Studies Toward the Synthesis of Benzfuzed Azoles

A Thesis Submitted
in Partial Fulfillment of the Requirements
for the Degree of

DOCTOR OF PHILOSOPHY

by

Rapolu Kiran Kumar

Department of Chemistry
Indian Institute of Technology Guwahati
Guwahati 781039
March 2013

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Dedicated

To

My Mother

INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI

Department of Chemistry

STATEMENT

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the Department of Chemistry, Indian Institute of Technology Guwahati, Guwahati, India under the supervision of Prof. Tharmalingam Punniyamurthy.

In keeping with the general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigators.

Guwahati — Rapolu Kiran Kumar

March, 2013

INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI

Department of Chemistry

CERTIFICATE

This is to certify that Mr. Rapolu Kiran Kumar has been working under my supervision since September 2009. I am forwarding his thesis entitled "*Studies Toward the Synthesis of Benzfuzed Azoles*" being submitted for the Ph.D. degree of this institute. I certify that he has fulfilled all the requirements according to the rules of this institute, and regarding the investigations embodied in his thesis and this work has not been submitted elsewhere for a degree.

Guwahati

March 2013

Prof. Tharmalingam Punniyamurthy

Supervisor

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I thank all the faculty members, research scholars, supporting staff of the department of chemistry and CIF for their kind cooperation in all respects.

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Finally, my deepest gratitude goes to my family for their unflagging love and support throughout my life. I feel deeply indebted to them for whatever I have achieved so far.

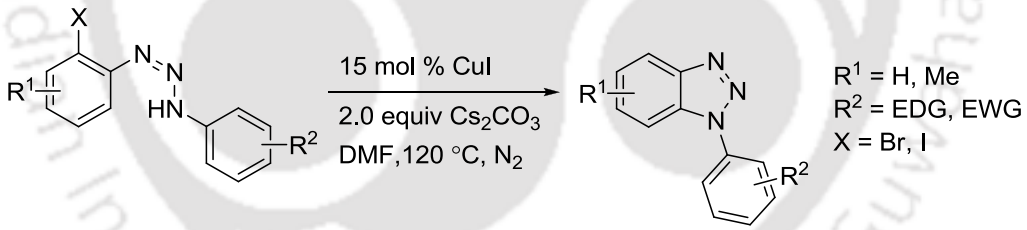
Rapolu Kiran Kumar

Abstract

The thesis contains four chapters. The first two chapters describe the synthesis of 1-aryl-1*H*-benzotriazoles by copper-catalyzed *C-N* cross-coupling and palladium-catalyzed intramolecular C-H activation/*C-N* bond formation reactions. The third chapter deals with the synthesis of *N*-aryl benzimidazoles *via* palladium-catalyzed intramolecular C-H amination, while the fourth chapter focuses on $PhI(OAc)_2$-promoted oxidative synthesis of benzfuzed azoles.

I. Copper(I)-Catalyzed Synthesis of 1-Aryl-1*H*-benzotriazoles

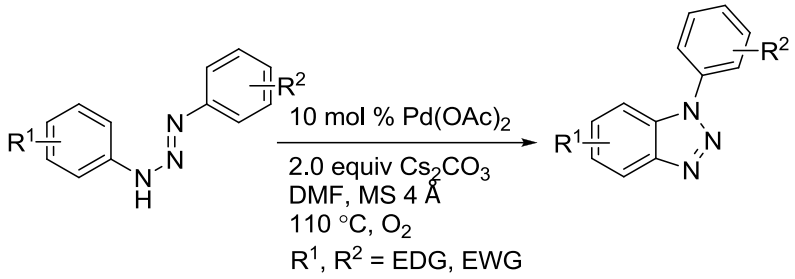
1-Aryl-1*H*-benzotriazoles are among the most important classes of heterocyclic compounds in biological and medicinal sciences. This chapter describes copper(I)-catalyzed synthesis of 1-aryl-1*H*-benzotriazoles from 2-halophenylimino-2-phenyl-hydrazines by intramolecular *C-N* cross-coupling reaction (Scheme 1). A variety of substrates undergo reactions to give the target products in high yield. This procedure provides a straightforward route for the regioselecitve and efficient synthesis of functionalized 1-aryl-1*H*-benzotriazoles under external ligand-free conditions.



Scheme 1. Copper(I)-Catalyzed Synthesis of 1-Aryl-1*H*-benzotriazoles

II. Palladium(II)-Catalyzed Synthesis of 1-Aryl-1*H*-benzotriazoles

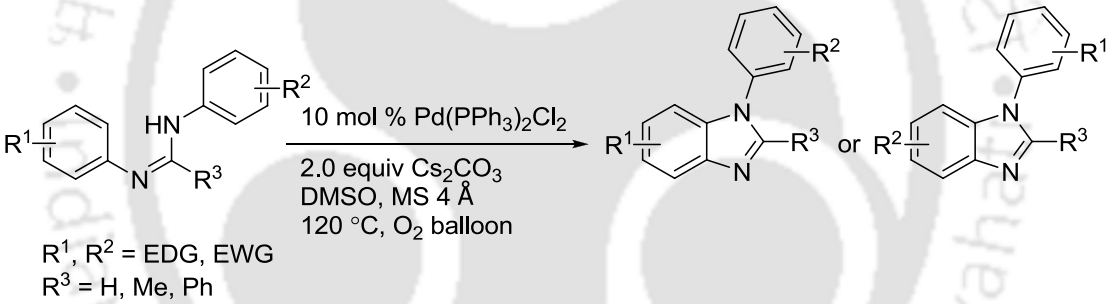
C-H activation protocols are attractive because they make methodology atom economical, step efficient and obviate the need for preactivated substrate precursors. This chapter focuses on the synthesis of 1-aryl-1*H*-benzotriazoles from phenylimino-2-phenyl-hydrazines (Scheme 2). The substrates undergo intramolecular C-H activation followed by *C-N* bond formation reactions in presence of catalytic amount of $Pd(OAc)_2$ to afford the corresponding 1-aryl-1*H*-benzotriazoles.



Scheme 2. Palladium(II)-Catalyzed Synthesis of 1-Aryl-1*H*-benzotriazoles

III. Palladium(II)-Catalyzed Synthesis of *N*-Aryl Benzimidazoles

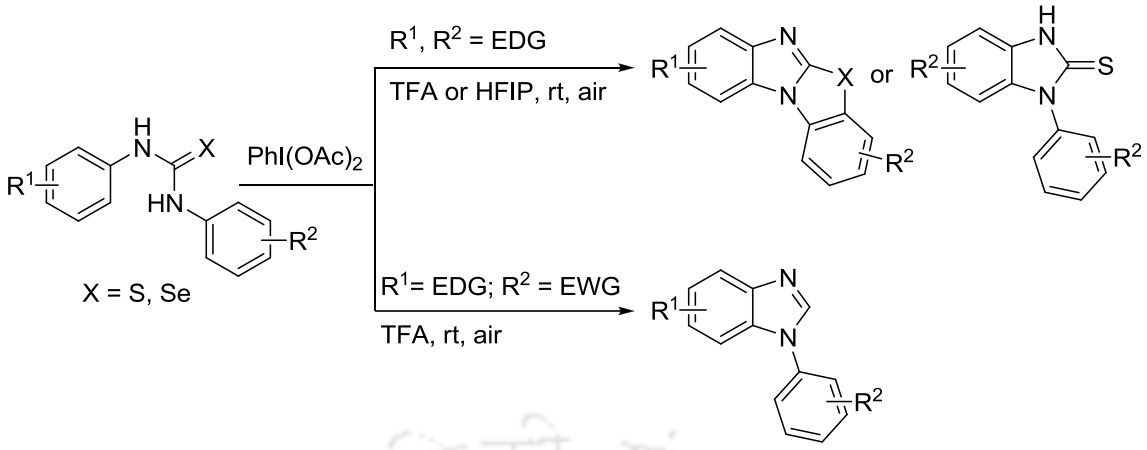
Benzimidazoles are the class of prominent heterocyclic motifs that exhibit a wide range of applications in therapeutic and biological sciences. This chapter describes the synthesis of *N*-aryl benzimidazoles from 1,3-diaryl amidines (Scheme 3). Use of molecular oxygen as an external oxidant makes the methodology green. This protocol is also applicable for the synthesis of both 2-unsubstituted and 2-alkyl/-aryl substituted *N*-aryl benzimidazoles.



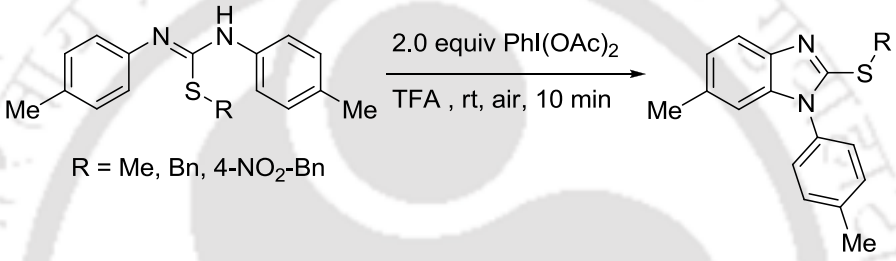
Scheme 3. Palladium(II)-Catalyzed Synthesis of *N*-Aryl Benzimidazoles

IV. $PhI(OAc)_2$-Promoted Oxidative Synthesis of Benzo-fuzed Azoles

The construction of carbon-heteroatom bonds *via* C-H functionalization has received intensive attention in recent years. Transition-metal based systems such as Cu, Pd, Rh, Ru and Ag have been considerably explored for this purpose. This chapter describes $PhI(OAc)_2$-promoted oxidative *C-N* and tandem *C-N* and *C-S*/*C-Se* bonds formation *via* mono and double C-H functionalizations at ambient conditions for the synthesis of benzo[*d*]imidazo[2,1-*b*]benzothiazole, benzimidazole-2-thione, benzo[*d*]imidazo[2,1-*b*]benzoselenoazole, 2-alkylthio-*N*-aryl benzimidazoles and *N*-aryl benzimidazoles that are important in biological and medicinal sciences (Schemes 4-5).



Scheme 4. $PhI(OAc)_2$ Promoted Synthesis of Benzo-fuzed Azoles



Scheme 5. $PhI(OAc)_2$ Promoted Synthesis of 2-Alkylthio-*N*-Aryl Benzimidazoles

Contents

Chapter I

Copper(I)-Catalyzed Synthesis of 1-Aryl-1*H*-benzotriazoles

1-Aryl-1*H*-benzo[*d*][1,2,3]triazoles are among the most important classes of heterocyclic compounds in biological and medicinal sciences (Figure 1)[1]. For example, 1-aryl-1*H*-benzotriazoles are structural motifs of many compounds that possess antibacterial,[1a] anticancer,[1b] antidepressant,[1c] antifungal[1d] and antimalarial activities.[1e] They are also useful synthons in some versions of the Graebe-Ullmann reaction,[2] especially in the synthesis of pyridoacridine,[3] carboline[4] and tetraazapentalenes.[5] 1*H*-Benzotriazoles also serve as synthetic auxiliaries in amidoalkylation, insertion and imidoylation that have been used for the synthesis of heterocyclic compounds.[6] Development of newer methods from readily available substrate precursors and devoid of harsh reaction conditions for the construction of the functionalized 1-aryl-1*H*-benzotriazoles is thus important in synthetic organic chemistry.

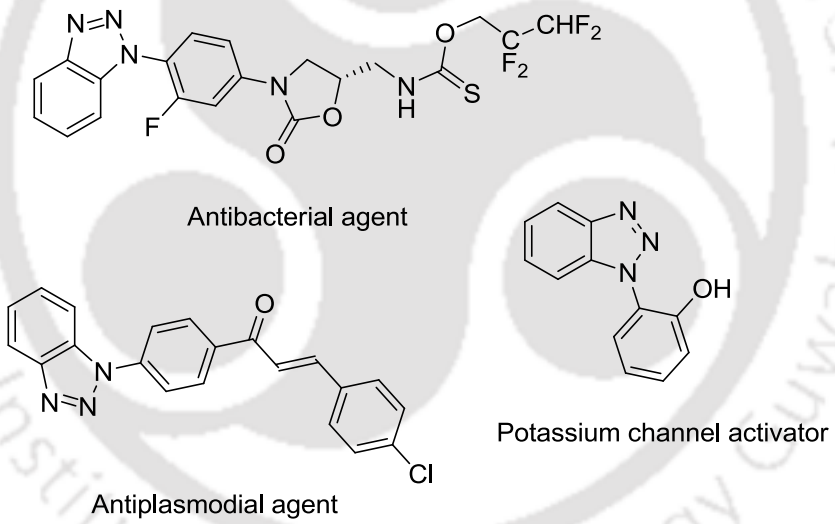


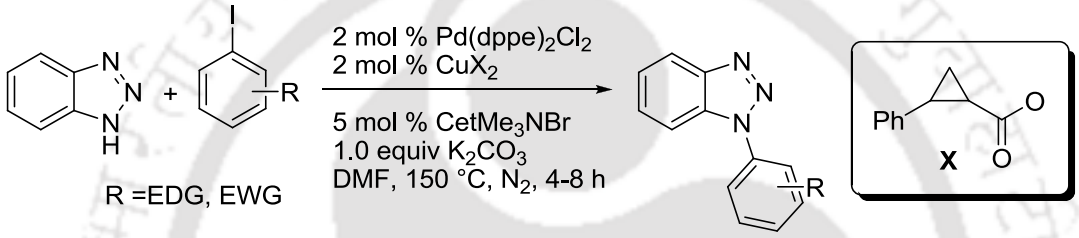
Figure 1. Some Examples of Biologically Active 1-Aryl-1*H*-benzo[*d*][1,2,3]triazoles

The common methods used for the synthesis of 1-aryl-1*H*-benzotriazole framework involve a three step process having the arylation of *o*-nitroaniline, reduction of nitro group and diazotization followed by cyclization.[4b,7] However, the drawbacks of these methods include the unavailability of suitably substituted *o*-nitroanilines, harsh reaction conditions and lack of regioselectivity. Some of these drawbacks have been recently overcome by the development of more sustainable cross-coupling reactions using copper and palladium based catalytic systems, which allow the assembly of the target

heterocycles under relatively milder reaction conditions. The alternative method involves 1,3-dipolar cycloaddition of azides with benzynes and diynes with limited studies.

1.1 Palladium-Catalyzed Synthseis of 1-Aryl-1*H*-benzo[*d*][1,2,3]triazoles

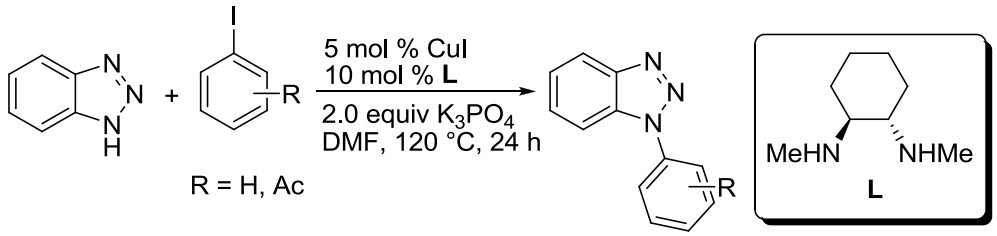
Over the past few years palladium-catalyzed intermolecular *C–N* cross-coupling reaction has been explored for the synthesis of nitrogen containing heterocyclic compounds. Mareno-Manas and co-workers described the combined palladium and copper-catalyzed *N*-arylation of benzotriazole structural framework with aryl iodides under phase transfer conditions to afford the corresponding 1-aryl-1*H*-benzotriazoles (Scheme 1).[14]



Scheme 1. Palladium Catalyzed *N*-Arylation of 1*H*-Benzotriazoles

1.2 Copper-Catalyzed Synthesis of 1-Aryl-1*H*-benzo[*d*][1,2,3]triazoles

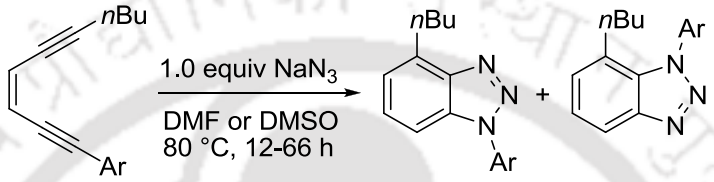
The recent development in cross-coupling reactions using transition-metal-catalysis provides powerful tools for the formation of carbon-heteroatom bonds.[8,9,10] Among them, the copper-based processes are attractive because the catalyst is abundant and cheap.[11] Recently, copper-catalyzed strategies have been successfully applied for the assembly of various substituted heterocycles by *C–N* cross-coupling reaction.[12] Buchwald and co-workers developed a copper-catalyzed *N*-arylation of benzotriazoles with aryl iodides to afford the corresponding 1-aryl-1*H*-benzotriazoles (Scheme 2).[13]



Scheme 2. Copper Catalyzed *N*-Arylation of 1*H*-Benzotriazoles

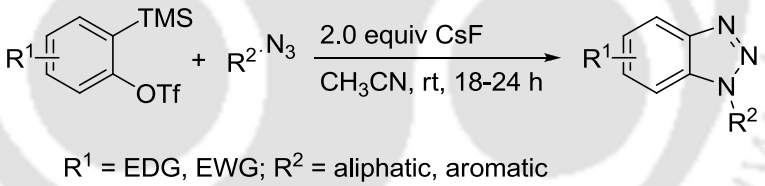
1.3 1,3-Dipolar Cycloaddition Reactions

1,3-Dipolar cycloaddition reactions are powerful methods for the preparation of variety of cyclic compounds. It is well-known that 1,3-dipolar cycloaddition of an azide with an alkyne leads to the formation of 1,2,3-triazoles.[15] Wu and co-workers described the synthesis of substituted benzotriazoles by reaction of (*Z*)-1-aryl-3-hexene-1,5-diynes with sodium azide in DMF or DMSO at 80 °C. This reaction involves a tandem anionic cascade cyclization reaction and sigmatropic rearrangement in the benzotriazole systems with moderate to good yield (Scheme 3).[16]



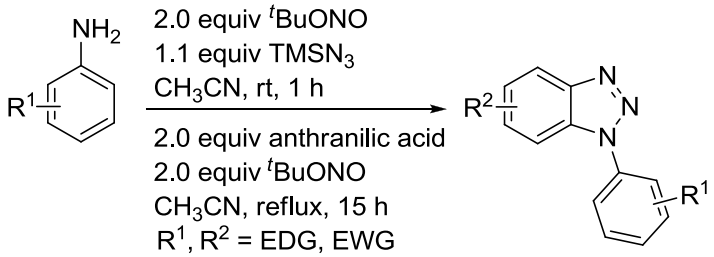
Scheme 3. Synthesis of 1-Aryl-1*H*-benzotriazoles from 1,5-Diynes

Larock and co-workers reported the synthesis of a variety of 1-aryl-1*H*-benzotriazoles by the [3+2] cycloaddition of azides to benzynes (Scheme 4).[17] The reaction is general and affording the functionalized benzotriazoles under mild reaction conditions.



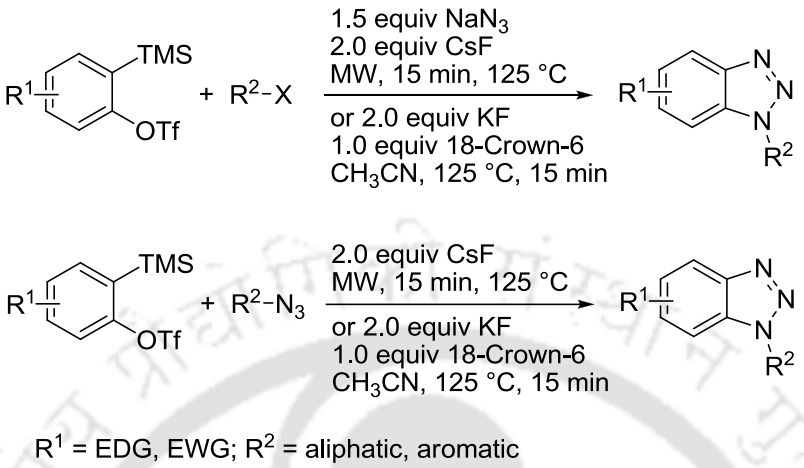
Scheme 4. Synthesis of 1-Aryl-1*H*-benzotriazoles *via* Benzyne Click Chemistry

Moses and co-workers reported the synthesis of substituted 1-aryl-1*H*-benzotriazoles from anilines and anthranilic acid (Scheme 5).[18] The key procedure is the *in situ* generation of aromatic azide and benzyne reaction partners.



Scheme 5. One-Pot Synthesis of 1-Aryl-1*H*-benzotriazoles

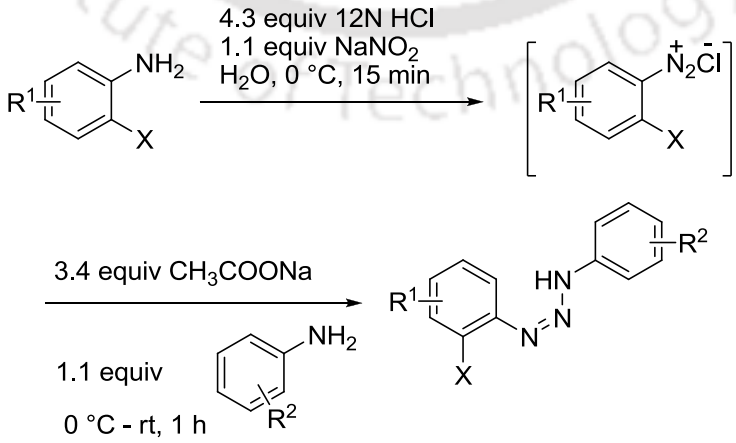
Ed Biehl and co-workers reported the synthesis of substituted 1-aryl-1*H*-benzotriazoles *via* microwave assisted three component and two component benzyne "click" chemistry (Scheme 6).[19]



Scheme 6. Microwave Assisted Synthesis of 1-Aryl-1*H*-benzotriazoles

1.4 Present Study

In this chapter, we describe a general method for the synthesis of substituted 1-aryl-1*H*-benzotriazoles *via* intramolecular *C*-*N* cross-coupling between aryl halides and triazene moities using copper-catalysis. The protocol is simple, general and provides a straight forward route for the regioselective efficient synthesis of functionalized 1-aryl-1*H*-benzotriazoles with excellent yield under ligand-free conditions. 2-Halophenylimino-2-phenyl-hydrazines were prepared in good yield by diazotization of 2-haloanilines followed by condensation with corresponding anilines in the presence of sodium acetate in aqueous media (Scheme 7).[20]

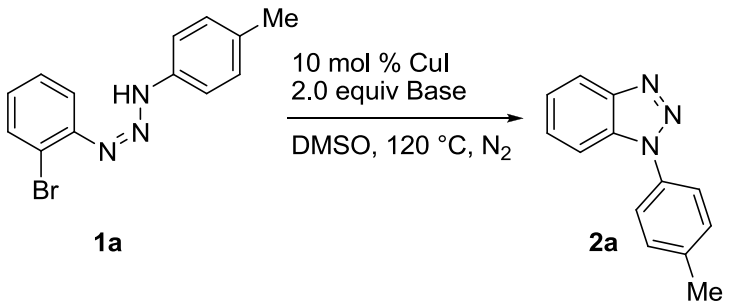


Scheme 7. Synthesis of 2-Halophenylimino-2-phenyl-hydrazines

The reaction conditions for the cyclization of 2-haloaryltriazines were carried out with 2-bromophenylimino-2-*p*-tolyl-hydrazine **1a** as a model substrate using different bases, copper sources and solvents at varied temperature (Table 1). When the reaction is carried out with 10 mol % of CuI and 2.0 equiv of Cs_2CO_3 in DMSO at 120 °C under N_2 atmosphere afforded 50% conversion of the desired 1-*p*-tolyl-1*H*-benzotriazole **2a.** Bases such as DBU, K_2CO_3, K_3PO_4 and NaOAc were less effective providing the target product with 19-45% yield. No product was obtained using KO^{t}Bu, KOH, CsOH.H_2O, DABCO and pyridine as the base. Replacing the solvent from DMSO to DMF gave **2a** in 70% conversion (Table 2). Using CH_3CN, dioxane and 2-propanol as the solvent yielded **2a** in <19% conversion. The catalytic activities of the copper sources were compared, and CuI was found to be superior to others. Using CuBr as the catalyst afforded **2a** in 35% conversion. In contrast, no product was obtained using $Cu(OAc)_2 \cdot H_2O$, $Cu(OTf)_2$ and CuO nanoparticles as the catalyst. Increasing the catalyst loading to 15 mol % provided **2a** with 100% conversion. Control experiments confirmed that no product was obtained in the absence of the copper source. The reactivities of other aryl halides were compared. 2-Iodophenylimino-2-*p*-tolylhydrazine readily proceeded the cyclization with 100% conversion, while 2-chlorophenylimino-2-*p*-tolylhydrazine did not show any reaction. The reason for these observations may be the BDE (Ar-I) < BDE (Ar-Br) < BDE (Ar-Cl). Under these conditions, the cyclization *via* C-H activation did not occur.

Next, with the optimized conditions in hand, the scope of the protocol studied for other substrates (Table 3). 2-Bromophenylimino-2-phenylhydrazine **1b** proceeded the cyclization to give 1-phenyl-1*H*-benzo[*d*][1,2,3]triazole **2b** with 98% yield. Similarly, a series of substituted triazines **1c-o** underwent cyclization *via* intramolecular *C-N* cross-coupling to afford the corresponding substituted 1-aryl-1*H*-benzotriazoles **2c-o** in 75-99% yield. Both the substrates having electron donating and electorn withdrawing groups could be readily converted to the respective 1-aryl-1*H*-benzotriazoles without affecting the functional groups. For examples, a series of 1-aryl-1*H*-benzotriazoles **2b-o** having 2-Br, 2-Cl, 2-I, 3-Me, 4-COMe, 4-Cl, 4-CO_2Et, 4-OMe, 2,4-diF, 2-I-4-Me, 2,4-diMe and 3,4-diMe functional groups could be prepared from the corresponding triazines **1b-o** in high yields. It is noteworthy that the reactions were selective and no by-product was obtained. These results clearly suggest that the protocol is simple, general and efficient for the straight forward synthesis of functionalized 1-aryl-1*H*-benzo[*d*][1,2,3]triazoles.

Table 1. Effect of Base on the Synthesis of 1-*p*-Tolyl-1*H*-benzo[*d*][1,2,3]triazole[a]



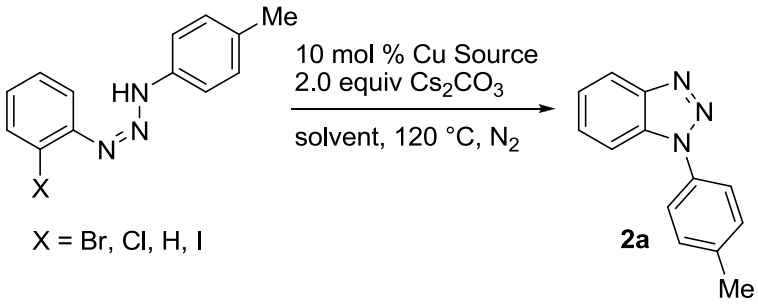
1a **2a**

entry	base	time (h)	conversion (%)[b]
1	DBU	5	45
2	Cs_2CO_3	3	50, 25,[c] 30[d]
3	KO^{t}Bu	7	n.d.
4	K_2CO_3	6	25
5	K_3PO_4	6	19
6	CH_3COONa	6	19
7	KOH	6	n.d.
8	$CsOH.H_2O$	4	n.d.
9	DABCO	7	n.d.
10	pyridine	7	n.d.

[a]Reaction condition: Substrate **1a** (1.0 mmol), CuI (10 mol %) and base (2.0 equiv) were stirred at 120 °C in DMSO (1.0 mL) under nitrogen atmosphere. [b]Determined from 400 MHz ^{1}H NMR. [c]Reaction temperature = 110 °C . [d]Cs_2CO_3 (1.5 equiv) was used. n.d. = Not detected.

To study an application of the protocol, the cyclization of 1-(2-iodophenylimino)-2-(2-iodophenyl)-hydrazine **1p** was studied to afford 1-(2-iodophenyl)-1*H*-benzo[*d*][1,2,3]triazole **2p** in 99% yield. Whose single crystal X-ray structure is presented in Figure 2. The latter could be readily converted into potassium channel activator 2-(1*H*-benzotriazol-1-yl)phenol[1c] **3a** by CuI and 2-methylquinolin-8-ol **L** in 90% yield (Scheme 8).

Table 2. Effect of Copper Sources and Solvents[a]



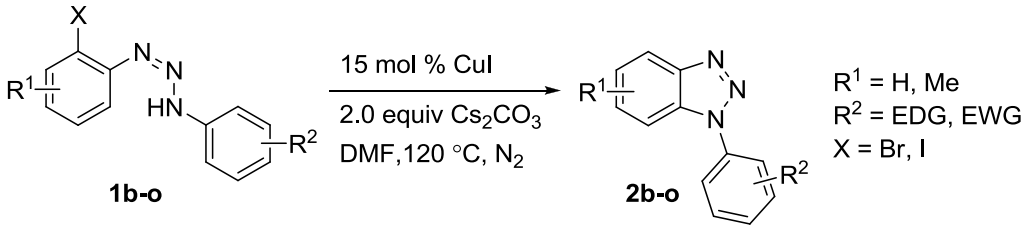
X = Br, Cl, H, I

2a

entry	X	copper source	solvent	time (h)	conversion (%)[b]
1	Br	CuBr	DMSO	7	35
2	Br	$Cu(OAc)_2.H_2O$	DMSO	7	n.d.
3	Br	$Cu(OTf)_2$	DMSO	7	n.d.
4	Br	CuO(nano)	DMSO	7	n.d.
5	Br	CuI	DMSO	7	n.d.
6	Br	CuI	DMF	3	70
7	Br	CuI	^{i}PrOH	7	19
8	Br	CuI	CH_3CN	8	n.d.
9	Br	CuI	dioxane	5	trace
10	Br	CuI	DMF	3	100[c]
11	I	CuI	DMF	1	100[c]
12	Cl	CuI	DMF	5	n.d.
13	H	CuI	DMF	7	n.d.

[a]Reaction condition: Substrate **1a** (1.0 mmol), Copper sorce (10 mol %) and Cs_2CO_3 (2.0 equiv) were stirred at 120 °C in solvent (1.0 mL) under nitrogen atmosphere. [b]Determined from 400 MHz ^{1}H NMR. [c]CuI (15 mol %) was used. n.d. = Not detected.

Table 3. Copper-Catalyzed Intramolecular Aryl Triazenylation: Substrate Scope[a,b]



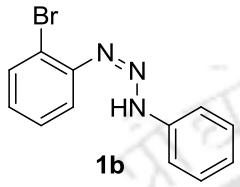
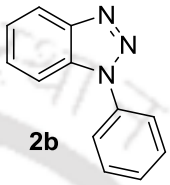
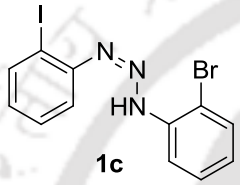
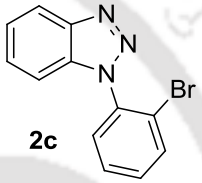
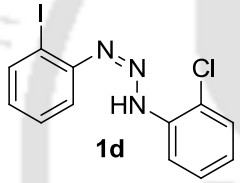
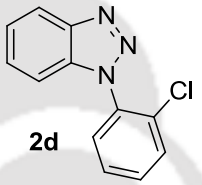
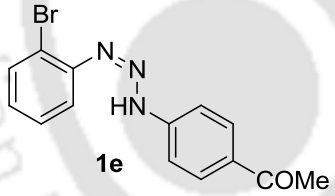
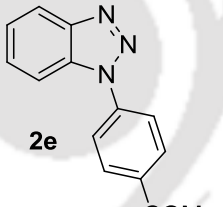
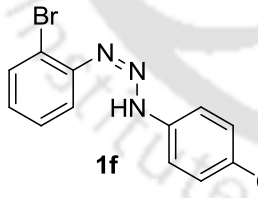
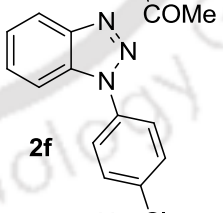
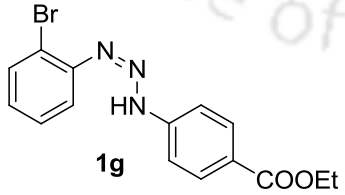
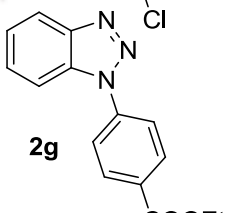
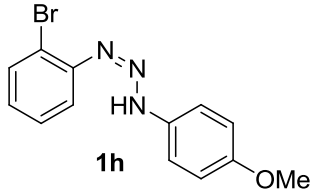
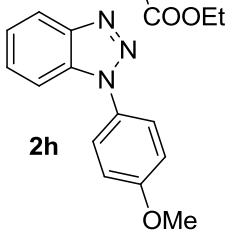
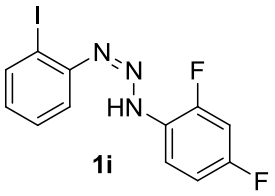
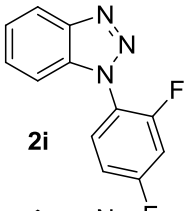
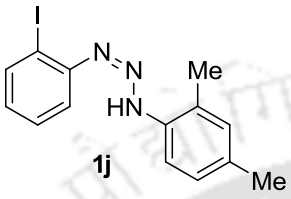
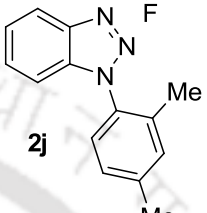
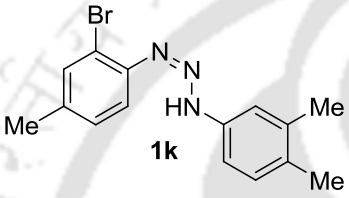
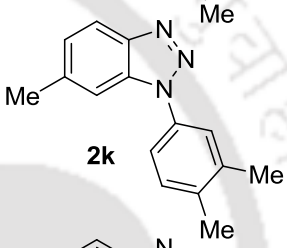
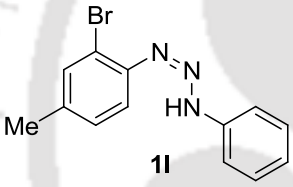
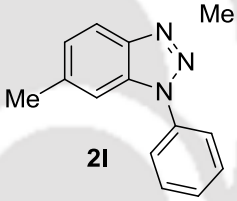
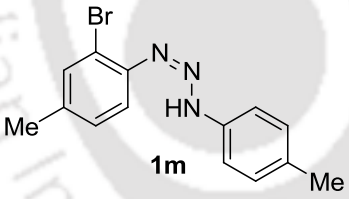
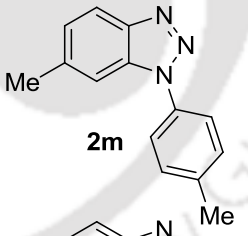
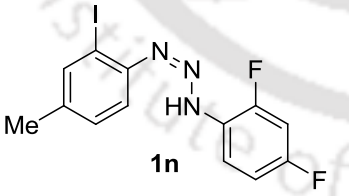
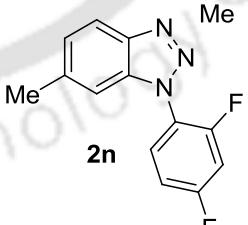
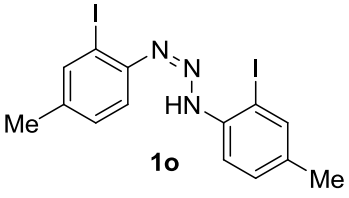
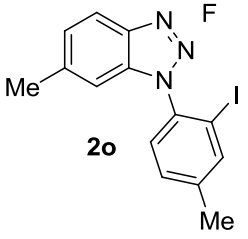
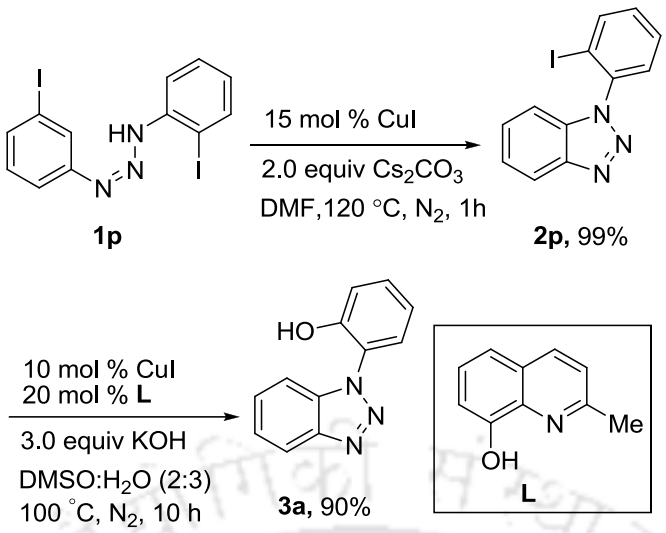
entry	substrate	time (h)	product	yield (%)[b]
1	 **1b**	3.0	 **2b**	98
2	 **1c**	3.0	 **2c**	98
3	 **1d**	3.0	 **2d**	98
4	 **1e**	2.0	 **2e**	99
5	 **1f**	2.0	 **2f**	99
6	 **1g**	2.0	 **2g**	99
7	 **1h**	3.0	 **2h**	90

Table 3 continues…

entry	substrate	time (h)	product	yield (%)[b]
8	 **1i**	1.0	 **2i**	99
9	 **1j**	1.0	 **2j**	98
10	 **1k**	3.0	 **2k**	92
11	 **1l**	2.0	 **2l**	92
12	 **1m**	3.0	 **2m**	95
13	 **1n**	1.0	 **2n**	99
14	 **1o**	1.0	 **2o**	96

[a]Reaction condition: **1a-o** (1.0 mmol), CuI (15 mol %) and Cs_2CO_3 (2.0 equiv) were stirred at 120 °C in DMF (1.0 mL) under nitrogen atmosphere. [b]Isolated yield.



Scheme 8. Synthesis of 2-(1*H*-Benzotriazol-1-yl)phenol: A Potassium Channel Activator

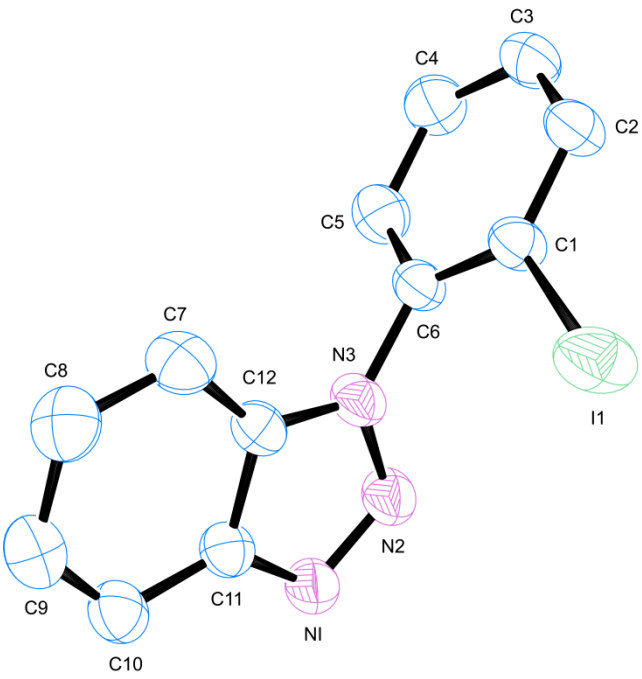
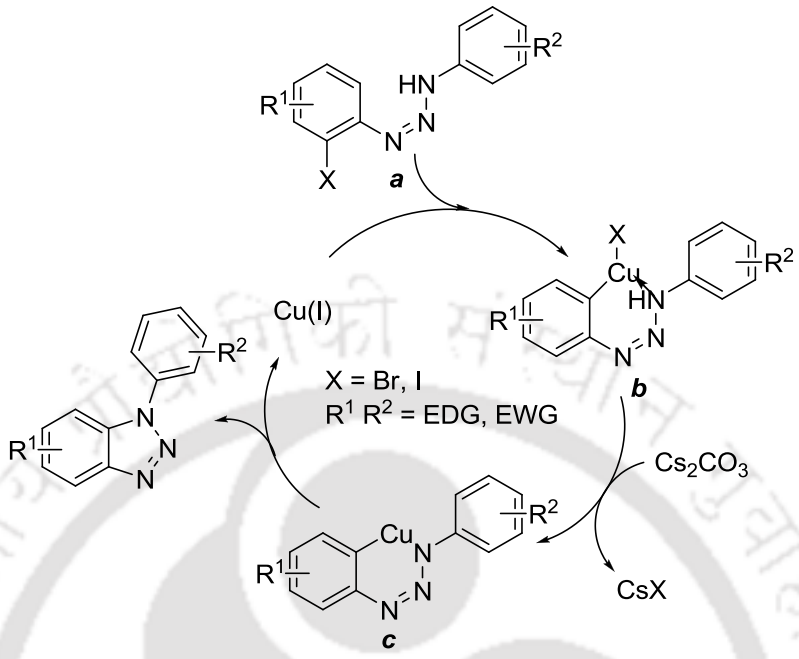


Figure 2. ORTEP Diagram of 1-(2-Iodophenyl)-1*H*-benzotriazole **2p**. Thermal ellipsoids are drawn at 50% probability level. H-Atoms are omitted for clarity

The proposed catalytic cycle is shown in scheme 9. The substrate ***a*** may undergo oxidative addition with copper(I) to give the intermediate ***b***. The latter in the presence of

base may transform into the intermediate ***c*** that could complete the catalytic cycle by reductive elimination of 1-aryl-1*H*-benzotriazole.



Scheme 9. Proposed Catalytic Cycle

Conclusion

We have developed a general method for the synthesis of substituted 1-aryl-1*H*-benzo[*d*][1,2,3]triazoles *via* intramolecular *C-N* cross-coupling between aryl halide and triazene moities using copper-catalysis under ligand-free conditions. The protocol is simple, general and provides a straight forward route of the regioselecitve and efficient synthesis of functionalized 1-aryl-1*H*-benzotriazoles with excellent yield.

1.4 Experimental Section

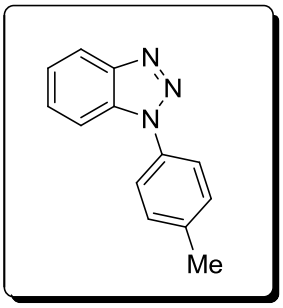
General Information. Anilines, $Cu(OAc)_2 \cdot H_2O$ (98%), CuI (98%), CuBr (98%), CuO nano (97%), $Cu(OTf)_2$ (98%), Cs_2CO_3 (99%), $CsOH \cdot H_2O$, KO^tBu (95%) and K_3PO_4 (98%) were purchased from Aldrich and used without further purification. The column chromatography was performed with Rankem silica gel (60-120 mesh). NMR (^1H and ^{13}C) spectra were recorded with a Varian 400 spectrometer. Melting points were determined with a Büchi B-545 apparatus and are uncorrected. Elemental analysis were recorded using Perkin Elmer CHNS analyzer. X-Ray data were collected on a Bruker SMART APEX equipped with a CCD area detector using Mo Kα radiation. The structures were solved by direct method using *SHELLX-97* (Göttingen, Germany).

General Procedure for Synthesis of 1,3-Di-aryltriaz-1-enes. To a stirred solution of water (8 mL) and 12N HCl (2 mL) in a 100 mL beaker for 5 min at ambient temperature, 2-haloanilines (15.0 mmol) were added. The resultant stirring mixture was cooled to 0 °C and treated dropwisely with 0 ^{o}C cooled $NaNO_2$ solution (8.24 mmol in 2 mL of water) for 15 min followed by 0 °C cooled NaOAc solution (25.48 mmol in 5 mL of water) for 15 min. The stirring was continued at 0 °C for 1 h and the resultant yellow precipitate was filtered by a Buchner funnel, washed with cold water (20 mL) and dried at room temperature to give the target triazenes **1a-p** 70-95% yield.

General Procedure for Synthesis of 1-Aryl-1*H*-benzotriazoles. An oven dried 10 mL single necked round bottom flask was charged with CuI (15 mol %), Cs_2CO_3 (2.0 equiv) and triazene (1.0 mmol). The resultant mixture was stirred at 120 °C in DMF (1.0 mL) under nitrogen atmosphere for appropriate time (Table 3). The progress of reaction was monitored by TLC using ethyl acetate and hexane as an eluent. After completion, the reaction mixture was cooled to room temperature and diluted with ethyl acetate (25 mL). The organic layer was washed successively with brine (1 x 3 mL) and water (3 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using 9:1 hexane and ethyl acetate as eluent.

General Procedure for Synthesis of 2-(1*H*-Benzotriazol-1-yl)phenol. An oven dried 10 mL round bottom flask was charged with CuI (19.0 mg, 10 mol %) and 8-hydroxyquinaldine (31.8 mg, 20 mol %) and the mixture was stirred in DMSO (0.4 mL) for 10 min. Then, the reaction mixture was treaed with 1-(2-iodophenyl)-1*H*-benzo[*d*][1,2,3]triazole (**2p**) (321.0 mg, 1.0 mmol), KOH (168 mg, 3.0 equiv) and H_2O (0.6 mL), and the resulting mixture was stirred at 100 °C for 10 h. The reaction mixture was then cooled to room temperature and acidified with 0.5 M HCl (0.5 mL). The reaction mixture was then cooled to room temperature and diluted with ethyl acetate (15 mL). The organic layer was washed successively with brine (1 x 4 mL) and water (2 x 4 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using ethyl acetate and hexane as eluent.

1.5 Characterization Data



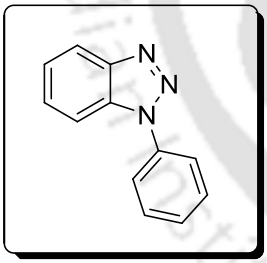
1-*p*-Tolyl-1*H*-benzo[*d*][1,2,3]triazole (2a). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.35; brown solid; yield 96%.

Mp: 94-96 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08-8.05 (m, 1H), 7.66-7.63 (m, 1H), 7.59-7.57 (m, 2H), 7.48-7.44 (m, 1H), 7.37-7.33 (m, 3H), 2.40 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.4, 138.7, 134.5, 132.3, 130.3, 128.0, 124.2, 122.6, 120.0, 110.4, 21.1.

Elemental analysis calcd (%) for $C_{13}H_{11}N_3$: C, 74.62; H, 5.30; N, 20.08. Found: C, 74.60; H, 5.29; N, 20.11.



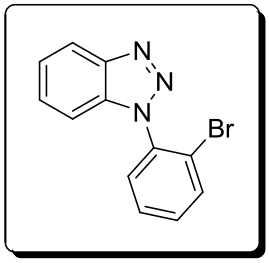
1-Phenyl-1*H*-benzo[*d*][1,2,3]triazole (2b).[13] Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.35; red solid; yield 98%.

Mp: 86-88 °C (lit.[13] 85-87 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 8.4 Hz, 1H), 7.78-7.72 (m, 3H), 7.59 (t, *J* = 7.6 Hz, 2H), 7.55-7.47 (m, 2H), 7.41 (t, *J* = 8.4 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.4, 136.9, 132.2, 129.8, 128.6, 128.2, 124.3, 122.7, 120.1, 110.3.

Elemental analysis calcd (%) for $C_{12}H_9N_3$: C, 73.83; H, 4.65; N, 21.52. Found: C, 73.81; H, 4.64; N, 21.55.



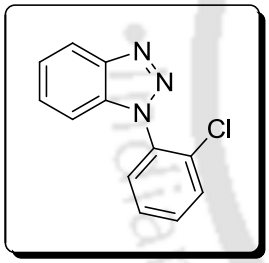
1-(2-Bromophenyl)-1*H*-benzo[*d*][1,2,3]triazole (2c). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.40; orange solid; yield 98%.

Mp: 132-134 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.55-7.33 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.8, 135.9, 134.3, 133.9, 131.7, 129.6, 128.8, 128.3, 124.4, 121.0, 120.3, 110.7.

Elemental analysis calcd (%) for $C_{12}H_8BrN_3$: C, 52.58; H, 2.94; N, 15.33. Found: C, 52.60; H, 2.95; N, 15.30.



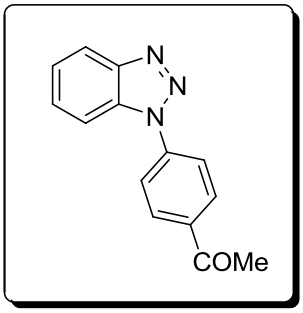
1-(2-Chlorophenyl)-1*H*-benzo[*d*][1,2,3]triazole (2d). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.40; yellow solid; yield 98%.

Mp: 84-86 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 8.4 Hz, 1H), 7.64 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.56-7.47 (m, 4H), 7.42 (dt, *J* = 7.2, 1.2 Hz, 1H), 7.36 (dd, *J* = 8.4, 0.8 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.7, 134.2, 133.9, 131.4, 131.2, 131.0, 129.3, 128.3, 128.2, 124.4, 120.3, 110.7.

Elemental analysis calcd (%) for $C_{12}H_8ClN_3$: C, 62.76; H, 3.51; N, 18.30. Found: C, 62.74; H, 3.49; N, 18.34.



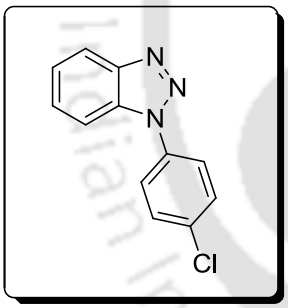
1-(4-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)phenyl)ethanone (2e).[13] Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.25; yellow solid; yield 99%.

Mp: 159-160 °C (lit.[13] 151-152 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21-8.15 (m, 3H), 7.94 (d, *J* = 8.4 Hz, 2H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.59 (t, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 1H), 2.68 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.9, 146.9, 140.7, 136.7, 131.1, 130.3, 128.9, 124.9, 122.2, 120.8, 110.5, 26.9.

Elemental analysis calcd (%) for $C_{14}H_{11}ON_3$: C, 70.87; H, 4.67; N, 17.71. Found: C, 70.84; H, 4.65; N, 17.74.



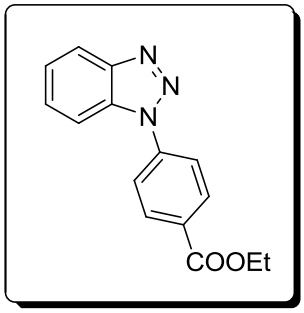
1-(4-Chlorophenyl)-1*H*-benzo[*d*][1,2,3]triazole (2f).[19] Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.40; brown solid; yield 99%.

Mp: 153-154 °C (lit.[19] 153-154 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.4 Hz, 1H), 7.74-7.69 (m, 3H), 7.59-7.54 (m, 3H), 7.43 (t, *J* = 7.6 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.7, 135.7, 134.6, 132.3, 130.2, 128.7, 124.8, 124.1, 120.6, 110.3.

Elemental analysis calcd (%) for $C_{12}H_8ClN_3$: C, 62.76; H, 3.51; N, 18.30. Found: C, 62.79; H, 3.50; N, 18.32.



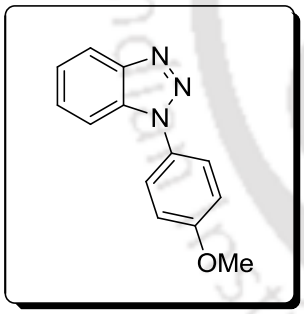
Ethyl-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)phenyl)benzoate (2g).[16] Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.25; white solid; yield 95%.

Mp: 86-88 °C (lit.[16] 87-88 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.31 (d, *J* = 8.0 Hz, 2H), 8.18 (d, *J* = 8.4 Hz, 1H), 7.92 (d, *J* = 8.8 Hz, 2H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.61 (t, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 1H), 4.44 (q, *J* = 6.8 Hz, 2H), 1.45 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.7, 146.9, 140.6, 132.1, 131.5, 130.5, 128.9, 124.9, 122.1, 120.8, 110.5, 61.6, 14.5.

Elemental analysis calcd (%) for $C_{15}H_{13}N_3O_2$: C, 67.40; H, 4.90; N, 15.72. Found: C, 67.36; H, 4.88; N, 15.70.



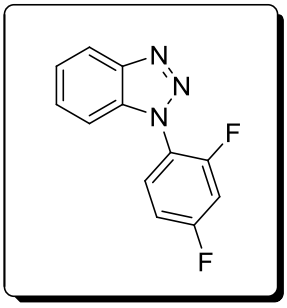
1-(4-Methoxyphenyl)-1*H*-benzo[*d*][1,2,3]triazole (2h).[18] Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.30; brown solid; yield 90%.

Mp: 96-98 °C (lit.[18] 98-99 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 8.4 Hz, 1H), 7.66-7.64 (m, 3H), 7.51 (t, *J* = 8.4 Hz, 1H), 7.43-7.39 (m, 1H), 7.10 (d, *J* = 8.8 Hz, 2H), 3.89 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.9, 146.4, 132.8, 130.1, 128.2, 124.7, 124.4, 120.3, 115.1, 110.4, 55.8.

Elemental analysis calcd (%) for $C_{13}H_{11}ON_3$: C, 69.32; H, 4.92; N, 18.66. Found: C, 69.35; H, 4.94; N, 18.64.



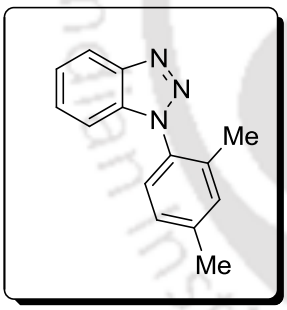
1-(2,4-Difluorophenyl)-1*H*-benzo[*d*][1,2,3]triazole (2i). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.40; white solid; yield 99%.

Mp: 126-128 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.4 Hz, 1H), 7.70-7.65 (m, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.45-7.41 (m, 2H), 7.15-7.10 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.5 (d, *J* = 11.4 Hz), 162.0 (d, *J* = 10.7 Hz), 157.5 (d, *J* = 13.0 Hz), 154.9, 145.9, 133.7, 128.8 (d, *J* = 32.1 Hz), 124.6, 120.3, 112.7 (d, *J* = 23.9 Hz), 110.3, 105.7 (t, *J* = 26.7 Hz).

Elemental analysis calcd (%) for $C_{12}H_7F_2N_3$: C, 62.34; H, 3.05; N, 18.17. Found: C, 62.30; H, 3.03; N, 18.14.

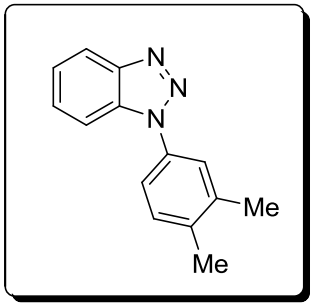


1-(2,4-Dimethylphenyl)-1*H*-benzo[*d*][1,2,3]triazole (2j). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.35; yellow liquid; yield 75%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16-8.13 (m, 1H), 7.51-7.47 (m, 1H), 7.43-7.39 (m, 1H), 7.34-7.32 (m, 1H), 7.28-7.26 (m, 2H), 7.21-7.19 (m, 1H), 2.45 (s, 3H), 2.08 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.8, 140.3, 135.1, 134.2, 132.9, 132.4, 128.1, 127.8, 126.9, 124.2, 120.2, 110.3, 21.4, 17.8.

Elemental analysis calcd (%) for $C_{14}H_{13}N_3$: C, 75.31; H, 5.87; N, 18.82. Found: C, 75.34; H, 5.88; N, 18.78.



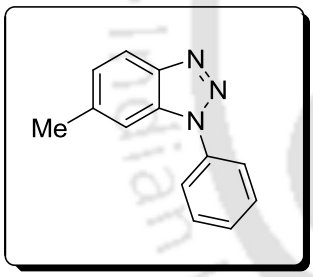
1-(3,4-Dimethylphenyl)-1*H*-benzo[*d*][1,2,3]triazole (2k). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.35; brown solid; yield 92%.

Mp: 68-69 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 8.4 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.53-7.32 (m, 5H), 2.37 (s, 3H), 2.35 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.5, 138.7, 137.6, 134.9, 132.6, 130.9, 128.1, 124.4, 124.2, 120.3, 110.6, 20.1, 19.7.

Elemental analysis calcd (%) for $C_{14}H_{13}N_3$: C, 75.31; H, 5.87; N, 18.82. Found: C, 75.29; H, 5.86; N, 18.85.



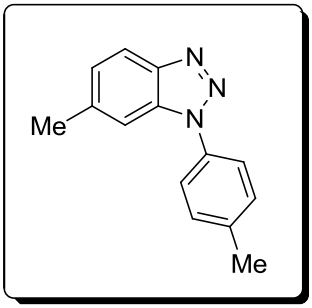
6-Methyl-1-phenyl-1*H*-benzo[*d*][1,2,3]triazole (2l). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.35; yellow solid; yield 93%.

Mp: 119-120 °C

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 2H), 7.60 (t, *J* = 7.6 Hz, 2H), 7.51-7.47 (m, 2H), 7.24 (d, *J* = 8.4 Hz, 1H), 2.55 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ = 144.9, 138.8, 136.9, 132.5, 129.6, 128.3, 126.5, 122.5, 119.4, 109.5, 21.9.

Elemental analysis calcd (%) for $C_{13}H_{11}N_3$: C, 74.62; H, 5.30; N, 20.08. Found: C, 74.59; H, 5.31; N, 20.10.



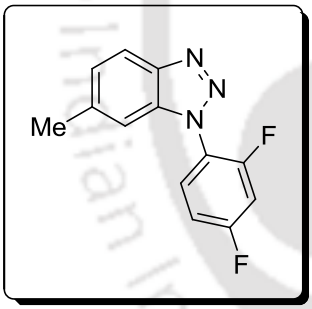
6-Methyl-1-*p*-tolyl-1*H*-benzo[*d*][1,2,3]triazole (2m). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.35; yellow solid; yield 95%.

Mp: 92-93 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 8.8 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.47 (s, 1H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 1H), 2.52 (s, 3H), 2.46 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.1, 138.9, 138.7, 134.7, 132.9, 130.4, 126.6, 122.9, 119.6, 109.7, 22.1, 21.3.

Elemental analysis calcd (%) for $C_{14}H_{13}N_3$: C, 75.31; H, 5.87; N, 18.82. Found: C, 75.28; H, 5.86; N, 18.86.



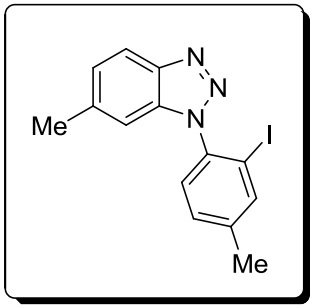
1-(2,4-Difluorophenyl)-6-methyl-1*H*-benzo[*d*][1,2,3]triazole (2n). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.40; white solid; yield 99%.

Mp: 125-127 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 8.4 Hz, 1H), 7.70-7.64 (m, 1H), 7.28-7.12 (m, 4H), 2.53 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.4, 162.0 (d, *J* = 10.7 Hz), 157.5 (d, *J* = 12.2 Hz), 155.1, 144.6, 139.5, 134.2, 129.0 (t, *J* = 10.7 Hz), 126.8, 121.9 (d, *J* = 10.7 Hz), 119.7, 112.8 (t, *J* = 22.8 Hz), 109.5, 106.0-105.4 (m), 22.1.

Elemental analysis calcd (%) for $C_{13}H_9F_2N_3$: C, 63.67; H, 3.70; N, 17.14. Found: C, 63.64; H, 3.68; N, 17.17.



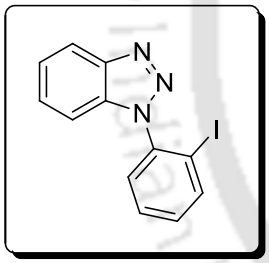
1-(2-Iodo-4-methylphenyl)-6-methyl-1*H*-benzo[*d*][1,2,3]triazole (2o). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.40; yellow solid; yield 96%.

Mp: 100-101 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (d, *J* = 8.4 Hz, 1H), 8.07 (s, 1H), 7.53-7.40 (m, 4H), 2.67 (s, 3H), 2.62 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.3, 142.4, 140.8, 138.9, 136.7, 134.2, 130.2, 128.4, 126.5, 119.5, 109.7, 95.7, 22.1, 20.9.

Elemental analysis calcd (%) for $C_{14}H_{12}IN_3$: C, 48.16; H, 3.46; N, 12.03. Found: C, 48.18; H, 3.44; N, 12.00.



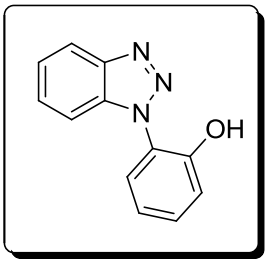
1-(2-Iodophenyl)-1*H*-benzo[*d*][1,2,3]triazole (2p). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.40; yellow solid; yield 99%.

Mp: 99-100 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 8.4 Hz, 1H), 8.07 (d, *J* = 7.6 Hz, 1H), 7.58-7.28 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.8, 140.6, 139.2, 133.6, 131.8, 129.6, 129.0, 128.3, 124.4, 120.3, 110.6, 95.8.

Elemental analysis calcd (%) for $C_{12}H_8IN_3$: C, 44.88; H, 2.51; N, 13.09. Found: C, 44.85; H, 2.52; N, 13.12.



2-(1*H*-Benzotriazol-1-yl)phenol (2q). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.20; yellow solid; yield 90%.

Mp: 187-189 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.41 (br s, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.8 Hz, 1H), 7.62 (t, *J* = 8.8, 2H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.38 (t, *J* = 7.2 Hz, 1H), 7.29-7.26 (m, 1H), 7.13 (t, *J* = 7.6 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$-$DMSOd_6$ 3:1): δ = 151.5, 145.3, 133.7, 130.8, 130.6, 127.5, 127.1, 123.8, 119.7, 119.2, 117.5, 111.5.

Elemental analysis calcd (%) for $C_{12}H_9ON_3$: C, 68.24; H, 4.29; N, 19.89. Found: C, 68.20; H, 4.30; N, 19.92.

Crystal Data and Structure Refinement for 2p at 298(2) K

Identification code	2p	
Empirical formula	$C_{12}H_8IN_3$	
Formula weight	321.11	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P-21/n	
	Loop xyz	
	‘x, y, z’ ‘-x, -y, -z’	
Unit cell dimensions	*a* = 9.9946 (4) Å	α(°) = 9.9946 (4)
	b = 7.6083 (4) Å	β(°) = 109.39 (19)
	c = 15.0195 (7) Å	γ(°) = 101.989 (13)
Volume	1123.34(9) Å^3	
Z	4	
Density (calculated)	1.899 Mg/m^3	

Absorption coefficient	2.824 mm^{-1}
F(000)	616.0
Crystal size	0.42 x 0.35 x 0.25 mm
Theta range for data collection	0.945 to 28.39 °
Index ranges	-10<=h<=10, -11<=k<=11, -13<=l<=13
Reflections collected	2662
Independent reflections	2314
Completeness to theta = 24.31°	94.5 %
Absorption correction	Multi-scan
Max. and min. transmission	0.317 and 0.493
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2800 / 0 /116
Goodness-of-fit on F^2	1.129
Final R indices [I>2sigma (I)]	*R1* = 0.042, *wR2* = 0.0387
R indices (all data)	*R1* = 0.0366, *wR2* = 0.1325

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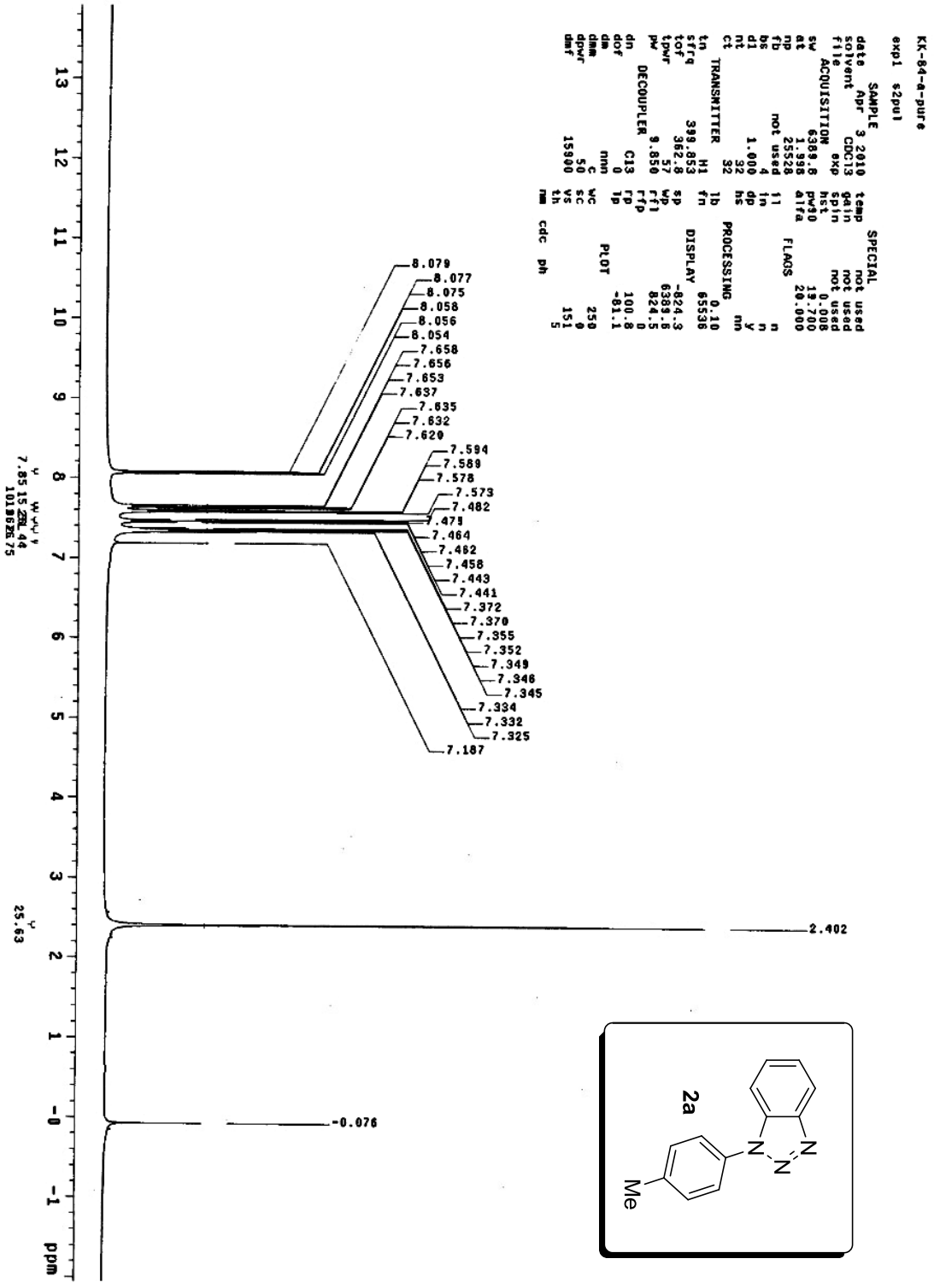
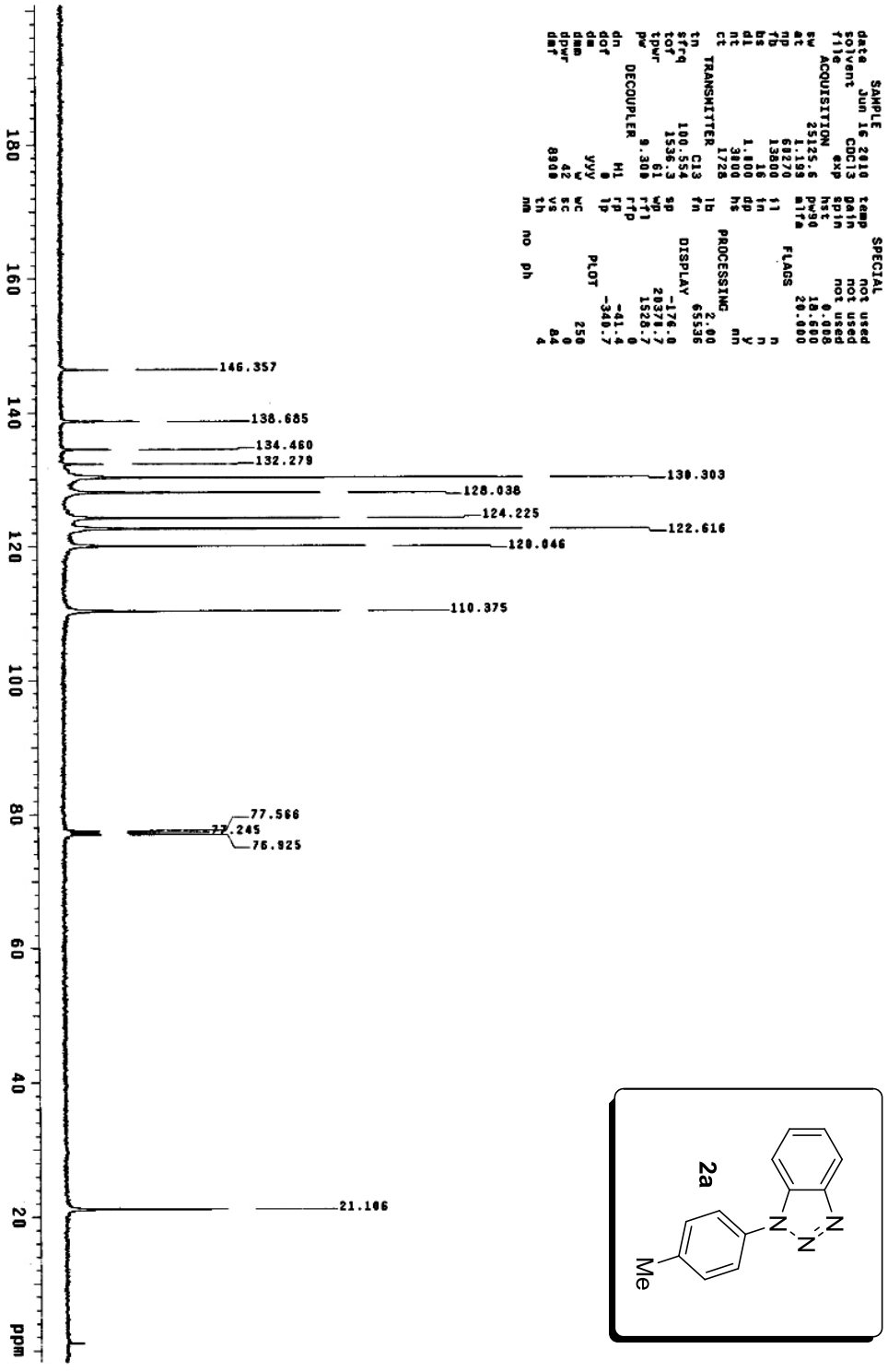
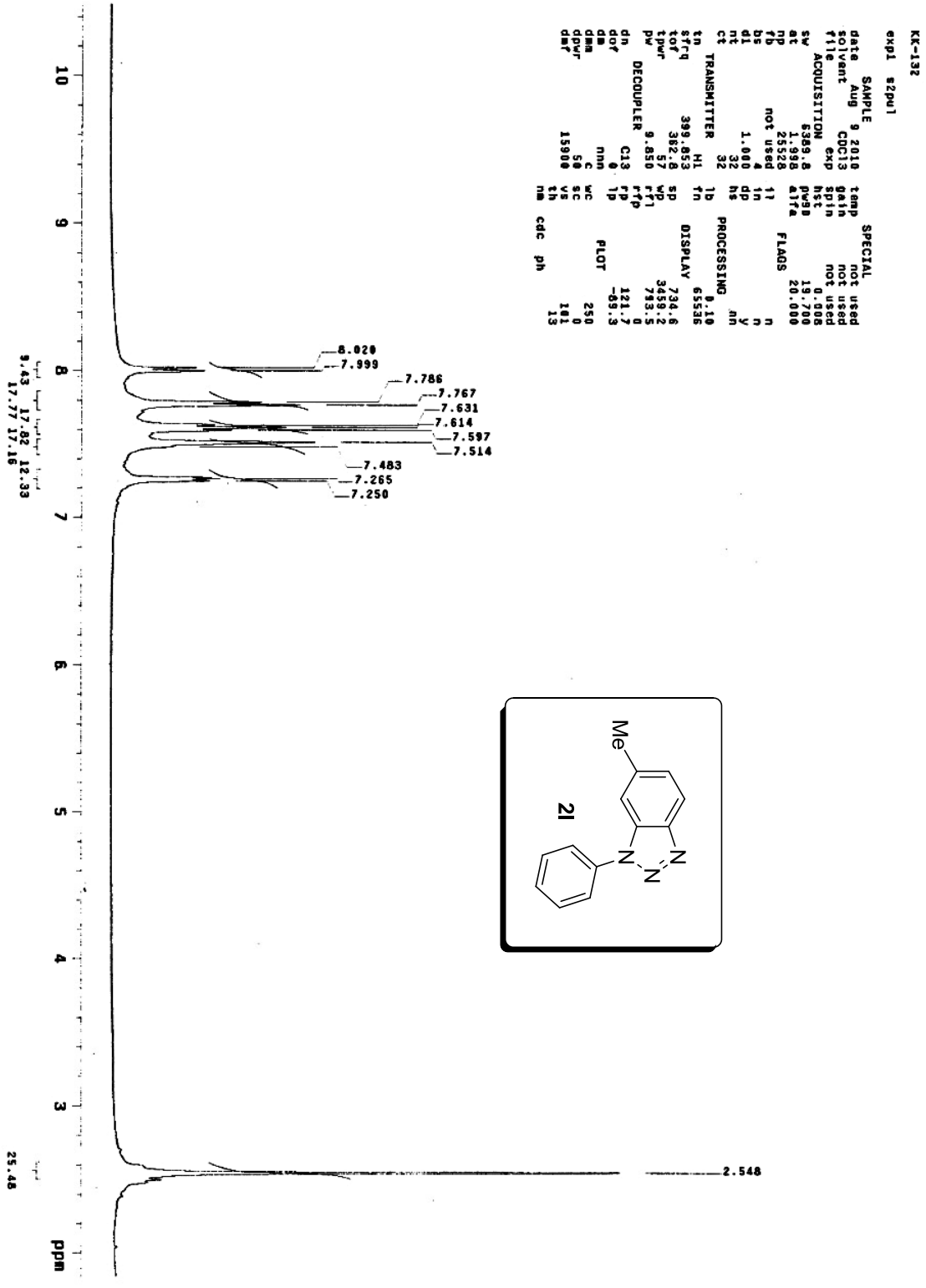
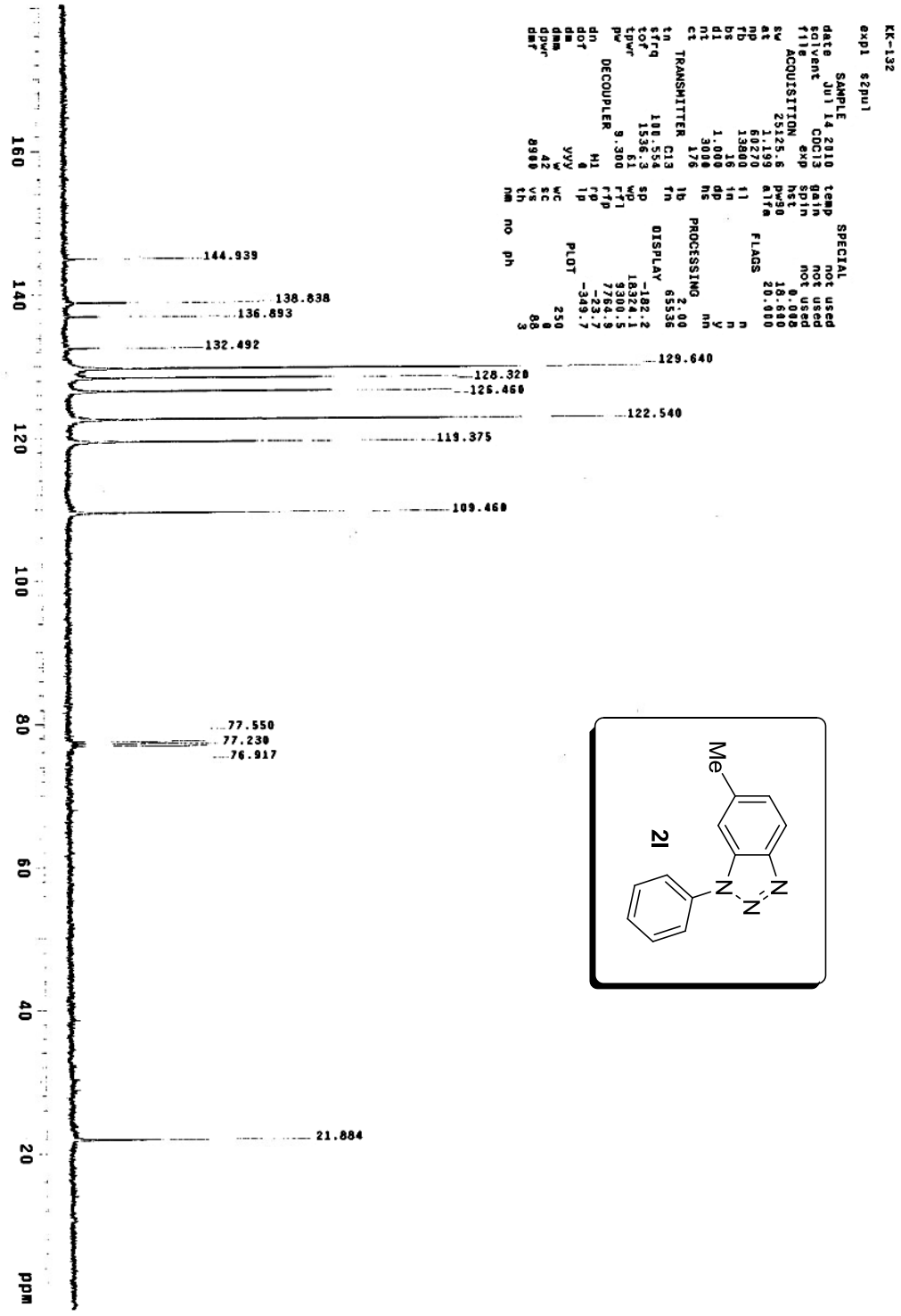
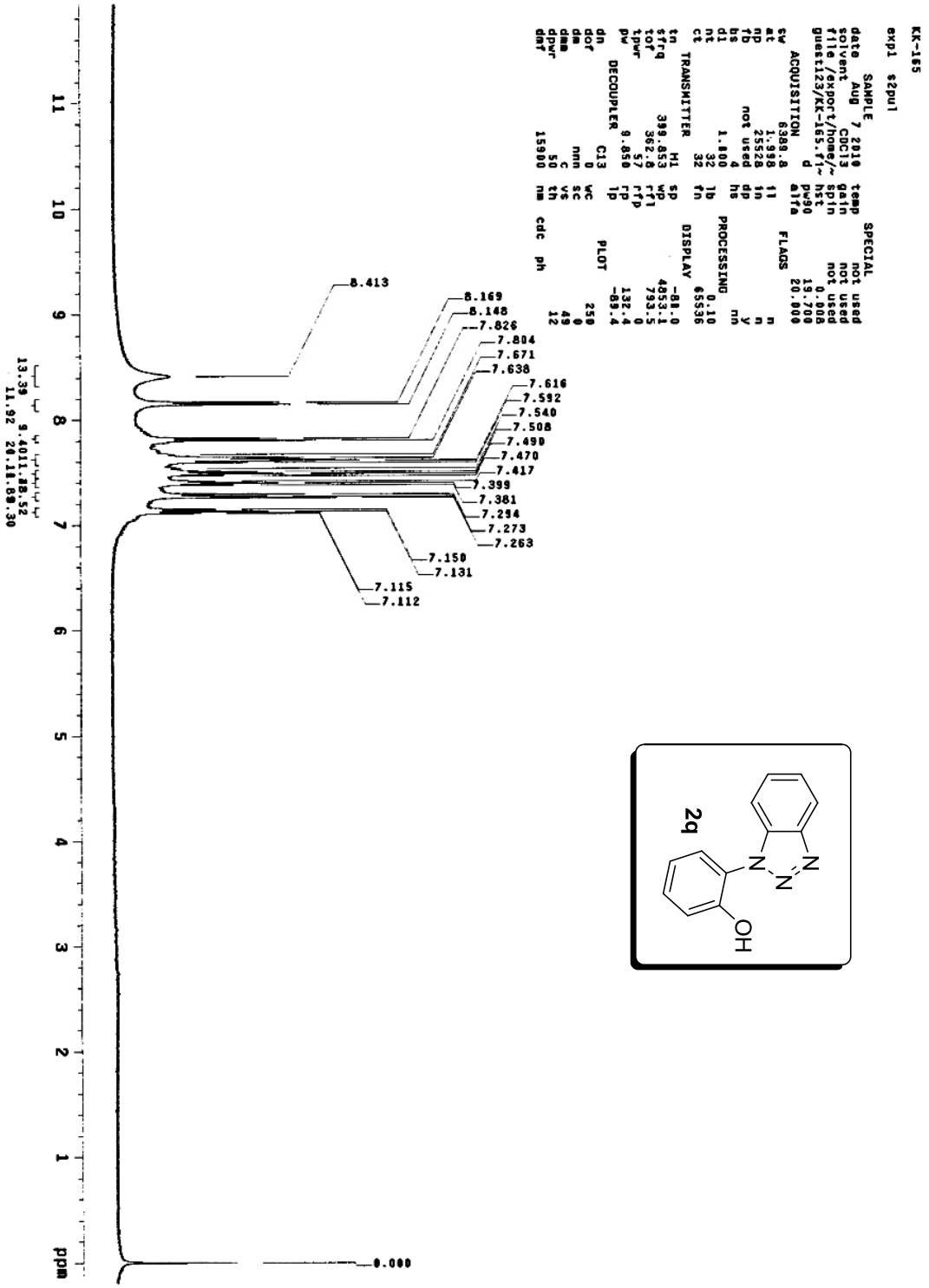
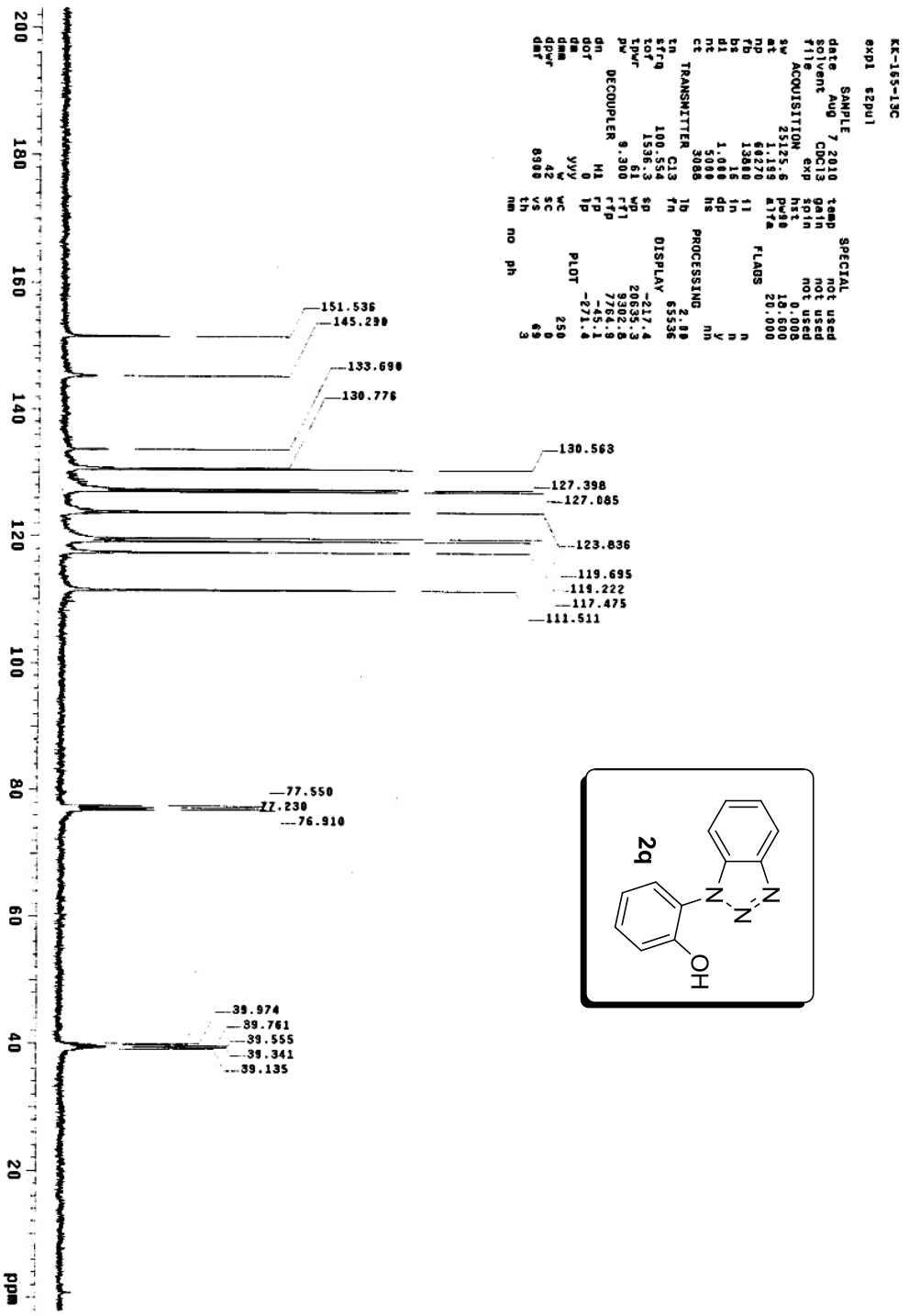












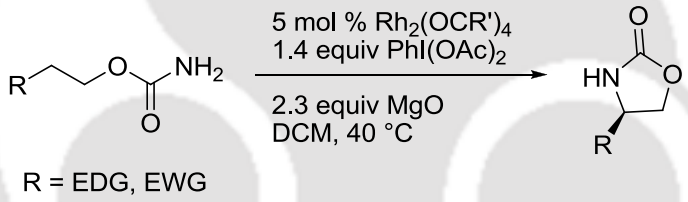
Chapter II

Palladium(II)-Catalyzed Synthesis of 1-Aryl-1*H*-benzotriazoles

C-H activation protocols are attractive because they make methodology atom economical, step efficient and obviate the need for preactivated substrate precursors.[1] Transition metal catalyzed functionalization of unreactive C-H bonds to carbon-carbon and carbon-heteroatom bonds formation has brought a revolution in synthetic methodology.[2,3] Notable progress has been made using predominantly Rh, Ru, Ag, Cu and Pd based systems.

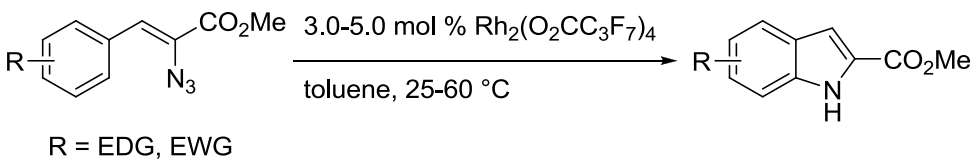
2.1 Rhodium Catalyzed C-H Activation

Du Bois and co-workers described Rh(II)-carboxylate catalyzed C-H amination of primary carbamates to afford oxazolidinone derivatives, which can be converted into vicinal amino alcohols (Scheme 1).[4]



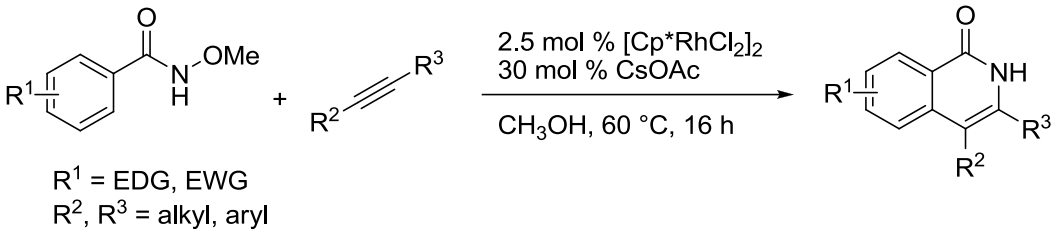
Scheme 1. Synthesis of Oxazolidinone Derivatives.

Driver and co-workers demonstrated a dirhodium(II)-catalyzed intramolecular C-H activation/C-H amination protocol for the synthesis of 1*H*-indole-2-carboxylates. The reaction proceeds *via* decomposition of azidocarboxylates to afford 1-[*H*]indole-2-carboxylates (Scheme 2).[5]



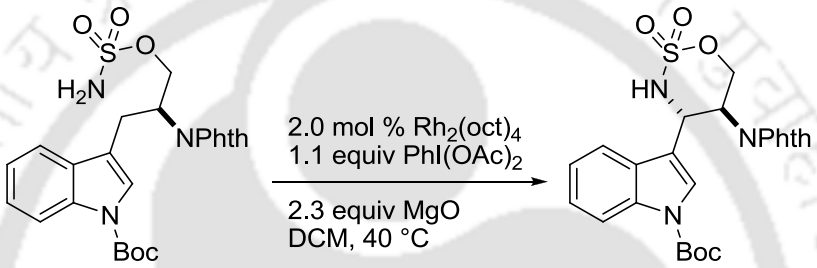
Scheme 2. Synthesis of 1*H*-Indole-2-carboxylates.

Fagnou and co-workers showed a rhodium(III)-catalyzed annulation of benzhydroxamic acids with alkynes to afford suitably substituted isoquinolone derivatives (Scheme 3).[6]



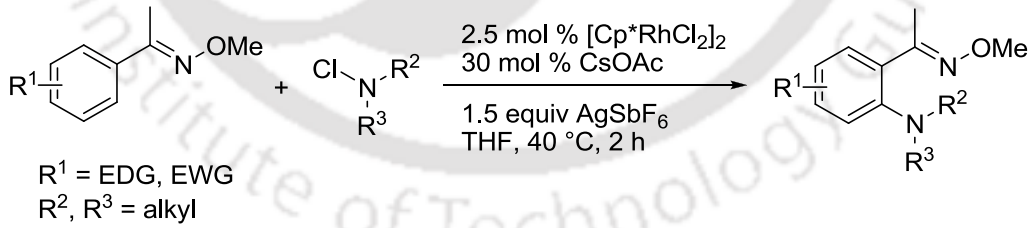
Scheme 3. Synthesis of Isoquinolones.

Du Bois and co-workers showed Rh(II)-carboxylate catalyzed intramolecular oxidative C-H amination of chiral sulfamate esters. The reaction proceeds with good diastereoselectivity (Scheme 4).[7]



Scheme 4. C-H Amination of Chiral Sulfamate Ester.

Yu and co-workers developed a Rh(III)-catalyzed intermolecular *ortho*C-H amination of acetophenone *O*-methyloximes using *N*-chloroamines. The protocol has broad substrate scope and proceeds under mild reaction conditions (Scheme 5).[8]

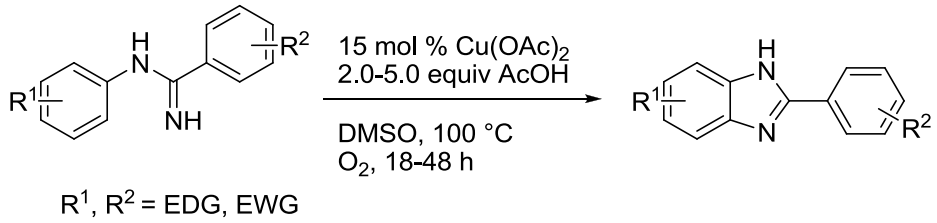


Scheme 5. Intermolecular C-H Amination.

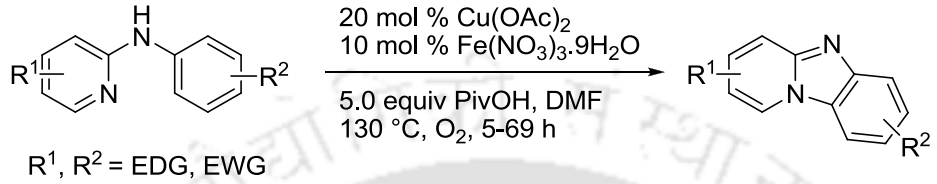
2.2 Copper Catalyzed C-H Activation

Buchwald and co-workers developed a copper(II)-catalyzed synthesis of benzimidazoles from amidines *via* C-H functionalization followed by intramolecular *C-N* bond formation (Scheme 6).[9]

Zhu and co-workers employed the combination of copper(II) and iron(III) salts for the synthesis of pyrido[1,2-*a*]benzimidazoles from *N*-aryl-2-aminopyridines (Scheme 7).[10]

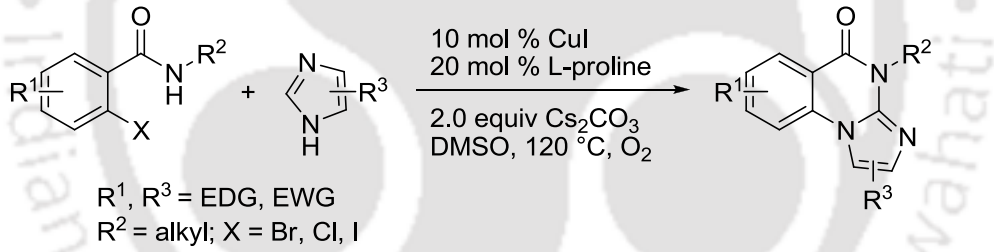


Scheme 6. Synthesis of 2-Substituted Benzimidazoles.



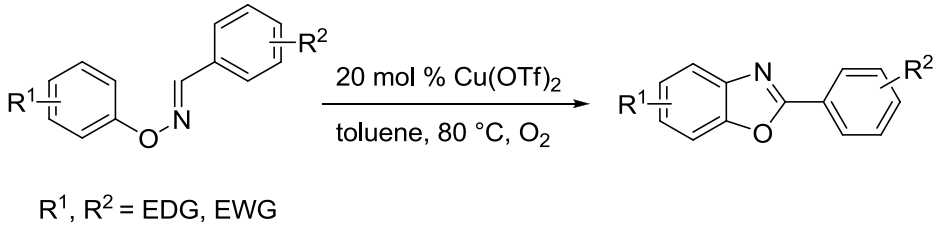
Scheme 7. Synthesis of of Pyrido[1,2-*a*]benzimidazoles.

Fu and co-workers described copper catalyzed synthesis of imidazo/benzimidazoquinazolinones *via* sequential Ullmann type coupling followed by aerobic oxidative intramolecular C-H amidation (Scheme 8).[11]



Scheme 8. Synthesis of Imidazo/Benzimidazoquinazolinones.

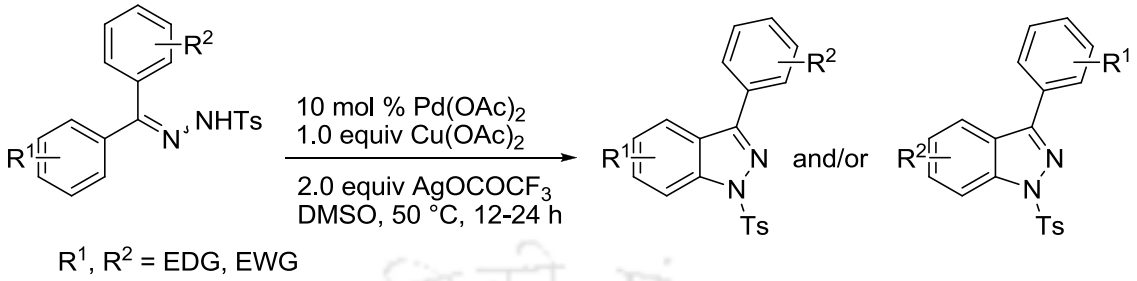
Our group developed new route for the synthesis of suitably substituted 2-aryl benzoxazoles from bisaryloxime ethers *via* copper(II)-catalyzed C-H activation followed by *C-N* bond formation (Scheme 9).[12]



Scheme 9. Copper(II)-Catalyzed Synthesis of 2-Arylbenzoxazoles.

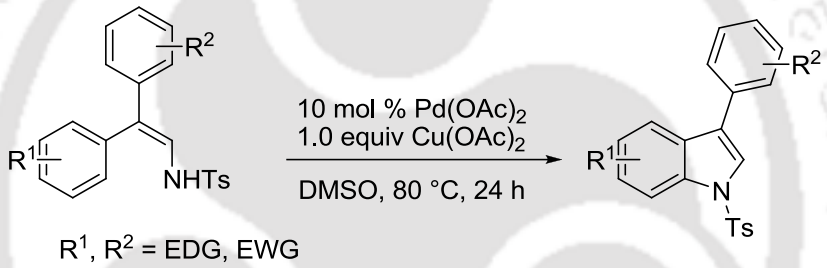
2.3 Palladium Catalyzed C-H Activation

Hiroya and co-workers reported a palladium(II)-catalyzed C-H activaion followed by intramolecular C-H amination for the synthesis of indazole derivatives (Scheme 10).[13]



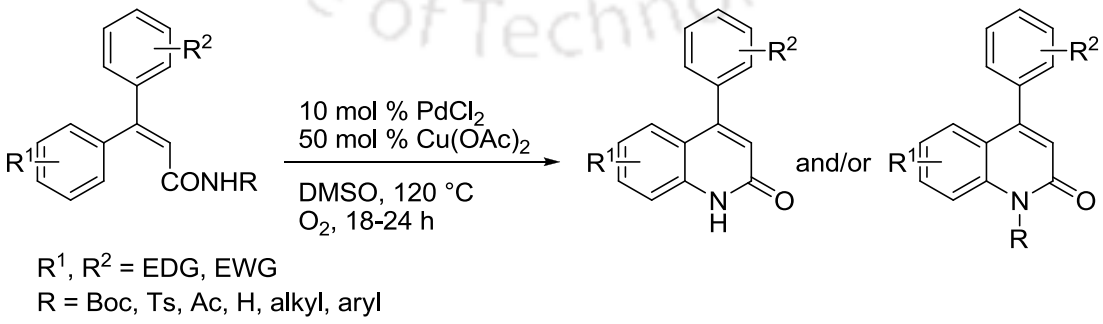
Scheme 10. Synthesis of Indazole Derivatives.

They also further demonstrated palladium(II)-catalyzed C-H activation followed by intramolecular C-H amination for the synthesis of indole derivatives (Scheme 11).[14]



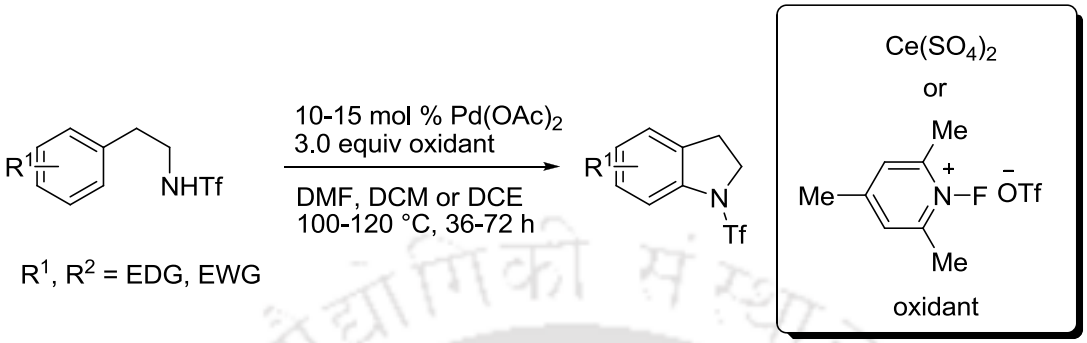
Scheme 11. Synthesis of Indole Derivatives.

In addition, $PdCl_2$ catalyzed cyclization of 3,3-diarylacrylamides through intramolecular C-H amination has been shown to produce variously substituted 2-quinolinones. The use of O_2 atmosphere along with a semicatalytic amount of $Cu(OAc)_2$ as a reoxidation system proved to be crucial for the process (Scheme 12).[15]



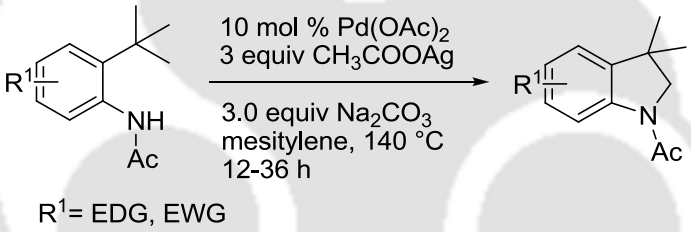
Scheme 12. Synthesis of 2-Quinolinones.

Yu and co-workers developed a $Pd(OAc)_2$-catalyzed intramolecular C-H amination to afford indoline derivatives. The reaction involves use of either $Ce(SO_4)_2$ or F^+ source as the oxidant (Scheme 13).[16]



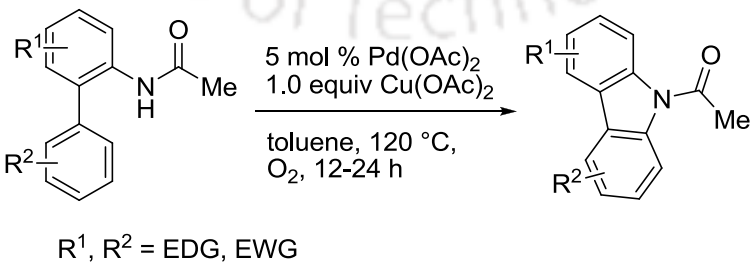
Scheme 13. Synthesis of Indoline Derivatives.

Glorius and co-workers reported a palladium-catalyzed amidation of unactivated sp^3 C-H bonds to afford the substituted indolines (Scheme 14).[17]



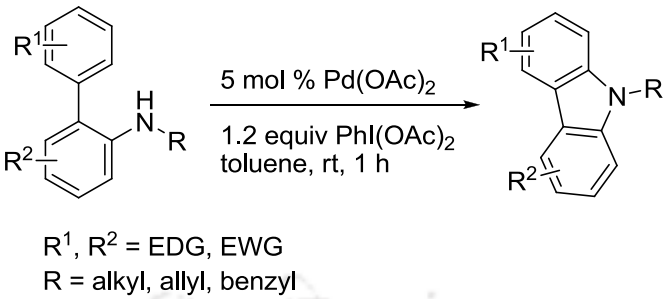
Scheme 14. Synthesis of Indoline Derivatives.

Buchwald and co-workers showed $Pd(OAc)_2$ catalyzed C-H functionalization followed by *C-N* bond formation for the synthesis of carbazoles. This reaction involves of use of $Cu(OAc)_2$ as an external oxidant (Scheme 15).[18]



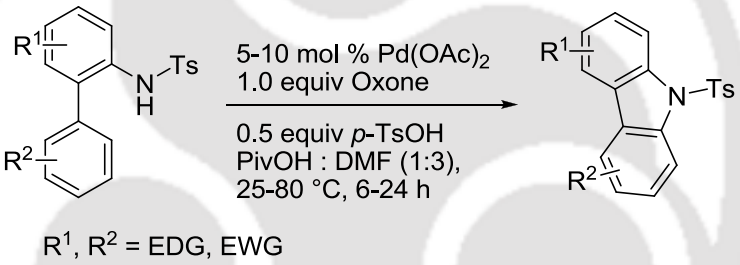
Scheme 15. Synthesis of Carbazoles.

Gaunt and co-workers described Pd(II)-catalyzed C-H amination to give carbazoles. The protocol involves use of $PhI(OAc)_2$ as an external oxidant (Scheme 16).[19]



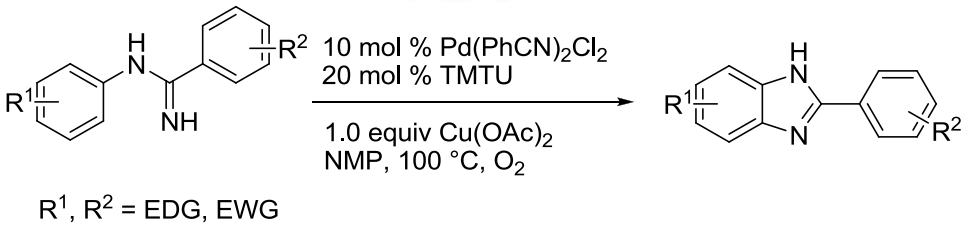
Scheme 16. Synthesis of Carbazoles.

Kim and co-workers developed a palladium-catalyzed intramolecular C-H amination of *N*-tosyl-2-arylanilines to afford carbazoles under ambient temperature. The protocol employs oxone as an external oxidant (Scheme 17).[20]



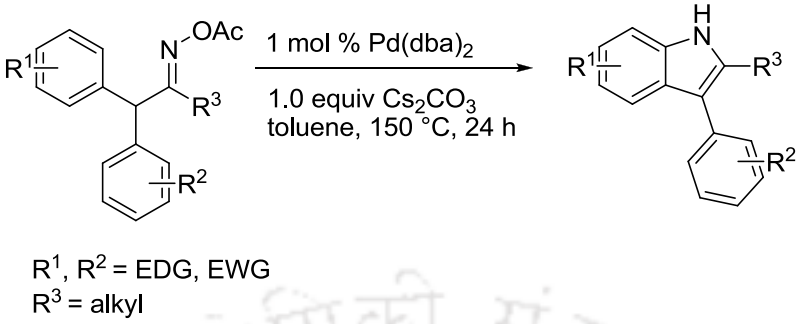
Scheme 17. Synthesis of Carbazoles.

Shi and co-workers showed a straight forward method to construct 2-substituted 1*H*-benzo[*d*]imidazoles by means of Pd(II)-catalyzed intramolecular C-H activation/*C*-*N* bond formation from *N*-phenylbenzimidamides. The reaction uses tetramethyl thiourea (TMTU) to promote the catalytic efficiency (Scheme 18).[21]



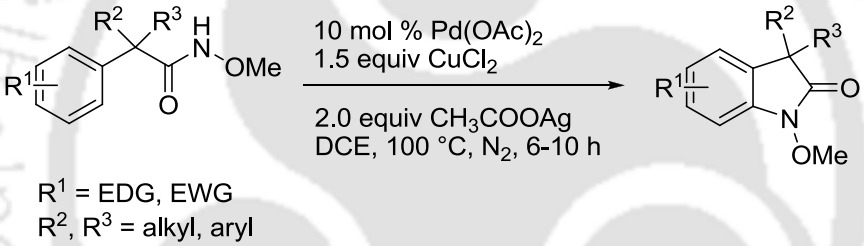
Scheme 18. Synthesis of 2-Substituted 1*H*-Benzo[*d*]imidazoles.

Hartwig and co-workers developed $Pd(dba)_2$ catalyzed intramolecular C-H amination of oxime esters to afford substituted 1*H*-indoles (Scheme 19).[22]



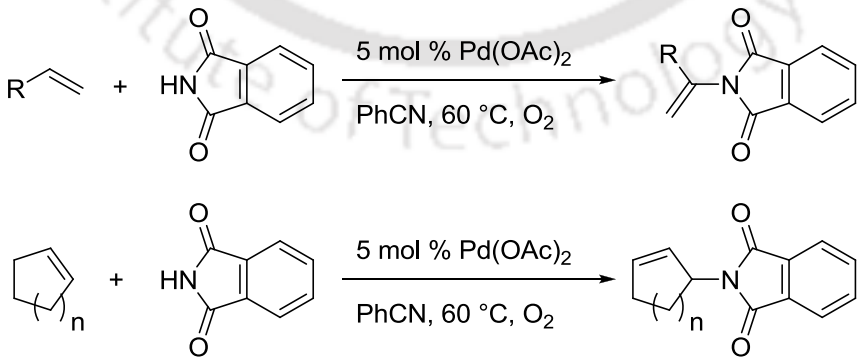
Scheme 19. Synthesis of Substituted 1*H*-Indoles.

Yu and co-workers described $Pd(OAc)_2$ catalyzed intramolecular C-H amination of *N*-methoxyhydroxamic acids to afford β-, γ- and δ-lactams (Scheme 20).[23]



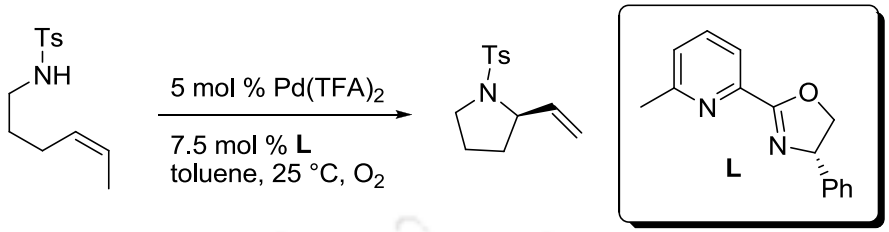
Scheme 20. C-H Amination of *N*-Methoxyhydroxamic acids.

Stahl and co-workers reported a Pd(II)-catalyzed aerobic oxidative intermolecular C-H amination of unactivated alkenes and cycloalkenes with phthalimide (Scheme 21).[24]



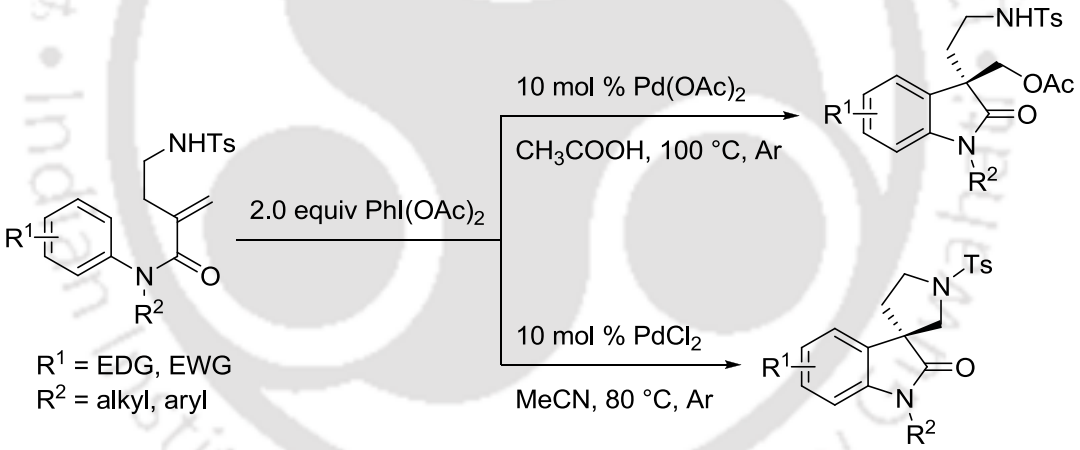
Scheme 21. C-H Amination of Alkenes and Cycloalkenes with Phthalimide.

They also further showed Pd(II) catalyzed intramolecular oxidative allylic amidation of alkenes. This protocol affords the amidation products with high enantioselectivity (Scheme 22).[25]



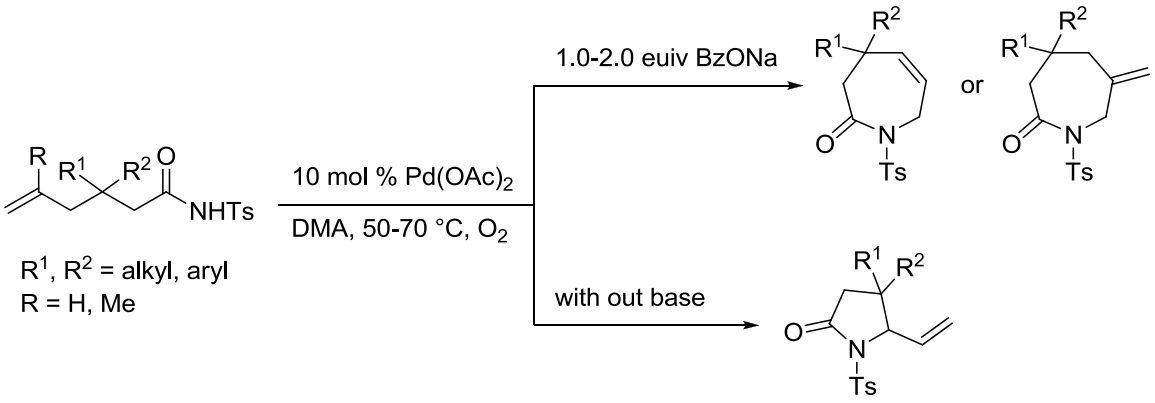
Scheme 22. Allylic C-H Amination of Alkenes.

Zhu and co-workers demonstrated Pd(II)-catalyzed direct C-H functionalization and C-X bond formation. Changing the reaction conditions like solvent and catalyst leads to the formation of either 3,3'-disubstituted oxindole or spirooxindole from the same substrate precursor (Scheme 23).[26]



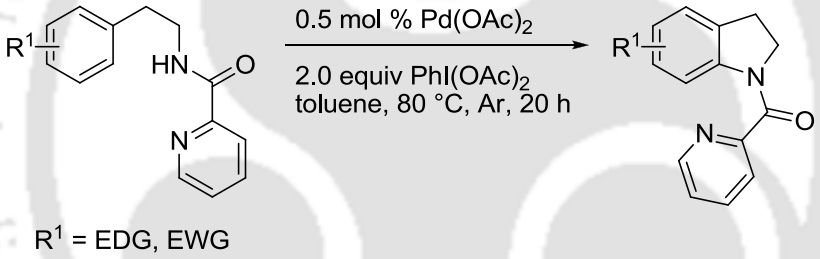
Scheme 23. Intramolecular C-H Amination Reaction.

Liu and co-workers showed Pd-catalyzed intramolecular aerobic oxidative allylic C-H amination of olefins. Bronsted base modulates the regioselectivity and product formation (Scheme 24).[27]



Scheme 24. Allylic C-H Amination of Olefins.

Chen and co-workers described Pd-catalyzed intramolecular amination for the synthesis of indoline compounds from picolinamide protected β-arylethylamine substrates. The reaction features high efficiency, low catalyst loading and mild operating conditions (Scheme 25).[28]

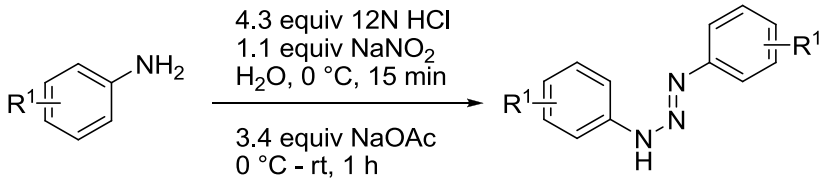


Scheme 25. Synthesis of Indoline Compounds.

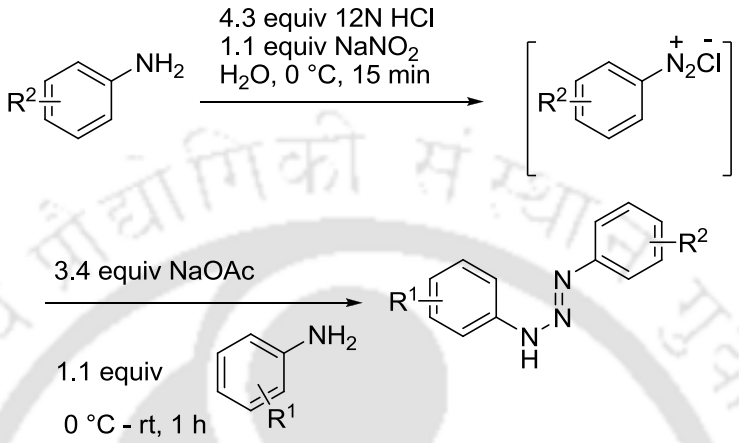
2.4 Present Study

In this chapter, we describe a general method for the synthesis of substituted 1-aryl-1*H*-benzotriazoles *via* Pd-catalyzed C-H activation followed by intramolecular *C-N* bond formation of 1,3-diaryl triazenes. The protocol is simple, general and provides a straight forward route for the efficient synthesis of functionalized 1-aryl-1*H*-benzotriazoles with excellent yield.

The substrate precursors 1,3-diaryltriazenes were prepared from the readily available anilines according to literature procedure (Schemes 26-27).[29]



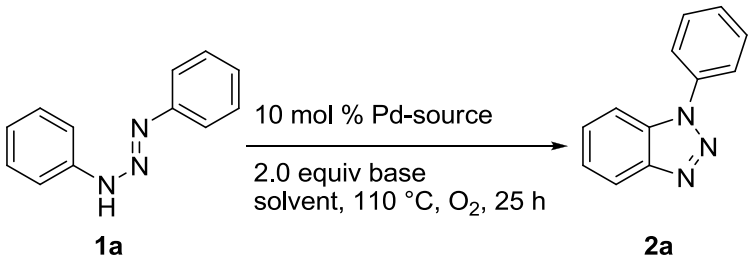
Scheme 26. Synthesis of Symmetrical Phenylimino-2-phenyl-hydrazines



Scheme 27. Synthesis of Unsymmetrical Phenylimino-2-phenyl-hydrazines

First, the reaction conditions were optimized using phenylimino-2-phenylhydrazine **1a** as a model substrate with different palladium sources, solvents and bases at varied temperature (Table 1). The reaction occurred to afford the desired 1-aryl-1*H*-benzotrizole **2a** in 36% yield when the substrate was stirred with 10 mol % $Pd(OAc)_2$ in DMSO at 110 °C under oxygen balloon. The catalytic activity of the Pd(II) sources were compared, and $Pd(OAc)_2$ was found to be superior to $PdCl_2$ and $PdCl_2(PPh_3)_2$. Replacing the solvent from DMSO to DMF gave **2a** in 65% yield. The yield of **2a** was further increased to 80% when freshly activated 4Å molecular sieve was added as an additive. In contrast, solvents such as xylene, chlorobenzene and 1,4-dioxane gave inferior results. The reaction was effective with Cs_2CO_3, K_2CO_3, K_3PO_4, KOH and Na_2CO_3, and Cs_2CO_3 yielded the best results. No product was obtained using KO^tBu as the base. Lowering the reaction temperature (100 °C) or the amount of the catalyst (5 mol %) or the base (1.5 equiv) gave **2a** in < 55% yield. Control experiments confirmed that no product was obtained in the absence of the palladium source. In summary, the optimal conditions in DMF include $Pd(OAc)_2$ (10 mol %) and Cs_2CO_3 (2.0 equiv) at 110 °C for 25 h under oxygen balloon.

Table 1. Optimization of Reaction Conditions[a]

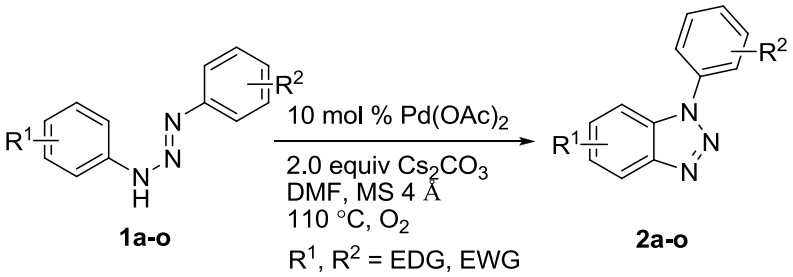


entry	Pd-sorce	base	solvent	yield (%)[b]
1	$Pd(OAc)_2$	Cs_2CO_3	DMSO	36
2	$PdCl_2$	Cs_2CO_3	DMSO	30
3	$Pd(PPh_3)_2Cl_2$	Cs_2CO_3	DMSO	15
4	**$Pd(OAc)_2$**	**Cs_2CO_3**	**DMF**	65**(80)**[c]
5	$Pd(OAc)_2$	Cs_2CO_3	DMF	23[d]
6	$Pd(OAc)_2$	Cs_2CO_3	xylene	n.d.
7	$Pd(OAc)_2$	Cs_2CO_3	chlorobenzene	n.d.
8	$Pd(OAc)_2$	Cs_2CO_3	1,4-dioxane	3
9	$Pd(OAc)_2$	Na_2CO_3	DMF	12
10	$Pd(OAc)_2$	K_2CO_3	DMF	72
11	$Pd(OAc)_2$	KOH	DMF	5
12	$Pd(OAc)_2$	K_3PO_4	DMF	25
13	$Pd(OAc)_2$	KO^tBu	DMF	n.d.
14	$Pd(OAc)_2$	Cs_2CO_3	DMF	55[e]
15	$Pd(OAc)_2$	Cs_2CO_3	DMF	32[f]
16	-	Cs_2CO_3	DMF	n.d.

[a]Reaction condition: Phenylimino-2-phenylhydrazine **1a** (1.0 mmol), Pd source (10 mol %), base (2.0 equiv) were stirred at 110 °C in solvent (1.0 mL) under oxygen balloon. [b]Isolated yield. [c]With MS 4 Å (100 mg). [d]$Pd(OAc)_2$ (5 mol %) used. [e]1.5 equiv. of Cs_2CO_3 was used. [f]Reaction temperature = 100 °C. n.d. = Not dected.

With the optimization condition in hand, the scope of the protocol was studied for the substrates having substituents on the aryl rings (Table 2).

Table 2. Palladium Catalyzed Synthesis of 1-Aryl-1*H*-benzotriazoles: Substrate Scope[a]



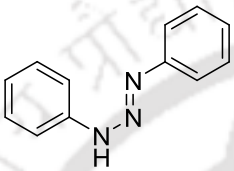
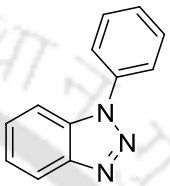
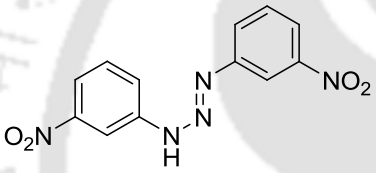
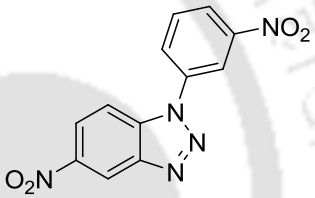
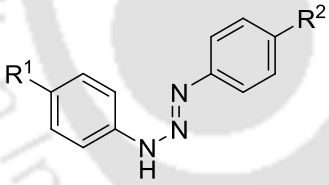
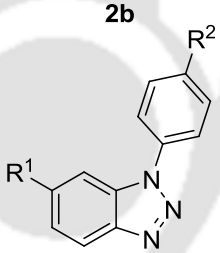
entry	substrate		time (h)	product		yield (%)[b]
1		**1a**	25		**2a**	80
2		**1b**	30		**2b**	80
3		**1c**	3		n.d.	
4	R^1, R^2 = CO_2Et	**1d**	4	n.d.		
5	R^1, R^2 = Br	**1e**	5	R^1, R^2 = H	**2a**	55
6	R^1, R^2 = Cl	**1f**	6	R^1, R^2 = Cl	**2c**	85
7	R^1, R^2 = Et	**1g**	7	R^1, R^2 = Et	**2d**	70
8	R^1, R^2 = OMe	**1h**	8	n.d.		
9	R^1, R^2 = Me	**1i**	9	R^1, R^2 = Me	**2e**	84

Table 2 continues…

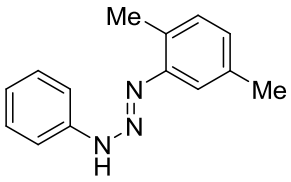
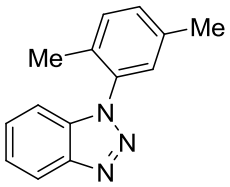
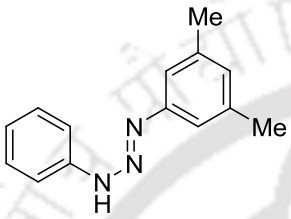
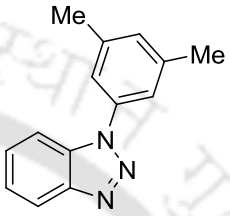
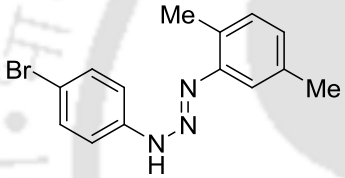
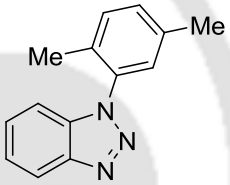
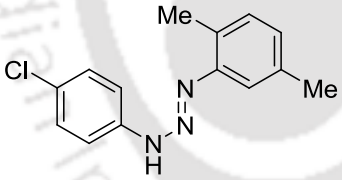
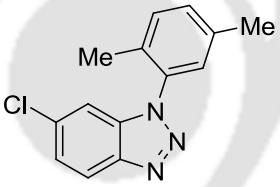
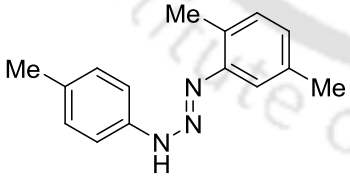
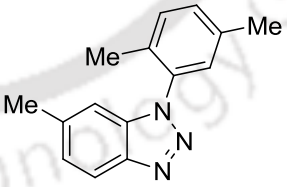
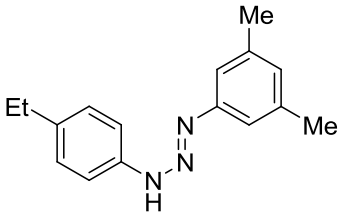
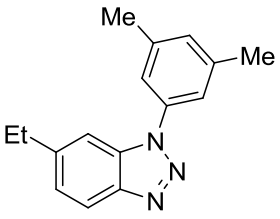
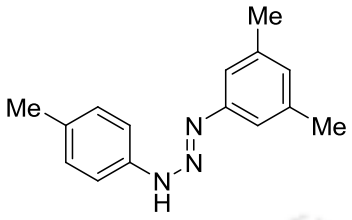
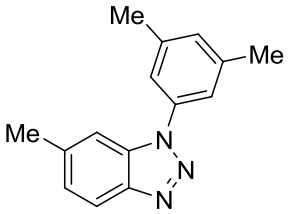
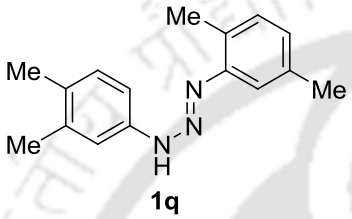
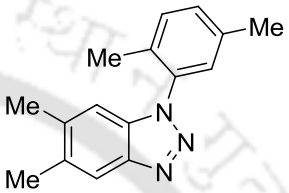
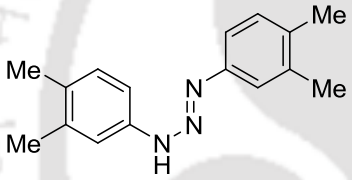
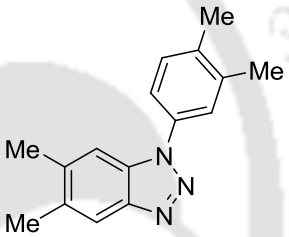
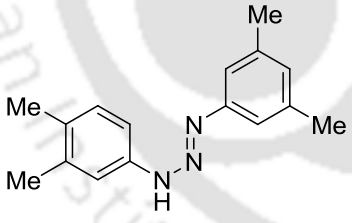
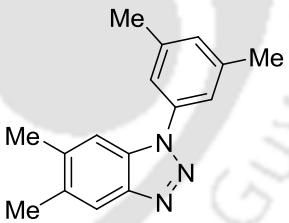
entry	substrate	time (h)	product	yield (%)[b]
10	 **1j**	25	 **2f**	72
11	 **1k**	30	 **2g**	72
12	 **1l**	30	 **2f**	57
13	 **1m**	30	 **2h**	60
14	 **1n**	30	 **2i**	72
15	 **1o**	30	 **2j**	75

Table 2 continues…

entry	substrate	time (h)	product	yield (%)[b]
16	 **1p**	25	 **2k**	72
17	 **1q**	30	 **2l**	75
18	 **1r**	30	 **2m**	88
19	 **1s**	30	 **2n**	77

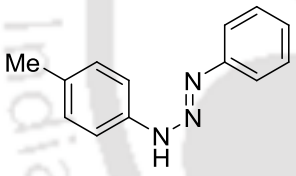
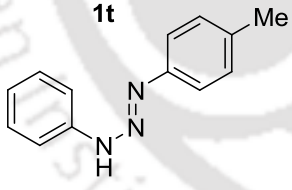
[a]Reaction condition: Substrate **1a-s** (1.0 mmol), $Pd(OAc)_2$ (10 mol %), Cs_2CO_3 (2.0 equiv) and MS 4Å (100 mg) were stirred at 110 °C in DMF (1.0 mL) under oxygen balloon. [b]Isolated yield. [c]Single isomer. n.d. = Not detected.

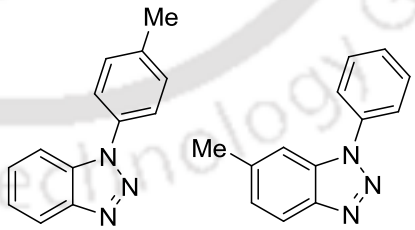
Phenylimino-2-phenylhydrazines **1b, 1f-g** and **1i** having 3-NO_2, 4-Br, 4-Cl, 4-Et, and 4-Me substituents proceeded the C-H amination to afford the benzotriazoles **2b** and **2c-e** in 70-85% yield. In contrast, the substrates **1c-d** and **1h** with 4-COMe, 4-CO_2Et and 4-OMe groups showed no cyclization and the starting materials were recovered intact. Whereas

phenylimino-2-phenylhydrazines **1j-s** having Cl, Me and Et substituents readily underwent cyclization to give the corresponding benzotriazoles **2f-n** in 57-88% yield. Recrystallization of **2m** in CH_2Cl_2 gave single crystals whose structure was confirmed by X-ray analysis. The substrates **1e** and **1l** with Br group provided the debrominated products **2a** and **2f** exclusively.[4a]

Finally, to reveal the regioselectivity, the reactions of the unsymmetrical substrates **1t-u** were studied (Table 3). Both the substrates underwent cyclization to provide a 2:1 mixture of the regioisomers **2o** and **2p** in 75% yield. In both the substrates, the cyclization occurred preferentially on the nonsubstituted aryl ring. These results suggest that the isomerization of triazenes can occur easily under the conditions used in this system.

Table 3. Cyclization of Unsymmetrical Phenylimino-2-phenylhydrazines[a]

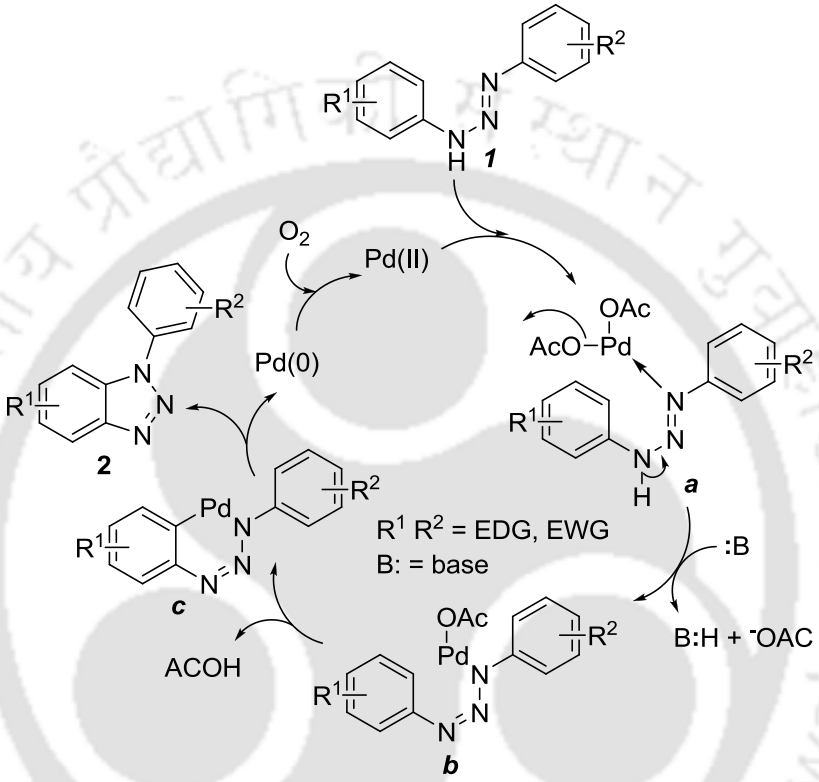
entry	substrate	time (h)	products[c] **2o : 2p**	yield (%)[b]
1	 **1t**	25	2 : 1	75
2	 **1u**	25	2 : 1	75



2o **2p**

[a]Reaction condition: Substrate **1t-u** (1.0 mmol), $Pd(OAc)_2$ (10 mol %), Cs_2CO_3 (2.0 equiv) and MS 4Å (100 mg) were stirred at 110 °C in DMF (1.0 mL) under oxygen balloon. [b]Isolated yield. . [c]Regioisomeric ratio was determined by 400 MHz ^{1}H NMR of the crude reaction mixture.

The proposed catalytic cycle is shown below (Scheme 28).[13] The substrates **1** may undergo coordination with Pd(II) to give intermediate ***a*** that could lead to the formation of ***b*** in the presence of base. The latter may undergo C-H activation to give the six-membered palladacycle ***c*** that could afford the target 1-aryl-1*H*-benzotriazole **2** and Pd(0). The reduced Pd could be oxidized in the presence of oxygen to complete the catalytic cycle.



Scheme 28. Proposed Catalytic Cycle.

Conclusion

We have developed a novel protocol for the synthesis of 1-aryl-1*H*-benzotriazoles *via* C-H activation followed by intramolecular amination employing a $Pd(OAc)_2$ as a catalyst under relatively milder conditions. The protocol involves of molecular oxygen as an terminal oxidant.

Experimental Section

General Information. Anilines, $Pd(OAc)_2$ (99.9%), $PdCl_2$ (99.9%), $Pd(PPh_3)_2Cl_2$ (98%), Cs_2CO_3 (99%), K_2CO_3, KO^tBu (95%) and K_3PO_4 (98%) were purchased from Aldrich and used without further purification. The column chromatography was performed with Rankem

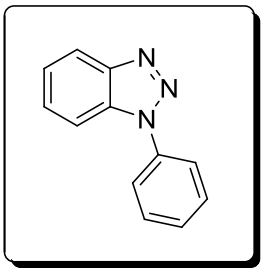
silica gel (60-120 mesh). NMR (^{1}H and ^{13}C) spectra were recorded with a Varian 400 spectrometer. Melting points were determined with a Büchi B-545 apparatus and are uncorrected. Elemental analyses were recorded using Perkin Elmer CHNS analyzer. X-Ray data were collected on a Bruker SMART APEX equipped with a CCD area detector using Mo Kα radiation. The structures were solved by direct method using *SHELLX-97* (Göttingen, Germany). IR spectra were recorded using FT-IR spectrometer.

General Procedure for Synthesis of Symmetrical Triazenes 1a-i and **1r.**[29] To a stirred solution of water (8.0 mL) and 12N HCl (2.0 mL) in a 100 mL beaker for 5 min at ambient temperature, anilines (15.0 mmol) were added. The resultant stirring mixture was cooled to 0 °C and treated drop wise with a 0 °C cooled $NaNO_2$ solution (8.24 mmol in 2.0 mL of water) for 15 min followed by 0 °C cooled NaOAc solution (25.48 mmol in 5.0 mL of water) for 15 min. The stirring was continued at 0 °C for 1 h and the resultant yellow precipitate was filtered by a Buchner funnel, washed with cold water (20.0 mL) and dried at room temperature to give the target triazenes **1a-i** and **1r** in 70-85% yield.

General Procedure for Synthesis of Unsymmetrical Triazenes 1j-q and **1s-u.**[29] To a stirred solution of water (8.0 mL) and 12 NHCl (2.0 mL) for 5 min at ambient temperatures, R^2 substituted anilines (7.49 mmol) were added. The stirring reaction mixture was cooled to 0 °C and treated drop wise with a 0 °C cooled $NaNO_2$ solution (8.24 mmol in 2 mL of water) for 15 min followed by a 0 °C cooled NaOAc solution (25.48 mmol in 5.0 mL of water) for 15 min. Then R^1 substituted anilines (7.49 mmol) were added and the stirring was continued for an additional 1 h at 0 °C. The resultant yellow precipitate was filtered by a Buchner funnel, washed with cold water (20.0 mL) and dried at room temperature to afford the target unsymmetrical triazenes **1j-q** and **1s-u** in 70-80% yield.

General Procedure for Aryl Triazenylation. An oven dried 10 mL round bottom flask was charged with $Pd(OAc)_2$ (10 mol %), Cs_2CO_3 (2.0 equiv), triazene **1a-u** (1.0 mmol) and 4Å molecular sieve (100 mg). The mixture was stirred at 110 °C in DMF (1.0 mL) under oxygen balloon. The progress of reaction was monitored by TLC using ethyl acetate and hexane. The reaction mixture was cooled to room temperature and diluted with ethyl acetate (25 mL). The organic layer was washed successively with brine (1 x 3 mL) and water (3 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using 9:1 hexane and ethyl acetate as eluent.

2.5 Characterization Data



1-Phenyl-1*H*-benzo[*d*][1,2,3]triazole (2a).[30] Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.35; yellow solid; yield 80%.

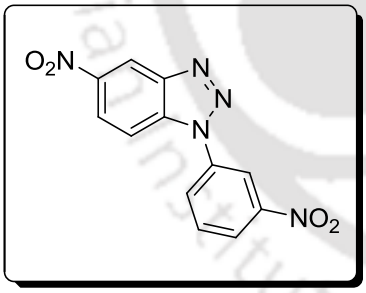
Mp: 86-87 °C (lit.[30] 85-87 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, *J* = 8.4 Hz, 1H), 7.77-7.71 (m, 3H), 7.59 (t, *J* = 7.6 Hz, 2H), 7.54-7.46 (m, 2H), 7.41 (t, *J* = 8.4 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.5, 137.0, 132.3, 129.9, 128.7, 128.3, 124.4, 122.9, 120.3, 110.4.

FT-IR (KBr): *v* = 3056, 2923, 1595, 1500, 1275, 1186, 1089, 1059 cm^{-1}.

Elemental analysis calcd (%) for $C_{12}H_9N_3$: C, 73.83; H, 4.65; N, 21.52. Found: C, 73.70; H, 4.67; N, 21.63.



5-Nitro-1-(3-nitrophenyl)-1*H*-benzo[*d*][1,2,3]triazole (2b). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.35; yellow solid; yield 80%.

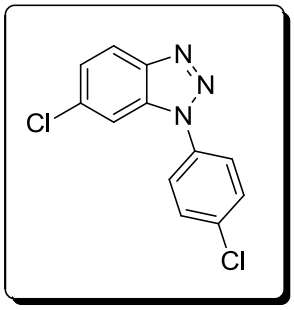
Mp: 172-174 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.13-9.12 (m, 1H), 8.69 (t, *J* = 1.6 Hz, 1H), 8.56 (dd, *J* = 9.2, 2.0 Hz, 1H), 8.46-8.43 (m, 1H), 8.22-8.19 (m, 1H), 7.92-7.88 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 148.6, 144.9, 144.8, 136.3, 134.8, 131.8, 129.5, 124.1, 123.7, 118.3, 116.9, 112.3.

FT-IR (KBr): *v* = 3105, 2924, 2851, 1633, 1526, 1354, 1025, 1001 cm^{-1}.

Elemental analysis calcd (%) for $C_{12}H_7N_5O_4$: C, 50.53; H, 2.47; N, 24.55. Found: C, 50.40; H, 2.49; N, 24.65.



6-Chloro-1-(4-chlorophenyl)-1*H*-benzo[*d*][1,2,3]triazole (2c). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.40; yellow solid; yield 85%.

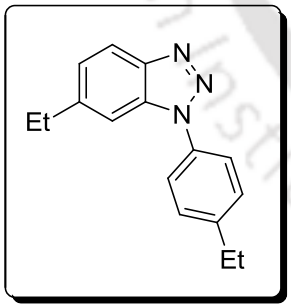
Mp: 202-203 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 9.2 Hz, 1H), 7.70-7.68 (m, 3H), 7.60-7.58 (m, 2H), 7.42 (dd, *J* = 1.6, 8.8 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.3, 135.3, 135.2, 135.1, 132.9, 130.4, 126.0, 124.2, 121.6, 110.2.

FT-IR (KBr): *v* = 3055, 2918, 1613, 1500, 1464, 1270, 1235, 1071 cm^{-1}.

Elemental analysis calcd (%) for $C_{12}H_7Cl_2N_3$: C, 54.57; H, 2.67; N, 15.91. Found: C, 54.39; H, 2.69; N, 16.03.



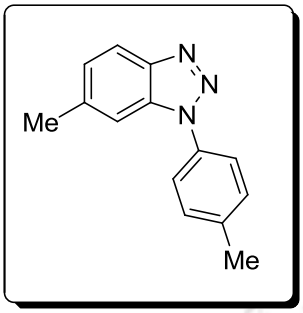
6-Ethyl-1-(4-ethylphenyl)-1*H*-benzo[*d*][1,2,3]triazole (2d). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.40; yellow liquid; yield 70%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 8.8 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.48 (s, 1H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 1H), 2.84-2.73 (m, 4H), 1.33-1.27 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.4, 145.1, 135.0, 133.1, 129.4, 125.7, 123.2, 120.0, 108.5, 29.6, 28.8, 15.9, 15.7.

FT-IR (neat): ν = 2965, 2932, 1616, 1518, 1454, 1277, 1073, 1044 cm^{-1}.

Elemental analysis calcd (%) for $C_{16}H_{17}N_3$: C, 76.46; H, 6.82; N, 16.72. Found: C, 76.34; H, 6.84; N, 16.82.



6-Methyl-1-*p*-tolyl-1*H*-benzo[*d*][1,2,3]triazole (2e). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.25; yellow solid; yield 84%.

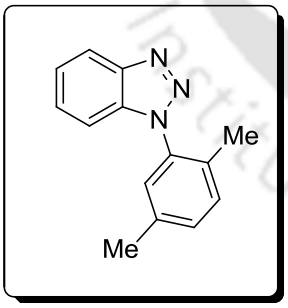
Mp: 92-93 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 8.8 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 2H), 7.47 (s, 1H), 7.40 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 1H), 2.52 (s, 3H), 2.46 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.1, 138.9, 138.7, 134.7, 132.9, 130.4, 126.6, 122.9, 119.6, 109.7, 22.1, 21.3.

FT-IR (KBr): ν = 3030, 2957, 2921, 2856, 1613, 1513, 1455, 1275, 1064 cm^{-1}.

Elemental analysis calcd (%) for $C_{14}H_{13}N_3$: C, 75.31; H, 5.87; N, 18.82. Found: C, 75.18; H, 5.88; N, 18.94.



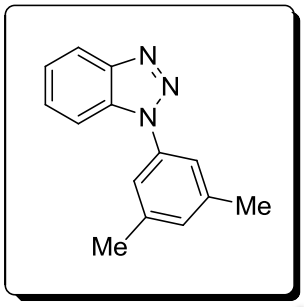
1-(2,5-Dimethylphenyl)-1*H*-benzo[*d*][1,2,3]triazole (2f). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.40; yellow liquid; yield 72%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 8.4 Hz, 1H), 7.53 (t, *J* = 8.4 Hz, 1H), 7.47-7.43 (m, 1H), 7.39-7.29 (m, 4H), 2.44 (s, 3H), 2.10 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.5, 136.9, 134.9, 133.8, 131.8, 131.4, 130.7, 127.9, 127.3, 124.0, 119.9, 110.2, 20.7, 17.2.

FT-IR (neat): ν = 2923, 1621, 1511, 1457, 1272, 1067 cm^{-1}.

Elemental analysis calcd (%) for $C_{14}H_{13}N_3$: C, 75.31; H, 5.87; N, 18.82. Found: C, 75.19; H, 5.89; N, 18.92.



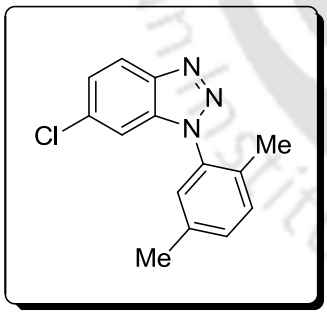
1-(3,5-Dimethylphenyl)-1*H*-benzo[*d*][1,2,3]triazole (2g). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.25; yellow liquid; yield 72%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (d, J = 8.4 Hz, 1H), 7.74 (d, J = 8.4 Hz, 1H), 7.52 (t, J = 7.2 Hz, 1H), 7.43-7.37 (m, 3H), 7.12 (s, 1H), 2.43 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.6, 139.9, 137.0, 132.5, 130.4, 128.2, 124.4, 120.7, 120.3, 110.7, 21.5.

FT-IR (neat): ν = 2920, 1616, 1492, 1470, 1282, 1237, 1165, 1065 cm^{-1}.

Elemental analysis calcd (%) for $C_{14}H_{13}N_3$: C, 75.31; H, 5.87; N, 18.82. Found: C, 75.16; H, 5.90; N, 18.94.



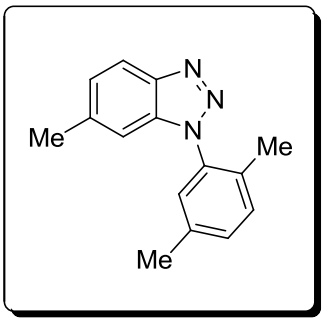
6-Chloro-1-(2,5-dimethylphenyl)-1*H*-benzo[*d*][1,2,3]triazole (2h). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.25; yellow liquid; yield 74%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05 (dd, J = 0.4, 8.8 Hz, 1H), 7.38-7.27 (m, 4H), 7.16 (s, 1H), 2.40 (s, 3H), 2.04 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.3, 137.3, 134.7, 132.1, 131.7, 131.3, 127.5, 125.5, 121.2, 110.1, 21.0, 17.4.

FT-IR (neat): ν = 2962, 2924, 1609, 1511, 1458, 1273, 1263, 1067 cm^{-1}.

Elemental analysis calcd (%) for $C_{14}H_{12}ClN_3$: C, 65.25; H, 4.69; N, 16.30. Found: C, 65.13; H, 4.71; N, 16.40.



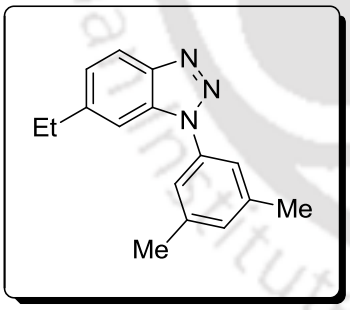
6-Methyl-1-(2,5-dimethylphenyl)-1*H*-benzo[*d*][1,2,3]triazole (2i). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.40; yellow liquid; yield 72%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 8.4 Hz, 1H), 7.34-7.23 (m, 3H), 7.19 (s, 1H), 7.09 (s, 1H), 2.50 (s, 3H), 2.41 (s, 3H), 2.07 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.3, 138.8, 137.0, 135.2, 134.4, 132.1, 131.5, 130.8, 127.6, 126.4, 119.5, 109.4, 22.0, 20.9, 17.4.

FT-IR (neat): *v* = 2922, 1620, 1512, 1461, 1274, 1117, 1066 cm^{-1}.

Elemental analysis calcd (%) for $C_{15}H_{15}N_3$: C, 75.92; H, 6.37; N, 17.71. Found: C, 75.79; H, 6.40; N, 17.81.



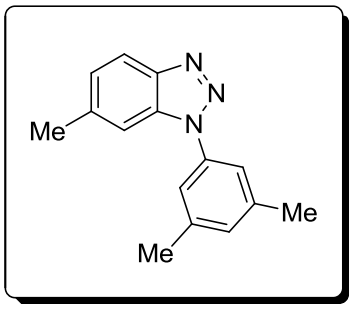
6-Ethyl-1-(3,5-dimethylphenyl)-1*H*-benzo[*d*][1,2,3]triazole (2j). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.40; yellow liquid; yield 75%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 8.4 Hz, 1H), 7.47 (s, 1H), 7.35 (s, 2H), 7.27 (d, *J* = 8.4 Hz, 1H), 7.11 (s, 1H), 2.85 (q, *J* = 8.0 Hz, 2H), 2.43 (s, 6H), 1.29 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.3, 139.9, 137.1, 133.0, 130.4, 129.3, 125.6, 123.1, 120.9, 119.9, 108.6, 29.5, 21.5, 16.0.

FT-IR (neat): *v* = 2964, 2928, 2862, 1619, 1475, 1283, 1073 cm^{-1}.

Elemental analysis calcd (%) for $C_{16}H_{17}N_3$: C, 76.46; H, 6.82; N, 16.72. Found: C, 76.31; H, 6.84; N, 16.85.



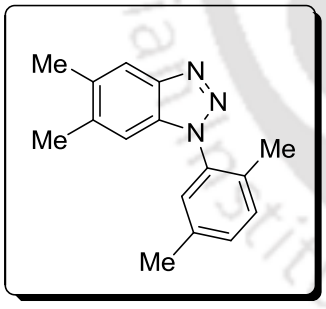
6-Methyl-1-(3,5-dimethylphenyl)-1*H*-benzo[*d*][1,2,3]triazole (2k). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.40; yellow liquid; yield 72%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 8.4 Hz 1H), 7.49 (s, 1H), 7.37 (s, 2H), 7.27 (d, *J* = 8.8 Hz, 1H), 7.14 (s, 1H), 2.55 (s 3H), 2.45 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.2, 139.9, 138.9, 137.0, 132.9, 130.4, 126.6, 120.8, 119.7, 109.8, 22.2, 21.5.

FT-IR (neat): *v* = 2920, 1612, 1597, 1475, 1283, 1234, 1135, 1065 cm^{-1}.

Elemental analysis calcd (%) for $C_{15}H_{15}N_3$: C, 75.92; H, 6.37; N, 17.71. Found: C, 75.80; H, 6.40; N, 17.80.



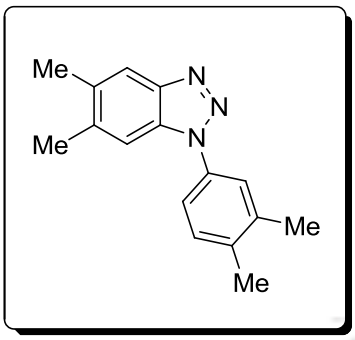
5,6-Dimethyl-1-(2,5-dimethylphenyl)-1*H*-benzo[*d*][1,2,3]triazole (2l). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.40; yellow liquid; yield 75%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87 (s, 1H), 7.33-7.27 (m, 2H), 7.19, (s, 1H), 7.09 (s, 1H), 2.44 (s, 3H), 2.41 (s, 3H), 2.39 (s, 3H), 2.06 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.8, 138.4, 136.9, 135.2, 133.9, 133.0, 131.9, 131.3, 130.6, 127.4, 119.0, 109.6, 20.9, 20.8, 20.4, 17.3.

FT-IR (neat): *v* = 3028, 2923, 2862, 1625, 1511, 1465, 1254, 1224, 1069 cm^{-1}.

Elemental analysis calcd (%) for $C_{16}H_{17}N_3$: C, 76.46; H, 6.82; N, 16.72. Found: 76.31; H, 6.85; N, 16.84.



5,6-Dimethyl-1-(3,4-dimethylphenyl)-1*H*-benzo[*d*][1,2,3]triazole (2m). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.40; yellow solid; yield 88%.

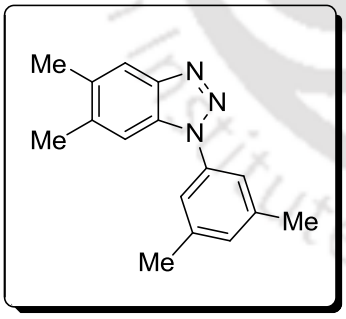
Mp: 134-136 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83 (s, 1H), 7.52 (s, 1H), 7.44-7.43 (m, 2H), 7.33 (d, *J* = 8.0 Hz, 1H), 2.41 (s, 6H), 2.37 (s, 3H), 2.35 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.8, 138.5, 137.3, 135.1, 134.1, 131.6, 130.8, 124.1, 120.1, 119.3, 110.0, 21.1, 20.5, 20.1, 19.6.

FT-IR (KBr): *v* = 2947, 2862, 1611, 1504, 1466, 1385, 1065 cm^{-1}.

Elemental analysis calcd (%) for $C_{16}H_{17}N_3$: C, 76.46; H, 6.82; N, 16.72. Found: 76.32; H, 6.85; N, 16.83.



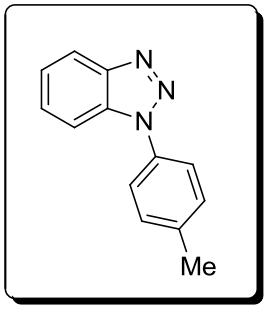
5,6-Dimethyl-1-(3,5-dimethylphenyl)-1*H*-benzo[*d*][1,2,3]triazole (2n). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.45; yellow liquid; yield 75%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83 (s, 1H), 7.46 (s, 1H), 7.35 (s, 2H), 7.10 (s, 1H), 2.43 (s, 12H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.8, 139.9, 138.6, 137.3, 134.2, 131.6, 130.2, 120.7, 119.4, 110.1, 21.5, 21.2, 20.6.

FT-IR (neat): ν = 2921, 1628, 1469, 1236, 1071 cm^{-1}.

Elemental analysis calcd (%) for $C_{16}H_{17}N_3$: C, 76.46; H, 6.82; N, 16.72. Found: C, 76.30; H, 6.84; N, 16.86.



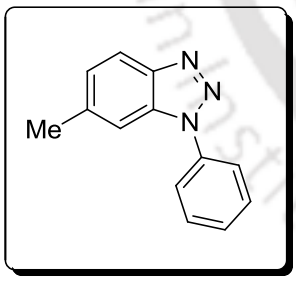
1-*p*-Tolyl-1*H*-benzo[*d*][1,2,3]triazole (2o). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.35; brown solid.

Mp: 94-96 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08-8.05 (m, 1H), 7.66-7.63 (m, 1H), 7.59-7.57 (m, 2H), 7.48-7.44 (m, 1H), 7.37-7.33 (m, 3H), 2.40 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.4, 138.7, 134.5, 132.3, 130.3, 128.0, 124.2, 122.6, 120.0, 110.4, 21.1.

Elemental analysis calcd (%) for $C_{13}H_{11}N_3$: C, 74.62; H, 5.30; N, 20.08. Found: C, 74.60; H, 5.29; N, 20.11.



6-Methyl-1-phenyl-1*H*-benzo[*d*][1,2,3]triazole (2p). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.35; yellow solid.

Mp: 99-100 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, J = 8.4 Hz, 1H), 7.76 (d, J = 8.0 Hz, 2H), 7.60 (t, J = 7.6 Hz, 2H), 7.51-7.47 (m, 2H), 7.24 (d, J = 8.4 Hz, 1H), 2.55 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.9, 138.8, 136.9, 132.5, 129.6, 128.3, 126.5, 122.5, 119.4, 109.5, 21.9.

Elemental analysis calcd (%) for $C_{13}H_{11}N_3$: C, 74.62; H, 5.30; N, 20.08. Found: C, 74.59; H, 5.31; N, 20.10.

Single Crystal X-ray structure of 2m

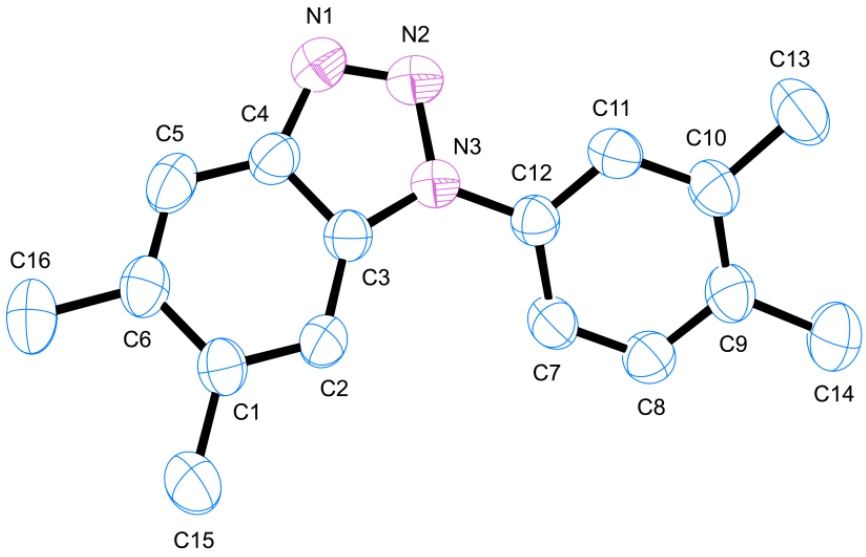


Figure 1. ORTEP Diagram of 5,6-Dimethyl-1-(3,4-dimethylphenyl)-1*H*-benzotriazole **2m**. Thermal ellipsoids are drawn at 50% probability level. H-Atoms are omitted for clarity

Crystal Data and Structure Refinement for 2m at 296(2) K

Identification code	2m	
Empirical formula	$C_{16}H_{17}N_3$	
Formula weight	251.3304	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	Pbca	
	Loop xyz	
	'x, y, z' '-x, -y, -z'	
Unit cell dimensions	*a* = 13.2943 (7) Å	α(°) = 90.00
	b = 7.4099 (4) Å	β(°) = 90.00

	c = 27.6216 (14) Å γ(°) = 90.00
Volume	2721.0(2) $Å^3$
Z	8
Density (calculated)	1.227 Mg/m^3
Absorption coefficient	0.075 mm^{-1}
F(000)	1072
Crystal size	0.44 x 0.36 x 0.26 mm
Theta range for data collection	0.981 to 28.02 °
Index ranges	-17<=h<=17, -8<=k<=9, -35<=l<=36
Reflections collected	3161
Independent reflections	1810
Completeness to theta = 24.31°	99.5 %
Absorption correction	Multi-scan
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3161 / 0 /177
Goodness-of-fit on F^2	0.995
Final R indices [I>2sigma (I)]	*R1* = 0.0952, *wR2* = 0.1369
R indices (all data)	*R1* = 0.0497, *wR2* = 0.1191

2.6 References

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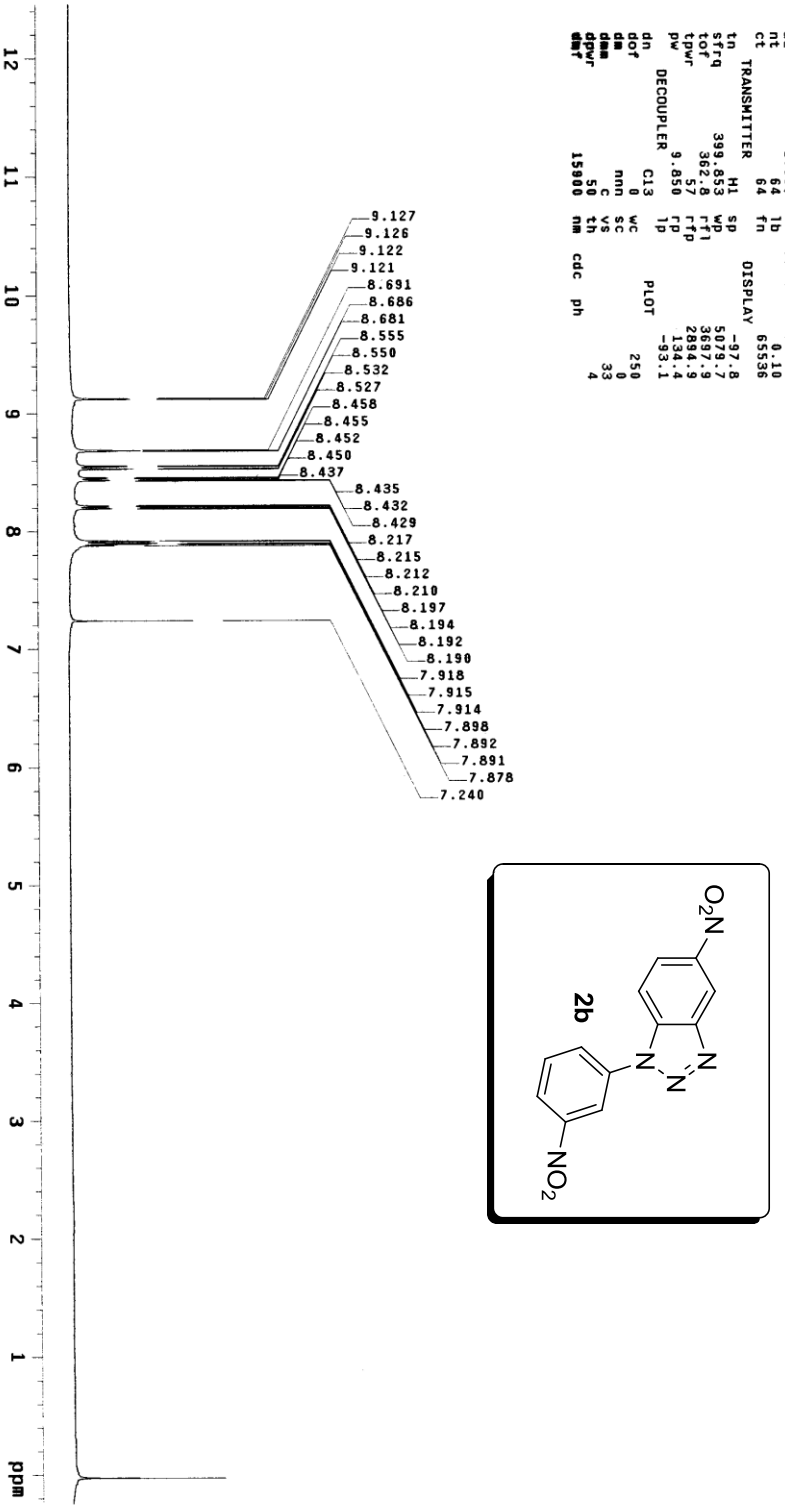
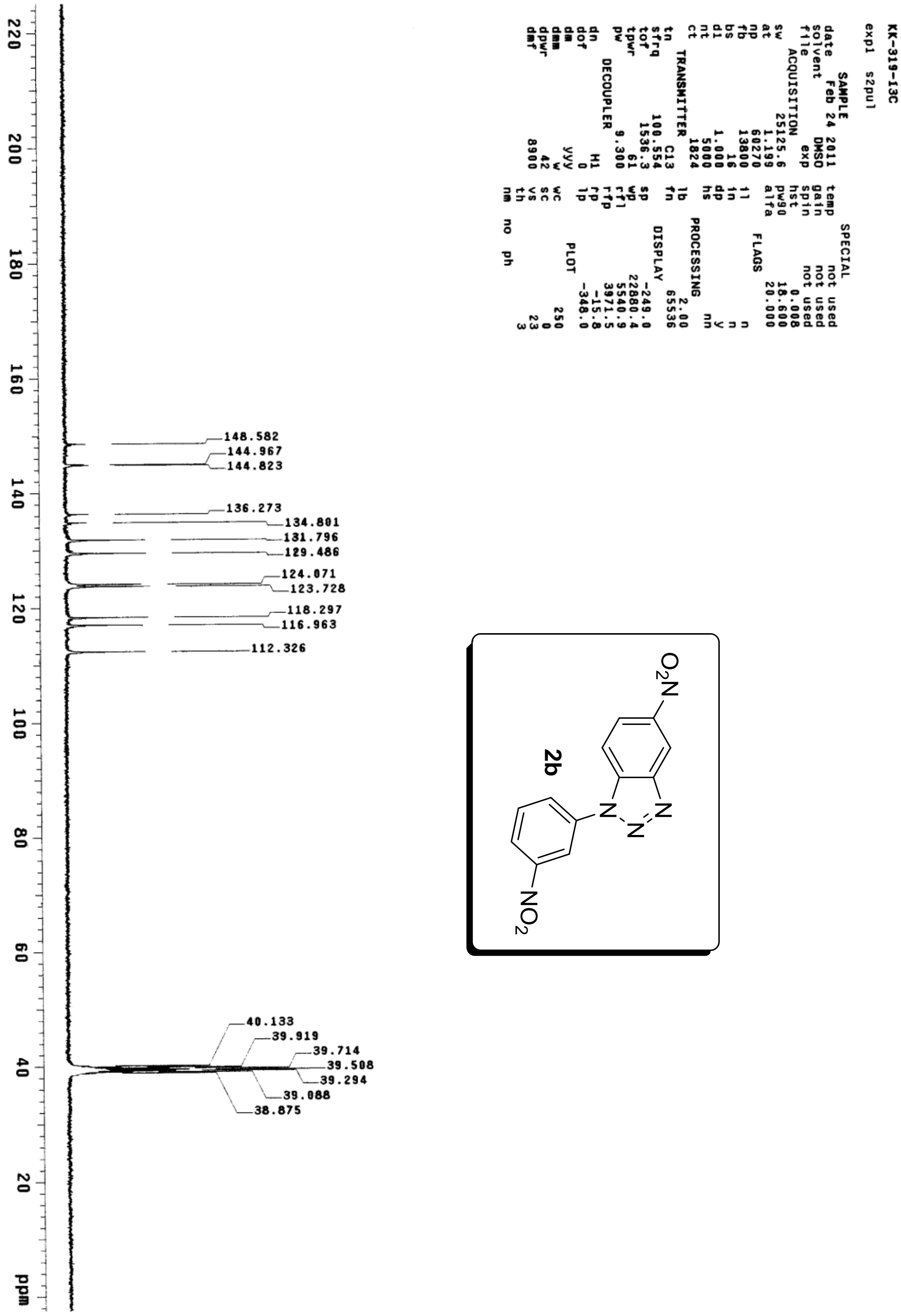
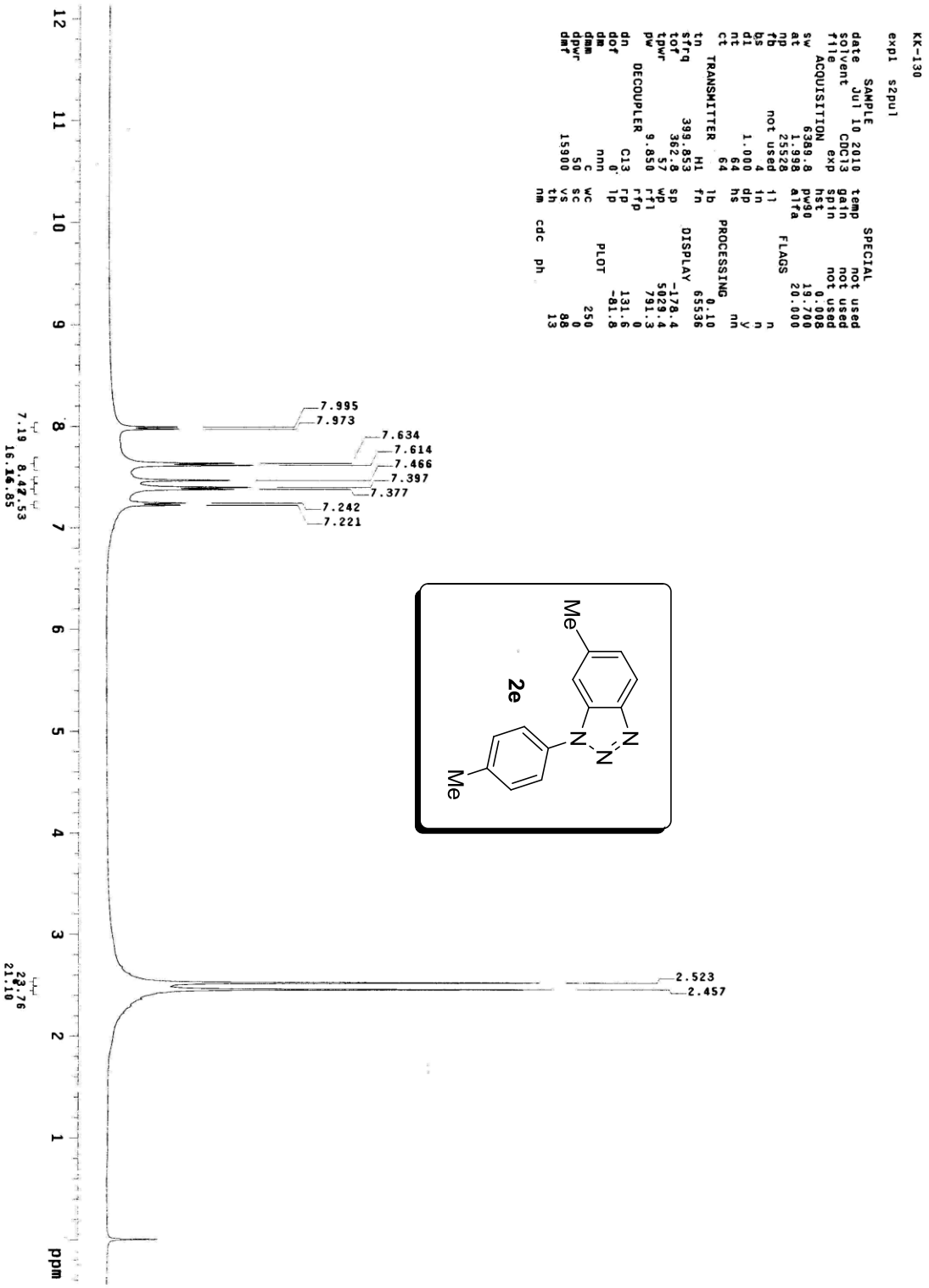
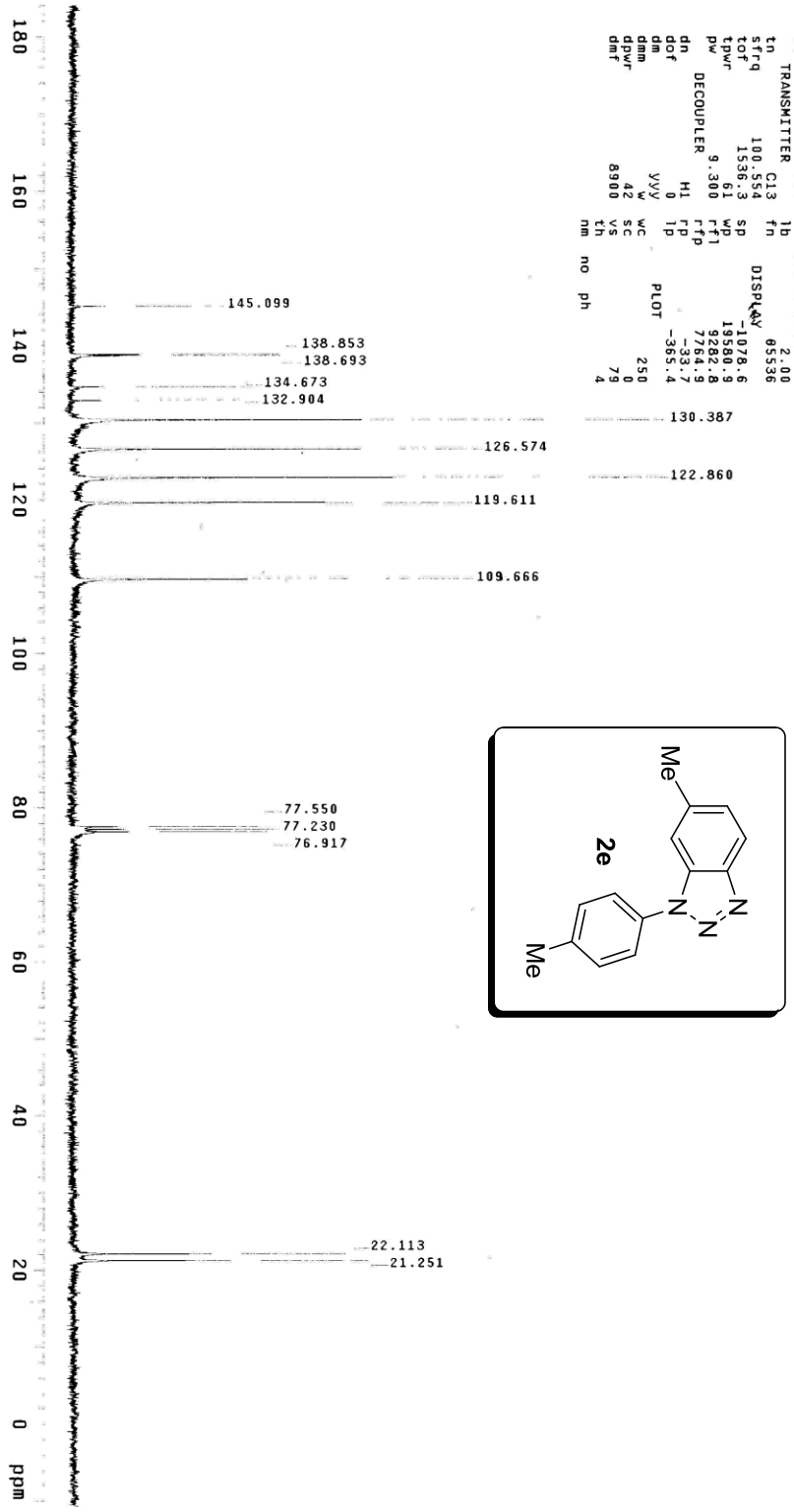
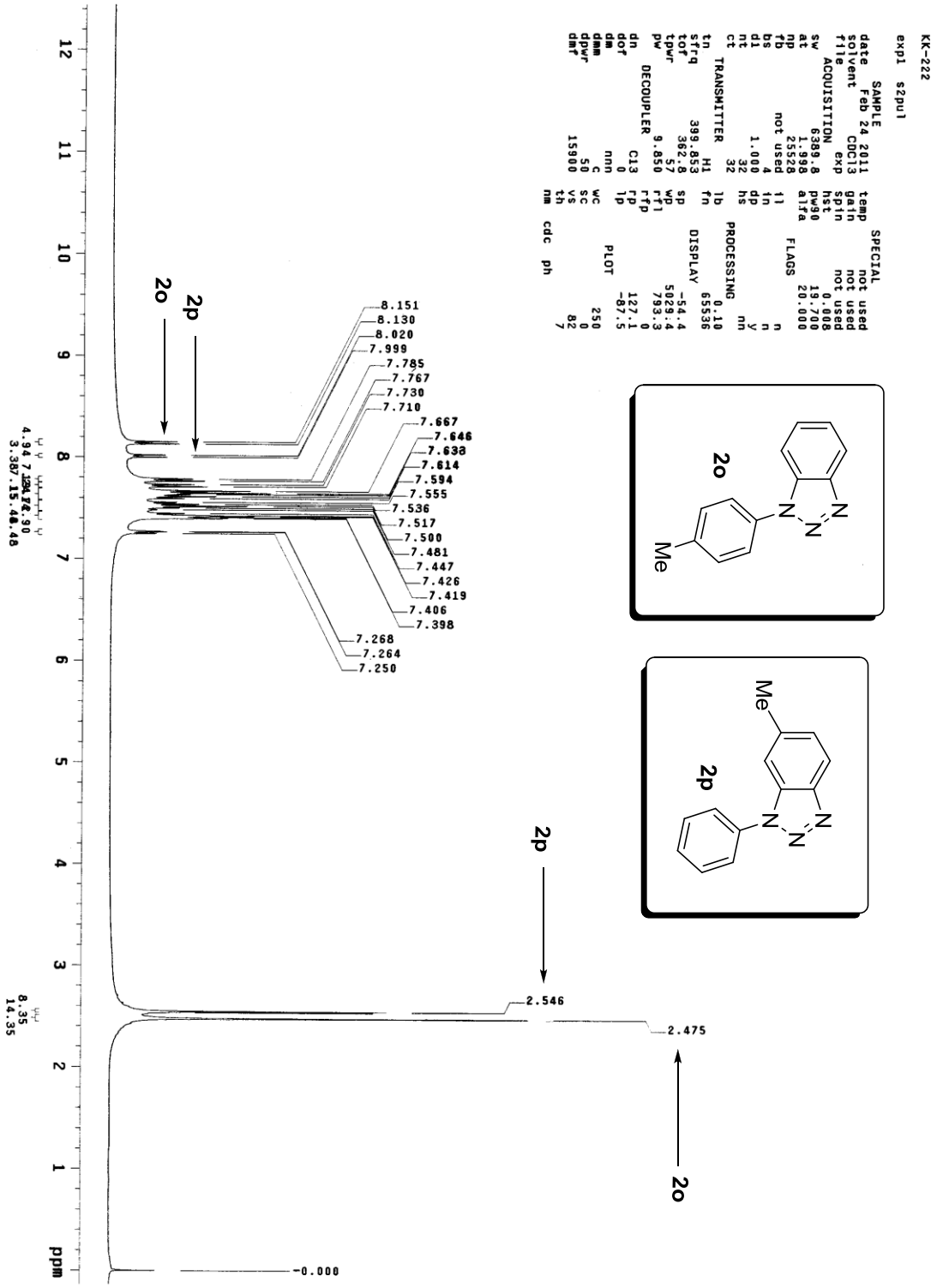










Chapter III

Palladium(II)-Catalyzed Synthesis of *N*-Aryl Benzimidazoles

Benzimidazoles are the class of prominent heterocyclic motifs that exhibit a wide range of applications in therapeutic and biological sciences.[1,2] In the field of medicinal chemistry *N*-aryl benzimidazoles have been characterized as Nek2 inhibitor[3a] and lymphocyte specific kinase (Lck) inhibitor (Figure 1).[3b] In addition, they are substrate precursors for the preparation of an important class of *N*-heterocyclic carbenes (NHCs)[4] that have been successfully utilized as ligands in organo catalysis as well as in transition metal catalysis. Development of newer methods for the construction of the functionalized benzimidazoles[5] is thus important in synthetic organic chemistry.

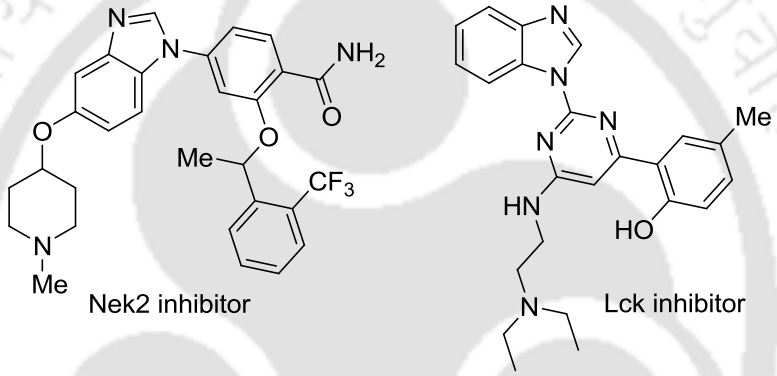
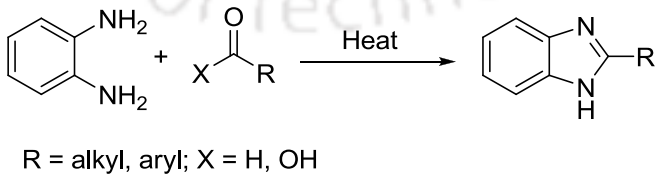


Figure 1. Some Examples of Biologically Active *N*-Aryl Benzimidazoles.

3.1 Classical Methods of Synthesis of Benzimidazoles

The classical approaches employed for the synthesis of the benzimidazoles involve condensation followed by oxidative cyclization of *o*-phenylenediamine with carboxylic acids or carboxylic acid derivatives (Scheme 1).[6]



Scheme 1. Classical Methods of Synthesis of Benzimidazoles.

o-Nitroanilines can also be used in the place of the 1,2-diaminoarene derivatives under reducing conditions.[7] However, these processes often suffer due to the unavailability of

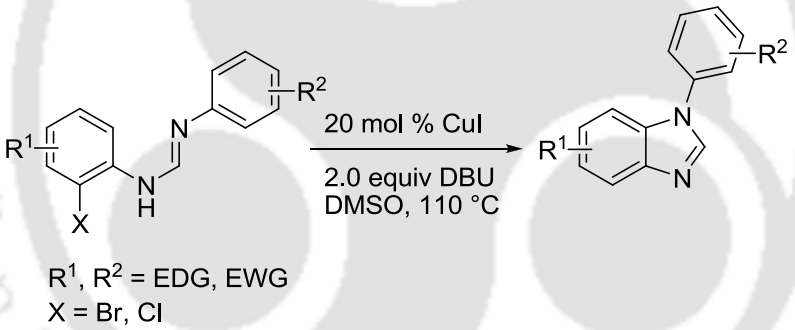
the suitably substituted substrate precursors. Furthermore, the oxidative cyclization requires the combination of strong acid and elevated temperature.

3.2 Cross Coupling Methods for the Synthesis of Benzimidazoles

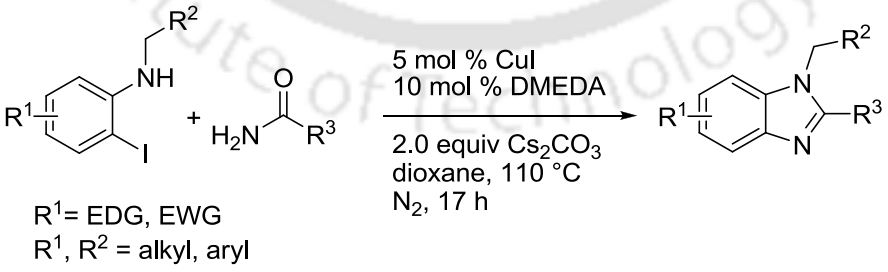
Some of these drawbacks have been overcome by the recent development in the transition-metal-catalyzed cross-coupling reactions that allow the construction of the target heterocyclic frameworks under relatively milder conditions.

Copper Catalyzed Synthesis of Benzimidazoles

Copper catalysts, because of its less-toxic nature and low cost, have been extensively used for synthesis of various substituted benzimidazoles *via C–N* cross-coupling reactions. Glorius and co-workers developed a copper(I)-catalyzed intramolecular arylation of formamidines to afford 2-unsubstituted *N*-aryl benzimidazoles. This protocol provides rapid access to *N*-aryl benzimidazoles with sterically demanding aromatic groups (Scheme 2).[8]



Scheme 2. Synthesis of 2-Unsubstituted *N*-Aryl Benzimidazoles

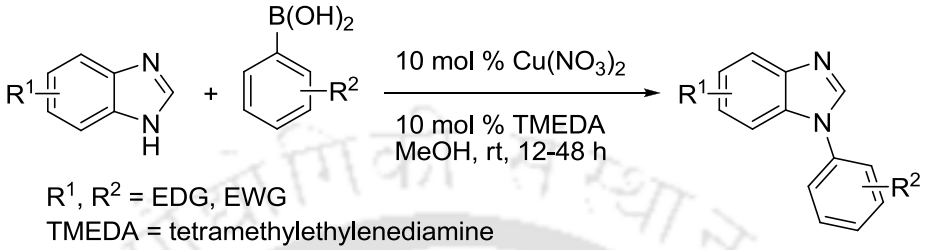


Scheme 3. Synthesis of *N*-Alkyl Benzimidazoles

Buchwald and co-workers developed a CuI and *trans-N,N'*-dimethyl-1,2-cyclohexanediamine (DMEDA) based catalytic system for the synthesis of *N*-alkyl

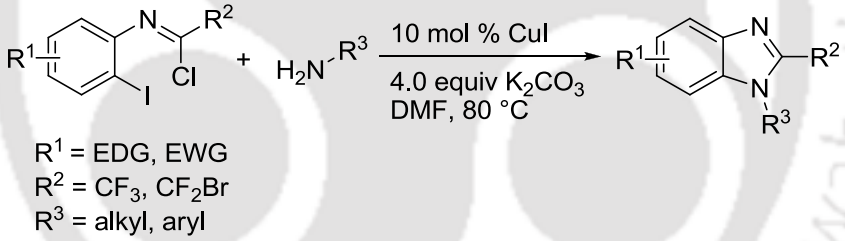
benzimidazoles in regioisomerically pure form starting from readily available 2-iodo anilines (Scheme 3).[9]

Kozlowski and co-workers described a mild, efficient copper-diamine based catalytic system for the coupling of benzimidazoles with substituted arylboronic acids in good to excellent yields. The methodology works at ambient temperature (Scheme 4).[10]



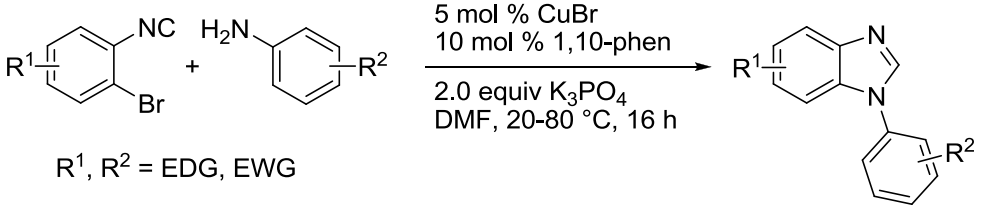
Scheme 4. Synthesis of Sterically hindered *N*-Aryl Benzimidazoles

Wu and co-workers reported a copper(I)-catalyzed synthesis of 2-fluoroalkyl benzimidazoles *via* tandem *C-N* cross coupling reaction between fluorinated imidoylchlorides and primary amines (Scheme 5).[11]



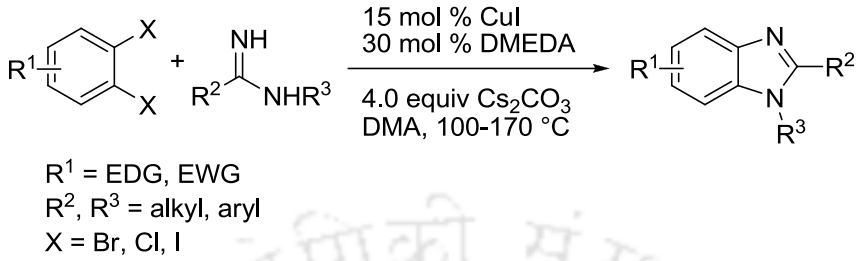
Scheme 5. Synthesis of 2-Fluoroalkyl Benzimidazoles

Meijere and co-workers developed a CuBr catalyzed synthesis of 2-unsubstituted *N*-arylbenzimidazoles from 2-bromo arylisocyanides and primary amines. The protocol proceeds *via* cascade addition reaction between 2-bromo arylisocyanides followed by intramolecular *C-N* cross-coupling to afford the corresponding *N*-aryl benzimidazoles (Scheme 6).[12]



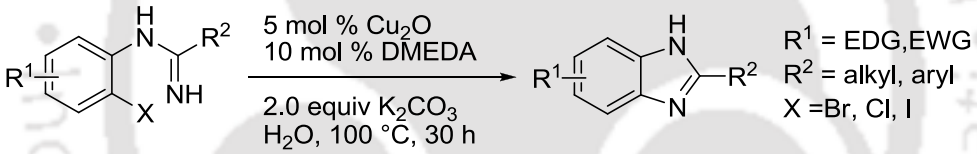
Scheme 6. Synthesis of 2-Unsubstituted *N*-Aryl Benzimidazoles

Deng and co-workers demonstrated a CuI/*N*,*N'*-dimethylethylenediamine (DMEDA) as an efficient catalytic system for the guanidinylation of aryl iodides. The catalytic system provides ready access to 1,2-disubstituted benzimidazoles from readily available 1,2-dihaloarenes and guanidine in single step (Scheme 7).[13]



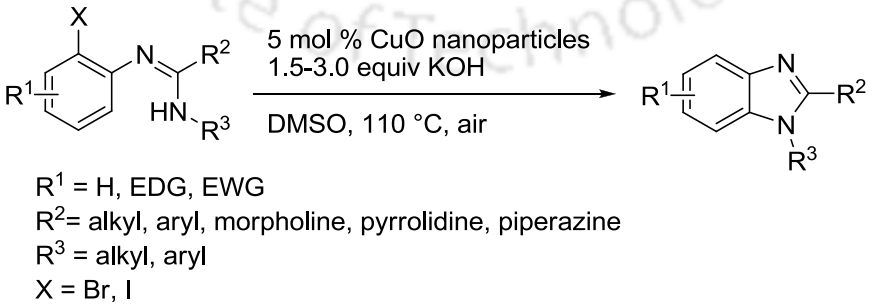
Scheme 7. Synthesis of Benzimadazoles from 1,2-Dihaloarenes

Peng and co-workers successfully developed a straightforward route of intramolecular *N*-arylation method for providing the benzimidazole ring system. The protocol involves the use of Cu_2O in combination with a DMEDA (*N*,*N*'-Dimethylethylenediamine) catalytic system. The protocol uses water as the solvent (Scheme 8).[14]



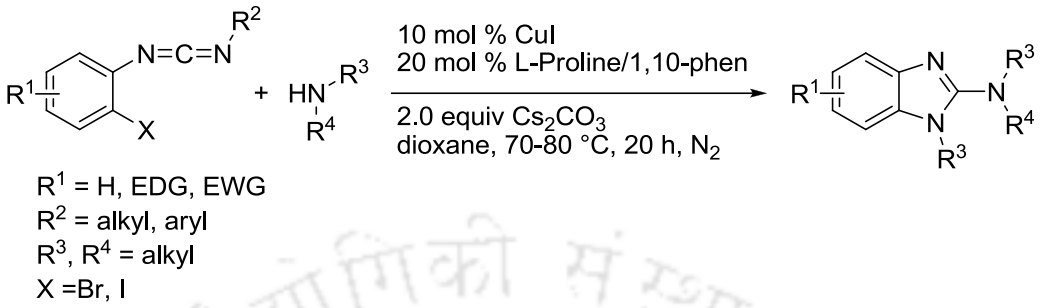
Scheme 8. Synthesis of 2-Substituted Benzimidazoles

Our group showed the synthesis of benzimidazoles, and 2-aminobenzimidazoles *via* intramolecular cyclization of 2-bromoarylamidine derivatives using CuO nanoparticles in DMSO under air. The procedure is experimentally simple, general, efficient and free from addition of external chelating ligands (Scheme 9).[15]



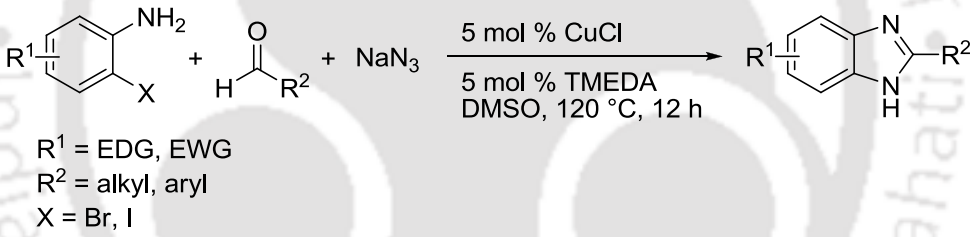
Scheme 9. Synthesis of Substituted Benzimidazoles

Bao and co-workers reported the synthesis of *N*-substituted 2-heterobenzimidazoles. The protocol proceeds *via* Cu(I)-catalyzed cascade intermolecular addition followed by intramolecular *C-N* coupling process (Scheme 10).[16]



Scheme 10. Synthesis of *N*-Substituted Benzimidazoles

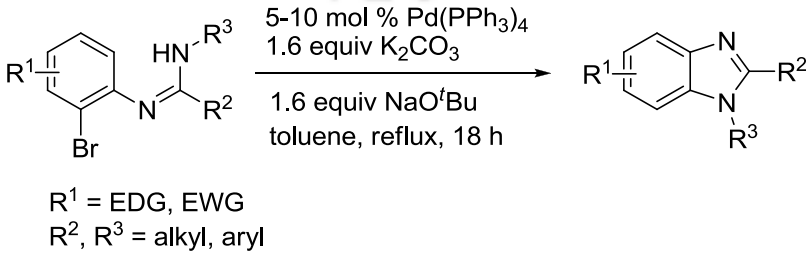
Lee and co-workers reported an efficient synthesis of 2-substituted 1-*H*-benzimidazoles. The protocol involves a three-component reactions of 2-haloanilines, aldehydes and NaN_3 in the presence of CuCl and TMEDA (tetramethylethylenediamine) (Scheme 11).[17]



Scheme 11. Copper Catalyzed One-Pot Three-Component Synthesis of Benzimidazoles

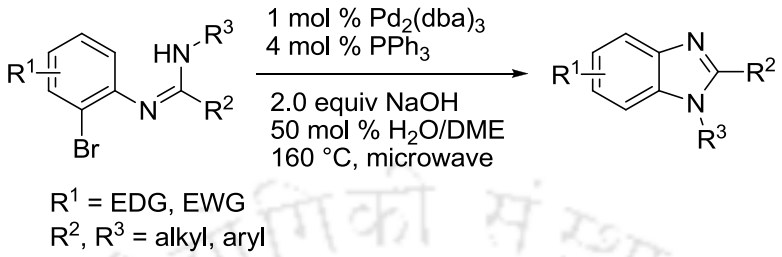
Palladium Catalyzed Synthesis of Benzimidazoles

Brain and co-workers reported the synthesis of benzimidazoles by a palladium-catalyzed intramolecular *N*-arylation from 2-bromophenylamidine precursors (Scheme 12).[18]



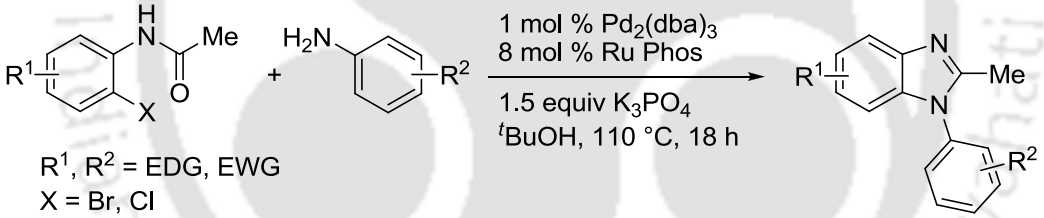
Scheme 12. Synthesis of 1,2-Disubstituted Benzimidazoles

Later, same group modified the reaction procedure for the synthesis of substituted benzimidazoles. They have used the combination of palladium and triphenylphosphine as a catalytic system under microwave conditions in presence of NaOH in aqueous DME (Scheme 13).[19]



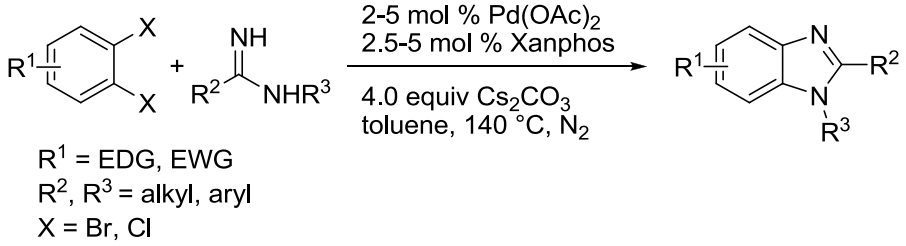
Scheme 13. Microwave Assisted Synthesis of Benzimidazoles

Buchwald and co-workers have developed a catalytic method for the synthesis of *N*-aryl benzimidazoles. This protocol involves a cascade amination of 2-bromoacetanilides followed by condensation to afford the corresponding *N*-aryl benzimidazoles (Scheme 14).[20]



Scheme 14. Regiospecific Synthesis of *N*-Aryl Benzimidazoles

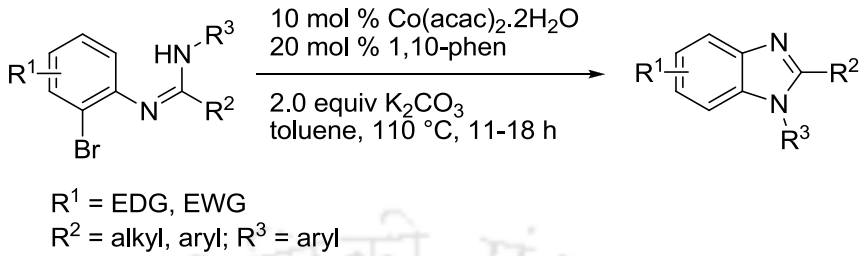
You and co-workers described a $Pd(OAc)_2$ catalyzed cascade intermolecular and intramolecular amination 1,2-dihaloarenes with guanidines that allows, regiospecific and modular synthesis of a library of structurally diverse 1,2-disubstituted benzimidazoles (Scheme 15).[21]



Scheme 15. Synthesis of 1,2-Disubstituted Benzimidazoles

Cobalt Catalyzed Synthesis of Benzimidazoles

Our group has developed cobalt(II)-complex catalyzed intramolecular *C-N* cross-coupling of *Z-N'*-2-halophenyl-*N*-phenylamidines to afford the benzimidazoles (Scheme 16).[22]

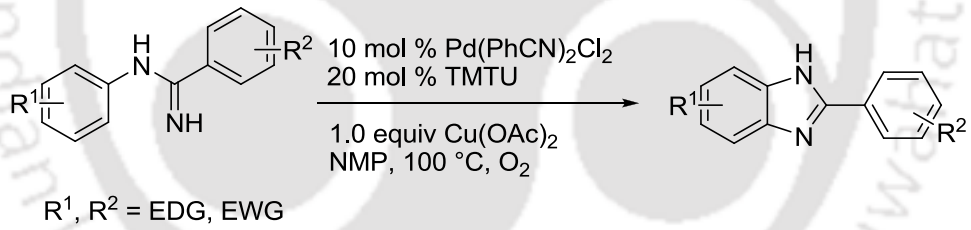


Scheme 16. Synthesis of Substituted Benzimidazoles

3.3 C-H Activation Methods for the Synthesis of Benzimidazoles

3.3.1 Palladium Catalyzed Synthesis of Benzimidazoles

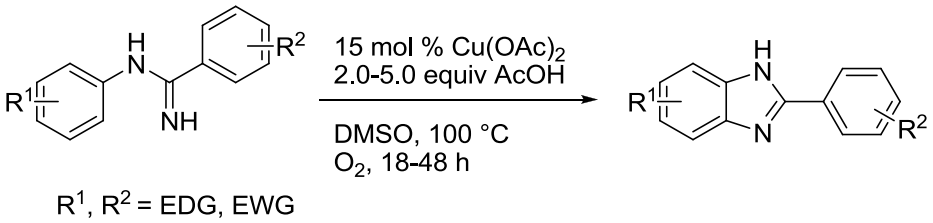
Shi and co-workers reported a straightforward method to construct 1*H*-benzo[*d*]imidazoles by means of Pd(II)-catalyzed intramolecular C-H amination starting from readily available *N*-aryl benzimidamides (Scheme 17).[23]



Scheme 17. Synthesis of 2-Substituted-1*H*-Benzo[*d*]imidazoles

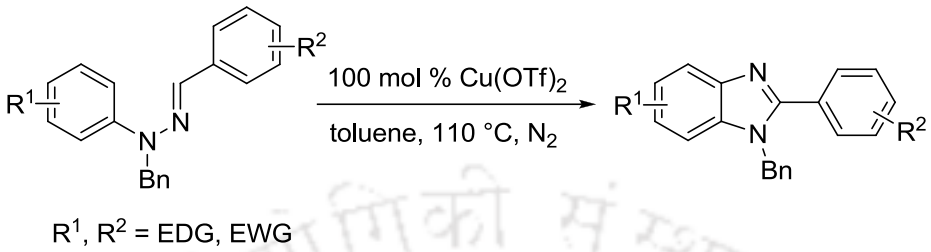
3.3.2 Copper Catalyzed Synthesis of Benzimidazoles

Buchwald and co-workers reported a $Cu(OAc)_2$ catalyzed intramolecular C-H activation followed by C-H amination protocol for the synthesis of suitably substituted benzimidazoles starting from readily accessible amidines (Scheme 18).[24]



Scheme 18. Synthesis of Benzimidazoles from Amidines

Our group has developed an new method for the transformation of *N*-benzyl bisarylhydrazones to functionalized 2-aryl-*N*-benzylbenzimidazoles. The protocol involves a copper(II)-mediated cascade C-H functionalization followed by *C*-*N* bond formation under neutral conditions (Scheme 19).[25]

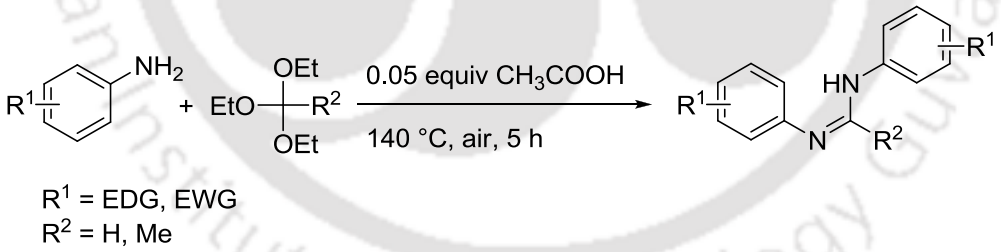


Scheme 19. Synthesis of 2-Aryl-*N*-Benzylbenzimidazoles

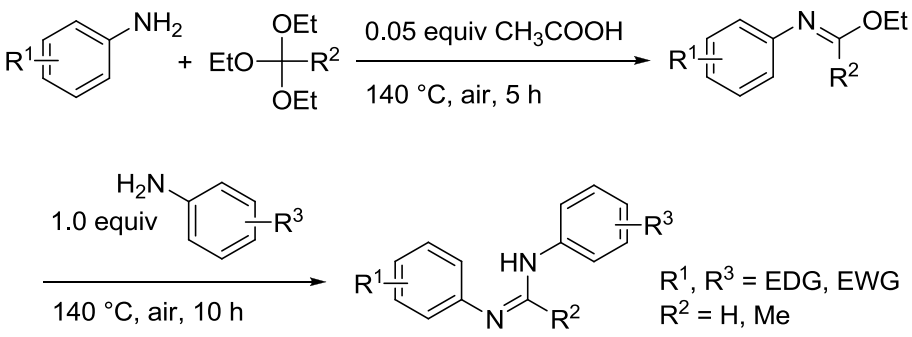
3.4 Present Study

In this chapter, we describe a general method for the synthesis of substituted *N*-aryl benzimidazoles *via* palladium catalyzed C-H activation followed by intramolecular *C*-*N* bond formation of bisarylamidines. The protocol is simple, general and provides a straight forward route for the efficient synthesis of functionalized 2-unsubstituted and 2-alkyl/-aryl substituted 1-aryl-1*H*- benzimidazoles with excellent yield.

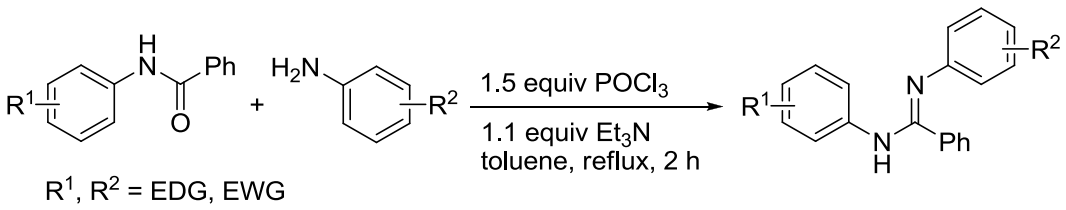
The substrate precursors 1,3-diarylamidines were prepared from readily available anilines according to literature procedures (Schemes 20-22).[26]



Scheme 20. Synthesis of Substrate Precursors Symmetrical 1,3-Diarylamidines



Scheme 21. Synthesis of Unsymmetrical 1,3-Diarylamidines

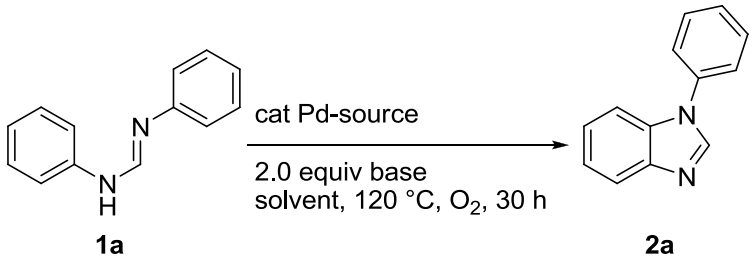


Scheme 22. Synthesis of Unsymmetrical 1,3-Diarylbenzimidines

The optimization of the reaction conditions was carried out with *N,N'*-diphenyl formamidine **1a** as a model substrate. The substrate **1a** underwent the C–H activation followed by intramolecular C–N bond formation to afford the desired *N*-phenyl benzimidazole **2a** in 46% yield when the reaction was carried out in the presence of 10 mol % $Pd(PPh_3)_2Cl_2$ and 2.0 equiv Cs_2CO_3 in DMSO under molecular oxygen (Table 1, entry 1). Yield of the heterocycle **2a** could be further increased to 63% when freshly activated 4Å molecular sieves were added as an additive (entry 2). Palladium sources such as $Pd(PPh_3)_2(OAc)_2$, $Pd(CH_3CN)_2Cl_2$ and $Pd(PhCN)_2Cl_2$ were less effective compared to $Pd(PPh_3)_2Cl_2$ affording **2a** in 10-30% yield (entries 3-5), whereas the reaction with $Pd(OAc)_2$ led to decomposition of the starting material **1a** and no desired **2a** was obtained. DMSO was found to be the solvent of choice. The reaction using DMF gave **2a** in 45% yield (entry 6). In contrast, the solvents such as NMP, toluene and acetonitrile showed no reaction (entries 7-9). Among the bases screened, Cs_2CO_3, K_2CO_3, Ag_2CO_3, K_3PO_4 and Na_2CO_3, the former yielded the best results. While the reactions with K_2CO_3, K_3PO_4 and Na_2CO_3 gave **2a** in 10-50% yield, whereas Ag_2CO_3 and KOH showed no reaction (entries 10-14). Lowering of the reaction temperature (110 °C) or amount of the palladium catalyst (5 mol %) or base (1.5 equiv) or performing the reaction under air led to the formation of **2a** in < 63% yield (entries 15-18). Control experiments confirmed that no product **2a** formation was observed in the absence of the palladium catalyst (entry 19). In summary, the standard reaction conditions in DMSO include $Pd(PPh_3)_2Cl_2$ (10 mol %) and Cs_2CO_3 (2.0 equiv) at 120 °C for 30 h under oxygen balloon.

Next, the scope of the procedure was studied for the reactions of the substituted *N,N'*-bis(aryl)formamidines (Table 2, entries 1-8). *N,N'*-Bis(phenyl)formamidine **1b** with methyl substituents at *o*-position of both the phenyl rings did not cyclize, which may be due to the steric hindrance of the methyl groups (entry 2). However, the symmetrical substrates **1c-g** having methyl, ethyl, fluoro and 2-propyl substituents at *m*- as well as *p*-positions of both the phenyl rings proceeded the cyclization at less hindered aryl C–H

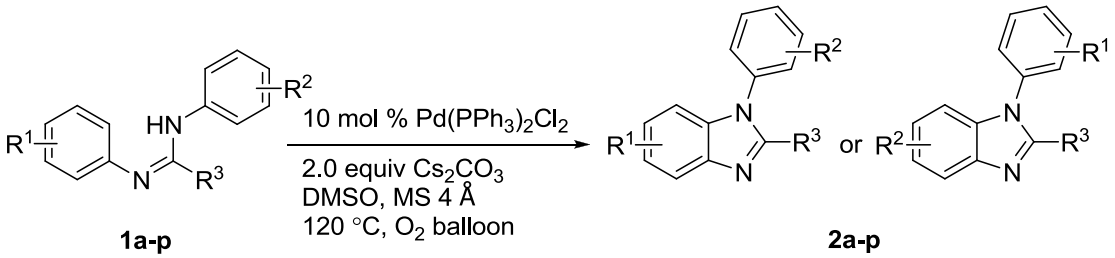
Table 1. Optimization of Reaction Conditions[a]



entry	Pd-sorce	base	solvent	yield (%)[b]
1	$Pd(PPh_3)_2Cl_2$	Cs_2CO_3	DMSO	46[c]
2	**$Pd(PPh_3)_2Cl_2$**	**Cs_2CO_3**	**DMSO**	**63**
3	$Pd(PPh_3)_2(OAc)_2$	Cs_2CO_3	DMSO	30
4	$Pd(CH_3CN)_2Cl_2$	Cs_2CO_3	DMSO	11
5	$Pd(PhCN)_2Cl_2$	Cs_2CO_3	DMSO	10
6	$Pd(PPh_3)_2Cl_2$	Cs_2CO_3	DMF	45
7	$Pd(PPh_3)_2Cl_2$	Cs_2CO_3	NMP	n.d.
8	$Pd(PPh_3)_2Cl_2$	Cs_2CO_3	toluene	n.d.
9	$Pd(PPh_3)_2Cl_2$	Cs_2CO_3	CH_3CN	n.d.
10	$Pd(PPh_3)_2Cl_2$	K_2CO_3	DMSO	50
11	$Pd(PPh_3)_2Cl_2$	Na_2CO_3	DMSO	10
12	$Pd(PPh_3)_2Cl_2$	K_3PO_4	DMSO	40
13	$Pd(PPh_3)_2Cl_2$	KOH	DMSO	n.d.
14	$Pd(PPh_3)_2Cl_2$	Ag_2CO_3	DMSO	n.d.
15	$Pd(PPh_3)_2Cl_2$	Cs_2CO_3	DMSO	35[d]
16	$Pd(PPh_3)_2Cl_2$	Cs_2CO_3	DMSO	45[e]
17	$Pd(PPh_3)_2Cl_2$	Cs_2CO_3	DMSO	50[f]
18	$Pd(PPh_3)_2Cl_2$	Cs_2CO_3	DMSO	35[g]
19	-	Cs_2CO_3	DMSO	n.d.

[a]Reaction condition: *N,N'*-diphenyl formamidine **1a** (0.5 mmol), Pd-source (10 mol %), base (2.0 equiv) and 4Å MS (50 mg) were stirred at 120 °C in solvent (1.0 mL) under oxygen balloon. [b]Isolated yield. [c]Without 4 Å MS. [d]$Pd(PPh_3)_2Cl_2$ (5 mol %) was used. [e] Cs_2CO_3 (1.5 equiv.) was used. [f]Reaction temperature = 110 °C. [g]Under air. n.d. = Not detected.

Table 2. Palladium Catalyzed Synthesis of *N*-Aryl Benzimidazoles[a]



1a-p **2a-p**

R^1, R^2 = EDG, EWG; R^3 = H, Me, Ph

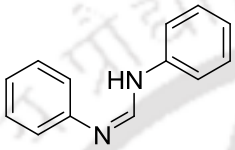
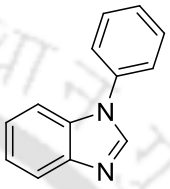
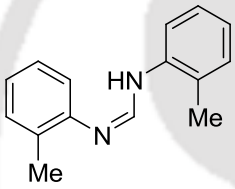
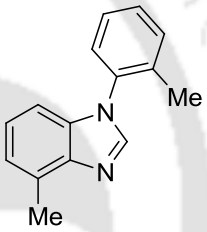
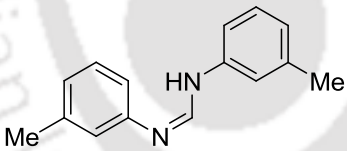
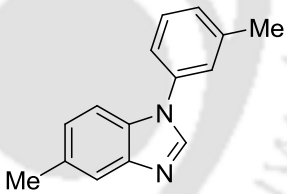
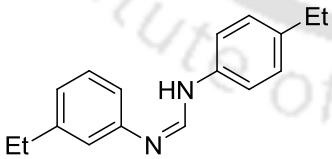
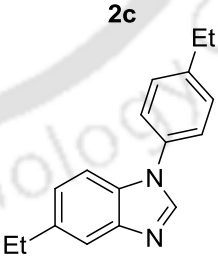
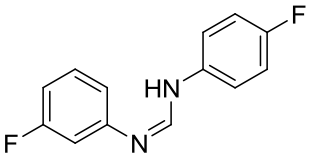
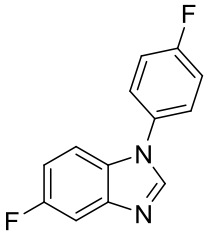
entry	substrate	time (h)	product	yield (%)[b,c]
1	 **1a**	30	 **2a**	63
2	 **1b**	30	 **2b**	n.d.
3	 **1c**	36	 **2c**	70
4	 **1d**	36	 **2d**	66
5	 **1e**	38	 **2e**	74

Table 2 continues…

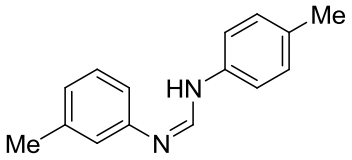
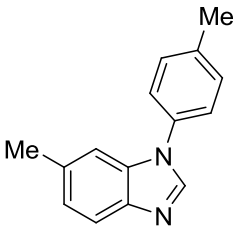
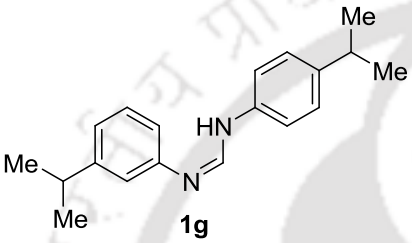
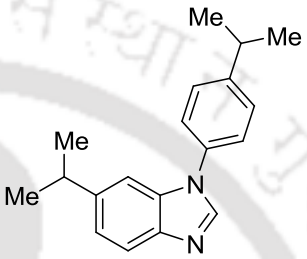
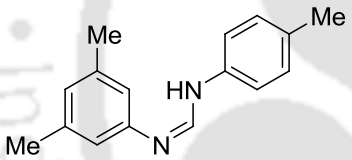
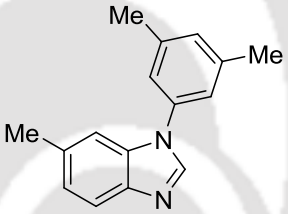
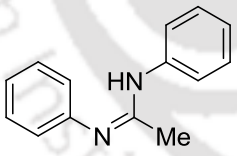
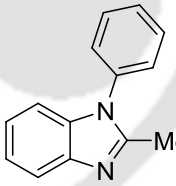
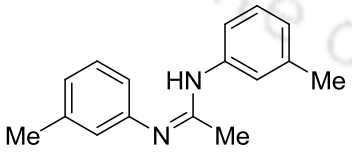
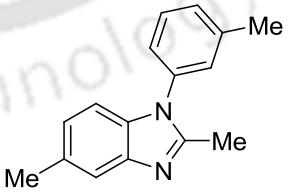
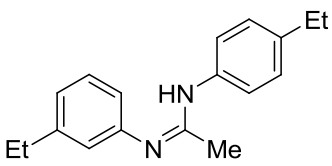
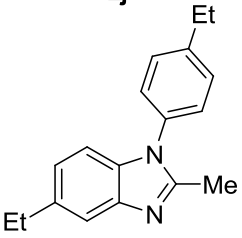
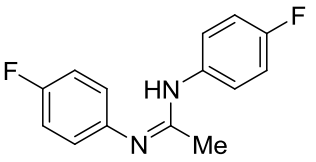
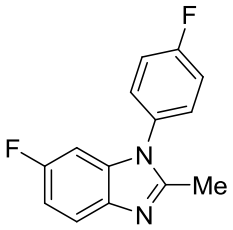
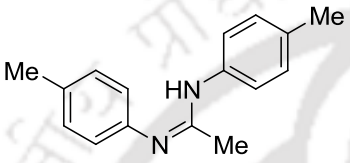
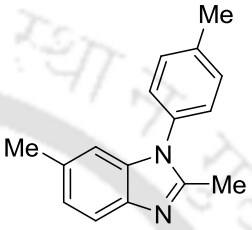
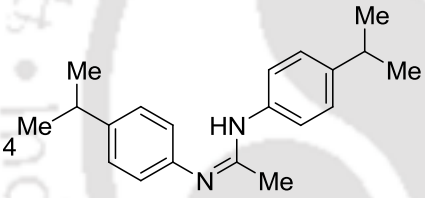
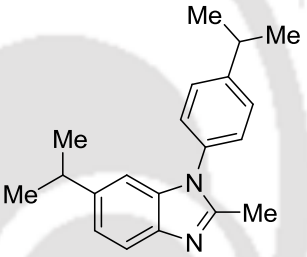
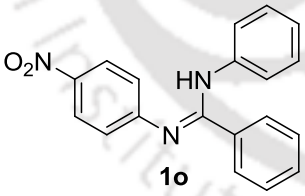
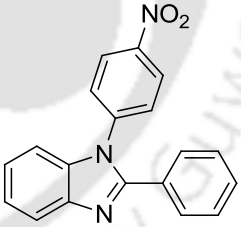
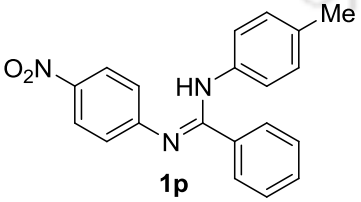
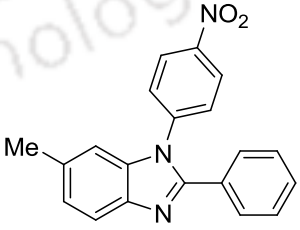
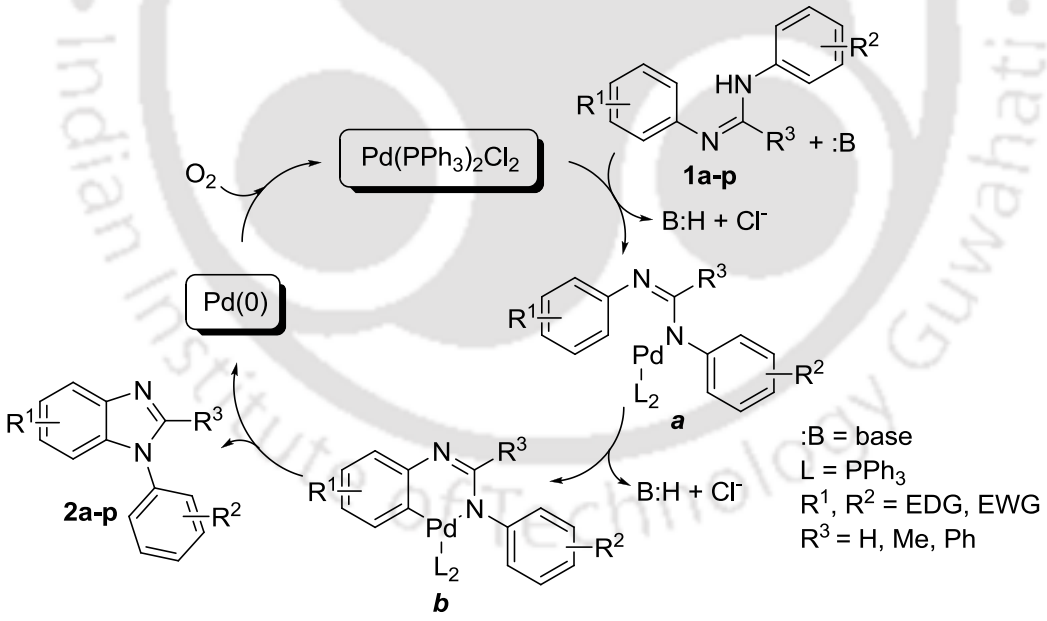
entry	substrate	time (h)	product	yield (%)[b,c]
6	 **1f**	30	 **2f**	63
7	 **1g**	48	 **2g**	75
8	 **1h**	30	 **2h**	75
9	 **1i**	48	 **2i**	65
10	 **1j**	60	 **2j**	70
11	 **1k**	48	 **2k**	68

Table 2 continues…

entry	substrate	time (h)	product	yield (%)[b,c]
12	 **1l**	30	 **2l**	75
13	 **1m**	48	 **2m**	75
14	 **1n**	50	 **2n**	78
15	 **1o**	60	 **2o**	80
16	 **1p**	60	 **2p**	82

[a]Reaction condition: Substrate **1a-p** (0.5 mmol), $Pd(PPh_3)_2Cl_2$ (10 mol %), Cs_2CO_3 (2.0 equiv) and MS 4Å (50 mg) were stirred at 120 °C in DMSO (1.0 mL) under oxygen balloon. [b]Isolated yield. [c]Single isomer. n.d. = Not detected.

bonds to give the respective *N*-aryl benzimidazoles **2c-g** as a single regioisomer in 63-75% yield (entries 3-7). Similarly, unsymmetrical *N,N,*-bis(aryl)formamidine having methyl substituents at *m*- and *p*-positions **1h** could be converted into benzimidazole **2h** in 75% yield (entry 8). The protocol was also compatible for the cyclization of *N,N'*-bis(aryl)acetamidines and *N,N'*-bis(aryl)benzamidines to afford 2-substituted *N*-aryl benzimidazoles (Table 2, entries 9-16). For example, bis(aryl)acetamidine **1i** proceeded cyclization to give 2-methyl *N*-aryl benzimidazole **2i** in 65% yield (entry 9). Likewise, the symmetrical bis(aryl)acetamidines **1j-n** having methyl, ethyl, fluoro and 2-propyl substituents at *m*- as well as *p*-positions of both the phenyl rings underwent reaction to give the corresponding 2-methyl *N*-aryl benzimidazoles **2j-n** in 68-78% yield (entries 10-14). Furthermore, the unsymmetrical *N,N'*-bis(aryl)benzamidines **1o-p** having methyl and nitro groups at *p*-position of one of the phenyl rings could be cyclized to give the respective 1,2-diaryl benzimidazoles **2o-p** in 80-82% yield. Recrystallization of **2n** and **2p** in CH_2Cl_2 gave crystals whose structures were confirmed unambiguously by single crystal X-ray analysis.



Scheme 23. Plausible Catalytic Cycle

The proposed catalytic cycle is shown in Scheme 23.[27] The substrates **1a-p** may undergo nitrogen directed association with Pd(II) complex to give an intermediate ***a*** that could lead to the formation of a six-membered palladacycle ***b*** *via* C–H activation, which may undergo reductive elimination to give the target heterocylces **2a-p** and Pd(0).

Molecular oxygen may be involved in the reoxidation of Pd(0) to Pd(II) to complete the catalytic cycle.

Conclusion

Pd-catalyzed C–H aerobic oxidative amination of bis(aryl)amidines has been developed to afford *N*-aryl benzimidazoles. The protcol involves the use of molecular oxygen an external oxidant. The reaction provided general route for the synthesis of 2-unsubstituted as well as 2-alkyl/-aryl substituted *N*-aryl benzimidazoles.

Experimental Section

General Information. Anilines, $Pd(PPh_3)_2Cl_2$ (98%), $Pd(PPh_3)_2(OAc)_2$ (98%), $Pd(CH_3CN)_2Cl_2$ (98%), $Pd(PhCN)_2Cl_2$ (98%), Cs_2CO_3 (99%), Ag_2CO_3 (99%), KO^tBu (95%) and K_3PO_4 (98%) were purchased from Aldrich. Triethylorthoformate (98%) and triethylorthoacetate (97%) were purchased from Avra synthesis. K_2CO_3 (99.9%) was procured from Central Drug House (P) LTD. Purification of the reaction products was carried out by column chromatography using Rankem silica gel (60-120/230-400 mesh). Analytical TLC was performed on Merck silica gel G/GF 254 plate. NMR spectra were recorded on DRX-400 Varian spectrometer using $CDCl_3$ as solvent and Me_4Si as internal standard. Chemical shifts (δ) are reported in ppm and spin-spin coupling constants (J) are given in Hz. Melting points were determined using Buchi B-540 melting point apparatus and are uncorrected. FT-IR spectra were recorded using Perkin Elmer IR spectrometer. Elemental analysis was recorded using Perkin Elmer CHNS analyzer. X-Ray data were collected on a Bruker SMART APEX equipped with a CCD area detector using Mo/Kα radiation. The structures were solved by direct method using *SHELLX-97* (Göttingen, Germany).

Synthesis of Symmetrical *N,N'*-Bis(aryl)formamidines 1a-g.[26a] An oven dried round bottom flask (50 mL) was charged with triethylorthoformate (2.22 g, 15.0 mmol, 1.0 equiv), corresponding aniline (30.0 mmol, 2.0 equiv) and glacial acetic acid (45.0 mg, 0.75 mmol, 0.05 equiv). The resulting mixture was stirred for 10 h at 140 °C and allowed to cool to room temperature. The resulting white solid was triturated with cold hexane (30 mL), collected by vaccum filteration and dried in vacuo to give the symmetrical *N,N'*-bis(aryl)formamidines **1a-g** (80-90%) as a white solid.

Synthesis of Unsymmetrical Symmetrical *N,N'*-Bis(aryl)formamidine 1h.[26a] An oven dried round bottom flask (50 mL) was charged with 3,5-dimethylaniline (913.5 mg, 7.5 mmol, 1 equiv), triethylorthoformate (1.11 g, 7.5 mmol, 1.0 equiv) and glacial acetic acid (22.5 mg, 0.375 mmol, 0.05 equiv). The resulting mixture was stirred for 5 h at 140 °C, then cooled to rt. 4-Methylaniline (803.7 mg, 7.5 mmol, 1.0 equiv) was then added to the reaction mixture and the resulting mixture was stirred for 10 h at 140 °C and allowed to cool to rt. The resulting white solid was triturated with cold hexane (30 mL), collected by vaccum filteration and dried in vacuo to provide unsymmetrical *N,N'*-bis(aryl)formamidine **1h** (700 mg, 39.2%) as a white solid.

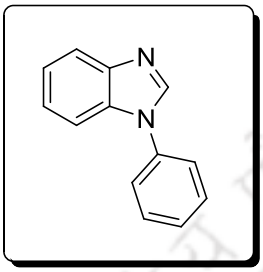
Synthesis of Symmetrical *N,N'*-Bis(aryl)acetamidines 1j-n.[26b] An oven dried round bottom flask (50 mL) was charged with triethylorthoacetate (2.43 g, 15.0 mmol, 1.0 equiv), corresponding aniline (30.0 mmol, 2.0 equiv) and glacial acetic acid (45.0 mg, 0.75 mmol, 0.05 equiv). The resulting mixture was stirred for 10 h at 140 °C and allowed to cool to rt. The resulting brown viscous oil was scratched in ice cold hexane and the resulting white solid was triturated with cold hexane (30 mL), collected by vaccum filteration and dried in vacuo to give the symmetrical *N,N'*-bis(aryl)acetamidines **1i-n** (70-80%) as a white solid.

Synthesis of *N,N'*-Bis(aryl)benzamidines 1o-p.[26c] An oven dried two neck round bottom flask (25 mL) was charged with 4-nitroaniline (345.0 mg, 2.49 mmol, 1.0 equiv) and corresponding benzamide (2.74 mmol, 1.1 equiv) under nitrogen atmosphere. Toluene (5.0 mL), triethylamine (381.0 µl, 2.74 mmol, 1.1 equiv) and $POCl_3$ (342.9 µl, 3.67 mmol, 1.5 equiv) were added and the resulting mixture was stirred for 5 h at 120 °C and allowed to cool to rt. Toluene was evaporaped in vacuo and saturated $NaHCO_3$ (10 mL) was added. The resulting yellow viscous oil was extraced with ethyl acetate (3 x 20 mL), dried over Na_2SO_4 and evaporated in vacuo. The residue was purified by silica gel column chromatography (60-120 mesh) using hexane and ethylacetate (1:9) as eluent to afford *N,N'*-bis(aryl)benzamidines **1o-p** (50-60%) as a yellow solid.

Pd-Catalyzed Synthesis of *N*-Aryl Benzimidazoles. Bis(aryl)amidines **1a-p** (0.5 mmol), $Pd(PPh_3)_2Cl_2$ (35.0 mg, 10 mol %), Cs_2CO_3 (325.8 mg, 2.0 equiv) and freshly activated 4Å molecular sieves (50 mg) were stirred at 120 °C in DMSO (1.0 mL) under oxygen balloon. The progress of the reaction was monitored by TLC using ethylacetate and hexane as eluent. After the appropriate time, the reaction mixture was cooled to room temperature and water (5 mL) was added. The resulting solution was extracted with ethyl acetate (3 x 10 mL) and

washed sucessively with brine (2 x 5 mL) and water (2 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using hexane and ethylacetate as eluent to afford analytically pure *N*-aryl benzimidazoles.

3.5 Characterization Data



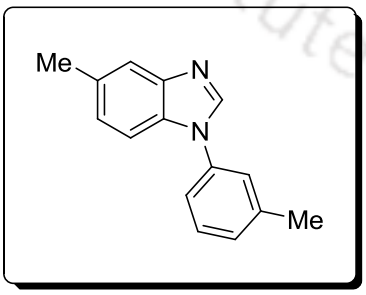
1-Phenyl-1*H*-benzo[*d*]imidazole (2a).[28] Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.20; yellow liquid; yield 63%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (s, 1H), 7.87-7.85 (m, 1H), 7.58-7.43 (m, 6H), 7.36-7.29 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.7, 142.3, 136.2, 133.7, 130.1, 128.2, 124.6, 124.1, 123.0, 120.3, 110.6.

FT-IR (neat): ν = 3065, 2927, 2846, 1599, 1503, 1454, 1382, 1319, 1286, 1248, 1231, 1201, 1028 cm^{-1}.

Elemental analysis calcd (%) for $C_{13}H_{10}N_2$: C 80.39, H 5.19, N 14.42, found: C 80.29, H 5.21, N 14.50.



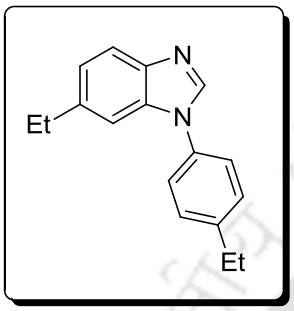
5-Methyl-1-(3-methylphenyl)-1*H*-benzo[*d*]imidazole (2c). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.30; brown liquid; yield 70%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (s, 1H), 7.63 (s, 1H), 7.41(d, *J* = 8.4 Hz, 1H), 7.29-7.23 (m, 4H), 7.14 (d, *J* = 8.0 Hz, 1H), 2.48 (s, 3H), 2.44 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.5, 142.4, 140.4, 136.6, 132.6, 131.9, 129.9, 128.8, 125.3, 124.6, 121.0, 120.4, 110.2, 21.6.

FT-IR (neat): *v* = 2967, 2922, 2857, 1610, 1497, 1264, 1218, 1196, 1091, 850, 786, 739, 697 cm^{-1}.

Elemental analysis calcd (%) for $C_{15}H_{14}N_2$: C 81.05, H 6.35, N 12.60, found: C 80.93, H 6.37, N 12.70.



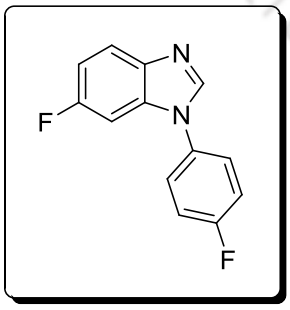
6-Ethyl-1-(4-ethylphenyl)-1*H*-benzo[*d*]imidazole (2d). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.30; yellow liquid; yield 66%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (s, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.39 (s, 4H), 7.30 (s, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 2.78-2.71 (m, 4H), 1.32-1.23 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.5, 142.4, 142.2, 140.5, 134.3, 129.5, 124.3, 123.4, 120.3, 109.3, 29.5, 28.7, 16.4, 15.6.

FT-IR (neat): *v* = 2964, 2928, 2862, 1615, 1518, 1283, 1264, 1229, 1015, 836, 738 cm^{-1}.

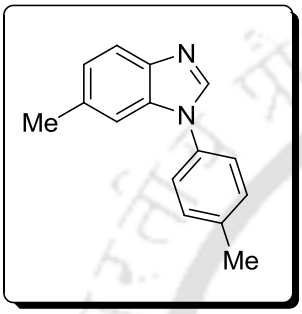
Elemental analysis calcd (%) for $C_{17}H_{18}N_2$: C 81.56, H 7.25, N 11.19, found: C 81.45, H 7.26, N 11.29.



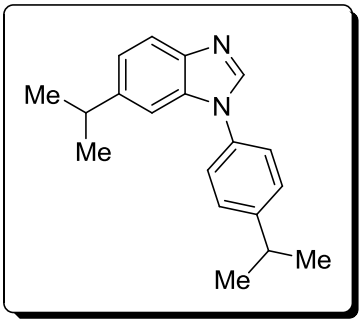
6-Fluoro-1-(4-fluorophenyl)-1*H*-benzo[*d*]imidazole (2e). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.40; yellow solid; yield 74%.

Mp: 109-111 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02 (s, 1H), 7.79 (dd, *J* = 8.8, 5.2 Hz, 1H), 7.46-7.42 (m, 2H), 7.28 (d, *J* = 8.4, Hz, 1H), 7.12-7.03 (m, 2H), 6.83 (dd, *J* = 10.4, 8.4 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.5, 161.6, 161.0, 159.2, 143.0, 140.3, 134.2, 132.1, 126.1 (d, *J* = 8.3 Hz), 121.6 (d, *J* = 9.9 Hz), 117.4 (d, *J* = 22.7 Hz), 111.7 (d, *J* = 25.0 Hz), 97.2 (d, *J* = 28.0 Hz).
FT-IR (KBr): *v* = 2917, 2846, 1625, 1516, 1259, 1208, 1152, 1094, 832, 803, 738 cm^{-1}.
Elemental analysis calcd (%) for $C_{13}H_8F_2N_2$: C 67.82, H 3.50, N 12.17, found: C 67.69, H 3.52, N 12.18.



6-Methyl-1-(4-methylphenyl)-1*H*-benzo[*d*]imidazole (2f). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.30; yellow liquid; yield 65%.
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (s, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.35 (s, 4H), 7.27 (s, 1H), 7.14 (d, *J* = 8.0 Hz, 1H), 2.45 (s, 3H), 2.44 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.1, 138.1, 134.3, 134.0, 133.8, 130.7, 124.4, 124.2, 120.1, 110.4, 21.9, 21.3.
FT-IR (neat): *v* = 2967, 2924, 2851, 1633, 1518, 1500, 1292, 1265, 1235, 1017, 809, 739 cm^{-1}.
Elemental analysis calcd (%) for $C_{15}H_{14}N_2$: C 81.05, H 6.35, N 12.60, found: C 80.95, H 6.36, N 12.69.



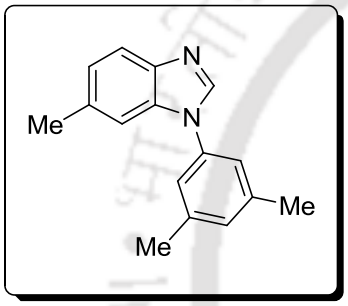
6-Isopropyl-1-(4-isopropylphenyl)-1*H*-benzo[*d*]imidazole (2g). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.30; yellow liquid; yield 75%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (s, 1H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.41 (s, 4H), 7.33 (s, 1H), 7.22 (dd, *J* = 8.4, 1.2 Hz, 1H), 3.05-2.97 (m, 2H), 1.32 (s, 3H), 1.30 (s, 3H), 1.28 (s, 3H), 1.26 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14149.0, 145.2, 142.4, 142.3, 134.3, 128.1, 124.2, 121.9, 120.2, 107.8, 34.7, 34.0, 24.6, 24.1.

FT-IR (neat): *v* = 2960, 2928, 2862, 1639, 1517, 1489, 1289, 1265, 1229, 1053, 812, 740 cm^{-1}.

Elemental analysis calcd (%) for $C_{19}H_{22}N_2$: C 81.97, H 7.97, N 10.06, found: C 81.85, H 7.99, N 10.16.



6-Methy-1-(3,5-dimethylphenyl)-1*H*-benzo[*d*]imidazole (2h). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.30; yellow solid; yield 76%.

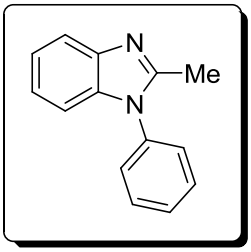
Mp: 130-132 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99 (s, 1H), 7.72 (d, *J* = 8.4 Hz, 1H), 7.29 (s, 1H), 7.14 (d, *J* = 8.4 Hz, 1H), 7.08 (s, 3H); 2.46 (s, 3H), 2.40 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.1, 140.0, 136.4, 133.7, 129.7, 124.4, 121.9, 120.1, 110.5, 22.0, 21.4.

FT-IR (KBr): *v* = 2956, 2921, 2857, 1623, 1497, 1294, 1268, 1215, 1037, 845, 808, 699 cm^{-1}.

Elemental analysis calcd (%) for $C_{16}H_{16}N_2$: C 81.32, H 6.82, N 11.85, found: C 81.20, H 6.83, N 11.96.



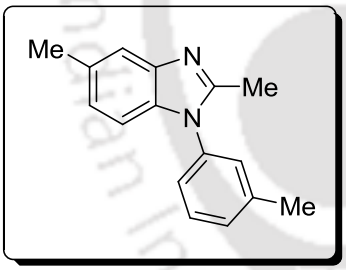
2-Methyl-1-phenyl-1*H*-benzo[*d*]imidazole (2i). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.18; yellow liquid; yield 65%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 7.6 Hz, 1H), 7.59 (t, *J* = 7.2Hz, 2H), 7.53 (d, *J* = 6.8 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.21 (t, *J* = 8.0 Hz, 1H), 7.13 Hz (d, *J* = 8.0 Hz, 1H), 2.51 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.5, 142.4, 136.4, 135.9, 129.9, 128.8, 127.0, 122.6, 122.4, 119.9, 118.8, 110.0, 14.3.

FT-IR (neat): *v* = 3056, 2956, 2923, 1672, 1597, 1499, 1457, 1395, 1324, 1287, 1248, 1181, 1016, 797, 760, 744, 698 cm^{-1}.

Elemental analysis calcd (%) for $C_{14}H_{12}N_2$: C 80.74, H 5.81, N 13.45, found: C 80.63, H 5.82, N 13.55.



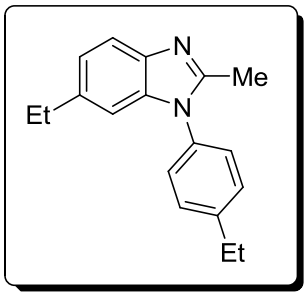
2,5-Dimethyl-1-(3-methylphenyl)-1*H*-benzo[*d*]imidazole (2j). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.23; yellow liquid; yield 70%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49 (s, 1H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 2H), 6.98 (d, *J* = 0.8 Hz, 2H), 2.46 (s, 3H), 2.45 (s, 3H), 2.42 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.3, 142.7, 139.9, 136.0, 134.5, 131.8, 129.5, 127.4, 123.8, 118.6, 109.5, 21.4, 21.2, 14.3.

FT-IR (neat): *v* = 3054, 2956, 2922, 2857, 1607, 1520, 1493, 1262, 1085, 1017, 793, 745, 703 cm^{-1}.

Elemental analysis calcd (%) for $C_{15}H_{15}N_3$: C 81.32, H 6.82, N 11.85, found: C 81.21, H 6.83, N 11.95.



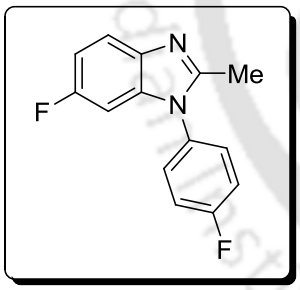
6-Ethyl-1-(4-ethylphenyl)-2-methyl-1*H*-benzo[*d*]imidazole (2k). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.30; yellow liquid; yield 68%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 8.8 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.12 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.92 (s, 1H), 2.80 (q, *J* = 8.0 Hz, 3H), 2.72 (q, *J* = 7.6 Hz, 3H), 2.47 (s, 3H), 1.35 (t, *J* = 7.6 Hz, 3H), 1.24 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.1, 144.8, 140.7, 139.0, 136.7, 133.6, 129.2, 126.8, 122.5, 118.4, 108.6, 29.1, 28.5, 16.2, 15.3, 14.2.

FT-IR (neat): *v* = 3033, 2965, 2931, 2872, 1619, 1515, 1450, 1394, 1320, 1254, 1210, 1055, 1009, 818 cm^{-1}.

Elemental analysis calcd (%) for $C_{18}H_{20}N_2$: C 81.78, H 7.63, N 10.60, found: C 81.65, H 7.65, N 10.70.



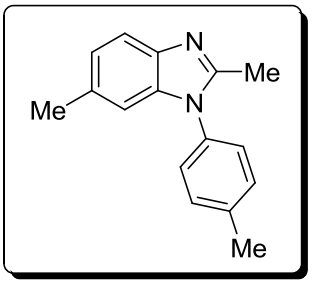
6-Fluoro-1-(4-fluorophenyl)-2-methyl-1*H*-benzo[*d*]imidazole (2l). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.35; yellow liquid; yield 75%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 (dd, *J* = 8.8, 5.2 Hz, 1H), 7.34 (m, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 6.75 (dt, *J* = 9.2, 2.4 Hz, 1H), 6.75 (dd, *J* = 8.4, 2.4 Hz, 1H), 2.44 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.7, 161.2, 160.8, 158.4, 152.1, 138.7, 136.5, 136.4, 131.6, 128.8, 128.7, 119.6, 119.5, 117.1, 116.9, 110.6, 110.3, 96.7, 96.4, 14.1.

FT-IR (neat): *v* = 3074, 2961, 2930, 1620, 1513, 1480, 1396, 1311, 1261, 1228, 1145, 1105, 1010, 969, 836, 796, 619 cm^{-1}

Elemental analysis calcd (%) for $C_{14}H_{10}F_2N_2$: C 68.85, H 4.13, N 11.47, found: C 68.73, H 4.14, N 11.58.



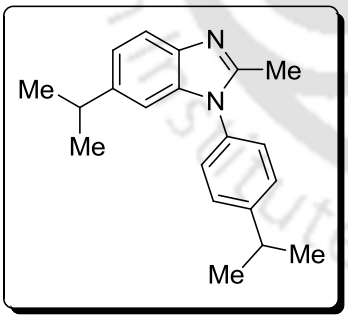
2,6-Dimethyl-1-(4-methylphenyl)-1*H*-benzo[*d*]imidazole (2m). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.40; yellow liquid; yield 75%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 (d, *J* = 8.4 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.05 (d, *J* = 8.4 Hz, 1H), 6.87 (s, 1H), 2.44 (s, 3H,) 2.44 (s, 3H), 2.37 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.0, 140.5, 138.7, 136.7, 133.4, 132.3, 130.4, 126.8, 123.6, 118.3, 109.8, 21.5, 21.1, 14.2.

FT-IR (neat): *v* = 3035, 2967, 2922, 2862, 1626, 1515, 1484, 1448, 1396, 1318, 1257, 1212, 1108, 1010, 808, 715 cm^{-1}.

Elemental analysis calcd (%) for $C_{16}H_{16}N_2$: C 81.32, H 6.82, N 11.85, found: C 81.22, H 6.81, N 11.97.



6-Isopropyl-1-(4-isopropylphenyl)-2-methyl-1*H*-benzo[*d*]imidazole (2n). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.30; yellow solid; yield 78%.

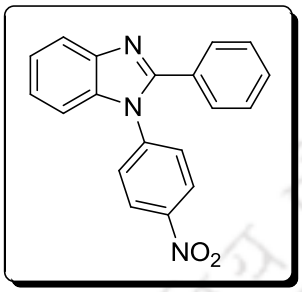
Mp: 126-128 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 8.4 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.16 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.96 (s, 1H), 3.06-2.92 (m, 2H), 2.46 (s, 3H), 1.35 (s, 3H), 1.33 (s, 3H), 1.25 (s, 3H), 1.23 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.2, 149.4, 143.8, 140.9, 136.6, 133.7, 127.8, 126.8, 121.0, 118.5, 107.3, 34.4, 33.8, 24.5, 23.9, 14.3.

FT-IR (KBr): *v* = 3035, 2960, 2923, 2870, 1621, 1515, 1480, 1448, 1394, 1324, 1298, 1263, 1210, 1100, 1056, 1008, 817 cm^{-1}.

Elemental analysis calcd (%) for $C_{20}H_{24}N_2$: C 82.15, H 8.27, N 9.58, found: C 82.05, H 8.28, N 9.67.



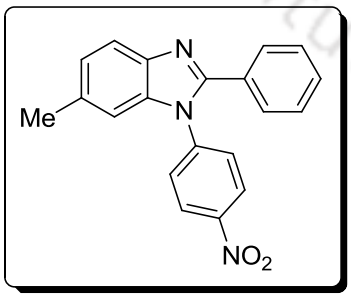
1-(4-Nitrophenyl)-2-phenyl-1*H*-benzo[*d*]imidazole (2o). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.50; yellow solid; yield 80%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.36 (d, *J* = 8.8 Hz, 1H), 8.25 (d, *J* = 9.2 Hz, 1H), 7.89-7.82 (m, 3H), 7.52-7.46 (m, 4H), 7.39-7.29 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.4, 143.4, 142.7, 136.3, 130.2, 129.7, 128.9, 128.1, 127.4, 125.3, 120.5, 110.1.

FT-IR (KBr): *v* = 2923, 2862, 1638, 1500, 1329, 1300, 1282, 1176, 1111, 790, 743, 695 cm^{-1}.

Elemental analysis calcd (%) for $C_{19}H_{13}N_3O_2$: C 72.37, H 4.16, N 13.33, found: C 72.25, H 4.17, N 13.44.



6-Methyl-1-(4-nitrophenyl)-2-phenyl-1*H*-benzo[*d*]imidazole (2p). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.50; yellow solid; yield 82%.

Mp: 167-169 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.34 (d, *J* = 9.2 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.46-7.45 (m, 4H), 7.37-7.30 (m, 4H), 7.19 (d, *J* = 8.4 Hz, 1H), 7.06 (s, 1H), 2.45 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.8, 147.0, 142.8, 141.4, 136.5, 134.4, 129.9, 129.5, 129.4, 128.7, 128.0, 125.4, 119.9, 109.9, 21.9.

FT-IR (KBr): *v* = 3076, 2923, 2851, 1594, 1520, 1350, 1214, 1109, 1028, 855, 810, 771, 735, 698 cm^{-1}.

Elemental analysis calcd (%) for $C_{20}H_{15}N_3O_2$: C 72.94, H 4.59, N 12.76, found: C 72.83, H 4.60, N 12.86.

Single Crystal X-Ray Structure of 2n

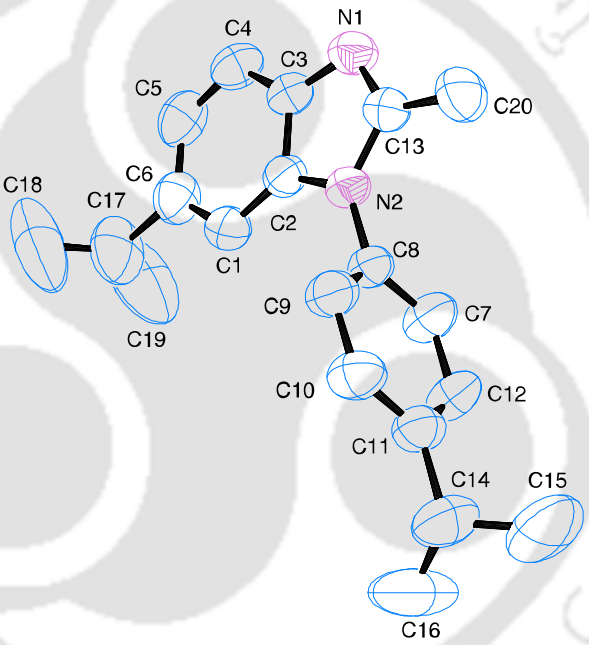


Figure 2. ORTEP diagram of the single-crystal X-ray structure of 6-Isopropyl-1-(4-isopropylphenyl)-1*H*-benzo[*d*]imidazole **2n.** Thermal ellipsoids are drawn at 50% probability level. H-Atoms are omitted for clarity (CCDC 863007).

Crystal Data and Structure Refinement for 2n at 296(2) K

Identification code	2n	
Empirical formula	$C_{20}H_{24}N_2$	
Formula weight	292.41	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
	Loop xyz	
	'x, y, z' '-x, -y, -z'	
Unit cell dimensions	*a* = 8.8353 (18) Å	α(°) = 106.121 (18)
	b = 10.145(2) Å	β(°) = 109.391(19)
	c = 11.616 (4) Å	γ(°) = 101.989(13)
Volume	890.3(5) $Å^3$	
Z	2	
Density (calculated)	1.091 Mg/m^3	
Absorption coefficient	0.064 mm^{-1}	
F(000)	316	
Crystal size	0.46 x 0.34 x 0.22 mm	
Theta range for data collection	0.981 to 28.02 °	
Index ranges	-10<=h<=10, -11<=k<=11, -13<=l<=13	
Reflections collected	2900	
Independent reflections	2049	
Completeness to theta = 24.31 °	99.5 %	
Absorption correction	Multi-scan	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3161 / 0 /177	
Goodness-of-fit on F^2	0.995	
Final R indices [I>2sigma (I)]	*R1* = 0.0952, *wR2* = 0.1369	
R indices (all data)	*R1* = 0.0767, *wR2* = 0.1902	

Single Crystal X-Ray Structure of 2p

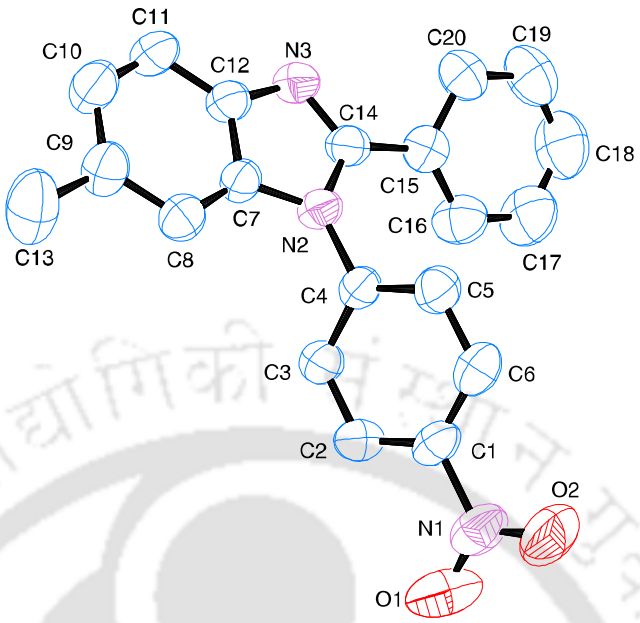


Figure 3. ORTEP diagram of the single-crystal X-ray structure of 6-Methyl-1-(4-nitrophenyl)-2-phenyl-1*H*-benzo[*d*]imidazole **2p.** Thermal ellipsoids are drawn at 50% probability level. H-Atoms are omitted for clarity (CCDC 863008).

Crystal Data and Structure Refinement for 2p at 296(2) K

Identification code	2p	
Empirical formula	$C_{20}H_{15}N_3O_2$	
Formula weight	329.35	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
	Loop xyz	
	‘x, y, z’ ‘-x, -y, -z’	
Unit cell dimensions	*a* = 8.2036 (6) Å	α(°) = 76.796 (5)
	b = 10.3079 (8) Å	β(°) = 78.813 (5)
	c = 10.9919 (9) Å	γ(°) = 0.229 (5)
Volume	844.64 (12) $Å^3$	
Z	2	

Density (calculated)	1.295 Mg/m^3
Absorption coefficient	0.086 mm^{-1}
F(000)	344.0
Crystal size	0.36 x 0.24 x 0.18 mm
Theta range for data collection	1.92 to 25.25 °
Index ranges	-9<=h<=9, -12<=k<=12, -13<=l<=13
Reflections collected	3053
Independent reflections	1869
Completeness to theta = 25.25 °	100.0 %
Absorption correction	Multi-scan
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3053 / 0 / 227
Goodness-of-fit on F^2	1.066
Final R indices [I>2sigma (I)]	*R1* = 0.0502, *wR2* = 0.1387
R indices (all data)	*R1* = 0.0873, *wR2* = 0.1784

3.6 References

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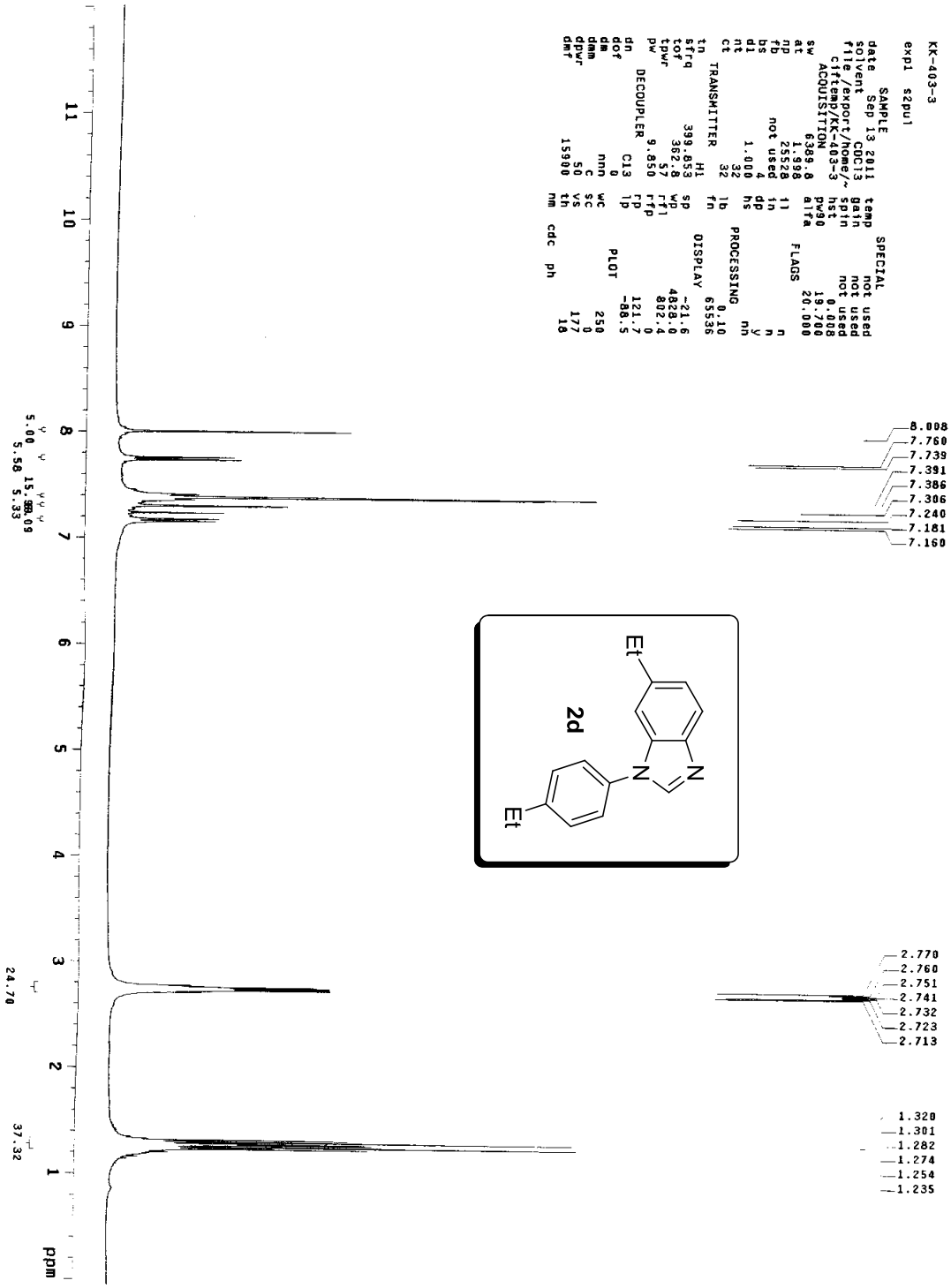
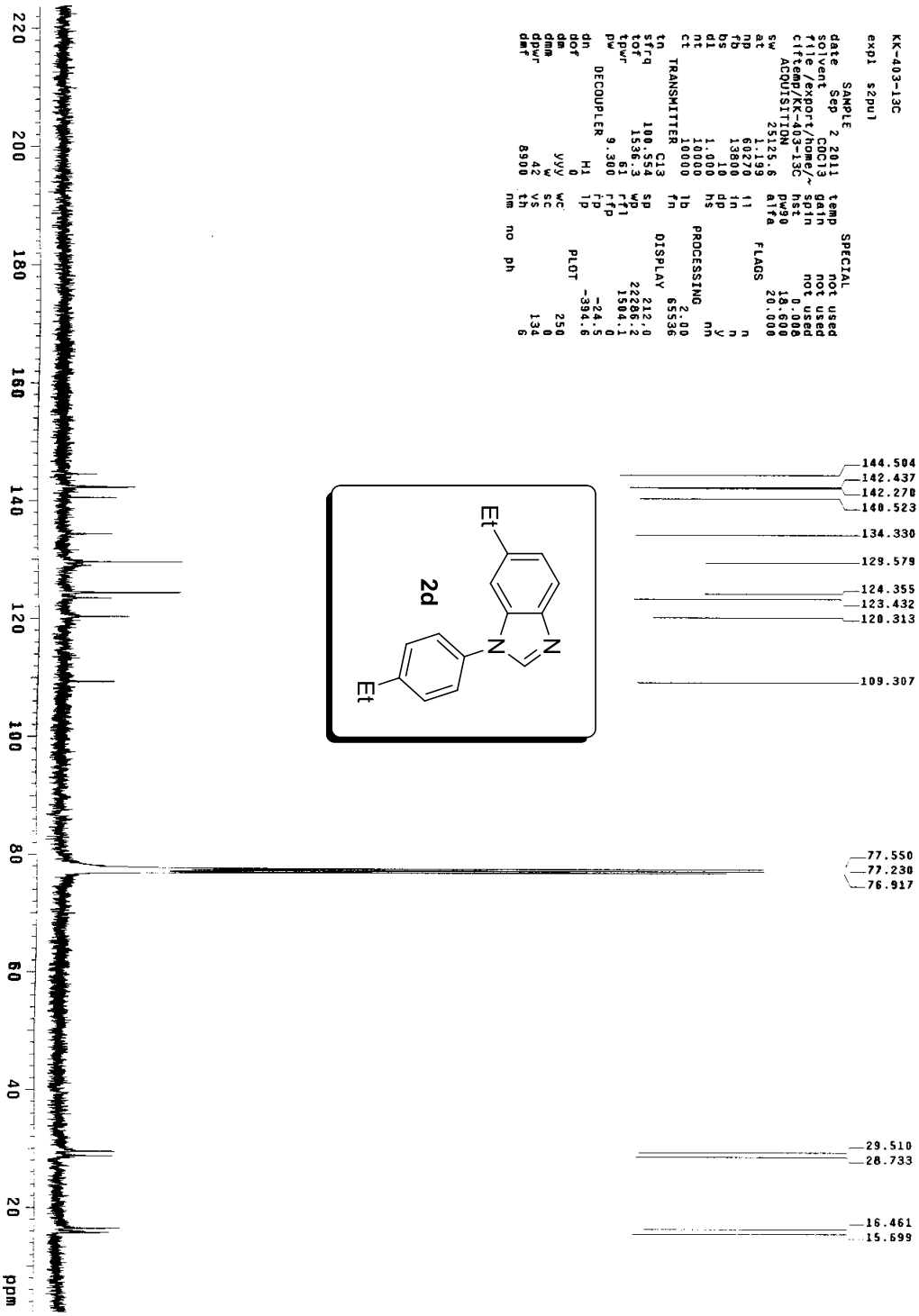
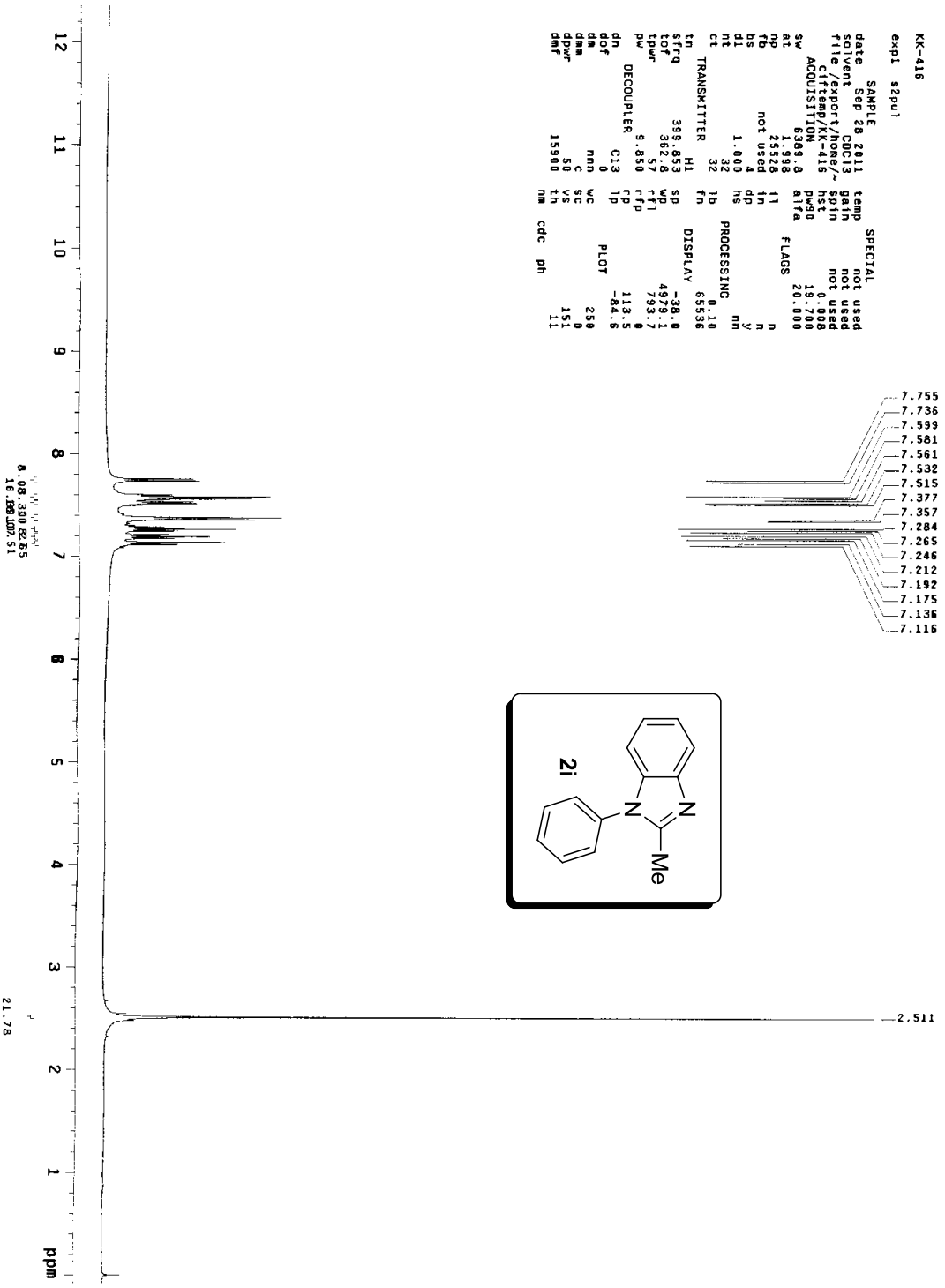
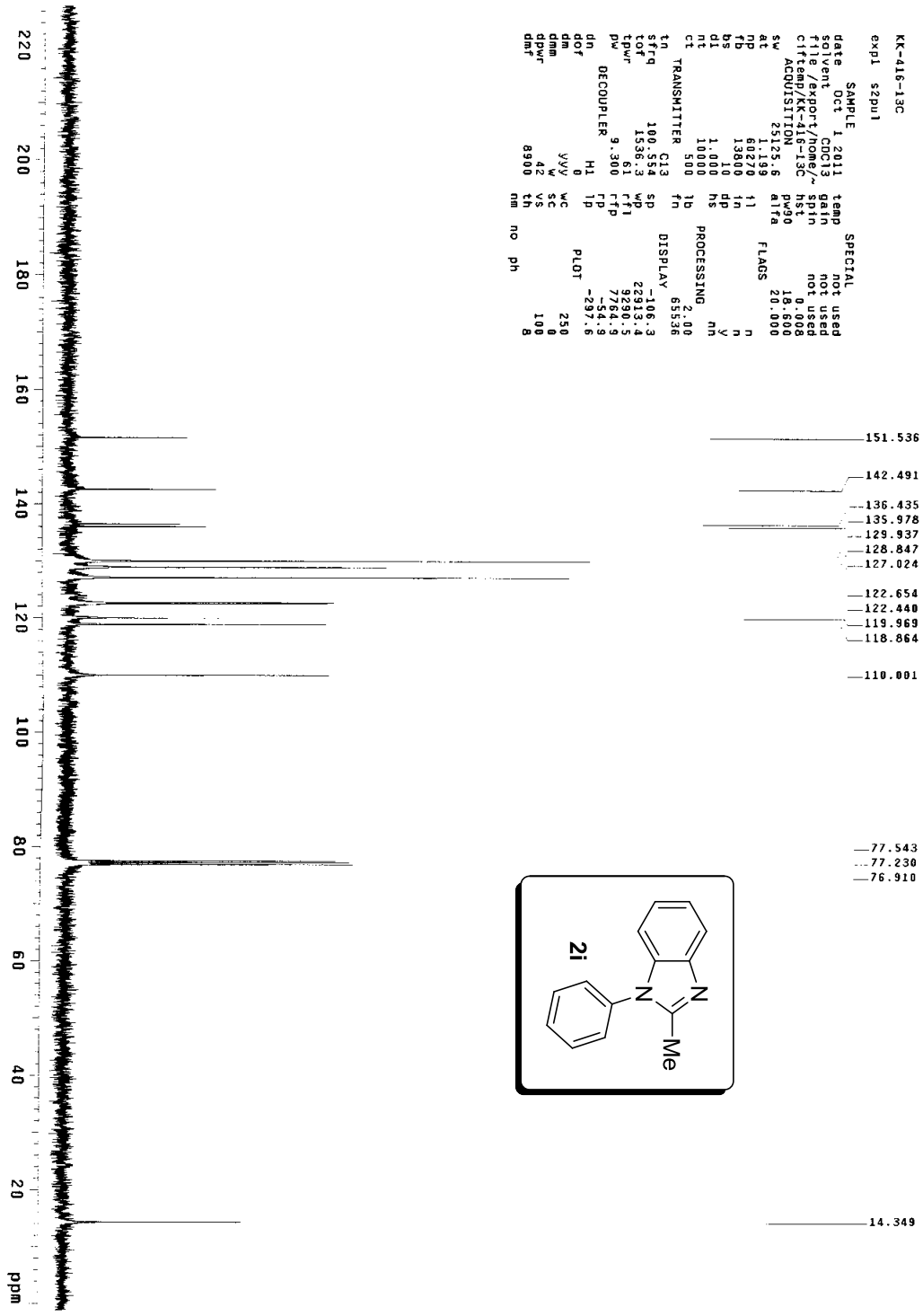
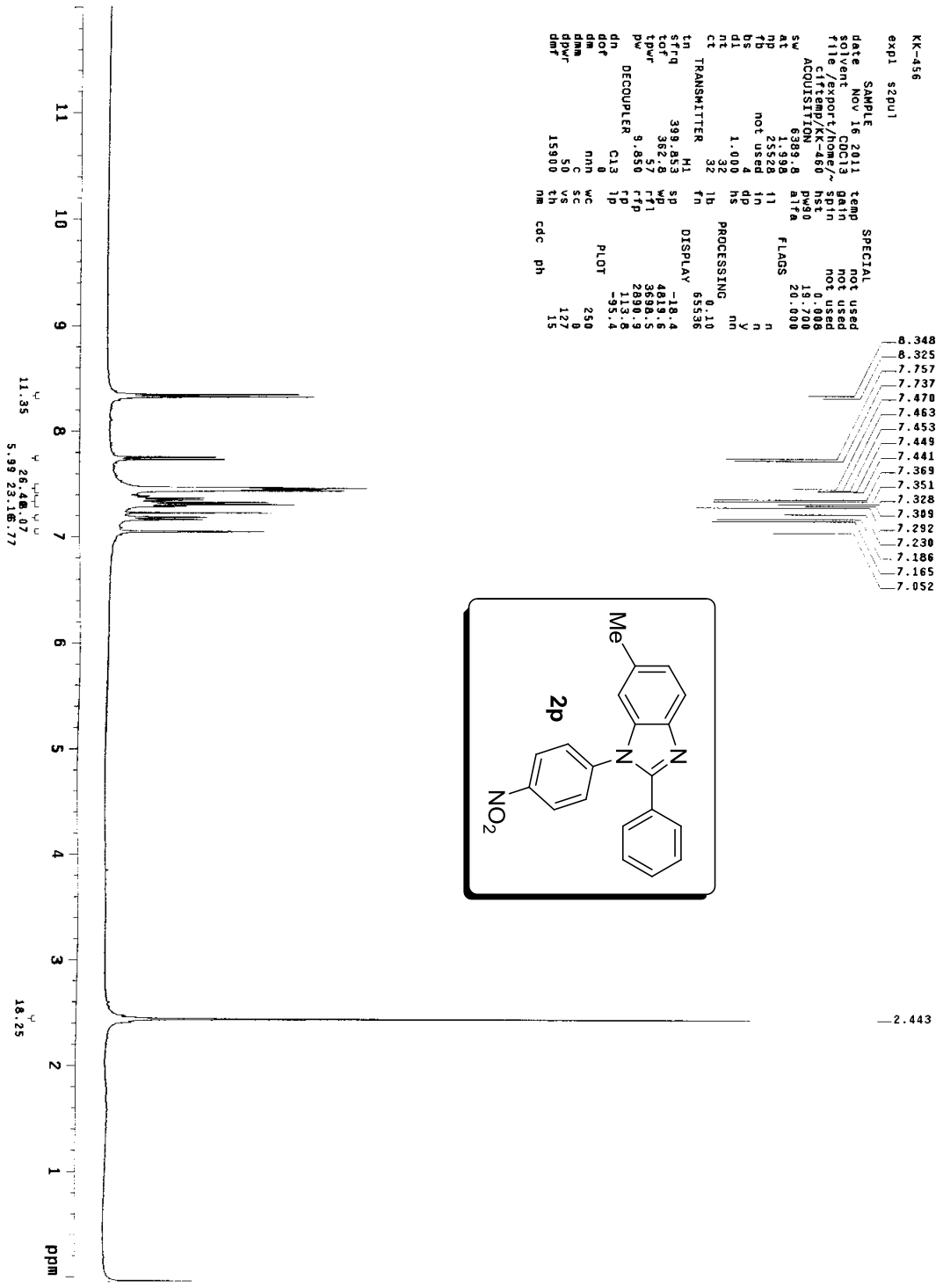
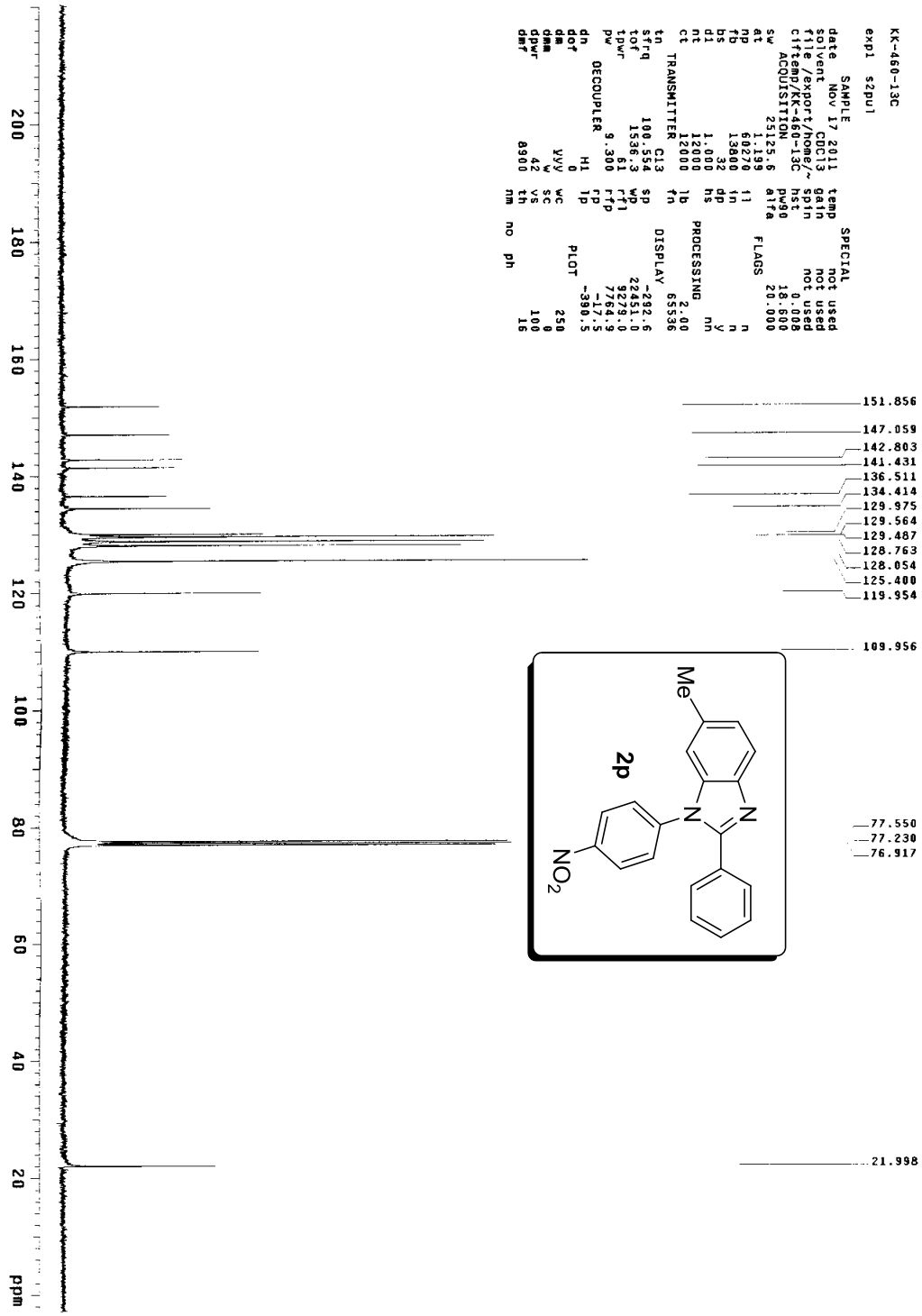












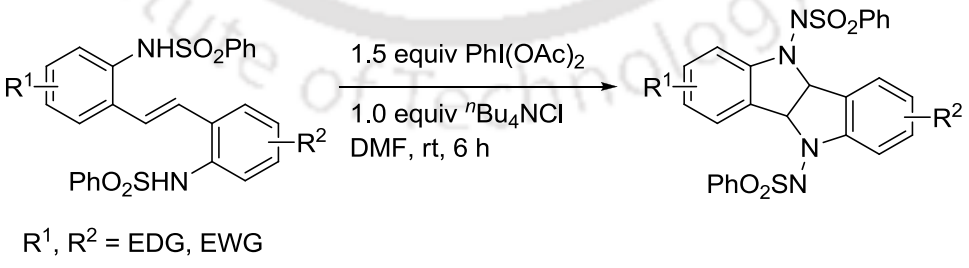
Chapter IV

$PhI(OAc)_2$-Promoted Oxidative Synthesis of Benzo-fuzed Azoles

The construction of carbon-heteroatom bonds *via* C-H functionalization has received intensive attention in recent years.[1] Because this methodology makes the protocol step efficient and atom economical with broad substrate scope. Transition-metal based systems such as Cu, Pd, Rh, Ru, and Ag have been considerably explored for this purpose. Concerning the cost and convenience issues associated with the classical versions of the metal based systems such as the higher temperature and the metal contamination with the target products, the development of alternative methods that can devoid the use of metal catalysts is of much significance for the large scale synthesis.[2] Thus, effort has been made on the development of the metal-free conditions for the construction of *C-N* bonds, and a few studies with *C-O* and *C-S* bonds. In addition, a one-step protocol that can perform the functionalization of multiple C-H bonds *via* tandem *C-N* and *C-S/C-Se* bonds formation will be attractive for the synthesis of pharmaceutically important benzfuzed heterocycles.

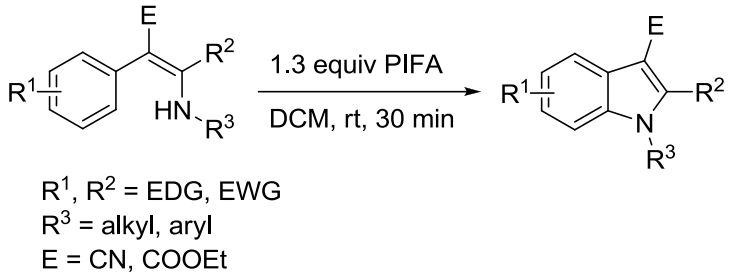
4.1 Metal-Free C-H Functionalization/C-N Bond Formation

Chang and co-workers developed a procedure for intramolecular oxidative diamination of olefins. The protocol involves the use of iodobenzene diacetate (PIDA) as an oxidant and halide additive to furnish the corresponding bisindoline compounds (Scheme 1).[3]



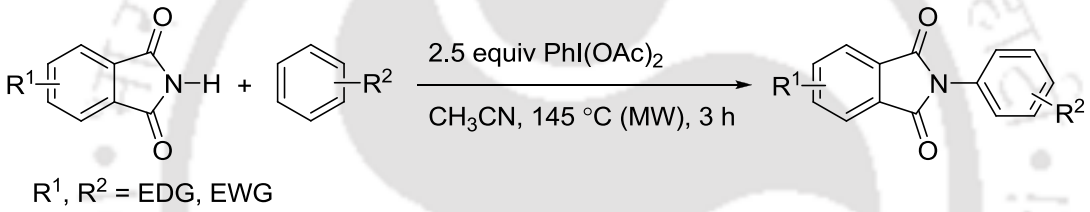
Scheme 1. Intramolecular Diamination of Olefins

Zhao and co-workers have demonstrated the synthesis of substituted *N*-arylated and *N*-alkylated indole derivatives *via* phenyliodine bis(trifluoreacetate) (PIFA) promoted intramolecular cyclization at room temperature (Scheme 2).[4]



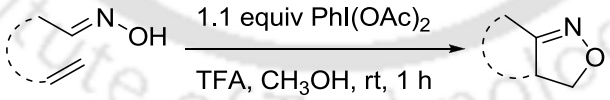
Scheme 2. Synthesis of *N*-Substituted Indoles *via* PIFA Promoted C-H Activation

DeBoef and co-workers reported an intermolecular oxidative amination reaction, a synthetic transformation that involves the simultaneous functionalization of both an N-H and C-H bond, is described. The process, which is mediated by an I(III) oxidant and contains no metal catalyst, provides a rapid and green method for synthesizing protected anilines from simple arenes and phthalimide (Scheme 3).[5]



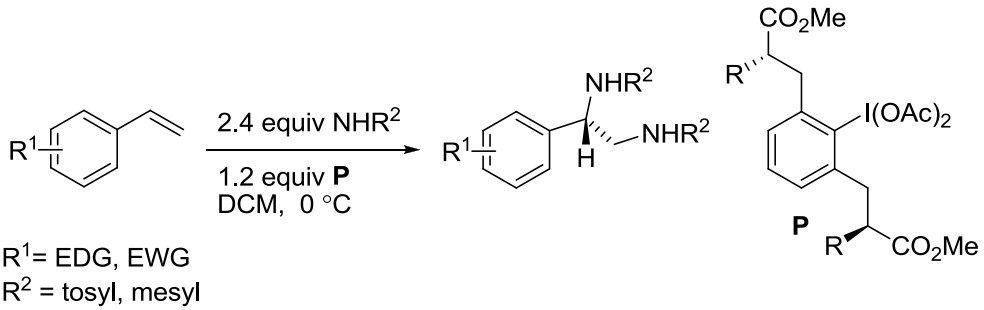
Scheme 3. Intermolecuar Oxidative C-H Amination of Unactivated Arenes

Ciufolini and co-workers reported $PhI(OAc)_2$ catalzyed oxidation of aldoximes to nitrile oxides, which could be trapped in situ with olefins in a bimolecular or an intramolecular mode (Scheme 4).[6]



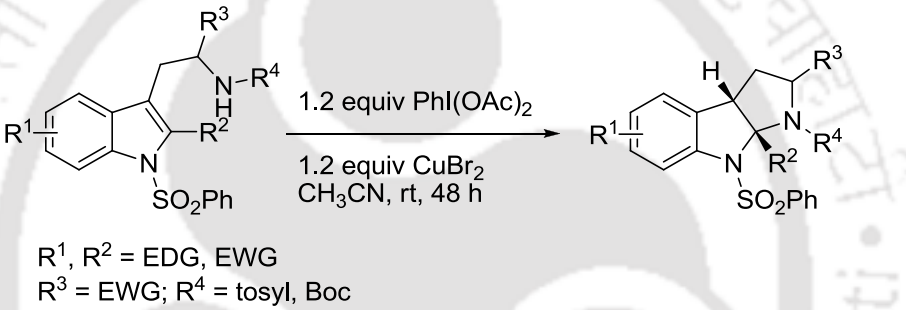
Scheme 4. Oxidation of Oximes to Nitrile Oxides

Muniz and co-workers developed an intermolecular enantioselective diamination of alkenes. This oxidation reaction transforms styrenes into diamine derivatives under metal-free conditions using a chiral iodine(III) reagent and bismesylimide or bistosylimide as the nitrogen source (Scheme 5).[7]



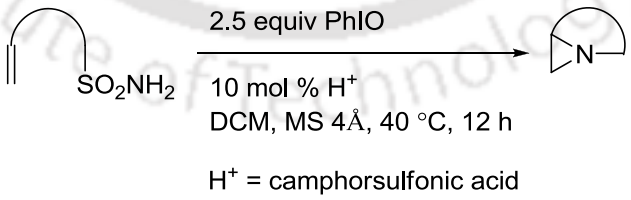
Scheme 5. Enantioselective Diamination of Styrenes

Xia and co-workers have developed a synthetic procedure for the pyrrolo[2,3-*b*]indole skeleton *via* intramolecular annulation of indole derivatives promoted by $PhI(OAc)_2$ (Scheme 6).[8]



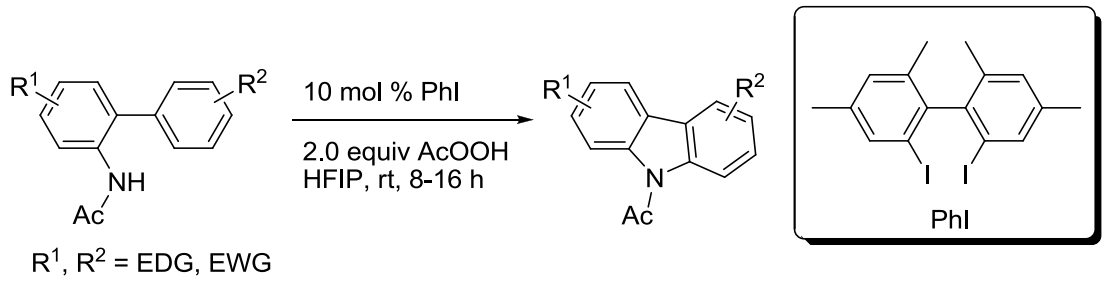
Scheme 6. Synthesis of Pyrrido[2,3-*b*]indole Derivatives

Moriarty and co-workers successfully developed an intramolecular aziridation of alkene under transition metal-free conditions. The protocol involves the use of iodosyl benzene as an oxidant (Scheme 7).[9]



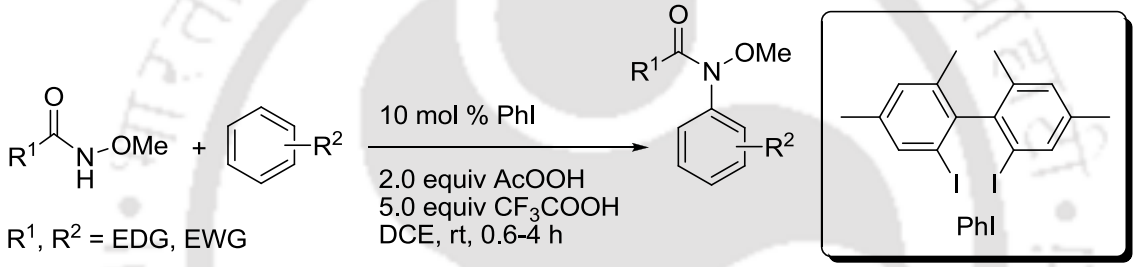
Scheme 7. Intramolecular Aziridation of Alkenes

Lee and co-workers described a metal-free organocatalytic protocol for the synthesis of carbazoles *via* intramolecular C-H functionalization and C-H amination method. The protocol can be used for synthesis various substituted carbazoles without addition of any additives like transition metals and alkali metals (Scheme 8).[10]

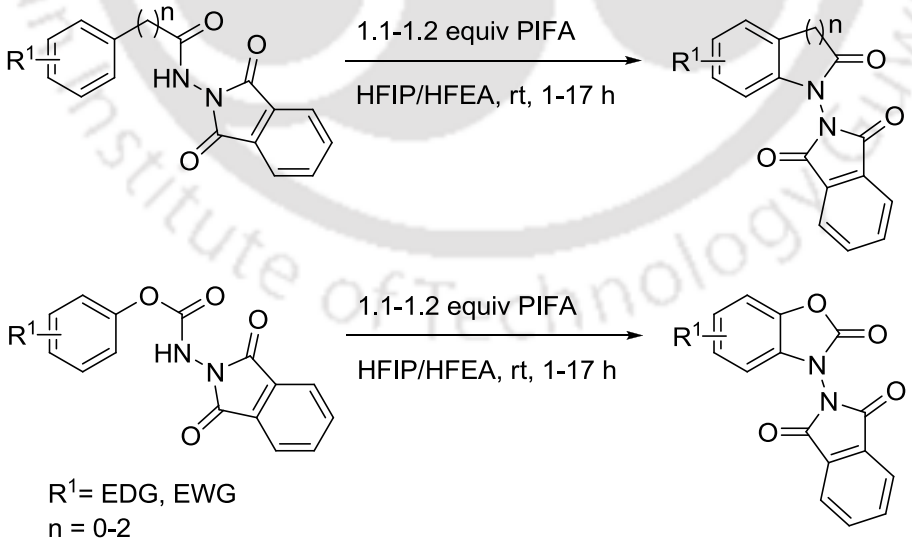


Scheme 8. Cross-Amination of Arenes

Later they reported oxidative intermolecular process for the introduction of amine group into unactivated arenes. The protocol involves the use of 10 mol % of aryl iodide as an organocatalyst and 2.0 equiv. of peracetic acid as a terminal oxidant at ambient conditions (Scheme 9).[11]



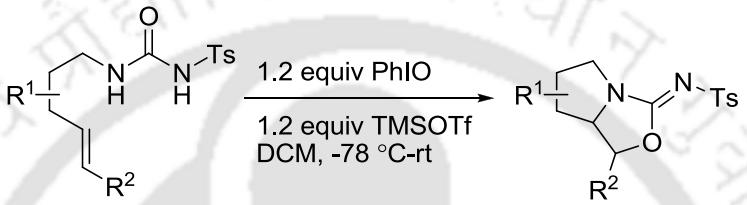
Scheme 9. Intermolecular Amination of Arenes



Scheme 10. Synthesis of Benzannulated Compounds

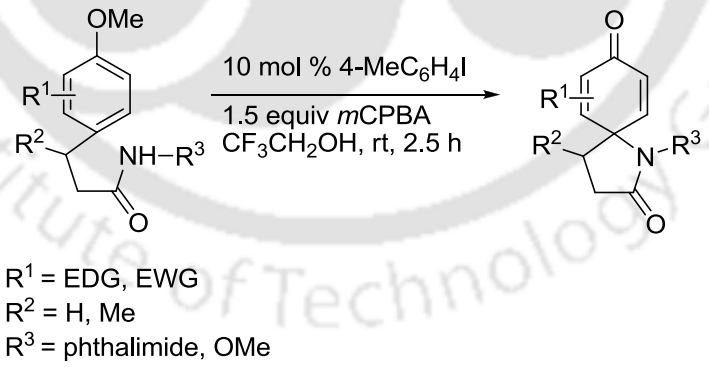
Kikugawa and co-workers showed PIFA-based cyclization of *N*-acylaminophthalimides for the synthesis of benzannulated 3*H*-benzol-3-ones and 3*H*-benzoxazin-3-ones from *N*-acylaminophthalimides bearing phenoxy group. The protocol involves generation of *N*-phthalimido-*N*-acylnitrenium ions (Scheme 10).[12]

Michael and co-workers reported a metal-free oxidative cyclization of ureas onto unactivated alkenes using iodosylbenzene and a Lewis acid promoter. The products are predominantly bicyclic isourea derivatives resulting from an intramolecular oxyamination reaction (Scheme 11).[13]



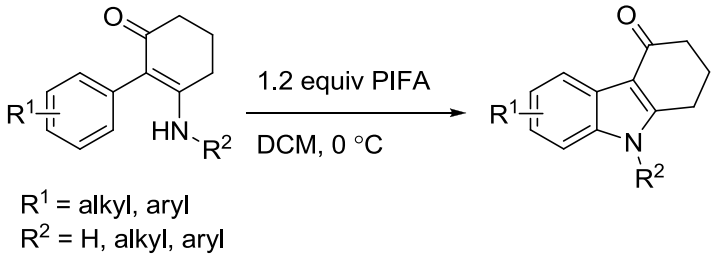
Scheme 11. Oxidative Cyclization of Urea-Tethered Alkenes with Iodosylbenzene

Kita and co-workers established the catalytic spirolactam forming reaction induced by *in situ* generated hypervalent iodine(III). The protocol involves the use of 4-iodotoluene as organocatalyst and *m*-chloroperbenzoic acid (*m*CPBA) as an oxidant for the generation of hypervalent iodine(III) reagent (Scheme 12).[14]



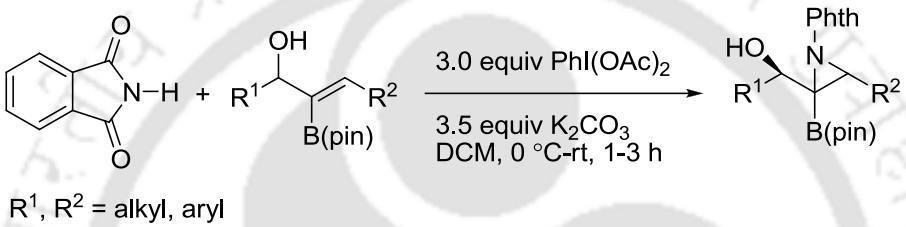
Scheme 12. Spirocyclization of Amides to *N*-Fused Spirolactams

Wang and co-workers reported an alternative approach to synthesize the carbazolone derivatives. This method uses phenyliodine bis(trifluoreacetate) (PIFA) as the promoter (Scheme 13).[15]



Scheme 13. Synthesis of Carbazoles from 2-Aryl Enaminones

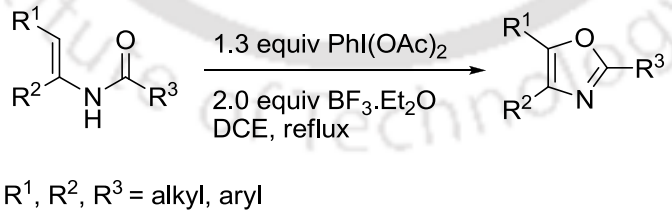
Walsh and co-workers demonstrated the aziridination of B(pin)-substituted allylic alcohols in the presence of $PhI(OAc)_2$ and *N*-aminophthalimide. This reaction gives rise to *syn*-B(pin)-substituted hydroxyaziridines in good yields (Scheme 14).[16]



Scheme 14. Diastereoselective Aziridazation of B(pin)-Susbstituted Ally Alcohols

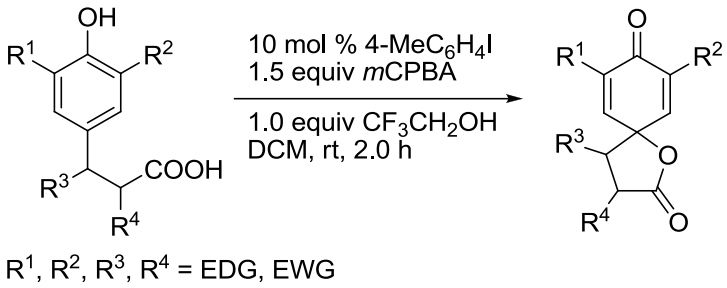
4.2 Metal-Free C-H Functionalization/C-O Bond Formation

Zhao and co-workers successfully developed the synthesis of functionalized oxazoles *via* $PhI(OAc)_2$-mediated intramolecular cyclization. This protocol has broad substrate scope and the heavy-metal-free characteristic of the oxidative carbon–oxygen bond formation process (Scheme 15).[17]



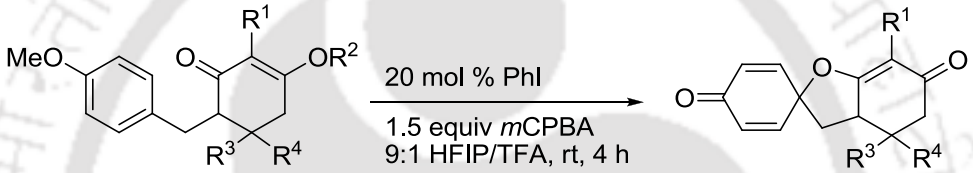
Scheme 15. Synthesis of Oxazoles from Enamines

Kita and co-workers reported organocatalytic spirocyclization of phenols. The protocol involves the use of catalytic amount of 4-iodotoluene along with 1.5 equiv of *m*CPBA as a co-oxidant (Scheme 16).[18]



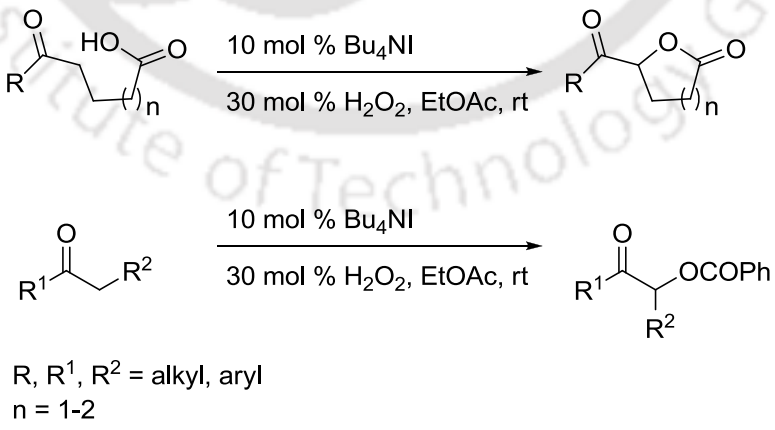
Scheme 16. Spirocyclization of Phenols

Hutt and co-workers reported an iodobenzene catalyzed synthesis of spirofurans *via* oxidative cyclization of vinylogous esters. The protocol involves the use of 20 mol % iodobenzene as an organocatalyst and 1.5 equiv of *m*CPBA as a terminal oxidant (Scheme 17).[19]



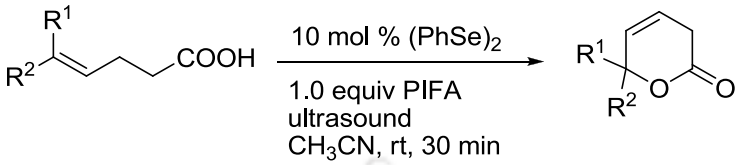
Scheme 17. Synthesis of Spirofurans

Ishihara and co-workers developed organocatalytic intra and intermolecular direct α-oxyacylation of carbonyl compounds with carboxylic acids. The protocol involves the *in situ* generation of ammonium(hypo)iodite species using either hydrogen peroxide or TBHP (Scheme 18).[20]



Scheme 18. α-Oxyacylation of Carbonyl Compounds

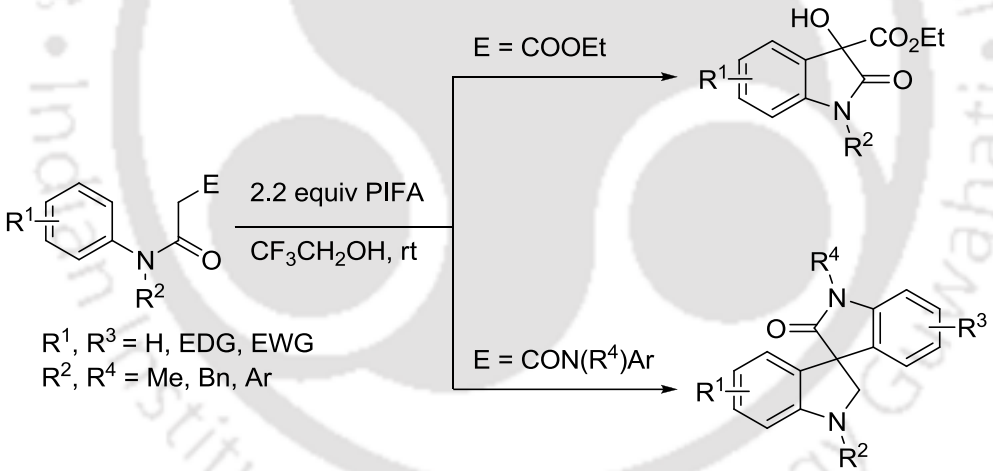
Wirth and co-workers described selenium catalyzed regioselective cyclization of γ,δ-unsaturated carboxylic acids to 3,6-dihydro-2*H*-pyran-2-ones. The cyclization products have been obtained in good to excellent yields using diphenyl diselenide as a catalyst and bis(trifluoroacetoxy)iodobenzene (PIFA) as a stoichiometric oxidant (Scheme 19).[21]



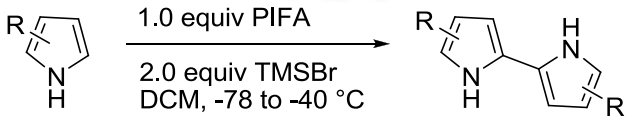
Scheme 19. Synthesis of 3,6-Dihydro-2*H*-pyran-2-ones

4.3 Metal-Free C-H Functionalization/C-C Bond Formation

Zhao and co-workers reported a metal-free synthesis of 3-hydroxy-2-oxindoles and spirooxindoles. The protocol proceeds *via* PIFA mediated cascade oxidation of anilide derivatives. The nature of the product depends on substituents of anilides (Scheme 20).[22]



Scheme 20. Synthesis of 3-Hydroxy-2-oxindoles and Spiroindoles



Scheme 21. Synthesis of Bipyrroles

Kita and co-workers developed the phenyliodine bis(trifluoroacetate) (PIFA) mediated oxidative coupling pyrroles to give α-linked bipyrroles (Scheme 21).[23]

4.4 Present Study

The –NH group attached to electron withdrawing substituents such as acyl (-$COCH_3$), mesyl (-SO_3Me) and tosyl (-SO_3Ph) groups has been demonstrated to undergo *C-N* bond formation *via* oxidative C-H activation in the presence of hypervalent iodine reagents such as $PhI(OAc)_2$ (PIDA), $PhI(OOCF_3)_2$ (PIFA) and PhIO. These studies led us to investigate the metal-free C-H activation for intramolecular *C-N* bond formation reactions of readily accessible 1,3-diaryl-thiourea. In this context, we describe a simple, mild and general metal-free oxidative protocol for *C-N* and tandem *C-N* and *C-S/C-Se* bonds formation *via* mono and double C-H activations using $PhI(OAC)_2$ at ambient conditions for the diversified synthesis of benzo[*d*]imidazo[2,1-*b*]benzothiazoles,[24] benzimidazole-2-thiones, benzo[*d*]imidazo[2,1-*b*]benzoselenoazoles, 2-alkylthio-*N*-aryl benzimidazoles and 2-unsubstituted *N*-aryl benzimidazoles[25-26] that are important in biological and medicinal sciences.

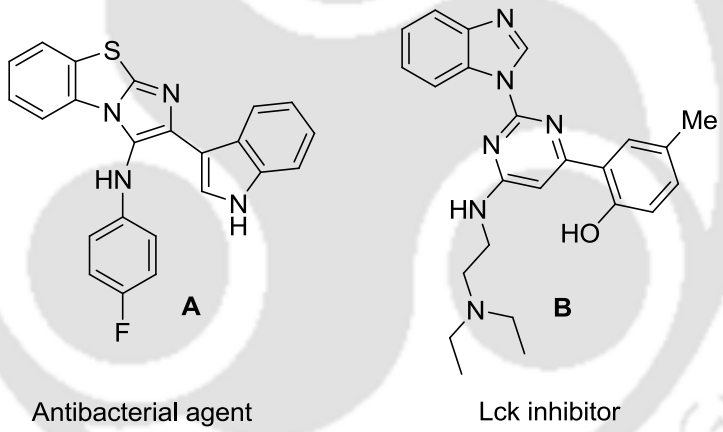
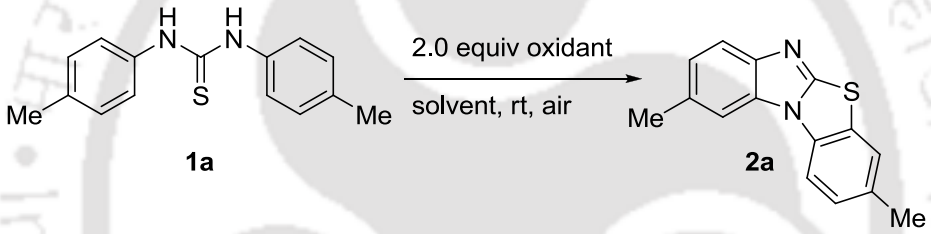


Figure 1. Some Examples of Biologically Active Benzfuzed Azoles.

Benzo[*d*]imidazo[2,1-*b*]benzothiazole is an interesting scaffold to chemists with four fused rings that are found in many bioactive molecules such as antibacterial agent (Figure 1, **A**), and plays a key role in imaging β-amyloid plaques in patients with Alzheimer's disease by means of positron emission tomography.[27] Reports reveal that these core structures could be constructed from either 2-iodobenzothiaozle or 2-mercaptobenzimidazole.[24b] However, the time taking tedious multi-step synthesis of the preactivated substrate precursors and the requirement of elevated temperature (≥120 °C) limit the accessibility of these classical synthetic transformations.

Further, *N*-aryl benzimidazole is an important structural unit that can be found in many medicinally significant compounds.[28] For example, the compound with 2-unsubstituted *N*-aryl benzimidazole structural framework has been shown to exhibit lymphocyte specific kinase (Lck) inhibition (Figure 1, **B**) and Nek2 inhibition. Although considerable studies have been done ranging from classical condensation to modern cross-coupling and C-H activation reactions for the synthesis of *N*-aryl benzimidazoles, most of these protocols rely on the use of metal based systems and effective under heating. Development of a general metal-free protocol that can be effective at ambient conditions for the construction of the above described fuzed heterocyclic compounds and their analogues from the readily accessible substrate precursors having wide substrate would be thus valuable in drug discovery.

Table 1. Optimization of Reaction Conditions[a]



entry	oxidant	solvent	yield (%)[b]
1	PIDA	CH_2Cl_2	n.d.
2	PIDA	toluene	n.d.
3	PIDA	H_2O	n.d.
4	PIDA	DMF	n.d.
5	PIDA	CH_3CN	n.d.
6	PIDA	CH_3COOH	n.d.
7	PIDA	^{i}PrOH	n.d.
8	PIDA	HFIP	n.d.
9	**PIDA**	**TFA**	30**(70)**[c]
10	PIFA	TFA	10
11	PhIO	TFA	n.d.
12	Oxone	TFA	n.d.

[a]Reaction condition: A mixture mixture of 1,3-Di-*p*-tolylthiourea **1a** (0.5 mmol), oxidant (2.0 equiv.) were stirred in solvent (0.5 mL) at rt under air. [b]Isolated yield. [c]Oxidant 4.0

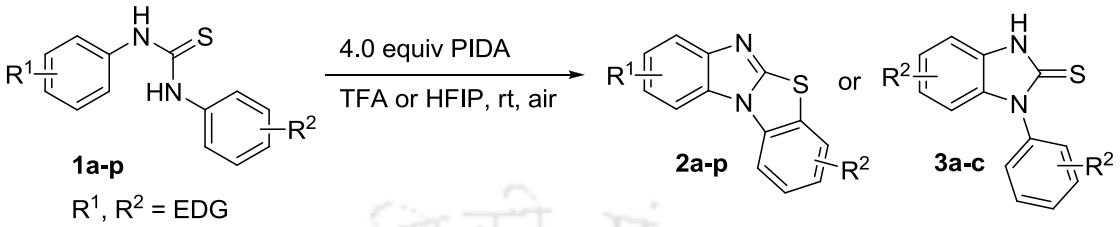
equiv was used. n.d. = Not detected. PIDA = Phenyliodine(III) diacetate, PIFA = Phenyliodine(III) bis(trifluoroacetate), PhIO = Iodosyl benzene, TFA = Trifluoro acetic acid, HFIP = 1,1,1,3,3,3,-Hexafluoro-2-propanol.

First optimization of reaction condition was carried out by taking 1,3-di-*p*-tolylthiourea **1a** as a model substrate for the C-H activation followed by carbon-heteroatom bond formation using hypervalent iodine reagents at ambient conditions (Table 1). When the substrate **1a** was reacted with 2.0 equiv of PIDA in a series of solvents such as CH_2Cl_2, toluene, water, DMF, CH_3CN, CH_3COOH, $^{i}PrOH$ and 1,1,1,3,3,3,-hexafluoro-2-propanol (HFIP) at 25 °C, C-H activation and *C-N* bond formation was not observed (Table 1, entries 1-8). These reactions were further examined using 1.0 equiv of Cs_2CO_3 as a base, but no effect was observed. However, to our delight, the use of CF_3COOH (TFA) as a solvent led to the double C-H activation and tandem *C-N* and *C-S* bonds formation leading to the construction of benzo[*d*]imidazo[2,1-*b*]benzothiazole **2a** in 30% yield (entry 9). Recrystallization of **2a** in CH_2Cl_2 gave a single crystal whose structure was confirmed by X-ray analysis. Increasing of the quantity of PIDA from 2.0 equiv to 4.0 equiv led to the formation of the target **2a** in 70% yield. While other oxidants such as PIFA was less effective producing **2a** in 10% yield (entry 10), while PhIO and oxone showed no reaction, and the starting material **1a** was recovered intact (entries 11-12).

Next, the scope of the procedure was studied for the reactions of a series of substituted 1,3-diaryl thiourea derivatives having both the electron withdrawing and electron donating substituents on the aryl rings (Table 2). The substrates **1b** and **1f-g** having 4-ethyl, 2,4-dimethyl and 3,4-dimethyl substituents on the aryl rings underwent reaction to give benzo[*d*]imidazo-[2,1-*b*]benzothiazoles **2b** and **2e-f** in high yields (entries 1, 7 and 8). While the substrates **1c-e** in that the aryl rings are substituted with the combination of 4-methoxy and 4'-methyl or 4,4'-dimethoxy groups underwent mono C-H activation to afford benzimidazole-2-thiones **3a** and **3b-c** in 72-80% yields (entry 2, 3 and 5). Further, when the reaction medium was changed from TFA to HFIP, the substrates **1d-e** underwent tandem *C-N* and *C-S* bonds formation to give benzo[*d*]imidazo[2,1-*b*]benzo-thiazoles **2c** and **2d** in 50% and 30% yield, respectively (entries 4 and 6). On the other hand, the substrates in which one or both the aryl rings are substituted with electron withdrawing groups such as 4-chloro, 4-fluoro and 2,4-difluoro substituents led to the

formation of 2-unsubstituted *N*-arylbenzimidazoles **4a-b**, **4f, 4j** and **4l** in 55-75% yields *via C-N* bond formation and desulphurization (Table 3). In case of the substrate having

Table 2. Substrate Scope of the Metal-Free C-H Activation of Electron Rich Thioureas[a]



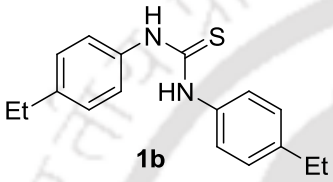
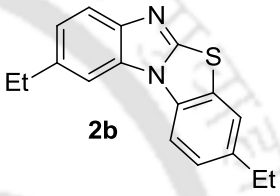
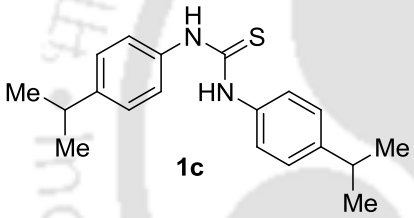
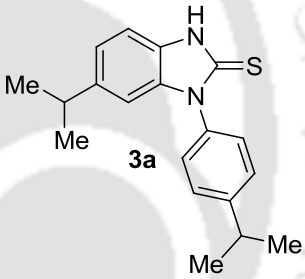
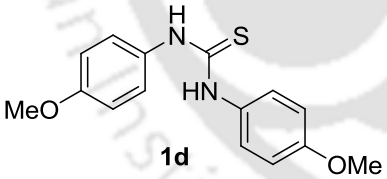
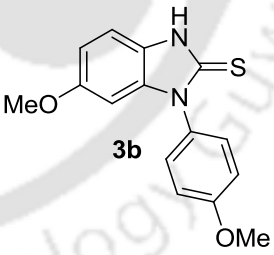
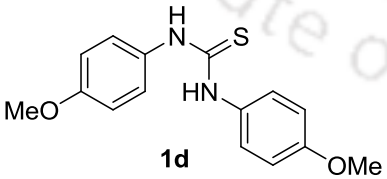
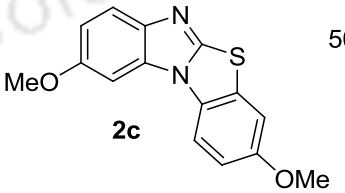
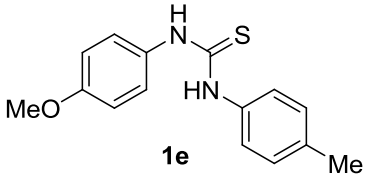
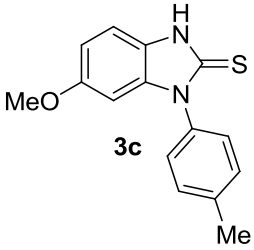
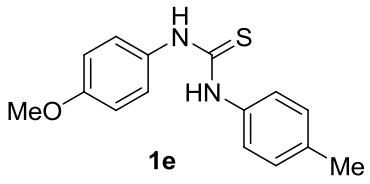
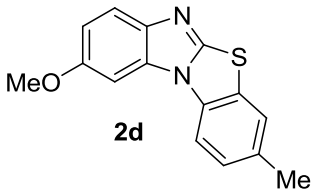
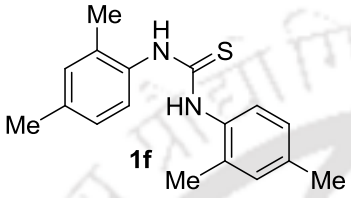
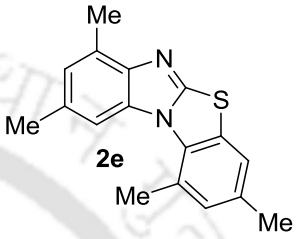
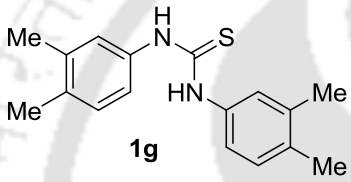
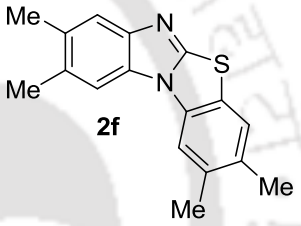
entry	substrate	time (h)	solvent	product	yield (%)[b,c]
1		1	TFA		75
2		1	TFA		72
3		1	TFA		80
4		6	HFIP		50
5		1	TFA		75

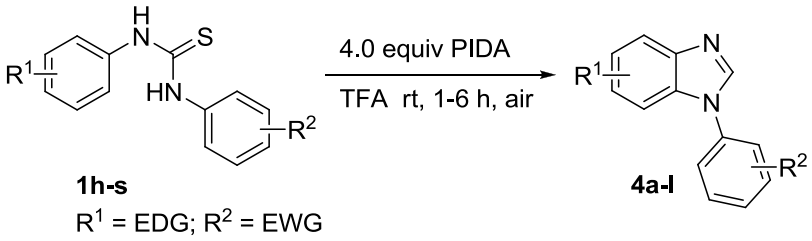
Table 2 continues…

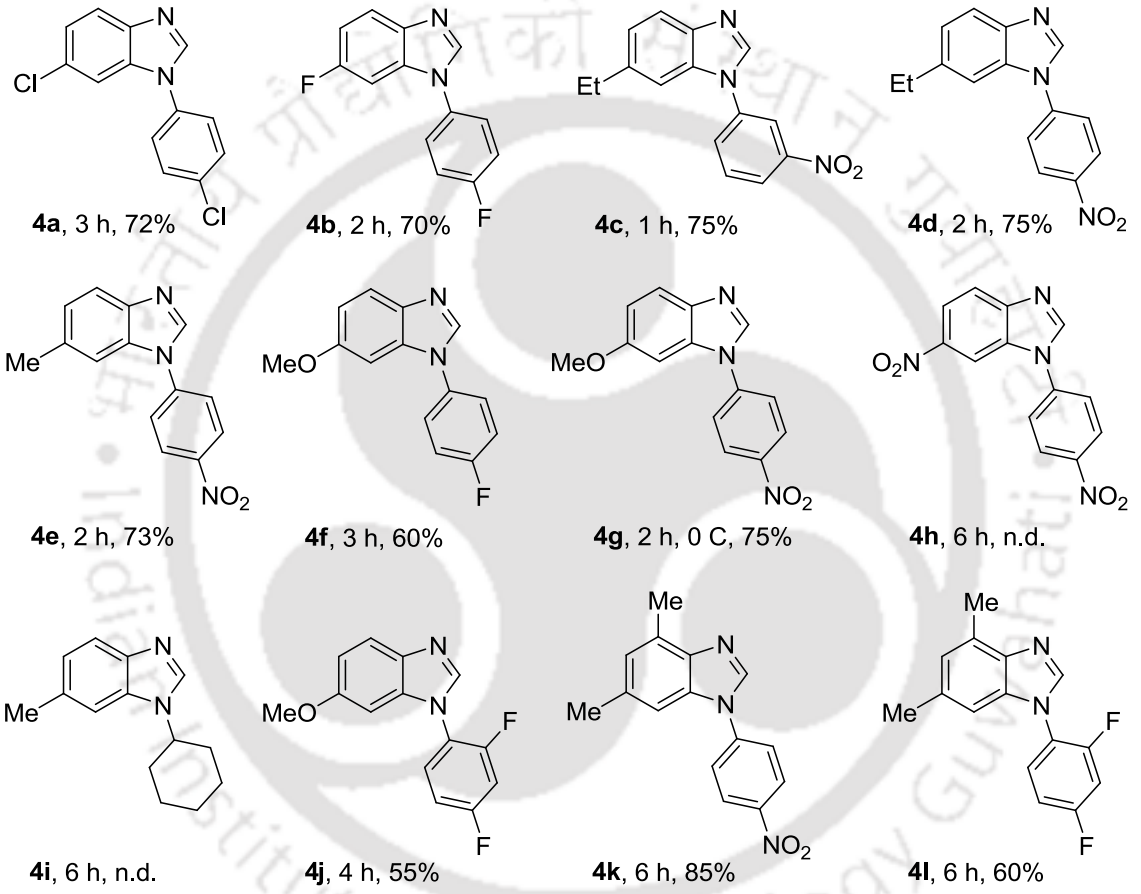
entry	substrate	time (h)	solvent	product	yield (%)[b,c]
6	 **1e**	6	HFIP	 **2d**	30
7	 **1f**	6	TFA	 **2e**	82
8	 **1g**	4	TFA	 **2f**	80

[a]Reaction condition: 1,3-diaryl thiourea **1b-g** (1.0 mmol), PIDA (2.0 equiv) were stirred in solvent (1.0 mL) at rt under air. [b]Isolated yield. [c]Single isomer. n.d. = Not detected.

nitro substituents, if one of the aryl rings has the nitro group and the other aryl ring has electron donating group, the reaction occurred as above to give the target *N*-arylbenzimidazoles **4c-e**, **4g** and **4k** in 73-85% yields. In contrast, if both the aryl rings are substituted with nitro group **1o**, the formation of benzimidazole **4h** was not observed. This may be due to the more electron deficiency of the aryl ring that may not be able to react with the electron deficient nitrogen radical intermediate that may be involved in the reaction. Furthermore, the substrate having 1-alkyl-3-aryl substituents showed no reaction to give **4i**, and the starting material was recovered intact. These experimental results suggest that the nature of the solvent, oxidant and substituent on the aryl ring is important for the target reaction. Recrystallization of **3b** and **4g** in CH_2Cl_2 gave the single crystals whose structures were confirmed by X-ray analysis.

Table 3. Substrate Scope of the Metal-Free C-H Activation of Electron Deficient Thioureas[a,b,c]



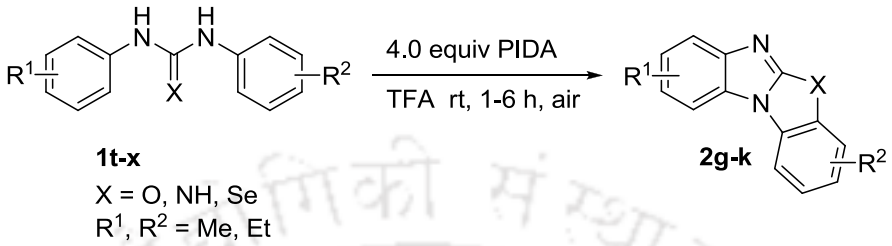


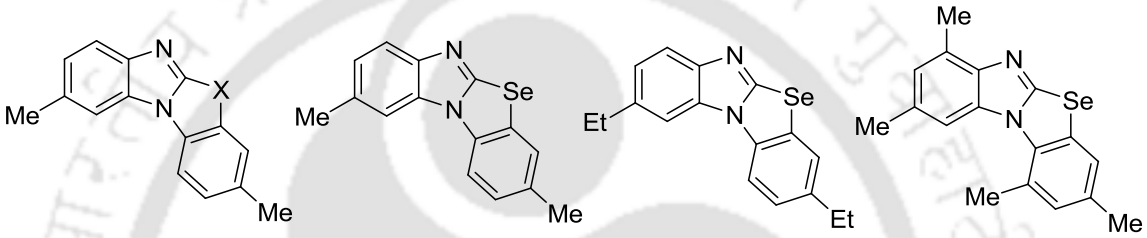
[a]Reaction condition: 1,3-diaryl thiourea **1h-s** (1.0 mmol), PIDA (4.0 equiv) were stirred at in TFA (1.0 mL) at rt under air. [b]Isolated yield. [c]Single isomer. n.d. = Not detected.

The procedure was further examined for the reactions of analogue guanidine, urea and selenourea derivatives (Table 4). The substrates, 1,3-di-*p*-tolylurea **1t** and 1,3-di-*p*-tolyl guanidine **1u** showed no reaction, and the starting material was recovered intact. However, 1,3-diarylselenourea derivatives having alkyl substituents such as 4-ethyl, 4-methyl and 2,4-dimethyl substituents on the aryl rings **1v-x** readily underwent the tandem *C-N* and *C-Se* bonds formation *via* double C-H activations to give the corresponding

benzo[*d*]imidazo-[2,1-*b*]benzoselenoazoles **2i-k** in 70-78% yields. The reactivity of the 1,3-diarylselenourea derivatives was similar to that of the 1,3-diarylthiourea derivatives.

Table 4. Metal-Free C-H Activation of 1,2,3-Triarylguanidine, 1,3-Diarylurea and 1,3-Diarylselenourea Derivatives[a,b,c]





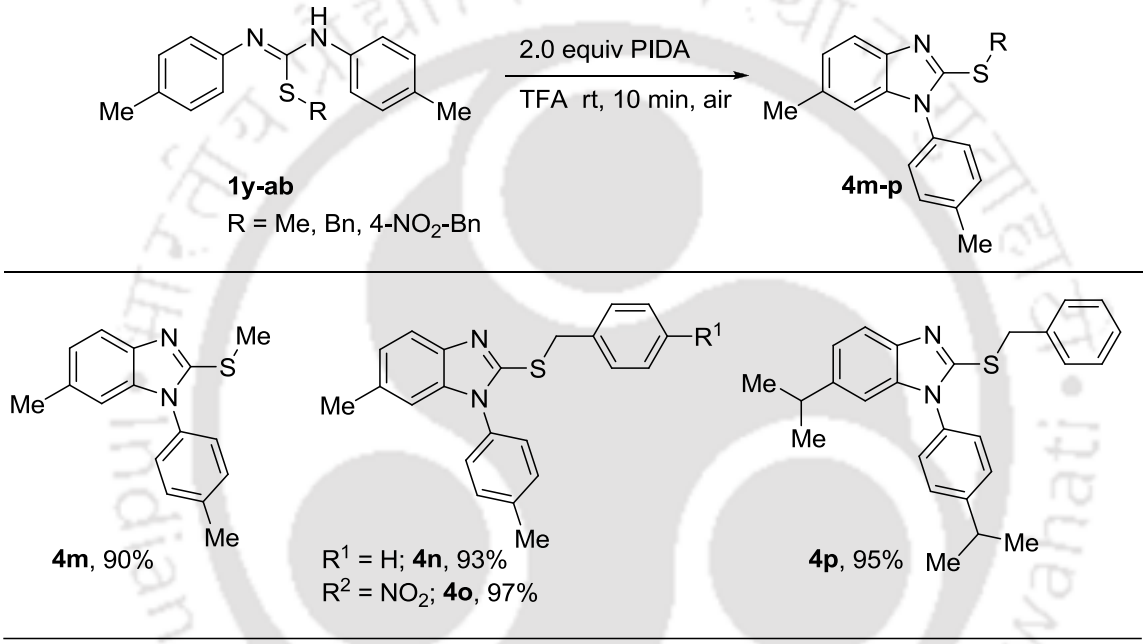
[a]Reaction condition: Substrate **1t-x** (1.0 mmol), PIDA (4.0 equiv) were stirred in TFA (1.0 mL) at rt under air. [b]Isolated yield. [c]Single isomer. n.d. = Not detected.

Finally, the cyclization of alkyl substituted 1,3-diaryl isothiourea derivatives was investigated (Table 5). The reactions were effective using 2 equiv of PIDA affording the target 2-thio benzimidaozles in quantitative yield. For example, 1,3-diaryl isothiourea derivatives **1y-ab** having methyl and isopropyl groups on the aryl rings readily underwent reaction to give the corresponding 2-alkylthio *N*-aryl benzimidazoles **4m-p** in 90-97% yield.

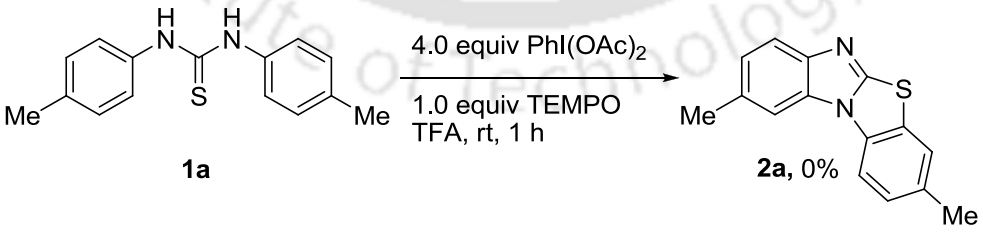
To reveal whether protocol invovles a radical intermediate, the reaction of 1,3-ditolylurea **1a** using 4.0 equiv PIDA was performed in the presence of 1.0 equiv of TEMPO in TFA (1.0 mL) (Scheme 22). No reaction was observed and the starting material was recovered intact. This result clearly suggests that the reaction may be involved a radical intermediate.[29] Thus, the reaction of thiourea **1** with PIDA can generate an intermedate **B** *via* **A** upon release of AcOH (Scheme 23). Homolytic cleavage of **B** can lead to the formation of the radical **C** that could undergo cyclization to give the

intermediate **D**. The latter may react with hypervalent iodine(III) centered radical *via* single electron transfer (SET) to give cyclohexadienyl cation **E**. The subsequent H-abstraction by the acetate anion can give the target product **3**. If R = EDG, the product **3** may undergo further reaction with $PhI(OAc)_2$ via intermediates **F**-I to afford the product **2**. Alternatively, if R = EWG, **3** may undergo desulphurization in the presence of $PhI(OAc)_2$ to give the *N*-aryl benzimidazole **4**.

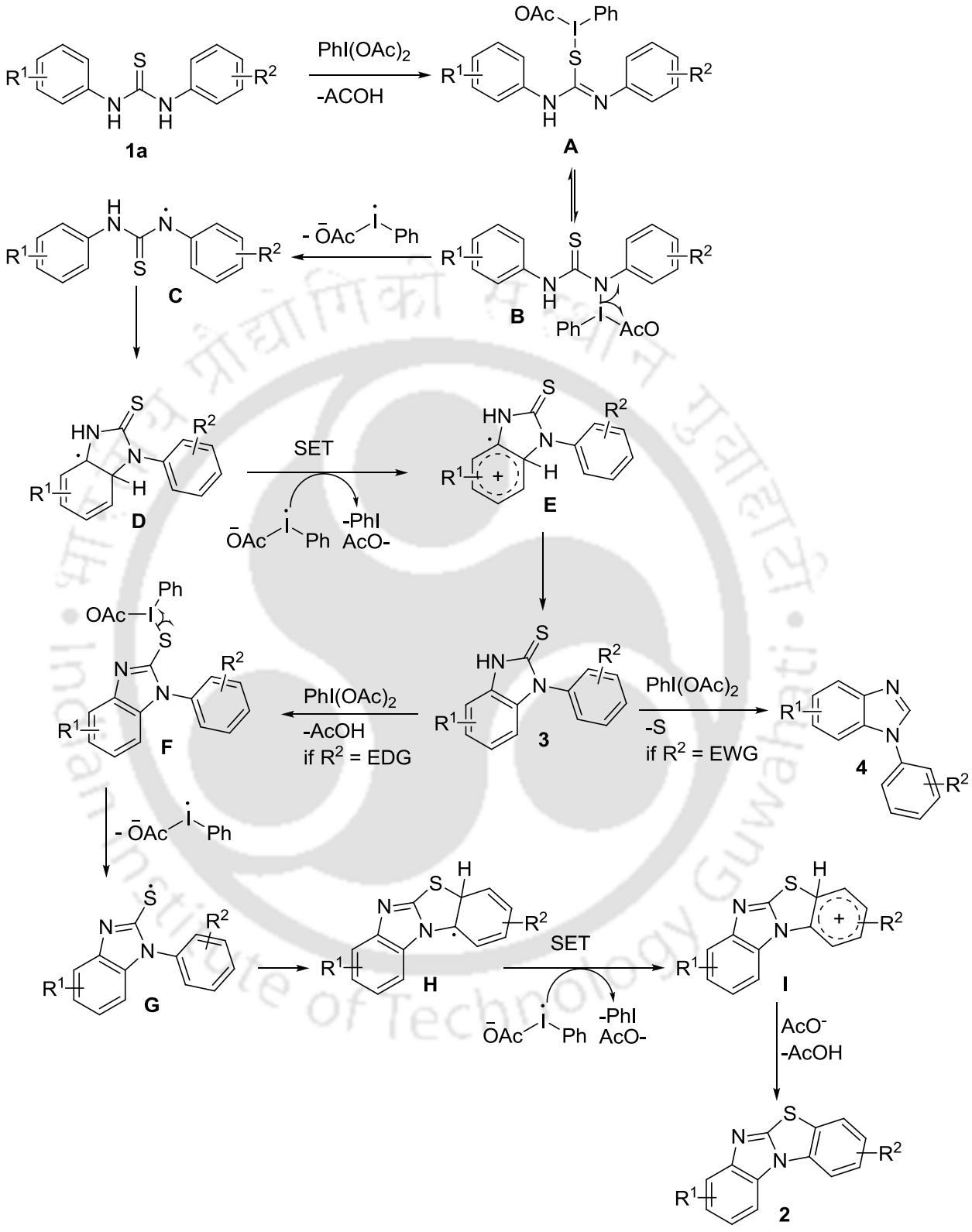
Table 5. Metal-Free C-H Activation Intramolecular C-H Amination of 1,3-Diarylisothiurea Dervatives[a,b]



[a]Reaction condition: 1,3-diaryl isothiourea **1y-ab** (1.0 mmol), PIDA (2.0 equiv) were stirred in TFA (1.0 mL) at rt under air. [b]Isolated yield.



Scheme 22. Reaction of 1,3-Di-*p*-Tolylthiourea with PIDA in Presence of TEMPO



Scheme 23. Mechanism.

Conclusion

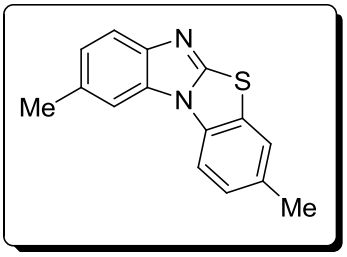
A general metal-free protocol has been developed for the synthesis of functionalized benzo[*d*]imidazo[2,1-*b*]benzothiazoles, benzimidazole-2-thiones, *N*-aryl benzimidazoles and benzo[*d*]imidazo[2,1-*b*]benzoselenoazoles 1,3-diarylthiourea/-selenourea derivatives using PIDA at ambient conditions. The reaction takes place *via* oxidative C-H activation followed by *C-N* or *C-N* and *C-S/C-Se* bonds formation. This protocol can also be used for the construction of 2-alkylthio *N*-aryl benzimidazoles with quantitative yield.

Experimental Section

General Information. Anilines, $PhI(OAc)_2$ (98%) and HFIP (99%) were purchased from Aldrich and were used as received. TFA (98%) was purchased from Merck. PIFA[30] and PhIO[31] were prepared according literature procedures. Purification of the reaction products was carried out by column chromatography using Rankem silica gel (60-120/230-400 mesh). Analytical TLC was performed on Merck silica gel G/GF 254 plate. NMR spectra were recorded on DRX-400 Varian spectrometer using $CDCl_3$ as solvent and Me_4Si as internal standard. Chemical shifts (δ) are reported in ppm and spin-spin coupling constants (J) are given in Hz. Melting points were determined using Buchi B-540 melting point apparatus and are uncorrected. FT-IR spectra were recorded using Perkin Elmer IR spectrometer. Elemental analysis was recorded using Perkin Elmer CHNS analyzer. X-Ray data were collected on a Bruker SMART APEX equipped with a CCD area detector using Mo/Kα radiation. The structures were solved by direct method using *SHELLX-97* (Göttingen, Germany).

General Procedure for the C-H Activation Reaction. Substrate **1a-ab** (1.0 mmol) and PIDA (2.0-4.0 equiv) were stirred in solvent (1 mL) under air. Progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluent. After the appropriate time, the reaction mixture was then diluted with ethylacetate (25 mL). The organic phase was washed with saturated $NaHCO_3$ (1 x 5 mL), brine (3 x 5 mL) and water (3 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using hexane and ethyl acetate as eluent to afford to afford analytically pure products.

4.5 Characterization Data



3,9-Dimethyl-benzo[*d*]imidazo[2,1-*b*]benzothiazole (2a). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.20; yellow solid; yield 70%.

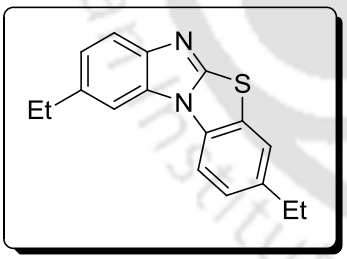
Mp: 119-121 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 10.0 Hz, 2H), 7.47 (s, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.20 (d, *J* = 8.4 Hz, 1H), 2.55 (s, 3H), 2.45 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.5, 146.0, 134.2, 131.7, 129.9, 127.3, 124.7, 124.2, 120.7, 120.8, 120.4, 118.7, 111.8, 110.5, 21.8, 21.2.

FT-IR (KBr): *ν* = 2950, 2829, 2257, 2126, 1638, 1517, 1495, 1462, 1380, 1348, 1253, 1217, 1168, 1119, 1025, 995, 828, 765, 613 cm^{-1}.

Elemental analysis calcd (%) for $C_{15}H_{12}N_2S$: C 71.40, H 4.79, N 11.10, S 12.71 found: C 71.21, H 4.81, N 11.19, S 12.69.



3,9-Diethyl-benzo[*d*]imidazo[2,1-*b*]benzothiazole (2b). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.20; yellow solid; yield 75%.

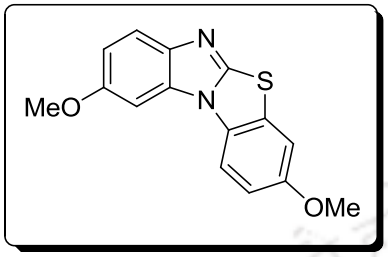
Mp: 139-141 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.0 Hz, 1H), 7.70-7.683 (m, 2H), 7.49 (d, *J* = 0.8 Hz, 1H), 7.31 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.23 (dd, *J* = 8.4, 1.6 Hz, 1H), 2.87 (q, *J* = 7.6 Hz, 2H), 2.77 (q, *J* = 7.6 Hz, 2H), 1.36 (t, *J* = 7.2 Hz, 3H), 1.30 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.7, 146.3, 140.7, 138.4, 131.1, 130.6, 128.9, 126.2, 123.6, 123.2, 118.9, 111.9, 109.4, 29.3, 28.6, 16.4, 15.7.

FT-IR (KBr): ν = 293024, 2960, 2928, 2870, 1620, 1871, 1621, 1603, 1583, 1507, 1476, 1447, 1313, 1275, 1255, 1233, 1198, 1054, 934, 907, 834, 802, 625, 565 cm^{-1}.

Elemental analysis calcd (%) for $C_{17}H_{16}N_2S$: C 81.05, H 6.35, N 12.60, found: C 72.82, H 5.75, N 9.99, S 11.44 found: C 72.67, H 5.77, N 10.07, S 11.49.



3,9-Dimethoxy-benzo[*d*]imidazo[2,1-*b*]benzothiazole (2c). Analytical TLC on silica gel, 2:8 ethyl acetate/hexane R_f = 0.25; brown solid; yield 50%.

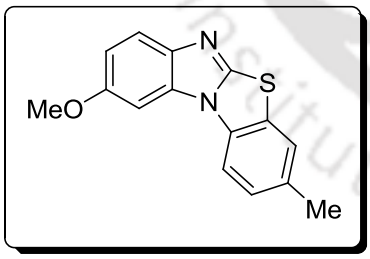
Mp: 139-141 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 8.8 Hz, 1H), 7.64 (s, 1H), 7.29 (d, *J* = 2.4 Hz, 1H), 7.17 (d, *J* = 2.4 Hz, 1H), 7.00-6.95 (m, 2H), 3.90 (s, 3H), 3.84 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 155.6, 152.8, 141.2, 130.2, 129.5, 126.3, 119.0, 113.5, 112.1, 109.4, 95.2, 56.1, 55.9.

FT-IR (KBr): ν = 2923, 2851, 1645, 1459, 1256, 1045, 1024, 998, 827, 765 cm^{-1}.

Elemental analysis calcd (%) for $C_{15}H_{12}N_2O_2S$: C 63.36, H 4.25, N 9.85, S 11.28, found: C 63.20, H 4.27, N 9.93, S 11.34.



3-Methyl-9-methoxy-benzo[*d*]imidazo[2,1-*b*]benzothiazole (2d). Analytical TLC on silica gel, 2:8 ethyl acetate/hexane R_f = 0.25; brown solid; yield 30%.

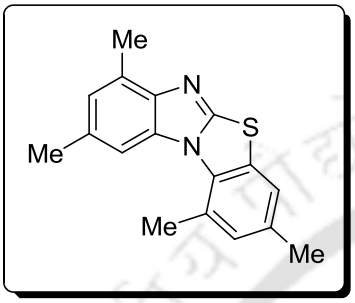
Mp: 133-135 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66 (d, *J* = 3.2 Hz, 1H), 7.64 (d, *J* = 4.0 Hz, 1H), 7.43 (s, 1H), 7.32 (d, *J* = 2.4 Hz, 1H), 7.25-7.23 (m, 1H), 6.29 (dd, *J* = 9.2, 2.8 Hz, 1H), 3.91 (s, 3H), 2.42 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 155.6, 153.7, 142.4, 134.3, 130.7, 130.6, 128.8, 127.2, 124.2, 119.5, 111.5, 111.4, 95.3, 56.0, 21.2.

FT-IR (KBr): *v* = 2921, 2829, 2049, 1887, 1623, 1504, 1481, 1382, 1244, 1207, 1151, 1108, 1056, 1030, 809, 798 cm^{-1}.

Elemental analysis calcd (%) for $C_{15}H_{12}N_2OS$: C 67.82, H 3.50, N 12.17, found: C 67.14, H 4.51, N 10.44, S 11.95, found: C 66.97, H 4.53, N 10.54, S 12.00.



1,3,7,9-Tetramethyl-benzo[*d*]imidazo[2,1-*b*]benzothiazole (2e). Analytical TLC on silica gel, 2:8 ethyl acetate/hexane R_f = 0.25; yellow liquid; yield 82%.

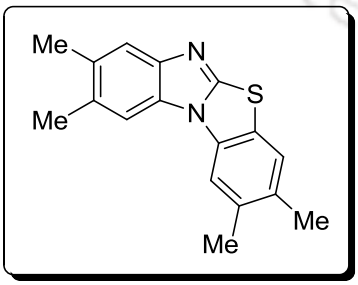
Mp: 180-182 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (s, 1H), 7.25 (s, 1H), 6.99 (d, *J* = 6.4 Hz, 2H), 3.03 (s, 3H), 2.63 (s, 3H), 2.47 (s, 3H), 2.36 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.3, 145.5, 134.3, 131.8, 131.1, 130.7, 130.4, 129.4, 128.1, 125.0, 122.8, 121.9, 110.6, 24.0, 22.1, 20.6, 16.9.

FT-IR (KBr): *v* = 3010, 2961, 2914, 2851, 2730, 1610, 1510, 1453, 1407, 1377, 1348, 1209, 1037, 845, 823, 751 cm^{-1}.

Elemental analysis calcd (%) for $C_{17}H_{16}N_2S$: C 72.82, H 5.75, N 9.99, S 11.44, found: C 72.66, H 5.78, N 10.08, S 11.48.



2,3,8,9-Tetramethyl-benzo[*d*]imidazo[2,1-*b*]benzothiazole (2f). Analytical TLC on silica gel, 2:8 ethyl acetate/hexane R_f = 0.25; yellow liquid; yield 80%.

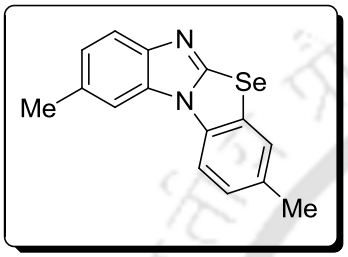
Mp: 175-177 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43 (s, 1H), 7.37 (s, 1H), 7.29(s, 1H), 7.16 (s, 1H), 2.35 (s, 3H,) 2.31 (s, 3H), 2.25 (s, 3H), 2.16 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.2, 145.2, 134.4, 131.0, 130.7, 130.6, 129.4, 128.0, 125.1, 122.8, 121.9, 110.6, 24.0, 22.1, 20.6, 16.9.

FT-IR (KBr): *v* = 3016, 2967, 2917, 2857, 2725, 1608, 1500, 1465, 1385, 1319, 1183, 1021, 997, 842 cm^{-1}.

Elemental analysis calcd (%) for $C_{17}H_{16}N_2S$: C 72.82, H 5.75, N 9.99, S 11.44, found: C 72.66, H 5.78, N 10.08, S 11.48.



3,9-Dimethyl-benzo[*d*]imidazo[2,1-*b*]benzoselazole (2i). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.30; brown solid; yield 70%.

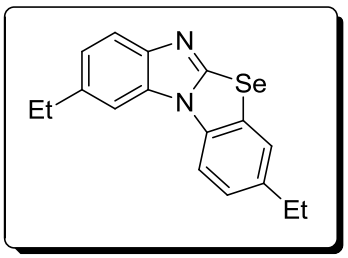
Mp: 120-122 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (d, *J* = 10.4 Hz, 1H), 7.66 (d, *J* = 6.0 Hz, 1H), 7.62 (s, 1H), 7.47 (s, 1H), 7.27 (d, *J* = 9.2 Hz, 1H), 7.16 (d, *J* = 10.4 Hz, 1H) 2.55 (s, 3H), 2.42 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.6, 145.4, 134.3, 132.0, 131.7, 127.4, 124.3, 118.1, 112.5, 110.6, 21.8, 21.0.

FT-IR (KBr): *v* = 3030, 2922, 2856, 2736, 1868, 1714, 1621, 1602, 1479, 1378, 1308, 1267, 1238, 1210, 1152, 1119, 1038, 861, 805, 736, 705, 596 cm^{-1}.

Elemental analysis calcd (%) for $C_{15}H_{12}N_2Se$: C 60.21, H 4.04, N 9.36 found: C 60.05, H 4.06, N 9.50.



3,9-Diethyl-benzo[*d*]imidazo[2,1-*b*]benzoselazole (2j). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.20; brown solid; yield 75%.

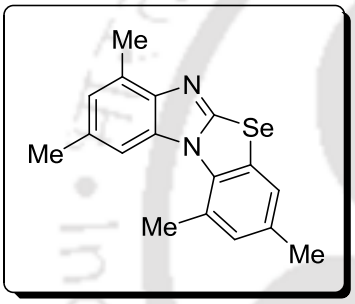
Mp: 137-139 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 10.8 Hz, 1H), 7.74 (s, 1H), 7.70 (dd, *J* = 12.0, 3.2 Hz, 1H), 7.54 (s, 1H), 7.34 (d, *J* = 10.4 Hz, 1H), 7.23 (d, *J* = 11.6 Hz, 1H), 2.90 (q, *J* = 10.4 Hz, 2H), 2.78 (q, *J* = 11.2 Hz, 2H), 1.3-1.23 (m, 6H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.1, 144.5, 141.3, 139.0, 132.3, 131.3, 128.0, 127.6, 126.1, 123.8, 117.9, 113.2, 109.7, 29.3, 28.5, 16.4, 15.6.

FT-IR (neat): *v* = 3038, 2965, 2930, 2872, 1675, 1618, 1601, 1498, 1447, 1373, 1313, 1236, 1202, 1155, 1061, 1017, 908, 872, 818, 719 cm^{-1}.

Elemental analysis calcd (%) for $C_{17}H_{16}N_2Se$: C 62.39, H 4.93, N 8.56 found: C 62.22, H 4.96, N 8.70.



1,3,7,9-Tetramethyl-benzo[*d*]imidazo[2,1-*b*]benzoselazole (2k). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.20; brown solid; yield 78%.

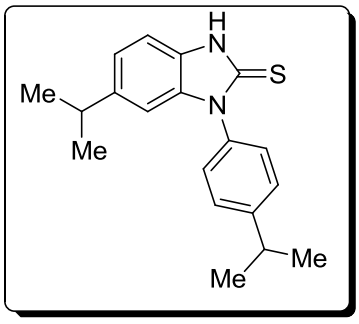
Mp: 129-131 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.82 (s, 1H), 7.27 (s, 1H), 7.02 (s, 1H), 6.98 (s, 1H), 2.96 (s, 3H), 2.64 (s, 1H) 2.47 (s, 3H), 2.35 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.1, 143.9, 135.0, 132.8, 132.4, 131.7, 131.1, 128.6, 127.4, 125.4, 125.1, 124.2, 111.5, 24.5, 22.1, 205, 16.9.

FT-IR (KBr): *v* = 3005, 2917, 2851, 1725, 1711, 1670, 1596, 1547, 1501, 1445, 1366, 1333, 1316, 1251, 1237, 1179, 1034, 822, 625 cm^{-1}.

Elemental analysis calcd (%) for $C_{17}H_{16}N_2Se$: C 62.39, H 4.93, N 8.56 found: C 62.24, H 4.95, N 8.69.



6-Isopropyl-1-(4-isopropylphenyl)-1*H*-benzo[*d*]imidazole-2(3*H*)-thione (3a). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.40; yellow solid; yield 72%.

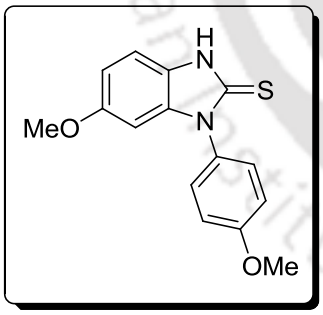
Mp: 175-177 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 12.09 (br, 1H), 7.46 (s, 4H), 7.24(d, *J* = 8.0 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 6.80 (s, 1H), 3.07 (q, *J* = 6.8 Hz, 1H), 2.93 (q, *J* = 7.2 Hz, 1H), 1.35 (d, *J* = 6.8 Hz, 3H), 1.21 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.7, 149.8, 144.7, 134.5, 133.1, 129.2, 127.8, 127.7, 122.3, 110.1, 107.9, 34.4, 34.1, 24.4, 24.0.

FT-IR (KBr): *ν* = 3124, 3042, 2958, 2868, 2703, 1614, 1514, 1491, 1440, 1384, 1357, 1324, 1248, 1225, 1176, 1058, 1017, 808, 739, 617 cm^{-1}.

Elemental analysis calcd (%) for $C_{19}H_{22}N_2S$: C 73.51, H 7.14, N 9.02, S 10.33, found: C 73.37, H 7.16, N 9.10, S 10.37.



6-Methoxy-1-(4-methoxyphenyl)-1*H*-benzo[*d*]imidazole-2(3*H*)-thione (3b). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.37; brown solid; yield 80%.

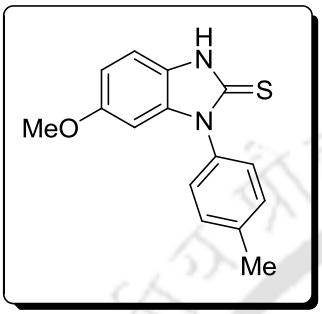
Mp: 158-160 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.94 (br, 1H), 7.41 (d, *J* = 8.8 Hz, 2H), 7.15 (d, *J* = 8.8 Hz, 1H), 7.08 (d, *J* = 8.8 Hz, 2H), 6.77 (d, *J* = 8.8 Hz, 1H), 6.42 (d, *J* = 2.0 Hz, 1H), 3.86 (s, 3H), 3.70 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$:DMSO-d_6 2:1): δ = 168.6, 158.9, 155.7, 134.5, 128.4, 127.4, 124.7, 120.1, 114.1, 113.3, 110.0, 94.2, 55.1, 54.8.

FT-IR (KBr): *v* = 3081, 3000, 2950, 2929, 2829, 2697, 2049, 1895, 1720, 1615, 1585, 1517, 1496, 1464, 1348, 1302, 1254, 1216, 1171, 1149, 1122, 1029, 832, 612 cm^{-1}.

Elemental analysis calcd (%) for $C_{15}H_{14}N_2O_2S$: C 62.92, H 4.93, N 9.78, S 11.20, found: C 62.77, H 4.95, N 9.86, S 11.27.



6-Methoxy-1-*p*-tolyl-1*H*-benzo[*d*]imidazole-2(3*H*)-thione (3c). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.36; brown solid; yield 75%.

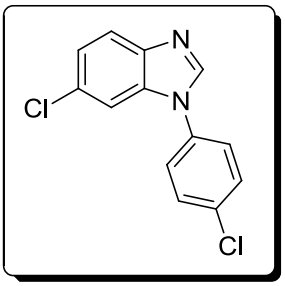
Mp: 155-157 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41 (d, *J* = 9.2 Hz, 2H), 7.16(d, *J* = 8.0Hz, 1H), 7.08 (d, *J* = 8.8 Hz, 2H), 7.00 (d, *J* = 8.0 Hz, 1H), 6.71 (s, 1H), 3.87 (s, 3H), 2.56 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.6, 159.9, 134.6, 133.1, 129.9, 128.9, 128.0, 124.7, 114.9, 110.2, 110.0, 55.6, 21.5.

FT-IR (KBr): *v* = 3137, 3057, 2956, 2930, 2835, 2049, 1860, 1610, 1583, 1517, 1500, 1455, 1381, 1338, 1283, 1256, 1209, 1170, 1105, 1027, 831, 799, 695, 612, 580 cm^{-1}.

Elemental analysis calcd (%) for $C_{15}H_{14}N_2OS$: C 66.64, H 5.22, N 10.36, S 11.86, found: C 66.54, H 5.21, N 10.44, S 11.91.



6-Chloro-1-(4-chlorophenyl)-1*H*-benzo[*d*]imidazole (4a). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.40; yellow solid; yield 72%.

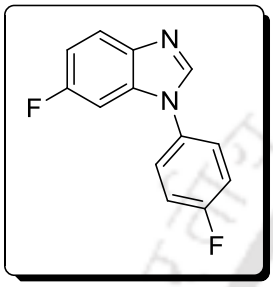
Mp: 110-112 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (s, 1H), 7.75 (d, *J* = 8.4, Hz, 1H), 7.54 (dd, *J* = 6.8, 2.0 Hz, 2H), 7.43-7.39 (m, 3H), 7.28 (dd, *J* = 8.4, 2.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.7, 142.0, 134.0, 133.8, 130.2, 129.6, 125.0, 123.6, 121.2, 110.3.

FT-IR (KBr): *v* = 3091, 3032, 2994, 1692, 1610, 1595, 1505, 1461, 1296, 1281, 1235, 1202, 1149, 1090, 836, 798, 553 cm^{-1}.

Elemental analysis calcd (%) for $C_{13}H_8Cl_2N_2$: C 59.34, H 3.06, N 10.65 found: C 59.18, H 3.09, N 10.78.



6-Fluoro-1-(4-fluorophenyl)-1*H*-benzo[*d*]imidazole (4b). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.40; yellow solid; yield 70%.

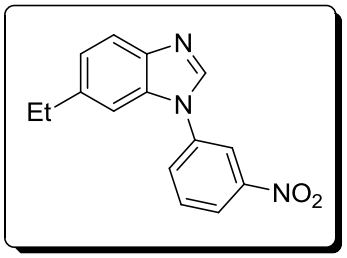
Mp: 109-111 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06 (s, 1H), 7.81-7.77 (m, 1H), 7.48-7.45 (m, 2H), 7.30-7.26 (m, 2H), 7.14-7.06 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.5, 161.6, 161.0, 159.2, 143.0, 140.3, 134.2, 132.1, 126.1 (d, *J* = 8.3 Hz), 121.6 (d, *J* = 9.9 Hz), 117.4 (d, *J* = 22.7 Hz), 111.7 (d, *J* = 25.0 Hz), 97.2 (d, *J* = 28.0 Hz).

FT-IR (KBr): *v* = 2917, 2846, 1625, 1516, 1259, 1208, 1152, 1094, 832, 803, 738 cm^{-1}.

Elemental analysis calcd (%) for $C_{13}H_8F_2N_2$: C 67.82, H 3.50, N 12.17, found: C 67.69, H 3.52, N 12.18.



6-Ethyl-1-(3-nitrophenyl)-1*H*-benzo[*d*]imidazole (4c). Analytical TLC on silica gel, 5:5 ethyl acetate/hexane R_f = 0.40; yellow solid; yield 75%.

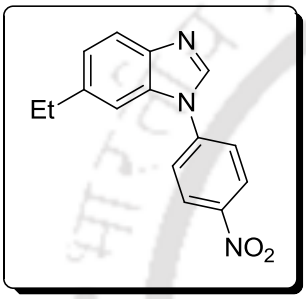
Mp: 158-160 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.37 (t, *J* = 2.0, Hz, 1H), 8.29-8.26 (m, 1H), 8.10 (s, 1H), 7.87-7.84 (m, 1H), 7.78-7.73 (m, 2H),7.30 (s, 1H), 7.20 (dd, *J* = 8.4, 2.0 Hz, 1H), 2.78 (q, 2H),1.26 (t, *J* = 7.6, Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.6, 141.3, 141.2, 140.8, 136.9, 132.7, 130.8, 129.1, 123.6, 121.9, 119.7, 118.1, 108.4, 28.8, 15.7.

FT-IR (KBr): *v* = 3095, 2965, 2931, 2872, 1615, 1533, 1500, 1451, 1350, 1295, 1235, 1203, 1090, 821, 769, 738, 680 cm^{-1}.

Elemental analysis calcd (%) for $C_{15}H_{13}N_3O_2$: C 67.40, H 4.90, N 15.72 found: C 67.27, H 4.92, N 15.83.



6-Ethyl-1-(4-nitrophenyl)-1*H*-benzo[*d*]imidazole (4d). Analytical TLC on silica gel, 4:6 ethyl acetate/hexane R_f = 0.36; yellow solid; yield 75%.

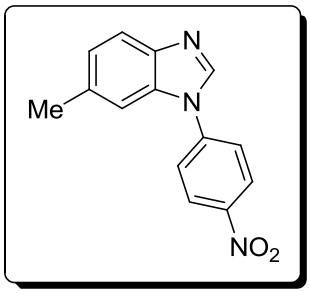
Mp: 166-168 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.49 (d, *J* = 9.2 Hz, 2H), 8.15 (s, 1H), 7.80 (d, *J* = 8.4 Hz, 1H), 7.75 (d, *J* = 9.2 Hz, 2H), 7.41 (s, 1H), 7.26 (s, 1H), 2.81 (q, *J* = 7.6 Hz, 2H), 1.31 (t, *J* = 7.6, Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.5, 142.2, 141.7, 141.5, 141.4, 133.0, 128.9, 125.8, 124.8, 124.3, 123.7, 120.5, 109.1, 29.3, 16.2.

FT-IR (KBr): *v* = 3085, 3032, 2960, 2934, 2868, 1594, 1505, 1446, 1336, 1195, 1107, 852, 811, 751 cm^{-1}.

Elemental analysis calcd (%) for $C_{15}H_{13}N_3O_2$: C 67.40, H 4.90, N 15.72 found: C 67.27, H 4.93, N 15.82.



6-Methyl-1-(4-nitrophenyl)-1*H*-benzo[*d*]imidazole (4e). Analytical TLC on silica gel, 4:6 ethyl acetate/hexane R_f = 0.36; yellow solid; yield 73%.

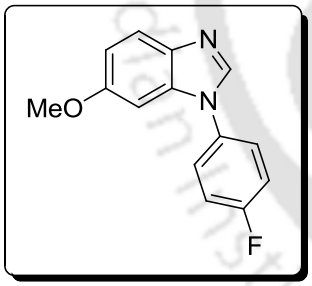
Mp: 164-166 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.62 (s, 1H), 8.44 (d, *J* = 9.2 Hz, 2H), 8.00 (d, *J* = 9.2 Hz, 2H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.56 (s, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 2.45 (s, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 145.4, 142.5, 142.2, 141.3, 133.6, 132.4, 125.3, 124.5, 123.3, 119.7, 110.6, 21.3.

FT-IR (KBr): *v* = 23071, 2920, 2857, 2434, 1596, 1516, 1445, 1348, 1297, 1188, 1114, 1037, 932, 854, 804, 691 cm^{-1}.

Elemental analysis calcd (%) for $C_{14}H_{11}N_3O_2$: C 66.40, H 4.38, N 16.59 found: C 66.34, H 4.40, N 16.73.



1-(4-Fluorophenyl)-6-methoxy-1*H*-benzo[*d*]imidazole (4f). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.30; brown solid; yield 60%.

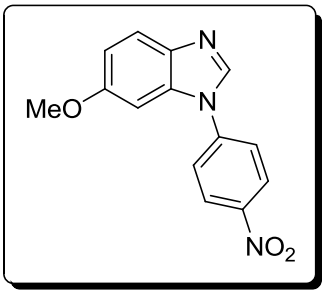
Mp: 90-92 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (s, 1H), 7.18 (d, *J* = 9.2 Hz, 1H), 7.46-7.43 (m, 2H), 7.27 (t, *J* = 10.0 Hz, 2H), 6.96 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.87 (dd, *J* = 2.0 Hz, 1H) 3.80 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.2, 160.7, 157.5, 141.5, 137.7, 134.4, 132.3, 126.1 (d, *J* = 8.4 Hz), 120.8, 117.1 (d, *J* = 22.1 Hz), 115.2, 112.4, 93.7, 55.8.

FT-IR (KBr): *v* = 2960, 2928, 2862, 1639, 1517, 1489, 1289, 1265, 1229, 1053, 812, 740 cm^{-1}.

Elemental analysis calcd (%) for $C_{14}H_{11}N_2FO$: C 69.41, H 4.58, N 11.56, found: C 69.24, H 4.60, N 11.71.



6-Methoxy-1-(4-nitrophenyl)-1*H*-benzo[*d*]imidazole (4g). Analytical TLC on silica gel, 5:5 ethyl acetate/hexane R_f = 0.40; yellow solid; yield 75%.

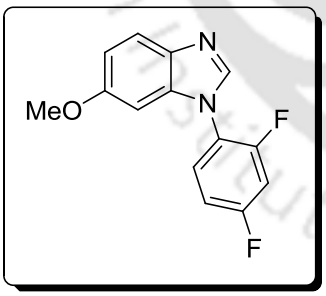
Mp: 171-173 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 (d, *J* = 10.0 Hz, 1H), 7.94 (s, 1H), 7.59-7.53 (m, 3H), 6.86 (d, *J* = 2.0 Hz, 1H), 6.82-6.79 (m, 1H), 3.67 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$: DMSO-d_6 1:3): δ = 157.5, 146.0, 141.4, 140.7, 138.2, 133.1, 125.5, 124.7, 123.3, 120.9, 117.6, 112.4, 93.8, 55.6.

FT-IR (KBr): *v* = 3111, 3076, 2961, 2840, 2439, 1698, 1595, 1522, 1508, 1342, 1215, 1110, 1027, 938, 828, 749 cm^{-1}.

Elemental analysis calcd (%) for $C_{14}H_{11}N_3O_3$: C 62.45, H 4.12, N 15.61, found: C 62.30, H 4.14, N 15.74.



1-(2,4-Difluorophenyl)-6-methoxy-1*H*-benzo[*d*]imidazole (4j). Analytical TLC on silica gel, 3:7 ethyl acetate/hexane R_f = 0.30; brown solid; yield 55%.

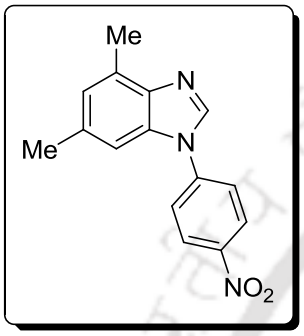
Mp: 91-93 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 1.6 Hz, 1H), 7.72 (d, *J* = 8.8 Hz, 1H), 7.49-7.43 (m, 1H), 7.12-7.04 (m, 2H), 6.96 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.70 (d, *J* = 1.6 Hz, 1H), 3.79 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.6 (d, *J* = 10.6 Hz), 161.1 (d, *J* = 10.7 Hz), 158.1 (d, *J* = 12.2 Hz), 157.5, 155.6 (d, *J* = 12.2 Hz), 141.9, 137.6, 134.8, 128.5 (d, *J* = 10.0 Hz), 120.9, 120.4 (d, *J* = 12.9 Hz), 112.3 (t, *J* = 22.9 Hz), 105.7 (t, *J* = 25.9 Hz), 93.7, 55.8.

FT-IR (KBr): *v* = 2923, 2862, 1638, 1500, 1329, 1300, 1282, 1176, 1111, 790, 743, 695 cm^{-1}.

Elemental analysis calcd (%) for $C_{14}H_{10}N_2F_2$: C 64.61, H 3.87, N 10.76, found: C 64.43, H 3.89, N 10.92.



4,6-Dimethyl-1-(4-nitrophenyl)-1*H*-benzo[*d*]imidazole (4k). Analytical TLC on silica gel, 4:6 ethyl acetate/hexane R_f = 0.30; yellow solid; yield 85%.

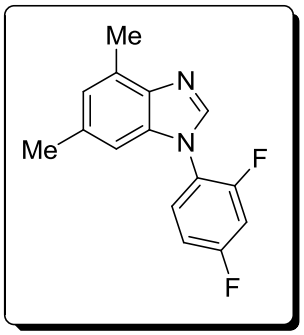
Mp: 181-183 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.44 (d, *J* = 9.2 Hz, 2H), 8.08 (s, 1H), 7.70 (d, *J* = 9.2 Hz, 2H), 7.20 (s, 1H), 7.01 (s, 1H), 2.65 (s, 3H), 2.44 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.3, 141.9, 141.6, 140.2, 134.7, 132.6, 130.5, 125.8, 125.7, 124.8, 123.6, 107.6, 21.8, 16.6.

FT-IR (KBr): *v* = 3091, 2915, 2846, 2439, 1950, 1597, 1520, 1456, 1347, 1296, 1280, 1193, 1185, 1138, 1108, 1031, 943, 855, 749, 696, 658 cm^{-1}.

Elemental analysis calcd (%) for $C_{15}H_{13}N_3O_2$: C 67.40, H 4.90, N 15.72, found: C 67.23, H 4.91, N 15.84.



1-(2,4-Difluorophenyl)-4,6-dimethyl-1*H*-benzo[*d*]imidazole (4l). Analytical TLC on silica gel, 2:8 ethyl acetate/hexane R_f = 0.41; brown solid; yield 60%.

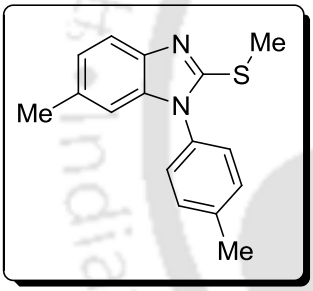
Mp: 90-92 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 1.2 Hz, 1H), 7.48-7.43 (m, 1H), 7.11-7.03 (m, 2H), 6.96 (s, 1H), 6.90 (s, 1H), 2.66 (s, 3H), 2.41 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.5 (d, *J* = 10.7 Hz), 161.0 (d, *J* = 10.7 Hz), 158.2 (d, *J* = 12.9 Hz), 155.6 (d, *J* = 12.2 Hz), 141.5, 140.7, 134.0, 130.0, 128.5 (d, *J* = 10.0 Hz), 125.1, 120.7 (d, *J* = 13.0 Hz), 112.2 (t, *J* = 18.3 Hz), 107.5, 105.7 (t, *J* = 23.6 Hz), 21.7, 16.6.

FT-IR (KBr): *v* = 3097, 3019, 2972, 2919, 2857, 1934, 1725, 1610, 1602, 1522, 1461, 1435, 1340, 1300, 1272, 1272, 1230, 1195, 1145, 1106, 1034, 969, 855, 835, 680, 598 cm^{-1}.

Elemental analysis calcd (%) for $C_{15}H_{12}N_2F_2$: C 69.76, H 4.69, N 10.85,found: C 69.60, H 4.71, N 10.99.



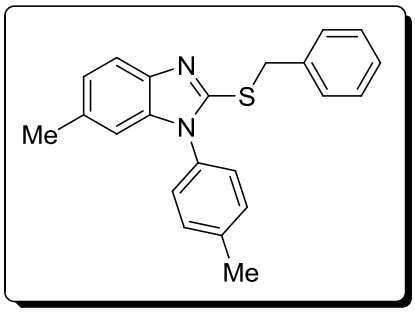
6-Methyl-2-(methylthio)-1-*p*-tolyl-1*H*-benzo[*d*]imidazole (4m). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.20; colourless liquid; yield 90%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60 (d, *J* = 8.0 Hz, 1H), 7.32-7.26 (m, 4H), 7.04 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.88 (d, *J* = 0.8 Hz, 1H), 2.70 (s, 3H), 2.42 (s, 3H), 2.36 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.7, 141.7, 138.9, 137.7, 132.6, 132.0, 130.4, 130.0, 126.7, 123.5, 117.5, 114.7, 109.3, 21.6, 21.2, 14.6.

FT-IR (neat): *v* = 3032, 2923, 2857, 2730, 1609, 1511, 1484, 1444, 1325, 1311, 1268, 1231, 988, 808, 714, 609 cm^{-1}.

Elemental analysis calcd (%) for $C_{16}H_{16}N_2S$: C 71.61, H 6.01, N 10.44, S 11.95, found: C 71.42, H 6.04, N 10.53, S 12.01.



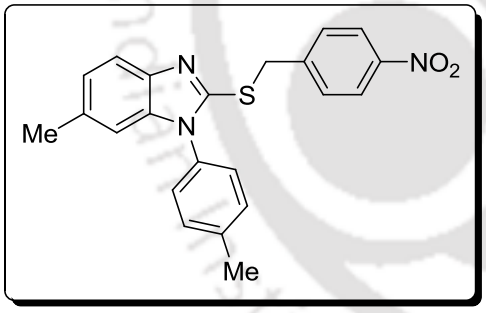
2-Benzylthio-6-methyl-1-*p*-tolyl-1*H*-benzo[d]imidazole (4n). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.25; yellow liquid; yield 93%.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 8.4 Hz, 1H), 7.36 (d, *J* = 7.4 Hz, 2H), 7.26-7.17(m, 7H), 7.06 (d, *J* = 8.0, 1H), 6.88 (s, 1H), 4.57 (s, 3H), 2.36 (s, 6H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.6, 141.9, 139.0, 137.8, 136.7, 132.7, 132.3, 130.4, 129.3, 128.7, 127.6, 126.8, 123.8, 117.9, 109.6, 36.9, 21.8, 21.3.

FT-IR (neat): *v* = 3230, 3188, 3053, 2923, 2840, 1625, 1601, 1572, 1492, 1446, 1248, 921, 744, 720, 592 cm^{-1}.

Elemental analysis calcd (%) for $C_{22}H_{20}N_2S$: C 76.71, H 5.85, N 8.13, S 9.31, found: C 76.51, H 5.87, N 8.23, S 9.39.



2-(4-Nitrobenzylthio)-6-methyl-1-*p*-tolyl-1*H*-benzo[d]imidazole (4o). Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.25; white solid; yield 97%.

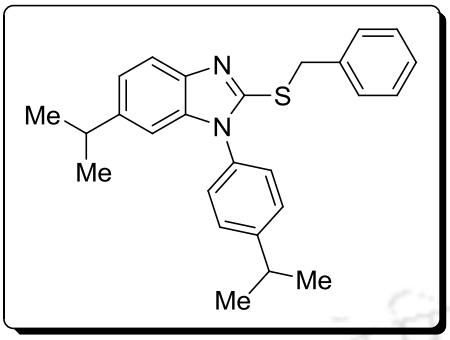
Mp: 123-125 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10 (d, *J* = 8.8 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 1H),7.57(d, *J* = 8.8 Hz, 2H),7.33 (d, *J* = 8.4 Hz, 2H),7.22 (d, *J* = 8.4 Hz, 2H),7.08-7.05 (m, 1H), 6.89 (d, *J* = 0.8 Hz,1H), 4.60 (s, 3H), 2.43 (s, 3H), 2.38 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.2, 147.1, 145.1, 141.4, 139.2, 137.7, 132.6, 132.3, 130.5, 130.0, 126.7, 123.9, 123.6, 117.8, 109.6, 35.6, 21.7, 21.3.

FT-IR (KBr): *v* = 3060, 3036, 2926, 2857, 2445, 1936, 1906, 1868, 1796, 1733, 1677, 1598, 1508, 1435, 1329, 1226, 1107, 1015, 900, 804, 726, 599 cm^{-1}.

Elemental analysis calcd (%) for $C_{22}H_{19}N_3O_2S$: C 67.84, H 4.92, N 10.79, S 8.23, found: C 67.69, H 4.94, N 10.87, S 8.28.



2-Benzylthio-6-isopropyl-1-(4-isopropylphenyl)-1*H*-benzo[*d*]imidazole (4p).

Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.25; yellow solid; yield 95%. Mp: 139-141 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (d, *J* = 8.4 Hz, 1H), 7.39-7.35 (m, 4H), 7.30-722 (m, 5H), 7.16 (dd, *J* = 8.4, 1.6 Hz, 1H),6.96 (d, *J* = 1.6 Hz, 1H), 4.58(s, 3H), 3.02-2.92 (m, 2H), 1.31 (s, 3H), 1.29 (s, 3H), 1.25 (s, 3H), 1.23 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.9, 149.7, 143.8, 143.0, 137.6, 136.6, 132.9, 129.3, 128.7, 127.8, 127.6, 126.9, 121.2, 118.0, 107.0, 36.9, 34.6, 34.0, 24.7, 24.0.

FT-IR (KBr): *v* = 3027, 3006, 2960, 2926, 2867, 1906, 1617, 1512, 1441, 1274, 1226, 1102, 828, 710, 614 cm^{-1}.

Elemental analysis calcd (%) for $C_{26}H_{28}N_2S$: 77.96, H 7.05, N 6.99, S 8.00, found: C 77.88, H 7.07, N 7.09, S 7.96.

Single Crystal X-ray Structure of 2a

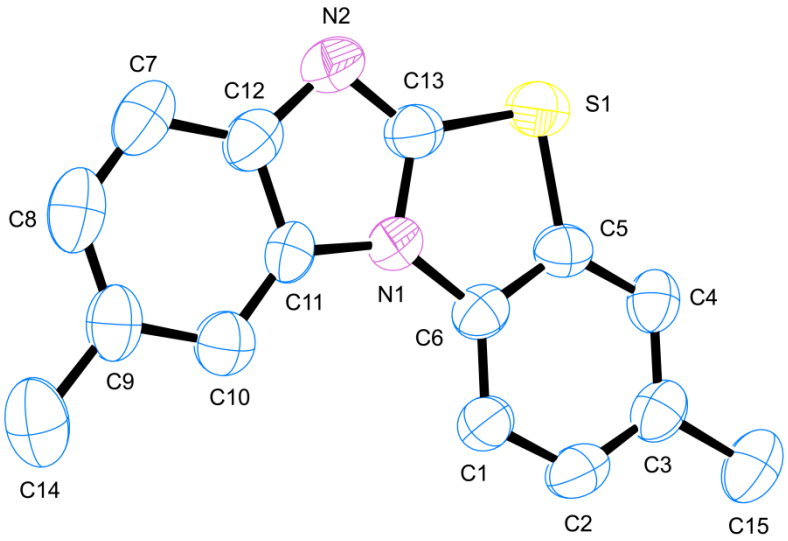


Figure 2. ORTEP diagram of the single-crystal X-ray structure of 3,9-dimethyl-benzo[*d*]imidazo[2,1-*b*]benzothiazole **2a.** Thermal ellipsoids are drawn at a 50% probability level. H-Atoms are omitted for clarity (CCDC 924487).

Crystal Data and Structure Refinement for 2a at 296(2) K

Identification code	123	
Empirical formula	$C_{15}H_{12}N_2S$	
Formula weight	252.33	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
	Loop xyz	
	'x, y, z' '-x, -y, -z'	
Unit cell dimensions	*a* = 9.075 (10) Å	α(°) = 111.015 (5)
	b = 10.8169 (15) Å	β(°) = 92.346(7)
	c = 14.0918 (18) Å	γ(°) = 100.762(7)
Volume	1260.1(3) $Å^3$	
Z	4	
Density (calculated)	1.330Mg/m^3	
Absorption coefficient	0.238mm^{-1}	

F(000)	528
Crystal size	0.32 x 0.25 x 0.18 mm
Theta range for data collection	1.56 to 25.24 °
Index ranges	-10<=h<=10, -12<=k<=12, -16<=l<=16
Reflections collected	4502
Independent reflections	2835
Completeness to theta = 25.24°	99.0 %
Absorption correction	Multi-scan
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4502 / 0 /329
Goodness-of-fit on F^2	1.002
Final R indices [I>2sigma (I)]	*R1* = 0.01021, *wR2* = 0.1906
R indices (all data)	*R1* = 0.0725, *wR2* = 0.1787

Single Crystal X-ray Structure of 3b

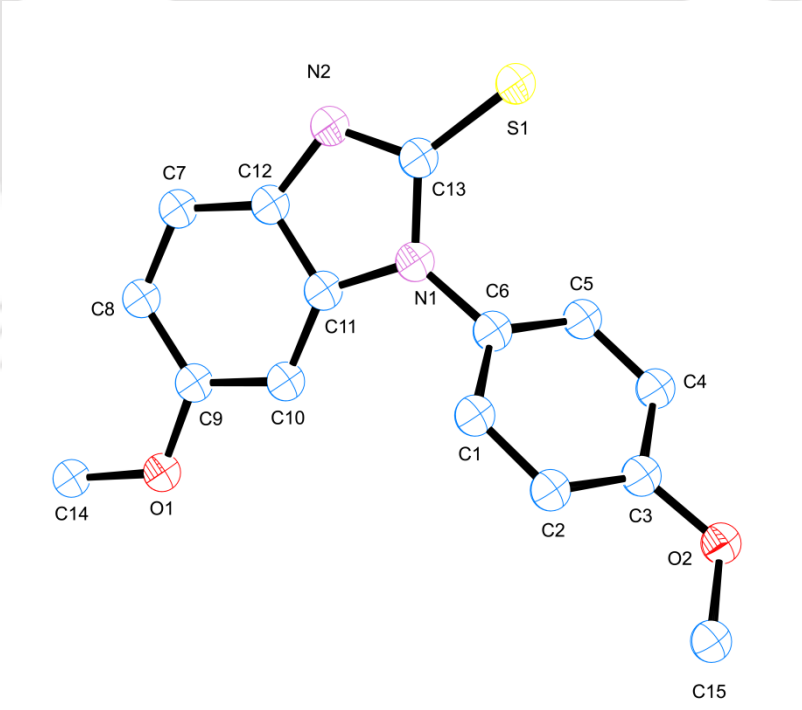


Figure 3. ORTEP diagram of the single-crystal X-ray structure of 6-methoxy-1-(4-methoxyphenyl)-1*H*-benzo[*d*]imidazole-2(3*H*)-thione **3b.** Thermal ellipsoids are drawn at 50% probability level. H-Atoms are omitted for clarity (CCDC 924488).

Crystal Data and Structure Refinement for 2p at 296(2) K

Identification code	kk	
Empirical formula	$C_{15}H_{14}N_2O_2S$	
Formula weight	286.34	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
	Loop xyz	
	'x, y, z' '-x, -y, -z'	
Unit cell dimensions	*a* = 9.2821 (10) Å	α(°) = 86.286(5)
	b = 9.8225 (10) Å	β(°) = 79.493(6)
	c = 15.9680 (17) Å	γ(°) = 77.163(5)
Volume	844.64 (12) $Å^3$	
Z	1395.2(3) $Å^3$	
Density (calculated)	4	
Absorption coefficient	1.363 Mg/m^3	
F(000)	0.234 mm^{-1}	
Crystal size	600.0	
Theta range for data collection	0.32 x 0.25 x 0.19 mm	
Index ranges	1.30 to 25.50 °	
Reflections collected	-11<=h<=11, -11<=k<=11, -18<=l<=19	
Independent reflections	5146	
Completeness to theta = 25.25 °	3940	
Absorption correction	99.1 %	
Refinement method	Multi-scan	
Data / restraints / parameters	Full-matrix least-squares on F^2	
Goodness-of-fit on F^2	5146 / 0 /365	
Final R indices [I>2sigma (I)]	1.066	
R indices (all data)	*R1* = 0.0525, *wR2* = 0.920	

Single Crystal X-ray Structure of 4g

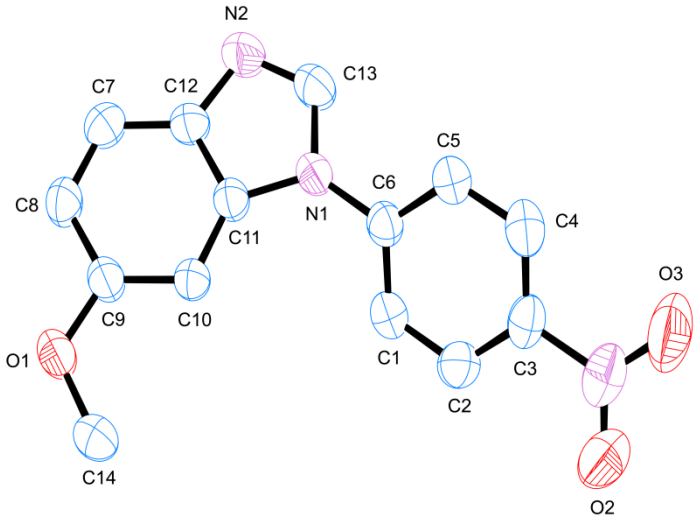


Figure 4. ORTEP diagram of the single-crystal X-ray structure of 6-Methoxy-1-(4-nitrophenyl)-1*H*-benzo[*d*]imidazole **4g.** Thermal ellipsoids are drawn at a 50% probability level. H-Atoms are omitted for clarity (CCDC 924486).

Crystal Data and Structure Refinement for 4g at 296(2) K

Identification code	11	
Empirical formula	$C_{14}H_{11}N_3O_3$	
Formula weight	269.26	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	*P-1*	
	Loop xyz	
	'x, y, z' '-x, -y, -z'	
Unit cell dimensions	*a* = 7.9271(3) Å	α(°) = 94.799(2)
	b = 8.3482(3) Å	β(°) = 102.504(2)
	c = 10.2367(4) Å	γ(°) = 105.761(2)
Volume	629.14(4) $Å^3$	
Z	2	
Density (calculated)	1.421Mg/m^3	
Absorption coefficient	0.103 mm^{-1}	

F(000)	280
Crystal size	0.32 x 0.25 x 0.19 mm
Theta range for data collection	2.06 to 28.34 °
Index ranges	-9<=h<=10, -11<=k<=11, -13<=l<=13
Reflections collected	3108
Independent reflections	1969
Completeness to theta = 24.31 °	98.9%
Absorption correction	Multi-scan
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3108 / 0 /182
Goodness-of-fit on F^2	1.142
Final R indices [I>2sigma (I)]	*R1* = 0.0783, *wR2* = 0.1858
R indices (all data)	*R1* = 0.0595, *wR2* = 0.1732

4.6 References

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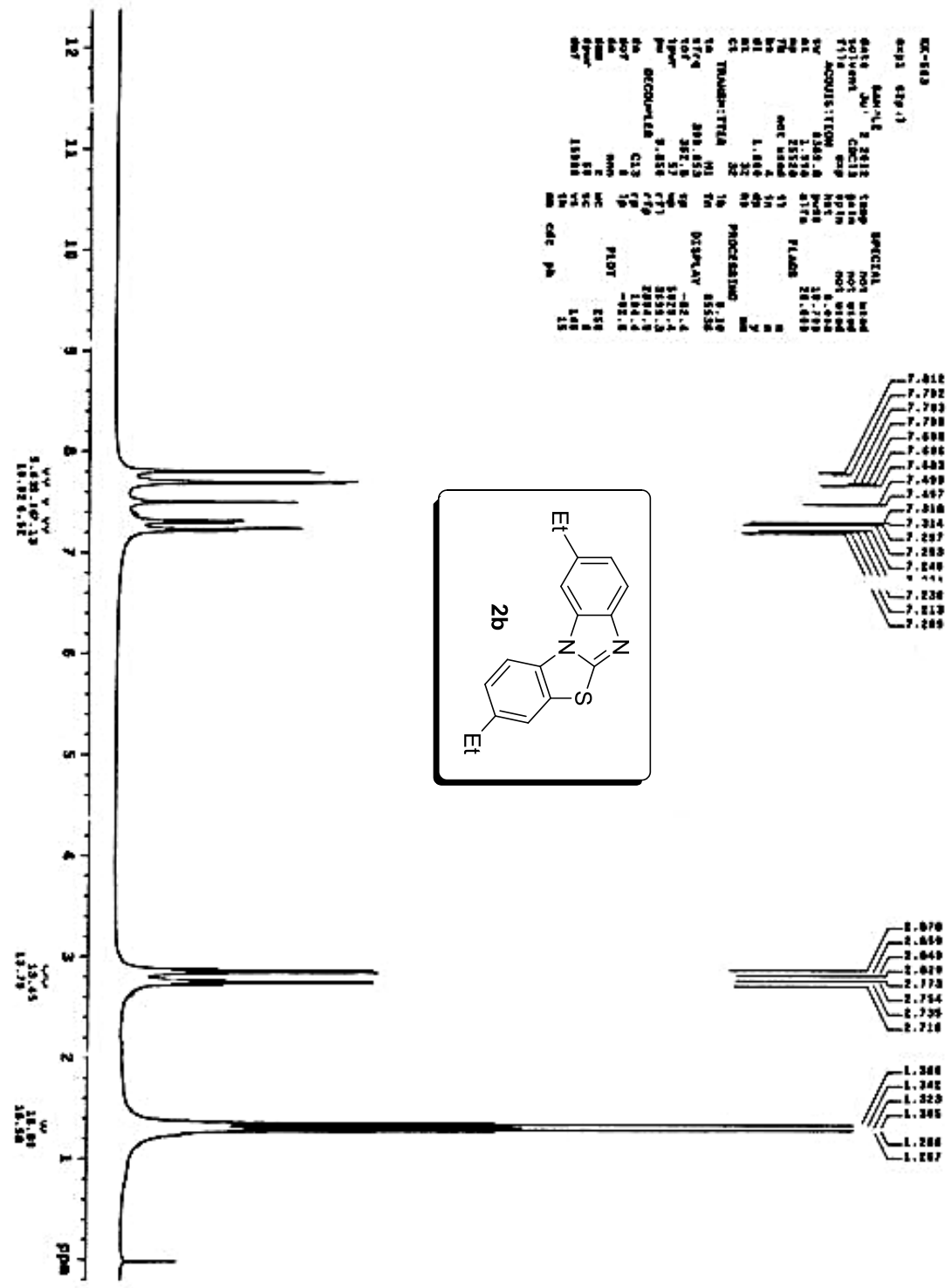

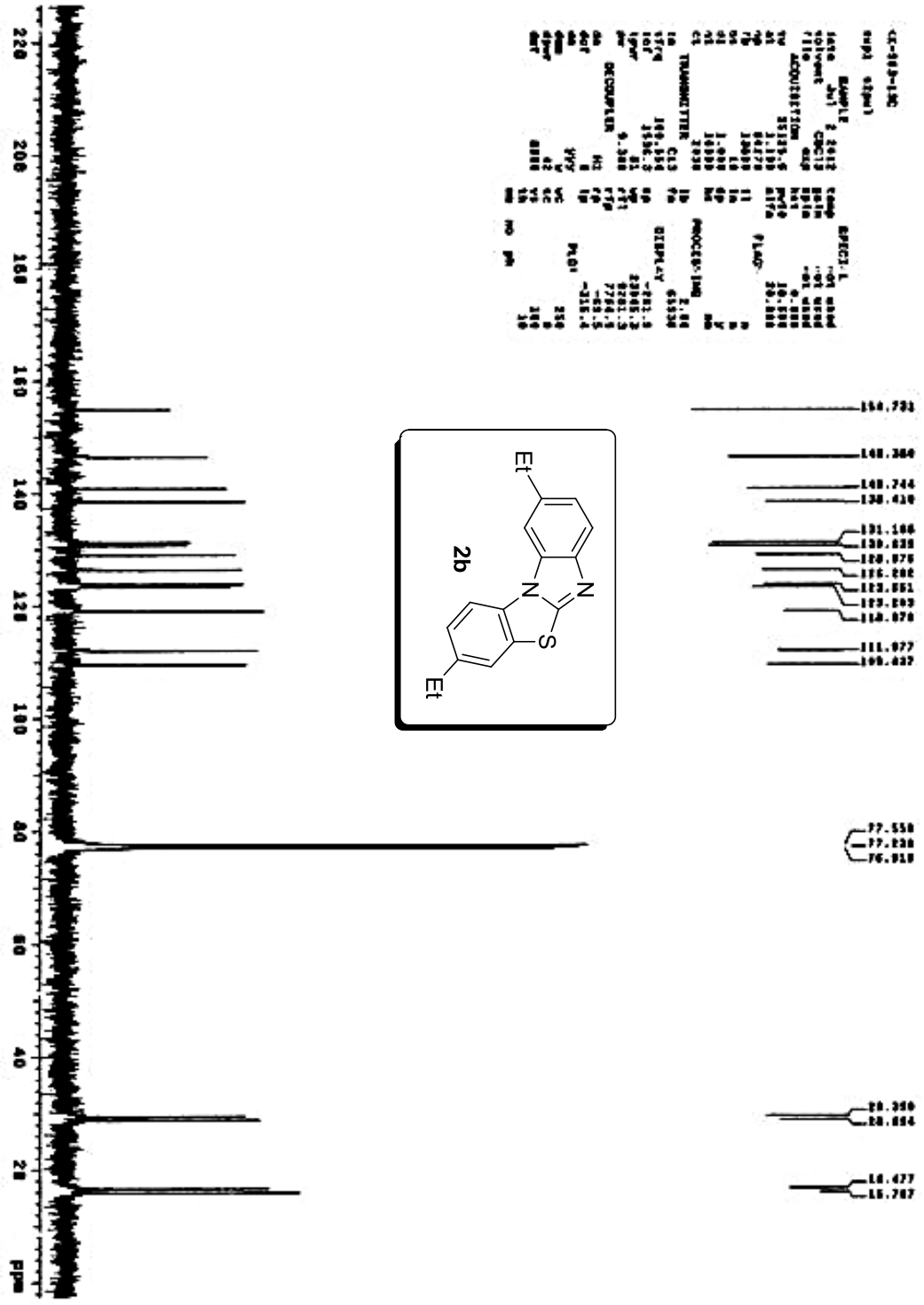

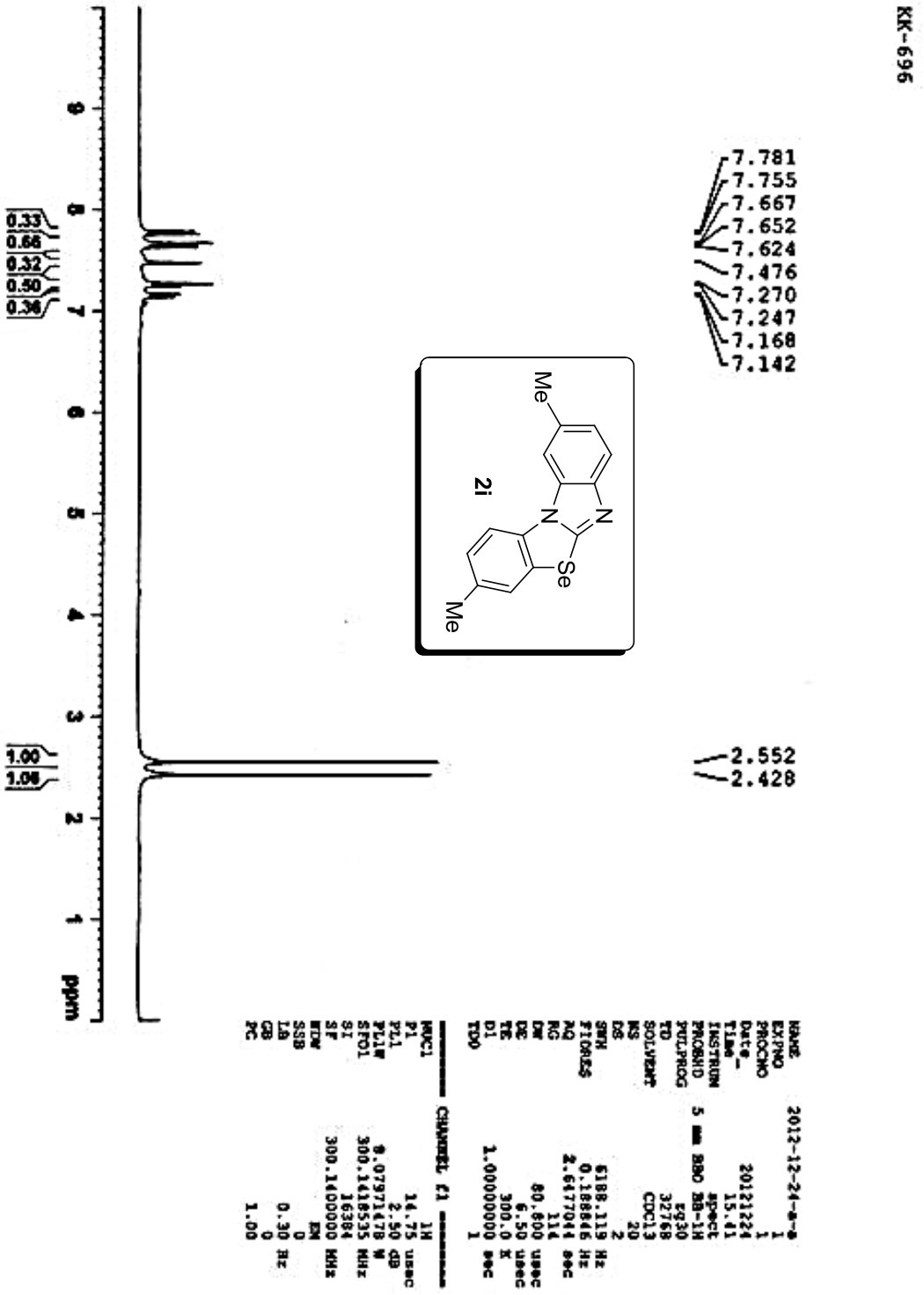

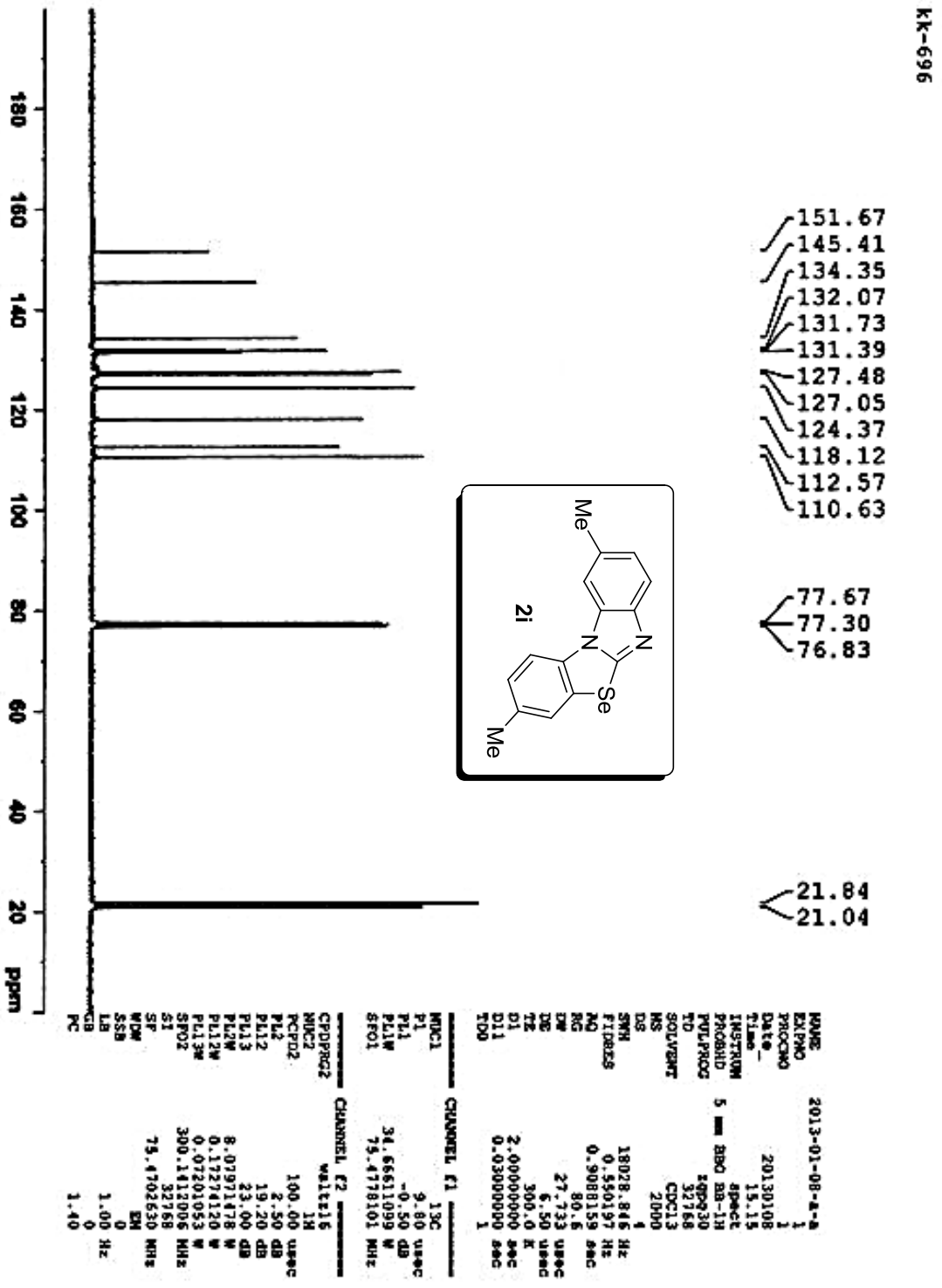

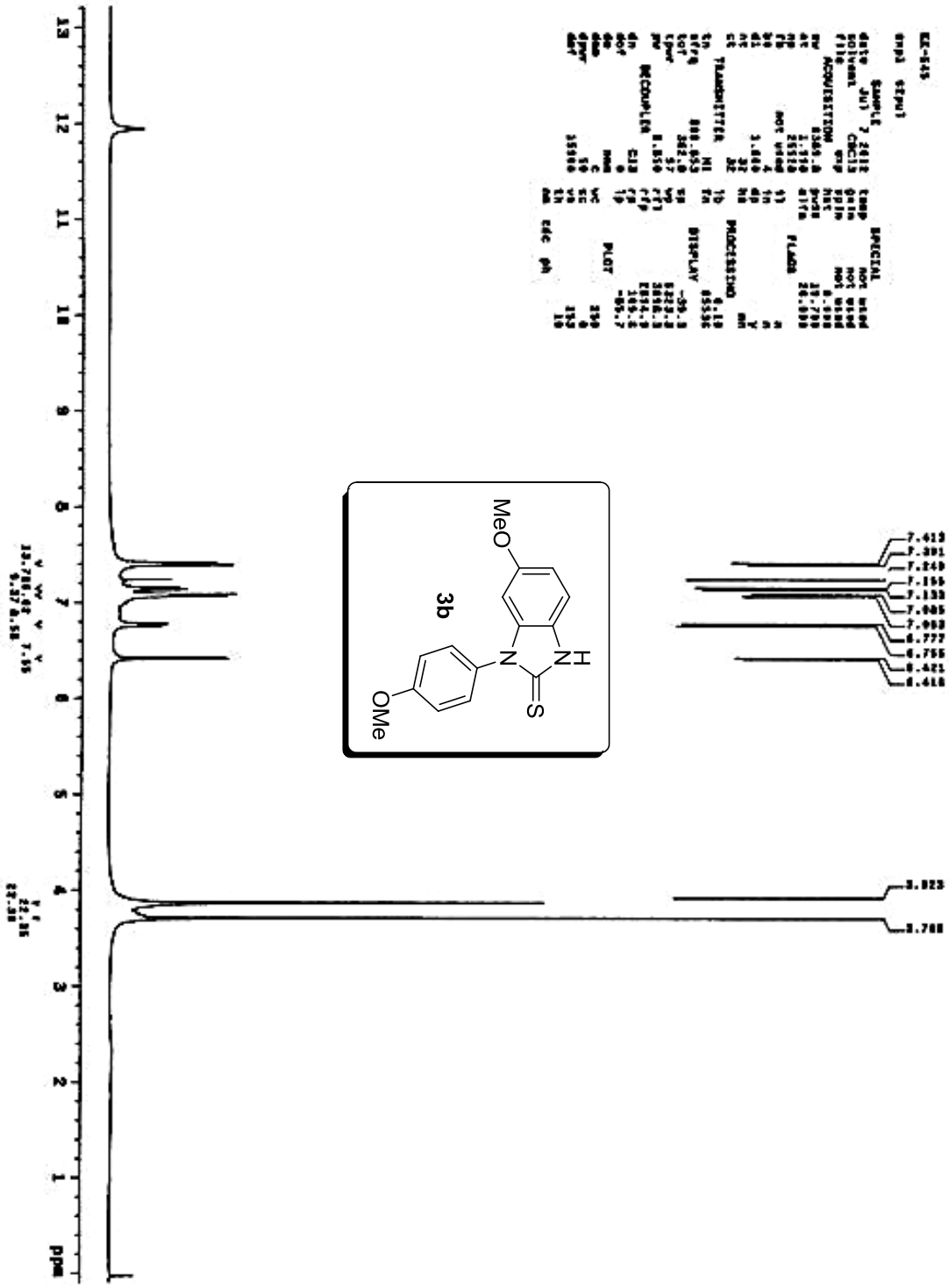

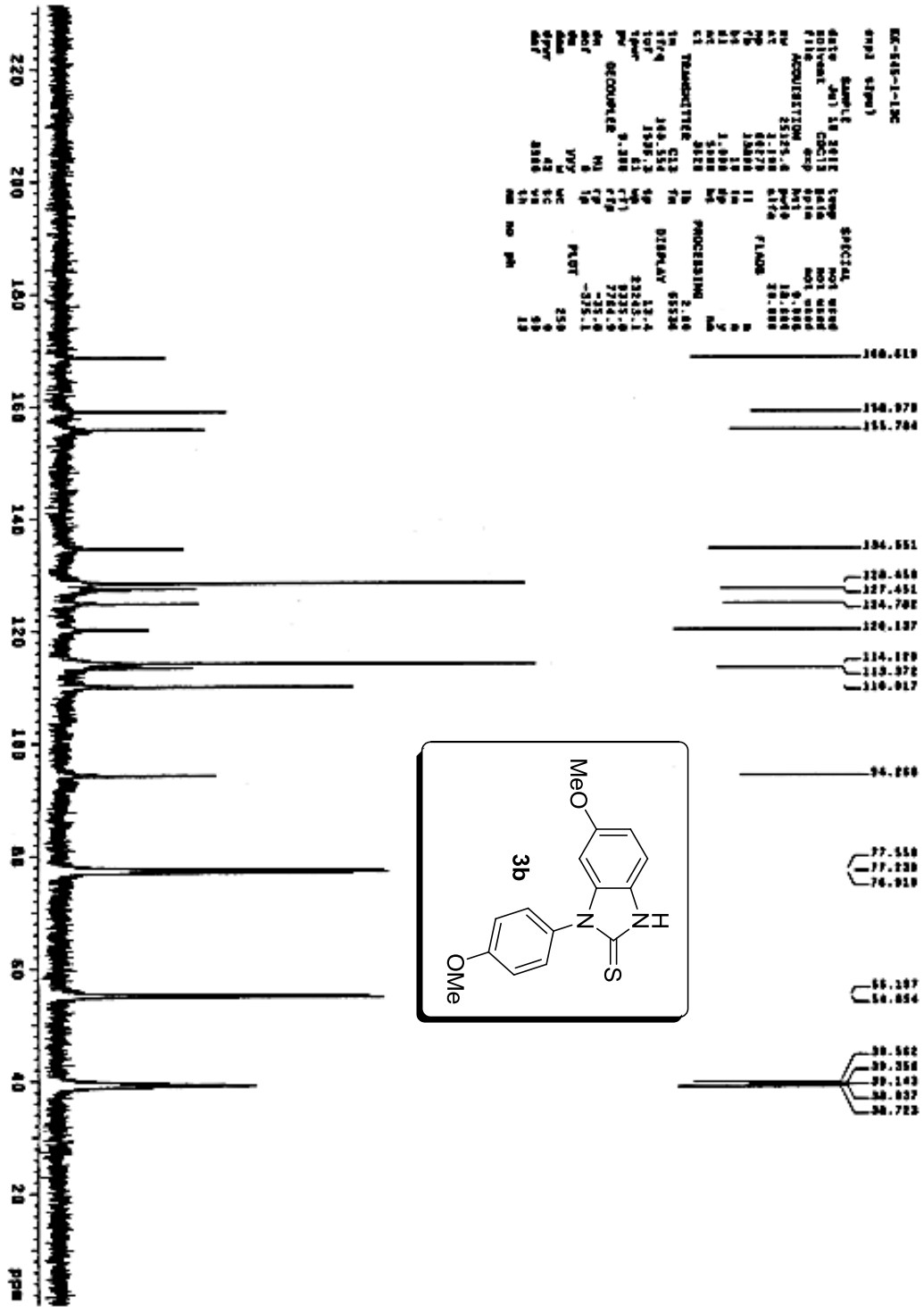

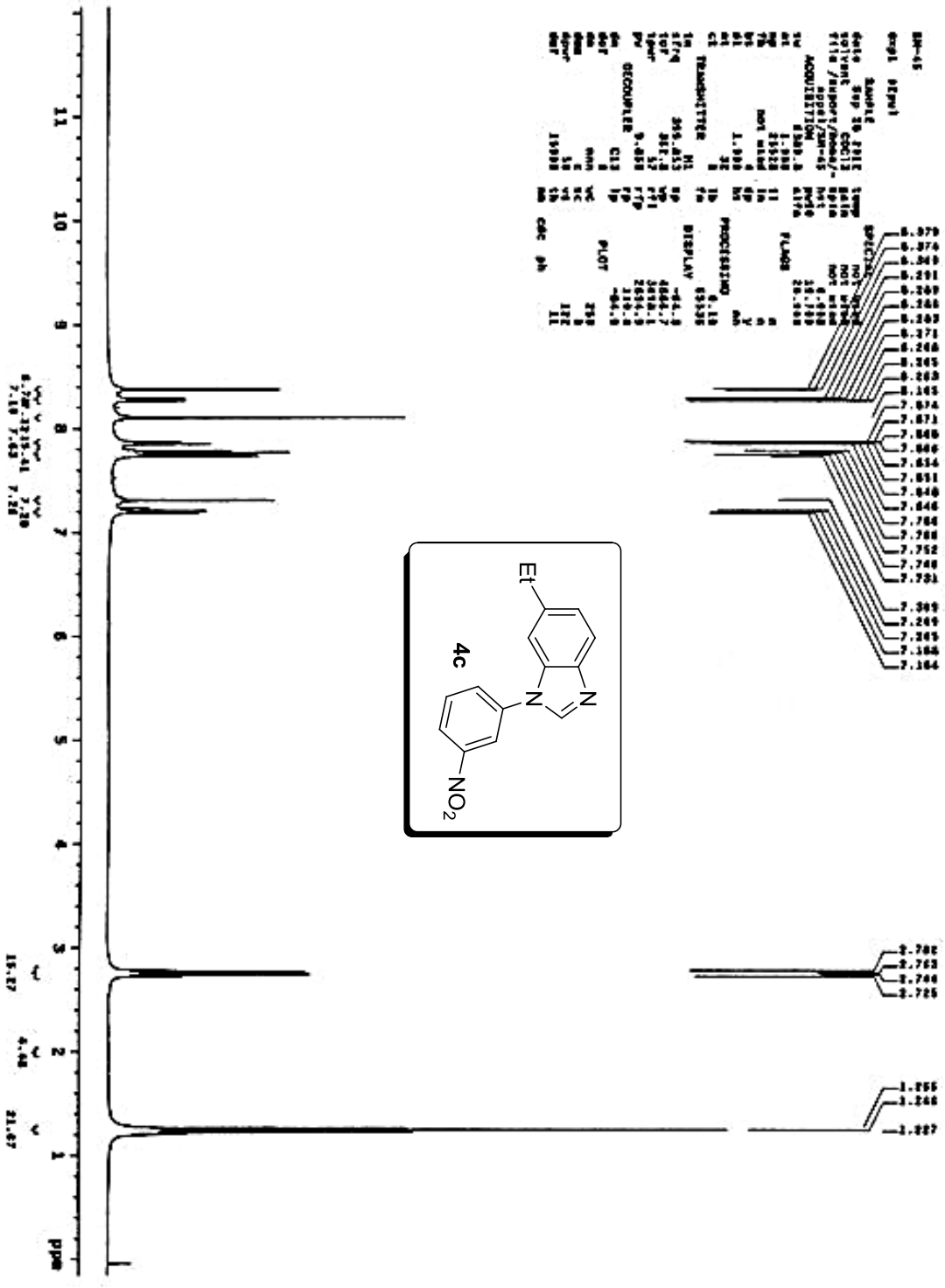

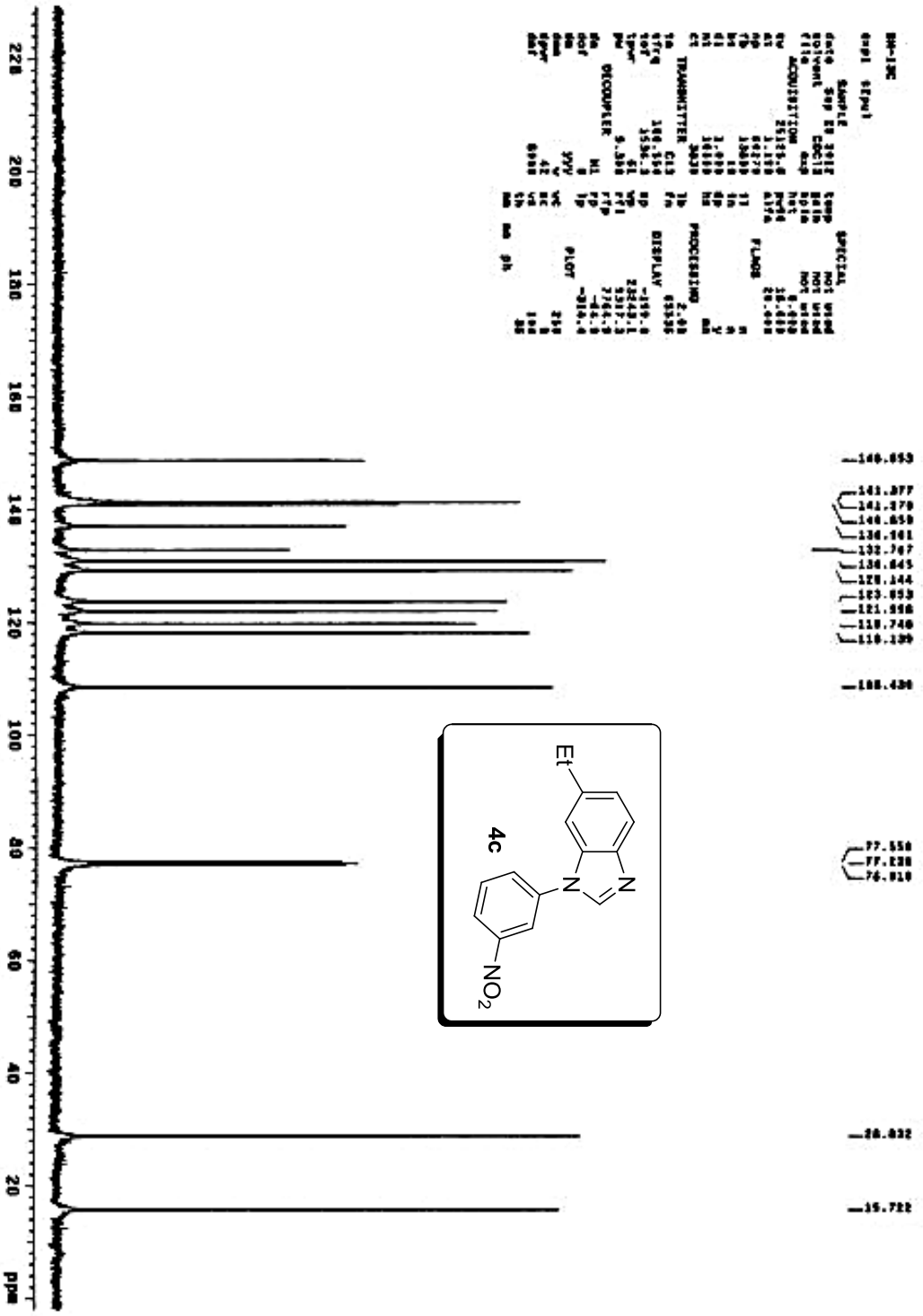

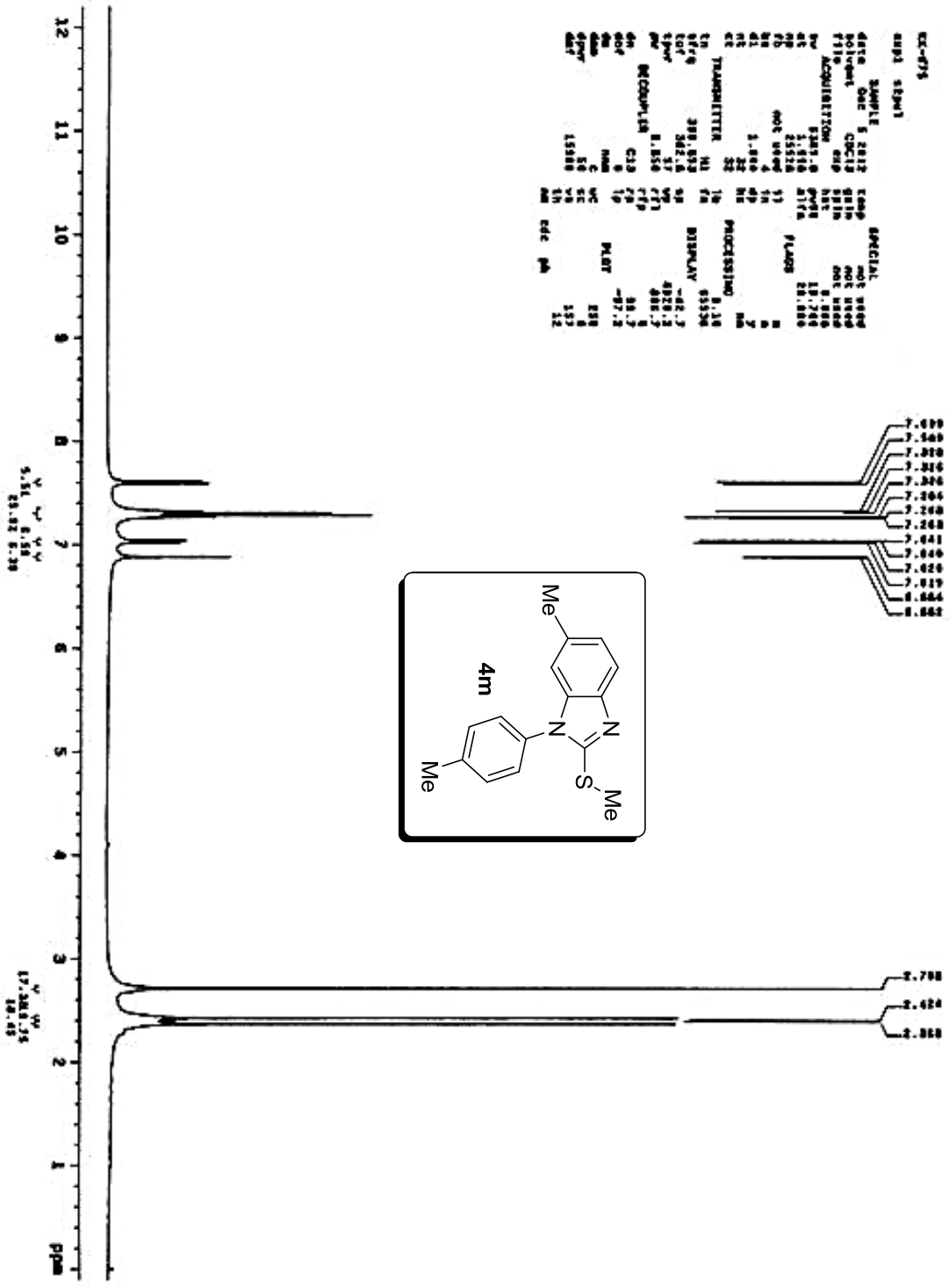

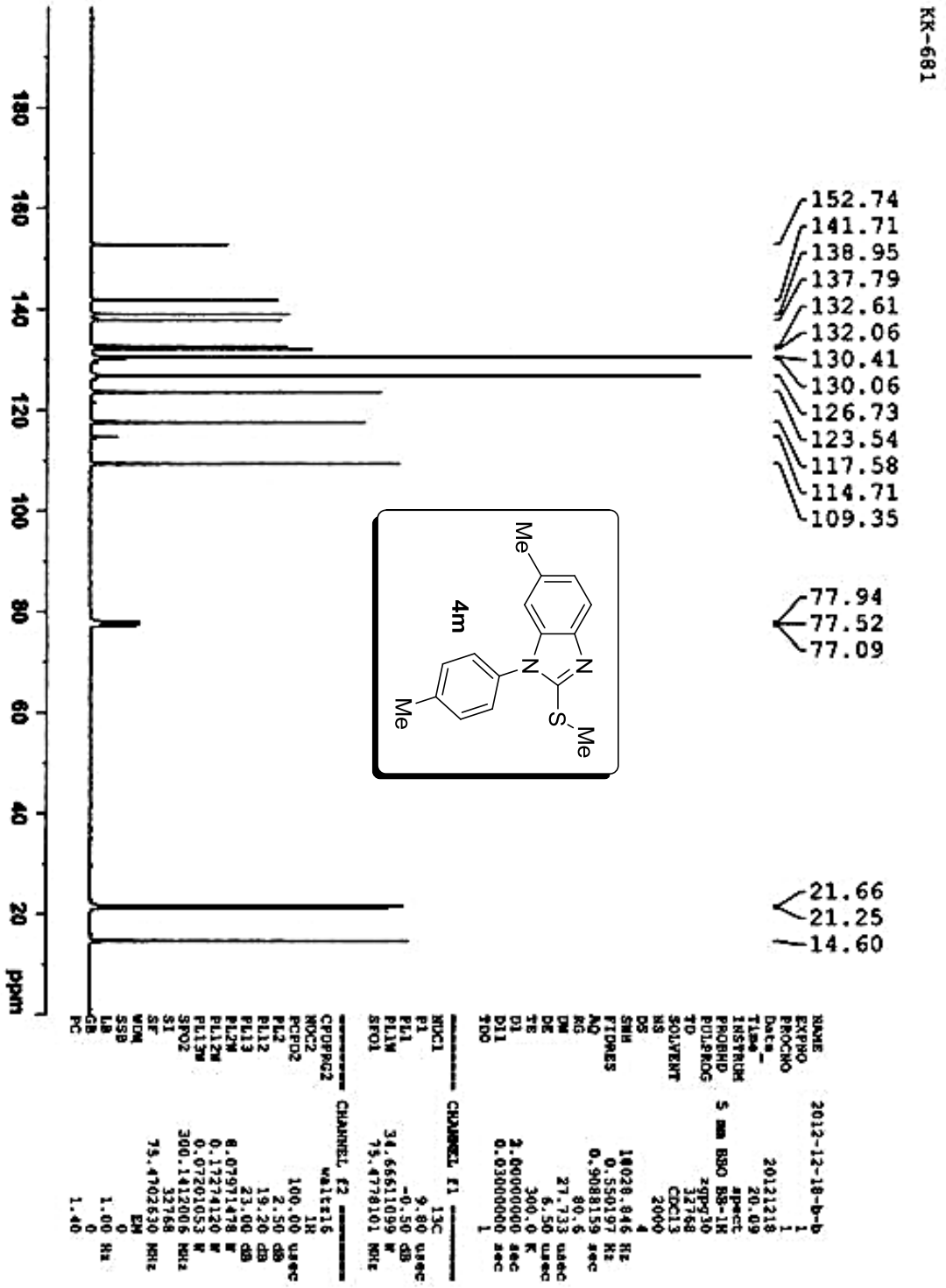

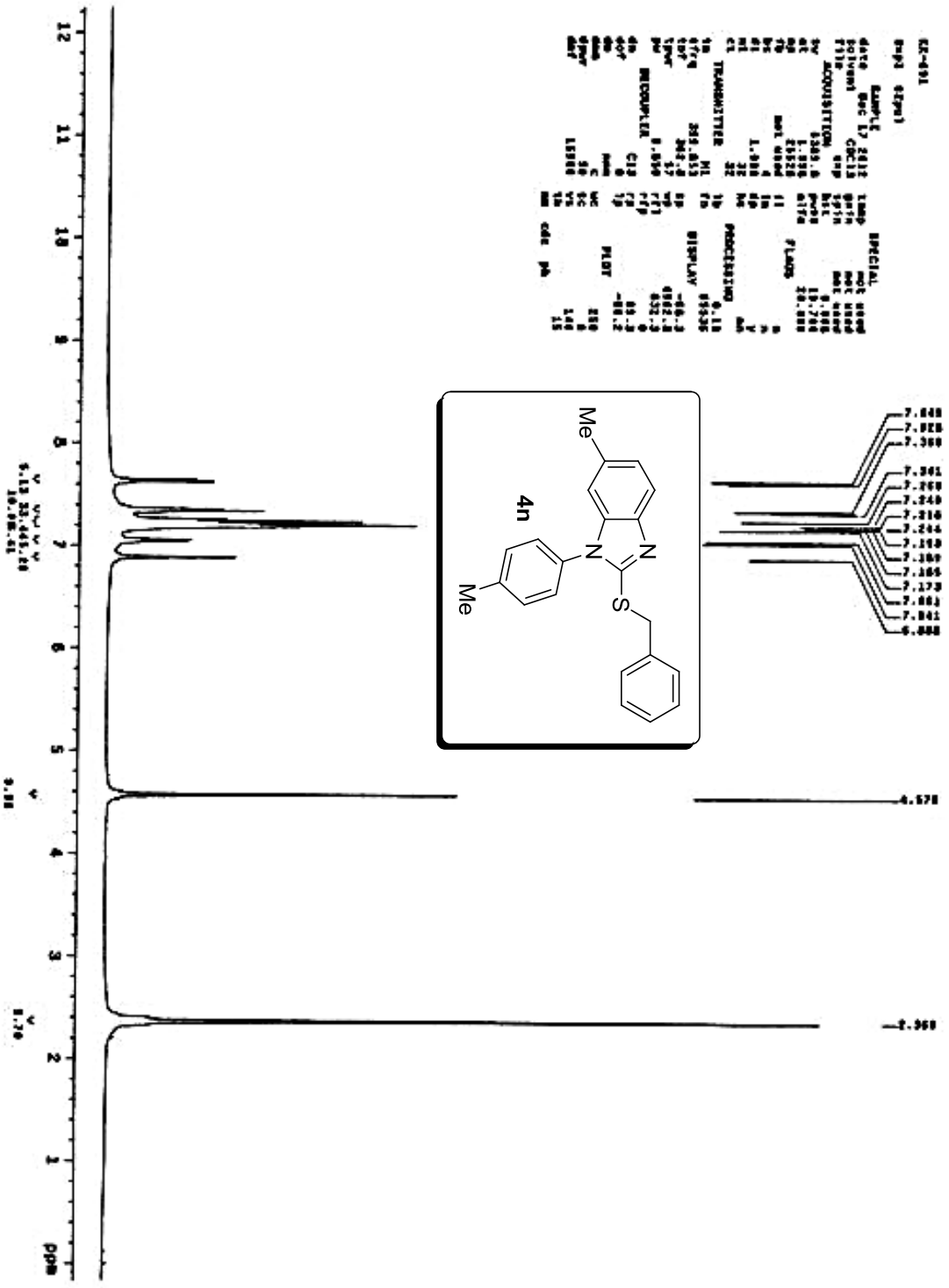

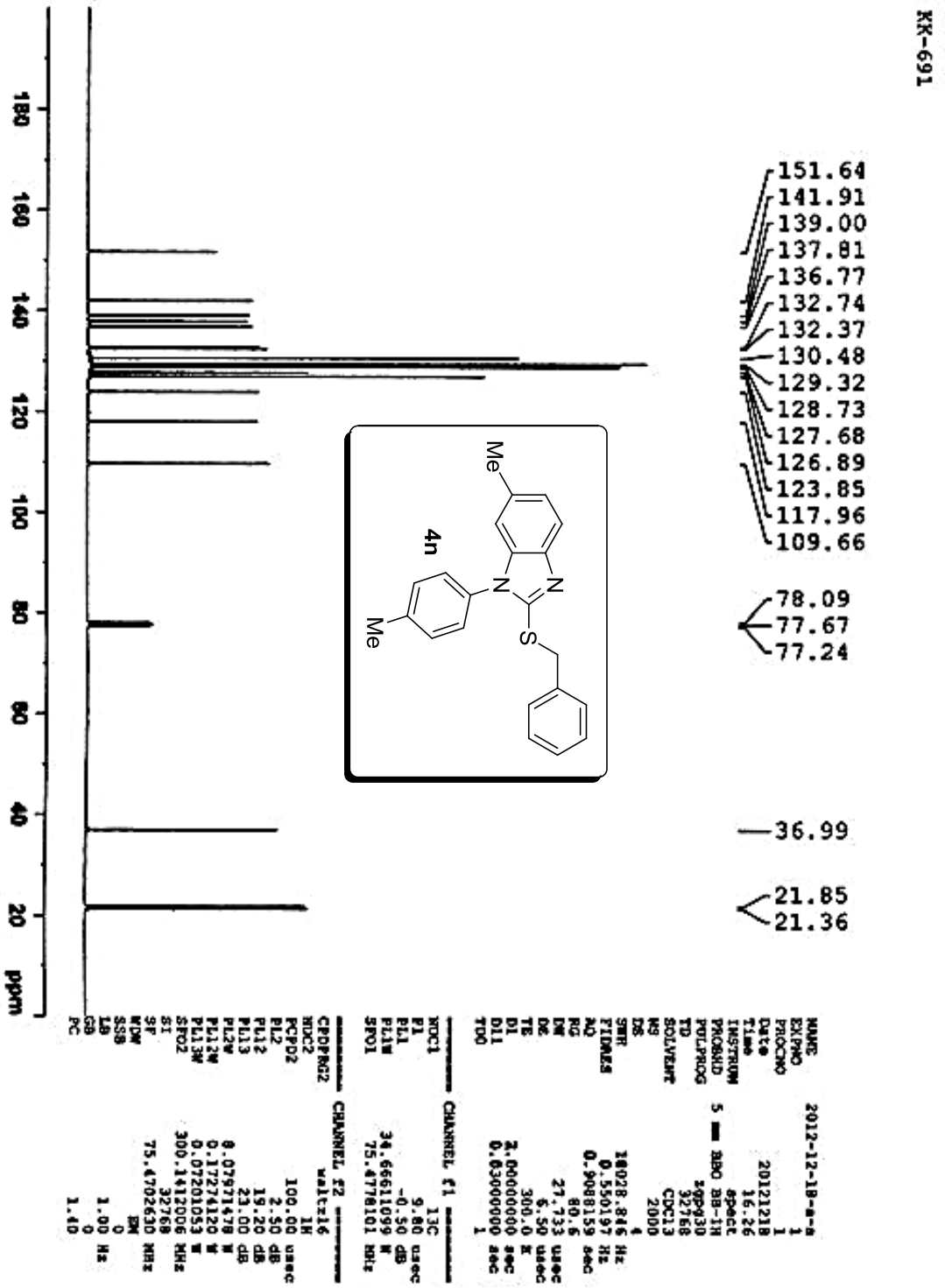

List of Publications

1. Pd-Catalyzed C-H Activation/C-N Bond Formation: A New Route to 1-Aryl-1*H*-benzotriazoles.
   Kumar, R. K.; Ali, M. A.; Punniyamurhty, T. *Org. Lett.* **2011**, *13*, 2102.
2. Palladium-Catalyzed Aerobic Oxidative C-H Amination: Synthesis of 2-Unsubstituted and 2-Substituted *N*-Aryl Benzimidazoles.
   Kumar, R. K.; Punniyamurhty, T. *RSc. Adv.* **2012**, *2*, 4616.
3. Iodobenzene Catalyzed C-H Amination *N*-Substituted Amidines Using *m*-Chloroperbenzoic Acid.
   Alla, S. K.; **Kumar, R. K.**; Sadhu, P.; Punniyamurhty, T. *Org. Lett.* **2013**, *15*, 1334.
4. ‘‘Metal-Free”: Oxidative *C-N* and Tandem *C-N* and *C-S/C-Se* Bonds Formation *via* Mono and Double C-H Activations.
   Kumar, R. K.; Manna, S.; Mahesh, D.; Punniyamurhty, T. (Communicated)