CHAPTER – III

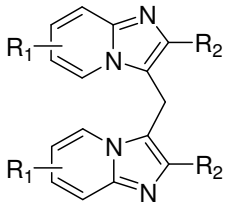
SYNTHESIS OF NOVEL BIS IMIDAZO[1,2- a] PYRIDINYLMETHANES DERIVATIVES

CHAPTER - III

SYNTHESIS OF NOVEL BIS-IMIDAZO[1,2-a]PYRIDINYLMETHANE DERIVATIVES

3.1 INTRODUCTION:-

Bis-imidazo[1,2-a]pyridine is an aromatic heterocyclic organic compound having one carbon atom attaching two imidazo[1,2-a]pyridine ring system**.** Bis-imidazo[1,2-a]pyridine derivatives are important intermediates in organic synthesis, especially in the synthesis of biologically active and medicinally useful agents. For instance, they are widely used in the synthesis of cyclin-dependent Kinases (CDK) inhibitors,[1] sleep inducers,[2] anticonvulsant agents,[3] anti-inflammatory [4] and antiviral agent.[5-7]

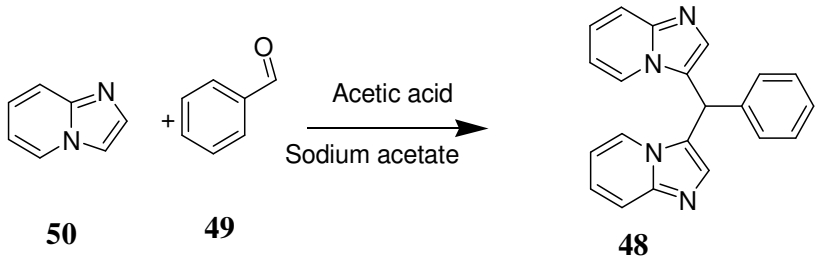


In recent years a significant portion of research work in heterocyclic chemistry has been devoted to dimer compounds. A wide variety of pharmacological properties and industrial applications have been encountered with several dimer products, such as, Antimicrobial,[9] Antiinflammatory,[10] Anticancer,[11] Analgesic,[12] Antifungal,[13] Anti-HIV,[14] Antiprotozoal,[15] Antimalarial,[16] Cytotoxic Activity,[17] Antitumor[18] activities.

Bis-imidazo[1,2-a]pyridine derivatives, containing different aryl, alkyl and heteroaryl groups as substituents shown interesting biological activities. Hence we prepared a series of bis-imidazo[1,2-a]pyridine derivatives and presented in this work.

3.2 LITERATURE BACKGROUND

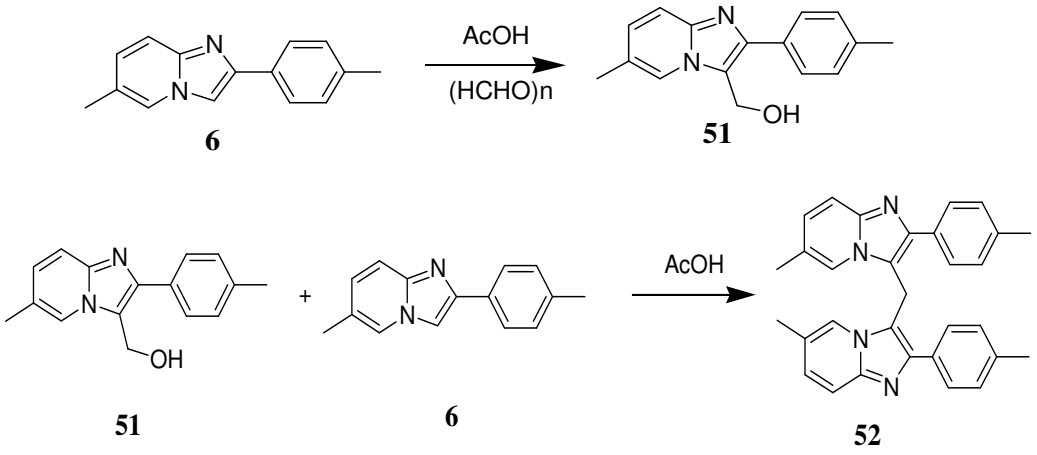
Rui Zhang and YongzhouHu[18] et al reported the synthesis of 3-(imidazo[1,2-a]pyridin-3-yl)(phenylmethane)imidzo[1,2-a]pyridine **48,** by the reaction of imidazo[1,2-a]pyridine **50** with benzaldehyde **49** in the aceticacid and sodium acetate to produce **48 (Scheme-3.1).**



50 **49** **48**

(Scheme-3.1)

Bollikonda Satyanarayana and Yasareni Sumalatha [19] et al reported the synthesis of bis-(6-methyl-2-(p-tolyl)imidazo[1,2-a] pyridin-3-yl) methane **52**, by the reaction of 6-methyl-2-(p-tolyl)imidazo [1,2-a]pyridine **6** with paraformaldehyde in aceticacid to produce (6-methyl-2-(p-tolyl)imidazo{1,2-a]pyridin-3-yl)methanol **51**. Obtained alcohol **51** on condensation with 6-methyl-2-(p-tolyl)imidazo [1,2-a]pyridine in aceticacid to give **52 (Scheme-3.2).**

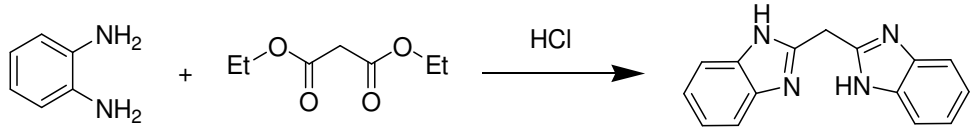


6 **51** **51** **6** **52**

(Scheme-3.2).

Fabio da Silva Miranda and Fabricio Gava Menezes[20] et al reported

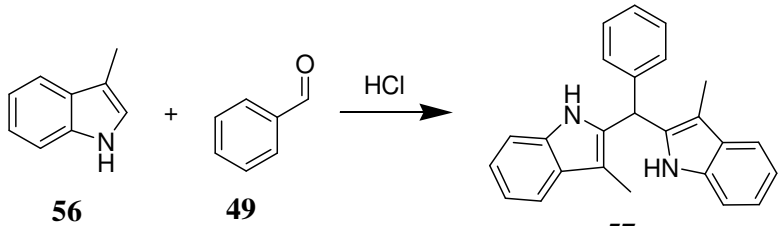
the synthesis of di(1*H*-benzoimidazol-2-yl)methane **55**, by the reaction of 1,2-diaminobenzene **53** with diethylmalonate **54** in the presence of hydrochloric acid to produce **55 (Scheme-3.3).**



53 **54** **55**

(Scheme-3.3).

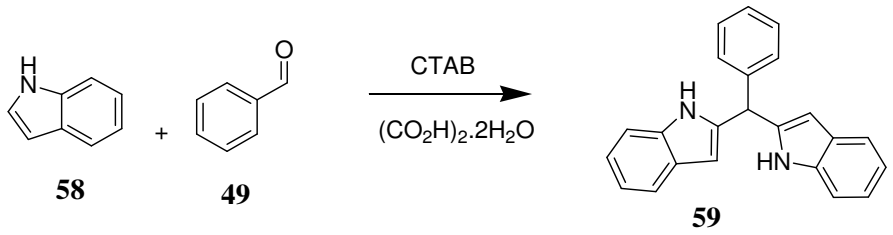
Wataru and Kazuaki[21] et al reported the synthesis of 3-methyl-2-(3-methyl-1*H*-indol-2-yl)(phenyl)-1*H*-indole **57**, Starting from the reaction of 3-methyl-1*H*-indole **56** with benzaldehyde **49** in diluted hydrochloric acid to provide compound **57 (Scheme-3.4).**



56 **49** **57**

(Scheme-3.4).

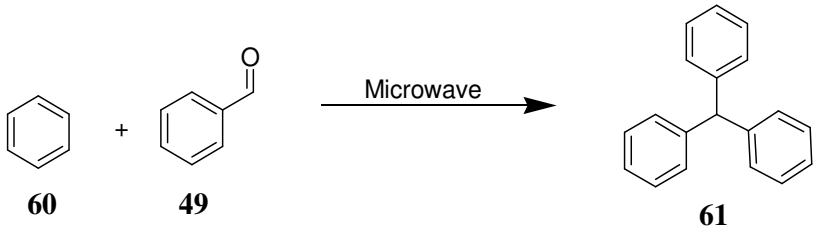
Ramin Ghorbani-Vaghel, Hojat Veisi[22] et al reported the synthesis of 2-(1*H*-indole-2-yl)(phenyl)methyl)-1*H*-indole **59** by the reaction of indole **58** with benzaldehyde **49** to produce **59 (Scheme-3.5).**



58 **49** **59**

(Scheme-3.5).

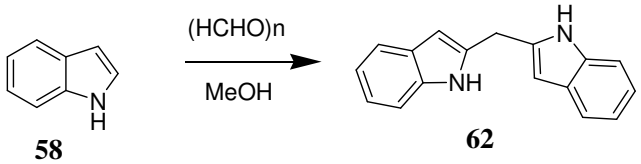
G. Surya, K. Prakash and Gabriella Fogassy[22] et al reported the synthesis of triphenylmethane **61** by reacting benzaldehyde **49** with benzene **60** to give **61 (Scheme-3.6).**



60 **49** **61**

(Scheme-3.6).

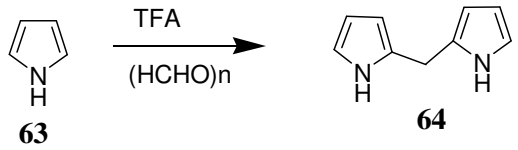
Sun, Chunlou[23] et al reported the synthesis of di(1*H*-indole-2-yl)methane **62** by the reaction of indole **58** with paraformaldehyde in methanol to produce **62** **(Scheme-3.7).**



58 **62**

(Scheme-3.7).

Edgardo N. Durantin[24-25] et al reported the synthesis of di(1*H*-pyrrol-2-yl)methane **64** by the reaction of pyrrole **63** with paraformaldehyde using TFA as catalyst to produce **64** **(Scheme-3.8).**



63 **64**

(Scheme-3.8).

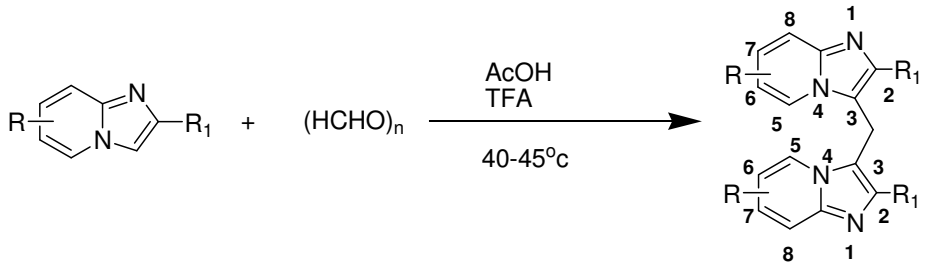
3.3 PRESENT WORK:

Bis-imidazo[1,2-a]pyridines are important class of heterocyclic compounds which are key intermediates during drug discovery. We have developed a new synthetic route for the synthesis of novel bis-imdizo[1,2-a]pyridines. The synthesis involves use of paraformaldehyde and aceticacid followed by simple workup process to give higher yields.

3.4 RESULT AND DISCUSSION

We have synthesized total 11 bis derivatives as shown in (**Scheme 3.9)** and presented in **Table 3.1**. Imidazo[1,2-a]pyridine derivatives reacted with paraformaldehyde in the presence of aceticacid containing trifluoroaceticacid (TFA) at 40-45^{o}C for 12h. Reaction monitored by TLC and the product is clearly different from the starting material. After regular work up and further purification with silica gel column chromatography obtained pure bis derivatives in 60-72% yield. The structure elucidation of these compounds is interesting. Typically, the structure of **65b** elucidated on the basis of its analytical and spectral data. Its **^{1}H NMR** ($CDCl_3$/TMS) spectrum (**Fig-3.1**) showed a signal at δ 6.15ppm for a single proton in contrast to a CH_2 carbon at δ 21.1ppm

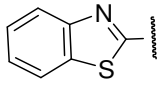
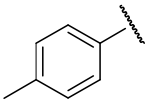
by its ^{13}C-DEPT spectrum. The molecular ion peak in mass spectrum shows peak at 543.7, related to bis compound. Based on these studies, δ 6.15ppm in ^{1}H NMR assigned to methylene group attached to two imidazo[1,2-a]pyridine rings. Except this proton, all other protons of imidazo[1,2-a]pyridine ring are symmetrical with another imidazo[1,2-a]pyridine ring and doubled in their integration. Other proton signals are at δ 2.27 (s, 6H, 2xCH_3), 6.15 (s, 2H), 6.40 (d, *J* = 6.8 Hz, 2H, aromatic-**CH**), 7.35 (s, 2H, aromatic-**CH**), 7.45 (t, *J* = 7.6 Hz, 2H, aromatic-**CH**), 7.52 (t, *J* = 7.3 Hz, 2H, aromatic-**CH**), 8.06 (m, 4H, aromatic-**CH**), 8.56 (d, *J* = 8.0 Hz, 2H, aromatic-**CH**). Its **^{13}C NMR** ($CDCl_3$/TMS) spectrum **(Fig-3.2)** showed signals at δ 19.8, 21.1, 115.6, 115.9, 118.3, 121.7, 122.8, 124.9, 125.1, 126.0, 135.1, 136.0, 136.8, 145.8, 154.3, 185.3; **ESI** mass spectrum **(Fig-3.3.)** showed molecular ion peak at 543.7 (M+1). This reaction was further studied by reacting different substituted imidazo[1,2-a]pyridines to extend the synthetic methodology shown in the **Table 3.1** and analyzed their spectral data.



(Scheme-3.9)

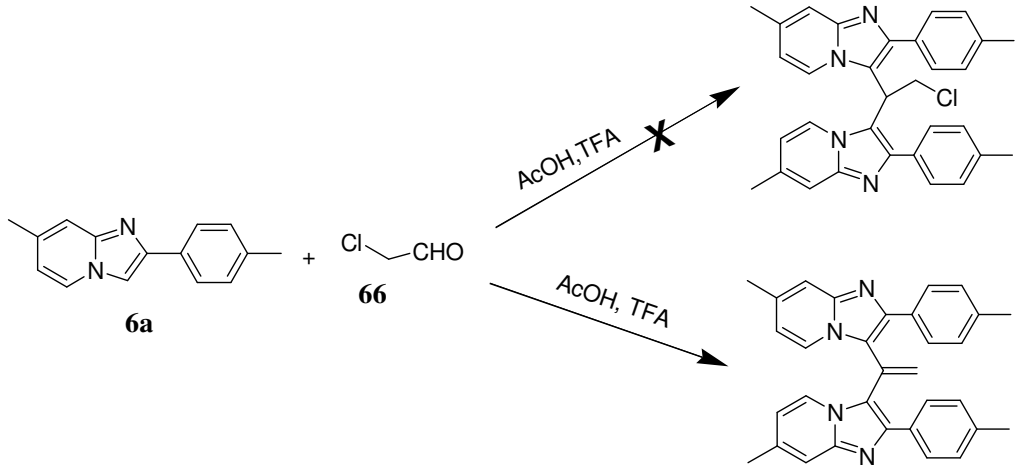
Table 3.1: Various Bis-imidazo[1,2-a]pyridinyl methane derivatives.

S.NO	PRODUCT	R	R_1	YIELD

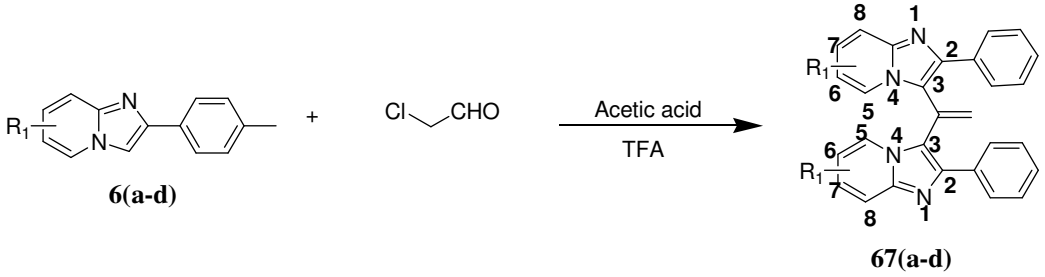
1	65a	6-methyl		72%
2	65b	7-methyl		68%
3	65c	6-chlor		62%
4	65d	6-bromo		60%
5	65e	H		69%
6	65f	H		72%
7	65g	6-methyl		70%
8	65h	6-chloro		62%
9	65i	6-bromo		65%
10	65j	7-methyl		62%
11	65k	6-bromo,7-methyl		72%

We attempted this reaction using chloroacetaldehyde in lieu of paraformaldehyde by expecting a chloromethyl as substituent on bridged methylene. When reacting 7-methyl-2-(p-tolyl)imidazo [1,2-a]pyridine with chloroacetaldehyde **66** in aceticacid containing TFA as catalyst and at reflux for 24h expecting for the formation of 3-(2-chloro-1-(7-methyl-2-(*p*-tolyl)imidazo[1,2-a]pyridin-3-yl)-7-methyl -2-(*p*-tolyl)imidazo[1,2-a]pyridine. But to our surprise, 7-methyl -3-(1-(7-methyl-2-(*p*-tolyl)imidazo[1,2-a]pyridin-3-yl)vinyl)-2-(*p*-tolyl)im idazo[1,2-a]pyridine **67a** (**Scheme 3.10)** a vinyl derivative, obtained . It could be due to dehydro halogenation reaction of the expected product. We prepared a series of vinyl derivatives using substituted imidazo[1,2-a]pyridine derivatives and chloroacetaldehyde as depicted

in (**Scheme 3.1)** and **Table 3.2**.



(Scheme 3.10)

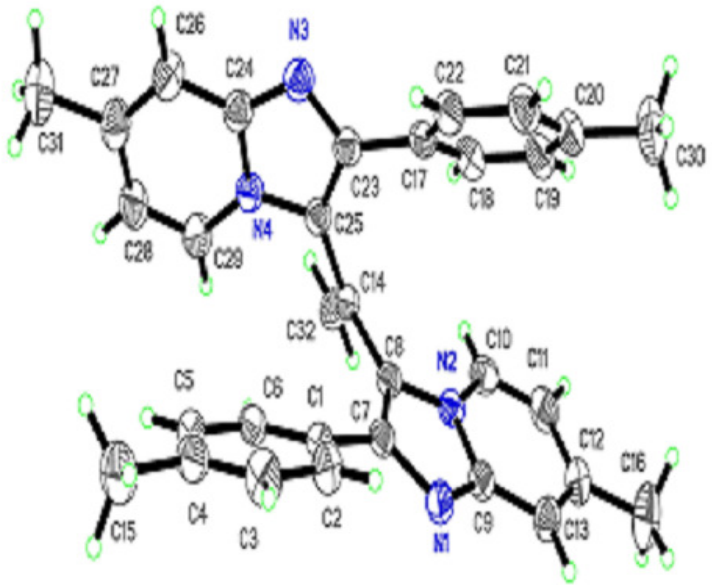


(Scheme 3.11)

Table 3.2: Various Bis-imidazo[1,2-a]pridinyl vinyl derivatives.

S.NO	Product	R	Yield
1	67a	7-methyl	58%
2	67b	H	56%
3	67c	6-chloro	59%
4	67d	6-methyl	62%

The structure of compound **67a**, 7-methyl-3-(1-(7-methyl-2-(*p*-tolyl) imidazo[1,2-a]pyridin-3-yl)vinyl)-2(*p*-tolyl)imidazo[1,2-a]pyridine is concluded on the basis of its analytical and spectral data. Thus its **^{1}H NMR** ($CDCl_3$/TMS) spectrum **(Fig-3.4)** showed signals at δ 2.24 (s, 6H 2xCH_3), 2.36 (s, 6H 2xCH_3), 5.88 (s, 2H, for =C**H_2**), 6.54 (d, *J* = 6.2 Hz, 2H aromatic -C**H**), 6.94 (d, *J* = 7.8 Hz, 4H aromatic -C**H**), 7.29 (s, 2H aromatic -C**H**), 7.45 (d, *J* = 7.9 Hz, 4H aromatic -C**H**), 7.94 (d, *J* = 7.0 Hz, 2H aromatic -C**H**). Its **^{13}C NMR** ($CDCl_3$/TMS) spectrum **(Fig-3.5)** showed signals at δ 18.39, 21.15, 116.52, 119.42, 121.74, 122.49, 122.57, 126.33, 127.63, 127.99, 128.26, 131.72, 136.52, 143.74, 144.32; The peak at 5.88ppm in ^{1}H NMR related to vinyl group, it confirmed by presence of a CH_2 carbon in ^{13}C-DEPT spectrum present at 121.4ppm and a quaternary carbon at 126.5ppm. The presence of this two carbon peaks in aromatic region leads to dehydro halogenated vinyl derivative. **ESI** mass spectrum **(Fig-3.6)** showed molecular ion peak at 469.4. (M+1) correspond to the molar mass of compound **67a**. The assigned structure for **67a** is further confirmed by its single crystal X-Ray analysis as shown below.



X-ray crystal structure of compound 67a, 7-methyl-3-(1-(7-methyl-2-(*p*-tolyl)imidazo[1,2-a]pyridin-3-yl) vinyl)-2-(*p*-tolyl)imidazo[1,2-a]pyridine

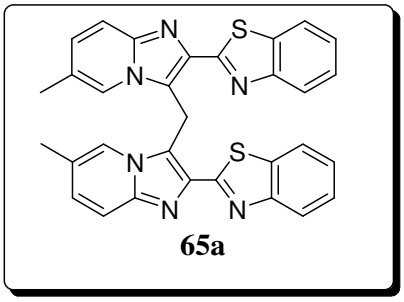
3.5 EXPERIMENTAL SECTION:-

General procedure for the preparation of Bis-imidazo[1,2-a]pyridinyl methane derivatives (65 a-k):

A mixture of imidazo[1,2-a]pyridine derivative (2.41g, 9.1mmol) and 10ml of acetic acid was stirred at 25-30^{o}C for 10-15 minutes and then paraformaldehyde (0.2g, 6.75mmol) was added followed by addition of 2 drops of trifluoroaceticacid (TFA) at room temperature. The reaction mixture was heated to 40-45^{o}C for 12h and the progress of the reaction was monitored by TLC. After completion of the reaction, aceticacid was distilled under reduced pressure and the residue diluted with water (10 ml). The solution was basified with sodium bicarbonate and the product

was extracted with MDC (2 X 20 ml). Obtained organic layer was washed with water (20 ml) and dried over anhydrous sodium sulphate. The solution was filtered, concentrated and purified by silica gel column chromatography by using MDC: MeOH (10:1) as eluent. Prepared compounds analytical and spectral data follows.

65a: Bis-(2-(benzothiazol–2-yl)-6-methylimidazo[1,2-a]pyridine -3-yl)methane:



65a

Description : White solid.

Melting point: Up to 260°C (Not clear).

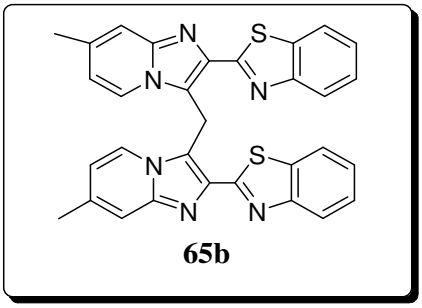
IR (In KBr) : 3391, 3075, 2918, 1941, 1730, 1556, 1493, 1435, 1356, 1239, 1155, 943, 795, 776, 758, 725, 682 cm^{-1} .

^{1}H NMR ($CDCl_3$/TMS): δ 2.77 (s, 6H, 2xCH_3), 5.96 (s, 2H), 7.77 (m, 4H), 7.93 (m, 4H), 8.13 (t, *J* = 8.2 Hz, 4H), 9.00 (s, 2H).

^{13}C NMR ($CDCl_3$/TMS): δ 17.98, 19.91, 116.76, 118.59, 121.86, 122.82, 122.86, 124.20, 125.15, 126.28, 129.00, 135.14, 136.31, 144.43, 154.23, 165.60.

ESI-MS:m/z: 543.4 (M+1).

65b: Bis-(2-(benzothiazol-2-yl)-7-methylimidazo[1,2-a]pyridine -3-yl)methane.



65b

Description : White solid.

Melting point: Up to 260.0°C (Not clear).

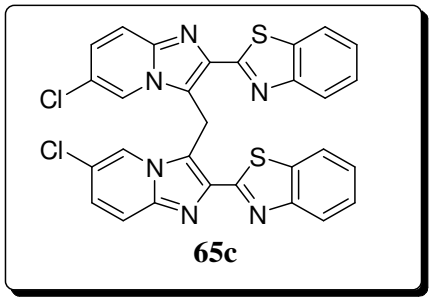
IR (In KBr) : 3390, 3052, 2915, 1892, 1646, 1566, 1556, 1434, 1360, 1315, 1255, 1234, 1234, 1165, 924, 815, 752, 725, 681 cm^{-1} .

^{1}H NMR ($CDCl_3$/TMS): δ 2.27 (s, 6H 2xCH_3), 6.15 (s, 2H), 6.40 (d, *J* = 6.8 Hz, 2H), 7.352 (s, 2H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.52 (t, *J* = 7.3 Hz, 2H), 8.06 (m, 4H), 8.56 (d *J* = 8.0 Hz, 2H).

^{13}C NMR ($CDCl_3$/TMS): δ 19.8, 21.1, 115.6, 115.9, 118.3, 121.7, 122.8, 124.9, 125.1, 126.0, 135.1, 136.0, 136.8, 145.8, 154.3, 165.3;

ESI-MS:m/z: 543.4 (M+1).

65c: Bis-(2-(benzothiazol-2-yl)-6-chloroimidazo[1,2-a]pyridine -3-yl)methane.



65c

Description : White solid.

Melting point 256.1 – 258.6°C.

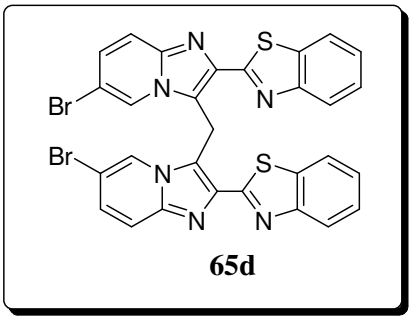
IR (In KBr) : 3412, 3062, 3007, 1927, 1736, 1366, 1313, 1229, 1094, 1014, 939, 810, 749, 672 cm^{-1} .

^{1}H NMR ($CDCl_3$/TMS): δ 6.02 (s, 2H), 7.13 (m, 2H), 7.49 (t, *J* = 7.42 Hz, 2H), 7.58 (m, 4H), 8.05 (d, *J* = 8.0 Hz, 2H), 8.13 (d, *J* = 8.0 Hz, 2H), 9.31 (s, 2H).

^{13}C NMR ($CDCl_3$/TMS): δ 19.88, 117.79, 118.67, 121.55, 121.75, 123.00, 124.71, 125.36, 126.31, 127.36, 135.07, 137.37, 143.69, 153.96, 164.65.

ESI-MS: (m/z): 583.1 (M+H).

65d: Bis-(2-(benzothiazol-2-yl)-6-bromoimidazo[1,2-a]pyridine -3-yl)methane.



65d

Description : Brown colour solid.

Melting point: 224.7–225.9^{o}C.

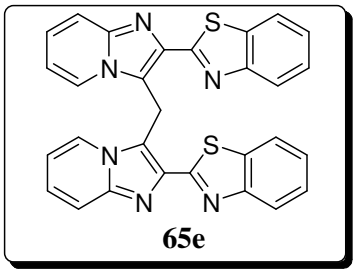
IR (In KBr) : 3437, 3076, 1734, 1366, 1230, 1085, 1018, 942, 812, 761, 577.

^{1}H NMR ($CDCl_3$/TMS): δ 6.00 (s, 2H), 7.21 (d, *J* = 8.0Hz, 2H), 7.57 (m, 6H), 8.04 (d, *J* = 8.0 Hz, 2H), 8.15 (d, *J* = 8.0 Hz, 2H), 9.43 (s, 2H);

^{13}C NMR ($CDCl_3$/TMS): δ 19.83, 108.00, 118.01, 118.52, 121.73, 123.11, 125.36, 126.30, 127.04, 129.48, 135.07, 137.11, 143.71, 153.98, 164.64.

ESI-MS (m/z): 673.1 (M+1).

65e: Bis(2-(benzothiazol-2-yl)imidazo[1,2-a]pyridin-3-yl)methane:



65e

Description : White solid.

Melting point: Up to 260.0°C (Not clear).

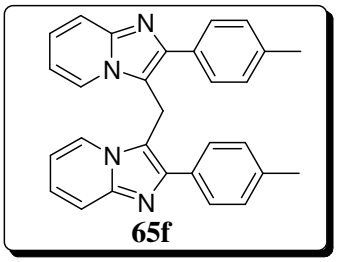
IR (In KBr) : 3390, 3051, 2725, 2526, 1893, 1730, 1634, 1563, 1493, 1451, 1433, 1365, 1313, 1233, 1135, 926, 783, 751, 743, 723, 690 cm^{-1} .

^{1}H NMR ($CDCl_3$/TMS): δ 6.28 (s, 2H), 7.38 (t, *J* = 6.6 Hz, 2H), 7.70 (m, 4H), 7.98 (t, *J* = 8.2 Hz, 2H), 8.15 (m, 6H), 9.30 (d, *J* = 6.5 Hz, 2H).

^{13}C NMR ($CDCl_3$/TMS): δ 19.79, 113.33, 116.21, 118.52, 118.77, 122.36, 123.72, 127.68, 127.90, 128.40, 134.96, 135.17, 140.73, 152.82, 154.07.

ESI-MS (*m*/*z*): 515.5 (M+1).

65f: Bis-(2-(p-tolyl)imidazo[1,2-a]pyridin-3-yl)methane:



65f

Description : White solid.

Melting point: 251.4 – 253.4°C (Decomposed).

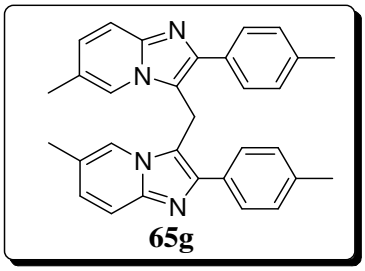
IR (In KBr) : 3420, 3023, 2918, 2361, 1632, 1500, 1375, 1352, 1234, 1114, 829, 749, 743, 509 cm^{-1} .

^{1}H NMR ($CDCl_3$/TMS): δ 2.44 (s, 6H 2xCH_3), 4.99 (s, 2H), 6.47 (t, *J* = 6.7 Hz, 2H), 7.06 (t, *J* = 8.1 Hz, 2H), 7.34 (m, 6H), 7.56 (m, 2H), 7.71 (m, 4H).

^{13}C NMR ($CDCl_3$/TMS): δ 19.72, 21.23, 112.07, 114.01, 117.23, 123.74, 124.04, 128.69, 129.44, 131.29, 137.93, 144.13, 144.85;

ESI-MS:m/z: 429.3 (M+1).

65g: Bis-(6-methyl-2-(p-tolyl)imidazo[1,2-a]pyridin-3-yl)methane.



65g

Description : White solid.

Melting point: Up to 260.0°C (Not clear).

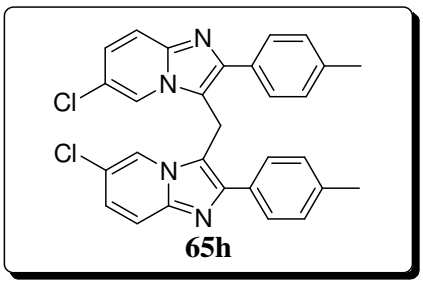
IR (In KBr) : 3385, 3085, 2919, 1907, 1639, 1532, 1493, 1377, 822, 801, 728, 507 cm^{-1} .

^{1}H NMR ($CDCl_3$/TMS): δ 1.89 (s, 6H 2xCH_3), 2.45 (s, 6H 2xCH_3), 4.91 (s, 2H), 6.85 (d, *J* = 8.9 Hz, 2H), 7.04 (s, 2H), 7.38 (d, *J* = 8.3 Hz, 6H), 7.73 (d, *J* = 7.8 Hz, 4H).

^{13}C NMR ($CDCl_3$/TMS): δ 17.81, 18.96, 21.25, 114.17, 116.29, 121.41, 122.01, 127.22, 128.81, 129.59, 131.90, 137.85, 143.56, 143.83.

ESI-MS:m/z: 457.3 (M+H).

65h: Bis-(6-chloro-2-(p-tolyl)imidazo[1,2-a]pyridin-3-yl)methane.



65h

Description : White solid.

Melting point: 251.4 – 253.4°C (Decomposed).

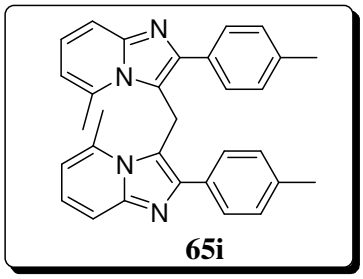
IR (In KBr) : 3098, 2739, 2677, 2491, 1519, 1495, 1105, 1025, 825, 797, 506 cm^{-1} .

^{1}H NMR ($CDCl_3$/TMS): δ 2.46 (s, 6H 2xCH_3), 4.89 (s, 2H), 7.02 (q, 2H), 7.29 (s, 2H), 7.38 (d, *J* = 7.7 Hz, 4H), 7.46 (d, *J* = 9.4 Hz, 2H), 7.66 (d, *J* = 7.8 Hz, 4H).

^{13}C NMR ($CDCl_3$/TMS): δ 21.28, 114.54, 117.53, 120.29, 121.91, 125.59, 128.78, 129.77, 130.67, 138.52, 143.24, 145.30;

ESI-MS:m/*z*: 497.3 (M+1).

65i: Bis-(5-methyl-2-(p-tolyl)imidazo[1,2-a]pyridin-3-yl)methane.



65i

Description : White solid.

Melting point: 230.1 – 233.8°C (Decomposed).

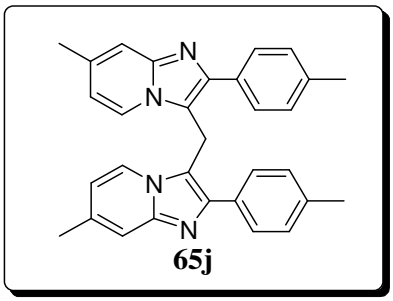
IR (In KBr) : 3401, 3032, 2915, 1894, 1633, 1509, 1497, 1386, 1357, 1178, 1141, 830, 819, 787, 772, 727 cm^{-1} .

^{1}H NMR ($CDCl_3$/TMS): δ 2.21(s, 6H 2xCH_3), 2.68 (s, 6H 2xCH_3), 5.29 (s, 2H), 6.36 (d, *J* = 6.6 Hz, 2H), 6.95 (m, 6H), 7.18 (d, *J* = 7.6 Hz, 4H), 7.31 (d, *J* = 8.8 Hz, 2H).

^{13}C NMR ($CDCl_3$/TMS): δ 20.57, 20.95, 26.51, 113.76, 115.68, 118.50, 124.09, 127.97, 128.12, 131.06, 135.62, 136.67, 145.71, 146.11.

ESI-MS: (m/z): 457.2 (M+H).

65j: Bis-(7-methyl-2-(p-tolyl)imidazo[1,2-a]pyridin-3-yl)methane.



65j

Description : White solid.

Melting point: Up to 260.0°C (Not clear).

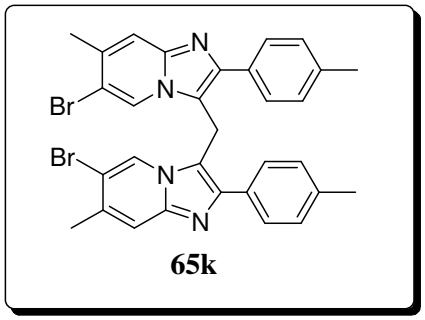
IR (In KBr) : 3413, 3037, 2916, 1909, 1646, 1502, 1378, 1361, 1179, 1171, 823, 771, 508 cm^{-1} .

^{1}H NMR ($CDCl_3$/TMS): δ 2.26 (s, 6H 2xCH_3), 2.44 (s, 6H 2xCH_3), 4.94 (s, 2H), 6.28 (d, *J*= 6.9 Hz, 2H), 7.21 (d, *J* = 7.0 Hz, 2H), 7.26 (s, 2H), 7.34 (d, *J* = 7.6 Hz, 4H), 7.71 (d, *J* = 7.8 Hz, 4H).

^{13}C NMR ($CDCl_3$/TMS): δ 19.65, 21.03, 21.23, 113.60, 114.63, 115.54, 123.01, 128.65, 129.43, 131.55, 134.97, 137.72, 143.64, 145.27;

ESI-MS(m/z): 457.2 (M+1).

65k: Bis-(6-bromo-7-methyl-2-(p-tolyl)imidazo[1,2-a]pyridin-3-yl) methane.



65k

Description : White solid.

Melting point: Up to 260.0°C (Not clear).

IR (In KBr) : 3429, 3091, 1633, 1496, 1428, 1374, 1318, 1167, 1070, 982, 853, 830, 801 cm^{-1} .

^{1}H NMR ($CDCl_3$/TMS): δ 2.31 (s, 6H 2xCH_3), 2.46 (s, 6H 2xCH_3), 4.87 (s, 2H), 7.38 (t, *J* = 7.3 Hz, 6H), 7.45 (s, 2H), 7.68 (d, *J* = 7.8 Hz, 4H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 19.05, 21.27, 22.33, 110.77, 113.55, 116.15, 123.99, 128.83, 129.72, 130.85, 134.75, 138.24, 144.19, 144.68;

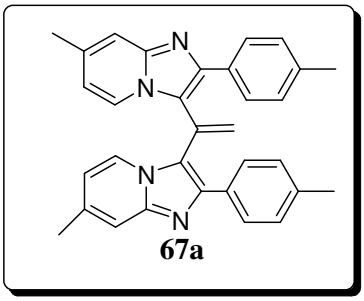
ESI-MS:m/z: 617.2 (M+1).

General procedure for the preparation of Bis-imidazo[1,2-a]pyridinyl vinyl derivatives (67a-d).

A mixture of imidazo[1,2-a]pyridine derivative (2.0g, 9.1mmol) and 10 ml of aceticacid was stirred at 25-30°C for 10-15 minutes then added chloroacetaldehyde (0.53g, 6.75mmol) drop wise and heated for

24h. The progress of the reaction was monitored by TLC. After completion, aceticacid was distilled under reduced pressure and the residue diluted with water (10 ml). Obtained solution was basified with sodium bicarbonate and extract with MDC (2 X 20 ml). MDC layer washed with water (10 ml) and dried over anhydrous sodium sulphate. The solution was filtered, concentrated and purified by Column chromatography by using MDC : MeOH (10:1) as eleunt. Spectral data of the prepared compounds presented below.

67a: 7-Methyl-3-(1-(7-methyl-2-(p-tolyl)imidazo[1,2-a]pyridin-3-yl)vinyl)-2-(p-tolyl)imidazo [1,2-a]pyridine.



67a

Description : White solid,

Melting point: : 259.3 – 259.8^{o}C.

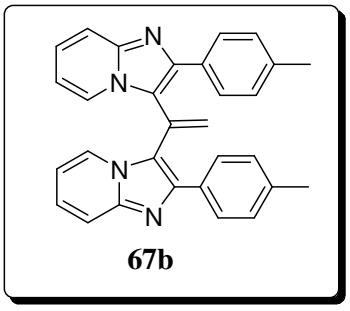
IR (In KBr) : 3389, 3013, 2913, 1922, 1643, 1501, 1413, 1348, 903, 829, 796, 784, 513 cm^{-1} .

^{1}H NMR ($CDCl_3$/TMS): δ 2.24 (s, 6H 2xCH_3), 2.36 (s, 6H 2xCH_3), 5.88 (s, 2H), 6.54 (d, *J* = 6.2 Hz, 2H), 6.94 (d, *J* = 7.8 Hz, 4H), 7.29 (s, 2H), 7.45 (d, *J* = 7.9 Hz, 4H), 7.94 (d, *J* = 7.0 Hz, 2H).

^{13}C NMR ($CDCl_3$/TMS): δ 21.08, 21.11, 115.27, 115.88, 118.15, 121.42, 122.76, 126.49, 127.84, 128.35, 131.12, 135.46, 137.13, 145.00, 145.57.

ESI-MS:(m/z): 469.4 (M+1).

67b: 2-(p-tolyl)-3-(2-(p-tolyl)imidazo[1,2-a]pyridine-3-yl)vinyl imidazo[1,2-a]pyridine:.



67b

Description : White solid.

Melting point: : 191.2 –195.4°C.

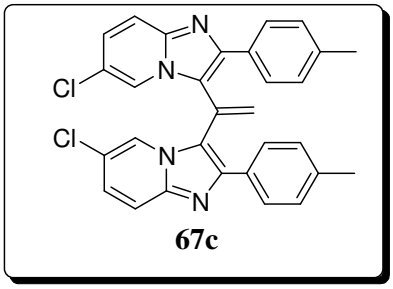
IR (In KBr) : 3367, 3077, 2919, 1923, 1698, 1501, 1417, 1346, 1239, 1141, 825, 756, 743, 512 cm^{-1} .

^{1}H NMR ($CDCl_3$/TMS): δ 2.19 (s, 6H 2xCH_3), 6.02 (s, 2H), 6.84 (m, 6H), 7.19 (t, *J* = 7.9 Hz, 2H), 7.28 (s, 6H), 7.56 (d, *J* = 9.0 Hz, 2H), 8.25 (d, *J* = 6.8 Hz, 2H).

^{13}C NMR ($CDCl_3$/TMS): δ21.02, 112.76, 117.47, 118.71, 121.01, 123.25, 124.62, 126.77, 127.73, 128.17, 130.63, 137.33, 145.07, 145.31.

ESI-MS:(m/z): 441.2 (M+1).

67c: 6-Chloro-3-(1-(6-chloro-2-(p-tolyl)imidazo[1,2-a]pyridin-3-yl) vinyl-2-(p-tolyl)imidazo[1,2-a] pyridine.



67c

Description : White solid.

Melting point: : 217.2 – 218.8°C.

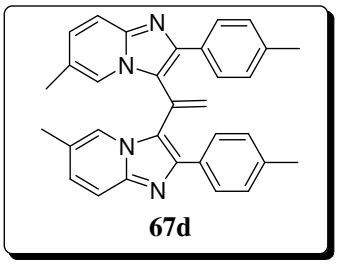
IR (In KBr) : 3636, 3213, 1900, 1615, 1520, 1494, 1421, 1403, 1329, 1143, 1090, 1076, 828, 806, 513 cm^{-1} .

^{1}H NMR ($CDCl_3$/TMS): δ 2.15 (s, 6H 2xCH_3), 6.14 (s, 2H), 6.77 (d, *J* = 7.8 Hz, 4H), 7.03 (d, *J* = 3.1 Hz, 4H), 7.17 (m 2H), 7.44 (d, *J* = 9.4 Hz, 2H), 8.43 (s, 2H).

^{13}C NMR ($CDCl_3$/TMS): δ 21.14, 117.87, 119.41, 120.73, 120.93, 121.13, 126.01, 127.14, 127.57, 128.12, 130.18, 137.79, 143.44, 146.61.

ESI-MS:(m/z): 509.2 (M+1).

67d: 6-Methyl-3-(1-(6-methyl-2-(p-tolyl)imidazo[1,2-a]pyridin-3-yl) vinyl-2-(p-tolyl)imidazo [1,2-a]pyridine.



67d

Description : White solid.

Melting point: : 232.1 – 235.3°C.

IR (In KBr) : 3636, 3367, 3059, 1953, 1606, 1536, 1508, 1398, 1337, 1250, 1126, 1018, 919, 819, 516 cm^{-1} .

^{1}H NMR ($CDCl_3$/TMS): δ 2.21 (s, 6H 2xCH_3), 2.25 (s 6H 2xCH_3), 6.02 (s 2H), 6.88 (d, *J* = 7.8 Hz, 4H), 7.00 (d, *J* = 8.6 Hz, 2H), 7.33 (d, *J* = 7.9 Hz, 4H), 7.43 (d, *J* = 9.0 Hz, 2H), 7.93 (s, 2H).

^{13}C NMR ($CDCl_3$/TMS): δ 18.39, 21.15, 116.52, 119.42, 121.74, 122.49, 122.57, 126.33, 127.63, 127.99, 128.26, 131.72, 136.52, 143.74, 144.32.

ESI-MS:m/z: 469.3 (M+1).

REFERENCES:

1) Anderson, M.; Beattie, G. A.; Breed, J.; Byth, K. F.; Culshaw, J. D.; Ellston, R. P. A.; Green, S; Minshull, C. A. *Bioorg Med Chem Lett* **2003** *13* 3021.

2) Hempel, G.; Blaschke, D. *J .Chromatogr.B* **1996** *675* 131.

3) Trapani, G.; Latrofa, A.; Franco, M.; Carrieri, A.; Snoeck, R. A.; Sanna, E. B. G. *Eur. J. Pharma Sci* **2003** *18* 231.

4) Lacerda, R. B.; de Lime, C. K.; da Silva, L. L. *Bioorg Med Chem Lett* **2009** *17* 74.

5) Gueiffier, A.; Lhassani, M.; Elhnkmaoui, A.; Snoeck, R.; Andrei, G.; Chavignon, O.; Teulade, J. C.; Kerbal, A.; Essassi, E. M.; Debouzy, J. C.; Witvrouw, M.; Blache, Y.; Balzarini, J.; de Clercq, E.; Chapate, J. P. *J Med Chem* **1996** *39* 2856.

6) Gueiffier, A.; Mavel, S.; Lhassan, M.; Elthakmaoui, A.; Snoeck, R.; Andrei, G.; Andre, A.; Chavignon, O.; Teulade, J. C.; Witvrouw, M.; Balzarini, R.; de Clercq, E. *J Med Chem* **1998** *41* 5108.

7) Mavel, S.; Renou, J.; Galter, C.; Allouchi, H.; Snoeck, R.; Andrei, G.; de Clereq, E.; Balzarini, J. *Bioorg Med Chem Lett* **2002** *10* 941.

8) Sanghani, S. G.; Ganatra, K. J. *Pharma Chemica,* **2010** *2(4)* 378.

9) Lacerda, R. B.; de Lima, C. K. F.; da Silva, L. L.; Romeiro, N. C.; Miranda, A. P.; Barreiro, E. J.; Fraga, C. A. M. *Bioorg. Med. Chem.,* **2009** *17(1)* 74.

10) Price, S.; Heald, R.; Lee, W.; Zak, M. E.; Hewitt, J. F. M. PCT Int. Appl. WO 2009085983 **2009**.

11) Hosni, H. M.; Abdulla, M. M. *Acta Pharmaceutica,* **2008** *58(2)* 175.

12) Cesur, Z.; Cesur, N.; Birteksoz, S.; Otuk, G. *Acta Chimica Slovenica,* **2010** *57(2)* 355.

13) Rida, S. M.; El-Hawash, S. A. M.; Fahmy, H. T. Y.; Hazzaa, A. A.; El-Meligy, M. M. *Archives of Pharmacal Research,* **2006** *29* 826.

14) Ismail, M. A.; Arafa, R. K.; Wenzler, T.; Brun, R.; Tanious, F. A.; Wilson, W. D.; Boykin, D. W. *Bioorg. Med. Chem.,* **2008** *16* 683.

15) Ash, A. B.; Stevens, C. L.; Markovac, A. US3600396 **1971**.

16) Heerding, D. A.; Clark, T. J.; Drewry, D. H.; Leber, J. D.; Safonov, I.; Yamashita, D. S. WO 2005011700 **2005**.

17) Ohtsuka, M.; Haginoya, N.; Chikawa, M.; Matsunaga, H.; Saito, H.; Shibata, Y.; Tsunemi, T. WO 2010016490 **2010**.

18) Zhang, R.; Yongzhou, H. *Synth Comm* **2004** *34* 3955.

19) Sumalatha, Y.; Reddy, P. P.; Reddy, R.; Satyanarayana, B. *ARKIVOC* **2009** 8 143.

20) da Silva, F. M.; Menezes, F. G.; Vicente, J.; Adailton, J. B.; Cesar, Z.; Ademir, N.; Sanches, N. G. *Journal of Molecular Structure* ,

2009 *938* 1.

21) Nishiki, W. O.; Lto, K. *Letters in Org Chem* **2007** *2(4*) 112.

22) Surya, G. K. P.; Fogassy, G.; Olah, G. A. *Catalysis Letters* **2009** *138* 155.

23) Chunlou, S.; Xiaoyuan, Z.; Feng, L. *Chemistry A European Journal* **2013** *19* 14030.

24) Edgardo, N. D. *Molecules* **2001** *6* 533.

25) Chang-Hee, L.; Lindsey, J. S. *Tetrahedron* **1994** *50* 11427.