Supporting Information

Efficient Synthesis of Biazoles by Aerobic Oxidative Homocoupling of Azoles Catalyzed by Copper(I) / 2-pyridonate Catalytic System

Mingwen Zhu,[a] Ken-ichi Fujita,*[,a,b] and Ryohei Yamaguchi*[,a]

[a]Graduate School of Human and Environmental Studies, Kyoto University, Sakyo-ku, Kyoto 606-8501, Japan

Email: yamaguchi.ryohei.8c@kyoto-u.ac.jp

[b]Graduate School of Global Environmental Studies, Kyoto University, Sakyo-ku, Kyoto 606-8501, Japan

Email: fujitak@kagaku.mbox.media.kyoto-u.ac.jp;

Experimental Section:

General: All reactions and manipulations were carried out by means of standard Schlenk techniques. ^{1}H and ^{13}C NMR spectra were recorded on JEOL ECS-400 and ECX-500 spectrometers. Column chromatography was carried out by using Wako-gel C-200. Elemental analyses were carried out at the Microanalysis Center of Kyoto University. Melting points were measured using a Yanagimoto melting point measurement apparatus. Solvents were dried by standard procedures and distilled prior to use. 1-(4-methylbenzyl)-1*H*-imidazole (**8**), 1-(4-trifluorobenzyl)-1*H*-imidazole (**9**), 1-(4-bromobenzyl)-1*H*- imidazole (**10**), 1-(4-chlorobenzyl)-1*H*-imidazole (**11**), 1-(3-chlorobenzyl)-1*H*-imidazole (**12**), 1-(2-chlorobenzyl)-1*H*-imidazole (**13**), were prepared according to the literature method[1]. All other reagents are commercially available and were used without further purification.

Preparation of 2-pyridonate ligands: To an oven-dried, argon purged flask were added 1.0 mmol of functionalized hydroxypyridine (2-hydroxypyridine, 3-hydroxypyridine, 4-hydroxypyridine, phenol, 5-trifluoromethyl-2-hydroxypyridine, 5-nitro-2-hydroxypyridine, 6-methyl-2-hydroxypyridine, 5-methyl-2-hydroxypyridine, 4-methyl-2-hydroxypyridine, 3-methyl-2-hydroxypyridine, 3-methoxy-2-hydroxypyridine), 1.0 mmol of sodium ethoxide and ethanol (2.5 mL), respectively. The mixture was stirred at room temperature for 2 hours. Then the solvent was removed and residue was dried in vacuo to give a colorless or yellow solid.

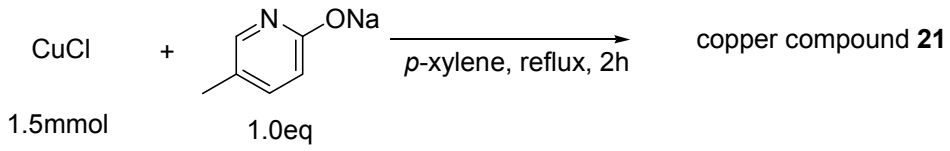
Sodium 2-pyridonate (**L1**) ^{1}H NMR (500 MHz, D_2O): δ 7.72 (br, 1H, Ar-H), 7.55 (t, 1H, J = 8.0 Hz, Ar-H), 6.54 (t, 1H, J = 5.3 Hz, Ar-H), 6.47 (d, 1H, J = 7.5 Hz, Ar-H).
Sodium 3-methoxy-2-pyridonate (**L5**) ^{1}H NMR (400 MHz, D_2O): δ 7.17 (br, 1H, Ar-H), 7.04 (d, 1H, J = 7.6 Hz, Ar-H), 6.47 (br, 1H, Ar-H), 3.76 (s, 3H, OCH_3).
Sodium 3-methyl-2-pyridonate (**L6**) ^{1}H NMR (400 MHz, D_2O): δ 7.50 (d, 1H, J = 5.2 Hz, Ar-H), 7.44 (d, 1H, J = 5.2 Hz, Ar-H), 6.47 (t, 1H, J = 5.2 Hz, Ar-H), 2.06 (s, 3H, CH_3).
Sodium 4-methyl-2-pyridonate (**L7**) ^{1}H NMR (500 MHz, D_2O): δ 7.50 (d, 1H, J = 6.0 Hz, Ar-H), 6.43 (d, 1H, J = 6.0 Hz, Ar-H), 6.37 (br, 1H, Ar-H), 2.22 (s, 3H, CH_3).
Sodium 5-methyl-2-pyridonate (**L8**) ^{1}H NMR (500 MHz, D_2O): δ 7.55 (s, 1H, Ar-H), 7.44 (d, 1H, J = 9.0 Hz, Ar-H) 6.43 (d, 1H, J = 8.5 Hz, Ar-H), 2.12 (s, 3H, CH_3).
Sodium 6-methyl-2-pyridonate (**L9**) ^{1}H NMR (500 MHz, D_2O): δ 7.49 (br, 1H, Ar-H), 6.39 (br, 1H, Ar-H), 6.31 (br, 1H, Ar-H), 2.27 (br, 3H, CH_3).
Sodium 5-(trifluoromethyl) -2-pyridonate (**L10**) ^{1}H NMR (400 MHz, D_2O): δ 8.08 (s, 1H, Ar-H), 7.61 (d, 1H, J = 7.2 Hz, Ar-H), 6.38 (d, 1H, J = 7.2 Hz, Ar-H).
Sodium 5-nitro-2-pyridonate (**L11**) ^{1}H NMR (500 MHz, D_2O): δ 8.84 (br, 1H, Ar-H), 8.18 (br, 1H, Ar-H), 6.39 (br, 1H, Ar-H).

Procedure for the homocoupling of 1-methyl-1*H*-imidazole shown in Table 1: To an oven-dried, argon purged two-necked flask were added sodium 2-pyridonate (0.04 mmol, 2.0 or 1.0 mol%), Cu-catalyst (0.02 mmol, 2.0 or 1.0 mol%), 1-methyl-1*H*-imidazole (1.0 or 2.0 mmol), and *p*-xylene (4 mL). The flask was sealed and preheated at 140 °C under argon for

about 1 minute and then the mixture was stirred at 140 °C under open air for 20 h. The mixture was cooled to room temperature. The solvent was removed in vacuo and the crude reaction mixture was diluted with chloroform and filtered through a filter-paper. Chloroform was removed in vacuo and 1,3,5-trimethoxybenzene was added as an internal standard for NMR analysis. The yield of 1,1'-dimethyl-1*H*,1*H'*-2,2'-biimidazole (**1**) was calculated by ^{1}H-NMR analysis in chloroform-d.

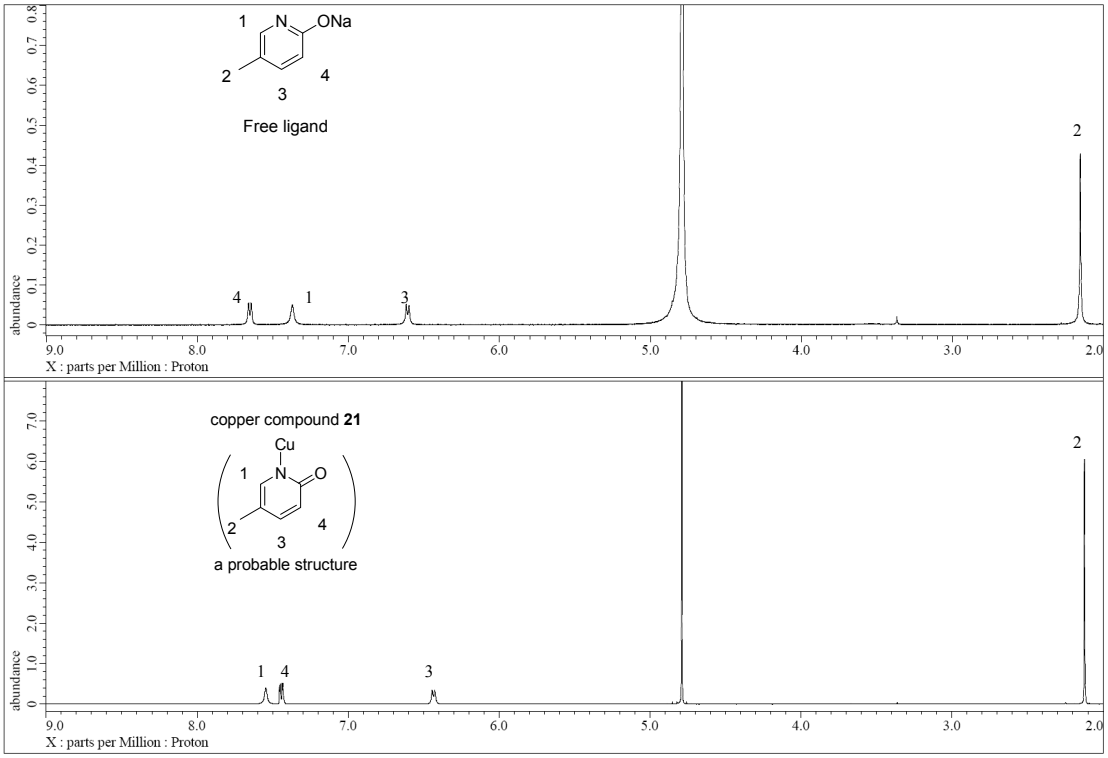
General Procedure for the oxidative homocoupling of various azoles shown in Table 2 and 3: To an oven-dried, argon purged flask were added sodium 5-methyl-2-pyridonate (**L8**) (0.04 mmol, 2.0 mol%), CuCl (0.02 mmol, 1.0 mol%), an azole (2.00 mmol) and *p*-xylene (4 mL). The flask was sealed and preheated at 140 °C under argon for about 1 minutes and then the mixture was stirred at 140 °C under open air for 20 h. The mixture was cooled to room temperature. The solvent was removed in vacuo and the crude reaction mixture was diluted with chloroform and filtered through a filter-paper. The filtrate was concentrated by evaporation and purified by a silica gel column chromatography.

Stoichiometric reaction of CuCl with sodium 5-methyl-2-pyridonate (L8) to afford copper compound 21:

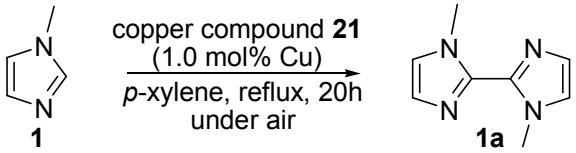


To an oven-dried, argon purged two-necked flask were added CuCl (1.5 mmol), sodium 5-methyl-2-pyridonate (1.5 mmol) and *p*-xylene (10 mL). The suspension was heated under reflux in an oil bath for 2 h under argon. Then the mixture was cooled to room temperature and washed with, MeOH, (5 mL, 2 times) and Et_2O (5 mL, 2 times) . Drying in vacuum gave a yellow solid (**21**) (229.1 mg, 89%). M. p.: 192 °C (dec.). ^{1}H NMR (500 MHz, D_2O) δ 7.65 (d, 1H, J = 9.0 Hz), 7.37 (s, 1H), 6.61 (d, 1H, J = 9.5 Hz), 2.15 (s, 3H). ^{13}C NMR (125.7 MHz, D_2O) δ 163.7, 146.5, 132.5, 119.3, 118.2, 16.0. Anal.Calcd for CuC_6H_6NO: C, 41.98; H, 3.52; N, 8.16. Found: C, 41.74; H, 3.53; N, 8.11.

^{1}H NMR spectra of copper compound 21 and free ligand L8 in D_2O:



Aerobic oxidative homocoupling of N-methylimidazole catalyzed by the copper compound 21:

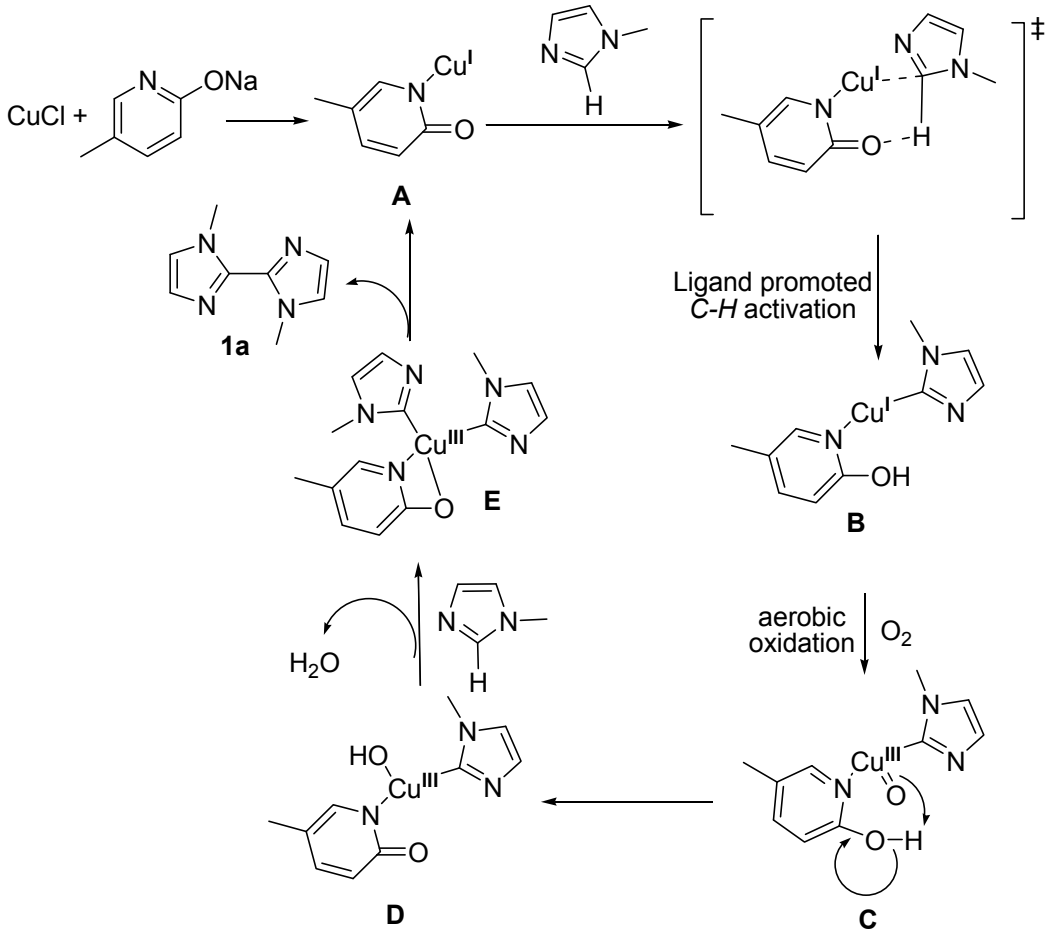


92% NMR yield

To an oven-dried, argon purged two-necked flask were added the copper compound **21** (3. 2 mg, 2.0 mol% Cu), 1-methyl-1*H*-imidazole (2.00 mmol), and *p*-xylene (4 mL). The flask was sealed and preheated at 140 ^oC under argon for about 1 minute and then the mixture was stirred at 140 ^oC under open air for 20 h. The mixture was cooled to room temperature. The solvent was removed in vacuo and the crude reaction mixture was diluted with chloroform and filtered through a filter-paper. Chloroform was removed in vacuo and 1,3,5-trimethoxybenzene was added as an internal standard for NMR analysis. The yield of 1,1'-dimethyl-1*H*,1*H'*-2,2'-biimidazole (**1a**) was calculated by the integration in ^{1}H-NMR analysis in chloroform-d.

Explanation of a Plausible Mechanism:

Although the mechanism for the CuCl/2-pyridonate catalyzed aerobic oxidative homo-coupling of azoles is not completely clear so far, a plausible one is shown in Scheme S1. The reaction would start with the formation of a Cu(I) species **A** bearing 2-pyridonate as a ligand by the reaction of CuCl with sodium 2-pyridonate. Then, 2-pyridonate ligand-promoted C-H activation of azole would occur to afford a Cu(I) species **B** which would be oxidized by oxygen to form a Cu(III)-oxo species **C**. Subsequent hydrogen transfer from hydroxyl group in the ligand to copper-oxo moiety would occur to afford a Cu(III) species **D**. Ligand promoted C-H activation of azole followed by dehydration would proceed to give a bis-imidazolyl Cu(III) species **E**. Reductive elimination would take place to give the corresponding biazoles and regenerate the Cu(I) species **A**.



Scheme S1. A plausible mechanism

Data for the Products of oxidative homocoupling of azoles:

1,1'-dimethyl-1*H*,1*H*'-2,2'-biimidazole (**1a**)[2]:
Purification was performed by column chromatography on silica gel eluting with EtOAc (100%) to give **1a** as a colorless solid (152.2 mg, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (d, 2H, *J* = 1.0 Hz, Im-H), 6.96 (d, 2H, *J* = 1.0 Hz, Im-H), 4.04 (s, 6H, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 138.82, 127.96, 122.74, 35.49.

1,1'-diethyl-1*H*,1*H*'-2,2'-biimidazole (**2a**)[3]:
Purification was performed by column chromatography on silica gel eluting with EtOAc/Hexane (3:1) to give product **2a** as a colorless solid (182.2 mg, 96% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (d, 2H, *J* = 1.0 Hz, Im-H), 7.02 (d, 2H, *J* = 1.0 Hz, Im-H), 4.50 (q, 4H, *J* = 7.5 Hz, CH_2), 1.41 (t, 6H, *J* = 7.5 Hz, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 138.04, 128.24, 120.56, 42.63, 16.63.

1,1'-di-n-butyl-1*H*,1*H*'-2,2'-biimidazole (**3a**)[3]:
Purification was performed by column chromatography on silica gel eluting with EtOAc/Hexane (1:1) to give **3a** as a pale yellow oil (221.0 mg, 90% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (s, 2H, Im-H), 6.99 (s, 2H, Im-H), 4.44 (t, 4H, *J* = 7.5 Hz, $CH_2CH_2CH_2CH_3$), 1.74-1.68 (m, 4H, $CH_2CH_2CH_2CH_3$), 1.30-1.25 (m, 4H, $CH_2CH_2CH_2CH_3$), 0.89-0.86 (t, 6H, *J* = 7.5 Hz, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 138.24, 128.05, 47.20, 33.25, 19.81, 13.73.

1,1'-divinyl-1*H*,1*H*'-2,2'-biimidazole (**4a**):
Purification was performed by column chromatography on silica gel eluting with EtOAc/Hexane (1:1) to give **4a** as a colorless solid (117.5 mg, 63% yield). M. p.: 125-126^{o}C, ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.02 (q, 2H, *J* = 8.0 Hz, CH=CH_2), 7.37 (d, 2H, *J* = 1Hz, Im-H), 7.17 (d, 2H, *J* = 1 Hz, Im-H), 5.28 (dd, 2H, *J* = 16.0 Hz, 1.5 Hz, CH=CH_2), 4.95 (dd, 2H, *J* = 8.0 Hz, *J* = 1.5 Hz, CH=CH_2). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 137.3, 131.3, 129.6, 117.1, 102.5. Anal.Calcd for $C_{10}H_{10}N_4$: C, 64.50; H, 5.41; N, 30.09. Found; C, 64.59; H, 5.38; N, 30.04.

1,1'-di(4-methoxyphenyl)-1*H*,1*H*'-2,2'-biimidazole (**5a**)[4]:
Purification was performed by column chromatography on silica gel eluting with EtOAc (100%) to give **5a** as a colorless solid (266.1 mg, 77% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (d, 2H, *J* = 1.0 Hz, Im-H), 7.02 (d, 2H, *J* = 1.0 Hz, Im-H), 6.75-6.70 (m, 8H, Ar-H), 3.79 (s, 6H, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 158.95, 137.81, 130.45, 129.73, 125.60, 121.63, 114.26, 55.67.

1,1'-dibenzyl-1*H*,1*H*'-2,2'-biimidazole (**7a**)[2]:
Purification was performed by column chromatography on silica gel eluting with EtOAc/Hexane (1:1) to give **7a** as a pale yellow solid (291.6 mg, 92% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24-7.23 (m, 6H, Ar-H), 7.12 (d, 2H, *J* = 1.0 Hz, Im-H), 7.04-7.03 (m, 4H, Ar-H), 6.93 (d, 2H, *J* = 1.0 Hz, Im-H), 5.71 (s, 4H, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ

138.41, 137.46, 128.80, 128.53, 127.76, 127.58, 121.57, 50.94.

1,1'-di(4-methylbenzyl)-1*H*,1*H*'-2,2'-biimidazole (**8a**):
Purification was performed by column chromatography on silica gel eluting with EtOAc (100%) to give **8a** as a pale red solid (294.2 mg, 86% yield). M.p.: 154-155 ^{o}C, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (s, 2H, Im-H), 7.04 (d, 4H, *J* = 7.5 Hz, Ar-H), 6.94-6.92 (m, 6H, Ar-H and Im-H), 5.63 (s, 4H, CH_2), 2.31 (s, 6H, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 138.43, 137.48, 134.44, 129.46, 128.47, 127.69, 121.48, 50.75, 21.27. Anal. Calcd for $C_{22}H_{22}N_4$: C, 77.16; H, 6.48; N, 16.36. Found: C, 77.39; H, 6.31; N, 16.45.

1,1'-di(4-trifluoromethylbenzyl)-1*H*,1*H*'-2,2'-biimidazole (**9a**):
Purification was performed by column chromatography on silica gel eluting with EtOAc/Hexane (1:1) to give **9a** as a pale red solid (379.7 mg, 88% yield). M.p.: 122-123 ^{o}C, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, 4H, *J* = 8.0 Hz, Ar-H), 7.15-7.13 (m, 6H, Ar-H and Im-H), 6.95 (d, 2H, *J* = 1.0 Hz, Im-H), 5.85 (s, 4H, CH_2). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 141.54, 138.25, 130.10 (q, *J* = 32.8 Hz, C-F coupling), 128.86, 127.65, 125.76, 124.08 (q, *J* = 271.8 Hz, C-F coupling), 121.85, 50.56. Anal. Calcd for $C_{22}H_{16}F_6N_4$: C, 58.67; H, 3.58; N, 12.44. Found: C, 59.14; H, 3.93; N, 12.07.

1,1'-di(4-bromobenzyl)-1*H*,1*H*'-2,2'-biimidazole (**10a**):
Purification was performed by column chromatography on silica gel eluting with EtOAc/Hexane (1:1) to give **10a** as a pale yellow solid (414.9 mg, 90% yield). M.p.: 149-150 ^{o}C, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, 4H, *J* = 8.0 Hz, Ar-H), 7.12 (d, 2H, *J* = 1.0 Hz, Im-H), 6.93 (s, 2H, *J* = 1.0 Hz, Im-H), 6.88 (d, 4H, *J* = 8.0 Hz, Ar-H), 5.66 (s, 4H, CH_2). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 138.20, 136.46, 131.92, 129.24, 128.66, 121.83, 121.68, 50.37. Anal. Calcd for $C_{22}H_{16}Br_2N_4$: C, 50.87; H, 3.42; N, 11.87. Found: C, 50.89; H, 3.38; N, 11.54.

1,1'-di(4-chlorobenzyl)-1*H*,1*H*'-2,2'-biimidazole (**11a**):
Purification was performed by column chromatography on silica gel eluting with EtOAc (100%) to give **11a** as a pale yellow solid (348.1 mg, 90% yield). M.p.:161-162 ^{o}C, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, 4H, *J* = 8.0 Hz, Ar-H), 7.12 (d, 2H, *J* = 1.5 Hz, Im-H), 6.95 (d, 4H, *J* = 8.0 Hz, Ar-H), 6.93 (d, 2H, *J* = 1.5 Hz, Im-H), 5.68 (s, 4H, CH_2). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 138.21, 135.96, 133.71, 128.96, 128.94, 128.67, 121.65, 50.32. Anal. Calcd for $C_{22}H_{16}Cl_2N_4$: C, 62.67; H, 4.21; N, 14.62. Found; C, 62.73; H, 4.22; N, 14.67.

1,1'-di(3-chlorobenzyl)-1*H*,1*H*'-2,2'-biimidazole (**12a**):
Purification was performed by column chromatography on silica gel eluting with EtOAc (100%) to give **12a** as a pale yellow solid (318.4 mg, 83% yield). M.p.: 106-107 ^{o}C, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23-7.10 (m, 8H, Ar-H and Im-H), 6.92-6.94 (m, 4H, Ar-H and Im-H), 5.73 (s, 4H, CH_2) ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 139.49, 138.25, 134.69, 130.15, 128.76, 128.09, 127.70, 125.67, 121.69, 50.44. Anal. Calcd for $C_{22}H_{16}Cl_2N_4$: C, 62.67; H, 4.21; N, 14.62. Found: C, 62.46; H, 4.37; N, 14.59.

1,1'-di(2-chlorobenzyl)-1*H*,1*H*'-2,2'-biimidazole (**13a**):
Purification was performed by column chromatography on silica gel eluting with EtOAc (100%) to give **13a** as a pale yellow solid (313.1 mg, 81% yield). M.p.: 157-158 °C, ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.21 (t, 2H, *J* = 7.5 Hz, Ar-H), 7.12 (s, 2H, Im-H), 7.11 (t, 2H, *J* = 7.5 Hz, Ar-H), 6.95 (s, 2H, Im-H), 6.87 (d, 2H, *J* = 8.0 Hz, Ar-H), 5.89 (s, 4H, CH_2). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 138.58, 135.27, 133.26, 129.73, 129.34, 129.19, 128.72, 127.34, 121.66, 48.67. Anal. Calcd for $C_{22}H_{16}Cl_2N_4$: C, 62.67; H, 4.21; N, 14.62. Found: C, 62.67; H, 4.17; N, 14.54.

1,1'-dimethyl-1*H*,1*H*'-2,2'-bibenzo[*d*]imidazole (**14a**)[2]:
Purification was performed by column chromatography on silica gel eluting with EtOAc/Hexane (1:5) to give **14a** as a colorless solid (224.1 mg, 85% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.48 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.42-7.35 (m, 4H, Ar-H), 4.32 (s, 6H, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 143.36, 142.68, 136.33, 124.06, 122.98, 120.43, 110.21, 32.56.

4,4'-diphenyl-2,2'-bioxazole (**15a**):
Purification was performed by column chromatography on silica gel eluting with EtOAc/Hexane (1:5) to give product **15a** as a colorless solid (241.9 mg, 84% yield). M.p.: 249-250 °C, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (s, 2H, Im-H), 7.87 (d, 4H, *J* = 7.5 Hz, Ar-H), 7.46 (t, 4H, *J* = 7.5 Hz, Ar-H), 7.38 (t, 2H, *J* = 7.5 Hz, Ar-H). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 151.32, 142.97, 135.12, 129.94, 128.95, 128.89, 125.97. Anal. Calcd for $C_{18}H_{12}N_2O_2$: C, 74.99; H, 4.20; N, 9.72. Found: C, 75.39; H, 4.48; N, 9.45.

2,2'-bibenzo[*d*]oxazole (**16a**)[2]:
Purification was performed by column chromatography on silica gel eluting with EtOAc/Hexane (1:5) to give product **16a** as a colorless solid (216.4 mg, 92% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.73 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.55–7.47 (m, 4H, Ar-H). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 152.03, 151.13, 141.31, 127.70, 125.92, 121.67, 111.63.

2,2'-bibenzo[*d*]thiazole (**17a**):
Purification was performed by column chromatography on silica gel eluting with EtOAc (100%) to give **17a** as a colorless solid (218.2 mg, 81% yield). M.p.: 239-240 °C (dec.), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, 2H, *J* = 8.0 Hz, Ar-H), 8.00 (d, 2H, *J* = 8.0 Hz, Ar-H), 7.57 (t, 2H, *J* = 7.0 Hz, Ar-H), 7.50 (t, 2H, *J* = 7.0 Hz, Ar-H). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 161.63, 153.65, 135.90, 126.94, 126.73, 124.18, 122,14. Anal.Calcd for $C_{14}H_8N_2S_2$: C, 62.66; H, 3.00; N, 10.44. Found: C, 62.63; H, 2.97; N,10.42.

4,4'-dimethyl-2,2'-bithiazole (**18a**)[2]:
Purification was performed by column chromatography on silica gel eluting with EtOAc/Hexane (1:5) to give **18a** as a pale green solid (180.9 mg, 91% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.96 (s, 4H, Im-H), 2.51 (s, 6H, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 160.96, 154.30, 115.56, 17.32.

4,4',5,5'-tetramethyl-2,2'-bithiazole (**19a**)[2]:
Purification was performed by column chromatography on silica gel eluting with EtOAc/Hexane (1:5) to give **19a** as a colorless solid (209.1 mg, 92% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.39 (s, 6H, CH_3), 2.36 (s, 6H, CH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 157.23, 149.68, 128.30, 14.96, 11.76.

(4,4'-dimethyl-2,2'-bithiazole-5,5'-diyl)bis(methylene) dipropionate (**20a**):
Purification was performed by column chromatography on silica gel eluting with EtOAc/Hexane (1:1) to give **20a** as a colorless solid (367.6 mg, 98% yield). M.p.: 118-119 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.26 (t, 4H, OCH_2), 3.10 (t, 4H, Im-CH_2), 2.41 (s, 6H, Im-CH_3), 2.08 (s, 6H, $COCH_3$). ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 170.97, 158.36, 150.74, 129.34, 64.04, 26.31, 21.08, 15.20. Anal. Calcd for $C_{16}H_{20}N_2O_4S_2$: C, 52.15; H, 5.47; N, 7.66. Found: C, 52.11; H, 5.43; N, 7.59.

X-ray Structure Analysis of 14a: Diffraction data for **14a** were obtained with a Rigaku RAXIS RAPID instrument. Reflection data were corrected for Lorentz and polarization effects. Empirical absorption corrections were applied. The structures was solved by direct method[5,6] and refined anisotropically for non-hydrogen atoms by full-matrix least-squares calculations. Atomic scattering factors and anomalous dispersion terms were taken from the literature.[7] Hydrogen atoms were located on the idealized positions. The calculations were performed using the program system CrystalStructure.[8, 9] ORTEP drawing of **14a** is shown in Figure S1. The crystal data and details are shown in CIF file.

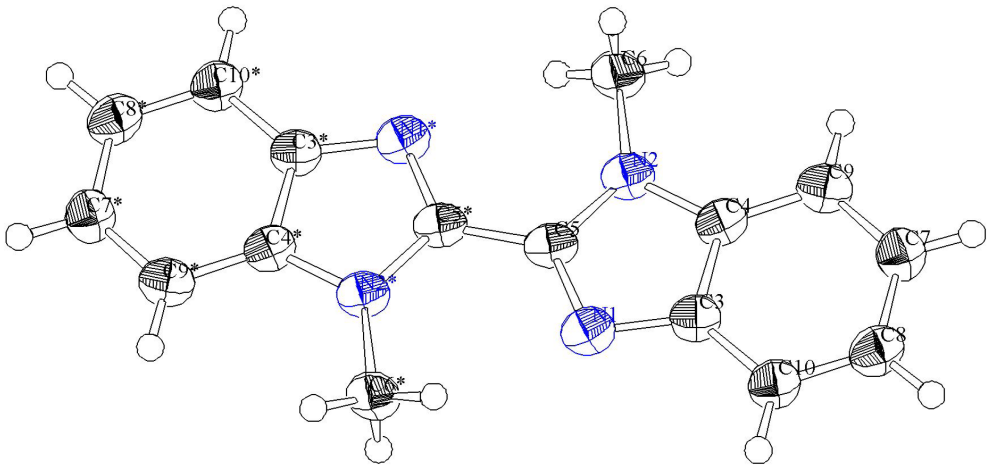
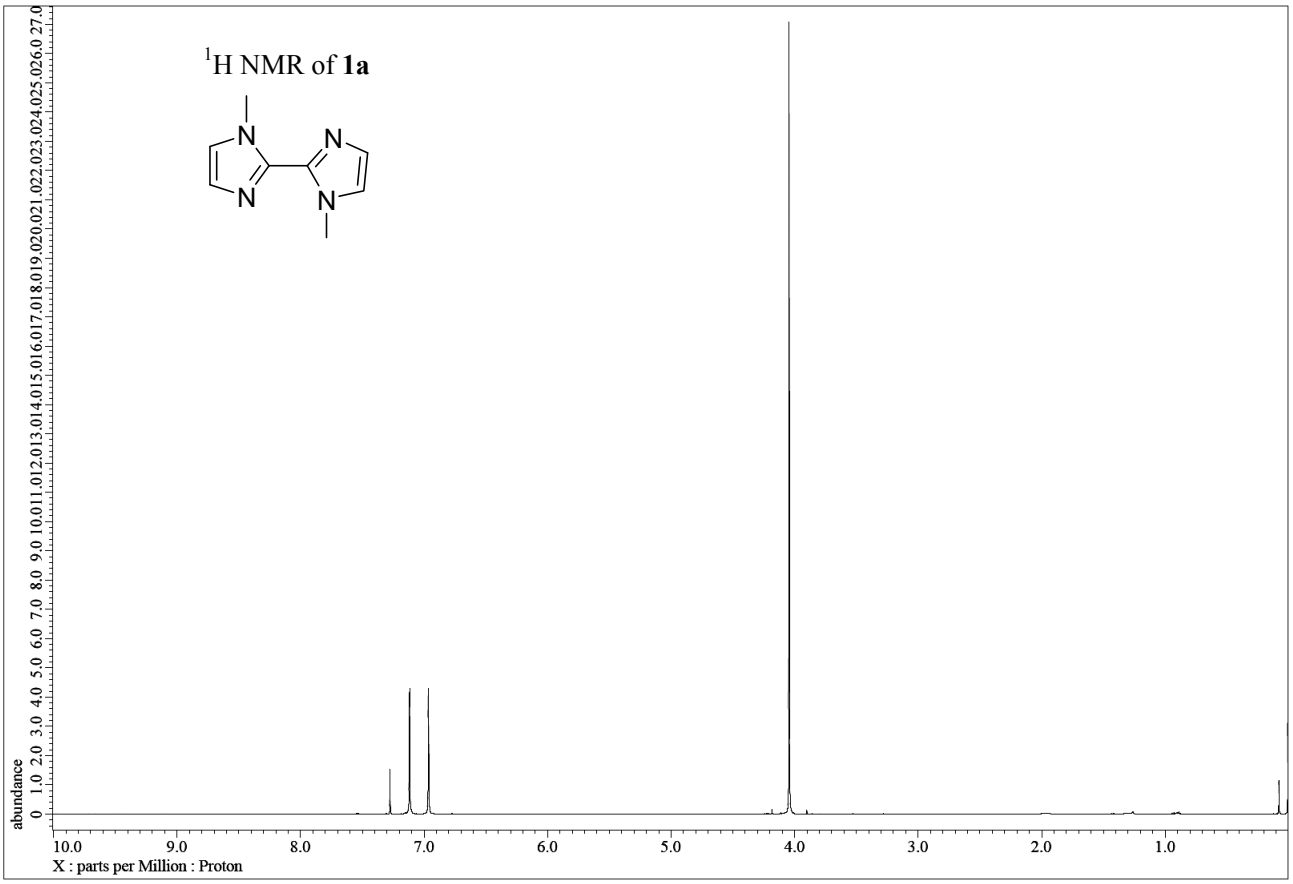
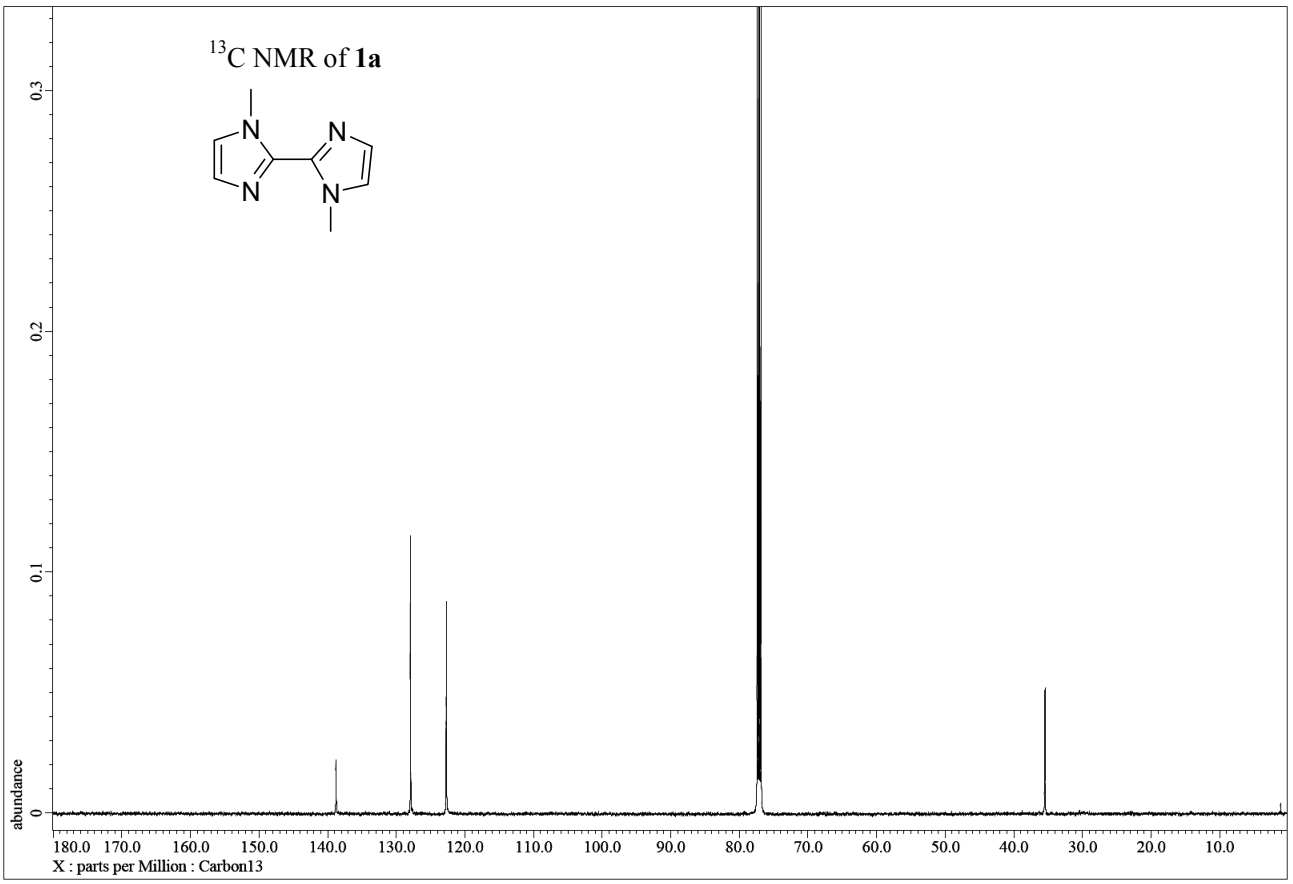
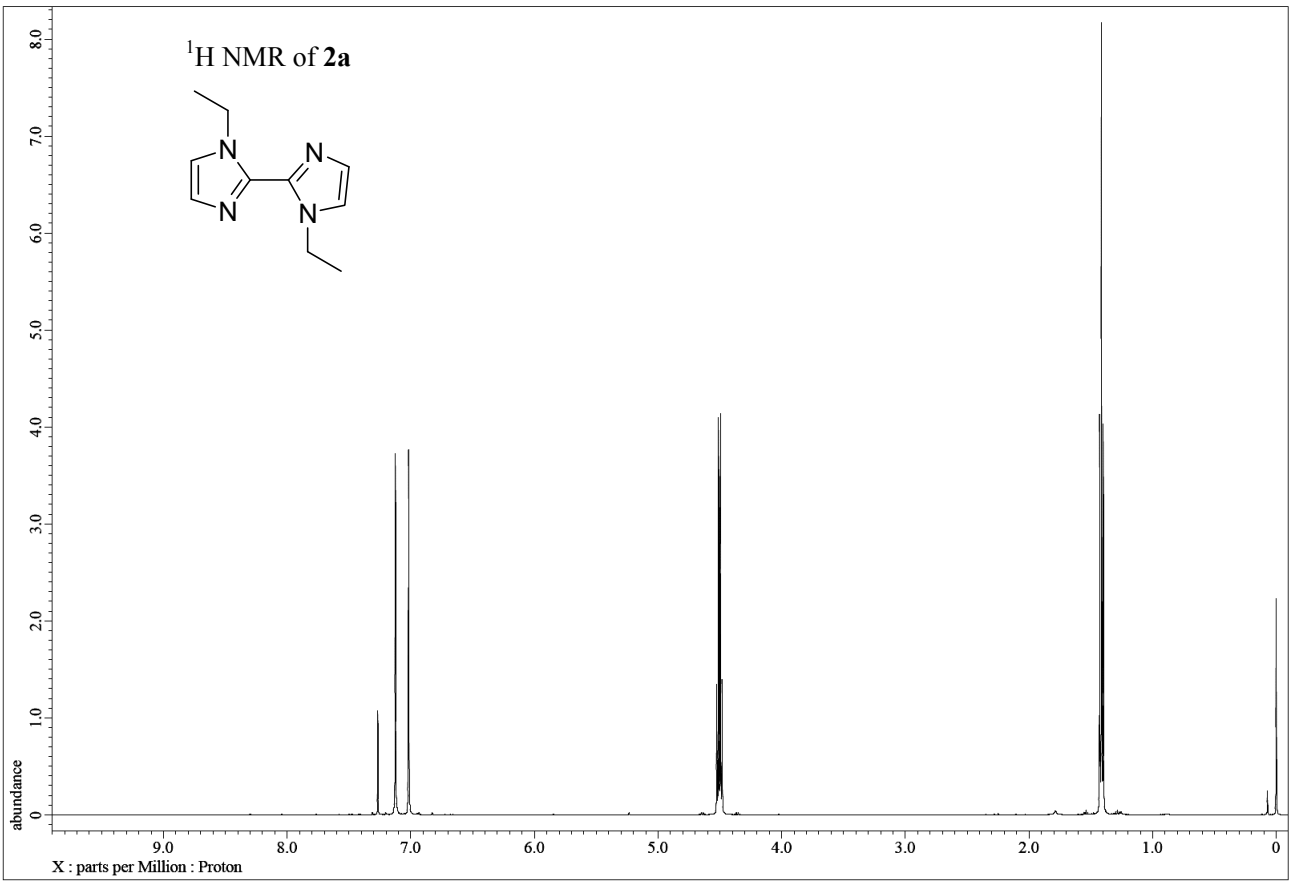
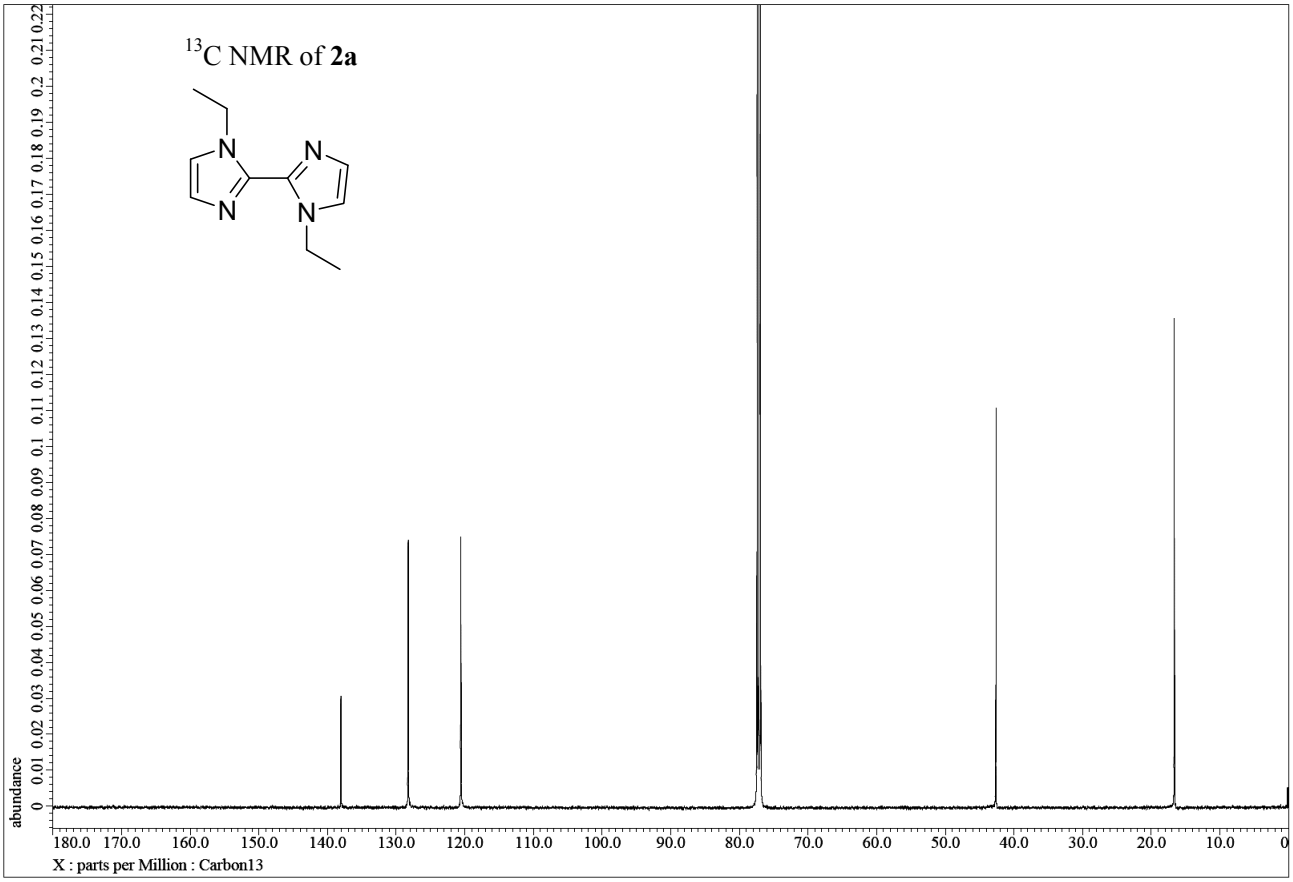


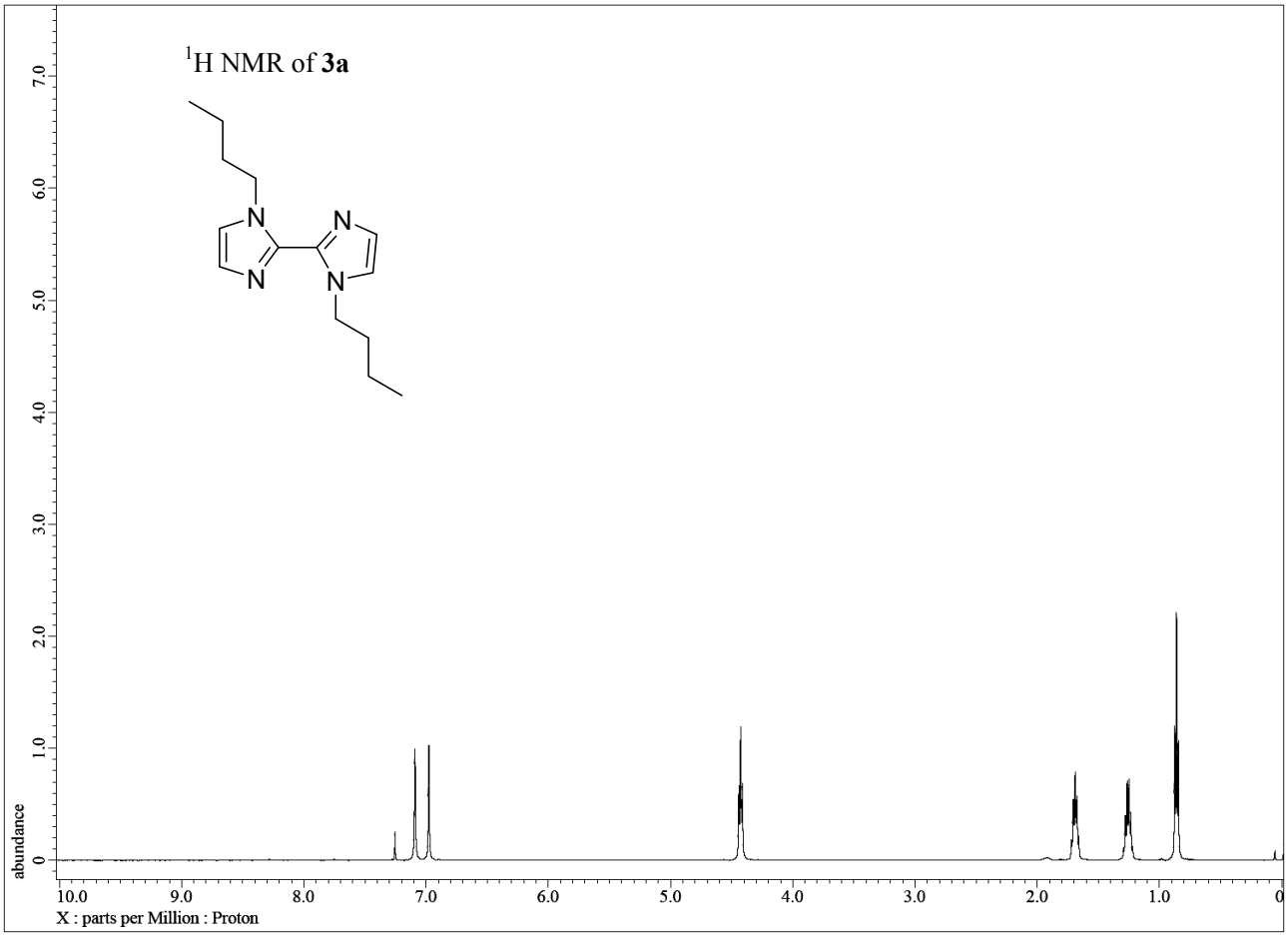
Figure S1. ORTEP drawings of 1,1'-dimethyl-1*H*,1*H'*-2,2'-bibenzo[*d*]imidazole (**14a**) with 50% thermal probability ellipsoids.

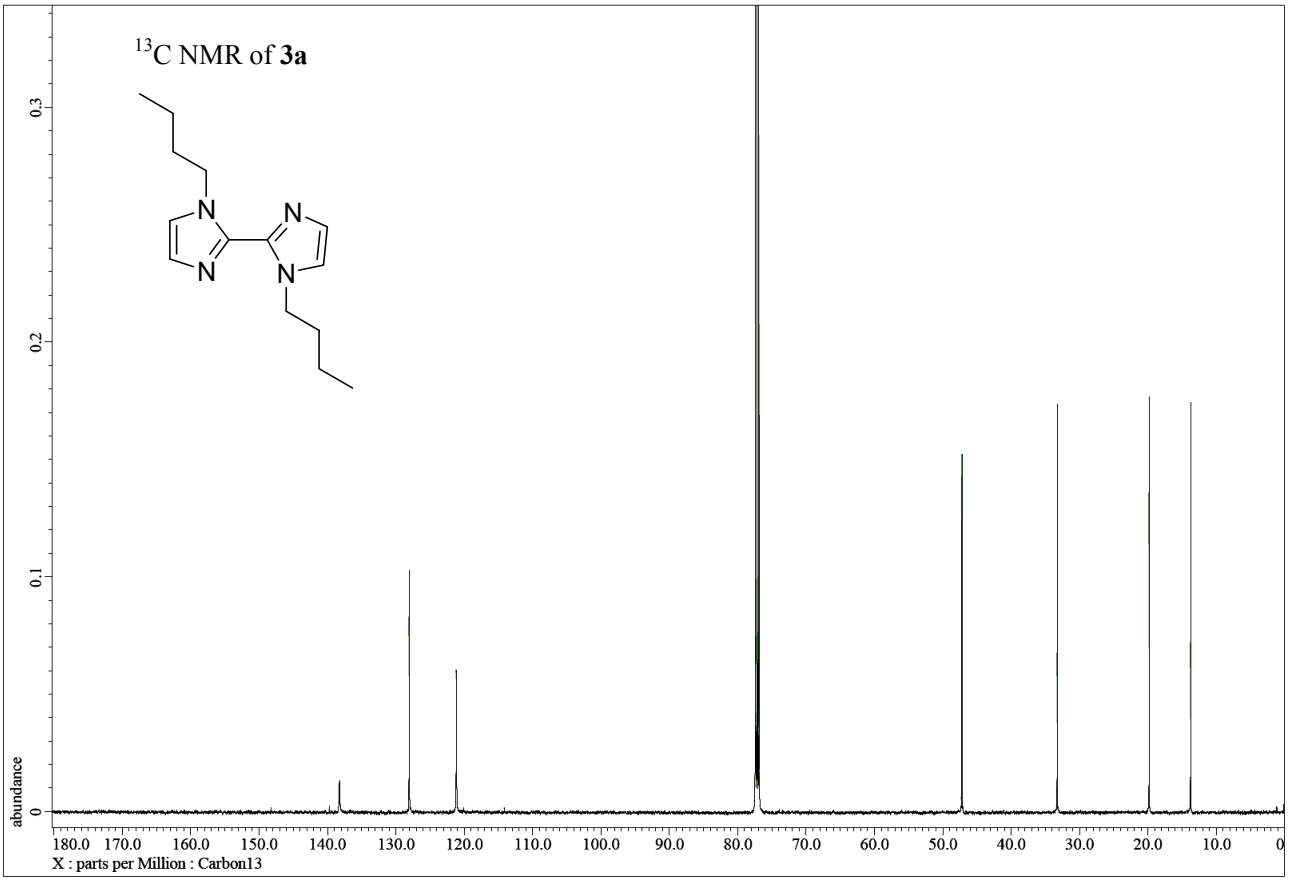

^{1}H NMR of **1a**
abundance
X : parts per Million : Proton

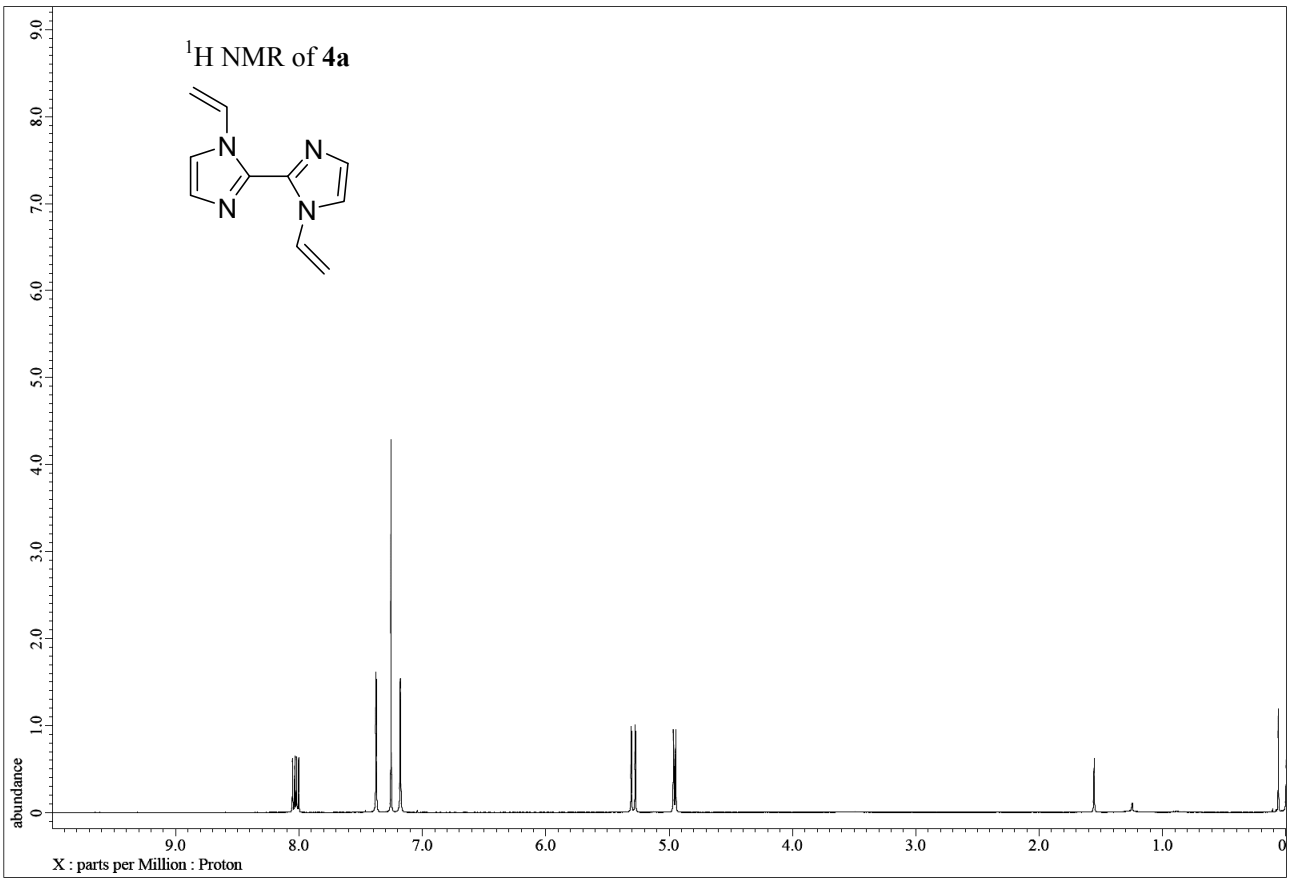

^{13}C NMR of **1a**
abundance
X : parts per Million : Carbon13

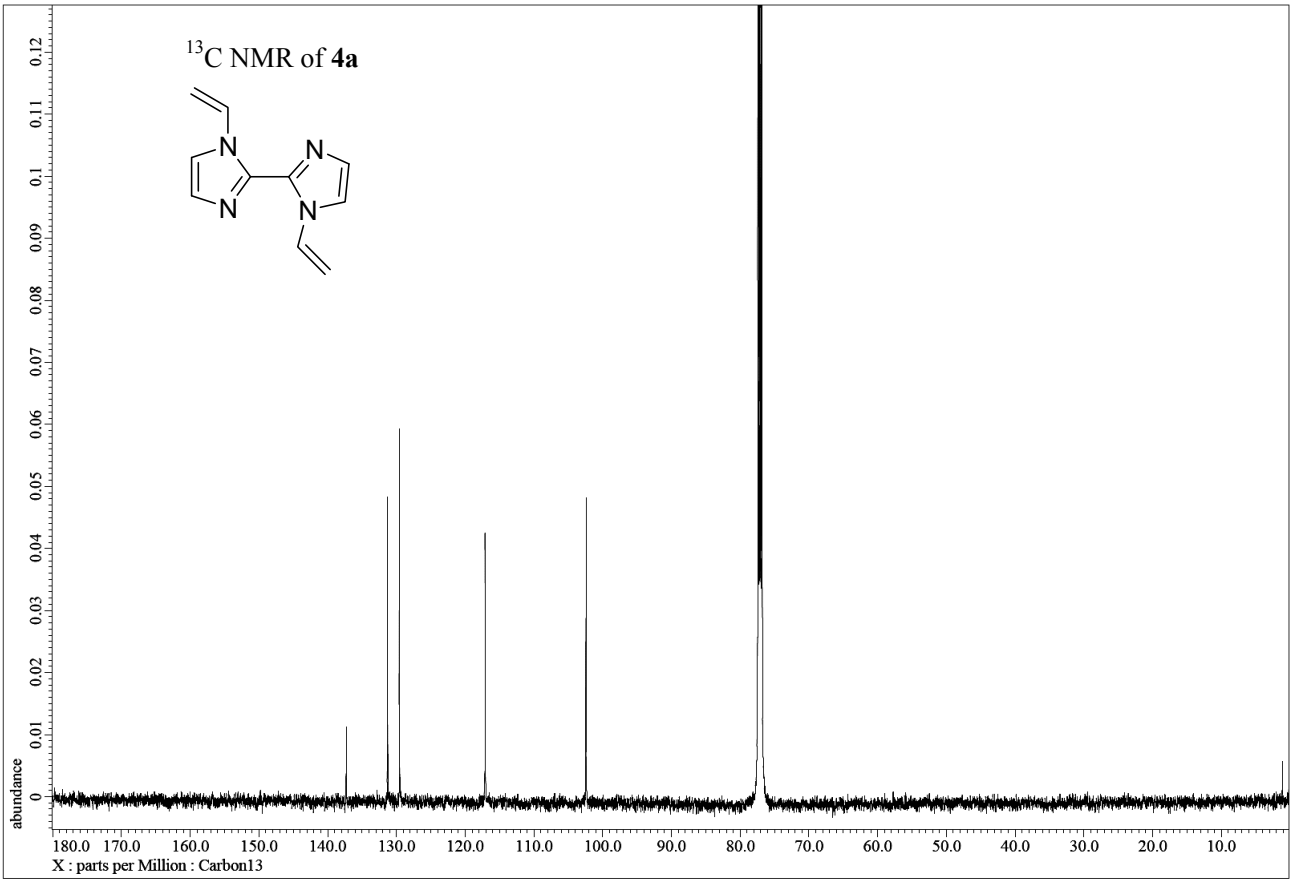

^{1}H NMR of **2a**
abundance
X : parts per Million : Proton

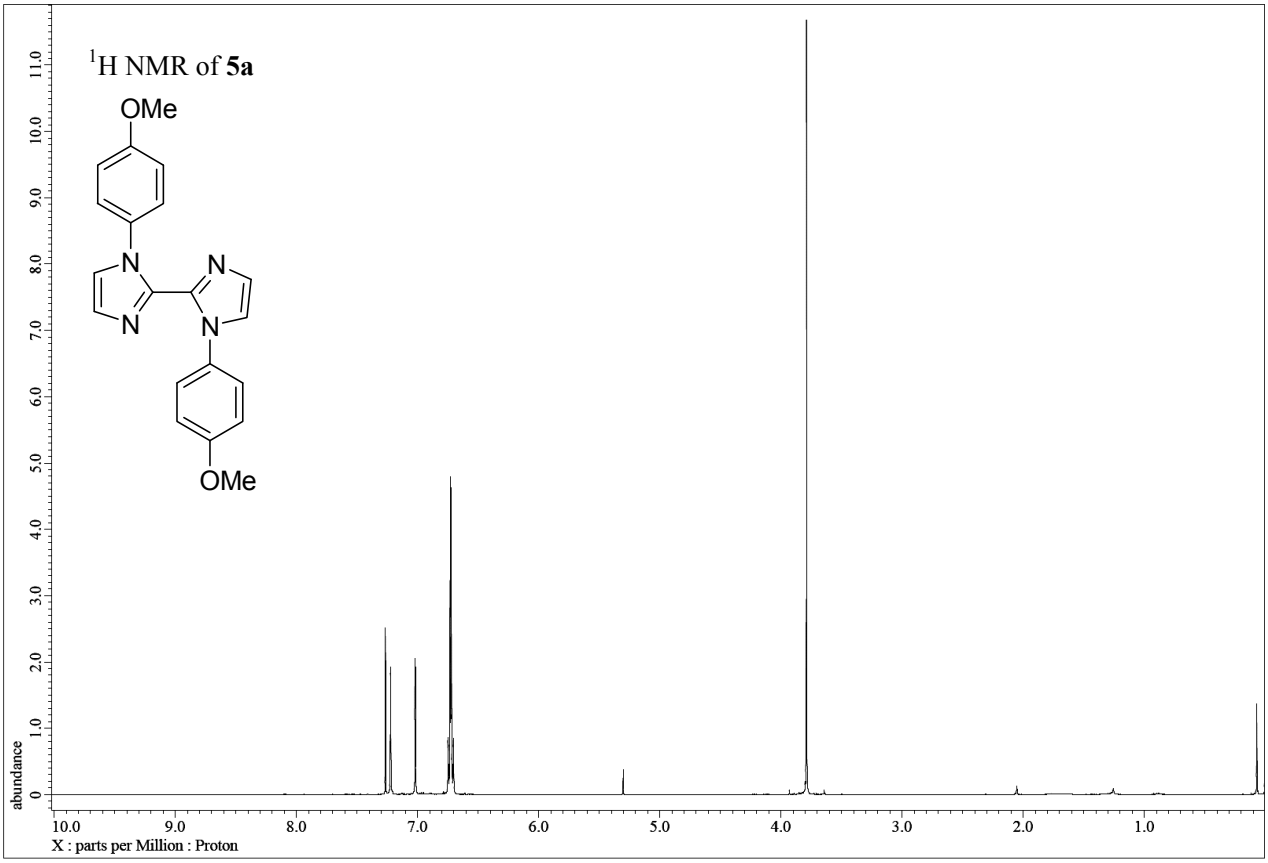

^{13}C NMR of **2a**
abundance
X : parts per Million : Carbon13

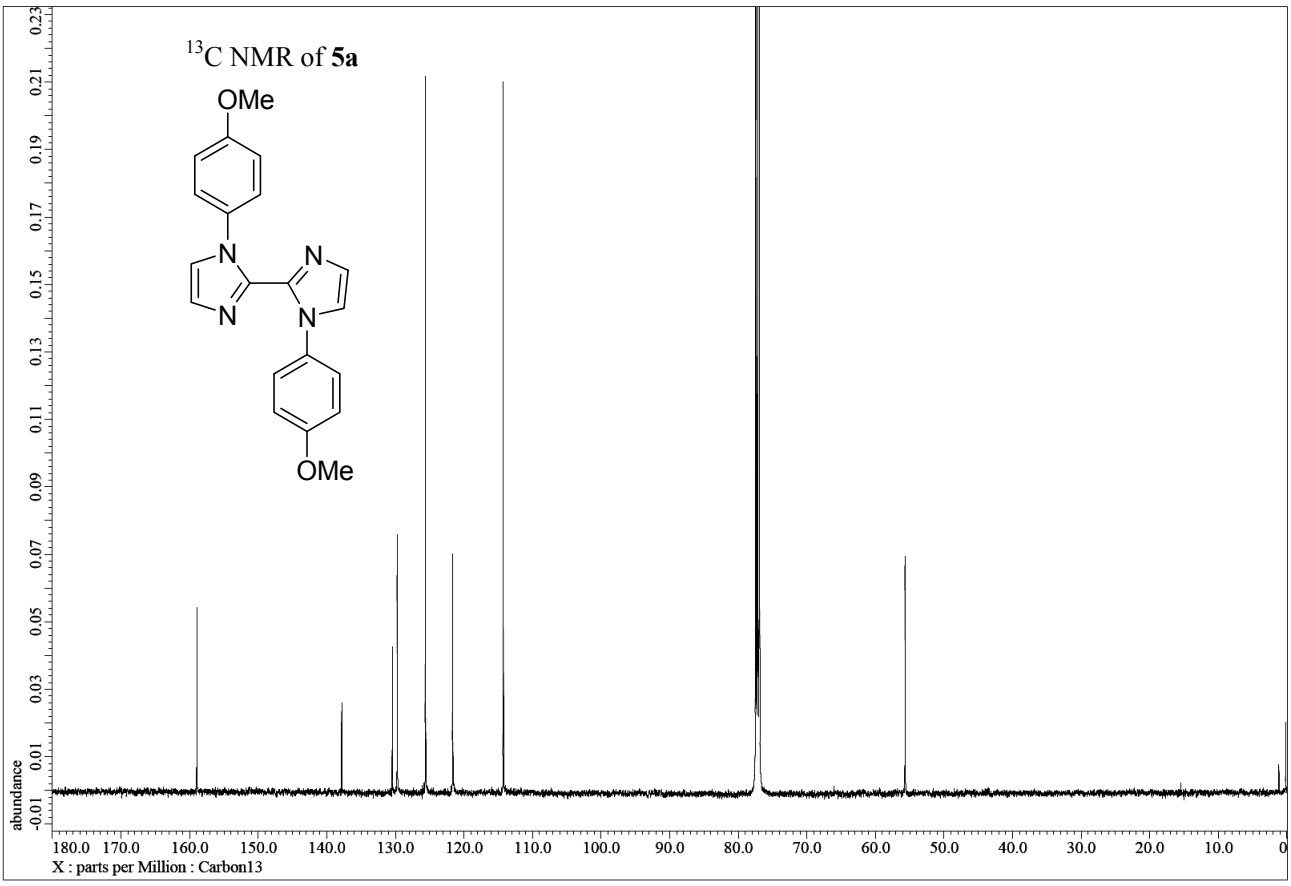

^{1}H NMR of **3a**
abundance
X : parts per Million : Proton

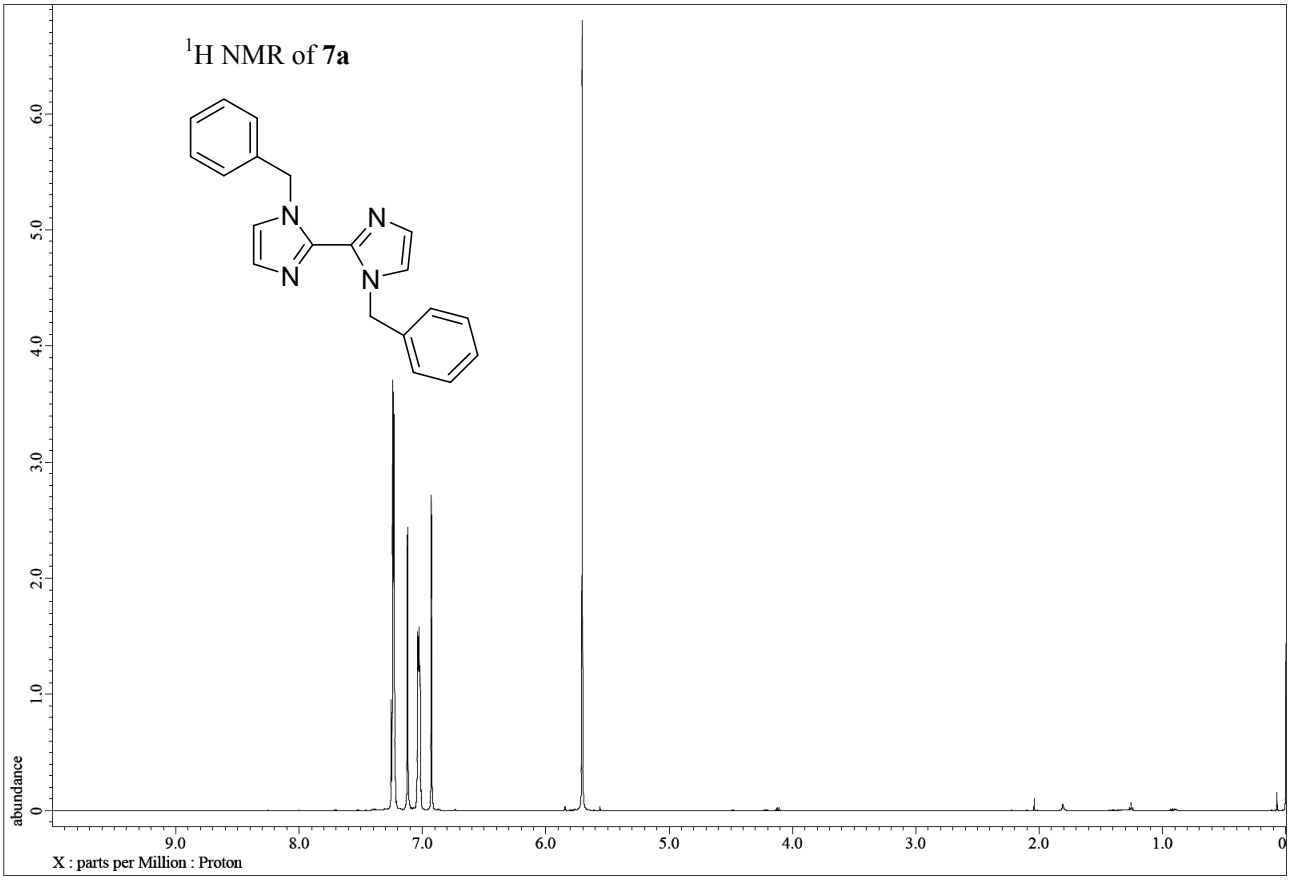

^{13}C NMR of **3a**
abundance
X : parts per Million : Carbon13

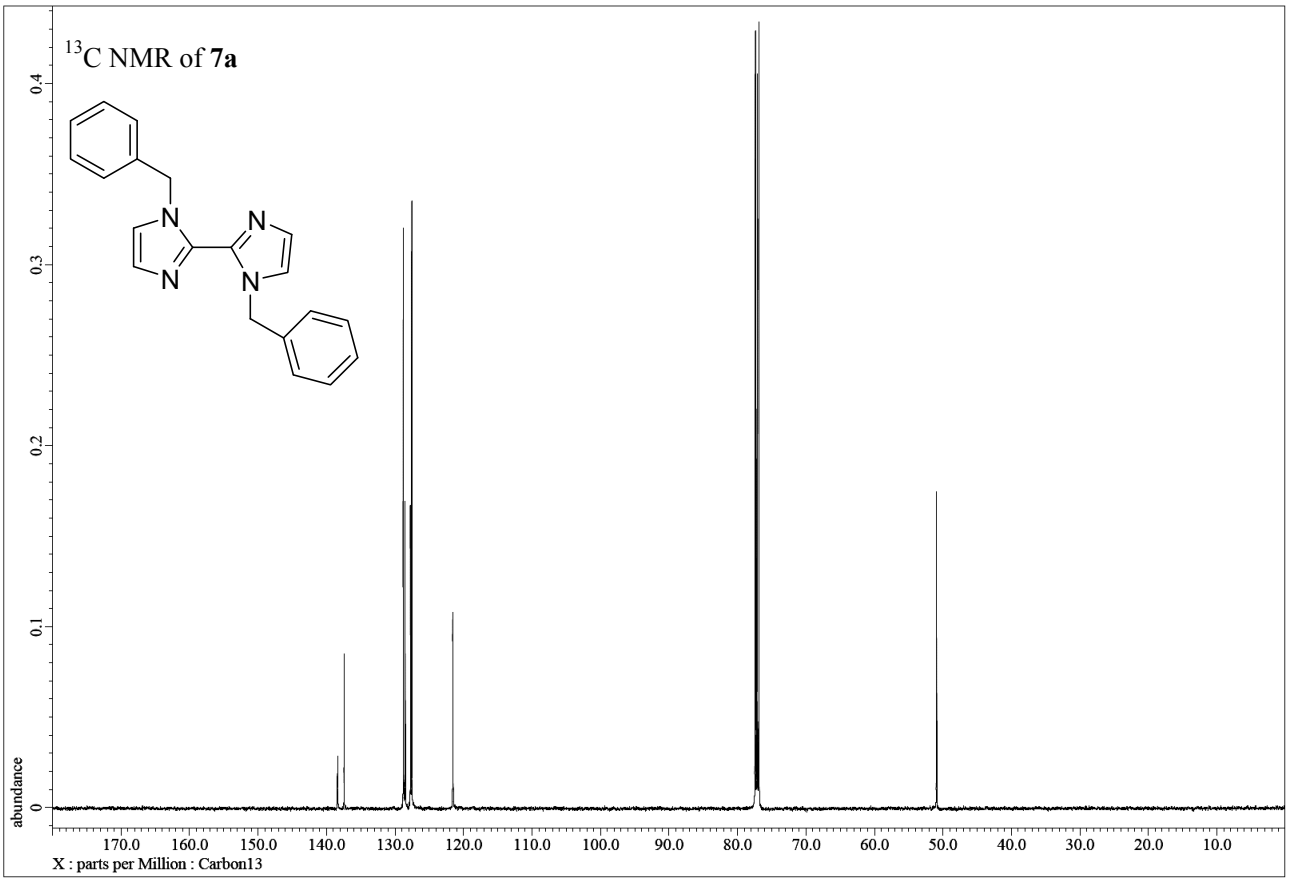

^{1}H NMR of **4a**
abundance
X : parts per Million : Proton

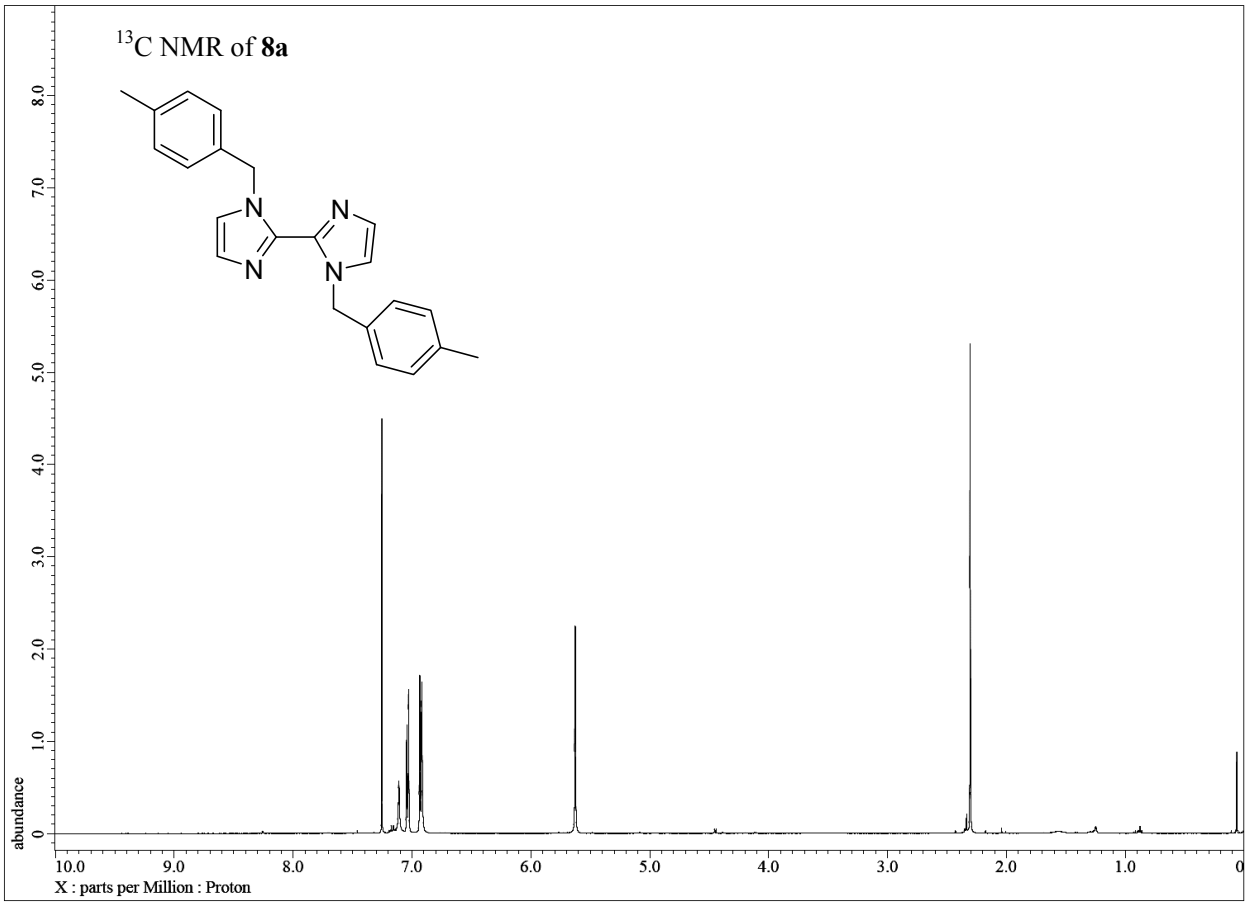

^{13}C NMR of **4a**
abundance
X : parts per Million : Carbon13

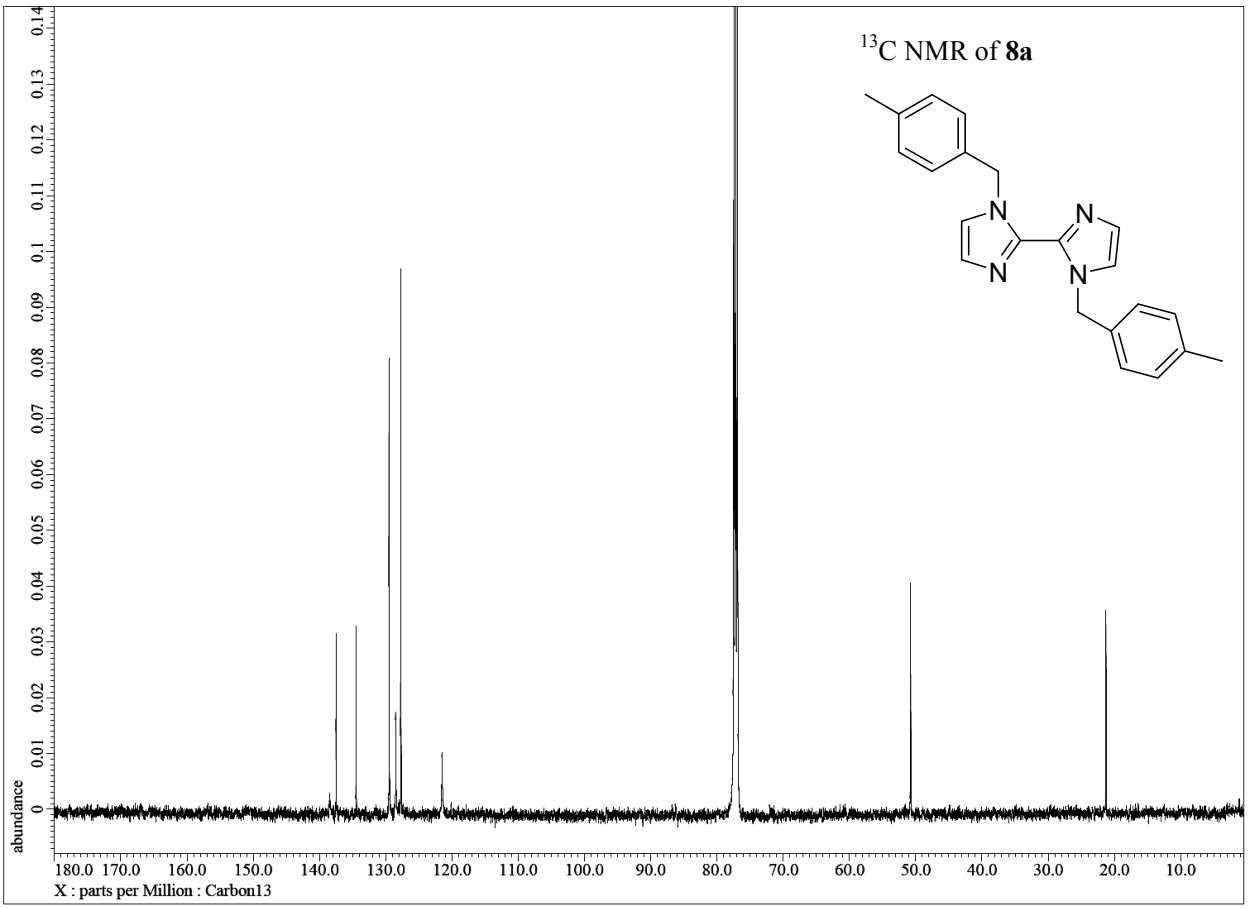

1H NMR of 5a
OMe
N
N
N
N
OMe
abundance
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
X : parts per Million : Proton

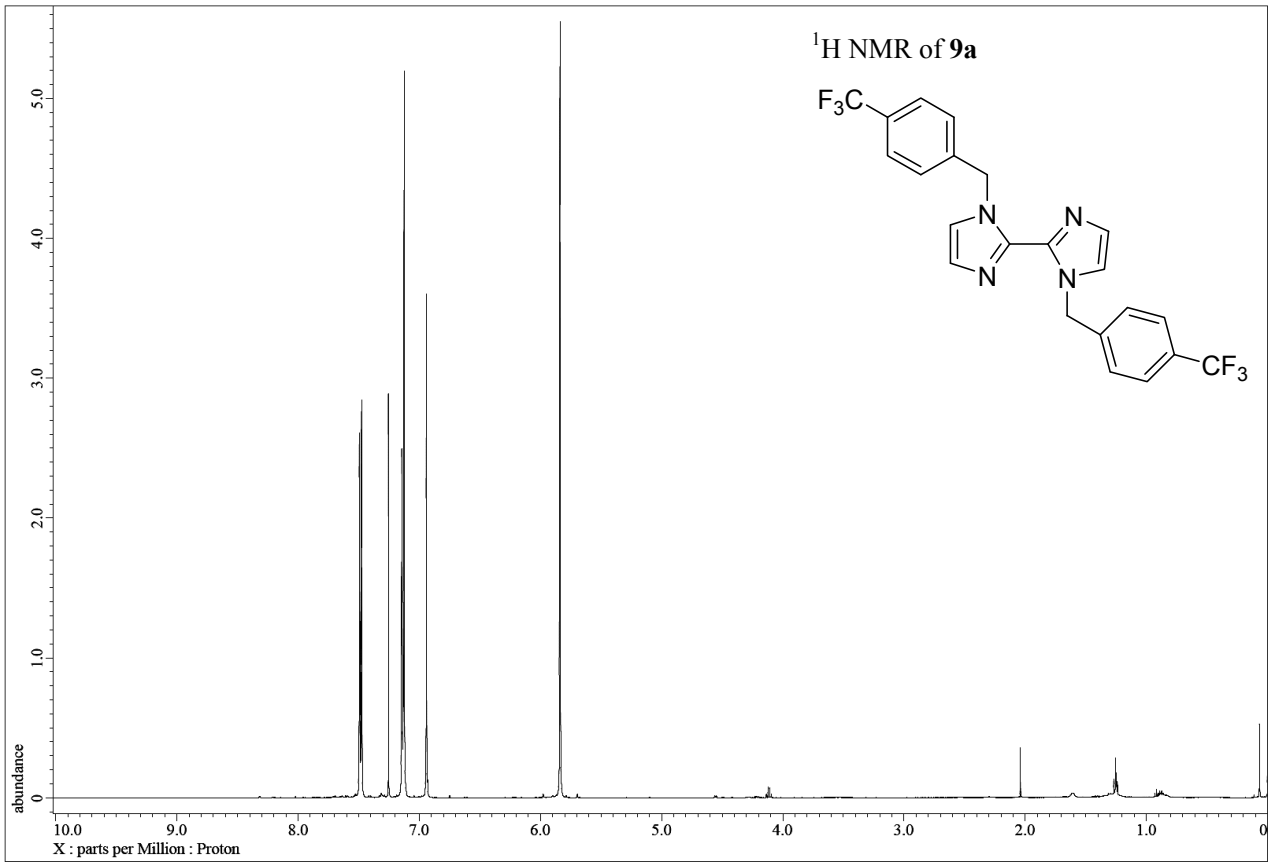

13C NMR of 5a
OMe
N
N
N
N
OMe
abundance
0.23
0.21
0.19
0.17
0.15
0.13
0.11
0.09
0.07
0.05
0.03
0.01
-0.01
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
X : parts per Million : Carbon13

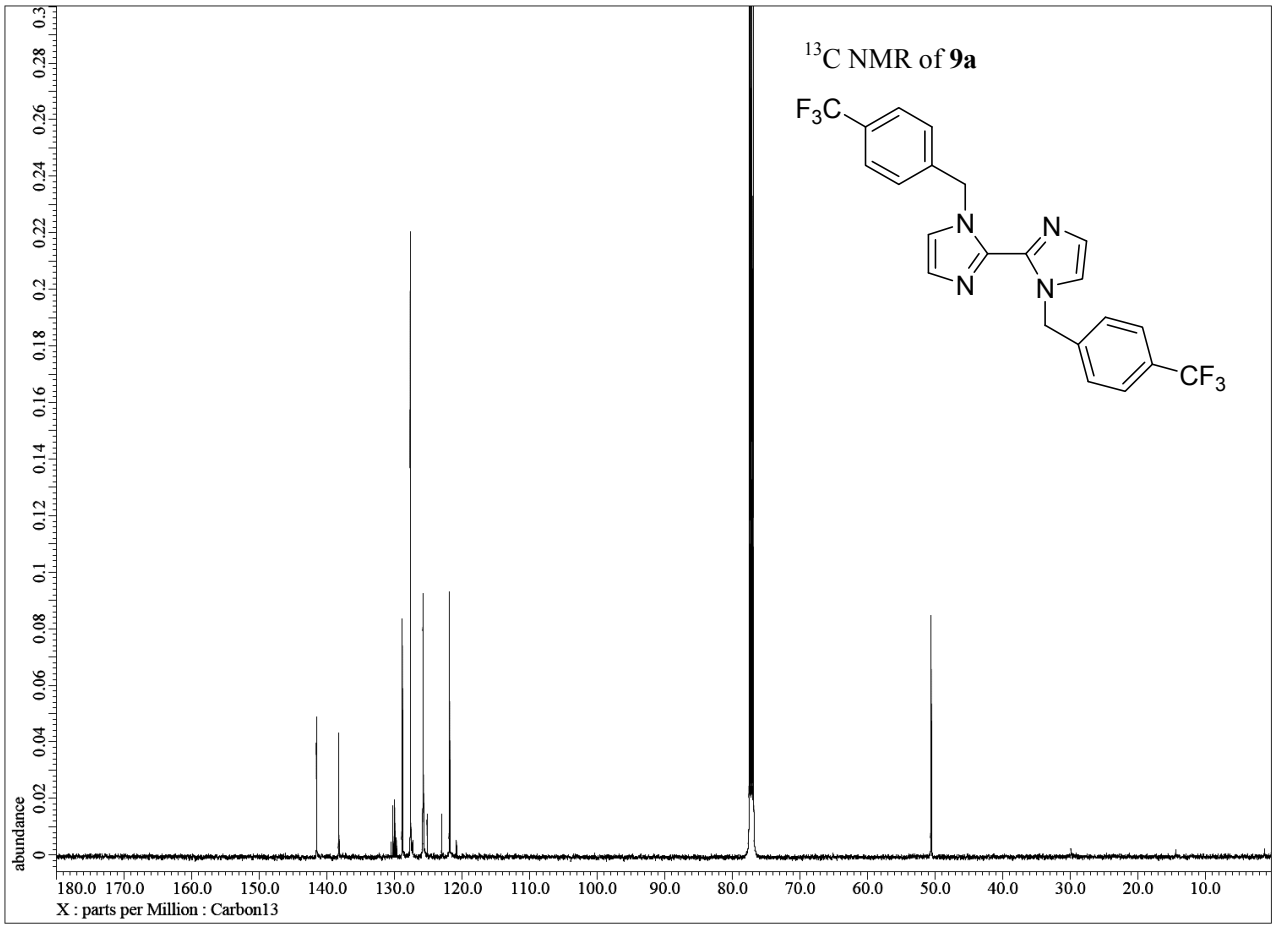

1H NMR of 7a
abundance
X : parts per Million : Proton

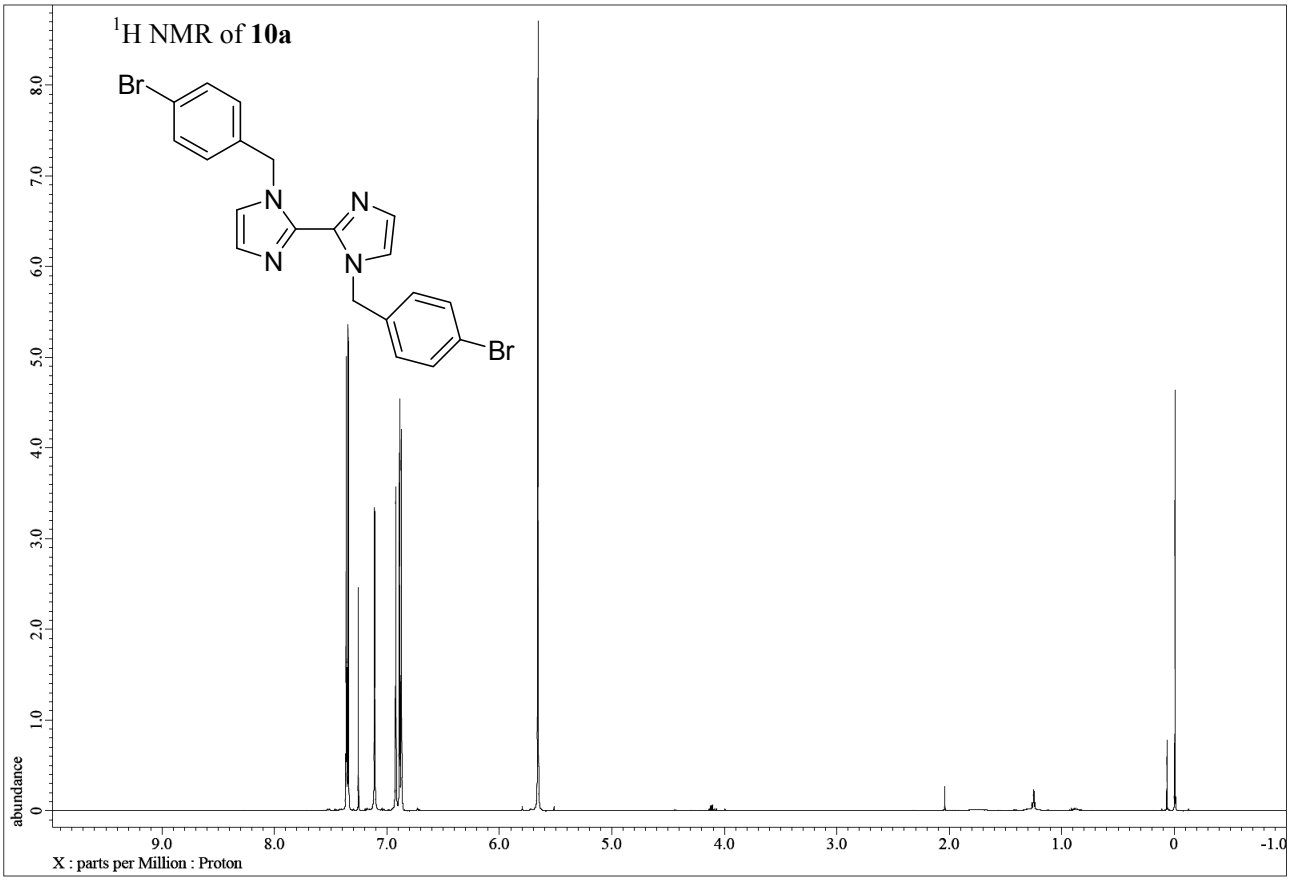

13C NMR of 7a
abundance
X : parts per Million : Carbon13

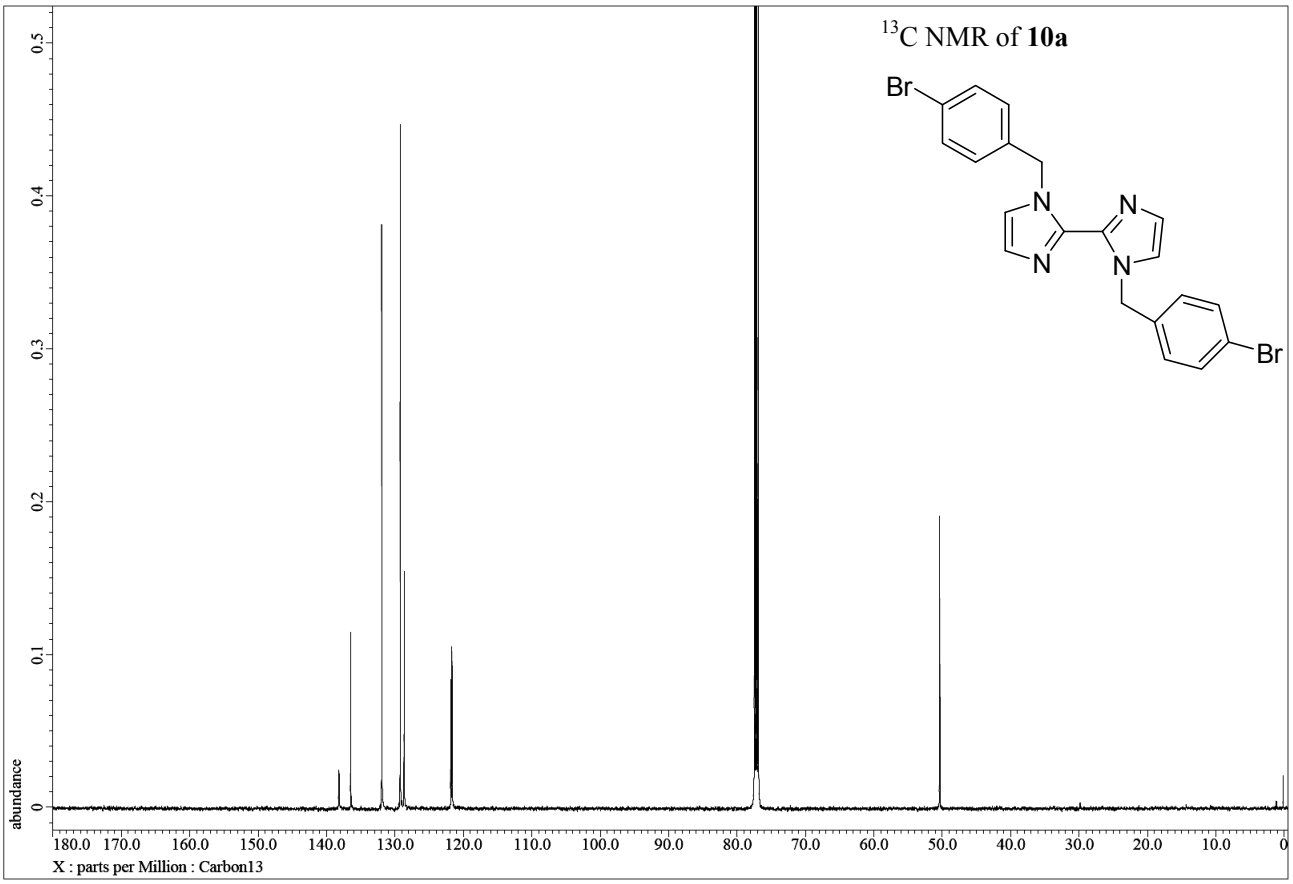

13C NMR of 8a
N
N
N
N
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

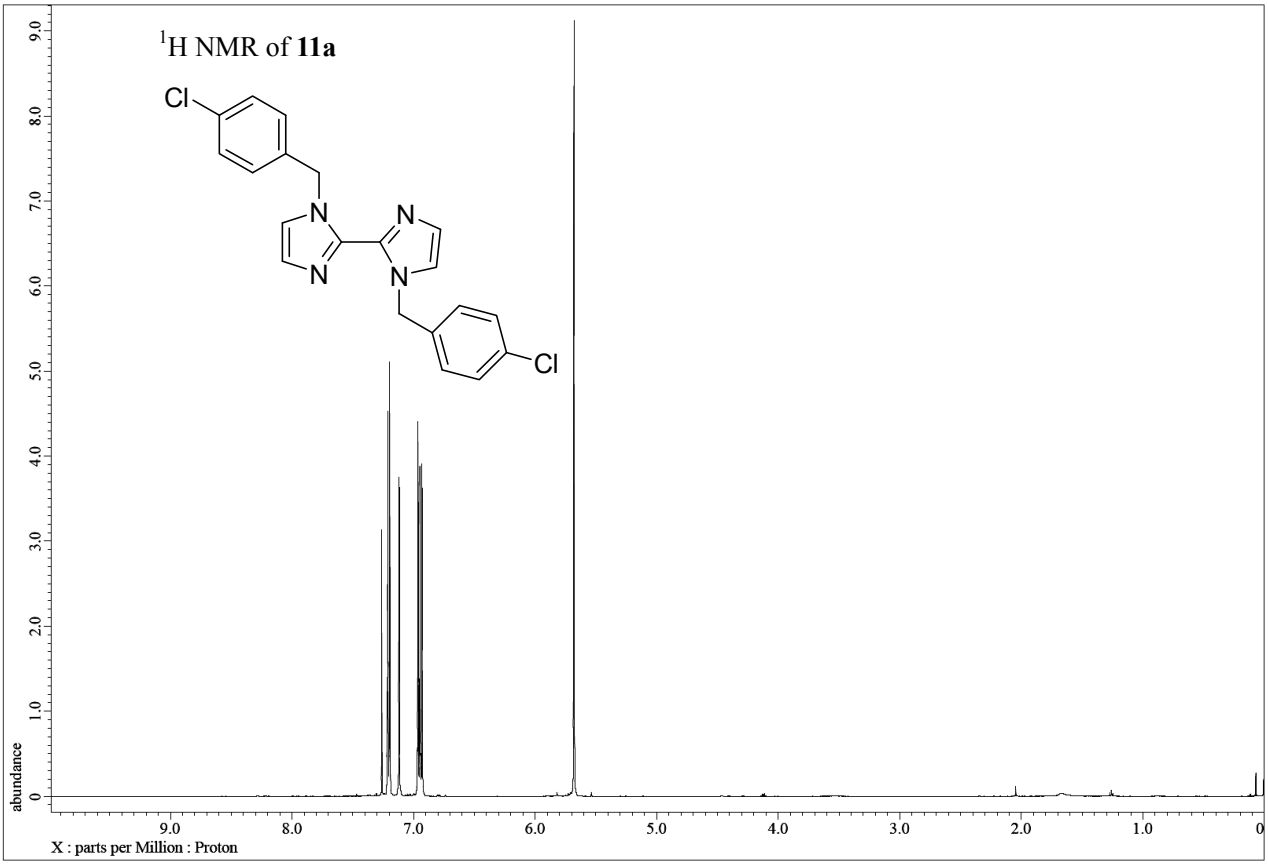

13C NMR of 8a
N
N
N
N
abundance
0
0.01
0.02
0.03
0.04
0.05
0.06
0.07
0.08
0.09
0.1
0.11
0.12
0.13
0.14
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
X : parts per Million : Carbon13

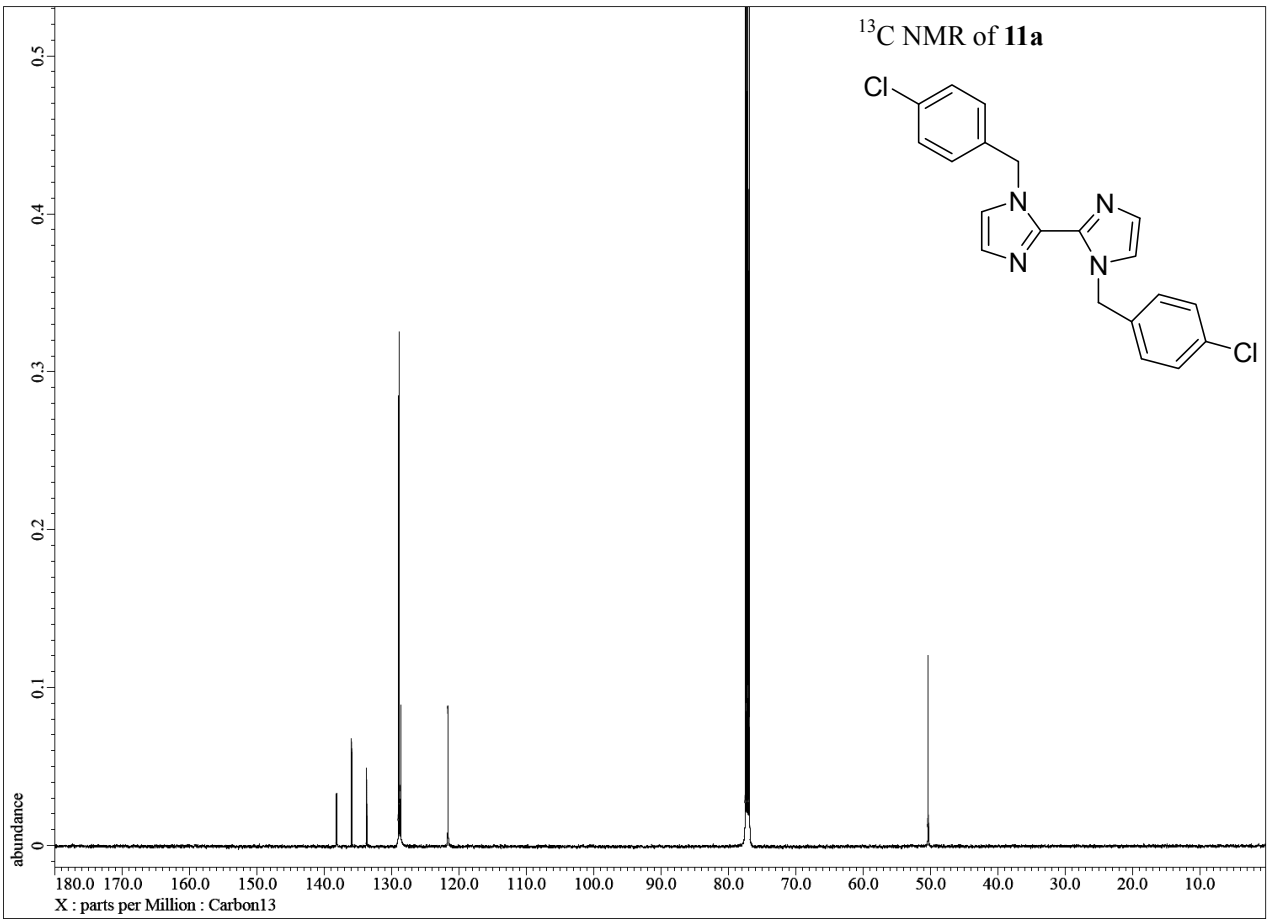

^{1}H NMR of **9a**
F_3C
N
N
N
N
CF_3
abundance
0
1.0
2.0
3.0
4.0
5.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

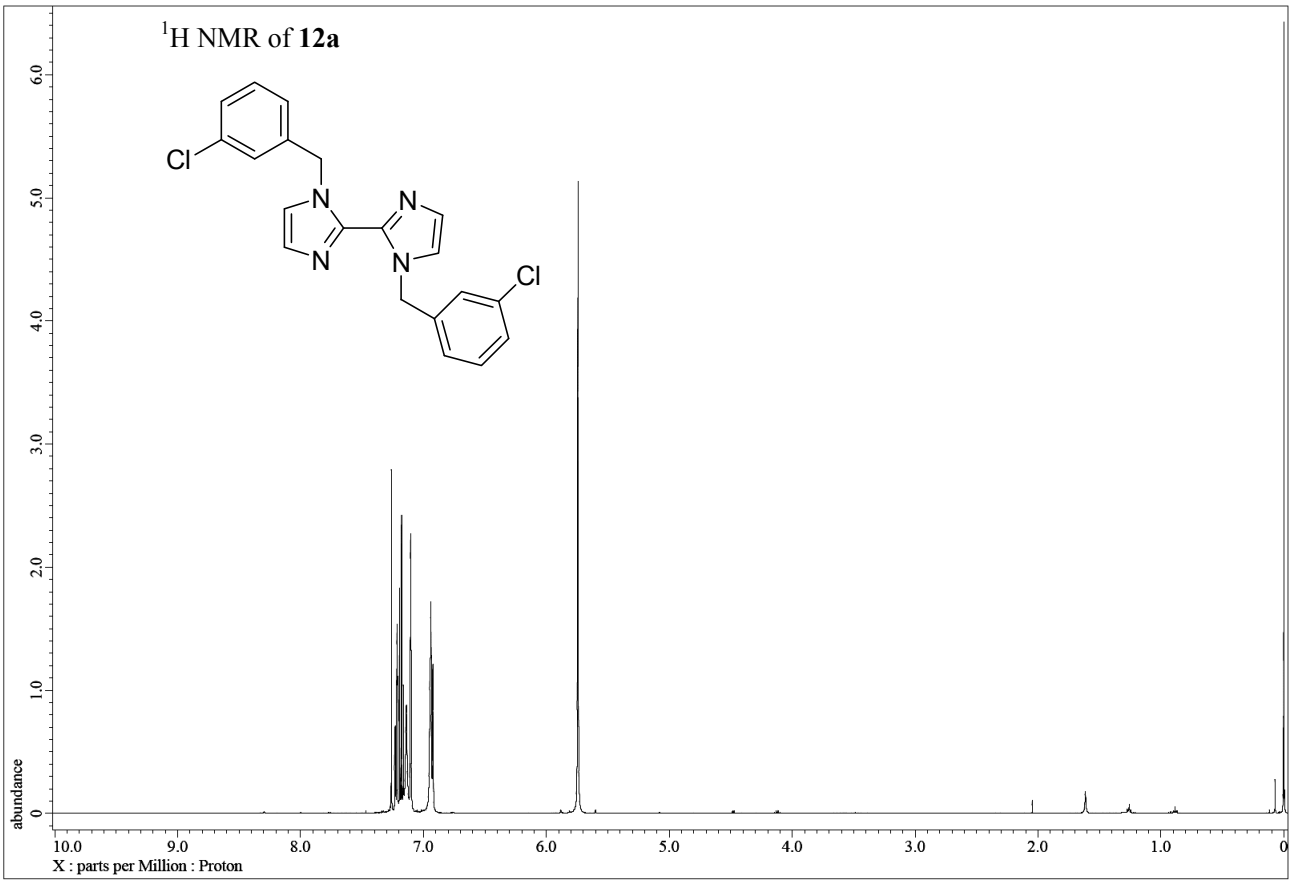

^{13}C NMR of **9a**
F_3C
N
N
N
N
CF_3
abundance
0
0.02
0.04
0.06
0.08
0.1
0.12
0.14
0.16
0.18
0.2
0.22
0.24
0.26
0.28
0.3
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
X : parts per Million : Carbon13

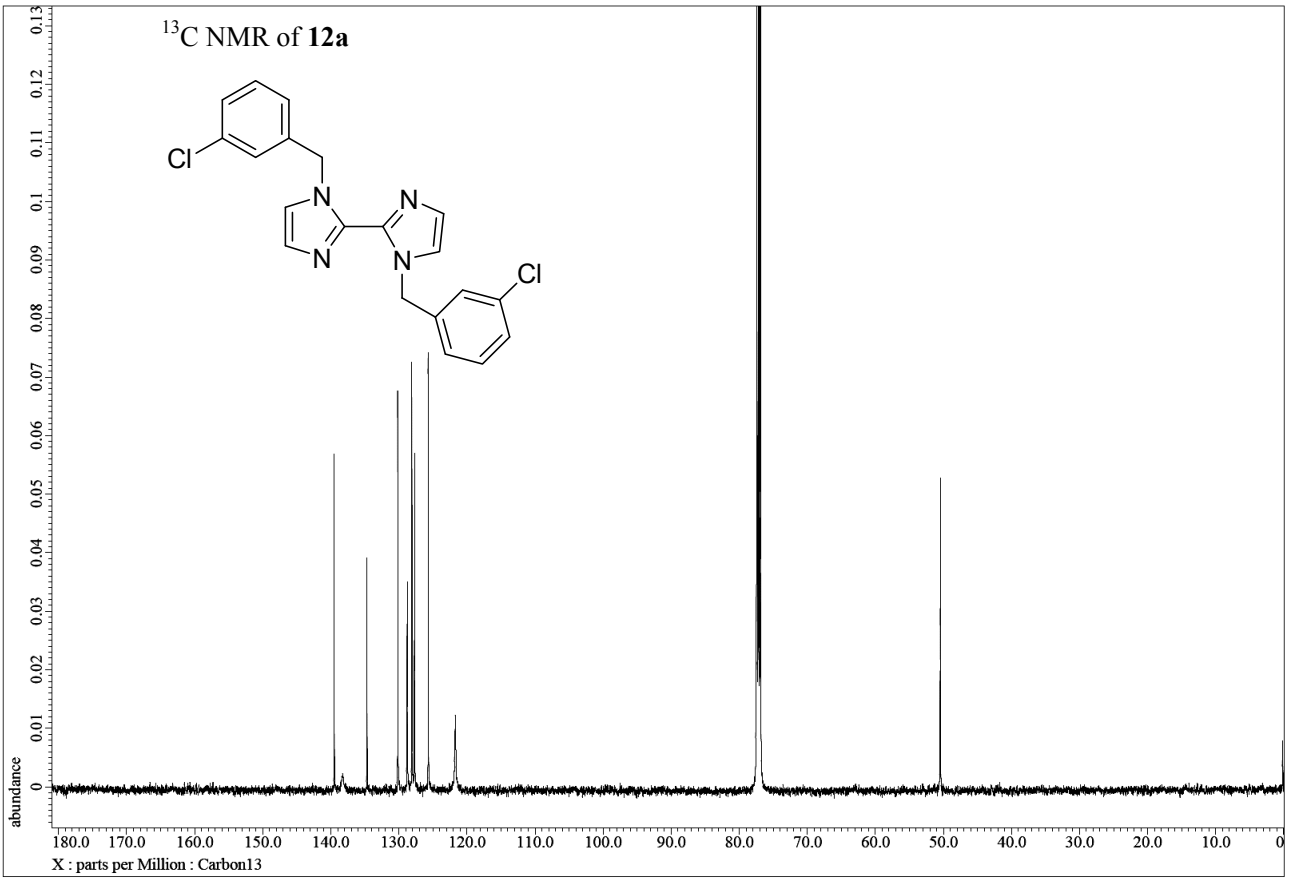

^{1}H NMR of **10a**
Br
N
N
N
N
Br
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
-1.0
X : parts per Million : Proton

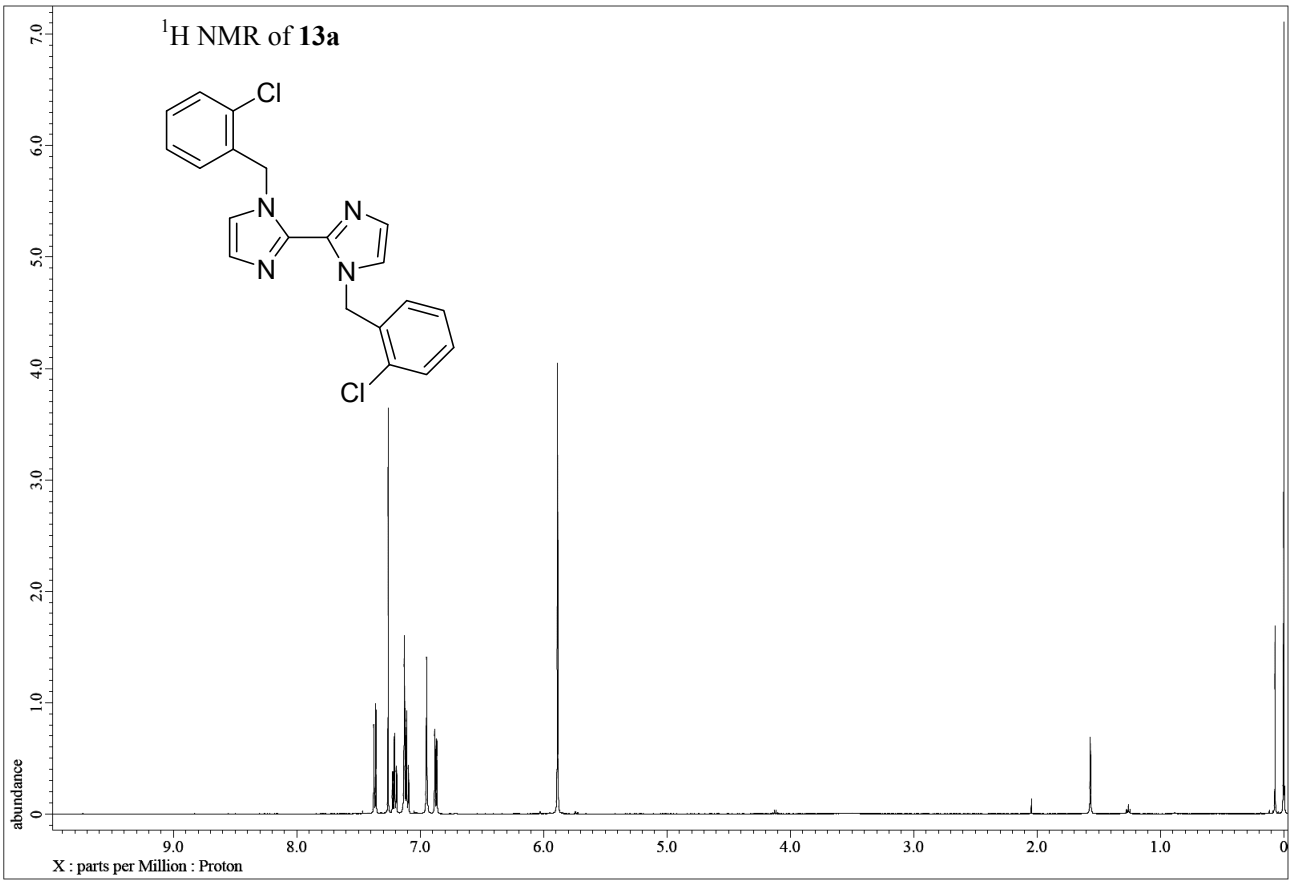

^{13}C NMR of **10a**
Br
N
N
N
N
Br
abundance
0
0.1
0.2
0.3
0.4
0.5
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
X : parts per Million : Carbon13

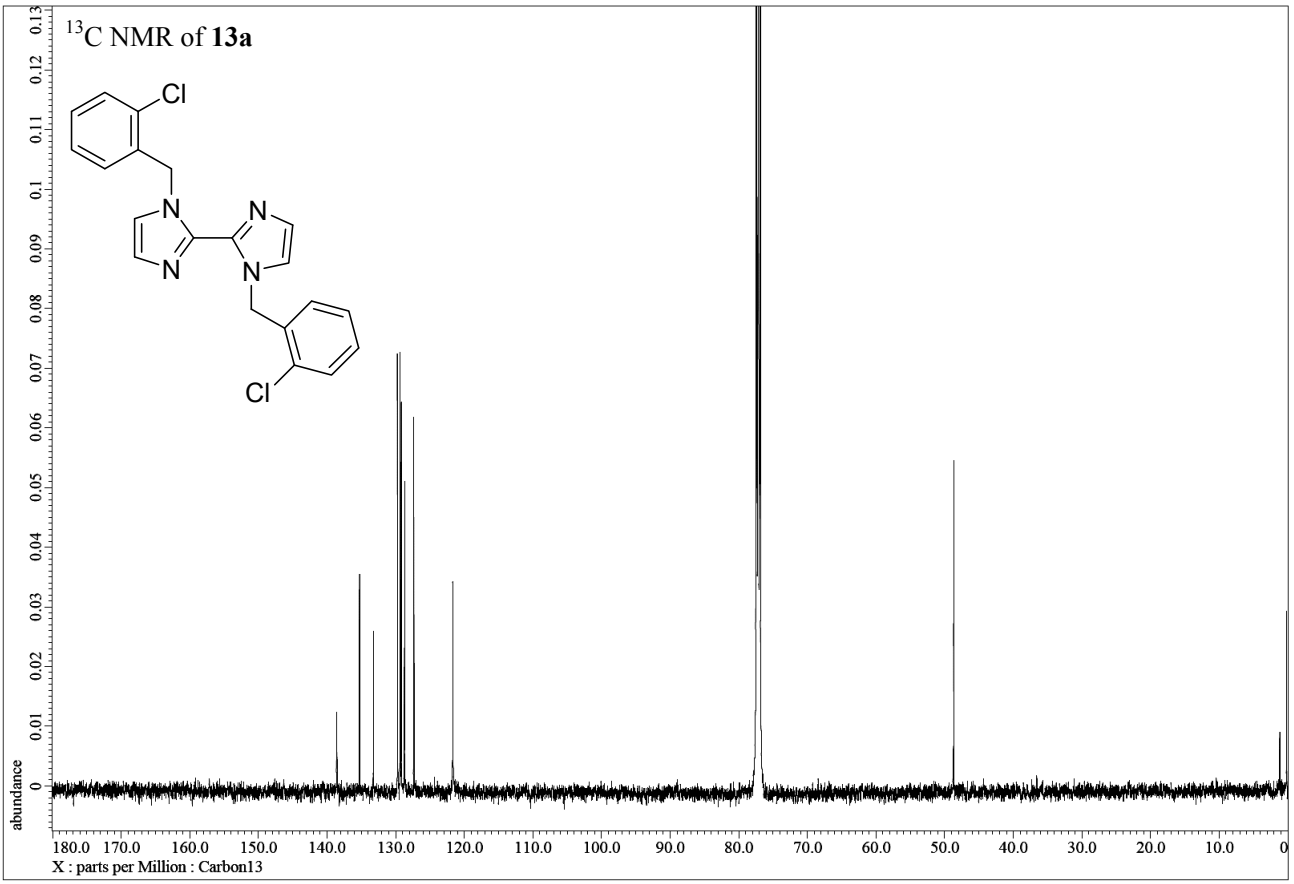

^{1}H NMR of **11a**
Cl
N
N
N
N
Cl
abundance
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

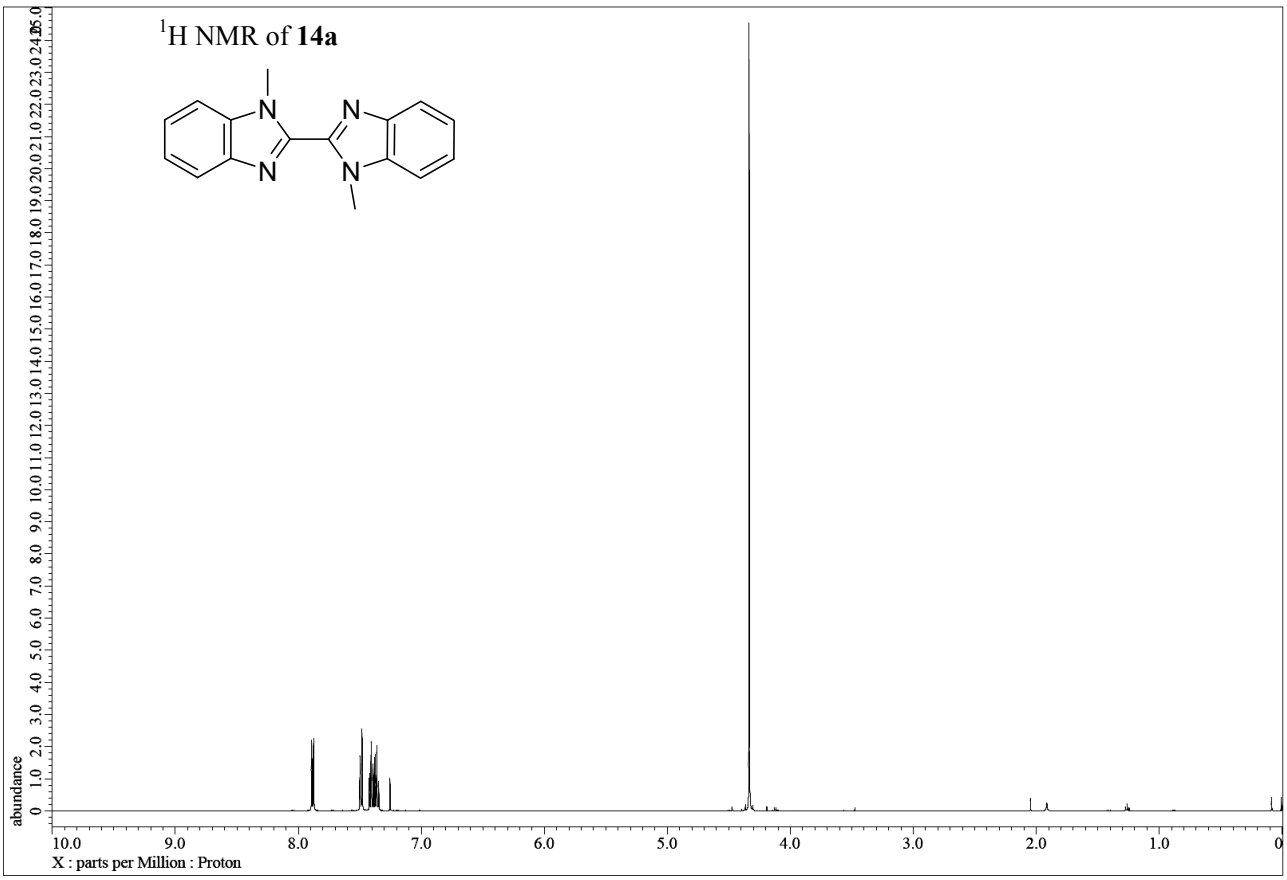

^{13}C NMR of **11a**
Cl
N
N
N
N
Cl
abundance
0.5
0.4
0.3
0.2
0.1
0
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0
X : parts per Million : Carbon13

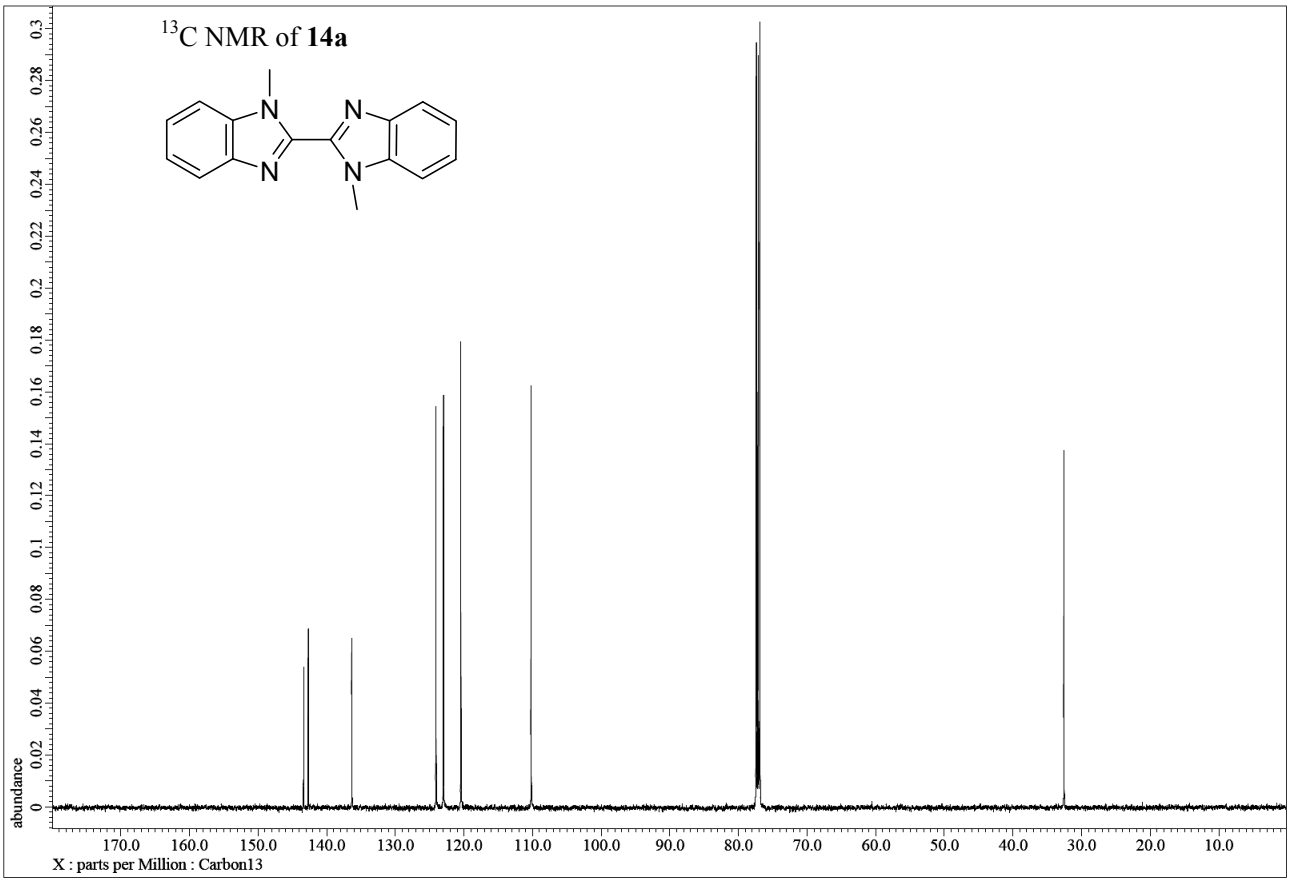

^{1}H NMR of **12a**
Cl
N
N
N
N
Cl
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

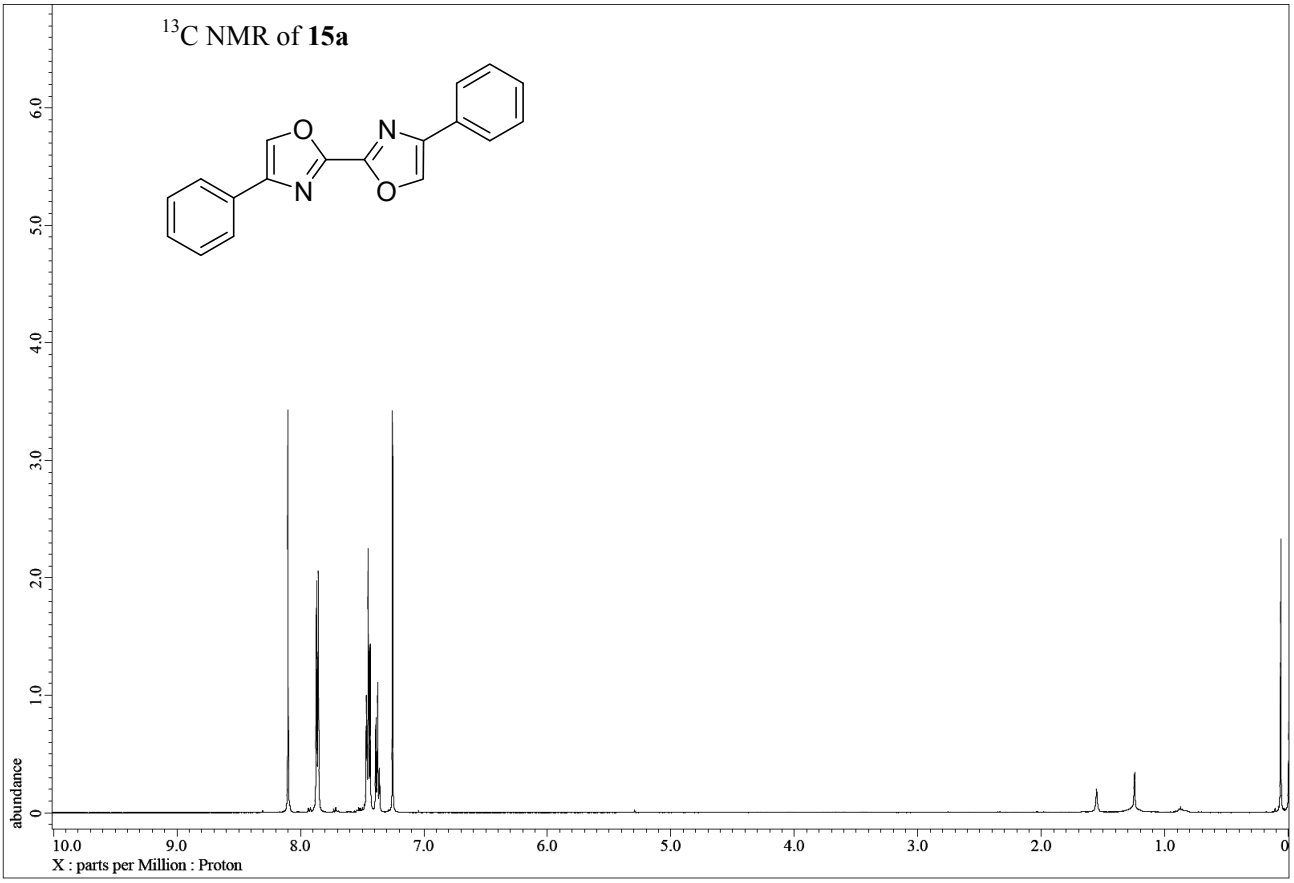

^{13}C NMR of **12a**
Cl
N
N
N
N
Cl
abundance
0
0.01
0.02
0.03
0.04
0.05
0.06
0.07
0.08
0.09
0.1
0.11
0.12
0.13
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
X : parts per Million : Carbon13

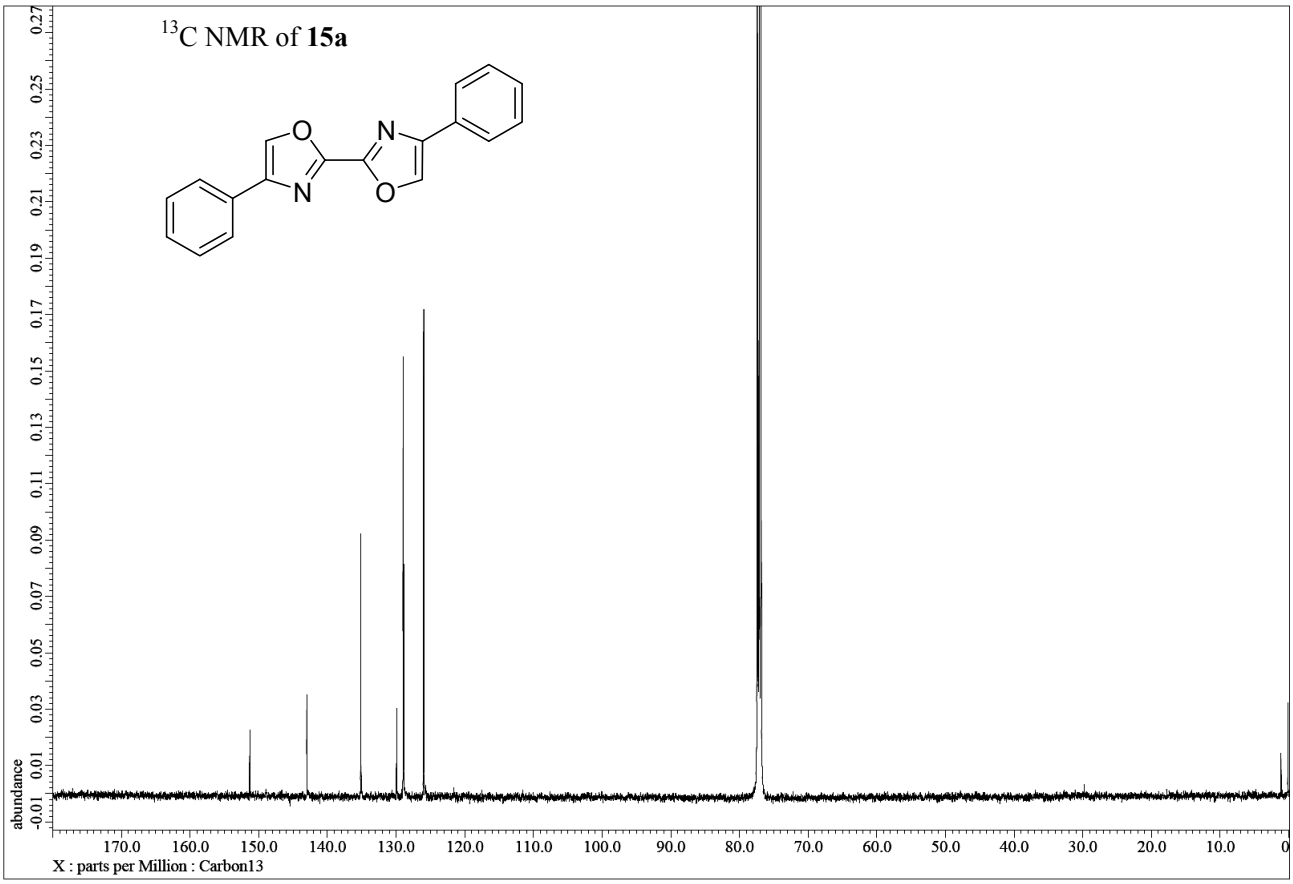

^{1}H NMR of **13a**
Cl
N
N
N
N
Cl
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

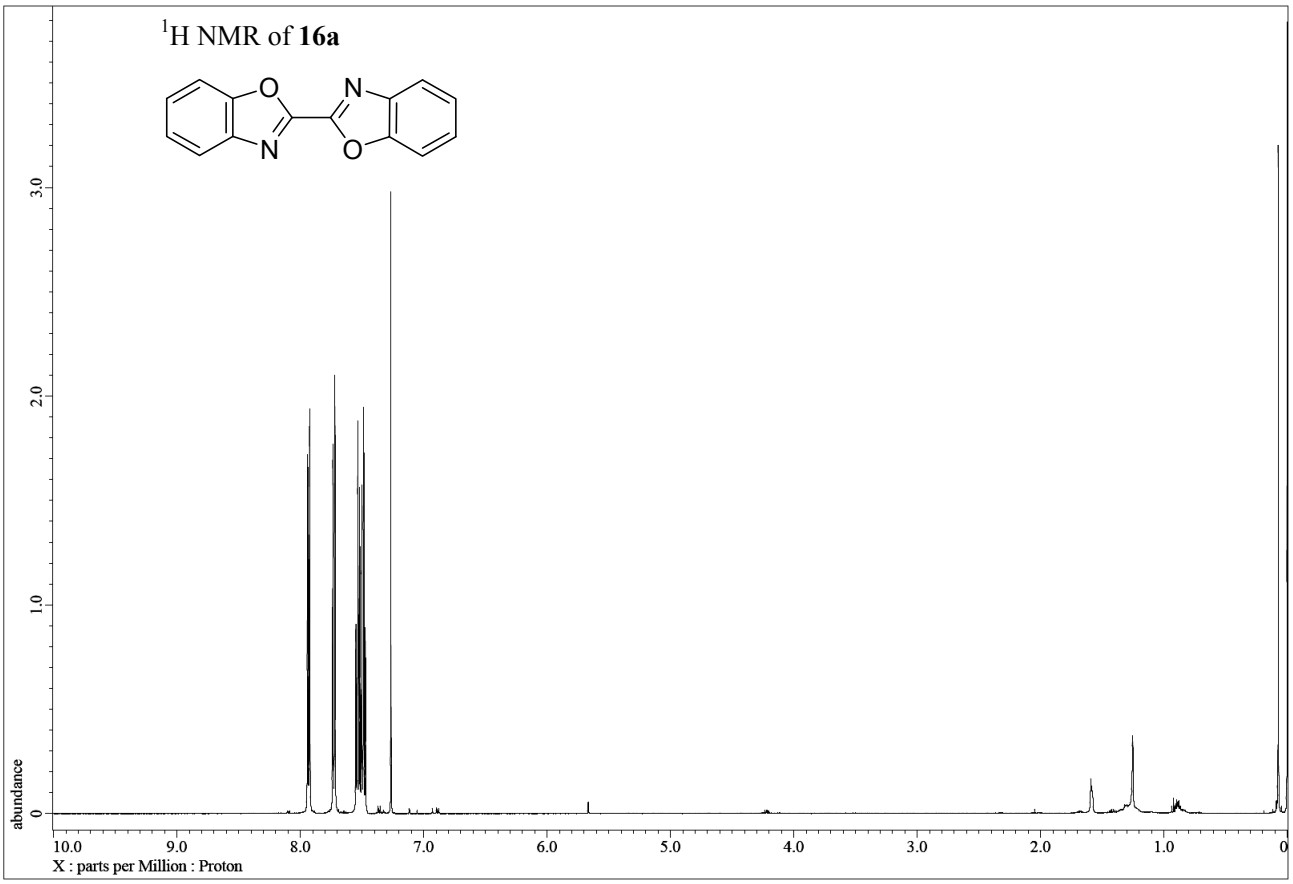

^{13}C NMR of **13a**
Cl
N
N
N
N
Cl
abundance
0
0.01
0.02
0.03
0.04
0.05
0.06
0.07
0.08
0.09
0.1
0.11
0.12
0.13
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
X : parts per Million : Carbon13

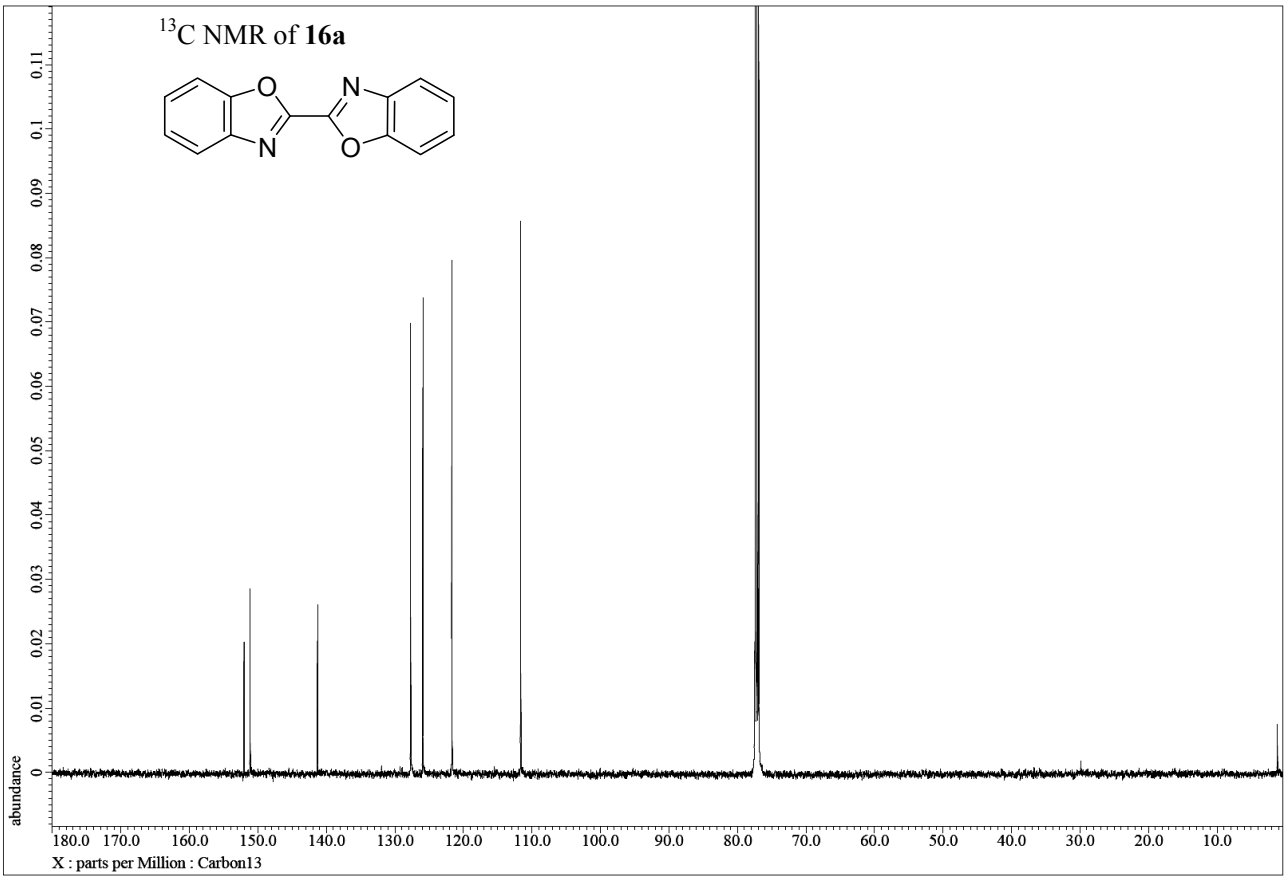

^{1}H NMR of **14a**
abundance
X : parts per Million : Proton

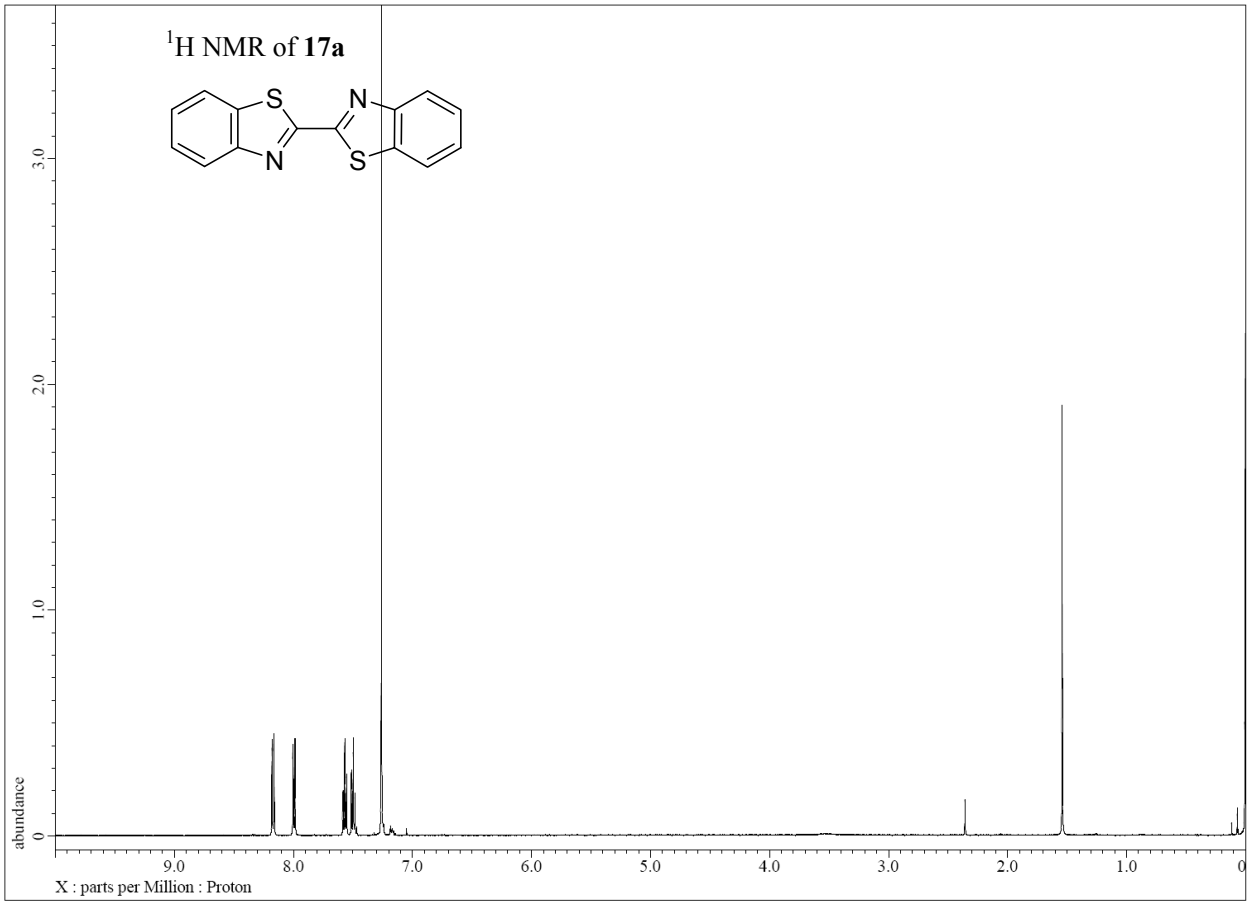

^{13}C NMR of **14a**
abundance
X : parts per Million : Carbon13

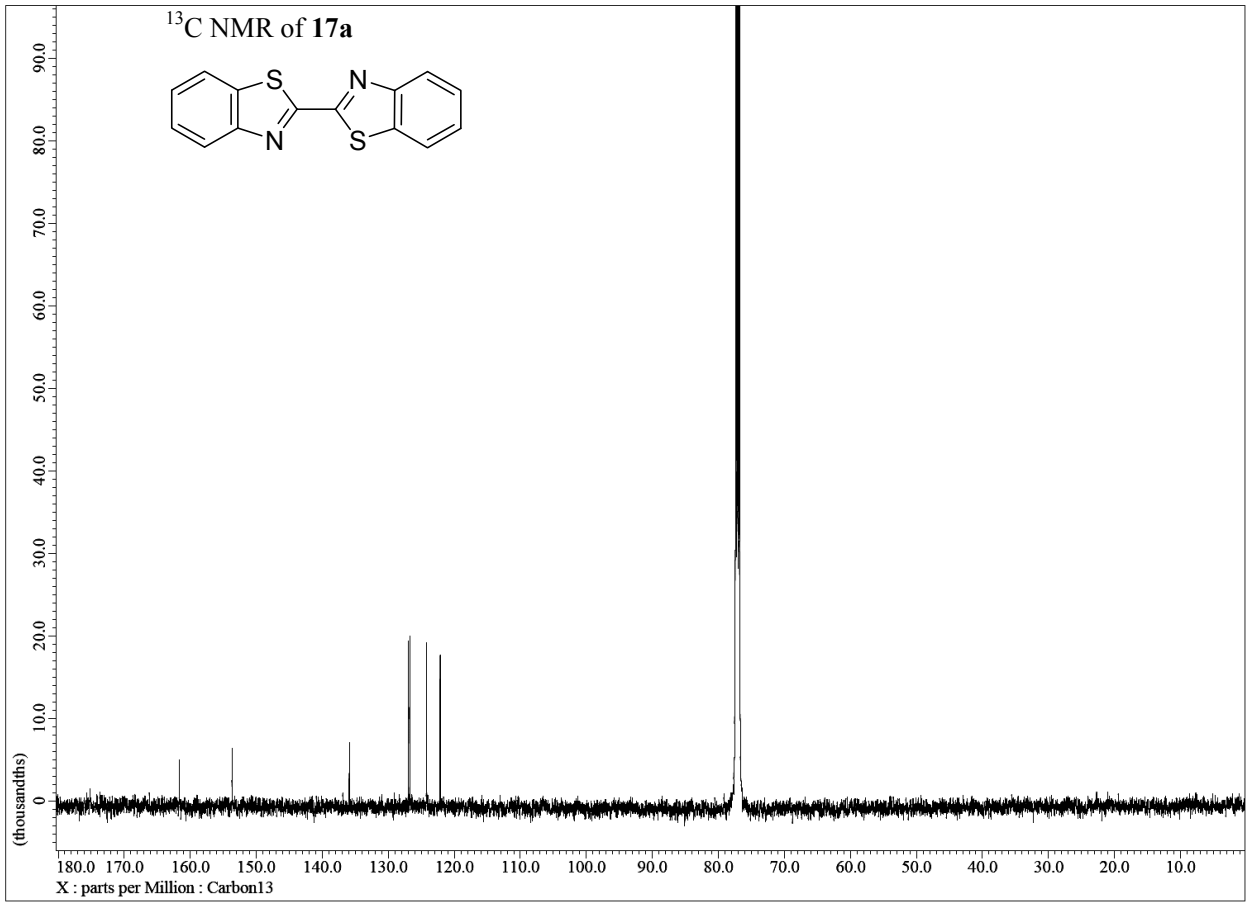

13C NMR of 15a
O
N
N
O
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

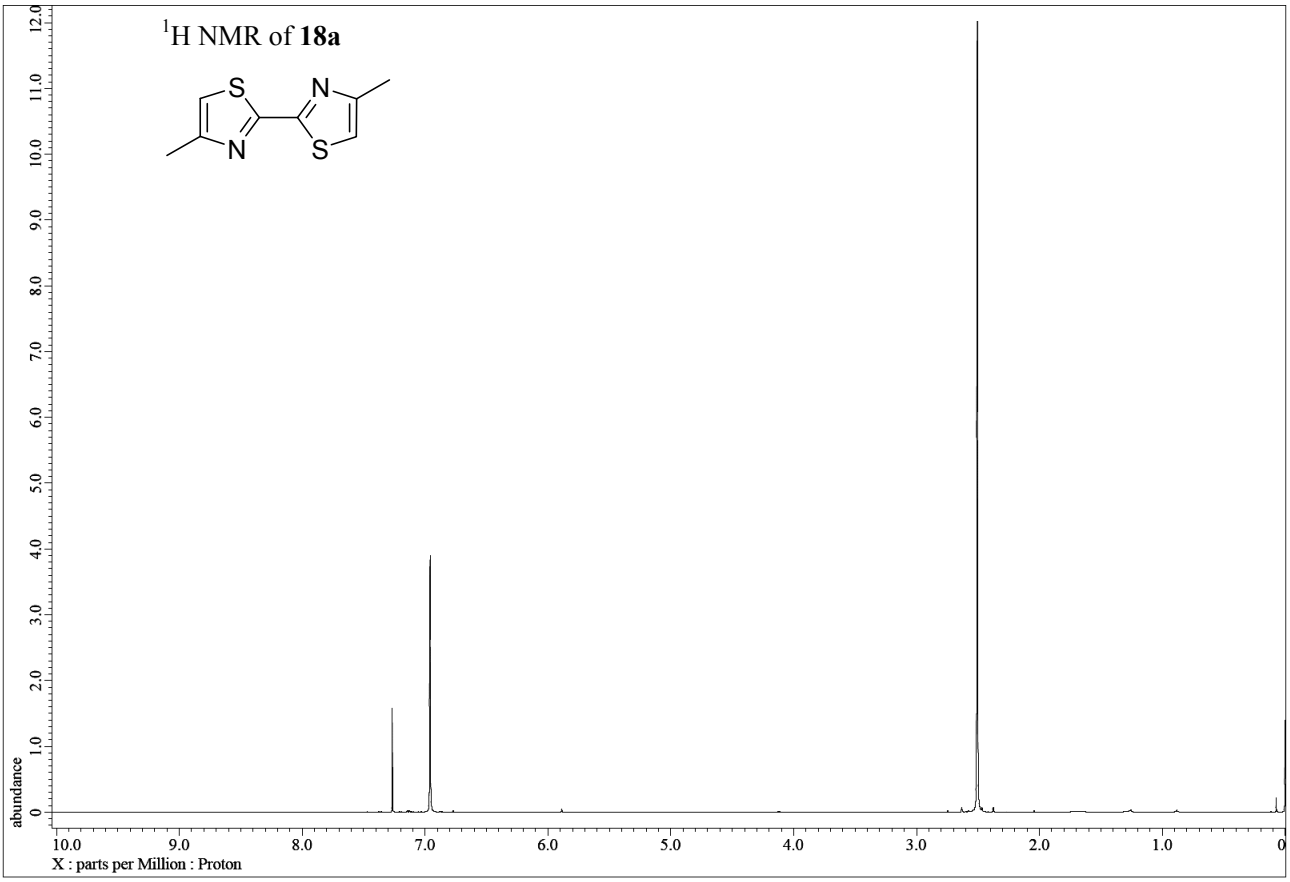

13C NMR of 15a
O
N
N
O
abundance
-0.01
0.01
0.03
0.05
0.07
0.09
0.11
0.13
0.15
0.17
0.19
0.21
0.23
0.25
0.27
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
X : parts per Million : Carbon13

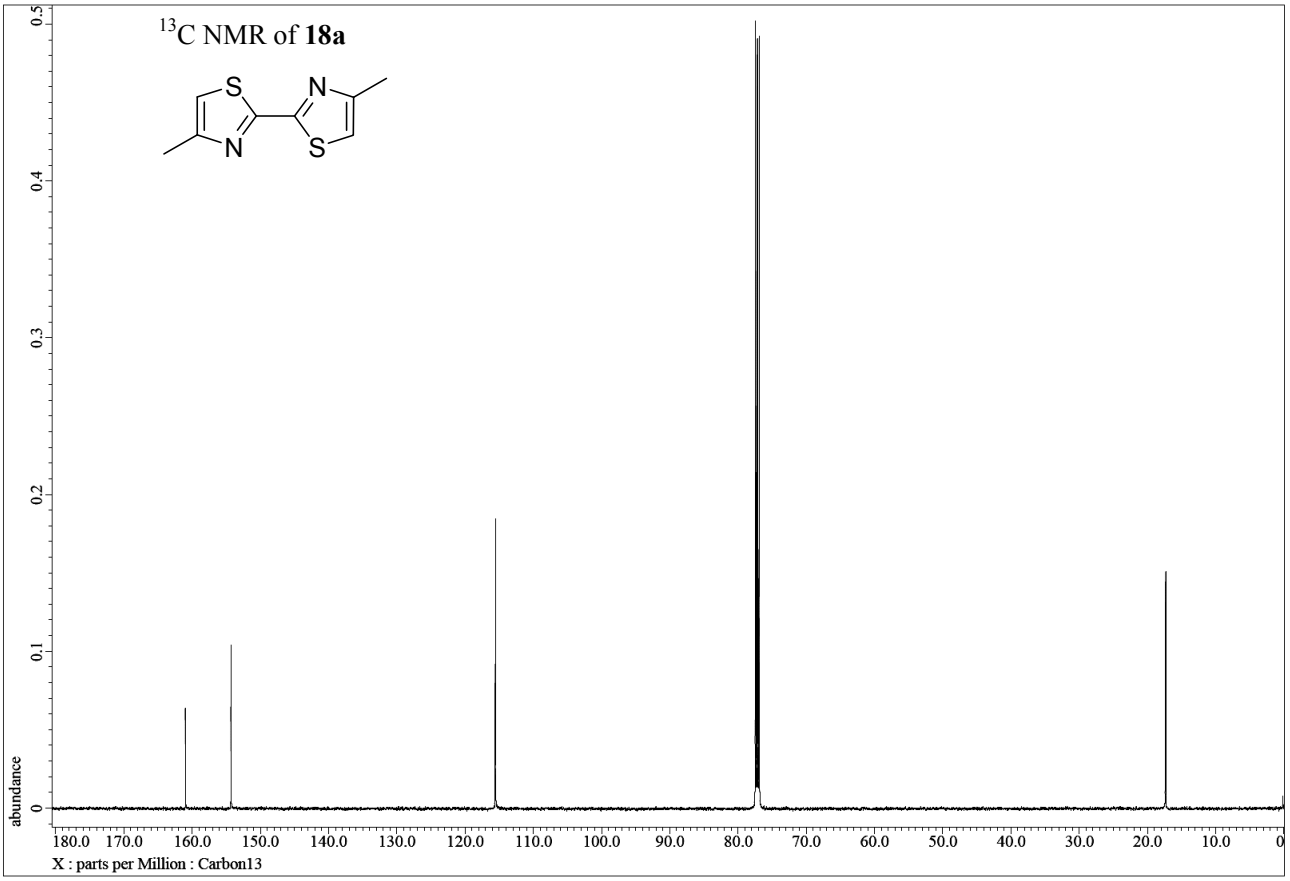

1H NMR of 16a
O
N
N
O
3.0
2.0
1.0
0
abundance
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

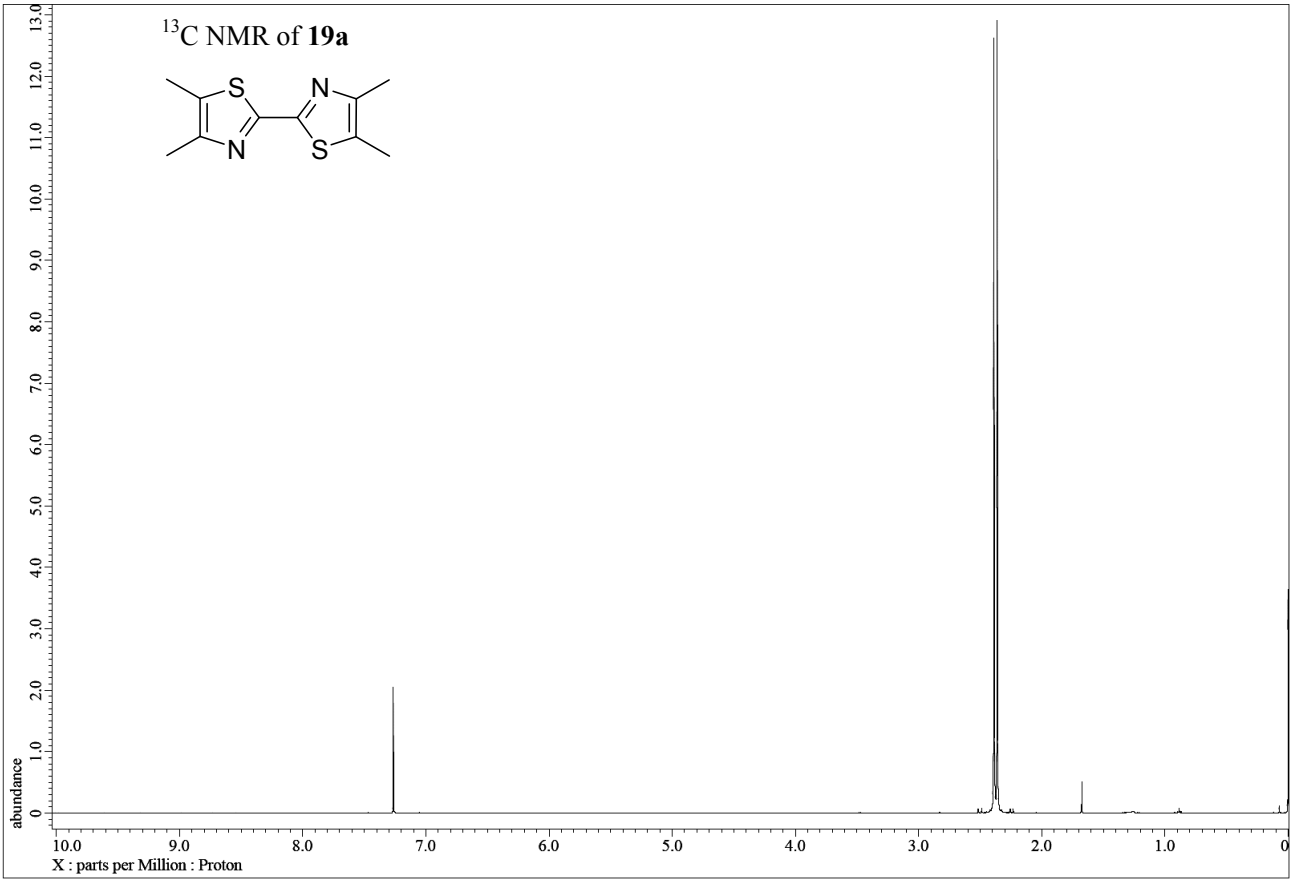

13C NMR of 16a
O
N
N
O
0.11
0.1
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
abundance
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
X : parts per Million : Carbon13

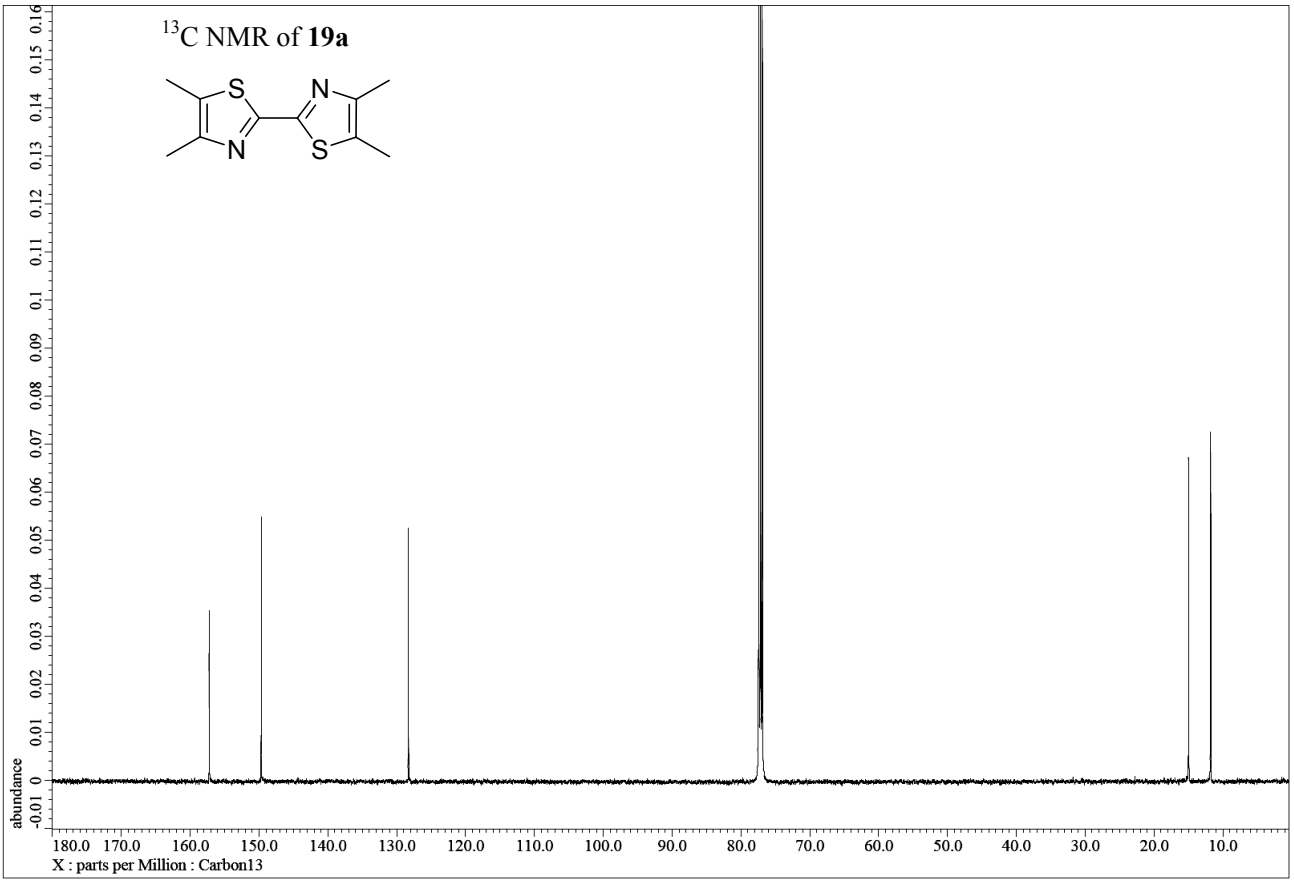

1H NMR of 17a
S
N
N
S
abundance
3.0
2.0
1.0
0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

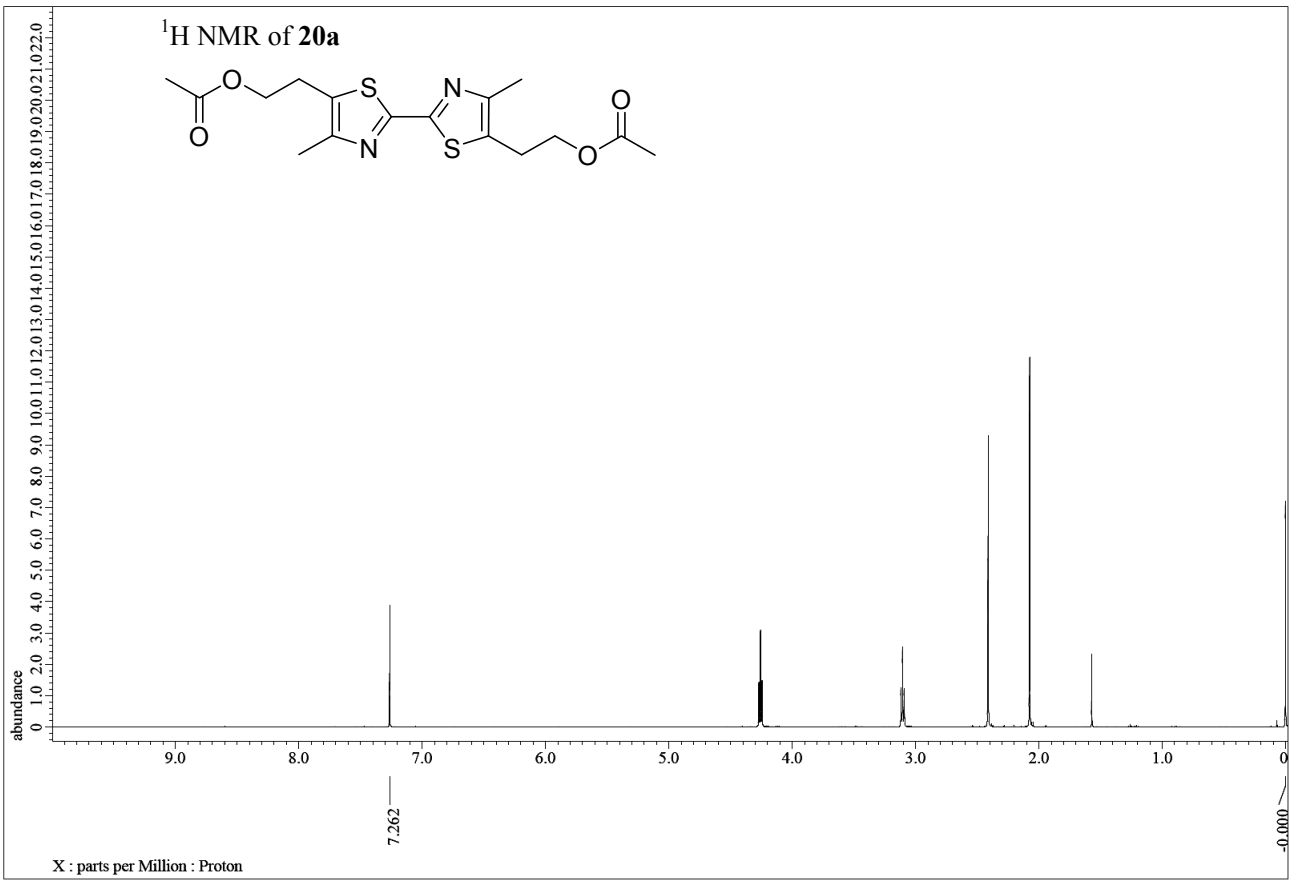

13C NMR of 17a
S
N
N
S
(thousandths)
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0
X : parts per Million : Carbon13

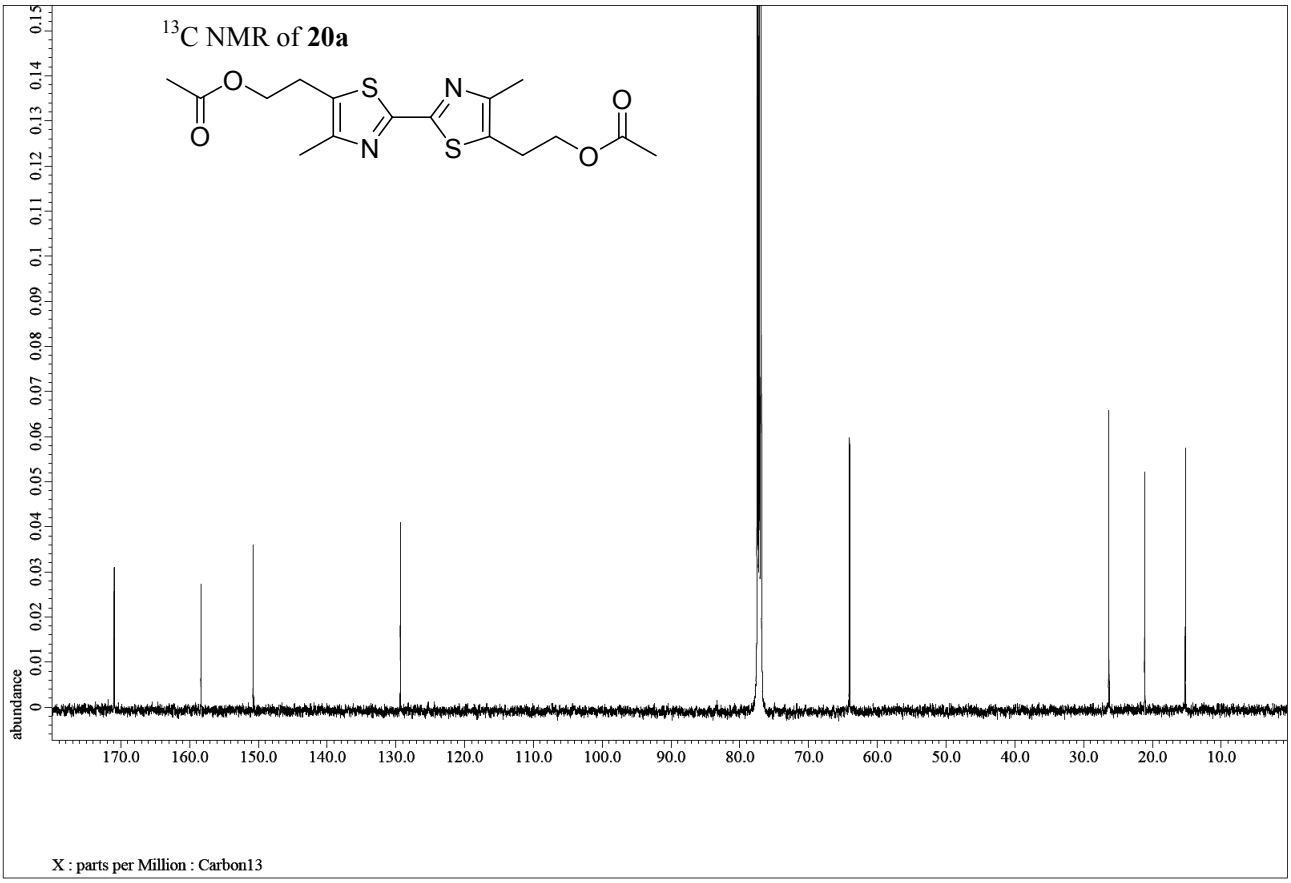

^{1}H NMR of **18a**
S
N
N
S
abundance
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : Proton

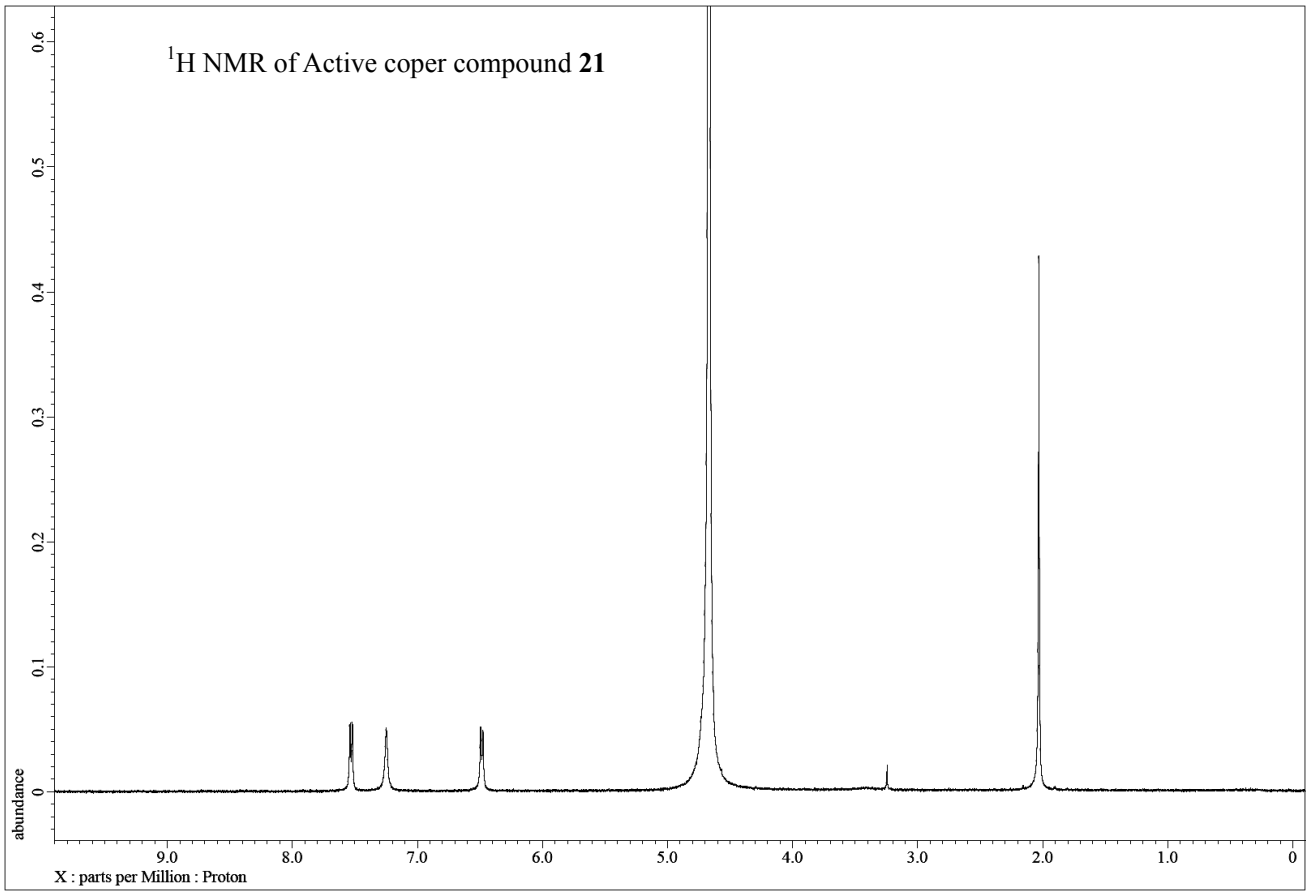

^{13}C NMR of **18a**
S
N
N
S
abundance
0.5
0.4
0.3
0.2
0.1
0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
X : parts per Million : Carbon13


13C NMR of 19a
S
N
N
S
abundance
X : parts per Million : Proton

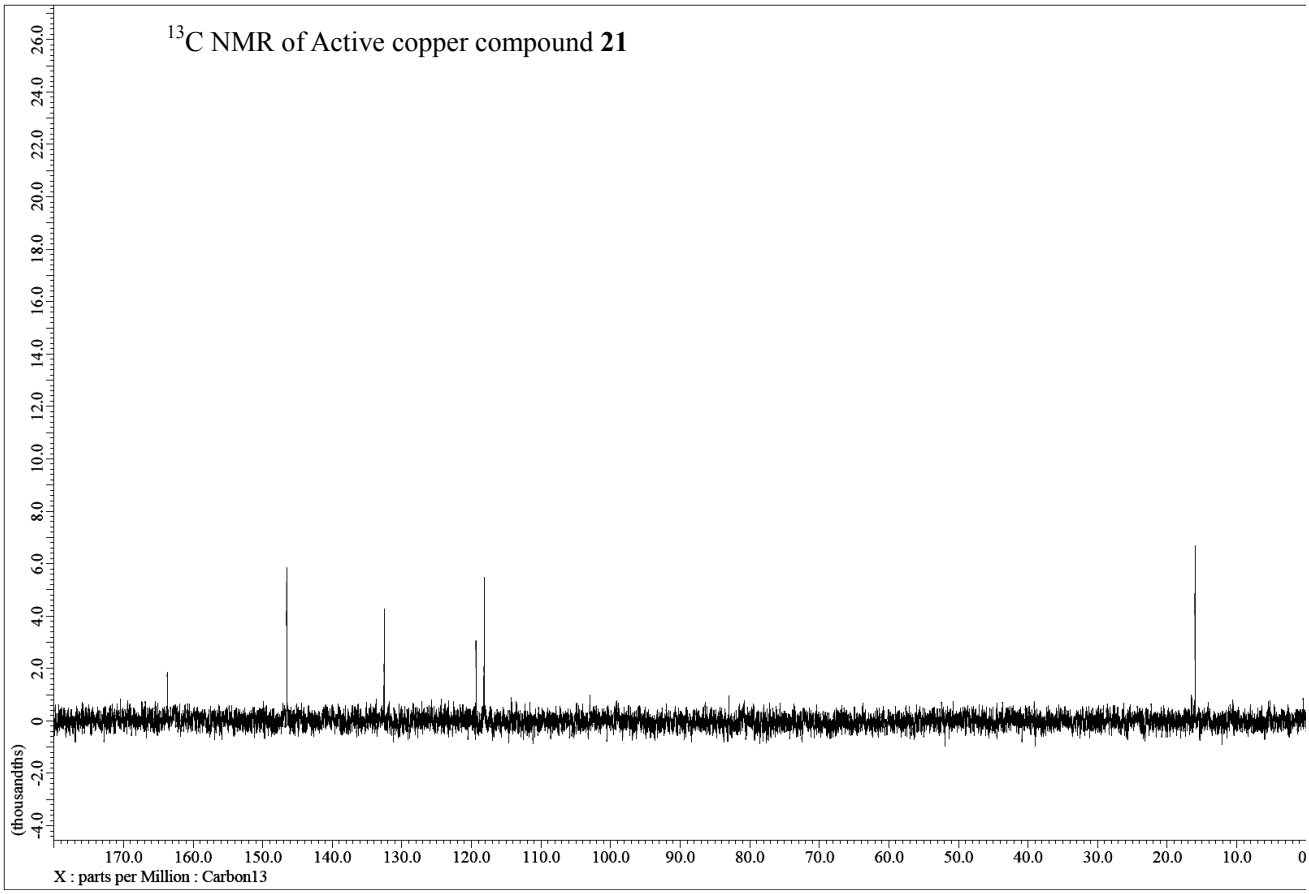

13C NMR of 19a
S
N
N
S
abundance
X : parts per Million : Carbon13







^{1}H NMR of Active coper compound **21**



^{13}C NMR of Active copper compound **21**

Reference:

1. L. Roumen, J. W. Peeters, J. M. A. Emmen, I. P. E. Beugels, E. M. G. Custers, M. de Gooyer, R. Plate, K. Pieterse, P. A. J. Hilbers, J. F. M. Smits, J. A. J. Vekemans, D. Leysen, H. C. J. Ottenheijm, H. M. Janssen, and J. J. R. Hermans, *J. Med. Chem.*, 2010, **53**, 1712.

2. Y. Li, J. Jin, W. Qian and W. Bao, *Org. Biomol. Chem.*, 2010, 8, 326.

3. J. Xiao and J. M. Shreeve, *J. Org. Chem.*, 2005, **70**, 3072.

4. K. Stippich, R. Kretschmer, R. Beckert and H. Goerls, *Synthesis*, 2010, **14**, 1311

5. P. T. Beurskens, G. Admiraal, G. Beurskens, W. P. Bosman, R. de Gelder, R. Israel and J. M. M. Smits, The DIRDIF-99 program system, Technical Report of the Crystallography Laboratory University of Nijmegen, Nijmegen, The Netherlands, 1999.

6. A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M. Burla, G. Polidori and M. Camalli, *J. Appl. Crystallogr.*, 1994, **27**, 435.

7. (a) D. T. Cromer, G. T. Waber, International Table for X-Ray Crystallography, The Kynoch Press, Birmingham, U.K., 1974; vol. IV, table 2.2 A; (b) J. A. Ibers, W. C. Hamilton, *Acta Crystallogr.*, 1964, **17**, 871; (c) D. C. Creagh, W. J. McAuley, in International Tables for X-Ray Crystallography, ed. A. J. C. Wilson, Kluwer Academic Publishers, Boston, 1992; vol. C, pp. 219–222, table 4.2.6.8; (d) D. C. Creagh, J. H. Hubbell, in International Tables for X-Ray Crystallography, ed. A. J. C. Wilson, Kluwer Academic Publishers, Boston, 1992; vol. C, pp. 200–206, table 4.2.4.3.

8. CrystalStructure 3.8, Crystal Structure Analysis Package, Rigaku and Rigaku/Molecular Structure Corp., 2000–2006.

9. J. R. Carruthers, J. S. Rollett, P.W. Betteridge, D. Kinna, L. Pearce, A. Larsen, E. Gabe, CRYSTALS Issue 11, Chemical Crystallography Laboratory, Oxford, 1999.