Electronic Supplementary Material (ESI) for Green Chemistry

Electronic Supplementary Information

Solvent-free Huisgen Cyclization Using Heterogeneous Copper Catalysts Supported on Chelate Resin

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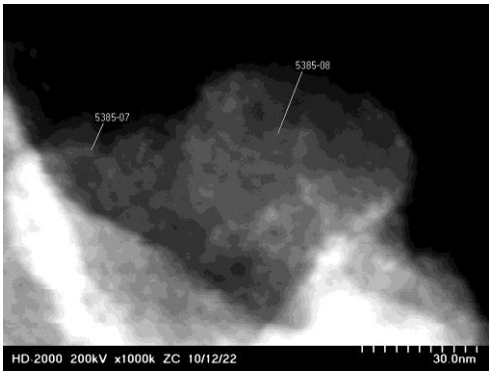
General

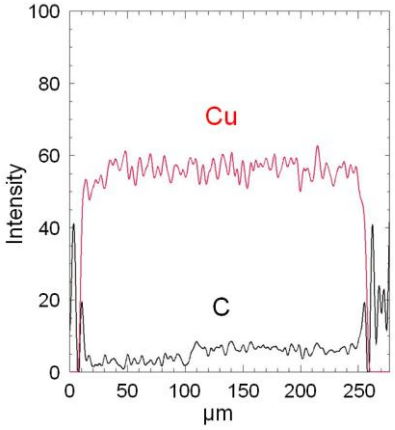
All reagents and solvents were obtained from commercial sources and used without further purification. The DIAION CR11 was obtained from Mitsubishi Chemical Corporation (Japan). Flash column chromatography was performed using silica gel 60N [spherical neutral (63–210 μm)] from Kanto Chemical Co., Inc. The ^{1}H and ^{13}C NMR spectra were recorded by a JEOL JEOL JNM AL-400 (400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR). Chemical shifts (δ) are expressed in parts per million and internally referenced [0.00 ppm for tetramethylsilane (TMS)/$CDCl_3$ for ^{1}H NMR and 77.0 ppm for $CDCl_3$ for ^{13}C NMR]. The mass spectra were taken by JEOL JMS Q1000GC Mk II Quad GC/MS for EI and JEOL JMS-T100TD for ESI.

STEM image and EPMA data for 12% Cu/CR11

Copper particles in the 12% Cu/CR11 were found to be approximately 3 nm in diameter by scanning transmission electron microscopy (STEM) and uniformly distributed on the support based on an electron probe microanalysis (EPMA). These results indicated that fine copper nanoparticles are highly dispersed on the DIAION CR11 and suggest the potential catalyst activity of the 12% Cu/CR11 toward the copper-catalyzed reactions including the Huisgen cycloaddition.



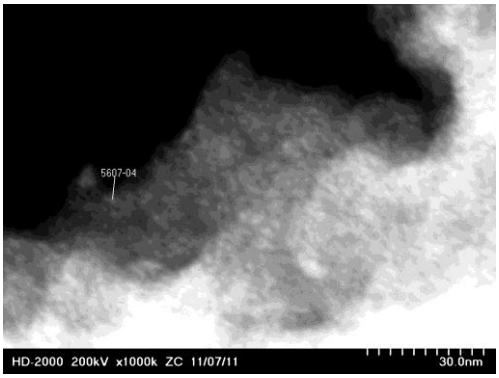
STEM image of 12% Cu/CR11.



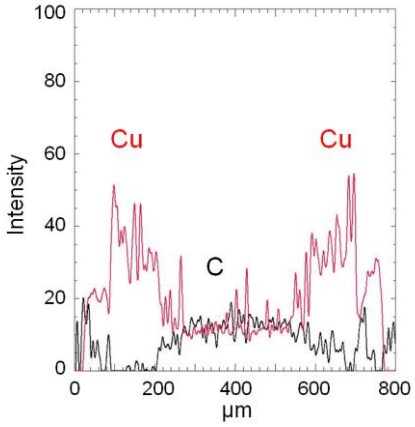
EPMA of 12% Cu/CR11.

STEM image and EPMA data for 7% Cu/CR20

The STEM and EPMA of 7% Cu/CR20 indicated that 3–5 nm copper particles were disproportionately distributed on the relatively surface areas of the DIAION CR20.



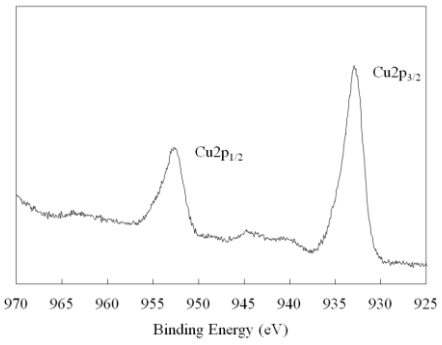
STEM image of 7% Cu/CR20.



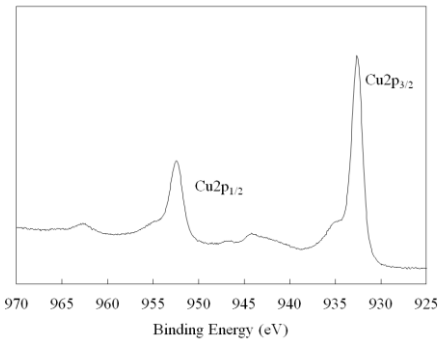
EPMA of 7% Cu/CR20.

XPS spectra of 12% Cu/CR11 and 7% Cu/CR20

X-ray photoelectron spectroscopy (XPS) analysis of the Cu $2p_{3/2}$ for 12% Cu/CR11 and 7% Cu/CR20 shows a single peak at approximately 932.5 eV, which is corresponding to Cu(I) (932.5 eV for Cu_2O) or Cu(0) (932.7 eV). The shoulder peaks at 935 eV of both catalysts are supposed to be those for Cu(II) [935.1 eV for $Cu(OH)_2$; 935.5 eV for $Cu(NO_3)_2$]. These results suggest that the copper species would exist mainly as Cu(I) or/and Cu(0). Copper ion of $Cu(NO_3)_2$ might be reduced to Cu(I) or Cu(0) by the iminodiacetate (CR11) or polyamine (CR20) moiety on the supports during the preparation. Although peaks of Cu(I) and Cu(0) on the XPS chart could not be completely-distinguished, the reaction efficiency and high regioselectivity for the 2,4-disubstituted triazole synthesis strongly suggest the formation of Cu(I) species.



XPS spectrum of 12% Cu/CR11



XPS spectrum of 7% Cu/CR20

Reuse test of 12% Cu/CR11

A mixture of the benzylazide (666 mg, 5.00 mmol), ethynylbenzene (605 μL, 5.50 mmol), Et_3N (154 μL, 1.10 μmol), and 12% Cu/CR11 (26.0 mg, 50.0 μmol) in a 50 mL-round bottom flask was stirred at 70 °C for 4 h. CH_2Cl_2 (50 mL) was added, and the mixture was passed through a filter paper [Kiriyama, No. 5C (1 μm)]. To the filtrate was added H_2O (50 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (50 mL × 2), and the combined organic layers were washed with brine (50 mL × 2), dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/EtOAc, 10 : 1) to give 1-benzyl-4-phenyl-1,2,3-triazole (1.14 g, 97%). The recoverd Cu/CR11 (26.0 mg, 100%) was washed with H_2O (20 mL) and MeOH (20 mL), dried under vacuum for 2 h, and then used for the 2nd run. The quantities of reagents for the reuse test are indicated in the Table below.

Run	Used 12% Cu/CR11	Azide	Alkyne	Yield	Recovered 12% Cu/CR11
1st	26.0 mg	666 mg (5.00 mmol)	605 μL (5.50 mol)	1.14 g (97%)	26.0 mg (100%)
2nd	26.0 mg	666 mg (5.00 mmol)	605 μL (5.50 mol)	1.15 g (98%)	25.0 mg (96%)
3rd	23.4 mg	599 mg (4.50 mmol)	545 μL (4.95 mmol)	1.04 g (98%)	22.1 mg (94%)
4th	20.8 mg	533 mg (4.00 mmol)	439 μL (4.40 mmol)	933 mg (99%)	19.5 mg (94%)
5th	18.2 mg	466 mg (3.50 mmol)	423 μL (3.85 mmol)	611 mg (74%)	16.1 mg (88%)

Reuse test of 7% Cu/CR20

A mixture of the benzylazide (666 mg, 5.00 mmol), ethynylbenzene (605 μL, 5.50 mmol), and 7% Cu/CR20 (45.0 mg, 50.0 μmol) in a 50 mL-round bottom flask was stirred at 70 °C for 5 h. CH_2Cl_2 (50 mL) was added, and the mixture was passed through a filter paper [Kiriyama, No. 5C (1 μm)]. To the filtrate was added H_2O (50 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (50 mL × 2), and the combined organic layers were washed with brine (50 mL × 2), dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (hexane/EtOAc, 10 : 1) to give 1-benzyl-4-phenyl-1,2,3-triazole (1.17 g, 100%). The recoverd Cu/CR20 (45.0 mg, 100%) was washed with H_2O (20 mL) and MeOH (20

mL), dried under vacuum for 2 h, and then used for the 2nd run. The quantities of reagents for the reuse test are indicated in the Table below.

Run	Used 7% Cu/CR20	Azide	Alkyne	Yield	Recovered 12% Cu/CR11
1st	45.0 mg	666 mg (5.00 mmol)	605 μL (5.50 mol)	1.17 g (100%)	45.0 mg (100%)
2nd	40.5 mg	599 mg (4.50 mmol)	545 μL (4.95 mol)	1.05 g (99%)	40.5 mg (100%)
3rd	36.0 mg	532 mg (4.00 mmol)	484 μL (4.40 mmol)	941 mg (100%)	34.6 mg (96%)
4th	31.5 mg	466 mg (3.50 mmol)	424 μL (3.85 mmol)	823 mg (100%)	30.8 mg (98%)
5th	27.0 mg	400 mg (3.00 mmol)	363μL (3.30 mmol)	705 mg (100%)	24.8 mg (92%)

Assay of residual copper species in the reaction mixture

The reaction was carried out according to the typical procedure for 12% Cu/CR11-catalyzed, solvent-free Husigen cyclization using benzylazide (6.66 g, 50.0 mmol), ethynylbenzene (6.05 mL, 55.0 mmol), Et_3N (1.54 mL, 11.0 mmol), and 12% Cu/CR11 (260 mg, 500 μmol). After 4 h, the reaction was pssed through a filter paper [Kiriyama, No. 5C (1 μm)], and the filter was washed with CH_2Cl_2 (100 mL × 2) and H_2O (40 mL × 2). The combined filtrates were separeted into two layers, and the organic layer was concentrated in vauo to approximately 80 mL. Both layers were transfered to each 100 mL-volumetric flask, and CH_2Cl_2 and H_2O were added to each flask up to 100 mL of total volume. The concentration of the residual copper in each layer was assayed using Shimadzu ICPS-8100; aqueous layer: 0.86 mg/L (0.86 ppm); organic layer: 8.6 mg/L (6.6 ppm). The leached Cu species 0.946 mg (3.0% of total used Cu).

Spectral Data of Products

1-Benzyl-4-phenyl-1*H*-1,2,3-triazole (Table 3, Entry 1; Table 6 Entry 1)[1]

^{1}H NMR δ 7.78 (2H, d, *J* = 8.3 Hz), 7.41–7.29 (8H, m), 5.57 (2H, s); ^{13}C NMR δ 148.2, 134.7, 130.5, 129.1, 128.8, 128.1, 128.0, 125.6, 119.4, 54.1; MS (EI) m/z (%) 235 (M^+, 11%), 206 (61), 180 (11), 116 (87), 104 (21), 91 (100), 65 (20).

1-(4-Fluorobenzyl)-4-phenyl-1*H*-1,2,3-triazole (Table 3, Entry 3)[2]

^{1}H NMR δ 7.76 (2H, d, *J* = 8.0 Hz), 7.69 (1H, s), 7.37 (2H, t, *J* = 7.0 Hz), 7.24–7.30 (3H, m), 7.02 (2H, t, *J* = 8.5 Hz); ^{13}C NMR δ 164.0, 161.5, 148.2, 130.55, 130.50, 130.4, 129.8, 128.7, 128.2, 125.6, 119.4, 116.1, 115.9, 53.3; MS (EI) m/z (%) 253 (M^+, 11%), 224 (47), 198 (8), 116 (100), 89 (39), 63 (12).

1-(4-Methoxybenzyl)-4-phenyl-1*H*-1,2,3-triazole (Table 3, Entry 4; Table 6, Entry 2)[3]

^{1}H NMR δ 7.79 (2H, m), 7.61 (1H, s), 7.39 (2H, m), 7.25–7.32 (3H, m), 6.91 (2H, m), 5.50 (2H, s), 3.81 (3H, s); ^{13}C NMR δ 160.0, 148.1, 130.6, 129.7, 128.8, 128.1, 126.7, 125.7, 119.2, 114.5, 55.3, 53.8; MS (EI) m/z (%)265 (M^+, 11%), 236 (17), 134 (11), 121 (100), 103 (10), 89 (11), 77 (24).

1,4-Diphenyl-1*H*-1,2,3-triazole (Table 3, Entry 5)[1]

^{1}H NMR δ 8.20 (1H, s), 7.91 (2H, d, *J* = 7.4 Hz), 7.78 (2H, d, *J* = 8.0 Hz), 7.53 (2H, t, *J* = 7.5 Hz), 7.45–7.48 (3H, m), 7.38 (1H, m); ^{13}C NMR δ 148.4, 137.1, 130.2, 129.8, 128.9, 458.8, 128.4, 125.8, 120.5, 117.6; MS (EI) m/z (%) 221 (M^+, 1%), 193 (100), 165 (46), 116 (24), 90 (29), 77 (42), 51 (22).

Ethyl 4-(4-phenyl-1*H*-1,2,3-triazol-1-yl)benzate (Table 3, Entry 6; Table 6, Entry 3)

^{1}H NMR δ 8.27–8.22 (3H, m), 7.94–7.90 (4H, m), 7.50–7.39 (3H, m), 4.46 (2H, q, *J* = 6.4 Hz), 1.46 (3H, t, *J* = 7.2 Hz); ^{13}C NMR δ 165.4, 148.7, 140.0, 131.3, 130.6, 130.0, 129.0, 128.6, 125.9, 119.8, 117.3, 61.4, 14.3; MS (ESI) m/z (%) 293 (M^+, 2%), 265 (100), 237 (89), 220 (22), 207 (23), 192 (65), 165 (37), 116 (52), 89 (46), 76 (26), 65 (11); HRMS (ESI) calcd for $C_{17}H_{15}N_3O_2$ [$(M+Na)^+$] 316.10620. Found 316.10547.

1-(4-Benzoylphenyl)-4-phenyl-1*H*-1,2,3-triazole (Table 3, Entry 7)

^{1}H NMR δ 8.29 (1H, s), 8.02–7.82 (5H, m), 7.62 (1H, tt, *J* = 7.6, 1.2 Hz), 7.55–7.47 (3H, m), 7.41–7.38 (1H, m); ^{13}C NMR δ 148.9, 139.6, 137.5, 137.1, 132.9, 131.8, 131.1, 123.0, 129.9, 129.0, 128.7, 128.5, 125.9, 124.7, 119.8, 117.3; MS (EI) m/z 325 (M^+, 0.03%), 279 (2), 167 (28), 149 (100), 104 (11), 83 (12), 70 (38), 57 (39); HRMS (ESI) calcd for $C_{21}H_{15}N_3O$ [$(M+H)^+$] 326.12934. Found 326.12914.

1-(4-Methoxyphenyl)-4-phenyl-1*H*-1,2,3-triazole (Table 3, Entry 8; Table 6, Entry 4)[1]

^{1}H NMR δ 8.11 (1H, s), 7.89 (2H, dd, *J* = 7.5, 1.0 Hz), 7.67 (2H, dd, *J* = 11, 2.5 Hz), 7.43 (2H, t, *J* = 9.5 Hz), 7.36 (1H, t, *J* = 9.5 Hz), 7.02 (2H, dd, *J* = 11, 2.5 Hz), 3.87 (3H, s); ^{13}C NMR δ 159.8, 148.2, 130.5, 130.4, 128.8, 128.3, 125.8, 122.1, 117.8, 114.8, 55.6; MS (EI) m/z (%) 251 (M^+, 0.4), 223 (100), 208 (82), 180 (51), 152 (22), 116 (12), 89 (24), 77 (24), 64 (19).

1-Cyclohexyl-4-phenyl-1*H*-1,2,3-triazole (Table 3, Entry 9; Table 6, Entry 5)[4]

^{1}H NMR δ 7.84 (2H, m), 7.78 (1H, s), 7.41 (2H, m), 7.31 (1H, m), 4.48–4.41 (1H, m), 2.22 (2H, m), 1.94 (2H, m), 1.81–1.72 (3H, m), 1.46 (2H, m), 1.31 (1H, m); ^{13}C NMR δ 147.1, 130.8, 128.6, 127.8, 125.5, 117.3, 60.0, 33.4, 25.0, 25.0; MS (EI) m/z (%) 227 (M^+, 22%), 198 (24), 156 (34), 117 (100), 104 (25), 90 (28), 55 (61).

1-Hexyl-4-phenyl-1*H*-1,2,3-triazole (Table 3, Entry 10; Table 6, Entry 6)[4]

^{1}H NMR δ 7.88 (2H, m), 7.73 (1H, s), 7.41–7.30 (3H, m), 4.35 (2H, q, *J* = 3.6 Hz), 1.95–1.88 (2H, m), 1.3 (2H, m), 0.87 (3H, m); ^{13}C NMR δ 147.5, 130.7, 128.7, 127.9, 125.5, 119.4, 50.3, 31.0, 26.0, 22.3, 13.8; MS (EI) m/z (%) 229 (M^+, 19%), 200 (23), 172 (17), 144 (18), 130 (16), 117 (100), 104 (27), 89 (23), 17 (14), 55 (11).

1-Benzyl-4-(4-tolyl)-1,2,3-1*H*-triazole (Table 4, Entry 1; Table 6, Entry 7)[4]

^{1}H NMR δ 7.68–7.61(3H, m), 7.38–7.18 (7H, m), 5.52 (2H, s), 2.34 (3H, s); ^{13}C NMR δ148.1, 137.9, 134.7, 129.3, 129.0, 128.5, 127.9, 125.5, 119.1, 54.0, 21.1; MS (EI) m/z (%)249 (M^+, 14%), 220 (67), 206 (17), 179 (18), 130 (100), 103 (20), 91 (79), 77 (18), 65 (19).

1-Benzyl-4-(4-methoxyphenyl)-1*H*-1,2,3-triazole (Table 4, Entry 2; Table 6, Entry 8)[4]

^{1}H NMR δ 7.72 (2H, d, *J* = 8.4 Hz), 7.58 (1H, s), 7.36–7.27 (5H, m), 6.92 (2H, m), 5.52 (2H, s), 3.80 (3H, s); ^{13}C NMR δ 159.5, 148.0, 134.7, 129.0, 128.6, 128.0, 126.9, 123.2, 118.7, 114.1, 55.2, 54.1; MS (EI) m/z (%) 265 (M^+, 18%), 236 (16), 146 (44), 104 (25), 91 (100), 65 (21).

1-Benzyl-4-propyl-1*H*-1,2,3-triazole (Table 4, Entry 3)[5]

^{1}H NMR δ 7.36–7.21 (6H, m), 5.47 (2H, s), 2.67 (2H, t, *J* = 7.2 Hz), 1.70–1.63 (2H, m), 0.95 (3H, t, *J* = 7.2 Hz); ^{13}C NMR δ 148.6, 134.9, 128.9, 128.4, 127.8, 120.5, 53.8, 27.6, 22.5, 13.6; MS (EI) m/z (%) 201 (M^+, 2%), 173 (5), 144 (10), 130 (11), 104 (11), 91 (100), 65 (28).

1-Benzyl-4-butyl-1*H*-1,2,3-triazole (Table 4, Entry 4; Table 6, Entry 9)[6]

^{1}H NMR δ 7.35–7.21 (6H, m), 5.47 (2H, s), 2.70 (2H, t, *J* = 7.6 Hz), 1.66-1.58 (2H, m), 1.40–1.31 (2H, m), 0.92 (3H, t, *J* = 7.2 Hz); ^{13}C NMR δ 148.8, 134.9, 128.9, 128.4, 128.0, 127.8, 120.4, 53.8, 31.3, 25.2, 22.2, 13.6; MS (EI) m/z (%) 229 (M^+, 18%), 173 (13), 144 (7), 91 (100), 65 (18).

1-Benzyl-4-pentyl-1*H*-1,2,3-triazole (Table 4, Entry 5)[7]

^{1}H NMR δ 7.37–7.21 (6H, m), 5.48 (2H, s), 2.69 (2H, t, *J* = 7.6 Hz), 1.66–1.60 (2H, m), 1.34–1.29 (4H, m), 0.89 (3H, t, *J* = 6.8 Hz); ^{13}C NMR δ 148.9, 134.9, 128.9, 128.4, 127.8, 120.4, 53.8, 31.3,

28.9, 25.5, 22.2, 13.8; MS (EI) m/z (%) 243 (M^+, 3%), 186 (5), 173 (14), 144 (7), 124 (4), 104 (5), 91 (100), 65 (18).

1-Benzyl-4-*n*-hexyl-1*H*-1,2,3-triazole (Table 4, Entry 6; Table 6, Entry 10)[7]

^{1}H NMR δ 7.35–7.22 (6H, m), 5.47 (2H, s), 2.70 (2H, t, *J* = 7.6 Hz), 1.67–1.60 (2H, m), 1.35–1.27 (6H, m), 0.88 (3H, t, *J* = 7.2 Hz); ^{13}C NMR δ 148.8, 134.9, 128.8, 128.3, 127.7, 120.5, 53.7, 31.3, 29.17, 28.7, 25.5, 22.3, 13.8; MS (EI) m/z (%) 215 (M^+, 1%), 186 (4), 173 (14), 144 (9), 104 (8), 91 (100), 77 (3), 65 (21).

Ethyl 1-benzyl-1*H*-1,2,3-triazole-4-carboxylate (Table 4, Entry 9)[1]

^{1}H NMR δ 8.02 (1H, s), 7.39–7.28 (5H, m), 5.58 (2H, s), 4.41 (2H, q, *J* = 6.8 Hz), 1.39 (3H, t, *J* = 6.8 Hz); ^{13}C NMR δ 160.5, 140.4, 133.7, 129.1, 128.9, 128.1, 127.2, 61.1, 54.2, 14.1; MS (EI) m/z (%) 231 (M^+, 0.1%), 174 (25), 130 (20), 91 (100), 77 (4), 65 (17).

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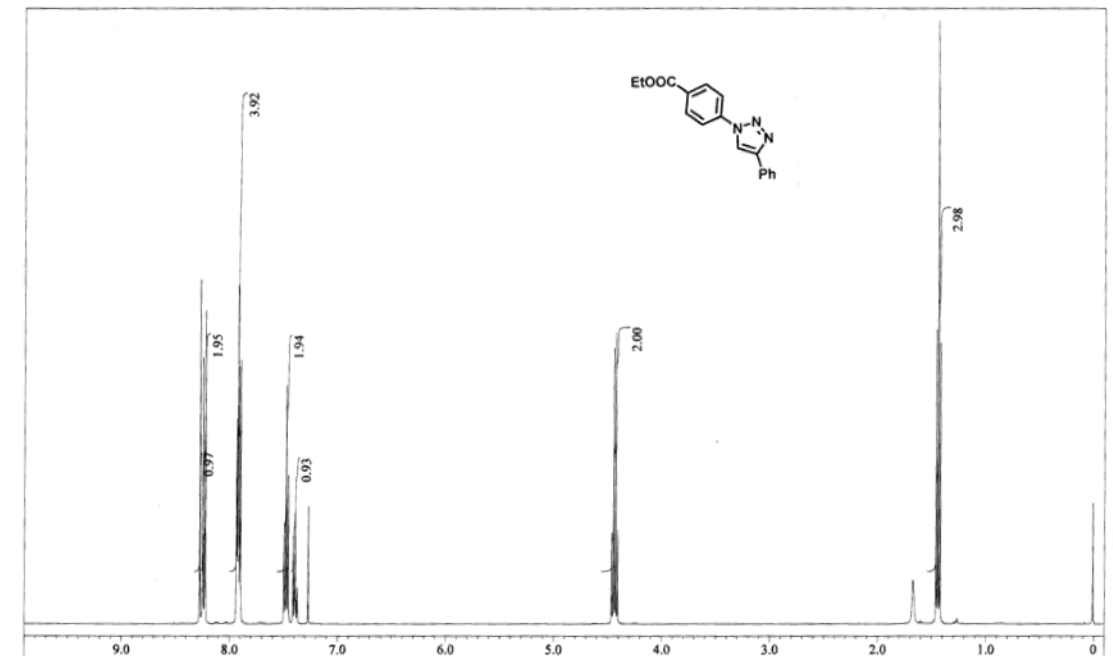
NMR spectra of new compounds

Table 3, Entry 6



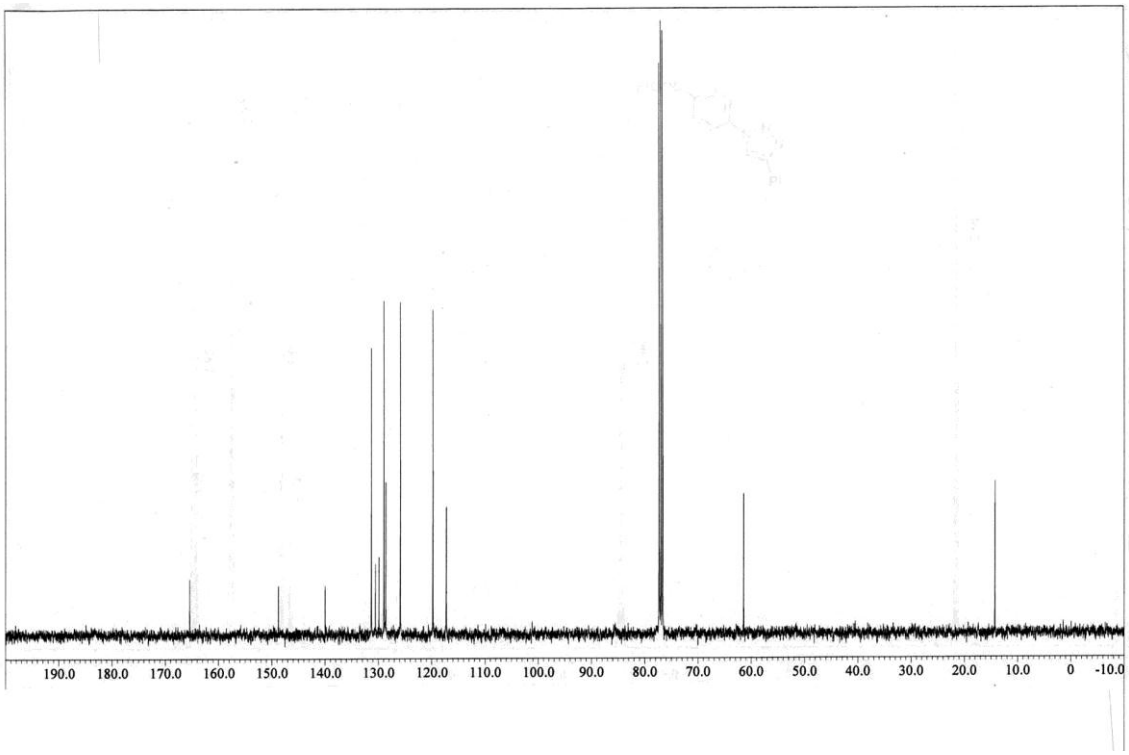


Table 3, Entry 7