

Supplementary Information

Perchloric acid modified-cellulose: a versatile, novel and biodegradable heterogeneous solid acid catalyst for single-pot synthesis of novel Bis-Pyran annulated heterocyclic scaffolds under solvent-free conditions

Tabassum Khan and Zeba N. Siddiqui*

Department of Chemistry, Aligarh Muslim University, Aligarh, 202002, India.

Corresponding author. Email: siddiqui_zeba@yahoo.co.in

Table of contents

General Experimental Methods	S2
Experimental procedure for preparation of catalyst.....	S2-S3
Experimental procedure for synthesis of compounds 4a-r	S3
Spectral data of compounds.....	S4-11
¹ H and ¹³ C NMR spectra for the novel compounds.....	S12-33

Experimental

General information

Melting points of all synthesized compounds were taken in a Riechert Thermover instrument and are uncorrected. The IR spectra (KBr) were recorded on Perkin Elmer RXI spectrometer. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker DRX-300 and Bruker Avance II 400 spectrometer using tetramethylsilane (TMS) as an internal standard and $\text{DMSO-}d_6/\text{CDCl}_3$ as solvent. ESI-MS were recorded on a THERMO Finnigan LCQ Advantage max ion trap mass spectrometer having an ESI source. Elemental analyses (C, H and N) were conducted using the Elemental vario EL III elemental analyzer and their results were found to be in agreement with the calculated values. Chemicals were of commercial grade and used without further purification. The homogeneity of the compounds was checked by thin layer chromatography (TLC) on glass plates coated with silica gel G254 (E. Merck) using chloroform-methanol (3:1) mixture as mobile phase and visualized using iodine vapors. All acid catalyst such as perchloric- SiO_2 , PEG- OSO_3H , $\text{Zn}(\text{L-proline})_2$, sulfuric acid- SiO_2 , $\text{P}_2\text{O}_5/\text{SiO}_2$, $\text{NaHSO}_4\text{-SiO}_2$, xanthan- OSO_3H and sulfamic acid- SiO_2 used in optimization study were synthesised by reported procedures and rest were commercially available. X-ray diffractograms (XRD) of the catalyst were recorded in the 2θ range of $10\text{-}70^\circ$ with scan rate of $4^\circ/\text{min}$ on a Rigaku Minifax X-ray diffractometer with Ni-filtered $\text{Cu K}\alpha$ radiation at a wavelength of $1.54060^\circ \text{ \AA}$. The SEM-EDX characterization of the catalyst was performed on a JEOL JSM-6510 scanning electron microscope equipped with energy dispersive X-ray spectrometer operating at 20 kV. TG/DTA was obtained with DTG-60H, with a heating rate of $20^\circ\text{C}/\text{min}$ from 0 to 500°C under N_2 atmosphere.

Preparation of catalyst

Cellulose- HClO_4 was prepared by the drop wise addition of perchloric acid (1.0 g, 10 mmol) to a magnetically stirred mixture of cellulose (5.0 g) in n-hexane (20 mL) at 0°C during 2 h. After the addition was complete, the mixture was stirred for another 2 h. Then, the mixture was filtered,

washed with acetone (30 mL) and dried at room temperature to afford cellulose-HClO₄ as white powder (5.25 g).

Back titration analysis of Cellulose-HClO₄

NaOH solution (20 mL, 0.1 N) was added to the Cellulose-HClO₄ (100 mg) in an Erlenmeyer flask. This solution was stirred for 10 min. Excess amount of base was neutralized by addition of HCl solution (1 N) to the equivalence point of titration. NaOH solution (20 mL, 0.1 N) when added to cellulose (100 mg) without HClO₄ and subjected to back titration under similar condition, no change in the strength of NaOH was observed. This ruled out the possible reaction of NaOH with cellulosic-OH groups.

General procedure for the synthesis of bis-pyran annulated heterocyclic scaffolds (4a-r) and dihydropyrano[c]chromene scaffolds (4s-u) under solvent-free conditions

A mixture of terephthalaldehyde/isophthalaldehyde (**1a-b**) (1.00 mmol), substituted benzaldehydes (**1c-e**, 1.00 mmol), ethyl cyanoacetate/malononitrile (**2a-b**) (2.00/1.00 mmol), a variety of C-H activated acids (**3**) (2.00/1.00 mmol) and cellulose-HClO₄ (0.08 g) were mixed in a 25 mL round bottom flask for the specific period of time (Table 4-7) at 70°C. After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature and added EtOAc (5 mL). The reaction mixture was filtered to recover the catalyst and then evaporated under reduced pressure to afford the product (**4a-u**). The products were further recrystallized from ethanol. The recovered catalyst was washed with EtOAc (2 mL x 2) dried in oven at 70 °C and reused for further catalytic cycles.

Spectral data of compounds

Diethyl-4,4'-(1,4-Phenylene)bis(2-amino-5-oxo-4,5-dihydropyrano[3,2-c]chromene-3-carboxylate) (4a)

White solid; m.p. 289-291 °C; IR (KBr) cm^{-1} : 1603 (C=C, vinylamine), 1674 (CO), 1710 (COO), 3198, 3321, 3396 (NH_2). ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ = 1.21-1.31 (6H, m, 2 x CH_3), 3.98-4.14 (4H, m, 2 x OCH_2), 4.44 (2H, s, 2 x CH), 6.77 (4H, s, 2 x NH_2), 7.16 (4H, s, C_6H_4), 7.29-7.75 (8H, m, Ar-H). ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ = 13.94 (2 x CH_3), 37.12 (2 x CH), 61.20 (2 x CH_2), 74.72 (2 x C3), 105.14 (2 x C13), 115.36 (2 x C11), 121.10, 122.32, 124.01, 125.84, 130.11, 138.20 (Ar-C), 152.54 (2 x C12, C14), 161.21 (2 x C2), 169.30 (2 x C5), 174.71 (2 x CO). ESI-MS: (m/z) 649.2 (M^++1). Anal. calcd. for $\text{C}_{36}\text{H}_{28}\text{N}_2\text{O}_{10}$: C, 66.66; H, 4.35; N, 4.31; found: C, 66.67; H, 4.33; N, 4.27.

4,4'-(1,4-Phenylene)bis(2-amino-5-oxo-4,5-dihydropyrano[3,2-c]chromene-3-carbonitrile) (4b)

White solid; m.p. >280 °C (lit. >280 °C); IR (KBr) cm^{-1} : 1605 (C=C, vinylnitrile), 1698 (CO), 2201 (CN), 3170, 3262, 3271, 3367 (NH_2). ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ = 4.40 (2H, s, 2 x CH), 7.20 (4H, s, 2 x NH_2), 7.34 (3H, d, Ar-H), 7.40 (3H, s, Ar-H), 7.46 (2H, d, Ar-H), 7.72 (2H, s, Ar-H), 7.87 (2H, d, Ar-H). ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ = 36.30 (2 x CH), 58.20 (2 x C3), 103.20 (2 x C13), 116.90 (2 x C11), 119.55 (2 x CN), 122.91, 125.11, 126.95, 128.13, 129.94, 134.24, 143.70 (Ar-C), 151.93 (2 x C12), 153.80 (2 x C14), 157.40 (2 x C2), 163.90 (2 x C5). ESI-MS: 555.1 (M^++1). Anal. calcd. for $\text{C}_{32}\text{H}_{18}\text{N}_4\text{O}_6$: C, 69.31; H, 3.27; N, 10.10; found: C, 69.29; H, 3.25; N, 10.08.

4,4'-(1,3-Phenylene)bis(2-amino-5-oxo-4,5-dihydropyrano[3,2-c]chromene-3-carbonitrile) (4c)

White powder; m.p. 280-282 °C (lit. 281-283 °C); IR (KBr) cm^{-1} : 1673 (C=C, vinylnitrile), 1719 (CO), 2198 (CN), 3198, 3214, 3337 (NH_2). ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ = 4.40 (1H, s, CH), 4.46 (1H, s, CH), 7.07-7.18 (3H, m, C_6H_4), 7.27 (1H, s, C_6H_4), 7.36 (2H, s, NH_2), 7.40 (2H, s, NH_2), 7.45-7.53 (4H, m, Ar-H), 7.65-7.73 (2H, m, Ar-H), 7.82-7.90 (2H, m, Ar-H). ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ = 36.91 (2 x CH), 57.9 (2 x C3), 103.74 (2 x C13), 116.51 (2 x C11),

119.12 (2 x CN), 122.54, 124.73, 126.11, 127.32, 131.33, 135.42, 143.31 (Ar-C), 152.3 (2 x C12), 154.43 (2 x C14), 158.57 (2 x C2), 159.42 (2 x C5). ESI-MS: (m/z) 555.1 ($M^+ + 1$). Anal. calcd. for $C_{32}H_{18}N_4O_6$: C, 69.31; H, 3.27; N, 10.10; found: C, 69.28; H, 3.27; N, 10.07.

Diethyl-4,4'-(1,4-Phenylene)bis(2-amino-7-methyl-5-oxo-4,5-dihydropyrano[4,3-b]pyran-3-carboxylate) (4d)

White solid; m.p. > 280 °C; IR (KBr) cm^{-1} : 1646 (C=C, vinylamine), 1670 (CO), 1706 (COO), 3198, 3317, 3369 (NH_2). 1H NMR (400 MHz, $DMSO-d_6$): δ = 1.25-1.38 (6H, m, 2 x CH_3), 2.31 (6H, s, 2 x CH_3), 3.99-4.07 (4H, m, 2 x OCH_2), 4.19 (2H, s, 2 x CH), 6.31 (2H, s, 2 x H_8), 6.89 (4H, s, 2 x NH_2), 7.16 (4H, s, C_6H_4). ^{13}C NMR (100 MHz, $DMSO-d_6$): δ = 15.6 (2 x CH_3), 20.9 (2 x CH_3), 39.46 (2 x CH), 61.8 (2 x CH_2), 69.21 (2 x C3), 100.1 (2 x C8), 101.9 (2 x C10), 127.52, 130.11, 136.60, 142.43 (Ar-C), 160.64 (2 x C2), 162.23 (2 x C7), 164.88 (2 x C9), 167.5 (2 x C5), 175.1 (2 x CO). ESI-MS: (m/z) 577 ($M^+ + 1$). Anal. calcd. for $C_{30}H_{28}N_2O_{10}$: C, 62.49; H, 4.89; N, 4.85; found: C, 62.50; H, 4.91; N, 4.83.

4,4'-(1,4-Phenylene)bis(2-amino-7-methyl-5-oxo-4,5-dihydropyrano[4,3-b]pyran-3-carbonitrile) (4e)

White solid; m.p. > 280 °C (lit. > 280 °C); IR (KBr) cm^{-1} : 1680 (C=C, vinyl nitrile), 1713 (CO), 2198 (CN), 3180, 3375 (NH_2). 1H NMR (400 MHz, $DMSO-d_6$): δ = 2.25 (6H, s, 2 x CH_3), 4.29 (1H, s, CH), 4.46 (1H, s, CH), 6.20 (1H, s, H_8), 6.27 (1H, s, H_8), 7.14 (1H, s, NH_2), 7.23 (1H, s, NH_2), 7.28 (2H, s, NH_2), 7.49 (2H, d, C_6H_4), 7.65 (2H, d, C_6H_4). ^{13}C NMR (100 MHz, $DMSO-d_6$): δ = 19.7 (2 x CH_3), 36.93 (2 x CH), 56.24 (2 x C3), 101.04 (2 x C8), 103.05 (2 x C10), 119.48 (2 x CN), 129.49, 130.34, 132.12, 142.07 (Ar-C), 159.64 (2 x C2), 162.02 (2 x C7), 164.42 (2 x C9), 166.3 (2 x C5). ESI-MS: 483.2 ($M^+ + 1$). Anal. calcd. for $C_{26}H_{18}N_4O_6$: C, 64.72; H, 3.76; N, 11.61; found: C, 64.70; H, 3.73; N, 11.58.

4,4'-(1,3-Phenylene)bis(2-amino-7-methyl-5-oxo-4,5-dihydropyrano[4,3-b]pyran-3-carbonitrile)
(4f)

White solid; m.p. 253-255 °C; IR (KBr) cm^{-1} : 1670 (C=C, vinyl nitrile), 1702 (CO), 2198 (CN), 3198, 3329, 3424 (NH_2). ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ = 2.15 (6H, s, 2 x CH_3), 4.39 (2H, s, 2 x CH), 6.21 (2H, s, 2 x H_8), 6.99 (4H, s, 2 x NH_2), 7.15-7.53 (3H, m, C_6H_4), 7.44 (1H, s, C_6H_4). ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ = 21.9 (2 x CH_3), 40.2 (2 x CH), 59.1 (2 x C3), 101.9 (2 x C8), 104.2 (2 x C10), 119.41 (2 x CN), 124.7, 128.5, 130.9, 138.1 (Ar-C), 159.2 (2 x C2), 161.2 (2 x C7), 164.6 (2 x C9), 167.5 (2 x C5). ESI-MS: (m/z) 483.1 (M^++1). Anal. calcd. for $\text{C}_{26}\text{H}_{18}\text{N}_4\text{O}_6$: C, 64.72; H, 3.76; N, 11.61; found: C, 64.70; H, 3.71; N, 11.64.

Diethyl-5,5'-(1,4-Phenylene)bis(7-amino-1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrano[2,3-d]pyrimidine-6-carboxylate) (4g)

Yellow solid; m.p. >300 °C; IR (KBr) cm^{-1} : 1684 (C=C, vinylamine), 1711 (CO), 1721 (COO), 3165, 3218 (NH_2). ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ = 1.24-1.39 (6H, m, 2 x CH_3), 3.16 (6H, s, 2 x CH_3), 3.30 (6H, s, 2 x CH_3), 4.13-4.20 (4H, m, 2 x OCH_2), 4.32 (2H, s, 2 x CH), 7.06 (4H, s, 2 x NH_2), 7.26 (4H, s, C_6H_4). ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ = 14.7 (2 x CH_3), 28.9 (2 x CH_3), 29.7 (2 x CH_3), 39.85 (2 x CH), 62.1 (2 x CH_2), 75.1 (2 x C3), 79.5 (2 x C10), 129.13, 141.1 (Ar-C), 151.40 (2 x C7), 160.30 (2 x C2), 162.7 (2 x C9), 166.9 (2 x C5), 172.2 (2 x CO). ESI-MS: (m/z) 637.1 (M^++1). Anal. calcd. for $\text{C}_{30}\text{H}_{32}\text{N}_6\text{O}_{10}$: C, 56.60; H, 5.06; N, 13.20; found: C, 56.54; H, 5.03; N, 13.17.

5,5'-(1,4-Phenylene)bis(7-amino-1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrano[2,3-d]pyrimidine-6-carbonitrile) (4h)

Light yellow powder; m.p. >300 °C; IR (KBr) cm^{-1} : 1697 (C=C, vinyl nitrile), 1715 (CO), 2198 (CN), 3188, 3336 (NH_2). ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ = 3.08 (6H, s, 2 x CH_3), 3.13 (6H, s, 2 x CH_3), 4.45 (2H, s, 2 x CH), 6.96 (4H, s, 2 x NH_2), 7.16 (4H, s, C_6H_4). ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$): δ = 28.10 (2 x CH_3), 29.50 (2 x CH_3), 50.11 (2 x CH), 59.31 (2 x C3), 81.51 (2 x

C10), 119.10 (2 x CN), 128.16, 135.31(Ar-C), 152.40 (2 x C7), 159.20 (2 x C2), 160.10 (2 x C9), 163.4 (2 x C5). ESI-MS: (m/z) 543.1 ($M^{+}+1$). Anal. calcd. for $C_{26}H_{22}N_8O_6$: C, 57.56; H, 4.08; N, 20.65; found: C, 57.54; H, 4.03; N, 20.67.

5,5'-(1,3-Phenylene)bis(7-amino-1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrano[2,3-d]pyrimidine-6-carbonitrile) (4i)

Light yellow powder; m.p. >300 °C; IR (KBr) cm^{-1} : 1699 (C=C, vinyl nitrile), 1714 (CO), 2195 (CN), 3178, 3341 (NH_2). 1H NMR (400 MHz, DMSO- d_6): δ = 3.07 (6H, s, 2 x CH_3), 3.15 (6H, s, 2 x CH_3), 4.41 (2H, s, 2 x CH), 6.97 (4H, s, 2 x NH_2), 7.40-7.48 (3H, m, C_6H_4), 7.66 (1H, s, C_6H_4). ^{13}C NMR (100 MHz, DMSO- d_6): δ = 28.19 (2 x CH_3), 29.13 (2 x CH_3), 49.20 (2 x CH), 56.01 (2 x C3), 80.23 (2 x C10), 118.98 (2 x CN), 129.34, 136.01(Ar-C), 151.21 (2 x C7), 159.12 (2 x C2), 162.10 (2 x C9), 164.84 (2 x C5). ESI-MS: (m/z) 543 ($M^{+}+1$). Anal. calcd. for $C_{26}H_{22}N_8O_6$: C, 57.56; H, 4.08; N, 20.65; found: C, 57.53; H, 4.03; N, 20.68.

Diethyl-4,4'-(1,4-Phenylene)bis(2-amino-5-oxo-4,5-dihydroindeno[1,2-b]pyran-3-carboxylate) (4j)

Green powder; m.p. > 280 °C; IR (KBr) cm^{-1} : 1610 (C=C, vinylamine), 1689 (CO), 1721 (COO), 3222, 3387, 3400 (NH_2). 1H NMR (400 MHz, DMSO- d_6): δ = 1.19-1.21 (6H, m, 2 x CH_3), 4.11-4.17 (4H, m, 2 x OCH_2), 4.71 (2H, s, 2 x CH), 6.97 (4H, s, 2 x NH_2), 7.11 (4H, s, C_6H_4), 7.36, 7.52, 7.57, 7.64 (8H, m, Ar-H). ^{13}C NMR (100 MHz, DMSO- d_6): δ = 13.98 (2 x CH_3), 45.18 (2 x CH), 61.7 (2 x CH_2), 72.3 (2 x C3), 102.5 (2 x C12), 127.4, 128.9, 134.4, 136.5, 137.6, 140.2 (Ar-C), 159.1 (2 x C2), 167.2 (2 x C13), 171.2 (2 x CO), 192.5 (2 x C5). ESI-MS: (m/z) 617.1 ($M^{+}+1$). Anal. calcd. for $C_{36}H_{28}N_2O_8$: C, 70.12; H, 4.57; N, 4.54; found: C, 70.15; H, 4.59; N, 4.51.

4,4'-(1,4-Phenylene)bis(2-amino-5-oxo-4,5-dihydroindeno[1,2-b]pyran-3-carbonitrile) (4k)

Green powder; m.p. > 280 °C; IR (KBr) cm^{-1} : 1610 (C=C, vinyl nitrile), 1689 (CO), 2210 (CN), 3232, 3332, 3407 (NH_2). 1H NMR (400 MHz, DMSO- d_6): δ = 4.29 (2H, s, 2 x CH), 6.91 (4H, s, 2 x NH_2), 7.24 (4H, s, C_6H_4), 7.36-7.58 (8H, m, Ar-H). ^{13}C NMR (100 MHz, DMSO- d_6): δ = 52.18

(2 x CH), 58.1 (2 x C3), 106.1 (2 x C12), 117.2 (2 x CN), 126.2, 128.4, 130.1, 134.4, 136.6 (Ar-C), 158.31 (2 x C2), 161.2 (2 x C13), 190.3 (2 x C5). ESI-MS: (m/z) 523.1 ($M^+ + 1$). Anal. calcd. for $C_{32}H_{18}N_4O_4$: C, 73.55; H, 3.47; N, 10.72; found: C, 73.52; H, 3.49; N, 10.69.

4,4'-(1,3-Phenylene)bis(2-amino-5-oxo-4,5-dihydroindeno[1,2-b]pyran-3-carbonitrile) (4l)

Green powder; m.p. > 280 °C; IR (KBr) cm^{-1} : 1630 (C=C, vinyl nitrile), 1685 (CO), 2210 (CN), 3232, 3339, 3411 (NH_2). 1H NMR (400 MHz, $DMSO-d_6$): δ = 4.54 (2H, s, 2 x CH), 6.95 (4H, s, 2 x NH_2), 7.23-7.68 (3H, m, C_6H_4), 7.43 (1H, s, C_6H_4), 7.76-8.08 (8H, m, Ar-H). ^{13}C NMR (100 MHz, $DMSO-d_6$): δ = 49.08 (2 x CH), 59.91 (2 x C3), 105.51 (2 x C12), 118.3 (2 x CN), 126.34, 129.14, 131.1, 134.81, 135.96 (Ar-C), 157.5 (2 x C2), 165.82 (2 x C13), 191.1 (2 x C5). ESI-MS: (m/z) 523.1 ($M^+ + 1$). Anal. calcd. for $C_{32}H_{18}N_4O_4$: C, 73.55; H, 3.47; N, 10.72; found: C, 73.52; H, 3.49; N, 10.69.

Diethyl-4,4'-(1,4-Phenylene)bis(2-amino-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carboxylate) (4m)

Shining white powder; m.p. 262 °C (lit. 260-261 °C); IR (KBr) cm^{-1} : 1634 (C=C, vinylamine), 1682 (CO), 1717 (COO), 3176, 3222, 3387 (NH_2). 1H NMR (400 MHz, $DMSO-d_6$): δ = 0.99 (12H, s, 4 x CH_3), 1.29-1.32 (6H, m, 2 x CH_3), 1.88-1.94 (8H, m, 2 x CH_2), 2.29-2.35 (4H, m, 2 x OCH_2), 4.43 (2H, s, 2 x CH), 6.99 (4H, s, 2 x NH_2), 7.23 (4H, s, C_6H_4). ^{13}C NMR (100 MHz, $DMSO-d_6$): δ = 16.21 (2 x CH_3), 27.5 (4 x CH_3), 32.3 (2 x C7), 35.2 (2 x C8), 41.8 (2 x CH), 51.5 (2 x C6), 61.7 (2 x CH_2), 69.2 (2 x C3), 113.9 (2 x C10), 128.9, 141.4 (Ar-C), 155.0 (2 x C9), 162.1 (2 x C2), 167.2 (2 x CO), 198.9 (2 x C5). ESI-MS: (m/z) 605 ($M^+ + 1$). Anal. calcd. for $C_{34}H_{40}N_2O_8$: C, 67.53; H, 6.66; N, 4.63; found: C, 67.50; H, 6.67; N, 4.66.

4,4'-(1,4-Phenylene)bis(2-amino-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile) (4n)

White solid; m.p. 273-275 dec. °C (lit. 270 dec. °C); IR (KBr) cm^{-1} : 1621 (C=C, vinyl nitrile), 1674 (CO), 2201 (CN), 3121, 3254, 3331 (NH_2). 1H NMR (400 MHz, $DMSO-d_6$): δ = 0.99 (6H, s,

2 x CH₃), 1.05 (6H, s, 2 x CH₃), 2.17-2.24 (4H, m, 2 x CH₂), 2.48-2.58 (4H, m, 2 x CH₂), 4.15 (2H, s, 2 x CH), 6.90 (4H, s, 2 x NH₂), 7.13 (4H, s, C₆H₄). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 27.8 (2 x CH₃), 28.21 (2 x CH₃), 30.11 (2 x C7), 34.28 (2 x C8), 39.2 (2 x CH), 51.18 (2 x C6), 59.22 (2 x C3), 114.12 (2 x C10), 121.26 (2 x CN), 126.18, 144.7 (Ar-C), 159.25 (2 x C9), 164.43 (2 x C2), 196.86 (2 x C5). ESI-MS: (*m/z*) 511.2 (M⁺+1). Anal. calcd. for C₃₀H₃₀N₄O₄: C, 70.57; H, 5.92; N, 10.97; found: C, 70.56; H, 5.95; N, 11.01.

4,4'-(1,3-Phenylene)bis(2-amino-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile) (4o)

White powder; m.p. 163-164 dec. °C (lit. 165 dec.) °C; IR (KBr) cm⁻¹: 1622 (C=C, vinyl nitrile), 1672 (CO), 2204 (CN), 3142, 3263, 3334 (NH₂). ¹H NMR (400 MHz, DMSO-*d*₆): δ = 0.98 (6H, s, 2 x CH₃), 1.04 (6H, s, 2 x CH₃), 2.09 (2H, d, CH₂), 2.25 (2H, d, CH₂), 2.36 (2H, d, CH₂), 2.46-2.56 (2H, m, CH₂), 4.15 (2H, s, 2 x CH), 6.72 (1H, s, C₆H₄), 6.87 (4H, s, 2 x NH₂), 6.98-7.02 (2H, m, C₆H₄), 7.21 (1H, s, C₆H₄). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 27.38 (4 x CH₃), 30.68 (2 x C7), 34.32 (2 x C8), 38.32 (2 x CH), 48.14 (2 x C6), 114.26 (2 x C10), 121.53 (2 x CN), 124.23, 127.31, 129.67, 144.21 (Ar-C), 159.40 (2 x C9), 165.31 (2 x C2), 196.11 (2 x C5). ESI-MS: (*m/z*) 511.1 (M⁺+1). Anal. calcd. for C₃₀H₃₀N₄O₄: C, 70.57; H, 5.92; N, 10.97; found: C, 70.59; H, 5.90; N, 10.99.

Diethyl-4,4'-(1,4-Phenylene)bis(6-amino-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carboxylate) (4p)

Reddish brown solid; m.p. > 300°C (lit. 296 dec.) °C; IR (KBr) cm⁻¹: 1620 (C=C, vinylamine), 1695 (CO), 2201 (CN), 3104, 3260, 3327 (NH₂). ¹H NMR (400 MHz, DMSO-*d*₆): δ = 1.24-1.29 (6H, m, 2 x CH₃), 1.93 (6H, s, 2 x CH₃), 4.20-4.23 (4H, m, 2 x OCH₂), 4.74 (2H, s, 2 x CH), 6.99 (4H, s, 2 x NH₂), 7.34 (4H, s, C₆H₄), 7.45-7.62 (10H, m, Ar-H). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 13.5 (2 x CH₃), 14.8 (2 x CH₃), 36.7 (2 x CH), 61.7 (2 x CH₂), 75.9 (2 x C3), 119.0 (2 x C9), 122.5, 126.2, 128.9, 129.3, 137.5, 139.3 (Ar-C), 147.1 (2 x C5), 153.9 (2 x C8), 159.0 (2 x C2),

169.5 (2 x CO). ESI-MS: (*m/z*) 673.1 ($M^+ + 1$). Anal. calcd. for $C_{38}H_{36}N_6O_6$: C, 67.84; H, 5.39; N, 12.49; found: C, 67.86; H, 5.38; N, 12.44.

4,4'-(1,4-Phenylene)bis(6-amino-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile) (4q)

Reddish brown solid; m.p. >300 dec. °C (lit. 296 dec.) °C; IR (KBr) cm^{-1} : 1622 (C=C, vinyl nitrile), 1697 (CO), 2201 (CN), 3108, 3252, 3318 (NH₂). ¹H NMR (400 MHz, DMSO-*d*₆): δ = 2.16 (6H, s, 2 x CH₃), 4.75 (2H, s, 2 x CH), 7.23-7.26 (4H, s, 2 x NH₂), 7.39-7.49 (6H, m, Ar-H), 7.60-7.62 (4H, m, C₆H₄), 7.70-7.75 (4H, m, Ar-H). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 13.32 (2 x CH₃), 36.35 (2 x CH), 59.39 (2 x C3), 117.2 (2 x CN), 119.95 (2 x C9), 123.23, 126.11, 127.52, 128.62, 132.22, 136.24 (Ar-C), 144.37 (2 x C5), 146.52 (2 x C8), 158.23 (2 x C2). ESI-MS: (*m/z*) 579.2 ($M^+ + 1$). Anal. calcd. for $C_{34}H_{26}N_8O_2$: C, 70.57; H, 4.52; N, 19.36; found: C, 70.60; H, 4.49; N, 19.39.

4,4'-(1,3-Phenylene)bis(6-amino-3-methyl-1-phenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile) (4r)

Reddish brown solid; m.p. 196-199 °C (lit. 198 dec.) °C; IR (KBr) cm^{-1} : 1619 (C=C, vinyl nitrile), 1698 (CO), 2200 (CN), 3100, 3248, 3338 (NH₂). ¹H NMR (400 MHz, DMSO-*d*₆): δ = 1.75 (6H, s, 2 x CH₃), 4.69 (2H, s, 2 x CH), 7.13-7.17 (6H, m, 2 x NH₂, Ar-H), 7.27-7.34 (4H, m, Ar-H), 7.49 (4H, t, C₆H₄), 7.75 (4H, d, Ar-H). ¹³C NMR (100 MHz, DMSO-*d*₆): δ = 13.23 (2 x CH₃), 36.13 (2 x CH), 57.19 (2 x C3), 118.45 (2 x CN), 120.17 (2 x C9), 121.28, 126.12, 127.14, 128.31, 131.21, 137.21 (Ar-C), 143.26 (2 x C5), 145.22 (2 x C8), 160.32 (2 x C2). ESI-MS: (*m/z*) 579.1 ($M^+ + 1$). Anal. calcd. for $C_{34}H_{26}N_8O_2$: C, 70.57; H, 4.52; N, 19.36; found: C, 70.60; H, 4.53; N, 19.34.

2-Amino-4-(4-chlorophenyl)-5-oxo-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile (4s)

White solid; m.p. 260-263 °C (lit. 262-264 °C); IR (KBr) cm^{-1} : 1673 (C=C, vinyl nitrile), 1713 (CO), 2198 (CN), 3189, 3285, 3326, 3389 (NH₂). ¹H NMR (400 MHz, DMSO-*d*₆): δ = 4.43 (1H, s, CH), 7.29 (2H, d, Ar-H), 7.33 (2H, d, Ar-H), 7.40 (2H, d, Ar-H), 7.45 (2H, br s, NH₂), 7.66 (1H,

t, Ar-H), 7.86 (1H, d, Ar-H). ^{13}C NMR (100 MHz, DMSO- d_6): δ = 35.83 (CH), 56.69 (C3), 104.18 (C13), 115.46 (C11), 119.23 (CN), 122.39, 124.38, 127.23, 130.35, 131.19, 132.12, 134.22, 142.27 (Ar-C), 152.11 (C12), 153.95 (C2), 157.23 (C14), 160.23 (C5). ESI-MS: 351.1 ($\text{M}^+ + 1$). Anal. calcd. for $\text{C}_{19}\text{H}_{11}\text{ClN}_2\text{O}_3$: C, 65.06; H, 3.16; N, 7.98; found: C, 65.08; H, 3.14; N, 7.945.

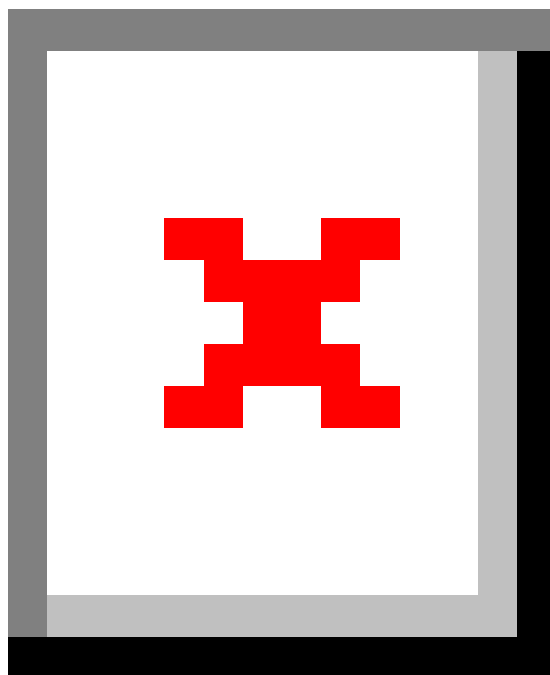
2-Amino-5-oxo-4-(p-tolyl)-4,5-dihydropyrano[3,2-c]chromene-3-carbonitrile (4t)

White solid; m.p. 256-258 °C (lit. 257-259 °C); IR (KBr) cm^{-1} : 1611 (C=C, vinyl nitrile), 1693 (CO), 2196 (CN), 3182, 3293, 3372 (NH_2). ^1H NMR (400 MHz, DMSO- d_6): δ = 2.24 (3H, s, CH_3), 4.42 (1H, s, CH), 7.14 (4H, m, Ar-H), 7.35 (2H, s, NH_2), 7.44 (1H, d, Ar-H), 7.49 (1H, t, Ar-H), 7.68 (1H, t, Ar-H), 7.78 (1H, d, Ar-H). ^{13}C NMR (100 MHz, DMSO- d_6): δ = 20.23 (CH_3), 36.27 (CH), 56.25 (C3), 103.13 (C13), 115.43 (C11), 119.67 (CN), 122.39, 124.12, 127.92, 129.04, 132.03, 135.32, 140.12 (Ar-C), 150.31 (C12), 154.11 (C2), 156.34 (C14), 159.85 (C5). ESI-MS: 331.1 ($\text{M}^+ + 1$). Anal. calcd. for $\text{C}_{20}\text{H}_{14}\text{N}_2\text{O}_3$: C, 72.71; H, 4.27; N, 8.48; found: C, 72.69; H, 4.25; N, 8.50.

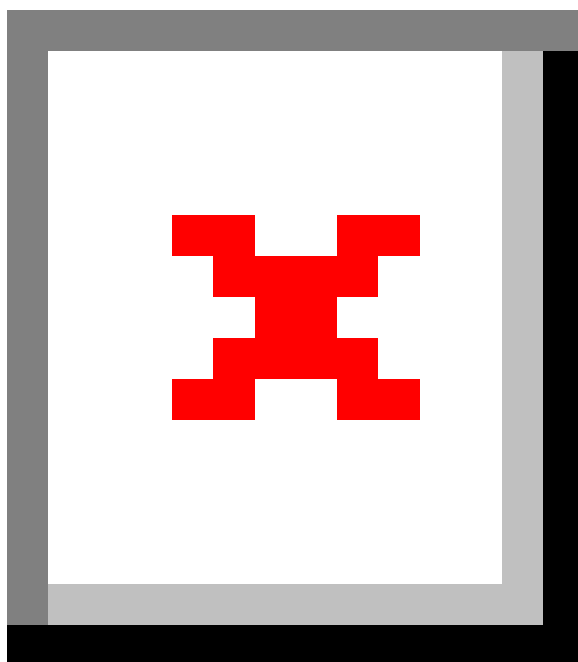
2-Amino-4-(3-nitrophenyl)-5-oxo-4,5-dihydropyrano[3,2-c]chromene-3-carbonitrile (4u)

White solid; m.p. 255-257 °C (lit. 254-256 °C); IR (KBr) cm^{-1} : 1697 (C=C, vinyl nitrile), 1778 (CO), 2199 (CN), 3342, 3346 (NH_2). ^1H NMR (400 MHz, DMSO- d_6): δ = 4.70 (1H, s, CH), 7.40 (1H, d, Ar-H), 7.47 (1H, t, Ar-H), 7.55 (2H, s, NH_2), 7.60 (1H, t, Ar-H), 7.71 (1H, td, Ar-H), 7.84 (1H, d, Ar-H), 7.93 (1H, d, Ar-H), 8.10 (1H, d, Ar-H), 8.14 (1H, s, Ar-H). ^{13}C NMR (100 MHz, DMSO- d_6): δ = 37.16 (CH), 57.56 (C3), 102.02 (C13), 116.54 (C11), 119.65 (CN), 121.49, 122.65, 123.32, 124.31, 131.37, 133.92, 134.17, 144.87 (Ar-C), 153.56 (C12), 155.98 (C2), 158.95 (C14), 162.76 (C5). ESI-MS: 362.1 ($\text{M}^+ + 1$). Anal. calcd. for $\text{C}_{19}\text{H}_{11}\text{N}_3\text{O}_5$: C, 63.16; H, 3.06; N, 11.63; found: C, 63.13; H, 3.04; N, 11.65.

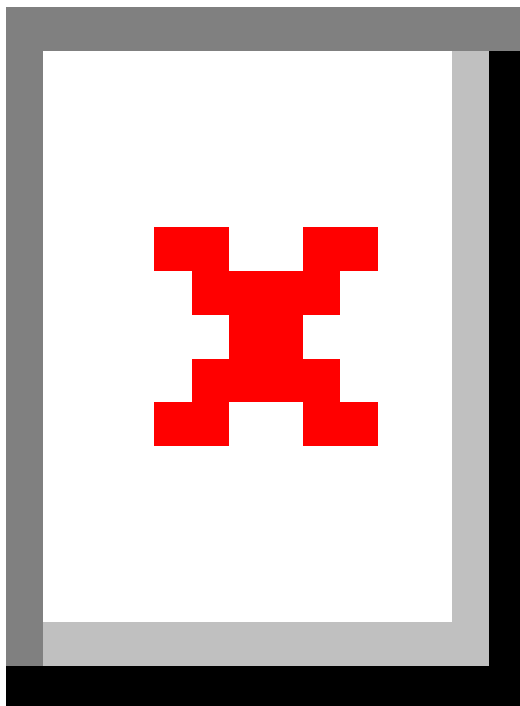
^1H NMR of 4a



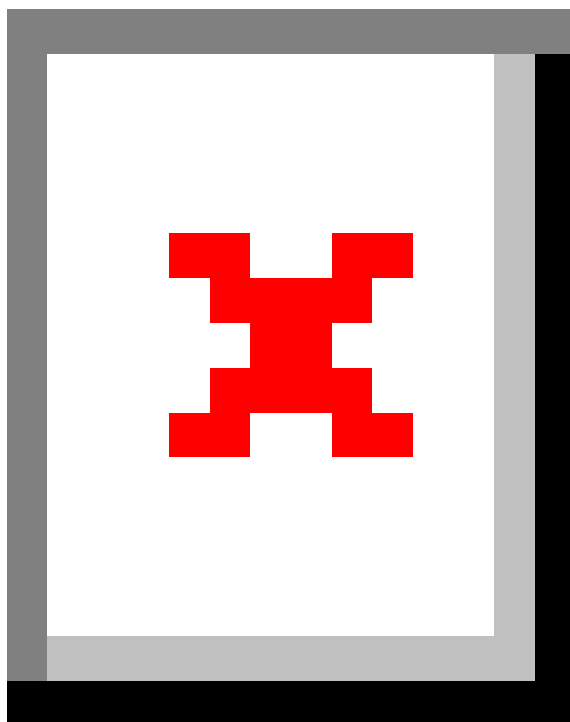
^{13}C NMR of 4a



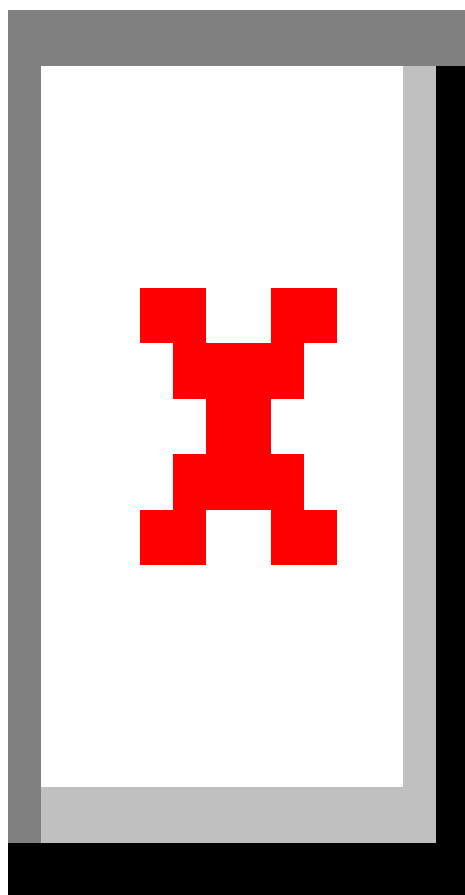
^1H NMR of 4d

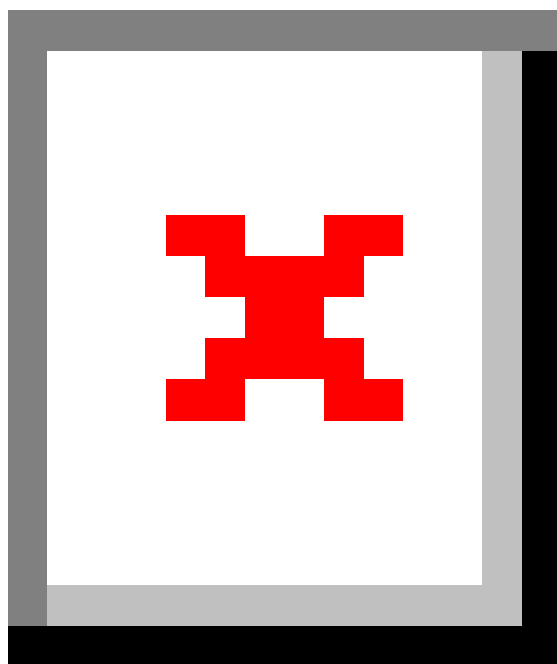


^{13}C NMR of 4d

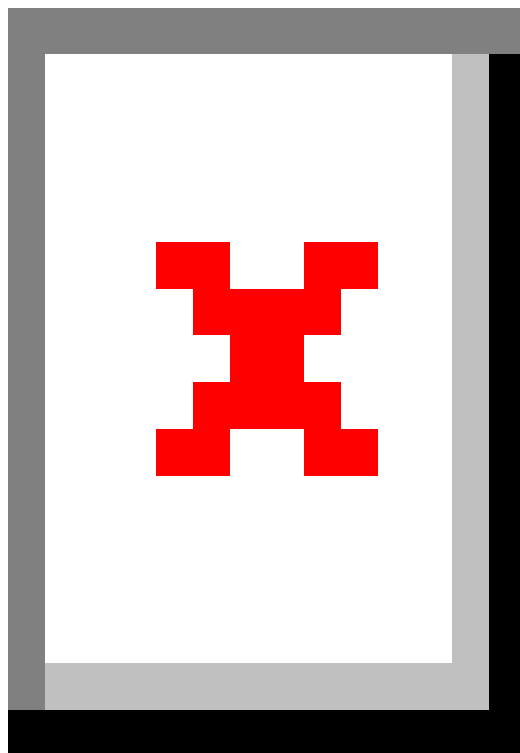


^1H NMR of 4f

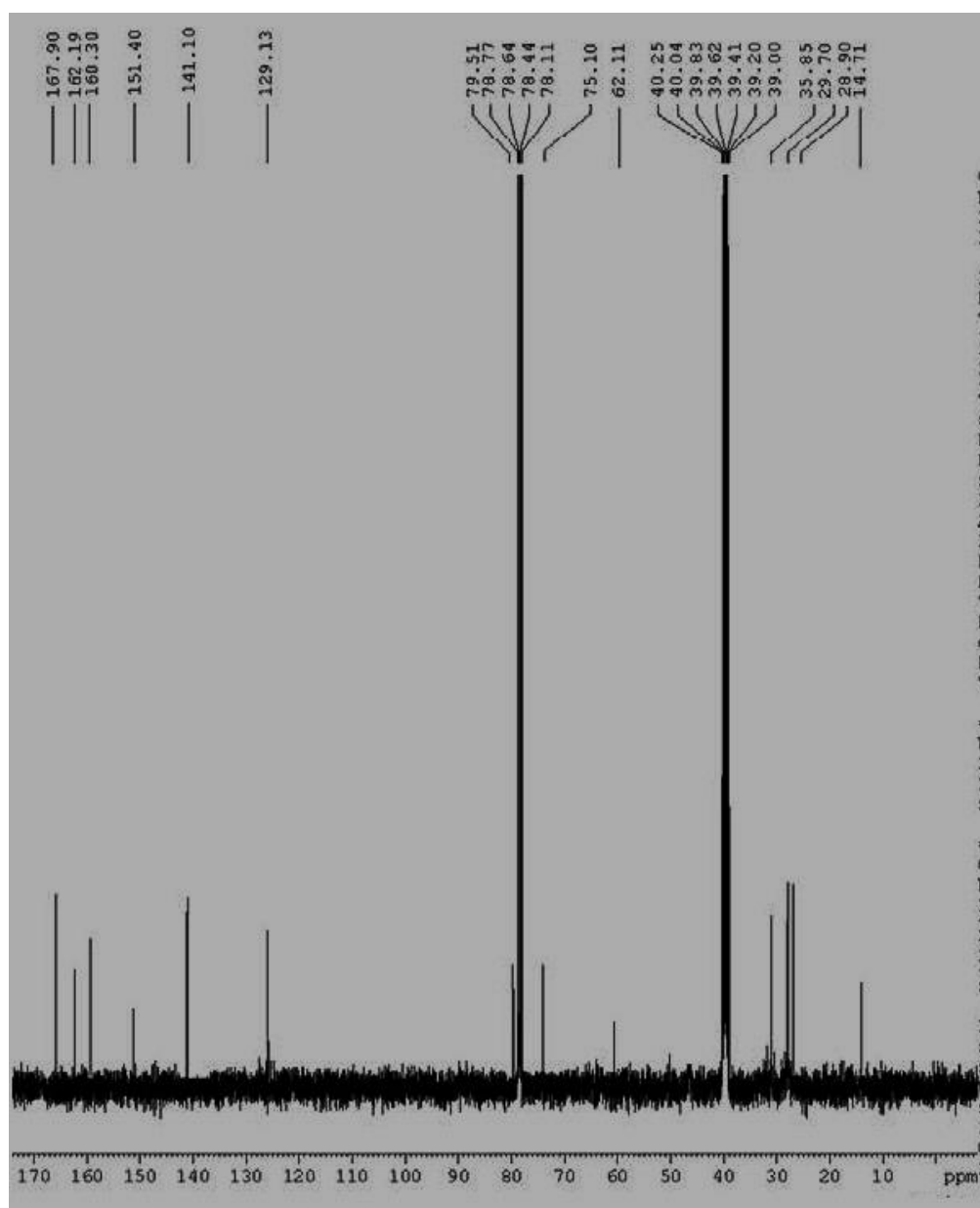




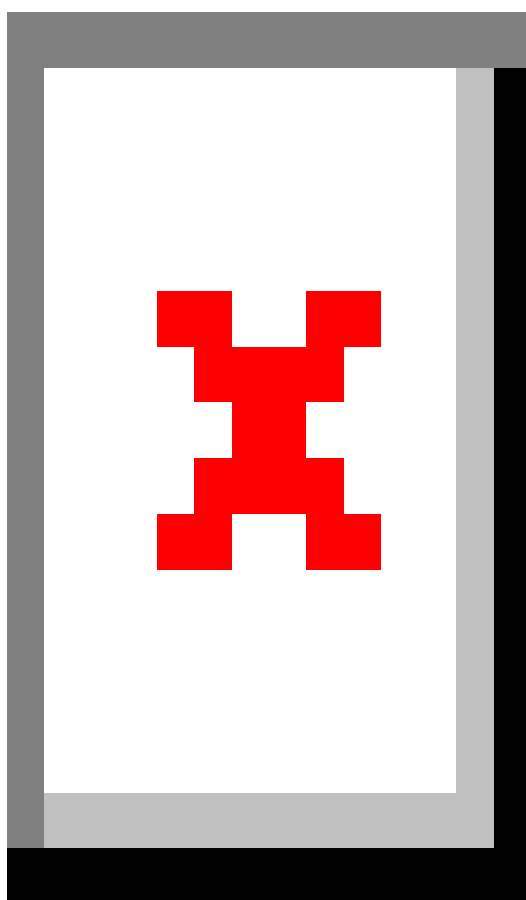
^1H NMR of 4g



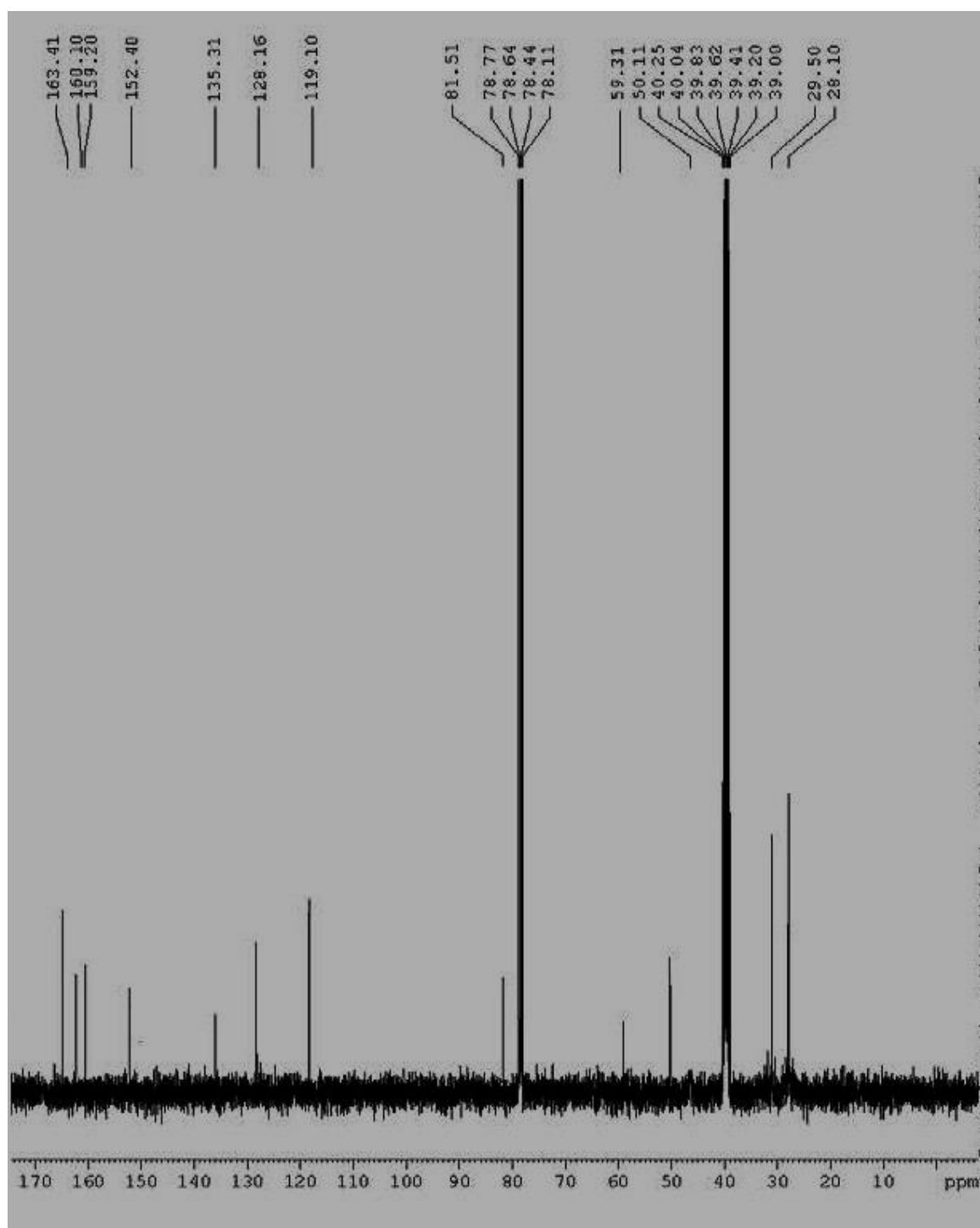
^{13}C NMR of 4g



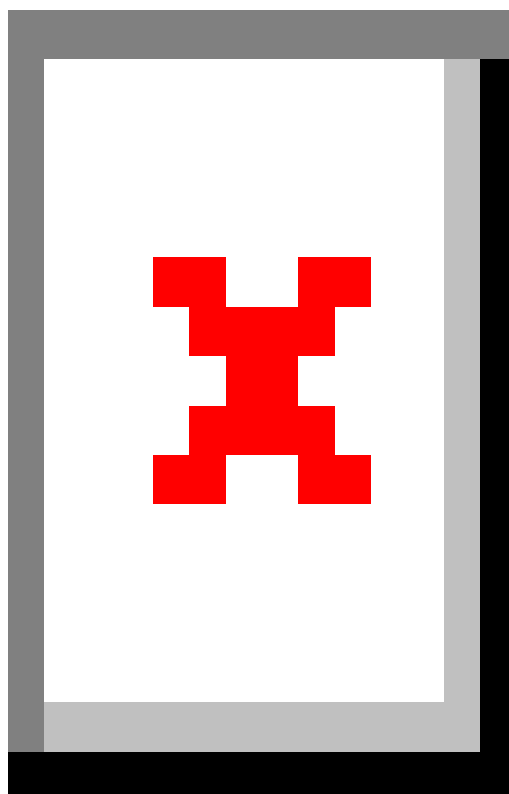
^1H NMR of 4h



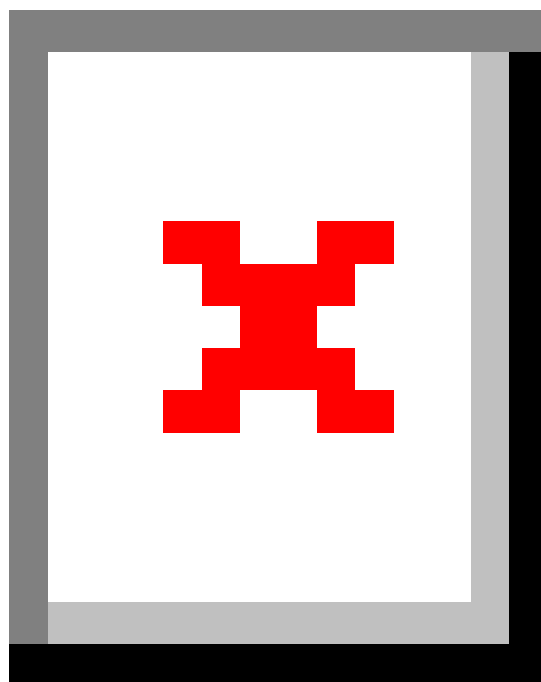
^{13}C NMR of 4h



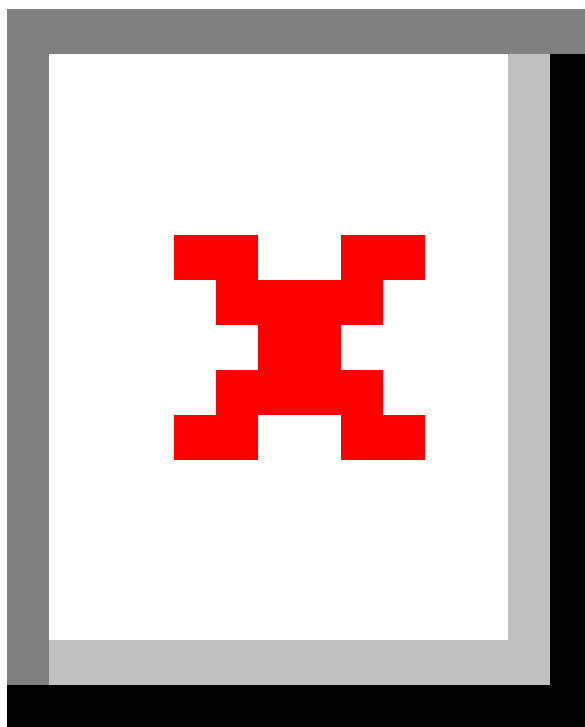
^1H NMR of 4i



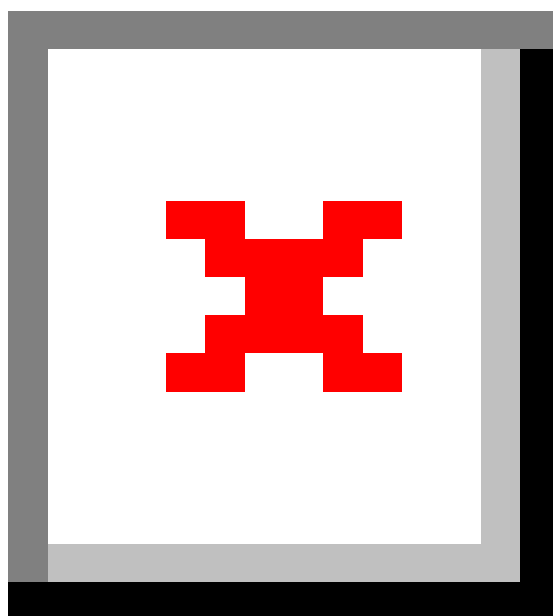
^{13}C NMR of 4i



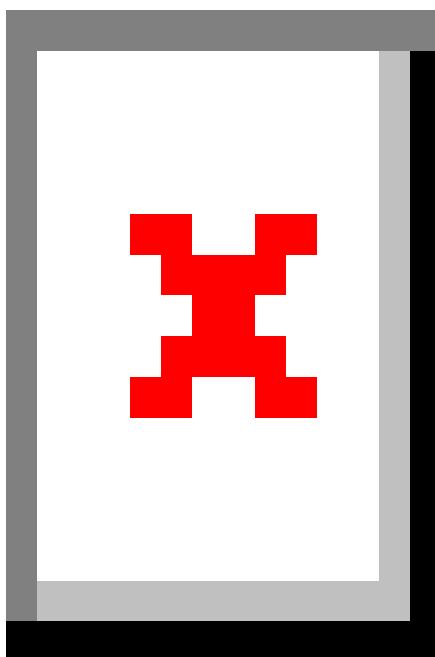
^1H NMR of 4j

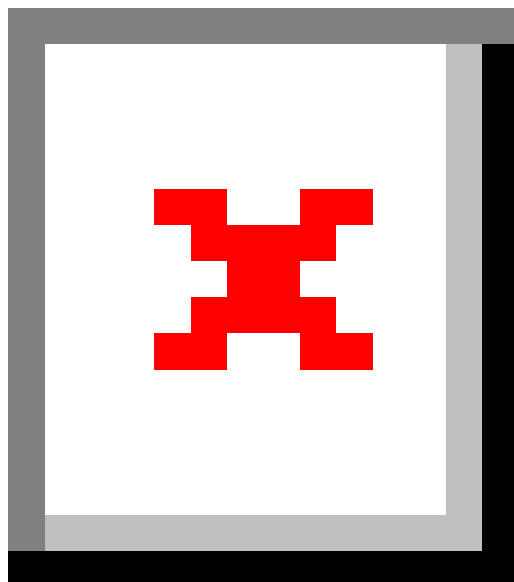


^{13}C NMR of 4j

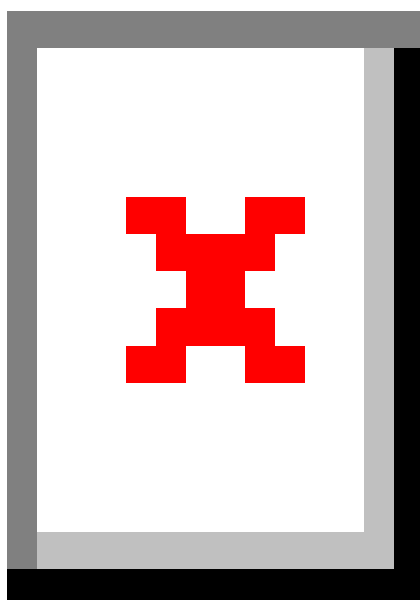


^1H NMR of 4k

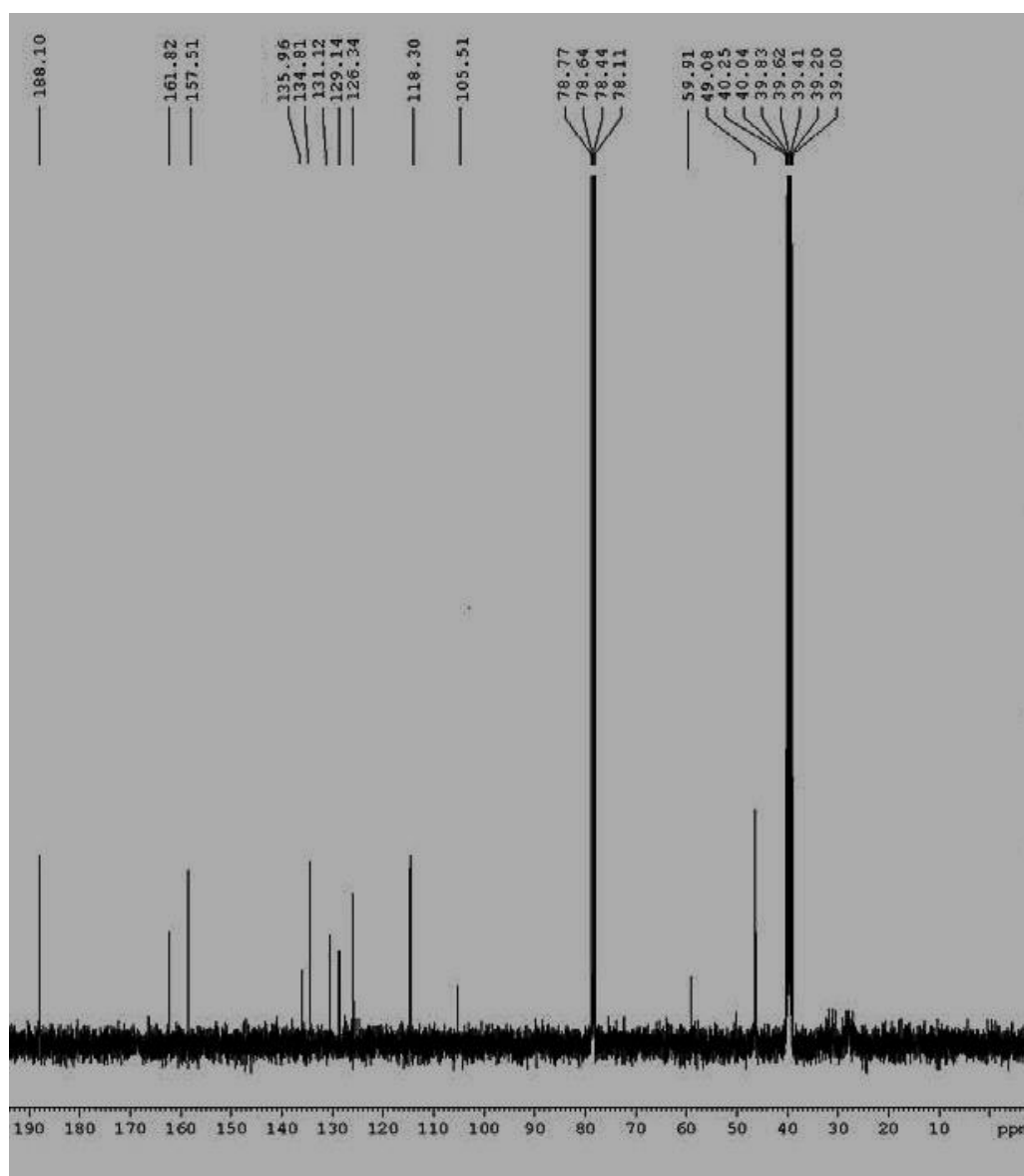




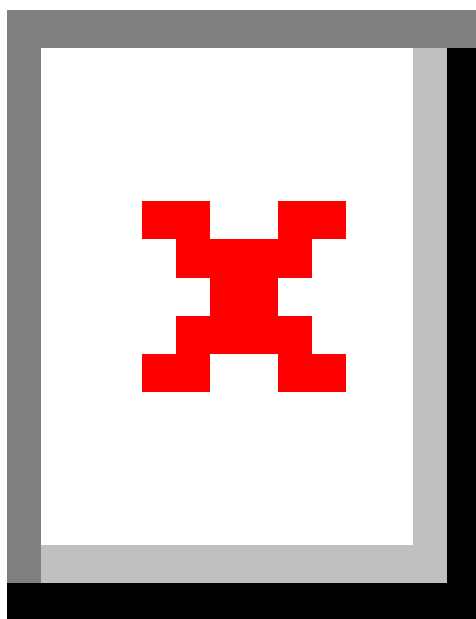
^1H NMR of 4l



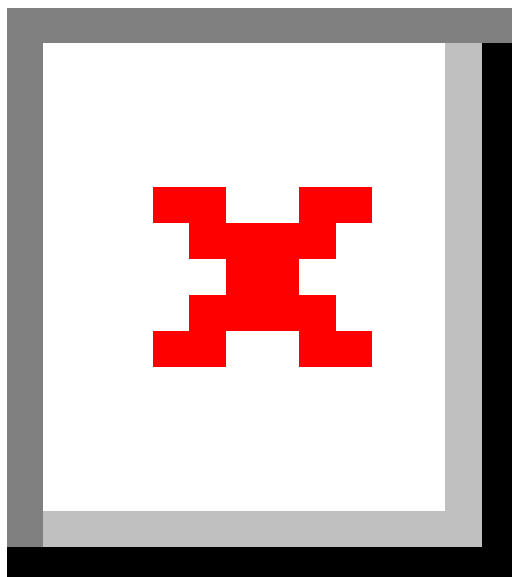
^{13}C NMR of 4l



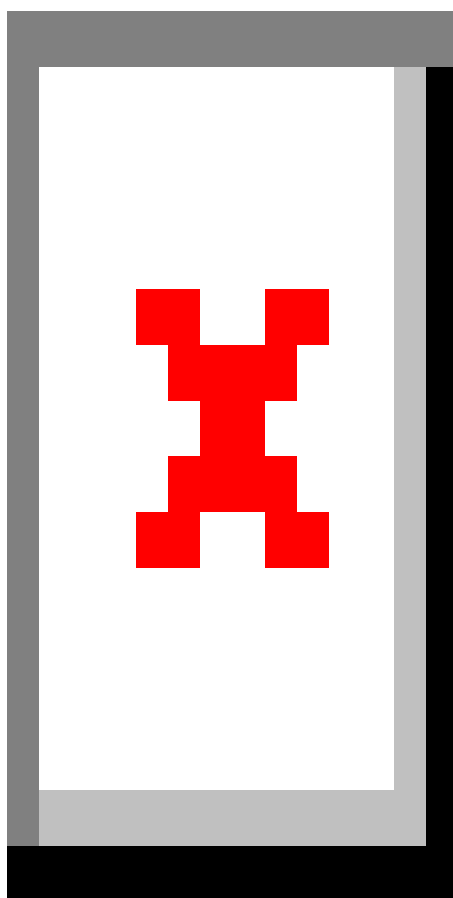
^1H NMR of 4m



^{13}C NMR of 4m



^1H NMR of 4p



^{13}C NMR of 4p

