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Utilizing *o*-quinone methide chemistry: synthesis of sterically hindered acridin-4-ols

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Experimental. Solvents and anilines were purified routinely [S1]. 3,5-Di-*tert*-butyl-6-(methoxymethyl)catechol was prepared according to known procedure [S2]. The CHN elemental analysis was performed using a Vario EL cube analyzer. The NMR spectra were recorded on Bruker AV-200 and Bruker ARX 400, the solvents used are DMSO-d_6 and $CDCl_3$. The IR spectra were obtained using a PerkinElmer 577 spectrometer in the 4000–450 cm^{-1} region in Nujol mull on KBr plates. The UV-vis absorption spectroscopy experiments were performed in a 1 cm quartz cuvette using a PerkinElmer Lambda-25 in a range from 200 to 700 nm; excitation and emission spectra were obtained with PerkinElmer LS-55 in the 200–700 nm range.

3-(2-Amino-5-bromobenzyl)-4,6-di-tert-butylcatechol 3a. 3,5-Di-*tert*-butyl-6-(methoxymethyl)-catechol **2** (2.66 g, 0.01 mol) and *p*-bromoaniline (1.07 g, 0.01 mol) were dissolved in toluene (20 ml). The mixture was brought to boiling, and the solvent was slowly evaporated until still temperature reached 140 °C (24 h). The mixture was then cooled to 60 °C, and hexane (20 ml) was added. White-yellow solid was filtered off, washed with hexane and dried under vacuum. Yield 0.6 g (15%). ^{1}H NMR (200 MHz, DMSO-d_6): 1.22 (s, 9H, *t*-Bu), 1.38 (s, 9H, *t*-Bu), 3.81 (s, 2H, CH_2), 5.22 (s, 2H, OH), 6.25 (d, J = 2.2 Hz, 1H, C_{ar}-H). 6.58 (d, J = 8.4 Hz, 1H, C_{ar}-H), 6.85 (s, 1H, C_{cat}H), 6.95 (dd, J = 8.4 Hz, 2.2 Hz, 1H, C_{ar}-H), 7.82 (s, 2H, NH_2), ^{13}C NMR (50 MHz, DMSO-d_6): 29.06, 29.67, 31.73, 34.53, 35.30, 106.51, 115.07, 115.42, 122.70, 127.38, 128.04, 128.82, 129.11, 133.97, 138.58, 142.13, 145.18. IR (KBr, ν, cm^{-1}): 3476 (s), 3401 (s), 335 (s), 2750-2400 (br w), 1607 (m), 1410 (s), 1337 (w), 1292 (s), 1260 (m), 1211 (m), 1175 (m), 1163 (m), 1061 (m), 1042 (s), 974 (s), 928 (w), 918 (w), 880 (s), 860 (m), 809 (m), 747 (w), 699 (w), 652 (w), 631 (w), 614 (w), 538 (m), 517 (m), 469 (w). Anal. Calcd. (%) for $C_{21}H_{28}BrNO_2$: C, 62.07; H, 6.95; N, 3.45. Found (%) C, 62.57; H, 7.05; N, 3.35.

7-Bromo-1,3-di-tert-butylacridin-4-ol 4a. Compound **3a** (0.20 g, 0.5 mmol) was dissolved in diethyl ether and stirred vigorously for 1 h with a KOH (0.002 mol) solution in H_2O (5 ml). The

mixture was extracted, washed with water and dried over Na_2SO_4. Product **4a** was isolated by column chromatography (*n*-hexane used as eluent) as yellow solid. Yield 0.18 g (95%).

Similar synthesis without isolation of **3a** provides 1.32 g (34%) of **4a**. M.p . 162-163 °C. ^{1}H NMR (200 MHz, $CDCl_3$): 1.57 (s, 9H, *t*-Bu), 1.66 (s, 9H, *t*-Bu), 7.60 (s, 1H, C_{ar}-H), 7.78 (dd, *J*=9.1 Hz, 2.0, 1H, C_{ar}-H), 8.05 (d, *J*=9.1 Hz, 1H, C_{ar}-H), 8.23 (d, *J*=2.0 Hz, 1H, C_{ar}-H), 9.19 (s, 1H, C_{ar}-H), 9.39 (br s, 1H, OH). ^{13}C NMR (50 MHz, $CDCl_3$): 29.55, 32.04, 35.17, 36.16, 119.16, 123.72, 124.28, 126.18, 129.85, 130.36, 133.59, 134.44, 134.83, 141.81, 143.50, 146.98. IR (nujol, ν, cm^{-1}): 3323 (m), 1628 (m), 1609 (w), 1572 (w), 1557 (w), 1513 (m), 1418 (s), 1389 (s), 1363 (s), 1346 (s), 1287 (m), 1273 (m), 1262 (m), 1229 (s), 1205 (s), 1156 (s), 1132 (m), 1094 (m), 1049 (m), 1024 (w), 991 (m), 964 (w), 950 (w), 935 (w), 917 (s), 891 (m), 869 (w), 855 (m), 824 (s), 803 (m), 733 (s), 697 (w), 635 (s), 625 (s), 615 (s), 561 (m), 541 (w), 516 (w), 499 (w), 477 (m). Anal. Calcd. (%) for for $C_{21}H_{24}BrNO$: C, 65.29; H, 6.26; N, 3.63. Found (%) C, 65.35; H, 6.38; N, 3.50.

1,3-Di-tert-butylacridin-4-ol 4b was obtained as described for **4a** from reactant **1** and aniline without isolation of **3b**. M.p. 84-85°C. Yield 0.6 g (15%). ^{1}H NMR (400 MHz, $CDCl_3$): 1.59 (s, 9H, *t*-Bu), 1.69 (s, 9H, *t*-Bu), 7.50-7.60 (m, 1H, C_{ar}-H), 7.61 (s, 1H, C_{ar}-H), 7.74-7.84 (m, 1H, C_{ar}-H), 8.05 (d, *J*=9.1 Hz, 1H, C_{ar}-H), 8.16-8.32 (br s, 1H, C_{ar}-H), 9.34 (s, 1H, C_{ar}-H), 9.38-9.94 (br s, 1H, OH). ^{1}H NMR (400 MHz, DMSO-d_6): 1.51 (s, 9H, *t*-Bu), 1.62 (s, 9H, *t*-Bu), 7.50 (s, 1H, C_{ar}-H), 7.56-7.63 (m, 1H, C_{ar}-H), 7.81-7.87 (m, 1H, C_{ar}-H), 8.16 (d, *J*=8.7 Hz, 1H, C_{ar}-H), 8.37 (d, *J*=8.3, 1H, C_{ar}-H), 9.52 (s, 1H, C_{ar}-H), 9.71 (s, 1H, OH). ^{13}C NMR (100 MHz, DMSO-d_6): 29.79, 32.14, 35.11, 36.28, 123.12, 123.26, 125.73, 126.05, 127.57, 128.15, 129.80, 131.10, 135.08, 135.93, 141.58, 145.40, 147.34. IR (nujol, ν, cm^{-1}): 3296 (m), 3261 (m), 1634 (m), 1623 (w), 1563 (w), 1522 (s), 1431 (s), 1412 (s), 1397 (m), 1366 (s), 1299 (m), 1267 (w), 1233 (s), 1198 (m), 1179 (m), 1161 (m), 1131 (m), 1052 (w), 1026 (w), 1009 (m), 991 (m), 952 (w), 916 (s), 885 (m), 852 (m), 814 (w), 808 (w), 762 (s), 748 (s), 731 (s), 683 (w), 656 (s), 627 (m), 609 (w), 574 (m), 549 (w), 523 (w), 492 (w), 470 (m). Anal. Calcd. (%) for $C_{21}H_{25}NO$: C, 82.04; H, 8.20; N, 4.56. Found (%) C, 82.20; H, 8.35; N, 4.40.

1,3-Di-tert-butyl-7-methylacridin-4-ol 4c was obtained as described for **4a** from reactant **1** and *p*-toluidine without isolation of **3c**. M.p . 132-133°C. Yield 0.64 g (20%). ^{1}H NMR (400 MHz, $CDCl_3$): 1.63 (s, 9H, *t*-Bu), 1.71 (s, 9H, *t*-Bu), 2.58 (s, 3H, CH_3), 7.50-7.65 (m, 2H, C_{ar}-H), 7.80 (s, 1H, C_{ar}-H), 8.08 (d, *J*=8.3, 1H, C_{ar}-H), 9.21 (s, 1H, C_{ar}-H), 9.2-9.9 (br s, 1H, OH). ^{13}C NMR (100 MHz, $CDCl_3$): 21.73, 29.64, 32.05, 35.06, 36.15, 123.30, 123.49, 125.51, 126.80, 127.32, 127.82, 132.96, 134.44, 134.59, 135.12, 141.18,144.15, 146.94. IR (nujol, ν, cm^{-1}): 3266 (m), 1639 (m), 1520 (s), 1396 (s), 1369 (s), 1352 (s), 1318 (w), 1290 (m), 1266 (m), 1227 (s), 1195 (w), 1177 (w), 1165 (m), 1140 (m), 1096 (m), 1037 (m), 1029 (m), 994 (m), 952 (w), 920 (s), 902 (m), 885 (m), 859 (w), 819 (s), 801 (m), 735 (s), 672 (m), 645 (s), 633 (m), 621 (m), 563 (m), 519 (w), 505 (w), 478 (m), 466 (w). Anal. Calcd. (%) for $C_{22}H_{27}NO$: C, 82.20; H, 8.47; N, 4.36. Found (%) C, 82.25; H, 8.50; N, 4.38.

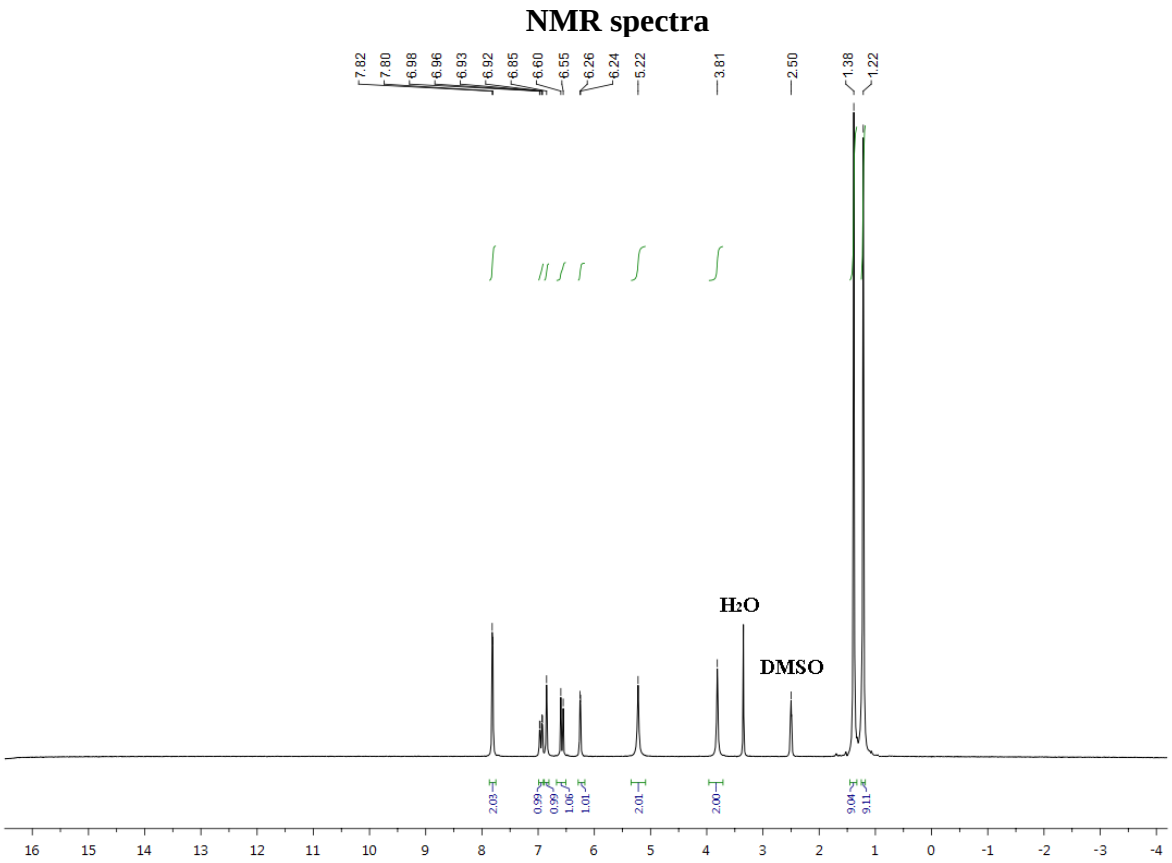

Figure S1. ^{1}H NMR spectrum of **3a** in DMSO-d_6.

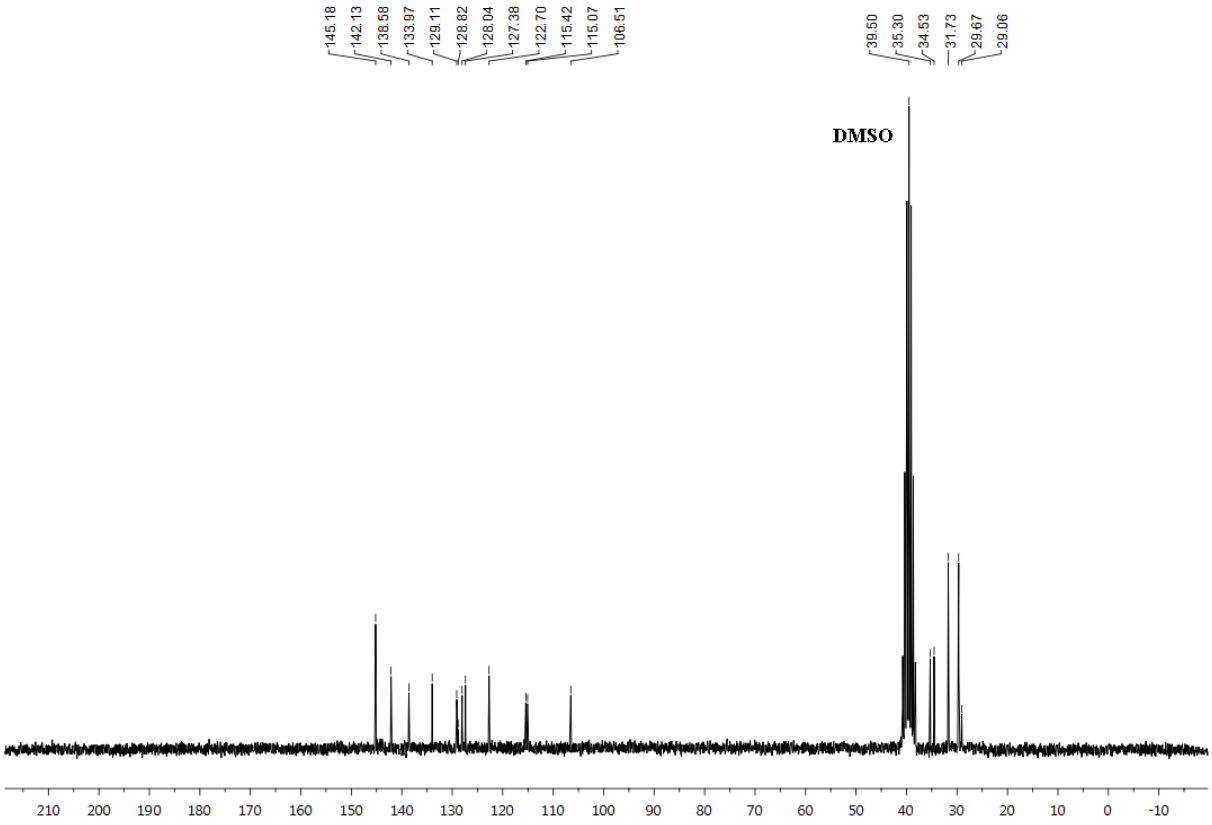

Figure S2. ^{13}C NMR spectrum of **3a** in DMSO-d_6.

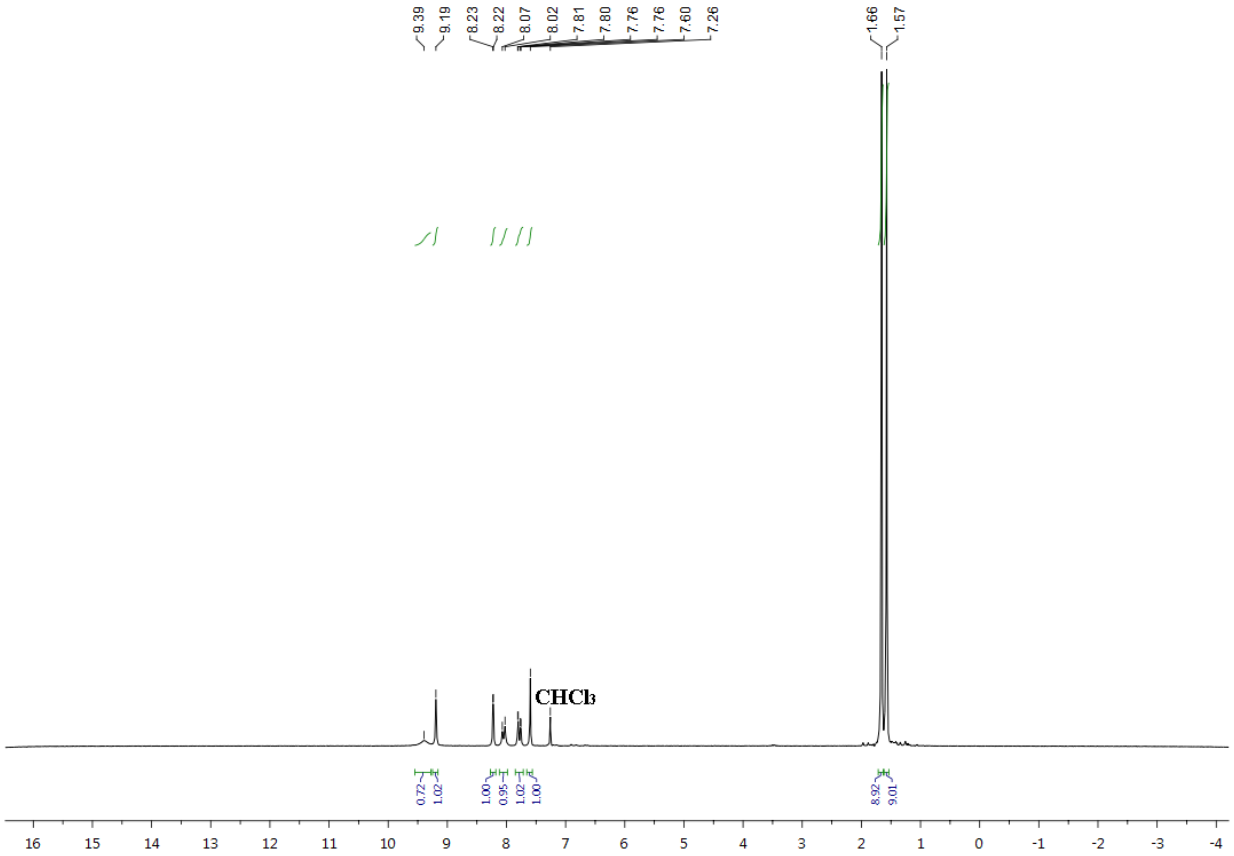

Figure S3. ^{1}H NMR spectrum of **4a** in $CDCl_3$.

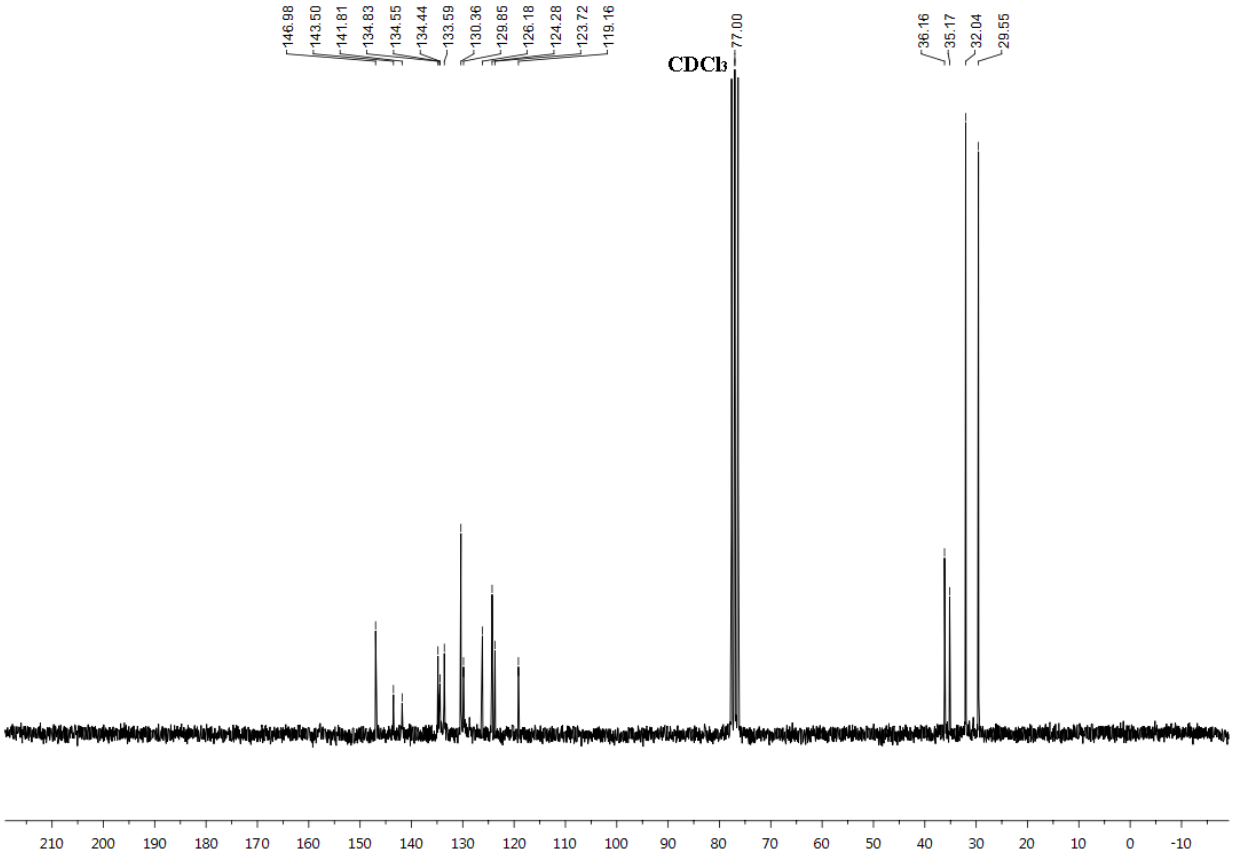

Figure S4. ^{13}C NMR spectrum of **4a** in $CDCl_3$.

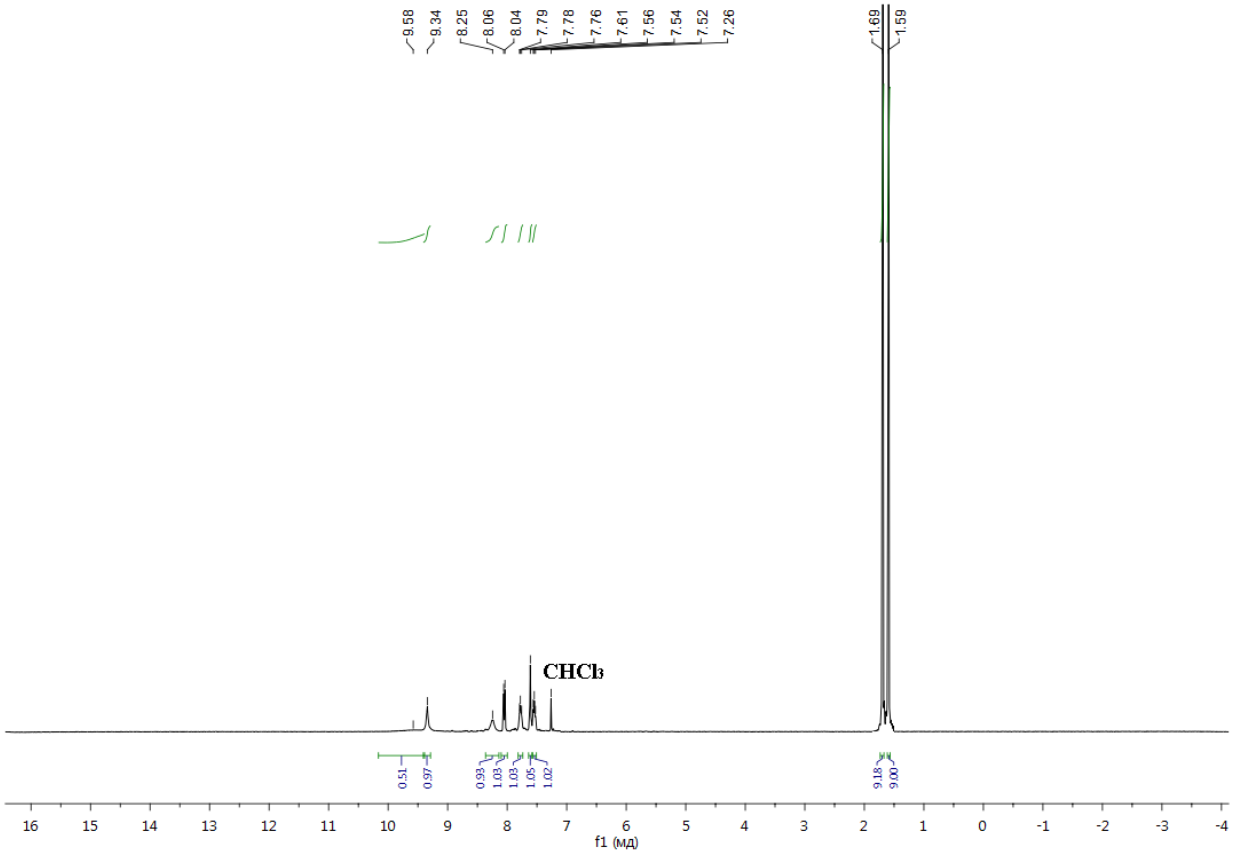

Figure S5. ^{1}H NMR spectrum of **4b** in $CDCl_3$.

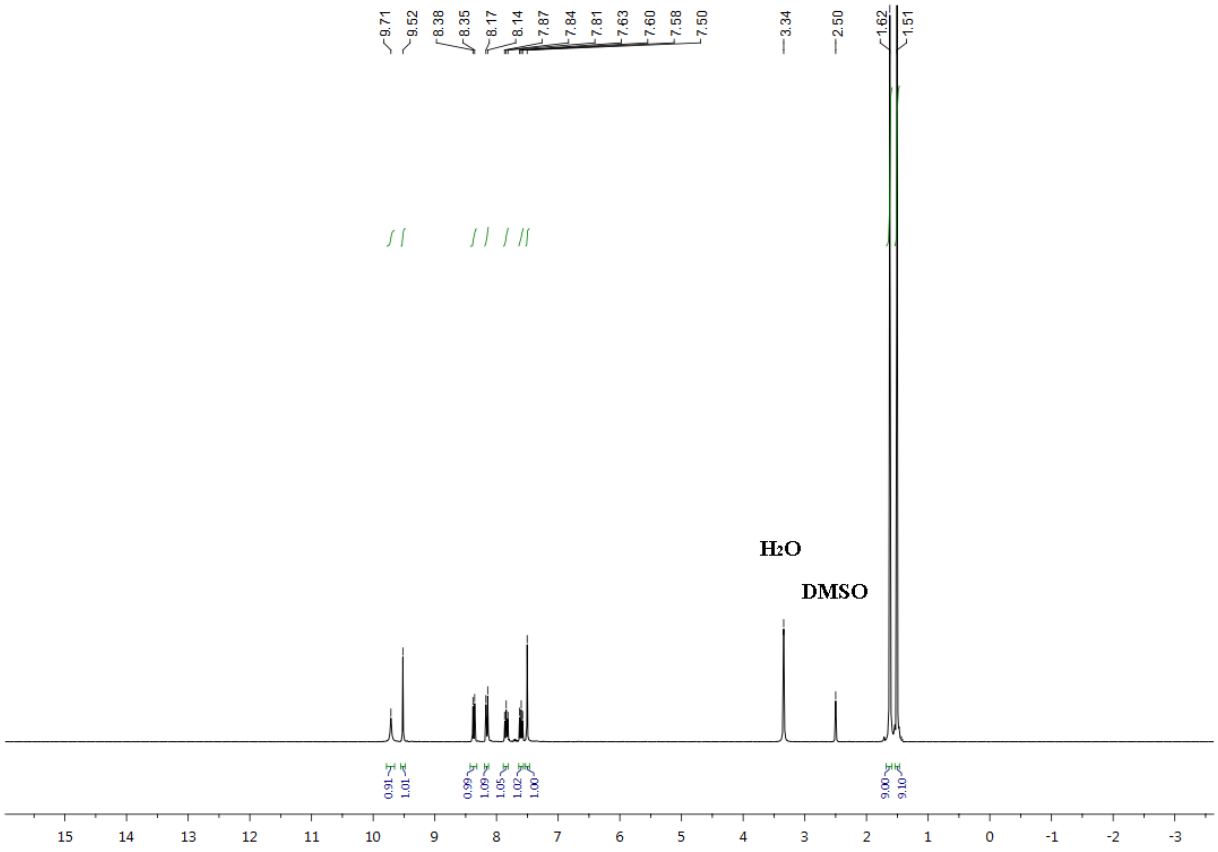

Figure S6. ^{1}H NMR spectrum of **4b** in DMSO-d_6.

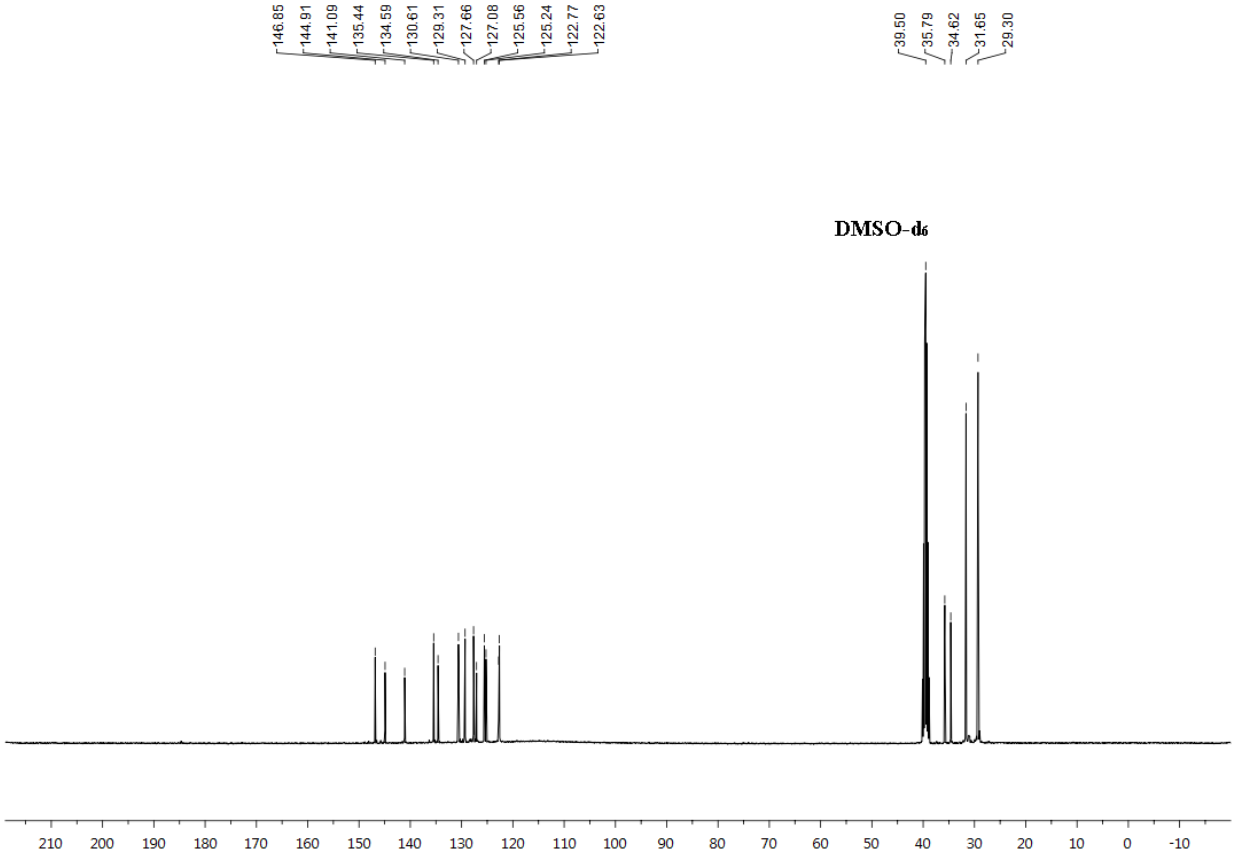

Figure S7. ^{13}C NMR spectrum of **4b** in DMSO-d_6.

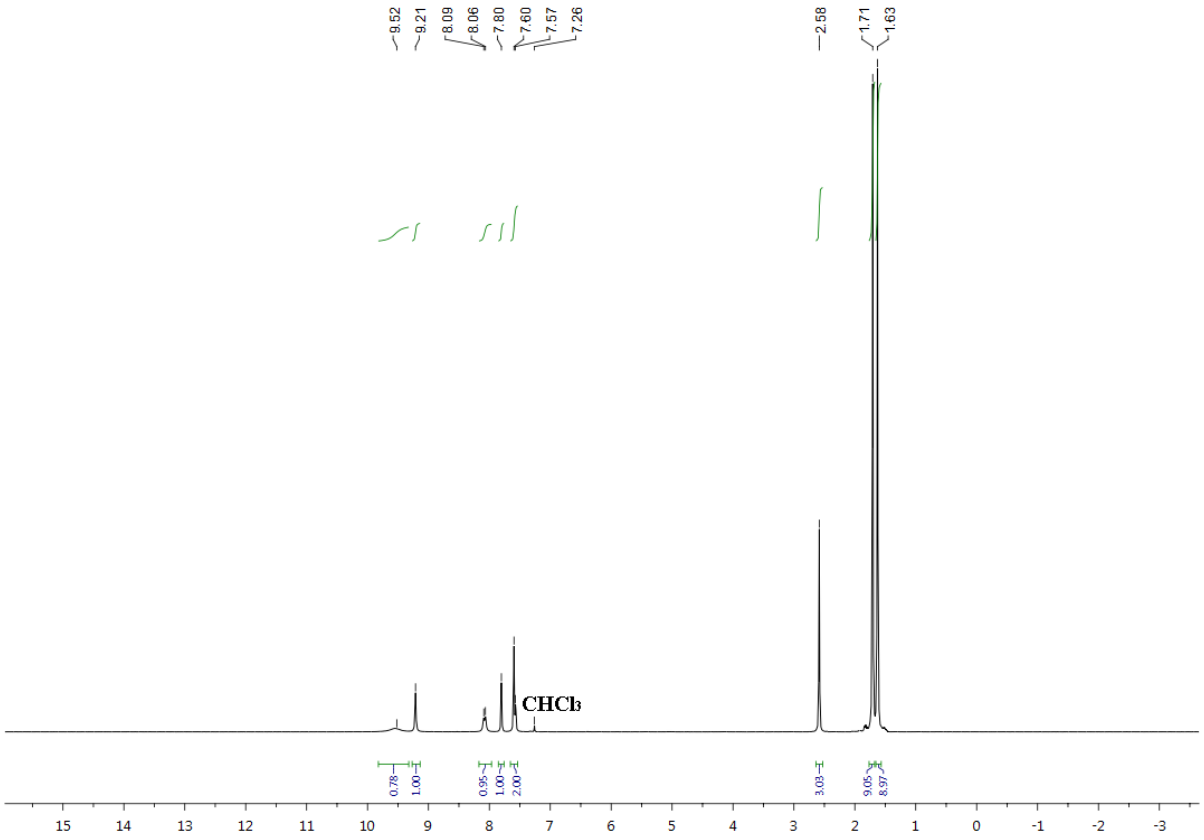

Figure S8. ^{1}H NMR spectrum of **4c** in $CDCl_3$.

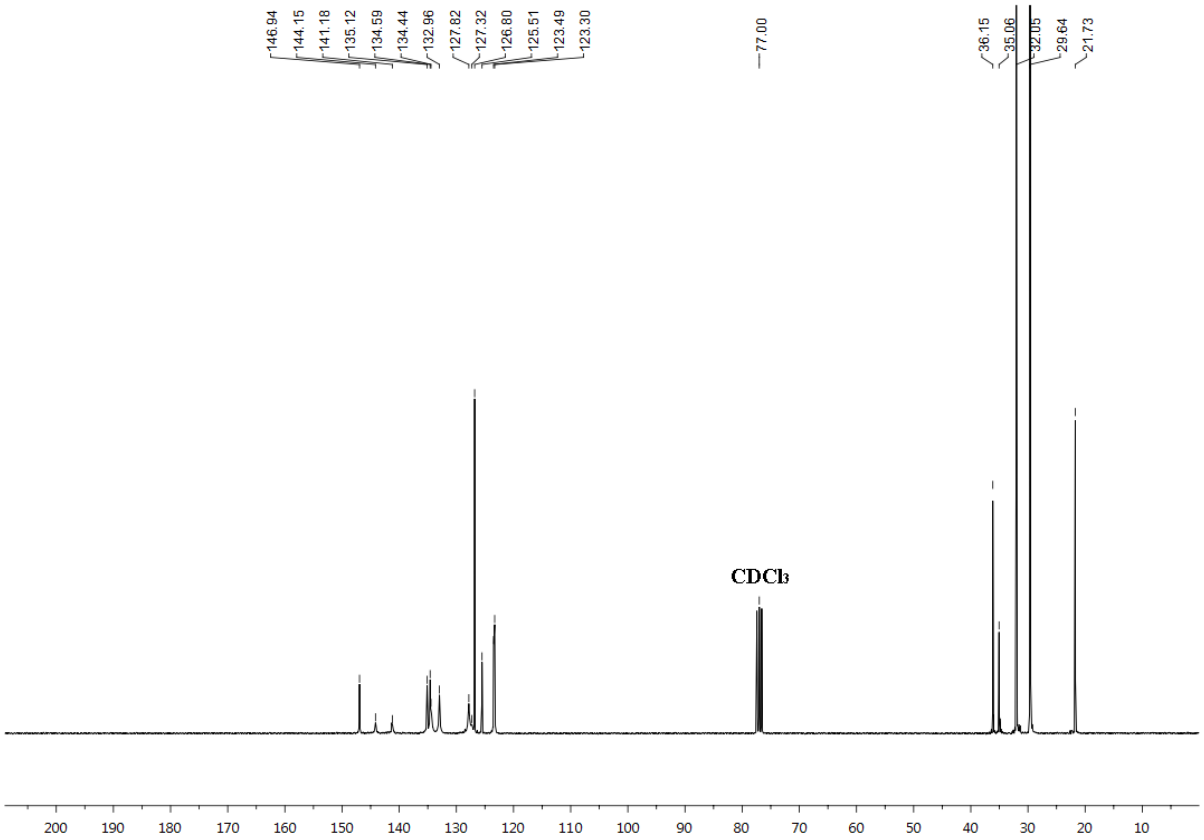

Figure S9. ^{13}C NMR spectrum of **4c** in $CDCl_3$.

X-Ray analysis

Table S1. The selected bond lengths (Å) and angles (°) in **4a** and **4c**.

Bond, Å	**4a**	**4c**	Angle, °	**4a**	**4c**
O(1)-C(1)	1.363(2)	1.372(3)	C(1)-O(1)-H(1)	106.4(15)	99(3)
N(1)-C(2)	1.346(2)	1.345(3)	O(1)-C(1)-C(2)	116.42(10)	115.2(2)
C(1)-C(2)	1.430(2)	1.441(3)	N(1)-C(2)-C(1)	114.48(11)	114.4(2)
O(1)-H(1)	0.83(2)	0.93(4)	C(3)-N(1)-C(2)	118.69(11)	118.2(2)
N(1)···H(1)	2.06(2)	1.91(4)	O(1)-H(1)···N(1)	121.3(19)	128(3)
C_{Ar}-Br	1.898(2)	-			
C_{Ar}-C_{Me}	-	1.506(4)			

References

[S1]. W. L. F. Armarego and C. L. L. Chai, *Purification of Laboratory Chemicals*. Elsevier, Butterworth-Heinemann, Amsterdam, 2003.

[S2]. M. V. Arsenyev, E. V. Baranov, M. P. Shurygina, S. A. Chesnokov and G. A. Abakumov, *Mendeleev Commun.*, 2016, **26**, 552.