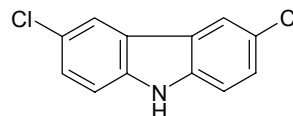


1,8-Diamino-3,6-dichlorocarbazole – a promising building block for anion receptors

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3,6-Dichlorocarbazole (7)



To a 3-neck, 500 mL round-bottomed flask, carbazole (20 g, 0.12 mol) and CH_2Cl_2 (200 mL) were added and the flask was equipped with a septum, a mechanical stirrer and a thermometer. The suspension was cooled to 0°C . While vigorous stirring, SO_2Cl_2 (19.2 mL, 0.24 mol) was added dropwise at such rate, that the temperature did not exceed 2°C . Following the addition, the cooling bath was removed and the reaction mixture was stirred for another 4 h at RT. After this time, the solid precipitate was filtered off, washed with CH_2Cl_2 and dried to give 17.668 g of raw 3,6-dichlorocarbazole contaminated with traces of 3-chlorocarbazole. 3-Chlorocarbazole seemed to be more soluble in hexane than the major product, so the raw 3,6-dichlorocarbazole was suspended in 0.5 L of hexane and boiled for 0.5 h. The suspension was filtered, giving pure product (17.130 g, 60.6%); **m.p.** $205\text{--}208^\circ\text{C}$ (lit.⁸ 198°C);

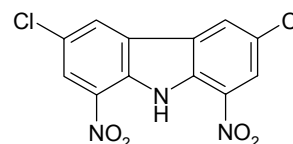
^1H NMR (DMSO-d_6) δ_{DMSO} : 11.58 (s, 1H, NH), 8.28 (d, 2H, $J_1 = 2.0\text{Hz}$, aromatic H-4 and H-5), 7.52 (d, 2H, $J_1 = 8.6\text{Hz}$, aromatic H-1 and H-8), 7.42 (dd, 2H, $J_1 = 8.6\text{Hz}$, $J_2 = 2.0\text{Hz}$, aromatic H-2 and H-7);

^{13}C NMR (DMSO-d_6) δ_{DMSO} : 138.7 (4°), 126.1 (3°), 123.2 (4°), 122.8 (4°), 120.2 (3°), 112.7 (3°);

HR MS (EI): m/z calcd. for $\text{C}_{12}\text{H}_7\text{NCl}_2$ $[\text{M}]^{+}$: 234.9956, found: 234.9961;

Elemental Analysis calcd. for $\text{C}_{12}\text{H}_7\text{NCl}_2$: C, 61.05; H, 2.99; N, 5.93; Cl, 30.03; found: C, 61.10; H, 2.80; N, 5.92; Cl, 29.95.

3,6-Dichloro-1,8-dinitrocarbazole (8)



To a 3-neck, 500 mL round-bottomed flask, 3,6-dichlorocarbazole (28.32 g, 0.12 mol), acetic acid (96 mL) and acetic anhydride (72 mL) were added. Afterwards, the flask was equipped with a dropping funnel, a mechanical stirrer and a thermometer. The solution was then cooled to 1°C and 100% HNO_3 (14.4 mL, 0.35 mol) began to be added dropwise while the solution was being stirred and the temperature was being kept low. After the addition of 1/8 of the whole volume of HNO_3 , the cooling bath was replaced with an oil bath. The mixture was heated to 60°C and kept at this

temperature until half of HNO_3 was added. During the addition of the remaining HNO_3 , the reaction mixture was further heated, until it reached 75°C . When the addition was completed, temperature of the mixture was elevated to 110°C for next ten minutes. Afterwards, the suspension was filtered while hot and the product was washed with boiling acetic acid (30 mL) and diethyl ether. 28.73 g (73.4%); **m.p.** $284\text{--}288^\circ\text{C}$ (lit.⁸ m.p. $285\text{--}286^\circ\text{C}$);

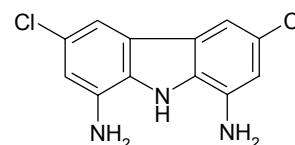
^1H NMR (DMSO-d_6) δ_{DMSO} : 11.24 (bs, 1H, NH), 8.93 (d, 2H, $J_1 = 2.0\text{Hz}$, aromatic H-4 and H-5), 8.44 (d, 2H, $J_1 = 2.0\text{Hz}$, aromatic H-2 and H-7);

^{13}C NMR: low solubility of the compound made it impossible to obtain ^{13}C NMR spectrum;

HR MS (EI): m/z calcd. for $\text{C}_{12}\text{H}_5\text{N}_3\text{O}_4\text{Cl}_2$ $[\text{M}]^{++}$: 324.9657, found: 324.9673;

Elemental Analysis calcd. for $\text{C}_{12}\text{H}_5\text{N}_3\text{O}_4\text{Cl}_2$: C, 44.20; H, 1.55; N, 12.89; found: C, 44.40; H, 1.58; N, 12.74.

1,8-Diamino-3,6-dichlorocarbazole (9)



To a 250 mL round-bottomed flask equipped with a magnetic stirrer, 3,6-dichloro-1,8-dinitrocarbazole (2.00 g, 6.13 mmol) was added.

The flask was purged with argon and 5% Pd/C (200 mg) and CH_3CN (100 mL) were added. Then the flask was flushed with hydrogen and the reduction was stirred under hydrogen atmosphere overnight. The next day, the catalyst was filtered off and the solvent was evaporated. The solid residue was purified by flash chromatography (gradient elution with $\text{CH}_2\text{Cl}_2 - \text{CH}_3\text{OH}$ from 99:1 to 49:1) to yield a gray powder (1.452 g, 89.0%); **m.p.** decomposition at 300°C (lit.⁸ decomposition at 205°C);

^1H NMR (DMSO-d_6) δ_{DMSO} : 10.66 (s, 1H, NH), 7.34 (d, 2H, $J_1 = 2.0\text{Hz}$, aromatic H-4 and H-5), 6.65 (d, 2H, $J_1 = 2.0\text{Hz}$, aromatic H-2 and H-7), 5.34 (bs, 4H, NH_2);

^{13}C NMR (DMSO-d_6) δ_{DMSO} : 135.1 (4°), 127.5 (4°), 123.9 (4°), 123.3 (4°), 108.9 (3°), 108.0 (3°);

HR MS (ESI): m/z calcd. for $\text{C}_{12}\text{H}_{10}\text{N}_3\text{Cl}_2$ $[\text{M}+\text{H}]^+$: 266.0246, found: 266.0261;

Elemental Analysis calcd. for $\text{C}_{12}\text{H}_9\text{N}_3\text{Cl}_2$: C, 54.16; H, 3.41; N, 15.79; found: C, 54.08; H, 3.47; N, 15.70.

General Procedure for Preparation of the Ligands

To a 100 mL round-bottomed flask equipped with a magnetic stirrer, 1,8-diamino-3,6-dichlorocarbazole **9** (532 mg, 2.00 mmol) was added. The flask was closed with a septum and purged with argon. Afterwards, freshly dried CH₃CN (50 mL) and triethylamine (0.67 mL, 4.8 mmol) were added from a syringe. After cooling the reaction mixture to -30°C, an appropriate acid chloride (4.8 mmol) was slowly added dropwise. Then the suspension was allowed to achieve room temperature and stirred overnight.

1,8-Di(benzoylamino)-3,6-dichlorocarbazole (**5**)

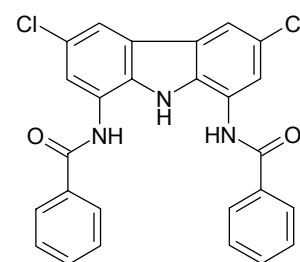
As an acyl reagent, benzoyl chloride (0.557 mL, 4.80 mmol) was used. When the reaction was finished, the precipitated product was filtered off (0.80 g), and purified by crystallization from acetic acid (400 mL) to obtain 0.653 g of white powder (68.8%); **m.p.** decomposition at 350°C;

¹H NMR (DMSO-*d*₆) δ_{DMSO} : 10.93 (s, 1H, carbazole NH), 10.48 (s, 2H, NH), 8.23 (d, 2H, $J_1 = 2.0\text{ Hz}$, aromatic H-4 and H-5), 8.03 (dd, 4H, $J_1 = 7.8\text{ Hz}$, $J_2 = 1.7\text{ Hz}$, *ortho*-H of the phenyl ring), 7.86 (d, 2H, d, $J_1 = 2.0\text{ Hz}$, aromatic H-2 and H-7), 7.7-7.5 (m, 6H, *meta*-H and *para*-H of the phenyl ring);

¹³C NMR (DMSO-*d*₆) δ_{DMSO} : 166.0 (4°), 134.3 (4°), 132.0 (3°), 131.9 (4°), 128.5 (3°), 128.0 (3°), 124.22 (4°), 124.16 (4°), 123.3 (4°), 120.6 (3°), 117.0 (3°);

HR MS (ESI): *m/z* calcd. for C₂₆H₁₇N₃O₂NaCl₂ [M+Na]⁺: 496.0590, found: 496.0615.

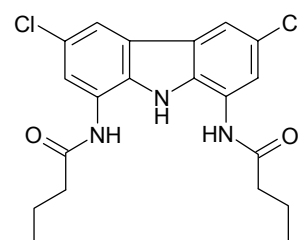
Elemental Analysis calcd. for C₂₆H₁₇N₃O₂Cl₂: C, 65.84; H, 3.61; N, 8.86; found: C, 66.10; H, 3.72; N, 8.96.



1,8-Di(butyrylamino)-3,6-dichlorocarbazole (**6**)

As an acyl reagent, butanoic acid chloride (0.50 mL, 4.8 mmol) was used. When the reaction was finished, the precipitated product was filtered off (0.61 g), and purified by crystallization from acetic acid (600 mL) to obtain 0.485 g of white powder (59.7%); **m.p.** >350°C;

¹H NMR (DMSO-*d*₆) δ_{DMSO} : 10.57 (s, 1H, carbazole NH), 10.13 (s, 2H, NH), 8.10 (d, 2H, $J_1 = 1.6\text{ Hz}$, aromatic H-4 and H-5), 7.74 (d, 2H, $J_1 = 1.6\text{ Hz}$, aromatic H-2 and H-7), 2.46 (t, 4H, $J_1 = 7.2\text{ Hz}$, CH₂CH₂CO), 1.71 (m, 4H, CH₂CH₂CO), 0.99 (t, 6H, $J_1 = 7.2\text{ Hz}$, CH₃);



^{13}C NMR (DMSO- d_6) δ_{DMSO} : 171.6 (4°), 130.7 (4°), 124.3 (4°), 124.0 (4°), 123.3 (4°), 118.8 (3°), 116.2 (3°), 37.9 (2°), 18.5 (2°), 13.6 (1°);

HR MS (ESI): m/z calcd. for $\text{C}_{20}\text{H}_{21}\text{N}_3\text{O}_2\text{NaCl}_2$ $[\text{M}+\text{Na}]^+$: 428.0903, found: 428.0927;

Elemental Analysis calcd. for $\text{C}_{20}\text{H}_{21}\text{N}_3\text{O}_2\text{Cl}_2$: C, 59.12; H, 5.21; N, 10.34; found: C, 59.08; H, 5.24; N, 10.30.

Titration experiments:

All salts and ligands were dried at 60°C under high vacuum. Initial water content of DMSO-d₆ (99.9% isotopic purity, purchased from ARMAR AG) was measured by the Fisher method, and then the calculated amount of H₂O was added to obtain 0.5% water concentration in DMSO-d₆.

0.40 - 0.50 ml of 1.2 –17 mM solution of a ligand was titrated in NMR tube with aliquots (10 – 50 µl) of a solution of the respective tetrabutylammonium salt (12-164 mM) in the ligand solution (to prevent diluting of the ligand). 11-13 data points were recorded. The association constants were calculated from changes in chemical shifts in the amide and carbazole protons of the ligands. Nonlinear curve fit for simple 1:1 binding model was carried out using the Origin software. Association constants K and asymptotic change in chemical shift $\Delta\delta_{\max}$ were set as free parameters for fitting. The following equation was applied:

$$\Delta\delta = \frac{\Delta\delta_{\max} \left(L + LX + \frac{1}{K} - \sqrt{\left(L + LX + \frac{1}{K} \right)^2 - 4LLX} \right)}{2L}$$

where:

$\Delta\delta$ – chemical shift change at given point (ppm),

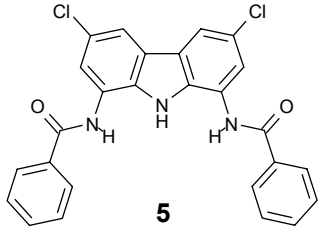
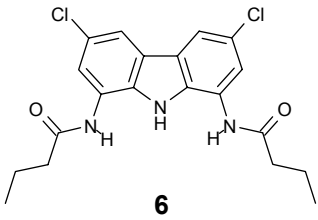
$\Delta\delta_{\max}$ – asymptotic, maximum change in chemical shift (parameter, ppm),

X – number of anion equivalents added to the NMR tube,

L – initial concentration of the ligand solution (mol·dm⁻³),

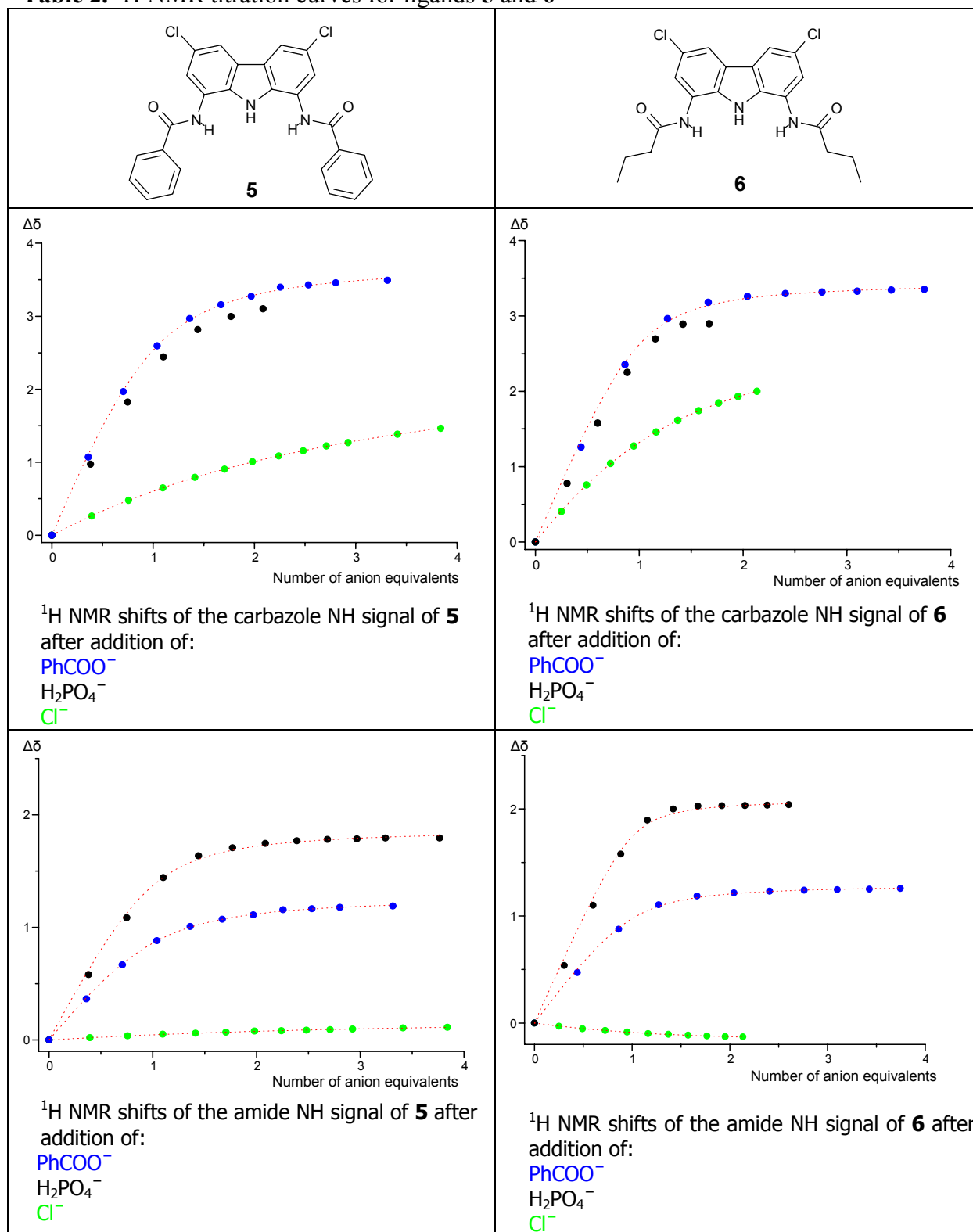
K – association constant (parameter, mol⁻¹·dm³).

Table 1. Concentrations of solutions used in the titration experiments and the results of data fitting.

Anion	 5				 6			
	L [mol·dm ⁻³]	A [mol·dm ⁻³]	K [M ⁻¹]	Δδ _{max} [ppm]	L [mol·dm ⁻³]	A [mol·dm ⁻³]	K [M ⁻¹]	Δδ _{max} [ppm]
Cl ⁻	0.03004	0.30755	13.1±0.2 12.9±0.9	2.60 (NH _{carb.}) 0.20 (NH _{amde})	0.01499	0.1919	100±2 131±13	2.92 (NH _{carb.}) -0.18 (NH _{amde})
PhCOO ⁻	0.005176	0.095096	1241±64 1218±61	3.75 (NH _{carb.}) 1.28 (NH _{amde})	0.001499	0.03369	8544±1037 8138±930	3.46 (NH _{carb.}) 1.30 (NH _{amde})
H ₂ PO ₄ ⁻	0.005176	0.1007	^a 1908±225	≈3.7 (NH _{carb.}) 1.88 (NH _{amde})	0.001499	0.02342	^a 19800±6234	≈3 (NH _{carb.}) 2.09 (NH _{amde})

^a The signal disappears during titration.

Table 2. ^1H NMR titration curves for ligands **5** and **6**



*Crystal data for (5)₂×(TBACl)₂×(C₂H₅)₂O: C₈₈H₁₁₆Cl₆N₈O₅, M = 1578.59 triclinic, *P*-1, *a* = 12.783(3), *b* = 16.815(3), *c* = 20.440(4) Å, α = 91.31(3)°, β = 104.04(3)°, γ = 95.84(3)°, *V* = 4234.9(15) Å³, *T* = 110(2) K, *Z* = 2, μ(Mo–K_α) = 0.258 mm⁻¹, 60713 reflections measured, 14861 unique (*R*_{int} = 0.0474) which were used in all calculations. The final *R*1(*F*²) = 0.0597 and *wR*(*F*²) = 0.1616 [*I* > 2σ]. All non-hydrogen atoms were refined anisotropically. All hydrogen atoms, except those connected to disordered atoms, were found from a difference density map and refined without any constraints.*

The X-ray measurements were undertaken in the Crystallographic Unit of the Physical Chemistry Lab. at the Chemistry Department of the University of Warsaw.

Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 234806. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].