Preparation and Characterization of New Amino-Substituted Crowns and Podands

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A number of macrocyclic (**1b–3b**) and linear oligoether compounds (**4b–8b**) with 2,2′-methylenebis(4-aminophenol) or 2-aminophenol characteristic building blocks have been synthesized by reduction of the corresponding nitro derivatives with Pd–C/hydrazine hydrate. The pKa′ values of the new compounds have been determined by potentiometric titration. These and the observed spectroscopic data are discussed and compared with related compounds. A crystalline 1:1 complex of the diamino crown **3b** with NaSCN has also been prepared and characterized.

Introduction

During the last two decades, crown ethers (coronands) [1] and their noncyclic analogues (podands) [1] have been of considerable interest due to the salient complexation properties to cations and uncharged organic molecules [2]. These have found many applications in theoretical, analytical and preparative chemistry [3]. The particular ligation behaviour of crowns and podands depends on different parameters including the number of donor atoms, the nature of donor atoms, ring size as well as topological and conformational parameters [4]. Extra functional groups have also been introduced into crown and podand frameworks in order to make them more specific complexants. Typical examples of compounds are the so-called self-ionizable (protonizable) crowns and podands [5]. Others use the extra functional groups for coloration effects [6]. In these cases the functional groups are intended to converge the complexation site of the crown or podand. By way of contrast, functional groups in a lateral position of the crown are useful to attach additional complexation arms [7] or lipophilic side groups [8], to bind the crown or podand to a polymer backbone [9], to tie together two or more crown compounds (bis-crown ethers) [10] or to build new host topologies [11]. In the latter context, amino functional groups are very promising since they open broad chemical connectivities. However, relatively few coronands and podands with extra amino groups are known [12].

Here, we report on the synthesis of a series of crown compounds (**1b–3b**) and podands (**4b–8b**) incorporating two aniline building blocks obtained from previously synthesized nitro compounds (**1a–8a**) [13] and give characterization of the new compounds in respect of analytical, physical, spectroscopic and PKa data; the latter exceed a preliminary study [14]. Crystalline complex formation between **3b** and NaSCN is reported and since the X-ray crystal structure of dianilino crown **1b** is known [15], a structural comparison based on the previous solid state and the present spectroscopic data in solution is drawn.

Results and Discussions

Synthesis

The catalytic reduction of aromatic nitro compounds by hydrazine has been known since 1929 [16]. Numerous aromatic nitro compounds have been treated in neutral or basic solution with hydrazine and in the presence of several catalysts, *e.g.* Pd–C, Pd–$CaCO_3$ (1%), Pt–C, Ru–Ca or Raney Ni [17]. Selectivity at these reductions is ob-

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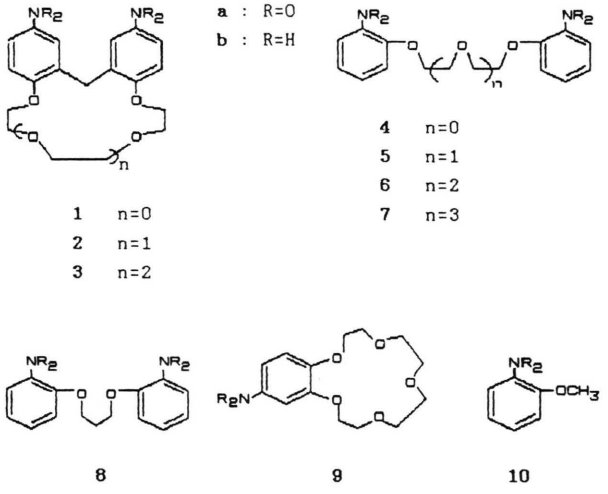
served only for aromatic nitro compounds containing O-benzyl, N-benzyl and chloro substituents [18]. So far, no systematic investigation has been made on the hydrazine-effected reduction of cyclic and open-chain oligoether derivatives with two nitro groups on different benzene rings, such as the present compounds **1a–7a.** These compounds and also **8a** and **10a** gave the corresponding diamines **1b–8b** and monoamine **10b** smoothly and in high yields if the reduction is carried out



in neutral refluxing ethanol solution using hydrazine hydrate (80%) and a Pd–C catalyst (Table I). However, when nitrobenzo crown ether **9a** was subjected to the same reduction conditions, the reduction was very incomplete showing the presence of unreacted nitro compound **9a** and large quantities of intermediate reduction products but only low amount of amine **9b,** detected by TLC (CH_2Cl_2/THF, 1:1). The observed difference in reactivity is possibly a result of the particular complexation behaviour of **9a,** considering the fact that 18-crown-6 is capable of forming stable complexes with hydrazines [19]. Moreover, it was found that the addition of base (KOH) helps to distinctly speed up the reaction rate. Under this condition, the reductions are generally complete in 0.5–1.0 h, except of **9a** which was again insufficient. Hence, reduction of **9a** was alternatively carried out by Raney Ni/hydrazine hydrate (80%) in neutral ethanol to give a 70% yield of **9b** [20]. Isolation and purification of the amino compounds **1b–10b** were effected by column chromatography (SiO_2) using hexane/CH_2Cl_2 (1:2) for elution and subsequent recrystallization (solvents and other experimental data for each compound are given in Table I). Amino crown **9b** was obtained as a viscous oil which crystallized hardly from isopropanol in two months at the dark. When dry hydrogen chloride was passed through a solution of **9b** in CH_2Cl_2, the corresponding hydrochloride (**9b**·HCl) resulted in crystals (Table I). The 1:1 complex between diamino crown **3b** and NaSCN was obtained by combining solutions of **3b** in acetonitrile and NaSCN in hot methanol.

Titration studies

In previous experiments [14], we have attempted to investigate correlation between structural characteristics and basicity properties of some of the crowns and podands the synthesis of which is re-

Table I. Experimental details for compounds **1b–10b.**

Compound	Reaction time (h)	Crystallization solvent	Yield (%)	M.p. (°C) [Literature][a]
1b	2.0	Ethanol/Isopropanol (1:2)	74	169
2b	2.0	Isopropanol	73	93
3b	2.5	Isopropanol	82	115
4b	2.0	Isopropanol	94	128 (128) [27]
5b	2.5	Ethanol	92	65 (65) [27]
6b	2.5	Isopropanol	86	33
7b	2.0	–	67	oil (oil) [28]
8b	2.0	Ethanol	74	79
9b	2.0	Isopropanol	70	75 (75) [20]
9b·HCl	0.5	Methylene chloride	66	225
10b	1.5	Isopropanol	76	6 (6.22) [26]

[a] Literature m.p.'s are in parentheses.

ported here. Complementary studies including the remaining compounds are required to round off the discussion. They involve using of the same experimental method as before [14]. In this nexus, solutions of the compounds (0.001 M) in nitrobenzene were titrated potentiometrically with perchloric acid (0.034 M) in nitrobenzene and their pKa′ values were calculated. The complete pKa'_1 and pKa'_2 data, compounds of comparison included, are given in Table II. For the diamino coronands **1b–3b** and podands **4b–8b,** a linear relationship between the pKa'_1 values and the present number of oxygen atoms is evident. This suggests that in these compounds, the ether oxygens may considerably be involved in the proton interaction which is reasonable since hydronium complexes of crowns are established [21]. Aniline and 2-methoxyaniline (**10b**), which were included for comparison, fall into line while 2,2′-diaminobiphenyl shows a distinct deviation, possibly due to a certain proton sponge property [22]. On the other hand, amino crown **9b** with five ether oxygens in the macroring has a pKa'_1 close to that of **1b** with only three ether oxygens in the ring, which is not obvious from the above reasoning. Also, the pKa'_2 values found for the series of crowns **1b–3b** are difficult to understand.

Consequently, further work is required to establish the effects which control the protonation/deprotonation equilibria of this class of compounds.

Spectroscopy

Selected IR data for the new amino crowns and podands are listed in Table III. All compounds show characteristic NH_2 absorptions at 3500–

Compound	HNP_1 [mV]	HNP_2 [mV]	pKa'_1	pKa'_2
Aniline	432	–	−0.72	–
2,2′-Diaminobiphenyl	370	–	+0.29 (for two protons)	–
1b	284	331	+1.75	+0.95
2b	264	325	+2.09	+1.05
3b	248	388	+2.36	−0.02
4b	364	455	+0.39	−1.15
5b	324	465	+1.07	−1.32
6b	278	488	+1.85	−1.71
7b	254	494	+2.26	−1.82
8b	359	455	+0.47	−1.15
9b	281	–	+1.80	–
10b	407	–	−0.34	–

Table II. Potentiometric titration data[a].

[a] Half-neutralization potentials (HNPs), pKa'_1 and pKa'_2 values of various amines titrated potentiometrically with perchloric acid in nitrobenzene solvent. Potentials recorded against a buffer solution; readings, −17 mV and pH 7.

Table III. Selected IR bands[a,b].

Compound	ν_{NH}	ν_{C-H} (arom.)	ν_{C-H} (aliph.)	C−N, C=C	C−O−C as. (arom.)	C−O−C as.	C−O−C sym. (arom.)
1b	3490; 3340	3050	2920; 2880	1610; 1595	1240	1140–1090	1045
2b	3495–3200	3040	2915; 2875	1620; 1595	1235	1135–1080	1050
3b[c]	3500–3200	3030	2910; 2880	1630	1240	1140–1080	1040
4b	3460; 3380	3080	2960	1610	1230	1150–1080	1050
5b	3460; 3380 ; 3360	3060	2960; 2880 2900; 2850	1610	1225	1150–1100	1050
6b	3495; 3395	3070	2950; 2900	1620; 1600	1230	1140–1080	1060
7b	3480; 3380 ; 3340	3360	2960; 2870 2910; 2850	1615; 1600	1230	1150–1080	1040
8b	3500; 3400	3070	2950 2900	1620	1230	1150–1090	1060
9b[d]	3390; 3340	3060	2920; 2870	1610; 1600	1235	1135–1095	1040

[a] In KBr, $\nu_{cm^{-1}}$; [b] the corresponding nitro derivatives, show ν_{NO_2} 1510, 1340 cm^{-1} bands; [c] the corresponding NaNCS complex of **3b** gives a $\nu_{(C-N)}$ 2070 cm^{-1} band; [d] the hydrochloride salt of **9b** gives ν_{NH_3Cl} 3400 (broad), 2910, 2870, and 2600 cm^{-1} bands.

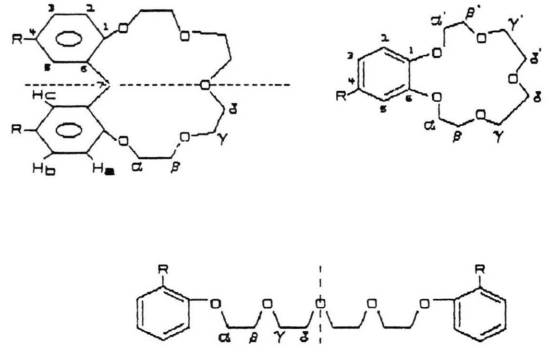
3200 cm^{-1} while the NO_2 bands (1510 and 1340 cm^{-1}) present in the IR spectra of the corresponding nitro derivatives have disappeared [13, 23]. Alkylether and arylether stretching bands are also observed at 1150–1080 cm^{-1} and ~1240 cm^{-1}, respectively.

The ^1H NMR data are given in Table IV (assignment of atoms in Scheme 1).

On comparing the α-CH_2 proton chemical shifts of the previously reported [13] nitro coronands and podands with amino coronands and podands, we note a shielding of 0.005 to 0.20 ppm on passing from the nitro to the corresponding amino compounds which is reasonable since NO_2 and NH_2 are electron withdrawing and donating groups, respectively. A similar, but lesser, effect is observed for the β-CH_2 and γ-CH_2 protons.

Benzylic protons give a singlet (average δ = 3.96 ppm) in amino derivatives **1b–3b** just as the corresponding nitro compounds [13].

The ^{13}C NMR data for the new coronands (**1b–3b** and **9b**) are summarized in Table V (*cf.* Scheme 1). It is possible to make a complete assignment of the ^{13}C NMR spectra which furnishes clear proof of the structures. In the ^{13}C-proton de-



Scheme 1. The numbering scheme of crowns and podands.

Table IV. ^1H NMR data (δ [ppm] and J_{HH} [Hz][a,b].

Compound	α-CH_2	β-CH_2	γ-CH_2	δ-CH_2	CH_2 (Benzylic)	Aromatic protons (Ha, Hb, Hc)	NH_2 (NH_3)$^+$
1b	4.05 (t, 4H, J = 5.0)	3.75 (t, 4H, J = 5.0)	–	–	3.94 (s, 2H)	6.80 (d, 2H, Ha) 6.60 (dd, 2H, Hb, Jab = 8.5, Jbc = 2.5) 6.50 (d, 2H, Hc)	3.10 (bs, 4H
2b	4.05 (m, 4H)	3.78 (m, 4H)	3.75 (s, 4H)	–	3.98 (s, 2H)	6.72 (d, 2H, Ha) 6.50 (dd, 2H, Hb, Jab = 8.5, Jbc = 3.0) 6.40 (d, 2H, Hc)	2.65 (bs, 4H
3b	4.05 (m, 4H)	3.78 (m, 4H)	3.75 (s, 8H,	γ-CH_2+δ-CH_2)	3.96 (s, 2H)	6.70 (d, 2H, Ha) 6.50 (dd, 2H, Hb, Jab = 8.5, Jbc = 3.0) 6.32 (d, 2H, Hc)	2.30 (bs, 4H
4b	4.20 (s, 4H)	–	–	–	–	6.70–7.00 (m, 8H)	3.80 (bs, 4H
5b	4.15 (t, 4H, J = 5.0)	3.85 (t, 4H, J = 5.0)	–	–	–	6.50–7.00 (m, 8H)	3.70 (bs, 4H
6b	4.15 (t, 4H, J = 5.0)	3.85 (t, 4H, J = 5.0)	3.80 (s, 4H)	–	–	6.50–7.00 (m, 8H)	3.68 (bs, 4H
7b	4.10 (t, 4H, J = 5.0)	3.83 (t, 4H, J = 5.0)	3.76 (s, 8H,	γ-CH_2+δ-CH_2)	–	6.50–6.95 (m, 8H)	3.65 (bs, 4H
8b	4.21 (t, 4H)	2.26 (q, 2H)				6.70–7.00 (m, 8H)	3.75 (bs, 4H
9b	4.05 (m, 4H)	3.80 (m, 4H)	3.65 (s, 8H,	γ-CH_2+δ-CH_2)	–	6.60 (d, Ha) 6.20 (d, Hc) 6.10 (dd, Hb, Jab = 8.0, Jbc = 3.0)	3.10 (bs, 2H
9b·HCl	4.20 (m, 4H)	3.95 (m, 4H)	3.77 (m, 8H,	γ-CH_2+δ-CH_2)		6.96 (dd, Hb, Jab = 7.0, Jbc = 2.0) 7.04 (d, Ha) 7.09 (d, Hc)	[2.08 (s, 3H)]
10b	3.70	–	–	–	–	6.50–7.10	3.50

[a] In $CDCl_3$ (room temperature) at 199.5 MHz; [b] bs: broad singlet, s: singlet, d: doublet, t: triplet, q: quintet.

Table V. ^{13}C NMR data (δ [ppm], J_{CH} [Hz])[a,b].

Compd. No.	C_α	C_β	C_γ	C_δ	C_1	C_2	C_3	C_4	C_5	C_6	C_7
1b	71.56	69.07	–	–	147.45	112.76	116.50	142.31	118.08	132.78	28.38
2b	69.34	68.82	68.82	–	149.02	112.87	113.93	139.74	117.23	130.63	28.50
3b	71.16	70.66	69.79	69.09	150.15	113.44	113.44	139.81	118.00	130.99	29.23
9b	68.79 68.17 (α')	67.47 (β,β')	67.40 (γ,γ')	67.08 (δ,δ')	147.54	112.56	106.97	122.01	114.80	147.14	

[a] In $CDCl_3$ (room temperature) at 50.10 MHz; [b] $^1J_{CH}$ (aliph.) = ~142 Hz, $^3J_{CCCH}$ = 4.5–5.0 Hz, $^1J_{CH}$ (arom.) = ~165 Hz.

Table VI. Analytical data.

Compound	Formula	M (M^+) Calcd (found)[a]	Elemental analysis (%) Calcd (found) C	H	N
1b	$C_{17}H_{20}N_2O_3$	300 (300)	67.98 (67.86)	6.71 (6.83)	9.33 (9.18)
2b	$C_{19}H_{24}N_2O_4$	344 (344)	66.26 (66.34)	7.02 (7.15)	8.13 (7.96)
3b	$C_{21}H_{28}N_2O_5$	388 (388)	64.93 (64.83)	7.27 (7.26)	7.21 (7.10)
6	$C_{18}H_{24}N_2O_4$	332 (332)	65.04 (65.17)	7.28 (7.32)	8.43 (8.25)
7	$C_{20}H_{28}N_2O_5$	376 (376)	63.81 (63.72)	7.50 (7.61)	7.44 (7.34)
8b	$C_{15}H_{18}N_2O_2$	258 (258)	69.75 (69.87)	7.02 (6.93)	10.84 (10.72)
9b·HCl	$C_{14}H_{22}NO_5Cl$	319 (283)[b]	52.58 (52.32)	6.93 (6.97)	4.38 (4.58)
9b·NaSCN	$C_{21}H_{28}N_3O_5SNa$	469 (388)[c]	56.28 (56.23)	6.01 (6.08)	8.95 (8.86)

[a] Based on the mass of the most abundant isotope; [b] (M^+ – HCl); [c] (M^+ – NaNCS).

coupled NMR spectra of **1b–3b,** one benzylic and six different aromatic carbon lines have been observed. For the more flexible oligoether segments of the molecules $C\alpha-C\delta$ signals, respectively, are separated, with the exception of **9b** where the $C\beta$ and $C\gamma$ signals overlap.

As determined by X-ray crystallography [15] crown compound **1b** shows a highly non-symmetric irregular conformation in the solid state with high distortion at the benzylic carbon (bonding angle 116.1°). The torsion angle between the phenylene planes is 65.6° and there is short contact (2.41 Å) between one of the benzylic H atom and a neighbouring oxygen, unlike a similar compound of larger ring size [24]. The ^1H NMR spectra indicate no such irregular conformations in solution, neither of **1b** nor of **2b** and **3b.** This, it is likely that conformations of the higher diphenylmethano crowns are also rather different in solution and in the solid state.

In the electron impact (EI) mass spectra of the amino crowns **1b–3b,** relative height of 100% of the M^+-peaks (see Table VI) suggests high stability of the macrocycles. Fragmentations mostly proceed by the loss of C_4H_7O, $C_4H_8O_2$ or C_2H_4O groups. For the NaNCS complex of **3b,** the fragmentation patterns are similar to uncomplexed **3b.**

Experimental

General

Melting points were measured on a Thomas-Hoover apparatus using a capillary tube. IR spectra were obtained from a Perkin Elmer 377 spectrophotometer in KBr discs. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution (90 MHz and 200 MHz NMR spectrometers, δ-scale, $SiMe_4$ as internal standard). Mass spectra were obtained from a VG 7070 mass spectrometer (electron impact mode 70 eV, source temperature 240 °C). Microanalyses were carried out by the microanalytical service of TÜBITAK-MAE, Gebze-Kocaeli (Turkey).

Chemicals

Hydrazine hydrate (80%), Pd–C (10%) and nickel catalyst were purchased from Fluka. 2,2'-diaminobiphenyl [25] and the nitro precursors **1a–10a** were prepared by the literature methods

[13, 25]. The new amino crowns and podands **1b–8b** as well as **9b** [20] and **10b** [26] were synthesized from the corresponding nitro derivatives **1a–10a** by catalytic reduction with hydrazine hydrate. Experimental details are summarized in Table I, analytical data in Table VI. The procedure given for the synthesis of **3b** is representative of all amino compounds, except **9b** [20].

Preparation of diamino crown **3b**

To a refluxing suspension of Pd–C (0.10 g, 10% Pd) and dinitro crown **3a** (0.90 g, 2.0 mmol) in ethanol (100 ml) was dropped a solution of hydrazine hydrate (80%, 8 ml) in ethanol (50 ml) over a period of 0.5 h. Refluxing was continued for 2 h. The mixture was filtered and the solvent removed *in vacuo*. The residue was subjected to column chromatography (75 g SiO_2 to 1.0 g residue, eluents hexane/CH_2Cl_2 1:2) to give solid **3b** which was crystallized from isopropanol and recrystallized from ether-isopropanol (1:4).

Hydrochloride of **9b**

This compound was obtained by passing dry hydrogen chloride through a solution of **9b** in methylene chloride. Further details in Table I and VI.

Preparation of complex **3b** · *NaNCS (1:1)*

The macrocycle **3b** (0.388 g, 1.0 mmol) dissolved in acetonitrile (15 ml) was added to a hot solution of NaNCS (0.081 g, 1.0 mmol) in methanol (10 ml). The mixture was concentrated and diethyl ether (10 ml) was added. On refrigerating for two days, needle-shaped crystals formed which were collected and washed with cold ether. Recrystallization from acetonitrile/diethyl ether (1:3) yielded 0.33 g (70%) of the 1:1 complex, m.p. > 250 °C (decomp.), analytical data in Table VI.

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