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# Novel 1,10-diaza-18-crown-6 derivatives

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Reaction of 1,10-bis(methoxymethyl)-1,10-diaza-18-crown-6 (**1**) with trimethylsilyl azide resulted in hitherto unknown 1,10-bis(azidomethyl)-1,10-diaza-18-crown-6 (**2**) and novel ionic compound 1,10-bis(azide anion)-1,10-dihydro-1,10-diaza-18-crown-6 (**3**). Compound **2** reacted with dimethyl acetylenedicarboxylate to give 1,10-bis(4,5-dimethoxycarbonyltriazolomethyl)-1,10-diaza-18-crown-6 (**4**). Carbamoylation of 1,10-diaza-18-crown-6 (**5**) with optically active α-phenylethyl amine yielded optically active 1,10-bis(α-phenylethylcarbamoyl)-1,10-diaza-18-crown-6 (**6**).

**Key words:** 1,10-diaza-18-crown-6, 1,10-bis(methoxymethyl)-1,10-diaza-18-crown-6, 1,10-bis(azidomethyl)-1,10-diaza-18-crown-6, 1,10-bis(azide anion)-1,10-dihydro-1,10-diaza-18-crown-6, 1,10-bis(4,5-dimethoxycarbonyltriazalomethyl)-1,10-diaza-18-crown-6, trimethylsilyl azide, aminomethyl-substituted triazoles, dimethyl acetylenedicarboxylate.

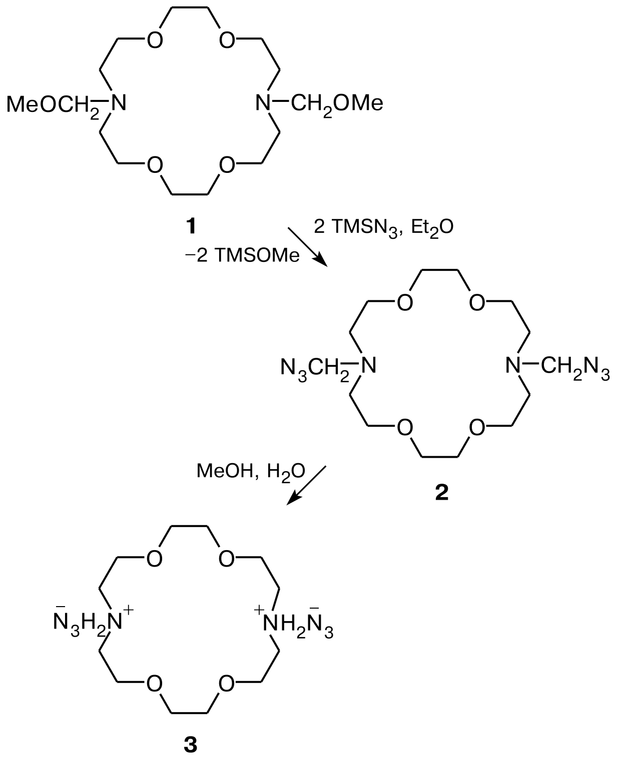
Earlier, we developed synthetic procedures towards azido- and cyanomethylamines by the reaction of alkoxymethylamines with trimethylsilyl azide ($TMSN_3$) or trimethylsilyl cyanide (TMSCN). For the compounds synthesized, structures and anomeric effects in crystalline state and gaseous phase were studied. Novel fragmentation of azidomethoxymethyldimethylamine and novel rearrangement of triazolylmethylamines were found. Cycloaddition of azidomethylamines to dimethyl acetylenedicatboxylate (DMAD) resulted in hitherto unknown aminomethyl-substituted triazoles, and their based-catalyzed isomerization were studied.[1]

In the present work, we describe the reactions of $TMSN_3$ with 1,10-bis(methoxymethyl)-1,10-diaza-18-crown-6 (**1**) and 1,10-diaza-18-crown-6 (**5**) with optically active α-phenylethyl isocyanate.

Compound **1** reacts with $TMSN_3$ in diethyl ether at room temperature to give 1,10-bis(azidomethyl)-1,10-diaza-18-crown-6 (**2**). Novel ionic compound 1,10-bis(azide anion)-1,10-dihydro-1,10-diaza-18-crown-6 (**3**) was synthesized by refluxing compound **2** in aqueous MeOH for 2 h with the subsequent keeping of the reaction mixture at −2 °C for 24 h (Scheme 1).

Azide anion, one of the well-studied pseudohalogenides, attracts considerable attention from organic and physical organic chemists.[2] Covalently bound azide groups do not prone to participate in intramolecular interactions; at the same time, the role of the uncoordinated azide an-

**Scheme 1**



$N_3^- = N^-{=}N^+{=}N^-$

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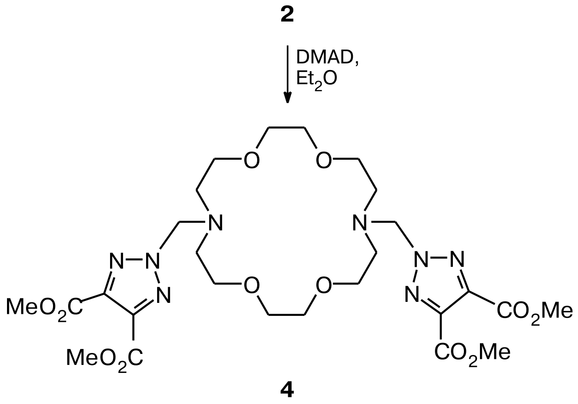
ion in the crystal packing and the intermolecular contact formation is not almost studied, since the compounds bearing this species in a free state are poorly available.* Weak interactions of the coordinated azide ions play an important role in the crystal packing of metal complex compounds and the free azide anion is the best species for their investigation.

The azide group, a promising building block for supramolecular systems, was studied by X-ray diffraction in both coordinated and uncoordinated anionic states on the example of compound **3**.[2] X-ray diffraction of compound **3** reveals that the diprotonated crown ether cation forms hydrogen bonds with two uncoordinated azide anions. Refinement and analysis of the experimental electron density distribution show that along with formation of the strong hydrogen bonds, the azide anion participates in several weak C—H...N interactions. A comparison of the experimental and calculated data allows us to develop a general approach to the description of the role of the azide anion in the crystal packing, which links the integrated charge of the terminal atoms of the azide anion with their ability to participate in nonvalent and coordination interactions.[2] Structure of compound **3** is also confirmed by $^1$H NMR spectroscopy (see Experimental).

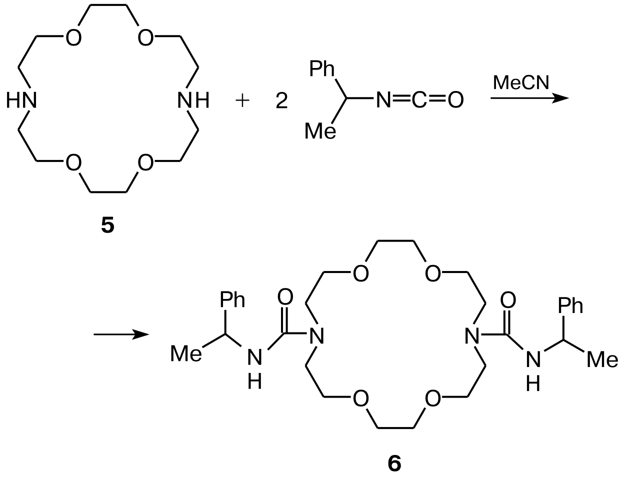
1,10-Bis(azidomethyl)-1,10-diaza-18-crown-6 (**2**) reacts with dimethyl acetylenedicarboxylate (DMAD) to give triazole derivative, 1,10-bis(4,5-dimethoxycarbonyltriazol-2-ylmethyl)-1,10-diaza-18-crown-6 (**4**) (Scheme 2). Similar cycloaddition accompanied the reaction of azidomethylamines with DMAD.[1] In contrast to cycloaddition of azidomethylamines to DMAD, in the reaction of compound **2** with DMAD no isomerization of the triazole derivative occurs; therefore, the reaction is performed without base addition.

**Scheme 2**



We also studied carbamoylation of 1,10-diaza-18-crown-6 (**5**) with optically active α-phenylethyl isocyanate. This reaction under mild conditions affords optically active 1,10-bis(α-phenylethylcarbamoyl)-1,10-diaza-18-crown-6 (**6**) in excellent yield (Scheme 3).

**Scheme 3**



In summary, in the present work ionic compound 1,10-bis(azide anion)-1,10-dihydro-1,10-diaza-18-crown-6 (**3**) was first synthesized by the reaction of novel crown ether, *e.g.*, 1,10-bis(azidomethyl)-1,10-diaza-18-crown-6 (**2**), with trimethylsilyl azide ($TMSN_3$).

## Experimental

Starting compounds, 1,10-bis(methoxymethyl)-1,10-diaza-18-crown-6 (**1**), 1,10-diaza-18-crown-6 (**5**), trimethylsilyl azide ($TMSN_3$), dimethyl acetylenedicarboxylate (DMAD), and α-phenylethyl isocyanate, are commercially available. $^1$H NMR spectra were recorded on a Bruker WM-400 spectrometer (400.13 MHz) in $CDCl_3$ or DMSO-$d_6$ relatively to the residual solvent signal ($\delta_H$ 7.26 for $CDCl_3$ and $\delta_H$ for DMSO-$d_6$).

The optical rotations were measured with a POLAMAT A polarimeter (Carl Zeiss JENA). Melting points were determined on a Stuart Scientific Melting point apparatus SMP3 (Great Britain) in sealed capillaries. Microanalyses were performed on Perkin Elmer 2400 CHN elemental analyzer.

**1,10-Bis(azidomethyl)-1,10-diaza-18-crown-6 (2).** To a solution of compound **1** (0.77 g, 2.2 mmol) in anhydrous diethyl ether (3 mL), trimethylsilyl azide (0.51 g, 4.4 mol) was slowly added at 20 °C. The reaction mixture was kept for 12 h at room temperature, the crystals formed were collected and crystallized from methanol—diethyl ether (1 : 1) to give compound **2** in the yield of 0.74 g (90%), m.p. 129—131 °C. $^1$H NMR ($CDCl_3$), δ: 2.98 (t, 8 H, 4 $CH_2N$, $^3J$ = 5.6 Hz); 3.69 (s, 8 H, 2 $O(CH_2)_2O$); 3.76 (t, 8 H, 4 $CH_2O$, $^3J$ = 5.6 Hz); 4.55 (s, 4 H, 2 $NCH_2N_3$). Found (%): C, 45.13; H, 7.74; N, 30.23. $C_{14}H_{28}N_8O_4$. Calculated (%): C, 45.16; H, 7.53; N, 30.11.

**1,10-Bis(azide anion)-1,10-dihydro-1,10-diaza-18-crown-6 (3).** Compound **2** (0.372 g, 1 mmol) was refluxed in MeOH for 2 h

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* Cambridge structural database (CSD version 5.30, November 2008 with 3 updates) contains structures of 43 organic compounds bearing the azide anions.

and then kept at –2 °C for 20 h. Compound **3** was obtained in the yield of 0.32 g (92%), crystals, m.p. 142—144 °C. $^1$H NMR (DMSO-d$_6$), δ: 3.16 (t, 8 H, 4 $CH_2N$, $^3J$ = 6.2 Hz); 3.58 (s, 8 H, 2 $O(CH_2)_2O$); 3.71 (t, 8 H, 4 $CH_2O$, $^3J$ = 6.2 Hz). Found (%): C, 41.43; H, 8.12; N, 32.20. $C_{12}H_{28}N_8O_4$. Calculated (%): C, 41.38; H, 8.05; N, 32.18. Structure of compound **3** was confirmed by X-ray diffraction[2] (CCDC 801422).

**1,10-Bis(4,5-dimethoxycarbonyltriazol-2-ylmethyl)-1,10-diaza-18-crown-6 (4).** To a solution of 1,10-bis(azidomethyl)-1,10-diaza-18-crown-6 (**2**) (0.085 g, 0.228 mmol) in anhydrous MeOH (2 mL), DMAD (0.065 g, 0.46 mmol) was slowly added. The reaction mixture was kept for 12 h at room temperature, then solvent was removed *in vacuo*, the crystalline residue was recrystallized from methanol—diethyl ether (1 : 1) to give compound **4** in the yield of 0.14 g (93%), m.p. 132—134 °C. $^1$H NMR (CDCl$_3$), δ: 3.46 (t, 8 H, 4 $CH_2N$, $^3J$ = 6.1 Hz); 3.57 (s, 8 H, $O(CH_2)_2O$); 3.64 (t, 8 H, 4 $CH_2O$, $^3J$ = 6.1 Hz); 3.92 (s, 12 H, 4 $CH_3O$); 4.64 (c, 4 H, 2 $NCH_2N$). Found (%): C, 47.60; H, 6.15; N, 17.22. $C_{26}H_{40}N_8O_{12}$. Calculated (%): C, 47.56; H, 6.10; N, 17.07.

**1,10-Bis(α-phenylethylcarbamoyl)-1,10-diaza-18-crown-6 (6).** To a solution of compound **5** (0.8 g, 3 mmol) in anhydrous MeCN (3 mL), *R*-(+)-α-phenylethyl isocyanate (0.9 g, 6 mmol) was added and the reaction mixture was kept at 20 °C for 12 h. The solvent was removed *in vacuo*, the residue was crystallized from diethyl ether to give compound **6** in the yield of 1.63 g (96%), crystals, m.p. 130—131 °C, $[\alpha]_D$ +8.35 (*c* 1.5, MeOH). $^1$H NMR (CDCl$_3$), δ: 1.43 (d, 6 H, 2 $C\underline{H}_3CH$, $^3J$ = 6.7 Hz); 3.46 (t, 8 H, 4 $CH_2N$, $^3J$ = 6.7 Hz); 3.53 (s, 8 H, 2 $O(CH_2)_2O$); 3.62 (t, 8 H, 4 $CH_2O$, $^3J$ = 6.7 Hz); 4.89 (dq, 2 H, 2 CH, $^{33}J_{CH-CH_3}$ = = 6.7 Hz, $^3J_{CH-NH}$ = 6.7 Hz); 6.26 (d, 2 H, $N\underline{H}CH$, $^3J_{NH-CH}$ = = 6.7 Hz); 7.3 (m, 10 H, Ph). Found (%): C, 64.69; H, 7.97; N, 10.14. $C_{30}H_{44}N_4O_6$. Calculated (%): C, 64.75; H, 7.91; N, 10.07.

## References

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