NUCLEOPHILIC SUBSTITUTION REACTIONS IN TETRANITRODIBENZO-18-CROWN-6

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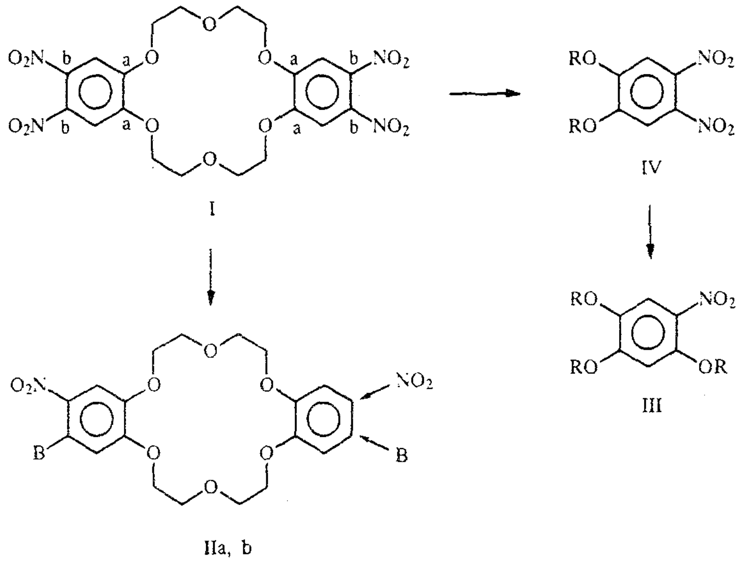
The nature of the reaction of a reagent with tetranitrodibenzo-18-crown-6 was found to depend on its basicity. This behavior was interpreted in the framework of the theory of hard and soft acids and bases.

We have shown that the reactions of tetranitrodibenzo-18-crown-6 (I) with bases may proceed either with retention or cleavage of the macroheterocycle [1-5].



II B=i-PrS$^-$, PhO$^-$, a) cis isomer, b) trans-isomer;III, IV R=Me, Et.

In order to determine the effect of the nature of the reagent on the reaction course leading to products II and III, we correlated the results of our previous work [1-5] on the reaction of crown ether I with various bases in DMSO at room temperature (~20°C). The following bases were used: acetamide, aniline, aliphatic amines, hydrazines, piperidine, thiocyanate anions, azide anions, phenolate anions,* isopropylthiolate anions,* and alcoholate anions (Fig. 1).

This correlation showed that I is cleaved by strong bases such as sodium methylate and sodium ethylate under the given reaction conditions (analogously to our previous findings [1]), participates in nucleophilic substitution of the nitro groups by the action of aliphatic amines and piperidine (analogously to our subsequent work [2, 3]), phenolate anions, and isopropylthiolate anions, and does not react with such weak bases as thiocyanate anions, azide anions, and aromatic amines. However, in the case of aniline, heating the reaction mixture to 100°C yields type-II products [2]. The characteristics of previously unreported compounds are given in the Experimental.

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*The experimental results are given in the present communication.

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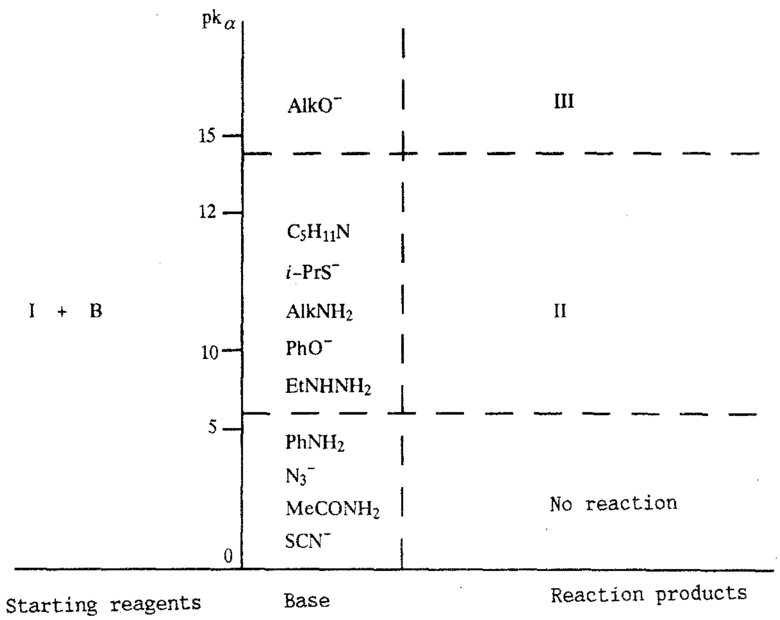
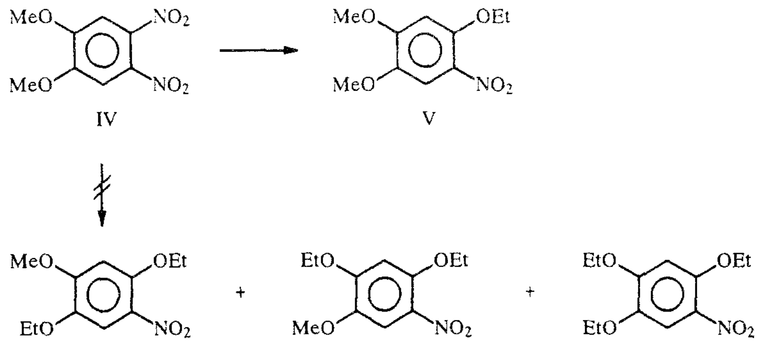


Fig. 1. Dependence of the nature of the product of the reaction of tetranitrodibenzo-18-crown-6 on the basicity of reagent B (handbook pK_a values were used [7]).

Our calculation of the partial charges on the atoms in tetranitrodibenzo-18-crown-6 (I) carried out according to our previous procedure [6] showed that $C_{(a)}$ and $C_{(b)}$ in the benzene rings, which are alternative reaction sites, should differ markedly relative to attack by soft and hard bases ($qC_{(a)} = 0.11235$ and $qC_{(b)} = 0.0618$).

In accord with this calculation, the results obtained may be interpreted in the framework of the theory of hard and soft acids and bases as follows: AlkO$^-$ anions, which are hard bases, attack hard electrophilic $C_{(a)}$ sites, leading to cleavage of the macroheterocycle. In the case of softer bases such as PhO$^-$, i-PrS$^-$, RNH_2, and $RNHNH_2$, the attack proceeds at the $C_{(b)}$ sites and leads to the products of nitro group substitution.



From this viewpoint, we may readily explain the finding that heating crown ether I with sodium methylate in methanol at reflux yields a mixture of isomeric type-II products (B = OCH_3) [4]. The hardness of CH_3O^- as a base should be markedly diminished upon going from aprotic, dipolar DMSO or DMF to protic methanol, which alters the regioselectivity of the reaction. In this case, the attack of the soft solvated methoxy anion proceeds at the soft $C_{(b)}$ electrophilic site.

However, in our opinion, the pathway for the reaction of tetranitrodibenzo-18-crown-6 (I) with sodium alcoholates is a function not only of the basicity of the reagent. Another, not less important reason for this reaction is found in the formation of a complex of crown ether I with the sodium cation during the reaction, which facilitates cleavage of the macrocycle. This is supported by the finding that only V is formed upon treatment of 1,2-dinitro-4,5-dimethoxybenzene (IV), which is a structural analog of crown ether I, by sodium ethylate in DMSO and products of the replacement of the methoxy groups by the ethoxy anion were not isolated.

The addition of catalytic amounts of simple crown ethers such as dibenzo-18-crown-6, which has higher complexing capacity than I, does not alter the reaction course.

EXPERIMENTAL

Monitoring of the reaction and purity of the products was carried out by thin-layer chromatography on Silufol UV-254 plates using 1:1 acetone—hexane or 5:1 chloroform—ethanol as the eluent. Silica gel 100/250 was used for the column chromatography. The IR spectra were taken on a Specord 75-IR spectrometer in chloroform. The mass spectra were taken on a Varian MAT 112 mass spectrometer with direct sample inlet at 70 eV and a temperature 40-50°C above the melting point of the samples. The PMR spectra were taken on a Tesla BS 497 spectrometer at 100 MHz in $CDCl_3$ with TMS as the internal standard.

The elemental analysis data for C, H, N, and S corresponded to the calculated values.

3,13-Dinitro-2,14-di(phenoxy)dibenzo-18-crown-6 and 3,14-Dinitro-2,13-di(phenoxy)dibenzo-18-crown-6 (IIa,b, B = OPh, $C_{32}H_{30}N_2O_{10}$). A sample of 0.54 g (1 mmole) tetranitrodibenzo-18-crown-6 (I) was dissolved in 100 ml DMSO and 0.232 g (2 mmoles) sodium phenolate was added. The reaction mixture was stirred at 20°C for 4 h and poured into 500 ml water. The precipitate formed was filtered off and the individual products were isolated by column chromatography. The yield of product IIa was 0.2 g (32%), mp 188°C, M^+ 634. IR spectrum: 1510 (NO_2), 1180 cm^{-1} (C—O—C). PMR spectrum: 7.59, 6.56 (4H, s, =CH), 6.34 (10H, m, Ph), 3.92 ppm (16H, m, CH_2O. The yield of IIb was 0.2 g (32%), mp 124°C, M^+ 634. IR spectrum 1510 (NO_2), 1165 cm^{-1} (C—O—C). PMR spectrum: 7.61, 6.58 (4H, s, =CH), 6.37 (10H, m, Ph), 3.94 ppm (16H, m, CH_2O).

3,13-Dinitro-2,14-di(isopropylthio)dibenzo-18-crown-6 and 3,14-dinitro-2,13-dinitro(isopropylthio)dibenzo-18-crown-6 (IIa,b, B = i-PrS, $C_{26}H_{34}N_2O_{10}S_2$). A sample of 0.54 g (1 mmole) tetranitrodibenzo-18-crown-6 (I) was dissolved in 100 ml DMSO and 0.196 g (2 mmoles) sodium isopropylthiolate. The reaction mixture was stirred for 0.5 h at 20°C and then poured into 500 ml water. The solution was brought to pH 7 by the addition of dilute hydrochloric acid. The reaction products were extracted with chloroform. The individual products were isolated by column chromatography. The yield of IIa was 0.2 g (34%), mp 78°C, M^+ 598. IR spectrum: 1505 (NO_2), 1160 cm^{-1} (C—O—C). PMR spectrum: 7.32, 6.54 (4H, s, =CH), 3.86 (16H, m, CH_2O), 3.54 (2H, q, CHS), 1.24 ppm (12H, d, CH_3). The yield of IIb was 0.2 g (34%), mp 82°C, M^+ 598. IR spectrum: 1505 (NO_2), 1180 cm^{-1} (C—O—C). PMR spectrum: 7.35, 6.58 (4H, s, =CH), 3.90 (16H, m, CH_2O), 3.56 (2H, q, CHS), 1.25 ppm (12H, d, CH_3).

1-Nitro-2-ethoxy-4,5-dimethoxybenzene (V). A sample of 2.28 g (0.01 mole) IV was dissolved in 100 ml DMSO and 1.16 g (0.02 mole) sodium ethylate was added. The reaction mixture was stirred for 3 h at 20°C and then poured into 500 ml water. The precipitated product was filtered off. The yield of V was 1.95 g (86%), mp 104°C, M^+ 227. PMR spectrum: 7.59, 6.61 (2H, s, =CH), 4.12 (2H, q, CH_2O), 3.86, 3.78 (6H, s, CH_3O), 1.52 ppm (3H, t, CH_3).

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