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SYNTHESIS OF N-CYANO MONOAZA CROWN ETHERS

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Abstract: N-Cyano monoaza crown ethers were prepared by the reaction of cyanamide with oligoethylene glycol dichlorides or ditosylates in the NaH/DMSO reaction system and led to the derivatives.

Crown ethers with functional groups such as hydroxymethyl,1) bromomethyl2) or monoaza crown ethers3) are important as intermediates in the synthesis of bis-crown compounds,4) crown ether polymers5) or surface active crown ethers.6) As a new type of reactive crown ethers, N-cyano monoaza crown ethers (IIa, b) have been synthesized in one-step by the N-alkylation of cyanamide with oligoethylene glycol dichlorides or ditosylates and their reactivity was investigated.

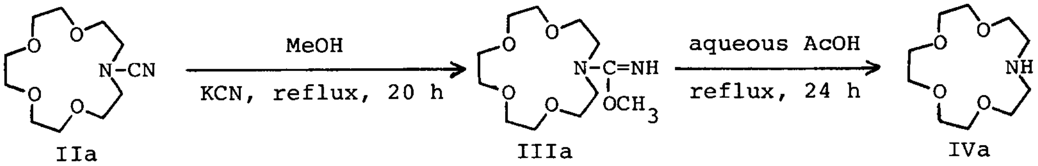
Ia: n=2, X=Cl
Ib: n=3, X=Cl
Ic: n=2, X=OTs

IIa: n=2
IIb: n=3

For example, cyanamide (0.84 g, 0.02 mol) and pentaethylene glycol dichloride Ia (5.50 g, 0.02 mol) were dissolved in 50 ml of dimethyl sulfoxide and the solution was added at 40°C over a period of 1 h into a stirred solution of sodium methylsulfinylmethide prepared *in situ* from sodium hydride (1.06 g, 0.044 mol) and 120 ml of dimethyl sulfoxide. After the addition, the reaction was continued for 20 h, then the reaction mixture was filtered, and the solvent was evaporated off from the filtrate. Water (50 ml) was added to the residue and the solution was extracted several times with dichloromethane. Upon removing the solvent from the combined solution, a viscous liquid (4.6 g) was obtained. It was distilled using kugelrohr distillation apparatus under reduced pressure to afford N-cyano monoaza 15-crown-5 IIa as a pale yellow liquid. Yield: 1.62 g (33%). b.p. 110-112°C/0.005 Torr. IR (neat, cm^{-1}): 2940s, 2860s, 2200s, 1450m, 1350m, 1120s. MS (m/e): 244 (M^+), 201, 157, 129, 113, 100, 69, 56, 45. ^1H-NMR ($CDCl_3$, δ): 3.34 (t, 4H), 3.62-3.82 (s+m, 16H). Analysis for $C_{11}H_{20}N_2O_4$: Calcd; C: 54.09, H: 8.25, N: 11.47, Found; C: 54.28, H: 8.41, N: 11.30. When sodium bromide (0.04 mol, 4.12 g) was added into the system, the reaction was appreciably accelerated and completed within 2 h, although remarkable improvement in yield was not attained (34%). This result may be explained by suggesting the exchange of halogen atom. Besides, IIa was also obtained by using ditosylate instead of dichloride in rather lower yield (12%).

In the same manner, the reaction of Ib with cyanamide and sodium hydride in dimethyl sulfoxide gave N-cyano monoaza 18-crown-6 IIb as an yellowish liquid in 17% yield. b.p. 118-120°C/0.005 Torr (Kugelrohr). IR (neat, cm^{-1}): 2940s, 2860s, 2200s, 1450m, 1350m, 1120s. MS (m/e): 288 (M^+), 245, 201, 157, 129, 113, 100, 89, 69, 56, 45. ^{1}H-NMR ($CDCl_3$, δ): 3.34 (t, 4H), 3.60-3.86 (s+m, 20H). Analysis for $C_{13}H_{24}N_2O_5$: Calcd; C: 54.15, H: 8.39, N: 9.72, Found; C: 54.06, H: 8.62, N: 9.35.

These crown ethers can be converted to the derivatives utilizing the reactivity of cyano group. For example, a base promoted addition of methanol to N-cyano monoaza 15-crown-5 IIa gave easily its O-methylisourea derivative IIIa, which was hydrolyzed almost quantitatively to monoaza 15-crown-5 IVa by refluxing in aqueous acetic acid. IIIa: pale yellow liquid; Yield: 95%. IR (neat, cm^{-1}) 3350w, 2940s, 2860s, 1630s, 1470m, 1350m, 1120s. MS (m/e): 276 (M^+), 231, 218, 145, 130, 102, 87, 45. ^{1}H-NMR ($CDCl_3$, δ), 3.44 (t, 4H), 3.58-3.78 (m, 19H), 4.46 (s, 1H). Analysis for $C_{12}H_{24}N_2O_5$: Calcd; C: 52.16, H: 8.75, N: 10.14, Found; C: 52.09, H: 8.79, N: 10.05. IVa: white crystals; b.p. 80-82°C/0.02 Torr, m.p. 30-32°C.[3)]



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