Tetrahedron Letters,Vol.24,No.13,pp 1327-1328,1983 0040-4039/83/131327-02$03.00/0
Printed in Great Britain

SYNTHESIS OF HYDROXYMETHYL-21-CROWN-7 AND HYDROXYMETHYL-24-CROWN-8

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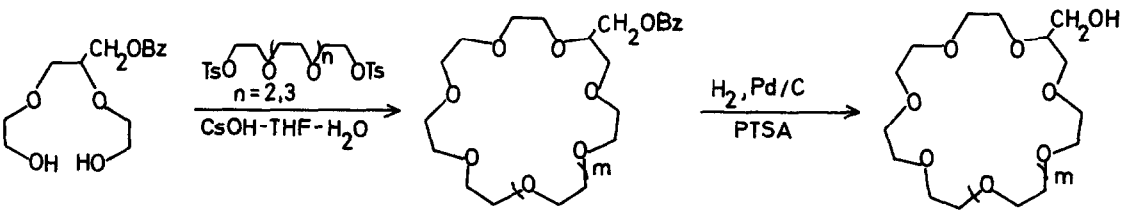
Summary: Reactions of 3,6-dioxa-4-(benzyloxymethyl)-1,8-octanediol with appropriate ditosylates followed by hydrogenolysis produce two new functionalized crown ethers.

Hydroxymethyl crown ethers are versatile intermediates for further structural modification[1] and for the formation of polymer-supported crown ethers.[2] Although hydroxymethyl derivatives of 12-crown-4, 15-crown-5 and 18-crown-6 are well-known,[3] the preparation of similarly-functionalized forms of larger-ring crown ethers has not been reported.

In this paper we describe the first syntheses of hydroxymethyl-21-crown-7 (1) and hydroxymethyl-24-crown-8 (2). Both preparations utilize the accessible[4] 3,6-dioxa-4-(benzyloxymethyl)-1,8-octanediol (3) as a key synthetic intermediate.



3

4 m = 1

5 m = 2

1 m = 1

2 m = 2

Treatment of diol 3 with CsOH in refluxing THF-H_2O followed by addition of tetraethylene glycol ditosylate provided benzyloxymethyl-21-crown-7 (4)[5] in 27% yield. Hydrogenolysis of 4 over Pd/C in the presence of a catalytic amount of p-toluenesulfonic acid gave, after chromatography, an 81% yield of hydroxymethyl-21-crown-7 (1).[6] Similarly, reaction of 3 with pentaethylene glycol ditosylate formed benzyloxymethyl-24-crown-8 (5)[7] in 14% yield. Debenzylation of 5 produced hydroxymethyl-24-crown-8 (2)[8] in 72% yield. Structural assignments of 1, 2, 4 and 5 are supported by elemental analysis and by IR, ^{1}H NMR, and mass spectral data.

In a typical experiment, diol 3 (20 mmol) was dissolved in 20 ml of THF-H_2O (40:1) and CsOH (50 mmol) was added. The reaction mixture was stirred and gently heated under nitrogen at 60°C until the base dissolved completely after which a solution of the ditosylate (20 mmol) in THF (10 ml) was added dropwise. The reaction mixture was stirred and heated (70°C) overnight. An additional amount of ditosylate (4 mmol) was added in one portion and stirring and heating were

continued for an additional 5 h. After cooling the reaction mixture to room temperature, the THF was removed *in vacuo* and CH_2Cl_2 was added to the residue. The cesium tosylate was filtered and washed with CH_2Cl_2. The combined filtrate and washings were evaporated *in vacuo* and the residue was chromatographed on neutral alumina (petroleum ether-EtOAc, 1:1). The resulting benzyloxymethyl crown ether was dissolved in EtOH and 10% Pd/C (100 mg/g of crown ether) and a catalytic amount of *p*-toluenesulfonic acid was added. After hydrogenolysis (slightly more than 1 atmosphere of hydrogen) at room temperature for 24 h, the catalyst was filtered and the filtrate was evaporated *in vacuo*. The residue was chromatographed on neutral alumina (EtOAc-MeOH, 10:1) to yield the hydroxymethyl crown ether.

It is anticipated that these new, functionalized, large-ring crown ethers and suitabile derivatives will exhibit selectivity for Rb^+ and Cs^+ in complexation of the alkali metal cations. This possibility is currently under investigation in our laboratories.

Acknowledgement. This research was supported by grant D-775 from the Robert A. Welch Foundation.

References and Notes

(1) G. W. Gokel, S. H. Korzeniowski, "Macrocyclic Polyether Syntheses," Springer Verlag, Berlin-Heidelberg-New York, 1982.

(2) a) M. Tomoi, O. Abe, M. Ikeda, K. Kihara, K. Kakiuchi, Tetrahedron Lett., 1978, 3031; b) F. Montanari, P. Tundo, J. Org. Chem., 47, 1298 (1982); c) K. Fukunishi, B. Czech, S. L. Regen, J. Org. Chem., 46, 1218 (1981); d) A. van Zon, F. de Jong, Y. Ouwezen, Recl. Trav. Chim. Pays-Bas., 100, 429 (1981).

(3) a) C. J. Pedersen, J. Am. Chem. Soc., 92, 386 (1970); b) R. N. Greene, Tetrahedron Lett., 1972, 1793; c) J. Dale, P. O. Kristiansen, Acta Chem. Scand., Ser. B, 26, 1471 (1972); d) I. Ikeda, S. Yamamura, Y. Nakatsuji, M. Okahara, J. Org. Chem., 45, 5355 (1980); e) B. R. Bowsher, A. J. Rest, Inorg. Chim. Acta, 53, L175 (1981); f) R. Chenevert, N. Voyer, R. Plante, Synthesis, 1982, 782.

(4) B. Czech, D. A. Babb, R. A. Bartsch, Org. Proc. Prep. Int., in press.

(5) Data for 4: Colorless viscous oil, ^1H NMR ($CDCl_3$, δ) 3.65 (s + m, 29H), 4.51 (s, 2H), 7.29 (s, 5H). IR (neat) 1116 (C-O) cm^{-1}. MS 429 (M+1). Elem. Anal. Calcd. for $C_{22}H_{36}O_8$: C, 61.66; H, 8.47. Found: C,61.64; H, 8.44.

(6) Data for 1: Colorless viscous oil, ^1H NMR ($CDCl_3$, δ) 2.71 (br s, 1H), 3.65 (s, 29H). IR (neat) 3458 (O-H), 1112 (C-O) cm^{-1}. MS 339 (M+1). Elem. Anal. Calcd. for $C_{15}H_{30}O_8$: C, 53.24; H, 8.93. Found: C, 53.05; H, 9.06.

(7) Data for 5: Colorless viscous liquid, ^1H NMR ($CDCl_3$, δ) 3.63 (s + m, 33H), 4.51 (s, 2H), 7.29 (s, 5H). IR (neat) 1114 (C-O) cm^{-1}. MS 473 (M+1). Elem. Anal. Calcd. for $C_{24}H_{40}O_9$: C, 61.00; H, 8.53. Found: C, 60.74; H, 8.34.

(8) Data for 2: Colorless viscous liquid, ^1H NMR ($CDCl_3$, δ) 2.85 (br s, 1H), 3.65 (s, 33H). IR (neat): 3454 (O-H), 1114 (C-O) cm^{-1}. MS 383 (M+1). Elem. Anal. Calcd. for $C_{17}H_{34}O_9$: C, 53.39; H, 8.96. Found: C, 53.19; H, 8.99.

(Received in USA 15 December 1982)