Tetrahedron Letters,Vol.26,No.15,pp 1787-1790,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

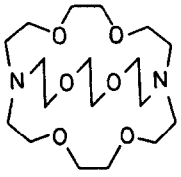
SYNTHESIS OF CRYPTANDS WITH ONE CARBON AND ONE NITROGEN BRIDGEHEAD ATOM

Byungki Son, Bronislaw P. Czech and Richard A. Bartsch*

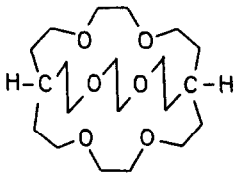
Department of Chemistry, Texas Tech University, Lubbock, Texas 79409

Summary: Two novel cryptands which each contains one carbon and one nitrogen atom at the bridgehead positions are synthesized and found to form strong complexes with lithium cations.

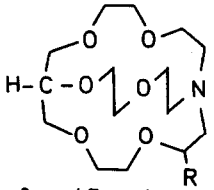
Macrobicyclic polyethers (cryptands) which contain two nitrogen atoms at the bridgehead positions (eg. 1) were prepared by Lehn[1-3] and found to be strong and selective binders for various metal cations. Another type of cryptand has two carbon bridgehead positions (eg. 2).[4-8] In general, such compounds are poorer metal ion complexing agents than the nitrogen bridgehead cryptands. We now report the first examples of novel cryptands 3 which contain one carbon and one nitrogen atom at the bridgehead positions.



1



2

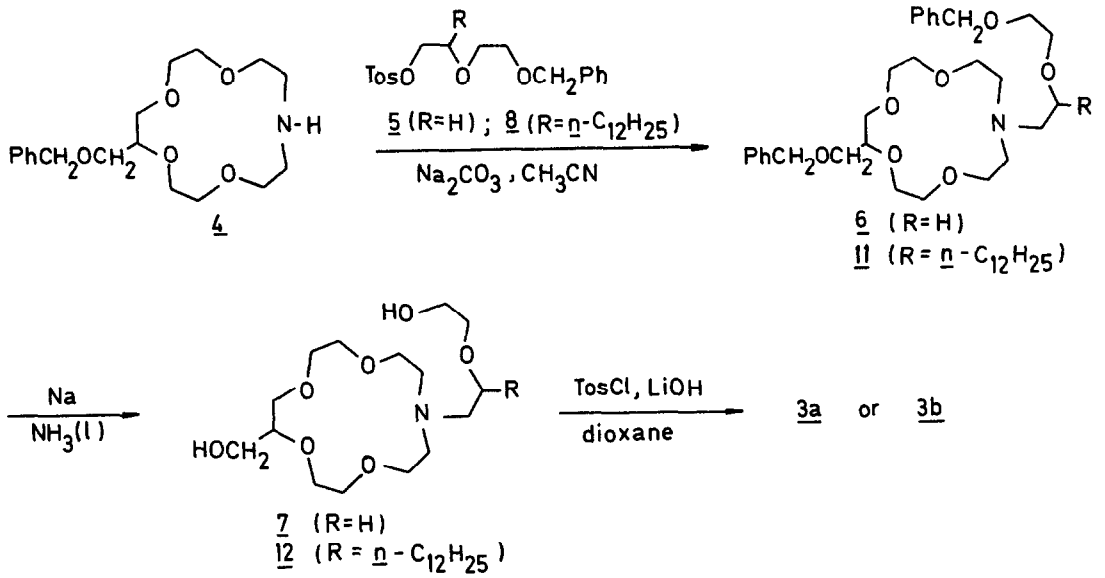


3a (R=H)

3b (R=n-$C_{12}H_{25}$)

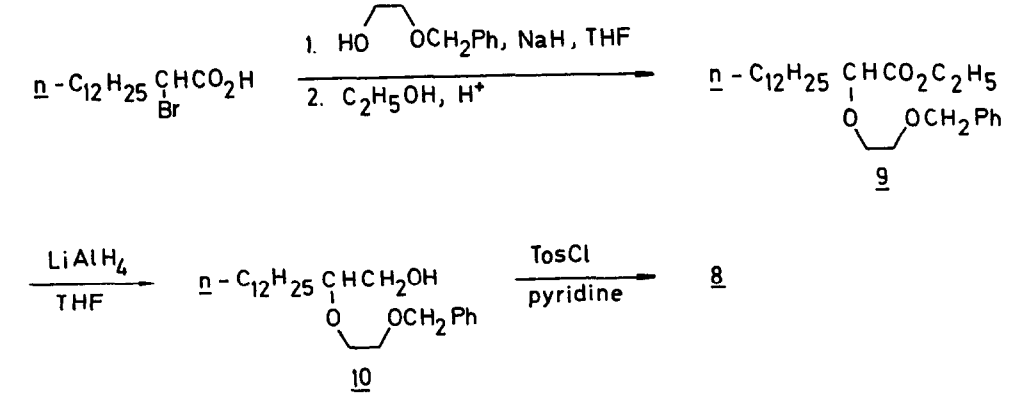
Synthesis of the parent cryptand 3a (Scheme 1) began with reaction of the benzyloxymethyl monoazacrown 4 [9] and the tosylate of monobenzyl-protected diethylene glycol (5)[10] in the presence of anhydrous sodium carbonate in acetonitrile to afford the dibenzyl ether 6 [12] in 76% yield. Debenzylation of 6 with sodium in liquid ammonia[13] produced a 93% yield of the macrocyclic diol 7.[14] An Okahara-type cyclization[15] of diol 7 in dioxane which involves in situ monotosylation with tosyl chloride and subsequent cyclization in the presence of lithium hydroxide gave, after column chromatography on alumina (EtOAc-MeOH, 3:1), cryptand 3a as a lithium hydroxide complex[16] in 35% yield.

The monobenzyl-protected diethylene glycol 8 required for the synthesis of the lipophilic cryptand 3b was prepared by the synthetic sequence shown in Scheme 2. Reaction of monobenzyl-protected ethylene glycol[17] with sodium hydride in THF and then with 2-bromotetradecanoic



Scheme 1

acid gave a crude product which was readily esterified to give the ethyl ester 9 [18] in 55% yield. Reduction of 9 with lithium aluminum hydride in THF provided an 81% yield of the lipophilic alcohol 10 [19] which was converted into its tosylate 8 in 97% yield.



Scheme 2

Treatment of monoazacrown 4 with tosylate 8 and sodium carbonate in acetonitrile gave the lipophilic dibenzyl-protected compound 11 [21] in 30% yield. Debenzylation with sodium in liquid ammonia produced a 58% yield of the lipophilic diol 12,[22] which was cyclized with tosyl

chloride and lithium hydroxide in dioxane to afford, after column chromatography on alumina (EtOAc-MeOH, 24:1), a 23% yield of lipophilic cryptand 3b as a complex with lithium hydroxide.[23]

Isolation of the lithium hydroxide complexes of cryptands 3a and 3b was verified by infrared and proton magnetic resonance spectra and by elemental analysis. The mass spectrum of each complex exhibited a molecular ion peak for the free cryptand. Strong complexation of lithium cations by 3a and 3b is in accord with the reported strong binding of lithium cations by Lehn's two nitrogen bridgehead atom cryptand [2.1.1][3] which should have an internal cavity of similar dimensions to those of 3a and 3b.

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

References and Notes

1. B. Dietrich, J. M. Lehn and J. P. Sauvage, Tetrahedron Lett., 2885, 2889 (1969).
2. B. Dietrich, J. M. Lehn, J. P. Sauvage and J. Blanzat, Tetrahedron 29, 1629 (1973).
3. B. Dietrich, J. M. Lehn and J. P. Sauvage, Tetrahedron 29, 1647 (1973).
4. A. C. Coxon and J. F. Stoddart, J. Chem. Soc., Perkin I, 767 (1977).
5. B. J. Gregory, A. H. Haines and P. Karntiang, J. Chem.Soc., Chem. Commun., 918 (1977).
6. A. H. Haines and P. Karntiang, J. Chem. Soc., Perkin I, 2577 (1979).
7. Y. Nakatsuji, T. Mori and M. Okahara, J. Chem. Soc., Chem. Commun. 1045 (1984).
8. B. L. Allwood, S. E. Fuller, P.C.Y.K. Ning, A.M.Z. Slawin, J. F. Stoddart and D. J. Williams, J. Chem. Soc., Chem. Commun., 1356 (1984).
9. B. Son, B. Czech and R. A. Bartsch, Synthesis, 776 (1984).
10. Compound 5 was obtained from monobenzyl diethylene glycol[11] by tosylation in 93% yield as a pale yellow oil: ^{1}HNMR ($CDCl_3$,δ)2.32(s,3H), 3.3-3.85(m,6H), 3.9-4.3(m,2H), 4.45(s,2H), 7.1-7.9(m,9H); IR(neat,cm^{-1}) 1356, 1190, 1176 [$S(=O)_2$], 1140, 1097 (C-O). Elem. anal. calcd. for $C_{18}H_{22}O_5S$: C, 61.69; H, 6.33. Found: C, 61.76; H, 6.48.
11. H. Johnson, J. Pharm. Sci., 64, 693 (1975).
12. Data for 6: colorless oil; ^{1}HNMR ($CDCl_3$,δ) 2.6-3.1(m,6H), 3.2-4.1(m,23H), 4.64(s,4H), 7.33(s,10H); IR(neat,cm^{-1}) 1105(C-O). Elem. anal. calcd. for $C_{29}H_{43}NO_7$: C,67.29; H.8.37. Found: C,67.11; H,8.25.
13. E. J. Reist, V. J. Bartuska and L. Goodman, J. Org. Chem., 29, 3725 (1964).
14. Data for 7: colorless oil; ^{1}HNMR ($CDCl_3$,δ)2.5-3.1(m,6H); 3.1-4.3(m,25H); IR(neat,cm^{-1}) 3488(O-H), 1112(C-O). Elem. anal. calcd. for $C_{15}H_{31}NO_7$: C,53.40; H,9.26. Found : C,53.10; H,9.30.
15. P. L. Kuo, M. Miki and M. Okahara, J. Chem. Soc., Chem. Commun., 504 (1978).
16. Data for 3a·LiOH : colorless oil; ^{1}HNMR ($CDCl_3$,δ)2.6-3.1(m,6H), 3.3-4.2(m,23H); IR(neat, cm^{-1})1124(C-O); MS 319 (M^+ for 3a). Elem. anal. calcd. for $C_{15}H_{29}NO_6$·LiOH : C,52.47; H,8.80. Found : C,52.44; H,8.85.
17. C. L. Butler, A. G. Renfrew and M. Clapp, J. Am. Chem. Soc., 60, 1472 (1938).
18. Data for 9 : colorless oil; ^{1}HNMR ($CDCl_3$,δ)0.65-1.90(m,28H), 3.63(brs,4H), 3.7-4.35(m,3H), 4.51(s.2H), 7.28(s,5H); IR(neat,cm^{-1}) 1755(C=O),1115(C-O). Elem. anal. calcd. for

$C_{25}H_{42}O_4$: C,73.85; H,10.41. Found : C,74.07; H,10.24.

19. Data for 10 ; colorless oil; ^{1}HNMR($CDCl_3$,δ)0.7-1.6(m,25H), 2.8-3.85(m,8H), 4.42(s,2H), 7.28(s,5H); IR(neat,cm^{-1}) 3448(O-H), 1101(C-O). Elem. anal. calcd. for $C_{23}H_{40}O_3$: C,75.78; H,11.06. Found : C,75.73; H,11.21.
20. Data for 8 : pale yellow oil; ^{1}HNMR($CDCl_3$,δ)0.7-1.6(m,25H),2.40(s,3H), 3.57(m+s,5H), 3.98 (d,2H), 4.47(s,2H), 7.25(s,5H), 7.45(ABq.4H); IR(neat,cm^{-1}) 1363, 1190,1178[$S(=O)_2$], 1097(C-O). Elem. anal. calcd. for $C_{30}H_{46}O_5S$: C,69.46; H,8.94. Found : C,69.79; H,8.95.
21. Data for 11 : colorless oil; ^{1}HNMR($CDCl_3$,δ)0.7-1.7(m,25H), 2.3-3.1(m,6H), 3.2-4.0(m,22H), 4.54(s,4H),7.31(s,10H); IR(neat,cm^{-1}) 1105(C-O). Elem. anal. calcd. for $C_{41}H_{67}NO_7$: C,71.79; H,9.84. Found : C,71.50; H,9.65.
22. Data for 12 : pale yellow oil; ^{1}HNMR($CDCl_3$,δ)0.7-1.8(m,25H), 2.4-3.1(m,6H), 3.2-4.2(m,24H); IR(neat,cm^{-1}) 3281(O-H), 1116(C-O). Elem. anal. calcd. for $C_{27}H_{55}NO_7 \cdot 0.5H_2O$: C,63.00; H,10.97. Found : C,62.89; H,10.85.
23. Data for 3b·LiOH : colorless oil; ^{1}HNMR($CDCl_3$,δ)0.7-1.6(m,25H),2.4-3.1(m,6H), 3.2-4.2 (m,22H); IR(neat,cm^{-1}) 1132(C-O); MS 488(M^+ for 3b). Elem. anal. calcd. for $C_{27}H_{53}NO_6 \cdot$ LiOH : C,63.38; H,10.64, Found : C,63.63; H,10.52.

(Received in USA 28 December 1984)