

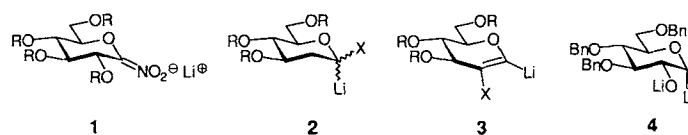
- [4] A. Schmidpeter, G. Jochem, *Tetrahedron Lett.* **1992**, *33*, 471–474.
 [5] K. Karaghiosoff, G. Jochem, A. Schmidpeter, unpublished.
 [6] S. Lochschmidt, A. Schmidpeter, *Phosphorus Sulfur* **1986**, *29*, 73–109.
 [7] a) G. A. Gray, *J. Am. Chem. Soc.* **1973**, *95*, 7736–7742; b) G. Fronza, P. Bravo, C. Ticozzi, *J. Organomet. Chem.* **1978**, *157*, 299–310; c) M. Schlosser, T. Jenny, B. Schaub, *Heteroat. Chem.* **1990**, *1*, 151–156.
 [8] If the phosphonio group at the C atom and the substituent at the P atom of a phosphalkene are fixed *cis* to each other in a ring, then $^2J(\text{P,P}) \approx 50$ Hz. E. Fluck, G. Becker, B. Neumüller, R. Knebl, G. Heckmann, H. Riffel, *Z. Naturforsch. B* **1987**, *42*, 1213–1221.
 [9] In fact, compound **5b** stays ionic and the bromide ion does not associate with the two-coordinate phosphorus. The same applies to compound **5c**, which is generated from **3c** and $\text{Et}_3\text{NSiMe}_3$ and has NEt_2 instead of SCH_2Ph and Cl^- instead of Br^- [4], for which similar ^{31}P NMR data were obtained.
 [10] A. Schmidpeter, G. Jochem, K. Karaghiosoff, C. Robl, *Angew. Chem.* **1992**, *104*, 1420–1441; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1350–1352.
 [11] a) 2,4,6-Tri-*tert*-butylphenyldithioxophosphorane: R. Appel, F. Knoch, H. Kunze, *Angew. Chem.* **1983**, *95*, 1008–1009; *Angew. Chem. Int. Ed. Engl.* **1983**, *22*, 1004–1005. b) 2,6-Di-*tert*-butyl-4-methylphenyldithioxophosphorane: A. S. Ionkin, V. M. Nekhoroshkov, Y. Y. Efremov, *Izv. Akad. SSSR Ser. Khim.* **1991**, 1654–1656; *Chemical Abstracts* **1991**, *115*, 208108s; see also [11 c]. c) 2,6-Bis(trifluoromethyl)phenyldithioxophosphorane: G. Grossmann, G. Ohms, H. Beckmann, K. Friedrich, E. Niecke, M. Nieger, R. Serwas, V. von der Gönna, W. W. Schoeller, *Abstr. XIth Int. Conf. Phosphorus Chem.*, Toulouse, **1992**. Proceedings: *Phosphorus Sulfur Silicon Relat. Elem.* **1993**, *77*, 248.
 [12] X-ray diffraction crystal structure determination: Data were collected at 293 K, Siemens P4/V diffractometer, MoK_α radiation ($\lambda = 0.71073$ Å), graphite monochromator. The structures were solved by direct methods (SHELXTL PLUS, PC version). (Non-hydrogen atoms anisotropic, H atoms in calculated positions and included in the refinement using the riding model $U_{i,H} \approx 1.2 U_{eq}$. c). – **4b**: orange-yellow plates, $\text{C}_{21}\text{H}_{20}\text{P}_2\text{S}$, $M_r = 366.4$, triclinic, space group $P\bar{1}$; $a = 9.343(4)$, $b = 10.791(5)$, $c = 10.816(5)$ Å, $\alpha = 62.72(1)^\circ$, $\beta = 86.55(1)^\circ$, $\gamma = 85.95(2)^\circ$, $V = 966(1)$ Å³, $Z = 2$, $\rho_{\text{calcd.}} = 1.259$ g cm⁻³, $F(000) = 756$, $\mu = 3.32$ cm⁻¹; ω -scans, $2.0^\circ \leq 2\theta \leq 48^\circ$, 3125 measured reflections, of which 2929 were independent ($R_{\text{int}} = 0.0333$), 1904 with $|F| > 3\sigma(F)$. The full-matrix least-squares refinement resulted in $R = 0.0572$ and $R_w = 0.0576$. – **6c**: $0.5 \text{ C}_6\text{H}_6$: yellow prisms, $\text{C}_{29}\text{H}_{23}\text{P}_2\text{S}_2$, $M_r = 485.5$, triclinic, space group $P\bar{1}$; $a = 9.182(2)$, $b = 11.063(2)$, $c = 13.327(2)$ Å, $\alpha = 89.99(1)^\circ$, $\beta = 76.68(1)^\circ$, $\gamma = 78.21(1)^\circ$, $V = 1288.0(5)$ Å³, $Z = 2$, $\rho_{\text{calcd.}} = 1.252$ g cm⁻³, $F(000) = 506$, $\mu = 3.45$ cm⁻¹; ω -scans, $2.0 \leq 2\theta \leq 50^\circ$, 5398 measured reflections, of which 4486 were independent ($R_{\text{int}} = 0.159$), 3671 with $|F| > 3\sigma(F)$. The full-matrix least-squares refinement resulted in $R = 0.0528$ and $R_w = 0.0569$. Further details of the crystal structure investigation may be obtained from the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-76344 Eggenstein-Leopoldshafen (FRG), on quoting the depository number CSD-57193, the names of the author, and the journal citation.
 [13] a) H. Schmidbauer, J. Jeong, A. Schier, W. Graf, D. L. Wilkinson, G. Müller, *New J. Chem.* **1989**, *13*, 341–352; b) M. A. Vincent, H. F. Schaefer III, A. Schier, H. Schmidbauer, *J. Am. Chem. Soc.* **1983**, *105*, 3806–3811, and references therein.
 [14] V. D. Romanenko, L. N. Markovskii, A. V. Ruban, *Compounds of Low-Valent Five-Coordinate Phosphorus* (English translation of title), Naukova Dumka, Kiev, **1992**, p. 138.
 [15] H. W. Roesky, R. Ahlrichs, S. Brode, *Angew. Chem.* **1986**, *98*, 91–93; *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 82–83.

Stereoselective Synthesis of C-Glycosides with a Glycosyl Dianion**

By Valentin Wittman and Horst Kessler*

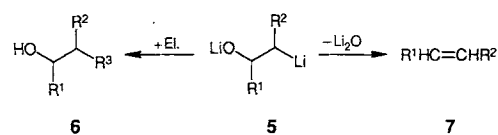
During the past few years the interest in the synthesis of C-glycosides^[1] has greatly increased. This is chiefly due to the discovery of C-glycosidic or analogue structures in many natural products,^[2] and their potential use as antimetabolites.^[3] As with the synthesis of O-glycosides, the traditional

approach to C-glycosides is based upon the addition of a suitable C-nucleophile to the electrophilic anomeric center of a 1-activated carbohydrate. The use of glycosyl radicals^[1,4] and glycosylidene carbenes^[5] has also been described. Direct 1-C-lithiation of sugars generally leads to the elimination of functional groups in the 2-position.^[6] Paulsen et al. first reported the C-elongation of open-chain carbohydrates by polarity inversion (umpolung) at the anomeric center via dianions of hydroxy-1,3-dithianes.^[7] However, in the case of pyranoses the concept of umpolung has been limited so far to 1-nitrosugars **1**,^[8] 2-deoxysugars **2** ($X = \text{H}$,^[6 a,9] SO_2PH ,^[10] PPh_3 ,^[11] CO_2R ^[12]), and glycols **3** ($X = \text{H}$,^[9 d,13] SOPh ,^[14] SPh ,^[15] OBn ^[15]). Chain elongation of nitrosugars **1** followed by substitution of the nitro group by a hydroxy group leads to higher ketopyranoses with the added residue in the equatorial position. Glycols **3** offer the possibility of subsequent introduction of the missing hydroxy group and therefore access to β -C-glycosides.

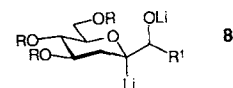


In this communication we present the application of the dilithio compound **4** in the synthesis of C-glycosides. Simple lithiation of the 2-hydroxy group functions both as a means of protection, and efficiently prevents β elimination. Subsequent reaction with electrophiles directly produces 2-hydroxy-substituted C-glucopyranosides, exclusively with α -configuration (see Scheme 1).

Dianions of the general type **5** may be obtained from β -hydroxy organomercury compounds,^[16] chlorohydrins,^[17] epoxides,^[18] carbonyl compounds,^[10 a,19] or hydroxy-1,3-dithianes,^[7] and were used either as carbanions for C–C-coupling reactions (**5** \rightarrow **6**, $\text{El.} = \text{electrophile}$)^[7,16–18,19 a] or in the synthesis of olefins by Li_2O elimination (**5** \rightarrow **7**).^[19,20]



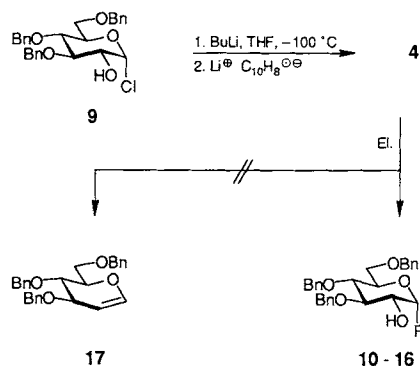
The suitability of **4** for chain elongation reactions at the anomeric center or its tendency to eliminate to give the glucal were not readily predictable. It was reported,^[17] for example, that compounds **5** in which lithium is located at a primary carbon ($\text{R}^2 = \text{H}$) are stable up to -60°C . On the other hand in the case of $\text{R}^2 = \text{alkyl}$, they decompose spontaneously even at -100°C to the olefin by β elimination. Only compounds **5** with stabilizing substituents like $\text{R}^2 = \text{Ph}$ or CO_2Et , or cyclic β -lithiocyclohexanolate ($\text{R}^1,^{[10]} \text{R}^2 = -(\text{CH}_2)_4-$) can be converted into the corresponding deuterated alcohols **6** ($\text{R}^3 = \text{D}$). Beau and Sinay have postulated^[10] the presence of the dilithio derivative **8** and demonstrated that protonation without β elimination is possible.



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In a first experiment we treated 3,4,6-tri-O-benzyl- α -D-glucopyranosyl chloride **9**^[21] in THF at -78°C dropwise with 1.1 equivalents of *n*-butyllithium (to generate the alcoholate), and after 15 minutes with 2.2 equivalents of lithium naphthalenide. After a further 15 minutes, quenching with MeOD, work up under acidic conditions, and chromatography on silica gel yielded a mixture of deuterated sugar **10** (66%), the corresponding β -configured compound (3.1%), and the protonated compound **11** (17%) (Scheme 1). These products suggest that the dilithio com-



Scheme 1. Synthesis of the α -C-glucosides **10–16** (cf. Table 1). Bn = CH_2Ph , El. = electrophile.

ound **4** was formed intermediately during the reaction. The axial configuration of deuterium in **10** is based on the ^1H NMR spectrum (250 MHz, CDCl_3 , $^3J_{\text{H}1, \text{H}2} = 5.3$ Hz). The α/β ratio of 21:1 was determined by deuterium NMR spectroscopy. Obviously no Li_2O elimination leading to 3,4,6-tri-O-benzyl-D-glucal **17** takes place under these conditions.

Table 1. Results of the C-glucoside synthesis according to Scheme 1.

Electrophile	Product [a]	R	Yield [%] [b]
MeOD	10	D	75
MeOH	11	H	82
MeCHO	12 a/b	CH(OH)Me	62
PhCHO	13 a/b	CH(OH)Ph	70
<i>i</i> PrCHO	14 a/b	CH(OH) <i>i</i> Pr	59
HCHO	15 [23]	CH_2OH	17
MeI [c]	16	Me	72

[a] Products were characterized by ^1H and ^{13}C NMR spectroscopy (see Table 2) and FAB-MS. [b] Yields of α -anomers after chromatography on silica gel. [c] Addition of 10% CuI.

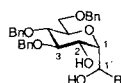
The best yields were obtained by *quick* addition of the lithiated sugar **4** in the synthesis of α -C-glucosides. To avoid undue increase of reaction temperature, a precooled lithium naphthalenide solution (-78°C) is recommended. However, since the solubility of lithium naphthalenide in THF is greatly reduced at this temperature, it is better to work at -100°C and add the reagent uncooled. The results presented in Table 1 were obtained by using the latter method.

We next turned our attention to the possibility of using the lithiated sugar **4** in the synthesis of α -C-glucosides. The reaction of **4** with acetaldehyde affords a mixture of diastereomers **12 a/b**^[22] (ratio 1.4:1) in 62% yield. In the same manner benzaldehyde and isobutyraldehyde produced **13 a/b** (1:1, 70%) and **14 a/b** (1:1, 59%), respectively. In all cases axial configured C-glucosides were produced with high stereoselectivity ($\alpha/\beta \geq 20:1$). The use of gaseous formalde-

Table 2. Selected ^1H and ^{13}C NMR chemical shifts (δ values) and coupling constants J [Hz] of **10–16** [a,b]. ax = axial, eq = equatorial, n.d. = not determinable.

Compd.	H-1	H-2	H-1'	C-1	C-2	C-1'	$^3J_{\text{H}1, \text{H}2}$
10	3.95	3.69		69.1	70.0		5.3
11	3.97 (eq)	3.69		69.5	70.1		5.3 (eq-ax)
	3.18 (ax)						11.1 (ax-ax)
12 a	3.50	3.69	4.04	73.6	67.6	67.7	1.6
12 b	3.57	3.98	4.10	73.7	68.4	67.0	2.9
13 a	3.75	3.34	4.97	73.8	66.1	73.9	1.0
13 b	3.93	3.93	5.00	72.4	67.4	74.0	n.d. [c]
14 a	3.78	3.75	3.60	69.2	68.9	76.8	<1.0
14 b	3.77	3.97	3.77	69.8	68.1	74.3	2.0
15	3.97	3.76	3.76	71.1	68.7	62.2	2.7
			3.87				
16	4.09	3.61	1.23	68.1	70.4	14.2	3.8

[a] NMR spectra in CDCl_3 at 300 K, internal standard TMS. ^1H : 500 MHz, ^{13}C : 125 MHz. [b] To facilitate comparison, atoms are numbered following that used for the starting sugar **9**.



[c] Identical chemical shifts of H1 and H2.

hyde gave the desired hydroxymethyl C-glucoside **15** in an unsatisfactory 17% yield; in this case large quantities of polyoxymethylene were formed. However, alkylation of the dianion **4** with MeI proceeded without complications to give α -methyl-C-glucoside **16** in 58% yield. An improved yield of 72% could be obtained by addition of 10% of CuI before addition of the electrophile.

It is remarkable that the formation of tribenzylglucal **17** was not observed under any circumstances. Thus, the dilithio compound **4** proves to be a species which is stable at -78°C and reacts with electrophiles with *retention* of configuration at the anomeric center to give a variety of 2-hydroxy- α -C-glucosides. The precursor **9** is crystalline and stable at -20°C ,^[21] and is easily obtained from acetobromoglucose in a four-step synthesis in an overall yield of approximately 55%.

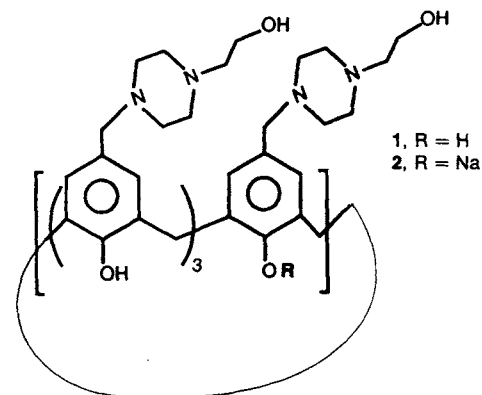
Experimental Procedure

Under argon a 0.15 M solution of **9** in dry THF at -100°C was treated with 1.1 equivalents of *n*BuLi (1.6 M in THF), followed by quick addition of 2.2 equivalents of lithium naphthalenide (1 M in THF). After 15 minutes, 1.5 equivalents of aldehyde or MeI were added, and the mixture was stirred for 1 h at -100°C and then allowed to warm up to room temperature. A saturated aqueous solution of NH_4Cl was added and the mixture extracted with dichloromethane. After the organic layer had been dried over MgSO_4 , the product was purified by chromatography on silica gel (eluent: toluene/ethyl acetate or hexane/ethyl acetate).

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- [1] For an excellent overview see: M. H. D. Postema, *Tetrahedron* **1992**, *48*, 8545–8599 and references cited therein.
- [2] a) G. Franz, M. Grün, *Planta Med.* **1983**, *47*, 131–140; b) S. Hanessian, *Total Synthesis of Natural Products: The 'Chiron' Approach*, Pergamon Press, Oxford, **1983**.
- [3] a) C. Bertozzi, M. Bednarski, *Carbohydr. Res.* **1992**, *223*, 243–253; b) K. Krohn, H. Heins, K. Wielckens, *J. Med. Chem.* **1992**, *35*, 511–517; c) R. R. Schmidt, H. Dietrich, *Angew. Chem.* **1991**, *103*, 1348–1349; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1328–1329.
- [4] a) B. Giese, T. Linker, R. Muhn, *Tetrahedron* **1989**, *45*, 935–940; b) H. Kessler, V. Wittmann, M. Köck, M. Kottenhahn, *Angew. Chem.* **1992**, *104*, 874–877; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 902–904.
- [5] A. Vasella, C. Witzig, R. Husi, *Helv. Chim. Acta*, **1991**, *74*, 1362–1372.
- [6] a) J.-M. Lancelin, L. Morin-Allory, P. Sinaÿ, *J. Chem. Soc. Chem. Commun.* **1984**, 355–356; b) R. R. Schmidt, J. Kast, *Tetrahedron Lett.* **1986**, *27*, 4007–4010.

- [7] H. Paulsen, K. Roden, V. Sinnwell, P. Luger, *Liebigs Ann. Chem.* **1981**, 2009–2027.
- [8] a) B. Aebischer, J. H. Bieri, R. Prewo, A. Vasella, *Helv. Chim. Acta* **1982**, *65*, 2251–2272; b) K. Mahmood, A. Vasella, B. Bernet, *ibid.* **1991**, *74*, 1555–1583.
- [9] a) P. Lesimple, J.-M. Beau, P. Sinaÿ, *J. Chem. Soc. Chem. Commun.* **1985**, 894–895; b) J.-M. Beau, P. Sinaÿ, *Tetrahedron Lett.* **1985**, *26*, 6185–6188; c) P. Lesimple, J.-M. Beau, P. Sinaÿ, *Carbohydr. Res.* **1987**, *171*, 289–300; d) J. Prandi, C. Audin, J.-M. Beau, *Tetrahedron Lett.* **1991**, *32*, 769–772; e) D. K. Hutchinson, P. L. Fuchs, *J. Am. Chem. Soc.* **1987**, *109*, 4930–4939.
- [10] a) J.-M. Beau, P. Sinaÿ, *Tetrahedron Lett.* **1985**, *26*, 6189–6192; b) J.-M. Beau, P. Sinaÿ, *ibid.* **1985**, *26*, 6193–6196.
- [11] J. B. Ousset, C. Mioskowski, Y.-L. Yang, J. R. Falck, *Tetrahedron Lett.* **1984**, *25*, 5903–5906; Cf. also: S. V. Ley, B. Lygo, *ibid.* **1984**, *25*, 113–116.
- [12] a) D. Crich, L. B. L. Lim, *Tetrahedron Lett.* **1990**, *31*, 1897–1900; b) K. Wallimann, A. Vasella, *Helv. Chim. Acta* **1991**, *74*, 1520–1532.
- [13] a) K. C. Nicolaou, C.-K. Hwang, M. E. Duggan, *J. Chem. Soc. Chem. Commun.* **1986**, 925–926; b) S. Hanessian, M. Martin, R. C. Desai, *ibid.* **1986**, 926–927; c) P. Lesimple, J.-M. Beau, G. Jaurand, P. Sinaÿ, *Tetrahedron Lett.* **1986**, *27*, 6201–6204; d) K. A. Parker, C. A. Coburn, *J. Am. Chem. Soc.* **1991**, *113*, 8516–8518.
- [14] a) R. Preuss, R. R. Schmidt, *Liebigs Ann. Chem.* **1989**, 429–434; b) R. R. Schmidt, R. Preuss, *Tetrahedron Lett.* **1989**, *30*, 3409–3412; c) S. Maier, R. Preuss, R. R. Schmidt, *Liebigs Ann. Chem.* **1990**, 483–489.
- [15] R. R. Schmidt, R. Preuss, R. Betz, *Tetrahedron Lett.* **1987**, *28*, 6591–6594.
- [16] J. Barluenga, F. J. Fananas, J. Villamana, M. Yus, *J. Org. Chem.* **1982**, *47*, 1560–1564.
- [17] a) C. Najera, M. Yus, D. Seebach, *Helv. Chim. Acta* **1984**, *67*, 289–300; b) J. Barluenga, J. Florez, M. Yus, *J. Chem., Soc. Perkin Trans. 1* **1983**, 3019–3026.
- [18] a) T. Cohen, I.-H. Jeong, B. Mudryk, M. Bhupathy, M. M. A. Awad, *J. Org. Chem.* **1990**, *55*, 1528–1536; b) E. Bartmann, *Angew. Chem.* **1986**, *98*, 629–631; *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 653–654.
- [19] a) J. Barluenga, J. L. Fernandez-Simon, J. M. Concellon, M. Yus, *J. Chem. Soc., Perkin Trans. 1* **1988**, 3339–3343; b) J. Barluenga, F. Alvarez, J. M. Concellon, M. Yus, *J. Chem. Res. (S)* **1987**, 402–403; (*M*) 3265–3285.
- [20] K. N. Gurudutt, B. Ravindranath, *Tetrahedron Lett.* **1980**, *21*, 1173–1174.
- [21] H. Yamaguchi, C. Schuerch, *Carbohydr. Res.* **1980**, *81*, 192–195.
- [22] Here **a** and **b** refer to the diastereomers produced by addition to both stereoheterotopic faces of the prochiral aldehyde, which are separable by chromatography on silica gel.
- [23] G. Stork, H. S. Suh, G. Kim, *J. Am. Chem. Soc.* **1991**, *113*, 7054–7056.



remove the compound causing these signals were unsuccessful. Subsequently, a single-crystal X-ray diffraction study^[12] revealed the presence of a guest in the cavity (Fig. 1). This molecule appears to be unreacted, excess 1-(2-hydroxyethyl)piperazine that has been methylated at the position of the secondary nitrogen. Although the hydroxyethyl chain of this molecule is badly disordered (and thus not shown in Fig. 1), the remainder of the atoms are better defined. The ¹H and ¹³C NMR spectra are also consistent with the presence of two different hydroxyethylpiperazine moieties.^[13] As Figure 1 reveals, the arms of the calix[4]arene are spread wide to provide a shallow cavity similar to that found in *p*-sulfonatocalix[4]arene.^[3–9]

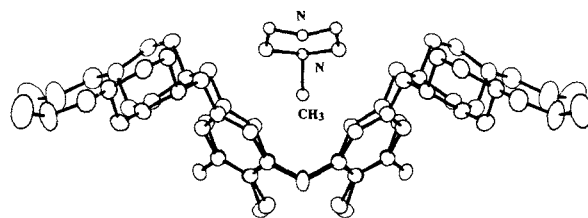


Fig. 1. Structure of *p*-[4-(2-hydroxyethyl)piperazinomethyl]calix[4]arene with the guest $\text{CH}_3\text{N}(\text{CH}_2\text{CH}_2)_2\text{NCH}_2\text{CH}_2\text{OH}$. The $-\text{CH}_2\text{CH}_2\text{OH}$ portion of the guest molecule was badly disordered and is not shown.

Supramolecular Complexes of Flexible, Extended Cavity Calix[4]arenes—Structural Characterization of a Molecular Venus Flytrap**

By Jerry L. Atwood,* G. William Orr, Simon G. Bott, and Kerry D. Robinson

The ability of calix[4]arenes to form supramolecular complexes has been responsible for much of the current interest in these macrocycles.^[1, 2] While *p*-sulfonatocalix[4]arene has been shown to bind to a range of small molecules and ions,^[3–9] there exists a need for calix[4]arenes with larger cavities possessing more binding possibilities. In search of deep-cavity calix[4]arenes, Gutsche and Nam reported^[10] in 1988 that calix[4]arene undergoes acetic acid-catalyzed aminomethylation in the presence of formaldehyde and dimethylamine in THF. We have now expanded on this Mannich reaction^[11] to synthesize a wide range of aminomethylcalix[4]arenes. One of these, *p*-[4-(2-hydroxyethyl)piperidinomethyl]calix[4]arene (**1**), possesses a flexible binding capability reminiscent of the capture of insects by the Venus flytrap.

In the original synthesis of **1** unidentified resonances appeared in both the ¹H and ¹³C NMR spectra, and efforts to

Preparation of **1** and subsequent neutralization with 10% Na_2CO_3 solution to pH 9 leads to the removal of one of the phenolic protons resulting in the complex **2**. Following crystallization from ethyl acetate, **2** was dried under vacuum for 48 h at 120 °C. The ¹H NMR spectrum revealed that even

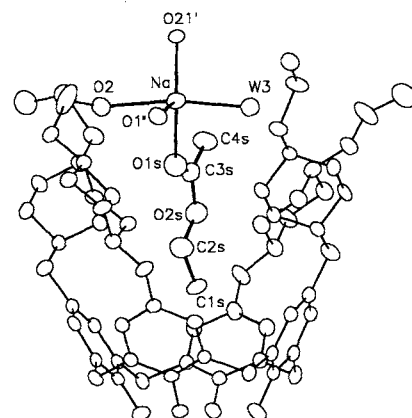


Fig. 2. Structure of $\text{Na}[p\text{-[4-(2-hydroxyethyl)piperazinomethyl]calix[4]arene}] \cdot \text{CH}_3\text{COOCH}_2\text{CH}_3$.

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