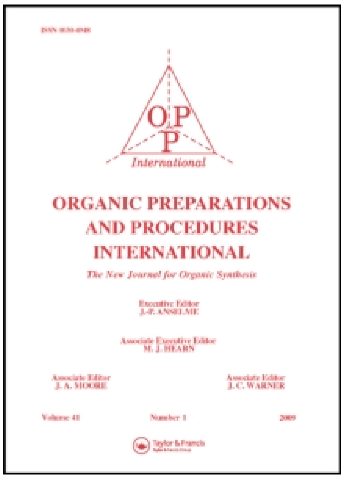


Organic Preparations and Procedures International

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

PREPARATION OF NEW 4',5'-DISUBSTITUTED BENZOCROWN ETHERS

Haluk Akkus[a]; Ahmet Gül[a]
[a] Department of Chemistry, Technical University of Istanbul, Maslak, Istanbul, TURKEY

To cite this Article Akkus, Haluk and Gül, Ahmet(1995) 'PREPARATION OF NEW 4',5'-DISUBSTITUTED BENZOCROWN ETHERS', Organic Preparations and Procedures International, 27: 6, 668 — 670
To link to this Article: DOI: 10.1080/00304949509458528
URL: http://dx.doi.org/10.1080/00304949509458528

PREPARATION OF NEW 4',5'-DISUBSTITUTED BENZOCROWN ETHERS

Submitted by
(12/19/94)

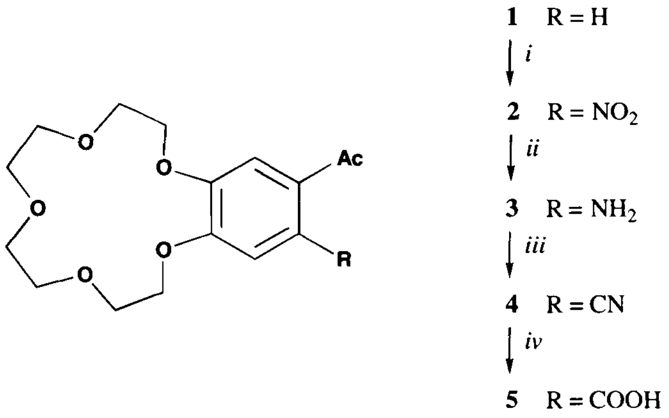
Haluk Akkus and Ahmet Gül*

Department of Chemistry
Technical University of Istanbul
80626 Maslak, Istanbul, TURKEY

Crown ethers have proved to be efficient building blocks in the design and synthesis of many chemical systems capable of performing specific functions with high selectivity.[1,2] In this context reactive groups are needed on the macrocycles to accomplish these functions. In the case of benzo-crown ethers, functional groups on the aromatic rings provide the only possibility for further reactions. Although it appears possible to prepare these macrocycles by starting from a suitably derived pyrocatechol,[2] it is usually not practical because of low yields of cyclization or difficulty in work-up procedures. Consequently, mono- and difunctional derivatives of benzocrown ethers are generally obtained starting from the parent macrocyclic compound.[3] The present paper describes new synthetic routes to previously unreported 4',5'-disubstituted benzocrown ethers.

Initial attempts to brominate 4'-acetylbenzo-15-crown-5 or to acetylate 4'-cyano- or 4'-bromo derivative at the *ortho* position were unsuccessful under a variety of conditions. The synthesis to 4'-acetylbenzo-15-crown-5-5'-carboxylic acid (**5**) was accomplished, starting with 4'-acetylbenzo-15-crown-5 (**1**) obtained by Friedel Crafts acetylation using polyphosphoric acid as catalyst, by the sequence of reactions shown.

The new compounds were characterized by elemental analyses, IR, ^{1}H NMR, ^{13}C NMR and mass spectra.



i) Conc.HNO$_3$; ii) Tin powder and conc. HCl; iii) diazotization with NaNO$_2$ and conc. HCl and then CuCl + NaCN; NaOH and then HCl.

EXPERIMENTAL SECTION

^{1}H and ^{13}C NMR Spectra were obtained on a Bruker 200 MHz spectrometer. IR spectra were recorded as KBr pellets on a Perkin Elmer 598 spectrophotometer. Elemental analyses were performed by the Instrumental Analysis Laboratory of TUBITAK Marmara Research Center. Benzo-15-crown-5 and 4'-acetylbenzo-15-crown-5 were synthesized according to the reported procedures.[4,3a]

4'-Acetyl-5'-nitrobenzo-15-crown-5 (2).- To a solution of 4'-acetylbenzo-15-crown-5 (11.47 g, 37 mmol) in 120 mL of glacial acetic acid was added 40 mL of conc. HNO_3 (65%) dropwise in 30 min at room temperature and the mixture was stirred overnight. Then 100 mL of water was added and the product was extracted with chloroform (8 x 50 mL). The organic phase was neutrallized with Na_2CO_3 solution (5%), washed with water and dried over anhydrous sodium sulfate. The yellow oily residue obtained after evaporation of the solvent, was triturated and crystallized from n-heptane to yield 7.88 g (60%) of pale yellow solid, mp.104°.

Hydrochloride Salt of 4'-Acetyl-5'-aminobenzo-15-crown-5 (3•HCl). -A mixture of **2** (35.5 g, 0.1 mol) and coarse tin powder (23.5 g, 0.2 mol) was treated with small portions of conc. HCl (150 mL) with cooling in ice. After completion of gas evolution, the reaction was continued for additional one hour at 100°. The solution was cooled to room temperature and made alkaline by addition of NaOH solution (100 mL, 50%). Then it was extracted with chloroform (8 x 50 mL) and the organic layer was dried over anhydrous Na_2SO_4. After evaporation of about 3/4 of chloroform the solution was treated with dry HCl gas to yield 27.4 g (75%) of the product as hydrochloride salt, mp. 202°.

4'-Acetyl-5'-cyanobenzo-15-crown-5 (4).- A solution of $NaNO_2$ (3.10 g, 45 mol) in water (15 mL) was added with stirring into a solution of **3•HCl** (16 g, 44 mol) in water in 15 min and the temperature was kept at 0° by addition of crushed ice. The presence of free nitrous acid was verified by testing with starch iodide paper. Then the mixture was cautiously neutralized by adding sodium carbonate. A cuprous cyanide solution[5] was prepared by reduction of $CuSO_4 \cdot 5H_2O$ (12.5 g, 50 mmol) with 3.15 g Na_2SO_3 in water (200 mL) and subsequent addition of excess NaCN (6.5 g, 130 mmol). The cold neutralized aqueous diazonium solution **(CAUTION!)** prepared above was added dropwise in 30 min to the CuCN solution (400 mL) also containing toluene (20 mL) while the temperature was kept in 0-5° range by external cooling. Reaction was immediate as evidenced by evolution of N_2 gas; the yellowish oily product formed was extracted into the toluene phase. The pure product (6.04 g, 41%) was obtained by evaporation of the solvent and subsequent recrystallization from toluene, mp. 92°. *m/z* (EI) = 336 $(M+1)^+$, 335 (M^+), 310 $(M\text{-}CN)^+$, 293 $(M\text{-}COCH_3)^+$.

4'-Acetylbenzo-15-crown-5-5'-carboxylic Acid (5).- A stirred mixture of 4 (3 g, 9 mmol), NaOH solution (10 %, 20 mL) and ethanol (0.5 mL) was refluxed for 1.5 hr during which time ammonia evolution was detected by wet litmus paper. The mixture was further heated for another 60 min to complete the ammonia evolution and ethanol evaporation. After cooling to room temperature, it was acidified with conc. HCl and the product was extracted with chloroform. The chloroform layer was washed with water until neutral and then dried over anhydrous sodium sulfate. Evaporation of the solvent resulted with an orange product of 2.4 g (75%) which was recrystallized from ethanol, mp.156°.

TABLE. Elemental Analyses and Characteristic Spectral Data

Compd.	IR (cm^{-1})	^1H NMR (δ)	^{13}C NMR (δ)	Analyses (Found) C	H	N
2	1695	7.59 (s, 1H)	192.3	54.08	5.92	3.94
	1290	6.73 (s, 1H)	154.06	(54.31)	(5.86)	(3.85)
	1125	2.48(s,3H)	151.3			
3•HCl	3400	7.24 (s, 1H)	186.3	53.11	6.64	3.87
	1660	7.01 (s, 1H)	150.2	(52.85)	(6.83)	(3.80)
	1625	5.85 (brs, 3H)	149.1			
4	2220	7.39 (s, 1H)	194.3	60.88	6.31	4.18
	1680	7.15 (s, 1H)	152.0	(60.63)	(6.25)	(4.30)
	1130	2.70 (s, 3H)	148.2			
5	3300-	10.03 (s, 1H)	194.3	57.63	6.21	-
	2500 (br)		174.8	(57.86)	(6.33)	-
	1740	7.49 (s, 1H)	153.6			
	1680	6.85 (s, 1H)	148.4			

Acknowledgement.- Financial support of this research from TÜBITAK-Turkey (No.TBAG 1326) is gratefully acknowledged.

REFERENCES

1. F. C. J. M. van Veggel, W. Verboom and D. N. Reinhoudt, *Chem. Rev.*, **94**, 279 (1994); H. An, J. S. Bradshaw, R. M. Izatt and Z. Yan, *Ibid.*, **94**, 939 (1994); I. O. Sutherland, in *"Crown Compounds: Toward Future Applications"* S. R. Cooper, Ed., VCH, Weinheim, 1992, p. 235.

2. E. M. Hyde, B. L. Shaw and I. Shephered, *J. Chem. Soc. Dalton Trans.*,1696 (**1978**).

3. a) R. Ungaro, B. El Haj and J. Smid, *J. Am. Chem. Soc.*, **98**, 5198 (1976); b) F. Wada and T. Matsuda, *Bull. Chem. Soc. Jpn*, **53**, 421 (1980); c) F. Wada, R. Arata, T. Goto, K. Kikukawa and T. Matsuda, *ibid.*, **53**, 2061 (1980); d) F. Wada, H. Hirayama, H. Namiki, K. Kikukawa and T. Matsuda, *ibid.*, **53**, 1473 (1980); e) A. Gül, A. I. Okur, A. Cihan, N. Tan and Ö. Bekaroglu, *J. Chem. Res. (S)*, 90 (1986); (M) 881 (1986); f) A. Gül, A. I. Okur, S. Can and and Ö. Bekaroglu, *Chem. Ber.*, **119**, 3870 (1986); g) V. Ahsen, E. Yılmazer, M. Ertas and Ö. Bekaroglu, *J. Chem. Soc. Dalton Trans.*, 401 (**1988**).

4. C. J. Pedersen, *J. Am. Chem. Soc.*, **89**, 7017 (1967).

5. C. S. Marvel and S. M. Mc Elvain, *Org. Syn. Coll. Vol. I*, 170 (**1941**).

****