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CAPPED CYCLOFRUCTAN. PREPARATION AND STRUCTURE DETERMINATION OF $6^A,6^C$-DI-*O*-(BIPHENYL-4,4'-DISULFONYL)-CYCLOINULOHEXAOSE

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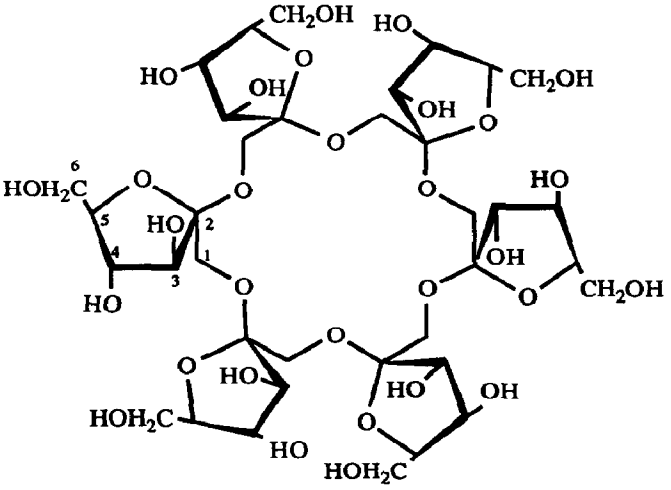
Abstract: A capped cyclofructan, $6^A,6^C$-di-*O*-(biphenyl-4,4'-disulfonyl)-cycloinulohexaose was selectively prepared by the reaction of cycloinulohexaose with biphenyl-4,4'-disulfonyl chloride in pyridine.

Cycloinulohexaose **1** [hereafter abbreviated as CF-6 (cyclofructan-6)] is a β-(2→1)-linked cyclohexaose of fructofuranose. This compound is an interesting molecule because it is produced from inulin by cycloinulooligosaccharide fructanotransferase[1] and has a chiral 18-crown-6 structure.[2,3] Its chemical modification should be investigated to apply the unique structure for constructing artificial enzymes or receptors. However, there has been only one example for chemically modified CF-6; per-*O*-methylated CF-6.[4]



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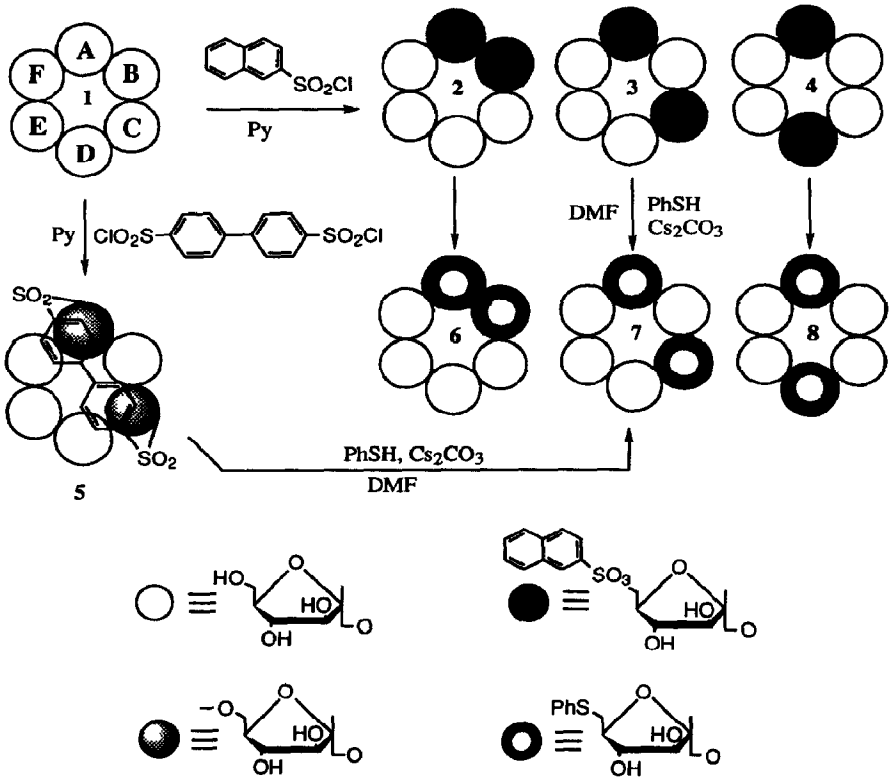
Sulfonylation on hydroxyls of CF-6 is important since the hydroxyls should be activated usually before their modification. Recently, we reported stepwise di-sulfonylation on the primary hydroxyls of CF-6 and

structure determination of the regiochemical isomers, $6^A,6^X$-bis[*O*-(2-naphthalenesulfonyl)]-CF-6 (X = B, C, and D) **2**-**4**[5] by the extended Körner method.[6] But, the stepwise preparation method is not appropriate for producing the disulfonates because the reaction was not regiochemically selective and the yield of each disulfonate was very low (**2**, 3.1%; **3**, 2.6%; **4**, 1.9%)

In this report, we describe one-stage di-sulfonylation on 6^A-OH and 6^C-OH of CF-6.[7] This reaction gives an interesting chiral crown ether capped on the one side and a useful starting compound for preparing many bifunctional CF-6 where the functional groups are located on the given positions, 6^A and 6^C.



A solution of CF-6 **1** (500 mg, 5.14 x 10^{-4} mol; dried over P_2O_5 at 100°C overnight) in dry pyridine (150 mL; dried over KOH under refluxing and distilled) was concentrated to 100 mL by distillation under atmospheric pressure to eliminate water included in CF-6. During this procedure, the solution became a suspension because the solubility of CF-6 in pyridine decreases with increasing the temperature. After the mixture was cooled (the mixture became clear), 180 mg (5.14 x 10^{-4} mol) of biphenyl-4,4'-disulfonyl chloride was added to the mixture. After the mixture was stirred for 10 h at room temperature, the reaction

was stopped by addition of water. The reversed-phase HPLC[8] showed selective formation of one product (Fig. 1). The mixture was concentrated in vacuo and the residue was dissolved into 30% aqueous MeOH and applied on a reversed-phase column[9] with a gradient elution from 30% aqueous MeOH (1 L) to 80% aqueous MeOH (1 L) to give $6^A,6^C$-di-*O*-(biphenyl-4,4'-disulfonyl)-CF-6 **5** (111.2 mg, 17.3%). The FAB mass and ^1H- and ^{13}C-NMR spectra supported this structure-determination but cannot be decisive tools for determining the kind and the relative positions of the two sulfonylated hydroxyls. These problems were solved as shown below.

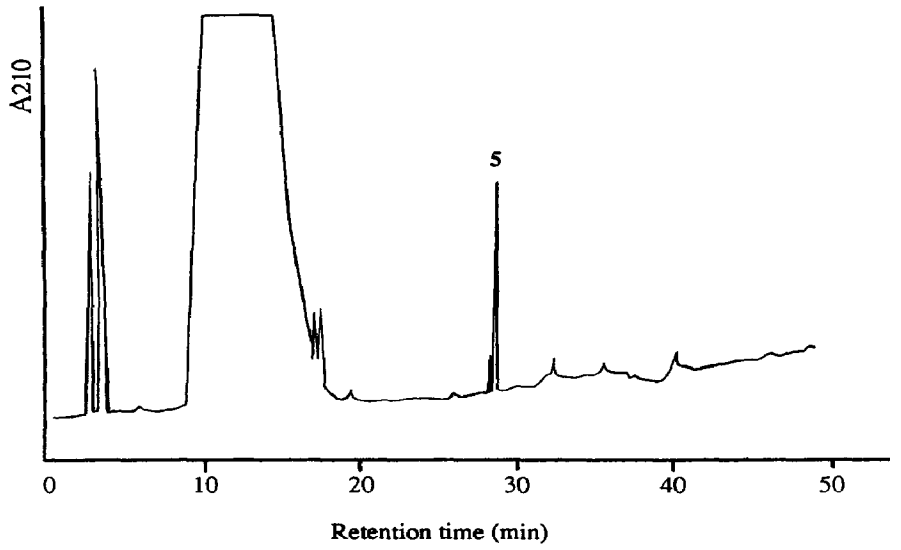


Fig. 1. Reversed-phase HPLC of the mixture obtained by the reaction of cycloinulohexaose with biphenyl-4,4'-disulfonyl chloride in pyridine: a gradient elution from 10% aqueous CH_3CN (30 mL) to 60% aqueous CH_3CN (30 mL); flow rate, 1.0 mL/min

The capped CF-6 was treated with thiophenol/Cs_2CO_3 in DMF to give the corresponding sulfide whose FAB mass spectrum contained the molecular ions ($M+H^+$ and $M+Na^+$). By comparing its retention time on reversed-phase HPLC[8] with those (Fig. 2) of the authentic sulfides **6**-**8**[10] which were prepared by the similar reaction of $6^A,6^X$-bis[*O*-(2-naphthalenesulfonyl)]-CF-6 (X = B, C, and D) **2**-**4**, respectively, it was assigned to the $6^A,6^C$-isomer **7**. Therefore, **5** is $6^A,6^C$-di-*O*-(biphenyl-4,4'-disulfonyl)-CF-6. Since the transannular sulfonates can be substituted with appropriate nucleophiles, we will be able to obtain many chiral crown ethers having appropriate functional groups at the specific positions, 6^A and 6^C.

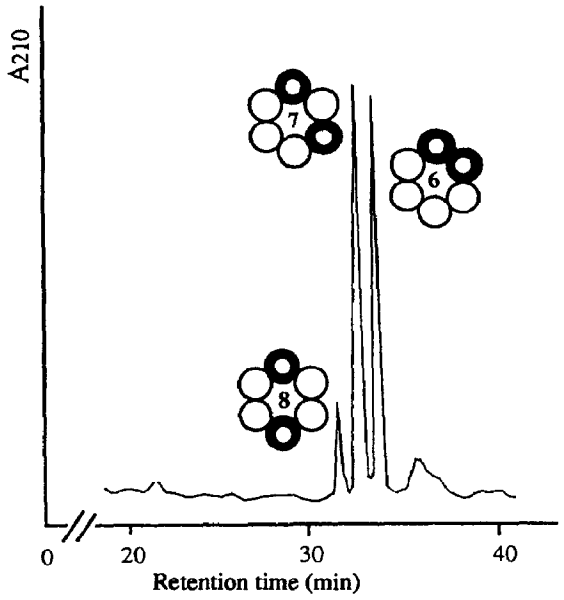


Fig. 2. Reversed-phase HPLC of the mixture of sulfides **6-8** which were obtained by the reaction of $6^A,6^X$-bis[*O*-(2-naphthalenesulfonyl)]-cycloinulohexaose (X = B, C, and D) **2-4** with thiophenol, respectively: a gradient elution from 10% aqueous CH_3CN (30 mL) to 60% aqueous CH_3CN (30 mL); flow rate, 1.0 mL/min

References and Notes

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4. Y. Takai, Y. Okumura, S. Takahashi, M. Sawada, M. Kawamura, and T. Uchiyama, *J. Chem. Soc., Chem. Commun.*, **1993**, 53.
5. K. Fujita, M. Atsumi, K. Ohta, and N. Imaki, *Tetrahedron Lett.*, in press.
6. K. Fujita, A. Matsunaga, and T. Imoto, *J. Am. Chem. Soc.*, **106**, 5740 (1984); G. Körner, *Gazz. Chem. Ital.*, **4**, 305 (1874).
7. Transannular di-sulfonylation was developed with β-cyclodextrin by Tabushi and his coworkers. For example; I. Tabushi, K. Shimokawa, N. Shimizu, H. Shirakata, and K. Fujita, *J. Am. Chem. Soc.*, **98**, 7855 (1976): I. Tabushi, Y. Kuroda, K. Yokota, and L. C. Yuan, *Ibid.*, **103**, 3574 (1981).
8. TSKgel ODS-120A (4.6 x 250) column was used.
9. Merck Lobar column RP18 (size C) was used.
10. Each sulfide was isolated and analyzed by FAB mass spectrum, which contained the molecular ion.

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