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# 6-*O*-SULFONATES OF CYCLOINULOHEXAOSE (CYCLOFRUCTAN-6)

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***Abstract:*** Mono-, di-, and tri-6-*O*-sulfonylated cycloinulohexaoses were prepared and regiochemistry of di- and tri-sulfonates was determined by the extended Körner method.

Cycloinulohexaose [hereafter abbreviated as CF-6 (cyclofuractan-6)] is a β-(2-1)-linked cyclohexaose of fructofuranose. This compound is an interesting molecule because it is produced from inulin by cycloinulo-oligosaccharide fructanotransferase[2] and has a chiral 18-crown-6 structure.[3,4] Its chemical modification should be investigated to apply the unique structure for constructing artificial enzymes or receptors. However, there is only one example for chemically modified CF-6; per-*O*-methylated CF-6.[5] Sulfonylation of hydroxyls of CF-6 is important since the hydroxyls should be activated usually before their modification. We describe here sulfonylation on the primary hydroxyls of CF-6 and structure determination of the regiochemical isomers.

To a solution of CF-6 (200 mg, 2.06 x $10^{-4}$ mol) in pyridine (20 mL) was added 2-naphthalenesulfonyl chloride (117 mg, 5.16 x $10^{-4}$ mol) and the reaction mixture was stirred at room temperature for 40 min. After water was added, the mixture was concentrated in vacuo and the residue was dissolved in 20% aqueous MeOH. The solution was analyzed by reversed-phase HPLC (ODS 80TM, TOSOH) (Figure 1A). The mixture was chromatographed on a reversed-phase column (Lobar column Rp 18, Merck) to give **1** (36.0 mg, 15.1%), **2** (8.5 mg, 3.1%), a mixture of **3** and **4**, and a mixture (5.1 mg) of **5-8**. The compounds **3** (7.1 mg, 2.6%) and **4** (5.2 mg, 1.9%) were isolated from the mixture by reversed-phase preparative HPLC (Cosmosil 10C18, Waters).

Their fast-atom-bombardment (FAB) mass spectra showed that **1** was a mono-sulfonate and **2-4** were di-sulfonates. The $^{13}C$ NMR signal at δ 74.8 in the case of **1** demonstrated the sulfonylation on 6-OH (Fig. 2A).[6] This is reasonable result because sulfonylation with sulfonyl chloride in pyridine occurs selectively on a primary hydroxyl. While two H-1 signals around δ 8.0 for 2-naphthalenesulfonyl moieties were observed in the cases of **3** (Fig. 2C) and **4** (Fig. 2D), only one was observed around δ 8.5 with **2** (Fig. 2B). This suggests that **2** has $C_2$ symmetry, therefore, is $6^A,6^D$-bis[*O*-(2'-naphthalenesulfonyl)]-CF-6. However, the structure of other two cannot be determined on the basis of the spectral data.

We apply our extended Körner method[7] to elucidate the regiochemical structure of **2-4** as shown below. The compounds **5-8** were isolated by HPLC (Polyamine, YMC) from the mixture (Fig. 1B). Their FAB mass spectra showed that they were the tri-sulfonates. On the basis of the extended Körner method for determining the regiochemical structure absolutely, the regiochemistry of the trisulfonates were related to the regiochemistry of the disulfonates (Scheme 1). According to the Scheme 1, additional sulfonylation of the $6^A,6^B$-, $6^A,6^C$-, or $6^A,6^D$- disulfonate should give three ($6^A,6^B,6^C$-, $6^A,6^B,6^D$-, and $6^A,6^B,6^E$-trisulfonates), four

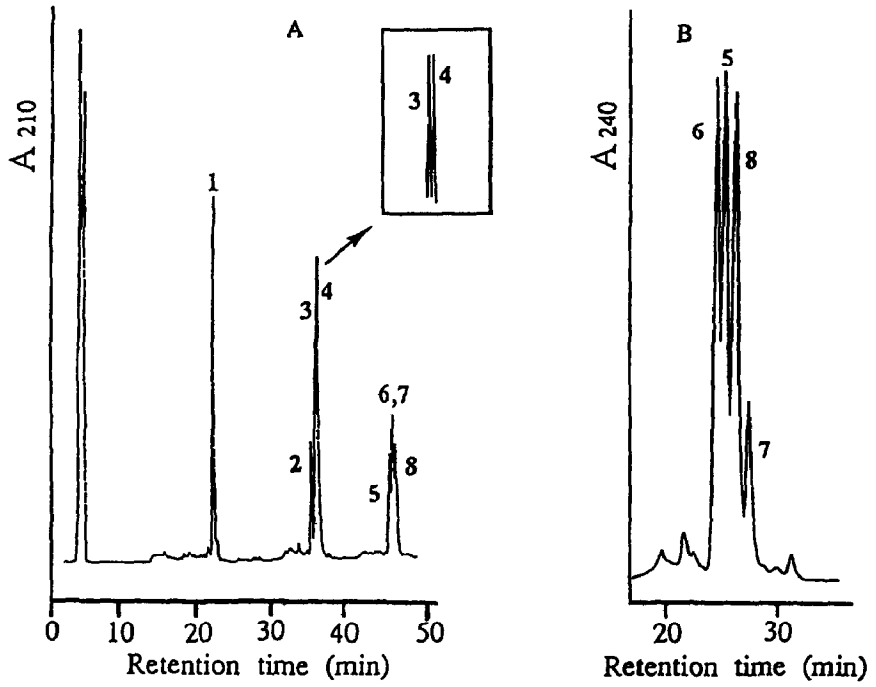


Fig. 1. HPLC separation of **1-8**. A; Reversed-phase HPLC of the reaction mixture obtained by the reaction of CF-6 with 2-naphthalenesulfonyl chloride with gradient elution from 10% (30 mL) to 60% (30 mL) aqueous $CH_3CN$ solution; flow rate, 1.0 mL/min. B; HPLC of the mixture of trisulfonates **5-8** with gradient elution from $CH_3CN$/n-PrOH/$H_2O$ (60/30/10, v/v/v) to $CH_3CN$/n-PrOH/$H_2O$ (40/30/30); flow rate, 1.0 mL/min.

($6^A,6^B,6^C$-, $6^A,6^B,6^D$-, $6^A,6^B,6^E$-, and $6^A,6^C,6^E$- trisulfonates), or two ($6^A,6^B,6^D$- and $6^A,6^B,6^E$- trisulfonates) products, respectively. As expected, additional 2-naphthalenesulfonylation of **2**, **3**, and **4** gave two (**5** and **6**), four (**5-8**), and three (**5**, **6**, and **8**) trisulfonates, respectively. Therefore, **2**, **3**, and **4** are $6^A,6^D$-, $6^A,6^C$-, and $6^A,6^B$-bis[*O*-(2'-naphthalenesulfonyl)]-CF-6, respectively. Furthermore, **5**, **6**, **7**, and **8** are assigned as $6^A,6^B,6^D$- (or $6^A,6^B,6^E$-), $6^A,6^B,6^E$- (or $6^A,6^B,6^D$-), $6^A,6^C,6^E$-, and $6^A,6^B,6^C$-tris[*O*-(2'-naphthalenesulfonyl)]-CF-6, respectively.

Now the mono-, di- and tri-sulfonylated CF-6s of known structures are available for a wide variety of uses; their sulfonyl groups can be easily converted to other groups including functional groups.

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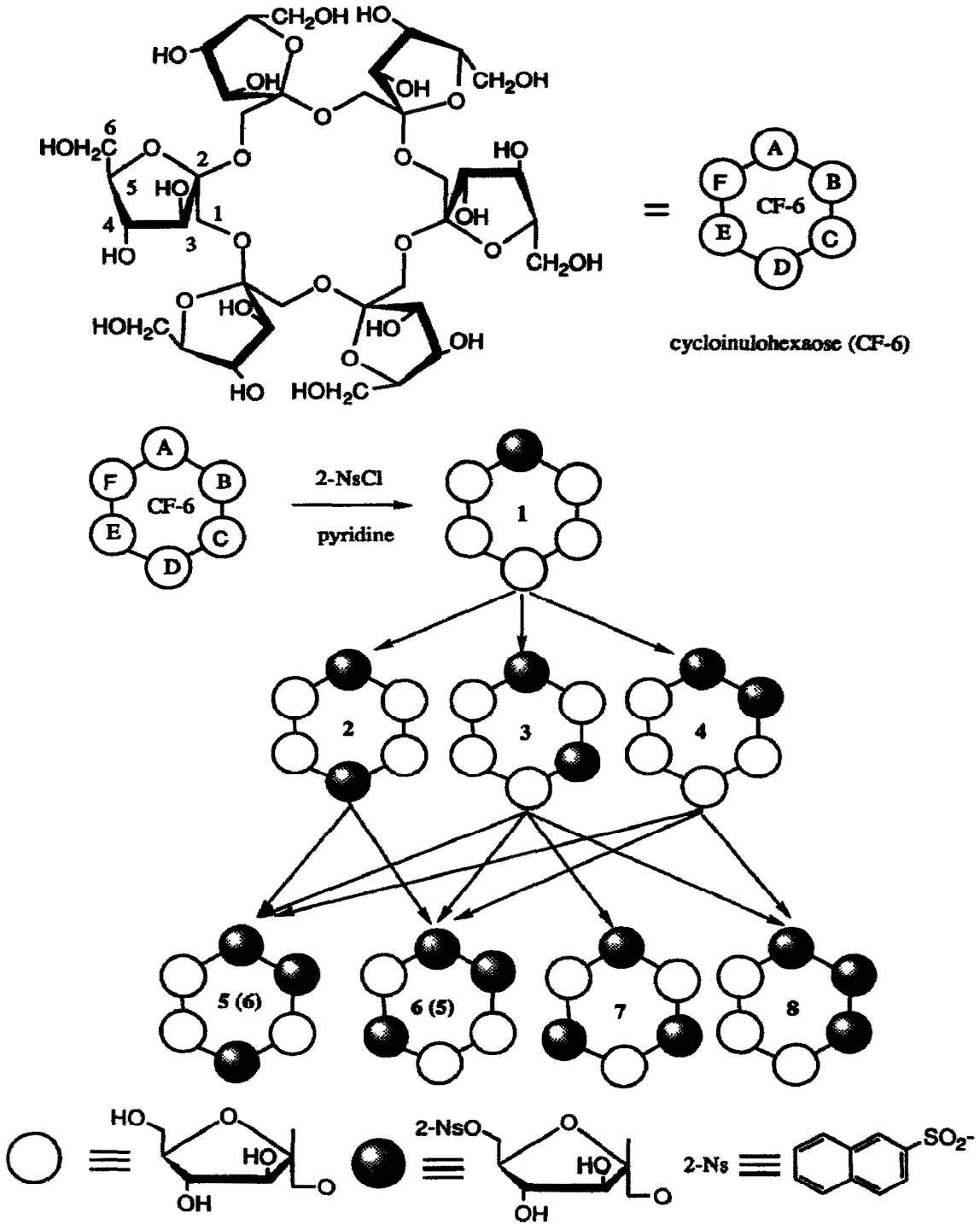


Scheme 1. Preparation and structure-determination of mono-, di-, and tri-sulfonates

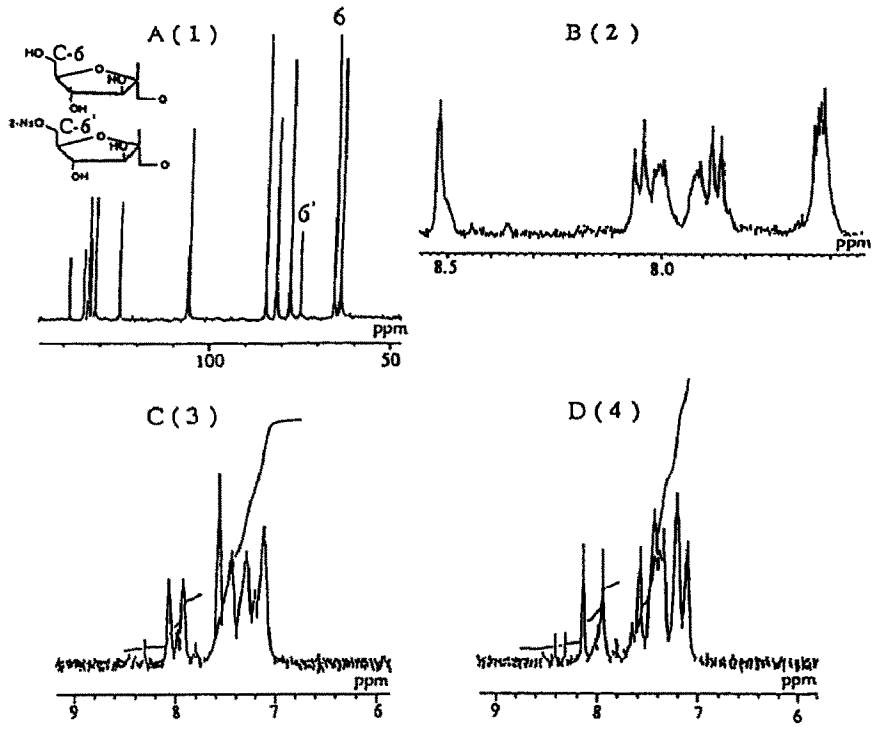


Fig.2. NMR spectra of **1** (A, $D_2O$), **2** (B, $D_2O$ + $CD_3CN$), 3 (C, $D_2O$ + $CD_3CN$), and **4** (D, $D_2O$ + $CD_3CN$)

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6. Sulfonylation on a primary hydroxyl causes down-field shift (9~10 ppm) of the α-carbon signal[7c] and the C-6 signals of CF-6 are observed at δ 65.5.
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