BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 45, 2895—2898 (1972)

Studies on Tritylated Sucrose. II. Di-O-Tritylsucroses

Toshiki OTAKE
Nippon Electric Varian, Ltd., Azabu, Iigura-machi, Minato-ku, Tokyo

(Received January 31, 1972)

Three isomeric di-*O*-tritylsucrose were isolated from a mixture of tritylated sucrose by the reaction of sucrose and trityl chloride in mole ratio 1: 2. Structures of isomeric diethers were established by application of NMR to the hexa acetyl derivatives. They are recognized as 6,6′-, 1′,6-, and 1′,6′-di-*O*-tritylsucrose. The former two substances were crystallized as colorless prisms.

In the preceding paper,[1] the isolation and structure of mono-*O*-tritylsucroses through the reaction of sucrose with trityl chloride in mole ratio 1: 1.2 were described. The content of monoether in the reaction product was 53% for total tritylated sucrose. The trityl groups on monoethers obtained were at 6- and 6′-position of sucrose. No other positional isomer such as 1′-mono-*O*-tritylether was detected. However, by thin-layer chromatography, at least three kinds of di-*O*-tritylsucroses and one triether were recognized in the reaction mixture. Formation of the three diethers suggests that at least one reactive hydroxyl group against trityl chloride should be present on sucrose in addition to the hydroxyl groups of 6- and 6′-position. The structures of diethers were established by NMR spectra. The structure of the triether was confirmed by McKeown *et al.*[2] McKeown and Hayward[3] and Bredereck *et al.*[4] to be 1′,6′,6-tri-*O*-trityl sucrose from the analysis according to the complex chemical procedures. In both works, one mole of sucrose was tritylated with 3 mol of trityl chloride, followed by acetylation in the same vessel, no description being given on mono- and di-*O*-tritylethers.

Results and Discussions

After removal of mono-*O*-tritylsucrose from the product obtained by the reaction of sucrose and trityl chloride in 1: 2 mole ratio, the residue was chromatographed on silica gel to divide it into fractions of di-*O*-tritylsucroses, tri-*O*-tritylsucroses, and non-sugar trityl compounds. On the total solid recovered by chromatography, the yields of mono-*O*-tritylsucroses, di-*O*-tritylsucroses, tri-*O*-tritylsucrose, and non-sugar trityl-compounds were accounted for in 27, 37, 17, and 19% weight, respectively. The thin-layer chromatogram of diethers showed that the diethers fraction consisted of at least three isomers and the order of amount of each isomer was IIa (R_f value 0.62)>IIb (R_f value 0.67)>IIc (R_f value 0.72).

Diethers IIa and IIc were crystallized, and melted at 124.5—126.5 and 133°C (corr), respectively, while IIb was obtained as colorless amorphous powder, softening at 129°C. The yield for crystalline IIa was 74%, as compared with 14% for IIb and 12% for IIc, on the total weight of the di-*O*-tritylsucroses. The IR spectra of all the diethers exhibited the O–H stretching absorption near 3500 cm^{-1} and the characteristic phenyl absorption at 1600, 1495, and 1450 cm^{-1}. On the UV spectra, the diethers and trityl chloride showed almost the same absorption pattern (λ_{max}= 260 mμ) and the molar extinction coefficient of the diethers (ε_{max}: IIa 1440, IIb 1415, and IIc 1460) gave twice the value of trityl chloride (ε_{max} 720). Thus, it is confirmed that IIa, IIb, and IIc are all di-*O*-tritylsucroses. The peracetyl derivative of III was crystallized in 70% yield against the total acetyl product of III-fraction. Its melting point (mp 234.4°C corr) was equal to that of 1′,6′,6-tri-*O*-trityl penta-*O*-acetylsucrose which had been reported by McKeown and Bredereck.

Diethers IIa, IIb, and IIc were acetylated with

---

[1] T. Otake, This Bulletin, **43**, 3199 (1970).

[2] G. G. McKeown, R. S. E. Serenius, and L. D. Hayward, *Can. J. Chem.*, **35**, 28 (1957).

[3] G. G. McKeown, and L. D. Hayward, *ibid.*, **35**, 992 (1957).

[4] H. Bredereck, H. Zinner, A. Wagner, G. Faber, W. Greiner, and W. Huber, *Chem. Ber.*, **91**, 2824 (1958).

acetic anhydride in a pyridine solution. The residues on evaporation were chromatographed on silica gel to obtain di-*O*-trityl-hexa-*O*-acetylsucroses (IVa, IVb, and IVc) in good yield. The product IVa was crystallized as colorless prisms (mp 102°C), while the others remained as amorphous solid by the same treatment. IR data of each product showed no absorption corresponding to the O–H stretching vibration, and the thin-layer chromatogram showed the products to be homogeneous. It was thus revealed that acetylation of the diether was completed.

In the NMR spectra of the acetyl derivatives, the integrated intensities of acetyl, trityl, and other protons agreed with the theoretical values calculated as di-*O*-trityl-hexa-*O*-acetylsucrose. The chemical shifts of the acetyl-group protons were in the δ value 1.5—2.0, showing certain differences between them: IVa; δ 1.57 (3H), 1 88 (3H), 1.92 (3H), 1.98 (3H), 2.00 (6H), IVb; δ 1.78 (3H), 1.91 (3H), 1.95 (3H), 1.96 (3H), 1.98 (3H), 2.03 (3H), IVc; δ 1.66 (3H), 1.88 (3H), 1.97 (3H), 2.00 (9H).

In each case, signals arising from the methine and the methylene protons fell into the region between δ 2.5 and δ 5.9, which could be subdivided into the three non-overlapping regions; A (δ 2.5—3.5 (4H)), B (δ 3.6—4.5 (4H)), and C (δ 4.5—5.9 (6H)).

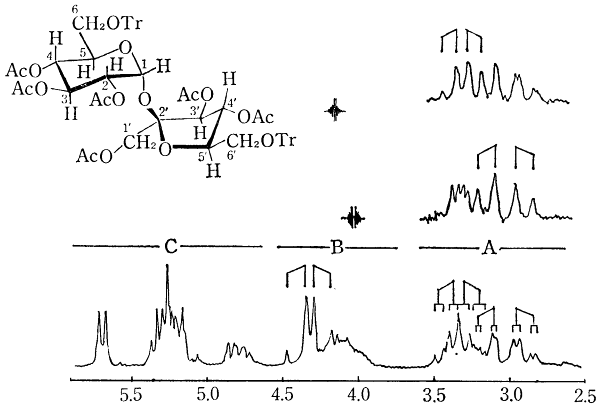

Fig. 1. Partial NMR spectrum of 100 MHz of IVa in $\mathrm{CDCl_3}$.

The signals in region A may be assigned to the protons of the methylene groups to which *O*-trityl group is directly attached.[1] For IVa, the signals in A are considered to consist of the two independent AB parts in each ABX system (Fig. 1). This was confirmed for IVa by carrying out irradiation near δ 4.0 and observing the perturbation of the signals, as it gives the two groups of signals with each four transitions. The following simulation spectrum was obtained by a computer, confirming the proposed ABX system defined by δ (1) 2.91, δ (2) 3.15, and δ (3) 4.15, with *J* (1, 2) −10.8, *J* (1, 3) 4.0, and *J* (2, 3) 2.0 Hz, δ (1′) 3.28, δ (2′) 3.41, and δ (3′) 4.15 with *J* (1′, 2′) −10.0, *J* (1′, 3′) 6.8, *J* (2′, 3′) 6.3 Hz,

	1	2	3	4	5	6	7	8
Observed (δ)	2.83	2.88	2.94	2.98	3.10	3.12	3.21	3.23
Generated (δ)	2.83	2.86	2.93	2.97	3.10	3.12	3.21	3.23

	1′	2′	3′	4′	5′	6′	7′	8′
Observed (δ)	3.17	3.24	3.27	2.34×2		3.40	3.44	3.50
Generated (δ)	3.17	3.24	3.27	3.34×2		3.41	3.44	3.51

On the basis of these observations, the signals in region A can be assigned to the methylene protons of H-6 and H-6′, and the original diether IIa **should** be 6,6′-di-*O*-tritylsucrose. By comparison with the chemical shifts of H-6 or H-6′ on mono-*O*-trityl-sucrose,[1] it is concluded that the signals of lower field in region A is ascribed to H-6′, and those of high field to H-6. The AB quartet observed in the lower field of region B is assigned to protons of C-1′methylene-group to which an *O*-acetyl group is directly attached, giving further confirmation of the structure.

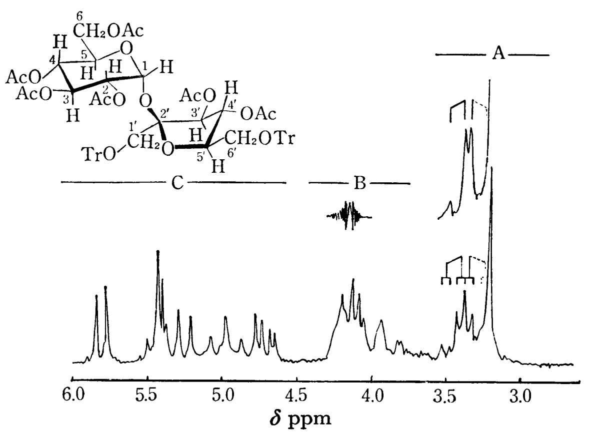

Fig. 2. Partial NMR spectrum at 100 NHz of IVb in $\mathrm{CDCl_3}$.

In the spectrum of IVb (Fig. 2) a broad singlet at δ 3.30 is considered to be due to protons of C-1′ methylene. The other signals in region A (δ 3.3—3.6) are assumed to be AB part of an ABX system which is turned to four-transition signals by irradiation near 4 ppm. The generated spectra in NMR spin simulation defined by δ (1) 3.31, δ (2) 3.43, and δ (3) 4.10, with *J* (1, 2) −10.5, *J* (1, 3) 4.5, and *J* (2, 3) 5.0 Hz, agreed with the observed spectrum of region A:

	1	2	3	4	5	6	7	8
Observed (δ)	—*	3.29	3.32	3.37×2		3.42	3.46	3.52
Generated (δ)	3.21	3.26	3.32	3.36	3.37	3.42	3.48	3.53

* overlapped with the protons of H-1′.

This system is almost consistent with that formed with the protons of C-6′methylene and H-5′ on 6′-mono-*O*-trityl-hepta-*O*-acetylsucrose. Thus the original diether IIb is perceived to be 1′,6′-di-*O*-tritylsucrose.

Signals in region A of IVc (Fig. 3) are considered to be overlapping signals of part AB in system ABX and system AB. The latter is assigned to the protons of C-1′methylene to which a trityl group is directly attached. Irradiation near 4 ppm gave rise to the collapse of signals other than those of C-1′methylene in region A and the appearance of four-transition signals. Comparison of the observed and the generated spectra in region A which is defined by δ (1) 2.85, δ (2) 3.3, and δ (3) 4.15 with *J* (1, 2) −10.7, *J* (1, 3)

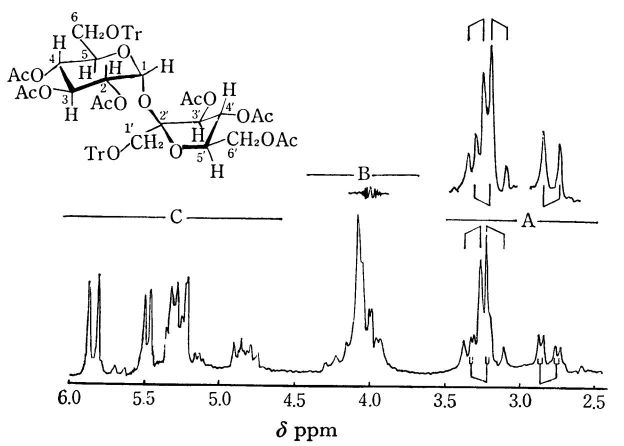

Fig. 3. Partial NMR spectrum at 100 NHz of IVc in $CDCl_3$.

3.2, and J (2, 3) 2 Hz, and δ (1′) 3.22, δ (2′) 3.33 with J (1′, 2′) −10.2 Hz, is as follows.

	1	2	3	4	5	6	7	8
Observed (δ)	2.78	2.81	2.88	2.91	3.23	3.25	3.34	3.36
Generated (δ)	2.77	2.81	2.88	2.91	3.24	3.26	3.34	3.37

	1′	2′	3′	4′
Observed (δ)	3.16	3.26	3.30	3.40
Generated (δ)	3.15	3.25	3.30	3.40

The above approximate three-spin system agreed well with that consisting of the proton of C-6 methylene and H-5 on 6-mono-trityl-hepta-*O*-acetylsucrose. Thus, the original diether should be 1,6-di-*O*-trityl-hepta-*O*-acetylsucrose.

The three possible isomeric diethers through the tritylation at two of the three primary alcohol (1′-, 6′-, and 6-position) are all recognized in the reaction mixture. The trityl group at the 1′-position was not observed in mono-*O*-tritylsucroses.[1] It should be noted that the tritylation at 1′-position is only observed in the ethers of higher trityl content.

Inactivity of 1′-hydroxyl group has also been observed in the *trans*-esterification of sucrose.[5] Formation of 1′,6-, and 1′,6′-di-*O*-tritylsucrose may take place through 6-, or 6′-mono-*O*-tritylsucrose gradually.

Experimental

General Methods. Thin-layer chromatography was carried out using Merck silica gel G as an adsorbent in a thickness of 0.25 mm and with the solvent systems: (A) methanol–water–acetone–chloroform (20: 4: 2: 56) for tritylated sucrose, (B) methyl ethyl ketone (MEK)–toluene for the *O*-acetyl derivatives of sucrose. The developed plates were sprayed with 50% sulfuric acid and heated at 120°C. Column chromatography was carried out using silica gel, 60—80 mesh (Kanto Chemical Co.). IR and UV spectra were measured with a Hitachi EPI-II RI spectrometer and a Cary Model 14R recording spectrophotometer, respectively. The NMR spectra were recorded with a Varian HA-100D (100 MHz) spectrometer using chloroform-*d* with tetramethylsilane as an internal lock, the signal positions being expressed in δ values. The NMR simulations were accomplished by a Varian Spectro. System SS-100 equipped with a Varian 620/i computer.

Tritylation of Sucrose. Commercial granulated sucrose (6.84 g) was reacted with recrystallized trityl chloride (11.4 g) in dry pyridine (100 m*l*) at room temperature. The reaction was accelerated by agitation of the reaction solution for 96 hr. At the end of the reaction period, the solution was dried *in vacuo* on a rotary evaporator. The residue was dissolved in 1-butanol (200 m*l*) and then washed with a Mckirrvin buffer (pH 7.0) and water in order to remove the free sucrose. Evaporation of the butanol solution under reduced pressure left 15.25 g of tritylated sucrose as colorless glass.

*Separation of di-*O*-tritylsucroses.* The mixture of tritylated sucrose was then subjected to counter currentgraphy for separation **into** mono-*O*-tritylsucroses and a mixture of ethers of higher trityl content. Evaporation of non-polar layer yielded the mixture (11.25 g) as colorless glass, which was subsequently chromatographed on 50 g of silica gel. After washing the column with chloroform (1 *l*) and with 2% methanol/chloroform (1 *l*), the diethers were eluted with 6% methanol/chloroform (1 *l*). Evaporation of the last solution left 5.319 g of a mixture of diethers.

*6,6′-di-*O*-tritylsucrose (IIa).* The mixture of diethers was resolved in an admixture of *n*-hexane and trichloroethylene (1: 1 vol/vol) (50 m*l*) at 55°C. The solution was then left at room temperature to precipitate an admixture of IIa and IIb. The residue of the filtration was dissolved in 80% methanol (30 m*l*) to crystallize IIa. By crystallization twice, 1.893 g of IIa was obtained as colorless prisms, melting at 125—126°C. Further 0.941 g of crystalline IIa was obtained from the mother liquid of recrystallization by recycling column chromatography.

Found: C, 70.78; H, 6.39%. Calcd for $C_{50}H_{58}O_{11}\cdot H_2O$: C, 71.09; H, 6.16%.

*1′,6′-di-*O*-tritylsucrose (IIb).* Evaporation residue (0.9 g) from the mother liquid of the recrystallization of IIa from 80% methanol was added to silica gel (10 g) column as a chloroform solution; the column was then gradually washed with 4, 5, 6, and 7% methanol/chloroform (200 m*l* each). The eluent was divided into sixteen 50 m*l*-fractions after all the solvent passed through the column, each fraction was returned gradually to the column. After repeating the recycling procedure, each fraction was examined by thin-layer chromatography to find out the fractions consisting of IIb. Evaporation of the fractions yielded 0.602 g of IIb as amorphous colorless powder melting at 129°C.

Found: C, 72.72; H, 6.37%. Calcd for $C_{50}H_{58}O_{11}$: C, 72.63; H, 6.09%.

*1′,6-di-*O*-tritylsucrose (IIc).* The evaporation residue of the mother liquid of the crystallization of IIa with an admixture of *n*-hexane and trichloroethylene was chromatographed in the same manner as in the separation of IIb. The residue of IIc fraction (0.536 g) was crystallized twice from 5 m*l* of 80% methanol solution to yeild about 0.4 g of crystalline IIc melting at 133°C.

Found: C, 71.37; H, 6.22%. Calcd for $C_{50}H_{58}O_{11}\cdot H_2O$: C, 71.09; H, 6.16%.

*Di-*O*-trityl-hexa-*O*-acetylsucroses (IVa, IVb, and IVc).* Acetylation of di-*O*-tritylsucroses was caried out as reported.[1] Each residue of reaction solution was chromatographed on a silica gel (10 g) column. After washing the column with 200 m*l* of toluene, each hexa-*O*-acetyl derivative (IVa, IVb, and IVc) was eluted with 7% methyl ethyl ketone (MEK)/toluene (200 m*l*) in an almost theoretical yield. IVa was

---

[5] T. Otake, *Nippon Kagaku Zasshi*, **90**, 393 (1969).

obtained in a crystalline form, melting at 102°C, by recrystallization with 10 m*l* of 80% methanol, in about 85% yield against the evaporation residue; attempts to crystallize the other hexa-*O*-acetyl derivatives were unsuccessful. Each acetyl derivative was found to be homogeneous on the thin-layer chromatogram developed with MEK–toluene (1:1 vol/vol); every compound had the same R_f value of 0.89.

Found, IVa: C, 69.28; H, 5.72%. Calcd for $C_{62}H_{62}O_{17}$: C, 69.01; H, 5.79%.

The author wishes to thank Professor Tetsuo Suami, Keio University, for his helpful advice and Mr. Iwao Miura for determination of NMR spectra.