Carbohydrate Research, 237 (1992) 283–287
Elsevier Science Publishers B.V., Amsterdam

Note

^1H and ^{13}C NMR study of nonsymmetrical α,α-trehalose derivatives

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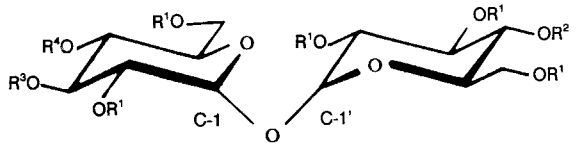
(Received March 16th, 1991; accepted September 21st 1991)

A detailed study[1] of the reaction of α,α-trehalose with pivaloyl chloride showed the high efficiency of this acyl chloride for obtaining symmetric and nonsymmetric hepta, hexa-, and penta-pivalate derivatives. These derivatives are of great utility as starting materials for the synthesis of deoxy-, amino-, and chloro-α,α-trehalose derivatives having biological activity[2,3]. In that study, the ^1H NMR spectra of the symmetric trehalose derivatives were assigned, but owing to instrumental limitations, those of the nonsymmetric derivatives, such as 2,4,6-tri-*O*-pivaloyl-α-D-glucopyranosyl 2,3,4,6-tetra-*O*-pivaloyl-α-D-glucopyranoside (**1**), 2,3,6-tri-*O*-pivaloyl-α-



1 $R^1 = R^2 = R^4 = Pv$; $R^3 = H$
2 $R^1 = R^2 = R^3 = Pv$; $R^4 = H$
3 $R^1 = R^4 = Pv$; $R^2 = R^3 = H$
4 $R^1 = R^2 = R^3 = R^4 = Pv$
5 $R^1 = R^3 = Pv$; $R^2 = R^4 = H$

Pv = Me_3CCO

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TABLE I

^{1}H NMR chemical shifts and coupling constants for α,α-trehalose derivatives [a]

Assignment	1	2	3
Chemical shifts (δ) [b]			
H-1	5.32(d)	5.35(d)	5.34(d)
H-2	4.93(dd)	4.98(dd)	4.90(dd)
H-3	4.15(dt) [c]	5.33(t)	4.13(dt) [c]
H-4	4.98(t)	3.52(t)	4.96(t)
H-5	3.88(ddd)	3.73(ddd)	3.93(ddd)
H-6a	4.01(dd)	4.33(dd)	4.09(dd)
H-6b	4.01(dd)	4.26(dd)	4.09(dd)
H-1′	5.38(d)	5.43(d)	5.31(d)
H-2′	5.03(dd)	5.02(dd)	4.98(dd)
H-3′	5.62(t)	5.60(t)	5.38(t)
H-4′	5.14(t)	5.13(t)	3.50(dt) [d]
H-5′	3.92(ddd)	3.88(ddd)	3.84(ddd)
H-6′a	4.13(dd)	4.12(dd)	4.30(dd)
H-6′b	4.00(dd)	4.00(dd)	4.30(dd)
Coupling constants (Hz)			
$J_{1,2}$	3.7	3.9	3.7
$J_{2,3}$	10.1	9.7	10.2
$J_{3,4}$	10.1	9.7	10.2
$J_{4,5}$	10.1	9.7	10.2
$J_{5,6a}$	2.1	2.1	2.1
$J_{5,6b}$	5.7	5.7	5.7
$J_{6a,6b}$	12.0	12.0	12.0
$J_{1',2'}$	3.7	3.9	3.7
$J_{2',3'}$	9.8	9.8	9.8
$J_{3',4'}$	9.8	9.8	9.8
$J_{4',5'}$	9.8	9.8	9.8
$J_{5',6'a}$	1.5	1.5	1.5
$J_{5',6'b}$	6.1	6.0	6.0
$J_{6'a,6'b}$	12.3	12.3	12.3

[a] Measured for solutions in $CDCl_3$ and Me_4Si as the internal reference at 300 MHz. [b] Chemical shifts for *tert*-butyl groups are not given since they are similar to those reported[4]. [c] $J_{H\text{-}3,OH} = 4.1$ Hz. [d] $J_{H\text{-}4',OH} = 4.1$ Hz.

D-glucopyranosyl 2,3,4,6-tetra-*O*-pivaloyl-α-D-glucopyranoside (**2**), and 2,4,6-tri-*O*-pivaloyl-α-D-glucopyranosyl 2,3,6-tri-*O*-pivaloyl-α-D-glucopyranoside (**3**), could not be completely assigned, nor were the ^{13}C NMR signals of compounds **1–5** assigned. We report herein the complete and unequivocal assignment of the signals of the ^{1}H (Table I) and ^{13}C NMR (Table II) spectra of these compounds, determined by two-dimensional COSY and HETCOR multipulse sequences, as exemplified for **2**.

In the ^{1}H–^{1}H-COSY contour plot of **2** (Fig. 1), the broadened triplet at δ 3.52 was assigned to H-4 from its chemical shift, since it is the only hydrogen atom geminal to a hydroxyl group. This assignment was further confirmed by the sharpening of the signal after addition of D_2O. The H-4 signal is coupled to H-5, which appears as a double double doublet (ddd) at δ 3.73, and to H-3, which

TABLE II

^{13}C NMR chemical shifts of α,α-trehalose derivatives [a]

Chemical shifts(δ) [b]	1	2	3	4	5
C-1	90.00	89.39	89.99	89.13	89.56
C-2	72.39	69.70	72.63	70.42	69.72
C-3	70.44	73.10	70.43	69.37	73.16
C-4	70.42	70.05	70.48	67.80	70.18
C-5	68.70	70.60	68.52	68.41	70.58
C-6	61.94	62.77	61.87	61.61	62.76
C-1′	89.58	89.22	89.89	89.13	89.56
C-2′	70.42	70.34	69.91	70.42	69.72
C-3′	69.52	69.40	72.63	69.37	73.16
C-4′	67.86	67.88	69.85	67.80	70.18
C-5′	68.25	68.31	72.55	68.41	70.58
C-6′	61.63	61.62	62.81	61.61	62.76

[a] Measured for solutions in $CDCl_3$ and Me_4Si as the internal standard. [b] Chemical shifts for pivaloyl groups are: (**1**) 177.90, 177.87, 177.80, 177.74, 177.04, 176.90, 176.36, 39.01, 38.87, 38.83(2), 38.75(2), 38.72, 27.37, 27.31, 27.23, 27.09(2), 27.03, and 27.01. (**2**) 179.73, 177.87, 177.51, 177.51, 177.39, 176.80, 176.40, 38.97, 38.90(2), 38.88, 38.84, 38.73(2), 27.37, 27.32, 27.22, 27.13, 27.06, 27.04, and 26.89. (**3**) 179.29, 179.02, 178.20, 177.96, 177.88, 177.16, 39.04, 39.98, 38.94, 38.90, 38.86, 38.84, 27.36, 27.27, 27.18, 27.15, 27.10, and 27.01. (**4**) 177.86(2), 177.40(2), 176.66(2), 176.42(2), 38.88(2), 38.85(2), 38.74(2), 38.72(2), 27.37(2), 27.23(2), and 27.06(4). (**5**) 179.83(2), 178.80(2), 177.57(2), 39.01(2), 38.92(4), 27.35(2), and 27.17(4).

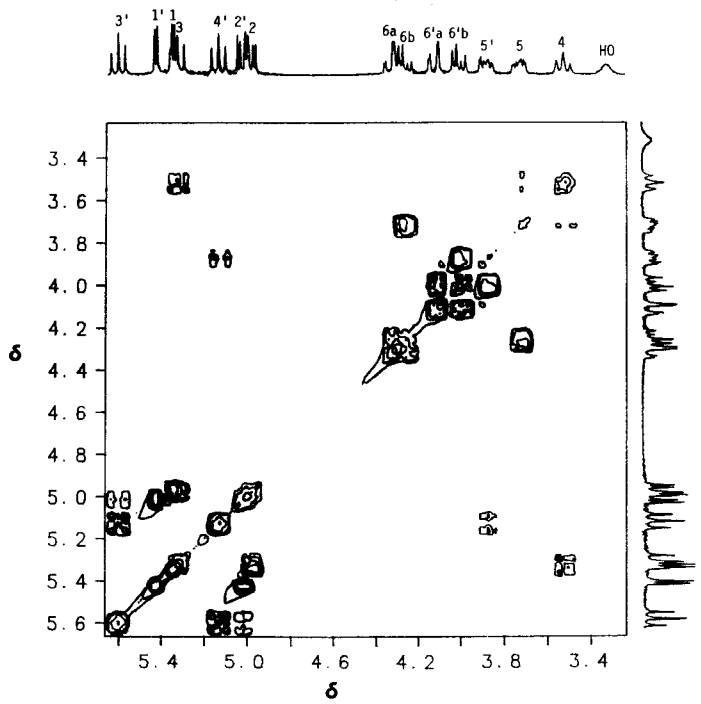

Fig. 1. COSY, homonuclear-correlation spectrum of heptapivalate **2** in $CDCl_3$ at 300 MHz.

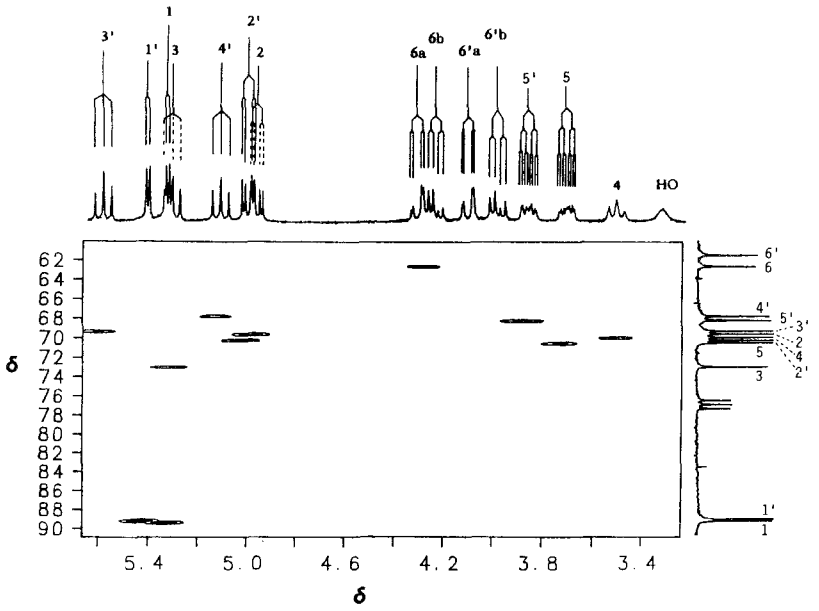

Fig. 2. HETCOR contour-plot of heptapivalate **2** in $CDCl_3$ at 300 MHz.

appeared as a triplet at δ 5.33. It was also observed that H-3 is coupled to the signal at δ 4.98, which appears as a double doublet and was ascribed to H-2, which in turn is coupled to the doublet at δ 5.35, which is therefore assigned to H-1. As mentioned, the signal for H-5 is found upfield; it is coupled to two sets of double doublets, the first one corresponding to H-6a at δ 4.33, and the second one to H-6b at δ 4.26. The coupling of H-4 with the hydroxyl proton allowed the distinction between the signals for H-4 and H-4′ and, therefore, between the two groups of signals for each D-glucopyranosyl residue. Thus, the signals for the second D-glucopyranosyl residue (H-1′–H-6b′) were easily assigned by comparison of individual multiplicities with those of the first D-glucopyranosyl residue and by the correlations shown in the COSY contour plot.

Once the ^1H NMR spectrum of **2** had been fully assigned, the ^{13}C signals could be assigned by 2D ^{13}C–^1H heteronuclear shift correlation (HETCOR, Fig. 2). Thus, the signals at δ 89.39 and 89.22 correspond to C-1 and C-1′, respectively, since they show correlation to the corresponding ^1H NMR signals, and those at δ 73.10 and 69.40 to C-3 and C-3′, respectively. The signals for C-5, C-4, and C-2 appear at δ 70.60, 70.05, and 69.70, respectively, and those for C-5′, C-4′, and C-2′ at δ 68.31, 67.88, 70.34, respectively, as again deduced from the correlations. The signals for C-6 and C-6′ are found upfield, at δ 62.77 and 61.62, respectively, although it should be noted that only the correlation of the CH_2-6 signals was observed on Fig. 2. However, the assignment of C-6′ could be deduced as it is the only nonobserved correlation. In an analogous way, the ^1H–^1H COSY and the

$^{13}C-^{1}H$ HETCOR contour plots of all remaining compounds provided the assignments summarized in Tables I and II.

EXPERIMENTAL

Methods.—Compounds **1–5** were prepared as published[1]. The NMR measurements were carried out on a Varian XL-300GS spectrometer operated with the software package version 6.1D, provided by the manufacturer, at ambient probe temperature (22°C). Chemical shifts were measured in δ values from the signal of internal Me_4Si. The two-dimensional $^{1}H-^{1}H$ and $^{13}C-^{1}H$ chemical-shift correlated spectra were obtained with the standard COSY and HETCOR pulse sequences.

ACKNOWLEDGMENT

Partial financial support from SEP and from CoNaCyT is acknowledged.

REFERENCES

1 R.C. Garcia, L. Hough, and A.C. Richardson, *Carbohydr. Res.,* 200 (1990) 307–317.
2 F. Arcamone and F. Bizioli, *Gazz. Chim. Ital.,* 87 (1957) 896–902; F. Arcamone, L. Valentini, and M. Reggianini, *Gazz. Chim. Ital.,* 87 (1957) 1499–1506; M. Ghione and A. Sanfilippo, *G. Microbiol.,* 3 (1957) 189–196; M. Uramoto, N. Otake, and H. Yanehara, *J. Antibiot.,* 20 (1967) 236–2340; L.A. Dolak, T.M. Castle, and A.L. Laborde, *ibid.,* 33 (1980) 690–694.
3 S.Z. Dzeidzic and G. Birch, *J. Sci. Food Agric.,* 32 (1981) 283–287.
4 D. Ljevakouic, S. Tomic, and H. Tomasic, *Carbohydr. Res.,* 182 (1988) 197–205.