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CATALYTIC REARRANGEMENT OF A 20(S),24(R)-EPOXYDAMMARANE-3β,12α,25-TRIOL (α-D-GLUCOSE 1,2-ORTHOACETATE). II.

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UDC 547.455+547.597+547.917+547.918

The catalytic rearrangement of 20(S),24(R)-epoxydammarane-3β,12α,25-triol 3,12-di(β-D-glucose orthoacetate) leads to the formation of a complex mixture of products, predominating among which are the corresponding 12-monoglucoside and 20(S),24(R)-epoxydammar-12-ene-3β,25-diol. As compared with the rearrangement of the 20(S),24(R)-epoxydammarane-3β,12β,25-triol 3,12-diorthoester the rearrangement of the 20(S),24(R)-epoxydammarane-3β,12α,25-triol 3,12-diorthoester takes place less regioselectively, which is apparently due to the strength of an intramolecular hydrogen bond. The results of IR, PMR, and ^{13}C NMR spectroscopy for the compounds newly obtained are given.

Continuing a study of the influence of intramolecular hydrogen bonds (intraHBs) on the regiochemistry of the catalytic rearrangements of orthoesters of polyhydric polycyclic alcohols [1], we have effected the synthesis and catalytic transformation of 20(S),24(R)-epoxydammarane-3β,12α-25-triol 3,12-di(3',4',6'-tri-O-acetyl-α-D-glucopyranose orthoacetate) (II). The catalytic isomerization of the 3β,12β-diorthoester (X) under conditions given previously [2] lead, as was shown in [1], to the formation of a mixture of the 12-monoglucoside (XI) and the 12,25-diglucoside (XII).

The anomalous regioselectivity of the catalytic rearrangement of (X) is apparently due to the influence of a strong intraHB between the protons of the hydroxy group at C^{25} and the alkoxyl carbon atom of the orthoester (OE) grouping at C^{12}.

In the light of the idea of the decisive role of an intraHB in the positional directivity of the rearrangement of the 3β,12β-diorthoester (X) put forward in [1], particular interest was presented by the results of the rearrangement of the 3β,12α-diorthoester (II), since the intraHB between the proton of the hydroxy group at C^{25} and the alkoxyl oxygen atom of the OE grouping at C^{12} in (II) is considerably weaker than in (X).

Unfortunately, in the IR spectroscopy of organic compounds there is no strict quantitative relationship between the integral intensity of the absorption bands of the vibrations of a O–H...O bond in the 3300-3600 cm^{-1} region and the energy of an intraHB, and therefore

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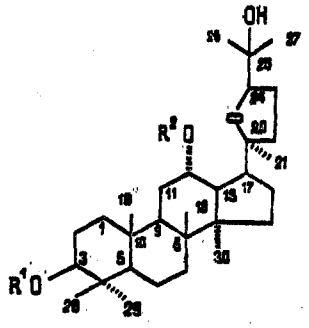
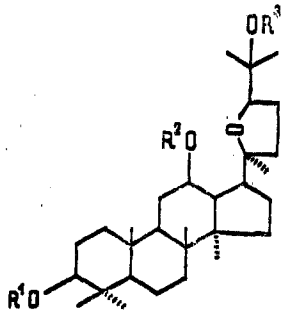
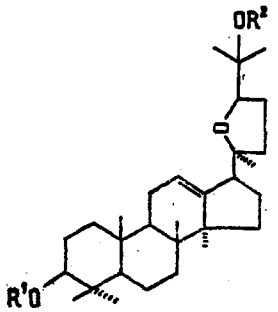
the strengths of the intraHBs and the compounds studied were evaluated only qualitatively. Thus, in the IR spectrum of (X) an intense broad band is observed at 3406 cm^{-1} which does not depend on the concentration of the solution in $CHCl_3$ (~25-fold dilution), while in the IR spectrum of (II) an analogous band is observed at 3527 cm^{-1} the peak intensity of which is ~5 times and the integral intensity ~11 times less than in the IR spectrum of (X).



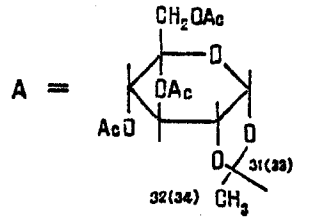
I. $R^1=R^2=H$
II. $R^1=R^2=A$
III. $R^1=H$, $R^2=A$
IV. $R^1=H$, $R^2=B$
V. $R^1=B$, $R^2=H$

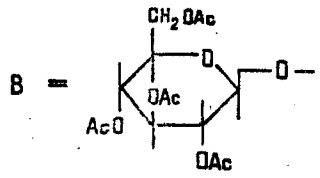


X. $R^1=R^2=A$, $R^3=H$
XI. $R^1=R^3=H$, $R^2=B$
XII. $R^1=H$, $R^2=R^3=B$



VI. $R^1=R^2=H$
VII. $R^1=A$, $R^2=H$
VIII. $R^1=B$, $R^2=H$
IX. $R^1=H$, $R^2=B$





The orthoester (II) was obtained by the reaction of α-acetobromoglucose with the alcohol (I) under the conditions described by Mazurek and Perlin [3]. The formation of the 3,12-diorthoester (II) took place considerably more slowly than that of the analogous 3,12-diorthoester (X). The structure of (II) was confirmed by acid hydrolysis and by the results of an investigation by the methods of ^1H and ^{13}C NMR. The positions of attachment of the OE groupings in (II) were established by comparing the ^{13}C spectra of the triol (I) and of the orthoester (II) (Table 1). The orthoester (II) was subjected to catalytic rearrangement in CH_3NO_2 under the action of $HgBr_2$ in the conditions given previously [2]. The rearrangement of (II) took place less regioselectively than that of (X) and led to the formation of a complex mixture of products (III-IX), predominating among which were the 12-monoglucoside (IV) and the enediol (VI). The predominant formation of (IV) and (VI) permits the assumption that the rearrangement of the diorthoester (II) probably took place in accordance with the scheme proposed previously [1] for the rearrangement of the diorthoester (X). The absence of the 12,25-diglucoside and of the free triol (I) from the products of the rearrangement of (II) is apparently connected with the occurrence of a process of dehydration of the suggested intermediates with a free hydroxy group at C^{12} through a 1,2-trans-diaxial splitting out of a molecule of water under the action of $HgBr_2$, which leads to the formation of 12-ene compounds (VI-IX), competing with the glycosylation reaction.

TABLE 1. ^{13}C Chemical Shifts of Compounds (I-IX) (δ, ppm relative to TMS)

C atom	Compound								
	I	II	III	IV	V	VI	VII	VIII	IX
1	38,9	39,3	39,1	39,0	38,9	38,9	38,9	39,0	38,9
2	27,4	25,6	27,4	27,4	25,9	27,4	25,3	25,8	27,5
3	78,8	81,0	78,8	78,8	90 6	78,9	81,2	90,6	79,0
4	38,9	38,7	39,1	39,0	39,1	38,9	38,7	39,0	38,8
5	56,0	56,5	56,0	55,7	56,3	56,0	56,5	56,2	55,9
6	18,3	18,4	18,3	18,3	18,2	18,3	18,4	18,1	18,3
7	35,3	35,3	35,3	35,2	35,3	34,8	34,8	34,7	34,7
8	40,4	40,5	40,6	40,3	40,4	38,1	38,1	38,0	38,0
9	45,5	45,6	45,8	45,8	45,5	47,8	47,8	47,7	47,7
10	36,8	36,7	37,0	36,8	36,6	37,2	36,9	36,8	37,1
11	29,4	28,6	28 5	28,0	29,5	23,5	23,5	23,5	23,4
12	68,3	77 5	77,4	79,9	68,3	116,0	116,0	116,0	115,7
13	44,5	43,2	43,3	43,2	44,6	147,3	147,3	147,2	147,3
14	49,0	49,8	49,9	49,7	49,0	50,6	50,6	50,5	50,5
15	31,9	32,2	32,3	32,8	31,9	31 8	31,7	31,7	31,7
16	25,0	26,6	26,6	26,1	25,0	26,9	26,9	26,8	27,3
17	46,3	45,9	45,9	45,6	46,4	51,1	51,0	51,0	51,3
18	16,1	16,4	16,4	16,4	16,1	16,8	16,8	16,7	16,8
19	15,5	15,1	15,5	15,4	15,1	15,7	15,8	15,6	15,6
20	86,2	87,1	87,1	86,8	86,1	85,7	85,8	85,7	85,8
21	24,1	24,9	24,6	25,0	24,0	21,5	21,5	21,4	23,4
22	34,1	33,3	33,3	33,1	34,2	37,5	37,5	37,5	37,4
23	26,3	26,0	25,9	25,7	26,3	26,5	26,5	26,5	26,9
24	83,3	83,6	83,6	83,2	83 2	83,1	83 1	83,0	82,0
25	71,1	71,5	71,6	71,2	71,2	71,3	71,3	71,2	79,7
26	27,3	27,0	27,3	27,4	27,6	27,5	27 5	27,5	23,4
27	24,7	24,9	25,7	25 5	24,7	24,4	24,3	24,3	22,8
28	28,0	28,3	28,1	28,0	27,7	28,2	28,5	27,7	28,1
29	15,1	16,4	15,1	15,0	16,3	15,7	16,5	16,4	15,6
30	19,6	20,1	20,3	19,6	19,6	25,3	25,3	25,2	25,2
31	—	122,0	121,8	—	—	—	122,2	—	—
32	—	22 3	22,6	—	—	—	22,6	—	—
33	—	121,7	—	—	—	—	—	—	—
34	—	22,7	—	—	—	—	—	—	—

TABLE 2. ^{13}C Chemical Shifts of the Sugar Components of Compounds (II-V) and (VII-IX) (δ, ppm relative to TMS)*

C atom	Compound							
	II		III	IV	V	VII	VIII	IX
1	97,0	97,0	97,0	101,8	103,0	97,1	103 0	95 8
2	68 2	68,5	68,4	71,2	71,5	68,2	71 6	71,6
3	70,5	70,2	70,3	73 2	72 9	70,6	72,9	73,3
4	73,4	72 9	73,0	68,7	68,8	73 6	68 8	68,9
5	67,4	67,1	67,1	71,8	71,6	67,5	71,7	71,6
6	63,2	63 2	63,2	62,2	62,3	63,2	62,3	62,4

*Emissions from the ^{13}C nuclei of acetate groups of sugar components of compounds (II-V) and (VII-IX) appear in the ranges 170.0-170.6 and 20.8-21.3 ppm.

Thus, the results obtained show a considerable dependence of the regiochemistry of the catalytic rearrangements of the diorthoesters (II) and (X) on the strength of the intra-HBs, although in the case of (II) this dependence is considerably distorted by the auxiliary influence of the steric factor.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were recorded on a Bruker HX-90 E instrument in the Fourier regime at 30°C using 8% solutions of the substances in $CDCl_3$ with a working frequency of 90.0 MHz for ^1H and 22.63 MHz for ^{13}C. The accuracy of measurement was ±0.15 Hz for ^1H and ±1.5 Hz for ^{13}C. The assignment of the signals in the ^{13}C spectra was made by analogy with [1]. The melting points of the substances were determined on a Boetius stage. Solvents were prepared by a published method [4]. Column chromatography was performed on KSK SiO_2, 100-115 mesh, treated as described by Wulff and Schmidt [5], in the petroleum–acetone (40:1) → (5:1) system, and TLC in a fixed layer of SiO_2 in the petroleum ether–acetone

(3:1) and (2:1) systems. The TLC plates were visualized with a mixture of concentrated H_2SO_4 and MeOH (1:10) at 100-200°C. The hydrolytic test for sugar orthoesters was carried out under the conditions given by Wulff and Schmidt [5]. The triterpene (I) was obtained by the hydride reduction of its 3,12-diketo derivative. The 3,12-diketo derivative of the triterpene (I) was obtained from 20(S),24(R)-epoxydammarane-3α,12β,25-triol as described by Nagai et al. [6]. The 20(S),24(R)-epoxydammarane-3α,12β,25-triol was isolated from the leaves of the Far Eastern species *Betula platyphylla*.

Preparation of 20(S),24(R)-Epoxydammarane-3β,12α,25-diol (I). With stirring, a solution of 1.8 g of the 3,12-diketo derivative of the triol (I) in 15 ml of absolute THF was added dropwise to a suspension of 7.5 g of $LiAlH(OC_4H_9)_3$ in 100 ml of absolute THF. The mixture was boiled for 7 h and was left overnight at 25°C. The excess of hydride was decomposed by the addition of 5 ml of C_2H_5OAc and, with vigorous stirring, 50 ml of 20% H_2SO_4. The aqueous solution was extracted with ether (4 × 50 ml), and the combined extracts were dried over Na_2SO_4 and the solvent was driven off. The residue was separated on a column of SiO_2. This gave 1.35 g (72%) of (I), $C_{30}H_{52}O_4$, mp 247-250°C (petroleum ether). ^1H spectrum (δ, ppm): 0.79 (s, 3 H); 0.87 (s, 3 H); 0.94 (s, 3 H); 0.99 (s, 3 H); 1.12 (s, 6 H); 1.16 (s, 3 H); 1.22 (s, 3 H); 3.21 (m, 1 H, $\Sigma J \approx 16$ Hz, H_a^3); 3.74 (t, 1 H, J = 7.0 Hz, H^{24}); 4.23 (broadened singlet, 1 H, $\Sigma J \approx 0$ Hz, H_e^{12}).

Preparation of the Orthoester (II). A mixture of 0.952 g (2 mmole) of the triol (I), 2.466 g (6 mmole) of α-acetobromoglucose, and 8 ml of collidine in 20 ml of CH_3NO_2 was stirred at 25°C for 96 h. The precipitate that had deposited was separated off and was washed with benzene, and the filtrate was evaporated to dryness. The residue was dissolved in $CHCl_3$ and the solution was washed with water. The organic phase was dried, the solvent was separated off, and the residue was chromatographed on a column of SiO_2. This gave 1.30 g (57%) of the amorphous diorthoester (II). $C_{58}H_{88}O_{22}$. ^1H spectrum (δ, ppm); 0.75 (s, 3 H); 0.85 (s, 3 H); 0.94 (s, 6 H); 0.99 (s, 3 H); 1.14 (s, 3 H); 1.17 (s, 3 H); 1.22 (s, 3 H); 1.73 (s, 3 H, C^{31} $-CH_3$); 1.77 (s, 3 H, C^{33} $-CH_3$); 2.09 (s, 15 H, 5 OAc); 2.12 (s, 3 H, OAc); 3.13 (m, 1 H, $\Sigma J \approx 15$ Hz, H_a^3); 3.77 (t, 1 H, J = 7.0 Hz, H^{24}); 3.94 (q, 2 H, J = 3.7 and 8.7 Hz, 2 H_5'); 418 (d, 4 H, J = 3.7 Hz, 4 H_6'); 4.40 (q, 2 H, J = 2.5 and 5.0 Hz, 2 H_2'); 4.40 (m, 1 H, $\Sigma J \approx 9$ Hz, H_e^{12}); 4.90 (q, 2 H, J = 2.5 and 8.7 Hz, 2 H_4'); 5.18 (t, 2 H, J = 2.5 Hz, 2 H_3'); 5.67 (d, 2 H, J = 5.0 Hz, 2 H_1').

Rearrangement of the Orthoester (II). One quarter of the solvent was distilled off from a solution of 1.136 g (1 mmole) of (II) in 10 ml of CH_3NO_2, and then a solution of 0.13 g (0.36 mmole) of $HgBr_2$ and 4 ml of CH_3NO_2 were added and the reaction mixture was heated at 100-105°C for 30 min. After a few drops of pyridine had been added, the solvent was evaporated off completely, and the residue was washed four times with hot water, dried, and chromatographed on a column of SiO_2. This led to the successive isolation of:

1) 20(S),24(R)-epoxydammar-12-ene-4β,25-diol (VI), 0.035 g (17%), $C_{30}H_{50}O_3$. ^1H spectrum (δ, ppm): 0.80 (s, 6H); 0.94 (s, 3 H); 1.00 (s, 3 H); 1.04 (s, 3 H); 1.12 (s, 6 H); 1.21 (s, 3 H); 2.75 (m, 1 H, H_e^{11}); 3.21 (q, 1 H, J = 7.4 and 8.9 Hz, H_a^3); 3.71 (t, 1 H, J = 7.4 Hz, H^{24}), 5.35 (q, 1 H, J = 2.6 Hz, H^{12});

2) 20(S),24(R)-epoxydammar-12-ene-3β,25-diol 3-(3',4',6'tri-O-acetyl-α-D-glucopyranose 1',2'-O-orthoacetate) (VII), 0.019 g (5%), $C_{44}H_{68}O_{12}$. ^1H spectrum (δ, ppm): 0.77 (s, 3 H); 0.79 (s, 3 H); 0.93 (s, 3 H); 1.04 (s, 3 H); 1.12 (s, 6 H); 1.21 (s, 3 H); 1.26 (s, 3 H); 1.74 (s, 3 H, C^{31}—CH_3); 2.08 (s, 3 H, OAc); 2.09 (s, 3 H, OAc); 2.11 (s, 3 H, OAc); 3.12 (m, 1 H, $\Sigma J \approx 16$ Hz, H_a^3); 2.71 (t, 1 H, J = 7.0 Hz, H^{24}); 3.95 (q, 1 H, J = 4.0 and 9.0 Hz, H_5'); 4.20 (d, 2 H, J = 4.0 Hz, 2 H_6'); 4.33 (q, 1 H, J = 3.0 and 5.3 Hz, H_2'); 4.91 (q, 1 H, J = 3.0 and 9.0 Hz, H_4'); 5.18 (t, 1 H, J = 3.0 Hz, H_3'; 5.33 (m, 1 H, H^{12}); 5.67 (d, 1 H, J = 5.3 Hz, H_1');

3) 20(S),24(R)-epoxydammar-12-ene-3β,25-diol 3-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranoside) (VIII), 0.02 g (5%), $C_{44}H_{68}O_{12}$. ^1H spectrum (δ, ppm): 0.75 (s, 3 H); 0.79 (s, 3H); 0.92 (s, 6 H); 1.03 (s, 3 H); 1.11 (s, 6 H); 1.22 (s, 3 H); 2.00 (s, 3 H, OAc); 2.02 (s, 3 H, OAc); 2.05 (s, 3 H, OAc); 2.07 (s, 3 H, OAc); 3.10 (m, 1 H, $\Sigma J \approx 16$ Hz, H_a^3);

3.69 (m, 1 H, H_5'); 3.71 (t, 1 H, J = 6.7 Hz, H^{24}); 4.18 (m, 2 H, 2 H_6'); 4.54 (d, 1 H, J = 7.4 Hz, H_1'); 4.92-5.20 (m, 3 H, H_2', H_3', and H_4'); 5.33 (m, 1 H, H^{12});

4) 20(S),24(R)-epoxydammar-12-ene-3β,25-diol 25-O-(2',3',4',6'-tetra O-acetyl-β-D-glucopyranoside) (IX), 0.024 g (7%), $C_{44}H_{68}O_{12}$. ^1H spectrum (δ, ppm): 0.80 (s, 6 H); 0.93 (s, 3 H); 0.99 (s, 3 H); 1.06 (s, 6H); 1.15 (s, 3 H); 1.18 (s, 3 H); 1.99 (s, 3 H, OAc); 2.02 (s, 6H, 2 OAc); 2.06 (s, 3 H, OAc); 2.74 (m, 1 H, H_e^{11}); 3.22 (q, 1 H, J = 7.5 and 8.7 Hz, H_a^3); 3.84 (t, 1 H, J = 7.5 Hz, H^{24}); 3.50-5.47 (m, 7 H, H_5', 2 H_6', H_2', H_3', H_4' and H_1');

5) 20(S),24(R)-epoxydammarane-3β,12α-25-triol 12-O-(3',4',6'-tri-O-acetyl-α-D-glucopyranose 1',2'-orthoacetate) (III), 0.015 g (4%), $C_{44}H_{70}O_{13}$. ^1H spectrum (δ, ppm): 0.77 (s, 3 H); 0.85 (s, 3 H); 0.95 (s, 3 H); 0.98 (s, 6 H); 1.13 (s, 3 H), 1.16 (s, 3 H); 1.22 (s, 3 H); 1.76 (s, 3 H, C^{31}—CH_3); 2.09 (s, 6 H, 2 OAc); 2.11 (s, 3 H, OAc); 3.21 (q, 1 H, J = 7.4 and 8.6 Hz, H_a^3); 3.78 (t, 1 H, J = 6.1 Hz, H^{24}); 3.93 (m, 1 H, H_5'); 4.19 (m, 2 H, 2 H_6'); 4.37 (m, 2 H, H_e^{12}, H_2'); 4.88 (q, 1 H, J = 3.5 and 10.0 Hz, H_4'); 5.20 (t, 1 H, J = 2.6 Hz, H_3'); 5.68 (d, 1 H, J = 5.0 Hz, H_1');

6) 20(S),24(R)-epoxydammarane-3β,12α-25-triol 12-O-(2',3',4',6-tetra-O-acetyl-β-D-glucopyranoside) (IV), 0.078 g (21%). $C_{44}H_{70}O_{13}$. ^1H spectrum (δ, ppm): 0.77 (s, 3 H); 0.83 (s, 3 H); 0.94 (s, 6 H); 0.98 (s, 3 H); 1.15 (s, 3 H); 1.19 (s, 3 H); 1.22 (s, 3 H); 2.01 (s, 6 H, 2 OAc); 2.07 (s, 6 H, 2 OAc); 3.20 (m, 1 H, $\Sigma J \simeq 16$ Hz, H_a^3); 3.70 (t, 1 H, J = 6.8 Hz, H^{24}); 4.29 (m, 1 H, $\Sigma J \simeq 9$ Hz, H_e^{12}); 4.64 (d, 1 H, J = 7.8 Hz, H_1'); 3.50-5.30 (m, 6 H, H_2', H_3', H_4', H_5', 2 H_6'); and

7) 20(S),24(R)-epoxydammarane-3β,12α,25-triol 3-O-(2',3',4',6'-tetra-O-acetyl-β-D-glucopyranoside) (V), 0.019 g (5%), $C_{44}H_{70}O_{13}$. ^1H spectrum (δ, ppm): 0.74 (s, 3 H); 0.86 (s, 3 H); 0.93 (s, 6 H); 1.10 (s, 3 H); 1.12 (s, 3 H); 1.16 (s, 3 H); 1.22 (s, 3 H); 2.00 (s, 3 H, OAc); 2.03 (s, 6 H, 2 OAc); 2.08 (s, 3 H, OAc); 3.08 (m, 1 H, $\Sigma J \simeq 16$ Hz, H_a^3); 3.73 (t, 1 H, J = 6.8 Hz, H^{24}); 3.76 (m, 1 H, H_5'); 4.17 (m, 2 H, 2 H_6'); 4.23 m, 1 H, $\Sigma J \simeq 8$ Hz, H_e^{12}); 4.54 (d, 1 H, J = 7.1 Hz, H_1'); 4.91-5.30 (m, 3 H, H_2', H_3', H_4').

SUMMARY

The catalytic rearrangement of a 20(S),24(R)-epoxydammarane-3β,12α,25-triol 3,12-diorthoester takes place less regioselectively than that of a 20(S),24(R)-epoxydammarane-3β,12β,12-triol 3,12-diorthoester which is apparently due to the strength of an intramolecular hydrogen bond.

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