Carbohydrate Research, 150 (1986) 151–162
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

DIRECT SYNTHESIS OF 6-OXABICYCLO[3.2.1]OCTANE DERIVATIVES FROM DEOXYINOSOSES*†

REGINE BLATTNER AND ROBERT J. FERRIER
Department of Chemistry, Victoria University of Wellington, Private Bag, Wellington (New Zealand)
(Received October 9th, 1985; accepted for publication, November 12th, 1985)

ABSTRACT

In the presence of bases, even those (for example, pyridine) normally used for acylation reactions, 2L-(2,4,5/3)-2,3,4-tribenzoyloxy-5-hydroxycyclohexanone (**3**) readily gives 2L-(2,4/3)-2,3,4-tribenzoyloxycyclohex-5-enone or aromatic products. Under acid conditions, efficient *O*-acylation and tetrahydropyranylation can be effected. The main product (60% isolated) formed on treatment of **3** with diazomethane is (1*R*,2*S*,3*R*,4*S*,5*S*)-2,3,4-tribenzoyloxy-1-hydroxy-6-oxabicyclo [3.2.1]octane (**15**); small proportions of the epimeric spiro-epoxides and 1-acetyl-6-benzoyloxy-7-methoxy-1*H*-indazole are also formed. On photobromination, the acetate (**17**) of **15** undergoes substitution at C-7 and, from the product, *C*-formyl-deoxyinositol derivatives are produced.

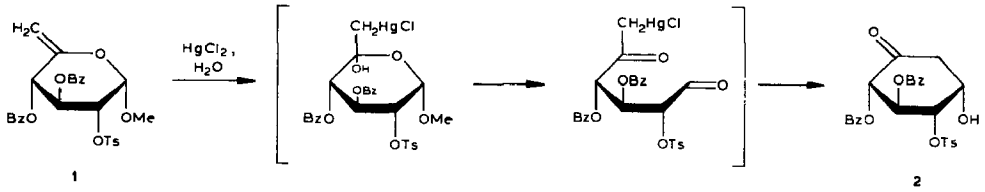
INTRODUCTION

A simple and efficient method by which 6-deoxyhex-5-enopyranose derivatives, *e.g.*, **1**, may be converted into 2-deoxyinosose compounds, *e.g.*, **2**, by use of mercury(II) salts in aqueous media was first reported[1] in 1979. Since then the procedure has been used in the preparation of inosamine derivatives of interest in the study of aminoglycoside antibiotics[2–7] and for making pseudo-sugars[8,9] and pseudo-oligosaccharides[2,3,10]. Mercury(II) acetate[11], mercury(II) trifluoroacetate[7], and mercury(II) sulphate[8,12] have been found to be more effective for promoting the reaction than mercury(II) chloride, which was used in the initially reported[1] examples (**1**→**2**).

As part of a programme concerned with the conversion of carbohydrates into non-carbohydrate compounds of significance in medicinal chemistry[13], we have investigated some reactions of the 2,3,4-tri-*O*-benzoyl analogue of the tosylate **2** with a view to preparing polyfunctional cyclohexanes, in particular derivatives having

*Dedicated to Professor N. K. Kochetkov.
†Functionalised Carbocycles from Carbohydrates, Part 9. For Part 8, see ref. 11.

0008-6215/86/$ 03.50



1 2

carbon–carbon bonded substituents on the rings.

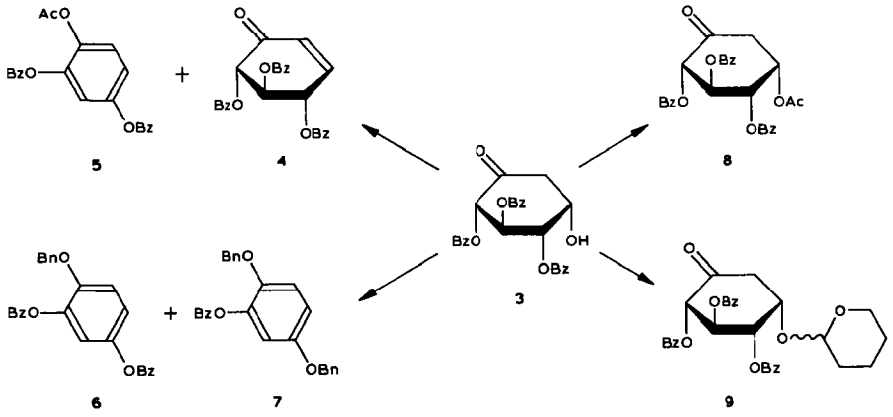
Compounds, like **2**, with potential leaving-groups in both positions β to the carbonyl function readily undergo β-elimination reactions and hence aromatisation. Thus, treatment of **2** with acetic anhydride–pyridine[1,2], methanesulphonyl chloride–pyridine[3], or triflic anhydride–pyridine[7] causes enone formation on the methylene (C-6) side of the carbonyl group, and eliminations on the other side, *i.e.*, from C-3, have been noted when tosyloxy[12] or azido[6] groups are present at that position. The enone produced in each of these reactions is subject to base-catalysed aromatisation[1].

Notwithstanding the ease with which compounds of the deoxyinosose class may undergo eliminations, members have been found to react in several useful ways without such eliminations. Thus, acetylation of the free hydroxyl group in **2** occurred efficiently with acetic anhydride in trifluoroacetic anhydride[4], and glycosylation of an analogue with 1,5-anhydro-2,3,4,6-tetra-*O*-benzoyl-D-*arabino*-hex-1-enitol in the presence of boron trifluoride also occurred without complication[10]. Several reactions have been accomplished specifically at the carbonyl group. Thus, oximes[2,4,5] and hydrazones[4] can be formed, and reduction with sodium borohydride[5,7] and reductive amination with sodium cyanoborohydride[2] can be effected. Furthermore, methylene condensations can be carried out by use of Wittig reagents[3,8], and cyclic acetals and thioacetals can be formed with ethylene glycol (sulphuric acid as catalyst) and ethane-1,2-dithiol (boron trifluoride as catalyst)[14].

RESULTS

Investigations of the chemical characteristics of compounds of the 2-deoxyinosose class were carried out on the tribenzoate **3**[11], which is readily obtainable from 1,2,3,4,6-penta-*O*-benzoyl-β-D-glucose *via* its 5-bromo derivative[15] and the derived 6-deoxy-5-enose[16]. Acylation of the hydroxyl group in **3** under normal circumstances was seriously impeded by the propensity of the products to undergo elimination to give the enone **4**. Treatment of **3** at room temperature with acetic anhydride in pyridine gave 60% of **4** and also the acetylated phenol **5** (28%). Such eliminations and aromatisations have been observed with related inosose derivatives and the structures of the products can be assigned by analogy[1,17,18].

Attempted benzylation of **3** with benzyl bromide in *N,N*-dimethylformamide in the presence of silver oxide led completely to aromatisation and the isolation of the phenolic derivatives **6** and **7**, the former being the product of two β-eliminations followed by benzylation and the latter the product of these two processes preceded

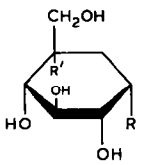


by an O-4→O-5 benzoyl migration.

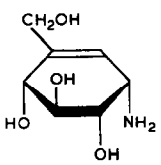
Comparable eliminations did not occur with similar ease under acid conditions. Treatment of **3** with acetic anhydride and boron trifluoride as catalyst gave the 5-acetate **8** in high yield when the reaction was carried out at ~0°. However, at room temperature, small proportions of the enone **4** were produced.

Treatment of **3** with 2,3-dihydropyran in the presence of toluene-*p*-sulphonic acid as catalyst gave, in high yield, the diastereoisomeric tetrahydropyranyl ethers **9**, which had very similar ^{1}H-n.m.r. spectra except that the resonances of H-3 (1,3-diaxial relationship to the new chiral acetal centres) appeared as two distinct broad triplets of roughly equal intensities. In spite of the presence of mixed isomers, the ethers **9** crystallised well, but the components were not separable by recrystallisation.

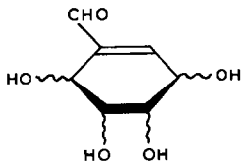
Our particular interest was to investigate the use of **3** or its analogues or derivatives as synthetic precursors of pseudo-sugars, in particular pseudo-α-D-glucopyranose[19] (**10**), which we have succeeded in preparing by this approach[9], and such related substances as validamine[20] (**11**), valiolamine[20] (**12**), valienamine[20] (**13**), and the rancinamycins which are esters of the configurationally uncharacterised aldehyde **14**[21]. With this objective in mind, therefore, **3** was treated with diazomethane following the precedent that inososes[22] and their acetals[23] and esters[24] give



	R	R'
10	OH	H
11	NH_2	H
12	NH_2	OH



13



14

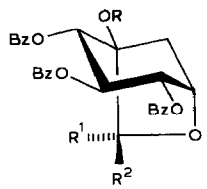
TABLE I

^{1}H-N.M.R. DATA FOR COMPOUND **15** AND ITS DERIVATIVES

Compound	*Chemical shifts and multiplicities*							
	H-2	*H-3*	*H-4*	*H-5*	*H-6e*	*H-6a*	*H-7endo*	*H-7exo*
3	5.83d	6.42t	5.77dd	4.60m		2.88	—	—
15	5.63dd	6.16t	5.21dd	4.58dd	2.48dd	2.13d	4.33d	3.69dd
17	6.1–6.2		5.20d	4.67d	2.51dd	3.08d	4.58d	3.85d
22	6.26d	5.98t	5.25d	4.95d		3.1	6.82s	—
24	5.80d	6.04t	5.21d	4.72d	2.62dd	2.12d	6.40s	—
25	5.7–6.3		5.48dd	5.13dd	3.42dd	2.69d	—	—
26	6.17d	6.07t	5.24d	4.89d	2.66dd	3.13d	6.70s	—

Compound	*Coupling constants*							
	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6e}$	$J_{5,6a}$	$J_{6,6'}$	$J_{7,7'}$	$J_{2,7exo}$
3	10	10	2.5	3[a]	4[a]	14[a]	—	—
15	8.5	8.5	0.5	6.5	0	12.5	8.5	1.6
17	—	—	0	6.5	0	12.5	8.5	—
22	7.5	7.5	0	5	—	—	—	—
24	8.5	8.5	0	7	0	12.5	—	—
25	8	8	1	7	0	12.5	—	—
26	7.5	7.5	0	7	0	13	—	—

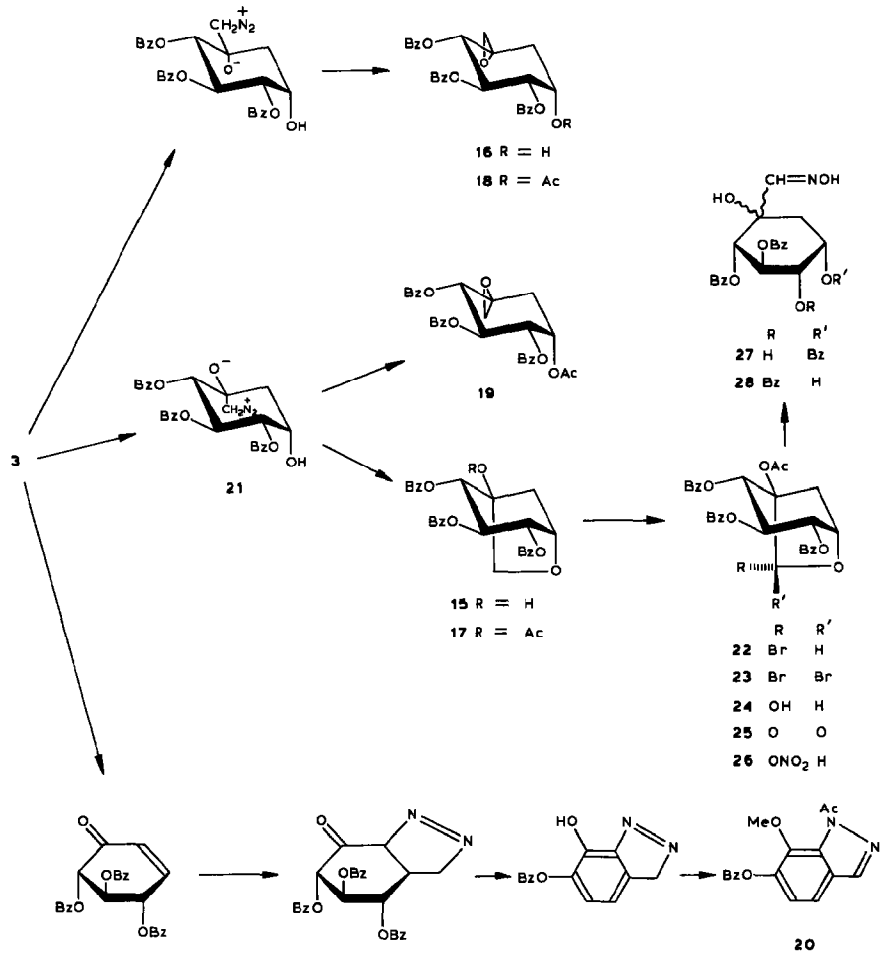
[a]Determined from a spectrum recorded for a solution in deuterated acetone.



	R	R^1	R^2
15	H	H	H
17	Ac	H	H
22	Ac	Br	H
24	Ac	OH	H
25	Ac	O	O
26	Ac	ONO_2	H

spiro-epoxides with this reagent. T.l.c. indicated the formation of two products which were isolated crystalline in yields of 60 and 15%.

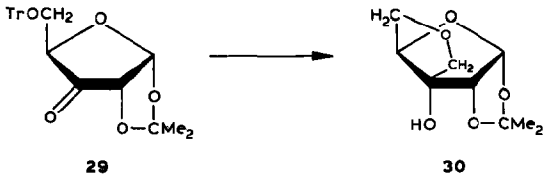
The major product was assigned structure **15**. In the ^{13}C-n.m.r. spectrum, the C-6 methylene carbon atom resonated at δ 39 and there were six signals in the range δ 71–79. Reaction had therefore occurred at the carbonyl group, but the compound was neither an epoxide (expected δ values 46–60)[25] nor a ring-expanded ketone[26]. In the ^{1}H-n.m.r. spectrum (Table I), resonances for a new methylene group were present; the upfield proton resonance showed small coupling (decoupling experiment) with H-2 which is typical[27] of $J_{4,6exo}$ splitting observed for 1,6-anhydrohexopyranose derivatives that have axial protons at C-4 and are structurally analogous to **15**. The geminal ^{1}H–^{1}H coupling observed for the new



methylene group (8.5 Hz) is also diagnostic of this type of bicyclic system[28].

Resonances at δ 47 and 56 in the ^{13}C-n.m.r. spectrum of the minor product indicated the presence of a spiro-epoxide[25]; a geminal ^{1}H–^{1}H coupling constant for the new methylene group of 4.5 Hz is consistent with this conclusion[23,29], and this compound was assigned the structure **16**. Acetylation of **15** and **16** gave the esters **17** and **18**, respectively, in high yield.

The mother liquors remaining after the isolation of **16** contained material which, after acetylation and column chromatography, yielded the acetate **18** of **16**,



the C-1 epimer (**19**) of **18**, and the indazole **20**, each in a yield of 2% (based on **3**).

The formation of the anhydro compound **15** as the main product of reaction of the ketone **3** with diazomethane can be rationalised by invoking attack by O-5 at the diazo carbon centre in the intermediate **21** from which compound **19** is also derived. Transannular reactions of this kind have been noted before in carbohydrate examples (*e.g.*, **29**–**30**)[30], and with terpenoid hydroxyketones[31].

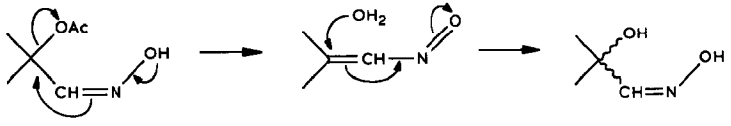
Assignment of the configurations at C-1 of the epoxides **18** and **19** was based on the method of Andrews *et al.*[32]. In the ^{1}H-n.m.r. spectrum of **19**, the two resonances of the downfield and upfield doublets given by H-7 and H-7′ had $W_{1/2}$ values of 3 and 1.5 Hz, respectively, and the methylene group is therefore pseudo-axial. In the spectrum of the isomer **18**, the corresponding values were 1 Hz, which is consistent with a pseudo-equatorial methylene group. It is notable also that **19** is dextrorotatory, like **17** which has the same configuration at C-1, whereas the epimer **18** is levorotatory.

The route to the indazole **20** depends upon 1,3-dipolar addition of diazomethane to intermediate **4**[33] produced by diazomethane-catalysed β-elimination from **3**. The ^{1}H-n.m.r. spectrum of **20** was consistent with published data for 1*H*-indazole[34], in particular, a $J_{4,5}$ value of 9 Hz, a δ value of 7.79 for H-3, and resonances for acetyl, benzoyl, and methoxyl groups.

Treatment of the acetate **8** of **3** with diazomethane gave a mixture of products, and the tetrahydropyranyl ethers **9** afforded mainly **15** so that neither substituted derivative protected O-5 to allow efficient access to spiro-epoxide products.

Since 2,3,4-tri-*O*-acetyl-1,6-anhydro-β-D-glucopyranose can be functionalised at C-6 by photobromination[28], **17**, a stereochemical analogue, was subjected to this reaction. The microcrystalline product, obtained in high yield, could not be purified by recrystallisation and was found to be a 9:1 mixture of the bromide **22** and the dibromide **23**[28] (Br analysis and hydrolysis products; see below). The ^{1}H-n.m.r. spectrum (Table I) of the mixture showed that substitution had occurred at C-7, since one resonance initially associated with this site had been removed and the other had been deshielded by ~2.2 p.p.m.[28]. As the substitution also caused deshielding of H-5 and H-6*e* by 0.4 and 0.6 p.p.m., respectively, the bromine is assigned to the *exo*-position[28]. Consistent with this assignment, H-3 was not deshielded. Compound **22** was appreciably more dextrorotatory than was its precursor **17**, which again established the *exo*-substitution site since the *exo*-bromide formed from 2,3,4-tri-*O*-acetyl-1,6-anhydro-β-D-glucopyranose (an analogue of the enantiomer of **17**) is more levorotatory than its precursor[28]. Reduction of **22** and **23** with zinc–acetic acid regenerated **17**, indicating that no rearrangement had occurred during the halogenation step.

Hydrolysis of the mixed bromides **22** and **23** over silica gel afforded 80% of the crystalline hemiacetal **24** together with 10% of the lactone **25** derived from the dibromide **23**. When the reaction was carried out with silver nitrate as reagent, **24** and **25** were formed in similar proportions and 9% of the nitrate **26** was also isolated. Compounds **24** and **26** were, like the bromide **22**, assigned the 7*S* or *exo*



31 32 33

configuration on the bases of the chemical shifts of H-5, H-6*e*, and H-3, and their more dextrorotatory nature than the precursor **17**.

Heating of the hemiacetal **24** with hydroxylamine hydrochloride in ethanolic pyridine gave a mixture of the isomeric oximes **27** and **28**, in the ratio 1:1, from which pure **27** was isolated. From the ^{1}H-n.m.r. spectrum of **27**, it was clear that deacetylation had taken place as well as benzoyl migration. The spectrum of the second product, obtained by difference, indicated that deacetylation, but no ester migration, had taken place. It is not clear whether loss of the acetyl groups was hydrolytic (although no water other than that produced in the oxime formation was present) or whether the process[35] **31**→**33** had occurred. Consequently, the configurations at the tertiary centres of the oximes remain uncertain.

EXPERIMENTAL

General methods. — Unless otherwise stated, ^{1}H- and ^{13}C-n.m.r. spectra were recorded for solutions in $CDCl_3$ at 80 and 20 MHz, respectively, using a Varian FT80A spectrometer. Optical rotations were measured on 0.5–1.5% solutions in chloroform.

2L-(2,4/3)-2,3,4-Tribenzoyloxycyclohex-5-enone (**4**). — A solution of 2L-(2,4,5/3)-2,3,4-tribenzoyloxy-5-hydroxycyclohexanone (**3**, 0.45 g) in pyridine (10 mL) was treated with acetic anhydride (7 mL) for 16 h at 20°. On pouring on to ice, a crystalline product (0.41 g) was formed. Three recrystallisations from methanol gave **4** (0.26 g, 60%), m.p. 149–151°, $[\alpha]_D$ +106°. ^{1}H-N.m.r. data: δ 5.9–6.4 (m, 4 H, H-2,3,4,6), 7.02 (d, 1 H, $J_{5,6}$ 11 Hz, H-5), 7.1–8.1 (m, 15 H, 3 Bz).

Anal. Calc. for $C_{27}H_{20}O_7$: C, 71.0; H, 4.4. Found: C, 70.9; H, 4.3.

2,4-Dibenzoyloxyphenyl acetate (**5**). — On standing at −10°, the mother liquors from the above reaction deposited a second product (0.1 g, 28%). Three recrystallisations from methanol gave **5**, m.p. 139–140°. Mass spectrum: *m/z* 376 (M^+), 334 $(M - CH_2CO)^+$, 230 $[(M + 1) - CH_2CO - PhCO]^+$. ^{1}H-N.m.r. data: δ 2.16 (2, 3 H, Ac), 7.1–8.2 (m, 13 H, H-2,3,5, 2 Bz).

Anal. Calc. for $C_{22}H_{16}O_6$: C, 70.2; H, 4.3. Found: C, 70.2; H, 4.4.

2,5-Dibenzyloxyphenyl benzoate (**7**) *and 2-benzyloxy-5-benzoyloxyphenyl benzoate* (**6**). — Several portions of silver oxide (total, 0.67 g) were added during 1 h to a solution of **3** (0.40 g) in dry *N,N*-dimethylformamide (4 mL) containing benzyl bromide (2 mL). The mixture was stirred for 16 h, and the solids were collected, and washed with *N,N*-dimethylformamide (4 mL) and chloroform (4 mL). Water (30 mL) was added to the combined filtrate and washings, and the

mixture was extracted with chloroform (3 × 15 mL). The combined extracts were washed with water (3 × 10 mL), dried, and concentrated to leave a brown residue which contained mainly two components (t.l.c.). Column chromatography (light petroleum–ether, 1:1) on silica gel gave, first, **7** (0.10 g, 29%) which, after two recrystallisations from methanol, had m.p. 82–84°. Mass spectrum: *m/z* 410 (M^+), 319 ($M - PhCH_2$)$^+$. ^{1}H-N.m.r. data: δ 4.92, 4.96 (2 s, 4 H, 2 CH_2), 6.6, 6.9–7.5, 7.9–8.2 (3 m, 8 H, H-3,4,6, Bz), 7.15, 7.25 (2 s, 10 H, 2 Ph).

Anal. Calc. for $C_{27}H_{22}O_4$: C, 79.0; H, 5.4. Found: C, 79.4; H, 5.5.

The second product (0.11 g, 31%) was **6** which, after two recrystallisations from methanol, had m.p. 139–140°. Mass spectrum: *m/z* 424 (M^+). ^{1}H-N.m.r. data: δ 5.03 (s, 2 H, CH_2), 6.9–7.7, 8.0–8.25 (2 m, 13 H, H-3,4,6, 2 Bz), 7.17 (s, 5 H, Ph).

Anal. Calc. for $C_{27}H_{20}O_5$: C, 76.4; H, 4.8. Found: C, 76.1; H, 4.9.

2L-(2,4,5/3)-5-Acetoxy-2,3,4-tribenzoyloxycyclohexanone (**8**). — Boron trifluoride etherate (0.2 mL) was added dropwise to a cooled, stirred solution of **3** (0.5 g) in acetic anhydride (15 mL), and the mixture, after storage at 0° for 1 h with stirring, was poured on to ice. The white solid which formed after further stirring for 1.5 h was collected, washed with water, and recrystallised twice from methanol to give **8** (0.45 g, 83%), m.p. 149–151°, $[\alpha]_D$ +42.5°. ^{1}H-N.m.r. data: δ 2.13 (2, 3 H, Ac), 2.99 (m, 2 H, H-6,6'), 5.7–5.95 (m, 3 H, H-2,4,5), 6.34 (t, 1 H, $J_{2,3} = J_{3,4}$ = 10 Hz, H-3), 7.1–8.1 (m, 15 H, 3 Bz).

Anal. Calc. for $C_{29}H_{24}O_9$: C, 67.4; H, 4.7. Found: C, 67.4; H, 4.8.

When the reaction was carried out using 0.99 g of **3** at room temperature, only 50% of **8** was obtained after recrystallisation. From the mother liquors, after concentration and storage at −10°, the enone **4** (20%) was obtained; m.p. 149–150° (from methanol), $[\alpha]_D$ +107°.

2L-(2,4,5/3)-2,3,4-Tribenzoyloxy-5-(tetrahydropyran-2-yloxy)cyclohexanone (**9**). — A suspension of **3** (1.0 g) in dry benzene (20 mL) and 2,3-dihydropyran (2.0 g) containing toluene-*p*-sulphonic acid (2 mg) was stirred at 20° for 16 h during which the solid dissolved. Anhydrous potassium carbonate (0.25 g) was added, stirring was continued for 0.5 h, and the solids and solvent were then removed to give a colourless oil. Column chromatography (light petroleum–ether, 1:1) then gave crystalline **9** (1.08 g, 92%). A sample, after purification on a second column, had m.p. 156–160°, $[\alpha]_D$ +8°. ^{1}H-N.m.r. data: δ 2.85–3.0 (m, 2 H, H-6,6'), 4.60 (m, 1 H, H-5), 5.77 (dd, 1 H, $J_{3,4}$ 10, $J_{4,5}$ 2 Hz, H-4), 5.87 (d, 1 H, $J_{2,3}$ 10 Hz, H-2), 6.37, 6.44 (2 t, 1 H, H-3), 7.1–8.1 (m, 15 H, 3 Bz), together with the resonances expected for the tetrahydropyranyl group.

Anal. Calc. for $C_{32}H_{30}O_9$: C, 68.8; H, 5.4. Found: C, 69.0; H, 5.5.

Reaction of **3** *with diazomethane.* — A solution of **3** (1.0 g) in chloroform (20 mL) was treated with diazomethane [produced from *N*-methyl-*N*-nitrosourea (5 g)] in ether (50 mL) for 2 days at 4°. Removal of the solvent gave a light-yellow oil which crystallised on trituration with methanol. Four recrystallisation of the product (0.21 g, 20%) from ethanol gave (1*R*,2*S*,3*R*,4*S*,5*S*)-2,3,4-tribenzoyloxy-1-hydroxy-6-oxabicyclo[3.2.1]octane (**15**), m.p. 178–179°, $[\alpha]_D$ +50.5°. N.m.r. data:

^{1}H, δ 2.13 (d, 1 H, $J_{6,6'}$ 12.5 Hz, H-6*a*), 2.46 (dd, 1 H, $J_{5,6}$ 6.5 Hz, H-6*e*), 3.2 (s, 1 H, OH), 3.69 (dd, 1 H, $J_{7,7'}$ 8.5, $J_{2,7exo}$ 1.6 Hz, H-7*exo*), 4.33 (d, 1 H, H-7*endo*), 4.58 (dd, 1 H, $J_{4,5}$ 0.5 Hz, H-5), 5.21 (dd, 1 H, $J_{3,4}$ 8.5 Hz, H-4), 5.63 (dd, 1 H, $J_{2,3}$ 8.5 Hz, H-2), 6.16 (t, 1 H, H-3), together with benzoyl signals; ^{13}C, δ 38.7 (C-6), 71.3, 72.5, 76.35, 77.6, 77.7, 78.4 (C-1,2,3,4,5,7, not assigned).

Anal. Calc. for $C_{28}H_{24}O_8$: C, 68.8; H, 5.0. Found: C, 68.7; H, 5.0.

Column chromatography (light petroleum–ether, 1:2) of the remaining products gave more **15** (0.42 g, 60% total), m.p. 177–179°, $[\alpha]_D$ +50°. Eluted later was (1*S*,2*S*,3*R*,4*S*,5*S*)-2,3,4-tribenzoyloxy-5-hydroxycyclohexane-1-spiro-oxirane (**16**; 0.15 g, 15%) obtained by crystallisation from methanol at −10° (several weeks). After four recrystallisations from this solvent, **16** had m.p. 151–154° $[\alpha]_D$ −5°. N.m.r. data: ^{1}H, δ 1.99 (dd, 1 H, $J_{6,6'}$ 15, $J_{5,6'}$ 4.5 Hz, H-6′), 2.46 (dd, 1 H, $J_{5,6}$ 3 Hz, H-6), 2.67 (d, 1 H, $J_{7,7'}$ 4.5 Hz, H-7), 2.73 (d, 1 H, H-7′), 3.10 (bs, 1 H, OH), 4.55 (m, 1 H, H-5), 5.48 (dd, 1 H, $J_{3,4}$ 9.5, $J_{4,5}$ 2.5 Hz, H-4), 5.71 (d, 1 H, $J_{2,3}$ 9.5 Hz, H-2), 6.34 (t, 1 H, H-3), together with benzoyl signals; ^{13}C, δ 34.5 (C-6), 47.2 (C-7), 56.4 (C-1), 67.8, 70.1, 70.3, 74.8 (C-2,3,4,5, not assigned).

Anal. Calc. for $C_{28}H_{24}O_8$: C, 68.8; H, 5.0. Found: C, 68.7; H, 5.0.

The mother liquors (0.4 g) from a repeat of the above isolations (carried out on 5.9 g of **3**) were treated conventionally with acetic anhydride in pyridine. Column chromatography (light petroleum–ether, 1:2) of the products gave (1*S*,2*S*,3*R*,4*S*,5*S*)-5-acetoxy-2,3,4-tribenzoyloxycyclohexane-1-spiro-oxirane (**18**; 0.12 g, 2%), m.p. 159–160° (from methanol), $[\alpha]_D$ −5°. N.m.r. data: ^{1}H, δ 1.7–2.5 (m, 2 H, H-6,6′), 2.17 (s, 3 H, Ac), 2.64 (d, 1 H, $J_{7,7'}$ 4.5 Hz, H-7), 2.71 (d, 1 H, H-7′), 5.52 (dd, 1 H, $J_{3,4}$ 9.5, $J_{4,5}$ 3 Hz, H-4), 5.7 (m, 1 H, H-5), 5.70 (d, 1 H, $J_{2,3}$ 9.5 Hz, H-2), 6.29 (t, 1 H, H-3), together with benzoyl signals; ^{13}C, δ 21.0 (CH_3), 32.2 (C-6), 47.15 (C-7), 55.7 (C-1), 68.9, 69.95, 70.3, 72.0 (C-2,3,4,5, not assigned).

Anal. Calc. for $C_{30}H_{26}O_9$: C, 67.9; H, 5.0. Found: C, 67.9; H, 5.0.

An earlier fraction was 1-acetyl-6-benzoyloxy-7-methoxy-1*H*-indazole (**20**; 0.075 g, 2%). After three recrystallisations from methanol, it had m.p. 173–175° (sealed tube). Mass spectrum: *m/z* 310 (M^+), 268 ($M - CH_2O)^+$, 163 ($M - CH_2O - PhCO)^+$. ^{1}H-N.m.r. data: δ 2.36 (s, 3 H, Ac), 4.10 (s, 3 H, OMe), 6.90, 7.02 (2 dd, 2 H, $J_{4,5}$ 9 Hz, H-4,5), 7.79 (s, 1 H, H-3), 7.3–8.3 (m, 5 H, Bz).

Anal. Calc. for $C_{17}H_{14}N_2O_4$: C, 65.8; H, 4.6; N, 9.0. Found: C, 65.4; H, 4.6; N, 9.2.

The first fraction was (1*R*,2*S*,3*R*,4*S*,5*S*)-5-acetoxy-2,3,4-tribenzoyloxycyclohexane-1-spiro-oxirane (**19**; 0.1 g, 2%), which, after four recrystallisations from methanol, had m.p. 163–165°, $[\alpha]_D$ +26.5°. N.m.r. data: ^{1}H, δ 1.96 (dd, 1 H, $J_{5,6}$ 4.5, $J_{6,6'}$ 14 Hz, H-6), 2.11 (s, 3 H, Ac), 2.45 (dd, 1 H, $J_{5,6'}$ 3 Hz, H-6′), 2.62 (d, 1 H, $J_{7,7'}$ 4.5 Hz, H-7), 3.13 (d, 1 H, H-7′), 5.55 (dd, 1 H, $J_{3,4}$ 9.5, $J_{4,5}$ 3 Hz, H-4), 5.7 (m, 1 H, H-5), 5.74 (d, 1 H, $J_{2,3}$ 9.5 Hz, H-2), 6.11 (t, 1 H, H-3), together with benzoyl signals: ^{13}C, δ 20.8 (CH_3), 33.1 (C-6), 49.6 (C-7), 55.7 (C-1), 67.9, 69.95, 70.8,. 72.2 (C-2,3,4,5, not assigned).

Anal. Calc. for $C_{30}H_{26}O_9$: C, 67.9; H, 5.0. Found: C, 67.6; H, 4.9.

(1R,2S,3R,4S,5S)-1-Acetoxy-2,3,4-tribenzoyloxy-6-oxabicyclo[3.2.1]octane **(17)**. — (*a*) *From the alcohol* **15**. Treatment of **15** (0.52 g) with acetic anhydride (5 mL) in pyridine (10 mL) for 40 h at 20° gave **17** (0.52 g, 91%), which, after three recrystallisations from ethanol, had m.p. 157–157.5°, $[\alpha]_D$ +15°. For ^{1}H-n.m.r. data, see Table I.

Anal. Calc. for $C_{30}H_{26}O_9$: C, 67.9; H, 5.0. Found: C, 67.9; H, 5.1.

(*b*) *From the bromide* **22**. Compound **22** (0.26 g) in acetone (5 mL) was shaken with a suspension of zinc dust (0.5 g) and a solution of sodium acetate (0.5 g) in aqueous acetic acid (1:1, 3 mL) for 16 h. The solids were removed, the filtrate was partitioned between water and chloroform, and the chloroform phase was washed with water, dried, and concentrated to give a colourless oil (0.25 g). Column chromatography (light petroleum–ether, 1:1) then gave **17** (0.14 g, 61%). After recrystallisation from ethanol, **17** had m.p. and mixture m.p. 156–157.5°, $[\alpha]_D$ +50°.

(1S,2S,3R,4S,5S)-5-Acetoxy-2,3,4-tribenzoyloxycyclohexane-1-spiro-oxirane **(18)**. — Acetylation of **16** (0.08 g) in pyridine (2 mL) containing acetic anhydride (1 mL) for 20 h at 20° gave **18** (0.08 g, 93%), which, after two recrystallisations from methanol, had m.p. 160–161°, $[\alpha]_D$ −7°.

Reactions of the acetate **8** *and the tetrahydropyranyl ethers* **9** *with diazomethane*. — Treatment of a solution of **8** in chloroform, ether, or benzene at 20° or −10° with ether–diazomethane gave mixtures containing at least five products.

A solution of **9** (0.09 g) in chloroform (10 mL) and methanol (3 mL) was treated with diazomethane in ether (20 mL) for 24 h at 4°. The solvents were then removed to give a two-component residue. Column chromatography (light petroleum–ether, 1:1) gave, first, an unidentified compound and then **15** (0.048 g, 53%), which, after two recrystallisations from ethanol, had m.p. 174–177°, $[\alpha]_D$ +50°.

Photobromination of the anhydro derivative **17**. — A solution of **17** (0.3 g) in carbon tetrachloride (10 mL) containing bromine (0.18 g) was boiled under reflux and exposed to a 275-W heat lamp for 0.5 h. The solvents were then removed to give a foam which crystallised on trituration with light petroleum. Recrystallisation of the product (0.31 g, ~90%) from light petroleum–benzene gave material with m.p. 104–106°, $[\alpha]_D$ +116° (benzene). ^{1}H-N.m.r. data are given in Table I.

Anal. Calc. for $C_{30}H_{25}BrO_9$: Br, 13.1. Found: Br, 13.8.

This was mainly (1*S*,2*S*,3*R*,4*S*,5*S*,7*R*)-1-acetoxy-2,3,4-tribenzoyloxy-7-bromo-6-oxabicyclo[3.2.1]octane (**22**) contaminated with ~10% of the 7,7-dibromo derivative **23**.

Photobromination of a second sample (0.3 g) with *N*-bromosuccinimide (0.3 g) in refluxing carbon tetrachloride (10 mL), for 1 h under the heat lamp, gave a similar mixture of products.

A solution of the crude mixture of **22** and **23** in aqueous acetone (30 mL, 10:1) was shaken with silica gel (0.5 g, Merck G) for 48 h at 20°, then filtered, and concentrated. A solution of the residue in chloroform was washed with water, dried, and concentrated. Column chromatography (light petroleum–ether, 1:3) of

the syrupy residue gave, first, (1*S*,2*S*,3*R*,4*S*,5*S*)-1-acetoxy-2,3,4-tribenzoyloxy-7-oxo-6-oxabicyclo[3.2.1]octane (**25**; 0.03 g, 10%), which, after three recrystallisations from light petroleum–acetone, had m.p. 214–215°, $[\alpha]_D$ +40°. ^{1}H-N.m.r. data are given in Table I.

Anal. Calc. for $C_{30}H_{24}O_{10}$: C, 66.2; H, 4.5. Found: C, 66.1; H, 4.6.

A second fraction (0.25 g, 80%) was the hemiacetal (1*S*,2*S*,3*R*,4*S*,5*S*,7*S*)-1-acetoxy-2,3,4-tribenzoyloxy-7-hydroxy-6-oxabicyclo[3.2.1]octane (**24**) which, after three recrystallisations from ethanol, had m.p. 162–164°, $[\alpha]_D$ +74°. ^{1}H-N.m.r. data are given in Table I.

Anal. Calc. for $C_{30}H_{26}O_{10}$: C, 65.9; H, 4.8. Found: C, 65.7; H, 5.0.

In a second reaction, a solution of the unpurified bromide (0.95 g) in acetone (30 mL) was stirred with silver nitrate (0.4 g) in water (2 mL) for 0.5 h. The precipitated silver bromide was collected and washed with acetone, and the combined filtrate and washings were concentrated and extracted with chloroform (3 × 30 mL). The combined extracts were washed with water, dried, and concentrated. Column chromatography (light petroleum–ether, 1:3) of the syrupy residue gave **25** (0.08 g, 10%), m.p. 214–215°, $[\alpha]_D$ +44°; **24** (0.61 g, 72%), m.p. 163–164°, $[\alpha]_D$ +75°; and (1*S*,2*S*,3*R*,4*S*,5*S*,7*R*)-1-acetoxy-2,3,4-tribenzoyloxy-7-nitrato-6-oxabicyclo[3.2.1]octane (**26**; 0.77 g, 8%), which, after three recrystallisations from light petroleum–acetone, had m.p. 109–110°, $[\alpha]_D$ +61°. ^{1}H-N.m.r. data are given in Table I.

Anal. Calc. for $C_{30}H_{25}NO_{12}$: C, 60.9; H, 4.3; N, 2.4. Found: C, 61.1; H, 4.4; N, 2.2.

Reaction of the hemiacetal **24** *with hydroxylamine.* — A mixture of **24** (0.65 g) and hydroxylamine hydrochloride (0.4 g) was heated under reflux for 3 h in ethanol (5 mL) and pyridine (5 mL). The solvents were removed and toluene (10 mL) was evaporated from the residue. Trituration with water then gave a 1:1 mixture (0.75 g, 95%) of **27** and **28**, which, after three recrystallisations from chloroform–ethanol, had m.p. 206–212°, $[\alpha]_D$ −44° (acetone).

Anal. Calc. for $C_{28}H_{25}NO_9$: C, 64.8; H, 4.9; N, 2.7. Found: C, 65.1: H, 4.9; N, 2.8.

Recrystallisation of the mixture from ethanol gave (2*S*)-(2,4,5/3)-2,3,5-tribenzoyloxy-1,4-dihydroxycyclohexane-1-carbaldehyde oxime (**27**), m.p. 209–211°, $[\alpha]_D$ −48° (acetone). ^{1}H-N.m.r. data: δ 2.34 (dd, 1 H, $J_{5,6}$ 3, $J_{6,6'}$ 15 Hz, H-6), 2.72 (dd, 1 H, $J_{5,6'}$ 4 Hz, H-6′), 4.44 (dd, 1 H, $J_{3,4}$ 9.5, $J_{4,5}$ 3.5 Hz, H-4), 5.69 (d, 1 H, $J_{2,3}$ 9.5 Hz, H-2), 5.7 (m, 1 H, H-5), 5.98 (t, 1 H, H-3), 10.22 (s, 1 H, OH), together with benzoyl signals.

The ^{1}H-n.m.r. data for the isomer (2*S*)-(2,4,5/3)-2,3,4-tribenzoyloxy-1,5-dihydroxycyclohexane-1-carbaldehyde oxime (**28**) (obtained by difference): δ 2.41 (m, 2 H, H-6,6′), 4.6 (m, 1 H, H-5), 5.54 (dd, 1 H, $J_{3,4}$ 10, $J_{4,5}$ 3 Hz, H-4), 5.76 (d, 1 H, $J_{2,3}$ 10 Hz, H-2), 6.14 (t, 1 H, H-3), 10.37 (s, 1 H, OH), together with benzoyl signals.

REFERENCES

1 R. J. FERRIER, *J. Chem. Soc., Perkin Trans. 1*, (1979) 1455–1458.
2 F. SUGAHARA AND H. KUZUHARA, *Agric. Biol. Chem.*, 45 (1981) 301–304.
3 N. SAKAIRI AND H. KUZUHARA, *Tetrahedron Lett.*, (1982) 5327–5330.
4 I. PINTÉR, J. KOVÁCS, A. MESSMER, G. TÓTH, AND S. D. GERO, *Carbohydr. Res.*, 116 (1983) 156–161.
5 D. SEMERIA, M. PHILIPPE, J.-M. DELAUMENY, A.-M. SEPULCHRE, AND S. D. GERO, *Synthesis*, (1983) 710–713.
6 I. PELYVÁS, F. SZTARICSKAI, AND R. BOGNÁR, *J. Chem. Soc., Chem. Commun.*, (1984) 104–105.
7 F. CHRETIEN AND Y. CHAPLEUR, *J. Chem. Soc., Chem. Commun.*, (1984) 1268–1269.
8 A. S. MACHADO, A. OLESKER, S. CASTILLON, AND G. LUKACS, *J. Chem. Soc., Chem. Commun.*, (1985) 330–332.
9 R. BLATTNER AND R. J. FERRIER, unpublished results.
10 R. BLATTNER, R. J. FERRIER, AND P. PRASIT, *J. Chem. Soc., Chem. Commun.*, (1980) 944–945.
11 R. BLATTNER, R. J. FERRIER, AND S. R. HAINES, *J. Chem. Soc., Perkin Trans. 1*, (1985) 2413–2416.
12 A. S. MACHADO, A. OLESKER, AND G. LUKACS, *Carbohydr. Res.*, 135 (1985) 231–239.
13 R. J. FERRIER, S. CHEW, P. PRASIT, AND P. C. TYLER, *Proc. IUPAC Symp. Org. Synth., Vth, Freiburg*, 1984, pp. 247–254.
14 R. J. FERRIER AND S. R. HAINES, *Carbohydr. Res.*, 130 (1984) 135–146.
15 R. J. FERRIER AND P. C. TYLER, *J. Chem. Soc., Perkin Trans. 1*, (1980) 1528–1534.
16 R. BLATTNER, R. J. FERRIER, AND P. C. TYLER, *J. Chem. Soc., Perkin Trans. 1*, (1980) 1535–1539.
17 S. J. ANGYAL AND M. E. TATE, *J. Chem. Soc.*, (1965) 6949–6955.
18 W. MEYER ZU RECKENDORF, *Chem. Ber.*, 101 (1968) 3652–3654.
19 T. SUAMI, K. TADANO, Y. KAMEDA, AND Y. IIMURA, *Chem. Lett.*, (1984) 1919–1922.
20 S. HORII, H. FUKASE, AND Y. KAMEDA, *Carbohydr. Res.*, 140 (1985) 185–200.
21 A. D. ARGOUDELIS, R. W. SPRAGUE, AND S. A. MIZSAK, *J. Antibiot.*, 29 (1976) 787–796.
22 T. POSTERNAK AND J.-G. FALBRIARD, *Helv. Chim. Acta*, 43 (1960) 2142–2147.
23 T. SUAMI, S. OGAWA, T. ISHIBASHI, AND I. KASAHARA, *Bull. Chem. Soc. Jpn.*, 49 (1976) 1388–1390.
24 A. GIDDEY, F. G. COCU, B. POCHELOU, AND T. POSTERNAK, *Helv. Chim. Acta*, 57 (1974) 1963–1974.
25 D. R. PAULSON, F. Y. N. TANG, G. F. MORAN, A. S. MURRAY, B. P. PELKA, AND E. M. VASQUEZ, *J. Org. Chem.*, 40 (1975) 184–186.
26 C. D. GUTSCHE, *Org. React.*, 8 (1954) 364–429.
27 D. HORTON AND J. S. JEWELL, *Carbohydr. Res.*, 5 (1967) 149–160.
28 R. J. FERRIER AND R. H. FURNEAUX, *Aust. J. Chem.*, 33 (1980) 1025–1036.
29 L. M. JACKMAN AND S. STERNHELL, *Applications of N.M.R. Spectroscopy in Organic Chemistry*, 2nd edn., Pergamon, Oxford, 1969, p. 270.
30 J. P. HORWITZ, N. MODY, AND R. GASSER, *J. Org. Chem.*, 35 (1970) 2335–2339.
31 W. A. TEMPLE, Ph.D. Thesis, University of Otago, 1975.
32 L. J. T. ANDREWS, J. M. COXON, AND M. P. HARTSHORN, *J. Org. Chem.*, 34 (1969) 1126–1127.
33 J. S. PIZEY, *Synthetic Reagents*, Vol. 2, Wiley, New York, 1974, p. 65.
34 P. J. BLACK AND M. L. HEFFERNAN, *Aust. J. Chem.*, 16 (1963) 1051–1055.
35 c.f. R. U. LEMIEUX, F. F. Z. GEORGES, AND Z. SMIATACZ, *Heterocycles*, 13 (1979) 169–173.