# Functionalised Carbocycles from Carbohydrates. Part 4.[1] The Synthesis of the Epoxy Lactone Prostaglandin Intermediate *via* Bicyclo[3.2.0]heptane Derivatives. *X*-Ray Crystal Structure of (1*R*)-5-*endo*-Acetyl-2-*exo*,3-*endo*-dibenzoyloxybicyclo[2.2.1]heptane

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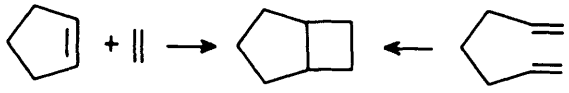
Irradiation of the nona-3,8-dienulose derivative (2) at 350 nm gave the bicyclo[3.2.0]heptyl methyl ketone (3) in good yield. This was converted *via* the acetate (5) into the corresponding bicycloheptanol (6) which, with base, gave the cyclopentenyl aldehyde (9). This is an intermediate in the preparation of the epoxy lactone (11), a synthetic precursor of the prostaglandins, and this procedure therefore represents a new route to these natural products. With base, compound (3) gave the tricyclic product (4) in good yield. Ring-opening reactions of the latter afford trinorbornane derivatives, one of which, compound (13), was characterised by *X*-ray diffraction analysis.

We are concurrently reporting the preparation of the (*E*)-nona-3,8-dienulose derivative (2) from the 5,6-dideoxyhex-5-enose 2,3,4-triester (1),[2] and our interest in the preparation of functionalised cyclopentanes from carbohydrates [1] led us to consider this dienone as a possible precursor of such compounds. Although cyclobutanes are the invariable products of [2 + 2]-cycloaddition reactions applied to pairs of alkene double bonds, the process can be used in two ways to obtain compounds which also contain fused five-membered rings *i.e.* bicyclo[3.2.0]heptanes: either cyclopentenes can be used as at least one of the alkenes, or the two rings can be formed concurrently by intramolecular reaction of 1,6-dienes (Scheme 1). Frequently, [2 + 2]cycloaddition reactions are effected photochemically with compounds in which one of the alkene groups is a component of a conjugated enone,[3] and the bicyclo[3.2.0]heptane ring system may be produced in this way by use of cyclopent-2-enones and alkenes [4] (also cyclopentadienes and ketenes [4]) or intramolecularly from dienone derivatives exemplified by compound (2). Such reactions applied intramolecularly to obtain bicyclo[3.2.0]heptanes from wholly acyclic compounds are apparently rare, although related bicyclic systems have been made in this way.[5] However, alicyclic conjugated enones have been utilised on many occasions [6] and many syntheses of natural products depend upon their use.[7]

When the diene (2) was irradiated at 350 nm in dilute benzene solution a crystalline compound (3) was obtained which was the product of a [2 + 2]cycloaddition reaction with the cyclobutane ring fused in the *trans*-relationship to the adjacent ester groups, and with the acetyl group in the *exo*-orientation (Scheme 2). This is sterically the most favoured product and would be expected to predominate in a reaction which is believed to occur in stepwise fashion and to involve a triplet excited enone.[8] In related, but intermolecular, examples sterically favoured products have likewise been found to predominate; for example, photoinduced addition of propene to cyclopent-2-enone gives mainly *exo*-products and, similarly, cyclopentene added photochemically to the same enone affords a large preponderance of the product with the two five-membered rings in the *anti*-relationship.[3] Consistent with the assigned structure, compound (3) on treatment with 1,5-diazabicyclo[5.4.0]undec-5-ene gave the crystalline tricyclic product (4) in high yield following proton abstraction from

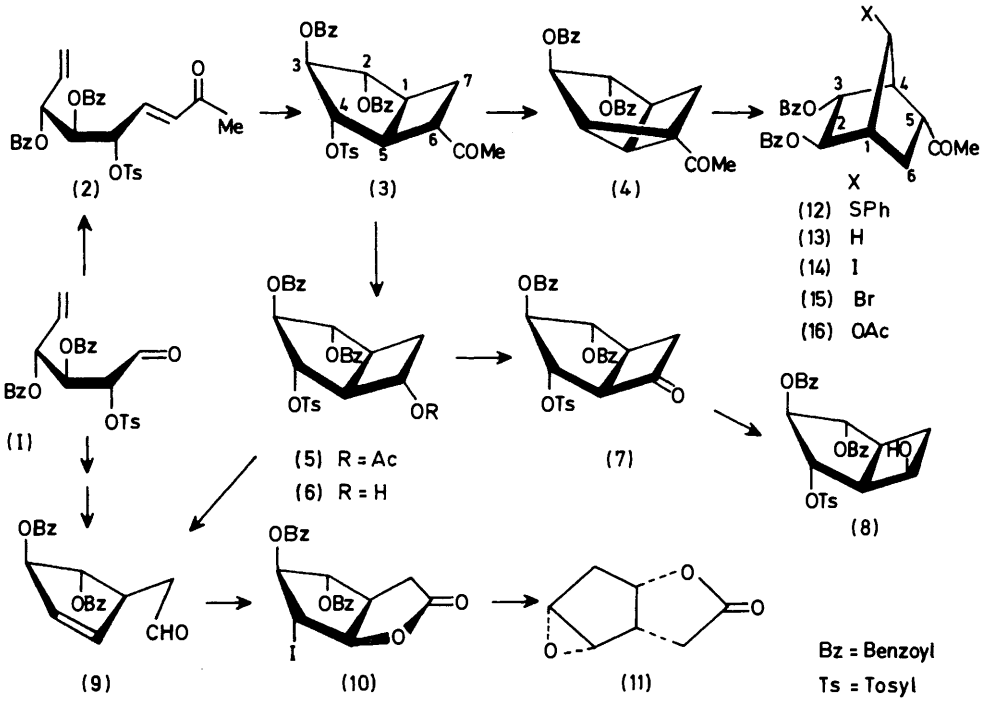


**Scheme 1.**

C-6 and nucleophilic displacement of the sulphonyloxy group which, it is assumed, was suitably orientated for displacement, *i.e. exo*. It has previously been found that carbanions generated at C-6 of bicyclo[3.2.0]heptanes readily displace *exo*-leaving groups at C-4 to give tricyclo[3.2.0.0$^{4,6}$]heptanes,[9] one such product derived in this manner having been characterised by *X*-ray diffraction analysis.[10] While in the cases cited in the literature the required carbanion stabilisation was provided by a carbonyl group at C-7, in the present case the exocyclic ketonic group was responsible.

Baeyer–Villiger oxidation of cycloalkyl methyl ketones [11] and, in particular, cyclobutyl methyl ketone,[12] proceeds mainly with migration of the cycloalkyl group to give cycloalkyl acetates with retention of configuration and, in agreement with this, the ketone (3) afforded the acetate (5) in high yield on treatment with trifluoroperacetic acid.[14] When boron trifluoride and hydrogen peroxide [14] were used for the reaction the oxidation was inconsistent and the derived acetate underwent hydrolysis to the alcohol (6). This latter observation led to suitable means of obtaining this compound, the ester (5) giving it in high yield when heated in tetrahydrofuran (THF) containing aqueous hydrogen chloride. On oxidation with pyridinium dichromate [15] the alcohol (6) gave the ketone (7) and this, on treatment with sodium borohydride, afforded the C-6 epimeric alcohol (8). Since it has been shown [4] that such alcohols derived in this way are produced by *exo*-attack of the reagent and thus have the *endo*-configuration, it is established that its epimer (6) has the *exo*-configuration as, therefore, have the acetate (5) and the original methyl ketone (3).

A common method of opening the four-membered rings of bicyclo[3.2.0]heptan-6-one derivatives to allow access to cyclopentanes carrying two-carbon substituents (at C-1) utilises the Baeyer–Villiger oxidation to give the corresponding lactones.[4,16] The alcohol (6) on treatment with sodium hydride provided another method, being converted quantitat-




**Scheme 2.**

ively into the cyclopentene (9) (which has the two-carbon substituent at C-5). This ring-opening reaction is analogous to others which have been observed in cyclobutane derviatives which can readily accept an electron pair at one ring carbon atom and which have a leaving group at a β-related carbon atom (either in the ring or attached exocyclically to the α-related carbon atom).[17]

Since the aldehyde (9) and the crystalline iodo lactone (10), into which it was converted for characterisation purposes, are both synthetic precursors of the epoxy lactone (11) [1] which is a prostaglandin intermediate, the above synthesis of the aldehyde represents a new approach to the prostaglandins. This route, in our opinion, is to be preferred to the previously reported procedure by which the enal (1) is converted into the aldehyde (9) by way of a bicyclic isoxazolidine intermediate;[1] in particular, the two-carbon side-chain is introduced more readily by the present methods.

Any general approach to prostaglandin precursors from compound (3) requires a method for the reductive removal of the sulphonyloxy group and, to this end, it was of interest to determine whether, on treatment with nucleophiles, the triester would give analogous products with the nucleophilic group bonded to C-4. The main compound obtained by use of sodium benzenethiolate gave a $^1$H n.m.r. spectrum which indicated that its carbon skeleton was structurally different from that of the starting material. In particular, there were ring proton resonances in the region δ 1.6—2.1 which were not present in the spectrum of compound (3). This same product was then observed to result from analogous treatment of the tricyclic ketone (4) (which is therefore assumed to have been formed as an intermediate) and the product was thus assigned the bicyclo[2.2.1]heptane structure (12).

When compound (4) was treated with zinc dust in acetic acid a crystalline compound was obtained which gave an analogous $^1$H n.m.r. spectrum to that of compound (12), and it was shown by *X*-ray diffraction analysis to have structure (13) (see below). It was also obtained from compound (4), and in better yield, by use of tributyltin hydride. Likewise, when the tricyclic ketone was heated with sodium iodide in refluxing acetic anhydride the iodide (14) belonging to the same series ($^1$H n.m.r. evidence) was formed and, with hydrogen bromide in acetic acid–acetic anhydride, two products, assumed from their closely similar spectra to be the bromide (15) and the acetate (16), were produced. The n.m.r. parameters of these compounds were consistent with their being trinorbornyl derivatives,[18] and in spin decoupling experiments carried out on the iodide (14) the ' iodo proton ' was shown to be coupled to the higher field ester ring proton, *i.e.* the 2-H *endo*, as is characteristic of proton pairs in this particular relationship in the trinorbornyl system.[19] Had the iodine atom simply replaced the sulphonyloxy group of compound (3) the corresponding proton (4-H) would conceivably have been coupled to the low-field ester ring proton (3-H) but not to the other (2-H). The *endo*-proton at C-2 showed no measurable coupling with 1-H whereas the *exo*-proton at C-3 gave $J_{3,4}$ values of *ca.* 4 Hz. Except in the case of compound (13) the 5-H resonances overlapped with those of 4-H, but with this compound 5-H gave a five-band signal indicating $J_{4,5}$, $J_{5,6}$(*endo*), and $J_{5,6}$(*exo*) values of *ca.* 5, 5, and 10 Hz, respectively. This is consistent with expectations for an *exo*-proton at this position.[18] An *X*-ray diffraction analysis of compound (13) confirmed its trinorbornyl character (Figure) It is noteworthy that the acetyl group is *endo* despite the fact that the nearer ester group also has this orientation so the compound presumably resulted from a kinetically controlled *exo*-protonation step.

Compound (4), therefore, underwent attack by nucleophilic reagents at C-5 (path a, Scheme 3). The bond common to the two smallest rings was cleaved, and this is consistent with several cases of analogous ring opening of tricyclo[3.2.0.0$^{2,7}$]-heptan-6-ones which also give 7-substituted trinorbornanes.[10,16,18a]

The encountered method by which the tricyclic compound (4) reacted with nucleophiles therefore precluded its use as a means of desulphonylating compound (3). Had path b (Scheme 3) been followed, reductive removal of this ester group would have been greatly facilitated, but the above findings are not

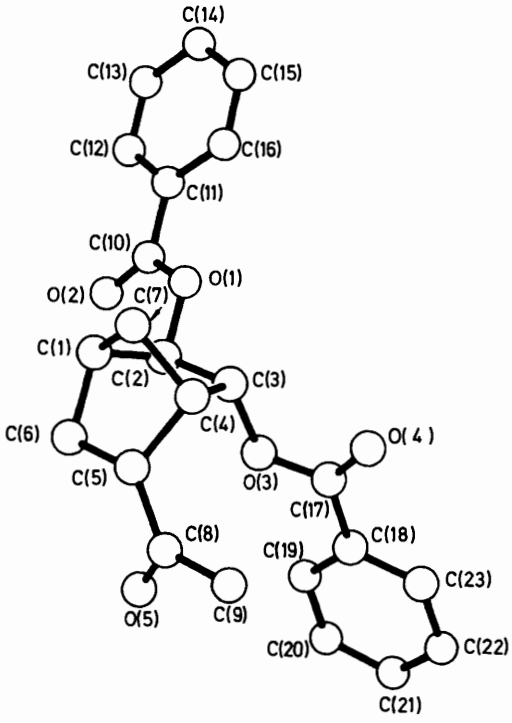



**Figure.** *X*-Ray crystal structure of (1R)-5-*endo*-acetyl-2-*exo*,3-*endo*-dibenzoyloxybicyclo[2.2.1]heptane (13)

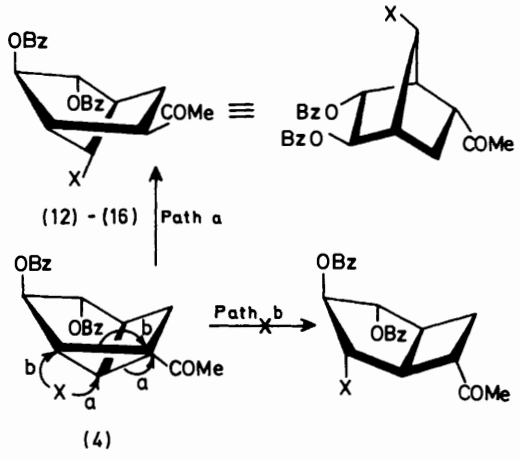
necessarily without relevance to prostaglandin synthesis since one approach is entirely dependent upon stereospecific introduction of ω-chain nucleophilic groups at C-7 of trinorbornane derivatives.[16]

## Experimental

N.m.r. spectra were measured in deuteriochloroform solutions with a Varian FT 80A instrument. Optical rotations were measured in chloroform and within the concentration range 0.5—1.5%. light petroleum refers to that fraction boiling in the range 60—80 °C. Organic solutions were dried with sodium sulphate or magnesium sulphate.

(1S,5S)-6-exo-*Acetyl*-2-exo,3-endo-*dibenzoyloxy*-4-exo-*tosyloxybicyclo*[3.2.0]*heptane* (3).—A solution of the dienone (2)[2] (3.5 g) in benzene (610 ml) was photolysed in a water-cooled Rayonet reactor with a 350-nm source for 3 d. Removal of the solvent gave the crystalline *bicyclic ketone* (3) which was recrystallised from ethyl acetate–light petroleum (3.02 g, 86%), m.p. 139—140 °C, $[\alpha]_D$ +7° (Found: C, 65.3; H, 5.4; S, 5.7. $C_{30}H_{28}O_8S$ requires C, 65.7; H, 5.1; S, 5.8%); $\delta_H$ 2.15 (3 H, s, Ac), 2.34 (3 H, s, $C_6H_4CH_3$), 2.2—3.4 (5 H, m, 1-, 5-, 6-, 7-, and 7-H), 5.13 (1 H, dd, $J_{4,5}$ 1.4, $J_{3,4}$ 3.1 Hz, 4-H), 5.38 (1 H, dd, $J_{2,3}$ 3.2, $J_{1,2}$ 1.9 Hz, 2-H), 5.77 (1 H, t, 3-H), and 7.1—8.0 (14 H, m, ArH); $\delta_C$ 21.62 ($C_6H_4CH_3$), 24.63 (C-7), 27.33 ($COCH_3$), 40.21 (C-6), 45.57 and 46.81 (C-5 and -1), 81.58, 82.61, and 86.72 (C-4, -3, and -2), and 206.39 p.p.m. ($COCH_3$), as well as ester-carbon signals.

In several repetitions of the above photochemical reaction the yields were 55—60%. When compound (1) was converted into the dienone and the product photolysed without purification, a 30% yield based on the original 6-iodo compound [precursor of the enone (1)] was obtained. This represents a simple way of making the ketone (3), but under these conditions longer irradiation times are required.




**Scheme 3.**

(1S,5R)-6-exo-*Acetyl*-2-exo,3-endo,4-exo-*dibenzoyloxytricyclo*[3.2.0.$0^{2,7}$]*heptane* (4).—The ketone (3) (1.0 g) was stirred for 15 h at 60 °C with 1,5-diazabicyclo[5.4.0]undec-5-ene (0.42 g, 1.5 mol equiv.) in *N*,*N*-dimethylformamide (12 ml). The solvent was removed, the dark residue was dissolved in chloroform, and the solution was washed successively with aqueous hydrochloric acid (dilute), aqueous sodium hydrogen carbonate, and water. After being dried the organic phase was evaporated to give a brown residue (0.87 g) which was passed in solution through a short column of silica gel and gave a chromatographically pure product (0.68 g). Recrystallisation from diethyl ether–light petroleum gave the *tricyclic ketone* (4) (0.57 g, 83%), m.p. 81—83 °C; $[\alpha]_D$ −215° (Found: C, 73.0; H, 5.3. $C_{23}H_{20}O_5$ requires C, 73.4; H, 5.3%); $\delta_H$ 1.6—1.9 (2 H, m, 7-Hz), 1.97 (3 H, s, Ac), 2.68 (1 H, br d, $J_{1,7}$ 5.8 Hz, 1-H), 3.04 (1 H, t, $J_{4,5} = J_{3,4}$ 5 Hz, H-4), 3.30 (1 H, br d, H-5) 5.16 (1 H, s, H-2), 5.92 (1 H, dd, *J* 1.4 and 4.7 Hz, 3-H), and 7.2—8.1 (10 H, ArH); $\delta_C$ 24.36 ($COCH_3$), 25.29 (C-7), 35.44 (C-6), 36.24, 38.09, and 40.24 [C-1, -4, -5 specific resonances unassigned)], 81.69 and 82.87 [C-2, -3, (specific resonances unassigned)], and 204.46 p.p.m. ($COCH_3$), together with ester-carbon resonances.

(1S,5S)-6-exo-*Acetoxy*-2-exo,3-endo-*dibenzoyloxy*-4-exo-*tosyloxybicyclo*[3.2.0]*heptane* (5).—A solution of trifluoroperacetic acid in dichloromethane [prepared by the slow addition at 0 °C of trifluoroacetic anhydride (1.7 ml) to a stirred mixture of hydrogen peroxide (0.35 ml; 90%) and dichloromethane (5 ml)] was added dropwise at 0 °C during 6 h to a stirred solution of the methyl ketone (3) (1.28 g) in dry dichloromethane (15 ml) containing powdered anhydrous disodium hydrogen phosphate. The mixture was then stirred at 20 °C for 15 h, diluted with dichloromethane, and washed successively with aqueous sodium hydrogen sulphite and water. After being dried the solution was evaporated and the product was freed from small amounts of starting material by chromatography on a column of silica gel to give the *acetate* (5) (1.12 g, 85%). Recrystallisation from ethyl acetate–light petroleum gave m.p. 120—123 °C, $[\alpha]_D$ −39° (Found: C, 63.6; H, 5.1; S, 5.8. $C_{30}H_{28}O_9S$ requires C, 63.8; H, 5.0; S, 5.7%); $\delta_H$ 2.06 (3 H, s, OAc), 2.35 (3 H, s, $C_6H_4CH_3$), 2.4—2.6 (2 H, m, 7-$H_2$), 2.9—3.3 (2 H, m, 1- and 5-H), 4.95—5.25 (2 H, m, 4- and 6-H), 5.31 (1 H, t, *J* 2.4 Hz, 2-H), 5.73 (1 H, br s, 3-H), and 7.1—8.0 (14 H, ArH).

(1S,5S)-2-exo,3-endo-*Dibenzoyloxy*-6-exo-*hydroxy*-4-exo-*tosyloxybicyclo*[3.2.0]*heptane* (6).—A solution of the acetate

(5) (1.0 g) in freshly distilled THF (30 ml) containing aqueous hydrogen chloride (1M; 1 ml) was heated under reflux for 12 h whence a more polar product was formed. The solvent was removed and the residue partitioned between chloroform and aqueous sodium hydrogen carbonate. The organic phase was washed with water, dried, and evaporated to dryness to leave a syrup (0.93 g). After chromatography on a column of silica gel the alcohol (6) (0.77 g, 83%) was crystallised from benzene–light petroleum and had m.p. 125—127 °C, [α] −36° (Found: C, 63.9; H, 5.2; S, 6.2. $C_{28}H_{26}O_8S$ requires C, 64.4; H, 5.0; S, 6.1%); $\delta_H$ 2.29 (3 H, s, $C_6H_4CH_3$), 2.4—2.6 (2 H, m, 7-$H_2$), 2.93 (1 H, s, OH), 3.06 (2 H, m, 1- and 5-H), 4.5 (1 H, m, 6-H), 5.08 (1 H, m, $w_{\frac{1}{2}}$ 7 Hz, 4-H), 5.28 (1 H, m, $w_{\frac{1}{2}}$ 10 Hz, 2-H), 5.75 (1 H, m, $w_{\frac{1}{2}}$ 10 Hz, 3-H), and 6.9—8.0 (14 H, ArH).

(1S,5R)-2-exo,3-endo-*Dibenzoyloxy*-6-*oxo*-4-exo-*tosyloxybicyclo*[3.2.0]*heptane* (7).—The alcohol (6) (0.42 g) was stirred for 15 h at 20 °C in dichloromethane (5 ml) with pyridinium dichromate (0.48 g, 1.5 mol equiv.), diethyl ether (30 ml) was then added, and the solids and solvents were removed to afford the *ketone* (7) (0.4 g, 95%) which was essentially pure. The product was recrystallised from methanol and had m.p. 131—132 °C, $[\alpha]_D$ −38° (Found: C, 64.4; H, 4.8; S, 5.3. $C_{28}H_{24}O_8S$ requires C, 64.6; H, 4.6; S, 6.1%); $\delta_H$ 2.40 (3 H, s, $C_6H_4CH_3$), 2.95—3.6 (3 H, m, 1-, 7-, and 7-H), 4.15 (1 H, m, 5-H), 5.15 (1 H, s, 4-H), 5.45 (1 H, s, 2-H), 5.71 (1 H, s, 3-H), and 7.1—8.1 (14 H, ArH); $\delta_C$ 21.70 ($C_6H_4CH_3$), 35.70 (C-7), 51.84 (C-1), 70.32 (C-5), 80.54, 81.83, and 83.46 (C-4, -3, and -2), and 203.02 p.p.m. (C-6), together with ester-carbon signals.

(1S,5S)-2-exo,3-endo-*Dibenzoyloxy*-6-endo-*hydroxy*-4-exo-*tosyloxybicyclo*[3.2.0]*heptane* (8).—A saturated solution of sodium borohydride in ethanol (*ca.* 0.2 ml) was added to a solution of the ketone (7) (50 mg) in THF–ethanol (3 ml; 2 : 1) at −70 °C and the temperature of the mixture was kept below −60 °C for 2 h. Acetic acid (0.2 ml) was added, the solvent was removed, and the residue was partitioned between water and chloroform. The dried chloroform phase contained two components which were isolated by p.l.c. The more mobile faction (35 mg, 70%) was the required endo-*alcohol* (8) which, when crystallised from ethyl acetate–light petroleum, had m.p. 141—142 °C, $[\alpha]_D$ −37° (Found: C, 64.0; H, 5.2; S, 6.2. $C_{28}H_{26}O_8S$ requires C, 64.4; H, 5.0; S, 6.1%); $\delta_H$ 2.25 (3 H, s, $C_6H_4CH_3$), 2.4—3.0 (4 H, m, 1-, 7-, and 7-H and OH), 3.30 (1 H, m, 5-H), 4.55 (1 H, m, 6-H), 5.12 (1 H, dd, $J_{4,5}$ 2.7, $J_{3,4}$ 6.4 Hz, 4-H), 5.48 (1 H, dd, $J_{2,3}$ 7.4, $J_{1,2}$ 5.1 Hz, 2-H), 5.95 (1 H, t, 3-H), and 7.0—8.0 (14 H, ArH).

The less mobile component (5 mg) was crystallised from benzene–light petroleum, m.p. 125—127 °C [undepressed on admixture with a sample of the *exo*-alcohol (6)].

(1R,5R)-6-exo,7-endo-*Dibenzoyloxy*-8-exo-*iodo*-3-*oxo*-2-*oxabicyclo*[3.3.0]*octane* (10).—A solution of the alcohol (6) (0.05 g) in dichloromethane (2 ml) was added slowly at 0 °C to a stirred suspension of sodium hydride (5 mg) in dichloromethane (0.5 ml). The mixture was stirred at 0 °C for 0.5 h and then for 6 h at 20 °C. Dichloromethane was added, the mixture was washed with water and dried, and the solvent was removed to give the essentially pure syrupy aldehyde (9) (0.033 g, 100%) $[\alpha]_D$ −200°; the $^1H$ n.m.r. spectrum was identical to that previously reported.[1]

Pyridinium dichromate (0.11 g) was added to a solution of the aldehyde (9) (0.033 g) in *N*,*N*-dimethylformamide (1 ml) and the mixture was stirred at 20 °C for 5 h and was then poured into water and extracted with diethyl ether. The extract was dried and filtered through silica gel to give the corresponding carboxylic acid (0.033 g, 96%) which was treated in THF (1 ml) with iodine (0.035 g) at 0 °C for 4 h. Work-up as before[1] gave the iodo lactone [0.039 g, 83% based on the alcohol (6)], m.p. 162—164 °C; $[\alpha]_D$ +9.6° (lit.,[18] 162—164 °C; +11°). The $^1H$ n.m.r. spectrum was identical to that of the earlier sample.

(1S,7S)-5-endo-*Acetyl*-2-exo,3-endo-*dibenzoyloxy*-7-*phenylthiobicyclo*[2.2.1]*heptane* (12).—The ketone (3) (0.2 g) was stirred for 15 h in *N*,*N*-dimethylformamide in the presence of sodium benzenethiolate (0.27 g) and the three products formed were isolated by p.l.c. The most mobile (53 mg) was apparently a product of aldol condensation, the slowest (21 mg) was not characterised, and the intermediate, main compound (71 mg, 40%) was the *phenylthiotrinorbornane* (12) which was crystallised from methanol, m.p. 143—144 °C; $[\alpha]_D$ −81° (Found: C, 71.5; H, 5.6; S, 6.5. $C_{29}H_{26}O_5S$ requires C, 71.6; H, 5.4; S, 6.6%); $\delta_H$ 1.85 (1 H, m, 6-$H_{endo}$), 2.11 (3 H, Ac), 2.27 (1 H, m, 6-$H_{exo}$), 2.70 (1 H, br d, $J_{1,6(exo)}$) 4 Hz, 1-H), 3.0—3.2 (2 H, m, 4- and 5-H), 3.53 (1 H, br s, $w_{\frac{1}{2}}$ 5 Hz, 7-H), 5.06 (1 H, dd, $J_{2,3} = J_{2,7}$ 2.1 Hz, 2-H), 6.05 (1 H, dd, $J_{3,4}$ 4.1 Hz, 3-H), and 7.1—8.1 (15 H, ArH).

The compound was also produced by treatment of the tricyclic ketone (4) (40 mg) with sodium benzenethiolate (14 mg) in *N*,*N*-dimethylformamide (1 ml) for 6 h at 20 °C. Isolated by p.l.c., the product (33 mg, 64%) had the same $^1H$ n.m.r. spectrum as the previous sample.

(1R)-5-endo-*Acetyl*-2-exo,3-endo-*dibenzoyloxybicyclo*-[2.2.1]*heptane* (13).—The tricyclic ketone (4) (0.1 g) was stirred in acetic acid (2 ml) in the presence of zinc dust (0.6 g) for 15 h, further zinc (0.1 g) was then added, and the mixture was stirred for a further 6 h. The solids and solvent were removed and the products were resolved into a mobile (50 mg, 50%) and a much less mobile fraction (34 mg) by p.l.c. The latter fraction was not a discrete compound ($^1H$ n.m.r.) but the former was the *trinorbornyl derivative* (13) which was recrystallised from ethyl acetate–light petroleum, m.p. 134—136 °C; $[\alpha]_D$ −129° (Found: C, 73.3; H, 6.3. $C_{23}H_{22}O_5$ requires C, 73.0; H, 5.9%); $\delta_H$ 1.6—2.0 (3 H, m, 6-$H_{endo}$ and 7-$H_2$), 1.99 (3 H, s, Ac), 2.25 (1 H, m, 6-$H_{exo}$), 2.55 (1 H, d, $J_{1,2(exo)}$ 5 Hz, 1-H), 2.80 (1 H, ddd, $J_{4,5} = J_{5,6(endo)}$ 5, $J_{5,6(exo)}$ 10 Hz, 5-H), 3.25 (1 H, m, 4-H), 4.87 (1 H, t, $J_{2,3} = J_{2,7}$ 2.2 Hz, 2-H), 5.52 (1 H, dd, $J_{3,4}$ 3.5 Hz, 3-H), and 7.2—8.0 (10 H, ArH).

Treatment of compound (4) (110 mg) with tributyltin hydride (150 mg) and azobisisobutyronitrile (5 mg) in refluxing benzene (2 ml) for 1 h gave the same product specifically ($^1H$ n.m.r. analysis).

*Treatment of Compound* (4) *with Other Nucleophiles.*—A solution of the ketone (4) (0.1 g) in acetic acid (1 ml) containing small proportions of acetic anhydride was treated at 0 °C with hydrogen bromide in acetic acid (0.2 ml; 33%) for 1 h. The two products were isolated by standard procedures, separated by p.l.c., and characterised by $^1H$ n.m.r. spectroscopy as the bromide (15) and the acetate (16). Both gave all n.m.r. resonances within 0.2 p.p.m. of the corresponding resonances for the phenylthio compound (12) except for 7-H which resonated at $\delta_H$ 4.07 and 4.90 for the bromide (15) and acetate (16), respectively.

A further portion of the ketone (4) (0.1 g) was heated under reflux in acetic anhydride (1 ml) with sodium iodide (0.1 g) for 0.5 h to give essentially one product which, after p.l.c., gave a $^1H$ n.m.r. spectrum closely similar to that of compound (12) (all resonances within 0.2 p.p.m.) except that 7-H resonated at $\delta_H$ 3.92.

**Table 1.** Atomic co-ordinates for compound (13) with e.s.d.s in parentheses

| | $10^4x$ | $10^4y$ | $10^5z$ | | $10^4x$ | $10^4y$ | $10^5z$ |
|---|---|---|---|---|---|---|---|
| O(1) | 133(2) | 5 773(2) | 47 062(3) | C(10) | −1 003(3) | 6 530(3) | 45 695(4) |
| O(2) | −1 896(2) | 7 519(2) | 46 549(3) | C(11) | −1 017(3) | 5 959(3) | 43 057(4) |
| O(3) | 383(2) | 4 529(2) | 53 121(3) | C(12) | −1 971(3) | 6 761(3) | 41 357(4) |
| O(4) | 1 982(2) | 2 375(2) | 53 574(3) | C(13) | −2 008(3) | 6 273(3) | 38 864(4) |
| O(5) | 934(2) | 7 258(2) | 57 282(3) | C(14) | −1 081(3) | 4 984(3) | 38 089(4) |
| C(1) | 1 533(3) | 7 758(3) | 49 611(4) | C(15) | −133(3) | 4 184(3) | 39 801(4) |
| C(2) | 369(3) | 6 347(3) | 49 618(4) | C(16) | −93(3) | 4 665(3) | 42 286(4) |
| C(3) | 1 312(3) | 5 027(3) | 50 971(4) | C(17) | 845(3) | 3 151(3) | 54 255(4) |
| C(4) | 2 908(3) | 5 829(3) | 51 665(4) | C(18) | −212(3) | 2 774(3) | 56 417(4) |
| C(5) | 2 632(3) | 7 136(3) | 53 687(4) | C(19) | −1 489(3) | 3 733(3) | 57 072(4) |
| C(6) | 1 590(3) | 8 391(3) | 52 322(4) | C(20) | −2 419(4) | 3 346(4) | 59 132(4) |
| C(7) | 3 135(3) | 6 881(3) | 49 320(4) | C(21) | −2 067(4) | 2 000(4) | 60 539(4) |
| C(8) | 2 082(3) | 6 643(3) | 56 264(4) | C(22) | −780(4) | 1 032(4) | 59 887(4) |
| C(9) | 3 096(4) | 5 432(4) | 57 627(4) | C(23) | 136(4) | 1 419(3) | 57 798(4) |

**Table 2.** Intramolecular bond distances and angles for compound (13) with e.s.d.s in parentheses

| Atoms | Distance (Å) | Atoms | Distance (Å) |
|---|---|---|---|
| O(1)–C(2) | 1.461(3) | O(1)–C(10) | 1.358(3) |
| O(2)–C(10) | 1.208(3) | O(3)–C(3) | 1.449(3) |
| O(3)–C(17) | 1.361(3) | O(4)–C(17) | 1.211(3) |
| O(5)–C(8) | 1.220(3) | C(1)–C(2) | 1.535(4) |
| C(1)–C(6) | 1.542(3) | C(1)–C(7) | 1.541(4) |
| C(2)–C(3) | 1.541(4) | C(3)–C(4) | 1.544(4) |
| C(4)–C(5) | 1.556(4) | C(4)–C(7) | 1.543(3) |
| C(5)–C(6) | 1.550(4) | C(5)–C(8) | 1.509(3) |
| C(8)–C(9) | 1.512(4) | C(10)–C(11) | 1.487(3) |
| C(11)–C(12) | 1.384(4) | C(11)–C(16) | 1.396(4) |
| C(12)–C(13) | 1.393(3) | C(13)–C(14) | 1.395(4) |
| C(14)–C(15) | 1.385(4) | C(15)–C(16) | 1.387(3) |
| C(17)–C(18) | 1.489(3) | C(18)–C(19) | 1.384(4) |
| C(18)–C(23) | 1.386(4) | C(19)–C(20) | 1.387(4) |
| C(20)–C(21) | 1.388(4) | C(21)–C(22) | 1.395(4) |
| C(22)–C(23) | 1.393(4) | | |

| Atoms | Angle (°) | Atoms | Angle (°) |
|---|---|---|---|
| C(2)–O(1)–C(10) | 116.3(2) | C(3)–O(3)–C(17) | 116.3(2) |
| C(2)–C(1)–C(6) | 106.4(2) | C(2)–C(1)–C(7) | 100.8(2) |
| C(6)–C(1)–C(7) | 103.4(2) | O(1)–C(2)–C(3) | 105.7(2) |
| O(1)–C(2)–C(1) | 109.8(2) | C(3)–C(2)–C(1) | 103.2(2) |
| O(3)–C(3)–C(4) | 113.7(2) | O(3)–C(3)–C(2) | 107.6(2) |
| C(4)–C(3)–C(2) | 104.1(2) | C(3)–C(4)–C(5) | 110.2(2) |
| C(3)–C(4)–C(7) | 99.3(2) | C(5)–C(4)–C(7) | 100.3(2) |
| C(4)–C(5)–C(6) | 103.6(2) | C(4)–C(5)–C(8) | 119.0(2) |
| C(6)–C(5)–C(8) | 116.2(2) | C(1)–C(6)–C(5) | 103.0(2) |
| C(4)–C(7)–C(1) | 94.8(2) | O(5)–C(8)–C(5) | 122.1(3) |
| O(5)–C(8)–C(9) | 120.9(2) | C(5)–C(8)–C(9) | 116.8(2) |
| O(1)–C(10)–O(2) | 123.7(2) | O(1)–C(10)–C(11) | 111.3(2) |
| O(2)–C(10)–C(11) | 125.0(2) | C(10)–C(11)–C(12) | 118.0(2) |
| C(10)–C(11)–C(16) | 121.7(2) | C(12)–C(11)–C(16) | 120.4(2) |
| C(11)–C(12)–C(13) | 119.8(2) | C(12)–C(13)–C(14) | 119.9(2) |
| C(13)–C(14)–C(15) | 120.0(2) | C(14)–C(15)–C(16) | 120.3(3) |
| C(11)–C(16)–C(15) | 119.7(2) | O(3)–C(17)–O(4) | 123.2(2) |
| O(3)–C(17)–C(18) | 110.8(2) | O(4)–C(17)–C(18) | 126.0(2) |
| C(17)–C(18)–C(19) | 122.2(2) | C(17)–C(18)–C(23) | 117.4(2) |
| C(19)–C(18)–C(23) | 120.3(2) | C(18)–C(19)–C(20) | 120.0(3) |
| C(19)–C(20)–C(21) | 120.0(3) | C(20)–C(21)–C(22) | 120.2(3) |
| C(21)–C(22)–C(23) | 119.4(3) | C(18)–C(23)–C(22) | 120.0(3) |

**Table 3.** Selected torsion angles for compound (13). The torsion angle of the bonded atoms A–X–Y–B is the angle between the planes A–X–Y and X–Y–B and is positive when clockwise [a]

| Atoms | Angle (°) |
|---|---|
| C(10)–O(1)–C(2)–C(1) | −85.6 |
| C(2)–O(1)–C(10)–O(2) | −7.1 |
| C(17)–O(3)–C(3)–C(2) | 116.6 |
| C(3)–O(3)–C(17)–O(4) | 1.3 |
| C(6)–C(1)–C(2)–O(1) | 174.7 |
| C(7)–C(1)–C(2)–O(1) | −77.7 |
| C(2)–C(1)–C(6)–C(5) | 75.8 |
| C(7)–C(1)–C(6)–C(5) | −29.9 |
| C(2)–C(1)–C(7)–C(4) | −56.7 |
| O(1)–C(2)–C(3)–O(3) | −122.3 |
| C(1)–C(2)–C(3)–O(3) | 122.4 |
| O(3)–C(3)–C(4)–C(5) | −48.9 |
| C(2)–C(3)–C(4)–C(5) | 67.9 |
| C(3)–C(4)–C(5)–C(6) | −64.9 |
| C(3)–C(4)–C(7)–C(1) | 56.9 |
| C(4)–C(5)–C(6)–C(1) | −5.7 |
| C(4)–C(5)–C(8)–O(5) | −129.0 |
| C(6)–C(5)–C(8)–O(5) | −4.0 |
| O(1)–C(10)–C(11)–C(12) | −172.0 |
| O(2)–C(10)–C(11)–C(12) | 9.2 |
| C(10)–O(1)–C(2)–C(3) | 163.7 |
| C(2)–O(1)–C(10)–C(11) | 174.0 |
| C(17)–O(3)–C(3)–C(4) | −78.6 |
| C(3)–O(3)–C(17)–C(18) | −179.6 |
| C(6)–C(1)–C(2)–C(3) | −73.0 |
| C(7)–C(1)–C(2)–C(3) | 34.6 |
| C(3)–C(4)–C(5)–C(8) | 66.0 |
| C(7)–C(4)–C(5)–C(8) | 170.0 |
| C(6)–C(1)–C(7)–C(4) | 53.2 |
| O(1)–C(2)–C(3)–C(4) | 116.7 |
| C(1)–C(2)–C(3)–C(4) | 1.4 |
| O(3)–C(3)–C(4)–C(7) | −153.5 |
| C(2)–C(3)–C(4)–C(7) | −36.7 |
| C(7)–C(4)–C(5)–C(6) | 39.1 |
| C(5)–C(4)–C(7)–C(1) | −55.8 |
| C(1)–C(6)–C(5)–C(8) | 138.3 |
| C(4)–C(5)–C(8)–C(9) | 55.5 |
| C(6)–C(5)–C(8)–C(9) | −179.4 |
| O(3)–C(17)–C(18)–C(19) | 0.8 |
| O(2)–C(10)–C(11)–C(16) | −171.4 |

[a] W. Klyne and V. Prelog, *Experientia*, 1960, **16**, 521.

*X-Ray Crystal Analysis of Compound* (13).—*Crystal data.* $C_{23}H_{22}O_5$, tetragonal, $a = b = 8.3895(9)$, $c = 53.378(6)$ Å, $U = 3756.94$ Å$^3$, $Z = 8$, $D_c = 1.34$ g cm$^{-3}$. Space group $P4_12_12$, $\mu$(Cu-$K_\alpha$) = 7.8 cm$^{-1}$. Intensities were collected on a Picker Facs-II diffractometer at 115 K with graphite monochromatized Cu-$K_\alpha$ radiation with line-profile analysis.[20]

A total of 1 584 independent reflections, up to $\theta$ 61.5°, were measured with intensities greater than 2.5 times their standard

deviation. The intensities were corrected for measured direct beam polarization,[21] and a Gaussian absorption correction was performed. The structure was solved by direct methods.

All hydrogen atoms were located and refined with isotropic thermal parameters, while the other atoms were refined anisotropically by block-diagonal least-squares using counting statistics weights. The quantity minimized was $\Sigma\omega\Delta^2$, [$\Delta = |F_o| - |F_c|$, $\omega = 1/\sigma^2(F_o)$]. An extinction correction was included [22] and the scattering curves for neutral atoms were taken from International Tables.[23] The final residuals $R$, $R_w$ are 0.031 and 0.022, respectively. All the calculations were performed using the National Research Council PDP8-E system of programmes.[24]

Atomic co-ordinates, bond lengths and angles (non-hydrogen), and selected torsion angles are given in Tables 1—3. Observed and calculated structure factors, thermal parameters, and some additional bond lengths are listed in Supplementary Publication No. SUP 23633 (12 pages).*

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* For details of the Supplementary Publications Scheme, see Instructions for Authors (1983), *J. Chem. Soc., Perkin Trans. 1*, 1983, Issue 1.

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