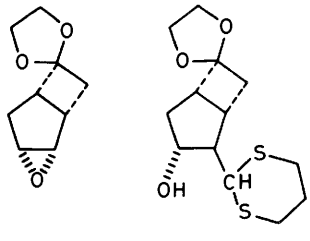
Functionalised Carbocycles from Carbohydrates. Part 7.[1] A Route to Carbacyclin from a D-Glucose Derivative. *X*-Ray Crystal Structure of 3-*endo*-Benzoyloxy-2-*exo*-(1,3-diphenyl-1,3,2-diazaphospholan-2-yloxymethyl)-6-oxobicyclo[3.3.0]-octane

Robert J. Ferrier* and Peter C. Tyler
Department of Chemistry, Victoria University of Wellington, Private Bag, Wellington, New Zealand
Graeme J. Gainsford
Chemistry Division, Department of Scientific and Industrial Research, Private Bag, Petone, New Zealand

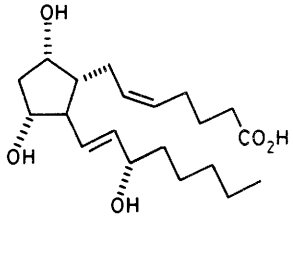
A specific method for converting the epoxide (**7**), which was previously obtained from methyl α-D-glucopyranoside, into the prostaglandin intermediate (**1**) is described, and a route from this latter compound into the previously reported bicyclo[3.3.0]octan-3-one (**4**) has been developed (using racemic material). Compound (**4**) is a synthetic precursor of carbacyclin and its analogues. In the course of this work a functionalised bicyclo[3.3.0]octan-2-one was encountered; it was characterised by *X*-ray diffraction analysis of the derivative (**19**).

In the same way as the cyclobutanone acetal (**1**) and derived compounds such as (**2**)[2] are synthetic intermediates from which a range of prostaglandins *e.g.* $PGF_{2\alpha}$ (**3**) and analogues can be prepared,[3] related bicyclo[3.3.0]octan-3-ones [e.g. (**4**)] are general precursors for carbacyclin (**5**) and its analogues.[4] Compound (**5**), a chemically stabilised modification of natural prostaglandin I_2 (**6**) (prostacyclin),[4] has valuable physiological activity, in particular in inhibiting the aggregation of blood platelets without side-effects while being resistant to the ready hydrolysis exhibited by the natural vinyl ether,[5] and it has been the subject of several synthetic studies all of which have used racemic compounds as starting materials.[5a,6] We now report a specific synthesis of the acetal (**1**) from compound (**7**), which we have previously prepared from methyl α-D-glucopyranoside,[7] and then conversion of the acetal into compound (**4**). For practical convenience this latter part of the work was carried out using racemic material, but, nevertheless, the methodology used delineates a formal route from D-glucose to carbacyclin.

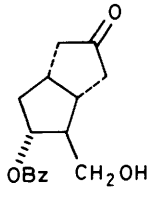


(**1**)

(**2**)

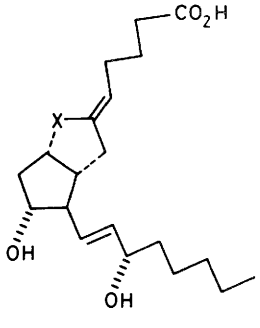


(**3**)



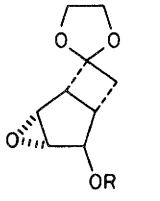
Bz = benzoyl

(**4**)

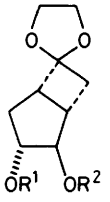


(**5**) X = CH_2
(**6**) X = O

Our initial route to the epoxide (**1**) involved a photochemical ring closure of a nona-3,8-dienulose derivative and the production of the epoxide (**7**) with good selectivity.[7] The derived diol (**8**) was, however, surprisingly non-selective in undergoing dehydration to the required product (**1**), and we therefore now report a means of overcoming this difficulty. Treatment of the previously prepared silyl ether (**9**) with lithium aluminium hydride and benzoylation of the product gave the ester (**10**) from which the silyl group was cleaved by use of tetrabutylammonium fluoride. Immediate tosylation of the resulting alcohol was effected by tosylimidazole present in the desilylating solution and gave the diester (**11**) which, on direct treatment with potassium carbonate in methanol, afforded the required epoxide (**1**) specifically.



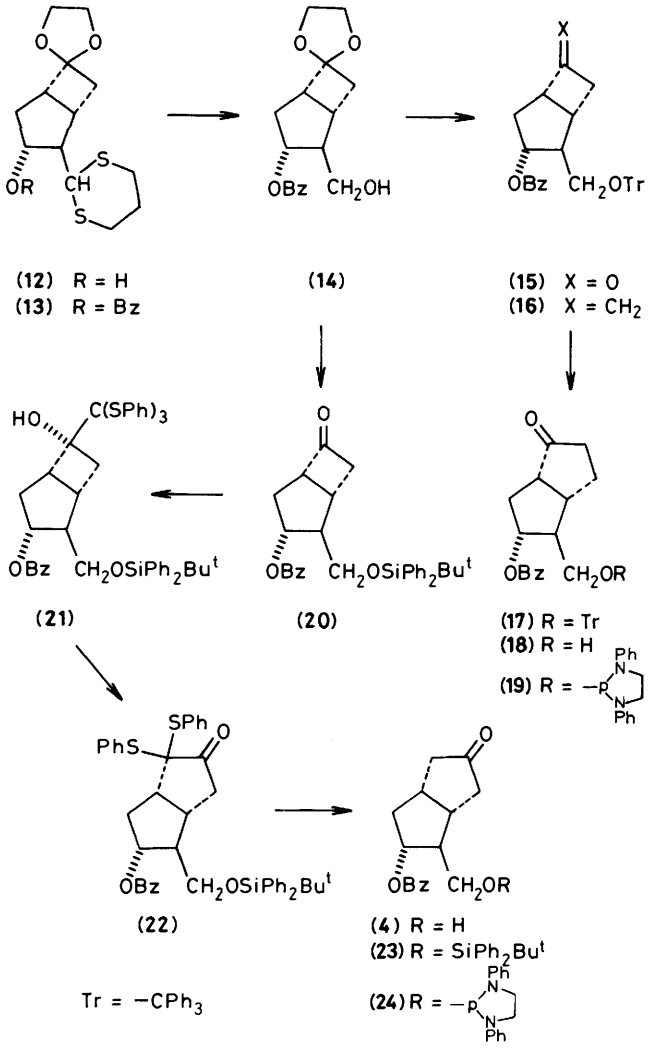
(**7**) R = H
(**9**) R = $SiMe_2Bu^t$



	R^1	R^2
(**8**)	H	H
(**10**)	Bz	$SiMe_2Bu^t$
(**11**)	Bz	$SO_2C_6H_4Me$-*p*

Although the above route affords a means of obtaining the epoxide (**1**) in its appropriate enantiomeric form the following steps were developed with racemic material which was more readily and inexpensively available from cyclopentadiene and dichloroketene following the method of the Glaxo workers.[2] This group have shown that, with nucleophiles, this epoxide undergoes preferential reaction at the carbon atom nearer the ring junction and with dithianyl-lithium afforded 66% of compound (**12**), but they did not separate it from the isomeric product. We have now effected this separation chromatographically† and have converted the highly crystalline major alcohol into the crystalline cyclobutanone (**15**) by successive *O*-benzoylation to give the ester (**13**), hydrolysis of the dithiane ring by use of *N*-bromosuccinimide (NBS) in an aqueous

† The isomers can also be separated by preferential crystallisation of the derived acetates (W. Bartmann, G. Beck, J. Knolle, and R. H. Rupp, *Tetrahedron Lett.*, 1982, **23**, 3647).



medium, reduction of the derived aldehyde to give the alcohol (**14**), acid-catalysed hydrolysis of the acetal ring and *O*-tritylation of the primary alcohol group.

Ring expansion of cyclobutanones to cyclopentanones[8] is frequently carried out by use of diazomethane, but with a ketone closely related to compound (**15**) Newton and Wadsworth,[9] by use of this reagent, were not able to effect selectivity in the production of the bicyclo[3.3.0]octan-2- and 3-ones formed. Preliminary studies showed that, in similar fashion, the cyclobutanone (**15**) also gave two products in similar proportions when treated with diazomethane.

Epoxides can be rearranged into carbonyl compounds with high efficiency by use of lithium bromide in benzene in the presence of an equivalent of hexamethylphosphoramide,[10] and spiro-epoxides derived from cyclobutanones give cyclopentanones under these conditions.[8] Furthermore, there is evidence that the reaction affords products which have the carbonyl group disposed furthest from ring substituents[11] and therefore it seemed probable that the required cyclopentanone (**4**) could be obtainable from epoxides derived from the ketone (**15**). Treatment with methylenetriphenylphosphorane gave the crystalline alkene (**16**) which was converted into epimeric epoxides by use of *m*-chloroperbenzoic acid (MCPBA). When these products were heated in benzene containing hexamethylphosphoramide with lithium bromide, two ketones were formed of which the major isomer (**17**) was isolated chromatographically in 70% yield. Although the ^{13}C n.m.r. spectrum was generally consistent with that to be expected for the desired 7-one, when the trityl group was removed the syrupy alcohol (**18**) gave an ^{1}H n.m.r. spectrum which was not identical with that of the previously reported alcohol (**4**)[6f] and the compound was converted into the crystalline *O*-(1,3-diphenyl-1,3,2-diazaphospholane) derivative (**19**)[12] for characterisation by *X*-ray diffraction analysis. As shown in the Figure this indicated that, whereas the functionality and stereochemistry were as required, the ring-expansion procedure gave as main product the 6- rather than the 7-one.

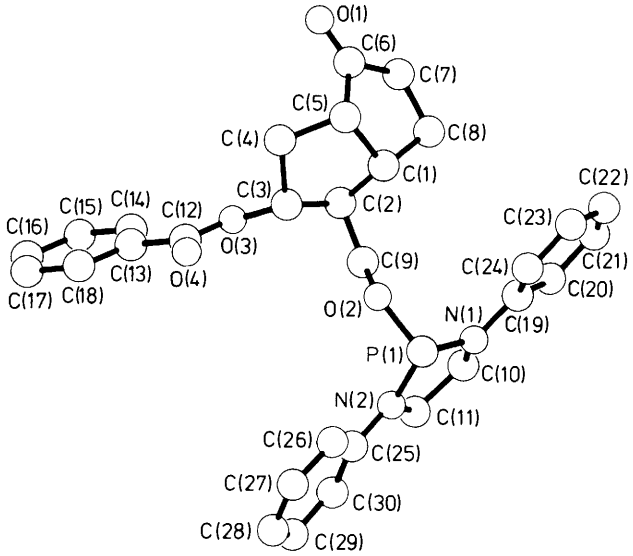


Figure. *X*-Ray crystal structure of 3-*endo*-benzoyloxy-2-*exo*-(1,3-diphenyl-1,3,2-diazaphospholan-2-yloxymethyl)-6-oxobicyclo[3.3.0]-octane (**19**). The diagram was prepared by use of the PLUTO programme.[22]

A method which has been applied to a compound with the same bicyclo[3.2.0]heptan-6-one system as is present in the ketone (**15**), and which afforded the required bicyclo-[3.3.0]octan-3-one product almost specifically,[13] was then investigated. The ketone (**15**) in various procedures gave products which underwent loss of the trityl group and the work was therefore continued on the analogous t-butyldiphenylsilyl ether (**20**). This was treated with tris(phenylthio)methyllithium[14] and afforded a product giving a ^{1}H n.m.r. spectrum consistent with that expected for the derived tris(phenylthio)methyl tertiary alcohol (**21**). When this product was treated with mercury(II) chloride in *NN*-dimethylformamide (DMF) rearrangement occurred to give the expected α,α-bis(phenylthio)ketone (**22**) which, on reduction with Raney nickel, afforded the required monobenzoate (**23**) which was converted into the crystalline *O*-(1,3-diphenyl-1,3,2-diazaphospholane) derivative (**24**) by way of the alcohol (**4**).

Although this latter alcohol (**4**), having been produced from racemic epoxide (**1**), was not obtained in the enantiomerically pure form required for the production of 'natural' carbacyclin, the above methodology establishes that this compound is derivable in optically pure form from a carbohydrate starting material.

The isomeric alcohols (**4**) and (**18**) gave similar poorly resolved but distinguishable ^{1}H n.m.r. spectra, only that of the former bearing close resemblance to one previously obtained for the 7-one.[6f] The ^{13}C spectra were distinctly different and bore close resemblances to those reported[9] for two closely related 2,3-disubstituted 7- and 6-oxobicyclo[3.3.0]octanes. In particular, the resonances for the methylene carbon atoms of the cyclopentanone rings were within the range δ_C 43—46 p.p.m.

for compound (**4**) and its reference compound, whereas compound (**18**) and its reference gave these resonances near δ_C 25 and 35 p.p.m. Also, the ring-junction atoms had distinguishable resonances near δ_C 36 and 42 p.p.m. for the 7-one (**4**) and its reference, and near δ_C 43 and 49 p.p.m. for the isomer (**18**) and its reference.

Experimental

^1H and ^{13}C n.m.r. spectra were measured in deuteriochloroform on a Varian FT 80A instrument with $SiMe_4$ as internal standard. Optical rotations were measured in chloroform within the concentration range 0.5—1.5%. Light petroleum refers to that fraction boiling in the range 60—80 °C.

(1S,5S)-3-endo-*Benzoyloxy*-2-exo-(*t-butyldimethylsilyloxy*)-*spiro*{*bicyclo*[3.2.0]*heptane*-6,2′-[1,3]*dioxolane*} (**10**).—The previously described epoxyalcohol (**7**)[7] (250 mg) was stirred in DMF (3 ml) with imidazole (270 mg) and t-butyldimethylsilyl chloride (300 mg)[15] at 18 °C for 2 h. Dichloromethane was added, the solution was washed with water (× 2) and dried, and the volatiles were removed, the last traces under high vacuum. The residue was dissolved in dry ether (5 ml) and the solution was stirred at 18 °C with lithium aluminium hydride (100 mg) for 2 h. Usual work-up gave a chromatographically discrete syrupy monohydroxy product which was benzoylated in pyridine (3 ml) by use of benzoyl chloride (230 mg) for 15 h. Normal work-up and purification by preparative thin layer chromatography (p.l.c.) gave the silylated benzoate (**10**) (465 mg, 85% based on the epoxide), $[\alpha]_D$ +17° (Found: C, 65.4; H, 8.1. $C_{22}H_{32}O_5Si$ requires C, 65.3; H, 8.0%; δ_H 0.08 (3 H, s, Me), 0.10 (3 H, s, Me), 0.87 (9 H, s, Bu^t), 2.1—2.45 (5 H, m, 1-H and 4- and 7-H_2), 3.00 (1 H, m, 5-H), 3.75—3.90 (4 H, m, OCH_2), 4.15 (1 H, d, $J_{2,3}$ 1.4 Hz, 2-H), 5.20 (1 H, m, $w_{\frac{1}{2}}$ 13 Hz, 3-H), and 7.3—8.2 (5 H, 2 m, ArH).

(1′S, 2′S, 4′R, 6′S)-*Spiro*{[1,3]*dioxolane*-2,7′-[3]*oxatricyclo*-[4.2.0.0^{2,4}]*octane*} (**1**).—To a solution of the silyl ether (**10**) (95 mg) in tetrahydrofuran (THF) (3 ml) containing tosylimidazole[16] (510 mg) was added a dry solution of tetrabutylammonium fluoride (0.7 ml) in THF (3 ml) and the mixture was stirred under nitrogen at 18 °C for 1 h. A single, more polar product was formed and potassium carbonate (200 mg) and methanol (3 ml) were then added and the mixture was stirred for 3 h. Chloroform was added and the mixture was washed with water, the organic phase was dried, and the solvent was removed to leave the epoxide (**1**) (32 mg, 81%) which was purified by flash chromatography.[17] The ^1H n.m.r. spectrum was identical with those of the previous sample[7] and of racemic material.[2]

3-endo-*Benzoyloxy*-2-exo-(1,3-*dithian*-2-*yl*)*spiro*{*bicyclo*-*heptane*-6,2′-[1,3]*dioxolane* (**13**).—Racemic epoxide (**1**) was prepared as previously described[2] and was treated with 1,3-dithian-2-yl lithium to give the alcohol (**12**) and its stereoisomer in the ratio 2:1 as also described by the Glaxo workers. These were separated by flash chromatography[17] [ether–light petroleum (3:2)] and the major isomer (0.81 g) was benzoylated in pyridine (10 ml) with benzoyl chloride (0.34 ml) for 10 min at 18 °C. Usual work-up gave the benzoate (**13**) (1.05 g, 95%) (Found: C, 60.9; H, 6.6; S, 15.9. $C_{20}H_{24}O_4S_2$ requires C, 61.2; H, 6.2; S, 16.3%); δ_H 1.8—3.0 (13 H, m), 3.7—3.9 (4 H, m, OCH_2), 4.20 (1 H, d, *J* 5.9 Hz, CHS_2), 5.52 (1 H, q, *J* 6 Hz, 3-H), and 7.3—8.1 (5 H, 2 m, ArH).

3-endo-*Benzoyloxy*-2-exo-*hydroxymethylspiro*{*bicyclo*[3.2.0]-*heptane*-6,2′-[1,3]*dioxolane*} (**14**).—A solution of NBS (2.04 g) in aqueous acetonitrile[18] (25 ml; 20%) was added dropwise at 0 °C to a solution of the dithiane (**13**) (0.75 g) in acetonitrile (10 ml) and the solution was stirred for 5 min. Dichloromethane was added and the mixture was washed successively with aqueous sodium hydrogen sulphite, saturated aqueous sodium hydrogen carbonate, and brine. The organic solution was dried and the solvent was removed to give a syrupy residue which was dissolved in ethanol (15 ml) and the solution was cooled to −40 °C. Saturated ethanolic sodium borohydride (10 ml) was added and the mixture was stirred at −25 °C for 3 h and then allowed to warm to −5 °C. Acetic acid (5 ml) was added and the solvents were removed. Dichloromethane was added to the residue and the extract was filtered through Celite. Again the solvent was removed and column chromatography gave the *alcohol* (**14**) (0.44 g, 76%), m.p. 77—78 °C (from ether–light petroleum) (Found: C, 66.9; H, 6.7. $C_{17}H_{20}O_5$ requires C, 67.1; H, 6.6%); δ_H 2.1—3.1 (8 H, m), 3.52 (2 H, d, *J* 6.1 Hz, CH_2OH), 3.8—3.9 (4 H, m, OCH_2), 5.37 (1 H, q, *J* 4.5 Hz, 3-H), and 7.4—8.1 (5 H, 2 m, ArH).

3-endo-*Benzoyloxy*-6-*oxo*-2-exo-(*triphenylmethoxymethyl*)-*bicyclo*[3.2.0]*heptane* (**15**).—A solution of the acetal (**14**) (400 mg) in aqueous methanol (5 ml; 10%) containing toluene-*p*-sulphonic acid (100 mg) was heated under reflux for 0.25 h and, after being cooled, was passed through a short flash-column of silica gel. The column was washed with ethyl acetate and the combined eluate and washings were evaporated to give a syrupy residue, δ_H 1.9—3.4 (7 H, m), 3.64 (2 H, d, *J* 7.2 Hz, CH_2O), 3.8 (1 H, m, OH), 5.58 (1 H, d, *J* 3.9 Hz, 3-H), and 7.1—8.1 (5 H, 2 m, ArH). The alcohol was dissolved in pyridine (5 ml), triphenylmethyl chloride (735 mg) was added, and the solution was stored at 18 °C for 2 days. Usual work-up and isolation by p.l.c. gave the *tritylketone* (**15**) (595 mg, 90%), m.p. 138 °C (from light petroleum) (Found: C, 81.3; H, 6.1. $C_{34}H_{30}O_4$ requires C, 81.3; H, 6.0%); δ_H 1.7—3.8 (9 H, m), 5.62 (1 H, d, *J* 3.8 Hz, 3-H), 7.1—8.1 (20 H, 2 m, ArH).

3-endo-*Benzoyloxy*-6-*methylene*-2-exo-(*triphenylmethoxy-methylbicyclo*[3.2.0]*heptane* (**16**).—Butyl-lithium (0.15 ml; 1.6M in hexane) was added to a solution of methyltriphenylphosphonium bromide (100 mg) in toluene (1.0 ml) and the mixture was stirred for 2 h, then cooled to 0 °C and a solution of the ketone (**15**) (80 mg) in toluene (0.5 ml) was added dropwise. The mixture was stirred for 20 min at 0 °C and the ketone was consumed. After the mixture had been stirred for a further 1.5 h at 18 °C the betaine intermediate had decomposed to give the alkene and the mixture was extracted with ether, the extract was washed with water and dried, and the solvent was removed. Purification of the residue (p.l.c.) gave the *alkene* (**16**) (69 mg, 86%), m.p. 113—115 °C (from light petroleum) (Found: C, 84.1; H, 6.6. $C_{35}H_{32}O_3$ requires C, 84.0; H, 6.4%); δ_H 2.0—3.4 (9 H, m), 4.78 (2 H,br s, $w_{\frac{1}{2}}$ 6 Hz, $=CH_2$), 5.56 (1 H,br s, $w_{\frac{1}{2}}$ 10 Hz, 3-H), and 7.0—8.0 (20 H, m, ArH).

3-endo-*Benzoyloxy*-2-exo-(1,3-*diphenyl*-1,3,2-*diazaphospho-lan*-2-*yloxymethyl*)-6-*oxobicyclo*[3.3.0]*octane* (**19**).—A solution of MCPBA (48 mg; 85%) in dichloromethane (1 ml) was added dropwise at 0 °C to a solution of the alkene (**16**) (94 mg) in the same solvent (2 ml) and the mixture was kept at 4 °C for 15 h. After the mixture had been washed with aqueous sodium hydrogen carbonate and dried, removal of the solvent gave a product whose ^1H n.m.r. spectrum was consistent with that expected for the epoxide. It was dissolved in benzene (3 ml) containing lithium bromide and hexamethylphosphoramide (each 1.5 mol equiv.) and the solution was heated under reflux under nitrogen for 16 h. Ether was added and the solution was washed with water, dried, and the solvent was removed to yield mainly the cyclopentanone (**17**) which was isolated (p.l.c.) [development (× 3) with ether–light petroleum] (68 mg, 70%),

Table 1. Atomic co-ordinates[a] for non-hydrogen atoms of compound (**19**)

Atom[b]	*x*	*y*	*z*	Atom	*x*	*y*	*z*
P(1)	0.634 9(3)	0.816 1(2)	0.479 0(5)	C(13)	0.876 8(9)	1.059 1(4)	0.949 5(16)
O(1)	0.335 8(12)	1.038 5(6)	0.834 9(18)	C(14)	0.894 0(9)	1.029 6(4)	1.075 3(16)
O(2)	0.620 7(6)	0.871 8(4)	0.576 3(11)	C(15)	0.985 5(9)	1.046 2(4)	1.193 2(16)
O(3)	0.716 1(8)	0.998 8(5)	0.841 7(11)	C(16)	1.059 7(9)	1.092 3(4)	1.185 4(16)
O(4)	0.761 6(10)	1.069 0(6)	0.709 6(13)	C(17)	1.042 4(9)	1.121 8(4)	1.059 6(16)
N(1)	0.588 7(9)	0.749 9(6)	0.532 8(13)	C(18)	0.951 0(9)	1.105 2(4)	0.941 7(16)
N(2)	0.769 2(8)	0.789 1(6)	0.556 4(13)	C(19)	0.474 6(10)	0.741 1(5)	0.503 9(10)
C(1)	0.443 7(13)	0.927 8(8)	0.652 9(18)	C(20)	0.443 1(10)	0.693 4(5)	0.573 8(10)
C(2)	0.567 4(11)	0.921 6(6)	0.746 5(16)	C(21)	0.330 6(10)	0.682 9(5)	0.546 7(10)
C(3)	0.609 5(13)	0.986 2(8)	0.724 8(17)	C(22)	0.249 7(10)	0.720 1(5)	0.449 8(10)
C(4)	0.519 0(15)	1.035 6(9)	0.724 6(19)	C(23)	0.281 2(10)	0.767 8(5)	0.380 0(10)
C(5)	0.410 3(13)	0.996 5(6)	0.672 5(18)	C(24)	0.393 7(10)	0.778 3(5)	0.407 0(10)
C(6)	0.355 7(13)	0.995 6(11)	0.775 6(20)	C(25)	0.854 9(8)	0.816 4(6)	0.522 1(12)
C(7)	0.339 0(30)	0.925 9(15)	0.799 6(46)	C(26)	0.837 4(8)	0.868 4(6)	0.434 5(12)
C(8)	0.366 9(13)	0.886 5(10)	0.697 5(24)	C(27)	0.925 5(8)	0.893 3(6)	0.404 9(12)
C(9)	0.626 0(13)	0.867 6(8)	0.714 7(20)	C(28)	1.031 2(8)	0.866 3(6)	0.462 9(12)
C(10)	0.672 8(15)	0.711 5(9)	0.636 8(19)	C(29)	1.048 7(8)	0.814 3(6)	0.550 6(12)
C(11)	0.785 3(15)	0.732 7(9)	0.638 8(21)	C(30)	0.960 6(8)	0.789 3(6)	0.580 1(12)
C(12)	0.780 7(15)	1.044 4(8)	0.819 1(22)				

[a] Estimated standard deviations (in parentheses) are those derived from the final least-squares inversion matrix; note that atoms C(13)—C(18), C(19)—C(24), and C(25)—C(30) were refined as rigid (phenyl) groups. [b] Crystallographic numbering scheme.

Table 2. Intramolecular bond distances and angles for compound (**19**)[a] with e.s.d.s in parentheses

Atoms[b]	Distance (Å)	Atoms	Distance (Å)
P(1)–O(2)	1.614(10)	P(1)–N(2)	1.717(11)
O(2)–C(9)	1.425(17)	O(3)–C(12)	1.357(18)
N(1)–C(10)	1.462(19)	N(2)–C(11)	1.440(17)
C(1)–C(2)	1.537(18)	C(1)–C(8)	1.526(23)
C(2)–C(9)	1.479(20)	C(4)–C(5)	1.547(20)
C(6)–C(7)	1.527(30)	C(10)–C(11)	1.520(22)
P(1)–N(1)	1.702(12)	O(1)–C(6)	1.182(19)
O(3)–C(3)	1.483(15)	O(4)–C(12)	1.196(18)
N(1)–C(19)	1.406(16)	N(2)–C(25)	1.415(17)
C(1)–C(5)	1.553(20)	C(2)–C(3)	1.522(19)
C(3)–C(4)	1.571(20)	C(5)–C(6)	1.495(20)
C(7)–C(8)	1.504(38)	C(12)–C(13)	1.492(23)
Atoms	**Angle (°)**	**Atoms**	**Angle (°)**
O(2)–P(1)–N(1)	104.8(6)	C(1)–C(5)–C(6)	108.4(15)
P(1)–O(2)–C(9)	128.4(10)	O(1)–C(6)–C(7)	125.7(21)
P(1)–N(1)–C(19)	120.8(10)	C(1)–C(8)–C(7)	104.9(17)
P(1)–N(2)–C(25)	119.9(10)	N(2)–C(11)–C(10)	108.4(13)
C(2)–C(1)–C(8)	113.6(23)	O(4)–C(12)–C(13)	125.7(18)
C(1)–C(2)–C(9)	115.1(13)	N(1)–C(19)–C(20)	118.5(7)
O(3)–C(3)–C(4)	110.2(13)	N(2)–C(25)–C(30)	117.3(6)
C(1)–C(5)–C(4)	106.5(13)	N(1)–P(1)–N(2)	89.5(6)
O(1)–C(6)–C(5)	128.7(21)	P(1)–N(1)–C(10)	116.6(10)
C(6)–C(7)–C(8)	109.5(21)	P(1)–N(2)–C(11)	116.8(10)
N(1)–C(10)–C(11)	106.7(14)	C(2)–C(1)–C(5)	105.8(13)
O(3)–C(12)–C(13)	110.3(16)	C(1)–C(2)–C(3)	100.1(13)
C(12)–C(13)–C(18)	116.7(9)	O(3)–C(3)–C(2)	108.3(13)
N(2)–C(25)–C(26)	122.7(6)	C(3)–C(4)–C(5)	103.0(13)
O(2)–P(1)–N(2)	106.5(6)	C(4)–C(5)–C(6)	111.7(16)
C(3)–O(3)–C(12)	115.4(13)	C(5)–C(6)–C(7)	105.4(19)
C(10)–N(1)–C(19)	121.0(12)	O(2)–C(9)–C(2)	110.3(15)
C(11)–N(2)–C(25)	122.6(11)	O(3)–C(12)–O(4)	123.9(18)
C(5)–C(1)–C(8)	104.5(13)	C(12)–C(13)–C(14)	123.3(9)
C(3)–C(2)–C(9)	114.7(13)	N(1)–C(19)–C(24)	121.5(7)
C(2)–C(3)–C(4)	106.8(12)		

[a] Phenyl groups were refined as rigid groups with C–C 1.395 Å, C–C–C 120°. [b] Crystallographic numbering scheme.

δ_H 1.6—2.75 (9 H, m), 3.25 (2 H, d, *J* 5.7 Hz, CH_2O), 5.27 (1 H, q, *J* 6 Hz, 3-H), and 7.0—8.0 (20 H, m, ArH).

The tritylated ketone (**17**) (74 mg) was heated in a refluxing mixture of acetic acid, THF, and water (5 ml; 3:1:1) for 0.5 h and gave the primary alcohol (**18**), δ_H 1.5—2.9 (10 H, m), 3.70 (2 H, d, *J* 5.9 Hz, CH_2O), 5.27 (1 H, q, *J* 5 Hz, 3-H), and 7.2—8.0 (5 H, m, ArH), these signals being clearly distinguishable from those in the 90 MHz spectrum kindly supplied by Dr. Skuballa;[6f] δ_C 25.3 (C-8), 34.6 (C-7), 36.2 (C-4), 41.9 (C-1), 50.4 (C-5), 54.8 (C-2), 62.6 (CH_2O), and 78.7 (C-3), together with

Table 3. Selected torsion angles for compound (**19**).* 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 when viewed down the bond X–Y.

Atoms[a]	Angle (°)	Atoms	Angle (°)
N(1)–P(1)–O(2)–C(9)	30.0	C(11)–N(2)–C(25)–C(26)	175.0
O(2)–P(1)–N(1)–C(19)	72.0	C(5)–C(1)–C(2)–C(9)	−163.0
O(2)–P(1)–N(2)–C(11)	99.0	C(2)–C(1)–C(5)–C(4)	23.0
N(1)–P(1)–N(2)–C(25)	164.0	C(8)–C(1)–C(5)–C(6)	23.0
C(12)–O(3)–C(3)–C(4)	−82.0	C(1)–C(2)–C(3)–O(3)	160.0
P(1)–N(1)–C(10)–C(11)	−16.0	C(9)–C(2)–C(3)–C(4)	165.0
P(1)–N(1)–C(19)–C(24)	14.0	O(3)–C(3)–C(4)–C(5)	−145.0
P(1)–N(2)–C(11)–C(10)	−1.0	C(3)–C(4)–C(5)–C(6)	121.0
P(1)–N(2)–C(25)–C(30)	−175.0	C(4)–C(5)–C(6)–O(1)	49.0
C(5)–C(1)–C(2)–C(3)	−39.0	C(5)–C(6)–C(7)–C(8)	−8.0
C(8)–C(1)–C(2)–C(9)	83.0	O(3)–C(12)–C(13)–C(14)	−1.0
C(8)–C(1)–C(5)–C(4)	143.0	O(4)–C(12)–C(13)–C(18)	−1.0
C(5)–C(1)–C(8)–C(7)	−27.0	C(12)–C(13)–C(18)–C(17)	180
C(9)–C(2)–C(3)–O(3)	−76.0	O(2)–P(1)–N(1)–C(10)	−94.0
C(3)–C(2)–C(9)–O(2)	−57.0	N(2)–P(1)–N(1)–C(19)	179.0
C(3)–C(4)–C(5)–C(1)	3.0	N(1)–P(1)–N(2)–C(11)	−7.0
C(1)–C(5)–C(6)–C(7)	−9.0	C(12)–O(3)–C(3)–C(2)	161.0
O(1)–C(6)–C(7)–C(8)	176.0	C(3)–O(3)–C(12)–C(13)	172.0
N(1)–C(10)–C(11)–N(2)	10.0	P(1)–N(1)–C(19)–C(20)	−167.0
O(4)–C(12)–C(13)–C(14)	179.0	C(10)–N(1)–C(19)–C(24)	179.0
N(2)–P(1)–O(2)–C(9)	−64.0	P(1)–N(2)–C(25)–C(26)	5.0
N(2)–P(1)–N(1)–C(10)	13.0	C(11)–N(2)–C(25)–C(30)	−5.0
O(2)–P(1)–N(2)–C(25)	−91.0	C(8)–C(1)–C(2)–C(3)	−153.0
P(1)–O(2)–C(9)–C(2)	−158.0	C(2)–C(1)–C(5)–C(6)	−97.0
C(3)–O(3)–C(12)–O(4)	−8.0	C(2)–C(1)–C(8)–C(7)	88.0
C(19)–N(1)–C(10)–C(11)	179.0	C(1)–C(2)–C(3)–C(4)	41.0
C(10)–N(1)–C(19)–C(20)	−2.0	C(1)–C(2)–C(9)–O(2)	59.0
C(25)–N(2)–C(11)–C(10)	−172.0	C(2)–C(3)–C(4)–C(5)	−28.0
C(1)–C(5)–C(6)–O(1)	166.0	N(1)–C(19)–C(24)–C(23)	179.0
C(4)–C(5)–C(6)–C(7)	−126.0	N(2)–C(25)–C(26)–C(27)	180.0
C(6)–C(7)–C(8)–C(1)	23.0	N(1)–C(19)–C(20)–C(21)	−179.0
O(3)–C(12)–C(13)–C(18)	180.0	N(2)–C(25)–C(30)–C(29)	−180.0
C(12)–C(13)–C(14)–C(15)	−180.0		

* The e.s.d.s for the dihedral angles are within the range 1—2.5°. [a] Crystallographic numbering scheme.

signals from aromatics, ester C=O, and ketonic C=O. The product was dried by evaporation in the presence of added toluene, and was then dissolved in this solvent (5 ml) together with 2-diethylamino-1,3-diphenyl-1,3,2-diazaphospholidine (60 mg) and acetic acid (12 mg) and the mixture was heated under reflux for 0.3 h under nitrogen. The solution was evaporated and the 2-*alkoxy* 1,3-*diphenyl*-1,3,2-*diazaphospholane* (**19**) (45 mg, 61%) was isolated by p.l.c., m.p. 108—110 °C (from light petroleum) (Found: C, 70.2; H, 6.2; N, 5.4. $C_{30}H_{31}N_2O_4P$ requires C, 70.0; H, 6.1; N, 5.4%); δ_H 1.6—2.6 (9 H, m), 3.5—4.0 (6 H, m, CH_2O, and CH_2N), 4.98 (1 H, q, 5.4 Hz, 3-H), and 6.7—7.9 (15 H, m, ArH).

3-endo-*Benzoyloxy*-2-exo-(*t-butyldiphenylsilyloxymethyl*)-6-*oxobicyclo*[3.2.0]*heptane* (**20**).—The alcohol (0.77 g), prepared by acetic acid-catalysed hydrolysis of ketone (**15**), was stirred at 20 °C in DMF (10 ml) with imidazole (0.5 g) and t-butyldiphenylsilyl chloride (1.0 ml) for 2 h. Ether was added and the mixture was washed successively with water, dil. hydrochloric acid, and aqueous sodium hydrogen carbonate, and dried. Removal of the solvent gave the substituted product which was purified by flash chromatography. The *silyl ether* (**20**) (1.33 g, 90%), recrystallised from aqueous ethanol, had m.p. 116—117 °C (Found: C, 74.5, H, 7.0. $C_{31}H_{34}O_4Si$ requires C, 74.7; H, 6.9%); δ_H 1.08 (9 H, s, CH_3), 2.2—3.5 (7 H, m), 3.65 (2 H, m, CH_2O), 5.55 (1 H, d, *J* 4 Hz, 3-H), 7.2—7.9 (15 H, m, ArH).

3-endo-*Benzoyloxy*-2-exo-(*t-butyldiphenylsilyloxymethyl*)-6-endo-*hydroxy*-6-exo-*tris*(*phenylthio*)*methylbicyclo*[3.2.0]*heptane* (**21**).—Butyl-lithium (0.45 ml; 1.4M in hexane) under nitrogen was added dropwise at −78 °C to a stirred solution of tris(phenylthio)methane (0.21 g) in THF (4 ml) under nitrogen and the mixture was stirred for 15 min. Ether (4 ml) was added slowly to the rapidly stirred mixture, followed by a solution of the ketone (**20**) (0.24 g) in ether (3 ml). The mixture was stirred for 1 h, water and ether were added, and the product was recovered from the organic phase. Purification (p.l.c.) gave the *tertiary alcohol* (**21**) (0.28 g, 70%) (Found: C, 71.7; H, 6.1; S, 11.3. $C_{50}H_{50}O_4S_3Si$ requires C, 71.6, H, 6.0; S, 11.5%); δ_H 1.00 (9 H, s, CH_3), 1.6—2.5 (5 H, m), 2.7—3.1 (3 H, m), 3.45 (2 H, d, CH_2O), 5.26 (1 H, m, $w_{\frac{1}{2}}$ 14 Hz, 3-H), and 7.2—8.1 (30 H, m, ArH).

3-endo-*Benzoyloxy*-2-exo-(*t-butyldiphenylsilyloxymethyl*)-7-*oxobicyclo*[3.3.0]*octane* (**23**).—A solution of mercury(II) chloride (82 mg) in DMF (0.5 ml) was added to a solution of the alcohol (**21**) (0.2 g) in DMF (5 ml) containing ethyldiisopropylamine (0.08 ml) at −40 °C and the solution was stirred at this temperature for 2 h. Toluene was added, the solution was washed successively with water, dil. hydrochloric acid, aqueous sodium hydrogen carbonate, and water before being dried, and the solvent was removed. T.l.c. indicated that a discrete product had been formed. This was stirred with Raney nickel in ethanol for 0.5 h at 50 °C to give a single product which was purified by flash chromatography to afford the *ketone* (**23**) (0.09 g, 74%) (Found: C, 75.1; H, 7.1. $C_{32}H_{36}O_4Si$ requires C, 75.0; H, 7.1%); δ_H 1.05 (9 H, s, CH_3), 1.3—2.7 (9 H, m), 3.77 (2 H, d, *J* 5.2 Hz, CH_2O), 5.35 (1 H, q, *J* 7 Hz, 3-H), and 7.2—8.0 (15 H, ArH).

3-endo-*Benzoyloxy*-2-exo-(1,3-*diphenyl*-1,3,2-*diazaphospholan*-2-yloxy*methyl*)-7-*oxobicyclo*[3.3.0]*octane* (**24**).—A solution of the silyl ether (**23**) (110 mg) in THF (3 ml) was treated with tetrabutylammonium fluoride (0.35 ml; 1M in THF) for 30 min at 20 °C. The solution was diluted with ether, washed with water, dried, and the solvent was removed to leave the primary alcohol which was purified by flash chromatography to give the syrupy alcohol (**4**) (50 mg, 82%); δ_H 1.7—3.0 (10 H, m), 3.70 (2 H, d, *J* 5.4 Hz, CH_2O), 5.34 (1 H, q, *J* 5.9 Hz, 3-H), 7.2—8.1 (5 H, m, ArH), closely similar to the 90 MHz spectrum kindly supplied by Dr. Skuballa;[6f] δ_C 37.3 (C-5), 38.6 (C-4), 40.9 (C-1), 44.0 (C-6), 44.6 (C-8), 55.1 (C-2), 62.4 (CH_2O), and 78.6 (C-3), together with signals from aromatics, ester C=O, and ketonic C=O.

This alcohol was treated with a solution of 2-diethylamino-1,3-diphenyl-1,3,2-diazaphospholidine (90 mg) in toluene (10 ml) containing acetic acid (15 mg) and the mixture was heated under reflux for 0.5 h. The solvent was removed and the *phospholane* (**24**) (74 mg, 79%) was purified by flash chromatography. Recrystallisation from toluene–light petroleum gave crystals, m.p. 111—113 °C (Found: C, 70.0; H, 6.1; N, 5.4. $C_{30}H_{31}N_2O_4P$ requires C, 70.0; H, 6.1; N, 5.4%); δ_H 1.6—2.7 (9 H, m), 3.6—3.9 (6 H, m, CH_2O and CH_2N), 5.07 (1 H, q, *J* 6 Hz, 3-H), and 6.7—7.9 (15 H, m, ArH).

X-*Ray Crystal Analysis of Compound* (**19**).—*Crystal data.* $C_{30}H_{31}N_2O_4P$, monoclinic, a = 12.967(6), b = 21.179(7), c = 10.451(8) Å, β = 112.16(4)°, U = 2 658.1 Å^3, Z = 4, D_c = 1.28 g cm^{-3}. Space group $P2_1/c$, μ(Mo–K_α) = 1.5 cm^{-1}. Intensities were collected on a Nicolet R3m diffractometer at 294 K with graphite-monochromatized Mo–K_α radiation.

A total of 2 677 reflections including standards with $2 \leqslant 2\theta \leqslant 39°$ were measured; 989 independent reflections had intensities greater than 3.0 times their standard deviations. The intensities were corrected for direct beam polarization and Lorentz effects. The structure was solved using random-phasing direct methods (program RANT[19]) and successive difference Fourier calculations.

Full-matrix least-squares refinement[20] was performed minimizing the function $\Sigma\omega(|F_o|-|F_c|)^2$, where ω, the weight, was $[\sigma^2(F_o) + 0.000\,6\,|F_o|^2]^{-1}$ and F_o and F_c are the observed and calculated structure factors respectively. Scattering factors were taken from standard compilations.[21] All non-hydrogen atoms were refined with anisotropic thermal parameters, with the remaining non-hydrogen atoms refined isotropically. The phenyl groups were refined as rigid groups (C_6H_5) with C–C, 1.395 Å, C–H, 1.0 Å, and C–C–C, C–C–H 120°. The thermal parameters for the hydrogen atoms were refined in five groups: those bound to carbon atoms in the fused five-membered rings, those methylene hydrogen atoms on C(9), C(10), and C(11), and the three sets on the three phenyl groups. The final residuals R, R_w are 0.065, 0.067 respectively. Calculations were performed using two related systems written by Sheldrick.[19,20]

Atomic co-ordinates, bond lengths and angles (non-hydrogen), and selected torsional angles are given in Tables 1—3. Observed and calculated structure factors are available from the editorial office on request. All thermal parameters and hydrogen co-ordinates and some additional geometrical parameters are listed in Supplementary Publication No. SUP 56119 (5 pp.).

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