# Preparation and Properties of some Phytotoxic 2-Benzyloxy-8-oxabicyclo[3.2.1]octane Derivatives

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The preparation and biological activity of a novel group of herbicides is described. These 2-benzyloxy-8-oxabicyclo[3.2.1]octanes are readily obtained from the cycloadducts formed between various olefins and 3-oxidopyrylium ylides, prepared from 6-acetoxypyran-3(6*H*)-ones.

In a recent paper [1] we reported the generation and trapping of the 3-oxidopyrylium derivatives (1)—(3). For example, with an excess of ethyl vinyl ether the 1,3-dipole (1) afforded the 2,6-adduct (7) in 60% yield. Herein is described the chemical transformation of such cycloadducts into a group of biologically active compounds related to the glycerol ether herbicides.[2] The 2-benzyloxy-glycerol ethers and related compounds have been of interest for some time as plant growth inhibitors.[3] The first group of compounds shown to possess such activity was derived from acyclic systems and have the general structure (44), in which $R^1$ is a benzyl group and $R^2$ is an alkyl substituent. Several bicyclic systems, *e.g.* compound (45), were developed from the earlier studies. A steric requirement was observed for the cyclic systems in which, for herbicidal activity, the benzyloxy group and oxygen bridge had to be placed in a *syn*-relationship, *i.e.* for the present systems, *exo*-substituted.† On the basis of these earlier studies the cycloadducts prepared from the pyranulose acetates (4)—(6) have been transformed into related structures,

The cycloadducts (7)—(9), (12), and (13) were prepared as described previously.[1] The benzyl ether (10) was prepared by stirring the pyranulose acetate (4) with benzyl vinyl ether [4] in the presence of triethylamine, whilst the intramolecular cycloadduct (11) was obtained by pyrolysis of the acetate (6) in acetonitrile. All the adducts were obtained as one major regio- and stereo-isomer. The oxygen bridge in these adducts imparts conformational rigidity on an otherwise flexible system. As a consequence of the rigidity it was possible to transform chemically the ring systems with a high degree of stereochemical control. For example, the cycloadducts reacted with lithium dimethylcuprate to produce the *exo*-conjugate adducts only. The stereochemical assignments were made on the basis of detailed $^1$H n.m.r. studies. For example, the observed $J_{4,5}$ of *ca.* 1.5 Hz, in the methylated derivatives, *e.g.* (14)—(17), suggested a dihedral angle of *ca.* 90°, as expected for *exo*-addition.[1] The stereoselectivity of the addition possibly reflects complexing of the incoming organocuprate reagents with the oxygen bridge. The upper, *exo*-face of the bicyclic system is also less hindered.

In the presence of 5% palladium on carbon, the norbornylene cycloadduct (13) was regioselectively hydrogenated to compound (18).

In order to introduce the desired 2-benzyloxy substituent into the above derivatives the ketone function was reduced with lithium aluminium hydride to afford the respective alcohols. The results are summarised in Table 1. The adduct (18) with lithium aluminium hydride gave the *endo*-alcohol (36), stereoselectively. Similarly, direct reduction of the enone system of, for example, compound (7), afforded the single epimer (42). These reductions can also be explained in terms of hydride attack from the less hindered *exo*-face. Reduction of compound (7) with sodium borohydride in the presence of ceric chloride [5] also afforded the alcohol (42), a result which can be explained by complexing of the cerium with the bridgehead oxygen before directing the hydride attack.

**Table 1.** Percentage of products obtained from the reduction reactions

| Compound | *exo*-OH (%) [a] | *endo*-OH (%) [a] |
|---|---|---|
| (14) [b] | (21) 43 | (22) 38 |
| (15) [b] | (23) 61 | (24) 22 |
| (16) [b] | (25) 36 | (26) 45 |
| (17) [b] | (30) 26 | (31) 38 |
| (18) [b] | 0 | (36) 92 |
| (19) [b] | (32) 30 | (33) 40 |
| (19) [d] | (32) 29 | (33) 45 |
| (20) [b] | (38) 64 | (39) 30 |
| (7) [c] | 0 | (42) 85 |

[a] Yields after column chromatography. [b] With $LiAlH_4$. [c] With $CeCl_3/NaBH_4$[5]. [d] With $NaBH_4$.

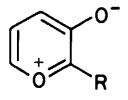
The stereochemical assignments for the alcohols were also aided by $^1$H n.m.r. measurements; the observed coupling constant between the allylic 2-H and 4-H protons for the alcohol (42) was 1.5 Hz, as expected for the presence of an *endo*-hydroxy group.

Reduction of the ketones (14)—(17), (19), and (20) [6] with lithium aluminium hydride gave epimeric mixtures of alcohols, readily separable by silica gel chromatography. The loss of stereoselectivity in the reduction of these compounds probably reflects steric hindrance on the *exo*-face by the presence of the *exo*-C-4 methyl group. Although reduction of the ketones (14)—(16) gave the *exo*-alcohols as the major product, stereospecific *endo*-hydride attack could not be achieved. The use of sodium borohydride or mixed reducing agents afforded similar mixtures of alcohols.

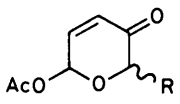
The separated alcohols were benzylated as the sodium salt with either benzyl bromide or 2,6-dichlorobenzyl bromide in dimethylformamide, to afford a series of ethers. The $^1$H n.m.r. data of representative compounds are listed in Table 2. Usually the proton $H_B$ in the *exo*-benzyl ether (see Table 2) occurs at higher field than the corresponding proton in the *endo*-isomer, possibly explained by a deshielding effect of the oxygen bridge on $H_B$ when the latter is *syn* to the oxygen bridge.

The herbicidal activity of the benzyl ether derivatives was evaluated against a range of plants in both pre-emergence and

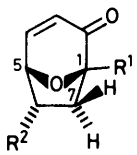
† Herein the terms *exo*- and *endo*- refer to the stereochemical relationships between the substituents on the bicyclic ring and the ether bridge, *exo*-substituents being on the same side of the molecule as the oxygen bridge. All products were prepared as racemates.



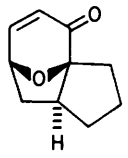
(1) R = H
(2) R = Me
(3) R = $CH_2{=}CH(CH_2)_3$



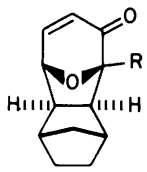
(4) R = H
(5) R = Me
(6) R = $CH_2{=}CH(CH_2)_3$



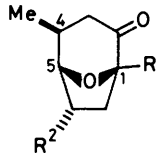
(7) $R^1$ = H; $R^2$ = OEt
(8) $R^1$ = H; $R^2$ = Ph
(9) $R^1$ = Me; $R^2$ = OEt
(10) $R^1$ = H; $R^2$ = $OCH_2Ph$



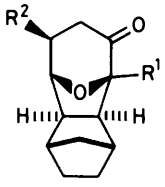
(11)



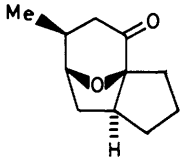
(12) R = H
(13) R = Me



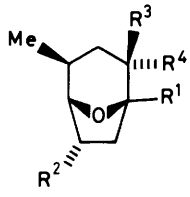
(14) $R^1$ = H; $R^2$ = OEt
(15) $R^1$ = Me; $R^2$ = OEt
(16) $R^1$ = H, $R^2$ = Ph



(17) $R^1$ = H; $R^2$ = Me
(18) $R^1$ = Me; $R^2$ = H
(19) $R^1$ = Me; $R^2$ = Me



(20)



(21) $R^1$ = $R^4$ = H; $R^2$ = OEt; $R^3$ = OH
(22) $R^1$ = $R^3$ = H; $R^2$ = OEt; $R^4$ = OH
(23) $R^1$ = Me; $R^2$ = OEt; $R^3$ = OH; $R^4$ = H
(24) $R^1$ = Me; $R^2$ = OEt; $R^3$ = H; $R^4$ = OH
(25) $R^1$ = $R^4$ = H; $R^2$ = Ph; $R^3$ = OH
(26) $R^1$ = $R^3$ = H; $R^2$ = Ph; $R^4$ = OH
(27) $R^1$ = $R^4$ = H; $R^2$ = OEt; $R^3$ = $OCH_2Ph$
(28) $R^1$ = $R^3$ = H; $R^2$ = OEt; $R^4$ = $OCH_2Ph$
(29) $R^1$ = Me; $R^2$ = OEt; $R^3$ = $OCH_2Ph$; $R^4$ = H

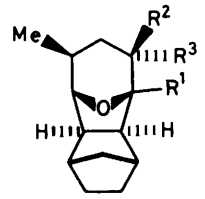
post-emergence assays; some results are given in Table 3. Several structural requirements are apparent for the derivatives to possess significant biological activity. Of utmost importance is the *syn*-relationship between the benzyloxy functionality and the bridgehead oxygen atom. Compounds with an *endo*-stereochemical relationship, for example, adduct (10), were devoid of activity. Indeed, the biological results served to confirm the assigned *endo*-mode of addition between the vinyl ether and the oxidopyrylium intermediate. Similarly the *endo*-benzyl ethers such as (37) and (34) were inactive, in this case providing complementary evidence for the stereoselective *exo*-attack of hydride ion on the ketone adducts, (18) and (17) respectively. Of the active derivatives, the greatest intrinsic activity was recorded for compounds containing the least degree of alkyl substitution. For example, the compounds derived from the ethyl vinyl ether adducts, (7) and (9), or the intramolecular adduct (20), are more active than those derived from the norbornylene and styrene adducts.[7] Of interest is that, in the bicyclic adducts, *e.g.* compounds (27) and (34), the presence of a tertiary alkyl group adjacent to the bridged ether is not imperative for activity, *cf.* (44), $R^2$ = alkyl for active compounds.[3]

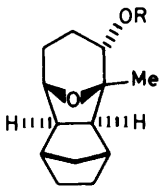
## Experimental

M.p.s were determined on a Kofler hot-stage apparatus and are uncorrected. I.r. spectra were recorded with a Perkin-Elmer 297 spectrophotometer either on films or, for solids, as Nujol mulls. Unless otherwise stated, $^1H$ n.m.r. spectra were recorded on either a Perkin-Elmer R32 (90 MHz) instrument or a Jeol FX90Q spectrometer for solutions in deuteriochloroform using tetramethylsilane as internal reference. Mass spectra were recorded on either a Kratos MS25 or MS9/50 instrument.

Thin layer chromatography (t.l.c.) and short column chromatography were carried out on Kieselgel $GF_{254}$ (Merck) silica gel. Solvents were generally distilled and dried before use. Light petroleum refers to the fraction of boiling range 40—60 °C and ether refers to diethyl ether. Solvent ratios are described in ratios of volumes before mixing.

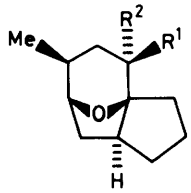
The intermolecular cycloadducts were prepared under either thermal conditions, in glass tubes, sealed under vacuum, or by base-catalysed reaction at room temperature, using triethylamine as base in the manner described previously.[1]

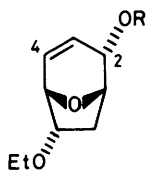




(30) $R^1$ = H; $R^2$ = OH; $R^3$ = H
(31) $R^1$ = H; $R^2$ = H; $R^3$ = OH
(32) $R^1$ = Me; $R^2$ = OH; $R^3$ = H
(33) $R^1$ = Me; $R^2$ = H; $R^3$ = OH
(34) $R^1$ = H; $R^2$ = 2,6-$Cl_2C_6H_3CH_2O$; $R^3$ = H
(35) $R^1$ = Me; $R^2$ = $PhCH_2O$; $R^3$ = H

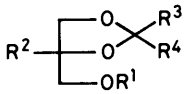
(36) R = H
(37) R = 2,6-$Cl_2C_6H_3CH_2$

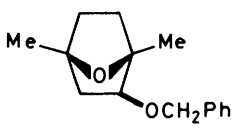




(38) $R^1$ = OH; $R^2$ = H
(39) $R^1$ = H; $R^2$ = OH
(40) $R^1$ = $OCH_2Ph$; $R^2$ = H
(41) $R^1$ = H; $R^2$ = $OCH_2Ph$

(42) R = H
(43) R = $CH_2Ph$





(44) $R^1$ = $CH_2Ph$; $R^2$ = alkyl; $R^3$, $R^4$ = alkyl, aryl or benzyl

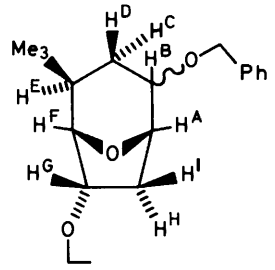
(45)

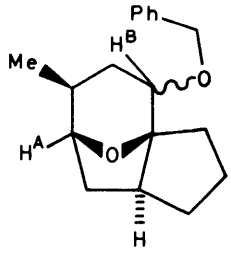
6-endo-6-*Benzyloxy*-8-*oxabicyclo*[3.2.1]*oct*-3-*en*-2-*one* (10).—Benzyl vinyl ether was prepared by the method of Watanabe *et al.*[4] 6-Acetoxy-2*H*-pyran-3(6*H*)-one (4) [8] (2 g), benzyl vinyl ether (10.3 g, 6 equiv.), and triethylamine (2.3 g, 2 equiv.) in dichloromethane (6 ml) were stirred at room temperature for 16 h; the solvents were then removed under reduced pressure and the residue chromatographed through silica gel (250 g) using ether–light petroleum (1.5 : 1) as eluant to afford the *title compound* (10) (1.3 g, 44%) as a colourless oil, $\nu_{max.}$ 1 690 $cm^{-1}$; δ 1.55 (1 H, m, *J* 2, 5, 13 Hz, 7-*endo*-H) 2.60 (1 H, m, *J* 8, 10, 13 Hz, 7-*exo*-H), 4.2 (1 H, m, *J* 5, 7, 10 Hz, C*H*OBz), 4.35 (2 H, s, $CH_2$Ph), 4.5 (1 H, m, *J* 1.5, 2, 8 Hz, CHCO), 4.6 (1 H, dd, *J* 5.5, 7 Hz, 5-H), 6.1 (1 H, dd, *J* 1.5, 11 Hz, 3-H), 7.1 (1 H, dd, *J* 5.5, 11 Hz, 4-H,) and 7.2 (5 H, m, ArH) (Found: $M^+$, 230.094 53. $C_{14}H_{14}O_3$ requires $M^+$, 230.094 288).

6-*Acetoxy*-2-*pent*-4-*en*-1-*yl*-2H-*pyran*-3(6H)-*one* (6).—To a solution of 5-bromomagnesiopent-1-ene, prepared from 5-bromopent-1-ene (25 g) and magnesium (4.3 g) in ether (300 ml), was added a solution of 2-furaldehyde (16 g) in ether (100 ml). The reaction mixture was stirred at room temperature for 30 min before being quenched with saturated aqueous $NH_4Cl$, and extraction with ether (600 ml). The combined extract was washed with water, dried, and the solvent removed under reduced pressure. The crude product was distilled (88 °C/2 mmHg) to give 2-(1-hydroxyhex-5-enyl)furan (23.5 g, 85%), $\nu_{max.}$ 3 360, 3 080, 2 930, and 1 640 $cm^{-1}$; δ 1.3—2.4 (6 H, m, $CH_2$), 2.5 (1 H, br s, OH), 4.6 (1 H, m, C*H*OH), 5.1 (2 H, m, $CH_2$=C), 5.6 (1 H, m, C*H*=$CH_2$), 6.2 (2 H, m, ArH), 7.4 (1 H, m, ArH) (Found: $M^+$, 166.098 57. $C_{10}H_{14}O_2$ requires $M^+$, 166.099 37).

The pentenylfurfuryl alcohol (5 g) was oxidised with *m*-chloroperbenzoic acid (5.7 g, 95%) in dichloromethane (150 ml) 5—10 °C for 30 min and thereafter at room temperature for 2.5 h. The *m*-chlorobenzoic acid was filtered off, the solution washed with aqueous $NaHCO_3$, and the solvent removed under reduced pressure. The residue was chromatographed through silica gel (200 g) using ether–$CHCl_3$ (1 : 1) as eluant to produce 6-*hydroxy*-2-*pent*-4-*enylpyran*-3(6H)-*one* (4.4 g, 80%), as a waxy solid, m.p. 38—42 °C; $\nu_{max.}$ 3 400, 1 690, and 1 640 $cm^{-1}$; δ 1.2—2.5 (6 H, m, $CH_2$), 2.4 (1 H, broad s, (OH), 4.6 (1 H, m, CHO), 5.0 (2 H, m, $CH_2$=C), 5.6 (1 H, d, *J* 5 Hz, C*H*OH), 5.6—5.8 (1 H, m, CH=C), 6.20 (1 H, d, *J* 10 Hz, CH–CO), and 6.9 (1 H, dd, *J* 5, 10 Hz, C*H*=CH) (Found: C, 65.7; H, 7.85. $C_{10}H_{14}O_3$ requires C, 65.9; H, 7.7%.)

**Table 2.** $^1$H N.m.r. data of benzyl ether adducts





(27) OBz = *exo*
(28) OBz = *endo*

(40) OBz = *exo*
(41) OBz = *endo*

| Benzyl ether | A | B | C |
|---|---|---|---|
| (27) [a] | 4.28 (1.5, 2, 8) | 3.21 (1.5, 2, 5) | 2.14 (5, 6.5, 15) |
| (28) [a] | 4.28 (1 25, 1.8, 3.7, 7.5) | 3.78 (3.7, 6.25, 11.25) | 1.91 (6.25, 11.25, 13.5) |
| (40) [b] | 4.15 (1.5, 2, 8) | 3.15 (2, 4) | |
| (41) [b] | 4.05 (1.5, 2, 8) | 3.65 (8, 10) | |

| | D | E | F |
|---|---|---|---|
| (27) [a] | 1.6 (2, 2, 15) | 1.86 (1.2, 2, 6.5, 7) | 4.0 (1.2, 1.2, 7) |
| (28) [a] | 1.65 (1.5, 2, 6.25, 13.5) | 2.11 (1.8, 2, 6.25, 7) | 3.84 (1.5, 1.8, 7.5) |

| | G | H | I |
|---|---|---|---|
| (27) [a] | 4.14 (2, 4.5, 15) | 1.41 (2, 4.5, 15) | 2.4 (8, 10.5, 15) |
| (28) [a] | 4.13 (5, 7.5, 10.5) | 1.83 (1.8, 5, 13.75) | 2.17 (7.5, 10.5, 13.75) |

[a] Spectra recorded at 400 MHz; $CDCl_3$ as solvent; δ values (*J* in Hz). [b] Carried out at 90 MHz.

**Table 3.** Herbicidal activity of benzyl ether derivatives [a]

| Compd. | Dose kg/ha | Phytotoxicity rating (0—9) [b] Post emergence (plants) Foliar spray [c] Mz | R | BG | O | L | M | SB | S | Seeds Pre-emergence Mz | R | BG | O | L | M | SB | S | Stereochemistry of benzyl ether group |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (27) | 5 | 5 | 2 | 8 | 0 | 3 | 0 | 0 | 5 | 9 | 9 | 9 | 6 | 0 | 0 | 0 | 0 | *syn* |
| | 1 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 2 | 3 | 2 | 9 | 0 | 0 | 0 | 0 | 0 | |
| (28) | 5 | | | | Inactive | | | | | | | | Inactive | | | | | *anti* |
| | 1 | | | | | | | | | | | | | | | | | |
| (29) | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 8 | 2 | 0 | 0 | 0 | 5 | *syn* |
| (40) | 5 | 7 | 2 | 9 | 5 | 6 | 3 | 5 | 5 | 7 | 7 | 9 | 5 | 6 | 5 | 5 | 5 | *syn* |
| | 1 | 5 | 0 | 8 | 3 | 3 | 0 | 2 | 4 | 7 | 6 | 9 | 3 | 5 | 4 | 2 | 3 | *syn* |
| (41) | 5 | | | | Inactive | | | | | | | | Inactive | | | | | *anti* |
| | 1 | | | | | | | | | | | | | | | | | |
| (34) | 1 | 0 | 0 | 6 | 2 | 4 | 6 | 3 | 5 | 0 | 0 | 9 | 2 | 0 | 3 | 2 | 3 | *syn* |
| (10) | 5 | | | | Inactive | | | | | | | | Inactive | | | | | *anti* |
| | 1 | | | | | | | | | | | | | | | | | |
| (35) | 1 | 2 | 0 | 5 | 2 | 2 | 0 | 0 | 3 | 0 | 0 | 8 | 0 | 0 | 0 | 0 | 0 | *syn* |
| (37) | 5 | | | | Inactive | | | | | | | | Inactive | | | | | *anti* |
| | 1 | | | | | | | | | | | | | | | | | |
| (43) | 5 | | | | Inactive | | | | | | | | Inactive | | | | | *anti* |
| | 1 | | | | | | | | | | | | | | | | | |

[a] Assessed at the Biosciences Division, Shell Research Centre, Sittingbourne. [b] 0 = no effect; 9 = complete death of plant. [c] Mz = maize; R = rice; BG = barnyard grass; O = oat; L = linseed; M = mustard; SB = sugar beet; S = soya bean.

The alcohols were acetylated with pyridine–acetic anhydride at 0 °C for 3 h. Work-up in the normal manner afforded the *title acetate* (5.5 g, 89%) isolated as a pale yellow oil, $\nu_{max.}$ 1 735, 1 690, and 1 640 $cm^{-1}$ (Found: $M^+$, 224.104 82. $C_{12}H_{16}O_4$ requires $M^+$, 224.104 85).

1,5-*Epoxybicyclo*[5.3.0]*dec*-3-*en*-2-*one* (11).—The acetate (6) (2 g) in acetonitrile (6 ml) was heated at 150 °C for 16 h before removal of solvent under reduced pressure; the product was then filtered through silica gel (150 g) using ether–light petroleum (1 : 1) as eluant to afford the *title adduct* (1 g, 78%) as a pale yellow oil, $\nu_{max.}$ 1 690 $cm^{-1}$; δ 1.2—2.4 (9 H, m), 4.95 (1 H, m, CH–O), 6.05 (1 H, d, *J* 11 Hz, CHCO), and 7.25 (1 H, dd, *J* 4.5, 11 Hz, C*H*=CH) (Found: $M^+$, 164.083 62. $C_{10}H_{12}O_2$ requires $M^+$, 164.083 72).

*Methylation of the Adduct Esters.*—To a solution of lithium dimethylcuprate [prepared from methyl lithium–lithium bromide complex (23.5 ml of 1.5M solution in hexane) and cuprous iodide (3.4 g)] in ether (70 ml) under $N_2$ at −20 °C was added a solution of the adduct enone (10 mmol) in ether (10 ml). The reaction mixture was warmed to room temperature and stirred for a further 1.5 h before being poured into saturated aqueous $NH_4Cl$ (50 ml) and extraction with ether (3 × 100 ml). The combined ether extract was washed with brine (50 ml) and water (50 ml), dried ($Na_2SO_4$), filtered and the solvent removed under reduced pressure. The residue was chromatographed through silica gel (100 g) using ether–chloroform mixture as eluant to give the desired adducts.

In this manner the following adducts were prepared. 4-exo,-6-endo-6-*Ethoxy*-4-*methyl*-8-*oxabicyclo*[3.2.1]*octan*-2-*one* (14) (94%), $\nu_{max.}$ 2 960 and 1 730 $cm^{-1}$; δ 1.0 (3 H, d, *J* 7 Hz, Me), 1.2—2.6 (5 H, m, methine and methylenes), 1.15 (3 H, t, *J* 8 Hz, $CH_3CH_2$), 3.6 (2 H, q, *J* 8 Hz, $CH_2CH_3$), 4.2 (1 H, m, 6-H), 4.5 (1 H, dd, *J* 2, 9 Hz, 1-H), and 4.55 (1 H, d, *J* 8 Hz, 5-H) (Found: $M^+$, 194.109 96. $C_{10}H_{16}O_3$ requires $M^+$, 184.109 94).

4-exo,6-endo-6-*Ethoxy*-1,4-*dimethyl*-8-*oxabicyclo*[3.2.1]-*octan*-2-*one* (15) (92%), $\nu_{max.}$ 1 720 $cm^{-1}$; δ 1.2 (3 H, d, *J* 7 Hz, $CH_3CH$), 1.35 (3 H, s, $CH_3$), 1.6—3.2 (5 H, m, CH and $CH_2$), 1.40 (3 H, t, *J* 7 Hz, $CH_3CH_2$), 3.5 (2 H, q, *J* 7 Hz, $OCH_2CH_3$), 4.3 (1 H, m, CHO), and 4.4 (1 H, m, C*H*OEt) (Found: $M^+$, 198.125 07. $C_{11}H_{18}O_3$ requires $M^+$, 198.125 59).

5,9-*Epoxy*-1,2,3,4,4a,5,7,8,9,9a-*decahydro*-8-*methyl*-1,4-*methanobenzocycloheptan*-6-*one* (17) (90%), m.p. 42 °C, $\nu_{max.}$ 1 725 $cm^{-1}$; δ 1.1 (3 H, d, *J* 7 Hz, $CH_3$), 0.8—2.8 (13 H, m), 3.8 (1 H, s, CH–O), and 4.0 (1 H, s, CHCO) (Found: $M^+$, 206.130 61. $C_{13}H_{18}O_2$ requires $M^+$, 206.130 67).

5,9-*Epoxy*-1,2,3,4,4a,5,7,8,9,9a-*decahydro*-5,8-*dimethyl*-1,4-*methanobenzocycloheptan*-6-*one* (19) (96%), as a colourless oil, $\nu_{max.}$ 1 725 $cm^{-1}$; δ 1.1 (3 H, d, *J* 7 Hz, $CH_3$), 1.3 (3 H, s, $CH_3$), 1.0—2.8 (13 H, m), and 3.85 (2 H, broad s, CHO) (Found: $M^+$, 220.146 18. $C_{14}H_{20}O_2$ requires $M^+$, 220.146 32).

4-exo-1,5-*Epoxy*-4-*methylbicyclo*[5.3.0]*decan*-2-*one* (20) (95%), m.p. 39—40 °C, $\nu_{max.}$ 1 740 $cm^{-1}$; δ 1.2 (3 H, d, *J* 8 Hz, $CH_3$), 1.4—2.7 (12 H, m), and 4.3 (1 H, m, C*H*O) (Found: $M^+$, 180.114 72. $C_{11}H_{16}O_2$ requires $M^+$, 180.115 03).

*Hydrogenation of the Norbornylene Adduct* (13).—The adduct (2 g) in ethanol (75 ml) was hydrogenated at room temperature at 40 lb $in^{-2}$, using 5% Pd/C (200 mg) as catalyst. After adsorption of 1 equiv. of hydrogen the solution was filtered and the filtrate concentrated under reduced pressure. The residue was filtered through silica gel, using ether–light petroleum (1 : 2) as eluant to afford the *dihydro-ketone* (18) (1.8 g, 90%) as a colourless oil, $\nu_{max.}$ 1 720 $cm^{-1}$; δ 1.25 (3 H, s, $CH_3$), 0.9—2.5 (14 H, m), and 4.15 (1 H, m, CH–O) (Found: C, 75.8; H, 8.8. $C_{13}H_{18}O_2$ requires C, 75.6: H, 8.7%).

2-exo,4-exo,6-endo-6-*Ethoxy*-2-*hydroxy*-4-*methyl*-8-*oxa-bicyclo*[3.2.1]*octane* (21).—The ketone (14) [1] (1.3 g) in dry tetrahydrofuran (60 ml) was treated with lithium aluminium hydride (0.43 g) at 0 °C for 30 min before being quenched with methanol, acidified with dilute HCl, and extracted with ether (2 × 75 ml). The combined ether extract was washed with saturated aqueous $NaHCO_3$, brine, and water, dried, filtered, and the solvent removed under reduced pressure. The residue was chromatographed through $SiO_2$ (100 g) using ethyl acetate as eluant to afford two compounds. The less-polar endo-*alcohol* (22) (0.50 g, 38%) was obtained as a colourless

oil, $\nu_{max.}$ 3 440 $cm^{-1}$; δ 1.25 (3 H, t, *J* 7 Hz, $CH_3CH_2$), 1.35 (3 H, d, *J* 6 Hz, $CH_3CH$), 1.5—2.5 (5 H, m), 2.5 (1 H, br s, OH), 3.45 (2 H, q, *J* 7 Hz, $CH_3CH_2O$), 3.75 (1 H, m, CHOH), 4.15 (3 H, m, CHO) (Found: $M^+$, 186.126 04. $C_{10}H_{18}O_3$ requires $M^+$, 186.125 59).

The more polar compound was the *title alcohol* (0.56 g, 43%), $\nu_{max.}$ 3 340 $cm^{-1}$; δ 1.25 (3 H, t, *J* 7 Hz, $CH_3CH_2$), 1.35 (3 H, d, *J* 6.5 Hz, $CH_3CH$), 1.5—2.4 (5 H, m), 2.6 (1 H, br s, OH), 3.5 (2 H, q, *J* 7 Hz, $CH_3CH_2O$), 3.55 (1 H, m, CHOH), and 4.1 (3 H, m, CHO) (Found: $M^+$, 186.125 89. $C_{10}H_{18}O_3$ requires $M^+$, 186.125 59).

2-exo,4-exo,6-endo-6-*Ethoxy*-1,4-*dimethyl*-2-*hydroxy*-8-*oxabicyclo*[3.2.1]*octane* (23).—In the above described manner, the ketone (15) (0.9 g) was reduced with lithium aluminium hydride (0.17 g) in tetrahydrofuran (50 ml). The product was separated by chromatography through $SiO_2$ to yield, as the less polar product, the endo-*alcohol* (24) (0.2 g, 22%) as a colourless oil, $\nu_{max.}$ 3 450 $cm^{-1}$; δ 1.2 (3 H, t, *J* 7 Hz, $CH_3CH_2$), 1.3 (3 H, d, *J* 7 Hz, $CH_3CH$), 1.35 (3 H, s, $CH_3$), 1.4—2.5 (5 H, m), 2.4 (1 H, br s, OH), 3.4 (2 H, q, $CH_3CH_2O$), 3.65 (1 H, m, CHOH), 4.1 (1 H, m, CHO), 4.3 (1 H, m, CH–O) (Found: $M^+$, 200.141 41. $C_{11}H_{20}O_3$ requires $M^+$, 200.141 124).

The more polar compound was the *title alcohol* (0.55 g, 61%), obtained as a colourless oil, $\nu_{max.}$ 3 450 $cm^{-1}$; δ 1.2 (3 H, t, *J* 7 Hz, $CH_3CH_2$), 1.3 (3 H, d, *J* 7 Hz, $CH_3CH$), 1.35 (3 H, s, $CH_3$), 1.4—2.4 (5 H, m), 2.4 (1 H, m, br s, OH), 3.3 (1 H, m, CHOH), 3.4 (2 H, q, *J* 7 Hz, $CH_3CH_2O$), 4.1 (1 H, m, CH–O), and 4.25 (1 H, m, CH–O) (Found: C, 65.7; H, 10.0. $C_{11}H_{20}O_3$ requires C, 66.0; H, 10.0%).

2-exo,4-exo,6-endo-2-*Hydroxy*-4-*methyl*-6-*phenyl*-8-*oxabicyclo*[3.2.1]*octane* (25).—In the manner described above, the ketone (16) (1.8 g) was reduced with lithium aluminium hydride (0.32 g). Chromatography of the product through $SiO_2$, with ether–light petroleum (3 : 1) as eluant gave, as the less polar material, the *title alcohol* (0.65 g, 36%), as a colourless oil, $\nu_{max.}$ 3 440 $cm^{-1}$; δ 1.1 (3 H, d, *J* 7 Hz, $CH_3CH$), 0.8—2.5 (5 H, m), 2.4 (1 H, br s, OH), 3.55 (1 H, m, CH), 3.95 (1 H, m, CH–OH), 4.1 (1 H, m, CHO), 4.25 (1 H, m, CH–O), and 7.3 (5 H, m, ArH) (Found: C, 77.1; H, 8.7. $C_{14}H_{18}O_2$ requires C, 77.1; H, 8.3%).

The more polar material was the epimeric alcohol (26) (0.82 g, 45%), m.p. 86 °C, $\nu_{max.}$ 3 440 $cm^{-1}$; δ 1.15 (3 H, d, *J* 7 Hz, $CH_3CH$), 0.8—2.5 (5 H, m), 2.35 (1 H, br s, OH), 3.5 (1 H, m, CH), 4.1 (1 H, m, CH–O), 4.25 (1 H, m, CH–OH), 4.25 (1 H, m, CH–O), and 7.25 (5 H, m, ArH) (Found: $M^+$, 218.130 36. $C_{14}H_{18}O_2$ requires $M^+$, 218.130 67).

*Reduction of the Ketone* (20).—The ketone (1.71 g) was reduced with lithium aluminium hydride (0.54 g) in tetrahydrofuran (75 ml) at 0 °C in the usual manner. Chromatography of the product through $SiO_2$, using ether–light petroleum (3 : 1) as eluant, afforded the less polar endo-*alcohol* (39) (0.55 g, 36%), as a colourless oil, $\nu_{max.}$ 3 420 $cm^{-1}$; δ 1.25 (3 H, d, *J* 7 Hz, $CH_3CH$), 1.1—2.4 (12 H, m), 2.5 (1 H, br s, OH), 3.65 (1 H, m, CHOH), and 4.15 (1 H, m, CH–O) (Found: $M^+$, 192.130 81. $C_{11}H_{18}O_2$ requires $M^+$, 182.130 672).

The more polar product was the exo-*alcohol* (38) (0.93 g, 64%), m.p. 43 °C, $\nu_{max.}$ 3 420 $cm^{-1}$; δ 1.25 (3 H, d, *J* 7 Hz, $CH_3CH$), 1.1—2.4 (12 H, m), 2.5 (1 H, br s, OH), 3.5 (1 H, m, CH–OH), and 4.2 (1 H, m, CH–O) (Found: C, 72.75; H, 10.05. $C_{11}H_{18}O_2$ requires C, 72.5; H, 9.9%).

*Reduction of the Ketone* (17).—The ketone (17) (10.9 g) was reduced with lithium aluminium hydride (0.19 g) in tetrahydrofuran (75 ml) by the usual method. Chromatography of the product through $SiO_2$, using ether–chloroform (3 : 1) as eluant gave, as the less polar component, the exo-*alcohol* (30) (0.24 g, 26%), as a colourless oil, $\nu_{max.}$ 3 390 $cm^{-1}$; δ 1.2 (3 H, d, *J* 7 Hz, $CH_3CH$), 0.8—2.3 (13 H, m), 2.2 (1 H, br s, OH), 3.1 (1 H, br s, CH–OH), 3.6 (1 H, m, CHO), and 4.0 (1 H, s, CHO) (Found: $M^+$, 208.145 99. $C_{13}H_{20}O_2$ requires $M^+$, 208.146 32).

The more polar endo-*alcohol* (31) was also obtained as a colourless oil (0.34 g, 38%), $\nu_{max.}$ 3 390 $cm^{-1}$; δ 1.2 (3 H, d, *J* 7 Hz, $CH_3$), 0.8—2.3 (13 H, m), 2.15 (1 H, br s, OH), 3.25 (1 H, br s, CH–OH), 3.6 (1 H, m, CHO), and 4.0 (1 H, s, CH–O) (Found: $M^+$, 208.146 30. $C_{13}H_{20}O_2$ requires $M^+$, 208.146 32).

*Reduction of the Ketone* (18).—The ketone (18) (1.5 g) was reduced with lithium aluminium hydride (0.26 g) in tetrahydrofuran (75 ml) by the usual method. Filtration of the product through $SiO_2$, using ether–chloroform (3 : 1) as eluant, afforded the endo-*alcohol* (36) (1.4 g, 93%), m.p. 41 °C, $\nu_{max.}$ 3 400 $cm^{-1}$; δ 1.2 (3 H, s, $CH_3$), 0.8—2.3 (14 H, m), 2.2 (1 H, br s, OH), 3.45 (1 H, m, CHOH), and 3.9 (1 H, m, CH–O) (Found: C, 75.4; H, 9.5. $C_{13}H_{20}O_2$ requires C, 75.0; H, 9.6%).

*Reduction of the Ketone* (19).—In the usual manner, the ketone (1.0 g) was reduced with lithium aluminium hydride (0.23 g) in tetrahydrofuran (75 ml). The product was chromatographed through $SiO_2$, using ether–light petroleum (3 : 2) as eluant, the less polar exo-*alcohol* (32) (0.3 g, 30%) as a colourless oil, $\nu_{max.}$ 3 400 $cm^{-1}$; δ 1.00 (3 H, d, *J* 7 Hz, $CH_3CH$), 1.2 (3 H, s, $CH_3$), 0.8—2.3 (13 H, m), 2.2 (1 H, br s, OH), 3.3 (1 H, m, CHOH), and 3.6 (1 H, m, CH–O) (Found: C, 75.6; H, 10.0. $C_{14}H_{22}O_2$ requires C, 75.8; H, 9.9%).

The more polar endo-*alcohol* (33) (0.4 g, 40%) was isolated as a colourless oil, $\nu_{max.}$ 3 400 $cm^{-1}$; δ 1.0 (3 H, d, *J* 7 Hz, $CH_3CH$), 1.2 (3 H, s, $CH_3$), 0.8—2.25 (13 H, m), 2.2 (1 H, br s, OH), 3.5 (1 H, m, CHOH), 3.8 (1 H, m, CH–O) (Found: $M^+$, 221.1620. $C_{14}H_{22}O_2$ requires $M^+$, 222.161 97).

2-endo,6-endo-6-*Ethoxy*-2-*hydroxy*-8-*oxabicyclo*[3.2.1]-*hept*-3-*ene* (42).—The ketone (7) [1] (1 g) was dissolved in methanol (15 ml) containing cerium(III) chloride hexahydrate (2.13 g) and sodium borohydride (0.23 g) added portionwise at room temperature during 15 min.[5] The mixture was then stirred at room temperature for a further 15 min before the reaction was quenched with 2M-HCl (20 ml) and the mixture extracted with ether (3 × 60 ml). The combined ether extract was washed with brine, dried, and evaporated under reduced pressure and the residue chromatographed through $SiO_2$ (50 g), using ether–light petroleum (2 : 1) as eluant. The *title alcohol* (0.6 g, 60%) was obtained as a colourless oil, $\nu_{max.}$ 3 400 $cm^{-1}$; δ 1.2 (3 H, t, *J* 7 Hz, $CH_3CH_2$), 2.2 (2 H, m, $CH_2$), 2.6 (1 H, s, OH), 3.5 (2 H, q, *J* 7 Hz, $CH_3CH_2$), 4.1—4.8 (3 H, m, CHO), 5.7 (1 H, dd, *J* 3, 9 Hz, C=CH–CHOH), and 6.0 (1 H, ddd, *J* 2, 4, 9 Hz, CH=CH–CH–OH) (Found: $M^+$, 170.094 22. $C_9H_{14}O_3$ requires $M^+$, 170.094 29).

*General Procedure for Benzylations.*—A solution of the alcohol (3 mmol) in dimethylformamide (10 ml) was added rapidly to a stirred suspension of sodium hydride (0.2 g, 50% suspension in oil, 4 mmol) in dimethylformamide (30 ml). After 15 min, the benzyl bromide (3.5 mmol) was added and the solution warmed to 65 °C for 30 min, before being cooled to ambient temperature with stirring for 16 h. It was then poured into water (50 ml) and extracted with ether (2 × 75 ml). The combined ether extracts were washed with water (3 × 40 ml), dried, and evaporated under reduced pressure. The oily products were generally purified by filtration through $SiO_2$ with ether–light petroleum mixtures as eluants, to afford the required ethers.

The ethers had the following properties. 2-exo,4-exo,6-endo-2-*Benzyloxy*-6-*ethoxy*-4-*methyl*-8-*oxabicyclo*[3.2.1]*octane* (27) (94%), a colourless oil; see Table 2 for the pertinent $^1$H n.m.r. data (Found: $M^+$, 276.172 51. $C_{17}H_{24}O_3$ requires $M^+$, 276.172 53).

2-endo,6-endo,4-exo-2-*Benzyloxy*-6-*ethoxy*-4-*methyl*-8-*oxabicyclo*[3.2.1]*octane* (28) (97%), as a colourless oil; see Table 2 for pertinent $^1$H n.m.r. data (Found: $M^+$, 276.172 42. $C_{17}H_{24}O_3$ requires $M^+$, 276.172 53).

2-exo,4-exo,6-endo-2-*Benzyloxy*-6-*ethoxy*-1,4-*dimethyl*-8-*oxabicyclo*[3.2.1]*octane* (29) (69%), a colourless oil, δ 1.3 (3 H, d, *J* 6.5 Hz, $CH_3CH$), 1.3 (3 H, t, *J* 7 Hz, $CH_3CH_2$), 1.35 (3 H, s, $CH_3$), 0.8—2.4 (5 H, m), 3.1 (1 H, m, CHO), 3.5 (2 H, q, *J* 7 Hz, $CH_3CH_2O$), 4.1 (1 H, m, CHO), 4.2 (1 H, m, CH–O), 4.6 (2 H, ABq, *J* 12 Hz, $CH_2Ph$), and 7.35 (5 H, s, ArH), (Found: $M^+$, 290.187 39; C, 74.9; H, 9.2. $C_{18}H_{26}O_3$ requires $M^+$, 290.188 18; C, 74.5; H, 9.0%).

exo-2,6-*Dichlorobenzyloxy ether* (34) (57%), a colourless oil, δ 0.6—2.2 (16 H, m), 3.2 (1 H, m, CH–O), 3.65 (1 H, s, CH–O), 4.0 (1 H, m, CH–O), 4.65 (2 H, ABq, *J* 12 Hz, $ArCH_2$), and 7.15 (3 H, m, ArH) (Found: C, 65.4; H, 6.5; Cl, 19.1. $C_{20}H_{24}Cl_2O_2$ requires C, 65.4; H, 6.5; Cl, 19.35%).

exo-*Benzyloxy ether* (35) (83%), a colourless oil, δ 1.2 (3 H, s, $CH_3$), 0.6—2.3 (16 H, m), 2.9 (1 H, m, CH–O), 3.7 (1 H, s, CH–O), 4.5 (2 H, ABq, *J* 12 Hz, $PhCH_2$), 7.2 (5 H, s, ArH) (Found: $M^+$, 321.209 79. $C_{21}H_{28}O_2$ requires $M^+$, 312.208 92).

2-endo-2,6-*Dichlorobenzyloxy ether* (37) (45%), m.p. 110 °C; δ 1.2 (3 H, s, $CH_3$), 0.7—2.3 (14 H, m), 3.4 (1 H, m, *J* 7, 8 Hz, CH–O), 3.9 (1 H, m, CH–O), 4.75 (2 H, ABq, *J* 12 Hz, $ArCH_2$), and 7.3 (3 H, m, ArH) (Found: C, 65.1; H, 6.9; Cl, 19.1. $C_{20}H_{24}Cl_2O_2$ requires C, 65.4; H, 6.5; Cl, 19.35%).

2-exo,4-exo-2-*Benzyloxy*-1,5-*epoxy*-4-*methylbicyclo*[5.3.0]-*decane* (40) (84%), a colourless oil, δ 1.28 (3 H, d, *J* 7 Hz, $CH_3CH$), 1.2—2.3 (12 H, m), 3.15 (1 H, dd, *J* 2, 4 Hz, CH–O), 4.15 (1 H, m, *J* 1.5, 2, 8 Hz, CH–O), 4.55 (2 H, ABq, *J* 13 Hz, $PhCH_2$), and 7.3 (5 H, m, ArH) (Found: $M^+$, 272.178 39. $C_{18}H_{24}O_2$ requires $M^+$, 272.177 62).

2-endo,4-exo-2-*Benzyloxy*-1,5-*epoxy*-4-*methylbicyclo*-[5.3.0]*decane* (41) (91%), a colourless oil, δ 1.05 (3 H, d, *J* 7 Hz, $CH_3CH$), 1.15—2.2 (11 H, m), 2.55 (1 H, m, CHMe), 3.65 (1 H, m, *J* 8, 10 Hz, CH–O), 4.05 (1 H, m, *J* 1.5, 2, 8 Hz, CHO), 4.52 (2 H, ABq, *J* 13 Hz, $PhCH_2$), and 7.28 (5 H, s, ArH) (Found: $M^+$, 272.178 17. $C_{18}H_{24}O_2$ requires $M^+$, 272.177 62).

2-endo,6-endo-2-*Benzyloxy*-6-*ethoxy*-8-*oxabicyclo*[3.2.1]-*oct*-3-*ene* (43) (65%), a colourless oil, δ 1.2 (3 H, t, *J* 7 Hz, $CH_3CH_2$), 2.25 (2 H, m, $CH_2$), 3.45 (2 H, q, *J* 7 Hz, $CH_3CH_2$), 4.15 (1 H, m, *J* 5, 7.5, 10.5 Hz, 6-H), 4.35 (1 H, m, *J* 4.5, 7.5 Hz, 5-H), 44.5 (1 H, m, *J* 1.8, 3.5, 7.5 Hz, 1-H), 4.5 (1 H, m, *J* 1.8, 3 Hz, 2-H), 4.55 (2 H, ABq, *J* 14 Hz, $PhCH_2$), 5.8 (1 H, dd, *J* 3, 10 Hz, 3-H), 5.95 (1 H, m, *J* 2, 3, 10 Hz, 4-H), and 7.35 (5 H, s, ArH) (Found: C, 73.5; H, 7.8. $C_{16}H_{20}O_3$ requires C, 73.8; H, 7.7%).

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