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STEREOCHEMICAL RELATIONS IN THE BORNANE SERIES

AN EXAMPLE OF PREFERRED EXO ATTACK

M. B. RUBIN and J. M. BEN-BASSAT

Department of Chemistry, Technion—Israel Institute of Technology, Haifa, Israel

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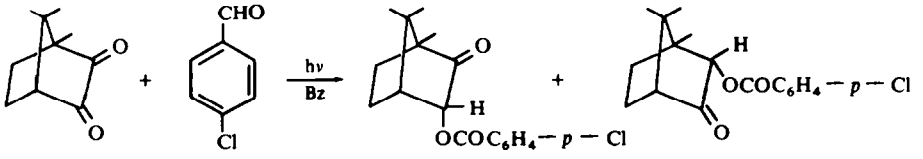
Abstract—The four α-hydroxybornanones have been obtained as their crystalline *p*-chlorobenzoates; the two *endo* ketoesters *via* photochemical reaction of camphorquinone and *p*-chlorobenzaldehyde and the two *exo*-isomers from *cis*, *exo*-bornanediol. *cis*-Diols were produced in every case by reaction of these ketoesters with *p*-methylbenzyl magnesium chloride, the *endo*-ketoesters affording *cis*, *endo*-diols via *exo* attack of the Grignard reagent on the bornane system. Two of the possible *trans*-diols were also synthesized.

IN CONNECTION with an investigation of photoreduction and photoaddition reactions of 2,3-bornandedione ("camphorquinone" **CQ**), it became necessary to provide unequivocal proof of the stereochemistry of a variety of hydroxyketones and substituted diols in the bornane series. Such compounds have been of considerable interest[1–4] but their characterization has not always been unambiguous or convenient due, in part, to formation of mixtures of difficultly separable products. In the present work we have obtained crystalline derivatives of the 3-hydroxy-2-ketones (hydroxycamphors) and 2-hydroxy-3-ketones (hydroxyepicamphors) as well as six of the eight possible 2- or 3-*p*-methylbenzyl-2,3-dihydroxybornanes. In addition, exclusive reaction of a Grignard reagent from the *exo* side of the bornanone system, to our knowledge the first such example, has been observed.

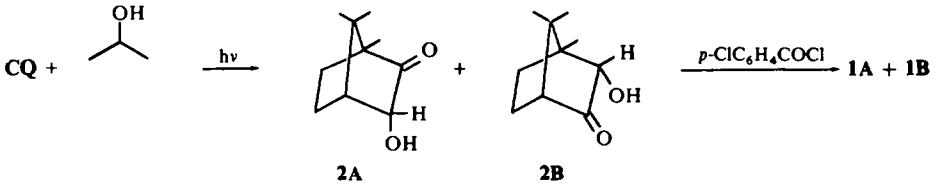
Irradiation[5] of CQ and *p*-chlorobenzaldehyde in benzene solution at wavelengths above 390 nm produced, in high yield, a 1:1 mixture of ketoesters which could be separated by chromatography on Florisil into crystalline 3-*endo*-hydroxy-2-bornanone *p*-chlorobenzoate (**1A**) and 2-*endo*-hydroxy-3-bornanone *p*-chlorobenzoate (**1B**).*



CQ **1A** **1B**

* Compounds in which the functionality and stereochemistry of C-2 and C-3 are interchanged have been designated by the same numeral followed by A or B. The A series refers to compounds in which the ester function or benzyl group is at C-3.

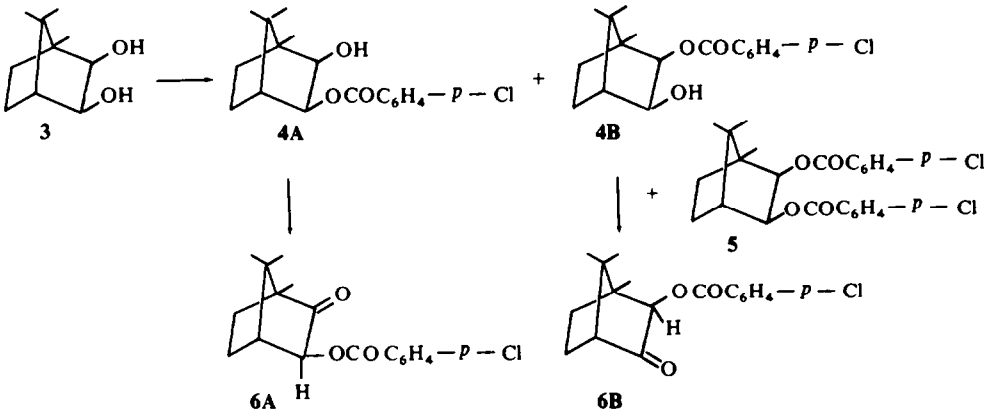
Identical products were obtained by esterification of the mixture of hydroxyketones (**2A**, **2B**) formed *via* photoreduction[3,4] of **CQ** in 2-propanol solution showing



2A **2B**

that both photoreactions lead to the same stereochemical outcome. The *endo*-configurations were consistent with the spectroscopic properties (*vide infra*) of **1A** and **1B** and were confirmed as follows.

The major product of LAH reduction of **CQ** has been shown[2,6] to be 2,3-*cis*, *exo*-bornanediol (**3**). Esterification of **3** with *p*-chlorobenzoyl chloride in pyridine for 15 min at room temperature followed by chromatographic separation afforded the 3-*p*-chlorobenzoate (**4A**) and the 2-*p*-chlorobenzoate (**4B**) in addition to a small amount of the diester **5**.* Oxidation of each isomer separately gave the crystalline *exo*-ketoesters **6A** and **6B** which were clearly different from the products (**1A**, **1B**) of the photochemical reaction.

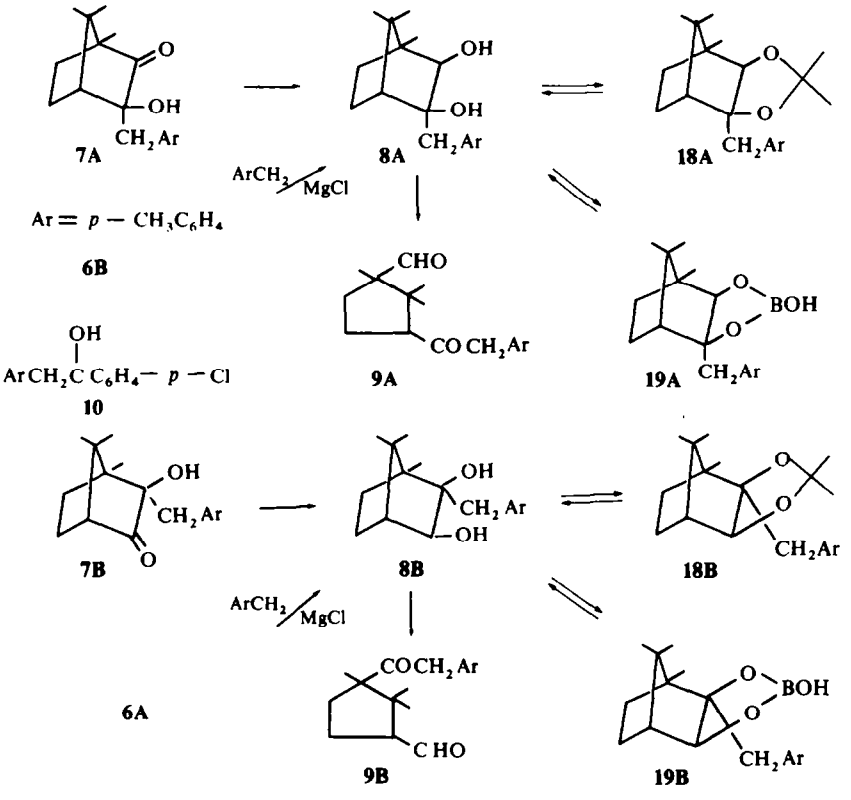


It should be noted that well-defined, crystalline derivatives of all four hydroxyketones are now available. Position isomers could be resolved by gas chromatography using XE-60 columns; the 3-*p*-chlorobenzoates being eluted first. Epimers, however, were not resolved.

The *exo*-ketoesters **6A** and **6B** could be interrelated with compounds obtained earlier in our investigation[8] of the photochemical reaction of **CQ** with *p*-xylene. It

* Previous workers[1,2,7] have reported that esterification of **3** with *p*-nitrobenzoyl chloride in pyridine for 72 hr gave a single monoester (the C-3 ester). It has also been reported[1] that reduction of 2-*exo*-hydroxy-3-bornanone *p*-nitrobenzoate gave a product identical with that reported earlier. However, it was noted that the NMR spectrum was most easily interpreted as that of a mixture of equal amounts of the two possible esters. In view of the results obtained in the present work, it appears most probable that the supposedly pure mono-*p*-nitrobenzoate is, in fact, a mixture.

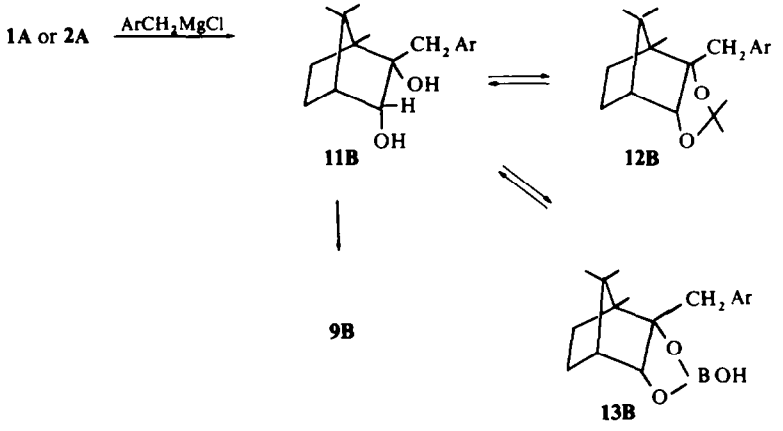
was shown that photoaddition of **CQ** and *p*-xylene or addition of *p*-methylbenzyl magnesium chloride to **CQ** gave the isomeric hydroxyketones **7A** and **7B** whose stereochemistry was assigned on the basis of the well-known preference for *endo* attack of Grignard reagents in the bornane series. Sodium borohydride reduction of



7A and **7B** afforded 2,3-*cis*, *exo*-dihydroxy-3-*endo*-(*p*-methylbenzyl)bornane (**8A**) and the 2-*endo*-(*p*-methylbenzyl) isomer (**8B**), each of which underwent facile cleavage with periodate to ketoaldehydes **9A** or **9B**. The *cis*-configuration of **8A** and **8B** were confirmed in the present work by formation of acetonides (**18A**, **18B**) and borate esters (**19A**, **19B**) from which the diols were regenerated by hydrolysis. As anticipated, reaction of the *exo*-ketoesters **6A** and **6B** with *p*-methylbenzyl magnesium chloride resulted in cleavage of the ester function and *endo* addition to the keto group affording the *cis*-diol **8B** from **6A** and the *cis*-diol **8A** from **6B**, both in nearly quantitative yield. In addition, *p*-chlorophenyl bis-*p*-methylbenzyl carbinol (**10**) was obtained; its structure was assigned on the basis of spectral data (Experimental). This interrelationship of the two series of compounds provides further confirmation for the structures assigned independently in each.

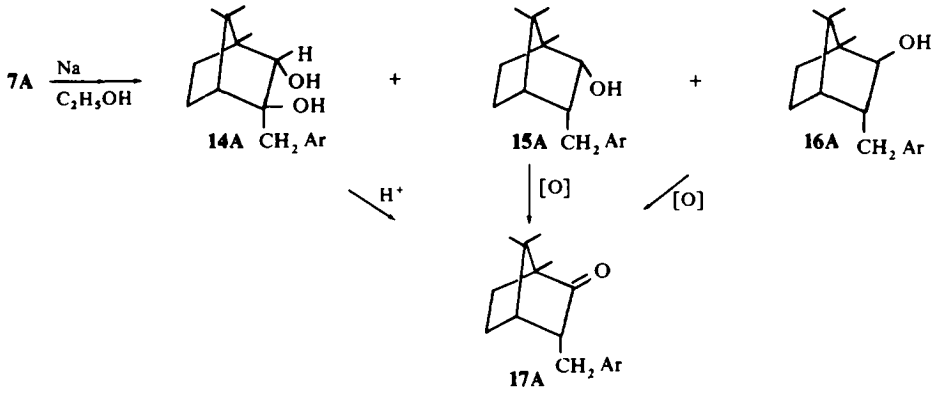
Grignard reaction of the *endo*-ketoesters **1A** and **1B** from the photoreaction of **CQ** was expected to proceed in a manner analogous to that observed with **6A** and **6B** to give *trans*-isomers of **8A** and **8B** in which the secondary OH group would have the *endo*-configuration. In fact, **1A** afforded a crystalline diol, **11B**, and **1B** a

crystalline diol, **11A**, both in 95% yield. Periodate cleavage of **11A** or **11B** afforded the same ketoaldehydes, **9A** or **9B**, obtained previously showing the epimeric relationship of **11A** and **8A** and of **11B** to **8B**. The mild conditions required for the quantitative periodate reaction (2 hr, room temp) were, however, not consistent with a *trans*-diol structure. Proof that **11A** and **11B** were, in fact, *cis*-diols, was obtained by formation of acetonides (**12A**, **12B**) and borate esters (**13A**, **13B**) from which **11A** or **11B** could be regenerated by hydrolysis. It then follows that **11A** must be 2,3-*cis*, *endo*-dihydroxy-3-*exo*-(*p*-methylbenzyl)bornane and **11B** is 2,3-*cis*, *endo*-dihydroxy-2-*exo*-(*p*-methylbenzyl)bornane formed by *attack of the Grignard reagent from the* exo *side of the bornane system.*



The reasons for these unexpected results are not clear at present. It seems probable that the first step in the Grignard reaction involves cleavage of the ester function since reaction of **1A** with a limited quantity of reagent gave unreacted starting material and equivalent amounts of the hydroxyketone **2B** and the carbinal **10**. Grignard reaction of a mixture of *endo*-hydroxyketones **2A** and **2B** also proceeded *via exo* attack and yielded **11A** and **11B**. Unexplained stereospecifity has been observed in Grignard reactions of a few open-chain α-hydroxyketones[9, 10, 14] and α-diketones[11, 14] and the results observed in the present work may reflect steric effects or coordination by magnesium in the solvated magnesium halide salts of **2A** and **2B** which may be intermediates in these reactions, This question is being investigated further.

In order to confirm the *cis*-configuration of the diols **11A** and **11B**, it appeared desirable to obtain *trans*-diols in this system and to establish that the usual criteria (facile periodate cleavage, acetonide and borate ester formation) for distinguishing between *cis* and *trans* isomers were valid. This could be achieved by reduction of the hydroxyketone **7A** with sodium in ethanol which yielded the desired 2-*endo*-3-*exo*-dihydroxy-3-*endo*-(*p*-methylbenzyl)bornane (**14A**) in addition to 2-*endo*-hydroxy- and 2-*exo*-hydroxy-3-*endo*-(*p*-methylbenzyl)-bornane (**15A**, **16A**) and traces of 3-*endo*-(*p*-methylbenzyl)-2-bornanone (**17A**). Both **15A** and **16A** were oxidized to **17A**. The *trans*-diol **14A** differed markedly in its properties from the *cis*-diols described above. It failed to react with sodium periodate even after four days in contrast to the two hours required for complete reaction of *cis*-diols and also failed to form a borate



ester. Attempted formation of an acetonide by reaction with perchloric acid in acetone resulted in conversion to the ketone **17A**. Since **17A** was obtained under the strongly alkaline conditions of the sodium, ethanol reduction as well as from the alcohols **15A** and **16A**, it is assumed to have the more stable *endo*-*p*-methylbenzyl configuration. The acid-catalyzed rearrangement of **14A** presumably, then, involves formation of the tertiary carbonium ion at C-3, followed by a 1,2-shift of the 2-*exo*-hydrogen in a manner analogous to that proposed[11] for the reaction of 2,3-*cis*, *exo*-dihydroxy-3-*endo*-phenylbornane.

Sodium in ethanol reduction of **7B** proceeded completely analogously to furnish the *trans*-diol **14B**, which showed the same type of behaviour as **14A**. The mono-alcohols **15B** and **16B** as well as the ketone **17B** were also obtained.

The chemical interrelationships of the compounds obtained in this work provide assignments of structure and stereochemistry which are internally consistent. Accepting the generalization that LAH reductions in the bornane system lead to *exo*-alcohols then allows definitive assignment of stereochemistry. These assignments were further supported by the spectroscopic properties of the various compounds as reported in the Experimental.

The nmr signals due to C-2 and C-3 protons were of particular value in assignment of structure. Anet[6] has shown, and numerous other workers[13] have confirmed, that these protons exhibit characteristic splitting patterns which depend on their position and configuration. In addition to vicinal couplings which fit the Karplus relationship, a 2-*exo* proton shows long range coupling with a 6-*exo* proton which results in broadening of the signal as compared to the signal of a 2-*endo* proton. In addition to long-range coupling (with C-5 proton), a 3-*exo* proton shows vicinal coupling (J = 4–5 Hz) with the C-4 proton while the 3-*endo* proton shows neither vicinal nor long-range coupling. Further, when both *endo* and *exo* epimers are available, the chemical shift of the *endo* proton is usually at higher field than the *exo* proton. The results obtained in the present work are summarized in the Table and are in complete agreement with the structures assigned on the basis of chemical evidence. Thus, for example, the *endo*-ketoester **1A** exhibits a doublet at τ 4·64 (J = 5 Hz) due to the 3-*exo* proton while the epimer **6A** shows a sharp singlet at τ 5·11.

An unexpected effect was observed in the spectrum of the acetonide of the 2-*endo*-(*p*-methylbenzyl)-*cis*, *exo*-diol **18B** where a three-proton singlet appeared at τ 9·63,

the region usually associated with protons of cyclopropane rings. The shift to higher field was not observed in the spectra of the isomeric acetonides **12A**, **12B** and **18A**. Examination of models shows that the benzyl group in **18B** is severely constrained so that the C-1 Me group lies above the plane of the aromatic ring and is therefore shielded because of the ring current effect. The methyl signals in most of the bornane derivatives obtained in this work were observed in the region τ 8·8–9·2.

TABLE 1. CHEMICAL SHIFTS AND COUPLING CONSTANT OR LINE WIDTHS OF C-2 AND C-3 PROTONS

Structural features	Compound	C-2 proton	C-3 proton
Ketoester	**1A**	—	*exo*, τ 4·64 (d, J = 5)
	1B	*exo*, 4·61 ($W_{\frac{1}{2}}$ = 3)	—
	6A	—	*endo*, 5·11 ($W_{\frac{1}{2}}$ = 1·5)
	6B	*endo*, 4·99 ($W_{\frac{1}{2}}$ = 1·5)	—
Diester	**5**	*endo*, 4·91 ($W_{\frac{1}{2}}$ = 1·5)	*endo*, 4·91 ($W_{\frac{1}{2}}$ = 5)
Hydroxyester	**4A**	*endo*, 6·20 (d, $J_{2,3}$ = 7[a]	*endo*, 5·30 (d, $J_{2,3}$ = 7)
	4B	*endo*, 5·45 (d, $J_{2,3}$ = 7)	*endo*, 6·04 (d, $J_{2,3}$ = 7)
p-Methylbenzyl, diol	**8A**	*endo*, 6·64 ($W_{\frac{1}{2}}$ = 2)	—
	8B	—	*endo*, 6·27 ($W_{\frac{1}{2}}$ = 2·5)[a]
	11A	*exo*, 6·38 ($W_{\frac{1}{2}}$ = 3·5)	—
	11B	—	*exo*, 5·99 (d, J = 4)[a]
	14A	*exo*, 6·00 ($W_{\frac{1}{2}}$ = 3·5)	—
	14B	—	*exo*, 5·70 (d, J = 5·5)[a]
p-Methylbenzyl, Acetonide	**18A**	*endo*, 6·36 ($W_{\frac{1}{2}}$ = 0·5)	—
	18B	—	*endo*, 6·14 ($W_{\frac{1}{2}}$ = 2)
	12A	*exo*, 5·74 ($W_{\frac{1}{2}}$ = 3)	—
	12B	—	*exo*, 5·29 (d, J = 5)
p-Methylbenzyl, Borate ester	**19A**	*endo*, 6·20 ($W_{\frac{1}{2}}$ = 1·5)	—
	19B	—	*endo*, 5·96 ($W_{\frac{1}{2}}$ = 1·5)
	13A	*exo*, 5·95 ($W_{\frac{1}{2}}$ = 2·5)	—
	13B	—	*exo*, 5·66 (d, J = 4·5)
Hydroxy, *p*-Methyl–benzyl	**15A**	*exo*, 6·05 (d, $J_{2,3}$ = 7)	*exo*, mult.
	15B	*exo*, mult.	*exo*, 5·64 ($J_{2,3} = J_{3,4}$ = 4·5)
	16A	*endo*, 6·82 (d, $J_{2,3}$ = 3·5)	*exo*, mult.
	16B	*exo*, mult.	*endo*, 6·55 (d, $J_{2,3}$ = 3·5)

[a] After exchange with deuterium oxide.

EXPERIMENTAL

Racemic camphorquinone was used; accordingly, all products were racemic mixtures. IR spectra were determined in KBr pellets except where noted otherwise. NMR spectra were determined at 60 MHz using TMS as internal standard.

Photoirradiation of camphorquinone and p-*chlorobenzaldehyde*

3-endo-*Hydroxy*-2-*bornanone* p-*chlorobenzoate* (**1A**) *and* 2-endo-*hydroxy*-3-*bornanone* p-*chlorobenzoate* (**1B**). A soln of camphorquinone (1·40 g) and freshly distilled *p*-chlorobenzaldehyde (2·0 g) in sufficient benzene to give a total volume of 20 ml was irradiated under N_2 in a Pyrex vessel using light from a General Electric high-pressure, mercury vapor lamp (AH-6) filtered through a Corning 3-73 glass color filter (0·5% T at 391 nm, 37% T at 418 nm) until the yellow color of the dione had disappeared. GC analysis indicated two major peaks of equal intensity with retention times of 5·0 and 5·35 min (1% XE-60 on 100/120 mesh Gaschrom

Q, 220°, 33 ml N_2/min). The soln was concentrated on a water bath under reduced press and the crude residue (2·6 g) chromatographed on 100 g Florisil.

Elution with 50% and 60% benzene-hexane afforded a colorless oil (1·04 g) which crystallized spontaneously, m.p. 91–94°. The analytical sample of **1A** was obtained by crystallization from hexane, m.p. 95·5–97·5° (GC retention time 5·0 min); IR_{max} 5·72, 5·78, 6·29 μ; NMR (CCl_4), τ 2·00 (d, J = 8 Hz, 2H), 2·60 (d, J = 8, 2H), 4·64 (d, J = 5, 1H) 7·4–7·6, 8·1–8·4 (m, 5H), 8·97 and 9·05 (9H). (Found: C, 66·65; H, 6·37, M^+ 306; $C_{17}H_{19}O_3Cl$ requires: C, 66·57; H, 6·24%; M^+ 306).

Elution with 60% and 70% benzene-hexane gave an oil (0·82 g) which partly crystallized on standing. Crystallization from hexane gave material (0·22 g) m.p. 119–124°. The analytical sample of **1B**, m.p. 132–132·5° (GC retention time 5·35 min) was obtained by further crystallization from the same solvent: IR_{max} 5·71, 5·81, 6·29 μ; NMR (CCl_4), τ 1·94 (d, J = 9, 2H), 2·55 (d, J = 9, 2H), 4·61 ($W_{\frac{1}{2}}$ = 3, 1H), 7·6–8·6 (m, 5H), 8·87, 8·97. (Found: C, 66·51; H, 6·16; M^+ 306; $C_{17}H_{19}O_3Cl$ requires: C, 66·65; H, 6·37%; M^+ 306).

Elution with 10% EtOAc-benzene and pure EtOAc afforded a mixture (0·25 g) of **2A** and **2B** as shown by comparison of IR spectra and GC analysis with the mixture obtained by photoreduction of CQ in 2-propanol.

Esterification of product of photoreduction of camphorquinone in isopropyl alcohol

The crude product (1·20 g) from photoreduction of camphorquinone in isopropyl alcohol[4] was treated with *p*-chlorobenzoyl chloride (1·4 ml) in pyridine (3 ml). After the initial exothermic reaction, the soln, containing crystals of pyridine hydrochloride, was allowed to stand for 15 min and then taken up in EtOAc. After washing with HCl, Na_2CO_3 aq and water, and drying over Na_2SO_4, the soln was concentrated to give a white solid (1·97 g). Chromatography as described above afforded pure **1A** (0·30 g), a mixture of **1A** and **1B** (0·44 g), and pure **1B** (0·11 g). Identity of the pure compounds with those obtained from the reaction with *p*-chlorobenzaldehyde was established by comparison of IR spectra and by GC retention times.

Esterification of 2,3-cis, exo-*bornandiol* (3) *with* p-*chlorobenzoyl chloride*

A solution of **3** (1·71 g) in anhyd pyridine (8 ml) was treated dropwise with *p*-chlorobenzoyl chloride (1·88 g, 1·1 equiv). After 15 min standing, the soln was worked up as described to give a crystalline product (3·1 g). A portion of this (1·80 g) was chromatographed on 60 g of neutral alumina. Elution with hexane afforded **5** (0·16 g, 10%). The analytical sample of **5** was obtained by crystallization from MeOH, m 138–139°; IR_{max} 5·8, 6·28 μ; NMR (CCl_4) τ 4·91 ($W_{\frac{1}{2}}$ = 1·5, 2H), 7·9–8·6 (m, 5H), 8·68 (3H), 9·03 (3H) and 9·07 (3H); lines corresponding to two overlapping AB systems (**8H**) were observed at 428, 433, 436, 441, 457 and 464 Hz downfield from TMS. (Found: C, 64·61; H, 5·51, M^+ 446; $C_{24}H_{24}O_4Cl_2$ requires: C, 64·44; H, 5·41%; M^+ 446).

Elution with 0·5 and 1% EtOAc in hexane gave a solid (0·45 g) m.p. 94–105°. Crystallization from hexane gave the analytical sample of **4A**, m.p. 104·5–105·5°; IR_{max} 2·88, 5·90 6·28 μ; NMR ($CDCl_3$) τ 2·15 (d, J = 8·5, 2H), 2·69 (d, J = 8·5, 2H **Q**, 5·30 (d, J = 7, (1H), 6·2 (broad, 1H), 7·5 (broad), 1H), 8·05–8·7 (m, 5H), 8·82 (3H), 9·10 (3H), 9·16 (3H); addition of D_2O resulted in the broad 6·2 resonance appearing as a doublet at 6·20 (J = 7) and disappearance of the resonance at 7·5. (Found: C, 66·12; H, 6·95, M^+ 308; $C_{17}H_{21}O_3Cl$ requires: C, 66·14; H, 6·85%; M^+ 308).

Elution with 1·5% and 10% EtOAc in hexane gave a solid (0·45 g) m.p. 128–131°. The analytical sample of **4B** was obtained by crystallization from hexane, m.p. 133·5–134·5; IR max 2·88, 5·9, 6·28 μ; NMR ($CDCl_3$) τ 2·12 (d, J = 8·5, 2H), 2·66 (d, J = 8·5, 2H), 5·45 (d, J = 7, 1H), 6 (broad, 1H), 7·46 (d, J = 4·5, 1H) 8·15–8·65 (m, 5H), 8·80 (3H, 9·07 (3H), 9·16 (3H); addition of D_2O causes disappearance of the 7·46 resonance and collapse of the broad resonance at 6 to a doublet, τ 6·00, J = 7; irradiation of the 5·45 resonance caused collapse of the doublet at 6·00 to a singlet. (Found: C, 65·98; H, 7·05; M^+ 308; $C_{17}H_{21}O_3Cl$ requires: C, 66·14; H, 6·85%; M^+ 308).

The isomers **4A** and **4B** were not separated by GC analysis on an XE-60 column. Oxidation as described below of a sample (42 mg) of the crude esterification product yielded a mixture which gave peaks corresponding to **6A** and **6B** in the ratio of 7:3.

3-exo-*Hydroxybornanone* p-*chlorobenzoate* (**6A**)

Oxidation of **4A** (0·25 g) as described below gave a crystalline product. The analytical sample of **6A** was obtained by crystallization from hexane, m.p. 131–132°; IR max 5·7, 5·8, 6·28 μ; NMR (CCl_4) τ 2·11 (d, J = 8, 2H), 2·64 (d, J = 8, 2H), 5·11 ($W_{\frac{1}{2}}$ = 1·5, 1H), 7·75–8·6 (m, 5H), 8·97 (3H), 9·05 (6H). (Found: C, 66·66; H, 6·29, M^+ 306. $C_{17}H_{19}O_3Cl$ requires: C, 66·57; H, 6·24%; M^+ 306).

The IR spectrum differed significantly from the spectra of **1A** and **1B**; mixture m.p. with **1B**, 105–111°. The GC retention time was almost identical with that of **1A**.

2-exo-*Hydroxy*-3-*bornanone* p-*chlorobenzoate* (**6B**)

A solution of **4B** (0·20 g) in 5 ml acetone was treated with 8N CrO_3 (0·25 ml). After 3 min, excess reagent was destroyed by addition of MeOH (2 ml). The reaction mixture was taken up in EtOAc, washed with water and saturated salt soln, dried over anhyd Na_2SO_4 and evaporated to dryness to give a crystalline product (0·19 g) m.p. 93·5–96·5°. The analytical sample of **6B** was obtained by crystallization from hexane, m.p. 99–100°; IR max 5·70, 5·80, 6·28 μ; NMR (CCl_4) τ 2·09 (d, J = 9, 2H), 2·64 (d, J = 9, 2H), 4·99 ($W_{\frac{1}{2}}$ = 1·5, 1H), 7·5–8·5 (m, 5H), 8·90 (3H), 9·07 and 9·08 (6H). (Found: C, 66·53; H, 6·31; M^+ 306; $C_{17}H_{19}O_3Cl$ requires: C, 66·57; H, 6·24%; M^+ 306).

The IR spectrum of **6B** was markedly different from spectra of **1A**, **1B** and **6A**; mixture m.p. with **1A**, 77–88°. The GC retention time was almost identical with that of **1B**.

Reaction of **1A** *with* p-*methylbenzyl magnesium chloride*

2,3-cis, endo-*Dihydroxy*-2-exo-(p-*methylbenzyl*) *bornane* (**11B**). A soln of **1A** (0·15 g) in anhyd ether (10 ml) was added dropwise with stirring to the Grignard reagent prepared from freshly distilled *p*-methyl-benzyl chloride (0·75 g) and Mg (0·13 g) in anhyd ether (2 ml) under N_2. After 2·5 hr stirring at room temp, cold dil H_2SO_4aq was added, the soln diluted with EtOAc, washed with Na_2CO_3aq and salt soln, dried and concentrated to give a crystalline product mixture (0·36 g) which was chromatographed on 14 g Florisil.

Elution with hexane afforded 1,2-di-(*p*-tolyl)ethane (88 mg). Elution with 30% benzene-hexane afforded **10** (160 mg) which crystallized on standing. Two crystallizations from hexane gave the analytical sample (90 mg), m.p. 83·5–84·5; IR max 3·0 μ; NMR (CCl_4) τ 2·88 (4H), 3·16 (d, J = 8·5, 4H), and 3·22 (d, J = 8·5, 4H), and 3·22 (d, J = 8·5, 4H), 6·93 (d, J = 14, 2H), 7·09 (d, J = 14, 2H), 7·8 (6H), 8·14 (1H, disappeared upon addition of D_2O. (Found: C, 78·69; H, 6·68. $C_{23}H_{23}ClO$ requires: C, 78·72; H, 6·61%. No molecular peak in mass spectrum).

Elution with pure benzene gave **11B** (122 mg, 91%) as white crystals, m.p. 167–169°. The analytical sample of **11B**, m.p. 171·5–172°, was obtained by crystallization from hexane; IR max 3·1 μ; NMR ($CDCl_3$) τ 2·85 (d, J = 8·5, 2H), 2·90 (d, J = 8·5, 2H), 5·99 (broadened triplet, J = 4·5, 1H), 6·94 ($W_{\frac{1}{2}}$ = 1·2, 1H), 7·25 ($W_{\frac{1}{2}}$ = 3, 2H), 7·72 (3H), 7·8–8·8 (m, 6H including 8·43, d, J = 5·5 1H), 8·91 (3H), 9·07 and 9·08 (6H). Addition of D_2O caused disappearance of the resonances at 6·94 and 8·43; the broad triplet at 5·99 was converted to a doublet (J = 4). (Found: C, 78·49; H, 9·47; M^+ 274. $C_{18}H_{26}O_2$ Requires: C, 78·79; H, 9·55%; M^+ 274).

The acetonide (**12B**, 88 mg from 83 mg of **11B**), prepared as described below, was obtained as a solid, m.p. 63–64°, after sublimation at 130°, 0·05 mm; IR max 9·4, 9·65 μ; NMR ($CDCl_3$) τ 2·77 (4H), 7·70 (3H), 7·8–9·0 (m, 5H), 8·45 (3H), 8·85 (3H), 9·05 and 9·10 (6H), 9·20 (3H).

The borate ester (**13B**, 50 mg from 50 mg of **11B**), prepared by procedure A below, was obtained as a solid, m.p. 145–154°. Crystallization from hexane gave material m.p. 149–155° which resolidified and then showed m.p. 177–179°; IR max (CH_2Cl_2) 2·8, 3·05, 6·8 μ; NMR ($CDCl_3$) τ 2·90 (4H), 4·61 (1H, disappeared upon addition of deuterium oxide), 5·66 (m, 1H, converted to a doublet, J = 4·5 upon addition of deuterium oxide), 7·12 (d, J = 15, 1H), 7·25 (d, J = 15, 1H), 7·70 (3H), 6·8–8·85 (m, 5H), 8·90 (3H), 9·02 (6H); M^+ 300.

Reaction of **1A** with 1·1 equivs of Grignard reagent afforded a mixture which contained equal amounts of **2A** and **10** in addition to unreacted starting material by GC analysis. No ether compounds were observed.

2,3-cis, endo-*Dihydroxy*-3-exo-(p-*methylbenzyl*) *bornane* **11A**

Reaction of **1B** (0·25 g) with *p*-methylbenzyl magnesium chloride and workup as described gave a thick oil (0·95 g) which was chromatographed on 25 g Florisil. Elution with hexane afforded 1,2-di-(*p*-tolyl)ethane (0·37 g) and elution with 20% benzene-hexane gave **10** (0·28 g).

Elution with 50% benzene-hexane and pure benzene afforded crystalline **11A** (0·21 g, 94%), m.p. 118–119°. The analytical sample of **11A**, m.p. 120–120·5° was obtained by crystallization from hexane; IR max 3·05 μ; NMR ($CDCl_3$) τ 2·87 (4H), 6·38 ($W_{\frac{1}{2}}$ = 3·7, 1H), 7·08 (2H), 7·70 (3H), 8·1–8·8 (m, 5H), 8·89 (3H), 9·07 (3H), 9·20 (3H). A broad absorption corresponding to about two protons was observed at 7·8–8·05 and disappeared upon addition of D_2O. (Found: C, 78·70; H, 9·73; M^+ 274. $C_{18}H_{26}O_2$ requires: C, 78·79; H, 9·55%; M^+ 274).

The acetonide (**12A**, 75 mg from 70 mg of **11A**), prepared as described, was a clear oil, IR max (liq. film)

9·4–9·6 μ; NMR ($CDCl_3$) τ 2·90 (4H), 5·74 ($W_{\frac{1}{2}}$ = 3, 1H), 6·87 (2H), 7·70 (3H), 8·0–8·9 (m, 5H), 8·46 (6H), 8·85 (3H), 9·05 and 9·10 (6H), M^+ 314.

The borate ester (**13A**, 26 mg from 24 mg of **11A**), prepared by procedure A, was obtained as a clear oil; IR max (CH_2Cl_2) 2·8–2·9, 6·7 μ; NMR ($CDCl_3$) τ 2·90 (4H), 5·95 ($W_{\frac{1}{2}}$ = 3, 1H), 6·98 (d, J = 14·5, 1H), 7·11 (d, J = 14·5, 1H), 7·70 (3H), 8·0–8·75 (m, 5H), 8·8 (1H, disappeared upon addition of D_2O), 8·90 (3H), 9·02 (3H), 9·15 (3H); M^+ 300.

2,3-cis, exo-*Dihydroxy*-2-endo-(p-*methylbenzyl*) *bornane* (**8B**)

Reaction of **6A** (0·13 g) with *p*-methylbenzyl magnesium chloride and workup afforded an oil (0·53 g) which was chromatographed on 15 g Florisil. Elution with hexane furnished 1,2-di-(*p*-tolyl)ethane (0·26 g) and with 30% benzene-hexane **10** (0·135 g). Elution with benzene gave the diol **8B** (0·11 g, 94%), m.p. 105–111°. Crystallization from hexane gave **8B**, m.p. 120·5–121°; IR spectrum identical with that of an authentic sample.[8]

The acetonide (**18B**, 41 mg from 37 mg of **8B**), prepared as described, was a crystalline solid, m.p. 100·5–101·5; IR max 9·65 μ; NMR ($CDCl_3$) τ 2·67 (d, J = 8, 2H), 2·92 (d, J = 8, 2H), 6·14 ($W_{\frac{1}{2}}$ = 2, 1H), 6·62 (d, J = 15, 1H), 7·18 (d, J = 15, 'H), 7·67 (3H), 7·9–9·1 (m, 5H), 8·37 and 8·42 (6H), 8·82 (3H), 9·23 (3H), 9·63 (3H); M^+ 314.

The borate ester* (**19B**, 12 mg from 10 mg of **8B**), obtained by procedure B, was a crystalline solid, m.p. 128–130°; IR max (CH_2Cl_2) 2·8, 3·02, 6·75 μ; NMR ($CDCl_3$) τ 2·94 (4H), 5·11 (1H, disappeared upon addition of D_2O), 5·96 ($W_{\frac{1}{2}}$ = 1·8 Hz, 1H), 7·10 (d, J = 14, 1H), 7·24 (d, J = 14, 1H), 7·70 (3H), 7·8–8·9 (m, 5H), 8·87 (3H), 9·03 and 9·10 (6H); M^+ 300.

2,3-cis, exo-*Dihydroxy*-3-endo-(p-*methylbenzyl*)*bornane* (**8A**)

Reaction of **6B** (0·125 g) with *p*-methylbenzyl magnesium chloride and work-up afforded a cloudy oil (0·41 g) which was chromatographed on 15 g Florisil. Elution with hexane gave 1,2-di-(*p*-totyl)ethane (0·11 g) and elution with 30% benzene-hexane gave **10** (0·12 g).

Elution with pure benzene afforded the diol **8A** (0·11 g, 95%). Crystallization from hexane gave material of m.p. 104–105°; the IR spectrum was identical with that of an authentic sample.

The acetonide (**18A**, 111 mg from 103 mg of **8A**) prepared as described, was obtained as a clear oil; IR max (liq. film) 9·3–9·8 μ; NMR ($CDCl_3$) τ 2·70 (d, J = 8, 2H), 2·92 (d, J = 8, 2H), 6·36 ($W_{\frac{1}{2}}$ = 1·5, 1H), 6·64 (d, J = 15, 1H), 7·18 (d, J = 15, 1H), 7·70 (3H), 8·40 (3H), 8·47 (3H), 8·70 (3H), 9·00 (3H), 9·23 (3H); M^+ 314. Hydrolysis of **18A** as described regenerated **8A** in nearly quantitative yield.

The borate ester* (**19A**, 50 mg from 47 mg of **8A**), prepared by procedure B, was obtained as a viscous oil; IR max (CH_2Cl_2) 2·8, 3·05, 6·7 μ; NMR ($CDCl_3$) τ 2·81 (d, J = 8), 2·90 (J = 8, total 4H), 5·25 (br., 1H), 6·20 ($W_{\frac{1}{2}}$ = 1·1, 1H), 7·05 (2H), 7·68 (3H), 7·9–8·9 (m, 5H), 8·85 (3H), 9·05 (3H), 9·13 (3H); the 5·25 signal disappeared upon addition of D_2O; M^+ 300.

Cleavage of diols with sodium periodate

A soln of diol (25–40 mg) in MeOH (5 ml) was treated with an aqueous soln (1·5 ml) sodium periodate (0·25 g) at room temp. After two hr, the soln, containing a mass of white needles of sodium iodate, was diluted with saturated salt soln and extracted with benzene. Drying and concentration of the benzene soln gave quantitative yield of colourless oil whose IR and NMR spectra were compared with spectra of authentic samples[8] of **9A** and **9B**.

Reaction of **11A** gave **9A**.

Reaction of **11B** gave **9B**.

The *trans*-diols **14A** and **14B** were recovered unchanged after 3 days standing with periodate.

Formation and hydrolysis of acetonides of cis*-diols*

A solution of *cis*-diol in anhydr acetone (10 ml) was treated with 70% aqueous perchloric acid (0·05 ml) at room temp. After 7 min, reaction was stopped by addition of excess solid $NaHCO_3$. In all cases GC analysis showed complete disappearance of starting diol and appearance of single new peak of shorter

* Reduction of **7A** or **7B** according to the previously reported[8] procedure afforded a single product, identical with **19A** or **19B**. Refluxing a solution of **19A** or **19B** (0·5 g) in methanol (15 ml) with 20% sodium hydroxide solution (5 ml) for 2·5 hr followed by extraction with benzene and evaporation of the benzene afforded 75–100% of **8A** or **8B**. No other products were observed.

retention time. The aceton soln was filtered, concentrated to about 2 ml and absorbed on 5 g Florisil. The acetonides were eluted with hexane.

Hydrolysis of the acetonides was achieved by heating ca. 15 mg in AcOH (1·5 ml) and water (1 ml) for 8 hr on the steam bath. In each case GC analysis showed a single product with retention time identical to that of the starting diol. The soln was taken up in EtOAc, washed, dried and concentrated. The IR spectra were identical with spectra of the starting diol in each case.

Formation of borate esters of cis*-diols*

A. *With boric acid.* A MeOH soln (3 ml) of the diol (25–50 mg) was added to a soln of boric acid (50 mg) in water (10·5 ml) containing AcOH (2 drops). After 3 hr at room temp, the soln was extracted with EtOAc which was washed with sat $NaHCO_3$ aq and sat salt soln, dried and concentrated.

B. *With sodium borohydride.* A soln of the diol (10–50 mg) in MeOH (1 ml) was treated with $NaBH_4$ (50 mg). After standing at room temp for 24 hr, AcOH (5 drops) followed by water (2 ml) was added and the soln extracted with benzene which was washed with sat $NaHCO_3$ aq, dried and concentrated. GC analysis of borate esters under conditions suitable for the corresponding diols gave no peaks whatsoever.

Reduction of 3-exo-*hydroxy*-3-endo-(p-*methylbenzyl*)-2-*bornanone* (**7A**) *with sodium in ethanol*

Sodium metal (2·0 g) was added in small portions to a soln of **7A** (0·87 g) in 60 ml EtOH. After completion of the addition, the soln was concentrated under reduced press and the residue taken up in benzene which was washed with dil H_2SO_4 aq, $NaHCO_3$ aq and water. After drying and concentration, an oil (0·84 g) was obtained. GC analysis (10′ × ⅛″ 1% XE-60 on Gaschrom Q, 170°, 30 ml N_2/min) indicated the following composition: **16A** (6·3 min, 35%), **17A** (7·0 min, 17%), **15A** (7·8 min, 8%), unreacted **7A** (14·7 min, 19%), and **14A** (24·7 min, 21%).

The crude product was chromatographed on 25 g Florisil. Elution with 25% benzene-hexane gave a mixture (0·31 g) of **15A**, **16A** and **17A**. Separation of **15A** and **16A** was achieved by preparative scale GC (5′ × ¼″ 3% XE-60 on Gaschrom Q, 180°, 120 ml helium/min). Compound **16A** was obtained as clear oil; IR max (liq. film) 2·9 μ; NMR ($CDCl_3$) τ 2·88 (4H), 6·82 (d, J = 3, 1H), 7·1–7·65 (m, 2H), 7·70 (3H), 8·45 (br. singlet, 5H), 8·97 (3H), 9·16 (6H); intensity of the broad absorption centered at 8·45 was reduced by addition of D_2O; M^+ 258.

Compound **15A** was also obtained as an oil; IR max ((liq. film) 2·9 μ; NMR ($CDCl_3$) τ 2·90 (4H), 6·05 (br. d, J = 7, 1H), 7·1–7·65 (m, 2H), 7·30 (3H), 8·2–8·5 (m, 6H), 9·12 and 9·17 (9H); addition of D_2O gave a sharp doublet at 6·05; M^+ 258.

Elution with 10% EtOAc-benzene afforded crystalline **14A** (0·12 g), m.p. 135–137°. Crystallization from hexane afforded the analytical sample of **14A**, m.p. 138–138·5°; IR max 2·95 μ; NMR ($CDCl_3$) τ 2·77 (d, J = 8, 2H), 2·90 (d, J = 8, 2H), 5·97 ($W_{\frac{1}{2}}$ = 3·5, 1H), 7·00 (d, J = 14, 1H), 7·30 (d, J = 14, 1H), 7·66 (3H), 8·25–8·8 (m, 7H), 8·90 (3H), 9·08 (3H), 9·13 (3H); addition of D_2O cause a decrease corresponding to two protons in the absorption at 8·25–8·8. (Found: C, 79·06; H, 9·33; M^+ 274. $C_{18}H_{26}O_2$ requires: C, 78·79; H, 9·55%; M^+ 274).

Attempted formation of a borate ester from **14A** resulted only in recovery of unchanged starting material.

Rechromatography (1% EtOAc–hexane) of early fractions on alkaline alumina gave pure **17A** (13 mg) as a clear oil; IR max (liq. film) 5·75 μ; NMR ($CDCl_3$) τ 2·89 (4H), 7·69 (3H), 7·9–8·9 (m, 5H), 9·03 (3H), 9·04 (3H), 9·15 (3H) and a complex pattern corresponding to three protons with lines at 145, 156, 168, 172, 185 and 197 Hz downfield from TMS. (Found: C, 84·08; H, 9·39; M^+ 256. $C_{18}H_{24}O$ requires: C, 84·32; H, 9·44%; M^+ 256).

3-endo-(p-*Methylbenzyl*)-2-*bornanone* (**17A**)

A. *From* 2-exo-*hydroxy*-3-endo-(p-*methylbenzyl*)*bornane* (**16A**). Oxidation of **16A** (65 mg) in acetone with 8N CrO_3 in H_2SO_4 soln afforded **17A** (60 mg, 93%) which was identical with the material obtained from Na–EtOH reduction of **7A** by comparison of IR and NMR spectra and identity of GC retention times.

B. *From a mixture of* **15A** *and* **16A**. A similar experiment with a 1:1 mixture of **15A** and **16A** gave **17A** in 95% yield.

C. *From* **14A**. Reaction of **14A** (44 mg) under conditions described for formation of the acetonides of *cis*-diols gave **17A** (37 mg).

Reduction of 2-exo-*hydroxy*-2-endo-(p-*methylbenzyl*)-3-*bornanone* (**7B**) *with sodium in ethanol*

Reduction of **7B** (0·68 g) in EtOH with Na as described afforded an oil (0·68 g) which was chromatographed on 25 g Florisil. Elution with 25% benzene–hexane afforded a mixture (0·26 g) of **15B**, **16B** and **17B** (by GC analysis).

Elution with 80% benzene–hexane and pure benzene gave crystalline **14B** (0·22 g). Crystallization from hexane yielded the analytical sample of **14B**, m.p. 112–112·5°; IR max 3·0 μ; NMR ($CDCl_3$) τ 2·72 (d, J = 8, 2H), 2·92 (d, J = 8, 2H), 5·7 (br. tr., J = 4·5, 1H), 7·01 (d, J = 14, 1H), 7·24 (d, J = 14, 1H), 7·70 (3H), 7·87 (d, J = 4·5, 1H), 8·15 (1H), 8–9 (m, 5H), 8·90 (3H), 9·15 (3H), 9·38 (3H); addition of D_2O caused disappearance of the lines at 7·87 and 8·15 and collapse of the 5·7 resonance to a doublet, J = 4·5. (Found: C, 79·09; H, 9·06; M^+ 274; $C_{18}H_{26}O_2$ requires: C, 78·79; H, 9·55%; M^+ 274).

Rechromatography of early fractions on Florisil afforded pure samples of **15B** and **16B**. Compound **14B** was obtained as an oil (pure by GC analysis); IR max (liq. film) 3·0 μ; NMR ($CDCl_3$) τ 2·88 (4H), 6·55 (br. d, J = 3·5, 1H), 7·1–7·6 (m, 2H), 7·70 (3H), 7·8–9·0 (m, 6H), 8·94 (3H), 9·15 (6H); addition of D_2O caused a reduction in intensity of the 7·8–9·0 multiplet and sharpening of the 6·55 doublet. Found: C, 83·72; H, 10·50; M^+ 258; $C_{18}H_{26}O$ requires: C, 83·66; H, 10·14%; M^+ 258).

Compound **15B** was obtained crystalline. Crystallization from pentane followed by sublimation at 140°, 0·05 mm afforded the analytical sample of **15B**, m.p. 63·5–64·5°; IR max (CH_2Cl_2) 2·95 μ; NMR ($CDCl_3$) τ 2·98 (4H), 5·64 (doublet of doublets, spacing of 4·5 Hz, 1H), 7·8–9·0 (m, 5H), 8·62 (1H), 9·10 (6H), 9·20 (3H); the singlet at 8·62 disappeared upon addition of D_2O. (Found: C, 83·72; H, 10·50; M^+ 258. $C_{18}H_{26}O$ requires: C, 83·66; H, 10·14%; M^+ 258).

2-endo-(p-*Methylbenzyl*)-3-*bornanone* (**17B**)

A mixture (82 mg) of **15B** and **16B** in acetone soln was oxidized as described with CrO_3 to give **17B** (18 mg, 95%) as a clear oil; IR max (liq. film) 5·75 μ; NMR ($CDCl_3$) τ 2·90 (4H), 7·71 (3H), 8–9 (m, 4H), 9·1 (6H), 9·30 (3H) and a complex pattern (4H) 124, 128, 133, 144, 153, 160, 167, 171 and 174 Hz downfield from TMS. (Found: C, 84·17; H, 9·28: M^+ 256. $C_{18}H_{24}O$ requires: C, 84·32; H, 9·44%; M^+ 256).

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