# Synthesis of α- and β-Branched Ethers from Alcohols by Reaction of Acetals with Grignard Reagents: Synthesis of Isopropyl and Isobutyl Ethers of (1*S**,2*R***S**,4*R**)-6-Methylenebicyclo[2.2.2]octan-2-ol†

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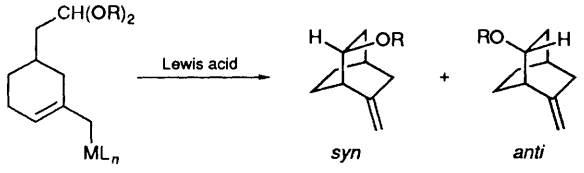
Non-symmetrical acetals have been combined with Grignard reagents in toluene at reflux to generate α- and β-branched ethers in moderate to high yields. The synthesis of isopropyl and isobutyl ethers of the bicyclic alcohol **1** was accomplished using this methodology, although reactions in the *syn*-series were complicated by the formation of tricyclic products by an intramolecular cyclisation. The scope and limitations of the ether-forming reactions were explored with a series of acetals derived from primary, secondary and tertiary alcohols. The halide component of the Grignard reagent and the solvent were found to be an important factor in facilitating these reactions.

In the context of our studies on the mechanism and origin of stereoselectivity in the reaction of acetals with allylmetal reagents we have examined the closure of a model system to a mixture of *syn* and *anti* bicyclic ethers, Scheme 1.[1] A critical

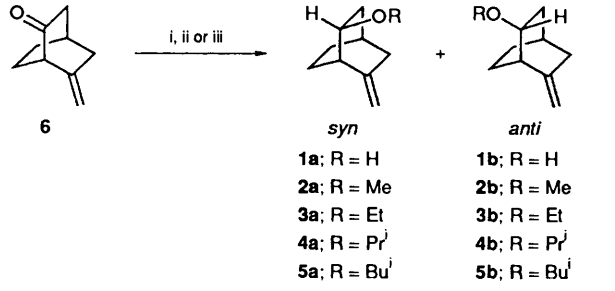



**Scheme 1**

component of these studies was the dependence of the *syn*:*anti* ratio on the nature of the acetal group R. Thus, the assignment of configuration of the products for R = Me, Et, Pr$^i$ and Bu$^i$ necessitated the synthesis of authentic samples in stereochemically pure form. This paper describes the preparation and characterization of these compounds. Specifically, we found that the hindered α- and β-branched ethers could not be synthesized directly. We have, therefore, investigated an alternative method for their preparation that involves the reaction of acetals with Grignard reagents. The reaction of acetals with Grignard reagents usually requires temperatures in excess of 100 °C and has rarely been used as a synthetic method.[2] Recently, however, Lewis acids have been employed to promote the reaction at lower temperatures.[3] We describe herein the successful application of this little-used method for the synthesis of the target compounds and a brief survey of the scope of this reaction for the synthesis of hindered ethers.

## Results

The synthesis of the bicyclic ethers **2**–**5** was designed to proceed *via* the known bicyclic alcohols **1a** and **1b**, which in turn were readily prepared by sodium borohydride reduction of the ketone **6**,[4] Scheme 2. The alcohols were isolated as a 2:1 mixture of diastereoisomers; the major isomer had the (1*S**,2*S**) configuration (designated *syn*), and the minor isomer had the (1*S**,1*R**) configuration (designated *anti*).[4] The mixture of alcohols could be separated into the constituent isomers by radial chromatography, facilitating the assignment

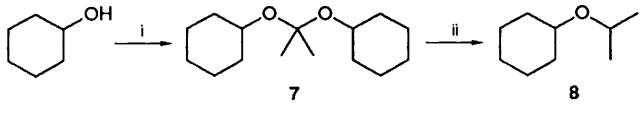



**Scheme 2** *Reagents* (*yields*): i, $NaBH_4$–EtOH (95%); ii, NaH–MeI–THF (89%); iii, KH–EtI–THF (75%)

of stereochemical configuration to derivatives of the pure isomers. For synthetic expediency, however, subsequent preparative experiments often employed the initial 2:1 mixture of alcohols.

The synthesis of simple linear ethers was straightforward, Scheme 2. Generation of the sodium alkoxide of the alcohols **1** with sodium hydride in tetrahydrofuran followed by alkylation with iodomethane, yielded the methyl ethers **2** uneventfully. Synthesis of the ethyl ethers **3** required the more potent potassium alkoxide of **1** for an efficient alkylation with iodoethane in tetrahydrofuran. The synthesis of α- or β-branched ethers proved more difficult. Attempted alkylation of either the sodium or potassium alkoxides of **1** with 2-iodopropane resulted in the formation of propene and recovery of the alcohol **1**. Use of a large excess of potassium hydride (fiftyfold) with dimethylformamide as the solvent gave identical results. Alkylation of 1-iodo-2-methyl-propane also failed, yielding isobutylene and recovered alcohol **1**.

A survey of the literature revealed a lack of general methods for the synthesis of α- or β-branched ethers from the corresponding alcohols.[5] One report described the conversion of cyclohexanol into its isopropyl ether **8** by the hydrogenation of the symmetrical acetone ketal **7** in an acidic medium,[6] Scheme 3. We attempted to employ a milder variant of this




**Scheme 3** *Reagents* (*yields*): i, $Me_2CO$; ii, Rh–$Al_2O_3$ $H_2$–HCl (60%)

reaction, since experience had shown that the bicyclic alcohols **1** were prone to undergo skeletal rearrangement in the presence of protic acids.[4] The non-symmetrical acetal **9** was obtained in

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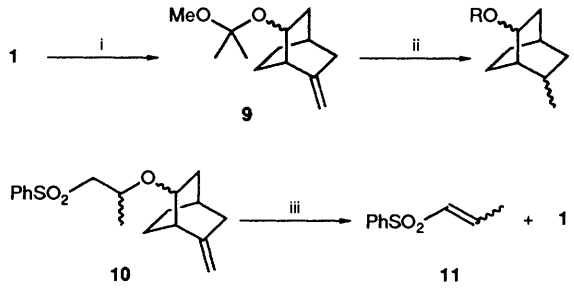
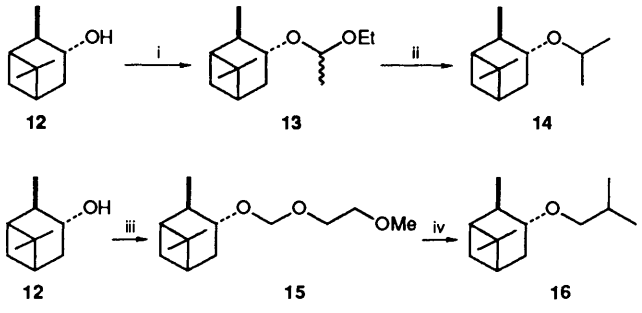
high yield by the reaction of alcohol **1** with 2-methoxypropene, Scheme 4. The reduction of aliphatic acetals to the



**Scheme 4** *Reagents:* i, 2-Methoxypropene–TsOH; ii, $Et_3SiH$–$Me_3Si$-OTf or $BF_3$·$OEt_2$; iii, 5% Na(Hg)–$Na_2HPO_4$

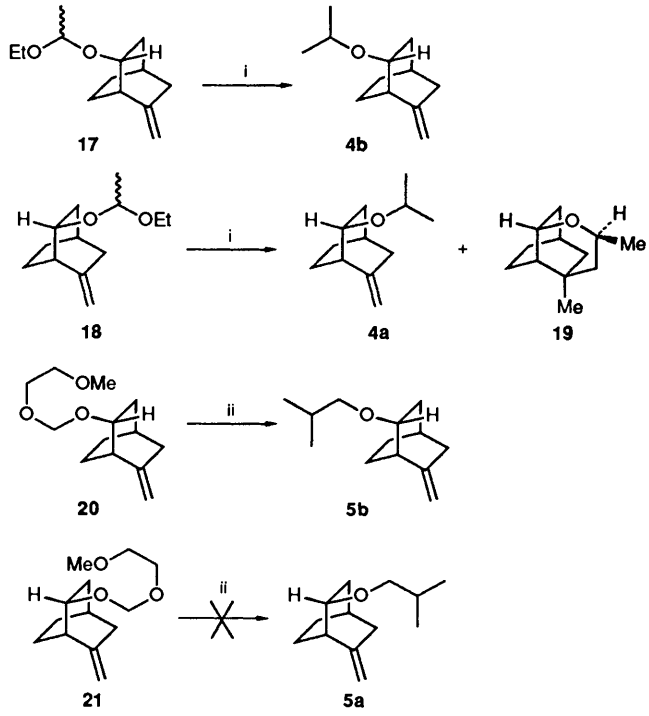
corresponding ethers has been reported by Noyori[7] using a hydride source in combination with mild Lewis-acid catalysis. Unfortunately, in our hands, the reduction of the acetal **9** using a silane Lewis-acid system gave only material in which the exocyclic double bond was absent. A similar result was obtained with the reduction of the phenyl sulphone **10** by Raney nickel. Sodium amalgam reduction of **10** yielded recovered **1** and the vinyl sulphone **11**, the product of β-elimination. We concluded that the presence of the exocyclic double bond in **1** precluded the use of reductive methods for the preparation of the ethers.

Since we were able to produce acetals from the bicyclic alcohol **1** in high yield, we postulated that their reaction with an organometallic reagent might yield the elusive ethers. We chose the hindered secondary alcohol pinan-3-ol **12** as a model substrate to investigate the synthesis of ethers by this route, Scheme 5. Reaction of **12** with ethyl vinyl ether gave the mixed



**Scheme 5** *Reagents* (*yields*): i, Ethyl vinyl ether–TsOH; ii, MeMgBr (3 equiv.)–toluene, reflux (54%); iii, MEMCl–Hunig's base–$CH_2Cl_2$ (86%); iv, $Pr^iMgBr$ (3 equiv.)–toluene, reflux or $Pr^iMgCl$ (3 equiv.)–$ZnBr_2$–toluene, reflux (67%)

acetal **13**. Without purification, the acetal was treated with an excess of methylmagnesium bromide. No reaction was observed in either diethyl ether or tetrahydrofuran at reflux; however, in toluene at reflux a rapid reaction occurred to yield the isopropyl ether **14**. Varying the reaction conditions revealed that 3 equiv. of commercial methylmagnesium bromide (Aldrich; 3.0 mol $dm^{-3}$ in diethyl ether) was the optimum nucleophile. The non-polar ether **14** was readily purified by column chromatography to remove traces of the starting alcohol **12**. Synthesis of isobutyl ether **16** required the methoxyethoxymethyl (MEM) ether **15**, which was obtained from **12** under standard conditions. Isopropylmagnesium bromide, generated as a 2.5 mol $dm^{-3}$ solution in diethyl ether from 2-bromopropane and magnesium, reacted with **15** in toluene at reflux to give the isobutyl ether **16**. Commercial isopropyl magnesium chloride (Aldrich; 2.0 mol $dm^{-3}$ in diethyl ether) failed to react with the acetal **15** unless zinc bromide was added to assist the displacement reaction.

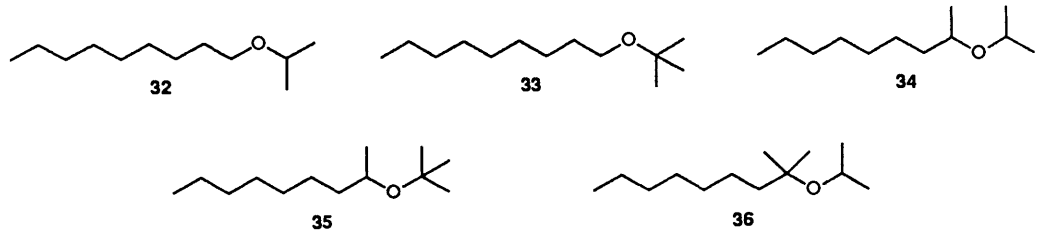


**Scheme 6** *Reagents:* i, MeMgBr (3 equiv.)–toluene, reflux; ii, $Pr^iMgBr$ (3 equiv.)–toluene, reflux or $Pr^iMgCl$ (3 equiv.)–$ZnBr_2$–toluene, reflux

The synthesis of the bicyclic ethers **4** and **5** was then attempted, Scheme 6. The reaction of methylmagnesium bromide with the crude acetal **17**, generated from the *anti*-alcohol **1b** and ethyl vinyl ether, gave the *anti*-isopropyl ether **4b** in high yield. Reaction of the corresponding *syn*-acetal **18** with methylmagnesium bromide gave the *syn*-isopropyl ether **4a**. A by-product was isolated from this reaction that lacked the characteristic exocyclic double bond and was assigned the tricyclic structure **19** based on its $^1H$ and $^{13}C$ NMR data. It is noteworthy that **19** was formed as a single stereoisomer (see the Discussion). Reaction of isopropylmagnesium bromide with the *anti*-MEM ether **20** gave the *anti*-isobutyl ether **5b** in high yield. However, the *syn*-MEM ether **21** yielded none of the desired ether **5a**, only products that lacked the exocyclic double bond could be isolated from the reaction mixture.

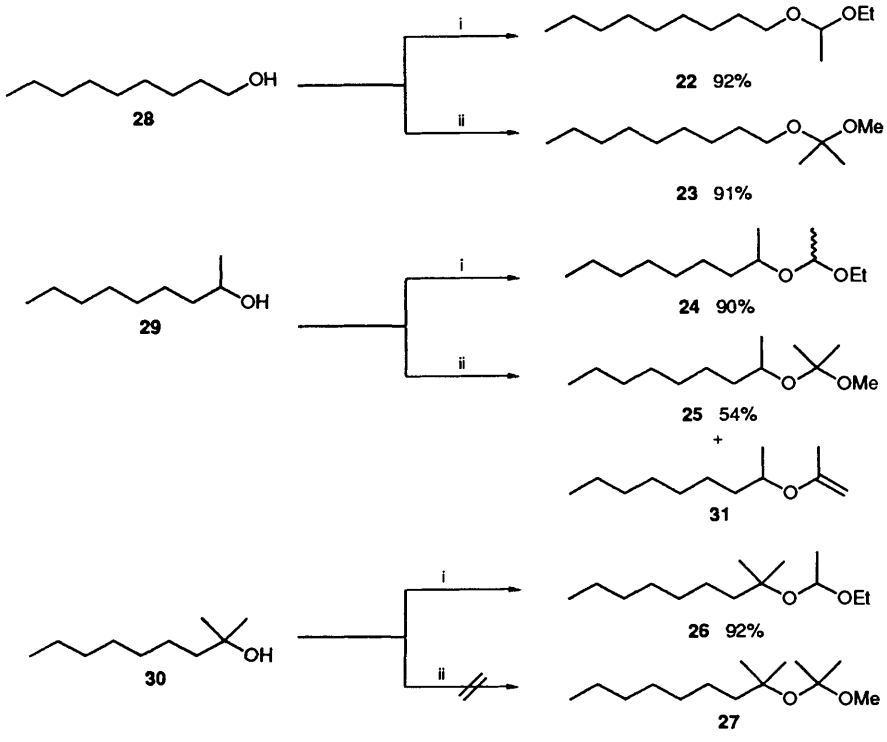
A series of isopropyl and *tert*-butyl ethers was then examined to explore the scope and limitations of the ether-forming reaction. The synthesis of the substrate acetals **22**–**27** was carried out by acid-catalysed condensation of the alcohols **28**–**30** with either 2-methoxypropene or ethyl vinyl ether, Scheme 7. The acetals **22**, **24** and **26** each derived from the appropriate alcohol and ethyl vinyl ether were obtained in excellent yields (≥90%) after chromatography on basic alumina followed by Kugelrohr distillation. Unfortunately, consistently high yields were not observed in the synthesis of acetals from condensation of alcohols **28**–**30** with 2-methoxypropene. Only the acetal **23**, derived from nonan-1-ol, was isolated in good yield (91%). Isolation of the acetal **25** was plagued by subsequent loss of methanol under the reaction conditions providing the enol ether **31** as a by-product. The synthesis of the acetal **27** could not be accomplished most probably because of instability under the reaction conditions. The reaction of these acetals, **22**–**26**, with methylmagnesium bromide (3 equiv.) was carried out in refluxing toluene solution. Conversion of acetals into mixtures of ethers and alcohols could be easily monitored by TLC and generally took 1–3 h. The yields of the products obtained after work-up and chromatographic purification are summarized in Table 1. In each case studied, the mass recovery was >75%,

**Table 1** Reactions of methylmagnesium bromide with acetals **22–26**[a]




| Entry | Acetal | Ether (% yield)[b] | Alcohol (% yield)[b] | Ether:Alcohol[c] |
|---|---|---|---|---|
| 1 | **22** | **32** (57) | **28** (25) | 2.3:1 |
| 2 | **23** | **33** (72) | **28** (8) | 9.0:1 |
| 3 | **24** | **34** (73) | **29** (3) | 24:1 |
| 4 | **25** | **35** (53) | **29** (35) | 1.5:1 |
| 5 | **26** | **36** (89) | **30** (6) | 15:1 |

[a] Reactions were performed on a 0.5 g scale of acetal in toluene (30 $cm^3$). [b] Yields reported are on an average of 2–3 runs and are based on recovery of ethers and alcohols after chromatography. [c] mol % of ether:mol % alcohol.

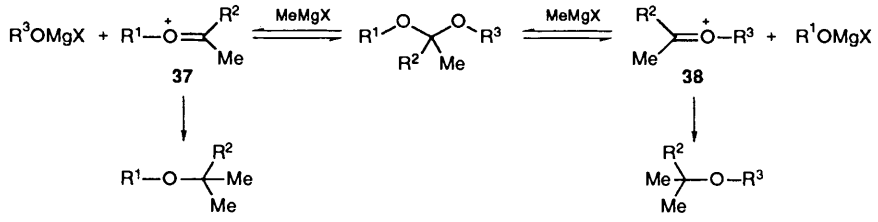



**Scheme 7** *Reagents:* i, Ethyl vinyl ether–TsOH; ii, 2-methoxypropene–TsOH

however structural variation of the acetal resulted in different ratios of isolated products. For example, the yields of ethers **32**, **34** and **36** from acetals **22**, **24** and **26** (entries 1, 3 and 5) increased from 57 to 89% as a function of increased α-branching on the parent alcohol. If the ether:alcohol ratio of 2.3:1 in entry 1 is interpreted as the selectivity for cleavage of an ethoxy compared with a nonyloxy group, then the ratio of 7.6:1 in entry 2 corresponds to the corresponding comparison for a methoxy compared with a nonyloxy group. A notable exception of this trend lies in the cleavage of the acetal **25**. However, it is possible that **25** is unstable under the reaction conditions thus providing the enol ether **31** which upon work-up is hydrolysed to the parent alcohol.

## Discussion

The choice of solvent and counter-ion was crucial to the outcome of these reactions. In the ethereal solvents diethyl ether and tetrahydrofuran, no reaction between the Grignard reagent and the acetals was observed. Furthermore, Grignard reagents formed from the corresponding alkyl chloride were inert unless the Lewis acid zinc bromide was added. In toluene, with Grignard reagents formed from the corresponding alkyl bromide, a rapid displacement of the acetal was observed to yield ethers. Clearly the solvation of the Grignard reagent and the magnesium salts by coordinating solvents suppresses their ability to react with the relatively non-basic acetals. Moreover, Westera *et al.*[8] have reported that the kinetics for the reaction of a dioxolane acetal with ethylmagnesium bromide in benzene was dependent on the basicity of ether or amine additives. It is not clear whether the organomagnesium halide itself is responsible for the activation of the acetal (see the Discussion below) or magnesium salts present in the reagent or due to the Schlenck equilibrium. Notably, studies on the solvent

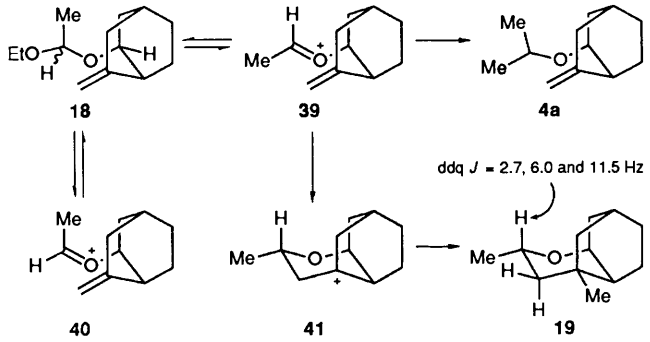



Scheme 8

dependence show that the Schlenck equilibrium shifts in favour of the organomagnesium halide in weakly coordinating solvents.[9] Our results are also consistent with the fact that magnesium bromides are more Lewis acidic than magnesium chlorides. Indeed, nearly all of the documented cases of reactions of ethers and acetals with Grignard reagents involve organomagnesium bromides.[2]

The nucleophilic displacement of acetals in the presence of Lewis acids can be explained by a continuum of mechanisms from $S_N2$-like to $S_N1$-like.[10] For the examples in Table 1, we favour an $S_N1$-like reaction with an oxocarbenium ion intermediate to explain the observed product distributions, Scheme 8. Under the reaction conditions, Lewis-acid-promoted ionization of the acetal results in the formation of two possible oxocarbenium ions **37** and **38**. One leads to the formation of the ether product the other to recovery of the parent alcohol. Since capture of the intermediates **37** and **38** is unlikely to be rate limiting, the ratio of the observed products reflects the ratio of the ions formed. In all cases the major product arose through capture of the more highly substituted, and presumably more stable, oxocarbenium ion. Even subtle differences in the stability of the ions were reflected in the product distribution. For example, in the reaction of **22** (Table 1, entry 1) a 2.3:1 ratio of ether **32** to alcohol **28** was obtained owing to the greater stability of intermediate **37** ($R^1$ = nonyl, $R^2$ = H) over intermediate **38** ($R^3$ = ethyl, $R^2$ = H). In other examples (entries 2, 3 and 5) the ratio of ether to recovered alcohol was at least 9:1, a reflection of a greater difference in energy between the respective oxocarbenium ions as the degree of substitution at $R^1$ increases from primary, **22**, to secondary, **24**, to tertiary, **26**. It is also possible that the increasing branching at $R^1$ hinders complexation by the metal cation. The anomolous results with the acetal **25** may be due, in part, to its instability under the reaction conditions.

An $S_N1$-like mechanism also accounts for the formation of tricyclic ether **19** as a by-product during the synthesis of the isopropyl ether **4a**, Scheme 9. Ionization of the diastereoisomeric mixture of acetals **18** would result in the formation of the *E*-oxocarbenium ion **39**. The *Z*-oxocarbenium ion **40** would be expected to be significantly higher in energy owing to the expected $A_{1,3}$-strain.[11] This primary intermediate can follow two pathways: (1) capture by the organometallic nucleophile to give the expected ether product **4a** and (2) cyclization onto the exocyclic double bond to form the bridgehead tertiary cation **41**. Capture of **41** by the organometallic nucleophile affords the tricyclic ether **19**. As previously noted, **19** is formed as single stereoisomer. The key methine resonance appeared as a ddq in the $^1H$ NMR spectrum which indicates an equatorial orientation of the 4-methyl group. Intramolecular capture of oxocarbenium ions to form five-,[12] six-,[13] and eight-membered[14] ring ethers has been well documented. In all of these cases however, the cyclic cation is captured by a heteroatom nucleophile (halide or alkoxide) or neutralized by the discharge of a proton or silicon electrofuge. This case is remarkable for the capture of the cyclic cation by an external carbon nucleophile.




Scheme 9

## Conclusion

We have demonstrated that, with the appropriate choice of solvent and counter-ion, acetals can function as electrophilic acceptors for Grignard reagents, and thus, a simple two-step conversion of alcohols into isopropyl, isobutyl and *tert*-butyl ethers has been developed. The reaction conditions are mild enough to permit the synthesis highly substituted α-branched ethers and a series of α- and β-branched bicyclic ethers that are unavailable by other routes.

## Experimental

*General.*—$^1H$ NMR and $^{13}C$ NMR were recorded on General Electric QE-300 (300 MHz, $^1H$; 75 MHz, $^{13}C$), General Electric GN-300NB (300 MHz, $^1H$; 75 MHz, $^{13}C$), Nicolet NT-360 (360 MHz, $^1H$; 90 MHz, $^{13}C$), or General Electric GN-500 (500 MHz, $^1H$) spectrometers in $CDCl_3$ with $CHCl_3$ as an internal reference ($^1H$, δ 7.26; $^{13}C$, δ 77.0). Resonances giving negative signals in $^{13}C$ NMR spectra using an attached proton test (APT) pulse sequence are indicated (*). Coupling constants, *J*, are given in Hz. FTIR spectra were recorded as thin films or as solutions in carbon tetrachloride on an IBM FTIR-32 spectrometer. Mass spectra were recorded on a Varian MAT CH-5 spectrometer with ionization voltages of 70 or 10 eV. Elemental combustion analyses were performed by the University of Illinois Microanalytical Service Laboratory. Column chromatography was performed with 32–63 μm silica gel (Merck). Column dimensions are indicated in the form (width × length). Radial chromatography was performed on a Harrison Research Chromatotron using silica gel plates. Analytical gas chromatography was performed on a Hewlett Packard 5890 equipped with split and on-column injectors. The columns used were either megabore HP-1 10 m methyl silicone gum or HP-20M Carbowax 20M 50 m. Retention times ($t_R$) and integrated ratios were obtained from a Hewlett Packard 3393A integrator. Bulb-to-bulb distillations were performed on a Buchi GKR-50 Kugelrohr; boiling points (b.p.) refer to air-bath temperatures and are uncorrected. Grignard reagents were titrated according to the method of Gilman.[15] Brine refers to a saturated aqueous solution of sodium chloride. Diethyl ether is abbreviated as ether. Tetrahydrofuran is abbreviated as THF. Solvents for extraction and chromatography were technical grade and distilled from the indicated drying agents: hexane

and dichloromethane (calcium chloride); ethyl acetate (potassium carbonate), ether (calcium sulphate). Solvents for recrystallization were spectroscopic grade. Toluene was distilled from calcium hydride prior to use. Commercial reagents were purified by standard procedures. (1*S**,2*S**,4*R**)-6-methylenebicyclo[2.2.2]octan-2-ol **1a** and (1*S**,2*R**,4*R**)-6-methylenebicyclo[2.2.2]octan-2-ol **1b** were prepared according to a literature procedure.[2]

(1S*,2S*,4R*)-2-*Methoxy*-6-*methylidenebicyclo*[2.2.2]*octane* **2a** *and* (1S*,2R*,4R*)-2-*Methoxy*-6-*methylenebicyclo*[2.2.2]-*octane* **2b**.—The alcohols **1** (2:1 *syn*:*anti*; 723 mg, 5.23 mmol) in THF (4.0 $cm^3$) were added dropwise to a stirred suspension of sodium hydride (251 mg, 10.5 mmol) in THF (6.0 $cm^3$). The resulting suspension was stirred at room temperature for 20 min after which iodomethane (977 $mm^3$, 15.7 mmol) was added dropwise. After an additional 40 min, the reaction mixture was poured into brine (50 $cm^3$) and extracted with ether (× 3). The organic extracts were washed with water (× 2) and brine, dried over magnesium sulphate, and concentrated to a yellow oil. Purification of the oil by radial chromatography (4 mm silica plate; 5% ether–hexane) followed by Kugelrohr distillation yielded first (1S*,2R*,4R*)-2-*methoxy*-6-*methylenebicyclo*-[2.2.2]*octane* **2b** (155 mg, 19%) as a colourless oil, b.p. 120–140 °C (air bath; 95 Torr) (Found: C, 78.9; H, 10.6. $C_{10}H_{16}O$ requires C, 78.9; H, 10.6%); $\nu_{max}$(neat)/$cm^{-1}$ 3066 w, 2976m, 2936s, 2864s, 2818m, 1653m, 1465m, 1448m, 1428m, 1364m, 1333w, 1227m, 1201m, 1130m, 1108s, 1080s, 1066m, 998m, 924m, 885m, 872m and 732m; $\delta_H$(300 MHz; $CDCl_3$) 4.82 (1 H, m, exocyclic methylene), 4.80 (1 H, dd, *J* 1.9 and 4.0, exocyclic methylene), 3.48 (1 H, dt, *J* 3.1 and 9.2, 2-H), 3.31 (3 H, s, $OCH_3$), 2.46 (1 H, dd, *J* 3.4 and 6.0, 1-H) and 2.40–1.35 (9 H, m); $\delta_C$(75 MHz; $CDCl_3$) 147.0, 108.4, 78.5*, 55.3*, 38.7*, 34.9, 34.6, 26.0*, 24.4 and 23.6; *m*/*z* (10 eV) 152 ($M^+$, 5%), 120 (81), 105 (57), 97 (39), 94 (47), 92 (100), 84 (7), 79 (46) and 44 (5). This was followed by mixed fractions (127 mg, 16%) and then (1S*,2S*,4R*)-2-*methoxy*-6-*methylenebicyclo*[2.2.2]*octane* **2a** (428 mg, 54%) as a colourless oil, b.p. 120–140 °C (air bath; 95 Torr) (Found: C, 79.1; H, 10.6. $C_{10}H_{16}O$ requires C, 78.9; H, 10.6%); $\nu_{max}$(neat)/$cm^{-1}$ 3069w, 2977m, 2931s, 2865s, 2818m, 1653m, 1465m, 1448m, 1366m, 1226w, 1204w, 1131w, 1101s, 1053w, 994w, 974w, 913w, 880s and 818w; $\delta_H$(300 MHz; $CDCl_3$) 4.86 (1 H, dd, *J* 2.0 and 4.2, exocyclic methylene), 4.74 (1 H, dd, *J* 2.0 and 4.0, exocyclic methylene), 3.46 (1 H, m, 2-H), 3.32 (3 H, s, $OCH_3$), 2.46 (1 H, dd, *J* 3.0 and 6.0, 1-H) and 2.30–1.30 (9 H, m); $\delta_C$(75 MHz; $CDCl_3$) 149.3, 107.8, 78.0*, 55.8*, 38.8*, 34.8, 34.4, 26.6*, 25.1 and 18.7; *m*/*z* (10 eV) 152 ($M^+$, 4%), 120 (79), 105 (59), 97 (35), 94 (53), 92 (100), 84 (7) and 79 (52).

(1S*,2S*,4R*)-2-*Ethoxy*-6-*methylenebicyclo*[2.2.2]*octane* **3a** *and* (1S*,2R*,4R*)-2-*Ethoxy*-6-*methylenebicyclo*[2.2.2.]*octane* **3b**.—The alcohols **1** (2:1 *syn*:*anti*; 150 mg, 1.09 mmol) in THF (1.0 $cm^3$) were added dropwise to a stirred suspension of potassium hydride (35% in mineral oil; 1.24 g, 10.9 mmol) in THF (2.0 $cm^3$). The resulting suspension was stirred at room temperature for 20 min and iodoethane (868 $mm^3$, 10.9 mmol) was added dropwise. After an additional 40 min, the reaction mixture was poured into brine (50 $cm^3$) and extracted three times with ether. The organic extracts were washed twice with water and brine, dried over magnesium sulphate, and concentrated to a yellow oil. Purification of the oil by radial chromatography (4 mm plate; 3% ether–hexane) and Kugelrohr distillation yielded first (1S*,2R*,4R*)-2-*ethoxy*-6-*methylene-bicyclo*[2.2.2]*octane* **3b** (50.6 mg, 27%) as a colourless oil, b.p. 120–125 °C (air bath; 90 Torr) (Found: C, 78.7; H, 10.6. $C_{11}H_{18}O$ requires C, 79.4; H, 10.8%); $\nu_{max}$(neat)/$cm^{-1}$ 3069w, 2976m, 2932s, 2866s, 1653m, 1445m, 1370m, 1354m, 1122m, 1102s, 1079m, 1058m and 880s; $\delta_H$(300 MHz; $CDCl_3$) 4.85 (1 H, d, *J* 2.1, exocyclic methylene), 4.73 (1 H, d, *J* 2.1, exocyclic methylene), 3.72–3.48 (3 H, m, 2-H and $OCH_2CH_3$), 2.62–1.50 (10 H, m) and 1.21 (3 H, t, *J* 7.0, $OCH_2CH_3$); $\delta_C$(90 MHz; $CDCl_3$) 149.7, 107.6, 76.1*, 63.3, 39.4*, 35.1, 34.5, 26.6*, 25.3, 19.0 and 15.6*; *m*/*z* (70 eV) 166 ($M^+$, 2%), 122 (23), 120 (100), 111 (21), 105 (55), 92 (98), 83 (18), 79 (14) and 45 (4) (Found: $M^+$, 166.136 10. $C_{11}H_{18}O$ requires *M*, 166.135 77). This was followed by (1S*,2S*,4R*)-2-*ethoxy*-6-*methylenebicyclo*[2.2.2]-*octane* **3a** (86.0 mg, 48%) as a colourless oil, b.p. 120–125 °C (air bath; 90 Torr) (Found: C, 79.0; H, 11.0. $C_{11}H_{18}O$ requires C, 79.4; H, 10.8%); $\nu_{max}$(neat)/$cm^{-1}$ 3067w, 2975m, 2932s, 2865s, 1653m, 1447m, 1370m, 1354m, 1109s, 1076m, 903w and 874m; $\delta_H$(300 MHz; $CDCl_3$) 4.83–4.77 (2 H, m, exocyclic methylene), 3.76–3.64 (2 H, m, $OCH_2CH_3$), 3.57–3.46 (1 H, m, 2-H), 2.63–1.55 (10 H, m) and 1.18 (3 H, t, *J* 7.0, $OCH_2CH_3$); $\delta_C$(90 MHz; $CDCl_3$) 147.4, 108.4, 76.8*, 62.7, 39.0*, 35.2, 35.1, 26.2*, 24.6, 23.9 and 15.4*; *m*/*z* (70 eV) 166 ($M^+$, 1%), 151 (5), 122 (21), 120 (100), 111 (24), 105 (59), 92 (99), 83 (17), 79 (15) and 45 (5) (Found: $M^+$, 166.136 30. $C_{11}H_{18}O$ requires *M*, 166.135 77).

(1S*,2R*,4R*)-2-(*Isobutoxy*)-6-*methylenebicyclo*[2.2.2]*octane* **5a**.—2-Methoxyethoxymethyl chloride (76.0 $mm^3$, 0.664 mol) was added dropwise to a solution of (1*S**,2*R**,4*R**)-6-methylenebicyclo[2.2.2]octan-2-ol **1b** (45.9 mg, 0.332 mmol) and *N*,*N*-di-(isopropyl)ethylamine (116 $mm^3$, 0.664 mmol) in dichloromethane (2.0 $cm^3$). The solution was stirred at room temperature for 3 h, quenched with water (5.0 $cm^3$) and extracted with ether (× 3). The organic extracts were washed with water (× 2) and brine, dried over magnesium sulphate, and concentrated. Purification of the residue by chromatography (2.0 × 13.5 cm; 25% ether–hexane) yielded (1S*,2R*,4R*)-2-(2-*methoxyethoxy*)*methoxy*-6-*methylenebicyclo*[2.2.2]*octane* **20** (63.9 mg, 85%) as a colourless oil, $\nu_{max}$(neat)/$cm^{-1}$ 3069w, 2928s, 1651w, 1449w, 1366w, 1132m, 1107s, 1048w, 994w, 972w, 912m, 882m, 851w and 733w; $\delta_H$(300 MHz; $CDCl_3$) 4.85 (1 H, m, exocyclic methylene), 4.76 (2 H, s, $OCH_2O$), 4.73 (1 H, m, exocyclic methylene), 3.74 (2 H, t, *J* 7.0, $OCH_2CH_2O$), 3.56 (2 H, t, *J* 7.0, $OCH_2CH_2O$), 3.22 (3 H, s, $OCH_3$) and 2.20–1.25 (11 H, m); *m*/*z* (70 eV) 150 (12%), 121 (16), 106 (60), 89 (100), 77 (28) and 59 (82).

To a solution of (1*S**,2*R**,4*R**)-2-(2-methoxyethoxy)-methoxy-6-methylenebicyclo[2.2.2]octane **20** (68.0 mg, 0.300 mmol) in toluene (2.0 $cm^3$) was added isopropylmagnesium bromide (2.5 mol $dm^{-3}$ in ether; 360 $mm^3$). The solution was heated at reflux for 15 min. A white precipitate formed during this period. The reaction mixture was cooled to room temperature, quenched with water (10 $cm^3$) and extracted with ether (× 3). The organic extracts were washed with brine, dried over magnesium sulphate, and concentrated. Purification of the residue by chromatography (1.2 × 15 cm; 5% ether–hexane) followed by Kugelrohr distillation yielded (1S*,2R*,4R*)-2-(*isobutoxy*)-6-*methylenebicyclo*[2.2.2]*octane* **5b** (47.2 mg, 81%) as a colourless oil, b.p. 150–160 °C (air bath; 30 Torr); $\nu_{max}$(neat)/$cm^{-1}$ 3069w, 2930s, 2867s, 1651m, 1466m, 1401w, 1379w, 1356m, 1296w, 1223w, 1169w, 1130m, 1098s, 1055w, 1001w, 916w, 880m, 822w, 741w and 698w; $\delta_H$(360 MHz; $CDCl_3$) 4.85 (1 H, d, *J* 2.0, exocyclic methylene), 4.74 (1 H, d, *J* 2.0, exocyclic methylene), 3.50 (1 H, m, 2-H), 3.19 (1 H, dd, *J* 8.9 and 6.9, $OCH_2$), 3.11 (1 H, dd, *J* 8.9 and 6.6, $OCH_2$), 2.43 (1 H, dd, *J* 5.8 and 2.8, 1-H), 2.25–1.30 (10 H, m), 0.88 (3 H, d, *J* 7.1, $CH_3CHCH_3$) and 0.87 (3 H, d, *J* 6.7, $CH_3CHCH_3$); $\delta_C$(90 MHz; $CDCl_3$) 149.9, 107.6, 76.3*, 75.1, 39.4*, 35.1, 34.6, 28.8*, 26.7*, 25.3, 19.5* and 19.0; *m*/*z* (70 eV) 164 (10%), 151 (21), 139 (25), 120 (70), 105 (38), 94 (85), 92 (73), 83 (26), 76 (61), 67 (18) and 57 (100) (Found: $M^+$, 194.166 09. $C_{13}H_{22}O$ requires *M*, 194.167 07).

(1S*,2R*,4R*)-2-*Isopropoxy*-6-*methylenebicycclo*[2.2.2]*octane* **4b**, (1S*,2S*,4R*)-2-*Isopropoxy*-6-*methylenebicyclo*[2.2.2]-*octane* **4a** *and* (1S*,3S*,5S*,7R*,10S*)-3,5-*Dimethyl*-2-*oxatricyclo*[5.3.1.0$^{5,10}$]*undecane* **19**.—The bicyclic alcohols **1** (2:1 *syn*:*anti*; 526 mg, 3.80 mmol) were dissolved in ethyl vinyl ether (5.0 cm$^3$) and toluene-*p*-sulphonic acid (2.0 mg) was added. The solution was stirred at room temperature for 40 min and poured into aqueous sodium hydrogen carbonate and extracted with ether (× 3). The organic extracts were washed with brine, dried over magnesium sulphate, and concentrated to a colourless oil. Purification of the oil by chromatography (3.0 × 13 cm; 10% ether–hexane) yielded the ethoxyethyl ethers **18** and **17** (2:1 *syn*:*anti*) as colourless oils (759 mg, 95%), $\nu_{max}$(neat)/cm$^{-1}$ 3067w, 2977s, 2867s, 1730s, 1655m, 1447m, 1377m, 1275m, 1127s, 1086s, 1059m, 1030s, 959m, 926m and 872m; *m*/*z* (70 eV) 210 (M$^+$, 1%), 195 (1), 181 (1), 164 (45), 121 (50), 93 (17), 79 (16) and 73 (100).

Methylmagnesium bromide (3.0 mol dm$^{-3}$ in ether, 3.56 cm$^3$) was added to a solution of the ethoxyethyl ethers **18** and **17** (2:1 *syn*:*anti*; 749 mg, 3.56 mmol) in toluene (25 cm$^3$). The solution was heated at reflux for 1 h. During this period a white precipitate formed. The reaction mixture was cooled to room temperature, quenched with water and extracted with ether (× 3). The organic extracts were washed with aqueous sodium hydrogen carbonate and brine, dried over magnesium sulphate and concentrated to a colourless oil. Purification of the oil by chromatography (3.0 × 17.5 cm; 5 to 30% ether–hexane) yielded first a 35:65 mixture of (1S*,2R*,4R*)-2-*isopropoxy*-6-*methylenebicyclo*[2.2.2]*octane* **4b** and (1S*,2S*,4R*)-2-*isopropoxy*-6-*methylenebicyclo*[2.2.2]*octane* **4a** (485 mg, 76%) followed by (1S*,3S*,5S*,7R*,10S*)-3,5-*dimethyl*-2-*oxatricyclo*-[5.3.1.0$^{5,10}$]*undecane* **19** (86.9 mg, 14%). The isopropyl ethers **4** were separated by radial chromatography (4 mm plate; 2.5% ether–hexane) followed by Kugelrohr distillation to yield first **4b** (137 mg, 21%) as a colourless oil, b.p. 120–125 °C (air bath; 60 Torr) (Found: C, 79.9; H, 11.2. $C_{12}H_{20}O$ requires C, 79.9; H, 11.2%); $\nu_{max}$(neat)/cm$^{-1}$ 3071w, 2971s, 2930s, 1651m, 1466m, 1377m, 1341m, 1325m, 1125s, 1094m, 1073s, 1034s and 880m; $\delta_H$(300 MHz; $CDCl_3$) 4.84 (1 H, d, *J* 2.0, exocyclic methylene), 4.73 (1 H, d, *J* 2.0, exocyclic methylene), 3.70–3.61 (2 H, m, 2-H and $CH_3CHCH_3$), 2.18–1.15 (10 H, m) and 1.15 (6 H, t, *J* 6.0, $CH_3CHCH_3$); $\delta_C$(75 MHz; $CDCl_3$) 149.9, 107.4, 73.1*, 68.1*, 40.2*, 35.5, 34.5, 26.7*, 25.4, 23.0*, 22.3* and 19.1; *m*/*z* (10 eV) 122 (40%), 120 (92), 105 (25), 94 (100), 92 (62), 83 (11), 79 (24) and 43 (9). This was followed by **4a** (235 mg, 36%) as a colourless oil, b.p. 120–125 °C (air bath; 60 Torr) (Found: C, 79.7; H, 11.05. $C_{12}H_{20}O$ requires C, 79.9; H, 11.2%); $\nu_{max}$(neat)/cm$^{-1}$ 3067w, 2971s, 2934s, 2865s, 1655m, 1466m, 1447m, 1377m, 1347m, 1320m, 1125s, 1100s, 1049s and 872m; $\delta_H$(300 MHz; $CDCl_3$) 4.80–4.76 (2 H, m, exocyclic methylene), 3.73–3.62 (2 H, m, 2-H and $CH_3CHCH_3$), 2.40–1.25 (10 H, m) and 1.13 (6 H, t, *J* 5.6, $CH_3CHCH_3$); $\delta_C$(75 MHz; $CDCl_3$) 147.3, 108.2, 73.9*, 67.7*, 39.5*, 35.6, 35.0, 26.2*, 24.5, 23.9, 23.1* and 21.8*; *m*/*z* (70 eV) 180 (M$^+$, 1%), 165 (1), 122 (37), 120 (100), 105 (23), 94 (92), 92 (63), 83 (12), 79 (21), 70 (3) and 43 (7).

The tricyclic ether **19** was further purified by radial chromatography (2 mm plate; 10% ether–hexane) followed by Kugelrohr distillation to yield a colourless oil (82.5 mg, 13%), b.p. 130–140 °C (air bath; 15 Torr) (Found: C, 79.5; H, 11.3. $C_{12}H_{20}O$ requires C, 79.9; H, 11.2%); $\nu_{max}$(neat)/cm$^{-1}$ 2932s, 2867s, 1474w, 1454m, 1446m, 1375m, 1174s, 1150m, 1109s, 1080m, 1044s, 1029w and 852w; $\delta_H$(500 MHz; $CDCl_3$) 3.96 (1 H, dt, *J* 3.4 and 9.2, 1-H), 3.86 (1 H, ddt, *J* 2.7, 6.0 and 11.5, 3-H), 1.87 (1 H, m), 1.76–1.64 (3 H, m), 1.58 (1 H, dd, *J* 1.2 and 12.8), 1.33–1.15 (6 H, m), 1.13 (3 H, d, *J* 6.0, 3-$CH_3$), 1.02 (1 H, t, *J* 11.5, 4-$H_{ax}$) and 0.94 (3 H, s, 5-$CH_3$); $\delta_C$(75 MHz; $CDCl_3$) 72.3*, 62.4*, 48.8, 38.9, 37.4*, 31.0, 30.1*, 28.2, 25.4*, 25.2, 22.0* and 18.8; *m*/*z* (10 eV) 180 (M$^+$, 24%), 166 (12), 165 (100), 147 (18), 121 (49), 107 (31), 105 (18), 95 (16), 94 (30), 93 (42), 91 (15), 80 (39), 77 (11), 67 (30) and 54 (19) (Found: M$^+$, 180.151 56. $C_{12}H_{20}O$ requires: *M*, 180.151 43).

(1S*,2R*,3R*)-3-(*Isopropoxy*)-2,6,6-*trimethylbicyclo*[3.1.1]-*heptane* **14**.—(1*S**,2*R**,3*R**)-2,6,6-Trimethylbicyclo[3.1.1]-heptan-3-ol **12** (211 mg, 1.37 mmol) was dissolved in ethyl vinyl ether (5.0 cm$^3$) and toluene-*p*-sulphonic acid (1.0 mg) was added. The solution was stirred at room temperature for 40 min and poured into aqueous sodium hydrogen carbonate and extracted with ether (× 3). The organic extracts were washed with brine, dried over magnesium sulphate and concentrated to yield (1*S**,2*R**,3*R**)-3-(1-ethoxyethoxy)-2,6,6-trimethylbicyclo[3.1.1]heptane **13** (311 mg, 100%) as a colourless oil. The crude ethoxyethyl ether **13** was dissolved in toluene (5.0 cm$^3$) and methylmagnesium bromide (3.0 mol dm$^{-3}$ in ether, 1.67 cm$^3$) was added. The mixture was heated at reflux for 3 h. During this period a white precipitate formed. The reaction mixture was cooled to room temperature, quenched with water (10 cm$^3$) and extracted with ether (× 3). The organic extracts were washed with aqueous sodium hydrogen carbonate solution and brine, dried over magnesium sulphate, and concentrated to a colourless oil. Purification of the oil by chromatography (2.3 × 16 cm; 5% ether–hexane) followed by Kugelrohr distillation yielded (1S*,2R*,3R*)-3-(*isopropoxy*)-2,6,6-*trimethylbicyclo*[3.1.1]*heptane* **14** (144 mg, 54%) as a colourless oil, b.p. 110–120 °C (air bath; 60 Torr) (Found: C, 79.3; H, 12.5. $C_{13}H_{24}O$ requires C, 79.5; H, 12.3%); $\nu_{max}$(neat)/cm$^{-1}$ 2971s, 2907s, 1456m, 1356m, 1325w, 1136m, 1124s, 1055s, 1022w and 951w; $\delta_H$(300 MHz; $CDCl_3$) 3.71 (1 H, m, 3-H), 3.67 (1 H, m, $CH_3CHCH_3$), 2.42 (1 H, m, 1-H), 2.34 (1 H, m, 5-H), 1.96 (2 H, m), 1.80–1.60 (3 H, m), 1.21 (3 H, s, 6-$CH_3$), 1.18 (3 H, d, *J* 6.2, $CH_3CHCH_3$), 1.15 (3 H, d, *J* 6.2, $CH_3CHCH_3$), 1.09 (3 H, d, *J* 6.6, 2-$CH_3$) and 0.93 (3 H, s, 6-$CH_3$); $\delta_C$(75 MHz; $CDCl_3$) 75.7*, 68.7*, 47.6*, 44.9*, 41.6*, 38.4, 33.8, 27.6*, 23.7*, 23.5*, 21.9* and 20.8*; *m*/*z* (70 eV) 196 (M$^+$, 1%), 141 (15), 136 (12), 127 (100), 113 (54), 112 (29), 110 (75), 100 (19), 95 (81), 85 (73), 81 (30), 71 (81), 58 (58) and 42 (67).

(1S*,2R*,3R*)-3-(*Isobutoxy*)-2,6,6-*trimethylbicyclo*[3.1.1]-*heptane* **16**.—A solution of pinan-3-ol **12** (66.3 mg, 0.430 mmol), 2-methoxyethoxymethyl chloride (98.2 mm$^3$, 0.860 mmol), and *N*,*N*-di(isopropyl)ethylamine (149.8 mm$^3$, 0.742 mmol) in dichloromethane (2 cm$^3$) was stirred at room temperature for 3 h. The mixture was poured into water (5 cm$^3$) and extracted with ether (× 3). The organic extracts were washed with water and brine, dried over magnesium sulphate, and concentrated under reduced pressure. Purification by chromatography (1.2 × 19 cm; 20% ether–hexane) yielded (1*S**,2*R**,3*R**)-3-(2-methoxyethoxymethyl)-2,6,6-trimethylbicyclo[3.1.1]heptane **15** (89.7 mg, 86%) as a colourless oil. To a solution of the MEM ether **15** (55.0 mg, 0.227 mmol) and zinc bromide (256 mg, 1.13 mmol) in toluene (2.0 cm$^3$) was added isopropylmagnesium chloride (2.0 mol dm$^{-3}$ in ether, 565 mm$^3$). The solution was heated at reflux for 18 h. A white precipitate formed during this period. The reaction mixture was cooled to room temperature and quenched with water (10 cm$^3$) and extracted with ether (× 3). The organic extracts were washed with brine, dried over magnesium sulphate, and concentrated. Purification of the residue by chromatography (1.2 × 15.5 cm; 5% ether–hexane) yielded (1S*,2R*,3R*)-3-(*isobutoxy*)-2,6,6-*trimethylbicyclo*[3.1.1]*heptane* **16** (31.9 mg, 67%) as a colourless oil, $\nu_{max}$(neat)/cm$^{-1}$ 2953s, 2905s, 2872s, 1472m, 1383w, 1366m, 1260m, 1157m, 1092s, 1028m, 955w and 804m; $\delta_H$(300 MHz; $CDCl_3$) 3.58 (1 H, quintet, *J* 6.1, 3-H), 3.26 (1 H, dd, *J* 8.0 and 11.0, $OCH_2$), 3.15 (1 H, dd, *J* 8.0 and 11.0, $OCH_2$), 2.39 (1 H, m, 1-H), 2.30 (1 H, m, 5-H), 1.70–1.25 (6 H, m, 2-H, 4-$H_2$, 7-$H_2$ and

$CH_3CHCH_3$), 1.22 (3 H, s, 6-$CH_3$), 1.14 (3 H, d, *J* 6.5, 2-$CH_3$), 0.91 (6 H, t, *J* 6.1, $CH_3CHCH_3$) and 0.91 (3 H, s, 6-$CH_3$); $\delta_C$(75 MHz; $CDCl_3$) 79.0*, 76.0, 47.7*, 44.6*, 41.5*, 35.8, 33.5, 28.7*, 27.6*, 23.7*, 21.4* and 19.6*; *m/z* (70 eV) 155 (13%), 141 (65), 127 (27), 110 (47), 95 (87), 85 (30), 81 (34), 71 (39) and 57 (100).

*General Method for the Preparation of Acetals.*—In a 100 $cm^3$ round-bottomed flask was placed the alcohol (*ca.* 2 g) in the enol ether (*ca.* 30 equiv.). The solution was cooled to 0 °C and treated with a catalytic amount of toluene-*p*-sulphonic acid (1–3 mg). The mixture was stirred at 0 °C as the progress of the reaction was monitored by TLC (silica; 25% ether–hexane). The reaction mixture was warmed to room temperature for 15 min and neutralized by the addition of solid potassium carbonate (*ca.* 1 g). After 20 min, the mixture was filtered and concentrated under reduced pressure. Purification was effected by column chromatography (basic alumina; eluting with 5% ether–hexane) followed by Kugelrohr distillation.

1-(1-*Ethoxyethoxy*)*nonane* **22**. Yield 92%, b.p. 70 °C (air bath; 0.025 Torr) (Found: C, 72.1; H, 13.1 $C_{13}H_{28}O_2$ requires C, 72.2; H, 13.0%); $\nu_{max}(CCl_4)/cm^{-1}$ 2928s, 2868s, 1462m, 1448m, 1419s, 1356m, 1225s, 1103s, 1072s, 966m and 902m; $\delta_H$(300 MHz; $CDCl_3$) 4.66 (1 H, q, *J* 5.4, OCHO), 3.66–3.35 (4 H, m, $OCH_2CH_3$ and 1-$H_2$), 1.54 (2 H, m, 2-$H_2$), 1.28 [3-H, d, *J* 5.4, $(CH_3CH_2O)OCHCH_3$], 1.25 (12 H, m), 1.17 (3 H, t, *J* 3.4, $OCH_2CH_3$) and 0.85 (3 H, t, *J* 6.2, 9-$H_3$); $\delta_C$(75 MHz; $CDCl_3$) 99.3 (OCHO), 64.9 (C-1), 60.2 ($OCH_2CH_3$), 31.8, 29.8, 29.5, 29.4, 29.2, 26.2, 22.5, 19.6, 15.1 ($OCH_2CH_3$) and 13.9 (C-9); *m/z* (70 eV) 75 (19%), 73 (100), 71 (18), 57 (16), 45 (73), 43 (21) and 41 (14); $t_R$ 15.5 min [HP-1, 100 °C (5 min), 10 °C $min^{-1}$, 250 °C].

1-(1-*Methoxy*-1-*methylethoxy*)*nonane* **23**. Yield 91%, b.p. 50 °C (air bath; 0.20 Torr) (Found: C, 72.3; H, 13.0. $C_{13}H_{28}O_2$ requires C, 72.2; H, 13.0%); $\nu_{max}(CCl_4)/cm^{-1}$ 2994m, 2928s, 2857s, 2828w, 1466m, 1379m, 1369m, 1257w, 1213s, 1184m, 1156m, 1080s, 1053m and 852w; $\delta_H$(300 MHz; $CDCl_3$) 3.35 (2 H, t, *J* 6.9, 1-$H_2$), 3.17 (3 H, s, $OCH_3$), 1.52 (2 H, m, 2-$H_2$), 1.32 (6 H, s, $CH_3CHCH_3$), 1.31–1.25 (12 H, m) and 0.86 (3 H, t, *J* 6.5, 9-$H_3$); $\delta_C$(75 MHz; $CDCl_3$) 99.5 ($CH_3CCH_3$), 60.5 (C-1), 48.1 ($OCH_3$), 31.8, 30.0, 29.5, 29.5, 29.2, 26.3, 24.3, 22.6 and 13.9 (C-9); *m/z* (70 eV) 98 (16%), 97 (16), 84 (18), 83 (22), 73 (17), 71 (16), 70 (45), 69 (39), 68 (12), 59 (76), 58 (28), 57 (40), 56 (68), 55 (65), 43 (100), 42 (34), 41 (88) and 39 (19); $t_R$ 15.5 min [HP-1, 100 °C (5 min), 10 °C $min^{-1}$, 250 °C].

2-(1-*Ethoxyethoxy*)*nonane* **24**. Yield 90%, b.p. 50 °C (air bath; 0.20 Torr) (Found: C, 72.3; H, 13.0. $C_{13}H_{28}O_2$ requires C, 72.2; H, 13.0%); $\nu_{max}(CCl_4)/cm^{-1}$ 2971s, 2930s, 2859s, 1548m, 1377, 1333m, 1132s, 1097s, 1059s, 1032m, 963m, 924w and 847w; $\delta_H$(300 MHz; $CDCl_3$) 4.73 (1 H, m, OCHO), 3.73–3.58 (2 H, m, $OCH_2CH_3$), 3.54–3.43 (1 H, m, $HCCH_3$), 1.58–1.45 (2 H, m, 3-$H_2$), 1.31 [3 H, d, *J* 5.4, $OCH(CH_3)O$], 1.28 (10 H, m), 1.20 (3 H, t, $OCH_2CH_3$), 1.12 (3 H, d, *J* 6.1, 1-$H_3$) and 0.88 (3 H, t, *J* 6.5, 9-$H_3$); $\delta_C$(75 MHz; $CDCl_3$) 98.9 (OCHO), 97.5 (OCHO), 72.8 (C-2), 71.4 (C-2), 59.6 ($OCH_2CH_3$), 59.5 ($OCH_2CH_3$), 37.4, 36.9, 31.8, 29.6, 29.2, 25.7, 25.4, 22.6, 20.9, 20.7, 20.5, 20.0, 15.2 and 13.9; *m/z* (70 eV) 73 (100%), 71 (12), 57 (11), 45 (54), 43 (15) and 41 (10); $t_R$ 14.4 and 14.6 min [HP-1, 100 °C (5 min), 10 °C $min^{-1}$, 250 °C].

2-(1-*Methoxy*-1-*methylethoxy*)*nonane* **25**. Yield 54%, b.p. 50 °C (air bath; 0.5 Torr) (Found: C, 72.2; H, 13.1. $C_{13}H_{28}O_2$ requires C, 72.2; H, 13.0%); $\nu_{max}(CCl_4)/cm^{-1}$ 2992s, 2930s, 2859s, 2928m, 1466m, 1379s, 1259w, 1206s, 1183s, 1156m, 1116m, 1070s, 1008m and 833w; $\delta_H$(300 MHz; $CDCl_3$) 3.79 (1 H, m, 2-H), 3.21 (3 H, s, $OCH_3$), 1.53–1.40 (2 H, m, 3-$H_2$), 1.32 (6 H, s, $CH_3CCH_3$), 1.20 (10 H, m), 1.10 (3 H, d, *J* 6.2, 1-$H_3$) and 0.85 (3 H, t, *J* 6.5, 9-$H_3$); $\delta_C$(75 MHz; $CDCl_3$) 99.9 ($CH_3CCH_3$), 66.8 (C-2), 48.5 ($OCH_3$), 38.1, 31.7, 29.6, 29.2, 25.5, 25.2, 25.1, 22.5, 21.3 and 13.8 C-9; *m/z* (70 eV) 70 (11%), 69 (19), 59 (20), 58 (19), 57 (16), 56 (13), 55 (20), 45 (100), 43 (36), 42 (10) and 41 (29).

2-*Methyl*-2-(1-*ethoxyethoxy*)*nonane* (**26**). Yield 92%, b.p. 60 °C (air bath; 0.55 Torr) (Found: C, 73.0; H, 13.1 $C_{14}H_{30}O_2$ requires C, 73.0; H, 13.1%); $\nu_{max}(CCl_4)/cm^{-1}$ 2977s, 2932s, 2857s, 1468m, 1379m, 1152m, 1117s, 1088s, 1057m, 1032m and 972s; $\delta_H$(300 MHz; $CDCl_3$) 4.85 (1 H, q, *J* 5.3, OCHO), 3.48 (2 H, m, $OCH_2CH_3$), 1.48–1.36 (2 H, m, 3-$H_2$), 1.31–1.21 (10 H, m), 1.24 (3 H, d, *J* 5.0, $CH_3CH$) 1.17 (3 H, s, 1-$H_3$) 1.15 (3 H, s, 1′-$H_3$), 1.14 (3 H, t, *J* 7.1, $OCH_2CH_3$) and 0.85 (3 H, t, *J* 6.7, 9-$H_3$); $\delta_C$(75 MHz; $CDCl_3$) 93.4 ($CH_3CH$), 75.5 (C-2), 58.3 ($OCH_2CH_3$), 42.1 (C-3), 31.8 (C-1), 30.1 (C-1′), 29.3, 26.4, 26.1, 24.0, 22.6, 21.7, 15.3 [($CH_3CH_2O$) and 13.9 (C-9)]; *m/z* (70 eV) 85 (10%), 73 (100), 71 (11), 59 (32), 57 (20), 56 (10), 45 (44), 43 (17) and 41 (15); $t_R$ 7.7 min [Carbowax, 100 °C (5 min), 10 °C $min^{-1}$, 250 °C].

*General Method for the Preparation of Ethers.*—In a flame-dried, three-necked 100 $cm^3$, round-bottomed flask was placed the acetal (*ca.* 550 mg) in anhydrous toluene (30 $cm^3$). Methylmagnesium bromide (3.0 mol $dm^{-3}$ in ether, 3.0 equiv.) was added and the solution heated to reflux. The mixture was allowed to reflux as the progress of the reaction was monitored by TLC. Formation of a white precipitate was usually observed. The reaction mixture was cooled and quenched by the addition of ice–water (30 $cm^3$). The layers were separated and the aqueous layer was extracted with pentane (3 × 30 $cm^3$). The organic layers were combined, dried over magnesium sulphate, filtered, and concentrated under reduced pressure. The crude mixture was purified by column chromatography (5–25% ether–pentane) and Kugelrohr distillation. For yields and products, see Table 1.

1-*Isopropoxynonane* **32**. Yield 57%, b.p. 40 °C (air bath; 0.5 Torr) (Found: C, 77.4; H, 14.0. $C_{12}H_{26}O$ requires C, 77.3; H, 14.1%); $\nu_{max}(CCl_4)/cm^{-1}$ 2973s, 2928s, 2857s, 1466m, 1379m, 1368m, 1335w, 1150m, 1129m and 1084m; $\delta_H$(300 MHz; $CDCl_3$) 3.53 (1 H, septet, *J* 6.1, $CH_3CHCH_3$), 3.37 (2 H, t, *J* 6.8, 1-$H_2$), 1.56–1.49 (2 H, m, 2-$H_2$), 1.25 (12 H, m), 1.13 (6 H, d, *J* 6.1, $CH_3CHCH_3$) and 0.86 (3 H, t, *J* 6.6, 9-$H_3$); $\delta_C$(75 MHz; $CDCl_3$) 71.2 ($CH_3CHCH_3$), 68.2 (C-1), 31.9, 30.2, 29.5, 29.3, 26.2 ($CH_3CHCH_3$), 23.6, 22.7, 22.1 and 14.1 (C-9); *m/z* (70 eV) 85 (26), 73 (28), 71 (48), 69 (12), 57 (39), 56 (12), 55 (20), 43 (100), 42 (11) and 41 (29); $t_R$ 12.7 min [HP-1, 100 °C (5 min), 10 °C $min^{-1}$, 250 °C].

1-tert-*Butoxynonane* **33**. Yield 72%, b.p. 98 °C (air bath; 1.1 Torr) (Found: C, 77.7; H, 13.9. $C_{13}H_{28}O$ requires C, 77.9; H, 14.1%); $\nu_{max}(CCl_4)/cm^{-1}$ 2972s, 2930s, 2857s, 1466m, 1387m, 1361m, 1255w, 1200s, 1117m, 1075w and 1013w; $\delta_H$(300 MHz; $CDCl_3$) 3.30 (2 H, t, *J* 6.8, 1-$H_2$), 1.52–1.47 (2 H, m, 2-$H_2$), 1.25 (12 H, m), 1.17 (9 H, s, $C(CH_3)_3$) and 0.85 (3 H, t, *J* 6.5, 9-$H_3$); $\delta_C$(75 MHz; $CDCl_3$) 72.1 [$C(CH_3)_3$], 61.5 (C-1), 31.9, 30.7, 29.6, 29.5, 29.3, 27.4, 26.2, 22.6 and 14.0 (C-9); *m/z* (70 eV) 185 (11), 71 (15), 59 (100), 57 (77), 56 (13), 43 (23) and 42 (23); $t_R$ 13.8 min [HP-1, 100 °C (5 min), 10 °C $min^{-1}$, 250 °C].

2-(*Isopropoxy*)*nonane* **34**. Yield 73%, b.p. 55 °C (air bath; 0.2 Torr) (Found: C, 77.6; H, 14.0. $C_{12}H_{26}O$ requires C, 77.4; H, 14.1%); $\nu_{max}(CCl_4)/cm^{-1}$ 2971s, 2928s, 2859s, 1466m, 1377s, 1329m, 1148m, 1117s and 1080m; $\delta_H$(300 MHz; $CDCl_3$) 3.61 (1 H, septet, *J* 6.1, $CH_3CHCH_3$), 3.40 (1 H, m, 2-H), 1.48–1.18 (12 H, m), 1.13 (3 H, d, *J* 6.1, $CH_3CHCH_3$), 1.11 (3 H, d, *J* 5.8, 1-$H_3$) 1.09 (3 H, d, *J* 6.1, $CH_3CHCH_3$) and 0.87 (3 H, t, *J* 6.6, 9-$H_3$); $\delta_C$(75 MHz; $CDCl_3$) 72.8 (C-2), 68.9 ($CH_3CHCH_3$), *37.4, 31.9, 29.7, 29.3, 25.8* ($CH_3CHCH_3$), 23.2 ($CH_3CHCH_3$), 22.7, 22.5, 20.8 and 14.1 (C-9); *m/z* (70 eV) 87 (94), 69 (26), 57 (12), 55 (13), 45 (100), 43 (45) and 41 (25); $t_R$ 11.45 min [HP-1, 100 °C (5 min), 10 °C $min^{-1}$, 250 °C].

2-(tert-*Butoxy*)*nonane* **35**. Yield 53%, b.p. 60 °C (air bath; 0.2 Torr) (Found: C, 78.1; H, 14.1. $C_{13}H_{28}O$ requires C, 77.9;

H, 14.1%); $\nu_{max}(CCl_4)/cm^{-1}$ 2970s, 2928s, 2856s, 1466m, 1387w, 1362m, 1256w, 1229w, 1198s, 1117w, 1075w and 1013w; $\delta_H$(300 MHz; $CDCl_3$) 3.54 (1 H, q, *J* 6.1, 2-$H_2$), 1.26–1.19 (12 H, m), 1.18 [9 H, s, $C(CH_3)_3$], 1.09 (3 H, d, *J* 6.1, 1-$H_2$) and 0.87 (3 H, t, *J* 6.7, 9-$H_3$); $\delta_C$(75 MHz; $CDCl_3$) 73.0 [$C(CH_3)_3$], 67.4 (C-2), 39.1, 31.9, 29.8, 29.3, 28.6 [$C(CH_3)_3$], 26.2, 23.0, 22.7 and 14.1 (C-9); *m/z* (70 eV) 101 (29%), 59 (25), 57 (100) and 41 (17); $t_R$ 12.75 min [HP-1, 100 °C (5 min), 10 °C $min^{-1}$, 250 °C].

2-(*Isopropoxy*)-2-*methylnonane* **36**. Yield 89%, b.p. 60 °C (air bath; 0.2 Torr) (Found: C, 78.5; H, 14.1. $C_{13}H_{28}O$ requires C, 77.9; H, 14.1%); $\nu_{max}(CCl_4)/cm^{-1}$ 2971s, 2930s, 2857m, 1466m, 1379m, 1366m, 1240w, 1202w, 1175m, 1119m and 1009s; $\delta_H$(300 MHz; $CDCl_3$) 3.75 (1 H, septet, *J* 6.1, $CH_3CHCH_3$), 1.42–1.27 (12 H, m), 1.12 (6 H, s, 1-$H_3$ and 1′$H_3$), 1.10 (6 H, d, *J* 6.1, $CH_3CHCH_3$) and 0.87 (3 H, t, *J* 6.5, 9-$H_3$); $\delta_C$(75 MHz; $CDCl_3$) 75.1 (C-2), 62.9 ($CH_3CHCH_3$), 41.5 (C-3), 31.9 (C-1), 30.3 (C-1′), 29.3, 26.0, 25.0 ($CH_3CHCH_3$), 24.2 ($CH_3CHCH_3$), 22.6 and 14.0 (C-9); *m/z* (70 eV) 101 (40), 59 (100), 57 (12), 43 (15) and 41 (15); $t_R$ 12.75 min [HP-1, 100 °C (5 min), 10 °C $min^{-1}$, 250 °C].

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