66. β-Cleavage of Potassium Bicyclo[2.2.2]oct-5-en-2-olates. Stereoselective Synthesis of (±)-Trichodiene

by **Roger L. Snowden***, **Robert Brauchli**, and **Philippe Sonnay**

Firmenich SA, Research Laboratories, CH-1211 Geneva 8

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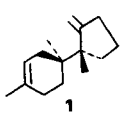
The transformations of **12** bicyclo[2.2.2]oct-5-en-2-ols (**V** or **VI**) to 3-(cyclohex-3-enyl)-2-alkanones (**III** or **IV**), *via* β-cleavage of their potassium alkoxides in HMPA, has been investigated *(cf. Table 1)*. As an illustration of this synthetic methodology, a stereoselective synthesis of (±)-trichodiene ((±)-**1**) is described which involves the β-cleavage of the tricyclic potassium alkoxides **46a** and **47a** to cyclopentanone **4** *(cf. Scheme 7)*.

Introduction. – Trichodiene (**1**), a naturally occurring sesquiterpene hydrocarbon isolated from various microorganisms [1], has attracted synthetic interest due mainly to the fact that it is the biogenetic precursor of a wide range of biologically active trichothecanes [2]. Up to now, relatively few stereoselective approaches to **1** have been reported[1]), reflecting the general problem of stereochemical control between two adjacent chiral quaternary C-centres where there is free rotation about the common C–C bond[2]).



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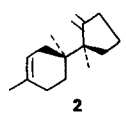
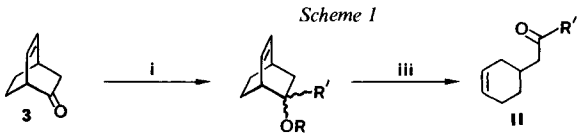


2

We now present a diastereoselective synthesis of (±)-**1** with full experimental details[3]) and also describe model studies which were originally designed to provide access to both (±)-**1** and (±)-bazzanene (**2**)[4]), its naturally occurring diastereoisomer.

Synthetic Strategy A. – In 1981 [6], we reported the preparation of 1-(cyclohex-3′-enyl)-2-alkanones (**II**) from 2-substituted bicyclo[2.2.2]oct-5-en-2-ols (**I**) *via* β-cleavage of

Scheme 1

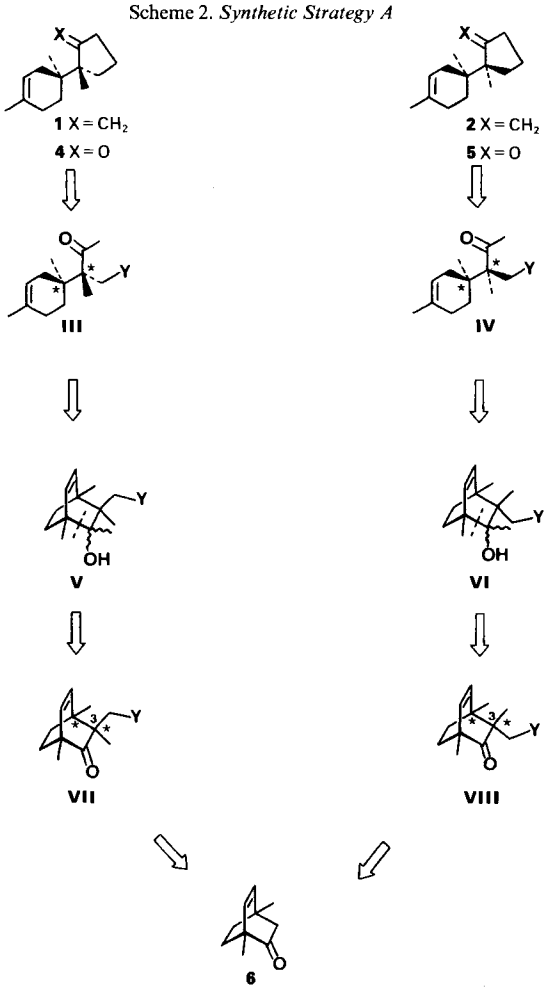


i) R′MgX, Et_2O, then aq. NH_4Cl soln.
ii) KH, HMPA, r.t.
iii) HMPA, Δ t, then. aq. NH_4Cl soln.

I R = H ⇄ **Ia** R = K (ii)

[1]) For stereoselective syntheses of (±)-**1**, see [3a–f]; for nonstereoselective approaches, see [3g–k].
[2]) For a review on methodology for the construction of quaternary C-centres, see [4].
[3]) Part of this work has been the subject of a preliminary communication [3d].
[4]) For a stereoselective synthesis of (±)-**2**, see [5].

Scheme 2. *Synthetic Strategy A*

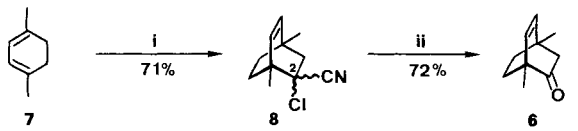


their potassium alkoxides **Ia**[5]) *(cf. Scheme 1)*. Retrosynthetic analysis of **1** and **2** *(cf. Scheme 2)* indicated that the known cyclopentanones **4** and **5** [3] [5], their logical precursors, might be synthesised from ketones **III** and **IV**, which in turn would result from *β*-cleavage of the potassium alkoxides of bicyclic alcohols **V** and **VI**, respectively. Access to **V** and **VI** was envisaged *via* sequential alkylation of bicyclic ketone **6** to either **VII** or **VIII** followed by reaction with a methyl organometallic reagent. It is thus evident that the configuration at C(3) in **VII** and **VIII** fixes the relative configuration of the two connected quaternary C-centres in **III** and **IV**[6]).

[5]) For other synthetic applications of the *β*-cleavage of homoallylic potassium alkoxides, see [7] and ref. cit. therein.

[6]) These quaternary C-centres are marked with an asterisk in *Scheme 2*.

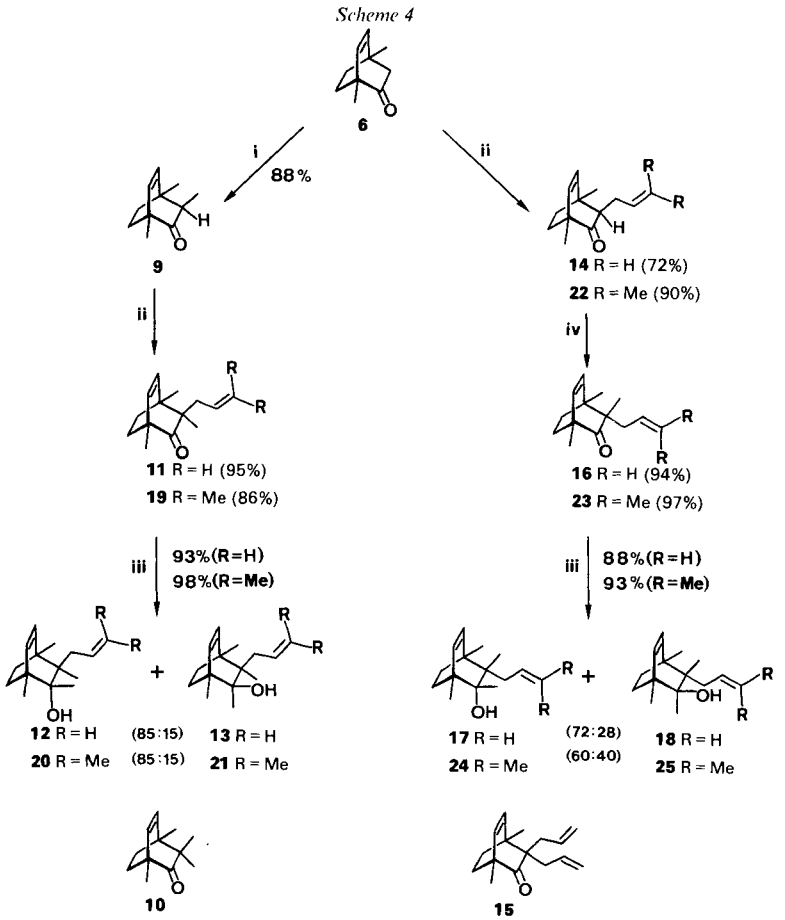
Scheme 3



i) CH_2=C(Cl)CN, toluene, 90°. ii) $Na_2S \cdot 9\,H_2O$, EtOH, reflux.

Results and Discussion. Synthesis of **6** (*Scheme 3*). 1,4-Dimethylcyclohexa-1,4-diene (**7**) [8][7]) was treated with 2-chloroacrylonitrile (1.5 mol-equiv.) in toluene containing a catalytic amount of hydroquinone at 90° during 60 h, and the resulting *Diels-Alder*

Scheme 4



i) LDA, THF/hexane, −70°, then MeI, HMPA, −30°. ii) LDA, THF/hexane, −70°, then allyl iodide (R = H) or prenyl bromide (R = Me), HMPA, −30°. iii) MeLi, Et_2O, 0–r.t. iv) LDA, THF/hexane, −70°, then MeI, HMPA, −60°.

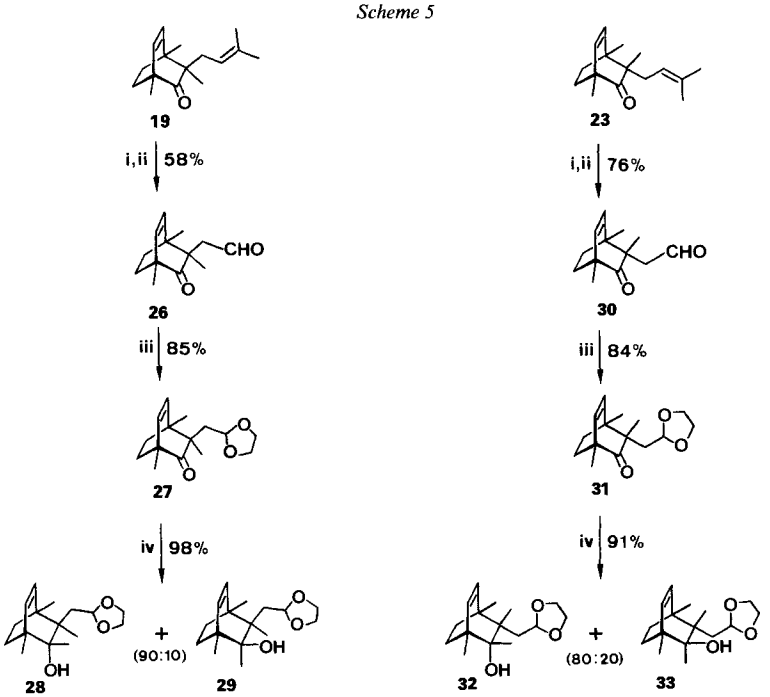
[7]) Compound **7** was synthesised using a three-step sequence starting from 4-methylanisole *(cf. Exper. Part)*. After completion of our work, *Brady* and co-workers described a practical two-step synthesis of **7** from *p*-xylene [9].

cycloadducts **8** (4:1 diastereoisomeric mixture, 71% yield) were then hydrolysed using $Na_2S \cdot 9\ H_2O$ in refluxing EtOH [10] to give **6**[8]) in 72% yield.

Synthesis of **12**, **13**, **17**, **18**, **20**, **21**, **24**, *and* **25** (*Scheme 4*). Deprotonation of **6** with lithium diisopropylamide (LDA) in THF/hexane at −70° followed by treatment of the resulting lithium enolate with MeI at −30°, with hexamethylphosphoric triamide (HMPA) as co-solvent, afforded **9** in 88% yield[9]). Using analogous conditions, allylation or prenylation of **6** led to the isolation of **14** (72%)[9]) and **22** (90%), respectively, whereas allylation and prenylation of **9** afforded **11** (95%) and **19** (86%), respectively. Similarly, methylation of **14** and **22** furnished **16** and **23**, respectively, in almost quantitative yields. The excellent stereoselectivities ($\geq$ 95%)[10]) of these alkylations, which thus allow ready access to **11**, **16**, **19**, and **23** from **6**, is due to exclusive capture of the electrophile on the sterically less hindered face of the corresponding lithium enolate.

Treatment of **11** and **19** with MeLi in Et_2O at 0° led to the formation of 5.7:1 mixtures **12**/**13** (93%) and **20**/**21** (98%), respectively. Under identical conditions, **16** and **23** afforded **17**/**18** (2.6:1, 88%) and **24**/**25** (1.5:1, 93%), respectively. All four pairs of

Scheme 5



i) O_3, CH_2Cl_2, −60°. ii) Me_2S, CH_2Cl_2. iii) $HOCH_2CH_2OH$, TsOH (cat.), C_6H_6, reflux. iv) MeLi, Et_2O, 0°.

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[8]) After the publication of our synthesis of **1** [3d], Prof. *Kreiser* (University of Braunschweig) informed us of independent syntheses of **6**, **8**, **9**, **10**, and **46**, also in the context of a synthetic approach to **1** [11]. We thank Prof. *Kreiser* for providing us with this information.

[9]) The methylation and allylation of **6** led to the formation of small amounts (*ca.* 5%) of dialkylated ketones **10** and **15** (*cf. Exper. Part*).

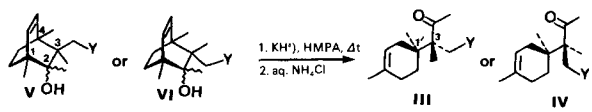
[10]) This lower stereoselectivity limit was estimated by ^{1}H-NMR spectral analysis of the crude reaction mixture.

diastereoisomeric alcohols were separated by chromatography, and each alcohol was fully characterised by spectral analysis. The stereochemical outcomes of these reactions are in qualitative agreement with nucleophilic attack of MeLi on the less hindered face of the substrate ketone. However, it is not clear why this stereoselectivity is higher for **11** and **19** when compared with **16** and **23**[11]).

Synthesis of **28**, **29**, **32**, *and* **33** (*Scheme 5*). Chemoselective ozonolysis of the trisubstituted C=C double bond in **19** followed by reduction of the intermediate ozonide with Me_2S led to keto aldehyde **37** in 58% yield. Subsequent treatment of **26** with ethylene glycol and a catalytic amount of TsOH in refluxing benzene resulted in selective acetalisation of the aldehyde group to furnish keto acetal **27**[12]) (85%). Reaction of **27** with MeLi in Et_2O at 0° then afforded hydroxy-acetal mixture **28**/**29** (9:1, 98%), inseparable by chromatography. Using the same methodology, **23** was transformed, *via* keto aldehyde **30** and keto acetal **31**[12]), to **32**/**33** (4:1, 58% overall yield from **23**) which were separated by chromatography.

β-Cleavage of Potassium Alkoxides **12a**, **13a**, **17a**, **18a**, **20a**, **21a**, **24a**, **25a**, **28a**, **29a**, **32a**, *and* **33a**. For these reactions, a general experimental procedure was followed. Thus,

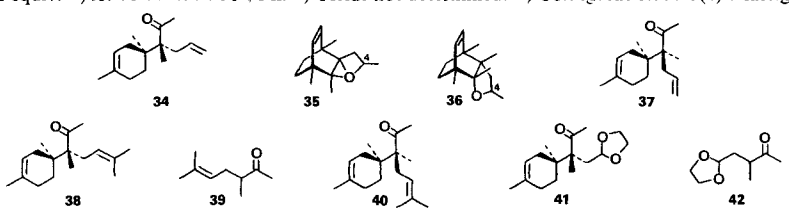
Table 1. *β-Cleavage of Substituted Potassium Bicyclo[2.2.2]oct-5-en-2-olates*



V OH VI OH III IV

Entry	Alcohol V	Alcohol VI	Reaction conditions[b])	Product (*ex β*-cleavage) III	Product (*ex β*-cleavage) IV	Yield [%]	Side products[c])
1	**12**		*A*	**34**	–	6	–
2	**13**		*A*	–	–	–	**35**[d])
3		**17**	*A*	–	–	–	**36**[d])
4		**18**	*A*	–	**37**	4	–
5	**20**		*A*	**38**	–	16	**39**
6	**21**		*A*	**38**	–	2	**39**
7		**24**	*B*	–	**40**	26	**39**
8		**25**	*B*	–	**40**	2	**39**
9	**28** + (9:1)	**29**	*A*	**41**	–	10	**42**
10		**32**	*A*	–	–	–	–
11		**33**	*A*	–	–	–	**42**

[a]) 1.2 mol-equiv. [b]) *A*: 70°, 1 h; *B*: 50°, 1 h. [c]) Yields not determined. [d]) Configuration at C(4) unassigned.



[11]) For further examples involving the reaction of MeLi with bicyclo[2.2.2]oct-5-en-2-ones, *cf.* **27**→**28**/**29**; **31**→**32**/**33** (*Scheme 5*) and **6**→**57**/**58**; **10**→**59**/**60** (*Scheme 13*).

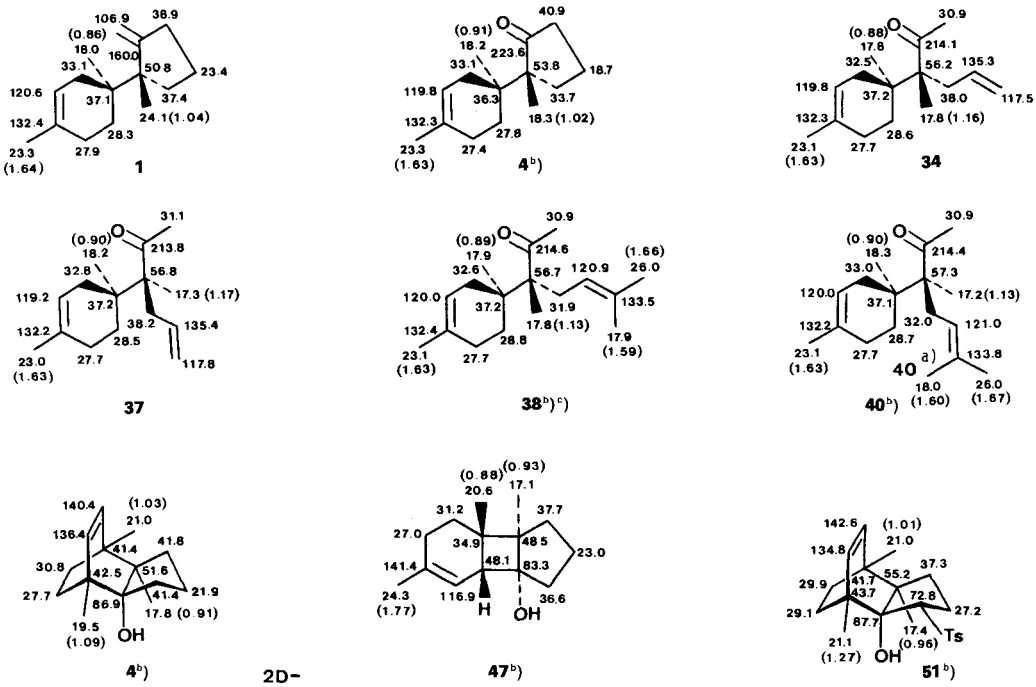
[12]) Direct syntheses of **27** and **31** *via* alkylation of **19** and **6** (*i.e.* LDA followed by 2-iodomethyl-1,3-dioxolan) were unsuccessful.

a solution of each substrate alcohol (**V** or **VI**) in HMPA was added to KH (1.2 mol-equiv.) in HMPA at 20° under N_2 to form the corresponding potassium alkoxide (**Va** or **VIa**) which was then heated under the reaction conditions *A* or *B (cf. Table 1)*. The evolution of each reaction was followed by TLC, and isolation of the products was effected by aqueous workup, extraction, and chromatography. Several conclusions may be drawn from the results.

i) Only five substrates (*cf. Entries 1, 4, 5, 7,* and *9*) afforded isolable quantities of ketones **III** and **IV** resulting from the desired β-cleavage reaction. In addition, only **20** and **24** (*cf. Entries 5* and *7*) gave yields in excess of 15%. It can, thus, be concluded that the transformation of **I** to **II** *(cf. Scheme 1)* is inefficient, when there is substitution at C(1), C(3), and C(4) in the substrate alcohol. The principal competing reaction is a facile *retro-Diels-Alder* reaction of the corresponding alkoxide [12] which involves cleavage of both C(1)–C(2) and C(3)–C(4) bonds and was confirmed by the isolation of ketones **39** and **42**.

ii) The β-cleavage reaction occurs without loss of the configurational integrity at C(3) and C(4). For example, both **20** and **21** afforded **38**, whereas **24** and **25** both led to the formation of **40**. Similarly, **12** and **18** gave **34** and **37**, respectively. The diastereoisomeric purity ($\geq 95\%$) of the product ketones was determined by GC analysis and inspection of their ^{1}H- and ^{13}C-NMR spectra (*cf.* the *Fig.*), thus demonstrating that the relative

Figure. *^{13}C-NMR Assignments for* **1**, **4**, **34**, **37**, **38**, **40**, **46**, **47**, *and* **51**[a])



[a]) Numbers in brackets refer to ^{1}H-NMR chemical shifts. [b]) C,H Correlation. [c]) 2D-Inadequate.

configuration of C(3) and C(4) in substrates **V** and **VI** is maintained in C(3) and C(1') of the products **III** and **IV**. This result demonstrates that interconversion of **III** and **IV**, *via* a possible base-catalysed isomerisation of the cyclohexenyl C=C bond, is not taking place under the strongly basic reaction conditions.

iii) The efficiency of the β-cleavage process is strongly dependent on the C(2)-configuration of the substrate alcohol. A comparison of the behaviour of the four diastereoisomeric alcohols, **20**, **21**, **24**, and **25** *(cf. Entries 5–8)*, illustrates this point. Whereas **20** and **24** afforded the desired β-cleavage products, **38** and **40**, in acceptable yields, **21** and **25**[13]), under identical reaction conditions, gave only trace amounts (*ca.* 2%) of the same compounds. An explanation of these results is that initial heterolytic cleavage of the C(1)–C(2) bond in **20a** and **24a** leads to a transient intermediate in which 1,5-H transfer is conformationally favoured. In contrast, a similar cleavage of the C(1)–C(2) bond in **21a** and **25a** affords an intermediate where 1,5-H transfer requires a C–C bond rotation to acquire a favourable conformation. This phenomenon, previously observed in analogous substrates [6] as a slight reduction in yield between two alcohol substrates epimeric at C(2), is thus amplified in the more substituted systems examined in the present study.

iv) Other important factors are competing reactions under the strongly basic reaction conditions. For example, **13** and **17** are converted to the tetrahydrofurans **35** and **36**, respectively (*cf. Entries 2* and *3*) *via* intramolecular addition of the 2-olato to the adjacent 3-allyl group[14]). Moreover, the presence of an acetal function *(cf. Entries 9–11)* leads to extensive decomposition of the substrate.

Attempted Transformations of **38**. Because of the poor yields of the β-cleavages, little time was spent on the eventual transformation of ketones **III** and **IV** to **1** to **2** in continuation of *Synthetic Strategy A (cf. Scheme 2)*. Nevertheless, preliminary experiments were conducted in order to investigate the possibility of chemical differentiation between the two trisubstituted C=C bonds in **38**. Disappointingly, treatment of **38** with equimolar amounts of either O_3 (CH_2Cl_2, $-70°$) or $NaIO_4$ in the presence of OsO_4 as catalyst [14] gave only complex mixtures. An attempted chemoselective bromination with pyridinium bromide perbromide [15] in either CH_2Cl_2 or THF was also unsuccessful. It can be concluded that both C=C bonds in **38** are of similar reactivity towards electrophiles and, thus, this line of research was abandoned.

Synthetic Strategy B. – Due to the unsurmountable problems encountered in *Synthetic Strategy A (vide supra)*, it was decided to investigate a second approach which would be specific for the synthesis of **1**. In this new strategy, the key step involves β-cleavage of the potassium alkoxide derived from the tricyclic homoallylic alcohol **46** whose stereoselective synthesis was envisaged starting from **6** *(cf. Scheme 6)*. Although an analogous approach would be theoretically possible for an analogous synthesis of **2**, the key step (*i.e.* **IX**→**5**) would be strongly disfavoured by the unfavourable configuration at C(2); for this reason, no attempt was made to investigate this putative approach to **2**. Our attention was thus fully concentrated on the synthesis of **1** and, primarily, on the stereoselective construction of **46** from **6**.

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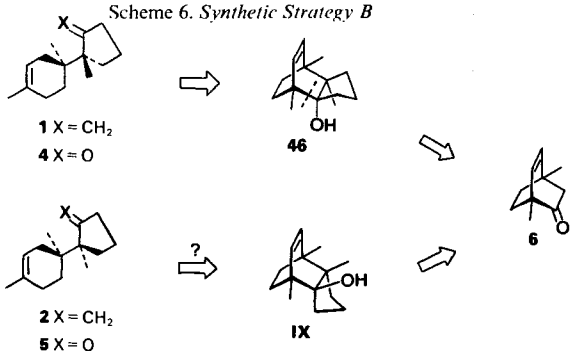
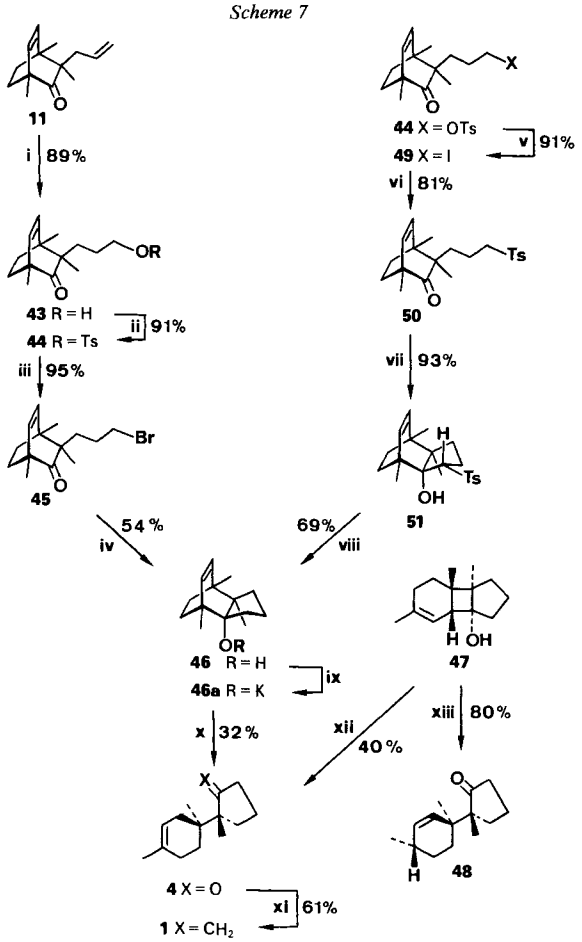
[13]) An attempted transformation of **25** to **40** *via* a thermal *retro*-ene reaction was unsuccessful: gas-phase pyrolysis at 300–400° led mainly to the formation of non-identified volatile products.

[14]) For a recent discussion of this cyclisation reaction in analogous systems, see [13].

Scheme 6. *Synthetic Strategy B*



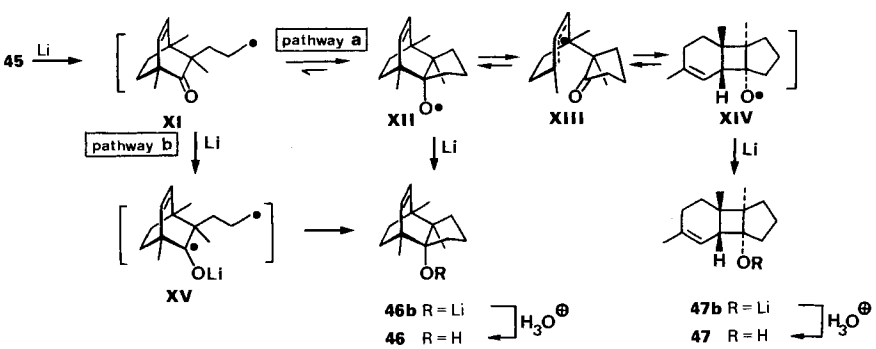
Scheme 7



i) 9-BBN, THF, r.t., then 30% aq. H_2O_2, NaOH, H_2O. ii) TsCl, pyridine. iii) LiBr, acetone, reflux. iv) Li, THF, ultrasound, 0°. v) NaI, acetone, r.t. vi) NaTs, DMF, 60°. vii) LDA, THF/hexane, −70°. viii) Li, NH_3, −60°. ix) KH, HMPA, r.t. x) HMPA, 140°, then aq. NH_4Cl soln. xi) $Ph_3P{=}CH_2$, DMSO, 80°. xii) *t*-BuOK, HMPA, r.t. xiii) toluene, 200°.

Results and Discussion. Synthesis of **46**[15]) (*Scheme 7*). Treatment of **11** with 9-borabicyclo[3.3.1]nonane (9-BBN; 1.1 mol-equiv.) in THF at 25° resulted in a chemoselective and regioselective hydroboration of the monosubstituted C=C bond to afford, after oxidation with basic 30% aqueous H_2O_2, hydroxy ketone **43** in 89% yield. The corresponding tosylate **4** was prepared in 91% yield using TsCl in pyridine, and then two synthetic routes to **46** were investigated. The first route involved treatment of **44** with LiBr in acetone at reflux to afford bromo ketone **45** (91%). Reaction of **45** with Li wire in THF at 0° in a sonicator [16] resulted in the formation of a 5:1 mixture **46**/**47** (65%) which was readily separated by chromatography. In the absence of sonication at 25°, the result was similar: in THF, a 6:1 mixture **46**/**47** (53%) was obtained which changed to a 3:1 mixture (56%), when Et_2O was used as solvent. The formation of **46** *via* an intramolecular *Barbier* reaction [17] was anticipated, but the presence of **47**[16]) was unexpected and merits discussion. The observed results are consistent with a radical mechanism[17]) whereby the first step is the conversion of **45** to radical **XI** *via* an initial single-electron transfer (SET) process (*cf. Scheme 8*). Two reaction pathways are now possible. *Pathway*

Scheme 8



a involves radical cyclisation [19] to the tricyclic alkoxy radical **XII** which is then either reduced to lithium alkoxide **46b** or undergoes β-cleavage of the C(1)–C(2) bond [20] to afford the allylic radical **XIII**. Cyclisation of **XIII** at the less substituted allylic position leads to the formation of a second tricyclic alkoxy radical **XIV** whose reduction then gives lithium alkoxide **47b**. The fact that a change of solvent from THF to Et_2O results in a higher proportion of **47b** can be explained by the more strongly reducing nature of the former system which favours reduction of **XII** to **46b** rather than β-cleavage to **XIII** [21].

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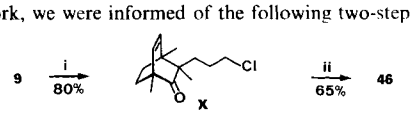
[15]) After completion of our work, we were informed of the following two-step synthesis of **46** from **9** *via* the chloro ketone **X** [11a].



i) LDA, THF/hexane, then I(CH$_2$)$_3$Cl, HMPA, –40°. ii) Li, THF, r.t.

[16]) The structure of **47** was elucidated by ^{1}H- and ^{13}C-NMR spectroscopy (including nuclear *Overhauser* effect (NOE) experiments) and confirmed by its transformation to the known cyclopentanone **48** [3b] *via* a thermal *retro*-ene reaction (*cf. Scheme 7*).

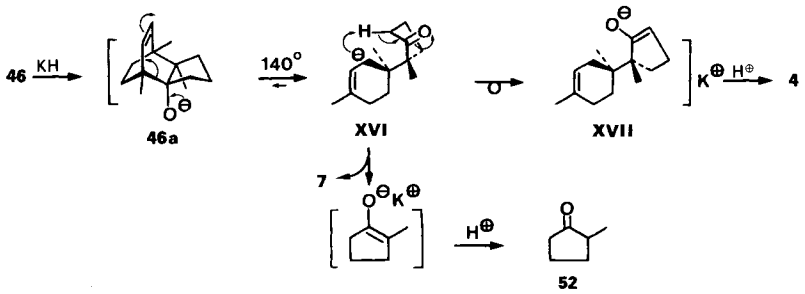
[17]) For evidence supporting a radical mechanism for the *Barbier* reaction, see [18].

Pathway b, the purported mechanism of the intermolecular *Barbier* reaction [18], may also account for the formation of **46b** from **XI** *via* the intermediacy of ketyl-anion radical **XV**. However, this latter pathway does not explain the formation of **47b**[18]).

The second route to **46** involved treatment of **44** with NaI in refluxing acetone to afford iodo ketone **49** (m.p. 55–56°, 91%)[19]) which was then transformed into keto sulfone **50** (m.p. 90–91°, 81%) using either sodium *p*-toluenesulfinate in DMF [23] or tetrabutylammonium *p*-toluenesulfinate in THF [24]. Deprotonation of **50** with LDA at −70° resulted in stereoselective cyclisation to the tricyclic hydroxy sulfone **51**[20]) (m.p. 93–94°, 93%) which was subsequently reduced with lithium in NH_3/THF at −70° [25] to furnish **46** in 69% yield.

β-Cleavage of Potassium Alkoxides **46a** *and* **47a**. *Synthesis of* **4**. Treatment of **46** with KH (1.6 mol-equiv.) in HMPA at 25° and heating the resulting HMPA solution of potassium alkoxide **46a** at 140° during 1 h, followed by an aqueous workup, afforded **4** in 30% yield. Also detected by ^{1}H-NMR analysis were small amounts of **5** (*ca.* 2%) which are believed to result from base-mediated isomerisation of **4**. Indeed, separate treatment of **4** with a large excess of KH (*ca.* 15 mol-equiv.) in HMPA at 140° during 1 h afforded a 3:1 mixture **4**/**5**. In analogy with our previous work [6], the reaction mechanism involves heterolytic cleavage of the allylic C(1)–C(2) bond, rearrangement of the resultant allylic anion **XVI**, *via* 1,5-H transfer, to the potassium enolate **XVII** and finally protonation to afford **4** *(cf. Scheme 9)*. It is noteworthy that no trace of **48** was detected, an observation which confirms the excellent regioselectivity of the 1,5-H transfer, **XVI**→**XVII**. The

Scheme 9



only moderate yield of **4** is due to a competing alkoxide-accelerated *retro-Diels-Alder* reaction which probably occurs stepwise *via* **XVI**. The isolation of both 2-methylcyclopentan-1-one (**52**) and *p*-xylene, the oxidation product of **7**, supports this hypothesis. The relatively high reaction temperature for the *β*-cleavage of **46a** also merits comment, especially as the potassium alkoxides, **Va** and **VIa,** described in the model studies invariably underwent reaction at 50–70° *(cf. Table 1)*. This reactivity difference is most

[18]) The non-interconversion of **46b** and **47b** under the reaction conditions was experimentally verified by independently treating **46** and **47** with LiH (1.2 mol-equiv.) in either THF or Et_2O.

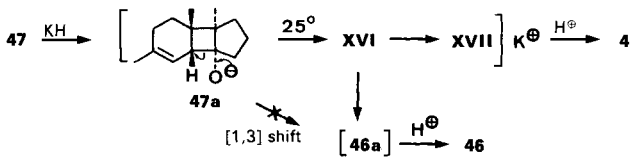
[19]) A direct preparation of **49** from **11** using a one-pot hydroboration procedure [22] afforded a complex mixture containing ⩽ 20% of **49**.

[20]) The anticipated C(3)-configuration with the tosyl group pseudoequatorial was confirmed by ^{1}H-NMR NOE experiments.

probably a consequence of the higher torsional strain of a cyclopentanone in comparison with an aliphatic ketone, a factor which directly influences the rate of the β-cleavage reactions leading to their formation.

Although not part of our original synthetic plan, it was appreciated that **47** could also provide access to **4** *via* β-cleavage of the C(1)–C(2) bond of its potassium alkoxide **47a**. Accordingly, treatment of **47** with KH (1.2 mol-equiv.) in HMPA at 25° during 2 h afforded, after the usual aqueous workup, a 3:1 mixture **46**/**4** (*ca.* 60%). The same experiment using THF as solvent, at either 25° or reflux, resulted in the quantitative recovery of unchanged **47**; alternatively, a 3:1 solution of THF/HMPA at reflux during 1 h gave complete conversion to the same 3:1 mixture **46**/**4**. At first sight these results appear to contradict the mechanistic conclusions concerning the β-cleavage of **46a** *(vide supra)*. How can **47a** be transformed into both **46** and **4**? The direct formation of **46a** from **47a** might be explained by an alkoxide accelerated [1,3]-sigmatropic rearrangement [26] *(cf. Scheme 10)*. However, this hypothesis is weakened by the observation that **47a**

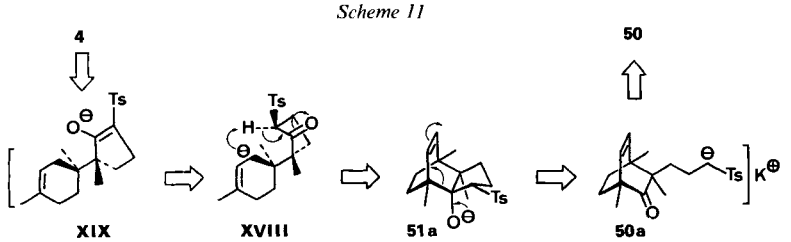
Scheme 10



remains unchanged in refluxing THF and also by the fact that such a rearrangement would be disfavoured by the rigidity of the system. The following explanation is proposed. Due to increased ring strain, the C(1)–C(2) allylic bond in **47a** readily undergoes β-cleavage to **XVI** which then either undergoes ring closure to **46a** or rearranges to **XVII** by 1,5-H transfer *(cf. Scheme 10)*. As it has already been established that **46a** is stable in HMPA solution at 25°, the 3:1 product ratio of **46** and **4** is thus kinetically controlled. Precedents for the β-cleavage of functionalised cyclobutoxides [26b,c] [27] also encouraged us to investigate the β-cleavage of **47a** in the presence of an external proton source. Indeed, although MeONa (1.2 mol-equiv.) in refluxing MeOH during 3 h gave no reaction, treatment of **47** with *t*-BuOK (2 mol-equiv.) in HMPA at 25° during 24 h afforded a 4:1 mixture **4**/**46** (*ca.* 50%). This result indicates that intermolecular protonation of **XVI** by *t*-BuOH to give **4** is regioselective and more rapid than ring closure to **46a**.

Attempted Synthesis of **4** *from* **50**. Another possible route to **4** was investigated starting from **50**. Retrosynthetic analysis *(cf. Scheme 11)* envisaged that the carbanion

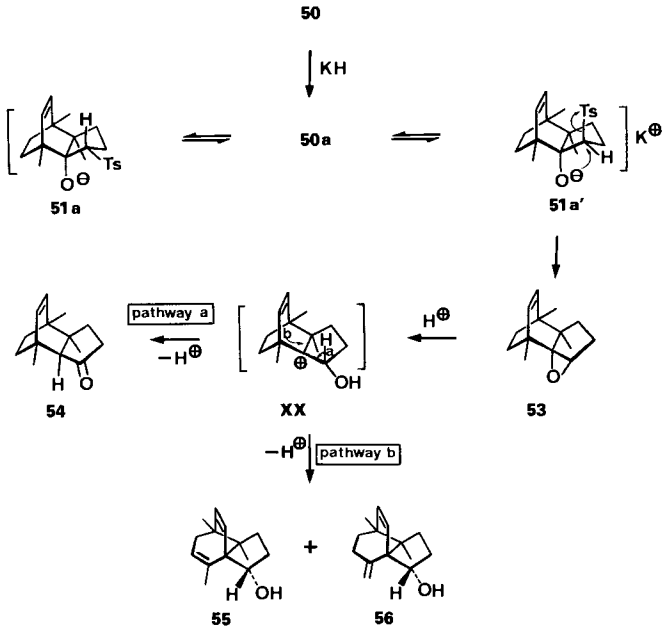
Scheme 11



50a would cyclise to alkoxide **51a** which, although in equilibrium with **50a**, might undergo an irreversible β-cleavage to the allylic carbanion **XVIII**. 1,5-H transfer would then give potassium enolate **XIX** whose conversion to **4** simply involves reductive removal of the sulfonyl group. It was hoped that the increased acidity of the α-carbonyl proton in **XVIII** would favour this pathway.

In practice, treatment of **50** with KH (1.5 mol-equiv.) in HMPA at 25° led to the rapid formation of **51a** (TLC analysis) which, on heating at 60° during 30 min, afforded a less polar compound, believed to be epoxide **53**. Aqueous workup and filtration through silica gel resulted in the transformation of **53** into tricyclic ketone **54** (*ca.* 20% from **50**) and tricyclic alcohols **55**/**56** (2:1 mixture, *ca.* 10% from **50**) whose separation was effected by preparative GC. The formation of these products may be rationalised in the following manner *(cf. Scheme 12)*. Equilibration of **51a** to **51a'** *via* **50a** is followed by epoxide

Scheme 12



formation to **53** with elimination of potassium *p*-toluenesulfinate. Ring strain in **53** then probably provides the driving force for a facile acid-catalysed ring opening to the carbonium ion **XX** which either loses a proton directly to give **54** or indirectly, after migration of the adjacent alkenyl C–C bond, to give **55** and **56**.

Synthesis of **1** *(Scheme 7)*. The preparation of **1** from **4** by means of a standard *Wittig* reaction is problematic due to competing enolatisation which results in inacceptably low yields. However, by using a large excess of (methylidene)triphenylphosphorane (10 mol-equiv.) in DMSO at 80° [3b], we were able to convert **4** to **1** in 42% yield. The application of a modification of this reaction, performed in a sealed tube [3c], improved the yield to 61%. An alternative methylidenation procedure (CH_2Br_2, Zn, $TiCl_4$ [28]), generally useful for readily enolisable ketones, was unsuccessful.

Table 2. *^{13}C- and ^{1}H-NMR Assignments for*

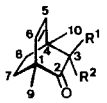
Compound	R^1	R^2	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)	C(9)	C(10)
6[a][b]	H	H	49.2	213.4	47.2	37.3	141.4	133.3	31.8	33.9	17.4	24.0
9[a]	CH_3	H	48.7	215.8	49.1	40.5	140.0	132.5	31.2	35.0	17.8	22.0
10	CH_3	CH_3	48.6	217.7	46.5	42.9	143.5	131.0	30.8	30.8	18.1	19.0
11[a]	Allyl	CH_3	48.9	215.3	49.9	42.9	143.6	129.2	30.8	31.4	18.1	19.1
14[a]	Allyl	H	48.9	213.5	53.6	40.4	140.6	131.1	30.9	35.7	17.8	22.4
15[a]	Allyl	Allyl	49.1	212.8	52.9	43.3	145.1	128.3	29.9	31.6	18.1	19.8
16	CH_3	Allyl	48.9	215.8	48.9	43.7	144.4	131.2	30.2	30.8	18.2	19.8
19[a]	Prenyl	CH_3	48.9	216.0	50.2	43.0	143.4	129.2	31.2	31.4	18.2	19.4
22[a]	Prenyl	H	48.8	214.2	54.3	40.4	140.5	131.3	31.2	35.6	17.8	22.4
23[a]	CH_3	Prenyl	48.8	216.3	49.4	43.6	144.5	131.0	30.2	30.9	18.2	19.9
27	(1,3-Dioxolan-2-yl)methyl	CH_3	49.0	216.1	47.6	43.2	142.5	130.5	30.9	31.4	18.2	19.1
30	CH_3	CH_2CHO	48.8	216.2	49.4	43.7	142.9	131.5	30.4	30.5	17.9	19.2
31	CH_3	(1,3-Dioxolan-2-yl)methyl	49.0	216.1	46.7	43.7	143.9	131.1	29.7	30.7	18.1	19.2
43[a]	$(CH_2)_3OH$	CH_3	49.0	216.7	48.9	42.9	143.4	129.2	31.0	31.4	18.1	19.1
45[a]	$(CH_2)_3Br$	CH_3	49.0	215.8	48.7	42.9	143.1	129.5	31.0	31.4	18.1	19.0
49[a]	$(CH_2)_3I$	CH_3	49.0	215.9	48.8	42.9	143.1	129.6	31.0	31.4	18.1	19.0
50[a]	$(CH_2)_3Ts$	CH_3	49.0	215.5	49.0	42.7	143.1	129.6	30.9	31.4	18.1	19.0

[a]) C,H Correlation. [b]) 2D-Inadequate. [c]) Interchangeable.

Table 3. *^{13}C- and ^{1}H-NMR Assignments for*

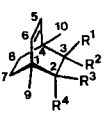
Compound	R^1	R^2	R^3	R^4	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)	C(9)	C(10)	C of R^1			CH_3
12[a]	Allyl	CH_3	CH_3	OH	43.4	79.7	47.2	41.8	140.0	136.0	28.9	32.0	20.0	21.4	42.5	139.2	115.6	
13[a]	Allyl	CH_3	OH	CH_3	44.3	80.3	48.2	41.8	142.2	136.3	28.0	33.4	19.9	20.6	42.8	139.3	116.5	
17	CH_3	Allyl	CH_3	OH	43.2	78.9	46.7	42.0	140.5	136.1	29.5	29.9	20.0	21.2	21.8			
18[a]	CH_3	Allyl	OH	CH_3	44.2	80.4	47.6	42.7	143.0	136.6	28.6	31.5	20.2	21.0	20.4			
20[a]	Prenyl	CH_3	CH_3	OH	43.5	79.6	47.0	41.9	140.0	135.9	28.6	32.4	20.0	21.5	36.3	124.6	130.2	17.8 26.1
21[a]	Prenyl	CH_3	OH	CH_3	44.1	80.2	48.7	41.7	141.7	136.2	28.0	33.5	19.9	20.6	36.0	124.2	132.3	17.8 26.2
24[a]	CH_3	Prenyl	CH_3	OH	43.1	78.6	47.1	42.1	140.7	136.1	29.6	29.9	20.0	21.2	21.8			
25[a][b]	CH_3	Prenyl	OH	CH_3	44.2	80.2	47.9	42.8	142.9	136.4	28.8	31.3	20.1	21.1	20.3			
57[a]	H	H	CH_3	OH	42.1	76.3	52.7	35.5	138.0	137.9	30.1	34.3	18.2	25.0				
58[a]	H	H	OH	CH_3	42.4	76.1	55.1	35.5	139.9	137.2	30.9	34.6	18.5	24.9				
59[a][b]	CH_3	CH_3	CH_3	OH	42.9	78.4	43.9	41.2	140.3	136.1	29.5	30.6	20.1	20.9	25.3			
60[a]	CH_3	CH_3	OH	CH_3	43.9	79.6	45.1	41.6	142.7	136.4	28.4	32.6	20.0	20.2	23.6			

[a]) C,H Correlation. [b]) 2D-Inadequate.



Bicyclo[2.2.2]oct-5-en-2-ones

C of R^1				C of R^2				CH_3–C(9)	CH_3–C(10)	CH_3–(R^1)	CH_3–(R^2)
			CH_3				CH_3				
								1.21	1.26		
14.9								1.20	1.20	1.01	
25.0				21.2				1.22[c])	1.19[c])	1.02	1.02
42.5	136.7	115.5		20.3				1.20	1.16		1.00
34.1	137.6	115.2						1.24	1.21		
40.2	137.1	115.3		39.7	135.2	117.0		1.20	1.20		
22.6				39.5	135.4	116.6		1.18	1.19	1.01	
36.2	122.2	131.3	17.6 25.9	19.9				1.19	1.14		0.99
28.6	123.6	131.0	17.7 25.7					1.20	1.21		
22.4				33.3	120.9	132.3	17.7 26.0	1.19	1.20	1.00	
41.7	102.6	64.3 64.7		19.9				1.20	1.17		1.08
23.0				47.5	202.6			1.18[c])	1.22[c])	1.24	
22.5				38.3	102.4	64.1 65.1		1.17[c])	1.19[c])	1.12[c])	
34.0	29.9	63.1		20.8				1.19	1.15		0.99
36.5	29.9	34.5		20.6				1.20	1.16		1.00
38.8	30.6	7.7		20.6				1.20	1.16		1.00
36.3	20.3	56.9		20.6				1.16	1.10		0.95

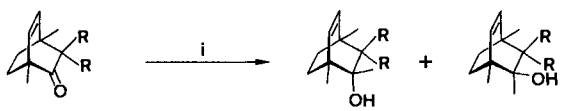


Bicyclo[2.2.2]oct-5-en-2-ols

C of R^2				R^3	R^4	CH_3–C(9)	CH_3–C(10)	CH_3–(R^1)	CH_3–(R^2)	CH_3–(R^3)	CH_3–(R^4)
			CH_3								
18.0				24.9		1.08	1.05		0.95	1.15	
20.0					19.5	1.12	1.06		0.91		1.08
38.3	139.2	116.8		26.4		1.06	1.05	0.88		1.01	
40.9	138.0	116.1			18.4	1.13	1.07	0.83			1.19
17.8				24.4		1.08	1.04		0.97	1.13	
20.3					19.6	1.12	1.07		0.90		1.10
31.9	123.3	133.6	17.9 26.3	26.5		1.06	1.05	0.91		1.02	
34.2	123.5	130.7	17.8 26.1		18.0	1.12	1.07	0.83			1.18
				28.5		1.08	1.08			1.10	
					23.3	1.17	1.10				1.20
19.7				24.4		1.08	1.03	0.92	0.81	1.02	
23.2					17.7	1.14	1.04	0.78	0.91		1.08

NMR Structural Assignments. – *Synthesis of Alcohols* **57–60**. *Tables 2* and *3* together with the *Figure* contain complete ^{13}C-NMR assignments for the majority of the compounds described in the present work. In addition, ^{1}H-NMR assignments have been made for the numerous CH_3 groups in these structures. In most cases C,H-CORR experiments were effected and in four examples (*viz.* **6**, **25**, **38**, and **59**) 2D-INADEQUATE experiments were performed. In the context of the NMR structural assignments of bicyclo[2.2.2]oct-5-en-2-ols, the four alcohols **57–60** were also prepared. Accordingly, treatment of **6** and **10** with MeLi in Et_2O afforded a 1:1 mixture **57**/**58** (86%) and 4:1 mixture **59**/**60** (82%), respectively *(cf. Scheme 13)*.

Scheme 13



6 R = H	86%	**57**	(1 : 1)	**58**
10 R = Me	82%	**59**	(4 : 1)	**60**

i) MeLi, Et_2O, 0–r.t., then aq. NH_4Cl soln.

In the light of previous examples concerning the stereochemistry of nucleophilic attack by MeLi on bicyclo[2.2.2]oct-5-en-2-ones *(vide supra)*, it is interesting to comment on these two results. Because a stereochemical bias due to substitution at C(3) is absent, the difference in stereoselectivity between the ketones **6** and **10** is unexpected. Whereas **10** affords predominantly **59**, the alcohol resulting from nucleophilic attack on the less hindered face, the attack of MeLi on **6** is totally non-stereoselective. It would appear that subtle changes in substitution at C(3) structurally modify the bicyclooctane skeleton and thus influence the direction of nucleophilic attack on the 2-carbonyl group.

Experimental Part

General. See [7a]. Li wire and MeLi (*ca.* 1.6M soln. in Et_2O) were obtained from *Fluka*, 9-borabicyclo[3.3.1]nonane (9-BBN) from *Aldrich*. Solns. of LDA in THF/hexane were freshly prepared by adding BuLi (*ca.* 1.5M soln. in hexane, *Degussa*) dropwise to a soln. of $(i\text{-}Pr)_2NH$ (1.1 mol-equiv.) in THF at −20° under N_2. Workup implies: drying of the org. phase (Na_2SO_4), filtration, and evaporation. Petroleum ether refers to petroleum ether (b.p. 30–50°). M.p.: *Büchi-510* melting-point apparatus; uncorrected. NMR: *Bruker WH-360*, modified in a *AM*-model and interfaced to an *Aspect 2000* computer; in $CDCl_3$; chemical shifts (δ) in ppm relative to TMS.

1,4-Dimethylcyclohexa-1,4-diene (**7**). Following a published procedure [29], a soln. of 4-methylanisole (61 g, 0.5 mol) in Et_2O (300 ml) was added dropwise within 30 min to a freshly-prepared soln. of Li wire (14 g, 2 mol) in liq. NH_3 (800 ml) at −40°. After 1 h at −40°, EtOH (103 g) was added dropwise and NH_3 allowed to evaporate. After addition of ice-H_2O (400 g) and saturation with NaCl, the mixture was extracted with Et_2O. A soln. of oxalic acid (32 g) in H_2O (200 ml) was added to the combined org. phase, and the mixture was then mechanically stirred at r.t. during 1 h. Workup and fractional distillation (spinning-band column) *i.v.* gave *4-methylcyclohex-3-en-1-one* as a colourless oil (43 g, 78%). B.p. 55–57°/12 Torr ([29a]: 74°/17 Torr; [29b]: 36°/4 Torr). IR: 1720, 1440, 1340, 1200, 1060, 898, 780, 600. ^{1}H-NMR: 1.77 (*s*, 3 H); 2.43 (4 H); 2.83 (2 H); 5.42 (*m*, 1 H). MS: 110 (73, $M^{+\cdot}$), 82 (9), 68 (100), 67 (94), 53 (28), 39 (21).

A soln. of MeI (540 g, 3.8 mol) in Et_2O (500 ml) was added dropwise within 45 min to a stirred mixture of Li wire (30 g, 4.3 mol) in Et_2O (1 l) at −60°. The mixture was allowed to attain −10° during 2 h and then re-cooled to −60° prior to the dropwise addition, within 1 h, of a soln. of 4-methylcyclohex-3-en-1-one (90 g, 0.82 mol) in

Et_2O (1 l). After further 30 min at −60°, MeOH (50 ml) was added dropwise cautiously, and the mixture was then poured into cold 10% aq. NH_4Cl soln. Extraction (Et_2O), workup and distillation *i.v.* afforded *1,4-dimethylcyclohex-3-en-1-ol* [30] as a colourless oil (100 g, 97%). B.p. 38–40°/0.2 Torr. IR: 3380 (br.), 1440, 1378, 1170, 1122, 1102, 1060, 1040, 924, 910, 880. ^{1}H-NMR (+D_2O): 1.20 (*s*, 3 H); 1.68 (*s*, 3 H); 1.30–2.30 (6 H); 5.29 (*m*, 1 H). MS: 126 (11, M^+), 108 (62), 93 (35), 83 (42), 68 (62), 58 (100).

A soln. of 2,6-di(*tert*-butyl)-4-methylphenol (BHT) (50 mg) in 1,4-dimethylcyclohex-3-en-1-ol (100 g, 0.79 mol) was added within 6 h to $KHSO_4$ (30 g) and BHT (50 mg) at 120° (bath: 200°) with continual distillation at 730 Torr. Separation of the org. phase from the distillate (b.p. 80–90°), workup, and redistillation afforded a colourless oil (84 g, 98%), b.p. 130–138°/730 Torr, containing **7**[21]) (53%) ([31]: 39%; ^{1}H-NMR: 1.73 (br. *s*, 6 H); 2.10 (br. *s*, 4 H); 5.54 (br. *s*, 2 H)) and *p*-xylene (8%).

2-Chloro-1,4-dimethylbicyclo[2.2.2]oct-5-ene-2-carbonitrile (**8**; 5:1 diastereoisomeric mixture). A soln. of **7** (purity: 53%; 86 g) and 2-chloroacrylonitrile (86 g, 0.98 mol) in toluene (350 ml) containing hydroquinone (50 mg) was heated at 90° during 60 h under N_2. Fractional distillation *i.v.* afforded **8** as a colourless oil (58 g, 71%). B.p. 66–70°/0.1 Torr. Crystallisation from petroleum ether at −60° resulted in the purification of the major diastereoisomer[22]). IR: 1460, 1390, 1370, 1120, 1020, 952, 898, 810, 752, 702. ^{1}H-NMR: 1.17 (*s*, 3 H); 1.30 (*m*, 1 H); 1.46 (*m*, 2 H); 1.47 (*s*, 3 H); 1.95 (*m*, 1 H); 2.01 (*dd*, J = 14.5, 3.5, 1 H); 2.42 (*d*, J = 14.5, 1 H); 5.86 (*d*, J = 8, 1 H); 6.11 (*d*, J = 8, 1 H). ^{13}C-NMR: 139.0 (*d*); 133.6 (*d*); 119.7 (*s*); 63.5 (*s*); 53.6 (*t*); 42.8 (*s*); 34.9 (*s*); 33.0 (*t*); 31.4 (*t*); 23.8 (*q*); 20.9 (*q*). MS: 195 (0, M^+), 132 (31), 116 (12), 108 (100), 93 (51), 91 (14), 77 (12).

1,4-Dimethylbicyclo[2.2.2]oct-5-en-2-one (**6**). A mixture of **19** (5:1 diastereoisomeric mixture; 47 g, 0.24 mol) and $Na_2S \cdot 9\,H_2O$ (228 g, 0.95 mol) in EtOH (300 ml) was stirred a reflux for 24 h under N_2. The cooled mixture was poured into 10% aq. NaOH soln. (1.5 l). Saturation with NaCl, continuous extraction (petroleum ether), workup, and fractional distillation *i.v.* afforded **6** as a colourless oil (26 g, 72%). B.p. 68–70°/10 Torr ([11a]: 80°/13 Torr). IR: 1720, 1458, 1406, 1380, 1370, 1320, 1260, 1220, 1160, 1080, 1070, 840, 704, 672. ^{1}H-NMR: 1.21 (*s*, 3 H); 1.26 (*s*, 3 H); 1.39–1.71 (4 H); 1.95 (2 H); 5.71 (*d*, J = 8, 1 H); 6.33 (*d*, J = 8, 1 H). ^{13}C-NMR: *(cf. Table 2)*. MS: 150 (1, M^+), 108 (100), 93 (81), 91 (14), 79 (8), 77 (11), 65 (5).

(1RS,3RS,4SR)-1,3,4-Trimethylbicyclo[2.2.2]oct-5-en-2-one (**9**). A soln. of **6** (11.6 g, 0.076 mol) in THF (50 ml) was added dropwise within 45 min to a stirred soln. of LDA (0.085 mol) in THF/hexane 2:1 (150 ml) at −60° under N_2. After 30 min at −60°, the mixture was allowed to attain −30° and a soln. of MeI (26 g, 0.18 mol) in HMPA (50 ml) was added dropwise. After a further 10 min at −30°, the mixture was poured into cold 10% aq. NH_4Cl soln. (500 ml). Saturation with NaCl, continuous extraction (petroleum ether), and workup gave a brown oil (13.6 g) which was filtered through silica gel (100 g) with Et_2O. Fractional distillation *i.v.* afforded **9** as a pale-yellow oil (11 g, 88%). B.p. 78–80°/10 Torr. IR ($CDCl_3$): 1715, 1450, 1380, 1370, 1210, 1040, 978. ^{1}H-NMR: 1.01 (*d*, J = 7, 3 H); 1.20 (2*s*, 6 H); 1.00–2.00 (5 H); 5.76 (*d*, J = 8, 1 H); 6.02 (*d*, J = 8, 1 H). ^{13}C-NMR: *(cf. Table 2)*. MS: 164 (1.5, M^+), 108 (100), 93 (66), 91 (10), 77 (8), 65 (2).

Also isolated, by fractional distillation *i.v.* and prep. GC was *1,3,3,4-tetramethylbicyclo[2.2.2]oct-5-en-2-one* (**10**): colourless oil, *ca.* 5% yield. B.p. 83–85°/10 Torr. IR: 1722, 1470, 1380, 1320, 1280, 1240, 1202, 1122, 1036, 1020, 910, 856, 780, 712. ^{1}H-NMR: 1.02 (2*s*, 6 H); 1.19 (*s*, 3 H); 1.22 (*s*, 3 H); 1.10–2.00 (4 H); 5.74 (*d*, J = 8, 1 H); 6.14 (*d*, J = 8, 1 H). ^{13}C-NMR: *(cf. Table 2)*. MS: 178 (1.5, M^+), 135 (11), 119 (3), 108 (100), 93 (50), 91 (13), 77 (8).

(1RS,3RS,4SR)-1,3,4-Trimethyl-3-(prop-2′-enyl)bicyclo[2.2.2]oct-5-en-2-one (**11**). A soln. of **9** (13.5 g, 0.082 mol) in THF (130 ml) was added dropwise within 30 min to a stirred soln. of LDA (0.1 mol) in THF/hexane 2:1 (210 ml) at −60° under N_2. After a further 30 min at −60°, a soln. of allyl iodide (38.6 g, 0.23 mol) in HMPA (75 ml) was added dropwise within 30 min. The mixture was left at −60° for an additional 30 min and then poured into cold 10% aq. NH_4Cl soln. (500 ml). Saturation with NaCl, continuous extraction (petroleum ether), filtration through silica gel (100 g) with Et_2O, concentration, and fractional distillation *i.v.* afforded **11** as a pale-yellow oil (16 g, 95%). B.p. 53–55°/0.05 Torr. IR: 1720, 1640, 1460, 1376, 1220, 1010, 1000, 918, 780, 717, 660. ^{1}H-NMR: 1.00 (*s*, 3 H); 1.16 (*s*, 3 H); 1.20 (*s*, 3 H); 1.23 (*m*, 1 H); 1.45 (*m*, 1 H); 1.56 (*m*, 1 H); 1.81 (*m*, 1 H); 2.09 (*m*, 1 H); 2.33 (*m*, 1 H); 4.88 (*m*, 2 H); 5.64 (*m*, 1 H); 5.65 (*d*, J = 8, 1 H); 6.14 (*d*, J = 8, 1 H). ^{13}C-NMR: *(cf. Table 2)*. MS: 204 (1, M^+), 135 (6), 108 (100), 93 (66), 91 (23), 79 (9), 77 (15).

(1RS,2RS,3RS,4SR)- and (1RS,2SR,3RS,4SR)-1,2,3,4-Tetramethyl-3-(prop-2′-enyl)bicyclo[2.2.2]oct-5-en-2-ol (**12** and **13**, resp.). A soln. of MeLi (0.127 mol) in Et_2O (80 ml) was added dropwise within 30 min to a stirred soln. of **11** (16 g, 0.078 mol) in Et_2O (320 ml) at 0° under N_2. After a further 10 min at 0°, MeOH (5 ml) was added

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[21]) For spectral data of **7**, *cf.* [8b].

[22]) Configuration at C(2) unassigned.

dropwise, and then the mixture was poured cautiously into cold 10% aq. NH_4Cl soln. (800 ml). Saturation with NaCl, extraction (Et_2O), workup, and distillation *i.v.* afforded a 85:15 mixture **12**/**13** (16.1 g, 93%). B.p. 68–83°/0.1 Torr. Purification of a 5 g aliquot was effected by CC (silica gel (300 g), cyclohexane/AcOEt 9:1).

Data of **12**. Colourless oil, R_f (cyclohexane/AcOEt 9:1) 0.30. IR: 3520 (br.), 1640, 1470, 1380, 1090, 1060, 1000, 920, 720. ^{1}H-NMR (+D_2O): 0.92 (2 H); 0.95 (*s*, 3 H); 1.05 (*s*, 3 H); 1.08 (*s*, 3 H); 1.15 (*s*, 3 H); 1.82 (2 H); 2.06 (*dd*, *J* = 14, 8, 1 H); 2.19 (*dd*, *J* = 14, 8, 1 H); 4.93 (br. *dd*, *J* = 11, 1 H); 4.94 (br. *d*, *J* = 18, 1 H); 5.78 (*d*, *J* = 8, 1 H); 5.92 (*d*, *J* = 8, 1 H); 5.94 (*m*, 1 H). ^{13}C-NMR *(cf. Table 3)*. MS: 220 (0, M^+), 161 (6), 133 (20), 119 (9), 108 (100), 93 (67), 91 (25), 77 (16).

Data of **13**. Colourless oil, R_f (cyclohexane/AcOEt 9:1) 0.40. IR: 3600, 3530 (br.), 1640, 1470, 1390, 1330, 1120, 1078, 1040, 920, 810, 720. ^{1}H-NMR (+D_2O): 0.91 (*s*, 3 H); 0.93 (*m*, 1 H); 1.06 (*s*, 3 H); 1.07 (*m*, 1 H); 1.08 (*s*, 3 H); 1.12 (*s*, 3 H); 1.49 (*m*, 1 H); 1.65 (*m*, 1 H); 1.98 (2 H); 4.99 (br. *d*, *J* = 11, 1 H); 5.00 (br. *d*, *J* = 18, 1 H); 5.81 (*d*, *J* = 8, 1 H); 6.11 (*m*, 1 H); 6.17 (*d*, *J* = 8, 1 H). ^{13}C-NMR: *(cf. Table 3)*. MS: 220 (0, M^+), 133 (14), 119 (7), 108 (100), 93 (64), 91 (22), 77 (15).

(1RS,3RS,4SR)-1,4-Dimethyl-3-(prop-2'-enyl)bicyclo[2.2.2]oct-5-en-2-one (**14**). As described for **11**, with **6** (13 g, 0.085 mol) in THF (120 ml), LDA (0.1 mol) in THF/hexane 4:1 (250 ml), and allyl iodide (38 g, 0.22 mol) in HMPA (80 ml). The mixture was stirred for 1 h at −60° and 3 h at −30° and then worked up as described for **11**: **14** as a colourless oil (11.7 g, 72%). B.p. 110–112°/12 Torr. IR: 1720, 1640, 1382, 1218, 1000, 916, 712. ^{1}H-NMR: 1.21 (*s*, 3 H); 1.24 (*s*, 3 H); 1.46 (2 H); 1.60 (2 H); 1.87 (*dd*, *J* = 7, 7, 1 H); 2.26 (*m*, 1 H); 2.40 (*m*, 1 H); 4.90 (br. *d*, *J* = 11, 1 H); 4.98 (br. *d*, *J* = 18, 1 H); 5.68 (*m*, 1 H); 5.70 (*d*, *J* = 8, 1 H); 6.05 (*d*, *J* = 8, 1 H). ^{13}C-NMR: *(cf. Table 2)*. MS: 190 (4, M^+), 108 (100), 93 (47), 91 (12), 79 (6), 77 (9).

Also isolated, by fractional dist. *i.v.* and prep. GC, was *1,4-dimethyl-3,3-bis(prop-2'-enyl)bicyclo[2.2.2]oct-5-en-2-one* (**15**): pale-yellow oil, 0.6 g (3%). B.p. (bulb-to-bulb dist.) 60–80°/0.2 Torr. IR: 1720, 1642, 1440, 1388, 1210, 1000, 918, 720. ^{1}H-NMR: 1.20 (2*s*, 6 H); 1.24 (*m*, 1 H); 1.47 (*ddd*, *J* = 13, 13, 3.5, 1 H); 1.63 (*m*, 1 H); 1.90 (*ddd*, *J* = 13, 9, 3.5, 1 H); 2.09 (*dd*, *J* = 14.5, 9, 1 H); 2.21 (*d*, *J* = 7, 2 H); 2.55 (*dd*, *J* = 14.5, 6, 1 H); 4.86 (br. *d*, *J* = 11, 1 H); 4.89 (br. *d*, *J* = 18, 1 H); 5.03 (br. *d*, *J* = 18, 1 H); 5.04 (br. *d*, *J* = 11, 1 H); 5.52 (*m*, 1 H); 5.55 (*d*, *J* = 8, 1 H); 5.95 (*m*, 1 H); 6.09 (*d*, *J* = 8, 1 H). ^{13}C-NMR: *(cf. Table 2)*. MS: 230 (9, M^+), 122 (6), 109 (100), 93 (51), 91 (13), 77 (9).

(1RS,3SR,4SR)-1,3,4-Trimethyl-3-(prop-2'-enyl)bicyclo[2.2.2]oct-5-en-2-one (**16**). A soln. of **14** (9.5 g, 0.05 mol) in THF (40 ml) was added dropwise within 30 min to a soln. of LDA (0.061 mol) in THF/hexane 2:1 (120 ml) at −60° under N_2. After 30 min at −60° a soln. of MeI (20 g, 0.14 mol) in HMPA (40 ml) was added dropwise within 30 min. After further 30 min at −60°, the mixture was worked up as described for **9** (21 g of brown oil, 200 g of silica gel): **16** as a pale-yellow oil (95 g, 94%). B.p. 118–120°/12 Torr (spinning-band column). IR: 1720, 1640, 1460, 1390, 1370, 1214, 1018, 918, 850, 718. ^{1}H-NMR: 1.01 (*s*, 3 H); 1.18 (*s*, 3 H); 1.19 (*s*, 3 H); 1.29 (*m*, 1 H); 1.49 (*m*, 1 H); 1.63 (*m*, 1 H); 1.90 (*m*, 1 H); 2.15 (*m*, 2 H); 4.95–5.05 (*m*, 2 H); 5.73 (*d*, *J* = 8, 1 H); 5.98 (*m*, 1 H); 6.11 (*d*, *J* = 8, 1 H). ^{13}C-NMR: *(cf. Table 2)*. MS: 204 (1, M^+), 135 (13), 108 (100), 93 (20), 91 (6), 77 (4).

(1RS,2RS,3SR,4SR)- and (1RS,2SR,3SR,4SR)-1,2,3,4-Tetramethyl-3-(prop-2'-enyl)bicyclo[2.2.2]oct-5-en-2-ol (**17** and **18**, resp.). As described for **12**/**13**, MeLi (0.068 mol) in Et_2O (40 ml), **16** (8.5 g, 0.042 mol) in Et_2O (170 ml), MeOH (5 ml), and 10% aq. NH_4Cl soln. (500 ml): 72:28 mixture **17**/**18** (8.1 g, 88%) which was purified by CC (silica gel (500 g), cyclohexane/AcOEt 9:1).

Data of **17**. Colourless oil. B.p. 64–68°/0.1 Torr. R_f (cyclohexane/AcOEt 9:1) 0.50. IR: 3600 (br.), 1640, 1460, 1380, 1100, 1060, 1008, 912, 718. ^{1}H-NMR (+D_2O): 0.88 (*s*, 3 H); 0.96 (2 H); 1.01 (*s*, 3 H); 1.05 (*s*, 3 H); 1.06 (*s*, 3 H); 1.84 (*m*, 1 H); 1.91 (*m*, 1 H); 2.01 (*m*, 1 H); 2.68 (*dd*, *J* = 14, 7, 1 H); 5.06 (br. *d*, *J* = 11, 1 H); 5.14 (br. *d*, *J* = 18, 1 H); 5.79 (*d*, *J* = 8, 1 H); 5.86 (*d*, *J* = 8, 1 H); 6.14 (*m*, 1 H). ^{13}C-NMR: *(cf. Table 3)*. MS: 220 (0, M^+), 161 (1), 121 (3), 108 (100), 93 (51), 91 (13), 77 (8).

Data of **18**. Colourless oil. B.p. 70–73°/0.1 Torr. R_f (cyclohexane/AcOEt 9:1) 0.33. IR: 3600, 3510 (br.), 1640, 1460, 1390, 1332, 1000, 918, 722. ^{1}H-NMR (+D_2O): 0.83 (*s*, 3 H); 0.93 (*ddd*, *J* = 12.5, 12.5, 7, 1 H); 1.07 (*s*, 3 H); 1.12 (*m*, 1 H); 1.13 (*s*, 3 H); 1.19 (*s*, 3 H); 1.58 (*m*, 1 H); 1.68 (*m*, 1 H); 2.20 (br. *d*, *J* = 7, 2 H); 4.99 (br. *d*, *J* = 11, 1 H); 5.01 (br. *d*, *J* = 18, 1 H); 5.80 (*d*, *J* = 8, 1 H); 6.00 (*m*, 1 H); 6.10 (*d*, *J* = 8, 1 H). ^{13}C-NMR: *(cf. Table 3)*. MS: 220 (0, M^+), 161 (3), 133 (5), 121 (4), 108 (100), 93 (54), 91 (16), 77 (11).

(1RS,3RS,4SR)-1,3,4-Trimethyl-3-(3'-methylbut-2'-enyl)-bicyclo[2.2.2]oct-5-en-2-one (**19**). As described for **11**, with **9** (11 g, 0.064 mol) in THF (100 ml), LDA (0.082 mol) in THF/hexane 3:1 (200 ml), 1-bromo-3-methylbut-2-ene (28 g, 0.19 mol) in HMPA (60 ml), and 10% aq. NH_4Cl soln. (600 ml): **19** as a colourless oil (12.7 g, 86%). B.p. 70–75°/0.05 Torr. IR: 1720, 1460, 1380, 1320, 1220, 1030, 1010, 1000, 908, 840, 712, 618. ^{1}H-NMR: 0.99 (*s*, 3 H); 1.14 (*s*, 3 H); 1.19 (*s*, 3 H); 1.20 (*m*, 1 H); 1.43 (*m*, 1 H); 1.52 (*s*, 3 H); 1.53 (*m*, 1 H); 1.64 (*s*, 3 H); 1.79 (*m*, 1 H); 2.03 (*dd*, *J* = 14, 7, 1 H); 2.25 (*dd*, *J* = 14, 7, 1 H); 5.02 (*m*, 1 H); 5.66 (*d*, *J* = 8, 1 H); 6.13 (*d*, *J* = 8, 1 H). ^{13}C-NMR: *(cf. Table 2)*. MS: 232 (4, M^+), 135 (5), 108 (100), 93 (28), 91 (6), 77 (3).

(1RS,2RS,3RS,4SR)- and (1RS,2SR,3RS,4SR)-1,2,3,4-Tetramethyl-3-(3'-methylbut-2'-enyl)bicyclo-[2.2.2]oct-5-en-2-ol (**20** and **21**, resp.). A soln. of **19** (9 g, 0.035 mol) in Et_2O (200 ml) was added dropwise within 30 min to a stirred soln. of MeLi (0.064 mol) in Et_2O (500 ml) at 0° under N_2. After a further 15 min at 0°, the mixture was worked up as described for **12/13** (500 ml of 10% aq. NH_4Cl soln.): 85:15 mixture **20/21** (9.4 g, 98%). B.p. 80–90°/0.05 Torr. Purification of a 5 g aliquot was effected by CC (silica gel (350 g), cyclohexane/AcOEt 19:1).

Data of **20**. Colourless oil. R_f (cyclohexane/AcOEt 19:1) 0.28. IR: 3640, 3520 (br.), 1460, 1380, 1310, 1080, 1060, 918, 718. ^{1}H-NMR (+D_2O): 0.97 (*s*, 3 H); 1.04 (*s*, 3 H); 1.08 (*s*, 3 H); 1.13 (*s*, 3 H); 0.85–1.05 (2 H); 1.53 (*s*, 3 H); 1.67 (*s*, 3 H); 1.70–1.95 (3 H); 2.08 (br. *dd*, J = 14.5, 7, 1 H); 5.30 (*m*, 1 H); 5.78 (*d*, J = 8, 1 H); 5.93 (*d*, J = 8, 1 H). ^{13}C-NMR: *(cf. Table 3)*. MS: 248 (1.5, M^+), 230 (26), 215 (13), 187 (24), 161 (33), 133 (35), 119 (21), 108 (100), 93 (40), 77 (17), 69 (23).

Data of **21**. Colourless oil. R_f (cyclohexane/AcOEt 19:1) 0.35. IR: 3600, 3570 (br.), 1460, 1384, 1328, 1120, 1070, 1040, 920, 910, 720. ^{1}H-NMR (+D_2O): 0.90 (*s*, 3 H); 0.92 (*m*, 1 H); 1.00–1.10 (1 H); 1.07 (*s*, 3 H); 1.10 (*s*, 3 H); 1.12 (*s*, 3 H); 1.47 (*m*, 1 H); 1.59 (*s*, 3 H); 1.69 (*s*, 3 H); 1.64 (*m*, 1 H); 1.77 (br. *dd*, J = 14.5, 4.5, 1 H); 2.09 (*dd*, J = 14.5, 8.5, 1 H); 5.44 (*m*, 1 H); 5.78 (*d*, J = 8, 1 H); 6.15 (*d*, J = 8, 1 H). ^{13}C-NMR: *(cf. Table 3)*. MS: 248 (0, M^+), 230 (7), 161 (8), 140 (9), 108 (100), 99 (28), 93 (29), 85 (16), 71 (10).

(1RS,3RS,4SR)-1,4-Dimethyl-3-(3'-methylbut-2'-enyl)bicyclo[2.2.2]oct-5-en-2-one (**22**). As described for **11**, with **6** (11 g, 0.072 mol) in THF (100 ml), LDA (0.088 mol) in THF/hexane 3:1 (240 ml), 1-bromo-3-methylbut-2-ene (30 g, 0.2 mol) in HMPA (70 ml). The mixture was left at −60° for a further 1.5 h at −60° and 1 h at −30° before being worked up as described for 11 (800 ml of 10% aq. NH_4Cl soln.): **22** as a colourless oil (14.2 g, 90%). B.p. 65–70°/0.05 Torr. IR: 1720, 1452, 1380, 1210, 1070, 1040, 830, 706, 660. ^{1}H-NMR: 1.20 (*s*, 3 H); 1.21 (*s*, 3 H); 1.35–1.70 (4 H); 1.57 (*s*, 3 H); 1.65 (*s*, 3 H); 1.80 (*t*, J = 6, 1 H); 2.20 (br. *t*, J = 6, 2 H); 5.07 (*m*, 1 H); 5.73 (*d*, J = 8, 1 H); 6.04 (*d*, J = 8, 1 H). ^{13}C-NMR: *(cf. Table 2)*. MS: 218 (3, M^+), 108 (100), 93 (35), 91 (8), 77 (5), 69 (2).

(1RS,3SR,4SR)-1,3,4-Trimethyl-3-(3'-methylbut-2'-enyl)bicyclo[2.2.2]oct-5-en-2-one (**23**). As described for **16**, with **22** (14.1 g, 0.064 mol) in THF (60 ml), LDA (0.078 mol) in THF/hexane 2:1 (150 ml), and MeI (25 g, 0.18 mol) in HMPA (50 ml). The mixture was left at −60° for a further 30 min and then worked up as described for **9** (600 ml of 10% aq. NH_4Cl soln.): **23** as a colourless oil (14.5 g, 97%). B.p. 70–75°/0.05 Torr. IR: 1720, 1460, 1380, 1370, 1320, 1220, 1024, 1016, 990, 904, 860, 840, 710, 610. ^{1}H-NMR: 1.00 (*s*, 3 H); 1.19 (*s*, 3 H); 1.20 (*s*, 3 H); 1.27 (*m*, 1 H); 1.48 (*m*, 1 H); 1.60 (*s*, 3 H); 1.62 (*m*, 1 H); 1.71 (*s*, 3 H); 1.89 (*m*, 1 H); 2.05 (*dd*, J = 14, 7, 1 H); 2.17 (*dd*, J = 14, 7, 1 H); 5.30 (*m*, 1 H); 5.71 (*d*, J = 8, 1 H); 6.10 (*d*, J = 8, 1 H). ^{13}C-NMR *(cf. Table 2)*. MS: 232 (5, M^+), 135 (5), 108 (100), 93 (27), 91 (6), 77 (4).

(1RS,2RS,3SR,4SR)- and (1RS,2SR,3SR,4SR)-3-(3'-Methylbut-2'-enyl)-1,2,3,4-tetramethylbicyclo-[2.2.2]oct-5-en-2-ol (**24** and **25**, resp.). As described for **12/13** with MeLi (0.036 mol) in Et_2O (22 ml; dropwise addition within 10 min at 20°), **23** (5 g, 0.022 mol) in Et_2O (100 ml), MeOH (2 ml; after 15 min at 20°), and 10% aq. NH_4Cl soln. (200 ml): 60:40 mixture **24/25** (5 g, 93%). B.p. 75–85°/0.05 Torr. Purification was effected by CC (silica gel (350 g), cyclohexane/AcOEt 19:1).

Data of **24**. Colourless oil. R_f (cyclohexane/AcOEt 19:1) 0.46. IR: 3560 (br.), 1460, 1380, 1326, 1102, 1062, 904, 808, 718, 670, 620. ^{1}H-NMR (+D_2O): 0.91 (*s*, 3 H); 1.02 (*s*, 3 H); 1.05 (*s*, 3 H); 1.06 (*s*, 3 H); 0.80–1.05 (2 H); 1.68 (*s*, 3 H); 1.73 (*s*, 3 H); 1.75–1.95 (2 H); 2.05 (*m*, 1 H); 2.60 (*dd*, J = 14.5, 8.5, 1 H); 5.45 (*m*, 1 H); 5.79 (*d*, J = 8, 1 H); 5.87 (*d*, J = 8, 1 H). ^{13}C-NMR: *(cf. Table 3)*. MS: 248 (0, M^+), 140 (9), 108 (100), 93 (32), 85 (16), 69 (11).

Data of **25**. Colourless oil. R_f (cyclohexane/AcOEt 19:1) 0.23. IR: 3600, 3510 (br.), 1460, 1390, 1330, 1130, 1090, 1064, 1042, 938, 918, 720. ^{1}H-NMR (+D_2O): 0.83 (*s*, 3 H); 0.93 (*ddd*, J = 12, 12, 6, 1 H); 1.07 (*s*, 3 H); 1.12 (*s*, 3 H); 1.13 (*m*, 1 H); 1.18 (*s*, 3 H); 1.57 (*m*, 1 H); 1.60 (*s*, 3 H); 1.69 (*s*, 3 H); 1.70 (*m*, 1 H); 2.09 (*m*, 2 H); 5.34 (*m*, 1 H); 5.80 (*d*, J = 8, 1 H); 6.11 (*d*, J = 8, 1 H). ^{13}C-NMR: *(cf. Table 3)*. MS: 248 (0, M^+), 161 (4), 133 (5), 108 (100), 93 (36), 91 (11), 82 (13), 69 (9).

(1RS,3RS,4SR)-(1,2,4-Trimethyl-3-oxobicyclo[2.2.2]oct-5-en-2-yl)acetaldehyde (**26**). O_3 (*ca.* 0.96 g/h) was introduced into a soln. of **19** (4.9 g, 0.019 mol) in CH_2Cl_2 (120 ml) at −65° during 62 min. After the dropwise addition of Me_2S (8.4 g, 0.135 mol) at −65°, the mixture was allowed to attain 20° during 30 min. Evaporation was followed by an extractive workup (petroleum ether) to give a yellow oil (4.3 g) which was purified by CC (silica gel (300 g), cyclohexane/AcOEt 7:3) to afford **26** as a colourless oil (2.4 g, 61%). B.p. 78–82°/0.1 Torr. R_f (cyclohexane/AcOEt 7:3) 0.40. IR: 1720, 1460, 1420, 1380, 1320, 1030, 780, 720, 612. ^{1}H-NMR: 1.17 (2*s*, 6 H); 1.23 (*s*, 3 H); 1.10–2.00 (4 H); 2.38 (*ABX*, J = 14, 4.5, 2.5, 2 H); 5.78 (*d*, J = 8, 1 H); 6.13 (*d*, J = 8, 1 H); 9.60 (*dd*, J = 4.5, 2.5, 1 H). MS: 206 (0.5, M^+), 120 (13), 108 (100), 93 (66), 91 (12), 77 (7).

(1RS,3RS,4SR)-3-[(1',3'-Dioxolan-2'-yl)methyl]-1,3,4-trimethylbicyclo[2.2.2]oct-5-en-2-one (**27**). A mixture of **26** (2.3 g, 0.011 mol), ethylene glycol (1.1 g, 0.018 mol), and $TsOH \cdot H_2O$ (60 mg) in benzene (30 ml) was heated at reflux during 2 h using a *Dean-Stark* water separator. The mixture was cooled to r.t., washed with sat. aq. $NaHCO_3$ soln. and the org. phase dried (Na_2SO_4). Evaporation and distillation *i.v.* afforded **27** as a white

crystalline solid (2.35 g, 85%). B.p. 90–93°/0.1 Torr. M.p. 45–46°. IR: 1720, 1460, 1420, 1378, 1320, 1210, 1130, 1050, 1020, 960, 910, 860, 716. ^{1}H-NMR: 1.08 (*s*, 3 H); 1.17 (*s*, 3 H); 1.20 (*s*, 3 H); 1.24 (*m*, 1 H); 1.45 (*m*, 1 H); 1.53 (*m*, 1 H); 1.75 (*ABX*, J = 18, 6, 4, 2 H); 1.82 (*m*, 1 H); 3.81 (4 H); 4.97 (*dd*, J = 6, 4, 1 H); 5.74 (*d*, J = 8, 1 H); 6.17 (*d*, J = 8, 1 H). ^{13}C-NMR: *(cf. Table 2)*. MS: 250 (0, M^{+}), 108 (100), 93 (34), 91 (5), 87 (17), 73 (26).

*(1*RS*,2*RS*,3*RS*,4*SR*)- and (1*RS*,2*SR*,3*RS*,4*SR*)-3-[(1',3'-Dioxolan-2'-yl)methyl]-1,2,3,4-tetramethylbicyclo[2.2.2]oct-5-en-2-ol* (**28** and **29**, resp.). As described for **12**/**13**, with MeLi (0.013 mol) in Et_2O (8 ml; dropwise addition within 5 min), **27** (2.1 g, 7.9 mmol) in Et_2O (80 ml), MeOH (2 ml), and 10% aq. NH_4Cl soln. (100 ml): *ca.* 9:1 mixture **28**/**29**, inseparable by CC, as a colourless oil (2.2 g, 98%). B.p. 103–107°/0.05 Torr. R_f (cyclohexane/AcOEt 7:3) 0.28. IR: 3520 (br.), 1460, 1380, 1120, 1040, 960, 920, 840, 718. ^{1}H-NMR (+D_2O): 1.03 (*s*, 3 H); 1.06 (*s*, 3 H); 1.10 (*s*, 3 H); 1.16 (*s*, 3 H); 1.00–1.70 (4 H); 1.76 (*d*, J = 4, 2 H); 3.88 (4 H); 4.94 (*dd*, J = 4, 4, 1 H); 5.85 (*AB*, J = 8, 2 H). MS: 266 (0, M^{+}), 115 (13), 108 (100), 93 (52), 91 (20), 77 (14), 73 (83).

*(1*RS*,2*RS*,4*SR*)-(1,2,4-Trimethyl-3-oxobicyclo[2.2.2]oct-5-en-2-yl)acetaldehyde* (**30**). As described for **26**, with O_3 (*ca.* 0.96 g/h; for 13 min), **23** (1 g, 4.1 mmol) in CH_2Cl_2 (50 ml), and Me_2S (1.7 g, 0.027 mol). Evaporation and purification of the residue by CC (silica gel (100 g), cyclohexane/AcOEt 7:3) afforded **30** as a colourless oil (0.64 g, 76%). B.p. (bulb-to-bulb dist.) 80–100°/0.1 Torr. R_f (cyclohexane/AcOEt 7:3) 0.42. IR: 1720, 1460, 1378, 1320, 1280, 1210, 1030, 1020, 910, 712. ^{1}H-NMR: 1.18 (*s*, 3 H); 1.22 (*s*, 3 H); 1.24 (*s*, 3 H); 1.35 (*m*, 1 H); 1.54 (*m*, 1 H); 1.61 (*m*, 1 H); 1.76 (*m*, 1 H); 2.27 (*ABX*, J = 14, 3.5, 3.5, 2 H); 5.81 (*d*, J = 8, 1 H); 6.14 (*d*, J = 8, 1 H); 9.94 (*dd*, J = 3.5, 3.5, 1 H). ^{13}C-NMR: *(cf. Table 2)*. MS: 206 (0, M^{+}), 108 (100), 93 (48), 91 (7), 77 (4), 58 (7).

*(1*RS*,3*SR*,4*SR*)-3-[(1',3'-Dioxolan-2'-yl)methyl]-1,3,4-trimethylbicyclo[2.2.2]oct-5-en-2-one* (**31**). As described for **27**, with **30** (3.8 g, 0.018 mol), ethylene glycol (1.8 g, 0.029 mol), $TsOH \cdot H_2O$ (100 mg), and benzene (50 ml): **31** as a colourless oil (3.9 g, 84%). B.p. 95–100°/0.1 Torr. IR: 1720, 1460, 1420, 1380, 1320, 1212, 1130, 1050, 1030, 960, 910, 840, 718. ^{1}H-NMR: 1.12 (*s*, 3 H); 1.17 (*s*, 3 H); 1.19 (*s*, 3 H); 1.29 (*ddd*, J = 12, 12, 7, 1 H); 1.47 (*ddd*, J = 12, 12, 3, 1 H); 1.65 (*m*, 1 H); 1.73 (*ABX*, J = 14, 6, 3, 2 H); 1.85 (*ddd*, J = 12, 10, 3, 1 H); 3.88 (4 H); 5.23 (*dd*, J = 6, 3, 1 H); 5.71 (*d*, J = 8, 1 H); 6.10 (*d*, J = 8, 1 H). ^{13}C-NMR: *(cf. Table 2)*. MS: 250 (0, M^{+}), 108 (100), 93 (39), 91 (7), 84 (4), 73 (7).

*(1*RS*,2*RS*,3*SR*,4*SR*)- and (1*RS*,2*SR*,3*SR*,4*SR*)-3-[(1',3'-Dioxolan-2'-yl)methyl]-1,2,3,4-tetramethylbicyclo[2.2.2]oct-5-en-2-ol* (**32** and **33**, resp.). As described for **12**/**13**, with MeLi (0.022 mol) in Et_2O (14 ml; dropwise addition within 10 min), **31** (3.8 g, 0.015 mol) in Et_2O (140 ml), MeOH (2 ml), and 10% aq. NH_4Cl soln. (100 ml): 80:20 mixture **32**/**33** (3.6 g, 91%) which was separated by CC (silica gel (200 g), cyclohexane/AcOEt 7:3).

Data of **32**. White crystalline solid. M.p. 38–40°. B.p. 100–103°/0.1 Torr. R_f (cyclohexane/AcOEt 7:3) 0.44. IR: 3490 (br.), 1460, 1412, 1390, 1375, 1130, 1040, 988, 950, 920, 840, 720. ^{1}H-NMR (+D_2O): 0.89 (*m*, 2 H); 0.90 (*s*, 3 H); 1.04 (2*s*, 6 H); 1.11 (*s*, 3 H); 1.65–1.75 (2 H); 2.05 (*m*, 1 H); 2.24 (*dd*, J = 14, 9, 1 H); 3.88 (2 H); 4.03 (2 H); 4.97 (*dd*, J = 9, 3, 1 H); 5.84 (*s*, 2 H). MS: 266 (0, M^{+}), 158 (28), 115 (22), 108 (100), 93 (65), 73 (62).

Data of **33**. White crystalline solid. M.p. 57–59°. R_f (cyclohexane/AcOEt 7:3) 0.22. IR: 3500 (br.), 1460, 1410, 1390, 1330, 1120, 1070, 1040, 920, 840, 720. ^{1}H-NMR (+D_2O): 0.92 (*s*, 3 H); 1.07 (*s*, 3 H); 1.14 (*s*, 3 H); 1.21 (*s*, 3 H); 0.87–1.00 (2 H); 1.48–1.67 (2 H); 1.79 (*dd*, J = 16, 6.5, 1 H); 1.93 (*d*, J = 16, 1 H); 3.89 (4 H); 5.01 (*dd*, J = 6.5, 2, 1 H); 5.82 (*d*, J = 8, 1 H); 6.11 (*d*, J = 8, 1 H). MS: 266 (0, M^{+}), 186 (3), 171 (5), 134 (7), 115 (7), 108 (44), 93 (100), 73 (62).

General Procedure for the β-Cleavage of Alkoxides: Preparation of Ketones **34**, **37**, **38**, **40**, *and* **41**. In 11 separate experiments, a soln. of **12**, **13**, **17**, **18**, **20**, **21**, **24**, **25**, **28** + **29** (9:1), **32** and **33** in HMPA (1 ml for 1 mmol of substrate) was added dropwise to a stirred slurry of KH (1.5 mmol for 1 mmol of substrate) in HMPA (4 ml for 1 mmol of substrate) at 20° under N_2. After 30 min at 20°, the mixture was heated at 50° or 70° until disappearance of substrate (TLC analysis). The mixture was then cooled to 5° and cautiously poured into an excess of sat. aq. NH_4Cl soln. Extraction (Et_2O), workup, CC (silica gel, cyclohexane/AcOEt 9:1), and distillation *i.v.* afforded the products described in *Table 1*.

*(3*RS*,1'*SR*)-3-(1',4'-Dimethylcyclohex-3'-enyl)-3-methylhex-5-en-2-one* (**34**; 6% yield from **12**, reaction conditions: 70°/1 h). B.p. (bulb-to-bulb dist.) 140–150°/0.1 Torr. R_f (cyclohexane/AcOEt 9:1) 0.45. IR: 1700, 1642, 1440, 1380, 1360, 1220, 1002, 962, 920, 810, 780, 610. ^{1}H-NMR: 0.88 (*s*, 3 H); 1.16 (*s*, 3 H); 1.36 (*m*, 1 H); 1.53 (*m*, 1 H); 1.63 (br. *s*, 3 H); 1.50–2.00 (4 H); 2.11 (*s*, 3 H); 2.28 (*m*, 1 H); 2.83 (*dd*, J = 14, 6, 1 H); 4.99 (*m*, 1 H); 5.00 (*m*, 1 H); 5.26 (*m*, 1 H); 5.55 (*m*, 1 H). ^{13}C-NMR: (*cf.* the *Fig.*). MS: 220 (0, M^{+}), 121 (4), 109 (26), 108 (100), 93 (47), 79 (12), 67 (23).

*(1*RS*,2*SR*,6*RS*,7*SR*)-1,2,4,6,7-Pentamethyl-3-oxatricyclo[5.2.2.0^{2,6}]undec-8-ene* (**35**; 52% yield from **13**; reaction conditions: 70°/1 h). B.p. (bulb-to-bulb dist.) 150–160°/0.1 Torr. M.p. 34–36°. IR: 1470, 1390, 1150, 1100, 1080, 1060. ^{1}H-NMR: 0.97 (*s*, 3 H); 1.02 (*s*, 3 H); 1.07 (*s*, 3 H); 1.12 (*s*, 3 H); 0.80–2.00 (9 H); 3.77 (*m*, 1 H); 5.81 (2 H). MS: 220 (0, M^{+}), 112 (100), 108 (34), 97 (10), 93 (23), 77 (6), 69 (15).

(1RS,2RS,6SR,7SR)-1,2,4,6,7-Pentamethyl-3-oxatricyclo[5.2.2.0^{2,6}]undec-8-ene (**36**; 47% yield from **17**; reaction conditions: 70°/1 h). B.p. (bulb-to-bulb dist.) 150–160°/0.1 Torr. IR: 1460, 1390, 1370, 1100, 1060, 1012. ^{1}H-NMR: 0.90 (*s*, 3 H); 0.99 (2*s*, 6 H); 1.00 (*s*, 3 H); 1.26 (*d*, *J* = 6, 3 H); 0.90–2.40 (6 H); 4.09 (*m*, 1 H); 5.73 (*d*, *J* = 8, 1 H); 5.96 (*d*, *J* = 8, 1 H). MS: 220 (0, M^+), 112 (100), 108 (68), 97 (18), 93 (44), 77 (13), 69 (30).

(3RS,1'RS)-3-(1',4'-Dimethylcyclohex-3'-enyl)-3-methylhex-5-en-2-one (**37**; 4% yield from **18**, reaction conditions: 70°/1 h). B.p. (bulb-to-bulb dist.) 150–160°/0.1 Torr. IR: 1700, 1642, 1440, 1380, 1360, 1216, 1002, 962, 920, 810, 780, 610. ^{1}H-NMR: 0.90 (*s*, 3 H); 1.17 (*s*, 3 H); 1.63 (br. *s*, 3 H); 1.40–1.70 (7 H); 2.13 (*s*, 3 H); 2.83 (*dd*, *J* = 14, 6, 1 H); 5.02 (*m*, 1 H); 5.03 (*m*, 1 H); 5.27 (*m*, 1 H); 5.60 (*m*, 1 H). ^{13}C-NMR: (*cf.* the *Fig.*). MS: 220 (0, M^+), 121 (3), 109 (25), 108 (100), 93 (41), 79 (12), 67 (28), 55 (27).

(3RS,1'SR)-3-(1',4'-Dimethylcyclohex-3'-enyl)-3,6-dimethylhept-5-en-2-one (**38**; 16% yield from **20**; reaction conditions: 70°/1 h). B.p. (bulb-to-bulb dist.) 150–160°/0.1 Torr. R_f (cyclohexane/AcOEt 7:3) 0.63. IR: 1700, 1450, 1380, 1360, 1220, 1170, 1080, 960, 890, 810, 780. ^{1}H-NMR: 0.89 (*s*, 3 H); 1.13 (*s*, 3 H); 1.00–2.10 (6 H); 1.58 (*s*, 3 H); 1.63 (*s*, 3 H); 1.66 (*s*, 3 H); 2.10 (*s*, 3 H); 2.28 (*d*, *J* = 15, 1 H); 2.66 (*dd*, *J* = 15, 6, 1 H); 4.87 (*m*, 1 H); 5.27 (*m*, 1 H). ^{13}C-NMR: (*cf.* the *Fig.*). MS: 248 (0, M^+), 192 (7), 139 (21), 121 (7), 108 (100), 93 (27), 85 (18), 69 (25).

Also isolated was *3,6-dimethylhex-5-en-2-one* (**39**)[23]). R_f (cyclohexane/AcOEt 7:3) 0.52. IR: 1720, 1380, 1360, 1240, 1170, 1120, 1083, 1060, 960, 882, 840, 780. ^{1}H-NMR: 1.08 (*d*, *J* = 6, 3 H); 1.63 (*s*, 3 H); 1.71 (*s*, 3 H); 2.13 (*s*, 3 H); 1.70–2.80 (3 H); 5.06 (*m*, 1 H). MS: 140 (0, M^+), 124 (16), 109 (7), 95 (20), 81 (12), 68 (23), 57 (100).

With **32** as substrate (reaction conditions: 70°/1 h), **38** was isolated (*ca.* 2% yield) together with **39**[23]) *(vide supra)*.

(3RS,1'RS)-3-(1',4'-Dimethylcyclohex-3'-enyl)-3,6-dimethylhept-5-en-2-one (**40**; 26% yield from **24**; reaction conditions: 50°/1 h). B.p. (bulb-to-bulb dist.) 150–160°/0.1 Torr. R_f (cyclohexane/AcOEt 7:3) 0.63. IR: 1698, 1440, 1380, 1350, 1220, 1170, 1080, 1060, 960, 808. ^{1}H-NMR: 0.90 (*s*, 3 H); 1.13 (*s*, 3 H); 1.40–2.10 (6 H); 1.60 (*s*, 3 H); 1.63 (*s*, 3 H); 1.66 (*s*, 3 H); 2.11 (*s*, 3 H); 2.19 (*d*, *J* = 15, 1 H); 2.65 (*dd*, *J* = 15, 6, 1 H); 4.91 (*m*, 1 H); 5.28 (*m*, 1 H). ^{13}C-NMR: (*cf.* the *Fig.*). MS: 248 (0, M^+), 139 (27), 121 (6), 108 (100), 93 (28), 85 (20), 69 (28).

Also isolated was **39**[23]) *(vide supra)*.

With **25** as substrate (reaction conditions: 50°/1 h), **62** was isolated (*ca.* 2% yield) together with **39**[23]) *(vide supra)*.

(3RS,1'SR)-3-(1',4'-Dimethylcyclohex-3'-enyl)-4-(1'',3''-dioxolan-2''-yl)-3-methylbutan-2-one (**41**; 10% yield from **28**, **29** (*ca.* 9:1, *vide supra*); reaction conditions: 70°/1 h). B.p. (bulb-to-bulb dist.) 150–170°/0.05 Torr. R_f (cyclohexane/AcOEt 7:3) 0.36. ^{1}H-NMR: 0.86 (*s*, 3 H); 1.30 (*s*, 3 H); 0.90–2.60 (8 H); 1.63 (br. *s*, 3 H); 2.17 (*s*, 3 H); 3.80 (*m*, 4 H); 4.90 (*dd*, *J* = 7, 4, 1 H); 5.25 (*m*, 1 H).

Also isolated was **42**[23]). R_f (cyclohexane/AcOEt 7:3) 0.20. IR: 1718, 1360, 1160, 1040, 960, 840, 800, 770. ^{1}H-NMR: 1.13 (*d*, *J* = 7, 3 H); 1.75 (*m*, 2 H); 2.13 (*s*, 3 H); 2.77 (*m*, 1 H); 3.88 (*m*, 4 H); 4.88 (*t*, *J* = 4.5, 1 H).

With **32** as substrate (reaction conditions: 70°/1 h), no products were isolated.

With **33** as substrate (reaction conditions: 70°/3 h), only **42** was isolated[23]).

(1RS,3RS,4SR)-3-(3'-Hydroxypropyl)-1,3,4-trimethylbicyclo[2.2.2]oct-5-en-2-one (**43**). A soln. of 9-BBN (2.1 g, 0.017 mol) in THF (50 ml) was added dropwise within 1 h to a stirred soln. of **11** (32 g, 0.016 mmol) at 25° under N_2. After further 2 h at 25°, the mixture was cooled and maintained at 5° during the addition of 3N aq. NaOH soln. (7 ml) followed by 35% aq. H_2O_2 soln. (7 ml). The mixture was then heated at 50° for 1 h. Evaporation and addition of H_2O (100 ml) was followed by extraction (Et_2O). Workup gave a pale-yellow oil (3.9 g) which was purified by CC (silica gel, cyclohexane/AcOEt 7:3). Distillation *i.v.* afforded **43** as a colourless oil (3.1 g, 89%). B.p. 100–102°/0.05 Torr. R_f (cyclohexane/AcOEt 1:1) 0.27. IR: 3420 (br.), 1710, 1450, 1370, 1060, 990, 900, 710, 610. ^{1}H-NMR (+D_2O): 0.99 (*s*, 3 H); 1.15 (*s*, 3 H); 1.19 (*s*, 3 H); 1.10–1.70 (7 H); 1.81 (*m*, 1 H); 3.44 (*t*, *J* = 6.5, 2 H); 5.65 (*d*, *J* = 8, 1 H); 6.20 (*d*, *J* = 8, 1 H). ^{13}C-NMR: *(cf. Table 2)*. MS: 222 (0, M^+), 135 (6), 114 (4), 108 (100), 93 (55), 91 (17), 77 (10).

(1RS,3RS,4SR)-3-[3'-(p-Toluenesulfonyloxy)propyl]-1,3,4-trimethylbicyclo[2.2.2]oct-5-en-2-one (**44**). A soln. of **43** (3.1 g, 0.014 mmol), TsCl (4.5 g, 0.024 mmol), and pyridine (3 g, 0.038 mmol) in CH_2Cl_2 (60 ml) was stirred at reflux during 8 h. Evaporation, addition of 10% aq. HCl soln. (100 ml), extraction (Et_2O), and workup gave a viscous yellow oil (6.2 g). Purification by CC (silica gel (250 g), cyclohexane/AcOEt 7:3) afforded **44** as a viscous colourless oil (6.0 g, 91%). R_f (cyclohexane/AcOEt 7:3) 0.34. ^{1}H-NMR: 0.96 (*s*, 3 H); 1.11 (*s*, 3 H); 1.17 (*s*, 3 H); 1.00–1.60 (7 H); 1.79 (*m*, 1 H); 2.42 (*s*, 3 H); 3.86 (*m*, 2 H); 5.64 (*d*, *J* = 8, 1 H); 6.12 (*d*, *J* = 8, 1 H); 7.52 (*AB*, *J* = 8, 4 H).

(1RS,3RS,4SR)-3-(3'-Bromopropyl)-1,3,4-trimethylbicyclo[2.2.2]oct-5-en-2-one (**45**). A soln. of **44** (9 g, 0.024 mol) and LiBr (5.5 g, 0.063 mol) in acetone (200 ml) was stirred at reflux for 1.5 h. Evaporation was followed

[23]) Yield undetermined.

by addition of H_2O (150 ml) to the residue. Extraction (Et_2O), workup, and distillation *i.v.* afforded **45** as a colourless oil (6.5 g, 95%). B.p. 88–90°/0.05 Torr. IR: 1720, 1372, 1264, 1230, 1020, 862, 716. ^{1}H-NMR: 1.00 (*s*, 3 H); 1.16 (*s*, 3 H); 1.20 (*s*, 3 H); 1.25 (*m*, 1 H); 1.40–1.90 (7 H); 3.27 (*t*, J = 6, 2 H); 5.69 (*d*, J = 8, 1 H); 6.19 (*d*, J = 8, 1 H). ^{13}C-NMR: *(cf. Table 2)*. MS: 284 (0, M^+), 135 (6), 108 (100), 93 (43), 91 (12), 79 (5), 77 (8).

(1RS,2RS,6RS,7SR)-1,6,7-Trimethyltricyclo[5.2.2.0^{2,6}]undec-8-en-2-ol (**46**) *and (1RS,2RS,6RS,7SR)-6,7-10-Trimethyltricyclo[5.4.0.0^{2,6}]undec-10-en-2-ol* (**47**). A soln. of **45** (5.3 g, 0.019 mol) in THF (60 ml) containing small pieces of Li wire (0.52 g, 0.074 mol) was submitted to sonication[24]) at 0° for 2 h. The mixture was then poured cautiously into cold 20% aq. NH_4Cl soln. (100 ml). Extraction (Et_2O), workup, and CC (silica gel (300 g), toluene) afforded **46** and **47** as the major products.

Data of **46**. Colourless oil (2.1 g, 54%). B.p. 70–72°/0.05 Torr. R_f (toluene) 0.20. IR ($CDCl_3$): 3640, 3300 (br.), 1465, 1370, 1222, 1126, 1010, 990, 950, 850. ^{1}H-NMR (+D_2O): 0.91 (*s*, 3 H); 1.03 (*s*, 3 H); 1.09 (*s*, 3 H); 0.90–1.80 (10 H); 5.75 (*d*, J = 8, 1 H); 5.85 (*d*, J = 8, 1 H). ^{13}C-NMR: (*cf.* the *Fig.*). MS: 206 (0, M^+), 188 (2), 173 (3), 145 (5), 108 (100), 93 (46), 91 (12), 77 (8).

Data of **47**. Colourless oil (0.42 g, 11%). B.p. (bulb-to-bulb dist.) 70–80°/0.04 Torr. R_f (toluene) 0.14. IR: 3480 (br.), 1450, 1376, 1298, 1200, 1096, 1060, 1026, 944, 910, 858. ^{1}H-NMR (+D_2O): 0.88 (*s*, 3 H); 0.93 (*s*, 3 H); 1.20–2.10 (10 H); 1.77 (*s*, 3 H); 2.23 (*m*, 1 H); 5.30 (*m*, 1 H). ^{13}C-NMR: (*cf.* the *Fig.*). MS: 206 (0, M^+), 108 (100), 98 (7), 93 (55), 91 (14), 83 (4), 77 (9), 67 (6).

The above experiment was repeated without sonication at 25° for 24 h to afford, after isolation, **46** and **47** (45 and 8%, resp., from **45**).

Another experiment using Et_2O as solvent, without sonication, at 25° for 1 h afforded, after isolation, **46** and **47** (42 and 14%, resp., from **45**).

Thermolysis of **47**: *Preparation of (2RS,1′SR,4′SR)-2-(1′,4′-Dimethylcyclohex-2′-enyl)-2-methylcyclopentan-1-one* (**48**). A soln. of **47** (103 mg, 0.5 mmol) in toluene (0.5 ml) was passed through a 3-m 5% *Carbowax*-packed GC column at 200° (carrier gas: He). Collection of the pyrolysate afforded **48** as a colourless oil (82 mg, 80%). B.p. (bulb-to-bulb dist.) 60–80°/0.01 Torr ([3b]: 60–65°/0.2 Torr). R_f (toluene) 0.25. IR ($CDCl_3$): 1730. ^{1}H-NMR: 0.95 (*d*, J = 7, 3 H); 1.02 (2*s*, 6 H); 1.10–2.40 (11 H); 5.47 (*d*, J = 10.5, 1 H); 5.77 (br. *d*, J = 10.5, 1 H). MS: 206 (0.2, M^+), 109 (100), 108 (32), 98 (18), 93 (22), 81 (14), 67 (38).

(1RS,3RS,4SR)-3-(3′-Iodopropyl)-1,3,4-trimethylbicyclo[2.2.2]oct-5-en-2-one (**49**). A soln. of **44** (4.1 g, 0.011 mol) and NaI (6.6 g, 0.044 mol) in acetone (80 ml) was stirred at 25° for 96 h. After evaporation, H_2O (50 ml) was added to the residue and the mixture extracted (Et_2O). The combined org. phase was washed with 5% aq. Na_2SO_4 soln., dried (Na_2SO_4), and evaporated. CC of the residue (silica gel (100 g), cyclohexane/AcOEt 19:1) afforded **49** as a white crystalline solid (3.3 g, 91%). M.p. 55–56°. B.p. 108–100°/0.1 Torr. R_f (cyclohexane/AcOEt 7:3) 0.57. IR ($CDCl_3$): 1710, 1370, 1210, 1200, 1170, 1010, 860, 710. ^{1}H-NMR: 1.00 (*s*, 3 H); 1.16 (*s*, 3 H); 1.20 (*s*, 3 H); 1.10–1.75 (7 H); 1.82 (*m*, 1 H); 3.04 (*m*, 2 H); 5.68 (*d*, J = 8, 1 H); 6.18 (*d*, J = 8, 1 H). ^{13}C-NMR: *(cf. Table 2)*. MS: 332 (0, M^+), 205 (4), 135 (6), 108 (100), 93 (40), 91 (15), 77 (9).

(1RS,3RS,4SR)-1,3,4-Trimethyl-3-[3′-(p-toluenesulfonyl)propyl]bicyclo[2.2.2]oct-5-en-2-one (**50**). *Method A* [23]. A mixture of **49** (3.2 g, 9.6 mmol), sodium *p*-toluenesulfinate (2 g, 0.011 mol) and DMF (70 ml) was stirred at 50° for 18 h under N_2. The mixture was then poured into H_2O (400 ml) and continuously extracted (Et_2O). Drying ($Na_2S_2O_3$), evaporation of the org. phase and CC of the residue (silica gel (350 g), cyclohexane/AcOEt 7:3) afforded **50** as a white crystalline solid (2.8 g, 81%). M.p. 90–91°. R_f (CH_2Cl_2) 0.10. IR ($CDCl_3$): 1715, 1602, 1456, 1300, 1240, 1164, 1090, 1020, 990, 820, 780, 670. ^{1}H-NMR: 0.95 (*s*, 3 H); 1.10 (*s*, 3 H); 1.16 (*s*, 3 H); 1.10–1.70 (7 H); 1.79 (*m*, 1 H); 2.45 (*s*, 3 H); 2.90 (*t*, J = 7, 2 H); 5.64 (*d*, J = 8, 1 H); 6.13 (*d*, J = 8, 1 H); 7.35 (*d*, J = 8, 2 H); 7.74 (*d*, J = 8, 2 H). ^{13}C-NMR: 144.5 (*s*); 136.4 (*s*); 129.8 (2*d*); 128.1 (2*d*); 21.6 (*q*) (for rest of data, *cf. Table 2*). MS: 360 (0, M^+), 157 (2), 135 (5), 108 (100), 97 (6), 93 (31), 91 (21).

Method B [24]. A soln. of Bu_4NBr (13 g, 0.04 mmol) and sodium *p*-toluenesulfinate (14.5 g, 0.082 mol) in H_2O (30 ml) was extracted (CH_2Cl_2, 3 × 20 ml). The combined org. phase was evaporated and THF (300 ml) added to the residue. The mixture was stirred at 40° and then filtered. The filtrate was evaporated and benzene (100 ml) added to the residue prior to re-evaporation of solvent (azeotropic removal of H_2O). This latter operation was repeated twice. Finally, the residue was dried *i.v.* to afford a sticky beige solid (14 g). To this solid was added THF (200 ml), followed by a soln. of **49** (2.3 g, 7.0 mmol) in THF (50 ml). The mixture was stirred at 25° for 18 h under N_2 and evaporated. Addition of H_2O (200 ml), saturation with NaCl and extraction (Et_2O) was followed by workup and CC (silica gel (200 g), cyclohexane/AcOEt 7:3) to afford **50** (2.03 g, 81%). *Vide supra* for physical and spectral data.

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[24]) Sonication was effected using a *Bransonic 221* (48 kHz/50 W) ultrasonic bath.

(1RS,2RS,3SR,6RS,7SR)-1,6,7-Trimethyl-3-(p-toluenesulfonyl)tricyclo[5.2.2.0^{2,6}]undec-8-en-2-ol (**51**). A soln. of **50** (2.03 g, 5.6 mmol) in THF (20 ml) was added dropwise within 30 min to a stirred soln. of LDA (6.7 mmol) in THF/hexane 3:1 (13 ml) at −70° under N_2. After a further 30 min at −70°, the reaction was poured into cold 20% aq. NH_4Cl soln. (100 ml). Saturation with NaCl, extraction (Et_2O), workup, and CC (silica gel (350 g), cyclohexane/AcOEt 8:2) afforded **51** as a white crystalline solid (1.9 g, 93%). M.p. 93–94°. R_f (CH_2Cl_2) 0.23. IR ($CDCl_3$): 3530 (br.), 1602, 1466, 1300, 1140, 1090, 780, 720, 698, 640. ^{1}H-NMR (+D_2O): 0.91 (*m*, 2 H); 0.95 (*s*, 3 H); 1.01 (*s*, 3 H);1.27 (*s*, 3 H); 1.38 (*m*, 2 H); 1.59 (*m*, 2 H); 1.96 (*m*, 2 H); 2.44 (*s*, 3 H); 3.28 (*dd*, *J* = 11, 7, 1 H); 5.72 (*d*, *J* = 8, 1 H); 5.92 (*d*, *J* = 8, 1 H); 7.33 (*d*, *J* = 8, 2 H); 7.77 (*d*, *J* = 8, 2 H). ^{13}C-NMR: 144.4 (*s*); 137.5 (*s*); 129.6 (2*d*); 128.6 (2*d*); 21.6 (*q*) (for rest of data *cf.* the *Fig.*). MS: 360 (0, M^+), 108 (100), 97 (25), 93 (30), 91 (16), 77 (7), 65 (5), 55 (5).

46 *from* **51**. Li wire (0.6 g, 0.086 mol) was added portionwise within 1.5 h to a soln. of 51 (2.2 g, 6.1 mmol) in liq. NH_3 (350 ml) and THF (35 ml) at −70° under N_2. After further 30 min at −70°, MeOH (1 ml) was added cautiously and the mixture allowed to attain r.t. (evaporation of NH_3). Addition of cold 20% aq. NH_4Cl soln. (50 ml), saturation with NaCl, continuous extraction (Et_2O) and workup gave a brown oil which was purified by CC (silica gel (100 g), cyclohexane/AcOEt 9:1) to afford **46** (0.87 g, 60%). *Vide supra* for physical and spectral data.

(2RS,1′SR)-2-(1′,4′-Dimethylcyclohex-3′-enyl)-2-methylcyclopentan-1-one (**4**) *from* **46**. A soln. of **46** (1.83 g, 8.9 mmol) in HMPA (20 ml) was added dropwise within 10 min to a stirred slurry of KH (0.014 mol) in HMPA (30 ml) at 25° under N_2. After 2 h at 25°, the mixture was heated at 140° for 1 h. The dark mixture was then cooled and poured into cold 20% aq. NH_4Cl soln. (100 ml). Continuous extraction (petroleum ether), workup, and CC (silica gel (350 g), cyclohexane, then toluene) afforded a 13:1 mixture **4**/**5** as a colourless oil (0.59 g, 32%)[25]. B.p. (bulb-to-bulb dist.) 80–100°/0.05 Torr ([3b]: 60–65°/0.2 Torr). R_f (toluene) 0.26. IR: 1730, 1410, 1380, 1370, 1160, 1060, 940, 820, 802, 780, 630. ^{1}H-NMR: 0.91 (*s*, 3 H); 1.02 (*s*, 3 H); 1.33 (*m*, 1 H); 1.63 (*s*, 3 H); 1.65–2.05 (8 H); 2.12 (*m*, 2 H); 2.31 (*m*, 1 H); 5.28 (*m*, 1 H). ^{13}C-NMR: (*cf.* the *Fig.*). MS: 206 (0, M^+), 123 (3), 108 (100), 98 (9), 93 (48), 91 (12), 83 (7), 79 (10), 67 (24).

Also isolated was a 2:1 mixture (0.28 g) of *p*-xylene and *2-methylcyclopentan-1-one* (**52**), separated by prep. GC and identified by spectral comparison (^{1}H-NMR, MS) with authentic samples.

4 *from* **47**. *Method A.* A soln. of **47** (0.1 g, 0.49 mmol) in HMPA (1 ml) was added dropwise to a stirred slurry of KH (1 mmol) in HMPA (2 ml) at 25° under N_2. After 2 h at 25°, the cooled mixture was poured cautiously into cold 20% aq. NH_4Cl soln. (10 ml). Extraction (Et_2O), workup, CC (silica gel (10 g), cyclohexane/AcOEt 7:3), and distillation *i.v.* afforded a 73:27 mixture **46**/**4** (60 mg) which was separated by prep. GC and identified by spectral comparison with authentic samples *(vide supra)*.

Method B. A soln. of **47** (0.1 g, 0.49 mmol) in THF (1 ml) was added to a stirred slurry of KH (1 mmol) in THF (2 ml) at 25° under N_2. After 2 h at 25° (no reaction detected by TLC), the mixture was refluxed for 16 h (still no reaction detected). HMPA (1 ml) was now added and the mixture refluxed for 2 h. Workup and purification as described above *(cf. Method A)* furnished a 73:27 mixture **46**/**4** (80 mg).

Method C. A soln. of **47** (0.1 g, 0.49 mmol) in HMPA (1 ml) was added to a stirred mixture of *t*-BuOK (112 mg, 1 mmol) in HMPA (2 ml) at 25° under N_2. After 18 h at 25°, the mixture was poured into 20% aq. NH_4Cl soln. (10 ml). Extraction (Et_2O) and workup as described above *(vide supra)* afforded a 80:20 mixture **4**/**46** (50 mg).

Method D. A soln. of **47** (0.1 g, 0.49 mmol) and MeONa (32 mg, 0.6 mmol) in MeOH (2 ml) was refluxed for 3 h. No reaction was observed (TLC).

Base-Promoted Isomerisation of **4**. A soln. of **4** (20 mg, 0.1 mmol) in HMPA (0.1 ml) was added to a stirred slurry of KH (*ca.* 1.5 mmol) in HMPA (0.5 ml) at 140° under N_2. After 1 h at 140°, the mixture was cooled to 5° and 20% aq. NH_4Cl soln. (1 ml) added dropwise. Extraction (Et_2O), workup, CC (silica gel (10 g), cyclohexane, then Et_2O), and distillation *i.v.* afforded a 3:1 mixture[26]) of **4**/**5** (20 mg).

(4RS,1′SR)-1,4-Dimethyl-4-(1′-methyl-2′-methylidenecyclopentyl)cyclohex-1-ene (= *(±)-Trichodiene;* **1**). Following the procedure in [3c], **4** (206 mg, 1 mmol) was transformed into **1** (colourless oil, 124 mg, 61%); isolation by CC (silica gel (20 g), petroleum ether) and distillation *i.v.* B.p. 60–80° (bulb-to-bulb distillation)/0.07 Torr ([3b]: 65–70°/0.5 Torr). IR ($CDCl_3$): 2975, 1640, 1440, 1375, 1160, 1080, 810. ^{1}H-NMR: 0.86 (*s*, 3 H); 1.04 (*s*, 3 H); 1.30–2.40 (12 H); 1.64 (*s*, 3 H); 4.74 (br. *s*, 1 H); 4.96 (br. *s*, 1 H); 5.30 (*m*, 1 H). ^{13}C-NMR: (*cf.* the *Fig.*). MS: 204 (2, M^+), 189 (2), 121 (6), 109 (100), 108 (66), 93 (34), 81 (22), 67 (46), 55 (17), 41 (28).

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[25]) Ketones **4** and **5** were not separable by chromatography; their relative proportions were estimated by ^{1}H-NMR (360 MHz; integration of the CH_3–C(2) signals).

[26]) Estimated by ^{1}H-NMR (360 MHz).

Ketone **54** *and Alcohols* **55**/**56** *from* **50** *and KH.* A soln. of **50** (0.36 g, 1 mmol) in HMPA (1 ml) was added dropwise to a stirred slurry of KH (1.5 mmol) in HMPA (2 ml) at 25° under N_2. After 30 min at 25°, the mixture was heated at 60° for 30 min, cooled to 5°, and then poured into cold 20% aq. NH_4Cl soln. (5 ml). Extraction (Et_2O), workup, filtration through silica gel (50 g, cyclohexane/AcOEt 7:3), and evaporation afforded a pale-yellow oil which was re-purified by CC (silica gel (50 g), toluene, then MeOH) and prep. GC to afford: *(1RS,2SR,3SR,4SR)-1,6,7-trimethyltricyclo[5.2.2.0^{2,6}]undec-8-en-3-one* (**54**; colourless oil, 40 mg, 20% from **50**) *and (1RS,2SR,5RS,6SR)-5,6-9-trimethyltricyclo[4.3.2.0^{1,5}]undeca-8,10-dien-2-ol* (**55**)/*(1RS,2SR,5RS,6SR)-5,6-dimethyl-9-methylidenetricyclo[4.3.2.0^{1,5}]undec-10-en-2-ol* (**56**; colourless oil, 2:1 mixture; 20 mg, 10% from **50**).

Data of **54**. B.p. (bulb-to-bulb dist.) 60–80°/0.02 Torr. R_f (toluene) 0.28. ^{1}H-NMR: 1.00–1.20 (2 H); 1.15 (*s*, 3 H); 1.16 (*s*, 3 H); 1.30–1.60 (4 H); 1.60 (*s*, 1 H); 1.70–1.85 (3 H); 2.01 (*m*, 1 H); 2.18 (*m*, 1 H); 5.84 (*d*, J = 8, 1 H); 5.95 (*d*, J = 8, 1 H). MS: 204 (0, M^+), 120 (6), 108 (100), 93 (53), 91 (15), 77 (9).

Data of **55**. B.p. (bulb-to-bulb dist.) 60–80°/0.02 Torr. R_f (toluene) 0.20. ^{1}H-NMR (+D_2O): 0.99 (*s*, 3 H); 1.06 (*s*, 3 H); 1.55 (*s*, 3 H); 4.45 (*m*, 1 H); 5.10 (*m*, 1 H); 5.24 (*d*, J = 8, 1 H); 5.72 (*d*, J = 8, 1 H). MS: 204 (30, M^+), 186 (43), 171 (100), 158 (26), 147 (63), 131 (52), 119 (53), 105 (60), 91 (84), 77 (48).

Data of **56**. B.p. (bulb-to-bulb dist.) 60–80°/0.02 Torr. R_f (toluene) 0.20. ^{1}H-NMR (+D_2O): 1.01 (*s*, 3 H); 1.02 (*s*, 3 H); 4.54 (*m*, 1 H); 4.81 (*m*, 1 H); 4.99 (*m*, 1 H); 5.35 (*d*, J = 8, 1 H); 5.54 (*d*, J = 8, 1 H). MS: 204 (33, M^+), 189 (14), 171 (28), 160 (61), 145 (79), 131 (83), 119 (50), 105 (76), 91 (100), 77 (80).

(1RS,2SR,4RS)- and (1RS,2RS,4RS)-1,2,4-Trimethylbicyclo[2.2.2]oct-5-en-2-ol (**57** and **58**, resp.). A soln. of **6** (0.75 g, 5.0 mmol) in Et_2O (10 ml) was added dropwise within 10 min to a stirred soln. of MeLi (8.5 mmol) in Et_2O (10 ml) at 20°. After a further 10 min at 20°, the mixture was cautiously poured into cold 10% aq. NH_4Cl soln. (50 ml). Saturation (NaCl), continuous extraction (Et_2O), workup, and bulb-to-bulb dist. *i.v.* afforded **57**/**58** (*ca.* 1:1) as a colourless oil (0.71 g, 86%). Separation was effected by prep. GC *(Carbowax)*.

Data of **57** (higher t_R). B.p. (bulb-to-bulb dist.) 100–120°/0.2 Torr. M.p. 47–48°. R_f (cyclohexane/AcOEt 7:3) 0.42. IR: 3450 (br.), 3050, 2950, 1460, 1375, 1140, 1080, 914, 834, 712. ^{1}H-NMR (+D_2O): 0.97 (*m*, 1 H); 1.08 (2*s*, 6 H); 1.10 (*s*, 3 H); 1.23 (*m*, 1 H); 1.33 (*dd*, J = 14, 3.5, 1 H); 1.41 (*d*, J = 14, 1 H); 1.48 (*m*, 1 H); 1.98 (*m*, 1 H); 5.85 (*s*, 2 H). ^{13}C-NMR: *(cf. Table 3)*. MS: 166 (0, M^+), 108 (100), 93 (65), 91 (5), 77 (3), 43 (8).

Data of **58** (lower t_R). B.p. (bulb-to-bulb dist.) 100–120°/0.2 Torr. R_f (cyclohexane/AcOEt 7:3) 0.40. IR: 3490 (br.), 3050, 2950, 1460, 1378, 1200, 1120, 1060, 920, 836, 718. ^{1}H-NMR (+D_2O): 1.10 (*s*, 3 H); 1.17 (*s*, 3 H); 1.20 (*s*, 3 H); 1.08–1.25 (2 H); 1.26 (*m*, 1 H); 1.38 (*dd*, J = 14, 3.5, 1 H); 1.52 (*d*, J = 14, 1 H); 1.55 (*m*, 1 H); 5.87 (*d*, J = 8, 1 H); 6.10 (*d*, J = 8, 1 H). ^{13}C-NMR: *(cf. Table 3)*. MS: 166 (0, M^+), 108 (100), 93 (63), 91 (7), 77 (4), 43 (12).

(1RS,2SR,4SR)- and (1RS,2RS,4SR)-1,2,3,3,4-Pentamethylbicyclo[2.2.2]oct-5-en-2-ol (**59** and **60**, resp.). As described for **57**/**58** with **10** (0.9 g, 5.1 mmol) in Et_2O (10 ml) and MeLi (0.01 mol) in Et_2O (8 ml) at 20°: **59**/**60** (4:1) as a partially crystalline solid (0.80 g, 82%). Separation was effected by CC (silica gel (350 g), cyclohexane/AcOEt 9:1).

Data of **59**. B.p. 110–120° (bulb-to-bulb dist.)/0.1 Torr. M.p. 41–43°. R_f (cyclohexane/AcOEt 7:3) 0.50. IR: 3530 (br.), 3050, 2975, 1460, 1374, 1082, 1060, 918, 716. ^{1}H-NMR (+D_2O): 0.81 (*s*, 3 H); 0.92 (*s*, 3 H); 1.02 (*s*, 3 H); 1.03 (*s*, 3 H); 1.08 (*s*, 3 H); 0.85–1.05 (2 H); 1.76 (*m*, 1 H); 1.88 (*m*, 1 H); 5.80 (*d*, J = 8, 1 H); 5.89 (*d*, J = 8, 1 H). ^{13}C-NMR: *(cf. Table 3)*. MS: 194 (0, M^+), 108 (100), 93 (47), 91 (4), 77 (3), 43 (13).

Data of **60**. B.p. 110–120° (bulb-to-bulb dist.)/0.1 Torr. R_f (cyclohexane/AcOEt 7:3) 0.55. IR ($CDCl_3$): 3600, 3050, 2975, 1470, 1386, 1370, 1328, 1074, 1044, 658. ^{1}H-NMR (+D_2O): 0.78 (*s*, 3 H); 0.91 (*s*, 3 H); 1.04 (*s*, 3 H); 1.08 (*s*, 3 H); 1.14 (*s*, 3 H); 0.90–1.70 (4 H); 5.78 (*d*, J = 8, 1 H); 6.14 (*d*, J = 8, 1 H). ^{13}C-NMR: *(cf. Table 3)*. MS: 194 (0, M^+), 108 (100), 93 (44), 78 (2), 43 (14).

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