^{13}C magnetic resonance studies. 144.[1] An examination of β-enolization in the bicyclo[3.3.1]- and [3.2.2]nonan-2-one system

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While 3,3-dimethylbicyclo[3.3.1]nonan-2-one (**5**) is stable under strongly basic conditions (*t*-BuO$^-$/*t*-BuOH/185°C), its isomer, 3,3-dimethylbicyclo[3.2.2]nonan-2-one (**6**), is slowly transformed to **5**. Similarly, 3,3-dimethylbicyclo-[3.2.2]non-6-en-2-one (**8***b*) rearranges to a [3.3.1] isomer but the latter is not stable. Experiments with 3,3-dimethylbicyclo[3.3.1]non-6-en-2-one (**7**) revealed that it is converted to five compounds, none of which is **8***b*. The major product, 8,8-dimethylbicyclo[4.3.0]non-1$^{(6)}$-en-7-one (**11**) arises from β-enolate rearrangement. Enone **11** undergoes slow reduction to *cis*- and *trans*-8,8-dimethylbicyclo[4.3.0]nonan-7-one, presumably by single electron transfer. Experiments with **11** alone showed that β-enolate rearrangement of **7** → **11** is unidirectional. Haller–Bauer cleavage to acidic products occurs as a minor process in the reactions of the unsaturated ketones. The structures of the products were established primarily from their ^1H and ^{13}C magnetic resonance spectra.

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Alors que la diméthyl-3,3-bicyclo[3.3.1]nonanone-2 (**5**) est stable dans des conditions fortement basiques (*t*-BuO$^-$/*t*-BuOH/185°C), son isomère la diméthyl-3,3-bicyclo[3.2.2]nonanone-2 (**6**) se transforme lentement en diméthyl-3,3-bicyclo[3.3.1]nonanone-2 (**5**). De la même façon, la diméthyl 3,3-bicyclo[3.2.2]nonèn-6-one-2 (**8***b*) se transpose en un isomère [3.3.1] instable. Des expériences révèlent que la diméthyl-3,3-bicyclo[3.3.1]nonèn-6-one-2 (**7**) se transforme en cinq composés parmi lesquels on ne retrouve pas le composé **8***b*. Le produit majoritaire, la diméthyl-8,8-bicyclo[4.3.0]nonèn-1$^{(6)}$-one-7 (**11**) provient d'une transposition β-énolate. L'énone **11** subit une lente réduction en *cis*- et *trans*-diméthyl-8,8-bicyclo[4.3.0]nonanone **7** probablement par simple transfert d'électron. Des expériences réalisées avec le composé **11** uniquement révèlent que la transposition β-énolate **7** → **11** est unidirectionnelle. Le clivage Haller–Bauer en produits acides intervient comme un processus mineur dans les réactions des cétones insaturées. On a établi la structure des produits principalement à partir de leurs spectres de résonnance magnétique nucléaire du ^1H et du ^{13}C.

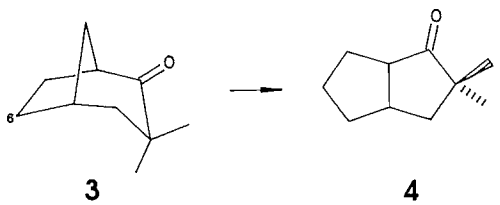
[Traduit par la rédaction]

Introduction

The discovery of the homoenolization process by Nickon and Lambert, who found that 3,3-dimethylbicyclo[2.2.1]-heptan-2-one (camphenilone) is racemized by treatment with strong base at elevated temperatures, *t*-BuO$^-$/*t*-BuOH/185°C (1), revealed that proton abstraction occurred from sites more than one bond from the carbonyl group. Their finding led to studies of several related polycyclic ketones of which the majority were found to exhibit abstraction from β-carbons, or β-enolization (2), with a few examples of γ-enolate formation (3). More recently, some examples of β-enolization in acyclic (4) and monocyclic systems (5) have been described. With few exceptions (6), α-enolization has been blocked in these homoenolizable ketones by α-methyl substitution or structurally such that only anti-Bredt α-enolates could form.

The β-enolization process may be viewed as the formation of a cyclopropoxide anion, e.g., **A** in Scheme 1, whose fate is governed by the regioselectivity of its subsequent protonation, via path *a* to return to the initial ketone or path *b* to form an isomeric ketone. The regioselectivity of the process has attracted some interest because of the potential utility for new synthetic approaches to carbon skeletons not readily accessible by other routes. Sequences in which a β-enolate rearrangement is a key step have been developed for linear and angular triquinanes (7) and a [3.3.3]propellane.[2] Since paths *a* and *b* may proceed with either retention or inversion of configuration, the stereoselectivity of protonation has mechanistic interest and may be established by isotopic labelling experiments.

The regio- and stereoselectivity of β-enolization has been examined in detail for several saturated bicyclic ketones. For example, the [2.2.2] and [3.2.1] ketones, **1** and **2**, are slowly equilibrated under the usual homoenolization conditions (8) while **3** rearranges slowly but irreversibly to **4** (9). It was also found that, under these conditions, Δ^5-**1** rearranged >100 times faster than **1** to a mixture of Δ^2- and Δ^3-**2**, with the equilibrium more strongly biased toward the [3.2.1] skeleton (10). Each of these reactions proceeds cleanly with little evidence of other products. In contrast, Δ^6-**3** is transformed to a mixture of six products, none of which is an unsaturated ketone (11). As an extension of these studies of simple bicyclic systems, we have examined the behavior of the related [3.3.1] and [3.2.2] ketones, **5**, **6**, **7**, and **8***b*, under typical homoenolization conditions. We wish to present the results of these experiments in this paper.



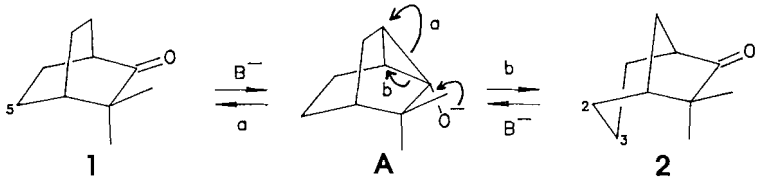
3 **4**

Results and discussion

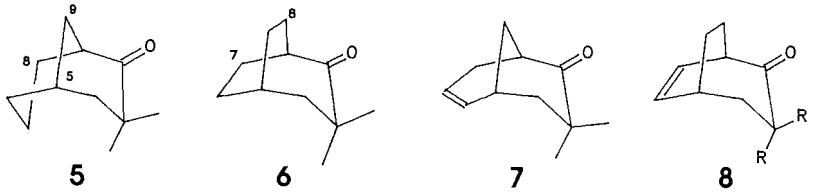
Ketone **5** (12) was obtained by methylation (MeI/$NaNH_2$/Et_2O) of bicyclo[3.3.1]nonan-2-one prepared from cyclohexanone by the four-step sequence described by Inouye et al. (13). Following our standard methods (14), **5** was dissolved in anhydrous *t*-BuO$^-$/*t*-BuOH (1.00 M) to furnish a solution 0.25 M in **5**. Aliquots of this solution were rapidly transferred to glass tubes under nitrogen, degassed, and sealed

[1]For Part 143, see ref. 5.

[2]H.A. Patel, J.B. Stothers, and S.E. Thomas. Paper in preparation.



SCHEME 1

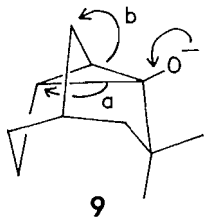


a R = H
b R = Me

under vacuum. After heating at 185°C in an oil-bath for various times (24, 48, 112, 240 h), the tubes were cooled and the neutral product isolated by pentane extraction. The alkaline washings were acidified and extracted with ether to isolate any acidic product but none was found even after 240 h at 185°C. In all cases, **5** was the only component detected (glc and ^{13}Cmr) in the neutral fractions and was recovered in >85% yields.

Under the same reaction conditions, however, **6** was found to rearrange slowly to **5**. Neutral fractions (>85% yields) containing 56:44, 42:58, and 35:65 mixtures of **6**:**5** were isolated after 96, 192, and 240 h, respectively, with no evidence of acidic products. Ketone **6** was prepared by catalytic hydrogenation of **8***b*, obtained by α,α-dimethylation of **8***a*, which was generated by ring expansion of bicyclo[2.2.2]octenone as described in an earlier report (15).

Ketones **5** and **6** are, in principle, interconvertible through the β-enolate **9**, which can be generated by abstraction of a proton from C-8 in **5** and C-7 or -8 in **6**. Subsequent cleavage via paths *a* or *b* would led to **5** or **6**, respectively. The results above showed that **9**, or an equivalent species, is formed from **6**, but there was no evidence that **9** is generated from **5**.



To examine this point, **5** was treated with *t*-BuO$^-$/*t*-BuOD at 185°C for various times and the ^{2}H content of the recovered **5**-d_x samples was assayed by mass spectrometry and ^{2}Hmr. The ^{2}H spectra of samples collected after treatment for 3, 6, 12, and 24 h in the deuterated base contained only two signals indicating that exchange occurred at C-1 (δ 2.38) and the *exo*-methyl site (δ 1.13). Earlier work (16) had shown that bridgehead exchange occurs under milder conditions (101°C in NaOMe/MeOD) and the methyl assignment followed from previous studies, which established that *exo*-methyl exchange is significantly faster than that at *endo*-methyl sites

TABLE 1. Deuterium incorporation in **5** at 185°C

Time (h)	Atoms D/molecule[b]	% Exchange/hydrogen[a] H-1	*exo*-Methyl
3	1.12	0.89	0.08
6	1.33	0.90	0.14
12	1.67	0.90	0.25
24	2.20	0.88	0.44

[a]Assayed by ^{2}Hmr (±2%).
[b]Determined by mass spectrometry.

in many related systems (2). From the proton spectrum of **5**, we can be certain that signals from other deuterated sites in **5**-d_x would not be obscured by the observed signals. The incorporation data are listed in Table 1. There was no evidence of proton abstraction from C-8 in **5**; thus, it must be a very slow process if, in fact, **9** is formed from **5**. An upper limit for a rate constant for C-8 exchange can be estimated to be ca. 10^{-7} s, which is an order of magnitude less than the observed rate for the **6** → **5** rearrangement. It may be noted that the ^{13}C spectra of the **5**-d_x samples confirm the ^{13}C assignments reported by Yamada et al. (12), since bridgehead (C-1) deuteration produced ^{2}H-induced isotope shifts of 125 and 111 ppb for the methylene signals at δ_C 29.5 (C-9) and 32.5 (C-8).

The fate of **7** under the homoenolization conditions was then examined. This ketone was prepared from bicyclo[3.3.1]nona-2,6-dione (17) through the sequence described by Bishop et al. (18), but using a modified procedure for ketalization of the dione (19). A series of runs (6, 12, 24, 48, and 72 h) gave neutral fractions (72–76% yields), containing five components after the longer reaction times, while small amounts of a single acidic component were obtained; the acid fraction represented 12% of the product after 72 h.

The ^{13}C spectra of the neutral products, isolated after 3 and 6 h, revealed two neutral components, in addition to **7**. Both were ketones and the more abundant contained a disubstituted double bond. Although attempts to isolate pure samples of this new ketone by column chromatography were unsuccessful, its ^{13}C shieldings strongly support structure **10**,

TABLE 2. ^{13}C shielding data[a] for **7**, **8***b*, and **10**

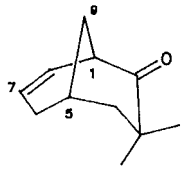
Compound	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	Me
7	42.4	221.6	42.8	43.9	29.4	126.5	132.1	32.0	29.2	30.2 30.5
10	47.0	215.4	42.7	45.5	25.8	33.6	131.0	126.8	29.0	30.2 32.2
8*b*	50.1	213.2	45.9	44.5	32.6	136.7	127.7	26.7	23.4	30.5 32.5

[a]In ppm from TMS in $CDCl_3$ solutions.

the Δ^7-isomer of **7**. The data are listed in Table 2 with those for **7** and **8***b*. The specific assignments for **7** followed from the results of $^1H\{^1H\}$ and $^{13}C\{^1H\}$ correlation spectra; the long-range $^{13}C\{^1H\}$ interactions of the methyl protons were found using the FLOCK sequence (20). For **10** and **7**, the shielding differences for the carbonyl and methine carbons are entirely consistent with isomerization of **7** to its Δ^7 isomer. The −6.2 ppm shift of the carbonyl signal in **10** relative to **7** is indicative of a homoconjugative interaction in a β,γ-enone (21) and the +4.6 and −3.6 ppm shifts for C-1 and -5, respectively, are as expected for this change in the position of the double bond. Since the allylic protons in **7** are the most acidic, equilibration of **7** and **10** may be anticipated under the strongly basic conditions and, in fact, the relative proportion of **7** and **10** was 3:2 in all of the neutral product mixtures.

The third ketone detected in the products from the shorter reaction times was readily isolated from the neutral mixture by chromatography on alumina. Its ^{13}Cmr spectrum contained signals for a tetrasubstituted double bond, δ_C 136.0 and 170.3, and a carbonyl carbon, δ_C 213.3, as well as those for five methylene carbons and a pair of equivalent methyl groups. The absence of methine signals clearly showed that a major skeletal change had occurred and the data indicated that this compound was **11**. The ^{13}C spectrum was the same as that of an authentic sample, prepared by 2,2-dimethylation of 4,5,6,7-tetrahydrindan-1-one (22); thus, the structural assignment was confirmed.

In the product mixtures from runs longer than a few hours, the presence of two additional compounds was apparent from glc analysis and ^{13}Cmr. Flash chromatography furnished a sample containing ca. 80% of these compounds and ca. 20% of a mixture of **7** and **10**. The ^{13}Cmr spectrum showed that these are ketones, δ_C 222.4 and 224.4, containing no olefinic carbons. There were signals for two methyl, five methylene, two methine, and one quaternary carbon for each of the two compounds. Identical sets of signals were found in the ^{13}C spectrum of the product from tetra-*n*-propylammonium per-ruthenate (TPAP) oxidation (23) of the alcohol mixture obtained by reduction of authentic **11** with lithium in liquid ammonia (24). Thus, these are the *cis* and *trans* isomers **12***b*. Specific ^{13}C assignments for the skeletal carbons of each isomer were made by comparison of the observed shieldings with the data for the parent ketones **12***a* (25). The ^{13}C data are collected in Table 3 from which it is evident that the methyl substituents have little effect on the shieldings of the methylene carbons in the six-membered ring. The synthetic sample was a 60:40 mixture of *cis*- and *trans*-**12***b*, while a 52:48 mixture was isolated from the runs with **7**.



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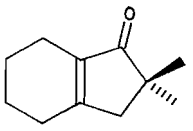

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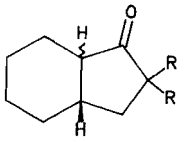

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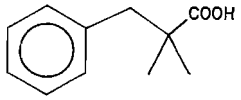
a R = H
b R = Me



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The acidic fraction contained a single carboxylic acid that exhibited a remarkably simple ^1Hmr spectrum having two singlets in the high-field region, δ 1.23 (6H) and 2.92 (2H), accompanied by low-field absorption, 7.15–7.35 ppm (5H), characteristic of a phenyl group. The ir, ms, and ^1H and ^{13}Cmr data indicated that the acid was **13** and this assignment was confirmed by the synthesis of an authentic sample from hydrocinnamic acid.

The compositions of the products isolated from the experiments with **7** are listed in Table 4 as a function of time. Although **8***b* was not detected in the neutral mixtures from the runs with **7**, its behavior under homoenolization conditions was of interest. A series of experiments showed that **8***b* is transformed slowly to **7** and, thence, to its rearrangement products. The compositions of the neutral products isolated in 72–80% yields are collected in Table 5. The acidic fractions, constituting <5% of the product after the longer reaction times, contained a single component, **13**. It may be noted that the ratio of **7** to **10** was 3:2, as in the product mixtures from **7** itself.

A series of runs with **11** was also carried out and the results clearly showed that the major mode of reaction involved reduction to *cis*- and *trans*-**12***b* in *t*-BuO^-/*t*-BuOH at 185°C, together with a minor process leading to a relatively small acidic fraction. Both glc analysis and ^{13}Cmr showed that the neutral fractions contained only **11** and the **12***b* isomers; there was no evidence of the presence of **7** and (or) **10**. The product compositions after various reaction times are listed in Table 6.

The generation of the neutral product mixtures found for the unsaturated ketones may be interpreted as outlined in Scheme 2. Irreversible rearrangement of the [3.2.2] ketone

TABLE 3. ^{13}C shielding data[a] for **12***a*[b] and *b*

Compound	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	Me
cis-**12***a*	36.0	28.0	23.9	22.7	22.4	49.3	219.5	34.6	25.5	
cis-**12***b*	32.5	28.1	23.0	23.8	22.5	48.0	224.4	44.2	40.7	26.5 27.2
trans-**12***a*	43.1	32.4	25.7	25.4	24.8	55.3	217.7	36.8	27.5	
trans-**12***b*	39.7	32.7	26.1	25.8	25.4	55.0	222.4	44.9	43.9	24.7 26.3

[a]In ppm from TMS in $CDCl_3$ solutions.
[b]Data from ref. 25.

TABLE 4. Composition[a] of the product mixtures from homoenolization of **7** (*t*-BuO^-/*t*-BuOH/185°C)

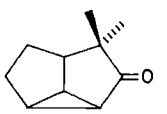
				12*b*		
Time (h)	**7**	**10**	**11**	*cis*	*trans*	**13**
6	37	24	12	–	–	5
12	20	14	26	7	6	6
24	13	9	33	11	10	8
48	6	4	34	15	14	8
72	<2	<1	31	21	20	12

[a]Ratios of the neutral products (>70% yields) estimated by ^{13}Cnmr.

TABLE 5. Composition[a] of the neutral product from homoenolization of **8***b* (*t*-BuO^-/*t*-BuOH/185°C)

					12*b*	
Time (h)	**8***b*	7	**10**	**11**	*cis*	*trans*
12	56	9	6	4	–	–
24	47	13	8	9	<2	<1
48	27	11	8	22	6	5
96	15	8	5	27	13	12
144	7	4	3	26	17	16

[a]Estimated by ^{13}Cnmr as percentage of isolated material (>70% yields).



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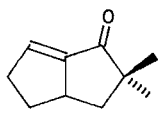

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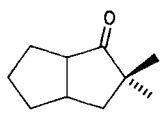

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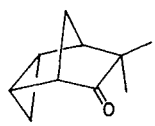

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for ketones **19** (3) and **20** (11). It is interesting that the reduction of **20** (→ **21**) is faster than that observed for either **11** or **19** under these conditions. Both **11** and **19** (generated by γ-enolate rearrangement of **22**) are the primary rearrangement products whose concentrations increase in the early stages of reaction, before passing through a maximum and then decreasing as these are slowly consumed by reduction. In contrast, no unsaturated ketones were found as products from homoenolization of Δ^6-**3**, although **20**, or an isomeric enone, must be an intermediate in the generation of **21**, which is the major product from Δ^6-**3**.

In all experiments **13** was the only acidic product, presumably arising by dehydrogenation of **23**, or a double bond isomer. Haller–Bauer cleavage of **10**, after addition of *tert*-butoxide anion to the carbonyl carbon, would generate **23** (R = *tert*-butyl), a cyclohexenyl analog of **13**, as outlined in Scheme 3. Migration of the double bond in **23** should occur readily under these strongly basic conditions because of the acidity of the allylic protons; this is analogous to the observed equilibration of **7** and **10**. It is conceivable that hydride transfer to **11** from an intermediate cyclohexenyl anion could occur, thereby generating a cyclohexadienyl analog of **13**. Allylic proton abstraction from the latter species and subsequent hydride loss would lead to the formation of **13**.

In summary, the saturated [3.3.1] ketone **5** shows no tendency to rearrange to the [4.3.0] ring skeleton. Its unsaturated analog **10** undergoes this transformation, but, under the homoenolization conditions, the olefinic bond in the initial **8***b* via β-enolate **14**, or an equivalent species, affords **7**, which would be expected to equilibrate rapidly with **10** through a common allylic anion. Proton abstraction from C-9 in **10** could lead to the formation of β-enolate **15**, or an equivalent intermediate, which undergoes unidirectional cleavage to the [4.3.0] skeleton. This rearrangement is strictly analogous to that of **3** → **4** (9) but is significantly faster. The **3** → **4** conversion exhibited a half-life of ca. 60 h while more than 50% of the **7**:**10** mixture is consumed in less than 12 h (Table 4). While formation of an isomeric β-enolate from **7** may be envisaged, we suggest that this is less likely since **5** is stable under these conditions. In any event, it is clear that the incorporation of a double bond in the [3.3.1] skeleton enhances β-enolate formation. An analogous enhancement for **1** and **2** was noted in the Introduction. In principle, γ,δ-enone **16** or the β,γ isomer would be the initial product(s) from cleavage of **15** and, under the basic conditions, can be expected to isomerize rapidly. Only α,β-enone **11** was identified among the products, but traces of other isomers may have escaped detection.

The formation of the saturated ketone **12***b* clearly shows that **11** undergoes slow reduction. We propose that single electron transfer from the *tert*-butoxide anion to the carbonyl carbon of **11** to generate ketyl **17** or homolysis of the addition product **18** are the most probable intermediates in this process. Similar reduction processes have been observed

TABLE 6. Composition[a] of the product mixtures from **11** after treatment with *t*-BuO^-/*t*-BuOH at 185°C

		12*b*		
Time (h)	**11**	*cis*	*trans*	**13**
3	71	11	10	–
12	63	17	15	–
24	41	20	18	5
48	31	25	23	10
96	19	28	26	15

[a]Ratios of neutral components estimated by ^{13}Cmr.

rearrangement product **11** is subsequently reduced to furnish the saturated [4.3.0] system as the end product.

Experimental

Boiling points and melting points are uncorrected. Gas–liquid chromatography (glc) was done with Varian 940 or 3300 instruments using 1/8-in. columns of OV-101 (10 ft, 1.5% and 6 ft, 5%, respectively) on Chromosorb G. Tetrahydrofuran (THF) and ether were dried over sodium/benzophenone and freshly distilled before use.

Infrared spectra were recorded with a Bruker/IBM FTIR instrument. Mass spectral data were obtained with a Finigan MAT 8230 spectrometer at 70 eV for routine spectra and 20 eV for precise mass measurements. The nmr spectra were recorded with Varian Gemini-200, XL-200, or XL-300 instruments, with digital resolution of 0.1 (^{1}H) and 0.6 Hz (^{13}C). The protonation level for each carbon signal was found from APT or DEPT spectra. Assignments for the sp^3 carbon signals were aided by $^{13}C\{^1H\}$ correlations. Comparisons of the intensities of clearly resolved signals (CH_3 vs. CH_3 and CH_2 vs. CH_2) permitted estimation of the compositions of some product mixtures. The HETCOR sequence of the Varian software with 2048 × 512 data point matrices was used to show one-bond interactions and the FLOCK sequence (20) to identify longer range interactions. The HOMCOR sequence of the Varian software was used to record $^1H\{^1H\}$ COSY-45 spectra with 1024 × 1024 data matrices.

Materials

The parent ketones required to prepare the reactants for these experiments were obtained by published procedures. The four-step sequence from cyclohexanone employed by Inouye et al. (13) gave bicyclo[3.3.1]nonan-2-one, which was methylated in 67% yield, as described below, to furnish **5** (12). Bicyclo[3.3.1]nona-2,6-dione was obtained from Meerwein's ester as reported by Lightner et al. (17) and monoketalized, as described by Momose et al. (19). Then, with minor modifications, the sequence employed by Bishop et al. (18) was followed. The carbonyl group was reduced and the hydroxyketal treated with *p*-toluenesulfonyl chloride. Elimination of the tosyl group by refluxing in pyridine and deketalization with *p*-TsOH furnished bicyclo[3.3.1]non-6-en-2-one. Ring expansion of bicyclo[2.2.2]otenone by ketonization of its cyclopropanated silyl enol ether gave bicyclo[3.2.2]non-6-en-2-one (**8***a*) (15).

General procedure for the α,α-dimethylation of the bicyclic ketones

To a stirred suspension of freshly powdered $NaNH_2$ (30 mmol) in dry ether (5 mL) was added a solution of the ketone (5 mmol) in dry ether (5 mL) and the mixture heated under reflux for 2 h with vigorous stirring. The mixture was cooled and methyl iodide (30 mmol) was added slowly before the mixture was refluxed for 16 h, at which time a second addition of methyl iodide (10 mmol) was made. After a reflux period of 3 h, the mixture was cooled to 0°C and the excess $NaNH_2$ destroyed by the addition of cold water (20 mL). The ether layer was separated and the aqueous phase extracted with ether (2 × 25 mL). The combined extracts were washed with brine before drying over anhydrous $MgSO_4$. Evaporation of the solvent afforded the desired dimethylated ketone. The purification method, yield, and physical data for each product are listed below.

3,3-Dimethylbicyclo[3.3.1]non-6-en-2-one (7): isolated in 85% yield by flash chromatography (fc) with hexane as eluent; ir (liquid film): 1700 m^{-1}; ^{13}Cmr ($CDCl_3$) see Table 2; ^{1}Hmr ($CDCl_3$) δ: 1.11 (s, 3H, Me), 1.08 (s, 3H, Me), 1.77 ("dt," 1H, *J* = 13.8, 2.5 Hz, *endo*-H-4), 1.84 (dd, 1H, *J* = 5.3, 13.8 Hz, *exo*-H-4), 1.90 (bd, 1H, *J* = 12 Hz, *anti*-H-9), 2.00 (bd, 1H, *J* = 12 Hz, *syn*-H-9), 2.12 (bd, 1H, *J* = 18 Hz, *endo*-H-6), 2.34 (bd, 1H, *J* = 18 Hz, *exo*-H-6), 2.45 (m, 1H, H-5), 2.65 (m, 1H, H-1), 5.64 (m, 1H, H-7), 5.78 (m, 1H, H-8). Exact Mass calcd. for $C_{11}H_{16}O$: 164.1202; found: 164.1203.

3,3-Dimethylbicyclo[3.2.2]non-6-en-2-one (8b): isolated in 73% yield by fc (hexane – ethyl acetate, 95:5) and slowly crystallized on standing to a waxy solid that sublimed readily at room temperature to provide an analytical sample; mp 38–39°C; ir ($CHCl_3$): 1694 cm^{-1}; ^{13}Cmr ($CDCl_3$): see Table 2; ^{1}Hmr ($CDCl_3$) δ: 1.14 (s, 3H, Me), 1.16 (s, 3H, Me), 1.6–1.95 (m, 6H), 2.64 (m, 1H, H-5), 3.17 (m, 1H, H-1), 6.0 (bdd, 1H, *J* = 7, 8 Hz, H-6), 6.35 (bt, 1H, *J* = 8 Hz, H-7). Exact Mass calcd. for $C_{11}H_{16}O$: 164.1202; found: 164.1200.

3,3-Dimethylbicyclo[3.2.2]nonan-2-one (6)

To a solution of **8***b* (254 mg) in ethyl acetate (10 mL) was added palladium on activated carbon catalyst (10% Pd, 70 mg) and the mixture placed in a Parr hydrogenation bottle. Then the bottle was filled to 58 psi (1 psi = 6.9 kPa) with hydrogen before shaking for 30 min at room temperature. The mixture was filtered and the solvent evaporated to furnish **6** quantitatively; ir (liquid film): 1692 cm^{-1}; ^{13}Cmr ($CDCl_3$) δ_C: 30.8 $(CH_3)_2$, 21.8 (2), 24.8 (2), 45.1, (5 × CH_2), 29.4, 46.6 (2 × CH), 45.0 (quat C), 220.1 (C=O); ^{1}Hmr ($CDCl_3$) δ: 1.18 (s, 6H, Me_2), 1.6–1.8 (m, 8H), 2.17 (m, 1H, H-5), 2.58 (m, 1H, H-1). Exact Mass calcd. for $C_{11}H_{18}O$: 166.1358; found: 166.1360.

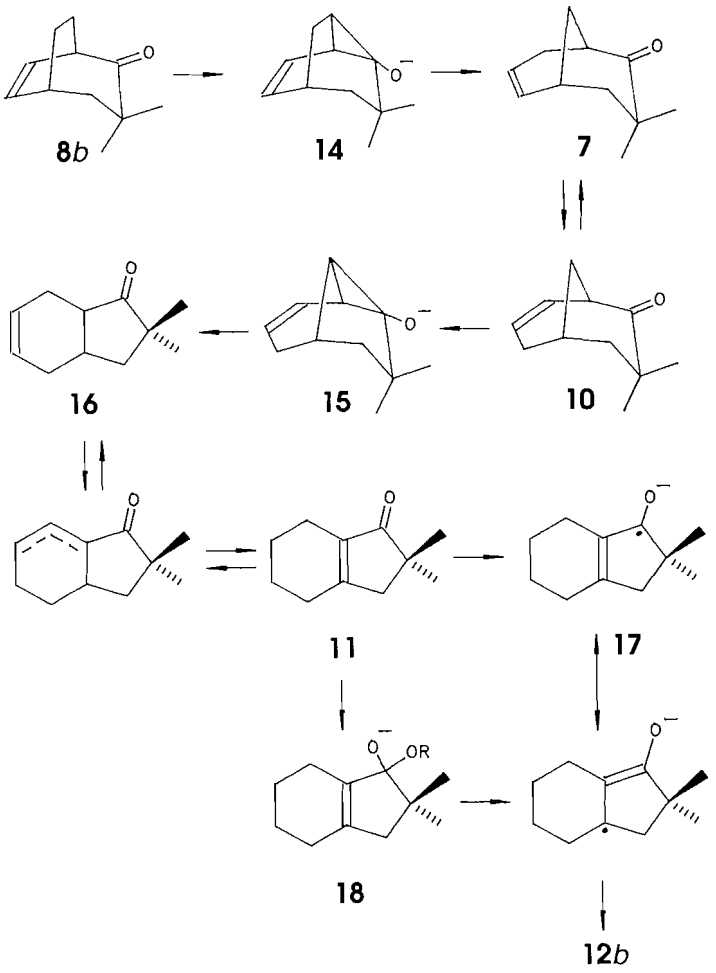
For the homoenolization experiments, samples were chromatographed over silica before use.

8,8-Dimethylbicyclo[4.3.0]non-1(6)-en-7-one (11)

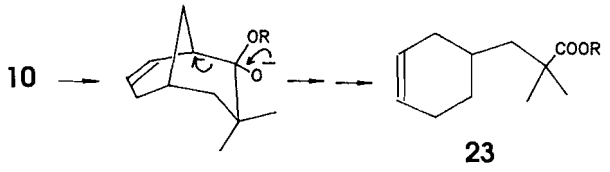
To diisopropylamine (0.6 mL) in 12 mL of THF at −60°C was added *n*-butyllithium (1.5 mL, 2.5 M in hexane) and the mixture stirred for 10 min. Then, 4,5,6,7-tetrahydrohydrindan-1-one (360 mg) (22) was added and the mixture stirred for 10 min before methyl iodide (0.5 mL) was added and stirring was continued for 15 min. The mixture was then poured into 1 M HCl solution (25 mL) and the product was isolated by ether extraction. After a second methylation cycle, the product was purified by column chromatography on silica to give **11** (390 mg, 89% yield); ir (liq. film) 1649, 1698 cm^{-1}; ^{13}Cmr ($CDCl_3$) δ_C: 25.3 $(CH_3)_2$, 20.2, 21.8, 22.3, 28.4, 47.2 (5 × CH_2), 43.2 (quat C), 135.9, 170.2 (C=C), 213.2 (C=O); ^{1}Hmr ($CDCl_3$) δ: 1.06 (s, 6H, $(CH_3)_2$), 1.55–1.75 (m, 4H), 2.03–2.13 (m, 2H), 2.22–2.28 (m, 2H), 2.29–2.34 (m, 2H, H-9). Exact Mass calcd. for $C_{11}H_{16}O$: 164.1202; found: 164.1200. This compound was identical to one of the products from the homoenolization experiments with **7**.

cis- *and* trans-*8,8-Dimethylbicyclo[4.3.0]nonan-7-one (12b)*

Following the procedure of House et al. (24), a solution of enone **11** (35 mg) in THF (2 mL), containing *tert*-butyl alcohol (40 μL), was added to a cold (−78°C) solution of lithium (6 mg) in ammonia (4 mL). After the addition, the cold-bath was removed and the mixture allowed to reflux for 2 h. The reaction was quenched by the addition of water (2 mL) and the ammonia was allowed to evaporate before water (10 mL) and ether (10 mL) were added. The organic layer was separated and the aqueous phase extracted twice with Et_2O (10 mL). The solvent was evaporated and the residual oil (34 mg) was oxidized directly by the addition of *N*-methylmorpholino-*N*-oxide (35 mg) in CH_2Cl_2 (10 mL) with



SCHEME 2



SCHEME 3

1 mg of tetra-*n*-propyl ammonium per-ruthenate (23). This reaction mixture was allowed to stand for 0.5 h before dilution with 20 mL of CH_2Cl_2. The solution was washed with 15 mL of each of saturated aqueous Na_2SO_3, brine, saturated aqueous $CuSO_4$, and brine before drying over anhydrous $MgSO_4$. Evaporation of the solvent left an oil (28 mg, 79% overall yield), which by ^{13}Cmr and glc was a 60:40 mixture of the desired *cis*- and *trans*-**12***b*; ir (liquid film): 1738 cm^{-1}; ^{13}Cmr ($CDCl_3$): see Table 3. Exact Mass calcd. for $C_{11}H_{18}O$: 166.1358; found: 166.1366 (*cis* isomer), 166.1353 (*trans* isomer); these data were obtained by gc/ms using a 30-m capillary column coated with DB-5.

2,2-Dimethyl-3-phenylpropanoic acid (13)

Methyl hydrocinnamate (500 mg) was methylated as described above for **11** (diisopropylamine (0.5 mL), THF (12 mL), n-BuLi (1.8 mL, 2.5 M in hexane), methyl iodide (0.5 mL). After a second methylation cycle, the methyl ester of **13** (550 mg, 94% crude yield) was isolated. The crude ester (37 mg) was heated in 3 M NaOH solution at 80°C for 5 h. The reaction mixture was extracted with ether (2 × 50 mL) and the aqueous phase acidified to pH 2 before extraction with ether (3 × 50 mL). After drying over $MgSO_4$, the solvent was removed to yield **13** (28 mg, 82%) with the following properties: ir (liquid film): 2400–3400, 1701 cm^{-1}; ^{13}Cmr ($CDCl_3$) δ_C: 24.7 (2 × CH_3), 45.9 (CH_2), 43.5 (quat C), 126.6, 128.1 (2), 130.3 (2) (5 × aryl CH), 137.6 (aryl C), 184.5 (COOH); ^{1}Hmr ($CDCl_3$) δ: 1.23 (s, 6H, Me_2), 2.92 (s, 2H, H-3), 7.15–7.35 (m, 5H, aryl H). Exact Mass calcd. for $C_{11}H_{14}O_2$: 178.0994; found: 178.0996.

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