69. Unexpected Configurational and Conformational Preference in Bicyclo[3.2.0]heptane Systems

by **Max Rey, Stanley M. Roberts**[1]) and **André S. Dreiding**

Organisch-chemisches Institut der Universität Zürich, Winterthurerstrasse 190, CH-8057 Zürich

and **Albert Roussel, Huguette Vanlierde, Suzanne Toppet**[2]) and **Léon Ghosez**

Laboratoire de Chimie Organique de Synthèse, Université Catholique de Louvain, Place L. Pasteur 1, B-1348 Louvain-La-Neuve

Zusammenfassung

Einige 7*endo*-monosubstituierte Bicyclo[3.2.0]hept-2-en-6-one and Bicyclo-[3.2.0]heptan-6-one zeigen eine unerwartete thermodynamische Stabilität gegenüber den entsprechenden 7*exo*-Isomeren. Die basenkatalysierte Epimerisierung (NaOH oder $N(CH_2CH_3)_3$) verschiedener 7-monosubstituierter Bicyclo[3.2.0]-hept-2-en-6-one (**1**–**7**) und Bicyclo[3.2.0]heptan-6-one (**8**–**10**) führt je nach Substituent (R) zu folgenden *endo*/*exo*-Gleichgewichtsgemischen: a) Bicyclo[3.2.0]-hept-2-en-6-one: R = F: 89/11, R = Cl: 87/13, R = CH_3: 76/24, R = CH_2CH_3: 65/35, R = $CH(CH_3)_2$: 57/43, R = $C(CH_3)_3$: 10/90, R = C_6H_5: 66/34; b) Bicyclo[3.2.0]-heptan-6-one: R = Cl: 85/15, R = CH_3: 45/55, R = $C(CH_3)_3$: 0,4/99,6. In jedem Fall wurde das gleiche Epimerengemisch erhalten, ausgehend sowohl vom *endo*- wie auch vom *exo*-Isomeren.

Die bemerkenswerte *endo*-Stabilität wird einer Bevorzugung der Konformation **11** des Cyclobutanonringes zugeschrieben, verursacht durch geringere *Pitzer*-Spannung. So kann ein *endo*-Substituent an C(7) eine pseudoäquatoriale Lage am Cyclobutanonring einnehmen. Bei sehr sperrigen Substituenten mit zunehmender Raumerfüllung nimmt eine 1,2-abstossende Wechselwirkung langsam überhand, bis im Falle des *t*-Butylsubstituenten die *exo*-Konfiguration die stabilere wird.

Die Dehalogenierung von 7-Halo-substituierten Bicyclo[3.2.0]hept-2-en-6-onen (**15** bis **21**) mit Zink und Eisessig und mit Tributylzinnhydrid führte zu den folgenden *endo*/*exo*-Epimerengemischen der entsprechenden 7-monosubstituierten Bicyclo[3.2.0]hept-2-en-6-one (**2** bis **7**): R = Cl: 92/8, R = CH_3: 93/7, R = CH_2CH_3: 93/7, R = $CH(CH_3)_2$: 92/8, R = $C(CH_3)_3$: 93/7, R = C_6H_5: 93/7. In allen Fällen, also unabhängig vom Substituenten R, war das *endo*-Isomere stark bevorzugt. Es muss sich also um eine kinetische Kontrolle im isomerenbestimmenden Schritt handeln: Die Reduktion verläuft über das Enolat, bzw. über eine Radikalspezies

[1]) British Science Research Council Post-doctoral Fellow 1969–1970.

[2]) Laboratory of Macromolecular Chemistry, K.U.L. Leuven.

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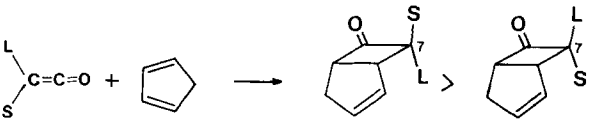
mit trigonal-planarer Anordnung am C(7), so dass die (irreversible) Wasserstoffanlagerung von der weniger behinderten Seite, der *exo*-Seite her erfolgt.

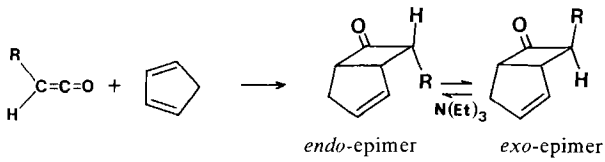
1. Introduction. – The cycloaddition of unequally substituted ketenes to cyclopentadiene has been reported [1–4] to give specifically the isomers of bicyclo[3.2.0]-hept-2-en-6-ones with the larger of the two moieties at C(7) in the *endo*-position (*Scheme 1*, L = large, S = small).

Scheme 1



The ketenes were generated *in situ* by treatment of acid chlorides with excess of triethylamine. Subsequent to the highly stereospecific kinetically controlled cycloaddition of aldoketenes (S = H) to cyclopentadiene, we occasionally observed a thermodynamically controlled epimerization of the product at C(7) *(Scheme 2)*. On closer examination we were surprised to find that the equilibrium of this epimerization was not always biased in the direction of the *exo*-epimer.

Scheme 2



endo-epimer *exo*-epimer

In the present paper we describe a study of this epimerization with several 7-monosubstituted bicyclo[3.2.0]hept-2-en-6-ones and with some corresponding bicyclo[3.2.0]heptan-6-ones. The results are of interest not only because they contradict our intuition with regard to steric effects *(Section 4)*, but also because they bear on the arguments [1–4] for the 'orthogonal' approach in the cycloaddition of ketenes to olefines *(Section 5)*. Since the completion of this work, some of the results presented here have been reported by *Brook et al.* [5].

2. Epimerization. – In the bicyclo[3.2.0]hept-2-en-6-ones (**A**) subjected to epimerization, the substituent at C(7) was fluorine (**1**), chlorine (**2**), methyl (**3**), ethyl (**4**), isopropyl (**5**), *t*-butyl (**6**) or phenyl (**7**). In the bicyclo[3.2.0]heptan-6-one (**B**) series only chlorine (**8**), methyl (**9**) and *t*-butyl (**10**) were examined. In all cases, both the *endo*-epimers (*endo*-**1** to *endo*-**10**) and the *exo*-epimers (*exo*-**1** to *exo*-**10**) were used (for formulae, see *Table 1*). The methods of their preparation, purification and configurational assignment will be described in later sections below. The compounds subjected to equilibration were of high epimer purity[3]) (see *Table 1*).

[3]) The 'epimer purity' is the % content of the major epimer in the mixture of the two (*endo*- and *exo*-)-epimers, not counting the presence of other components in the mixture.

Table 1. *Equilibration of* 7exo- *and* 7endo-*substituted bicyclo[3.2.0]hept-2-en-6-ones* (**A**) *and bicyclo[3.2.0]heptan-6-ones* (**B**)

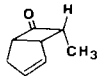
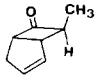
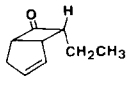
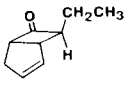
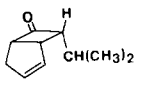
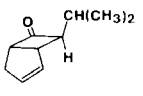
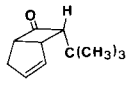
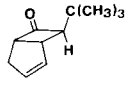
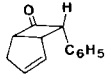
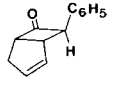
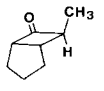
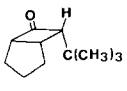
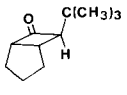
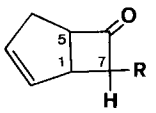
No.	Starting with	Epimer purity %	Epimer ratio after equilibration *endo*:*exo*	Epimerization conditions[a])	$\Delta G°_{endo\text{-}exo}$ (for the reaction *exo* → *endo*)	Epimer ratio after equilibration *endo*:*exo*	Epimer purity %	Starting with	No.
endo-**1**			89 :11	Method C 80°, 7 days	−1.24	88.7:11.3			*exo*-**1**
endo-**2**		98.2	86.8:13.2	Method B ~20°, 3 days	−1.22	86.7:13.3	97.8		*exo*-**2**
endo-**3**		97.0	76.6:23.4	Method A ~20°, 20 h Method A in D_2O ~20°, 24 h	−0.68	76.3:23.7 78.3:21.7	100 presumed[b])		*exo*-**3**
endo-**4**		97.0	65.1:34.9	Method A	−0.37	64.4:35.6	98.5		*exo*-**4**
endo-**5**		97.4	57.0:43.0	Method A ~20°, 90 h	−0.17	56.9:43.1	99.3		*exo*-**5**

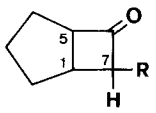
Table 1 (continued)

No.	Starting with	Epimer purity %	Epimer ratio after equilibration *endo*:*exo*	Epimerization conditions[a])	$\Delta G^\circ_{endo\text{-}exo}$ (for the reaction *exo* → *endo*)	Epimer ratio after equilibration *endo*:*exo*	Epimer purity %	Starting with	No.
endo-**6**		93.5	9.7:90.3	Method A ~20°, 120 h	+1.30	9.6:90.4	97.9		*exo*-**6**
endo-**7**		97	65 :35	Method D ~20°, 18 h	−0.40	67 :33	87.5		*exo*-**7**
endo-**8**		97.8	84.7:15.3	Method C 80°, 20 days	−1.02	84.9:15.1	97.0		*exo*-**8**
endo-**9**		97.5	44.9:55.1	Method A ~20°, 20 h	+0.12	44.7:55.3	97.0		*exo*-**9**
endo-**10**		91.5	0.4:99.6	Method A ~20°, 100 h	+3.26	0.4:99.6	99.7		*exo*-**10**

[a]) For details see *Exper. Part.* [b]) This sample was generated *in situ*, under the conditions of epimerization by a rearrangement reaction which is considered to lead stereospecifically to *exo*-**3** (see also text).



Series **A**: **1** to **7**



Series **B**: **8** to **10**

The basic conditions used for the epimerization were aqueous NaOH-solution (method A) or triethylamine in benzene (methods B, C and D). In most cases, the reaction mixture was kept at room temperature; with two of the halo-derivatives (**1** and **8**) the temperature was 80°. Sufficient reaction time was allowed in each case so that the same epimer composition (*i.e.* equilibrium) was reached from both epimers. The epimer ratio before and after equilibration was determined by gas chromatography (GC.) in all the cases except the 7-phenylbicycloheptenones (**7**) where it was assessed by integration of the well-separated NMR. signals due to H_{exo}- and H_{endo}–C(7) ($\delta = 4.75$ and 4.02 ppm). That these epimerizations proceed by enolization at C(7) was shown by deuterium exchange experiments [6]. No products other than the *7endo*- and *7exo*-epimers of the bicyclic ketones **1** to **10** could be detected at any stage, during the epimerization process, as evidenced by GC. or NMR.

The experimental results, especially the free enthalpy difference $\Delta G^\circ_{endo-exo}$ of the *exo* → *endo* epimerization are summarized in *Table 1*. The following generalizations emerge:

a) For most of the ketones examined, the epimer with the substituent R at C(7) in the *endo*-position is the more stable one (by 0.2 to 1.2 kcal/mol).

b) This stability bias toward the *endo*-epimer decreases with the substituent R at C(7) in the order fluorine (**1**), chlorine (**2**), methyl (**3**), phenyl (**7**), ethyl (**4**), isopropyl (**5**) and *t*-butyl (**6**) in the unsaturated series (**A**), and in the order chlorine (**8**), methyl (**9**) and *t*-butyl (**10**) in the saturated series (**B**). In the cases of **6**, **9**, and **10**, the stability bias has switched over to the *exo*-epimer.

c) Compared to the unsaturated (**A**) series, there is a decrease of the *endo*-preference for corresponding substituents R in the saturated (**B**) series.

These observations will be analyzed in *Section 4*.

3. Configuration and conformation of the epimeric ketones. – The configurational assignments of the epimers of all the 7-monosubstituted bicyclo[3.2.0]hept-2-en-6-ones (**A**) and bicyclo[3.2.0]heptan-6-ones (**B**) were made in accord with the arguments used previously [1] [7]. Since they are interrelated with arguments on the preferred conformations, they will be treated together.

The conformational variants to be considered in this connection are best seen in the four-membered ring. This is sufficient since the torsional motions available to the 5-membered-ring atoms are largely not independent. Intramolecular motion may involve considerable deviation from planarity (angle of puckering up to 30°) in cyclobutanes [8] and probably also in cyclobutanones [9]. The exact position of the energy-minimum along this four-membered-ring flipping path (= pseudo-rotation) undoubtedly varies from case to case; it is likely that the folded confor-

mations are favored. In the bicyclo[3.2.0]heptan- or hept-2-en-6-one systems we must consider two conformers, the one represented by conformation **11** with the carbonyl group folded in, towards the *endo*-side of the bicyclic ring system, the other one represented by conformation **12** with the carbonyl group folded out, towards the *exo*-side. To illustrate the salient structural features, conformation **11** and **12** are also shown in projectional views along the C(5),C(4)-bond (**a**) and along the C(7),C(1)-bond (**b**). All the compounds under investigation here appear to show a strong bias of the flipping motion toward conformation **11**. The evidence is as follows:

a) In the NMR. spectra (all values given for CCl_4 or $CDCl_3$ solutions) of compounds **1** to **10** (see *Table 2*) H–C(5) couples fairly strongly ($J = 7.3$–9.7 Hz) with one of the two H–C(4), but only weakly ($J = 1$–3.3 Hz) with the other H–C(4).

Table 2. Cis- *and* trans-*NMR.-coupling constants of vicinal protons relating to the conformation of the four-membered ring in bicyclo[3.2.0]hept-2-en-6-ones* (**A**) *and bicyclo[3.2.0]heptane-6-ones* (**B**)

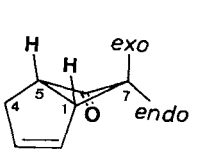
Compound	Coupling constants[a])			
	H–C(5) to H_{endo}–C(4)[b])	H–C(5) to H_{exo}–C(4)	H–C(1) to H_{endo}–C(7)[c])	H–C(1) to H_{exo}–C(7)
endo-**1**	1.5	7.3		8.3
exo-**1**	3.3	9.5	2.4	
endo-**2**	2.1	7.8		8
exo-**2**	3.2	9.4	2.6	
endo-**3**	2.2	8.2		?
exo-**3**	3.0	8.8	3.2	
endo-**4**	2.3	8.4		6.3
exo-**4**	3.0	8.9	3.0	
endo-**5**	2.1	7.8		8.6
exo-**5**	3.1	9.5	3	
endo-**6**	2.2	?		?
exo-**6**	2.2	9.7	3.1	
endo-**7**	2.2	7.3		9
exo-**7**	2.2	9.6	3.1	
endo-**8**	1	7.5		9.7
exo-**8**	2	8	4.0	
endo-**9**	1	8		10.5
exo-**9**	3	8.5	4.4	
endo-**10**	1	7.5		10.5
exo-**10**	3	8.5	5.0	
13	2.2	9.5	3.0	8.5
14	?	?	2.8	8.6

[a]) The coupling constants are derived from a first-order analysis and are thus accurate in most cases only to ± 0.3 Hz. When no figure after the decimal point is given, the accuracy is only ± 1 Hz.

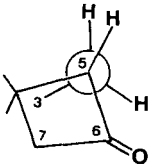
[b]) The H_{exo}- and the H_{endo}–C(4) are identified by the larger and the smaller coupling constants with H–C(5) as well as by the larger ($\delta_{CCl_4} - \delta_{C_6H_6} = \Delta\delta = 0.3$–$0.6$ ppm) and the smaller ($\Delta\delta = 0.05$–0.2 ppm) benzene shift, respectively. The chemical shift of the H_{exo}–C(4) is invariably at higher field by about 0.2 ppm than that of its geminal *endo*-neighbour (both in the δ-range of 2.3 to 2.7 ppm).

[c]) The identification of the H_{exo}- and H_{endo}–C(7) signals are, of course, equivalent to the assignment of the *endo*- and *exo*-configurations to compounds **1** to **10**, as has been described previously [1]. The assignment is based on the fact that, of each epimer pair, one epimer shows a large H–C(1)/H–C(7)-coupling (J_{cis}), the other, a small one (J_{trans}).

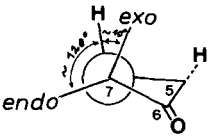
The same is true for the unsubstituted bicyclo[3.2.0]hept-2-en-one (**13**) and bicyclo-[3.2.0]heptan-6-one (**14**). This is only possible if the H,C(5)-bond lies staggered somewhere (but not halfway) in between the two H,C(4)-bonds when viewed in vicinal projection along the C(5),C(4)-axis. Such an arrangement is realized in conformation **11** (see **11a**), but not in **12** (see **12a**). This argument for the preponderance of conformer **11** is independent of the assignment of the two H–C(4) signals to the *exo*- and *endo*-protons; in fact, it permits such an assignment since only the H_{exo}–C(4) can be the one with the large H,C(5)-coupling constant.



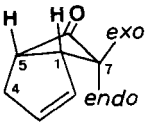
11



11a



11b



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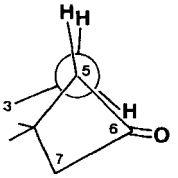
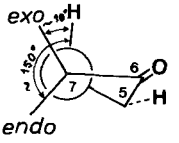
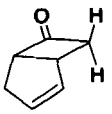


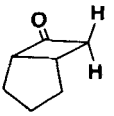
12a



12b



13



14

b) One epimer of each of the compounds **1** to **10** is characterized by a small coupling constant ($J = 2.4$–5.0 Hz) between H–C(1) and H–C(7). Such a small coupling is not in accord with the *endo*-epimers either in conformation **11** or **12** (see *H–C(1)/H_{exo}–C(7) torsional angle of ~10° in **11b** and in **12b**)*, nor does it fit for the *exo*-epimers in conformation **12** (see *H–C(1)/H_{endo}–C(7) torsional angle of ~150° in **12b**)*. The small coupling constant, therefore, in addition to indicating the *exo*-configuration for these epimers (*exo*-**1** to *exo*-**10**) [1], also confirms the above conclusion that they prefer to exist as conformer **11**.

c) The other epimers of compounds **1** to **10** must thus belong to the *endo*-series (*endo*-**1** to *endo*-**10**). As to their conformational preference, no confirmation of the above conclusion can be derived from the relatively large coupling ($J = 6.3$–10.5 Hz) between H–C(1) and H_{exo}–C(7) since an appropriate torsional angle of about 10° is available both in conformation **11** and **12** (see **11** and **12b**).

d) The unsubstituted compounds **13** and **14** display the coupling of H–C(1) with both H_{endo}- and H_{exo}–C(7). The fact that the first of these constants is small ($J = 3.0$ and 2.8 Hz) and the second is large ($J = 8.5$ and 8.6 Hz) indicates, as above, a staggered position of H–C(1) between (but not halfway) the two

H–C(7)'s when viewed along the C(1), C(7)-bond. Since this is realized only in conformations near **11**, it means that the compounds with two H-atoms at C(7) also prefer that conformer.

e) A recent X-ray analysis of 7*endo*-chloro-7*exo*-methoxycarbonylbicyclo[3.2.0]-hept-2-en-6-one confirms the preference of conformation **11** with a four-ring puckering angle along the C(1), C(6)-axis of 13,4° [10].

4. Rationalization. – In this section we consider a possible rationalization of the observed energy difference due to the two configurations at C(7) (*exo* and *endo*) of different 7-monosubstituted bicyclo[3.2.0]hept-2-en-6-ones (**A**) and bicyclo-[3.2.0]heptan-6-ones (**B**) in terms of intramolecular strains, which, of course must also account for the preferred conformations. The discussion is necessarily qualitative in nature since only free enthalpies were determined. Even though the overall effects are small, they pose some interesting problems.

A closer inspection of the values of *Table 1* shows that *two opposing effects* must be operating, as follows: since the free enthalpy of epimerization, $\Delta G^\circ(R_{endo\text{-}exo})$, is due to the difference in strain contributions of the various substituents as compared to that of a H-atom in the *endo*- and *exo*-position, we have:

$$\Delta G^\circ(R_{endo\text{-}exo}) = (\Delta G^\circ(R_{endo}) - \Delta G^\circ(R_{exo})) - (\Delta G^\circ(H_{endo}) - \Delta G^\circ(H_{exo})),$$

which we call the *endo*-strain of a group R and abbreviate with $E(R)$. The larger $E(R)$, the more effective is the substituent R in stabilizing the *exo*- (over the *endo*-)-epimer of the systems studied here. In *Table 3*, the $E(R)$-values are listed in increasing order for both the unsaturated (**A**) and the saturated series (**B**).

We note that the order of the substituents R according to $E(R)$ is the same as the one according to $A(R)$ and conclude that an increasing bulk[4]) of R destabilizes its *endo*-position. The actual value of $E(R)$ and $A(R)$ are not comparable, $E(R)$ referring to an *endo-exo*-difference in a bicyclo[3.2.0]heptane and $A(R)$ to an axial-equatorial-difference in a cyclohexane system.

Table 3. E-*Values for the substituent R at C(7) of bicyclo[3.2.0]heptene and -heptane derivatives and* A-*values for these substituents R in cyclohexane derivatives*

Substituent	$E(R)$[a])		$A(R)$[b])
R	Bicycloheptanones	Bicycloheptanes	Cyclohexanes
F	−1.24		+0.25
Cl	−1.22	−1.02	+0.5
CH_3	−0.68	+0.12	+1.7
C_6H_5	−0.40		+3.0
C_2H_5	−0.37		+1.75
$CH(CH_3)_2$	−0.17		+2.15
$C(CH_3)_3$	+1.30	+3.26	> +4

a) $\Delta G^\circ(R_{endo\text{-}exo}) = E(R)$-values taken from *Table 1*.
b) $\Delta G^\circ(R_{ax\text{-}eq}) = A(R)$-values [11].

4) The term bulk is used here to express the repulsive strain between the substituent and nearby atoms or groups of atoms.

The postulate of an *endo*-destabilizing bulk effect receives some confirmation from a comparison of the E(R)-values for corresponding R's in the unsaturated (**A**) with those in the saturated series (**B**). The three values available for such a comparison (R = chlorine, methyl and *t*-butyl) are all larger in series **B** than in **A**. This can be rationalized by the increased bulk of the saturated five-membered ring.

A H-atom is generally considered to be smaller than any of the substituents R listed in *Table 3*, and indeed, all A(R)-values (of the cyclohexane systems) are positive. If the same bulk effect were operating in our bicyclo[3.2.0]heptane systems one would expect all substituents R to compete favourably with the H-atom for the *exo*-position; *i.e.* all E(R)-values should also be positive. However, this is not the case. In fact, among the substituents examined, only methyl and *t*-butyl in the saturated series (**B**) and only *t*-butyl in the unsaturated series (**A**) are more stable in the *exo*-position. Therefore, we conclude that there must be a second effect operating in these systems, an *endo*-stabilization effect, which opposes the bulk effect.

The existence of this second (non-bulk) effect can also be inferred from conformational considerations: in *Section 3* it was shown that all *endo*- and also all *exo*-epimers of **1** to **10** prefer to exist as conformer **11** rather than **12**. While the bulk effect explains this preference in the *endo*-epimer, it cannot account for it in all the *exo*-epimers. The fact that even the *exo-t*-butyl derivatives (*exo*-**6** and *exo*-**10**) prefer conformer **11** (see *Section 3*) must be due to another effect.

The preference of conformation **11** in all compounds **1** to **10** (both epimers) can be rationalized by a smaller hindrance of the carbonyl group when turned toward the *endo*-side (conformation **11**) than of the tetrahedral C(7) when turned the same way (conformation **12**). Conformation **11** could also be stabilized by H–C(5) lying orthogonally to the carbonyl plane.

A rationalization of the *endo*-stabilization effect could be offered by postulating that H–C(7) prefers to be in an orthogonal orientation with respect to the carbonyl plane. This effect would, of course, be counteracted by the bulk effect, which destabilizes the *endo*-orientation of the substituents R in proportion to the size of R. With R sufficiently large, the *exo*-orientation of R is even preferred.

The stabilization effect of a C(α),H-bond orthogonal to a carbonyl plane has been utilized in the α-alkyl ketone effect and was rationalized by hyperconjugation [12]. In this connection it is of interest that the epimerization of compounds **3** in D_2O led to an *endo:exo* equilibrium in which the *endo*-epimer is slightly preferred as compared to that in the non-deuteriated **3**. This does not correlate with the published smaller hyperconjugative capacity of deuterium as compared to hydrogen [13] but it fits in with the generally accepted smaller size of deuterium *vs.* hydrogen [14].

5. Argument on the transition state of ketene-cycloaddition. – The argument made previously [4] for the 'orthogonal' rather than the 'parallel' approach in the cycloaddition of ketenes to olefines was based on the C(7)-epimer ratios of the bicyclo[3.2.0]hept-2-en-6-ones with two different substituents at C(7), which are formed in the addition of unequally substituted ketenes to cyclopentadiene. It was observed that the C(7)-epimer with the bulkier substituent in the *endo*-position

was always favored. The addition of carbomethoxychloroketene to cyclopentadiene is presently the only known exception to this rule[5]).

The conclusion with respect to the transition state was based on the assumption that less space was available in the *endo*- than in the *exo*-position; for, if there were more space available on the *endo*-side, then a parallel approach could also have led to the observed product composition. The assumption on the relative space availability on the *endo*- and *exo*-sides at C(7) of bicyclo[3.2.0]heptanes appeared justified from model considerations only.

'Orthogonal' approaches

'Parallel' approaches

The present results, which show that the *exo*-stabilization is a bulk effect, confirm the above mentioned assumption. The possibility that the *endo*-stabilization effect, postulated in this investigation, is responsible for the predominance of the *endo*-epimers in these cycloadditions (thus pointing to a parallel approach) can be excluded by the following arguments:

a) In many observed cases of *endo*-specificity of cycloaddition, the structural feature postulated for the *endo*-stabilization effect is not present and thus cannot be involved in the transition state.

b) In those four cases where available experimental results permit a direct comparison of the epimer ratio in the cycloaddition product with that at the epimerization equilibrium, the *endo*-epimer still predominates in the cycloaddition product to greater extent than in the equilibrium. These cases are the fluoro-, the chloro-, the methyl- and the phenyl-derivative (**1**, **2**, **3** and **6**), where the *endo*:*exo* ratios are 94:6, 97:3, 98:2 and $>95:<5$ in the cycloadditions reported earlier [1][6]) and 89:11, 87:13, 76:24 and 65:35 in the epimerizations reported here. Since it is unlikely that the *endo*-stabilization (not being of the bulk-type, as postulated) would act more strongly through partially formed (transition state) than fully established bonds (equilibrium), this greater effectiveness of *endo*-stabilization in the cycloaddition shows it to be a bulk effect.

The present results, therefore, confirm the orthogonal approach during the ketene-cyclopentadiene cycloaddition.

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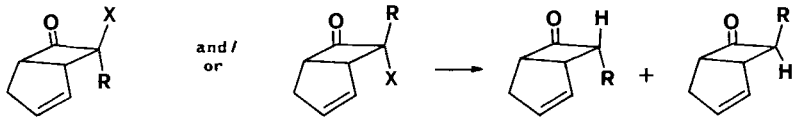
5) This unusual behavior has been rationalized by coulombic interactions or secondary orbital effects opposing the bulk effects of the substituents [10].

6) The cycloaddition of fluoroketene to give the epimer mixture of the 7-fluoro-derivative **1** is described in the *Exper. Part* of this paper.

6. Synthetic procedures. – The compounds needed for the investigation described in the preceding sections had to be prepared by various methods. The choice of synthetic procedure in each case was so as to obtain samples in which the desired epimer was present in sufficient amount to permit its chromatographic purification or, in one case, its direct use in the epimerization. The 7*endo*-substituted bicyclo-[3.2.0]hept-2-en-6-ones (*endo*-**1** to *endo*-**7**) were synthesized as follows: In the case of the fluoro- (*endo*-**1**), the chloro- (*endo*-**2**), the methyl- (*endo*-**3**) and the phenyl-derivative (*endo*-**7**) advantage was taken of the *endo*-stereospecificity [1] of aldoketene cycloadditions. *In situ*-generated fluoro-[6]), chloro-, methyl- and phenylketene were added to cyclopentadiene by the described [1] [7] [15–18] procedures. Another method involved two steps: first the cycloaddition of dihalo- or alkylhaloketenes [1] [3] [15–22] to cyclopentadiene to give the 7,7-dihalo (**15**) and the 7-alkyl-7-halo-derivative (**16** to **21**) (the latter mostly as 7-epimeric mixtures) of bicyclo[3.2.0]hept-2-en-6-one and then reductive removal of one halogen using zinc and acetic acid or tributyltinhydride [23] to give the chloro- (*endo*-**2**), the methyl- (*endo*-**3**), the ethyl- (*endo*-**4**), the isopropyl- (*endo*-**5**), the *t*-butyl- (*endo*-**6**) and the phenyl-derivative (*endo*-**7**).



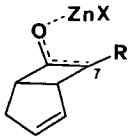
				> 90%		< 10%
15	R = X = Cl		**15**	*endo*-**2**	R = Cl	*exo*-**2**
16A	$R = C_2H_5$	X = Br	**16B**	*endo*-**4**	$R = C_2H_5$	*exo*-**4**
17A	$R = C_3H_7$	X = Br	**17B**	*endo*-**5**	$R = C_3H_7$	*exo*-**5**
18	$R = C_4H_9$	X = Br		*endo*-**6**	$R = C_4H_9$	*exo*-**6**
19A	$R = CH_3$	X = Br	**19B**	*endo*-**3**	$R = CH_3$	*exo*-**3**
20A	$R = CH_3$	X = Cl	**20B**	*endo*-**3**	$R = CH_3$	*exo*-**3**
21	$R = C_6H_5$	X = Cl		*endo*-**7**	$R = C_6H_5$	*exo*-**7**

The reduction of 7-halobicyclo[3.2.0]hept-2-en-6-ones with zinc and acetic acid is assumed to proceed *via* the zinc enolate **22** which is protonated at C(7) from the *exo*-face in a kinetically controlled reaction to give stereoselectively a 7*endo*-monosubstituted bicycloheptenone in over 90% epimeric purity [24]. The compounds that have been reduced by this method and the ratio of epimers in the dehalogenated products are listed in *Table 4*.

Table 4. *Reduction of 7-halobicyclo[3.2.0]hept-2-en-6-ones with zinc and acetic acid*

Starting material (7-halobicyclo[3.2.0]hept-2-en-6-one)	Product (bicyclo[3.2.0]hept-2-en-6-one)	Ratio *endo*:*exo*
15	*endo*-+*exo*-**2**	92:8
16A:**16B** = 57:43	*endo*-+*exo*-**4**	93:7
17A:**17B** = 73:27	*endo*-+*exo*-**5**	92:8
18	*endo*-+*exo*-**6**	93:7
20A	*endo*-+*exo*-**3**	93:7
20B	*endo*-+*exo*-**3**	93:7
21	*endo*-+*exo*-**7**	93:7

An analogous dehalogenation can be achieved with tributyltin hydride [23]. For this reaction with 7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one (**15**), which yielded exclusively *7endo*-chlorobicyclo[3.2.0]hept-2-en-6-one (*endo*-**2**), *Brady et al.* [18] suggested a preferential (for steric reasons) removal of the *exo*-Cl-atom from C(7) to give a non-planar (four-ring strain) radical (**23**), which is thought to pick up a H-atom faster than it can invert.



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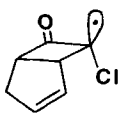

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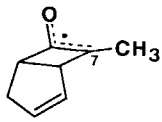

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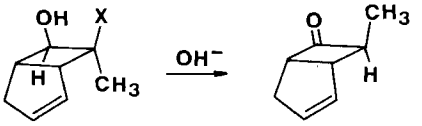
We prefer an explanation which postulates the intermediacy of a planar or a very rapidly inverting radical at C(7) (**24**). The high stereoselectivity of the reduction is due to a kinetically controlled attack of a H-atom on the sterically more available *exo*-face of the intermediate radical. Our observation that the reduction of the 7-bromo-7-methyl-isomers **19A** and **19B** or the 7-chloro-7-methyl-isomer **20A** with tributyltin hydride gave the same mixture (~95:5) of *7endo*-methylbicyclo[3.2.0]hept-2-en-6-one (*endo*-**3**) and of *7exo*-methylbicyclo[3.2.0]hept-2-en-6-one (*exo*-**3**) suggests a common intermediate.

The *7exo*-substituted bicyclo[3.2.0]hept-2-en-6-ones were synthesized as follows: Base-catalyzed equilibration of epimer mixtures containing largely the *endo*-epimers increased the concentration of the *7exo*-substituted bicycloheptenones (*exo*-**1**–**7**) in these mixtures sufficiently so that they could be purified by distillation and preparative gas chromatography. In some cases further enrichment of the *exo*-epimers was achieved by controlled pyrolysis, which preferentially destroys the *endo*-isomers by a kinetically controlled cycloreversion reaction [25]. In the case of the methyl derivative (*exo*-**3** and 7-deuterio-*exo*-**3**) a rearrangement reaction was used. Treatment of either of the two *7exo*-halo-*7endo*-methylbicyclo[3.2.0]-hept-2-en-6*exo*-ols (**25** and **26**) with base (2 N NaOH or 2 N NaOD in D_2O) for



25 X = Cl
26 X = Br

exo-**3**

20 h at room temperature gave stereospecifically [6] *7exo*-methylbicyclo[3.2.0]-hept-2-en-6-one (*exo*-**3**) directly in the solution; this was subsequently equilibrated. The supposition that this procedure is effectively equivalent to an epimerization of the *exo*-epimer of **3** (compare *Footnote b* in *Table 1*) is based on mechanistic considerations with respect to the H-migration during the dehydrohalogenation of **25** and **26**, which must take place on the *endo*-side [6].

The saturated ketones (series **B**), namely the three *7endo*-substituted (*endo*-**8**–**10**) and the three *exo*-substituted bicyclo[3.2.0]heptan-6-ones (*exo*-**8**–**10**) were prepared

by catalytic reduction of the correspondingly substituted unsaturated ketones (series **A**), in some cases followed by equilibration and purification by preparative gas chromatography.

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Experimental Part

1. General. – The purity of the compounds or epimer mixtures was determined mainly by gas chromatography (GC.). The percentage composition was measured with an electronic integrator (*Varian* model *480*). The purity was confirmed in each case by their spectroscopic properties. All compounds gave correct elemental analyses except the 7-fluoro-compounds **1**, which were not analyzed. The NMR. spectra were measured in the NMR. laboratories of the Organic Chemistry Department, University of Zürich and at the *F. Hoffmann-La Roche & Co. AG* in Basel. The IR. spectra (absorption bands in cm^{-1}) and the elemental analyses were obtained from the microanalytical laboratories of the Organic Chemistry Department, University of Zürich. Abbreviations: RT. = room temperature, RV. = rotatory evaporator.

1.1. *^{1}H-NMR.-Spectra.* The signals were measured with a *Varian A-100* spectrometer). See also [1].

1.2. *Gas Chromatography* (GC.): The different methods (GC.-A, -B, -C,...) are described in the following manner: purpose/apparatus/detector: oven temperature, column length × diameter, liquid phase on support, carrier gas and gas flow. *GC.-A:* analytical/*Aerograph A-350-B*/catharometer: 90°, 0.9 m × 6.4 mm, 20% *Silicon SE-30* on *Chromosorb W-AW/DMCS* 60/80 mesh, He 37 ml/min. *GC.-B:* prep./*Aerograph A-700* (Autoprep)/hot wire: 130°, 3 m × 9.5 mm, 30% *Silicon SE-30* on *Chromosorb W-AW/DMCS* 60/80 mesh, He 150 ml/min. *GC.-C:* analytical/*Aerograph 1520-B*/hot wire: 148°, 1.5 m × 3 mm, 5% *Emulphor-O* on *Chromosorb W-AW/DMCS* 100/120 mesh, He 25 ml/min. *GC.-D:* as for GC.-C but with oven temperature 98°. *GC.-E:* as for GC.-C but with oven temperature 112°. *GC.-F:* prep./*Aerograph 1520-B*/hot wire: 190°, 6 m × 9.5 mm, 20% *Emulphor-O* on *Chromosorb W* 60/80 mesh, He ~200 ml/min. *GC.-G:* as for GC.-C, but with oven temperature 122°.

2. Methods of equilibration. – One of the four following methods (A, B, C or D) was used in the equilibration of individual epimer pairs. Equilibrium was approached from both sides in each case. The reaction time varied widely and is recorded separately for each epimer pair. The method, the reaction time and the resulting epimer ratio are summarized in *Table 1*.

Method A. Portions of 7-monosubstituted bicyclo[3.2.0]hept-2-en-6-one or -heptan-6-one (3 mmol) were stirred with 1N aqueous NaOH (3 ml) at RT. The mixtures were extracted three times with ether and the combined extracts dried over $NaSO_4$. The ether was evaporated using a RV. and each residue was analyzed gas chromatographically (GC.-D, -E, -G). The compositions were determined with an electronic integrator. After distillation of the crude product at reduced pressure in a bulb tube the yield was in the range of 80–95%.

Method B. A molar solution (3 ml) of the 7-monosubstituted bicyclo[3.2.0]hept-2-en-6-one (series **A**) or -heptan-6-one (series **B**) in benzene was treated with 50 ml triethylamine at RT. The product was analyzed gas chromatographically using an electronic integrator. After distillation of the crude product at reduced pressure in a bulb tube the yield of the epimer mixtures was always 85–90%.

Method C. A solution of 327 mg *7endo*-fluorobicyclo[3.2.0]hept-2-en-6-one (*endo*-**1**) and 4 drops triethylamine in 0.5 ml benzene was warmed to 80° for 5 days. A further 2 drops of triethylamine were added and warming at 80° was continued for 2 days. In the case of *7exo*-fluorobicyclo[3.2.0]-hept-2-en-6-one (*exo*-**1**), a solution of 29 mg compound and 1 drop triethylamine in 0.1 ml benzene was warmed to 80° for 5 days. A second drop of triethylamine was added and warming at 80° was continued for 2 days. Each solution was analyzed gas chromatographically (GC.-A) and the percentage composition of epimers was estimated by determining the peak areas.

Method D. A solution of 7-monosubstituted bicyclo[3.2.0]hept-2-en-6-one (1M in 1 ml benzene) and 20 µl triethylamine was allowed to stand for 20 h at RT. in a NMR. tube. The percentage composition was determined by digital integration of the NMR. signals due to H–C(7) of both epimers (*endo-* and *exo-*) in the mixture using a *Varian A-60* spectrometer.

3. General procedures for the zinc reduction, hydrogenation and purification using the semicarbazone derivative. – The following three general procedures were used for the synthesis and purification of the starting materials for the epimerization. They will not be repeated in detail in the description of the individual cases.

3.1. *Zinc reduction.* To a stirred solution of 7-halobicyclo[3.2.0]hept-2-en-6-one in acetic acid an excess of zinc powder was added in small portions over 30–60 min. No attempt was made to control the attendant warming of the mixture. The reaction mixture was stirred for 30–60 min, treated with water and extracted four times with ether. The combined ether extracts were washed five times with water and once with a satd. $NaHCO_3$-solution. After drying, the ether was removed using a RV. and the residue was distilled under reduced pressure.

3.2. *Hydrogenation.* A mixture of 10% Pd/C and a solution of the 7-substituted bicyclo[3.2.0]hept-2-en-6-one in hexane was shaken under a H_2-atmosphere (760 Torr). When the hydrogen take-up had stopped, the catalyst was filtered off, the hexane evaporated and the residue distilled under reduced pressure.

3.3. *Purification using the semicarbazone derivative.* The 7*endo*-alkylbicyclo[3.2.0]hept-2-en-6-one (50 mmol in 20 ml ethanol) was added to a well stirred solution of 8.4 g (75 mmol) semicarbazide hydrochloride and 12.6 g crystalline CH_3COONa in 75 ml water. After stirring for 10 h the precipitated semicarbazone was filtered off and dissolved in 250 ml boiling ethanol. After standing overnight at RT. the recrystallized derivative was filtered off and dried. The semicarbazone was decomposed by steam-distillation from 100 ml of a 10% aqueous oxalic acid solution. The distillate was extracted three times with ether, the combined extracts were dried over Na_2SO_4, concentrated and the residue was distilled under reduce pressure.

4. Preparation of the monosubstituted bicyclo[3.2.0]hept-2-en-6-ones. – 4.1. *Preparation of* 7endo-*fluoro-*(endo-**1**) *and* 7exo-*fluorobicyclo[3.2.0]hept-2-en-6-one* (exo-**1**). To a well-stirred solution of 20 g (302 mmol) freshly distilled cyclopentadiene and 8.5 g (84 mmol) triethylamine in 40 ml dry ether, cooled to −70°, a solution of 8.1 g (84 mmol) fluoroacetyl chloride in 10 ml ether was added dropwise. After stirring for 6 h, the reaction mixture was allowed to warm to RT. and the precipitated triethylamine hydrochloride was filtered off. The ether solution was washed successively with 5% HCl-, 5% $NaHCO_3$-solutions and water and then dried ($CaSO_4$). The ether was distilled off using a RV. and the residue was distilled. The first fraction b.p. 58–60°/15–20 Torr contained 81% dicyclopentadiene (GC.-A). The second fraction (2.7 g), b.p. 65–66°/6–7 Torr, contained, in addition to a small amount of dicyclopentadiene, 81% 7*endo*-fluoro-(*endo*-**1**) and 5% 7*exo*-fluorobicyclo[3.2.0]hept-2-en-6-one (*exo*-**1**) (GC.-A). Total yield of both fractions 26%. The epimers were separated by preparative scale gas chromatography (GC.-B).

The faster moving component was 7*exo*-fluorobicyclo[3.2.0]hept-2-en-6-one (*exo*-**1**). – IR. (CCl_4): 1790 (C=O). – ^{1}H-NMR. (CCl_4): 5.97–5.73 (*m*, 2 H, H–C(2) and H–C(3)); 4.86 ($d\times d\times d$, J = 54.3, 2.4 and 2.2, 1H, H–C(7)); 4.17–3.87 (*m*, 1H, H–C(5)); 3.76–3.40 (*m*, 1H, H–C(1)); 2.71 ($d\times d\times d\times d\times d$, J = 3.8, ~2, ~2, 17.5 and 2.3, 1H, H_{endo}–C(4)); 2.55 ($d\times d\times d\times d\times d$, J = 2.6, ~2, ~2, 17.5 and 9.5, 1H, H_{exo}–C(4)).

The second component was 7*endo*-fluorobicyclo[3.2.0]hept-2-en-6-one (*endo*-**1**). – IR. (CCl_4): 1800 (C=O). – ^{1}H-NMR. (CCl_4): 6.00–5.86 and 5.77–5.63 (2 *m*, each 1H, H–C(2) and H–C(3)); 5.52 ($d\times d\times d$, J = 53.3, 8.3 and 3.4, 1H, H–C(7)); 3.99–3.72 (*m*, 1H, H–C(1)); 3.58–3.34 (*m*, 1H, H–C(5)); 2.72 ($d\times d\times d\times d\times d$, J = 2.6, ~2, ~2, 1.5 and 17.5, 1H, H_{endo}–C(4)); 2.52 ($d\times d\times d\times d\times d$, J = 1.8, ~2, ~2, 17.5 and 7.5, 1H, H_{exo}–C(4)).

4.2. *Preparation of* 7endo-*chlorobicyclo[3.2.0]hept-2-en-6-one* (endo-**2**). A solution of 88.6 g (650 mmol), 7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one (**15**) [19] in 400 ml acetic acid was treated with 38 g (580 mmol) zinc powder. The crude product was shown (GC.-C) to contain 92% 7*endo*-chloro-(*endo*-**2**) and 8% 7*exo*-chlorobicyclo[3.2.0]hept-2-en-6-one (*exo*-**2**). Distillation gave 57.2 g (80%) 7*endo*-chlorobicyclo[3.2.0]hept-2-en-6-one (*endo*-**2**), b.p. 98–100°/11 Torr. The epimer purity was shown (GC.-C) to be at least 98%. The IR. and NMR. spectra were identical with those of a sample prepared by the reaction of cyclopentadiene and monochloroketene [1] [17].

4.3. *Preparation of* 7exo-*chlorobicyclo[3.2.0]hept-2-en-6-one* (exo-**2**). A mixture of 16.0 g (112 mmol) 7*endo*-chlorobicyclo[3.2.0]hept-2-en-6-one (*endo*-**2**) and 0.6 g trioctylamine was heated carefully at 80–85°/15 Torr so that only the lower boiling *exo*-epimer (*exo*-**2**) distilled very slowly through a 25-cm-*Vigreux* column. After 20 h, 9.48 g (60%) 7*exo*-chlorobicyclo[3.2.0]hept-2-en-6-one (*exo*-**2**)

was obtained as a colorless oil. The epimer purity was shown (GC.-C) to be at least 97%. – IR. (CCl_4): 1797 (C=O). – ^{1}H-NMR. (C_6H_6): 5.37–5.25 and 5.23–5.12 (2 *m*, each 1H, H–C(2) and H–C(3)); 3.88 (*d*×*d*, *J* = 2.6 and 2.0, 1H, H–C(7)); 3.70–3.45 (*m*, 1H, H–C(5)); 3.12–2.92 (*m*, 1H, H–C(1)); 2.32 (*d*×*d*×*d*×*d*×*d*, *J* = 2.2, 2.1, 2.1, 17.8 and 3.2, 1H, H_{endo}–C(4)); 1.87 (*d*×*d*×*d*×*d*×*d*, *J* = 2.0, 2.1, 2.1, 17.8 and 9.4), 1H, H_{exo}–C(4)).

4.4. *Preparation of* 7endo-*methylbicyclo[3.2.0]hept-2-en-6-one* (endo-**3**). As described by *Jaz & Denis* [16], purification by formation of the semicarbazone derivative. The isomer purity was shown (GC.-D) to be 98%.

4.5. *Preparation and epimerization of* 7exo-*methylbicyclo[3.2.0]hept-2-en-6-one* (exo-**3**). After treating 7*exo*-chloro-7*endo*-methylbicyclo[3.2.0]hept-2-en-6*exo*-ol (**25**) with 2N NaOH [6] the product (*exo*-**3**) was isomerized directly in the same solution. The total procedure entailed stirring 3mmol **25** with 3 ml 2N NaOH. The rapidly formed ketone *exo*-**3** was equilibrated by continued stirring of the solution for 20 h at RT. Isolation yielded a mixture of 76.3% 7*endo*-methyl-(*endo*-**3**) and 23.7% 7*exo*-methylbicyclo[3.2.0]hept-2-en-6-one (*exo*-**3**) (GC.-D). Repetition of this experiment using 2N NaOD in D_2O yielded a mixture of 78.3% 7*exo*-deuterio-7*endo*-methyl-([^{2}H]-*endo*-**3**) and 21.7% 7*endo*-deuterio-7*exo*-methylbicyclo[3.2.0]hept-2-en-6-one ([^{2}H]-*exo*-**3**) (GC.-D).

4.6. *Preparation of* 7endo-*ethylbicyclo[3.2.0]hept-2-en-6-one* (endo-**4**). A solution of 46.5 g (216 mmol) 7-bromo-7-ethylbicyclo[3.2.0]hept-2-en-6-one [3] [21] (containing 57% of the 7*exo*-bromo-7*endo*-methyl-(**19A**) and 43% of the 7*endo*-bromo-7*exo*-methyl-(**19B**) epimer) in 250 ml acetic acid was treated with 19.9 g (304 mmol) zinc powder as described under *Section 3.1*. The crude product was distilled at 77–82°/16 Torr to give 22.9 g (78%) of a colorless oil, which contained (GC.-E) 93% 7*endo*-ethyl-(*endo*-**4**) and 7% 7*exo*-ethylbicyclo[3.2.0]hept-2-en-6-one (*exo*-**4**). The isomer purity of *endo*-**4** was increased to 98% by purification through the semicarbazone derivative as described above in 64% yield. – IR. (CCl_4): 1775 (C=O). – ^{1}H-NMR. (CCl_4): 5.91–5.78 and 5,77–5.64 (2 *m*, each 1H, H–C(2) and H–C(3)); 3.80–3.60 (*m*, 1H, H–C(5)); 3.65–3.40 (*m*, 1H, H–C(1)); 3.28 (*t*×*d*×*d*, *J* = 7.8, 6.3 and 2.3, 1H, H–C(7)); 2.59 (*d*×*d*×*d*×*d*×*d*, *J* = 2.3, 2.3, 2.3, 17.5 and 2.3, 1H, H_{endo}–C(4)); 2.33 (*d*×*d*×*d*×*d*×*d*, *J* = 2.5, 2.5, 2.5, 17.5 and 8.4, 1H, H_{exo}–C(4)); 1.73–1.15 (*m*, 2H, H_2C–C(7)); 0.94 (*t*, *J* = 7.5, 3H, CH_3).

4.7. *Preparation of* 7exo-*ethylbicyclo[3.2.0]hept-2-en-6-one* (exo-**4**). A mixture of 11.2 g (82.4 mmol) 7-ethylbicyclo[3.2.0]hept-2-en-6-one (**4**), containing 93% of the 7*endo*-ethyl-(*endo*-**4**) and 7% of the 7*exo*-ethyl-epimer (*exo*-**4**), was stirred in 110 ml 1N NaOH for 30 h at RT. The organic material was extracted into ether and the combined ether extracts were dried over Na_2SO_4. The solvent was evaporated and the residue distilled at 80–90°/11 Torr to give 9.65 g (86%) of a mixture (GC.-E) of 7*endo*-ethyl-(*endo*-**4**) (65%) and 7*exo*-ethylbicyclo[3.2.0]hept-2-en-6-one (*exo*-**4**) (35%). Gas chromatography (GC.-F) separated the faster moving fraction, which contained 7*exo*-ethylbicyclo[3.2.0]hept-2-en-6-one (*exo*-**4**) in 98% epimer purity (GC.-E). – IR. (CCl_4): 1775 (C=O). – ^{1}H-NMR. (CCl_4): 5.88–5.77 and 5.75–5.66 (2 *m*, each 1H, H–C(2) and H–C(3)); 3.75 (*d*×*d*×*d*×*d*, *J* = 8.9, 7.7, 3.0 and 3.0, 1H, H–C(5)); 3.17–2.97 (*m*, 1H, H–C(1)); 2.69 (*t*×*d*×*d*, *J* = 7.8, 3.0 and 3.0, 1H, H–C(7)); 2.65 (*d*×*d*×*d*×*d*×*d*, *J* = 2.5, 2.5, 2.5, 17.6 and 3.0, 1H, H_{endo}–C(4)); 2.44 (*d*×*d*×*d*×*d*×*d*, *J* = 2, 2, 2, 17.6 and 8.9, 1H, H_{exo}–C(4)); 1.67 (*qa*×*d*, *J* = 7.0 and 7.8, 2H, H_2C–C(7)); 0.98 (*t*, *J* = 7.0, 3H, CH_3).

4.8. *Preparation of* 7endo-*isopropylbicyclo[3.2.0]hept-2-en-6-one* (endo-**5**). A solution of 46,5 g (203 mmol) 7-bromo-7-isopropylbicyclo[3.2.0]hept-2-en-6-one (**17**) [3] (containing 73% 7*exo*-bromo-7*endo*-isopropyl-(**17A**) and 27% 7*endo*-bromo-7*exo*-isopropylbicyclo[3.2.0]hept-2-en-6-one (**17B**)) in 250 ml acetic acid was treated with 19.9 g (304 mmol) of zinc powder as described above. Distillation of the crude product at 88–94°/11 Torr gave 24.9 g (82%) of a colorless oil. Gas chromatography (GC.-E) showed the oil to contain 92% 7*endo*-isopropyl-(*endo*-**5**) and 8% 7*exo*-isopropylbicyclo[3.2.0]-hept-2-en-6-one (*exo*-**5**). Purification *via* the semicarbazone derivative as described above gave in 58% yield 7*endo*-isopropylbicyclo[3.2.0]hept-2-en-6-one (*endo*-**5**) of 98% isomer purity. – IR. (CCl_4): 1775 (C=O). – ^{1}H-NMR. (CCl_4): 5.90–5.80 and 5.80–5.70 (2 *m*, each 1H, H–C(2) and H–C(3)); 3.76–3.54 (*m*, 1H, H–C(5)); 3.62–3.38 (*m*, 1H, H–C(1)); 3.02 (*d*×*d*×*d*, *J* = 11.0, 8.6 and 3.0, 1H, H–C(7)); 2.59 (*d*×*d*×*d*×*d*×*d*, *J* = 2.5, 2.5, 2.5, 17.0 and 2.1, 1H, H_{endo}–C(4)); 2.32 (*d*×*d*×*d*×*d*×*d*, *J* = 2.5, 2.5, 2.5, 17.0 and 7.8, 1H, H_{exo}–C(4)); 2.00–1.50 (*m*, 1H, CH–C(7)); 1.02 (*d*, *J* = 6.3, 3H, CH_3); 0.88 (*d*, *J* = 6.3, 3H, CH_3).

4.9. *Preparation of* 7exo-*isopropylbicyclo[3.2.0]hept-2-en-6-one* (exo-**5**). A mixture of 12.0 g (79.5 mmol) 7-isopropylbicyclo[3.2.0]hept-2-en-6-one (**5**), containing 92% of the 7*endo*-isopropyl-(*endo*-**5**) and 8% of the 7*exo*-isopropyl-epimer (*exo*-**5**), with 120 ml 1N NaOH was stirred for 90 h. Ether

extraction and bulb-tube distillation of the crude product at 105–115°/15 Torr yielded 10.1 g (84%) of a mixture (GC.-E) containing 57% 7*endo*-isopropyl-(*endo*-**5**) and 43% 7*exo*-isopropylbicyclo[3.2.0]hept-2-en-6-one (*exo*-**5**). Gas chromatographic separation (GC.-F) of the minor, faster moving component gave 7*exo*-isopropylbicyclo[3.2.0]hept-2-en-6-one (*exo*-**5**) in 98% purity. – IR. (CCl_4): 1770 (C=O). – ^{1}H-NMR. (CCl_4): 5.86–5.65 (2 H, H–C(2) and H–C(3)); 3.67 ($d\times d\times d\times d$, J = 9.5, 7.8, 3.1 and 3.1, 1 H, H–C(5)); 3.25–3.04 (*m*, 1 H, H–C(1)); 2.61 ($d\times d\times d\times d\times d$, J = 2.3, 2.3, 2.3, 17.6 and 3.1, 1 H, H_{endo}–C(4)); 2.53 ($d\times d\times d$, J = 9.0, 3 and 3.1, 1 H, H–C(7)); 2.47 ($d\times d\times d\times d\times d$, J = 1.8, 1.8, 1.8, 17.6 and 9.5, 1 H, H_{exo}–C(4)); 2.18–1.63 (*m*, 1 H, CH–C(7)); 0.98 (*d*, J = 6.7, 6 H, 2 CH_3).

4.10. *Preparation of* 7endo-t-*butylbicyclo[3.2.0]hept-2-en-6-one* (endo-**6**). A solution of 39.2 g (162 mmol) 7*exo*-bromo-7*endo*-*t*-butylbicyclo[3.2.0]hept-2-en-6-one (**18**) [3] in 200 ml acetic acid was reacted with 16.0 g (245 mmol) zinc powder. Distillation of the crude product at 96–100°/15 Torr gave 22.6 g (85%) of a mixture (GC.-G) of 7% 7*exo*-*t*-butyl-(*exo*-**6**) and 93% 7*endo*-*t*-butylbicyclo[3.2.0]-hept-2-en-6-one (*endo*-**6**).

Spectroscopic properties of endo-**6**. – IR. (CCl_4): 1772 (C=O). – ^{1}H-NMR. (CCl_4): 5.93–5.79 and 5.79–5.65 (2 *m*, each 1 H, H–C(2) and H–C(3)); 3.66–3.40 (*m*, 2 H, H–C(5) and H–C(1)); 3.35–3.18 (*m*, 1 H, H–C(7)); 2.63 ($d\times d\times d\times d\times d$, J = 2.2, 2.2, 2.2, 17.3 and 2.2, 1 H, H_{endo}–C(4)); 2.46–2.05 (*m*, 1 H, H_{exo}–C(4)); 0.95 (*s*, 9 H, $C(CH_3)_3$).

4.11. *Preparation of* 7exo-t-*butylbicyclo[3.2.0]hept-2-en-6-one* (exo-**6**). A mixture of 4.93 g (30 mmol) 7-*t*-butylbicyclo[3.2.0]hept-2-en-6-one (**6**), containing 93% of the 7*endo*-*t*-butyl-(*endo*-**6**) and 7% of the 7*exo*-*t*-butyl-epimer (*exo*-**6**), with 50 ml 1N NaOH was stirred for 120 h. The product was extracted into ether and the residue obtained on evaporation of the solvent yielded, after distillation at 110–120°/11 Torr, 4.32 g (88%) of a colorless oil. The oil was shown (GC.-G) to be a mixture containing 90% of the 7*exo*-*t*-butyl-(*exo*-**6**) and 10% of the 7*endo*-*t*-butylisomer-(*endo*-**6**). Gas chromatographic separation (GC.-F) of the faster travelling major component yielded 99% pure 7*exo*-*t*-butylbicyclo[3.2.0]-hept-2-en-6-one (*exo*-**6**). – IR. (CCl_4): 1772 (C=O). – ^{1}H-NMR. (CCl_4): 5.84–5.63 (*m*, 2 H, H–C(2) and H–C(3)); 3.68–3.45 (*m*, 1 H, H–C(5)); 3.30–3.19 (*m*, 1 H, H–C(1)); 2.61 ($d\times d\times d\times d\times d$, J = 2.5, 2.5, 2.5, 17.4 and 2.2, 1 H, H_{endo}–C(4)); 2.61–2.54 (*m*, 1 H, H–C(7)); 2.45 ($d\times d\times d\times d\times d$, J = 2, 2, 2, 17.4 and 9.7, 1 H, H_{exo}–C(4)); 0.98 (*s*, 9 H, $C(CH_3)_3$). – On the addition of the europium-shift reagent ($Eu(fod)_3$) the signal corresponding to H–C(7) was shown to be $d\times d$, J = 3.2 and 3.0.

4.12. *Preparation of* 7endo-*phenylbicyclo[3.2.0]hept-2-en-6-one* (endo-7). – *a*) As described previously [1], using phenylacetylchloride, cyclopentadiene and triethylamine. The epimer purity was at least 97%.

b) A solution of 10.9 g (50 mmol) 7*exo*-chloro-7*endo*-phenylbicyclo[3.2.0]hept-2-en-6-one (**21**) [1] in 90 ml acetic acid was reacted with 4.9 g (75 mmol) zinc powder as described above. Distillation of the crude product at 110–120°/0.05 Torr gave 7.93 g (85%) of a viscous oil which contained ~7% 7*exo*-phenyl-(*exo*-**7**) and ~93% 7*endo*-phenylbicyclo[3.2.0]hept-2-en-6-one (*endo*-**7**). The epimer ratio was assessed by NMR. integration.

Spectroscopic properties of endo-**7**. – ^{1}H-NMR. ($CDCl_3$): 7.3–6.8 (*m*, 5 H, arom. H); 5.89–5.77 and 5.53–5.43 (2 *m*, each 1 H, H–C(2) and H–C(3)); 4.75 ($d\times m$, J = 8–9, 1 H, H–C(7)); 4.02–3.78 (*m*, 2 H, H–C(5) and H–C(1)); 2.76 ($d\times d\times d\times d\times d$, J = 2.2, 2.2, 2.2, 16.8 and 2.2, 1 H, H_{endo}–C(4)); 2.46 ($d\times d\times d\times d\times d$, J = 2.4, 2, 2, 16.8 and 7.3, 1 H, H_{exo}–C(4)).

4.13. *Preparation of* 7exo-*phenylbicyclo[3.2.0]hept-2-en-6-one* (exo-7). This compound was prepared by the method to be described in another publication [25]: the epimer purity of *exo*-**7** was 87%.

5. Preparation of the monosubstituted bicyclo[3.2.0]heptan-6-ones. – 5.1. *Preparation of* 7endo-*chlorobicyclo[3.2.0]heptan-6-one* (endo-**8**). A solution of 14.3 g (100 mmol) 7*endo*-chlorobicyclo[3.2.0]-hept-2-en-6-one (*endo*-**2**) in 150 ml hexane was hydrogenated in 60 min as described above using 0.5 g of catalyst. Distillation at 120–130°/11 Torr of the crude product gave 13.4 g (92%) 7*endo*-chlorobicyclo[3.2.0]heptan-6-one (*endo*-**8**) in 98% epimer purity (GC.-C). – IR. (CCl_4): 1795 (C=O). – ^{1}H-NMR. (CCl_4): 5.00 ($d\times d$, J = 9.7 and 3.5, 1 H, H–C(7)); 3.66 ($d\times d\times d\times d$, J = 7.5, 1, 7.5 and 3.5, 1 H, H–C(5)); 3.39–3.09 (*m*, 1 H, H–C(1)); 2.3–1.2 (*m*, 6 H, 2 H–C(2), 2 H–C(3) and 2 H–C(4)).

5.2. *Preparation of* 7exo-*chlorobicyclo[3.2.0]heptan-6-one* (exo-**8**). – 7*exo*-Chlorobicyclo[3.2.0]-hept-2-en-6-one (*exo*-**2**) (2.14 g (15 mmol) dissolved in 80 ml hexane) was hydrogenated in 40 min using 0.1 g of catalyst in the manner described above. The crude product was distilled at 105–115°/11 Torr to give 1.97 g (90%) of *exo*-**8** in at least 97% epimer-purity (GC.-C). – IR. (CCl_4): 1794 (C=O). – ^{1}H-NMR. (CCl_4): 4.18 ($d\times d$, J = 4.0 and 3.0, 1 H, H–C(7)); 3.73 ($d\times d\times d\times d$, J = 8, 2, 8

and 3.0, 1H, H–C(5)); 2.98–2.76 (*m*, 1H, H–C(1)); 2.3–1.5 (*m*, 6H, 2H–C(2), 2H–C(3) and 2H–C(4)).

5.3. *Preparation of 7*endo-*methylbicyclo[3.2.0]heptan-6-one* (endo-**9**). *7endo*-Methylbicyclo[3.2.0]-hept-2-en-6-one (*endo*-**3**) (10.0 g (82 mmol) dissolved in 200 ml hexane) was hydrogenated during 2 h using 0.5 g of catalyst in the manner described above. Distillation of the crude product at 80–90°/11 Torr gave 8.63 g (86%) of *endo*-**9** in 98% purity (GC.-D). – IR. (CCl_4): 1776 (C=O). – ^{1}H-NMR. (CCl_4): 3.54 (*d*×*d*×*d*×*d*, *J* = 8, 1, 8 and 3.4, 1H, H–C(5)); 3.31 (*qa*×*d*×*d*, *J* = 7.3, 10.5 and 3.4, 1H, H–C(7)); 3.03–2.75 (*m*, 1H, H–C(1)); 2.1–1.05 (*m*, 6H, 2H–C(2), 2H–C(3) and 2H–C(4)); 0.93 (*d*, *J* = 7.3, 3H, H_3C–C(7)).

5.4. *Preparation of 7*exo-*methylbicyclo[3.2.0]heptan-6-one* (exo-**9**). *7endo*-Methylbicyclo[3.2.0]-heptan-6-one (*endo*-**9**) (5.00 g, 41 mmol) was stirred for 20 h with 50 ml 1N NaOH at RT. Distillation of the ether soluble products at 100–110°/40 Torr gave 4.16 g (81%) of a mixture (GC.-D) composed of 55% of the *7exo*-methyl-(*exo*-**9**) and 45% of the *7endo*-methyl-epimer (*endo*-**9**). Gas chromatographic separation (GC.-F) of the faster moving major component gave *exo*-**9** in 99% epimer-purity. – IR. (CCl_4): 1775 (C=O). – ^{1}H-NMR. (CCl_4): 3.46 (*d*×*d*×*d*×*d*, *J* = 6.7, 3, 8.5 and 3.1, 1H, H–C(5)); 2.57 (*qa*×*d*×*d*, *J* = 7.2, 4.4 and 3.1, 1H, H–C(7)); 2.50–2.30 (*m*, 1H, H–C(1)); 2.15–1.4 (*m*, 6H, 2H–C(2), 2H–C(3) and 2H–C(4)); 1.15 (*d*, *J* = 7.2, 3H, H_3C–C(7)).

5.5. *Preparation of 7*endo-t-*butylbicyclo[3.2.0]heptan-6-one* (endo-**10**). *7endo-t*-Butylbicyclo[3.2.0]-hept-2-en-6-one (*endo*-**6**) (8.21 g, 50 mmol) dissolved in 200 ml hexane) was hydrogenated in 60 min in the presence of 0.4 g of catalyst. The crude product was distilled at 115–120°/11 Torr to give 7.71 g (95%) of *endo*-**10** of epimer purity > 93% (GC.-G). – IR. (CCl_4): 1772 (C=O). – ^{1}H-NMR. (CCl_4): 3.36 (*d*×*d*×*d*×*d*, *J* = 7.5, 1, 7.5 and 3.5, 1H, H–C(5)); 3.13 (*d*×*d*, *J* = 10.5 and 3.5, 1H, H–C(7)); 3.10–2.80 (*m*, 1H, H–C(1)); 2.4–1.2 (*m*, 6H, 2H–C(2), 2H–C(3) and 2H–C(4)); 1.00 (*s*, 9H, $C(CH_3)_3$).

5.6. *Preparation of 7*exo-t-*butylbicyclo[3.2.0]heptan-6-one* (exo-**10**). *7endo-t*-Butylbicyclo[3.2.0]-heptan-6-one (*endo*-**10**) (3.25 g, 19.6 mmol) was stirred at RT. with 35 ml 1N NaOH for 100 h. The product was extracted with ether and the ether soluble material was distilled at 105–115°/11 Torr to give 3.10 g (96%) of *exo*-**10**. The epimer purity of > 99% was increased to 99.8% by preparative scale gas chromatography (GC.-F). – IR. (CCl_4): 1770 (C=O). – ^{1}H-NMR. (CCl_4): 3.21 (*d*×*d*×*d*×*d*, *J* = 7.0, 3, 8.5 and 3.2, 1H, H–C(5)); 2.73–2.51 (*m*, 1H, H–C(1)); 2.33 (*d*×*d*, *J* = 5.0 and 3.2, 1H, H–C(7)); 2.1–1.35 (*m*, 6H, 2H–C(2), 2H–C(3) and 2H–C(4)); 0.94 (*s*, 9H, $C(CH_3)_3$).

6. Dehalogenations of 7-halobicyclo[3.2.0]hept-2-en-6-one. – 6.1. *Zinc reduction of the pure epimers of 7-chloro-7-methylbicyclo[3.2.0]hept-2-en-6-one* (**20A** *and* **20B**). – a) To a solution of 3.13 g (20 mmol) *7exo*-chloro-*7endo*-methylbicyclo[3.2.0]hept-2-en-6-one (**20A**) [1] [20] [22] in 15 ml acetic acid and 15 ml pyridine was added 1.60 g (24 mmol) zinc powder in small portions with stirring. The exothermic reaction was not controlled by external cooling. On completion of the addition the reaction mixture was stirred for a further 2 h and poured into iced dilute sulfuric acid. The aqueous solution was extracted three times with ether and the combined ether extracts were washed with water and saturated $NaHCO_3$-solution, dried over Na_2SO_4 and concentrated using a RV. The residue contained (GC.-D) 7% *7exo*-methyl-(*exo*-**3**) and 93% *7endo*-methylbicyclo[3.2.0]hept-2-en-6-one (*endo*-**3**). Distillation at 80–90°/11 Torr in a bulb tube gave 1.92 g (79%) of a 7:93 epimer mixture of *7exo*-(*exo*-**3**) and *7endo*-methylbicyclo[3.2.0]hept-2-en-6-one (*endo*-**3**).

b) A 1.57 g (10 mmol) sample of *7endo*-chloro-*7exo*-methylbicyclo[3.2.0]hept-2-en-6-one (**20B**) [1] [20] [22] in 7.5 ml acetic acid and 7.5 ml pyridine was reacted with 0.9 g (14 mmol) zinc powder as described above. The crude product contained (GC.-D) 7% *7exo*-methyl-(*exo*-**3**) and 93% *7endo*-methyl-bicyclo[3.2.0]hept-2-en-6-one (*endo*-**3**). Distillation at 80–90°/11 Torr in a bulb tube gave 0.92 g (75%) of a 7:93 mixture of *exo*-**3** and *endo*-**3**.

6.2. *Tributyltin hydride reduction of the 7-halo-7-methylbicyclo[3.2.0]hept-2-en-6-ones* **19A**, **19B** and **20A**. – *a*) To a solution of 3.0 g (10.3 mmol) tributyltin hydride in 50 ml benzene was added 2.0 g (10.0 mmol) *7exo*-bromo-*7endo*-methylbicyclo[3.2.0]hept-2-en-6-one (**19A**) [1] [21] [22]. A mildly exothermic reaction took place and the homogenous solution was allowed to stand for 16 h at RT. The benzene was removed in a RV. and the residue was distilled in a bulb tube. The fraction boiling at 100–110°/20 Torr weighed 0.50 g (66%) and was shown to consist of *7endo*-methylbicyclo[3.2.0]-hept-2-en-6-one (*endo*-**3**) and *7exo*-methylbicyclo[3.2.0]hept-2-en-6-one (*exo*-**3**) in a ratio of 95:5 by a comparison of the NMR. spectrum of the mixture with the spectra of authentic samples of the two epimers.

b) 7*endo*-Bromo-7*exo*-methylbicyclo[3.2.0]hept-2-en-6-one (**19B**) [1] [21] [22] (2.0 g, 10.0 mmol) was reacted with 3.0 g (10.3 mmol) tributyltin hydride in 50 ml benzene as described above. The NMR. spectrum of this product and that of the mixture obtained in the preceding experiment were superimposable. The mixture of 7*endo*-methylbicyclo[3.2.0]hept-2-en-6-one (*endo*-**3**) (≈95%) and 7*exo*-methylbicyclo[3.2.0]hept-2-en-6-one (*exo*-**3**) (≈5%) was obtained in 62% yield.

c) A solution of 1.8 g (11.5 mmol) 7*exo*-chloro-7*endo*-methylbicyclo[3.2.0]hept-2-en-6-one (**20A**) [1] [20] [22] and 3.5 g (12.1 mmol) tributyltin hydride in 35 ml benzene was refluxed for 16 h. The benzene was removed in a RV. and the residue was distilled in a bulb tube. The fraction boiling at 100–110°/20 Torr gave a NMR. spectrum identical with that obtained in *a*) and *b*). The combined yield of 7*endo*-methylbicyclo[3.2.0]hept-2-en-6-one (*endo*-**3**) (≈95%) and 7*exo*-methylbicyclo[3.2.0]-hept-2-en-6-one (*exo*-**3**) (≈5%) was 61%.

REFERENCES

[1] *M. Rey, S. Roberts, A. Dieffenbacher & A. S. Dreiding*, Helv. *53*, 417 (1970); *A. Roussel & L. Ghosez*, unpublished work.

[2] *W. T. Brady, F. H. Parry III, R. Roe, jr. & E. F. Hoff, jr.*, Tetrahedron Letters *1970*, 819; *P. R. Brook, J. M. Harrison & A. J. Duke*, Chem. Commun. *1970*, 859.

[3] *W. T. Brady & R. Roe, jr.*, J. Am. Chem. Soc. *92*, 4618 (1970).

[4] *L. Ghosez, M. J. O'Donnell*, 'Pericyclic Reactions of Cumulenes' in 'Pericyclic Reactions' (A. M. Marchand and R. E. Lehr, Ed.), Organic Chemistry, A Series of Monographs, Vol. 35-II, pp. 79, Academic Press 1977.

[5] *P. R. Brook, A. J. Duke, J. M. Harrison & K. Hunt*, J. Chem. Soc. Perkin *1*, *1974*, 927.

[6] *P. R. Brook, A. J. Duke, J. G. Griffiths, S. M. Roberts, M. Rey & A. S. Dreiding*, Helv. *60*, 1528 (1977); *P. R. Brook & A. J. Duke*, Chem. Commun. *1970*, 652.

[7] *W. T. Brady & E. F. Hoff, jr.*, J. Org. Chem. *35*, 3733 (1970).

[8] *D. Seebach*, «Isocyclische Vierring Verbindungen» in Houben-Weyl, «Methoden der Organischen Chemie», Vol. 4/4 (E. Müller, Ed.), Georg Thieme Verlag, Stuttgart 1971.

[9] *J. M. Conia & J. L. Ripoll*, Bull. Soc. Chim. France *1963*, 768; *B. Braillon, J. Salaün, J. Goré & J. M. Conia*, Bull. Soc. Chim. France *1964*, 1981.

[10] *S. Goldstein, P. Vannes, C. Houge, A. M. Frisque-Hesbain, C. Wiaux, L. Ghosez, G. Germain, J. P. Ferclercq, M. Van Meersche & J. M. Arrieta*, J. Am. Chem. Soc. *103*, 4616 (1981).

[11] *J. March*, 'Advanced Organic Chemistry', McGraw-Hill, London 1977, p. 130.

[12] *W. D. Cotterill & M. J. T. Robinson*, Tetrahedron Lett. *1963*, 1833; Tetrahedron *20*, 765, 777 (1964).

[13] *J. March*, 'Advanced Organic Chemistry', McGraw-Hill, London 1977, p. 206.

[14] *H. C. Brown, M. E. Azzaro, J. G. Koelling & G. J. McDonald*, J. Am. Chem. Soc. *88*, 2520 (1966); *R. E. Carter & L. Dahlgren*, Acta Chem. Scand. *24*, 633 (1970).

[15] *W. Rellensmann & K. Hafner*, Chem. Ber. *95*, 2579 (1962).

[16] *E. Jaz & E. Denis*, Bull. Soc. Chim. Belge *75*, 845 (1966).

[17] *W. T. Brady & E. F. Hoff, jr.*, J. Am. Chem. Soc. *90*, 6256 (1968).

[18] *W. T. Brady, E. F. Hoff, jr., R. Roe, jr. & F. H. Parry, jr.*, J. Am. Chem. Soc. *91*, 5679 (1969).

[19] *H. C. Stevens, D. A. Reich, D. R. Brandt, D. R. Fountain & E. J. Gaughan*, J. Am. Chem. Soc. *87*, 5257 (1965); *L. Ghosez, R. Montaigne & P. Mollet*, Tetrahedron Lett. *1966*, 135; *L. Ghosez, R. Montaigne, H. Van Lierde & P. Mollet*, Tetrahedron *27*, 615 (1971).

[20] *W. T. Brady & B. M. Holifield*, Tetrahedron Letters *1966*, 5511.

[21] *W. T. Brady & B. M. Holifield*, Tetrahedron *23*, 4251 (1967).

[22] *W. T. Brady, R. Roe, jr., E. F. Hoff, jr. & F. H. Parry, III*, J. Am. Chem. Soc. *92*, 146 (1970).

[23] *H. G. Kuivila & O. F. Beunel, jr.*, J. Am. Chem. Soc. *83*, 1246 (1961); *H. G. Kuivila*, Accounts Chem. Res. *1*, 299 (1968); *H. G. Kuivila*, Synthesis *1970*, 499.

[24] *M. Rey, U. A. Huber & A. S. Dreiding*, Tetrahedron Letters *1968*, 3583.

[25] *M. Rey & A. S. Dreiding*, unpublished results.