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STEREOCHEMISTRY OF CYCLOBUTANONE RESULTED FROM CYCLOADDITIONS OF t-BUTYLCYANOKETENE TO BICYCLO[2.2.1]HEPTENE DERIVATIVES, AS EVIDENCE FOR A $_\pi 2_s + _\pi 2_a$ REACTION MODE

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Abstract—The stereochemistry of the cyclobutanones **1–7**, resulted from the reaction of t-butylcyanoketene with bicyclo[2.2.1]heptene, bicyclo[2.2.1]heptadiene, 1,4 - dihydro - 1,4 - methanonaphthalene, 1,4 - dihydro - 9 - (1 - methylethylidene) - 1,4 - methanonaphthalene, 1,4 - dihydro - 1,4 - epoxynaphthalene, 1,4,4a,8b - tetrahydro - 1,4 - methanobiphenylene (1α,4α,4aα,8bα) and 1,4,4a,8b - tetrahydro - 1,4 - methanobiphenylene(1α,4α,4aβ,8bβ) was established as having the cyclobutanone ring *exo* and the t-Bu group in the α configuration. These findings represent a stereochemical argument in favour of a $_\pi 2_s + _\pi 2_a$ reaction mode of t-butylcyanoketene to the above mentioned bicyclo[2.2.1]heptene derivatives. Observations regarding preservation of the original configurations of alkenes as well as the geometrical distorsion of the cyclobutanones are shortly discussed.

Since Moore's discovery in 1970[1] of the synthesis and chemistry of t-butylcyanokete (TBCK), several papers have been published pointing out its extraordinary reactivity in cycloaddition reaction. Not only the pedestrian entry into the chemistry of TBCK precursors[2-5] and the unorthodox preparation of this particular ketene are remarkable, but also the ever increasing number of ketenophiles, spanning over a variety of structures, which in general all give 4-membered ketones in clean and stereospecific reactions. Thus, reactions were reported with alkenes,[1,6-10] dienes[6,11,12] alkynes,[13] allenes,[10,14-17] iminoethers[18] and carbodiimide.[1,6]

The cyclobutanones obtained, for example, from alkenes and TBCK have a stereochemistry of the 4-membered ring with the bulky group always *cis* to the largest group from the olefinic moiety,[6,8-10] in other words the isomer with the most crowded steric arrangements of the substituents. These results are easily rationalized if a $_\pi 2_s + _\pi 2_a$ reaction mode is accepted, as it has been defined by Woodward and Hoffmann.[19]

In the present paper, we would like to present new evidence for a $_\pi 2_s + _\pi 2_a$ reaction mode of TBCK in its reaction with bicyclo[2.2.1]heptene derivatives. Our evidence is based on the stereochemistry of the resulted polycyclobutanones as it was derived from ^{1}H-NMR and qualitative lanthanide induced shift (LIS) spectra.[20]

DISCUSSION OF THE RESULTS

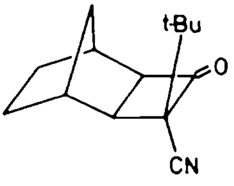
We have chosen as ketenophiles the bicyclo[2.2.1]heptene derivatives, which have been already mentioned in the summary of the present paper. Paradoxically, though substrates possessing this skeleton have generated many fundamental concepts and reactions in organic chemistry,[21-24] they were subjected to reactions with ketenes[25] only seldom and in a non-systematic manner. By analogy with other reactions, such as the electrophilic additions,[24] we think that the study of the reaction between ketenes and bicyclo[2.2.1]heptene derivatives could shed light on the mechanism of cycloaddition reactions. In the present paper we discuss only one feature of the reaction mechanism, derived from the finding that the cyclobutanone ring in the adducts **1–7** is *exo* in respect to the bicyclo[2.2.1]heptane skeleton and has an α-configuration for the t-Bu group. In a future publication we would like *inter alia*, to comment the observation that in the reactions of olefins mentioned in the summary with TBCK, only cyclobutanones were isolated but never, so far, rearranged products, even in the case of those substrates known to rearrange very rapidly, if a carbenium (or a carbenium-like) ion were involved. Thus, one could conclude the transition state of the cycloadditions is concerted.

A. *The cyclobutanone ring has an* exo-*configuration*

The reaction between ketene and an alkene could be regarded as involving in its early stage an electrophilic attack of the carbonyl C atom on the double bond. In our case, the double bond is part of the bicyclo[2.2.1]heptene skeleton, for which it is well documented that the electrophilic attack occurs from the *exo* side (see 8).[23,24] Indeed such a reaction course has been observed based on thorough experimental support for diphenyl,[25a] dichloro-,[25b] chloroalkylketenes[25c,d] and TBCK[7,8] especially with bicyclo[2.2.1]heptene and only occasionally to bicyclo[2.2.1]heptadiene. To these known examples, we would like to add five new ketenophiles giving the cyclobutanones **3–7** not yet used to our best knowledge for this purpose. Although the stereochemistry of compound **1**, has been discussed in one of our previous publications,[9] as it resulted from quantitative LIS spectra simulations, and that of compound **2**, independently synthesized in our laboratory, for which the stereochemistry has been established only partly based on chemical means,[7] both compounds are discussed again in this paper. Our present new arguments support for compound **1** and complete for compound **2** the previous conclusions.

The *exo* configuration of the cyclobutanone ring in compounds **1–7** results from two reliable features of their ^{1}H NMR spectra.

(i) It is documented that the vicinal coupling constant between the bridgehead proton and the *endo*-proton is smaller (0–1 Hz) than the vicinal coupling constant bet-



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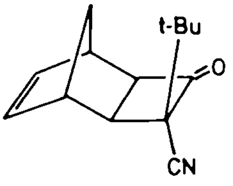

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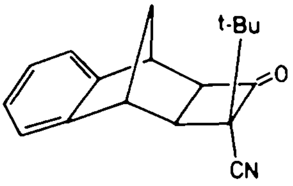

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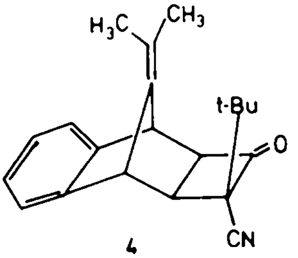

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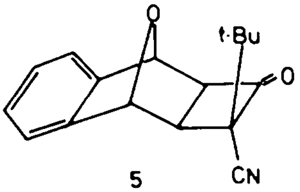

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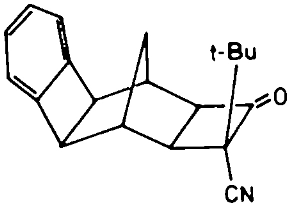

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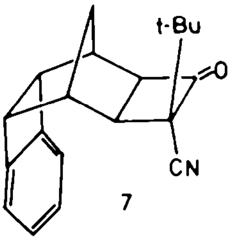

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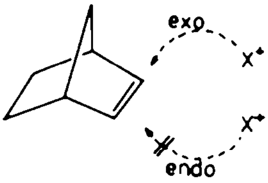

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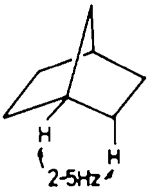

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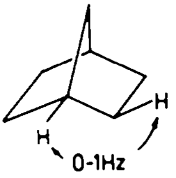

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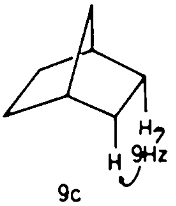

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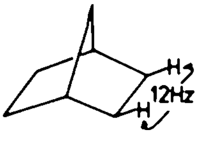


9d

ween the bridgehead proton and an *exo*-proton (2–5 Hz)[26] (see **9a** and **9b**). All cyclobutanones **1–7** display in their ^{1}H-NMR spectra low values for the coupling constants between the cyclobutanone and bridgehead proton. This observation resulted from the examination of the ^{1}H-NMR spectra, simplified especially for compound **4** and **5**, then from the ^{1}H-NMR-LIS of compound **1–3**, **6** and **7**, confirming the assignments of signals and finally from the double resonance experiments carried out on the complex of compound **1** with Eu(fod)$_3$.[27] Thus we tentatively conclude that even in the case in which the bicyclo[2.2.1]heptane system is condensed to a cyclobutane ring, the value of vicinal coupling constants between the original bridgehead protons of the bicyclo[2.2.1]heptane derivatives and the proton from the cyclobutane ring, common to both cyclic systems, is still valid as in the parent system. However we are aware that definite conclusions will be drawn only after more elaborate NMR study of such polycyclic systems.

(ii) Careful ^{1}H-NMR studies[26a,b] of the bicyclo[2.2.1]heptane system have shown that the coupling constant between *endo–endo* protons is about of 9 Hz, while the coupling between *exo–exo* protons is higher, of *ca.* 12 Hz (see **9c** and **9d**). The vicinal coupling constant, between the cyclobutanone protons, in all compounds **1–7**, are in the range 7.5–8 Hz, revealing therefore their *endo* nature and by extension the *exo* configuration of the cyclobutanone ring.

Table 1. ^{1}H-NMR chemical shifts (in δ, ppm, internal TMS) of protons H^1 and H^2, their coupling constant (in Hz) and their relative molar induced shifts

Compound	H^1	H^2	J_{H^1,H^2}	MIS_{H^2}/MIS_{H^1}
1	3.72	2.73	7.5	1.22
2	3.68	2.73	7.5	1.29
3	3.77	2.73	7.5	1.21
4	3.67	2.87	8	—
5	3.87	2.98	8	—
6	3.74	2.60	7.5	1.29
7	3.28	2.36	7.5	1.21

B. *The t-butyl group has an α-configuration*

Next we would like to present some arguments concerning the configuration of the t-Bu group in the cyclobutanones **1–7**, concluding that it has according to the Chemical Abstracts nomenclature the configuration α, e.g. pointing toward the methylene bridge of the bicyclo[2.2.1]heptane skeleton. Compounds with such configuration correspond to the isomer with the higher steric strain. Such a reaction course is a normal outcome in the chemistry of ketenes, being, in fact, the steric argument for the $_{\pi}2_{s} + _{\pi}2_{a}$ reaction mode. The t-butylcyanoketene approaches the double bond, in the early stage of the reaction with the bulky t-Bu group such as to minimize any steric interactions with other substituents. As the reaction goes on the $_{\pi}2_{s} + _{\pi}2_{a}$ reaction mode requires three simultaneous rotations I, II and III, which have as final result the isomer with the highest steric crowding (Fig. 1).

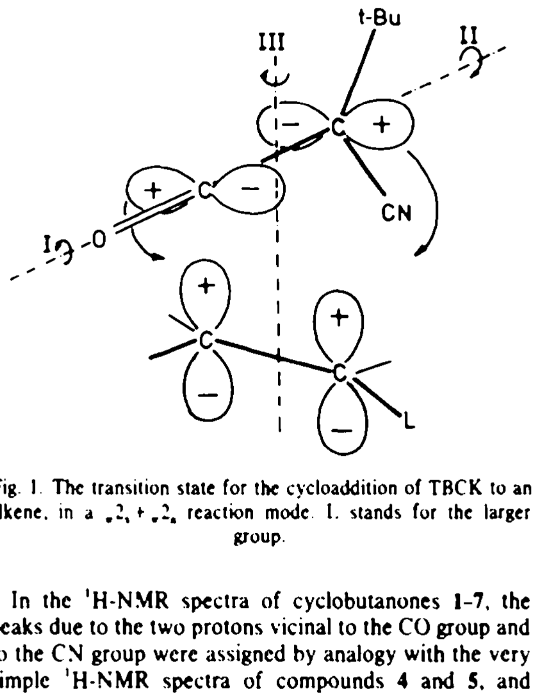


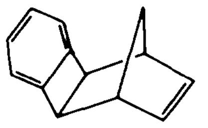
Fig. 1. The transition state for the cycloaddition of TBCK to an alkene, in a $_{\pi}2_{s} + _{\pi}2_{a}$ reaction mode. L stands for the larger group.

In the ^{1}H-NMR spectra of cyclobutanones **1–7**, the peaks due to the two protons vicinal to the CO group and to the CN group were assigned by analogy with the very simple ^{1}H-NMR spectra of compounds **4** and **5**, and confirmed by LIS-spectra of the remaining cyclobutanones **1–3**, **6** and **7**. We have assigned peak at lower field, appearing at δ = 2.3–3.0 ppm (see **10** and Table 1) to the proton H^2 (vicinal to the CO group), chemical shift in the range of the reported signal for the corresponding protons from the parent cyclobutanone **11**.[28] The chemical shift of the proton H^1, *cis* to the cyano group being deshielded has a value of δ = 3.3–3.9 ppm (see **10** and Table 1). In the parent cyclobutanone **11**, the protons belonging to the nonvicinal methylene group have a chemical shift of δ = 1.96 ppm. This dramatic downfield shift of the same protons in compounds **1–7**, *could be reasonably attributed to the presence of a* cis-*cyano group*. The argument regarding the deshielding effect of a cyano group *cis* to a proton is nicely supported by Moore *et al.*,[10] who isolated both isomers **12a** and **12b** from the reaction of 1,2-cyclononadiene with TBCK. Our experiments in the reaction of TBCK with olefins,[8,9] never gave rise to other isomers, preventing the possibility of a comparison with the compound having a cyano group *trans* to a vicinal proton.

The above assignments are supported also by qualitative LIS experiments carried out for compounds **1–3**, **6** and **7**. The molar induced shift (MIS) obtained by extrapolating[29] the induced shifts to 1:1 molar ratio of $Eu(fod)_3$ and substrate is, expected, higher for the proton H^2 closer to the CO group, assigned here as having the higher field chemical shift. Indeed in all cyclobutanones studied here by LIS method (**1–3**, **6** and **7**), the ratio MIS_{H^2}/MIS_{H^1} is equal to 1.21–1.29 (Table 1).

C. *The olefin preserves its original configuration*

The cyclobutanones **6** and **7** have the benzo ring with the same configuration as in the starting olefins, **13** and **14**, respectively, *exo* in **6** and *endo* in **7**.



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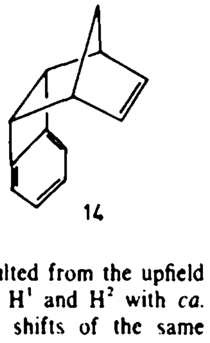

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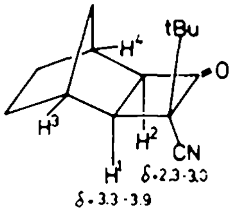
The *endo* configuration in **7** resulted from the upfield position of the signals of protons H^1 and H^2 with *ca.* 0.24–0.5 ppm, than the chemical shifts of the same protons in the case of similar cyclobutanones presented in Table 1. An *exo* configuration of the benzene ring increases the distances from this one to H^1 and H^2 protons, together with an unfavourable geometrical position of the ring. Therefore the configuration of the aromatic ring in **6** resulted from the lack of its shielding effect on the chemical shifts of protons H^1 and H^2 (Table 1). Should a carbenium ion be involved in the transition state of the cycloaddition reactions, then the skeleton of hydrocarbons **13** and especially **14**[30] would undergo inversion of configuration of the benzene ring.

D. *The cyclobutanone ring is generally nonplanar*

In the case of polycyclic cyclobutanones, having substituents with small or modest steric requirements, attached only on the cyclobutanone ring, one would expect planarity of the 4-membered ring. Cyclobutanones **1–4**, **6** and **7**, however, since the t-Bu group is pointing toward the methylene group, one would expect



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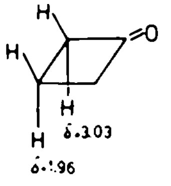

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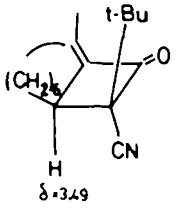
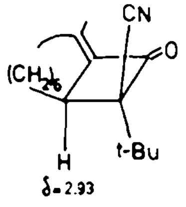


12a



12b

some nonplanarity in the cyclobutanone ring and some distorsions of the bicyclo[2.2.1]heptane skeleton, owing to steric strain. We think that the distorsions are more important along the side having the t-Bu group and protons H^1 and H^3. Since the t-Bu group is rotated, presumably outward, the dihedral angle between H^1 proton and the bridgehead proton H^3, is becoming favourable for a coupling constant observable in the ^{1}H-NMR signal of both protons (Fig. 2). Indeed H^1 signals, in the case of cyclobutanones **1-3**, **6** and **7** appear as a doublet of triplets, as a consequence of coupling with the proton H^3 as well as with the long range coupling with that proton from the methylene bridge, which completes the W-shaped pattern. These conclusions were nicely supported by double resonance experiments carried out compounds **6** and **7** at 100 M Hz. In the case of compound **4**, this long-range coupling is no longer possible, and indeed the H^1 signal is a doublet of doublets (Fig. 2). The side bearing the CO group the H^2 and H^4 protons are probably not or less distorted, since the signals of H^2 and H^4 protons in the case of compounds **1-4**, **6** and **7** appear as a doublet, as in fact one would expect for a normal pattern.

The replacement of the methylene group in the bridge of a bicyclo[2.2.1]heptane skeleton by oxygen, lead to steric repulsions with the bulky t-Bu group more diminished, conclusion resulted from the fact that in the cyclobutanone **5** the H^1 signal (Fig. 2) is a doublet, as result of the coupling only with the H^2 proton. This is what one would expect if the cyclobutanone ring were planar.

Concluding remarks

Our aim in the present paper was to bring new stereochemical evidence for a $_{\pi}2_{s}+{}_{\pi}2_{a}$ reaction mode in the cycloaddition of ketenes to nonpolar olefins: all substrates presented here possessing the bicyclo[2.2.1]heptene skeleton. They yield with TBCK cyclobutanones with *exo*-configuration and the t-Bu group has the α-configuration. These conclusions have resulted from the ^{1}H-NMR and qualitative ^{1}H-NMR-LIS spectra of cyclobutanones **1-7**.

EXPERIMENTAL

The cyclobutanones **1-7** gave all satisfactory elemental analyses, their IR and ^{1}H-NMR spectra support the proposed structures. Experimental details of their preparation will be published in a forthcoming paper.[11] The LIS-spectra were obtained with a Varian A-60A ^{1}H-NMR spectrometer, using as shift reagent $Eu(fod)_3$, which was added incrementally to a weighed amount of ketones **1-3**, **6** and **7** in CCl_4 (with internal TMS). The double resonance experiments for compound **6** and **7** were carried out on a HA-100 NMR spectrometer. The MIS values were calculated using first degree polynomial regression. The calculated values have acceptable standard errors and r^2 values. Calculations were carried out on a HP-3980 A calculator using the program "Polynomial Regression", *HP Stat. Pac.* Vol. 1, Part 09830-70800, page 1.

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REFERENCES

[1] H. W. Moore and W. Weyler, Jr., *J. Am. Chem. Soc.* **92**, 4132 (1970).
[2] H. W. Moore and W. Weyler, Jr., *Ibid.* **93**, 2812 (1971).
[3] H. W. Moore, D. L. Maurer, D. S. Pearce and M. S. Lee, *J. Org. Chem.* **37**, 1984 (1972).
[4] R. J. Wikholm and H. W. Moore, *J. Am. Chem. Soc.* **94**, 6152 (1972).
[5] M. D. Gheorghiu and M. Avram, *Org. Proced. Prepr. Intern.* **6**, 231 (1974).
[6] W. Weyler, Jr., W. G. Duncan and H. W. Moore, *J. Am. Chem. Soc.* **97**, 6187 (1975).
[7] P. R. Brook and K. Hunt, *J. Chem. Soc.* Chem. Comm. 989 (1974).
[8] M. D. Gheorghiu, F. Kerek and M. Avram, *Rev. Roumaine Chim.* **20**, 75 (1975).
[9] M. D. Gheorghiu, P. Filip, C. Drăghici and L. Pârvulescu, *J. Chem. Soc.* Chem. Comm. 635 (1975).
[10] W. Weyler, Jr., L. R. Byrd, M. C. Caserio and H. W. Moore, *J. Am. Chem. Soc.* **93**, 1027 (1972).
[11] A. Hassner, R. M. Cory and N. Sartoris, *Ibid.* **98**, 7698 (1976).
[12] M. D. Gheorghiu and L. Pârvulescu, unpublished observation concerning the reaction of TBCK with cyclopentadiene and 1,3-cyclohexadiene.
[13] M. D. Gheorghiu, C. Drăghici, L. Stănescu and M. Avram, *Tetrahedron Letters* 9 (1973).
[14] W. G. Duncan, W. Weyler, Jr. and H. W. Moore, *Ibid.* 4391 (1973).
[15] H. A. Bampfield and P. R. Brook, *J. Chem. Soc.* Chem. Comm. 171 (1974).

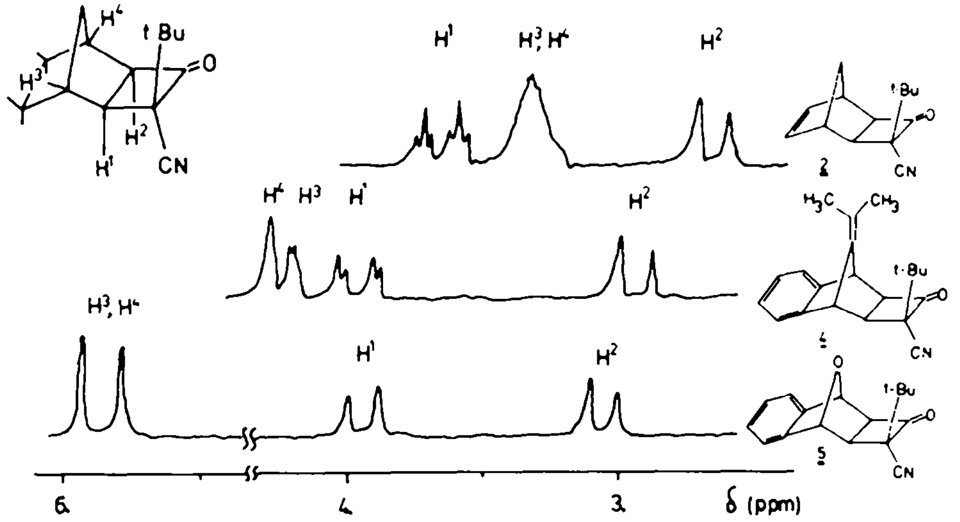

Fig. 2. ^{1}H-NMR spectra at 60 M Hz for protons H^1, H^2, H^3 and H^4 for compounds **2**, **4** and **5**.

[16] H. A. Bampfield, P. R. Brook and W. S. McDonald, *Ibid.* Chem. Comm. 132 (1975).

[17] H. A. Bampfield, P. R. Brook and K. Hunt, *Ibid.* Chem. Comm. 147 (1976).

[18] D. H. Aue and D. Thomas, *J. Org. Chem.* **40**, 2553 (1975).

[19] R. B. Woodward and R. Hoffmann, *The Conservation of Orbital Symmetry*, p. 163. Academic Press, New York (1970).

[20] A detailed discussion concerning simulation of LIS-spectra for some of the cyclobutanones mentioned here was reported in part at the 5th National Conference of Physical Chemistry, Bucharest, 1–4 Sept. 1976, M. D. Gheorghiu, C. Drăghici, P. Filip and L. Pârvulescu, Abstract No. I-40. It will be reported in a forthcoming paper from this laboratory.

[21] D. Sargent, *Carbonium Ions* (Edited by G. A. Olah and P. von R. Schleyer), Vol. III, p. 1099. Wiley-Interscience, New York (1972).

[22] G. M. Kramer, *Advances in Physical Organic Chemistry* (Edited by V. Gold and D. Bethele), Vol. 11, p. 177. Academic Press, London (1975).

[23] H. C. Brown and J. H. Kawakan, *J. Am. Chem. Soc.* **97**, 5521 (1975).

[24] For a recent review see F. Freeman, *Chem. Rev.* **75**, 439 (1975).

[25] For examples regarding reactions of norbornene and various ketenes see: [a] R. Huisgen and L. A. Feiler, *Chem. Ber.* **102**, 3391 (1969); [b] L. Ghosez, R. Montaigne, A. Russel, V. Vanheirde and P. Mollet, *Tetrahedron* **27**, 615 (1971); [c] R. C. De Selms and F. Delay, *J. Org. Chem.* **37**, 2908 (1972); [d] D. C. England and C. G. Krespan, *Ibid.* **35**, 3300 (1970); for examples regarding reactions of norbornadiene with various ketenes see: [e] R. C. De Selms and F. Delay, *J. Am. Chem. Soc.* **95**, 274 (1973); [f] Ref. 25*c*; [g] Ref. 7.

[26a] J. Marshall and S. R. Walter, *J. Am. Chem. Soc.* **96**, 6358 (1974); [b] J. Marshall, S. R. Walter, M. Barfield, A. P. Marchand, N. W. Marchand and D. L. Segre, *Tetrahedron* **32**, 537 (1976); [c] L. M. Jackman and S. Sternhell, *Applications of Nuclear Magnetic Spectroscopy in Organic Chemistry*, 2nd Edn, p. 289. Pergamon Press, Oxford (1969); [d] A. P. Marchand and N. W. Marchand, *Tetrahedron Letters* 5207 (1969).

[27] fod = 1,1,2,2,3,3-heptafluoro-7,7-dimethyloctane-dionate ion.

[28] C. D. Gutsche and T. S. Smith, *J. Am. Chem. Soc.* **82**, 4067 (1960); K. B. Wiberg and B. J. Nist, *Ibid.* **83**, 1226 (1961).

[29] See the Experimental.

[30] M. Avram, I. Pogany, F. Badea, I. G. Dinulescu and C. D. Nenitzescu, *Tetrahedron Letters* 3851 (1969); M. Avram, I. Pogany, I. G. Dinulescu, F. Chiraleu and C. D. Nenitzescu, *Rev. Roumaine Chim.* **15**, 1207 (1970); R. Baker and J. S. Salter, *J. Chem. Soc.* Perkin 2, 150 (1973); R. Baker and T. J. Mason, *Ibid.* 18 (1972).

[31] M. D. Gheorghiu and L. Pârvulescu, to be published.