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THE STEREOCHEMISTRY OF 2-t-BUTYL-2-CYANO-3-PHENYLCYCLOBUTANONE BY COMPLETE ANALYSIS OF ITS ^{1}H NMR SPECTRUM

ADDITIONAL EVIDENCE FOR A $_2\pi_s + {}_2\pi_a$ CYCLOADDITION OF t-BUTYLCYANOKETENE TO STYRENE[1]

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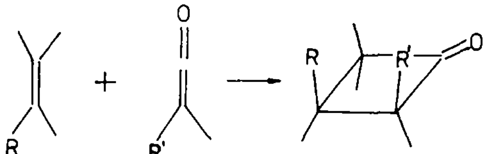
Abstract—The unique ^{1}H NMR spectral parameters obtained by computer simulation of the experimental spectrum of the three protons belonging to the 4-membered ring of the title cyclobutanone, can be rationalized if is accepted that the phenyl and t-Bu groups are *vicinal* and *cis*. The spectra parameters have been retained as results of the analysis of the six real solutions for the experimental ^{1}H NMR spectrum of the title cyclobutanone in chloroform-d. ^{1}H NMR spectra of deuterium labelled cyclobutanones obtained from mono- and dideuteriated styrenes and t-butylcyanoketene support the preferred theoretical solution. The conservation of the configuration of monodeuteriated styrenes in the cycloaddition reaction with t-butylcyanoketene strengthens our proposal that in this reaction the Woodward–Hoffmann $_2\pi_s + {}_2\pi_a$ reaction mode is operating.

The formation of the most crowded isomer I in the cycloadditions of a ketene to a nonpolar alkenes, was interpreted as an evidence for a $_2\pi_s + {}_2\pi_a$ reaction mode,[2] being evidenced convincingly on numerous alkenes.[3-25]



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The discovery in 1970 by Moore[25a] of t-butylcyanoketene (TBCK), a very reactive ketene, provided the possibility for enlarging the area of examples of cycloadditions occurring via a $_2\pi_s + {}_2\pi_a$ reaction mode.[15,19-25] Indeed, TBCK adds according to these rules to *cis* and *trans*-cyclooctene,[15,25a] styrene, indene and acenaphthalene,[19] bicyclo-(2.2.1)heptene derivatives[21-23] and 3,3-dimethylcyclopentene.[24]

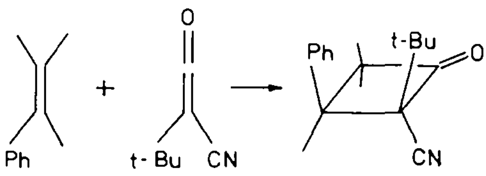
In a previous communication[19] one of us (MDG) based on the chemical shifts of the protons of the t-Bu group of the title cyclobutanone, relative to suitable models represented by 2-t-butyl-2-cyanocyclobutanones reported in the literature or synthesized in this laboratory, concluded that the stereochemistry of the title cyclobutanone has the phenyl and the t-Bu groups *vicinal* and *cis*. In other words the cycloadduct has the stereochemistry that one would expect if the styrene reacts with TBCK via a $_2\pi_s + {}_2\pi_a$ reaction mode.

Here, we would like to present new arguments, which independently support the same stereochemistry for the 2-t-butyl-2-cyano-3-phenylcyclobutanone as proposed previously.[19] Our conclusions resulted from the exact analysis[26,27] of all theoretical NMR spectral frequencies of the experimental ^{1}H NMR spectrum of the three protons belonging to the 4-membered ring. Only one set of the spectral parameters gave theoretical intensities which fitted with the experimental spectrum. The accepted spectral parameters are easily rationalized if one accepts as structural model a cyclobutanone having the t-Bu and phenyl groups both *vicinal* and *cis*. The chemical shifts and the coupling constants generally in accordance with other NMR studies on cyclobutanones,[28-33] obtained from the exact analysis of the experimental spectrum, are nicely supported by deuterium labelled cyclobutanones prepared from α, *cis*-, *trans*-, or *β,β'*-di-deuteriated styrene and TBCK. It also remarkable to note that the relative configuration of deuteriated styrenes are preserved during the cycloaddition to TBCK, suggesting a concerted mode for these reactions.

DISCUSSION OF THE RESULTS

The phenyl and t-butyl groups are vicinal *and* cis

The experimental ^{1}H NMR spectrum of the cyclobutanone **3** in $CDCl_3$ is best simulated with the following parameters $\delta_{H^1} = 4.41$ ppm, $\delta_{H^2} = 3.85$ ppm, $\delta_{H^2} = 3.44$ ppm, $J^{gem} = -18.24$ Hz, $J^{cis} = 11.14$ Hz and $J^{trans} = 10.07$ Hz. We consider that the chemical shifts obtained are best rationalized as follows.



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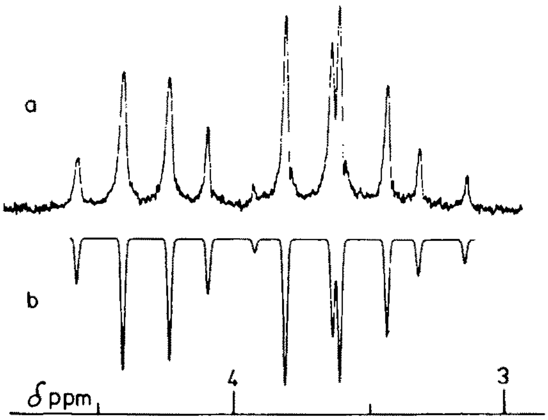
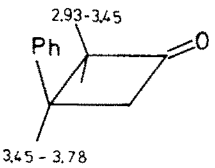


Fig. 1. (a) Experimental spectrum of cyclobutanone **3**. (b) The simulated spectrum.

The proton appearing at $\delta = 4.41$ ppm could be assigned as the benzylic proton H^1. Let us examine the chemical shift of such a proton in some 3-phenylcyclobutanones. Thus in 3-phenylcyclobutanone (**4**)[34] the chemical shift of the benzylic proton is at $\delta = 3.45$–3.78 ppm, in 2,2-dimethyl-3-phenylcyclobutanone (**5**)[35] the benzylic proton signal has the chemical shift at $\delta = 3.25$ ppm, while on replacement of the dimethyl groups with diphenyl groups as in cyclobutanone **6**, the benzylic proton is shifted downfield to 4.32 ppm[36] (or 4.48 ppm[37]). We conclude that, indeed, the H^1 proton in the cyclobutanone **3** has a deshielded shift. The acceptance of this deshielded position for the benzylic proton in the cyclobutanone **3** is crucial for the configurational assignment. The *cis* proximity of the cyano group is responsible for the position of the downfield shift of the benzylic proton in the cyclobutanone **3**. Furthermore the above quoted value for the chemical shift of the benzylic proton from the cyclobutanone **3** was confirmed by the exact analysis of its proton spectrum in various solvents and with shift reagents.[38] Then, we have obtained from β,β'-dideuteriated styrene and TBCK, the cyclobutanone **8** in which the benzylic proton appears at $\delta = 4.37$ ppm.

The chemical shift of the remaining protons, H^2 and H^3 fit well with structure **3**.

The chemical shift occurring at $\delta = 3.85$ ppm, we assign to proton H^2, which is *cis* to the phenyl group (Fig. 2). Its position is shifted with *ca* 0.8 ppm toward lower fields than the same proton in the parent cyclobutanone **7**[28 32] and with *ca* 0.5 ppm with respect to the position found in the 3-phenylcyclobutanones **4**, **5** and **6**. We consider this relative deshielding of H^2 in the cyclobutanone **3**, as a result of its position near or in the plane of the phenyl ring, as a consequence of the locking or only slightly oscilating Ph group by the neighboring t-Bu group (Fig. 2). If the phenyl group in the cyclobutanone rotated freely, as in the case of the



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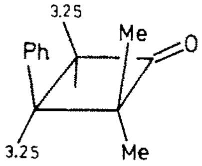

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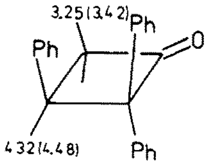

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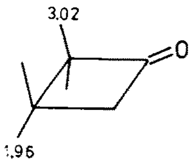

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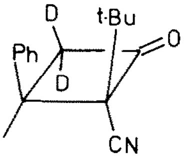

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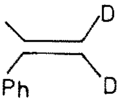

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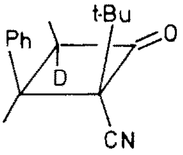

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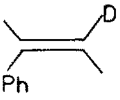

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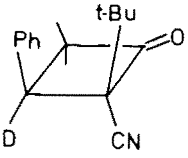

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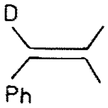

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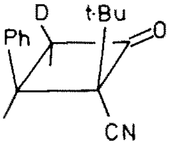

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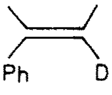

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cyclobutanones **4**, **5** and **6**, its average magnetic effect upon H^2 would have conferred a higher-field chemical shift. Again, the theoretical chemical shift for H^2 from cyclobutanone **3**, is supported by experimental value obtained from the ^1H NMR spectra of the deuteriated cyclobutanones **10** and **12**, obtained from *trans*- and α-deuteriated styrenes with TBCK (Table 1).

The theoretical chemical shift for H^3 as proposed above is supported by value obtained from the ^1H NMR spectra of deuteriated cyclobutanones **12** and **14** obtained from α-deuteriated styrene (**13**) and *cis*-deuteriated styrene (**15**) with TBCK.

At this point we would like to comment the magnitude and the signs of the coupling constants, belonging to the accepted solution chosen from the six real ones for the experimental spectrum in $CDCl_3$.

The calculated geminal coupling constant of − 18.24 Hz is only slightly different in magnitude from that obtained in the case of the parent cyclobutanone.[28–32] The absolute value of the geminal coupling constant has also resulted from the AB ^1H NMR spectrum of the monodeuteriated cyclobutanone 12.

The *cis* coupling constant, 10.07 Hz, is also fairly close to the magnitude of the same coupling constant found in the case of the parent cyclobutanone 7.

The *trans* coupling constant, 11.14 Hz, is however higher than the calculated value, 6 Hz, in the case of the parent cyclobutanone. We believe that this discrepancy results from the distorsions between the t-butyl group and the phenyl group. It is, however, less obvious why only *trans* coupling constant is affected by these conformational changes while the *cis* coupling constant is virtually unaffected.

The cycloaddition of TBCK to styrene derivatives is a concerted reaction

The concertedness of the cycloaddition of ketenes to nonpolar alkenes is receiving an increasing attention, not only on a particular substrate as it was for many years the case of cyclopentadiene,[2b] but also with an increasing number of other substrates belonging, in general, to nonpolar alkenes. Evidence for such a reaction course is based predominantly on the stereochemistry of the only cyclobutanone derivative resulted in the cycloaddition, which according to the Woodward–Hoffmann mechanism, if the reaction is concerted, should give the most sterically crowded isomer.[2] Along with these steric arguments, the concertedness of a few cycloadditions of ketene to alkenes was also supported by kinetic results and isotopic effects.[37,40]

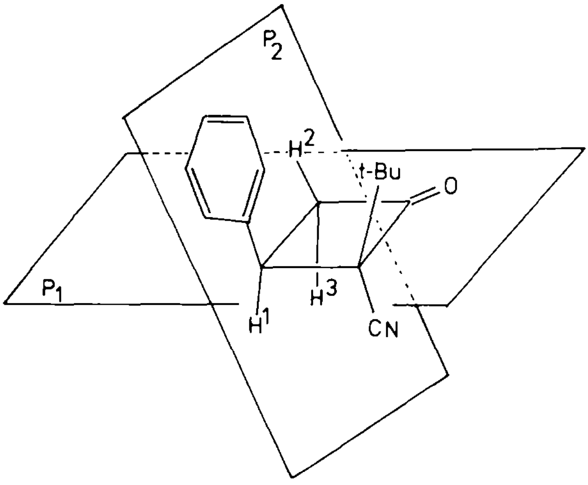
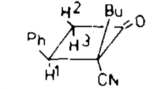
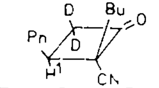
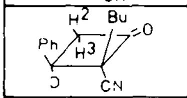
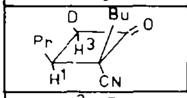
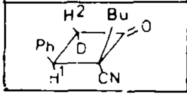


Fig. 2. Structure and protons assignment for cyclobutanone 3.

As in our previous paper,[19] we would like to conclude again that the reaction of styrene with TBCK is concerted. This conclusion is based on the fact that in the reaction of TBCK with deuteriated styrenes, *the original configuration of alkenes is preserved in the resulting cyclobutanones*. In the previous contributions regarding the cycloaddition of diphenylketene to deuteriated styrenes such observation were not commented.[37,40] In our case, *cis*- and *trans*-

Table 1. Calculated (first entry) and experimental chemical shifts (δ, ppm) and coupling constants (in Hz) for the parent and deuteriated cyclobutanones

	H^1	H^2	H^3	$J_{H^2H^3}$	$J_{H^1H^2}$	$J_{H^1H^3}$
	4.41	3.85	3.44	-18.24	11.14	10.07
	4.37	—	—	—	—	—
	—	3.81	3.42	18.0	—	—
	4.37	—	3.41	—	—	10.0
	4.39	3.80	—	—	11.0	—

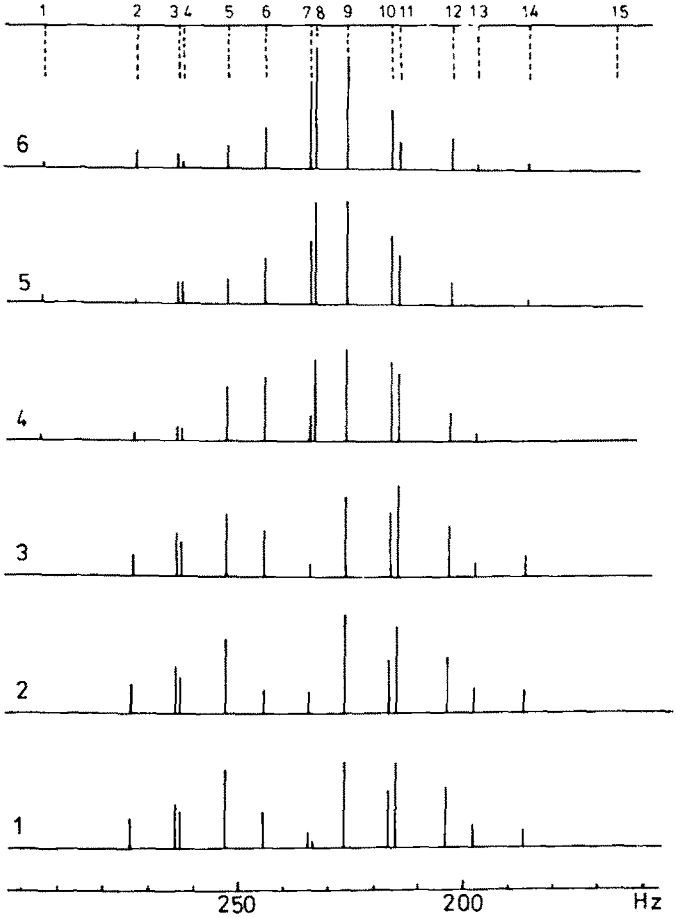


Fig. 3. Theoretical frequencies solutions obtained from the experimental spectrum of cyclobutanone **3** (in $CDCl_3$). The true spectral parameters are generating solution 1. The pairs of conjugated solutions are 1 with 6, 2 with 4 and 3 with 5.

deuteriated styrenes gave with TBCK cyclobutanones **10** and **14**, respectively. Styrenes substituted at the alkenic double bond with methyl or phenyl groups, as markers for the study of the stereochemistry of the reaction course, have so far failed to react with TBCK in our hands. Therefore, we evaluate our results regarding the cycloaddition of TBCK to deuteriated styrenes, as being among the few examples of concerted cycloaddition of a ketene to a cyclic and/or nonrigid alkene.[26,41]

EXPERIMENTAL

Compound **9**, was obtained from 1-phenyl-ethanol-2-d_3 and 30% phosphoric acid. The 1-phenylethanol-2-d_3 was obtained from acetophenone-d_3[42] by reduction with LAH.

The monodeuteriated styrenes were obtained from the corresponding bromostyrene by conversion into Grignard derivatives and then quenching with D_2O. The α-bromo, *trans*-bromo, and *cis*-bromostyrenes were treated with Mg turnings in absolute ether or THF using an excess of EtMgBr to ensure the retention of the original configuration of the bromostyrene in the Grignard derivative.[43] α-Bromostyrene was obtained from styrene dibromide and NaOH aq (1:1 molar ratio dibromo derivative: NaOH).[44]

cis-Bromostyrene was obtained from *trans*-cinamic acid dibromide and sodium carbonate in dry acetone.

trans-Bromostyrene (80% purity) was obtained from the same dibromide as above but with an aqueous solution of sodium hydroxide[45,46]

The content of deuteriated styrenes, estimated from ^1H NMR spectra were for *cis*-deuteriostyrene 90%, *trans*-deuteriostyrene 93%, α-deuteriostyrene 90%, *β,β'*-dideuteriostyrene 100%.

All the cycloaddition were carried out in anhyd benzene under argon. TBCK was obtained as soln in benzene, by thermolysis of 2,5-diazido-3,6-di-t-butylbenzoquinone, using for synthesis of the latter compound a modified version[47,48] of Moore's procedure.[25b]

The exact analysis of the experimental ^1H NMR spectrum of **3** was carried out using programmes written in BASIC for a Hewlett Packard 9830A calculator. The calculations were run in two distinctive steps. In the first step we calculated the real solns of the experimental spectrum of the cyclobutanone **3**, using the procedure devised by Castellano and Waugh[26] and Cavanaugh.[27] The resulting spectral parameters were fed into a second program designed to calculate the corresponding theoretical spectrum and to plot the spectrum (considering the signals as gaussian curves) with a Hewlett Packard 9862A Calculator Plotter.

Acknowledgements We are grateful to Prof. E. Ciorănescu-Nenitzescu Director of the Center of Organic Chemistry (Bucharest) for much understanding and support which made possible this project to be carried out. We are also

grateful to Prof. Lawrence T. Scott (University of Nevada, Reno, Nevada) for providing a copy of the NMR spectrum of 3-phenylcyclobutanone.

REFERENCES

[1] Presented in part at the National Congress of Chemistry, Bucharest, 11–14 September, 1978; M. D. Gheorghiu, L. Parvulescu, C. Draghici and M. Elian, Abstract No. 5-A-84.

[2a] R. B. Woodward and R. Hoffmann, *The Conservation of Orbital Symmetry*. Academic Press, New York

[2a] R. B. Woodward and R. Hoffmann, *The Conservation of Orbital Symmetry*, p 163. Academic Press, New York (1970); for reviews regarding the cycloaddition of ketenes see [b] R. W. Holder, *J. Chem. Educ.* **53,** 81 (1976); [c] D. Seebach, S. Beckman and H. Geiger, *Methoden der Organischen Chemie* (Edited by E. Muller) Band IB, Teil 4. Georg Thieme Verlag, Stuttgart (1971).

[3] R. Montaigne and L. Ghosez, *Angew. Chem.* **80,** 194 (1968).

[4] R. Huisgen, L. A. Feiler and G. Binsch, *Chem. Ber.* **102,** 3460 (1969).

[5] M. Rey, S. Roberts, A. Dieffenbacher and S. Dreiding, *Helv. Chim. Acta* **53,** 417 (1970).

[6] P. R. Brook, J. M. Harrison and A. J. Duke, *Chem. Commun.* 589 (1970).

[7] P. R. Brook, A. J. Duke and J. R. C. Duke, *Ibid.* 574 (1970).

[8] T. DoMinh and O. P. Strausz, *J. Am. Chem. Soc.* **92,** 1766 (1970).

[9] W. T. Brady, F. H. Parry, III, R. Roe, Jr., and E. F. Hoff, Jr., *Tetrahedron Letters* 819 (1970).

[10] W. T. Brady and R. Roe, Jr., *J. Am. Chem. Soc.* **92,** 4618 (1970).

[11] N. S. Isaacs and P. F. Stanfury, *Chem. Commun.* (1970) 1061.

[12] H. M Frey and N. S. Isaacs, *J. Chem. Soc.* (*B*) 830 (1970).

[13] L. Ghosez, R. Montaigne, A. Roussel, H. Vanlierde and P. Mollet, *Tetrahedron* **27,** 615 (1971).

[14] A. Hassner, V. K. Fletcher and D. P. G. Hamon, *J. Am. Chem. Soc.* **93,** 264 (1971).

[15] W. Weyler, Jr., L. R. Byrd, M. C. Caserio and H. W. Moore, *Ibid.* **94,** 1027 (1972).

[16] K. W. Egger and A. T. Cocks, *J. Chem. Soc.* Perkin II, 211 (1972).

[17] R. C De Selms and F. Delay, *J. Org. Chem.* **37,** 2908 (1972).

[18] N. S. Isaacs and P. Stanbury, *J. Chem. Soc.* Perkin II, 166 (1973).

[19] M. D. Gheorghiu, F. Kerek and M. Avram, *Rev. Roumaine Chim.* **20,** 75 (1975).

[20] W. Weyler, Jr., W. G. Duncan and H. W. Moore, *J Am. Chem. Soc.*, **97,** 6187 (1975).

[21] M. D. Gheorghiu, P. Filip, C. Draghici and L. Parvulescu, *J. Chem. Soc.* 635 (1975); P. R. Brook and K. Hunt, *Ibid.* Chem. Commun. 989 (1974).

[22] M. D. Gheorghiu, C. Draghici and L. Parvulescu, *Tetrahedron* **33,** 3295 (1977).

[23] M. D. Gheorghiu, L. Parvulescu and C. Draghici, *Rev. Roumaine Chim.* **24,** 1005 (1979).

[24] A. Hassner, R. M. Cory and N. Sartoris, *J. Am. Chem. Soc.* **98,** 7698 (1976).

[25a] H. W. Moore and W. Weyler, Jr., *Ibid.* **92,** 4132 (1970). [b] W. Weyler, Jr., W. G. Duncan, M. B. Liewen and H. W. Moore, *Org. Synth.* **55,** 32 (1976).

[26] S. Castellano and J. S. Waugh, *J. Chem. Phys.* **34,** 295 (1961).

[27] J. R. Cavanaugh, *Ibid.* **39,** 2378 (1963).

[28] K. B. Wiberg and B. J. Nist, *J. Am. Chem. Soc.* **83,** 1126 (1961).

[29] H. Weitkamp and F. Korte, *Tetrahedron Suppl.* 7, 75 (1966).

[30] L. H. Sutcliffe and S. M. Walker, *J. Phys. Chem.* **71,** 1155 (1967).

[31] B. Braillon, *J. Mol. Spect.* **27,** 313 (1968).

[32] R. G. Green, P. Shaw, L. H. Sutcliffe, B. Taylor and S. N. Walker, *Spectrochim. Acta* **30A,** 529 (1974).

[33] R. J. Abraham, *Analysis of High Resolution NMR Spectra*, p. 137. Elsevier, New York (1971).

[34] L. T. Scott and M. A. Minton, *Synthesis* 411 (1977).

[35] A. P. Krapcho and J. H. Lesser, *J. Org. Chem.* **31,** 2030 (1966).

[36] R. Huisgen and L. A. Feiler, *Chem. Ber.* **102,** 3391 (1969).

[37] J. E. Baldwin and J. A. Kapecki, *J. Am. Chem. Soc.* **92,** 4374 (1970).

[38] M. D. Gheorghie, O. Ciobanu and M. Elian, *J. hagn. Resonance* to be published.

[39a] It is generally accepted that the exact soln for an experimental spectrum of a three spin system is not necessarily unique.[26,27,39b] Although the search for unique solns is evident, in practice it is only seldom found in the lit. In order to strengthen the confidence in the spectral parameters which led us to infer the structure of **3**, we have undertaken a complete analysis of the experimental spectrum, obtaining six real solns (see Fig. 3). The true soln (1 on Fig. 3) is presented in Table 1. For other discussion see Ref. 38. Details regarding the six real solutions are available upon request; [b] P. Diehl, H. Kellerhalls and E. Lustig, *Computer assistance in the analysis of high-resolution NMR spectra*, in *NMR Basic Principles and Progress* (Edited by P. Diehl, E. Fluck, R. Kosfeld) vol. 6, p. 54. Springer-Verlag, Berlin (1972).

[40] C. J. Collins, B. M. Benjamin and G. W. Kabalka, *J. Am. Chem. Soc.* **100,** 2570 (1978).

[41] P. R. Brook, private communication (1978), cycloaddition of *cis*-2-butene with TBCK.

[42] D. S. Noyce, G. L. Woo and H. J. Jorgenson, *J. Am. Chem. Soc.* **83,** 1162 (1960).

[43] T. Yoshino, Y. Manabe and Y. Kikuki, *Ibid.* **86,** 4670 (1964).

[44] S. J. Cristol and W. P. Norris, *Ibid.* **75,** 2645 (1953), *Ibid.* **76,** 3005 (1954).

[45] E. Grovenstein, Jr., and D. E. Lee, *Ibid.* **75,** 2639 (1953).

[46] J. D. Bergman and C. C. Price, *Ibid.* **79,** 5474 (1957).

[47] M. D. Gheorghiu and M. Avram, *Org. Proced. Prepr. Intern.* **6,** 231 (1974).

[48] M. D. Gheorghiu, L. Parvulescu and I. Manolescu, unpublished results. Essentially our version uses in the elimination steps aqueous solution of sodium or potassium carbonate, triethylbenzylammonium chloride as phase transfer catalyst and a solution of the organic substrat in methylene dichloride or benzene.