The Mechanism of Diazoalkane Additions to Cyclopropanones[1]

Nicholas J. Turro[2] **and Robert B. Gagosian**[3]

Contribution from the Chemistry Department, Columbia University, New York, New York 10027. *Received August 25, 1969*

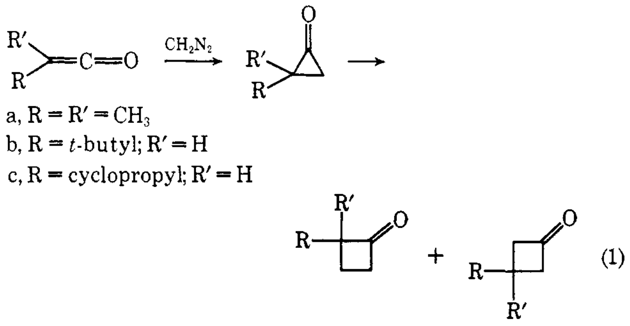
Abstract: The reaction of diazomethane and diazoethane with 2,2,3-trimethylcyclopropanone (**1**) and 2-methylcyclopropanone (**14**) to yield cyclobutanone products is reported. The reactions of diazoethane with **1** and **14** appear to be stereoselective. The mechanisms of these reactions are discussed in terms of the stereoelectronics of diazoalkane ring expansions and the role of conformational equilibria on the product distribution is discussed in the light of the Curtin–Hammett principle. Results of equilibrium studies performed on the various cyclobutanone products are reported and discussed.

Diazoalkane ring expansion reactions have been a subject of much discussion and have recently been extensively reviewed.[4] It has been shown that diazoalkanes react with ketones to produce a homologous ketone or an isomeric epoxide *via* a 1,2-nucleophilic rearrangement involving a charge separated intermediate.[4]

Usually, electronic and steric factors govern which group will migrate in unsymmetrical ketones; however, Gutsche[5] has shown that often solvent, temperature, concentration of diazoalkane, and method of introducing the diazoalkane (*in situ* or *ex situ*) are sometimes important in determining the ratio of the isomeric ring expanded ketones. As is expected for a 1,2-nucleophilic rearrangement mechanism, electron withdrawing groups at or near the α-carbon of the carbonyl generally diminish migratory reactivity while favoring epoxide formation; however, electron-donating groups tend to favor migration to form the homologous ketone.[4]

The role of stereochemistry in the mechanism of diazoalkane ring expansion reactions has been studied by several groups.[5,6] Gutsche has pointed out that there are two steric factors to consider: the steric approach of the diazoalkane attack on the carbonyl and conformational control over the rearrangement of the resulting betaine intermediate.[6a] Recently Marshall and Partridge used transition state energy arguments to show that various steric interactions in the transition state may be responsible for the products obtained from diazoethane ring expansions on 4-alkylcyclohexanones.[6b] Both steric approach control[7] and conformational interactions in the intermediates played important roles in their work. Carlson and Behn have recently reported their results of a study of steric and conformational effects of ring expansion reactions.[6c] They compared the product ratios of the diazoalkane ring expansion of ketones *vs.* the Tiffeneau–Demjanov ring expansion of two isomeric amino alcohols. Steric approach control and conformational interactions in the transition state for zwitterion to homologous ketone product also had an important role in their study. Thus, their findings lent support to the Marshall and Partridge steric scheme.[6b]

Conia and coworkers have recently studied the ring expansion of the formal two ring system, ketene (eq 1).[8] They found that various substituted ketenes upon reaction with diazomethane yielded cyclobutanones with migration of the most highly substituted carbon–carbon bond.[8] The intermediate in these reactions was presumably the corresponding cyclopropanone.[9]



a, R = R′ = CH_3
b, R = *t*-butyl; R′ = H
c, R = cyclopropyl; R′ = H

Per cent

a, 35%	65%
b, 30%	70%
c, 35%	65%

Results and Discussion

We have found that (a) indeed cyclopropanones are the intermediates in diazoalkane ring expansion of ketenes, (b) the migration aptitudes are dependent on

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[1] (a) Cyclopropanones. XVI. Paper XV: C. Rappe, L. Knutsson, N. J. Turro, and R. B. Gagosian, *J. Am. Chem. Soc.*, **92**, 2032 (1970). See N. J. Turro and R. B. Gagosian, *Chem. Commun.*, 949 (1969), for a preliminary report of this work. (b) The authors thank the Air Force Office of Scientific Research for their generous support of this work (Grants AFOSR-66-1000 and AFOSR-68-1381). A gift from the Upjohn Co. is also gratefully acknowledged.

[2] Alfred P. Sloan Fellow, 1966–1970.

[3] National Science Foundation Trainee, 1967–1968; Ferguson Teaching Fellow 1968–1969.

[4] (a) C. D. Gutsche, *Org. Reactions*, 8, 364 (1954); (b) C. D. Gutsche and D. Redmore, "Carbocyclic Ring Expansion Reactions," Academic Press, New York, N. Y., 1968.

[5] C. D. Gutsche and H. H. Peter, *J. Am. Chem. Soc.*, 77, 5971 (1955).

[6] (a) C. D. Gutsche, H. F. Strohmayer, and J. M. Change, *J. Org. Chem.*, **23**, 1 (1958); (b) J. A. Marshall and J. J. Partridge, *ibid.*, **33**, 4090 (1968); (c) R. G. Carlson and N. J. Behn, *ibid.*, **33**, 2069 (1968); (d) C. D. Gutsche and J. E. Bowers, *ibid.*, **32**, 1203 (1967).

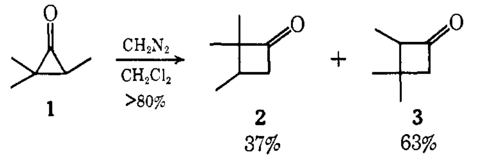
[7] E. L. Eliel, N. K. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," John Wiley & Sons, Inc., New York, N. Y., 1966, p 116.

[8] (a) H. Audier, J. M. Conia, M. Fetizon, and J. Gore, *Bull. Chim. Soc. France*, 787 (1967); (b) B. Braillon, J. Salaun, J. Gore, and J. M. Conia, *ibid.*, 1981 (1964); (c) J. M. Conia and J. Gore, *ibid.*, 1968 (1964); (d) J. M. Conia and J. Salaun, *ibid.*, 2751 (1965); (e) J. L. Ripoll and J. M. Conia, *ibid.*, 2755 (1965); (f) J. Salaun and J. M. Conia, *ibid.*, 3730 (1968); (g) J. M. Conia, personal communication; (h) W. B. Hammond, Ph.D. Dissertation, Columbia University, New York, N. Y., 1967.

[9] (a) R. L. Camp and F. D. Greene, *J. Am. Chem. Soc.*, **90**, 7349 (1968); (b) J. Smith and A. Pings, *J. Org. Chem.*, **2**, 95 (1937); (e) W. L. Mock, Ph.D. Dissertation, Harvard University, Cambridge, Mass., 1967.

the diazoalkane used, and (c) a complete steric scheme incorporating the methods of Marshall[6b] and Carlson[6c] can be drawn to account for the product ratios of the reactions studied.

2,2,3-Trimethylcyclopropanone (**1**) yields 2,2,3-trimethylcyclobutanone (**2**) and 2,3,3-trimethylcyclobutanone (**3**) in the ratio of 37:63 in over 80% yield upon reaction with diazomethane (eq 2). Preferential migration of the *most* substituted bond has occurred.

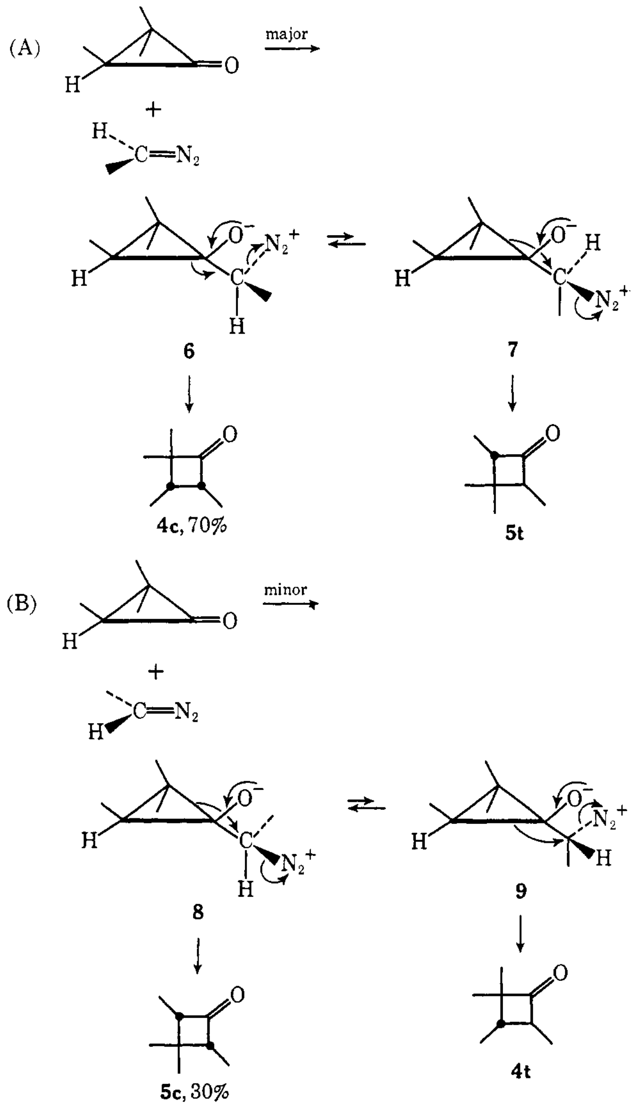


(2)

However, when **1** is allowed to react with diazoethane, preferential migration of the *least* substituted bond occurs stereoselectively to yield *cis*-2,2,3,4-tetramethylcyclobutanone (**4c**) and *cis*-2,3,3,4-tetramethylcyclobutanone (**5c**) in the ratio of 7:3 (eq 3).[10] Since the rate-determining step in diazoalkane ring expansions has been found to be addition of the diazoalkane to the ketone,[11] it is possible to look at (a) the steric approach of the diazoethane on **1** (see Schemes I and II) and (b) the steric interactions of the transition state of the zwitterionic rotameric intermediates to the cyclobutanone products, to determine which C–C bond migrates.

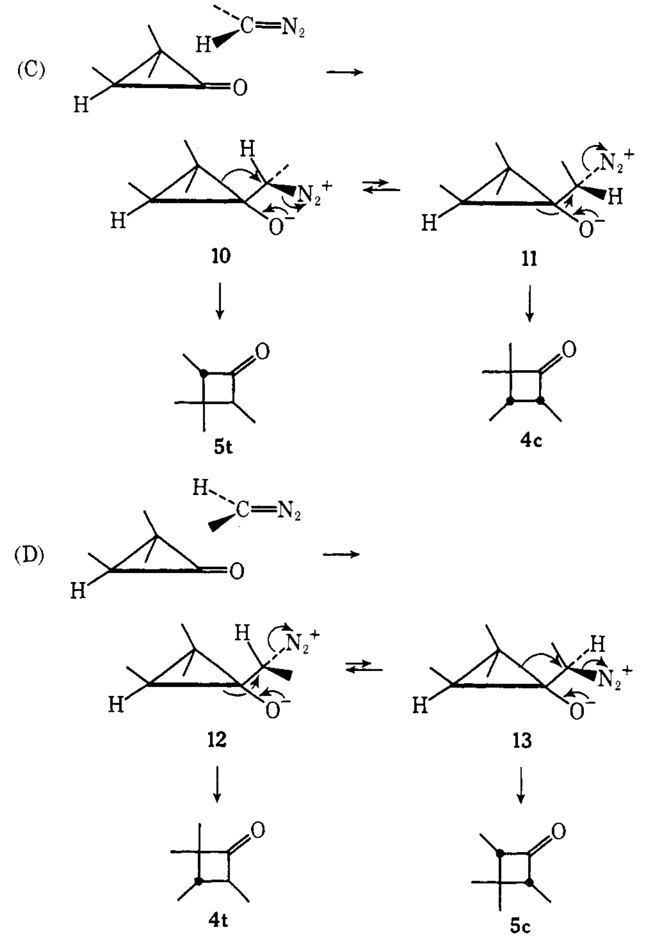
Scheme I. Stereochemistry of Attack of Diazoethane on **1** (Favored)

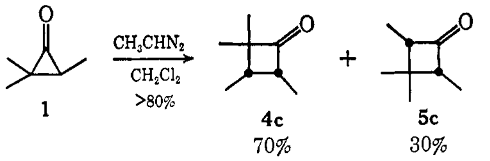
Bottom Attack



Scheme II. Stereochemistry of Attack of Diazoethane on **1** (Unfavored)

Top Attack





(3)

A reasonable assumption is that the 1,3 interactions of the zwitterionic rotamers should be approximately the same as the 1,3 interactions of the transition state of the zwitterion to cyclobutanone product (see **13a**). Therefore, we have calculated the 1,3 interaction energies of the zwitterions and compared them with the cyclobutanone product ratios.[12]

Attack by the diazoethane on **1** can occur from the "bottom" or the "top," as shown by Scheme I and Scheme II, respectively. From Dreiding models it has been found that the 1,3 interactions of the zwitterion are approximately 97% of a 1,3 diaxial interaction in cyclohexanone;[12] therefore, the transition state inter-

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[10] N. J. Turro, *Accounts Chem. Res.*, **2**, 25 (1969).

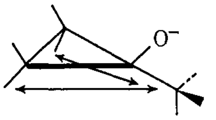
[11] J. N. Bradley, C. W. Cowell, and A. Ledwith, *J. Chem. Soc.*, 4334 (1964).

[12] The 1,3 diaxial interaction energies which were used were taken from ref 7.

Table I. Calculation of Interaction Energies for Intermediates **6–13**

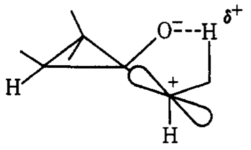
Intermediate	Interaction energies, kcal/mole: CH_3H	CH_3CH_3	Total
6	1 (0.9)		0.9
7	1 (0.9)	1 (3.6)	4.5
8	1 (0.9)		0.9
9	1 (0.9)	1 (3.6)	4.5
10	2 (0.9)		1.8
11		2 (3.6)	7.2
12	2 (0.9)		1.8
13		2 (3.6)	7.2

action energies for the cyclobutanone products from intermediates **6–13** can be calculated (Table I). From Table I, **4c**, **5c**, **4t**, and **5t** are all expected products in 40, 40, 10, and 10% yields, respectively. The analysis, however, has only included steric interactions in the transition state for the zwitterion to cyclobutanone product. Using steric approach control, attack of the cyclopropanone from the "top" would be eliminated due to steric crowding, thereby eliminating intermediates **10**, **11**, **12**, and **13**, the precursors of **5t**, **4c**, **4t**, and **5c**, respectively. One would also expect attack of the diazoethane with the hydrogen opposed to the cyclopropanone methyl, *e.g.*, step A in Scheme I, leading to **6** and **7**, rather than opposed to the cyclopropanone hydrogen, *e.g.*, step B in Scheme I leading to **8** and **9**. Combining both arguments, one comes to the conclusion that **4c** and **5c** are the expected products with **4c** being the major.



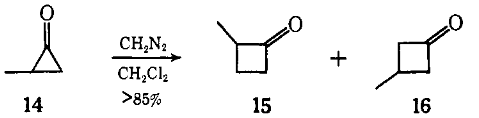
13a

An alternative mechanism would involve product formation *via* a carbonium ion, **13b**. However, in this case preferential migration of the most substituted bond is expected in contradiction to the observed results.



13b

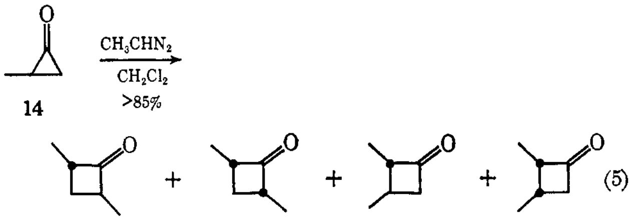
2-Methylcyclopropanone (**14**)[10] reacts with diazomethane to yield 2-methylcyclobutanone (**15**) and 3-methylcyclobutanone (**16**) (eq 4).[8a,g] Migration of the *most* substituted bond occurs again. However, when **14** reacts with diazoethane, a more complex pathway is followed, to yield *trans*-2,4-dimethylcyclobutanone (**17t**), *cis*-2,4-dimethylcyclobutanone (**17c**), *trans*-2,3-dimethylcyclobutanone (**18t**), and *cis*-2,3-dimethylcyclobutanone (**18c**), in the ratio of 12:31:17:40 (eq 5). Attack by diazoethane on **14** can occur from both the "bottom" or the "top" as shown in Schemes III and IV, respectively.



14 **15** **16**

43% 57%

(4)

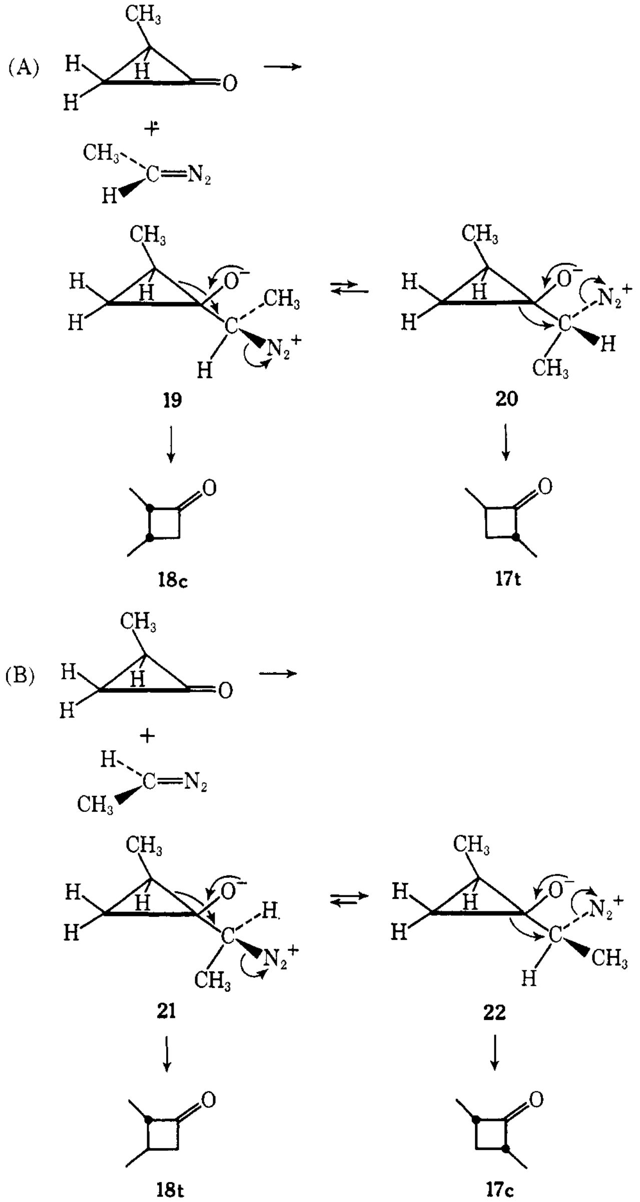


14

	17t	**17c**	**18t**	**18c**
Exptl	12%	31%	17%	40%
Calcd	10%	40%	10%	40%

Scheme III. Stereochemistry of Attack of Diazoethane on **14** (Favored Slightly)

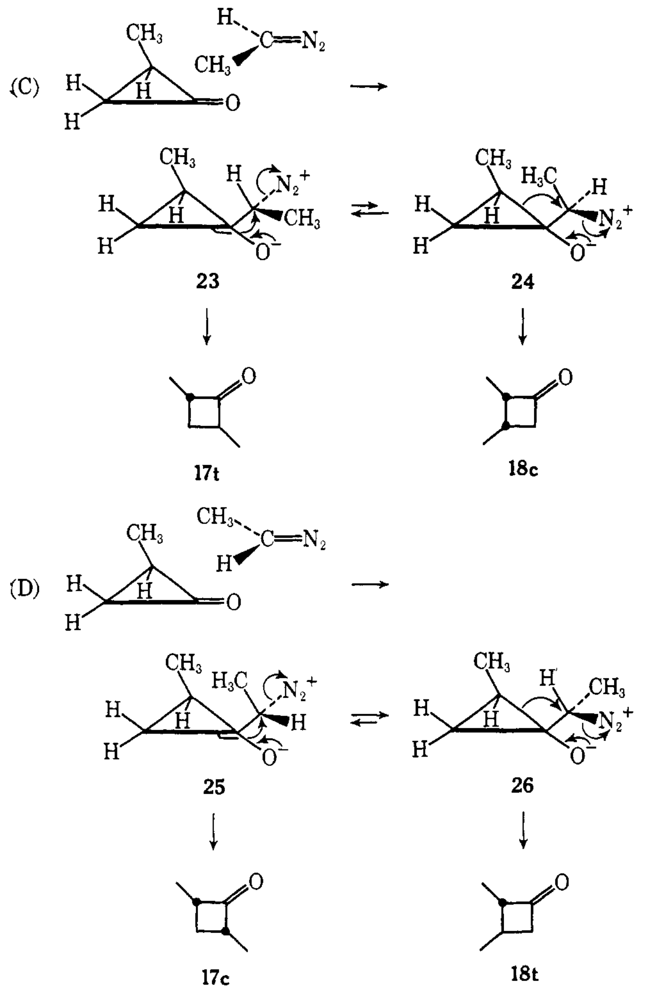
Bottom Attack



As in the reaction of **1** with diazoethane, it is possible to calculate the transition state 1,3 interaction energies for the intermediates **19–26** (Table II and Appendix). From Table II, the calculated yields are 10% **17t**, 40% **17c**, 10% **18t**, and 40% **18c**. From

Scheme IV. Stereochemistry of Attack of Diazoethane on **14** (Unfavored Slightly)

Top Attack



steric approach control, attack from the "bottom" is only slightly favored over attack from the "top." Step B in Scheme III is sterically the same as step A; therefore, the percentages calculated from Table II are the expected percentages of the product cyclobutanones. Although a reasonable correlation has been found, it is difficult to assess an exact value since steric approach control between "top" and "bottom" attack is different and the exact correlation between interactions in the transition state with those of the zwitterion will yield only qualitative results.

Table II. Calculation of Interaction Energies for Intermediates **19–26**

Intermediate	Interaction energies, kcal/mole CH_3H	 CH_3CH_3	 Total
19			0
20	2 (0.9)		1.8
21	2 (0.9)		1.8
22			0
23	1 (0.9)		0.9
24	1 (0.9)	1 (3.6)	4.5
25	1 (0.9)	1 (3.6)	4.5
26	1 (0.9)		0.9

It should be pointed out, however, that this treatment is only one explanation for the product ratios and the fact that the ratio of zwitterionic transition state interaction energies correlates with the ratio of their respective cyclobutanone products could be fortuitous, especially if the first step is reversible in Schemes I–IV.

It should also be noted that the arguments presented here, when interpreted in light of the Curtin–Hammett principle,[13a] imply that the activation energy, required to proceed from the intermediate (formed by addition of a diazoalkane to a cyclopropanone) to the transition state for ring expansion, is small and that the equilibration of rotomers is rapid relative to rearrangement. In other words, since ground state conformational arguments are capable of qualitatively predicting otherwise unexpected product ratios, an assumption implicit in the Curtin–Hammett principle,[13a] *i.e.*, that the activation energy for reaction is large relative to the barrier of internal rotation, probably does not hold. Indeed, our conclusions suggest strongly that product ratios are determined mainly by the conformer ratios of intermediates such as those shown in Scheme I, Scheme III, and Scheme IV. Furthermore, if one employs Hammond's postulate[13b] to guess at the position of the transition state for rearrangement along the reaction coordinate, the rapid rate and exothermicity of the ring expansion of cyclopropanones by diazoalkanes indicates that starting materials, the intermediate adduct, and the transition state for rearrangement all occur at some very early stage of the reaction. This suggests further that an intermediate need not even be involved, since one can explain product ratios simply on the basis of the energy contents of transition states for a synchronous addition–rearrangement. Since the starting materials are the same and must have the same free energy no matter which cyclobutanone is formed, then the 1,3-interactions can be viewed as the factors which favor one mode of attack (and transition state) over another.[6b]

Equilibration Studies

Relatively few equilibration studies of cyclobutanones have been reported.[8] In order to assess better the factors involved in determining the relative energy contents of cyclobutanones, equilibration studies of **4**, **5**, **17**, and **18** were performed (Table III).

Table III. Isomer Composition of Cyclobutanone Products

Cyclobutanone	Conditions[a]	% composition *cis*	 *trans*
4	a	100	0
	b	22.5	77.5
5	a	100	0
	b	100	0
17	a	72	28
	b	71	29
18	a	70	30
	b	23.5	76.5

[a] a = kinetic; b = equilibrium.

From Table III the following ΔF values for the corresponding isomers were calculated (Table IV).

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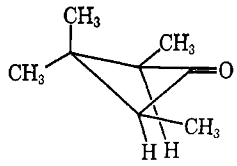
(13) (a) W. B. Hammond, Ph.D. Dissertation, Columbia University, 1967; D. Y. Curtin, *Rec. Chem. Progr.*, **15**, 111 (1954); E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., p 151; (b) G. S. Hammond, *J. Am. Chem. Soc.*, 77, 334 (1954).

Table IV. Free Energy Values for Cyclobutanone Products

Equilibrium	ΔF, kcal/mole
4c $\rightleftharpoons$ **4t**	-0.72
5c $\rightleftharpoons$ **5t**	$\geq +2.0$
17c $\rightleftharpoons$ **17t**	$+0.52$
18c $\rightleftharpoons$ **18t**	-0.71

Tables III and IV clearly demonstrate that the ring expansion reaction is kinetically controlled. Both tables also show that **4c** and the **18t**/**18c** ratio are kinetic products whereas **5c** and the **17t**/**17c** ratio are probably the kinetic and thermodynamic products. **5c** is both the kinetic and thermodynamic product. The fact that both methyl groups α to the carbonyl can occupy equatorial positions (27)[8a,e,14] explains the greater stability of **5c** over **5t**. It is interesting to note that no **5t** could be detected when **5c** was equilibrated (nmr and vpc). On the basis of infrared and Raman[14b] data, it has recently been proposed that cyclobutanones are planar. Our equilibration studies seem to us to support Conia's suggestion[8f] that cyclobutanones are puckered and that substituents can assume "equatorial" and "axial" type of positions.



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Conclusions

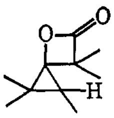
Conformational restrictions appear to play a very important role in the diazoethane ring expansions of substituted cyclopropanones. Steric approach control along with transition state energetic arguments appear to give a qualitative understanding of the product percentages.

Experimental Section

Infrared spectra were taken on a Perkin-Elmer 137 spectrometer. Nuclear magnetic resonance spectra were taken on a Varian A-60 or A-60A analytical high resolution nmr spectrometer. Chemical shifts are reported in δ (parts per million) from internal tetramethylsilane (δ 0.00) or from internal methylene chloride (δ 5.30) unless specified. Mass spectra were taken on a Hitachi Perkin-Elmer RMU-6D mass spectrometer. Vpc analyses were performed on an Aerograph Model A90P or Model 1200 gas chromatograph. The following liquid phases were used: 1,2,3-tris(2-cyanoethoxy)propane ($\beta\beta\beta$), Carbowax 20M (CWX 20M), and SE-30. Chromosorb P (Chrom P) was used as solid support. Elemental analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y. Unless specified, yields are based on nmr integrations of product absorption *vs.* methylene chloride. All commercial chemicals used were reagent quality. Preparation of 2-methylcyclopropanone (**14**) was accomplished as described previously.[15]

Preparation of 2,2,3-Trimethylcyclopropanone (1). A cold ($-78°$) CH_2Cl_2 solution of diazoethane[15] was added to a twofold excess of dimethylketene ($-78°$).[16a] The mixture was stirred during the addition and then vacuum distilled. The distillation apparatus was flushed with N_2 whenever the distillation was interrupted. During the distillation, the pot was maintained at 10–20°, the column at -5 to 0°, and the condenser and receiver at $-78°$. Aliquots were removed periodically for nmr analysis. The distillation was continued until the excess dimethylketene had been removed and the resulting CH_2Cl_2 solution of **1** was at the proper concentration of approximately 10% determined by nmr. Excess CH_2Cl_2 (80 ml) usually had to be added during the distillation. After the dimethylketene was removed, the solution was flash distilled on a high vacuum line (10^{-4} mm). This method usually gave a CH_2Cl_2 solution of **1** of greater than 85% purity. The purity was determined by nmr integrations of product absorption *vs.* CH_2Cl_2, tetramethyl-1,3-cyclobutanedione, *cis*-2,2,3,4-tetramethylcyclobutanone, and *cis*-2,3,3,4-tetramethylcyclobutanone being the main impurities. The usual yield of **1** (based on diazoethane) is greater than 60%. **1** shows the following spectral properties: ir $\nu_{max}^{CH_2Cl_2}$ 1822 cm^{-1} (C=O), 1387 and 1380 cm^{-1} (*gem*-dimethyl); nmr (CH_2Cl_2) δ 1.4–1.1 (m, 1 H), 1.36 (s, 3 H), 1.22 (d, 3 H, J = 5 Hz), 1.12 (s, 3 H).

Characterization of 1. 1,1,2,6,6-Pentamethyl-5-oxo-4-oxaspiro[2.3]hexane (28). To a 10% solution of dimethylketene (*ca.* 30 mmoles) in CH_2Cl_2 was added a CH_2Cl_2 solution (50 ml) of diazoethane (*ca.* 20 mmoles). The solution was allowed to stand for 6 days at $-78°$. The resulting solution was concentrated and analyzed by vpc (6 ft × 0.25 in., 22% CWX 20M, Chrom P, 200°, 120 cc of He/min). The major product was collected and identified as adduct **28** by the following spectral properties:[15] ir $\nu_{max}^{CCl_4}$ 1830 cm^{-1} (C=O), 1385 and 1365 cm^{-1} (*gem*-dimethyl); nmr (CCl_4–TMS), δ 1.39 (s, 3 H), 1.29 (s, 3 H), 1.13 (s, 3 H), 1.09 (s, 3 H), 1.06 (d, 3 H, J = 7 Hz), 0.82 (q, 1 H, J = 7 Hz); mass spectrum (75 eV) *m/e* (relative intensity) 168 (3, M$^+$), 153 (2), 124 (1), 123 (2), 108 (7), 70 (100), 55 (25), 42 (41). The instability of **28** precluded analysis.



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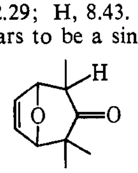
2,2,4-Trimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one (29). A dilute (2–3%) CH_2Cl_2 solution of **1** (15 ml) was mixed with 5 ml of purified furan (~69 mmoles). After 1 hr at room temperature, evaporation of the solvent followed by preparative vpc (6 ft × 3/8 in., 22% CWX 20M, Chrom P, 200°, 120 cc of He/min) led to the isolation of adduct **29** which was identified by the following spectral properties:[16a] ir ν_{max}^{neat} 1715 cm^{-1} (C=O), 1380 and 1360 cm^{-1} (*gem*-dimethyl), 725 cm^{-1} (>C=C<); nmr (CCl_4–TMS) δ 6.36–6.13 (m, 2 H),[16b] 4.65 (d, 1 H, J = 5 Hz), 4.29 (s, 1 H), 2.81 (d of q, 1 H, J = 7, 5 Hz), 0.89 (s, 3 H), 0.88 (d, 3 H, J = 7 Hz), 1.26 (s, 3 H); mass spectrum (75 eV) *m/e* (relative intensity) 166 (M$^+$, 37), 151 (15), 123 (6), 110 (12), 96 (81), 95 (67), 81 (100), 70 (31), 68 (13), 67 (22), 55 (23), 53 (17), 42 (28), 41 (65), 39 (64). *Anal.* Calcd for $C_{10}H_{14}O_2$: C, 72.29; H, 8.43. Found: C, 72.10; H, 8.67. From nmr, **29** appears to be a single isomer; however, of the four possible isomers, we do not know which isomer we have isolated.



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2,2,3-Trimethylcyclobutanone (2) and 2,3,3-Trimethylcyclobutanone (3). A CH_2Cl_2 solution (25 ml) of diazomethane (25 mmoles) was added slowly with stirring to a CH_2Cl_2 solution (20 ml) of **1** (14 mmoles) at $-78°$. The solution was allowed to stir for 30 min. The pale yellow solution was allowed to warm to room temperature. It was then concentrated on a short column condenser (10 cm) and the residue was analyzed by vpc (6 ft × 0.25 in., 20% $\beta\beta\beta$, Chrom P, 95°, 65 cc of He/min). Two cyclobutanones, **2** and **3**, were formed in the ratio of 38:62 and were identified by their spectral properties: 2,2,3-trimethylcyclobutanone (*2*)[8a–c] [ir $\nu_{max}^{CCl_4}$ 1777 cm^{-1} (C=O); nmr (CCl_4–TMS) δ 3.18 (d of d, 1 H, of AB, $\Delta\nu_{AB}$ = 36.2 Hz, J = 17, 9 Hz), 2.55 (d of d, 1 H, B of AB, $\Delta\nu_{AB}$ = 36.2 Hz, J = 17, 6.5 Hz), 2.12 (m, 1 H), 1.16 (d, 3 H, J = 7 Hz), 1.15 (s, 3 H), 1.03 (s, 3 H); mass spectrum[17] (75 eV)

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[14] (a) J. Salaun and J. M. Conia, *Bull. Soc. Chim. France*, 3730, 3735 (1968); (b) J. R. Durig and W. H. Green, *J. Mol. Spectrosc.*, **27** 95 (1968).

[15] N. J. Turro and W. B. Hammond, *Tetrahedron*, **24**, 6017 (1968).

[16] (a) N. J. Turro, S. S. Edelson, J. R. Williams, T. R. Darling, and W. B. Hammond, *J. Am. Chem. Soc.*, **91**, 2283 (1969). (b) Apparently this multiplet is an AB quartet with $\Delta\nu_{AB}$ = 3.5 Hz, J_{AB} = 6 Hz. Some further splitting is also evident.

[17] D. S. Weiss, R. B. Gagosian, and N. J. Turro, *J. Org. Mass Spectrosc.*, in press.

m/*e* (relative intensity) 112 (M$^+$, 5), 97 (1), 84 (3), 70 (100), 55 (88), 42 (93), 41 (70)]; 2,3,3-trimethylcyclobutanone (**3**)[8a–c] [ir $\nu_{max}^{CCl_4}$ 1775 cm^{-1} (C=O); nmr (CCl$_4$–TMS) δ 2.89 (m, 1 H), 2.85 (d of d, 1 H, A of AB, $\Delta\nu_{AB}$ = 9.8 Hz, *J* = 17, 2 Hz), 2.52 (d, 1 H, B of AB, $\Delta\nu_{AB}$ = 9.8 Hz, *J* = 17 Hz), 1.41 (s, 3 H), 1.11 (s, 3 H), 0.95 (d, 3 H, *J* = 7 Hz); mass spectrum[17] (75 eV) *m*/*e* (relative intensity) 112 (M$^+$, 4), 97 (2), 84 (5), 70 (89), 56 (76), 55 (100), 42 (45), 41 (77), 39 (43)].

***cis*-2,2,3,4-Tetramethylcyclobutanone (4c) and *cis*-2,3,3,4-Tetramethylcyclobutanone (5c).** A CH$_2$Cl$_2$ solution (25 ml) of diazoethane (22.5 mmoles) was added slowly with stirring to a CH$_2$Cl$_2$ solution (15 ml) of **1** (10.5 mmoles) at −78°. The solution was allowed to stir for 30 min. The pale orange solution was allowed to warm to room temperature. It was then concentrated on a short column condenser (10 cm) and the residue was analyzed by vpc (6 ft × 0.25 in., 20% $\beta\beta\beta$, Chrom P, 60°, 40 cc of He/min). Two cyclobutanones, **4c** and **5c**, were found in the ratio of 70:30 and were identified by their spectral properties: *cis*-2,2,3,4-tetramethylcyclobutanone (**4c**)[8a–c; 18] [ir $\nu_{max}^{CCl_4}$ 1770 cm^{-1} (C=O); nmr (CCl$_4$–TMS), δ 3.46 (q of d, 1 H, *J* = 10, 7 Hz), 2.15 (d of q, 1 H, *J* = 10, 7 Hz), 1.27 (s, 3 H), 0.98 (d, 3 H, *J* = 7 Hz), 0.95 (s, 3 H), 0.93 (d, 3 H, *J* = 7 Hz); mass spectrum[17] (75 eV) *m*/*e* (relative intensity) 126 (M$^+$, 9), 111 (2), 98 (2), 83 (6), 70 (100), 56 (9), 55 (51), 42 (39), 41 (27)]; *cis*-2,3,3,4-tetramethylcyclobutanone (**5c**) [ir $\nu_{max}^{CCl_4}$ 1770 cm^{-1} (C=O); nmr (CCl$_4$–TMS) δ 2.90 (q, 2 H, *J* = 7 Hz), 1.37 (s, 3 H), 0.93 (d, 6 *H*, *J* = 7 Hz), 0.87 (s, 3 H); nmr (benzene, TMS) δ 2.68 (q, 2 H, *J* = 7 Hz), 1.12 (s, 3 H), 0.81 (d, 6 H, *J* = 7 Hz), 0.67 (s, 3 H); mass spectrum[17] (75 eV) *m*/*e* (relative intensity) 126 (M$^+$, 11), 111 (2), 98 (3), 83 (5), 70 (100), 56 (11), 55 (58), 42 (19), 41 (18)]. From vpc methods, **4c** and **5c** were found to be in over 80% yield based on **1**.

Equilibration of *cis*- and *trans*-2,2,3,4-Tetramethylcyclobutanone (4c) and (4t). A catalytic amount of sodium methoxide (0.3 mmole) was added to a MeOH (10 ml) solution of vpc pure **4c** (4 mmoles) and allowed to stir for 6 hr. Analysis by vpc (6 ft × 0.25 in., 20% $\beta\beta\beta$, Chrom P, 80°, 40 cc of He/min) detected two peaks in the ratio of 77.5/22.5, assigned structures **4t** and **4c**, respectively, based on their spectral properties: *trans*-2,2,3,4-tetramethylcyclobutanone[8a–c, 18] (**4t**) [ir $\nu_{max}^{CCl_4}$ 1778 cm^{-1} (C=O); nmr (CCl$_4$–TMS) δ 2.87 (d of q, 1 H, *J* = 7, 4 Hz), 1.36–1.91 (m, 1 H), 1.18 (d, 3 H, *J* = 7 Hz), 1.15 (d, 3 H, *J* = 7 Hz), 1.09 (s, 6 H); mass spectrum[17] (75 eV) *m*/*e* (relative intensity) 126 (M$^+$, 12), 111 (2), 98 (2), 83 (9), 70 (100), 56 (13), 55 (40), 42 (24), 41 (23)]. The equilibration was repeated using pure 4t. The same results were obtained.

Equilibration of *cis*- and *trans*-2,3,3,4-Tetramethylcyclobutanone (5c) and (5t). The same method was used as for the equilibration of **4c** and **4t**. From both vpc and nmr analysis *only* one compound was detected, **5c**.

***trans*-2,4-Dimethylcyclobutanone (17t), *cis*-2,4-Dimethylcyclobutanone (17c), *trans*-2,3-Dimethylcyclobutanone (18t), and *cis*-2,3-Dimethylcyclobutanone (18c).** A CH$_2$Cl$_2$ solution (25 ml) of diazoethane (22.5 mmoles) was added slowly with stirring to a CH$_2$Cl$_2$ solution (15 ml) of **14**[15] (10.5 mmoles) at −78°. The solution was allowed to stir for 30 min. The pale yellow solution was allowed to warm to room temperature at which time it was vacuum distilled (60°, 10 mm). The solution was analyzed by vpc (10 ft × 3/8 in., 20% $\beta\beta\beta$ with SE-30 scrubber, Chrom P, 50°, 60 cc of He/min). Four cyclobutanones, **17t**, **17c**, **18t** and **18c**, were formed in the ratio of 12:31:17:40 and were identified by their spectral properties: *trans*-2,4-dimethylcyclobutanone (**17t**)[8e, 18] [ir $\nu_{max}^{CCl_4}$ 1774 cm^{-1} (C=O); nmr (CCl$_4$–TMS) δ 3.17 (m of q, 2 H, *J* = 7 Hz), 1.78 (t, 2 H, *J* = 7.5 Hz), 1.19 (d, 6 H, *J* = 7 Hz) (**17t** appears to equilibrate with **17c** in the mass spectrometer)[8a, f, 17] *cis*-2,4-dimethylcyclobutanone (**17c**)[8e, 18] [ir $\nu_{max}^{CCl_4}$ 1774 cm^{-1} (C=O); nmr (CCl–TMS) δ 3.5–2.9 (m, 1 H), 3.11 (m of q, 2 H, *J* = 7.5 Hz), 2.52 max (m, 1 H), 1.11 (d, 6 H, *J* = 7 Hz); mass spectrum[17] (75 eV) *m*/*e* (relative intensity) 98 (M$^+$, 24), 70 (6), 56 (100), 55 (25), 42 (12), 41 (20), 39 (19)]; *trans*-2,3-dimethylcyclobutanone (**18t**)[8e, 18] ir $\nu_{max}^{CCl_4}$ 1778 cm^{-1} (C=O); nmr (CCl$_4$–TMS) δ 2.78 (m, 3 H), 1.97 (m, 1 H), 1.33 (d, 3 H, *J* = 7 Hz), 1.11 (d, 3 H, *J* = 7 Hz); mass spectrum[17] (75 eV) *m*/*e* (relative intensity) 98 (M$^+$, 22), 70 (6), 56 (100), 55 (22), 42 (11), 41 (44), 39 (20)]; *cis*-2,3-dimethylcyclobutanone (**18c**)[8e, 18] [ir $\nu_{max}^{CCl_4}$ 1780 cm^{-1} (C=O); nmr (CCl$_4$–TMS) δ 3.66–2.95 (m, 2 H, *J* = 7.5 Hz), 2.80–2.16 (m, 2 H), 1.10 (d, 3 H, *J* = 7.5 Hz), 1.02 (d, 3 H, *J* = 7.5 Hz); mass spectrum[17] (75 eV) *m*/*e* (relative intensity) 98 (M$^+$, 25), 70 (7), 56 (100), 55 (21), 42 (12), 41 (49), 39 (23)].

Equilibration of *cis*- and *trans*-2,4-Dimethylcyclobutanones (17c) and (17t). The same method was used as for the equilibration of **4c** and **4t**. Analysis by vpc (8 ft × 1/8 in., 20% $\beta\beta\beta$, Chrom P, 50°) detected two peaks in the ratio of 29.2:70.8, assigned structures **17t** and **17c**, respectively, by their vpc retention times and spectral properties. The same results were obtained from an nmr analysis.

Equilibration of *cis*- and *trans*-2,3-Dimethylcyclobutanones (18c) and (18t). The same method was used as for the equilibration of **17c** and **17t**. Vpc analysis detected two peaks in the ratio of 76.5:23.5, assigned **18t** and **18c**, respectively, by their vpc retention times and spectral properties. The same results were obtained from an nmr analysis.

Reaction of 2,2,3-Trimethylcyclobutanone (2) and 2,3,3-Trimethylcyclobutanone (3) with Diazomethane. To a 38:62 ratio of **2** and **3** (*ca.* 1 mmole) in 5 ml of CH$_2$Cl$_2$ was added a fivefold molar excess of a CH$_2$Cl$_2$ solution of diazomethane.[15] The solution was allowed to stir for 6 hr at room temperature. The resulting solution was concentrated and analyzed by vpc (6 ft × 0.25 in., 20% $\beta\beta\beta$, Chrom P, 95°, 65 cc of He/min). The only products found by vpc and nmr in a 38:62 ratio were **2** and **3** as determined by their spectral properties and vpc retention times.

Appendix

Correlation of the 1,3 interactions in the transition state for intermediates **19–26** to cyclobutanone product percentages were carried out as follows.

From Table II, Table V can be constructed by converting kilocalories to percentage relative to intermediates **19** and **22**. Since **20** and **23** lead to **17t**, and **21** and **26** leads to **18t**, the percentages are added for 23 and 20 and also for 21 and 26. After addition all the percentages are normalized (see Table VI).

Table V. Conversion of Interaction Energies to Percentages of Zwitterions

	Kcal	%
Bottom attack		
19	0	48
20	1.8	2
21	1.8	2
22	0	48
Top attack		
23	0.9	10
24	4.5	0
25	4.5	0
26	0.9	10

Table VI. Calcu'ation of Product Percentages for **18c**, **17t**, **18t**, and **17c**

	Cyclobutanone products, %			
	18c	**17t**	**18t**	**17c**
Per cent from bottom attack	48	2	2	48
Per cent from top attack	0	10	10	0
Total	48	12	12	48
Normalization	40	10	10	40

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