Table I. Metastable Peaks from $C_3H_7^+ \xrightarrow{m_1^*} C_3H_5^+ + H_2$ and $C_3H_7^+ \xrightarrow{m_2^*} C_2H_3^+ + CH_4$

	<10⁻⁶ torr[a]		5 × 10⁻⁶ torr[a]			1 × 10⁻⁵ torr[a]		
	KE of m_1^*, eV	$[m_1^*]/[C_3H_7^+]$ [f]	$\Delta[m_1^*]/[C_3H_7^+]$ [b,f]	$[m_2^*]/[C_3H_7^+]$ [f]	$\Delta[m_1^*]/[m_2^*]$	$\Delta[m_1^*]/[C_3H_7^+]$ [b,f]	$[m_2^*]/[C_3H_7^+]$ [f]	$\Delta[m_1^*]/[m_2^*]$
n-Hexane	0.20	1.60	0.98	0.67	1.46	1.88	1.24	1.52
2-Methylpentane	0.20	1.18	0.91	0.67	1.36	2.04	1.33	1.53
3-Methylpentane	0.21	1.10	*c*	0.64		1.91	1.29	1.48
2,2-Dimethylbutane	0.21	0.59	0.99	0.68	1.44	1.85	1.24	1.49
2,3-Dimethylbutane	0.20	1.09	*d*	0.64		*d*	1.25	
2-Bromopropane	0.21	1.61	*c*	0.67		1.85	1.27	1.46
1-Bromopropane	0.20	1.71	*c*	*c*		2.32[e]	1.50[e]	1.54

[a] Approximate pressure in drift region. [b] Abundance in excess of that at $<10^{-6}$ torr. [c] Data not determined. [d] Interference from $C_3H_6^+ \rightarrow C_3H_5^+$ metastable. [e] Pressure in drift region approximately 1.3×10^{-5} torr. [f] Per cent.

teristics of Table I confirm this and illustrate the use of collision-induced metastables.

Table I reports the kinetic energy released in the metastable transition, $C_3H_7^+ \rightarrow C_3H_5^+ + H_2$ (m_1^*), plus the collision-induced metastables of $C_3H_7^+$ measured on a Bendix Model 12 time-of-flight mass spectrometer specially modified for the observation of metastable ions.[5-7] Raising the pressure in the drift tube of the spectrometer with air increases the abundance of m_1^* and causes an abundant new metastable to appear, corresponding to $C_3H_7^+ \rightarrow C_2H_3^+ + CH_4$ (m_2^*). The neutral fragment formed by the pressure-dependent reaction $N_2\cdot^+ \rightarrow N_2$ is used as an internal indicator of the drift tube pressure. Note that at a particular pressure *the values of* $[m_2^*]/[C_3H_7^+]$ *are equal within experimental error* for all of the molecules studied, despite the fact that the abundances of the metastable ions from the unimolecular decomposition $C_3H_7^+ \rightarrow C_3H_5^+$ are not constant. In addition, the fractions of the latter metastable ions which are caused by collision-induced fragmentation are also constant within experimental error, and the abundance ratio of the two collision-induced metastables produced at different pressures is also constant. Thus the abundance of the collision-induced metastable ion products appears to be *independent* of the original energy distribution of the precursor ions, indicating that most collisions impart considerably more energy to the $C_3H_7^+$ ions than the activation energy for the decompositions. The reaction producing m_2^* should require a higher activation energy than m_1^*, yet $\Delta[m_1^*]/[m_2^*]$ appears to be independent of the internal energy of the precursor $C_3H_7^+$ ions. Also $[m_2^*]/[C_3H_7^+]$ is independent of ionizing electron energy between 20 and 70 eV, consistent with previous observations showing that a collision-induced metastable exhibits the same ionization efficiency curve as its precursor ion.[8]

The usefulness of this tool for ion structure determination would be lowered if the collision process greatly increased the chance for isomerization of the ion.[9] We plan studies to check this; however, it is encouraging to note that the shape and width of the flat-topped metastable m_1^* appears to be identical for both the unimolecular and collision-induced processes, indicating comparable transition states for these processes. Also, in preliminary measurements collision-induced metastables, corresponding to $C_3H_6O\cdot^+ \rightarrow C_2H_3O^+ + CH_3$ in the spectra of acetone, 2-pentanone, and 4-heptanone, are produced in differing relative abundances, as would be expected from the different structures indicated for their respective $C_3H_6O\cdot^+$ ions.[10]

Thus, the abundance of a single collision-induced metastable should serve to characterize the structure of an ion. It may be possible that an even higher sensitivity for such metastables can be gained by utilizing the drift region between the ion source and electric sector of a double-focusing mass spectrometer[11] as the collision chamber, hopefully making this an ion structure tool of broad applicability.[12]

(3) This could not be confirmed [F. W. McLafferty and T. A. Bryce, *Chem. Commun.*, 1215 (1967)] by measurement of the abundances of the metastables, as only the transition $C_3H_7^+ \rightarrow C_3H_5^+$ was found;[4] although different relative abundances were observed for different sources of $C_3H_7^+$, this could be due to the formation of the same $C_3H_7^+$ isomer structure with different energy distributions.

(4) C. Ottinger, *J. Chem. Phys.*, 47, 1452 (1967), reports the very weak transition $C_3H_7^+ \rightarrow C_3H_6^+ + H$.

(5) F. W. McLafferty, R. S. Gohlke, and R. C. Golesworthy, Annual Meeting on Mass Spectrometry, ASTM E-14, Montreal, June 1964, p 331; R. E. Ferguson, K. E. McCulloh, and H. M. Rosenstock, *J. Chem. Phys.*, 42, 100 (1965); W. W. Hunt, Jr., R. E. Huffman, J. Saari, G. Wassel, J. F. Betts, E. H. Paufve, W. Wyess, and R. A. Fluegge, *Rev. Sci. Inst.*, **35**, 88 (1964).

(6) This instrument, which will be described in a separate publication, was especially modified to defocus ions of masses higher than the precursor.

(7) Measurements on a magnetic sector instrument (Hitachi RMU-6D) of the kinetic energy released in this *m/e* 39.09 metastable peak agree well with these data, despite interference of the $C_3H_3^+$ peak.

(8) K. R. Jennings, Annual Meeting on Mass Spectrometry, ASTM E-14, Denver, Colo., June 1967, p 73.

(9) Even the activation energy for ordinary metastable ion decompositions can be sufficient to cause isomerization of the precursor ion structure (*e.g.*, $C_2H_5O^+$ ions from several types of molecules[1]). However, higher energies generally discriminate *against* reactions with low "frequency factors," such as rearrangements.

(10) W. T. Pike and F. W. McLafferty, *J. Am. Chem. Soc.*, **89**, 5953 (1967).

(11) M. Barber and R. M. Elliott, Conference on Mass Spectrometry, ASTM E-14, Montreal, June 1964, p 30; T. W. Shannon, T. E. Mead, C. G. Warner, and F. W. McLafferty, *Anal. Chem.*, **39**, 1748 (1967).

(12) The generous support of National Institutes of Health Grants GM 12755 and FR 00354 is gratefully acknowledged.

(13) To whom inquiries should be addressed at Department of Chemistry, Cornell University, Ithaca, N. Y. 14850.

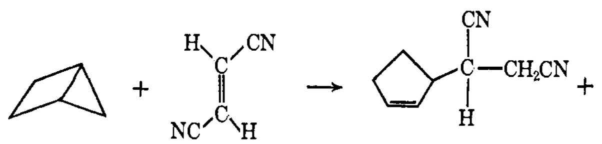
W. F. Haddon, F. W. McLafferty[13]
Department of Chemistry, Purdue University
Lafayette, Indiana 47907
Received May 13, 1968

The Mechanism and Stereochemistry of the Addition of Olefins to Bicyclo[2.1.0]pentane

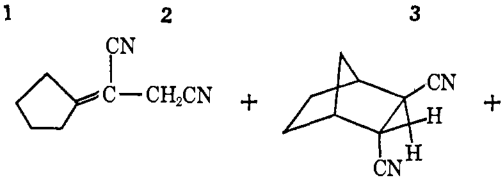
Sir:

The cycloaddition of carbon–carbon multiple bonds to highly strained carbon–carbon single bonds is one of the more remarkable reactions to appear in the recent chemical literature. Although numerous examples of this class of reactions have been noted,[1] it is only now that detailed studies of the mechanism of these cycloadditions have begun to appear.[2] It has been proposed, on the basis of kinetic and product studies in the reaction of dicarbomethoxyacetylene with bicyclo[2.1.0]pentane, that this cycloaddition occurs *via* the formation of a diradical intermediate.[2] In order to obtain definitive evidence concerning the mechanism of the addition of carbon–carbon multiple bonds to strained cyclopropanes we have investigated the stereochemical aspects of the reaction of olefins with bicyclo[2.1.0]pentane. This communication summarizes the results of these studies.

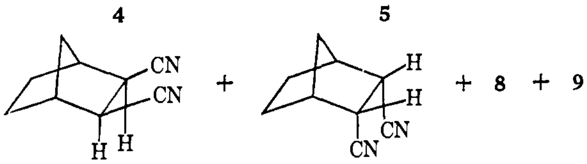
When bicyclo[2.1.0]pentane (**1**) was treated with fumaronitrile (**2**) in tetrahydrofuran for 2 days at 160° a mixture of seven products was obtained. Five of these products, **3** through **7**, were identified by comparison with authentic samples.[3,4] The "ene" type products **3** and **4** constituted 80.0 and 6.2%[3] of the



1 **2** **3**



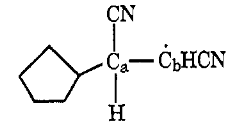
4 **5**



6 **7**

product mixture, respectively. The "cycloaddition" products, **5**, **6**, and **7**, were identified as *exo,endo*-2,3-dicyanobicyclo[2.2.1]heptane (6.7%),[3] *exo,exo*-2,3-dicyanobicyclo[2.2.1]heptane (0.3%), and *endo,endo*-2,3-dicyanobicyclo[2.2.1]heptane (0.4%), respectively. Under the same reaction conditions **1** reacted with maleonitrile (**10**) to give the same seven products with the following relative amounts of the identified components: **3**, 88.7%; **4**, 2.2%; **5**, 1.2%; **6**, 2.1%; **7**, 3.0%.

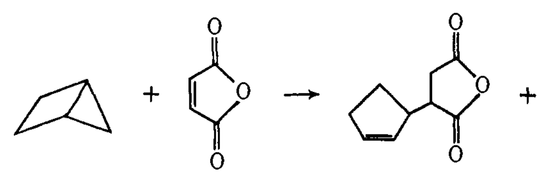
Since mixtures of **5**, **6**, and **7** were obtained in the reactions of **1** with **2** and **10**, the reaction must have proceeded *via* a mechanism which allowed rotation about the central bond of maleonitrile and fumaronitrile. Since maleonitrile, fumaronitrile, and the reaction products were stable under the reaction conditions, an intermediate must have been generated in which this rotation was permitted. This requires a two-step mechanism which rules out any concerted cycloaddition.[5] Previous studies[2] conclusively eliminated the possibility of a zwitterionic mechanism. Hence, the reaction must involve the formation of the diradical **11**.



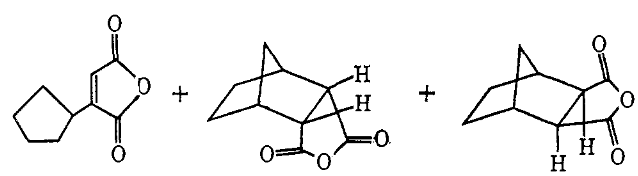
11

As Bartlett has shown,[6] intramolecular radical recombination is competitive with rotation about a carbon–carbon single bond. In our case this would involve rotation about the bond between C_a and C_b. The different product ratios observed in the reactions of **1** with **2** and **10** were consistent with expectations. Starting with fumaronitrile we noted *ca.* 10% rotation about the C_a–C_b bond, while with the *cis* starting material (maleonitrile), we found *ca.* 20% rotation about the same bond. These results would appear to provide definitive evidence for the formation of a diradical intermediate in the reaction of carbon–carbon multiple bonds with bicyclo[2.1.0]pentane.

The only stereochemical question which remained unanswered was whether the olefin approached the bicyclo[2.1.0]pentane envelope from the top or the bottom of the "flap." We used the reaction of **1** with maleic anhydride (**12**) to answer this question. When **12** was heated to 120° for 2 days with **1**, a mixture of **13**, **14**, **15**, and **16** was obtained. The yields of these products were 68.0, 17.4, 4.5, and 0.5%, respectively. In order to determine the stereochemical approach of the olefin,



1 **12** **13**



14 **15** **16**

the addition of maleic anhydride was carried out on stereospecifically labeled 2,3-dideuteriobicyclo[2.1.0]pentane (**17**) prepared *via* dideuteriodiimide reduction of bicyclo[2.1.0]pentene (**18**).[7] The deuteriums in **17** were exclusively in the *exo* position within the limits of

(1) P. G. Gassman and K. T. Mansfield, *Chem. Commun.*, 391 (1965); A. Cairncross and E. P. Blanchard Jr., *J. Am. Chem. Soc.*, **88**, 496 (1966); C. D. Smith, *ibid.*, **88**, 4273 (1966); M. Pomerantz, *ibid.*, **88**, 5349 (1966); H. J. Reich and D. J. Cram, *ibid.*, **89**, 3078 (1967); M. R. Rifi, *ibid.*, **89**, 4442 (1967); P. G. Gassman and K. T. Mansfield, *ibid.*, **90**, 1517 (1968).

(2) P. G. Gassman and K. T. Mansfield, *ibid.*, **90**, 1524 (1968).

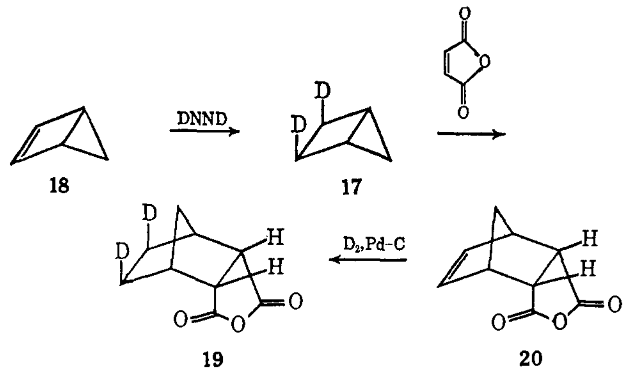
(3) The over-all yields in the reaction of **1** with **2** and **10** were 85 and 74%, respectively. The per cents quoted for the individual components are per cents of the product mixture. These values were obtained by vpc, utilizing an internal standard which had been calibrated *vs.* authentic samples. Compounds **3** through **7** were isolated *via* preparative vpc and were shown to be spectroscopically identical with authentic samples.

(4) The two remaining components, **8** and **9**, which constituted about 6% of the reaction product, were not identified.

(5) A concerted reaction is also forbidden according to molecular orbital symmetry considerations. See R. Hoffmann and R. B. Woodward, *J. Am. Chem. Soc.*, 87, 2046 (1965).

(6) P. D. Bartlett, L. K. Montgomery, and B. Siedel, *ibid.*, **86**, 616 (1964); L. K. Montgomery, K. Schueller, and P. D. Bartlett, *ibid.*, **86**, 622 (1964); P. D. Bartlett and L. K. Montgomery, *ibid.*, **86**, 628 (1964); P. D. Bartlett, *Nucleus* (Cambridge, Mass.), 251 (1966); P. D. Bartlett, *Science*, **159**, 833 (1968).

(7) J. I. Brauman, L. E. Ellis, and E. E. van Tamelen, *J. Am. Chem. Soc.*, **88**, 846 (1966). We wish to thank Professor Brauman for providing us with the experimental details of the photochemical conversion of cyclopentadiene to **18** and of the diprotiodiimide reduction of **18** prior to publication.



analysis by nmr.[8] The reaction of **17** with **12** was run under the same conditions as the reaction of **1** with **12**, and the *endo*-anhydride, **19**, was isolated. Within the limits of detection by nmr all of the deuterium in **19** was in the *exo* position. In order to confirm this assignment the Diels–Alder adduct of cyclopentadiene and maleic anhydride, **20**, was reduced with deuterium over palladium on carbon to yield a sample of **19** which was identical with the *endo*-anhydride obtained from **17** in all respects. In order for the deuteriums in **19** to be in the *exo* position, *the addition to bicyclo[2.1.0]pentane must have occurred from below the "flap" of the bicyclo[2.1.0]pentane envelope.*[9]

It would appear that the initial attack by an electron-deficient carbon–carbon multiple bond on the bicyclo[2.1.0]pentane system involves a "back-side" attack on the "bent" C_1–C_4 bond. This attack would involve an initial overlap of the electron-deficient orbitals of the carbon–carbon multiple bond with the "back orbital" of the C_1–C_4 bond, leading to homolytic cleavage with the relief of most of the strain energy of the bicyclo[2.1.0]pentane molecule. Studies designed to further elucidate the nature of the transition state preceding diradical formation are in progress.

Acknowledgments. We are indebted to the National Science Foundation for Grant GP 7063 and to The Ohio State University Development Fund for a grant-in-aid which supported this research.

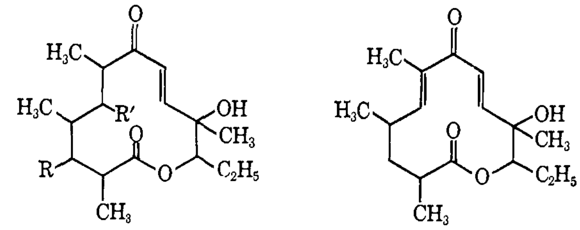
(8) P. G. Gassman and K. T. Mansfield, *J. Org. Chem.*, **32**, 915 (1967); W. R. Roth and M. Martin, *Ann. Chem.*, **702**, 1 (1967).
(9) For an example of another reaction of a substituted bicyclo[2.1.0]-pentane which was reported to occur from below the "flap" see W. R. Roth and M. Martin, *Tetrahedron Letters*, 4695 (1967).
(10) Alfred P. Sloan Research Fellow, 1967–1969.
(11) The Ohio State University Fellow, 1962–1963.
(12) National Institutes of Health Postdoctoral Fellow, 1967–1968.

Paul G. Gassman,[10] Kevin T. Mansfield,[11] Thomas J. Murphy[12]
Department of Chemistry, The Ohio State University
Columbus, Ohio 43210
Received May 17, 1968

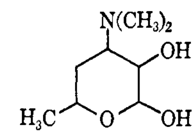
The Structure of Pikromycin

Sir:

Pikromycin was the first macrolide antibiotic[1] isolated.[2] It has long been considered to be an isomer of methymycin (**1**), which was the first macrolide of fully elucidated structure.[3] In order to account for the considerable difference in the chemical behavior of pikromycin and methymycin (**1**), structure **2** has been proposed for pikromycin[4,5] and structure **3** for its anhydro aglycone, kromycin.[4,5] Kromycin and desosamine (pikrocin) (**4**)[6] are formed upon treatment of pikromycin in water at pH 6.5.

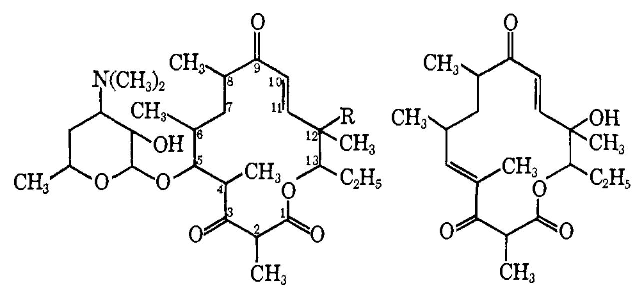


1, R = desosamine residue; R′ = H
2, R′ = desosamine residue; R = H
3



4

We now wish to report evidence that pikromycin has structure **5** and that kromycin has structure **6**. Pikromycin therefore appears to be a hydroxylated narbomycin (**7**).[7]



5; R = OH
7; R = H
6

The molecular ion of pikromycin has been found at *m/e* 525 (525.3298; calcd for $C_{28}H_{47}NO_8$: 525.3302).[8] Therefore the unit C_3H_4O has to be added to the formerly accepted structure **2**.[4,5] Since kromycin has a molecular ion at *m/e* 350 (350.2093; calcd for $C_{20}H_{30}O_5$: 350.2093.), this unit has also to be added to the old structure **3** for kromycin[4,5,8] and must therefore be part of the macrocyclic ring.

It becomes evident from the nmr spectrum[9] that the C_3H_4O unit must be added to the macrocyclic ring of kromycin as shown in structure **6**. This spectrum shows a quartet with a coupling constant consistent with a proton at a carbon atom substituted by two carbonyl groups and a methyl group (1 H, δ 4.30, q, J = 6 Hz).[10]

(1) The name macrolide antibiotic was introduced by R. B. Woodward, *Angew. Chem.*, **69**, 50 (1957).
(2) H. Brockmann and W. Henkel, *Naturwissenschaften*, **37**, 138 (1950); *Chem. Ber.*, **84**, 284 (1951).
(3) C. Djerassi, and J. A. Zderic, *J. Amer. Chem. Soc.*, **78**, 2907, 6390 (1956).
(4) H. Brockmann and R. Oster, *Chem. Ber.*, **90**, 605 (1957).
(5) A. Anliker and K. Gubler, *Helv. Chim. Acta*, **40**, 1768 (1957), and preceding paper.
(6) H. Brockmann, H. B. König, and R. Oster, *Chem. Ber.*, **87**, 856 (1954); E. H. Flynn, M. V. Sigal, Jr., P. F. Wiley, and K. Gerzon, *J. Amer. Chem. Soc.*, **76**, 3121 (1954); R. K. Clark, Jr., *Antibiot. Chemotherapy*, **3**, 663 (1953).
(7) V. Prelog, A. M. Gold, G. Talbot, and A. Zamojski, *Helv. Chim. Acta*, **45**, 4 (1962).
(8) Mass spectra were taken with an MS-9 mass spectrometer. The analytical data[4,5] reported earlier are in excellent agreement with this composition.
(9) Unless otherwise stated the nmr spectra were measured in $CDCl_3$.
(10) In this region the nmr spectrum for pikromycin is not as clean as it is for kromycin because of the absorption of the desosamine moiety.