Intramolecular Keten Cycloadditions in Unconstrained Systems

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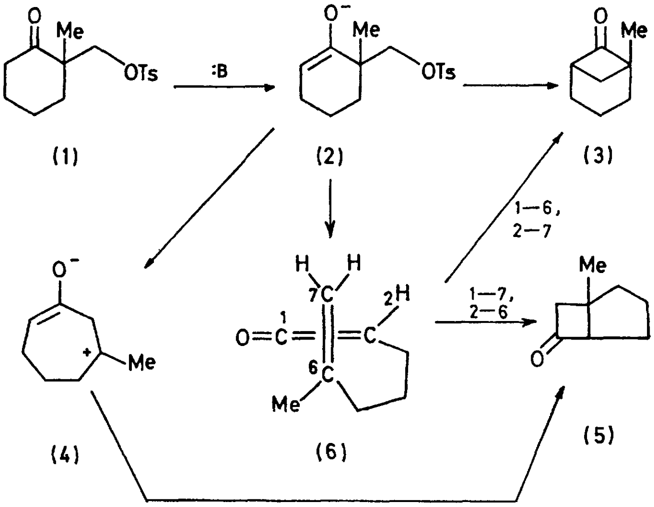
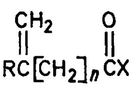
Summary The feasibility of intramolecular keten cycloadditions in acyclic systems is demonstrated; these results implicate keten intermediates in the formation of the cyclobutanone (**5**) from the cyclohexanone (**1**).

IN 1963 Wiberg and Kline[1] reported the formation of cyclobutanones (**3**) and (**5**) from base treatment of the cyclohexanone (**1**). Compound (**3**) was shown to be the product of an intramolecular alkylation reaction. Compound (**5**) was thought to arise through the ring-expanded zwitterion (**4**), which in turn was produced by migration of the oxyvinyl group of enolate (**2**).[2] There are similar possibilities for the formation of (**5**), involving varying degrees of oxygen participation in related intermediates.

While considering other mechanisms for this reaction we realised that an entirely different pathway, an intramolecular 2 + 2 olefin–keten cycloaddition, could account for the results. Keten (**6**), which might be formed by elimination of the toluene-*p*-sulphonate anion from enolate (**2**), is of interest since it is a potential precursor of both cyclobutanones (**3**) and (**5**). Assuming the accepted perpendicular geometry of the reacting π systems,[3] bond formation between carbons 1,6 and 2,7 would lead to cyclobutanone (**3**) while the alternate bonding between carbons 1,7 and 2,6 would afford cyclobutanone (**5**).

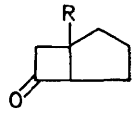
There are examples reported of intramolecular keten cycloadditions.[4] In general, however, these reactions have been observed only where conformational mobility between the addends is minimized by the incorporation of one or more rings. This is particularly true in those cases involving aldoketens (ketens substituted with one carbon-containing group and one hydrogen). The chemistry of aldoketens is characterized by dimerization and trimerization reactions. That these processes are actually catalysed by the tertiary amines required to generate the ketens from the corresponding acid chlorides still further reduces their effectiveness in cycloadditions.[5] Intermolecular cycloadducts of aldoketens and unactivated olefins are rarely observed because of the high propensity of the ketens for oligomerization.[6]





$$\overset{CH_2}{\overset{\|}{R C}}[CH_2]_n\overset{O}{\overset{\|}{C X}}$$

(**7**) R = Me, X = OH, n = 4
(**8**) R = Me, X = Cl, n = 4
(**9**) R = Ph, X = OH, n = 4
(**10**) R = Ph, X = Cl, n = 4
(**12**) R = Me, X = CHN_2, n = 3



(**5**) R = Me
(**11**) R = Ph

When a 0·2% methylene chloride solution of (**8**) was treated at room temperature with 1·1 equiv. of triethylamine and stirred for 10 h, a 65% yield of distilled cyclobutanone (**5**) was obtained. No isomeric cyclobutanone (**3**) was detected. The identity of (**5**) was established by comparison of published spectral data[1] and by independent synthesis.[7] Similar treatment of the acid chloride (**10**) of

(**9**)† resulted in a 58% yield of a single homogeneous cyclobutanone which was shown to have structure (**11**)† from spectral data and independent synthesis.[7] Thus the cyclobutanone formed in each cycloaddition reaction, (**8**) → (**5**) and (**10**) → (**11**), was the product of a highly regiospecific process. That none of the alternative cyclobutanone was observed in either instance is curious unless one assumes some degree of ionic or radical character in the transition state.

The formation of cyclobutanones (**5**) and (**11**) from the respective acid chlorides must reasonably proceed through keten intermediates as indicated. Additional confirmation was obtained when a 0·5% pentane solution of diazoketone (**12**) was exposed to u.v. (Pyrex). After the evolution of nitrogen had ceased (0·5 h), a low yield of cyclobutanone (**5**) was obtained as well as several other as yet unidentified products. The production of (**5**) by two routes which must rationally afford the same keten intermediate (**6**) is strong evidence for the suggested pathway. Attempts to observe the keten by low temperature spectroscopy have as yet been unsuccessful.

In the preceding discussion no attempt was made to determine whether the formation of (**5**) from (**1**) as described by Wiberg and Klein[1] had proceeded through keten (**6**). Instead, we concentrated on showing that such a process can occur.

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† All new compounds gave satisfactory elemental analyses and spectroscopic data.

[1] K. Wiberg and G. W. Kline, *Tetrahedron Letters*, 1963, 1043.

[2] It has also been shown that base treatment of 2-bromomethyl-2-methylcyclopentanone gives rise to (**7**) as well as cyclobutanones (**3**) and (**5**). The formation of (**7**) is consistent with, but not unique to, the intermediacy of keten (**6**); S. Julia and C. Gueremy, *Bull. Soc. chim. France*, 1965, 2994.

[3] R. B. Woodward and R. Hoffmann, *Angew. Chem. Internat. Edn.*, 1969, **8**, 781.

[4] D. Becker, M. Nagler, and P. Birnbaum, *J. Amer. Chem. Soc.*, 1972, **94**, 4771; R. R. Sauers and K. W. Kelley, *J. Org. Chem.*, 1970, **35**, 3286; P. Yates and A. G. Fallis, *Tetrahedron Letters*, 1968, 2493; O. L. Chapman, M. Kane, J. D. Lassila, R. L. Loeschen, and H. E. Wright, *J. Amer. Chem. Soc.*, 1969, **91**, 6856; H. Hart and G. M. Love, *ibid.*, 1971, **93**, 6266; Ch. Jutz, I. Rommel, I. Lengyel, and J. Feeney, *Tetrahedron*, 1966, **22**, 1809; S. Masamune and K. Fukumoto, *Tetrahedron Letters*, 1965, 4647.

[5] D. G. Farnum, J. R. Johnson, R. E. Hess, T. B. Marshall, and B. Webster, *J. Org. Chem.*, 1965, **30**, 5191.

[6] H. Ulrich, 'Cycloaddition Reactions and Heterocumulenes,' Academic Press, New York, 1967; R. N. Lacey, 'Ketenes,' in 'The Chemistry of Alkenes,' ed. S. Patai, Interscience, London, 1964.

[7] P. W. Jeffs and G. Molina, *J.C.S. Chem. Comm.*, submitted for publication. We thank Professor Jeffs for disclosing the details of an independent cyclobutanone synthesis prior to publication.