

Iodocyclization of Alkene Thioethers. Kinetic Evidence against an Iodonium Ion Intermediate

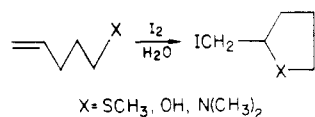
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The kinetics and mechanism of the facile iodocyclization of two alkene thioethers (4-pentenyl methyl sulfide and 5-methylene-1-thiacyclooctane) are presented. Both compounds exhibit the same rate law, $d[I_3^-]/dt = -k_2[\text{alkene thioether}][I_3^-][I^-]^{-1}$. Because of the inverse first-order dependence on the iodide concentration, the mechanism of the reaction is consistent with an intermediate π -complex between the iodine molecule and the alkene rather than an iodonium ion.

The iodination of simple alkenes in aqueous solution has not been observed, but in the presence of neighboring nucleophiles, an iodocyclization reaction takes place.¹ Although this is a synthetically valuable reaction, a detailed analysis of the mechanism of the iodocyclization reaction is not available. An often cited^{2,3} report by Rengevich et al. in 1962¹ listed some second-order rate constants and activation parameters for the iodocyclization of a series of acyclic molecules in water. These molecules contained different functional groups (alcohol, amide, amine, carboxylic acid, thioether) attached to the ω position of a terminal alkene such that a five-membered ring would form by iodocyclization. The rate laws were first order in alkene and first order in I_2 . Of most interest to us was the series of 4-pentenyl derivatives which cyclized as follows:



The rate constants, k_2 (20 °C) M⁻¹ s⁻¹, for X = SCH₃, OH, and N(CH₃)₂ were 3×10^{-3} :1.5:2.8 $\times 10^5$. The value of the rate constant reported for the thioether derivative was low relative to the less nucleophilic hydroxyl group. In fact when we used our best estimate of the conditions employed by Rengevich et al.¹ the reported reaction rate was so slow that oxidation of the thioether to the sulfoxide should have occurred.⁴

Based on the apparent slowness of the iodocyclization of the alkene thioether, Rengevich et al.¹ pointed out that the differences in the rate of iodocyclization reactions "correspond to 8 orders with a change from thioether to amine" and Capon² concluded that "factors other than nucleophilicity are important here".

We have been investigating the effect of neighboring nucleophiles on the rate of thioether oxidation with aqueous iodine and were interested in studying the reaction of a thioether in the vicinity of a neighboring alkene. For this purpose we prepared 5-methylene-1-thiacyclooctane in order to optimize the interaction between thioether and alkene groups and, since there were no primary data available to confirm the results of Rengevich et al.,¹ we reinvestigated the reaction of 4-pentenyl methyl sulfide.

(1) Rengevich, E. N.; Staninets, V. I.; Shilov, E. A. *Dokl. Akad. Nauk. SSSR* 1962, 146, 111; *Dokl. Akad. Nauk. SSSR (Engl. Transl.)* 1962, 146, 787.

(2) Capon, B.; McManus, S. P. "Neighboring Group Participation"; Plenum Press: New York, 1976; p 211.

(3) Kline, M. L.; Beutow, N.; Kim, J. K.; Caserio, M. C. *J. Org. Chem.* 1979, 44, 1904.

(4) Hirschon, A. S.; Doi, J. T.; Musker, W. K. *J. Am. Chem. Soc.* 1982, 104, 725.

Table I. Kinetic Data for the Iodocyclization of 4-Pentenyl Methyl Sulfide in Acetate Buffer^a

run	10 ³ [RSR]	[KI], M	[acetate buffer], M	pH	10 ³ k, s ⁻¹ b	k ₂ , M ⁻¹ s ⁻¹
1	1.00	0.0500	0.500	4.0	50 ± 3	50
2	0.75	0.0500	0.500	4.0	32 ± 2	43
3	0.50	0.0500	0.500	4.0	19.3 ± 0.1	38
4	0.25	0.0500	0.500	4.0	8.1 ± 0.4	32
5	1.00	0.400	0.500	4.0	7.0 ± 0.5	7
6	1.00	0.200	0.500	4.0	15.3 ± 0.2	15
7	1.00	0.100	0.500	4.0	29.8 ± 0.4	30
8	1.00	0.0250	0.500	4.0	94 ± 6	94
9	1.00	0.0125	0.500	4.0	149 ± 4	149
10	1.00	0.0500	0.500	6.0	46 ± 1.6	46
11	1.00	0.0500	0.500	5.0	47 ± 1	47
12	1.00	0.0500	0.0125	6.0	48 ± 2	48
13	1.00	0.0500	0.113	6.0	48.6 ± 0.3	49

^a Constant ionic strength was maintained by the addition of KCl, such that [KI] + [KCl] = 1.000 M at 26.0 °C. ^b Error determined from replicate runs. Correlation coefficients ≥ 0.992 .

Results

Kinetics. The reaction were followed in the usual way by monitoring at 353 nm the decay of $[I_3^-]$ in aqueous solution containing an excess of alkene.⁵ The pseudo-first-order rate constant can then be determined from the following equation. $k_{\text{obsd}} = k_2[\text{alkene thioether}]$. Because

$$\frac{d[\text{alkene thioether}]}{dt} = \frac{d[I_3^-]}{dt} = -k_{\text{obsd}}[I_3^-]$$

the triiodide preequilibrium step involves iodide ion and subsequent steps in the mechanism may involve further dissociation of iodide ion from substrate-iodine complexes, the dependence of the rate on the $[I^-]$ is important to determine. The iodide dependence, which can vary from 0 to -3, is related to the number of iodine atoms remaining attached to the substrate-iodine complex in the rate-determining step. Therefore, the effect of varying both substrate and iodide ion concentration on the rate *must* be determined in order to propose an acceptable mechanism.

The kinetic data for the iodocyclization of 4-pentenyl methyl sulfide are given in Table I. The rate law is approximately first order in thioether concentration. The apparent order is 1.3 with a correlation coefficient of 0.999, calculated from runs 1-4 of Table I. The rate is approximately inversely proportional to the iodide concentration. The apparent order is -0.9 with a correlation coefficient of 0.997 (see runs 1, 5, 6, 7, 8, and 9, of Table I). The pseudo-second-order rate constant k_2 was calculated by dividing the pseudo-first-order rate constant k_{obsd} by the

(5) Doi, J. T.; Musker, W. K. *J. Am. Chem. Soc.* 1981, 103, 1159.

Table II. Kinetic Data for the Iodocyclization of 5-Methylene-1-thiacyclooctane by Aqueous Iodine in Acetate Buffer^a

run	10 ⁴ [RSR]	[acetate buffer], M	pH	<i>k</i> , s ⁻¹ ^b	10 ⁻⁵ <i>k</i> ₂ , M ⁻¹ s ⁻¹
1	2.5	0.200	6.0	77 ± 8	3.1
2	5.0	0.100	6.0	315 ± 19	6.3
3	3.75	0.100	6.0	230 ± 11	6.1
4	2.5	0.100	6.0	143 ± 13	5.7
5	2.5	0.0500	6.0	252 ± 14	10
6	2.5	0.200	6.0	65 ± 7	2.6
7	2.5	0.100	5.0	73 ± 7	2.9
8	2.5	0.100	4.0	73 ± 7	2.9

^a Constant ionic strength was maintained by the addition of KCl, such that [KI] + [KCl] = 1.000 M at 26.0 °C. ^b Error determined from measurement of curves obtained from oscilloscope traces. Correlation coefficient of ≥ 0.994.

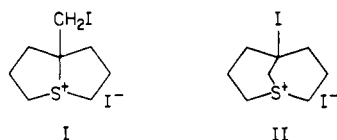
thioether concentration. The reaction was pH and buffer independent; see runs 1, 10, 11, and 10, 12, 13, respectively.

The kinetic data for the iodocyclization of 5-methylene-1-thiacyclooctane were obtained by use of a stopped-flow spectrophotometer. The rate law for 5-methylene-1-thiacyclooctane is approximately first order in thioether concentration. Runs 2, 3, and 4 of Table II give an apparent order of 0.9, with a correlation coefficient of 0.996. The iodocyclization rate is approximately inverse first order in iodide concentration. The apparent order calculated from runs 1, 4, and 5 of Table II is -1.2 with a correlation coefficient of 0.999. The pseudo-second-order rate constant *k*₂ given in the table was obtained by dividing the pseudo-first-order rate constant *k*_{obsd} by the thioether concentration. There is no buffer and very little pH dependence; see runs 1, 6 and 4, 7, 8, respectively, of Table II. Thus, the rate law for the iodocyclization of both 5-methylene-1-thiacyclooctane and 4-pentenyl methyl sulfide is given below.

$$\frac{d[\text{alkene thioether}]}{dt} = -k_2[\text{alkene thioether}][\text{I}_3^-][\text{I}^-]^{-1} \quad (1)$$

$$= -k_2'[\text{alkene thioether}][\text{I}_2] \quad (2)$$

Products. The product of the iodocyclization of 4-pentenyl methyl sulfide was previously determined to be 2-(iodomethyl)tetrahydrothiophene.¹ We anticipated that the product resulting from the iodocyclization of 5-methylene-1-thiacyclooctane should be either 5-(iodomethyl)-1-thioniabicyclo[3.3.0]octane iodide (I) or the isomeric, 5-iodo-1-thioniabicyclo[3.3.1]nonane iodide (II). Spectral evidence and chemical analysis did not distinguish between the two. However, a single-crystal X-ray structure of the iodide salt confirmed the bicyclooctane structure (I).⁶ No unusual bond lengths or bond angles were noted in the structure. The iodide counterion is located far from the cationic sulfur and no interaction is apparent. There was no evidence of sulfoxide formation.



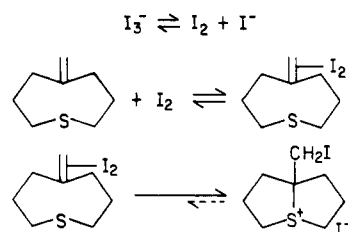
Discussion

The value of the the second-order rate constant, *k*₂, for the iodocyclization of 4-pentenyl methyl sulfide is 46 M⁻¹

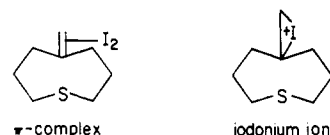
s⁻¹ in 0.05 M KI in acetate buffer at pH 6. The value of *k*₂ given by Rengevich¹ is 3 × 10⁻³ M⁻¹ s⁻¹, but, since only the range of [I⁻] (0.1–0.05 M) was reported, a direct comparison cannot be made. Nevertheless, it appears that the iodocyclization of 4-pentenyl methyl sulfide proceeds at a rate which is at least 10⁴ times faster than that reported previously. Thus it would appear that cyclization of the 4-pentenyl derivatives occurs N(CH₃)₂ > SCH₃ > OH which is more in line with the nucleophilicity of the respective substituents.

A comparison of the rate of iodocyclization of 5-methylene-1-thiacyclooctane and 4-pentenyl methyl sulfide with the rate of iodine oxidation of a simple thioether (thiacyclooctane) is 8 × 10⁶:4 × 10³:1, respectively, at pH 8.0 and an iodide concentration of 0.05 M. Thus, iodocyclization to form five-membered ring systems is an extremely facile process relative to a simple thioether oxidation.

A mechanism for the iodocyclization of both 5-methylene-1-thiacyclooctane and 4-pentenyl methyl sulfide which is consistent with both the rate law and the products obtained is given below. Since both compounds exhibit the same rate law, the mechanism is written with 5-methylene-1-thiacyclooctane.



After a preequilibrium between triiodide, iodine, and iodide has been established, an iodine molecule forms a π-complex with the alkene. The proximate thioether sulfur atom then interacts with the π-complex in the rate-determining step to give 5-(iodomethyl)-1-thioniabicyclo[3.3.0]octane (I).



If the initial attack of the iodine were on sulfur, the electrophilic thioether-iodine complex would have added to the alkene to give the more stable tertiary carbocation and the product would have had the bicyclo[2.2.1]nonane structure (II).

Since the [I⁻] dependence of the rate was shown to be inverse first order, an alternative mechanism of the iodocyclization reaction that involves an iodonium ion⁷ is inconsistent with the rate law and can be eliminated. In order for an iodonium salt to be included in the mechanism, an additional iodide ion would have to dissociate from the π-complex prior to the rate-determining step. Should this event occur, the rate law (eq 1) would contain an inverse-squared dependence on [I⁻]. Although kinetic analysis cannot distinguish between a π-complex and an ion pair in which the iodide ion is not solvated, we feel that an ion pair should not be included since there is no need to postulate its existence in the addition reaction. Since a free iodonium ion does not form in a polar solvent (water) where anion solvation is favorable, its existence in addition

(6) Olmstead, M. M., unpublished results.

(7) Kwart, H.; Drayer, D. *J. Org. Chem.* 1974, 39, 2157.

reactions in less polar solvents is even less likely.

Experimental Section

Materials. 5-Thiacyclooctanone was synthesized according to the literature.⁸ 5-Bromo-1-pentene was purchased from Aldrich Chemical Co.

5-Methylene-1-thiacyclooctane. The procedure followed was an adaptation of the method developed by Greenwald.⁹ Sodium hydride (4.2 mmol, 0.1 g as a 50% oil dispersion) was placed in a 300-mL three-necked round-bottom flask and washed with three 5-mL portions of pentane to remove the oil. The flask was then fitted with a magnetic stirrer, thermometer, condenser, and septums. The system was evacuated and filled with nitrogen; 3 mL of Me₂SO was added via syringe and the mixture heated for 45 min at 75–80 °C. The flask was then cooled in an ice bath and 1.5 g (4.2 mmol) of methyltriphenylphosphonium bromide dissolved in 8 mL of warm Me₂SO was added. The resulting dark green solution was stirred for 10 min at room temperature. A solution of 0.57 g (4.3 mmol) 5-thiacyclooctanone in 8 mL of Me₂SO was added and the reaction mixture was stirred for an additional 30 min at room temperature. The solution was extracted with pentane, the pentane was removed, and the residue was distilled under reduced pressure: b/p 113 °C (13 mm); yield 0.9 g (50%); ¹H NMR (CDCl₃/Me₄Si) δ 4.85 (s, 2 H), 2.63 (m, 4 H), 2.28 (m, 4 H), 1.91 (m, 4 H); IR (film) ν 3075 cm⁻¹ (=CH₂); mass spectrum (70 eV), *m/z* (reactive intensity) 142 (87, M⁺).

5-(Iodomethyl)-1-thioniabicyclo[3.3.0]octane. To 0.065 g (0.5 mmol) of 5-methylene-1-thiacyclooctane dissolved in 2 mL of methanol was added 0.55 mmol of iodine in methanol dropwise while stirring. The iodine color disappeared immediately. After adding one-third of the iodine a white precipitate formed. The solution became yellow after all the iodine was added and the

solution was stirred for an additional 30 min. The precipitate was removed by suction filtration and washed with 2 mL of methanol. The crystals, which were dried in a desiccator, were suitable for X-ray analysis: mp 120–122 °C. Anal. Calcd for C₈H₁₄I₂S: C, 24.27; H, 3.54. Found: C, 24.57; H, 3.61.

4-Pentenyl Methyl Sulfide. 4-Pentenyl methyl sulfide was synthesized according to the method of Kline,³ but acetonitrile was used instead of ethanol. The final product was purified by gas chromatography. NMR and IR spectra were identical with those in the literature.

Kinetics. Kinetic procedures have been described previously.⁵ The buffered solutions contained invariant concentrations of KI and KCl, balanced so that the total molarity of salts was 1.0. At the concentrations used, >99% of the iodine was consumed at 10 half-lives. The decay of [I₃⁻] at 353 nm in solutions containing an excess of alkene was monitored on a Beckman DU quartz monochromator equipped with a Gilford Instrument 2415A automatic curvette positioner, 252 photometer, and 6051 recorder. The cells were thermostated at 26.0 ± 0.1 °C. The stopped-flow kinetic data were obtained on a Durrum Model 110 spectrophotometer and the output was displayed on a Tektronix 5103N single-beam storage oscilloscope. Reaction time courses were recorded photographically with a Tektronix C-50 oscilloscope camera. The syringes, mixing chamber, and cells were thermostated at 25.0 ± 0.1 °C. A Brinkmann Instrument Lauda type K-2R constant temperature circulator was used on both instruments.

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Registry No. 1, 96096-00-3; 5-methylene-1-thiacyclooctane, 96095-99-7; methyltriphenylphosphonium bromide, 1779-49-3; 5-thiacyclooctanone, 20701-80-8; 4-pentenyl methyl sulfide, 69632-05-9.

(8) Leonard, N. J.; Milligan, T. W.; Brown, T. L. *J. Am. Chem. Soc.* 1960, 82, 4075.

(9) Greenwald, R.; Chaykovsky, M.; Corey, E. J. *J. Org. Chem.* 1963, 28, 1128.

Dichlorocarbene from Flash Vacuum Pyrolysis of Trimethyl(trichloromethyl)silane. Possible Observation of 1,1-Dichloro 3-Phenyl Carbonyl Ylide

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Flash vacuum pyrolysis of trimethyl(trichloromethyl)silane **3** at 500–700 °C was shown to be a simple and efficient method for the production of :CCl₂ in the gas phase. The copyrolysis of silane **3** and benzaldehyde (**7**) at 600 °C led to 1,1,1-trichloro-2-phenyl-2-(trimethylsiloxy)ethane (**8**), a 1:1 adduct, in addition to benzal chloride (**15**) and α-chlorophenylacetyl chloride (**16**), products thought to arise from 1,1-dichloro 3-phenyl carbonyl ylide **17** as outlined in Scheme I. An orange-red material trapped at 77 K could be photobleached as well as thermally bleached and had an IR band at 1650 cm⁻¹ and a significant absorption with λ_{max} 510 nm (and a broad shoulder at 580 nm).

Dihalo carbonyl ylides **1** have been implicated as key intermediates required to explain the variety of chemical reactions which take place when appropriate phenyl(trihalomethyl)mercurials are thermally decomposed in benzene in the presence of aromatic and aliphatic aldehydes and ketones.¹⁻³ We now report a convenient pre-

cursor for the generation of ¹A₁ :CCl₂ in the gas phase and its use in the preparation of a trapped species with chem-

(1) (a) Huan, Z.; Landgrebe, J. A.; Peterson, K. *J. Org. Chem.* 1983, 48, 4519. (b) Huan, Z.; Landgrebe, J. A.; Peterson, K. *Tetrahedron Lett.* 1983, 24, 2829.

(2) (a) Gill, H. S.; Landgrebe, J. A. *J. Org. Chem.* 1983, 48, 1051. (b) Gill, H. S.; Landgrebe, J. A. *Tetrahedron Lett.* 1982, 23, 5099. (c) Martin, C. W.; Lund, P. R.; Rapp, E.; Landgrebe, J. A. *J. Org. Chem.* 1978, 43, 1071. (d) Martin, C. W.; Landgrebe, J. A.; Rapp, E. *Angew. Chem., Int. Ed. Engl.* 1972, 11, 326. (e) Martin, C. W.; Landgrebe, J. A.; Rapp, E. *J. Chem. Soc., Chem. Commun.* 1971, 1438.

(3) (a) Martin, C. W.; Gill, H. S.; Landgrebe, J. A. *J. Org. Chem.* 1983, 48, 1898. (b) Martin, C. W.; Landgrebe, J. A. *Ibid.* 1971, 36, 15.