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THE PREPARATION AND ISOMERIZATION OF <u>CIS</u>- AND <u>TRANS</u>-3,4-DIMETHYLCYCLOBUTENE.*

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The thermal isomerization of cyclobutene was first observed in 1905 by Willstatter and von Schaedel;(1) they reported the formation of considerable amounts of 1,3-butadiene in addition to cyclobutene during the decomposition of trimethylcyclobutylammonium hydroxide at elevated temperatures. In recent years the ring opening of a variety of substituted cyclobutenes has also been reported(2) and thus thermal lability is recognized as a general characteristic and indeed diagnostic of unsaturated four-membered rings.

Two features of these isomerizations are worthy of special note: (1) the unimolecular reaction proceeds at relatively low temperatures (compared with the pyrolysis of cyclobutane) and is insensitive to environmental changes(3) and (2) a 1,3-butadiene derivative is formed stereospecifically in the isomerization of 3- and 3,4-substituted cyclobutenes.(2) The extensive investigations by Criegee and his coworkers in the field of cyclobutene chemistry has led to a simple formulation of

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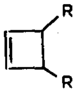
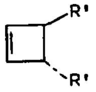
* This work was carried out in 1963 at the Technische Hochschule in Karlsruhe, West Germany. The author is sincerely grateful to Professor R. Criegee for his hospitality and for suggesting the problem.

cyclobutene isomerizations which incorporates both of these features$^{(4)}$. Stated briefly, this mechanism suggests that the process of breaking the C_3-C_4 bond involves participation of the double bond and requires that the substituents (or hydrogens) at carbon atoms 3 and 4 move in the same sense (clockwise or counterclockwise) with respect to the ring. (In a recent communication, Woodward and Hoffmann introduce the term "conrotatory twisting" to describe this process.$^{(9)}$) Our studies on the isomeric 3,4-dimethylcyclobutene (I and II) further exemplify the stereospecificity of the cyclobutene isomerizations.

Cis-3,4-dicarbomethoxycyclobutene (III)$^{(2a)}$ served as the starting material for the preparation of both cis-3,4-dimethylcyclobutene (I) and trans-3,4-dimethylcyclobutene (II). Reduction of (III) with lithium aluminum hydride and subsequent reaction at 0° with p-toluenesulfonyl chloride in pyridine furnished the cis-ditosylate (V) (m.p. 66-67° from methanol).* In similar manner, trans-3,4-dicarbomethoxycyclobutene (IV) (b.p. 42-44°/0.01, n_D^{21} 1.4552)** obtained from (III) by basic hydrolysis and subsequent re-esterification with diazomethane$^{(5)}$ was converted to trans-ditosylate (VI) (m.p. 46-47° from methanol).***



(I) R = CH_3
(III) R = $COOCH_3$
(V) R = CH_2OTs



(II) R' = CH_3
(IV) R' = $COOCH_3$
(VI) R' = CH_2OTs

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* Calc. for $C_{20}H_{22}O_6S_6$: C, 56.85; H, 5.25. Found: C, 56.75; H, 5.19.

** Calc. for $C_8H_{10}O_4$: C, 56.47; H, 5.92. Found: C, 55.56; H, 5.96.

*** Found: C, 57.02; H, 5.28.

The reduction of ditosylates (V) and (VI) with lithium aluminum hydride was carried out in anisole at 85-95°; the volatile products were swept from the reaction mixture by a slow stream of nitrogen, and trapped at -78°. In each case a mixture of hydrocarbons was obtained; these could be separated conveniently only by preparative vapor phase chromatography.(6) Thus the reduction of *cis*-ditosylate (V) furnished *cis*-3,4-dimethylcyclobutene (I), along with 1-methylcyclopentene[*] and a third substance tentatively identified as 3- or 4-methylcyclopentene[**] (approximate ratio 1 : 2 : 1.6). Similarly, lithium aluminum hydride reduction of *trans*-ditosylate (VI) produced a mixture consisting of *trans*-3,4-dimethylcyclobutene (II) 1-methylcyclopentene[*], the same 3- or 4-methylcyclopentene obtained in the reduction of (V)[**] and *trans*-*trans*-2,4-hexadiene (VII)(7) (Approximate ratio 1 : 0.2 : 1 : 0.6).

Both *cis*- and *trans*-3,4-dimethylcyclobutene underwent clean isomerization at 175°. Each furnished a single different butadiene derivative; *trans*-3,4-dimethylcyclobutene (II) produced only *trans*-*trans*-2,4-hexadiene (VII)(7), whereas *cis*-*trans*-2,4-hexadiene (VIII)(7) was formed to the exclusion of other isomers on heating *cis*-3,4-dimethylcyclobutene (I). Vapor phase chromatographic analysis(6) clearly distinguished among isomers (I), (II), (VII) and (VIII); furthermore as little as 2% (VII) in (VIII) or visa versa could be detected by this method of analysis. Clearly the isomerizations of (I) and (II) are stereospecific; the products are those expected on the basis of the mechanism presented by Criegee.(4)

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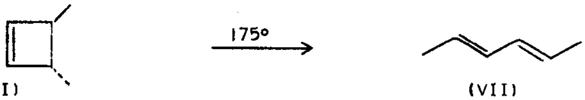
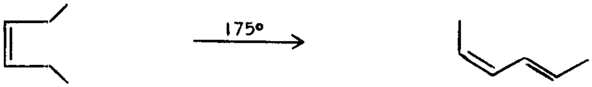
[*] Identified by comparison of its infrared spectrum with that of an authentic sample.

[**] Characterized by a strong absorption band in the infrared at 720 cm^{-1} (olefinic protons of an unsubstituted cyclopentene).



(II) (VII)



(I) (VIII)

The formation of considerable amounts of *trans-trans*-2,4-hexadiene (VII) during the preparation of *trans*-3,4-dimethylcyclobutene (II) and the *lack* of a similar by-product during the preparation of *cis*-3,4-dimethylcyclobutene (I) under approximately the same reaction conditions suggested a greater thermal lability of *trans*-cyclobutene (II) vis-a-vis the *cis* isomer (I). A comparison of the ease of isomerization of pure samples of (I) and (II) isolated by preparative vapor phase chromatography(6) revealed that this was indeed the case. After heating an approximately 1:1 mixture of (I) and (II) in a sealed ampule at 175° (oil bath temperature) for 10 minutes, less than 1% of the *trans*-3,4-dimethylcyclobutene remained whereas only 49% of the *cis*-3,4-dimethylcyclobutene had isomerized. Increased thermal lability due to 3,4-*trans* disubstitution on the cyclobutene ring (compared with the corresponding *cis* arrangement) has been demonstrated also in the 1,2,3,4-tetramethylcyclobutene series(4) and seems to be the case as well with the isomeric 3,4-dichlorocyclobutenes.(4) Thus eclipsing of substituents at C_3 and

C_4 on the cyclobutene ring cannot be a major factor contributing to the thermal lability of that ring system, as has been suggested,(8) for on this basis the greater thermal lability would have been expected of the cis isomers in each case. Furthermore the fact that cyclobutene itself would be only 64% isomerized after 10 minutes at 175° (calculated from gas phase kinetic data(3)) indicates that trans-3,4-disubstitution increases the ease of cyclobutene isomerization, whereas cis-3,4-disubstitution does not appreciably affect the rate of isomerization. An adequate explanation of this apparent acceleration of the cyclobutene - butadiene isomerization and definite conclusions on this point will have to await a quantitative study of the 3,4-dimethylcyclobutene isomerization, preferably in the gas phase.

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References

1. R. Willstätter and W. von Schaedel, Ber. Chem. 38, 1992 (1905).

2. (a) For examples from the earlier literature, see E. Vogel, Ang. Chem. 66, 640 (1954); Ann. 615, 1, 14 (1958).

   (b) Some more recent illustrations of cyclobutene isomerizations are reported by R. Criegee and K. Noll, Ann., 627, 1 (1959); R. Srinivasan, J. Am. Chem. Soc., 84, 4141 (1962); K. J. Crowley, Proc. Chem. Soc., 334 (1962); R. Criegee, J. Decker, W. Engel, P. Ludwig and K. Noll, Chem. Ber., 96, 2362 (1963); W. Adam, ibid, 97, 1811 (1964); R. Criegee and W. Funke, ibid., 97, 2934 (1964); E. Gil-Av and J. Shabtai, J. Org. Chem., 29, 257 (1964). See also ref. 4 and literature cited therein.

3. W. Cooper and W. D. Walters, J. Am. Chem. Soc., 80, 4220 (1958).

4. R. Criegee, D. Seebach, R. E. K. Winter, B. Börretzen and H. Brune, Chem. Ber. in press. The author thanks Professor Criegee for making this manuscript available prior to publication.

5. *Trans*-3,4-cyclobutenedicarboxylic acid was very labile. One of the purest samples obtained melted at 95° with simultaneous resolidification and final melting at 295-300° (*trans*-*trans*-muconic acid melts at 298°). The diester (IV) was completely isomerized within ten minutes at 130°, and furnished *trans*-*trans*-dimethylmuconate, m.p. 156-157°, undepressed on admixture with an authentic sample.

6. A six meter polyethyleneglycol-bis-β-cyanoethyl ether column was used for vapor phase chromatographic analysis and a twelve meter column was used for preparative separations.

7. A mixture of *trans*-*trans*-2,4-hexadiene and *cis*-*trans*-2,4-hexadiene was prepared by dehydrohalogenation of 2,5-dibromohexane according to Duden and Lemme. (Ber. Chem. 35, 1338 (1902). Preparative vapor phase chromatography (6) furnished each isomer pure: *trans*-*trans*-2,4-hexadiene, b.p. 81°, n_D^{21} 1.4558, λ_{max} 225mμ (log ε 4.63), ν_{max} 955 cm^{-1} (trans olefinic hydrogens); and *cis*-*trans*-2,4-hexadiene, b.p. 81° n_D^{21} 1.4519, λ_{max} 227mμ (log ε 4.25), ν_{max} 700 cm^{-1} (cis olefinic hydrogens) and 980 cm^{-1} (*trans* olefinic hydrogens). Identification of the hexadienes obtained during isomerization of dimethylcyclobutenes (I) and (II) was assured by comparison of infrared spectra and retention times in vapor phase chromatographs.

8. Vogel has attributed the lability of the cyclobutene ring at least in part to the unfavorable constellation of hydrogens (or substituents) at C$_3$ and C$_4$. (2a) Gil-Av and Shabtai have attempted to rationalize the greater lability of 3-methylcyclobutene vis-a-vis cyclobutene in terms of increase in Pitzer strain.(2b)

9. R. B. Woodward and R. Hoffman, J. Am. Chem. Soc., 87, 395 (1965).