

secologanin derivative is the diacetal sarracenin **6**.¹⁰ In view of the rapid disappearance of bitterness upon ripening of fruits, it is clear that xylomollin is transformed into other product(s), the hemiacetal acetal moiety being ideally suited for further transformations. It is conceivable that xylomollin is a key intermediate subsequent to secologanin in the biosynthesis of indole alkaloids.^{11,12}

Acknowledgments. The authors are grateful to Mr. V. Salmach for mass spectral measurements.¹³

References and Notes

- (1) The plant was collected near Mombasa. The studies of other bioactive principles are in progress.
- (2) This was not the reason for studying the unripe fruits.
- (3) N. Abo-Khatwa and I. Kubo, to be submitted for publication.
- (4) Probe temperatures 120 °C, 14 eV. The M^+ peak was generally very weak under a variety of conditions on both the GIC and Finnigan instruments. One condition under which the M^+ could be detected (one-half the intensity of the $M + 1$ peak) was at 130 °C, 15 eV.
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- (14) Japan Society for the Promotion of Science Research Fellow, 1974–1975.

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Thermal Isomerization of (+)-(1*S*,2*S*)-*trans*,*trans*-2-Methyl-1-propenylcyclopropane: Quantification of Four Stereochemical Paths in a Vinylcyclopropane Rearrangement

Sir:

Since discovery of the vinylcyclopropane rearrangement in 1959 and 1960,¹ considerable effort has been expended in unsuccessful efforts to define the stereochemical characteristics of the cyclopentene-forming reaction; not a single unconstrained monocyclic vinylcyclopropane derivative has been studied so as to define the quantitative importance of the four possible stereochemical rearrangement modes. Molecules conceptually suitable for stereochemical investigations have been synthesized, but rapid enantiomerization and diastereomerization reactions of the judiciously labeled substrates have vitiated the work: product distributions from a single starting material have not been gained.²

The most complete solution to the vinylcyclopropane stereochemical problem to date has been derived from the rearrangements of *trans*-1-cyano-2-isopropenylcyclopropane (**1**) and its *cis* isomer (**2**).³ The absence of stereochemical markers on the double bond termini makes the values of 69% inversion for *trans*-**1** and 39% inversion for *cis*-**2** the maximum information which can be gained from these systems.

The work we now report solves this long-standing problem. The key to our simplified kinetic analysis is appreciation of the kinetic behavior of *trans*- and *cis*-2-methyl-1-vinylcyclopropane (**3** and **4**).^{4,5} *trans*-2-Methyl-1-vinylcyclopropane (**3**) was

Table I. Isomeric Composition of Hydrocarbons Recovered from Pyrolysis of (+)-**7**

| Time (min) | (product mole fraction \pm standard deviation) ^a | | | |
|------------|---|------------------------|--------------------------|--------------------|
| | 7 | 8 | 9 | 8/9 |
| 60 | 0.527 \pm 0.004 | 0.0225 \pm 0.0005 | 0.00825 \pm 0.00052 | 2.73 \pm 0.11 |
| 120 | 0.280 \pm 0.001 | 0.0301 \pm 0.0003 | 0.0118 \pm 0.0002 | 2.56 \pm 0.03 |

^a The remainder of the C_7H_{12} hydrocarbons consisted of *cis*-1,4-heptadiene (the heptadiene to **8** + **9** ratio was 12.4 ± 0.5) and other heptadiene isomers which increased with decreasing pressure.

shown to rearrange to a 13 to 1 mixture of *cis*-1,4-hexadiene (**5**) and 4-methylcyclopentene (**6**), the former presumably arising from *cis*-**4** which rearranges to diene **5** via a concerted retro-ene reaction nearly three orders of magnitude faster than it is formed from *trans*-**3**. One consequence of these rate differences is that the 4-methylcyclopentene is formed only from **3**; diastereomerization of **3** to **4** does not lead to complications in the kinetic scheme governing formation of 4-methylcyclopentene. Thus with optically active *trans*,*trans*-2-methyl-1-propenylcyclopropane (**7**)⁶ as substrate, all four stereochemical paths could be traced quantitatively.

Optically pure (+)-(1*S*,2*S*)-*trans*,*trans*-2-methyl-1-propenylcyclopropane (**7**) was prepared from optically pure (+)-(1*S*,2*S*)-2-phenylcyclopropanecarboxylic acid, $[\alpha]_D^{+303}$. The phenyl acid was converted, by esterification, lithium aluminum hydride (LAH) reduction, mesylation, LAH reduction, and destructive ozonolysis, to (+)-(1*S*,2*S*)-*trans*-2-methylcyclopropanecarboxylic acid, $[\alpha]_D^{+95.8}$.^{7,8} Both carboxylic acids were shown to be optically pure by NMR analysis of the derived methyl esters with added Eu-Opt (tris[3-(trifluoromethylhydroxymethylene)-*d*-camphorato]europium(III)), an optically active NMR shift reagent. The methyl acid was converted to **7** by LAH reduction, Collins oxidation,⁹ and Wittig-Schlosser reaction.¹⁰ The optically pure (+)-(1*S*,2*S*)-**7** had $[\alpha]_D^{25} + 586 \pm 18^\circ$ and $[\alpha]_D^{25} + 528 \pm 18^\circ$.

Synthesis of optically pure *trans*- and *cis*-3,4-dimethylcyclopentenones (**8**) and (**9**) began with (+)-(R)-3-methylcyclopentanone, $[\alpha]_D^{+153}$. The ketone was converted to its hydroxymethylene derivatives and thence to a mixture of the corresponding butylthiomethylene compounds.¹¹ These were reduced to the ketones with Raney nickel¹¹ and converted to the six isomers of dimethylcyclopentene by LAH reduction, xanthate ester formation, and pyrolysis. Assurance of the geometrical relationships in **8** and **9** was obtained through alternative syntheses from commercial samples of *dl* and *meso*-3,4-dimethylcyclopentanone, and a racemic sample of **8** was reduced to give *trans*-1,2-dimethylcyclopentane identical with an optically active sample.¹² Assurance of the optical purities of **8** and **9** was secured as follows. The (+)-(S)-1,4-dimethylcyclopentene had $[\alpha]_D^{28} + 16.21^\circ$ (lit.³ $[\alpha]_D^{27} + 16.02^\circ$ for the *R* enantiomer). Epoxidation of the (+)-(R)-1,5-dimethylcyclopentene and NMR analysis with added Eu-Opt under conditions known to resolve the enantiomeric epoxide methine protons demonstrated its optical purity. The (–)-(3*S*,4*R*)-*trans*-3,4-dimethylcyclopentene (**8**) had $[\alpha]_D^{25} - 2850 \pm 160^\circ$ and $[\alpha]_D^{25} - 1720 \pm 70^\circ$, and the (+)-(3*R*,4*R*)-*cis*-3,4-dimethylcyclopentene (**9**) had $[\alpha]_D^{25} + 1220^\circ$ and $[\alpha]_D^{25} + 900^\circ$. Pyrolyses of 500-mg samples of (+)-(1*S*,2*S*)-**7** were carried out at 60 and 120 min at 296.5 °C, in the gas phase at about 40 mm, corresponding to one and two half-lives for the disappearance of **7**. Combination of these disappearance rates with two sealed tube kinetic runs (temperature range: 58 °C) leads to a calculated activation energy of 47.1 ± 2.3 kcal/mol and $\log A$ 14.3 ± 0.8 ; the corresponding

Table II. Optical Purities of Recovered **7**, **8**, and **9** from Pyrolysis of (+)-**7** (optical purity \pm standard deviation)¹³

| Time (min) | (+)-(1 <i>S</i> ,2 <i>S</i>)- 7 | (-)-(3 <i>S</i> ,4 <i>R</i>)- 8 | (-)-(3 <i>S</i> ,4 <i>S</i>)- 9 |
|------------|---|---|---|
| 60 | 0.600 \pm 0.017 | 0.632 \pm 0.018 | 0.512 \pm 0.057 |
| 120 | 0.344 \pm 0.012 | 0.544 \pm 0.020 | 0.447 \pm 0.040 |

Table III. The Stereochemistry of the Vinylcyclopropane Rearrangement of *trans,trans*-2-Methyl-1-propenylcyclopropane (**7**)¹³

| Time (min) | si (%) | ar (%) | sr (%) | ai (%) |
|------------|----------------|---------------|----------------|---------------|
| 60 | 65.0 \pm 2.8 | 7.6 \pm 0.9 | 21.6 \pm 2.6 | 4.8 \pm 1.0 |
| 120 | 65.0 \pm 2.9 | 7.6 \pm 1.1 | 21.8 \pm 2.6 | 4.6 \pm 0.9 |
| Av | 65 \pm 2 | 8 \pm 1 | 22 \pm 2.6 | 5 \pm 1 |

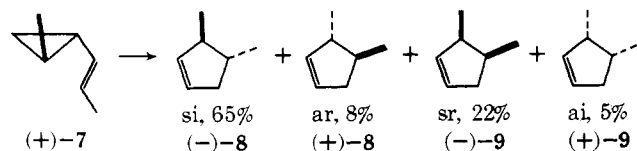
literature values for **3** are 48.6, 45.7 and 14.7, 13.7.^{4,5} The isomeric compositions of the C₇H₁₂ hydrocarbons recovered (95%) from the two pyrolyses are recorded in Table I. Unreacted starting material and the cyclopentene products were separated and purified by preparative GLC; the optical purities of these materials are shown in Table II.

The expression for the effective optical purity of a substrate undergoing racemization and competitive first-order formation of several products, where P_i is the initial optical purity of the starting material, k is the disappearance rate constant of starting material, and k_α is the one-way racemization rate constant of starting material, is¹⁴ $\bar{P} = P_i k / (k + 2k_\alpha) (1 - \exp(-(k + 2k_\alpha)t)) / (1 - \exp(-kt))$.

The data in Tables I and II yield $k = (1.773 \pm 0.008) \times 10^{-4} \text{ s}^{-1}$ and $k_\alpha = (7.25 \pm 0.16) \times 10^{-5} \text{ s}^{-1}$. These values, combined with $P_i = 100\%$, give $\bar{P}(60 \text{ min}) = 80.1 \pm 0.4\%$ and $\bar{P}(120 \text{ min}) = 68.8 \pm 0.5\%$. Combinations of the \bar{P} values with the optical purities in Table II and the (2.65 \pm 0.12):1 ratio of **8** to **9** lead to the values for the percent contribution of each of the four possible stereochemical outcomes for the vinylcyclopropane rearrangement of (+)-**7** (Table III).

Interestingly, the two migration-with-inversion stereochemical paths account for 70% of the reaction, in remarkable agreement with the 69% value for **1** reported by Doering and Sachdev.³

A detailed discussion of extensions of this investigation and the mechanistic implications will be given in the full paper. The high degree of maintenance of optical purity in both the allowed products **8** and the forbidden products **9** rule out the



possibility of freely rotating diradical intermediates in the cyclopentene-forming reaction of **7**. The kinetic scheme interrelating hypothetical, slowly interconverting diradicals is much too complex to be solved with the product distributions observed here. For these reasons we presently favor competition among four concerted processes, two allowed, and two forbidden, with the possible intervention of a planar π -vinylcyclopropane intermediate, having an orbital structure appropriate for disrotatory ring closure to racemic **9** accounting for the formation of the ai product and part of the sr product. An analogous intermediate has been postulated in the rearrangements of some vinyl epoxides.¹⁵

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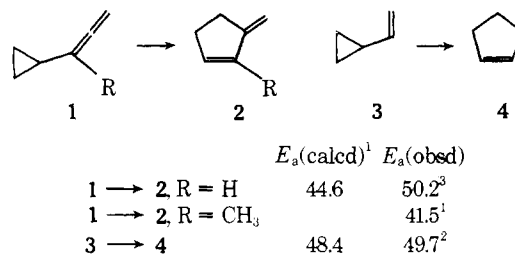
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Stereochemical Specificity in the Vinylcyclopropane Rearrangement vs. MINDO/3 Calculations

Sir:

A recent paper reports experimentally determined activation parameters for the isomerization of 3-cyclopropyl-1,2-butadiene to 2-methyl-3-methylenecyclopentene (**1** \rightarrow **2**, R = CH₃), MINDO/3 calculations modeling the cyclopropylallene rearrangement to 3-methylenecyclopentene (**1** \rightarrow **2**, R = H) and the vinylcyclopropane to cyclopentene conversion (**3** \rightarrow **4**), and assertions regarding the stereochemistry and mechanism of these reactions.¹



The Arrhenius parameters for conversion of 3-cyclopropyl-1,2-butadiene to 2-methyl-3-methylenecyclopentene were measured over a 20° temperature range to give $\log A = 12.8$ and $E_a = 41.5 \text{ kcal/mol}$.¹ Application of Benson's expression for propagation of error in calculation of Arrhenius parameters⁴ using the stated $\pm 1^\circ$ limits on temperature and 5% probable error in rate constants leads to calculated error limits of $\pm 3.7 \text{ kcal/mol}$ for E_a and ± 1.44 for $\log A$.

The activation parameters for the conversion of cyclopropylallene to 3-methylenecyclopentene have been found by Roth