Supplementary Material Available: Further spectroscopic data for 23,24-dioxa-5-oxophlorin 5 (6 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Rearrangements of 2,2'-Bis(methylene)dicyclopropyl

Kristi J. Snellings and Edward S. Lewis*

Department of Chemistry, Rice University, P.O. Box 1892, Houston, Texas 77251

Received May 22, 1990 (Revised Manuscript Received January 25, 1992)

Introduction

The substance 2,2'-bis(methylene)dicyclopropyl, 1, became available a few years ago. It was of interest to see if there were any new thermal reactions of this substance attributable to simultaneous reaction of both rings; the methylenecyclopropane rearrangement[1] of either half of the molecule was expected.

Results

A new synthesis of 1 as a separable diastereomeric mixture is described, as are the rates and equilibrium of the interconversion of the two diastereomers and the identification of all detected monomeric products of thermal reaction in solution in mesitylene. A brief study in the gas phase at higher temperatures is also reported.

The measured initial rate constants and equilibrium constants of the *meso*- to *dl*-conversion are given in Table I. Equilibrium constants were calculated as the ratio of the forward to reverse rate constants. At higher temperatures in solution and in the gas phase we used the equation $K = [dl\text{-}1]/[meso\text{-}1]$ since kinetic data were unavailable and substantial reaction had taken place. This calculation assumes that the stereoisomer interconversion is fast compared to all irreversible reactions. The discrepancy between the solution- and gas-phase results can be attributed either to the different conditions or to a failure of the above assumption. There was no significant variation of the equilibrium constants with temperature either in solution or in the gas phase.

The rate data in Table I are described by the expressions (1) and (2). The activation energies (in kcal/mol) are slightly smaller than some literature values for related compounds,[2] and the preexponential values are also somewhat higher. The analytical problems at less than

$$k_f = 10^{14.1} \exp(-36.7 \pm 0.7/RT) \quad (1)$$

$$k_r = 10^{15.1} \exp(-38.5 \pm 0.2/RT) \quad (2)$$

5% reaction with (even at this low conversion) perceptible amounts of other products leads us to mistrust the precision given; the two expressions may not differ significantly.

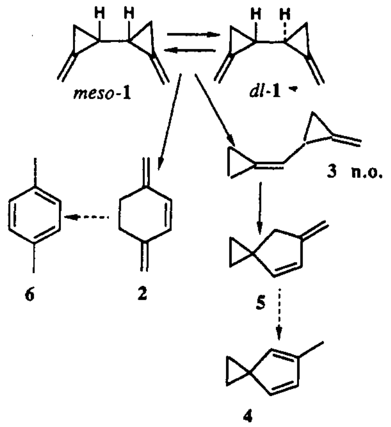
Scheme I shows the observed products from either isomer of 1, as well as one plausible intermediate, 3, the methylenecyclopropane rearrangement product which should rearrange rapidly to 5, in conformity with earlier results on vinylmethylenecyclopropanes.[3]

Table I. Rates[a] for the Conversion of the *meso*-1 to *dl*-1, k_f, the Reverse, k_r, and the Equilibrium Constant, *K*, in Mesitylene

t, °C	k_f s^{-1} × 10^6	k_r s^{-1} × 10^6	*K*
131.1	1.61 ± 0.03	1.81 ± 0.06	0.89 ± 0.03[b]
141.1	4.77 ± 0.10	5.5 ± 0.10	0.86 ± 0.16[b]
151.1	14.0 ± 0.17	17.5 ± 0.01	0.80 ± 0.02[b]
195[c]			0.85 ± 0.07[c]
292–352[c]			1.12 ± 0.09[c,d]

[a] Rate constants are the average of three to four individual measurements. [b] The equilibrium constant was calculated as ratio of the two rate constants given. [c] The equilibrium constant was calculated from the average ratio of *dl*-1 to *meso*-1 at the temperatures indicated; no kinetic data were collected at these temperatures. [d] These are gas-phase flash vacuum pyrolysis results; no systematic variation with temperature was noted.

Scheme I[a]



[a] And several dimers. Dashed arrows are secondary reactions. n.o. = not observed.

All other reactions were slower than the stereoisomer interconversion; no kinetic data on these were obtained. The structures shown in Scheme I were determined by NMR on samples separated by preparative GC methods. The major initial product was 2, which is itself thermally unstable. The other initial product is 5. Compounds 4, and 6, were shown to be artifacts derived from surface reactions and the GC separation artifacts of 5 and 2 respectively. Only 6 is stable for very long periods of heating.

The apparent 1,3 hydrogen shifts to give 4 and 6 suggested a possible free-radical chain with abstraction and readdition of allylic hydrogen. However, in mesitylene-d_{12}, no deuterium was incorporated from the solvent into either compound as shown by GCMS, so this radical chain does not occur in mesitylene solution.

The conversion to identified products was not quantitative; at least six dimers identified only as $C_{16}H_{20}$ by GC-mass spectra were found as well as higher molecular weight products. Yields were therefore not well determinable. However, at small extents of conversion the major product from 1 is 2, and in the gas phase the yield of 2 is always greater than that of 5 (counting 6 as part of 2 and 4 as part of 5) and is possibly as high as 70%. The fall in the product ratio with extent of conversion is presumably due to the low thermal stability of 2. Clearly, both

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[1] Gajewski, J. J. *Hydrocarbon Thermal Rearrangements*; Academic Press: New York, 1981; p 51–58.

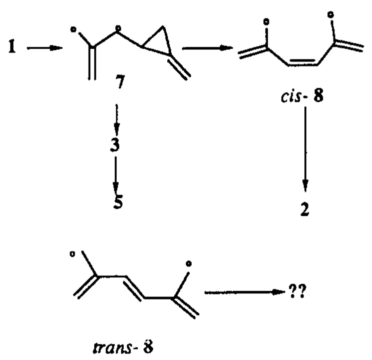
[2] Chesick, J. P. *J. Am. Chem. Soc.* **1963**, *85*, 2720.

[3] Billups, W. E.; Leavell, K. H.; Lewis, E. S.; Vanderpool, S. *J. Am. Chem. Soc.* **1973**, *95*, 8096.

[4] A reviewer suggests that the Cope product of 1, 1,2-dicyclopropenylethane, might be an intermediate in the *meso*- to *dl*-1. However, group additivity calculations show that this Cope product is less stable than 1 by about 51 kcal/mol. The observed activation energy for the *meso*- to *dl*-1 of 36–39 kcal/mol can hardly be this much in error, so this mechanism must be rejected.

0022-3263/92/1957-4315$03.00/0

Scheme II



2 and 5 are both formed at the earliest stages.

No structural assignment could be given to any dimer. The amount of dimers decreased when the thermolysis was done in dilute solution, but not nearly enough to be accounted for only by a bimolecular reaction. The dimers are in part derived from 2 since adding 2 to 1 before heating gave a different distribution of apparently the same (from retention time) dimers. By itself, 2 does not give dimers, although it polymerizes in mesitylene.

Experiments at higher temperature in the gas phase using flash vacuum pyrolysis (FVP) showed that the major products were the same. No dimers resulted, but some less volatile material was detected. A new uncharacterized isomer of 1 was a minor product. It was apparently formed at the cost of 4 or 5. At temperatures over 300 °C small amounts of nonisomeric styrene and *p*-ethyltoluene were identified.

Discussion

The mechanism of the interconversion of stereoisomers is presumably similar to that of other methylenecyclopropane rearrangements.[1,4] No further mechanistic conclusions can be drawn. The presence of the fast stereoisomer interconversion makes the use of other mechanistic tools (such as using optically active or isotopically labeled starting materials) very unpromising, since the methylene groups are presumably rapidly shuffled.

The most interesting result is the formation of 2, an apparently new reaction. Since completion of this work a report by Wendt and Berson[5] shows the analogous reaction with a stereochemically confined cyclic case. Unlike the present case, they were able to see only the single bismethylenecyclohexene analogous to 2 and were able to get good kinetics for its formation. An elegant study of optically active starting material allowed them to reject the exclusive intermediacy of an achiral diradical. Our reaction is the parent case of this rearrangement.

We considered the reaction sequence of Scheme II, which shows the diradical 7 often suggested for methylenecyclopropane rearrangements, but with an extra cyclopropane ring. Cyclopropylcarbinyl radicals are known to rearrange rapidly,[6] but not instantly. The rearrangement of 7 to the open diradical 8 must be faster than the unsubstituted cyclopropylcarbinyl radical since the product has extra allylic stabilization. This reaction is probably not reversible, since the product lacks the ring strain of 7 and has an extra allylic resonance. The closure of *cis*-8 to 2 is quite plausible, and *cis*-8 is entirely analogous to Wendt and Berson's achiral diradical. However, there seems no reason to exclude the formation of *trans*-8. The simple closure of *trans*-8 to 1 is not allowed since this completes a cyclic path forbidden by microscopic reversibility, yet no reasonable product from it appears. If *trans*-8 is absent, then *cis*-8 is also absent. *The logical conclusion is that 2 is not formed by the pathway of Scheme II but instead results from a direct reaction without intermediates from 1.* This interesting conclusion is not completely rigorous, however, since a possible exclusive fate of *trans*-8 to give dimers or polymers is still conceivable. However, the large initial yields of 2, especially in the gas phase, make it unlikely that a major product, such as some product from *trans*-8, was overlooked.

It is tempting to write a mechanism showing orbital interactions leading from 1 to 2. We are unwilling to do this, since the relation of the four methylene groups in 1 to the four in 2 is quite obscure; a mechanism assuming a particular fate of each CH_2 would be very weakly founded.

Experimental Section

Materials. Mesitylene was a commercial material distilled to avoid GC interferences. Mesitylene-d_{12} was made following the Organic Syntheses[7] preparation of ordinary mesitylene using deuterated acetone and D_2SO_4. The low yield (4.4%) after GC purification was not optimized since enough resulted from the first attempt. The MS showed extensive deuteration. Reagents and solvents were commercial materials.

2,2′-Dichloro-2,2′-dimethyldicyclopropyl. The formal addition of CH_3CCl to 1,3-butadiene using 1 equiv of CH_3CHCl_2 and butyllithium in ether followed closely the literature method,[8] using 0.29 mol of butadiene. Before distilling the product a second equivalent of CH_3CHCl_2 and butyllithium were added as before. Final workup gave the product as a mixture of stereoisomers, bp 29–40 °C (0.4 Torr), yield 8.2g, 16%. The first step alone is reported to give a 43% yield[8a] the second step is new: ^{1}H NMR (90 MHz, $CDCl_3$) δ 0.72–1.08 (4 H, m), 1.12–1.48 (2 H, m), 1.6 (6 H, s). No peaks were sharp, presumably because of the isomeric mixture, so coupling constants were undetermined. MS 178, with the expected peaks for ^{37}Cl content.

***meso*- and *dl*-2,2′-Bis(methylene)dicyclopropyl (1).** The isomeric mixture from the above paragraph was treated with potassium *tert*-butoxide in DMSO following similar literature methods.[8] The usual workup was followed by a bulb-to-bulb distillation and a preliminary preparative GC separation on a short diethyleneglycol succinate (DEGS) column. The *meso*- and *dl*-isomers present in about equal amounts were separated by further GC following Bergman.[9] *meso*-1: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.80 (2 H), 1.20 (2 H), 1.65 (2 H), 5.35 (4 H, s); the first three showed poorly resolved fine structure; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 9.36, 16.14, 103.66, 133.34. MS 106. *dl*-1: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85 (2 H), 1.10 (2 H), 1.70 (2 H), 5.33 (2 H, s), 5.37 (2 H, s); as above, coupling perceptible but unresolved for the first three; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 6.72, 15.60, 103.01, 134.13. MS 106.

3,6-Bis(methylene)cyclohexene was prepared for comparison of NMR by cracking the product of a double Wittig reaction on the reduced quinone–cyclopentadiene adduct, described below. This is a more expeditious synthesis than the literature one.[10]

3,6-Bis(methylene)-*endo*-tricyclo[6.2.1.0^{2,7}]undec-9-ene. The adduct of *p*-benzoquinone and cyclopentadiene was reduced following Chapman[11] giving light yellow low-melting crystals. Of this, 2.0 g (slightly wet with ligroine, about 0.01 mol) was dissolved

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(10) Bailey, W. J.; Barclay, R. *J. Am. Chem. Soc.* **1959**, *81*, 5393.

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in DMSO and added dropwise to a solution of methylenetriphenylphosphine (made from dimsylsodium and methyltriphenylphosphonium bromide, 7.85 g, 0.022 mol, in DMSO[12]). The solution was stirred at room temperature for 2 h. The solution was diluted with an equal volume of water and extracted three times with pentane. The pentane solution was dried with $MgSO_4$ and the solvent removed under vacuum. After column chromatography and elution with petroleum ether, the product was obtained as an oil, yield 843 mg, 45%: ^1H NMR (90 MHz, $CDCl_3$) δ 1.43 (2 H, s), 2.07 (4 H, s), 3.00 (4 H, d), 4.76 (4 H, s), 6.03 (2 H, s); MS 172.

3,6-Bis(methylene)cyclohexene (2). The product of the double Wittig reaction above (94 mg, 0.55 mmol) was added dropwise to a vertical pyrolysis tube packed with broken Pyrex tubing with a slow flow of nitrogen. The tube was held at 260 °C by a furnace. The lower end of the tube was connected to a trap containing pentane cooled by dry ice. After addition was complete and a volume of nitrogen several times the volume of the tube had passed, the trap was removed and maleic anhydride (54 mg, 0.55 mmol) dissolved in 1 mL acetone was added to remove the cyclopentadiene formed. The contents of the trap after warming to room temperature were then distilled to remove solvent and then subjected to preparative scale GC purification at about 75 °C. **2** was free from xylene and was isolated in 41% yield as found by analytical GC with an internal *p*-xylene standard: ^1H NMR (90 MHz, $CDCl_3$) δ 2.45 (4 H, s), 4.90 (4 H, s), 6.20 (2 H, s), the peak at 4.90 is just perceptibly split at 300 MHz; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 30.30, 112.03, 130.49 (the quaternary carbons were not observed in this spectrum).

Isolation and Identification of Products from 1. Samples (about 500 mg) of the mixture of stereoisomers of **1** in mesitylene were heated in sealed evacuated tubes for typically about 1.5 h; very long heating times led to much reduced quantities of the isomers, short times gave isolable amounts of major products only (**2** was the major early product). The tubes were then opened and subjected to bulb-to bulb distillation, the first distillate contained the C_8H_{10} products with mesitylene, the later fraction contained mesitylene and the $C_{16}H_{20}$ materials. A preliminary preparative-scale GC on a short DEGS column gave a sample with very little mesitylene. On further GC **1**, **2**, **6**, and **4** were in that order eluted and trapped. The analytical "microbore" column also showed **5**, not isolated in these experiments. Compound **5** did not survive this chromatography, but it was later isolated in a mixture with **2** and the NMR spectrum was obtained by difference; it is given below.

An identical run using mesitylene-d_{12} as the solvent and analyzed on the GCMS showed products of parent mass 106 and 212 only, not distinguishable from products in ordinary mesitylene.

The samples were identified by NMR spectroscopy. The ^1H NMR spectrum of isolated **2** agrees with that for the synthetic sample above. The ^1H NMR spectral data of **6**, δ 2.30 (6 H, s), 7.04 (4 H, s) have been reported. Those of **4**, ^1H (300 MHz, $CDCl_3$) δ 1.55 (4 H, s), 2.00 (3 H, s), 5.70 (1 H, s), 6.00 and 6.40 (2 H, AB system), agree with the data reported;[13] ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 12.17, 15.55, 37.19, 132.63, 139.65, 140.08. A DEPT spectrum showed that only the 12.17 resonance was for carbon with two attached protons. The identifications of **2** and **6** were confirmed by comparison of GC retention with those of authentic samples. Diene **4** was further identified by a UV maximum at 261 nm compared to the reported[14] peak at 257 nm for the parent compound without the methyl. No structure was assigned to any dimer. Similar experiments in mesitylene but in far more dilute solution still showed substantial although somewhat less dimer. Experiments with added broken glass to the solution of **1** showed slightly larger relative amounts of **4**, suggesting a heterogeneous rearrangement of **5**.

The flash vacuum pyrolysis described below gave a sample of the retention time of **2** after preparative GC isolation; it gave two peaks on the analytical GC. The ^1H NMR (300 MHz, $CDCl_3$) of this mixture, after subtraction of the NMR peaks of **2**, gave a spectrum of the other smaller component, assigned to **5**: δ 0.80 (4 H, d), 2.65 (2 H, d), 4.85 (2 H, d), 5.70 and 6.10 (2 H, AB system). The quality of this difference spectrum did not allow evaluation of coupling constants. The characterization of **5** resulted from improved preparative GC technique which minimized rearrangement to **4**, not to the conditions of the experiment yielding it. **5** was present in the analytical GCs of all the reaction samples.

Flash vacuum pyrolysis allowed short exposure to much higher temperatures. A Vycor tube packed with broken glass tubing was heated by a horizontal tube furnace. At one end was a small flask containing **1** (ca. 20 mg) and an inlet for a slow flow of N_2. The other end led to a trap cooled in dry ice and then to a vacuum pump with the pressure controlled by a leak. The N_2 flow was started, the flask of **1** was immersed in liquid N_2, the pump was started, and when the pressure was stable the flask was allowed to warm, leading to quiet evaporation of **1**. The trap was warmed, and the contents were rinsed out with pentane for the analytical GC, which only showed peaks corresponding to **1**, **2**, **4**, **5**, and **6** at FVP temperatures up to 300 °C. At the higher temperatures three other minor products were found. One of these, an isomer of **1** by GCMS, appeared to come from **4** or **5**, because the amounts of these decreased as the new isomer increased. Amounts were too small for identification, although it was shown that the species was thermally stable in solution up to 162 °C for 20 h, by noting that the mixture isolated from FVP after most of the **1** had disappeared showed no decrease in the concentration of this new isomer compared to an internal standard. The other two were (by NMR) styrene and *p*-ethyltoluene, from more drastic reactions. No dimers were found, but a substantial amount of less volatile material was seen. Temperatures were determined by the furnace setting and checked before a run with a thermometer in the tube.

Kinetics of the Interconversion of the Stereoisomers of 1. Approximately 13-mg samples of the separated isomers (>98% stereochemically pure) were dissolved in 1 mL of mesitylene, with heptane as internal standard. Samples (20 μL) were sealed in small capillary tubes and immersed in a thermostated oil bath. Analytical GC of samples removed from time to time gave the extent of isomerization. The reactions were followed only to <5% completion, minimizing the further reactions and the reverse reaction. The resulting plots of extent of completion vs time gave the first-order rate constants summarized in Table I.

Acknowledgment. This work was supported by a grant from the Robert A. Welch Foundation. It is based on the PhD thesis of K.J.S., 1990. Thanks are due to Alan Kook for help with the NMR. The preparation of **1** is based on preliminary results from the group of Prof. W. E. Billups.

Supplementary Material Available: ^1H NMR spectra of 6-methylenespiro[2.4]hept-4-ene (**5**) and 3,6-bis(methylene)-*endo*-tricyclo[6.2.1.0]undec-9-ene (2 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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Alteramide A, a New Tetracyclic Alkaloid from a Bacterium *Alteromonas* sp. Associated with the Marine Sponge *Halichondria okadai*

Hideyuki Shigemori,[1a] Myung-Ae Bae,[1b] Kazunaga Yazawa,[1b]
Takuma Sasaki,[1c] and Jun'ichi Kobayashi*,[1a]

*Faculty of Pharamceutical Sciences, Hokkaido University,
Sapporo 060, Japan, Sagami Chemical Research Center,
Kanagawa 229, Japan, and Cancer Research Institute,
Kanazawa University, Kanazawa 920, Japan*

Received March 24, 1992

Marine microorganisms have proven to be a rich source of structurally novel and biologically active compounds

0022-3263/92/1957-4317$03.00/0