Homoallylic Participation in the Acid-Catalyzed Rearrangement of an α,β-Epoxy Ketone

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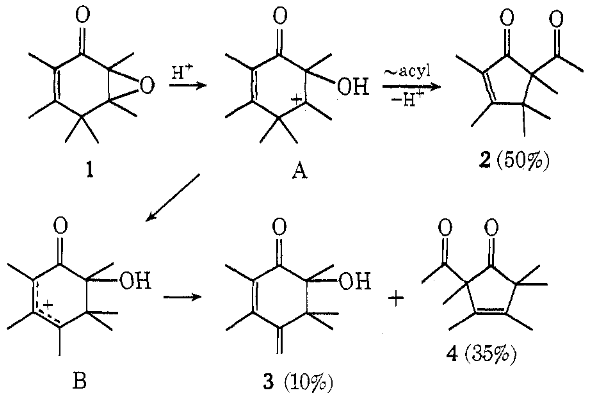
The α,β-epoxy ketones **6c** and **6t** (*cis-* and *trans*-2,3-epoxy-2,3,4,5,6-pentamethyl-4-vinyl-5-cyclohexenones) rearrange in acid exclusively by vinyl migration, in preference to the acyl and methyl migration observed previously in analogous compounds with a methyl group in place of the 4-vinyl substituent. When the vinyl group and epoxide ring were trans (**6t**) rearrangement was much faster than with the cis isomer (**6c**), owing to homoallylic participation during the epoxide ring opening. However the rearrangement products in both instances were identical, i.e., a 1:4 mixture of *cis-* and *trans*-2-acetyl-5-vinyl-2,3,4,5-tetramethyl-3-cyclopentenones (**7c** and **7t**).

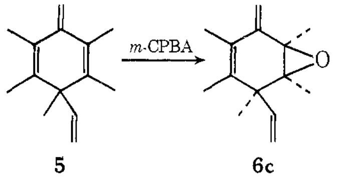
In a recent study[1] it was shown that acyl and methyl migration compete approximately equally in the acid-catalyzed rearrangement of the α,β-epoxy ketone **1**. Thus on treatment with trifluoroacetic acid, **1** rearranged (Scheme I) to nearly equal mixtures of **2** and (**3** + **4**).[1] Protonation and ring opening of **1** occur in such a manner as to place the positive charge remote from the carbonyl group, giving ion A. Acyl migration and proton loss affords the major product **2**. Methyl migration competes effectively, giving the allylic ion B, which may either lose a proton to give **3** or rearrange by a more complex process, eventually to give **4**.[2]

Scheme I

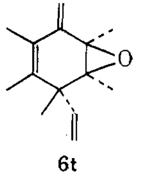


We now wish to report that replacement of one of the *gem*-dimethyl groups in **1** by a vinyl group markedly alters the outcome of the rearrangement, and that the reaction rate depends upon whether the vinyl group and epoxide ring are cis or trans to one another.

Preparation of 6c and 6t. Treatment of the vinyl cyclohexadienone **5**[3] with *m*-chloroperbenzoic acid (*m*-CPBA) in methylene chloride gave a mixture of two monoepoxides, **6c** and **6t**, in which the vinyl group and epoxide ring are cis or trans to one another, respectively.[4] Although it was not possible to separate the two isomers, it was clear from the nmr spectrum of the mixture that epoxidation had occurred exclusively at the α,β double bond. The area ratio of vinyl protons (multiplet, δ 4.8–6.1) to aliphatic protons (δ 1.1–1.7) was 1:5. With the aid of europium shift reagent and a 100-Mhz spectrometer, and as a consequence of isolating one of the isomers in pure form (**6c**, vide infra), it was possible to completely assign the NMR spectrum of each isomer. The ratio of **6c** to **6t**, as determined by integration of the europium-shifted NMR spectrum, was approximately 3:2.

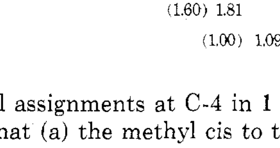


5 **6c**

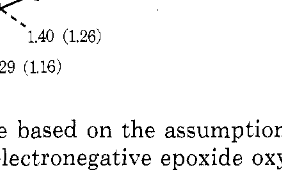


6t

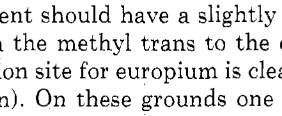
When a methylene chloride solution of the mixture of **6c** and **6t** was treated with trifluoroacetic acid for 1 hr at room temperature, *only one of the two isomers reacted.* The unreacted isomer was separated from the rearrangement products by preparative VPC, and we assign it structure **6c**. The chemical shifts and europium shift slopes[5] of the five methyl groups are shown on the structure. The most striking difference in the NMR spectra of **6c** and **6t** is the chemical shift of the methyl at C-4; these signals are 0.22 ppm apart in the two isomers. This result is consistent with the NMR spectrum of **1**,[6] shown for comparison. The methyl assignments at C-4 in **1** were based on the assumptions that (a) the methyl cis to the electronegative epoxide oxygen should appear at lowest field, and (b) the methyl cis to the epoxide oxygen, a possible coordination site for europium shift reagent should have a slightly larger europium-shift slope than the methyl trans to the epoxide ring (the main coordination site for europium is clearly, however, the carbonyl oxygen). On these grounds one can assign structure **6c** to the epoxy ketone which is recovered from mild treatment of **6c** + **6t** with trifluoroacetic acid, since its C-4 methyl appears at higher field (thus trans to the epoxide ring) than the C-4 methyl in its isomer. As will be seen, this assignment is consistent with mechanistic rationalizations of the acid-catalyzed rearrangement of **6**.



6c



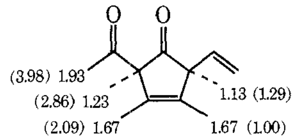
6t



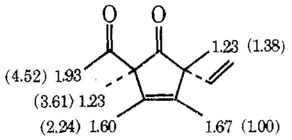
1

Structures of the Rearrangement Products. In addition to recovered **6c**, two rearrangement products were isolated from the mild treatment of **6c** + **6t** with trifluoroacetic acid. They were separated by preparative VPC and are assigned structures **7c** and **7t** (ratio 1:4), in which the methyls at C-2 and C-5 of the cyclopentenone ring are cis or trans, respectively. Each isomer showed two strong carbonyl bands in the infrared (~1700, 1740 cm^{-1}) for the acetyl and cyclopentenone carbonyl groups; the uv spectra also showed that neither carbonyl group was conjugated with a carbon–carbon double bond. The NMR spectrum of each isomer showed an acetyl methyl, two allylic methyls, two aliphatic methyls, and three vinyl protons. The mass spectra of **7c** and **7t** were nearly identical; striking features were a very weak parent peak (*m/e* 206), a base peak at *m/e* 164 corresponding to the loss of ketene, and three additional intense peaks for the further loss of 15, 28, and 43 amu. All of the spectra resemble closely the published spectra of 4.[1]

The distinction between **7c** and **7t** is based on different chemical shifts and europium slopes of the C-5 methyl (adjacent to the vinyl substituent). This signal appears at lower field and is affected more by shift reagent when the methyl is cis to the acetyl group at C-2 (i.e., in **7t**). Also noteworthy are the lower overall europium shift slopes in **7c** compared with **7t**, presumably because the large vinyl group cis to the acetyl group in **7c** diminishes the interaction with the shift reagent.

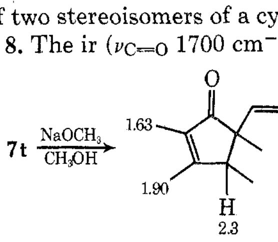


7c



7t

Chemical evidence for the structure of **7** was obtained by base cleavage. The major isomer (**7t**) was treated with sodium methoxide in methanol at room temperature (12 hr) to give a mixture of two stereoisomers of a cyclopentenone assigned structure **8**. The ir ($\nu_{C=O}$ 1700 cm^{-1}) and uv spectra [λ_{max} (MeOH) 237 nm (ϵ 8800)] support the presence of a cyclopentenone moiety, and the NMR spectrum showed two homoallylically coupled methyls (δ 1.63, 1.90, J = 1 Hz), three vinyl protons (δ 4.6–5.8), two aliphatic methyls (δ ~1.0), and the methine proton (m, δ 2.3). The structure of **8** was further supported by the observation that treatment with NaOCH$_3$–CH$_3$OD gave **8**-d_4, in which the NMR signals at δ 1.90 and 2.3 were absent, that at δ 1.63 sharpened to a singlet, and the aliphatic methyl signals simplified to sharp singlets.



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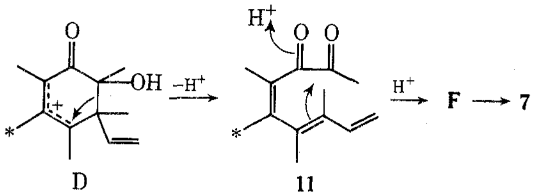
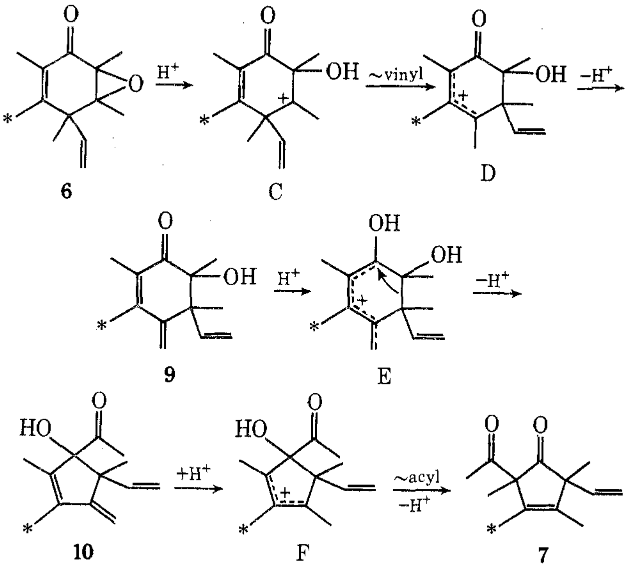
Rearrangement Mechanism. A plausible mechanism for the formation of **7** from **6** is shown in Scheme II (the question of stereochemistry is deferred for later discussion; vide infra). Protonation of the epoxide oxygen and ring opening gives ion C (analogous to A from **1**, Scheme I). Vinyl migration would give the allylic cation D (analogous to B from A, Scheme I). Proton loss could give **9** (analogous to **3**, Scheme I), which, however, was not observed. Reprotonation, ring contraction (to give **10**), and a 1,2-acetyl migration account for the product. Alternatively D could suffer ring opening to **11**, which, on protonation and ring closure, could lead directly to F, then **7**. These schemes are analogous to the mechanisms established for the formation of 4 from **1**.[1]

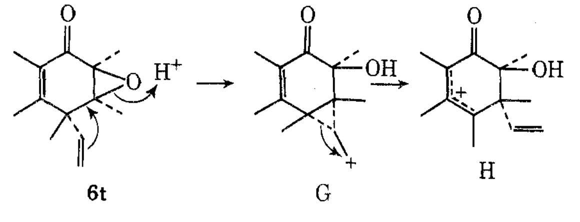


Scheme II

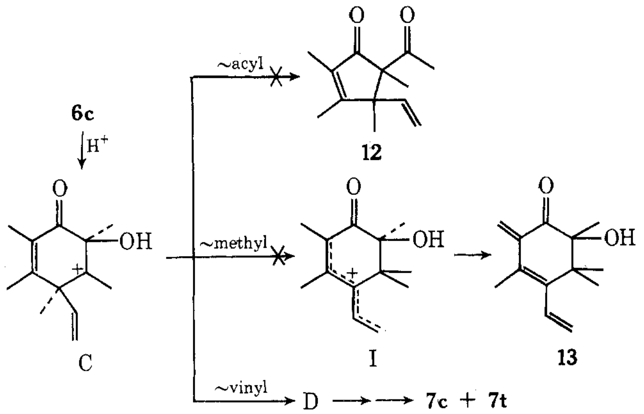


A labeling experiment was performed to test the general accuracy of Scheme II. Treatment of **6** (a mixture of cis and trans isomers) with DMSO-d_6 and potassium *tert*-butoxide gave **6***, whose NMR spectrum was identical with that of **6** except that the area of the peak at δ 1.67 was reduced in area by 50% (label at C-5). Treatment of **6*** with TFA at room temperature for 1 hr gave **6c*** (signal at δ 1.67 reduced in area by 50%, and a somewhat sharper singlet than for **6c**) and **7t*** whose NMR spectrum lacked the signal at δ 1.60 and had a sharpened singlet at δ 1.67.[7] These results clearly establish that a vinyl migration occurred during the rearrangement of **6** to **7** (the vinyl and labeled methyl in **6*** are on adjacent carbons, whereas in **7*** they are separated by an additional carbon) as outlined in Scheme II.

The observation that **6t** is rapidly converted by TFA into **7** under conditions where **6c** is recovered unchanged strongly suggested that Scheme II is oversimplified, and that homoallylic participation occurs in the ring opening of epoxide **6t**. That is, the initially formed ion from **6t** is not the tertiary carbonium ion C but a cyclopropylcarbinyl cation, one contributor of which is shown as structure G. Vinyl migration should give H (corresponds to D in Scheme II) in which the vinyl and hydroxyl groups are trans. Unfortunately, further steps in the mechanistic scheme allow for stereochemical ambiguity and the product is a mixture of **7t** and **7c**.



In isomer **6c**, where the vinyl and epoxide groups are cis, homoallylic participation in the ionization step is not possible. Consequently, **6c** is recovered unchanged under these reaction conditions. It seemed important to determine whether **6c** would also rearrange in acid under more forcing conditions. We found that **6c** was inert to TFA at room temperature, even after 12 hr. However, when the temperature was raised to 60°, **6c** did rearrange slowly, reaction being 85% complete in 7.5 hr. The products were **7c** and **7t**, identical with those obtained from **6t**. We conclude that



both **6c** and **6t** rearrange exclusively by vinyl migration. They do so, however, by different mechanisms, **6t** rearranging with homoallylic participation (via G, H, etc.) and **6c** rearranging without participation (via C, D, etc.). Even when the reaction occurs *without* participation, however, acyl or methyl migration are unable to compete with vinyl migration. Thus products such as **12** (which could be formed via acyl migration) or **13** (which could be formed by proton loss from the highly delocalized intermediate cation I) were not observed. One can conclude that vinyl migration is preferred over acyl or methyl migration even when homoallylic participation in the ionization step is not possible.

Experimental Section[8]

Epoxidation of 2,3,4,5,6-Pentamethyl-4-vinyl-2,5-cyclohexadienone (5). To a solution containing 100 mg (0.53 mmol) of **5**[3] in 5 ml of methylene chloride was added, at 0°, a solution of *m*-chloroperbenzoic acid (93.5 mg, 0.54 mmol) in 3 ml of methylene chloride. The reaction, which was followed by NMR, was complete in about 2 hr, during which time *m*-chlorobenzoic acid precipitated from solution. The solvent was removed by rotary evaporation, petroleum ether (bp 30–60°) was added, and the *m*-chlorobenzoic acid was removed by filtration. The filtrate was washed with aqueous sodium bicarbonate, then with saturated sodium chloride, and dried (Na_2SO_4). The solvent was rotary evaporated, and the residue was chromatographed on Florisil (80–100 mesh) using ethyl acetate–hexane (1:4) as eluent. The first fraction was a mixture of the monoepoxides **6c** and **6t** (43 mg, 88% based on unrecovered dienone). The second fraction was unreacted **5** (55 mg, 55%). The mixture of **6c** and **6t** had the following properties: ir (neat) 1660 (s), 1625 (w), 1385 (m), 1350 (w), 1030 (w), 885 (w), 685 cm^{-1} (w); uv λ_{max} (MeOH) 253 nm (ϵ 12,700), 212 (6800); NMR (CCl_4) δ 1.15 (s) and 1.31–1.40 (overlapping singlets), combined area 9 H, 1.67 (m, 6 H), 4.9–6.1 (m, 3 H). Europium shift reagent,[5] Eu(fod)$_3$, resolved the spectrum and at 100 MHz separate peaks due to the five methyl groups in each stereoisomer were discernible. The area ratio for peaks assigned to **6c** and **6t** was 3:2. The mass spectrum (70 eV) of the epoxide mixture was *m/e* (rel intensity) 206 (11), 191 (30), 190 (39), 175 (53), 174 (39), 165 (16), 164 (100), 163 (56), 159 (36), 149 (83), 147 (57), 136 (52), 135 (85), 121 (67), 120 (32), 119 (78), 108 (25), 107 (36), 105 (55), 93 (65), 91 (78), 79 (65), 77 (55), 65 (37).

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.73; H, 8.82.

In an effort to decrease the amount of unreacted **5** in the above epoxidation, the ratio of peracid to dienone was increased to 3:1. To a solution containing 100 mg (0.53 mmol) of **5** in 5 ml of methylene chloride was added, at 0°, a solution of 280 mg (1.62 mmol) of *m*-chloroperbenzoic acid in 10 ml of methylene chloride. The mixture was stirred at room temperature overnight, then worked up as described above. Chromatography of the crude product over Florisil (80–100 mesh) with ethyl acetate–hexane (1:4) as eluent gave as the first fraction the diepoxides[4] i_c and i_t (58 mg, 50%) and as the second fraction the monoepoxides **6c** and **6t** (43 mg, 40%). There was no unreacted **5**. The diepoxide mixture (2,3:5,6-diepoxy-2,3,4,5,6-pentamethyl-4-vinylcyclohexanone) had the following properties: ir (KBr) 1690 (s), 1380 (m), 1100 (m), 950 (m), 870 (w), 680 cm^{-1} (w), uv λ_{max} (MeOH) 210 nm (ϵ 2900); NMR (CCl_4) δ 1.07 (s), 1.20 (overlapping singlets), 1.33 (s), 1.50 (s), area from δ 1.07–1.50, 15 H, 4.8–6.4 (m, 3 H); Eu(fod)$_3$ shift reagent showed that there were two sets of methyl singlets, each with area ratios 1:2:2; for the NMR assignments and europium shift slopes, see the structures in ref 4; the two isomers were present in a 3:2 ratio; mass spectrum (70 eV) *m/e* (rel intensity) 222 (<1), 179 (18), 165 (13), 151 (49), 137 (70), 125 (23), 124 (24), 109 (100), 93 (34), 91 (30), 81 (34), 79 (37), 77 (31), 67 (35), 55 (29), 53 (54).

Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.28; H, 8.21.

Repetition of the epoxidation exactly as above but with 374 mg (2.2 mmol) of *m*-chloroperbenzoic acid and 100 mg (0.53 mmol) of **5** in a total of 20 ml of methylene chloride gave 99 mg (85%) of the diepoxide mixture i_c and i_t and, as the second fraction from Florisil chromatography, 10 mg (8%) of triepoxide ii: ir (CCl_4) 1695 (s), 1450 (w), 1375 (m), 1080 cm^{-1} (w); uv λ_{max} (MeOH) 215 nm (ϵ 6000); NMR (CCl_4) δ 0.83 (s), 1.35–1.6 (overlapping singlets; total area from δ 0.8–1.7, 15 H), 2.60–3.32 (m, 3 H), no vinyl protons; mass spectrum (70 eV) *m/e* (rel intensity) 238 (1), 195 (13), 167 (77), 164 (33(= [63 (28), 153 (50), 150 (30), 149 (100), 147 (33), 137 (73), 135 (65), 133 (42), 125 (86), 123 (86), 121 (36), 119 (44), 109 (70), 107 (94), 105 (55), 97 (28), 95 (26), 93 (52), 91 (97), 84 (20), 81 (45), 79 (80), 77 (64), 67 (60), 65 (39), 55 (63), 53 (75).

Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.63; H, 7.59.

Acid-Catalyzed Rearrangement of *cis*- and *trans*-2,3-Epoxy-2,3,4,5,6-pentamethyl-4-vinyl-5-cyclohexenone (6c and 6t). A solution of **6c** and **6t** (200 mg, 0.97 mmol) in 1 ml of trifluoroacetic acid was stirred at room temperature for 1 hr, then poured into a slurry of aqueous sodium bicarbonate solution and methylene chloride. The organic layer was separated, washed successively with aqueous sodium bicarbonate and saturated aqueous sodium chloride, and dried (Na_2SO_4). Evaporation of the solvent left 186 mg of a light yellow oil which, when subjected to analytical VPC (5 ft × 0.125 in. column, 3% SE-30 on Raroporl 30, 100–120 mesh, 125°), showed two peaks corresponding to **7c** + **7t** (retention time 5.5 min, 42%) and unreacted **6c** (retention time 9.5 min, 51%). Preparative VPC (5 ft × 0.25 in. column, 10% SE-30 on Chromosorb W, 80–100 mesh, 125°) gave pure ***cis*-2,3-epoxy-2,3,4,5,6-pentamethyl-4-vinyl-5-cyclohexenone (6c):** ir (CCl_4) 1660 (s), 1630 (w), 1390 (m), 1250 (m), 935 (w), 880 cm^{-1} (s); uv λ_{max} (MeOH) 250 nm (ϵ 10,000), 215 (4830); NMR (CCl_4), see structure; all methyl peaks were sharp singlets except that at δ 1.67, which was slightly broadened; the three vinyl protons appeared as a multiplet, δ 4.8–6.0; mass spectrum (70 eV) *m/e* (rel intensity) 206 (12), 191 (22), 164 (50), 163 (40), 149 (62), 147 (20), 137 (10), 136 (50), 135 (100), 121 (57), 120 (35), 119 (65), 107 (25), 105 (49), 93 (45), 91 (55), 77 (48), 65 (22). By comparing the NMR spectrum of the mixture of **6c** and **6t** with that of pure **6c** and by plotting the chemical shifts vs. europium shift reagent concentration and extrapolating back to zero shift reagent it was possible to assign the NMR spectrum of **6t** (see structure).

VPC [5 ft × 0.125 in. column, 5% TCEP (tetracyanoethylated pentaerythritol) on Chromosorb W, 80–100 mesh, 125°, FID] resolved the chromatograph of **7c** and **7t** into two peaks, **7t** (80%, retention time 75 min) and **7c** (20%, retention time 90 min). Preparative VPC (5 ft × 0.25 in. column, 15% TCEP on Chromosorb W, 80–100 mesh, 125°) gave each pure isomer. ***trans*-2-Acetyl-5-vinyl-2,3,4,5-tetramethyl-3-cyclopentenone (7t):** ir (CCl_4) 1740 (s), 1710 (s), 1250 (s), 935 (w), 875 cm^{-1} (s); uv λ_{max} (MeOH) 219 nm (ϵ 2650), 285 (720); NMR (CCl_4), see structure; the peaks at δ 1.60 and 1.67 were mutually coupled quartets, J = 1.5 Hz, other methyl peaks were sharp singlets, and the vinyl protons appeared at δ 4.6–5.8 (m, 3 H); mass spectrum (70 eV) *m/e* (rel intensity) 206 (<1), 164 (100), 149 (63), 136 (54), 135 (29), 121 (73), 119 (28), 105 (30), 91 (26), 77 (19), 66 (27), 65 (23), 44 (36).

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.56; H, 9.03.

***cis*-2-Acetyl-5-vinyl-2,3,4,5-tetramethyl-3-cyclopentenone (7c):** ir (CCl_4) 1740 (m), 1700 (s), 1250 (s), 875 cm^{-1} (s); uv λ_{max} (MeOH) 218 nm (ϵ 1150), 283 (30); NMR (CCl_4), see structure; all peaks were sharp singlets except for the vinyl protons at δ 4.7–5.4 (m, 3 H); mass spectrum (70 eV) *m/e* (rel intensity) 206 (<1), 164 (100), 149 (69), 136 (52), 135 (24), 121 (76), 119 (26), 105 (30), 91 (28), 77 (23), 66 (77), 65 (56).

Cleavage of 7t with Base. A solution of **7t** (26 mg) and sodium methoxide (20 mg) in 3 ml of methanol was stirred at room temperature for 12 hr, then poured into ice-water and extracted with ether. The combined ether layers were washed with saturated sodium chloride and dried (Na_2SO_4). Evaporation of the solvent and analysis of the residue by VPC (5 ft × 0.125 in. column, 3% SE-30 on Raroporl 30, 100–120 mesh, 120°) showed that all the **7t** was converted to a single product, assigned the structure **2,3,4,5-tetramethyl-5-vinyl-2-cyclopentenone (8).** Pure **8** was collected by preparative VPC (5 ft × 0.25 in. column, 10% SE-30 on Chromosorb W, 80–100 mesh, 120°): ir (CCl_4) 1700 (s), 1650 (w), 1250 (m), 885 cm^{-1} (s); uv λ_{max} (MeOH) 237 nm (ϵ 8820); NMR (CCl_4) δ 1.0–1.2 (m, 6 H), 1.63 (q, 3 H, J = 1 Hz), 1.90 (q, 3 H, J = 1 Hz), 2.3 (m, 1 H), 4.6–5.8 (m, 3 H); mass spectrum (70 eV) m/e (rel intensity) 164 (85), 149 (100), 135 (49), 121 (60), 119 (20), 105 (38), 93 (30), 91 (29), 79 (25), 77 (23), 67 (25), 65 (15), 53 (26).

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.83. Found: C, 80.47; H, 9.92.

Treatment of **8** (10 mg) with excess sodium methoxide in CH_3OD for 5 hr at room temperature followed by work-up analogous to that used in the preparation of **8** from **7t** gave **8-d_4**, whose NMR spectrum consisted of two sharp singlets at δ 1.00 and 1.13 (3 H), a sharp singlet at 1.63 (3 H), and a vinyl proton multiplet at 4.6–5.8 (3 H).

5-Trideuteriomethyl-2,3-epoxy-2,3,4,6-tetramethyl-4-vinyl-5-cyclohexenone (6*). To a solution containing 145 mg (0.7 mmol) of a mixture of **6c** and **6t** (as obtained from epoxidation of **5**) in 5 ml of dimethyl sulfoxide-d_6 was added, with stirring and under N_2, 95 mg (0.85 mmol) of potassium *tert*-butoxide. The mixture was stirred at room temperature for 4.5 hr, then quenched with ice–water and extracted with ether. The combined organic layers were dried (Na_2SO_4) and the solvent was evaporated to give a nearly quantitative yield of **6***. The NMR spectrum was identical with that of the starting material, except that the peak at δ 1.67 was decreased in area by 50%.

Acid-Catalyzed Rearrangement of 6*. The procedure and work-up were as described for the treatment of **6c** and **6t** with trifluoroacetic acid. The recovered unreacted **6c*** had an NMR spectrum identical with that of pure **6c** except that the signal at δ 1.67 had sharpened and was reduced in area to only 3 H. The major rearrangement product **7t*** had an NMR spectrum identical with that of pure **7t** except that the signal at δ 1.60 was absent, and that at δ 1.67 had sharpened to a singlet. The amount of **7c*** collected was insufficient for an NMR spectrum.

Acid-Catalyzed Rearrangement of 6c. A solution of pure **6c** (22 mg, recovered from the treatment of a mixture of **6c** and **6t** with trifluoroacetic acid at room temperature for 1 hr) in 0.5 ml of trifluoroacetic acid was allowed to stand at room temperature for 12 hr. There was no change in the NMR spectrum. The solution was then heated at 60° and the NMR spectrum gradually changed. After 7.5 hr the reaction was essentially complete and the solution was poured into a slurry of aqueous sodium bicarbonate and methylene chloride and worked up (vide supra). VPC (5 ft × 0.25 in. column, 10% SE-30 on Chromosorb W, 80–100 mesh, 135°) gave 15% recovered **6c** and 85% of a mixture (4:1) of **7t** and **7c** whose spectra (ir, NMR) were identical with those described above.

Acknowledgment. We are indebted to the National Institutes of Health for a grant (GM-15997) in support of this research.

Registry No.—i_c, 54277-18-8; i_t, 54353-09-2; ii, 54325-80-3; **5,** 54277-19-9; **6c,** 54325-81-4; **6t,** 54353-10-5; **7c,** 54277-20-2; **7t,** 54277-21-3; **8c,** 54277-22-4; **8t,** 54277-23-5.

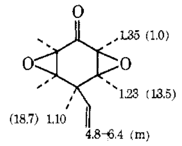
References and Notes

(1) H. Hart, I. Huang, and P. Lavrik, *J. Org. Chem.*, **39,** 999 (1974).

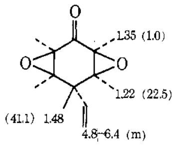
(2) For the mechanistic details of the latter process, including deuterium labeling experiments, see ref 1.

(3) H. Hart and M. Nitta, *Tetrahedron Lett.*, 2113 (1974).

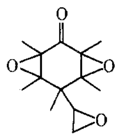
(4) When excess *m*-chloroperbenzoic acid was used, di- and triepoxides of **5** were formed. The diepoxides were a mixture of i_c and i_t in which the two epoxide rings are cis to one another and either cis or trans to the vinyl group. There was no detectable amount of the isomer with the two epoxide rings trans to one another. The stereochemistry of the triepoxide ii is not known, though it seems probable that the two epoxide oxygens on the cyclohexanone ring are cis. Spectral properties of i and ii are given in the Experimental Section.



i_c



i_t



ii

(5) Chemical shifts are in δ units, with relative downfield shifts in the presence of $Eu(fod)_3$ given in parentheses; see D. R. Kelsey, *J. Am. Chem. Soc.*, **94,** 1764 (1972).

(6) H. Hart, M. Verma, and I. Wang, *J. Org. Chem.*, **38,** 3418 (1973).

(7) Insufficient **7c*** was isolated for spectral examination.

(8) NMR spectra were obtained on either a Varian Associates T-60 or HA-100 spectrometer; ir spectra were measured on a Unicam SP-200 spectrophotometer and were calibrated against a polystyrene film, uv spectra on a Unicam SP-800 spectrophotometer, and mass spectra at 70 eV on a Hitachi Perkin-Elmer RMU-6 spectrometer. Elemental analyses were performed by Spang Microanalytical Laboratories, Ann Arbor, Mich., or Clark Microanalytical Laboratories, Urbana, Ill. Analytical gas chromatography (VPC) was done on a Varian Aerograph Model 1400 (flame ionization detector), and preparative VPC was done with a Varian Aerograph Autoprep Model 700 instrument (thermal conductivity detector).

Generalized Syntheses of γ Diketones. I. Addition of Dimetalloacetylides to Aldehydes. II. Dialkylation of Bisdithianes[1a]

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γ diketones are synthetically very useful but not generally accessible. Extensive preliminary studies revealed that the addition of dimetalloacetylides to aldehydes followed by catalytic reduction of the carbon–carbon triple bond and then oxidation of the saturated glycol to the diketone was one of the more promising approaches. The development of this method into a general, preparative procedure yielding a variety of 1,4 diketones in 20–60% overall yields is reported. The generality of application of the Corey–Seebach bisthio carbanions to the preparation of γ diketones via both single-step and stepwise dialkylations has also been examined. For the less reactive primary alkyl derivatives, the single-step approach and, for all other primary alkyl halides, the stepwise approach seem to offer the best general route to the target compounds. Thus this procedure is complementary to the dimetalloacetylide route which is superior when R is secondary or tertiary alkyl, and in which the bisthio carbanion approach generally fails. Many of the compounds made have not been reported heretofore.

γ diketones (1,4-dicarbonyl compounds) have great utility in organic synthesis, e.g., they readily undergo enolic dehydration and Knorr–Paal condensations to form furans, pyrroles, and thiophenes. Work carried out in this laboratory[2] has expanded the application of the Knorr–Paal pyrrole synthesis to produce a number of highly sterically