***cis*-Methyl 4-Oxo-2-pentenoate (9):** IR (NaCl) 1725 (COOMe), 1680, 1650 cm^{-1} (C═O, C═C); NMR (CCl_4) δ 2.27 (s, 3, CH_3CO), 3.74 (s, 3, $COOCH_3$), 6.06 (d, 1, J = 12.2 Hz, HC═CH), 6.30 (d, 1, J = 12.2 Hz, HC═CH); mass spectrum (70 eV) *m/e* (rel intensity) 128 (5), 114 (5), 113 (81), 97 (28), 85 (9), 69 (9), 59 (24), 55 (11), 54 (9), 53 (6), 43 (100).

***trans*-Methyl 4-Oxo-2-pentenoate (10):** IR (NaCl) 1730 (COOMe), 1675, 1650 cm^{-1} (CO, C═C); NMR (CCl_4) δ 2.38 (s, 3, CH_3CO), 3.86 (s, 3, $COOCH_3$), 6.63 (d, 1, J = 15.7 Hz, HC═CH), 7.00 (d, 1, J = 15.7 Hz, HC═CH); mass spectrum (70 eV) *m/e* (rel intensity) 128 (22), 114 (6), 113 (100), 98 (4), 97 (37), 85 (9), 69 (13), 59 (23), 55 (6), 54 (5), 53 (8), 43 (67).

***trans*-Methyl 4,4-Dimethoxy-2-pentenoate (11):** IR (NaCl) 1730 (COOMe), 1600 cm^{-1} (C═C); NMR (CCl_4) δ 1.33 (s, 3, CH_3), 3.13 (s, 6, OCH_3), 3.69 (s, 3, $COOCH_3$), 6.17 (d, 1, J = 16.0 Hz, HC═CH), 6.53 (d, 1, J = 16.0 Hz, HC═CH); mass spectrum (70 eV) *m/e* (rel intensity) 174 (23), 159 (36), 145 (30), 143 (100), 129 (60), 113 (23), 97 (37), 83 (24), 75 (11), 69 (14), 59 (10), 43 (33).

Reaction of (*E*)-5,5-Dichloro-4-methoxy-3-penten-2-one (5) with Sodium Methoxide. This reaction was carried out in the same way as in the case of **3**.

5,5-Dichloro-4,4-dimethoxypentan-2-one (12): NMR (CCl_4) δ 2.20 (s, 3, CH_3CO), 2.97 (s, 2, CH_2CO), 3.34 (s, 6, OCH_3), 5.87 (s, 1, $CHCl_2$).

***cis*-5,5,5-Trimethoxy-3-penten-2-one (13):** IR (NaCl) 1690, 1645 cm^{-1} (CO, C═C); NMR (CCl_4) δ 2.25 (s, 3, CH_3CO), 3.20 (s, 9, OCH_3), 6.33 (s, 2, HC═CH); mass spectrum (70 eV) *m/e* (rel intensity) 159 (3), 144 (8), 143 (100), 115 (12), 113 (6), 105 (37), 99 (14), 85 (8), 84 (45), 65 (46), 59 (18), 55 (8), 53 (6), 43 (33).

4,5,5,5-Tetramethoxy-2-pentanone (14): IR (NaCl) 1725 cm^{-1} (CO); NMR (CCl_4) δ 2.10 (s, 3, CH_3CO), 2.45–2.66 (m, 2, $CHCH_2CO$), 3.27 (s, 9, OCH_3), 3.37 (s, 3, OCH_3), 3.66–3.80 (m, 1, $-CHCH_2CO$); mass spectrum (70 eV) *m/e* (rel intensity) 175 (14), 106 (5), 105 (100), 99 (2), 75 (14), 59 (16), 43 (30).

Acknowledgments. The "Fonds voor Kollektief Fundamenteel Onderzoek" and the "Nationaal Fonds voor Wetenschappelijk Onderzoek" are thanked for financial support to the laboratory.

Registry No.—1, 53009-77-1; **2,** 61203-72-3; **3,** 61203-73-4; **4,** 61203-74-5; **5,** 61203-75-6; **6,** 61203-76-7; **7,** 61203-77-8; **8,** 61203-78-9; **9,** 19522-27-1; **10,** 2833-24-1; **11,** 42997-93-3; **12,** 61203-79-0; **13,** 61203-80-3; **14,** 61203-81-4; methyl dichloroacetate, 116-54-1; acetone, 67-64-1; diazomethane, 334-88-3; sodium methoxide, 124-41-4.

References and Notes

(1) N. De Kimpe, "Aangesteld Navorser" of the Belgian "Nationaal Fonds voor Wetenschappelijk Onderzoek"

(2) Postdoctoral Fellow, A.B.O.S.

(3) N. Schamp and W. Coppens, *Tetrahedron Lett.*, 2697 (1967).

(4) N. Schamp, N. De Kimpe, and W. Coppens, *Tetrahedron*, **31**, 2081 (1975).

(5) N. Schamp, L. De Buyck, and R. Verhé, unpublished results. Presented in part at the 25th IUPAC Congress, Jerusalem, July 1975, Abstract, p 103.

(6) L. Panizzi, *Gazz. Chim. Ital.*, **71**, 216 (1941).

(7) F. G. Bordwell and M. W. Carlson, *J. Am. Chem. Soc.*, **91**, 3951 (1969).

(8) F. G. Bordwell, M. W. Carlson, and A. C. Knipe, *J. Am. Chem. Soc.*, **91**, 3949 (1969).

(9) F. G. Bordwell, R. G. Scamehorn, and W. R. Springer, *J. Am. Chem. Soc.*, **91**, 2087 (1969).

A Simple Synthesis of *trans*-8,10-Dimethyl-1(9)-octal-2-one via an Acid-Catalyzed Michael Reaction

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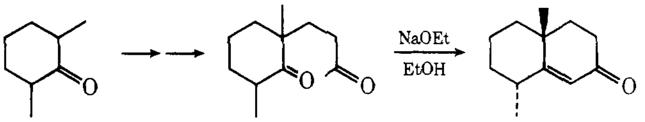
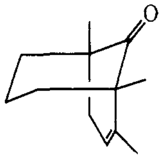
Received August 24, 1976

The structural similarity of *trans*-8,10-dimethyl-1(9)-octal-2-one (**1**) to the eudesmane sesquiterpenes makes it a valuable compound for natural product synthesis. Indeed, our concern with **1** stemmed from a project directed toward the synthesis of certain eudesmanolides. It is also of interest that octalone **1** has found commercial application as a flavorant and perfume constituent,[2] and was recently discovered to be a minor component of vetiver oil.[3] Use of **1**, however, has been limited by its unavailability. Failure of the Robinson annulation sequence to provide a viable route to this material has prompted other workers to develop new pathways to **1**.[4,5a] The alternate syntheses involve multistep conversion of 2,6-dimethylcyclohexanone to the 1,5 diketone **2** followed by a high-yield base-catalyzed cyclization to **1**.[5] Although overall yields of **2** as high as 46% were realized, the reported pathways are four to five steps in length and would require considerable effort for the preparation of large quantities of material. We wish to report that a one-step synthesis of **2** may be effected via an acid-catalyzed Michael addition and that **2** so prepared undergoes the previously reported cyclization in high yield to the octalone **1**.



2 1

Our initial experiments were directed toward the preparation of **1** via the convenient acid-catalyzed Robinson annulation procedure developed by Heathcock, Ellis, McMurry, and Coppolino.[6] Earlier studies by Marshall and Schaeffer[5a] on the Wichterle reaction indicated, however, that acid-catalyzed aldol cyclization of the intermediate 1,5 diketone **2** might lead preferentially to the bridged enone **3**. This proved to be the case. When 2,6-dimethylcyclohexanone and methyl vinyl ketone were refluxed with sulfuric acid in benzene, the bicyclo[3.3.1]nonenone **3** was isolated as the major product. We found, however, that stopping the reaction after only a few minutes at reflux allowed chromatographic isolation of substantial quantities of the intermediate Michael adduct **2**.[7] Further experimentation showed that by conducting the reaction at 0 °C, **2** could be prepared in 50–58% yield (70–75% conversion) with concurrent formation of only a trace of the bridged enone **3**. The product was readily isolated by distillation.



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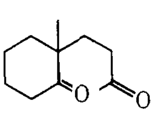

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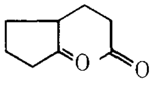

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Preliminary experiments suggest that this preparation of 1,5 diketones could have considerable generality. For example, sulfuric acid catalyzed addition at 0 °C of methyl vinyl ketone to 2-methylcyclohexanone and even cyclopentanone gave diones **4** and **5** in unoptimized yields of 55 and 31%, respectively.

Experimental Section

2,6-Dimethyl-2-(3-oxobutyl)cyclohexanone (2). A solution of 9.50 g (75 mmol, 10.3 ml) of 2,6-dimethylcyclohexanone, 5.25 g (75 mmol, 6.1 ml) of freshly distilled methyl vinyl ketone, and 50 ml of benzene was cooled to 0 °C under a drying tube. The mixture was stirred while 1.5 ml of concentrated sulfuric acid was added, and then allowed to stand at 0 °C for 2 h. The orange mixture was then stirred and second portions of methyl vinyl ketone (3.0 ml) and sulfuric acid (0.5 ml) were added. After an additional 2 h, final portions of methyl vinyl ketone (3.0 ml) and sulfuric acid (0.5 ml) were mixed with the dark reaction mixture. After standing for an additional 12 h at 0 °C, the orange reaction mixture was decanted from the dark polymer and poured into 100 ml of ether. The polymer was rinsed with a little fresh ether. The combined ethereal solutions were washed with 1 N sodium hydroxide and brine. The aqueous washings were back-extracted with ether, and the combined ether solutions were dried ($MgSO_4$) and the solvents removed at reduced pressure to give an orange oil (13.9 g).

The crude product was fractionated through a 4-in. Vigreux column. The first fraction was collected at water pump pressure (~25 mm) and had bp 90–94 °C. This material was essentially pure 2,6-dimethylcyclohexanone (2.7 g). The product **2** was collected at 0.6 mm with bp 80–100 °C [lit.[5a] bp 82–100 °C (0.2 mm)] as a pale yellow oil (5.3 g, 51% yield at 71% conversion). The spectral properties of this material were identical with those reported previously for **2**.[5a]

***trans*-8,10-Dimethyl-1(9)-octal-2-one (1).** Diketone **2** was cyclized according to the procedure of Marshall and Schaeffer[5a] in sodium ethoxide/ethanol to give an 87% yield of distilled octalone (≥95% pure by VPC).

Acknowledgment. The authors wish to thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the Vanderbilt University Research Council for their support of this work.

Registry No.—**1**, 17990-00-0; **2**, 4071-74-3; **4**, 4071-58-3; **5**, 1489-27-6; 2,6-dimethylcyclohexanone, 2816-57-1; methyl vinyl ketone, 78-94-4; 2-methylcyclohexanone, 583-60-8; cyclopentanone, 120-92-3.

References and Notes

(1) Undergraduate Research Fellow.
(2) *Chem. Abstr.*, **78**, P33809j (1973); **81**, P13187p (1974).
(3) B. Maurer, M. Fracheboud, A. Grieder, and G. Ohloff, *Helv. Chim. Acta*, **55**, 2371 (1972).
(4) J. A. Marshall and W. I. Fanta, *J. Org. Chem.*, **29**, 2501 (1964).
(5) (a) J. A. Marshall and D. J. Schaeffer, *J. Org. Chem.*, **30**, 3642 (1965); (b) D. Caine and F. N. Tuller, *ibid.*, **34**, 222 (1969).
(6) C. H. Heathcock, J. E. Ellis, J. E. McMurry, and A. Coppolino, *Tetrahedron Lett.*, 4995 (1971). Note that there is an error in the experimental procedure given in that paper. The correct procedure should read: "... and 0.3 ml of concentrated sulfuric acid *in 100 ml of benzene* is refluxed ..."
(7) A very recent report from the Heathcock group mentions isolation of a 1,5 diketone in an acid-catalyzed Robinson annulation reaction. See footnotes 14–16 in J. E. Ellis, J. S. Dutcher, and C. H. Heathcock, *J. Org. Chem.*, **41**, 2670 (1976). See also R. Maki, Y. Ishida, K. Satake, and R. Oda, *J. Chem. Soc. Jpn., Ind. Chem. Sect.*, **57**, 42 (1954).

Conformational Equilibria in the *cis*-1,2,3,6-Tetrahydrophthalic Anhydride Series

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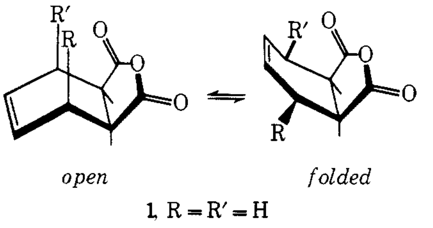
The use of lanthanide shift reagents (LSR) for conformational analysis can be approached in two ways. One method relates a ratio of proton slopes for the molecule being studied to the ratio of similar environmentally situated protons in skeletally homogeneous standards (the method of Servis and Bowler[2]). The second method utilizes the computer program PDIGM[3] to search for a conformer mix of lowest R values.[4] When suitable conformationally rigid molecules are available, the first method would appear to be more simple. This paper describes some of our work to test this assumption.

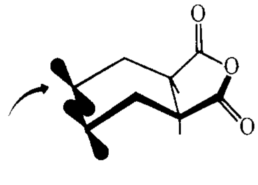
As part of our continuing program to evaluate how heteratoms can affect structure and reactivity of heterocyclic molecules,[5] we had the occasion to examine the anhydrides **1**,[6] **2**,[7] and **3**.[8] These can have, as seen by Dreiding models, two major contributing conformers which we designate as *"open"* and *"folded"*.



open *folded*

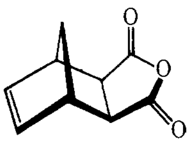
1, R = R′ = H
2, R = R′ = Me
3, R = H; R′ = Me

Epoxidation of **1** has been reported to give, as the major product, the epoxide syn to the anhydride moiety.[9] Although some participation of the anhydride functionality with the peroxy acid was not ruled out as a factor directing stereoselectivity, the major effect was thought to be conformational. In the *open* conformer, the steric effects are greater on the side of the π bond anti to the anhydride moiety.



Using NMR coupling constant data, however, **1** was determined to exist preferentially in the *folded* conformation.[10] Based primarily on the seemingly severe steric interactions of the methyl groups in the *open* conformation of **2**, this anhydride was also suggested to exist preferentially as a *folded* conformer. Anhydride **3** was also determined to be *folded*.

Since in our laboratories the anhydride functional group has been particularly well behaved toward LSR studies,[11] and because of the availability of **4** and **5** as models for the *open* and *folded* conformers, respectively, we chose to examine the conformer mix of **1–3** by the method of Servis. Additional representative *open* and *folded* models were available with **6–8**.[11]



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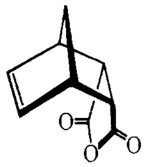

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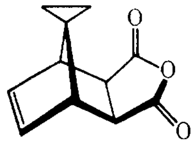

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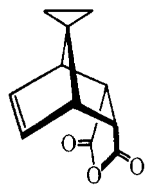

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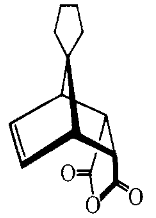

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To a weighed sample of the anhydride in deuteriochloroform was added Eu(fod)$_3$ in portions such that each spectrum constituted a 0.1 increment in the Eu(fod)$_3$ to substrate ratio. The chemical shifts for the vinyl and juncture protons (H_V and H_J, respectively) were obtained from the shifted spectra, and are listed in Table I.

In the experimental approach to this problem, we chose to compare the characteristic slope (S), obtained from a least-squares analysis of δ_{H_V} vs. ($\delta_{H_V} + \delta_{H_J}$) for each addition of shift reagent, where δ_{H_V} and δ_{H_J} are the chemical shifts for the vinyl and juncture protons, respectively. That the values for S do reflect the particular geometrical arrangement can be dramatically emphasized by comparing S values for the anhydrides **4–7** (Table I). Entries **4** and **6**, representative of *open* conformers, have very similar S values ($\bar{S}$ = 0.156 ± 0.002). Entries **5**, **7**, and **8** represent the *folded* conformer ($\bar{S}$ = 0.402 ± 0.004). Using the average values ($\bar{S}$) for the model compounds, 0.156 and 0.402 for 0.00 and 100% *folded*, respectively, we find that the three anhydrides do prefer the *folded* conformation: **1** (52%); **2** (71%); **3** (68%).

At this juncture it seemed appropriate to test the confor-