Tieffeneau–Demjanov Ring Homologations of Two Pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-diones

Alan P. Marchand,* D. Rajapaksa,[1a] and S. Pulla Reddy[1b]

Department of Chemistry, University of North Texas, Denton, Texas 76203-5068

William H. Watson* and Ante Nagl

Department of Chemistry, Texas Christian University, Fort Worth, Texas 76129

Received May 5, 1989

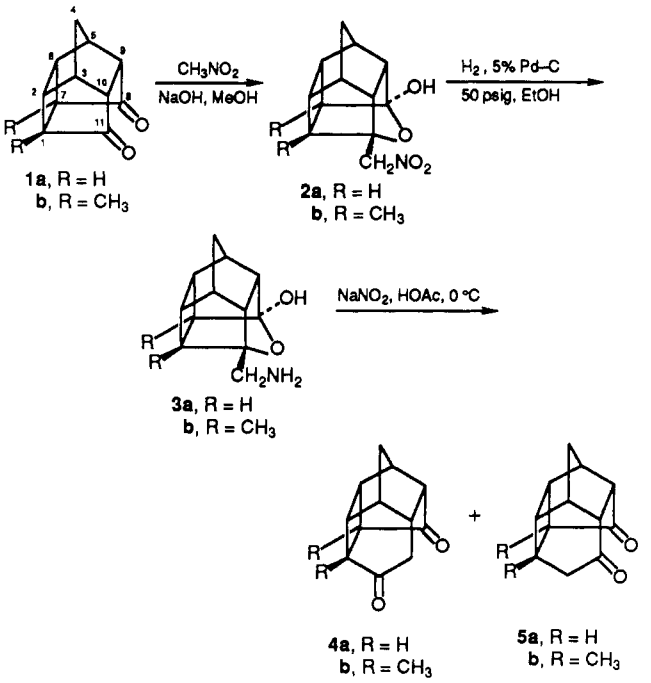
Tieffeneau–Demjanov ring homologation of pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione (PCUD-8,11-dione, **1a**) and of 1,7-dimethyl-PCUD-8,11-dione (**1b**) has been studied. Thus, nitrous acid deamination of 3-hydroxy-4-oxa-5-(aminomethyl)hexacyclo[5.4.1.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]dodecane (**3a**) results in ring expansion, thereby affording a mixture of cage diketones **4a** and **5a**. Reaction of this product mixture with *p*-toluenesulfonic acid produced **4a** (14%) and a tetracyclic compound, **6a** (56%), which most likely was formed via acid-promoted retro-Michael reaction of **5a**. Catalytic hydrogenation of **6a** afforded a tetracyclic diketone, **7**, whose structure was elucidated by X-ray crystallography. The corresponding reaction sequence when applied to 1,7-dimethyl-3-hydroxy-4-oxa-5-(aminomethyl)hexacyclo[5.4.1.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]dodecane (**3b**) gave cage diketone **4b** (26%) and a tetracyclic compound **6b** (39%) that is analogous to **6a**.

Introduction and Experimental Results

Ring expansions of substituted polycyclic ketones provide a convenient and versatile method for the construction of novel polycyclic "cage" systems.[2] Recently, we have reported some examples of boron trifluoride promoted ring homologations of substituted pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-diones (PCUD-8,11-diones) with ethyl diazoacetate (EDA).[3,4] The substituted pentacyclododecanes and pentacyclotridecanes thereby obtained have been employed as intermediates in the synthesis of a new class of molecular clefts.[5,6] By way of contrast, reaction of 1,9-dihalo-PCUD-8,11-diones with ethyl diazoacetate in the presence of boron trifluoride etherate ($F_3B{\cdot}OEt_2$) resulted in ring expansion with concomitant rearrangement to afford substituted dihydrocyclopent[*a*]indenes.[7] The present study was undertaken in an effort to delineate and to extend the scope of ketone homologations of appropriately substituted PCUDs.

An approach based upon the Tieffeneau–Demjanov rearrangement,[8] shown in Scheme I, has been adopted to perform the requisite ring expansions of **1a** and of **1b**. In each case, the substrate was condensed initially with nitromethane in the presence of base. The resulting adduct (**2a** or **2b**, respectively) next was subjected to catalytic reduction with hydrogen gas over palladized charcoal catalyst, thereby affording a primary amine (**3a** or **3b**, respectively). Finally, the amine was diazotized with sodium nitrite in aqueous acetic acid. This resulted in deamination with concomitant rearrangment, thereby affording the corresponding ring-expanded diketones (**4a** + **5a** and **4b** + **5b**, respectively).

Scheme I



In practice, compounds of the type **5** are not isolated. Instead, they undergo acid-catalyzed retro-Michael reaction to afford the corresponding tetracyclic enedione, **6** (Scheme II). Thus, application of the reaction sequence shown in Scheme I to **1a** afforded **4a**[4] and **6a** (product ratio 1:4).

Chloroform solutions of each of the product mixtures obtained via nitrous acid deamination of **3a** and of **3b** (i.e., **4a** + **5a** and **4b** + **5b**, respectively), when treated with *p*-toluenesulfonic acid monohydrate at 50 °C, afforded exclusively mixtures of **4a** + **6a** and of **4b** + **6b**, respectively. No other products were formed in these reactions. In a control experiment, it was established that pure **4a** or **4b**, when subjected to identical reaction conditions, could be recovered unchanged. Hence, the ratios **4a**:**6a** and **4b**:**6b** are considered to reflect the corresponding product

(1) (a) Robert A. Welch Postdoctoral Fellow, 1987–1989. (b) Robert A. Welch Postdoctoral Fellow, 1987.

(2) (a) van Seter, A. J. C.; Buza, M.; Klunder, A. J. H.; Zwanenburg, B. *Tetrahedron* **1981**, *37*, 1027. (b) Hirao, K.; Kajikawa, Y.; Abe, E.; Yonemitsu, O. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1791. (c) Nakazaki, M. *Top. Stereochem.* **1984**, *15*, 199. (d) For a review, see: Krow, G. R. *Tetrahedron* **1987**, *43*, 3.

(3) Marchand, A. P.; Arney, B. E., Jr.; Gilardi, R.; Flippen-Anderson, J. L. *J. Org. Chem.* **1987**, *52*, 3455.

(4) Marchand, A. P.; Annapurna, P.; Reddy, S. P.; Watson, W. H.; Nagl, A. *J. Org. Chem.* **1989**, *54*, 187.

(5) Marchand, A. P.; Annapurna, P.; Flippen-Anderson, J. L.; Gilardi, R.; George, C. *Tetrahedron Lett.* **1988**, *29*, 6681.

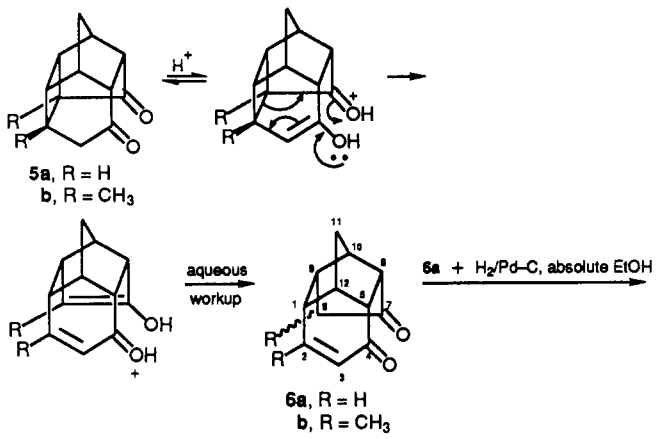
(6) Marchand, A. P.; Annapurna, P.; Flippen-Anderson, J. L.; Gilardi, R.; George, C.; Watson, W. H.; Nagl, A. *Abstracts of Papers*, 197th National Meeting of the American Chemical Society, Dallas, TX; April 9–14, 1989; American Chemical Society: Washington, DC, 1989; CHED 104.

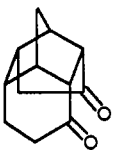
(7) Marchand, A. P.; Reddy, G. M.; Watson, W. H.; Nagl, A. *J. Org. Chem.* **1988**, *53*, 5969.

(8) Smith, P. A. S.; Baer, D. R. *Org. React. (N.Y.)* **1960**, *11*, 157.

0022-3263/89/1954-5086$01.50/0

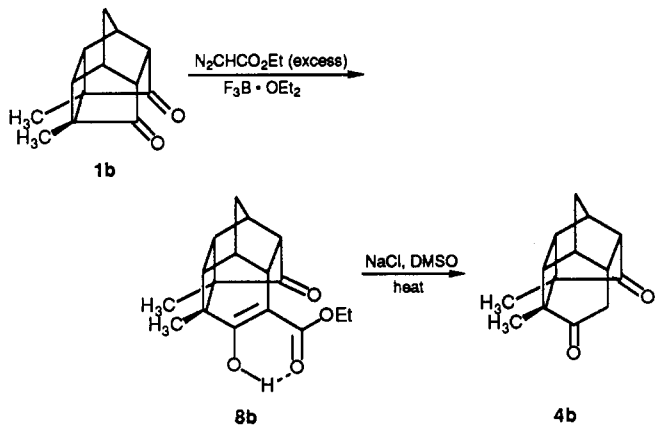
Scheme II





7

Scheme III



ratios **4a**:**5a** and **4b**:**5b**, respectively.

Compound **6a** proved to be unstable and difficult to handle. Structural characterization of **6a** was accomplished via its facile catalytic hydrogenation to the corresponding saturated tetracyclic diketone, **7**. The structure of **7** was established unequivocally by single-crystal X-ray structural analysis (vide infra).

1,7-Dimethyl-PCUD-8,11-dione (**1b**), when subjected to the reaction sequence shown in Scheme I, afforded diketone **4b** and enedione **6b** (product ratio 2:3). Compound **4b** was found to be identical in all respects with authentic material that was synthesized independently by using the route shown in Scheme III. Thus, reaction of **1b** with EDA (excess) in the presence of $F_3B{\cdot}OEt_2$ afforded **8b**. Decarboxylation of **8b**, which occurred when this compound was heated with NaCl–DMSO,[9] afforded material that was identical in all respects with **4b**. The structure of intermedate **8b** has been established previously via single-crystal X-ray structural analysis.[10]

The structure of the other product obtained from ring expansion of **1b** (i.e., **6b**) was established by analysis of its proton and carbon-13 NMR spectra and by comparison of these NMR spectra with the corresponding spectra of **6a**. Thus, the broad singlet in the proton NMR spectrum of **6b** at δ 6.55 (area 1 H) corresponds to the α-enone proton, H(3) (the corresponding proton in **6a** absorbs at δ 6.90). The C(8) methyl group protons at δ 0.95 appear as a doublet (J = 7.2 Hz) due to vicinal coupling to H(8), while the C(2) methyl group protons at δ 1.90 display allylic coupling to H(3) (J = 1.0 Hz). The carbon-13 NMR spectrum of **6b** reveals the presence of a conjugated (enone) carbonyl carbon resonance at δ 198.76 and an isolated carbonyl carbon resonance at δ 218.19. The α- and β-enone carbon atom resonances in **6b** [i.e., C(3) and C(2), respectively] occur at δ 125.78 (d) and at δ 163.53 (s), respectively. While the foregoing NMR data is consistent with structure **6b** in Scheme II, it is not sufficient to permit assignment of exo/endo stereochemistry to the C(8) methyl group.

X-ray Crystal Structure of 7

Compound **7** contains a norbornane moiety with a cyclohexanone ring fused across the 2,6-positions and a cyclopentanone ring fused across the 3,5-positions. The three five-membered rings in **7** reside in slightly twisted envelope conformations, while the six-membered ring occupies a slightly flattened chair conformation. Carbonyl carbon C(4) is in a planar environment, while the C(7) carbonyl carbon atom is slightly pyramidalized [i.e., C(7) lies 0.022 (5) Å out of the plane defined by the three atoms that are attached to C(7)]. The closest intramolecular contact of significance is H(3b)···H(8a) = 2.13 (5) Å. The bond lengths between contiguous carbon atoms that reside within the norbornane moiety are consistent with those observed and calculated previously for norbornane itself.[11-13]

Discussion

Recently, we reported the results obtained when several 1-substituted PCUD-8,11-diones were reacted with EDA (1 equiv) at 0 °C in tyhe presence of $F_3B{\cdot}OEt_2$.[4] Attack of the diazo ester occurred at the less hindered of the two carbonyl groups in the substrate [i.e., at C(8)]. This was followed by loss of nitrogen with concomitant C–C bond migration, thereby resulting in ring expansion. At first, it appeared that ring expansion in these systems occurred via regiospecific migration of the C(8)–C(9) bond in the substrate. However, it was found subsequently that these ring expansions are not regiospecific. The fact that a single monohomologation product was isolated in each case is due to the instability of the other monohomologation product [i.e., that which is formed via migration of the C(7)–C(8) bond in the substrate] to the reaction conditions. Similar results have been obtained for Tieffenau–Demjanov ring homologations of **1a** and **1b** in that both reactions proceed in nonregiospecific fashion to afford two monohomologation products, one of which is not stable to the workup conditions.

An important feature that distinguishes cage diketones **4a** and **4b** from cage diketones **5a** and **5b** is the fact that retro-Michael reaction in the former system would result in cleavage of a norbornane C–C bond but in the latter system results in cleavage of a cyclobutane C–C bond.

(9) (a) Krapcho, A. P.; Lovey, A. J. *Tetrahedron Lett.* **1973**, 957. (b) Krapcho, A. P.; Jahngen, E. G. E., Jr.; Lovey, A. J.; Short, F. W. *Tetrahedron Lett.* **1974**, 1091.

(10) Watson, W. H.; Nagl, A.; Marchand, A. P.; Reddy, G. M.; Reddy, S. P.; Dave, P. R. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1989**, *C45*, 263.

(11) Doms, L.; Van den Enden, L.; Geise, H. J.; Van Alsenoy, C. *J. Am. Chem. Soc.* **1983**, *105*, 158.

(12) Doms, L.; Van Hamelrijk, D.; Van de Mieroop, W.; Lenstra, A. T. H.; Geise, H. J. *Acta Crystallogr., Sect. B* **1985**, *B41*, 270.

(13) Allinger, N. L.; Geise, H. J.; Pyckhout, N.; Paquette, L. A.; Gallucci, J. C. *J. Am. Chem. Soc.* **1989**, *111*, 1106.

Since the former system is stable to acid but the latter is not, we conclude that the driving force for retro-Michael reaction can be found in the relief of strain that accompanies cleavage of a cyclobutane ring C–C bond in **5a** and **5b** and in other derivatives[4] of this ring system.

Interestingly, greater regioselectivity was observed to accompany nitrous acid deamination of **3a** (product ratio **4a**:**6a** = 1:4) as compared with the corresponding reaction of **3b** (product ratio **4b**:**6b** = 2:3). This result stands in contrast with the earlier observation by Liu and Majumdar[14] that monohomologation of unsymmetrically α-substituted cycloalkanones with EDA–$F_3B{\cdot}OEt_2$ generally proceeds with preferential migration of the *less substituted* of the two α-carbon atoms. Thus, we conclude that the regioselectivities of Tieffenau–Demjanov ring expansions and of the corresponding EDA-promoted ring expansions of substituted PCUD-8,11-diones are likely to be controlled by different factors.

Experimental Section

Melting points are uncorrected.

Base-Promoted Reaction of 1a with Nitromethane. To a cooled (0 °C) solution of **1a** (2.00 g, 11.5 mmol) and nitromethane (700 mg, 11.5 mmol) in methanol (10 mL) was added dropwise with stirring an aqueous solution of sodium hydroxide (700 mg, 17.5 mmol) in water (3 mL). After the addition of base had been completed, the reaction mixture was allowed to warm to ambient temperature and then was stirred for 2 h. Dilute 50% (v/v) aqueous acetic acid solution (2 mL) was then added, and the reaction mixture was concentrated in vacuo. Water (20 mL) was added to the residue, and the resulting mixture was extracted with methylene chloride (3 × 10 mL). The combined organic extracts were washed with water (3 × 10 mL), dried (anhydrous magnesium sulfate), and filtered. The filtrate was concentrated in vacuo, and the residue was recrystallized from a 1:1 ethyl acetate–hexane mixed solvent. Compound **2a** (2.1 g, 83%) was thereby obtained as a colorless microcrystalline solid: mp 133 °C; IR (KBr) 3300 (vs), 1520 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 1.60 (*AB*, J_{AB} = 10.2 Hz, 1 h), 1.95 (*AB*, J_{AB} = 10.2 Hz, 1 H), 2.50–2.95 (m, 8 H), 4.10 (br m, 1 H), 4.72 (br s, 2 H); ^{13}C NMR ($CDCl_3$) δ 41.75 (d), 42.08 (t), 43.52 (d), 43.84 (d), 44.94 (d), 47.21 (d), 47.64 (d), 57.29 (d), 57.62 (d), 81.03 (t), 88.31 (s), 119.20 (s); mass spectrum (70 eV), *m/e* (relative intensity) (no molecular ion), 174 (100), 92 (21), 91 (97).

Anal. Calcd for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.53. Found: C, 61.28; H, 5.63.

Base-Promoted Reaction of 1b with Nitromethane. This reaction was performed by using **1b** (2.0 g, 9.9 mmol) in the manner described above for the corresponding reaction of **1a** with nitromethane. Workup afforded **2b** (2.08 g, 80%) as a colorless microcrystalline solid: mp 156 °C; IR (KBr) 3300 (vs), 1520 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 1.00 (s, 3 h), 1.05 (s, 3 H), 1.50 (*AB*, J_{AB} = 10.2 Hz, 1 H), 1.80 (*AB*, J_{AB} = 10.2 Hz, 1 H), 2.10–3.10 (m, 7 H), 4.45 (*AB*, J_{AB} = 10.8 Hz, 1 H), 4.60 (*AB*, J_{AB} = 10.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 10.80 (q), 12.23 (q), 42.01 (d), 43.51 (t), 46.43 (d), 46.46 (d), 50.56 (d), 52.35 (s), 54.70 (s), 56.52 (d), 57.62 (d), 75.57 (t), 87.73 (s), 117.38 (s); mass spectrum (70 ev), *m/e* (relative intensity) (no molecular ion), 202 (100), 174 (34), 159 (61), 146 (32), 145 (26).

Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51. Found: C, 63.73; H, 6.55.

Catalytic Hydrogenation of 2a. To a solution of **2a** (1.50 g, 6.38 mmol) in 95% aqueous ethanol (25 mL) was added 5% palladized charcoal (200 mg). The resulting mixture was placed on a Parr shaker and hydrogenated at 50 psig at room temperature until hydrogen uptake had ceased (ca. 6 h). The catalyst was then removed by filtration through a Celite pad, and the filtrate was concentrated in vacuo. The residue was recrystallized from ethyl acetate, thereby affording **3a** (1.4 g, 93%) as a colorless microcrystalline solid: mp 131–132 °C; IR (KBr) 3400 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 1.50 (*AB*, J_{AB} = 10.2 Hz, 1 H), 1.90 (*AB*, J_{AB} = 10.2 Hz, 1 H), 2.40–3.00 (m, 11 H), 3.25 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 41.13 (d), 41.38 (d), 42.09 (t), 43.10 (t), 43.29 (d), 44.25 (d), 45.06 (d), 46.79 (d), 55.37 (d), 56.84 (d), 77.02 (s), 90.95 (s).

Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37. Found: C, 70.22; H, 7.57.

Catalytic Hydrogenation of 2b. This reaction was performed by using **2b** (2.0 g, 7.6 mmol) in the manner described above for the corresponding reaction of **2a**. Workup afforded **3b** (1.35 g, 90%) as a colorless microcrystalline solid: mp 164 °C; IR (KBr) 3400 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 0.90 (s, 3 H), 0.95 (s, 3 H), 1.40 (*AB*, J_{AB} = 10.2 Hz, 1 H), 1.75 (*AB*, J_{AB} = 10.2 Hz, 1 H), 2.20–3.10 (m, 8 H), 3.60 (br m, 3 H); ^{13}C NMR ($CDCl_3$) δ 10.99 (q), 12.30 (q), 41.17 (d), 42.01 (t), 43.12 (t), 43.51 (d), 46.50 (d), 46.63 (d), 51.83 (s), 52.87 (s), 55.35 (d), 57.82 (d), 75.57 (s), 90.72 (s).

Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.20. Found: C, 72.09; H, 8.28.

Nitrous Acid Deamination of 3a. To a cooled (0 °C) solution of **3a** (1.00 g, 4.80 mmol) in glacial acetic acid (10 mL) was added dropwise with vigorous stirring a solution of sodium nitrite (2.00 g, 29.9 mmol) in water (5 mL). After the addition of the aqueous sodium nitrite solution had been completed, the reaction mixture was allowed to warm to ambient temperature, and stirring was continued for 2 h. The resulting mixture was diluted with water (50 mL) and extracted with methylene chloride (3 × 20 mL). The combined extracts were washed successively with water (20 mL), saturated aqueous sodium bicarbonate solution (10 mL), and again water (10 mL). The organic layer was dried (anhydrous magnesium sulfate) and filtered, and the filtrate was concentrated in vacuo. The residue, judged by analysis of its ^{13}C NMR spectrum to be a mixture of **4a** and **5a**, was used as obtained without further purification.[15]

Reaction of the Product of Nitrous Acid Deamination of 3a with *p*-Toluenesulfonic Acid. To a solution of the product mixture, **4a** + **5a**, obtained above via nitrous acid deamination of **3a** (1.0 g, 5,3 mmol) in chloroform (20 mL) was added *p*-toluenesulfonic acid monohydrate (100 mg, 0.526 mmol). The resulting mixture was heated with stirring at 50 °C for 1 h. The reaction mixture was allowed to cool to room temperature, then washed successively with saturated aqueous sodium bicarbonate solution (10 mL) and water (10 mL), dried (anhydrous magnesium sulfate), and filtered. The filtrate was concentrated in vacuo, thereby affording an oil, which was purified by column chromatography (silica gel stationary phase, 30% ethyl acetate–hexane mixed solvent as eluent). The first chromatography fraction afforded diketone **4a** (140 mg, 14%) as a colorless microcrystalline solid: mp 233–234 °C (lit.[4] mp 233–234 °C). This material was identical in all respects with an authentic sample of **4a** that had been synthesized previously in our laboratory.[4] A control experiment established that pure **4a**, after treatment with *p*-toluenesulfonic acid monohydrate in chloroform solution at 50 °C for 1 h, could be recovered unchanged.

The second chromatography fraction afforded enedione **6a** (560 mg, 56%) as a colorless microcrystalline solid: mp 183–186 °C dec; IR (KBr) 1725 (s), 1660 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 1.60 (*AB*, J_{AB} = 10.5 Hz, 1 H), 1.90 (*AB*, J_{AB} = 10.5 Hz, 1 H), 2.20 (br s, 2 H), 2.70–3.05 (m, 6 H), 5.90 (*AB*, J_{AB} = 10.8 Hz, 1 H), 6.90 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 37.07 (t), 37.59 (d), 38.37 (d), 41.49 (t), 46.69 (d), 49.55 (d), 53.26 (d), 53.72 (d), 127.92 (d), 150.35 (d), 198.15 (s), 217.98 (s). Compound **6a** was unstable and proved to be difficult to handle and to purify. Accordingly, characterization of **6a** was completed via its facile reduction (via catalytic hydrogenation) to **7**, whose structure in turn was established unequivocally via single-crystal X-ray crystallography (vide infra).

Catalytic Hydrogenation of 6a. To a solution of enedione **6a** (600 mg, 3.19 mmol) in absolute ethanol (15 mL) was added 5% palladized charcoal (100 mg). The reaction mixture was hydrogenated with H_2 gas at 1 atm until uptake of hydrogen had ceased. The catalyst was removed by filtration through a Celite pad, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (silica gel stationary phase, 30% ethyl acetate–hexane as eluent). The eluate was recrystallized

(14) Liu, H. J.; Majumdar, S. P. *Synth. Commun.* **1975**, *5*, 125.

(15) The 300-MHz proton NMR spectra of product mixtures **4a** + **5a** and **4b** + **5b** are incompletely resolved, and each spectrum contains a large number of individual resonance peaks. Accordingly, we were unable to determine the product ratios in each case directly via spectral integration.

from an ethyl acetate–hexane mixed solvent, thereby affording pure **7** (540 mg, 90%) as a colorless microcrystalline solid: mp 274 °C dec; IR (KBr) 1715 (s), 1680 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 1.47 (*AB*, J_{AB} = 10.8 Hz, 1 H), 1.74 (*AB*, J_{AB} = 10.8 Hz, 1 H), 1.80–1.98 (m, 2 H), 2.12–2.30 (m, 3 H), 2.31 (br s, 1 H), 2.45 (*AB*, J_{AB} = 12.3 Hz, 2 H), 2.58–2.75 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 23.00 (t), 34.96 (t), 34.98 (d), 36.89 (t), 38.74 (d), 40.34 (t), 44.26 (d), 46.73 (d), 54.03 (d), 56.93 (d), 210.65 (s), 220.38 (s); mass spectrum (70 eV), *m/e* (relative intensity) 190 (molecular ion, 70), 162 (11).

Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.88; H, 7.48.

X-ray Crystallographic Analysis of 7. A colorless crystal of dimensions 0.18 × 0.43 × 0.45 mm was mounted on a Nicolet R3m/μ update of a $P2_1$ diffractometer. Unit cell dimensions were obtained via a least-squares refinement of 25 reflections: a = 14.765 (3) Å, b = 13.448 (2) Å, c = 11.420 (2) Å, β = 122.52 (1)°, V = 1912.0 (4) Å^3, monoclinic, $C2/c$, Z = 8, D_{calcd} = 1.322 g cm^{-3}, μ = 0.83 cm^{-1}. Intensity data were collected in the ω-scan mode ($3° \leq 2\theta \leq 45°$) with a variable scan rate of 4–29.3 deg min^{-1}) and graphite-monochromated Mo Kα radiation (λ = 0.710 73 Å). A total of 1251 independent reflections were measured, of which 1039 were $\geq 3\sigma(I)$. Lorentz and polarization corrections were made, and a ψ-scan based absorption correction was applied (transmission factors 0.891–0.866). The structure was solved by direct methods and refined by a block-cascade least-squares procedure. Hydrogen atoms were located in a difference map and were refined with isotropic thermal parameters. The structure was refined to R = 0.0520 and wR = 0.0716 with 183 parameters and 1039 reflections, S = 1.815, and $(\Delta/\sigma)_{max}$ = 0.007. The largest peaks in the final difference map were −0.18 and +0.37 e Å^{-3}. The function $\sum w(|F_o| - |F_c|)^2$ was minimized with $w = [\sigma^2(F_o) + 0.00091F_o^2]^{-1}$. All computer programs were supplied by Nicolet Instrument Corporation for Desktop 30 Microeclipse and Nova 4/C configuration. Atomic scattering factors and anomalous dispersion corrections were taken from the *International Tables for X-ray Crystallography*.[16] A structure drawing of **7** is shown in Figure 1 (supplementary material).

Nitrous Acid Deamination of 3b. This reaction was performed in the manner described above for the corresponding deamination of **3a**. The product, judged by analysis of its ^{13}C NMR spectrum to be a mixture of **4b** and **5b**, was used as obtained without further purification.[15]

Reaction of the Product of Nitrous Acid Deamination of 3b with *p*-Toluenesulfonic Acid. A chloroform solution of the product mixture, **4b** + **5b**, obtained above via nitrous acid deamination of **3b** (1.0 g, 4.3 mmol) was reacted with *p*-toluenesulfonic acid monohydrate in the manner described above for the corresponding reaction of **4a** + **5a**. Workup of the reaction mixture followed by column chromatographic purification of the residue afforded the two pure reaction products **4b** and **6b**. The first chromatography fraction afforded diketone **4b** (240 mg, 26%) as a colorless microcrystalline solid: mp 109.0–109.5 °C; IR (KBr) 1700 (s), 1450 (s), 1380 (s), 1160 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 0.80 (s, 3 H), 1.05 (s, 3 H), 1.45 (*AB*, J_{AB} = 10.6 Hz, 1 H), 1.65 (*AB*, J_{AB} = 10.6 Hz, 1 H), 2.35 (m, 4 H), 2.40–2.55 (m, 2 H), 2.68 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 12.96 (q), 17.77 (q), 38.51 (t), 39.16 (d), 39.69 (t), 40.59 (d), 43.14 (d), 43.30 (d), 46.14 (d), 48.09 (s), 53.05 (d), 53.09 (s), 210.10 (s), 220.21 (s); mass spectrum (70 eV), *m/e* (relative intensity) 216 (molecular ion, 27.0), 147 (18.9) 146 (49.4), 122 (17.6), 121 (100.0), 109 (15.9), 91 (25.3). A control experiment established that pure **4b**, after treatment with *p*-toluenesulfonic acid monohydrate in chloroform solution at 50 °C for 1 h, could be recovered unchanged.

Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.65; H, 7.49.

The second chromatography fraction afforded enedione **6b** (362 mg, 39%) as a colorless microcrystalline solid: mp 115–116 °C; IR (KBr) 1720 (s), 1645 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 0.95 (d, J = 7.2 Hz, 3 H), 1.60 (*AB*, J_{AB} = 10.5 Hz, 1 H), 1.80 (*AB*, J_{AB} = 10.5 Hz, 1 H), 1.90 (d, J = 1.0 Hz, 3 H), 2.42 (m, 2 H), 2.61–2.80 (m, 5 H), 6.55 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 10.54 (q), 26.24 (q), 37.03 (t), 42.67 (d), 45.15 (d), 48.15 (d), 49.06 (d), 49.12 (d), 51.80 (d), 52.18 (d), 125.78 (d), 163.53 (s), 198.76 (s), 218.19 (s); mass spectrum (70 eV), *m/e* (relative intensity) 216 (molecular ion, 22), 82 (100).

Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.96; H, 7.58.

Reaction of 1b with EDA/F_3B·OEt_2. Cage dione **1b** (700 mg, 3.49 mmol) was dissolved in anhydrous ether (50 mL) and cooled to 0 °C by application of an external ice bath. Boron trifluoride etherate (990 mg, 6.98 mmol) was then added slowly with stirring during 5 min. After all of the boron trifluoride etherate had been added, ethyl diazoacetate (1.19 g, 10.5 mmol) was then added slowly at such a rate that nitrogen was evolved at a slow, steady rate. The reacting mixture was stirred for 2 h after the addition of ethyl diazoacetate had been completed. The reaction mixture was allowed to warm slowly to room temperature and then stirred overnight (ca. 12 h) at room temperature. The reaction mixture was then cooled (ice bath), and the reaction was quenched via the addition of saturated aqueous sodium bicarbonate solution (15 mL). The ether layer was separated, and the aqueous layer was extracted with methylene chloride (25 mL). The combined organic extracts were washed with water (15 mL), dried (anhydrous sodium sulfate), and filtered, and the filtrate was concentrated in vacuo. The residue was purified via column chromatography (silica gel stationary phase, 10% ethyl acetate–hexane mixed solvent as eluent), thereby affording **8b** (740 mg, 74%). Analytically pure **8b** was obtained by recrystallization from hexane as a colorless microcrystalline solid: mp 111.5–112.5 °C; IR (KBr) 1720 (s), 1625 (s), 1595 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 1.03 (s, 3 H), 1.25 (t, J = 7.2 Hz, 3 H), 1.35 (s, 3 H), 1.50 (m, 1 H), 1.75 (d, J = 10.7 Hz, 1 H), 2.12 (br s, 1 H), 2.30 (m, 1 H), 2.50–2.75 (m, 3 H), 3.40–3.50 (m, 1 H), 4.05 (q, J = 7.2 Hz, 2 H), 12.08 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 12.63 (q), 14.06 (q), 17.20 (q), 37.91 (t), 40.40 (d), 41.08 (d), 41.89 (s), 42.67 (d), 44.20 (d), 44.60 (d), 55.02 (d), 56.83 (s), 60.40 (t), 99.02 (s), 170.93 (s), 175.85 (s), 218.22 (s); mass spectrum (70 eV), *m/e* (relative intensity) 288 (molecular ion, 20.1), 242 (100.0), 214 (47.0), 193 (25.0), 147 (95.2), 115 (20.0), 91 (40.1).

Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.95; H, 7.09.

Decarboxylation of 8b. The procedure of Krapcho and coworkers[9] was utilized to decarboxylate **8b**. Thus, a mixture of **8b** (500 mg, 1.73 mmol), sodium chloride (300 mg, 5.13 mmol), DMSO (5 mL), and water (5 drops) was heated at 150 °C under argon for 4 h. The reaction mixture was then poured into ice–water, and the resulting mixture was extracted with dichloromethane (2 × 35 mL). The combined organic layers were washed sequentially with water (3 × 25 mL) and brine (20 mL). The resulting dichloromethane solution was dried (anhydrous sodium sulfate) and filtered, and the filtrate was concentrated in vacuo. The residue was purified via column chromatography (silica gel stationary phase, 15% ethyl acetate–hexane mixed solvent as eluent) to afford the corresponding cage diketone, **4b** (340 mg, 91%). Recrystallization of this material from a 1:1 ethyl acetate–hexane mixed solvent afforded pure **4b** as a colorless microcrystalline solid: mp 109.0–109.5 C. Compound **4b** thereby obtained was identical in all respects with the corresponding material synthesized previously via reaction of the product of nitrous acid deamination of **3b** with *p*-toluenesulfonic acid (vide supra).

Acknowledgment. We thank the Air Force Office of Scientific Research (Grant AFOSR-88-0132, to A.P.M.), the Robert A. Welch Foundation (Grant B-963 to A.P.M., P-074 to W.H.W.), and the Faculty Research Committees of the University of North Texas and Texas Christian University for financial support of this study.

Supplementary Material Available: A structure drawing of **7** (Figure 1) and tables of atomic coordinates and isotropic thermal parameters, bond lengths, bond angles, anisotropic thermal parameters, and hydrogen atom coordinates and isotropic displacement parameters for **7** (4 pages). Ordering information is given on any current masthead page.

(16) *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, 1974; Vol. IV. (Present distributor, D. Reidel: Dordrecht.)