87682-13-1; (*R*)-R-CH(OH)-C≡C-R′ (R = *t*-Bu,R′ = *n*-Bu), 87682-14-2; (*R*)-R-CH(OH)-C≡C-R′ (R = *n*-Pr,R′ = H), 74364-79-7; (*R*)-R-CH(OH)-C≡C-R′ (R = *i*-Pr,R′ = H), 73522-97-1; (*R*)-R-CH(OH)-C≡C-R′ (R = T-Bu,R′ = H), 61317-72-4; (*S*)-R-CH(OH)-C≡C-R′ (R = Ph, R′ = H), 64599-56-0; (*R*)-R-CH(OH)-C≡C-R′ (R = *t*-Bu,R′ = $SiMe_3$), 89017-38-9; (*S*)-R-CH(OH)-C≡C-R′ (R = Ph, *R*′ = $SiMe_3$), 70975-25-6; R-CO-C≡C-R′ (R = Me,R′ = *n*-Bu), 1119-58-0; R-CO-C≡C-R′ (R = Et,R′ = *n*-Bu), 1817-61-4; R-CO-C≡C-R′ (R = *i*-Pr,R′ = *n*-Bu), 63098-60-2; R-CO-C≡C-R′ (R = *t*-Bu,R′ = *n*-Bu), 53723-95-8; R-CO-C≡C-R′ (R = *n*-Pr,R′ = H), 689-00-9; R-CO-C≡C-R′ (R = *i*-Pr,R′ = H), 13531-82-3; R-CO-C≡C-R′ (R = *t*-Bu,R′ = H), 5891-25-8; R-CO-C≡C-R′ (R = Ph, R′ = H), 3623-15-2; R-CO-C≡C-R′ (R = *t*-Bu,R′ = $SiMe_3$), 53723-94-7; R-CO-C≡C-R′ (R = Ph,R′ = $SiMe_3$), 13829-77-1; ((*S*)-2-MeBu)$_3$Al, 4023-25-0; *i*-$Bu_3Al_2Cl_3$, 12090-38-9; *i*-BuAl$Cl_2$, 1888-87-5; ((*S*)-2-MeBu)Al$Cl_2$, 82732-01-2; ((*S*)-2-MeBu)$_2$AlCl, 17303-81-0; 3,3-dimethyl-2-butanol, 464-07-3; (*S*)-3,3-dimethyl-2-butanol, 1517-67-5; 3,3-dimethyl-2-butanone, 75-97-8; isopropylphenylcarbinol, 611-69-8; (*S*)-isopropylphenylcarbinol, 34857-28-8; 1-chloro-1-phenyl-2-methylpropane, 936-26-5; 1-phenyl-2-methylpropene, 768-49-0; isopropyl phenyl ketone, 611-70-1; *tert*-butylphenylcarbinol, 3835-64-1; (*S*)-*tert*-butylphenylcarbinol, 24867-90-1; 1-chloro-1-phenyl-2,2-dimethylpropane, 1688-17-1; *tert*-butyl phenyl ketone, 938-16-9; cyclohexen-3-ol, 822-67-3; 1,3-cyclohexadiene, 592-57-4; 1-isobutylidene-2-cyclohexene, 89530-37-0; 2-isobutyl-1,3-cyclohexadiene, 89530-38-1; 3-chloro-cyclohexene, 2441-97-6; cyclohexen-3-one, 4096-34-8; 2-methyl-4-nonyl-3-ol, 6579-56-2; 1-(trimethylsilyl)-3-hydroxy-4,4-dimethylpentyne, 71321-14-7; 1-(trimethylsilyl)-3-hydroxy-3-phenylpropyne, 89530-34-7; 2,2,7-trimethyl-5-phenyl-2-silaoct-3-yn-5-ol, 89530-35-8; 2,2,7-trimethyl-5-phenyl-2-silaoct-3-yn-5-ene, 89530-36-9.

# Cyclopentannulation of Bicyclo[3.3.0]octane-3,7-dione. A More Convenient Synthesis of the [5]Peristylane System

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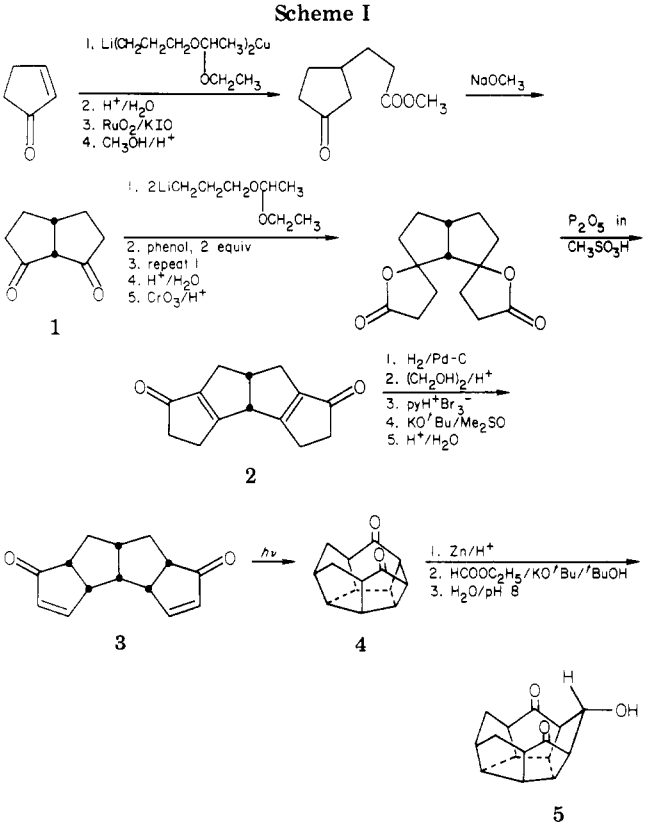
Mono- and biscyclopentannulation of the bicyclic title dione (**6**) is described. The first breaks the symmetry of the starting material and provides a triquinane (**19**) suited for elaboration into natural products having this skeleton. The second provides a pair of tetraquinane diones: one new (**13**), the other (**2**) the key precursor for the synthesis of the norperistylane (**4**) and peristylane (**5**) systems. The cyclopentannulation method used involves hydroxypropynylation, dehydration, and acid-catalyzed Nazarov cyclization.

Polyquinanes have achieved exceptional importance in the last decade; many new natural products with fused five-membered rings have been found, and there is increasing interest in fundamentally significant nonnatural products of this architecture.[1] Our particular concern has been with the convex, all-cis, all-syn polyquinanes that are precursors to new homo- and heteropolyhedranes. For example, our work toward a practical and logical synthesis of dodecahedrane has been focused on the elaboration of the $C_{15}$-hexaquinane system called peristylane (e.g., **5**). Our original synthesis of this system is shown in summary form in Scheme I.[2]

Although much used, the method in Scheme I suffers annoying practical limitations, e.g., the difficult solubility of bicyclo[3.3.0]octane-2,8-dione (**1**, 20 g/L in diethyl ether) and the little understood loss of yield with scale-up in stage 3. The effects of inflation have made these limitations more serious. The feedstocks (lithium metal, 3-bromo(or chloro)propanol, cuprous iodide, 2-cyclopentenone, etc.) have become so expensive, as has the labor to combine them, we have had no choice but to search out a new approach more suitable to our budget.

Bicyclo[3.3.0]octane-3,7-dione (**6**) is the most readily available biquinane functionalized in both rings. It was first prepared by Vossen and Schroeter decades ago.[3] Now it is accessible simply, cheaply, and in large quantities by the Bertz, Cook, and Weiss modification[4] of the early Weiss and Edwards method[5] for condensation of dimethyl 3-ketoglutarate with glyoxal followed by hydrolysis/decarboxylation.[3a,6] In 3 days of moderate effort it is no

Scheme I




(1) For an overview, see: Paquette, L. A. *Tetrahedron* **1981**, *37*, 4359–4559.

(2) (a) Eaton, P. E.; Mueller, R. H.; Carlson, G. R.; Cullison, D. A.; Cooper, G. F.; Chou, T-C.; Krebs, E. P. *J. Am. Chem. Soc.* **1977**, *99*, 2751. (b) Eaton, P. E.; Mueller, R. H. *Ibid.* **1972**, *94*, 1014.

(3) (a) Vossen, G. Dissertation, University of Bonn, 1910. (b) Schroeter, G. *Justus Liebigs Ann. Chem.* **1922**, *426*, 1.

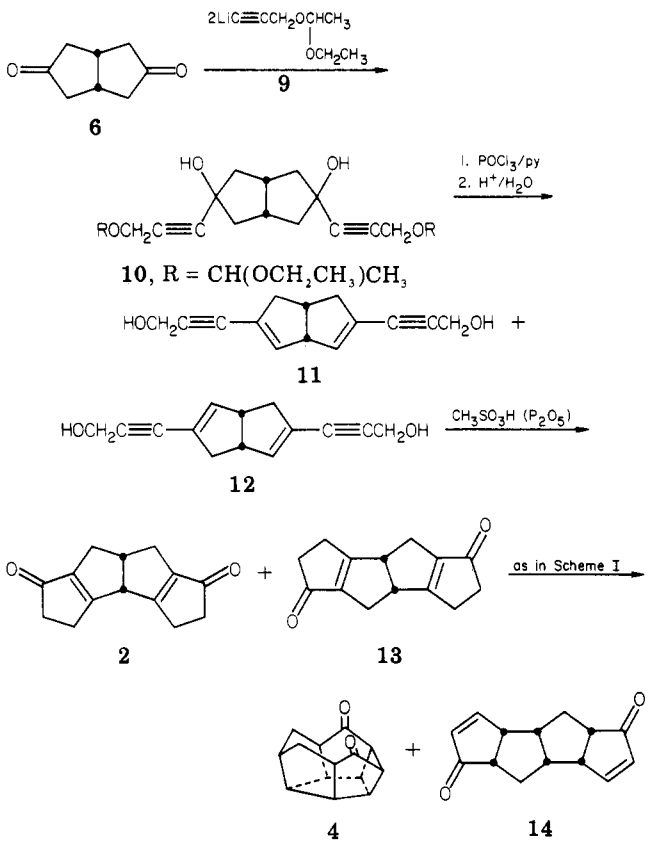
(4) (a) Bertz, S. H.; Cook, J. M.; Gawish, A.; Weiss, U. *Org. Synth.*, in press. We are grateful to Drs. Bertz and Cook for information concerning this procedure. (b) Bertz, S. H.; Rihs, G.; Woodward, R. B. *Tetrahedron* **1982**, *38*, 63.

(5) Weiss, U.; Edwards, J. M. *Tetrahedron Lett.* **1968**, 4885.

(6) Yates, P.; Hand, E. S.; French, G. B. *J. Am. Chem. Soc.* **1960**, *82*, 6347.

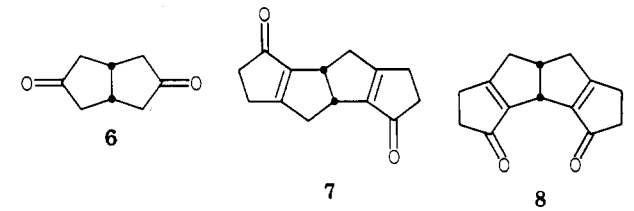
0022-3263/84/1949-1728$01.50/0 

Scheme II




problem to accumulate 150 g of this dione at very reasonable cost.

Cyclopentannulation via hydroxypropylation,[2,7] the method in Scheme I, always puts the "new" carbonyl carbon $\alpha$ to what was the "old" carbonyl carbon. Application of this methodology to the 3,7-dione **6** therefore gives the tetraquinanes **7** and **8**, interesting compounds but not at the focus of this paper.[8,9] The conversion of **6** to




the needed tetraquinane **2** requires a different cyclopentannulation strategy, one that places the new carbonyl carbon directly attached to what was the old one. Fortunately, the methodology is already available from the work of Raphael et al.[10] and its extensions.[9,11] In the derived form used here (Scheme II) the 3,7-dione **6** is added to an excess of the lithium propargylide **9**, prepared from the corresponding protected propargyl alcohol.[12] The diadduct **10** is formed readily in good yield provided the propargylide is used in excess. Hydrolysis to the corresponding tetrol can be accomplished cleanly, but Nazarov cyclization[13] of this tetrol under a wide variety of conditions gives only a low to moderate yield of the expected tetraquinanes **2** and **13** and then in an unfavorable 1:6 ratio. It is better to proceed stepwise. Dehydration of **10** with phosphorus oxychloride in pyridine followed by mild hydrolysis with aqueous methanolic acid gives the bis-enynol **11** and its double-bond positional isomer **12** in good overall yield and in a ratio of almost 1:1.

These isomers are very similar. It is possible, albeit tedious, to separate them almost completely by careful HPLC. Fortunately, the only overlap of resonances in the 500-MHz $^1$H NMR spectrum is that of the carbinol methylene protons. Thus, their individual identities can be determined: isomer **11** ($C_s$ symmetry) shows two types of ring junction protons ($\delta$ 3.88 and 3.05); isomer **12** ($C_2$ symmetry) shows only one ($\delta$ 3.49).

Acid cyclization of bis-enynol **11** with methanesulfonic acid at room temperature gives the known tetraquinane **2** and little if any of the alternative **13**. Vice versa, cyclization of **12** gives the previously unknown tetraquinane **13** and little or none of **2**. Thus, and remarkably, under the conditions of reaction, **11** and **12** do not interconvert.

The separation of **11** and **12** is too difficult to make part of a practical synthetic scheme, but cyclization of the mixed isomers proceeds well, particularly in methanesulfonic acid containing 0.5 wt % of $P_2O_5$. The yield is higher (77% vs. 64%) than that in the absence of the $P_2O_5$, and the ratio of **2**:**13** (2:3 vs. 1:2) is distinctly more favorable. The reason for these changes is not understood. Interestingly, the use of more concentrated $P_2O_5$ in methanesulfonic acid,[14] although very successful in other instances,[2,9] gives much lower yields in the case at hand.

Like their precursors, **2** and **13** are separable only with difficulty. They can, however, be taken together without hazard through the ketalization/bromination/dehydrobromination/hydrolysis procedure developed earlier for the original preparation of the peristylane system (Scheme I).[2] At the end, the product bis-enones **3** and **14** are separable; **14** is much less soluble in benzene than **3**. Alternatively, advantage can be taken of the ready photochemical closure of **3** to the norperistylane **4**; $2\pi + 2\pi$ photoclosure of **14** is geometricallly difficult (vide infra).

It is routinely possible by this method to prepare 15 g of pure norperistylane **4** (and thence the peristylane **5**) from 100 g of **6**. Although this does not compare favorably on a gram-for-gram basis with the approach in Scheme I (20 g of **1** gives 5 g of **4**), the much greater availability of **6**, the lesser expense of the required reagents, and the ease of scale-up make the new scheme clearly the one of choice. In addition, there is the potentially profitable fallout of the otherwise unknown tetraquinane **14** (25 g from 100 g of **6**).

The structure assignment to the tetraquinane bis-enone **14** follows reasonably from the compound's origins. Further, its proton-decoupled $^{13}$C NMR spectrum is completely consistent with the $C_2$ symmetry of the structure; the 14 carbons give rise to only seven resonance lines. Although the all-cis, all-syn stereochemistry of the junctions in **14** holds the molecule in a convex geometry forcing the outer rings close together, they are not positioned properly for $2\pi + 2\pi$ photocyclization as inspection of a

(7) Eaton, P. E.; Cooper, G. F.; Johnston, R. C.; Mueller, R. H. *J. Org. Chem.* **1972**, *37*, 1947.

(8) Both compounds have actually been prepared by this method [Eaton, P. E.; Kunai, A., this Laboratory, unpublished results]: **7**, mp 208–209 °C (lit.[9] mp 205–206.5 °C); **8**, mp 170–171 °C.

(9) McKervey, M. A.; Vibuljan, P.; Ferguson, G.; Siew, P. Y. *J. Chem. Soc., Chem. Commun.* **1981**, 912.

(10) (a) Raphael, R. A.; Islam, A. M. *J. Am. Chem. Soc.* **1953**, 2247. (b) MacAlpine, G. A.; Raphael, R. A.; Shaw, A.; Taylor, A. W.; Wild, H. J. *J. Chem. Soc., Perkin Trans. 1* **1976**, 410.

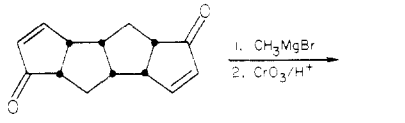
(11) (a) Karpf, M.; Dreiding, A. S. *Helv. Chim. Acta* **1976**, *59*, 1226. (b) Baumann, M.; Hoffmann, W.; Müller, N. *Tetrahedron Lett.* **1976**, *40*, 3585.

(12) Salomon, R. G.; Ghosh, S.; Zagorski, M. G.; Reitz, M. *J. Org. Chem.* **1982**, *47*, 829.

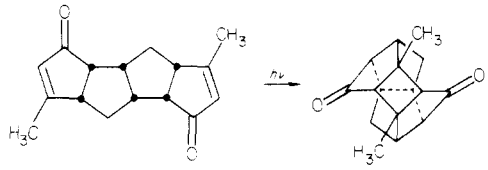
(13) For a review, see: Santelli-Rouvier, C.; Santelli, M. *Synthesis* **1983**, 429.

(14) Eaton, P. E.; Carlson, G. R.; Lee, J. T. *J. Org. Chem.* **1973**, *38*, 4071.

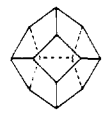
molecular model will show. Indeed, quite unlike its sibling **3**, **14** is resistant to light-induced closure. On the other hand, after a double enone transposition,[15] as shown, **14** becomes **15**[16] in which the double bonds are arranged neatly for photocyclization to the cyclobutane **16**. These processes proceed smoothly in 70% overall yield. Compound **16** and its desmethyl analogue (available from **7**) seem choice precursors for the $D_{3h}$-($4^3.5^6$)nonahedrane skeleton **17**. Work along these lines is in progress.




14

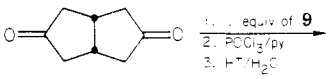



15 16

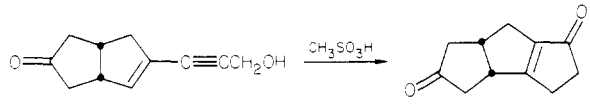


17

Cyclopentannulation of dione **6** can be controlled to give mono- rather than bis-annulated product, that is, the triquinane **19** instead of the tetraquinanes **2** and **13**. The only modification required in the general scheme is to use inverse addition of the lithium propargylide **9** in correct stoichiometry *to* dione **6** in THF at dry ice–acetone temperature. Careful quenching of the cold product suspension *into* aqueous pH 7.5 phosphate buffer sidesteps otherwise troublesome aldol condensations. Subsequent dehydration, deprotection (→ **18**), and cyclization gives **19** in 26% overall yield (not optimized). This monocyclopentannulation breaks the symmetry of **6** usefully and should thereby provide a way to incorporate this readily available starting material into, for example, the synthesis of natural products with the triquinane skeleton.[1]




6




18 19

## Experimental Section

Proton magnetic resonance ($^1$H NMR) spectra at 500 MHz (University of Chicago DS-1000 instrument) of solutions in deuteriochloroform (or deuteriobenzene) were taken in the pulsed-Fourier mode and were referenced to internal chloroform ($\delta$ = 7.26 ppm). Shifts are reported in ppm downfield from $Me_4Si$ to a precision of ±0.02 ppm. Splittings are reported in standard fashion; "st" indicates additional fine structure. Coupling constants are precise to ±1 Hz. Carbon magnetic resonance ($^{13}$C NMR) spectra were taken similarly at 50.31 MHz on a Nicolet NTC/200 W.B. spectrometer. Chemical shifts were referenced to the center line of internal deuteriochloroform ($\delta$ = 77.0 ppm) and are reported in ppm downfield from $Me_4Si$ to the nearest 0.1 ppm. Ultraviolet spectra were taken of methanol solutions with a Perkin-Elmer Lambda 5 spectrophotometer. Infrared spectra were recorded on a Pye-Unicam SP-1000 instrument using the polystyrene 1602-cm$^{-1}$ band for calibration. Absorptions of importance are reported to ±3 cm$^{-1}$. VPC analyses were performed on a Hewlett-Packard 5830A analytical instrument using 2% OV-17 (6 ft × $^1/_4$ in. glass) column at oven temperatures in the range of 200–220 °C.

Solvents were purchased as bulk reagent grade and then dried and distilled before use by standard procedures. "Evaporation" and "concentration" of solvents refers to the use of a rotary evaporator operating at about 40 torr with the bath near room temperature. Silica gel columns were slurry packed with E. Merck 70–230-mesh material. The composition of the eluents is given in volume percentage.

Melting points are uncorrected. Microanalyses were done by MicAnal, Tucson, AZ.

**3,7-Bis(3-hydroxypropynyl)bicyclo[3.3.0]octa-2,7- and -2,6-dienes (11 and 12). A. Formation and Addition of Lithium Reagent 9.** A solution of α-ethoxyethyl propargyl ether[12] (384 g, 3.00 mol) in dry THF (1.5 L) was placed in a 6-L kettle equipped with a Vibromixer, thermometer, addition funnel, and nitrogen inlet. The solution was cooled to −70 °C by using a dry ice–acetone bath. A commercial solution of *n*-butyllithium in hexane (Aldrich, 10.2 M, 275 mL, 2.80 mol) was added over 1 h. The brown reaction mixture was then allowed to warm up to 0 °C overnight. The solution of the organolithium reagent **9** so formed was recooled to −70 °C, and dione **6** (96.6 g, 0.70 mol) in 300 mL of dry THF was added slowly over about 2 h. The cold bath was removed; the reaction mixture was allowed to warm to room temperature over 1 h. The reaction was quenched carefully by slow addition with vigorous stirring of saturated aqueous ammonium sulfate (400 mL). The organic layer was separated; the aqueous phase was extracted with ethyl acetate (4 × 300 mL). The combined organic phase was washed with brine and dried over $Na_2SO_4$. Filtration and evaporation of the solvents left a brown oil, from which the residual propargyl ether was removed by distillation at 50 °C (1 torr). The crude residue of diadduct **10** [296 g, 110%; IR ($CHCl_3$) 3400 cm$^{-1}$, no carbonyl absorption] was used in the next step without further purification.

**B. Dehydration and Deprotection.** Phosphorus oxychloride (245 g, 1.6 mol) was added to a cold (ice bath), mechanically stirred solution of crude **10** in pyridine (700 mL) at a rate sufficient to maintain the temperature of the reaction mixture below 20 °C. After the addition was completed (1.5 h), the heterogeneous mixture was stirred for 1 h at room temperature and then poured into 2.5 L of ice water. The dark solution was extracted with ethyl acetate (4 × 600 mL). The extract was washed with 10% hydrochloric acid (2 × 500 mL), followed by brine. Evaporation of the solvent left a crude olefin mixture (240 g), which was deprotected by stirring for 5 h at room temperature with 1:9 aqueous methanol (1 L) containing 10 mL of concentrated hydrochloric acid. Solid potassium carbonate (15 g) was added, and the suspension was stirred for 0.5 h. Methanol was evaporated. The residue was taken up in ethyl acetate (1.2 L), and the solution was washed with brine and dried over $Na_2SO_4$. Evaporation of the solvent left 140 g of solid; this was stirred with 400 mL of methylene chloride. Filtration gave 76 g (51%) of a mixture of the two isomers **11** and **12** in a ratio of 47:53 (by $^1$H NMR). The mother liquor was concentrated and passed through a silica gel column using 10% ethyl acetate in methylene chloride as eluent. Evaporation of the eluate provided another 14 g (total yield 60% from **6**) of material. Careful high-pressure liquid chromatography using the Waters Prep 500 with a silica gel column and the same eluting solvent gave the individual components in better than 90% purity; **11** was eluted a little faster than **12**: UV of the mixture λ 229 nm (ε 23 000); IR of the mixture (KBr) ν 3280, 2220 cm$^{-1}$. $^1$H NMR ($CDCl_3$) of **11**: $\delta$ 5.93 (2 H, br s), 4.38 (4 H, s), 3.88 (1 H, m), 3.05 (1 H, m), 2.79 (2 H, d of d, $J$ = 16, 8 Hz), 2.28 (2 H, d with st, $J$ = 16 Hz), 1.55 (2 H, br s). $^1$H NMR ($CDCl_3$) of **12**: $\delta$ 5.82 (2 H, br s), 4.38 (4 H, s), 3.49 (2 H, m), 2.72 (2 H, m), 2.31 (2 H, d, $J$ = 16.5 Hz), 1.55 (2 H, br s). Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.14; H, 6.66.

(15) (a) Dauben, W. G.; Michno, D. M. *J. Org. Chem.* **1977**, *42*, 1977. (b) Buchi, G.; Egger, B. *Ibid.* **1971**, *36*, 2021. (c) Mehta, G.; Srikrishna, A.; Reddy, A. V.; Nair, M. S. *Tetrahedron* **1981**, *37*, 4543.

(16) This particular tetraquinanedione should also be available via hydroxypropylation, etc., starting with bicyclo[3.3.0]octane-2,6-dione.[9]

**Tetracyclo[6.6.0.0$^{2,6}$.0$^{9,13}$]tetradeca-2(6),9(13)-diene-5,12-dione (13) and Tetracyclo[6.6.0.0$^{2,6}$.0$^{10,14}$]tetradeca-2(6),10-(14)-diene-5,11-dione (2).** A suspension of phosphorus pentoxide (15 g, 0.11 mol) in methanesulfonic acid (Aldrich, 98%, 3 kg) was placed in a 4-L, jacketed kettle equipped with a Vibromixer, funnel, and nitrogen inlet. Cold water (20 °C) was circulated through the jacket. The powdered bis-enynol mixture of **11** and **12** (76 g) was added slowly over 3 h with vigorous stirring (faster addition resulted in a marked decrease in yield). The dark reaction mixture was stirred for another 4 h and then poured into 6 L of water with stirring. The solution was extracted with methylene chloride (5 × 500 mL). The extract was washed with water (1 L), followed by brine, and dried over $Na_2SO_4$. Evaporation of the solvent left a dark residue, which was charged onto a silica gel (1 kg) column. Elution with methylene chloride removed most of the dark colored material. Subsequent elution with ethyl acetate furnished a mixture of bis-enones **2** and **13** (58 g, 77%) as a pale yellow solid. Further purification was not pursued. IR ($CHCl_3$) $\nu$ 1692, 1640 cm$^{-1}$.

**Tetracyclo[6.6.0.0$^{2,6}$.0$^{9,13}$]tetradeca-3,10-diene-5,12-dione (14) and Hexacyclo[6.6.0.0$^{2,6}$.0$^{3,13}$.0$^{4,12}$.0$^{10,14}$]tetradecane-5,11-dione (Norperistylanedione, 4). A. Hydrogenation.** The crude mixture of bis-enones **2** and **13** (58 g) obtained in the last experiment was hydrogenated in acetone (2 L) over 10% Pd–C (8 g) as described earlier[2] to furnish 59 g (quantitative) of the corresponding saturated diketones. VPC analysis of this mixture indicated a 3:2 ratio of the two isomers, favoring tetrahydro **13**.

**B. Ketalization.** The diketone mixture (10 g) was ketalized as described earlier[2] with ethylene glycol (50 mL) in benzene (350 mL) in the presence of methanesulfonic acid (0.2 mL). Refluxing under a Dean–Stark trap for 20 h and workup furnished 13 g of the mixture of bis-ketals.

**C. Bromination.** Bromination of the bis-ketal mixture (13 g) with pyridinium hydrobromide perbromide (90%, 31.5 g, 0.089 mol) in dry THF (200 mL) as described earlier[2] gave 21 g of the mixture of dibromides.

**D. Dehydrobromination.** The bromide mixture was stirred with potassium *tert*-butoxide (23 g, 0.21 mol) in dry (!) $Me_2SO$ (200 mL) for 40 h at room temperature.[2] The dark mixture was diluted with water (200 mL) and extracted with benzene (800 mL and then 2 × 200 mL). The extract was washed with water (3 × 200 mL), followed by brine, and then dried over $Na_2SO_4$ and evaporated. The residue was flushed through a silica gel (50 g) column with 10% ethyl acetate in methylene chloride. Evaporation of the eluate gave a mixture of bis-ketals (11 g), which solidified on standing.

**E. Hydrolysis.** Methanesulfonic acid was added dropwise to a solution of the bis(ene ketal) mixture in THF–water (2:1, 50 mL) until the solution was at pH 2. The solution was stirred for 5 min and then neutralized with aqueous $NaHCO_3$ and extracted with methylene chloride (3 × 50 mL). The extract was washed with brine and dried over $Na_2SO_4$. Evaporation of the solvent left a mixture of bis-enones **3** and **14** (8 g). This was triturated with 100 mL of benzene; the less soluble bis-enone **14** was removed as white, sugarlike crystals. These were washed with more benzene (20 mL) and dried in vacuo to furnish 4 g of pure **14**: mp 218–220 °C ($CH_2Cl_2$–hexane); UV $\lambda$ 226 ($\epsilon$ 14370), 320 (84) nm; IR (KBr) $\nu$ 1692, 1580 cm$^{-1}$; $^1$H NMR ($C_6D_6$) $\delta$ 6.62 (2 H, d, of d, $J$ = 5.7, 2.7 Hz), 5.74 (2 H, d of d, $J$ = 5.7, 2 Hz), 2.78 (2 H, t, $J$ = 7.5 Hz), 2.51 (2 H, d of t, $J$ = 9.5, 7.2 Hz), 2.12 (2 H, q, $J$ = 7 Hz), 1.5 (2 H, m), 1.04 (2 H, q, $J$ = 10.5 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 211.9 (s), 163.8 (d), 133.3 (d), 51.9 (d), 49.61 (d), 49.59 (d), 27.2 (t). Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.42; H, 6.63. No attempt was made to isolate **3**.

**F. Photoclosure.** The benzene solution of **3** obtained above was taken in a Pyrex vessel, purged with a slow stream of nitrogen for 10 min, and then irradiated with use of an Hanovia, 450-W, medium-pressure, mercury arc lamp as described earlier,[2] monitoring the reaction by $^1$H NMR. Afterward the solvent was evaporated. The residue was charged on to a silica gel (70 g) column. Elution with 5% ethyl acetate in methylene chloride furnished norperistylanedione (**4**, 2.7 g, 67% from **2**), whose identity was confirmed by spectral comparison with an authentic sample. Elution with 20% ethyl acetate in methylene chloride furnished an additional 0.5 g (total yield 75% from **13**) of the bis-enone **14**.

**5,12-Dimethyltetracyclo[6.6.0.0$^{2,6}$.0$^{9,13}$]tetradeca-4,11-diene-3,10-dione (15).** A solution of methylmagnesium bromide in diethyl ether (Aldrich, 2.5 M, 1.5 mL, 3.7 mmol) was added to a magnetically stirred suspension of bis-enone **14** (0.214 g, 1.0 mmol) in dry THF (5 mL) under nitrogen. The reaction mixture was stirred for 15 min at room temperature and then quenched by a careful addition of saturated aqueous ammonium sulfate solution. The mixture was extracted with methylene chloride (2 × 20 mL). The extract was washed with brine and dried over $Na_2SO_4$. Evaporation of the solvent left crude solid diol (245 mg, quantitative). This was dissolved in acetone and the solution cooled in an ice bath. Standard Jones reagent[17] (1.26 M, 1.6 mL, 2.1 mmol) was added with stirring. After 15 min at room temperature, the excess reagent was destroyed by addition of isopropyl alcohol (1 mL). The volatiles were evaporated. The green residue was taken up in water (10 mL) and the solution extracted with methylene chloride (2 × 10 mL). The extract was washed with aqueous $NaHCO_3$, followed by brine, and dried over $Na_2SO_4$. Concentration of the solvent and clean up through a silica gel (10 g) column using 30% ethyl acetate in methylene chloride as eluent furnished the transposed bis-enone **15** (170 mg, 70% from **14**): mp 184–86 °C ($CH_2Cl_2$–hexane); UV $\lambda$ 229 ($\epsilon$ 25700), 310 (130) nm; IR ($CHCl_3$) $\nu$ 1682, 1611 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 5.66 (2 H, br s), 3.25 (2 H, q, $J$ = 8 Hz), 3.03 (2 H, t, $J$ = 8 Hz), 2.96 (2 H, m), 2.2 (2 H, t of d, $J$ = 11, 7.5 Hz), 2.03 (6 H, s), 0.93 (2 H, q, $J$ = 11 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 209.9 (s), 182.0 (s), 128.9 (d), 53.7 (d), 52.5 (d), 48.9 (d), 30.9 (t), 18.2 (q). Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.23; H, 7.75.

**5,12-Dimethylhexacyclo[6.6.0.0$^{2,6}$.0$^{4,12}$.0$^{5,11}$.0$^{9,13}$]tetradecane-3,10-dione (16).** An ethyl acetate solution (50 mL) of the transposed bis-enone **15** (100 mg) was purged with a slow stream of nitrogen for 10 min and then irradiated through Pyrex with use of a Hanovia, 450-W, medium-pressure mercury vapor lamp. The progress of the reaction was monitored by VPC. When it was over (15–20 min), the solvent was evaporated. The residue was crystallized from ethyl acetate and then sublimed at 100 °C (0.1 torr) to give the hexacyclic dione **16**: mp 285 °C dec; IR $\nu$ 1715 cm$^{-1}$; $^1$H NMR ($C_6D_6$) $\delta$ 2.68 (2 H, t, $J$ = 8 Hz), 2.44 (2 H, m), 2.28 (2 H, s), 2.22 (2 H, t, $J$ = 8 Hz), 2.08 (2 H, d, $J$ = 14 Hz), 1.4 (2 H, t of d, $J$ = 14, 7 Hz), 0.93 (6 H, s); $^{13}$C NMR ($CDCl_3$) $\delta$ 216.1 (s), 64.6 (d), 58.9 (d), 55.4 (d), 45.3 (d), 41.0 (s), 33.7 (t), 31.4 (q). Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.45; H, 7.51.

**7-(3-Hydroxypropynyl)bicyclo[3.3.0]oct-6-en-3-one (18). A. Addition of Lithium Propargylide 9.** A solution of lithium propargylide **9** [prepared from ethoxyethyl propargyl ether (1.4 g, 11.0 mmol) and *n*-butyllithium (1.5 M in hexane, 7 mL, 10.5 mmol) in dry THF (10 mL) as described earlier] was added slowly to a cold (−70 °C, dry ice–acetone bath), magnetically stirred solution of diketone **6** (1.38 g, 10 mmol in dry THF (15 mL). The brown mixture was stirred at −70 °C for 1 h and then poured into a stirred solution of disodium hydrogen phosphate–sodium dihydrogen phosphate buffer (pH 7.5, 20 mL). The aqueous phase was extracted with ethyl acetate (3 × 30 mL). The extract was washed with brine and dried over $Na_2SO_4$. Evaporation of solvent left crude alcohol (2.4 g, 90%), which was used in the next step without purification.

**B. Dehydration and Deprotection.** Phosphorus oxychloride (1.6 g, 10.5 mmol) was added dropwise to a cold (ice bath), magnetically stirred solution of the crude alcohol in pyridine (10 mL). The reaction mixture was stirred for 2 h at room temperature and then poured in ice water (20 mL). The solution was extracted with ethyl acetate (4 × 20 mL). The extract was washed with 5% hydrochloric acid (2 × 20 mL), followed by brine, and then dried over $Na_2SO_4$. Evaporation of the solvent left 1.4 g of a viscous oil, which was stirred for 5 h at room temperature with 1:9 aqueous methanol (30 mL) containing 0.3 mL of concentrated hydrochloric acid. Solid potassium carbonate (2 g) was added and the suspension stirred for 30 min. The methanol was evaporated. The residue was taken up in ethyl acetate (70 mL); the solution was washed with brine and dried over $Na_2SO_4$. The residue left on evaporation was charged onto a silica gel (12 g) column. Elution with 5% ethyl acetate in methylene chloride

(17) Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley: New York, 1967; Vol. 1, p 142.

furnished the enynolone **18** (670 mg, 38% from **6**), which was crystallized from $CH_2Cl_2$–hexane: mp 77–79 °C; UV λ 232 nm (ε 12 200); IR ($CHCl_3$) ν 3450, 2215, 1738 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 5.72 (1 H, s), 4.39 (2 H, s), 3.52 (1 H, m), 3.02 (1 H, quintet with st, $J$ = 8 Hz), 2.86 (1 H, t of d of d, $J$ = 17, 8, 3 Hz), 2.52 (1 H, d of d, $J$ = 19, 10 Hz), 2.47 (1 H, d of d of d, $J$ = 19, 10, 2.5 Hz), 2.32 (1 H, d of d, $J$ = 17, 2 Hz), 2.26 (1 H, d, $J$ = 19 Hz), 2.06 (1 H, d of d, $J$ = 19, 8 Hz), 1.7 (1 H, br s). Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 74.98; H, 7.13. Further elution of the column with 10% ethyl acetate in methylene chloride gave a mixture of bis-enynols **11** and **12** (160 mg, 7.5% from **6**).

**Tricyclo[6.3.0.0$^{2,6}$]undec-1(8)-ene-4,9-dione (19).** The enynolone **18** (200 mg) was added in small batches to 7 mL of magnetically stirred methanesulfonic acid over a period of 30 min. The dark mixture was stirred at room temperature for 3 h and then poured in water (20 mL). The solution was extracted with methylene chloride (3 × 15 mL). The extract was washed with water, followed by brine, and dried over $Na_2SO_4$. Evaporation of the solvent followed by passage of the residue through a silica gel (10 g) column using 20% ethyl acetate in methylene chloride as eluent furnished triquinane **19** (140 mg, 70%) as an oil, which was distilled bulb-to-bulb: bp 120 °C (bath) (0.1 torr); UV λ 241 (ε 11 350), 298 (980) nm; IR ($CHCl_3$) ν 1730, 1692, 1638 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 3.57 (1 H, m), 3.46 (1 H, quintet with st, $J$ = 8 Hz), 2.78 (2 H, t, $J$ = 5 Hz), 2.75 (1 H, m), 2.65 (1 H, d of d, $J$ = 18, 9 Hz), 2.55 (1 H, d of d, $J$ = 18, 10 Hz), 2.51 (2 H, m), 2.36 (1 H, d with st, $J$ = 16 Hz), 2.26 (1 H, d, $J$ = 16 Hz), 2.09 (1 H, d of d, $J$ = 18, 7.5 Hz); $^{13}C$ NMR ($CDCl_3$) δ 217.4 (s), 203.9 (s), 186.0 (s), 147.6 (s), 44.8 (d), 44.7 (t), 42.9 (d), 40.8 (t), 39.3 (t), 32.0 (t), 24.2 (t); mp 60–61 °C (ether). Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.98% H, 6.86. Found: C, 74.78; H, 6.75.

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**Registry No.** **2**, 89487-21-8; **2** (tetrahydro derivative), 36269-15-5; **2** (tetrahydro bisketal), 63127-34-4; **2** (tetrahydro dibromo bisketal), 63127-35-5; **3**, 36269-16-6; **4**, 36269-18-8; **6**, 51716-63-3; **6** (adduct with **9**), 89487-28-5; **9** (alkyne), 18669-04-0; **10**, 89487-16-1; **11**, 89487-18-3; **11** (α-ethoxyethoxy ether), 89487-17-2; **12**, 89487-19-4; **12** (α-ethoxyethoxy ether), 89487-32-1; **13**, 89487-20-7; **13** (tetrahydro derivative), 89487-22-9; **13** (tetrahydro bisketal), 89487-23-0; **13** (tetrahydro dibromo bisketal), 89487-24-1; **14**, 89487-25-2; **15**, 89487-26-3; **16**, 89487-27-4; **18**, 89487-30-9; **18** (α-ethoxyethoxy ether), 89487-29-6; **19**, 89487-31-0.

# Synthesis of Trialkylacetic Acids by the Anodic Oxidation of 3,3-Disubstituted-2-oxo Carboxylic Acids

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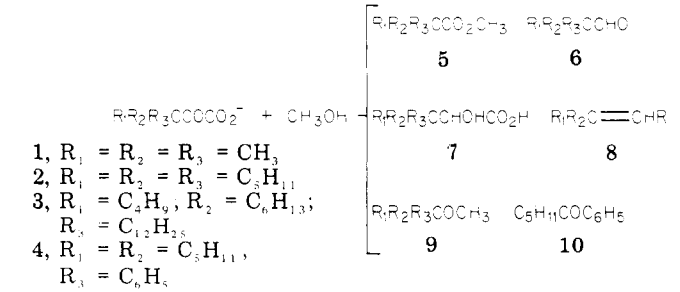
The "non-Kolbe" electrolysis of 3,3-disubstituted-2-oxo carboxylates **1–3** in methanol produced mixtures of methyl trialkylacetates **5**, trialkylacetaldehydes **6**, in some cases 2-hydroxy-3,3,3-trialkylpropionic acids **7**, trialkylethylenes **8**, and methyl trialkylmethyl ethers **9**. When one of the substituents on the 3-carbon of the 2-oxo carboxylate was phenyl **4**, molecular rearrangement was not observed. In addition to products **5–9**, with the exception of **7**, there was obtained with **4** an alkyl phenyl ketone **10**. The methyl trisubstituted acetates were saponified to the desired trialkylacetic acids.

Although the oxidative decarboxylation of 3,3-dialkyl-2-oxo carboxylic acids ($R_1R_2R_3CCOCO_2H$) offers a possible way for preparing trialkylacetic acids with variations in the substituents,[1] it was thought that the Kolbe electrolysis method might afford an alternative way of obtaining these materials. This was based on the demonstrated fact that carbocations may be present in anodic oxidations and produce "non-Kolbe" materials, the nature of which varies with solvent and other conditions.[2]

Substitution in the 2-position of an acid by a carbocation stabilizing group, e.g., alkyl, alkoxyl, aryl, etc., decreases the yield of Kolbe dimers, and alcohols, olefins, ethers, etc. are formed by carbonium ion mechanisms. Previous studies of the anodic oxidation of pyruvic, α-oxobutyric, and α-oxovaleric acids in methanol showed that good yields of methyl esters were realized in addition to other products.[3]

Scheme I. Products of Electrolysis of $R_1R_2R_3COCO_2^-$ in $CH_3OH$




In the present investigation four 2-keto acids **1–4** (Scheme I) were studied. They contained 6–25 carbon atoms, and the substituents were varied, including phenyl in the last case. It was thought that the aryl system might

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