H, br s, $W_{1/2}$ = 3 Hz, CHO), 3.03–1.93 (8 H), 2.20 (3 H, s, $COCH_3$), 1.17 (3 H, d, J = 6.6 Hz, Me-10), 0.86 (3 H, s, Me-5); GC/MS, m/e (relative intensity) 210 (3, M^+), 168 (61), 139 (16), 138 (25), 125 (22), 111 (21), 110 (53), 97 (100). Minor diastereomer **3a** (1*S*,5*S*,10*R*): NMR (270 MHz, $CDCl_3$) δ 9.61 (1 H, Br s, $W_{1/2}$ = 3 Hz, CHO), 3.02–1.22 (8 H), 2.17 (3 H, s, $COCH_3$), 1.16 (3 H, d, J = 6.6 Hz, Me-10), 0.96 (3 H, s, Me-5); GC/MS, m/e (relative intensity) 210 (1, M^+), 168 (57), 139 (20), 138 (9), 125 (13), 111 (21), 110 (95), 97 (100).

Anal. Calcd for $C_{12}H_{18}O_3$ (mixture of diastereomers): C, 68.55; H, 8.63. Found: C, 68.27, H, 8.46.

Aldol 4. Diketo aldehyde **3** (154 mg, 0.73 mmol) was dissolved in 10 mL of absolute methanol, and 2 mL of 10% aqueous potassium hydroxide was added, while the mixture was allowed to stir for 4 h at 25 °C. The resulting brown solution was cooled in an ice bath and acidified to pH 2 with 37% hydrochloric acid (0.4 mL). The mixture was concentrated in vacuo, and the residue was extracted with ethyl acetate three times. The combined extracts were washed with saturated sodium chloride, dried over anhydrous magnesium sulfate, and concentrated in vacuo to give a crude aldol **4**. Purification on a short silica gel column (ethyl acetate) resulted in 143 mg (0.68 mmol, 92%) of **4** (R_f 0.34) as a colorless oil: NMR (270 MHz, $CDCl_3$) δ 4.46 (1 H, br s, OH), 4.00 (1 H, tdd, J = 11.2, 4.4, 2.6 Hz, H-7), 3.01 (1 H, dd, J = 11.2, 10.0 Hz, H-8), 2.61 (1 H, dt, J = 10.0, 2.6 Hz, H-8), 2.59–1.32 (8 H), 1.22 (3 H, d, J = 7.0 Hz, Me-10), 0.78 (3 H, s, Me-5); IR (neat) 3460 (OH), 1739, 1700 cm^{-1}; MS, m/e (relative intensity) 210 (79, M^+), 192 (14), 97 (100).

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.74; H, 8.72.

Acknowledgment. This work was supported by the National Institutes of Health (Grant No. CA-16432). The author is grateful to Professor Frederick E. Ziegler for his enlightening suggestions and to Mr. P. Damou for recording high-field NMR spectra (NSF Northeast Regional NMR Facility, Department of Chemistry, Yale University).

Registry No. (±)-**1**, 74645-43-5; (±)-**2**, 60426-81-5; (±)-**3a**, 76156-83-7; (±)-**3b**, 81939-03-9; (±)-**4**, 81875-17-4; **5**, 34780-08-0; **6a**, 609-02-9; **6b**, 609-08-5; **6c**, 56834-42-5; **7a**, 69027-55-0; **7b**, 66446-63-7; **8a**, 81875-18-5; **8b**, 81875-19-6; **8c**, 81875-20-9; **8d**, 81875-21-0; **8e**, 81875-22-1; (±)-*cis*-**9** (isomer 1), 81875-23-2; (±)-*cis*-**9** (isomer 2), 81939-04-0; (±)-*trans*-**9** (isomer 1), 81939-05-1; (±)-*trans*-**9** (isomer 2), 81939-06-2; (±)-*cis*-**10** (isomer 1), 81875-24-3; (±)-*cis*-**10** (isomer 2), 81939-07-3; (±)-*trans*-**10** (isomer 1), 81939-08-4; (±)-*trans*-**10** (isomer 2), 81939-09-5; (±)-**11**, 81875-25-4; **12**, 81875-26-5; **13**, 81875-27-6; **14**, 81875-28-7; **15b**, 81875-29-8; (±)-**16** (isomer 1), 81875-30-1; (±)-**16** (isomer 2), 81939-10-8; (±)-**17** (isomer 1), 81875-31-2; (±)-**17** (isomer 2), 81939-11-9; (±)-**18** (isomer 1), 81875-32-3; (±)-**18** (isomer 2), 81939-12-0; (±)-**19** (isomer 1), 81875-33-4; (±)-**19** (isomer 2), 81939-13-1; **20**, 81875-34-5; **21**, 81875-35-6; ethyl propionate copper salt, 81875-36-7; ethyl propionate, 105-37-3; ethyl propionate lithium enolate, 81355-01-3; allyl bromide, 106-95-6; 2-methyl-2-cyclopentenone, 1120-73-6; ethyl 2-(1-hydroxy-2-methyl-2-cyclopenten-1-yl)propanoate, 81875-37-8.

Synthesis of the D_{2d}-Dinoradamantane Derivatives Having Two Coaxially Oriented Unsaturated Centers. 6-Methylene-D_{2d}-dinoradamantan-2-one and D_{2d}-Dinoradamantane-2,6-dione

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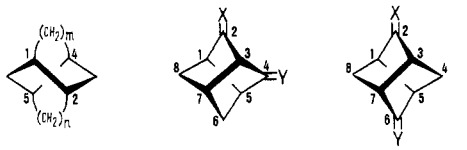
From the cyclopentadiene–maleic anhydride adduct was prepared the norbornenecarboxylic acid **22**. Treatment of the acid chloride **23** with triethylamine afforded the tetracyclic ketone **24** which was converted into the dinoradamantanecarboxylic acid **25** by a basic ring-opening reaction. The sequence of conversions involving the Cope elimination of the amine oxide derived from the amine **31** provided 6-methylene-D_{2d}-dinoradamantan-2-one (**6**) whose OsO_4–$NaIO_4$ oxidation eventually yielded D_{2d}-dinoradamantane-2,6-dione (**7**) of D_2 symmetry.

Bridging the 1,4 and 2,5 positions with CH_2 or CH_2CH_2 groups freezes cyclohexane's conformational mobility to make it assume a twist–boat conformation confined in the resulting tricyclic cage-shaped molecules.

Twistane (**1**) of D_2 symmetry and *twist*-brendane (**2**) of C_2 symmetry can be cited as examples (Chart I). They are both chiral, and their preparation in optically active modifications and determination of their absolute configuration have been reported from our laboratory.[1]

Bridging these positions with two CH_2 groups, however, provides an achiral tricyclic compound, D_{2d}-dinoradamantane (**3**), because introduction these CH_2 groups eventually creates another twist–boat cyclohexane moiety of opposite chirality interlocked with the original one. Since four CH_2 groups in D_{2d}-dinoradamantane (**3**) are a pair of enantiotopic molecular subunits, conversion of one

Chart I



(-) 1 D_2 m = n = 2 (-) 4 X=O, Y=H_2 6 X=O, Y=CH_2
(-) 2 C_2 m=1, n=2 (-) 5 X=O, Y=CH_2 7 X = Y = O
3 D_{2d} m = n = 1

of these CH_2 groups into carbonyl group desymmetrizes the D_{2d} symmetry inherent to **3**, leading to formation of D_{2d}-dinoradamantan-2-one (**4**) of C_2 symmetry. After having established the absolute configuration[2] of this interesting cage-shaped compound **4**, in which four among eight carbon atoms are asymmetric, we carried out its microbial[3] and horse liver alcohol dehydrogenase

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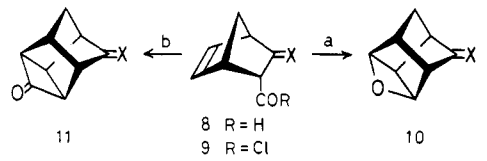
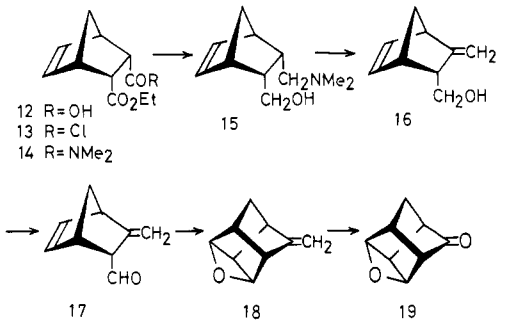
(2) Nakazaki, M.; Naemura, K.; Arashiba, N. *J. Chem. Soc., Chem. Commun.* **1976**, 678. Nakazaki, M.; Naemura, K.; Arashiba, N. *J. Org. Chem.* **1978**, *43*, 888.

0022-3263/82/1947-3470$01.25/0

Scheme I



Scheme II



(HLADH)[4] mediated oxidoreduction to disclose that although this gyrochiral ketone **4** is peculiar in its reluctance toward these biological systems, both the microbial *P*-C_2-ketone rule and the HLADH *M*-C_2-ketone rule are successfully applicable to predict the stereochemistry of its metabolites.

In the course of these investigations, we happened to notice that 4-methylene-D_{2d}-dinoradamantan-2-one (**5**) exhibits a λ_{max} (isooctane) of 300.5 nm (ϵ 445) in its UV spectrum, suggesting an unusually strong homoconjugation.

This coupled with a suggestion made from Professor J. Bernstein, Ben-Gurion University of the Negev, prompted us to prepare its gyrochiral regioisomers, 6-methylene-D_{2d}-dinoradamantan-2-one (**6**) (C_2 symmetry) and D_{2d}-dinoradamantane-2,6-dione (**7**) (D_2 symmetry), both with the unsaturated centers coaxially oriented along their C_2 axes, and to study their electron spectra as well as their microbiological transformations.[5]

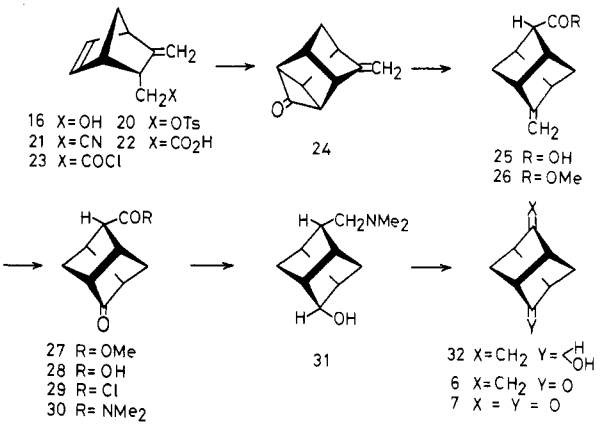
Results and Discussion

There have been reported two feasible synthetic routes to the D_{2d}-dinoradamantane molecular framework (Scheme I), one (a)[6] involving the Paterno–Büchi photocyclization of the unsaturated aldehyde **8** to the oxetane **10** and the other (b)[7] involving intramolecular cyclization of the ketene intermediate generated from the unsaturated acid chloride **9**.

As for the functional group which could be transformed into a carbonyl group in a later stage of the synthetic route, our choice was an exocyclic methylene group (X = CH_2, Scheme I), and this strategy required **17** and **23** as our primary synthetic targets.

Synthetic Approach Involving the Paterno–Büchi Photocyclization (Scheme II). The half-ester **12** obtained from the cyclopentadiene–maleic anhydride adduct

Scheme III



was converted into the *N*,*N*-dimethyl amide **14** via the acid chloride **13**. $LiAlH_4$ reduction of the amide **14** provided the tertiary amine **15** whose *N*-oxide was pyrolyzed (140–160 °C) to yield the diene–alcohol **16**.

The diene–aldehyde **17**, secured by pyridinium chlorochromate (PCC) oxidation of **16**, was irradiated in benzene with a medium-pressure mercury lamp for 14 h to give a 28% yield of an oxetane, bp 70 °C (20 mm) after purification through silica gel column chromatography and distillation. Having two unsaturated centers at the β,γ- and γ,δ-positions from the aldehyde group, the diene–aldehyde **17** has two alternative reaction routes opened in the Paterno–Büchi photocyclization. Although the dinoradamantane structure **18** was favored because of its IR and NMR spectra, both of which indicate the presence of an exocyclic methylene group in the product, direct support for **18** was provided by its ozonolysis to the oxetane ketone **19** (36% yield; mp 155–157 °C), whose IR spectrum exhibits a carbonyl band at 1765 cm^{-1}.[8]

Usual reductive cleavage of the oexetane rings in **18** and **19** with $LiAlH_4$ failed, and under more strenuous conditions (e.g., refluxing with excess $LiAlH_4$ in *N*-methylmorpholine for 50 h)[6b] these compounds appeared to suffer deep-seated cleavage reactions to afford no definite isolable products.

Having encountered these difficulties, we were forced to abandon this photochemical approach (a) and had recourse to the second route (b) shown in Scheme I.

Synthetic Approach via the Tetracyclic Ketone Intermediate 24 (Scheme III). The acid chloride **23** required as the prime intermediate in route b in Scheme I was prepared from the diene–alcohol **16** by the routine sequence of conversions via the tosylate **20**, the nitrile **21**, and the carboxylic acid **22**. Refluxing of the acid chloride **23** with triethylamine in benzene for 1 h afforded a 38% yield of a cyclobutane derivative, bp 79–80 °C (6 mm). As in the Paterno–Büchi photocyclization of the diene–aldehyde **17**, cycloaddition of the ketene intermediate occurred with the endocyclic double bond to yield the ketone **24** with a dinoradamantane framework, and this was borne out by its NMR spectrum which exhibits two singlets centered at δ 4.44 and 4.48 corresponding to C=CH_2 protons. Contrary to our expectation that the basic ring opening of the cyclobutanone moiety in **24** should yield a mixture of two isomeric carboxylic acids depending upon the direction of bond cleavage, 6-methylene-D_{2d}-dinoradamantane-2-carboxylic acid (**25**: mp 97–98 °C; 36% yield) was the sole product isolated from the reaction mixture, and the confirmative evidence supporting struc-

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(4) Nakazaki, M.; Chikamatsu, H.; Naemura, K.; Suzuki, T.; Iwasaki, M.; Sasaki, Y.; Fujii, T. *J. Org. Chem.* **1981**, *46*, 2726.
(5) We have reported microbial stereodifferentiating reduction of 2,6-adamantanedione and hexahydrodibenzoheptalene-5,11-dione both with two carbonyl groups coaxially oriented along the C_2 axis: Nakazaki, M.; Chikamatsu, H.; Nishino, M.; Murakami, H. *J. Org. Chem.* **1981**, *46*, 1151.
(6) (a) Sauers, R. R.; Shinski, W.; Mason, M. M. *Tetrahedron Lett.* **1969**, 79; (b) Sauers, R. R.; Kelly, K. W.; Sickles, B. R. *J. Org. Chem.* **1972**, *37*, 537. Sauers, R. R.; Schinski, W.; Mason, M. M.; O'Hara, E.; Byrne, B. *Ibid.* **1973**, *38*, 642.
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ture **25** was to be secured at the last stage of synthetic sequence (vide infra).

Removal of the exocyclic methylene was accomplished by ozonolysis of the ester **26**, and the resulting keto ester **27** was hydrolyzed to the acid **28** which was converted into the *N,N*-dimethyl amide **30** via the acid chloride **29**. $LiAlH_4$ reduction of the amide **30** gave a mixture of diastereomeric amino alcohols **31** whose *N*-oxides were pyrolyzed (160 °C) to afford a 18% yield of the unsaturated alcohol **32**, bp 110 °C (20 mm). The unsaturated ketone **6** (mp 35.5–36.5 °C) was obtained by PCC oxidation of **32**, and the spectroscopic comparison with an authentic specimen of the 4-methylene isomer **5**[9] indicated that they are pair of regioisomers, confirming the previous structural assignment for the acid **25**. Finally, removal of the exocyclic methylene group from the unsaturated ketone **6** by osmium tetraoxide oxidation followed by sodium metaperiodate oxidation concluded the sequence of steps leading to D_{2d}-dinoradamantane-2,6-dione (**7**), mp 94–97 °C.

The UV spectra of the 6-methylene 2-one **6** and the 2,6-dione **7** exhibit λ_{max} at 286 (ϵ 24.3) and 281 nm (ϵ 28.7), respectively, and comparison with the UV spectrum of D_{2d}-dinoradamantan-2-one (**4**) which shows λ_{max} at 282 nm (ϵ 25.3) seems to indicate that much less intramolecular interactions between the unsaturated centers are noticeable in these molecules than in **5**.

Detailed studies on their electronic spectra as well as their X-ray crystallographical analyses are to be reported by Professor J. Bernstein elsewhere.

Experimental Section

Infrared spectral data were obtained from a Hitachi 260-10 spectophotometer. NMR spectra were obtained from a JNM-C-60 and a JNM-FX-100. Chemical shifts are reported in parts per million (δ) downfield from tetramethylsilane. UV spectra were measured with a Beckman DB spectrometer. Elemental analyses were performed on a Yanagimoto CHN-Corder, Type II. All melting and boiling points are uncorrected.

***endo-cis*-2-Carboxy-3-(ethoxycarbonyl)bicyclo[2.2.1]hept-5-ene (12).** After the cyclopentadiene–maleic anhydride adduct[10] (240 g, 1.46 mol) was refluxed in ethanol (127 g, 2.76 mol) for 3 h, the excess ethanol was removed under reduced pressure. The residue was recrystallized from hexane to afford half-ester **12**: 254 g (83% yield); mp 72–73 °C (lit.[11] mp 74–75 °C).

Anal. Calcd for $C_{11}H_{14}O_4$: C, 62.84; H, 6.71. Found: C, 62.77; H, 6.67.

***endo-cis*-2-(Dimethylcarbamoyl)-3-(ethoxycarbonyl)bicyclo[2.2.1]hept-5-ene (14).** After a mixture of **12** (254 g, 1.21 mol), thionyl chloride (188 g, 1.58 mol), dimethylformamide (10 mL), and dry benzene (1.2 L) was stirred for 1 h at room temperature, the mixture was gently refluxed for 2.5 h. Volatile substances were removed from the reaction mixture in vacuo, and the residual oil was dissolved in dry benzene (550 mL). The benzene solution of the acid chloride **13** was added dropwise to a chilled solution of dimethylamine (238 g, 5.28 mol) in dry benzene (700 mL). The mixture was stirred for 1 h at 0–5 °C and allowed to stand overnight at room temperature. After the mixture was washed with water, 5% aqueous HCl, 5% aqueous NaOH, and water and dried ($MgSO_4$), the solvent was removed to give an oil which was distilled to provide **14**: 245 g (85% yield); bp 130–136 °C (0.7 mm); IR (neat film) 3080, 1735, 1645, 725 cm^{-1}.

Anal. Calcd for $C_{13}H_{19}O_3N$: C, 65.80; H, 8.07; N, 5.90. Found: C, 65.65; H, 7.98; N, 5.96.

***endo-cis*-2-[(Dimethylamino)methyl]-3-(hydroxymethyl)bicyclo[2.2.1]hept-5-ene (15).** A solution of **14** (111 g, 0.468 mol) in dry ether (1 L) was added dropwise to a suspension of $LiAlH_4$ (23.0 g, 0.606 mol) in dry ether (1 L), and the mixture was gently refluxed for 12 h. To the chilled reaction mixture was carefully added saturated aqueous NH_4Cl (90 mL) and an inorganic solid was filtered off. The filtrate was washed with water, dried (Na_2SO_4), and concentrated to give a white solid which was recrystallized from hexane to afford **15**: 68.7 g (81% yield); mp 90–92 °C; IR (KBr) 3150, 3050, 1045, 720 cm^{-1}.

Anal. Calcd for $C_{11}H_{19}ON$: C, 72.88; H, 10.57; N, 7.73. Found: C, 72.68; H, 10.42; N, 7.55.

***endo*-2-(Hydroxymethyl)-3-methylenebicyclo[2.2.1]hept-5-ene (16).** To a chilled and stirred solution of **15** (48.0 g, 0.265 mol) in methanol (55 mL) was slowly added a 30% H_2O_2 solution (21 mL), and the temperature was gradually brought to room temperature with stirring. After 3- and 6-h periods, 30% H_2O_2 solution (each 21 mL) was added, and the homogeneous solution was stirred at room temperature for 2 days. The excess hydrogen peroxide was destroyed by stirring with platinum black (300 mg) for 12 h at room temperature. After the platinum black was removed, the filtrate was concentrated in vacuo to give a white wax. The wax was transfered into a distilling flask equipped with a cold trap (dry ice–acetone) and heated at 140–160 °C in vacuo until an effusion of products ceased. The condensate in the trap was dissolved in benzene, and the solution was washed with water and dried ($MgSO_4$). After removal of the solvent, the residue was distilled to give **16**: 24.8 g (69% yield); bp 109 °C (20 mm); IR (neat film) 3320, 3070, 1660, 1020, 880, 740, 680 cm^{-1}.

Anal. Calcd for $C_9H_{12}O$: C, 79.37; H, 8.88. Found: C, 79.30; H, 8.80.

***endo*-2-Formyl-3-methylenebicyclo[2.2.1]hept-5-ene (17).** A solution of **16** (10.0 g, 0.0734 mol) in CH_2Cl_2 (17 mL) was added to a suspension of pyridinium chlorochromate (23.6 g, 0.109 mol) in CH_2Cl_2 (150 mL), and the mixture was stirred for 2 h at room temperature. The CH_2Cl_2 solution was separated by decantation, and the inorganic residue was rinsed with CH_2Cl_2. Combined CH_2Cl_2 extracts were washed with 2% aqueous NaOH and water and dried ($MgSO_4$). After removal of the solvent, the residue was chromatographed on silica gel. The fractions eluted with CH_2Cl_2 gave an oil which was distilled to afford **17**: 3.43 g (35% yield); bp 79–81 °C (27 mm); IR (neat film) 3070, 2720, 1720, 1655, 880, 740, 690 cm^{-1}.

8-Methylene-4-oxatetracyclo[4.2.1.$0^{2,5}$.$0^{3,7}$]nonane (18). A solution of **17** (2.00 g, 0.0149 mol) in benzene (300 mL) was irradiated for 14 h with a mercury lamp (100 UV, Toshiba) under an N_2 atmosphere. After removal of the benzene, pentane was added to the residue, and an insoluble solid was filtered off. The pentane solution was chromatographed on silica gel, and fractions eluted with pentane–ether (95/5 v/v) gave an oily product which was distilled to afford **18**: 560 mg (28% yield); bp 70 °C (20 mm); IR (neat film) 3070, 1675, 850, 660 cm^{-1}; NMR (CCl_4) δ 1.65–1.75 (m, 2 H), 2.18 (br s, 1 H), 2.6–2.9 (m, 2 H), 3.20 (br s, 1 H), 4.3–4.7 (m, 4 H).

Anal. Calcd for $C_9H_{10}O$: C, 80.56; H, 7.51. Found: C, 80.36; H, 7.51.

8-Oxo-4-oxatetracyclo[4.2.1.$0^{2,5}$.$0^{3,7}$]nonane (19). A stream of oxygen containing about 7% ozone was passed into a chilled solution (−78 °C) of **18** (980 mg, 7.30 mmol) in dry CH_2Cl_2 (40 mL) until an intense blue color persisted. The solution was allowed to warm to room temperature, and excess ozone was purged by passing a stream of N_2 through the solution. The solution was poured into a mixture of zinc powder (900 mg), acetic acid (1.5 mL), water (150 mL), and CH_2Cl_2 (30 mL), and the mixture was stirred vigorously for 3 h. After 3 h, zinc powder (900 mg) and acetic acid (1.5 mL) were added, and stirring was resumed for an additional 3 h. Excess zinc powder was removed by filtration, and the aqueous layer separated from the organic layer was extracted with CH_2Cl_2. The extracts were combined and washed with saturated aqueous $NaHCO_3$ and water and dried ($MgSO_4$). The solvent was removed, the residue was chromatographed on silica gel, and the eluates with CH_2Cl_2 gave a white solid which was further purified by sublimation at 70 °C (5 mm) to afford **19**: 350 mg (36% yield); mp 155–157 °C (in a sealed tube); IR (KBr) 1765, 1040, 940, 850 cm^{-1}; NMR ($CDCl_3$) δ 1.9–2.2 (m, 3 H), 2.75 (br s, 1 H), 2.97 (br s, 1 H), 3.56 (br s, 1 H), 4.7–5.0 (m, 2 H).

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(11) Rice, L. M.; Reid, E. E. *J. Am. Chem. Soc.* **1952**, *74*, 3955.

Anal. Calcd for $C_8H_8O_2$: C, 70.57; H, 5.92. Found: C, 70.42; H, 6.05.

***endo*-2-Methylene-3-[[(*p*-toluenesulfonyl)oxy]methyl]-bicyclo[2.2.1]hept-5-ene (20).** To a solution of **16** (100 g, 0.734 mol) in pyridine (350 mL) was added *p*-toluenesulfonyl chloride (168 g, 0.881 mol) with ice cooling. The mixture was stirred for 6 h in an ice bath and then allowed to stand overnight at room temperature. The reaction mixture was poured into ice–water, acidified with aqueous HCl, and extracted with ether. The extract was washed with aqueous $NaHCO_3$ and water and dried ($MgSO_4$). Removal of the solvent afforded **20** (197 g, 92% yield), which was recrystallized from ether–hexane to give an analytical sample, mp 41–42 °C.

Anal. Calcd for $C_{16}H_{18}O_3S$: C, 66.18; H, 6.25; S, 11.04. Found: C, 66.20; H, 6.30; S, 11.07.

***endo*-2-(Cyanomethyl)-3-methylenebicyclo[2.2.1]hept-5-ene (21).** A mixture of **20** (194 g, 0.670 mol), NaCN (98.0 g, 2.00 mol), and *N,N*-dimethylformamide (1 L) was heated at 130 °C for 14 h and cooled to room temperature. A solid deposite was filtered, and the filtrate was concentrated. The residue was diluted with water and extracted with ether. The extract was washed with water and dried ($MgSO_4$). The solvent was removed to give an oily product which was distilled to afford **21**: 67.9 g (70% yield); bp 118 °C (20 mm); IR (neat film) 3060, 2250, 1660, 890, 755, 740, 690 cm^{-1}.

Anal. Calcd for $C_{10}H_{11}N$: C, 82.72; H, 7.64; N, 9.65. Found: C, 82.53; H, 7.62; N, 9.44.

***endo*-2-(Carboxymethyl)-3-methylenebicyclo[2.2.1]hept-5-ene (22).** A mixture of **21** (29.7 g, 0.205 mol), KOH (34.7 g, 0.619 mol), and ethylene glycol (280 mL) was stirred at 150 °C for 15 h. After cooling, the reaction mixture was poured into water, acidified with aqueous HCl, and extracted with ether. The extract was washed with water, dried ($MgSO_4$), and concentrated to give a solid. Recrystallization of the solid from pentane afforded **22**: 29.6 g (88% yield); mp 70–72 °C; IR (KBr) 1700, 1310, 940, 880, 820, 745, 680 cm^{-1}.

Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 73.01; H, 7.27.

***endo*-2-[(Chloroformyl)methyl]-3-methylenebicyclo-[2.2.1]hept-5-ene (23).** To a chilled (dry ice–acetone) solution of **22** (8.00 g, 0.0487 mol) and triethylamine (8.8 mL, 0.0634 mol) in $CHCl_3$ (120 mL) was added thionyl chloride (7.53 g, 0.0633 mol). After the reaction mixture was stirred for 4 h at −78 °C, the chloroform was removed in vacuo to give a white solid. Extraction with ether (150 mL) followed by removal of the solvent left a residue which was distilled to afford **23**: 7.12 g (80% yield); bp 45–50 °C (0.13 mm); IR (neat film) 3070, 1790, 960, 880, 820, 740, 680 cm^{-1}.

8-Methylenetetracyclo[4.2.1.$0^{2,5}$.$0^{3,7}$]nonan-4-one (24). A solution of **23** (13.4 g, 0.0736 mol) in dry benzene (220 mL) was added dropwise to a refluxing solution of triethylamine (11.2 mL, 0.0810 mol) in dry benzene (1 L) over a 4.5-h period, and refluxing was resumed for an additional 1 h. After being cooled to room temperature, the reaction mixture was washed with 10% aqueous HCl, saturated aqueous $NaHCO_3$, and water and dried ($MgSO_4$). Removal of the solvent left a residue which was chromatographed on neutral alumina. Fractions eluted with pentane were combined and distilled to give **24**: 4.03 g (38% yield); bp 79–80 °C (6 mm); IR (KBr) 3080, 1800, 1775, 1695, 880, 685 cm^{-1}; NMR (CCl_4) δ 1.6–1.9 (m, 2 H), 2.6–2.9 (m, 6 H), 4.44 (s, 1 H), 4.48 (s, 1 H).

Anal. Calcd for $C_{10}H_{10}O$: C, 82.16; H, 6.90. Found: C, 82.02; H, 6.89.

6-Methylenetricyclo[3.3.0.$0^{3,7}$]octane-2-carboxylic Acid (25). To a chilled and vigorously stirred suspension of potassium *tert*-butoxide (88.4 g, 0.787 mol) in dry ether (280 mL) was added water (4.30 g, 0.236 mol) under a N_2 atmosphere, and then the mixture was warmed to room temperature. The tetracyclic ketone **24** (14.4 g, 0.0984 mol) was added all at once to the mixture, and the mixture was stirred for 3 h at room temperature in a N_2 atmosphere. The reaction mixture was poured into ice–water, and the water layer was separated, acidified with aqueous HCl, and extract with ether. The extract was washed with water, dried ($MgSO_4$), and concentrated to give a syrup. The syrup was triturated with pentane to afford a solid, which was further purified by sublimation at 80 °C (5 mm) to afford **25**: 5.07 g (31% yield); mp 97–98 °C (in a sealed tube); IR (KBr) 1690, 870 cm^{-1}.

Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 72.95; H, 7.35.

Methyl 6-Methylenetricyclo[3.3.0.$0^{3,7}$]octane-2-carboxylate (26). To a solution of **25** (3.00 g, 0.0183 mol) in ether (60 mL) was added ethereal diazomethane solution containing ca. 2 g of CH_2N_2, and the mixture was stirred for 40 min at room temperature. The routine workup afforded **26**: 3.11 g (96% yield); bp 91 °C (1 mm); IR (neat film) 3070, 1730, 1210, 865 cm^{-1}; NMR (CCl_4) δ 1.3–1.6 (m, 4 H), 2.5–2.7 (m, 5 H), 3.59 (s, 3 H), 4.18 (s, 2 H).

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 73.90; H, 7.82.

Methyl 6-Oxotricyclo[3.3.0.$0^{3,7}$]octane-2-carboxylate (27). By the same procedure described for the preparation of **19**, the tricyclic olefin **26** (2.94 g, 0.0165 mol) was converted into **27**. After the same workup, the crude product was chromatographed on neutral alumina. The fractions eluted with pentane–ether (95/9 v/v) gave **27** as a white solid: 470 mg (16% yield); mp 64–65.5 °C (in a sealed tube); IR (KBr) 1765, 1730, 1215 cm^{-1}; NMR ($CDCl_3$) δ 1.5–1.8 (m, 4 H), 2.39 (br s, 2 H), 2.82 (br s, 2 H), 2.90 (br s, 1 H), 3.70 (s, 3 H).

Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.65; H, 6.69.

6-Oxotricyclo[3.3.0.$0^{3,7}$]octane-2-carboxylic Acid (28). A mixture of **27** (500 mg, 2.77 mmol), KOH (300 mg, 5.35 mmol), methanol (3 mL), and water (3 mL) was refluxed for 3 h. The reaction mixture was diluted with water, acidified with aqueous HCl, and extracted with ether. The extract was washed with water, dried ($MgSO_4$), and concentrated to give a solid which was sublimed at 110 °C (5 mm) to afford **28**: 370 mg (81% yield); mp 125–126 °C (in a sealed tube); IR (KBr) 1765, 1705 cm^{-1}.

Anal. Calcd for $C_9H_{10}O_3$: C, 65.05; H, 6.07. Found: C, 64.99; H, 6.04.

***N,N*-Dimethyl-6-oxotricyclo[3.3.0.$0^{3,7}$]octan-2-amide (30).** To a solution of **28** (3.99 g, 0.0240 mol) in dry benzene (150 mL) was added thionyl chloride (5.14 g, 0.0432 mol), and the mixture was stirred for 5 days at room temperature to complete the rather sluggish reaction. After the mixture was concentrated in vacuo at 30 °C, the residue was dissolved in dry benzene (120 mL). The solution was added to a solution of dimethylamine (ca. 20 mL) in dry benzene (120 mL) with ice cooling, and the mixture was stirred for 12 h at room temperature. After addition of water, the organic layer was separated, and the water layer was extracted with ether. Combined extracts were washed with water and dried ($MgSO_4$). Removal of the solvent afforded **30** (2.56 g) as a solid. The aqueous layer and washings were combined and extracted continuously with ether for 3 days. The ethereal extract was dried ($MgSO_4$) and concentrated to give a second crop of **30**: 1.78 g; mp 168 °C dec; IR (KBr) 1760, 1635 cm^{-1}.

Anal. Calcd for $C_{11}H_{15}O_2N$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.28; H, 7.70; N, 7.03.

2-(Dimethylamino)-6-hydroxytricyclo[3.3.0.$0^{3,7}$]octane (31). A solution of **30** (2.73 g, 0.0141 mol) in dry THF (180 mL) was added dropwise to a suspension of $LiAlH_4$ (1.07 g, 0.0283 mol) in dry THF (40 mL), and the mixture was refluxed for 18 h. After successive addition of water (2 mL) and 40% aqueous NaOH (4 mL), an inorganic solid deposited was filtered and rinsed thoroughly with ether. The ethereal extracts were combined with the original filtrate, and the mixture was washed with water and dried ($MgSO_4$). Removal of the solvent gave **31** (2.47 g, 97% yield) as a colorless liquid. This material was used for the next reaction without further purification.

2-Hydroxy-6-methylenetricyclo[3.3.0.$0^{3,7}$]octane (32). By the same procedure described for the preparation of **16**, the amine **31** (5.17 g, 0.0285 mol) was converted into the corresponding *N*-oxide (a syrup). The *N*-oxide was placed in a distilling flask equipped with a trap cooled in dry ice–acetone bath and heated at 160 °C for 1 h under reduced pressure. The condensate in the trap was dissolved in ether, washed with aqueous HCl, aqueous $NaHCO_3$, and water, and dried ($MgSO_4$). After removal of the solvent, the residue was distilled to give **32**: 710 mg (18% yield); bp 110 °C [air-bath temperature (20 mm)]; IR (neat film) 3300, 1680, 860 cm^{-1}.

Anal. Calcd for $C_9H_{12}O$: C, 79.37; H, 8.88. Found: C, 79.10; H, 8.65.

6-Methylenetricyclo[3.3.0.0^{3,7}]octan-2-one (6). A solution of **32** (361 mg, 2.65 mmol) in CH_2Cl_2 (4 mL) was added to a suspension of pyridinium chlorochromate (943 mg, 4.37 mmol) in CH_2Cl_2 (5 mL), and the mixture was stirred for 3 h at room temperature. The CH_2Cl_2 solution was separated, and the inorganic residue was rinsed with CH_2Cl_2. The combined CH_2Cl_2 solutions were concentrated, and the residue was chromatographed on neutral alumina. Fractions eluted with pentane gave a solid which was sublimed at 30 °C (5 mm) to afford **6**: 125 mg (35% yield); mp 35.5–36 °C (in a sealed tube); UV (isooctane) λ_{max} 286 nm (ϵ 24.1); IR (KBr) 3075, 1770, 860 cm^{-1}; NMR (CCl_4) δ 1.65 (s, 4 H), 2.22 (br s, 2 H), 2.72 (br s, 2 H), 4.62 (s, 2 H).

Anal. Calcd for $C_9H_{10}O$: C, 80.56; H, 7.51. Found: C, 80.56; H, 7.52.

Tricyclo[3.3.0.0^{3,7}]octane-2,6-dione (7). A mixture of **6** (84 mg, 0.626 mmol), osmium tetraoxide (100 mg, 0.393 mmol), THF (2 mL), and water (2 mL) was stirred for 30 min at room temperature, and sodium metaperiodate (268 mg, 1.25 mmol) was added by portions over 40 min. After the mixture was stirred at room temperature for 14 h, the deposited inorganic solid was filtered, and this was rinsed with CH_2Cl_2. The CH_2Cl_2 extracts were combined with the original filtrate, and the mixture was made basic with 2 N aqueous NaOH (4 mL) and extracted with CH_2Cl_2. The extracts were washed with water and dried ($MgSO_4$). After removal of the solvent, the residue was chromatographed on neutral alumina. Early pentane–ether eluates recovered **6** (40 mg), and subsequent pentane–ether eluates afforded **7** (7 mg, 8% yield) which was recrystallized from hexane: mp 94–97 °C (in a sealed tube); UV (hexane) λ_{max} 281 nm (ϵ 28.7), 294 (sh) (ϵ 25.7); IR (KBr) 1765 cm^{-1}; NMR ($CDCl_3$) δ 1.85 (s, 4 H), 2.55 (s, 4 H).

Anal. Calcd for $C_{10}H_8O_2$: C, 74.99; H, 5.03. Found: C, 74.75; H, 5.15.

Registry No. 6, 82431-26-3; **7**, 82431-27-4; **12**, 67913-05-7; **13**, 82431-28-5; **14**, 82431-29-6; **15**, 56679-25-5; **16**, 82431-30-9; **17**, 82431-31-0; **18**, 82431-32-1; **19**, 82431-33-2; **20**, 82431-34-3; **21**, 82431-35-4; **22**, 82431-36-5; **23**, 82431-37-6; **24**, 82431-38-7; **25**, 82431-39-8; **26**, 82431-40-1; **27**, 82431-41-2; **28**, 82431-42-3; **29**, 82431-43-4; **30**, 82431-44-5; **31**, 82431-45-6; **31** *N*-oxide, 82431-46-7; **32**, 82431-47-8; cyclopentadiene–maleic anhydride adduct, 129-64-6.

Geometrically Biased Homoconjugated Ketones. Synthetic Avenues to 1-Acyl-2,4-cyclohexadienes

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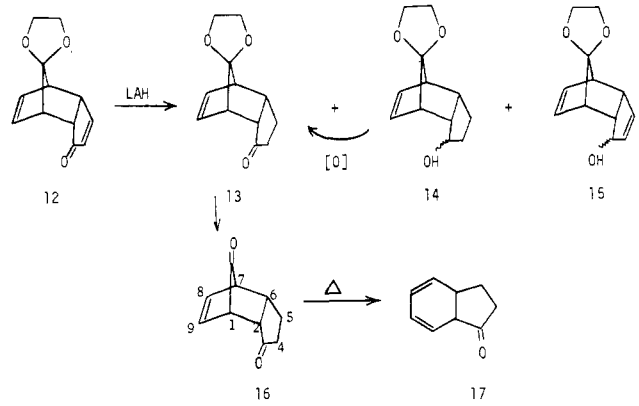
Synthetic approaches to a series of open (**1**), fused (**2**), and spiroannelated (**3**) 2,4-cyclohexadien-1-yl ketones, which differ in the geometrical juxtaposition of the homoconjugated chromophores, have been worked out. A series of prototropic rearrangements was found to occur, establishing an equilibrium between **28**–**30**.

We have recently initiated an investigation of the photochemical and photophysical properties of (homoconjugated) $\beta,\gamma,\delta,\epsilon$-unsaturated ketones as a function of the spacial juxtaposition of the respective chromophores. For reasons given elsewhere[1,2] we chose 1-acyl-2,4-cyclohexadiene as the basic system for study. We present now an account of the preparative methods and procedures we have worked out in this framework.

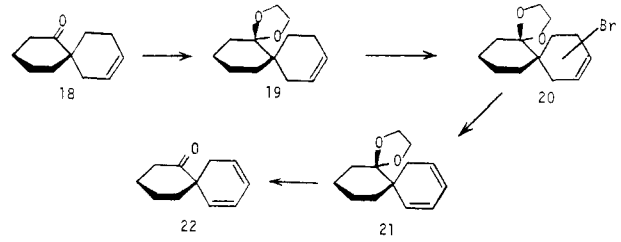
The attainment of open members of the series, adequately substituted to avoid aromatization, was relatively simple, and, e.g., **1** (Chart I) was secured by following largely literature procedures.[3] It is readily seen that in **1** and its analogues, the acyl group can freely rotate to assume various, albeit conformationally biased, spacial positions of the carbonyl vs. the π system. This bias becomes configurational and therefore much more severe in fused systems of type **2** or in spiro ketones of type **3**.

Following past experience,[4] we thought of developing a unified synthetic approach to all the needed compounds of types **2** and **3**, with the first step being a Diels–Alder cycloaddition to a cyclopentadienone ketal (**4**).[4-6] Thus, the reaction of **4** with, e.g., cyclopenten-3-one (**5**) was supposed to yield the precursor **7** for **2** (n = 1) whereas with 2-methylenecyclohexanone (**6**) the intermediate **8** was expected, leading to **3** (n = 3).

Scheme I



Scheme II



Unfortunately none of these cycloadditions could be realized. This, and further unsuccessful experiments with various dienophiles (e.g., **9**), led us to the conclusion that *4 cannot cycloadd to nonplanar or substituted dienophiles* and dimerizes instead. It appears that the steric hindrance (exercised by tetrahedral substituents) to the diene–

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