threo-**4-Methyl-2,3-diaminopentane Dihydrochloride (26a).**—Hydrogenation of the diazide (**25a**, 5.0 g) as described yielded the free diamine, a colorless oil, that was immediately converted to the dihydrochloride in ether solution from which it immediately precipitated: 4.0 g, 71% yield; mp 239–242° (ethanol); infrared showed 2800, 2000, 1580, 1505, and 1550 cm^{-1} (NH_3^+).

Anal. Calcd for $C_6H_{18}Cl_2N_2$: C, 38.10; H, 9.59; Cl, 37.49; N, 14.81. Found: C, 38.05; H, 9.27; Cl, 37.42; N, 14.68.

This compound was identical in every respect with **13** obtained *via* the aziridine route from the *cis* olefin.

trans-**2,3-Diethylaziridine (20b).**—Compound **20b** was prepared as previously described but from *trans*-3-hexene (**18b**, 8.4 g, 0.1 mole), silver cyanate (15 g, 0.1 mole), and iodine (25.4 g, 0.1 mole) in dry ether (250 ml) followed by successive reaction of the intermediate iodoisocyanate with methanol (200 ml) and then with potassium hydroxide (8.4 g) dissolved in water (30 ml), without separate isolation of **19b**. The pure aziridine (**20b**) was isolated as a colorless liquid by vacuum distillation: 2.3 g, 45%; bp 45° (32 mm) and 26–29° (15 mm); infrared showed 3200 (>NH) and 875 cm^{-1} (*trans*-aziridine).

Anal. Calcd for $C_6H_{13}N$: C, 72.66; H, 13.21; N, 14.12. Found: C, 72.67; H, 13.08; N, 14.05.

The phenylurea of **20b** had mp 85–86°.

Anal. Calcd for $C_{13}H_{18}N_2O$: C, 71.53; H, 8.31; N, 12.83. Found: C, 71.71; H, 8.48; N, 12.74.

The α-naphthylurea of **20b** had mp 114–115°.

Anal. Calcd for $C_{17}H_{20}N_2O$: C, 75.82; H, 7.60; N, 10.56. Found: C, 75.94; H, 7.42; N, 10.71.

erythro-**3,4-Azidoaminohexane (21b).**—Compound **21b** was prepared in the same way as **12** and **21a** but from **20b** (3.5 g). The pure azidoamine (**21b**) was isolated as a colorless liquid by vacuum distillation: 2.7 g, 56%; bp 78–79° (18 mm); infrared showed 3350 and 1610 (NH_2) and 2100 and 1275 cm^{-1} (N_3).

Anal. Calcd for $C_6H_{14}N_4$: C, 50.67; H, 9.93; N, 39.43. Found: C, 50.68; H, 9.91; N, 39.05.

meso-**3,4-Diaminohexane Dihydrochloride (22b).**—The azidoamine (**21b**, 2.0 g) was hydrogenated as described for **12** and **21a**, and the resulting diamine was converted directly to the dihydrochloride in the ethanol solution followed by evaporation to dryness. Recrystallization of the residue from ethanol yielded pure **22b**: 1.7 g, 72%; mp 263–266°; infrared showed 2800, 2000, 1600, and 1515 cm^{-1} (NH_3^+).

Anal. Calcd for $C_6H_{18}Cl_2N_2$: C, 38.10; H, 9.59; Cl, 37.49; N, 14.81. Found: C, 38.22; H, 9.60; Cl, 37.39; N, 14.74.

trans-**3,4-Epoxyhexane (23b).**—This was prepared in the usual way from **18b** and peroxyacetic acid containing sodium acetate.[21]

threo-**3,4-Diaminohexane Dihydrochloride (26b).**—By procedures already described the *trans* epoxide (**23b**, 6.0 g) was converted to the azidohydrin (**24b**) [infrared showed 3375 (OH) and 2100 and 1270 cm^{-1} (N_3)], which was then converted to the *threo*-3,4-diazidohexane (**25b**) *via* the intermediate azidomesylate. The usual reduction procedure over Adams catalyst yielded the diamine from **25b** which was converted to its dihydrochloride (**26b**) in ether solution. The precipitate of crude **26b** was recrystallized from ethanol to yield the pure compound: 4.0 g (35% from epoxide); mp 298–300°; infrared showed 2800, 2000, 1620, and 1520 cm^{-1} (NH_3^+).

Anal. Calcd for $C_6H_{18}Cl_2N_2$: C, 38.10; H, 9.59; Cl, 37.49; N, 14.81. Found: C, 37.98; H, 9.23; Cl, 37.01; N, 14.95.

Registry No.—**3,** 10027-78-8; *trans*-2-azidocyclohexyl methanesulfonate, 10043-43-3; **4,** 10027-79-9; **5,** 10027-80-2; **6,** 1199-15-1; **7,** 10027-82-4; **8,** 10027-83-5; *trans*-2-azidocyclohexylamine, 10043-36-4; **27,** 10027-84-6; **29,** 10027-85-7; **31,** 5456-63-3; **37,** 10039-14-2; *cis* isomer of **3,** 10027-87-9; **11,** 10027-88-0; phenylurea of **11,** 10027-89-1; 2-naphthylurea of **11,** 10039-15-3; phenylurea of **12,** 10027-90-4; **13,** 10027-91-5; **15,** 10027-92-6; **16,** 10027-93-7; **17,** 10027-94-8; **20a,** 10027-95-9; phenylurea of **20a,** 10027-96-0; 2-naphthylurea of **20a,** 10027-97-1; phenylurea of **21a,** 10027-98-2; **26b,** 10027-99-3; **24a,** 10028-00-9; **25a,** 10028-01-0; **20b,** 10028-02-1; phenylurea of **20b,** 10028-03-2; 2-naphthylurea of **20b,** 10028-04-3; **21b,** 10028-05-4; **22b,** 10028-06-5.

Acknowledgment.—The authors acknowledge with thanks support of this investigation by U. S. Public Health Service Research Grants No. CA-07803 and CA-07174 from the National Cancer Institute.

A Study of the Acid-Catalyzed Cyclization of Some Condensed Cyclohexenone and Cyclohexanone Aliphatic Acids

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Received September 12, 1966

Condensed cyclohexenone aliphatic acids of type **5** can be cyclized under acid-catalyzed conditions to bicycloalkenediones of type **6**, when n = 1–3. The corresponding cyclization of some saturated keto acids of type **7** appears to proceed preferentially toward the more substituted α-carbonyl position, or, in the absence of substitution, toward the direction of preferred enolization of the ketone group. The unusual spectroscopic properties of some of the bridged-ring compounds obtained have been noted.

In a synthesis of (±)-gibberone (**1**), a degradation product of gibberellic acid, formation of the bicyclo[3.2.1]octane system was achieved by the acid-catalyzed cyclization of unsaturated keto acid **3**, which gave in high yield diketone **2**.[2] A similar approach was followed in a total synthesis of (±)-gibberic acid (**4**).[3] The object of the present work was to try to evaluate this type of carbon–carbon bond formation more fully as applicable in particular to the formation of a bridged-ring system.[4,5] This involved determining (a) the generality of the cyclization of a cycloalkenone aliphatic acid of type **5** to give a bicyclo[3.n.1]alkenedione of type **6**, and (b) whether the same type of cyclization could be applied to the corresponding saturated keto acid of type **7**, and, if so, which of the two possible bicycloalkanediones (**8** or **9**) would be formed depending on the nature of the substituents R and R′ (see Scheme I).

Hydrophenanthrone 10a-aliphatic acids, as exemplified by structures **17–19**, **23** and **25**, and **30–32**, appeared very suitable as model keto acids, both because of their potential synthetic relationship to some of the tetra-

(1) From the M.S. Thesis of Z. Neuwirth, Israel Institute of Technology, 1964.

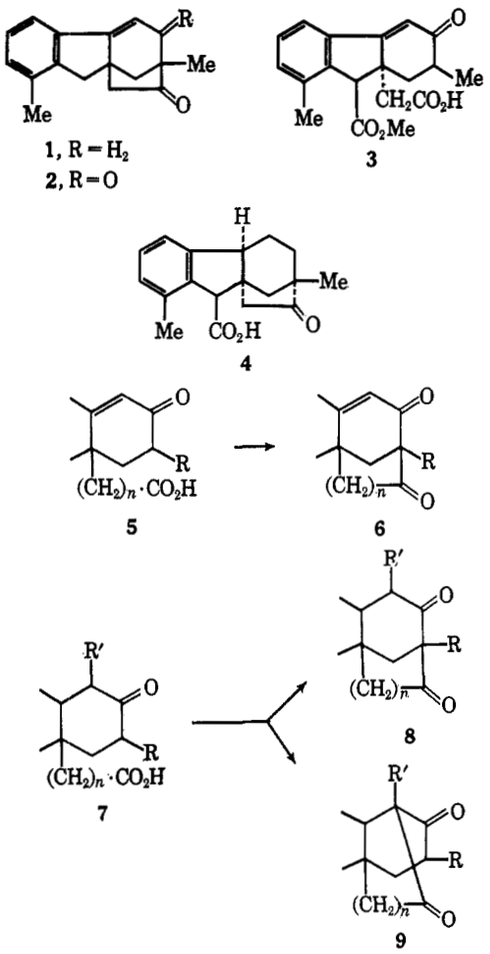
(2) H. J. E. Loewenthal, *Proc. Chem. Soc.*, 355 (1960); Y. Kos and H. J. E. Loeewnthal, *J. Chem. Soc.*, 605 (1963).

(3) H. J. E. Loewenthal and S. K. Malhotra, *Proc. Chem. Soc.*, 230 (1962); *J. Chem. Soc.*, 990 (1965).

(4) D. Becker and H. J. E. Loewenthal, *ibid.*, 1338 (1965).

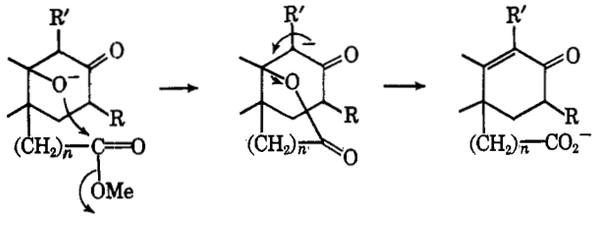
(5) J. A. Findlay, W. A. Henry, T. C. Jain, Z. Valenta, K. Wiesner, and C. M. Wong, *Tetrahedron Letters*, 869 (1962).

SCHEME I



cyclic diterpenes and because of their accessibility from α-tetralone.

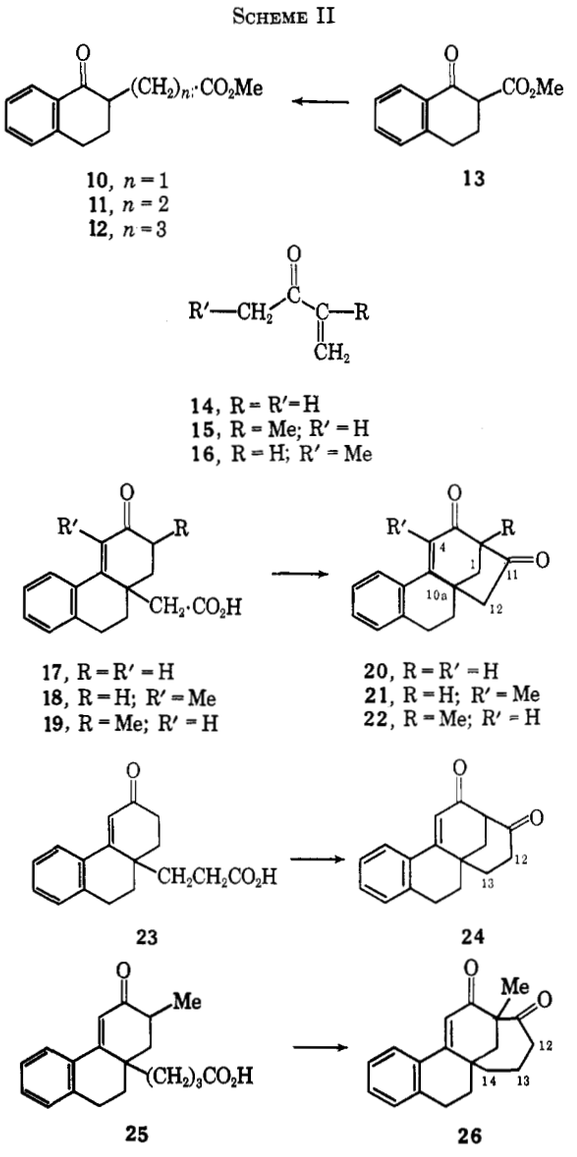
The synthesis of 1,2,3,4-tetrahydronaphthalen-1-one 2-aliphatic acids, by appropriate alkylation of methyl 1,2,3,4-tetrahydronaphthalen-1-one 2-carboxylate (**13**), has already been described by Bachmann[6] and Huisgen[7] and their co-workers. Their annelation to give phenanthrene derivatives, by reaction of the corresponding methyl esters (**10–12**, Scheme II) with the appropriate vinyl ketones (**14–16**) in the presence of methanolic sodium methoxide, proceeded smoothly and gave directly the desired unsaturated keto acids (**17–19** and **23**) in satisfactory yields. However, in the case of ester **12**, annelation (with methyl isopropenyl ketone) resulted in the formation of an appreciable proportion of the unsaturated ketonic product in the neutral fraction of the reaction. These facts point again to the participation of the carboxylate ester function in the Michael–Aldol annelation mechanism, *via* an aldol



lactone,[2–4,8] and such participation would naturally be expected to decrease with increasing length of the ester side chain.

The unsaturated keto acids (**17–19** and **23**) were all cyclized in satisfactory to excellent yields to the expected bridged-ring diketones (**20–22** and **24**, respectively), by refluxing with naphthalene-2-sulfonic acid in toluene. The corresponding four-carbon side-chain homolog (**25**), however, cyclized to the bicyclo-[4.3.1]decane derivative (**26**) in very low yield even after prolonged reaction. Cyclization with boron trifluoride etherate in acetic acid–acetic anhydride[2–4] was less satisfactory in most of the cases studied.

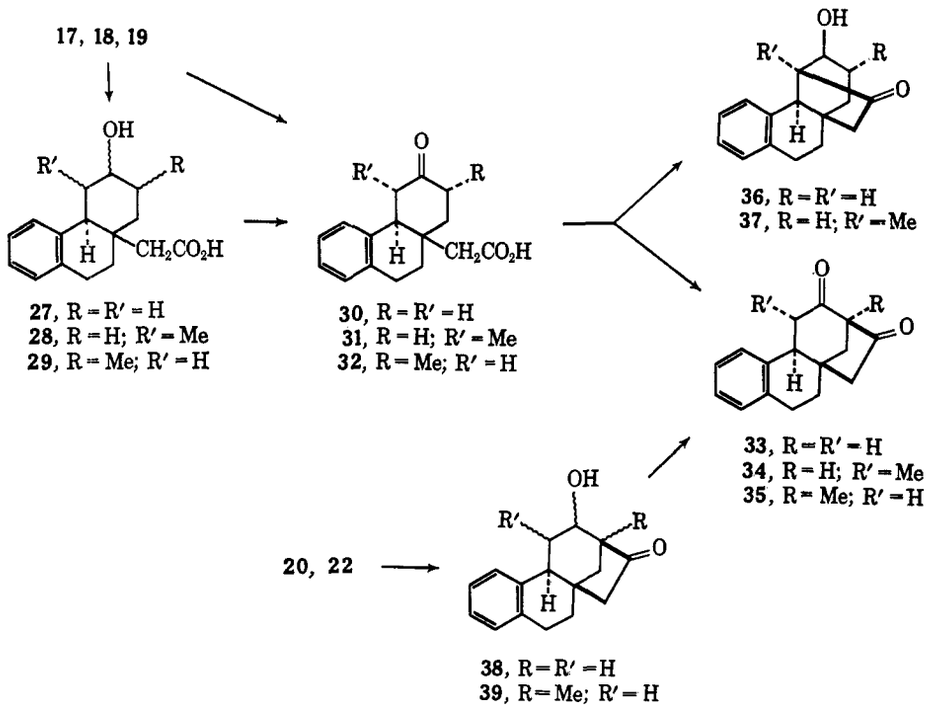
SCHEME II



The corresponding saturated keto acids could be obtained in two ways. The first was reduction of the enone system of unsaturated keto acids **17–19** by reaction with lithium in liquid ammonia which naturally ensured the obtention of a *trans*-ring junction.[9,10] The second method consisted of catalytic hydrogenation, usually in alkaline solution. This resulted in every

(6) W. E. Bachmann and G. D. Johnson, *J. Am. Chem. Soc.*, **71**, 3462 (1949).
(7) I. Ugi, R. Huisgen, and D. Pawellek, *Ann.*, **641**, 63(1961).
(8) W. L. Meyer and B. S. Bielaski, *J. Org. Chem.*, **28**, 1896 (1963).
(9) G. Stork and S. D. Darling, *J. Am. Chem. Soc.*, **86**, 1761 (1964).
(10) D. H. R. Barton and C. H. Robinson, *J. Chem. Soc.*, 3045 (1954).

SCHEME III

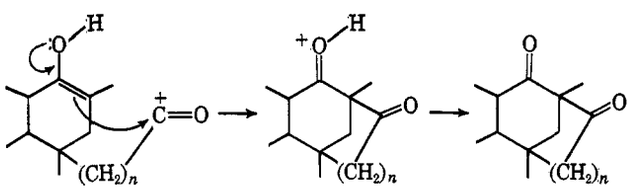


case in the uptake of 2 molar equiv of hydrogen to give an epimeric mixture of hydroxy acids **27–29** from which, by oxidation with chromic acid in acetone,[11] the same keto acids could be obtained in moderate yields. It appeared, therefore, that catalytic hydrogenation resulted mostly in addition of hydrogen from the side opposite the carboxylic side chain, though no attempt was made to characterize any products of opposite stereochemistry. From the stability of acids **31** and **32** in alkaline solution it must be assumed that in these the methyl group has the equatorial configuration, though it is not certain whether this represents the case in the initial product (*e.g.*, when obtained by lithium–ammonia reduction) or whether this was brought about during the work-up process.

Treatment of keto acids **30–32** with naphthalene-2-sulfonic acid in refluxing toluene led again to cyclization in reasonably good yields. The product from **30** could be separated by chromatogaphy on Florisil into the diketones **33** and **36** which were present in the proportion of 3:1. The structure of the former product was established by its alternative preparation from unsaturated diketone **20**, whose hydrogenation gave hydroxy ketone **38**, which could be further oxidized to **33**. Cyclization of methyl-substituted homolog **31** gave a 23:1 mixture of diketones **37** and **34**, while from isomeric acid **32** only diketone **35** could be obtained. The assignment of the structures of these products follows from examination of their nmr spectra. Compound **34** shows a C-methyl doublet at 1.40 ppm (J = 7 cps), while compounds **37** and **35** show a singlet, at 1.55 and at 1.26 ppm, respectively. The appearance of these signals at relatively lower field in **34** and **37**, compared with **35**, is presumably due to the fact that in the former two diketones the methyl group is nearly in the plane of the benzene ring.[12] (See Scheme III.)

(11) C. Djerassi, R. R. Engle, and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956).

The mechanism of the above cyclizations would appear to involve transfer of the π electrons of the enolic form of the ketone group to the acylium cation formed from the carboxyl group.



This is borne out by the fact that cyclization of acids **31** and **32** is directed primarily toward the carbon bearing the methyl group. In the case of acid **30**, the preponderance of product **33** is what might be expected from the known preferential direction of enolization of 10-substituted *trans*-2-decalones.[13]

The ultraviolet spectra of some of the compounds mentioned present some unusual features (see Table I). Unsaturated keto acids **17**, **19**, **23**, and **25** show

TABLE I

ULTRAVIOLET SPECTRA[a]

Unsatd keto acid	λ, mμ (ε)	Bridged diketone	λ, mμ (ε)
17	297 (19,700)	**20**	303 (20,000), 323 (18,000)[b]
18	288 (14,400)	**21**	292 (14,000), 325 infl (7500)
19	296 (19,200)	**22**	303 (22,000), 326.5 (19,500)
23	297 (24,100)	**24**	304 (20,000)
25	296 (22,300)	**26**	291 (20,300)

[a] In methanol. [b] See Figure 1.

the high-intensity maximum at 296–298 mμ (ε 19,000 to 24,000) expected from the type of chromophore present,[14] though acid **18** shows a distinct hypso-

(12) L. M. Jackman, "Applications of Nuclear Magnetic Resonance in Organic Chemistry," Pergamon Press Ltd., London, 1959, p 125.

(13) A. R. Pinder and R. Robinson, *J. Chem. Soc.*, 1224 (1952).

(14) A. L. Wilds, L. W. Beck, W. J. Close, C. Djerassi, J. H. Johnson, T. L. Johnson, and C. H. Shunk, *J. Am. Chem. Soc.*, **69**, 1985 (1947).

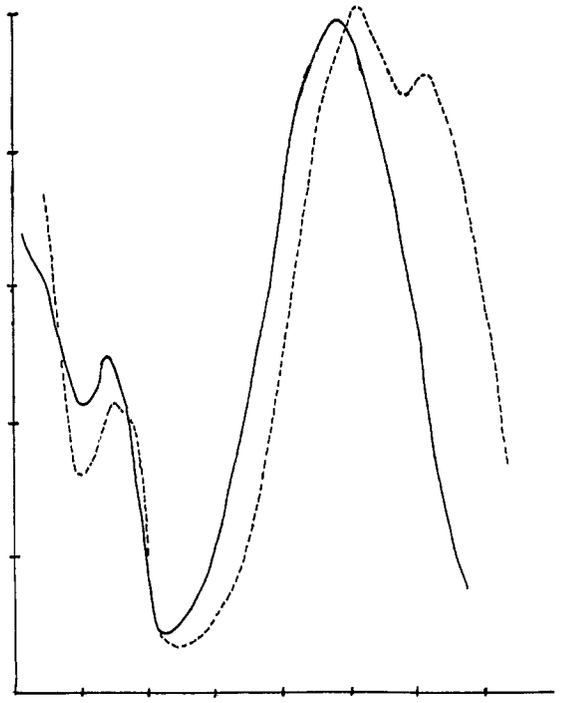


Figure 1.—Ultraviolet spectra: ———, keto acid **17**; – – – –, diketone **20**.

chromic shift in this maximum to 288 mμ in place of the calculated bathochromic shift of 10 mμ, with accompanying reduction in intensity (ε 14,400); the most reasonable explanation seems to be that the 4-methyl group is crowded by the C_5 hydrogen of the benzene ring,[15] thus causing some departure from coplanarity of the chromophore. Imposition of a bridge, as in diketones **20–22** and **24** leads to a bathochromic shift in this maximum, *e.g.*, Figure 1.

This may possibly be explained on the basis of Moore and Fisher's suggestion[16] that constraint imposed on a chromophore by a carbon bridge imposes a lateral distortion which would tend to favor the excited state.[17,18] However, an increase in the size of the bridge, *e.g.*, in compound **26**, appears to have the opposite effect.

On the other hand, bridged diketones **20** and **22** show an additional band at higher wavelengths. This phenomenon, also shown in compound **2**,[2,3] has been discussed in the case of gibberone (**1**),[19] and, since it does not appear to be connected with the carbonyl group in the bridge,[2,20] its origin remains obscure.

Another point of interest arises from examination of the infrared spectra of diketones **36** and **37** when compared with those of their bridge isomers **33–35**. All these compounds show carbonyl bands in the expected ranges of 1712–1724 (cyclohexanone) and 1745–1764 cm^{-1} (cyclopentanone), but, while these are of similar intensities in compounds **33–35**, the intensity of the cyclohexanone absorption in their isomers **36** and **37** (relative to that of the C–H band) is reduced to half or even less. The only difference in molecular geometry in the last three compounds which could influence a carbonyl dipole is the fact that in these the two-carbon bridge bearing the cyclopentanone carbonyl is vertical, and closer, to the benzene ring. However, this cannot explain why it is the cyclohexanone carbonyl absorption whose intensity is affected, even allowing for possible conformational differences in the six-membered ring.

(15) *Cf.*, H. J. E. Loewenthal, *J. Chem. Soc.*, 1421 (1961).

(16) R. N. Moore and G. S. Fisher, *J. Am. Chem. Soc.*, **78**, 4362 (1956).

(17) E. R. H. Jones, G. H. Mansfield, and M. C. Whiting, *J. Chem. Soc.*, 4073 (1956).

(18) G. Buechi, R. E. Erickson, and N. Wakabayashi, *J. Am. Chem. Soc.*, **83**, 927 (1961).

(19) H. Birnbaum, R. C. Cookson, and N. Lewin, *J. Chem. Soc.*, 1224 (1961).

(20) Private communication from Professor R. C. Cookson, University of Southampton.

Experimental Section[21]

Methyl 1,2,3,4-tetrahydro-1-oxonaphthalene-2-acetate (**10**), mp 58–59° (lit.[6] mp 55–56.5°), methyl 1,2,3,4-tetrahydro-1-oxonaphthalene-2-propionate (**11**), bp 140° (0.1 mm) [lit.[7] bp 115–120° (0.01 mm)], and methyl 1,2,3,4-tetrahydro-1-oxonaphthalene-2-butyrate (**12**), bp 142° (0.05 mm) [lit.[7] bp 130–135° (0.01 mm)], were prepared as described in the literature *via* appropriate alkylation of methyl 1,2,3,4-tetrahydro-1-oxonaphthalene-2-carboxylate (**13**),[22] except that in the case of the ester **12** γ-bromobutyronitrile was used as alkylating agent. The yields were comparable with those quoted in the literature.

Homologous 1,2,3,9,10,10a-Hexahydro-3-oxophenanthrene-10a-carboxylic Acids.—The methyl ester (**10**, **11**, or **12**; 26 mmoles), dissolved in the minimum amount of methanol or benzene, was added at 0° under nitrogen to a solution of sodium (62.5 mmoles) in dry methanol (35 ml), followed by dropwise addition of the vinyl ketone (**14**, **15**, or **16**; 37.5 mmoles) with stirring. The reaction mixture was allowed to reach room temperature overnight and acidified with a slight excess of acetic acid. The residue obtained after removal of most of the methanol was partitioned between chloroform–ether and 5% potassium carbonate, and the acidic product was obtained by acidification of the aqueous layer, filtration or extraction with chloroform, and crystallization. The following were thus obtained.

1,2,3,9,10,10a-Hexahydro-3-oxophenanthrene-10a-acetic acid (**17**) was obtained from **10** and methyl vinyl ketone (**14**) in 88% yield, mp 195–195.5° (from methanol–benzene). *Anal.* Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.83; H, 6.27.

The corresponding **methyl ester**, obtained with ethereal diazomethane, had mp 97.5–98° (from methylene chloride–isopropyl ether), ν_{max} 1660 and 1750 cm^{-1}. *Anal.* Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.71; H, 6.80.

1,2,3,9,10,10a-Hexahydro-4-methyl-3-oxophenanthrene-10a-acetic acid (**18**) was obtained from **10** and ethyl vinyl ketone (**15**) in 75% yield, mp 143–143.5° (from chloroform–isopropyl ether), ν_{max} 1660 and 1708 cm^{-1}. *Anal.* Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.48; H, 6.71.

1,2,3,9,10,10a-Hexahydro-2-methyl-3-oxophenanthrene-10a-acetic acid (**19**) was obtained from **10** and isopropenyl methyl ketone (**16**) in 90% yield, mp 213.5–214° (from methanol–benzene). *Anal.* Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.66; H, 6.62.

1,2,3,9,10,10a-Hexahydro-3-oxophenanthrene-10a-propionic acid (**23**) was obtained from **11** and methyl vinyl ketone (**14**) in 98% yield, mp 173.5–174° (from chloroform–isopropyl ether), ν_{max} 1660 and 1730 cm^{-1}. *Anal.* Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.37; H, 6.82.

1,2,3,9,10,10a-Hexahydro-2-methyl-3-oxophenanthrene-10a-butyric acid (**25**) was obtained from **12** and isopropenyl methyl ketone (**16**) in 32% yield, mp 153.5–154° (from methylene chloride–isopropyl ether). *Anal.* Calcd for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43. Found: C, 76.44; H, 7.37.

From the neutral product from the reaction in this case (ν_{max} 1720, 1670 cm^{-1}) more of the acid could be obtained by hydrolysis at room temperature overnight under nitrogen with 5% methanolic potassium hydroxide, followed by repeated recrystallization of the acidic product.

(21) Melting points are uncorrected. Ultraviolet spectra were measured on a Cary 14 instrument. Infrared spectra were taken on a Perkin-Elmer 21 instrument and are for chloroform solutions unless contraindicated. Nuclear magnetic resonance spectra are for deuteriochloroform solutions, with tetramethylsilane as internal reference on a Varian A-60 instrument.

(22) W. E. Bachmann and D. G. Thomas, *J. Am. Chem. Soc.*, **63**, 598 (1941).

Cyclization to Unsaturated Bridged-Ring Diketones. Procedure A.—The unsaturated keto acid (1.0 g) was refluxed in toluene (50 ml) in the presence of naphthalene-2-sulfonic acid (100 mg) for 24 hr with azeotropic separation of water. The cooled solution was washed with 10% potassium bicarbonate to remove unreacted starting material, then with water, and dried ($MgSO_4$), and the toluene was removed *in vacuo*, followed by crystallization of the neutral residue or purification by chromatography on Florisil.

Procedure B.—The unsaturated keto acid (1 g) was dissolved in a mixture of acetic acid (5 ml) and acetic anhydride (0.5 ml), redistilled boron trifluoride etherate (1.1 ml) was added, and the mixture was kept overnight, after which water was added, the product was extracted with chloroform, the extract was washed with bicarbonate solution to recover unchanged starting material and dried, and the neutral product was purified as above. The following were thus obtained.

1,2,3,9,10,10a-Hexahydro-2,10a-ethanophenanthrene-3,11-dione (20) was obtained from **17** in 91% yield (procedure A) or 32% yield (procedure B), mp 112–112.5° (from cold ether), ν_{max} 1750 and 1666 cm^{-1}. *Anal.* Calcd for $C_{16}H_{14}O_2$: C, 80.64; H, 5.92. Found: C, 80.58; H, 6.02.

1,2,3,9,10,10a-Hexahydro-2,10a-ethano-4-methylphenanthrene-3,11-dione (21) was obtained from **18** in 80% yield (procedure A), mp 153–153.5° (from chloroform–isopropyl ether), ν_{max} 1754 and 1669 cm^{-1}. *Anal.* Calcd for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 80.67; H, 6.26.

1,2,3,9,10,10a-Hexahydro-2,10a-ethano-2-methylphenanthrene-3,11-dione (22) was obtained from **19** in 89% yield (procedure A), mp 183–183.5° (from methylene chloride–isopropyl ether), ν_{max} 1750 and 1660 cm^{-1}. *Anal.* Calcd for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 80.73; H, 6.56.

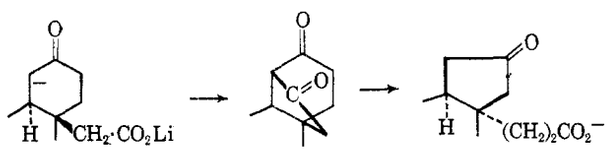
1,2,3,9,10,10a-Hexahydro-2,10a-trimethylenephenanthrene-3,11-dione (24) was obtained from **23** in 70% yield (procedure A) or 22% yield (procedure B), mp 168–168.5° (from methylene chloride–isopropyl ether), ν_{max} 1773 and 1660 cm^{-1}. *Anal.* Calcd for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 80.75; H, 6.41.

1,2,3,9,10,10a-Hexahydro-2-methyl-2,10a-tetramethylenephenanthrene-3,11-dione (26) was obtained from **25** in 8% yield (not raised by prolonging the reaction time or increasing the amount of acid catalyst) by procedure A, mp 150.5–151°, ν_{max} 1710 and 1660 cm^{-1}. *Anal.* Calcd for $C_{19}H_{20}O_2$: C, 81.39; H, 7.19. Found: C, 81.31; H, 7.11.

Homologous 1,2,3,4,4aα,9,10,10a-Octahydro-3-oxophenanthrene-10aβ-acetic Acids. A. By Reduction with Lithium in Liquid Ammonia.—The unsaturated keto acid (400–600 mg) was suspended in liquid ammonia (50–100 ml) and lithium was added with stirring at −60° in small pieces until a deep blue color persisted for at least 30 min, after which solid ammonium chloride was added and the ammonia was allowed to evaporate. The remaining solid was dissolved in water and the solution was acidified and extracted with chloroform. Removal of solvent from the dried solution left a residue which was dissolved in acetone (10 ml) and treated with 8 *N* chromic acid in aqueous sulfuric acid[11] with stirring until an orange color persisted, in order to reoxidize any overreduction product (this treatment was not necessary in the case of acid **31**). After addition of isopropyl alcohol and removal of acetone, water was added and the product was extracted with chloroform containing some tetrahydrofuran. The residue obtained after removal of solvent from the dried extract was crystallized once from ether and then recrystallized. The following were thus obtained.

1,2,3,4,4aα,9,10,10a-Octahydro-3-oxophenanthrene-10aβ-acetic acid (30) was obtained from **17** in 43% yield, mp 201–202° (from chloroform–isopropyl ether), ν_{max} 1720 cm^{-1} (KBr). *Anal.* Calcd for $C_{16}H_{18}O_3$: C, 74.39; H, 7.02. Found: C, 74.29; H, 6.87.

The lowered yield of this acid may be due to an internal Claisen cyclization in alkaline solution, followed by reversal to a cyclopentanone–propionic acid.



This is borne out by the fact that the methyl ester (prepared with diazomethane) of the mother liquors of this acid shows a shoulder at *ca.* 1760 cm^{-1} in addition to a band showing inflections at 1715 (cyclohexanone) and 1730 cm^{-1} (carboxylic ester); the ester prepared from the pure acid shows only the latter bands.[23]

1,2,3,4,4aα,9,10,10a-Octahydro-2-methyl-3-oxophenanthrene-10aβ-acetic acid (32) was obtained from **19** in 34% yield, mp 192–194° (from chloroform–isopropyl ether), ν_{max} 1700 cm^{-1} (KBr). *Anal.* Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 74.83; H, 7.21.

The over-all yield of this acid was raised to 54% by dissolving the mother liquors at room temperature overnight in 2 *N* sodium hydroxide, followed by isolation and recrystallization of the recovered acidic product.

1,2,3,4,4aα,9,10,10a-Octahydro-4-methyl-3-oxophenanthrene-10aβ-acetic acid (31) was obtained from **18** in 66% yield, mp 131.5–132.5° (from isopropyl ether or cyclohexane), ν_{max} 1710 cm^{-1}. *Anal.* Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 75.44; H, 7.60.

B. Catalytic Hydrogenation. i.—Acid **17** (307 mg) was dissolved in methanol and the equivalent amount of 1.045 *N* sodium hydroxide, and the solution was hydrogenated in the presence of palladium on charcoal (30%, 30 mg). During 8 hr 2 molar equiv of hydrogen was absorbed. After filtration the methanol was removed and the residual solution was acidified. Filtration gave **hydroxy acid 27** (307 mg), which after recrystallization from acetone–isopropyl ether had mp 203–204° dec. *Anal.* Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.74; H, 7.66.

The above hydroxy acid (200 mg) dissolved in acetone (40 ml) was treated with 8 *N* chromic acid in aqueous sulfuric acid (0.5 ml)[11] to the development of a permanent orange color. Isopropyl alcohol was added, acetone was removed *in vacuo*, and the product was isolated with chloroform. After recrystallization the acid **30** was obtained, identical in melting point and mixture melting point with the product obtained by procedure A.

ii.—Acid **19** (2.4 g) dissolved in methanol (300 ml) was catalytically reduced in the presence of palladium on charcoal (30%, 240 mg). Two molar equivalents of hydrogen was absorbed in the course of 3 hr. Filtration and removal of solvent left a mixture of epimers of the hydroxy acid **29**, from which one epimer could be separated pure by fractional crystallization, mp 201–202° (from chloroform–isopropyl ether, 0.51 g). *Anal.* Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.36; H, 8.03.

Oxidation of this epimer as described above gave the keto acid **32**, identical in melting point and mixture melting point with the product described in A.

iii.—Acid **18** (2.0 g) dissolved in 1 *N* sodium hydroxide (7.6 ml) and methanol was hydrogenated overnight at 50–60 psi in the presence of palladium on charcoal (30%, 80 mg). The filtered reaction mixture was concentrated and acidified, and the product was isolated with chloroform. The resulting epimeric mixture of **hydroxy acids 28** could not be separated into pure constituents, and it was therefore oxidized as described above, to give keto acid **31** (1.30 g), which after crystallization from cyclohexane was identical in melting point and mixture melting point with the corresponding product obtained by procedure A.

Cyclization to Saturated Bridged-Ring Diketones. i. Acid 30.—The acid (1.0 g) was refluxed for 24 hr in toluene (40 ml) in the presence of naphthalene-2-sulfonic acid (200 mg), with azeotropic removal of water. After cooling water was added and the organic layer was washed with 5% sodium carbonate and again with water. The residue (0.89 g) obtained after drying and removal of the toluene *in vacuo* was repeatedly chromatographed on Florisil, in combination with fractional crystallization of the various fractions obtained. Thus, in order of elution (using methylene chloride–hexane mixtures as eluents), the following were obtained.

a.—1,2,3,4,4aα,9,10a-Octahydro-2,10a-ethanophenanthrene-3,11-dione (33, 235 mg) was obtained, mp 142–142.5° (from methylene chloride–isopropyl ether), ν_{max} 1710 and 1750 cm^{-1}. *Anal.* Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 80.01; H, 6.86.

b.—1,2,3,4,4aα,9,10,10a-Octahydro-4,10a-ethanophenanthrene-3,11-dione (36, 80 mg) was obtained, mp 152–152.5° (from methylene chloride–isopropyl ether), ν_{max} 1762 and 1720 (weak) cm^{-1}

(23) *Cf.* J. F. Grove and T. P. C. Mulholland, *J. Chem. Soc.*, 3007 (1960).

(no significant change when taken in KBr). *Anal.* Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 80.01; H, 6.67.

ii. **Acid 31.**—The acid (1.036 g) was refluxed for 15 hr in toluene (40 ml) in the presence of naphthalene-2-sulfonic acid (100 mg) with azeotropic removal of water, after which the reaction mixture was treated as indicated above. The crude neutral product (0.94 g) was twice recrystallized from methylene chloride–isopropyl ether and then from benzene–cyclohexane to give 1,2,3,4,4aα,9,10,10a-octahydro-4-methyl-4,10a-ethanophenanthrene-3,11-dione (**37**, 667 mg), mp 153–153.5°, ν_{max} 1752 and 1710 (weak) cm^{-1}, nmr spectrum singlet at 1.55 ppm. *Anal.* Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13. Found: C, 80.42; H, 7.18.

The mother liquors were chromatographed on Florisil (12 g) using methylene chloride–hexane mixtures for elution. At first another 216 mg of the diketone **37** was obtained, followed by 38 mg of 1,2,3,4,4a,9,10,10a-octahydro-4-methyl-2,10a-ethanophenanthrene-3,11-dione (**34**), mp 144–145°, ν_{max} 1700 and 1755 cm^{-1} (KBr), nmr spectrum doublet centered at 1.40 ppm (J = 7 cps). *Anal.* Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13. Found: C, 79.43; H, 7.31.

iii. **Acid 32.**—The acid (0.35 g) was refluxed for 24 hr in toluene (20 ml) containing naphthalene-2-sulfonic acid (90 mg). The neutral residue obtained after the aforementioned work-up (0.32 g) was crystallized several times from methylene chloride–isopropyl ether, to give 1,2,3,4,4a,9,10,10a,9,10a-octahydro-2-methyl-2,10a-ethanophenanthrene-3,11-dione (**35**, 0.18 g), mp 119–119.5°, ν_{max} 1715 and 1755 cm^{-1}, nmr spectrum singlet at 1.26 ppm. *Anal.* Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 71.3. Found: C, 80.17; H, 7.05. Chromatography of the mother liquors on Florisil (3 g) gave only a further quantity of diketone **35** (86 mg); no other material could be isolated.

Catalytic Hydrogenation of Diketone 20.—The diketone (0.35 g) was shaken with hydrogen in methanol in the presence of palladium on charcoal (30%, 30 mg) until 2 molar equiv of gas was absorbed in the course of 0.5 hr. The residue obtained after filtration and removal of solvent was chromatographed through Florisil to remove a small nonpolar fraction (apparently an overreduction product) which was then followed on elution by 1,2,3,4,4aα,9,10a-octahydro-2,10a-ethano-3-hydroxyphenanthren-11-one (**38**, 0.32 g), mp 160.5–161° (from methylene chloride–isopropyl ether), ν_{max} 1740 and 3600 cm^{-1}. *Anal.* Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.15; H, 7.32.

The above ketol (100 mg) was added to the complex prepared from chromic oxide (100 mg) in pyridine (1 ml). After 12 hr at room temperature ether–methylene chloride was added, the mixture was filtered, and the filtrate was washed with 1 N hydrochloric acid containing 5% ferrous sulfate, with water, with dilute sodium carbonate, again with water, and dried ($MgSO_4$). The residue, after crystallization from methylene chloride–isopropyl ether, gave the diketone **33** (90 mg) identical with the specimen obtained above in melting point, mixture melting point, and infrared spectrum.

Catalytic Hydrogenation of Diketone 22.—The diketone (0.26 g) was catalytically reduced in methanol as above. The resulting 1,2,3,4,4aα,9,10,10a-octahydro-2,10a-ethano-3-hydroxy-2-methylphenanthren-11-one (**39**, 0.25 g) had mp 148–149° (from methylene chloride–isopropyl ether), ν_{max} 1735 and 3590 cm^{-1}. *Anal.* Calcd for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 79.60; H, 7.74.

Oxidation of this ketol with chromic oxide–pyridine as described above gave diketone **35** identified by melting point, mixture melting point, and infrared spectrum.

Registry No.—**17**, 7442-56-0; **18**, 7442-57-1; **19**, 7442-58-2; **20**, 7442-59-3; **21**, 7442-60-6; **22**, 7442-61-7; **23**, 7442-62-8; **24**, 7442-63-9; **25**, 7442-64-0; **26**, 7442-65-1; **27**, 7442-66-2; **29**, 7442-68-4; **30**, 7442-31-1; **31**, 7442-32-2; **32**, 7442-33-3; **36**, 7442-34-4; **37**, 7442-35-5; **38**, 7442-36-6; **39**, 7442-37-7; **33**, 7430-85-5; **34**; 7442-38-8; **35**, 7430-86-6; methyl ester of **17**, 7442-39-9.

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Conformational Analysis. LIV. The 2-Bromo Derivatives of 4-*t*-Butylcyclohexanone, 4,4-Dimethylcyclohexanone, 6,6-Dimethylcyclohexanone, and 2,6,6-Trimethylcyclohexanone[1,2]

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The conformations of title compounds have been studied by the dipole-moment method. *trans*-2-Bromo-4-*t*-butylcyclohexanone contains no detectable amount of boat form, while the *cis* isomer contains about 10% as shown by the variation of dipole moment with solvent. The *syn*-axial methyl–bromine interaction energy between the 2-bromo and a methyl group in either the 4 or 6 position is 2.2 kcal/mole in these compounds. The 2,6-*syn*-axial dimethyl interaction energy is greater than 2 kcal/mole.

While the conformational energies of most common substituents on cyclohexane rings are now known with more or less accuracy,[3-5] extension of these studies to systems of increasing complexity requires that the conformational energies for interactions between substituents be examined. A few are known: the *syn*-diaxial interactions between two methyl groups and that between a methyl and a hydroxyl for example.[3,6] There has not yet been reported any reliable method for predicting such interaction energies, and this is a goal for the future. At present it is desirable to determine more of these interaction energies experimentally, and this paper is concerned with the *syn*-diaxial methyl–bromine interaction. This interaction occurs in different ways in various methylated 2-bromocyclohexanones, and some qualitative information concerning certain of these compounds is available from earlier studies by Corey.[5,7] We have chosen dipole moments as a convenient property to measure to obtain this interaction energy in the present work.

(1) Paper LIII: N. L. Allinger and L. A. Tushaus, *Tetrahedron*, in press.

(2) This research was supported by Grant GP 4290 from the National Science Foundation.

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