(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.

Acknowledgment.—This work was supported by the Petroleum Research Fund administered by the American Chemical Society (Grant No. 1370-A-1); we wish to express our appreciation to the donors of this fund.

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.

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[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.

[3] For a summary and leading references, see E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, Inc., New York, N. Y., 1965.

[4] E. L. Eliel and T. J. Brett, *J. Am. Chem. Soc.*, **87**, 5039 (1965).

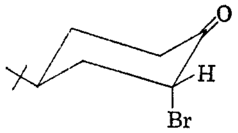
[5] N. L. Allinger, H. M. Blatter, L. A. Freiberg, and F. M. Karkowski, *ibid.*, **88**, 2999 (1966).

[6] B. Waegell, P. Pouzet, and G. Ourisson, *Bull. Soc. Chim. France*, 1821 (1963).

[7] E. J. Corey, T. H. Topie, and W. A. Wozniak, *J. Am. Chem. Soc.*, **77**, 5415 (1955).

The α-halo ketones represent a class of compounds which can be and have been studied by a large variety of experimental methods.[8] In general, simple substituted 2-bromocyclohexanones are equilibrium mixtures of chair forms in which the halogen is either axial or equatorial. The equatorial halogen is destabilized by the electrostatic repulsion between the C—Br and C═O dipoles, while steric effects may favor either form, depending on the situation. Steric effects are essentially invariant with respect to the nature of the solvent in which the equilibrium is established, while the electrostatic energy does vary with solvent. This variation of equilibrium with solvent can be used to obtain information on the relative importance of the steric and electrostatic effects present in the system. A study of the conformational equilibrium of 2-bromocyclohexanone itself was interpreted in terms of the chair conformations represented by the *cis* and *trans* isomers of 2-bromo-4-*t*-butylcyclohexanone.[9] At that time there was no reason to suspect that these molecules existed in anything other than chair forms. More recent work has, however, shown that the conformational energy of a cyclohexanone ring is considerably less than that of a cyclohexane ring,[5] and this problem has now been reconsidered.

The *trans* isomer (Ia) of 2-bromo-4-*t*-butylcyclohexanone has an axial bromine, and the only unfavorable interaction present is the small steric interaction between the bromine and the *syn*-axial hydrogens (0.4 kcal/mole). Taking the free energy of the cyclohexanone ring in the boat form as 2.8 kcal,[5] the energy of the chair form in Ia must be lower than that of the boat by at least 2.4 kcal, and hence the amount of boat form present in this compound must be at most 2% at room temperature. The equilibrium between boat and chair forms in Ia is thus so one-sided that it should be essentially invariant to changes in solvent, at least over the range considered, and hence it was predicted that the dipole moment of this compound would be solvent independent. Experimental measurements confirmed this prediction. The dipole moment of the compound is the same to within experimental error in heptane, benzene, and dioxane (Table I).



Ia

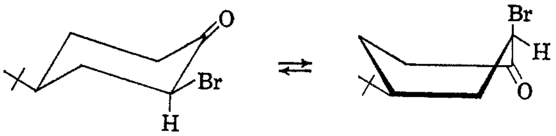
Table I

Experimental Dipole Moments of 4-*t*-Butylcyclohexanones

Ketone	Solvent		
	Heptane	Benzene	Dioxane
trans-2-Bromo (Ia)	3.19	3.20	3.17
cis-2-Bromo (Ie)	4.20	4.27	4.33
cis-2-Fluoro[a]	4.37	4.35	4.39

[a] N. L. Allinger, and H. M. Blatter, *J. Org. Chem.*, **27**, 1523 (1962).

The *cis* isomer (Ie) of 2-bromo-4-*t*-butylcyclohexanone represents a more complicated situation. In the chair form there is an unfavorable electrostatic interaction between the dipoles, which can be relieved if the molecule takes up a boat form. For the enantiomer pictured, the boat form is of optimum energy only when the pseudo-rotational angle (θ) is near −60°, as pictured. The free energy of this conformation can be estimated only approximately, since the experimental literature value and the value for this compound are expected to differ some in entropy. However, using the experimental value of 2.8 kcal/mole for the conformational energy of the ring in the boat form, taking the electrostatic energy to be that of the axial chair form (since the interdipole angles are quite similar), and neglecting the steric interaction of the bromine, which must be small, one is in a position to estimate the chair–boat equilibrium in Ie. The equatorial bromine in the chair form has an unfavorable electrostatic energy, relative to the axial-like bromine in the boat form, which varies from 1.4 kcal/mole in heptane to 1.0 kcal/mole in benzene and 0.8 kcal/mole in dioxane.[10] The free energy increase in going from the chair to boat in Ie can therefore be estimated to be variable from 1.4 kcal/mole in heptane to 2.0 kcal/mole in dioxane; and the percentage of boat form should vary from 9 down to 2% over this solvent range.



Ie (chair) Ie (boat, θ = −60°)

The dipole moment of Ie should be high in dioxane, and, as the polarity of the solvent decreases, the boat form increases at the expense of the chair, and the observed dipole moment should decrease. In benzene, the dipole moment of Ie is 4.27 D.,[9] and this should, according to the calculations, correspond to a mixture of 95% chair and 5% boat. The moment of the latter should be 3.19 D. (same as the *trans* isomer, average value), and from these data, the moment of the chair form of Ie can be calculated to be 4.31 D. From the calculated compositions of the equilibrium mixtures in heptane, benzene, and dioxane, one predicts dipole moments for the compound in these solvents of 4.22, 4.27, and 4.30 D., which is just sufficient variation to be detectable with certainty. The dipole moment of Ie was therefore determined in these different solvents, and the variation was indeed observed. It was the same as that calculated to within experimental error (Table I). A comparison of Ie with the corresponding fluoro derivative is of interest.[11] In this compound the electrostatic energy of the boat form is lower than that of the chair by an amount that varies from 0.7 kcal/mole in heptane to 0.2 kcal/mole in dioxane. The fraction of boat present would change only from 3 to 1% under these circumstances; so the observed dipole moment of the compound should be invariant with solvent, as was found.

Having now some confidence in our ability to deal with boat forms, we examined the 4,4- and the 6,6-dimethyl derivatives of 2-bromocyclohexanone (II and

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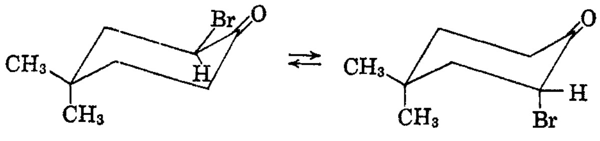
(8) Reference 3, p 460.

(9) N. L. Allinger and J. Allinger, *J. Am. Chem. Soc.*, **80**, 5476 (1958).

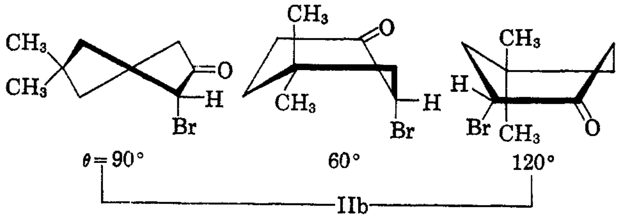
(10) N. L. Allinger, J. G. D. Carpenter, and M. A. DaRooge, *J. Org. Chem.*, **30**, 1423 (1965).

(11) See Table I, footnote *a*.

III, respectively). An axial methyl in the 4 position on a cyclohexanone ring is sterically similar to the corresponding methyl on a cyclohexane ring,[5] and the relative energy of IIe in heptane solvent is thus 1.7 (steric) + 1.4 (electrostatic) = 3.1 kcal/mole. The energy of IIa is 0.9 (Me|H) + 0.2 (Br|H) + Me|Br = 1.1 kcal, plus the (Me|Br) interaction. The best arrangement of the boat form which has the bromine in an axial-like position is with $\theta = 90°$ as pictured.



IIe IIa



The energies of the interactions in the $\theta = 90°$ form do not correspond to experimentally known ones, but they can be estimated from those at $\theta = 60$ and 120°. At $\theta = 60°$, the following are present: Me|C_6H = 0.9 kcal, and Br|C_5H = about 2 kcal, plus the ring energy. At $\theta = 120°$ there is present the (Me|Br) interaction we wish to determine (2.2 kcal), and the bromine is now in a bisected position (0.7 kcal) plus the ring energies. At $\theta = 90°$, the electrostatic energy will be half that at 120°, or 0.35 kcal. The other interactions will be reduced[10] to an amount between one-quarter and one-half the values at 60 and 120°, or to a value in the range of 1.4 to 2.1 kcal. Adding this to the ring energy (2.8 kcal) and the electrostatic energy, we obtain a total energy of 4.4 to 5.7 kcal/mole. The ratio of IIb to IIe is therefore going to be in the range of 0.10 to 0.02 and its presence can be allowed for. This conformation will have a dipole moment of approximately 3.55 D.

The experimental dipole moment of 2-bromo-4,4-dimethylcyclohexanone was found to be 3.93 D. in heptane (Table II). The moments for axial and equatorial conformers were calculated from the group moments of 2,2-dimethylcyclohexanone and the C—Br dipole (Table III) as before and found to be 3.12 and 4.29 D.,[12] if interdipole angles were like those of the unmethylated compound (Table IV). Actually, the molecule with equatorial bromine should have similar angles, but the *syn*-diaxial arrangement will have the methyl pushing the bromine out away from the ring, which would decrease the angle between the dipoles, and hence increase the dipole moment of the conformation. We can estimate the result from data available on steroid systems. The dipole moment of 2α-bromo-3-cholestanone, where the bromine is equatorial, is to about within experimental error the same as that of Ie, while 4β-bromo-3-cholestanone has a moment 0.30 D. larger than does Ia.[10] This difference was interpreted earlier as a result of a similar bending in the 4β-bromide brought about by the 19-methyl. In the present case the methyl is positioned similarly and the result will be the bromine bending in an almost identical manner with that observed in the steroid case. The axial conformation (IIa) would thus have its dipole moment increased to 3.42 D. when this bending is allowed for.

TABLE II

OBSERVED DIPOLE MOMENTS[a] AT 25°

Compound	Solvent[b]	μ, D.	Ref
1-Bromo-1-methylcyclohexane	B	2.26	*c*
2,2-Dimethylcyclohexanone	B	2.96	7
2,2,6-Trimethylcyclohexanone	B	2.85	*d*
2-Bromo-4,4-dimethylcyclohexanone	H	3.93	*e*
2-Bromo-6,6-dimethylcyclohexanone	B	3.98	7
2-Bromo-2,6,6-trimethylcyclohexanone	B	3.02	*d*
2-Bromo-2,6,6-trimethylcyclohexanone	D	3.12	*d*

[a] Least-squares treatment of the data gives the probable errors in the dipole moments as not more than ±0.02 D. in each case. [b] H, B, and D indicate heptane, benzene, and dioxane, respectively. [c] J. G. Traynham and O. S. Pascual, *J. Org. Chem.*, 21, 1362 (1956). [d] C. L. Stevens and A. J. Weinheimer, *J. Am. Chem. Soc.*, 80, 4072 (1958). [e] E. J. Corey, *ibid.*, 75, 2301 (1953).

TABLE III

GROUP MOMENTS FOR THE BROMOCYCLOHEXANONES[a]

Group	Bromine Axial	Bromine Equatorial
Cyclohexanone		
2,2-Dimethyl-	2.96	2.74
4,4-Dimethyl-[b]	3.06	2.83
2,2,6-Trimethyl-	2.85	2.64
Cyclohexyl		
1-Bromo-	2.26	1.93
1-Bromo-1-methyl-	2.24	1.91

[a] The dipole moment observed for a given methylated cyclohexanone and that observed for 1-methylcyclohexyl bromide were used for the group moments for the respective groups in the bromo ketone in conformations where the bromine is axial. If the bromine is equatorial it is necessary to reduce the group moments to allow for mutual induction; see N. L. Allinger, J. Allinger, L. A. Freiberg, R. F. Czaja, and N. A. LeBel, *J. Am. Chem. Soc.*, **82**, 5876 (1960). Geometries were those used previously. [b] These values were taken from those of cyclohexanone itself.

TABLE IV

DIPOLE MOMENTS CALCULATED FOR THE VARIOUS BROMO KETONE CONFORMATIONS[a]

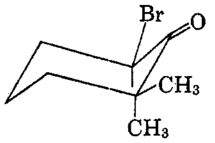
Conformation	μ, D.
IIa	3.42[b]
IIe	4.29
IIIa	3.35[b]
IIIe	4.20
IVa	2.98
IVe	4.12

[a] Calculated from the group moments in Table III except where indicated. [b] Including an increase in moment of 0.30 D. to allow for deformation of the carbon–bromine bond.

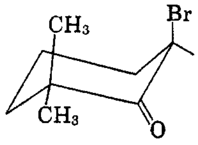
If the energy of the boat form is high enough that its concentration is negligible, the observed moment of II (3.93 D.) corresponds to a mixture containing 56% IIe and 44% IIa. If the lower limit in energy is taken for the boat form, the mixture contains 6% boat, 53% IIe, and 41% IIa. The presence or absence of the boat form makes no significant difference; the difference in energy between IIe and IIa is 0.2 kcal/mole, with the former being more stable. One can now write for IIa ⇌ IIe $\Delta G° = -0.4$ kcal/mole, and $G_e° - G_a° =$

-0.2 kcal/mole. Assuming the entropy change is zero, putting in the numbers given earlier, we have $(1.7 + 1.4) - (0.9 + 0.2 + \mathrm{Me|Br}) = -0.2$, which when solved gives the (Me|Br) interaction an energy of 2.2 kcal/mole. The energy is clearly a large one, but considerable smaller than the methyl–methyl *syn*-axial interaction (3.7 kcal/mole).[3] As a check, the above calculation was repeated without allowing for the bending of the carbon–bromine bond, using 3.12 for the moment of IIa. In this case the (Me|Br) interaction energy is found to be 2.4 kcal/mole, showing that error introduced by neglect of such bending is not very large.

An independent determination of the quantity in question was undertaken by measurements on 2-bromo-6,6-dimethylcyclohexanone (III), and similar considerations apply. The moments calculated for IIIe and IIIa in this case are 4.20 and 3.35 D., while the experimental value determined for III was 3.98 D. in benzene (Tables II and III). The interaction energies of the axial methyl with hydrogen are 1.6 kcal/mole in IIIe and 0.8 kcal/mole in IIIa. There is a steric bromine–hydrogen interaction of 0.2 kcal in IIIa, and an electrostatic interaction of 1.0 kcal in IIIe. The observed moment corresponds to 28% of IIIa and 72% of IIIe, which corresponds to a free-energy difference of 0.6 kcal/mole, IIIe being the more stable. (As before, this number is not really changed appreciably by allowing for the presence of a reasonable amount of boat form or by neglecting the carbon–bromine bond bending.) The energy equation for IIIa $\rightleftharpoons$ IIIe becomes $(1.6 + 1.0) - (0.8 + 0.2 + \mathrm{Me|Br}) = -0.6$, which gives a methyl–bromine interaction energy of 2.2 kcal/mole, exactly the same as that found in the 4,4-dimethyl case, which would not be expected from an examination of models in view of the fact that the 2- and 6-axial substituents tend to lean away from one another, but, as we have previously pointed out,[5] the Dreiding models are inaccurate in this respect.

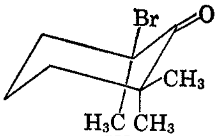


IIIe

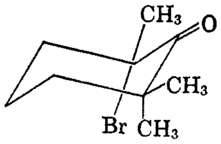


IIIa

Finally, 2-bromo-2,6,6-trimethylcyclohexanone (IV) was examined with the hope that the 2,6-*syn*-axial methyl–methyl interaction could be evaluated. If no carbon–bromine bond bending is allowed for, which seems a better approximation with the tertiary bromide, the calculated values for the dipole moments are, for IVe, 4.12, and IVa, 2.98 D. In benzene solution the experimental value (3.02 D.) showed that the compound was 97% in the axial conformation (which is within experimental error of 100%). In dioxane the experimental value (3.12 D.) indicated 89% axial. For the change IVe $\rightleftharpoons$ IVa, the energy equation in dioxane solution is $(2.2 + 0.8 + 0.2) - (\mathrm{Me|Me} + 1.6 + 0.8) = -1.2$ kcal/mole, which gives the (Me|Me) interaction as 2.0 kcal/mole. The experimental errors add up in such a way that this number could be quite a bit too low, and a conservative interpretation of the data is simply to conclude that the 2,6-*syn*-axial methyl–methyl interaction is 2 kcal/mole or greater. Unfortunately, the equilibrium is too one sided to allow more definite conclusions to be drawn in this case.



IVe



IVa

Experimental Section

The compounds were all prepared by known methods and had properties in agreement with the literature. The dipole moments were obtained using previously described methods and apparatus.[1] The results are summarized in Table II.

Registry No.—Ia, 7443-39-2; Ie, 7443-33-6; *cis*-2-fluoro ketone, 7443-34-7; IIa $\rightleftharpoons$ IIe, 7443-35-8; IIIa $\rightleftharpoons$ IIIe, 7431-07-4; IVe, 7428-18-4; 1-bromo-1-methylcyclohexane, 931-77-1; 2,2-dimethylcyclohexanone, 1193-47-1; 2,2,6-trimethylcyclohexanone, 2408-37-9; IVa, 7428-19-5.