38. **Seiichi Inayama**: The Correlation between the Spectra and Structures in Cyclohexanone Derivatives. I. Effect of α-Bromination and Conjugation on the Infrared and Ultraviolet Absorption Spectra of the Carbonyl Group.*

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The stereochemistry of various steroidal α-haloketones was progressively developed by Jones and his co-workers on the ground of infrared spectrographic evidence, in which the C=O stretching vibration regularly exhibits a higher frequency shift due to the configuration of halogen atom introduced into the neighboring carbon atom.[1] In cyclohexanone and decalone derivatives a similar effect may also be expected, but as far as is known, only Corey reported his work on α-bromocyclohexanone derivatives,[2a,2b] on the basis of which the configuration of α-bromoketosteroids was discussed,[2c] and further, the argument was extended to the prediction of a stable isomer.[2d]

The present paper includes both the infrared and ultraviolet spectral data of 33 kinds of α-bromoketones, additional ketones with α,β- and α,β : α′,β′-conjugated double bonds in mono- and bicyclic systems. On this ground the correlation between spectra and structure of these compounds is discussed. In Tables I and II are recorded the carbonyl stretching frequencies of the compounds, the structures of which are shown in Fig. 1 and their ultraviolet absorption maxima are listed in Table III.

Effect of Conjugation by Ethylenic Double Bond

Conjugation of a carbonyl group with an ethylenic linkage are found to lower the frequency by an amount depending on the nature of the double bond. The carbonyl stretching frequency($\nu_{c=0}$)of α,β- and α,β;α′,β′-unsaturated ketones are generally less than that in the corresponding saturated ketones, e.g. $\nu_{c=0}$ 1676 cm^{-1} in cholest-4-en-3-one[1a] and 1656 cm^{-1} in cholesta-1,4-dien-3-one,[1b] are significantly lower than that of 1718 cm^{-1} in cholestan-3-one,[1d] and the carbonyl frequency shifts ($\Delta\nu$) are 42 cm^{-1} and 52 cm^{-1}, respectively (all in carbon disulfide solution). In the case of cyclohexanone series, as indicated in Table I, the stretching band maxima of all saturated ketones fall within a very narrow range of 1718∼1724 cm^{-1}, whereas the cyclohexanones and cyclohexadienones respectively absorb maximally in the range of 1672∼1681 cm^{-1} and 1667∼1672 cm^{-1}. Then the magnitude of lower frequency shift in this series are 33∼46 cm^{-1} and 49∼52 cm^{-1}, respectively, which agrees with the result obtained in steroidal 3-ketones. The sensibly higher maximum of 6-methyl-2-cyclohexenone (II′c), being a less substituted monoenone compared to 2-methyl-2-cyclohexenone (IIc), agrees with the slight difference found between $\nu_{c=0}$ of Δ^1-3-one

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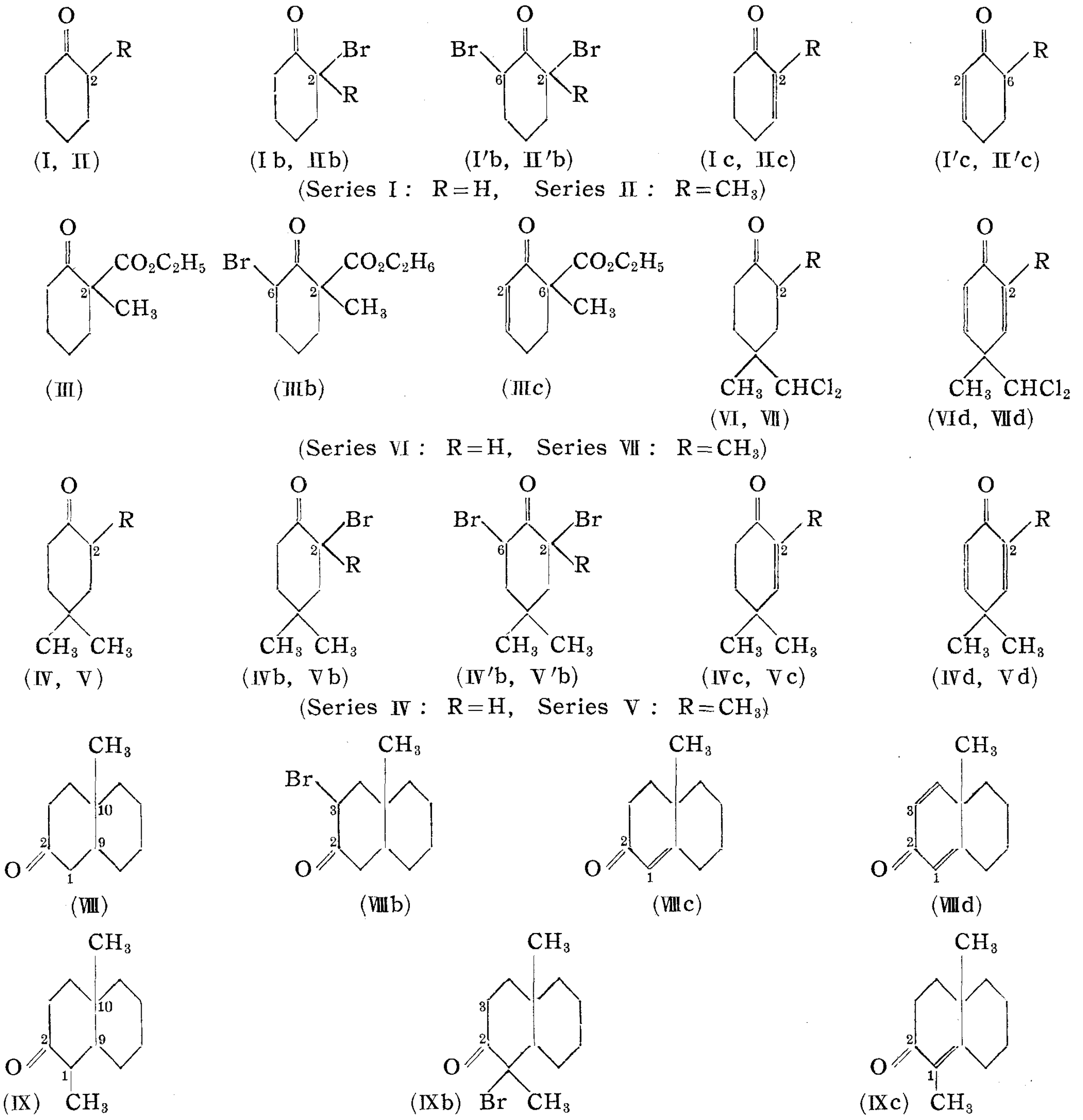
1) (*a*) R. N. Jones, P. Humphries, E. Packard, K. Dobriner: J. Am. Chem. Soc., **72**,86 (1950); **70**, 2024(1948); **71**, 241(1949); Vitamins and Hormones, **7**, 293(1949). (*b*) R. N. Jones, P. Humphries, K. Dobriner: J. Am. Chem. Soc., **72**, 956(1950). (*c*) R. N. Jones, D. A. Ramsay, D. S. Keir, K. Dobriner: *Ibid.*, **74**, 80(1952). (*d*) R. N. Jones, D. A. Ramsay, F. Herling, K. Dobriner: *Ibid.*, **74**, 2828(1952).

2) (*a*) E. J. Corey: *Ibid.*, **75**, 2301(1953). (*b*) E. J. Corey: *Ibid.*, **75**, 3297(1953). (*c*) E.J. Corey: Experientia, **9**, 329(1953). (d) E. J. Corey: J. Am. Chem. Soc., **76**, 175(1954).

Fig. 1. Structures of Cyclohexanone Derivatives



Series (b) : α-bromoketone. Series (c) : monoenone. Series (d) : dienone.

(1680~1684 cm^{-1}) and $\nu_{C=O}$ of Δ^4-3-one (1677~1674 cm^{-1}) in steroids.[1a] This may be explained from the fact that the contribution of the mesomeric structure in α,β-unsaturated system increases with the increasing number of ethylenic double bond conjugated to a carbonyl group and this influences the dipolemoment of the carbonyl group, resulting in reduction of the carbonyl frequency.

In connection with the foregoing infrared data, the ultraviolet absorption maximum of carbonyl group (the so-called R-band) is also displaced upward according to increment of the conjugated system.[3]

As given in Table III, the absorption maxima of several cyclohexanones, 283~287 mμ (ε 15~20), shift to a longer wave length, appearing at about 320 mμ (ε 25~60) ($\Delta\lambda$ +34~36 mμ) in cyclohexenones and at 325~337 mμ (ε 25~30) ($\Delta\lambda$ +40~50 mμ) in cyclohexadienones. Between the bathochromic shift of absorption maximum of cyclic monoenone and cross-dienone to the parent ketone, no significant difference

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[3] L. K. Evans, A. E. Gillam : J. Chem. Soc., **1941**, 815.

was found, either in infrared or ultraviolet spectra, viz. the shift value for cross-dienone is only ca. 10 cm^{-1} in the infrared and ca. 10 mμ in the ultraviolet more than that for monoenone. This is an interesting fact in connection with a pronounced fact that no considerable displacement is produced between the intense band maxima occurring at a shorter wave length region (the so-called K-band) due to monoenone and crossed dienone conjugated system (each maximum is described in experimental section).

Thus it becomes obvious that in these unsaturated compounds the infrared carbonyl frequency decreases by 35~50 cm^{-1}, whereas the ultraviolet carbonyl maximum increases by 35~50 mμ from the corresponding saturated ketones. No clear-cut correlation was found between the degree of alkyl substitution on the double bond

TABLE I. Effect of Conjugation on Infrared Absorption Maxima (Frequencies in cm^{-1})

Compound	$\nu_{\mathrm{C=O}}^{\mathrm{CCl_4}}$	$\Delta\nu$
2-Methylcyclohexanone (II)	1718	—
2-Methylcyclohexen-2-one (IIc)	1681	−37
6-Methylcyclohexen-2-one (II′c)	1684	−34
2-Ethoxycarbonyl-2-methylcyclohexanone (III)	1718	—
6-Ethoxycarbonyl-6-methylcyclohexen-2-one (IIIc)	1675	−43
2,4,4-Trimethylcyclohexanone (V)	1718	—
2,4,4-Trimethylcyclohexen-2-one (Vc)	1681	−37
2,4,4-Trimethylcyclohexa-2,5-dienone (Vd)	1669	−49
4-Dichloromethyl-4-methylcyclohexanone (VI)	1724	—
4-Dichloromethyl-4-methylcyclohexa-2,5-dienone (VId)	1672	−52
4-Dichloromethyl-2,4-dimethylcyclohexanone (VII)	1721	—
4-Dichloromethyl-2,4-dimethylcyclohexa-2,5-dienone (VIId)	1672	−49
trans-10-Methyl-2-decalone (VIII)	1718	—
2-Oxo-10-methyl-2,3,4,5,6,7,8,10-octahydronaphthalene (VIIIc)	1681	−37
2-Oxo-10-methyl-2,5,6,7,8,10-hexahydronaphthalene (VIIId)	1667	−51
trans-1,10-Dimethyl-2-decalone (IX)	1712	—
1,10-Dimethyl-2-oxo-2,3,4,5,6,7,8,10-octahydronaphthalene (IXc)	1672	−40

TABLE II. Effect of α-Bromination on Infrared Absorption Maxima (Frequencies in cm^{-1})

Compound	$\nu_{\mathrm{C=O}}^{\mathrm{CCl_4}}$	$\Delta\nu$	Conformation of α-bromine
Cyclohexanone (I)	1718*	—	—
2-Bromocyclohexanone (Ib)	1724* 1736*(sh.)	+6 +18	*a* *e*
cis-2,6-Dibromocyclohexanone (I′b)	1754*	+36	*e*, *e*
2-Methylcyclohexanone (II)	1718*	—	—
2-Bromo-2-methylcyclohexanone (IIb)	1724*	+6	*a*
trans-2,6-Dibromo-2-methylcyclohexanone (II′b)	1739*	+21	2*a*, 6*e*
2-Ethoxycarbonyl-2-methylcyclohexanone (III)	1718	—	—
6-Bromo-2-ethoxycarbonyl-2-methylcyclohexanone (IIIb)	1733	+15	*e*
4,4-Dimethylcyclohexanone (IV)	1718*	—	—
2-Bromo-4,4-dimethylcyclohexanone (IVb)	1736*	+18	*e*
cis-2,6-Dibromo-4,4-dimethylcyclohexanone (IV′b)	1754	+36	*e*, *e*
2,4,4-Trimethylcyclohexanone (V)	1718	—	—
2-Bromo-2,4,4-trimethylcyclohexanone (Vb)	1724 1738(sh.)	+6 +20	*a* *e*
trans-2,6-Dibromo-2,4,4-trimethylcyclohexanone (V′b)	1739	+21	2*a*, 6*e*
trans-10-Methyl-2-decalone (VIII)	1718	—	—
trans-3-Bromo-10-methyl-2-decalone (VIIIb)	1736	+18	*e*
trans-1,10-Dimethyl-2-decalone (IX)	1718	—	—
trans-1-Bromo-1,10-dimethyl-2-decalone (IXb)	1718	0	*a*

* Values in reference (from above): 1712[2a,2b]; 1716, 1730(sh.)[2b]; 1750[2b]; 1715[10]; 1722[10]; 1738[10]; 1728[2a].

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Table III. Effect of α-Bromination and Conjugation on Ultraviolet Maxima (Wave length in mμ)

Compound	λ_{max}^{EtOH}	$\Delta\lambda$	Orientation of α-bromine
Cyclohexanone (I)	284	—	—
2-Bromocyclohexanone (Ib)	306	+22	*a*
2-Methylcyclohexanone (II)	287	—	—
2-Bromo-2-methylcyclohexanone (IIb)	307	+20	*a*
2-Methylcyclohexen-2-one (IIc)	321	+21	—
6-Methylcyclohexen-2-one (II′c)	321	+21	—
2-Ethoxycarbonyl-2-methlcyclohexanone (III)	257	—	—
6-Bromo-2-ethoxycarbonyl-2-methylcyclohexanone (IIIb)	260(infl.)	+3	*e*
6-Ethoxycarbonyl-6-methylcyclohexen-2-one (IIIc)	305	+48	—
2,4,4-Trimethylcyclohexanone (V)	285	—	—
2-Bromo-2,4,4-trimethylcyclohexanone (Vb)	310	+25	*a*
2,4,4-Trimethylcyclohexen-2-one (Vc)	321	+36	—
2,4,4-Trimethylcyclohexa-2,5-dienone (Vd)	325	+40	—
4-Dichloromethyl-4-methylcyclohexanone (VI)	285	—	—
4-Dichloromethyl-4-methylcyclohexa-2,5-dienone (VId)	335	+50	—
trans-4-Dichloromethyl-2,4-dimethylcyclohexanone (VII)	287	—	—
4-Dichloromethyl-2,4-dimethylcyclohexa-2,5-dienone (VIId)	337	+50	—
trans-10-Methyl-2-decalone (VIII)	282	—	—
trans-4-Bromo-10-methyl-2-decalone (VIIIb)	283.5	+1.5	*e*
2-Oxo-10-methyl-2,4,5,6,7,10-hexahydronaphthalene (VIIId)	314	+32	—

and the position of the carbonyl band maximum both in infrared and ultraviolet spectra. In respect to this point, the adaptation of K-band to the above correlation, known as Woodward's rule, is quite useful.

Effect of α-Bromination

The stereochemistry of α-bromine atom in cyclic ketones is closely connected with reactivity of the bromine in the compound and the determination of its configuration has been made not only by chemical means,[4] but also by some convenient physical methods, including molecular rotation difference,[5] infrared,[1,2] and ultraviolet spectroscopy.[6] Hitherto, discrepancy between the results from them does not seem to be found.[*1]

Jones *et al.* observed in α-bromoketosteroids that if the bromine atom is equatorial (*e*) the carbonyl stretching frequency increases by 15~20 cm^{-1}, and on the contrary, no shift is virtually produced if axially (*a*) oriented.[1a] In the former, the C-Br link and the C=O bond are coplanar and increment of $\nu_{C=O}$ occurs, depending on increasing mutual interference between the C=O and C-Br dipoles, but those are so perpendicular in the latter that no appreciable surpression of the C-Br dipole to the vibration due to the C=O dipole is produced. Now since the validity of this postulation has already been confirmed,[2] the configuration of the bromine in a few of such cyclic secondary bromides, derived from cyclohexanone (I), 2-ethoxycarbonyl-2-methylcyclohexanone (III), 4,4-dimethylcyclohexanone (IV), and *trans*-10-methyl-2-decalone (VIII), may be predicted on the ground of carbonyl frequency shifts,

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4) (*a*) L. F. Fieser, R. Ettorre: J. Am. Chem. Soc., **75**, 1700(1953). (*b*) L. F. Fieser, X. A. Dominguez: *Ibid.*, **75**, 1704(1953). (*c*) L. F. Fieser, Wei-Yuan Huang: *Ibid.*, **75**, 4837(1953). (*d*) E. J. Corey: *Ibid.*, **75**, 4832(1953).

5) C. Djerassi: J. Org. Chem., **12**, 823(1947); cf. Footnote (4b).

6) R. C. Cookson: J. Chem. Soc., **1954**, 282.

[*1] On the conformation of bromine atom in 2-bromocholestan-3-one, Fieser declared that the conclusion of α-bromine being axially oriented from chemical evidence was a contradiction to that from the molecular rotation difference (Djerassi[5]), infrared (Jones *et al.*[1a] and Corey[2c]) and ultraviolet (Cookson[6])[4b], but Corey pointed out later the inapproprietness of Fieser's decision by chemical disproval.[4d] The former thus reëxamined and convinced the validity of the experiment and the approprietness of his prediction by the work of Corey.[4d]

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insofar as these cyclohexanone rings take the most probable chair conformation. As given in Table II, 2-bromocyclohexanone (Ib) absorbs strongly at 1724 cm^{-1} with a shoulder at 1736 cm^{-1}. By the introduction of a bromine atom at C_2, $\nu_{C=O}$ of cyclohexanone, therefore, increases to the intense band maximum by 6 cm^{-1} and to a weak shoulder by 18 cm^{-1}. This datum, agreeing with the result of Corey's determination,[2a,2b] reveals indeed that the bromoketone consists largely of the bromide corresponding to axial bromine, and in part, of the one corresponding to equatorial bromine atom. Since the electrostatic repulsion between the C–Br and C=O dipoles increases if the bromine is equatorial, Br(*a*) (XI*a*) $\rightleftharpoons$ Br(*e*) (XI*e*) equillibrium for the converted isomers (Fig. 2) tends to become thermodynamically more stable (Br(*a*)), causing no epimerization by hydrogen bromide. The isomer corresponding to kinetic and thermodynamic control[2c] is thus the one in which the bromine is axial. In 2-bromo-4,4-dimethylcyclohexanone (IVb), however, it is considered that the C–Br link lies approximately in the plane including the C=O bond on account of increasing steric interaction between α-bromine atom (*a*) and γ-methyl group (*a*), so that $\nu_{C=O}$ produces increments by 18 cm^{-1}, indicating that the stable conformation of the bromine in converted equilibrium (XII*a*) $\rightleftharpoons$ (XII*e*) for the compound should be equatorial. On adopting a similar argument to *trans*-3-bromo-10-methyl-2-decalone (VIIIb), which involves the same geometrical specificity as (IV*a*), the bromine atom causing no epimerization by hydrogen bromide[7] should also be predicted as α-oriented. The infrared determination value of 1736 cm^{-1}, indicating the displacement to a higher frequency by 18 cm^{-1}, substantiates the exclusive equatorial bromine in the equilibrium (XIII*a*) $\rightleftharpoons$ (XIII*e*) for the compound, that is parallel with the result for 2-bromocholestan-3-one ($\Delta\nu$ +15 cm^{-1}).[1d],[*1],[*2]

Next, in the case of 6-bromo-2-ethoxycarbonyl-2-methylcyclohexanone (IIIb) including two asymmetric carbon atoms, it may be expected that in the four possible isomers, two are stable, both carrying axial ethoxycarbonyl and equatorial methyl groups as shown by (XIV*a*) and (XIV*e*) in Fig. 2, because of the destabilizing effect due to the electrical repulsion between the C=O bond and the electronegative COOEt group if those are coplanar.[*3] Then the equilibrium (XIV*a*) $\rightleftharpoons$ (XIV*e*) for the compound, in which the severe steric interaction between the C=O group and either of the bulky axial substituents at α or α' position in (XIV*a*) is so much greater than

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[*2] After an intense discussion between Fieser and Corey on the configuration of the bromine in 2-bromocholestan-3-one, Jones suggested that, though the C_2-Br is axial (β), the spectrographic condition corresponding to the axial bromine would be satisfactory provided that the A-ring including the C=O group at C_3 takes a boat conformation.[8] This probability for (VIIIb), however, does not seem to be derived from the viewpoint of either simplicity of the C=O bond or thermodynamic stability of the compound.

7) M. Yanagita, K. Yamakawa : J. Org. Chem., **20**, 1473(1955).

8) R. N. Jones : J. Am. Chem. Soc., **75**, 4839(1953).

[*3] The electronegativity of ethoxycarbonyl group is assumed to be almost identical with that of bromine atom on comparison of dipole moments for the standard compounds, i.e. CH_3CO_2-C_2H_5 : 1.85(liquid), 1.76(vapor); CH_3Br : 1.80(vapor); *tert*- or *sec*-butyl bromide : 2.15(liquid).[9a] 2-Ethoxycarbonylcyclohexanone possesses chelation ($\nu_{C=O}$ 1642 cm^{-1} due to the presence of an enol system of the compound, whereas 2-ethoxycarbonyl-2-methylcyclohexanone (III) produces no chelation ($\nu_{C=O}$ 1724 cm^{-1}) (ester) and 1712 cm^{-1}(ketone)) as reported by Bellamy and Beecher.[9b] Thus it seems that the ethoxycarbonyl group in the latter compound is situated perpendicularly in the general plane of methylcyclohexanone. The possibility of the converted structures of (XIV*a*) and (XIV*e*), respectively, viz. (XIV′*a*) and (XIV′*e*), should therefore be discarded, because of much more enhanced destabilizing effect in the compound. An interaction being assumed between CH_3(*e*)-O-Br(*e*) would not amount to much.

9) (*a*) G. E. K. Branch, M. Calvin : "The Theory of Organic Chemistry, An Advanced Course," Prentice-Hall Inc., New York, Table 16, 146(1941). (*b*) L. J. Bellamy, L. Beecher : J. Chem. Soc., **1954**, 4487.

10) E. J. Corey, T.H. Topie, W. A. Wozniak : J. Am. Chem. Soc. **77**, 5415(1955).

the electrical repulsion between C–Br and C=O dipoles in (XIV*e*) would result in proceeding in the direction to stabilize (XIV*e*). In practice the first frequency shift ($\Delta\nu$ +15 cm^{-1}) fully substantiates the above equilibrium scheme and the second minute one indicates only a presence of the other epimer (XIV*a*).

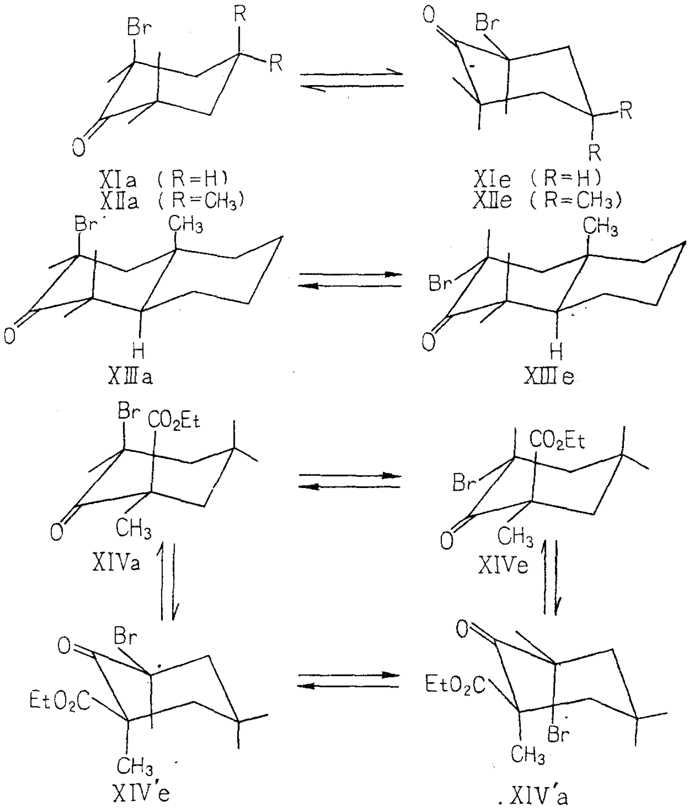

Fig. 2.

Conformation of Secondary Bromides

Series a : The bromine oriented axially

Series e : The bromine oriented equatorially

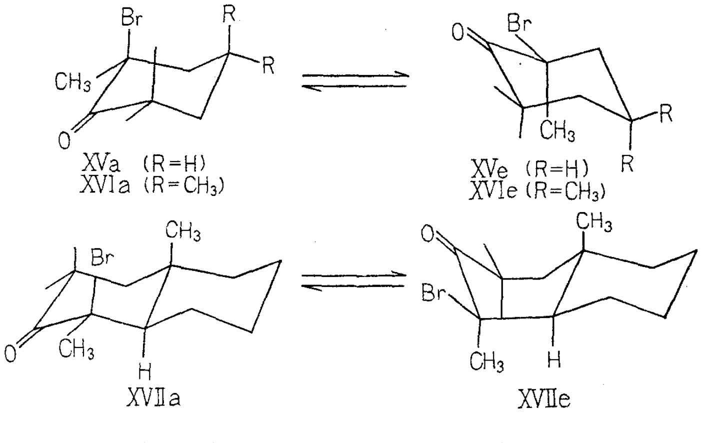

Fig. 3.

Conformation of Tertiary Bromides

After all, it has been clarified that in *sec*-bromides mentioned above, $\nu_{C=O}$ produces an upward shift by 15~18 cm^{-1} if the bromine is equatorial and only a little (less than 6 cm^{-1}) if axial. This agrees well with the statements made by Jones *et al.*[1d)] and Corey,[2a),2d)] but it is a question whether a similar argument as in *sec*-bromides could also be made for *tert.* ones derived from 2-methylcyclohexanone (II), 2,4,4-trimethylcyclohexanone (V), and *trans*-1,10-dimethyl-2-decalone (IX).[*4]

[*4] During the preparation of this paper for publication, it appeared that the conformation of bromine in several α-bromocyclohexanones including (IIb) and (II'b) was discussed by Corey *et al.* only on the basis of infrared carbonyl shift.[10)]

In view of the chemical behavior represented by ready dehydrobromination resulting in the formation of the corresponding monoenone,[11,12] and the assumption of destabilizing effect by interaction between the C=O and C–Br dipoles, it may be expected that the isomer carrying axial bromine surpasses the equatorial one in the equilibrium of the converted isomers, and also that the bromine atom in the compound is inevitably axial, provided that *tert*-bromides formed under kinetically controlled conditions are stabilized with retention of conformation of the bromine because of no possible epimerization, viz. enolization. In the latter two cases, however, an appreciable interaction between the bulky axial substituent at α-position and the axial methyl group at γ-position should be taken into the consideration. The infrared shifts for (IIb), (Vb), and (IXb), the bromides in question, in fact show $+6\,\mathrm{cm^{-1}}$, $+6\,\mathrm{cm^{-1}}$(except $+20\,\mathrm{cm^{-1}}$ to a shoulder band), and 0, respectively, indicating that the bromine in each compound all takes an axial conformation, except for the small amount of the equatorial in (Vb).

The C–Br link and the C=O bond in (IIb) might be assumed to become coplanar by ring conversion, but the bromine forced to an equatorial orientation would simultaneously tend to the parental axial orientation by reconversion due to the enhanced electrical repulsion between these dipoles in coplane, resulting in preferential stabilization to (XV*a*) in the equilibrium (XV*a*) $\rightleftharpoons$ (XV*e*) for the converted isomers (Fig. 3). Therefore, the axial isomer (XVa) should also be what corresponds to a thermodynamic control. The very facile elimination of hydrogen bromide,[11] indicating that the requirement for the geometry of the four reacting centres Br(*a*)–C_2–C_3H(*a*) is well satisfied, serves enough to support the above discussion. Since a single and shoulderless peak of the carbonyl band mentioned above and the following ultraviolet displacement substantiate it further, it will be self evident that the stereoformula for (IIb) corresponds to (XV*a*).

On applying the same scheme as above to 2-bromo-2,4,4-trimethylcyclohexanone (Vb), the axial isomer (XVI*a*) may be expected to amount to both kinetic and thermodynamic control in the equilibrium (XVI*a*) $\rightleftharpoons$ (XVI*e*) for the converted isomers. It should especially be considered that the axial isomer (XVIa) was converted to another equatorial one (XVI*e*) due to the strong steric interaction between C_2–Br(*a*) and C_4–CH_3(*a*), because of no possibility of epimerization of C_2–Br by enolization. In (XVI*e*), however, the destabilizing effect of both the electrical repulsion and the additional steric interaction between *cis*-axial methyl groups at *meta*-position would force the reconversion, which results in taking stabilization of the bromine as an equilibrium mixture carrying the preponderance of (XVI*a*). The present infrared data for (Va), in which a strong band at $1724\,\mathrm{cm^{-1}}$ ($\Delta\nu$ $+6\,\mathrm{cm^{-1}}$) indicates a larger proportion of the axial isomer and a very weak band at $1738\,\mathrm{cm^{-1}}$($\Delta\nu+20\,\mathrm{cm^{-1}}$) suggests only a little contamination of the equatorial one, well support the above expectation with the ultraviolet analysis described below and the facile dehybrobromination resulting in the quantitative formation of the corresponding monoenone (Vc).[11]

Next, in *trans*-1-bromo-1,10-dimethyl-2-decalone (IXb), the orientation of the bromine at C_1 corresponding both to kinetic and thermodynamic control may be expected to be axial as in (Vb), because of no possible epimerization of C_1–Br(*a*) by enolization and the impossible ring conversion due to the rigid structure of substituted *trans*-decaline system, which appears to make the structure of the bromide more stabilized, surpassing the destabilizing steric effect between C_1–Br(*a*)

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11) (*a*) M. Yanagita, S. Inayama : J. Org. Chem., **19**, 1724(1954). (*b*) M. Yanagita, S. Inayama, R. Kitagawa : *Ibid.*, in press.

12) M. Yanagita, R. Futaki : To be published.

and C_{10}-angular methyl group. Only a little possibility that the bromocyclohexanone ring of (XVII*a*) might equilibrate to the boat conformation (XVII*e*) is also ruled out by the minute shift of a single and strong band, and the ready dehydrobromination favorable to the axial orientation of the bromine.12) Thus, it is clear that the stable isomer of *tert*-bromo ketone is the one carrying an axially oriented bromine.

From the above discussion on the infrared analysis of α-bromocyclic ketones, it has been found that if the bromine is axial, no appreciable shift of $\nu_{C=O}$ is produced, irrespective of *sec*- or *tert*-bromides, whereas an augmentative shift to a higher frequency by $15\sim20\,\mathrm{cm}^{-1}$ occurs if the bromine is equatorial. The conformation of the bromine in some dibromides can also be discussed on this basis. The upward shift of $\nu_{C=O}$ by $36\,\mathrm{cm}^{-1}$ for 2,6-dibromocyclohexanone (I′b) (m.p. 110°) indicates that both α-bromines in the compound are equatorially substituted, viz. the dibromide corresponds to the *cis* isomer (XVIII*e*). If $\Delta\nu$ were about $18\,\mathrm{cm}^{-1}$, the dibromide might be engraved *trans* isomer (XVIII or XVIII′) carrying one equatorial and another axial bromine, and if a slight shift, the other *cis* isomer (XVIIIa) with two axial bromines. This seems not probable owing to the destabilizing effect between *cis*-axial bromines at the *meta*-position. Corey demonstrated that another isomer (m.p. 36°) derived from the *cis* isomer (I′b) under the acidic equilibrating condition was *trans* (XVIII or XVIII′) because of the upward shift by $20\,\mathrm{cm}^{-1}$.2b) This *trans* isomer carrying one coplanar C–Br dipole is obviously more stable than the *cis* isomer (XVIIIe) carrying two codirectional and coplanar C–Br dipoles with the C=O dipole in the equilibria (XVIII*a*) $\rightleftharpoons$ (XVIII) $\rightleftharpoons$ (XVIII′) $\rightleftharpoons$ (XVIII*e*) for the

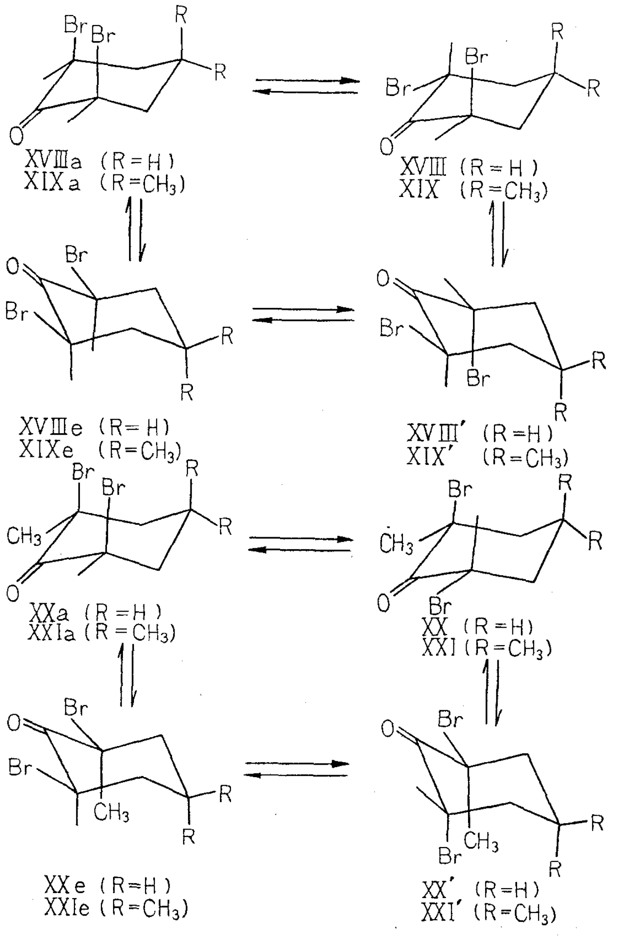

Fig. 4.

Conformation of Dibromides

Series a : The bromines axially oriented

Series e : The bromines equatorially oriented compound (Fig. 4).[*5] The more stable conformation of 2,6-dibromo compound (IV′b) formed by dibromination of 4,4-dimethylcyclohexanone (IV) under the equilibrating condition, is thought to be a *cis* dibromide (XIXe) (both equatorial bromines), as indicated by the upward shift by 36 $\mathrm{cm^{-1}}$, rather than the *trans* isomer (XIX) (equatorial and axial bromines), and further less stable another *cis* isomer (XIXa) (both axial bromines), both of which would be expected if $\Delta\nu$ were about $+18\,\mathrm{cm^{-1}}$ and $+6\,\mathrm{cm^{-1}}$, respectively. It is notable that the destabilizing effect due to the steric interaction between C_2-Br(*a*) and C_4-CH_3(*a*) is far larger than that due to the electrical one between C_2-Br(*e*) and C=O dipoles to favor the stabilization of the equilibria (XIX*a*) $\rightleftharpoons$ (XIX) $\rightleftharpoons$ (XIX′) $\rightleftharpoons$ (XIX*e*) for the compound to the *cis* one (XIX*e*).[*5]

The most stable conformation of the 2,6-dibromo compound (II′b), equally formed by the bromination of 2-methylcyclohexanone (II) with or without the presence of a proton, would be preferentially reduced to (XX) if the isomer carrying less destabilizing effect were chosen from the two *trans*- dibromides (XX and XX′) remaining after screening the four possible isomers by means of the presence of the upward shift by 21 $\mathrm{cm^{-1}}$ (Br(*e*,*a*)) in the equilibria (XX) $\rightleftharpoons$ (XX′) $\rightleftharpoons$ (XX*a*) $\rightleftharpoons$ (XX*e*) for the compound including the other two *cis* ones, viz. (XX*a*) (Br(*a*,*a*), $\Delta\nu$ calcd. ab. $+6\,\mathrm{cm^{-1}}$) and (XX*e*) (Br(*e*,*e*), $\Delta\nu$ calcd. ca. $+36\,\mathrm{cm^{-1}}$). That the bromination product of 2-methylcyclohexanone (II) corresponding both to kinetic and thermodynamic control may be (XX) alone is fully indicated by the single and shoulderless carbonyl maximum with less shift.10),[*4] Also, the 2,6-dibromo compound (V′b) produced by dibromination of 2,4,4-trimethylcyclohexanone (V) under equilibrating condition will be given a sole *trans* configuration (XXI) due to the single band with no shoulder ($\Delta\nu$ $+21\,\mathrm{cm^{-1}}$), which is regarded as the most stable isomer because of having the least destabilizing effect due to one electrical and one steric interaction in the four possible ones in the equilibria (XXI) $\rightleftharpoons$ (XXI′) $\rightleftharpoons$ (XXI*a*) $\rightleftharpoons$ (XXI*e*) for the compound. On the contrary, in the remainder of three structures, the other *trans* isomer (XXI′), $\Delta\nu$ of which is calculated to be 18 $\mathrm{cm^{-1}}$ for Br(*a*,*e*), includes three steric and one electrical interactions as the destabilizing factor. Then one *cis* isomer (XXIa), $\Delta\nu$ being calculated to be $+6\,\mathrm{cm^{-1}}$ for Br(*a*,*a*), carries the destabilizing effect due to three steric interactions, and the last *cis* compound (XXIe) ($\Delta\nu$ calcd. ca. $+36\,\mathrm{cm^{-1}}$) includes one steric and two electrical repulsions. The three configurational structures for the dibromide, which includes more unstable factor and indicates a sharp discrepancy of $\Delta\nu$ between calculation and determination, seems therefore to be improbable in equilibria for the compound, the stereospecified dibromination observed above may be ascribed to the stereochemical equilibration between the possible configurations of each dibromide or to the inherent stereoselectivity on the second bromination of each *tert*-monobromide (cf. Corey10)).

The conviction of the validity of conformation for various bromides is strengthened by an additional evidence on ultraviolet spectra given in Table III. If the bromine is axial, in the case of (Ib), (IIb), or (Vb), R-band produces a large bathochromic displacement by 25 mμ, whereas no considerable deviation occurs if equatorial, as in the case of (IIIb) or (VIIIb). These results parallel the observation on α-bromo ketosteroids, in which the shift for the axial isomer is bathochromic by an average of 28 mμ and that for the equatorial one is hypsochromic by ca. 5 mμ according to Cookson.7)

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[*5] The interaction being assumed between CH_3(*e*)-O-Br(*e*) in (XX) or (XXI), and Br(*e*)-O-Br(e) in (XVIII*e*), (XIX*e*), (XX*e*), or (XXI*e*) seems to be negligible too.

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Co., Ltd., for the infrared determinations, to Miss Suzuki of this school for the measurement of ultraviolet spectra, and to Miss Shibuya of this laboratory for microanalyses.

Experimental

2-Bromocyclohexanone (Ib)—Prepared from cyclohexanone (I) and one equivalent of Br_2 in CCl_4 or in AcOH in the presence of HBr; b.p$_4$ 80～93°.

cis-**2,6-Dibromocyclohexanone (I′b)**[13]—Prepared from (I) and 2 equiv. of Br_2 in AcOH in the presence of HBr; m.p. 108～110°.

2-Bromo-2-methylcyclohexanone (IIb)[14]—Prepared from 2-methylcyclohexanone (II) and 1 equiv. of Br_2 in CCl_4 or in AcOH in the presence of HBr[11a]; b.p$_{3.5}$ 62～66°.

trans-**2,6-Dibromo-2-methylcyclohexanone (II′b)**[13]—Prepared from (II) and 2 equiv. of Br_2 in AcOH; m.p. 43～45°.

6-Bromo-2-ethoxycarbonyl-2-methylcyclohexanone (IIIb)[15]—Prepared from 2-ethoxycarbonyl-2-methylcyclohexanone (III) and 1 equiv. of Br_2 in CCl_4[11b]; b.p$_4$ 123～124°.

2-Bromo-4,4-dimethylcyclohexanone (IVb)[2a]—Prepared from 4,4-dimethylcyclohexanone (VI), described below, and 1 equiv. of N-bromosuccinimide (N. B. S.) in CCl_4 or of Br_2 in AcOH[11a]; m.p. 58～60°.

cis-**2,6-Dibromo-4,4-dimethylcyclohexanone (IV′b)**[16]—Prepared from (IV) and 2 equiv. of Br_2 in AcOH; m.p. 95～97°.

2-Bromo-2,4,4-trimethylcyclohexanone (Vb)[11a]—Prepared from 2,4,4-trimethylcyclohexanone (V) and 1 equiv. of N. B. S. or of Br_2 in CCl_4 or in AcOH in the presence of HBr. Each of the distilled pure bromide, regardless of the method of bromination, provided in a good yield the corresponding monoenone (Vc) described below.

trans-**2,6-Dibromo-2,4,4-trimethylcyclohexanone (V′b)**[11a]—Prepared from (V) and 2 equiv. of Br_2 in CCl_4. On distilling the crude dibromide, the main fraction of b.p$_4$ 115～125° was collected as colorless liquid (72% yield) which solidified on standing over night in a refrigerator. White crystals of m.p. 55～58° washed with petr. ether on porous plate was recrystallized from petr. benzine to colorless prism, m.p. 62～64°. The mixed fusion of this crystal with 6-bromo-2,4,4-trimethylcyclohexen-5-one,[11a] m.p. 76～79°, indicated m.p. 40～52°, showing depression. *Anal.* Calcd. for $C_9H_{14}OBr_2$: C, 36.25; H, 4.74. Found: C, 36.73; H, 5.01.

This produced a 2,4-dinitrophenylhydrazone of 6-ethoxy-2,4,4-trimethyl-2-cyclohexenone in moderate yield with the Brady's reagent containing 1 equiv. of 2,4-dinitrophenylhydrazine. Orange needles (recrystallized 3 times from AcOEt), m.p. 171～173°. *Anal.* Calcd. for $C_{17}H_{22}O_5N_4$: N, 15.43. Found: N, 15.3.

After 2 g. of the crude dibromide, obtained by dibromination in AcOH in the presence of HBr,[11a] was treated with hot γ-collidine, as previously reported, the fractionated neutral substance (0.29 g., 32% yield) of b.p$_{10}$ 80～85° was redistilled to give a colorless liquid, b.p$_7$ 65～67°, with aromatic odor and paralytic taste. The 2,4-dinitrophenylhydrazone, quantitatively formed from the oil as fine scarlet needles, m.p. 178～180°, showed no depression on admixture with an authentic sample derived from 2,4,4-trimethylcyclohexa-2,5-dienone (Vd) mentioned below.

trans-**3-Bromo-10-methyl-2-decalone (VIIIb)**[8]—Prepared from *trans*-10-methyl-2-decalone (VIII) and 1 equiv. of Br_2 in CCl_4, m.p. 98～100°.

trans-**1-Bromo-1,10-dimethyl-2-decalone (IXb)**[12]—Prepared from *trans*-1,10-dimethyl-2-decalone (IX) and 1 equiv. of Br_2 in $CHCl_3$; b.p$_3$ ～130° (bath temp.).

2-Methylcyclohexen-2-one (IIc)[11]—Prepared by dehydrobromination of the bromoketone (IIb) as previously reported and purified through its semicarbazone; b.p$_7$ 75～78°, λ_{max}^{EtOH} 235 mμ (log ε 4.03).

6-Methylcyclohexen-2-one (II′c)[11b]—Prepared by the decarboxylation of the monoenone (IIIc) according to the reported procedure; b.p$_9$ 46～49°, λ_{max}^{EtOH} 225 mμ (log ε 4.01).

6-Ethoxycarbonyl-6-methylcyclohexen-2-one (IIIc)[15]—Prepared by the dehydrobromination of the bromoketone (IIIb) as previously reported; b.p$_7$ 95～97°, λ_{max}^{EtOH} 225 mμ (log ε 3.95).

4,4-Dimethylcyclohexanone (IV)[16]—Prepared in four steps via the intermediate 4-dichloromethyl-4-methyl-2,5-cyclohexadienone (VId) according to the method of Auwers *et al.*[17]; b.p$_7$ 55～56°.

2,4,4-Trimethylcyclohexanone (V)[11a]—Conveniently prepared by the catalytic hydrogenation of the monoenone (Vc); b.p$_{30}$ 81～83°.

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2,4,4-Trimethylcyclohexen-2-one (Vc)[11a]—Prepared by the cyclization of ethyl vinyl ketone with isobutyraldehyde as previously reported or by dehydrobromination of the bromoketone (Vb); b.p$_{20}$ 80~85°, λ_{max}^{EtOH} 235 mμ (ε 12030).

2,4,4-Trimethylcyclohexa-2,5-dienone (Vd)[11a]—Prepared by the dehydrobromination of the dibromoketone (V′b); b.d$_{15}$ 87~89°, λ_{max}^{EtOH} 237 mμ (ε 12623).

4-Dichloromethyl-4-methylcyclohexanone (VI)[17]—Prepared by catalytic hydrogenation of the dienone (Ⅵd); m.p. 51~52°.

4-Dichloromethyl-4-methylcyclohexa-2,5-dienone (VId)[17]—Prepared by Tiemann-Reimer reaction of *p*-cresol, m.p. 53~55°.

trans-**4-Dichloromethyl-2,4-dimethylcyclohexanone (VII)**[11a]—Prepared by catalytic hydrogenation of the dienone (Ⅶd); m.p. 51~53°.

4-Dichloromethyl-2,4-dimethylcyclohexa-2,5-dienone (VIId)[11a]—Prepared form *asym*-*m*-xylenol essentially according to the procedure of Auwers *et al.*[17] as above; m.p. 54~56°, λ_{max}^{EtOH} 235 mμ (ε 25625).

trans-**10-Methyl-2-decalone (VIII)**[7),*6]—Prepared in four steps via the intermediate, *trans*-1,4-dioxo-2-methoxy-10-methyl-1,4,5,8,9,10-hexahydronaphthalene[18] according to Woodward's procedure; b.p$_{21}$ 130~133°.

2-Oxo-10-methyl-2,3,4,5,6,7,8,10-octahydronaphthalene (VIIIc)[19]—Prepared by the condensation of 2-methylcyclohexanone and diethylaminobutan-2-one methiodide according to the Robinson's procedure and purified through its semicarbazone; b.p$_{15}$ 139~141°, λ_{max}^{EtOH} 240 mμ (ε 12350).

2-Oxo-10-methyl-2,5,6,7,8,9-hexahydronaphthalene (VIIId)[8]—Prepared by the condensation of 2-formyl-2-methylcyclohexanone and acetone according to the method of Woodward *et al.*[20]; b.p$_{3}$ 112~113°, λ_{max}^{EtOH} 240 mμ (ε 12650).

trans-**1,10-Dimethyl-2-decalone (IX)**[12),*6]—Prepared by the catalytic hydrogenation of the monoenone (Ⅸc) and purified through its 2,4-dinitrophenylhydrazone; b.p$_{6}$ 104~106°.

2-Oxo-1,10-dimethyl-2,3,4,5,6,7,8,10-octahydronaphthalene (IXc)[21]—Prepared by the condensation of 2-methylcyclohexanone and diethylaminopentan-2-one methiodide according to the procedure of Gunstone *et al.*[21] and purified through its semicarbazone; b.p$_{3}$ 108~110°, λ_{max}^{EtOH} 250 mμ (ε 16550).

Infrared and Ultraviolet Absorption Spectra—Infrared spectra were determined on a Perkin-Elmer Model 21 double beam spectrometer equipped with a NaCl prism, using CCl_4 as the solvent. The absorbtion bands of the solution were measured at concentrations of 2.5~3% in rock salt cell of 1.008 mm. thickness. Ultraviolet spectra were determined by a Beckman Model DU Spectrophothometer, employing EtOH as the solvent in a concentration of ca. $10^{-4}M$.

Samples for the measurement were prepared carefully by the direction described above. All temperatures are not corrected. All the liquid monobromides, except the crystalline (Ⅷb), were prepared before use and stored in ampules in a refrigarator till measurement. Samples of monoenones and dienones in a liquid state were stored in a cold place in sealed ampules after each preparation and survey of purity.

Summary

The infrared and ultraviolet absorption spectra of several mono- and bicyclic α-bromo-, α,β-, and α,β:α′,β′-conjugated ketones were investigated. The conformation of bromine atom in α-bromoketones was discussed mainly on the basis of the spectral data. The conclusion obtained for these compounds was in good agreement with that of α-bromoketosteroids. It was especially found that the foregoing argument about secondary α-bromo ketones applied well to tertiary α-bromo compounds.

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