Beckman IR-2 spectrophotometer. The analysis revealed only about 1.4 and 3.0 atoms of deuterium per mole for samples A and B, respectively. The oxidations were carried out at 65° using azodiisobutyronitrile as the catalyst and chlorobenzene as the solvent. A sensitive constant pressure apparatus was used to measure the volumes of oxygen consumed. The results are summarized in Table I.

TABLE I

THE RELATIVE RATE OF OXIDATION OF CUMENE AND DEUTEROCUMENE

Compound	Added inhibitor	k_H/k_D
Deuterocumene A	None	0.91
Deuterocumene B	None	0.85
Deuterocumene A	*p*-Nitrophenol	1.05
Deuterocumene B	*p*-Nitrophenol	1.07
Deuterocumene A	2,4-Dichlorophenol	1.19
Deuterocumene B	2,4-Dichlorophenol	1.27

From the data in Table I it can readily be seen that both of the effects discussed above are in operation. The two effects were separated by the addition of an inhibitor to replace the usual termination step.[6] The ratio of the inhibited rates represent the secondary isotope effect and indicate that hyperconjugation is important in stabilizing free radicals. The effect on the chain terminating step is much larger since it completely overshadows the secondary effect, even though the over-all rate of oxidation is proportional to the inverse square root of the termination rate constant. Such an effect probably means that the chain terminating step involves scission of a β-carbon-hydrogen bond and could be written thusly[7]

$$2C_6H_5C(CH_3)_2OO \longrightarrow C_6H_5\text{-}C(CH_3)_2OOH + C_6H_5C(CH_3)=CH_2 + O_2$$

Acknowledgment.—The authors are indebted to the Research Corporation for a Frederick Gardner Cottrell grant which made this work possible.

(6) G. S. Hammond, C. E. Boozer, C. E. Hamilton and J. N. Sen, THIS JOURNAL, **77**, 3238 (1955).

(7) A referee suggested $C_6H_5CCH_3CH_2$. or $C_6H_5COCH_3$ + CH_2O (with O—O) as other possible products.

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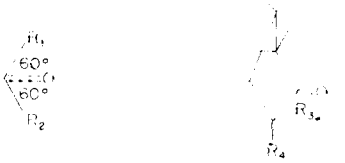
INFRARED ANALYSIS OF α-HALOCYCLOPENTANONES

Sir:

The well known *differences*[1] between substituted cyclopentane and cyclohexane rings stand in marked contrast to *similarities* recently found[2] when planar four center reactions were studied. These similarities, which might have arisen from common stereochemistry, led us to consider that when a carbon atom in the cyclopentane ring is puckered out of the plane about 0.7 Å.,[3] two adjacent *trans* groups will be coplanar much like two adjacent diaxial substituents on the chair form of the cyclohexane ring.

This communication which presents spectral evidence that α-halocyclopentanones are not planar lends support to these views. We have employed the method of R. N. Jones[4] and E. J. Corey[5] which distinguishes between axial and equatorial halogen atoms α- to a carbonyl group, to establish the hitherto unknown carbonyl frequency shifts due to the intermediate position of a halogen atom in a planar α-halocyclopentanone (I, R_1 = Br, Cl, R_2 = H).



I II

By measuring the α-halocamphors[6] where the rigid R—C—C=O geometry, in projection, is virtually the same as in a planar cyclopentanone,[7] we have obtained for α-bromine a shift of 14 cm.$^{-1}$ and α-chlorine a shift of 18-19 cm.$^{-1}$. These are intermediate[4,5c] or borderline values[5a,b] between those reported for axial and equatorial halogens in six membered rings.

The good agreement (Table I) between the shifts for α-chlorocamphor (II, R_3 = H, R_1 = Cl) and α′-chlorocamphor (II, R_3 = Cl, R_4 = H) and the further shift for dichlorocamphor are in keeping with their assigned geometry.

TABLE I[a]

Ketone	ν_{max} C=O, cm.$^{-1}$	$\Delta\nu$, cm.$^{-1}$
Camphor	1744	..
α-Bromo-	1758	14
α,α′-Dibromo-	1766	22
α-Chloro-	1763	19
α′-Chloro-	1762	18
α,α′-Dichloro-	1774	30
2-Indanone[b]	1753	..
1-Bromo-	1766	13
1-Chloro-[c]	1772	19
Cyclopentanone	1742	..
1-Bromo-	1750	8
1-Chloro-	1755[5a]	13

[a] Measured in carbon tetrachloride solution on a Perkin–Elmer Model 21 Double Beam Infrared Spectrophotometer. [b] Kindly prepared by Mr. Elmer Maurer, Eastern Regional Research Laboratories, Phila. 18, Pa. [c] Prepared as in reference 8, m.p. 70.0–70.5°. *Anal.* Calcd. for C_9H_7OCl: Cl, 21.28. Found: Cl, 21.33, 21.39.

(1) H. C. Brown, J. H. Brewster and H. Schechter, THIS JOURNAL, **76**, 467 (1954).

(2) F. V. Brutcher, Jr., and T. Roberts, Abstracts of Papers, 127th Meeting, American Chemical Society, Cincinnati, Ohio, April, 1955, p. 39N.

(3) Derived from the bicyclo[2.2.1]heptane ring system which has a puckered five membered ring with this geometry. It is considerably larger than the 0.2Å. puckering reported by Kilpatrick, Pitzer and Spitzer, THIS JOURNAL, **69**, 2483 (1947), for cyclopentane itself.

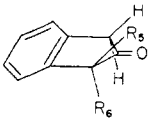
(4) R. N. Jones, D. A. Ramsay, F. Herling and K. Dobriner, THIS JOURNAL, **74**, 2828 (1952).

(5) (a) E. J. Corey and H. J. Burke, *ibid.*, **77**, 5418 (1955); (b) E. J. Corey, T. H. Topie and W. A. Wozniak, *ibid.*, **77**, 5415 (1955); (c) E. J. Corey, *ibid.*, **75**, 2301, 3297 (1953).

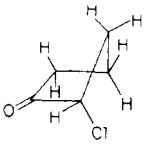
(6) J. Simonsen and L. N. Owen, "The Terpenes," Vol. II, Cambridge University Press, Cambridge, England, 1949, Chap. 5.

(7) R. C. Cookson, *J. Chem. Soc.*, 282 (1954).

Our intermediate values check closely with some 1-halo-2-indanones[8] which should have the same halo-carbonyl geometry (III) since the five membered ring has four carbon atoms which must be in one plane and a fifth, the carbonyl group, which can maintain favorable bisections with the α-substituents by remaining in the plane.



III



IV

It follows that if the α-halocyclopentanones were planar, the shift for α-bromine should be about 14 cm.$^{-1}$ and α-chlorine 18–19 cm.$^{-1}$. In actual fact the shift for α-bromocyclopentanone, as measured by Corey[5c] and confirmed by us is only 8 cm.$^{-1}$ and for α-chlorocyclopentanone[5c] the shift is only 13 cm.$^{-1}$, within the axial range.

The species most likely predominant in solution (IV) involves puckering of the C_3 atom about 0.7 Å. which develops a favorable staggered C_2-C_3-C_4 interaction, reduces the repulsion of R—C—C=O by increasing the distance between dipoles, yet maintains the favorable bisection of the C_5 methylene group by the carbonyl substituent.

As a consequence it can be inferred that the anion of *trans*-2-chlorocyclopentol[2] must be quite puckered in the transition state for epoxide formation, unexpectedly favoring a coplanar transition state, since the repulsive forces in Cl—C—C—C$\ominus$ with a full negative charge on oxygen must be considerable even though the geometry is not quite the same as in α-chlorocyclopentanone.

The framework outlined previously[2] and herein will accommodate recent comments on the puckered cyclopentane ring,[9,10] while LeFevre's recent polarizability data[11] are also in general argeement.

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(8) N. Creeth and J. F. Thorpe, *J. Chem. Soc.*, 1507 (1908).
(9) H. Kwart and W. G. Vosburgh, THIS JOURNAL, **76**, 5400 (1954).
(10) D. J. Cram, N. L. Allinger and H. Steinberg, *ibid.*, **76**, 6132 (1954).
(11) R. J. LeFevre and C. G. LeFevre, *Chem. and Ind.*, 54 (1956).
(12) Du Pont Predoctoral Fellow, 1954–1955.
(13) University of Pennsylvania Undergraduate Scholar.

THE HALIDE METABOLISM OF *STREPTOMYCES AUREOFACIENS* MUTANTS. THE BIOSYNTHESIS OF 7-CHLORO-, 7-CHLORO[36]- AND 7-BROMOTETRACYCLINE AND TETRACYCLINE

Sir:

We wish to report recent studies of the halide metabolism of two classes of experimental mutants of *Streptomyces aureofaciens* Duggar. These studies are concerned with the utilization of inorganic chloride and bromide by the mutants of the two classes to form 7-chlorotetracycline[1] and 7-bromotetracyline[2] and with the behavior of the mutants in the absence of halide.

Class I, represented by Mutant BC-41, contains those mutants whose rate of utilization of chloride for 7-chlorotetracycline (CTC) is independent of chloride concentration over the wide range of chloride concentrations from 0.02 to 10 stoichiometric equivalents of the total tetracyclines potential of the system. The total tetracyclines potential is the sum of the millimoles per liter of CTC, 7-bromotetracycline (BTC), and tetracycline (TC)[3] present at the end of the fermentation cycle. Class II, represented by Mutants S-580 and S-1055, contains those mutants whose rate of utilization of chloride for CTC depends on chloride concentration over the above range.

Chlorination by BC-41 to yield CTC is slightly inhibited by bromide; chlorination by S-580 and by S-1055 is substantially inhibited by bromide. Within limits, these inhibitions are reversible by excess chloride and competitive in nature. Halogenation in all three mutants is substantially inhibited by thiocyanate. The thiocyanate inhibition of BC-41 is not reversible by excess chloride; within limits, the thiocyanate inhibitions of S-580 and S-1055 are reversible by excess chloride. The response of all three mutants to the repression of halogenation, either through inhibition by bromide or by thiocyanate or through halide denial, is the biosynthesis of the unsubstituted product, TC.

In the absence of chloride, BC-41 utilizes bromide for BTC at a rate independent of bromide concentration over the above range; the over-all rate of bromide utilization for BTC is 0.3 times the rate of chloride utilization. Utilization by S-580 and by S-1055 of bromide for BTC could not be detected.

The total tetracyclines potential of each of the three mutants is independent of halide concentration over the 0.02 to 10 equivalents range; that is, the effect of halide variation is solely a change in the identity of product.

In the case of BC-41, the magnitude of the chlorination rate and its independence of chloride concentration allow complete utilization of chloride for CTC for chloride concentrations up to 93% that equivalent to the total tetracyclines potential of the system. Lesser initial chloride concentrations result in chloride exhaustion. Similarly, BC-41 completely utilizes bromide for BTC when bromide concentrations do not exceed 25% of that equivalent to the total tetracyclines potential of the system. S-1055 approaches complete utilization of chloride for CTC when chloride concentrations do not exceed 25% of the equivalent concentration. In the case of S-580, chloride is never completely utilized for CTC, and chloride exhaustion is not observed.

At high excess chloride concentrations, under the particular uniform fermentation conditions of these

(1) The trademark of the American Cyanamid Company for 7-chlorotetracycline is Aureomycin.
(2) A. P. Doerschuk, B. A. Bitler and J. R. D. McCormick, THIS JOURNAL, **77**, 4687 (1955); P. Sensi, *Il. Farmaco Sci. Ed.*, **10**, 346 (1955).
(3) The trademarks of the American Cyanamid Company and of Charles Pfizer and Co. for tetracycline are Achromycin and Tetracyn, respectively.