[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Stereochemistry of α-Haloketones. VII. The Stereochemistry and Spectra of Some α-Chlorocyclohexanones

BY E. J. COREY AND H. J. BURKE

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Measurements of the infrared spectra of a number of α-chlorocyclohexanones indicate that the carbonyl absorption is displaced +26 to +31 cm.$^{-1}$ for equatorial chlorine and +10 to +18 cm.$^{-1}$ for axial chlorine from the absorption maxima of the parent ketones. In the ultraviolet, an equatorial chlorine causes a slight hypsochromic shift and an axial chlorine a marked bathochromic shift of the low intensity carbonyl absorption, in agreement with earlier findings for axial and equatorial α-bromine. The relative stability of the possible rotational isomers of monocyclic α-chlorocyclohexanones is almost exactly the same as for the α-bromo counterparts. Chlorine seems to have a slightly greater tendency to adopt the equatorial orientation than does bromine, contrary to what might be expected.

Considerable data have been accumulated concerning the infrared absorption,[1,2] ultraviolet absorption[1,3] and stereochemistry[1,2] of α-bromocyclohexanones, both monocyclic and polycyclic. Both the infrared and ultraviolet methods allow a decision to be made between the axial and the equatorial orientations of bromine. In the infrared the introduction of an equatorial α-bromine substituent causes a shift of carbonyl absorption of +16 to +22 cm.$^{-1}$, whereas the introduction of an axial α-bromine causes a much smaller shift of −2 to +8 cm.$^{-1}$. In the ultraviolet an equatorial bromine produces only a slight, usually hypsochromic shift in the low-intensity carbonyl absorption band (at *ca.* 290 mμ) whereas an axial bromine produces a considerable bathochromic shift of +25 to +30 mμ.[3]

In order to determine the effectiveness of these methods with α-chlorocyclohexanones and to gain further information with regard to stereochemistry, we have carried out a brief study, the results of which are presented herein. For this study a number of chlorinated cyclohexanones were prepared and their infrared and in some cases ultraviolet spectra were compared with those of the parent ketones. The results are shown in Table I.

The data in Table I indicate that in the infrared the carbonyl shift due to an α-chlorine is greater than for an α-bromine, and amounts to 26–31 cm.$^{-1}$ for equatorial chlorine and 10–18 cm.$^{-1}$ for axial chlorine. Because of the fact that a considerable shift occurs with axial chlorine, the distinction between axial and equatorial orientations, although still possible, is less sharp for chlorine than for bromine. The ultraviolet absorption data in Table I is in complete agreement with the infrared data and also with the generalization previously made for α-bromoketones.[3]

The orientations of chlorine cited in Table I for the α-chloro derivatives of 2,2-, 3,3- and 4,4-dimethylcyclohexanone parallel to those found for bromine in the corresponding α-bromoketones. In both 2-chloro- and 2-bromocyclohexanone and both 2-chloro- and 2-bromo-3,3-dimethylcyclohexanone, the halogen is exclusively axial.[2] In the case of both 2-chloro- and 2-bromo-4,4-dimethylcyclohexanone the halogen is exclusively equatorial.[2]

TABLE I

Ketone	ν_{max} C=O, cm.$^{-1}$ (i.r.)	Shift due to α-Cl, Δν, cm.$^{-1}$	λ_{max} C=O, mμ (u.v.)	Shift due to α-Cl, Δλ, mμ	Cl orientation
Cyclohexanone	1712	..	282	..	...
2-Chloro-	1722	10	293	11	a
2,2-Dichloro-	1745	33	..	..	a, e
2,2,6,6-Tetrachloro-	1766	54	311	31	2a, 2e
2,2-Dimethylcyclohexanone	1702	..	289	..	...
6-Chloro-	1730	28	286	−3	e
	1715[a]	13	..	..	a
3,3-Dimethylcyclohexanone	1712	..	..	..	...
2-Chloro-	1730	18	..	..	a
4,4-Dimethylcyclohexanone	1712	..	283	..	...
2-Chloro-	1738	26	281	−2	e
Spiro(4.5)decane-6-one	1701	..	289	..	...
7-Chloro-	1732	31	285	−4	a
	1713[b]	12	..	..	e

[a] Weak shoulder on main band at 1730. [b] Medium weak shoulder on main band at 1732. Spectra determined in carbon tetrachloride solution.

With 6-chloro-2,2-dimethylcyclohexanone and 7-chlorospiro(4.5)-decane-6-one *both* the forms having axial and equatorial halogen are present with the equatorial predominating. The presence of the axial form in each instance is indicated by the appearance of a weak to moderately weak shoulder on the low wave length side of the main carbonyl band. A mixture of axial and equatorial forms was encountered also with 6-bromo-2,2-dimethylcyclohexanone and 7-bromo-spiro(4.5)decane-6-one,[3,4] however, comparison of the relative intensities of the carbonyl bands indicates that there is *relatively less* of the axial rotational isomer in the case of the chloroketones than in the case of the corresponding bromoketones. This result is unexpected in view of the smaller size and greater electronegativity of chlorine as compared with bromine. Both these factors might be expected to make the axial orientation relatively more favorable for chloroketones than for bromoketones. It is possible, however, that steric repulsions involving equatorial halogen are important and that equatorial halogen–carbonyl oxygen steric interactions increase more rapidly with the size of halogen than *cis*-axial steric interactions.

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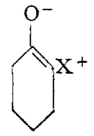
(1) R. N. Jones, D. A. Ramsay, F. Herling and K. Dobriner, THIS JOURNAL, **74**, 2828 (1952).

(2) E. J. Corey, *ibid.*, **75**, 2301, 3297 (1953).

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

(4) E. J. Corey, T. Topie and W. A. Wozniak, THIS JOURNAL, **77**, 5415 (1955).

Another possible explanation for this apparent anomaly, which is suggested by the ultraviolet data on α-halocyclohexanones and also by earlier work on stereoselective bromination,[5] is that the axial orientation of halogen is favored electronically over the equatorial orientation because of a greater contribution of resonance form I when halogen is axial.[4] Since form I should contribute more when X = Br than when X = Cl, this electrical effect should favor axial bromine more than axial chlorine. The observation that an axial halogen produces a bathochromic shift in the ultraviolet absorption of the carbonyl group, whereas equatorial halogen does not, agrees with the above argument, as does the fact that the shifts observed in the ultraviolet for axial chlorine are somewhat less than for axial bromine.[3,6]



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The α-chloroketones mentioned above exhibit every sort of chlorine–methyl, chlorine–methylene and chlorine–hydrogen interaction encountered in ketosteroids and, hence, serve as useful monocyclic reference compounds.[5]

It was hoped that the isomeric 2,6-dichlorocyclohexanones could be prepared for comparison with the dibromo analogs and for use as monocyclic reference compounds, but all attempts to isolate them from the direct dichlorination of cyclohexanone so far have been unsuccessful.

Meyer[7] had reported the isolation of a liquid, b.p. 106° (7 mm.), n^{20}_{D} 1.5031, which he regarded as 2,6-dichlorocyclohexanone from the chlorination of cyclohexanol in the presence of calcium carbonate. This liquid afforded a good analysis for a dichlorocyclohexanone, and after standing for several months crystallized to a colorless solid, m.p. 72–73°, which was taken to be the 2,6-dichloride although no analysis was reported.

This work was repeated and the distillate boiling at 105–107° (7 mm.) was separated into a liquid and a solid component by dilution with a little dry ether and cooling to −80°. The long, colorless needles thus obtained melted at 72.2–73.2° and were identical with authentic 2-chlorocyclohexenone. Fractionation of the liquid component yielded only 2,2-dichlorocyclohexanone, identical with a sample prepared in an unambiguous manner from 2-carbethoxycyclohexanone by the procedure described previously for 2,2-dibromocyclohexanone.[2] It is apparent that neither Meyer's solid nor liquid was 2,6-dichlorocyclohexanone.

An attempt also was made to prepare 2,6-dichlorocyclohexanone by dichlorination of cyclohexanone-2,6-dicarboxylic acid, followed by decarboxylation. The only product isolated from this reaction, however, was 3-chlorocyclohexan-1,2-dione (25% yield) identified by infrared and elemental analysis and color formation with ferric chloride.

Experimental

7-Chloro-spiro(4.5)decane-6-one.—One gram (0.0066 mole) of spiro-(4.5)decane-6-one[2] was dissolved in 1 ml. of glacial acetic acid and 4 ml. of methylene chloride. Slightly less than 1 molar equivalent of chlorine dissolved in carbon tetrachloride was added dropwise while cooling the solution in an ice-bath. The chlorine was consumed instantly at first; more slowly at the end.

The slightly yellow solution was allowed to stand a few minutes after completion of addition of the chlorine solution, then was extracted with 20 ml. of water. The water was back-extracted with 10 ml. of methylene chloride, the combined organic layers extracted with excess sodium bicarbonate solution, and the aqueous layer extracted with 15 ml. of methylene chloride. The combined organic layers were dried over calcium chloride and concentrated in vacuum. Recrystallization of the residue from low-boiling petroleum ether at −80° yielded 0.870 g. (71%) of white rosettes, m.p. 40–41°. An analytical sample, obtained by repeated recrystallization followed by sublimation melted at 40.8–41.8°.

Anal. Calcd. for $C_{10}H_{15}OCl$: C, 64.34; H, 8.10; Cl, 18.99. Found: C, 64.35; H, 8.09; Cl, 19.24.

6-Chloro-2,2-dimethylcyclohexanone.—This compound, m.p. 62.8–63.5°, was prepared using the method given above.

Anal. Calcd. for $C_8H_{13}OCl$: C, 59.81; H, 8.15; Cl, 22.07. Found: C, 59.46; H, 8.15; Cl, 22.23.

2-Chloro-4,4-dimethylcyclohexanone.—This compound, m.p. 58.5–60.7°, was prepared by the direct chlorination procedure described above.

Anal. Calcd. for $C_8H_{13}OCl$: C, 59.81; H, 8.15; Cl, 22.07. Found: C, 59.67; H, 8.45; Cl, 22.67.

2-Chloro-3,3-dimethylcyclohexanone.—To a solution of 528 mg. (0.0031 mole) of 3,3-dimethylcyclohexanone-2-carboxylic acid, freshly prepared by saponification of the methyl ester, in a few ml. of cold chloroform was added dropwise an equivalent amount of a standard solution of chlorine in carbon tetrachloride. When the fuming caused by evolution of hydrogen chloride had ceased, 20 ml. of water and excess sodium acetate were added and the solution was warmed on a steam-bath to complete decarboxylation.

The layers were separated and the aqueous layer was extracted with methylene chloride. The combined organic layers were washed with water, the water back-extracted with methylene chloride, and the combined organic layers were dried over magnesium sulfate. Removal of solvents left a little yellow oil from which, on fractional distillation in a micro column, was obtained 230 mg. (46%) of a colorless oil, b.p. 60° (1.5 mm.), n^{21}_{D} 1.4800.

Anal. Calcd. for $C_8H_{13}OCl$: C, 59.81; H, 8.15; Cl, 22.07. Found: C, 58.82; H, 7.76; Cl, 22.41.

2,2,6,6-Tetrachlorocyclohexanone.—The method used to prepare 2-chloro-3,3-dimethylcyclohexanone was applied to cyclohexanone-2,6-dicarboxylic acid.[8] The product was recrystallized from ether-*n*-pentane at −40 to −60°, m.p. 82.4–83.4°. Large quantities of this compound are better prepared by chlorination of cyclohexanone.

Anal. Calcd. for $C_6H_6OCl_4$: C, 30.54; H, 2.56; Cl, 60.11. Found: C, 30.56; H, 2.52; Cl, 58.11, 58.07.

2-2-Dichlorocyclohexanone.—Treatment of cyclohexanone-2-carboxylic acid with 2 molar equivalents of standard chlorine solution as described for 2-chloro-3,3-dimethylcyclohexanone produced 2,2-dichlorocyclohexanone, b.p. 71° (1.5 mm.), n^{20}_{D} 1.4941.

Anal. Calcd. for $C_6H_8OCl_2$: C, 43.14; H, 4.83; Cl, 42.45. Found: C, 43.01; H, 4.87; Cl, 42.27.

For large-scale preparation of the compound the following procedure was more useful: About 60 ml. of liquid chlorine was allowed to vaporize, over a period of 12 hours, into 56.5 g. (0.575 mole) of cyclohexanone containing 1 ml. of concentrated hydrochloric acid and kept continuously stirred at salt–ice-bath temperature. The resulting yellow slush was taken up in ether and washed with potassium carbonate solution until neutral, then with water. After drying over magnesium sulfate the ether solution was cooled overnight in a refrigerator. Filtration followed by repeated concen-

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(5) E. J. Corey, THIS JOURNAL, **76**, 175 (1954).

(6) The shift for α-chlorocyclohexanone (11 mμ) is much less than observed for axial α-bromocyclohexanones (25–30 mμ).

(7) R. E. Meyer, *Helv. Chim. Acta*, **16**, 1291 (1933).

(8) P. C. Guha and N. K. Seshardreingar, *Ber.*, **69B**, 1208 (1936).

tration and cooling, filtration, etc., until no more precipitate formed yielded 4.51 g. of crude white needles, m.p. 173–180°. A sample recrystallized from ethanol melted at 184–184.8° dec. The compound's infrared spectrum was blank between 1500 and 2800 cm.$^{-1}$ and showed no hydroxyl absorption.

Anal. Found: C, 40.88; H, 4.44; Cl, 50.67.

No further work was done on the solid product.

Fractionation of the crude mother liquors yielded 11.62 g. (12%) of pure 2,2-dichlorocyclohexanone.

2-Chlorocyclohexenone.—Cyclohexenone was converted to 2-chlorocyclohexenone according to the directions of Richter and Kotz.[9] Infrared absorption occurred at 1705, 1675 (shoulder), 1657 (w) and 1617 cm.$^{-1}$.

Anal. Calcd. for C_6H_7OCl: C, 55.18; H, 5.40; Cl, 27.15. Found: C, 55.15; H, 5.31; Cl, 26.88.

3-Chlorocyclohexane-1,2-dione.—To a solution of 727 mg. (0.0039 mole) of cyclohexanone-2,6-dicarboxylic acid[8] in 5 ml. of water was added a solution of *ca.* 20 molar equivalents of chlorine in carbon tetrachloride. After allowing the solution to stand for a few minutes with frequent shaking, excess chlorine was removed by subjecting the solution to a water-pump vacuum, the solution was made alkaline with a saturated solution of potassium bicarbonate and warmed to 60–65° for 15 minutes, the aqueous layer turning yellow in the process.

After cooling, the layers were separated and the aqueous layer extracted with four 50-ml. portions of ether. The combined organic layers were dried over magnesium sulfate and concentrated in vacuum to a brownish solid weighing 399 mg. Sublimation at 55° (0.02 mm.) yielded 157 mg. of square white plates contaminated with a colorless oil.

Recrystallization from ether–*n*-pentane at 0° gave 143 mg. (25%) of square plates, m.p. 119–122°. Repeated sublimation and recrystallization from low-boiling petroleum ether at 0° raised the melting point to 120.2–122°. The compound gave a strong violet color with ferric chloride, dissolved readily in 10% potassium carbonate solution, and gave a positive Beilstein test. Infrared absorption occurred at 3450, 1685 and 1656 cm.$^{-1}$.

Anal. Calcd. for $C_6H_7O_2Cl$: C, 49.17; H, 4.81; Cl, 24.19. Found: C, 49.14; H, 5.02; Cl, 24.05.

This material is different from Reimschneider's[10] Δ^3-3-chlorocyclohexen-1,2-dione which manifested infrared absorption at 3470, 1770 and 1725 cm.$^{-1}$.

URBANA, ILLINOIS

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[9] A. Kotz and K. Richter, *J. prakt. Chem.*, **111**, 373 (1925).

[10] R. Reimschneider, *Monatsh.*, **85**, 417 (1954).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, BUCKNELL UNIVERSITY]

On Cyclic Intermediates in Substitution Reactions. VII. The Alkaline Solvolysis of Some N-Aryl-4-bromobutanamides

BY HAROLD W. HEINE, PETER LOVE AND JOHN L. BOVE

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The rates of alkaline solvolysis of three N-aryl-4-bromobutanamides have been studied in methanol. The rates of reaction as determined by the measurement of the release of bromide ion are of the first order with respect to bromoamide and first order with respect to methoxide ion. The reaction products are the corresponding pyrrolidones. These results are discussed in terms of a mechanism involving the formation and conversion of a bromoamido ion to a pyrrolidone. The syntheses of three new bromoamides and one new pyrrolidone are described.

Earlier papers of this series[1] examined quantitatively the ease of participation of neighboring groups in internal displacement reactions in systems where the distance between the carbon atom on which displacement occurs and the participating neighboring group is increased.

The present investigation concerns itself with the alkaline solvolysis of some N-aryl-4-bromobutanamides. The products obtained in high yields from the solvolytic reactions were the corresponding N-arylpyrrolidones. Since 1-*p*-tolylpyrrolidone and 1-phenylpyrrolidone have previously been characterized[2,3] only the isolation of 1-*p*-chlorophenylpyrrolidone is described in detail in the Experimental section. The kinetics of the reaction, as followed by measurement of released bromide ion as a function of time, was found to be first order with respect to methoxide ion and first order with respect to bromoamide. The N-aryl-4-bromobutanamides studied were so chosen as to provide a test of the basis for a mechanism which involved a rapid reversible proton transfer from amide to methoxide ion followed by an internal displacement of bromide by the formed amido ion.

Method of Rate Measurement.—The measurements were carried out in a water-bath in which the temperature was thermostatically controlled to ±0.02°. A quantity of bromoamide sufficient to make the concentration lie within the range of 0.04–0.05 *M* was introduced into a 100-ml. volumetric flask which contained a known quantity of preheated standardized sodium methoxide solution sufficient to make the final concentration of methoxide 0.04–0.19. Anhydrous methanol preheated to bath temperature was then quickly added to the mark, the solution was shaken, and at convenient time intervals 10-ml. aliquots were removed with a pipet and immediately delivered into a 125-ml. separatory funnel containing 10 ml. of 6 *M* HNO_3, 25 ml. of distilled water and 20 ml. of chloroform. The mixture was shaken thoroughly and the chloroform removed. The water layer was extracted further with another 20 ml. of chloroform. Finally the chloroform extracts were washed once with 5 ml. of water and the water layers combined. The bromide ion was determined by the Volhard method.

In calculating the rate constants the first sample was taken as the starting point of the reaction because solution of the bromoamide required 1–2 minutes of shaking. The release of bromide ion followed a second-order rate law over 70% of the reaction range, after which the velocity coefficients exhibited a slight downward drift.

Typical rate data for the reaction of N-*p*-chlorophenyl-4-bromobutanamide and N-phenyl-4-bro-

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[1] H. W. Heine and B. L. Kapur, THIS JOURNAL, **77**, 4892 (1955); H. W. Heine and W. Siegfried, **76**, 489 (1954); **75**, 4778 (1953); **75**, 4514 (1953); **73**, 1348 (1951).

[2] J. Tafel and M. Stern, *Ber.*, **33**, 2235 (1900).

[3] T. B. Baillie and J. Tafel, *ibid.*, **32**, 74 (1898)