Haloacyloxylation. III. Reaction of Alkyl Iodides with Peracetic Acid in the Presence of Cyclohexene[1]

YOSHIRO OGATA AND KEIZO AOKI

Department of Applied Chemistry, Faculty of Engineering, Nagoya University, Chikusa-ku, Nagoya, Japan

Received April 18, 1969

Reaction of cyclohexyl iodide with peracetic acid in acetic acid at 30° affords 1-iodo-2-acetoxycyclohexane (70–80%), together with smaller amounts of cyclohexyl acetate, iodine, and 1,2-diacetoxycyclohexane. Treatment of alkyl iodides with peracetic acid in the presence of cyclohexene in acetic acid also affords 1-iodo-2-acetoxycyclohexane in moderate yields (33–55%). In general, secondary alkyl iodides give yields higher than those from primary alkyl iodides. A mechanism is suggested which involves the reaction of alkyl iodides with peracetic acid to give acetyl hypoiodite, which then adds to the double bond of cyclohexene.

In our previous paper[2] we have reported the reaction of *n*-alkyl iodides with peracetic acid in the presence of aromatic compounds, affording iodoarenes in good yields (70–80%) (eq 1), whereas secondary and tertiary alkyl iodides give little or no iodoarenes (0–0.8%).

$$\mathrm{RI + CH_3CO_3H + ArH \longrightarrow ArI + CH_3CO_2R + H_2O} \quad (1)$$

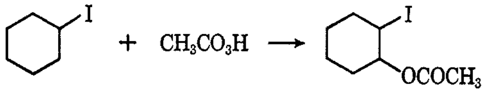
It was suggested that acetyl hypoiodite, CH_3COOI, formed by the reaction of alkyl iodides with peracetic acid may be the iodinating agent of aromatic compounds.[2-4] With cyclohexyl iodide, no aromatic iodination, but a different reaction, was observed to occur, giving a product identical with that from the Prévost reaction of acetyl hypoiodite with cyclohexene. Reaction of other alkyl iodides with peracetic acid in the presence of cyclohexene has also been studied to examine the possibility of Prévost-type addition.

Results and Discussion

Iodination of *m*-xylene was not observed in the reaction of cyclohexyl iodide with peracetic acid in acetic acid at 30° in the presence of *m*-xylene.[2] The products of the reaction were identical in glpc analyses with those obtained by the reaction of cyclohexyl iodide with peracetic acid in the absence of *m*-xylene.

The reaction of cyclohexyl iodide (0.096 mol) with peracetic acid (0.0726 mol) was conducted in acetic acid (100 ml) at 30°. The reaction products were separated by column chromatography and identified by glpc, ir, and nmr spectral analyses by comparison with the corresponding authentic specimens. The results are listed in Table I.

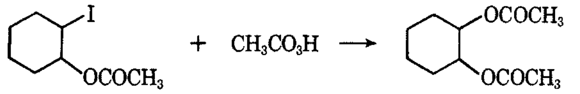
As shown in the table, the main product is 1-iodo-2-acetoxycyclohexane (70–80%), when the molar ratio of the reactants, $[CH_3CO_3H]/[\text{cyclohexyl iodide}]$, is in a range of 0.42–0.76. The other products were



(2)

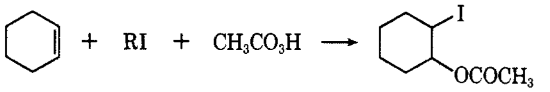
smaller amounts of cyclohexyl acetate (*ca.* 20%), 1,2-diacetoxycyclohexane (2–13%), and iodine (*ca.* 25%).

When the ratio was raised to 1.71, the iodoacetate disappeared and 1,2-diacetoxycylohexane was obtained as a main product together with cyclohexyl acetate and iodine.



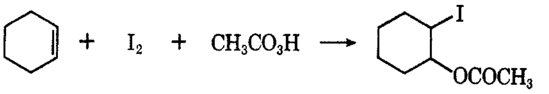
(3)

The reaction of other alkyl iodides with peracetic acid in acetic acid in the presence of cyclohexene affords 1-iodo-2-acetoxycyclohexane in 33–55% yield. The results are shown in Table II. Methyl iodide gives the iodoacetate in a smaller yield (33%). Secondary and tertiary alkyl iodides such as isopropyl, *sec*-butyl, and *t*-butyl iodides afford 1-iodo-2-acetoxycyclohexane in yields better than primary alkyl iodides. Conversely, aromatic iodination with a mixture of secondary or tertiary alkyl iodides and peracetic acid gives little iodoarenes (0–0.8%) and much iodine, but with *n*-alkyl iodides high yields of iodoarenes (70–80%) are obtained.[2]



(4)

The reaction of iodine with peracetic acid in the presence of cyclohexene also affords 1-iodo-2-acetoxycyclohexane (41%).[5]



(5)

It is interesting to note that cyclohexyl iodide reacts with peracetic acid in acetic acid in the absence of cyclohexene to give 1-iodo-2-acetoxycyclohexane in a high yield (77%). The yield is higher than that (57%) in the presence of cyclohexene.

Second-order rate constants (k) for the reaction of cyclohexyl iodide with peracetic acid in acetic acid at 30° was calculated by the equation $v = k[\text{cyclohexyl iodide}][CH_3CO_3H]$, where k was 9.0×10^{-3} M^{-1} sec^{-1}. The k value is higher than those of other *n*-alkyl iodides, *e.g.*, methyl, 2.2×10^{-3}, ethyl, 4.0×10^{-3}, and *n*-butyl iodides, 5.0×10^{-3} M^{-1} sec^{-1} at 30°.[2]

The second-order rate constant for epoxidation of cyclohexene by peracetic acid in acetic acid has been reported to be *ca.* 2.15×10^{-3} M^{-1} sec^{-1} at 25.8° and *ca.* 6.73×10^{-3} M^{-1} sec^{-1} at 39.6°.[6] This epoxidation rate is comparable with the rate of reaction of cyclohexyl iodide with peracetic acid. Thus the

---

(1) Contribution No. 136.

(2) Y. Ogata and K. Aoki, *J. Org. Chem.*, **34**, 3974 (1969).

(3) Y. Ogata and K. Aoki, *J. Amer. Chem. Soc.*, **90**, 6187 (1968).

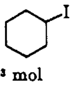
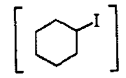
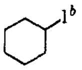
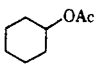
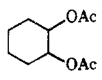
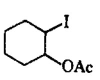
(4) Y. Ogata and K. Nakajima, *Tetrahedron*, **20**, 43 (1964).

(5) Y. Ogata, K. Aoki, and Y. Furuya, *Chem. Ind.* (London), 304 (1965).

(6) D. Swern, *Chem. Rev.*, **45**, 49 (1949).

TABLE I

YIELD OF PRODUCTS IN THE REACTION OF CYCLOHEXYL IODIDE WITH PERACETIC ACID IN ACETIC ACID AT 30°

Reactants			Molar ratio,		Products, %[a]			
Concn,  10^{-3} mol	Concn, CH_3CO_3H, 10^{-3} mol	Solvent CH_3CO_2H, ml	$[CH_3CO_3H]$/ 	Reaction time, hr	 [b]			
4.89	2.03	11	0.42	216	46	19	2	79
5.24	3.55	11	0.68	14	32	20	3	77
96	72.6	100	0.76	169	17	17	13	70
100	171	300	1.71	25	0	20	30	0

[a] The yields are based on peracetic acid used. [b] Recovered per cent.

TABLE II

REACTION OF ALKYL IODIDES WITH PERACETIC ACID IN THE PRESENCE OF CYCLOHEXENE IN ACETIC ACID AT ROOM TEMPERATURE

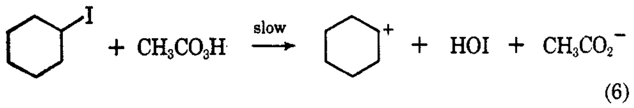
Reactants				Product, 1-iodo-2-acetoxycyclohexane[a]	
Alkyl iodide,	10^{-3} mol	Cyclohexene, 10^{-3} mol	Reaction time, hr	10^{-3} mol	%[b]
Methyl	5.23	9.98	16	1.18	33
Ethyl	5.14	9.89	16	1.54	43
n-Propyl	5.13	9.87	13	1.54	43
Isopropyl	4.96	9.96	13	1.96	55
n-Butyl	5.07	9.94	13	1.53	43
Isobutyl	5.37	9.87	13	1.35	38
sec-Butyl	6.16	9.92	13	1.87	53
t-Butyl	5.99	9.92	14	1.70	48
n-Amyl	5.36	9.95	16	1.67	47
Isoamyl	5.04	9.93	14	1.62	46
n-Hexyl	5.11	9.94	16	1.57	44
n-Octyl	5.92	9.92	16	1.49	42
Benzyl	4.73	9.93	14	1.39	39
Cyclohexyl	5.32	9.93	14	2.01	57
Cyclohexyl	5.24	0.00	14	2.72	77
Iodine[c]	2.00[c]	9.91	17	1.44	41

[a] Conformation (*cis* or *trans*) is unknown. [b] The yields are based on peracetic acid used (3.55×10^{-3} mol). [c] Iodine was used in place of alkyl iodide.

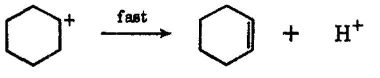
epoxidation may compete with iodoacetoxylation to lower the yield of 1-iodo-2-acetoxycyclohexane from cyclohexene with a mixture of alkyl iodides and peracetic acid.

It has been reported that the reaction of cyclohexyl iodide with silver nitrate gives cyclohexene.[7]

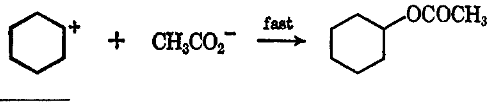
These facts suggest that the reaction may proceed through abstraction of an iodide ion from cyclohexyl iodide by peracetic acid, forming cyclohexyl cation which reacts mainly with acetate ion to eliminate a proton, giving cyclohexene, or to form cyclohexyl acetate in a minor amount. The carbonium ion formation such as step 6 should be favored in the order primary < secondary < tertiary alkyl iodide.



(6)

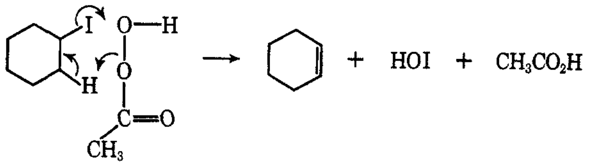


(7)



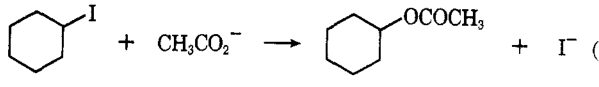
(8)

An alternative mechanism to eq 6 and 7 might be as follows.



(6′)

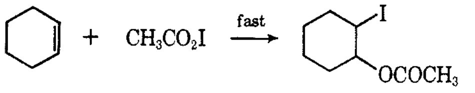
An alternative to eq 8 might be a direct displacement of iodide ion by acetate ion.



(8′)

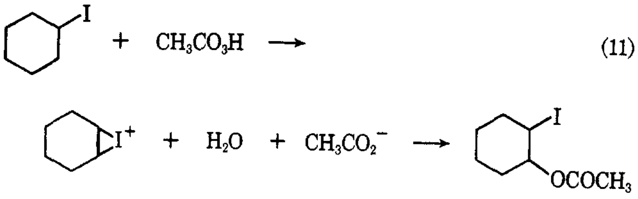
Abstracted iodide ion may be oxidized by peracetic acid to give acetyl hypoiodite, which then adds to the double bond of cyclohexene to form the observed 1-iodo-2-acetoxycyclohexane.

$$HOI + CH_3CO_2H \overset{\text{fast}}{\rightleftharpoons} CH_3CO_2I + H_2O \quad (9)$$



(10)

Another mechanism alternative to that shown in eq 6–10 might be as follows (eq 11), but at present no decisive evidence is available.



(11)

A smaller amount of iodine may be formed by the attack of acetyl hypoiodite on cyclohexyl iodide. Excess peracetic acid may oxidize iodoacetoxycyclohexane to form diacetoxycyclohexane (eq 3).

Experimental Section

Materials.—A *ca.* 3.5 *M* peracetic acid solution was prepared by adding dropwise acetic anhydride (407 g) to a stirred solution of 60% hydrogen peroxide (100 g) and concentrated H_2SO_4 (1 ml) as catalyst at 30–40° over a period of 3 hr. The solution contained a small concentration (*ca.* 0.2 *M*) of diacetyl peroxide.[8]

Alkyl iodides were prepared by refluxing the respective alcohols with a mixture of iodine and red phosphorus.[3] Cyclohexyl iodide had bp 59.0–59.8° (7 mm) [lit.[9] bp 74.4° (9 mm)].

---

[7] M. Tiffeneau, *Compt. Rend.*, **159**, 773 (1914).

[8] Y. Ogata and K. Aoki, *J. Org. Chem.*, **31**, 4181 (1966).

[9] P. W. Clutterbuck and J. B. Cohen, *J. Chem. Soc.*, **123**, 2511 (1923).

Cyclohexene was prepared by dehydration of cyclohexanol (400 g) with concentrated H_2SO_4 (13 ml) at 130–150° for several hours. Cyclohexene was salted out, dried ($CaCl_2$), and distilled, bp 83–84°.[10] Acetic acid was purified by rectifying 99.5% acetic acid over P_2O_5, bp 117.5–118.0°. Iodotoluene, bp 204–207°, was prepared by the reaction of toluene with a mixture of iodine and peracetic acid.[3,11] Cyclohexyl acetate was prepared by sulfuric acid catalyzed esterification of cyclohexanol with acetic acid, bp 173–175° [lit.[12] bp 74.5–76.5° (23 mm)]. 1-Iodo-2-acetoxycyclohexane was prepared by the reaction of cyclohexene (4.2 g, 0.051 mol) with a mixture of iodine (12.7 g, 0.05 mol) and silver acetate (8.4 g, 0.05 mol) in ether (100 ml) at 22–35° for 80 min. The reaction mixture, after treatment with aqueous $Na_2S_2O_3$ and then anhydrous Na_2SO_4, gave 10.6 g of 1-iodo-2-acetoxycyclohexane (79%), bp 100° (4 mm) [lit.[13] bp 120° (12 mm)]. The ir spectrum showed strong absorption at 1740 and 1235 cm^{-1}, characteristic of the acetoxyl group. Other bands were at 2930 (s), 2855 (m), 1445 (m), 1370 (m), 1355 (m), 1170 (m), 1122 (w), 1090 (w), 1045 (m), 1035 (m), 1007 (w), 960 (w), 908 (w), 890 (w), 850 (w), 838 (w), 796 (w), 663 (w), and 600 cm^{-1} (w). 1,2-Diacetoxycyclohexane[14] was prepared by the reaction of 1-iodo-2-acetoxycyclohexane (5.4 g, 0.02 mol) with silver acetate (4.5 g, 0.026 mol) in a mixed solvent of acetic acid (50 ml) and benzene (60 ml) by heating to reflux for 9 hr. The ordinary work-up gave 1,2-diacetoxycyclohexane (0.55 g), which was confirmed by glpc analyses, ir (liquid film) 1740 and 1240 cm^{-1} (ester C=O).

Analyses of Products.—Products were analyzed by glpc employing a Yanagimoto Model GCG 550F with a flame ionization detector operated with a 2 m × 3 mm column packed with Apiezon L grease 15% on Celite 545 of 80–100 mesh with nitrogen flow rate 20–30 ml/min, injection temperature 230–300°. Iodotoluene was used as an internal standard which was added to the extract of the reaction products just before analyses. Infrared spectra were determined as liquid film using KBr cell by a Perkin-Elmer Model 337 spectrophotometer; nmr spectra were determined as neat liquids using tetramethylsilane as an internal standard by Varian Model HA-100 instrument.

Reaction of Cyclohexyl Iodide with Peracetic Acid.—An acetic acid solution (20 ml) of 3.64 *M* peracetic acid (0.0726 mol) was added dropwise into an acetic acid solution (80 ml) of cyclohexyl iodide (19.2 g, 0.096 mol) at 30° over a period of 6 hr and the mixture was allowed to stand at room temperature for 7 days. The mixture was diluted with water (300 ml) and extracted with benzene (200 ml). The solution was washed with aqueous $Na_2S_2O_3$ to remove iodine and dried (Na_2SO_4). Solvent benzene was vacuum distilled, leaving a liquid (18.1 g). The liquid (2 g) was separated by column chromatography using an automatic fraction collector through silicic acid (30 g) packed in a 2 cm × 19 cm column, eluting successively with *n*-hexane (200 ml), benzene (100 ml), and diethyl ether (100 ml). The reaction products eluted in the order cyclohexyl iodide, 1-iodo-2-acetoxycyclohexane, cyclohexyl acetate, and 1,2-diacetoxycyclohexane. Solvents were vacuum distilled and the remaining liquids were identified by their ir spectra and by glpc analyses compared with the authentic samples. The products consisted of cyclohexyl acetate (14%), cyclohexyl iodide (17%), 1,2-diacetoxycyclohexane (11%), and 1-iodo-2-acetoxycyclohexane (58%). Their retention times were 2.3, 4.4, 6.6, and 14.9 min, respectively, at column temperature 160° and nitrogen carrier 15 ml/min.

In another run, excess peracetic acid was used. Cyclohexyl iodide (21 g, 0.1 mol) was treated with peracetic acid (0.171 mol) in acetic acid (300 ml) at 30° for 1 day. The mixture was worked up as above, giving, after evaporation of benzene, a residual liquid (7.9 g). The liquid was vacuum distilled and a fraction, bp 80–81° (2 mm), was obtained: ir 1740 and 1240 cm^{-1} (CH_3COO); nmr (neat liquid, standard TMS) τ 5.00 and 5.07 (CHOAc), 8.05 singlet ($OCOCH_3$) and 8.35 and 8.44 (CH_2 of cyclohexane ring). The liquid was identified as 1,2-diacetoxycyclohexane when compared with the authentic sample.

Reaction of Alkyl Iodides with Peracetic Acid in the Presence of Cyclohexene.—An acetic acid solution (1 ml) of 3.55 *M* peracetic acid was added to an acetic acid solution (10 ml) containing alkyl iodide (*ca.* 5×10^{-3} mol) and cyclohexene (*ca.* 10×10^{-3} mol) at room temperature (*ca.* 20°). The mixture became warm (*ca.* 45°) in a few minutes and the solution was colorless and transparent in most cases. The mixture was allowed to stand overnight and then poured into a separatory funnel containing water (50 ml) and benzene (20 ml). The benzene layer was washed with aqueous $Na_2S_2O_3$, dried (Na_2SO_4), and analyzed by glpc using indotoluene as an internal standard to estimate the yield of 1-iodo-2-acetoxycyclohexane.

Reaction of Cyclohexene with a Mixture of Iodine and Peracetic Acid.—An acetic acid solution (10 ml) of cyclohexene (9.91×10^{-3} mol) was added to a benzene solution (20 ml) of iodine (0.508 g, 2×10^{-3} mol). An acetic acid solution (1 ml) of 3.55 *M* peracetic acid was added to the mixture at 24–27°. After standing overnight at room temperature, the mixture was worked up as above. The yield of 1-iodo-2-acetoxycyclohexane was 41% by glpc analyses.

Registry No.—Peracetic acid, 79-21-0; cyclohexene, 110-83-8.

Acknowledgments.—The authors are grateful to Toyo-Rayon Co., Daicel Co., and Tokai Electro-Chemical Co. for their gifts of materials and also to the referees for their suggestions.

---

(10) G. H. Coleman and H. F. Johnston, "Organic Syntheses" Coll. Vol. I, 2nd ed., John Wiley & Sons, Inc., New York, N. Y., 1964, p 183.

(11) Y. Ogata and K. Nakajima, *Tetrahedron*, **20**, 2751 (1964).

(12) S. L. Friess, *J. Amer. Chem. Soc.*, **71**, 14 (1949).

(13) L. Birkenbach, J. Goubeau, and E. Berninger, *Ber.*, **65**, 1339 (1932).

(14) S. Winstein and R. E. Buckles, *J. Amer. Chem. Soc.*, **65**, 413 (1943).