Iodohydrins and Epoxides from Olefins

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Reaction of olefins with iodine in the presence of water and a suitable oxidizing agent such as iodic acid, or oxygen catalysed by nitrous acid, gives iodohydrins. These form epoxides readily on treatment with bases.

ALTHOUGH formation of chlorohydrins and bromohydrins from olefins and dilute aqueous solutions of the halogens is a well-known preparative and industrial procedure, the chemical literature provides no clear-cut example of an iodohydrin being formed from an olefin, iodine, and water. Pogorzelsky [1] reported that isobutene was absorbed by aqueous potassium tri-iodide and that subsequent addition of potassium hydroxide yielded some isobutene oxide along with a much larger amount of t-butanol. The epoxide arose possibly, but not necessarily, from iodohydrin formed in the first stage. This doubtful exception apart, it has always been found necessary to add mercuric oxide (or occasionally silver nitrate) to the mixture of olefin, iodine, water, and a suitable solvent such as ether; a procedure due originally to Bougault.[2]

We found that a solution of iodine in aqueous dioxan becomes acidic after propene has passed through it for a few seconds; an observation difficult to explain unless propene iodohydrin is being formed by equation (1):

$$C_3H_6 + I_2 + H_2O \longrightarrow C_3H_6(OH)I + HI \qquad (1)$$

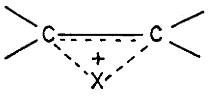
There are at least two reasons why this reaction should not proceed smoothly to completion, as it does with chlorine and bromine.

(i) Formation of trihalide ion in the equilibrium (2)

$$X_2 + X^- \rightleftharpoons X_3^- \qquad (2)$$

lowers the actual concentration of halogen. With iodine, the position of equilibrium lies far to the right; thus the concentration of iodine diminishes rapidly with accumulation of iodide ion.

(ii) Formation of a halohydrin from an olefin and halogen probably proceeds *via* an intermediate cationic



(I)

species such as (I), and whether this is formed directly by equation (3) or whether hydrolysis of the halogen

$$>C{=}C< + X_2 \rightleftharpoons (I) + X^- \qquad (3)$$

occurs first and is followed by reaction of hypohalous acid with the olefin [equations (4) and (5)] accumulation of the ion X^- dis-favours formation of the intermediate. This is less important for chlorine and bromine than it is for the less reactive iodine.

$$X_2 + H_2O \rightleftharpoons XOH + H^+ + X^- \qquad (4)$$

$$>C{=}C< + XOH + H^+ \longrightarrow (I) + H_2O \qquad (5)$$

Thus, the role of mercuric oxide in the Bougault procedure is probably to remove iodide ion continuously as the insoluble and poorly ionized mercuric iodide.

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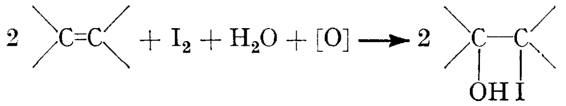
[1] S. Pogorzelsky, *J. Russ. Phys. Chem. Soc.*, 1905, **37**, 814.
[2] J. Bougault, *Compt. rend.*, 1900, **130**, 1766; **131**, 528.

Another and potentially more attractive device is to remove iodide ion by continuous reoxidation to iodine. Provided that the oxidizing species does not itself attack the olefin, equation (6) then becomes possible:



$$2\,\gt C{=}C\lt + I_2 + H_2O + [O] \longrightarrow 2\,\gt \underset{OH}{C}-\underset{I}{C}\lt \qquad (6)$$

whereby all iodine, instead of one-half as in Bougault's procedure, is incorporated into iodohydrin.

When a dilute aqueous solution of iodic acid was stirred with iodine in a propene atmosphere at 50°, propene iodohydrin was formed in 80% yield according to equation (7):

$$2I_2 + HIO_3 + 5C_3H_6 + 2H_2O \longrightarrow 5C_3H_6(OH)I \qquad (7)$$

The propene iodohydrin formed in this and in subsequent experiments was shown by g.l.c., and examination of n.m.r. spectra of the mixture, to consist of 1-iodopropan-2-ol containing *ca.* 8% of 2-iodopropan-2-ol. Iodic acid was generated *in situ* from potassium iodate and sulphuric acid (acetic acid, though a weaker acid than iodic, served equally well).

It has been known to analytical chemists for a very long time that traces of nitrous acid enormously accelerate the oxidation of hydriodic acid to iodine by oxygen, although we have been unable to trace this finding to its original source. An alternative oxidizing system was thus available; and in the event, when iodine in aqueous dioxan containing a little sodium nitrite was stirred at 70° with a 4 : 1 (v/v) mixture of propene and oxygen the gas was absorbed rapidly and propene iodohydrin was subsequently isolated in 87% yield (on iodine) according to equation (8):

$$2I_2 + O_2 + 4C_3H_6 + 2H_2O \longrightarrow 4C_3H_6(OH)I \qquad (8)$$

Nitrous acid presumably catalyses reaction between hydrogen iodide and oxygen by forming nitric oxide, which is continuously oxidized to nitrogen dioxide and formed again by reduction of the latter [equations (9)—(11)].

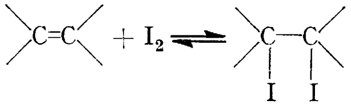
$$2HNO_2 + 2HI \longrightarrow 2NO + 2H_2O + I_2 \qquad (9)$$

$$2NO + O_2 \longrightarrow 2NO_2 \qquad (10)$$

$$NO_2 + 2HI \longrightarrow NO + H_2O + I_2 \qquad (11)$$

From sodium nitrite, sodium tri-iodide is eventually formed and consumption of iodine becomes slow towards the end of the reaction with propene: it was found best to add sulphuric acid at intervals in total amount equivalent to the nitrite used. Residual iodine was then as low as 0·1%.

When a chlorohydrin or a bromohydrin is formed from an olefin with aqueous chlorine or bromine, dilute solutions must be used or a side reaction which produces olefin dihalide becomes too important: the formation of dihalide is dependent on the concentration of halide ion in solution and presumably is due to competition of halide ion with water in reaction with the cationic intermediate. With iodine, however, this reaction is easily reversed (12), especially when the reaction is warmed.



$$\gt C{=}C\lt + I_2 \rightleftharpoons \gt \underset{I}{C}-\underset{I}{C}\lt \qquad (12)$$

Thus, higher initial concentrations (up to 20%) of iodine can be used and the factor limiting the yield, in the reaction with propene, is formation of di-iodopropyl ether, presumably formed according to equation (13) by competition of iodopropanol with water in the reaction

$$2I_2 + O_2 + 4C_3H_6 + 4C_3H_6(OH)I \longrightarrow 4(C_3H_6I)_2O + 2H_2O \qquad (13)$$

described in equation (8). The proportion of this ether formed at 10% initial concentration of iodine was *ca.* 0·85%, and at 20% initial concentration *ca.* 2·4%. The n.m.r. spectrum of the ether, and its separation by g.l.c. into at least two major components, suggested that it consisted principally of the racemic and meso forms of $[ICH_2CH(CH_3)]_2O$. When the iodohydrination was run in water alone, in quantity insufficient to prevent the formation of a large organic liquid layer containing the iodohydrin, the yield of the ether was much higher (44%). Thus, a water-soluble organic solvent is useful when the iodohydrin is required. Dioxan, sulpholane, t-butanol, and acetonitrile have been used with success.

Iodohydrins readily yield epoxides on treatment with bases, and potentiometric titration of aqueous solutions of iodopropanol at ambient temperature indicated that cyclization proceeds at perceptible rates at pH exceeding 8. When calcium hydroxide was added to a reaction mixture from the iodohydrination of propene, propene oxide could be recovered in 83—87% yields (based on iodine). Alternatively, the epoxide was made in 98% yield from the iodohydrin by the action of moist sodium aluminate suspended in ethylene dichloride.

Isobutene reacted readily with iodine and nitrite-catalysed oxygen to give, after addition of calcium hydroxide, an 85·5% yield of epoxide. No ether was detectable as a by-product, doubtless because the iodohydrin is a tertiary alcohol and unable to compete with water. This view was supported by an experiment in which water alone was the solvent: the iodohydrin was formed in high yield and little if any ether was produced, although propene under the same conditions gave an ether as the major product.

With ethylene, the unique stability of the di-iodide lowered the yield of iodohydrin below 60%. With allyl chloride, reaction was slow but an iodohydrin was isolated and shown to give epichlorohydrin on treatment with calcium hydroxide. *cis*-2-Butene gave, *via* an iodohydrin, *cis*-2,3-epoxybutane containing no *trans*-isomer, indicating as expected that the iodohydrin was formed by stereospecific *anti*-addition; if the temperature during iodohydrination was too high, solvolysis of the intermediate iodohydrin to butan-2-one occurred.

A new route to iodohydrins and epoxides was thus established. It seems possible that an analogous but much less efficient process was operative in the experiments of Sumrell *et al.*,[3] who treated preformed olefin di-iodides with acetone and hydrogen peroxide at room temperature. They obtained iodohydrins along with iodoacetone, and they stated that in the absence of acetone no iodohydrin was formed. About 40% of the iodine taken was found in iodohydrins.

EXPERIMENTAL

Propene Iodohydrin.—(*a*) Iodine (2·54 g.), potassium iodate (1·07 g.), water (75 ml.), and sulphuric acid (1 ml.; 5N) were stirred together at 50° under propene. After 8 hr., 600 ml. of the gas had been absorbed. An ether extract of the cooled solution was dried and distilled. Propene iodohydrin (3·7 g.) was collected at 28°/0·05 mm. and was identified (i.r. spectra, g.l.c.) with a specimen of similar composition prepared from propene oxide by the sodium iodide–acetic acid method.[4] G.l.c. (10% polyethylene glycol succinate; 150°; 20 lb./in.^{2} nitrogen) showed the presence of a major and a minor component. The n.m.r. spectrum (in carbon tetrachloride) showed the major component to be 1-iodopropan-2-ol (91·5%): τ 8·73 (d, J 6 Hz, CH_3), τ 6·83 (d, J 6 Hz, CH_2I), and the minor component to be 2-iodopropan-1-ol (8·5%), evaluated from the integral of the methyl-group doublet (τ 8·14; d, J 6·25 Hz, CH_3). Propene iodohydrin prepared by this and the following methods had about the same composition. Freshly distilled, it was a colourless oil, soluble in approximately 9 parts of water at room temperature (Found: C, 19·1; H, 3·9; I, 68·1. Calc. for C_3H_7IO: C, 19·4; H, 3·8; I, 68·2%).

(*b*) Iodine (50·8 g.), potassium iodate (23·55 g.), water (1280 ml.), dioxan (320 ml.), and acetic acid (43 ml.; 5N) were stirred under propene. When absorption had ceased the solution was extracted with chloroform which was then decolourized by being shaken with a little aqueous sodium thiosulphate. The dried solution on distillation through a 12 in. Widmer column gave propene iodohydrin (73 g., 78%), b.p. 49—52°/4 mm.

(*c*) The reaction vessel for propene–oxygen experiments was a 1 l. Pyrex Büchner filter flask containing a 6 cm. polytetrafluoroethylene-coated magnetic stirring bar and fitted with a rubber stopper carrying a stopcock tube. The side-arm of the flask was connected by rubber tubing and a 3-way tap to either of two gas reservoirs (of 2·5 l. and 1 l. capacity). These were filled with a mixture of propene and oxygen (4 : 1, by volume), mixed carefully after being filled by inversion of the reservoirs several times. The flask was charged with reagents and solvents, evacuated *via* the stopcock tube, and filled with gas from the smaller reservoir. It was then isolated from the reservoirs, immersed within 5 cm. of the side-arm in water pre-heated to the reaction temperature, and magnetic stirring was started. After a minute or two when the initial rise of pressure due to heating had subsided, the larger reservoir was connected. When necessary, additional reagents were added through the stopcock tube after slight reduction of the internal pressure to avoid loss of gas. When reaction was complete the flask was removed from the bath and allowed to cool while connected with the smaller reservoir.

The reactor was charged with iodine (5·08 g.), dioxan (25 ml.), water (25 ml.), and sodium nitrite (0·12 g.). The reaction ran at 70° and 1230 ml. of gas were absorbed during 75 min. The mixture required 2·0 ml. of 0·8N-sodium thiosulphate to decolourize it; this corresponds to 0·20 g. (4%) of unchanged iodine. Extraction with ether and distillation of the dried extract gave propene iodohydrin (6·50 g., 87%), b.p. 46—48°/3·6 mm. The small residue (*ca.* 0·2 g.) contained a little more iodohydrin and the by-product di-iododipropyl ether.

Propene Oxide.—(*a*) The reactor described in (*c*), above, contained iodine (10·16 g.), dioxan (25 ml.), water (25 ml.), and sodium nitrite (0·24 g.); the temperature was 70°. Six successive additions of N-sulphuric acid (0·5 ml. aliquots) were made at 5-min. intervals after the reaction had run for 15 min.; after 60 min., the gas uptake was 2530 ml. The resulting yellow solution (pH *ca.* 3) was added during 10—15 min. to a stirred suspension of calcium hydroxide (4 g.) in a little water. The pressure was reduced to *ca.* 50 mm. and the mixture was warmed. Propene oxide with some solvent, water, and di-iododipropyl ether distilled off and were collected in a cold trap (−70°). The epoxide (b.p 36°) in other experiments was isolated by fractional distillation at this stage and identified by comparison (i.r., g.l.c.) with authentic material; for determination of yield the distillate was diluted to 100 ml. with water and 5 ml. portions were added to 0·3M-sodium thiosulphate (50 ml.) containing phenolphthalein. Acetic acid (0·22N) was added gradually to the mixture, an excess of acid being avoided; as the reaction slowed, it was increasingly warmed, until the pink colour ceased to reappear. This required 15·8 ml. of acid equivalent to 4·04 g. (87% yield) of propene oxide. This analytical method is modified from Ross.[5] The aqueous alkaline residue from the distillation was shown to contain some propene glycol. The yield of di-iodopropyl ether under these conditions was *ca.* 0·35 g. (2·4%).

(*b*) Propene iodohydrin (19 g.) in ethylene dichloride (100 ml.) was stirred and heated under a 12 in. Widmer spiral with moist sodium aluminate on alumina (75 g.; prepared by mixing 100 g. chromatographic grade alumina with 20 ml. 10N-sodium hydroxide). Propene oxide (6·0 g.) distilled at 36°; after being dried, it weighed 5·8 g. (98%).

Di-iododipropyl Ether.—The reactor described above contained iodine (10·16 g.), water (50 ml.), and sodium nitrite (0·24 g.); the temperature was 70°. Sulphuric acid (0·5 ml. of N) was added at 25, 35, 45, 55, 65, and 75 min.; an addition of sodium nitrite (0·1 g.) was made at 77 min. Absorption ceased after several hours: the gas absorbed was 2600 ml. The two-phase mixture was added to calcium hydroxide (4 g.) and propene oxide was distilled at 50 mm. and determined as before (24·2% yield). Distillation was then continued at atmospheric pressure and the heavy oily ether was extracted from the distillate and distilled, b.p. 136°/12 mm. (6·2 g.), as a colourless oil. As shown by g.l.c. it contained at least two major components (Found: C, 20·7, 20·4; H, 3·3, 3·6. $C_6H_{12}I_2O$ requires C, 20·3; H, 3·4%). Identical samples gave divergent results for iodine (66·5 to 77%; calc., 71·8%). The ether was steam-volatile. On treatment with zinc in acetic acid the expected reduction to propene occurred rapidly at room temperature. Silver nitrate solution also reacted fast at room temperature and silver iodide was formed. The

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[3] G. Sumrell, B. M. Wyman, R. G. Howell, and M. C. Harvey, *Canad. J. Chem.*, 1964, **42**, 2710.

[4] J. W. Cornforth, R. H. Cornforth, and K. K. Mathew, *J. Chem. Soc.*, 1959, 112.

[5] W. C. J. Ross, *J. Chem. Soc.*, 1950, 2257.

n.m.r. spectrum in carbon tetrachloride showed a doublet (J 6 Hz) at τ 8·72 and a much smaller doublet (J 6·25 Hz) at τ 8·12. The ratio of the two integrals was *ca.* 16 : 1. From the assignments for propene iodohydrin (above), 94% of the methyl groups in the specimen were $CH_3CH{-}O$ and 6% were $CH_3CH{-}I$. A propene iodohydrin containing 92% of 1-iodo-propan-2-ol and 8% 2-iodo-propan-1-ol, and reacting with propene and iodine with similar preference for attachment of oxygen to the 2-position, would afford an ether consisting of 84·6% bis-(1-iodomethylethyl) ether, 14·7% of 2-iodopropyl 1-iodomethylethyl ether, and 0·6% of bis-(2-iodopropyl) ether: in such a mixture, 92% of the methyl groups would be $CH_3{-}CH{-}O$. Since the two major peaks shown by g.l.c. each contained over 40% of the specimen, it appears that both the racemic and meso isomers of bis-(1-iodomethylethyl) ether were present and that these were separable by g.l.c.

1-*Iodo*-2-*methylpropan*-2-*ol and* 1,2-*Epoxy*-2-*methylpropane*.—The reactor already described was used, the gas phase being isobutene–oxygen (4 : 1; v/v). (*a*) The reactor charge was iodine (10·16 g.), dioxan (25 ml.), water (25 ml.), and sodium nitrite (0·24 g.); the temperature was 70°. N-Sulphuric acid (0·5 ml.) was added at 6·5, 10, 15, 25, 30, and 35 min. Additional sodium nitrite (0·02 g.) was added after 43 min; the total reaction time was 60 min. and the gas uptake was 2695 ml. Almost no iodine remained. The mixture was added to calcium hydroxide (4 g.) as before and the epoxide was distilled at 50 mm. and determined as for propene oxide (yield: 4·83 g., 85·5%). No analogue of di-iodopropyl ether was detected.

(*b*) The reactor charge was iodine (10·16 g.), water (50 ml.), and sodium nitrite (0·12 g.); the temperature was 70°. N-sulphuric acid (0·5 ml.) was added at 10, 15, 20, 25, 30, 35, and 40 min. Additional sodium nitrite (0·12 g. at 27 min. and 0·06 g. at 75 min.) was added; the total reaction time was 100 min. and the gas absorbed was 2430 ml. Sodium thiosulphate reduced 0·48 g. (4·7%) of unchanged iodine. The two-phase mixture was extracted with ether and the dried extract was distilled to give 1-*iodo*-2-*methylpropan*-2-*ol* (11·8 g.; 74%), b.p. 52°/5 mm. (Found: C, 24·2; H, 4·7; I, 63·7. C_4H_9IO requires C, 24·0; H, 4·5; I, 63·5%). The n.m.r. spectrum in deuteriochloroform presented three singlet peaks: τ 8·60 ($2CH_3$), 7·25 (OH), and 6·68 (CH_2) in the ratio 6 : 1 : 2.

Iodochloropropanol and Epichlorohydrin.—The gas phase was pure oxygen. The reactor contained iodine (12·7 g.), dioxan (100 ml.), water (100 ml.), and sodium nitrite (0·3 g.). The mixture was stirred at 50° and allyl chloride (7·65 g.) was introduced gradually. The reaction was slow; after 6 hr. 530 ml. of gas had been absorbed (0·15 g. sodium nitrite added after 3 hr.). The residual iodine (6·0 g., 47%) was reduced by thiosulphate and the liquid was extracted with ether. Distillation gave chloroiodopropanol (8·6 g.; 75% on iodine used), b.p. 52—54°/0·2 mm. (Found: C, 16·3; H, 2·8; Cl, 16·1; I, 57·5. Calc. for C_3H_6ClIO: C, 16·2; H, 2·7; Cl, 16·3; I, 57·6%). The specimen was presumably a mixture of 1-chloro-3-iodopropan-2-ol and 3-chloro-2-iodopropan-1-ol. Treatment of this product with calcium hydroxide gave epichlorohydrin (identified by b.p., i.r., and g.l.c.).

Ethylene Iodohydrin.—The reactor contained iodine (10·16 g.), sulpholane (25 ml.), water (25 ml.), and sodium nitrite (0·24 g.); the temperature was 80° and the gas phase was ethylene–oxygen (4 : 1). N-Sulphuric acid (0·5 ml.) was added at 20, 25, 38, 45, 55, 65, and 75 min., and sodium nitrite (0·12 g.) at 55 min. When heating was stopped after 195 min., 2·2 g. of iodine remained and this was reduced by sodium thiosulphate. Ethylene di-iodide was filtered off and the filtrate was saturated with salt and extracted with ether (5 × 25 ml.). The extract was dried and distilled to give discoloured ethylene iodohydrin (6 g., 55% on iodine used), b.p. 84—86°/16 mm.; this was decolourized with sodium thiosulphate and redistilled (Found: C, 13·8; H, 3·0; I, 73·9. Calc. for C_2H_5IO: C, 13·95; H, 2·90; I, 73·85%).

cis-2,3-*Epoxybutane*.—The gas phase was *cis*-2-butene. The reactor contained iodine (10·16 g.), potassium iodate (4·3 g.), dioxan (25 ml.), and 0·8N-sulphuric acid (25 ml.); the temperature was 40°, the reaction time 60 min., and the amount of residual iodine was 0·8 g. The decolourized mixture was added to calcium hydroxide (4·0 g.) and distilled at 200 mm. Hg. pressure into cold traps, the contents of which were then distilled up to 80°. The distillate was dried ($CaCl_2$) and redistilled slowly through a short Vigreux column to give *cis*-2,3-epoxybutane (2·7 g.), b.p. 59—61°. The i.r. spectrum[6] was that of *cis*-2,3-epoxybutane uncontaminated by the *trans*-isomer.

At a reaction temperature of 67°, butan-2-one was formed and was identified by m.p. and mixed m.p. (113—114°) of the 2,4-dinitrophenylhydrazone.

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[6] H. van Risseghem, *Bull. Soc. chim. France*, 1959, 1661.