144. *Investigations of the Olefinic Acids. Part IX. The Addition of Hydrogen Bromide to Unsaturated Acids.*

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The addition of hydrogen halide to an olefin is directed largely by the degree of alkyl substitution of the two carbon atoms carrying the double bond—this is expressed empirically in Markownikoff's rule.

Provided that certain factors due to the presence of the carboxyl group are borne in mind, the olefinic acids are particularly suitable for the investigation of this subject. Their chief advantages over the olefins themselves are: (1) the greater accessibility of homogeneous unsaturated compounds with varied types of alkyl substitution and known positions of the double bond; (2) the greater ease of determination of the nature of the addition products; (3) both the unsaturated acids and the addition products which are required for reference can nearly always be obtained as pure crystalline solids.

The early work on the addition of hydrogen halides to olefinic acids is well known (Erlenmeyer senr., *Ber.*, 1880, **13**, 304; Fittig and collaborators, *Annalen*, 1880, **200**, 21;

Ber., 1880, **13**, 955; *Annalen*, 1881, **208**, 71; 1889, **255**, 18; 1894, **283**, 73; Fichter and Langguth, *Annalen*, 1900, **313**, 371) and the results are usually summarised by the statement that Δ^{α}- and Δ^{β}-acids add hydrogen halide so that the halogen seeks the position further from the carboxyl group, whereas in Δ^{γ}-acids the reverse obtains.* These conclusions, although correct for Δ^{α}-acids, are now shown to be invalid for the other types.

Walker and Lumsden (J., 1901, **79**, 1191) showed that undecenoic acid, when dissolved in toluene, added hydrogen bromide to give the terminal bromo-acid $CH_2Br{\cdot}CH_2{\cdot}[CH_2]_8{\cdot}CO_2H$, but in ethereal solution yielded mainly the isomeric acid, $CH_3{\cdot}CHBr{\cdot}[CH_2]_8{\cdot}CO_2H$ (confirmed by Chuit *et al.*, *Helv. Chim. Acta*, 1926, **9**, 1074; 1927, **10**, 173).

The direction of addition of hydrogen bromide to an olefinic acid is now shown to depend generally on (i) the external conditions (as indicated by Walker and Lumsden's discovery) and (ii) the alkyl substitution about the double bond; but, with the sole exception of Δ^{α}-acids, is *independent* of the position of the double bond with respect to the carboxyl group.

(i) *Effect of solvents.* In hydrocarbon solvents, the acid behaves as a " hydrogen ester "; the carboxyl group controls the orientation and the bromine adds to the " distant " carbon atom (this vol., p. 563), regardless of the alkyl substitution. As far as our experiments have gone, the addition to the acid in these solvents goes in the same direction as that to the corresponding ester in the absence of solvent. Without solvent, or in the presence of ether, acetic acid, or water, the double bond of the acid behaves independently of the carboxyl group.

(ii) *Effect of alkyl substitution.* This only becomes operative in additions of the second of the types indicated above, which proceed in accordance with the Markownikoff rule.

These generalisations indicate some remarkable differences in orientation. For instance, the direction of addition of hydrogen bromide to vinyl- and allyl-acetic acids alone is completely reversed if the acids are dissolved in toluene. Moreover, the direction of addition to these acids in the pure state is exactly the reverse of that to their esters. Although these differences are in the direction expected on theoretical grounds (see below), yet the completeness of the reversal of the orientation was an unexpected, though welcome, feature of these investigations.

The work was carried out with crystalline unsaturated acids, and the products of addition were analysed by methods which were controlled in every case by reference to the pure bromo-acids, independently synthesised. Many crystalline bromo-acids could be identified by direct comparison. The results are summarised in the table.

Addition of Hydrogen Bromide to Unsaturated Acids and Esters.

Acid (or ester).	Position of double bond.	Solvent.	% Composition of bromo-acid (ester) formed (±2%). β-.	γ-.	δ-.
$CH_3{\cdot}CH{:}CH{\cdot}CO_2H$ (I)	$\alpha\beta$	None (fused)	100	—	—
$C_2H_5{\cdot}CH{:}CH{\cdot}CO_2H$ (II)	,,	None	100	—	—
$(CH_3)_2CH{\cdot}CH{:}CH{\cdot}CO_2H$ (III)	,,	None	100	—	—
$CH_2{:}CH{\cdot}CH_2{\cdot}CO_2H$ (IV)	$\beta\gamma$	None	100	0	—
,, ,,	,,	Water	100	0	—
,, ,,	,,	Ether	100	0	—
,, ,,	,,	Acetic acid	100	0	—
,, ,,	,,	Toluene	0	100	—
,, ,,	,,	Petroleum	0	100	—
$CH_2{:}CH{\cdot}CH_2{\cdot}CO_2Et$ (V)	,,	None	0	100	—
$CH_3{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CO_2H$ (VI)	,,	None	8	92	—
,, ,,	,,	Water	8	92	—
$(CH_3)_2C{:}CH{\cdot}CH_2{\cdot}CO_2H$ (VII)	,,	None	0	100	—
,, ,,	,,	Water	0	100	—
$CH_2{:}CH{\cdot}[CH_2]_2{\cdot}CO_2H$ (VIII)	$\gamma\delta$	None	—	100	0
,, ,,	,,	Water	—	100	0
,, ,,	,,	Ether	—	100	0
,, ,,	,,	Toluene	—	0	100
$CH_2{:}CH{\cdot}[CH_2]_2{\cdot}CO_2Et$ (IX)	,,	None	—	0	100
$(CH_3)_2C{:}CH{\cdot}[CH_2]_2{\cdot}CO_2H$ (X)	,,	None	—	0	100
,, ,,	,,	Water	—	0	100

* Some standard works of reference even generalise incorrectly, stating that the halogen always enters at a point as far as possible from the carboxyl group.

In 1881, Fittig and Geisler (*Annalen*, **208**, 44) showed that pyroterebic acid (VII) differed from all other known unsaturated acids both in the ease with which it reacted with hydrogen bromide in water and in the fact that no hydrobromide then separated : distillation in steam of the solution so obtained yielded *iso*hexolactone, the isolation of which led to the recognition of lactones as a class. These authors observed the formation of a crystalline solid when hydrogen bromide was passed into the acid, but could not isolate the presumed hydrobromide owing to its unusual instability. We have obtained it as a solid, m. p. 10°, and followed its decomposition into the lactone (p. 576).

General Methods for the Synthesis of Bromo-acids.—The results indicate that a pure bromo-acid, $R'R''CBr\cdot[CH_2]_x\cdot CO_2H$, can be prepared by the following general methods.

If $x = 1$: By the addition of HBr to $R'R''C{:}CH\cdot[CH_2]_{x-1}\cdot CO_2H$. The solvent and the nature of R',R'' determine the rate, but not the direction, of addition.

If $x = 2$ *or more*: (i) If $R'R'' = H,H$ or H, alkyl; by the addition of HBr to $R'R''C{:}CH\cdot[CH_2]_{x-1}\cdot CO_2H$ in toluene or, better, petroleum solution, or to

$$R'R''C{:}CH\cdot[CH_2]_{x-1}\cdot CO_2Et.$$

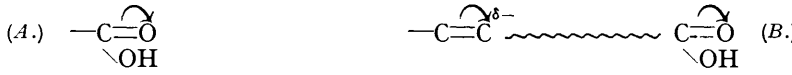
(ii) If $R'R'' =$ alkyl, alkyl; by the addition of HBr to $R'R''C{:}CH\cdot[CH_2]_{x-1}\cdot CO_2H$ under any conditions.

These observations, in conjunction with recent work on the synthesis of unsaturated acids, have rendered accessible a number of bromo-acids with the halogen atom in the β- or a more remote position. The utilisation of these for synthetic purposes is being further investigated; but their application to the preparation of adipic, pimelic, β-methylglutaric, and β-methyladipic acids is now described.

Theory of the Addition.—The addition of hydrogen bromide to an olefinic acid may be considered as irreversible under the experimental conditions used. Any spontaneous elimination of hydrogen bromide from the product takes place with the formation of a lactone and not of the parent acid. This type of elimination, which only occurs appreciably in the presence of water, can be neglected for the additions here studied. The addition being irreversible, the proportion of the hydrobromides formed in no way represents an equilibrium, but rather the resultant of two competing reactions. The fact that the product is in most cases homogeneous, or nearly so, merely shows that the velocity (and hence the activation) of one mode of addition is considerably greater than that of its competitor.

The influence both of solvents and of substituents on the direction of the addition, which has been shown experimentally to be of such importance, can be interpreted on the basis of the electrochemical theory of reaction developed by Lapworth, Robinson, and Ingold. Although doubtless other factors are operative to some extent, the agreement of the experimental facts with the demands of this theory is such as to render discussion along other lines unnecessary at the present stage. In its relation to the present work, this theory is based on the recognition by Lapworth of the anionoid reactivity of the double bond (*Nature*, 1925, **115**, 625) and on the distinction drawn by Robinson between the operation of the permanent (inductive) polar effects of groups and those latent polarisations which lead to reaction (J., 1926, 401). It is appropriate to refer more particularly to the work of Lucas, who was the first to connect the directing influence of alkyl groups on the addition of hydrogen halide to olefins with the capacity of these groups for repelling electrons in comparison with hydrogen (*J. Amer. Chem. Soc.*, 1924, **46**, 2475; 1925, **47**, 1459); to that of Ingold and his collaborators (particularly J., 1931, 2354, 2746); and to that of Burkhardt and Cocker (*Rec. trav. chim.*, 1931, **50**, 837).

The carboxyl group of an unsaturated acid dissolved in an inert solvent polarises like an ester (*A*). This effect, provided that some mechanism is available for its transmission, will facilitate polarisation of the double bond in the sense (*B*). This will lead, following

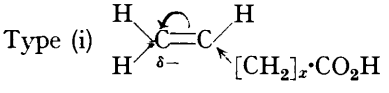


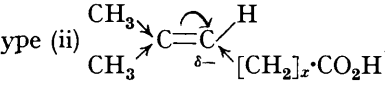
the general theory of addition to olefins, to preferential combination of hydrogen (δ +) to the proximate carbon, and of bromine (δ —) to the distant carbon atom. The effect

of the carboxyl group will be transmitted along the methylene chain only to a considerable extent through one carbon atom (from the evidence, for example, of the dissociation constants; preceding paper), and its main effect must operate through space, probably that immediately surrounding the molecule. No appreciable disturbance will be caused either by the inert solvent or by the equally inert methylene chain of the acid and a considerable effect will reach the double bond, however distant, provided the solution of the acid be sufficiently dilute. The operation of this " direct " or " field " effect has been recognised in the case of undecenoic acid by Robinson (" Outline of Electrochemical Theory of Organic Reactions," Institute of Chem., 1932. Cf. Robinson and Robinson, J., 1926, 2204; Ingold, *4me Conseil de Chimie, Inst. Solvay*, 1931, 493; Ingold and Ramsden, J., 1931, 2746). Robinson further suggests that, if a polar solvent such as water be present, the effect of the carboxyl group is interrupted by the presence of ions, and the same may be presumed to occur in the acid alone and in ethereal solution. Evidence in support of these views is supplied by the results obtained for vinylacetic and allylacetic acids and their esters.

It must, however, be admitted that the exact agreement between the results obtained for additions to the wet acid and those to the acid alone (that is, surrounded by similar molecules) or in ethereal solution is unexpected, in view of the large differences between these solvents in such properties as dielectric constant. It might be suggested that the distinction between the two types of solvent (p. 569) is connected with the capacity of the oxygenated solvents to form oxonium compounds with the hydrogen bromide, which is not possible in the case of the hydrocarbons (cf. McIntosh and his co-workers, J., 1904, **85**, 919; *J. Amer. Chem. Soc.*, 1908, **30**, 1103; *etc.*). Such an explanation, however, fails to account for the fact that unsaturated esters containing the group $CH_2{:}CH{\cdot}$, which will undoubtedly tend to form oxonium compounds (cf. Maass and McIntosh, *J. Amer. Chem. Soc.*, 1912, **34**, 1273, for ethyl acetate), add hydrogen bromide in the absence of solvent in the same direction as the corresponding acids dissolved in toluene. Neither does any explanation based on the association of the acid in oxygenated solvents appear tenable in view of the known association of acetic acid in benzene solution, whence it may be assumed that the unsaturated acids are also associated in toluene solution.

If the field effect of the carboxyl group be eliminated as in additions in water, acetic acid, or ether, or in the absence of solvent, the direction of addition will be determined by the inductive effects of the alkyl groups surrounding the double bond. The operation of these effects can be recognised, for example, in a comparison of the dissociation constants of the unsaturated acids concerned (this vol., p. 562). The two extreme preferred polarisations may be represented as:

Type (i)  , leading to $CH_3{\cdot}CHBr{\cdot}[CH_2]_x{\cdot}CO_2H$

and Type (ii)  , leading to $[CH_3]_2CBr{\cdot}CH_2{\cdot}[CH_2]_x{\cdot}CO_2H$

in complete agreement with the experimental results for both Δ^{β}- and Δ^{γ}-acids [Found for $x = 1$ or 2: Type (i), 100% proximate Br; type (ii), 100% distant Br].

In the more balanced system $CH_3{\cdot}CH{:}CH{\cdot}[CH_2]_x{\cdot}CO_2H$, if x is 1, we may expect that the carboxyl group, exerting its influence along the chain, will weaken the inductive effect of the methylene group on the double bond, so that there will be an advantage for the polarisation $CH_3 \longrightarrow \overset{\frown}{CH{=}CH} \longleftarrow CH_2{\cdot}CO_2H$, leading to the formation mainly of a γ-bromo-acid (Found: 92% γ-bromo-acid). If x is 2 or more, the balance should become more even and the amount of the proximate bromo-acid formed should rapidly rise to about 50%. We have not yet examined any such systems, but it is of interest that Fichter and Langguth (*loc. cit.*), by the addition of aqueous hydrogen bromide to Δ^{γ}-*n*-hexenoic acid ($x = 2$), obtained a bromo-acid which yielded γ-hexolactone on

decomposition with boiling water. No yield of lactone is stated, but it is clear that the γ-bromo-acid must have been formed to a considerable extent.

Experimental.

The unsat. acids were prepared by the methods given in the preceding papers, unless otherwise stated. The addition of HBr was carried out as follows:

HBr (from Br and $C_{10}H_8$) was passed through U-tubes containing $C_{10}H_8$, P_2O_5, and dry glass wool into the acid (about 4 g.) in a U-tube, fitted with ground glass taps and cooled in H_2O (for the expts. with solvents a larger U-tube containing three bulbs was employed which permitted the use of some 25 c.c. of solution. All joints were of ground glass), until weighing showed that an excess of HBr had been absorbed. If no solvent was used, the tube, having been kept closed over-night for completion of the reaction, was transferred to a vac. desiccator containing KOH and left with the taps open until there was no further loss in wt. In the expts. in which a small amount of H_2O was added, the products were treated similarly, but in this case the reaction was generally more rapid. The Et_2O and C_7H_8 used as solvents were dried over Na and redistilled before use. The U-tube containing solutions of acids in these solvents was cooled in ice and a large excess of HBr was absorbed. The tube was left closed over-night and the solvent and excess of HBr were then removed by means of a pump and finally in a vac. desiccator containing KOH.

1. *Butenoic Acids.*

Crotonic acid (I), m. p. 72·5°, was fused at 80° and treated with dry HBr for 2 hr; the oily product was allowed to cool and again saturated with the gas. After 12 hr., removal of the excess of HBr left a const. wt. of a pale yellow liquid, which solidified at − 15° to white plates of β-bromo-*n*-butyric acid, m. p. 17—17·5° (Brulé, *Bull. Soc. chim.*, 1909, **5**, 1019, gives m. p. 17—18°) (Found: *M*, by titration with baryta, 169·2. Calc., 167·1).

γ-Bromobutyric acid, prepared from γ-butyrolactone by Henry's method (*Compt. rend.*, 1886, **102**, 369), crystallised from light petroleum at − 15° in white flattened needles, m. p. 32—33° (lit., 32—33°) (Found: *M*, 166·5).

Analysis of Mixtures of β- and γ-Bromobutyric Acids.—This was the most troublesome of all the analyses of mixed bromo-acids. The method which was successfully applied to other pairs of bromo-acids depends on the fact that their barium salts decompose in boiling aq. solution. Both yield lactones, but the β-lactone from the β-bromo-acid decomposes irreversibly into the β-hydroxy-acid and some olefin, whereas the γ-lactone forms only a trace of hydroxy-acid. β-Bromobutyric acid, however, yielded a small amount of ψ-acidic material under these conditions and analyses of mixtures therefore tended to give results about 5% high in γ-bromo-acid content.

In a modification of the method the bromo-acid (or a known mixture) was neutralised with $Ba(OH)_2$ aq., the solution boiled under reflux for 15 min., an excess of $Ba(OH)_2$ aq. added, and the solution boiled, filtered, and after the addition of an excess of H_2SO_4, boiled for 15 min., to ensure lactonisation of all γ-hydroxy-acid; it was then cooled and exactly neutralised with $Ba(OH)_2$ aq., a known excess of standard $Ba(OH)_2$ aq. added, and, after boiling and cooling, the excess of $Ba(OH)_2$ titrated with H_2SO_4 (cf. Linstead, J., 1932, 121). The γ-lactone corresponding to the γ-bromo-acid in the original material could thus be estimated. The two pure bromo-acids gave the following figures: γ-bromo-acid, 100% γ; β-bromo-acid, 4·7% "γ."

This method was employed for the analysis of the addition products and the results were corrected by comparison with those obtained for the pure bromo-acids. For confirmation, the actual conversion of the bromo-acids into γ-butyrolactone was also carried out.

Addition of Hydrogen Bromide to Vinylacetic Acid (IV).—(i) *Without solvent.* The acid (m. p. − 36°; this vol., p. 560) reacted slowly with HBr and the usual process had to be repeated several times before reaction was complete. The hydrobromide, isolated in two expts. in quant. yield, had *M* 168·6, 167·2 (calc., 167) and, by the analytical method described above, contained 6·9, 6·5% (observed) or 1—2% (corr.) of γ-bromo-acid.

(ii) *With ½% of water.** The products of three expts. had *M* 164·0, 165·0, 164·2 and contained 5·2, 0·9, 2·0 (obs.) = 0% (corr.) of γ-bromo-acid.

The hydrobromides formed in these five expts. were united and neutralised with aq. $Ba(OH)_2$ and the solution was boiled for 15 min. under reflux, neutralised with $NaHCO_3$,

* This small amount of water was used throughout to prevent appreciable lactone formation from the less stable γ-bromo-acids.

and extracted continuously with Et_2O: 7·11 g. of bromo-acid thus gave 0·15 g. of ψ-acidic material, from which scarcely any γ-butyrolactone (0·016 g.) could be obtained by distillation in vac. The amount of γ-bromobutyric acid produced by addition either with or without H_2O was thus less than $\frac{1}{2}$%.

(iii) *In ether* (50% *by vol.*). The bromo-acid formed would not solidify at — 15°. An attempt to convert it into γ-butyrolactone by the method described above showed that it contained only a trace (0·4%) of γ-bromobutyric acid.

(iv) *In toluene.* A preliminary expt. was made with a solution containing 50% of vinylacetic acid by vol. After removal of the solvent, the residue readily solidified in a freezing mixture, leaving a few drops of a purple liquid. This impurity, unlike the two bromo-acids, was insol. in light petroleum (b. p. 40—60°), and the bromo-acid was accordingly extracted with this solvent. On removal of petroleum by means of a pump, the residue formed white crystals, m. p. 32°, after draining on porous tile.

The expt. was repeated with the acid dissolved in toluene (4 vols.), the trace of impurity being separated as before. The product had m. p. 32° and *M* 167·1. It was analysed by the general method described on p. 574 for γ-bromovaleric acid (Found: 99% γ-bromobutyric acid). After treatment with boiling $Ba(OH)_2$ aq. and $NaHCO_3$ aq., extraction with Et_2O as described above yielded 95% of γ-butyrolactone, *M* 86·6 (calc. 86), m. p. (corr.) —48°, mixed m. p. with authentic γ-butyrolactone —48·5° (cf. following paper).

(v) *In glacial acetic acid* (50% *by vol.*). Absorption was rapid. After removal of the AcOH and excess of HBr, the yellow liquid had *M* 168·0 and contained less than 1% of γ-bromo-acid. The m. p. (8°) was rather low, possibly owing to the presence of a trace of lactone. A mixture with authentic β-bromo-acid melted at 12—13°.

(vi) *In petroleum.* A 20% solution of the acid in Na-dried petroleum (b. p. 40—60°) was used. Absorption was rapid and the bromo-acid commenced to separate from the ice-cold solution as an oil. Removal of the solvent after a few hours left a residue, which solidified in a freezing mixture to the pure γ-bromo-acid, m. p. and mixed m. p. 33° (Found: 99·3% γ-bromo-acid; *M*, 167·1). This acid was converted as before into γ-butyrolactone, *M* 86·3, m. p. (corr.) — 48°, mixed m. p. —48·5°. The γ-bromo-acid made in this way is free from the oily impurity obtained by using toluene as solvent.

Addition of Hydrogen Bromide to Ethyl Vinylacetate (V).—The ester, prepared from the silver salt and EtI, had $n_D^{20°}$ 1·4102, $d_4^{20°}$ 0·9192, $[R_L]_D$ 30·74 (calc., 30·98) (cf. Bruylants, *Bull. Soc. chim. Belg.*, 1929, **38**, 133).

The ethyl esters required for reference were prepared from β- and γ-bromobutyric acids by the method used by Wohlgemuth (*Ann. Chim.*, 1914, **2**, 298) for the prepn. of ethyl γ-bromovalerate. Ethyl β-bromobutyrate (Lespieau, *Compt. rend.*, 1904, **139**, 739), obtained in 75% yield, had b. p. 81°/17·5 mm., $n_D^{20°}$ 1·4485, $d_4^{20°}$ 1·3214; whence $[R_L]_D$ 39·75 (calc., 40·31). Ethyl γ-bromobutyrate (Henry, *loc. cit.*) had b. p. 94°/18 mm., $n_D^{20°}$ 1·4569, $d_4^{20°}$ 1·3540; whence $[R_L]_D$ 39·41. Both bromo-esters set to a glass at a low temp.

The addition of HBr to ethyl vinylacetate was carried out exactly as for the acid, no solvent being used. The reaction was fairly fast, only one saturation being required. After removal of the excess of HBr over KOH, the product was distilled and gave an almost theo. yield of bromo-ester, a little high-boiling substance being the only by-product. The addition product was almost pure ethyl γ-bromobutyrate; it had b. p. 96°/18·5 mm., $n_D^{20°}$ 1·4558, $d_4^{20°}$ 1·3577, which agree closely with the corresponding constants of the γ-bromo-ester and differ considerably from those of the β-bromo-ester, and gave an 86% yield of adipic acid, m. p. ("crude") 149°, mixed m. p. 150°, on treatment as in the following method, which was found satisfactory for pure bromo-esters.

Ethyl sodiomalonate, prepared in suspension in C_6H_6 (dried over Na) from Na (pressed into thin sheets under light petroleum) and 10% excess of ethyl malonate (cf. Gabriel and Colman, *Ber.*, 1909, **42**, 1244), was boiled under reflux ($CaCl_2$ guard-tube) with the bromo-ester (exactly equiv. to the Na used) for 24 hr. The C_6H_6 was removed *completely* from the neutral product by means of a pump, and the ester, isolated by extraction with Et_2O, was boiled under air reflux for 20 hr. with conc. HCl (2 vols.), the HCl then removed, and the decarboxylation completed by heating the residue at 150—170°; the acid was finally dried in a desiccator and weighed. Ethyl β-chloropropionate thus gave 85% of glutaric acid; ethyl β-bromobutyrate gave 85% of β-methylglutaric acid, m. p. (crude) 75—77°, 86° after crystn. from C_6H_6–light petroleum, mixed m. p. 85—86°; and ethyl γ-bromobutyrate gave 72% of adipic acid, m. p. ("crude") 149·5°, mixed m. p. 150°.

2. n-*Pentenoic Acids.*

Δ^{α}-*n*-Pentenoic acid (II) was prepared by the method of v. Auwers (*Annalen*, **1923**, **432**, 46), modified as described by Boxer and Linstead (J., **1931**, 747) for the prepn. of the higher homologue, and was purified by fractional melting of the solidified acid. It had b. p. 106°/20 mm., m. p. 9·5°, $n_D^{20°}$ 1·4513, $d_{4°}^{20°}$ 0·9903 (cf. v. Auwers, *loc. cit.*). A small excess of HBr was led into the acid, which then rapidly solidified with evolution of the uncombined gas. The product crystallised from light petroleum in long white needles of pure β-bromovaleric acid, m. p. 58·5—59° (Found : Br, 44·3; *M*, 180·8. Calc. : Br, 44·2%; *M*, 180·9); * yield, theo. This method of prepn. is more convenient than that used by Fittig and Spenzer (*Annalen*, **1894**, **283**, 73) and Fittig and McKenzie (*ibid.*, p. 82).

A cold aq. solution of the acid yields no HBr during 16 hr., but addition of aq. $AgNO_3$ at any time gives a ppt. of AgBr in 4 sec. After boiling, the aq. solution gives an immediate ppt. with $AgNO_3$.

γ-Bromo-*n*-valeric acid was prepared from γ-valerolactone by Wohlgemuth's method (*loc. cit.*), and was purified by freezing a conc. solution in light petroleum, filtering the solid acid at a low temp., and drying it in a vacuum desiccator in a cold room. Yield, 77% ; burr-like needles, m. p. 22·5° (lit. 21°); *M*, 182·4. The reversal of this reaction is described below.

Estimation of Mixtures of β- *and* γ-*Bromo*-n-*valeric Acids.*—The principle of the method has been indicated on p. 572.

β-Bromovaleric acid (3 g.) was boiled under reflux with H_2O until there was no more smell of olefin ; the solution was neutralised with $NaHCO_3$ and extracted continuously with Et_2O for 24 hr. The extract gave a trace (0·4%) of the original acid and no lactone. Similarly treated, the γ-bromo-acid gave a 75% yield of γ-valerolactone, b. p. 88°/14 mm., m. p. — 35°; *M*, by back titration, 101·1 (calc., 100·1). For quant. purposes, a known wt. of the acid (*ca.* 0·2 g.) was dissolved in 100 vols. of neutral 50% H_2O–EtOH, exactly neutralised with $Ba(OH)_2$ aq., and boiled under reflux for not less than 80 min. The liquid was cooled and titrated with $Ba(OH)_2$ to neutralise the trace of acid present. The lactone was then determined by boiling the solution with a known excess of $Ba(OH)_2$ and titrating the excess. The following results were obtained :

% γ-Bromo-acid (true)	100	46·5	93·5
,, ,, (found)	101	46·8	92·8

Addition of Hydrogen Bromide to Δ^{β}-n-*Pentenoic Acid* (VI).—The acid (this vol., p. 560) had m. p. 1·5°. The addition of HBr was carried out as before, and the product analysed by the method given above :

	Equiv. (calc. 180·9).	% Br (calc. 44·2).	% γ-Bromo-acid.		Equiv. (calc. 180·9).	% Br (calc. 44·2).	% γ-Bromo-acid.
Dry acid	182·4	43·6	92·8	Acid + ½% water	185·7	—	93·2
,,	183·8	—	91·8	,, ,,	185·6	43·5	92·4
,,	187 (?)	—	91·4	,, ,,	185·0	—	92·5

It will be seen that there is a slight lactonisation of the product, giving a high equiv. and low % Br. The main product of the addition was confirmed to be γ-bromovaleric acid by its conversion into γ-valerolactone by the method already described. The product from the " wet " hydrobromination gave a lactone, b. p. 92—93°/18 mm., m. p. — 35·5°, *M* 100·4; that from the " dry " hydrobromination was similar.

Addition of Hydrogen Bromide to Δ^{γ}-n-*Pentenoic* (*Allylacetic*) *Acid* (VIII).—A solution of δ-valerolactone (this vol., p. 583) in rather less than half its wt. of H_2O was saturated with HBr at 0°, kept for 24 hr., heated at 100° for 30 min., cooled, and saturated with HBr; the process was repeated and from the product, diluted with H_2O, Et_2O extracted δ-bromovaleric acid (90% yield), m. p. 40°, after recrystn. from light petroleum [Found : Br (Carius), 44·6. Calc., 44·2%]. Cloves (*Annalen*, **1901**, **319**, 367) gives m. p. 39—40°. The acid may be kept for 6 months without change.

Δ^{γ}-*n*-Pentenoic acid, m. p. — 22·5° (this vol., p. 582), was treated with HBr in various

* The determination of the equiv. by titration with *N*/10-$Ba(OH)_2$ was done rapidly, as the end-point faded owing to the liberation of HBr from the barium salt. The determination of Br in this and similar acids was readily carried out by boiling the acid with a slight excess of halogen-free NaOH aq. for 15 min., acidifying the solution with conc. HNO_3, and estimating the halogen as AgBr.

solvents by the methods already described. The products were removed from the U-tubes and cooled to 0°.

(i) *In the absence of solvent.* The product readily solidified and after being dried on a porous tile had m. p. 19—21°, alone or mixed with γ-bromovaleric acid.

(ii) *With ½% water.* The product had m. p., and mixed m. p. with γ-bromovaleric acid, 18—20°.

To remove traces of lactone, the above products were recrystallised from light petroleum and then yielded the pure γ-bromo-acid, m. p. 22°.

(iii) *In ether* (50% *by vol.*). Addition was somewhat slower than to the pure acid. A trace of ester was formed, probably from EtOH produced by the action of HBr on the solvent. The products of two expts. had m. p. 22°, 20°, not depressed by admixture with the γ-bromo-acid.

(iv) *In toluene* (50% *by vol.*). Addition was rapid. The solvent was removed immediately after complete absorption of the HBr; the residue, which solidified completely in ice, had m. p. 40°, unchanged by admixture with δ-bromovaleric acid. A similar product, m. p. 40°, was obtained when the mixture was kept over-night. This is undoubtedly the readiest way of preparing δ-bromovaleric acid.

Addition of Hydrogen Bromide to Ethyl Δ$^{\gamma}$-n-*Pentenoate* (IX).—The unsaturated ester, prepared *via* the silver salt, had b. p. 144—144·5°, $d_4^{20°}$ 0·9014, $n_D^{20°}$ 1·4142, whence $[R_L]_D$ 35·53 (calc., 35·71). Ethyl γ-bromo-*n*-valerate (Wohlgemuth, *loc. cit.*) had b. p. 105—107°/20 mm., $d_4^{20°}$ 1·2814, $n_D^{20°}$ 1·4533, $[R_L]_D$ 44·12 (calc., 43·83). Ethyl δ-bromo-*n*-valerate, similarly prepared from the solid δ-bromo-acid, had b. p. 105—107°/15 mm., $d_4^{20°}$ 1·2804, $n_D^{20°}$ 1·4543, $[R_L]_D$ 44·23. These bromo-esters do not exhibit differences in physical properties comparable with those between ethyl β- and γ-bromobutyrates.

The addition of HBr to the unsaturated ester, which was effected without the use of solvent and was comparatively slow, yielded 70% of a product, b. p. 104—110°/15 mm., $d_4^{20°}$ 1·2801, $n_D^{20°}$ 1·4547, resembling the δ-bromo-ester. To prove the orientation, the method of malonation and hydrolysis described on p. 573 was employed. By this method, ethyl γ-bromo-*n*-valerate gave an 80% yield of β-methyladipic acid, m. p. (crude) 92°, 95° after crystn. from C_6H_6 and a little light petroleum, not depressed by admixture with authentic β-methyladipic acid. Ethyl δ-bromo-*n*-valerate similarly gave 71% of pimelic acid, m. p. (crude) 96—99°, 104° after crystn. from C_6H_6, 105° admixed with an authentic specimen.

The hydrobromide of ethyl Δ$^{\gamma}$-pentenoate gave a 75% yield of a product, m. p. 97—99°, 105° after crystn. from C_6H_6, not depressed by admixture with authentic pimelic acid.

3. iso*Hexenoic Acids.*

Δ$^{\alpha}$-*iso*Hexenoic acid (III) (Goldberg and Linstead, J., 1928, 2343), b. p. 105°/11 mm., m. p. — 32°, *M* 114·2 (calc., 114·1), when treated with HBr in the absence of a solvent, yielded β-bromo*iso*hexoic acid as a pale yellow liquid, which formed a glass at — 78° (cf. Braun, *Monatsh.*, 1896, **17**, 218) (Found: Br, 41·0; *M*, 195·1. Calc.: Br, 40·9%; *M*, 194·9). The acid is sparingly sol. in H_2O, and the solution develops no free HBr. When the acid was boiled with H_2O, the usual decompositions observed by Fittig for β-bromo-acids occurred, but a little ψ-acidic material, probably β-lactone, also appeared. This was also obtained when a neutral aq. solution of the sodium salt was boiled for 30 min. The solution produced was extracted with ether; the small amount of liquid isolated from the extract was treated with aq. $NaHCO_3$, and from this solution Et_2O extracted practically nothing, the absence of a stable ψ-acid such as the γ-lactone thus being proved.

γ-Bromo*iso*hexoic acid was prepared as follows: *iso*Hexolactone, prepared by boiling Δ$^{\beta}$-*iso*hexenoic acid for 5 hr. (Linstead, *loc. cit.*), was freed from traces of acid over K_2CO_3 and redistilled; b. p. 94°/20 mm., m. p. 8·5°, *M* 114·1. Dry HBr was passed into the lactone at 100° for 30 min., and the liquid allowed to cool in the stream of the gas and kept in a closed vessel over-night. The mixture was freed from a trace of brown oil by extraction with light petroleum, and the solvent removed. The residue slowly solidified at — 15° to the characteristic burr-like masses of a γ-bromo-acid; m. p. — 4° (Found: Br, 35·1. Calc., 40·9%). It is doubtful whether this bromo-acid can be obtained pure from the very stable lactone, into which there is a great tendency for it to revert.

Addition of Hydrogen Bromide to Δ$^{\beta}$-iso*Hexenoic* (*Pyroterebic*) *Acid* (VII).—The Δ$^{\beta}$-acid was prepared in 50% yield from the Δ$^{\alpha}$-isomeride (Linstead, *loc. cit.*) and had b. p. 84/4° mm., m. p. — 2°, $n_D^{20°}$ 1·4455, $d_4^{20°}$ 0·9758, *M* 114·2. The physical properties were determined immediately after the final distillation of the freshly prepared acid and are slightly different

from, and probably more correct than, those previously reported (m. p. — 4·5°, $n_D^{20°}$ 1·4465, $d_4^{20°}$ 0·978). The iodine addition was 93·5% in 5 min. at 20°.

The acid reacted with dry HBr with the greatest ease, and on removal of the excess of gas and cooling, the product formed needles, m. p. 10°. This is much purer γ-bromo*iso*hexoic acid than that prepared from the lactone (above) (Found : Br, 41·55. Calc., 40·9%). A mixture of the two prepns. melted at about 4°.

The position of the Br atom was determined by the method used for the hydrobromide of Δ^{β}-*n*-pentenoic acid. The products of two additions, using dry HBr, gave 100·0 and 100·2% of γ-bromo-acid. To check the method, a synthetic mixture containing 94·6% of the γ-bromo-acid (m. p. 10°) and 5·4% of the β-bromo-acid was analysed; 94·2% of γ-bromo-acid was found.

The products of two additions of HBr in the presence of ½% H_2O contained 100·2 and 99·3% of γ-bromo-acid.

The composition of the hydrobromides prepared by these processes was confirmed as follows : the addition products were neutralised with NaOH aq., and the solutions boiled for 5 min. under reflux, acidified with H_2SO_4, and again boiled for 5 min. to lactonise all γ-hydroxy-acid. The solutions were cooled, saturated with $NaHCO_3$, and extracted with Et_2O. The γ-lactone, thus extracted, was distilled and its m. p., alone and mixed with γ-*iso*hexolactone, determined. The properties of the lactonic products are tabulated below.

	Yield, %.	B. p.	M. p.	Mixed m. p.	Equiv.
From " dry " hydrobromide	92	93°/19 mm.	8·4°	8·2°	113·9
From " wet " hydrobromide	87	97/22 mm.	8·5	8·2	113·8
Pure γ-*iso*hexolactone	—	94/20 mm.	8·5	—	114·1

It is thus established that (i) Δ^{β}-*iso*hexenoic acid adds HBr to give entirely the γ-bromo-acid, and (ii) this bromo-acid is decomposed by alkali to yield pure γ-*iso*hexolactone. The bromo-acid is very unstable in H_2O, being completely dissolved in 1 min., and gives an immediate ppt. with $AgNO_3$.

4. Δ^{γ}-iso*Heptenoic Acid* (X).

The acid was prepared from isoprene and purified as described on p. 584. It had m. p. — 33° and the other properties there stated.

γ-Bromo-δ-methylhexoic acid, prepared by passing HBr into moist γ-*iso*propyl-γ-butyrolactone (this vol., p. 584) for 1 hr. and cooling the product in a freezing mixture, formed (theo. yield) flattened needles, m. p. 41°, after draining on porous earthenware and recrystn. from light petroleum (Found : Br, 38·0. $C_7H_{13}O_2Br$ requires Br, 38·2%). Fittig and Zanner (*Annalen*, **1889, 255, 93**) describe the prepn. of the hydrobromide of Δ^{β}-*iso*heptenoic acid, which was considered to be this γ-bromo-acid. Their prepn. was, however, an oil, and probably contained some β-bromo-acid.

δ-Bromo-δ-methylhexoic acid was similarly prepared by passing HBr into 2 g. of δ-*iso*heptolactone (this vol., p. 585) diluted with 1 c.c. of H_2O. After 30 min. the product became solid; it then crystallised from light petroleum in large flattened needles (3·1 g.), m. p. 45° (Found : Br, 37·9. $C_7H_{13}O_2Br$ requires Br, 38·2%). The addition of a small quantity of the γ-bromo-acid depressed the m. p.

When HBr was passed into the dry unsaturated acid (X) there was considerable evolution of heat and absorption was complete in 30 min. On being cooled and scratched, the product solidified. It melted at 45°, alone or mixed with pure δ-bromo-δ-methylhexoic acid. In a similar expt. in the presence of ½% H_2O there was an even greater evolution of heat but absorption of the gas appeared to be complete only in 45 min. The product melted at 45°, alone or mixed with the pure δ-bromo-acid.

Addition of HBr had thus occurred to give solely the δ-bromo-isomeride.

The authors are much indebted to Professor R. Robinson, F.R.S., for his helpful suggestions and to the Chemical Society and the Royal Society for grants.

IMPERIAL COLLEGE, LONDON, S.W. 7. [*Received, February 9th*, 1933.]