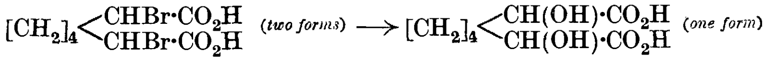
CXCII.—*The Conditions underlying the Formation of Unsaturated and Cyclic Compounds from Halogenated Open-chain Derivatives. Part IX. Products derived from Suberic and Azelaic Acids.*

By Frank Robert Goss and Christopher Kelk Ingold.

According to the hypothesis underlying this series of investigations, the action of concentrated methyl-alcoholic alkali on ethyl αα′-dibromosuberate should pursue a course similar to that observed in the pimelic acid series.

The bromination of suberic acid has been investigated by Gauthier, Hell, and Rempel (*Ber.*, 1882, **15**, 149; 1885, **18**, 814), who isolated a dibromo-acid of m. p. 173°. αα′-Dibromosuberic acid (I) should exist in meso- and racemic modifications, and a second form, m. p. 118—120°, has now been isolated. Both forms are produced together in the ordinary Hell-Volhard process of bromination, the less fusible acid in the greater quantity.

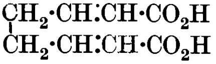
It appears impossible at present to assign configurations to these two acids, because, on treatment with dilute alkalis, both yield the same αα′-dihydroxysuberic acid (II), so that in one case or the other an inversion must occur at one of the two asymmetric carbon atoms.



$$[CH_2]_4<\begin{matrix}CHBr\cdot CO_2H\\ CHBr\cdot CO_2H\end{matrix}\ \textit{(two forms)} \longrightarrow [CH_2]_4<\begin{matrix}CH(OH)\cdot CO_2H\\ CH(OH)\cdot CO_2H\end{matrix}\ \textit{(one form)}$$

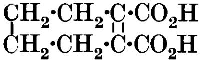
(I.) (II.)

By the action of alcoholic alkali on the less fusible dibromo-acid, Hell and Rempel (*loc. cit.*) obtained an acid, $C_8H_{10}O_4$, which they termed "suberocolic acid," but they were unable to ascertain whether it was a doubly unsaturated open-chain acid (III) or a *cyclo*hexene acid such as (IV). It has now been found that the acid has an open-chain structure, for, on partial reduction, it forms a dihydro-derivative which is still unsaturated, and on vigorous reduction gives suberic acid.

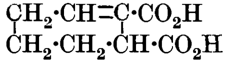


$$\begin{array}{l} CH_2{\cdot}CH{:}CH{\cdot}CO_2H \\ | \\ CH_2{\cdot}CH{:}CH{\cdot}CO_2H \end{array}$$

(III.)



(IV.)



(V.)

The acids (IV) and (V) are, however, produced along with (III) when ethyl dibromosuberate is treated with concentrated alkalis under the conditions described in the experimental part of this paper. It is probable that (IV) is the first product, although it changes into (V) to a large extent under the conditions employed in its formation.

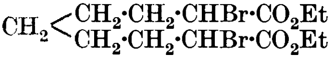
The cyclic acids had previously been prepared by the reduction of benzene derivatives, and Baeyer observed the conversion of (IV) into (V) by the action of alkalis (*Annalen*, 1890, **258**, 209). He appears, however, to have regarded the change as complete, whereas, actually, the action is a balanced one, the acid (V) undergoing limited conversion into (IV) under identical experimental conditions.

When methyl-alcoholic alkali is used, considerable quantities of the meso- and racemic forms of the dimethoxy-acid

$$CO_2H{\cdot}CH(OMe){\cdot}[CH_2]_4{\cdot}CH(OMe){\cdot}CO_2H \quad (VI.)$$

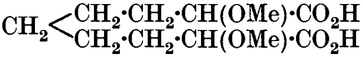
are produced in agreement with the prediction made in the preceding paper.

The general rules deduced in the preceding parts of this series suggest that the principal product of the action of concentrated methyl-alcoholic alkali on ethyl $\alpha\alpha'$-dibromoazelate (VII) should be the dimethoxy-acid (VIII) (in which the methoxyl groups occupy 1 : 9-positions) and that the by-products, if any, should consist of the dihydroxy-acid (IX) and the unsaturated acid (X). Further, it is not to be expected that *cyclo*heptane ring closure would take place to any considerable extent, although some might occur, as in the *cyclo*butane series (Part II); an acid of constitution (XI) (if formed) might pass into its open-chain ketonic isomeride (XII).



$$CH_2{<}\begin{array}{l} CH_2{\cdot}CH_2{\cdot}CHBr{\cdot}CO_2Et \\ CH_2{\cdot}CH_2{\cdot}CHBr{\cdot}CO_2Et \end{array}$$

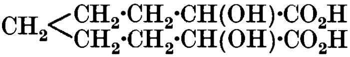
(VII.)



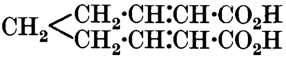
$$CH_2{<}\begin{array}{l} CH_2{\cdot}CH_2{\cdot}CH(OMe){\cdot}CO_2H \\ CH_2{\cdot}CH_2{\cdot}CH(OMe){\cdot}CO_2H \end{array}$$

(VIII.)

(IX.)

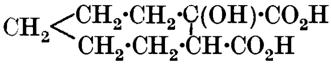


$$CH_2{<}\begin{array}{l} CH_2{\cdot}CH_2{\cdot}CH(OH){\cdot}CO_2H \\ CH_2{\cdot}CH_2{\cdot}CH(OH){\cdot}CO_2H \end{array}$$

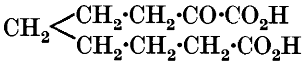


$$CH_2{<}\begin{array}{l} CH_2{\cdot}CH{:}CH{\cdot}CO_2H \\ CH_2{\cdot}CH{:}CH{\cdot}CO_2H \end{array}$$

(X.)



(XI.)



$$CH_2{<}\begin{array}{l} CH_2{\cdot}CH_2{\cdot}CO{\cdot}CO_2H \\ CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H \end{array}$$

(XII.)

The experiments now described show that under the conditions of hydrolysis which have been uniformly employed during these investigations the dibromo-ester (VII) is converted to the extent of at least 80% into a mixture of meso- and racemic methoxy-acids of formula (VIII) in striking agreement with the conclusions summarised in the preceding paper. Considerable difficulty was experienced in isolating the by-products of the reaction, but the dihydroxy-acid (IX) was obtained as a mixture of meso- and racemic isomerides, and an unsaturated acid, which may have been (X), was present. The production of the ring-acid (XI) could not be established with certainty, but an acid which appears to have the open-chain ketonic structure (XII) was isolated.

EXPERIMENTAL.

Suberic acid was prepared from castor oil, as described by Baker and Ingold (J., 1923, **123**, 128).

αα′-Dibromosuberic Acid (A-form).—Suberic acid (60 g.) was warmed with 60 c.c. of thionyl chloride until sulphur dioxide ceased to be evolved, and the product treated on the steam-bath with 45 c.c. of bromine, added gradually to keep pace with the absorption. The product was poured into absolute formic acid and boiled until carbon monoxide ceased to be evolved; on cooling, 60 g. of the dibromo-acid, m. p. 160—170°, separated. After two crystallisations from water, this acid melted at 172—173° (Found: Br, 48·3. Calc.: Br, 48·2%).

αα′-Dibromosuberic Acid (B-form).—The formic acid mother-liquors were evaporated, and the pasty residue was drained on porous porcelain, and extracted with boiling chloroform until the m. p. of the undissolved portion rose above 160°. (This, after crystallisation from water, yielded a further 6 g. of the A-acid.) The residue from the chloroform solution was drained and crystallised several times from the same solvent; 20 g. of B-acid, m. p. 120—121°, were thus obtained (Found: Br, 48·0. $C_8H_{12}O_4Br_2$ requires Br, 48·2%).

Ethyl αα′-Dibromosuberate.—Suberic acid (60 g.) was brominated as before, and the product poured into ethyl alcohol. The ester was extracted with ether after the addition of water, washed with dilute sodium carbonate solution, and distilled. It boiled constantly at 230°/31 mm., the yield being almost theoretical (Found: Br, 41·0. $C_{12}H_{20}O_4Br_2$ requires Br, 41·2%).

αα′-Dihydroxysuberic Acid.—This substance is formed when either the A- or the B-form of αα′-dibromosuberic acid is boiled with 2*N*-aqueous sodium carbonate. The product, which is extracted with ether after acidification, is purified through the barium salt, and thus obtained as a colourless gum which sets to a hard, crystalline mass, m. p. 166—168°, during the course of several months (Found : C, 46·8; H, 6·8. $C_8H_{14}O_6$ requires C, 46·6; H, 6·8%).

Suberocolic Acid.—Ethyl αα′-dibromosuberate was treated with 6*N*-methyl-alcoholic potassium hydroxide under conditions comparable with those used in the previous investigations of this series. The cooled product was mixed with an equal volume of absolute ethyl alcohol, and the insoluble salts were collected, washed with ethyl alcohol, drained, dissolved in the minimal amount of water, and decomposed with concentrated hydrochloric acid. The sparingly soluble acid thus obtained was crystallised from boiling water (100 parts), from which it separated in branched needles, m. p. 253° (decomp.)—a considerably higher m. p. than that recorded by Hell and Rempel (Found : C, 56·5; H, 5·9. Calc. : C, 56·5; H, 5·9%). The yield was 11% of the theoretical.

Oxidation of Suberocolic Acid.—On oxidation with alkaline permanganate, suberocolic acid gives (as it should) succinic and oxalic acids, but not in the expected yields. In one experiment, 0·8 g., on treatment with 140 c.c. of 3% permanganate (7 atoms of available oxygen), gave 0·5 g. of calcium oxalate (theory, 1·2 g.) and 0·3 g. of succinic acid (theory, 0·55 g.).

Reduction of Suberocolic Acid.—The acid (0·5 g.) was reduced with 30 g. of 4% sodium amalgam on the steam-bath during 3 hours. After the mercury had been removed, the solution was acidified and extracted with much ether.

Dihydrosuberocolic Acid (*A-form*).—The residue from the ether, after draining on porous porcelain, melted at 125—160°. After twice crystallising from water, small rosettes of needles were obtained, m. p. 170° (Found : C, 55·6; H, 7·0. $C_8H_{12}O_4$ requires C, 55·8; H, 7·0%). The acid instantly decolorises cold alkaline permanganate, and on vigorous reduction (see below) yields suberic acid.

Dihydrosuberocolic Acid (*B-form*).—This acid is formed along with suberic acid when suberocolic acid is reduced by boiling an aqueous solution with 50 g. of 4% sodium amalgam, added gradually during 4 hours. It separates from water in needles, m. p. 125° (Found : C, 55·7; H, 7·0%). The acid instantly decolorises cold alkaline permanganate, and on prolonged boiling with water and sodium amalgam yields suberic acid.

Suberic acid was separated from the B-form of dihydrosuberocolic acid by fractional crystallisation from hot water, and was identified by analysis (Found : C, 55·1; H, 8·0. Calc. : C, 55·2; H, 8·0%) and by comparison with a genuine specimen.

Δ^1-cyclo*Hexene*-1 : 2-*dicarboxylic Acid.*—The aqueous filtrate from the suberocolic acid was extracted with ether, the residue obtained on evaporating the ether was rubbed with water, and the filtered solution evaporated in a vacuum. The residue obtained on evaporating the alcoholic solution with water was extracted with ether after acidification, and the residue from the concentrated and filtered ethereal solution was fractionally crystallised from ether. The combined residues were evaporated with water on the water-bath, and the crystals obtained after partial esterification of the residue were crystallised from water and identified by their properties, by analysis (Found: C, 56·3; H, 6·0. Calc.: C, 56·5; H, 5·9%), and by the m. p. of the anhydride (74°) prepared from them.

Δ^2-cyclo*Hexene*-1 : 2-*dicarboxylic Acid.*—The acids separated by means of water contained this *cyclo*hexene acid and suberocolic acid, which were separated by fractional crystallisation from water. The combined residues from the other ethereal and aqueous solutions were boiled with acetyl chloride for a short time, and the residue obtained by vacuum desiccation over potassium hydroxide was dissolved in ether and washed with sodium carbonate solution. The residue from the ether was dissolved in boiling water, from which the *cyclo*hexene acid (4·7%) was obtained in a pure condition by evaporation and three crystallisations from water. It was identified by its properties, by analysis (Found: C, 56·4; H, 6·0. Calc.: C, 56·5; H, 5·9%), and by conversion into the anhydride of the Δ^1-acid, as described by Baeyer (*loc. cit.*).

αα'-Dimethoxysuberic Acid (*A-form*).—The sodium carbonate washings, on acidification and extraction with ether, yielded a mixture of acids which was separated into two fractions by boiling with ether. The sparingly soluble portion crystallised from a small amount of water in leaflets or rosettes of small needles (yield 20·4%), m. p. 145—146° (Found: C, 51·0; H, 7·6. $C_{10}H_{18}O_6$ requires C, 51·3; H, 7·7%).

αα'-Dimethoxysuberic Acid (*B-form*).—On subjecting the more soluble fraction to repeated fractional crystallisation, from ether and water alternately, a further quantity of A-acid was obtained, whilst the B-acid became concentrated in the mother-liquors, partly on account of its greater solubility, and partly because of its much slower speed of crystallisation. It was finally obtained (2·8%) as rosettes of needles, m. p. 117—118° (Found: C, 51·7; H, 7·6%).

Azelaic acid was prepared by the oxidation of ricinoleic acid, as described by Baker and Ingold (J., 1923, **123**, 128), and dibrominated in the form of its acid chloride. The dibromo-ester prepared from the dibromo-chloride was hydrolysed with 6*N*-methyl-alcoholic potassium hydroxide, as described in the earlier investigations of this series. The acid product, a yellow syrup, was treated in various ways in the hope of inducing crystallisation, but without success, and it was therefore esterified with ethyl alcohol, and the ester carefully fractionated under reduced pressure, through a short column. After four distillations, the following fractions were obtained :

	(i).	(ii).	(iii).	(iv).	(v).	Residue.
B. p./30 mm. ...	198—205°	205—218°	218—221°	221—240°	240—260°	260°
Wt. (g.) ...	5·2	7·9	125·3	6·9	4·4	6·0
G./degree	0·7	0·6	41·8	0·4	0·2	—

αα′-*Dimethoxyazelaic Acid* (II).—The main fraction (iii), b. p. 218°/30 mm., on redistillation boiled mainly at 218—219°/30 mm. (Found : C, 58·9; H, 9·3. *Ethyl dimethoxyazelate*, $C_{15}H_{28}O_6$, requires C, 59·2 ; H, 9·2%). Both the main fraction and the central fraction gave on hydrolysis by hydrochloric acid a liquid mixture of the *meso*- and racemic forms of *αα′-dimethoxyazelaic acid* (Found : C, 52·8 ; H, 8·4. $C_{11}H_{20}O_6$ requires C, 53·2 ; H, 8·0%), which, even after purification through the *silver* salt (Found : Ag, 46·5. $C_{11}H_{18}O_6Ag_2$ requires Ag, 46·8%), could not be induced to solidify, and was therefore digested with thionyl chloride until sulphur dioxide ceased to be evolved. After the excess of thionyl chloride had been removed in a vacuum at 100°, the acid chloride was dissolved in ether and treated with dry ammonia; a crystalline precipitate, which, however, was a mixture of isomerides, was then obtained. Repeated crystallisation from water yielded one of the individuals in a pure condition as small plates, m. p. 164—165° (Found : C, 54·0 ; H, 8·6. $C_{11}H_{22}O_4N_2$ requires C, 53·7 ; H, 8·8%). The same *αα′-dimethoxyazelamide* was obtained by digesting the ester with aqueous ammonia (*d* 0·880) for a month. Stellate clusters of crystals were formed which, after two crystallisations from water and one from ethyl acetate, gave small plates identical with the above. The more soluble isomeride could not be isolated in a pure condition. Crystals of the correct composition, having m. p. 143—146°, were obtained, but as in the course of numerous crystallisations small amounts of the amide, m. p. 164—165°, were obtained from them, they were concluded to be a difficultly separable mixture.

αα′-Dihydroxyazelaic Acid (III).—Fractions (iv) and (v) obtained in the above preparation were combined with corresponding fractions in three similar experiments and fractionally distilled four times. *Ethyl αα′-dihydroxyazelate*, b. p. 235—240°/16 mm., was thus obtained (3·7 g.) (Found : C, 56·9; H, 8·9. $C_{13}H_{24}O_6$ requires C, 56·5; H, 8·7%). The *acid* obtained from it by hydrolysis with hydrochloric acid was a clear syrup which did not solidify, and from which no crystalline amide could be prepared (Found : C, 49·4; H, 7·7.

$C_9H_{16}O_6$ requires C, 49·1; H, 7·3%. Found for the *silver* salt: Ag, 49·7. $C_9H_{14}O_6Ag_2$ requires Ag, 50·2%).

α-*Ketoazelaic Acid* (VI).—Fractions (i) and (ii) obtained in the preceding preparations gave on hydrolysis with mineral acids a syrupy acid which instantly decolorised cold alkaline permanganate, but the only crystalline products which could be obtained from it had not this property. Fractional distillation of the esters yielded no fraction of constant boiling point, and treatment with ammonia gave an impure mixture of amides from which only the dimethoxyamide described above could be isolated. By hydrolysis of a fraction, b. p. 198—205°/23 mm., however, an acid was obtained which partly solidified after several months. On crystallisation from ether, rosettes of needles, m. p. 175°, were obtained (Found by microanalysis: C, 53·5, 53·7; H, 7·1, 7·1. $C_9H_{14}O_5$ requires C, 53·4; H, 7·0%). The amount obtained (0·05 g.) was insufficient for a detailed examination, but since the substance resembled α-ketoglutaric acid in giving a dull reddish-brown colour with ferric chloride, it is believed to be α-ketoazelaic acid, and not the isomeric hydroxy*cyclo*heptane acid.

We desire to record our thanks to the Royal Society for a grant with the aid of which some of the expense of this investigation has been defrayed.

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