424. *Muconic and Hydromuconic Acids. Part VI.* cis- *and* trans-Δ^{α}-*Dihydromuconic Acids.*

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In the course of an earlier investigation in this series (Farmer, J., 1923, **123**, 2531) several attempts were made to produce a homogeneous Δ^{α}-dihydromuconic acid from its Δ^{β}-isomeride by heating the latter with aqueous caustic soda as prescribed by Rupe (*Annalen*, 1890, **256**, 13). Rupe records that he obtained under specified conditions, and presumably as the sole product, a Δ^{α}-acid, m. p. 168—169°, from the corresponding Δ^{β}-acid, m. p. 195°. All repetitions of his work at that time, however, led to the production of obvious mixtures of acids of indefinite melting point, which clearly contained much of the original acid; moreover, all attempts to isolate a pure Δ^{α}-acid by fractional crystallisation of the mixtures failed. Ingold (J., 1921, **119**, 965), however, states that he obtained the Δ^{α}-acid by the interaction of α-bromoadipic ester with 6*N*-methyl-alcoholic potash and assigns to it the melting point observed by Rupe (169°); and Ingold and Shah (J., 1933, 885) prepared the Δ^{α}-acid by Rupe's method and, believing their product to be a homogeneous compound, utilised it for observations relating to the mode of catalytic reduction of ethyl muconate.

Both the *trans*- and the *cis*-form of the Δ^{α}-acid have become of interest owing to their evident production during the step-wise hydrogenation of *trans-trans*- and *cis-cis*-muconic acids respectively (preceding paper). Now there was every reason to believe that the mixtures of acids obtainable under Rupe's conditions, or under certain modifications of these, were essentially equilibrium mixtures of the Δ^{α}- and Δ^{β}-acids in which the Δ^{β}-form probably preponderated. This view has proved to be correct, for as the result of our recent observation that Δ^{α}- and Δ^{β}-dihydromuconic acids behave differently when a mixture of the two is submitted to esterification with methyl-alcoholic hydrogen chloride (the former yielding an extremely tractable solid half-ester, $MeO_2C{\cdot}CH_2{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CO_2H$, of m. p. 60°, and the latter the neutral ester, $MeO_2C{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CO_2Me$, of b. p. 125°/14 mm. and m. p. 16° : compare Farmer, *loc. cit.*, p. 2541; Farmer and Duffin, J., 1927, 405), it has become an easy matter to isolate simple ester derivatives of the pure Δ^{α}- and Δ^{β}-acids from Rupe's preparation. These derivatives are obtainable (respectively) in roughly the proportion 1 : 3. By careful hydrolysis of the Δ^{α}-half-ester with acid or alkali the corresponding Δ^{α}-acid is obtainable, and it is to be observed that, although this acid melts at 191°, *i.e.*, within a few degrees of its Δ^{β}-isomeride (m. p. 195°), there is a very large depression of melting point (24°) when the acids are mixed; furthermore, the crystalline habit of the Δ^{α}-acid is very different from that of its isomeride, and the neutral methyl ester of the Δ^{α}-acid, unlike that of its Δ^{β}-isomeride, does not solidify in ice–salt. Both the compound now designated as the pure Δ^{α}-acid and its solid half-ester are converted almost quantitatively into succinic and oxalic acids when oxidised with permanganate, and since the same (mono-olefinic) solid half-ester had already been observed by us to be formed when sodium *trans-trans*-muconate is semi-hydrogenated catalytically and the product partially esterified, there can be no doubt that both compounds possess the *trans*-configuration.

The *trans*-Δ^{α}-half-ester yielded with bromine a viscous liquid dibromide, and this on hydrolysis with hydrobromic acid gave a mainly solid product from which only one dibromo-acid (m. p. 171—173°) was isolated. This was converted, on debromination with zinc, into the same Δ^{α}-acid as was obtained by direct hydrolysis of the half-ester. No further attempts to obtain the corresponding *cis*-Δ^{α}-acid by debromination of one or other of the two theoretically possible stereo-forms of the dibromide, $HO_2C{\cdot}CH_2{\cdot}CH_2{\cdot}CHBr{\cdot}CHBr{\cdot}CO_2H$, were made, because its methyl (or ethyl) ester was found to form one of the partial reduction products of methyl (or ethyl) *cis-cis*-muconate (see this vol., p. 1932). The isolation of the *cis*-acid, which melts at 81°, is described in the experimental portion (p. 1940), and this substance, like its *trans*-isomeride, gives succinic and oxalic acids in good yield on oxidation. Of the four theoretically possible dihydromuconic acids, therefore, three are now known.

EXPERIMENTAL.

Formation of trans-Δ^{α}-*Dihydromuconic Acid.*—(a) *By equilibration of* Δ^{β}-*dihydromuconic acid.* The ordinary form of Δ^{β}-dihydromuconic acid, m. p. 195°, was prepared in quantity by the method of Farmer (*loc. cit.*, p. 2541). Portions of this were heated with caustic soda solution, and the supposed Δ^{α}-dihydromuconic acid so formed was isolated in the manner prescribed by Rupe (*loc. cit.*). In all cases an acid of indefinite melting point was obtained from which a homogeneous product could not be isolated by fractional crystallisation : a large proportion of the product appeared, however, to be unchanged Δ^{β}-acid. Modifications of Rupe's method of treatment involving alteration in the duration of heating and the concentration of the alkali yielded similar results. When the product obtained under Rupe's conditions was submitted to partial esterification with $0{\cdot}25N$-methyl-alcoholic hydrogen chloride for 16 hours, and the reaction mixture worked up in the usual way, a neutral ester, b. p. 125°/14 mm., and a crystalline half-ester were obtained. The former was crystallisable methyl Δ^{β}-dihydromuconate (m. p. 16° : compare Farmer and Duffin, *loc. cit.*, p. 402) and yielded pure Δ^{β}-dihydromuconic acid, m. p. 195° (mixed m. p. with an authentic specimen, 195°) on hydrolysis, whilst the latter was quite unlike the half-ester of Δ^{β}-dihydromuconic acid which had been recently obtained in quantity by one of us in connexion with another investigation. The half-ester crystallised from light petroleum, in which it was sparingly soluble, in pearly plates, m. p. 60°, and gave on oxidation at 0° with alkaline 3% permanganate almost quantitative yields of oxalic acid (isolated as calcium oxalate) and succinic acid, m. p. 184° (mixed m. p. with authentic specimen,184—185°). It was accordingly *methyl hydrogen* Δ^{α}-*dihydromuconate* [Found : C, 53·05; H, 6·2; M (monobasic), 162. $C_7H_{10}O_4$ requires C, 53·15; H, 6·3% ; M, 158]. Since it was formed by partial esterification of the unsymmetrical Δ^{α}-acid, it must be represented by the formula $MeO_2C{\cdot}CH_2{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CO_2H$ (the isomeric half-ester $HO_2C{\cdot}CH_2{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CO_2Me$ is as yet unknown), and for the reason given on p. 1932 must unquestionably be regarded as a *trans*-form.

When the half-ester was hydrolysed by heating for several minutes with 25% (by vol.) sulphuric acid, or more satisfactorily, by boiling for about 15 minutes with twice the theoretical quantity of dilute sodium carbonate or caustic soda solution, the corresponding acid, trans-Δ^{α}-*dihydromuconic acid*, was obtained. This differed from the isomeric (*trans*) Δ^{β}-acid considerably in crystalline habit but by only a few degrees in melting point. It dissolved readily in hot water and partly separated from concentrated aqueous solution, on cooling, in small prisms or as a coarsely crystalline powder, m. p. 191° ; in small quantities it could be conveniently recrystallised from ether [Found : C, 49·95; H, 5·50; M (dibasic), 142. $C_6H_8O_4$ requires C, 50·0; H, 5·55% ; M, 144].

(b) *By partial hydrogenation of* trans-trans-*muconic acid.* The 50% hydrogenation of ordinary muconic acid (employed in the form of its sodium salt in aqueous solution) invariably consisted to a considerable extent (32—57%) of the above-described *trans*-Δ^{α}-dihydromuconic acid when the catalyst was nickel or palladium (see preceding paper). This acid was conveniently isolated from the crude reduction product by submitting the latter to partial esterification and crystallising the methyl hydrogen *trans*-Δ^{α}-dihydromuconate so formed from light petroleum This half-ester, m. p. 60°, was identical with that described above and gave the corresponding free *trans*-Δ^{α}-acid, m. p. 191°, on hydrolysis.

Esterification of the half-ester by refluxing its silver salt with methyl iodide yielded the corresponding neutral ester, *methyl* trans-Δ^{α}-*dihydromuconate*, b. p. 127°/14 mm., which did not solidify on cooling in ice–salt (Found : C, 55·65; H, 6·9. $C_8H_{12}O_4$ requires C, 55·8; H, 6·9%).

Addition of bromine (1 mol. in chloroform) to the half-ester yielded a pale yellow liquid bromide (methyl hydrogen αβ-dibromoadipate) which did not solidify on cooling or keeping. Hydrolysis of this bromide with boiling hydrobromic acid yielded a solid bromo-acid which was evidently one of the possible stereo-forms of *αβ-dibromoadipic acid*, since it reverted on debromination with zinc and acetone to the original geometrical form (*trans*) of Δ^{α}-dihydromuconic acid. This bromo-acid separated from ether–petroleum as a white crystalline powder, m. p. 171—173° (Found : Br, 52·3. $C_6H_8O_4Br_2$ requires Br, 52·6%).

Prolonged heating of methyl hydrogen Δ^{α}-dihydromuconate or the corresponding free acid with dilute mineral acid, or boiling with 50% sulphuric acid for 15 minutes, yielded an oil which on distillation was obtained as a non-homogeneous colourless liquid which proved to consist partly of the lactone of β-hydroxyadipic acid (compare Farmer, *loc. cit.*, p. 3331).

Formation of cis-Δ^{α}-*Dihydromuconic Acid.*—This acid was obtained by the 50% reduction of methyl *cis-cis*-muconate. This ester, m. p. 75°, was obtained by the method of Farmer (*loc. cit.*, p. 2547) and was hydrogenated in alcohol in the presence of activated nickel (see preceding paper). The reduction product, freed from catalyst by filtration, and from alcohol by gentle warming under reduced pressure, was taken up in light petroleum and cooled. A little unchanged methyl *cis-cis*-muconate crystallised, but no further separation could be effected. The residual ester mixture was therefore hydrolysed by refluxing it with twice the theoretical amount of aqueous 15% caustic soda *until dissolution was just complete.* The product was boiled for a further few minutes without a condenser to expel alcohol, then cooled and extracted with ether to remove any trace of neutral ester. The alkaline liquor was well cooled and very cautiously acidified with the calculated amount of well-cooled concentrated hydrochloric acid and *immediately* extracted with ether. The ethereal extract yielded a solid mixture of acids, from which cis-Δ^{α}-*dihydromuconic acid* [Found : C, 49·8; H, 5·57; *M* (dibasic), 144. $C_6H_8O_4$ requires C, 50·0; H, 5·55; *M*, 144] was directly isolable by several extractions with boiling (dry) benzene. This *cis*-acid, after recrystallisation from benzene, melted at 81°, and gave by oxidation in the usual way with cold alkaline permanganate good yields of succinic acid (m. p. 185°; mixed m. p. 185°) and oxalic acid. Complete separation of the acids contained in the residue of the hydrogenation product was not effected, but by repeated fractional crystallisation of the mixture specimens of Δ^{β}-dihydromuconic acid (*trans*, m. p. 193—195°) and adipic acid (m. p. 148°) were isolated.

Slightly impure ethyl *cis-cis*-muconate (Found : C, 59·9; H, 6·9. Calc. for $C_{10}H_{14}O_4$: C, 60·6; H, 7·05), when similarly submitted to 50% hydrogenation in presence of nickel, also yielded an appreciable proportion of the corresponding *cis*-Δ^{α}-dihydro-product, since the *cis*-Δ^{β}-dihydromuconic acid, m. p. 81°, was readily isolable from the hydrolysed reduction product.

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