143. *Polyene Acids. Part V.* Catalytic Semi-hydrogenation of the Three Isomeric Muconic Acids and Comfirmation of their Configurations.*

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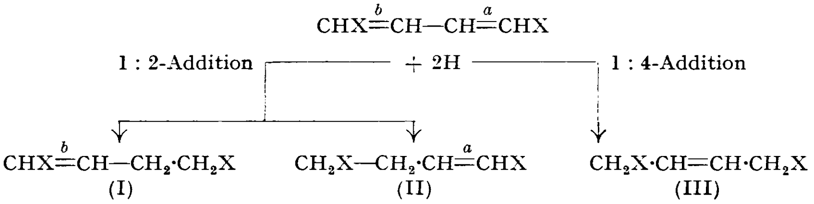
The geometrical configurations previously given to the three isomeric muconic acids have been confirmed by semi-hydrogenation. Under the same conditions the *cic-cis*-acid yields *cis*-Δ^{α}-dihydromuconic acid; the *trans-trans-*, the *trans*-Δ^{α}-dihydro-acid; and the *cis-trans*-acid a mixture of *cis-* and *trans*-Δ^{α}-dihydromuconic acids. *trans*-Δ^{β}-Dihydromuconic acid is a by-product in all these experiments. These results are discussed in the light of previous work.

In Part I of this series (*J.*, 1950, 2235), the preparation of the three geometrical forms of muconic acid was described and configurations were assigned to them. We now report the confirmation of these configurations by means of catalytic semi-hydrogenation.

The semi-hydrogenation of a conjugated diene of this type can be represented as follows :



$$CHX\overset{b}{=}CH-CH\overset{a}{=}CHX$$

1 : 2-Addition + 2H 1 : 4-Addition

$$\underset{(I)}{CHX\overset{b}{=}CH-CH_2{\cdot}CH_2X} \qquad \underset{(II)}{CH_2X-CH_2{\cdot}CH\overset{a}{=}CHX} \qquad \underset{(III)}{CH_2X{\cdot}CH=CH{\cdot}CH_2X}$$

If no inversion in configuration occurs, then the Δ^{α}-acid formed by 1 : 2-addition of hydrogen (I and II) can have either of the configurations *a* or *b* present in the original diene and if $a = b$ then only one Δ^{α}-acid will be formed. The three forms of muconic acid would thus give the following Δ^{α}-products : *cis-cis* → *cis*; *trans-trans* → *trans*; *cis-trans* → *cis* + *trans*. If, however, this line of attack were invalidated by inversion over the catalyst the same product would be expected from all three isomerides. Δ^{β}-Acid (III), formed by 1 : 4-addition, is a further possibility, but this is not immediately relevant to the argument and we return to this aspect later.

Literature on the catalytic semi-hydrogenation of conjugated dienes is scanty and, for the muconic acid system, contradictory. Thus Farmer and Hughes (*J.*, 1934, 304, 1929; cf. Farmer and Galley, *J.*, 1932, 430) isolated dihydro-acids but Ingold and Shah (*J.*, 1933, 885) obtained only complete hydrogenation. A likely explanation for this discrepancy arises from our work.

We have studied the hydrogenation of the neutral sodium salts of the three muconic acids over palladised charcoal with the results summarised in the Table. The products were analysed by a method (described in the Experimental section) which is more accurate than that of Farmer and Hughes (the order of accuracy may be gauged by the divergence of the total yields from 100%). The first point which emerges is that good yields of dihydro-

Semi-hydrogenation of the muconic acids.

Starting material	Acids produced (%)				
	Unchanged muconic	*cis*-Δ^{α}-Dihydro-muconic	*trans*-Δ^{α}-Dihydro-muconic	Δ^{β}-Dihydro-muconic	Adipic
(a) *trans-trans*	0	0	76	13	12
(b) *cis-trans*	21	22	50	11	0
(c) *cis-cis*	18	56	0	10	17
(d) 1 : 1 Mixture of *cis-cis* and *trans-trans*	19 (13% *cis-cis*, 6% *trans-trans*)	33	34	11	12

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* Part IV, *J.*, 1952, 1026.

acids were obtained under our experimental conditions, as in Farmer's work. The second is that the Δ^{α}-dihydro-acids from the symmetrical muconic acids were strictly homogeneous, whereas the Δ^{α}-product from the *cis-trans*-muconic acid was a mixture of the *cis-* and the *trans*-form. The configurations of the three muconic acids are therefore confirmed.

The *trans*-Δ^{α}-dihydromuconic acid (isolated as the half methyl ester) was identified by comparison with authentic material (Elvidge, Linstead, Orkin, Sims, Baer, and Pattison, *J.*, 1950, 2228). The *cis*-Δ^{α}-acid agreed with Farmer and Hughes' description (*loc. cit.*) and its structure was confirmed by its inversion to the *trans*-isomeride by cold dilute hydrochloric acid containing a trace of sulphur dioxide. The same inversion could not be brought about by irradiation with ultra-violet light in the presence of iodine. Pure *cis-cis*-muconic acid is easily inverted by this means although its inversion does not occur in the presence of its semi-hydrogenation products.

The Table shows that the *cis*-double bond is hydrogenated rather more readily than the *trans* when they are in direct competition within the same molecule: a similar difference is not, however, shown by the experiments with an equimolecular mixture of symmetrical acids [Section (d) of Table].

Δ^{β}-Dihydromuconic acid was formed in all our experiments, presumably by direct 1 : 4-addition. The Δ^{β}-acid isolated from the semi-hydrogenation of *cis-cis*-muconic acid was the well-known and presumably *trans*-form, m. p. 195°, and appeared to be free from *cis*-isomeride. The formation of a *trans*-Δ^{β}-acid from *cis-cis*-muconic acid indicates that the diene system is adsorbed on the catalyst in an *s-trans*-form. This is the preferred configuration for the acid on general grounds (see Part I, *loc. cit.*). The stereochemical aspect of 1 : 4-hydrogenation is especially interesting and is being investigated further.

The fact that dihydro-acids were obtained in good yields in our experiments and those of Farmer and his collaborators means that in aqueous solution the muconate ions must be more readily hydrogenated than their dihydro-products. Rate measurements supported this. In methanol over palladised charcoal the rate of hydrogen uptake by *cis-cis*-muconic acid was some 6 times that of the ions in water. Equivalent amounts of *trans*-Δ^{α}- and -Δ^{β}-dihydromuconic acid were hydrogenated about as rapidly under these conditions, but *cis*-Δ^{α}-dihydromuconic acid at only half the rate. Yet semi-hydrogenation of *cis-cis*-muconic acid in alcohol gave less than 5% of *cis*-Δ^{α}-dihydromuconic acid, the reaction mixture consisting largely of adipic acid and starting material. Measurements on separated components or systems are therefore not necessarily pertinent. Ingold and Shah's result (see above) with (*trans-trans-*)muconic ester may well be attributable to their use of alcohol as medium.

EXPERIMENTAL

Partial Hydrogenation of the Muconic Acids.—(*a*) *trans-trans-* (10 g.) and (*b*) *cis-trans-*Muconic acid (10 g.), in water (*a*, 150 c.c.; *b*, 200 c.c.) containing sodium hydrogen carbonate (12 g.), were separately shaken with 5% palladium–charcoal (0·5 g.) in hydrogen (allowed uptake: *a*, 1760 c.c. at 771 mm./15°, in 65 minutes; *b*, 1705 c.c. at 743 mm./16°). (*c*) Sodium *cis-cis*-muconate (from 10 g. of acid), and (*d*) a mixture of the *cis-cis-* (5 g.) and *trans-trans*-acid (5 g.), in water (*c*, 200 c.c.; *d*, 200 c.c. containing 12 g. of sodium hydrogen carbonate), were similarly semi-hydrogenated.

Separation of the Products.—This will be exemplified by the product from experiment (*d*). The filtered solution was acidified with hydrochloric acid, and the precipitate washed with water. Washings and filtrate were combined. Extraction of the precipitate with hot ethanol gave (*A*) insoluble *trans-trans-* and (*B*) soluble *cis-cis*-muconic acid. The preceding aqueous filtrate was extracted exhaustively with ether, the extract evaporated, and the residue extracted with boiling benzene. The soluble portion (*C*), *cis*-Δ^{α}-dihydromuconic acid, was recrystallised from benzene and had m. p. 78—80°, and the insoluble (*D*) was partially esterified (3 days at room temperature) in ether (*ca.* 10 vols.) with methanol (2—3 fold excess) containing 0·1% of hydrogen chloride. These mild conditions esterify adipic and Δ^{β}-dihydromuconic acid completely: the amount of *trans*-Δ^{α}-dihydro-acid converted into diester is appreciable but much smaller than by the method of Farmer and Hughes (*loc. cit.*). The neutral-ester fraction was hydrolysed by brief boiling with 2N-sodium hydroxide (slight excess) to yield a mixture (*E*) of Δ^{β}-dihydromuconic and adipic acid, with some *trans*-Δ^{α}-dihydromuconic acid. Extraction of the acidic fraction (from the esterification) with light petroleum removed (*F*) (δ)-methyl hydrogen *trans*-Δ^{α}-dihydromuconate,* m. p. 58°. Insoluble residue (*G*) was *cis-cis*-muconic acid.

The product from experiment (*a*) on similar treatment yielded nothing at points (*B*), (*C*), and (*G*) in the above scheme. Experiment (*b*) gave *cis-trans*-muconic acid at (*G*), but no product at (*A*) and (*B*). Experiment (*c*) afforded a mixture of *cis-cis*-muconic and adipic acid at (*B*) and *cis-cis*-muconic acid at (*G*), but no product at (*A*) and (*F*) and no *trans*-Δ^{α}-dihydro-acid in the mixture at (*E*).

Analysis of the Separated Products.—Unchanged *trans-trans-*, *cis-cis-*, or *cis-trans*-muconic acid, and *cis*-Δ^{α}-dihydromuconic acid were weighed at (*A*), (*B* + *G*), (*G*), and (*C*), severally. When *cis-cis*-muconic acid at (*B*) was contaminated with adipic acid, hydrogenation and/or bromometric analysis (see below) gave the relative proportions. The removal of *cis*-Δ^{α}-dihydro-acid at (*C*) prevented interference with bromometric analyses at later stages. At (*D*), portions of the benzene-insoluble material were hydrogenated quantitatively and analysed bromometrically to give, respectively, total unsaturation (i) and Δ^{β}-dihydromuconic acid (ii). At (*E*), hydrogenation gave total dihydro-acids there present (iii), and bromometric analysis the Δ^{β}-dihydromuconic acid (iv). Agreement between the values (ii) and (iv) showed that there was no loss of Δ^{β}-dihydro-acid to (*F*) and (*G*). Adipic acid at (*E*) was given by 100 − (iii)%, and *trans*-Δ^{α}-dihydromuconic acid by (iii) − (iv), the remainder being isolated at stage (*F*) as the half methyl ester. A check on the hydrogenation values was available because (i) − (iii) represented the muconic plus *trans*-Δ^{α}-dihydromuconic acids, later isolated at (*G*) and (*F*).

The experimental values are recorded in the Table.

Bromometric Analysis for Δ^{β}-Dihydromuconic Acid in the Mixtures (D) and (E).—*Calibration studies.* The *trans*-Δ^{β}- and -Δ^{α}-dihydromuconic acids and iodine in ethanol, or their sodium salts in water and iodine in potassium iodide, did not react appreciably during several hours. Bromine in chloroform reacted at a convenient rate. Solutions of *trans*-Δ^{β}- (758 mg.), *trans*-Δ^{α}-dihydromuconic (109 mg.), and *cis-cis*-muconic acid (723 mg.) in ethanol (5 c.c. portions) were separately treated with 2% bromine in chloroform (50 c.c.), and the solutions diluted with chloroform to 250 c.c. in dark flasks. 25-C.c. aliquots were withdrawn at intervals and the unchanged bromine was determined iodometrically (% uptake of 2 atoms of Br, severally : 70, 21, 14 in 5 minutes; 82, 28, 18 in 10 minutes; 92, 38, 22 in 20 minutes; 100, 49, 28 in 40 minutes; 102·5, 64, 36% in 80 minutes). The greater rate of reaction of the Δ^{β}-dihydro-acid enabled it to be determined in mixtures.

Binary mixtures (70—75 mg.) of *trans*-Δ^{β}-dihydromuconic acid with *cis-cis*-muconic and *trans*-Δ^{α}-dihydromuconic acid were separately dissolved in methanol (5-c.c. portions) in dark flasks. To each solution, chloroform (10 c.c.) was added and then freshly standardised 1% bromine in chloroform (10·0 c.c.). After 10 minutes, the unchanged bromine was determined iodometrically. The % uptake of 2 equivs. of Br in 10 minutes (% reaction) was plotted against % of Δ^{β}-dihydro-acid in the mixtures. The two curves for the two series of mixtures were almost coincident. Thus *cic-cis*-muconic acid behaved effectively as Δ^{α}-dihydro-acid and could be reckoned as such (with equiv. 72) in the calculation of the bromometric analyses, with negligible error. The mean of the two curves was used, given by :

Δ^{β}-Acid, %	0	10	20	30	40	50	60	70	80	90	100
Reaction, % (defined)	15	22·5	29·5	36·5	43	49·5	55·5	60·5	64	66·5	68

Adipic acid (72 mg.) reacted under the standard conditions to the extent of 7%.

Method. The samples taken at (*D*) and (*E*) of weights chosen to contain 70—75 mg. of unsaturated acids (" effective dihydro-acids "), respectively calculated from the values (i) and (*G*), and (iii), were treated with 1% bromine in chloroform under the foregoing standard conditions. The apparent % reaction was corrected for the adipic acid present (x%) {at (*D*), [100 − (iii)](*E*)/(*D*); at (*E*), 100 − (iii)%} by deducting 7% of x. The % of Δ^{β}-acid in the unsaturated acids was then read from the curve described. Finally, the % of Δ^{β}-acid in the sample was calculated.

The accuracy of the analyses exemplified below showed that the method used for binary mixtures could be extended to ternary and quaternary mixtures; and also justified the other approximations.

Examples. (*a*) 119·0 Mg. of an artificially prepared mixture of *trans*-Δ^{β}- and *trans*-Δ^{α}-dihydromuconic acid, containing 39·0% of adipic acid (∴ 61% of dihydro-acids, equiv., 72), consumed under the standard conditions bromine equivalent to 11·20 c.c. of 0·0508N-thiosulphate.

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* For nomenclature see *J.*, 1951, 3386.

Apparent amount of reaction = 11·2 × 0·0508 × 100 × 72 × 100/(61 × 119) = 56·4%.
Correction for adipic acid = 39 × 7/100 = 2·7.

Hence, amount of reaction = 53·7%, whence (from graph) amount of Δ^{β}-dihydro-acid in the mixed dihydro-acids = 57%. Therefore amount of Δ^{β}-dihydro-acid in the ternary mixture = 61 × 57/100 = 34·7% (Given: 34·9%).

(*b*) 158·6 Mg. of a mixture of *trans*-Δ^{β}-, *trans*-Δ^{α}-dihydromuconic, and *cis-cis*-muconic acid containing 48·2% of adipic acid (∴ 51·8% of "effective dihydro-acids," equiv., *ca.* 72), consumed under the standard conditions bromine equivalent to 10·20 c.c. of 0·0508 N-solution.

Apparent amount of reaction = 10·2 × 0·0508 × 100 × 72 × 100/(51·8 × 158·6) = 45·4%.

Reaction, corrected for adipic acid = 42·0%, whence (from graph) Δ^{β}-dihydro-acid in the mixed unsaturated acids = 38·2%. Therefore, Δ^{β}-dihydro-acid in the quaternary mixture = 51·8 × 38·2/100 = 19·8% (Given: 20·1%). (The amount of *cis-cis*-muconic acid in the mixture was 10%.)

Isolation of trans-Δ^{β}-*Dihydromuconic Acid.*—Sodium *cis-cis*-muconate (10 g.) in water (200 c.c.) and 5% palladium–charcoal (0·2 g.) were shaken in hydrogen until 1 l. had been taken up (Calc. for 1 double bond: 1·7 l.). The filtered solution was acidified with hydrochloric acid and the precipitated *cis-cis*-muconic acid (3·9 g.) washed with cold water. The filtrate and washings were extracted continuously with ether overnight, and the solid residue from the extract was crystallised from benzene, yielding *cis*-Δ^{α}-dihydromuconic acid (4·6 g.). The benzene-insoluble portion (0·6 g.) was esterified partially (under the conditions given above) and the neutral fraction hydrolysed with cold 2N-sodium hydroxide. Acidification precipitated an acid (0·17 g.), m. p. 194—195° alone and when mixed with authentic *trans*-Δ^{β}-dihydromuconic acid (Farmer and Hughes, *loc. cit.*).

Isomerisation of cis-Δ^{α}-*Dihydromuconic Acid.*—A solution of the acid (1·5 g.) in N-hydrochloric acid (20 c.c.), containing a trace of sulphur dioxide, deposited crystals (0·41 g.), m. p. 190—192°, when kept for 7 days. Continuous extraction of the filtrate with ether yielded a solid, which was extracted with boiling benzene. The benzene-insoluble solid (0·56 g.) was combined with the foregoing crystals. Recrystallisation from water gave *trans*-Δ^{α}-dihydromuconic acid (0·96 g.), m. p. and mixed m. p. 190—192°.

The *cis*-Δ^{α}-acid (0·3 g.) in ethanol containing a trace of iodine was recovered (m.p. 78—80°) after irradiation for 5 hours with ultra-violet light from a Hanovia lamp.

Hydrogenation Rate Measurements.—*Methanol.* The dihydro-acids (0·5 g. of each) and muconic acid (0·25 g.) in methanol (30-c.c. portions) were hydrogenated (at 16°/762·5 mm.) over 5% palladium–charcoal (0·1-g. portions):

	Uptake (c.c.)			
Time (min.)	*cis*-Δ^{α}	*trans*-Δ^{α}	*trans*-Δ^{β}	*cis-cis*-
3	8	17	22	24
5	15	27	34	38
7	22	36	47	48
10	29	50	62	61
12	36	59	68	69
14	39	68	71	74
16	43	72	—	—
18	46	73	—	—
36	69	—	—	—

Aqueous alkali. The acids were similarly hydrogenated in 5% aqueous sodium carbonate (30-c.c. portions):

	Uptake (c.c.)				Uptake (c.c.)		
Time (min.)	*trans*-Δ^{α}	*trans*-Δ^{β}	*cis-cis*-	Time (min.)	*trans*-Δ^{α}	*trans*-Δ^{β}	*cis-cis*-
5	5	9	10	40	42	41	63
10	11	16	20	50	51	48	72
15	16	21	30	70	67	61	85
20	21	26	39	100	85	79	91
30	32	34	53				

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