230. *Lævulic Acid. Part I. The Knoevenagel Reaction.*

By Roger Stevens.

Lævulic acid and its esters condense with ethyl cyanoacetate, cyanoacetamide, and malononitrile to give derivatives of 5-cyano-4-methylpent-4-enoic acid. During condensations with cyanoacetic acid some rearrangement to the pent-3-enoic acid takes place. Hydrogenation of these products gives the saturated compounds and thence β-methyladipic acid. Hydrolysis of the product from ethyl lævulate and cyanoacetic acid affords αδ-dihydro-β-methylmuconic acid, but the condensation product with ethyl cyanoacetate reverts to lævulic and malonic acid.

LÆVULIC ACID (I; R = H), produced by acid degradation of materials which contain hexose residues, is potentially cheap.[1] We are therefore examining its conversion into dicarboxylic acids suitable for use as textile intermediates, *e.g.*, for modified nylons.[2] Preliminary work showed that preparation of α-methyladipic acid by way of pentane-1,4-diol and the corresponding dihalide and dinitrile was unattractive on account of the high pressures and critical conditions needed for the hydrogenation,[3] and attention was turned to the synthesis of β-methyladipic acid.

Earlier workers [4] showed that the Reformatsky reaction between ethyl lævulate and ethyl bromoacetate produced γ-ethoxycarbonyl-γ-methylbutanolide (VI; R = Et); hydrolysis then gave a crude acid (V; R = H) which could be reduced to β-methyladipic acid.[4b] The intermediate dihydromuconic acid did not crystallise in the early work [4b,5] and later workers [4c,5,6] record a wide range of melting points (118—161°). β-Methyladipic acid has also been prepared by desulphurisation of the condensation product of lævulic acid with rhodanine, but the overall yield was less than 10%.[7] In view of the low yields in these two procedures an alternative route using the Knoevenagel reaction has been investigated. Ethyl lævulate with cyanoacetic acid in the presence of piperidine [8] gives ethyl 5-cyano-4-methylpent-4-enoate (II; R = Et, R′ = H) in 26% yield; its condensation with ethyl cyanoacetate has also been investigated [9] although in neither case has the position of the double bond in the product been established. In the presence of alcoholic ammonia, ethyl lævulate condenses with two molecules of ethyl cyanoacetate to give a Guareschi imide, hydrolysis of which leads to β-carboxymethyl-β-methyladipic acid.[10]

In the present investigation, diethyl 2-cyano-3-methylhex-2-enedioate (II; R = Et, R′ = CO_2Et) has been prepared in good yield by using the conditions developed by Cope *et al.*[11] Hydrogenation of this ester with palladium–charcoal proceeded smoothly at atmospheric pressure to give the saturated ester (III; R = Et, R′ = CO_2Et) which, on acid-hydrolysis, gave the required β-methyladipic acid. Alternatively, alkaline hydrolysis

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[1] Wiggins, *Adv. Carbohydrate Chem.*, 1949, **4**, 306; Leonard, *Ind. Eng. Chem.*, 1956, **48**, 1330; Dunlop, " Furfural from Agricultural Sources," *Roy. Inst. Chem. Lectures, Monographs, Reports*, 1956, No. 4, p. 15.

[2] Caruthers, U.S.P. 2,130,948 (*Chem. Abs.*, 1938, **32**, 9519).

[3] Christian, Brown, and Hixon, *J. Amer. Chem. Soc.*, 1947, **69**, 1961.

[4] (*a*) Duden and Freydag, *Ber.*, 1903, **36**, 953; (*b*) Staudinger and Ruzicka, *Helv. Chim. Acta*, 1924, **7**, 251; (*c*) Linstead, Lunt, Weedon, and Shephard, *J.*, 1952, 3621; Baumgarten, *J. Amer. Chem. Soc.*, 1953, **75**, 979.

[5] Kuhn, Kohler, and Kohler, *Z. physiol. Chem.*, 1936, **242**, 171.

[6] Penfold, Ramage, and Simonsen, *J.*, 1939, 1486; Elvidge, Linstead, and Sims, *J.*, 1951, 3386.

[7] Allan, Maclean, and Newbold, *J.*, 1952, 5053.

[8] Shemyakin and Trakhtenberg, *J. Gen. Chem.* (*U.S.S.R.*), 1943, **13**, 552 (*Chem. Abs.*, 1945, **39**, 497).

[9] Bannerjee, *Science and Culture*, 1940, **5**, 566; *J. Indian Chem. Soc.*, 1940, **17**, 423.; Raha, *ibid.*, 1953, **30**, 129, 205.

[10] Farmer and Ross, *J.*, 1925, **127**, 2368.

[11] Cope, *J. Amer. Chem. Soc.*, 1937, **59**, 2327; Cope, Hofmann, Wyckoff, and Hardenbergh, *ibid.*, 1941, **63**, 3452.

of the saturated cyano-ester afforded 2-methylbutane-1,1,4-tricarboxylic acid[12] (IV; R = H, R′ = CO_2H) which was readily decarboxylated to β-methyladipic acid.

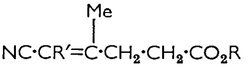
Similarly, cyanoacetic acid with lævulic acid and its methyl, ethyl, and benzyl ester gave the corresponding derivatives of 5-cyano-4-methylpentenoic acid. Hydrogenation of these esters with palladium–charcoal afforded the corresponding pentanoates. During hydrogenation of the benzyl ester two mols. of hydrogen were absorbed and the debenzylated acid (III; R = R′ = H) was obtained. All the derivatives of 5-cyano-4-methylpentanoic acid were hydrolysed almost quantitatively to β-methyladipic acid (IV; R = R′ = H).

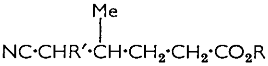
Alexander and Cope[13] have described a technique whereby the equilibrium in the Knoevenagel reaction is displaced by hydrogenation of the unsaturated product; in this way the saturated esters (III; R = Et, R′ = H and CO_2Et) have been prepared directly but the slow hydrogen absorption, even with regular renewal of the palladium–charcoal catalyst, and the low yields make the method unattractive. Attempts to hydrogenate the crude undistilled Knoevenagel reaction product were also unsuccessful.

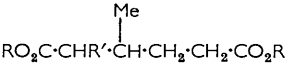
When Raney nickel was used as catalyst in the hydrogenation of ethyl 5-cyano-4-methylpentenoate either at 27° or at 100°/150 atm. only a small quantity of the saturated ester (III; R = Et, R′ = H) was obtained, together with large basic fraction which, although not completely characterised, behaved as ethyl 6-amino-4-methylhexanoate and polymerised on attempted distillation.[14] Acid-hydrolysis of the polymer gave a deliquescent hydrochloride thought to be 6-amino-4-methylhexanoic acid hydrochloride.[15]

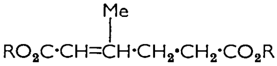
Attempts to condense ethyl lævulate with ethyl acetoacetate, diethyl malonate, and acetonitrile were unsuccessful but condensations with cyanoacetamide and malononitrile yielded the substituted esters (II; R = Et, R′ = $CO\cdot NH_2$ and CN). The amide was hydrogenated over palladium–charcoal to the saturated derivative (III; R = Et, R′ = $CO\cdot NH_2$), which on hydrolysis gave β-methyladipic acid, but under similar conditions the dinitrile (II; R = Et, R′ = CN) was unchanged.

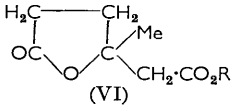
$CH_3\cdot CO\cdot CH_2\cdot CH_2\cdot CO_2R$
(I)

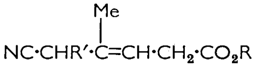

$NC\cdot CR'{=}\overset{Me}{\overset{|}{C}}\cdot CH_2\cdot CH_2\cdot CO_2R$
(II)

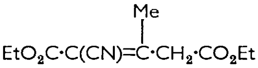

$NC\cdot CHR'\cdot\overset{Me}{\overset{|}{C}H}\cdot CH_2\cdot CH_2\cdot CO_2R$
(III)

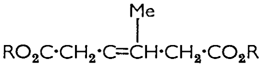

$RO_2C\cdot CHR'\cdot\overset{Me}{\overset{|}{C}H}\cdot CH_2\cdot CH_2\cdot CO_2R$
(IV)

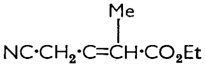

$RO_2C\cdot CH{=}\overset{Me}{\overset{|}{C}}\cdot CH_2\cdot CH_2\cdot CO_2R$
(V)


(VI)


$NC\cdot CHR'\cdot\overset{Me}{\overset{|}{C}}{=}CH\cdot CH_2\cdot CO_2R$
(VII)


$EtO_2C\cdot C(CN){=}\overset{Me}{\overset{|}{C}}\cdot CH_2\cdot CO_2Et$
(VIII)


$RO_2C\cdot CH_2\cdot\overset{Me}{\overset{|}{C}}{=}CH\cdot CH_2\cdot CO_2R$
(X)


$NC\cdot CH_2\cdot\overset{Me}{\overset{|}{C}}{=}CH\cdot CO_2Et$
(IX)

Following the practice of the earlier workers, we generally write the products of the Knovenagel reaction as αβ-unsaturated nitriles, *i.e.*, as derivatives of 5-cyanopent-4-enoic acid (II), though Zaar[16] reported them to be mixtures of $\Delta^{\alpha\beta}$- and $\Delta^{\beta\gamma}$-forms (*e.g.*, II and VII). Kitson and Griffiths[17] found that the nitrile stretching frequency of saturated or

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[12] Noyes and Cox, *J. Amer. Chem. Soc.*, 1903, **25**, 1093.

[13] Alexander and Cope, *J. Amer. Chem. Soc.*, 1944, **66**, 886.

[14] Cf. Ruzicka, *Helv. Chim. Acta*, 1921, **4**, 479.

[15] Cf. Ungnade and McLaren, *J. Org. Chem.*, 1945, **10**, 29.

[16] Zaar, *Ber. Schimmel and Co. Akt. Ges.*, Jubilee No., 1929, 299 (*Chem. Abs.*, 1930, **24**, 2107).

[17] Kitson and Griffiths, *Analyt. Chem.*, 1952, **24**, 334.

unconjugated nitriles lies in the range 2249—2260 cm.$^{-1}$ while conjugated nitriles absorb at about 2221 cm.$^{-1}$. The stretching frequencies of some of the nitriles obtained in this work are collected in Table 1 where it can be seen that the condensation product of ethyl lævulate and ethyl cyanoacetate absorbs at 2222 cm.$^{-1}$, confirming the conjugated structure (II) in this case. The infrared spectra of the products from cyanoacetamide and malononitrile are also in agreement with the conjugated structure (II). On the other hand, the spectrum of the product from cyanoacetic acid has bands at both 2217 and 2252 cm.$^{-1}$, suggesting that it is a mixture of the conjugated (II; R = Et, R′ = H) and the unconjugated form (VII; R = Et, R′ = H), in which the former predominates. This rearrangement made the spectra of the condensation products of ethyl acetoacetate with ethyl cyanoacetate and cyanoacetic acid of interest. Ethyl acetoacetate and ethyl cyanoacetate [18] gave a small yield of what, on the basis of the nitrile stretching frequency (2232 cm.$^{-1}$), is thought to be diethyl 2-cyano-3-methylpent-2-enedioate (VIII). For the product from ethyl acetoacetate and cyanoacetic acid,[8] both the nitrile stretching frequency (2242 cm.$^{-1}$) and a band at 1631 cm.$^{-1}$, associated with a conjugated carbonyl group, indicate that the product is ethyl 4-cyano-3-methylbut-2-enoate (IX). It therefore appears that when the Knovenagel condensation is accompanied by decarboxylation some rearrangement occurs but that in other cases the product is almost entirely the αβ-saturated nitrile.

Before the infrared spectra had clarified the situation, hydrolysis of the product from ethyl lævulate and cyanoacetic acid was studied. Alkaline hydrolysis afforded an oil which on long storage gave a small yield of an acid, m. p. 128—130°. The same acid was obtained if the crude hydrolysate was esterified and the distilled ester hydrolysed. That it was a dihydro-β-methylmuconic acid was established by analysis and hydrogenation to β-methyladipic acid and it was shown to be the *trans*-$\Delta^{\beta\gamma}$-isomer (X; R = H) by comparison of its infrared spectrum with those of authentic samples of the isomeric *trans*-dihydro-β-methylmuconic acids kindly provided by Dr. J. A. Elvidge. In particular, the spectrum of the acid obtained in this work and that of the authentic αδ-dihydro-β-methylmuconic acid lacked the absorption at about 1630 cm.$^{-1}$ (conjugated C=O) which was present in the spectra of the other two isomers and of the methyl ester of the crude hydrolysate of the condensation product. The isolation of the αδ-dihydro-β-methylmuconic acid (X; R = H) on hydrolysis of a nitrile which on spectral evidence was itself chiefly in the $\Delta^{\alpha\beta}$-form may be due to relative solubilities but is more probably an example of three-carbon tautomerism. The many examples given by Linstead and his co-workers [19] lead to the view that in the dihydro-β-methylmuconic acid series the $\Delta^{\beta\gamma}$-form will be the most stable.

TABLE 1. *Infrared nitrile stretching frequencies* (*cm.*$^{-1}$).

	Thickness	ν		Thickness	ν
Me·CN	0·025 mm.	2257 *	(II; R′ = CN)	Nujol mull	2198
$NC{\cdot}CH_2{\cdot}CO_2Et$	0·025 mm.	2268	(II and VII; R′ = H)	0·025 mm.	2217s, 2252m
(III; R′ = H)	0·025 mm.	2257			
(III; R′ = CO_2Et)	0·025 mm.	2252	(VIII)	0·05 mm.	2232
(II; R′ = CO_2Et	0·025 mm.	2222	(IX)	0·025 mm.	2242
(II; R′ = $CO{\cdot}NH_2$)	Nujol mull	2198			

* Kitson and Griffiths [17] report 2254 cm.$^{-1}$.

It was thought that a study of the hydrolysis of the ester which was shown by infrared evidence to have the structure (II; R = Et, R′ = CO_2Et) might help to elucidate the tautomerism of this series, but after alkaline hydrolysis only malonic acid and lævulic acid could be recovered. The absence of any dihydro-β-methylmuconic acid was shown

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[18] Kon and Nanji, *J.*, 1931, 560.

[19] See table by Linstead in " Organic Chemistry " (ed. Gilman), Wiley, New York, 2nd edn., 1943, p. 1042, and references there cited.

by esterification of the crude hydrolysate and examination by vapour-phase chromatography. In a similar manner, it was shown that only lævulic acid resulted from acid-hydrolysis of this ester. Ethanolysis of ethyl 5-cyano-4-methylpentenoate gave diethyl dihydro-β-methylmuconate, presumably a mixture of (V) and (X) (R = Et), which was smoothly hydrogenated to diethyl β-methyladipate.

EXPERIMENTAL

Infrared spectra were measured on a Perkin-Elmer spectrophotometer model 137. For determination of the nitrile stretching frequencies, the spectrum of polystyrene was superimposed on the chart, and wavelengths were corrected to the bands at 3·42, 3·50, and 6·24 μ in that spectrum.

Lævulic acid (I; R = H) as a film had $\nu_{max.}$ 2941—3333s, 1695—1754s, 1404s, 1370s, 1211s, 1166s, 1064w, 1026w, and 990w cm.$^{-1}$.

Ethyl lævulate (I; R = Et) as a film had $\nu_{max.}$ 3030s, 2985s (infl.), 1779m (infl.), 1733s, 1481m (infl.), 1462m (infl.), 1445s (infl.), 1410s, 1370s, 1311s, 1209s, 1160s, 1099m, 1064m, 1033s, 990w, 926m, 874w, 787w, and 767w cm.$^{-1}$.

β-*Methyladipic Acid.*—A sample prepared by oxidation of 4-methylcyclohexanone with alkaline potassium permanganate [20] had m. p. 92—94° and $\nu_{max.}$ (Nujol mull) 2900—3030s, 1695—1724s, 1471s, 1418s, 1388s, 1351m, 1266—1316s, 1224s, 1176s, 1127m, 961m, 781w, and 787w cm.$^{-1}$.

Knoevenagel Condensations.—These were carried out by Cope's method; [11] the lævulic derivative (0·5 mol.), the cyanoacetic derivative (0·5 mol.), glacial acetic acid (6 g.), and ammonium acetate (3·85 g.) in benzene (50 ml.) were heated under reflux under a Dean-Stark adaptor until no more water separated (usually overnight). Working up of the products is described below.

Ethyl 2-*Cyano*-3-*methylhex*-2-*enedioate* (II; R = Et, R′ = CO_2Et).—The product from ethyl lævulate (86 g.) and ethyl cyanoacetate (49 g.) was washed twice with both 2N-sodium carbonate and water, dried ($MgSO_4$), and distilled; the ester had b. p. 145—148°/1 mm., n_D^{27} 1·4708 (67·4 g., 65%) (Found: C, 60·3; H, 7·1; N, 5·7. Calc. for $C_{12}H_{17}O_4N$: C, 60·3; H, 7·1; N, 5·9%) (lit.,[9] b. p. 154—160°/5·5 mm.), $\nu_{max.}$ 2976s, 2222m, 1701—1754s, 1600s, 1449s, 1377s, 1163—1361s, 1075s, 1301s, 943m, 905w, 862m, and 784s cm.$^{-1}$.

Ethyl α-*Cyano*-β-*methyladipate* (III; R = Et, R′ = CO_2Et).—(i) The preceding ester (22·2 g.) in ethanol (50 ml.) was shaken in hydrogen with 5% palladised charcoal (0·5 g.). The calculated absorption (2·3 l. at 27°/760 mm.) was achieved in 6 hr. After the removal of catalyst and solvent, the saturated ester had b. p. 147—152°/0·5 mm., n_D^{27} 1·4415 (17·7 g., 79%) (Found: C, 59·2; H, 7·7; N, 5·7. Calc. for $C_{12}H_{19}O_4N$: C, 59·7: H, 7·9; N, 5·8%) (Noyes and Cox [12] report b. p. 175—185°/20 mm.), $\nu_{max.}$ 3021s, 2252w, 1724—1761s, 1623w (infl.), 1471s, 1425m, 1395s, 1377s, 1163—1282s, 1099s, 1020—1042s, 947w, 862m, 794m, 769m (infl.), and 685s cm.$^{-1}$.

(ii) Ethyl cyanoacetate (28·3 g.), ethyl lævulate (39·6 g.), ammonium acetate (1·95 g.), and acetic acid (3 g.) in ethanol (50 ml.) were shaken with 5% palladised charcoal (0·5 g.) in hydrogen. The catalyst was replaced by fresh portions after 4, 48, 76, and 99 hr. After 120 hr. the hydrogenation was stopped (uptake 4·3 l. at 27°/760 mm., 70% of theory), the catalyst was removed, and the residue was distilled; the fraction having b. p. 142—147°/0·3 mm., n_D^{27} 1·4490 (38 g., 63%) (Found: C, 59·2; H, 7·9; N, 5·7%), was collected. The saturated ester (8 g.) was heated under reflux overnight with 5N-hydrochloric acid, and the hydrolysate diluted with water and extracted with ether to give β-methyladipic acid (5·3 g., 98%), m. p. and mixed m. p. 90—93° (from benzene).

2-*Methylbutane*-1,1,4-*tricarboxylic Acid* (IV; R = H, R′ = CO_2H).—Ethyl α-cyano-β-methyladipate (5 g.) and sodium hydroxide (10 g.) in aqueous ethanol (50 ml.) were heated under reflux overnight, cooled, acidified, and continuously extracted with ether. The ethereal extract gave the tricarboxylic acid (4·15 g.), m. p. 123—128° raised to 128—130° by recrystallisation from water (Found: C, 47·7; H, 5·9. Calc. for $C_8H_{12}O_6$: C, 47·1; H, 5·95%). Noyes and Cox [12] record m. p. 127°. The acid (IV; R = H, R′ = CO_2H) was heated at 200° for 30 min., cooled, and recrystallised from benzene (charcoal), to give β-methyladipic acid (0·8 g.), m. p. and mixed m. p. 90—93°.

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[20] Wallach, *Annalen*, 1896, **289**, 344.

TABLE 2. *5-Cyano-4-methylpentenoic acid derivatives* (II and VII; R′ = H).

			Yield		Found (%)			Required (%)		
R	B. p./mm.	n_D^{27}	(%)	Formula	C	H	N	C	H	N
H	163—165°/1·5	1·4760	50	$C_7H_9O_2N$ *	60·1	6·3	10·0	60·4	6·5	10·1
Me	159—161°/30	1·4540	51	$C_8H_{11}O_2N$	63·1	7·5	8·9	62·8	7·2	9·2
Et	162—163°/30 †	1·4510	78	$C_9H_{13}O_2N$	65·0	7·9	7·9	64·7	7·8	8·4
CH_2Ph	172—178°/1	1·5180	56	$C_{14}H_{15}O_2N$	73·1	6·6	6·1	73·4	6·6	6·1

* Found: equiv., 140. Required: equiv., 139.
† Shemyakin and Trakhtenberg [8] report b. p. 136—140°/22 mm.

TABLE 3. *5-Cyano-4-methylpentanoic acid derivatives* (III; R′ = H).

			Yield		Found (%)			Required (%)		
R	B. p./mm.	n_D^{27}	(%)	Formula	C	H	N	C	H	N
H	144—146°/0·4	1·4510	67	$C_7H_{11}O_2N$	59·1	7·5	10·0	59·6	7·8	9·9 †
Me	154—156°/30	1·4320	94	$C_8H_{13}O_2N$	62·3	8·5	8·8	61·9	8·4	9·0
Et	159—160°/30	1·4316	82	$C_9H_{15}O_2N$	63·8	8·7	8·1	63·9	8·9	8·3
CH_2Ph	166—168°/0·3	1·5020	81 *	$C_{14}H_{17}O_2N$	72·5	7·2	5·8	72·7	7·4	6·1

* By esterification. † Meluch and Mislow, *J. Org. Chem.*, 1955, **20**, 1311, found b. p. 120—124°/0·25 mm., n_D^{35} 1·4559, for the (+)-form.

5-Cyano-4-methylpentenoic Acid and its Esters (II; R = H).—These were made by the Knoevenagel reaction as described above; the products were washed with water, the solvent removed, and the residue heated at 180° for 30 min. to ensure complete decarboxylation before distillation. The yields, b. p.s, and analyses are recorded in Table 2. Ethyl 5-cyano-4-methylpentenoate had $\nu_{max.}$ 3226s, 3030s, 2994s (infl.), 2252m, 2217s, 1695—1770s, 1639m, 1370—1449s, 1149—1333s, 1089m, 1080w, 1036s, 935m, 787—862m cm.$^{-1}$.

Ethyl 5-Cyano-4-methylpentanoate (III; R = Et, R′ = H).—(i) Ethyl 5-cyano-4-methylpentenoate (20 g.) in ethanol (100 ml.) containing 5% palladised charcoal (0·5 g.) was shaken in hydrogen until the calculated volume of hydrogen was absorbed (9·5 hr.); after filtration and removal of the solvent, the reduced *ester* was distilled. The physical properties are recorded in Table 3. The compound had absorption at 3571m, 3205m, 2941s, 2262m, 1773m (infl.), 1724s, 1626m, 1458s, 1422s, 1372s, 1340s, 1098s, 1031s, 975w, 952m, 902w, 858m, and 787m cm.$^{-1}$. The *methyl ester* (III; R = Me, R′ = H) was prepared similarly.

(ii) Ethyl lævulate (43 g.), cyanoacetic acid (21·3 g.), ammonium acetate (1·95 g.), and acetic acid (3 g.) were shaken in ethanol (50 ml.) with 5% palladised charcoal (0·5 g.) in hydrogen. The catalyst was changed after 5, 29, 47, 72, and 97 hr. After 7 days (hydrogen uptake 4·8 l., 78%) the catalyst and solvent were removed and the residue heated at 180° and then fractionally distilled; the ester (III; R = Et, R′ = H) had b. p. 156—165°/30 mm., n_D^{27} 1·4450 (5·2 g.) (Found: C, 63·7; H, 8·6; N, 8·5%).

(iii) Ethyl 5-cyano-4-methylpentenoate (32 g.) in methanol (50 ml.) was shaken with hydrogen and Raney nickel W-2 (*ca.* 3 g.) at 27°/150 atm. for 24 hr. After removal of the catalyst and solvent the residue was dissolved in 2N-hydrochloric acid and extracted with ether. The ethereal extract gave an oil (7·5 g.) which was combined with the non-basic fraction from a similar hydrogenation carried out at 100° (2·5 g.) and distilled, to give the ester b. p. 142—144°/25 mm., n_D^{27} 1·4480 (5·2 g.) (Found: N, 8·0, 8·1%).

Ethyl 6-Amino-4-methylhexanoate.—By hydrogenation of ethyl 5-cyano-4-methylpentenoate (32 g.) at 100°/150 atm. with Raney nickel W-2, an oil was obtained which was completely soluble in 2N-hydrochloric acid. After the removal of the non-basic fraction in ether (see above) the solution was made basic by the addition of potassium carbonate and re-extracted with ether, to give an oil (19·4 g.), n_D^{25} 1·4370, which polymerised on attempted distillation at 30 mm. (cf. ethyl 6-aminohexanoate [13]). The polymer dissolved in boiling 5N-hydrochloric acid in 2 hr.; the excess of acid was removed by repeated distillation in a vacuum, to leave a deliquescent *hydrochloride* (Found: N, 6·1, 6·2. $C_7H_{15}O_2N,HCl$ requires N, 7·7%).

5-Cyano-4-methylpentanoic Acid (III; R = R′ = H).—(i) 5-Cyano-4-methylpentenoic acid (14·5 g.) in ethanol, when shaken in hydrogen with palladised charcoal, absorbed only 73% of the theoretical quantity of hydrogen. Renewal of the catalyst resulted in no further absorption. The physical properties of the reduced acid are given in Table 2. Hydrolysis of this acid (1·1 g.) with 2N-methanolic sodium hydroxide, followed by acidification and ether-extraction, gave the theoretical yield of β-methyladipic acid, m. p. and mixed m. p. 89—93° (from benzene).

(ii) Benzyl 5-cyano-4-methylpent-4-enoate (15 g.) in a similar hydrogenation rapidly absorbed 1 mol. of hydrogen (50 min.) and then slowly (14 hr.) took up a further mol. After removal of catalyst and solvent, the *acid* had b. p. 148—150°/0·4 mm., n_D^{27} 1·4490 (7·2 g., 78%) (Found: N, 9·9%).

Benzyl 5-*Cyano*-4-*methylpentanoate* (III; R = CH_2Ph, R′ = H).—The acid (6·5 g.) obtained as above and benzyl alcohol (6·5 ml.) in toluene were heated overnight under a Dean–Stark adaptor, the mixture was then cooled, washed with a saturated solution of sodium hydrogen carbonate and water, dried, and distilled. The physical properties of the *ester* are recorded in Table 2. Hydrolysis gave β-methyladipic acid, m. p. and mixed m. p. 92—94°.

β-*Methyladipic Acid* (IV; R = R′ = H).—Ethyl 5-cyano-4-methylpentanoate (36 g.) and potassium hydroxide (40 g.) in ethanol (100 ml.) were heated under reflux overnight, water being added after about 1 hr. to dissolve the solid formed. The majority of the solvent was distilled off, and the mixture cooled, acidified, and extracted with ether. The material extracted (33 g., 98%) recrystallised from benzene, to give β-methyladipic acid, m. p. 89—93°. Two further recrystallisations from benzene gave a sample of m. p. and mixed m. p. 93—94 (Found: C, 52·4; H, 7·9%; equiv., 80·2, 80·5. Calc. for $C_7H_{12}O_4$: C, 52·5; H, 7·6%; equiv., 80·1). The ethyl ester had b. p. 150—154°/30 mm. (lit., 130—138°/15 mm.), the amide m. p. 188—189° (lit., m. p. 191°), and the *p*-*bromophenacyl derivative*, m. p. 83—84° (from aqueous ethanol) (Found: C, 49·8; H, 4·4. $C_{23}H_{22}O_6Br_2$ requires C, 49·8; H, 4·0%).

Ethyl 5-*Carbamoyl*-5-*cyano*-4-*methylpent*-4-*enoate* (II; R = Et, R′ = $CO{\cdot}NH_2$).—Cyanoacetamide [21] (42 g.) was condensed with ethyl lævulate (86 g.) in Cope's conditions, and water (11 ml.) was eliminated, but on cooling some cyanoacetamide, m. p. and mixed m. p. 118°, crystallised. On further storage at 0°, the required *amide* separated; it had m. p. 82—87° (from benzene) (20·7 g., 20%) (Found: C, 56·6; H, 6·7; N, 13·0. $C_{10}H_{14}O_3N_2$ requires C, 57·1; H, 6·7; N, 13·3%) and $\nu_{max.}$ (mull in Nujol) 3448m, 3226m, 2198w, 1736s, 1645s, 1613s, 1290m, 1205m, 1124w, 1099w, 1058w, 1036w, 980w, 870w, 800m, 735m, and 690m cm.$^{-1}$. No further solid could be isolated from the mother-liquors.

Ethyl 5-*Carbamoyl*-5-*cyano*-4-*methylpentanoate* (III; R = Et, R′ = $CO{\cdot}NH_2$).—The amide obtained above (8 g.) was shaken in ethanol (75 ml.) with 5% palladised charcoal (0·5 g.) in hydrogen until the theoretical quantity was absorbed (11 hr.). Removal of the catalyst and solvent left a solid residue, m. p. 53—56°. Two recrystallisations from water gave the *amide*, m. p. 67—69° (Found: C, 56·9; H, 7·6; N, 13·3. $C_{10}H_{16}O_3N_2$ requires C, 56·6; H, 7·6; N, 13·2%). A sample (1·0 g.) was boiled under reflux for 16 hr. with 5N-hydrochloric acid (20 ml.), cooled, diluted, and extracted with ether, which gave β-methyladipic acid (0·8 g.), m. p. 91—93° (from benzene).

Ethyl 5,5-*Dicyano*-4-*methylpent*-4-*enoate* (II; R = Et, R′ = CN).—A solution of malononitrile [22] (41·9 g.), ethyl lævulate (100 g.), acetic acid (6 g.), and ammonium acetate (3·85 g.) in benzene (50 ml.) was heated under reflux for 5 hr., water (16·7 ml.) being collected in a Dean–Stark adaptor. The cooled mixture was washed three times with water, and the solvent removed. After storage at 0° crystals, m. p. 135—150°, were deposited (17·4 g. 14·6%), which after several recrystallisations from ethanol gave the *dinitrile*, m. p. 148—151° (Found: C, 62·0; H, 6·7; N, 14·7. $C_{10}H_{12}O_2N_2$ requires C, 62·5; H, 6·3; N, 14·6%), $\nu_{max.}$ (Nujol mull) 3378m, 3247m, 2198m, 1730s, 1658s, 1645s (infl.), 1585m, 1235m, 1202s, 1179s, 1018—1031m, 862w, and 833m cm.$^{-1}$. A solution of the dinitrile (6 g.) in ethanol (1·5 ml.) at 40° absorbed no hydrogen over 5% palladised charcoal (0·5 g.), and the dinitrile was recovered.

Diethyl 2-*Cyano*-3-*methylpent*-2-*enedioate* (VIII).—The Knoevenagel condensation was carried out as described above, with ethyl acetoacetate (65 g.) and ethyl cyanoacetate (56 g.). The calculated quantity of water separated but on distillation at the reported pressure the product largely polymerised. The ester which distilled (21 g., 19%) had b. p. 178°/25 mm., n_D^{22} 1·4640 (Found: N, 6·6. Calc. for $C_{12}H_{15}O_4N$: N, 6·2%) (Kon and Nanji [18] record b. p. 170°/25 mm. n_D^{18} 1·4092), $\nu_{max.}$ 2976s, 2232s, 1712—1761s, 1613m, 1370—1471s, 1149—1302s, 1010—1116s, 961·5m, 930m, 860s, 820m, 781s, and 730m cm.$^{-1}$.

Ethyl 4-*Cyano*-3-*methylbut*-2-*enoate* (IX).—In a similar condensation ethyl acetoacetate (32·5 g.) and cyanoacetic acid (24 g.) gave the ester, b. p. 100—102°/5 mm., n_D^{20} 1·4529 (17·6 g., 72%) (Found: N, 9·0. Calc. for $C_8H_{11}O_2N$: N, 9·1%) (lit.,[8] b. p. 116—118°/12 mm.), $\nu_{max.}$ 3003s, 2242s, 1736s, 1631m, 1460m (infl.), 1441s, 1385s, 1370s, 1316s, 1250s, 1149—1220s, 1112m, 1099m, 1058m (infl.), 1040s, 928m, 877w, 840m, 816m, and 725w cm.$^{-1}$.

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[21] Carson, Scott, and Vose, *Org. Synth.*, Coll. Vol. I, 2nd edn., p. 179.

[22] *Idem, ibid.*, Coll. Vol. II, p. 379.

αδ-*Dihydro*-β-*methylmuconic Acid.*—Ethyl 5-cyano-4-methylpentenoate (11 g.) was heated under reflux with potassium hydroxide (10 g.) in methanol (90 ml.) and water (10 ml.) for 18 hr. The solvent was removed, and the residue acidified with 10N-sulphuric acid and extracted continuously overnight with ether. The ethereal extract was evaporated and after prolonged storage gave a semicrystalline solid which was drained on porous tile and recrystallised from benzene–ethyl acetate several times, to give a product, m. p. 129—130° (Found: C, 53·0; H, 6·5%; equiv., 79·1, 79·2. Calc. for $C_7H_{10}O_4$: C, 53·2; H, 6·4%, equiv., 79·1). The infrared spectrum of this acid in a potassium bromide disc was identical with that of αδ-dihydro-β-methylmuconic acid (see below). The authentic sample had m. p. 133—134° and m. p. 128—129° when mixed with the above acid. The acid (85 g.), shaken with Adams catalyst in hydrogen until no further absorption occurred, gave β-methyladipic acid, m. p. and mixed m. p. 93·5°. In another experiment the hydrolysate of ethyl 5-cyano-4-methylpentenoate was heated under reflux with methanol containing concentrated sulphuric acid. After dilution and extraction with ether the *dimethyl ester* had b. p. 138—142°/25 mm., n_D^{27} 1·4460 (Found: C, 58·4; H, 7·2. $C_9H_{14}O_4$ requires C, 58·1; H, 7·5%), $\nu_{max.}$ (film) 1653w cm.$^{-1}$. Hydrolysis gave the same dihydro-β-methylmuconic acid, m. p. 127—128°.

Dihydro-β-*methylmuconic Acids.*—The authentic samples provided by Dr. J. A. Elvidge showed the following bands in potassium bromide discs: *trans*-$\Delta^{\alpha\beta}$ (V; R = H), 2941m, 2597m (infl.), 1684s, 1623s, 1433m, 1292m, 1258s, 1214m, 1053w, 986w (infl.), 935m, 862m, and 714 cm.$^{-1}$.

trans-$\Delta^{\beta\gamma}$ (X; R = H), 2941s, 2703m, 2509m, 1692s, 1406s, 1355w, 1325m, 1285m, 1242s, 1222s, 1170m, 1096w, 1020w, 926m, 794m, and 707m cm.$^{-1}$.

trans-$\Delta^{\gamma\delta}$, 2899s, 2703m, 1689s, 1639m, 1408m, 1342w, 1282s, 1217w, 1176m, 1081w, 989w, 952m, 873w, 735w, and 685w cm.$^{-1}$.

Hydrolysis of Diethyl 2-*Cyano*-3-*methylhex*-2-*enedioate.*—(i) The ester (II; R = Et, R′ = CO_2Et) (20 g.) was heated under reflux for 24 hr. with potassium hydroxide (20 g.) in methanol (80 ml.) and water (20 ml.). After removal of most of the methanol the mixture was cooled in ice, acidified dropwise by 10N-sulphuric acid (35 ml.), and extracted with ether for 48 hr. The extract (19·4 g.) was examined in two portions. The first (12·9 g.) was esterified by heating under reflux with ethanol (100 ml.) containing concentrated sulphuric acid (5 ml.). After dilution of the solution the esters were extracted with ether. Vapour-phase chromatography of the crude mixed esters on Apiezon M at 170° with nitrogen as the eluting gas showed a double peak similar to that given by a mixture of ethyl lævulate and diethyl malonate and no material with the retention volume expected for diethyl dihydro-β-methylmuconate. The esters had b. p. 194—196° (lit., ethyl lævulate b. p. 206—208°, diethyl malonate b. p. 199°), and the distillate gave ethyl lævulate 2,4-dinitrophenylhydrazone (from ethanol), m. p. and mixed m. p. 96—97° (lit., 101°). The residue partially crystallised overnight. The crystals were recovered and after recrystallisation from benzene–ether had m. p. 129—130° (Found: equiv., 54·0, 54·1. Calc. for $C_3H_4O_4$: equiv., 52·0) and the infrared absorption (Nujol mull) of malonic acid (m. p. 135—136°). The combined mother-liquors were heated at 180° for 30 min. to decarboxylate any remaining malonic acid and distilled, to give lævulic acid, b. p. 108°/3 mm., n_D^{20} 1·4396 (Found: equiv., 121·8, 121·0. Calc. for $C_5H_8O_3$: equiv., 116) (lit., b. p. 137—139°/10 mm., n_D^{16} 1·442), with the authentic infrared spectrum.

(ii) The ester (II; R = Et, R′ = CO_2Et) (10·1 g.) was heated under reflux with 5N-hydrochloric acid for 24 hr. After evaporation to small bulk, dilution with water, and continuous extraction with ether, the ethereal extract was esterified and examined by vapour-phase chromatography. Only a peak corresponding to ethyl lævulate was present. The crude ester was distilled at *ca.* 200° (bath) to give ethyl lævulate having n_D^{20} 1·4196 (lit., b. p. 206°, n_D^{20} 1·4229) and the authentic infrared absorption.

Diethyl Dihydro-β-*methylmuconate.*—A solution of ethyl 5-cyano-4-methylpentenoate (30 g.) in dry ethanol (200 ml.) was cooled to 0°, saturated with dry hydrogen chloride, and set aside overnight. The solution was then boiled under reflux for 2 hr., then cooled, and the ammonium chloride was removed. The filtrate was evaporated and heated at 180° for 2 hr., cooled, taken up in ether, washed with water, and distilled. After a small fore-run, the required ester had b. p. 110—112°/0·7 mm., n_D^{27} 1·4470 (13·1 g., 34%) (Found: C, 61·3; H, 8·0. $C_{11}H_{18}O_4$ requires C, 61·7; H, 8·5%). Baumgarten [4c] records b. p. 101—102°/0·5 mm. The unsaturated ester (V; R = Et) (7·7 g.) in ethanol (50 ml.) was shaken in hydrogen with 5% palladised charcoal (0·5 g.) until the theoretical quantity (0·9 l.) was absorbed. After removal of catalyst and solvent, diethyl β-methyladipate was obtained having b. p. 158—161°/35 mm., n_D^{27} 1·4300 (4·2 g., 54%), which on hydrolysis gave the parent acid, m. p. and mixed m. p. 91—93°.

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