excess of pyridine) described above, except that the reaction mixture was held at 43° for 25 hours and then at room temperature for another 20 hours after addition was complete. The yield was 4.8 g. (27%) of material, b.p. 135–150° (3–3.5 mm.), which gave the crude oxime in 56% yield.

This oxime (2.9 g.) was chromatographed from chloroform on activated alumina. The product was extracted from the chloroform eluate with dilute hydrochloric acid and reprecipitated with dilute sodium hydroxide solution. After crystallization from benzene and benzene–petroleum ether, there remained 1.2 g. of pure material, m.p. 148.5–149.5°.

Anal. Calcd. for $C_{11}H_{16}N_2O$: C, 68.72; H, 8.39. Found: C, 68.91; H, 8.41.

Nitriles.—For each gram of oxime, about 10 cc. of acetic anhydride was added, and the solution was heated on the steam-bath for one hour in the preparation of dimethylaminobenzonitrile, and for five hours with the other examples. Water was then added, and the acetic acid solution was neutralized with ammonia, whereupon the crude nitrile precipitated.

***p*-Dimethylaminobenzonitrile.**—The crude product was chromatographed from benzene on activated alumina, and crystallized three times from methanol–water. From 1.67 g. of oxime was obtained 0.42 g. (32%) of the nitrile, m.p. 75–76°; reported[13,14] m.p. 75–76°.

7-Dimethylamino-4-indancarbonitrile.—The crude product was extracted from benzene solution with dilute hydrochloric acid, and then reprecipitated with ammonia. It was then chromatographed from benzene on activated alumina, and crystallized from methanol–water. From 1.5 g. of the oxime was obtained 0.39 g. (29%) of nitrile, m.p. 55–56°.

Anal. Calcd. for $C_{12}H_{14}N_2$: C, 77.38; H, 7.58. Found: C, 77.06; H, 7.67.

4-Dimethylamino-5,6,7,8-tetrahydro-1-naphthonitrile.—The crude product was chromatographed from benzene on activated alumina. From 0.69 g. of the oxime was obtained 0.36 g. (56%) of nitrile, m.p. 46.5–47.5°. After two crystallizations from methanol–water, there remained 0.26 g. (41%) of the desired nitrile; m.p. 46–47°.

Anal. Calcd. for $C_{13}H_{16}N_2$: C, 77.96; H, 8.05. Found: C, 77.84; H, 8.37.

4-Dimethylamino-2,3-xylonitrile.—The crude product was chromatographed from benzene on activated alumina, and crystallized from methanol at −80°. The yield from 0.63 g. of oxime was 0.34 g. (60%) of nitrile, m.p. 25–26°.

Anal. Calcd. for $C_{11}H_{14}N_2$: C, 75.82; H, 8.10. Found: C, 75.52; H, 8.30.

MINNEAPOLIS 14, MINNESOTA RECEIVED JULY 6, 1951

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[14] K. Matsumura, THIS JOURNAL, **57**, 955 (1935).

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES, GENERAL MILLS, INC.]

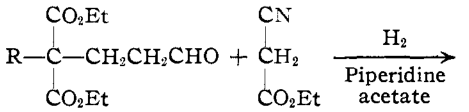
Synthesis of Pimelic Acid and α-Substituted Pimelic Acid and Intermediates[1]

BY DONALD T. WARNER AND OWEN A. MOE

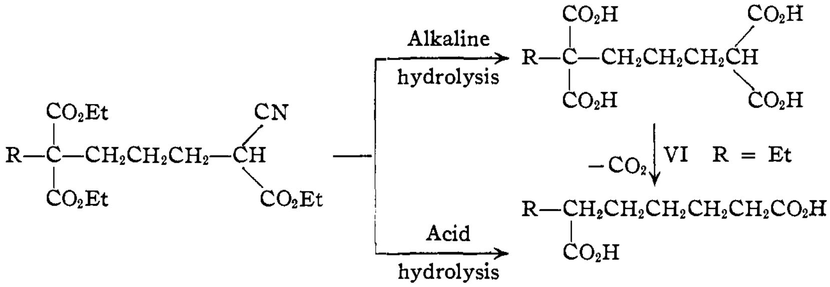
Several aldehydo compounds, obtained by 1,4-addition reactions of malonate systems with acrolein, have been utilized in simultaneous condensation–reduction reactions with ethyl cyanoacetate. The resulting products are intermediates in the synthesis of pimelic acid and mono-α-substituted pimelic acids. The hydrolyses of three of the intermediates and the identification of pimelic acid, α-aminopimelic acid and α-ethylpimelic acid are described.

The 1,4-additions of malonate systems to α,β-unsaturated aldehydes have resulted in the convenient preparation of a number of aldehydo compounds.[2] These compounds have been utilized for the preparation of amino acids and other products.[3] In the present work, these aldehydes have been condensed with ethyl cyanoacetate[4] to produce intermediates which may be hydrolyzed to pimelic acid and mono-α-substituted pimelic acids. The results obtained indicate that the aldehydo compounds, although formed by a reversible 1,4-addition reaction, can be conveniently used with the mild alkaline catalysts required in this method.

The compounds studied and the reactions involved may be illustrated as



$$\mathrm{R{-}\underset{CO_2Et}{\overset{CO_2Et}{C}}{-}CH_2CH_2CHO + \underset{CO_2Et}{\overset{CN}{CH_2}} \xrightarrow[\text{Piperidine acetate}]{H_2}}$$



$$\mathrm{R{-}\underset{CO_2Et}{\overset{CO_2Et}{C}}{-}CH_2CH_2CH_2{-}CH(CN)(CO_2Et)} \xrightarrow[\text{hydrolysis}]{\text{Alkaline}} \mathrm{R{-}\underset{CO_2H}{\overset{CO_2H}{C}}{-}CH_2CH_2CH_2CH(CO_2H)_2} \xrightarrow[-CO_2]{\text{VI}\quad R = Et} \mathrm{R{-}\underset{CO_2H}{CH_2}CH_2CH_2CH_2CH_2CO_2H}$$

$$\mathrm{R{-}\underset{CO_2Et}{\overset{CO_2Et}{C}}{-}CH_2CH_2CH_2{-}CH(CN)(CO_2Et)} \xrightarrow[\text{hydrolysis}]{\text{Acid}} \mathrm{R{-}\underset{CO_2H}{CH_2}CH_2CH_2CH_2CH_2CO_2H}$$

I, R = H
II, R = C_2H_5
III, R = $NHCOCH_3$
IV, R = $nC_{10}H_{21}$
V, R = —O—$COCH_3$
VII, R = H
VIII, R = Et
IX, R = NH_2

All of the aldehydo compounds tested readily undergo a simultaneous condensation–reduction with ethyl cyanoacetate to form the pimelic acid intermediates I–V. We have used alcohol as the solvent for these reductions with satisfactory results. The cyanotricarboxylate products may be purified by distillation without decomposition even at the elevated distillation temperatures which are required in some instances.

Since the yields of the condensation–reduction products are known to be dependent upon the purity of the aldehydo compounds,[4] we have attempted to determine the optimum results when freshly distilled γ,γ-dicarbethoxy-caproaldehyde was employed in the preparation of II. The condensation–reduction product was obtained in a yield of 75% based on the weight of redistilled II.

The cyanotricarboxylate compounds I, II and III

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[1] Paper No. 122, Journal Series, Research Laboratories, General Mills, Inc.

[2] For previous references to this work see O. A. Moe, D. T. Warner and M. I. Buckley, THIS JOURNAL, **73**, 1062 (1951).

[3] (a) O. A. Moe and D. T. Warner, *ibid.*, **71**, 1251 (1949); (b) D. T. Warner and O. A. Moe, *ibid.*, **70**, 2765 (1948); (c) D. T. Warner and O. A. Moe, *ibid.*, **70**, 3918 (1948).

[4] E. R. Alexander and A. C. Cope, *ibid.*, **66**, 886 (1944).

were hydrolyzed to the known pimelic acids VII, VIII and IX, which were obtained as crystalline solids having the expected melting points. VII and IX were further characterized as known derivatives. Compound VIII, α-ethylpimelic acid, has been previously reported,[5a,b] as a crystalline solid melting at 42–43°; but to our knowledge derivatives of this product have not been reported. We have, therefore, completed the identification of VIII by the preparation of the dianilide. The derivative melted at 163–163.8°. A small quantity of monoanilide was also obtained by alkaline extraction of the crude dianilide preparation.

In the hydrolysis of the cyanotricarboxylate compounds, to the corresponding pimelic acids, I was hydrolyzed with difficulty by 50 volume per cent. aqueous sulfuric acid. In the case of II, prolonged heating with 50 volume per cent. aqueous sulfuric acid failed to convert the product to α-ethylpimelic acid. This resistance to hydrolysis by aqueous sulfuric acid of carbethoxy groups attached to a quaternary carbon atom[5c] was previously noted in the cyclization of the phenylhydrazone of γ-acetamido-γ,γ-dicarbethoxybutyraldehyde.[3b] Alkaline hydrolysis of II was successful and the tetracarboxylic acid VI was isolated as an intermediate and decarboxylated to VIII.

In contrast to the action of aqueous sulfuric acid on the ester groups of the quaternary carbon atom, concentrated hydrochloric acid attacks such ester linkages more readily. We first observed this in the hydrolysis of ethyl α,ε-diacetamido-α-carbethoxycaproate to DL-lysine.[3c] In the present work, concentrated hydrochloric acid also readily hydrolyzed III to α-aminopimelic acid (m.p. 216° dec.).[6] Similarly II with aqueous HCl was conveniently hydrolyzed to α-ethylpimelic acid (VIII).

Products IV and V were purified by distillation and were subjected to elementary analysis. However, they were not hydrolyzed to the corresponding pimelic acids.

Experimental[7,8]

Ethyl α-Carbethoxy-α'-cyanopimelate (I).—A solution containing 21.6 g. of γ,γ-dicarbethoxybutyraldehyde[9] and 50 cc. of anhydrous dioxane was mixed with 11.3 g. of ethyl cyanoacetate and 1.2 g. of glacial acetic acid. After cooling to 4°, piperidine (0.35 g.) and 5% palladium-on-charcoal (0.4 g.) were added, and the reduction was carried out at an initial pressure of 32 pounds hydrogen. About 60% of the theoretical amount of hydrogen was consumed. The catalyst was removed by filtration and the filtrate was concentrated *in vacuo*, yielding a residual oil which was dissolved in benzene. The benzene solution was washed with water and dried over anhydrous sodium sulfate. After filtration the benzene was removed by concentration *in vacuo*, yielding an oil which was distilled under diminished pressure. A small amount of forerun was discarded and the purified (I) (12.2 g.) was collected at 156–164° (0.12–0.15 mm.) (39%).

Pimelic Acid (VII).—A portion of the redistilled I (3.9 g.) was refluxed with 47 g. of 50 volume per cent. aqueous sulfuric acid. After one hour the reaction mixture had darkened appreciably; hence, water (15 cc.) was added, and the reflux temperature was maintained for an additional 7-hour period. The cooled reaction mixture failed to deposit any crystalline material. It was extracted with ether, and after drying over anhydrous sodium sulfate, the ether was removed by distillation and the residual white solid was recrystallized in benzene. The pimelic acid VII was obtained as a white crystalline product melting at 103–104°. The di-*p*-bromophenacyl ester and the dianilide were also prepared and melted at 136–137° and 153–155°, respectively (given[10]: for di-*p*-bromophenacyl ester, 137°; for dianilide, 155°).

Ethyl α-Carbethoxy-α-ethyl-α'-cyanopimelate (II).—48.8 g. (0.2 mole) of γ,γ-dicarbethoxycaproaldehyde[9] (freshly redistilled) was dissolved in 120 ml. of absolute ethanol and 25 g. (0.22 mole) of ethyl cyanoacetate was added. The mixture was cooled to about 10° and 2 ml. of glacial acetic acid was added, followed by 0.8 g. of piperidine dissolved in a small quantity of alcohol. No temperature rise was observed. The hydrogenation was carried out in the presence of 2 g. of 5% Pd-on-Charcoal (American Platinum Works) and 0.2 mole of hydrogen were taken up in 40 minutes. The catalyst was filtered and the solution was concentrated *in vacuo*. The crude product was washed as in (I) and then distilled *in vacuo*; 63.1 g. of II distilled at 137–150° (0.10–0.16 mm.) (84.5%).

46.3 g. of II was redistilled through a short Vigreux column and 40.9 g. was collected at 151–162° (0.13–0.08 mm.). This represents an over-all yield of 75% based on redistilled product. A center fraction ($n^{30}D$ 1.4450) was submitted for analysis.

Anal. Calcd. for $C_{17}H_{27}O_6N$: C, 59.78; H, 7.97; N, 4.10. Found: C, 59.87; H, 7.78; N, 4.19.

α-Ethyl-α,α'-dicarboxypimelic Acid (VI).—10.23 g. (0.03 mole) of II was refluxed for 72 hours with 75 ml. of 20% sodium hydroxide solution. The hydrolyzate was then cooled in an ice-bath and acidified with 32 ml. of concentrated HCl. The water solution was then extracted with four 120-ml. portions of ether. The combined ether extracts were dried over anhydrous sodium sulfate. The ether was removed and 5 g. of crude crystalline VI remained. This material was not completely soluble in 35 ml. of warm anhydrous ether. The insoluble portion (3 g.) melted at 172.5° (dec.). The ether filtrate was diluted with an equal volume of benzene and an additional 1.3 g. of crystalline VI (m.p. 173–173.5° dec.) was obtained.

The crude VI dissolved readily in ether containing about 5% ethanol, and upon addition of an equal volume of benzene, VI was obtained as an amorphous product which precipitated slowly; m.p. 173–173.5° dec.

Anal. Calcd. for $C_{11}H_{16}O_8$: C, 47.82; H, 5.84; neut. equiv., 69.06. Found: C, 48.31; H, 5.84; neut. equiv., 70.5, 71.6.

α-Ethylpimelic Acid (VIII).—(A) 2.69 g. of VI was heated for five minutes at 170–180° until the major portion of the decarboxylation had occurred. The product was then distilled at 153–157° (0.2 mm.) (Carter[5a] reports 218–223° (17 mm.)); weight 1.65 g. (90%). The undistilled residue weighed 0.2 g. The loss in weight was equivalent to two carboxyl groups.

Anal. Calcd. for $C_9H_{16}O_4$: C, 57.42; H, 8.57. Found: C, 56.95; H, 8.51.

The distilled VIII persisted as a liquid for several weeks at room temperature but solidified overnight in the refrigerator; m.p. 41–42° (given[5a,b] for α-ethylpimelic acid: 41.5–43°, 42–43°).

The liquid VIII was heated to reflux with excess aniline for 3 hours. The reaction product was a mixture of monoanilide and dianilide. The crude product could not be readily purified from 50% ethanol, so the monoanilide was removed by extraction with 5% sodium bicarbonate solution. The crude dianilide melted at 158–159.5°; and after two crystallizations from 50 volume per cent. ethanol, it melted at 163–163.8°.

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(5) (a) A. S. Carter, THIS JOURNAL, **50**, 1967 (1928); (b) S. J. A. Allen and J. G. N. Drewitt, U. S. Patent 2,527,509 (Oct. 31, 1950).

(5c) The recent article by H. Schechter, and J. C. Kirk, THIS JOURNAL, **73**, 3087 (1951), also describes the difficult hydrolysis by sulfuric acid of 2-alkyl-2-carbethoxycycloalkanones containing an ester group on a quaternary carbon atom. Their results with the hydrolysis of 2-carbethoxy-2-alkylcyclohexanones are comparable to those reported in the present work. The more rapid hydrolysis of 2-carbethoxy-2-alkylcyclopentanones may be related to the planar ring structure in these compounds.

(6) W. Dieckmann, *Ber.*, **38**, 1654 (1905).

(7) Melting points uncorrected.

(8) Microanalyses by J. R. Kerns.

(9) D. T. Warner and O. A. Moe, THIS JOURNAL, **70**, 2470 (1948).

(10) R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds." John Wiley and Sons, Inc., New York, N. Y., 1940, p. 192.

Anal. Calcd. for $C_{21}H_{26}O_2N_2$: C, 74.51; H, 7.75; N, 8.28. Found: C, 74.53; H, 7.52; N, 8.67.

The sodium bicarbonate solution was acidified with dilute hydrochloric acid. The precipitate of crude monoanilide was crystallized twice from 40% ethanol and melted at 119.5–120.5°.

Anal. Calcd. for $C_{15}H_{21}O_3N$: C, 68.45; H, 8.04; N, 5.32. Found: C, 68.42; H, 7.62; N, 5.42.

(B) 4.1 g. of II was refluxed for 24 hours with 40 ml. of concentrated hydrochloric acid. The clear solution was concentrated *in vacuo* to about 20 ml. and an oil separated. The mixture was extracted with two 30-ml. portions of ether. The combined ether extracts were washed with four 10-ml. portions of water and the ether layer was dried over anhydrous sodium sulfate. Filtration and evaporation of the ether yielded 1.8 g. of viscous, oily VIII which solidified on cooling; m.p. 36.5–39.5°.

Ethyl α-Acetamido-α-carbethoxy-α'-cyanopimelate (III).—The condensation–reduction reaction employing crude γ-acetamido-γ,γ-dicarbethoxy-butyraldehyde[11] (84.7 g.) and ethyl cyanoacetate (36.2 g.) was carried out essentially as described under II. The crude reaction product weighed 121.5 g. Distillation of 86 g. of the crude oil yielded 28.4 g. of product collected at 210–220° (0.8 mm.). A large amount of a dark brown residue remained. Redistillation yielded 22 g. of III collected at 195–198° (0.25 mm.) (27%).

α-Aminopimelic Acid (IX).—A portion (5.2 g.) of the redistilled III was refluxed with 50 cc. of concentrated hydrochloric acid for a period of 24 hours. After filtration, the reaction mixture was concentrated *in vacuo*. The residue was dissolved in 8 cc. of water and neutralized to a *p*H of 3.1 with aqueous sodium hydroxide solution. The resulting solution was heated and filtered. When the filtrate was permitted to cool slowly, it yielded a crystalline product which was melted at 216° with decomposition.

Anal. Calcd. for $C_{17}H_{13}O_4N$: C, 47.98; H, 7.48; N, 8.00. Found: C, 47.90; H, 7.28; N, 7.95.

The α-aminopimelic acid was further characterized as the N-benzoyl derivative which melted at 164–165°.

Anal. Calcd. for $C_{14}H_{17}O_5N$: C, 60.18; H, 6.13; N, 5.02. Found: C, 60.44; H, 5.82; N, 5.34.

Ethyl α-Cyano-ε,ε-dicarbethoxyhexadecanoate (IV).—The condensation–reduction reaction was carried out using 51.9 g. of crude γ-decyl-γ,γ-dicarbethoxybutyraldehyde[9] and 20.3 g. of ethyl cyanoacetate essentially as described under II. Distillation of the reaction product yielded 29 g. of IV collected at 200–205° (0.7–0.8 mm.). Redistillation yielded 21 g. (32%) of IV collected at 189–198° (0.12 mm.). An analytical sample was prepared by collecting a middle cut from another distillation at 176° (0.06 mm.), $n^{25}D$ 1.4515.

Anal. Calcd. for $C_{25}H_{43}O_6N$: C, 66.22; H, 9.49; N, 3.09. Found: C, 66.27; H, 9.36; N, 3.49.

Ethyl α-Acetoxy-α-carbethoxy-α'-cyanopimelate (V).—Crude γ-acetoxy-γ,γ-dicarbethoxybutyraldehyde[9] (27 g.) was condensed with ethyl cyanoacetate (12.5 g.) essentially as described under II. In the first distillation, 19 g. of crude V was collected at 167–182° (0.2–0.3 mm.). Upon redistillation, 13 g. (35%) was collected at 160–168° (0.1 mm.). A center fraction was collected at 162.5–163° (0.1 mm.); $n^{25}D$ 1.4512.

Anal. Calcd. for $C_{17}H_{25}O_8N$: C, 54.95; H, 6.79; N, 3.78. Found: C, 54.77; H, 6.66; N, 3.64.

MINNEAPOLIS, MINNESOTA RECEIVED AUGUST 3, 1951

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[11] O. A. Moe and D. T. Warner, THIS JOURNAL, 70, 2763 (1948).

[CONTRIBUTION FROM THE SHELL DEVELOPMENT COMPANY, EMERYVILLE, CALIFORNIA]

Selective Hydrogenation of Polyolefins with Metal Sulfide Catalysts in the Liquid Phase

BY R. J. MOORE, R. A. TRIMBLE AND B. S. GREENSFELDER

The use of the sulfides of molybdenum and nickel as liquid phase selective hydrogenation catalysts is described; these materials were found to be highly selective for the hydrogenation of polyolefins to monoölefins. Advantageously, they retain their activity in the presence of as much as one per cent. mercaptan or alkyl sulfide. Evidence is presented to show that hydrogenation proceeds through the conjugated form of the polyolefin, with preliminary catalyzed isomerization of nonconjugated double bonds to this form when structurally permissible.

Although metal sulfides have been proposed as liquid phase olefin hydrogenation catalysts,[1,2] finely divided active metals such as nickel, platinum, etc., have remained the most widely used catalysts for this type of reaction. It is very difficult, however, to hydrogenate an olefin with these metal catalysts in the presence of common sulfur compounds, except for some limited reactions involving thiophenes. In view of the successful development and application of metal sulfide catalysts for commercial high temperature vapor phase hydrogenation and dehydrogenation, the use of catalysts of this type with sufficient activity for liquid phase reactions at low to moderate temperatures was investigated.

When operating in the range 100 to 200°, metal sulfides, notably the sulfides of nickel and molybdenum, have been found to have a remarkable activity and selectivity for hydrogenation of certain polyolefins to monoölefins in the liquid phase, but are virtually inactive for hydrogenation of monoolefins or of the benzene ring. However, only those polyolefins which are conjugated or are capable of conjugation by double bond shift isomerization were found to be susceptible to this selective hydrogenation. These catalysts are highly selective in that the rate of monoölefin hydrogenation is so low as to be negligible under the applied conditions. In contrast, previous work with elementary metals[3] appears to be based on relatively smaller differences in reactivity in favor of the more unsaturated component, and the reaction must be externally interrupted at the desired extent of hydrogenation.

Experimental Part

Preparation of Catalysts.—The catalysts used here were prepared by impregnating a porous support with an aqueous solution of a readily decomposable metal salt. The dried mixture was then heated with hydrogen sulfide to convert the metal to the sulfide. In general, the finished catalysts contained about 10% metal by weight.

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[1] U. S. Patent 1,908,286, E. Dorrer (to I. G. Farbenindustrie, A. G.), May 9, 1933; U. S. Patent 2,402,493, B. S. Greensfelder and W. H. Peterson (to Shell Development Co.), June 18, 1946; U. S. Patent 2,488,145, W. M. Smith and R. B. Mason (to Standard Oil Development Co.), November 15, 1949.

[2] W. A. Lazier, F. K. Signaigo and co-workers have described the preparation of various sulfide hydrogenation catalysts and their use in introducing sulfur into organic compounds, as covered by U. S. Patents 2,402,613 to –15; –39 to –45; –85 and –86 (to E. I. du Pont de Nemours and Co.).

[3] K. N. Campbell and B. K. Campbell, *Chem. Revs.*, 31, 77 (1942).