melting point was determined. This compound is fairly soluble in acetone and benzene, but is insoluble in water.

N-Phenyl-N′-(2-alkoxycinchoninyl)-piperazines.—A hot solution of 8.8 g. (0.025 mole) of N-phenyl-N′-(2-chlorocinchoninyl)-piperazine in 140 ml. of benzene was added to a solution of 1.0 g. of sodium dissolved in 25 ml. of the appropriate alcohol, and the resulting mixture was refluxed four to fifty hours, after which it was filtered free from sodium chloride. In the cases of the methyl, ethyl, propyl and allyl compounds, the filtrate was evaporated to dryness, washed with water and recrystallized from 95% ethanol. In the cases of the others, the filtrate was washed with water and then evaporated to an oil, which was then dissolved in ethanol. Crystals eventually appeared from these alcoholic solutions, although with difficulty in some cases. All of the compounds were crystallized again from ethanol before their melting points were determined. These compounds are fairly soluble in acetone and benzene, but are insoluble in water.

N-(2-Alkoxycinchoninyl)-morpholines.—A hot solution of 5.5 g. (0.02 mole) of N-(2-chlorocinchoninyl)-morpholine in 50 ml. of benzene was added to a solution of 1.0 g. of sodium dissolved in 50 ml. of the appropriate alcohol. This mixture was refluxed for four hours, filtered and then evaporated to a solid. This was washed with water and then dissolved in ethanol. The crystals which later appeared were again crystallized before the melting points were determined.

A summary of the new nupercaine analogs is shown in Table I.

Summary

1. Thirteen new quinoline compounds analogous to nupercaine have been prepared and characterized.
2. At least one of these compounds has anesthetic properties.
3. Pharmacological studies of these compounds are now under way under the direction of Dr. James C. Munch of John Wyeth and Brother.
4. Work on these series of compounds is being continued in this Laboratory.

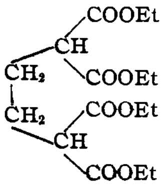
GAINESVILLE, FLA. RECEIVED NOVEMBER 16, 1936

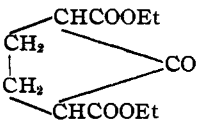
[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Reaction of Certain Monosubstituted Malonic Esters and Methylene Dimalonic Esters with Sodium Ethoxide

BY J. R. ROLAND AND S. M. MCELVAIN

The fact that ethylene dimalonic ester (I) undergoes intramolecular condensation to give a dicarbethoxycyclopentanone[1] (II), led to the expectation that two molecules of methylmalonic ester (III), on account of their similarity to I in structure, should condense intermolecularly. As a matter of fact, such an intermolecular condensation of monosubstituted malonic esters had been predicted by Dieckmann[2] on the basis of his interpretation of the mechanism of the acetoacetic ester condensation. Later, however, Dieckmann and Kron[3] mentioned briefly in a footnote the failure of methylmalonic ester to undergo this condensation.


I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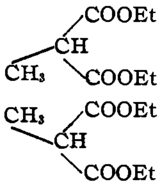
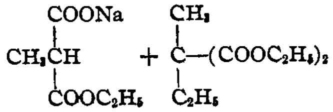

III

In view of this reported failure to realize an intermolecular condensation of III, it seemed worth while to ascertain what products, if any, result from the reaction of sodium ethoxide and methylmalonic ester. Of course the first product formed from these reactants is the sodium enolate of methylmalonic ester and an equivalent of alcohol. When the latter is removed by distillation the reactants remaining are this enolate and the excess methylmalonic ester. Such enolates are, therefore, the real condensing agents when such an ester as I is condensed.

When the sodium enolate of methylmalonic ester was heated at 140–160° with an excess of the ester, the reaction products isolated were monoethylmethylmalonate, methylethylmalonic ester and α-methylbutyric ester. The first two of these products are the result of the alkylation of the enolate by methylmalonic ester,[4] thus

$$CH_3CH(COOC_2H_5)_2 + [CH_3C(COOC_2H_5)_2]^- Na^+ \longrightarrow$$



$$CH_3\underset{COOC_2H_5}{\overset{COONa}{CH}} + \underset{C_2H_5}{\overset{CH_3}{C}}\text{—}(COOC_2H_5)_2$$

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[1] Meincke, Cox and McElvain, THIS JOURNAL, **57**, 1133 (1935). *Cf.* also the condensation of the homologous trimethylene dimalonic ester [Guha and Seshadriengar, *Current Sci.*, **3**, 20 (1934)].

[2] Dieckmann, *Ber.*, **33**, 2678 (1900).

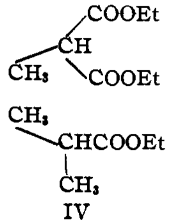
[3] Dieckmann and Kron, *ibid.*, **41**, 1260 (footnote 1) (1908).

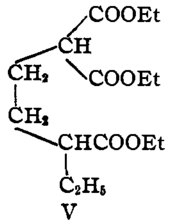
[4] *Cf.* Walter and McElvain, THIS JOURNAL, **57**, 1891 (1935).

The α-methyl butyric ester results from the decarboxylation of the methylethylmalonic ester. At lower temperatures (100–120° and 50–60°) this alkylation reaction did not occur and the only product under these conditions was due to the hydrolysis of the enolate[5] when the reaction mixture was worked up, since none of it was obtained when the reaction mixture was decomposed with dry hydrogen chloride. Apparently, therefore, the only reaction which methylmalonic ester shows with sodium ethoxide at 140–160° is self alkylation, and this reaction takes place to the extent of 72% of the theoretical.

It seemed necessary to determine whether or not this alkylation reaction was preventing any acetoacetic ester condensation of the malonic ester from taking place. This was done by using isopropylmalonic ester instead of methylmalonic ester. The isopropyl group has been shown[6] to be effective in blocking certain alkylations. With this group present, the alkylation amounted to only 45% of the theoretical at 140–160°, but no trace of any condensation product could be isolated from the reaction.

Just as methylmalonic ester failed to undergo an acetoacetic ester condensation with itself, it also failed to condense with ethyl isobutyrate. This intermolecular condensation would be expected from the similarity in structure between these esters (IV) and ethyl α-ethyl-α′-carbethoxyadipate (V) which has been shown[7] to undergo intramolecular condensation with the formation of 2-ethyl-2,5-dicarbethoxycyclopentanone.

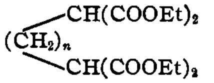

IV

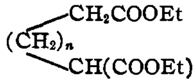

V

These esters (IV) failed to enter into any intermolecular condensation. The only product, besides the starting materials, which was isolated from the reaction was a small amount of monoethyl methylmalonate.

On the basis of our present knowledge no reasonable explanation is available to account for the ready intramolecular condensation of such esters as I and V and the failure of such esters as III and IV to undergo an intermolecular condensation. This failure, however, by emphasizing the necessity of a structure that permits an intramolecular condensation, suggested the investigation of the behavior of some other methylene dimalonic esters, the intramolecular condensation of which would yield cyclic products containing cycles other than those of conventional five or six members.

In this connection methylene dimalonic ester (VI, $n = 1$), pentamethylene dimalonic ester (VI, $n = 5$) and decamethylene dimalonic ester (VI, $n = 10$) were investigated. These esters, if they condensed intramolecularly in the manner of I, would yield products containing four, eight and thirteen membered rings, respectively.


VI


VII

None of these dimalonic esters gave any evidence of intramolecular condensation when heated with sodium ethoxide. Methylene dimalonic ester yielded ethyl acrylate, malonic ester, ethyl α-carbethoxyglutarate (VII, $n = 1$) and a relatively large amount of an undistillable tar. The first two of the products are probably the result of a retrograde Michael reaction on VII ($n = 1$). The best explanation for the unusually large amount of tar is from the polymerization of methylene malonic ester which, along with malonic ester, would result from a retrograde Michael reaction on the starting ester (VI, $n = 1$). Pentamethylene dimalonic ester yielded only de-carboxylated products, ethyl azelate and ethyl α-carbethoxyazelate (VII, $n = 5$). Decamethylene dimalonic ester yielded no product boiling lower than itself. The reaction product was a viscous liquid which could not be distilled and appeared to be an intermolecular condensation product.

Experimental

Methylmalonic ester was prepared by the Wislicenus[8] procedure, in yields of 60–70% of the theoretical. The product obtained boiled at 194–196°.

Reaction of Methylmalonic Ester with Sodium Ethoxide.—One mole (174 g.) of methylmalonic ester was heated with 0.5 mole of sodium ethoxide at 160° for eight hours. The apparatus was arranged so that any distillate could be collected. The distillate on fractionation yielded the following fractions: (a) alcohol, b. p. 75–78°, 25.8 g.; (b) ethyl propionate, b. p. 98–104°, 7.0 g.; (c) ethyl α-

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[5] *Cf.* Michael, *J. prakt. Chem.*, [2] **72**, 547, 550 (1905).

[6] Preiswerk, *Helv. Chim. Acta*, **6**, 192 (1923).

[7] Meincke and McElvain, THIS JOURNAL, **57**, 1443 (1935).

[8] Wislicenus, *Ann.*, **246**, 315 (1888); *Ber.*, **27**, 796 (1894).

methylbutyrate, b. p. 125–132°, sap. equiv. 129 (calcd. 130), 2.2 g.

The reaction mixture, after cooling, was treated with a cold solution of 35% sulfuric acid, the precipitated $Na_2SO_4 \cdot 10H_2O$ filtered off, and the filtrate fractionated. The following fractions were collected from this filtrate: (d) ethyl propionate, b. p. 98–100°, 4 g.; (e) ethyl α-methylbutyrate, b. p., 130–131°, 10.7 g.; (f) methylmalonic ester, b. p. 194–196°, 53.4 g.; (g) ethyl methylethylmalonate, b. p. 205–208°, sap. equiv., 102 (calcd. 101), 57.0 g.; (h) monoethyl methylmalonate, b. p. 100–102° (2 mm.), 13.0 g., sap. equiv. 71 (calcd. 73), n^{25}_{D}, 1.4235, d^{25}_{25}, 1.1192.[9] Analyses calcd. for $C_6H_{10}O_4$: C, 49.3, H, 6.85; OC_2H_5, 30.8. Found: 49.4, 6.84, 30.2.

The total quantity of alkylated products, methylethylmalonic ester and α-methylbutyric ester from the above run amounted to 72.1% of the theoretical.

When methylmalonic ester was allowed to react with sodium ethoxide at 50–60° and also at 120° for six hours and the product worked up in the same manner as described above, the only product which was isolated was the mono-ethyl methylmalonate. If, however, dry hydrogen chloride instead of 35% sulfuric acid was used to decompose the reaction mixture, unchanged methylmalonic ester was the only product recovered.

Isopropylmalonic Ester.—This ester was prepared in 56% yield by alkylation of sodiomalonic ester suspended in alcohol with isopropyl bromide. The product, washed free of unreacted malonic ester with 25% potassium hydroxide, boiled 211–212°.[10]

Reaction of Isopropyl Malonic Ester with Sodium Ethoxide.—One-half mole (101 g.) of isopropylmalonic ester was allowed to react with 0.25 mole of sodium ethoxide for eighteen hours at 150–160°. During this time 8.5 g. of alcohol distilled from the reaction mixture. When the reaction mixture was worked up as described above, the following fractions were collected: (a) ethyl isovalerate, b. p. 132–134°, sap. equiv. 133 (calcd. 130), 11.0 g.; (b) ethyl α-isopropylbutyrate, b. p. 158–162°, 4.7 g., derived acid, b. p. 203°,[11] neut. equiv. 130 (calcd. 130); (c) isopropylmalonic ester, b. p. 91–92° (8 mm.), 29.8 g.; (d) ethylisopropylmalonic ester, b. p. 81–82° (2 mm.), 15.5 g., derived acid, m. p. 132–133°;[11] (e) b. p., 100–110° (2 mm.), 5.0 g.

Fraction e was heated to 140° in order to decarboxylate any mono-ethyl ester. Only 75 cc. of carbon dioxide was obtained from a 4-g. sample, the theoretical amount being 560 cc., had the sample been pure half ester. This amount of carbon dioxide corresponds to 0.67 g. of half ester. The remainder boiled 134–136° (10 mm.) and was found to be identical with ethylisopropylmalonic ester (fraction d).

The alkylated products, fractions b, d, and e, are equivalent to 23.4 g. of starting material and represent a yield of 45% of the theoretical.

Attempted Condensation of Ethyl Isobutyrate with Methylmalonic Ester.—To one-half mole of sodium ethoxide was added one mole (174 g.) of methylmalonic ester. (The alcohol formed was removed at 50° under diminished pressure.) To this was added two moles (232 g.) of ethyl isobutyrate and the mixture refluxed for ten hours. The amounts of the various products isolated were: 195 g. of ethyl isobutyrate (107–110°); 126 g. of methylmalonic ester (194–196°); 7 g. of monoethyl methylmalonate [100–110° (2 mm.)].

Reaction of Methylene Dimalonic Ester with Sodium Ethoxide.—A mixture of one-half mole of sodium ethoxide and one-half mole (166 g.) methylene dimalonic ester, prepared according to Welch,[12] was heated at 110–115° for eight hours. During this period of heating 11.6 g. of alcohol distilled out. The pressure was then reduced to 400 mm. and 2.8 g. of ethyl carbonate distilled over. The reaction mixture was decomposed with 35% sulfuric acid, cooled, and the $Na_2SO_4 \cdot 10H_2O$ filtered off. Fractionation of the filtrate yielded (a) 21.2 g. of a fraction, b. p. 80–110°, composed of a mixture of alcohol and ethyl acrylate which from saponification values contained 7.6 g. of ethyl acrylate; (b) 12.2 g. of malonic ester, b. p. 195–198°; (c) 13.2 g. α-carbethoxyglutaric ester, b. p. 149–151° (7 mm.);[13] (d) 15.2 g. of starting ester, methylene dimalonic ester, b. p. 150–153° (2 mm.). The undistilled residue from this run amounted to 78 g.

Preparation of Pentamethylene Dimalonic Ester.—This was prepared according to the method of Perkin[14] except that the sodiomalonic ester was prepared in benzene. The ester, boiling 194–199° (1 mm.), was obtained in 24% yield.

Reaction of Pentamethylene Dimalonic Ester with Sodium Ethoxide.—Sixty two grams (0.14 mole) of pentamethylene dimalonic ester was heated with 0.08 mole of sodium ethoxide at 120–130° for eight hours. During this time 2.2 g. of alcohol distilled from the reaction. The reaction mixture was treated with 35% sulfuric acid and after filtering off the $Na_2SO_4 \cdot 10H_2O$ the filtrate fractionated. Fraction (a) 5 g., b. p. 115–125°, was ethyl azelate; sap. equiv. 131 (calcd. 122), m. p. of derived azelaic acid 105–106° and its *p*-phenylphenacyl ester 145–146°;[15] fraction (b) 10 g., b. p., 125–150°; fraction (c) 17.8 g., b. p. 150–165°; fraction (d) 12.2 g., b. p. 165–170°.

The acids derived from (d) were decarboxylated to determine the amount of α-carboxyazelaic acid, a compound which has not been described previously. The carbon dioxide obtained when the acids from (d) were heated indicated that the mixed acids from (d) contained 67% α-carboxyazelaic acid. The acid remaining after the evolution of the carbon dioxide was azelaic acid.

Considerable evolution of carbon dioxide was observed during the isolation of the acids from fractions (b) and (c). This indicates that these fractions were also mixtures of ethyl azelate and ethyl α-carbethoxyazelate.

Decamethylene dimalonic ester was prepared by reaction of decamethylene bromide with a benzene suspension of sodiomalonic ester.[16] All material boiling below 160° (0.2 mm.) was removed. The residue, which could not be readily distilled, amounted to 36% of the theoretical yield.

Reaction of Decamethylene Dimalonic Ester with Sodium Ethoxide.—Two hundred twenty-nine grams of the residue obtained above was heated with one-half mole

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(9) *Cf.* Marguery, *Bull. soc. chim.*, [3] **33**, 542 (1905).

(10) Conrad and Bischoff, *Ann.*, **204**, 144 (1880).

(11) Crossley and LeSueur, *J. Chem. Soc.*, **77**, 92 (1900).

(12) Welch, *ibid.*, 673 (1931).

(13) Emery, *Ber.*, **24**, 282 (1891).

(14) Perkin, *J. Chem. Soc.*, **65**, 92 (1894).

(15) Drake and Sweeney, THIS JOURNAL, **54**, 2059 (1932).

(16) Franke and Hankam, *Monatsh.*, **31**, 177 (1910).

of sodium ethoxide at 130° for six hours. During this time, only 3.2 g. of alcohol distilled from the reaction. On working up the reaction mixture in the manner described for the other dimalonic esters nothing could be distilled from the reaction product even at 230° and under 0.4 mm. pressure. This product, which was much more viscous than the starting material, was probably an intermolecular condensation product, and was not investigated further.

Summary

A study of the behavior of methylmalonic ester, isopropylmalonic ester, methylene dimalonic ester, pentamethylene dimalonic ester and decamethylene dimalonic ester with sodium ethoxide has been made. The main reaction product in the cases of the monosubstituted malonic esters was the dialkylmalonic ester resulting from self-alkylation of the starting esters. There was no evidence of an intermolecular condensation product in either case.

With the methylene dimalonic esters no intramolecular condensation could be effected. When the reaction products could be identified they were found to be decomposition products, resulting from retrograde Michael reactions and decarboxylation, of the starting esters.

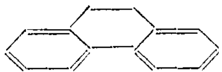
MADISON, WISCONSIN RECEIVED OCTOBER 20, 1936

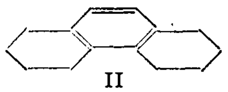
[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

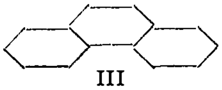
Hydrogenation of Phenanthrene

BY JOHN R. DURLAND AND HOMER ADKINS

Three substances, 9,10-dihydrophenanthrene[1,3] (I), 1,2,3,4,5,6,7,8-octahydrophenanthrene[2,3,4] (II), and tetradecahydrophenanthrene[5] (III), have been made by the catalytic hydrogenation of phenanthrene. Incidental to an investigation of the relation of structure to the hydrogenation of certain phenanthrene derivatives we have developed procedures for the preparation of these compounds which may be of immediate value to others.


I


II


III

Burger and Mosettig took advantage of the greater activity of copper–chromium oxide[6] toward olefinic double bonds as compared with benzenoid nuclei[7] and selectively hydrogenated phenanthrene at 220°, obtaining 9,10-dihydrophenanthrene in yields of about 80%. We have duplicated their results. However, with a purer sample of phenanthrene we have obtained no dihydrophenanthrene at 220°. With this purer sample of phenanthrene we have been able to hydrogenate in the 9,10-position with copper–chromium oxide at 130° within four hours, as compared with the eight to ten hours at 220° reported by Burger and Mosettig. The best temperature for the production of 9,10-dihydrophenanthrene with copper–chromium oxide appears to be about 150°, the yield being 87%. At 180° a little octahydrophenanthrene was produced, while at 220° the latter is produced to the exclusion of the dihydro compound.

The fact that phenanthrene may be hydrogenated in the 9,10-position over copper–chromium oxide at 130° is rather striking evidence of the olefinic character of the double bond in that position. Copper–chromium oxide is not usually active toward any type of unsaturation at temperatures much below 130°.

With pure phenanthrene, Raney nickel may also be used for the preparation of dihydrophenanthrene. When the reaction was carried out at 96°, a 61% yield was obtained after five hours. However, nickel is not so satisfactory as copper–chromium oxide for this selective hydrogenation. With copper–chromium oxide there is a difference of about 50° between the temperature at which hydrogenation begins in the 9,10-position and the temperature required for further hydrogenation. With Raney nickel the temperature differential for these two types of reaction is no more than 10°. These facts are indicated by a com-

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(1) Burger and Mosettig, THIS JOURNAL, **57**, 2731 (1935); **58**, 1857 (1936).

(2) Van de Kamp and Mosettig, *ibid.*, **57**, 1107 (1935).

(3) Schroeter, *Ber.*, **57**, 2025 (1924); Schroeter, Müller and Huang, *ibid.*, **62**, 645 (1929).

(4) Ipatieff, *ibid.*, **41**, 999 (1908).

(5) Pinkney and Marvel, THIS JOURNAL, **58**, 976 (1936).

(6) Connor, Folkers and Adkins, *ibid.*, **54**, 1138 (1932).

(7) Adkins and Connor, *ibid.*, **53**, 1091 (1931).