

Malon-*p*-phenetidic Acid and Some of its Derivatives

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Malon-*p*-phenetidic acid, its ethyl ester, amide, and hydrazide have been prepared. By condensing the acid with appropriate aldehydes, benzylidenemalon-*p*-phenetidic acid, cinnam-*p*-phenetidide, 2-thenal-malon-*p*-phenetidic acid, 2-thenal-acryl-*p*-phenetidide, γ -trichlorocroton-*p*-phenetidide, and *N*-*p*-ethoxyphenylacrylamide have been obtained. The effect of various condensing agents like pyridine, pyridine acetate, piperidine, piperidine acetate, glacial acetic acid, and polyphosphoric acid on these condensations has been studied. The $\alpha\beta$ -dibromo and the dihydro derivatives of benzylidenemalon-*p*-phenetidic acid and cinnam-*p*-phenetidide have also been prepared.

By the action of malonic ester on primary aromatic amines, several derivatives of malonic acid can be prepared. Recently, the three malon-chloroanilic acids¹, malon-3,4-xylydic acid², malon-*p*-iodoanilic acid³, and malon-2, 5-xylydic acid⁴ have been obtained in this laboratory. The method followed was similar to the one recommended by Chattaway and Olmsted⁵ for the preparation of malon-*o*-toluidic acid. Presence of a reactive methylene group in these compounds makes them valuable intermediates in the synthesis of several substances, some of which have found important practical applications.

The present communication deals with the preparation of malon-*p*-phenetidic acid, its ethyl ester, amide, and hydrazide. By condensing malon-*p*-phenetidic acid with appropriate aldehydes, benzylidenemalon-*p*-phenetidic acid, cinnam-*p*-phenetidide, 2-thenal-malon-*p*-phenetidic acid, 2-thenal-acryl-*p*-phenetidide, γ -trichlorocroton-*p*-phenetidide, and *N*-*p*-ethoxyphenylacrylamide have been obtained. These condensations were carried out in presence of condensing agents like pyridine, pyridine acetate, piperidine, piperidine acetate, glacial acetic acid, and polyphosphoric acid.

From benzylidene-malon-*p*-phenetidic acid and cinnam-*p*-phenetidide, the corresponding dihydro derivatives were prepared by reduction with sodium amalgam and the corresponding $\alpha\beta$ -dibromo derivatives by bromination in glacial acetic acid.

The use of malon-*p*-phenetidic acid in the synthesis of substituted coumarins and the use of the acid hydrazide as a reagent for detection of carbonyl compounds are under investigation.

1. George and Ittyerah, *Agra Univ. J. Res. (Sci.)*, 1955, **4**, 299.
2. Chellappa and Ittyerah, this *Journal*, 1953, **30**, 387.
3. Asthana and Ittyerah, *Agra Univ. J. Res. (Sci.)*, 1963, **12**, 81.
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5. *J. Chem. Soc.*, 1910, **97**, 938.

EXPERIMENTAL

Malon-p-phenetidic Acid and Malon-di-p-phenetidide.—A mixture of *p*-phenetidine (5 g.) and freshly distilled diethyl malonate (8.8 g.) was gently refluxed for 1 hr., allowing the alcohol formed to escape and the ester to flow back. While still warm, ethanol (50 ml) was added, the mixture, stirred well, and cooled. Malon-di-*p*-phenetidide crystallised was filtered. It was further purified by recrystallisation from ethanol, m.p. 224°, yield 3.8 g. (Found: N, 8.50. $C_{19}H_{22}O_4N_2$ requires N, 8.69%).

To the ethanolic extract activated charcoal (0.2 g.) and sodium carbonate (5 g. in 50 ml water) were added and steam was blown through for 30 min. The solution after cooling was filtered and acidified with HCl (conc.). Malon-*p*-phenetidic acid separating as a white crystalline mass was filtered and purified by recrystallisation from aqueous ethanol, m.p. 150° (decomp.), yield 2.1 g. (Found: N, 6.13. $C_{11}H_{13}O_4N$ requires N, 6.27%).

Effect of variation in the duration of heating and in the molecular proportion of the amine and the ester was studied and it was found that maximum yield was obtained under the above conditions.

Ethyl Malon-p-phenetide.—In another experiment, after refluxing the mixture of diethyl malonate and *p*-phenetidine and removal of malon-di-*p*-phenetidide, the ethanolic extract was refluxed with animal charcoal for a few minutes and filtered. The filtrate on evaporation on a steam bath left a sticky mass which after several recrystallisations from petroleum (b.p. 80–100°) melted at 105°. This was identified to be ethyl malon-*p*-phenetide. (Found: N, 5.20. $C_{13}H_{17}O_4N$ requires N, 5.58%).

Malon-p-phenetidamide.—Ethyl malon-*p*-phenetide (2 g.), dissolved in ethanol (10 ml), was added slowly with stirring to liquor ammonia (25 ml) and the mixture kept overnight. The crystalline mass formed was filtered and recrystallised from ethanol in glistening plates, m.p. 165°, yield 1.6 g. (Found: N, 13.08. $C_{11}H_{14}O_3N_2$ requires N, 12.70%).

Malon-p-phenetidic Acid Hydrazide.—Hydrazine hydrate (2 ml, 80%) was added to a solution of ethyl malon-*p*-phenetide (2 g.) in ethanol (10 ml) and the mixture was left aside for 30 min. Some heat was evolved. The hydrazide separating as needle-shaped crystals was filtered and recrystallised from ethanol, m.p. 175°, yield 1.5 g. (Found: N, 17.50. $C_{11}H_{15}O_3N_3$ requires N, 17.72%).

Benzylidenemalon-p-phenetidic Acid and Cinnam-p-phenetidide.—A mixture of benzaldehyde (0.6 g.) and malon-*p*-phenetidic acid (1.1 g.) was heated on a steam bath for 4 hr. On extraction in the usual manner, 1.1 g. of benzylidenemalon-*p*-phenetidic acid was obtained. This after recrystallisation from ethanol melted with decomposition at 199°. (Found: N, 4.85. $C_{18}H_{17}O_4N$ requires N, 4.50%). A better yield of the acid (88%) could be obtained by using glacial acetic acid as the condensing agent.

In another experiment, when a trace of pyridine was used as the condensing agent, the only product obtained was cinnam-*p*-phenetidide which could be recrystallised from aqueous ethanol, m.p. 145°. [Found: N, 6.01; M.W. (Rast), 262. $C_{17}H_{17}O_2N$ requires

N, 5.24%; M.W., 267]. The maximum yield (80%) was obtained when pyridine acetate was used as the condensing agent.

Benzylmalon-p-phenetidic Acid.—To benzylidenemalon-*p*-phenetidic acid (1.5 g.), dissolved in minimum amount of an aqueous 10% solution of NaOH, was added sodium amalgam (60 g., 4%) gradually with stirring and HCl (conc.) was added simultaneously to neutralise the reaction medium. After addition, the beaker was set aside for an hour. The mercury was then tapped off, the aqueous layer filtered, cooled in ice, and acidified. The white crystalline precipitate (1.2 g.) was recrystallised from aqueous ethanol. The glistening white crystals, m.p. 184° (decomp.), did not decolorise either alkaline potassium permanganate or bromine water. (Found: N, 4.36. $C_{18}H_{19}O_4N$ requires N, 4.47%).

Hydrocinnam-p-phenetide, m.p. 128°, was obtained by reducing cinnam-*p*-phenetide with sodium amalgam. It could be recrystallised from aqueous ethanol and did not respond to the usual tests for unsaturation. (Found: N, 5.12. $C_{17}H_{19}O_2N$ requires N, 5.2%).

$\alpha\beta$ -*Dibromobenzylidenemalon-p-phenetidic acid*, m.p. 220°, was obtained by mixing equimolecular quantities of benzylidenemalon-*p*-phenetidic acid and bromine, both dissolved in minimum quantities of acetic acid. The mixture was set aside for 2 hr. and then diluted with water. The pale yellow precipitate obtained (0.8 g.) was crystallised from ethanol. (Found: Br, 33.70. $C_{18}H_{17}O_4NBr_2$ requires Br, 33.97%).

$\alpha\beta$ -*Dibromocinnam-p-phenetide*, m.p. 186°, was prepared by bromination of cinnam-*p*-phenetide in glacial acetic acid. The bromo compound, when recrystallised from ethanol, was obtained in colorless needles. (Found: N, 3.37; Br, 36.73. $C_{17}H_{17}O_2NBr_2$ requires N, 3.25; Br, 37.47%).

2-Thenal-malon-p-phenetidic Acid and 2-Thienylacryl-p-phenetide.—Both these were formed when an equimolecular mixture of 2-thiophenylaldehyde and malon-*p*-phenetidic acid were heated for 4 hr. on a steam bath in presence of a trace of piperidine acetate. These were separated by using sodium carbonate solution and extracted in the usual manner. The acid product, m.p. 234° (decomp.), could be recrystallised from ethanol in 28% yield. (Found: N, 4.76; S, 9.90. $C_{16}H_{15}O_4NS$ requires N, 4.41; S, 10.09%).

The non-acid product could be recrystallised from aqueous ethanol in colorless needles, m.p. 146°, yield 40%. (Found: N, 5.02. $C_{15}H_{15}O_2NS$ requires N, 5.12%).

With no condensing agent or in presence of pyridine, pyridine acetate or glacial acetic acid, only the acid product was obtained, whereas in presence of piperidine or polyphosphoric acid, the product was a mixture of the acid and the non-acid.

γ -*Trichlorocroton-p-phenetide*, m.p. 154°, was obtained in almost quantitative yield when an equimolecular mixture of chloral hydrate and malon-*p*-phenetidic acid in presence of a trace of pyridine was heated on a steam bath for 4 hr. Recrystallisation from ethanol furnished colorless needles. (Found: N, 4.66. $C_{11}H_{12}O_2NCl_3$ requires N, 4.53%).

N-p-Ethoxyphenylacrylamide.—Malon-*p*-phenetidic acid (1.1 g.), formalin (2 ml, 36%), and two drops of pyridine were mixed and heated at 50° for 4 hr. The semisolid mass

left on cooling was extracted with a solution of sodium carbonate. The residue when recrystallised from aqueous ethanol was obtained in colorless flakes, m.p. 110°. (Found: N, 7.63. $C_{11}H_{13}O_2N$ requires N, 7.33%).

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