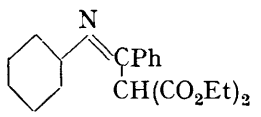
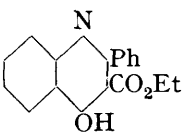
102. *Imidochlorides. Part III. Reaction of Anilide Imidochlorides and Ethyl Sodiomalonate.*

By R. C. SHAH and V. R. HEERAMANECK.

JUST condensed benzanilide imidochloride with ethyl sodiomalonate in ether and obtained ethyl mono- and di-(phenyliminobenzyl)malonate, the former (I) of which underwent ring closure on heating to give ethyl 4-hydroxy-2-phenylquinoline-3-carboxylate (II) (*Ber.*, 1885, **18**, 2623, 2632; 1886, **19**, 979, 1541; see also Seka and Feuchs, *Monatsh.*, 1931, **57**, 52).

(I.) 



(II.)

A substantial improvement of the method is the use of toluene as solvent and of ethyl malonate (1 mol.) together with its sodio-derivative (1 mol.), which minimises the formation of the dicondensation product. Crystalline monocondensation products have thus been obtained in good yields from various anilide imidochlorides, and cyclised to the corresponding quinolines, the yields of which are 30—40%, calculated on the imidochloride employed. The presence of substituents does not appear to influence appreciably the condensation or the cyclisation.

Cyclisation of (I) has also been effected by (i) phosphoryl chloride, which gives the carbethoxyquinoline, and (ii) concentrated sulphuric acid, which affords the quinoline-carboxylic acid.

The action of *p*-toluidine on (I) produces (*phenyliminobenzyl*)*malonodi*-p-*toluidide* at 110—120° and the p-*toluidide* of 4-hydroxy-2-phenylquinoline-3-carboxylic acid at 150°. Benzoylation of the sodium derivative of (I) affords *ethyl benzoyl*(*phenyliminobenzyl*)-*malonate*, which is not cyclised by heating.

The condensation product obtained from benzo-*m*-toluidide imidochloride gives on ring closure a mixture of *ethyl 4-hydroxy-2-phenyl*-5- and -7-*methylquinoline-3-carboxylate*, which are separable by fractional crystallisation.

Experimental.

Reaction of Benzanilide Imidochloride with Ethyl Sodiomalonate.—By Just's method, benzanilide imidochloride (10 g.) gave 2 g. of the monocondensation product, m. p. 75°, and 2 g. of the dicondensation product, m. p. 160°.

A solution of benzanilide imidochloride (150 g.; 1 mol.) in dry toluene was refluxed for 2 hours with a mixture of ethyl sodiomalonate (1 mol.), ethyl malonate (112 g.; 1 mol.), and toluene, and the whole mixed with water. The product extracted by ether was heated at 120—125°/30—40 mm. to remove toluene and the excess of malonic ester; the residual oil solidified at 0° and on crystallisation from alcohol gave 85 g. (38%) of ethyl (phenyliminobenzyl)malonate (I), m. p. 75°. No dicondensation product could be isolated. The product (I) was quantitatively converted at 150—170° into ethyl 4-hydroxy-2-phenylquinoline-3-carboxylate (II), m. p. 258—260° (Just, m. p. 260°) (yield 38%, calculated on the imidochloride employed), which was hydrolysed with aqueous-alcoholic sodium hydroxide to the carboxylic acid, m. p. 230—232° (Just, m. p. 232°).

Cyclisation of Ethyl (*Phenyliminobenzyl*)*malonate* (I) *by Phosphoryl Chloride and by Sulphuric Acid.*—(i) A mixture of (I) (2 g.) and phosphoryl chloride (16 c.c.) was refluxed for 1 hour, cooled, and poured on ice. The solid was washed with cold alcohol and crystallised from nitrobenzene, yielding 1·2 g. of (II), m. p. and mixed m. p. 259—260°. (ii) The compound (I) (2 g.) was mixed with concentrated sulphuric acid (8 c.c.) and kept at room temperature for a few days until a test portion gave an immediate white precipitate with water; the whole was then diluted with water. The precipitated acid crystallised from alcohol in colourless needles, m. p. and mixed m. p. with the carboxylic acid described above, 229—231°.

Action of p-*Toluidine on Ethyl* (*Phenyliminobenzyl*)*malonate* (I).—(i) The ester (0·5 g.) and *p*-toluidine (0·4 g.) were heated together at 110—120° for 4 hours and the cooled melt was treated with dilute hydrochloric acid. The oil obtained solidified (0·2 g.) and then crystallised from alcohol in needles of (*phenyliminobenzyl*)*malonodi*-p-*toluidide*, m. p. 208—210° (Found: N, 9·3. $C_{30}H_{27}O_2N_3$ requires N, 9·1%), soluble in hot methyl and ethyl alcohol and insoluble in hot chloroform and benzene. (ii) When the reaction was carried out at 150°, the product was the p-*toluidide* of *4-hydroxy-2-phenylquinoline-3-carboxylic acid*, crystallising from alcohol in needles, m. p. 255—257° (Found: N, 7·8. $C_{23}H_{18}O_2N_2$ requires N, 7·9%), and obtainable also from (II) and *p*-toluidine at 190—200° after 4 hours' heating.

Ethyl Benzoyl(*phenyliminobenzyl*)*malonate.*—An ethereal solution of (I) (5 g.) was slowly added to a mixture of pulverised sodium (0·5 g.) and dry ether, followed by a small excess of benzoyl chloride, the mixture refluxed for 2 hours, and dilute sodium hydroxide solution added. The *product* extracted by ether crystallised from benzene–light petroleum in colourless needles (3·5 g.), m. p. 156—158° (Found: N, 3·4. $C_{27}H_{25}O_5N$ requires N, 3·2%).

The following compounds were prepared by the methods described above and cyclisation was effected by heating, usually at 180—190°. The condensation products are easily soluble in common organic solvents, whereas the carbethoxyquinolines are only sparingly soluble; they were mostly crystallised from alcohol. The yields of the condensation products and quinolines given in parentheses are calculated on the imidochloride employed. By heating at a high temperature the mother-liquor from which the condensation product has been separated, a further small quantity of the quinoline can be obtained.

Ethyl (*phenylimino*-p-*nitrobenzyl*)*malonate* (45%), large, hard, monoclinic, highly refractive, yellow crystals with a blue fluorescence, m. p. 101° (Found: N, 7·2. $C_{20}H_{20}O_6N_2$ requires N, 7·3%); *ethyl 4-hydroxy-2-*(p-*nitrophenyl*)*quinoline-3-carboxylate* (38%), tiny, pale yellow needles, m. p. 239—241° (Found: N, 8·0. $C_{18}H_{14}O_5N_2$ requires N, 8·3%); the *carboxylic acid*,

needles (from acetic acid), m. p. 197—199° (efferv.) (Found: N, 9·5. $C_{16}H_{10}O_5N_2$ requires N, 9·0%).

Ethyl (phenylimino-o-chlorobenzyl)malonate (45%), monoclinic colourless crystals, m. p. 77° (Found: Cl, 9·3. $C_{20}H_{20}O_4NCl$ requires Cl, 9·5%); *ethyl 4-hydroxy-2-o-chlorophenylquinoline-3-carboxylate* (40%), colourless needles, m. p. 239—242° (Found: Cl, 11·2. $C_{18}H_{14}O_3NCl$ requires Cl, 10·8%); the *carboxylic acid*, colourless needles, m. p. 242—244° (Found: Cl, 12·2. $C_{16}H_{10}O_3NCl$ requires Cl, 11·9%). *Ethyl (p-nitrophenyliminobenzyl)malonate* (40%), lemon-yellow monoclinic crystals with a blue fluorescence, m. p. 103° (Found: N, 7·7. $C_{20}H_{20}O_6N_2$ requires N, 7·3%); *ethyl 6-nitro-4-hydroxy-2-phenylquinoline-3-carboxylate* (35%), light feathery crystals, m. p. above 300° (Found: N, 7·8. $C_{18}H_{14}O_5N_2$ requires N, 8·3%); the *carboxylic acid*, pale yellow needles (from acetic acid), m. p. 295—297° (Found: N, 9·2. $C_{16}H_{10}O_5N_2$ requires N, 9·0%). Ethyl (*o*-tolyliminobenzyl)malonate (35%), monoclinic crystals, m. p. 95° (Found: N, 4·1. Calc. for $C_{21}H_{23}O_4N$: N, 4·0%) (Just, *Ber.*, 1886, **19**, 1541, gives m. p. 95°); ethyl 4-hydroxy-2-phenyl-8-methylquinoline-3-carboxylate (30%), colourless needles, m. p. 242° (Found: N, 4·8. Calc. for $C_{19}H_{17}O_3N$: N, 4·6%) (Just, *loc. cit.*, gives m. p. 208·5°); the *carboxylic acid*, m. p. 201—203° (decomp.) (Found: N, 5·2. $C_{17}H_{13}O_3N$ requires N, 5·0%). *Ethyl (m-tolyliminobenzyl)malonate* (45%), colourless needles, m. p. 67—68° (Found: N, 4·2%); when heated, it gave a mixture (40%), m. p. 189—240°, separated by five crystallisations from ethyl acetate into sparingly soluble *ethyl 4-hydroxy-2-phenyl-(5 or 7)-methylquinoline-3-carboxylate*, m. p. 237—240° (Found: N, 4·6. $C_{19}H_{17}O_3N$ requires N, 4·6%), and easily soluble *ethyl 4-hydroxy-2-phenyl-(7 or 5)-methylquinoline-3-carboxylate*, m. p. 225—228° (Found: N, 4·8%); mixed m. p. 195—240°. *Ethyl (p-tolyliminobenzyl)malonate* (30%), colourless needles, m. p. 62—63° (described as a viscid oil by Just, *Ber.*, 1886, **19**, 979) (Found: N, 4·3%); ethyl 4-hydroxy-2-phenyl-6-methylquinoline-3-carboxylate (29%), m. p. 253—254° (Just gives m. p. 236°) (Found: N, 5·0. Calc. for $C_{19}H_{17}O_3N$: N, 4·6%); the *carboxylic acid*, needles, m. p. 209—211° (decomp.) (Found: N, 5·1. $C_{17}H_{13}O_3N$ requires N, 5·0%).

Benzo-o-chloroanilide imidochloride, prepared from benzo-*o*-chloroanilide (40 g.) and phosphorus pentachloride (41 g.), distilled at 214—215°/40 mm. Yield, 33 g. (Found: N, 5·5. $C_{13}H_9NCl_2$ requires N, 5·6%). It is easily soluble in all the common organic solvents. It was characterised by its amidine, prepared by Shah's modified method (*J. Indian Inst. Sci.*, 1925, **7**, 219). Aniline (2 g.) was slowly added to a mixture of freshly distilled diethylaniline (6 g.) and the imidochloride (2 g.), and the whole heated on the water-bath for 1 hour. Treatment with dilute hydrochloric acid gave the sparingly soluble hydrochloride, which on trituration with aqueous ammonia and alcohol gave *o'-chlorodiphenylbenzamidine*, which crystallised from alcohol in colourless needles, m. p. 113—114° (Found: Cl, 11·3. $C_{19}H_{15}N_2Cl$ requires Cl, 11·6%). The *hydrochloride*, obtained from the amidine and concentrated hydrochloric acid in glacial acetic acid, had m. p. 219—220° (Found: Cl, 20·8. $C_{19}H_{15}N_2Cl,HCl$ requires Cl, 20·7%). *Ethyl (o-chlorophenyliminobenzyl)malonate* (40%) formed colourless needles, m. p. 104—105° (Found: Cl, 9·7. $C_{20}H_{20}O_4NCl$ requires Cl, 9·5%), *ethyl 8-chloro-4-hydroxy-2-phenylquinoline-3-carboxylate* (32%) had m. p. 155—156° (Found: Cl, 11·0. $C_{18}H_{14}O_3NCl$ requires Cl, 10·8%), and the *carboxylic acid* m. p. 184—186° (Found: Cl, 11·8. $C_{16}H_{10}O_3NCl$ requires Cl, 11·9%).

Benzo-m-chloroanilide imidochloride, obtained from benzo-*m*-chloroanilide (45 g.) and phosphorus pentachloride (43 g.), distilled at 229—231°/50 mm. Yield, 35 g. (Found: N, 5·6%). m-*Chlorodiphenylbenzamidine* crystallised from alcohol in needles, m. p. 123—124° (Found: Cl, 11·3%), and its *hydrochloride* had m. p. 233—235° (Found: Cl, 20·6%). Ethyl (*m*-chlorophenyliminobenzyl)malonate, a viscous oil, on heating gave a product, m. p. 180—220°, from which, by fractional crystallisation from ethyl acetate, *ethyl (5 or 7)-chloro-4-hydroxy-2-phenylquinoline-3-carboxylate*, m. p. 234—237°, was isolated (Found: Cl, 10·5. $C_{18}H_{14}O_3NCl$ requires Cl, 10·8%).

Ethyl (p-chlorophenyliminobenzyl)malonate (35%) melted at 75° (Found: Cl, 9·5%), *ethyl 6-chloro-4-hydroxy-2-phenylquinoline-3-carboxylate* (30%) at 251—252° (Found: Cl, 11·1%), and the *carboxylic acid* at 300° (Found: Cl, 11·6%).

The work is being extended to the condensation of anilide imidochlorides with β-diketones and β-ketonic esters.

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ROYAL INSTITUTE OF SCIENCE, BOMBAY. [*Received, November 18th*, 1935.]