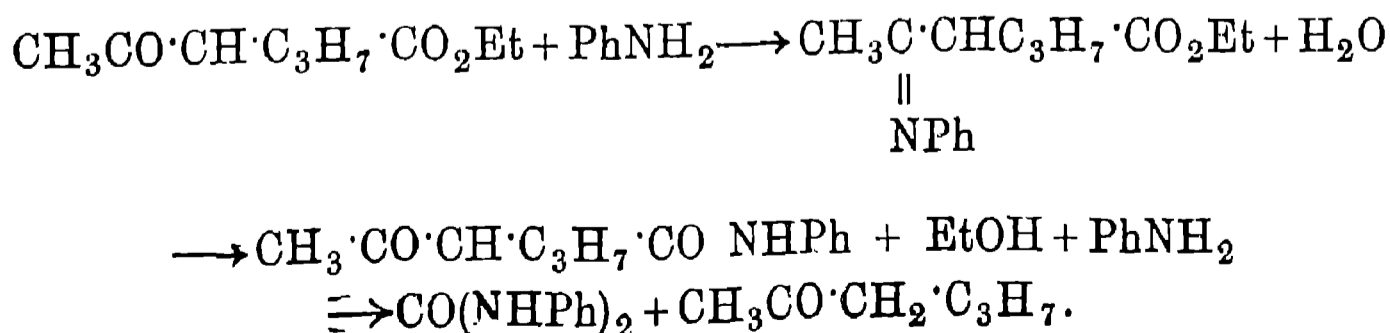


Condensation of Ethyl Propylacetoacetate with Aromatic Amines. Part I.

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Although the condensation of ethyl (or methyl) acetoacetate with various aromatic amines has been worked out, chiefly by Knorr (*Ber.*, 1883, 16, 2593; 1884, 17, 542), Conrad and Limpach (*Ber.*, 1888, 21, 521, 1654), Ewins and King (*J. Chem. Soc.*, 1913, 103, 106), no systematic work has been done to observe the effect of substitution of the methylene hydrogen atoms on such condensations. Knorr (*Annalen*, 1889, 245, 358) obtained methyl acetoacetanilide from ethyl methylacetoacetate and aniline, while Kermack and Smith (*J. Chem. Soc.*, 1931, p. 221) reported the formation of a compound $C_{21}H_{28}O_2N_4$ as a result of the interaction of *p*-anisidine and ethyl methylacetoacetate. Foglino (*Ann. Chem. Pharm.*, 1898, 26, 535) on the other hand obtained substituted carbamides from *p*-phenetidine and various substituted ethyl acetoacetates. Guareschi (*Chem. Zentr.*, 1905, 11, 685) describes *n*-propylacetoacetamide.

The present work was undertaken to examine the effect of substitution of the methylene hydrogen atom and also to prepare substituted quinoline derivatives. It has been found that the interaction of ethyl *n*-propylacetoacetate and aromatic amines (*viz.*, aniline, *o*-, *m*- and *p*-toluidines, *o*- and *p*-anisidines, *m*-xylydines (1:4:5 and 1:3:4) and *p*-phenetidine leads to the formation of the corresponding anilide, $MeCO \cdot CH \cdot C_3H_7 \cdot CONHR$ or the substituted carbamide $CO(NHR)_2$ or both. The carbamide invariably is formed and its yield increases with the duration of heating. This can be explained according to Hurst and Thrope (*J. Chem. Soc.*, 1915, 107, 934) as follows:



The carbamides are also formed on boiling the anilides with an excess of the appropriate amines.

The constitution of the carbamides was confirmed by preparing them according to Mistry and Guha (*J. Indian Chem. Soc.*, 1930, 7, 793) and finding their mixed melting point.

In the case of carbamide it was further confirmed by boiling it with acetic anhydride and fused sodium acetate when acetanilide was obtained.

EXPERIMENTAL.

Diphenyl Carbamide.—The mixture of ethyl *n*-propylacetoacetate (10 g.) and aniline (5 g.) was refluxed with an air condenser for about an hour. The red liquid was then put on a water-bath to remove the alcohol formed in the reaction. The crystalline solid obtained on cooling was triturated and washed with benzene, till it was free from the unaltered substances. It was crystallised from acetic acid, m.p. 235-36°. (Found: N, 13.18. $C_{13}H_{12}ON_2$ requires N, 13.21 per cent.).

The substance was also prepared according to Mistry and Guha (*loc. cit.*) and the mixed m. p. was found to be identical.

Some of the diphenyl carbamide obtained from ethyl *n*-propylacetoacetate was boiled with acetic anhydride and anhydrous sodium acetate and when the reaction mixture was diluted, a solid was obtained having m.p. 113-14°. It was proved to be acetanilide by mixed melting point.

n-Propylacetoacetanilide—The benzene filtrate from the above preparation was evaporated to dryness and the solid obtained was drained at the pump and dried on a porous plate, as it was found easily soluble in most organic solvents, *viz.*, alcohol, chloroform, petroleum ether, methyl alcohol etc. It was finally crystallised from dilute acetic acid (1:1), m.p. 96-97°. (Found: N, 6.03. $C_{13}H_{17}O_2N$ requires N, 6.39 per cent.).

The same procedure was followed in subsequent preparations, the ester and the respective amines being taken in molecular proportions. Carbamide derivatives were found to be insoluble in benzene, the anilides being soluble. The constitution of carbamide derivatives in the case of *p*-anisidine, *o*-anisidine *m*-xylylidine (1:3:4) and (1:4:5) and *p*-phenetidine was determined by preparing the compounds according to Mistry and Guha (*loc. cit.*) and by observing the mixed melting points which were found identical.

Di-o-tolyl Carbamide.—The heating was done for only half an hour and the solid was crystallised from dilute acetic acid, m.p. 246-47°. (Found: N, 11.26. $C_{15}H_{16}ON_2$ requires N, 11.67 per cent.).

n-Propylacetoacet-o-toluidide.—The solid obtained from benzene filtrate was crystallised from dilute acetic acid, m.p. 105-106°. (Found: N, 6.30. $C_{14}H_{19}O_2N$ requires N, 6.0 per cent.).

Di-p-tolyl carbamide was prepared and purified as in the above case, m.p. 262-63°. (Found: N, 11.29. $C_{15}H_{16}ON_2$ requires N, 11.67 per cent.).

n-Propylacetoacet-p-toluidide was crystallised from dilute acetic acid, m.p. 112-13°. (Found: N, 6.2. $C_{14}H_{19}O_2N$ requires N, 6.0 per cent.).

Di-m-tolyl carbamide was crystallised from alcohol, m.p. 220°. Cossack (*Ber.*, 1879, 12, 1449) gave 217° while Gattermann and Cantzler (*Ber.*, 1892, 25, 1089) gave 203°. Found: N, 11.35. $C_{15}H_{16}ON_2$ requires N, 11.67 per cent.).

Di-p-anisidyl Carbamide.—The heating was done for an hour and the product was crystallised from glacial acetic acid, m.p. 232-33°. Lossen (*Annalen*, 1875 175, 295) recorded m.p. 232-34°. (Found: N, 10.31. $C_{15}H_{16}O_3N_2$ requires N, 10.29 per cent.).

n-Propylacetoacet-p-anisidide—The solid from benzene filtrate was washed with petroleum ether and crystallised from dilute acetic acid, m.p. 115°. (Found: N, 5.44. $C_{14}H_{19}O_3N$ requires N, 5.62 per cent.).

Di-o-anisidyl Carbamide.—After heating the mixture as above, it was left at room temperature for four days, when crystals began to appear. It was then put inside a refrigerator for about twenty four hours for complete crystallisation after washing as usual, it was finally crystallised from dilute acetic acid, m.p. 185-86°. Conard and Limpach (*loc. cit.*) gave m.p. 182°. Mühlhäuser (*Annalen*, 1881 207, 244) gave 174°. (Found: N, 9.72. $C_{15}H_{16}O_3N_2$ requires N, 10.29 per cent.).

Di-m-xylidyl Carbamide (1:3:4).—Heating was done for only twenty minutes. It was crystallised from glacial acetic acid, m.p. 239-40°. (Found: N, 10.62. $C_{17}H_{20}ON_2$ requires N, 10.45 per cent.).

n-Propylacetoacet-m-xylidide (1:3:4).—The solid was first washed with petroleum ether and finally crystallised from dilute

alcohol, m.p. 100-101°. (Found: N, 5.92. $C_{15}H_{21}O_2N$ requires N, 5.66 per cent.).

Di-m-xylidyl carbamide (1:4:5) was prepared and crystallised as in the case of (1:3:4), m.p. above 275°. (Found: N, 10.17. $C_{17}H_{20}ON_2$ requires N, 10.45 per cent.).

n-Propylacetoacet-m-xylidide (1:4:5) was washed as in the case of (1:3:4), m.p. 113-14°. (Found: N, 5.86. $C_{15}H_{21}O_2N$ requires N, 5.67 per cent.).

Di-p-phenetidyl Carbamide.—The mixture was heated for an hour. The solid was crystallised from glacial acetic acid, m.p. 226°, (Fogolino, *loc. cit.*). (Found: N, 9.66. $C_{17}H_{20}O_3N_2$ requires N, 9.33 per cent.).

n-Propylacetoacet-p-phenetidide.—It was washed with petroleum ether and finally crystallised from dilute acetic acid, m.p. 115°. (Found: N, 5.57. $C_{15}H_{21}O_3N$ requires N, 5.32 per cent.).

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