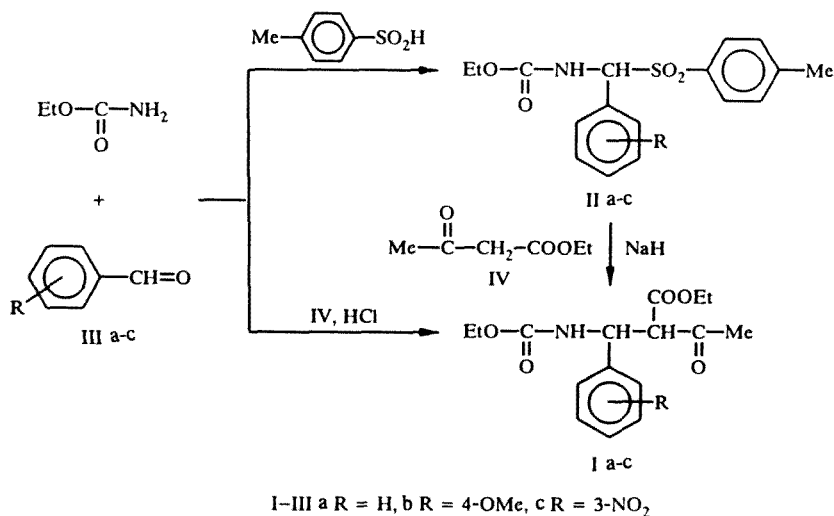


SYNTHESIS OF N-ETHOXYCARBONYL- β -AMINOKETONES — KEY INTERMEDIATES FOR THE PREPARATION OF NITROGEN-CONTAINING HETEROCYCLES

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We previously developed a new and effective method for the construction of pyrimidine rings, based on the α -aminoalkylation of 1,3-dicarbonyls with readily accessible α -arylsulfonyl substituted thioureas [1]. The products of this reaction, β -oxoalkylthioureas, spontaneously cyclized to the corresponding 4-hydroxyhexahydropyrimidin-2-thiones. We used an analogous approach in the present work to synthesize N-ethoxycarbonyl- β -aminoketones (Ia-c) which are key intermediates for the preparation of a variety of nitrogen-containing hydrogenated heterocycles of the pyrimidine, 1-3-oxazine and other series.



We have shown that α -(*p*-tolylsulfonyl)substituted carbamates (IIa-c) are readily formed in high yield by the reaction of ethyl carbamate with substituted benzaldehydes (IIIa-c) and *p*-toluenesulfonic acid in water. These compounds (IIa-c) react with the sodium derivative of the enol of acetoacetic ester in acetonitrile by nucleophilic displacement of the *p*-toluenesulfonyl group to give the required N-ethoxycarbonyl- β -aminoketones (Ia-c) in up to 75% yield.

Compound Ia was also obtained in 28% yield by reaction of ethyl carbamate with benzaldehyde and ethyl acetoacetate in boiling ethanol in the presence of hydrochloric acid.

The use of the carbamates I in the synthesis of heterocyclic compounds will be demonstrated in one of our forthcoming publications.

4-Phenyl-3-ethoxycarbonyl-4-ethoxycarbonylamino-2-one (Ia, C₁₆H₂₁NO₅). Yield 75% (from Ia). Mp. 98-99.5°C (3:1 ethanol-water). IR spectrum: 3350 (NH), 3065 3037 (=CH), 1737 (COOEt), 1714 (C=O), 1692 (amide I), 1589, 1497 (C=C), 1534 (amide II), 754, 700 cm⁻¹.

4-(*p*-Methoxyphenyl)-3-ethoxycarbonyl-4-ethoxycarbonylaminobutan-2-one (Ib, C₁₇H₂₃NO₆). Yield 63%. M.p. 88-89°C (petroleum ether). IR spectrum: 3355 (NH), 3058 (=CH), 1738 (COOEt), 1714 (C=O), 1689 (amide I), 1614, 1588 (C=C), 1535, 1514 (amide II), 826 cm⁻¹ (=CH).

4-(*m*-Nitrophenyl)-3-ethoxycarbonyl-4-ethoxycarbonylaminobutan-2-one (Ic, C₁₆H₂₀N₂O₇). Yield 44%. M.p. 98-100°C (3:1 ethanol-water). IR spectrum: 3345 (NH), 3069 (=CH), 1740 (COOEt), 1714 (C=O), 1688 (amide I), 1620 (C=C), 1547, 1533 (NO₂), 1531 (amide II), 808 cm⁻¹ (=CH).

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