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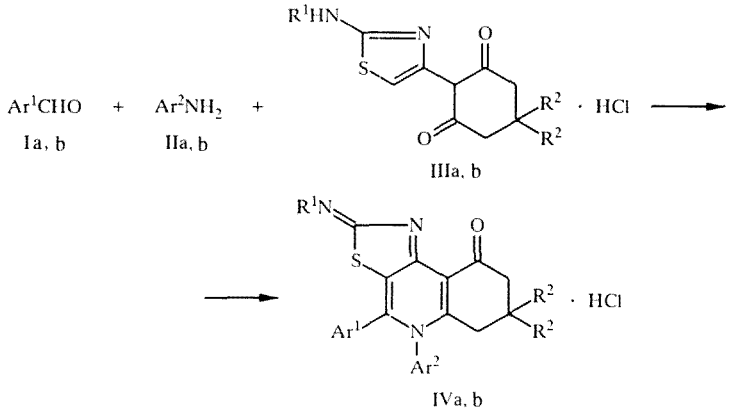
TRIPLE CONDENSATION OF 2-HETARYL-1,3-CYCLOHEXANEDIONES, AROMATIC ALDEHYDES AND ANILINES — A NEW APPROACH TO THE SYNTHESIS OF CONDENSED HETEROCYCLIC COMPOUNDS

O. V. Gulyakevich and A. L. Mikhal'chuk

The condensation of carbonyl compounds and their various derivatives with nitrogen bases is the basis of the synthetic methods for formation of the pyridine ring [1, 2]. Complex compounds with a given set of functional groups, which are, in essence, specially prepared fragments that may be fused in the final steps of the synthesis to give condensed heterocyclic structures, may be used [3]. The use of 2-hetaryl- and 2-aryl-1,3-dicarbonyl compounds in such reactions has not been reported.

In a continuation of previous work on the reaction of Schiff bases with β-dicarbonyl and β,β′-tricarbonyl compounds and their enol derivatives, we have found that 2-(4-thiazolyl)-1,3-cyclohexanediones condense with aromatic aldehydes and anilines to give thiazolo[c]quinoline. This reaction opens a fundamentally new area for the use of β-dicarbonyl compounds and is an extremely simple one-step approach to the synthesis of condensed heterocyclic compounds starting from 2-hetaryl- and 2-aryl-1,3-dicarbonyl compounds.

The condensation of benzaldehydes Ia and Ib with anilines IIa and IIb and 2-thiazolyl-1,3-cyclohexanediones IIIa and IIIb is carried out by heating their equimolar mixtures in alcohols in the presence of HCl at reflux. The desired thiazolino[c]quinolines IVa and IVb are formed in yields up to 45-50% as hydrochloride salts. The mechanism, limits of applicability, and optimization of the conditions for this reaction are presently under study.



I—IV a $Ar^1 = Ar^2 = R^1 = Ph$, $R^2 = Me$; b $Ar^1 = C_6H_4OMe$-4, $Ar^2 = C_6H_4Me$-4, $R^1 = R^2 = H$

Starting 2-thiazolyl-1,3-cyclohexanediones IIIa and IIIb were obtained according to our previous method [7]. The reactions were monitored by thin-layer chromatography on Silufol UV-254 plates with 8.5:1.0:0.5 chloroform—methanol—water as the eluent and development using UV light or iodine vapor with subsequent heating to 250-300°C. The melting points were determined on a Boetius heating block. The IR spectra were taken on a UR-20 spectrometer for KBr pellets. The electronic absorption spectra were taken on a Specord M-400 spectrophotometer for ethanol solutions. The mass spectra were taken on a Varian MAT-311 mass spectrometer.

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Hydrochloride Salt of 7, 7-Dimethyl-9-oxo-4, 5-diphenyl-2-phenylimino-6, 7, 8, 9-tetrahydrothiazolino-[5,4-*c*]-quinoline (IVa). A mixture of 0.51 ml (5 mmoles) benzaldehyde Ia, 0.65 g (5 mmoles) aniline hydrochloride IIa, and 1.63 g (5 mmoles) hydrochloride salt of 2-thiazolyldimedone IIIa in 20 ml ethanol was heated at reflux for 7 h in an argon atmosphere. The reaction mixture was then evaporated to half-volume and ether was added until slight turbidity was noted. The mixture was left for 24 h at +5°C. The precipitate was filtered off and recrystallized from 2:3 ethanol—ether to give 1.15 g (44.9%) IVa as bright yellow fine needles, mp 331-334°C. M 512.07, $[M - Cl]^+$ 476-477. IR spectrum: 3600-3200, 3100-2500, 1690, 1620-1590, 1565, 1500-1440, 1400, 1271, 1250, 1220, 760, 710 cm^{-1}. UR spectrum [λ_{max} (ε)]: 205 (45,750), 256 (21,100), 284 (12,400). 385 nm (14,350). Found: C, 70.28; H, 5.05, Cl, 7.00; N, 8.13; S, 6.19%. Calculated for $C_{30}H_{25}N_3OS \cdot HCl$: C, 70.37; H, 5.12; Cl, 6.72; N, 8.21; S, 6.26%.

Hydrochloride Salt of 2-Imino-5-(4-methylphenyl)-4-(4-methoxyphenyl)-9-oxo-6,7,8,9-tetrahydrothiazolino-[5,4-*c*]quinoline (IVb). A mixture of 0.3 ml (2.5 mmoles) aldehyde Ib, 0.27 g (2.5 mmoles) toluidine IIb, and 0.62 g (2.5 mmoles) hydrochloride salt of 2-thiazolyldihydroresorcinol IIIb in 20 ml 3% methanolic HCl was heated at reflux for 9 h in an argon atmosphere. The reaction mixture was then evaporated to two-thirds of its original volume and ether was added until slight turbidity was noted. The mixture was left for 48 h at from −5 to +5°C. The precipitate was filtered off and recrystallized from 1:2 ethanol—ether to give 0.55 g (50%) IVb as pale yellow flakes, mp >300°C (dec.), M 439.96, $[M - Cl]^+$ 404-405. IR spectrum: 3500-2600, 1693, 1630 sh, 1612, 1515, 1490, 1405, 1257, 1180, 1025, 845, 755 cm^{-1}. UV spectrum [λ_{max} (ε)]: 240 (26,240), 268.7 (20,790), 325 nm (22,150). Found: C, 62.67; H, 4.95; Cl, 8.17; N, 9.49; S, 7.31%. Calculated for $C_{23}H_{21}N_3O_2S \cdot HCl$: C, 62.79; H, 5.04; Cl, 8.06; N, 9.55; S, 7.29%.

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