

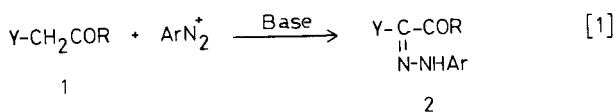
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Received May 13, 1981

Diazotized anthranilic acid and its methyl ester react with substituted phenacyl thiocyanates **3** to give in both cases the corresponding thiadiazolo[2,3-*b*]quinazolines **7a-e**. A mechanism is proposed and it is substantiated by alternate synthesis of **7a** from the hydrazidoyl chlorides **9a,b** and potassium thiocyanate.

J. Heterocyclic Chem., **19**, 73 (1982).

The reaction of aromatic diazonium salts with active methylene compounds **1** to give the corresponding hydrazone derivatives **2** has been extensively studied (1-4). In this communication we report the synthesis of the title



R = alkyl, aryl, OEt, NHR
Y = RCO, NC, ArSO₂, O₂N

compounds by coupling of diazotized anthranilic acid and its methyl ester with phenacyl thiocyanates. An examination of the literature reveals that coupling of active methylene thiocyanates has received little, if any, attention. In addition, the fused hetero tricyclic system **7** has not yet been reported.

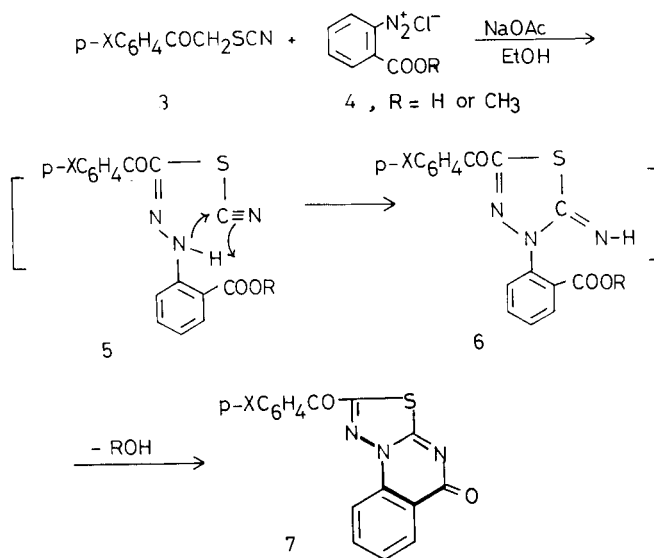
Results and Discussion.

Treatment of phenacyl thiocyanates **3a-e** with diazotized anthranilic acid in an ethanolic sodium acetate buffered solution yielded in each case, one isolable product, as evidenced by tlc, identified as thiadiazolo[2,3-*b*]quinazoline derivatives **7a-e**, respectively. Similar treatment of **3a-e** with diazotized methyl anthranilate gave identical products (ir, pmr, uv, mp and mixed mp) with **7a-e**. The structures of these products were inferred from their elemental and spectral analyses and independent synthesis. The infrared spectra of **7a-e** revealed the absence of bands due to SCN, NH and OH groups. They exhibited two characteristic bands near 1630 and 1680 cm⁻¹; in some cases only one broad band in the region 1630-1680 cm⁻¹ appeared. The pmr spectra of all compounds exhibited only the aromatic proton multiplet signal and no signal due to acidic proton appeared. This was confirmed by the observation that no change was noticed in the pmr spectra after shaking the sample solution with deuterium oxide. The ultraviolet spectra revealed, in each case, two intense maxima (log ε > 4) near 235 and 270 nm in ethanol.

To account for the formation of **7**, it is suggested that the reaction of **3** with diazotized anthranilic acid or its methyl ester leads to the formation of the hydrazone intermediate **5**. The latter undergoes spontaneous cycloaddition to give the iminothiadiazoline derivative **6** which

completes the reaction by the loss of water (in the case of **6**, R = H) or methanol (in the case of **6**, R = CH₃) to yield the final product **7** (Scheme 1).

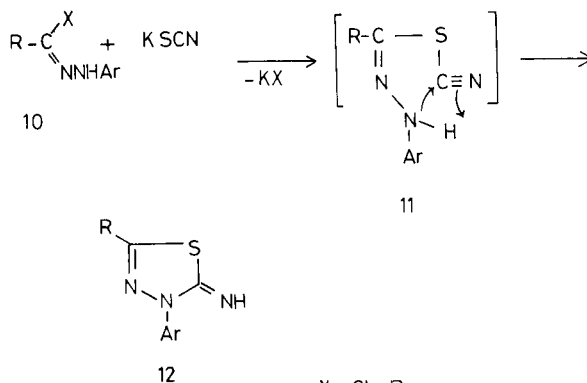
Scheme 1



a) X = H b) X = CH₃ c) X = Cl d) X = Br e) X = NO₂

To substantiate the involvement of **5** and **6** as intermediates in the present synthesis of **7**, the reaction of *C*-aroyl-*N*-(2-carboxyphenyl)hydrazidoyl chloride **9a** and its methyl ester analogue **9b** was studied. It is well known

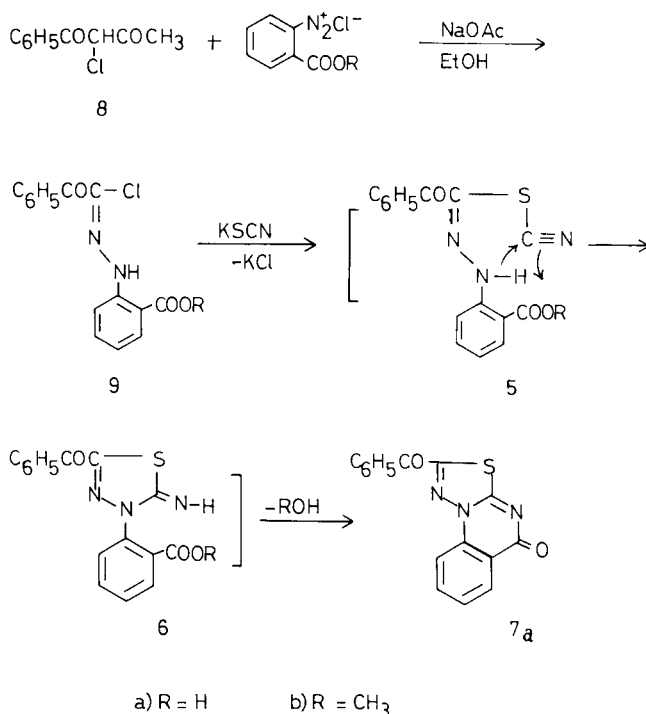
Scheme 2



X = Cl, Br
R = Alkyl, Aryl, Acyl or EtOOC-

that hydrazidoyl halides of type **10** react with potassium thiocyanate and give **12** in good yields (5-8). In no case were the intermediate α -thiocyanatohydrazones **11** isolated (Scheme 2). In our hands, treatment of **9a-b** (prepared by coupling of α -chlorobenzoylacetone with diazotized anthranilic acid and its methyl ester, respectively) with potassium thiocyanate in ethanol gave a product identical in all respects (spectra, mp and mixed mp) with **7a** obtained above from phenacyl thiocyanate and diazotized anthranilic acid or its methyl ester (Scheme 3).

Scheme 3



The reaction of phenacyl thiocyanates with diazotized anthranilic acid and its methyl ester appears to be an unequivocal method for the preparation of thiadiazolo[2,3-*b*]quinazoline derivatives. It is an efficient and rapid experimental procedure which requires only readily available starting materials.

EXPERIMENTAL

All melting points are uncorrected. Infrared spectra were recorded on a Beckman Acculab spectrophotometer, and ultraviolet spectra were obtained in ethanol using Cary 17 spectrophotometer. The ¹H nmr spectra in deuterated chloroform were recorded on a Varian T60A spectrometer using tetramethylsilane as an internal standard. Phenacyl thiocyanate and its ring substituted derivatives were prepared from the corresponding phenacyl bromide and potassium thiocyanate as previously described (10).

Thiadiazolo[2,3-*b*]quinazolines (**7a-e**).

General Procedure.

To a cold solution of the appropriate phenacyl thiocyanate (0.01 mole) and sodium acetate (1.3 g) in ethanol (50 ml) was added, dropwise a solution of diazotized anthranilic acid (or its methyl ester) (0.01 mole) while stirring. The addition took 30 minutes, after which stirring was continued for 3 hours. The solid formed was collected, washed with water and finally crystallized from dimethylformamide.

2-Benzoyl-5*H*-thiadiazolo[2,3-*b*]quinazolin-5-one (**7a**).

This compound was obtained in a yield of 75%, mp 235°; uv (ethanol): λ max (log ϵ) 335 (4.10), 267 nm (4.07).

Anal. Calcd. for C₁₆H₉N₃O₂S: C, 62.53; H, 2.94; S, 10.42. Found: C, 62.38; H, 2.88; S, 10.35.

2-*p*-Methylbenzoyl-5*H*-thiadiazolo[2,3-*b*]quinazolin-5-one, (**7b**).

This compound was obtained in a yield of 80%, mp 238°; uv (ethanol): λ max (log ϵ) 340 (4.14), 270 nm (4.81).

Anal. Calcd. for C₁₇H₁₁N₃O₂S: N, 13.07; S, 9.97. Found: N, 12.98; S, 10.00.

2-*p*-Chlorobenzoyl-5*H*-thiadiazolo[2,3-*b*]quinazolin-5-one (**7c**).

This compound was obtained in a yield of 78%, mp 239°; uv (ethanol): λ max (log ϵ) 339 (4.39), 274 nm (4.38).

Anal. Calcd. for C₁₆H₈ClN₃O₂S: N, 12.29; S, 9.38. Found: N, 11.89; S, 9.29.

2-*p*-Bromobenzoyl-5*H*-thiadiazolo[2,3-*b*]quinazolin-5-one (**7b**).

This compound was obtained in a yield of 76%, mp 256°; uv (ethanol): λ max (log ϵ) 340 (4.41), 275 nm (4.40).

Anal. Calcd. for C₁₆H₈BrN₃O₂S: N, 10.87; S, 8.30. Found: N, 10.68; S, 8.25.

2-*p*-Nitrobenzoyl-5*H*-thiadiazolo[2,3-*b*]quinazolin-5-one (**7e**).

This compound was obtained in a yield of 83%, mp 263°; uv (ethanol): λ max (log ϵ) 335 (4.13), 255 nm (4.00).

Anal. Calcd. for C₁₆H₈N₄O₄S: N, 15.89; S, 9.10. Found: N, 15.81; S, 9.08.

Preparation of Hydrazidoyl Chlorides (**9a,b**).

To a cold solution of α -chlorobenzoylacetone (1.96 g, 0.01 mole) (9) and sodium acetate (1.3 g) in ethanol (50 ml) was added dropwise while stirring a solution of diazotized anthranilic acid or its methyl ester (0.01 mole). Stirring was continued after the addition is complete for further 30 minutes and the reaction mixture was left overnight in a refrigerator. The solid formed was collected, and crystallized from ethanol.

C-Benzoyl-*N*-(2-carboxyphenyl)hydrazidoyl Chloride (**9a**).

This compound was obtained in a yield of 75%, mp 214°; ir (potassium bromide): 3300-2800 (OH, NH), 1670, 1652 (CO) cm⁻¹.

Anal. Calcd. for C₁₅H₁₁ClN₂O₃: C, 59.51; H, 3.66; Cl, 11.72. Found: C, 59.43; H, 3.59; Cl, 11.70.

C-Benzoyl-*N*-(2-methoxycarbonylphenyl)hydrazidoyl Chloride (**9b**).

This compound was obtained in a yield of 81%, mp 157-158°; ir (potassium bromide): 3200 (NH), 1670, 1700 (CO) cm⁻¹.

Anal. Calcd. for C₁₆H₁₃ClN₂O₃: C, 60.66; H, 4.13; Cl, 11.20. Found: C, 60.48; H, 4.09; Cl, 11.18.

Reaction of Hydrazidoyl Chlorides **9a,b** with Potassium Thiocyanate.

To a suspension of **9** (0.005 mole) in ethanol (30 ml) a solution of potassium thiocyanate (1 g, 0.015 mole) in water (10 ml) was added. The mixture was stirred for 4 hours at room temperature, then left overnight. The crude product formed was collected, washed with water and crystallized from dimethylformamide. The products obtained from **9a** and **9b** were identical in all respects with each other and with **7a** (mp, mixed mp and spectra).

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