

1,2,4-Triazolo[3,4-f][1,2,4]triazines

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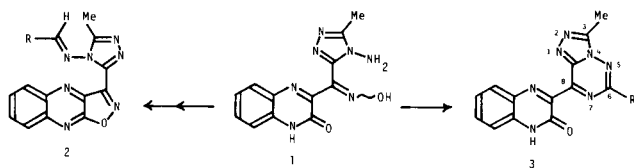
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Novel compounds 8-(quinoxalin-2-yl)-1,2,4-triazolo[3,4-f][1,2,4]triazines **3a,b** were obtained by a new annulation method in the 1,2,4-triazine synthesis.

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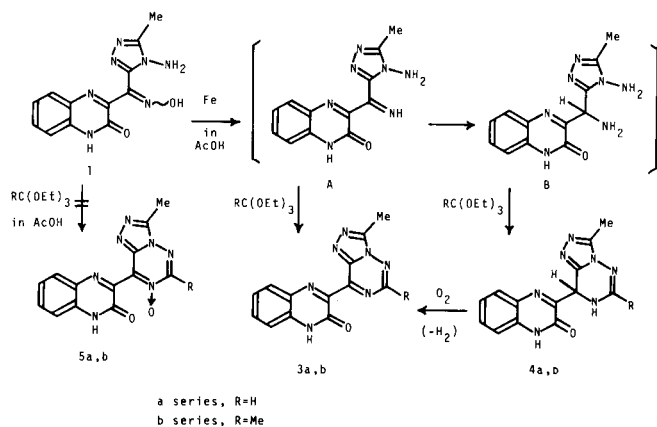
In a previous paper [1], we reported the synthesis of the oxime **1** and its facile cyclization into the isoxazolo[4,5-b]-quinoxalines **2** by dehydration between the quinoxaline and oxime moieties (Scheme 1). In continuation of this work, we also succeeded in the other type of one-step cyclization by insertion of the one-carbon moiety between the

Scheme 1



amino and oxime groups of **1**, giving 8-(3-oxo-3,4-dihydroquinoxalin-2-yl)-3-methyl-1,2,4-triazolo[3,4-f][1,2,4]triazine (**3a**) and 8-(3-oxo-3,4-dihydroquinoxalin-2-yl)-3,6-dimethyl-1,2,4-triazolo[3,4-f][1,2,4]triazine (**3b**). Namely, reduction of the oxime into the imino or amino group [2] would produce the intermediary ambident diamine **A** or **B** (Scheme 2), which easily incorporated the one-carbon moieties. Concerning the 1,2,4-triazolo[3,4-f][1,2,4]triazine ring system,

Scheme 2



only a report has been contributed by Becker *et al.* [3], who synthesized 6-substituted 8-oxo-7,8-dihydro-1,2,4-triazolo[3,4-f][1,2,4]triazines. The above successful cyclization enabled us to furnish novel 8-(quinoxalin-2-yl)-1,2,4-triazolo[3,4-f][1,2,4]triazines **3a,b**. In addition, the present annu-

lation method may be the first example in the 1,2,4-triazine synthesis [4]. This paper describes the convenient synthesis of the novel compounds **3a,b**.

The reactions of **1** with orthoesters (R = H, Me) and Fe powder in acetic acid afforded **3a,b** and the 7,8-dihydro-1,2,4-triazolo[3,4-f][1,2,4]triazines **4a,b**, while the absence of Fe powder did not provide the *N*-oxides **5a,b**, but recovered the starting material **1** (Scheme 2). The above 7,8-dihydro compounds **4a,b** were susceptible to oxidation, changing into **3a,b** during purification, and hence the production of **4a,b** had to be checked by high resolution mass spectrometry (ms). The molecular ion peaks of **4a,b** were observed as the base peaks [**4a**, Calcd. for C₁₃H₁₁N₇O 281.103, Found 281.103 (M⁺); **4b**, Calcd. for C₁₄H₁₃N₇O 295.118, Found 295.118 (M⁺)].

General Procedure.

A solution of **1** (2 g), the appropriate orthoester (20 ml), and Fe powder (2 g) in acetic acid (200 ml) was refluxed in an oil bath for 2 hours to precipitate yellow crystals of **4**, which were collected by suction filtration while hot [5]. A solution of the whole crystals **4** in DMF (100 ml) was refluxed in an oil bath for 30 minutes and then the solution was filtered. Removal of the solvent by evaporation *in vacuo* afforded yellow crystals of **3**, which were recrystallized from DMF/ethanol/*n*-hexane to provide yellow needles [**3a** (360 mg), **3b** (330 mg)].

Evaporation of the above filtrate (acetic acid solution) *in vacuo* gave yellow crystals, which were collected by suction filtration. Recrystallization from the same solvent system as the above afforded yellow needles **3** [**3a** (650 mg), **3b** (630 mg)]. Total yields, **3a** (56%), **3b** (47%).

Compound **3a** had mp 313-314° dec; ms: *m/z* 279 (M⁺); ir (potassium bromide): ν cm⁻¹ 1665, 1605; nmr (DMSO-d₆): δ 13.07 (brs, 1H, NH), 9.34 (s, 1H, C₆-H), 8.00-7.30 (m, 4H, aromatic), 2.80 (s, 3H, C₃-Me).

Anal. Calcd. for C₁₃H₉N₇O: C, 55.91; H, 3.25; N, 35.11. Found: C, 55.66; H, 3.23; N, 34.93.

Compound **3b** had mp 311-312° dec; ms: *m/z* 293 (M⁺); ir (potassium bromide): ν cm⁻¹ 1665, 1630, 1605; nmr (DMSO-d₆): δ 13.00 (brs, 1H, NH), 8.00-7.30 (m, 4H, aromatic), 2.77 (s, 6H, C₃- and C₆-Me).

Anal. Calcd. for $C_{14}H_{11}N_7O$: C, 57.33; H, 3.78; N, 33.43.
Found: C, 57.16; H, 3.96; N, 33.26.

REFERENCES AND NOTES

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[4] J. G. Erickson, P. F. Wiley and V. P. Wystrach, "The 1,2,3- and 1,2,4-Triazines, Tetrazines and Pentazines", A. Weissberger, ed, John Wiley and Sons, New York, London, Sydney, 1956, Vol 10, pp 44-132.

[5] The crystals of **4** were collected with a small amount of Fe powder.