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Note

Synthesis of a novel heterocyclic system: Oxazolo[2,3-*c*][1,2,4]benzotriazine

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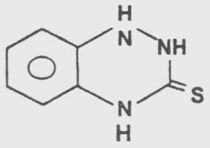
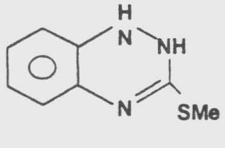
The synthesis of 10*H*-2-phenyloxazolo[2,3-*c*][1,2,4] benzotriazine **4**, a member of a new heterocyclic system, is described.

In continuation of our earlier studies on the orientation of cyclization in bicyclic compounds derived from 1,2,4-triazine[1-6], we now report in this communication our work on the synthesis of a novel heterocyclic system, oxazolo [2,3-*c*][1,2,4]benzotriazine **4**.

3-Thioxo-1,2-dihydro-1,2,4-benzotriazine **1**, obtained by the fusion of thiosemicarbazide with 1,2-diaminobenzene, was methylated by methyl iodide in the presence of sodium hydroxide to afford the corresponding 3-thiomethyl derivative **2**. Treatment of this compound with phenacyl bromide in the presence of triethylamine gave a single crystalline product (TLC).



(1)



(2)

The presence of a sharp band for carbonyl group in IR and the absence of M, M + 2 pattern in MS, characteristic for a monobromo compound and the exact mass measurement suggested the product to be a ketone. However, depending upon the nucleophilicity of nitrogen three structures, **3**,**3a** and **3b** are possible.

Treatment of the ketone with triethylamine for a long period gave a compound which was identified as 9*H*-2-phenyloxazolo [2,3-*c*][1,2,4]benzotriazine **4** from **3** or 5*H*-2-phenyloxazolo [3,2-*b*][1,2,4]benzotriazine **4a** from **3a**.

The structure of cyclized product as **3** was confirmed by the absence of the carbonyl band in IR and the accurate mass measurement. Further support for the cyclic structure for this TLC pure compound came from ^{1}H NMR spectrum. The signal at δ 6.65 (s, 1H, = CH) belonging to the oxazolo ring, thus corroborated the cyclic structure. The spectral data, however were not of much help in deciding in favour of either the angular product **4** or the linear product **4a**.

It has already been shown that in 1,2,4-benzotriazine N-4 is much more reactive than N-2. For this reason, structure **3** was assigned to the single product from the reaction of **2** with phenacyl bromide. Since **3** has now been considered as a precurssor, the cyclized product should have the structure **4** rather than **4a.** Compound **4** was also prepared in one-step using benzotriazine **1** and phenacyl bromide in an excess of triethylamine.

This ring system can be formed either by nucleophilic displacement of the thiomethyl group by the side chain in its ionized from or by hydrolysis of the thiomethyl group and subsequent cyclization. Compound **5** was prepared unambiguously by the hydrolysis of thiomethyl **2** but it did not undergo cyclization to the corresponding oxazolo[2,3- *c*] [1,2,4]benzotriazine **4**. The reaction proceeds as depicted in Scheme I.

Experimental Section

General. Melting points are uncorrected and were determined on a Kofler-Heizbank Richert 7841 melting point apparatus. IR spectra were obtained on a 4300 Shimadzu spectrometer. ^{1}H NMR spectra were recorded on a Varian 50 A spectrometer or a Brucker 80 AC spectrometer using TMS as internal reference (chemical shifts in

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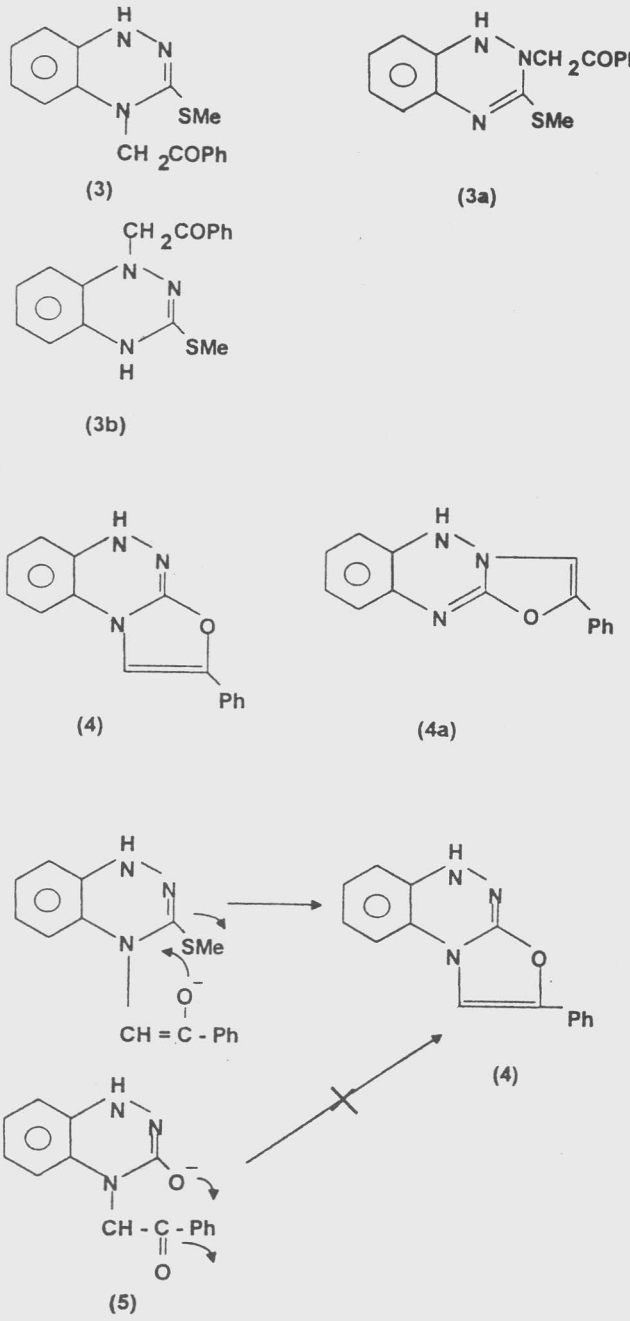

Scheme I

δ, ppm). Mass spectra were scanned on a Varian Mat CH-7 instrument at 70 eV.

3-Thiomethyl-1,2,4-benzotriazine 2. 3-Thioxo-1,2-dihydro-1,2,4-benzotriazine **1** (3g, 0.018 mole) was dissolved in 0.06*N* NaOH (300 mL). To this solution methyl iodide (1.2 mL, 0.018 mole) was added. The reaction mixture was stirred at room temperature for 4 hr. The precipitated solid was filtered, washed thoroughly with water and crystallized from EtOH to afford the title compound (1.08g, 56%), mp 194-96 °C, ^{1}H NMR (DMSO-d_6): 2.65 (s, 3H, CH_3), 7.1 (s, 4H, C_6H_4) (NH signals were not exhibited); MS (rel. intensity): m/z 179 (M^+, 10%), 152 (80), 129 (95), 119 (100), 111 (75), 89(23), 52(25); FIIR (KBr): 3100-3300 (NH), 1520, 1620, 1180 cm^{-1} (C-S); UV (DMSO): 323 mm.

1*H*-3-Thiomethyl-4-phenacyl-1,2,4-benzotriazine 3. Compound **2** (3.6, 0.02 mole) and phenacyl bromide (4g; 0.02 mole) were refluxed in a mixture of propan-2-ol (60 mL) and triethylamine (20 mole) for 1/2 hr. The solvent was evaporated and the obtained solid was thoroughly washed with water and crystallized from EtOH to yield the title compound **3** (5g, 54%), mp 119-21 °C, ^{1}H NMR (DMSO-d_6): 2.65 (s, 3H, CH_3), 5.4 (s, 2H, CH_2), 7.1 - 7.9 (m, 9H, C_6H_4 and Ph) (NH signal was not exhibited); MS: m/z, 297 (M^+); IR (KBr), 3051, 1700, 1394, 1234 cm^{-1}.

9*H*-2-Phenyloxazolo[2,3-*c*][1,2,4]benzotriazine 4. Compound **3** (1g, 0.003 mole) was refluxed in a mixture of propan-2-ol (30 mL) and triethylamine (20 mL) for 72 hr. The solvent was evaporated and the residue treated with water and crystallized from EtOH to yield the title compound **4** (0.54g, 60%), mp 227-29 °C; ^{1}H NMR (DMSO-d_6): 6.65 (s, 1H, =CH of oxazolo ring) 7.1-8 (m, 9H, C_6H_4 and Ph) (NH signal was not exhibited) ; MS: m/z 233 (M^+); IR (KBr): 3063, 1684, 1460, 1083 cm^{-1}.

Acknowledgement

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