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SYNTHESIS OF OXAZOLO [3, 2-b] 1, 2, 4-TRIAZINES A NOVEL HETEROCYCLIC SYSTEM

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Abstract

The synthesis of 6- methyl- 2- phenyl- 7H- oxazolo [3,2-b] 1,2,4- Triazine- 7- one (6, R=Ph) and its 2-*P*- bromophenyl analogue to the two members of a new heterocyclic system is described.

Introduction

Many compounds containing 1, 2, 4- triazine ring system have interesting pharmacological properties [1-5].

The literature survey disclosed no reference describing the preparation of oxazolo [3, 2-*b*] 1, 2, 4- triazine. Since oxazolo [3, 2-*b*] 1, 2, 4- triazines can be considered to be analogues of thiazolo [3, 2-*b*] 1, 2, 4- triazines and imidazo [1, 2-b] 1, 2, 4- triazines by virtue of [b] fusion of the five membered ring to the 1, 2, 4- triazine nucleus, they could be interesting from the view point of chemical reactivity and also biological activity.

Results and Discussion

The readily prepared 6- methyl- 1, 2, 4- triazin- 5 (4H)- one (**1**; R= SH) [6] was converted to its derivative (**1**; R= SMe) by action of methyl iodide [7]. Treatment of this compound with phenacyl bromide in the presence of triethylamine in propan- 2- ol gave a crystalline compound which was characterized as 6- methyl- 3- methylmercapto- 2- phenacyl- 1, 2, 4- triazin- 5 (4H)- one (2). The assigned structure was consistent with spectroscopic data and c, H, N analysis. But treatment of (1; R= SMe) with phenacyl bromide could also give the 4- phenacyl derivative **3** which is the isomer of **2**. Many spectroscopic aspects of **2** and **3** should be similar.

Key words: Oxazolotriazines, Novel Heterocycle

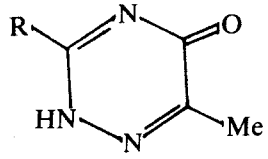
The structure of 2- phenacyl compound was established. This was done by comparison of the ultraviolet spectrum of the compound **2** or **3** with those of 2, 6- dimethyl- 3- methylmercapto- 1, 2, 4- triazin- 5 (4H)- one **4** and 4, 6- dimethyl- 3- methylmercapto- 1, 2, 4- triazin- 5 (4H)- one (**5**) [8] which have similar conjugated system to those of the two possible isomers **2** and **3** respectively. The ultraviolet spectrum of our N- condensed product **2** was similar to that of 2, 6- dimethyl- 1, 2, 4- triazine (**4**) which indicated the presence of the same cross conjugated bond system in the triazine ring.

Treatment of compound (**2**) with triethylamine for a long period of time gave the novel heterocyclic system, 6- methyl- 2- phenyl- 7H- oxazolo [3, 2-b] 1, 2, 4- triazin- 7- one. The second example of this new heterocyclic system (**6**; R= P- BrC_6H_4-) was made likewise by treating the same triazine with phenacyl bramide. Both compounds were also prepared in one step, using the same triazine and the α- haloketones, in excess triethylamine.

The ring system can either be formed by nucleophilic displacement of the methylmercapto group by side chain in its ionised form or by first hydrolysis of the methylmercapto group and subsequent cyclisation. The compound **7** was prepared unambiguously by hydrolysis of methylmercapto derivative **2** but did not undergo cyclisation to the corresponding oxazolo [3,2-b] 1, 2, 4- triazine (**6**, R= Ph). It seems likely that the reaction proceeds as depicted in Scheme I.

Scheme I

Ring cleavage of oxazolo [3,2-*b*] 1,2,4-triazin-7-ones, under acidic and basic conditions and their ring transformations with several amines have also been investigated.



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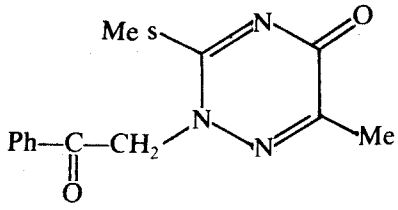

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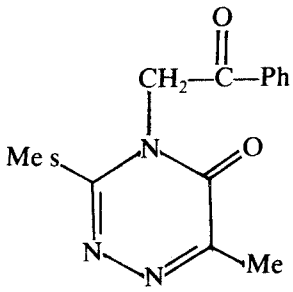

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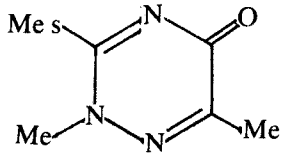

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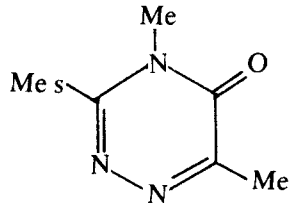

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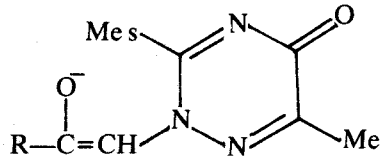
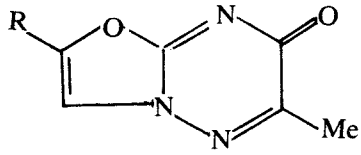
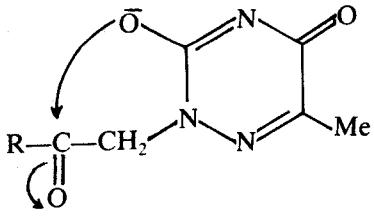




(6)



(7)

SCHEME 1

Experimental Section

Melting points were taken on a Kofler hot stage apparatus and are uncorrected. ^{1}H. N. M. R spectra were measured on a Perkin - Elmer R 32/90 MHZ model at normal temperature unless specified otherwise using tetramethylsilane as an internal standard. d_6 DMSO was used as solvent for all compounds. Infrared spectra were recorded using the Nujol mull technique on a Perkin- Elmer 297 double beam spectrometer. Mass spectra were recorded on an AEI MS 902 S mass spectrometer and U. V. spectra with a unicam SP 800 double beam UV/ visible spectrometer. Microanalysis were performed by Butterworth Laboratories LTD.

6- Methyl- 3- methylmercapto- 2- phenacyl- 1, 2, 4- triazin- 5- one

6- Methyl- 3- methylmercapto- 1, 2, 4- triazin- 5 (4H)- one (16 g) and phenacyl bromide (20 g) were refluxed in a mixture of propan- 2- ol (300 ml) and triethylamine (10 ml) for 2 hrs. The solvent was evaporated to dryness. The residue was dissolved in water (200 ml) and extracted with chloroform (3× 100 ml). The combined extracts were dried over $MgSO_4$ and evaporated to dryness. The residue was crystallised from ethyl acetate - light petroleum (b. P. 60-80°) to afford the title compound. (10.5 g; 37%). m. P. 159-160° [found; C, 56.76; H, 4.73; N, 15.19: M^+ (mass spectrum), 275. $C_{13}H_{13}N_3O_3S$ requires C, 56.71; H, 4.75; N, 15.26; M, 275] ^{1}H-N.M.R. δ[d_6- DMSO] 2.1 (s, 3H, Me), 2.45 (s, 3H, Me), 5.71 (s, 2H, CH_2), 7.9 (m, 5H, Ph); U. V. (H_2O) max, 274 nm.

6- Methyl- 2- phenyl- 7H- oxazolo [3, 2-b] 1, 2, 4- triazin- 7- one

6- Methyl- 3- methylmercapto- 2- phenacyl- 1, 2, 4- triazin- 5- one (2 g) was dissolved in propan- 2- ol (150 ml) and triethylamine (20 ml) was added. The reaction mixture was refluxed for 48 hrs and cooled to room temperature. The precipitated white solid was filtered, washed with ethanol and dried to yield the title compound (1 g; 60%), m. p. 281- 282° (from ethanol) [Found; C, 63.47; H, 4.08; N, 18.50, M^+ (mass spectrum) 297, $C_{12}H_9N_3O_2$ requires; C, 63.43; H, 3.99; N, 18.49; M, 227. ^{1}H. N. M. R. δ[d_6- DMSO] 2.21 (S, 3H, Me), 7.11 (s, 1H, CH), 7.45 and 7.75 (m, 5H, Ph).

2- *P*- Bromophenyl- 6- methyl- 7H- Oxazolo [3, 2-b] 1, 2, 4 - triazin - 7- one

6-Methyl- 3-methylmercapto- 1,2, 4-triazin-5 (4H)-one (2 g) and *P*- bromophenacyl bromide (3.45 g) were dissolved in a mixture of propan- 2- ol (150 ml) and triethylamine (30 ml). The reaction mixture was refluxed for 48 hrs and cooled to room temperature. The precipitated white solid was filtered, washed with water and dried to yield the title compound (1.7 g, 43%), m. p. 295- 296° (decomp) (from dimethylformamide). [Found; C, 47.20; H, 2.83; N, 13.46; M^+ (mass spectrum), 305 $C_{12}H_8N_3O_2Br$ requires; C, 47.08; H, 2.63; N, 13.73].

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