Vol.8 No.4
Autumn 1997

SYNTHESIS OF 1,2,4-TRIAZINO [3,4-c] [1,2,4] BENZOTRIAZINE, A NOVEL HETEROCYCLIC SYSTEM

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Abstract

3-Mercapto-1,2,4 benzotriazine (1) was methylated by methyl iodide in the presence of base to afford 1,2-dihydro-3-methylmercapto-1,2,4 benzotriazine (2). The latter was reacted with hydrazine hydrate to give the corresponding 3-hydrazine derivative (3). Compound (3) on condensation with phenacyl bromide gave 3-phenacyl hydrazino 1,2,4-benzotriazine (4). PPA cyclization of the ketone (4) yielded 1H, 2H, 10H-4-phenyl-triazino [3,4-c]-1,2,4-benzotriazine (5). Triazino benzotriazine (5) is a novel heterocyclic system and is reported for the first time.

Introduction

In continuation of our studies on the synthesis and structural elucidation of bicyclic compounds derived from 1,2,4-triazine [1-9], we wish to report in the present communication, the reaction of 3-hydrazino-1,2,4-benzotriazine with phenacyl bromide.

Results and Discussion

1,2-dihydro-3-mercapto-1,2,4-benzotriazine (1) obtained by the fusion of thiosemicarbazide with 1,2,-diaminobenzene [10] was methylated by methyl iodide in the presence of sodium hydroxide to give 1,2-dihydro 3-methylmercapto-1,2,4-benzotriazine (2).

We expected the compound to have the strucutre (2) rather than (2_a) because in (2), the double bond in trazine ring is in conjugation with the benzene ring whereas (2_a) has an isolated double bond. However, comparison of UV spectrum of compound (1) with that of compound (2) showed no differences. Therefore, the compound should have the structure (2_a).

Compound (2) was treated with hydrazine hydrate to afford, 3-hydrazino-1,2,4-benzotriazine (3)$\rightleftarrows$(3_a). When (3) was reacted with phenacyl bromide, a single product (TLC) was obtained (4)$\rightleftarrows$(4_a).

UV spectrum of (4) did not show any considerable difference from UV spectrum of (2) which is further evidence that the compound has structure (4_a).

The ketone (4) being unsymmetrical on cyclization was expected to yield 1H, 2H, 10H -4-phenyl-1,2,4-triazino [3,4-c] [1,2,4]-benzotriazine (5) or 1H, 2H, 5H-4-phenyl-1,2,4-triazino [4,3-b] [1,2,4]-benzotriazine (6) or both, depending upon the direction of cyclization. The ketone (4) however, on treatment with polyphosphoric acid underwent cyclization, giving a single compound confirmed by the absence of the carbonyl band in its IR spectrum.

Further support for the cyclic structure of this pure compound came from ^{1}H NMR spectra. The appearance of a signal at 6.8 (s,1H, = CH) and the disappearance of a

Keywords: Benzotriazine; Cyclization; Orientation; Triazinobenzotriazine

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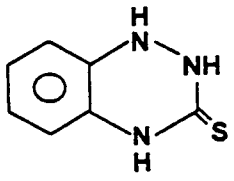
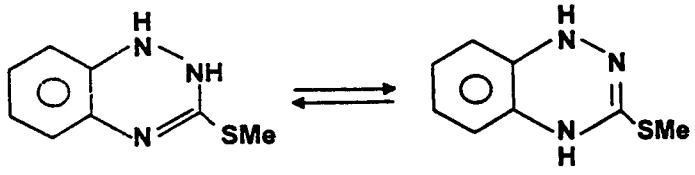


(1)



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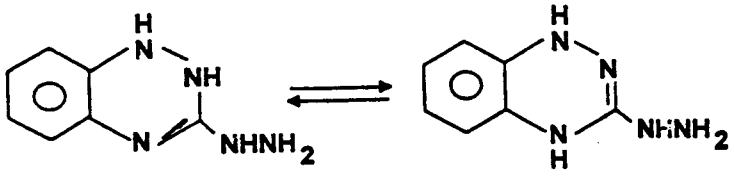

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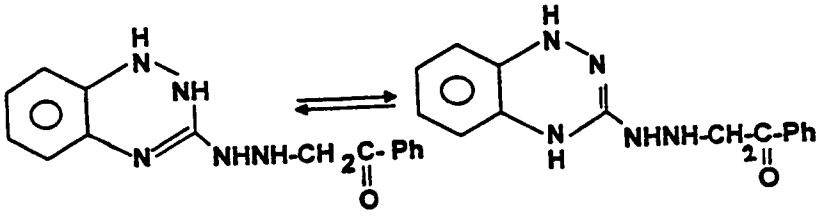
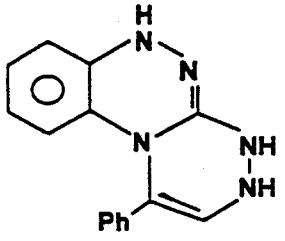


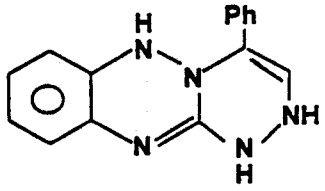
(4) (4a)

signal at 5.3 (s, 2H, CH_2) from the precursor (4), confirmed the cyclic structure. The ^1H NMR, IR, UV and mass spectral data were not of much help in deciding in favor of either product (5) or (6).

To establish the correct structure for cyclized compound (5) or (6), we have to decide which nitrogen in this asymmetric triazine is more nucleophilic and will attack the carbonyl carbon. To conclude this, we tried to synthesize a relevant model. Thus, 3-mercapto-1,2,4-benzotriazine-3-mercapto acetic acid (7) [10]. When this acid (7) was refluxed in a mixture of acetic anhydride and pyridine, cyclization was achieved giving a single product (TLC). Interpretation of ^1H NMR spectrum of this compound in the determination of the direction of cyclization can be crucial. In strucutre (9), all the aromatic protons (four protons) are expected to resonate in close proximity to each other, whereas in (8), H_a should be deshielded by the magnetic anisotropic effect of the carbonyl group in thiazolidone ring. As a result, H_a in (8) should resonate at down field in comparison to other aromatic protons [10]. ^1H NMR and ^{13}C NMR spectra of the cyclized product in CF_3 COOH were recorded.



(5)



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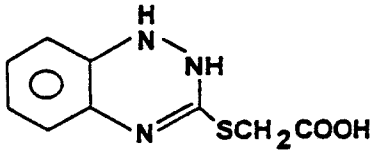

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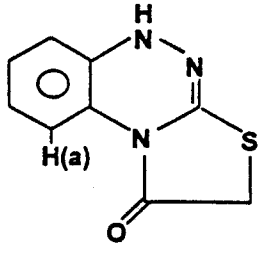

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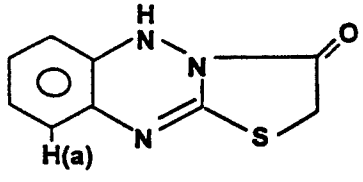

(9)

Aromatic protons of the cyclized product were separated in two signals with the difference of Ca.. 0.5 ppm. Three protons appeared at δ. 7.02 and one at δ. 7.65. This huge difference is due to the deshielding anisotropy of C= O on H_a, therefore, the compound should have structure (8). From this result we can conclude that in the 1,2,4-benzotriazine system (1) N_4 is more nucleophilic than N_2 and cyclization of ketone (4) has proceeded on N_4 giving (5) rather than (6).

Experimental Section

The melting points were obtained on a Kofler Heizband Richart type 7841 melting point apparatus and were uncorrected. The IR spectra were recorded on a 4300 Shimadzu spectrometer. The ^{1}H NMR spectra were performed on a Varian 50 A and a Bruker 80 AC spectrometer using TMS as internal reference; mass spectra were scanned on a Varian Matt CH-7 instrument at 70 eV. UV spectra were recorded on Beckman DU-6-spectrometers (UV-visible):

3-Methylmercapto-1,2,4-benzotriazine(2)

1,2-dihydro-3-methylmercapto-1,2,4-benzotriazine (1), (3 g, 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 h. The precipitated solid was filtered off, washed thoroughly with water and crystallized from EtOH to afford the title compound: yield 1.8 g., 56%, m.p. 194-196° C ^{1}H NMR δ (d6-DMSO), 2.65 (s,

3H, Me), 7.1 (s, 4H, C_6H_4), NH signals were not exhibited in the normal range, ms: m/z (rel) 179 (M^+ 10), 152 (80), 129 (95), 119 (100), 11 (75), 86 (23), 52 (25); FT-IR (KBr disk); 3300-3100, NH, 1920, 1520, 1180 C-S, cm^{-1}, UV (DMSO): λmax 323 nm.

1,2-Dihydro-3-hydrazino-1,2,4-benzotriazine

Compound (2) (1.79 g, 0.01 mol) and hydrazine hydrate (0.35 ml, 0.01 mole) in EtOH (100 mil was refluxed for 36 h. The volume of solvent was reduced to 10 ml and the precipitated solid was filtered off and crystallized from EtOH to give the title compound: yield 0.72, 44% m.p. 192-194°, ^1H NMR, (d6-DMSO), 2.5-2.8, (s, broad, 3H, NH_2, NH), 7.1 (s, 4H, C_6H_4), NH signals of the ring were not exhibited in normal range, ms, m/z (rel. intensity), 163 (M^+, 12), 161 (25), 129 (21), 83 (62), 69 (85), 56 (100), 43 (86) FTIR (KBr disk), 3500-3000, NH, NH_2, 1620, 1520 cm^{-1}, UV (DMSO) λmax 322 nm.

1, 2 - Dihydro - 3 - phenacyl hydrazino - 1, 2, 4-benzotriazine (4)

Compound (3) (1.63 g, 0.01 mol) and phenacyl bromide (1.99 g, 0.01 mol) were dissolved in EtOH (100 mil). The reaction mixture was refluxed for 8 h. The mixture was cooled down to room temperature and the precipitated solid was filtered off and crystallized from EtOH to afford the title compound: yield 1.94 g, 69%, m.p. 226-228 °C ^1H NMR, (d6-DMSO), 5.3 (s, 2H, CH_2) 7.2-8 (m, 9H, C_6H_4 and ph), ms, m/z, λ 281M^+, FTIR (KBr disk), 3100-2800 cm^{-1}. NH, 1700, C=O, 1600, 1540 cm^{-1} UV (DMSO) λmax 300 nm.

1H, 2H, 10H-4-phenyl-1,2,4-triazino [3,4-c] [1,2,4] benzotriazine (5)

A mixture of ketone (4) (2 g, 0.07 mol), phosphorus pentoxide (10 g) and orthophosphoric acid (7.5 mil) was heated to 170°C in an oil bath for 4 hours. The reaction mixture was cooled and basified with potassium carbonate. The solid thus obtained was crystallized from EtOH giving pale yellow crystals, identified to be the title compound: yield 0.99 g, 53% m.p. 130-131°C, ^1H NMR, δ (DC Cl_3), 6.8 (s, 1H = CH conjugated with benzene ring), 7.1-8 (m, 9H, C_6H_4, ph); m.s. m/z, (rel. intensity), 263 (M^+, very weak), 249 (100), 248 (99), 203 (65), 100 (77), 87 (70), 75 (80), 62 (32), 50 (37), FTIR (KBr disk), 3300-3600, NH, 1620, 1500 cm^{-1}, UV (DMSO) λmax 322 nm.

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