Synthesis and antibacterial activity of 3- substituted phenyl -5,7-dinitro-1,2,
4-triazolo-(3,4-b)-benzothiazole

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Abstract

2-hydrazino-4,6-dinitro benzothiazole (2) has been prepared by refluxing 2-amino-4,6-dinitro benzothiazole with hydrazine hydrate. Compound (2) condensed independently with benzaldehyde, 4-chloro benzaldehyde, 4-dimethylamino benzaldehyde, 2,4-dinitro benzaldehyde, 3-methoxy-4-hydroxy benzaldehyde to form corresponding hydrazone (3a-3e). These hydrazone heated with active MnO₂ to obtain cyclised 3-substituted-5, 7-dinitro-1,2,4-triazolo-(3,4-b)-benzothiazole. The structures of newly synthesized compounds were confirmed by elemental analysis and spectral analysis. The newly synthesized compounds were screened for their antibacterial activity.

Key Words : benzothiazole, hydrazone, triazolobenzothiazole, antibacterial activity.

Introduction :

Several five member aromatic system having three hetero atom at symmetrical position have been studied because of their interesting physiological properties. It is also well established that various derivatives of 1,2,4 triazole exhibit broad spectrum of pharmacological properties such as antibacterial & antifungal activities. The available therapeutically important medicines are terconazole, iterconazole, fluconazole & ribavirin etc are some of the example which contain one of these heterocyclic nucleus in view of the above mentioned fact & in continuation of our work on the synthesis of biological important heterocyclic compounds. Different methods were reported in the literature for the synthesis of triazole. Hence we synthesised some substituted triazole derivatives containing benzothiazole moiety. Therefore 2-amino-4,6-dinitro benzothiazole heated with hydrazine to obtained 2-hydrazino-4,6-dinitro benzothiazole 2. Compound 2 condensed with different aromatic aldehyde to afford corresponding hydrazone((3a-3e). These hydrazones were treated with active MnO₂ to form 3-substituted phenyl-5,7-dinitro-[1,2,4-triazolo-(3,4-b)] benzothiazole (4a-4e) & evaluated for their antibacterial activity.

Experimental:

All the melting points were determined in open capillary tube and may be uncorrected. The purity of compound was checked by TLC on silica gel coated glass plate. Infra-red spectra were monitored in Nujol / KBr palates on Bomen 104 FT infra-red spectrophotometer. 1HNMR spectra were obtained on a Gemani 200 Mz spectrometer with tetra methyl silane as an internal standard. Mass spectra were recorded on FTVG-7070H mass spectrometer using the EI technique at 70ev. Elemental analysis was performed on a Heraeus CHN-O rapid analyser.
Synthesis of 2-hydrazino-4,6-dinitro-benzothiazole (2):

Hydrazine hydrate (80%, 6 ml) was taken in 100ml R.B. and cooled to 5°C by keeping R.B. in ice bath. Concentrated HCl (4 ml) was added in drop wise fashion. The R.B. flask was kept at room temp for few minutes and then add 4 gm of 2-amino-4, 6-dinitro benzothiazole and 16 ml of ethylene glycol. The content of the flask heated on oil bath for 3hr maintaining temperature 140°C to 160°C. On filtered at pump washed with water and recrystallised by ethyl alcohol.

Yield : 3.2 gm , M.P. 112°C, IR (KBR) : 3452 cm⁻¹ (asymmetric N—H stretching in asymmetric) 3354 cm⁻¹ (N-H symmetric stretching, 3100 cm⁻¹ (N-N stretch)), 1584 (C= N Stretch), 1290 (C-N Stretch), Mass (m/e) : 255 (M⁺, 30%); Anal. Cal. For C₁₄H₆N₅O₄S, required C(48.98%) H(2.64%) N(20.40%) O (24.66%) S(8.24%) Found : C(38.35%) H(2.3%) N(20.72%) O(25.38%) S(8.35%)

Synthesis of 2-hydrazinoaryl-4,6-dinitro benzothiazoly1 hydrazone (3a-3e)

2-hydrazino-4,6-dinitro benzothiazole (0.01 M) and aryl aldehyde was dissolved in ethanol separately. Transferred these two solutions in a 100 ml round bottom flask and reflux on water bath for two hours. The reaction mixture was cooled and solid obtained was filtered at pump, washed with ethanol and recrystallised from hot benzene.

3a) Yield : 2.4 gm , M. P. : 2170°C, IR(KBr) : 3160 (N-N stretch), 1575 (C= N Stretch), 1292 (C-N Stretch), [Found : C: 47.90 %, H : 2.58%, N :20.33 %, S(9.30%), O(18.50%) S(9.10%) C₁₄H₆N₅O₄S, required C(48.98%) H(2.64%) N(20.40%) O(18.64%) S(9.34%)]

3b) Yield : 2.6 gm, M. P. : 218°C, IR(KBr) : 3155 (N-N stretch), 1570 (C= N Stretch), 1292 (C-N Stretch), [Found : C: 44.30 %, H : 2.10%, Cl : (9.20%), N :18.40 %, O : (18.50%), S(8.40%) C₁₄H₆ClN₃O₄S, required C(44.51%), H(2.13%), Cl(9.38%) N(18.54%) O(16.94%) S(8.49%)]

3c) Yield : 3.1 gm, M. P. : 216°C, IR(KBr) : 3202 (N-H stretch), 1575 (C= N Stretch), 1292 (C-N Stretch), [Found : C: 49.70 %, H : 3.60%, N :21.70 %, O : (16.50%), S(8.20%) C₁₄H₆N₅O₄S, required C (49.74%), H(3.65%), N(21.75%) O(16.56%) S(8.30%)]

3d) Yield : 2.4 gm, M. P. : 233°C, IR(KBr) : 3160 (N-N stretch), 1575 (C= N Stretch), 1292 (C-N Stretch), [Found : C: 38.70 %, H : 1.60%, N :22.50 %, O : (29.50%), S(7.20%) C₁₄H₆N₅O₄S, required C(38.81%), H(1.63%), N(22.63%) O(29.54%) S(7.40%)]

3e) Yield : 2.8 gm, M. P. : 244°C, IR(KBr) : 3448 cm⁻¹ (O-H stretching), 3200 cm⁻¹ (N-H stretching), 1575 (C= N Stretch), 1292 (C-N Stretch)Anal. [Found : C: 46.10 %, H : 2.70%, N :17.80 %, O : (24.50%), S(8.10%) C₁₄H₆N₅O₄S, required C(46.27%), H(2.85%), N(17.99%) O (24.66%) S(8.24%)]
Synthesis of 3-substituted phenyl-5,7-dinitro-1,2,4-triazolo-(3,4-b)-benzothiazole (4a-4e)

2-hydrazinoary-4,6 dintro-benzothiazolyl hydrazone was taken in 100 ml Round bottom flask and 20 ml anhydrous benzene added. The solution was refluxed on water bath for three hours with Attenburrow’s MnO$_2$ to obtain 3-(substituted phenyl)-5,7-dinitro-1,2,4-triazolo-[3,4-b]-benzothiazoles.

4a) Yield : 1.05 gm, M. P. : 143°C, IR(KBr) : 3160 (N-N) stretch), 1580 (C= N Stretch), 1292 (C-N Stretch).

[Found : C: 49.20 %, H : 1.90 %, O : (18.70 %), S(9.3 0%) C$_{14}$H$_{7}$N$_{5}$O$_{4}$S, required C(49.27 %), H(2.07 %), N(20.52 %) O (18.75 %) S(9.39 %)]

4b) Yield : 1.2 gm, M. P. : 136°C, IR(KBr) : 3150 (N-N stretch), 1575 (C= N Stretch), 1292 (C-N Stretch).

[Found : C: 44.70 %, H : 1.50 %, Cl : 9.30, N :18.50 %, O : (16.90 %), S(8.40 %) C$_{14}$H$_{6}$ClN$_{5}$O$_{4}$S, required C(44.75 %), H(1.61 %), Cl : (9.44 ) N(18.64 %) O (17.03 %) S(8.53 %)]

4c) Yield : 1.05 gm, M. P. : 194°C, IR(KBr) : 3145 (N-N stretch), 1570 (C= N Stretch), 1292 (C-N Stretch).

[Found : C: 49.90 %, H : 3.10 %, N :21.80 %, O : (16.50 %), S(8.20 %) C$_{14}$H$_{5}$N$_{5}$O$_{4}$S, required C(50.00 %), H(3.15 %), N(21.86 %) O (16.65 %) S(8.34 %)]

4d) Yield : 1.2 gm, M. P. : 154°C, IR(KBr) : 3160 (N-N stretch), 1575 (C= N Stretch), 1292 (C-N Stretch).

[Found : C: 38.90 %, H : 1.10 %, N :22.60 %, O : (29.50 %), S(7.30 %) C$_{14}$H$_{3}$N$_{5}$O$_{4}$S, required C(38.99 %), H(1.17 %), N(22.73 %) O (29.68 %) S(7.43 %)]

4e) Yield : 1.4 gm, M. P. : 168°C, IR(KBr) : 3279 cm$^{-1}$ broad O-H stretching band due to N-H stretching absent. 3160 (N-N stretch), 1575 (C= N Stretch), 1292 (C-N Stretch).

[Found : C: 46.10 %, H : 2.70 %, N :17.80 %, O : (24.50 %), S(8.10 %) C$_{15}$H$_{9}$N$_{5}$O$_{4}$S, required C(46.51 %), H(2.34 %), N(18.08 %) O (24.78 %) S(8.28 %)]
Result and Discussion:

The structures of these tricyclic triazolo benzothiazoles (6a–6f) were assigned on the basis of their elemental analysis and spectral data.

The hydrazones showed stretching absorption bands in IR spectra in the region 3450-3100 cm\(^{-1}\) due to –N-H stretching. The presence of broad singlet in their PMR spectra in the region \(\delta\) 2.5 to \(\delta\) 4.5 confirmed the presence of –NH proton. The mass spectrum of compound 3b shows molecular peak at 377 (M\(^+\)) which corresponds to molecular weight of the compound. The I. R. spectra of these triazolo benzothiazoles observed the absence of strong bands in the region 3450 cm\(^{-1}\) - 3100 cm\(^{-1}\) due to -NH stretching; however the absence of broad singlet in PMR spectra of these triazolo benzothiazole in the region \(\delta\) 2.5 - \(\delta\) 4.5 confirms the formation of cyclised products.
Antibacterial Activity

Procedure

The antibacterial activity is measured by agar cup method. Nutrient agar (HiMedia) was prepared and sterilized at 15 Psi for 15 min in the autoclave. It was allowed to cool below 45°C and seeded with turbid suspension of test bacteria separately, prepared for 24 hours old slant culture. 3% inocula were used every time. The bacterial cultures selected were, two gram negative cultures viz. Escherichia coli, Salmonella typhi and two gram positive cultures viz. Staphylococcus aureus, Bacillus Subtilis. This seeded preparations was then poured in sterile Petri plate under aseptic condition and allowed it to solidify.

Cup of 10mm diameter were bored in the agar plate with sterile cord borer. 100ul of compound solution preapared in Dimethyl Sulphoxide (1%) was added in cup under aseptic condition with the help of micro pipette. 100ul of DMSO was also placed in one of the cup of blank (Negative control) A standard antibiotic disk impregnated with 10 units of penicillin was also placed on the seeded nutrient agar surface at standard reference antibiotic (positive control).

The plates were kept in refrigerator for 15 min to allow diffusion of the compound from agar cup into the medium. The plates were shifted to incubator at 37°C and incubated for 24 hours.

After incubation plates were observed for the zone of inhabitation of bacterial growth around the agar cup. Results were recorded by measuring the zone of inhibition in millimeter (mm) using zone reder.

<table>
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<th>Sr. No.</th>
<th>Comp.</th>
<th>E.coli</th>
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</table>

Strong inhibition zone were found with compound 4b, 4e (11 mm) against against all pecies. While moderate inhibition zone were reported with compound 4c and low inhibition zone with compound 4a, 4d.

References

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