

SYNTHESIS AND BIOLOGICAL SCREENING OF SOME 6-(SUBSTITUTED ACRIDIN-9-YL AMINO)-2,3-DIHYDRO-3-THIOXO-[1,2,4] TRIAZOLO [4,3-f][1,2,4] TRIAZIN-8 (5H)-ONE.

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ABSTRACT

A new series of 6-(substituted acridin-9-yl amino)-2,3-dihydro-3-thioxo- [1,2,4] triazolo [4,3-f][1,2,4] triazin-8 (5H)-one were synthesized from the reaction of 9-chloro acridine and 6-amino-2,3-dihydro-3-thioxo-[1,2,4]triazolo[4,3-f][1,2,4]triazin-8(5H)-one. The structures of the compounds were confirmed by IR, ¹H NMR, Mass and CHN analysis. These compounds were evaluated for analgesic and diuretic activity.

Key words: triazolo triazinones, analgesic activity, diuretic activity.

INTRODUCTION

The chemistry of 1, 2, 4-triazoles and their fused heterocyclic derivatives has received considerable attention owing to their synthetic and effective biological importance. Among these heterocycles, the mercapto- and thione- substituted 1,2,4-triazole ring system have been well studied and so far a variety of biological activities have been reported for large number of their derivatives, such as anti bacterial¹, anti fungal², anticancer^{3,4} and hypoglycemic⁵ properties.

EXPERIMENTAL

Melting points were taken in open capillaries and are uncorrected. Purity of the compounds was checked by micro TLC using silica gel-G coated plates using chloroform and methanol (1: 1v/v) as irrigant and iodine vapour as detecting agent. The IR spectra of the compounds were recorded on Perkin-Elmer FT-IR using KBr pellet and PMR spectra wave recorded on Bruker AMX FT-NMR (400MHz) using TMS as internal standard and chemical shifts are reported in δ ppm. Mass spectra of the compounds were recorded by the direct inlet method using the UG micromass 70704 mass spectrophotometer and auto spec FAB + operating at 70 ev. Elemental analysis for C,H and N were performed on a PERKIN ELMER 240 elemental analyzer and were found to be within 0-4% of the theoretical values and physical properties are given in table-1.

6-(Substituted Acridin-9-yl amino)-2, 3-Dihydro-3-Thioxo-[1,2,4] Triazolo [4,3-f][1,2,4] Triazin-8 (5H)-One.

A mixture of 9-chloro acridines (0.001mol) and an equimolar amount of 6-amino-2, 3-dihydro-3-thioxo-[1, 2, 4] triazolo [4,3-f][1,2,4] triazin-8 (5H)-one (0.001mol) in dry DMF (10ml) containing 3drops TEA was stirred at room temperature for 2hrs, then heated under reflux for 16hrs.The mixture was then allowed to cool and water was added drop wise while stirring and cooling. The obtained precipitate was filtered and finally recrystallized from ethanol.

6-(acridin-9-ylamino)-2,3-dihydro-3-thioxo-(1,2,4)triazolo[4,3-f][1,2,4]triazin-8(5H)-one (3a):IR (KBr):3287 (N-H), 1715 (C=O), 1585 (C-N), 1068 (C=S). ¹H NMR (CDCl₃):δ7.42-8.02 (m, 8H,ArH). 6.4 (S,1H,N-H);MS:m/z,361. [Found:C,56.48,H,3.10,N,27.11 C₁₇H₁₁N₇OS requires C,56.50,H,3.07,N,27.13,O,4.43%].

6-(2-nitroacridin-9-ylamino)-2,3-dihydro-3-thioxo-[1,2,4]triazolo[4,3-f][1,2,4]triazin-8(5H)-one(3b): IR (KBr): 3262 (N-H), 1680 (C=O), 1520 (C=N), 1071(C=S), ¹H NMR (CDCl₃): δ 7.59-8.23 (m,7H,Ar-H), 6.9(S,1H,N-H); MS: m/z,406.[Found: C,50.21, H,2.45,N,27.60 C₁₇H₁₀N₈O₃S requires C,50.24,H,2.48,N,27.57 %].

6-(2-methoxyacridin-9-ylamino)-2,3-dihydro-3-thioxo-[1,2,4]triazolo[4,3-f][1,2,4]triazin-8(5H)-one(3c): IR (KBr) : 3281 (N-H), 1700 (C=O), 10873 (C=S), 1509 (C=N). ¹H NMR (CDCl₃): δ 7.3-8.05 (m, 6H,Ar-H). 6.8(S,1H,N-H); MS:m/z, 391. [Found: C,55.20, H,3.38,N,25.02 C₁₈H₁₇N₇O₂S requires C,55.23,H,3.35,N,25.05%].

6-(2_methoxy-7-nitroacridin-9-ylamino)-2,3-dihydro-3-thioxo-[1,2,4]triazolo[4,3-f][1,2,4]triazin-8(5H)-one(3d): IR (KBr) :3268 (N-H), 1581 (C=N), 1074 (C=S),1712 (C=O),¹H NMR (CDCl₃): δ 6.2 (S,1H,N-H), 3.73 (S,3H,OCH₃), 7.31 (S,1H,C4-H),7.92 (S,1H,C5-H),8.23(S,1H,C6-H); MS:m/z, 436.[Found:C,49.57, H,2.75,N,25.66 C₁₈H₁₂N₈O₄S requires C,49.54,H,2.77,N,25.68%].

6-amino-2,3-dihydro-3-thioxo-[1,2,4]triazolo[4,3-f][1,2,4]triazin-8(5H)-one **2** was prepared⁶ and refluxed with 9-chloro acridines in the presence of DMF containing TEA to get different 6-(substituted acridin-9-yl amino)-2,3-dihydro-3-thioxo-[1,2,4]triazolo[4,3-f][1,2,4]triazin-8(5H)-one (**3a-d**).The reactions leading to formation of different derivatives are outlined in scheme-1.Their structure were confirmed by IR,¹H NMR, Mass and CHN analysis.

Table-1: Details of Compound **3a-d**

Compound	R	R ¹	Yield (%)	M.P(°C)	R _f Value
3a.	H	H	91.63	Above 300	0.52
3b.	H	NO ₂	89.0	268	0.54
3c.	OCH ₃	H	65.2	232	0.37
3d.	OCH ₃	NO ₂	52.61	254	0.31

RESULT AND DISCUSSION

Analgesic activity

Synthesized compounds were evaluated for their analgesic activity by tail flick method⁸.Analgin was used as standard. Among the compounds tested, compound **3d** displayed significant analgesic activity.

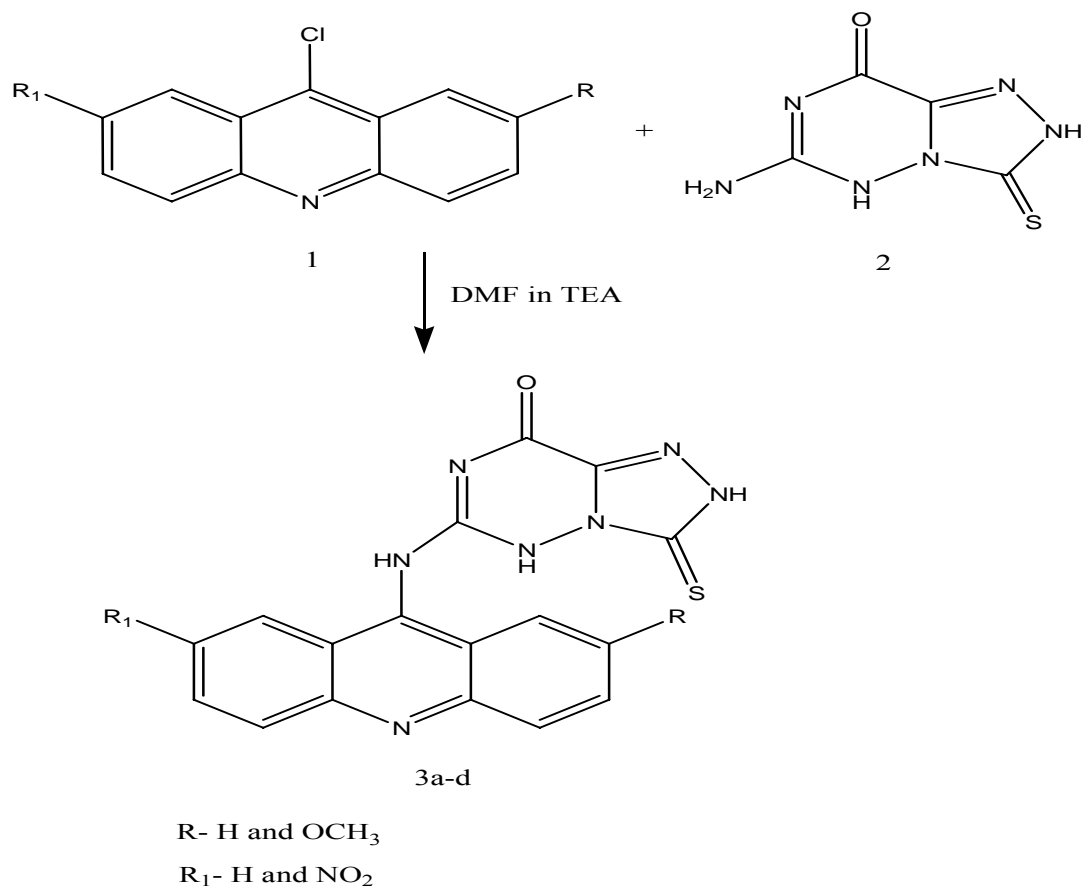
Diuretic activity

Albino rats of either sex weighing between 140-200gms were used to evaluate diuretic activity of some selected compounds hydrochlorothiazide was used as a standard drug at a dose of 5mg/kg body weight of albino rats. The test compounds were given at two dose levels (50 and 100mg/kg body weight) orally. Compounds **3b** and **3c** shown moderate diuretic activity.

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SCHEME-1



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