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Synthesis and anti-inflammatory activity of 6-(substituted acridin-9-yl amino)-2,3-dihydro -3-thioxo-[1,2,4] triazolo [4,3-*f*][1,2,4] triazin-8 (5*h*)-one

G. NAGARAJAN*, K.V.S. ANUSH, A. MAHESH, B.L.V.M. SPANDANA, K. SAMINATHAN, V. BALASUBRAMANIAM and K.S. MANJUNATH

*Department of Medicinal Chemistry,
Smt. Sarojini Ramulamma College of Pharmacy, Mahabub Nagar - 509 001 (India).

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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 (5*H*)-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(5*H*)-one. The structures of the compounds were confirmed by IR, ^{1}H NMR, Mass and CHN analysis. These compounds were evaluated for anti-inflammatory activity; compound 3b and 3c exhibited good anti inflammatory activity.

Key words: Antiinflammatory activity, compounds.

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 bacterial[1], anti fungal[2], anticancer[3], diuretic[4] and hypoglycemic[5] properties.

6-amino-2,3-dihydro-3-thioxo-[1,2,4]triazolo[4,3-*f*][1,2,4]triazin-8(5*H*)-one 2 was prepared[6] 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(5*H*)-one (3a-d).The reactions leading to formation of different derivatives are outlined in scheme-1.Their structure were confirmed by IR,^{1}H NMR, Mass and CHN analysis.

Anti-Inflammatory activity

The new synthesized compounds were evaluated for their anti-inflammatory activity in male albino Wistar rats (weighing 150-200 g) carageenan induced rat paw method. Indomethacin (10mg/kg, p.o.) was employed as standard drug. Anti-inflammatory activity study revealed that the compounds 3b and 3c with 2-nitroacridin-9-ylamino and 2-methoxyacridin-9-ylamino moieties, respectively, were found to possess significant anti-inflammatory activity.

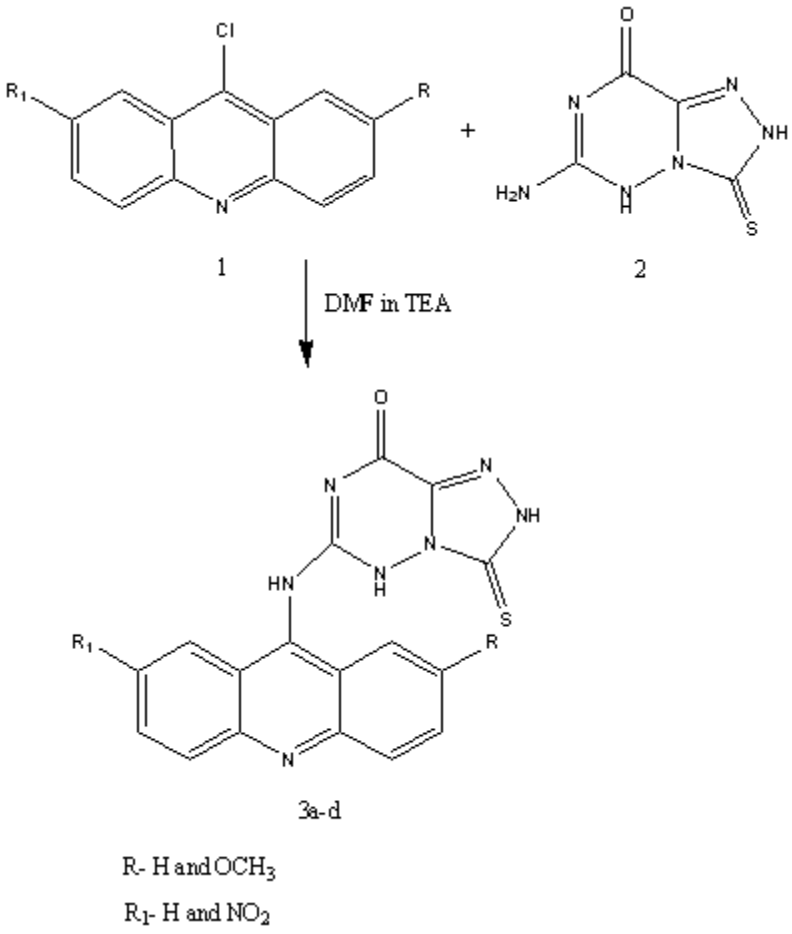
EXPERIMENTAL

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.

Table 1.

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



Scheme 1

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

IR (KBr):3287 (N-H), 1715 (C=O), 1585 (C-N), 1068 (C=S). ^{1}H 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 $C_{17}H_{11}N_7OS$ 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(5*H*)-one(3b)

IR (KBr): 3262 (N-H), 1680 (C=O), 1520 (C=N), 1071(C=S), ^{1}H 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 $C_{17}H_{10}N_8O_3S$ 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(5*H*)-one(3c): IR (KBr) : 3281 (N-H), 1700 (C=O), 10873 (C=S), 1509 (C=N. ^{1}H 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 $C_{18}H_{17}N_7O_2S$ 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(5*H*)-one(3d)

IR (KBr) :3268 (N-H), 1581 (C=N), 1074 (C=S),1712 (C=O),^{1}H NMR (CDCl3): ä 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 $C_{18}H_{12}N_8O_4S$ requires C,49.54,H,2.77,N,25.68%].

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