Asian Journal of Chemistry Vol. 4, No. 2 (1992), 197–200

Synthesis of a New Type of 5-Heteroaryl-3-Mercapto-4-Amino-1,2,4-Triazoles and their Derivatives

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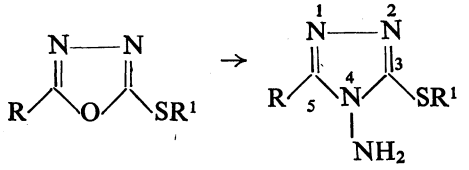
A series of 4-amino-3-substituted mercapto-5-aryl/heteroaryl-1,2,4-triazoles have been prepared by reaction of the corresponding 1,3,4-oxadiazoles with hydrazine hydrate in alcohol. The compounds have been screened for their antimicrobial properties.

INTRODUCTION

Compounds containing triazole rings have been found to possess fungicidal[1], bactericidal[2] and pesticidal[3] properties. Anticancer and antifungal activities have been displayed by a variety of heterocyclic sulfides[4]. Prompted by these observations, we wish to report here the synthesis of the title compounds starting with 5-aryl/heteroaryloxymethyl-2-mercapto-1,3,4-oxadiazoles(I) and their derivatives, synthesized earlier in these laboratories[5]. The treatment of (I) with ethanolic hydrazine hydrate at 50–60°C gave the corresponding 4-amino-3-substituted mercapto-1,2,4-triazoles (II).

Attempted alkylation and acylation of the 3-mercapto-4-amino-1,2,4-triazoles gave the corresponding *S*-alkylated and *S*-acylated products in low yields only. Better yields were obtained by starting with *S*-alkyl or *S*-acyl derivatives of 1,3,4-oxadiazoles and treating them with hydrazine hydrate in alcohol.



(I) (II)

It is interesting to note that the lactone moiety gets cleaved in case (IIg and IIh) at higher temperature.

EXPERIMENTAL

IR spectra were recorded on Perkin-Elmer 283 instrument. PMR spectra were recorded on a Varian A–90 D instrument using TMS as an internal standard (ppm), and mass spectra on a JMS–D 300 mass spectro-

meter at 70 eV. Melting points were uncorrected. Compounds were obtained in 45–65% yields.

4-Amino-3-Substituted Mercapto-5-Aryl Heteroaryl-1,2,4-Triazoles(II)

The corresponding 1,3,4-oxadiazole (0.01 mol), alcohol (60 ml) and hydrazine hydrate (0.01 mol) were refluxed for 3/2 hrs, cooled and acidified with dil. HCl. The precipitate was filtered, dried and recrystallised from a suitable solvent. Yield : 45–65%. The analytical and spectral data of these compounds are recorded in Table 1.

TABLE 1

PHYSICAL DATA OF 5-HETEROARYL-3-MERCAPTO-4-AMINO-1,2,4-TRIAZOLES AND THEIR DERIVATIVES (II)

Compound	R	R^1	M.pt.°C	% Nitrogen Found/(Calcd.)	% Sulphur Found/(Calcd.)
IIa	4-Methylcoumarin-7-yl-oxymethyl	H	117–119	18.51 (18.42)	10.50 (10.42)
IIb	,, ,,	CH_3	156–158	17.59 (17.61)	10.00 (10.06)
IIc	2,3-diphenylbenzofuran 6-yl oxy methyl	H	147–149	13.57 (13.52)	7.77 (7.72)
IId	,, ,,	C_2H_5	118–120	12.54 (12.66)	7.20 (7.24)
IIe	Benzoxazol-2-yl thio-methyl	H	141–143	25.16 (25.08)	22.90 (22.93)
IIf	,, ,,	C_2H_5	113–115	22.72 (22.80)	20.80 (20.84)
IIg	Coumarin-3-yl	H	214–216	21.58 (21.53)	12.27 (12.30)
IIh	,, ,,	$COCH_3$	134–136	18.50 (18.54)	10.90 (10.95)
IIi	4-Pyridyl	H	217–219	36.20 (36.26)	16.50 (16.58)
IIj	,, ,,	$COCH_3$	152–154	29.71 (29.78)	13.58 (13.61)

IIc ν_{max} (KBr) : 4550, 5150, 1600, 1075, 1055 and 750 cm^{-1}.
$\delta(CDCl_3)$: 3.5 (1H,s), 4.8 (2H, $-CH_2-$), 5.4 (d-NH_2), 7.8 (m, 13H, aromatic).
m/z : 4.14, 341, 325, 301, 286, 285, 154, 77.

RESULTS AND DISCUSSION

The IR (KBr/Nujol) bands for these compounds appeared at 2600–2550 cm^{-1} (C=S, SH stretching)[6,7], 3400 cm^{-1} and 3100 cm^{-1} (NH_2 and NH vibrations)[8,9] and 1200–1000 cm^{-1} (C=S and C—S—H tauto-

merism)[10,11]. Absorption patterns were noticed in the case of similar *S*-alkyl and *S*-acyl derivatives.

The ^1H NMR spectra of the compounds confirm the structures assigned. The –SH proton appears at δ 3.5 and —NH_2 at δ 6.0–7.0. The assignment of these signals was also confirmed by D_2O exchange. The characteristic signals for aryl/heteroaryl are also noticed in the anticipated region (δ 6–7).

The striking feature of the mass spectra of a few of these triazoles was the low abundance of the molecular ion and thus the base peak was not the molecular ion peak, but it was a fragment obtained by a series of cleavages. In all these compounds the ejection of the thiosemicarbazide ion was noticed. The prominent mass peaks appearing in the spectrum of IIa are m/z 304 (M^{+*}), 215 ($C_{12}H_9O_3$), 189 ($C_{11}H_9O_3$), 175 ($C_{10}H_7O_3$), 148 ($C_9H_8O_2$), 120 (C_8H_7O) and 91 (C_7H_7).

Antibacterial Activities

The antibacterial activity of these compounds was evaluated against *Bacillus megaterium* (Gram + ve) and *Proteus vulgaris* (Gram —ve) by the filter paper disc method at dose levels of 400 and 600 μg/ml. The activity of the compounds, when 5-substituent contained an ether link, was found to be low when compared to those of the corresponding thioether derivatives. Compound IIe is highly active at both these dose levels against *Bacillus megaterium* but less active against *Proteus vulgaris.* Compounds (IIa), (IIc) and (IIg) have no action at 400 μg/ml. Compound (IIc) is ineffective at both dose levels against the bacteria employed.

Antifungal Activity

The antifungal activities of these compounds were screened against *Drechslera speciferum* (brain) nicot and *Fusarium solani* (mart) app and woolen W by glass slides humid chamber technique. These compounds are less active at minimum dose level. Compound (IIg) is inactive against *Drechslera speciferum* but shows 100% inhibition at 840 μg/ml. The other compounds are inactive against both the fungi.

ACKNOWLEDGEMENT

Authors are thankful to the Principal, Regional Engineering College, Warangal for providing facilities.

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[*Received*: 5 March 1990; *Accepted*: 15 December 1990] AJC-251