

**SOME CHEMICAL ASPECTS OF 3-AMINO-1,2,4-TRIAZOLE**

**BY**

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**ABSTRACT**

3- Amino -1,2,4- Triazole undergoes a characteristic and condensation reactions, giving a new compounds which may have a biological activity.

**INTRODUCTION**

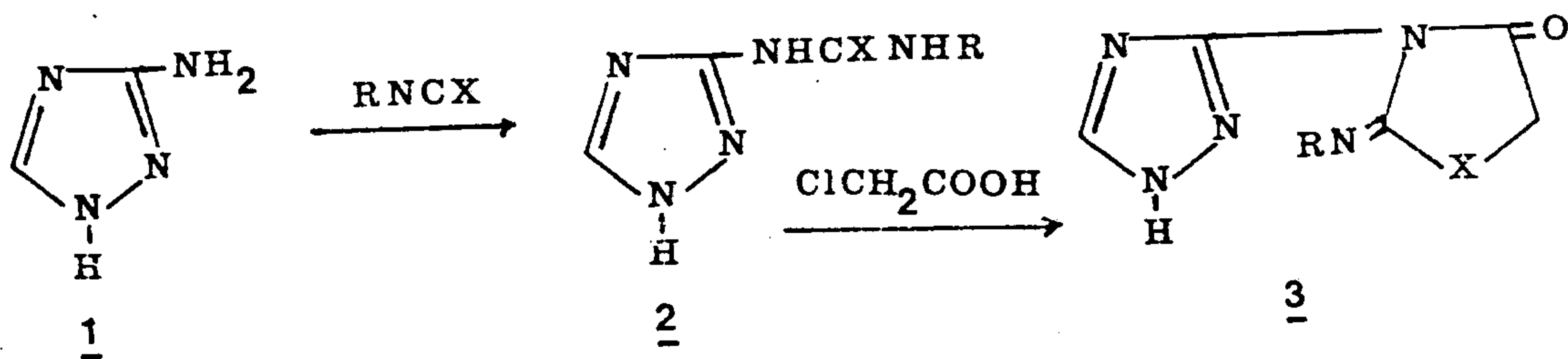
It is known that the amino group in a heterocyclic compounds is highly reactive and undergoes some characteristic and condensation reactions [1,4-6].

Accordingly, 3-amino-1,2,4-triazole, 1 reacts with phenyl isocyanate, ethyl and/ or phenyl isothiocyanate giving 3-(3-phenylcarbamido)-1,2,4- triazole 2a and 3- (3-alkyl (aryl) thiocarbamido)-1,2,4- triazole, 2b,c .

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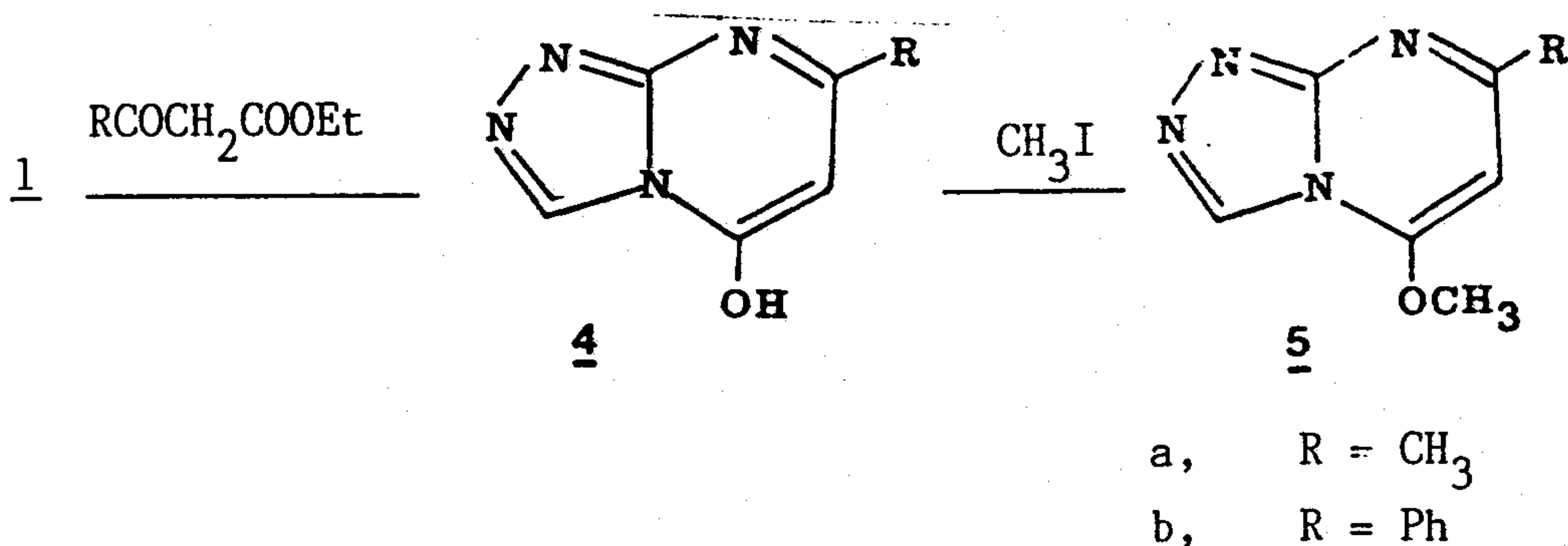
Refluxing compounds 2a-c with chloroacetic acid yield, through the elimination of  $H_2O$  and  $HCl$ , 3-(2-phenyl-imino-isoxazol-3-yl-5H-4-oxo)-1,2,4-triazole, 3a, and 3-(2-alkyl (aryl) iminoisothiazol-3-yl-5H-4-oxo) 1,2,4-triazole, 3a, and 3-(2-alkyl (aryl) iminoisothiazol-3-yl-5H-4-oxo) 1,2,4-triazole (3b-c), respectively.



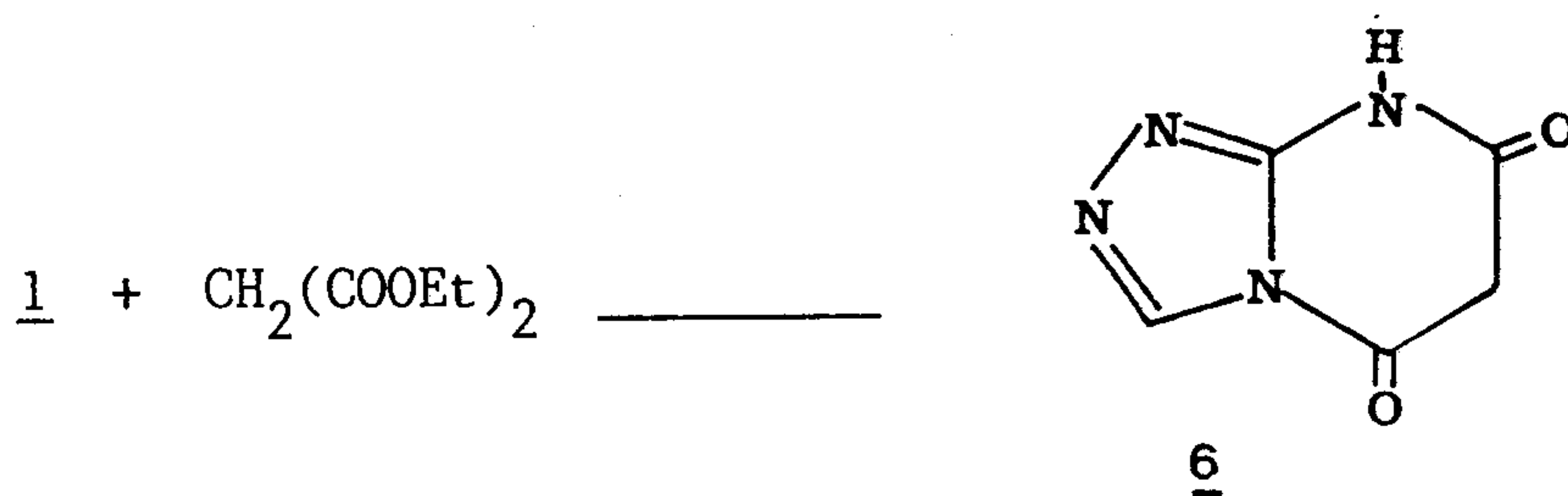
<u>2,3</u>	R	X
a	$C_6H_5$	O
b	$C_2H_5$	S
c	$C_6H_5$	S

Cyclocondensation reaction of 1 with ethylacetate or ethylbenzoyl acetate in glacial acetic acid yields 1-methyl or (phenyl)-3-hydroxy-1,2,4-triazole [4,3-a] pyrimidine, 4. Methylation of compound 4 with  $CH_3I$  in sodium methoxide gives 1-methyl-3-methoxy-1,2,4-triazolo [4,3-a] pyrimidine, 5.

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Similarly, cyclocondensation reactions of compound 1 with di-ethylmalonate yields 1,3-dioxo-2H-1,2,4-triazolo[4,3-a]pyrimidine. 6.



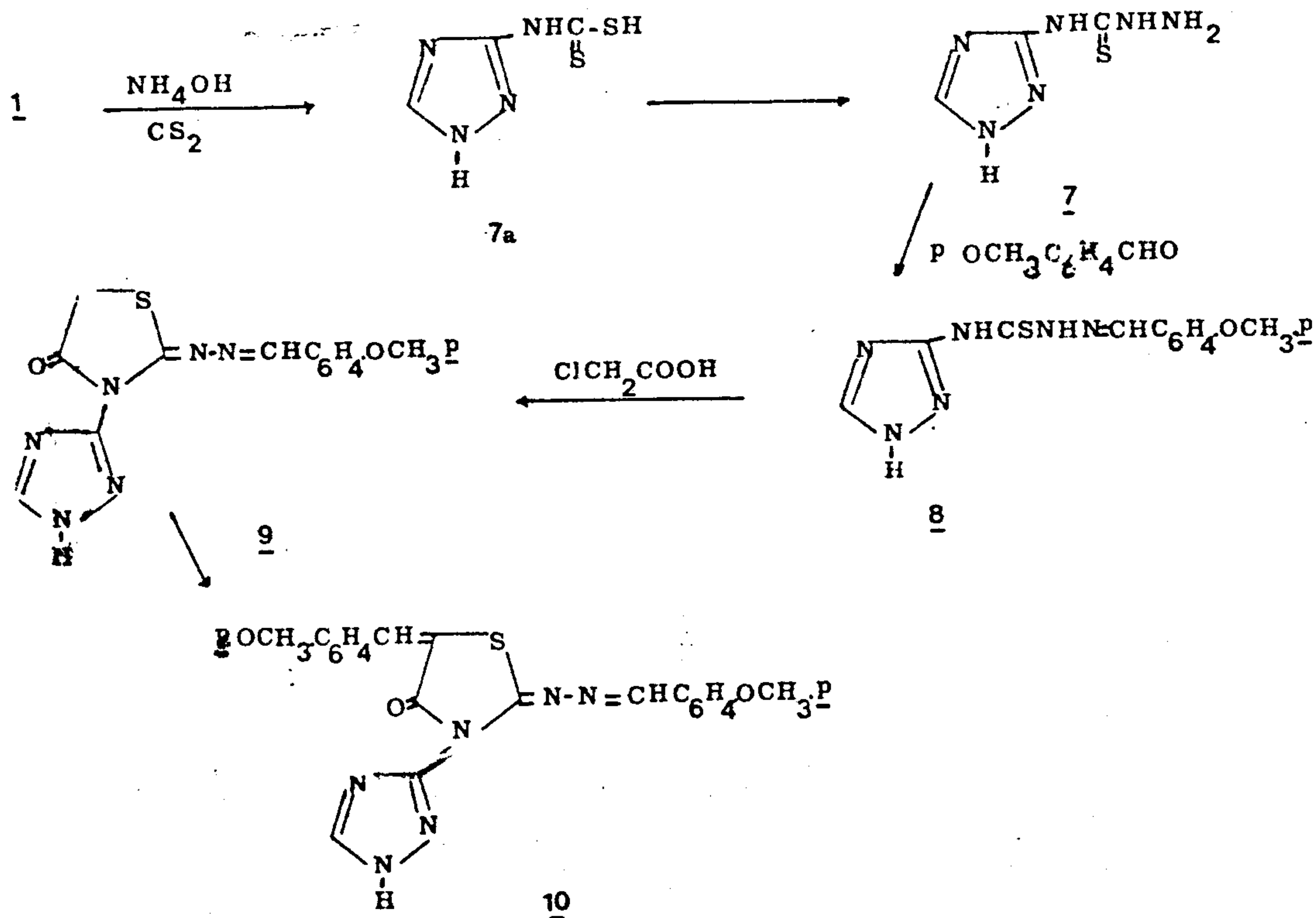
Compound 1 reacts with carbon disulphide at room temperature in the presence of conc. ammonia to give the nonisolable dithiocarbamate 7a, which on treatment with alkaline solution of a mixture of chloroacetic acid and hydrazine yields 3-thiocarboxyhydrazinoamine-1,2,4-triazole 7, which condenses with 4-methoxy benzaldehyde affording the condensation product 3-(p-methoxy benzylidene-4-thiosemicarbazone)-1,2,4-triazole, 8.

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Compound 8 reacts with chloroacetic acid in the presence of fused sodium acetate yielding the cyclized product dihydrazone-1-p-methoxy benzylidene-2-(2-thiazolideno-4-oxo-3-yl-3)-1,2,4-triazole, 9.

Condensation of 9 with 4-methoxy benzaldehyde gives dihydrazono-1-p-methoxy benzylidene-2-(2-thiazolideno-3-p-methoxy benzylidene-4-oxo-3-yl-3)-1,2,4-triazole, 10.

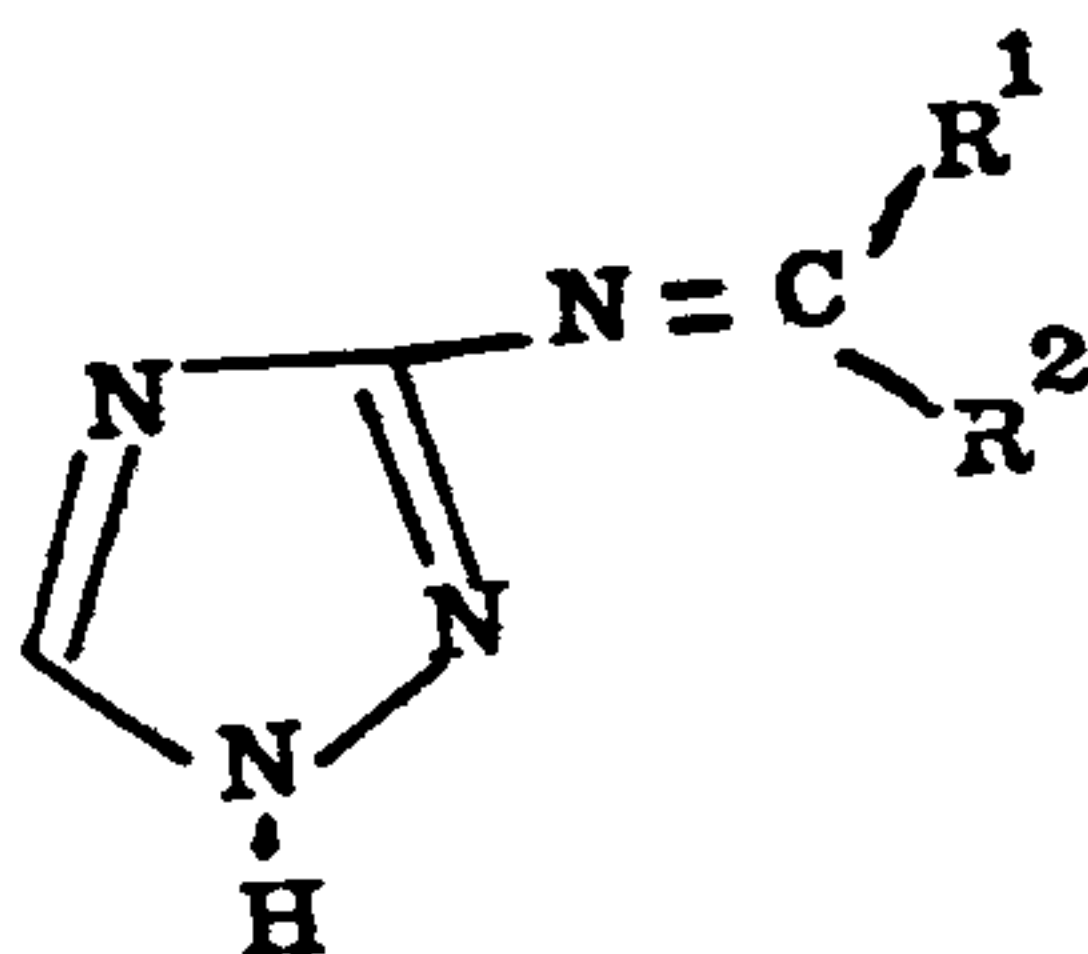
(Scheme 1).



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Compound 1 condenses with benzaldehyde, acetyl acetone and benzoylacetone to afford the corresponding products 11a-c.



<u>11</u>	a, R <sup>1</sup> = H	, R <sup>2</sup> = Ph
	b, R <sup>1</sup> = CH <sub>3</sub>	, R <sup>2</sup> = CH <sub>2</sub> COCH <sub>3</sub>
	c, R <sup>1</sup> = CH <sub>3</sub>	, R <sup>2</sup> = CH <sub>2</sub> COPh

The melting points were taken on a Gallenkamp Apparatus, and are uncorrected. The <sup>1</sup>H n.m.r. Spectra were recorded on a Variant 60. MHZ spectrometer in CDCl<sub>3</sub> and with TMS as internal reference. The i.r. Spectra were recorded on Unicam SP 200 G, using KBr Wafer technique.

Experimental and Spectral data are grouped in table 1.

### EXPERIMENTAL

3-amino-1,2,4-triazole 1 was prepared as usual [2,3,7].

Reaction of compound 1 with isocyanate and isothiocyanate :

A mixture of 1 (0.01 mole), and phenylisocyanate, ethyl and/ or phenylisothiocyanate (0.01 mole) was refluxed in anhydrous benzene (50 ml) for 3 hours. After cooling,

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the resulting solid was filtered off and crystallized from alcohol.

Cyclization of compound 2 :

A mixture of 2 (0.01 mole), chloroacetic acid (0.01 mole) and fused sodium acetate (0.01 mole) was refluxed in acetic acid (20 ml) for 6 hours. After cooling was poured into ice and kept overnight at room temperature, the resulting solid was filtered off and crystallized from acetic acid.

Reaction of 1 with B-keto-esters :

A mixture of 1 (0.025 mole), ethylacetoacetate (0.03 mole) and/ or benzoylacetoacetate (0.03 mole) was refluxed in acetic acid (30 ml) in presence or the absence of sodium methoxide for 3 hours. After cooling the precipitate was filtered off and crystallized from acetic acid, to yield 4.

Treatment of 4 (0.01 mole) with methyl iodide (0.01 mole) and sodium (0.05 mole) in methyl alcohol (30 ml) by boiling under reflux for 3 hours. After cooling, the resulting solid was filtered off and crystallized to give 5.

Formation of compound 7 :

A concentrated ammonium hydroxide solution was added

Table 1. Experimental and Analytical data of compounds 2 - 11.

Comp.	M.P. °C	Solvent	Yield %	Formula (Mol. wt.)	Analyses %			I.R. In $\text{cm}^{-1}$	$^1\text{H}$ N.m.r. $\delta$ ppm	
					C	H	N			
2a	360	E	90	$\text{C}_{11}\text{H}_{11}\text{N}_5\text{O}$ (203.2)	Calcd. 53.2 Found 53.7	4.5 4.0	34.5 34.6	3300(NH), 1700(C=O), 1670(C=N).		
2b	155	Ac	70	$\text{C}_5\text{H}_9\text{N}_5\text{S}$ (171.2)	Calcd. 35.1 Found 34.9	5.3 5.2	40.9 40.0	18.7 18.6	3220(NH), 1620(C=N), 1220(C=S).	
2c	162	E	90	$\text{C}_9\text{H}_9\text{N}_5\text{S}$ (219.3)	Calcd. 49.3 Found 49.1	4.1 4.3	31.9 31.8	14.6 14.3	3220(NH), 1610(C=N), 1220(C=S).	
3a	280	Ac	50	$\text{C}_{11}\text{H}_9\text{N}_5\text{O}_2$ (243.2)	Calcd. 54.3 Found 54.0	3.7 3.8	28.8 29.0		3220(NH), 1670(C=O), 1610(C=N).	
3c	290	Ac	55	$\text{C}_{11}\text{H}_9\text{N}_5\text{O}_2$ (259.3)	Calcd. 50.9 Found 51.0	3.5 3.4	27.0 27.1	12.4 12.7	3110(NH), 1700(C=O), 1560(C=N). 1.8, s/2(CH <sub>2</sub> )2.0.	t/3(CH <sub>2</sub> )0.5, q/2(CH <sub>2</sub> ), s/3(CH <sub>2</sub> )1.2, s/1(CH)2.9
4a	268	Ac	60	$\text{C}_6\text{H}_6\text{N}_4\text{O}$ (150.2)	Calcd. 48.0 Found 48.0	4.0 4.4	37.0 37.0		3230(OH), 3090(C-H), 1360(C-CH <sub>2</sub> ) s/1(OH)5.8.	s/3(CH <sub>2</sub> )2.2, s/3(OCH <sub>2</sub> )3.5 s/1(CH)5.6.
5a	360	E	80	$\text{C}_7\text{H}_8\text{N}_4\text{O}$ (164.2)	Calcd. 51.2 Found 51.1	4.9 4.6	34.1 34.8		1540(OCH <sub>2</sub> ).	s/3(CH <sub>2</sub> )2.2, s/3(OCH <sub>2</sub> )3.5 s/1(CH)5.6.
6	285	Ac	70	$\text{C}_5\text{H}_4\text{N}_4\text{O}$ (136.1)	Calcd. 44.1 Found 44.6	3.0 3.5	41.1 42.1		3090(C-H), 1660(C=O).	s/2(CH <sub>2</sub> )2.2, s/1(CH)7.8
8	360	Ac	50	$\text{C}_{11}\text{H}_{12}\text{N}_6\text{O}_5$ (276.3)	Calcd. 47.8 Found 47.8	4.4 4.6	30.4 30.0	11.6 11.5	3430(NH), 1640(C=O), 1220(C=S).	
9	190	Ac	45	$\text{C}_{13}\text{H}_{12}\text{N}_6\text{O}_2$ (316.4)	Calcd. 49.4 Found 49.0	3.8 3.6	26.6 25.6		3130(NH), 1610(C=N).	
10	360	Ac	60	$\text{C}_{21}\text{H}_{18}\text{N}_6\text{O}_3$ (434.5)	Calcd. 58.1 Found 58.7	4.2 4.6	19.4 20.4	7.4 7.2	3100(NH), 1720(C=O), 1610(C=N).	
11b	135	E	80	$\text{C}_7\text{H}_{10}\text{N}_4\text{O}$ (166.2)	Calcd. 50.5 Found 50.7	6.0 5.8	33.7 33.4		1640(C=O).	s/3(CH <sub>2</sub> )2.5, s/3(CH <sub>2</sub> )2.8 s/2(CH <sub>2</sub> )3.5, s/1(NH)7.3.

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slowly to an ethanolic solution of 1 (0.01 mole). After cooling, carbon disulphide (6 ml) was added dropwise during a period of 5 minutes. After one hour, an aqueous mixture of sodium hydroxide (0.01 mole) and monochloroacetic acid (0.01 mole) was added followed by the addition of hydrazine hydrate (0.01 mole). The reaction mixture was kept cool overnight. The resulting solid was filtered off and crystallized from acetic acid to give compound 7.

Reaction of 1 with B-diketones :

A mixture of 1 (0.025 mole) and acetyl acetone or benzoylacetone (0.03 mole) was refluxed for 4 hours in absolute ethanol containing 5 ml 1% KOH. The reaction mixture was cooled. The resulting solid was filtered off and crystallized to give 11.

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