BRIDGEHEAD NITROGEN HETEROCYCLES. PART III[c]. SYNTHESIS OF FUSED HETEROCYCLES FROM 3-(2,4-DICHLOROPHENYL)-5-MERCAPTO-1,2,4-*s*-TRIAZOLES

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Abstract - The condensation reaction of 3-(2,4-dichlorophenyl)-5-mercapto-1,2,4-*s*-triazole with chloroacetic acid, aromatic aldehydes, oxalyl chloride, dimethyl acetylenedicarboxylate, 1,2-diaminocompounds and 1,2-diketones leading to the formation of fused heterocycles was carried out.

The synthesis of condensed *s*-triazole heterocycles has been receiving attention during recent years.[1] Triazoles and their condensed products are reported to possess significant antifungal and antibacterial properties.[2,3] Potts and Hussain[4] studied the mode of cyclization of the 1,2,4-triazole-5-thiols both with alkyl and aryl groups as a substituent at 3-position. Puzari et al.[2] extensively studied the reaction and Goswami et al.[5] proved the formation of thiazolo[3,2-*b*]-*s*-triazole. Our interest in the chemistry of heterocycles[6] and the results obtained from these studies prompted us to synthesize some new bridgehead nitrogen heterocycles from 3-(2,3-dichlorophenyl)-5-mercapto-1,2,4-*s*-triazole (1) by reacting with chloroacetic acid, aromatic aldehydes, 1,2-diamines, 1,2-diketones, oxalyl chloride and dimethyl acetylenedicarboxylate (DMAD) and to investigate these new compounds. Exploration of the studies is principally directed towards the synthesis of new heterocyclic products. The results obtained during this attempt are reported in this paper.

The compound (1) underwent condensation with chloroacetic acid and aromatic aldehydes in acetic anhydride and glacial acetic acid in presence of sodium acetate giving 5-arylidene-2-(2,4-dichlorophenyl)thiazolo-[3,2-*b*][1,2,4]triazol-6(5H)-ones (2a-e) in 56-86% yield[7] (Scheme 1). The mode of cyclization was studied earlier[5,8a-c] and confirmed the formation of compounds (2a-e). The compound (1) on condensation with chloroaceticacid in ethanol in presence of sodium acetate gave 2-(2,4-dichlorophenyl)thiazolo[3,2-*b*]-[1,2,4]triazol-6(5H)-one (3), whereas with oxalyl chloride in presence of pyridine gave 2-(2,4-dichlorophenyl)-thiazolo[3,2-*b*][1,2,3]triazol-5,6-dione (4). Triazole (1) on condensation with DMAD in methanol in the presence of acetic acid gave 5-carbomethoxy-2-(2,4-dichlorophenyl)-7H-[1,2,4]triazolo[3,2-*b*][1,3]thiazin-7-one (7) in 40% yield.[9] Reaction of triazole (1) with 2,3-dichloroquinoxaline in ethanol in the presence of sodium acetate gave 2-(2,4-dichlorophenyl)[1,2,4]triazolo[3',2'-2,3]thiazolo[4,5-*b*]quinoxaline (5) in 96% yield.[8a] Reaction of triazole (1) with diketone like dimedone in ethanol in presence of bromine gave tetrahydrobenzothiazolone derivative (6) in 84% yield.[10]

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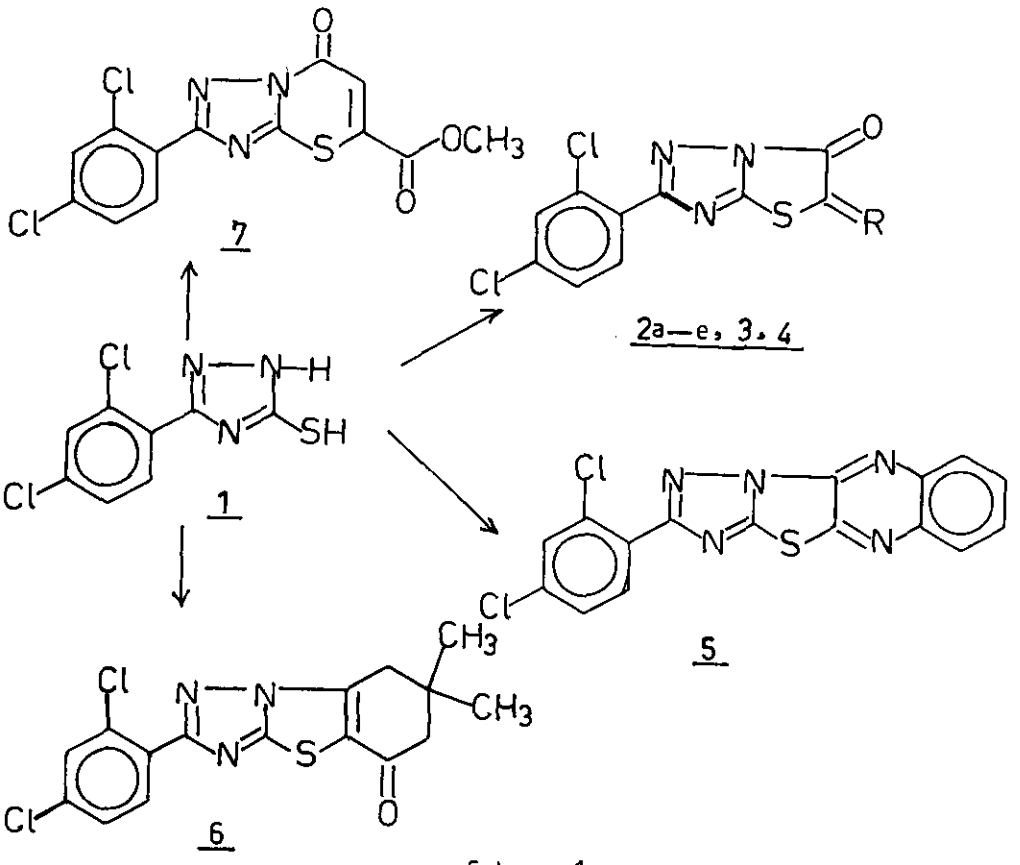
[c]Part II. P. C. Gogoi and J. C. S. Kataky, Heterocycles, 1990, 31, 2147.



Scheme 1

The structure of the compounds newly synthesized were deduced on the basis of analytical and spectral data (Table 1).

EXPERIMENTAL

Melting points were determined with a Buchi oil heated apparatus in open capillaries and are uncorrected Ir spectra were recorded with Perkin-Elmer 580B spectrophotometer using potassium bromide discs, unless otherwise stated (ν_{max} in cm^{-1}). ^1H Nmr spectra were recorded in solutions stated with TMS as the internal reference in 60 MHz on a Varian T-60 spectrometer (chemical shifts in δppm). 3-(2,4-Dichlorophenyl)-5-mercapto[1,2,4]triazole (1) was prepared following the method of Rao et al.[11]

6-Arylidene-2-(2,4-dichlorophenyl)thiazolo[3,2-*b*][1,2,4]-6(5H)-ones (2a-e)

General Procedure

A mixture of triazole (1) (2.46 g, 0.01 mol), chloroacetic acid (0.95 g, 0.01 mol), fused sodium acetate (2 g, 0.024 mol) and aromatic aldehyde (0.01 mol) in acetic anhydride (20 ml) and glacial acetic

Table 1

Physical and spectral data of compounds (2a-e, 3-7)

Compd No	R	mp (°C)	yield (%)	ir (KBr) ν cm^{-1} C=O	ir (KBr) ν cm^{-1} C=N	^{1}H nmr (δ ppm, DMSO-d_6)	Analysis (%) Found C	Found H	Found N	Calcd C	Calcd H	Calcd N
2a	CH-C_6H_5	183	86	1720	1600	7.0-7.5(m,Ar-H)	54.70	2.32	11.29	54.54	2.40	11.23
2b	CH-$C_6H_4(OCH_3)$(-p)	140	56	1700	1610	3.2(s,3H),6.8-7.4 (m,Ar-H)	53.40	2.62	10.35	53.46	2.72	10.39
2c	CH-$C_6H_4N(CH_3)_2$(-p)	190	77	1715	1610	2.6(s,6H),6.8-7.5 (m,Ar-H)	54.61	3.40	13.40	54.67	3.35	13.43
2d	CH-$C_6H_4(OH)$(-o)	123	64	1720	1610	7.0-7.5(m,Ar-H)	52.38	2.35	10.72	52.31	2.31	10.77
2e	CH-$C_6H_3(OCH_3)(OH)$(-m,-p)	210	56	1720	1610	3.4(s,3H),7.0-7.5 (m,Ar-H)	51.45	2.69	10.20	51.43	2.62	10.00
3	H_2	165	60	1720	1610	4.6(s,2H), 6.8-7.4 (m,Ar-H)	41.90	1.74	14.62	41.96	1.72	14.68
4	O	235	50	1760	1600	7.0-7.6(m,Ar-H)	40.01	1.05	14.10	40.00	1.00	14.00
5	-	225	96		1650	7.0-7.6(m,Ar-H)	51.62	1.80	18.85	51.61	1.88	18.82
6	-	193	84	1640	1610	1.6(s,6H), 4.2(s,4H), 7.0-7.6(m,Ar-H)	52.49	3.58	11.45	52.46	3.55	11.47
7	-	218	40	1750 1700	1620	3.8(s,3H), 7.4-7.6 (m,Ar-H)	43.81	1.85	11.85	43.82	1.92	11.80

acid (30 ml) was refluxed for 3 h. The reaction mixture was cooled to room temperature and diluted with water (30 ml). The precipitate formed was filtered, dried and then recrystallized from aqueous dioxane. The physical data of the compounds are given in Table 1.

2-(2,4-Dichlorophenyl)thiazolo[3,2-*b*][1,2,4]triazole-6(5H)-one (3)

A mixture of triazole (1) (2.46 g, 0.01 mol), chloroacetic acid (0.95 g, 0.01 mol) and sodium acetate (2 g, 0.024 mol) in ethanol (50 ml) was refluxed for 5 h. The mixture was then cooled, filtered the separated white solid. The solid was washed with water, dried and recrystallized from ethanol to get compound (3) (1.72 g, 60% yield). The compound (5) was also prepared in a similar method only 2,3-dichloroquinoxaline was used in place of chloroacetic acid. The physical data of compounds (3) and (5) are given in Table 1.

2-(2,4-Dichlorophenyl)thiazolo[3,2-*b*][1,2,4]triazol-5,6-dione (4)

A mixture of triazole (1) (2.46 g, 0.01 mol) and oxalyl chloride (1.27 g, 0.01 mol) was mixed with pyridine (1.58 g, 0.02 mol) in dry benzene (50 ml) and refluxed for 10 h. The precipitate pyridine hydrochloride was filtered. The organic layer was washed several times with water and then dried over anhydrous sodium sulphate. The solvent was removed under reduced pressure. The solid then formed was recrystallized from ethanol to get pure compound (4)(1.5 g, 50% yield). The physical data are given in Table 1.

7,7-Dimethyl-7,8-dihydro-2-(2,4-dichlorophenyl)triazolo[3,2-*b*]benzothiazolo-5(6H)-one (6)

To the equimolar mixture of triazole (1) (2.46 g, 0.01 mol) and dimedone (1.4 g, 0.01 mol) in ethanol (50 ml) was added bromine (3.2 g, 0.02 mol). The reaction mixture was refluxed for 30 h and then cooled. After removal of the solvent a solid was obtained which was kept in ether for 24 h. The solid was then recrystallized from ethanol to get compound (6) (3.1 g, 84% yield). The physical data of the compound (6) are given in Table 1.

7-Carbomethoxy-2-(2,4-dichlorophenyl)-7H-[1,2,4]triazolo[3,2-*b*][1,3]thiazine-7-one (7)

An equimolar amount of triazole (1) (2.46 g, 0.01 mol) and DMAD (1.42 g, 0.01 mol) in methanol (100 ml) and trace of glacial acetic acid were refluxed for 6 h. On cooling a white solid separated and then the solid filtered and recrystallized from methanol to get compound (7) (1.42 g, 40% yield). The physical data are given in Table 1.

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