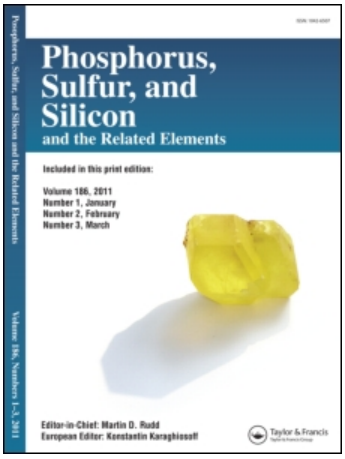

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SYNTHESIS OF NEW FUSED AND SPIRO HETEROCYCLES DERIVED FROM 4-AMINO-5-MERCAPTO-3-TRIFLUOROMETHYL-1,2,4-TRIAZOLE

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SYNTHESIS OF NEW FUSED AND SPIRO HETEROCYCLES DERIVED FROM 4-AMINO-5-MERCAPTO-3-TRIFLUOROMETHYL-1,2,4-TRIAZOLE

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Some new heterocyclic systems **2-9** were obtained through the reaction of 4-amino-5-mercapto-3-trifluoromethyl-1,2,4-triazole (**1**) with ylidenemalononitriles, 1,3-diketones, halonitriles, active nitriles, aromatic aldehydes or ketones. Also spiro systems **10-12** were achieved in one pot synthesis by addition of compound **1** to isatine, cycloalkanones or ylidenenitriles followed by cyclization. The reaction of compound **1** with 3 [di(methylthio)-methylene] pentan-2,4-dione afforded compound **13** treated with cycloalkanones to give compounds **14**.

Keywords: ylidenemalononitriles; halonitriles; cycloalkanones; thiadiazepinotriazole; thiadiazinotriazole; thiadiazolotriazole

INTRODUCTION

Several reports indicated the biological importance of 1,2,4-triazole derivatives [1-3]. Also mercaptotriazoles and their condensed products are strong CNS depressant [4] and posses antiinflammatory [5] or hypotensive [6] activities. The introduction of fluorine atom in hetero cyclic compounds does widen their spectrum as therapeutic agents [7] and insecticides [8]. So, in an extention of our previous studies [9-11] on the synthetic use of mecapto-1,2,4-triazole in our laboratory, the synthesis of fused thiadiazepinotriazole, thiadiazinotriazole and thiadiazolotriazole rings is reported, as well as, spiro heterocycles prepared.

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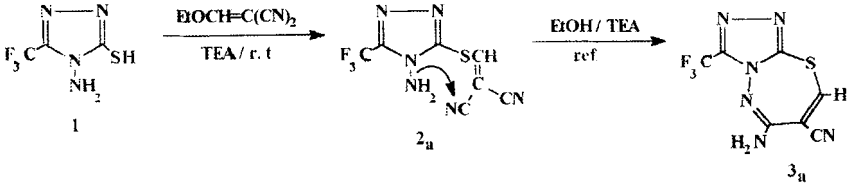
RESULTS AND DISCUSSION

The reaction of 4-amino-3-mercapto-5-trifluoromethyl-1,2,4-triazole (**1**) [7, 8] with ethoxymethylenemalononitrile or ethyl ethoxymethylenecyanoacetate in refluxing ethanol using triethylamine as a catalyst afforded s-triazolothiadiazepine derivatives $\mathbf{3}_{a,b}$. The reaction pathway was assumed to proceed via a nucleophilic addition of the thiol group of compound **1** to the ethylenic bond, with elimination of ethanol molecule, followed by intramolecular cyclization through the attack of the N-NH_2 group to the cyano group to give compounds $\mathbf{3}_{a,b}$. The sequence of the reaction was confirmed by reacting compound **1** with ethoxymethylenemalononitrile under the same conditions but on cold where S-vinyl product $\mathbf{2}_a$ was obtained. Its IR spectrum showed a characteristic bands corresponding to NH_2 (3300,3210) and CN (2201). The product $\mathbf{2}_a$ refluxed in ethanol in the presence of triethylamine as a catalyst gave compound $\mathbf{3}_a$.



1 $\quad$ 2_a $\quad$ 3_a

Compound **1** was reacted with ylidenenitriles, e.g. arylmethylenemalononitriles, heteromethylenemalononitriles or ethyl p-chlorophenylmethylenecyanoacetate to give new series of s-triazolothiadiazepine derivatives $\mathbf{4}_{a\text{-}f}$. The reaction pathway was assumed to proceed via addition of the thiol group to the activated double bond of ylidenenitrile to yield the intermediate Michael adduct which was cyclized through the addition of N-NH_2 to the cyano group. Aromatization was gained by elimination of hydrogen molecule and absorbed by another molecule of ylidenenitrile [12, 13]. IR spectra of products **4** showed a characteristic bands corresponding to NH_2 (3300-3115), CH(2960-2880) and CN(2180-2100), respectively. ^{1}H NMR spectra of products are in agreement with the proposed structures (c.f Table I).

Condensation and subsequent oxidative cyclization [14] of compound **1** with 1,3-diketones, namely, acetylacetone, ethyl acetoacetate or dibenzoylmethane in dimethylsulphoxide as a solvent afforded s-triazolothiadiazine derivatives $\mathbf{5}_{a\text{-}c}$. IR spectra of compounds **5** showed the absence of absorption bands corresponding to NH_2, SH groups and appearance of new absorption bands corresponding to NH at 3330-3230 cm^{-1}, CO_{ester} at 1736 cm^{-1} and CO_{ketone} at 1710, 1716 cm^{-1}, respectively. ^{1}H NMR spectral data were listed in Table I.

TABLE I: Analytical and Spectral Data of The New Compounds

Product No	M.P. (°C)[a] Cryst. Solvent	Yield (%)	Mol. Form. (Mol. Wt)	Analytical Data (Cal./Found)[b]		
				C	H	N
2a	81-82	80	$C_7H_3F_3N_6S$	32.31	1.16	32.29
	(benzene)		(260.19)	32.43	1.00	32.34
3a	156-157	67	$C_7H_3F_3N_6S$	32.31	1.16	32.29
	benzene		(260.19)	32.49	1.07	32.44
3b	160	66	$C_7H_3F_3N_5O_2S$	35.18	2.62	22.79
	(ethanol)		(307.24)	35.23	2.43	22.61
4a	130-131	77	$C_{13}H_7F_3N_6S$	46.43	2.09	25.09
	(ethanol)		(336.28)	46.53	2.12	25.19
4b	183	39	$C_{13}H_6ClF_3N_6S$	42.11	1.62	22.66
	(benzene)		(370.78)	42.43	1.40	22.68
4c	195-196	40	$C_{13}H_6F_3N_7O_2S$	40.95	1.58	25.71
	(ethanol)		(381.28)	40.63	1.43	25.61
4d	176	68	$C_{11}H_6F_3N_7S$	40.61	1.85	30.14
	(ethanol)		(325.26)	40.43	1.70	30.19
4e	200-201	39	$C_{12}H_7F_3N_8S$	40.91	2.00	27.82
	(dioxane)		(352.29)	40.63	2.21	27.61
4f	191	43	$C_{10}H_{10}F_3N_5O_2S$	37.38	3.13	21.79
	(dioxane)		(321.29)	37.43	3.00	21.61
5a	151	66	$C_8H_7F_3N_4OS$	36.36	2.66	21.29
	(ethanol)		(264.22)	36.43	2.36	21.33
5b	210-211	70	$C_9H_{11}F_3N_4OS$	36.73	3.08	19.11
	(dioxane)		(294.24)	33.63	3.23	19.31
5c	243	69	$C_{18}H_{11}F_3N_4OS$	55.66	2.85	14.48
	(DMF)		(388.35)	55.43	2.66	14.68
6a	167-168	78	$C_6H_3F_3N_6S$	29.03	1.21	34.00
	(benzene)		(248.18)	29.34	1.30	34.21
6b	173	83	$C_5H_4F_3N_5S$	26.91	1.80	31.51
	(ethanol)		(223.14)	26.75	1.76	31.77
7a	196	77	$C_6H_3F_3N_6S$	29.03	1.21	34.00
	(dioxane)		(248.18)	29.33	1.33	34.21
7b	233-234	68	$C_5H_4F_3N_5S$	26.91	1.80	31.51
	(benzene)		(223.14)	26.77	1.78	31.35
8a	220	46	$C_6H_2F_3N_5S$	30.91	0.86	30.16
	(ethanol)		(233.14)	30.66	0.99	30.00
8b	236-237	80	$C_8H_7F_3N_4O_2S$	38.40	2.81	22.48
	(ethanol)		(250.22)	38.55	2.76	22.57
9a	181-182	85	$C_{10}H_6ClF_3N_4S$	39.16	1.97	18.26
	(dioxane)		(306.70)	39.00	1.86	18.00
9b	186	67	$C_{10}H_6F_3N_5O_2S$	37.85	1.90	22.07
	(benzene)		(317.26)	37.69	1.77	22.14
9c	160	66	$C_{11}H_8ClF_3N_4S$	41.19	2.51	17.47
	(ethanol)		(320.73)	41.43	2.33	17.32
9d	220	77	$C_{11}H_8F_3N_5O_2S$	39.88	2.43	21.14
	(ethanol)		(331.28)	39.53	2.22	21.29

TABLE I *Continued*

Product No	M.P. (°C)[a] Cryst. Solvent	Yield (%)	Mol. Form. (Mol. Wt)	Analytical Data (Cal./Found)[b]		
				C	H	N
10	323 (DMF)	89	$C_{11}H_8F_3N_5OS$ (315.26)	44.90 44.63	2.55 2.44	22.21 22.48
11a	95 (ethanol)	80	$C_8H_9F_3N_4S$ (250.17)	38.40 38.63	3.62 3.43	22.39 22.61
11b	110 (benzene)	68	$C_9H_{11}F_3N_4S$ (264.28)	40.90 40.63	4.19 4.30	21.20 21.09
11c	100 (dioxane)	59	$C_{10}H_{13}F_3N_4S$ (278.28)	43.16 43.43	4.70 4..51	20.13 20.21
12a	191 (dioxane)	77	$C_{14}H_8F_3N_7OS$ (379.31)	44.33 44.55	2.12 2.00	25.95 25.71
12b	210 (ethanol)	66	$C_{16}H_{13}F_3N_6O_3S$ (426.36)	45.07 45.33	3.07 3.26	23.09 23.13
12c	110 (dioxane)	73	$C_{12}H_{13}F_3N_6S$ (330.32)	43.63 43.43	3.96 3.83	25.54 25.41
12d	200 (DMF)	69	$C_{14}H_{18}F_3N_5O_2S$ (377.36)	44.56 44.43	4.80 4.66	18.63 18.60
12e	179 (benzene)	78	$C_{13}H_8F_3N_7OS$ (367.30)	42.51 42.34	2.19 2.30	26.80 26.71
12f	163 (ethanol)	83	$C_{13}H_8F_3N_7S_2$ (383.37)	40.72 40.88	2.09 2.26	25.67 25.77
12g	121 (dioxane)	77	$C_9H_8F_3N_7OS$ (319.25)	33.85 33.66	2.52 2.43	30.83 30.76
13	233 (benzene)	68	$C_9H_7F_3N_4O_2S$ (292.22)	36.99 36.77	2.41 2.58	19.25 19.35
14a	101 (ethanol)	46	$C_{12}H_{11}F_3N_4OS$ (316.29)	45.56 45.66	3.50 3.69	17.78 17.67
14b	115 (ethanol)	80	$C_{13}H_{13}F_3N_4OS$ (330.31)	47.27 47.55	3.96 3.76	17.03 17.37
14c	81 (benzene)	90	$C_{14}H_{16}F_3N_4OS$ (345.34)	48.69 48.55	4.66 4..40	16.29 16.00

Product No.	IR (cm^{-1})[c]	^1H NMR(δ.ppm)[d]
2_a	3300,3210(NH_2), 2201(CN)	5.7-5.5(br,2H,NH_2), 5.0(s,1H,CH),
3a	3296,3125(NH_2), 2100(CN)	6.6(s,2H, NH_2), 3.9(s,1H,=CH).
3_b	3210,3120(NH_2), 2170(CN), 1730(CO)	4.6(s,2H, NH_2), 4.4-4.2(q,2H,CH_2),3.9(s, 1H,=CH), 1.3-1.0 (t,3H,CH_3).

TABLE I *Continued*

Product No.	IR (cm^{-1})[c]	^1H NMR(δ.ppm)[d]
4a	3200,3115(NH_2), 2100(CN)	7.9-6.7 (m,5H,aromatic), 5.5(s,2H,NH_2).
4_b	3230,3135(NH_2), 2180(CN)	8.1-7.4 (m,4H,aromatic), 6.5(s,2H,NH_2).
4_c	3290,3185(NH_2), 2170(CN)	8.5-7.7 (m,4H,aromatic), 6.1(s,2H,NH_2).
4_d	3350,3215,3110 (NH,NH_2), 2110(CN)	9.1 (s,1H,NH), 8.9-8.0 (m,3H,aromatic), 5.5(s,2H,NH_2).
4_e	3315,3215,3110(NH,NH_2), 2140(CN)	7.9-6.7 (m,5H,aromatic+NH), 5.5 (s,2H,NH_2).
4_f	3200,3100(NH_2), 2100(CN),1740(CO).	7.9-6.6 (m,4H,aromatic), 6.5 (s,2H,NH_2), 4.4-4.2 ((q,2H,CH_2), 1.3-1.0 (t,3H,CH_3).
5_a	3230(NH), 1710(CO).	9.1 (s,1H,NH), 3.1 (s,3H,CH_3), 2.6 (s,3H,CH_3 CO).
5_b	3330(NH), 1736(CO)	8.8-8.6(br,1H,NH), 4.4-4.1 (q,2H,CH_2), 2.9 (s,3H,CH_3),1.3-1.0 (t,3H,CH_3.).
5_c	3330(NH), 1716(CO)	10.0 (s,1H,NH), 7.7-6.8 (m,10H,aromatic).
6_a	3300,2210 (NH_2), 2100 (CN).	5.8-5.6 (br,2H,NH_2), 4.9 (s,2H,CH_2).
6_b	3219,3120(NH_2), 2130(CN).	5.8-5.6 (br,2H,NH_2), 5.1 (s,1H,CH).
7_a	3310,3210(NH_2).	4.5-4.1 (br,2H,NH_2), 4.0 (s,2H,CH_2).
7_b	3230,3140(NH_2), 2130(CN)	5.0-4.8 (br,2H,NH_2), 3.9 (s,1H,CH).
8_a	2950($CH_{aliph.}$), 2120(CN)	4.4 (s,2H,CH_2).
8_b	2930($CH_{aliph.}$), 1743(CO).	4.3-4.0 (q,2H,CH_2), 3.5 (s,2H,CH_2), 1.3-1.0 (t,3H,CH_3.).

TABLE I *Continued*

Product No.	IR (cm^{-1})[c]	^1H NMR(δ.ppm)[d]
9_a	3310(NH), 3015($CH_{aromatic}$)	9.1 (s,1H,NH). 7.7-7.0 (m,4H,aromatic).
9_b	3210(NH), 3010($CH_{aromatic}$)	10.1 (s,1H,NH), 8.8-7.8 (m,4H,aromatic).
9_c	3235(NH), 3010,2970($CH_{aromatic+aliph.}$)	8.8(s,1H,NH), 8.6-7.4 (m,4H,aromatic), 2.4 (s,3H,CH_3).
9_d	3210(NH), 3015,2890($CH_{aromatic+aliph.}$)	10.5 (s,1H,NH), 7.8-6.8 (m,4H,aromatic), 2.5 (s,3H,CH_3).
10	3340,3210($OH,NH_{isatine}$), 3128(NH),1720 (CO).	10.0 (s,1H,$NH_{isatine}$), 7.7-7.0 (m,4H,aromatic), 6.1 (s,1H,NH)
11_a	3350(NH), 2980-2870($CH_{aliph.}$)	6.3 (s,1H,NH), 2.7-1.5 (m,8H,cyclic CH_2).
11_b	3300(NH), 2940-2860($CH_{aliph.}$)	7.3 (s,1H,NH), 2.8-1.5 (m,10H,cyclic CH_2).
11_c	3310(NH), 2950-2850($CH_{aliph.}$)	6.3 (s,1H,NH), 2.6-1.3 (m,13H,cyclic CH_2 + CH_3).
12_a	3310,3220,3150(NH,NH_2), 2100(CN),1710 (CO)	11.0 (s,1H,NH), 7.7-6.8 (m,4H,aromatic), 4.6 (s,2H,NH_2), 3.4 (s,1H,CH).
12_b	3320,3211,3110(NH,NH_2), 1730(CO_{ester}), 1710($CO_{isatine}$)	10.5 (s,1H,NH), 7.6-6.7 (m,4H,aromatic), 4.9 (s,2H,NH_2), 4.4-4.1 (q,2H,CH_2), 3.6 (s,1H,CH), 1.3-1.0 (t,3H,CH_3).
12_c	3230,3115(NH_2), 2170(CN)	5.7 (s,2H,NH_2), 3.4 (s,1H,CH), 2.8-1.5 (m, 10H, cyclic CH_2).

TABLE I *Continued*

Product No.	IR (cm^{-1})[c]	^1H NMR(δ.ppm)[d]
12_d	3217,3150(NH_2), 1740(CO),	5.6 (s,2H,NH_2), 4.4-4.2 (q,2H,CH_2), 3.3 (s,1H,CH), 2.8-1.5 (m, 10H, cyclic CH_2), 1.3-1.0 (t,3H,CH_3).
12_e	3320,3215,3120(NH,NH_2), 2150(CN)	8.8 (s,1H,NH), 7.4-6.4 (m,4H,aromatic), 5.6 (s,2H,NH_2), 4.0 (s,1H,CH).
12_f	3340,3244,3136(NH,NH_2), 2140(CN)	10.0 (s,1H,NH), 7.8-6.8 (m,4H,aromatic), 4.7 (s,2H,NH_2), 3.4 (s,1H,CH).
12_g	3324,3215,3117(NH,NH_2), 2138(CN)	9.7 (s,1H,NH), 6.0 (s,2H,NH_2), 3.9 (s,1H,CH), 3.2 (s,4H,$2CH_2$).
13	3310(NH), 1710(CO), 1620(C=C)	7.0(s,1H,NH), 2.8 (s,6H,2 CH_3CO).
14_a	3300(NH), 2980-2870($CH_{aliph.}$), 1600(C=C).	8.0(s,1H,NH), 6.6 (s,1H,=CH), 2.8 (s,3H, CH_3), 2.5-1.5 (m,8H, cyclic CH_2).
14_b	3260(NH), 2955-2897 ($CH_{aliph.}$), 1603(C=C).	7.6 (s,1H,NH), 6.7(s,1H,=CH), 2.6(s,3H, CH_3),2.5-1.3(m,10H, cyclic CH_2).
14_c	3230(NH), 2945-2786($CH_{aliph.}$), 1608(C=C).	8.0(s,1H,NH), 6.2(s,1H,=CH), 2.8(s,3H, CH_3),2.7-1.3(m,13H, cyclic CH_2).

[a]) Uncorrected [b]) Satisfactory microanalyses obtained; C, 0.3%, H, 0.3%, N, 0.45% [c]) Measured on Nicolet 710 FT-IR spectrophotometer [d]) Measured with a Varian EM 360 L using TMS as internal standard.

Treatment of compound **1** with chloroacetonitrile or bromomalononitrile and triethylamine in equimolar ratio in p-xylene afforded the corresponding S-alkyl derivatives $\mathbf{6_{a,b}}$. On refluxing compound $\mathbf{6_{a,b}}$ with sodium ethoxide in ethanol gave triazolothiadiazine derivatives $\mathbf{7_{a,b}}$. IR spectra of $\mathbf{6_{a,b}}$ were exhibiting the absorption bands corresponding to NH_2 (3300-2120) and CN (2130-2100),

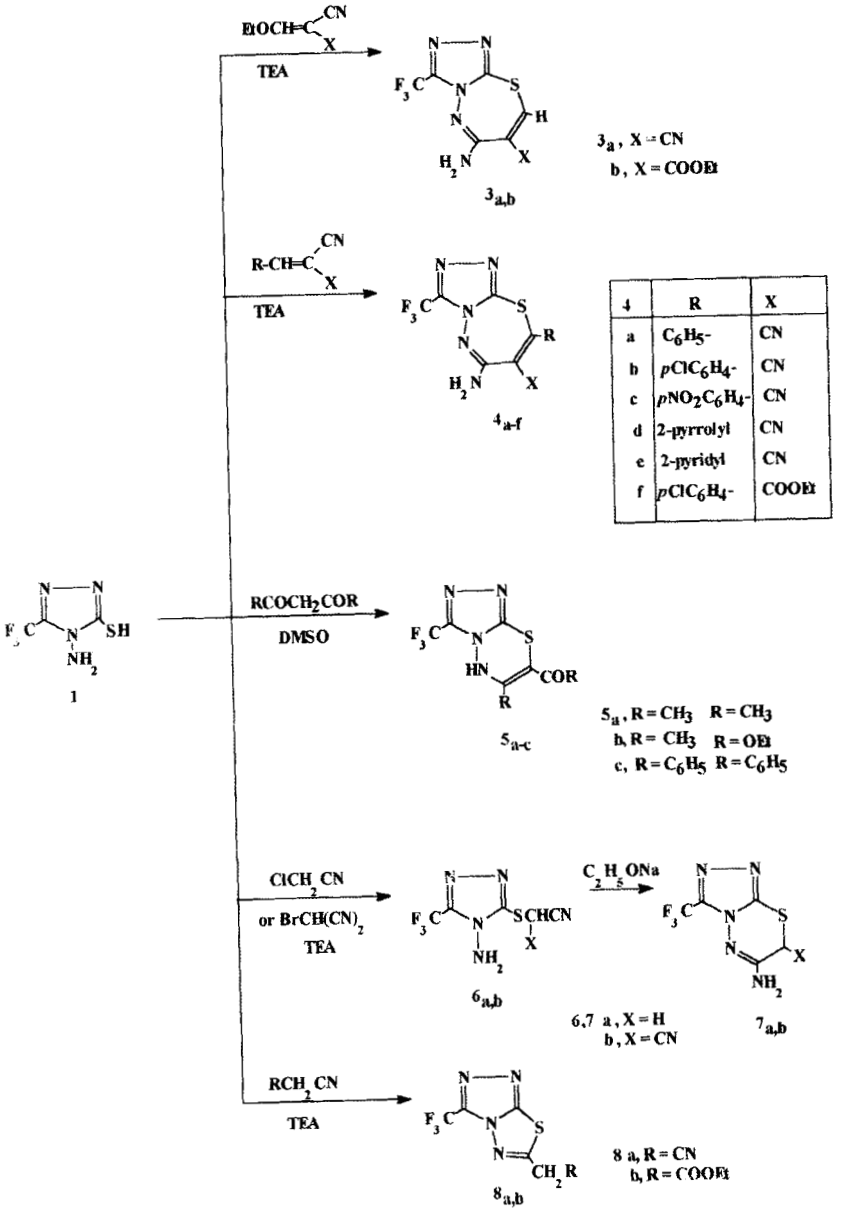
respectively. While IR spectrum of compound $\mathbf{7_a}$ showed the absence of the absorption band corresponding to CN group. ^{1}H NMR spectral data were listed in Table I.

6-Alkyl-3-trifluoromethyl-s-triazolo[3,4-b][1,3,4]thiadiazoles ($\mathbf{8_{a,b}}$) were synthesized by reaction of compound **1** with malononitrile or ethyl cyano-acetate, in presence of triethylamine as a catalyst. The reaction pathway was suggested to proceed via nucleophilic addition of sulphur anion to the cyano group [13] followed by cyclization through elimination of ammonia molecule from the intermediates. Also, 6-cyanomethyl-3-trifluoromethyl-s-triazolo[3,4-b] [1,3,4] thiadiazole ($\mathbf{8_a}$) was obtained on reacting compound **1** with cyano-acetamide or cyanoacetohydrazide in which the sulphur anion firstly attacks the carbonyl group followed by cyclization through elimination of NH_3 and H_2O or $NH_2{\cdot}NH_2$ and H_2O molecules, respectively. IR and ^{1}H NMR spectra are in agreement with the proposed structures (c.f. Scheme 1, Table I).

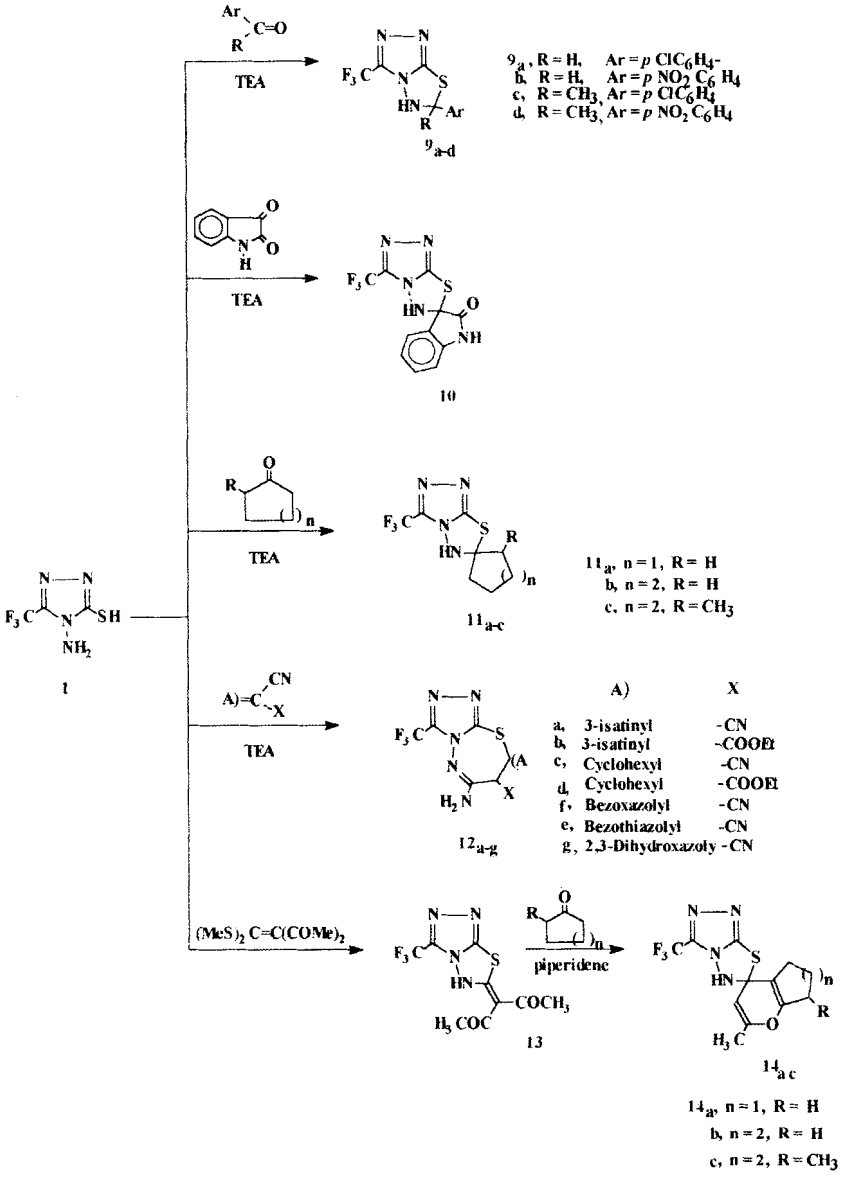
The reaction of compound 4-amino-3-mercapto-5-alkyl-1,2,4-triazole with aromatic aldehydes or ketones in refluxing acetic acid was reported to give Schiff bases [9]. But, when the reaction was carried out in benzene using *p*-toluenesulphonic acid as a catalyst gave s-triazolothiadiazole derivatives in 80% yield [14]. We report here, when compound **1** reacted with aromatic aldehydes or ketones in equimolar ratio using triethylamine catalyst afforded the corresponding 5,6-dihydro-6-trifluoromethyl-s-triazolo[3,4-b][1,3,4]thiadiazole derivatives $\mathbf{9_{a-d}}$ in 85%, 87% yields, respectively. IR spectra of compounds $\mathbf{9_{a-d}}$ showed the absence of absorption bands corresponding to NH_2, SH groups and appearance new band corresponding to NH at (3310–3210). ^{1}H NMR spectra were shown in Table I.

On applying our conditions (refluxing dioxane, TEA) on the reaction of compound **1** with isatine, cyclopentanone, cyclohexanone or 2-methylcyclohexanone, new spiro polyfused derivatives **10**, $\mathbf{11_{a-c}}$ were obtained (c.f. Table I, Scheme 2).

A one pot synthesis of fused triazolothiadiazepine attached with many heterocyclic rings in spiro system $\mathbf{12_{a-g}}$ were obtained through the reaction of compound **1** with different ylidenenitriles (e.g., isatinylmalononitrile, ethyl-isatinylcyanoacetate, cyclohexylidenemalononitrile, ethyl cyclohexylidenecyano acetate, benzoxazolidenemalononitrile, benzothiazolidenemalononitrile or 2,3-dihydrooxazolidenemalononitrile) in which the first step is the addition of SH group on styryl function [13] followed by addition of N-NH_2 on cyano group to give the proposed structures. Their IR spectra showed absorption bands corresponding to NH_2 (3320-3115), CH (2960-2880), CN (2170-2100), CO_{ester} (1740,1730) and $CO_{isatine}$ (1710), respectively. ^{1}H NMR spectra of products are in agreement with the proposed structures (c.f. Table I, Scheme 2).



Compound **1** reacted with 3-[di(methylthio)methylene] pentan-2,4-dione to give 2-(acetyl-2-oxopropylidene)-s-triazolothiadiazole **13** treated with cycloalkanones (e.g, cyclopentanone, cyclohexanone or 2-methylcyclohexanone) gave new spiro products $\mathbf{14}_{a\text{-}c}$. The reaction pathway was assumed to follow a



preliminary hydrolysis of one of the two acetyl groups followed by a nucleophilic addition of the formed carbanion of cycloalkanones at ethylenic bond with subsequent cyclization [16, 17]. The structure of products **14** was proved by elemental analysis and spectral data (c.f. Table I, Scheme 2).

EXPERIMENTAL

Synthesis of compound 2:

To a solution of compound **1** (0.003 mol) in 20 ml ethanol, ethoxymethylenemalononitrile (0.003 mol) and 0.003 mol of triethylamine were added. The reaction mixture was stirred at room temperature (20-25°C) for 6.5 h. and the solvent was evaporated under reduced pressure. The residual solid was washed with pet.ether (40/60°C), and crystallized from benzene. Poduct $\mathbf{3_a}$ was obtained by refluxing ethanolic solution of compound $\mathbf{2_a}$ in presence of catalytic amount of triethylamine for 3h. The disired product $\mathbf{3_a}$ was crystallized from ethanol. (cf. Table I).

Synthesis of compounds 3,4,8-12: (General procedure).

An equimolar mixture (0.005 mol) of compound **1**, ylidenenitriles, active nitriles, aromatic aldehydes, aromatic ketones, isatine, cycloalkanones, and triethylamine in 20 ml of ethanol was refluxed for 3 h. The solvent was evaporated under reduced pressure and the residual solid was filtered, washed with water and crystallized from the proper solvent to give products **3,4,8-12**, respectively.

Note: *In case of aryl or heteromethylenemalononitriles (0.02 mol) was used.*

Synthesis of s-triazolothiadiazines $\mathbf{5_{a-c}}$: (General procedure)

An equimolar mixture (0.01 mol) of compound **1** and 1,3-diketones (acetylacetone, ethylacetoacetate or dibenzoylmethane) in 20 ml dimethylsulfoxide was refluxed for 3 h. The reaction mixture was concentrated, cooled, poured on ice-water, the precipitant was collected by filteration and crystallized from the proper solvent.

Synthesis of compounds 6,7: (General procedure)

To a solution of compound **1** (0.01 mol) in 20 ml dry p-xylene, a suitable halonitrile compound (0.01 mol) and 0.01 mol of triethylamine were added. The

reaction mixture was refluxed for 3 hr. and the solvent was evaporated under reduced pressure. The residual solid was washed with water, and crystallized from appropriate solvent (c.f. Table I). Products $\mathbf{7_{a,b}}$ were obtained by refluxing ethanolic solution of compounds $\mathbf{6_{a,b}}$ in presence of catalytic amount of sodium ethoxide for 3h. and the residual solid was filtered, washed with water and crystallized from ethanol to give the desired products $\mathbf{7_{a,b}}$. (c.f. Table I)

Synthesis of compound 13:

An eqimolar mixture (0.005 mol) of compound **1** and 3-[di(methylthio) methylene]pentan-2,4-dione in 20 ml ethanol was refluxed until the evolution of CH_3SH finished (36 h.). The reaction mixture was concentrated and the residual solid was washed with pet.ether (40/60°C), and crystallized from benzene.

Synthesis of compounds 14:

An equimolar mixture (0.002 mol) of compound **13**, cycloalkanones, and piperidene in 20 ml of ethanol was refluxed for 3 h. The solvent was evaporated under reduced pressure and the residual solid was filtered off and crystallized from the proper solvent to give products $\mathbf{14_{a-c}}$, respectively.

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