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Microwave Assisted Synthesis of Fluorinated Hexahydro 1,3,5-Triazine Derivatives in Aqueous Medium and One Pot Synthesis of 1,2,4-Triazolo(4,3-a)1,3,5-triazines

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Microwave Assisted Synthesis of Fluorinated Hexahydro 1,3,5-Triazine Derivatives in Aqueous Medium and One Pot Synthesis of 1,2,4-Triazolo(4,3-a)1,3,5-triazines

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ABSTRACT

A multi-component condensation of substituted phenylthiourea/urea, aqueous formaldehyde and substituted aromatic/heterocyclic amines lead to 2-thioxohexahydro-1,3,5-triazines (4) in aqueous medium under microwave irradiation in 30-60 sec in quantitative yield with reasonable purity. Further, triazolo[4,3-a]triazines were also prepared by a one-pot reaction of 'in situ' synthesized triazinyl hydrazine (7) with CS₂ (9).

Key Words: Fluorinated hexahydro 1,3,5-triazine; Microwave irradiation; 1,2,4-Triazolo(4,3-a) 1,3,5-triazine.

1141

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1,3,5-Tri-*N*-substituted hexahydro-2-oxo-1,3,5-triazines (triazones) have been known for many years in literature.^[1-3] Triazones are used for protection of amino group^[4,5] as well as for the synthesis of poly amines,^[6a-d] poly functional amino acids and amino alcohols.^[4] Many water soluble triazones are used as fertilizers,^[7] while some have shown potent antitumor,^[8] muscle relaxant properties^[9] and are reactive azodyes^[10] and substituted triazine derivatives are patented^[11a-f] as herbicides, fungicides and treatment of HIV infection.

Incorporation of fluorine to different heterocycles is known to affect the course of the reaction besides, influencing the biological/pharmacological activity,^[12a,b] and more interest has been focused on synthesis of fluorinated 1,3,5-triazines due to wide variety of their uses.^[13a-e]

Conventionally, triazones are synthesized (a) by the reaction of phenylisocynate with azomethines in the presence of zinc chloride,^[14] (b) by the reaction of hydrochloride salt of a primary amine with 4-oxo-oxadiazinane, and (c) by the reaction of primary amines with N,N'-disubstituted ureas and aqueous formaldehyde with a co-solvent such as toluene/ethanol/ethyl acetate.^[4,5] All these methods suffer from many disadvantages like long reaction period, low yield, use of strong acids/dehydrating agents or use of high boiling solvent such as DMF.^[3]

Usage of microwave irradiation (MWI) is well known for the synthesis of variety of compounds^[15a,b] along with triazine derivatives^[16a,b] wherein chemical reactions are accelerated because of selective absorption of microwaves by polar molecules, but microwave assisted procedures involving the use of solvents are limited as they give rise to elevated temperatures and consequently high pressures which can lead to dangerous explosions. In view of this, more interest has now been focused on dry media synthesis, involving the coupling of MWI with solid supported reagents. The method provides unique chemical process with special attribute to enhanced reaction time, higher yield, greater selectivity and ease of manipulation.^[17a-e] But, the above technique requires an appreciable amount of solvent for adsorption of reactants and elution of products.

Recently, the use of aqueous media for organic reaction^[18] is under extensive investigation for synthesis and also to exploit hydrophobic effect.^[19a-c] Water has high dielectric constant with a permanent dipole moment, which allows the coupling between the oscillating electric field and the molecular tumbling to occur with high efficient heating. Hence, at elevated temperature it acts as a pseudo-organic solvent and in its use, isolation of products is also facilitated due to decreased solubility of organic material upon post reaction cooling.

In continuation to our earlier interest on the environmentally benign synthesis of biodynamic heterocycles^[20a-e] we report herein for the first time

1142

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the facile, one-pot, eco-friendly, multi-component synthesis of a new series of fluorinated 1,5-diarylhexahydro-2-thioxo-1,3,5-triazines (**4**); 1,5-diaryl[1,3,5-triazin]-2-yl hydrazine (**7**) and 1,5-diaryl[1,3,5-triazin]-2-yl thioaceticacid (**8**) in aqueous medium under microwave irradiation (Sch. 1).

In the present studies, under MW irradiation the condensation of fluorinated/heterocyclic amines (3) with formaldehyde (2) gave imine formaldehyde co-polymer in the beginning which was reacted with fluorinated phenyl thioureas to give thioxotriazines (4) in 30-60 sec in 94-98% yield with reasonable purity, with no need of further crystallization. The process is general for both the components, e.g. urea/thiourea (aromatic, fluorinated) and anilines (aromatic, fluorinated, heterocyclic). Thus a number of 1,3,5-triazines, triazinyl hydrazine/thioaceticacid and 1,2,4, triazolo [4,3-a]-1,3,5-triazines can be readily obtained by varying the two components.

4 was further reacted with hydrazine hydrate (5) or chloroacetic acid (6) to give 7 and 8 respectively. When 7 was treated with CS_2 , a cyclized product (10) was obtained in quantitative yields. The whole procedure for synthesis of 10 involved a one-pot reaction as the intermediates 4 and 7 were formed in quantitative yield with reasonable purity (TLC) and were used 'in situ' for further conversion.

For comparative studies some compounds were also synthesized under thermal conditions (Table 1). Conventional synthesis of **10** require a three step procedure with prolonged reflux in organic solvents using strong dehydrating agents/acids, leading to lower yields.

RESULT AND DISCUSSION

In the ¹H NMR spectra of triazines (4) the two methylene ring protons appeared at $\delta 4.32-4.51$ ppm (s, 2H, <u>CH</u>₂-N-Ph), 4.72–5.20 ppm (s, 2H, <u>CH</u>₂-NH) and multiplet at $\delta 6.57-7.62$ ppm for aromatic protons along with a broad peak at $\delta 7.41-7.82$ ppm (br, 1H, NH). IR spectra of these compounds revealed a strong band in the region 1160–1220 cm⁻¹ (C=S). The formation of **7** and **8** was confirmed by the IR spectra showing disappearance of C=S band and appearance of NHNH₂ band (3400–3220 cm⁻¹) in case of **7**, while a sharp band at 1690–1720 cm⁻¹ (>C=O, acidic), and a broad band at 3470– 3420 cm⁻¹ (OH) in case of **8**. The ¹H NMR spectra of **7** showed additional peaks at $\delta 1.52-1.56$ ppm (s, 1H, -<u>NHNH</u>₂) and a broad peak at 2.01– 2.06 ppm (br, 2H, -NH<u>NH</u>₂) along with usual signals of <u>CH</u>₂-N-Ph, <u>CH</u>₂-NH and Ar-H, while in case of **8**, **a** sharp peak was obtained at $\delta 3.95-3.42$ ppm (s, 2H, -<u>SCH</u>₂) and at 8.45–8.40 ppm (br, 1H, OH). Compounds **10**, showed a characteristic absorption at 3210–3240 cm⁻¹ (NH) and 1240–1245 (C=S) cm⁻¹ in IR spectra and disappearance of NH₂ peak and appearance

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Entry	Medium	Mode of reaction Δ/MW (Power W)	Temperature ^a (°C)	Time (min)	Yield ^b (%)
4a	DMF	Δ	40	720	58
	Aqueous medium	MW (640)	101	45 sec.	96
	Aqueous medium	Δ	101	45 sec.	34
	Aqueous medium	Δ	101	10	75
7a	Aqueous medium	Δ	Reflux	420	58
	Aqueous medium	MW (640)	102	1.5	86
	Aqueous medium	Δ	102	1.5	20
8a	Ethanol + Fused CH ₃ COONa	Δ	Reflux	420	60
	Neat	MW (640)	122	3	85
	Neat	Δ	122	3	30
10a	Anhydrous Pyridine	Δ	Reflux	240	60
	Neat	MW (520)	122	3	85
	Neat	Δ	122	3	30

Table 1. Comparative study of the synthesis of 4a, 7a, 8a, 10a.

^aFinal temperature is measured at the end of microwave irradiation by introducing a glass thermometer in the reaction mixture in the beaker.

^bYield of the isolated products.

1144

of a broad peak due to -NH at δ 7.54–7.48 ppm (br, 1H, NH) in ¹HNMR spectra along with the characteristic signals of CH₂-N-Ph, CH₂-NH and Ar-H confirmed the formation of **10**. Physical and spectral data of new synthesized compounds are given in Tables 2 and 3 respectively.

EXPERIMENTAL

Melting points were determined in open glass capillaries and were uncorrected. IR spectra were recorded on a Perkin-Elmer (Model-577) infracord spectophotometer using KBr pellets. ¹H NMR and ¹⁹F NMR spectra were recorded on Jeol (Model FX-90Q), using CDCl₃ as solvent at 89.95 MHz. TMS was used as an internal reference for ¹H NMR spectra and hexafluorobenzene as an external reference for ¹⁹F NMR spectra. All compounds were found homogeneous on TLC in solvent systems like benzene : ethyl acetate (8:2), in case of compound **4**, **7**, **8** and benzene : ethyl acetate (7:1:2) in case of **10**. The microwave induced reactions for the synthesis of **4**, **7** and **8** were carried out in unmodified BMO-700T domestic oven manufactured by BPL multimode Sanyo utilities and



appliances Ltd. operating at 700 W generating 2450 MHz frequency. Synthesis of **10** was carried out in a modified microwave oven attached with reflux condenser and magnetic stirrer fitted at the base of the oven.

1-(2-Trifluoromethylphenyl)-5(2-trifluoromethylphenyl)-2thioxo Hexahydro-1,3,5-triazine (4a)

It was prepared by two different methods: (A) Conventional synthesis and (B) Microwave mediated synthesis.

Conventional Synthesis

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An equimolar mixture of 2-trifluromethyl phenyl thiourea 1a (220 mg, 1 mmol), aqueous formaldehyde 2 (2 mL, 5 mmol) and 2-trifluromethyl aniline 3a (161 mg, 1 mmol) was stirred at $40-45^{\circ}$ C (room temperature) for 8 hr in presence of DMF (20 mL). On completion of reaction (TLC), the reaction mixture was cooled and poured into ice cold water the solid thus obtained was filtered, washed with water, dried and recrystallized from ethanol to give the respective product 4a.

Microwave Mediated Synthesis

An equimolar mixture (1 mmol) of **1a** and **3a** was gently mixed with excess of **2** (5 mmol). It was then irradiated inside a microwave oven at 640 watts for 30-60 sec to get a white colored solid which was filtered, washed with water and found to be pure (TLC), with no need of further crystallization or purification.

1-(2-Trifluoromethylphenyl)-5(2trifluoromethylphenyl)[1,3,5-triazin]-2-yl Hydrazine (7a)

Conventional Synthesis

4a (405 mg, 1 mmol) was refluxed with hydrazine hydrate (5) (30–40 mL) for 6 hr. A crude product appeared on cooling the reaction mixture, which was filtered, washed with water and recrystallized from ethanol to give the desired product.

ORDER		REPRINTS
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1146

Dandia, Arya, and Sati

Table 2. Physical data of synthesized compounds 4a-n, 7a-c, 8a,b, 10a-c.

	Reaction Time	: (min)/yield (%)				
					Elemental analysis	(%) Found (Calcd)
Compound No.	Classical method	Microwave method	Molecular formula ^b	M.P. (°C)	N	S
4a	720/58	45 sec/96	$C_{17}H_{13}N_3SF_6$	242	10.34 (10.37)	7.86 (7.90)
4b	690/53	$50 \sec/98$	$C_{16}H_{14}N_{3}SF_{3}$	150	12.49 (12.46)	9.46 (9.49)
4c	715/56	1/96	$C_{15}H_{14}N_3SF$	120	14.66 (14.63)	11.10 (11.14)
4d	650/52	55 sec/92	$C_{15}H_{14}N_3SF$	175	14.59 (14.63)	11.10(11.14)
4e	740/50	1/94	$C_{16}H_{14}N_{3}SF_{3}$	158	12.42 (12.46)	9.46 (9.49)
4f	750/53	48 sec/94	$C_{17}H_{13}N_{3}SF_{6}$	215	10.34(10.37)	7.92 (7.90)
4g	680/55	1/96	$C_{16}H_{13}N_{3}SF_{4}$	170	11.80 (11.83)	8.98(9.01)
4h	650/53	$50 \sec/95$	$C_{16}H_{13}N_{3}SF_{4}$	192	11.86 (11.83)	9.03 (9.01)
4i	715/51	1/95	$C_{16}H_{13}N_{3}SF_{4}$	195	11.80(11.83)	8.98 (9.01)

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4j	750/50	2/96	$C_{13}H_{13}N_6S_2F_3$	210	22.39 (22.45)	17.06 (17.11)
4k	760/55	2/96	$C_{19}H_{17}N_4S_2F_3$	208	13.23 (13.27)	15.19 (15.16)
41	720/53	1.5/98	$C_{16}H_{14}N_5SF$	242	21.45 (21.40)	9.75 (9.78)
4m	695/58	1.5/96	$C_{10}H_{13}N_{3}S$	205	20.22 (20.28)	15.48 (15.45)
4n	720/53	1/98	$C_{10}H_{13}N_3O_2$	138	20.33 (20.28)	
7a	640/58	1.5/86	$C_{17}H_{15}N_{5}F_{6}$	172	17.31 (17.36)	
7b	415/52	1.5/90	$C_{16}H_{16}N_5F_3$	152	20.94 (20.89)	
7c	430/55	2/89	$C_{15}H_{16}N_{5}F$	220	24.49 (24.56)	
8a	420/60	3/85	$C_{19}H_{15}N_3F_6O_2S$	265	9.04 (9.07)	6.91 (6.92)
8b	425/62	3.5/84	$C_{18}H_{16}N_3F_3O_2S$	225	10.60 (10.63)	8.08 (8.10)
10a	240/60	3/92	$C_{18}H_{13}N_5SF_6$	58	15.69 (15.73)	7.22 (7.19)
10b	245/56	4/88	$C_{17}H_{14}N_5SF_3$	275	18.51 (18.56)	8.45 (8.48)
10c	252/52	3/86	$C_{16}H_{14}N_5SF$	302	21.35 (21.40)	9.75 (9.78)
^a Final temper mixture in the ^b All compoun	ature is measured : beaker. ds gave satisfacto	at the end of m	icrowave irradiation by lyses (C and H) withir	y introduci 1 $\pm 0.25\%$	ng a glass thermome of theoretical value.	ter in the reaction

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Synthesis of Fluorinated Hexahydro 1,3,5-Triazine



4.42 (s, 2H)

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1148

Dandia, Arya, and Sati

-62.69 (s, CF₃), -120.85 (s, 2-F)

6.70-758 7.62 (br, 1H, NH) (m, 8H)

-63.12 (s, 2-CF₃), -118.85 (s, 4-F)

6.70–762 7.45 (br, 1H, NH) (m, 8H)

(two s, both 2-CF₃)

-64.07, -64.02

6.62-7.35 7.41 (br, 1H, NH) (m, 8H)

5.02 (s, 2H)

4.42 (s, 2H)

4.35 (s, 2H)

(C=S) 3330-3270 (NH), 2920-2860 (C=C), 1440, 1205-1170 (C=S) 3325-3280 (NH), 2920-2870 (C=C), 1450, 1210-1160 (C=S) 3330-3280 (NH), 2910-2860 (C=C), 1440, 1205-1170 (C=S)

48

4h

		Table 3. Spc	sctral data of the cc	spunoam		
		-		¹ H NMR (8), ppm)	
Compound No.	I IR (cm ⁻¹)	<u>CH</u> 2-NPh/H	CH ₂ -NH/CH ₂ -N	Ar-H	NH/NH ₂ /OH (Exchangeable with D ₂ O)	19F NMR (ô, ppm)
4a	3340-3280 (NH), 2920-2860 (C=C), 1460, 1220-1180 (C=S)	4.38 (s, 2H)	5.12 (s, 2H)	6.57–7.20 (m, 8H)	7.82 (br, 1H, NH)	-64.02, 64.12 (two s, both 2-CF ₃)
4b	3360-3290 (NH), 2920-2860 (C=) 1440, 1205-1185 (C=)	4.32 (s, 2H)	5.02 (s, 2H)	6.72-7.35 (m, 9H)	7.61 (br, 1H, NH)	–64.12 (s, CF ₃)
4c	(2-5) 3380-3295 (NH), 2910-2850 (2=C), 1420, 1210-1190 (7-5)	4.30 (s, 2H)	5.05 (s, 2H)	6.72-7.25 (m, 9H)	7.73 (br, 1H, NH)	– 119.20 (s, 3-F)
4d	(C—S) 3340–3290 (NH), 2905–2860 (C=C), 1410, 1205–1185 (C—S)	4.31 (s, 2H)	5.15 (s, 2H)	6.72–7.25 (m, 9H)	7.62 (br, 1H, NH)	– 120.92 (s, 2-F)
4e	3350–3290 (NH), 2910–2850 (C=C), 1450, 1210–1180	4.30 (s, 2H)	5.12 (s, 2H)	6.78–7.45 (m, 9H)	7.52 (br, 1H, NH)	-64.24 (s, CF ₃)

4f



(continued)						
-64.12 (s, 2-CF ₃)	0.70 (01, 111, 011)	(m, 8H)	(117 %) 00.0	2.27 (s, 211, 3- <u>CH2</u>) 4.25 (s, 2H, <u>CH2</u> NPh)	(NH), 2940-(C=C), 1720 (NH), 2940-(C=C), 1720 (C=O), 1620 (C=N)	00
	2.06 (br, 2H, -NH <u>NH</u> ₂)	(m, 9H)			2910-2870 (C=C), 1620 (C=N)	
–119.05 (s, 3-F)	1.56 (s, 1H, - <u>NH</u> NH ₂),	6.56-7.35	5.22 (s, 2H)	4.18 (s, 2H)	(C=N) 3410-3260 (NH ₂ and NH),	7с
	2.03 (br, 2H, $-NHNH_2$)	(m, 9H)			2920–2850 (C=C), 1625	2
-64.10 (s. 2-CF ₃)	1.54 (s. 1H. –NHNH ₃).	6.58-7.32	5.25 (s. 2H)	4.15 (s. 2H)	1620 (C=N) 3400-3240 (NH ² and NH).	dF D
s, both 2-CF ₃)	2.01 (br, 2H, -NH <u>NH</u> ₂)	(m, 8H)			2930-2870 (CH Stretching),	
–64.13, –64.02 (Two	1.52 (s, 1H, –NHNH ₂),	(m, 4H) 6.62–7.42	5.20 (s, 2H)	4.37 (s, 2H) 4.41 (s, 2H)	(C=C), 1680 (CONH ₂) 3380–3220 (NH ₂ and NH),	7а
I	7.42 (br, 2H, NH)	6.52-7.05	4.85 (s, 4H)	3.48 (s, 3H, OCH ₃)	3310-3280 (NH), 2925-2850	4n
		(m, 4H)		4.35 (s, 2H)	(C=C), 1205-1185 (C=S)	
I	7.85 (br, 2H, NH)	6.72-7.10	4.98 (s, 4H)	2.18 (s, 3H, CH ₃).	1090-1120 (C-O-C) 3320-3270 (NH), 2920-2865	4m
					1205–1170 (C=S),	
	(br, 1H, NH)	(m, 8H)			(C=C), 1625 (C=N), 1420,	
– 118.65 (s, 4-F)	7.72 (br, 1H, NH) 8.01	6.51-7.82	4.72 (s, 2H)	(s, 2H) 4.41 (s, 2H)	1360, 1205–1170 (C S) 3340–3280 (NH), 2920–2850	41
		(m, 7H)	(111 (0) -0.1	(t, 2H, CH ₂), 4.38	(C=C), 1620 (C=N), 1420,	1
- 63 87 (c - 2 CE.)	7 57 (br. 11 MHV)	122 229	S M G JHV	4.41(s, 2H, <u>CH</u> ₂ N-Ph) 1 33 (s, 3H, <u>CH</u> ₂) 3 72	1440, 1205–1170 (C=S) 3360 3300 (NHV) 2000 2840	ŧ
		(m, 4H)		(s, 3H, CH ₃)	(C=C), 2440–2420 (SH),	
-63.72 (s. 2-CF ₃)	7.65 (hr. NH. NH)	6.70-7.62	5.15 (s. 2H)	1.36 (s. 1H. SH). 2.32	(C=S) 3370-3320 (NH). 2930-2870	4i
- 02.00 (s, 2-Ur3), - 118.75 (s, 4-F)	/.02 (DI, 111, INH)	0./2 <i>C</i> ./-C/.0 (m, 8H)	(H17 '8) CI .C	(177 (S, 211)	C=C), 1430, 1210–1180 (C=C)	Ŧ
						;



1150

				¹ H NMR (8	, ppm)	
Compound No.	IR (cm ⁻¹)	<u>CH</u> 2-NPh/H	CH2-NH/CH2-N	Ar-H	NH/NH ₂ /OH (Exchangeable with D ₂ O)	19F NMR (ô, ppm)
8b	3450-3420 (OH), 3300-3240 (NH), 2960-2910 (C=C),	3.42 (s, 2H, S- <u>CH</u> ₂) 4.20 (s, 2H	5.12 (s, 2H)	6.52-7.58 (m, 9H)	8.45 (br, 1H, OH)	–64.13 (s, 2-CF ₃)
10a	1690 (C=O), 1610 (C=N) 3240-3220 (NH), 2930-2870 (C=C), 1620 (C=N), 1240	<u>CH₂NPh</u>), 4.35 (s, 2H)	5.12 (s, 2H)	6.59–7.42 (m, 8H)	7.54 (br, 1H, NH)	64.15 (s, 2-CF ₃) - 64.02 (s, 2-CF ₃)
10b	(C=S) 3230-3210 (NH), 2930-2870 (C=C), 1625 (C=N), 1245	4.48 (s, 2H)	5.15 (s, 2H)	6.62–7.46 (m, 9H)	7.58 (br, 1H, NH)	64.10 (s, 2-CF ₃)
10c	(C=S) 3240-3210 (NH), 2950-2880 (C=C), 1615 (C=N), 1240 (C=S)	4.52 (s, 2H)	5.12 (s, 2H)	6.62–7.40 (m, 9H)	7.52 (br, 1H, NH)	– 119.65 (s, 3-F)

Table 3. Continued.

Dandia, Arya, and Sati





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$H_2N = C = N = X + CH_2O + R = NH_2 = Z = S = X = S = X = S = X = S = X = S = X = S = X = S = X = S = S$	$ \begin{array}{c} \begin{array}{c} & X \\ & & \\ \end{array} \\ \\ \hline \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\$	$\begin{array}{c} X \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\$
Compound no.	Х	R
4 a	$2-CF_3C_6H_4$	2-CF ₃ C ₆ H ₄
4b	C_6H_5	$2-CF_3C_6H_4$
4c	C_6H_5	$3-FC_6H_4$
4 d	C_6H_5	$2-FC_6H_4$
4 e	C_6H_5	$3-CF_3C_6H_4$
4f	$2-CF_3C_6H_4$	$3-CF_3C_6H_4$
4g	$2-CF_3C_6H_4$	$2-FC_6H_4$
4h	$2-CF_3C_6H_4$	$4-FC_6H_4$
4i	$4-FC_6H_4$	$2-CF_3C_6H_4$
4j	$2\text{-}CF_3C_6H_4$	H ₃ C N N H ₃ C N N H ₃ C N SH
4k	$2\text{-}CF_3C_6H_4$	
41	4-FC ₆ H ₄	
4m	Н	$4-CH_3C_6H_4$
4n	Н	$4-OCH_3C_6H_4$
7a	$2-CF_3C_6H_4$	$2-CF_3C_6H_4$
7b	C_6H_5	$2-CF_3C_6H_4$
7c	C_6H_5	$3-FC_6H_4$
8a	$2-CF_3C_6H_4$	$2-CF_3C_6H_4$
8b	C_6H_5	$2-CF_3C_6H_4$
10a	$2-CF_3C_6H_4$	$2-CF_3C_6H_4$
10b	C_6H_5	$2-CF_3C_6H_4$
10c	C_6H_5	$3-FC_6H_4$

Scheme 1.

1151





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Microwave Mediated Synthesis

1152

To 4a (synthesized 'in situ'), hydrazine hydrate (5) (1 mL, 0.005 mole) was added and irradiated inside microwave oven at 640 watts till the completion of the reaction (1.5 min). The reaction mixture on cooling gave a crystalline product 7 with reasonable purity (TLC).

1-(2-Trifluoromethylphenyl)-5(2trifluoromethylphenyl)[1,3,5-triazin]-2-yl Thioaceticacid (8a)

Conventional Synthesis

A mixture of **4a** (405 mg, 1 mmol), chloroacetic acid (**6**) (94 mg, 1 mmol) and fused sodium acetate (1 mmol) in dry ethanol was heated under reflux for 6 hrs. The reaction mixture was cooled to room temperature and the solid thus separated, was filtered and recrystallized from ethanol to give **8**.

Microwave Mediated Synthesis

'In situ' synthesized compound 4a was mixed with chloroacetic acid (6) (94 mg, 0.001 mole) and irradiated inside microwave oven at 640 watts till the completion of the reaction (3 min). The product was then extracted from methanol and excess of solvent was evaporated on roto-evaporator to give a crystalline compound, which was found to be pure (TLC).

The compounds **4b–n**, **7b,c** and **8b** were prepared by following the same procedure.

1,2,4-Triazolo[4,3-a]-5-thioxo-1(2-trifluoromethylphenyl)-5(2trifluoromethylphenyl)-1,3,5-triazine (10a)

Conventional Synthesis

A mixture of 7a (403 mg, 1 mmol) and carbon disulphide 9 (10 mL) in anhydrous pyridine (30 mL) was refluxed for 4 hr. On cooling the reaction mixture, crude solid appeared which was filtered, and recrystallized from DMF to give the desired compound.



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Microwave Mediated Synthesis

In a 100 mL round bottom flask, a neat mixture of 7a (synthesized 'in situ') and carbon disulfide 9 (5 mL) was stirred using rotating magnet and irradiated with microwaves till the completion of the reaction (3 min) at 520 W. On completion of reaction, white colored needles appeared on cooling which were filtered and found to be of reasonable purity (TLC) with no need of further crystallization.

The compounds **10b,c** were also prepared on similar lines by following the same procedure.

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1154

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