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Microwave assisted one pot synthesis of a series of trifluoromethyl substituted spiro [indole–triazoles]

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Abstract

A series of trifluoromethyl substituted spiro [3H-indole-3,3′-[3H-1,2,4]triazoles]-2(1H)-ones have been synthesized in 85–90% yield by one pot environmentally benign microwave induced techniques involving the condensation of 3-arylimino-2H-indol-2-ones (**III**) with thiosemicarbazide (**IV**) using montmorillonite as solid support. This 3-arylimino-2H-indol-2-ones (**III**) was synthesized in situ by the reaction of fluorinated indole-2,3-diones (**I**) and fluorinated anilines (**II**). The advantages obtained by the use of microwave irradiation were demonstrated.

Keywords: Microwave irradiations; Indole-2,3-diones; 3-Arylimino-2H-indol-2-ones spiro [indole–triazoles]

1. Introduction

The indole nucleus has been found to be associated with diverse biological activities [1]. Further, if the indole-3-carbon is in the form of a spiro atom, the compounds exhibit enhanced biological activities [2,3]. Along with spiro indolines, the great importance of triazole derivatives in the field of biochemistry [4–6] and pesticidal chemistry has also attracted the attention of chemist and biochemists for a long time.

Fluorine incorporation in heterocycles is known to affect the course of the reaction besides influencing the biological activity [7]. It has been observed that introduction of a fluorine atom or CF_3 group to heterocycles may act as a pharmacophore, enhancing pharmacological properties of the compounds as compared to their non-fluorinated analogues [8]. Incorporation of a trifluoromethyl substituent also increases the phytotoxicity along with selectivity and arenes bearing a trifluoromethyl substituent comprise the largest sub-group of commercially promising pesticides and herbicides. Fluorinated 3-phenyl imino indol-2(3H)-ones have been reported to possess remarkable antimicrobial activities against *Mycobacterium paratuberculosis*, *E. coli*, *Salmonella typhi* and *Aspergillus niger* [9]. Trifluoromethyl substitutions in the aromatic ring are favorable for antimicrobial activity [10]. The derivatives also represent a novel class of anti HIV agents which appear to act by inhibiting virus dependent cell fusion. Fluorinated triazole derivatives have also shown remarkable antibacterial, antifungal and herbicidal activities [11–14].

In spiro indoles also, fluorine incorporation alters bioactivity and the chemistry of fluorinated spiro indole derivatives has been of considerable interest due to the variation in the physico-chemical properties of these derivatives as compared to their non-fluorinated analogues [2,15,16].

In spite of the immense biological activities displayed by fluorinated 3-arylimino-2H-indol-2-ones and fluorinated triazol derivatives, no attention has been paid so far to the synthesis of fluorinated spiro [3H-indole-3,3′-[3H-1,2,4]triazoles]-2(1H)-ones. Recently, we have reported a one pot synthesis of novel spiro [indole-1,2,4-triazoles] for the first time [17].

Further utilization of ‘microwave-oven induced reaction enhancement’ (MORE) chemistry for highly accelerated synthesis of divergent types of heterocycles is of current interest due to the rapid heating associated with microwave technology [18].

However, greater interest has been focused recently on ‘‘dry media’’ synthesis using inorganic solid supports under microwave irradiation. The coupling of a microwave heating mode with the use of a mineral solid support has allowed the synthesis of several organic compounds with higher selectivity, yield and purity compared to traditional methods [19]. Formation of fluoro compounds by usual methods is tedious and expensive, now that the potential of microwave chemistry can be utilized in the synthesis of these compounds.

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Table 1
Physical and analytical data **VI(a–e)**[a]

Compound number	*X*	*Y*	Reaction time (min)	Melting point (°C)	Yield (%)	Molecular formula	Elemental analysis (calculated/found) (%)	
							C	N
VI(a)	H	$2CF_3$	6 + 2	250	85.6	$C_{18}H_{14}F_3N_5O_2$	55.52/55.45	17.99/17.86
VI(b)	5Cl	$3CF_3$	6 + 2	280	84.8	$C_{18}H_{13}ClF_3N_5O_2$	51.00/51.22	16.52/16.70
VI(c)	5F	$3CF_3$	2 + 2	200	80.7	$C_{18}H_{13}F_4N_5O_2$	53.07/53.19	17.19/17.85
VI(d)	$7NO_2$	$3CF_3$	7 + 2	265–266 (d)	80.0	$C_{18}H_{13}F_3N_6O_4$	49.76/49.85	19.35/19.45
VI(e)	$5CH_3$	$3CF_3$	5 + 2	180	82.0	$C_{19}H_{16}F_3N_5O_2$	56.57/56.68	17.36/17.48

[a] **VI(a–e)** were synthesized at 360 W using ethanol as energy transfer medium, e.g. **VI(a)**, 6 + 2 indicates, first irradiation for 6 min gives compound **III** (detected by TLC) and then further irradiation after adding thiosemicarbazide for 2 min yield **VI(a)**.

Table 2
Comparative results of the synthesis of **V/VI** using ethanol/ethanol with acetic acid (method a) and montmorillonite/montmorillonite with acetic acid (method b) under microwave irradiation[a]

Compound number	*X*	*Y*	Classical method		Microwave method				Melting point (°C)	Molecular formula	Elemental analysis (calculated/found) (%)	
			Time (h) (first/second step)	Yield (%) (first/second step)	a		b				C	N
					Time (min)	Yield[b] (%)	Time (min)	Yield[b] (%)				
V(a)	5Cl	$2CF_3$	4/2	76/32	6 + 2	65.2	5 + 2	93.6	275 (d)	$C_{16}H_{11}ClF_3N_5O$	50.32/50.70	18.34/18.20
V(b)	$7NO_2$	$2CF_3$	–	–	6 + 1	60.2	4 + 2	95.2	285	$C_{16}H_{11}F_3N_6O_3$	48.97/48.85	21.42/21.50
VI(f)	5Cl	$2CF_3$	2/5	77/60	6 + 2	75.6	5 + 1	94.7	290	$C_{18}H_{13}ClF_3N_5O_2$	51.00/51.30	16.52/16.24
VI(g)	$7NO_2$	$2CF_3$	–	–	6 + 2	78.0	4 min + 4 s	92.8	260 (d)	$C_{18}H_{13}F_3N_6O_4$	49.76/49.84	19.35/19.40

[a] Irradiations were carried out at 360 and 480 W in methods a and b, respectively; montmorillonite 20 wt.%.
[b] Final isolated yield from single step.

Hence, in continuation to our earlier interest on the synthesis of fluorine containing bio-dynamic heterocycles [20–26] using non-conventional method of organic synthesis, we report here the one pot synthesis of fluorinated spiro [3H-indole-3,3′-[3H-1,2,4-triazoles]-2(1H)-ones, using (a) ethanol as energy transfer medium and (b) montmorillonite as inorganic solid support under microwave irradiation.

2. Results and discussion

The condensation of fluorinated indole-2,3-diones (**I**) with fluorinated anilines (**II**) yielded fluorine containing 3-arylimino-2H-indol-2-ones (**III**) which in situ were cyclo-condensed with thiosemicarbazide (**IV**) in the presence/absence of acetic acid to give **VI/V**, respectively.

Reaction occurs rapidly in both cases, i.e. with/without acetic acid with the evolution of H_2S gas [27], the presence of which is detected by its characteristic odor and rendering a filter paper wet with lead acetate, black during the progress of the reaction.

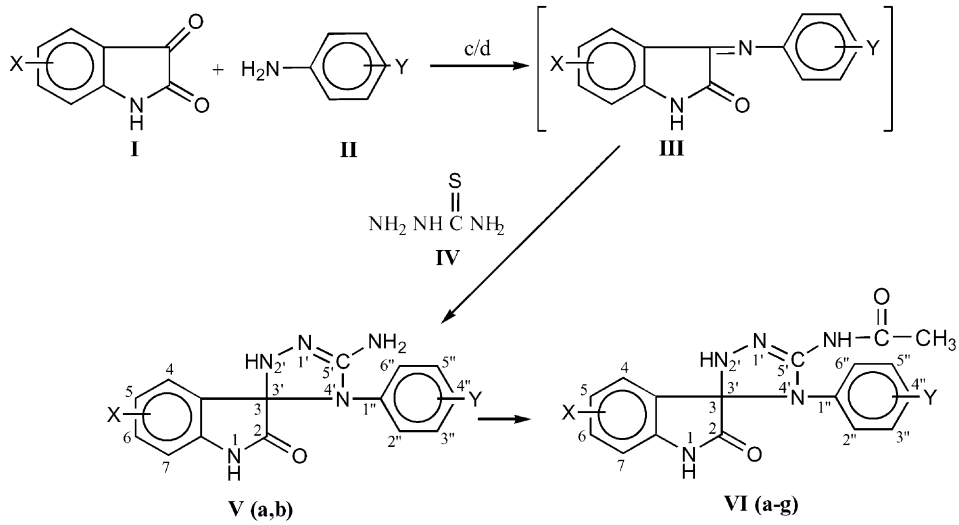
We have extensively studied the title reaction varying different parameters, viz. medium, solid support, power level, etc. Montmorillonite efficiently catalyzed the reaction giving maximum yield (94–98%) with shortest period and easiest work up.

Further, the amount of montmorillonite also plays a very important role as reactions occur rapidly along with enhanced yields when an optimum quantity (20 wt.%) of montmorillonite is used. However, excess of solid support (50 wt.%) reduces the yield with an increase in reaction time. The results are summarized in Tables 1 and 2. The possible existence of a specific microwave effect (non-thermal) has been studied by carrying out the reactions using a preheated oil bath under similar condition (same

Table 3
Comparative results obtained in the synthesis of **V(a)** and **VI(f)** using conventional synthesis (a) and microwave method (b) using ethanol as the energy transfer medium[a]

Compound number	Method	Reaction time	Temperature (b) (°C)	Yield (%)
V(a)	b	6 + 2	78	65.2
	a	6 + 2	78	Nil
	a	15 + 2	78	Traces
	a	15 + 8	78	39
VI(f)	b	6 + 2	78	75.6
	a	6 + 2	78	Nil
	a	15 + 2	78	Traces
	a	15 + 6	78	42.8

[a] Final temperature (b) is measured by immersing a glass thermometer in the reaction mixture at the end of exposure to microwave irradiation.



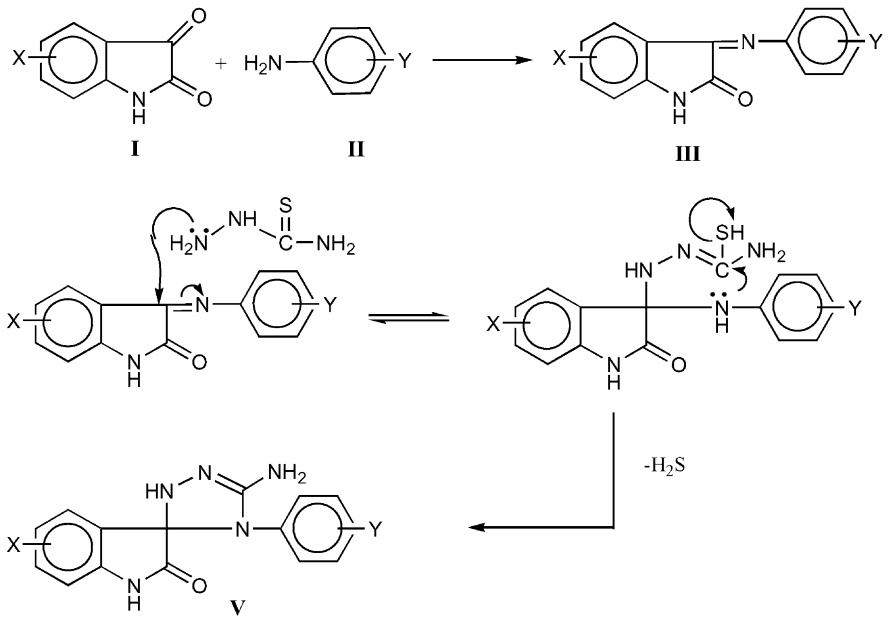
Synthetic Procedures

(a) EtOH + AcOH, μv
(b) Montmorillonite + AcOH, μv
(c) EtOH, μv
(d) Montmorillonite, μv

X = H, 5-Cl, 5-F, 7-NO_2, 5-Br

Y = 2-CF_3,3-CF_3

Mechanism



Scheme 1.

time, temperature and vessel) as carried out during microwave experiments. Under these conditions it has been observed that poor yields are obtained using the preheated oil bath which indicates that the effect of microwave irradiation is not purely thermal (Table 3).

The present new method of the formation of **V** and **VI** under microwave irradiation offers several advantages over traditional methods faster reaction rates, fewer byproducts (TLC), smaller amounts of solvent and simple, less expensive equipment while the classical method of formation of spiro [indole-4H-[1,2,3]triazoles] involves a long tedious process (more than 21 days) in two steps [28] with the requirement of purification and crystallization, while the present method involves the synthesis of spiro derivatives in only 10–15 min without any need of further purification.

Table 4
Spectroscopic data

Compound number	IR (cm^{-1})	^1H NMR (δ, ppm)	^{19}F NMR (δ, ppm)
V(a)	3400–3265 (NH_2 and NH), 1743 (C=O), 1625 (C=N), 1465, 1051, 920	6.91 (dd, 1H, $J_1 = 8.4$, $J_2 = 7.6$, 5″-H), 6.99 (dd, 1H, $J_1 = 8.9$, $J_2 = 2.4$, 6H), 7.07–7.58 (m, 2H, 6″-H, 7H), 7.66 (d, 1H, $J = 2.4$, 4H), 7.77 (dd, 1H, $J_1 = 8.4$, $J_2 = 7.5$, 4″-H), 7.91 (d, 1H, $J = 7.5$, 3″-H), 8.38 (br, 1H, NH of triazole) 8.85 (br, 2H, NH_2), 11.09 (br, 1H, indole NH)	−63.249 (s, CF_3)
V(b)	3400–3300 (NH_2 and NH), 1740 (C=O), 1620 (C=N), 1460, 1050, 920	6.86–7.15 (m, 3H, 5″-H, 5H, 6″-H), 7.24 (dd, 1H, $J_1 = 8.3$, $J_2 = 1.2$, 6′-H), 7.47 (dd, 1H, $J_1 = 8.9$, $J_2 = 1.2$, 4H), 7.71 (dd, 1H, $J_1 = 8.4$, $J_2 = 7.6$, 4″-H), 7.93 (d, 1H, 7.6, 3″-H), 8.39 (br, 1H, NH of triazo1e), 8.85 (br, 2H, NH_2), 11.09 (br, 1H, indole NH)	−64.046 (s, CF_3)
VI(a)	3300–3068 (NH), 1730 (C=O), 1697 (C=O), 1614 (C=N), 1465, 1396, 1336, 1269, 1240, 1120, 945, 842, 746	2.11 (s, 3H, $NHCOCH_3$), 6.85 (dd, 1H, $J_1 = 8.5$, $J_2 = 7.6$, 5″-H), 6.90 (dd, 1H, $J_1 = 8.5$, $J_2 = 7.4$, 4″-H), 7.21 (td, 1H, $J_1 = 8.3$, $J_2 = 6.8$, $J_3 = 1.3$, 5H), 7.24 (td, 1H, $J_1 = 8.4$, $J_2 = 6.8$, $J_3 = 1.3$, 6H), 7.65 (dd, 1H, $J_1 = 8.3$, $J_2 = 1.4$, 4H), 7.71 (d, 1H, $J_1 = 7.6$, 6″-H), 7.82 (d, 1H, $J_1 = 7.4$ (3″-H), 8.30 (s, 1H, NH triazole), 8.79 (s, 1H, $NHCOCH_3$), 11.09 (br, 1H, NH indole)	−63.021 (s, CF_3)
VI(b)	3290–3060 (NH), 1720 (C=O), 1695 (C=O), 1613 (C=N), 1460, 1390, 1335, 1260, 1240, 1120, 947, 843, 745	2.13 (s, 3H, $NHCOCH_3$), 6.89 (dd, 1H, $J_1 = 8.6$, $J_2 = 7.3$, 5″-H), 6.96 (d, 1H, $J = 7.3$, 6″-H), 7.15 (dd, 1H, $J_1 = 9.1$, J_2 =2.3, 6H), 7.31 (d, 1H, $J = 9.1$, 7H), 7.68 (d, 1H, $J = 2.3$, 4H), 7.75 (d, 1H, $J = 8.6$, 4″-H), 7.87 (s, 1H, 2″-H), 8.29 (br, 1H, NH triazole), 8.80 (br, 1H, $NHCOCH_3$), 11.08 (br, 1H, NH, indole)	−63.859 (s, CF_3)
VI(c)	3305–3060 (NH), 1725 (C=O), 1697 (C=O), 1610 (C=N), 1455, 1390, 1330, 1260, 1245, 1120, 947, 846, 745	2.09 (s, 3H, $NHCOCH_3$), 6.88 (dd, 1H, $J_1 = 8.7$, $J_2 = 7.6$, 5″-H), 6.97 (d, 1H, $J = 7.6$, 6″-H), 7.18 (dd, 1H, $J_1 = 9.2$, $J_2 = 2.5$, 6H), 7.35 (d, 1H, 9.2, 7H), 7.68 (d, 1H, $J = 2.5$, 4H), 7.76 (d, 1H, $J = 8.7$, 4″-H), 7.86 (s, 1H, 2″-H), 8.31 (br, 1H, NH triazole), 8.80 (br, 1H, $NHCOCH_3$), 11.09 (br, 1H, NH indole)	−63.041 (s, CF_3)
VI(d)	3300–3065 (NH), 1728 (C=O), 1698 (C=O), 1612 (C=N), 1465, 1385, 1330, 1260, 1240, 1120, 947, 840	2.12 (s, 3H, $NHCOCH_3$), 6.96–7.10 (m, 3H, 5″-H, 5H, 6″-H), 7.21 (dd, 1H, $J_1 = 8.1$, $J_2 = 1.1$, 6H), 7.40 (dd, 1H, $J_1 = 8.9$, $J_2 = 1.1$, 4H), 7.78 (d, IH, $J = 8.6$, 4″-H), 7.89 (s, 1H, 2″-H), 8.30 (br, 1H, NH triazole), 8.78 (br, 1H, $NHCOCH_3$), 11.09 (br, 1H, NH indole)	−65.142 (s, CF_3)
VI(e)	3285–3060 (NH), 1730 (C=O), 1690 (C=O), 1610 (C=N), 1460, 1390, 1250, 1230, 1120, 45, 840, 740	2.09 (s, 3H, $NHCOCH_3$), 2.27 (s, 3H, CH_3), 6.89 (dd, 1H, $J_1 = 8.8$, $J_2 = 7.6$, 5″-H), 6.92 (dd, 1H, $J_1 = 8.5$, $J_2 = 1.7$, 6H), 7.05 (d, 1H, $J = 7.6$, 6″-H), 7.13 (d, 1H, $J_1 = 1.7$, 4H), 7.55 (d, 1H, $J = 8.5$, 7H), 7.76 (d, 1H, $J_1 = 8.8$, 4″-H), 7.84 (s, 1H, 2″-H), 8.32 (br, 1H, NH triazole), 8.81 (br, 1H, $NHCOCH_3$), 11.10 (br, 1H, NH indole)	−62.698 (s, CF_3), −119.82 (s, 5-F)
VI(f)	3310–3100 (NH), 1725 (C=O), 1695 (C=O), 1610 (C=N), 1465, 1340, 1250, 1120, 945, 840, 740	2.11 (s, 3H, $NHCOCH_3$), 6.90 (dd, 1H, $J_1 = 8.4$, $J_2 = 7.6$), 6.99 (dd, 1H, $J_1 = 8.9$, $J_2 = 2.4$, 6H), 7.07–7.58 (m, 2H, 6″-H, 7H) 7.66 (d, 1H, $J = 2.4$, 4H), 7.77 (dd, 1H, $J_1 = 8.4$, $J_2 = 7.5$, 4″-H), 7.91 (d, 1H, $J = 7.5$, 3″-H), 8.31 (br, 1H, NH triazole), 8.79 (br, 1H, $NHCOCH_3$), 11.11 (br, 1H, NH indole)	−63.928 (s, CF_3)
VI(g)	3305–3068 (NH), 1730 (C=O), 1695 (C=O), 1614 (C=N), 1460, 1390, 1330, 1265, 1240, 1120, 945, 842, 746	2.13 (s, 3H, $NHCOCH_3$), 6.86–7.15 (m, 3H, 5″-H, 5H, 6″-H), 7.24 (dd, 1H, $J_1 = 8.3$, $J_2 = 1.2$, 6H), 7.47 (dd, 1H, $J_1 = 8.9$, $J_2 = 1.2$), 7.71 (dd, 1H, $J_1 = 8.4$, $J_2 = 7.6$, 4″-H), 7.93 (d, 1H, $J_1 = 7.6$, 3″-H), 8.33 (br, 1H, NH triazole), 8.80 (br, 1H, $NHCOCH_3$), 11.12 (br, 1H, NH indole)	−64.729 (s, CF_3)

Table 5
^{13}C NMR spectroscopic data

Compound number	^{13}C NMR (δ, ppm)
V(a)	164.02 (C=O), 152.08 (N–C=N), 125.55 (CF_3), 111.62 (spiro carbon), 148.28, 147.51, 146.31, 142.10, 132.34, 130.39, 123.01, 120.35, 119.39, 118.06, 117.22, 116.51 (12 aromatic ring carbons)
V(b)	165.12 (C=O), 152.76 (N–C=N), 126.05 (CF_3), 112.16 (spiro carbon), 150.01, 149.21, 147.98, 144.23, 140.05, 131.12, 130.62, 124.77, 121.03, 118.92, 117.56, 115.99 (12 aromatic ring carbons)
VI(a)	162.05 (C=O), 179.18 (C=O), 152.28 (N–C=N), 126.11 (CF_3), 110.78 (spiro carbon), 148.29, 147.55, 146.38, 142.11, 132.36, 130.38, 123.12, 120.38, 119.28, 118.10, 117.21, 116.52 (12 aromatic ring carbons), 38.62 (CH_3)
VI(b)	162.79 (C=O), 179.64 (C=O), 153.01 (N–C=N), 125.03 (CF_3), 111.09 (spiro carbon), 148.66, 147.11, 146.56, 143.02, 131.98, 130.65, 123.52, 121.36, 119.51, 118.96, 117.34, 116.92 (12 aromatic ring carbons), 38.65 (CH_3)
VI(c)	163.11 (C=O), 179.98 (C=O), 153.02 (N–C=N), 125.76 (CF_3), 111.48 (spiro carbon), 148.35, 147.66, 145.87, 146.21, 133.35, 131.27, 125.14, 122.26, 120.02, 118.92, 117.25, 116.88 (12 aromatic ring carbons), 39.01 (CH_3)
VI(d)	163.85 (C=O), 180.12 (C=O), 153.21 (N–C=N), 126.36 (CF_3), 111.52 (spiro carbon), 148.95, 147.68, 146.82, 143.15, 133.02, 130.78, 123.44, 121.05, 119.88, 119.01, 117.56, 116.72 (12 aromatic ring carbons), 39.05 (CH_3)
VI(e)	161.98 (C=O), 178.01 (C=O), 152.11 (N–C=N), 126.31 (CF_3), 110.56 (spiro carbon), 148.24, 147.51, 147.02, 142.22, 132.06, 132.99, 122.87, 121.06, 119.98, 118.21, 117.15, 116.39 (12 aromatic ring carbons), 38.34 (CH_3)
VI(f)	162.68 (C=O), 179.78 (C=O), 153.11 (N–C=N), 125.44 (CF_3), 111.15 (spiro carbon), 148.01, 147.23, 146.77, 143.56, 132.01, 130.48, 123.69, 121.91, 119.15, 118.71, 117.21, 116.98 (12 aromatic ring carbons), 38.45 (CH_3)
VI(g)	163.89 (C=O), 179.95 (C=O), 153.29 (N–C=N), 126.96 (CF_3), 111.41 (spiro carbon), 148.82, 147.99, 146.59, 143.38, 132.98, 131.01, 123.86, 120.97, 119.65, 118.03, 117.51, 116.81 (12 aromatic ring carbons), 38.86 (CH_3)

Formation of spiro compounds (**V** or **VI**) may be rationalized by the mechanism proposed in Scheme 1. The structures of synthesized compounds have been confirmed on the basis of analytical and spectral studies as given in Tables 1–5. On the basis of spectral data, compounds obtained in the presence and absence of acetic acid have been identified as 5′-(*N*-acetyl amino)-4′-aryl-2′,4′-dihydro-spiro[3H-indole-3,3′-[3H-1,2,4]triazoles]-2(1H)-ones (**VI**) and 5′-amino-4′-aryl-2′,4′-dihydro-spiro[3H-indole-3,3′-[3H-1,2,4]-triazoles]-2(1H)-ones (**V**).

3. Experimental

Melting points were determined in open glass capillaries and were uncorrected. IR spectra were recorded on a Perkin-Elmer (model 577) in KBr pellets. ^1H NMR and ^{13}C NMR were recorded on model Bruker MW-200, using $CDCl_3$ as solvent at 200.13 and 50.3 MHz, respectively. ^{19}F NMR was recorded on a Jeol (model FX-90Q) using $CDCl_3$ at 84.25 MHz. TMS was used as internal reference for ^1H NMR and ^{13}C NMR and hexafluorobenzene as external reference for ^{19}F NMR. All compounds were found homogeneous on TLC in various solvent systems.

The induced microwave convection system used has microwaves generated at a frequency of 2450 MHz. The oven has a range of microwave output energy of 1200 W.

Montmorillonite K10 and fluorinated anilines were Aldrich products and were used as received.

*3.1. 5′-Amino-4′-(2-trifluoromethyl phenyl)-2′,4′-dihydro-5-chloro-spiro[3H-indole-3,3′-[3H-1,2,4]triazoles]-2(1H)-ones (**V(a)**)*

The compound **V**(**a**) has been synthesized by (1) classical method; and (2) microwave irradiation method.

Classical method: **V**(**a**) has been synthesized by classical methods in two steps.

1. Synthesis of intermediate anil (**III**(**a**)): a mixture of 5-chloroindole-2,3-dione (**I**) (0.005 mol) and 2-trifluoromethyl aniline (**II**) (0.005 mol) was refluxed in dry toluene (15 ml) for 4 h. Crystals separated out on cooling were dried and recrystallized from ethanol [29].

   III(**a**) : $X = 5Cl$; $Y = 2CF_3$; mp = 167°C; yield = 76% (mp = 167°C; yield = 66.5%)

2. Synthesis of spiro product: a mixture of **III**(**a**) (0.005 mol) and thiosemicarbazide (**IV**) (0.005 mol) in ethanol (20 ml) was refluxed for 2 h. Reaction occurs with the evolution of H_2S. The solid obtained on cooling was crystallized from ethanol.

   V(**a**) : mp = 275°C (d); yield = 32%

Microwave irradiation method: **V**(**a**) has been synthesized in one step without isolation of the intermediate anil by two different methods under microwave irradiation.

(a) An equimolar mixture of **I** and **II** (0.001 mol) in the minimum quantity of ethanol required to form a slurry was irradiated inside a microwave oven at 360 W. After every 2 min an interval of 1 min is allowed, to avoid excessive evaporation of solvent, until the completion of the reaction (6 min). As the reactants disappeared (TLC), thiosemicarbazide (**IV**) (0.001 mol) was added to the reaction mixture which was again irradiated for 2 min. On cooling crystals separated out which were dried and found to be pure by TLC.

V(**a**) : mp = 275°C (d); yield = 65.2%

(b) The compounds **I** and **II** (0.001 mol) were taken in a borosil beaker (50 ml) and dissolved in minimum amount

of methanol and to this solution, montmorillonite K10 (20 wt.%) was added. The mixture was swirled for a while and the solvent was removed under vacuum to obtain free flowing powder and irradiated inside a microwave oven for 5 min at 480 W. As the reactants disappeared (TLC), **IV** (0.001 mol) adsorbed on montmorillinite K10 was added to the reaction mixture and again irradiated for 2 min. The product was extracted from methanol and the excess solvent was evaporated on a roto-evaporator to give a solid which was found to be pure by TLC.

V(**a**) : mp = 275°C (d); yield = 93.6%

The identity of the compounds synthesized by various methods was confirmed by mixed melting points and spectral studies. The presence of primary $N\underline{H}_2$ group in compounds **V** is also confirmed by the 'diazotization test' [30].

The compound **V**(**b**) was synthesized by methods (a) and (b) under microwave irradiation only because the thermal method gives poor yield.

*3.2. 5′-(N-acetylamino)-4′-(2-trifluoromethyl phenyl)-2′,4′-dihydro-5-chloro-spiro[3H-indole-3,3′-[3H-1,2,4]triazoles]-2(1H)-ones (**VI(f)**)*

Classical method: **VI**(**f**) was synthesized by the classical method in two steps.

1. Synthesis of intermediate anil (**III**(**a**)): a mixture of **I** (0.005 mol) and **II** (0.005 mol) was refluxed in glacial acetic acid (10 ml) for 2 h. On cooling, crystals separated out which were recrystallized from ethanol [29].

   III(**a**) : $X = 5Cl$; $Y = 2CF_3$; mp = 167°C; yield = 77% (mp = 167°C; yield = 66.5%)

2. Synthesis of spiro product: a mixture of **III**(**a**) (0.001 mol) and thiosemicarbazide (**IV**) (0.001 mol) in glacial acetic acid (20 ml) was refluxed for 5 h. Reaction occurs with evolution of H_2S. Crystals obtained on cooling were filtered, dried and recrystallized from ethanol.

   VI(**f**) : mp = 290°C; yield = 60%

Microwave irradiation method: **VI**(**f**) has been synthesized in one step without isolation of **III** by two different methods under microwave irradiation.

(a) An equimolar mixture of **I** and **II** (0.001 mol) in a minimum quantity of ethanol required to form a slurry was irradiated inside a microwave oven at 360 W until the completion of reaction (6 min). As the reactant disappeared (TLC), thiosemicarbazide (**IV**) (0.001 mol) and four drops of acetic acid were added to the reaction mixture which was again irradiated for 2 min. On cooling crystals separated out which were dried and found to be pure by TLC.

VI(**f**) : mp = 290°C; yield = 75.6%

(b) The compounds **I** and **II** (0.001 mol) were adsorbed on montmorillonite K10 and irradiated for 5 min at 480 W. As the reactants disappeared, **IV** (0.001 mol) and two to three drops of acetic acid were adsorbed on clay, added to the reaction mixture and irradiated for 1 min. The product was extracted from methanol and the excess solvent was evaporated on a roto-evaporator to give a solid which was found to be pure by TLC.

VI(**f**) : mp = 290°C; yield = 94.7%

The remaining compounds listed in Tables 1 and 2 were synthesized by methods (a) and (b) under microwave irradiation. Compounds **V**(**a**) and **VI**(**f**) were synthesized by the classical method for comparative yield.

The identity of the compounds synthesized by various methods was established by their mixed mp, IR and ^{1}H NMR spectral studies.

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