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Microwave-induced Synthesis of Spiro[indoline-3,2′-[1,3]thiazinane]-2,4′-diones

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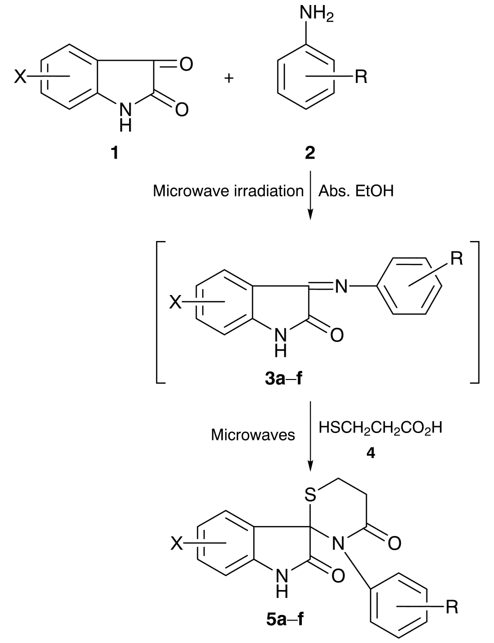
The potential of domestic microwave ovens has been utilized in an elegant one-step synthesis of spiro[indoline-3,2′-[1,3]thiazinane]-2,4′-diones.

The title reaction, incorporating two biodynamic heterocyclic moieties,[14–17] through the spiro carbon atom appeared interesting in view of the broad spectrum of bioactivity associated with sulfur-containing heterocyclic systems,[19,21] along with the presence of different reaction sites, which may lead to the formation of variety of products. The role of fluorine and perfluoro groups in indole chemistry is also noteworthy as compared with their non-fluorinated analogues.[24]

The field of application of microwaves to organic synthesis is just a decade old,[26–28] but the main activity in the area has been in 1990s. Activation of chemical reactions by exposure to microwaves results in faster and cleaner reactions with higher yields, as compared with conventional heating and the products of the reaction are easy to work-up. Reactions using milligrams to several hundred grams were conducted in minutes rather than hours, using highly polar solvents. Microwave technology is cost effective also, as organic reactions can be carried out without the need of standard organic laboratory paraphernalia such as reflux condensers, stirrers, water separators, *etc.*

We now report the one-step synthesis of fluorinated spiro[indoline-3,2′-[1,3]thiazinane]-2,4′-diones, both thermally and under microwave irradiation (Scheme 1). The reactions were studied under different reaction conditions. From the results of a comparative study of the synthesis of the spiro compounds by the classical method using Dean–Stark apparatus and microwave irradiation, it is clear that the reaction time is reduced from several hours to only a few minutes by using microwave irradiation (Table 1), indicating that the microwaves play an important role in the rate enhancement. The products are also obtained in excellent yields.



X = H, 5-Cl, 5-NO_2, 7-NO_2, 5,7-Me_2
R = 2-CF_3, 3-CF_3, 4-F, 2,3,5,6-F

Scheme 1

Table 1 Physical and analytical data of **5a–f**

Compound	X	R	MW Method Time (min/h)	Yield (%)	Mp (T/°C)	Mol. formula	Found (required %) C	H	N	S
5a	5-Cl	2-CF_3	14/15[a]	72/68[a]	205	$C_{18}H_{12}ClF_3N_2O_2S$	52.33 (52.36)	2.88 (2.90)	6.82 (6.78)	7.76 (7.75)
5b	5-Cl	3-CF_3	13/14[a]	76/61[a]	220	$C_{18}H_{12}ClF_3N_2O_2S$	52.37 (52.36)	2.86 (2.90)	6.80 (6.78)	7.79 (7.75)
5c	5,7-Me_2	3-CF_3	12/13[a]	84/74[a]	198	$C_{20}H_{17}F_3N_2O_2S$	59.09 (59.11)	4.16 (4.18)	6.92 (6.89)	7.85 (7.88)
5d	5-NO_2	4-F	18/16[a]	68/55[a]	260	$C_{17}H_{12}FN_3O_4S$	54.70 (54.69)	3.23 (3.21)	11.27 (11.26)	8.60 (8.57)
5e	H	2-CF_3	11/14[a]	82/74[a]	210	$C_{18}H_{13}F_3N_2O_2S$	57.16 (57.14)	3.39 (3.43)	7.18 (7.22)	8.32 (8.30)
5f	H	2,3,5,6-F	17/20[a]	62/14[a]	208	$C_{17}H_{10}F_4N_2O_2S$	53.42 (53.40)	2.64 (2.61)	7.42 (7.48)	8.68 (8.65)

[a] Reaction time and yield by method A (thermal).

Techniques used: ^1H and ^{19}F NMR, IR and mass spectrometry

References: 40

Schemes: 1

Tables: 1

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