Microwave-induced One-pot Synthesis and Biological Screening of 8-Substituted 2,5-Dihydro-1,5-benzothiazepin-2-spiro-3′-3′*H*-indol-2′-(1′*H*)-ones

J. Chem. Research (S), 1998, 752–753
J. Chem. Research (M), 1998, 3348–3355

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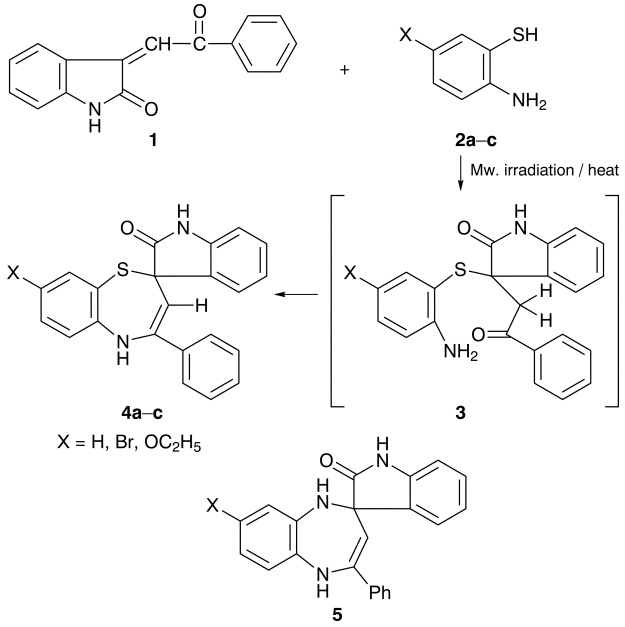
The concept of microwave-induced enhancement of organic reactions has been utilized in a one-pot synthesis of spiro[benzothiazepin-indol]ones.

3-Spiroindolines incorporating a 1,5-benzothiazepine ring at the 3-position of the 2-indolinone skeleton appear to be potentially bioactive compounds in view of the wide range of biological activities associated with both the 1,5-benzothiazepine and 3-spiroindoline[2–5] heterocyclic nuclei. The microwave-oven induced enhancement of organic reactions is currently a focus of attention for chemists due to the decreased reaction times, improved yields and easier work up, as compared to conventional methods.[30]

We have investigated the reaction of 1,3-dihydro-3-(2-phenyl-2-oxoethylidene)indol-2(1*H*)-one (**1**) with 2-aminobenzenethiols (**2a**–**c**) under thermal and microwave reaction conditions. Ethylene glycol was used as the energy transfer medium under microwave irradiation while the classical method involves reaction in ethanol staturated with hydrogen chloride gas. A comparison of the results obtained from the two synthetic approaches indicates that the effect of microwave irradiation is not purely thermal, besides giving decreased reaction times and improved yields.

In bioassay testing, the compounds showed activity against *Alternaria alternata*, *Fusarium oxysporium* and *Mycobacterium tuberculosis*.



Scheme

Table 1 Analytical and physical data for **4a**–**c**

Compound	Yield (%) (time)		Mp/°C	Formula	Found (Calc.) (%)		
	Classical[a]	MW[b]			C	H	N
4a	52 (6 h)	49 (15 min) 54 (8 min)[d] 57 (7 min)[e]	165–167	$C_{22}H_{16}N_2SO$	74.1 (74.15)	4.5 (4.49)	7.91 (7.86)
4b	51 (4 h)	54 (10 min)[e]	218	$C_{24}H_{20}N_2SO_2$	71.9 (72.0)	5.04 (5.00)	7.02 (7.00)
4c	62 (4 h)	65 (10 min)[e]	160	$C_{22}H_{15}N_2SOBr$	60.8 (60.68)	3.51 (3.45)	6.40 (6.43)

[a]Classical method; absolute ethanol + hydrogen chloride gas. [b]Microwave method. [c]Toluene + acetic acid. [d]Ethylene glycol + conc. hydrochloric acid. [e]Ethylene glycol + piperidine.

Table 2 Effect of synthesized compounds **4a**–**c** on the radial growth of different fungi

Compound	X	Radial growth of *Alternaria alternata*[a]/cm			Radial growth of *Fusarium oxysporium*[a]/cm		
		Conc./ppm			Conc./ppm		
		0	500	1000	0	500	1000
4a	H	3.30	1.80	1.50	3.50	2.80	2.00
4b	OEt	3.30	1.70	1.20	3.50	2.00	1.20
4c	Br	3.30	1.70	0.70	3.50	1.80	1.33

[a]Average of three replications.

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Table 3 Antitubercular activity[a]

Compound	X	Inhibition(%)	Comments[b]
4a	H	100	MIC RMP = 0.25 μg ml^{-1}, 98% inhibition *vs. M. tuberculosis*
4b	OC_2H_5	92	
4c	Br	97	

[a]Screening of compounds **4a**–**c** was conducted at a concentration of 12.5 μg ml. [b]Minimum inhibitory concentration (MIC) of control drug for comparison.

Tehniques used: ^{1}H NMR, ^{13}C NMR, IR and mass spectra

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Received, 2nd March 1998; Accepted, 1st September 1998
Paper E/8/01725E

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