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NOTE

Microwave Assisted Synthesis and Characterization of Some New Isatin Derivatives

ANKUR PATEL*, S.B. BARI, G.S. TALELE and J.S. PATEL
Department of Pharmaceutical Chemistry, R.C. Patel College of Pharmacy
Shirpur-425 405, India
E-mail: sbbari@rediffmail.com

3-[(5-Benzylidene-2-phenyl)-3,5-dihydro-4*H*-imidazol-4-one-3- (4-benzovlhydrazono)]-indole-2-ones (IV) were synthesized in high yield (82%) using a microwave method. In these, different isatin hydrazones (II) are reacted with 2-phenyl-5-bezylidene-3-N-(4-acetyl phenyl)-1,5-dihydro-imidazol-4-one to afford final compound (IV). Synthesis of 3-[(5-benzylidene-2-phenyl)-3,5 dihydro-4*H*-imidazol-4-one-3-(4-benzoyl hydrazono)]-indole-2-ones (IV) was found much easier and faster than conventional heating method. These compounds were characterized by IR, ^{1}H NMR and mass spectra.

Key Words: Isatin, Imidazolone, Irradiation, Microwave.

It is evident from literature that isatin derivatives are known to be associated with broad spectrum of biological activity like antibacterial[1], anti-cancer[2], anti-inflammatory[3], analgesic[4], antiviral[5], antifungal[6], antitubercular[7], anti-depressent[8]. Isatin hydrazones have been reported to possess anticonvulsant[8] activity also. The influence of microwave irradiation prompted us to synthesize 3-[(5-benzylidene-2-phenyl)-3,5-dihydro-4H-imidazol-4-one-3-(4-benzoyl- hydrazono)]-indole-2-ones (IV). Microwave irradiation is a non-conventional energy source, which has been of special interest in organic chemistry in recent years[9–12].

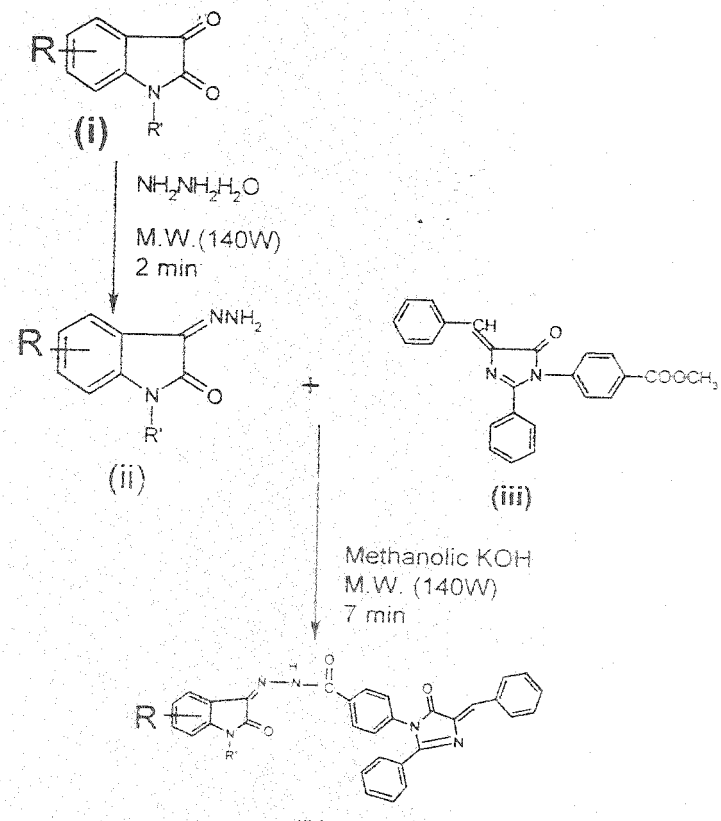
All the melting points were determined by open capillary method and are uncorrected. Purity of compounds was checked by TLC on silica gel-GF coated plates. Reactions were performed in RAGA Scientific microwave system model RG 31L with 220 V–50 Hz power source, 700 output and 2450 MHz operating frequency. IR spectra were recorded on Shimadzu FTIR 8400 using KBr. ^{1}H NMR were recorded on 300 MHz Bruker DPX using $CDCl_3$ and mass spectra was determined using EI-MS mode on VG Autospec instrument.

Synthesis of isatin hydrazone (II)

Conventional method: An appropriate isatin or indole-2,3-dione (I, 0.01 mol) was dissolved in alcohol and then added hydrazine hydrate (99%, 0.015 mol) while shaking. The reaction mixture was stirred well, warmed on a water bath for 10 min and left in the refrigerator for 3 h. The resultant yellow crystalline solid was filtered, washed rapidly with small protion of cold water and finally with small quantity of cold alcohol. The product was dried and purified by recrystallization from chloroform. The compounds thus obtained were characterized by comparison with their physical constant reported in literature[13]. m.w. 161, m.f. $C_8H_7N_3O$, m.p. 220°C, yield 74.5%.

Microwave synthesis: An equimolar quantity of isatin (I, 0.01 mol) and hydrazine hydrate (99%, 0.015 mol) in methanol were dissolved and subjected to microwave irradiation for 1 min at level-1 (140 W). Then, the reaction mixture was allowed to cool at room temperature. Then the product was filtered, dried and purified by recrystallization from methanol. Melting point of compound was found to be 220°C, yield 90%.

Similarly, other derivatives of isatin hydrazones are prepared by the above method.



Synthesis of 3-[(5-Benzylidene-2-phenyl) 3,5-dihydro-4*H*-imidazol-4-one-1-(4-benzoylhydrazono)]indole-2-ones (IV).

Conventional method (IV): A mixture of equimolar quantity of isatin hydrazone (II, 0.01 mol) and 2-phenyl-5-bezylidene 3-N-(4-acetyl phenyl)-1,5-dihydro-imidazol-4-one (III) (0.01 mol) was dissolved in methanol containing a catalytic amount of potassium hydroxide and heated under reflux for 6 h. The reaction mixture was cooled and neutralized with concentrated hydrochloric acid. Then filtered the resultant product, dried and purified by recrystallization from methanol. m.w. 546, m.f. $C_{31}H_{21}N_5O_3Cl$, m.p. 208°C, yield 70%.

Microwave synthesis (IV): An equimolar quantity of isatin hydrazones (II, 0.01 mol) and 2-phenyl-5-bezylidene-3-N-(4-acetylphenyl)-1,5-dihydro-imidazole-4-one (III) (0.01 mol) was dissolved in methanol containing a catalytic amount of potassium hydroxide and subjected to microwave irradiation for 7 min at level-1 (140 W). The reaction mixture was cooled and neutralized with concentrated hydrochloric acid. Then washed, filtered the resultant product and dried.

Then it was purified by recrystallization from methanol. The physical data of the synthesized compound is given in Table-1.

TABLE-1
PHYSICAL CHARACTERIZATION DATA OF SYNTHESIZED COMPOUNDS (IV)

S. No.	Compound code	R	R′	m.p. (°C)	m.f.	m.w.	Yield (%)
1.	**IVa**	H	H	208	$C_{13}H_{21}N_5O_3$	511	85
2.	**IVb**	5-Cl	H	252	$C_{31}H_{20}N_5O_3Cl$	546	75
3.	**IVc**	5-F	H	237	$C_{31}H_{20}N_5O_3F$	529	78
4.	**IVd**	5-Br	H	265	$C_{31}H_{20}N_5O_3Br$	591	80
5.	**IVe**	H	Acetyl	152	$C_{33}H_{23}N_5O_4$	554	72
6.	**IVf**	H	Methyl	143	$C_{32}H_{23}N_5O_3$	526	77
7.	**IVg**	5-Br	Acetyl	183	$C_{33}H_{22}N_5O_4Br$	634	70

Spectral interpretation of compound (IV): IR (ν_{max} KBr, cm^{-1}): 1643 ν(CO), 1689 ν(CONH), 2923 ν(ArCH), 3253 ν(NH). ^1H NMR (δ): 10.1 (s, 1H, aromatic NH), 10.2 (s, 1H, NHCO), 2.5 (s, 1H, CH), 7-8 (m, 18H, AR—H). Mass: molecular ion peak at m/z 546 and base peak at m/z 105.

Table-2 compares the synthetic condition of compound **(IV)** and its derivatives under microwave irradiation and conventional method. So the microwave method of new isatin hydrazones gives more yield, is less time consuming and more pure than the conventional method.

TABLE-2
COMPARISON OF THE TIME AND YIELDS ON THE FORMATION OF SOME NEW ISATIN DERIVATIVES USING MICROWAVE IRRADIATION AND CONVENTIONAL METHOD

Compounds	Conventional method (%)		Microwave method (%)	
	T (min)	Yield (%)	T (min)	Yield (%)
Isatin hydrazone (II)	120	74.5	1	90
Final compound (IV)	330	70.01	7	82

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