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NOTE

Microwave Activated Synthesis of 2-Imidazolin-5-ones Using Phenyl Isothiocyanate as Cyclocondensing Agent

PRADEEP K. TRIPATHY
Department of Chemistry, North Eastern Regional Institute of Science and Technology, Itanagar-791 109, India

The cyclocondensation reaction of N-acetyl and N-benzoylglycines (**1a, b**) with aromatic aldehydes in the presence of phenyl isothiocyanate as cyclizing agent and pyridine as a catalyst in an open vessel under microwave irradiation in dry media yielded 4-(arylmethylene)-1-phenyl-2-styryl- and 4-(arylmethylene-1,2-diphenyl-2-imidazolin-5-ones (**2f** and **2a–e**, respectively). It is noteworthy that the reaction is completed within 10 min with much better yields. All the steps are carried out in one pot.

Key Words: 1,2-Disubstituted 2-imidazolin-5-ones, Phenyl isothiocyanate, Microwave activation, Cyclocondensation, Green Chemistry.

Microwave assisted organic synthesis is a fast developing area in synthetic organic chemistry[1–3]. The use of such non-conventional reaction conditions reveals several features like a short reaction time compared to conventional heating[4], ease of work-up and simplicity. Interest in the chemistry of imidazolones continues unabated because of their usefulness as antibacterial[5] and antiinflammatory[6] agents and some of them may be useful in polymer chemistry. It is, therefore, thought worthwhile to critically examine the synthesis of imidazolones under microwave irradiation using phenyl isothiocyanate as cyclocondensing agent in a minimum possible time.

Melting points were recorded by Toshniwal melting point apparatus and are uncorrected. The UV, IR and ^{1}H NMR spectra were studied on a Cary-14, Perkin-Elmer 720 and/or 257 and Jeol FX 90 Q spectrometers, respectively. Microwave irradiation was carried out by using domestic LG-microwave oven, model MS 194A (1200W).

Synthesis of 1,2-Disubstituted-4-arylmethylene-2-imidazolin-5-ones (2)

General procedure: A mixture of compound **1**, aromatic aldehyde and phenyl isothiocyanate in a molar ratio of 1 : 1 : 1.2 with pyridine as a catalyst was thoroughly mixed and was irradiated by microwave for 10 min in an open vessel. The reaction mixture was cooled and the residue was triturated with ethanol. The product was isolated by suction, washed with ethanol and recrystallized from absolute ethanol. Relevant physical data are given in Table-1.

TABLE-1
MICROWAVE ASSISTED SYNTHESIS OF 2-IMIDAZOLIN-5-ONES (2)

Product	R^1	Ar	Yield (%)	m.p. (°C)[7, 8]
2a	C_6H_5	C_6H_5	80	180
2b	C_6H_5	$3\text{-}O_2NC_6H_4$	90	198–199
2c	C_6H_5	$3\text{-}CH_3O, 4\text{-}OHC_6H_3$	81	190
2d	C_6H_5	$4\text{-}Me_2NC_6H_4$	82	250–252
2e	C_6H_5	$C_6H_5CH{=}CH$	84	197–198
2f	$C_6H_5CH{=}CH$	C_6H_5	88	240–241

2a: IR (Nujol): 1710, 1650 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.26 (s, 1H, 4-C═CH); 7.35–8.30 (m, 15H, Ar—H); UV (95% ethanol) λ(nm) ($\varepsilon \times 10^{-4}$): 340 (2.0), 290 (1.21), 235 (1.26).

2b: IR (Nujol): 1710, 1630 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.22 (s, 1H, 4-C═CH); 7.35–9.30 (m, 14H, Ar—H); UV (95% ethanol) λ(nm) ($\varepsilon \times 10^{-4}$): 380 (0.83), 250 (1.01).

2c: IR (Nujol): 3300, 1690, 1650 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.04 (s, 3H, OCH_3); 6.88–8.27 (m, 15H, 4-C═CH, —OH and Ar—H); UV (95% ethanol) λ(nm) ($\varepsilon \times 10^{-4}$): 412 (3.70), 265 (2.44), 230 (2.22).

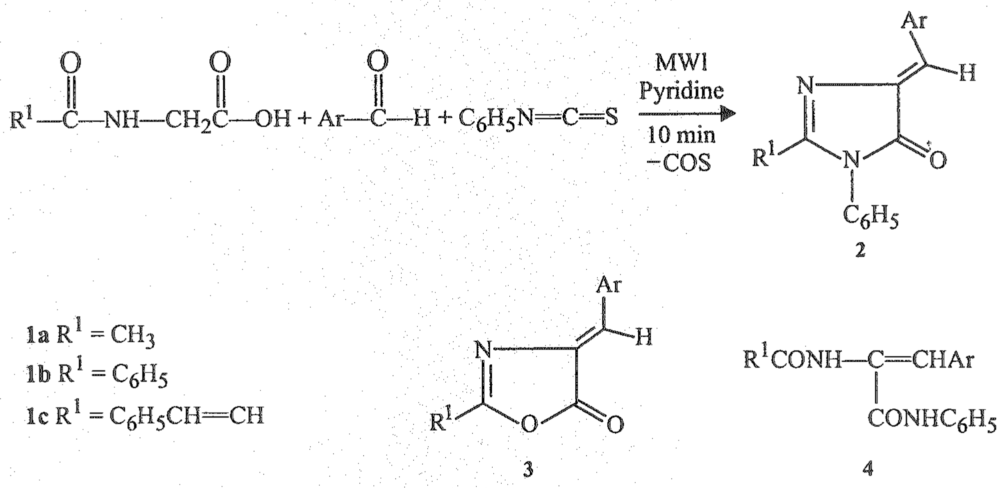
2d: IR (Nujol): 1700, 1670, 1630 cm^{-1}; ^1H NMR ($CDCl_3$): δ Insufficiently soluble in $CDCl_3$.

2e: IR (Nujol): 1710, 1610 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.94–7.70 (m, 18H, Ar—H, 4-C═CH and PhCH═CH—); UV (95% ethanol) λ(nm) ($\varepsilon \times 10^{-4}$): 395 (4.03), 275 (0.77), 240 (1.06).

2f: IR (Nujol): 1710, 1630, 1620 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.90–8.10 (m, 18H, Ar—H, 4-C═CH and PhCH═CH—); UV (95% ethanol) λ(nm) ($\varepsilon \times 10^{-4}$): 405 (1.7), 295 (2.14), 235 (1.26).

A facile and rapid synthesis of 1,2-disubstituted-2-imidazolin-5-ones **(2)** was carried out by the cyclocondensation reaction of N-acetyl and N-benzoylglycines **(1a, b)** with aromatic aldehydes in the presence of phenyl isothiocyanate as cyclizing agent and pyridine as a catalyst in an open vessel under microwave irradiation in domestic microwave oven without using solvent furnished 4-(arylmethylene)-1-phenyl-2-styryl-2-imidazolin-5-ones **(2f)** and 4-arylmethylene-1,2-diphenyl-2-imidazolin-5-ones **(2a–e)**, respectively. The reaction is completed within 10 min with much better yields (80–90%) **(Scheme-1).** On cyclocondensation of 2-(benzoylamino)cinnamic acid with phenyl isothiocyanate, **2a** (Ar = Ph) was obtained directly. The cyclocondensation of cinnamoylglycine **(1c)** under similar conditions afforded 4-(arylmethylene)-1-phenyl-2-styryl-2-imidazolin-5-ones **(2f)** as the main product.

A trace amount of 2-oxazolin-5-ones **(3)** and N-substituted 2-acylamino-2-alkenamides **(4)** was detected by TLC in some cases but these compounds could not be isolated due to poor yield. The detection of **3** and **4** helped to establish the possible pathways of the reaction mechanism. The reaction seems to be initiated by the formation of an adduct, followed by the cyclocondensation to 4-arylmethylene-



Scheme-1

2-oxazolin-5-ones (**3**) with the elimination of COS and aniline moiety. The cleavage of 1,5-bond of unsaturated 2-oxazolin-5-ones by aniline afforded the title compound (Z)-1,2-disubstituted 4-arylmethylene-2-imidazolin-5-ones (**2**) *via* N-phenyl-2-acylamine-2-alkenamides (**4**). The products were identified by comparison with authentic samples as well as spectroscopic techniques. It is not out of place to mention that the reaction afforded only the (Z)-imidazolones which seem to be thermostable under present conditions. In the UV spectrum, the higher values of ε_{max} supported for the (Z)-isomer than the corresponding (E)-isomer.

In conclusion, a simple and useful method for the synthesis of 1,2-disubstituted 4-arylmethylene-2-imidazolin-5-ones (**2**) under mild and environmentally benign reaction conditions using Green Chemistry methodology has been reported. The reactions can be carried out in one flask within the least possible time in contrast with the literature's multi-step methods. Considering the easy availability of the starting materials, the speed of the reaction and simplicity of the work-up, the present method appears to be useful.

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