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NOTE

A Facile and Fast One Flask Synthesis of Unsaturated Azlactones by Microwave Activation

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2-Substituted-2-oxazolin-5-ones (**2**), generated by cyclizing α-N-acylaminoacids (**1**) with ethylchloroformate in the presence of triethylamine in benzene, affords 2-substituted-4-arylmethylene-2-oxazolin-5-ones (**3**), on reaction with aromatic aldehydes by microwave irradiation. All the steps are carried out in one flask.

Key Words: α-N-acrylaminoacids, Azlactone, Oxazolones, 2-Substituted 4-arylmethylene-2-oxazolin-5-ones, Microwave activation.

The objective of the present investigation was to develop a method for a fast and facile synthesis of unsaturated azlactones (**3**) by using a non-conventional green chemistry methodology which led to higher yield and a remarkable reaction rate enhancement with the optimum utilization of energy. Interest in the chemistry of oxazolones continues unabated because of their usefulness as synthons and their diverse bio-potentiality.

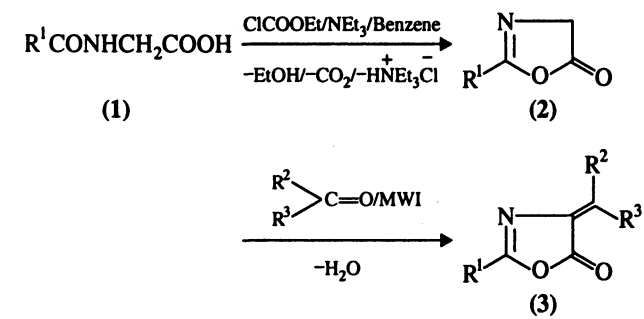
The conversion of α-N-acylaminoacids (**1**) to the unstable 2-substituted, 2-oxazolin-5-ones (**2**) was carried out at room temperature, which declined the risk of high-pressure development associated with solution phase reaction at higher temperature as well.

With a view to converting the unstable 2-substituted-2-oxazolin-5-ones (**2**), obtained by ethylchloroformate mediated cyclization of α-N-acylaminoacids (**1**) in benzene in the presence of triethylamine base at room temperature, into the more stable 2-substituted-4-arylmethylene-2-oxazolin-5-ones (**3**), the triethylamine hydrochloride salts were filtered under suction and the solvent was removed to dryness under reduced pressure, followed by the addition of suitable aromatic aldehydes to the reaction mixture. The contents were mixed thoroughly and then heated under microwave irradiation only for 2 min. On work-up, **3** was obtained as pure (Z)-isomer (**3a–g**) except in the case of **3h** where (E)-isomer was obained. (E)-azlactone was thermolabile and isomerized to corresponding (Z)-isomer (**3i**) when microwave heating was continued for 4 min. In the UV spectrum, both **3h**

and **3i** absorb in nearly the same regions, but the C_{max} values are higher for the (Z)-isomer than the corresponding (E)-compound, thereby confirming the assigned stereochemistry of the product[1]. The IR spectrum bands at 1810–1790, 1770 and 1650 cm^{-1} were in agreement with the product **3.** The result is obviously due to the aldol type condensation of aldehydes at 4-methylene position of the intermediate **2** with the elimination of water molecule.

The present procedure overcomes some of the disadvantages of the earlier methods[1] regarding speed of the reaction and stereochemical purity of the products. For example, the Erlenmeyer azalactone synthesis[2] employs acetic anhydride for cyclization and it affords a mixture of (E)- and (Z)-isomers of the unsaturated azalactones. Further, acetylation of the free —OH group of aldehydes usually occurs simultaneously, if present, which leads to the formation of acetoxybenzylidene moiety at 4-position of **3.** It should be emphasized that the present procedure is simple and straight forward and all the steps can be carried out in one flask. In view of the ready availability of the reactants, mild experimental conditions and excellent overall yields, the present proposed route appears to be potentially important.

The products reported were characterized by spectral data and by comparison with authentic samples.



Scheme-1

Melting points were recorded by Toshniwal melting point apparatus and are uncorrected. The UV, IR and ^{1}H-NMR were 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 no. MS 194A (1200W).

Preparation of 2-substituted-4-arylmethylene-2-oxazolin-5-ones (3)

To a suspension of α-N-acylaminoacids (1; 1.0 mol) in dry benzene (25 mL/g of the acid) containing triethylamine (1.2 mol), ethylchloroformate (1.1 mol) was added and the mixture was shaken at room tempeature until the crystals of the acid disappeared and triethylamine hydrochloride salt separated out which was filtered under suction and washed with benzene (5 mL). The solvent was removed to dryness under reduced pressure and to the viscous residue were added aromatic aldehydes, taken in molar ratio with respect to α-N-acylaminoacids and the

mixture was intimately mixed and heated in a microwave oven for 2 min only except for **3i** where heating was continued to 4 min. Trituration with ethanol gave a solid which was recrystallized from ethanol. Relevant physical data are given in Table-1.

TABLE-1
PHYSICAL DATA OF COMPOUNDS (3a–i)

Product	R^1	R^2	R^3	Yield (%)*	m.p. (°C)	
					Found	Reported†
3a	Me	Ph	H	85	152–154	148–150[3]
3b	Ph	Ph	H	92	166–167	165–166[4]
3c	Ph	3-O_2N—C_6H_4	H	95	175–176	175–176[5]
3d	Ph	4-Me_2N—C_6H_4	H	91	213–215	214[6]
3e	Ph	3-MeO, 4-HO-C_6H_3	H	90	157–158	158[7]
3f	Ph	2-Furyl	H	92	170–171	170–171[8]
3g	PhCH=CH	Ph	H	91	132–133	132–133[8]
3h	Ph	H	CH=CHPh	88	142–143	143[9]
3i	Ph	CH=CHPh	H	88	151–152	153[9]

*Yields of the pure products are based on the amount of α-N-acylamino acid used.

†All the compounds are known in literature, so the spectral data are not incorporated in the present text[1, 9, 10].

REFERENCES

1. Y.S. Rao and R. Filler, *Synthesis,* 749 (1975).
2. E. Erlenmeyer and O. Matter, *Liebigs Ann. Chem.*, **337,** 271 (1904).
3. R.M. Herbst and D. Shemin, *Org. Synth. Coll.* **2,** 1 (1950).
4. H.B. Gillespire and H.R. Snyder, *Org. Synth. Coll.* **2,** 489 (1950).
5. V.G. Zubenko, *Dopov. Akad. Nauk. Ukr. RSR. Ser., B,* **30,** 547 (1968); *Chem. Abstr.*, **69,** 106596 (1968).
6. H. Behringer and H. Taul, *Chem. Ber.*, **90,** 1398 (1957).
7. E. Baltazzi and E.A. Davis, *Chem. Ind. (London),* 929 (1962).
8. B. Sain, S.P. Singh and J.S. Sandhu, *Chem. Ind. (London),* 499 (1990).
9. P.K. Tripathy and A.K. Mukerjee, *Synthesis,* 418 (1984).
10. ———, *Acta Ciencia Indica,* **17C,** 850 (1991).

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