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NOTE

Synthesis of Some 2-Oxazolidinones in Mild Conditions

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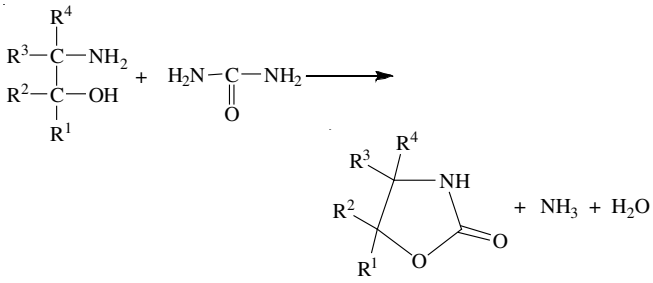
One step efficient protocol for the synthesis of 2-oxazolidinones in paste chemical medium is described under microwave activation with 80 % yield.

Key Words: Ethanolamines, Condensation, Microwaves, 2-Oxazolidinones, Urea.

2-Oxazolidinone derivatives are known for their antibacterial activity, drugs against methicillin-resistant *Staphylococcus aureus* (MRSA) and *Bacillus anthracis*[1,2], monoamine oxidase type A inhibitors[3,4], inhibitors of animal cell motility and growth[5,6], of the cytochrome P-450 enzyme aromatase[7,8] and fungicidal pest-controls[9].

Generally, the synthesis of these compounds are achieved with the use of organic solvents[10-13] and expensive metallic catalysts[14-17]. The reaction time usually takes several hours. The low yields and toxic reagents make the conventional methodologies not attractive for the organic chemists[10,11,14-18].

The syntheses were performed on an Optiquick Y71 microwave oven operating at 650 W. The 2-oxazolidinones **1-10** (**Scheme-I**, Tables 1 and 2) were identified by TLC (silica gel, eluent EtOH 100 %). They were characterized by elemental analysis (Carlo Erba® 1106 instrument) and IR spectra (KBr pellets on a Perkin-Elmer® 1600 spectrometer). Melting points were measured on a Boetius instrument and compared with the previously known values (Table-2).



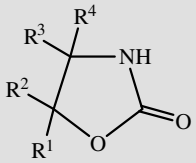
Scheme-I

General procedure for the synthesis of 2-oxazolidinones **1-10** (**Scheme-I**). Ethanolamine derivative (2 mmol) and urea (0.12 g, 2 mmol) were mixed in a 25 mL pyrex beaker. A few drops of nitromethane were then added. The resulting paste was irradiated in a microwave oven (λ = 12.2 cm) for the time indicated in Table-2. The resulting crude products were purified by recrystallisation from $CHCl_3$-EtOH to give the corresponding pure 2-oxazolidinones **1-10** (Tables 1 and 2). Single 4-ethyl-2-oxazolidinone **4** (Table-1) was purified by distillation.

TABLE-1
KEY IR ABSORPTION BANDS (cm^{-1}) OF 2-OXAZOLIDINONES

No.	ν(N-H)	$\nu_{as,s}(CH_3)$ $\nu_{as,s}(CH_2)$	Amide band I ν(C=O)	Amide band II δ(N-H)	ν_{as}(C-O)	ν_s(C-O)
1	3283 s	2960 m	1723 s	1527 w	1256 vs	1027 s
2	3280 s	2970 m	1719 s	1520 w	1264 s	1015 s
3	3265 m	2952 m	1711 s	1513 w	1248 s	1012 s
4	3293 s	2977 s	1716 s	1534 w	1233 s	1044 s
5	3310 m	2871 s	1730 s	1506 w	1247 vs	1035 s
6	3276 s	2910 m	1751 s	1515 w	1241 s	1024 s
7	3295 s	2941 m	1780 s	1537 w	1272 s	1039 s
8	3318 s	2973 m	1705 s	1517 w	1262 s	1041 s
9	3297 m	2948 s	1734 s	1539 w	1268 s	1037 m
10	3330 m	2961 s	1728 s	1541 w	1249 s	1031 m

TABLE-2
SYNTHESIS OF 2-OXAZOLIDINONE DERIVATIVES



Product No.	R^1	R^2	R^3	R^4	Elemental analysis (%) calcd./found			Time (min)	Yield (%)	m.p. (ºC)
					C	H	N			
1	H	H	H	H	54.02 (54.01)	4.43 (4.39)	12.58 (12.56)	4	97	90 86.5-88.5[23]
2	Me	H	H	H	47.52 (47.49)	6.93 (6.89)	13.86 (13.81)	5	92	22 20-22[24]
3	H	H	Me	H	47.52 (47.50)	6.93 (6.91)	13.86 (13.84)	5	94	49
4	H	H	Et	H	52.17 (52.13)	7.82 (7.79)	12.17 (12.16)	5.5	91	124* 119-126[24]
5	H	H	Me	Me	52.17 (52.14)	7.82 (7.81)	12.17 (12.15)	5	89	50 48-51[24]
6	Ph	H	H	Ph	75.31 (75.30)	5.43 (5.39)	5.85 (5.84)	5	82	167
7	CH_3	CH_3	H	H	52.17 (5.08)	7.82 (7.80)	12.17 (12.14)	3	86	81 79-82[25]
8	H	H	H	i-Pr	55.38 (55.35)	9.23 (9.18)	10.76 (10.75)	4	83	75
9	H	Ph	H	H	66.25 (66.21)	8.58 (8.54)	8.58 (8.51)	5	87	87 87-88[26]
10	*p*-ClPh	H	H	H	54.68 (54.67)	4.05 (4.01)	7.08 (7.03)	3	93	131 129-131[27]

*Boiling point.

We previously discussed green synthesis by using microwaves activation in heterogeneous medium[19-22]. These results prompted us to target several 2-oxazolidinones in a mild conditions (**Scheme-I**).

Reaction conditions and results are collected in Table-1. Table-2 lists the main IR data of the prepared compounds.

The ethanolamines and urea were mixed with a few drops of nitromethane. A paste like chemical medium resulted and was irradiated with microwave. The use of nitromethane is explained by its non-reactivity against the starting reagents, but its molecules create hot spots inside of the reaction medium. These hot spots are known to be catalytic centers[19]. That is, simple experimental equipments, easy separation of high purity 2-oxazolidinones, combined with short reaction time and high yields are obvious benefits of the present proposed method.

Conclusion

The heterogeneous medium is a very good site for the condensation of urea with ethanolamines assisted by microwaves. The short reaction time and the yields of synthesized 2-oxazolidinones are important advantages of the method. The mild experimental conditions of the synthesis make the proceeding quite attractively against conventional oxazolidinone synthesis.

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