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A NEW SYNTHESIS OF OXAZOLES

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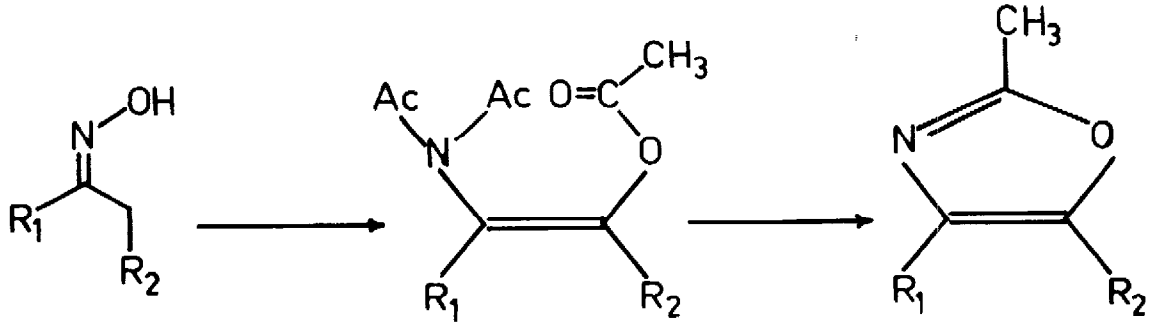
Abstract: Oxazoles are prepared from the ketoximes in a single pot sequence.

Oxazole rings, besides being present in a number of natural products[1] and biologically active compounds, can serve as versatile intermediates. The use of substituted oxazoles as azadienes in Diels-Alder synthesis has found many applications in the synthesis of pyridine derivatives, especially pyridoxine[1-5]. Intramolecular cyclization of propargylic imidates to oxazoles is described extensively in the literature[6]. Now, we wish to report a facile method for the synthesis of oxazoles from the ketoximes, based on a new reaction[7,8].

We reported that the ketoximes are converted to α-and α^1- acyloxyenimides, which on hydrolysis give α-acyloxy ketones[9]. When dry HCl gas is passed through an acetic anhydride solution of the enimides, oxazoles are obtained in good yield. Thus ketoximes are transformed into oxazoles in a single pot sequence.

The generality of the formation of substituted oxazoles from ketoximes has been demonstrated with a few representative examples (Table).

Procedure: In a typical run benzylmethylketoxime (3.0g 20mmol) is dissolved in dry pyridine (1.6 ml 20mmol) and acetic anhydride (2.0 ml, 20mmol). Acetyl chloride (2.0 ml 26mmol) is added to the above mixture at 0°C and heated over a boiling water bath for 4 hr. Then dry HCl gas is passed for 3 hr (at 100°C). The reaction mixture is cooled, poured in crushed ice, and extracted with methylene chloride. After the standard work up and solvent removal, the viscous residue is passed through the column (silica gel; benzene/hexane) to get 2.8g of 2,4-dimethyl-5-phenyl oxazole, m.p. 52°.



(a) $R_1 = CH_3$, $R_2 = Ph$; (b) $R_1 = CH_2Ph$, $R_2 = Ph$; (c) $R_1 = Ph$, $R_2 = CH_3$;
(d) $R_1R_2 = -[CH_2]_4-$; (e) $R_1R_2 = -[CH_2CH_2CH(CH_3)CH_2]-$; (f) $R_1 = R_2 = Ph$;
(g) $R_1 = R_2 = CH_3$.

TABLE

Ketoxime	Time hr.	Oxazole †	Yield % ‡
a	4	2,4-Dimethyl -5-phenyl oxazole	80
b	8	2-Methyl-4-benzyl -5-phenyl oxazole	83
c	9	2,5-dimethyl-4-phenyl oxazole	70
d	4	2-Methyl- 4,5,6,7-tetrahydro benzoxazole	61
e	4	2,6-dimethyl-4,5,6,7-tetrahydro benzoxazole	72
f	8	2-Methyl-4,5-diphenyl oxazole	58
g	24*	2,4,5-trimethyl oxazole	78

* Reaction is carried out at 140°C.

† The b.p. or m.p. of all the products conformed to those described in literature. The nmr, ir data were consistent with the structures or in agreement with literature data.

‡ All yields are based on isolated and purified products.

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