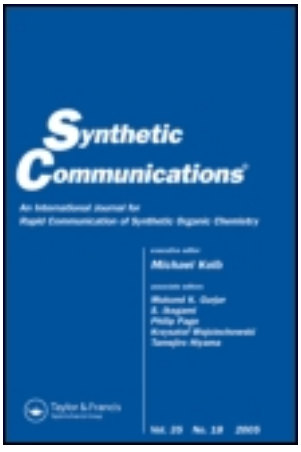

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Convenient Synthesis of 3,5-Disubstituted Isoxazoles

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Convenient Synthesis of 3,5-Disubstituted Isoxazoles

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Abstract: α,β-Unsaturated oximes obtained from the corresponding α,β-unsaturated ketones on treatment with 2 equivalents of manganese dioxide in refluxing chloroform gives 3,5-disubstituted isoxazoles in good yields.

Keywords: heterocycle, isoxazole, MnO_2, oxidative cyclisation

Isoxazoles[1] form an important class of aromatic heterocycles and have diverse applications. Their range of uses includes medicinal, herbicidal, fungicidal, pesticidal applications; dyes; insulating oils and lubricants. Isoxazoles contain a weak nitrogen–oxygen bond, which has been exploited to provide difunctionalized compounds such as 1,3-dicarbonyl, enaminoketone, γ-aminoalcohols, and β-hydroxy ketone. Thus, isoxazoles serve as building blocks in organic synthesis.

Earlier, we had reported dichloro dicyano benzoquinone (DDQ) as an oxidative cyclizing agent for the synthesis of 3,5-diaryl isoxazoles from the oximes of corresponding ketones.[2] Recently, MnO_2 has been used as a

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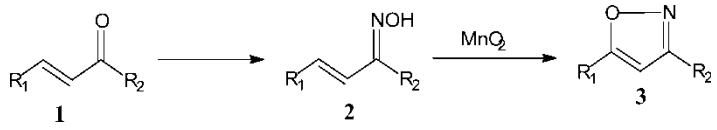

Scheme 1.

tandem oxidation process (TOP) agent[3] in a variety of synthetic manipulations including synthesis of heterocycles. Because MnO_2 is a mild, nontoxic, and cheaply available reagent, we thought of using this for the synthesis of isoxazoles (Scheme 1). Our initial attempt at oxidative cyclisation of the chalcone oxime **1a** in CH_2Cl_2 failed. When refluxing chloroform was used, we could get the corresponding 3,5-diphenyl isoxazole (**2a)** in 60% yield after 2 h. Similarly the other unsaturated oximes (Table 1, entries **2a**–**j**) yielded the corresponding isoxazoles. To check the feasibility of the TOP sequence,[3] a mixture of chalcone **1a**, MnO_2, $NH_2OH \cdot HCl$, and triethylamine (TEA) in refluxing $CHCl_3$ was attempted, but without success. When tetrahydrofuran (THF) was used as a solvent, some amount of direct formation of product was observed, but under the varying conditions tried, complete conversion could not be obtained. However, it was possible to obtain the isoxazole in a one-pot experiment wherein initially chalcone **1a**, 3 equivalents of $NH_2OH \cdot HCl$, and 3 equivalents of TEA were stirred for 30 min, followed by the addition of MnO_2 (5 equivalents) and refluxing for 2 h.

In conclusion, we have developed a convenient method for the synthesis of 3,5-disubstituted isoxazoles from α,β-unsaturated ketones. The procedure works well for differently substituted 3,5-diaryl isoxazoles (Table 1, entries **2a**–**h**). It also works well when one of the group is alkyl (entries **2i**–**j**). It fails to work when both the groups are alkyl and also with α,β-unsaturated aldehydes or

Table 1. Preparation of 3,5-disubstituted isoxazoles **3a-j**

Compound **1**–**3**	R_1	R_2	Yield of 3 (%)	Mp (°C) (lit.mp)
a	Ph	Ph	67	141 (140–141[4])
b	Ph	4-$MeOC_6H_4$	62	122 (122[5])
c	Ph	4-ClC_6H_4	69	175 (172–178[6])
d	Ph	4-BrC_6H_4	75	178 (178–180[6])
e	Ph	4-$NO_2C_6H_4$	65	228 (226–228[7])
f	4-$MeOC_6H_4$	4-ClC_6H_4	79	209 (210[7])
g	4-$MeOC_6H_4$	4-BrC_6H_4	65	130 (130–132[6])
h	4-$MeOC_6H_4$	4-$NO_2C_6H_4$	60	175 (172–175[6])
i	Ph	CH_3	70	67 (67[8])
j	4-$MeOC_6H_4$	CH_3	75	113 (111–112[9])

their oximes. Also, extending the method for the one-pot synthesis of corresponding pyrazoles using hydrazine did not work well in our hands.

EXPERIMENTAL

All melting points are uncorrected and were measured by the normal Thiels tube (paraffin) method. Column chromatography was performed on silica gel G (13% $CaSO_4$ as binder). IR spectra were recorded on a Shimadzu FT-IR spectrophotometer (KBr pellets). ^1H NMR and ^{13}CMR were recorded on a Brucker 300-MHz instrument. The multiplicities of carbon signals were obtained from distortionless enhancement by polarization transfer (DEPT) experiments.

General Procedure

A mixture of α,β-unsaturated oxime **2** (1 mmol), MnO_2 (2 mmol), and chloroform (15 mL) was refluxed for 2 h (or until the reaction was completed). After cooling, it was filtered and the black residue was washed with chloroform (5×5 mL). The combined filtrate after concentration was further purified by passing through a small column of silica gel using ethyl acetate–hexane (5:95) as an eluent.

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REFERENCES

1. (a) Barco, A.; Benetti, S.; Pollini, G. P.; Simoni, D. *Synthesis* **1987**, 857; (b) Kondo, Y.; Uchiyama, D.; Yamanaka, H. *Tetrahedron. Lett.* **1989**, *30*, 4249; (c) Monya, O.; Urata, Y. *Tetrahedron Lett.* **1989**, *30*, 3987.
2. Desai, V. G.; Tilve, S. G. *Synth. Commun.* **1999**, *29* (17), 3017.
3. Kanno, H.; Taylor, R. J. K. *Synlett* **2002**, 1287.
4. Wei, X.; Fang, J.; Hu, Y.; Hu, H. *Synthesis* **1992**, 1205.
5. Himo, F.; Lovell, T.; Hilgraft, R.; Rostovrsev, V. V.; Noodleman, L.; Sharpless, K. B.; Fokin, V. V. *J. Am. Chem. Soc.* **2005**, *127*.
6. Baranski, A. *Polish J. Chem.* **1989**, *63* (4–12), 483.
7. Deshmukh, A. Y.; Raghuvanshi, P. B.; Joshi, A. G. *Asian J. Chem.* **2002**, *14* (1), 548.
8. Bunelle, W. H.; Singam, P. R.; Narayan, B. A.; Bradshaw, C. W.; Lios, J. S. *Synthesis* **1997**, 436–442.
9. Palacios, F.; Aparicio, D.; Delos Santos, J. M.; Rodriguez, E. *Tetrahedron* **1998**, *54*, 599–614.