Reaction of 4,4-Dimethyloxazolidine-*N*-oxyl (Doxyl) Derivatives with Nitrogen Dioxide: A Novel and Efficient Reconversion into the Parent Ketone

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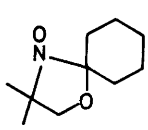
Summary 4,4-Dimethyloxazolidine-*N*-oxyl (doxyl) derivatives, an important class of spin labels, can be converted into their parent ketones in excellent yield by brief treatment with NO_2

STABLE nitroxyl radicals have been intensively investigated recently,[1] particularly with respect to their use as biological spin labels [2] Among the most useful are the 4,4-dimethyloxazolidine-*N*-oxyl (doxyl[3]) derivatives of ketones, originally prepared by Keana [4] We report a highly efficient and chemically novel method of reconverting doxyl derivatives into their parent ketones, a transformation for which no convenient alternative procedure exists



(I)

When a stream of commercial nitrogen dioxide is bubbled (room temp , 30 s) through a solution of the doxyl (I) in cyclohexane under nitrogen, cyclohexanone (71%) is obtained Longer treatment with NO_2 tends to lower the yield of ketone The most convenient procedure is to bubble commercial nitric oxide, which contains NO_2, through a solution of the doxyl in EtOH for 5 min Yields of ketones from several doxyls, using unpurified NO and cyclohexane or absolute ethanol as solvent, are listed in the Table The presence of NO_2 is essential, when the NO used is first bubbled through aqueous base to remove NO_2, no reaction occurs

TABLE

Reaction of doxyl derivatives with NO_2–NO *at room temperature*

	Yield[c] of ketone (%)	
Doxyl derivative[a]	In cyclohexane	In ethanol
Cyclohexanone[b]	66	95
2-Methylcyclohexanone	81	100
Cyclopentanone	55	Not run
Cycloheptanone	86	93
Heptan-2-one[b]	74	Not run
Cholestan-3 one[b]	68[d]	85[d]

[a] All prepared by the method of Keana, ref 4 New compounds gave appropriate analytical and spectral data [b] Previously reported, ref 4 [c] An average of several g l c determinations using an internal reference compound, unless otherwise noted [d] % Yield of isolated, recrystallized ketone with m p 127—130°

A tarry, intractable residue, obviously derived largely from the doxyl moiety, was the only other product found G l c analysis of the progress of the reaction shows, in addition to peaks from the doxyl (decreasing) and ketone (increasing), only a few very weak transient peaks

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[2] For a recent review see H M McConnell and B G McFarland, *Quart Rev Biophys* , 1970, **3**, 91.

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[4] J F W Keana, S B Keana, and D Beetham, *J Amer Chem Soc* , 1967, **89**, 3055