Conversion of Ketals to Ketones by Nitrogen Dioxide in the Presence of Silica Gel

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Nitrogen dioxide transforms ketals to ketones in the presence of silica gel under neutral, anhydrous and mild conditions.

Nitrogen dioxide, which is equilibrated with dinitrogen tetraoxide, has been reported to cause the oxidation of some organic compounds.[1] Field and Grundy reported that benzyl alcohols are oxidized to benzaldehydes by high concentrations of dinitrogen tetraoxide.[2] We have inferred that nitrogen dioxide is an active intermediate in the oxidation of alcohols and ethers by metallic nitrates supported on silica gel;[3,4] further, we have found that ethers and alcohols are oxidized to the corresponding aldehydes and ketones by nitrogen dioxide in the presence of silica gel.[5] These results suggested that ketals, which are ethers and popular protected forms of ketones, should be oxidatively cleaved to yield the original ketones. Here we report on the conversion of 2,2-disubstituted 1,3-dioxolanes (ethylene ketals) into the corresponding ketones by nitrogen dioxide in the presence of silica gel. This deprotective method may be useful for organic synthesis, because it can be used under neutral, anhydrous, and mild conditions in contrast to the acidic or wet conditions usually employed for cleavage of ketals.[6] Conversion of ethylene ketals into ketones under neutral conditions and ketal exchange reactions in acetone catalysed by $PdCl_2(MeCN)_2$ has been reported.[7]

Table 1 Transformation of ethylene ketals to ketones by nitrogen dioxide[a]

R^1	R^2	SiO_2/g	*t*/min	Yield (%)
Isopropyl	Isopropyl	0.33	40	100
		—	40	1
		—	120	2
		—[b]	40	98
Propyl	Propyl	0.17	60	97
		—	60	66
		—	140	84
Methyl	Phenyl	0.03	60	93
		—	60	58
		—	100	65
Butyl	Butyl	0.17	10	91
		—	10	43
		—	100	71
Methyl	Heptyl	0.17	40	88
		—	40	40
		—	160	70

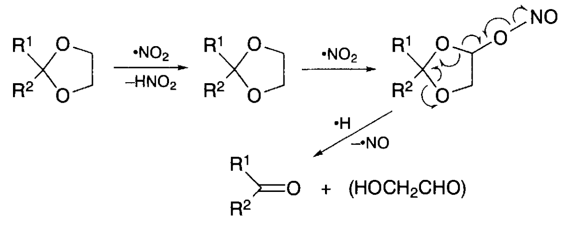
[a] A ketal (1 mmol), nitrogen dioxide (3 mmol) and dried silica gel in CCl_4 (6 ml) were stirred at 30 °C under an atmosphere of nitrogen. [b] Dried activated carbon (0.33 g) was added.

The ketones were obtained in high yields from the 2,2-disubstituted 1,3-dioxolanes in the presence of silical gel, as summarized in Table 1.† In the absence of silica gel the reactions proceeded more slowly and the yields of ketones were lower.

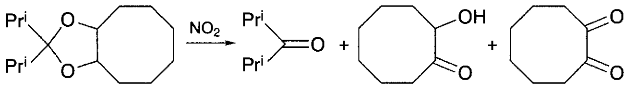
The function of silica gel is inferred to accumulate the ketals and nitrogen dioxide in high concentration on its surface by adsorption. The acidic character of silica gel is not important because cleavage did not occur at all in the absence of nitrogen dioxide and the addition of sodium hydrogencarbonate hardly influenced the performance of silica gel in the reaction. These inferences are supported by the observation that dried activated carbon promoted the ketal cleavage reaction nearly as effectively as dried silica gel.

We propose the radical process shown in Scheme 1 for the oxidative cleage of ketals based on the fact that nitrogen dioxide itself is a radical and from results obtained in previous studies.[3–5] The reaction of 10,10-bis(1-methylethyl)-9,11-dioxabicyclo[6,3,0]undecane (1 mmol) with nitrogen dioxide (0.5 mmol) in the presence of silica gel (0.2 g) at 50 °C for 5 h in CCl_4 (6 ml) gave diisopropyl ketone (0.35 mmol), 2-ketocyclooctanol (0.04 mmol) and 1,2-diketocyclooctanol (0.13 mmol). This result also supports the mechanism shown in Scheme 1. It was also confirmed that 2-ketocyclooctanol transforms readily to 1,2-diketocyclooctane in the presence of nitrogen dioxide and silica gel (Scheme 2).

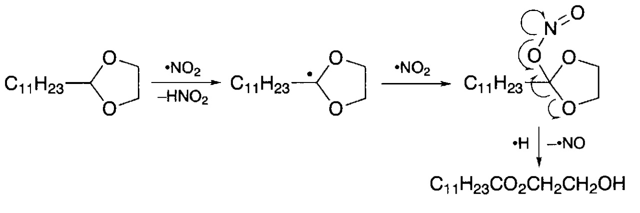
The first step of the process may be the abstraction of a hydrogen atom from a dimethylene moiety since nitrogen dioxide oxidatively cleaves ethers.[4,5] This assumption is supported by the reaction of 2-undecanyl-1,3-dioxolane, the ethylene acetal of dodecanal, with nitrogen dioxide which yielded the ester 2-hydroxyethyl decanoate as the main product and dodecanal as a minor product. This result shows that the 2-position of the acetal, which is activated by the two ether linkages, is more reactive than the dimethylene moiety of the substrate toward nitrogen dioxide. The mechanism of this reaction is implied in Scheme 3.



Scheme 1



Scheme 2



Scheme 3

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Footnote

† A typical experimental procedure was as follows: nitrogen dioxide was condensed in a vessel cooled in a ice-bath, weighed and then diluted with CCl_4. 230–400 Mesh chromatographic silica gel was dried at 200 °C for 2 h and to this (0.33 g) were added 2,2-diisopropyl-1,3-dioxolane (1 mmol) in CCl_4 (4 ml) and NO_2 (3 mmol) in CCl_4 (6 ml) along with pentadecane

(70 µl) used as a internal standard for GLC analysis under a nitrogen atmosphere. The mixture was stirred for 40 min at 30 °C and then the reaction mixture was submitted to GLC analysis.

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