New Synthesis of α-Nitroso Esters and Oximes of α-Keto Esters

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Ketene *O*-alkyl *O'*-silyl acetals on reaction with nitric oxide or isoamyl nitrite in the presence of titanium(IV) chloride provide either one of α-nitroso esters and oximes of α-keto esters.

It is well known that ketene *O*-alkyl *O'*-silyl acetals **1** are synthetically useful intermediates for the preparation of α-substituted carboxylic esters.[1-3] In this communication we report our findings concerning reactions of **1a–g** with nitric oxide and with isoamyl nitrite in the presence of titanium(IV) chloride. These reactions seem to provide a relatively direct way to introduce a nitrogen substituent at the α-carbon atom of carboxylic esters. Recently, the radical nitrosation using nitric oxide leading to the formation of a carbon–nitrogen bond has been reported.[4] On the other hand, the mode of reaction using alkyl nitrites is not clear though the radical character of alkyl nitrites has been proposed thirty years ago by Kharasch and co-workers.[5]

In the present reactions, the structure of products obtained depended not on the attacking reagent used, but on the presence or absence of α-hydrogen in the starting substrates **1a–g**. Thus, the products obtained from ketene *O*-alkyl *O'*-silyl acetals such as **1a–c** having no α-hydrogen were the corresponding α-nitroso esters **4a–c**; on the other hand, those obtained from ketene *O*-alkyl *O'*-silyl acetals such as **1d–g** having α-hydrogen were the oximes of α-keto esters **(5d–g)**, which were brought about by tautomerization of the intermediate α-nitroso esters **4d–g**. The structures of these products were confirmed by high-resolution mass spectrometry, IR spectra, and ^{1}H-NMR spectra.

The reactions using nitric oxide provided mainly the dimers of intermediate radical species **3** if titanium(IV) chloride was added prior to nitric oxide to the starting substrate.[6] This means that the reaction proceeds via a radical process and that the rate of reaction of **3** with nitric oxide is faster than dimerization. On the

Table. α-Nitroso Esters **4** and Oximes of α-Keto Esters **5** Prepared

Ketene Acetal	Reagent	Product[a]	Yield[b] (%)	mp[c] (°C)	Molecular Formula[d] or Lit. mp (°C)	IR (Nujol)[e] ν (cm^{-1})	^{1}H-NMR (CDCl$_3$)[f] δ, J (Hz)
1a	NO	**4a**	68	81–83	89[7]	2920, 1740, 1560	1.21 (t, 3H, J = 7); 1.62 (s, 6H); 4.20 (q, 2H, J = 7)
	i-C$_5$H$_{11}$ONO		75	82–83			
1b	NO	**4b**	72	78	C$_7$H$_{13}$NO$_3$ (159.2)	2935, 1735, 1520	0.88 (t, 3H, J = 7); 1.24 (t, 3H, J = 7); 1.57 (s, 3H); 2.15 (q, 2H, J = 7); 4.18 (q, 2H, J = 7)
	i-C$_5$H$_{11}$ONO		75	77			
1c	NO	**4c**	65	170	C$_{15}$H$_{13}$NO$_3$ (255.3)	3020, 2910, 1740 1610, 1535	3.71 (s, 3H); 7.28 (m, 10H)
	i-C$_5$H$_{11}$ONO		65	170			
1d	NO	**5d**	65	93	95[8]	3240, 2930, 1720, 1670	1.23 (t, 3H, J = 7); 2.12 (s, 3H); 4.32 (q, 2H, J = 8); 9.71 (br s, 1H)
	i-C$_5$H$_{11}$ONO		70	93–94			
1e	NO	**5e**	68	39	C$_7$H$_{13}$NO$_3$ (159.2)	3300, 2960, 1725, 1630	0.96 (t, 3H, J = 7); 1.26 (t, 3H, J = 7); 1.52 (m, 2H); 2.49 (t, 2H, J = 7); 2.23 (q, 2H, J = 7); 10.18 (br s, 1H)
	i-C$_5$H$_{11}$ONO		70	39–40			
1f	NO	**5f**	70	48–49	C$_7$H$_{13}$NO$_3$ (159.2)	3350, 2980, 1730, 1600	1.23 (m, 9H); 3.42 (m, 1H); 4.24 (q, 2H, J = 7); 9.88 (br s, 1H)
	i-C$_5$H$_{11}$ONO		75	48–49			
1g	NO	**5g**	65	44–45	42[9]	3250, 2950, 1720, 1640	0.86 (t, 3H, J = 7); 1.31 (t, 3H, J = 7); 1.49 (m, 4H); 2.59 (t, 2H, J = 8); 4.27 (q, 2H, J = 7); 10.10 (br s, 1H)
	i-C$_5$H$_{11}$ONO		70	45			

[a] For nitroso compounds **4a–c**, which are light-green crystalline solids, the IR bands in the region 1520–1560 cm^{-1} support the monomeric form. Also, the mass spectral data support the monomeric form. The simplicity of the ^{1}H-NMR data of **5d–g** as well as the observation that their IR spectra indicate a relatively sharp peak at 3240–3350 cm^{-1} are suggestive of simple isomers. Probably, the compounds **5d–g** possess the *Z* geometry, such that intramolecular hydrogen bonds are possible.

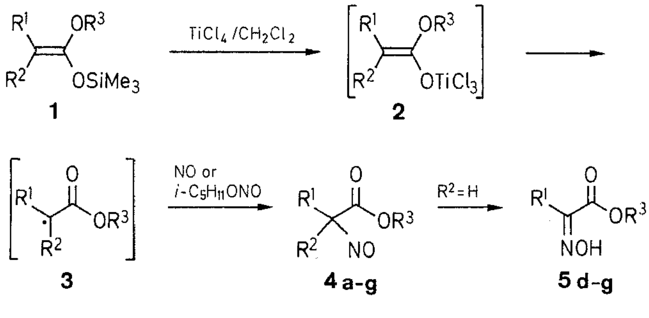
[b] Yield of product isolated by column chromatography.

[c] Recrystallized from hexane.

[d] Satisfactory microanalyses obtained: C ±0.25, H ±0.31, N ±0.29.

[e] Recorded on a JASCO IR-810 spectrophotometer.

[f] Measured at a 200 MHz instrument using TMS as internal standard.



1-4	R^1	R^2	R^3	1-5	R^1	R^2	R^3
a	Me	Me	Et	d	Me	H	Et
b	Et	Me	Et	e	n-Pr	H	Et
c	Ph	Ph	Me	f	i-Pr	H	Et
				g	n-Bu	H	Et

other hand, we have no evidence for that the reactions using isoamyl nitrite also proceed similarly via a radical process. In view of the initially mentioned report by Kharasch and coworkers,[5] however, the results using isoamyl nitrite also seem to be accommodated by assuming radical intermediates.

Reaction of Ketene *O*-Alkyl *O*′-Silyl Acetals (1a–g) with Nitric Oxide in the Presence of Titanium(IV) Chloride; General Procedure:

Nitric oxide is bubbled through a stirred and cooled (0–5 °C) solution of ketene *O*-alkyl *O*′-silyl acetal **1** (5 mmol) in CH$_2$Cl$_2$ (20 mL) for 30 min. TiCl$_4$ (0.55 mL, 5 mmol) is then added dropwise, and stirring is continued for 4 h. The reaction mixture is diluted with water (30 mL) and extracted with CH$_2$Cl$_2$ (3 × 30 mL). The organic extracts are dried (MgSO$_4$) and concentrated *in vacuo*. The residue is subjected to flash chromatography on silica gel using EtOAc/hexane (1 : 1) as eluent.

Reaction of Ketene *O*-Alkyl *O*′-Silyl Acetals (1a–g) with Isoamyl Nitrite in the Presence of Titanium(IV) Chloride; General Procedure:

To a stirred and cooled (10 °C) solution of ketene *O*-alkyl *O*′-silyl acetals **1** (5 mmol) and isoamyl nitrite (0.88 g, 7.5 mmol) in CH$_2$Cl$_2$ (20 mL) is added dropwise TiCl$_4$ (0.55 mL, 5 mmol). The reaction mixture is then stirred at room temperature for 24 h and diluted with cold water (30 mL). The organic layer is separated, and the aqueous layer is extracted with CH$_2$Cl$_2$ (3 × 30 mL). The combined organic extract is dried (MgSO$_4$) and concentrated *in vacuo* to afford a residue, which is subjected to flash chromatography on silica gel using EtOAc/hexane (1 : 1) as eluent.

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