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HYPERVALENT IODINE OXIDATION OF TRIMETHYLSILYL KETENE ACETALS: A CONVENIENT ROUTE TO α-METHOXYLATION OF ESTERS AND LACTONES

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Abstract: Hypervalent iodine oxidation of trimethylsilyl ketene acetals of esters and lactones using iodosobenzene in methanol affords the corresponding α -methoxylated carbonyl compounds in good yields.

Hypervalent iodine oxidation of silyl enol ethers under different conditions offers a very useful way of introducing various functionalities at the alpha position of ketones.¹ However, the scope of this approach to the α -functionalization of esters and lactones is not investigated in most cases. In an effort to extend the application of I(III) mediated method for α -functionalization of esters^{1c,2} and lactones, we now report α -methoxylation of trimethylsilyl ketene acetals of some esters and lactones. Part of the reason to undertake this study was that α -alkoxylation of esters and lactones is generally accomplished by using indirect methods^{3,4} which suffer from several drawbacks such as poor yields and low generality.

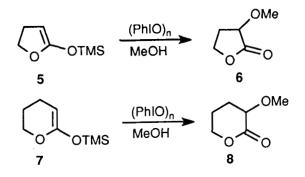
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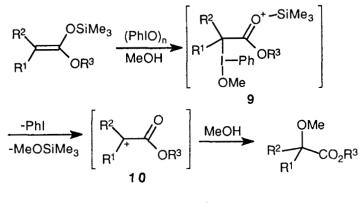
Based on our previous results on α -methoxylation of ketones^{1b} we first treated trimethylsilyl ketene acetal of ethyl phenylacetate (1a) with one equivalent of iodosobenzene and boron trifluoride etherate in methanol. But the reaction gave a complex mixture of several products. Interestingly, omitting the use of boron trifluoride etherate and treating the trimethylsilyl ketene acetal with iodosobenzene in methanol for 24 hours afforded ethyl α -methoxyphenylacetate (2a) in 65% yield. Other esters which were α -methoxylated by using this approach include methyl phenylacetate (silyl ketene acetal 1a'), methyl/ethyl *p*-substituted phenyl acetates (silyl ketene acetals 1b-d) and methyl isobutyrate (silyl ketene acetal 3) (Scheme 1).

R2 R1		(PhIO) _n MeOH ►		R ² R ¹ CO ₂ R ³
	1a-d 3			2a-d 4
Product	R ¹	R ²	R ³	% Yield
2a	Ph	Н	Et	65
2a'	Ph	Н	Me	74
2 b	$p-MeC_6H_4$	Н	Et	71
2 c	<i>p</i> -OMeC ₆ H ₄	Н	Me	73
2 d	p-ClC ₆ H ₄	Н	Me	57
4	Me	Me	Me	64
		Scheme	1	

The same approach was successfully applied to the α -methoxylation of γ butyrolactone (5 \rightarrow 6) and δ -valerolactone (7 \rightarrow 8). It is to be mentioned that syntheses of 6⁵ and 8⁶ have recently been reported by multistep procedures without providing complete characterization data. In particular, lactone 8 was synthesized by Wolff *et al.*⁶ as a viscous oil, very impure as judged by ¹H NMR (29% yield) which could nevertheless be used by them for the further synthetic work.



A plausible mechanistic pathway outlined in Scheme 2 involves the initial electrophilic attack of the reactive I(III) species- $PhI(OMe)_2$ (generated from iodosobenzene and methanol⁷) upon the acetal double bond to give intermediate 9. Loss of PhI and MeOSiMe₃ followed by nucleophilic attack of methanol on the resulting carbocation (10) leads to the α -methoxycarbonyl compound.



Scheme 2

The noteworthy features which make the present method more advantageous than literature procedures are: i) the procedure involves mild and neutral conditions with very simple experimentation, ii) the method works well on aromatic/aliphatic esters and lactones, iii) as evident by conversions $1a, b \rightarrow 2a, b$, the method does not give

any transesterification; literature procedures^{2,3} including hypervalent iodine oxidative alkoxylation of esters,² which involve strong alkoxide ions, normally yield the transesterified α -alkoxy derivatives.

Experimental

General Procedure. A suspension of iodosobenzene (2.4 g; 11 mmol) in dry methanol was stirred under nitrogen until a clear solution resulted (about 10 minutes). To this solution was added a trimethylsilyl ketene acetal (10 mmol) in one portion and the mixture was stirred at room temperature for 20-24 h. Methanol was removed in vacuo and the crude mixture was purified by column chromatography on silica gel using hexanes-ether as eluant.

Ethyl α -methoxy-p-tolylacteate (2b), liquid; IR (neat) 1730 cm⁻¹; ¹H NMR (CDCl₃) δ 1.22 (t, 3 H), 2.34 (s, 3 H), 3.38 (s, 3 H), 4.17 (q, 2 H), 4.72 (s, 1 H), 7.17 (d, 2 H), 7.32 (d, 2 H); MS (CI) m/z 209 (M⁺+1, 1), 179 (31), 177 (100); Anal. Calcd. for C₁₂H₁₆O₃ C 69.23, H 7.69; Found C 69.04, H 7.77%.

 α -Methoxy- γ -butyrolactone (6),⁵ liquid; IR (neat) 1785 cm⁻¹; ¹H NMR (CDCl₃) δ 2.35 (m, 2 H), 3.45 (s, 3 H), 4,48 (m, 3 H); MS (70 eV) m/z 116 (M⁺, 11), 84 (37); Anal. Calcd. for C₅H₈O₃: C 51.72, H 6.90; Found: C 51.81, H 6.82%.

 α -Methoxy- δ -valerolactone (8),⁶ liquid; IR (neat) 1750 cm⁻¹; ¹H NMR (CDCl₃) δ 1.83 (m, 4 H), 3.60 (s, 3 H), 4.22 (m, 3 H); MS m/z 130 (M⁺, 5), 98 (48); Anal. Calcd. for C₆H₁₀O₃: C 55.38, H 7.69; Found: C 55.32, H 7.63%. The spectral data of products 2a, 2a', 2c, 2d^{2a} and 4⁸ were in total agreement

The spectral data of products 2a, 2a', 2c, 2d²² and 4° were in total agreement with those previously reported.

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