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Robert M. Moriarty [a], Neena Rani [a], Cristian Condeiu [a], Michael P. Duncan [a] & Om Prakash [a]
[a] Department of Chemistry, University of Illinois, Chicago, IL., 60607, USA
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HYPERVALENT IODINE OXIDATION OF TRIMETHYLSILYL KETENE ACETALS: A CONVENIENT ROUTE TO α-METHOXYLATION OF ESTERS AND LACTONES

Robert M. Moriarty*, Neena Rani, Cristian Condeiu, Michael P. Duncan and Om Prakash*#
Department of Chemistry, University of Illinois at Chicago, IL. 60607 USA

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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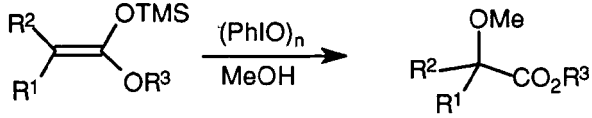
*To whom correspondence should be addressed.

On leave of absence from Kurukshetra University, Kurukshetra, 136119, India.

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).

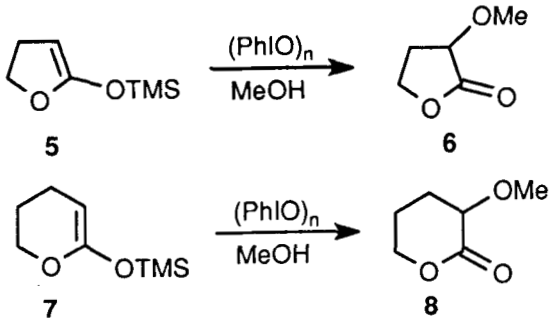


1a-d **2a-d**
3 **4**

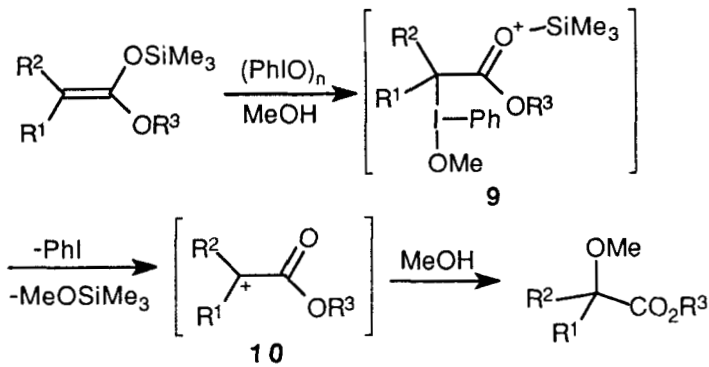
Product	R^1	R^2	R^3	% Yield
2a	Ph	H	Et	65
2a'	Ph	H	Me	74
2b	*p*-MeC_6H_4	H	Et	71
2c	*p*-$OMeC_6H_4$	H	Me	73
2d	*p*-ClC_6H_4	H	Me	57
4	Me	Me	Me	64

Scheme 1

The same approach was successfully applied to the α-methoxylation of γ-butyrolactone (**5**→**6**) and δ-valerolactone (**7**→**8**). It is to be mentioned that syntheses of **6**[5] and **8**[6] 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 ^{1}H 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 methanol[7]) upon the acetal double bond to give intermediate **9**. Loss of PhI and $MeOSiMe_3$ 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** →**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 ($CDCl_3$) 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 $C_{12}H_{16}O_3$ 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 ($CDCl_3$) 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 $C_5H_8O_3$: 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 ($CDCl_3$) 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 $C_6H_{10}O_3$: C 55.38, H 7.69; Found: C 55.32, H 7.63%.

The spectral data of products **2a, 2a', 2c, 2d**[2a] **and 4**[8] were in total agreement with those previously reported.

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