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ALKYLATION AND SILYLATION OF DIRECTED ENOLATES FROM DIETHYLKETENE AND ORGANOMETALLIC REAGENTS

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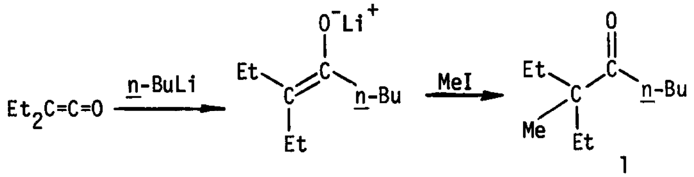
Abstract. Diethylketene and organometallic reagents form enolates capturable by methyl iodide or trimethylsilyl chloride with greater than 95% positional selectivity.

Despite their multiple functionality and high reactivity ketenes have found only limited utility as laboratory scale synthetic reagents.[1] Instead the use of "ketene equivalents"[2a] and "masked ketenes"[2b] has been emphasized. A recent review on preparative applications of ketenes emphasizes cycloadditions and states "ketene acylation reactions are generally not useful synthetically."[1d] Only occasional examples are reported of advantageous use of ketenes in synthesis,[3] although there has been intense recent interest in the reaction mechanisms of ketenes and related species[4] and in their role as reaction intermediates.[5]

There have been scattered reports[1,6] of nucleophilic additions to ketenes to generate enolates which were captured by protonation or acylation. The present communication reports the first examples of one flask nucleophilic addition-alkylation and nucleophilic addition-silylation sequences of a ketene. The procedures include the directed generation of an enolate which is formed to only a minor extent by conventional procedures.

Specifically reaction of n-butyllithium with diethylketene followed by methyl iodide led to the formation of 3-ethyl-3-methyl-4-octanone (1, eq. 1) in yields of up to 55%. The



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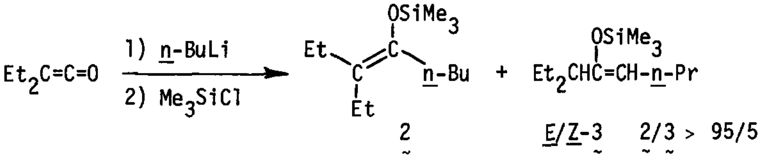
isomeric 3-ethyl-5-methyl-4-octanone was not detected and constituted no more than 3% of the product. A study of the effect of some reaction variables on this process reported in the Table revealed THF solvent at -70°C to be the optimum conditions for this procedure.[7]

Table Reaction of Diethylketene with n-Butyllithium and Methyl Iodide

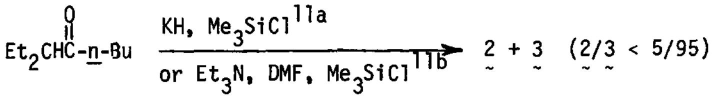
Solvent	T(°C)	% Yield **1**
THF	-70	55
THF	0	47
Et_2O	-70	8
DME	-70	2
pentane	-70	2

Reaction of diethylketene with PhMgBr and methyl iodide correspondingly led to $MeEt_2CCOPh$, but in only 5% yield.

Addition of trimethylsilyl chloride to the enolate prepared from diethylketene and n-butyllithium produced a 65% yield of vinyl silyl ether **2** and less than 5% of the E/Z isomers **3** (eq. 2).[10] This directed synthesis of **2** contrasts with the results of two conventional synthetic procedures,[11] which gave **2** as only a minor constituent of the mixture of isomeric products (eq. 3). The reaction of diethylketene with PhMgBr followed by Me_3SiCl gave 20% of $Et_2C{=}C(OSiMe_3)Ph$ (**4**).[10]



2 E/Z-3 2/3 > 95/5 (2)



$$Et_2CH\overset{O}{\overset{\|}{C}}\text{-}n\text{-}Bu \xrightarrow[\text{or } Et_3N,\ DMF,\ Me_3SiCl^{11b}]{KH,\ Me_3SiCl^{11a}} \mathbf{2} + \mathbf{3} \quad (\mathbf{2}/\mathbf{3} < 5/95) \qquad (3)$$

This work has thus established the utility of consecutive nucleophilic and electrophilic additions to diethylketene resulting in directed formation of products which are at best only minor constituents of the isomeric products available from conventional procedures. The study of the full scope of this reaction is being actively pursued.

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(7) In the standard procedure diethylketene (prepared as in ref. 8 and analyzed as in ref. 9) as a solution in the cold reaction solvent (8 ml of 0.4 *M* solution, 3.2 mmol $Et_2C=C=O$) was added over 5 min by a syringe to a stirred solution of 1.4 M *n*-BuLi in pentane (10 ml, 14 mmol) in 100 ml of the reaction solvent under N_2. After 30 min CH_3I (30 mmol) was added in one portion and the reaction was allowed to warm to room temperature overnight. The reaction mixture was poured into water, extracted, concentrated, and analyzed by gas chromatography.

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(10) The new compounds reported, namely **2**, *E*- and *Z*-**3**, and **4**, were characterized by NMR, ir, mass spectrometry, and correct C, H analysis. The assignment of the *E* and *Z* configurations of the separate isomers of **3** is not yet secure.

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