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EFFICIENT CONVERSION OF CARBONYL COMPOUNDS TO CONJUGATED DIENALS

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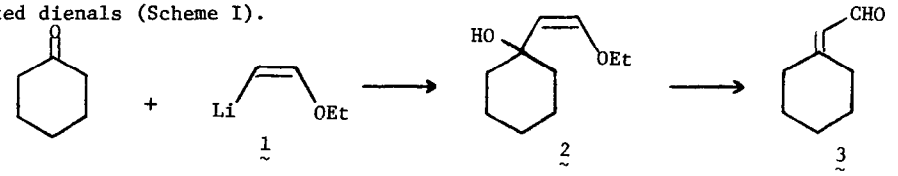
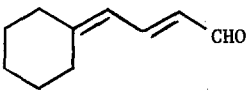
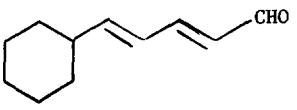
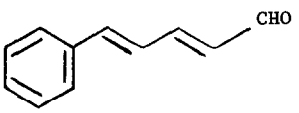
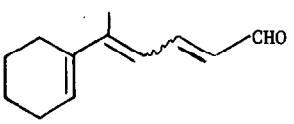
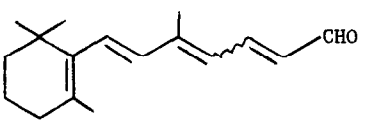
A useful preparation of the hitherto elusive compound cis-2-ethoxyvinyllithium[1] (1) was recently described.[2] The utility of this reagent was demonstrated by a range of applications. One particularly valuable use of 1 is in the extraordinarily simple and convenient two-carbon homologation of carbonyl compounds to α,β-unsaturated aldehydes. For example, addition of cyclohexanone to 1 (at -78°C) gave the detectable intermediate 2. Attempts to purify this and similar γ-hydroxy enol ethers have been unsuccessful owing to their facile allylic rearrangement into α,β-unsaturated aldehydes[3,4] (e.g. 3), even during rapid chromatography on Florisil. An extension of this methodology is now described whereby carbonyl substrates are efficiently converted to conjugated dienals (Scheme I).



1 2 3

Hydrostannation of 1-ethoxy-1-buten-3-yne[5] with one equiv of tri-n-butyltin hydride and a catalytic amount of azobisisobutyronitrile as a radical initiator (90°C, 10 h) gave the easily distillable [bp 120-130°C (0.3 mm)] vinylstannane 4 (mixture of geometric isomers). Transmetallation of 4 with n-butyllithium in THF proceeded smoothly at -78°C in 1 h to form anion 5. At -78°C, 5 reacts with aldehydes and ketones to produce the dienols 6 in good yields. These intermediate enol ethers are converted into conjugated dienals of type 7 during chromatography on silica gel or by treatment with p-toluenesulfonic acid (5 mol %) in 5% aqueous THF (25°C, 1 h; Table I).[6]

Table I. Reaction 1-Lithio-4-Ethoxybutadiene with Electrophiles

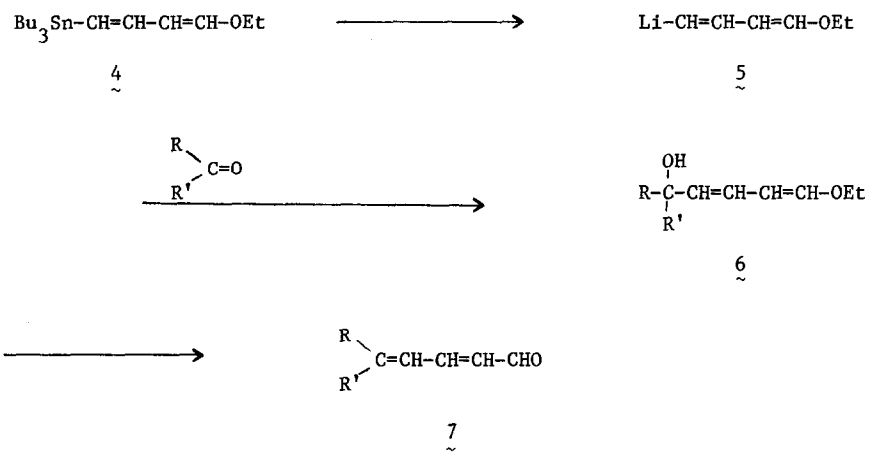
Electrophile	Adduct	Yield[a](%)
cyclohexanone		87
cyclohexanecarboxaldehyde		83
benzaldehyde		90
1-acetyl-1-cyclohexene		80[b,c]
β-ionone		82[b,c]

[a]The yields were based on products isolated by preparative TLC or column chromatography. All products exhibited satisfactory nmr, ir, and microanalysis data. Unless otherwise indicated the crude enol ethers 6 underwent allylic rearrangement to the dienals 7 during chromatography.

[b]The intermediate enol ether was stirred with p-TsOH in aqueous THF prior to chromatography.

[c]The isolated product was a ~5:1 mixture of E/Z isomers.

Scheme I



The experimental details are illustrated in the preparation of 5-phenyl-2,4-pentadienal. To a solution of 650 mg (1.68 mmol) of 1-tri-n-butylstannyl-4-ethoxybutadiene in 7 mL of dry THF at -78°C was added dropwise 1.10 mL (1.76 mmol) of 1.1 M n-butyllithium. After stirring for 1 h at -78°C, 162 mg (1.53 mmol) of benzaldehyde was added. The mixture was stirred at -78°C for 3 h and then quenched with aqueous sodium bicarbonate. The mixture was extracted with ether and the isolated crude product was purified by column chromatography on silica gel to give 217 mg (90%) of the desired dienal: IR (film) 1675, 1620 and 1595 cm^{-1}; NMR, aldehydic proton at δ9.55 (d, J = 8 Hz), aromatic and 3 vinylic protons at δ6.9-7.7, vinylic proton β to CHO at δ6.22 (ddd, J = 1, 8 and 17 Hz). A 2,4-DNP derivative was prepared and analyzed. Anal. Calcd for $C_{17}H_{14}N_4O_4$: C, 60.35; H, 4.17; N, 16.56. Found: C, 60.09; H, 4.25; N, 16.36.

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References and Notes

1. J. Ficini and J. C. Depezay, Tetrahedron Lett., 937 (1968).
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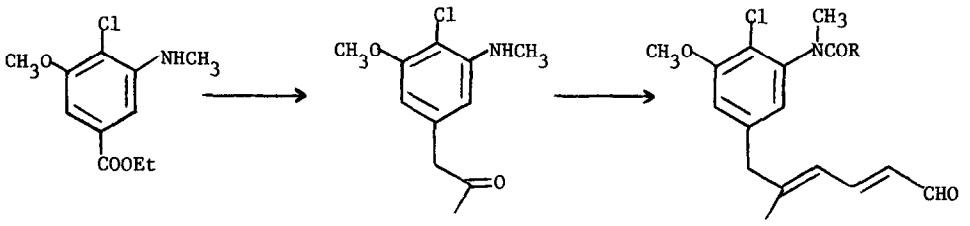
6. One application of reagent 5 may be in the synthesis of dienal 8, a compound which has been earmarked as a key synthetic intermediate corresponding to the benzoid part of maytansine. Corey has recently published a synthesis of amino ester 9 (ref 7), a reasonable precursor to ketone 10.



9 10 8

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