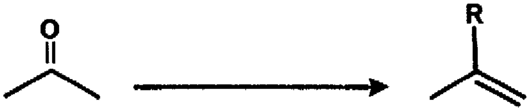
Tetrahedron Letters No. 49, pp 4405 - 4408, 1976. Pergamon Press. Printed in Great Britain.

A NEW SYNTHESIS OF OLEFINS FROM KETONES VIA COUPLING OF LITHIUM DIALKYLCUPRATES WITH ENOL DIPHENYLPHOSPHATE ESTERS

Larry Blaszczak*, Jeffrey Winkler, and Steven O'Kuhn
Mallinckrodt Chemical Laboratories
Harvard University
Cambridge, Massachusetts 02138 USA

(Received in USA 7 September 1976; received in UK for publication 19 October 1976)

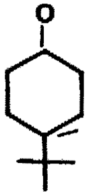
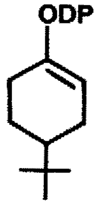
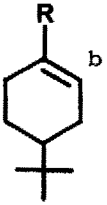
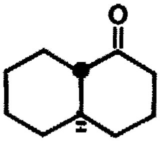
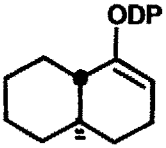
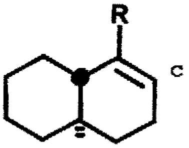
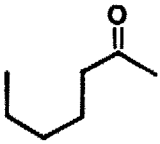
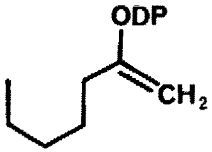
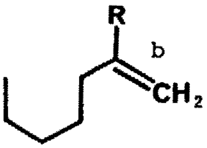
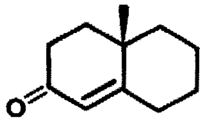
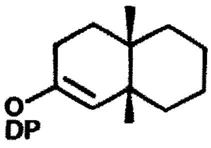
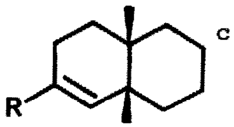
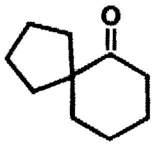
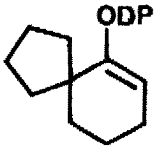
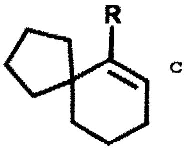
The conversion of a ketone to an alkyl-substituted olefin is an important process in synthesis (Scheme I). The classical method for effecting this overall transformation, i.e. nucleophilic addition of an alkyllithium or Grignard reagent followed by dehydration of the resultant alcohol, generally affords olefin mixtures and/or skeletal rearrangement products.[1] Corey and Posner[2] have shown that vinyl halides and lithium dialkylcuprate reagents react to form alkyl-substituted olefins.[3] However, the formation of vinyl halides from ketones requires harsh conditions and gives mixtures of all possible isomeric products.[4] Considering the accessibility of a wide variety of ketone enolate ions, particularly the regiospecifically generated enolates of unsymmetrical ketones,[5-7] we felt that a method for the replacement of an enolate oxygen by an alkyl substituent would constitute a powerful new approach to the synthesis of isomerically pure olefinic compounds. We now wish to record a preliminary communication of our work in this area.



Scheme I

Ireland[8,9] and others[10] have reduced enol tetramethylphosphoroamidate and enol diethylphosphate esters of ketones to olefins with lithium in ammonia/t-butanol, replacing enol oxygen by hydrogen. This result suggested to us that an enol phosphate might also undergo reduction by a cuprate reagent affording an alkyl-substituted olefin. Indeed, when the enol diphenylphosphate ester of 4-t-butylcyclohexanone was treated with lithium di(n-butyl)cuprate (3 equiv) in THF at -30°C

Table

Ketone	Enol Phosphate^a	R, R_2CuLi	Product	% Yield
		n-Bu Me		59 11
		Me		12
		n-Bu		74
		n-Bu		52^e
		n-Bu		<10

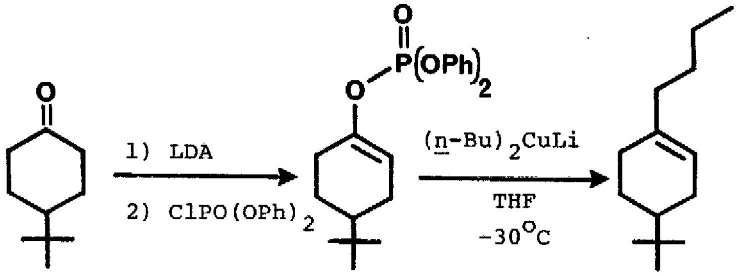
a) DP = -PO(OPh)$_2$

b) Identified by spectral (ir, nmr) and chromatographic comparison with material prepared *via* an alternate route

c) Spectral (ir, nmr, ms) data consistent with proposed structure

d) Isolated yield from starting ketone unless otherwise indicated

e) Isolated yield from enol diphenylphosphate ester for 12 hr, reaction occurred smoothly to furnish 1-n-butyl-4-t-butyl-1-cyclohexene in 59% yield overall from 4-t-butylcyclohexanone (Scheme II).



Scheme II

Several representative olefins which have been prepared using this new method are listed in the table. It is noteworthy that the less reactive[11] lithium dimethylcuprate has thus far failed, even under forcing conditions (6 equiv, -10°C, 30 hr), to undergo this novel substitution reaction. Enol phosphates which are sterically hindered also fail to react.

The following experimental procedure is illustrative.

1-n-butyl-4-t-butyl-1-cyclohexene. A solution of 4-t-butylcyclohexanone (463 mg, 3 mmol) in dry THF (5 ml) was added dropwise to a stirred solution of lithium diisopropylamide (3.3 mmol) in dry THF (10 ml) at 0°C under an argon atmosphere. After 15 min, diphenylphosphorochloridate[12] (0.93 ml, 4.5 mmol) was added in one portion. The cooling bath was removed and the mixture allowed to stand at ambient temperature for 2 hr. The pale yellow solution was partitioned between ether and water; the combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo*. Rapid chromatography of the residue on silica gel using ether/hexane (1:1, v/v) as eluent gave 1.248 gm (104% recovery) of enol diphenylphosphate ester which was sufficiently pure for use in the coupling reaction.

To a stirred solution of lithium di(n-butyl)cuprate (8.9 mmol) in dry THF (20 ml) under argon at -30°C was added dropwise a solution of the crude enol diphenylphosphate ester in dry THF (10 ml). The reaction mixture was stirred at -30°C for 12 hr, quenched with excess methanol, and then partitioned between pentane and saturated aqueous NH_4Cl/aqueous NH_3 (1:1, v/v). The organic extracts were combined, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was taken up in pentane and filtered through alumina (activity I, neutral). Concentration[13] of the filtrate afforded 343 mg (59% yield) of 1-n-butyl-4-t-butyl-1-cyclohexene as a colorless oil, identical (ir, nmr, tlc) to material prepared by an alternate route.

While the yields are not optimized, we feel that this procedure represents an important addition to the methodology now available for olefin synthesis. We are continuing our investigation of this new reductive coupling reaction.[14]

References and Notes

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7. Enolates obtained by cuprate addition to α,β-enones: D. C. Muchmore, Org. Synth., 52, 109 (1972) and references therein.
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12. Aldrich "Diphenyl Chlorophosphate" D20,655-5 was distilled (157-160°C/2.3 Torr) prior to use.
13. Concentration by means of a rotary evaporator under aspirator pressure left residual n-octane which was conveniently removed at the oil pump (ca. 1 Torr, 25-30°C, 20 min) prior to analysis. The octane presumably results from decomposition of the lithium di(n-butyl)cuprate.

14. The authors wish to thank Professor E. J. Corey and the Department of Chemistry, Harvard University, for their generous financial support.