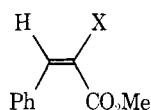


ample, when the Li complex was prepared from $\text{LiAlD}(\text{OCH}_3)_3$ ¹² and allowed to react with methyl cinnamate, methyl 3-deuterio-3-phenylpropionate was obtained in 20% yield.¹³ With same reagent, 2,2,6,6-tetramethylheptanone gave 2,2,6,6-tetramethyl-5-deuterio-3-heptanone in 87% yield.¹⁴ With the Li complex under the usual conditions, but with D_2O being added instead of water during isolation, methyl cinnamate led to 3-phenylpropionate with deuterium only in the α position.¹⁵ These results suggest that the hydrogen added in the β position arises from the copper hydride, while the hydrogen added in the α position results from protons in the medium or added during isolation.

That the 2-butanol acts as a proton donor (and not a hydrogen atom donor, from C-2) was shown by the formation of unlabeled methyl phenylpropionate (82% yield) from reduction of methyl cinnamate in the presence of 2-deuterio-2-butanol.¹⁶ On the other hand, 2-butanol-*O-d* leads to methyl phenylpropionate with 24% deuterium at the α position ($\sim 50\%$ labeling of one proton) and $<1\%$ deuterium in the β position. The effectiveness of 2-butanol appears to result from selective proton transfer—slow toward the copper hydride but rapid enough toward an intermediate (e.g., 2) to inhibit oligomerization reactions.¹⁷

Two acetylenic esters undergo successful reduction. The reaction with methyl phenylpropiolate is highly selective for single stage reduction, giving predominately the cis-unsaturated ester upon proteolytic isolation. Consistent with an α -carboxyvinyl metal intermediate (e.g., 4), the yield and geometry of the products depend on temperature and duration of reaction before quenching.¹⁸ Longer reaction times give lower yields and more trans isomer. Quenching with D_2O provides a mixture of *cis*- and *trans*-cinnamates with $>98\%$ α deuterium (i.e., 5) from methyl phenylpropiolate and the Na complex.^{19,20}



4, X = Cu

5, X = D

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- R. K. Boeckman, Jr., and R. Michalak, *J. Am. Chem. Soc.*, **96**, 1623 (1974). This paper includes one example of reduction of an acrylate in 40% yield. No general method of reduction of conjugated esters is claimed, however.
- Eastman Chemical's sodium bis(2-methoxyethoxy)aluminum hydride in benzene.
- Cuprous bromide and iodide were purified according to the procedure of G. B. Kauffman and L. A. Teter, *Inorg. Synth.*, **7**, 9 (1963).
- The purity and identity of this compound were established by spectral (^1H NMR, ir, mass) and chromatographic (GPC) means.
- Compound 1 was identified by interpretation of ^1H NMR and mass spectra and by comparison of melting point with the literature value: found mp $174\text{--}175^\circ$; literature mp $174\text{--}175^\circ$ [D. Y. Curtin and S. Dayagi, *Can. J. Chem.*, **42**, 867 (1964)].
- Cf., K. W. Bowers, R. W. Giese, J. Grimshaw, H. O. House, N. H. Kolodny, K. Kronberger, J. P. Kaplan, and J. F. Simone, *J. Am. Chem. Soc.*, **92**, 2800 (1970).
- H. O. House and M. J. Umen, *J. Org. Chem.*, **38**, 3893 (1973), and references therein.
- This compound was prepared from lithium aluminum deuteride and methyl alcohol in tetrahydrofuran. A filtered, titrated solution of lithium aluminum deuteride was employed.
- The deuterium was ascertained to be specifically at the β position by ^1H NMR analysis, using rare earth shift reagents to separate and simplify the multiplets due to the α - and β -hydrogen atoms. Integration of the NMR signals and abundances of peaks in the molecular ion region of the mass spectrum suggested replacement of one hydrogen by deuterium to the extent of $\sim 85\%$.
- The position of the deuterium in the 2,2,6,6-tetramethyl-5-deuterio-3-heptanone was obvious from the ^1H NMR spectrum (CDCl_3). The multiplet which appears as a triplet ($J = 7.8$ Hz) of area 2 at δ 1.50 in 2,2,6,6-tetramethylheptan-3-one now appears as triplet of triplets at δ 1.50, of area 1.1 ($J_{\text{H-H}\beta} = 7.8$ Hz, $J_{\text{H-D}\beta} = 1.0$ Hz). The area of the signals (doublet of triplets) due to the α hydrogens is 2.0 (no deuterium incorporation). The relative abundances of ions in the parent ion region of the mass spectrum also indicated the presence of one deuterium in $\sim 90\%$ of the molecules.
- The extent of incorporation was low (45% of one hydrogen in the β position), perhaps owing to exchange with aqueous solutions during isolation. The experiment was designed to show the absence of proton (deuteron) delivery to the β position.
- The labeled alcohol was prepared by reduction of acetone with lithium aluminum deuteride and contained $>96\%$ deuterium at C-2 by NMR analysis.
- On the other hand, methyl alcohol is too reactive toward the copper hydride species and drastically decreases the reducing ability, while *tert*-butyl alcohol has no significant effect on the reactions.
- Maximum yield is obtained after 15 min at -20° (*cis*, 55%; *trans*, 21%) but drops if the reaction is quenched after 30 min at 0° (*cis*, 14%; *trans*, 13%).
- The extent of deuterium incorporation was determined by NMR spectral analysis, using integration of the signal appearing at δ 5.90 (d, α H, $J = 13$ Hz, *cis* isomer), and δ 6.38 (d, α H, $J = 16$ Hz, *trans* isomer). Cf., K. Brocklehurst, H. S. Price, and K. Williamson, *Chem. Commun.*, 884 (1968).
- We are pleased to acknowledge financial support for this work from the National Institutes of Health (AI-08687).
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Olin Chemistry Laboratory
Cornell University
Ithaca, New York 14853

M. F. Semmelhack*²¹
R. D. Stauffer²²

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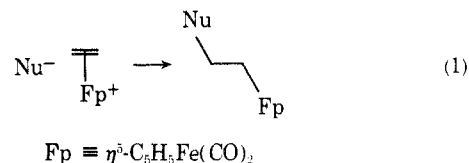
Metal Assisted C—C Bond Formation. Use of a Methyl Vinyl Ketone Complex in Michael Condensations

Summary: Methyl vinyl ketone complexed by $\text{C}_5\text{H}_5\text{Fe}(\text{CO})_2^+$ is shown to be a powerful acceptor of nucleophiles in Michael-type reactions.

Sir: The addition of kinetically generated enolates to vinyl ketones is generally complicated by polymerization of the acceptor component under the aprotic conditions required to minimize proton transfer and consequent equilibration of the donor enolate.¹

It has recently been shown² that the polymerization problem may be resolved through the use of α -silylated vinyl ketones, and a number of such reagents have been successfully employed with regioselectively generated lithium enolates in ring annelation reactions.^{2,3}

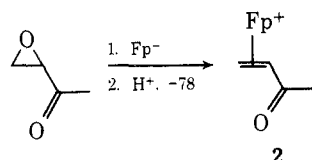
Since we had previously reported⁴ that enolates of β -dicarbonyls could be condensed with isolated olefins activated by coordination with $\eta^5\text{-C}_5\text{H}_5\text{Fe}(\text{CO})_2^+$ (eq 1), we were



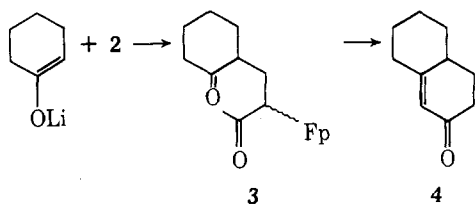
led to consider extension of these reactions to Michael condensations. Moreover, the powerful activating influence exerted upon an olefin by metal complexation left open the possibility that such reactions might also be effected with regioselectively generated enol derivatives.

The present paper describes the use of a novel methyl vinyl ketone acceptor component (2) in both electroneutral and cationic Michael-type condensations.

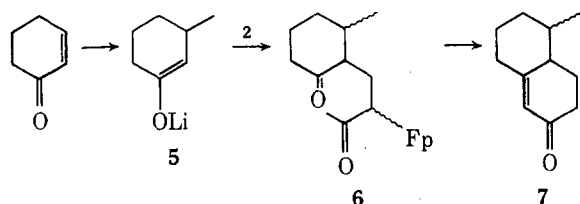
Complex 2, which is readily obtained in high yield from methyl vinyl ketone epoxide⁵ following a procedure previously reported⁶ may be stored at 0° for prolonged periods. A brief description of its preparation follows. Methyl vinyl ketone epoxide (1.3 g, 15 mmol) was added to an equivalent of $C_6H_5Fe(CO)_2Na^7$ in 30 ml of THF cooled to 0°. After 30 min at 0°, the reaction mixture was cooled to -78° and 30 mmol of $HBf_4 \cdot Et_2O$ was added dropwise. The resulting yellow solid was collected and recrystallized from acetone-ether at 0° to give 4.87 g (97%) of 2: ir (KBr) 2092, 2049, 1704 cm^{-1} ; NMR (acetone- d_6) τ 3.93 (s, 5, Cp), 4.73 (dd, 1, $J = 8, 14$ Hz, $CH=$), 5.32 (d, 1, $J = 8$ Hz, $cis-CH_2=$), 5.92 (d, 1, $J = 14$ Hz, $trans-CH_2=$).



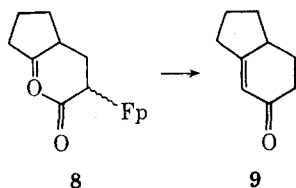
The complex cation is an effective and powerful acceptor of nucleophiles. Thus, when acetonitrile solutions of 2 are treated at -78° with cyclohexanone lithium enolate, the adduct (3) is obtained in 45% yield. This substance may be cyclized, with concurrent loss of the Fp group, to the octalones (4,⁸ 76%) on refluxing in methylene chloride solutions for 19 hr in the presence of activity I basic alumina. The facile loss of the organometallic group under these relatively mild conditions suggests that cleavage of the metal-carbon bond may be promoted by the acyl group through base attack on the organometallic group and release of an enolate ion.



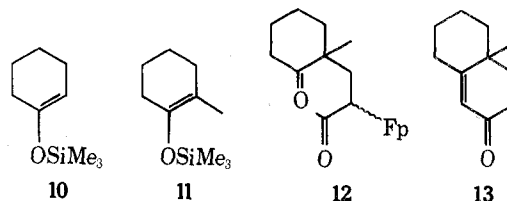
The regioselectively generated enolate (5), formed by $LiCuMe_2$ addition to cyclohexenone^{10,3a} similarly gave the adduct (6, 70%), as a mixture of diastereomers.¹¹ Cyclization with 2% KOH in methanol led, as before, to concurrent removal of the Fp group and to the formation of methyl octalones (7,¹² 70%).



Significantly, complex 2 may serve as an acceptor component with uncharged donors as well. Both cyclohexanone and cyclopentanone enamines react rapidly at 0° with 2 affording 3 or the corresponding cyclopentone adduct (8), both in 85% yield. The latter was cyclized to the hydroindanone (9)¹⁴ in 72% yield by refluxing in CH_2Cl_2 solution in the presence of basic alumina for 6 hr.



Except in terms of the mildness of reaction conditions, these reactions provide no synthetic advantage over the use of the nonactivated acceptor component in a normal enamine reaction. However, the use of silyl enol ethers as reaction partners with 2 provides a means for carrying out Michael condensations under mild conditions with regioselectively generated enol derivatives.¹⁶ Thus, cyclohexanone enol silyl ether (10) was found to react at 0° in 2 hr with 2 in acetonitrile solution. Cyclization of the crude adduct (3) in the presence of basic alumina gave 4 in 65% overall yield. The regioisomeric enol silyl ether (11), also added within 1 hr at 0° to 2, affording the methyl octalone (13)¹⁷ in 58% yield, after cyclization of 12 in the presence of basic alumina.



Our experience with Fp(olefin) complexes of simple monosubstituted olefins suggests that similar cationic complexes of other vinyl ketones should prove as accessible at 2. The use of these components as well as cationic complexes of cyclic enones and of substituted vinyl ketones as components in metal-assisted Michael reactions is being examined.

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- Prepared in 67% yield, from methyl vinyl ketone and 30% hydrogen peroxide, following the procedure used for the preparation of isophorone oxide [R. L. Wasson and H. O. House, *Org. Synth.*, **37**, 58 (1957)], except that only 20% as much sodium hydroxide solution was used and the product was extracted with $CHCl_3$ rather than ether.
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- Obtained as a mixture of $\Delta^{1,9}$ and $\Delta^{9,10}$ isomers, λ_{max}^{EtOH} 239 nm (lit.¹⁰ 239 nm), 2,4-dinitrophenylhydrazone mp 165–167° (lit.¹⁰ mp 168–170°).
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- At least three and possibly all four stereoisomers of 6 are formed, as is indicated by the presence of three cyclopentadienyl proton signals ($CDCl_3$) at τ 5.15, 5.19, and 5.23 in a ratio of 1:1:2.
- This material crystallizes on standing to give colorless needles, mp 33.5–34.5°. A 2,4-dinitrophenylhydrazone had mp 181–183 (lit.¹³ mp 188–189°).
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Department of Chemistry
Brandeis University
Waltham, Massachusetts 02154

A. Rosan
M. Rosenblum*

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