if 1,1,3,3-tetramethylguanidine (TMG) was employed as the catalyst.[11] The yield of stereoisomeric bridged products was >90%. Elimination of the hydroxyl group could be effected in reasonable yield by refluxing the derived mesylate in acetic acid with sodium acetate for 1 day.[12] Olefin **8** was isolated in ~50% yield in addition to some of the unreacted mesylate possessing equatorial methyl and mesylate groups.

A Wittig reaction with ethylidenetriphenylphosphorane proceeded readily to afford the trisubstituted olefin **9** of predominantly *Z* stereochemistry, a stereochemical result reminiscent of that found for α-oxygenated cyclohexanones.[13] The *Z*/*E* mixture was isomerized to a mixture **10** comprised predominantly of the *E* olefin (90:10 ratio) by heating with thiophenol and AIBN.[14] Interestingly, hydrolysis of the *E*/*Z* mixture of esters could be carried out to provide solely the acid of *E* stereochemistry in addition to the unreacted, more sterically encumbered ester of *Z* olefin stereochemistry.

The acid was treated sequentially with thionyl chloride, sodium azide, and methanol to provide the urethane **11** through the Curtius rearrangement.[15] Lastly, trimethylsilyl iodide was employed to effect both N- and O-deprotection.[16] Huperzine A, isolated in racemic form, was identical with the natural material by 300 MHz NMR, IR, and mass spectral analysis.[17,18] Furthermore, racemic huperzine A was found to be nearly equipotent to natural huperzine A in its inhibition of rat brain acetylcholinesterase.[19]

In summary, the synthesis developed for this important natural product is relatively efficient, an accomplishment dependent upon the remarkable ability of TMG to catalyze the tandem Michael/aldol sequence. Current efforts are aimed at improving upon the biological profile of this nootropic agent through computer aided structural modification of the huperzine A molecule. Efforts to identify more effective anticholinesterase-based therapies for the palliative treatment of Alzheimer's dementia lie at the heart of these efforts.

Acknowledgment. We are indebted to Professor J.-S. Liu of the Shanghai Institute of Materia Medica for a sample of natural huperzine A. We thank the National Institute on Aging (Grant No. IR01AG07591) for their generous support of our program. Y. Xia thanks the University of Pittsburgh for an Andrew Mellon Predoctoral Fellowship (1986-1988).

Supplementary Material Available: R_f, IR, NMR, and mass spectral data for compounds **2-11** and huperzine A (5 pages). Ordering information is given on any current masthead page.

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(17) Satisfactory spectroscopic data (including ^{1}H NMR, IR, high resolution MS, and/or ^{13}C NMR) were obtained for all intermediates.

(18) Dr. D. W. Armstrong of the University of Missouri-Rolla has found that a cyclodextrin-bonded phase column can be used to separate racemic huperzine A into its enantiomers on an analytical scale. We thank him and H. L. Jin for carrying out these studies. Efforts to resolve huperzine A by classical methods of diastereomeric salt formation have so far proven unsuccessful.

(19) The cholinesterase studies were conducted by Dr. Israel Hanin of Loyola University Stritch School of Medicine on a subcontract from NIA Grant No. 1R01AG07591. Huperzine A has also been found to have an action at the NMDA receptor complex by Dr. German Barrionuevo of the Behavioral Neuroscience Department of the University of Pittsburgh. A full report on the biological activity of huperzine A and its analogues will be published separately.

Reactions of the (η^3-Allyl)iron Tricarbonyl Anion with Carbon Electrophiles

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Numerous synthetically useful carbon-carbon bond-forming reactions are based on the fact that unsaturated hydrocarbon ligands bound to neutral or cationic metal carbonyl moieties are activated toward addition of nucleophiles.[1] Recently, several reports have described the complementary approach: activation of unsaturated hydrocarbons toward electrophilic attack by complexation with anionic metal carbonyl fragments. Examples of such anionic complexes which form carbon-carbon bonds upon reaction with carbon electrophiles include diene-$Mn(CO)_3^-$,[2] cyclohexadienyl-$Cr(CO)_3^-$,[3] cycloheptadienyl-$Fe(CO)_2^-$,[4] (arene)$Mn(CO)_2^-$,[5] $Cr(CO)_2(arene)^{2-}$,[6] and η^4-$C_8H_8Mn(CO)_3^-$.[2e,f] Attack of the electrophile is usually endo[2-5] suggesting the intermediacy of metal alkyl complexes which have been observed in certain cases.[5] Acyl products are isolated in some systems indicating CO insertion prior to metal-to-ligand migration.[3-5] We report here a synthetic and mechanistic study of the reaction of the simple anionic allyl complex, η^3-$C_3H_5Fe(CO)_3^-$, **1**, with alkyl halides which leads to α,β- or β,γ-unsaturated ketones.

Treatment of η^3-$C_3H_5Fe(CO)_3^-Na^+$ (**1**)[7] with alkyl halides in THF (0 °C, 10-20 min) followed by addition PPh_3 (2 equiv, 25 °C, 2-6 h) gives α,β-unsaturated ketone complexes, (η^4-enone)-$Fe(CO)_2(PPh_3)$, **2** (see Scheme I).[8] Results using several alkyl halides are summarized in Table I. The complexes obtained with PPh_3 are exclusively the trans isomers (≥95%); yields are good for both primary and secondary halides.

Substantial evidence has been obtained for the reaction pathway shown in Scheme I. Thermally unstable allyliron tricarbonyl alkyl complexes **3a**,**b** have been obtained and spectroscopically char-

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(7) A procedure for generation of **1** was described by Gubin and Denisovich (Gubin, S. P.; Denisovich, L. A. *J. Organomet. Chem.* **1968**, *15*, 471). We have used a modified procedure which involves use of a larger excess (10 equiv) of sodium-mercury amalgam (2.5%) and gives better yields. In addition, the PPN^+ salt of **1** can be prepared by addition of PPNCl to the Na salt of **1**, which was purified by several recrystallizations using THF/hexane. The PPN^+ salt is unstable in the air but can be stored under nitrogen at -10 °C for several days.

(8) All new compounds were characterized by ^{1}H and ^{13}C NMR and IR spectroscopy and combustion analysis. Details are given in Supplementary Material. Some spectropic data for selected compounds are as follows: η^4-[CH_3CH=$CHCOCH_3$]$Fe(CO)_2PPh_3$, **2a**; IR ν_{max} (THF) 1990, 1930, 1835, 1475, 1435 cm^{-1}; ^{1}H NMR (C_6D_6, δ) 7.78-7.65 (m, 5 H, Ph), 7.10-6.95 (m, 10 H, 2 Ph), 4.82 (dd, J_{H-P} = 2.3 Hz, J = 8.2 Hz, 1 H, =C*H*CO), 2.10 (d, J_{H-P} = 2.5 Hz, 3 H, $COCH_3$), 1.62-1.50 (m, 1 H, CH_3CH=), 1.10 (dd, J = 1.8, 6.4 Hz, 3 H, CH_3CH=); ^{13}C NMR (C_6D_6, δ, decoupled) 17.1 (CH_3CH=), 21.1 ($COCH_3$), 55.2 (CH_3CH=), 84.2 (=*C*HCO). Anal. Calcd for $C_{25}H_{23}O_3FeP$: C, 65.52; H, 5.06. Found: C, 65.59; H, 5.37. η^4-[CH_3CH=$CHCOCH_2Ph$]$Fe(CO)_2PPh_3$, **2b**: IR ν_{max} (THF) 1990, 1925, 1470, 1430 cm^{-1}; ^{1}H NMR (C_6D_6, δ) 7.78-7.68 (m, 5 H, Ph), 7.11-6.98 (m, 15 H, 3Ph), 4.95 (dd, J_{H-P} = 2.0 Hz, J = 8.4 Hz, 1 H, =C*H*CO), 4.04, 3.69 (ABq, J_{H-P} = 1.7 Hz, J = 14.8 Hz, 2 H, CH_2Ph), 1.52 (dq, J = 2.0, 7.3 Hz, 1 H, CH_3CH=), 0.99 (dd, J = 0.6, 7.3 Hz, 3 H, CH_3CH=); ^{13}C NMR ($CDCl_3$, δ, decoupled) 17.6 (CH_3CH=), 42.4 ($COCH_2Ph$), 56.5 (CH_3CH=), 85.0(=*C*HCO). Anal. Calcd for $C_{31}H_{27}O_3FeP$: C, 69.67; H, 5.09. Found: C, 69.80; H, 5.12.

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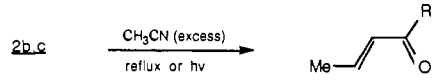
Table I

entry	RX	product (R =)	yield (%)
a	MeI	Me **2a**	74,[a] 79[b]
b	$PhCH_2Br$	$PhCH_2$ **2b**	87,[a] 93[b]
c	$Me(CH_2)_3I$	$Me(CH_2)_2CH_2$ **2c**	78[a]
d	Me_2CHBr	Me_2CH **2d**	73[a]
e	$CH_2{=}CHCH_2Br$	$CH_2{=}CHCH_2$ **2e**	61[c]

[a] Yields are based on the starting $C_3H_5Fe(CO)_3I$, **1**, generated in situ as sodium salt. [b] Yields based on reaction with pure isolated $C_3H_5Fe(CO)_3^-PPN^+$. [c] $(\pi\text{-}C_3H_5)_2Fe(CO)_2$ is also obtained as reported previously.[9]

acterized[10] at low temperature (−40 °C) by reaction of **1** with CH_3I and $PhCH_2Br$ in the absence of PPh_3. Treatment of **3a,b** with PPh_3 at −78 °C results in immediate formation of acyl complexes **4a,b** ($t_{1/2}$ < 10 min, −78 °C) which were characterized by ^1H NMR spectroscopy.[11] In a first-order process, complexes **4a,b** convert to **2a,b** via an acyl migration reaction. Rates measured by ^1H NMR were $k_{4a\rightarrow 2a} = 5.1 \times 10^{-2}\ s^{-1}$, 21 °C, $\Delta G^{\ddagger} = 18.9$ kcal/mol for CH_3CO migration and $k_{4b\rightarrow 2b} = 6.1 \times 10^{-2}\ s^{-1}$, 21 °C, $\Delta G^{\ddagger} = 18.8$ kcal/mol for $PhCH_2CO$ migration. No intermediates (i.e., neither **5** nor π-allylhydride species) were detected by ^1H NMR in the conversion of **4a,b** to **2a,b**.

Free α,β-unsaturated ketones may be readily obtained from **2a–e**. Refluxing enone complexes **2b,c** in CH_3CN (2–6 h) gives metal-free enone compounds **6b,c** in good yields (70–77%). Alternatively irradiation (GE sunlamp) of enone complexes in CH_3CN under mild conditions (0 °C, 2–6 h) leads to **6b,c** in somewhat better yields (80–85%).

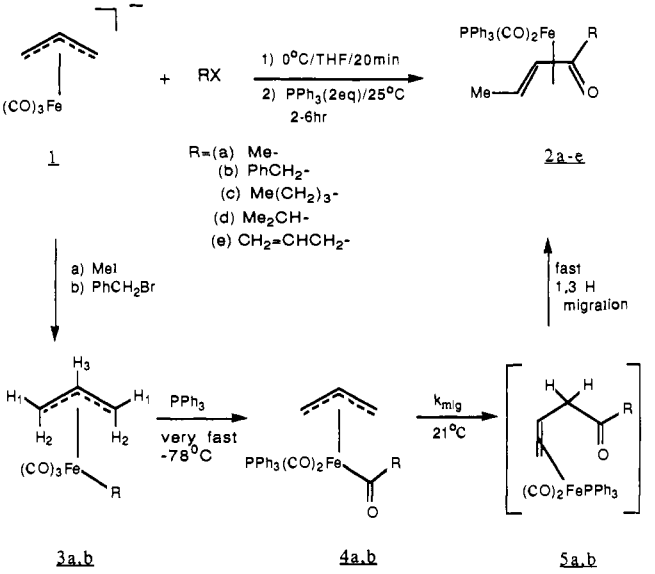


6b,c

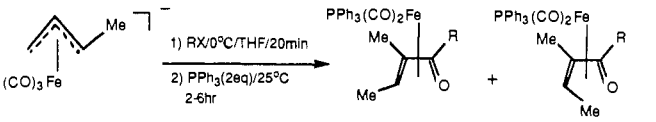
On the basis of the mechanism in Scheme I, if the 16-electron olefin complexes, **5a–e**, could be intercepted and displaced prior to its isomerization to **2a–e**, then a reaction sequence would be available to prepare not only α,β-enones but also the less readily available unconjugated β,γ-isomers. This proved possible using the following procedure: After alkylation of anion **1** (R = CH_2Ph, $-CHMe_2$, 0 °C, 30 min), the reaction mixture was quenched with excess CH_3CN. Irradiation of this mixture at 0 °C for 2–6 h gave the β,γ-unsaturated ketones in good yields (75–80%). The products were contaminated by small amounts of α,β-unsaturated ketone (<10%).

Preliminary results using a substituted allyl system indicate that substantial regioselectivity in the migration reaction is observed. For example, in situ generation of η^3-$(CH_2{\cdots}CH{\cdots}CHCH_3)Fe(CO)_3^-Na^+$ from the (η^3-methallyl)iron tricarbonyl iodide followed by treatment with CH_3I or $PhCH_2Br$ and then with PPh_3 yields complexes **8** and **9** in an ca. 2:1 ratio (75–81% yield).[12] Isolation of complexes **8** and **9** indicates that acyl migration occurs

Scheme I



regioselectively to the more hindered methyl-substituted carbon of the π-allyl moiety.



Acknowledgment is made to the National Institutes of Health (GM 28938) for support of this research.

Supplementary Material Available: ^1H, ^{13}C NMR, IR, and microanalytical data for **2c**, **2d**, **2e**, **6b**, **8a**, **9a**, **8b**, **9b**, η^4-$[CH_2{=}C(CH_2CH_3)COCH_3]Fe(CO)_2PPh_3$, η^4-$[CH_2{=}C(CH_2CH_3)COCH_2Ph]Fe(CO)_2PPh_3$, and $CH_3CH{=}CHCOCH_2CH_2CH_2CH_3$ and ^1H, NMR, and high resolution mass spectroscopic data for $CH_3CH{=}CHCOCH_2Ph$ and $CH_2{=}CHCH_2COCH_2Ph$ (4 pages). Ordering information is given on any current masthead page.

Metallabenzene: Synthesis, Structure, and Spectroscopy of a 1-Irida-3,5-dimethylbenzene Complex

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Replacement of a methine group in benzene with a nitrogen, phosphorus,[1] or arsenic[1] atom leads to stable heterocyclic compounds in which aromaticity is retained. However, little is known about analogous replacements involving transition metals and their associated ligands. Particularly intriguing is the question of whether such "metallabenzenes" would exhibit aromatic properties.[2]

To date, only one family of stable metallabenzenes has been reported.[3,4] These species, obtained via a cyclization reaction involving acetylene and an osmium–thiocarbonyl complex, were reported by Roper in 1982.[3] The X-ray crystal structure of Roper's parent compound, $[Os{\cdots}C(S){\cdots}CH{\cdots}CH{\cdots}CH{\cdots}CH]$-

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(10) η^3-$C_3H_5Fe(CO)_3(CH_3)$, **3a**: Obtained as a mixture of two isomers (15:1 at −58 °C); IR ν_{max} (THF) 2050, 1985 cm^{-1}; ^1H NMR ($CDCl_3$, −58 °C, δ) major isomer 3.92 (m, 1 H, 3-H), 3.04 (d, J = 7.5 Hz, 2 H, 1-H), 2.18 (d, J = 12.2 Hz, 2 H, 2-H), −0.51 (s, 3 H, CH_3); minor isomer, 4.20 (m, 1 H, 3-H), 3.52 (d, J = 7.6 Hz, 2 H, 1-H), 1.74 (d, J = 12.5 Hz, 2 H, 2-H), −0.42 (s, 3 H, CH_3). η^3-$C_3H_5Fe(CO)_3(CH_2Ph)$, **3b**: obtained as a mixture of two isomers (5:1 at −13 °C); IR ν_{max} (THF) 2057, 1994, 1711 cm^{-1}; ^1H NMR (CD_2Cl_2, −13 °C, δ) major isomer 7.18–6.92 (m, 5 H, Ph), 3.92 (m, 1 H, 3-H), 3.16 (d, J = 7.5 Hz, 2 H, 1-H), 2.36 (d, J = 12.4 Hz, 2 H, 2-H), 1.80 (s, 2 H, CH_2Ph); minor isomer, 7.18–6.92 (m, 5 H, Ph), 4.21 (m, 1 H, 3-H), 3.58 (d, J = 7.5 Hz, 2 H, 1-H), 1.90 (d, J = 12.5 Hz, 2 H, 2-H), 1.80 (s, 2 H, CH_2Ph).

(11) η^3-$C_3H_5Fe(CO)_3(COCH_3)$, **4a**: IR ν_{max} (CH_2Cl_2) 1991, 1932, 1639 cm^{-1}; ^1H NMR (CD_2Cl_2, −40 °C, δ) 7.56–7.24 (m, 15 H, 3Ph), 4.20 (m, 1 H, 3-H), 2.92 (s, 3 H, $COCH_3$), 2.86 (d, J = 6.9 Hz, 2 H, 1-H), 1.92 (dd, $J_{H\text{-}P}$ = 3.7 Hz, J = 12.2 Hz, 2 H, 2-H); η^3-$C_3H_5Fe(CO)_3(COCH_2Ph)$, **4b**: IR ν_{max} (CH_2Cl_2) 1990, 1930, 1630 cm^{-1}; ^1H NMR (CD_2Cl_2, −45 °C, δ) 7.80–7.12 (m, 20 H, 4Ph), 4.81 (s, 2 H, CH_2Ph), 4.38–4.04 (m, 1 H, 3-H), 2.98 (d, J = 7.5 Hz, 2 H, 1-H), 2.04 (dd, $J_{H\text{-}P}$ = 3.5 Hz, J = 12.3 Hz, 2 H, 2-H).

(12) A minor product is η^4-$[CH{=}C(CH_2CH_3)COR]Fe(CO)_2PPh_3$.

(1) Ashe, III, A. J. *J. Am. Chem. Soc.* **1971**, *93*, 3293.

(2) For a theoretical discussion of delocalization in metallacycles, see: Thorn, D. L.; Hoffmann, R. *Nouv. J. Chem.* **1979**, *3*, 39.

(3) Elliot, G. P.; Roper, W. R.; Waters, J. M. *J. Chem. Soc., Chem. Commun.* **1982**, 811.

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