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(11) Heptanoic acid was used in this study instead of acetic acid for two reasons: (a) it absorbs much less strongly in the 1900–2200-cm^{-1} region than acetic acid and (b) analytical proof of acetic acid formation becomes simpler.

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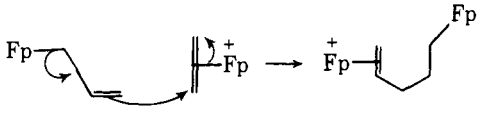
Metal Assisted Carbon–Carbon Bond Formation. Synthesis of Hydroazulene Complexes

Sir:

Synthetic methods for the construction of hydroazulenes, especially those which provide for the stereospecific introduction of groups into the five- and seven-membered rings, are of particular importance for the synthesis of the large number of sesquiterpenes with this skeleton.[1] Of the several approaches at present available, few provide direct access to substituted hydroazulenes and convenient avenues for their subsequent elaboration.[2]

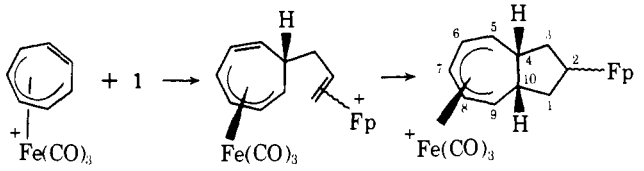
We report here a novel and efficient synthesis of hydroazulene-iron complexes, which either directly or in the course of demetalation provides ready access to hydroazulenes of diverse substitutional pattern and type.

We recently described a new carbon–carbon bond synthesis based on the condensation of metal activated olefin components.[3] This is exemplified in terms of the simplest donor (**1**) and acceptor components by eq 1. (The symbol Fp is used to designate the radical η^5-$C_5H_5Fe(CO)_2$.)



1 2 3

We now find that tropyliumiron tricarbonyl (**4**)[4] reacts rapidly with **1**, in two successive condensations, to give the dinuclear hydroazulene complex (**6**)[5] as a mixture of C_2-

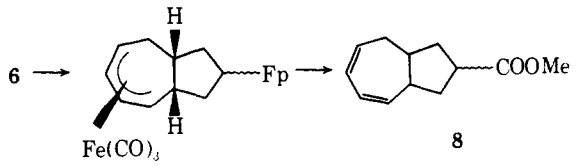


4 5 6

epimers in 75% yield: NMR (CD_3NO_2) τ 2.61 (t, 1, H_7), 4.1 (m, 2, $H_{6,8}$), 5.0 (br m, 2, $H_{5,9}$), 5.15, 5.18 (two s, 5, Cp), 6.3 (br m, 2, $H_{4,10}$), 7–8.5 (br m, 5, $H_{1,2,3}$).[6] The reaction, in 1,2-dichloroethane solution, is complete within 3 h at 55 °C. At lower temperatures the formation of the intermediate **5** may be detected in the NMR spectrum by the appearance of two resonances at τ 4.35 and 4.36, characteristic of the cyclopentadienyl protons in the Fp(olefin) cation.

The structure of the condensation product (**6**) was confirmed by reduction with $NaBH_4$ in aqueous acetonitrile to **7** (78%), oxidation with $Ce(NH_4)_2(NO_3)_6$ in methanol tetrahydrofuran to the unsaturated ester **8** (61%),[7] and dehydrogenation by brief heating in xylene in the presence of dichlorodicyanoquinone to methyl azulene-2-carboxylate (**9**), mp 107–109 (lit.[8] mp 108–109).

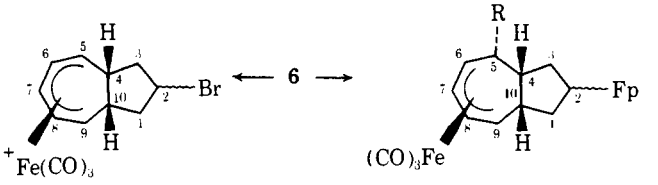
The stereochemistry assigned to **6** is based on ample precedent for initial alkylation of **4** trans to the $Fe(CO)_3$ group[9] followed by preferential cis closure of the C_5-ring.[10]



7 8

The potential synthetic utility of the new condensation reaction is illustrated by alternative transformations of **6** which allow for the introduction of diverse substituents at C_5 and of halogen at C_2. Furthermore, the use of donor components other than **1** provides a means for the introduction of substituents at C_1 and of unsaturation into the cyclopentane ring.

Thus, **6** reacts with lithium dimethylmalonate to give **10**, mp 129–133 °C (58%): ir 2050, 2000, 1970, 1937, 1765, 1740; NMR (CS_2) τ 4.73 (m, 2, $H_{7,8}$), 5.29 (s, 5, Cp), 6.34, 6.36, 6.41 (s, 3, OMe), 6.85 (m, 2, H_5, $CH(COOMe)_2$), 7.5 (m, 4, $H_{6,9,4,10}$), 8.0–8.8 (m, 5, $H_{1,2,3}$).



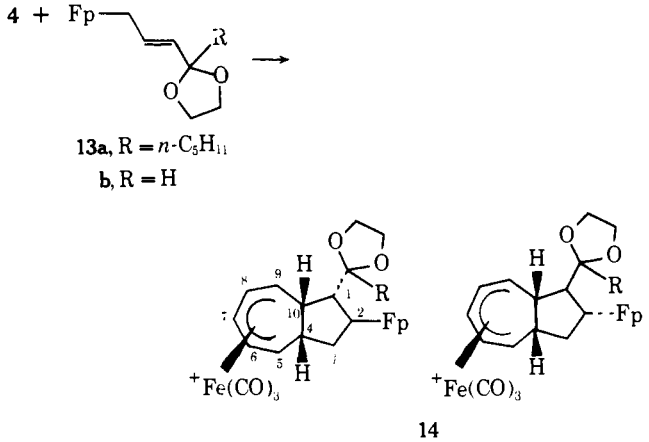
12

10, R = $CH(COOMe)_2$
11, R = OMe

The complex cation **6** also reacts with methanol in the presence of K_2CO_3 to give **11**, >150 °C dec (41%); NMR (CS_2) τ 4.68 (m, 2, $C_{7,8}$), 5.38, 5.39 (2s, 5, Cp), 6.13 (dt, 1, J = 5.5, 2 Hz, H_5), 6.74, 6.79 (s, 3, OMe), 7.4–8.8 (br m, 8, $H_{1,2,3,4,6,9,10}$).

Oxidation demetalation of **6**, employing bromine in methylene chloride, is complete within 5 min at −78 °C, and leads to the selective replacement of the Fp group by halogen, yielding **12** (62%): NMR (CD_3NO_2) τ 2.50 (m, 1, H_7), 3.88 (m, 2, $H_{6,8}$), 4.98 (m, 2, $H_{5,9}$), 6.0–6.3 (m, 3, $H_{2,4,10}$), 7.2–8.8 (m, 4, $H_{1,3}$).

With 1-substituted (η^1-allyl)Fp complexes, which are readily available from the parent complex,[11] reaction with **4** affords 1-substituted hydroazulene complexes. The reaction of **13a** in 1,2-dichloroethane solution is essentially complete in 10 min at room temperature and yields **14a** (41%) as a mixture of trans 1,2-disubstituted complexes;[12] NMR (CD_3NO_2) τ 2.50 (t, 1, J = 7 Hz, H_7), 3.97 (dd, 2, J = 9,7 Hz, $H_{6,8}$), 4.9 (m, 2, $H_{5,9}$), 5.18 (s, 5, Cp), 5.96 (m, 4, OCH_2CH_2O), 5.9–6.8 (m, 2, $H_{4,10}$) 7.7–9.0 (m, 15, $H_{1,2,3}$ + C_5H_{11}). The reaction of **13b** with **4** is equally facile, affording **14b** in 73% yield: NMR (CD_3NO_2) τ 2.6 (m, 1,

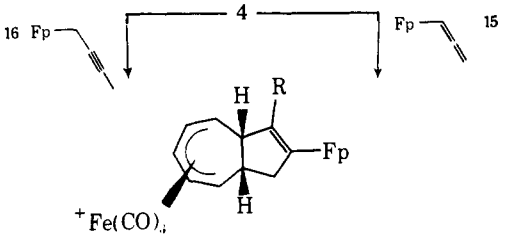


13a, R = n-C_5H_{11}
b, R = H

14

H_7), 4.05 (m, 2, $H_{6,8}$), 5.0 (m, 3, $H_{5,9}$ OCHO) 5.12, 5.14 (2 s, 5, Cp) 6.0 (m, 4, OCH_2CH_2O), 6.4 (m, 2, $H_{4,10}$), 7.5–8.7 (m, 4, $H_{1,2,3}$).

The use of (η^1-allenyl)Fp or (η^1-propargyl)Fp complexes as partners in condensations with **4** is illustrated by the conversion of **15** and **16** to the hydroazulene complexes **17a** (55%) and **17b** (78%), respectively, by treatment with **4** in nitromethane solution at room temperature for 15 min.



17a, R = H
b. R = Me

Further elaborations of these reactions are being examined.

Acknowledgment. This work was supported by grants from the National Institutes of Health (GM-16395) and by the National Science Foundation (GP-27991) which are gratefully acknowledged.

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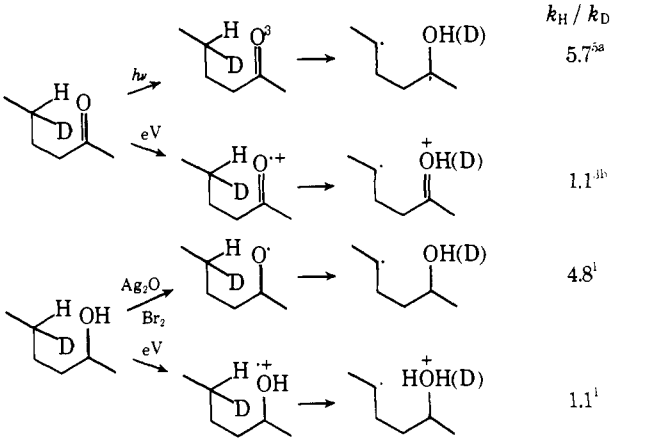
The Hofmann–Loeffler–Freytag Bridge between Mass Spectrometry and Free Radical Chemistry

Sir:

The regiospecific γ-hydrogen transfers observed in alkoxy radicals and triplet ketones are analogues on many levels to the formally similar hydrogen transfers observed in the molecular cation radicals of alcohols and ketones (McLafferty rearrangement), respectively.[1,2] Nevertheless, the isotope effects for the reactions occurring in the mass spectrometer are nearly unity[3,4] while the neutral analogues exhibit high discrimination against transfer of deuterium[5,6] (Scheme I).

Scheme I



Established theory[7] offers a ready explanation for the differing isotope effects in these otherwise similar intramolecular γ-hydrogen transfers (Scheme I). Reactions involving breaking of carbon hydrogen bonds have been observed to occur with a wide range of hydrogen deuterium isotope effects. These isotope effects have been directly related to the energy of activation for the process and through transition state theory to the extent of carbon hydrogen bond breaking and bond making in the activated complex. Thus, bromine atom and chlorine atom, in abstraction of benzylic hydrogen vs. deuterium from toluene, exhibit, under identical conditions, isotope effects of 4.6 and 1.3, respectively.[8] There is a great deal of support for these ideas.[9]

For the reactions exhibited in Scheme I the electron denying character of *both* sources of reactivity for the radical cations may reasonably be hypothesized to lead to abstraction of carbon bound hydrogen with lowered energy of activation compared to the related neutrals. As seen above, this would lead to decreased isotope effects[7] in line with the observations (Scheme I).

If this view were correct the decreased isotope effects (Scheme I) should be observed whatever the source of the cation radicals. To test this hypothesis we have determined the isotope effect for the γ-hydrogen transfer to amminium cation radical in the Hofmann–Loeffler–Freytag reaction[10] of deuterated *N*-chloro-2-hexylamine (**1**). Furthermore we have taken advantage of the chirality of **1** to simultaneously determine the stereoselectivity for the γ-hydrogen transfer. The compounds studied and the deuterium incorporation results are shown in Scheme II.

The d_1/d_0 ratio of the pyrrolidine obtained from **1** is equal to the isotope effect (k_H/k_D). The average of the d_1/d_0 ratios for the pyrrolidines from **1A** and **1B**, prepared independently, is within experimental error of the value obtained for **1** as it should be. The values for d_1/d_0 from **1A** and **1B** may be treated by Curtin's analysis[15] to yield the stereoselectivity for abstraction of the C-5 diastereotopic hydrogens[16] from (*R*)-*N*-chloro-2-hexylamine. These results of these calculations as well as comparable data on other γ-hydrogen abstracting reactions are presented in Table I.

The common regioselectivity for γ-hydrogen for all the intramolecular rearrangements shown (Table I) as well as the preferential abstraction of H_a over H_b for the *R* configuration at the chiral center in all cases is very strong evi-