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STEREOCONTROLLED ACYLATION OF (η^4-CYCLOHEPTATRIENE)IRON TRICARBONYL

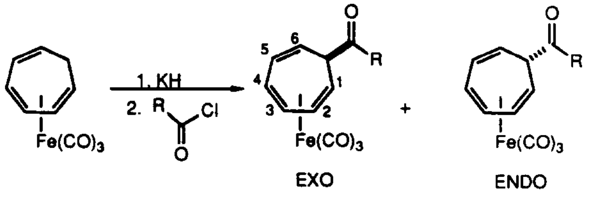
Gregory M. Williams* and Duane E. Rudisill

Department of Chemistry, University of California, Irvine,
Irvine, California 92717 USA

Abstract: The anion derived by deprotonating (cycloheptatriene)Fe(CO)$_3$ reacts with acid chlorides to give exo C-7 substitution. The acyl group is^3 readily isomerized to C-5 on treatment with base. The C-7 acylated products can be deprotonated; the resulting anions react at oxygen with acyl chlorides and Me$_3$SiCl, and at carbon with MeI.

Deprotonation of (cycloheptatriene)Fe(CO)$_3$ provides a species which can be considered as a tropylium anion stabilized by a metal fragment.[1,2] Although this organometallic anion has been known for several years, its development as a reagent for carbon-carbon bond-forming reactions is limited to a brief account of its reaction with methyl chloroformate.[2] We felt that [(C$_7$H$_7$)Fe(CO)$_3$]$^{-1}$ would be an excellent substrate for stereocontrolled elaboration of a seven-membered ring. As our initial effort in this area we have examined the reaction between the anion and several acid chlorides. We find that acylation occurs at C-7 with very high selectivity for the exo face of the coordinated ring.

The addition of a THF solution of (C$_7$H$_8$)Fe(CO)$_3$ to a suspension of KH in THF results in the formation of the bright red (C$_7$H$_7$)Fe(CO)$_3$ anion (2 hrs; 25°C). Filtration through Celite under an inert atmosphere removes excess KH. The anion is added dropwise to a solution of the acid chloride (2 equiv; 35 min; 25°C). The products are isolated by flash-chromatography on Florisil (petroleum ether:ether). The reaction is illustrated in eq 1 and the results are summarized in the Table.



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The ^{1}H-NMR spectra of the acylated products all show the characteristic signals of an η^4-cycloheptatriene.[4] One-proton multiplets at ca. δ 5.1 and 6.0 can be assigned to the protons of the non-complexed double bond (H-6 and H-5 respectively). Thus acylation has occurred at C-7 of the coordinated ring. The stereochemistry at C-7 could not be determined from the NMR spectra. A thorough analysis of both isomers of the acetyl derivative (entry 1) revealed that the coupling constants of the ring hydrogens are too similar to allow assignment of stereochemistry. However, an X-ray crystal structure of the benzoyl complex (entry 6) shows that acylation takes place on the exo face

Table: A Summary of Results for the Reaction Illustrated in Eq. 1

Entry	R	exo/endo[b]	% yield[c]
1	CH_3	35	75
2	OCH_3	55	60
3	i-Pr	50	40
4	t-Bu	>70	90
5	$CH_2CH_2CH_2Cl$	50	85
6	C_6H_5	>70	85

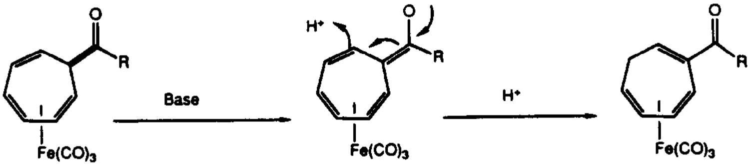
a) All new compounds have been characterized by full spectral data and elemental analysis and/or high resolution mass spectroscopy.4

b) Ratios determined by integration of H-NMR spectra of crude reaction mixtures.

c) Yields are reported for isolated purified products.

of the coordinated ring.5 The minor isomer (endo) probably arises from direct attack at the metal center. Ambident nuclophilicity for this organoiron anion has been noted previously.[1c,f]

The (exo-7-acyl-C_7H_7)$Fe(CO)_3$ complexes are isomerized readily by excess base. Thus, treatment of the benzoyl derivative (entry 6) with KH followed by a rapid proton quench provided the C-5 conjugated material in 65-80% yield, (eq 2). The substitution pattern was evident from the ^{1}H-NMR which showed no signal in the vicinity of δ 6.0. Stirring in the presence of sodium ethoxide



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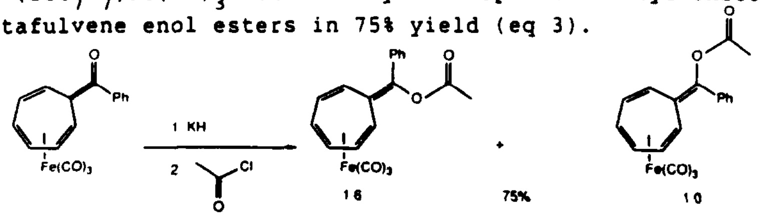
in ethanol for several hours results in a number of products (as detected by thin layer chromatography). The ^{1}H-NMR spectra of crude reaction mixtures suggest that the acyl group is distributed to a number of positions around the ring. We have made no effort to analyze these mixtures except to note that the C-6 substituted product can be obtained in 30% yield (R = CH_3). The C-6 substituted isomer was reported to be the major isolated product from reaction of the iron anion with methylchloroformate.[2]

Electrophiles that are less reactive than acid chlorides fail to react with $(C_7H_7)Fe(CO)_3^-$. Neither n-BuOTs nor acetaldehyde show a reaction with the anion. However, we have recently found that a BF_3-acetaldehyde complex reacts with $(C_7H_7)Fe(CO)_3^-$ to provide the expected alcohol in 70% yield.[6] The scope of Lewis acid activation is currently under examination.

The C-7 proton on the 7-exo-acylated product is quite acidic and is removed readily even though it is on the endo face of the coordinated ring. Deprotonation of $(BzC_7H_7)Fe(CO)_3$ followed by work-up with acetyl chloride gave a mixture of heptafulvene enol esters in 75% yield (eq 3).



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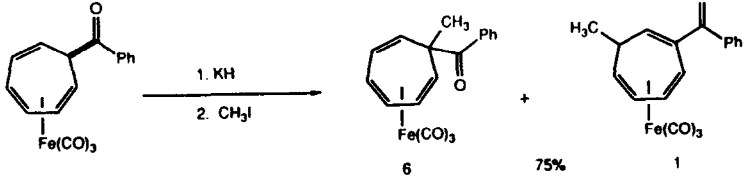
An NOE experiment established the predominance of the Z isomer. Thus irradiation of H-6 in the major isomer gave an enhancement in both H-5 and the ortho protons of the phenyl ring; similar irradiation of the minor isomer gave an enhancement only in H-5. The $(Bz\text{-}C_7H_6)Fe(CO)_3$ anion also reacted readily with benzoyl chloride (1.6:1; 90%), Me_3SiCl (3:1; 80%) and methyl triflate (2.8:1; 30%). In each of the four reactions, ^1H-NMR signals for H-5 and H-6 of the major isomer appear upfield of the signals for the minor isomer. Based on these data we suggest that the Z isomer predominates in all of these cases.

Methyl iodide C-alkylates $(Bz\text{-}C_7H_6)Fe(CO)_3$ anion in 75% yield.[7] Reactivity at the alpha carbon of the dienolate predominates ($\alpha/\gamma = 6:1$). The stereochemistry of methylation (exo vs. endo) could not be determined from the NMR



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spectra; a crystallographic analysis will be conducted. Allyl bromide reacts with the anion in a similar manner ($\alpha/\gamma = 6:1$, 75%). Reaction with n-PrI requires refluxing THF and gives a mixture of O- and α-alkylated products (α/O = 3.7:1; 61%). No γ-alkylation was detected.

Although limited in scope at present, (cycloheptatriene)$Fe(CO)_3$ and its substituted derivatives show significant promise for highly stereoselective carbon-carbon bond-forming reactions. Further studies of (cycloheptatriene)-$Fe(CO)_3$ as a reagent for organic synthesis are in progress.

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4. Spectroscopic properties for all compounds in the Table are quite similar. The benzoyl derivative, entry 6, is representative: ^{1}H-NMR (250 MHz, $CDCl_3$): δ 7.96 (m, 2H, H_0); 7.55 (m, 3H, $H_{m,p}$); 6.03 (dtd, 1H, H-5; J_{45}=8.6 Hz, J_{56}=10.65, J_{57}=1.85); 5.57 (dddd, 1H, H-3; J_{13}=1.41, J_{23} = 4.79, J_{34}=7.67); 5.47 (dddd, 1H, H-2); 5.27 (dddd, 1H, H-6; J_{46}=1.38; J_{67}=4.57); 4.55 (t of d, 1H, H-7; J_{17}=4.56); 3.12 (m, 2H, H-1,4). ^{13}C-NMR (62.89 MHz, $CDCl_3$): δ 211.1 (Fe-CO); 200.0 (C(O)Ph); 136.8, 133.9, 129.5, 129.2 (Ph); 132.4, 123.9 (C-5,6); 95.7, 89.9 (C-2,3); 58.5, 55.8 (C-1,4); 52.9 (C-7). Elemental Analysis: Calc. C: 60.75, H: 3.60; Found C: 60.90, H: 3.55. Spectra of all compounds will be reported in a full paper.

5. Monoclinic crystals; space group $P2_1/C$; 3119 reflections through $0^\circ < 2\Theta < 50^\circ$; R_w = 0.051. Structural details will be presented in a full paper.

6. Williams, G.M.; McMillan, J.W. unpublished data. ^{1}H NMR (250 MHz, $CDCl_3$): δ 5.95 (m, H-5); 5.52 (m, H-2); 5.40 (m, H-3); 5.18 (m, H-6); 3.90 (m, H-8); 3.14 (m, H-1); 2.96 (br t, H-1); 2.70 (m, H-7); 1.40 (br s, OH); 1.21 (2 d's, CH_3). Mixture of diastereomers. Full spectral datda, including decoupling, will be published in a full paper.

7. ^{1}H-NMR (250 MHz, C_6D_6, δ) α-product: 7.58 (m, 2H, H_0); 7.05 (m, 3H, $H_{m,p}$); 5.55 (dd, 1H, H-5); 5.44 (d of m, 1H, H-6); 4.69 (m, 2H, H-2,3); 3.83 (dt, 1H, H-1); 2.49 (t, 1H, H-4); 1.33 (s, 3H, CH_3). γ-product: 7.74 (H_o); 7.08 ($H_{m,p}$); 5.68 (H-6), 4.82, 4.55 (H-2,3); 3.89 (H-4); 2.58 (H-1); 2.24 (H-7); 0.73 (d, CH_3).

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