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MICHAEL-TYPE ADDITIONS TO α,β-ENOYLIRON(CYCLOPENTADIENYL)DICARBONYL COMPLEXES AND ITS APPLICATION TO β-LACTAM SYNTHESIS

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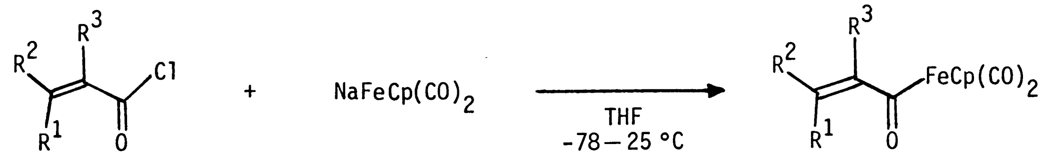
Michael-type additions of amines and thiols to α,β-enoyliron-(cyclopentadienyl)dicarbonyl complexes were carried out to give the corresponding new β-aminoalkanoyl- and β-thioalkanoyliron complexes in good to excellent yields. A β-aminoalkanoyliron complex was treated with bromine in the presence of triethylamine to give the expected β-lactam in an excellent yield.

Organometallic and organic chemistry of organo-iron complexes have brought about the development of many interesting and useful methodologies in organic synthesis.[1] Among those organo-iron complexes, [CpFe(CO)$_2$](Cp = η^5-cyclopentadienyl) and [CpFe(CO)(PPh$_3$)] complexes have recently been studied extensively as effective reagents for selective organic transformations.[2] However, little attention has been paid to Michael-type additions of nucleophiles to α,β-enoyl-iron complexes. This is mainly due to some difficulties in the preparation of the α,β-enoyliron complexes.[3] We have found that α,β-enoyl-FeCp(CO)$_2$ (1) complexes can be obtained in high yields by the reaction of NaFeCp(CO)$_2$ and α,β-enoyl chlorides followed by a flash chromatography on silica gel (Eq. 1). This improved procedure of preparation enabled us to look at the reactivity of these complexes toward nucleophiles. During our research on the Michael-type addition of nitrogen and sulfur nucleophiles to 1, Davies et al. reported[4] recently the Michael addition of *n*-butyllithium to acryloyl-FeCp(CO)(PPh$_3$) followed by methylation with methyl iodide. This prompted us to disclose our results as a communication.[5]

As for α,β-enoyl-FeCp(CO)$_2$ complexes, the procedure for the preparation of 3-methylcrotonoyl-FeCp(CO)$_2$ is typically described. [FeCp(CO)$_2$]$_2$ (1.77 g, 5 mmol) in dry THF (25 mol) was added to sodium amalgam prepared from sodium (341 mg) and mercury (34 g) at ambient temperature, and the mixture as stirred vigorously for 4 h until the color changed from reddish-brown to yellowish-brown and excess amalgam was removed. To this solution was added 3-methylcrotonoyl chloride (1.45 ml, 12.6 mmol) at -78 °C with stirring, and the reaction mixture was gradually warmed to ambient temperature and stirred for 24 h. After the solvent was evaporated, the residue was extracted with chloroform and the extract was filtered through a small pad of neutral alumina. Then, the solvent was removed and the residue was washed with pentane and submitted to a flash chromatography on silica gel to give 3-methylcrotonoyl-FeCp(CO)$_2$ (1a)(2.07 g, 79.5% yield based on [FeCp(CO)$_2$]$_2$) as yellow needles. Mp 62-63 °C.$^{6)}$

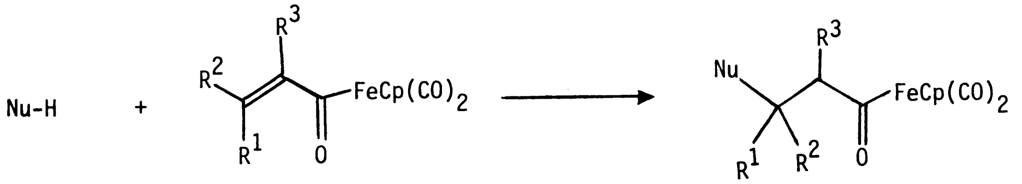


(1)

a) $R_1 = R_2 = Me, R_3 = H$, 79.5%
b) $R_1 = H, R_2 = Me, R_3 = H$, $R_1 = Me, R_2 = H, R_3 = H$ } 74.5%
c) $R_1 = R_2 = H, R_3 = Me$, 70.1%
d) $R_1 = R_2 = R_3 = H$, 72.2%

1

Michael-type additions of amines and thiols to the α,β-enoyl-FeCp(CO)$_2$ (1) complexes thus obtained, were carried out without solvent at ambient temperature to give the corresponding new β-aminoalkanoyl-FeCp(CO)$_2$ (2) and β-thioalkanoyl-FeCp(CO)$_2$ (3) complexes in good to excellent yields (Eq. 2).$^{6)}$ The use of bases such as sodium hydride, sodium hydroxide, sodium methoxide, lithium diisopropylamide and butyllithium in organic solvents to generate metalated amines decreased the yields by promoting a decomposition of 1 to [FeCp(CO)$_2$]$_2$. Additions of Lewis acids did not give good results: BF$_3$.OEt$_2$ did not show any effects and TiCl$_4$ and SnCl$_4$ did not give any of the desired products. Consequently, it turned out that the simplest procedure, i.e., a mixture of 1 and 3-5 equiv. of Nu-H was stirred without any solvent at ambient temperature for 48 h, gave the best results. Typical results are summarized in Table 1.

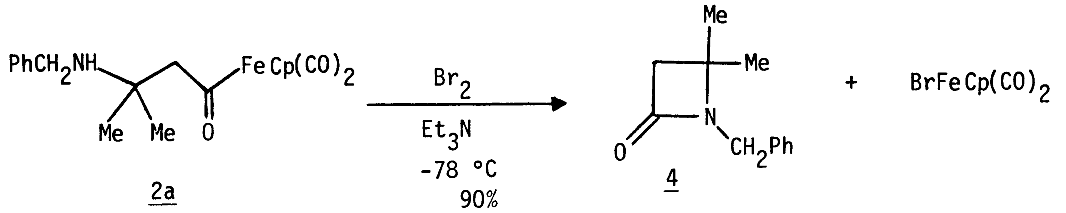


(2)

1

2: Nu = RR'N-
3: Nu = R"S-

As the primary amine adducts (2, Nu=RNH) have a similar structure to those obtained from the reaction of an iron enolate, FeCp(CO)(PPh$_3$)-C(OM)=CH$_2$ (M=Li or Et$_2$Al), with a Schiff base, reported recently by Davies et al.$^{2g)}$ and Liebskind et al.,$^{2h)}$ we carried out a β-lactam synthesis using a benzylamine adduct (2a) (Eq. 3). Thus, to a solution of (2a) ($R^1 = R^2 = Me$, $R^3 = H$, Nu = PhCH$_2$NH) in dichloromethane was added bromine(3 equiv.) at -78 °C with stirring. After 1 h, triethylamine (6 equiv.)was added to the mixture at -78 °C and the reaction mixture as gradually warmed to ambient temperature. GLC analysis showed that the desired β-lactam, 1-benzyl-4,4-dimethylazetidin-2-one (4), was formed in 90% yield, which was isolated by a column chromatography on silica gel.



2a 4

(3)

Table 2. Synthesis of New β-Aminoalkanoyl- and β-Thioalkanoyl-FeCp(CO)$_2$ Complexes

Entry	R^1	R^2	R^3	NuH	Conditions[a]		Isolated yield/%[b]	^{1}H NMR(ppm)($CDCl_3$)[c]	IR(ν/cm^{-1})[d]
					Temp/°C	Time/h			
1.	Me	Me	H	$PhCH_2NH_2$ (3 equiv.)	25	48	62 (91) *mp 68-70 °C*	1.13(s,6H)(Me) 4.83(s,5H)(Cp)	3320 (ν_{NH})[e] 2020, 1965, 1631 ($\nu_{C=O}$)
2.	Me	H	H	$PhCH_2NH_2$ (3 equiv.)	25	48	78 *oil*	1.10(d,J=5.7 Hz,3H)(Me) 4.82(s,5H)(Cp)	3320 (ν_{NH}) 2019, 1963 1645 ($\nu_{C=O}$)
3.	Me	H	H	$(CH_2)_4NH$ (3 equiv.)	25	48	51 (93) *oil*	1.06(d,J=6.2 Hz,3H)(Me) 4.85(s,5H)(Cp)	2022, 1975 1647 ($\nu_{C=O}$)
4.	Me	H	H	$O(C_2H_4)_2NH$ (3 equiv.)	25	48	57 (96) *mp 69-70 °C*	0.98(d,J=6.3 Hz,3H)(Me) 4.87(s,5H)(Cp)	2015, 1945[e] 1659 ($\nu_{C=O}$)
5.	Me	H	H	PhSH (4.5 equiv.)	25	48	95 *oil*	1.14(d,J=6.6 Hz,3H)(Me) 4.82(s,5H)(Cp)	2020, 1950 1630 ($\nu_{C=O}$)
6.	Me	H	H	$HOCH_2CH_2SH$ (3 equiv.)	25	48	66 *oil*	1.21(d,J=6.5 Hz,3H)(Me) 4.86(s,5H)(Cp)	3440 (ν_{OH}) 2015, 1950 1625 ($\nu_{C=O}$)
7.	Me	H	H	$CH_2=CHCH_2NH_2$ (5 equiv.)	25	24	89 *oil*	0.95(d,J=5.4 Hz,3H)(Me) 4.80(s,5H)(Cp)	3310 (ν_{NH}) 2020, 1955 1640 ($\nu_{C=O}$)
8.	Me	H	H	*n*-Bu-NH_2 (3.8 equiv.)	25	3	98 *oil*	0.96(d,J=5.7 Hz,3H)(Me) 4.83(s,5H)(Cp)	3315 (ν_{NH}) 2020, 1955 1640 ($\nu_{C=O}$)
9.	H	H	Me	$(CH_2)_4NH$ (3 equiv.)	25	48	50 (94) *oil*	0.98(d,J=6.9 Hz,3H)(Me) 4.89(s,5H)(Cp)	2026, 1955 1639 ($\nu_{C=O}$)
10.	H	H	Me	$O(C_2H_4)_2NH$ (3 equiv.)	25	48	75 (96) *oil*	0.94(d,J=6.9 Hz,3H)(Me) 4.90(s,5H)(Cp)	2015, 1956 1644 ($\nu_{C=O}$)
11.	H	H	Me	PhSH (4.5 equiv.)	25	48	90 *oil*	1.11(d,J=6.6 Hz,3H)(Me) 4.84(s,5H)(Cp)	2020, 1955 1630 ($\nu_{C=O}$)
12.	H	H	Me	$HOCH_2CH_2SH$ (3 equiv.)	25	48	78 *oil*	1.06(d,J=6.9 Hz,3H)(Me) 4.89(s,5H)(Cp)	3420 (ν_{OH}) 2015, 1950 1625 ($\nu_{C=O}$)

a) All reactions were run with 0.5 mmol of an α,β-enoyl-FeCp(CO)$_2$ and 1.5-2.5 mmol of an amine or a thiol at 25 °C without solvent. *b*) Values in the parentheses are the yields determined by NMR using 1,1,2,2-tetrachloroethane as the internal standard. *c*) Selected signals. *d*) Selected absorptions. Measured as neat liquid unless otherwise noted. *e*) Measured as KBr disk.

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References

1) For example, "The Organic Chemistry of Iron," ed by E.A. Koerner von Gustorf, F.-W. Grevels, and I. Fischer, Academic Press, New York (1978), Vol. 1; M. Rosenblum, Acc. Chem. Res., 7, 122 (1974); M. Rosenblum, A. Bucheister, T.C.T. Chang, M. Cohen, M. Marsi, S.B. Samuels, D. Scheck, N. Sofen, and J.C. Watkins, Pure Appl. Chem., 56, 129 (1984), and references therein.

2) For example a) M. Marsi and M. Rosenblum, J. Am. Chem. Soc., 106, 7264 (1984); b) M. Brookhart, D. Timmers, J.R. Tucker, G.D. Williams, and G.R. Husk, ibid., 105, 6721 (1983); c) N. Aktogu, H. Felkin, and S.G. Davies, J. Chem. Soc., Chem. Commun., 1984, 1303; d) S.G. Davies, I.M. Dordor, and P. Warner, ibid., 1984, 956; e) G.J. Baird, S.G. Davies, R.H. Jones, K. Prout, and P. Warner, ibid., 1984, 745; f) S.G. Davies, I.M. Dordor, J.C. Walker, and P. Warner, Tetrahedron Lett., 25, 2709 (1984); g) K. Broadley and S.G. Davies, ibid., 25, 1743 (1984); h) L.S. Liebskind, M.E. Walker, and V. Goedken, J. Am. Chem. Soc., 106, 441 (1984); i) L.S. Liebskind and M.E. Walker, Tetrahedron Lett., 25, 4341 (1984); j) Idem, Organometallics, 2, 194 (1983); k) C.P. Casey, W.H. Miles, and H. Tukuda, J. Am. Chem. Soc., 107, 2924 (1985); l) G.-H. Kuo, P. Helquist, and R.C. Kerber, Organometallics, 3, 806 (1984); m) K.A.M. Kremer, G.-H. Kuo, E.J. O'Conner, P. Helquist, and R.C. Kerber, J. Am. Chem. Soc., 104, 6119 (1982).

3) R.B. King and M.B. Bisnette, J. Organometal. Chem., 2, 15 (1964). According to King's procedure, cinnamoyl-FeCp$(CO)_2$ was prepared in 80% yield whereas acryloyl-FeCp$(CO)_2$ (1d) was obtained in only 5% yield. Recently, the preparation of 1c was improved to 64-70% yield level by Casey,[2k] who employed a high vacuum distillation ($<10^{-2}$ Torr).

4) S.G. Davies and J.C. Walker, J. Chem. Soc., Chem. Commun., 1985, 209.

5) As a private communication. Prof. L.S. Liebskind has succeeded in the stereoselective Michael additions of carbon and nitrogen nucleophiles to α,β-enoyl-FeCp(CO)(PPh_3) complexes. The authors thank Prof. Liebskind for communicating his results to us prior to publication.

6) Satisfactory spectral and analytical data were obtained for all new compounds.

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