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Nitroalkenylferrocene. I. Preparation of 2-Nitro-1-ferrocenylalkenes

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A wide variety of nitroalkenylferrocenes and their derivatives were synthesized by the condensation of formylferrocene and nitroalkanes. As a condensing agent, either sodium methoxide or a cyclic amine, such as piperidine, pyrrolidine and morpholine, was employed. Condensation using a cyclic amine, which is analogous to the Mannich reaction in nature, gave better results than that using sodium methoxide. The mechanism of the Mannich-type reaction has been discussed, and the formation of a molecular complex between formylferrocene and piperidine has been proposed as an intermediacy.

Many condensation reactions involving formylferrocene have been appeared in the literature. However, the reaction of the aldehyde with nitroalkane has not yet been studied except with nitromethane.

The present paper will report the preparation of several kinds of nitroalkenylferrocenes by two different methods; one is a method using sodium alkoxide[1,2] as a condensing agent, while the other uses a cyclic amine.[3-5] The reaction mechanism of the latter method, which is analogous to that of the Mannich reaction in nature, will also be discussed.

The Condensation Using Sodium Methoxide. The condensation of formylferrocene with nitroalkane by sodium methoxide was carried out as follows: A methanolic solution of sodium methoxide was gradually added to a cooled mixture of formylferrocene (**1**) and nitromethane in methanol. At the end of the reaction, an insoluble sodium salt of nitroalcohol (**2**) separated out as a yellow solid; this solid was apt to decompose to the starting materials in the presence of water. Dark violet crystals of 2-nitro-1-ferrocenylethylene (**3a**) (mp 139—140 ℃), which has been reported on as an oil by Flores *et al.*,[6] were isolated in an excellent yield by acidifying the salt with dilute hydrochloric acid. The NMR spectrum of **3a** exhibits two singlet peaks, at τ 5.46 and τ 5.81, corresponding to protons in the substituted and in the unsubstituted cyclopentadienyl ring respectively, and two doublets, centered at τ 2.03 and τ 2.80 ($J_{\alpha\beta}$= 12.5 cps), assignable to the vinyl α-proton and the vinyl β-proton*1 respectively. The IR spectrum of the nitroolefin showed absorption peaks at 1290 and 950 cm^{-1}; these peaks are indicative of *trans*-olefin.

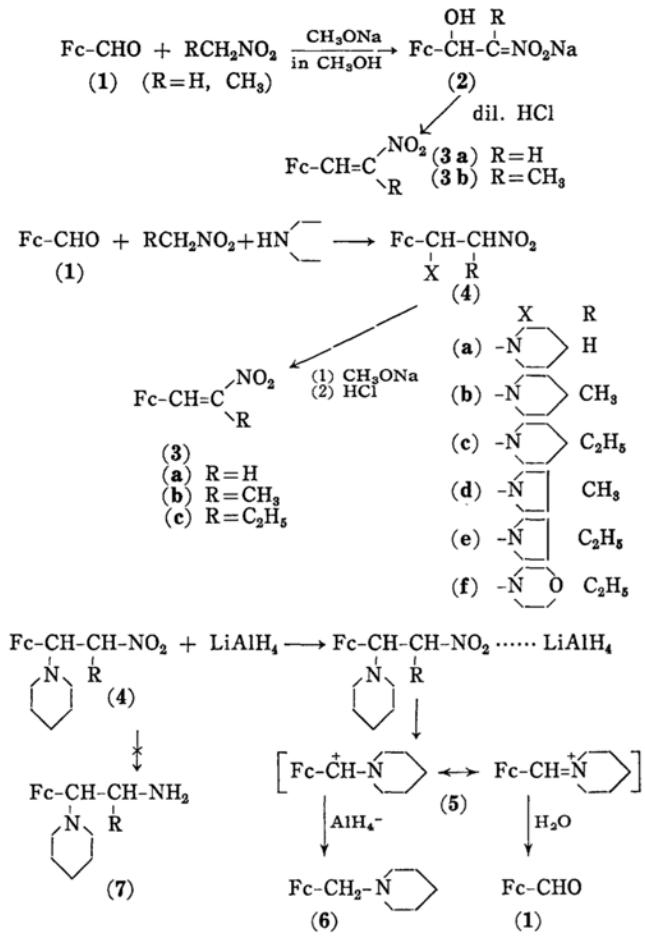
In the reaction of formylferrocene with nitroethane, 2-nitro-1-ferrocenylpropene (**3b**), (mp 57—58℃), obtained in a low yield (12%), was the only isolated product; no salt intermediate **2** was isolated. The NMR spectrum of **3b** exhibits two singlet peaks, at τ 5.49 and τ 5.83, corresponding to the ring protons, and two singlets, at τ 2.08 and τ 7.70, assignable to the vinyl α-proton and the methyl proton respectively (Table 3).

The Condensation Using Cyclic Amines. This condensation was conducted by using a cyclic amine, such as piperidine, pyrrolidine, or morpholine, as the condensing agent in a way similar to that using sodium methoxide. The nature of this condensation seems to be analogous to the Mannich reaction; in fact, the reaction afforded a Mannich-type product,[7] aminonitroalkane (**4**), which could eventually converted into a nitroolefin (**3**) if the right conditions were employed. The condensation

1) L. Bouveault and A. Wahl, *Compt. rend.*, **135**, 41 (1902).
2) B. Preib, *Ber.*, **18**, 1362 (1885).
3) N. Campbell, W. Anderson and J. Gillore, *J. Chem. Soc.*, **1940**, 446.
4) E. Pratt and E. Werble, *J. Am. Chem. Soc.*, **72**, 4638 (1950).
5) M. Kamlet, *ibid.*, **77**, 4896 (1955).
6) B. Loev and M. Flores, *J. Org. Chem.*, **26**, 3595 (1961).

*1 The α- and β- symbols refer to the ferrocene ring throughout this paper.

7) "Organic Reactions," Vol. 1, p. 304 (1942).



of nitromethane, nitroethane, and 1-nitropropane with formylferrocene in the presence of piperidine gave only aminonitroalkanes (**4**) as yellow crystals. The reduction of these products with $LiAlH_4$ afforded reddish-orange crystals (mp 84—86℃), along with the original aldehyde **1**; the expected amino compounds **7** were not obtained. The reddish-orange substance was identified as piperidinomethylferrocene (**6**)[8] by means of elementary analysis and a study of the IR spectrum and the NMR spectrum. Accordingly, it appears that the reaction proceeds through a cationic intermediate **5**, as is shown in the scheme.

On the other hand, nitromethane condensed with formylferrocene in the presence of pyrrolidine to form nitroolefin **3a** exclusively, while nitroethane and 1-nitropropane gave only aminonitroalkanes, **4d** and **4e** respectively. Furthermore, in the presence of morpholine, which is a weaker base than the others, the condensation of nitromethane and nitroethane with formylferrocene gave exclusively nitroolefin **3a** and **3b** respectively, whereas 1-nitropropane gave only aminoalkane **4f** as is shown in Table 1. When the Mannich bases, **4c** and **4e**, were converted to sodium salt by sodium methoxide and then treated with hydrochloric acid, the basic group on α-carbon was readily eliminated to afford quantitatively 2-nitro-1-ferrocenyl-1-butene **3c**, mp 77—78℃, whose NMR spectrum is shown in Table 3. A characteristic color change from yellow to violet was observed when a Mannich base **4** was converted into a nitroolefin **3**.

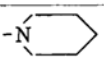
Discussion of the Mechanism of the Condensation Reaction. As the mechanism of the Mannich-type reaction[9] affording an aminonitroalkane **4**, the three courses shown in Fig. 1 can be considered. Course A involves the nucleophilic substitution of cyclic amine on the nitroalcohol **8** formed by the nucleo-

8) J.M. Osgerby and P.L. Pauson, *J. Chem. Soc.*, **1958**, 656.

9) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Company, New York (1956), p. 263.

TABLE 1. THE CONDENSATION OF FORMYLFERROCENE WITH NITROALKANE AND CYCLIC AMINE

Nitroalkane	Cyclic amine	Product	Yield (%)
Nitromethane	Piperidine	$FcCHCH_2NO_2$[a] (**4a**)	86
		X_1	
Nitroethane	Piperidine	$FcCHCH(CH_3)NO_2$[a] (**4b**)	88
		X_1	
1-Nitropropane	Piperidine	$FcCHCH(C_2H_5)NO_2$[a] (**4c**)	95
		X_1	
Nitromethane	Pyrrolidine	$FcCH=CHNO_2$ (**3a**)	81
Nitroethane	Pyrrolidine	$FcCHCH(CH_3)NO_2$[b] (**4d**)	89
		X_2	
1-Nitropropane	Pyrrolidine	$FcCHCH(C_2H_5)NO_2$[b] (**4e**)	94
		X_2	
Nitromethane	Morpholine	$FcCH=CHNO_2$ (**3a**)	74
Nitroethane	Morpholine	$FcCH=C(CH_3)NO_2$ (**3b**)	—
1-Nitropropane	Morpholine	$FcCHCH(C_2H_5)NO_2$[c] (**4f**)	72
		X_3	

a) X_1 =  b) X_2 =  c) X_3 = 

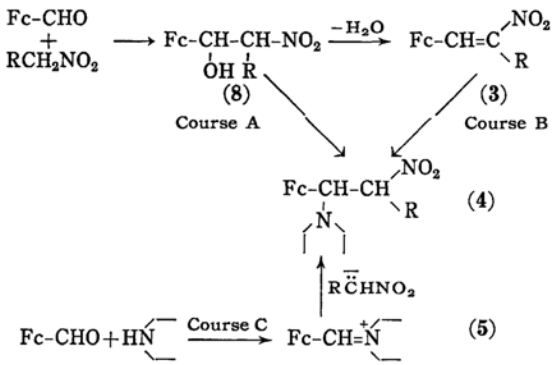
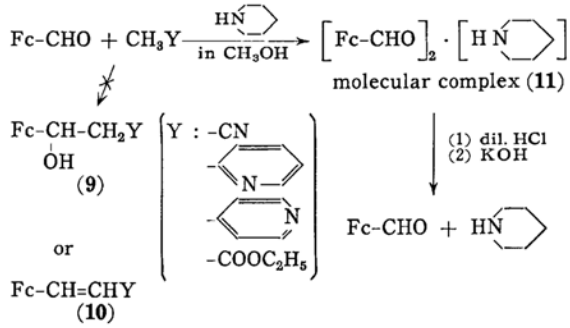


Fig. 1. Eventual mechanism of the Mannich-type condensation.

philic attack of nitroalkane on formylferrocene. Course B involves the addition of amine to the nitroolefin **3** produced by the dehydration of the nitroalcohol **8**. Course C involves the intermediacy of the enamine **5**,[10] which is subjected to attack by a carbanion derived from nitroalkane. Of these three possibilities, Course A may be eliminated because of the fact that no alcoholic product was isolated from the reaction. In addition, Courses A and B can both be ruled out by the fact that the formation of aminonitroalkane **4** is not retarded, but even accelerated, when the nitroalkane with a bulkier alkyl substituent is used.

In order to obtain further information, condensation reactions of formylferrocene with compounds less acidic than nitroalkane, such as acetonitrile, α- and γ-picoline, and ethyl acetate, were attempted in the presence of piperidine in methanol. Neither the expected alcohol **9** nor the olefin **10** was thus formed; the only product isolated was a yellow, crystalline substance. When an ethereal solution of the yellow substance was shaken with dilute hydrochloric acid, the substance easily transferred to the aqueous layer to give a red solution. The neutralization of the aqueous layer with alkali gave the original aldehyde and amine. Moreover, the yellow substance was not isolated in the absence of a nucleophile, such as acetonitrile and the like, under the same conditions as above. This substance, therefore, seems to be something like a molecular complex; its elementary analysis suggests a structure corresponding to the formula **11**. The proposed structure is consistent with the following observations. The IR spectrum showed the characteristic absorption band of the carbonyl group of

10) S.P. Makarov, *J. Prakt. Chem.*, **141**, (2), 77 (1934).



formylferrocene and that of the methylene group of piperidine, but no peak in the region of ν_{NH}. The UV spectrum of this compound is almost identical with that of formylferrocene. The complex **11** gradually decomposed into formylferrocene and piperidine when left standing in the air. Furthermore, the aminonitroalkane **4** was produced when the complex was dissolved in nitroalkane.

On the basis of these experimental results, it seems reasonable to conclude that Course C is the most likely, although there is no direct evidence for the formation of the enamine **5**.

For the preparation of 2-nitro-1-ferrocenylalkanes, piperidine is the most effective condensing agent among the cyclic amines employed in those reactions. The reactions of the nitroalkenes and the aminonitroalkanes will be reported in the following papers.

Experimental

Materials. Commercial cyclic amines and nitroalkanes were used without any further purification. Formylferrocene was prepared by the modified Vilsmeier reaction previously reported.[11]

TABLE 2. THE IR SPECTRA OF 1-FERROCENYL-2-NITROALKENES (KBr disk)

Compound	Mp(°C)	Frequency (cm^{-1})	
		$\nu_{C=C}$	ν_{NO_2}
FcCH=CHNO$_2$ (**3a**)	139—140	1630	1503 1328
FcCH=C(CH$_3$)NO$_2$ (**3b**)	57—58	1655	1499 1303
FcCH=C(C$_2$H$_5$)NO$_2$ (**3c**)	77—78	1639	1509 1298

Identification of the Reaction Products. The reaction products were identified by means of the NMR spectra, the IR spectra, and the results of elementary analyses. These results are tabulated in Tables 2, 3, and 4 respectively.

2-Nitro-1-ferrocenylethylene (3a). To an ice-cooled solution of formylferrocene (21.4 g, 0.1 mol) and nitromethane (12.2 g, 0.2 mol) in 60 m*l* of absolute methanol, there was gradually added a methanolic solution of sodium methoxide (10.8 g, 0.2 mol). Within a few minutes, about 30 g of a yellow-brown solid separated out. The solid salt was collected and washed with dry ether. Treating the solid with dilute hydrochloric acid gave 19.5 g (76% yield) of 2-nitro-1-ferrocenylethylene (**3a**) as violet crystals, mp 139—140 °C. The analytical sample was prepared by recrystallization from ethanol.

The nitroolefin **3a** was also well prepared as

TABLE 4. RESULTS OF THE ELEMENTARY ANALYSES

Compound	Found			Calcd		
	C%	H%	N%	C%	H%	N%
3a	55.64	4.79	5.36	56.07	4.28	5.42
3b	57.00	4.90	5.63	57.61	4.80	5.17
3c	57.08	5.24	4.62	58.99	5.27	4.92
4a	59.67	6.53	8.04	59.66	6.48	8.19
4b	60.69	6.79	7.86	60.05	6.78	7.81
4c	61.63	7.08	7.57	61.45	6.97	7.61
4d	59.09	6.39	7.69	59.68	6.44	8.19
4e	59.92	6.82	8.19	60.71	6.75	7.87
4f	57.69	6.46	7.34	58.10	6.46	7.53
6	67.45	7.38	4.66	68.10	7.42	4.92
11	65.58	7.41	2.59	65.40	6.10	2.88

TABLE 3. THE NMR SPECTRA OF 1-FERROCENYL-2-NITROALKENES (τ-value, in $CDCl_3$)

Compound	Unsubstituted ring protons	Substituted ring protons	Vinyl protons α	Vinyl protons β	Alkyl protons	
FcCH=CHNO$_2$ (**3a**)	5.81 (s) 5[a]	5.46 (s) 4	2.03 (d) 1	2.80 (d)[b] 1		
FcCH=C(CH$_3$)NO$_2$ (**3b**)	5.83 (s) 5	5.49 (s) 4	2.08 (s) 1		7.70 (s) 3	
FcCH=C(C$_2$H$_5$)NO$_2$ (**3c**)	5.80 (s) 5	5.49 (s) 4	2.09 (s) 1		7.21 (q) 2	8.75 (t)[c] 3

a) Figures under the τ-values indicate the ratio of intensities.
b) $J_{\alpha\beta}$=12.5 cps. c) J=6.7 cps.

11) M. Sato, H. Kono, M. Shiga, I. Motoyama and K. Hata, This Bulletin, **41**, 252 (1968).

follows: (a) Pyrrolidine (1.42 g, 0.02 mol) or morpholine (1.74 g, 0.02 mol) was gradually added to an ice-cooled solution of formylferrocene (2.14 g, 0.01 mol) and nitromethane (1.22 g, 0.02 mol) in 10 m*l* of absolute methanol. After standing for a few hours, the reaction mixtue was poured into dilute hydrochloric acid in order to be acidified, and then extracted with chloroform. The extract was washed with water, and then dried over anhydrous magnesium sulfate. After the removal of the solvent, the residue was chromatographed on alumina, using benzene as a solvent, to give the olefin **3a** in an excellent yield (Table 1).

(b) Aminonitroalkane (**4a**) (1.7 g, 0.005 mol), to be described below, was added to 10 m*l* of absolute methanol containing 1.08 g (0.02 mol) of sodium methoxide. The reaction mixture was stirred for an hour on an ice bath and then acidified with dilute hydrochloric acid to give the olefin **3a** quantitatively.

2-Nitro-1-ferrocenylpropene (3b). Sodium methoxide (3.6 g, 0.07 mol) in methanol was gradually added with cooling to a solution of formylferrocene (4.00 g, 0.02 mol) and nitroethane (3.0 g, 0.04 mol) in 20 m*l* of absolute methanol. After it had then been let stand for four days at room temperature, the reaction mixture was poured into 70 m*l* of 15% hydrochloric acid and extracted with chloroform. The organic layer was separated, washed with water, and dried over anhydrous magnesium sulfate. After the evaporation of the solvent, the crude product was chromatographed on alumina, using dry benzene as a solvent. From the first fraction, 2-nitro-1-ferrocenylpropene was obtained as violet crystals, mp 57—58 °C. From the following fractions 2.26 g (57%) formylferrocene were recovered.

For the preparation of nitroolefin **3b**, pyrrolidine and piperidine gave much better results than sodium methoxide, but morpholine gave only a low yield.

Aminonitroalkane, **4b** (1.78 g, 0.005 mol) and **4d** (1.71 g, 0.005 mol), prepared in excellent yields by the procedure to be described below, were quantitatively converted to the nitroolefin **3b** by treating them for an hour with 10 m*l* of a methanolic solution containing 1.08 g (0.02 mol) of sodium methoxide, followed by acidification with dilute hydrochloric acid.

2-Nitro-1-ferrocenyl-1-butene (3c). By the same procedure as has been described above, 2-nitro-1-ferrocenyl-1-butene was quantitatively prepared from the aminoalkanes **4c**, **4e**, and **4f** as violet crystals, mp 77—78 °C.

1-Ferrocenyl-1-piperidino-2-nitroethane (4a). Formylferrocene (2.14 g, 0.01 mol), nitromethane (1.22 g, 0.02 mol), and piperidine (1.70 g, 0.02 mol) were dissolved in 20 m*l* of absolute methanol. The solution was let stand at room temperature for a few hours to give 1-ferrocenyl-1-piperidino-2-nitroethane as yellow-brown crystals (2.9 g, 86%). It was filtered and washed with water and then with a small portion of ether. The pale yellow crystals obtained by recrystallization from dichloromethane - *n*-hexane melted at 116°C (dec.).

1-Ferrocenyl-1-piperidino-2-nitropropane (4b). Following the procedure described above, 1-ferrocenyl-1-piperidino-2-nitropropane was prepared from formylferrocene, nitroethane, and piperidine in a 94% yield. The pale yellow crystals obtained by recrystallization from dichloromethane - *n*-hexane melted at 121—122°C (dec.).

1-Ferrocenyl-1-piperidino-2-nitrobutane (4c). Yellow crystals of 1-ferrocenyl-1-piperidino-2-nitrobutane, mp 132°C (dec.), were similarly obtained.

Piperidinomethylferrocene (6). A mixture of 1-ferrocenyl-1-piperidino-2-nitropropane (**4b**) (1 g, 0.003 mol) and lithium aluminum hydride (0.8 g, 0.02 mol) in 50 m*l* of dry ether was stirred for 3 hr on an ice bath, and then 30 m*l* of methanol was gradually poured into the reaction mixture, followed by 100 m*l* of water. The mixture was then extracted with ether, and the extract was washed with water and dried over anhydrous magnesium sulfate. After the removal of the solvent, the residue was chromatographed on alumina, using benzene - *n*-hexane as a solvent. Reddish-orange crystals of piperidinomethylferrocene (**6**), mp 84—86°C, were obtained from the second fraction; yield 0.13 g (17%). The same compound **6** was obtained in a 15—17% yield from 1-ferrocenyl-1-piperidino-2-nitroethane (**4a**) by a similar procedure. The NMR spectrum of **6** exhibits two broad peaks, at τ 8.58 and τ 7.67, due to the methylene protons of the piperidine ring, and two singlets, at τ 6.66 and τ 5.93, due to α-methylene protons and ferrocene ring protons respectively.

1-Ferrocenyl-1-pyrrolidino-2-nitropropane (4d). By a procedure, using pyrrolidine as a condensing agent, similar to that used for the preparation of **4a**, **4d** was prepared in an 89% yield. The analytical sample, recrystallized from dichloromethane-*n*-hexane, melted at 75°C (dec.).

1-Ferrocenyl-1-pyrrolidino-2-nitrobutane (4e). From formylferrocene, 1-nitropropane, and pyrolidine, **4e** was obtained in a 88% yield as pale yellow crystals, mp 101—102°C, after recrystallization from dichloromethane - *n*-hexane.

1-Ferrocenyl-1-morpholino-2-nitrobutane (4f). A similar reaction of formylferrocene with 1-nitropropane and morpholine afforded **4f** as yellow-brown crystals, mp 139—140°C, in a 72% yield.

Molecular Complex (11) of Formylferrocene and Piperidine. Formylferrocene (1 g) was added to an ice-cooled solution of piperidine (1 g) and acetonitrile (0.5 g) in 5 m*l* of absolute methanol. After half an hour, the complex **11** separated from the solution as yellow crystals, which were then filtered and washed with methanol (yield, 0.7 g). Some discrepancies in the analytical data shown in Table 4 may be due to its instability in the air.

When 0.2 g of the complex **11** was dissolved in 2 g of nitromethane with stirring under ice cooling, the reaction mixture immediately turned to a brownish-violet. From the solution, 0.1 g of 1-ferrocenyl-1-piperidino-2-nitroethane (**4a**) was obtained as yellow crystals.