Methyl 3-oxa-5-oxoheptanoate (9d): IR 1750, 1730; ^{1}H NMR 1.1 (t, 3 H, CH_3, J = 8 Hz), 2.55 (q, 2 H, CH_2CO, J = 8 Hz), 3.8 (s, 3 H, OCH_3), 4.25 (s, 4 H, OCH_2CO); MS, m/e 160 (M^+), 103, 101, 75, 57.

Methyl 5-oxohexanoate (9e): IR 1735, 1710; ^{1}H NMR 1.6–2 (m, 2 H, CH_2), 2.13 (s, 3 H, CH_3), 2.2–2.7 (m, 4 H, CH_2), 3.65 (s, 3 H, OCH_3); MS, m/e 144 (M^+), 112, 99, 74, 71.

Registry No. **1a**, 87761-86-2; **1b**, 87761-87-3; **1c**, 83134-77-4; **1d**, 78947-93-0; **1e**, 87761-88-4; **1f**, 87761-89-5; **2b**, 87761-95-3; **3a**, 37160-77-3; **3b**, 87761-93-1; **3c**, 87761-94-2; **3d**, 4161-60-8; **3e**, 73397-68-9; **3f**, 76917-16-3; **4**, 83134-80-9; **5**, 87761-96-4; **6a**, 1729-32-4; **6b**, 1729-26-6; **6c**, 87761-90-8; **6d**, 87761-91-9; **6e**, 87761-92-0; **9a**, 624-45-3; **9b**, 74457-44-6; **9c**, 25359-49-3; **9d**, 61363-67-5; **9e**, 13984-50-4.

Direct Synthesis of Ferrocenyl Alcohols from Aldehydes and Ketones

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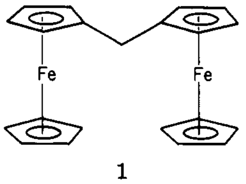
The number of reports dealing with the chemistry of ferrocene is staggering; if one limits the survey of the chemistry of ferrocene only to those reactions that are categorized under the name of the Friedel–Crafts reaction, the volume of literature seems little reduced. It is, therefore, surprising that the reaction of ferrocene with aldehydes and ketones in strongly acidic medium to produce ferrocenyl alcohols and olefins derived from these alcohols has not been previously described. To be sure, reaction conditions that might be expected to yield these products have been extensively employed, but none of the reports dealing with them, as far as we are able to determine, have described the isolation of these monomeric products. Instead, it appears that the alcohols and olefins have been assumed to be transient intermediates that give rise to dimeric and oligomeric products, depending on reaction conditions. Pauson and Watts, for example, have described the synthesis of diferrocenylmethane (1) from ferrocene and paraformaldehyde in concentrated sulfuric acid when ferrocene is present in relatively large excess,[1] while under similar conditions, others have reported that diferocenylethane (2) is the major product of the reaction.[2]



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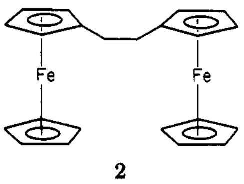
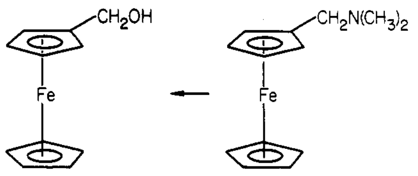


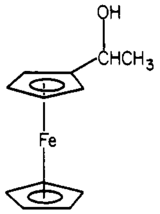
2

Similar results have been realized with other catalyst systems such as $ZnCl_2/HCl$ at elevated temperatures[3] and $AlCl_3$.[4] Analogous conclusions, using $AlCl_3$ as the Friedel–Crafts catalyst, were realized by Shiga et al., with the important difference that in some cases, e.g., when propiophenone and cyclohexanone were the carbonyl compounds employed, monomeric olefins containing only one ferrocenyl moiety were isolated.[5]

The monomeric products to which we have referred are often prepared in sequences involving a number of steps. For example, ferrocenylmethanol (3) has been most successfully prepared from [(dimethylamino)methyl]ferrocene (4) in three steps;[6] obvious methods of synthesis of 1-ferrocenylethanol (5) and 2-ferrocenyl-2-propanol (6) from acetylferrocene require two steps from ferrocene.



3 4



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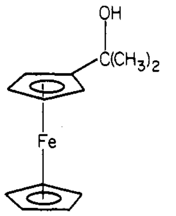

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By modifying the conditions that have been previously employed to provide oligomeric products, we have been able to produce a number of monomers containing a single ferrocene unit, and we believe our method is a general one for the synthesis of ferrocenylmethanols or the olefins derived from them. The conditions under which we have been able to isolate these monomeric products are, in contrast to those usually reported, extraordinarily mild, normally involving low temperatures and very short reaction times. In general, the carbonyl compound is dissolved in cold concentrated sulfuric acid, to which ferrocene is subsequently added, and after a short reaction time, the reaction mixture is worked up by addition of ice or cold water followed by ether extraction. We have found that most aldehydes provide the expected alcohol in good yield, while ketones, except for acetone, provide the olefin derived from the expected alcohol. (Acetone provides **6** in excellent yield.) In many cases, the reaction appears to be extraordinarily capricious; a first attempt, even in experienced hands, often leads to failure, and repeated attempts, even with no apparent modifications, may ultimately be rewarded. For this reason, we recommend that our directions for the synthesis of specific alcohols or olefins be followed exactly, and in only a general way when attempting the synthesis of one of these products not reported here, with the anticipation of repeated trials with small procedure modifications until success is realized.

We have studied the Friedel–Crafts syntheses of a number of ferrocenyl alcohols and their olefinic derivatives (in the usual cases, one or the other was isolated; often the alcohols appeared to be very unstable toward dehydration), using formaldehyde (as formalin), acetaldehyde, propionaldehyde, butyraldehyde, benzaldehyde, ferrocene carboxaldehyde, and the ketones acetone, 2-butanone, cyclopentanone, and cyclohexanone. With aldehydes, only alcoholic products were isolated and identified, in yields ranging from 39% in the case of propionaldehyde to 57%

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(1) Pauson, P. L.; Watts, W. E. *J. Chem. Soc.* **1962**, 3880.

(2) Rinehart, K. L.; Michejda, C. J.; Kittle, P. A. *J. Am. Chem. Soc.* **1959**, *81*, 3163.

(3) Sokolinskaya, T. A.; Vishnyakova, T. P.; Paushkin, Y. M.; Popova, Y. A. *Vysokomolecul. Soedin. Ser. A* **1967**, *9*, 677.

(4) Vishnyakova, T. P.; Sokolinskaya, T. A.; Pankova, N. A.; Sokolovskii, Y. S. *Zh. Obshch. Khim.* **1976**, *46*, 1612.

(5) Shiga, M.; Motoyama, I.; Hata, K. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 1891.

(6) Lindsay, J. K.; Hauser, C. R. *J. Org. Chem.* **1957**, *22*, 355.

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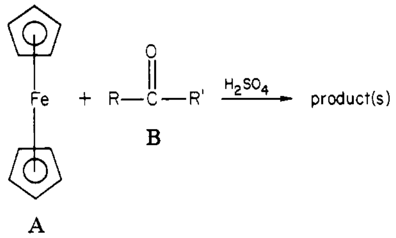
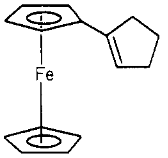
Table I



carbonyl compd	ratio A/B, mmol	ratio H_2SO_4/H_2O, mL	rctn time, min	rctn temp, °C	yield of alcohol, %	yield of olefin(s), %	product mp, mp, °C	lit. mp, °C (ref)
CH_2O (formalin)	2.5/2.6	8/1	1	−15	53		77-78	81-82 (*a*)
CH_2O (formalin)	5.0/5.0	8/0	2	−50	57		77-78	81-82 (*a*)
CH_3CHO	2.5/2.5	8/1	1	0	54		77-78	73-75 (*b*)
cyclohexanone	10/10	8/0	5	0		83	66-66.5	(*c*)
acetone	2.5/10	8/0	5	0	33	36	57-59 62-63	77.5-78.5 (*d*)
benzaldehyde	2.5/2.5	8/1.5	1	−10	42		80-81	81-82 (*e*)
2-pentanone	2.5/2.5	8/1	1	0	25		liquid	
propionaldehyde	2.5/2.5	8/0	1	−15	39	trace	liquid	(*f*)
2-butanone	10/10	8/0	1	0	trace	54[h]		(*f*)
cyclopentanone	10/100	10/0	90	27		83	68-69	64-65 (*g*)

[a] Reference 6, text. [b] Arimoto, F. S.; Haven, A. C., Jr. *J. Am. Chem. Soc.* **1955**, *77*, 6295. [c] Reference 5, text. [d] Rinehart, K. L.; Michejda, C. J.; Kittle, P. A. *J. Am. Chem. Soc.* **1960**, *82*, 2082. [e] Weliky, N.; Gould, E. S. *J. Am. Chem. Soc.* **1957**, *79*, 2742. [f] Schlogl, K.; Mohar, A. *Monatsh. Chem.* **1961**, *92*, 219. [g] Weinmayr, V. *J. Am. Chem. Soc.* **1955**, *77*, 3009. [h] Mixture of 2-ferrocenyl-1-butene and 2-ferrocenyl-2-butene.

with formaldehyde. In most of these syntheses, other products were obtained in small amounts and were not identified. The reaction of ferrocene with benzaldehyde in concentrated sulfuric acid did not provide a substantial amount of a compound, different from phenylferrocenylcarbinol, that has not yet been identified. Ketones, on the other hand, are not as well-behaved. While product yields were generally higher, mostly olefinic products were obtained. With acetone, 2-ferrocenyl-2-propanol (6) as well as the corresponding olefin, 2-ferrocenylpropene, was isolated; relative amounts depended on reaction conditions. Cyclopentanone and cyclohexanone gave 1-ferrocenylcyclopentene (7) and 1-ferrocenylcyclohexene (8), respectively, both in yields of 83%.



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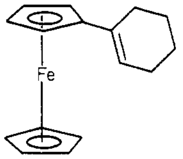

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Experimental Section

Melting points were obtained on a Fisher-Johns apparatus and are uncorrected. Because of the sensitive nature of some of the syntheses reported here, general descriptions of syntheses will contain parenthetical notes that refer to specific changes for some problem compounds. Table I summarizes our results and provides details of reaction temperature, time, and concentrations of reactants.

Typical Procedure for Reaction of Ferrocene with Aldehydes in Concentrated Sulfuric Acid. To a solution of 8 mL of concentrated sulfuric acid and 1 mL of water cooled to −10 °C (ice–HCl bath) was added 2.5 mmol of the aldehyde. After stirring of the mixture for about 1 min, 2.5 mmol of ferrocene was added. The mixture was vigorously stirred for 1 min, after which 10 mL of ice water was added dropwise over a 2-min period. In some cases, the separation of a solid was observed, but in all successful runs, the solid redissolved to produce a deep red solution. The reaction mixture was poured into about 150 mL of cold water and extracted four times with 20 mL of diethyl ether. The ether solution was washed with aqueous sodium bicarbonate solution and dried with magnesium sulfate and the solvent removed under reduced pressure. The oil or waxy solid thus produced was chromatographed on silica gel, first using hexane as the eluting solvent and gradually increasing the ether content of the eluting solvent to a maximum ether concentration of 30%. Alcohol products were normally recrystallized from hexane.

Typical Procedure for Reaction of Ferrocene with Ketones in Concentrated Sulfuric Acid. To 8 mL of concentrated sulfuric acid cooled to 0 °C was added 10 mmol of the ketone (in the case of cyclopentanone, 100 mmol was added). This mixture was stirred for 1 min, and 10 mmol of ferrocene was added. The mixture was stirred for 5 min, followed by addition of 10 mL of ice water over a 2-min period. The workup procedure followed that described for aldehydes above. The olefinic products were purified by chromatography on silica gel, using hexane as eluting solvent. In the cases of cyclohexanone and cyclopentanone, chromatography was not necessary; the cyclohexenyl- and cyclopentenylferrocene products, respectively, were purified directly by recrystallization from absolute ethanol.

Registry No. 3, 1273-86-5; 5, 1277-49-2; 6, 12093-87-7; 7, 12260-67-2; 8, 33183-07-2; CH_3CHO, 75-07-0; phenylferrocenylmethanol, 1277-68-5; 2-ferrocenyl-2-pentanol, 12302-37-3; 1-ferrocenyl-1-propanol, 1294-04-8; 2-ferrocenyl-1-butene, 32614-19-0; 2-ferrocenyl-2-butene, 12289-38-2; formalin, 50-00-0; cyclohexanone, 108-94-1; acetone, 67-64-1; benzaldehyde, 100-52-7; 2-pentanone, 107-87-9; propionaldehyde, 123-38-6; 2-butanone, 78-93-3; cyclopentanone, 120-92-3; ferrocene, 102-54-5; 2-ferrocenylpropene, 31725-14-1.

A Practical Enzymatic Synthesis of (S_P)-Adenosine 5′-*O*-(1-Thiotriphosphate) ((S_P)-ATP-α-S)[1]

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(S_P)-Adenosine 5′-*O*-(1-thiotriphosphate) ((S_P)-ATP-α-S) is an analogue of ATP useful in studying the mecha-

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