dibromopentane, b.p. 40° (4 mm.), $n^{20}D$ 1.4968, containing only 2% of the *meso* isomer.

The same procedure repeated for the *meso*-diol gave *meso*-dibromide containing substantial quantities of the alternative isomer, 5–20% depending on reaction conditions and the method of isolation. However, fractional distillation of such material through the column described above usually resulted in 25% recovery of a pure dibromide mixture, b.p. 45° (5 mm.), $n^{20}D$ 1.5015, containing not less than *ca.* 95% of the *meso*-dibromide.[33] Isomeric equlibration was noted on prolonged boiling of the product at 4 mm., so setting a limit to the degree of separation of the higher boiling (*meso*) product attainable by fractional distillation.

Anal. Calcd. for $C_5H_{10}Br_2$: C, 26.1; H, 4.35; Br, 69.5. Found: *meso*-isomer, C, 26.1; H, 4.15; Br, 69.6; racemic form, C, 26.1; H, 4.6; Br, 69.4.

Vapor Phase Chromatography.—The retention times given in Table I were obtained with a column 10 ft. long and 0.4-in. i.d., packed with 8% by weight of Carbowax (mol. wt., 9000) on 30/60-mesh firebrick, and with an inlet pressure of 40 p.s.i. of helium gas to an F. and M. Scientific Corporation Model 500 instrument. The retention times quoted in the table were for 1-μl. samples and a flow rate of 570 ml./min. The table also shows the maximum quantities of material in μl. which could be separated under the conditions described, indicating the degree of spreading of the various samples on the column.

N.m.r. Spectroscopy.—Samples of each isomeric form of 2,4-pentanediol with four times their volume of deuterium oxide were degassed and sealed under vacuum in thin-walled tubes, 6 × 0.5 in. in diameter. Spectra were run at room temperature on a Varian machine operating at 60 Mc./sec., equipped with a Varian 12-in. electromagnet, flux stabilizer, and field-homogeneity stabilizer. A side band of 250 c.p.s. was set off at high field from the signal due to the hydroxyl protons. Hence, the arbitrary scale on Fig. 1 and 2 is set at zero for the exchanging hydroxyl protons in an alcohol-water-HDO-deuterium oxide mixture containing *ca.* 4% H and 96% D.

TABLE I

RETENTION TIMES IN MINUTES FOR 2,4-DISUBSTITUTED PENTANE DERIVATIVES UNDER CONDITIONS SPECIFIED IN THE TEXT

Derivative	Temp., °C.	Retention time *meso*	Retention time Racemic	Max. quant. (μl.)
Diacetates	130	6.25	5.1	1
Cyclic sulfites	130	4.7	6.45	50
Dichlorides	80	3.8	3.15	1
Dibromides	100	6.7	5.5	10

Acknowledgment.—The authors wish to express their thanks to Mr. W. C. Lawrence for obtaining the n.m.r. spectra shown in Fig. 1 and 2, and to Mr. H. E. Frankfort for his contribution toward the elucidation of the nickel–hydrogen and sodium borohydride reductions of acetylacetone during the initial stages of this work. All microanalyses were by the Alfred Bernhardt Mikroanalytisches Laboratorium, Max-Planck-Institut für Kohlenforschung, Mülheim (Ruhr), Germany.

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The Acetylation of Some Substituted Ferrocenes[1]

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A number of mono- and disubstituted ferrocenes have been acetylated. It has been found that iodine is lost from iodoferrocene under the acetylation conditions employed. Contrary to another report, bromo- and chloroferrocenes are acetylated to give 1′-acetylbromo- and chloroferrocenes in good yield. Acetylation of acetamido- and urethanoferrocenes gives predominantly the heteroannularly substituted isomers, and these substituents are deactivating.

In recent years a number of reports have appeared on the electrophilic substitution reactions of ferrocene derivatives.[3] Rosenblum[4] has reported some studies of this type and has used a molecular orbital calculation to predict the effect of substituent groups. Recently Morrison and Pauson[5] have shown that Friedel–Crafts acetylation of chloro-, methylthio- and methoxyferrocenes leads to the replacement of the substituent by hydrogen. Thus chloroferrocene yields ferrocene and methoxyferrocene yields acetylferrocene. In connection with our work on metallocenyl carbonium ions and for other reasons it was desirable to have in hand substituted ferrocenes. This led to a study of the acetylation reactions of iodo-, bromo-, chloro-, acetamido-, methoxycarbonylamino-, ethoxycarbonylamino-, 1,1′-diethoxycarbonylamino-, and cyanoferrocenes.

Results and Discussion

The results are summarized in Table I.

Structural assignments were made chiefly on the basis of infrared spectral correlations. The pertinent data are summarized in Table II. It can be seen that all disubstituted compounds assigned the 1,2-homoannular structure possess bands near 9 and 10 μ (1111 and 1000 cm.$^{-1}$) in accordance with the 9–10 rule set forth by Rosenblum.[6] In addition the 1,2-disubstituted compounds clearly show hydrogen bonding between the amide hydrogen and the oxygen atom of the acetyl group.[7] 2-Acetyl-1,1′-di(ethoxycarbonylamino)ferrocene also possesses a spectrum indicative of hydrogen bonding whereas 3-acetyl-1,1′-di(ethoxycarbonylamino) ferrocene does not. The compounds assigned the 1,1′-disubstituted structure lack the bands near 9 and 10 μ but do show absorption near 8.95 μ (1117 cm.$^{-1}$) which is known to be indicative of a ferrocene possessing a cyclopentadienyl ring substituted only with an acetyl group.[6]

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[1] Supported in part by a grant from the National Science Foundation.

[2] (a) This paper is based on the Ph.D. thesis of D. W. Hall, December, 1962; (b) the Denver Research Center of the Marathon Oil Company.

[3] For a review see K. Plesske, *Angew. Chem.*, **74**, 301, 347 (1962).

[4] M. Rosenblum and W. G. Howells, *J. Am. Chem. Soc.*, **84**, 1167 (1962).

[5] J. G. Morrison and P. L. Pauson, *Proc. Chem. Soc.* (London), 177 (1962).

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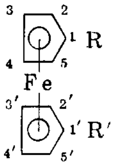
[7] R. E. Richards and H. W. Thompson, *J. Chem. Soc.*, 1248 (1947).

TABLE I

ACETYLATION OF MONO- AND DI-SUBSTITUTED FERROCENES



R	R'	Reagents	Starting material recovered, %	Isomer yields, % conversion 1'-	2-	3-
Acetamido-	H	1:1 Aluminum chloride–acetyl chloride	42	37.4	0[a]	0
		Silicon tetraacetate and stannic chloride	39.6	29.7	0[a]	0
		Boron trifluoride and acetic anhydride	17.8	69.2	3.3	0
Ethoxycarbonylamino-	H	Boron trifluoride and acetic anhydride	Not determined	Approx. 50	Under 5	0
Ethoxycarbonylamino-	R = R'	Boron trifluoride and acetic anhydride	21[b]	. . .	22[b]	46
Methoxycarbonylamino-	H	1:1 Acetyl chloride–aluminum chloride	Not determined	Approx. 50	Under 5	0
Cyano-	H	1:1 Acetyl chloride–aluminum chloride	0	100	0	0
Bromo-	H	1:1 Acetyl chloride–aluminum chloride	0	75	0	0
Chloro-	H	1:1 Acetyl chloride–aluminum chloride	0	81	0	0
Iodo-	H	1:1 Acetyl chloride–aluminum chloride	A mixture of iodoferrocene was recovered	Only acetylferrocene and 1,1'-diacetylferrocene were isolated		

[a] Probably present but not isolated. [b] Estimated; see Experimental.

In accord with the observations of other workers, the 2-substituted compounds were eluted from alumina before the other isomers.[8,9]

Ultraviolet absorption data are summarized in Table III.

Under our conditions, the acetylation of bromo- and chloroferrocenes proceeded smoothly to yield the heteroannularly substituted products. There was no evidence for the presence of homoannularly substituted products in either of these two cases. Nesmeyanov has also found that acetylation of bromoferrocene gives only 1'-acetylbromoferrocene.[10] These results are in contrast with those of Morrison and Pauson[5] and emphasize the influence of conditions on the course of these reactions. In the case of iodoferrocene, repeated attempts at acetylation led only to unchanged starting material and ferrocene, itself. Thus, as would be expected, the iodine is more susceptible to electrophilic displacement by a proton than is chlorine or bromine.

Acetylation of acetamido- and alkoxycarbonylaminoferrocenes yielded predominantly the heteroannularly substituted isomer. In some cases a small yield of 1,2-isomer was isolated though never was any 1,3-product observed. The presence of predominantly heteroannular product indicates that the acetamido and alkoxycarbonylamino groups are deactivating substituents.

Further confirmation for the deactivating effects of these substituents comes from the study of the competitive acetylation of acetamidoferrocene and ferrocene. In this reaction the ferrocene was found to be more reactive than its substituted analogue by a factor of about two.

The acetylation of 1,1'-di(ethoxycarbonylamino)-ferrocene with boron trifluoride and acetic anhydride yielded two or three times more 3-acetyl than 2-acetyl substituted product. These results are similar to those obtained in studies of the acetylation of 1,1'-dimethylferrocene[9] and 1,1'-diethylferrocene.[11,12] Formylation of 1,1'-diethylferrocene produces only the 3-formyl product.[11] Thus in the disubstituted case, the predominance of 3-isomer stands in marked contrast to the absence of the 3-substituted homoannular isomer in the acetylation of monosubstituted acetamido- and urethanoferrocenes.

Pauson[13] has found that another powerfully electron-donating substituent,[14] methylthio-, is also deactivating in the aminomethylation reaction of ferrocene.

The effects of the substituents so far discussed in deactivating the aromatic rings of ferrocene to further electrophilic substitution is quite different from the effects of these groups on the ease of removal of an electron from the iron atom. Thus, it has been found from chronopotentiometric oxidation studies that

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TABLE II

INFRARED ABSORPTION BANDS OF SOME SUBSTITUTED FERROCENES[a]

Compound	Solvent	Absorption maxima, cm.$^{-1}$				
Acetamidoferrocene	CCl$_4$	3460	1694		1107	1005
	CHCl$_3$	3450	1682		1103	1001
	Nujol	3265 3220[b]	1654	1289	1103	1001
2-Acetylacetamidoferrocene	CCl$_4$	3340	1695, 1653	1292	Poor resolution in other regions	
	CS$_2$	3360	1700, 1659	1300	1109	1004
	Nujol	3345	1686, 1650	1305	1107	1006
1′-Acetylacetamidoferrocene	CCl$_4$	3445 (3320)[c]	1695, 1666	1278	1117	
	CHCl$_3$	3450 (3320)[c]	1686, 1666	1279	1112	
Methoxycarbonylaminoferrocene	CCl$_4$	3450	1745		1106	1007
2-Acetylmethoxycarbonylaminoferrocene	CCl$_4$	3350 (3450)[c]	1740, 1656	1296	1107	1005
1′-Acetylmethoxycarbonylaminoferrocene	CCl$_4$	3450 (3320)[c]	1743, 1673	1278	1115	
Ethoxycarbonylaminoferrocene	Nujol	3245	1715		1106	1001
2-Acetylethoxycarbonylaminoferrocene	CS$_2$[d]	3315 (3415)[c]	1722, 1645	1287	1099	994
	Smear[e]	3350	1730, 1655	1295	1105	1003
1′-Acetylethoxycarbonylaminoferrocene	CCl$_4$	3445 (3320)[c]	1738, 1671	1277	1115	
	Nujol	3270	1717, 1652	1282	1115	
1,1′-Di(ethoxycarbonylamino)ferrocene	CCl$_4$[f]	3450 (3375)[g]	1735	1305[h]		
2-Acetyl-1,1′-di(ethoxycarbonylamino)-ferrocene	CCl4	3447[i] 3345[j]	1735, 1654	1296		
	Nujol	3358 3248	1723, 1652 (1675)[h]	1301	1113[h]	
3-Acetyl-1,1′-di(ethoxycarbonylamino)-ferrocene	CHCl$_3$	3450	1725, 1664	1305		
	Nujol	3310	1726, 1640 1702	1304		
Bromoferrocene	Neat				1107	1005
	CCl$_4$				1108	1005
1′-Acetylbromoferrocene	CCl$_4$		1682	1276	1114	
Chloroferrocene	CS$_2$				1107	1003
1′-Acetylchloroferrocene	CCl$_4$[d]		1690	1281	1118	
Cyanoferrocene	CCl$_4$	2232			1109	1012
1′-Acetylcyanoferrocene	CCl$_4$	2234	1685	1277	1117	

[a] These spectra were determined on a Beckman IR-7 recording spectrophotometer. [b] Shoulder. [c] Very faint peak, presence is uncertain. [d] Spectrum appears to be shifted slightly due to improper tracking. [e] Spectrum of crude material after chromatography but before the material had solidified. [f] Solution was very concentrated. [g] May be due to intermolecular hydrogen bonding in the concentrated solution. [h] Very weak, but definitely present. [i] This peak is due to the urethane group in the 1′-position. [j] This peak is due to the urethane group in the 2-position; the shift is due to hydrogen bonding with the adjacent acetyl group.

acetamido, alkoxycarbonylamino and methoxy groups are strongly electron donating substituents.[15]

If one accepts that the interaction of the electrophile with the iron atom is an important step in the detailed mechanism for the electrophilic substiution of metallocenes[16,17] one would then expect factors which enhance the ease of oxidation also to facilitate electrophilic substitution. This is, however, not true in the present cases and leads to the suggestion that it is not the neutral species alone which are involved in the reactions just discussed but that the substrates exist in the reaction mixtures in large measure as conjugate acids which are markedly less reactive than either their neutral analog or than unsubstituted ferrocenes. In short, the observed effects are the complex result of equilibria between the neutral and protonated species and of the reaction rates for each of these forms.

Precedence for this view can be found in the work of Rosenblum[18] on the anomalous acetylation of ferrocene and in work on the electrophilic substitution of acetanilide. Brown[19] and Stock[20] have reported that the acetamino group is a powerful electron donator in mercuration and bromination reactions of acetanilide. In contrast to this, however, there are several studies which indicate that acetanilide is less reactive than benzene in certain nitration[21] and acetylation[22,23] reactions. In these latter cases the formation of salts or

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TABLE III

ULTRAVIOLET ABSORPTION DATA FOR SOME SUBSTITUTED FERROCENES[a]

Compound	λ_{max}, mμ[b]	ϵ_{max}[b]
Acetylferrocene	226[c,d]	16,500[c,d]
	269	6,500
Acetamidoferrocene	268	...
1'-Acetylacetamidoferrocene	222	18,300
	262	8,000
2-Acetylacetamidoferrocene	233[c]	21,250[c]
	265–270	10,700
	338–339	3,750
	237–238[e]	19,900[e]
	269–271	9,400
1'-Acetylethoxycarbonylaminoferrocene	222–223	19,000
	222–223[c]	20,200[c]
	220[e]	23,400[e]
	280 (broad shoulder)	3,000
2-Acetyl-1,1'-di(ethoxycarbonylamino)ferrocene	230	22,500
	280 (broad shoulder)	7,550
3-Acetyl-1,1'-di(ethoxycarbonylamino)ferrocene	226–227	22,150
	290 (very broad shoulder)	6,100
1'-Acetylbromoferrocene	223–224	...
	250–260 (inflection)	...
1'-Acetylcholoroferrocene	224–225	...
	270	...
1'-Acetylcyanoferrocene	221	19,900
	253	10,600
	325 (shoulder)	950
	220–222[e]	...
	254	...
	310	...

[a] These spectra were taken on a Cary Model 11M recording spectrophotometer. [b] In methanol unless otherwise indicated. [c] In 95% ethanol. [d] Ref. 9. [e] In cyclohexane.

complexes with the amide group is highly likely making the substituent deactivating.

Experimental

All melting points are uncorrected and were determined on an Eimer and Amend melting point block unless otherwise indicated. Nuclear magnetic resonance spectra were determined on a Varian Associates Model A-60 spectrometer.[24] Elemental analyses were performed by Elek Microanalytical Laboratory, Los Angeles, California, Spang Microanalytical Laboratory, Ann Arbor, Michigan, and Schwartzkopf Microanalytical Laboratory, Woodside, New York.

All reactions were carried out under nitrogen. Chromatography was performed on columns wrapped with aluminum foil to protect the compounds from light.

Preparation of Substrates.—Carbazidoferrocene was prepared in part by a procedure reported in the literature wherein chlorocarbonylferrocene is treated with sodium azide.[25,26] The procedure was modified in that the crude reaction product was purified by extraction with low-boiling petroleum ether in a Soxhlet apparatus. Quite pure carbazidoferrocene (m.p. 84.5–85°; lit.[25,26] m.p. 74–75° and 84–86°) crystallized in the reboiling flask; the yield was about 65% based on the starting amount of ferrocenecarboxylic acid.

Carbazidoferrocene was also prepared in a conversion of 56% by adding an aqueous solution of sodium azide to the mixed anhydride formed by the reaction of ethylchloroformate with a mixture of ferrocenecarboxylic acid and triethylamine. The procedure is identical with that reported by Weinstock for the synthesis of a different carboxylic acid azide.[27] This procedure for the preparation of carbazidoferrocene is very much faster than previously reported methods and it gives good conversion with little decomposition of starting material.

Acetamidoferrocene was prepared by heating carbazidoferrocene in acetic anhydride at about 80° until nitrogen evolution ceased; the resulting diacetylated amine was hydrolyzed to acetamidoferrocene when the crude reaction product was stirred with water for 18 hr. at room temperature. After chromatography on alumina the product was isolated in 73% yield in the form of yellow platelets (m.p. 168–170°; lit.[25] m.p. 170.5–172°). Careful recrystallization gave material melting at 173–173.5°.

Anal. Calcd. for $C_{12}H_{13}NO_2Fe$: C, 59.29; H, 5.39; N, 5.76. Found (Elek): C, 59.32; H, 5.44; N, 5.69.

Methoxycarbonylaminoferrocene and ethoxycarbonylaminoferrocene were prepared from carbazidoferrocene by the procedure of Schlögl.[26] 1,1'-Di(ethoxycarbonylamino)ferrocene was prepared according to the procedure given by Rosenblum.[28] 1,1'-Dibromoferrocene and bromo-, chloro-,[29] cyano-,[30] and iodoferrocenes[31] were prepared by procedures reported by Nesmeyanov.

Acetylation Reactions.—Isomeric products were separated by chromatography on Merck acid-washed alumina. Isomer yields were calculated on the basis of the the weight of materials isolated after removal of solvent from the chromatographic fractions but before any further purification was done. The purity of the materials at this stage of purification was checked by comparing the infrared spectra with spectra determined from analytical samples.

A standard procedure was followed for the acetylation of the ferrocene compounds with acetyl chloride and aluminum chloride. The acetylating reagent was made up according to the Perrier modification of the Friedel–Crafts synthesis by mixing acetyl chloride and excess aluminum chloride in dichloromethane at 0° under nitrogen; the excess aluminum chloride was filtered with glass wool. The acetylating reagent was added by means of a dropping funnel equipped with a pressure-equalizing side tube over a period of about 1 hr. to a solution of the ferrocene compound in dichloromethane at 0°. The reaction mixture was stirred from one to three hours at 0° and then it was poured into ice–water. The organic phase was separated and then dichloromethane washings of the aqueous phase were added to it. The organic solution was washed with saturated sodium bicarbonate solution and with water; it was then dried over anhydrous sodium sulfate. The mixture was filtered and solvent was flash-distilled under reduced pressure. The crude product was then chromatographed.

1'-Acetylacetamidoferrocene.—Acetamidoferrocene (2.2 g., 9 mmoles) and an equimolar amount of the acetylating reagent gave, after a reaction time of 1 hr., 1'-acetylacetamidoferrocene (0.965 g., 37.4% conversion) melting at 115.5–116°.

Anal. Calcd. for $C_{14}H_{15}NO_2Fe$: C, 58.97; H, 5.30; N, 4.91. Found (Elek): C, 59.00; H, 5.41; N, 4.88.

Recovered acetamidoferrocene weighed 0.923 g. (42% recovery). It is very possible that a small amount of 2-acetylacetamidoferrocene was formed but was not detected.

1'-Acetylmethoxycarbonylaminoferrocene and 2-Acetylmethoxycarbonylaminoferrocene.—Methoxycarbonylaminoferrocene gave by this procedure a low yield of the 2-acetyl isomer; the compound was isolated in an impure state as an oil. 1'-Acetylmethoxycarbonylaminoferrocene (m.p. 135–136°) was isolated in a yield of approximately 50%. Only the 1'-isomer was analyzed.

Anal. Calcd. for $C_{14}H_{15}NO_3Fe$: C, 55.84; H, 5.02; N, 4.65. Found (Spang): C, 56.00; H, 5.10; N, 4.54.

1'-Acetylbromoferrocene.—Bromoferrocene and a threefold excess of the acetylating reagent were stirred for 1.5 hr. at 0° and then for an additional 1.0 hr. with the ice bath removed. Chromatography of the crude product which resulted after working up the reaction mixture in the usual manner gave only 1'-acetylbromoferrocene (75% yield, m.p. 56–58°, lit.[10] m.p. 61.5–63°). No bromoferrocene was recovered.

Anal. Calcd. for $C_{12}H_{11}BrOFe$: C, 46.95; H, 3.61; Br, 26.03. Found (Spang): C, 47.02; H, 3.65; Br, 26.10.

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[24] We are indebted to Mr. Milton I. Levenberg for the n.m.r. spectral determinations.

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1′-Acetylchloroferrocene.—Chloroferrocene was acetylated under the same conditions as bromoferrocene. The acetylating reagent (9 mmoles) and chloroferrocene (0.585 g., 2.7 mmoles) gave, after purification by chromatography, only 1′-acetylchloroferrocene (0.562 g., 81%; m.p., sealed tube, 53–55°). Although the ketone itself was not analyzed, the acetate of the alcohol resulting from its reduction with sodium borohydride was analyzed. The acetate is a red-orange liquid, n^{25}_D 1.5806.

Anal. Calcd. for $C_{14}H_{15}ClO_2Fe$: C, 54.85; H, 4.93; Cl, 11.57. Found (Spang): C, 54.79; H, 5.06; Cl, 11.45.

Attempted Preparation of Acetyliodoferrocene.—Two runs on iodoferrocene, one at 0° and one at room temperature, using a slight excess of the acetylating reagent, failed to give any acetyliodoferrocene. In the run at 0° only acetylferrocene and a mixture of ferrocene and iodoferrocene were obtained. The n.m.r. spectrum of the nonketonic fraction indicated that ferrocene and iodoferrocene were present in about equal amounts. The second run gave acetylferrocene in a yield less than 1% and 1,1′-diacetylferrocene in a yield of about 15%. These two compounds were identified by comparing their melting points, infrared spectra, and n.m.r. spectra with those determined from authentic samples. A nonketonic fraction was isolated in a recovery of 45–50% (by weight, based on the weight of starting material). Any coupling products or diiodoferrocene which might have been present could have gone undetected in these two experiments even if they were present in quantities as great as 20% by weight of the total material recovered. It seemed that considerably more ferricinium ion was present at the end of the reactions than was noted in the case of the acetylation of bromo- and chloroferrocenes.

1′-Acetylcyanoferrocene.—Slightly more vigorous conditions were employed in the acetylation of cyanoferrocene than were generally used in the standard procedure. The acetylating reagent (60 mmoles) was added over a period of 20 min. to cyanoferrocene (3.5 g., 17 mmoles) in dichloromethane (100 ml.) at 0°. The ice bath was removed immediately after the addition was completed; the reaction mixture was then stirred for 5 hr. and worked up in the usual manner. Chromatography of the crude product gave only 1′-acetylcyanoferrocene (3.98 g., quantitative conversion; m.p. 99.8–101°).

Anal. Calcd. for $C_{13}H_{11}NOFe$: C, 61.94; H, 4.38; N, 5.54. Found (Elek): C, 61.82; H, 4.48; N, 5.41.

Acetylations Using Acetic Anhydride and Boron Trifluoride. 1′-Acetyl- and 2-Acetylacetamidoferrocenes.—Acetamidoferrocene (2.55 g., 10 mmoles) and acetic anhydride (0.97 g., 10 mmoles) were dissolved in dichloromethane (150 ml.) in a 200-ml. three-necked, round-bottomed flask equipped with a magnetic stirrer and gas inlet and outlet tubes. The solution was flushed with nitrogen and cooled with an ice bath. Boron trifluoride was bubbled into the solution for 3 min.; the color of the solution changed to a deep purple. The reaction mixture was stirred at 0° for 15 min. and then the ice bath was removed. The mixture was stirred for an additional 2.5 hr. and then it was hydrolyzed and worked up in the usual manner. Chromatography of the crude product gave three bands. A leading narrow orange band eluted with ether gave 2-acetylacetamidoferrocene (0.098 g., 4% based on unrecovered starting material) melting at 109–109.5°. A yellow band eluted with ether gave acetamidoferrocene (0.453 g., 17.8% recovery). A broad orange band eluted last with 3% methanol in benzene gave 1′-acetylacetamidoferrocene (2.068 g., 85% of theory based on unrecovered starting material) melting at 115.5–116°. This last compound was chromatographed a second time. Three fractions were collected; each fraction yielded only material having a melting point and infrared spectrum identical with those determined from the sample before chromatography. It should be noted that 1′-acetylacetamidoferrocene sometimes crystallizes in the form of long red-amber needles melting around 50°. These needles will, if heated slowly, undergo transformations at several intermediate temperatures and eventually melt at 115–116°. The infrared and ultraviolet spectra of the low melting crystals are identical with those previously determined for the higher melting crystals. Only 2-acetylacetamidoferrocene was analyzed since the other isomer possessed physical properties identical with those of a previously analyzed sample of 1′-acetylacetamidoferrocene.

Anal. Calcd. for $C_{14}H_{15}NO_2Fe$: C, 58.97; H, 5.30; N, 4.91. Found (Schwarzkopf): C, 59.04; H, 5.31; N, 5.16.

1′-Acetyl- and 2-Acetylethoxycarbonylaminoferrocenes.—Ethoxycarbonylaminoferrocene was acetylated according to the procedure used to acetylate acetamidoferrocene with these same reagents. 2-Acetylethoxycarbonylaminoferrocene was isolated as an oil in low yield. 1′-Acetylethoxycarbonylaminoferrocene. (m.p. 149.5–150°) was isolated in a yield of approximately 50%. Only the heteroannularly substituted isomer was analyzed.

Anal. Calcd. for $C_{15}H_{17}NO_3Fe$: C, 57.16; H, 5.44; N, 4.44. Found (Schwarzkopf): C, 56.93; H, 5.50; N, 4.66.

2-Acetyl- and 3-Acetyl-1,1′-Di(ethoxycarbonylamino)ferrocenes.—A solution of 1,1′-di(ethoxycarbonylamino)ferrocene (0.40 g., 1.1 mmoles) and acetic anhydride (0.15 g., 1.5 mmoles) in dichloromethane (30 ml.) was saturated at 0° with boron trifluoride and then stirred for 5 hr. with the ice bath removed. Chromatography of the crude product resulting after work-up gave four distinct bands. The first two bands, a leading yellow band and an orange band were incompletely separated and were eluted together with 10% ether in benzene as fraction one. A broad orange band was eluted next with 20% ether in benzene as fraction two. A very narrow red-orange band remained at the top of the column; this band did not move down the column even upon elution with pure ether. The material (probably less than 5 mg.) in this last band was not isolated.

Fraction two gave 3-acetyl-1,1′-di(ethoxycarbonylamino)ferrocene (0.206 g., m.p. 140.8–142°).

The material isolated from fraction one was chromatographed a second time; a partial separation of starting material and 2-acetyl-1,1′-di(ethoxycarbonylamino)ferrocene was achieved. Two fractional crystallizations of samples richer in one or the other of the two compounds finally gave pure crystals of each compound. It is estimated that the two compounds were present in nearly equal amounts. Carefully purified crystals of 2-acetyl-1,1′-di(ethoxycarbonylamino)ferrocene melt at 109.5–110°. The yield of the 3-acetyl compound is 46% (58% based on the estimated amount of recovered starting material). The yield of the 2-acetyl- isomer is 22%, based on the estimated amount of starting material recovered. Only the 3-acetyl isomer was analyzed; the many purification steps required gave pure 2-isomer in an amount to small for analysis.

Anal. Calcd. for $C_{18}H_{22}N_2O_5Fe$: C, 53.75; H, 5.51. Found (Schwarzkopf): C, 53.86; H, 5.68.

Acetylation with Silicon Tetraacetate and Stannic Chloride.—Acetamidoferrocene (0.27 g., 1.1 mmoles), silicon tetraacetate (0.16 g., 0.6 mmole), and stannic chloride (0.29 g., 1.1 mmoles) were dissolved in benzene (5 ml.) in a 10-ml. erlenmeyer flask and stirred at room temperature under a nitrogen atmosphere for 28 hr. The reaction mixture was worked up in the customary manner and the crude reaction product was chromatographed on alumina. Three bands were eluted. A leading narrow orange band was eluted with benzene; this material was not isolated but it is likely that it was 2-acetylacetamidoferrocene on the basis of experiments conducted later with other acetylating reagents.

A yellow band eluted second with ether gave acetamidoferrocene (0.107 g.). The melting point and infrared spectrum were identical with those of starting material.

A broad orange band eluted last with 3% methanol in benzene gave 1′-acetylacetamidoferrocene (0.094 g., 50% based on recovered starting material).

Competitive Acetylation of Ferrocene and Acetamidoferrocene.—A 1:1 mixture of acetyl chloride and aluminum chloride (6.07 mmoles) was added over a period of 20 min. to ferrocene (1.13 g., 6.07 mmoles) and acetamidoferrocene (1.48 g., 6.07 mmoles) in 60 ml. of dichloromethane at 0°. The reaction mixture was stirred for 0.5 hr. at 0°; the ice bath was removed and the mixture was hydrolyzed and worked up in the usual manner. Recrystallization of the crude solid resulting gave well-formed platelets of acetamidoferrocene (0.854 g.). Chromatography of the filtrate on alumina gave ferrocene (0.837 g., 74% recovery), acetylferrocene (0.305 g., 22% conversion or 86% based on recovered ferrocene), acetamidoferrocene (0.445 g., total amount recovered is 88%) and 1′-acetylacetamidoferrocene (0.135 g., 7.8% conversion or 65% based on recovered acetamidoferrocene).

In a second run the reaction was carried out at room temperature. Ferrocene (1.052 g., 5.66 mmoles) and acetamidoferrocene (1.377 g., 5.66 mmoles) added initially gave acetylferrocene (0.317 g., 24.5% conversion or 96.5% based on recovered ferrocene) and 1′-acetylacetamidoferrocene (0.174 g., 10.8% conversion or 120% based on recovered acetamidoferrocene). Recrystallization of the 0.174 g. of 1′-acetylacetamidoferrocene isolated after chromatography gave 0.084 g. of well formed crystals (5.2% conversion of 58% based on recovered acetamidoferrocene). Ferrocene isolated after chromatography of the crude acetylation products weighed 0.784 g. (74.5% recovery); acetamidoferrocene similarly recovered weighed 1.256 g. (91.2% recovery).

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Base Strengths of Alkylpyridines Using Triethylaluminum as the Reference Acid. A Study in F Strain

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The heats of reaction of a series of alkylpyridines with triethylaluminum have been measured. The order of the relative base strengths observed suggests steric factors were operative in qualitatively the manner predicted on the basis of the F strain concept of Brown and coworkers. The magnitude of these effects, however, was considerably smaller than observed previously with trimethylboron as the reference acid. The source of these differences together with some anomalous results obtained are discussed and suggested reaction schemes presented.

Brown and co-workers in a series of investigations have shown that the relative base strengths of alkylpyridines depend on the structure of the reference acid.[3-5] The basicity towards proton increases with alkyl group substitutions on the pyridine ring, as one would predict from simple inductive effects. On the other hand, as the "steric requirements" of the reference acid (Lewis acid) increase, the order of the observed relative base strengths of the alkylpyridines is different than for protonic acids. The basicity of the alkylpyridines depends on the size and position of the alkyl groups. One of the most dramatic examples cited is that of 2,6-lutidine (2,6-dimethylpyridine). Although a strong base for protonic acid ($-\Delta H = 19.5$ kcal./mole for CH_3SO_3H), a very low heat of reaction was observed with trimethylboron.[3,4]

This result has been interpreted by Brown and coworkers to be due to the steric repulsion of the alkyl groups of the reference acid and the alkyl groups surrounding the nitrogen atom of the pyridine ring. This type of contribution of steric factors to chemical reactivity has been called F strain.[3] Due in large measure to the work of Brown and co-workers, an excellent fund of data is now available on the influence of steric strain in the reactions of hindered nitrogen bases with alkylboron compounds. In contrast, very little is known of the contribution of steric factors to the reactivity of hindered nitrogen bases with other structurally related organometallic compounds, in particular with trialkylaluminum.

In this present study, we have measured the heats of reaction of various alkylpyridines with triethylaluminum. One objective of this work has been to compare the importance of F strain in the chemical reactivity of alkylpyridines as the central atom of the reference acid was changed from boron to aluminum.

Experimental

Materials.—Normal decane was chosen as the solvent for these reactions because of its low vapor pressure at room temperature. A practical grade of normal decane was rapidly stirred with concentrated sulfuric acid (3 l. of decane/1 l. of concentrated sulfuric acid) for several days at room temperature. The ultraviolet spectrum of the decane was scanned to detect residual unsaturation (250–290 mμ). When no ultraviolet absorption was detected, the decane layer was separated, washed twice with dilute potassium hydroxide followed by three washings with distilled water. The *n*-decane was then dried with anhydrous calcium sulfate and finally stored over calcium hydride. The decane was purged with nitrogen and stored in a nitrogen atmosphere.[5b] The middle third (b.p. 115.2°, lit. b.p. 115.3°, $n^{20}D$ 1.5090, lit. b.p. 1.5092) was collected and stored over calcium hydride. The 2,6-dimethylpyridine (99% pure from Matheson, Coleman and Bell) was distilled from potassium hydroxide through a 12-in. Vigreux column under a reduced nitrogen pressure. The middle third ($n^{20}D$ 1.4967) was collected and stored over calcium hydride. The 2-methyl-6-ethylpyridine, 2-methyl-6-*n*-propylpyridine, and 2-methyl-6-isobutylpyridine were obtained as pure research samples from Reilly Tar and Chemical Company. Before use, they were stored over calcium hydride. The triethylaluminum was obtained from the Ethyl Corporation. According to their analysis, this sample was 97.5% by weight triethylaluminum (minimum), the remainder being primarily butylaluminum compounds. All handling of the triethylaluminum was carried out under a protective blanket of dry nitrogen. All of the equipment used in preparing the triethylaluminum solutions in *n*-decane was rigorously dried.

Colorimetric Procedure.—The calorimeter and technique used for measuring the heats of reaction was similar to that described by Brown and Horowitz.[6] Because of a slight difference in the geometry of the mixing chamber, we used 100 g. of mercury to provide the seal between the storage chambers. Thirty milliliters each of the 0.1 *M* solutions of the reagents were used in these experiments. All of these measurements were made at 27.4 ± 0.02°.

Even after completion of the reaction, care was taken to avoid oxidation of the triethylaluminum. After completion of the run, the solution and mercury were drawn out under vacuum. The calorimeter was then rinsed with cyclohexane, disassembled, washed, and dried.

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(2) From the thesis of S. Liebman submitted in partial fulfillment of the requirements for the degree of Master of Science, College of Arts and Sciences, American University, 1960.

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