Metalation of *o-tert*-Butylanisole (3) with *n*-Butyllithium and TMEDA. Condensation with Benzophenone to Produce 2-*tert*-Butyl-6-diphenylhydroxymethylanisole (6).—*o-tert*-Butylanisole (3) (3.28 g, 0.02 mol) was dissolved in 50 ml of dry ether. TMEDA (2.22 g, 0.0192 mol) was added, and under an argon atmosphere 12 ml (0.0192 mol) of 1.6 *M* *n*-butyllithium was slowly added. The mixture was stirred for 1 hr and treated with benzophenone (3.5 g, 0.0192 mol) in 20 ml of ether. The mixture was stirred for 4 hr and hydrolyzed with 20 ml of water. The ether layer was separated, washed with water, dried over MgSO₄, and stripped. The resulting oil was purified by heating in a steam bath overnight at 0.01 mm to remove unreacted *o-tert*-butylanisole (3) and benzophenone. An ir of the resulting oil indicated that some benzophenone still remained. The oil was subjected to steam distillation until an ir spectrum of the residue indicated that all the benzophenone had been removed. The absence of any definitive absorptions in an nmr spectrum of this residue indicated that it was contaminated by some paramagnetic material, probably a result of the steam distillation. The oil was dissolved in ether and washed through a column of sand

and magnetic stirring bars. Upon removal of the solvent an oil resulted and the nmr and elemental analysis data given below were consistent with the structure 2-*tert*-butyl-6-diphenylhydroxymethylanisole (6) (yield 1.73 g, 25%): ir 2.94 (–OH), 5.10, 5.31, 5.53 (1,2,3-trisubstituted benzene), 7.90 (–OCH₃), 8.20 *μ* [–C(CH₃)₃]; nmr (CDCl₃) *τ* 2.59–3.63 (multiplet, 13.9 protons, HO(C₆H₅)₂CC₆H₃–), 6.96 (singlet, 3.2 protons, –OCH₃), 8.58 [singlet, 8.9 protons, –C(CH₃)₃].

Anal. Calcd for C₂₄H₂₆O₂: C, 83.02; H, 7.56. Found: C, 82.96; H, 7.75.

Directed Metalation Reactions. IV.[1] 2-Metalation of N-Substituted Ferrocenecarboxamides

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Demonstration of the 2-metalating ability of the N-substituted carboxamide group in ferrocene is presented. By means of the 2-lithiated intermediate a series of 1,2-disubstituted ferrocenes, where one of the substituents is the carboxamide group, has been prepared. That this procedure will be useful for the preparation of 2-substituted ferrocenecarboxylic acids has been shown by the three-step synthesis, starting from ferrocene, of 2-methylferrocenecarboxylic acid.

Puterbaugh and Hauser in 1963[2] demonstrated the interesting phenomenon of the directing ability of the methyl amide substituent in the 2-metalation of the benzene nucleus. This served to extend the original observation from the Hauser group of the directing ability of the dimethylaminomethyl substituent in both the benzene[3] and ferrocene[4] systems. Metalation of the amide functional group was postulated to occur by successive removal of two protons: the first from the monosubstituted amide group to produce a resonance-stabilized anion; the second from the 2 position of the benzene ring, with a coordinated lithio intermediate similar to that described for the 2-lithiation of aromatics containing the dimethylaminomethyl substituent being proposed (Scheme I). The resonance-stabilized anion which was produced by the removal of the nitrogen proton was felt to significantly reduce the tendency of the carbonyl group to undergo nucleophilic attack. Hence electrophilic attack of the more reactive second position of metalation, *i.e.*, the 2 position of the aromatic ring, could be observed.

In these laboratories we have observed that directed metalation reactions of monosubstituted benzenes can be made to occur in their ferrocene counterparts, often

SCHEME I
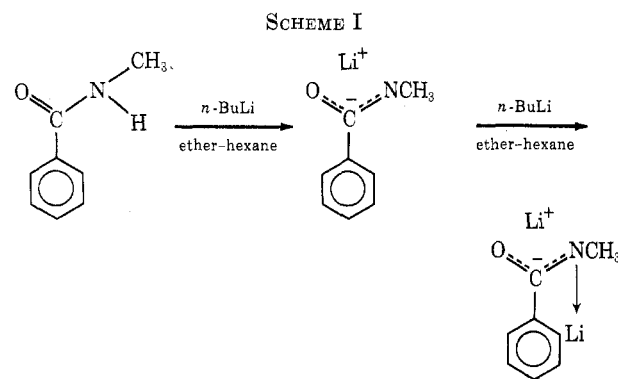
with greater facility.[5] These observations, coupled with our desire to examine methods of synthesizing 2-substituted ferrocene derivatives, prompted an investigation of the use of the directed metalation of N-ethylferrocenecarboxamide (1).

Results and Discussion

N-Ethylferrocenecarboxamide (1) was metalated with 1.5 equiv of *n*-butyllithium and condensed with various reagents in order to test the suitability of the procedure as a method of synthesizing 1,2-disubstituted ferrocenes. The N-ethyl derivative was chosen for examination because of its recorded preparation;[6] the

(1) For part III, *cf.* D. W. Slocum and B. P. Koonsvitsky, *J. Org. Chem.*, **38**, 1675 (1973).

(2) W. H. Puterbaugh and C. R. Hauser, *J. Amer. Chem. Soc.*, **85**, 2467 (1963).

(3) (a) F. N. Jones, M. F. Zinn, and C. R. Hauser, *J. Org. Chem.*, **28**, 663 (1963); (b) F. N. Jones, R. L. Vaulx, and C. R. Hauser, *ibid.*, **28**, 3461 (1963).

(4) D. W. Slocum, B. W. Rockett, and C. R. Hauser, *J. Amer. Chem. Soc.*, **87**, 1241 (1965).

(5) *Cf.*, for example, D. W. Slocum, C. A. Jennings, T. R. Engelmann, B. W. Rockett, and C. R. Hauser, *J. Org. Chem.*, **36**, 377 (1971); D. W. Slocum, B. P. Koonsvitsky, and C. R. Ernst, *J. Organometal. Chem.*, **38**, 125 (1972).

(6) M. D. Rausch, P. Shaw, D. Mayo, and A. M. Lovelace, *J. Org. Chem.*, **23**, 505 (1958).

N-methyl derivative was later found to be accessible by the same route. That one of the two substituents of the 1,2-disubstituted ferrocene systems thus produced was an amide was of particular interest, compared to the directing groups previously studied in the ferrocene system, since numerous additional derivative possibilities could be prepared through the hydrolysis product of the amides, namely, the 2-substituted carboxylic acids. Thus the scope of the reaction was limited only by the type of electrophilic condensing reagents that would react, the ease of hydrolysis of the amide, and the reactions the derived carboxylic moiety could undergo. As we shall see, these are significant limitations to the convenience of this particular synthetic technique for the preparation of 1,2-disubstituted ferrocenes.

The ability of the N-ethylamide functional group to direct lithiation to the 2 position of ferrocene was demonstrated by two independent routes. The first method, shown in Scheme II, was to synthesize 2-

SCHEME II
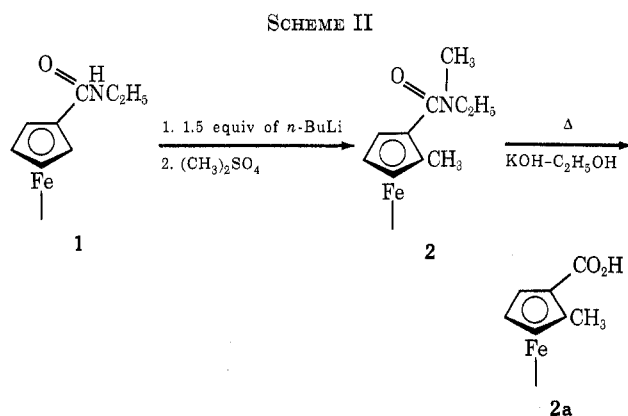
methylferrocenecarboxylic acid (2a) *via* the carboxamide route and match its properties with those reported for the known compound.[7] It was also found possible to prepare 2-methyldimethylaminomethylferrocene (4) by two separate methods (Scheme III). One of these was *via* the carboxamide route; the other was *via* the 2-lithiation of dimethylaminomethylferrocene (DMAMF) (3). The fact that the last-mentioned compound has clearly been demonstrated to undergo metalation in the 2 position establishes without question that the carboxamide functional group on ferrocene also directs metalation to the 2 position.

Scheme III contains two steps that deserve comment. It has been reported that certain ferrocene carboxamides cannot be hydrolyzed;[8] however, the N-methyl-N-ethylamide 2 was found to undergo basic hydrolysis but not with great ease. The two steps in Scheme III leading to 2-methyldimethylaminomethylferrocene (4) utilize an amine exchange reaction that was developed in this laboratory; recently Ugi and coworkers have reported a similar reaction.[9] This amine exchange procedure has proved to be convenient for the

substitution of a dimethylamine functional group in place of other types of substituted amines.

The conditions found to maximize the yield of 2-methylcarboxamide 2 from the metalation of carboxamide 1 followed by derivatization with dimethyl sulfate were a mole ratio of 1.5:1.0 n-butyllithium/carboxamide 1 in THF solvent. Higher ratios gave significant unsubstituted ring metalation, as noted in other ferrocene systems.[4,5] A time study of the reaction showed the yield of 2-methyl carboxamide 2 to reach a maximum after 10 min. In each trial of the study 0.6 g (2.30 mmol) of N-ethylferrocenecarboxamide (1), 2.5 ml of 1.6 M n-butyllithium in ether–hexane, and 50 ml of purified, dry THF were used. The data are shown in Table I.

TABLE I

TIME STUDY OF 2-METHYLATION OF LITHIATED
N-ETHYLFERROCENECARBOXAMIDE (1)

Time, min	Quantity of 2-methylcarboxamide 2, mmol	Quantity of N-methyl-N-ethyl-ferrocenecarbox-amide 9, mmol	Summation of the two products, mmol
1	0.49 (0.49)[a]	1.66 (1.61)	2.15 (2.10)
8	0.63	1.48	2.11
10	0.70 (0.66)	1.36 (1.36)	2.06 (2.02)
15	0.35	1.30	1.65
20	0.18 (0.21)	1.44 (1.48)	1.62 (1.69)
30	0.07	1.59	1.66

[a] Figures in parentheses represent duplicate runs.

Scheme IV depicts the proposed successive removal of protons from N-ethylferrocenecarboxamide (1) necessary to explain the reported observations. The mono-N-anion 1a could give rise to N-methyl-N-ethyl-ferrocenecarboxamide (9) when treated with dimethyl sulfate. This product could also be argued to arise just as easily from incomplete derivatization of the dianion intermediate 1b, but the fact that no product was detected arising from substitution at only the more reactive site, namely, the 2-lithio position, mitigates strongly against this supposition. The dianion 1b would be the only path leading to 2-methyl carboxamide 2.

The relative dianion (1b) and mono-N-anion (1a) concentrations were conveniently followed by the isolation of 2-methyl carboxamide (2) and N,N-disubstituted carboxamide (9) produced upon treatment with dimethyl sulfate. Since from Table I the dianion product can be seen to have increased at a rate similar to that for the decrease of the monoanion product over the first 10 min, it can be deduced that the 2-methyl N,N-disubstituted carboxamide 2 was derived from an equilibrium involving the mono-N-anion 1a. After a period of 10–15 min, the dianion 1b apparently abstracts a proton and regenerates the mono-N-anion. This seems plausible, since as further time passed the dianion product 2 decreased by the same magnitude as the mono-N-anion product 9 increased.

The yield of 2-methyl N,N-disubstituted carboxamide 2 falls off sharply after 10 min, as does the combined yield of products. After the maximum yield of product 2 was reached (10 min), it was observed that one-third of the starting material was lost. Up to this point the material balance had been within experimental error. Possibly a different reaction occurred at the

(7) G. Haller and K. Schlogl, *Monatsh. Chem.*, **98**, 603 (1967); H. Falk, G. Haller, and K. Schlogl, *ibid.*, **98**, 592 (1967).

(8) N. Weliky and E. S. Gould, *J. Amer. Chem. Soc.*, **79**, 2742 (1957).

(9) G. Gokel, P. Hoffmann, H. Kleimann, H. Klusacek, C. Marquarding, and I. Ugi, *Tetrahedron Lett.*, 1771 (1970).

SCHEME III

SCHEME IV
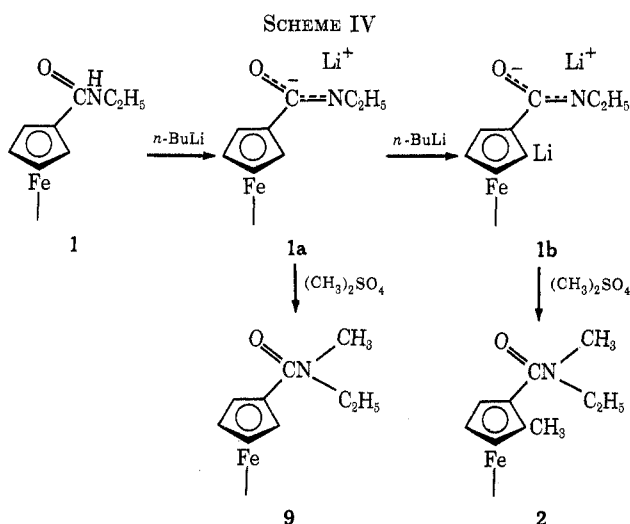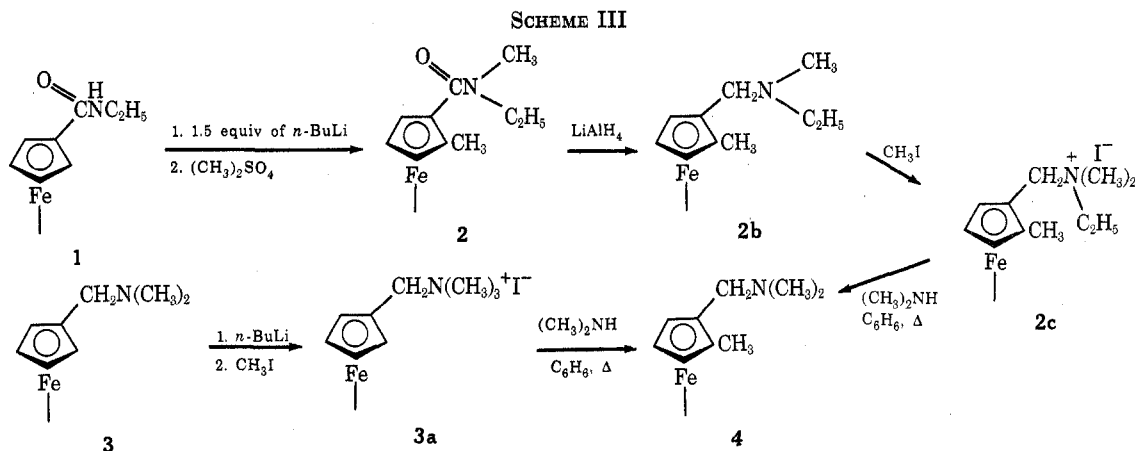
10-min point. This unknown reaction yielded no new identifiable products. After the initial decline in products was observed, the summation of the two products remained relatively constant over a 15-min interval, indicating that the competing reaction was no longer interfering. The nature of this very rapid reaction remains uncertain.

Table II lists the new 1,2-disubstituted ferrocenes

TABLE II

NEW 1,2-DISUBSTITUTED FERROCENES PREPARED FROM
N-ETHYLFERROCENECARBOXAMIDE (1)

Compd	Molecular formula[a]	Ir spectrum, cm^{-1}[b]
2-Methyl-*N*-methyl-*N*-ethyl-ferrocenecarboxamide (2)	$C_{15}H_{19}NOFe$	2950, 1625 (C=O), 825
2-Ethyl-*N*,*N*-diethylferrocene-carboxamide (5)	$C_{17}H_{23}NOFe$	2970, 1629 (C=O), 825
2-*n*-Propyl-*N*-*n*-propyl-*N*-ethyl-ferrocenecarboxamide (6)	$C_{19}H_{27}NOFe$	3000, 2980, 1630 (C=O), 825
2-Trimethylsilyl-*N*-ethyl-ferrocenecarboxamide (7)	$C_{16}H_{23}NOSiFe$	1670, 1280, 1240
2-Diphenylhydroxymethyl-*N*-ethylferrocenecarboxamide (8)	$C_{26}H_{25}NO_2Fe$	
2-Methyl-*N*,*N*-dimethylamino-methylferrocene (4)	$C_{14}H_{19}NFe^c$	2920, 1930, 735

[a] Satisfactory analytical data were reported for all compounds listed in the table, unless otherwise noted. [b] The usual 9- and 10-*μ* bands indicative of homoannular substitution were found for all ferrocenes and are not recorded. [c] *Anal.* Calcd: C, 65.41; H, 7.40; N, 5.45; Fe, 21.74. Found: C, 65.98; H, 7.63; N, 5.37; Fe, 20.35.

which have been prepared by 2-lithiation of *N*-ethyl-ferrocenecarboxamide (1) as a result of this investigation.

Experimental Section

General starting materials were obtained from Matheson Coleman and Bell. Arapahoe Chemical Co. supplied the ferrocene starting materials. All starting materials were checked for purity prior to use. Foote Mineral Co. supplied the organolithium reagents. All reactions involving the use of organolithium reagents were conducted under an inert atmosphere of argon. Ethyl isocyanate was a complimentary sample supplied by Ott Chemical Co. Nmr data were obtained on a Varian A 56/60 spectrometer at 44° with internal tetramethylsilane (TMS) standard. Concentrations were approximately 10% by volume in CDCl$_3$ unless otherwise stated. All ir spectra were obtained on a Perkin-Elmer Model 137 infracord either as smears or Nujol mulls using the 6.25-*μ* band of polystyrene as a reference. All ferrocene compounds possessed the 9–10-*μ* band which was characteristic of an homoannularly unsubstituted cyclopentadiene ring. The 9–10-*μ* bands are underlined. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and all melting points were corrected.

Metalations were performed by injecting the requisite amount of *n*-butyllithium into a closed flask containing a side arm fitted with a septum and a water-cooled condenser fitted with a drying tube.

A. Preparation of 2-Methyl-*N*-methyl-*N*-ethylferrocenecarboxamide (2).—To a solution of 0.6 g (0.023 mol) of *N*-ethylferrocenecarboxamide (1) in 50 ml of purified THF, 2.5 ml of a 1.6 *M* solution of *n*-butyllithium was injected. The lithiation was allowed to proceed for 10 min and then 0.5 ml of dimethyl sulfate was quickly injected into the solution and the solution was allowed to stir for 30 min. The reaction mixture was evaporated to constant weight, suspended in water, and extracted with several portions of methylene chloride. Anhydrous MgSO$_4$ was used to dry the combined extracts, which were evaporated and chromatographed on basic alumina II. The product was eluted with a 50:50 mixture of petroleum ether (bp 30–60°)–methylene chloride. Three bands were observed on the chromatography column. The first band eluted was an oil weighing 0.2 g (30.4%); the following analytical data identified it as 2-methyl-*N*-methyl-*N*-ethylferrocenecarboxamide (2). The second band was also an oil, weighing 0.37 g (59%), and was identified as *N*-methyl-*N*-ethylferrocenecarboxamide (9). The third band, a red material, was isolated in only a trace amount.

Nmr data for 2-methyl-*N*-methyl-*N*-ethylferrocenecarboxamide (2): δ 1.10 (t, 8.0, *J* = 7.6 Hz), 2.1 (s, 3.0), 2.95 (s, 3.0), 3.40 (AB quartet, 2.0, *J* = 7.3 Hz), 4.18 (m, 7.9). Nmr data for *N*-methyl-*N*-ethylferrocenecarboxamide (9): δ 1.18 (t, 3.0, *J* = 7.5 Hz), 3.06 (s, 3.0), 3.51 (AB quartet, 2.1, *J* = 7.0 Hz), 4.18 (s, 5.1), 4.26 (m, 1.9), 4.59 (m, 2.0). Ir data: major peaks at 2960, 1625 (C=O), 1110, 1000, and 830 cm^{-1}. *Anal.* Calcd for $C_{14}H_{17}NOFe$: C, 62.03; H, 6.28; N, 5.17; Fe, 20.62. Found: C, 62.25; H, 6.32; N, 5.22; Fe, 20.46.

Preparation of 2-Methylferrocenecarboxylic Acid (2a).—A solution of 0.1 g (0.35 mol) of 2-methyl-*N*-methyl-*N*-ethylferrocenecarboxamide (2) and 20.0 g of KOH in 30 ml of 95% ethanol was refluxed under an argon atmosphere for 3 days. At the end of the first day 25 ml of 95% ethanol was added and allowed to distil from the reaction mixture. The mixture was then brought up to approximately 50 ml volume and argon was flushed through the system, which was then allowed to reflux for another day. This procedure was repeated at the end of the second day. At the end of the third day the sample was distilled almost to dryness. This mixture was then partitioned between 10% NaOH and methylene chloride. The aqueous layer was acidified with 10% H₂SO₄ and extracted several times with methylene chloride. The combined methylene chloride extracts were washed several times with water, dried over anhydrous MgSO₄, and evaporated to dryness to yield 0.03 g (35.2%) of crystalline acid 2a, mp 151–153°. A sublimed sample had a melting point of 155–156° (lit.[7] mp 158–160°). Nmr data: δ 2.29 (s, 3.0), 4.17 (s, 5.0), 4.33 (m, 2.4), 4.79 (m, 1.5). The carboxyl group proton was not discernible; however, from integration it was probably broadly spread out under the δ 4.33 and 4.79 multiplet. Ir data: major peaks at 3300 (OH), 1670 (C=O), 1280, 1240, *1120*, and *1000* cm⁻¹.

Anal. Calcd for C₁₂H₁₂O₂Fe: C, 59.06; H, 4.92. Found: C, 59.36; H, 5.21.

Preparation of 2-Methyl DMAMF (4) from 2-Methylcarboxamide (2).—To a stirring suspension of ether and LiAlH₄, 1.0 g (3.5 mol) of 2-methyl-*N*-methyl-*N*-ethylferrocenecarboxamide (2) dissolved in ether was slowly added. The reaction was kept at reflux temperature for 24 hr. After this period water and 15% NaOH were added to decompose excess LiAlH₄. The reaction mixture was acidified and extracted with ether. The aqueous layer was then made basic and this basic solution was extracted with ether. Reduction afforded 0.8 g (82%) of 2-methyl-*N*-ethyl-*N*-methylaminomethylferrocene (2b). This amine was treated with an excess of methyl iodide to form the quaternary ammonium salt 2c. The quaternary salt 2c was subjected to an amine exchange reaction. Dimethylamine was passed for 3 days through a refluxing heterogeneous mixture of 100 ml of benzene and 1.0 g of methiodide 2c. The reaction mixture was acidified with 10% H₂SO₄ and extracted with ether. The aqueous layer was made basic with 10% NaOH and extracted with ether. This latter ether layer was dried over anhydrous MgSO₄, filtered, and stripped to give 0.6 g of an oily product. This oil was chromatographed on basic alumina IV. The material was eluted with petroleum ether (trace of ether) solvent to yield 0.6 g (92%) of 2-methyl DMAMF (4).

B. Preparation of 2-Ethyl-*N*,*N*-diethylferrocenecarboxamide (5).—To a solution of 0.6 g (2.4 mmol) of *N*-ethylferrocenecarboxamide (1) in 25 ml of purified THF, 2.5 ml (1.6 *M*) of *n*-butyllithium was injected and the solution was allowed to stir for 10 min. At the end of 10 min, the mixture was quickly treated with an excess of diethyl sulfate in THF and subsequently allowed to stir for 1 hr. After the solvent had been stripped, the resulting thick oil was taken up in methylene chloride, washed several times with water, dried over MgSO₄, and then chromatographed on basic alumina IV with a solvent system of 50:50 petroleum ether–methylene chloride. Three bands were observed and separated. Band I was eluted as an oil and was shown to be 2-ethyl-*N*,*N*-diethylferrocenecarboxamide (5), 0.16 g (22%). Band II, a crystalline solid, was *N*,*N*-diethylferrocenecarboxamide (10), 0.35 g (53%), mp 59–60°. Band III was starting material 1, 0.15 g (25%).

Nmr data for 2-ethyl-*N*,*N*-diethylferrocenecarboxamide (5): δ 1.10 and 1.11 (overlapping t, 9.0, *J* = 7.0 Hz each), 2.46 (m, 2.0), 3.30 (m, 4.0), 4.11 and 4.21 (m and s, respectively, 8.0).

Nmr data for *N*,*N*-diethylferrocenecarboxamide (10): δ 1.20 (t, 6.2, *J* = 7.5 Hz), 3.52 (AB quartet, 3.9, *J* = 7.0 Hz), 4.23 (m, 7.2), multiplet centered at 4.65 (m, 1.8).

Preparation of 2-Ethyl-*N*,*N*-diethylaminomethylferrocene (5a). —To a large excess of LiAlH₄ suspended in a vigorously stirred solution of ether, 0.16 g (0.5 mmol) of 2-ethyl-*N*,*N*-diethylferrocenecarboxamide (5) dissolved in ether was slowly added. The reaction mixture was refluxed overnight. Excess LiAlH₄ was hydrolyzed with 10 ml of water followed by 10 ml of 10% NaOH. The solution was extracted with ether and the ether extracts were evaporated to a dark oil, which was chromatographed with petroleum ether on basic alumina IV yielding 0.14 g (98%) of amine 5a as an oil. Nmr data: δ 1.06 (m,

9.0), 2.38 (m, 6.1), 3.42 (AB quartet, 2.0, ν₁ = 3.31, ν₂ = 3.54, *J* = 13.5 Hz), 4.00 (m, 8.3). Ir data: major peaks at 3010, *1110*, *1000*, and *830* cm⁻¹.

Preparation of 2-Ethyl DMAMF (5b).—2-Ethyl-*N*,*N*-diethylaminomethylferrocene (5a) (0.14 g) was treated with methyl iodide, producing the quaternary ammonium salt. The salt was filtered, dried, and found not to possess a sharp melting point. This quaternary salt was refluxed in benzene–dimethylamine for 3 days to produce 0.08 g of crude oil product. The oil was chromatographed on basic alumina IV; 0.01 g (7.7%) of an oil identified as 2-ethyl DMAMF (5b) was eluted. Physical and spectral properties of this oil were in accord with those reported by Nesmeyanov and coworkers[10] for this compound prepared by a less direct method. Nmr data: δ 1.17 (t, 3.0, *J* = 7.5 Hz), 2.27 (AB quartet and s, 8.1, *J* = 7.5 Hz), 3.25 (AB quartet, 2.0, ν₁ = 3.16, ν₂ = 3.35, *J* = 12.5 Hz).

C. Preparation of 2-*n*-Propyl-*N*-ethyl-*N*-*n*-propylferrocenecarboxamide (6).—To a stirring solution of 4.0 g (0.015 mol) of *N*-ethylferrocenecarboxamide (1) in THF, 20.0 ml (0.03 mol) of *n*-butyllithium was injected. The solution was allowed to react for 10 min and quickly treated with an excess of di-*n*-propyl sulfate. The reaction was allowed to stir for 1 hr at room temperature and hydrolyzed with water. The aqueous THF solution was stripped under vacuum and the resultant thick oil was taken up in ether and washed with water several times. The ether layer was dried over MgSO₄ and evaporated to a thick oil, which was chromatographed on a 50:50 mixture of alumina I–alumina IV using a 50:50 mixture of methylene chloride–petroleum ether, yielding first starting material (90% recovery) and 0.4 g (7.6%) of 2-*n*-propyl-*N*-ethyl-*N*-*n*-propylferrocenecarboxamide (6). Nmr data: δ 0.61–1.68 (m, 13.2), 2.13–2.45 (m, 1.9), 2.80–3.40 (m, 3.9), 4.08 (m, 8.0).

D. Preparation of 2-Trimethylsilyl-*N*-ethylferrocenecarboxamide (7).—To a stirring solution of 0.6 g (2.34 mmol) of *N*-ethylferrocenecarboxamide (1) in 25 ml of THF, 2.5 ml (1.6 *M*) of *n*-butyllithium was quickly added. The mixture was allowed to stir under an argon atmosphere for 10 min. Trimethylchlorosilane (1.5 ml, 0.014 mol) was added and allowed to stir for 1 hr. To ensure complete removal of THF, the reaction mixture was evaporated to dryness repeatedly with subsequent additions of methylene chloride. The material was then extracted several times with a water–methylene chloride system. The methylene chloride portion was dried with anhydrous MgSO₄, filtered, and evaporated to dryness. The solid material obtained was subjected to column chromatography on alumina IV. 2-Trimethylsilyl-*N*-ethylferrocenecarboxamide (7) was the first material eluted from the column with a solvent system of 50:50 petroleum ether–methylene chloride, 0.09 g (12.3%), mp 139–141°. Nmr data: δ 0.33 (s, 9.0), 1.22 (t, 2.9, *J* = 7.0 Hz), 4.17 (s, 5.1), 4.26 (m, 0.9), 4.40 (m, 1.0), 4.60 (m, 1.0).

E. Preparation of 2-Diphenylhydroxymethyl-*N*-ethylferrocenecarboxamide (8).—To a solution of 0.6 g (2.4 mmol) of *N*-ethylferrocenecarboxamide (1) in 50 ml of purified THF, 2.5 ml (1.6 *M*) of *n*-butyllithium was quickly added and the solution was allowed to stir for 10 min. The reaction was then treated with an excess of benzophenone in THF and allowed to stir for 12 hr. The solvent was removed by vacuum distillation, yielding a thick, syrupy material which was dissolved in ether and washed several times with water. The ether layer was dried with MgSO₄ and evaporated to dryness. The material was chromatographed on basic alumina IV with a 50:50 petroleum ether–methylene chloride solvent system and the products were eluted in the following order: 0.49 g (82%) starting material 1, 0.05 g (5%) 2-diphenylhydroxymethyl-*N*-ethylferrocenecarboxamide (8), mp 245–246°, and a trace of a red colored material. Nmr data: δ 0.96 (t, 3.0, *J* = 7.0), 3.15 (quartet, 2.0) 3.66 (m, 0.9), 4.38 (m, 7.0), 5.91 (s, 1.0), 7.38 (m, 10.0), 8.21 (s, 1.0).

F. Preparation of 2-Methyl DMAMF (4) *via* Amine Exchange Reaction.—Dimethylamine was passed for 3 days through a refluxing heterogeneous mixture of 100 ml of benzene and 1.0 g of the 2-methylmethiodide of DMAMF (3a).[11] The reaction mixture was acidified with 10% H₂SO₄ and extracted with ether. The aqueous layer was made basic with 10% NaOH and extracted with ether. This latter ether layer was dried over anhydrous MgSO₄, filtered, and stripped to give 0.6 g of an oily product.

(10) L. S. Shilovtseva, E. G. Perevalova, V. A. Nefedov, and A. N. Nesmeyanov, *Dokl. Akad. Nauk SSSR*, **7**, 2175 (1966).

(11) D. W. Slocum, W. E. Jones, T. F. Crimmins, and C. R. Hauser, *J. Org. Chem.*, **34**, 1973 (1969).

This oil was chromatographed on basic alumina IV. The material was eluted with petroleum ether (trace of ether) solvent to yield 0.6 g (92%) of 2-methyl DMAMF (4). Nmr data: δ 1.95 (s, 3.0), 2.13 (s, 6.0), 3.26 (AB quartet, 2.1, ν_1 = 3.21, ν_2 = 3.30, J = 13.0), 4.00 (m, 8.0).

Oxidation of Olefins by Palladium(II). VI. Ethylene Oxidation by Palladium(II) Acetate in Acetic Acid Promoted by Various Oxidants[1]

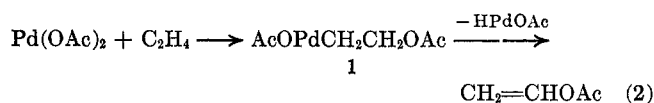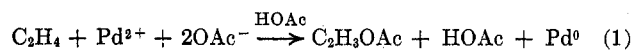Patrick M. Henry[2]

*Contribution No. 1605 from the Research Center,
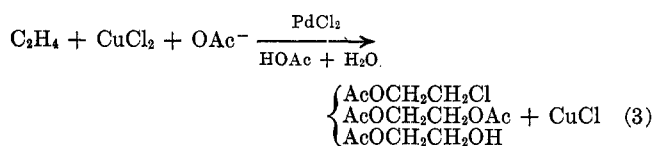Hercules Incorporated, Wilmington, Delaware 19899*

Palladium(II) salts alone in acetic acid oxidize ethylene to vinyl acetate. It has been previously reported that $CuCl_2$ and NO_3^- increase the rate of oxidation and change the product from vinyl acetate to 1,2-disubstituted ethanes such as ethylene glycol mono- and diacetate and 2-chloroethyl acetate. The present study was undertaken to determine the generality of this new reaction. A number of oxidants, including $K_2Cr_2O_7$, $NaNO_2$, $CuBr_2$, MnO_2, $Pb(OAc)_4$, $Tl(OAc)_3$, $TlCl_3$, and $HAuCl_4$, were also found to be active in this reaction. Others which had little or no activity include *p*-quinone, $FeCl_3$, $Fe(OAc)_3$, $Hg(OAc)_2$, $MoCl_5$, and $MoOCl_4$. $CuBr_2$ gave 2-bromoethyl acetate. In addition to the 1,2-disubstituted ethanes, $Tl(OAc)_3$, $TlCl_3$, and $HAuCl_4$ also formed appreciable quantities of ethylidene diacetate. The reaction probably proceeds by a mechanism similar to that of the previously studied aromatic substitution reaction. This mechanism involves formation of an intermediate with a palladium(II)–carbon bond. This intermediate reacts with the oxidant to give the observed products.

In the absence of other oxidants palladium(II) salts in acetic acid oxidize ethylene to vinyl acetate[3] and other olefins to mixtures of vinyl and allylic acetates.[4] A study of the product distributions obtained from oxidation of 1 and 2 olefins with palladium(II) acetate

$$C_2H_4 + Pd^{2+} + 2OAc^- \xrightarrow{HOAc} C_2H_3OAc + HOAc + Pd^0 \quad (1)$$

$$Pd(OAc)_2 + C_2H_4 \longrightarrow \underset{1}{AcOPdCH_2CH_2OAc} \xrightarrow{-HPdOAc}$$

$$CH_2{=}CHOAc \quad (2)$$

indicated that the reaction proceeds by way of an acetoxypalladation–Pd(II)–hydride elimination.[5]

Addition of copper(II) chloride to these reaction mixtures causes the rate of olefin oxidation to increase. In addition the main product changes from vinyl acetate to 1,2-disubstituted alkanes.[6] It has been demonstrated that both $PdCl_2$ and $CuCl_2$ are required for this reaction

$$C_2H_4 + CuCl_2 + OAc^- \xrightarrow[HOAc + H_2O]{PdCl_2}$$

$$\begin{cases} AcOCH_2CH_2Cl \\ AcOCH_2CH_2OAc + CuCl \quad (3) \\ AcOCH_2CH_2OH \end{cases}$$

to take place.[6b] On the basis of studies with the butenes[6b] and cyclohexene[1] the mechanism for this reaction has been postulated to involve the interception

of the acetoxypalladation intermediate, 1, by oxidant to give saturated products (X = OAc, Cl, or OH).

$$1 + 2CuCl_2 + X^- \longrightarrow$$
$$AcOCH_2CH_2X + PdCl_2 + 2CuCl + OAc^- \quad (4)$$
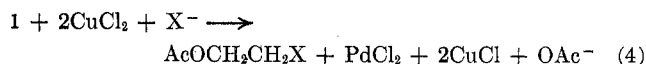
The reaction is not limited to $CuCl_2$, as it has been demonstrated that nitrate can replace $CuCl_2$.[7] The present study is aimed at defining the scope of this new reaction. In particular a number of oxidants will be surveyed to determine what types of oxidants are effective in interacting with Pd(II).

A related reaction is the Pd(II)-catalyzed aromatic substitution reaction, which also requires a second oxidant[8] (X^- = OAc^-, N_3^-, Cl^-, NO_2^-, Br^-, CN^-, or SCN^-).

$$\text{(5)}$$
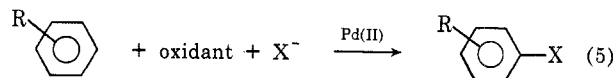
This reaction very likely proceeds by way of a Pd(II)–aryl intermediate analogous to 1 although Pd(IV) species cannot be eliminated by the experimental evidence.

Results

A number of oxidants were tested for their ability to change the nature of the oxidation of olefins in the same fashion as $CuCl_2$ or nitrate. In the present work ethylene was the olefin used. There are two criteria for a given reagent to be capable of interacting with Pd(II): first, the rate of ethylene oxidation in the presence of this reagent and Pd(II) as compared to the rate of oxidation in the absence of Pd(II); and second, the product distributions obtained in the oxidations containing Pd(II) and the reagent. Of course, Pd(II) alone gives only vinyl acetate.

Gas Uptake Experiments.—In Table I are listed the results of a series of experiments in which the $Pd(OAc)_2$

(1) Paper V: P. M. Henry, *J. Amer. Chem. Soc.*, **94**, 7305 (1972).

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(3) (a) I. I. Moiseev, M. N. Vargaftik, and Ya. K. Sirkin, *Dokl. Akad. Nauk SSSR*, **133**, 377 (1960); (b) E. W. Stern and M. L. Spector, *Proc. Chem. Soc.*, 370 (1961).

(4) (a) M. N. Vargaftik, I. I. Moiseev, and Ya. K. Sirkin, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 930 (1962); (b) I. I. Moiseev, A. P. Belov, and Ya. K. Sirkin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1527 (1963).

(5) W. Kitching, Z. Rappoport, S. Winstein, and W. G. Young, *J. Amer. Chem. Soc.*, **88**, 2054 (1966).

(6) (a) D. Clark, P. Hayden, and R. D. Smith, *Amer. Chem. Soc., Div. Petrol. Chem., Prepr.*, **14** (2), B10 (1969); (b) P. M. Henry, *J. Org. Chem.*, **32**, 2575 (1967).

(7) M. Tamura and T. Yahui, *Kogyo Kagaku Zasshi*, **72**, 578, 581 (1969).

(8) P. M. Henry, *J. Org. Chem.*, **36**, 1886 (1971).