Anal. Calcd. for $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92; N, 9.15. Found: C, 74.60; H, 5.69; N, 8.99.

Bis[p-(3-aminopropoxy)phenyl]methane. The above purified dinitrile, 30.3 g., was dissolved in 500 ml. of 1,2-dimethoxyethane and hydrogenated as in the preceding hydrogenation. Ten grams of freshly prepared Raney cobalt catalyst and 115 g. (7 moles) of ammonia were used. The hydrogenation proceeded smoothly between 84–116° while at 3280–3460 p.s.i.g. The crude diamine was flash-distilled at 0.5 mm. All distillate, boiling up to 240° was collected. This clear, colorless distillate was redistilled through a 4″-Vigreux column (Mini-Lab) at 0.5 mm. pressure. Nineteen and one-half grams of distillate boiling at 219–222° was collected.

Anal. Calcd. for $C_{19}H_{26}N_2O_2$: N, 8.91. Found: N, 7.70.

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Acid Constants of Heteroannular Substituted Ferrocenoic Acids

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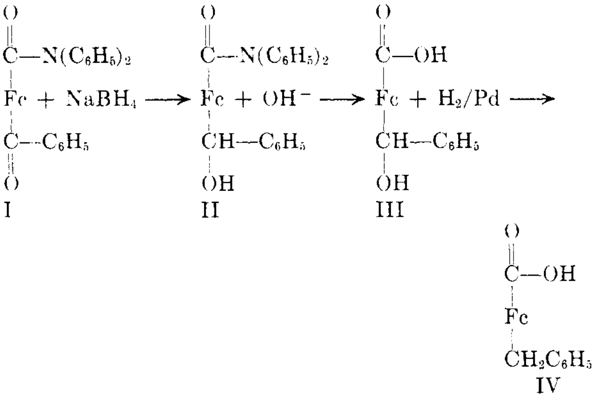
Since we reported the use of *N,N*-diphenylcarbamyl chloride as a useful reagent for preparation of ferrocenoic acid and its heteroannular substituted derivatives,[2] several additional ferrocenoic acids have been prepared and their pK_a values determined in 50% ethanol.

Although 1-benzoyl-1′-diphenylcarbamylferrocene was not reduced by hydrogen at 45 p.s.i. in ethyl acetate over palladium on charcoal for ten hours, it was readily reduced with sodium borohydride to 1-(α-hydroxybenzyl)-1′-diphenylcarbamylferrocene (II). Hydrolysis of II yielded 1-(α-hydroxybenzyl)-1′-ferrocenoic acid (III), and catalytic reduction of III gave 1-benzyl-1′-ferrocenoic acid (IV).

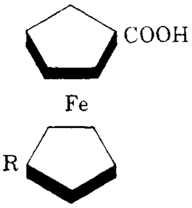
The pK_a values of III and IV, along with values determined for other previously prepared acids[2] are listed in Table I. Nesmeyanov[3,4] had previously reported pK_a values for some of these and other acids in 68% methanol. Table I lists the values from Nesmeyanov for comparison.



I II III IV

TABLE I

pK_a VALUES OF SUBSTITUTED FERROCENOIC ACIDS IN 50% ETHANOL AT 24°



R	pK_a, 50% Ethanol	pK_a 68% Methanol[3,4]
$—C_2H_5$	6.34 ± 0.01	6.43
$—CH_2C_6H_5$	6.25 ± 0.01	—
—H	6.11 ± 0.01	6.29
$—COC_6H_5$	5.90 ± 0.04	—
$—CH(OH)C_6H_5$	5.84 ± 0.01	—
$—COCH_3$	5.76 ± 0.02	5.90

pK_a for benzoic acid in 50% ethanol at 25°, 5.68[5]

It can be seen that the acid strengths of the substituted ferrocenoic acids vary in the expected manner according to the electron donating or withdrawing properties of the substituent. Further, a plot of our pK_a values against Hammett *para* sigma constants[5,6a] yielded a satisfactory straight line of slope 0.74. Nesmeyanov's values for 68% methanol similarly treated gave a slope of 0.81.

Although sigma constants are not known for the α-hydroxybenzyl group,[6b] it does appear that the α-hydroxybenzylferrocenoic acid is out of line with

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(1) Taken in part from a Ph.D. dissertation of Robert Eisenthal submitted to the University of North Carolina, January 1961.

(2) W. F. Little and R. Eisenthal, *J. Am. Chem. Soc.*, **82**, 1577 (1960).

(3) A. N. Nesmeyanov and O. A. Reutov, *Doklady Akad. Nauk., S.S.S.R.*, **115**, 518 (1957).

(4) A. N. Nesmeyanov and O. A. Reutov, *Izvest. Akad. Nauk., S.S.S.R.*, 926 (1959); *Chem. Abstr.*, **54**, 469 (1960).

(5) H. H. Jaffe, *Chem. Rev.*, **53**, 191 (1953).

(6)(a) Sigma constants are available for but four of the substituent groups used; acid constants are not reported for benzylbenzoic acid or α-hydroxybenzylbenzoic acid. (b) A reasonable estimate for the Hammett *para* sigma constant is +0.012. T. Kuwana, D. E. Bublitz, and G. Hoh, *J. Am. Chem. Soc.*, **82**, 5811 (1960), have reported chronopotentiometric quarter wave potentials, $E_{\frac{1}{4}}$, for a number of substituted ferrocenes, including α-hydroxybenzylferrocene. While these workers reported correlation of the quarter wave potentials with Taft polar sigma constants, we have found that the data are correlated much better with Hammett *para* sigma constants, and from such a plot the *para* sigma for the α-hydroxybenzyl group can be obtained as approximately +0.012. Using this value, our acid constant for α-hydroxybenzylferrocenoic acid does not fit on the line; it is a much stronger acid than predicted.

the others since it is a stronger acid than the benzoylferrocenoic acid. A possible explanation of the greater strength of this acid could lie in hydrogen bonding of the carboxylate ion with the α-hydroxy group, stabilizing the ionized form, similar to the explanation advanced by Branch[7] for the large acid constant of salicylic acid.

EXPERIMENTAL

Acetyl- and benzoylferrocenoic acids were prepared by the methods previously described.[2]

Ethylferrocenoic acid was prepared by Clemmensen reduction of acetylferrocenoic acid according to the procedure described by Nesmeyanov.[8]

1-(α-Hydroxybenzyl)-1′-carbamylferrocene. To a warm solution of 8.4 g. (0.017 mole) of 1-benzoyl-1′-diphenylcarbamylferrocene[2] in 200 ml. of methanol containing 0.2 ml. of 50% sodium hydroxide was added 27 ml. of a 10% sodium borohydride solution made up in 10% aqueous sodium hydroxide. The reaction mixture was stirred at room temperature for 30 min. and at gentle reflux for 5 hr. On cooling, the product crystallized. A yield of 6.7 g. (79.5%) was obtained, m.p. 152–154°. The analytical sample was recrystallized from hexane and melted at 154.5–156°.

Anal. Calcd. for $C_{30}H_{25}NO_2Fe$: C, 73.93; H, 5.17. Found: C, 74.04; H, 5.14.

α-Hydroxybenzylferrocenoic acid. α-Hydroxybenzyldiphenylcarbamylferrocene (2.60 g.) was dissolved in a mixture of 25 ml. of benzene and 50 ml. of 10% ethanolic potassium hydroxide. The mixture was held at reflux for 2 hr. and was allowed to stand overnight at 50°. The solvent was removed and the residue was shaken with water (75 ml.) for 3 hr. The aqueous suspension was filtered, and the filtrate yielded upon acidification with hydrochloric acid 1.45 g. (81%) of crude α-hydroxybenzylferrocenoic acid. Recrystallization from benzene yielded a product melting at 129.5–130°.

Anal. Calcd. for $C_{18}H_{16}O_3Fe$: C, 64.31; H, 4.80. Found: C, 64.54; H, 4.95.

Benzylferrocenoic acid. A solution of 2.33 g. (0.00694 mole) of α-hydroxybenzylferrocenoic acid in 100 ml. of ethyl acetate containing 5 ml. of acetic acid was placed in an atmospheric hydrogenator over 0.7 g. of prereduced palladium oxide. The reduction required 850 min. for the calculated hydrogen uptake. After filtration, the solvent was removed with reduced pressure. The orange crude product, 2.05 g. (92%), melted at 148–151°. Recrystallization from cyclohexane yielded a product melting at 151–152.5° dec.

Acid constants. The acid constants were measured in 50 volume % ethanol in water, essentially according to the method described by Roberts.[9] Three or more determinations were made on each acid, and the mean deviations of the determinations are shown in Table I.

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Steroidal Cyclic Ketal. XXIII.[1] Some Reactions of the 3-Ethylenedioxy-Δ^5 Grouping in Steroids

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We wish to report here on some aspects of the chemistry of the 3-ethylenedioxy-Δ^5 grouping in the presence of a double bond at C-9,11 in the steroid molecule.

When 21-acetoxy-3,20-bisethylenedioxy-5,9(11)-pregnadien-17α-ol (I)[2] was treated with one equivalent of perbenzoic acid an epoxide was formed in 63% yield which was assigned the structure, 21-acetoxy-3,20-bisethylenedioxy-5β,6β-epoxy-9(11)-pregnen-17α-ol (II). The structure II was established by its synthesis from 21-acetoxy-3,20-bisethylenedioxy-5β,6β-epoxypregnane-11β,17α-diol (IIIb)[3] by selective dehydration of the 11β-hydroxyl group with phosphorus oxychloride in pyridine.[4,5] It would appear then that in a 5,9(11)-diene 3,20-bisethylene ketal the C-5,6-double bond is more reactive toward epoxidation than the 9,11-double bond, and moreover frontal attack is favored.[6]

When the 5,9(11)-diene bisketal I was treated with two equivalents of perbenzoic acid, a diepoxide IV separated in 74% yield. As the same product could be obtained by reaction of 21-acetoxy-3,20-bisethylenedioxy-5β,6β-epoxy-9(11)-pregnen-17α-ol (II) with an additional equivalent of perbenzoic acid, the structure of IV was designated as 21-

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[1] Paper XXII, S. Bernstein, M. Heller, and W. S Allen, *J. Org. Chem.*, **26**, 1333 (1961).

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[4] R. Littell and S. Bernstein, *J. Am. Chem. Soc.*, **78**, 984 (1956).

[5] In this connection, the 11β-hydroxyl group in the 5α,6α-epimer of III has been shown to be stable to dehydration conditions with phosphorus oxychloride. However, this dehydration can be effected with thionyl chloride but with simultaneous elimination of the 17α-hydroxyl group. See, S. Bernstein, M. Heller, F. J. McEvoy, and S. M. Stolar, *J. Org. Chem.*, **26**, 505 (1961).

[6] This observation is of interest in view of the finding (ref. 3) that when the bisethylene ketal (Va) of hydrocortisone was treated with perbenzoic acid, an excellent separation (*ca*, 60% yield) of the 5α,6α-epoxide occurred. The 5β,6β-epoxide IIIa has now been isolated from the mother liquor by chromatography; m.p. 193–196°; $[\alpha]_D^{25}$ +5° (pyridine); ν_{max} 3495, 1110, and 1036 cm.$^{-1}$ *Anal.* Calcd for $C_{25}H_{38}O_8$ (466.55): C, 64.36; H, 8.21. Found: C, 64.15; H, 8.50.

Also epoxidation of the 3-ethylenedioxy-Δ^5 grouping in a number of steroids unsubstituted in Ring C has given a mixture of α- and β-epoxides in which the α-epimer is apparently the major product; see, *e.g.* A. Bowers, L. C. Ibáñez, and H. J. Ringold, *Tetrahedron*, **7**, 138 (1959).