The observed distributions are shown in the table. Two features are of great interest; first, the distribution of activities in carbons 1 and 2 immediately suggested the incorporation of an intact acetate molecule in these positions; second, the distribution of activity in carbons 3 to 6, assuming equal activities in carbons 4 and 5, is very close to that expected in the succinate moiety (carbons 2 to 5) of α-ketoglutarate arising from acetate via the citric acid cycle (see table). The theoretical basis for the calculation of acetate activities in citric acid cycle components has been described.[2] Despite certain deviations the activity patterns are remarkably close. The higher-than-calculated activities in the lysine carbons 1 and 2 are probably due to incomplete equilibration of acetate with citric acid cycle components, and the presence of low activity in carbons 1 and 6 of lysine formed from methyl-labeled acetate is probably due to recycling,[4] whereby methyl activity migrates to the carboxyl of acetate.

DISTRIBUTION OF ACETATE CARBONS IN LYSINE

Values are specific activities based on 100 for over-all activity of lysine

Lysine carbon number[a]	Precursor Acetate methyl Observed	Precursor Acetate methyl Calcd.	Acetate carboxyl Observed	Acetate carboxyl Calcd.
1	18	0	360	300
2	206	150	0	0
3	121	150	7	0
4	116	150	−11	0
5	116	150	−11	0
6	7	0	226	300

[a] Numbering begins with carboxyl carbon. The actual specific activities of the lysine hydrochlorides were: from methyl-labeled acetate, 6380 c./m. per standard dish; from COOH-labeled, 5708 c./m.

In speculating on a mechanism by which such a distribution might be achieved it has occurred to us that acetate may condense with α-ketoglutarate to yield a homolog of citric acid, which, by undergoing a series of reactions analogous to citrate in the citric acid cycle, should yield "homonisocitrate," oxaloglutarate, α-ketoadipate, and ultimately α-aminoadipic acid. The formation of lysine from α-aminoadipic acid, presumably by the same sequence of reactions involved in ornithine formation from glutamate, has been suggested by the *Neurospora* studies of Mitchell and Houlahan.[5] The existence of such a "homocitric" acid cycle represents an intriguing possibility which is now being investigated further.

An alternate possibility is that acetate condenses with an unsymmetrical succinate, possibly succinyl-CoA, but this is regarded as less likely since it does not as easily account for the formation of α-aminoacidic acid.

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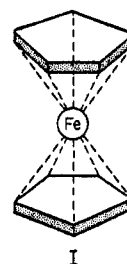RECEIVED MAY 29, 1952

(4) K. F. Lewis and S. Weinhouse, THIS JOURNAL, 73, 2500 (1951).

(5) H. K. Mitchell and M. B. Houlahan, J. Biol. Chem., 174, 883 (1948).

A NEW AROMATIC SYSTEM

Sir:

Recently we have assigned to iron biscyclopentadienyl[1] the structure I.[2] It is clear that this mole-

I

cule contains two rings, each of five equivalent C–H groupings. It seemed likely that the equivalent ring bonds connecting these C–H groups should be of effective order greater than 1. Considering one of the carbocyclic rings alone, then, the situation might be represented as in II. This expression calls to mind the very similar circumstances obtaining in the case of benzene (III).

II   III
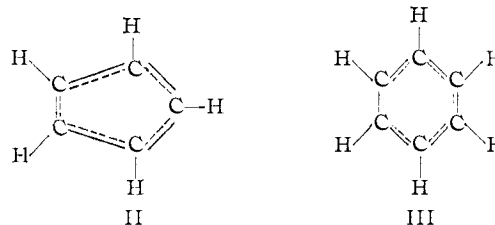
We were led by these considerations to the view that iron biscyclopentadienyl might behave as an aromatic substance. We now wish to record experiments which demonstrate typically aromatic properties of this unique iron compound, for which we propose the name *ferrocene*.

In spite of its high degree of formal unsaturation, ferrocene does not possess properties typical of polyolefinic substances. It does not react with maleic anhydride in boiling benzene, and is not hydrogenated under normal conditions over reduced platinum oxide. Its resistance to the action of acidic reagents, and its great thermal stability have been mentioned previously.[1,2]

When ferrocene in carbon bisulfide was treated with acetyl chloride in the presence of aluminum chloride, it was very smoothly converted to a beautifully crystalline red diacetyl derivative, m.p. 130–131° (calcd. for $C_{14}H_{14}O_2Fe$: C, 62.52; H, 5.22. Found: C, 62.56; H, 5.40), which formed a crystalline dioxime (decomposes above 200°; calcd. for $C_{14}H_{16}N_2O_2Fe$: C, 56.02; H, 5.37; N, 9.34; Fe, 18.40. Found: C, 56.13; H, 5.31; N, 9.53; Fe, 18.61). Similarly, β-chloropropionyl chloride gave bis-β-chloropropionylferrocene, m.p. 117–121° (calcd. for $C_{16}H_{16}O_2Cl_2Fe$: C, 52.34; H, 4.39; Cl, 19.32; Fe, 15.94. Found: C, 52.84; H, 4.59; Cl, 19.32; Fe, 16.04), and bisacryloylferrocene, m.p. 71–71.5° (calcd. for $C_{16}H_{14}O_2Fe$: C, 65.33; H, 4.82. Found: C, 64.92; H, 5.15). With

(1) T. J. Kealy and P. L. Pauson, *Nature*, 168, 1039 (1951); S. A. Miller, J. A. Tebboth and J. F. Tremaine, *J. Chem. Soc.*, 632 (1952).

(2) G. Wilkinson, M. Rosenblum, M. C. Whiting and R. B. Woodward, THIS JOURNAL, 74, 2125 (1952).

phthalic anhydride, bis-o-carboxybenzoylferrocene, characterized as its **dimethyl ester,** m.p. 144–144.5° (calcd. for $C_{28}H_{22}O_6Fe$: C, 65.31; H, 4.35. Found: C, 64.71, 65.08; H, 4.65, 4.70), was obtained.

Oxidation of diacetylferrocene by hypoiodite gave **ferrocene dicarboxylic acid** (sublimes unchanged above 230°); calcd. for $C_{12}H_{10}O_4Fe$: C, 52.59; H, 3.68; Fe, 20.40. Found: C, 52.36; H, 3.96; Fe, 19.91), which gave a **dimethyl ester,** m.p. 114–115° (calcd. for $C_{14}H_{14}O_4Fe$: C, 55.66; H, 4.67. Found: C, 55.66; H, 4.93).

The acylferrocenes dissolve readily in acids with marked halochromism, are photolabile, and so far as we have been able to ascertain, are not convertible to isolable derivatives of the **ferricinium** cation, $[(C_5H_5)_2Fe]^+$, which is readily formed from the parent ferrocene on oxidation.[2] From the structural point of view, it seems most probable that each of the acyl groups is attached to a different ring. For example, we formulate diacetylferrocene as IV, and leave open for the present the question of whether the barrier in the way of rotation of one ring with respect to the other is sufficient to permit the existence of isomeric disubstituted ferrocenes, such as V.
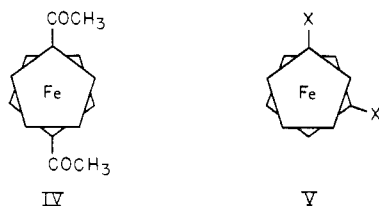
Many of the typical substitution reactions of classical aromatic systems are brought about by strongly oxidizing species, such as NO_2^+ and Br^+. The ready conversion of ferrocene to the ferricinium cation supervenes when attempts are made to carry out substitution reactions on ferrocene with such agents.

A comparison of relevant physical characteristics of ferrocene and its derivatives with the corresponding properties of analogous benzenoid compounds reveals certain similarities. There follows a tabulation of infrared band positions for opposite cases

	R = ferrocenyl, μ	R = phenyl, μ
H—R	3.26	3.27
		3.31
CH_3CR (‖ O)	5.97	5.93
CH_3OCR (‖ O)	5.82	5.81
$o\text{-}CH_3OOCC_6H_4CR$ (‖ O)	6.02	5.97

Of even greater interest are the acidity constants for the carboxylic acids (measured in 2/1 EtOH/H_2O).

Ferrocene dicarboxylic acid	pK_1	3.1×10^{-7}
	pK_2	2.7×10^{-8}
Benzoic acid	pK	2.4×10^{-7}

The very small differences between the two dissociation constants of ferrocene dicarboxylic acid indicates that the carboxyl groups interact very little, and must be very far apart (cf. IV), while the near identity of the first constant with that of benzoic acid demonstrates that *the ring carbon atoms of ferrocene, and thence necessarily the central iron atom as well, are substantially electrically neutral.* This observation is of importance in respect to the detailed electronic structure of ferrocene, since it excludes any form of hybridization which leads to charge separation within the molecule.

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