

1- β -D-Ribofuranosyl-1H-imidazo[4,5-*b*]pyridine (XVII).—The mother liquor resulting from crystallization of XVI¹⁰ gave, on evaporation of the solvent, 930 mg. of residue. The crude products were deblocked as described above. The deblocked products (350 mg.) contained nucleosidic compounds whose R_f values in solvent A were 0.60 and 0.43. The extract of the spot of R_f 0.60 had ultraviolet spectra identical with those of an authentic sample of 3- β -D-ribofuranosyl-3H-imidazo[4,5-*b*]pyridine (XVI).¹⁰ The ratio of the total optical density of the two spots (XVII to XVI) was 4:1, which means ribosylation of V gave rise to 68% yield of 9H isomer XVI and 3.3% of 7H isomer XVII. The mixture (345 mg.) was dissolved in 10 ml. of water and the solution was treated with activated carbon and filtered. The filtrate was concentrated to dryness (197 mg.) and suspended in 10 ml. of ethanol. To the suspension was added water until the residue almost dissolved. On standing for 39 days at room temperature, crystals deposited: m.p. 226–227.5; $\lambda_{\max}^{\text{D}} 0.11$ (cationic form) 278 m μ (ϵ 8890) (shoulder), 283.5 (10,000), 289 (ϵ 9700) (shoulder); $\lambda_{\min}^{\text{D}} 5.6$ (neutral form) 259 m μ (ϵ 3640); $pK_a = 2.95 \pm 0.02$; isosbestic points at 259.5, 271–272, and 281 m μ . Ultraviolet spectra of this nucleoside (XVII) for the neutral and cationic species were identical with those of 1-methyl-1H-imidazo[4,5-*b*]pyridine and differed appreciably from those of the 3-methyl-3H isomer.¹⁰

Anal. Calcd. for $C_{11}H_{13}N_3O_4$: C, 52.58; H, 5.22; N, 16.73. Found: C, 52.61; H, 5.16; N, 16.49.

Examination of Products Other Than the 9H Isomer in Ribosylation Products of Chloromercuri Salt of 6-Chloropurine (X).—Chloromercuri-6-chloropurine¹³ (5.45 g., 14 mmoles) was treated with XIII, prepared from 10 g. (19.8 mmoles) of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribose by the standard procedure.¹⁴ The residue (10.46 g.) obtained was fractionated into 39 parts on an alumina column. Each fraction was put into a bomb of stainless steel and treated with 5 ml. of methanolic ammonia (saturated at 0°) at 100–110° (bath temperature) for 4 hr. The solution was evaporated to dryness. To the residue was added 5 ml. of methanol and the solvent was removed *in vacuo*. The process was repeated four times to remove methyl benzoate and benzamide, and the resulting residue was subjected to paper chromatographic examination (solvent A). Each fraction contained, if any, only a single nucleosidic product, adenosine.

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Ferrocene-Containing Polymers. X. Isomeric Bis(ferrocenylmethyl)ferrocenes

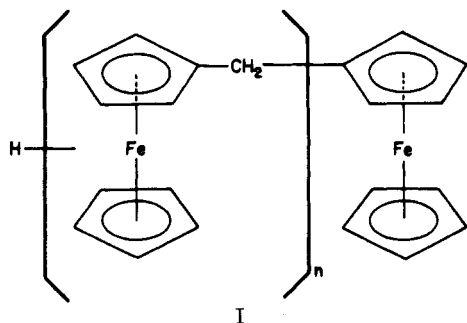
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From a trinuclear fraction of the methylene-bridged ferrocene polymer I, obtained in earlier investigations, the isomeric 1,2-, 1,3-, and 1,1'-bis(ferrocenylmethyl)ferrocenes IIa-c are separated by fractional crystallization in the approximate ratio, 1:5:4. The three isomers are identified by elemental analyses and spectroscopic techniques. Their structural assignments are confirmed by independent syntheses *via* Clemmensen reduction of the corresponding monoketones IIIa-c, obtained from ferrocenoyl chloride and diferrocenylmethane under Friedel-Crafts conditions. The established ratio of isomers II, while at best a very crude approximation, corroborates earlier qualitative predictions with regard to the sequence distribution of 1,2-, 1,3-, and 1,1'-substituted recurring units along the backbone of polymer I.

It was shown recently^{2a} that the ferrocenyl Mannich base, N,N-dimethylaminomethylferrocene, can be condensed with ferrocene in the presence of a zinc chloride-hydrochloric acid catalyst system to give polymeric products possessing the idealized structure I.^{2b} In this reaction (and, similarly so, in the self-



condensation of the Mannich base³), slightly prevailing homoannular substitution along the polymer chain of I was predicted on the basis of earlier publications demonstrating enhanced (inductive and hyperconjugative) activation of the substituted, compared with the

unsubstituted, π -cyclopentadienyl rings of alkyl ferrocenes in acylation reactions⁴ and was evidenced spectroscopically by a quantitative evaluation of the 9- μ absorption^{5,6} of a series of polyhomologous fractions.

To obtain a more precise measure of this prevailing homoannularity in I, in this earlier study^{2a} a monodisperse fraction composed of the three trinuclear (I, $n = 2$) isomers II was separated chromatographically. For this fraction, on which the distribution of the three substitution orientations could be studied without interference by branching (such interference has to be anticipated in homologs with $n \geq 3$), a 59.6% content of homoannular isomers was determined by the same quantitative spectroscopic technique. While the preponderance of homoannular bonding in the trinuclear isomer mixture (and, by inference, also in the chain of polymeric I) was thus clearly established, no efforts were made to separate this isomer mixture further into the individual components IIa-c.

In the present investigation, the earlier work was resumed, and this isolation of isomers IIa-c⁷ was

(1) (a) Douglas Aircraft Co., Inc.; (b) California Research Corp.

(2) (a) E. W. Neuse and K. Koda, paper submitted for publication. (b) As in the earlier work (ref. 2a and 3), the centered substituent link on the left of this simplified scheme denotes a random sequence distribution along the polymer backbone of 1,2-, 1,3-, and 1,1'-substituted units.

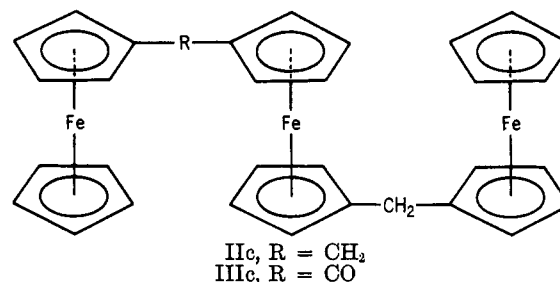
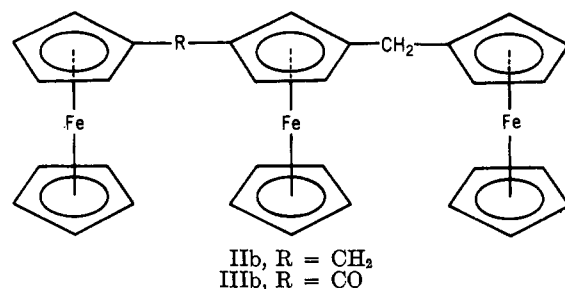
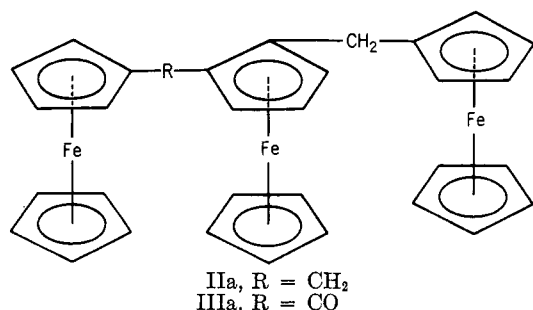
(3) E. W. Neuse and E. Quo, *J. Polymer Sci.*, **A3**, 1499 (1965).

(4) (a) M. Rosenblum and R. B. Woodward, *J. Am. Chem. Soc.*, **80**, 5443 (1958); (b) M. Rosenblum, *ibid.*, **81**, 4530 (1959); (c) K. L. Rinehart, Jr., D. E. Bublitz, and D. H. Gustafson, *ibid.*, **85**, 970 (1963); (d) D. W. Hall and J. H. Richards, *J. Org. Chem.*, **28**, 1549 (1963); (e) R. A. Benkeser, Y. Nagai, and J. Hooz, *J. Am. Chem. Soc.*, **86**, 3742 (1964).

(5) M. Rosenblum, Ph.D. Thesis, Harvard University, 1953.

(6) E. W. Neuse and D. S. Trifan, *J. Am. Chem. Soc.*, **85**, 1952 (1963).

(7) The heteroannular IIc was recently prepared by P. L. Pauson and W. E. Watts, *J. Chem. Soc.*, 3880 (1962).



brought about by fractional crystallization,⁸ furnishing in the order of increasing solubility the 1,2, 1,1', and 1,3 isomer in the very approximate ratio, 1:4:5 (average obtained from three independent fractionation series).⁹ This isomer ratio, while too crude to permit even semiquantitative interpretations, nonetheless represents an instructive reflection of the relative populations of the 1,2-, 1,1'-, and 1,3-substituted segments along the polymer chain of I and is, thus, well in accord with the earlier predicted¹⁰ substitution orientation in propagation sequences involving the ferrocenyl-carbinyl cation intermediate.

The over-all composition of the three isomers II was determined by elemental analyses and molecular weight measurements. IIc, occurring as two crystalline modifications of identical melting point (164–166°) and spectral behavior *in solution*, was characterized by a per cent homoannularity value⁶ of 69.1 (calculated, 66.7), which clearly demonstrated heteroannular substitution on the central ferrocene unit. This compound, therefore, was identified as 1,1'-bis(ferrocenylmethyl)ferrocene. Comparison in spectral behavior and melting point with an authentic product synthesized by the procedure of Pauson and Watts⁷ confirmed this assignment. The infrared spectra (potassium bromide pellets) of the two modifications resembled those of diferrocenylmethane and oligomeric fractions of I discussed previously.^{2a} Conspicuous was the 7.80- μ band, strong in one modification and of moderate intensity in the other (thus, again^{2a,6,11} attesting to the difficulty of utilizing this region for discrimination between homoannular substituent dispositions¹²), the doublet at 9.65–9.80 μ , of considerably higher intensity than in diferrocenylmethane or the two homoannular isomers IIa and IIb, and the doublet at 10.80–10.95 μ (the high wave length peak very weak in one of the modifications). Proton magnetic resonance (p.m.r.) signals were exhibited in

the τ region 5.9–6.1 (ferrocene multiplet) and at τ 6.67 (methylene singlet) in the expected 26:4 area ratio.

The remaining two isomers, as expected, were shown to be of the homoannular type, both giving per cent homoannularity values in the vicinity of 100. Compound IIb occurred as two modifications, both melting at 146–147° and showing weak infrared absorption at 10.59 μ in addition to a multiplet, somewhat dependent on the particular modification, in the 10.7–11.0- μ region. On the basis of earlier reports^{4c,13} suggesting infrared bands at this position to be typical of 1,3-dialkylated ferrocenes, the observed absorption pattern was taken as a tentative indication of the 1,3 disposition in IIb, leaving the 1,2 disposition for the third isomer, IIa. (Both existing modifications of the latter, m.p. 203–205°, while failing to exhibit the band near 10.6 μ under discussion, showed instead somewhat broad absorption near 10.9 μ ^{11,13}).

Corroboration of the tentative assignments IIa and IIb resulted from proton magnetic resonance (p.m.r.) data. IIb gave a methylene singlet at τ 6.67, *i.e.*, at the same position as IIc. In contrast, enhanced deshielding was experienced by the methylene protons of the 1,2 isomer IIa, in which the contribution by the π systems of all three substituted rings was expected to result in a considerably stronger total field induced around the two methylene bridges than realized in IIb or IIc. As a consequence, the methylene singlet appeared at τ 6.60, *i.e.*, by 0.07 p.p.m. downfield from that of IIb. For both IIa and IIb the ferrocene and methylene resonances were in the expected 26:4 ratio.

With the assignments of the homoannular isomers IIa and IIb admittedly resting on rather weak spectroscopic grounds, all three compounds were prepared by an independent route for further structural confirmation. To this end, diferrocenylmethane was interated with ferrocenoyl chloride under Friedel-Crafts conditions to give the three isomeric ketones III. The assignment of the substituent dispositions in these isomers, first suggested by the order in which they were eluted chromatographically^{4a,b} (IIIa > IIIc > IIIb), was made on the basis of unambiguous spectral correlations. In contrast to II, such correla-

(8) Both column chromatography and v.p.c. (the latter at temperatures up to 250°) had proved earlier to be impracticable for this isomer separation.

(9) X-Ray diffractographic identification techniques, while extensively employed in the course of this fractionation, had to be used judiciously because of a pronounced tendency of each of the isomers, when accompanying a fraction in minor concentrations, to crystallize isomorphously with the major component.

(10) See ref. 2a, 3, and 6. Prevalence of the 1,3 over the 1,2 disposition of the intrachain-type substituent positions (as contrasted to branch-point positions) in these poly(ferrocenylmethyl)enes was predicted largely on steric grounds. The analogous steric effects operative in acetylation reactions of alkylferrocenes with the resultant prevailing substitution at the 3 position (the degree of 3 substitution depending on the substituent's steric requirements) were demonstrated by the Rosenblum, Rinehart, Richards, and Benkeser groups (ref. 4).

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

(12) A. N. Nesmeyanov, L. A. Kazitsyna, and B. V. Lokshin, and V. D. Vilchevskaya, *Dokl. Akad. Nauk SSSR*, **125**, 1037 (1959).

(13) K. L. Rinehart, Jr., K. L. Motz, and S. Moon, *J. Am. Chem. Soc.*, **79**, 2749 (1957).

tions could clearly be established on these ketones because of the pronounced effects on the infrared and p.m.r. behavior arising from the presence of the carbonyl group.

The heteroannular derivative IIIc was easily identified by its low per cent homoannularity value (73.0). In the 10–11- μ region of the infrared spectrum (in chloroform solution), as expected, only a single peak was shown at 10.80 μ (with shoulder near 10.9 μ), *i.e.*, at the same position at which absorption appeared in the spectrum of diferrocenylmethane (ferrocenyl ketone fails to absorb in this region). Of the two homoannular isomers, IIIa showed a doublet at 10.75–10.80 μ , confirming its assignment to the 1,2 structure by analogy with Rinehart's findings on 1,2-acetylalkylferrocenes.¹³ Correspondingly, the 1,3 disposition was consistent with the peaks¹³ at 10.26 (very weak), 10.60, 10.84, and 11.0 μ exhibited by IIIb.

The p.m.r. spectra of all three isomers III showed clearly separated, though poorly resolved, multiplet signals for the protons flanking (α) the carbonyl group and those in "meta" position (β) to it. In keeping with the relative deshielding effects generally found to operate on protons located in the negative shielding region of a carbonyl group conjugated to a ferrocene ring,¹⁴ the signals shifted most strongly downfield ($\tau \sim 5.0$) were assigned to the α protons, leaving the multiplets positioned further upfield by some 0.5 p.p.m. ($\tau \sim 5.5$) to the somewhat less deshielded β protons. The τ values observed for the three isomers are collected in Table I, with relative intensities given in parentheses.

TABLE I

| Com- pound | Ferrocene protons ^a | | | Methylene protons ^a |
|---------------|--------------------------------|----------|-----------------------------|-----------------------------------|
| | α | β | Other ^b | |
| IIIa | 5.03 (3) | 5.49 (4) | 5.65–6.05 (19) | 6.17 (2) ^c |
| IIIb | 5.04 (4) | 5.51 (3) | 5.72–6.10 (19) | 6.50 (2) |
| IIIc | 5.01 (4) | 5.47 (4) | 5.70–6.03 (18) ^d | 6.72 (2) |

^a Chemical shifts are given in τ values. Deuteriochloroform was used as solvent. Relative intensities are in parentheses. ^b Protons of unsubstituted and methylene-substituted rings. ^c Signal of considerable broadness, indicating retarded rotation of the methylene bridge. ^d Resolved into 5-proton singlet at τ 5.79 (unsubstituted ring protons of ferrocenyl portion) and 13-proton multiplet near τ 5.92 (residual ferrocene protons).

The intensity values in the α and β columns immediately identify IIIa, b, and c as the 1,2, 1,3, and 1,1' species, respectively. Additional evidence was obtained from the positions of the methylene protons (last column, Table I). Being well within the negative shielding region of, and in close proximity to, the carbonyl group, the protons of the methylene bridge in IIIa experienced the highest downfield shift (τ 6.17, compared, *e.g.*, with τ 6.62 for the corresponding signal in diferrocenylmethane), followed by the methylene protons of IIIb (τ 6.50).¹⁵ On the other hand, the methylene protons of the heteroannular isomer IIIc, capable of spending ever so limited residence time in the positive shielding cone of the carbonyl group, gave a singlet resonance at a position (τ 6.72) upfield from that of diferrocenylmethane.

Clemmensen reduction of the ketones IIIa–c so identi-

(14) See, for instance, M. D. Rausch and V. Mark, *J. Org. Chem.*, **28**, 3225 (1963); R. A. Benkeser, Y. Nagai, and J. Hooz, *Bull. Chem. Soc. (Japan)*, **36**, 482 (1963); **37**, 53 (1964); M. I. Levenberg and J. H. Richards, *J. Am. Chem. Soc.*, **86**, 2634 (1964); R. A. Benkeser and J. L. Bach, *ibid.*, **86**, 890 (1964); Rinehart and co-workers, *ref. 4c*.

fied gave in smooth reaction the corresponding methylene compounds, which, in corroboration of the initial, tentative assignments, were found to be identical with IIa–c.

Experimental Section¹⁶

Trinuclear Fraction of I ($n = 2$).—A polycondensation was carried out as described (except 6, Table I, *loc. cit.*^{2a}) by fusing the mixture of 80.00 g. (0.329 mole) of N,N-dimethylamino-methylferrocene,¹⁷ 122.50 g. (0.658 mole) of ferrocene, 22.88 g. (0.166 mole) of anhydrous zinc chloride, and 31.44 g. (0.327 mole) of concentrated (38%) hydrochloric acid for 7 hr. at 170° with stirring under nitrogen. Removal of catalysts and salt-like by-products by water extraction left a crude polymer mixture which was reprecipitated from dioxane solution (600 ml.) by the threefold volume of methanol. Addition of excess water to the mother liquor furnished a second portion of solids (132.6 g. after drying for 24 hr. over phosphorus pentoxide *in vacuo*) consisting of oligomers and unreacted ferrocene. The cyclohexane extract from this oligomer-ferrocene mixture was chromatographed on 3000 g. of Alcoa, grade F-20, alumina partially deactivated by 14-hr. exposure to air of 70% relative humidity. Elution with hexane gave a broad, incompletely resolved zone containing ferrocene and diferrocenylmethane, followed by a clearly separated band consisting of the trinuclear isomer mixture I ($n = 2$). The crude solid recovered from the eluate of this band, 17.35 g. of orange-yellow crystals, melted in the range 105–135°. Analytical data and molecular weight are given in the first line of Table II.

TABLE II

| Com- pound | M.p., °C. | Found, ^a % | | | Mol. wt. ^b |
|----------------------------|--------------|-----------------------|------|-------|--------------------------|
| | | C | H | Fe | |
| I ($n = 2$) ^c | 105–135 | 66.30 | 5.25 | 28.90 | 575 |
| IIa | 203–205 | 65.97 | 5.23 | 28.83 | 590 |
| IIb | 146–147 | 66.13 | 5.21 | 28.52 | 585 |
| IIc | 164–166 | 66.10 | 5.31 | 28.69 | 580 |
| IIIa | 176–178 | 64.28 | 4.85 | | 570 |
| IIIb | 212–214 | 64.35 | 4.71 | | 590 |
| IIIc | 157–159 | 64.87 | 4.73 | | 585 |

^a Anal. Calcd. for C₃₂H₃₀Fe₃ (structures II, mol. wt. 582): C, 66.02; H, 5.19; Fe, 28.78. Calcd. for C₃₂H₂₈OFe₃ (structures III, mol. wt. 596): C, 64.42; H, 4.69. ^b Determined in dibromomethane, rounded off to the nearest 5. ^c Isomer mixture obtained by chromatography (see text).

Isomers IIa–c.—After all attempts at separating, without concomitant decomposition, the above fraction I ($n = 2$) into its components IIa–c by vapor phase chromatography (*v.p.c.*) or elution chromatography under a variety of conditions had met with failure, a conventional fractional crystallization technique was employed, using hexane as solvent. In three parallel, carefully conducted, time-consuming operations involving the isolation and further utilization of several hundred subfractions (identified by melting ranges and X-ray diffractograms⁹), the mixture was separated into the components IIa–c, with IIa being the least soluble and IIb the most soluble species. The crude, rounded-off yields (average of the three operations) obtained from 10.0 g. of starting mixture were 0.7 g. for IIa, 3.6 g. for IIb, and 3.0 g. for IIc (73% material recovery).

1,2-Bis(ferrocenylmethyl)ferrocene (IIa) formed fine, yellow crystals (X-ray diffractogram: 5.84, 4.99, 4.82, 3.79, and 4.32)

(15) This observation finds a parallel in the report by the Benkeser group (*ref. 14*) regarding the deshielding effect of the carbonyl group in acetylalkylferrocenes on the α hydrogens of alkyl substituents on the same ring.

(16) Melting points are uncorrected. Infrared spectra were obtained by Mr. R. J. DiMarzo on a Perkin-Elmer, Model 421, spectrophotometer. X-ray diffractograms were recorded by Mr. R. L. Harvey, using a Norelco X-ray diffractometer (vanadium-filtered K α chromium radiation); d spacings, in Å., given for the five strongest peaks in order of decreasing intensity within the angular range $2\theta = 10$ –35°. Dr. L. P. Lindeman (*ref. 1a*) recorded the p.m.r. spectra (in deuteriochloroform solution) on a Varian Associates, Model A-60, n.m.r. spectrometer operating at 60 Mc./sec.; chemical shifts, τ , are given in parts per million relative to tetramethylsilane as internal standard. Molecular weights were measured in dibromomethane solution with a Mechrolab vapor pressure osmometer, Model 301 A. Combustion analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

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