HIGHER HOMOLOGUES FROM PYRROLES AND DIPYRRYLMETHENES[1]

S. F. MacDonald and A. Markovac[2]
Division of Pure Chemistry, National Research Council, Ottawa, Canada

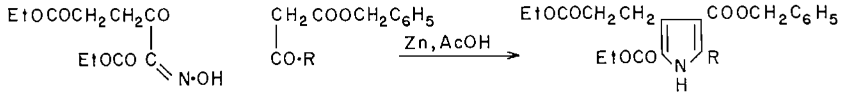
Received July 20, 1965

ABSTRACT

Higher alkyl derivatives were obtained from bromomethyl-pyrroles or -dipyrrylmethenes with the use of Grignard reagents.

INTRODUCTION

The synthesis of pyrro- and δ-phyllo-porphyrins related to the *Chlorobium* chlorophylls (1) required I*a* and its homologues, I*c* and I*d*. These were obtained conventionally as the need for them arose:



followed by

$$COOCH_2C_6H_5 \rightarrow COOH \rightarrow H \rightarrow CHO \rightarrow CH_3$$

The desirability of a general method for conversions such as that of I*a* into I*c* and I*d*, to obtain all three from common intermediates and avoid the use of propionyl- or butyrylacetic esters, was clear in retrospect. A sequence of established reactions was available for this: 2-$CH_3 \rightarrow COOH \rightarrow H \rightarrow CO{\cdot}R \rightarrow CH_2R$, and we have applied it to III*a* (see below). Modifications also reverse the β-substituents: 4-methyl-pyrrole-3-propionic acid (from II*a*), is acylated in the 5-position (2), and a general method follows from the conversion of III*a* into III (CHO for COOEt, R = COOEt) (1).

The well-known reactivity of bromomethyl-pyrroles suggested the shorter sequence now described: $CH_3 \rightarrow CH_2Br$ (+ RMgBr) $\rightarrow CH_2R$. The bromomethyl-pyrroles I*b*, II*b*, and III*b* reacted with methyl- or ethyl-magnesium iodide to form the homologues I (*c* or *d*), II (*c* or *d*), and III (*c* or *d*). By a standardized procedure yields of 55–70% were obtained. We have recorded the preparation of III*b* because, as noted by Fischer (3), earlier references (4) are to its hydrobromide. The less reactive pyrrole V did not react in the desired way, and 30% of it was recovered unchanged. The pyrrole IV*a* (5) (now prepared in double the reported yield) gave IV (*b*, *c*, *d*, and *e*) with the appropriate Grignard reagents. As expected, the pyrroles VI and VII did not react and were recovered in good yield.

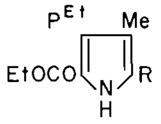
Of these homologues, I*c* (1), I*d* (1), IV*b* (6), and IV*c* (5, 7) were known, and II*c* could be hydrolyzed to the known half-ester (free propionic acid) (6, 8). The structures of III*c* and III*d* were confirmed by comparison with the products of the alternative sequence mentioned above, III ($a \rightarrow e \rightarrow f \rightarrow$ (g or h) $\rightarrow$ (c or d)). As all these Grignard reactions had taken the expected course, the structures of the remaining products, II*d*, IV*d*, and IV*e*, could be inferred.

Two moles of Grignard reagent were required for 55–70% yields; with 1 mole the yield was less than 30% and the products were difficult to purify. Presumably the Grignard

---

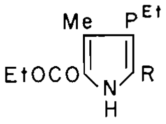
[1] *Issued as N.R.C. No. 8681.*
[2] *National Research Council Postdoctorate Fellow, 1963–1965.*

Canadian Journal of Chemistry. Volume 43 (1965)



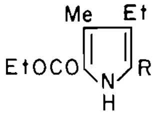
I

(a) R = CH_3
(b) R = CH_2Br
(c) R = Et



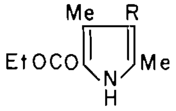
II

(d) R = CH_2Et
(e) R = COOH
(f) R = H



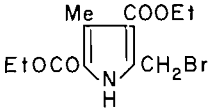
III

(g) R = $CO{\cdot}CH_3$
(h) R = $CO{\cdot}Et$
P^{Et} = CH_2CH_2COOEt

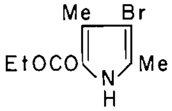


IV

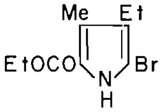
(a) R = CH_2Cl
(b) R = Et ≡ IIIa
(c) R = CH_2Et
(d) R = $(CH_2)_5CH_3$
(e) R = $(CH_2)_6CH_3$



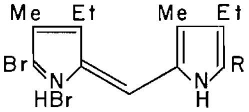
V



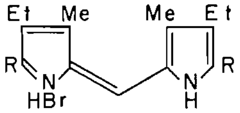
VI



VII



VIII



IX

(a) R = CH_3
(b) R = CH_2Br
(c) R = Et

reagent reacts also with the active hydrogen of the pyrrole. The formally analogous reaction of pyrryl magnesium bromides with III*b* required only 1.3 moles of the former for a >70% yield of dipyrrylmethane (3). Like the acylation of N-ethyl pyrryl magnesium bromide (9), the latter may be condensations rather than Grignard reactions, because pyrroles such as III*b* and even V readily undergo acid-catalyzed condensation with reactive pyrroles to dipyrrylmethanes (10).

Although dipyrrylmethenes without 5-hydroxy groups are amenable to few general reactions, their 5-bromomethyl derivatives, when these can be obtained, are very reactive. Thus the hydrobromides of the dipyrrylmethenes VIII*b* and IX*b* reacted with an excess of methyl magnesium iodide to give VIII*c* and IX*c* respectively, both of which were identified by comparison with the products of conventional syntheses. Nucleophiles, including Grignard reagents (11), frequently attack the bridge of negatively substituted dipyrrylmethenes. No such addition was observed here, and furthermore, VIII*a* and IX*a* were recovered as the free bases but otherwise unchanged after the same treatment.

EXPERIMENTAL

2-Bromomethyl-3-ethyl-4-methyl-5-carbethoxy-pyrrole (IIIb)

Bromine (8 ml) in 50 ml of carbon tetrachloride was slowly dropped into a stirred and water-cooled solution of 16 g of 2,4-dimethyl-3-ethyl-5-carbethoxy-pyrrole (III*a* (12)) in 100 ml of carbon tetrachloride. After 2 h, the yellow crystals of the hydrobromide (22 g, m.p. 128–134°; lit. (4):128–132°) were separated, washed with ether, and dried. This was treated by reflux with benzene (120 ml) until solution was complete and no more HBr was evolved. Colorless needles of the product (16.5 g, 73%, m.p. 144°) were separated from the cooled solution and washed with *n*-hexane.

For analysis it was recrystallized from benzene–*n*-hexane, m.p. 145°.

Calcd. for $C_{11}H_{16}NO_2Br$: C, 48.16; H, 5.87; N, 5.11; Br, 29.16. Found: C, 48.31; H, 5.78; N, 5.31; Br, 29.06.

2,3-Di-ethyl-4-methyl-5-carbethoxy-pyrrole (IIIc)

(a) General Procedure

2-Bromomethyl-3-ethyl-4-methyl-5-carbethoxy-pyrrole (III*b*, 3.4 g, 0.0125 mole) in 70 ml of dry tetrahydrofuran was added dropwise to the Grignard reagent from 0.65 g (0.027 g-atom) of magnesium, 3.54 g (0.025 mole) of methyl iodide and 100 ml of dry ether. The yellow suspension was stirred and heated under reflux for 4 h. Half of the solvent was removed *in vacuo* and ether (50 ml), then aqueous ammonium chloride, were added to the remainder. The aqueous layer was separated off and washed with ether. The combined ether layers were washed with water and dried (Na_2SO_4), and the ether was evaporated *in vacuo*. The crystalline residue was recrystallized from 70% ethanol, and yielded 1.8 g (69%) of colorless prisms, m.p. 68°.

The analytical sample was thrice recrystallized, m.p. 73–74°, which was unchanged when it was mixed with the product of (*b*) below.

Calcd. for $C_{12}H_{19}NO_2$: C, 68.86; H, 9.15; N, 6.69. Found: C, 68.98; H, 9.29; N, 6.83.

(b) The pyrrole III*a* was converted successively into III*e* (13), III*f* (14), and III*g* (8). This last was hydrogenated in ethanol with Raney nickel (1200 p.s.i., 120°, 40 h). The filtrate from the catalyst was concentrated and then cooled to give the crystalline product (90%), m.p. 72°.

The analytical sample was thrice recrystallized from 70% ethanol as colorless prisms, m.p. 73–74°. Found: C, 68.71; H, 9.13; N, 6.83.

2-n-Propyl-3-ethyl-4-methyl-5-carbethoxy-pyrrole (IIId)

(a) By the general procedure, III*b* and ethyl magnesium iodide gave an oily crude product which was distilled (170°, 1 × 10^{-4} mm). The distillate (58%, m.p. 77°) was recrystallized from 80% ethanol as long colorless prismatic rods, m.p. 82°, which was unchanged when it was mixed with the product of (*b*) below.

Calcd. for $C_{13}H_{21}NO_2$: C, 69.92; H, 9.48; N, 6.27. Found: C, 70.05; H, 9.58; N, 6.48.

(b) 2-Propionyl-3-ethyl-4-methyl-5-carbethoxy-pyrrole (III*h*, see below) was reduced in ethanol over Raney nickel (120°, 1200 p.s.i., 40 h). The filtrate from the catalyst was concentrated and cooled to give the colorless crystalline product (95%), m.p. 80°. When recrystallized from 80% ethanol it formed prismatic rods m.p. 82°.

2-Propionyl-3-ethyl-4-methyl-5-carbethoxy-pyrrole (IIIh)

The acylation of III*f* with propionyl chloride was analogous to that with acetyl chloride (8). A colorless product (57%), m.p. 78°, was obtained by recrystallizing the crude material from petroleum ether (30–60°).

The analytical sample was thrice recrystallized from petroleum ether as prismatic rods, m.p. 80°.

Calcd. for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07; N, 5.90. Found: C, 65.80; H, 8.08; N, 5.72.

2-Ethyl-3-methyl-5-carboxy-pyrrole-4-propionic Acid Di-ethyl Ester (Ic)

The oily crude product of the above general Grignard procedure applied to I*b* (15) and methyl magnesium iodide was distilled (140–150°, 1 × 10^{-4} mm), after which it solidified as colorless crystals (65%), m.p. 76°.

The analytical sample was recrystallized four times from 60% ethanol as colorless needles, m.p. 79–80°, which was undepressed by authentic material of m.p. 81–82° (1).

Calcd. for $C_{15}H_{23}NO_4$: C, 64.03, H, 8.24; N, 4.98. Found: C, 63.91; H, 8.42; N, 5.10.

2-n-Propyl-3-methyl-5-carboxy-pyrrole-4-propionic Acid Di-ethyl Ester (Id)

A reaction between ethyl magnesium iodide and I*b* was carried out in the same way, and the oily crude product was distilled (1 × 10^{-4} mm). For analysis it (57%, m.p. 74°) was recrystallized four times from 60% ethanol as colorless needles, m.p. 77–78°, which was undepressed when it was mixed with authentic material of m.p. 77–79° (1).

Calcd. for $C_{16}H_{25}NO_4$: C, 65.06; H, 8.53; N, 4.74. Found: C, 65.13; H, 8.69; N, 4.77.

2-Ethyl-4-methyl-5-carboxy-pyrrole-3-propionic Acid Di-ethyl Ester (IIc)

Methyl magnesium iodide and II*b* (15) similarly gave an oily crude product, which was distilled (160–170°, 1 × 10^{-4} mm). For analysis the colorless distillate (60%, m.p. 49–50°) was thrice recrystallized from petrol (20–40°) as colorless prisms, m.p. 52°.

Calcd. for $C_{15}H_{23}NO_4$: C, 64.03; H, 8.24; N, 4.98. Found: C, 64.12; H, 8.21; N, 5.16.

2-Ethyl-4-methyl-5-carbethoxy-pyrrole-3-propionic Acid

The above di-ester was heated under reflux with 1 equivalent of potassium hydroxide in ethanol, and the solvent was then evaporated. The product was precipitated with acid from a solution of the residue in water, then recrystallized from benzene – petrol ether as colorless prisms, m.p. 140° (lit. (6): 138°).

Calcd. for $C_{13}H_{19}NO_4$: C, 61.64; H, 7.56; N, 5.53. Found: C, 61.54; H, 7.54; N, 5.70.

2-n-Propyl-4-methyl-5-carbethoxy-pyrrole-3-propionic Acid Di-ethyl Ester (IId)

The oily crude product from the reaction between II*b* and ethyl mganesium iodide was distilled (150°, 1×10^{-4} mm) and the product (56%, m.p. 57°) was recrystallized thrice from 80% ethanol as long colorless needles, m.p. 63–64°.

Calcd. for $C_{16}H_{25}NO_4$: C, 65.06; H, 8.53; N, 4.74. Found: C, 64.99; H, 8.57; N, 4.96.

2,4-Dimethyl-3-chloromethyl-5-carbethoxy-pyrrole (IVa) (5)

A slurry of paraformaldehyde (6 g) in 75 ml of acetic acid was cooled in ice and stirred while a rapid current of dry hydrogen chloride was passed through. A solution of 31 g of 2,4-dimethyl-5-carbethoxy-pyrrole in 200 ml of acetic acid was then dropped in over a period of 15 min. Passage of the gas stream was continued for 2 h. The mixture was poured into 1 liter of dry ether and refrigerated overnight. The crude product (30 g, m.p. 160° after washing with ether) was recrystallized from benzene as colorless needles (24 g, 60%), m.p. 164–165° (lit. (5): 164–166°).

2,4-Dimethyl-3-ethyl-5-carbethoxy-pyrrole (IVb)

The crude light yellow product of the reaction between IV*a* and methyl magnesium iodide was recrystallized from 95% ethanol as colorless crystals (72%), m.p. 90°. For analysis it was thrice recrystallized as colorless needles, m.p. 94° (lit. (6): 96°), which was unchanged when it was mixed with authentic material.

Calcd. for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.78; N, 7.17. Found: C, 67.79; H, 8.96; N, 7.33.

2,4-Dimethyl-3-n-propyl-5-carbethoxy-pyrrole (IVc)

The crude product of the reaction between IV*a* and ethyl magnesium iodide was crystallized from 95% ethanol as colorless crystals (67%, m.p. 98°). For analysis it was thrice recrystallized as prisms, m.p. 97.5–98.5° (lit. (7): 98°).

Calcd. for $C_{12}H_{19}NO_2$: C, 68.86; H, 9.15; N, 6.69. Found: C, 68.57; H, 8.96; N, 6.81.

2,4-Dimethyl-3-n-hexyl-5-carbethoxy-pyrrole (IVd)

The oily crude product of the reaction between IV*a* and *n*-pentyl magnesium bromide was distilled (140–150°, 1×10^{-4} mm). The distillate solidified into colorless plates (70%), m.p. 59°. For analysis it was recrystallized thrice from 85% ethanol as colorless plates, m.p. 61–62°.

Calcd. for $C_{15}H_{25}NO_2$: C, 71.67; H, 10.03; N, 5.57. Found: C, 71.73; H, 10.13; N, 5.75.

2,4-Dimethyl-3-n-heptyl-5-carbethoxy-pyrrole (IVe)

The oily crude product of the reaction between IV*a* and *n*-hexyl magnesium bromide was distilled (140–150°, 1×10^{-4} mm). The crystalline distillate was recrystallized from 80% ethanol as colorless plates (61%), m.p. 52°. For analysis, it was thrice recrystallized, m.p. 54–55°.

Calcd. for $C_{16}H_{27}NO_2$: C, 72.41; H, 10.26; N,5.28. Found: C, 72.60; H, 10.41; N, 5.41.

2-Formyl-3-ethyl-4-methyl-5-bromo-pyrrole (16)

The corresponding 5-carboxy pyrrole (17) (1 g) was dissolved in 3 ml of acetic acid, a solution of bromine (0.3 ml) in acetic acid (1 ml) was added, and the mixture was heated for 1 h on a steam bath. The solvent was then removed *in vacuo* and the product extracted from the residue into hot petrol (40–60°), leaving the insoluble by-product. The petrol solution was washed with 5% ammonium hydroxide, then with water, and dried with sodium sulfate. The petrol was evaporated, and the residue was crystallized from petroleum ether as colorless prisms (0.4 g, 33%), m.p. 114–115° (lit. (16): 115°).

2,3-Di-ethyl-4-methyl-pyrrole (8)

The 5-carbethoxy derivative (III*c*, 1.5 g) was heated for 20 h at 180° with 10 ml of 15% sodium hydroxide in a Teflon lined screw-capped brass tube. After it was cooled, the product was extracted with ether and the solution was dried with potassium carbonate. The ether was evaporated, and the product distilled (110°, 15 mm) as a colorless oil (100 mg).

4,5,3′-Tri-ethyl-3,4′-dimethyl-5′-bromo-dipyrrylmethene Hydrobromide (VIIIc)

(a) The dipyrrylmethene hydrobromide (VIII*b*, 481 mg (3)), suspended in 80 ml of tetrahydrofuran, was dropped into a solution of Grignard reagent (4 moles, from 98 mg of magnesium, 567 mg of methyl iodide, and 50 ml of ether). The mixture was stirred under reflux for 2 h, then left for 2 h at 20°. Half the solvent was removed *in vacuo*, fresh ether was added, and the product was hydrolyzed with aqueous ammonium chloride. The ether layer and washings were washed with water, dried with sodium sulfate, and the solvent evaporated. The residue was treated by reflux with 3 ml of ethanol. An insoluble by-product separated out, after which the ethanol was evaporated. The residue was converted into the hydrobromide by dissolving it

in 32% hydrogen bromide in acetic acid. The latter was evaporated, and a crystalline product was left which was recrystallized from ethanol–ether as brown prisms (200 mg, 48%), m.p. 185° (dec.). The X-ray powder photograph of this product and of that of (*b*) below were identical.

For analysis, it was recrystallized thrice from chloroform–ether as red-brown prisms, m.p. 204–205° (dec.).

Calcd. for $C_{17}H_{24}N_2Br_2$: C, 49.04; H, 5.81; N, 6.73; Br, 38.42. Found: C, 48.87; H, 5.63; N, 6.89; Br, 38.24.

The hydrobromide (50 mg) was dissolved in ethanol, a drop of 5% aqueous sodium hydroxide was added, and the solution was cooled. The free base which separated was recrystallized from ethanol as orange–brown prisms, melting point and mixed melting point with the free base prepared by method (*b*) below, 85°.

(*b*) 2-Formyl-3-ethyl-4-methyl-5-bromo-pyrrole (55 mg), 2,3-di-ethyl-4-methyl-pyrrole (35 mg), and 0.2 ml of acetic acid were well mixed in a small beaker cooled in an ice bath. Hydrobromic acid (0.2 ml of 48%) was added and the mixture stirred for about 30 min. The crystalline hydrobromide was separated out, washed with ether then with acetic acid, and recrystallized from ethanol–ether as red-brown prisms, m.p. 190° (dec.).

For analysis, it was thrice recrystallized from chloroform–ether as red-brown prisms, m.p. 202–203° dec.). Found: C, 49.13; H, 5.76; N, 6.91.

The free base was obtained as under (*a*) above as orange–brown prisms, m.p. 85–86°.

3,5,3′,5′-Tetramethyl-4,4′-di-ethyl-dipyrrylmethene Hydrobromide (IXa) (18)

As in analogous cases, the 5-carbethoxy derivative is now more easily available than 2,4-dimethyl-3-ethyl-pyrrole itself, and the dipyrrylmethene can be more conveniently prepared directly from the former (19) by a general method devised by Fischer (20).

The hydrobromide was converted to the free base, m.p. 150° (lit. (18): 151°), which was unchanged when it was mixed with authentic material.

3,3′-Dimethyl-4,4′-di-ethyl-5,5′-di-bromomethyl-dipyrrylmethene Hydrobromide (IXb) (21)

The dipyrrylmethene hydrobromide (IX*a*, 3.5 g) was dissolved in 60 ml of acetic acid with warming, 4.5 g of bromine was added, and the mixture was heated for 2 h on a steam bath. After it was cooled, the crystals were separated out, washed with acetic acid, then with ether, and recrystallized from chloroform–ether as red–brown prisms (4 g, 78%).

4,5,4′,5′-Tetra-ethyl-3,3′-dimethyl-dipyrrylmethene Hydrobromide (IXc)

(*a*) The di-bromomethyl dipyrrylmethene hydrobromide (IX*b*, 496 mg), suspended in 80 ml of tetrahydrofuran, was dropped into a solution of Grignard reagent (4 moles, from 96 mg of magnesium, 567 mg of methyl iodide, and 50 ml of ether). The mixture was stirred under reflux for 1 h, then left for 2 h at 20°. Half the solvent was removed *in vacuo*, 10 ml of cold water was added, and the mixture was stirred for 10 min. Chloroform (50 ml) and hydrobromic acid (10 ml of 10%) were added and the mixture was well shaken. The chloroform layer and washings were washed with water and dried with sodium sulfate. The chloroform was evaporated and the residue crystallized from acetic acid as brown–red rods (150 mg, 41%), m.p. 180–184°, (lit. 180° (dec.) (8); 190° (21)). After it was recrystallized again from acetic acid, this product, m.p. 186°, and that obtained as under (*b*) below gave identical X-ray powder photographs.

The hydrobromide (100 mg) was dissolved in 3 ml of ethanol, a drop of ammonium hydroxide was added, the mixture was cooled, and the free base separated. It was recrystallized from aqueous ethanol as orange–brown needles, m.p. 116° (lit. 116° (8)), which was undepressed when it was mixed with the base obtained as under (*b*) below.

Calcd. for $C_{19}H_{28}N_2$: C, 80.23; H, 9.92; N, 9.85. Found: C, 80.33; H, 10.03; N, 10.09.

(*b*) 2,3-Di-ethyl-4-methyl-5-carbethoxy-pyrrole (III*c*, 300 mg), 3 ml of 98% formic acid, and 2 ml of 48% hydrobromic acid were heated for 1 h on a steam bath. After the mixture had stood overnight at 20°, the product was separated out and recrystallized from acetic acid as prismatic crystals (180 mg, 88%), m.p. 185–186°.

The free base, obtained as under (*a*) above, was thrice recrystallized from 95% ethanol as orange–brown needles, m.p. 116–117°. Found: C, 80.01; H, 9.74; N, 10.03.

VIIIa and IXa with the Grignard Reagent

The chloroform-insoluble perbromide of VIII*a* was treated under reflux for 10 min with 9 parts of acetone, then the mixture was refrigerated. On the next day orange–red prisms of the hydrobromide, VIII*a* (98%), were separated off and washed with ether, m.p. 215–217° (dec.) (lit. (3): 215°).

The dipyrrylmethene hydrobromides VIII*a* and IX*a*, suspended in tetrahydrofuran, were added to ethereal methyl magnesium iodide (3 and 4 moles respectively), heated under reflux, and worked up as in the preparation of VIII*c* by method *a*. When the ethanol was removed and the residues crystallized from aqueous ethanol, the starting methenes VIII*a* and IX*a* were obtained as the corresponding free bases.

The free base from VIII*a* (75%) had a melting point and mixed melting point with authentic material of 102° (lit. 103° (3)).

Calcd. for $C_{16}H_{21}N_2Br$: Br, 24.90. Found: Br, 25.02.

The free base from IX*a* (60%) had m.p. 152°, 151° when mixed with authentic material (lit. 151° (18)).

REFERENCES

1. J. L. Archibald, D. M. Walker, K. B. Shaw, A. Markovac, and S. F. MacDonald. In preparation. J. L. Archibald, S. F. MacDonald, and K. B. Shaw. J. Am. Chem. Soc. **85**, 644 (1963).
2. H. Fischer and Z. Csukas. Ann. **508**, 167 (1934).
3. H. Fischer, E. Baumann, and H. J. Riedl. Ann. **475**, 205 (1929).
4. H. Fischer and P. Ernst. Ann. **447**, 139 (1926). H. Fischer and H. Orth. Chemie des pyrrols. Vol. I. Akademische Verlagsgesellschaft, Leipzig. 1934. p. 95.
5. T. H. Curry. Dissertation. Ohio State University 1953.
6. H. Fischer and J. Klarer. Ann. **447**, 48 (1926).
7. H. Fischer, M. Goldschmidt, and W. Nüssler. Ann. **486**, 1 (1931).
8. H. Fischer and H. K. Weichmann. Ann. **492**, 35 (1932).
9. W. Herz. J. Org. Chem. **22**, 1260 (1957).
10. H. Fischer and P. Halbig. Ann. **447**, 123 (1926).
11. J. H. Paden, A. H. Corwin, and W. A. Bailey, Jr. J. Am. Chem. Soc. **62** 418 (1940). K. J. Brunings and A. H. Corwin. J. Am. Chem. Soc. **66**, 337 (1944). H. Booth, A. W. Johnson, F. Johnson, and R. A. Langdale-Smith. J. Chem. Soc. 650 (1963).
12. F. K. Signaigo and H. Adkins. J. Am. Chem. Soc. **58**, 709 (1936).
13. H. Fischer and H. Orth. Chemie des pyrrols. Vol. I. Akademische Verlagsgesellschaft, Leipzig. 1934. p. 252.
14. H. Fischer and H. Orth. Chemie des pyrrols. Vol. I. Akademische Verlagsgesellschaft, Leipzig. 1934. p. 241.
15. F. Morsingh and S. F. MacDonald. J. Am. Chem. Soc. **82**, 4377 (1960).
16. W. Siedel and H. Fischer. Z. Physiol. Chem. **214**, 145 (1933).
17. H. Fischer, E. Sturm, and H. Friedrich. Ann. **461**, 270 (1928).
18. H. Fischer, P. Halbig, and B. Walach. Ann. **452**, 296 (1927).
19. A. W. Johnson, I. T. Kay, E. Markham, R. Price, and K. B. Shaw. J. Chem. Soc. 3416 (1959).
20. H. Fischer, H. Friedrich, W. Lamatsch, and K. Morgenroth. Ann. **466**, 165 (1928).
21. H. Fischer and A. Kürzinger. Z. Physiol. Chem. **196**, 213 (1931).