was suspended in methanol and the suspension was saturated with carbon dioxide, heated, and filtered. This extraction process was repeated four times, and the combined extracts were evaporated at reduced pressure. The residue, a white solid, was extracted with chloroform. The chloroform extracts were evaporated and the residue was crystallized from methanol, yielding 0.4 g. (45.6%) of V, colorless needles, m.p. 179–180°.

Anal. Calcd. for $C_{12}H_{13}O_3N$: C, 65.74; H, 5.99. Found: C, 65.74; H, 6.15.

Dihydrodictamnine (VI). To a suspension of 0.02 g. (1 mmole) of sodium hydride in 25 ml. of tetrahydrofuran was added 0.2 g. (0.91 mmole) of 4-methoxy-2-hydroxy-3(2′-hydroxyethyl)quinoline. The resulting mixture was stirred overnight at room temperature. *p*-Toluenesulfonyl chloride (0.18 g., 0.94 mmole) was added at once and stirred for 1 hr. The excess reagents were decomposed by the addition of a few drops of water, followed by 5 ml. of dilute aqueous sodium hydroxide. This aqueous suspension was then stirred for an additional hour to ensure complete hydrolysis of the *p*-toluenesulfonyl chloride. The tetrahydrofuran was removed by distillation at reduced pressure and the aqueous residue was extracted three times with chloroform. The chloroform was evaporated on the steam bath, and the oily residue was extracted three times with boiling petroleum ether (b.p. 60–80°). Evaporation of the petroleum extracts and recrystallization of the residue from methanol-water gave 0.1 g. (55%) of dihydrodictamnine, m.p. 103–104.5°. (Reported[6] 103–104°.) Infrared: 1625 cm.$^{-1}$; ultraviolet $\lambda_{max}^{ethanol}$: 262 mμ, log ϵ 3.58; 272 mμ, log ϵ 3.67; 283 mμ, log ϵ 3.58; 308 mμ, log ϵ 3.40; 320 mμ, log ϵ 3.46.

Anal. Calcd. for $C_{12}H_{11}O_2N$: C, 71.62; H, 5.51. Found: C, 71.62; H, 5.22.

Acid hydrolysis of methyl 3-azabenzocycloheptene-4,7-dione-6-carboxylate. A suspension of 2 g. (0.086 mole) of the ester I in 50 ml. of 4*N* sulfuric acid was refluxed for 3 hr. The reaction mixture was allowed to stand overnight and filtered. The precipitate was digested with methanol and filtered hot. The residue (1.0 g., 53.5%) was soluble in aqueous sodium bicarbonate and its infrared spectrum was identical with that of the quinoline carboxylic acid (III) melting at 295–300° (dec.). A mixed melting point with a sample of III prepared from basic hydrolysis was undepressed.

The methanolic filtrate from above was concentrated and cooled, giving crystals melting at 200–205°, which then solidified, remelting at 310–315°. This material was insoluble in sodium bicarbonate and its infrared and ultraviolet spectra were identical with the methyl ester of 2,4-dihydroxyquinoline-3-acetic acid (IIIa).

Anal. Calcd. for (IIIa) $C_{12}H_{11}O_4N$: C, 61.80; H, 4.75. Found: C, 61.56; H, 4.48.

Basic hydrolysis of the methylation product. A solution of 2 g. (0.081 mole) of the methyl ether of VII in 200 ml. of 2% aqueous sodium hydroxide was refluxed for 35 min. The reaction mixture was made acid with 6*N* hydrochloric acid and cooled. The crystals formed were collected by filtration and recrystallized from methanol, yielding 0.6 g. (32%) of the acid VIIa, melting at 215–217° with evolution of a gas. Infrared: 1710 cm.$^{-1}$, 1665 cm.$^{-1}$; ultraviolet $\lambda_{max}^{ethanol}$: 279 mμ, log ϵ 3.46.

Anal. Calcd. for (VIIa), $C_{12}H_{11}O_4N$: C, 61.80; H, 4.75. Found: C, 61.97; H, 4.65.

Los Angeles 24, Calif.

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[6] R. G. Cooke and H. F. Haynes, *Australian J. Chem.*, 7, 273 (1954).

[Contribution from the Department of Chemistry, Duke University]

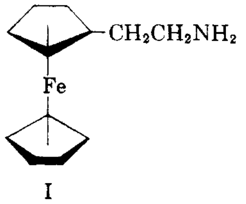
Structure of the Product of Anomalous Leuckart Reaction of 2-Ferrocylethylamine. A Route to 1,2-Disubstituted Ferrocenes[1]

DANIEL LEDNICER and CHARLES R. HAUSER

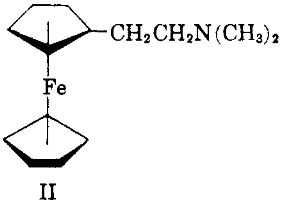
Received July 31, 1958

The product of the reaction of 2-ferrocylethylamine with formic acid and formaldehyde has been assigned the structure of the tetrahydroisoquinoline analog in the ferrocene series on the basis of degradative work. On treatment with strong base the methiodide of the cyclic product was opened to 1-*N*,*N*-dimethylaminomethyl-2-vinylferrocene. The structural features of the latter compound were demonstrated by spectra, hydrogenation, and displacement reactions.

It has been recently reported that the treatment of the primary amine I with formic acid and formaldehyde under the conditions of the Eschweiler-Clarke modification of the Leuckart reaction affords instead of the expected product II, a tertiary amine of unknown structure.[2] At that time it was suggested that the presumably first formed intermediate III undergoes cyclization into the ferrocene ring. Such a ring closure would result in a product that had the structure IV. Osgerby and Pauson[3] have recently made the same suggestion.



I



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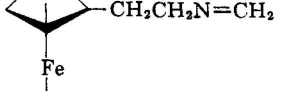
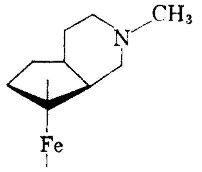


III



IV

In the present work, the methiodide of the Eschweiler-Clarke reaction product was prepared as

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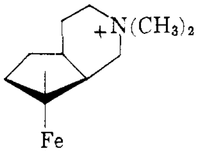
[1] Supported by the Office of Ordnance Research, U.S. Army.

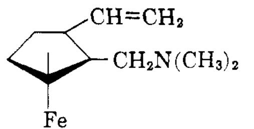
[2] D. Lednicer, J. K. Lidsay, and C. R. Hauser, *J. Org. Chem.*, 23, 653 (1958).

[3] J. M. Osgerby and P. L. Pauson, *Chem. and Ind. (London)*, 196 (1958).

described previously.[2] In the earlier report[2] the reaction of that methiodide with potassium amide to afford a tertiary amine was described. The reaction was repeated to give that amine in an almost quantitative yield. If the methiodide is assigned the structure V, treatment with the strong base would be expected to lead to a β-elimination to form the unsaturated amine VI.



V



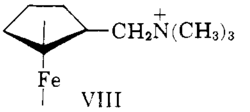
VI

It was found that the spectral data were in good agreement with the structure VI. Thus the product exhibited a sharp infrared band at 6.1 μ as well as one at 11.1 μ characteristic of a terminal methylene. While alkylferrocenes exhibit rather featureless ultraviolet absorption spectra, VI was found to show the absorption maximum at 273 mμ characteristic of vinylferrocene.[4] The latter was taken as evidence that the double bond of VI was conjugated with the ring.

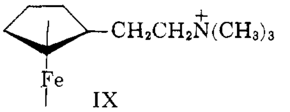
Treatment of the unsaturated amine VI with hydrogen over palladium-on-charcoal resulted in the uptake of an equivalent of the gas. The infrared spectrum of the resulting liquid amine, VII (see Scheme A) showed neither the band at 6.1 μ nor that at 11.1 μ. The 273 mμ band in the ultraviolet spectrum had similarly disappeared.

Although the above evidence for the presence of the conjugated vinyl group in VI leaves little choice for the formulation of the remainder of the molecule, it was nevertheless deemed desirable to demonstrate the presence of the "benzyl type" *N,N*-dimethylamino group.

It is known that the methiodide of *N,N*-dimethylaminomethylferrocene (VIII) readily reacts with hydroxide ion[5] or cyanide ion[2] to lose trimethylamine and form the corresponding alcohol or nitrile. In connection with the present investigation it was found that the homologous quaternary salt IX is unaffected by cyanide ion, and in the presence of hydroxide ion undergoes slow β-elimination to form vinylferrocene. These reactions would thus seem to be a useful diagnostic test for the presence of the "benzyl type" quaternary salt.

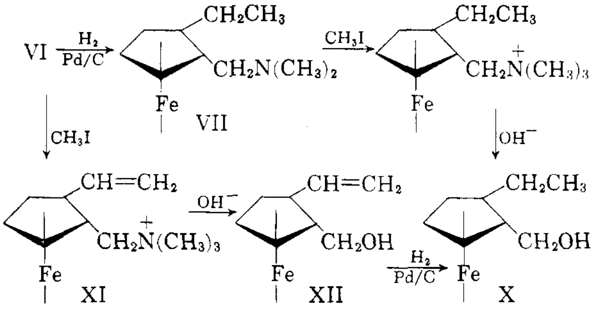


VIII

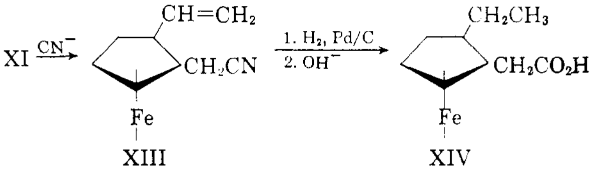


IX

Thus, it was found that treatment of the methiodide of the saturated amine VII with refluxing aqueous potassium hydroxide afforded the solid alcohol X. Similarly, the quaternary salt XI of the unsaturated amine VI produced on similar treatment the unsaturated alcohol XII. This product showed the same spectral earmarks (infrared bands at 6.1 μ and 11.1 μ and ultraviolet at 273 mμ) of the vinyl group as did the unsaturated amine VI. Catalytic reduction of XII resulted in the uptake of one equivalent of hydrogen. The product was shown by mixed melting point and infrared spectrum to be identical to X. The ultraviolet spectrum of this compound is the same as that of alkylferrocenes.



As further evidence for the ready displacement of trimethylamine from XI, this compound was treated with potassium cyanide. The liquid nitrile XIII which was obtained was reduced catalytically. The liquid saturated nitrile was in this case not purified but hydrolyzed directly to the acid XIV.



It is of interest that while ferrocylacetonitrile will readily undergo alkaline hydrolysis in refluxing ethanol,[2] these conditions did not appear to affect the 1-ethyl derrivative. The reaction of the sterically hindered compound was however achieved in good yield in refluxing alkaline aqueous ethylene glycol.

The experiments described above furnish evidence that in VI there are present a vinyl group and an *N,N*-dimethylaminomethyl group both of which are directly attached to the ferrocene ring. The fact that all the compounds in this series show infrared bands at 9 μ and 10 μ is taken as evidence that both groups are attached to the same ring.[6] Though the 1,2 relationship of the groups has not been proven, it is of interest that all these compounds show a very weak band at 10.5 μ which has been suggested to be characteristic of such disubstituted compounds.[7] The formation of a compound which has the structure of VI from the

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(4) F. S. Arimoto and A. C. Haven, Jr., *J. Am. Chem. Soc.*, **77**, 6295 (1955).

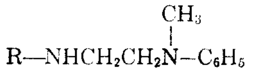
(5) J. K. Lindsay and C. R. Hauser, *J. Org. Chem.*, **22**, 355 (1957).

(6) M. Rosenblum, Ph.D. thesis, Harvard University, August 1953.

(7) K. K. Rinehart, Jr., K. L. Motz, and S. Moon, *J. Am. Chem. Soc.*, **79**, 2749 (1958).

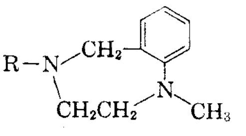
quaternary salt V on treatment with base can be rationalized only by assuming the abnormal Leuckart reaction to have involved a cyclization to IV.

The cyclization of the intermediate III[8] is not without precedent. Thus, it is known that tetrahydroisoquinolines may be obtained from β-arylethylamines by treating the condensation products of the latter and formaldehyde with hydrochloric acid.[9] Subsequent to our original work[2] a report appeared describing the cyclization of XV to XVI upon treatment with formic acid and formaldehyde under the conditions of the Eschweiler-Clarke reaction.[10]



$R{-}NHCH_2CH_2N(CH_3){-}C_6H_5$

XV R = 3 - tropanyl



XVI

It should be mentioned that it has been observed that ferrocylbutyric acid under acid conditions likewise undergoes cyclization into the ring to which the acid is attached.[11]

Finally the product of the ring opening, VI, may prove of synthetic value, since it contains two readily transformable functional groups in the 1,2 positions of a single ring of ferrocene. In principle at least, by reducing the nitrile group of XIII (or of the dihydro compound) to the primary amine and subjecting this again to the conditions of the Eschweiler-Clarke reaction a 1,2,3-trisubstituted ferrocene might be obtained.

EXPERIMENTAL[12]

Reduction of 1-dimethylaminomethyl-2-vinylferrocene (VI) *to 1-dimethylaminomethyl-2-ethylferrocene.* A suspension of 5.46 g. (0.020 mole) of the unsaturated amine[13] and 0.50 g. of 10% palladium-on-charcoal in 25 ml. of methanol was stirred under hydrogen at atmospheric pressure. Within 15 min., 493 ml. (theo. 496 ml.) of hydrogen had been absorbed. The catalyst was removed by filtration and washed with methanol. The filtrates were then diluted with water (200 ml.) and the oily product taken up in ether. After drying over sodium sulfate the solvent was removed from the ethereal solution. The residual oil was dried *in vacuo* to afford 5.36 g. (98%) of the amine VII.

Anal. Calcd. for $C_{15}H_{21}FeN$: C, 66.43; H, 7.81; N, 5.17. Found: C, 66.42; H, 7.72; N, 5.11.

A small sample (0.25 g.) of the amine was treated with 5 ml. of saturated ethanolic picric acid. The orange powder which was deposited was recrystallized twice from ethanol to afford the picrate as red needles m.p. 162–162.5°.

Anal. Calcd. for $C_{21}H_{24}FeN_4O_7$: C, 50.43; H, 4.84; Fe, 11.16; N, 11.20. Found: C, 50.19; H, 4.74; Fe, 11.45; N, 11.26.

Methiodide of VII. A solution of 5.36 g. of the amine in 15 ml. of acetonitrile was cooled in an ice bath and treated with 5 ml. of methyl iodide. A solid was almost immediately deposited. The suspension was stored in the cold overnight. From this there was obtained 5.65 g. (70% of light yellow granules), m.p. 172–175° (dark 150°). Further crystallization lowered the m.p. to 170°.

1-Ethyl-2-hydroxymethylferrocene (X). A suspension of 5.20 g. (0.019 mole) of the methiodide obtained above in 52 ml. of 10% aqueous sodium hydroxide was brought to reflux. Almost immediately an oil began to separate and trimethylamine was evolved. At the end of 2.5 hr. the suspension was allowed to cool. The oil was taken up in ether and this solution washed with water and then dried over sodium sulfate. The oil which remained when the solvent was removed crystallized to a waxy solid on scratching. Recrystallization from hexane afforded the alcohol as a light orange solid (2.15 g., 47%), m.p. 42–52°. One further crystallization from the same solvent gave 1.76 g. of X, m.p. 54–56°.

1-Vinyl-2-hydroxymethylferrocene XII. A suspension of 11.0 g. of the quaternary salt XI[14] in 110 ml. of 10% aqueous sodium hydroxide was brought to reflux. Trimethylamine was evolved as a steam volatile oil separated. At the end of 2.5 hr. the reaction mixture was allowed to cool and worked up in the same manner as the displacement reaction of the saturated compound. The oil which remained when the solvent was removed was distilled at 2 mm. to yield 2.86 g. (44%) of a dark red liquid b.p. 149–153°. λ_{max}, 2.92 μ, 6.1 μ, 11.1 μ; 273 mμ; ϵ_{max} 7000.

Anal. Calcd. for $C_{13}H_{14}FeO$: C, 64.49; H, 5.83; Fe, 23.07. Found: C, 64.87; H, 5.64; Fe, 22.87.

A considerable amount of nonvolatile tar remained in the pot.

Catalytic reduction of XII *to 1-ethyl-2-hydroxymethylferrocene* (X). A suspension of 0.25 g. of palladium-on-charcoal in a solution of 2.84 g. of the alcohol XII in 15 ml. of methanol was stirred under hydrogen at atmospheric pressure. Within 20 min. the theoretical amount (266 ml. of hydrogen had been taken up. The catalyst was removed by filtration and washed with methanol. The filtrates were diluted to 150 ml. with water. On scratching the oil which came out of this solidified. The alcohol was obtained as 2.40 g. (84%) of orange solid, m.p. 48–53°. Two recrystallizations from hexane afforded 2.05 g. of X, m.p. 55–57°. The mixed melting point of this with alcohol obtained above by the displacement reaction was 55–56.5°. The infrared spectra of the two samples were superposable.

A sample was recrystallized further from hexane to afford long, fine, orange needles, m.p. 57–57.5°.

Anal. Calcd. for $C_{13}H_{16}FeO$: C, 63.96; H, 6.61; Fe, 22.88. Found: C, 64.26; H, 6.56; Fe, 22.99.

Reaction of the methiodide of 1-dimethylaminomethyl-2-vinylferrocene with potassium cyanide to form 2-vinylferrocylacetonitrile (XIII). To a solution of 30.0 g. of potassium cyanide in 300 ml. of water there was added 30 25 g. of the quaternary salt. As the reaction was brought to reflux an oil began to separate and the odor of trimethylamine was noted. At the end of 6.5 hr. the reaction was allowed to cool. The oil was taken up in ether and this solution washed with water and dried over sodium sulfate. The oil which remained on stripping the solvent was distilled at 1.4 mm. to afford 13.26 g. (72%) of the nitrile, b.p. 156–159°; λ_{max} 4.4 μ, 6.1 μ, 11.1 μ.

Anal. Calcd. for $C_{14}H_{13}FeN$: C, 66.96; H, 5.22; Fe, 22.24; N, 5.58. Found: C, 67.01; H, 5.39; Fe, 21.93; N, 5.95.

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[8] Actually the intermediate in the cyclization is probably the protonation product of III bearing a positive charge on the terminal methylene group. That active intermediate could also be obtained by the loss of hydroxide from the methylol resulting from the addition of formaldehyde to the primary amine I.

[9] J. S. Buck, *J. Am. Chem. Soc.*, **56**, 1769 (1934).

[10] S. Archer, T. R. Lewis, M. J. Unser, J. O. Hoppe, and H. Lape, *J. Am. Chem. Soc.*, **79**, 5783 (1957).

[11] K. L. Rinehart, Jr., and R. J. Curby, Jr., *J. Am. Chem. Soc.*, **79**, 3290 (1957).

[12] All melting points are uncorrected. Analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

[13] Prepared in the same manner as compound XV.[2]

[14] Quaternary salt, XI, is identical with and is prepared in the same manner as the methiodide of compound XV.[2]

Catalytic reduction of XIII *to 2-ethylferrocylacetonitrile.* A solution of 13.2 g. of the nitrile in 50 ml. of methanol containing in suspension 1.3 g. of 10% palladium-on-charcoal was stirred vigorously under hydrogen at atmospheric pressure. In 30 min., 1428 ml. (theo. 1330) of gas had been taken up. The reaction mixture was worked up in the same manner as the other reductions to afford 12.6 g. of a dark oil; λ_{max} 4.4 μ, no absorption at 6.1 μ or 11.1 μ.

Hydrolysis of the saturated nitrile to 1-ethylferrocylacetic acid. A solution of 12.6 g. of the nitrile obtained above and 48 ml. of 50% aqueous potassium hydroxide in 100 ml. of ethanol was brought to reflux. After 30 min. heating no ammonia had been noted. At this point 100 ml. of ethylene glycol was added to the solution and solvent was removed by distillation until the temperature of the distillate reached 100°. The now copious evolution of ammonia had ceased at the end of 2 hr. The hot solution was poured onto 800 ml. of ice water and this solution washed three times with 100 ml. of ether. The alkaline portion was subsequently filtered and acidified with phosphoric acid under a stream of nitrogen. The precipitated solid was collected on a filter, dried, and crystallized from benzene-hexane to afford 9.50 g. (70%) of the acid as stout amber rod-like crystals m.p. 123–125°. Further crystallization from the same solvent pair gave a sample m.p. 124–125°.

Anal. Calcd. for $C_{14}H_{16}FeO_2$: C, 61.78; H, 6.13; Fe, 20.52. Found: C, 61.91; H, 6.20; Fe, 20.28.

Reaction of the methiodide IX *with sodium hydroxide.* A suspension of 5.0 g. of the quaternary salt[15] in 50 ml. of *N* sodium hydroxide was heated under reflux for 20 hr. At this temperature the salt went into solution. On cooling a crystalline solid came out of solution. This was collected on a filter and washed with ether to yield 3.70 g. (74%) of a material whose infrared spectrum was identical to that of starting material. The aqueous filtrate was extracted with ether and the organic solutions were combined. The residue obtained on removing the ether (0.08 g.) was chromatographed on an alumina column to afford 0.06 g. of a solid m.p. 46–52°, whose infrared spectrum is the same as that of vinylferrocene.

DURHAM, N. C.

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[15] C. R. Hauser, J. K. Lindsay, and D. Lednicer, *J. Org. Chem.*, **23**, 358 (1958).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Addition Reactions of the Methiodide of Benzophenonemethylimine and Its 4-Methyl Analog with Nucleophilic Reagents[1]

CHARLES R. HAUSER AND DANIEL LEDNICER

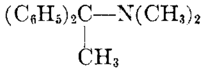
Received August 5, 1958

Benzophenone and 4-methylbenzophenone were condensed with methylamine to form the corresponding methylimines, which were converted to their methiodides. These methiodides were treated with potassium cyanide to give the corresponding α-aminonitriles. The α-aminonitrile from the methiodide of benzophenoneimine was obtained in low yield by the phenylation of the α-aminonitrile prepared from benzaldehyde, dimethylamine, and potassium cyanide. The methiodide of benzophenoneimine also underwent addition reactions with methylmagnesium iodide, potassio phenylacetonitrile, water, and liquid ammonia. The tertiary amine obtained from the methiodide and methylmagnesium iodide was prepared in better yield from the appropriate α-aminonitrile and the same Grignard reagent.

Some time ago, Sommelet[2] reported that the methiodide of benzophenonemethylimine (I) reacts with methylmagnesium iodide to form tertiary amine II, but the experimental details were not given.

$$(C_6H_5)_2C{=}\overset{+}{N}(CH_3)_2\ I^-$$

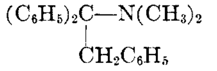
I



$$(C_6H_5)_2\underset{\displaystyle CH_3}{\underset{|}{C}}{-}N(CH_3)_2$$

II

More recently, the corresponding reaction of the methiodide I with benzylmagnesium chloride was effected in this laboratory[3] as an independent synthesis of tertiary amine III, which had been obtained from a Stevens type of rearrangement.



$$(C_6H_5)_2\underset{\displaystyle CH_2C_6H_5}{\underset{|}{C}}{-}N(CH_3)_2$$

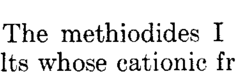
III

In the present investigation a further study along these lines was carried out. The methiodide I was prepared as indicated in Equation 1.[3]

$$(C_6H_5)_2C{=}O \xrightarrow[180^\circ]{CH_3NH_2} (C_6H_5)_2C{=}NCH_3 \xrightarrow{CH_3I} I \quad (1)$$

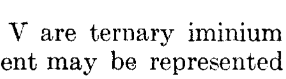
The yield of the intermediate benzophenonemethylimine was 89%, which is somewhat higher than that (49%) reported previously.[3] The methiodide of this imine was obtained as an ether-insoluble, crystalline solid.

Similarly 4-methylbenzophenone was condensed in 68% yield with methylamine to give the corresponding imine IV, which was methylated to form the methiodide V.



$$p\text{-}CH_3C_6H_4\overset{\displaystyle C_6H_5}{\overset{|}{C}}{=}NCH_3$$

IV



$$p\text{-}CH_3C_6H_4\overset{\displaystyle C_6H_5}{\overset{|}{C}}{=}\overset{+}{N}(CH_3)_2\ I$$

V

The methiodides I and V are ternary iminium salts whose cationic fragment may be represented by resonance forms such as Ia and Ib.

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[1] Supported by the Office of Ordnance Research, U. S. Army.

[2] M. Sommelet, *Compt. rend.*, **183**, 302 (1926).

[3] C. R. Hauser, R. M. Manyk, W. R. Brasen, and P. L. Bayless, *J. Org. Chem.*, **20**, 1119 (1955).