Pfitzinger reaction of ketone III. The reaction with the liquid ketone (III) was performed in a similar manner, giving a 65% yield of *2-(3-chloro-2-methoxy-4'-biphenylyl)-cinchoninic acid* (VIII), crystallizing from acetic acid in yellowish prisms, m.p. 209°.

Anal. Calcd. for $C_{23}H_{16}ClNO_3$: Cl, 9.1. Found: Cl, 9.0.

2-(3-Chloro-2-methoxy-4'-biphenylyl)quinoline (IX), obtained on thermal decarboxylation of the above acid, crystallized from ethanol in shiny colorless prisms, m.p. 199°.

Anal. Calcd. for $C_{22}H_{16}ClNO$: N, 4.1. Found: N, 4.1.

The corresponding *picrate* crystallized from ethanol in bright yellow needles, m.p. 188°.

Anal. Calcd. for $C_{28}H_{19}ClN_4O_8$: N, 9.7. Found: N, 9.8.

Other acylations of 3-chloro-2-methoxybiphenyl. (*a*) Reaction of 22 g. of I with 9.8 g. of propionyl chloride in the presence of 14 g. of aluminum chloride furnished a 73% yield of *propionyl-3-chloro-2-methoxybiphenyl*, viscous, pale yellow oil, b.p. 230–235°/20 mm., which failed to solidify even partly, on standing in the refrigerator. Red halochromism forms with sulfuric acid.

Anal. Calcd. for $C_{16}H_{15}ClO_2$: C, 70.2; H, 5.5. Found: C, 69.8; H, 5.5.

(*b*) Similar reaction with 11.2 g. of butyryl chloride afforded a 69% yield of an oily *butyryl-3-chloro-2-methoxybiphenyl*, b.p. 230°/15 mm.

Anal. Calcd. for $C_{17}H_{17}ClO_2$: C, 70.7; H, 5.9. Found: C, 70.8; H, 5.8.

(*c*) With 14.7 g. of benzoyl chloride, the reaction gave a 77% yield of a viscous, oily ketone, b.p. 265–270°/16 mm.

Anal. Calcd. for $C_{20}H_{15}ClO_2$: C, 74.4; H, 4.7. Found: C, 74.6; H, 4.6.

(*d*) With 16.3 g. of phenacetyl chloride, the reaction gave a 68% yield of an oil, b.p. 270–280°/16 mm.

Anal. Calcd. for $C_{21}H_{17}ClO_2$: C, 74.9; H, 5.1. Found: C, 74.9; H, 5.0.

This last ketone mixture underwent a positive Pfitzinger reaction with isatin, to give in 68% yield and after 5 days' refluxing, a *cinchoninic acid*, crystallizing from acetic acid in yellowish prisms, m.p. 295°.

Anal. Calcd. for $C_{29}H_{20}ClNO_3$: C, 74.8; H, 4.3. Found: C, 74.5; H, 4.3.

The corresponding *quinoline* crystallized from ethanol in colorless needles, m.p. 164°.

Anal. Calcd. for $C_{28}H_{20}ClNO$: C, 79.7; H, 4.8. Found: C, 79.7; H, 4.8.

PARIS V^e, FRANCE

[CONTRIBUTION FROM THE UNIVERSITY OF CALIFORNIA, LOS ANGELES]

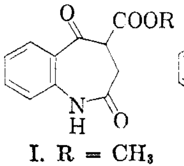
Rearrangement of Methyl 3-Azabenzocycloheptene-4,7-dione-6-carboxylate to 2,4-Dihydroxyquinoline-3-acetic Acid in Acid and Base

T. A. GEISSMAN AND A. K. CHO

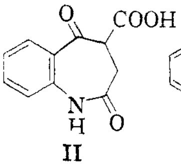
Received July 11, 1958

The preparation of methyl 3-azabenzocycloheptene-4,7-dione-6-carboxylate (I) and its rearrangement in aqueous acid and base to 2,4-dihydroxyquinoline-3-acetic acid (III) are described. The quinoline structure of the rearrangement product is shown by its ultraviolet spectrum and by its conversion to dihydrodictamnine (VI). The ring closure of 2,4-dihydroxy-3-(2'-hydroxyethyl)quinoline to dihydrodictamnine was achieved in this work with sodium hydride and *p*-toluenesulfonyl chloride.

The azabenzocycloheptenedione (I) was prepared by carrying out a Dieckmann cyclization of methyl *N*- β-carbomethoxypropionylanthranilate with sodium in boiling toluene. The corresponding ethyl ester has been prepared recently by MacPhillamy *et al.*[1] who described the resistance to decarboxylation of the acid obtained by hydrolysis of Ia. A similar observation was made in the course of this work and an explanation for the stability of the product, assumed to be the β-ketoacid (II), was provided by investigation of the acid obtained by the basic and acid hydrolysis of the azabenzocycloheptenedione (I). The ultraviolet spectrum and subsequent reactions of the hydrolysis product showed it to be 2,4-dihydroxyquinoline-3-acetic acid (III). The ultraviolet spectrum of the hydrolysis product had double maxima in the 270 mμ and 300–340 mμ range, characteristic of 2,4-dihydroxyquinolines.[2]



I. R = CH_3
Ia. R = C_2H_5



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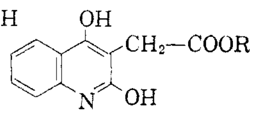

III. R = H
IIIa. R = CH_3

Further evidence for the quinoline nature of the hydrolysis product was provided by its conversion to dihydrodictamnine (VI). This was accomplished by treating III with excess ethereal diazomethane to give 4-methoxy-2-hydroxyquinoline-3-acetic acid methyl ester (IV), which was reduced to 4-methoxy-2-hydroxy-3-(2'-hydroxyethyl)quinoline (V). Cooke[3] has prepared dictamnine using this approach but was able to obtain the quinoline acetic acid ester (IIIa) directly. Treatment of V with sodium hydride in tetrahydrofuran followed by *p*-toluenesulfonyl chloride[4] gave dihydrodictamnine.

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[1] H. B. MacPhillamy, R. L. Dziemian, R. A. Lucas, and M. E. Kuehne, *J. Am. Chem. Soc.*, **80**, 2172 (1958).

[2] R. F. C. Brown, J. J. Hobbs, G. K. Hughes, and E. Ritchie, *Australian J. Chem.*, **7**, 348 (1954).

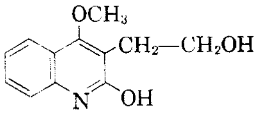
[3] R. G. Cooke and H. F. Haynes, *Australian J. Chem.*, **11**, 225 (1958).

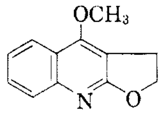
[4] J. D. Roberts, W. Bennett, R. E. McMahon, and E. W. Holroyd, Jr., *J. Am. Chem. Soc.*, **74**, 4283 (1952).

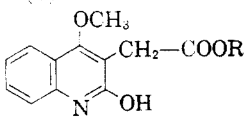
The ring closure to dihydrodictamnine was carried out by Cooke with polyphosphoric acid.

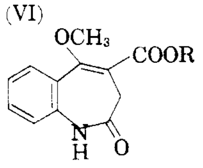
Treatment of I with excess ethereal diazomethane gave a methyl ether different from IV to which the structure VII was assigned. This reaction is consistent with the enolic spectral properties reported.[1] The enol ether VII was converted to the dihydroxyquinoline (IIIa) by the action of acid but treatment with aqueous base gave an acid, isomeric with IVa but which did not show the quinoline ultraviolet spectrum. The structure VIIa has been assigned to this acid.

The conversion of I to III is a facile one, occurring in aqueous base or acid. A small quantity of the methyl ester of III was isolated as a side product from a large scale preparation of I.


(V)


(VI)


IV. R = CH_3
IVa. R = H


VII. R = CH_3
VIIa. R = H

EXPERIMENTAL

Methyl 3-azabenzocycloheptene-4,7-dione-6-carboxylate (I). β-Carbomethoxypropionyl chloride was prepared as described by Cason and Rapoport.[5] A solution of all the acid chloride from 74 g. (0.55 mole) of methyl hydrogen succinate in 50 ml. of benzene was added dropwise with stirring and cooling to a solution of 75 g. (0.49 mole) of methyl anthranilate, and 40 g. (0.5 mole) of pyridine in 100 ml. of benzene. The mixture was allowed to stir at room temperature overnight, then it was washed with dilute acid, water, and aqueous sodium carbonate. The organic layer was evaporated at reduced pressure, and the residue upon cooling gave 66 g. (50%) of the acyl anthranilate, m.p. 67–70°, after recrystallization from ethanol.

A solution of 33 g. (0.123 mole) of the above mentioned amide in 100 ml. of toluene was added dropwise to 100 ml. of refluxing toluene containing 6 g. of sodium over a period of 1.5 hr. The reaction mixture was refluxed for 3.5 hr., then cooled and filtered. The tan precipitate was added to ethanol, neutralized with 6*N* HCl, and filtered. The resulting white flocculent precipitate was crystallized from ethanol, yielding 10.8 g. (38%) of fine needles melting at 222.5–224°. The ester I gave a dark purple coloration with ferric chloride. Infrared: 1670 cm.$^{-1}$, 1650 cm.$^{-1}$, 1610 cm.$^{-1}$; ultraviolet $^{\text{ethanol}}_{\max}$: 227 mμ, log ε 4.36; 243 (sh) mμ, log ε 4.15; 295 mμ, log ε 3.98.

Anal. Calcd. for $C_{12}H_{11}O_4$: C, 61.79; H, 4.75; N, 6.00. Found: C, 62.05; H, 4.83; N, 6.16.

The methanol-water filtrate obtained from the isolation of the main product from a run using 50 g. of the acyl anthranilate was concentrated on the steam bath. The residue, a mixture of water and dark oil, was cooled and a crystalline solid formed. The solid was recrystallized from methanol and 1.8 g. of the ester (IIIa) melting at 185–190°, resolidifying and decomposing at 305–307° (dec.) were obtained. The ultraviolet spectrum of this compound showed typical 2,4-dihydroxyquinoline absorption. It gave a brown color with ferric chloride. Infrared: 1725 cm.$^{-1}$, 1710 cm.$^{-1}$, 1650 cm.$^{-1}$, 1635 cm.$^{-1}$, 1605 cm.$^{-1}$; ultraviolet $\lambda_{\max}^{\text{ethanol}}$: 272 mμ, log ε 3.95; 282 mμ, log ε 3.92; 316 mμ, log ε 3.88; 328 mμ (sh), log ε 3.78.

Anal. Calcd. for $C_{12}H_{11}O_4N$: C, 61.79; H, 4.75. Found: C, 61.66; H, 4.91.

Methyl 4-methoxy-3-azabenzocyclohepta-1,5-dien-5-one-6-carboxylate. The ether solution of diazomethane from 17 g. of nitrosomethyl urea was added to a cooled suspension of 10 g. (0.042 mole) of I in 450 ml. of methanol and stirred with a magnetic stirrer. When the suspension became colorless, the ethereal diazomethane from another 17 g. of nitrosomethylurea was added. This process was repeated and the mixture was stirred overnight. The ice bath was allowed to melt during this period.

The excess diazomethane was decomposed with a few drops of glacial acetic acid and the clear solution was evaporated on the steam bath. The residue was recrystallized once from methanol and gave 10 g. (96%) of colorless plates, m.p. 145.5–146°. Infrared: 1665 cm.$^{-1}$, 1605 cm.$^{-1}$; ultraviolet $\lambda_{\max}^{\text{ethanol}}$: 230 mμ, log ε 4.58; 282 mμ, log ε 4.10.

Anal. Calcd. for $C_{13}H_{13}O_4N$: C, 63.15; H, 5.30; OCH_3, 25.12. Found: C, 63.09; H, 5.28; OCH_3, 24.32.

2,4-Dihydroxyquinoline-3-acetic acid (III). A solution of 5 g. (0.021 mole) of I in 100 ml. of 5% aqueous potassium hydroxide was refluxed for 3 hr. The reaction mixture was cooled and made acid with dilute hydrochloric acid. The resulting precipitate was collected and recrystallized from ethanol, yielding 3 g. (64%) of the acid III melting at 290–295° (dec.). The melting point reported by MacPhillamy *et al.*[1] for this compound is 322–323° (dec.). Infrared: 1680 cm.$^{-1}$, 1650 cm.$^{-1}$, 1635 cm.$^{-1}$; ultraviolet $\lambda_{\max}^{\text{ethanol}}$: 272 mμ, log ε 3.95; 281 mμ, log ε 3.95; 316 mμ, log ε 3.89; 326 mμ, log ε 3.80.

4-Methoxy-2-hydroxyquinoline-3-acetic acid methyl ester (IV). A suspension of 2 g. (0.0091 mole) of the acid III in ether was treated with an ethereal solution of diazomethane from 8 g. of nitrosomethylurea. The reaction mixture was initially cooled and stirred, and allowed to come to room temperature overnight. The excess diazomethane was decomposed with a few drops of glacial acetic acid and the solvent was removed by evaporation. Extraction of the residue with petroleum ether (b.p. 60–80°) and evaporation of the solvent gave crystals melting at 69–70°. The residue from the petroleum ether extract was recrystallized from ethanol. The weight of the latter fraction was 0.62 g. (30%) of the methyl ether ester (IV) melting at 171–171.5°. Infrared: 1725 cm.$^{-1}$, 1650 cm.$^{-1}$, 1605 cm.$^{-1}$; ultraviolet $\lambda_{\max}^{\text{ethanol}}$: 269 mμ, log ε 3.86; 278 mμ, log ε 3.82; 324 mμ, log ε 3.86; 336 mμ (sh), log ε 3.69.

Anal. Calcd. for $C_{13}H_{13}O_4N$: C, 63.15; H, 5.30. Found: C, 62.81; H, 5.22.

Analytical data and ultraviolet spectrum indicated the material melting at 69–70° was 2,4-dimethoxyquinoline-3-acetic acid methyl ester.

Anal. Calcd. for $C_{14}H_{15}O_4N$: C, 64.36; H, 5.79. Found: C, 64.64; H, 5.50.

4-Methoxy-2-hydroxy-3-(2′-hydroxyethyl)quinoline (V). A solution of one g. (0.004 mole) of the ester IV in about 70 ml. of dry tetrahydrofuran was added with stirring to a solution of 0.29 g. (0.008 mole) of lithium aluminum hydride in 100 ml. of tetrahydrofuran at room temperature. The addition process took about 20 min. After the addition, the mixture was refluxed for 15 min. and cooled. A solution of 1 ml. of methanol in 9 ml. of tetrahydrofuran was added dropwise. This was followed by the dropwise addition of a solution of 1 ml. of water in 9 ml. of tetrahydrofuran. The reaction mixture was then filtered and the filtrate was evaporated under reduced pressure. The residue was a small quantity of oily material which did not crystallize after numerous attempts. The precipitate of the metal hydroxides

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[5] J. Cason and H. Rapoport, *Laboratory Text in Organic Chemistry*, Prentice Hall Inc., New York, N. Y., 1950, p. 356.

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]

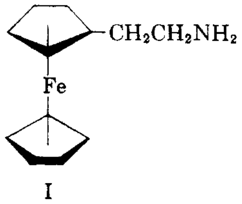
Structure of the Product of Anomalous Leuckart Reaction of 2-Ferrocylethylamine. A Route to 1,2-Disubstituted Ferrocenes[1]

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.



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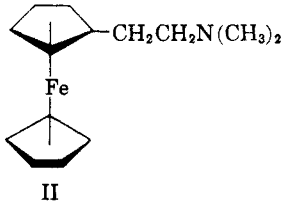

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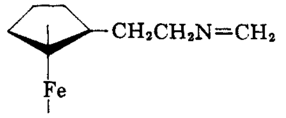
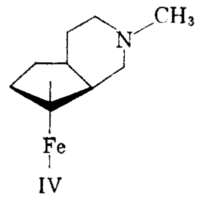


III



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. Lindsay, and C. R. Hauser, *J. Org. Chem.*, **23**, 653 (1958).

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