1152. *Alkaloids of* Macrorungia longistrobus *C.B. Cl.*

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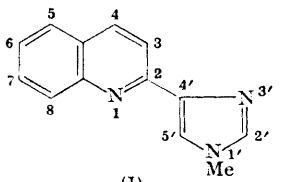
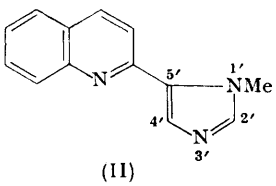
Three new alkaloids, macrorine (I), isomacrorine (II), and macrorungine (III), have been isolated from *Macrorungia longistrobus* C.B. Cl. Degradation experiments are reported which established the 1′-methyl-2-4′-(1′*H*-imidazolyl)quinoline, 1′-methyl-2-5′-[1′*H*-imidazolyl)quinoline, and 2′,3′-dihydro-1′-methyl-2-4′-(1′*H*-imidazolyl)quinolin-2′-one structures for macrorine, isomacrorine, and macrorungine, respectively.

The shrub *Macrorungia longistrobus*(A canthaceae) is of isolated occurrence in the Republic of South Africa. Although several plants of this family contain alkaloids,[1] only one alkaloid isolated has so far been fully characterized, *viz.*, vasicine.[2]

From the ethanol extract of the aerial portion of the plant, we have isolated three new alkaloids, macrorine ($C_{13}H_{11}N_3$), isomacrorine ($C_{13}H_{11}N_3$), and macrorungine ($C_{13}H_{11}N_3O$), for which we propose structures (I)—(III), respectively.



(I)



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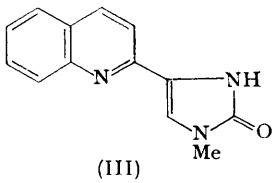


(III)

The inter-relationship of macrorine and isomacrorine was established through their methiodides, which were identical. On pyrolysis, this methiodide gave mainly macrorine with only a trace of isomacrorine, which could be detected by gas chromatography. In its infrared spectrum, macrorine showed bands at 1600, 1564, 1503, and 1490 cm.$^{-1}$ (aromatic). Macrorine also showed an *N*-methyl group at τ 6·3 and eight aromatic protons (440—490 c./sec. from tetramethylsilane) in its nuclear magnetic resonance (n.m.r.) spectrum. The aromatic character is further evident from its strong ultraviolet absorption spectrum, $\lambda_{max.}$ 217, 238, 265, and 341 mμ (ε 39,170, 15,380, 23,070, and 9370). Macrorine was unaffected on zinc-dust distillation and was recovered unchanged when fused with alkali. It absorbed 2 mol. of hydrogen over Adams catalyst in acetic acid. The infrared spectrum of tetrahydromacrorine showed a band at 3450 cm.$^{-1}$ (NH), and its ultraviolet spectrum, $\lambda_{max.}$ 207, 250, and 301 mμ (ε 27,280, 8590 and 2210), was closely comparable with that found for 1,2,3,4-tetrahydroquinoline-2-carboxyamide, $\lambda_{max.}$ 206, 242, and 295 mμ (ε 24,800, 8000, and 1700). In its n.m.r. spectrum tetrahydromacrorine indicated, besides an *N*-methyl group at τ 6·46 and an NH group at τ 5·70, two multiplets, τ 7·85 and 7·2, each representing two protons, and a quartet representing one proton at τ 5·53, indicative of the system $>N\cdot\underset{|}{C}H\cdot CH_2\cdot CH_2\cdot Ph$. The existence of this system was confirmed by the n.m.r. spectrum of tetradeuteriomacrorine, in which the two multiplets were replaced by two broad peaks, τ 7·90 and 7·25, each

[1] Alkaloid-bearing plants and their contained alkaloids, Technical Bulletin No. 1234, Agricultural Research Service, U.S. Department of Agriculture.

[2] J. N. Sen and T. P. Ghose, *Quart. J. Indian Chem. Soc.*, 1925, **1**, 315.

representing one proton only, and the absence of the quartet at τ 5·53 and the peak ascribed to the NH group at τ 5·7.

On treatment with acetic anhydride–pyridine, an *N*-acetyl derivative was obtained. The above data are consistent with structure (IV) proposed for tetrahydromacrorine. Tetrahydromacrorine could be reconverted into macrorine by zinc-dust distillation or mild oxidation (potassium permanganate–acetone).

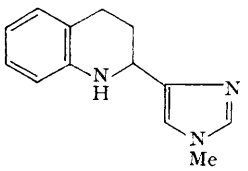
Macrorungine (III) in its infrared spectrum (KBr or Nujol) showed two carbonyl bands, at 1710 and 1690 cm.$^{-1}$, and in chloroform only one band, at 1695 cm.$^{-1}$. A similar phenomenon was observed in the infrared spectra of several cyclopentenones.[3] Its n.m.r. spectrum in trifluoroacetic acid showed an *N*-methyl peak at τ 7·9 and an AB pattern τ 2·99 ($\Delta\nu = 47$ c./sec., $J = 9$ c./sec.) of two isolated *ortho*-aromatic protons.

An inter-relationship between macrorungine and macrorine has also been established. Refluxing macrorungine in dioxan with lithium aluminium hydride gave macrorine and traces of tetrahydromacrorine. The latter was also formed when macrorine itself was treated with lithium aluminium hydride in the same way. That the amide-carbonyl group was situated between two nitrogen atoms was indicated by the resistance of macrorungine to acid and to alkaline hydrolysis.

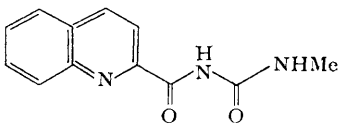
Macrorungine absorbed 6 mol. of hydrogen over Adams catalyst in acetic acid to give perhydromacrorungine. Dehydrogenation over palladium on charcoal of this substance afforded a mixture of quinoline, 2-methylquinoline (quinaldine), and 2-ethylquinoline.

Further information on the structure of these alkaloids was obtained from oxidation experiments. The oxidation of macrorine with potassium permanganate afforded a mixture which was resolved by chromatography over silica into two compounds. One of these was identical with quinoline-2-carboxyamide. The other compound, in its infrared spectrum, showed a band at 3330 cm.$^{-1}$ attributed to a secondary amide NH-group and two amide-carbonyl bands at 1708 and 1692 cm.$^{-1}$.

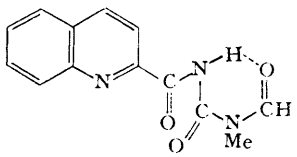
The n.m.r. spectrum of this compound showed a doublet peak ($J = 5$ c./sec.) at τ 7·0 (NHMe) which was converted into a singlet on equilibration with deuterium oxide in the presence of triethylamine. This is characteristic of a secondary amide. The ultraviolet spectrum was closely similar to that of quinoline-2-carboxyamide. Hydrolysis with methanolic hydrochloric acid afforded methyl quinoline-2-carboxylate and methylurea. Therefore, this oxidation product must have the ureide structure (V).



(IV)



(V)



(VI)

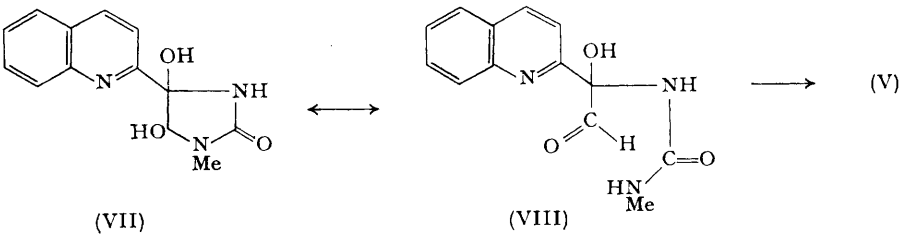
Isomacrorine, when oxidized with potassium permanganate, gave quinoline-2-*N*-methylcarboxyamide as the major product, in accordance with structure (II) proposed for this alkaloid.

Oxidation of macrorungine with chromic acid in acetic acid afforded a product for which we propose structure (VI). This showed the appropriate carbonyl bands at 1770, 1710, and 1690 cm.$^{-1}$. The n.m.r. spectrum showed an *N*-methyl group (τ 6·65), an NH-group (τ 1·28), and an *N*-formyl group (τ 1·82). On equilibration with deuterium oxide, no proton exchange occurred, indicating strong hydrogen bonding between the NH-proton and *N*-formyl carbonyl group as indicated (VI). Acid hydrolysis of (VI) gave the ureide (V) and formic acid.

Macrorungine, when oxidized with osmium tetroxide–periodate[4] afforded the ureide (V).

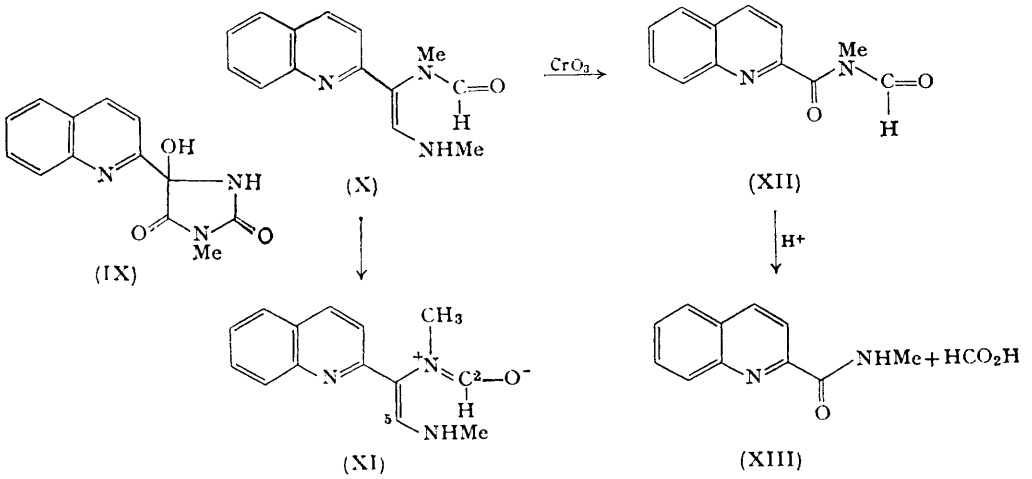
[3] P. Yates and L. L. Williams, *J. Amer. Chem. Soc.*, 1958, **80**, 5896.
[4] R. Pappo, D. S. Allen, R. U. Lemieux, and W. S. Johnson, *J. Org. Chem.*, 1956, **21**, 478.

The ureide formation is envisaged to proceed by way of the carbinolamine (VII) which is oxidized in the tautomeric form (VIII) to afford the ureide (V).



(VII) (VIII)

Oxidation of macrorungine with potassium permanganate in aqueous medium afforded a mixture of the ureide (V) and a second product, $C_{13}H_{11}N_3O_3$. Its ultraviolet spectrum resembled that of 2-substituted quinolines, its infrared spectrum showed bands at 3560 (NH), 3420 (OH), and two carbonyl bands at 1820 and 1750 cm.$^{-1}$, indicating a hydantoin grouping.[5] The methyl ether of this product was obtained on treatment with methanolic hydrochloric acid. This is characteristic of a carbinolamine.[6] This evidence leads us to propose structure (IX) for this oxidation product. A better yield of this hydroxy-hydantoin derivative was obtained when the permanganate oxidation was carried out in acetone.



The methiodides of macrorine and isomacrorine, on treatment with potassium hydroxide, afforded a non-quaternary product ($C_{14}H_{15}N_3O$) for which we suggest the seco-formamide structure (X). The infrared spectrum showed an amide-carbonyl band at 1672 cm.$^{-1}$. The n.m.r. spectrum showed two *N*-methyl groups, of which one, at τ 6·85, was a doublet, the splitting ($J = 0{\cdot}8$ c./sec.) arising from coupling of the allylic C-2 proton which appeared as a multiplet at τ 1·72 [cf. (XI)]. The second *N*-methyl group, at τ 6·80, was considerably sharpened after equilibration with deuterium oxide as was an olefinic proton at τ 3·2 (C-5). Oxidation with chromic acid–pyridine[7] afforded the amide derivative (XII). Its infrared spectrum showed bands at 1785 and 1667 cm.$^{-1}$ attributed to two amide groups. N.m.r. measurements confirmed the presence of only one *N*-methyl group and demonstrated the presence of an *N*-formyl group (τ 0·33). On treatment with dilute mineral acid, the oxidation product (XII) gave quinoline-2-*N*-methylcarboxyamide (XIII) and formic acid.

[5] M. Viscontini and H. Raschig, *Helv. Chim. Acta*, 1959, **42**, 570.
[6] H. L. Holmes and C. C. Lee, *J. Amer. Chem. Soc.*, 1947, **69**, 1996.
[7] G. I. Poos, G. E. Arth, R. E. Beyler, and L. H. Sarett, *J. Amer. Chem. Soc.*, 1953, **75**, 422.

Macrorine, isomacrorine, and macrorungine are the first members of a previously unknown group of imidazolylquinoline alkaloids. Macrorungine also represents the first known imidazolone alkaloid isolated.

Experimental

Unless otherwise stated, the infrared spectra were measured in chloroform solution on a Perkin-Elmer model 21 spectrometer, n.m.r. spectra were obtained in deuteriochloroform on a Varian A60 spectrometer, and ultraviolet spectra on a Unicam S.P. 500 spectrometer. Samples were dried *in vacuo* at 60° for analyses.

Extraction and Isolation of the Alkaloids.—Ground, air-dried branches and leaves (80 kg.) of *M. longistrobus* were extracted with hot ethanol. The extract was concentrated, treated with 2% tartaric acid, filtered, made alkaline, and extracted with chloroform. The chloroform solution was extracted with 3N-sulphuric acid and, after being made alkaline, the mixture of alkaloids (85 g.) was isolated with methylene dichloride. Chromatography on formamide-impregnated cellulose (36%, 2 kg.) and elution with 9:1 benzene–hexane, 1:1 benzene–hexane, and 1:1 benzene–methylene dichloride separated the alkaloid mixture into three main fractions: (i) isomacrorine (6·7 g.), (ii) macrorine (15·5 g.), and (iii) a mixture of alkaloids from which macrorungine (7·0 g.) could be separated by crystallization from acetone.

Macrorine (I).—The alkaloid was purified by way of its dipicrate (see below) from which it could be liberated by passage through basic alumina in acetone solution. *Macrorine* crystallized from acetone as colourless needles, m. p. 160°, $[\alpha]_D^{21}$ 0°, (*c* 1·0 in $CHCl_3$), pK_a 4·87 (toluene-*p*-sulphonic acid in 50% EtOH), $\lambda_{max.}$ (in EtOH) 217, 238, 265, and 341 mμ (ε 39,170, 15,380, 23,070, and 9370), (in 1% HCl–EtOH) 216, 260, 306, 320, 335, and 365 mμ (ε 26,770, 38,220, 6680, 7780, 9700, and 5560) (Found: C, 74·5; H, 5·2; N, 19·7; *N*-Me, 6·8. $C_{13}H_{11}N_3$ requires C, 74·6; H, 5·3; N, 20·1; *N*-Me, 7·2%).

The *monopicrate* crystallized from acetone–ether as yellow plates, m. p. 180° (decomp.) (Found: C, 52·0; H, 3·5. $C_{19}H_{14}N_6O_7$ requires C, 52·1; H, 3·2%). The *dipicrate* crystallized from acetone–ether as yellow needles, m. p. 202° (decomp.) (Found: C, 45·2; H, 2·9. $C_{25}H_{17}N_9O_{14}$ requires C, 45·0; H, 2·6%). The *perchlorate* crystallized from methanol–ether as colourless needles, m. p. 222° (Found: C, 50·3; H, 3·7. $C_{13}H_{11}N_3,HClO_4$ requires C, 50·3; H, 3·9%). Heating the alkaloid in a sealed tube with an excess of methyl iodide at 80° for 1 hr. afforded the *methiodide*, m. p. 196° (from methanol–benzene) (Found: C, 48·2; H, 4·2; N, 12·1. $C_{14}H_{14}IN_3$ requires C, 47·9; H, 4·0; N, 12·0%).

Tetrahydromacrorine (IV).—Macrorine (61 mg.) in acetic acid (5 ml.) over Adams catalyst (15 mg.) absorbed 2 mol. hydrogen. The *tetrahydro-derivative* (65 mg.) sublimed *in vacuo* at 90° and crystallized from acetone–hexane as colourless needles, m. p. 133°, $[\alpha]_D^{21}$ 0° (*c* 1·0 in $CHCl_3$), pK_a 5·63 (toluene-*p*-sulphonic acid in 50% EtOH), $\lambda_{max.}$ (in EtOH) 207, 250, and 301 mμ (ε 27,280, 8590, and 2210), (in 1% HCl–EtOH) 207, 247, and 345 mμ (ε 17,850, 4630, and 4010) (Found: C, 73·4; H, 7·1; N, 19·9; active H, 0·31. $C_{13}H_{15}N_3$ requires C, 73·2; H, 7·1; N, 19·7; 1 active H, 0·47%). Treatment with acetic anhydride–pyridine (1:1) afforded an oil which gave a crystalline *N-acetyl hydrochloride*, m. p. 207—211° (from methanol–ether) (Found: C, 61·7; H, 6·4; N, 14·2. $C_{15}H_{17}N_3O,HCl$ requires C, 61·8; H, 6·2; N, 14·4%).

Tetradeuteriomacrorine.—Macrorine (75·5 mg.) in $CH_3{\cdot}CO_2D$ (20 ml.) over Adams catalyst (70 mg.) absorbed 2 mol. deuterium. The tetradeuterio-derivative sublimed *in vacuo* at 90° and crystallized from acetone–hexane as colourless needles, m. p. 131–132°.

Isomacrorine (II).—*Isomacrorine* was sublimed *in vacuo* at 95° and crystallized from hexane–acetone to afford colourless needles, m. p. 110°, $[\alpha]_D^{21}$ 0° (*c* 0·5 in EtOH), pK_a 5·09 (toluene-*p*-sulphonic acid in 50% EtOH), $\lambda_{max.}$ (in EtOH) 214, 235, 269, 328, and 342 mμ (ε 27,820, 12,930, 28,460, 11,130, and 11,410), (in 1% HCl–EtOH) 218, 252, 292, 319, and 334 mμ (ε 21,480, 37,370, 7140, 7060, and 6410) (Found: C, 74·5; H, 5·3; N, 19·7; *N*-Me, 6·8. $C_{13}H_{11}N_3$ requires C, 74·6; H, 5·3; N, 20·1; *N*-Me, 7·2%).

The *diperchlorate* crystallized from methanol–water, m. p. 290° (decomp.) (Found: C, 38·1; H, 3·3; N, 10·2. $C_{13}H_{11}N_3,2HClO_4$ requires C, 38·1; H, 3·2; N, 10·2%).

The methiodide formed in the presence of an excess of methyl iodide after 18 hr. at room temperature. It crystallized from methanol–ether, m. p. 196° (decomp.), identical (m. p., mixed m. p., and infrared spectrum) with macrorine methiodide.

Macrorungine (III).—*Macrorungine* crystallized from methanol as pale yellow prisms, m. p.

267—270° (decomp.), $\lambda_{max.}$ (in EtOH) 220, 284, 301, and 354 mμ (ε 40,000, 17,400, 16,600, and 18,300), (in 0·1N-KOH–EtOH) 227, 283, 323, and 382 mμ (ε 28,300, 11,800, 8300, and 11,200), (in 0·2N-HCl–EtOH) 203, 225, 253, 300, and 413 mμ (ε 22,700, 29,500, 9300, 11,150, and 38,050), $\nu_{max.}$ (Nujol) 1710, 1690 (C=O), 1630, 1600 (aromatic), 750 cm.$^{-1}$ (disubstituted benzene) (Found: C, 69·3; H, 5·1; N, 18·8; O, 7·5; active H, 0·45. $C_{13}H_{11}N_3O$ requires C, 69·3; H, 4·9; N, 18·7; O, 7·1; 1 active H, 0·44%).

All salts of macrorungine reported below crystallized from methanol: the *picrate* m. p. > 250° (decomp.) (Found: C, 50·4; H, 3·3. $C_{19}H_{14}O_8N_6$ requires C, 50·2; H, 3·1%); the *hydrochloride* as red needles, m. p. > 290° (decomp.) (Found: C, 59·8; H, 5·0; N, 16·1. $C_{13}H_{11}ON_3$,HCl requires C, 59·7; H, 4·6; N, 16·1%); the *perchlorate* as yellow plates, m. p. > 290° (decomp.) (Found: C, 47·0; H, 3·6; N, 12·2. $C_{13}H_{11}N_3O$,$HClO_4$,0·5H_2O requires C, 46·8; H, 3·9; N, 12·5%); the *methiodide* as orange prisms, m. p. > 290° (decomp.) (Found: C, 45·0; H, 3·7; N, 11·3. $C_{14}H_{14}IN_3O$,0·5H_2O requires C, 44·8; H, 4·0; N, 11·2%).

Reduction of Macrorungine (III) *with Lithium Aluminium Hydride.*—Macrorungine (100 mg.) in dioxan (30 ml.) was refluxed with lithium aluminium hydride for 6 hr. The excess of lithium aluminium hydride was destroyed with ethyl acetate and the dioxan evaporated under reduced pressure. The residue, in 3N-sulphuric acid (25 ml.), was extracted with ether, basified with ammonia, and extracted with methylene dichloride to give a basic oil (78 mg.). Chromatography on silica (20 g.) and elution with 95:5 methylene dichloride–methanol gave a mixture (28 mg.) of tetrahydromacrorine (IV) and macrorine (I). Further elution with methanol afforded unreacted macrorungine (III). Rechromatography of the mixture on formamide-impregnated cellulose (20 g.) separated macrorine (12 mg.) from tetrahydromacrorine (1 mg.), both characterized by m. p., mixed m. p., and infrared spectrum. Macrorine (50 mg.) treated in the same way with lithium aluminium hydride for 24 hr. gave rise to tetrahydromacrorine (IV) (15 mg.) and traces of unreacted macrorine, identified by m. p., mixed m. p. and infrared spectrum.

Hydrogenation of Macrorungine (III).—Macrorungine (120 mg.) in acetic acid (25 ml.) over Adams catalyst (120 mg.) absorbed 6 mol. of hydrogen. After addition of water, the mixture was made alkaline with sodium carbonate, the product isolated with methylene dichloride as an oil (120 mg.) and purified by chromatography on silica (12 g.). Elution with 5:1 methylene dichloride–methanol and crystallization from acetone–hexane gave colourless needles of *perhydromacrorungine*, m. p. 130—135°, pK_a 7·93 (toluene-*p*-sulphonic acid in 50% EtOH), $\nu_{max.}$ 3500 (NH) and 1700 cm.$^{-1}$ (C=O), $\lambda_{max.}$ (in EtOH) 207 mμ (ε 4400) (Found: C, 65·6; H, 10·0; N, 17·7. $C_{13}H_{23}N_3O$ requires C, 65·8; H, 9·8; N, 17·7%). The n.m.r. spectrum showed a broad band at τ 8·1—9·0 (CH_2) and a peak at τ 7·23 (*N*-Me). Two peaks, at τ 3·80 and 4·16 (NH), disappeared when the solution was equilibrated with deuterium oxide. Perhydromacrorungine with acetic anhydride–pyridine (1:1) afforded the *mono-N-acetyl derivative* as colourless needles, m. p. 202—204° (from acetone–hexane) (Found: C, 64·3; H, 9·2; N, 14·7. $C_{15}H_{25}N_3O_2$ requires C, 64·5; H, 9·0; N, 15·0%).

Dehydrogenation of Perhydromacrorungine.—Perhydromacrorungine (900 mg.), heated with 30% palladium–charcoal (1 g.) at 250° under nitrogen for 6 hr., gave ammonia (200 mg., as picrate) and an oil (120 mg.). A sample of the oil was chromatographed in the gas phase (2% S.E. 30 on Embacel at 100°[8] and 10% diglycerol on Embacel at 100°[9]) behaving as a mixture of quinoline, quinaldine, and 2-ethylquinoline. Fractional distillation of the oil (120 mg.) at 150—160°/12 mm. gave fractions that yielded picrates on crystallization from methanol identical in m. p. and mixed m. p. with the authentic picrates of quinoline, quinaldine, and 2-ethylquinoline, respectively.

Oxidations with Potassium Permanganate.—(*a*) *Macrorine.* A suspension of macrorine (545 mg.) in water (20 ml.) was partly oxidized with 5% potassium permanganate (60 ml.) for 20 min. at room temperature. After acidification with sulphurous acid and a few drops of 3N-sulphuric acid, the product was extracted with ether. The extract, washed free from all traces of acid, gave a crystalline mixture (160 mg.). The acid solution, after being made alkaline with sodium carbonate and extracted with methylene dichloride, yielded unreacted starting material (180 mg.).

Chromatography on silica (20 g.) and elution with methylene dichloride separated the above-mentioned crystalline mixture into quinoline-2-carboxyamide (60 mg.), identified by m. p., mixed m. p., infrared spectrum, and thin-layer chromatography, and the *ureide* (V) (54 mg.), m. p. 150°, $\lambda_{max.}$ (in EtOH) 208, 243, and 292 mμ (ε 26,680, 40,330, and 5624) (Found: C, 63·0; H, 5·0; N, 18·3; *N*-Me, 6·9. $C_{12}H_{11}N_3O_2$ requires C, 62·9; H, 4·9; N, 18·3; *N*-Me, 6·6%).

A solution of the ureide (V) (73 mg.) was refluxed for 1 hr. with methanol (30 ml.) in the presence

[8] J. S. Fitzgerald, *Austral. J. Appl. Sci.*, 1961, **12**, 51.
[9] V. Rezl, J. Janak, and H. Hrivnac, *Z. analyt. Chem.*, 1963, **195**, 56.

of hydrogen chloride, evaporated, and the residue chromatographed on silica (20 g.). Elution with 95:5 methylene dichloride–methanol and methanol separated methyl quinoline-2-carboxylate which crystallized from hexane (m. p., mixed m. p., and infrared spectrum). A second product, after being passed through Amberlite IR-45 resin in methanol, gave the free base (10 mg.) which was sublimed *in vacuo* at 60° and was identical with methylurea (m. p., mixed m. p., and infrared spectrum).

(*b*) *Isomacrorine.* When isomacrorine (69 mg.) in water (10 ml.) was partly oxidized as above with 5% potassium permanganate (7 ml.), the product was isolated from the acid solution with methylene dichloride and purified by chromatography on silica (20 g.). Elution with 98:2 methylene dichloride–methanol, sublimation *in vacuo* at 60°, and crystallization from hexane gave colourless needles (2 mg.) m. p. 117—118° identical (m. p., mixed m. p., and infrared spectrum) with an authentic sample of quinoline-2-*N*-methylcarboxyamide.

(*c*) *Macrorungine.* When macrorungine (1·024 g.) in water (80 ml.) was partly oxidized with 5% potassium permanganate (40 ml.), an oil (444 mg.) was isolated with ether from the acid solution. Unreacted starting material (92 mg.) was isolated with methylene dichloride after the solution was made alkaline.

Chromatography on silica (60 g.) and elution with 99:1 methylene dichloride–methanol separated the above-mentioned oil into the ureide (V) (180 mg.) and the hydroxy-hydantoin derivative (IX) (170 mg.). This compound was obtained in better yield on oxidation of macrorungine (109 mg.) at 0° in acetone (50 ml.) with potassium permanganate (85 mg.) in acetone (5 ml.), added over a period of 30 min. The excess of permanganate was destroyed with sulphur dioxide and the brown mixture filtered through a short column of cellulose powder. The acetone was evaporated and the residual oil dissolved in methylene dichloride (30 ml.) and extracted with 0·5N-sulphuric acid (100 ml.). After being made alkaline with sodium carbonate, the *product* (IX) was extracted with methylene dichloride and was crystallized from acetone–hexane (37 mg.), m. p. 171°, $\lambda_{max.}$ (in EtOH) 206, 231, 278, 303, 309, and 317 mμ (ε 47,300, 48,200, 4900, 4400, 3400, and 4900), $\nu_{max.}$ 3560 (NH), 3420 (OH), and 1820, 1750 cm.$^{-1}$ (C=O). The n.m.r. spectrum (in acetone) showed a signal at τ 6·98 (*N*-Me). Two signals, τ 1·9 and 5·8, disappeared when the solution was equilibrated with deuterium oxide (Found: C, 60·7; H, 4·4; N, 15·9; active H, 0·97. $C_{13}H_{11}N_3O_3$ requires C, 60·7; H, 4·3; N, 16·3; 2 active H, 0·78%).

Refluxing of compound (IX) (55 mg.) with methanol (25 ml.) and a trace of hydrochloric acid gave the *methyl ether* (48 mg.), crystallized from acetone–hexane as colourless plates, m. p. 169—170°, $\nu_{max.}$ 3390 (NH) and 1800, 1730 cm.$^{-1}$ (C=O). The n.m.r. spectrum showed a signal at τ 6·55 (OMe) and 6·95 (*N*-Me); a broad signal at τ 3·1 (NH) disappeared on adding deuterium oxide (Found: C, 61·8; H, 5·3; N, 15·5; OMe, 11·6. $C_{14}H_{13}N_3O_3$ requires C, 62·0; H, 4·8; N, 15·5; OMe, 11·4%).

Chromium Trioxide Oxidation of Macrorungine.—Macrorungine (109 mg.) was oxidized in acetic acid (25 ml.) with an excess (14·8 ml.) of 0·25N-chromium trioxide and set aside for 1 hr. at room temperature. Propan-2-ol (3 ml.) was added and the solution evaporated under reduced pressure. Water (25 ml.) was added to the residue and the product extracted with methylene dichloride. The extract, freed from acid, gave a glass (105 mg.) that, on crystallization from acetone–hexane, gave *compound* (VI) as colourless needles, m. p. 161—162°, $\nu_{max.}$ 3500 (NH) and 1770, 1710, 1690 cm.$^{-1}$ (C=O) (Found: C, 60·9; H, 4·1; N, 16·3. $C_{13}H_{11}N_3O_3$ requires C, 60·7; H, 4·3; N, 16·3%).

Ureide (V) *from Compound* (VI).—The oxidation product (VI) (30 mg.), dissolved in 2N-aqueous hydrochloric acid (25 ml.), was shaken for 5 hr. and kept at room temperature for a further 72 hr. The product was isolated with methylene dichloride and crystallized from acetone–hexane to give rise to the ureide (V) (10 mg.) (m. p., mixed m. p., and infrared spectrum). Formic acid was detected in the acid solution by a positive chromotropic reaction after reduction.[10]

Oxidation of Macrorungine with Osmium Tetroxide and Sodium Periodate.—To macrorungine (55 mg.) in 80% acetic acid (15 ml.) was added osmium tetroxide (5 mg.) and sodium paraperiodate (137 mg.). After 6 hr. at room temperature, the solution was evaporated under reduced pressure, water (10 ml.) added, and the product extracted with methylene dichloride. The extract, washed free from acid, gave, after crystallization from acetone–hexane, ureide (V) (48 mg.) (m. p., mixed m. p., and infrared spectrum).

Reaction of Macrorine Methiodide with Potassium Hydroxide.—Macrorine methiodide (130 mg.) in methanol (30 ml.) was refluxed for 1 hr. with potassium hydroxide (800 mg.) under nitrogen.

[10] F. Feigl, "Qualitative Analysis by Spot Tests," Elsevier, Amsterdam, 1937.

Water (50 ml.) was added and the methanol evaporated under reduced pressure. The product was extracted with methylene dichloride. The extract, washed with water and dried (Na_2CO_3), gave, after crystallization from acetone–hexane, the *seco-amide* (X) as yellow plates (80 mg.), m. p. 123—124°, $\lambda_{max.}$ (in EtOH) 218, 287, 312, 323, and 380 mμ (ε 49,170, 14,380, 11,920, 10,820, and 12,830) (Found: C, 69·9; H, 6·4; N, 17·3. $C_{14}H_{15}N_3O$ requires C, 69·7; H, 6·3; N, 17·4%).

Chromium Trioxide Oxidation of Compound (X).—Compound (X) (100 mg.), in pyridine (2 ml.), was shaken for 4 hr. with chromium trioxide–pyridine complex[7] (100 mg. chromium trioxide in 2 ml. pyridine), poured into water (50 ml.), and the product extracted with ether. The extract, washed with water, gave a yellow oil. Chromatography on silica (20 g.) and elution with methylene dichloride separated the oil into quinoline-2-*N*-methylcarboxyamide (5 mg.) (m. p., mixed m. p., and infrared spectrum) and the *amide derivative* (XII) (14 mg.), m. p. 116° (from acetone–hexane), $\lambda_{max.}$ (in EtOH) 207, 237, and 290 mμ (ε 33,830, 48,640, and 4730) (Found: C, 67·6; H, 5·0. $C_{12}H_{10}N_2O_2$ requires C, 67·3; H, 4·7%).

Quinoline-2-N-*methylcarboxyamide from Compound* (XII).—Compound (XII) (5 mg.) dissolved in 2N-hydrochloric acid (20 ml.) was set aside overnight at room temperature and extracted with ether. The extract afforded, after chromatography on silica and crystallization from hexane, the *N*-methylamide (4 mg.), (m. p., mixed m. p., and infrared spectrum). Formic acid was detected in the acid solution by a positive chromotropic reaction after reduction.[10]

Quinoline-2-N-*methylcarboxyamide*.—Methyl quinoline-2-carboxylate (500 mg.) treated overnight with 25% aqueous methylamine (25 ml.), extracted with ether, and crystallized from hexane, yielded the N-*methylamide* (420 mg.), m. p. 117—118° (Found: C, 70·7; H, 5·5; N, 14·7. $C_{11}H_{10}N_2O$ requires C, 71·0; H, 5·4; N, 15·1%).

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