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MASS SPECTROMETRIC STUDIES OF QUINOLINE ALKALOIDS—I. SOME 2-ALKYL(ARYL)-4-QUINOLONES

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Abstract—The mass spectra of eight 2-substituted 4-quinolones have been determined and evaluated. In each case a path of fragmentation has been proposed, and parallels drawn between compounds which appear to have analogous fragmentation patterns.

The mass spectrometer has been used in the determination of the structure of numerous classes of alkaloids. However, to date, very little has been reported on the mass spectra of the 4-quinolone alkaloids. Tschesche and Werner[1] determined the mass spectrum of a 1-methyl-2-alkenyl-4-quinolone in their investigation of alkaloids from *Evodia rutacarpa*. The mass spectrum of a 2,3-dihydro-4-quinolone has also been reported.[2]

Numerous 4-methoxy-, 1-methyl-, and 2,3-furo-4-quinolones have been found in the plant family Rutaceae.[3a] In addition, the 2-n-heptyl-, 2-n-nonyl-, and 2-(n-Δ^1-nonenyl)-4-quinolones and their N-oxides have been found in bacteria.[3b]

Because of the need for obtaining reference spectra of this type of compound, we have taken the mass spectra of eight model 4-quinolone alkaloids and have proposed fragmentation pathways in each case.

Before discussing the individual mass spectra, it should be noted that in five of the eight compounds studied, the parent peak was the largest. In no other case did the intensity of the parent peak fall below 30 per cent of the base peak. One could, therefore, expect to obtain an accurate molecular weight at least from the mass spectra of alkaloids of this type.

In the figures the numbers refer to the mass to charge ratio of the ion or ion-radical pictured, and the percentages refer to the largest peak which is arbitrarily set at 100. Figure 1 shows the fragmentation mode of the parent compound 4-quinolone (I). Loss of carbon monoxide from the molecular ion-radical leads to the formation of the indole peak (m/e 117) whose fragmentation has been reported.[4] Rearrangement with loss of HCN gives the corresponding benzylium type ion-radical (50 per cent of the base peak) which further fragments to give peaks typical of a benzene derivative.[5] 2-Methyl-4-quinolone (II, Fig. 2)

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[1] R. Tschesche and W. Werner, *Tetrahedron* **23**, 1873 (1967).

[2] K. S. Brown, Jr. and D. Becher, *Tetrahedron Letters* **18**, 1732 (1967).

[3a] R. F. Manske and H. L. Holmes, editors, *The Alkaloids, Chemistry and Physiology*, Chapter 17. Academic Press, New York (1953).

[3b] H. G. Boit, *Ergebnisse der Alkaloid-Chemie bis 1960*, Chapters 46, 47 and 48. Akademie-Verlag, Berlin (1961).

[4] Catalog of Mass Spectral Data, American Petroleum Institute Research Project 44, Carnegie Institute of Technology, Pittsburg, Pa., spectrum no. 623.

[5] J. H. Beynon, *Mass Spectrometry and its Application to Organic Chemistry*, p. 397. Elsevier, Amsterdam (1960).

also undergoes a loss of CO giving the methylindole ion-radical whose spectrum has also been reported (Ref. 5, pp. 397 and 398).

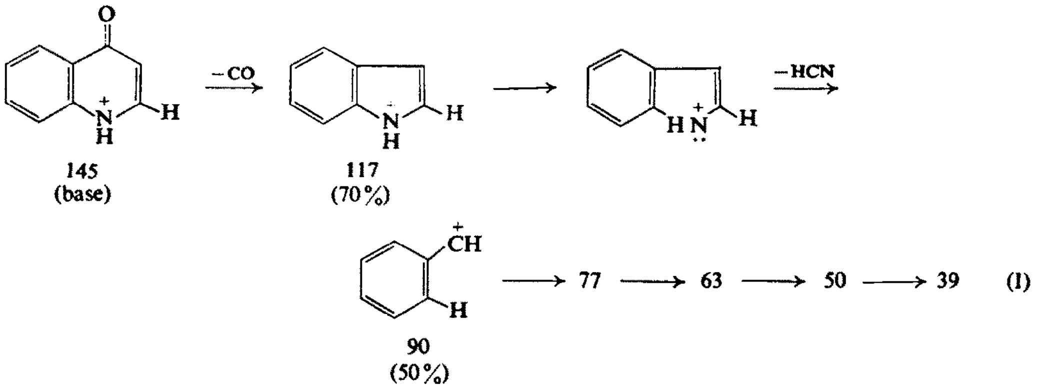


Fig. 1.

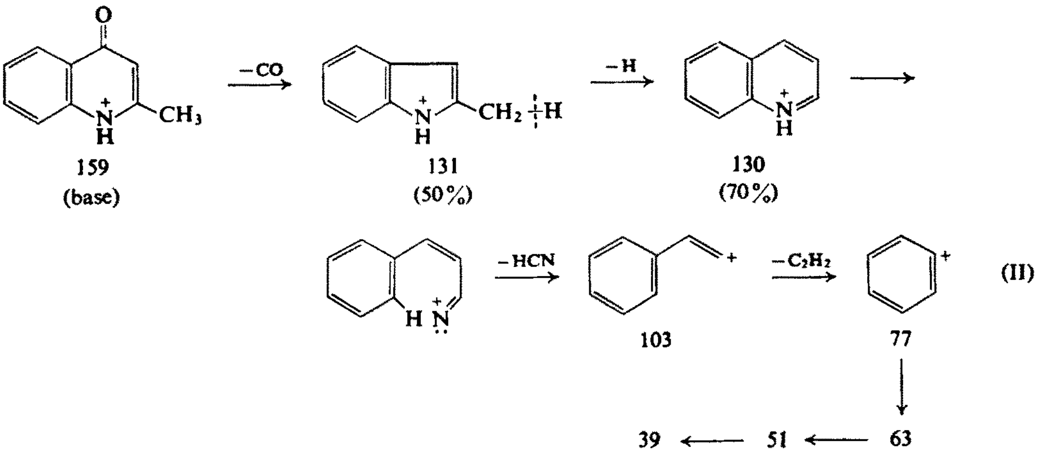


Fig. 2.

Placing an alkyl group larger than CH_3 in the 2-position leads to a multiplicity of fragmentation paths as shown for the 2-n-propyl (III) and 2-n-hexyl (IV) derivatives (Fig. 3). Four modes are shown for the 2-n-propyl compound, all leading to the formation of the 2-methylene indole ion (m/e 130), the fragmentation of which was mentioned above (Fig. 2). In the first case the parent ion-radical undergoes a loss of CO followed by a loss of C_2H_5 giving the m/e 130 peak. Secondly, the parent peak can undergo loss of a methyl radical followed by a loss of CO and then CH_2 again giving the m/e 130 peak. Two of the modes which seem to be of more importance are pictured at the bottom of Fig. 3. The C-3 position accepts an H-radical from either the α- or the γ-carbon of the alkyl chain with subsequent C—C splitting giving the corresponding rearranged ion-radical. A rearrangement of this type has been proposed for analogous alkylbenzenes.[1] Rearrangement of the γ-proton leads to the formation of the m/e peak at 159 which is the base peak. Rearrangement of the α-proton yields the m/e peak at 172 which is 70 per cent of the base peak. The m/e 159 ion-radical is

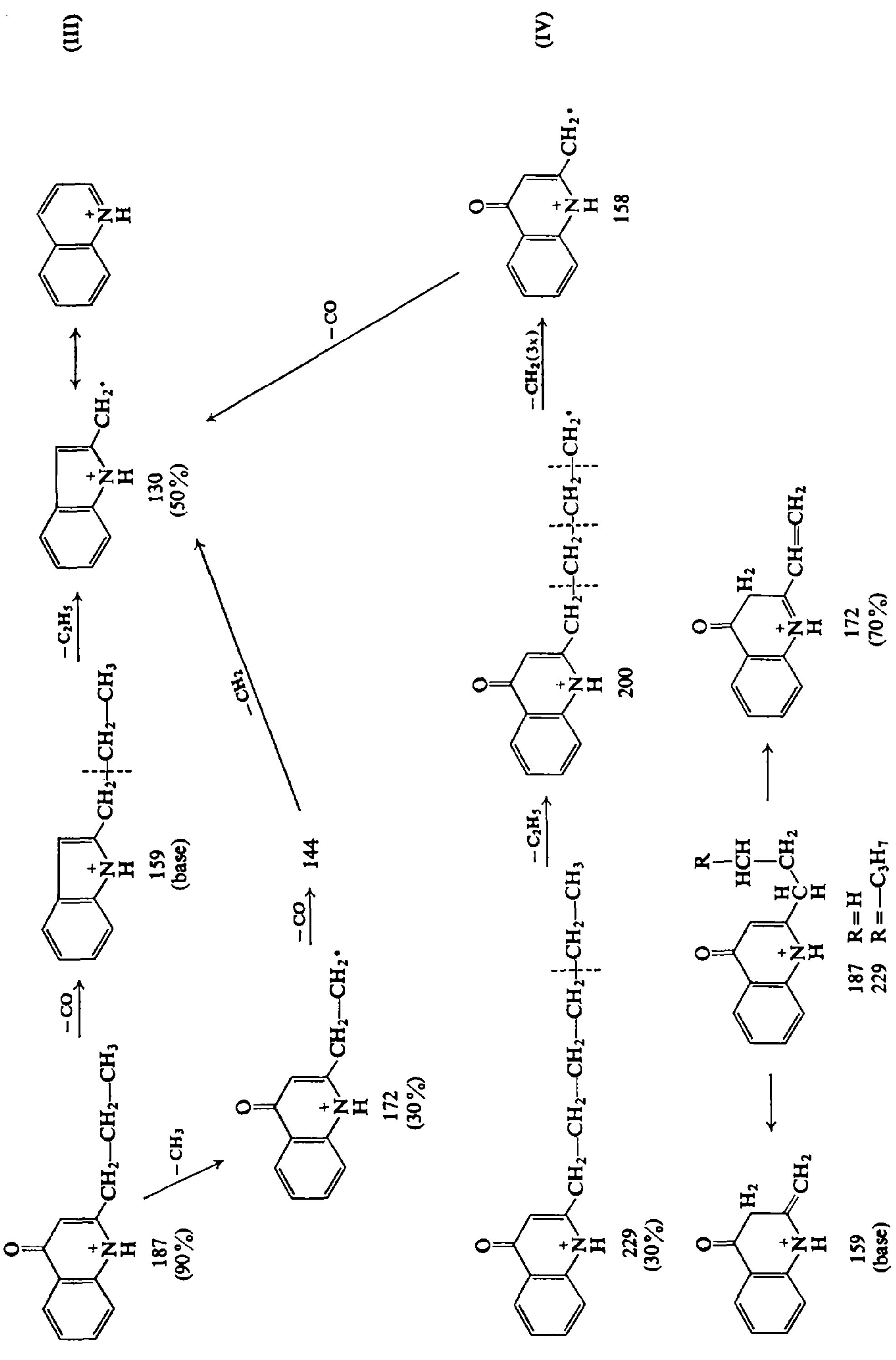

(III)
(IV)
187 (90%)
−CO
159 (base)
−C₂H₅
130 (50%)
−CH₃
172 (30%)
−CO
144
−CH₂
−CO
229 (30%)
−C₂H₅
200
−CH₂(3x)
158
187 R=H
229 R=—C₃H₇
159 (base)
172 (70%)

FIG. 3.

merely one resonance form of 3-methylindole whose spectrum has already been discussed. The m/e 172 peak undergoes the loss of ketene with subsequent rearrangement to give the usual m/e 130 peak which is 50 per cent of the base peak.

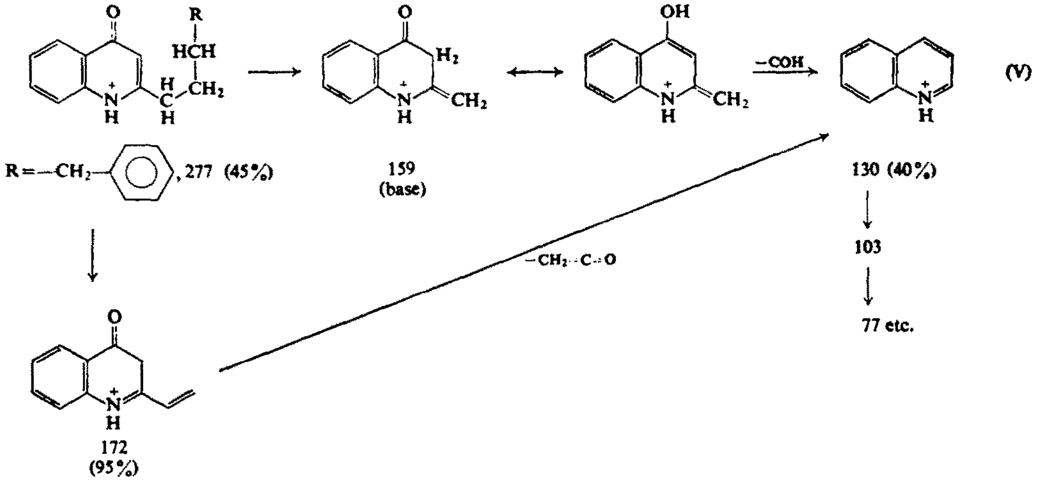


Fig. 4.

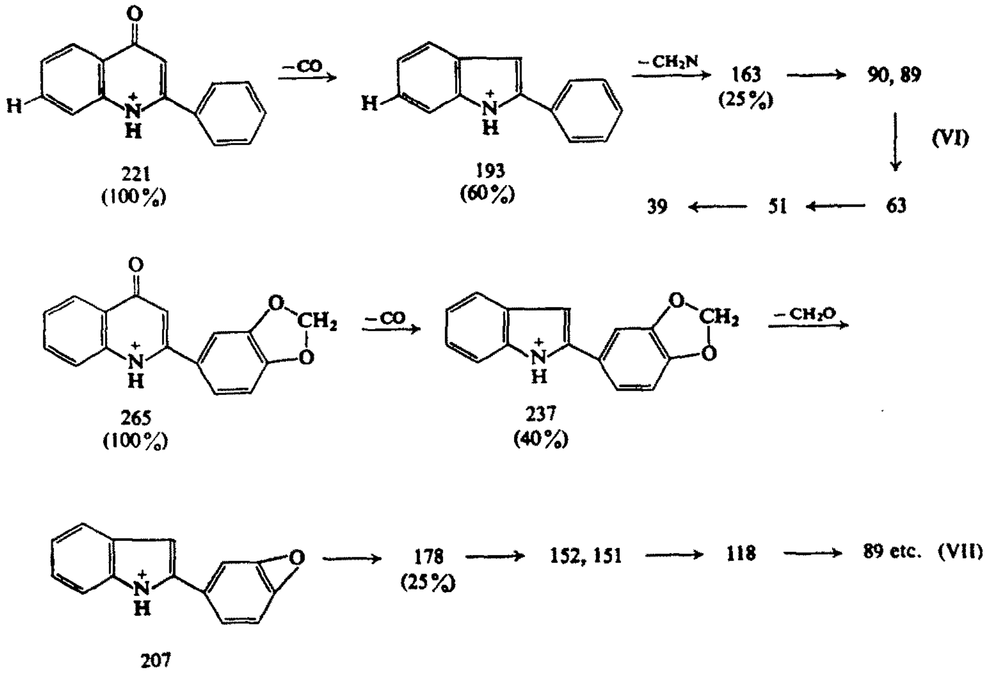
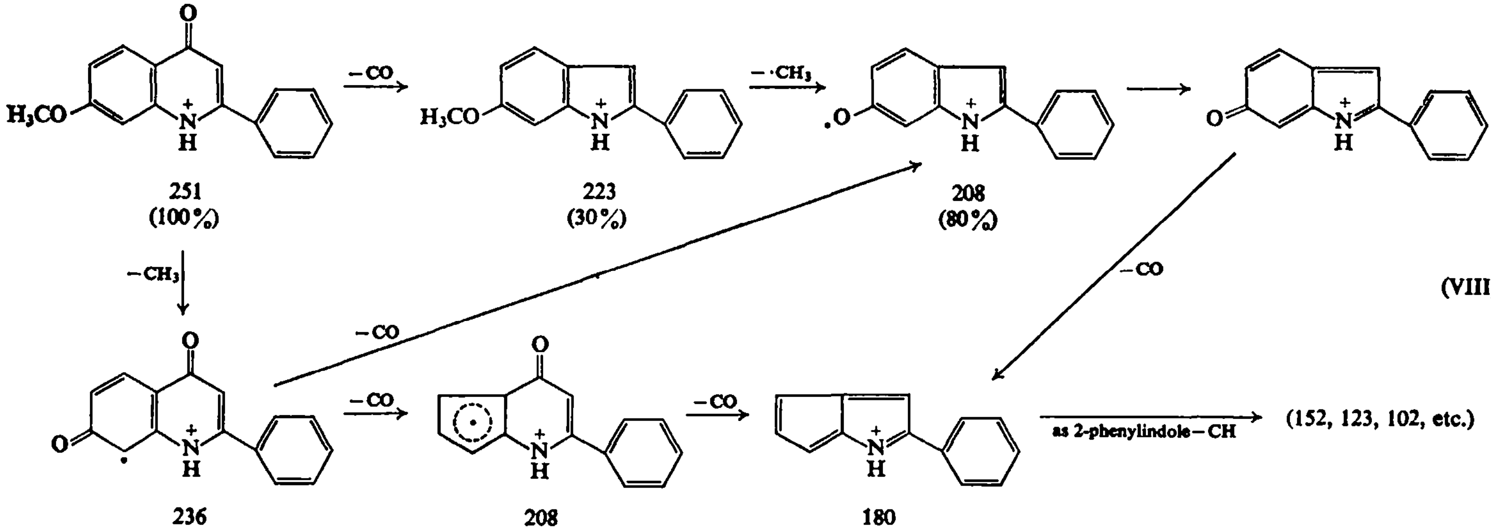


Fig. 5.


251
(100%)
−CO
223
(30%)
−·CH₃
208
(80%)
−CH₃
−CO
−CO
236
−CO
208
−CO
180
as 2-phenylindole−CH
(152, 123, 102, etc.)

(VIII)

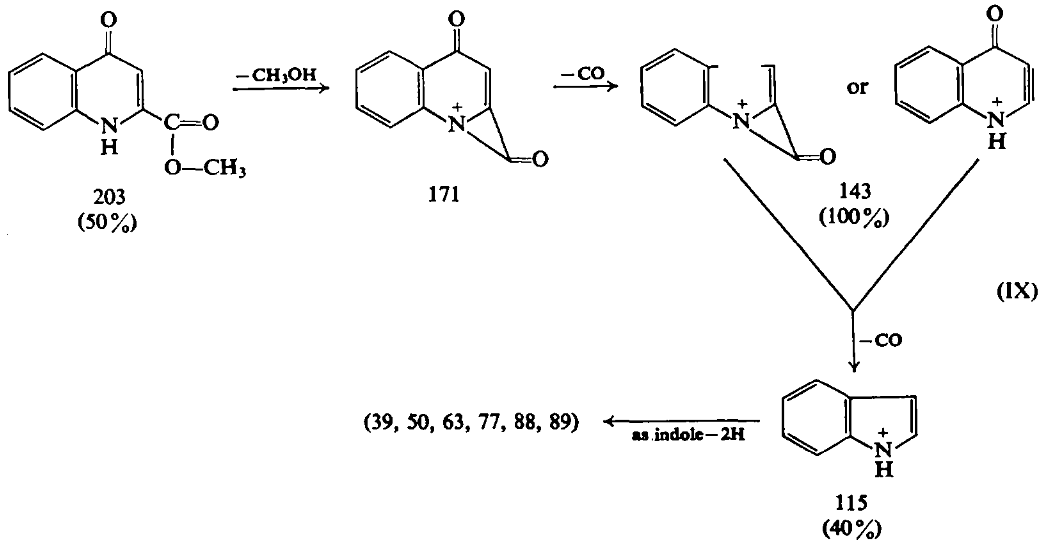
Fig. 6.

The 2-n-hexyl derivative also shown in Fig. 3 shows similar modes of fragmentation with the exception that no loss of CO from the parent (m/e 229) peak was noticed. The two modes of alkylbenzene type rearrangement are present plus a third path which shows the loss of ethyl radical from the parent peak and a series of CH_2 losses from the alkyl chain to give the 2-methylene quinolone ion peak m/e 158.

The 2-(4′-phenyl-n-butyl)-4-quinolone (V, Fig. 4) undergoes primarily the alkylbenzene type rearrangements yielding the 159 m/e peak as the base peak and the 172 m/e peak as 95 per cent of the base peak. However, the m/e 159 peak in this case appears to fragment not with the usual loss of CO, but rather with a rearrangement to the enolic form followed by loss of COH (Ref. 1, pp. 167 and 168). Why this should be the case with this molecule is not clear.

In the case of 2-phenyl-4-quinolone (VI, Fig. 5) fragmentation appeared once again to be a loss of CO from the parent (221) m/e peak. The 2-phenylindole ion-radical, whose spectrum is reported,[6] loses CH_2N and goes on to yield the typical benzene derivative peaks. Substitution on the 2-phenyl group as in 2-(2′,3′-methylenedioxyphenyl)-4-quinolone (VII) affects the pattern very little as shown in Fig. 5. The difference being in the second step where, as reported for other similar methylenedioxy compounds,[7] a loss of the elements of formaldehyde takes place.

When one places a methoxy group in the 7-position of the 2-phenyl compound (VIII) the pattern becomes more complex, with three principal fragmentation paths appearing, all leading to the m/e 180 peak. This then undergoes further fragmentation analogous to 2-phenylindole (Fig. 6). In the first process we see once again the loss of the carbonyl group followed by a loss of methyl radical to give the m/e 208 peak which, on rearrangement and loss of the second CO, gives the m/e 180 peak. Alternatively the parent molecule can first lose a methyl radical to give the m/e 236 peak which further fragments in two pathways, depending on whether the hetero-ring CO or the benzene ring CO is lost first.



(IX)

FIG. 7.

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[6] A. CORNU and R. MASSOT, *Compilation of Mass Spectral Data.* Heyden and Son, London (1966).

[7] B. WILLHALM, A. F. THOMAS and F. GAUTSCHI, *Tetrahedron* **20**, 1185 (1965).

In the last example (Fig. 7), the 2-methoxycarbonyl (IX) derivative, we invoke a rearrangement shown to occur in analogous compounds[8] to rationalize the first step, loss of the elements of methanol. That is, the 1-hydrogen is lost with simultaneous splitting of the O═C—O bond. Successive loss of two carbonyl groups results in the m/e 115 peak which fragments in the same manner as the earlier-mentioned indole.

In conclusion it should be repeated that all compounds gave a relatively large parent peak, and thus an accurate molecular weight was obtained. Close inspection and comparison of the mass spectra of these model substances with those of suspected alkaloids should prove very useful for the recognition of this structure type.

EXPERIMENTAL

All spectra were taken on a Hitachi-Perkin-Elmer RMU-6D Mass Spectrometer with an electron beam of 70 eV using the heated direct inlet system.

The compounds I,[9] II,[10] V,[11] VI,[12] VII[13] and IX[14] were prepared using methods described elsewhere. Compound III was prepared in a manner analogous to that described for II; m.p. 162–164°. (Found: C, 77·56; H, 7·05; N, 7·39. Calc. for $C_{12}H_{13}NO$: C, 76·97; H, 7·00; N, 7·48%.)

2-n-Hexyl-4-quinolone (*IV*). 3·4 g (0·02 mole) of methyl n-non-2-ynoate, 1·9 g (0·02 mole) of aniline and 0·2 m-mole of Cu_2O were heated within 5 min to a temperature of 180°. After the exothermic reaction had subsided the temperature was maintained at 230–250° for 15 min. The solid mass formed on cooling of the reaction mixture was washed with ether, then recrystallized from aqueous alcohol; m.p. 139° [lit. 139°[15]], yield 2·8 g (60%). (Found: C, 78·61; H, 8·36; N, 6·04. Calc. for $C_{15}H_{19}NO$: C, 78·56; H, 8·35; N, 6·11%.)

7-Methoxy-2-phenyl-4-quinolone (*VIII*). VIII was prepared according to the procedure described in[15]; m.p. 283–284° [lit. 282–283°[16]]. Further, the presence of the 4-quinolone structure was substantiated by analysis of the i.r. spectrum in each case.[17–19]

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[8] H. Budzikiewicz, C. Djerassi and D. H. Williams, *Interpretation of Mass Spectra of Organic Compounds*, p. 246. Holden-Day, San Francisco (1964).

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[15] J. Reisch, *Angew. Chem.* **75**, 1203 (1963).

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[17] H. Sterk and F. Ziegler, *Monatsh.* **98**, 101 (1967).

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