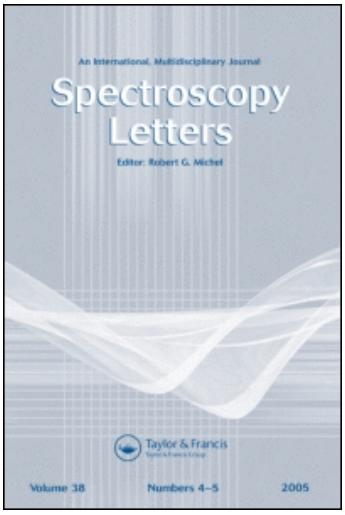


Spectroscopy Letters
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597299

N.M.R. Spectral Studies of Some Quinolone Derivatives. Part II.[1] Further Studies of the Effect of Substitution on the Degree of Hydrogen Bonding

Paul A. Claret[a]; Alan G. Osborne[a]
[a] Department of Chemistry, The City University, London, England

To cite this Article Claret, Paul A. and Osborne, Alan G.(1976) 'N.M.R. Spectral Studies of Some Quinolone Derivatives. Part II.[1] Further Studies of the Effect of Substitution on the Degree of Hydrogen Bonding', Spectroscopy Letters, 9: 3, 157 — 166
To link to this Article: DOI: 10.1080/00387017608067424
URL: http://dx.doi.org/10.1080/00387017608067424

SPECTROSCOPY LETTERS, 9(3), 157-166 (1976)

N.M.R. SPECTRAL STUDIES OF SOME QUINOLONE DERIVATIVES. Part II.[1] FURTHER STUDIES OF THE EFFECT OF SUBSTITUTION ON THE DEGREE OF HYDROGEN BONDING.

KEY WORDS : NMR, chemical shift, quinolone, hydrogen bonding

Paul A. Claret and Alan G. Osborne

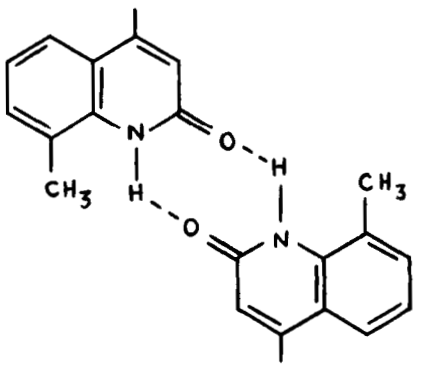
Department of Chemistry
The City University
London EC1V 4PB., England

Abstract : The chemical shift of the NH proton for a series of 4-quinolone derivatives has been studied. It is proposed that the inhibition of π-hydrogen bonding is a dominant factor which contributes to the observed NH chemical shift. Details of the ^{1}H n.m.r. spectra of some 2- and 4- quinolone derivatives are presented.

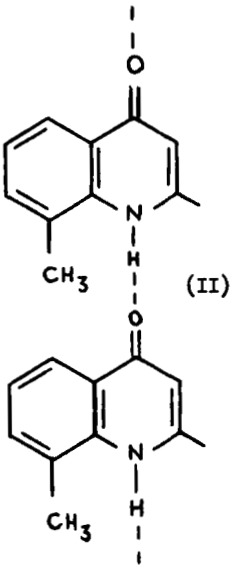
We reported in Part 1[1] that the substitution of a methyl group at position 8 in the 2- or 4- quinolone ring resulted in a characteristic upfield chemical shift of the NH proton compared with that of the unsubstituted quinolone. This was attributed to steric inhibition of hydrogen bonding and was supported by a corresponding loss of the broad nature of the N-H stretching region in the infra-red spectrum.

The generally accepted doubly hydrogen bonded dimeric structure (I) for 2-quinolone was considered[1] to be inconsistent with these observations which were more in accordance with the helical structure proposed by Penfold[2] for the structure of 2-pyridone in the crystalline state. Further consideration of the corresponding structure (II) for 4-quinolone showed, however, that both 5- and 8- substituents would be expected to

have similar space requirements, which did not appear to be consistent with the limited evidence available.



(I)



(II)

We have now undertaken further measurements with a series of substituted 2-methyl-4-quinolone derivatives and the results are shown in Table 1. These results together with a more detailed study of our previous data for the 4-methyl-2-quinolone series[1] shows that introduction of a methyl substituent at various positions of the quinolone ring induce the following approximate upfield chemical shifts for the NH proton (p.p.m.), both individually or in combination.

Ring position	2	4	5	6	7	8
2-quinolone	-	0.2	0.7	0.2	0.1	2.5
4-quinolone	0.05	-	0.4	0.1	0.2	1.4

The above figures (the mean of the shifts from Table 1, and from Table 1 of reference 1), although not precise, are sufficient to show the particular significance of the 8-substituent compared with all other

Table 1

Properties and chemical shifts of NH protons for a series of 4-quinolone derivatives

Substituents	m.p.	m.p.(lit.)	NH chemical shift (δ)(a)
nil	- (b)	-	11.70
2-Me	- (b)	-	11.65
2,6-Me_2	279-80°	278-9° (3)	11.54
2,7-Me_2	260-75° (c)	255-70° (4)	11.47
2,6,7-Me_3	271-3° (d)	(e)	11.36
2,5-Me_2	274-6°	274° (3)	11.36
2,5,6-Me_3	271-3° (d)	(e)	11.21
2,5,7-Me_3	285-7°	288° (4)	11.14
2,8-Me_2	269-70°	263-4° (3)	10.36
2,6,8-Me_3	273-4°	273° (3)	10.32
2,7,8-Me_3	292-4°	(e)	10.24
2,5,8-Me_3	246-7°	248° (3)	9.92
2,5,6,8-Me_4	285-6°	285° (5)	9.84

(a) NMR - 100 MHz, 5% w/v solution in DMSO-d_6.

(b) Commercial sample.

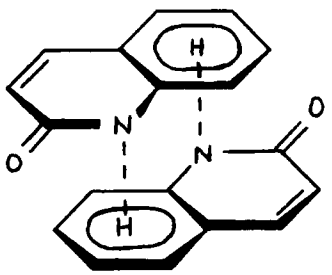
(c) In admixture with 2,5- isomer.

(d) Mixture of 2,5,6- and 2,6,7- isomers.

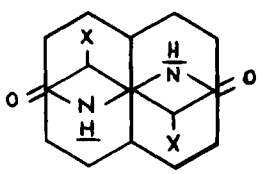
(e) Satisfactory elemental analyses (C,H,N) were obtained for all new compounds reported in this paper.

positions, and also that a methyl substituent at position 5 does have a slightly greater effect then when at position 6 or 7.

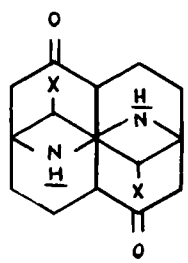
These experimental observations are consistent with the proposal of Petersen[6] that the structure of quinolones in solution involves cyclic dimers formed by π-hydrogen bonds as well as those with carbonyl-hydrogen bonds. Petersen's structure (III) may be represented in diagrammatic form by (IV) which shows the particular significance of the 8-substituent. The corresponding 4-quinolone is represented by (V).



(III)



(IV)

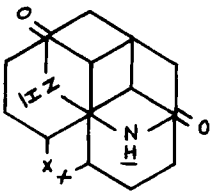


(V)

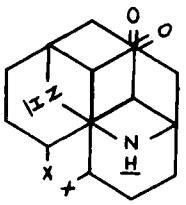
H - H bonded by π-bond.

X - 8-substituent.

Other arrangements, which also involve two π-hydrogen bonds such as (VI) and (VII) are possible which would again be sensitive to a substituent at position 8.



(VI)



(VII)

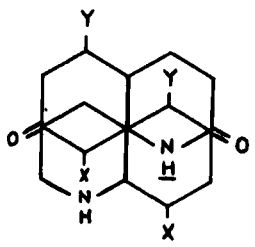
In addition, a series of less favourable structures involving only one π-hydrogen bond may be postulated viz. (VIII), (IX) and (X) for the 2-quinolones and (XI), (XII) and (XIII) for the 4-quinolones. Of these, (IX) and (XII) would be subject to steric interference by an 8-substituent, (X) and (XIII) by a 5-substituent and (VIII) and (XI) by both 5- and 8-substituents. In all cases the effects at other positions would be less significant.

It should be emphasised that although the intermediate effect of a 5-substituent is consistent with the above structures, only the upfield shift of the NH proton caused by the presence of an 8-substituent may be considered sufficiently significant to be of diagnostic value.

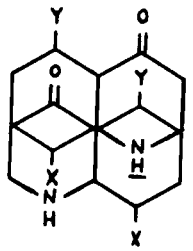
Since reports of the ^{1}H n.m.r. spectra of 2- and 4- quinolone derivatives appear to be scarce,[7-12] we have included some data for these compounds in Tables 2 and 3. Previous workers[7-9] either employed trifluoroacetic acid as solvent, or did not report data for the NH signal.[11,12] Some previous assignments[7,10] require correction.

The spectra have also facilitated confirmation of the identity of the 4-quinolone derivatives prepared by the Conrad-Limpach synthesis[5] commencing with m-toluidine and with 3,4-dimethylaniline.

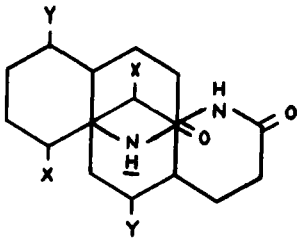
The presence of the 8-methoxy substituent in the alkaloid preskimmianine[13] may also be deduced from the reported chemical shift (9.15δ) for the NH proton.



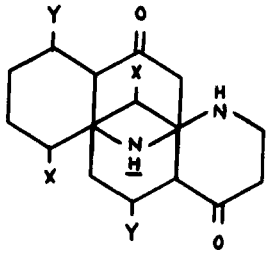
(VIII)



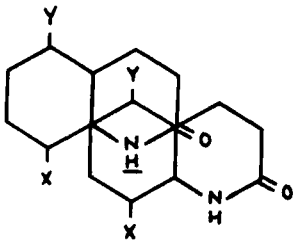
(XI)



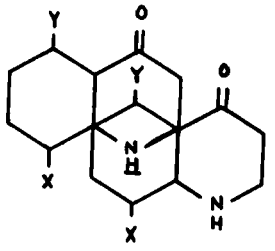
(IX)



(XII)



(X)



(XIII)

Y - 5 substituent

EXPERIMENTAL

N.m.r. spectra were measured at 100 MHz using tetramethylsilane as an internal standard. 2-Quinolone derivatives were 5% w/v solutions in $CDCl_3$,

Table 2

^{1}H N.m.r. spectra of some 2-quinolone derivatives[a]

Substituents	Chemical shift (δ)[b,c]						
	H-3	H-4	H-5	H-6	H-7	H-8	Notes[d]
nil	6.72	7.80					(i)
4-Me	6.59	(2.49)					
4,7-Me_2	6.53	(2.46)	7.53	7.02	(2.44)	7.25	(ii)
4,5,7-Me_3	6.45	(2.67)	(2.71)	6.80	(2.36)	7.05	(e)
4,5,8-Me_3	6.46	(2.66)	(2.72)	6.88	7.17	(2.41)	(iii)
4,6,7-Me_3	6.52	(2.46)	7.38			7.22	(iv)
4,6,8-Me_3	6.50	(2.45)	7.31	(2.38)	7.17	(2.45)	
4,7,8-Me_3	6.46	(2.43)	7.41	7.02			(v)

Notes (i) - J_{34} 9.5 Hz, (ii) - J_{56} 8.1 Hz, J_{68} 1.6 Hz, (iii) - J_{67} 7.5 Hz, (iv) - (2.32, 2.35), (v) - J_{56} 8.3 Hz, (2.39, 2.40).

(a) Determined on 5% w/v solution in $CDCl_3$, all spectra analysed by first order treatment.

(b) Values in parentheses are for the appropriate substituted methyl group.

(c) For chemical shifts of NH protons see reference 1.

(d) For coupling constants and chemical shifts of unassigned methyl groups see notes.

(e) Determined on ca. 1% w/v solution.

4-quinolone derivatives were 5% w/v solutions in DMSO-d_6. All spectra were determined on a Varian HA-100D spectrometer.

The substituted 4-methyl-2-quinolone derivatives were synthesised by the Conrad-Limpach procedure,[5] all products were recrystallised from water.

Table 3

^{1}H N.m.r. spectra of some 4-quinolone derivatives[a]

Substituents	Chemical shift (δ)[b,c]						
	H-2	H-3	H-5	H-6	H-7	H-8	Notes[d]
nil	7.92	6.07	8.13				(i)
2-Me	(2.35)	5.93	8.07				
2,7-Me_2	(2.39)	5.87	7.93	7.17	(2.32)	7.23	(ii)
2,5,6-Me_3	-	5.78	(2.78)	-	7.20	7.34	(iii)(e)
2,5,7-Me_3	(2.24)	5.73	(2.73)	6.73	(2.31)	7.04	
2,5,8-Me_3	(2.34)	5.82	(2.74)	6.83	7.24	(2.43)	(iv)
2,6,7-Me_3	-	5.82	7.78	-	-	7.24	(e)
2,6,8-Me_3	(2.34)	5.88	7.69	(2.38)	7.25	(2.48)	
2,7,8-Me_3		5.88	7.84	7.10			(v)
2,5,6,8-Me_4	(2.23)	5.79	(2.72)	(2.32)	7.19	(2.41)	

Notes (i) - J_{23} 7.4 Hz, (ii) - J_{56} 8.2 Hz,
(iii) - J_{78} 8.1 Hz, (iv) - J_{67} 7.2 Hz,
(v) - J_{56} 8.3 Hz, (2.37, 2.40, 2.40).

(a) Determined on 5% w/v solution in DMSO-d_6, all spectra analysed by first order treatment.

(b) Values in parentheses are for the appropriate substituted methyl group.

(c) For chemical shifts of NH protons see Table 1.

(d) For coupling constants and chemical shifts of unassigned methyl groups see notes.

(e) Assignment of methyl groups uncertain, for respective isomers.

The sample from m-toluidine after crystallisation from water was a mixture of 2,5- and 2,7- dimethyl-4-quinolone in the proportion 57:43

(as determined from the areas of the respective H-3 peaks), m.p. 260-75°, lit.[4] m.p. 255-70°. Spivey and Curd[14] reported an isomer proportion of 44:56. Careful recrystallisation from dilute ethanol gave pure 2,5-dimethyl-4-quinolone as colourless needles, m.p. 274-6°, lit.[4] m.p. 273°, lit.[14] m.p. 278°. The chemical shift of the NH proton of 2,5-dimethyl-4-quinolone showed only slight variation (0.02δ) as a pure sample or in admixture with the 2,7- isomer, each in DMSO-d_6 solution.

The sample from 3,4-dimethylaniline after crystallisation from water was a mixture of 2,5,6- and 2,6,7- trimethyl-4-quinolone in the proportion 24:76, m.p. 271-3°. Attempts to separate the isomers were unsuccessful.

It is considered that the variation between isomer proportions may be accounted for by varying degrees of separation which were effected in the crystallisations. Thus it was found possible to effect a partial separation of 2,5- and 2,7- dimethyl-4-quinolones by fractional crystallisation from water.

ACKNOWLEDGEMENTS

We thank Dr. J. C. Petersen, Laramie Energy Research Centre, Laramie, Wyoming, U.S.A. for bringing his paper to our attention and for helpful discussions.

We are also indebted to the Physico Chemical Measurements Unit, Harwell for the dertermination of the n.m.r. spectra.

REFERENCES

1. P. A. Claret and A. G. Osborne, Spectrosc. Letters, 1974, 7, 503 is now regarded as Part 1.
2. B. R. Penfold, Acta. Cryst., 1953, 6, 591.
3. B. P. Bangdiwala and C. M. Desai, J. Indian Chem. Soc., 1953, 30, 655.
4. O. G. Backeberg and C. A. Friedmann, J. Chem. Soc., 1938, 972.

5. M. Conrad and L. Limpach, Ber., 1888, 21, 523.

6. J. C. Petersen, J. Phys. Chem., 1971, 75, 1129.

7. E. Diaz and P. Joseph-Nathan, Spectrochim. Acta, 1969, 25A, 1547.

8. O. Buchardt, P. L. Kumler and C. Lohse, Acta Chem. Scand., 1969, 23, 159.

9. W. Werner, Tetrahedron, 1969, 25, 255.

10. K. M. Johnston, R. M. Luker and G. H. Williams, J. Chem. Soc. Perkin Trans. 1, 1972, 1648.

11. D. J. Gale and J. F. K. Wilshire, Austral. J. Chem., 1974, 27, 1295.

12. H. Sterk and H. Holzer, Org. Magn. Res., 1974, 6, 133.

13. R. Storer and D. W. Young, Tetrahedron Letters, 1972, 2199 ; Tetrahedron, 1973, 29, 1217.

14. A. M. Spivey and F. H. S. Curd, J. Chem. Soc., 1949, 2656.

Received: 12-15-75
Accepted: 12-19-75