Tautomerism in ketomethyl quinolines. Part 3. 4-Ketomethylquinolines[1]

JOHN V. GREENHILL[2] AND HOSSEIN LOGHMANI-KHOUZANI
Pharmaceutical Chemistry, School of Pharmacy, University of Bradford, Bradford, West Yorkshire, BD7 1DP, England
AND
DEREK J. MAITLAND
Chemistry and Chemical Technology, University of Bradford, Bradford, West Yorkshire, BD7 1DP, England

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A series of 4-ketomethylquinolines has been prepared and their tautomerism investigated. The compounds were prepared from 4-methylquinoline deprotonated with lithium diisopropylamide or potassium ethoxide and treated with esters. Attempted deprotonation with *tert*-butyllithium or phenyllithium led to 2-substituted-4-methylquinolines. The simple alkyl or aryl 4-ketomethylquinolines exist essentially as the keto forms, but the quinoline-4-pyruvates are exclusively or substantially in the enol forms.

Key words: ketomethyl quinolines, pyruvates, tautomerism, enols.

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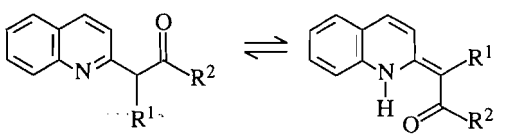
On a préparé une série de 4-cétométhylquinoléines et on a examiné leur tautomérie. On a préparé les produits à partir de la 4-méthylquinoléine déprotonée, à l'aide du diisopropylamide de lithium ou de l'éthylate de potassium, qui a été traitée par des esters. Des essais de déprotonation à l'aide du *tert*-butyllithium ou le phényllithium ont conduit à la formation de 4-méthylquinoléines substituées en position 2. Les 4-cétométhylquinoléines portant des groupements aryles ou alkyles simples existent essentiellement sous la forme cétonique; toutefois, les quinoléine-4-pyruvates existent exclusivement ou presque sous la forme énolique.

Mots clés : cétométhylquinoléines, pyruvates, tautomérie, enols.

[Traduit par la rédaction]

Introduction

We recently conducted detailed investigations into the tautomerism of 2-ketomethylquinolines (1), Scheme 1. By a combination of ir and nmr spectroscopy it was clearly shown that the enaminone form **B** was strongly favoured over the ketone form **A** for 2-ketomethylquinolines where R^1 = H, CN, or COOEt (R^2 = alkyl, aryl, CN, COOEt, etc.). For the compounds with R^1 = H, R^2 = Me, Et, *i*-Pr, or *t*-Bu, the tautomeric mixtures in chloroform had 12–20% of the ketone forms and signals for both forms **A** and **B** could clearly be seen in the ir and the ^{1}H, ^{13}C, and ^{15}N nmr spectra. The rest of the structures investigated showed only the enaminone signals. However, compounds of Scheme 1 where R^1 = Me or Br were found to be exclusively in the ketone form **A**.

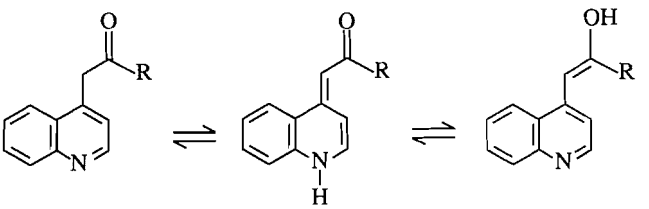


A **B**

SCHEME 1

We have now undertaken a study of 4-ketomethylquinolines by preparing and examining the compounds of Table 1. The few literature reports had reached differing conclusions regarding the tautomerism of compounds of this type. In principle, three forms are possible, Scheme 2.

It was claimed by Stock *et al.* (2) that the pyruvate **6** had 76%



A **B** **C**

SCHEME 2

of the enol form (**C**) after 20 min in methanol, which dropped to 22% at equilibrium (time unspecified). This investigation made use of bromine titration to determine the enol content, and intermolecular (O—H...N) hydrogen bonded stabilization was suggested to account for the enolic content of the mixture. In an nmr study of the same compound, Golankiewicz and Golankiewicz assigned a singlet, which appeared at δ 6.38 in both $CDCl_3$ and DMSO-d_6, to the vinyl proton of the enol form and in the absence of a methylene signal the pyruvate was concluded to be 100% enol (3). Mondelli and Merlini claimed to detect a small proportion of the dienaminone form (**B**) of this pyruvate (4). The 8-cyano derivative of compound **1** was claimed by Higishino *et al.* to be exclusively in the dienaminone form, based on the ir (1680 cm^{-1}) and 60 MHz nmr spectra (5). Compound **11** has recently been shown by Fukata *et al.*, using potentiometric titration, to have log K_T 1.78 in favour of the keto form (**A**) (6).

Synthesis

Compared with the 2-ketomethylquinolines, only a few 4-ketomethylquinolines have been reported (7). Those made from 4-methylquinoline and an ester usually required sodium diisopropylamide (SDA) as base (8), although compound **11** was obtained in good yield from methyl benzoate in the

[1]For Part 2, see ref. 1.

[2]Author to whom correspondence may be addressed. New address: Department of Chemistry, University of Florida, Gainesville, FL 32611-2046, U.S.A.

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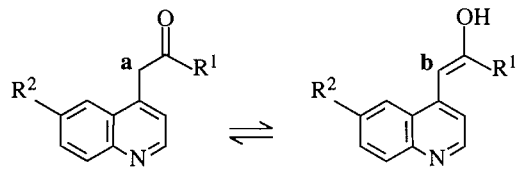
TABLE 1. 4-Ketomethylquinolines and their tautomerism data



A C

No.	R^1	R^2	Chemical shift Ha (integral)	Hb (integral)	Ca	Cb	Infrared (cm^{-1})		Ratio A:C	Ref.
1	Me	H	4.14 (2H)	—	47.91	—	1714 (C=O)		100:0	8
2	Et	H	4.13 (2H)	—	46.69	—	1717 (C=O)	—	100:0	8
3	Pr^i	H	4.17 (2H)	—	44.48	—	1714 (C=O)	—	100:0	8
4	Bu^t	H	4.30 (2H)	—	40.21	—	1711 (C=O)	—	100:0	8
5	COOMe	H	4.76 (0.06H)	6.71 (0.97H)	41.87	[a]	2665 (O–H)	1632 (C=C)	3:97	
6	COOEt	H	4.73 (0.2H)	6.70 (0.90H)	44.37	100.97	2639 (O–H)	1631 (C=C)	10:90	11
7	COOEt	OMe	4.68 (0.38H)	6.68 (0.81H)	41.92	103.39	2619 (O–H)	[a]	19:81	
8	COOEt	COOMe	—	6.73 (1H)	—	79.07	2775 (O–H)	1635 (C=C)	0:100	
9	COOEt	COOEt	—	6.74 (1H)	—	94.39	2657 (O–H)	1639 (C=C)	0:100	
10	COOBu	H	[a]	7.12	42.49	99.24	2936 (O–H)	1626 (C=C)	18:82[b]	
11	Ph	H	4.75 (2H)	—	42.14	—	1691 (C=O)	—	100:0	6
12	2-Py	H	5.05 (2H)	—	40.79	—	1702 (C=O)	—	100:0	8

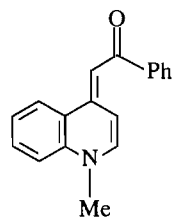
[a]Signal (band) not detected.
[b]Estimated from the ^{13}C nmr spectrum.

presence of sodium hydride (9). In our hands only **11** and the 2-pyridyl ketone **12** could be prepared by this technique.

Attempted use of *tert*-butyllithium or phenyllithium as ionizing bases with 4-methylquinoline, followed by a nitrile or an ester as the acylating agent, gave high yields of 2-*tert*-butyl-4-methylquinoline and 2-phenyl-4-methylquinoline respectively, see experimental section. No trace of any acylated product was detected. Attempted use of sodium hydride or N^1-*tert*-butyl-N^2,N^2,N^3,N^3-tetramethylguanidine (10) as base gave none of the required ketomethylquinolines; only starting materials were recovered. Finally, with lithium diisopropylamide (LDA), compounds **1**, **2**, **3**, and **4** were obtained in good yields. A literature report describes the preparation of ketone **3** from 4-methylquinoline and SDA followed by ethyl isobutyrate (8). The crude product was distilled and extracted with petroleum ether to give a soluble material, mp 45.5–46.6°C, and an insoluble product, mp 160–165°C. It was claimed that the low melting compound was the pure keto form and the high melting material was a mixture of the keto and enol forms. In our hands the same two products were obtained when LDA was substituted for SDA. The spectra of the low melting material showed it to be the required compound as a pure ketone, see experimental section. The nmr spectrum of the high melting material was as follows (δ $CDCl_3$): 1.28 (d), 1.52 (d), 2.94 (heptet), 3.45 (heptet), 4.55 (s), 7.86 (2H, m), 8.04 (2H, m), 8.85 (1H, d), 9.05 (1H, d), 9.40 (s, NH). We interpreted this to be a mixture of the required ketomethylquinoline hydrochloride and diisopropylamine hydrochloride (signals at δ 1.52, 3.45, and 9.4) in the proportions of 88:12. The mixture was dissolved in water, basified, and extracted with dichloromethane to give a further quantity of the low melting ketone.

The ethyl pyruvate **6** has been prepared from 4-methylquinoline and diethyl oxalate in the presence of potassium ethoxide (11). However, we found this compound to be only sparingly soluble in chloroform so that it was difficult to get good spectra for the study of its tautomerism. Therefore, the further pyruvates **5**, **7**, **8**, **9**, and **10** were prepared in the hope of finding more soluble examples. In this we were frustrated and had to rely on KBr discs for the ir spectra and prolonged acquisition times for the FT nmr spectra. The new compounds were prepared by the potassium ethoxide method except for the methyl ester **5**, which resulted from a transesterification of the ethyl ester **6** in methanol containing boron trifluoride.

To get an example of a fixed dienaminone, compound **13** was prepared from 1,4-dimethylquinolinium iodide by a Schotten–Baumann procedure (6).



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Discussion

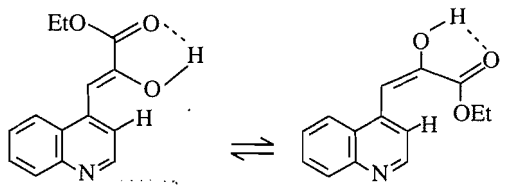
Aliphatic 4-ketomethylquinolines **1**, **2**, **3**, and **4** were clearly in the simple keto forms in chloroform with no trace of any other tautomers. They all had strong carbonyl bands in their ir spectra at about 1715 cm^{-1}. The ^1H nmr spectra showed two-proton singlets for the methylene groups between δ 4.1 and 4.3 and the ^{13}C spectra were characterized by methylene signals between δ 40 and 48 and by unconjugated carbonyl carbon signals in the δ 204—211 region. The uv spectra, Table 2, were closely similar to those of 4-methylquinoline.

The pyruvic ester **9** proved to be in the enol tautomeric form. The ir spectrum showed a very broad, strong band centred at 2657 cm^{-1} for the hydrogen bonded enolic O–H stretch. A strong band at 1723 cm^{-1} represented both ester carbonyl groups and a medium band at 1639 cm^{-1} was in the range for enol C=C stretch. This was much weaker than the carbonyl

TABLE 2. Ultraviolet spectra (λ_{max} (ε) EtOH)

4-Methylquinoline			313 (3 800) 300 (4 200)	277 (6 300)	224 (26 000)
1			315 (3 300) 301 (4 100)	283 (5 200)	231 (13 900)
2			315 (3 100) 301 (3 800)	288 (4 500)	231 (13 000)
3			314 (3 400) 301 (3 900)	288 (4 400)	231 (13 800)
4			314 (2 800) 302 (3 500)	283 (4 600)	227 (23 000)
5	468 (25 700)	446 (18 700)	323 (8 000)	281 (7 200)	230 (20 300)
6	468 (17 600)	448 (14 300)	315 (6 300)		217 (20 000)
7	472 (9 800)	452sh (7 500)	350 (4 600) 324 (6 500)		234 (24 200)
9	479 (14 000)	453 (12 800)		285 (6 500)	242 (28 000)
10	468 (23 800)		315 (7 700)	281 (6 900)	228 (21 400)
11	466 (460)	442 (320)	314 (3 400) 300 (4 400)	280 (7 100)	232 (19 400)
12	479 (1 300)	452 (960)	330 (2 000) 314 (4 200)	271 (8 200)	227 (27 800)
13	474 (52 300)	452 (37 500)		279 (9 700)	230 (26 000)

stretching band of the dienaminone **13** at 1631 cm^{-1}. In the uv spectrum the compound showed strong peaks at 479 and 453 nm, consistent with the proposed extended conjugated system. The ^1H nmr spectrum showed signals for the enol, in particular a full one-proton singlet at δ 6.74 for the vinyl proton. In the ^{13}C spectrum there were the expected signals for the enol and the highest field signal was at δ 165.12 for an ester carbonyl carbon. By contrast, the dienaminone carbonyl carbon of compound **13** absorbed at δ 187.96. Neither nmr spectrum had any sign of a methylene signal from the keto form or any other indication of a second tautomer. Thus both simple ketone and dienaminone forms were ruled out and the compound shown to exist as the enol form. The very low O–H band in the ir spectrum and the fact that the simple ketones **1**, **2**, **3**, **4**, **11**, and **12** showed negligible amounts of their enol forms strongly suggest that the hydrogen bond in **9** is intramolecular, and the compound adopts one of the planar forms **14***a* or **14***b*. Of these we prefer form **14***a*



14*a* **14***b*

since the steric interaction between the C3-H and the ethoxy group of **14***b* would be expected to destabilize it. The mixed ester **8** was also 100% enol, but the other pyruvates **5**, **6**, and **7** were mixtures of keto and enol forms. The tautomeric ratios, calculated from the ^1H nmr spectra, are given in Table 1. For ester **10** a complex proton nmr spectrum indicated the presence of two forms, but it was not possible to identify positively signals on which the tautomeric ratio could be calculated. In the ^{13}C nmr spectrum it was not possible to see two full sets of signals, but the methylene group (δ 42.49) of the keto form and the vinyl carbon (δ 99.24) of the enol form were clearly visible. Their relative intensities in the DEPT spectrum indicated an approximate tautomeric ratio of 18:82.

The aromatic ketone **11** was, like the simple aliphatic compounds, essentially in the keto form. The ir and nmr spectra gave no indication of a second tautomer, but there were two small long-wavelength absorptions in the uv spectrum. The 2-pyridyl derivative **12** was prepared in the hope that the pyridine nitrogen would stabilize the enol form. However, its lone pair is not ideally orientated for intramolecular hydrogen bonding in the way that the oxygen lone pairs of the pyruvates are. Again, it did show two weak long-wavelength absorptions in the uv spectrum. However, neither compound gave any clear signals for a second form in either the ^1H or the ^{13}C nmr spectrum.

The ultraviolet spectra in aqueous solutions for four of the compounds are given in Table 3. The simple ketones, compounds **1** and **11**, showed spectra little changed between water and molar acid, as would be expected. The pyruvates **6** and **10** showed long-wavelength absorption in water similar to that seen in ethanol. Clearly the enolic forms exist in neutral aqueous solution. In acid all four compounds gave very similar spectra. Under these conditions the pyruvates revert to the ketone structures, perhaps because the carbonyl groups are stabilized by hydrogen bonding to the H_3O^+ molecules. It was interesting that all four compounds showed strong absorption at 388–406 nm in molar sodium hydroxide. These conditions must be sufficiently basic to induce deprotonation of the methylene group.

In comparing the structures of the 2-ketomethylquinolines with those of the present report it is clear that the *intra*-molecular hydrogen bond in the enaminone form, Scheme 1, is essential for its stabilization. The energy difference between the two forms of Scheme 1 must be small since the simple alkyl derivatives (R^1 = H, R^2 = alkyl) show significant proportions of the ketone forms in solution. The equivalent compounds of the 4-ketomethyl series, Scheme 2, have no comparable *intra*-molecular hydrogen bonding available and show only ketone structures.

In comparing the freely chloroform-soluble compounds **1**–**4**, **11**, and **12** (all 100% ketones) with the esters **5**–**10** there was the possibility that the DMSO-d_6, which had to be used to obtain the ester nmr spectra, had helped to stabilize the enol forms detected. Compound **1** was therefore re-run in DMSO-d_6, but

TABLE 3. Ultraviolet spectra in aqueous solutions (λ_{max} (ϵ))

1	H_2O		314 (4 400)	301 (4 700)	289 (4 800)	226 (30 600)
	M HCl		314 (8 200)			233 (31 700)
	M NaOH	388 (900)			264 (9 900)	225 (41 200)
6	H_2O	444 (18 600)			277 (6 300)	227 (20 700)
	M HCl		315 (7 800)			236 (35 800)
	M NaOH	388 (19 100)			263 (9 000)	218 (18 700)
10	H_2O	445 (17 200)	314 (5 000)		277 (6 400)	230 (25 900)
	M HCl		314 (9 900)			235 (42 500)
	M NaOH	390 (17 700)			265 (9 500)	223 (44 800)
11	H_2O		314 (6 200)	300 (7 000)	284 (8 600)	226 (42 200)
	M HCl		314 (10 200)			236 (40 800)
	M NaOH	406 (16 800)			257 (8 600)	223 (42 400)

neither the ^1H nor the ^{13}C spectrum was significantly different from the $CDCl_3$ spectrum (see experimental). The methyl (δ 2.29) and methylene (δ 4.38) proton signals were in an exact 3:2 ratio and there were no detectable signals for an enol form. Further evidence for the conclusions reached was provided by the uv spectra. The compounds of Scheme 1, which have been shown to be substantially enaminones in chloroform, had strong absorptions in ethanol and in water at 430–440 nm (for R^1 = H, R^2 = alkyl) or 450–460 nm (for R^1 = H, R^2 = aryl), establishing that the enaminone forms are dominant in these solvents also (14). Reference to Tables 2 and 3 shows that the alkyl 4-ketomethylquinolines **1**–**4** show no trace of long-wavelength absorption, and the aryl derivatives **11** and **12** have very low absorption in the 440–480 region.

It is reasonable to assume that other simple 4-ketomethylquinolines would exist as ketones, but that enol formation, giving a system conjugated to the quinoline ring, will always be a possibility where it can be stabilized by intramolecular hydrogen bonding. Whether any firm examples will be found in which dienaminone forms exist remains to be seen, but the loss of aromaticity in the heterocyclic ring cannot be compensated by hydrogen bonding as is the case with the enaminone forms of 2-ketomethylquinolines (1).

Experimental

The ir spectra were run on Perkin–Elmer 1700-X and 1720-X FT spectrophotometers. The 270 MHz ^1H and 67.8 MHz ^{13}C nmr (broad band decoupled and DEPT 135) spectra were run on a JEOL GX 270 spectrometer fitted with a 5 mm C/H probe. The uv spectra were obtained on a Perkin–Elmer Lambda 5 UV/VIS spectrophotometer and mass spectra on an AEI MS 902 spectrometer. Chromatography columns were prepared with Aldrich silica gel 70–230 mesh.

2-(1,1-Dimethylethyl)-4-methylquinoline

A solution of 4-methylquinoline (2.86 g, 0.02 mol) in dry ether (10 mL) was added dropwise to a solution of *tert*-butyllithium (11.76 mL of 1.7 M solution in pentane, 0.02 mol) in dry ether (20 mL) and stirred under nitrogen at room temperature for 1 h. Acetonitrile (5.0 g, 0.06 mol) in dry ether (10 mL) was added and stirring continued for a further 20 h. The product was washed with water and extracted with dilute hydrochloric acid. The aqueous extracts were neutralized with solid sodium carbonate and extracted with chloroform (2 × 50 mL). The chloroform solution was dried ($MgSO_4$) and the solvent removed to give *2-(1,1-dimethylethyl)-4-methylquinoline* as a colourless oil (3.4 g, 85%); ^1H nmr (δ $CDCl_3$); 1.46 (9H, s, 3 × CH_3), 2.67 (3H, s, CH_3), 7.34 (H, s), 7.47 (H, dt), 7.65 (H, dt), 7.93 (H, dd), 8.06 (H, dd); ^{13}C nmr (δ $CDCl_3$); 18.95 (CH_3), 30.10 (3 × CH_3), 37.88 (C), 118.87 (CH), 123.36 (CH), 125.36 (CH), 126.51 (C), 128.66 (CH), 129.91 (CH), 143.58 (C), 147.27 (C), 168.90 (C); *m/z* 199. It gave the *hydrochloride*, mp 225–226°C (from ethanol–ether). Anal. calcd. for $C_{14}H_{18}ClN$: C, 71.3, H 7.65, Cl 15.1, N 5.95%; found: C 71.2, H 7.5, Cl 15.2, N 5.9%.

4-Methyl-2-phenylquinoline was similarly prepared from 2-phenyllithium: 82%, mp 65°C (from methanol) (lit. (12) mp 67°C); ^1H nmr (δ $CDCl_3$, 60 MHz); 2.52 (3H, s, CH_3), 7.3–8.3 (10H, m, C_9H_5N + C_6H_5); *m/z* 219.

1-(4-Quinolyl)propan-2-one (1)

4-Methylquinoline (2.86 g, 0.02 mol) was added dropwise to a solution of lithium diisopropylamide (13.3 mL of a 1.3 M solution in cyclohexane, 0.02 mol) in THF (15 mL) with stirring under nitrogen at −78°C. After 20 min methyl acetate (1.5 g, 0.02 mol) was added and stirring continued for 30 min at −78°C. The mixture was allowed to warm to room temperature and stirred for a further 40 min. Water (2 mL) and ether (50 mL) were added, the cooled solution carefully acidified with hydrochloric acid, and the layers separated. The aqueous solution was treated with sodium hydroxide solution until nearly neutral and finally basified with solid sodium carbonate. The product was extracted with chloroform, dried ($MgSO_4$), the solvent evaporated, and the residue chromatographed on a silica column eluted with 1% methyl acetate in chloroform to give 1-(4-quinolyl)propan-2-one (1.37 g, 37%) mp 70–71°C (from petroleum ether 40–60) (lit. (8) mp 71.8–72.6°C); ir ($CHCl_3$): 1714(s), 1594(m), 1572(w), 1511(m) cm^{-1}; ^1H nmr (δ $CDCl_3$): 2.20 (3H, s, CH_3), 4.14 (2H, s, CH_2), 7.28 (H, d, C3-H, J = 4.40), 7.57 (H, t), 7.73 (H, t), 7.87 (H, d), 8.14 (H, d), 8.87 (H, d, C2-H, J = 4.39); ^1H nmr (δ DMSO-d_6): 2.29 (3H, s), 4.38 (2H, s), 7.39 (H, d, J = 4.29), 7.64 (H, t), 7.77 (H, t), 7.90 (H, d), 8.04 (H, d), 8.84 (H, d, J = 4.28); ^{13}C nmr (δ $CDCl_3$): 29.50 (CH_3), 47.91 (CH_2), 122.78 (CH), 123.62 (CH), 127.07 (CH), 127.54 (C), 129.50 (CH), 130.29 (CH), 140.43 (C), 148.42 (C), 150.16 (CH), 204.48 (C); ^{13}C nmr (δ DMSO-d_6): 30.24, 46.66, 123.56, 125.07, 126.90, 127.98, 129.60, 129.86, 141.96, 148.17, 150.53, 205.34; *m/z* 185.

The following were prepared similarly:

1-(4-Quinolyl)butan-2-one (2): 35%, bp 135–140°C (0.3 Torr; 1 Torr = 133.3 Pa) (lit. (8) bp 134–135°C (0.55 Torr)). Analytical sample purified via a silica column eluted with 1% ethyl acetate in chloroform; ir ($CHCl_3$): 1717 (s), 1593 (m), 1572 (w), 1511 (m) cm^{-1}; ^1H nmr (δ $CDCl_3$): 1.03 (3H, t, CH_3), 2.52 (2H, q, CH_2), 4.13 (2H, s, CH_2), 7.26 (H, d, C3-H, J = 4.39), 7.56 (H, t), 7.72 (H, t), 7.87 (H, d, J = 8.42), 8.14 (H, d, J = 8.42), 8.86 (H, d, C-2H, J = 4.39); ^{13}C nmr (δ $CDCl_3$): 7.70 (CH_3), 35.51 (CH_2), 46.69 (CH_2), 122.73 (CH), 123.70 (CH), 127.02 (CH), 127.60 (C), 129.47 (CH), 130.18 (CH), 140.73 (C), 148.34 (C), 150.08 (CH), 207.12 (C); *m/z* 199.

3-Methyl-1-(4-quinolyl)butan-2-one (3): 55%, bp 145°C (0.8 Torr) (lit. (8) bp 133–135°C (0.55 Torr)). The oil (2.1 g) was refluxed with petroleum ether 40–60, filtered, and the filtrate cooled in liquid nitrogen. The product was collected and chromatographed through a silica column eluted with 1% methyl acetate in chloroform to give the pure ketone (1.2 g), mp 43–44°C (lit. (8) mp 45.4–46.6°C); ir ($CHCl_3$); 1714 cm^{-1}; ^1H nmr (δ $CDCl_3$): 1.14 (6H, d, 2 × CH_3), 2.77 (H, heptet, CH), 4.17 (2H, s, CH_2), 7.23 (H, d, C3-H, J = 4.40), 7.54

(H, t), 7.68 (H, t), 7.82 (H, d), 8.13 (H, d), 8.84 (H, d, C2-H, J = 4.40); ^{13}C nmr (δ $CDCl_3$): 18.40 (CH_3), 40.48 (CH), 44.48 (CH_2), 122.76 (CH), 123.62 (CH), 126.86 (CH), 127.71 (C), 129.34 (CH), 130.17 (CH), 140.83 (C), 148.31 (C), 149.99 (CH, 210.20 (C); m/z 213. The petroleum ether insoluble residue (0.6 g) was dissolved in water, basified with dilute ammonium hydroxide, and extracted with dichloromethane. The extracts were dried ($MgSO_4$) and the solvent evaporated to give a residue identical (^{1}H nmr) with the pure ketone base prepared above.

3,3-Dimethyl-1-(4-quinolyl)butan-2-one (**4**): Purified through a silica column eluted with 1% ethanol in dichloromethane, 26.5%, mp 119–120°C (from petroleum ether 60–80) (lit. (8) mp 119–120°C); ir ($CHCl_3$): 1711 (s), 1596 (m), 1572 (w), 1512 (s) cm^{-1}; ^{1}H nmr (δ $CDCl_3$): 1.32 (9H, s, 3 × CH_3), 4.30 (2H, s, CH_2), 7.23 (H, d, C3-H, J = 4.40), 7.57 (H, t), 7.76 (2H, m), 8.20 (H, d, J = 8.43), 8.90 (H, d, C2-H, J = 4.40); ^{13}C nmr (δ $CDCl_3$): 26.65 (CH_3), 40.21 (CH_2), 45.07 (C), 122.84 (CH), 123.60 (CH), 126.94 (CH), 127.95 (C), 129.60 (CH), 129.64 (CH), 142.39 (C), 147.55 (C), 149.31 (CH, 211.01 (C); m/z 227.

Methyl 2-hydroxy-3-(4-quinolyl)propenoate (**5**)

A solution of ethyl 2-hydroxy-3-(4-quinolyl)propenoate (0.8 g) in 14% boron trifluoride – methanol complex (40 mL) was refluxed on a water bath for 12 h. Most of the solvent was removed and the residue basified with saturated potassium bicarbonate solution and extracted with chloroform (5 × 100 mL). The combined extract was dried ($MgSO_4$) and the solvent evaporated to give the methyl ester (0.6 g, 78%) mp 198–200°C (from pyridine); ir (KBr): 2665 (br s), 1727 (s), 1632 (m), 1601 (m), 1533 (vs), 1505 (vs) cm^{-1}; ^{1}H nmr (δ DMSO-d_6, 16°C): 3.77 (s, OCH_3), 3.86 (s, OCH_3, keto form), 4.76 (s, CH_2, keto form), 6.71 (s, =CH), 7.4–8.6 (6H, m, C_9H_6N), 12.40 (s, OH), ratio keto:enol 3:97; at 60°C the spectrum was the same, but the keto:enol ratio was 6:94; ^{13}C nmr (δ DMSO-d_6, 60°C): 41.87 (CH_2, keto form), 51.77 (OCH_3), 52.69 (OCH_3, keto form), 123.25, 123.53, 125.31, 126.43, 127.46, 129.12, 129.47, 131.00, 139.89, 147.86, 165.76 (C); it was not possible to identify the other carbon signals due to the low solubility; m/z 229. Anal. calcd. for $C_{13}H_{11}NO_3$: C 68.1, H 4.8, N 6.1%; found: C 67.9, H 4.85, N 6.15.

General method for the preparation of esters **6–10**

A solution of the appropriate oxalic acid diester (0.005) mol) in dry ether (10 mL) was added to potassium ethoxide (0.01 mol from potassium (0.4 g) and ethanol (1.8 mL) in dry ether (20 mL)). A solution of the 4-methylquinoline (0.005 mol) in dry ether (10 mL) was added dropwise and the mixture stirred for 3 days and allowed to stand for 4 days. The precipitate was collected rapidly and immediately added to dilute acetic acid (10 mL). After stirring for 2 h, the new precipitate was collected to give the required ester:

Ethyl 2-hydroxy-3-(4-quinolyl)propenoate (**6**): 70%, mp 192–194°C (from pyridine) (lit. (11) mp 196°C); ir (KBr): 2639 (br. s), 1716 (s), 1631 (m), 1602 (m), 1529 (s), 1505 (s) cm^{-1}; ^{1}H nmr (δ DMSO-d_6): 1.31 (t, CH_3), 4.24 (q, CH_2), 4.73 (s, CH_2, keto form), 6.70 (s, =CH), 7.4–8.5 (6H, m, C_9H_6N), keto:enol ratio 1:9; ^{1}H nmr (δ DMSO-d_6/TFA 1:2); 1.50 (t, CH_3), 4.52 (q, CH_2), 5.12 (s, CH_2, keto form), 7.45 (s, =CH), 8.0–9.0 (6H, m, C_9H_6N), keto:enol ratio 1:4; ^{13}C nmr (δ DMSO-d_6/TFA 1:2), strong signals (enol form); 14.14 (CH_3), 65.80 (CH_2), 100.97 (CH), 122.04 (CH), 122.19 (CH), 125.97 (CH), 128.11 (C), 131.53 (CH), 136.37 (CH), 139.12 (C), 143.61 (CH), 151.35 (C), 153.17 (C), 165.77 (C); weak signals (keto form): 14.02 (CH_3), 44.37 (CH_2), 65.63 (CH_2), 122.45 (CH), 125.22 (CH), 126.94 (CH), 130.26 (C), 132.27 (CH), 137.08 (CH), 138.99 (C), 144.48 (CH), 155.59 (C), 161.39 (C), 189.96 C); m/z 243.

Ethyl 2-hydroxy-3-(6-methoxy-4-quinolyl)propenoate (**7**): 49%, mp 188–190°C (from ethanol); ir (KBr): 2619 (br s), 1718 (s), 1606 (s), 1504 (vs), 1477 (vs) cm^{-1}; ^{1}H nmr (δ DMSO-d_6 70°C): 1.32 (3H, t, CH_3), 3.92 (3H, s, OCH_3), 4.27 (2H, q, CH_2), 4.68 (s, CH_2, keto form), 6.68 (s, =CH), 7.3–8.4 (5H, m, C_9H_5N), keto:enol ratio 19:81; ^{13}C nmr (δ DMSO-d_6 70°C): 13.71 (CH_3 keto form), 14.02 (CH_3), 41.92 (CH_2 keto form), 55.62 (OCH_3), 60.88 (CH_2), 62.07 (CH_2 keto form), 103.39 (CH), 121.24 (CH), 121.55 (CH), 122.64 (CH), 123.51 (CH), 124.38 (C), 128.52 (C), 131.08 (CH), 138.39 (C), 144.01 (C), 147.38 (CH), 157.06 (C), 157.59 (C), 160.47 (C), 165.20 (C), 190.56 (C=O keto form); clearly, two forms were present, but the other signals could not be distinguished because of low solubility; m/z 273. Anal. calcd. for $C_{15}H_{15}NO_4$: C 65.9, H 4.5, N 5.1%; found: C 65.8, H 4.55, N 5.0%.

Ethyl 2-hydroxy-3-(6-methoxycarbonyl-4-quinolyl)propenoate (**8**): 20%, mp 215–216°C (from methanol); ir (KBr): 2775 (br s), 1718 (s), 1635 (m), 1602 (w), 1538 (s), 1504 (s) cm^{-1}; ^{1}H nmr (δ DMSO-d_6 20°C); 1.37 (3H, t, CH_3), 3.78 (3H, s, OCH_3), 4.39 (2H, q, CH_2), 6.73 (H, s, =CH), 7.71 (H, d), 8.08 (H, br s), 8.19 (H, dd), 8.46 (H, d), 8.69 (H, s); ^{13}C nmr (δ DMSO-d_6 70°C): 14.11 (CH_3), 51.96 (OCH_3), 61.07 (CH_2), 79.07 (CH), 165.12 (C), 165.39 (C); due to low solubility only four aromatic carbons were clearly visible at 125.39, 126.32, 130.06, and 130.50; m/z 301. Anal. calcd. for $C_{16}H_{15}NO_5$: C 63.8, H 5.0, N 4.65%; found: C 63.5, H 5.1, N 4.55%.

Ethyl 2-hydroxy-3-(6-ethoxycarbonyl-4-quinolyl)propenoate (**9**): 76%, mp 210°C (from ethanol); ir (KBr): 2657 (br s), 1723 (s), 1639 (m), 1500 (vs), 1470 (vs) cm^{-1}; ^{1}H nmr (δ DMSO-d_6): 1.31 (3H, t, CH_3), 1.38 (3H, t, CH_3), 4.24 (2H, q, CH_2), 4.39 (2H, q, CH_2), 6.74 (H, s, =CH), 7.71 (H, d, J = 8.80), 8.07 (H, d), 8.18 (H, d, J = 8.79), 8.45 (H, d), 8.68 (H, s); ^{13}C nmr (δ DMSO-d_6): 13.98 (CH_3), 14.08 (CH_3), 60.76 (CH_2, 60.99 (CH_2), 94.39 (CH), 110.68 (CH), 121.59 (CH), 121.80 (C), 125.36 (CH), 126.08 (C), 130.26 (CH), 140.70 (CH), 142.74 (C), 147.96 (C), 148.02 (C), 165.12 (C), 170.36 (C); m/z 315. Anal. calcd. for $C_{17}H_{17}NO_5$: C 64.7, H 5.4, N 4.4%; found: C 64.3, H 5.3, N 4.0%.

Butyl 2-hydroxy-3-(4-quinolyl)propenoate (**10**): From dibutyl oxalate (13) (26.5%), mp 145°C (from ethanol); ir (KBr): 2936 (br s), 1722 (s), 1626 (m), 1591 (m), 1549 (m), 1500 (vs), 1468 (vs) cm^{-1}; ^{1}H nmr (δ $CDCl_3$): 0.93 (3H, t, CH_3), 1.44 (2H, m, CH_2), 1.76 (2H, m, CH_2), 4.31 (2H, t, OCH_2), 7.12 (s, =CH), 7.0–9.2 (m, Ar); ^{13}C nmr (δ $CDCl_3$): 13.71 (CH_3), 19.08 (CH_2), 30.51 (CH_2), 34.85 (CH_2), 42.49 (CH_2), 62.72 (CH_2), 65.77 (CH_2), 66.82 (CH_2), 99.24 (CH), 118.57 (CH), 123.60 (CH), 124.93 (CH), 127.35 (CH), 127.49 (CH), 130.04 (CH), 131.27 (CH), 152.80 (C), 163.21 (C), 165.30 (C), 169.36 (C); m/z 271. Anal. calcd. for $C_{16}H_{17}NO_3$: C 70.8, H 6.25, N 5.15%; found: C 70.5, H 6.45, N 5.15%.

1-Phenyl-2-(4-quinolyl)ethanone (**11**): By the literature method (6) (75%), mp 118–119°C (lit. (6) mp 116–117°C); ir ($CHCl_3$): 1691 (vs), 1597 (s), 1512 (s) cm^{-1}; ^{1}H nmr (δ $CDCl_3$): 4.75 (2H, s, CH_2), 7.27 (H, d, J = 4.40), 7.4–8.2 (9H, m, Ar), 8.86 (H, d, J = 4.40); ^{13}C nmr (δ $CDCl_3$): 42.14 (CH_2), 122.79 (CH), 123.62 (CH), 126.86 (CH), 127.70 (C), 128.44 (CH), 128.87 (CH), 129.31 (CH), 130.31 (CH), 133.71 (CH), 136.21 (C), 141.08 (C), 148.36 (C), 150.03 (CH), 195.98 (C); m/z 247.

1-(2-Pyridyl)-2-(4-quinolyl)ethanone (**12**): From ethyl 2-picolinate by the method for compound **11** (88%), mp 87–88°C (from petroleum ether 60–80) (lit. (8) mp 88.4–89.6°C); ir (KBr): 1702 cm^{-1} (s); ^{1}Hnmr (δ $CDCl_3$): 5.05 (CH_2), 7.4–8.3 (8H, m, Ar), 8.6–9.1 (2H, m, Ar); ^{13}C nmr (δ $CDCl_3$): 40.79 (CH_2), 122.43 (CH), 123.36 (CH), 124.16 (CH), 126.72 (CH), 127.70 (CH), 127.98 (C), 129.28 (CH), 130.01, 130.01 (CH), 137.19 (CH), 141.82 (C), 148.23 (C), 149.10 (CH), 149.91 (CH), 152.60 (C), 197.76 (C); m/z 248.

2-(1,4-Dihydro-1-methylquinilyliden-4-yl)-1-phenylethanone (**13**): Prepared by the literature method (6) (15.3%), mp 139–140°C (dec.) (lit. (6) mp 141–143°C (dec.)); ir ($CHCl_3$); 1631 (s), 1611 (w), 1597 (m), 1589 (m), 1567 (m), 1553 (m), 1520 (s), 1498 (vs), 1484 (vs), 1475 (vs) cm^{-1}; ^{1}H nmr (δ $CDCl_3$): 3.68 (3H, s, NCH_3), 6.87 (H, s, =CH), 7.0–8.6 (11H, m, Ar); ^{13}C nmr (δ $CDCl_3$): 40.65 (CH_3). 96.28 (CH), 107.42 (CH), 115.23 (CH), 123.27 (C), 123.95 (CH), 124.42 (CH), 127.32 (CH), 128.11 (CH), 130.25 (CH), 130.96 (CH), 138.88 (C), 139.29 (CH), 143.04 (C), 147.60 (C), 187.96 (C); m/z 261.

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