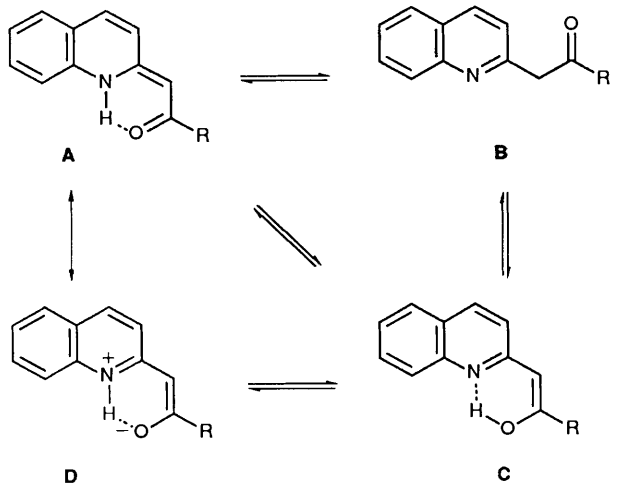
Tautomerism in Ketomethylquinolines. Part 2.[1] Further Results on 2-Ketomethylquinolines

John V. Greenhill,[a] Hossein Loghmani-Khouzani[a] and Derek J. Maitland[b,*]
[a] *Department of Pharmaceutical Chemistry;*
[b] *Chemistry and Chemical Technology, Department of Chemical Engineering; University of Bradford, Bradford BD7 1DP, UK*

A further series of 2-ketomethylquinolines has been prepared, many with α-substituents. Base-catalysed α-alkylation of unsubstituted ketomethylquinolines was successful in two instances. With excess sodium hydride and iodomethane α,*N*-dialkylation occurred. α-Bromination gave three new derivatives which were vulnerable to oxidation to 1,2-diketones. The preparation of two pyrroloquinolinones gave model compounds for the enaminone forms of the ketomethylquinolines. Examination of the compounds by IR and NMR spectroscopy has shown that compounds unsubstituted at the α-position and those carrying nitrile or ester groups strongly prefer the enaminone form in solution. The presence of a bromine atom or an alkyl group on the α-carbon gives compounds in which the major or sole tautomer is the ketone.

We have previously examined a series of 2-ketomethylquinolines and demonstrated by IR and NMR spectroscopy that 18 of the 19 compounds studied existed exclusively or predominantly as the enaminone tautomers.[1] The sole exception had a methyl group substituted at the α-position. We have now prepared further members of the series and have found that the ketone forms are favoured when there is an α-bromo or α-alkyl substituent and a bulky substituent such as Bu^t or phenyl on the γ-carbon. The investigation was stimulated by the realisation

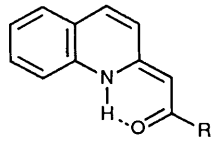


Scheme 1

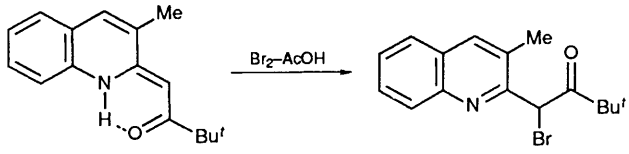
that several conflicting reports existed in the literature. Authors have assigned the enaminone structure **A**,[2,3] the enol structure **C**,[4,5] or the zwitterion structure **D**[6] to various members of the series (Scheme 1). A full discussion of the published work appears in a recent review.[7] The compounds examined in this study, most of which are new, are listed in Table 1. Some further results on two of the ketomethylquinolines described in Part 1 are also reported.

Synthesis.—The α-alkylated derivatives **8** and **12** were obtained from the parent enaminones by base-catalysed alkylations. The use of an excess of sodium hydride/iodomethane afforded the dialkyl derivatives **16** and **17**.

The reaction of 2-ketomethylquinolines with bromine in chloroform was studied in an attempt to effect α-bromination,

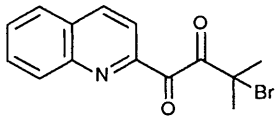


20

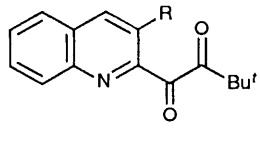


21 **10**

but this was only successful in one instance, thus **9** was obtained from **20**, R = Bu^t, in 82% yield. Similar bromination in glacial acetic acid gave compound **1**. Some experiments gave small amounts of compound **3** by bromination at the methyl group, but this material was best prepared from 2-methylquinoline and ethyl bromoacetate in the presence of lithium diisopropylamide. The *tert*-butyl ketomethylquinoline **21**[1] was readily brominated in acetic acid to give **10**, but when the acetophenone derivative **20**, R = Ph, was subjected to the same conditions, it gave a 38% yield of 1,2-bis(quinolin-2-yl)ethane;[8] the only isolated product. When the isopropyl derivative **20**, R = Pr^i was treated with bromine in glacial acetic acid it gave the bromo diketone **22**.



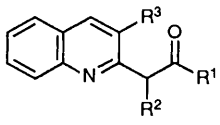
22



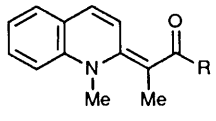
23 R = H
24 R = Me

The α-bromo derivative of **20**, R = Ph has been shown to give a comparable 1,2-diketone on warming in dimethyl sulphoxide.[9] Therefore two of the α-bromo compounds, **9** and **10**, were dissolved in dimethyl sulphoxide and allowed to stand at 45–50 °C. Under these mild conditions they were converted into the diketones **23** and **24**. Surprisingly, the latter was also obtained as the only product, when a mixture of 2,3-dimethylquinoline and phenyllithium was treated with pivalonitrile.

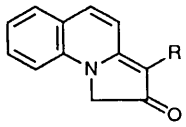
Table 1 2-Ketomethylquinolines



Compound	R^1	R^2	R^3	Ref.
1	Me	Br	H	
2	CH_2Cl	CN	H	26
3	CH_2Br	H	H	
4	CH_2I	CN	H	26
5	CF_3	H	H	
6	CCl_3	H	H	
7	Pr^i	H	Me	
8	Bu^t	Me	H	
9	Bu^t	Br	H	
10	Bu^t	Br	Me	
11	CO_2Et	H	Me	
12	Ph	CH_2Ph	H	
13	Ph	CO_2Et	H	14
14	2-Py	H	H	19
15	Ph	CN	H	28

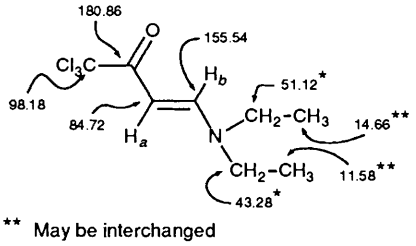


16 R = Et
17 R = Bu^t



18 R = H
19 R = CN

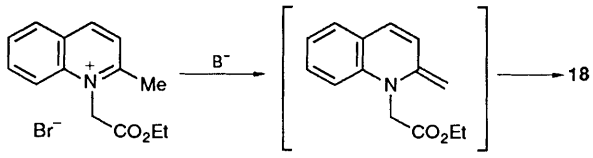
Compounds **5** and **6** were prepared by employing a reaction developed[10] for the preparation of 1-(2-pyridyl)-3,3,3-trichloropropanone. The reaction between 2-methylquinoline, and trichloroacetic anhydride in the presence of triethylamine gave the required ketomethylquinoline (38%), plus the enaminone **25**. The IR spectrum showed bands at ν/cm^{-1}



1660 (s, C=O) and 1560 (vs, C=C). The ^1H NMR spectrum had two doublets (J 12.4 Hz) at δ 5.65 and 7.81 for the *trans* olefinic protons H_a and H_b respectively. There were separate sets of signals for the two *N*-ethyl groups, triplets at δ 1.25 and 1.29 and quartets at δ 3.34 and 3.41. Similarly, the ^{13}C NMR spectrum had 4 distinct resonances for the two ethyl groups—further evidence for the partial double bond character of the CH–N bond, as expected for an enaminone.[11] A possible mechanism for the formation of this product is shown in Scheme 2. A search of the literature revealed that this compound had been prepared previously by two methods. Giger *et al.*[12] allowed trichloroacetyl chloride to react with triethylamine to obtain compound **25** in 69% yield, whereas Talley[13] obtained the latter from hexachloroacetone and triethylamine.

Treatment of 2,3-dimethylquinoline, with sodium hydride and methyl isobutyrate gave the enaminone **7**, whilst with diethyl oxalate and potassium ethoxide the enaminone ester **11** was formed. The enaminone **13** was prepared from quinoline 1-oxide, acetic anhydride and ethyl benzoylacetate, whereas reaction with benzoylacetonitrile gave compound **15**. Compounds **2**, **4** and **14** were prepared by literature methods.

In the hope of obtaining ketomethylquinolines fixed in the enaminone forms for comparison with the above compounds, the syntheses of the pyrroloquinolones **18** and **19** were undertaken. Babichev *et al.*[14] had shown that the chloromethyl compound **2** could be cyclised to the pyrroloquinolone **19** by heating in high boiling solvents such as chlorobenzene. During the present work it was discovered that the iodomethyl derivative **4** with sodium hydride in refluxing THF (tetrahydrofuran) gave **19** in high yield. Three approaches to the unknown pyrroloquinolone **18** were investigated. Hydrolysis of the nitrile **19** by prolonged reflux in concentrated hydrochloric acid gave the acid which spontaneously decarboxylated to the required product, but only in 23% yield. Several attempts were made to convert the quaternary salt **26** *via* the enamino ester **27** into **18**. A best yield of 16% was obtained with sodium hydroxide in ethanol. Finally, the bromomethyl compound **3** gave a good yield (85%) of the pyrroloquinolone **18** on refluxing in chlorobenzene.



26 **27**

Discussion

Tautomerism involves ionisation to and from carbon and such reactions can be quite slow; particularly in the absence of a catalyst and in non-polar solvents. As a consequence quite different tautomer ratios can sometimes be observed, depending on whether the sample has been freshly prepared from a crystalline solid, or has been allowed to stand and reach equilibrium. In order to minimise such effects, normally samples were prepared for NMR spectroscopy and then left for at least 6 h before the spectra were recorded. Usually the ^1H NMR spectrum was recorded, then the ^{13}C NMR spectra were acquired overnight, and the ^1H NMR spectrum recorded again to check for any changes in tautomer composition. Normally no change in composition was observed.

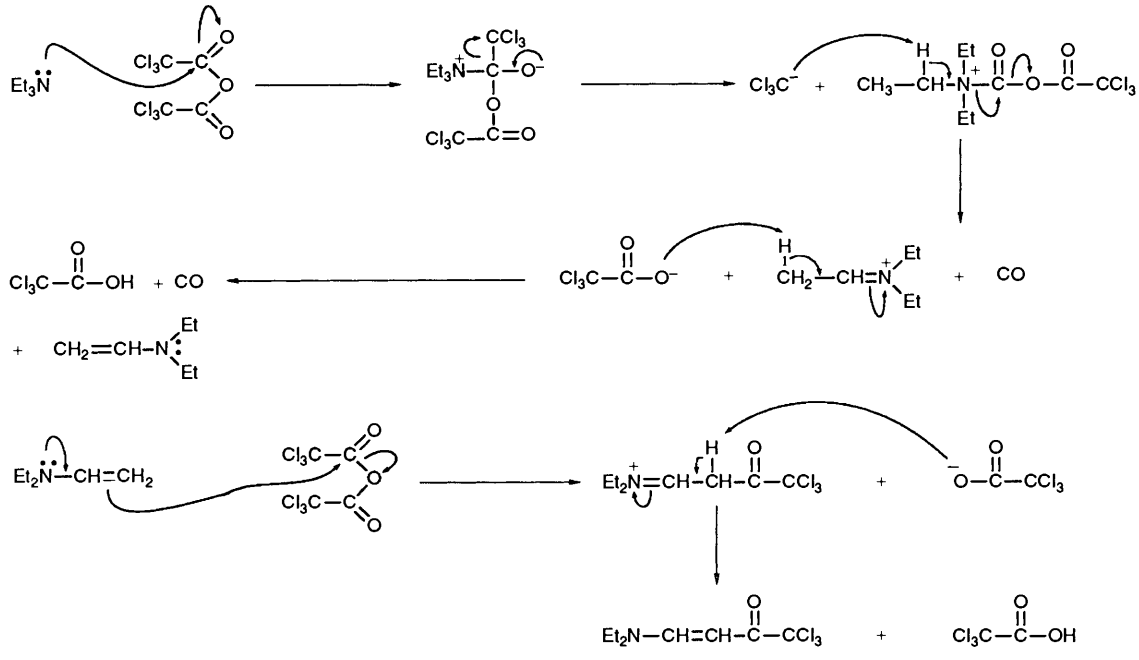
As with the earlier work,[1] several of the compounds listed in Table 1, namely **2**, **3**, **4**, **5**, **6**, **11**, **13**, **14** and **15** were found to exist exclusively in their enaminone forms. They showed typical enaminone IR spectra with strong bands in the ν/cm^{-1} 1630–1640 (C=O) and 1530–1580 (C=C) regions. There was also in each case a strong aromatic ring breathing band in the ν/cm^{-1} 1590–1600 region. The details are given Table 2. The significant ^1H NMR spectroscopic data and the tautomeric ratios derived from them are shown in Table 3 and relevant ^{13}C NMR spectroscopic data are given in Table 4.

The ^1H and ^{13}C NMR spectra of each of these compounds showed single sets of signals which were consistent with the enaminone form **A**. The ^1H NMR spectra of compounds **3**, **5**, **6**, **11** and **14**, each had vinyl signals that integrated to one proton (see Table 3) and no trace of any methylene signals. All compounds in the enaminone form **A** exhibited NH resonances in the range δ 14.8–16.8 due to the strong intramolecular hydrogen bonding between the NH proton and the carbonyl oxygen. With the exception of **13** these compounds have $J_{3,4}$ coupling constants of 9.2 Hz, which confirmed a heterocyclic ring system similar to 2(1*H*)-quinolone for which we have determined a $J_{3,4}$ of 9.4 Hz. Compounds in the ketone form **B** typically showed $J_{3,4}$ values of 8.4–8.6 Hz, which suggested a heterocyclic ring system analogous to quinoline for which a $J_{3,4}$ value of 8.2 Hz (CCl_4) has been reported.[15] Thus, as has been

Table 2 IR spectroscopic bands for the ν/cm^{-1} 1800–1500 region[a]

Compound	C=O	C=O/C=C	Ar	C=C/C=O	Other
1	1720(s)	1628(vs)	1596(s)	1529(s)	1506(m)
2		1632(vs)	1597(s)	1593(s)	1527(m)
3		1635(vs)	1591(s)	1561(vs)	
4		1633(vs)	1593(s)	1582(s)	1525(m)
5		1636(s)	1593(vs)	1581(vs)	
6		1635(vs)	1592(s)	1576(vs)	
7		1639(s)	1593(s)	1560(vs)	
8	1703(vs)	1620(vw)	1600(m)	1567(vw)	1506(m)
9	1713(s)	1620(vw)	1596(m)	1564(vw)	1505(m)
10	1725(s)		1601(w)	1566(w)	
11		1636(vs)	1595(s)	1575(vs)	COOEt 1723(s)
12	1682(s)	1620(w)	1598(s)	1582(w)	1566(w)
					1505(m)
13		1630(vs)	1590(s)	1544(s)	COOEt 1683(s)
					1517(s)
14		1632(s)	1588(m)	1555(vs)	1574(m)
15		1632(vs)	1589(s)	1553(m)	1521(s)
16	1708(vs)	1618(w)	1600(s)	1560(w)	
17	1693(s)	1618(w)	1595(m)	1559(w)	
18		1651(s)	1605(s)	1561(s)	1542(s)
19		1668(s)	1611(vs)	1567(s)	1536(vs)

[a] Figures are reported for chloroform solutions except for the insoluble compounds **7**, **16** and **19** which were run as potassium bromide discs.



Scheme 2 Possible mechanistic pathway to (*E*)-1,1,1-trichloro-4-(*N*,*N*-diethylamino)but-3-en-2-one **25**

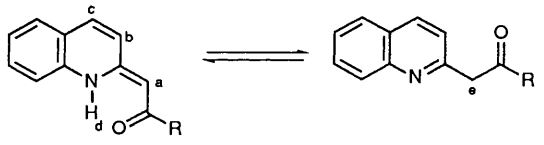
reported previously,[16] the values of $J_{3,4}$ can be correlated with the structure of the dominant tautomer, the larger $J_{3,4}$ value for compounds in the **A** form reflecting the increased bond fixation.

Inspection of the ^{13}C chemical shifts given in Table 4 reveals that except for compound **7** enaminone carbonyl resonances are found generally in the region δ 172–194, those of C-2 (c) at δ 150–156, those of C-9 at δ 135–139 except compound **13**, and those of C-10 between δ 122 and 124; except compound **11**. The different values for compounds **7** and **11** possibly reflect the hyperconjugative and steric effects of the methyl group on C-3, and for compound **13** the electron withdrawing effect of the ethoxycarbonyl group.

Four compounds, **8**, **9**, **10** and **12**, all carrying alkyl groups or bromine atoms at the α-positions, proved to be exclusively in the ketone forms. They had strong IR stretching bands within the range of typical ketone carbonyl groups.

The ^{13}C NMR spectra of these compounds exhibited signals in the range δ_C 198–216, typical of unconjugated ketone carbonyl carbon atoms, and showed only signals for single tautomeric forms. Resonances associated with C-2 (f) were found at δ 155–162, those of C-9 at δ 146–148, and those of C-10 between δ 127–128. There is a strong correlation between the values of these and the corresponding resonances of 2-methylquinoline, which occur[17] at δ 158.9, 147.9 and 126.5 respectively. Thus it would appear that the resonance frequencies of the carbon atoms at C-2, C-9, C-10 and those of the carbonyl groups generally reflect the structure of the tautomer. The resonance position of C-9 appears to be a particularly good indicator of structure; with the exceptions of compounds **13** and **17**, δ 135–139 for the enaminone form **A** and δ 146–148 for the keto form **B**. In the ^{1}H NMR spectrum, compound **8** showed the expected quartet for the methine proton at δ 4.76 and only had signals for the ketone form.

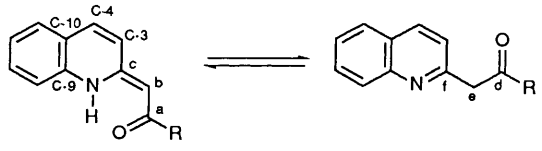
Table 3 ^{1}H NMR spectroscopic data ($CDCl_3$; 270 MHz)



A B

Compound	δ_H a	b	c	d	e	Ratio A:B	J/Hz$_{3,4}$
1	(Br)	7.66	8.21	16.29	5.74	34:66	8.4
2	(CN)	7.46	8.16	15.65		100:0	9.2
3	5.62	6.77	7.69	15.15		100:0	9.2
4	(CN)	7.47	8.14	15.75		100:0	9.2
5	5.79	6.96	7.91	15.29		100:0	9.2
6	6.17	6.98	7.85	14.84		100:0	9.2
7	5.37	(Me)	7.45	15.59	4.21	95:5	
8	(Me)	7.51	8.10		4.76	0:100	8.6
9	(Br)	7.90	8.19		6.16	0:100	8.6
10	(Br)	(Me)	7.99		6.32	0:100	
11	6.40	(Me)	7.74	16.40		100:0	
12	($PhCH_2$)	7.43	8.06		5.39	0:100	8.4
13	(CO_2Et)	7.96	8.14	16.85		100:0	9.5
14	6.82	6.97	7.68	15.73		100:0	9.2
15	(CN)	7.61	8.13	16.54		100:0	9.2
16	(Me)	7.13	8.07	(Me)		100:0	9.0
17	(Me)	7.71	8.16	(Me)		100:0	8.5
18	5.18	6.87	7.45	(CH_2)		100:0	9.2
19	(CN)	7.32	7.97	(CH_2)		100:0	9.2

Table 4 ^{13}C NMR spectroscopic data ($CDCl_3$; 67.8 MHz)



Compound	δ_C a	b	c	d	e	f	C-3	C-4	C-9	C-10
1				199.29	56.23	155.28	121.18	137.41	147.10	127.47
1	189.39	87.84	150.81				118.22	137.71	137.32	122.65
2	188.36	77.05	154.65				118.38	140.64	135.73	123.74
3	184.75	90.46	153.94				117.86	137.05	136.95	123.24
4	190.46	76.23	154.86				118.48	140.41	135.80	123.74
5	173.59	86.84	155.14				118.12	138.70	136.24	123.79
6	179.34	84.01	155.06				117.81	138.09	136.24	123.54
7	200.17	86.70	153.54				116.83	134.37	136.32	122.45
8				215.69	50.19	161.23	119.44	136.75	147.69	127.03
9				207.06	49.04	156.11	121.51	137.17	147.04	127.31
10				204.32	55.00	155.74	128.82[a]	137.87	146.15	128.08[a]
11	172.16	89.09	155.22				123.90	136.52	135.91	128.93
12				198.31	59.18	159.02	120.13	136.92	148.10	127.00
13	193.22	97.83	154.27				118.48	138.14	143.77	123.36
14	181.54	89.93	154.72				118.32	136.89	137.74	123.55
15	191.65	77.56	155.87				118.51	139.87[a]	139.18[a]	123.73
17	213.94	88.72	162.70				117.99	136.73	146.90	127.28
18	193.15	94.61	165.60				112.77	136.90	138.14	121.76
19	188.25	80.01	164.54				114.21	140.56	137.11	122.87

[a] Assignments within a row may be interchanged.

The benzyl substituted ketomethylquinoline **12** showed an ABX system associated with the chiral carbon atom. Groups of four signals were present at δ 3.32, 3.71 and 5.39 representing the two methylene protons and the methine proton respectively. Each doublet of doublets integrated for one proton. There was no sign of a methylene singlet to indicate the contribution of an enaminone form. For compounds **9** and **10** the methine signals were shifted downfield to δ 6.16 and 6.32 respectively due to influence of the bromine atoms, but each singlet integrated for one proton. Again, only the expected signals for the ketone forms were present. In quinolines 3-H is usually the most upfield signal about δ 7.0–7.2. Interestingly in compounds **1**,

8, **9** and **12**, which are in the **B** form, the 3-H protons are shifted downfield to between δ 7.4–7.9; the effect is most marked for compound **9**. This suggests that 3-H in these compounds must experience significant anisotropic deshielding by the carbonyl group. Therefore the preferred conformation, when there is a large group on C-1, must have the carbonyl oxygen adjacent to 3-H as depicted in Table 3. The IR spectra of compounds **8**, **9**, **10** and **12** (Table 2) showed weak or very weak bands in the two ranges normally associated with the enaminone bands. These may represent very small contributions from enaminone forms. Notwithstanding, careful re-examination of the 270 MHz ^{1}H NMR spectra, which had noiseless baselines, failed to reveal any enaminone signals. Any such contribution would certainly be less than 1%. Because of the very high IR extinction coefficients observed for enaminones[1,18] it is possible that these spectra would be more sensitive to very low concentrations of the enaminone forms than the ^{1}H NMR spectra.

Compound **1** clearly showed absorption bands for both enaminone and ketone forms in all spectra. In deuteriochloroform solution a tautomeric ratio of 34:66 was determined by comparing the integral for the methine absorption at δ 5.74 with the total aromatic integral and with the total methyl integral. The result (±2%) was an average of the two calculations. The only other ketomethylquinoline in this series to show a mixture of forms was compound **7**, which gave a set of ^{1}H NMR signals for each tautomer. The 95:5 tautomeric ratio was readily calculated from the integrals of the vinyl and methylene protons, and confirmed by the ratio of the methyl signals at δ 2.21 and 2.40. It is interesting that here no trace of the ketone carbonyl absorption (a weaker band than enaminone absorptions[1,11,18]) could be seen in the IR spectrum.

Compound **20** (R = Bu^t) has previously been shown[1] to exist as a tautomeric mixture in both deuteriochloroform and [$^2H_8$]dioxane. Since this compound was one of the most soluble of the compounds studied, it proved possible to obtain natural abundance ^{15}N NMR spectra on 50% w/v solutions. In order to obtain quantitative results, the spectra were acquired with a tip angle of 31° with NOE effects suppressed, and a long pulse delay to ensure complete relaxation of the different N-atoms present. In deuteriochloroform there was a strong signal at δ_N 148.13 and a weak one at δ_N 305.81 assigned to the sp^3 nitrogen of the enaminone form and the sp^2 nitrogen of the ketone form respectively.[20] In [$^2H_8$]dioxane similar signals were seen at δ_N 166.90 and 310.41. For comparison the ^{15}N NMR spectrum of 2-methylquinoline was run in deuteriochloroform and gave one signal at δ_N 301.19. A comparison of the intensities of the ^{15}N NMR signals of compound **20** (R = Bu^t) indicated a tautomeric ratio (enaminone:ketone) in deuteriochloroform of 84:16 (the ratio from the ^{1}H NMR spectrum[1] was 88:12). In [$^2H_8$]dioxane the ^{15}N NMR spectrum indicated a tautomeric ratio of 82:18. This led us to re-examine our ^{1}H NMR spectrum from which we had previously[1] derived a tautomeric ratio of 55:45 in this solvent. On re-running the spectrum in [$^2H_8$]dioxane a ratio of 84:16 was obtained, which suggested that our earlier measurement was subject to an instrumental error. ^{13}C NMR spectra of compound **20** (R = Bu^t) were also acquired with long pulse delays and NOE effects suppressed, and from these tautomeric ratios of 89:11 in deuteriochloroform and 86:14 in [$^2H_8$]dioxane were calculated. Thus, the true enaminone:ketone ratio for compound **20** (R = Bu^t) in [$^2H_8$]dioxane is 84:16 with an error of ±2%.

The pyruvic ester **28** was found to exist in chloroform exclusively in the enaminone form.[1] A single absorption in the ^{15}N NMR spectrum at δ_N 167.36 ($CDCl_3$), indicative of sp^3 hybridised nitrogen, provided further evidence against the enol form previously claimed.[3,4] An interesting change occurred when the protonated derivative was examined in a 2:1 TFA–[$^2H_6$]DMSO mixture. The relevant data are summarised in Table 5.

It was clear from the ^{1}H and ^{13}C NMR spectra that compound **28** had fully protonated in the mixed solvent and that it existed as the single tautomeric form **29**. In the ^{1}H NMR spectrum the aromatic signals moved from δ 7.2–7.9 in deuteriochloroform to δ 8.0–9.0 in TFA–[$^2H_6$]-DMSO. In the ^{13}C NMR spectrum the aromatic carbon signals also experienced downfield shifts in the mixed solvent. The most significant difference between the spectra of the free base **28** and the protonated form **29** was the loss of the quaternary carbon signal from the enaminone carbonyl group of structure **28**. The compound would be expected to protonate at the α-carbon atom as is normal for enamines. However, the signal at δ 6.95 in TFA–[$^2H_6$]-DMSO integrated for one proton and there was no signal assignable to a methylene group. Clearly the protonation had been followed by keto–enol tautomerism to give structure **29**, where the enol is stabilised by hydrogen bonding. This hypothesis was substantiated, when the ^{1}H and ^{13}C NMR spectra of compound **28** in [$^1H_2$]-TFA were examined. The pertinent data are given in Table 5. The spectra showed that the molecule was in the 'protonated' form **29** and that the proton (H-b) had been replaced by deuterium. The signal for H-b at δ 7.05 only integrated for 5% of one proton and in the ^{13}C NMR the signal for C-b appeared as a very small triplet at δ 102.63. This provided an interesting parallel with the behaviour of 3-(quinolin-4-yl)pyruvates which is discussed[21] in Part 3.

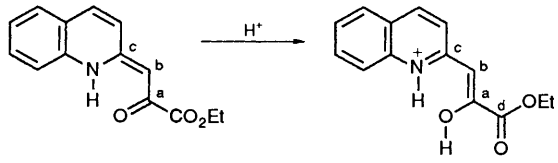
The ^{15}N NMR chemical shifts for quinoline in carbon tetrachloride, methanol and sulphuric acid have been reported[22] at δ_N 288.5, 273.7 and 159.4 respectively. The ^{15}N NMR spectrum of structure **29** in TFA–[$^2H_6$]-DMSO showed one signal at δ_N 174.65 confirming protonation of the nitrogen.

The IR spectra of the α,*N*-dimethylated derivatives **16** and **17** were characterised by strong carbonyl bands at ν/cm^{-1} 1708 and 1698 respectively. The longest wavelength absorption in the UV spectrum (EtOH) of compound **16** was 317 nm (ε 3650) and of compound **17** at 317 nm (ε 3750). These are very close to 2-methylquinoline, 314 nm (ε 4800). Clearly, steric hindrance in these molecules prevents planarity in the enaminone systems and essentially unconjugated ketone bands are seen. The extreme low solubility of compound **16** made ^{13}C NMR spectroscopy impossible, but compound **17** gave a spectrum showing two sets of signals. The carbonyl carbon signals (δ_C 213.94 and 216.61) were both in the lowfield region occupied by unconjugated ketones, suggesting the presence of two geometrical isomers.

The pyrroloquinolones **18** and **19** were prepared in the hope of obtaining fixed enaminone forms for comparison by IR and UV spectroscopy with the previous compounds, although it was recognised that keto–enol tautomerism was a possibility. It was also realised that the comparison would not be ideal since the acyclic ketomethylquinolines in the enaminone tautomers adopt a *cis*-s-*cis* conformation while these are fixed as the *cis*-s-*trans* forms. For compound **18** the ^{1}H NMR spectrum was clean for a single form with the 2 proton methylene signal at δ 4.26 and the one proton vinyl signal at δ 5.18. The ^{13}C NMR spectrum also showed only signals for the enaminone form as shown (see Table 4 and Experimental section). In the IR spectrum the frequency of the carbonyl band was increased to ν/cm^{-1} 1651. This was a consequence of its presence in a five membered ring and of the *cis*-s-*trans* form. Compound **19** was similar with the carbonyl band at ν/cm^{-1} 1688 and the methylene group proton signal at δ 4.57 indicative of the enaminone form.

Conclusions.—It has long been recognized that the mesomeric

Table 5 Selected ^1H and ^{13}C NMR chemical shifts (δ relative to Me_4Si) for ethyl 3-(quinolin-2-yl)pyruvate



28 **29**

Compound	δ_H b	δ_C a	b	c	d
28 ($CDCl_3$)	7.05	170.42	93.59	155.13	164.47
29 (TFA-[$^2H_6$]-DMSO)	6.95	152.31[a]	100.68	154.05[a]	163.70
29 ([$^2H_1$]-TFA)	7.05[b]	152.04[a]	102.63[b]	152.74[a]	165.68

[a] May be interchanged. [b] Very low intensity signal.

effect in enaminones is very strong and is the main stabilising mechanism of the system.[11] Unusually high relative permittivities have been measured for some members of the group.[23] This is supported by the present investigation where the enaminone system **A**, stabilised by the mesomer **D** and to a lesser extent by hydrogen bonding, is thermodynamically more stable than the aromatic forms **B** and **C**. As suggested in Part 1,[1] large groups at R^1 interact with α-substituents at R^2 to destabilize the enaminone. Where the group R^1 is small as in compound **1**; forms **A** and **B** coexist. It is interesting that large groups such as Pr^i, or Bu^t at R^1 in conjunction with a methyl group at R^3 exert pressure against a proton at R^2 to slightly destabilise form **A** (compounds **7** and **21**).[1] Six examples, four described in this paper and two in Part 1, which have nitrile or ester groups at R^2 exist exclusively in the enaminone form. It has been well demonstrated[24] that such molecules with one electron donor (N) and two electron receivers (CO, CN) suffer very strong electron movements through the whole system. This is clearly enough to stabilise these enaminones in spite of the steric interactions. It seems likely that the stability difference between the enaminone forms **A** and the ketone forms **B** is not great and that the substituent groups can tip the balance of the tautomeric ratio either way.

Experimental

IR spectra were run on Perkin-Elmer 1700-X and 1720-X FTIR spectrophotometers. UV spectra were obtained with a Perkin-Elmer Lambda 5 UV-VIS spectrophotometer. 270 MHz ^1H and 67.8 MHz ^{13}C NMR spectra (^1H broad band decoupled and DEPT 135) spectra were run ($CDCl_3$ solutions, unless specified otherwise, with Me_4Si as internal standard) on a JEOL GX 270 spectrometer fitted with a 5 mm C/H probe; unless specified otherwise. ^{15}N NMR spectra were obtained on the same instrument at 27.25 MHz using a tunable high sensitivity 10 mm probe in SGNNE mode (single pulse, no nuclear overhauser enhancement), tip angle 31° (8 μs), pulse delay 22 s. Spectra were referenced to external nitromethane (380.2 ppm relative to NH_3) in a co-axial 2 mm tube. All J values are given in Hz. Mass spectra (EI) were determind on an AEI MS 902 spectrometer. Chromatography columns were prepared from Aldrich silica gel 70-230 mesh.

1-Bromo-1-(quinolin-2-yl)propan-2-one **1**.—A solution of bromine (0.80 g, 5 mmol) in glacial acetic acid (10 cm^3) was added to a stirred solution of 1-(1,2-dihydroquinolin-2-ylidene)propan-2-one[25] (0.93 g, 5 mmol) in glacial acetic acid (50 cm^3) over 2 h at room temperature. Stirring was continued for 1 h and the product poured into a mixture of ice and saturated aqueous sodium acetate (50 g). The mixture was cooled in the refrigerator for 2 h and the product collected and washed with water to give the *ketone* (1.19 g, 90%), m.p. 70–71 °C [from light petroleum (b.p. 80–100 °C)] (Found: C, 54.5; H, 3.95; Br, 29.8; N, 5.4. $C_{12}H_{10}BrNO$ requires C, 54.4; H, 3.75; Br, 30.2; N, 5.3%); m/z 265 (M^+ + 2, 23%), 263 (M^+, 28), 223 (87), 221 (100), 184 (45) and 141 (28); δ_H 2.48 (1.98 H, s, Me), 2.49 (1.02 H, s, Me), 5.74 (0.66 H, s, CHBr), 7.29 (0.34 H, ddd, J 8.1, 7.0 and 1.1), 7.42–7.62 (2 H, m), 7.66 (0.66 H, d, $J_{3,4}$ 8.4, 3-H), 7.74 (0.66 H, ddd, J 8.4, 7.0 and 1.5), 7.82 (1 H, t), 8.06 (0.66 H, d, J 8.1), 8.21 (0.66 H, d, $J_{3,4}$ 8.4, 4-H) and 16.28 (0.34 H, s, NH); δ_C(keto form) 27.49 (Me), 56.23 (CH), 121.18 (CH), 127.47 (C), 127.48 (CH), 127.59 (CH), 129.34 (CH), 130.10 (CH), 137.41 (CH), 147.17 (C), 155.28 (C) and 199.29 (C), δ_C(enaminone form) 28.90 (Me), 87.84 (C), 118.22 (CH), 120.71 (CH), 122.65 (C), 124.08 (CH), 127.65 (CH), 131.48 (CH), 137.32 (C), 137.71 (CH), 150.81 (C) and 189.39 (C).

Similarly was prepared: *1-Bromo-3,3-dimethyl-1-(3-methylquinolin-2-yl)butan-2-one* **10** (77%), m.p. 135 °C (from aq. EtOH) (Found: C, 60.0; H, 5.9; Br, 24.8; N, 4.2. $C_{16}H_{18}BrNO$ requires C, 60.0; H, 5.6; Br, 25.0; N, 4.4%); m/z 321 (M^+ + 2, 0.5%), 319 (M^+, 0.4), 240 (13), 184 (38), 156 (31) and 57 (100); δ_H 1.09 (9 H, s, CMe_3), 2.65 (3 H, d, J 0.7, 3-Me), 6.32 (1 H, s, CBrH), 7.52 (1 H, ddd, J 8.1, 7.0 and 1.1), 7.64 (1 H, ddd, J 8.1, 7.0 and 1.1), 7.74 (1 H, dd, J 8.1 and 1.1), 7.99 (1 H, s, 4-H) and 8.00 (1 H, dd, J 8.1 and 1.1); δ_C 18.90 (Me), 27.46 (3 × Me), 44.03 (C), 55.0 (CH), 126.63 (CH), 127.44 (CH), 128.08 (C), 128.82 (C), 129.07 (CH), 129.56 (CH), 137.87 (CH), 146.15 (C), 155.74 (C) and 204.32 (C)

1,2-Bis(quinolin-2-yl)ethane. When the same procedure was applied to 2-(1,2-dihydroquinolin-2-ylidene)-1-phenylethan-1-one it gave as the only isolated product 1,2-bis(quinolin-2-yl)ethane (38%), m.p. 165 °C (from MeOH) (lit.,[8] m.p. 162–163 °C) (Found: C, 83.9; H, 5.6; N, 9.9. Calc. for $C_{20}H_{16}N_2$: C, 84.2; H, 5.3; N, 9.85%); m/z 284; ν_{max}(KBr)/cm^{-1} 1610, 1595 and 1540; δ_H 3.54 (4 H, s, CH_2CH_2), 7.5–8.1 (12 H, m, 2 × C_9H_6N); δ_C 38.68 (CH_2), 121.67 (CH), 125.76 (CH), 126.79 (C), 127.50 (CH), 128.82 (CH), 129.34 (CH), 136.22 (CH), 147.93 (C) and 161.61 (C).

3-Bromo-3-methyl-1-(quinolin-2-yl)butane-1,2-dione **22**. When the same procedure was applied to 1-(1,2-dihydroquinolin-2-ylidene)-3-methylbutan-2-one the product did not precipitate on pouring into water. The aqueous solution was extracted with dichloromethane (2 × 30 cm^3) and the organic solution dried, filtered and evaporated. The crude residue was chromatographed through a silica gel column to give from the first fraction the *bromo dione* (20%), m.p. 65–67 °C [from light petroleum (b.p. 60–80 °C)] (Found: C, 54.7; H, 3.95; N, 4.8. $C_{14}H_{12}BrNO_2$ requires C, 54.9; H, 3.9; N, 4.55%); m/z 226

(M^+ − Br, 53%), 156 (38), 129 (67) and 128 (100); ν_{max}(KBr)/cm^{-1} 1715, 1698, 1616 and 1585; δ_H(60 MHz) 2.0 (6 H, s, 2 × Me) and 7.1–8.4 (6 H, m, C_9H_6N).

1-*Chloro*-3-*cyano*-3-(1,2-*dihydroquinolin*-2-*ylidene*)*propan*-2-*one* **2**.—A mixture of 2-cyanomethylquinoline (1.68 g, 10 mmol) and chloroacetic anhydride (1.88 g, 11 mmol) was refluxed in toluene (35 cm^3) for 1 h. After cooling, diethyl ether (70 cm^3) was added and the resulting precipitate was chromatographed through a silica column. Elution with chloroform gave the enaminone (2 g, 82%), m.p. 196–198 °C (from toluene) (lit.,[26] 196–197 °C), *m/z* 244 (M^+, 27%); δ_H 4.54 (2 H, s, CH_2Cl), 7.46 (1 H, dd, *J* 9.2 and 1.5, 3-H), 7.53 (1 H, ddd, *J* 8.1, 7.0 and 1.1), 7.62 (1 H, dd, *J* 8.1 and 1.1), 7.73–7.80 (2 H, m), 8.16 (1 H, d, $J_{3,4}$ 9.2, 4-H) and 15.65 (1 H, s, NH); δ_C 46.41 (CH_2), 77.05 (C), 118.38 (CH), 118.76 (CH), 118.84 (CH), 123.74 (C), 126.35 (CH), 128.36 (CH), 132.88 (CH), 135.73 (C), 140.64 (CH), 154.65 (C) and 188.36 (C).

1-*Bromo*-3-(1,2-*dihydroquinolin*-2-*ylidene*)*propan*-2-*one* **3**.—A solution of lithium diisopropylamide (1.5 mol dm^{-3} solution in cyclohexane; 6.7 cm^3, 10 mmol) was added to a solution of 2-methylquinoline (1.43 g, 10 mmol) in dry THF (tetrahydrofuran) at −78 °C. Ethyl bromoacetate (1.72 g, 10 mmol) in THF (20 cm^3) was added over 10 min and stirring at −78 °C was continued for a further 20 min. The mixture was allowed to warm to room temperature and stirred for a further 2 h. The product was poured into water, extracted with dichloromethane and the extract dried ($MgSO_4$) and evaporated under reduced pressure at room temperature. The crude residue was chromatographed through a silica column eluted with chloroform. The first fraction was the *enaminone* (2.2 g, 83%), m.p. 60 °C [from light petroleum (b.p. 60–80 °C)] (Found: C, 54.6; H, 4.0; Br, 29.8; N, 5.2. $C_{12}H_{10}BrNO$ requires: C, 54.3; H, 3.75; Br, 30.2; N, 5.3%); *m/z* 265 (M^+ + 2, 17%), 263 (M^+, 19), 170 (100), 156 (19), 143 (95), 142 (62), 128 (18) and 115 (35); δ_H 3.96 (2 H, s, CH_2Br), 5.62 (1 H, s, =CHCO), 6.77 (1 H, d, $J_{3,4}$ 9.2, 3-H), 7.28 (1 H, ddd, *J* 8.8, 7.0 and 1.1), 7.40 (1 H, d, *J* 8.8), 7.51–7.57 (2 H, m), 7.69 (1 H, d, $J_{3,4}$ 9.2, 4-H) and 15.15 (1 H, s, NH); δ_C 34.53 (CH_2), 90.46 (CH), 117.86 (CH), 121.53 (CH), 123.24 (C), 124.17 (CH), 127.68 (CH), 131.29 (CH), 136.95 (C), 137.05 (CH), 153.94 (C) and 184.75 (C).

3-*Cyano*-3-(1,2-*dihydroquinolin*-2-*ylidene*)-1-*iodopropan*-2-*one* **4**.—A solution of sodium iodide (0.57 g, 3.8 mmol) in dry acetone (5 cm^3) was added to a warm solution of compound **2** (0.61 g, 2.5 mmol) in dry acetone (40 cm^3), the mixture refluxed for 10 min and allowed to stand overnight. The resultant precipitate was washed with ether, cold acetone, and recrystallised from toluene to give the enaminone (77%) m.p. 200–201 °C (lit.,[26] m.p. 202–203 °C); *m/z* 336 (M^+, 9%), 210 (24), 208 (100) and 195 (58); δ_H 4.27 (2 H, s, CH_2I), 7.47 (1 H, dd, *J* 9.2 and 1.5, 3-H), 7.49–7.55 (1 H, m), 7.63 (1 H, d, *J* 8.1), 7.72–7.79 (2 H, m), 8.14, (1 H, d, $J_{3,4}$ 9.2, 4-H) and 15.75 (1 H, s, NH); δ_C 4.35 (CH_2), 76.23 (C), 118.48 (CH), 118.93 (CH), 119.31 (C), 123.74 (C), 126.26 (CH), 128.33 (CH), 132.77 (CH), 135.80 (C), 140.42 (CH), 154.86 (C) and 190.46 (C).

3-(1,2-*Dihydroquinolin*-2-*ylidene*)-1,1,1-*trifluoropropan*-2-*one* **5**.—A solution of trifluoroacetic anhydride (12.6 g, 60 mmol) in benzene (10 cm^3) was carefully added to a solution of triethylamine (10 g, 100 mmol) and 2-methylquinoline (4.3 g, 30 mmol) in benzene (40 cm^3) under nitrogen. The mixture was stirred at room temperature for 3 days and the solvent evaporated. The residue was extracted with hot light petroleum (b.p. 60–80 °C), the solvent evaporated and the product chromatographed *via* a silica column eluted with chloroform to give the *enaminone* (4.9 g, 68%), m.p. 125–126 °C [from light petroleum (b.p. 60–80 °C)] (Found: C, 60.0; H, 3.55; F, 24.2; N, 5.8. $C_{12}H_8F_3NO$ requires C, 60.2; H, 3.35; F, 23.85; N, 5.9%); *m/z* 240 (M^+ + 1, 13%) and 239 (M^+, 71); δ_H 5.79 (1 H, s, =CHCO), 6.96 (1 H, d, $J_{3,4}$ 9.2, 3-H), 7.42 (1 H, ddd, *J* 8.5, 6.9 and 1.1), 7.54 (1 H, d, *J* 8.5), 7.63–7.69 (2 H, m), 7.91 (1 H, d, $J_{3,4}$ 9.2, 4-H) and 15.29 (1 H, s, NH); δ_C 86.84 (CH), 118.12 (CH), 118.19 (1 C, q, J_{C-F} 286.2, C-1), 121.46 (CH), 123.79 (C), 125.38 (CH), 128.04 (CH), 132.11 (CH), 136.24 (C), 138.70 (CH), 155.14 (C) and 173.59 (1 C, q, J_{C-C-F} 33.3, C-2).

1,1,1-*Trichloro*-3-(1,2-*dihydroquinolin*-2-*ylidene*)*propan*-2-*one* **6**. This compound was prepared by the above method. The silica gel column was eluted with dichloromethane, the first fraction collected, the solvent evaporated and the residue dried in the dark without heat to give the *enaminone* (11%), m.p. 91–92 °C [from light petroleum (b.p. 60–80 °C)] (Found: C, 50.1; H, 2.9; Cl, 36.9; N, 4.6. $C_{12}H_8Cl_3NO$ requires C, 49.9; H, 2.8; Cl, 36.9; N, 4.85%); δ_H 6.17 (1 H, s, =CHCO), 6.99 (1 H, d, $J_{3,4}$ 9.2, 3-H), 7.39 (1 H, ddd, *J* 8.4, 6.9 and 1.1), 7.48 (1 H, d, *J* 8.4), 7.60–7.66 (2 H, m), 7.85 (1 H, d, $J_{3,4}$ 9.2, 4-H) and 14.84 (1 H, s, NH); δ_C 84.01 (CH), 96.96 (CCl_3), 117.81 (CH), 122.16 (CH), 123.54(C), 125.09 (CH), 127.97 (CH), 131.97 (CH), 136.24 (C), 138.09 (CH), 155.06 (C) and 179.34 (C). Further elution with dichloromethane gave (*E*)-1,1,1-trichloro-4-(*N*,*N*-diethylamino)but-3-en-2-one **25** (38%) m.p. 51–52 °C [from light petroleum (b.p. 40–60 °C)] (lit.,[27] 55.5–57 °C) (Found: C, 38.9; H, 4.95; Cl, 43.6; N, 5.65. Calc. for $C_8H_{12}Cl_3NO$: C, 39.3; H, 4.9; Cl, 43.6; N, 5.7%); *m/z* (M^+, 5%) and 126 (100); ν_{max}(KBr)/cm^{-1} 1660 (s), 1590 (vs) and 1560 (vs); λ_{max}(EtOH)/nm 330 (ε 52 800); δ_H 1.24 (3 H, t, *J* 7.3, Me), 1.29 (3 H, t, *J* 7.3, Me), 3.34 (2 H, q, *J* 7.3, CH_2), 3.41 (2 H, q, *J* 7.3, CH_2), 5.65 (1 H, d, *J* 12.5, 3-H) and 7.81 (1 H, d, *J* 12.5, 4-H); δ_C 11.58 (Me), 14.66 (Me), 43.28 (CH_2), 51.12 (CH_2), 84.72 (CH), 98.18 (C), 155.54 (CH) and 180.86 (C).

1-(1,2-*Dihydro*-3-*methylquinolin*-2-*ylidene*)-3-*methylbutan*-2-*one* **7**.—A solution of 2,3-dimethylquinoline (0.79 g, 5 mmol) in THF (80 cm^3) was added dropwise over 10 min to sodium hydride (50% dispersion prewashed with light petroleum; 25 mmol, 1.2 g) in THF (20 cm^3) with stirring under nitrogen. A solution of methyl isobutyrate (0.72 g, 7 mmol) in THF (20 cm^3) was added and the mixture refluxed for 48 h. The cooled solution was diluted with ether (50 cm^3) and extracted with dilute hydrochloric acid (3 × 40 cm^3). The aqueous solution was basified with solid sodium carbonate and extracted with ether (3 × 50 cm^3). The combined organic extract was dried ($MgSO_4$), filtered and the solvent evaporated. The residue was chromatographed through a silica column eluted with chloroform to give the *enaminone* (0.8 g, 70%) m.p. 72 °C (from aq. EtOH) (Found: C, 79.0; H, 7.65; N, 5.95. $C_{15}H_{17}NO$ requires C, 79.3; H, 7.5; N, 6.15%); *m/z* 227 (M^+, 40%), 184 (79), 157 (100) and 43 (33); δ_H 1.21 (6 H, d, *J* 6.9, 2 × Me), 2.21 (3 H, s, 3-Me), 2.63 (1 H, sept., *J* 6.9, C*H*Me$_2$), 4.21 (0.05 H, s, CH_2 ketone form) 5.37 (0.95 H, s, =CH, enaminone form), 7.18 (1 H, dt, *J* 8.0 and 1.1), 7.35 (1 H, d, *J* 7.3), 7.41–7.45 (2 H, m), 7.45 (1 H, s, 4-H) and 15.59 (1 H, s, NH), plus very small signals 2.40 (s), 7.63 (t), 7.75 (d), 7.9 (s) and 8.0 (d); δ_C(enaminone form) 18.55 (Me), 20.26 (2 × Me), 39.64 (CH), 86.70 (CH), 116.83 (CH), 122.45 (C), 122.95 (CH), 126.72 (CH), 128.25 (C), 129.85 (CH), 134.37 (CH), 136.32 (C), 153.54 (C), 200.17 (C), plus small signals at 18.38 (Me) and 49.5 (CH_2) from the keto-form.

2,2-*Dimethyl*-4-(*quinolin*-2-*yl*)*penta*-3-*one* **8**.—A solution of 1-(quinolin-2-ylidene)-3,3-dimethylbutan-2-one (1.14 g, 5 mmol) in THF (20 cm^3) was added to sodium hydride (80% dispersion prewashed with light petroleum; 1.2 g, 5 mmol) in THF (30 cm^3), refluxed under nitrogen for 3 h and cooled. Iodomethane (0.7 g, 5 mmol) in THF (20 cm^3) was added and stirring continued at room temperature for 20 h. The product

was diluted with ether (50 cm^3) and extracted with dilute hydrochloric acid (2 × 40 cm^3). The acid solution was treated with sodium hydroxide solution until almost neutral and then basified with solid potassium carbonate. The mixture was extracted with ether (3 × 30 cm^3) and the combined extracts were dried ($MgSO_4$), filtered, and evaporated. The residue was chromatographed through a silica column eluted with chloroform to give the ketone (1.1 g, 98%) b.p. 135–137 °C/1.4 mmHg; *m/z* 241 (M^+, 12%), 184 (7), 157 (32), 156 (49) and 57 (100); δ_H 1.14 (9 H, s, 3 × Me), 1.52 (3 H, d, *J* 7.0, CH_3CHCO), 4.76 (1 H, q, *J* 7.0, CH_3CHCO), 7.50 (1 H, ddd, *J* 8.4, 6.9 and 1.5), 7.51 (1 H, d, $J_{3,4}$ 8.6, 3-H), 7.69 (1 H, ddd, *J* 8.4, 6.9 and 1.5), 7.78 (1 H, dd, *J* 8.4 and 1.5), 8.05 (1 H, dd, *J* 8.4 and 1.5) and 8.10 (1 H, d, $J_{3,4}$ 8.6, 4-H); δ_C($CDCl_3$) 19.52 (Me), 26.29 (3 × Me), 45.49 (C), 50.19 (CH), 119.44 (CH), 126.21 (CH), 127.03 (C), 127.51 (CH), 129.03 (CH), 129.47 (CH), 136.75 (CH), 147.69 (C), 161.23 (C) and 215.69 (C). Compound **8** gave the *hydrochloride* m.p. 176–178 °C (from ethanol–ether) (Found: C, 69.2; H, 7.15; Cl, 13.1; N, 5.1. $C_{16}H_{20}ClNO$ requires C, 69.2; H, 7.2; Cl, 12.8; N, 5.05%).

The following compounds were prepared in a similar manner:

2-(1,2-*Dihydro*-1-*methylquinolin*-2-*ylidene*)*pentan*-3-*one* **16** from 1-(1,2-dihydroquinolin-2-ylidene)butan-2-one [1] (1.07, g, 5 mmol), sodium hydride (10 mmol) and iodomethane (10 mmol); (0.75 g, 66%) m.p. 50–51 °C (from aq. EtOH) (Found: C, 79.0; H, 7.6; N, 6.0. $C_{15}H_{17}NO$ requires C, 79.3; H, 7.5; N, 6.15%); *m/z* 227 (M^+, 9%), 171 (64), 170 (100), 156 (15) and 57 (10); δ_H($CDCl_3$; 60 MHz) 0.95 (3 H, t, *J* 7.0, Me), 1.57 (3 H, s, MeC=), 2.22 (2 H, q, *J* 7.0, CH_2), 2.62 (3 H, s, NMe), 7.13 (1 H, d, *J* 9.0, 3-H), 7.15–8.1 (4 H, m) and 8.07 (1 H, d, *J* 9.0, 4-H).

2-(1,2-*Dihydro*-1-*methylquinolin*-2-*ylidene*)-4,4-*dimethylpentan*-3-*one* **17** from 1-(1,2-dihydroquinolin-2-ylidene)-3,3-dimethylbutan-2-one [1] (5 mmol), sodium hydride (10 mmol) and iodomethane (10 mmol); (42%) m.p. 85 °C (from aq. EtOH) (Found: C, 80.25; H, 8.45; N, 5.5. $C_{17}H_{21}NO$ requires C, 80.0; H, 8.25; N, 5.5%); *m/z* 255 (M^+, 7%), 172 (24), 171 (39), 170 (81), 129 (16), 128 (16) and 57 (100); δ_H 1.10 (9 H, s, 3 × Me), 1.71 (3 H, s, MeC=), 3.36 (3 H, s, NMe), 7.51 (1 H, ddd, *J* 8.5, 7.0 and 1.5), 7.67 (1 H, dd, *J* 8.5, 7.0 and 1.5), 7.71 (1 H, d, *J* 8.5, 3-H), 7.79 (1 H, d, *J* 8.5), 8.02 (1 H, d, *J* 8.5) and 8.16 (1 H, d, *J* 8.5, 4-H), δ_C 21.97 (Me), 28.24 (3 × Me), 44.61 (C), 52.33 (Me), 88.72 (C), 117.99 (CH), 126.16 (CH), 126.35 (CH), 127.28 (C), 127.47 (CH), 129.41 (CH), 136.73 (CH), 146.90 (C), 162.70 (C) and 213.94 (C); plus small signals for a second conformer: δ_H 0.98 (s), 1.64 (s), 7.32 (d, *J* 8.5) and 8.13 (d, *J* 8.5); δ_C 26.21 (Me), 29.20 (3 × Me), 45.35 (C), 56.45 (Me), 126.70 (CH), 127.48 (CH), 129.45 (CH), 164.11 (C) and 216.61 (C).

1,3-*Diphenyl*-2-(*quinolin*-2-*yl*)*propan*-1-*one* **12**. Prepared by following the above method using 1-phenyl-2-(quinolin-2-yl)-ethan-1-one [1] and benzyl chloride (72%); m.p. 115–116 °C (from EtOH) (Found: C, 85.5; H, 5.9; N, 4.15. $C_{24}H_{19}NO$ requires C, 85.5; H, 5.65; N, 4.15%); *m/z* 337 (M^+, 5%); δ_H 3.32 (1 H, dd, *J* 6.4 and 13.8, *H*CHPh), 3.71 (1 H, dd, *J* 8.2 and 13.8, HC*H*Ph), 5.39 (1 H, dd, *J* 6.4 and 8.2, C*H*CO), 7.08–7.22 (5 H, m), 7.29–7.36 (2 H, m), 7.41 (1 H, dt, *J* 6.8 and 1.3), 7.43 (1 H, d, *J* 8.4, 3-H), 7.48 (1 H, ddd, *J* 7.0, 6.8 and 1.3), 7.67 (1 H, ddd, *J* 7.0, 6.8 and 1.3), 7.74 (1 H, dd, *J* 8.1 and 1.3) and 8.06 (4 H, 'dd', *J* '8.4 and 1.5', 4-H, 8-H and PhCO 2-H and 6-H); δ_C 38.50 (CH_2), 59.18 (CH), 120.13 (CH), 126.21 (CH), 126.38 (CH), 127.00 (C), 127.52 (CH), 128.30 (2 × CH), 128.45 (2 × CH), 129.02 (2 × CH), 129.13 (2 × CH), 129.21 (CH), 129.53 (CH), 133.01 (CH), 136.74 (C), 136.92 (CH), 139.32 (C), 148.10 (C), 159.02 (C) and 198.31 (C).

1-*Bromo*-3,3-*dimethyl*-1-(*quinolin*-2-*yl*)*butan*-2-*one* **9**.—A solution of bromine (0.8 g, 5 mmol) in chloroform (10 cm^3) was added slowly to a stirred solution of 3,3-dimethyl-1-(quinolin-2-ylidene)butan-2-one (1.14 g, 5 mmol) in chloroform (50 cm^3) at room temperature. The mixture was stirred for 5 h and then evaporated to give the *ketone hydrobromide* (1.59 g, 82%) m.p. 197 °C (from EtOH–ether) (Found: C, 46.4; H, 4.55; Br, 40.9; N, 3.55. $C_{15}H_{17}Br_2NO$ requires C, 46.5; H, 4.4; Br, 41.3; N, 3.6%). The salt was neutralised with dilute ammonia solution and extracted with chloroform (2 × 50 cm^3). The solution was dried ($MgSO_4$) and evaporated to give the *ketone* m.p. 76–78 °C [from light petroleum (b.p. 60–80 °C)] (Found: C, 58.9; H, 5.35; Br, 26.3; N, 4.45. $C_{15}H_{16}BrNO$ requires C, 58.6; H, 5.2; Br, 26.1; N, 4.55%); *m/z* 307 (M^+ + 2, 1.4%), 305 (M^+, 1.1), 226 (5), 170 (40), 85 (20) and 57 (100); δ_H 1.26 (9 H, s, 3 × Me), 6.16 (1 H, s, CHBr), 7.56 (1 H, ddd, *J* 8.1, 7.0 and 1.1), 7.72 (1 H, ddd, *J* 8.1, 7.0 and 1.1), 7.81 (1 H, dd, *J* 8.1 and 1.1), 7.90 (1 H, d, *J* 8.6, 3-H), 8.05 (1 H, d, *J* 8.1) and 8.19 (1 H, d, *J* 8.6, 4-H); δ_C 26.50 (3 × Me), 45.33 (C), 49.04 (CH), 121.51 (CH), 127.32 (C), 127.36 (CH), 127.54 (CH), 129.28 (CH), 129.88 (CH), 137.17 (CH), 147.04 (C), 156.11 (C) and 207.06 (C).

Ethyl 3-(1,2-*Dihydro*-3-*methylquinolin*-2-*ylidene*)*pyruvate* **11**.—A solution of diethyl oxalate (0.73 g, 0.5 mmol) in dry ether (10 cm^3) was added to potassium ethoxide [10 mmol from potassium (0.4 g) and ethanol (1.8 cm^3) in dry ether (20 cm^3)]. A solution of 2,3-dimethylquinoline (0.78 g, 5 mmol) in dry ether (10 cm^3) was added dropwise and the mixture stirred for 3 d and allowed to stand for 4 d. The precipitate was rapidly collected and immediately added to dilute acetic acid (10 cm^3). After the mixture had been stirred for 2 h, the resultant precipitate was collected to give the *enaminone ester* (0.35 g, 27%), m.p. 129–130 °C (from aq. EtOH) (Found: C, 70.2; H, 5.75; N, 5.3. $C_{15}H_{15}NO_3$ requires C, 70.0; H, 5.85; N, 5.45%); *m/z* 257 (M^+, 12%); δ_H 1.42 (3 H, t, *J* 7.1, Me), 2.37 (3 H, d, *J* 0.7, 3-Me), 4.37 (2 H, q, *J* 7.1, CH_2), 6.40 (1 H, s, =CHCO), 7.36 (1 H, ddd, *J* 8.1, 6.8 and 1.6), 7.52–7.61 (3 H, m), 7.74 (1 H, s, 4-H) and 16.40 (1 H, s, NH); δ_C 14.23 (Me), 18.50 (Me), 61.69 (CH_2), 89.09 (CH), 118.32 (CH), 123.90 (C), 124.99 (CH), 127.06 (CH), 128.93 (C), 130.69 (CH), 135.91 (C), 136.52 (CH), 155.22 (C), 164.85 (C) and 172.15 (C).

Ethyl 2-(1,2-*Dihydroquinolin*-2-*ylidene*)-3-*oxo*-3-*phenylpropionate* **13**.—Ethyl benzoylacetate (1.73 g, 9 mmol) was added to a stirred solution of quinoline 1-oxide (1.3 g, 9 mmol) in acetic anhydride (5.2 g, 50 mmol) over 10 min. After 12 h at 40 °C the mixture was cooled and the excess of acetic anhydride decomposed with methanol (40 cm^3). The solvent was evaporated and the residue dissolved in ether and shaken with aq. sodium hydrogen carbonate until all traces of acid were removed. The ether solution was dried ($MgSO_4$) and evaporated and the residue chromatographed through a silica column eluted with dichloromethane to give the *enamino ester* (0.95 g, 33%), m.p. 84–85 °C [from light petroleum (b.p. 80–100 °C)] (Found: C, 75.3; H, 5.35; N, 4.2. $C_{20}H_{17}NO_3$ requires C, 75.2; H, 5.35; N, 4.4%); *m/z* 319 (M^+, 5%), 217. (13), 105 (100) and 77 (29); δ_H 0.71 (3 H, t, *J* 7.0, Me), 3.85 (2 H, q, *J* 7.0, CH_2), 7.36–7.44 (4 H, m), 7.51–7.70 (5 H, m), 7.96 (1 H, d, *J* 9.5, 3-H), 8.14 (1 H, dd, *J* 9.5 and 1.5, 4-H) and 16.85 (1 H, s, NH); δ_C 13.21 (Me), 60.01 (CH_2), 97.83 (C), 118.48 (CH), 119.71 (CH), 123.36 (C), 124.95 (CH), 126.58 (2 × CH, Ph), 127.67 (CH), 127.87 (2 × CH, Ph), 129.33 (CH), 131.57 (CH), 136.26 (C, Ph), 138.14 (CH), 143.77 (C), 154.27 (C), 169.92 (C) and 193.22 (C).

2-(1,2-*Dihydroquinolin*-2-*ylidene*)-1-(*pyridin*-2-*yl*)*ethan*-1-*one* **14**.—The title compound was prepared by the method of Case and Schilt,[19] (92%), m.p. 161–162 °C (from EOH) (lit.,[19] m.p. 158 °C), *m/z* 248 (M^+, 76%) and 170 (100); δ_H 6.82 (1 H, s, =CHCO), 6.97 (1 H, d, *J* 9.2, 3-H), 7.26 (1 H, ddd), 7.34 (1 H, ddd), 7.52 (3 H, m), 7.68 (1 H, d, *J* 9.2, 4-H), 7.83 (1 H, dt), 8.17 (1 H, dt), 8.65 (1 H, ddd) and 15.73 (1 H, s, NH); δ_C 89.93

(CH), 118.32 (CH), 121.09 (CH), 122.65 (CH), 123.55 (C), 123.99 (CH), 124.82 (CH), 127.67 (CH), 131.05 (CH), 136.51 (CH), 136.89 (CH), 137.74 (C), 148.59 (CH), 154.72 (C), 156.01 (C) and 181.54 (C).

2-Cyano-2-(1,2-dihydroquinolin-2-ylidene)-1-phenylethanone **15**.—Benzoylacetonitrile (1.3 g, 9 mmol) was added to a stirred solution of quinoline 1-oxide (1.3 g, 9 mmol) in acetic anhydride (2.6 cm^3) at 0 °C over 0.5 h. The mixture was stirred at 35–40 °C for 9 h and left in the refrigerator overnight. The product was collected and washed with cooled methanol (5 cm^3) to give the enaminone (1.2 g, 50%), m.p. 204–205 °C (from EtOH) (lit.,[28] m.p. 206–207 °C); *m/z* 273 (M^+ + 2, 25%), 272 (M^+, 100), 271 (73), 195 (46), 170 (21), 140 (23), 105 (48) and 77 (60); δ_H 7.44–7.55 (4 H, m), 7.61 (1 H, dd, *J* 9.2 and 1.8, 3-H), 7.66–7.78 (3 H, m), 7.90–7.94 (2 H, m), 8.13 (1 H, d, *J* 9.2, 4-H) and 16.54 (1 H, s, NH); δ_C 77.56 (C), 118.51 (CH), 119.41 (CH), 120.82 (CN), 123.73 (C), 125.90 (CH), 127.92 (2 × CH), 128.16 (3 × CH), 131.18 (CH), 132.44 (CH), 135.92 (C), 139.18 (C), 139.88 (CH), 155.87 (C) and 191.65 (C).

1-Ethoxycarbonylmethyl-2-methylquinolinium Bromide **26**.—A mixture of freshly distilled ethyl bromoacetate (6.7 g, 40 mmol) and 2-methylquinoline (2.9 g, 20 mmol) in acetonitrile (50 cm^3) was refluxed for 8 h and most of the solvent evaporated. After cooling the precipiate was collected and chromatographed through a silica column eluted with 1% methanol in chloroform to give the *quaternary ammonium salt* (2.3 g, 50%), m.p. 190–192 °C (from isopropyl alcohol) (Found: C, 54.0; H, 5.2; N, 4.4. $C_{14}H_{16}BrNO_2$ requires C, 54.2; H, 5.15; N, 4.5%); *m/z* 229 (M^+ − HBr); ν_{max}(KBr)/cm^{-1} 3450 and 1730; δ_H([$^2H_1$]-TFA) 1.38 (3 H, t, Me), 3.15 (3 H, s, Me), 4.43 (2 H, q, CH_2), 5.93 (2 H, s, NCH_2) and 7.8–9.0 (6 H, m, C_9H_6N).

Pyrrolo[1,2-a]*quinolin-2*(1H)*-one* **18**.—*Method A*. A solution of compound **3** (0.82 g, 3 mmol) in chlorobenzene (100 cm^3) was refluxed on an oil bath for 2 h. The reaction mixture was allowed to stand at room temperature for 12 h and the precipitate collected to give the *pyrroloquinoline hydrobromide* (0.7 g, 85%), m.p. 235–237 °C (from EtOH–ether) (Found: C, 54.3; H, 3.9; Br, 30.1; N, 5.7. $C_{12}H_{10}BrNO$ requires: C, 54.5; H, 3.8; Br, 30.3; N, 5.3%). The salt was made basic with dilute ammonia solution and extraction with chloroform gave the *free base*, m.p. 128–129 °C (decomp.); *m/z* 183 (M^+, 100%), 154 (32) and 129 (46); δ_H 4.26 (2 H, s, NCH_2CO), 5.18 (1 H, s, =CHCO), 6.87 (1 H, d, *J* 9.2, 3-H), 7.05 (1 H, d, *J* 8.6), 7.15 (1 H, ddd, *J* 8.1, 7.0 and 1.0), 7.45 (1 H, d, *J* 9.2, 4-H) and 7.53 (2 H, m); δ_C 54.97 (CH_2), 94.61 (CH), 112.77 (CH), 116.83 (CH), 121.77 (C), 122.46 (CH), 129.58 (CH), 132.24 (CH), 136.90 (CH), 138.14 (C), 165.60 (C) and 193.15 (C).

Method B. A solution of compound **19** (0.2 g) in conc. hydrochloric acid (10 cm^3) was refluxed for 12 h. The solvent was evaporated and the residue washed several times with ethanol to give the *pyrroloquinoline hydrochloride* (0.05 g, 23%), m.p. 220–222 °C (from EtOH–ether) (Found: C, 65.9; H, 4.35; Cl, 16.4; N, 6.25. $C_{12}H_{10}ClNO$ requires C, 65.6; H, 4.55; Cl, 16.2; N, 6.35%). The free base was identical (m.p. and mixed m.p., IR, TLC) with the compound obtained by method A.

Method C. A solution of 1-ethoxycarbonylmethyl-2-methylquinolinium bromide in ethanol (20 cm^3) was made alkaline with dilute sodium hydroxide and extracted with chloroform. The organic extract was dried ($MgSO_4$), filtered and evaporated. The residue was chromatographed through a silica column eluted with chloroform to give *pyrrolo*[1,2-a]*quinolin-2*(1H)*-one* (0.15 g, 16%) identical (m.p. and mixed m.p., IR, TLC) with the free bases prepared by methods A and B.

3-Cyanopyrrolo[1,2-a]*quinolin-2*(1H)*-one* **19**.—A solution of compound **4** (0.2 g) in THF (10 cm^3) was added dropwise to sodium hydride (80% dispersion prewashed with light petroleum; 0.038 g) in THF (20 cm^3) with stirring under nitrogen at room temperature. After addition was complete the mixture was refluxed for 2 h. The cooled product was diluted with ether (50 cm^3) and washed with dilute hydrochloric acid. The organic layer was separated, dried ($MgSO_4$), filtered and evaporated to give the pyrroloquinolone (0.12 g, 97%), m.p. 258–260 °C (from nitromethane) (lit.,[14] m.p. 270 °C); *m/z* 209 (M^+ + 1, 14%), 208 (M^+, 100), 153 (13) and 129 (15); δ_H 4.57 (2 H, s, NCH_2CO), 7.32 (1 H, d, *J* 9.2, 3-H), 7.34 (1 H, d, *J* 8.1), 7.43 (1 H, ddd, *J* 8.1, 7.0 and 1.0), 7.74 (1 H, ddd, *J* 8.1, 7.0 and 1.0) 7.76 (1 H, d, *J* 8.1) and 7.97 (1 H, d, *J* 9.2, 4-H); δ_C 55.51 (CH_2), 80.01 (C), 114.21 (CH), 115.03 (CH), 118.43 (CN), 122.87 (C), 124.98 (CH), 130.31 (CH), 133.72 (CH), 137.11 (C), 140.56 (CH), 164.54 (C) and 188.25 (C).

3,3-Dimethyl-1-(quinolin-2-yl)butane-1,2-dione **23**.—A solution of compound **9** (1.63 g) in dimethyl sulphoxide (DMSO) (10 cm^3) was stirred at 45–50 °C for 54 h. The resulting solution was poured into ice and extracted with ether (2 × 40 cm^3). The extracts were dried ($MgSO_4$), filtered and evaporated. The crude product was chromatographed through a silica column eluted with dichloromethane to give the *dione* (0.7 g, 54%), m.p. 66–68 °C [from light petroleum (b.p. 40–60 °C)] (Found: C, 75.0; H, 6.3; N, 5.85. $C_{15}H_{15}NO_2$ requires C, 74.7; H, 6.2; N, 5.8%); *m/z* 241 (M^+, 25%); ν_{max}($CHCl_3$)/cm^{-1} 1708, 1694, 1619 and 1590; δ_H(60 MHz) 1.33 (9 H, s, 3 × Me) and 7.0–9.0 (6 H, m, C_9H_6N).

3,3-Dimethyl-1-(3-methylquinolin-2-yl)butane-1,2-dione **24**.—*Method A*. By following the above method from compound **10** was obtained the *dione* (35%), m.p. 121–122 °C (from EtOH) (Found: C, 74.7; H, 6.85; N, 5.4. $C_{16}H_{17}NO_2$ requires C, 74.7; H, 6.65. N, 5.45%); *m/z* 255 (M^+, 26%), 170 (21), 143 (46), 142 (100), 115 (20) and 57 (62); ν_{max}($CHCl_3$)/cm^{-1} 1705, 1696, 1623 and 1588; δ_H(60 MHz) 1.39 (9 H, s, 3 × Me), 2.80 (3 H, s, Me) and 7.3–8.1 (6 H, m, C_9H_6N); δ_C 19.25 (Me), 26.68 (3 × Me), 42.33 (C), 126.81 (CH), 129.20 (C), 129.44 (CH), 129.48 (CH), 130.00 (CH), 131.82 (C), 138.42 (CH), 145.55 (C), 149.73 (C), 197.78 (C) and 214.47 (C).

Method B. To a solution of 2,3-dimethylquinoline (15.7 g, 100 mmol) and phenyllithium (8.4 g, 100 mmol) in dry ether (100 cm^3) was added dropwise with stirring, under nitrogen, at room temperature, a solution of pivalonitrile (8.3 g, 100 mmol) in dry ether (50 cm^3) and the mixture stirred at room temperature for 24 h. The resulting solution was washed with water (500 cm^3) and then extracted with hydrochloric acid (2 mol dm^{-3}). The extract was neutralised with solid sodium hydrogen carbonate, extracted with chloroform and the extract dried ($MgSO_4$), and subjected to rotary evaporation; recrystallisation of the residue from ethanol gave the *dione* **24** (12.7 g, 50%), identical m.p. and spectroscopically with the sample from method A.

Acknowledgements

We thank Mr. P. J. Taylor for helpful discussions and the Ministry of Higher Education, Islamic Republic of Iran for a grant to H. L.-K.

References

1 J. V. Greenhill, H. Loghmani-Khouzani and D. J. Maitland, *Tetrahedron*, 1988, **44**, 3319.

2 R. Roussel, M. Oteyza de Guerrero, P. Spegt and J. C. Galin, *J. Heterocycl. Chem.*, 1982, **19**, 785; A. R. E. Carey, G. Fukata, R. A. More O'Ferrall and M. G. Murphy, *J. Chem. Soc., Perkin Trans. 2*, 1985, 1711.

3 A. M. Stock, W. E. Donahue and E. D. Amstutz, *J. Org. Chem.*, 1958, **23**, 1840.
4 B. Golankiewicz and K. Golankiewicz, *Bull. Acad. Polon. Sci., Ser. Sci. Chim.*, 1966, **14**, 199 (*Chem. Abstr.*, 1966, **65**, 10466).
5 P. L. Compagnon, F. Gasqyez, O. Compagnon and T. Kinmy, *Bull. Soc. Chim. Belg.*, 1982, **91**, 931.
6 M. Hamana and H. Noda, *Chem. Pharm. Bull.*, 1966, **14**, 762.
7 J. V. Greenhill, in *The Chemistry of Heterocyclic Compounds: Quinolines*, vol. 32, Part 3, ed. G. Jones, John Wiley and Sons, 1990.
8 J. C. Carey and W. H. F. Sasse, *Aust. J. Chem.*, 1968, **21**, 207; A. K. Kuzmin, A. N. Chistyakov and V. A. Proskuryakov, *Zh. Prikl. Khim (Leningrad)*, 1981, **54**, 120 (*Chem. Abstr.*, 1981, **95**, 23 871).
9 B. Eistert and E. Enders, *Justus Liebigs Ann. Chem.*, 1970, **734**, 56.
10 V. V. Lapachev, S. A. Stekhova, I. Ya. Mainagashev, M. A. Fedotov, V. E. Khall and V. P. Mamaev, *Khim. Geterotsikl. Soedin.*, 1986, 802; *Chem. Heterocycl. Compd. (Engl. Transl.)*, 1986, **22**, 633.
11 J. V. Greenhill, *Chem. Soc. Rev.*, 1977, **6**, 277.
12 R. Giger, R. Allain, M. Rey and A. S. Dreiding, *Helv. Chim. Acta*, 1970, **53**, 120.
13 J. J. Talley, *Tetrahedron Lett.*, 1981, **22**, 823.
14 F. S. Babichev and Yu M. Volovenko, *Khim. Geterotsikl. Soedin.*, 1976, 1147; *Chem. Heterocycl. Compd. (Engl. Transl.)*, 1976, **12**, 949.
15 P. J. Black and M. C. Heffernan, *Aust. J. Chem.*, 1964, **17**, 558.
16 R. Mondelli and L. Merlini, *Tetrahedron*, 1966, **22**, 3253.
17 Ja-Au Su, E. Siew, E. V. Brown and S. L. Smith, *Org. Magn. Reson.*, 1977, **10**, 122.
18 D. Smith and P. J. Taylor, *Spectrochimica Acta*, 1976, **32A**, 1477.
19 F. H. Case and A. A. Schilt, *J. Heterocycl. Chem.*, 1979, **16**, 1135.
20 G. C. Levy and R. L. Lichter in *Nitrogen-15 Nuclear Magnetic Resonance Spectroscopy*, John Wiley and Sons, NY, 1979, pp. 78, 84.
21 J. V. Greenhill, H. Loghmani-Khouzani and D. J. Maitland, *Can. J. Chem.*, 1991, **69**, 696.
22 P. S. Pregosin, E. W. Randall and A. I. White, *J. Chem. Soc., Perkin Trans. 2*, 1972, 1.
23 D. Pitea and G. Favini, *J. Chem. Soc., Perkin Trans. 2*, 1972, 142.
24 D. Smith and P. J. Taylor, *J. Chem. Soc., Perkin Trans. 2*, 1979, 1376.
25 R. M. Acheson and G. Procter, *J. Chem. Soc., Perkin Trans. 1*, 1979, 2171.
26 F. S. Babichev, Yu M. Volovenko and A. A. Oleinik, *Khim. Geterotsikl. Soedin.*, 1977, 1515; *Chem. Heterocycl. Compd. (Engl. Transl.)*, 1977, **13**, 1211.
27 R. R. Fraser and R. B. Swingle, *Tetrahedron*, 1969, **25**, 3469.
28 R. A. Abramovitch, G. Grins, R. B. Rogers and I. Shinkai, *J. Am. Chem. Soc.*, 1976, **98**, 5671.

Paper 1/01947C
Received 24*th April* 1991
Accepted 24*th July* 1991