Determination of Electrophilic Aromatic Reactivities *via* Pyrolysis of 1-Arylethyl Acetates. Part VII.[1] The Total Reactivity of Quinoline

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All seven 1-(quinolyl)ethyl acetates have been prepared and their rates of elimination of acetic acid together with those of 1-phenylethyl acetate and the three 1-(pyridyl)ethyl acetates measured at temperatures between 348·2 and 413·5°. The results yield the first measure of the quantitative electrophilic reactivity of the neutral quinoline molecule and coupled with previous data show the relative reactivities as follows: α-naph > β-naph > 5-Q > phenyl > 8-Q = 6-Q > 3-Q > 7-Q > 3-P ≫ 2-Q > 4-Q > 2-P > 4-P. Each position in quinoline is consequently shown to be less reactive than the corresponding positions in naphthalene, more reactive than the corresponding positions in pyridine, and only the 5-position is activated relative to a position in benzene. Electrophilic substituent constants σ^+ are derived for the positions (in parentheses) as follows: −0·108(5); +0·063(8,6); +0·079(3); +0·152(7); +0·730(2); +0·747(4). Taken in isolation the positional reactivities are predicted satisfactorily by molecular orbital calculations of π-electron densities, but these are less satisfactory in predicting the reactivities relative to other molecules; calculated localisation energies are poor indicators of the positional reactivities, which appear to be particularly dependent upon inductive and/or field effects.

WHILST the electrophilic reactivity of benzene and its derivatives have been studied by many hundreds of workers leading to the accumulation of a large body of quantitative data and sophisticated analyses of these,[2] knowledge of the quantitative reactivity of heterocycles has, until recently been negligible. This arises from the tendency of heterocycles to protonate (*e.g.* pyridine, quinoline) or decompose (*e.g.* furan) under acid conditions which are either initially present, or produced as byproducts in most electrophilic substitutions. Reactions which involve or produce only mild acid conditions tend to have high ρ-factors so that determination of the quantitative electrophilic reactivity of the heterocycle becomes extremely difficult, if not impossible.

We have shown in this series of papers how the pyrolysis of 1-arylethyl acetates is a model reaction for determining quantitative electrophilic reactivities and has outstanding advantages over all other reactions in that there is no solvent, no possibility of protonation, and the ρ-factor is small enough for relative rates to be measured *directly* without the need for overlap techniques. In this way the first total quantitative electrophilic reactivities of pyridine, furan and thiophen were determined,[3,4] and for the last two compounds more recent work [5–8] has confirmed the validity of the prediction of the gas-phase reaction, but for pyridine there is still no other set of results available which indicates the extreme difficulties attendant upon the determination of the reactivity of nitrogen-containing heterocycles by traditional methods.

Previously we found [3] that the electrophilic reactivity of pyridine was quantitatively predicted by π-electron densities calculated by the Hückel method, using parameters *viz.* $\beta_{CN} = \beta_{CC}$, $\alpha_N = \alpha_C + 0{\cdot}5\beta$, and $\alpha_{C'}$ (2-carbon) $= \alpha_C + 0{\cdot}085\beta$ derived [9] from analysis of dipole moments, free radical and nucleophilic substitution data for N-containing heterocycles. Localisation energies [calculated with the additional parameter $\delta = (\alpha_C - \alpha_{C'})/0{\cdot}075\beta = 0{\cdot}45$ for substitution at the 2-position] also accurately predicted the quantitative

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reactivity; the ability of both π-electron densities and localisation energies to predict the reactivity stems from the inability of pyridine to respond to demands for resonance stabilisation of transition states.

The purpose of the present work was, therefore, to determine the electrophilic reactivity of quinoline, compare it with the related molecules naphthalene, benzene, and pyridine, and to see if its reactivity could be predicted by the method found to be so successful for pyridine.

RESULTS AND DISCUSSION

The rates of pyrolysis of the esters (reproducible to ±1%) at the indicated temperatures are given in the Table together with the values of log k/k_0 (log k_{Het}/k_{Ph}),

Pyrolysis of compounds CH_3·CHR·OAc

R	T/°C	10^3k/s^{-1}	log A/s^{-1}	E / kcal mol^{-1}	$\Delta S^{\ddagger}$ / cal mol^{-1} K^{-1}	log k/k_0 (at 625 K)
Phenyl	398·5	37·0	12·75	43·7	−1·7	0
	382·9	16·8				
	370·7	9·20				
	360·3	5·17				
	348·2	2·63				
2-Pyridyl	413·5	27·0	12·85	44·9	−1·2	−0·49
	398·5	12·8				
	382·4	5·48				
	370·6	3·03				
	360·3	1·72				
3-Pyridyl	398·5	25·7	12·85	44·3	−1·2	−0·185
	382·5	11·3				
	370·7	6·14				
	360·3	3·46				
	348·2	1·735				
4-Pyridyl	413·5	24·2	12·7	44·9	−2·0	−0·545
	398·5	11·2				
	382·9	5·17				
	370·7	2·70				
	360·3	1·515				
2-Quinolyl	413·5	28·3	12·6	44·5	−2·3	−0·46
	398·9	13·8				
	382·4	6·06				
	370·6	3·29				
	360·0	1·805				
3-Quinolyl	399·0	34·1	12·7	44·0	−1·8	−0·050
	382·4	15·3				
	374·0	9·68				
	370·6	8·23				
	360·7	4·74				
	348·2	2·35				
4-Quinolyl	413·5	27·9	12·5	44·5	−2·7	−0·47
	398·9	13·3				
	383·1	6·05				
	370·6	3·15				
	360·0	1·76				
5-Quinolyl	398·9	42·5	12·65	43·1	−2·1	+0·068
	382·5	18·8				
	370·6	10·4				
	360·0	5·75				
	348·3	3·12				
6-Quinolyl	398·9	34·7	12·8	43·9	−1·5	−0·040
	382·6	15·6				
	370·6	8·23				
	360·0	4·81				
	348·2	2·40				
7-Quinolyl	398·6	29·7	12·8	44·0	−1·5	−0·096
	382·9	14·0				
	382·5	13·6				
	370·6	7·16				
	360·0	4·12				
	348·2	2·11				
8-Quinolyl	398·7	35·2	12·8	43·8	−1·3	−0·040
	398·5	33·7				
	396·6	30·0				
	387·3	19·35				
	382·5	15·5				
	382·1	14·95				
	374·1	10·15				
	372·0	8·92				
	361·8	5·13				

and the energies and entropies of activation, determined at 625 K from the Arrhenius plot (Figure 1). The log k_{rel} values for the pyridyl esters are in excellent agreement (within 3%) with the values which we obtained earlier on a less sophisticated version of the apparatus,[3] and the present values should be taken as the more accurate; the agreement in the thermodynamic parameters from each work is well inside the experimental error.

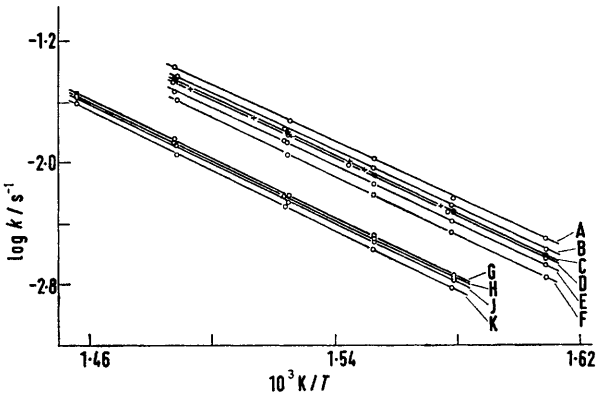

FIGURE 1 Arrhenius plot for the pyrolysis of 1-arylethyl acetates: aryl = (A) 5-quinolyl, (B) phenyl, (C) 8-quinolyl, 6-quinolyl, (D) 3-quinolyl, (E) 7-quinolyl, (F) 3-pyridyl, (G) 2-quinolyl, (H) 4-quinolyl, (J) 2-pyridyl, (K) 4-pyridyl

The log k_{rel} values are illustrated in Figure 2 together with the σ^+-values obtained by dividing the former

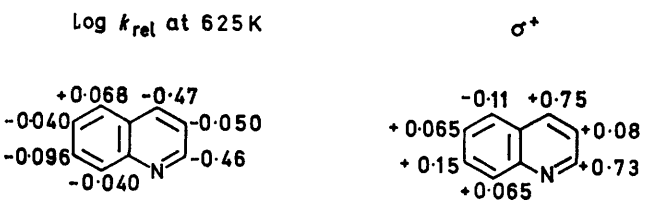

FIGURE 2

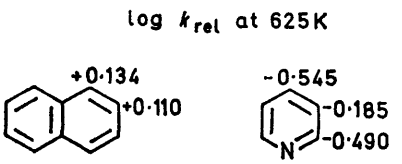

FIGURE 3

values by the ρ-value at 625 K of −0·63. The corresponding log k_{rel} values for pyridine and naphthalene (corrected for the temperature difference from those given in ref. 10) are given in Figure 3, and comparison of both sets reveals the following important qualitative features:

(i) All positions in quinoline are *less* reactive than the corresponding positions in naphthalene and this is as predicted from consideration of the electronegativity of nitrogen.

(ii) All positions in the N-substituted ring of quinoline are *more* reactive than the analogous positions in pyridine: again this fulfils the prediction from our knowledge of the activating effect of a benzo-substituent.

(iii) With the exception of the 5-position which is activated, all positions in quinoline are deactivated towards electrophilic substitution.

(iv) With the exception of the 2- and 4-positions, the reactivities at the other positions differ from that of a position in benzene by only a small amount relative to the range of substituent effects encountered in electrophilic substitutions.[2]

With the knowledge of the quantitative reactivities of both quinoline and pyridine we are now in the position to make the first quantitative analysis of some of the positional reactivities. Firstly the 3-position of quinoline is equivalent to a 3-position in pyridine which has a 3,4-benzo-substituent. Now the effect of the latter substituent in benzene is given by the reactivity of the β-position in naphthalene, for which log k_{rel} is +0·110 in the present reaction. Since log k_{rel} for the 3-position in pyridine is −0·185, then the predicted value of log k_{rel} for the 3-position of quinoline is −0·185 + 0·110 = −0·075, *cf.* the experimental value of −0·050; the agreement is extremely good and the small discrepancy is in the expected direction since the benzo-substituent has a variable response to demands for resonance stabilisation of transition states.[11] Substituted in the less reactive pyridine molecule giving quinoline the electron supply should be greater than when substituted in benzene (giving naphthalene), so that the 3-position of quinoline should be slightly greater than predicted, just as we observe.

It might be expected that a similar approach might predict the reactivities of the 2- and 4-positions in quinoline, but in fact the prediction turns out to be slightly less good here for no very obvious reason; possibly the fact that a full positive charge is placed on nitrogen in the principal canonical forms of the resonance hybrid of the transition states for reaction at these positions, and the effective electronegativity of nitrogen in the two molecules (which would significantly affect the stability of the transition states) may not be the same, is responsible. What is interesting is the fact that the 2- and 4-positions in quinoline differ from the corresponding positions in pyridine by virtue of the fact that the 2-position is β-naphthalene-like whereas the 4-position is α-naphthalene-like. Consequently we might expect that the difference in the reactivities of the 2-positions on one hand and the 4-positions on the other might reflect the difference in reactivity of the α- and β-position in naphthalene. This is emphatically borne out by the experimental results. From equations (1) and (2) we can predict that the difference log $f_{4\text{-Q}}$ − log $f_{2\text{-Q}}$ should be 0·045—0·024 = 0·021, which is extremely close to the experimental value of 0·010.

$$\log f_{4\text{-P}} - \log f_{2\text{-P}} = 0{\cdot}045 \quad (1)$$

$$\log f_{\alpha\text{-Naph}} - \log f_{\beta\text{-Naph}} = 0{\cdot}024 \quad (2)$$

[10] R. Taylor and G. G. Smith, *Tetrahedron*, 1963, **19**, 937; R. Taylor, G. G. Smith, and W. H. Wetzel, *J. Amer. Chem. Soc.*, 1962, **84**, 4817.

[11] C. Eaborn and R. Taylor, *J. Chem. Soc.*, 1961, 1012.

The 3-, 6-, and 8-positions are each formally '*meta*' to the nitrogen, *i.e.* reaction at these positions does not place a positive charge on nitrogen in the transition state so that following the arguments above, additivity of substituent effects should obtain here. It is interesting to note, therefore, that these positions differ in reactivity from those corresponding in naphthalene by a closely similar amount as indicated by equations (3)—(5), and further that the differences increase slightly as the position involved is nearer to nitrogen, so that

$$\log f_{6\text{-Q}} = \log f_{\beta\text{-Naph}} - 0{\cdot}155 \quad (3)$$

$$\log f_{3\text{-Q}} = \log f_{\beta\text{-Naph}} - 0{\cdot}160 \quad (4)$$

$$\log f_{8\text{-Q}} = \log f_{\alpha\text{-Naph}} - 0{\cdot}174 \quad (5)$$

this can be fairly confidently attributed to the inductive effect of the heteroatom.

The 7- and 6-positions are both β-naphthalene-like and so it is legitimate to compare their reactivities in the manner of equation (6). Likewise the 5- and 8-positions are both α-naphthalene-like which leads to

$$\log f_{6\text{-Q}} - \log f_{7\text{-Q}} = 0{\cdot}065 \quad (6)$$

equation (7). Two points of interest emerge from this.

$$\log f_{5\text{-Q}} - \log f_{8\text{-Q}} = 0{\cdot}095 \quad (7)$$

The first is that the group nearest to nitrogen is in both cases the least reactive, and secondly the greater reactivity difference given by equation (7) compared to that given by equation (6) follows the expectation arising from the $-I$ effect of nitrogen.

In the above discussion we have neglected any steric effects arising from the *peri*-hydrogen because they cancel out entirely or almost so in each of the comparisons. It should be noted that for naphthalene, the ratio $\log f_{\alpha\text{-Naph}} : \log f_{\beta\text{-Naph}}$ was less (1·22) than predicted (1·40) from analysis of electrophilic substitution data,[10] which suggested slight steric hindrance to attainment of coplanarity of the aryl *p*-orbitals and those of the forming carbonium ion in the transition state for reaction at the α-position. Using the value of 1·40, this predicts that the hindrance-free $\log k_{rel}$ value for reaction at the α-position should be 0·154 rather than 0·134, at 625 K. It is probable, therefore, that to obtain the true electrophilic reactivities we should increase the $\log k_{rel}$ values at the 4- and 5-position by *ca.* 0·02 units; the reactivity of the 8-position may be too low by perhaps 0·01 unit since the nitrogen lone pair is less bulky than a C–H bond. Making these corrections means that the true σ^+-values for the 4-, 5-, and 8-positions should be slightly more negative as follows: −0·14(5), +0·048(8), +0·715(4). The only difference these minor corrections make to our conclusions is that the 4-position becomes marginally *more* rather than *less* reactive than the 2-position.

Theoretical Calculations of the Electrophilic Reactivity of Quinoline.—We now turn our attention to the ability of calculations to predict the observed reactivities. π-Electron densities, calculated by the Hückel method using the parameters previously found satisfactory for pyridine,[3] are as shown in Figure 4 together with the values for pyridine. This leads to the reactivity sequence 8 > H > 6 > 3 > 5 > 7 > 3P ≫ 2P > 4P > 4Q > 2Q, and the plot in Figure 5 from which it can be seen that the experimental results are, with the principal

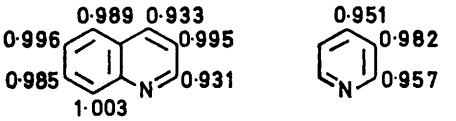

FIGURE 4 π-Electron densities

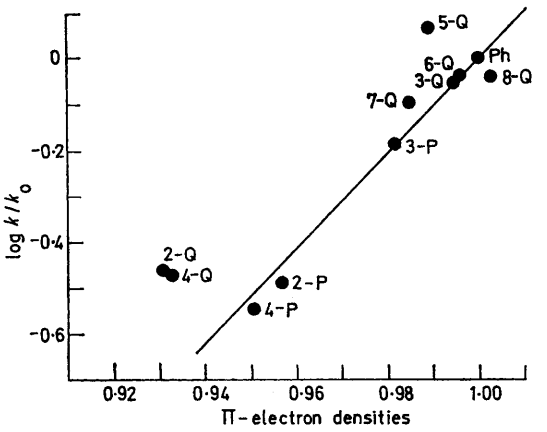

FIGURE 5 Plot of log k/k_0 values for pyrolysis of 1-arylethyl acetates against π-electron densities

exception of the 5- and 8-position reactivities, reasonably satisfactorily predicted by these parameters, though the data are best represented by separate lines for pyridine and quinoline. The order of reactivity of the 2- and 4-positions in pyridine relative to those in quinoline are also incorrectly predicted, and it appears that the calculations over-emphasise the importance in quinoline of transition-state structures which retain benzenoid or pyridinoid character. These structures are obtained in reaction at the 2-, 4-, and 5-positions and also place a positive change in nitrogen, *i.e.* the calculations predict the reactivities of these positions to be lower than is the case. Another factor which may account for the

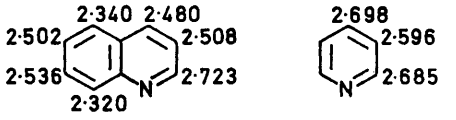

FIGURE 6 Localisation energies (−β)

reversal of the observed 5- and 8-positional reactivities from the prediction is the possibility of a direct-field effect from the nitrogen which would strongly deactivate the 8-position, whereas the interposition of the 9,10-bond could be expected to markedly diminish this effect at the 5-position.

Calculations of localisation energies by the Hückel method give the values in Figure 6 and these though satisfactory for pyridine are totally unsuccessful for quinoline; in particular they over-emphasise the

reactivity of α-naphthalene-like positions as can be seen from the reactivity order $8 > 5 > 4 > 6 > 3 > 7 = H > 3\text{-P} > 2\text{-P} > 4\text{-P} > 2$.

Calculations of localisation energies by a zero-overlap SCF-electron MO method in which the bond lengths are iterated to be self-consistent with the calculated bond orders and in which the bond angles are consistent with the bond lengths,* were equally unsuccessful at predicting the reactivities.

Qualitative Data from Electrophilic Substitutions.—Comparison of the experimental results with data for electrophilic substitutions is barely possible since the latter are very sparse and refer almost entirely to reactions of the quinolinium ion. Nitration,[12] bromination,[13] and sulphonation [14] (all under acidic conditions) give predominantly 5- and 8-substitution but this concerns reaction on the quinolinium ion. In nitration the reactivity was 10^{10} less than that of naphthalene,[15] whereas we predict that for the neutral molecule this factor should be between *ca.* 10, and 2×10^6 for reaction at the most, and least reactive positions, respectively. This confirms that in these electrophilic substitutions, the quinolinium ion is involved, as indicated also by reactivity-acidity profiles.[15,16]

Under less acidic conditions, nitration,[17] bromination,[18] and mercuration [19] give 3- > 6,8-substitution, more in keeping with our prediction. Unfortunately, however, in these reactions 95% of the products were tars so that little reliance can be placed upon this result; the lack of 5-substitution may not be real or it may reflect the bulkier nature of the electrophile usually encountered under more neutral conditions. It would clearly be valuable to have a reinvestigation of some of these reactions using modern analytical techniques.

EXPERIMENTAL

All compounds were indicated to be >99% pure by v.p.c. analysis and gave the expected i.r. spectra showing the absence of alcohol or ketone precursors.

All of the quinolyl esters were viscous yellow oils and the viscosities (determined visually) followed the order $4 \approx 5 > 8 \gg 2,3,6,7$ which suggests a relationship between viscosity and the most hindered sites in the molecule.

1-Phenylethyl acetate, 1-(2-, 3-, and 4-pyridyl)ethyl acetates were available from previous studies and were refractionated before use.

1-(2-*Quinolyl*)*ethyl Acetate*.—Quinaldine (229 g, 1·6 mol) was converted by the method of Campbell *et al.*[20] *via* tribromoquinaldine into quinoline-2-carboxylic acid, m.p. 153° (lit.,[20] 153—155°), and thence ethyl 2-quinolate, b.p. 120—122°/0·3 mm, n_D^{20}, 1·5969 (lit.,[20] 131—136°/0·3 mm, n_D^{20}, 1·5973). The ester was converted, also by the method of Campbell *et al.*,[20] into 2-acetylquinoline, m.p. 46° (lit.,[20] 47·5—48°, lit.,[21] 52°—we believe this latter value to be in error). 2-Acetylquinoline (14 g, 0·082 mol) was reduced by sodium borohydride in ethanol–water into 1-(2-*quinolyl*)-*ethyl alcohol* which was acetylated without further purification, with pyridine and acetic anhydride to give after normal work-up 1-(2-*quinolyl*)*ethyl acetate* (18·3 g, 47%, based on ketone), b.p. 96—100°/0·4 mm, n_D^{20}, 1·5708 (Found: C, 72·7; H, 6·1. Calc. for $C_{13}H_{13}NO_2$: C, 72·5; H, 6·1%).

1-(3-*Quinolyl*)*ethyl Acetate*.—3-Bromoquinoline (25 g, 0·12 mol) was treated with an excess of freshly prepared n-butyl lithium at −80° during 1 h. Acetaldehyde (excess) was added and the mixture was stirred for a further 1 h and allowed to come to room temperature. Hydrolysis and work-up gave crude 1-(3-*quinolyl*)*ethyl alcohol* which was acetylated directly as above. V.p.c. analysis indicated a wide variety of products in both alcohol and acetate. Fractional distillation of the crude acetate gave a fraction b.p. 100°/0·4 mm which was still contaminated with other products, especially 3-bromoquinoline and these could not be removed by further fractionation. Purification was affected by column chromatography using neutral Woelm alumina [22] and elution with chloroform–dichloromethane mixtures to give 1-(3-*quinolyl*)*ethyl acetate* (2 g; 7·5% based on bromo-compound) n_D^{20}, 1·5763 (Found: C, 72·4; H, 6·21%).

1-(4-*Quinolyl*)*ethyl Acetate*.—Quinoline-4-carboxylic acid (25 g, 0·145 mol) supplied by K and K Laboratories was converted into ethyl quinoline-4-carboxylate (23 g, 79%), b.p. 124°/0·9 mm by refluxing it with conc. sulphuric acid and ethyl alcohol (excess) during 5 h. This ester (15·5 g, 0·077 mol) was heated under reflux with a 5-fold excess of sodium ethoxide and ethyl acetate in toluene during 18 h. The progress of the reaction was followed by monitoring the disappearance of the ester by means of v.p.c. analysis. The crude sodium enolate obtained by removal of solvents under vacuum, was heated with excess of sulphuric acid (20%) during 2 h. Work-up gave crude 4-acetylquinoline (11 g, 83·5%) which was reduced to crude 1-(4-*quinolyl*)-*ethyl alcohol* and acetylated as above. Work-up and fractional distillation gave pure 1-(4-*quinolyl*)*ethyl acetate* (10 g, 72% based on ketone), b.p. 101°/0·2 mm, n_D^{20}, 1·5760 (Found: C, 72·8; H, 6·25%).

1-(5-*Quinolyl*)*ethyl Acetate*.—A Skraup reaction was carried out on 3-aminobenzoic acid (30 g, 0·22 mol), glycerol (50 g, 0·54 mol), sodium 3-nitrobenzenesulphonate (60 g, 0·27 mol), and 70% sulphuric acid (250 g); the reaction mixture was heated under reflux during 3 h according to the method of Bradfield *et al.*[23] Their work-up procedure was modified in that the precipitate obtained by the first addition of acetic acid was used directly for the preparation of pure ethyl quinoline-5-carboxylate (18 g, 41% based on aminobenzoic acid), b.p. 104—106°/0·4 mm, and the filtrate kept for preparation of ethyl quinoline-7-carboxylate (described below). This preparation was repeated a

* We thank Prof. J. Murrell and Dr. H. Benson for these calculations.

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number of times in order to obtain enough starting material for the 7-ester preparation.

Ethyl quinoline-5-carboxylate (33·5 g, 0·167 mol) was treated with a 5-fold excess of sodium ethoxide and ethyl acetate in toluene during 19 h with monitoring as for the 4-compound. Decomposition of the 5-enolate as above yielded *5-acetylquinoline* (11 g, 33·5%) which was reduced to *1-(5-quinolyl)ethyl alcohol* and acetylated as above. Work-up and fractional distillation gave pure *1-(5-quinolyl)-ethyl acetate* (10·4 g, 75%) b.p. 95°/0·4 mm, n_D^{20}, 1·5706 (Found: C, 72·8; H, 6·1%).

1-(6-Quinolyl)ethyl Acetate.—The method of Waley [24] employing the Skraup reaction was used to convert 4-aminobenzoic acid (55 g, 0·4 mol), 4-nitrobenzoic acid (42·6 g, 0·25 mol), ferrous sulphate (14 g), boric acid (24 g), glycerol (188 g, 2 mol), and concentrated sulphuric acid (70 ml) into crude quinoline-6-carboxylic acid (70 g, 54%). Esterification with sulphuric acid and ethanol as above gave ethyl quinoline-6-carboxylate (50 g, 61·5%), b.p. 136°/0·6 mm, lit.,[24] 130—150°/0·2 mm.

Ethyl quinoline-6-carboxylate (16 g, 0·08 mol) was converted into 6-acetylquinoline (6·5 g, 47·5%), b.p. 125°/0·5 mm (lit.,[24] 145°/2 mm) in the manner used for the 5-isomer. Sodium borohydride reduction of the ketone gave crude *1-(6-quinolyl)ethyl alcohol* which was acetylated directly as above to give after work-up and fractional distillation, *1-(6-quinolyl)ethyl acetate* (3 g, 36·5%), b.p. 104°/0·4 mm, n_D^{20}, 1·5812 (Found: C, 72·65; H, 6·3%).

1-(7-Quinolyl)ethyl Acetate.—The filtrate from the preparation of quinoline-5-carboxylic acid was extracted continuously with chloroform and the crude solid obtained by removal of the solvent was esterified as above. V.p.c. analysis of the ester product showed the presence of some of the 5-ester; fractional distillation with a 10-plate Vigreaux column gave pure ethyl quinoline-7-carboxylate (4 g, 9% based on 3-aminobenzoic acid), b.p. 108—112°/0·3 mm (lit.,[25] 145—150°/2 mm).

Ethyl quinoline-7-carboxylate (14 g, 0·07 mol) was heated under reflux with a 5-fold excess of sodium ethoxide and ethyl acetate in toluene during 13 h with v.p.c. monitoring as above. The crude enolate, after solvent removal, was heated with sulphuric acid (20%) during 3 h and normal work-up gave crude *7-acetylquinoline* (6·2 g, 52%). Sodium borohydride reduction of the ketone and work-up gave crude *1-(7-quinolyl)ethyl alcohol* which was acetylated as above to give after work-up and fractional distillation, pure *1-(7-quinolyl)ethyl acetate* (5 g, 64%), b.p. 100/0·3 mm, n_D^{20}, 1·5707 (Found: C, 72·3; H, 6·2%).

1-(8-Quinolyl)ethyl Acetate.—The Skraup method of Campbell *et al.*[26] was used to convert anthranilic acid (102 g, 0·75 mol), 2-nitrobenzoic acid (75 g, 0·45 mol), glycerol (250 g, 2·7 mol), and concentrated sulphuric acid (150 ml) into quinoline-8-carboxylic acid (60 g, 43%). The crude acid was converted into ethyl quinoline-8-carboxylate (20 g, 36%), b.p. 145°/0·8 mm (lit.,[26] 144—115°/0·5 mm) as above; the poor yield in the latter step was traced to insufficient cooling, and conditions which were too alkaline in the work-up procedure, so that the ester was partly hydrolysed back to the sodium salt of the acid. The ester was converted as for the 7-isomer into *8-acetylquinoline* (8·5g, 50%), b.p. 118°/0·5 mm and this was reduced with sodium borohydride to crude *1-(8-quinolyl)ethyl alcohol* which was acetylated as above to give after work-up and fractional distillation, pure *1-(8-quinolyl)ethyl acetate* (8·3 g, 77%), b.p. 100°/0·4 mm, n_D^{20}, 1·5720 (Found: C, 72·25; H, 6·1%).

The kinetic technique has been described in earlier papers in this series. Contrary to our earlier observations,[3] studies with the pyridine esters gave good first-order kinetics to at least 95% of reactions (80% before). We previously proposed that departure from linearity in the earlier work arose from significant decomposition of the acetic acid byproduct in the time taken for the primary elimination of these unreactive compounds. This cannot have been the case, and we now believe it to have been due to a small leak in the injection valve of the earlier apparatus so that traces of fresh compound were admitted to the reaction chamber during a run. However it should be noted that the k_{rel} values obtained in both sets of work (and determined in the earlier work from the first portions of the runs only) agree within experimental error, consequently only an insignificant error was introduced into the earlier work and all of the previous conclusions remain entirely valid.

Kinetic studies were carried out over a 50° range for each compound except the 8-isomer, the reaction products from which showed a tendency to polymerise at lower temperatures, so that accurate first-order kinetics could not be obtained for this compound below 360°. (This polymerisation tendency has been noted previously with other compounds at lower temperatures.[4,27]) A greater number of kinetic runs were, therefore, carried out with the 8-isomer than for the other compounds, in the temperature range 362—399° where this polymerisation was not a problem.

Calculations of π-electron densities and localisation energies were carried out on the University of Sussex ICL 1905 Computer using the parameters described previously.[3]

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