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The Synthesis and Physical Properties of Some 2-Alkylthio-4-oxoquinoline-3-carboxylate Esters

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Anilino(alkylthio)malonates, readily available by alkylation of the anions formed by the addition of malonate ions to isothiocyanates, have been found to undergo smooth cyclisation, upon being heated in o-dichlorobenzene, to give the title compounds in moderate to good yields. In certain cases the compounds so prepared may be isolated in the 4-quinolinol or 4-quinolone forms, this tautomeric behaviour depending on factors which include the solvent of crystallisation, the temperature of the sample, and the steric bulk of the 2-alkylthio-substituent. In solution this tautomerism has been studied spectroscopically, and in the solid state by means of differential-scanning calorimetry. Certain unusual features in the spectroscopy of these compounds are discussed.

THERE has been an increased interest recently in the preparation and properties of the thioamides formed by the addition of carbanions to isothiocyanates, and this reaction has formed the subject of a review.¹ Thus Barnikow and Kunzek,² following the work of Ross,³ have described the formation of the anions (I) by the addition of diethyl sodiomalonate to arylisothiocyanates which on alkylation give rise to the anilino(alkylthio)malonates (II; $X = Y = CO_2Et$). Gompper and Töpfl⁴ have prepared some related 1-cyanoacrylates (II; X = CN, $Y = CO_2Et$) and, for one case (II; Ar =Ph, R = Me, X = CN, $Y = CO_2Et$), have shown that with hot phosphorus oxychloride, this cyclised with chlorination to give a low yield of 4-chloro-3-cyano-2-methylthioquinoline (III).

We now report a general synthesis of 2-alkylthio-4-oxoquinoline-3-carboxylic esters (IV) formed in moderate to good yields under mild conditions by brief heating of compounds of type (II) in o-dichlorobenzene; further-

¹ W. Walter and K. D. Bode, Angew. Chem. Internat. Edn., 1966, 5 (5), 447.

more, we describe the unexpected tautomeric behaviour of certain members of this series.

The sodium salts of (I; $X = Y = CO_2Et$) were prepared using slight modifications of the procedure described by Ross.³ The reaction of these in dimethylformamide with alkyl or aralkyl halides gave compounds of type (II), which were often oils or low-melting solids difficult to purify; their direct conversion into the quinolones [(VI); see Table 5] was effected by heating o-dichlorobenzene solutions of them for one hour.

The reaction of (IV; $R^1 = H$, $R^2 = Et$, $R^3 = Me$) with acetic anhydride in pyridine afforded the O-acetate (V; X = OAc), and the reaction of (IV; $R^1 = H$, $R^2 = Et$, $R^3 = Me$) with phosphorus oxychloride gave (V; X = Cl) (cf. ref. 4).

Tautomerism.—When compound (VII) is dissolved in carbon tetrachloride, it shows ν (C=O) at 1653 cm.⁻¹ and other strong bands at 1621, 1582, and 1558 cm. $^{-1}$; the solid isolated from this solution has a similar i.r. spectrum. Isolated from methanol, however, it shows

² G. Barnikow and H. Kunzek, Annalen, 1967, 700, 36.

 ³ J. Ross, J. Amer. Chem. Soc., 1933, 55, 2672.
 ⁴ R. Gompper and W. Töpfl, Chem. Ber., 1962, 95, 2871.

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bands (other than aromatic) at 1721, 1695, 1647, 1575, and 1522 cm.⁻¹. Similarly, its u.v. spectra in methanol and cyclohexane (from which the former solid



crystallises) are quite distinct (Figure 1a). The process is completely reversible and analysis of the i.r. spectra (Tables 1 and 3) clearly shows it to be tautomeric; the first is the enol, the second the keto-form.

TABLE 1

Salient bands (cm.⁻¹) from the i.r. spectra of compounds in the quinolinol form (solutions in CCl_4) *

		(v,	Assign-
a) (IXa)	(Xa)	X = OAc)	ments
3000br	3000br		$\nu(OH)$
		1789s	Acetyl
			ν (C=O)
1650s	1653s	1730s	Ester
			ν (C=O)
s 1621ms	1621ms	1621m	Aromatic
s 1582s	1582s	1590ms	ν (C=C)
s 1560ms	$1560 \mathrm{ms}$	1555m	ν (C=N)
1486ms	1486ms	1486m	Aromatic
1450m	1451m	1453 mw	Aromatic
1412ms	1412 ms		δ(OH)
1353ms	1353m	1370ms	$\nu(COR)$
s 1236vs	1236vs		v(COH)
		1236s	$\nu(COAc)$
w 1205mw	1200 mw	1200 sh	sk
		1185vs	v(COAc)
1016m	1014m	1027m	$\nu(OR)$
d, $s = stron$	g, m = me	edium, w = ·	weak, sh =
skeletal. $v =$	= verv.	-	-
	 (IXa) 3000br 1650s s 1621ms s 1582s s 1582s s 1560ms 1486ms 1450m 1412ms 1353ms s 1236vs w 1205mw 1016m d, s = stron skeletal, v = 	 (IXa) (Xa) 3000br 3000br 1650s 1653s 1621ms 1621ms 1582s 1582s 1580ms 1560ms 1486ms 1486ms 1450m 1451m 1412ms 1412ms 1353ms 1353m 1236vs 1236vs w 1205mw 1200mw 1016m 1014m d, s = strong, m = me skeletal, v = verv. 	t) (IXa) (Xa) $X = OAc$) 3000br 3000br 1789s 1650s 1653s 1730s s 1621ms 1621ms 1621m s 1582s 1582s 1590ms s 1560ms 1560ms 1555m 1486ms 1486ms 1486m 1450m 1451m 1453mw 1412ms 1412ms 1353ms 1353m 1370ms s 1236vs 1236vs w 1205mw 1200mw 1200sh 1185vs 1016m 1014m 1027m d, s = strong, m = medium, w = skeletal, v = verv.

Most of the other compounds behave similarly. It is always true that the enol and keto-forms are those stable in carbon tetrachloride and methanol respectively, but the position as to the solid state is variable.

TABLE 2

Salient bands (cm. ⁻¹) from the i.r. spectra of (VI	Ia)
in its OH and OD forms (solutions in CCl_4)	

਼ਰਸ	OD	Assignments
20001	0170h-	(OH)
30000r	21700r	V(OL)
1653s	1647 s	ν (C=O)
1621ms	1616m	Aromatic
1582s	1555ms	$\nu(C=C)$
1558ms	1560 sh	$\nu (C=N)$
1486ms	1484m	Aromatic
1449m	1449 m	Aromatic
1351 ms	1300m	$\nu(COR)$
1412s		$\delta(OH) + \nu(COH)$
	1323vs	$\nu(COD)$
1236vs		ν (COH) + δ (OH)
	1253 ms	$\delta(OD) + sk$
1203m		sk
	1050m	$slr \perp \delta(OD)$
	1000111	SK -T- U(OD)
1016m	1019m	$\nu(OR)$

Generally, either form may be isolated by choosing the appropriate solvent, but this is not always so. The matter has been investigated by means of differentialscanning calorimetry (d.s.c.). When solid (VII), as



FIGURE 1 U.v. spectra taken in cyclohexane (A) and methanol (B) for: (a) (VII), (b) (IX), (c) (X), and (d) (V; X = OAc)

isolated from methanol, is heated, it absorbs some heat at 82° but much more at 117° ; this corresponds to the observed m.p. Above this, its i.r. spectrum shows it to exist as the enol, and upon being cooled until it crystallises, it remains in this form. On being heated again it

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melts at 82° , so that this and 117° are the m.p.'s of the quinolinol and quinolone forms respectively. The original, minor endotherm at 82° indicates that a small amount of the quinolinol form is present initially; its ability to melt substantially without depression is evidence, consistent with the separate m.p.'s, for the presence of a considerable energy barrier for the interconversion of the two forms in the solid state. It is too rapid in solution, however, to be observed. A précis of the d.s.c. trace of (VII) is reproduced in Figure 2; compound (VIII) behaves in the same way.

(e.g. Figure 1c) and i.r. spectra respectively. Table 4 summarises the position so far as it is known.

I.r. Spectroscopy.—The i.r. spectra of the enol forms (Table 1) possess four bands of very similar strength in the 6 μ region (see Figure 4). The band near 1650 cm.⁻¹ is v(C=O) and another, at 1621 cm.⁻¹, is aromatic in origin; it occurs unchanged in the keto-forms. The other two, near 1580 and 1550 cm.⁻¹, are considered as due to the essentially localised C=C and C=N vibrations of the pyridine ring. They are assigned on the basis of deuteriation studies (Table 2) which show that the

	Salier	nt bands (cr	n. ⁻¹) from tl	ne i.r. spect	ra of compo	unds in the	e quinolone f	orm (Nujol)
(VIIb)		(VIIc)	(VIIIb)		(VIIIc)	(IXb)		(IXc)	Assignments
	3185m		. ,	3190m	. ,	. ,	$3185 \mathrm{mw}$. ,	٧NH
1695ms	1647mw 1621ms 1603w	1721s	1710sh	1655vw 1620m 1602w	1724s	1710sh	(1647) <i>ª</i> 1621ms 1597m	1727s	Ester ν (C=O) Ring ν (C=O) Aromatic Aromatic
1522ms	1493m 1441m	1575vs	$1535 \mathrm{sh}$	$1502 \mathrm{ms}$ $1438 \mathrm{m}$	1560vs	1534w	1508s 1439m	1560s	ν(C=C) Aromatic Aromatic
$1330 \mathrm{ms}$	1031m	1344ms	?	1027m 4	1344ms In MeCN.	?	1027m	1344ms	$ \frac{\nu(\text{COR})}{\nu(\text{OR})} $

TABLE 3

Certain compounds show a quite different pattern. The keto-form of (IX) melts to give the enol but reverts slowly as the melt is supercooled (Figure 3): the whole process has been followed by i.r. examination (Figure 4).



FIGURE 2 Trace (d.s.c.) of (VII) followed through a complete cycle of heating, cooling, and re-heating (same sample throughout)



FIGURE 3 Trace (d.s.c.) of (IX) followed through a complete cycle of heating, cooling, and re-heating (same sample throughout)

When crystallisation of the melt is induced by scratching, the keto-form exclusively results. At the other extreme, certain compounds, such as (VI) and (X), remain in the quinolinol form throughout, and cannot be isolated as the quinolone either from methanolic or acetonitrile solution despite their indubitable existence as such in these solvents, as shown by their u.v. spectra v(C=O) and the 1580 cm.⁻¹ bands fall in frequency, whereas the other two do not. Since the C=C linkage is part of a *quasi*- β -diketone chelate ring, it is reasonable

FIGURE 4 I.r. spectrum of (IX) in the melt as a function of temperature (uncalibrated): (A) above m.p., (B) near room temperature

that v(C=C) rather than v(C=N) should be affected. The same two bands are found in (V; X = OAc) as well (Table 1). Deuteriation also allows $\delta(OH)$, v(COH), and a skeletal vibration, probably ester v(CC),

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to be identified. The complex coupling pattern which these compounds show will be discussed elsewhere.⁵ The unusual positions of the $\nu(COR)$ vibrations may probably be ascribed to the fact that, here, the alkoxy-radical is less part of an ester group than a

TABLE 4

Tautomers	present under various conditions	:
	e = enol, k = keto	

	a	MeOH			
Compound	in solid state	Crystals	Solution	solution	
(VI)	e	е	k	е	
(VII)	e	k	k	е	
(VIII)	е	k	k	е	
(IX)	k	k	k	е	
(\mathbf{X})	e	е	k	е	
	Also	o cyclohexa	.ne.		

substituent in a chelated β -diketone ring; at least one rather similar situation has previously been encountered.⁶ None of the other assignments calls for comment.

The keto-forms (Table 3) possess several features of unusual interest. Discounting aromatic vibrations, which are largely identical with those of the enol tautomers, there are five bands in the 6 μ region, not the three that might have been anticipated. Not all are resolved in every compound, but (VII) shows them clearly. Here there are two pairs of strong bands near 1720 and 1550 $cm.^{-1}$ and between these a weak band at 1647 cm.⁻¹. This last is assigned to the ring v(C=O) vibration since that of (XV) is at 1634 cm.⁻¹; its position is normal for a 4-quinolone.⁷ The others are assigned to ester ν (C=O) and ring v(C=C) respectively. Their occurrence in pairs we consider evidence for the co-existence in the solid state of (VIIb) and (VIIc), the s-trans and s-cis isomers. It is known⁸ that the *s*-trans forms of saturated ketones are thermodynamically the more stable, so that isomer (b) should normally be preferred, but here the 2-substituent is a potential source of steric hindrance which will increase as \mathbb{R}^2 becomes bulkier. Consistent with this theory, the lower frequency band of each pair diminishes in intensity as the series is ascended, until with (IX), where R^2 is a branched-chain alkyl group, isomer (c) predominates almost to the exclusion of the other. The simple "parent compound" (XIII) has bands at 1740s and 1564vs cm.⁻¹, with no sign of doubling, and so, presumably, exists entirely as the s-trans isomer.

The great strength of v(C=C), much the strongest band in the spectrum, is a characteristic feature of enamino-ketones,⁹ and the weakness of ring v(C=O) is also not without precedent.¹⁰ In (IX) it is almost This reversal of the normally expected invisible. intensities for v(C=O) and v(C=C) is common in enaminoketones, and one of us ⁶ has recently discussed the reasons for this with particular reference, inter alia, to 4-pyridone. These compounds carry that tendency to extremes. In compound (XIII) the ring v(C=O) band at 1625 cm.⁻¹ (Nujol) is of moderate strength, so the S-alkyl group may play some part in its abnormally low intensity elsewhere.

Deuteriation of the keto-forms has not been attempted since their easy reversion to the enol tautomer might make the results equivocal. In consequence, $\delta(NH)$ has not been positively identified.

U.v. Spectroscopy.—The quinolinol and quinolone spectra show the same type of relative frequencyshift reported previously.¹¹ No good models exist for a closer comparison. The one point of interest concerns the spectrum of (IX) in methanol, where the band near 270 m μ is abnormally weak (Figure 1b). Possibly the ester carbonyl is forced out of the plane of the ring by steric interaction with the S-isopropyl group sufficiently for appreciably diminished conjugation to result; molecular models show some hindrance to exist. No such effect is visible, however, in the solid state i.r. spectrum (Table 3) and the u.v. spectrum of (IXa) in cyclohexane is quite normal.

DISCUSSION

Hydroxy-pyridines generally exist, when possible, as pyridones, and the corresponding quinolines are expected to behave similarly.¹² Exceptions are known: ¹³ Katritzky^{13a} has found up to 70% of the enol-form to exist at equilibrium in aqueous solutions of some 4-pyridones containing electronegative substituents in the 2-position, but similar substitution in the 3-position has little effect. Katritzky has explained this difference in terms of proximity to the oxygen and nitrogen atoms: a 2-substituent disproportionately affects nitrogen basicity, whereas in the 3-position the effects on nitrogen and oxygen cancel. We believe the situation to be more complex than Katritzky's analysis so far reveals: we find, for example, that while (XIII) exists exclusively in the quinolone form under all conditions examined, (XIV) is present mostly as the quinolinol in acetonitrile solution (though not in the solid state). This difference must hinge on the greater electronegativity of the nitrile group.¹⁴ It is not to be explained as the result of intramolecular hydrogen bonding,

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¹¹ G. F. Tucker and J. L. Irvin, J. Amer. Chem. Soc., 1951, 73, 1923.

¹² A. R. Katritzky and J. M. Lagowski, Adv. Heterocyclic Chem., 1963, 7, 339.

¹³ (a) A. R. Katritzky, J. D. Rowe, and S. K. Roy, J. Chem.
 Soc. (B), 1967, 758; (b) J. M. Hearn, R. A. Morton, and J. C. E.
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⁵ I. T. Kay, G. A. Cockayne, and P. J. Taylor, to be published.

⁶ P. J. Taylor, Spectrochim. Acta, submitted for publication. ⁷ J. R. Price and J. B. Willis, Austral. J. Chem., 1959, **12**,

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⁸ R. Mecke and K. Noack, Spectrochim. Acta, 1958, 12, 391; F. H. Cottee, B. P. Straughan, C. J. Timmons, W. F. Forbes, and R. Shilton, J. Chem. Soc. (B), 1967, 1146. ⁹ See, inter alia, N. H. Cromwell, F. A. Miller, A. R. Johnson,

R. L. Frank, and D. J. Wallace, J. Amer. Chem. Soc., 1949, 71, 3337; B. Witkop, *ibid.*, 1956, 78, 2873; J. Dabrowski, Spectrochim. Acta, 1963, 19, 475.

known ^{13b} in the parallel case of 4-hydroxyquinoline-3-carboxylic acid to stabilise the enol-form, since in (XIV) such bonding is impossible. However, it must be conceded that 2-substitution is the more effective. While (XIII) remains in the quinolone form, despite its markedly electronegative 3-substituent, addition in (VII) of the only mildly electronegative S-methyl group is enough to tip the balance. It may be surmised that a more strongly electronegative 2-substituent might suppress quinolone formation altogether.

These results also provide good evidence that intramolecular hydrogen bonding, if a minor factor in determining how substituents affect the equilibrium, may still dominate its phase-dependence in borderline cases. Other things being equal, solvents that cannot form hydrogen bonds should favour the enol tautomer; the results of Table 4 are readily explained this way.

In addition to equilibria, rates must be considered. All the facts, bar one, will fit a simple hypothesis: the bulkier the S-alkyl substituent, the longer it takes for the tautomeric equilibrium to be established. Thus, while (VII) and (VIII) will crystallise from methanol in the metastable keto-form, the less-hindered (VI) comes out as the quinolinol; tautomerisation rate is faster here than rate of crystallisation. (However, it has not proved possible to observe tautomerisation taking place in solution.) In one case, (IX), steric hindrance in the

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However, since n.m.r. is a ground-state process the excited state should reflect this even more, so that its u.v. spectrum should show substantial changes. None are visible (Figure 1c) unless the considerably enhanced intensity of the band near 270 m μ in the quinolinol form is counted, a point of doubtful significance. The *para*-substituted derivatives (XI) and (XII) have been synthesised on the hypothesis that, if electron "leakage" occurs in (X), it should be enhanced in (XI) and retarded or removed in (XII). In fact, their tautomeric behaviour is similar. This phenomenon is not understood.

EXPERIMENTAL

The following procedure for compound (IV; $R^1 = H$, $R^2 = Et$, $R^3 = Me$) illustrates the general method employed for the preparation of the 4-quinolones described in Table 5.

Diethyl Anilino (methylthio)malonate (II; Ar = Ph, R = Me, $X = Y = CO_2Et$).—To a stirred suspension of sodium hydride (14.5 g., 50% dispersion in oil) in anhydrous ether (500 ml.) was added diethyl malonate (48 g.) dropwise during 30 min. Phenyl isothiocyanate (40 g.) was then added dropwise with stirring during 30 min. after which the mixture was heated under reflux for 1 hr. and then kept overnight at room temperature. The solid was separated, washed with anhydrous ether (400 ml.), and dried *in vacuo* to yield the sodium salt of (I; Ar = Ph, $X = Y = CO_2Et$) as a pale yellow powder (88 g.).

TABLE 5

Analytical and other data for compounds of type (IV)

Compound (IV)		Vield Cryst				Found (%)			Required (%)			
R1	R ²	R³	(%)	M.p.	solvent "	Formula	ĉ	H	N	ć	H	N
н	Me	Me	67	98—100°	LP	C ₁ ,H ₁ ,NO ₃ S	58.0	4.7	5.55	57.85	4.4	5.6
н	\mathbf{Et}	Me	78	116-118	E	C ₁₃ H ₁₃ NO ₃ S	59.1	4.95	5.25	59.3	4.95	5.35
н	\mathbf{Et}	Et	75	104 - 105	Е	C ₁₄ H ₁₅ NO ₃ S	60.8	5.55	5.05	60.65	5.4	5.05
н	Et	Pr ⁿ	66	116 - 117	E	C ₁₅ H ₁₇ NO ₃ S	62.1	6.05	4.6	61.85	5.85	4.8
н	Et	Pri	59	128 - 130	E	C ₁₅ H ₁₇ NO ₃ S	61.6	6.0	4 ·9	61.85	5.85	$4 \cdot 8$
\mathbf{H}	Et	Bu ⁿ	40	88-89	E	C ₁₆ H ₁₉ NO ₃ S	63.3	6.35	4.45	$62 \cdot 95$	6.25	$4 \cdot 6$
н	\mathbf{Et}	Bui	60	125 - 126	E	$C_{16}H_{19}NO_{3}S$	$62 \cdot 9$	6.25	4 ·6	62.95	6.25	$4 \cdot 6$
н	Et	$C_{8}H_{17}^{n}$	50	36 - 37	E	C ₂₀ H ₂₇ NO ₃ S	66·4	7.4	3.9	66.5	7.5	$3 \cdot 9$
н	Et	–ČH, Ph	67	92 - 93	E	C ₁₉ H ₁₇ NO ₃ S	67.1	5.3	3.95	67.15	$5 \cdot 0$	4.1
н	Et	CH₃Č₄H₄Cl-⊅	34	100 - 102	E	C ₁₉ H ₁₆ CINO ₃ S	60.9	4.3	3.45	61.3	$4 \cdot 3$	3.75
н	Et	CH _a C _a H _a ·NÔ _a -p	44	149 - 150	E-B	C ₁₉ H ₁₆ N ₂ O ₅ S	59.5	4.25	7.35	59.35	$4 \cdot 2$	7.3
н	Et	CH _a C _a H _a ·OMe-p	50	91	E	C ₂₀ H ₁₉ NO ₄ S	65.3	$5 \cdot 1$	3.95	65.05	5.15	$3 \cdot 8$
MeO	Et	Me	75	109 - 110	LP	C14H15NO4S	57.7	5.15	4 ·8	57.35	$5 \cdot 1$	4 ⋅8
MeO	Et	Et	70	120 - 121	E	C ₁₅ H ₁₇ NO ₄ S	58.7	5.65	4.45	58.65	5.55	4.55
MeO	Et	Bu ⁱ	66	105 - 106	E	C ₁₇ H ₂₁ NO ₄ S	61.3	6.3	4 ·0	60.9	6.25	$4 \cdot 2$
MeO	Et	-CH.Ph	50	111 - 112	E	C ₂₀ H ₁₀ NO ₄ S	64.8	$5 \cdot 0$	3.7	65.05	5.15	$3 \cdot 8$
MeO	Et	CH.C.H.Cl-b	61	155 - 156	E-B	C ₂₀ H ₁₀ CINO ₄ S	59.6	4.55	$3 \cdot 4$	59.5	4.45	3.45
C1	Et	Me	55	136 - 138	B-LP	C ₁₃ H ₁₂ CINO ₃ S	$52 \cdot 4$	4.15	4.8	$52 \cdot 45$	4.05	4 ·7
		<i>•</i> LP =	= Light p	etroleum (b.p	. 60—80°).	, $E = ethanol$, E	3 = be	nzene.				

crystal is so extreme that (IXc) is the stable tautomer; there is little of (IXb), and (IXa) is present only in the melt (Figure 4). The exceptional compound is (X). This behaves as (VI), *i.e.*, as if as little hindered as when $R^1 = R^2 = Me$, which, since $R^2 = CH_2Ph$, is unexpected. There is a peculiarity in its n.m.r. spectrum, namely that the phenyl-ring signal instead of being a singlet is a complex multiplet, which suggests an abnormal polarisation of its π -electrons towards the quinoline ring. This, if it happens, could lower the energy of the interconversion process and so account for its rapidity. To this salt (10 g.) dissolved in dimethylformamide (30 ml.) was added methyl iodide (6 ml.) with stirring. Following the mild exothermic reaction, the mixture was then kept overnight at room temperature. The addition of water followed by extraction into ether gave, after drying (MgSO₄) and removal of the solvent, the crude *product* (9.5 g.) as a pale yellow oil which, with time, solidified, m.p. 54—56° (lit.,³ 58°).

Ethyl 2-Methylthio-4-oxo-1,4-dihydroquinoline-3-carboxylate (VII; $R^1 = Et$, $R^2 = Me$) = (IV; $R^1 = H$, $R^2 = Et$, $R^3 = Me$).—The above crude ester (13 g.) in o-dichlorobenzene (40 ml.) was heated under reflux for 1 hr. The o-dichlorobenzene was removed under reduced pressure to afford the product as a pale yellow liquid which rapidly solidified on being scratched with a glass rod. Crystallisation from ethanol gave the *product* (8.7 g., 78%), in the quinolone form, as prisms, m.p. 116---118°. Alternatively, crystallisation from light petroleum (b.p. 60---80°) of the crude product, following the removal of the o-dichlorobenzene, gave the product in the quinolinol form as needles, m.p. 83---85° (Found: C, 59.1; H, 4.95; N, 5.25. C₁₃H₁₃NO₃S requires C, 59.3; H, 4.95; N, 5.35%); τ (CDCl₃) --3.2 (1H, s), 1.8---2.7 (4H, complex multiplet), 5.54 (2H, quartet, J 7.5 c./sec.), 7.46 (3H, s), and 8.53 (3H, t, J 7.5 c./sec.); u.v. spectrum as shown on Figure 1a; i.r. spectrum as shown in Tables 1---3.)

Ethyl 4-Acetoxy-2-methylthioquinoline-3-carboxylate (V; X = OAc).—To the foregoing quinolone (2.63 g.) in anhydrous pyridine (10 ml.) was added acetic anhydride (3 ml.) and the mixture, protected from moisture, was kept overnight at room temperature. The addition of water (50 ml.) then gave the product which was collected and washed with water. Crystallisation from ethanol gave the product as plates (2.2 g.), m.p. 101—102° (Found: C, 59.2; H, 4.85; N, 4.4; C₁₅H₁₅NO₄S requires C, 59.1; H, 4.95; N, 4.6%); u.v. spectrum as shown on Figure 1d).

Ethyl 4-Chloro-2-methylthioquinoline-3-carboxylate (V; X = Cl).—A mixture of (VII) (9 g.) with phosphorus oxychloride (30 ml.) was heated on a steam-bath for 1 hr. The solution was set aside to cool to room temperature and then it was slowly, and with stirring, poured onto crushed ice; the solution was basified with ammonium hydroxide, and then extracted into chloroform (50 ml.). Removal of the chloroform and distillation of the residue afforded the product (b.p. $165^{\circ}/0.8$ mm.) as an oil which slowly solidified, m.p. $41-42^{\circ}$ (Found: C, $55\cdot2$; H, $4\cdot3$; Cl, $11\cdot3$; N, $4\cdot7$. $C_{13}H_{12}ClNO_2S$ requires C, $55\cdot4$; H, $4\cdot25$; Cl, $11\cdot35$; N, $4\cdot95\%$).

¹⁵ C. C. Price, N. J. Leonard, and H. F. Herbrandson, J. Amer. Chem. Soc., 1946, **68**, 1251.

3-Cyano-1-methyl-4-oxo-1,4-dihydroquinoline (XV).—To compound (XIV) (0.34 g.) in N-sodium hydroxide (5 ml.) was added dimethyl sulphate (0.24 g.) after which the suspension was shaken for 1 hour at room temperature. The solid was separated, washed with water, and crystallised from ethanol to give the *product*, m.p. 252° (Found: C, 70.85; H, 4.5; N, 15.0. C₁₀H₆N₂O requires C, 71.7; H, 4.35; N, 15.2%); *m/e* 170 with prominent loss of CO; λ_{max} . (MeOH) 215, 248, 256, 305inf, 317, and 330 mµ (log ϵ 4.51, 4.23, 4.20, 4.07, 4.13, and 4.10); n.m.r. shows only one peak for Me.

Physical Measurements.—Spectra were run on a Perkin-Elmer model 21 i.r. spectrophotometer, a Perkin-Elmer 137 UV u.v. spectrophotometer, and a Varian A60 n.m.r. spectrometer. I.r. spectra of melts were examined by melting a crystal of the compound between heated NaCl plates; the holder was heated electrically by way of a rheostat but its temperature was not known. Deuteriations were carried out by shaking carbon tetrachloride solutions with an equal volume of deuterium oxide for up to 24 hr.; the organic layer was removed and examined at once without drying. Calorimetry was performed on 5-mg. samples in a Perkin-Elmer model DSC-1B differential scanning calormeter at a rate of $8^{\circ}/min$. with nitrogen flushing.

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¹⁶ B. Riegel, G. R. Lappin, B. H. Adelson, R. I. Jackson, C. J. Albisetti, R. M. Dodson, and R. H. Baker, J. Amer. Chem. Soc., 1946, **68**, 1264.