564. *Heterocyclic Syntheses with Malonyl Chloride. Part VII.* Dihydropyrano[3,4-e]-1,3-oxazines from Isocyanates, and their Degradation to Dihydro-2,4-dioxo-1,3-oxazines and thence Conversion into Pyridones.*

By M. Aslam Butt, J. A. Elvidge, and Arthur Brian Foster.

Isocyanates with malonyl chloride yield 3-substituted 7-chloro-3,4-dihydro-2,4,5-trioxo-2*H*,5*H*-pyrano[3,4-*e*]-1,3-oxazines (II; X = O). Phenyl isothiocyanate yields the 4,5-dioxo-3-phenyl-2-thio-compound (II; R = Ph, X = S).

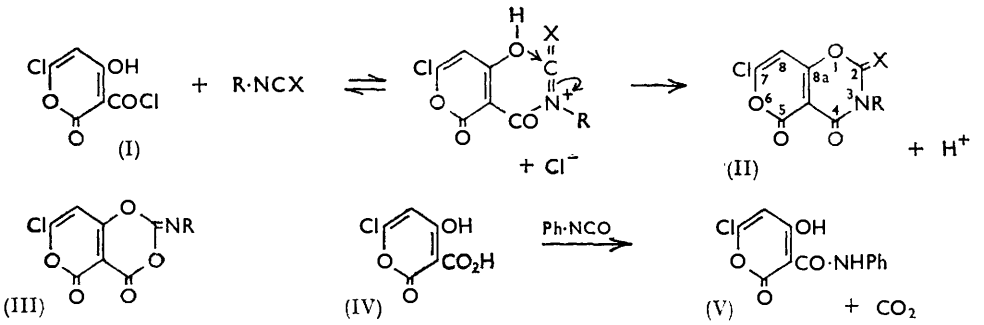
Alcohols open the chloropyrone ring of the new bicyclic compounds (II; X = O) and give derivatives of 3,4-dihydro-2,4-dioxo-2*H*-1,3-oxazine (VI). These are isomerisable by alkoxide to 1-substituted dialkyl 1,2-dihydro-4,6-dihydroxy-2-oxopyridine-3,5-dicarboxylates (IX), but aqueous alkali yields the corresponding monoesters (XII). The dihydrodioxo-oxazines (VI) react further with alcohol to give diester anilides of acetone-1,1,3-tricarboxylic acid, (VII) and (VIII), which are cyclised by alkali to hydroxypyridones (X) and (XII). The dihydroxypyridone ester (XII; R = Ph, R′ = Et) was converted into the 4,6-dichloropyridone ester (XIII; R = Ph, R′ = Et) and thence by alkaline hydrogenolysis into 1-phenylpiperidone.

Ultraviolet and infrared absorptions and proton magnetic resonance results provided information about the fine structures of some of these potentially tautomeric compounds.

The condensation reactions of malonyl chloride with ketones [1,2] and with nitriles [3,4] appeared capable of extension to other classes of compound. Here we describe the condensation of isocyanates and of phenyl isothiocyanate with malonyl chloride. Chlorodihydro-oxopyrano-1,3-oxazines (II; X = O or S) are formed.

From these new heterobicyclic compounds, we have prepared dihydrodioxo-oxazines (VI), monoamide diesters of acetonetricarboxylic acid, (VII) and (VIII), and the 4,6-dihydroxy-2-pyridone derivatives (IX), (X), and (XII).

Chlorodihydro-oxopyrano-oxazines (II).—When malonyl chloride was heated with phenyl isocyanate, hydrogen chloride was evolved and a crystalline product $C_{13}H_6ClNO_5$



was formed, evidently by the overall process $2CH_2(COCl)_2 + Ph{\cdot}NCO - 3HCl$. The same product arose (with hydrogen chloride) when the chloropyrone acid chloride [2] (I) was heated with phenyl isocyanate.

* Part VI, *J.*, 1962, 3638.

[1] Davis and Elvidge, *J.*, 1952, 4109.
[2] Elvidge, *J.*, 1962, 2606.
[3] Davis and Elvidge, *J.*, 1962, 3553.
[4] Davis, Elvidge, and Foster, *J.*, 1962, 3638.

The close analogy with the behaviour of ketones [1,2] and nitriles [3] made it probable that the new product was bicyclic and that it was formed from malonyl chloride in two main stages, the first being the formation of the pyrone acid chloride (I) (cf. ref. 2), induced by the weakly basic isocyanate. The second stage conceivably proceeded through acylation of either the nitrogen or the oxygen atom of the isocyanate to yield, as product, (II) or (III). Neither the infrared nor the ultraviolet light absorption of the product was structurally diagnostic (Tables 2 and 3), but subsequent degradation with alcohols excluded structure (III). For the second stage, therefore, the process (I) ⟶ (II) is favoured.

The alternative direction of cyclisation for the reaction (I) ⟶ (II), involving the 4-urethane of (I) as an intermediate, appeared unlikely because a urethane was not obtained from the hydroxypyrone acid (IV) with an excess of phenyl isocyanate. Instead,

TABLE 1.

Spectroscopic data for the pyrones (V) and (IV).

(i) Ultraviolet		(ii) Infrared (5—6·7 μ)		(iii) Proton magnetic resonance		
$\lambda_{max.}$ (mμ)	$10^{-3}\varepsilon$	Max. (cm.$^{-1}$)	Assignment	τ	Intensity	Assignment
			Compound (V)			
310	15·2	1711	O=C (2,H-bonded)	3·75	1	H (5)
				2·9—2·1	5	Ph
		1629	O=C, (at 3, ,,)	−0·62b	1	HN (bonded)
		1602, 1500	C=C	−6·96	1	HO (4, ,,)
		1538b	C=C + amide-II			
			Compound (IV)			
304	10·1	1717	O=C (2,H-bonded)	3·57	1	H (5)
		1676	O=C (at 3, ,,)	−1·50b	1	HO_2C (bonded)
		1621, 1554, 1527sh	C=C	−4·25	1	HO (4, ,,)

(i) In EtOH (ii) As a Nujol mull (iii) 10% in $CDCl_3$ + 0·5% $SiMe_4$

TABLE 2.

Ultraviolet absorption max. in mμ (with $10^{-3}\varepsilon$ in parentheses).

Chlorodihydro-oxopyrano-oxazines (II) (in dioxan)

X = O, R = Ph	238 (6·9),	317 (8·3)
,, R = Me		315 (9·3)
,, R = Et		315 (9·0)
,, R = α-$C_{10}H_7$	282 (8·8),	293 (9·9), 317 (11·3)
X = S, R = Ph	233 (12·3),	279 (20·8), 322 (7·1)

Dihydrodioxo-oxazines (VI) (in dioxan)

X = O, R = Ph, R′ = Et	236 (6·9)
,, ,, R′ = Me	238 (7·6)
,, R = α-$C_{10}H_7$, R′ = Et	270 (7·2), 280 (7·2)
,, ,, R′ = Me	272 (6·6), 282 (7·2)
X = S, R = Ph, R′ = Et	275 (22·0)
,, ,, R′ = Me	279 (17·6)

Enol ethers (in ethanol)

(VII; R′ = Et)	242 (30·7)
(VII; R′ = Me)	244 (24·5)

Enols (in ethanol)

(VIII; R′ = Et and Me)	244, 284
(XVIII)	244 (20·0) 282 (22·7)

Copper(II) derivatives of enols (VIII) (in ethanol)

R′ = Et	288 (47·3)
R′ = Me	288 (49·0)

2-Pyridones (in dioxan)

(IX; R = Ph, R′ = Et)	265 (17·7),	297 (16·4)
(,, ,, R′ = Me)	265 (17·5),	299 (15·6)
(,, R = α-$C_{10}H_7$, R′ = Et	265 (21·8),	300 (20·5)
(,, ,, R′ = Me)	268 (19·8),	294 (19·0)

2-Pyridones (in ethanol)

(X; R = Ph, R′ = Et and Me)		282 (21·0)
(XII; R = Ph, R′ = Et)		305 (18·7)
Morpholine salt *	266 (4·9),	307 (23·7)
(XII; R = Me, R′ = Et)		303 (17·6)
Morpholine salt *	264 (4·6),	305 (23·0)
(XII; R = α-$C_{10}H_7$, R′ = Et)		305 (24·3)
Morpholine salt *		305 (26·0)
(XII; R = α-$C_{10}H_7$, R′ = Me)		305 (22·8)
(XIX)		306 (32·6)
(XIII; R = Ph, R′ = Et and Me)		326 (8·2)
(XIII; R = Me, R′ = Et)		323 (7·5)

2-Pyridthione (in ethanol)

(XVI)	238 (29·5), 357 (15·8)

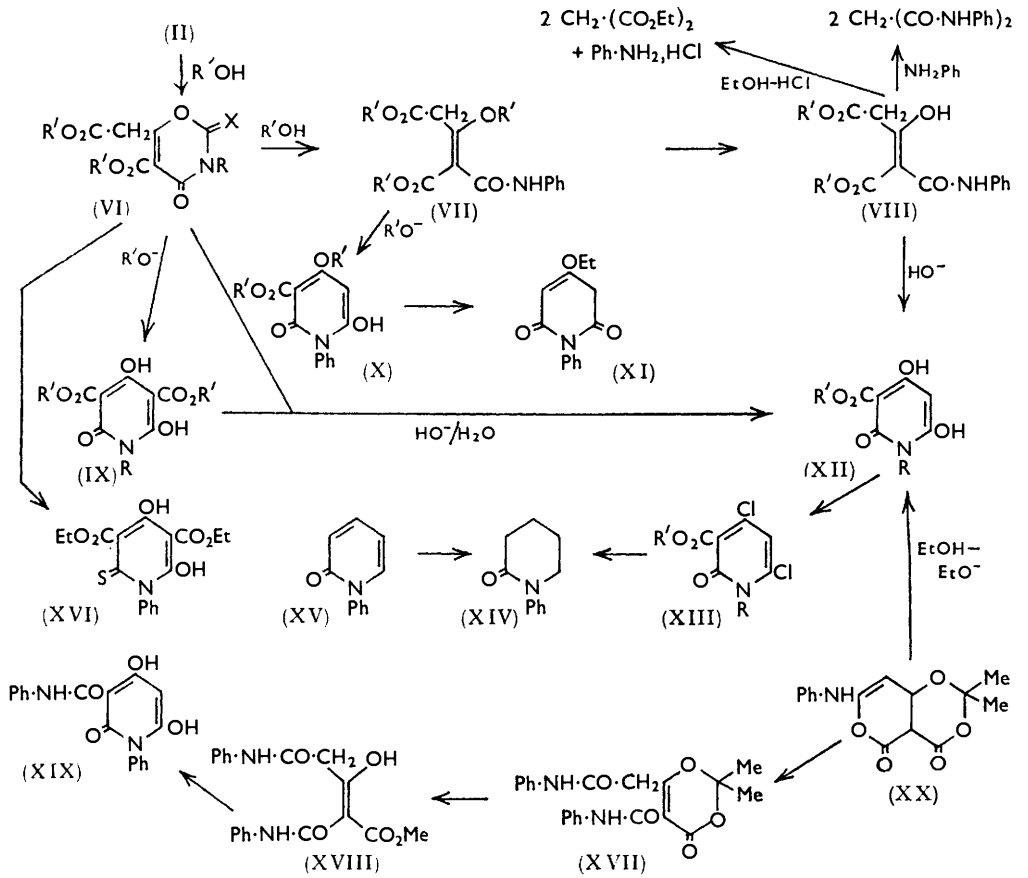
2-Piperidone (in ethanol)

(XIV)	232 (6·1)

* Salt of preceding item.

carbon dioxide was evolved and the enolic pyrone-3-carboxyanilide (V) was formed. The constitution of the latter was demonstrated by the spectroscopic data, given in Table 1. The assignments followed from the data for the established pyrone acid (IV), its ethyl ester,[2] and the related 3-benzamidocarbonyl- and 3-ethoxycarbonyl-4-hydroxy-6-morpholino-2-pyrone.[3]

Methyl, ethyl, and α-naphthyl isocyanate condensed with malonyl chloride similarly to phenyl isocyanate and yielded the products (II; X = O, R = Me, Et, and α-$C_{10}H_7$). These absorbed light in the 280 and the 315 mμ region (Table 2), like the related chloro-oxopyranodioxins.[1]



Phenyl isothiocyanate with malonyl chloride gave the analogous 2-thio-compound (II; X = S, R = Ph), which was also obtained from the pyrone acid chloride (I). The identity of the two products was checked by converting them into a monomorpholino-derivative.

Confirmation of the constitutions (II) for these new malonyl chloride products was provided by their reactions, shown in the accompanying scheme.

3,4-Dihydro-2,4-dioxo- and -4-oxo-2-thio-2H-1,3-oxazines (VI).—When the chloro-compounds (II) were heated in ethanol or methanol for a few minutes and the solution then cooled, chlorine-free, neutral products were obtained, which no longer showed light absorption in the 315 mμ region. It was evident that the pyrone ring had undergone alcoholysis. In agreement, there was no olefinic-proton signal in the proton magnetic resonance spectrum of the (arbitrarily selected) product from (II; X = O, R = Ph) and

TABLE 3.

Infrared absorption max. ($cm.^{-1}$) and assignments, mainly for the region 3—6·7 μ (Nujol mulls).

Dihydrodioxo-oxazines (VI; X = O)

R = Ph		R = α-$C_{10}H_7$		
R′ = Et	R′ = Me	R′ = Et	R′ = Me	
1769	1785	1776	1774	O=C (2)
1735sb	1735s	1733s	1721s	O=C (ester)
1694	1708	1698	1700	O=C (4)
1658	1666	1669	1653	C=C
1591w	1599w	1608w	1597w	C=C
1490w	1495w	1515w		C=C

Compound (II; X = O, R = Ph)

1799sh, 1761sb	O=C (2 + 5)
1695s	O=C (4)
1637, 1618w, 1565s	C=C

Compound (VI; X = S, R = Ph, R′ = Et)

1750s, 1738s	O=C (ester)
1705	O=C (4)
1666, 1599w, 1488w	C=C
1255s	S=C

Enol ethers (VII)		Enols (VIII; R′ = Et)	(XVIII)	
R′ = Et	R′ = Me			
3202w	3202w	3205w	3253	H–N
		2632wb	2667wb	H–O (bonded)
1738s	1726s	1742s		O=C (satd. ester)
1703s	1715	1675s	1677sh, 1664s	O=C (unsatd. ester)
1671s	1644			O=C (amide-I)
1625s, 1598w	1619s, 1599w	1600s, 1497w	1601, 1583w, 1498w	C=C
1551	1557	1554s	1564, 1532s	sec. amide-II

2-Pyridones

(IX; R = Ph, R′ = Et)	(XVI)	(X; R = Ph, R′ = Et)	
2660wb	2650wb		H–O (bonded)
1698s	1698s	1704s	O=C (ester)
1656		1637	O=C (2)
1629	1633		O=C (ester, H-bonded)
1603w, 1542s	1578, 1525w	1611, 1603, 1530s	C=C
	1268s		S=C

(XII; R = Ph, R′ = Et)	(XII; R = α-$C_{10}H_7$, R′ = Et)	(XII; R = Me, R′ = Et)	
2680, 2470, both wb	2700, 2565 both wb	2700, 2565, both wb	H–O (bonded)
1643sb	1643sb	1637sb	O=C (ester, H-bonded and 2)
1596, 1578w	1591, 1573w	1592w, 1520sb	C=C
1502, 1484w	1506, 1498w		C=C

(XIII; R = Ph, R′ = Et)	
1747	O=C (ester)
1656s	O=C (2)
1596, 1534s	C=C

Compound (XI)

1698, 1656s	O=C (2,6)
1621, 1595	C=C
1542w, 1493	C=C

methanol (Table 4). So the products were the diester derivatives (VI) of the dihydro-1,3-oxazine.

Support for this formulation came from the light absorptions. Thus in the ultraviolet region, the 3-phenyl compounds (VI; X = O, R = Ph, R′ = Me and Et) showed a maximum near 237 mμ as compared to 231 and 227 mμ for the simpler 3-phenyl and 3-alkyl derivatives of 3,4-dihydro-6-methyl-2,4-dioxo-2*H*-1,3-oxazine described by Lacey and Ward.[5] Our 3-α-naphthyl compounds (VI; X = O, R = α-$C_{10}H_7$) and the thio-analogues (VI; X = S, R = Ph) absorbed at longer wavelength (Table 2), the dominant effect of the substituents recalling the situation encountered with 4-oxo-1,3-dioxins [6] and not being unexpected. In the infrared region, the dihydrodioxo-oxazines (VI; X = O, R = Ph, R′ = Me and Et) showed maxima in the double-bond stretching region (Table 3) which correlated well with Lacey and Ward's data,[5] in spite of the difference in state. The information enabled a reasonable interpretation to be made of the infrared characteristics of the bicyclic precursor (II; X = O, R = Ph) (see Table 3). The 2-thio-compound

[5] Lacey and Ward, *J.*, 1958, 2134.
[6] Davis and Elvidge, *J.*, 1953, 2251.

TABLE 4.

Proton magnetic resonance results (for 5—10% solutions in $CDCl_3$).

Compound	τ	Intensity	Multiplicity	Assignment
(VI; X = O, R = Ph, R′ = Me)	6·20	3	Singlet	CH_3 (of ester at 6)
	6·13	3	,,	CH_3 (of ester at 5)
	6·15	2	,,	CH_2 (at 6)
	2·8—2·45	5	Complex	Ph
(VII; R′ = Me)	6·26	3	Singlet	CH_3 (satd. ester)
	6·20	3	,,	CH_3 (unsatd. ester)
	6·15	3	,, (vs)	$CH_3O{\cdot}C$
	5·97	2	,,	CH_2
	2·75—2·28	5	Complex	Ph
(VIII; R′ = Me)	6·34	3	Singlet	CH_3 (satd. ester)
	6·28	3	,,	CH_3 (unsatd. ester)
	6·31	2	,,	CH_2
	2·77—2·39	5	Complex	Ph
	−1·13 (concn.-independent)	1	Broadened	H—O (bonded intramolecularly)
(IX; R = Ph, R′ = Et)	8·63	3	Triplet, J = 7 c./sec.	CH_3 of ester
	5·59	2	Quartet, J = 7 c./sec.	CH_2 of ester
	8·55	3	Triplet, J = 7 c./sec.	CH_3 of other ester
	5·51	2	Quartet, J = 7 c./sec.	CH_2 of other ester
	2·86—2·31	5	Complex	Ph
	−5·21 (concn.-independent)	1	Broadened	H—O (bonded intramolecularly)
	ca. −6·08 (concn.-dependent)	1	,,	H—O (bonded intramolecularly)
(X; R′ = Et)	8·62	3	Triplet, J = 7·5 c./sec.	CH_3 of ester at 3
	5·63	2	Quartet, J = 7·5 c./sec.	CH_2 of ester at 3
	8·55	3	Triplet, J = 7·0 c./sec.	CH_3 of group at 4
	5·93	2	Quartet, J = 7·0 c./sec.	CH_2 of group at 4
	4·40	1	Singlet	H (5)
	2·93—2·21	5	Complex	Ph
	ca. −5·58 (concn.-dependent)	1	Broad	H—O (bonded intermolecularly)
(XIII; R′ = Et)	8·65	3	Triplet, J = 7·25 c./sec.	CH_3 of ester
	5·59	2	Quartet, J = 7·25 c./sec.	CH_2 of ester
	3·46	1	Singlet	H (5)
	2·82—2·24	5	Complex	Ph

(VI; X = S, R = Ph, R′ = Et) lacked the highest-frequency peak ascribed in the dihydrodioxo-oxazines (VI; X = O) to the 2-carbonyl group, but it showed strong absorption at 1255 cm.$^{-1}$ and so this is tentatively assigned to the 2-thiocarbonyl group: another difference was the resolution of the ester carbonyl band into two peaks.

Further support for the dihydrodioxo-oxazine structure of the compounds (VI; X = O) was provided by the ring-opening reaction which occurred with boiling alcohols.

Dialkyl 3-Hydroxy-2-N-phenylcarbamoylpent-2-enedioates (VIII) *and the Enol Ethers* (VII).—Whilst the dihydro-4-oxo-2-thio-1,3-oxazine (VI; X = S, R = Ph, R′ = Et) was stable in boiling ethanol, the dihydro-2,4-dioxo-oxazines were not. Thus, when the ethyl and methyl esters (VI; X = O, R = Ph, R′ = Et and Me) were boiled in ethanol and methanol, respectively, carbon dioxide was evolved and the neutral enol ethers (VII; R′ = Et and Me) were produced, attack at the 6-position in (VI) and ring-opening having occurred. Consistent with this were the products' light absorption maxima near 243 mμ (Table 2) and the infrared absorption of the ether (VII; R′ = Et) (Table 3), the proton magnetic resonance spectrum of the ether (VII; R′ = Me) (Table 4), and the hydrolysis of the two compounds with acid to the enols (VIII; R′ = Et and Me) which each readily afforded a copper(II) complex. As expected of acetone-1,1,3-tricarboxylic derivatives, degradation to malonic derivatives occurred on treatment with acid or base. Thus from

the enol (VIII; R′ = Et) with boiling ethanolic hydrochloric acid, 1·5 mol. of ethyl malonate were obtained and 0·88 mol. of aniline as hydrochloride. From scission of the enol (VIII; R′ = Me) with boiling aniline, 1·77 mol. of malondianilide were isolated.

The enol ether (VII; R′ = Me) was also obtained directly from the chlorodihydro-3-phenyl-4-oxopyrano-oxazine (II; X = O, R = Ph) by boiling methanol in 15 min. Longer refluxing of the 3-methyl compound (II; X = O, R = Me) with ethanol gave a mixture from which was isolated triethyl acetone-1,1,3-tricarboxylate as the copper(II) complex and diethyl malonate by distillation.

Whilst the enol ethers (VII) showed the expected three carbonyl absorption bands in the infrared spectrum (Table 3), the enols themselves (VIII) showed only two. These appear to arise from the saturated ester- and the amide-carbonyl. The " missing " unsaturated ester-carbonyl group is evidently bonded to the enolic hydroxyl, so that its carbonyl stretching is submerged under the amide-I absorption band, which is indeed rather broad. The proton magnetic resonance spectrum of the enol (VIII; R′ = Me) is consistent with an internally hydrogen-bonded constitution (Table 4).

4-Alkoxy-6-hydroxy-2-pyridones.—Brief treatment of the neutral enol ethers (VII; R′ = Et and Me) with alcoholic potassium hydroxide, and then acidification, afforded the acidic, enolic pyridone derivatives (X; R′ = Et and Me). These absorbed light strongly at 282 mμ, and exhibited normal ester- and amide-carbonyl absorption in the infrared spectrum (Table 3). The proton magnetic resonance spectrum of the 4-ethoxy-compound (X; R′ = Et) confirmed that it existed in the monoenolic form (at least in chloroform solution) and showed that the hydroxyl was bonded intermolecularly (see Table 4). It seems, therefore, that (X) is the preferred constitution: the alternative with the hydroxyl and the oxo-group interchanged would be more likely to show intramolecular hydrogen bonding.

The cyclisation (VII) ⟶ (X) must involve attack of amidic anion upon the remote ester-carbonyl group and elimination of alkoxide. There will be no hindrance to this because the ethers (VII) are glutaconic derivatives and in alkaline solution there will be equilibration of Δ^1- and Δ^2-isomers and their geometrical forms.

The pyridones (X) were more stable than the acyclic enols (VIII) and were not degraded to malonic derivatives by acids or bases. Alkaline hydrolysis of the pyridone derivative (X; R′ = Et) only effected removal of the 3-ethoxycarbonyl group. The product, formally 4-ethoxy-6-hydroxy-1-phenyl-2-pyridone, showed two absorption bands in the infrared carbonyl region at 1698 and 1656 cm.$^{-1}$ reminiscent of cyclic imides,[7a] for example, glutarimide,[7b] and so the glutaconimide constitution (XI) is preferred.

Alkyl 1,2-Dihydro-4,6-dihydroxy-2-oxopyridine-3-carboxylates (XII).—Cyclisation of the enolic ester amides (VIII; R = Ph, R′ = Et and Me) proceeded analogously with alkali and yielded the enolic 1,2-dihydro-4,6-dihydroxy-2-oxo-1-phenylpyridine-3-carboxylates (XII; R = Ph, R′ = Et and Me). These showed intense light absorption at 305 mμ, reminiscent of 3-alkoxycarbonyl-4-hydroxy-2-pyrones,[1] but unlike the latter showed no high-frequency carbonyl absorption in the infrared spectrum. There was a single, broad, unsymmetrical band around 1640 cm.$^{-1}$ attributable jointly to an amide-carbonyl and a hydrogen-bonded ester-carbonyl group (Table 3). Unfortunately, adverse solubility characteristics prevented an investigation of the constitution by proton magnetic resonance. The compounds (XII) were sufficiently acidic to form stable salts with morpholine: morpholides were not obtained, the ester groups being unreactive. It was verified that mineral acid regenerated the enol (XII; R = Ph, R′ = Et) from its salt.

Ethyl and methyl 1,2-dihydro-4,6-dihydroxy-2-oxo-1-phenylpyridine-3-carboxylate (XII; R = Ph, R′ = Et and Me) were encountered also as the products of treatment of the dihydro-dioxo-oxazines (VI; X = O, R = Ph, R′ = Et and Me) with aqueous alkali

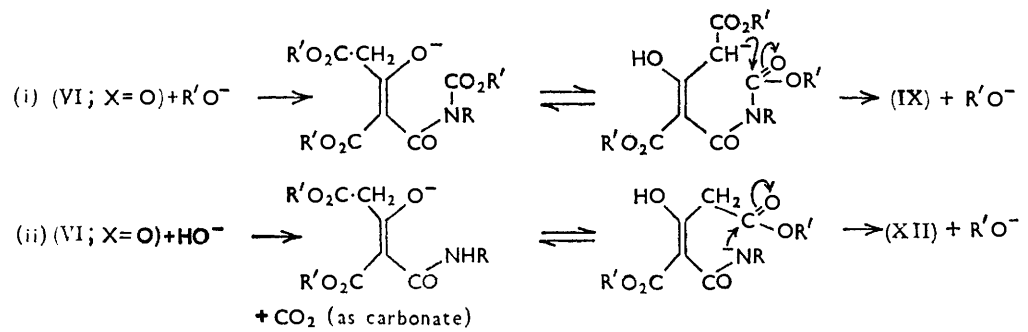
[7] (*a*) Bellamy, " Infrared Spectra of Complex Molecules," Methuen and Co. Ltd., London, 1958, p. 221; (*b*) Frank and McPherson, *J. Amer. Chem. Soc.*, 1949, **71**, 1387.

in dioxan, followed by acidification. Similarly, the dihydro-3-α-naphthyloxazine derivatives (VI; X = O, R = α-$C_{10}H_7$, R′ = Me and Et) afforded the dihydroxypyridone monoesters (XII; R = α-$C_{10}H_7$, R′ = Me and Et), the second of which was characterised as the morpholine salt. Treatment of the chlorodihydro-pyrano-oxazine derivative (II; X = O, R = Me) with boiling ethanol and then alkali afforded on acidification of the solution the 1-methylpyridone derivative (XII; R = Me, R′ = Et) directly.

Dialkyl 1,2-Dihydro-4,6-dihydroxy-2-oxopyridine-3,5-dicarboxylates (IX).—When the oxazine derivative (VI; X = O, R = Ph, R′ = Et) was treated with ethanolic, rather than aqueous, potassium hydroxide, and the solution acidified, the pyridone (XII; R = Ph, R′ = Et) was obtained in only small yield, the major product now being an enol, $C_{17}H_{17}NO_7$. This new isomer of the starting material was the sole product when sodium ethoxide in dry ethanol was the reagent. That the product was a pyridone diester (IX; R = Ph, R′ = Et) followed from mechanistic considerations. Unambiguous demonstration of the constitution (IX; R = Ph, R′ = Et) was provided by the proton magnetic resonance spectrum (Table 4). This showed that there was no hydrogen atom attached directly to the pyridone ring, and that the two ethyl ester groups were in non-equivalent environments. One of the acidic hydroxyl groups was internally bonded and the other was bonded intermolecularly (see Table 4).

From the appropriate dihydrodioxo-oxazine derivatives (VI; X = O) with alcoholic alkali, the dihydroxypyridone diester analogues (IX; R = Ph, R′ = Me; and R = α-$C_{10}H_7$, R′ = Et and Me) were also obtained. Repetition of the reaction upon the last methyl ester, but with omission of the acidification stage, afforded a hydrated dipotassium salt of the dihydroxypyridone diester (IX; R = α-$C_{10}H_7$, R′ = Me). Morpholine salts were also prepared from the dihydroxypyridones (IX; R = Ph, R′ = Me and R = α-$C_{10}H_7$, R′ = Me). The several dihydroxypyridone diesters (IX) were resistant to alkaline hydrolysis, but conversion of the compound (IX; R = Ph, R′ = Et) into the dihydroxypyridone monoester (XII; R = Ph, R′ = Et) was successfully accomplished with hot concentrated sulphuric acid (cf. ref. 8).

It was evident that the dihydro-oxazine ring in the compounds (VI; X = O) was attacked by nucleophiles at the 2-position, to give acyclic tautomeric anions which cyclised, as indicated in the annexed formulæ.



In agreement with mechanism (ii), the dihydro-4-oxo-2-thio-oxazine (VI; X = S, R = Ph, R′ = Et) interacted with potassium hydroxide in ethanol to give the known 2-pyridone monoester (XII; R = Ph, R′ = Et), together with a potassium salt, which liberated carbon dioxide and hydrogen sulphide on acidification. Anhydrous ethanolic sodium ethoxide, as expected from the mechanism (i), isomerised the dihydro-4-oxo-2-thio-oxazine (VI; X = S, R = Ph, R′ = Et) into a monothio-analogue of the pyridone diester (IX; R = Ph, R′ = Et). The product, (XVI), absorbed light more intensely

[8] Mumm and Hingst, *Ber.*, 1923, **56**, 2312.

and at longer wavelength than the dihydroxypyridone diester. In the infrared spectrum, there was strong absorption in the 1270 cm.$^{-1}$ region and no sign of S–H absorption near 2560 cm.$^{-1}$. These findings suggest that the compound exists in the 2-thione form. Further investigation of the fine structure and the chemistry of this compound and related 2-pyridthiones will be reported later.

The easy cyclisation of the acetonetricarboxylic derivatives (VIII) caused us to reinvestigate a previously described reaction.[6] This was the ring-opening of the 4-oxo-1,3-dioxin diamide derivative (XVII) with methoxide to give the methyl ester dianilide of acetonetricarboxylic acid (XVIII). Repetition of the experiment confirmed that 1 molecular proportion of sodium methoxide afforded the acyclic product (XVIII). (Light absorptions are given in Tables 2 and 3.) However, treatment with an excess of alkali rapidly caused cyclisation to the dihydroxypyridone-anilide (XIX), which showed the characteristic maximum at 306 mμ in the ultraviolet spectrum (Table 2). In a further experiment, the anilinopyronodioxin (XX) was treated with ethanolic alkali, and the known pyridone (XII; R = Ph, R′ = Et) was obtained directly: presumably the mono-anilide diester (VIII; R′ = Et) was formed intermediately.

Confirmation of the gross structures proposed for the foregoing compounds was finally obtained by converting the dihydroxypyridone (XII; R = Ph, R′ = Et) into the 4,6-dichloro-compound (XIII; R = Ph, R′ = Et) and thence by hydrogenation in alkaline solution into 1-phenylpiperidone (XIV). This product was identified with a specimen prepared by reduction of 1-phenyl-2-pyridone (XV).

The above conversion of the dihydroxypyridone into the dichloropyridone was effected smoothly by boiling phosphorus oxychloride. Two other examples of this reaction, given in the Experimental section, provide evidence of the generality of this procedure

Experimental

7-Chloro-3,4-dihydro-oxo-2H,5H-pyrano[3,4-e]-1,3-oxazines (II).—Phenyl isocyanate (6 g.) and malonyl chloride (14·3 g.) were warmed together for 5—10 min., with exclusion of moisture, and then heated at 100° until solidification occurred. The product was triturated with dry ether, collected (8·8 g., 60%), and crystallised from the minimum of acetone. *7-Chloro-3,4-dihydro-2,4,5-trioxo-3-phenyl-2H,5H-pyrano[3,4-e]-1,3-oxazine* formed plates, m. p. 265° (decomp.) (Found: C, 53·7; H, 2·3; N, 4·8. $C_{13}H_6ClNO_5$ requires C, 53·5; H, 2·1; N, 4·8%).

Similarly, phenyl isothiocyanate gave *7-chloro-3,4-dihydro-4,5-dioxo-3-phenyl-2-thio-2H,5H-pyrano[3,4-e]-1,3-oxazine* (61%), m. p. 200—204° (decomp.) (Found: C, 51·0; H, 2·4; N, 4·3. $C_{13}H_6ClNO_4S$ requires C, 50·75; H, 2·0; N, 4·55%); α-naphthyl isocyanate afforded the *3-α-naphthyl analogue* (87%) which crystallised from acetic acid as prisms, m. p. 282° (Found: C, 60·1; H, 3·0; N, 4·4. $C_{17}H_8ClNO_5$ requires C, 59·7; H, 2·4; N, 4·1%).

Methyl isocyanate [9] (2·7 g.) was added dropwise to ice-cold malonyl chloride (13·5 g.). When the initial reaction had subsided, the mixture was allowed to come to room temperature and then warmed on the steam-bath until solidification occurred. The solid was triturated with acetone at 0°, collected (9·8 g., 80%), and crystallised from acetic acid. The *7-chloro-3,4-dihydro-3-methyl-2,4,5-trioxo-2H,5H-pyrano[3,4-e]-1,3-oxazine* had m. p. 227° (Found: C, 41·6; H, 2·0; N, 6·1. $C_8H_4ClNO_5$ requires C, 41·8; H, 1·8; N, 6·1%).

Ethyl isocyanate [9] (5 g.) and malonyl chloride (2 g.) were mixed, with cooling, and then the temperature was slowly increased and finally kept at 60°. The solid was triturated with acetone, collected (11·5 g., 67%), and crystallised from acetone to afford the *3-ethyl analogue*, m. p. 198° (Found: C, 44·6; H, 2·7; N, 5·5. $C_9H_6ClNO_5$ requires C, 44·4; H, 2·5; N, 5·7%).

Condensation of Phenyl Isocyanate and of Phenyl Isothiocyanate with the Pyrone Acid Chloride (I).—(*a*) 6-Chloro-4-hydroxy-2-oxopyran-3-carboxylic acid (0·25 g.) was converted with thionyl chloride into the acid chloride.[2] Phenyl isocyanate (0·2 g.) was added and the mixture heated, whereupon solidification occurred. Trituration of the product (0·26 g., 69%) with dry ether and crystallisation from a minimum of acetone gave platelets, m. p. 265° undepressed by the 7-chloro-3,4-dihydro-2,4,5-trioxo-3-phenyl compound described above.

[9] Slotta and Lorenz, *Ber.*, 1925, **58**, 1320.

(*b*) Similarly, the acid chloride (I) (from 0·22 g. of the acid) was warmed with phenyl isothiocyanate until solidification occurred. After being triturated with ether, the product (0·26 g.) crystallised from acetone and then had m. p. 200—203° (decomp.), undepressed by 7-chloro-3,4-dihydro-4,5-dioxo-3-phenyl-2-thio-2*H*,5*H*-pyrano[3,4-*e*]-1,3-oxazine. The product was further characterised by conversion in chloroform with 2 mol. of morpholine into the 7-morpholino-derivative (see below), m. p. and mixed m. p. 268°.

Condensation of Phenyl Isocyanate with the Pyrone Acid (IV).—The acid (0·3 g.) was heated at 100° with phenyl isocyanate (0·5 g.), with exclusion of moisture. Carbon dioxide was evolved and the mixture solidified. From benzene, leaflets of the 6-*chloro*-4-*hydroxy*-2-*oxopyran*-3-*carboxyanilide* (V) (0·23 g.) crystallised; it had m. p. 160° (Found: C, 53·85; H, 2·95; N, 5·3. $C_{12}H_8ClNO_4$ requires C, 54·2; H, 3·0; N, 5·3%). The compound in aqueous ethanol gave a reddish-orange colour with ferric chloride.

Reaction of the 7-*Chlorodihydrodioxothiopyrano-oxazine* (II; X = S, R = Ph) *with Morpholine*.—To the chloro-compound (0·4 g.) in chloroform (10 c.c.), morpholine (0·24 g.) was added dropwise, with stirring and cooling. The chloroform solution was washed with water, dried ($CaCl_2$), and evaporated under reduced pressure, and the residue crystallised from acetone to yield 3,4-*dihydro*-7-*morpholino*-4,5-*dioxo*-3-*phenyl*-2-*thio*-2H,5H-*pyrano*[3,4-e]-1,3-*oxazine* (0·37 g., 79%), m. p. 268° (Found: C, 56·8; H, 4·2; N, 8·0; S, 8·8. $C_{17}H_{14}N_2O_5S$ requires C, 56·95; H, 3·95; N, 7·8; S, 8·9%).

3,4-*Dihydro*-2,4-*dioxo*-2H-1,3-*oxazines* (VI).—7-Chloro-3,4-dihydro-2,4,5-trioxo-3-phenyl-2*H*,5*H*-pyrano[3,4-*e*]-1,3-oxazine (1 g.) was boiled in ethanol (10 c.c.) for 10 min., and the solution was diluted with ether (30 c.c.), filtered through charcoal, and cooled. The *ethyl* 6-*ethoxycarbonylmethyl*-3,4-*dihydro*-2,4-*dioxo*-3-*phenyl*-2H-1,3-*oxazine*-5-*carboxylate* (0·8 g., 65%) that separated crystallised from ether and had m. p. 78° (Found: C, 58·9; H, 5·3; N, 4·0. $C_{17}H_{17}NO_7$ requires C, 58·8; H, 4·9; N, 4·0%). By boiling the chloro-compound (1 g.) in methanol (10 c.c.) for 10 min. and cooling the solution, the corresponding *dimethyl ester* (0·73 g., 64%) was obtained, which had m. p. 118° (from methanol) (Found: C, 56·2; H, 4·1; N, 4·3. $C_{15}H_{13}NO_7$ requires C, 56·4; H, 4·1; N, 4·4%).

7-Chloro-3,4-dihydro-3-α-naphthyl-2,4,5-trioxo-2*H*,5*H*-pyrano[3,4-*e*]-1,3-oxazine (2 g.) was treated with ethanol (10 c.c.), and the solution was worked up as for the 3-phenyl compound. *Ethyl* 6-*ethoxycarbonylmethyl*-3,4-*dihydro*-3-α-*naphthyl*-2,4-*dioxo*-2H-1,3-*oxazine*-5-*carboxylate* (1·28 g., 53%) crystallised from ethanol as needles, m. p. 132° (Found: C, 63·4; H, 5·1; N, 3·8. $C_{21}H_{19}NO_7$ requires C, 63·5; H, 4·8; N, 3·5%). The chloro-compound with boiling methanol similarly gave the 3-α-*naphthyldioxo-oxazine dimethyl ester* (67%), m. p. 150° (from methanol) (Found: C, 61·5; H, 4·3; N, 3·8. $C_{19}H_{15}NO_7$ requires C, 61·8; H, 4·1; N, 3·8%).

Analogous treatment of 7-chloro-3,4-dihydro-4,5-dioxo-3-phenyl-2-thio-2*H*,5*H*-pyrano[3,4-*e*]-1,3-oxazine with ethanol and with methanol afforded *ethyl* 6-*ethoxycarbonylmethyl*-4-*oxo*-3-*phenyl*-2-*thio*-2H-1,3-*oxazine*-5-*carboxylate* (54%), m. p. 121° (from ethanol) (Found: C, 56·7; H, 4·9; N, 3·9; S, 8·5. $C_{17}H_{17}NO_6S$ requires C, 56·2; H, 4·7; N, 3·9; S, 8·8%), and the *dimethyl ester* (64%), m. p. 168° (from methanol) (Found: C, 53·4; H, 4·6; N, 4·0; S, 9·5. $C_{15}H_{13}NO_6S$ requires C, 53·7; H, 3·9; N, 4·2; S, 9·6%).

The Enol Ethers (VII).—(*a*) *Preparation*. When ethyl 6-ethoxycarbonylmethyl-3,4-dihydro-2,4-dioxo-3-phenyl-2*H*-1,3-oxazine (1 g.) was boiled in ethanol (15 c.c.), carbon dioxide was evolved. After 1 hr., the solution was cooled. *Diethyl* 3-*ethoxy*-2-N-*phenylcarbamoylpent*-2-*enedioate* (0·6 g.) separated as long needles and recrystallised (m. p. 115°) from ether (Found: C, 62·2; H, 7·1; N, 4·3. $C_{18}H_{23}NO_6$ requires C, 61·9; H, 6·65; N, 4·0%). Similarly, the dimethyl ester (VI; X = O, R = Ph, R′ = Me) with boiling methanol yielded *dimethyl* 3-*methoxy*-2-N-*phenylcarbamoylpent*-2-*enedioate* (72%) which had m. p. 162° (from ether–methanol) (Found: C, 58·4; H, 5·5; N, 4·4. $C_{15}H_{17}NO_6$ requires C, 58·6; H, 5·6; N, 4·6%).

7-Chloro-3,4-dihydro-2,4,5-trioxo-3-phenyl-2*H*,5*H*-pyrano[3,4-*e*]-1,3-oxazine (II; X = O, R = Ph) (5 g.) was refluxed in dry methanol (35 c.c.) for 15 min. The hot solution was filtered through a thin layer of charcoal, evaporated to 15 c.c. under reduced pressure, and cooled. The enol methyl ether (3 g., 57%) crystallised from methanol and then had m. p. and mixed m. p. 162°.

(*b*) *Hydrolysis to the enols* (VIII). Treatment of the enol ethyl ether (VII; R′ = Et) (0·2 g.) in boiling dioxan (5 c.c.) with 2N-hydrochloric acid (0·5 c.c.) for 40 min. and evaporation of the solution under reduced pressure afforded *diethyl* 3-*hydroxy*-2-N-*phenylcarbamoylpent*-2-*enedioate* (VIII; R′ = Et) (0·08 g.), m. p. 57° (from aqueous ethanol) (Found: C, 59·3; H,

5·95; N, 4·3. $C_{16}H_{19}NO_6$ requires C, 59·8; H, 6·0; N, 4·4%). This gave a red colour with aqueous-ethanolic ferric chloride. With ethanolic copper(II) acetate, a yellowish-green *copper*-(II) *derivative* (47%) was obtained, having m. p. 155° (from ethanol) (Found: C, 54·7; H, 5·5; N, 4·1. $C_{32}H_{36}CuN_2O_{12}$ requires C, 54·6; H, 5·1; N, 4·0%).

Similar hydrolysis of the enol methyl ether (VII; R′ = Me) (0·26 g.) afforded the analogous *dimethyl ester* (VIII; R′ = Me) (0·05 g.), m. p. 66° (from aqueous methanol) (Found: C, 57·5; H, 5·2; N, 4·9. $C_{14}H_{15}NO_6$ requires C, 57·4; H, 5·1; N, 4·8%), which was converted in methanol into the yellowish-green *copper*(II) *enolate* (31%), m. p. 172° (from methanol) (Found: C, 51·8; H, 4·6; Cu, 10·4; N, 4·3. $C_{28}H_{28}CuN_2O_{12}$ requires C, 51·8; H, 4·3; Cu, 9·8; N, 4·3%).

Degradation of Acetonetricarboxylic Derivatives.—The diethyl ester anilide (VIII; R′ = Et) (0·63 g.) was boiled with ethanol (5 c.c.) and concentrated hydrochloric acid (1 c.c.) for 2 hr. Cooling the solution and addition of ether (100 c.c.) afforded aniline hydrochloride (0·23 g., 0·88 mol.), m. p. 200° (Found: C, 55·6; H, 6·75; Cl, 27·1; N, 10·7. Calc. for C_6H_8ClN: C, 55·6; H, 6·2; Cl, 27·4; N, 10·8%). Evaporation of the filtrate left diethyl malonate (0·49 g., 1·52 mol.), n_D^{24} 1·4123.

The dimethyl ester anilide (VIII; R′ = Me) (0·4 g.) was boiled with aniline (4 c.c.) for 1 hr. Cooling the solution and dilution with ether (100 c.c.) gave malondianilide, m. p. and mixed m. p. 228° (Found: C, 70·4; H, 5·6; N, 11·4. Calc. for $C_{15}H_{14}N_2O_2$: C, 70·85; H, 5·55; N, 11·0%).

Degradation of 7-Chloro-3,4-dihydro-3-methyl-2,4,5-trioxo-2H,5H-pyrano[3,4-e]-1,3-oxazine with Boiling Ethanol.—The chloro-compound (0·85 g.) was boiled in ethanol (5 c.c.) for 2 hr., the solution was evaporated somewhat, and copper(II) acetate (0·4 g.) in water (10 c.c.) was added with stirring. The mixture was warmed, filtered, and cooled. The pale green crystals (0·41 g., 30%) had m. p. 85° undepressed on admixture with the hydrated copper(II) complex of triethyl acetone-1,1,3-tricarboxylate.[10] After being kept under reduced pressure over concentrated sulphuric acid, the dark green anhydrous copper complex was obtained, m. p. 59°.[10]

The filtrate from the pale green crystals was extracted with ether (2 × 20 c.c.), and the ether solution was dried ($CaCl_2$) and evaporated to yield diethyl malonate (0·21 g., 35%), b. p. 90°/15 mm., n_D^{22} 1·4100 (Found: C, 52·4; H, 7·7. Calc. for $C_7H_{12}O_4$: C, 52·5; H, 7·55%).

Alkyl 4-Alkoxy-1,2-dihydro-6-hydroxy-2-oxopyridine-3-carboxylates (X).—The enol ether (VII; R′ = Et) (0·5 g.) was boiled for 10 min. in ethanol (5 c.c.) containing potassium hydroxide (0·5 g.), and the solution was cooled and acidified with 2N-hydrochloric acid. The precipitate was extracted in ether and the extract concentrated by evaporation. *Ethyl 4-ethoxy-1,2-dihydro-6-hydroxy-2-oxo-1-phenylpyridine-3-carboxylate* (0·3 g., 70%) crystallised with m. p. 160° from ether (Found: C, 63·3; H, 5·8; N, 5·0. $C_{16}H_{17}NO_5$ requires C, 63·4; H, 5·65; N, 4·6%).

After the enol methyl ether (VII; R′ = Me) (0·22 g.) had been boiled for 10 min. in methanol (10 c.c.) containing potassium hydroxide (0·2 g.), acidification yielded *methyl 6-hydroxy-4-methoxy-1,2-dihydro-2-oxo-1-phenylpyridine-3-carboxylate* (0·14 g., 74%) which crystallised from chloroform–methanol as needles, m. p. 252° (decomp.) (Found: C, 60·8; H, 5·1; N, 4·9. $C_{14}H_{13}NO_5$ requires C, 61·1; H, 4·8; N, 5·1%).

Both compounds gave a reddish-brown colour with aqueous-ethanolic ferric chloride.

Hydrolysis of Ethyl 4-Ethoxy-1,2-dihydro-6-hydroxy-2-oxo-1-phenylpyridine-3-carboxylate.—The compound (0·5 g.), potassium hydroxide (0·5 g.), and ethanol (10 c.c.) were refluxed together for 4 hr. The solution was cooled and acidified with 2N-hydrochloric acid, and starting material (0·1 g.) was removed. The filtrate was diluted with water (2 vol.) and kept at 0° for 2 days, whereupon *γ-ethoxy-N-phenylglutaconimide* (*4-ethoxy-1,2,3,6-tetrahydro-2,6-dioxo-1-phenylpyridine*) (XI) (0·25 g., 65%), m. p. 200° (from water), separated (Found: C, 67·0; H, 5·9; N, 5·9. $C_{13}H_{13}NO_3$ requires C, 67·5; H, 5·7; N, 6·1%).

Alkyl 1,2-Dihydro-4,6-dihydroxy-2-oxopyridine-3-carboxylates (XII).—The diester anilide (VIII; R′ = Et) (0·25 g.) was boiled with ethanolic potassium hydroxide (5 c.c., 5%) for 10 min. Cooling and neutralisation of the solution with 2N-hydrochloric acid afforded *ethyl 1,2-dihydro-4,6-dihydroxy-2-oxo-1-phenylpyridine-3-carboxylate* (0·19 g., 90%), m. p. 204° (decomp.) (from ethanol) (Found: C, 60·8; H, 5·0; N, 5·0. $C_{14}H_{13}NO_5$ requires C, 61·1; H, 4·8; N, 5·1%). Similarly, the dimethyl ester anilide (VIII; R′ = Me) gave the *methyl ester* (XII; R = Ph, R′ = Me) (99%), m. p. 210° (decomp.) (from methanol) (Found: C, 59·5; H,

[10] Willstätter, *Ber.*, 1899, **32**, 1272.

4·2; N, 5·3. $C_{13}H_{11}NO_5$ requires C, 59·8; H, 4·2; N, 5·4%). Both products gave reddish-brown colours with ferric chloride.

The ethyl ester (XII; R = Ph, R′ = Et) (1 g.) in chloroform (15 c.c.) was heated with morpholine (0·4 c.c.), the solution was evaporated under reduced pressure, and the residue triturated with ether. The *morpholine salt* (1·1 g.) crystallised with m. p. 182° (decomp.) from ethanol, was soluble in water, and gave a reddish colour with ferric chloride (Found: C, 59·7; H, 6·1; N, 7·7. $C_{18}H_{22}N_2O_6$ requires C, 59·7; H, 6·1; N, 7·7%). Acidification of a solution of the salt (0·23 g.) in water (10 c.c.) with 2N-hydrochloric acid (5 c.c.) precipitated the starting ester (XII) (0·175 g., 96%), m. p. 204—205° (decomp.) (after recrystallisation from ethanol), which had an infrared spectrum identical with that of authentic material. The *morpholine salt* of the methyl ester crystallised with m. p. 196° (decomp.) from methanol (Found: C, 58·8; H, 6·1; N, 8·2. $C_{17}H_{20}N_2O_6$ requires C, 58·6; H, 5·8; N, 8·0%).

Ethyl 6-ethoxycarbonylmethyl-3,4-dihydro-2,4-dioxo-3-phenyl-2*H*-1,3-oxazine-5-carboxylate (VI; X = O, R = Ph, R′ = Et) (1 g.) in dioxan (5 c.c.) was added to 10% aqueous potassium hydroxide (15 c.c.). The mixture was refluxed for 10 min., cooled, and acidified with 2N-hydrochloric acid, whereupon carbon dioxide was evolved and the ester (XII; R = Ph, R′ = Et) separated (0·5 g., 63%). From boiling ethanol, it formed needles, m. p. and mixed m. p. 204° (decomp.). In the same way, the dihydrodioxo-oxazine dimethyl ester (VI; X = O, R = Ph, R′ = Me) yielded carbon dioxide and the methyl ester (XII; R = Ph, R′ = Me), which crystallised from methanol and had m. p. and mixed m. p. 210° (decomp.).

Methyl 3,4-dihydro-6-methoxycarbonylmethyl-3-α-naphthyl-2,4-dioxo-2*H*-1,3-oxazine-5-carboxylate (VI; X = O, R = α-$C_{10}H_7$, R′ = Me) (1 g.) in dioxan (5 c.c.) was refluxed with 5% aqueous potassium hydroxide (20 c.c.) for 10 min. Cooling and acidification with 2N-hydrochloric acid caused evolution of carbon dioxide and precipitation of *methyl* 3,4-*dihydro*-4,6-*dihydroxy*-1-α-*naphthyl*-2-*oxopyridine*-3-*carboxylate* (0·8 g., 91%), m. p. 250° (decomp.) (from methanol) (Found: C, 65·4; H, 4·2; N, 4·5. $C_{17}H_{13}NO_5$ requires C, 65·6; H, 4·2; N, 4·5%). Similarly, the diethyl ester (VI; X = O, R = α-$C_{10}H_7$, R′ = Et) gave the corresponding *monoethyl ester* (XII) (90%), m. p. 208° (decomp.) from ethanol (Found: C, 66·2; H, 5·0; N, 4·3. $C_{18}H_{15}NO_5$ requires C, 66·45; H, 4·65; N, 4·3%), converted in chloroform into the *morpholine salt* (76%), m. p. 188° (decomp.) (from ethanol–ether) (Found: C, 64·0; H, 6·35; N, 6·9. $C_{22}H_{24}N_2O_6$ requires C, 64·1; H, 5·9; N, 6·8%).

7-Chloro-3,4-dihydro-3-methyl-2,4,5-trioxo-2*H*,5*H*-pyrano[3,4-*e*]-1,3-oxazine (2 g.) was boiled in ethanol (15 c.c.) for 20 min. The solution was cooled, mixed with 20% aqueous potassium hydroxide (20 c.c.), and boiled for 10 min. Acidification with 2N-hydrochloric acid and addition of water (1 vol.) yielded *ethyl* 1,2-*dihydro*-4,6-*dihydroxy*-1-*methyl*-2-*oxopyridine*-3-*carboxylate* (0·84 g., 92%), m. p. 170° (decomp.) (from ethanol) (Found: C, 50·9; H, 5·2; N, 6·3. $C_9H_{11}NO_5$ requires C, 50·7; H, 5·2; N, 6·6%). The *morpholine salt* (56%) had m. p. 144° (from ethanol) (Found: C, 52·1; H, 7·0. $C_{13}H_{20}N_2O_6$ requires C, 52·0; H, 6·7%).

Dialkyl 1,2-*Dihydro*-4,6-*dihydroxy*-2-*oxopyridine*-3,5-*dicarboxylates* (IX).—The dihydrodioxo-3-phenyloxazine diethyl ester (VI; X = O, R = Ph, R′ = Et) (0·95 g.) was boiled with ethanolic 5% potassium hydroxide (20 c.c.) for 10 min. Cooling and acidification of the solution with 2N-hydrochloric acid caused evolution of a little carbon dioxide and yielded *diethyl* 1,2-*dihydro*-4,6-*dihydroxy*-2-*oxo*-1-*phenylpyridine*-3,5-*dicarboxylate* (IX; R = Ph, R′ = Et) (0·63 g., 66%), m. p. 214° (decomp.) (from ethanol) (Found: C, 58·8; H, 5·4; N, 3·9. $C_{17}H_{17}NO_7$ requires C, 58·8; H, 4·9; N, 4·0%). This gave a reddish-brown colour with ferric chloride. Evaporation of the filtrate gave the 3-monoester (0·2 g., 27%), identified by the ultraviolet spectrum and the m. p. and mixed m. p. 204° (decomp.). The m. p. of a mixture with the preceding product was depressed.

Similar treatment of the dihydrodioxo-oxazine (VI; X = O, R = Ph, R′ = Et) with ethanolic sodium ethoxide afforded a crystalline sodium salt, which with 2N-hydrochloric acid yielded the preceding diester as sole product, m. p. and mixed m. p. 214° (decomp.).

The dihydrodioxo-3-phenyloxazine dimethyl ester (VI; X = O, R = Ph, R′ = Me) (0·5 g.) was boiled for 10 min. with methanolic 5% potassium hydroxide (10 c.c.). Cooling, and acidification with 2N-hydrochloric acid, gave *dimethyl* 1,2-*dihydro*-4,6-*dihydroxy*-2-*oxo*-1-*phenylpyridine*-3,5-*dicarboxylate* (0·44 g., 88%), m. p. 232° (decomp.) (from methanol) (Found: C, 56·6; H, 4·5; N, 4·3. $C_{15}H_{13}NO_7$ requires C, 56·4; H, 4·1; N, 4·4%), which on treatment in chloroform with morpholine and then evaporation yielded the *morpholine salt* (79%), m. p. 192° (from ethanol) (Found: C, 56·7; H, 5·9; N, 6·9. $C_{19}H_{22}N_2O_8$ requires C, 56·2; H, 5·5; N,

6·9%). Similarly, the 3-α-naphthyldihydrodioxo-oxazine dimethyl ester (VI; X = O, R = α-$C_{10}H_7$, R′ = Me) afforded the 1-α-*naphthyl dimethyl ester* (IX; R = α-$C_{10}H_7$, R′ = Me) (82%), m. p. 214° (decomp.) (from acetone) (Found: C, 62·1; H, 4·3. $C_{19}H_{15}NO_7$ requires C, 61·8; H, 4·1%), which gave a *morpholine salt* (92%), m. p. 208° (from methanol) (Found: C, 60·3; H, 5·6; N, 6·1. $C_{23}H_{24}N_2O_8$ requires C, 60·5; H, 5·3; N, 6·1%). The dihydrodioxo-oxazine diethyl ester (VI; X = O, R = α-$C_{10}H_7$, R′ = Me) (2 g.) with ethanolic 10% potassium hydroxide (20 c.c.) gave the 1-α-*naphthyl diethyl ester* (IX) (1·55 g., 75%), m. p. 209° (decomp.) (from ethanol) (Found: C, 63·4; H, 5·1; N, 3·7. $C_{21}H_{19}NO_7$ requires C, 63·5; H, 4·8; N, 3·5%).

Methyl 3,4-dihydro-6-methoxycarbonylmethyl-3-α-naphthyl-2,4-dioxo-2*H*-1,3-oxazine-5-carboxylate (0·81 g.) was refluxed with methanolic 7% potassium hydroxide (15 c.c.) for 10 min., and the solution was cooled. Crystals of the *hydrated dipotassium salt* of dimethyl 1,2-dihydro-4,6-dihydroxy-1-α-naphthyl-2-oxopyridine-3,5-dicarboxylate separated (0·95 g., 87%) (Found: C, 49·4; H, 3·5; K, 17·3; N, 3·1. $C_{19}H_{13}K_2NO_7,H_2O$ requires C, 49·2; H, 3·3 K, 16·9; N, 3·0%).

The dihydroxypyridone diester (IX; R = Ph, R′ = Et) (1·9 g.) was heated with concentrated sulphuric acid (1 c.c.) by means of a bath at 175°. When effervescence ceased (8 min.), the solution was strongly cooled and diluted with ice–water (20 c.c.). Ethyl 1,2-dihydro-4,6-dihydroxy-2-oxo-1-phenylpyridine-3-carboxylate separated (1·42 g., 95%); it had m. p. 204° (decomp.) from ethanol and was identical (mixed m. p.; ultraviolet and infrared spectra) with an authentic specimen.

Action of Alkaline Reagents upon the Dihydro-oxothio-oxazine (VI; X = S, R = Ph, R′ = Et).—(*a*) *Ethanolic hydroxide.* The thio-compound (0·89 g.) was refluxed with ethanolic 7% potassium hydroxide (15 c.c.) for 10 min. The solid which had separated gave, with hydrochloric acid, carbon dioxide and hydrogen sulphide. The filtrate on acidification evolved a similar mixture of gases and deposited a white solid. Crystallisation of the latter from ethanol afforded ethyl 1,2-dihydro-4,6-dihydroxy-2-oxo-1-phenylpyridine-3-carboxylate (XII; R = Ph, R′ = Et) (0·4 g., 67%), m. p. and mixed m. p. 204° (decomp.) (Found: C, 60·8; H, 5·0; N, 5·0%).

(*b*) *Alkoxide.* The thio-compound (3 g.) was boiled for 25 min. in ethanol (15 c.c.) containing sodium ethoxide (from 1 g. of sodium), and the solution was cooled and acidified with 2N-hydrochloric acid. During 1 hr., *diethyl 1,2-dihydro-4,6-dihydroxy-1-phenyl-2-thiopyridine-3,5-dicarboxylate* (XVI) separated (2·4 g., 80%), having m. p. 156° (from ethanol) (Found: C, 56·3; H, 4·8; N, 4·0. $C_{17}H_{17}NO_6S$ requires C, 56·2; H, 4·7; N, 3·9%). The compound dissolved in aqueous sodium hydrogen carbonate, and it gave a dark brown colour with aqueous-ethanolic ferric chloride.

Cyclisation of the Ester Dianilide (XVIII).—The ester dianilide [6] (0·3 g.) was boiled for 5 min. with methanol (10 c.c.) containing potassium hydroxide (0·3 g.). The solution was cooled, then acidified with 2N-hydrochloric acid, and the precipitate (0·15 g., 55%) was crystallised from methanol. *1,2-Dihydro-4,6-dihydroxy-2-oxo-1-phenylpyridine-3-carboxyanilide* (XIX) had m. p. 234° (decomp.) (Found: C, 67·3; H, 3·9; N, 8·8. $C_{18}H_{14}N_2O_4$ requires C, 67·1; H, 4·4; N, 8·7%) and gave a reddish-brown colour with ferric chloride in aqueous ethanol.

Conversion of 7-Anilino-2,2-dimethyl-4,5-dioxopyrano[4,3-d]-*1,3-dioxin into Ethyl 1,2-Dihydro-4,6-dihydroxy-2-oxo-1-phenylpyridine-3-carboxylate.*—The pyronodioxin [6] (XX) (1 g.) was boiled for 20 min. with 10% potassium hydroxide in ethanol (20 c.c.), and then the solution was cooled and acidified. The precipitate was washed with water and crystallised from ethanol to give the pyridone derivative (XII; R = Ph, R′ = Et) (0·4 g., 42%), m. p. and mixed m. p. 204° (decomp.).

Ethyl 4,6-Dichloro-1,2-dihydro-2-oxopyridine-3-carboxylates (XIII).—Ethyl 1,2-dihydro-4,6-dihydroxy-1-methyl-2-oxopyridine-3-carboxylate (XII; R = Me, R′ = Et) (2 g.) was refluxed with phosphorus oxychloride (15 c.c.) for 1·5 hr. The excess of the reagent was evaporated under reduced pressure, and the residue crystallised from aqueous ethanol, to give the *4,6-dichloro-ester* (0·7 g.), m. p. 117° (Found: C, 43·3; H, 3·5; Cl, 28·6; N, 5·9. $C_9H_9Cl_2NO_3$ requires C, 43·2; H, 3·6; Cl, 28·4; N, 5·6%). Similarly the 1-phenylpyridone (XII; R = Ph, R′ = Et) (2 g.) afforded the *dichloro-ester* (XIII; R = Ph, R′ = Et) (1·2 g.), m. p. 156° (from ethanol) (Found: C, 54·0; H, 3·7; Cl, 22·1; N, 4·4. $C_{14}H_{11}Cl_2NO_3$ requires C, 53·9; H, 3·55; Cl, 22·7; N, 4·5%), and the methyl ester derivative (XII; R = Ph, R′ = Me) (1 g.) gave methyl *4,6-dichloro-1,2-dihydro-1-phenyl-2-oxopyridine-3-carboxylate* (XIII; R = Ph, R′ = Me) (0·6 g.),

m. p. 154° (from methanol) (Found: C, 52·3; H, 3·0; Cl, 24·1; N, 4·9. $C_{13}H_9Cl_2NO_3$ requires C, 52·4; H, 3·0; Cl, 23·8; N, 4·7%).

1-*Phenyl*-2-*piperidone* (XIV).—When ethyl 4,6-dichloro-1,2-dihydro-1-phenyl-2-oxopyridine-3-carboxylate (1 g.), 0·4N-sodium hydroxide (60 c.c.), and W4 Raney nickel [11] (1 g.) were shaken together in hydrogen, *ca.* 3·4 mol. of the gas (280 c.c.) were absorbed in 2 days. Filtration, acidification with hydrochloric acid, and extraction with chloroform for 8 hr., and evaporation of the extract yielded 1-phenyl-2-piperidone (0·5 g., 85%), m. p. 101—102° (from ethanol) (Found: C, 75·3; H, 7·0; N, 8·0. Calc. for $C_{11}H_{13}NO$: C, 75·4; H, 7·5; N, 8·0%).

An identical product (mixed m. p.; infrared spectrum) was obtained in 78% yield from 1-phenyl-2-pyridone [12] (0·5 g.) by hydrogenation under similar conditions (uptake, 120 c.c. in 2 hr.) (Found: N, 7·9%).

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