695. *Heterocyclic Syntheses with Malonyl Chloride. Part V.* 5-Oxopyrano[3,4-e]-[1,3]-oxazines from Nitriles, and their Degradation to 4-Oxo-1,3-oxazines and Other Products.*

By S. J. Davis and J. A. Elvidge.

Benzo-, aceto-, and naphtho-nitrile with 2 mols. of malonyl chloride at 100° yield 2-substituted 7-chloro-4,5-dioxopyrano[3,4-*e*]-[1,3]-oxazines. The reactions of this new system are compared with those of the chloro-oxopyranodioxins.

Amines displace the chlorine substituent and yield 7-amino-oxopyranooxazines, and then cleave the pyrone ring to give biscarboxyamide derivatives of 4-oxo-1,3-oxazine. This new ring is split by alkali, alkoxide, and phenylhydrazine, and slowly by morpholine which with 5-morpholinocarbonyl-4-oxo-1,3-oxazin-6-ylacetomorpholide yields acetone-1,1,3-tricarboxymorpholide and trimeric benzonitrile.

Water with 7-chloro-4,5-dioxo-2-phenylpyrano[3,4-*e*]-[1,3]-oxazine gives the corresponding 7-hydroxy-compound and also attacks the ring-junction position, to afford the mixed imide of benzoic and acetone-1,3-dicarboxylic acid, and carbon dioxide. The 7-morpholino-analogue is similarly split to yield a second novel mixed imide of benzoic and 4-hydroxy-6-morpholino-2-oxopyran-3-carboxylic acid.

Ethanol degrades the 7-chloro-4,5-dioxo-2-phenylpyrano-oxazine system to hydrogen chloride, acetone-1,1,3-tricarboxylic ester, and benzamide.

Infrared- and ultraviolet-light absorptions, together with proton magnetic resonance results, provided essential structural evidence.

Ketones induce the self-condensation of malonyl chloride to the chlorohydroxypyrone acid chloride (I) and then react with this to form chloro-oxopyranodioxins.[1, 2] We have found that nitriles behave similarly with malonyl chloride and yield chloro-oxopyranooxazines (II).

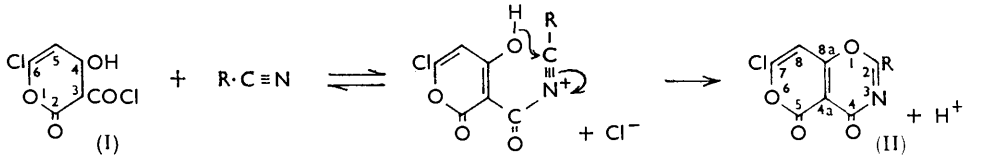
Chloro-oxopyrano-oxazines (II).—Benzonitrile and malonyl chloride interacted briskly at 100° with evolution of hydrogen chloride, to yield a sparingly soluble, yellowish product, $C_{13}H_6ClNO_4$, the formation of which could be represented as $Ph{\cdot}CN + 2CH_2(COCl)_2 - 3HCl$. The striking analogy with the ketone reaction [2] made it probable that the new product had the bicyclic constitution (II; R = Ph). Support came from the infrared

* Part IV, preceding paper.

[1] Elvidge, *J.*, 1962, 2606.

[2] Davis and Elvidge, *J.*, 1952, 4109.

absorption (Table 1). There was a strong carbonyl band at 1771 cm.$^{-1}$, as in related 2-pyrones,[1] whilst a second band at 1680 cm.$^{-1}$ could be attributed to the 4-carbonyl group of the 1,3-oxazine ring. Amide resonance must be inhibited in the latter system (because the group C=N$^+$=C requires to be linear) and so the stretching frequency of the 4-carbonyl group should occur in the ketone region.



(I) (II)

Further evidence for the new product's being 7-chloro-4,5-dioxo-2-phenylpyrano-[3,4-*e*]-[1,3]-oxazine (II; R = Ph) was provided by an alternative preparation from the pre-formed pyrone acid chloride (I) [1] and benzonitrile. This preparation also suggested that the reaction between malonyl chloride and benzonitrile occurred in two main stages, *via* the acid chloride (I), as with ketones,[1] and that the detailed steps were essentially

TABLE 1.

Infrared absorptions in the region 3·0—6·8 μ.

Max. (cm.$^{-1}$)	Assignment *
Compound (II; R = Ph)	
(*a*) 1771	O=C (5)
1680	O=C (4)
1624, 1591, 1536, 1496	C=C
1573	C=N
Compound (X)	
(*a*) 2660	H–O (bonded)
1786, 1706	O=C (5, free & H-bonded)
1674, 1637	O=C (4, free & H-bonded)
1607, 1581, 1532	C=C
1561	C=N
Compound (V)	
(*a*) 3185 (*b*) 3215	H–N (bonded)
2663 (broad) 2663 (broad)	H–O (bonded)
1770	O=C (2, free)
1725 1721	O=C (2, H-bonded)
1694 1701	O=C (remote in 3-substituent)
1645 1656	O=C (at 3-position, H-bonded)
1597, 1587, 1601, 1579, 1497 1486	C=C
Compound (VIII)	
(*a*) 2725	H–O (bonded)
1761	O=C (2)
1642	O=C (ester, H-bonded)
1605, 1548, 1496	C=C
Compound (IV; R = Ph)	
(*a*) 1669	O=C (4)
1650	O=C (in 6-substituent)
1637	O=C (at 5-position)
1600, 1587, 1488	C=C
1563	C=N

(*a*) As a Nujol mull. (*b*) In $CHCl_3$. * Cf. refs. 1 and 4.

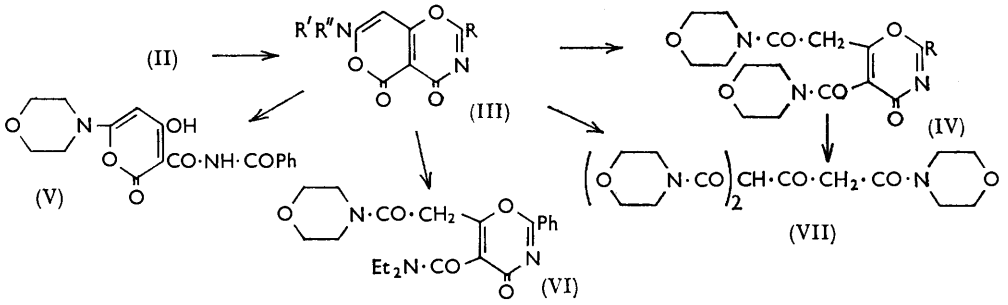
similar. The final stage could be written as formulated here. The alternative mechanism, involving initial attack by the oxygen in the 4-position of (I), upon protonated nitrile, and then cyclisation, is less likely because of the low electron-availability at the 4-hydroxyl group.

Acetonitrile and α- and β-naphthonitrile behaved similarly to benzonitrile and afforded with malonyl chloride the yellowish chloro-oxopyrano-oxazines (II; R = Me, α- and β-$C_{10}H_7$).

The new heterobicyclic compounds (II) reacted with amines, water, and alcohols, and the results served to substantiate the constitution. There emerged both similarities to, and differences from, the behaviour of oxopyranodioxins.[2, 3]

[3] Davis and Elvidge, *J.*, 1953, 2251.

Amino-oxopyrano-oxazines (III).—With 2 mol. of morpholine, the chloro-oxopyrano-oxazines (II; R = Ph, α- and β-$C_{10}H_7$) at once gave morpholine hydrochloride and the 7-morpholino-compounds (III; R′R″ = $[CH_2]_2{\cdot}O{\cdot}[CH_2]_2$). Similarly from the chloro-compound (II; R = Ph) and butylamine, a 7-butylamino-derivative (III; R = Ph, R′ = H, R″ = Bu) was obtained.



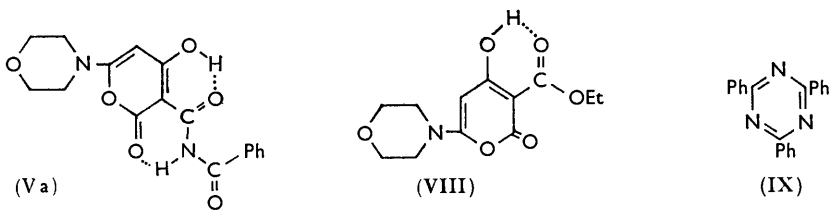
These substituted 7-amino-oxopyrano-oxazines (III) were not basic and they showed high-intensity light absorption at about 335 mμ (Table 2), like the 7-amino-oxopyrano-dioxins,[3] but in contrast the new compounds were all yellowish. Both of the rings were cleaved by base, and the 7-morpholino-derivative (III; R = Ph, R′R″ = $[CH_2]_2{\cdot}O{\cdot}[CH_2]_2$)

TABLE 2.

Ultraviolet light absorptions (λ in mμ).

Amino-oxopyrano-oxazines	Solvent	$\lambda_{max.}$	ε		Solvent	$\lambda_{max.}$	ε
(III; R = Ph, R′ = N<[CH₂·CH₂]₂>O)	Propylene carbonate	254	25,000	Pyrone (V)	$CHCl_3$	335	43,000
		333	34,500	Morpholine salt of hydroxypyrone (X) (XI)		251	14,000
(III; R = α-$C_{10}H_7$, R′ as above)	$CHCl_3$	338	40,300		Dioxan	335	37,000
					,,	237	17,000
(III; R = β-$C_{10}H_7$, R′ = as above)	,,	262	34,000			269	3000
		335	34,000			280	
4-Oxo-1,3-oxazines							
(IV; R = Ph)	,,	265	21,500				
(IV; R = α-$C_{10}H_7$)	,,	251	26,000				
		310	13,000				
(IV; R = β-$C_{10}H_7$)	,,	261	40,000				
		308	15,000				

with an excess of morpholine yielded acetone-1,1,3-tricarboxymorpholide (VII). Towards ethanol, the amino-oxopyrano-oxazines were apparently stable, but not to water: after storage without rigid protection from atmospheric moisture all the compounds showed an enol reaction to ferric chloride; the reason was hydrolysis of the 4-oxo-oxazine ring at the 1,8a-bond, as a detailed study of the 7-morpholino-compound showed. This compound, $C_{17}H_{14}N_2O_5$, rapidly gave with water a product $C_{17}H_{16}N_2O_6$, which was evidently the pyrone (V) because it was colourless and enolic, and it absorbed light intensely at



335 mμ (Table 2). Support for the pyrone structure came from the infrared absorption spectrum, the interpretation of which (Table 1) was assisted by the data previously

obtained in the 2-pyrone series [1] and by the absorption characteristics of the simpler, known 6-morpholino-2-pyrone (VIII).[3] It was evident that in the solid state the new pyrone had the doubly hydrogen-bonded constitution (Va), whilst in chloroform solution the pyrone 2-carbonyl group was to some extent free. Confirmation of structure was provided also by the proton magnetic resonance (Table 3). That the N–H and O–H groups were both strongly bonded was indicated by the exceptionally low τ values for the protons of these functions.

TABLE 3.

Proton magnetic resonance measurements (for 5% solutions in $CDCl_3$).

Compound	Line position (τ)	Proton assignment *
(V)	6·35, centre of A_2B_2 group	Morpholine ring
	4·75	H (5)
	2·62 to 1·80	Ph
	−2·28 (broad)	H–N (bonded)
	−4·87	H–O ,,
(IV; R = Ph)	6·31, centre of broad peak	Morpholine rings and CH_2
	2·39 (broad)	Ph

* Cf. Jackman, " Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Ltd., London, 1959.

4-Oxo-1,3-oxazines.—Under anhydrous conditions the 7-morpholino-oxopyrano-oxazines (III) reacted with a further mol. of morpholine to yield the colourless dicarboxymorpholide derivatives of 4-oxo-1,3-oxazine (IV; R = Ph, α- and β-$C_{10}H_7$), the pyrone ring having been split at the 5,6-bond. The product (IV; R = β-$C_{10}H_7$) was also obtained directly from the chloro-oxopyrano-oxazine (II; R = β-$C_{10}H_7$) with 3 mol. of morpholine. With 1 mol. of diethylamine, the 7-morpholino-compound (III; R = Ph, R′R″ = $[CH_2]_2{\cdot}O{\cdot}[CH_2]_2$) gave the mixed diamide (VI).

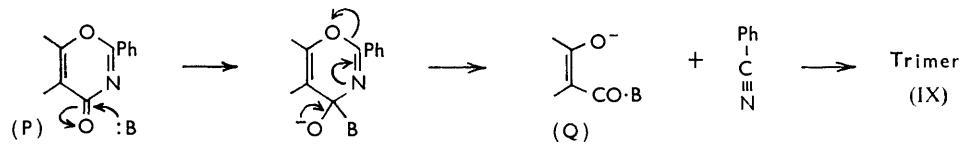
Evidence for the oxo-oxazine structure of these products, and thence for the course of their formation, came initially from the ultraviolet light absorptions (Table 2), which ruled out alternatives. More positive support, in respect of the phenyl compound (IV; R = Ph), was provided by the proton magnetic resonance spectrum (Table 3) which was significantly devoid of any olefinic-proton signal, and by the infrared absorptions. In the interpretation of the latter (Table 1), it seemed reasonable to assign the carbonyl band of highest frequency to the non-amidic 4-carbonyl group in (IV; R = Ph). The sharp absorption at 1563 cm.$^{-1}$ was tentatively assigned to C=N; in favour of this was the fact that absorption near this frequency was found only in those compounds of the present series (II; R = Ph), (IV; R = Ph), and (X), which were presumed to have that structural feature. Such a low frequency for C=N stretching is encountered in cyclic conjugated rings.[4] It should perhaps be emphasised that conjugation through the 4-oxo-1,3-oxazine ring is in no way restricted even though amide resonance must be inhibited.

No simple fully unsaturated 4-oxo-1,3-oxazines appear to have been described before, although 2,3-dihydro-derivatives are known.[5] The new oxo-oxazine derivatives (IV) and (VI) resembled the 4-oxo-1,3-dioxins [3] in showing a main absorption band at about 260 mμ (Table 2). Qualitative testing with ferric chloride for the appearance of an enolic hydroxyl group indicated that the simple oxo-oxazines were considerably more stable to water than the fused-ring oxopyrano-oxazines (II) and (III) in neutral and acid conditions, but that the ring of (IV; R = Ph) was split rapidly by alkoxide and by phenylhydrazine, and slowly by morpholine. From the last reaction, acetone-1,1,3-tricarboxymorpholide (VII) was isolated along with cyaphenine (IX), the trimer of benzonitrile.

It was thus evident that in these simple 4-oxo-1,3-oxazines the 4-position was most susceptible to nucleophilic attack, the reaction with morpholine (:B) proceeding as (P) ⟶ (Q). That the attack was slow by water and sluggish with morpholine was in accord

[4] Bellamy, " Infra-red Spectra of Complex Molecules," Methuen and Co. Ltd., London, 1958.
[5] Lacey, *J.*, 1954, 839, 845.

with the previous observations that reaction occurred preferentially at other sites in the dicyclic oxopyrano-oxazines (II) and (III). Morpholine first displaced the chloro-substituent in (II) and then attacked the pyrone 5-position in (III). The less bulky nucleophile, water, preferentially attacked the ring junction 8a-position in (III).



Reactions of the Chloro-oxopyrano-oxazine System with Water and Alcohols.—Whilst the behaviour of the chloro-oxopyrano-oxazine system (II) towards amines thus parallelled that of the oxopyranodioxins,[3] the behaviour to water and alcohols differed. To these reagents, the ring junction 8a-position was rivalled in reactivity by the 7-chloro-substituent and so 6-chloropyrone degradation products were not obtained as from the chloro-oxopyranodioxins.[2]

Treatment of compound (II; R = Ph) with boiling aqueous sodium hydroxide yielded benzoic acid, ammonia, and a resin. With 1 mol. of water in boiling dioxan, the 7-chlorine substituent was replaced by a hydroxyl group, and hydrogen chloride was evolved. The product, $C_{13}H_7NO_5$, was yellow and enolic, and it dissolved without effervescence in aqueous sodium hydrogen carbonate and was precipitated on acidification. It was therefore assigned the structure (X) because it resembled the pseudo-acidic glutaconic anhydrides,[6] which are best regarded as 6-hydroxy-2-pyrones.

In the infrared region (Table 1), the new hydroxy-compound (X) showed broad absorption at 2600 cm.$^{-1}$ (arising from bonded O–H) and four carbonyl bands. As the hydrogen-bonding could only be intermolecular, two pairs of carbonyl frequencies might be expected, corresponding to the free and hydrogen-bonded forms of each of the two carbonyl groups. Certainly, the respective frequencies were consistent with the assignments. Again there was a band at 1561 cm.$^{-1}$, attributable to C=N stretching.

With morpholine, the compound (X) afforded an adduct, $C_{17}H_{16}N_2O_6$, which was yellow, not acidic to hydrogen carbonate, and which showed intense light-absorption at 330 mμ (Table 2). The adduct therefore seemed best represented as the morpholinium salt of the 7-hydroxyoxopyrano-oxazine (X) rather than a 6-morpholinocarbonylmethyloxo-oxazine-5-carboxylic acid derived by scission of the pyrone ring of (X).

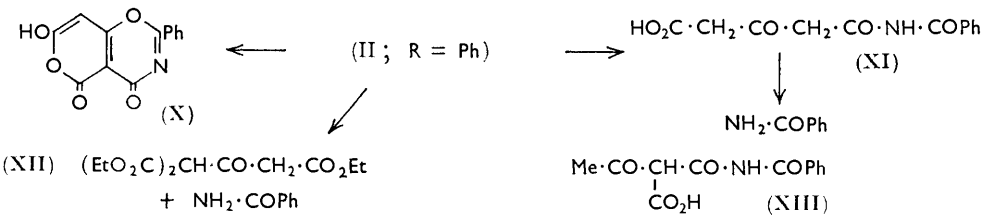
From the action of cold water on the chloro-oxopyrano-oxazine (II; R = Ph), which was slow, a second, colourless product $C_{12}H_{11}NO_5$ was isolated, evidently formed by the overall process $C_{13}H_6ClNO_4 + 3H_2O - HCl - CO_2$. The new product was an acid, which gave a deep red colour with ferric chloride and decomposed with vigorous evolution of gas at 137°. Attempted decarboxylation by sublimation resulted in gross decomposition, but treatment with hot water gave benzamide in good yield. The new product was therefore probably the mixed imide (XI) of benzoic and acetone-1,3-dicarboxylic acid, formed *via* the mild hydrolysis of both pyrone and oxo-oxazine rings in (II; R = Ph). The light absorption (Table 1) was consistent with the open-chain, substituted-benzamide formulation. The possible alternative structure (XIII) was discounted because acetylmalonic acid itself, unlike acetone-1,3-dicarboxylic acid, is apparently too unstable to exist.

With boiling ethanol, the chloro-oxopyrano-oxazine (II; R = Ph) was degraded to benzamide and ethyl acetone-1,1,3-tricarboxylate (XII), the latter being isolated as the copper enolate: the filtrate smelt of ethyl benzoate. Benzamide was also obtained on treatment of the chloro-oxopyrano-oxazine (II; R = Ph) with boiling methanol. Presumably, as in the reaction of the 7-morpholino-compound (III; R = Ph, R′ = N≺[CH$_2$·CH$_2$]$_2$≻O) with water to give (V), there was an initial nucleophilic attack (by

[6] Thole and Thorpe, *J.*, 1911, **99**, 2208.

ROH) at the ring-junction 8a-position to split the oxazine ring. Benzamide would then arise by alcoholysis of the mixed imide link in the first formed product.

Cold methanol reacted with the sparingly soluble chloro-oxopyrano-oxazine (II; R = Ph) slowly. After 3 weeks, the undissolved solid (50%) no longer gave a positive test



for chlorine. It was identified, unexpectedly, as the hydroxypyrone (X). Evaporation of the filtrate afforded some ammonium chloride, together with an oil, which was adjudged to be a mixture of benzoic and acetonecarboxylic esters.

Experimental

7-Chloro-4,5-dioxopyrano[3,4-e]-[1,3]-oxazines (II) *from Malonyl Chloride and Nitriles.*—The freshly purified reactants were mixed and heated on the steam-bath, and the *products* triturated with solvents and recrystallised, as indicated in Table 4.

Condensation of Benzonitrile with the Pyrone Acid Chloride (I).—6-Chloro-4-hydroxy-2-oxopyran-3-carboxylic acid (0·23 g.) was dissolved in hot thionyl chloride (2 c.c.). After 15 min. on the steam-bath, the solution was evaporated under reduced pressure, benzonitrile (2 c.c.) was added, and the solution heated under reflux for 10 min. The yellow 7-chloro-4,5-dioxo-2-phenylpyrano[3,4-*e*]-[1,3]-oxazine, which separated (0·2 g., 60%; m. p. >300°), was characterised by conversion with 1 mol. of water in boiling dioxan into the 7-hydroxy-derivative (see below), m. p. and mixed m. p. 245° (decomp.).

7-Amino-4,5-dioxopyrano[3,4-e]-[1,3]-oxazines (III).—(*a*) A stirred suspension of the powdered chloro-oxopyrano-oxazine No. 1 (5 g.) in chloroform (150 c.c.) was treated slowly with morpholine (3·16 c.c.) in chloroform (50 c.c.), and then heated under reflux for several minutes.

Table 4.

7-Chloro-4,5-dioxopyrano[3,4-*e*]-[1,3]-oxazines (II).

No.	R in R·CN	$CH_2(COCl)_2$ (c.c.)	Reaction time (min.)	Product triturated with	Derivatives of (II)	Yield (%)	Form and solvent *
1	Ph (10 c.c.)	10	30	Dioxan (anhyd.)	2-Ph	79	Pale yellow leaflets, $PhNO_2$
2	Me (25 c.c.)	5	5	—	2-Me	19	Orange, $PhNO_2$
3	1-$C_{10}H_7$ (1·53 g.)	1·95	7	Dioxan	2-1′-$C_{10}H_7$	60	Orange leaflets, PhCN
4	2-$C_{10}H_7$ (1·96 g.)	2·5	4	Dioxan + Et_2O	2-2′-$C_{10}H_7$	72	Orange leaflets, PhCN–Et_2O

			Found (%)				Required (%)			
No.	M. p.†	Formula	C	H	Cl	N	C	H	Cl	N
1	>300°	$C_{13}H_6ClNO_4$	56·8	2·5	12·55	5·05	56·65	2·2	12·85	5·1
2	268	$C_8H_8ClNO_4$	45·3	2·3	16·05	6·55	45·0	1·9	16·6	6·55
3	>300	$C_{17}H_8ClNO_4$	62·2	2·6	—	4·15	62·7	2·5	—	4·3
4	237	,,	62·2	2·8	—	4·75	,,	,,	—	,,

* Hot, but *not* boiling. † With decomp.

Unchanged chloro-compound (0·3 g.) was removed and the filtrate washed *rapidly* with water, dried (Na_2SO_4), and evaporated, and the residue triturated with ether. The *7-morpholino-2-phenyl derivative* (4·6 g.) formed yellowish prisms, m. p. 237° (decomp.), from tetrahydrofuran–ether (Found: C, 62·4; H, 4·7; N, 8·7. $C_{17}H_{14}N_2O_5$ requires C, 62·6; H, 4·3; N, 8·6%).

(*b*) The product obtained similarly from the chloro-compound No. 1 (1 g.) and butylamine

(0·72 c.c.) was triturated with ethanol and crystallised from chlorobenzene. The *7-butylamino-2-phenyl derivative* formed yellowish plates, m. p. 192° (decomp.) (Found: N, 8·6. $C_{17}H_{16}N_2O_4$ requires N, 9·0%).

(*c*) The chloro-compound No. 3 (1 g.) and morpholine (0·54 c.c.) similarly yielded the *7-morpholino-2-α-naphthyl compound* (0·22 g., 19%), which separated from nitrobenzene–dioxan as yellow leaflets, m. p. 233° (decomp.) (Found: C, 66·5; H, 4·4; H, 7·55. $C_{21}H_{16}N_2O_5$ requires C, 67·0; H, 4·3; N, 7·45%).

(*d*) The chloro-compound No. 4 (3 g.) was triturated with morpholine (1·6 c.c.). When the exothermic reaction subsided, the product was stirred with chloroform and then collected. The *7-morpholino-2-β-naphthyl compound* formed pale yellow plates (0·55 g., 16%), m. p. 285° (decomp.), from nitrobenzene (Found: C, 66·65; H, 4·55; N, 7·9).

Degradation of 4,5-Dioxo-7-morpholino-2-phenylpyrano[3,4-*e*]-[1,3]-*oxazine to Acetone-1,1,3-tricarboxymorpholide*.—The 7-morpholino-2-phenylpyrano-oxazine (cf. III) (0·65 g.) and morpholine (0·18 c.c.) were heated together in chloroform (5 c.c.) under reflux for 3 hr. Evaporation, and trituration of the residue with ethanol afforded acetone-1,1,3-tricarboxymorpholide, m. p. 178° raised to 185° on recrystallisation from ethanol. Admixture with authentic material (see below) caused no depression in m. p. The product gave a purple-red colour with ferric chloride.

Stability to water. None of the preceding 7-amino- and 7-chloro-oxopyrano-oxazines in ethanol or dioxan gave a red colour immediately with aqueous ferric chloride. However, after being kept in aqueous solvents for 5—10 min., or after normal storage for some months, strong red colours were given.

Formation of the Pyrone (V).—The reaction described in paragraph (*a*) above was repeated, and the chloroform solution shaken with several lots of water. Evaporation of the chloroform then yielded a crude product (3·6 g.) which was treated with boiling ethanol. Recrystallisation of the undissolved solid (3 g.) from dioxan afforded colourless needles, m. p. 221° (decomp.), of *3-benzamidocarbonyl-4-hydroxy-6-morpholino-2-oxopyran* (Found: C, 59·4; H, 4·8; N, 8·15. $C_{17}H_{16}N_2O_6$ requires C, 59·3; H, 4·7; N, 8·1%). This was sparingly soluble in ethanol and insoluble in cold water, but soluble in aqueous sodium carbonate. In dioxan with aqueous ferric chloride, a deep red colour was given at once.

4-Oxo-1,3-oxazine Derivatives.—(*a*) 4,5-Dioxo-7-morpholino-2-phenylpyrano[3,4-*e*]-[1,3]-oxazine (cf. III) (1 g.) in dioxan (20 c.c.) was treated with morpholine (0·27 c.c.). Next day, the solution was evaporated, and the residue triturated with dry ether until it had solidified. Water (2 c.c.) was added. After 24 hr., the remaining, purer solid (0·1 g.) was recrystallised from ethanol, to afford feathery needles, m. p. 226° of *5-morpholinocarbonyl-4-oxo-2-phenyl-1,3-oxazin-6-ylacetomorpholide* (IV; R = Ph) (Found: C, 61·2; H, 5·8; N, 10·5. $C_{21}H_{23}N_3O_6$ requires C, 61·0; H, 5·6; N, 10·15%). The aqueous filtrate, which gave a deep red colour with ferric chloride, was evaporated. Crystallisation of the residue from ethanol afforded acetone-1,1,3-tricarboxymorpholide (0·1 g.), m. p. 181—184° undepressed by authentic material (see below).

(*b*) Similarly, 4,5-dioxo-7-morpholino-2-α-naphthylpyrano[3,4-*e*]-[1,3]-oxazine (0·22 g.) and morpholine (0·05 c.c.) in boiling chloroform (5 c.c.) (3 hr.) yielded *5-morpholinocarbonyl-2-α-naphthyl-4-oxo-1,3-oxazin-6-ylacetomorpholide* (IV; R = α-$C_{10}H_7$) (0·22 g., 81%), which from ethanol formed laths, m. p. 189° (Found: C, 64·6; H, 5·7; N, 9·0. $C_{25}H_{25}N_3O_6$ requires C, 64·8; H, 5·45; N, 9·05%).

(*c*) (i) 5-Morpholinocarbonyl-2-β-naphthyl-4-oxo-1,3-oxazin-6-ylacetomorpholide was similarly obtained (92%), identical (mixed m. p.) with the product next described. (ii) A suspension of the 7-chloropyrano-oxazine No. 4 (2·15 g.) in chloroform (50 c.c.) was treated slowly with morpholine (1·72 c.c., 3 equiv.), and the solution was subsequently boiled for 1 hr., cooled, washed with water, dried (Na_2SO_4), and evaporated. Trituration of the residue with ether gave the *dimorpholide* (IV; R = β-$C_{10}H_7$) (2·4 g., 78%), which crystallised from ethanol as laths, m. p. 229° (Found: C, 65·05; H, 5·65; N, 9·3%).

(*d*) Treatment of the 7-morpholino-2-phenylpyrano-oxazine (cf. III), (0·3 g.) in boiling chloroform (5 c.c.) with diethylamine (0·095 c.c.) for 2 hr. afforded on evaporation of the solvent, a gum which was triturated with ether. From ethanol *5-dimethylcarbamoyl-4-oxo-2-phenyl-1,3-oxazin-6-ylacetomorpholide* (VI) formed needles, m. p. 181° (Found: C, 63·55; H, 6·55; N, 10·7. $C_{21}H_{25}N_3O_5$ requires C, 63·15; H, 6·3; N, 10·5%).

Properties of the Simple 4-Oxo-1,3-oxazines.—None of the compounds (IV) and (VI) gave a

colour with ferric chloride in aqueous ethanol. Their stability to hydrolysis was investigated by testing for enolic products with ferric chloride after any excess of acid or alkali had been neutralised. The derivative (IV; R = Ph) gave a purple colour after being refluxed with water for 10 min., but it was unaffected by 10% of water in dioxan at 95° for 1 hr. Cold aqueous and boiling methanolic hydrogen chloride had no effect in 5 min. With cold aqueous 10% sodium hydroxide and with boiling methanol containing sodium methoxide, ring-scission occurred and purple colours were given in 2 and 5 min., respectively. After treatment in ethanol with 1 mol. of phenylhydrazine for 5 min. at 60°, evaporation under reduced pressure did not lead to recovery of the oxo-oxazine: the residue in ethanol gave a dark reddish colour with ferric chloride. When the oxo-oxazine (IV; R = Ph) (110 mg.) was boiled in dioxan (10 c.c.) with morpholine (0·029 c.c.) for 1 hr. and the solution was evaporated, the starting oxazine was recovered (after trituration with a few drops of dioxan), with m. p. and mixed m. p. 218—220°, and the filtrate gave only a weak red colour with ferric chloride.

Degradation of 5-Morpholinocarbonyl-4-oxo-2-phenyl-1,3-oxazin-6-ylacetomorpholide with Morpholine.—The oxo-oxazine (IV; R = Ph) (2·8 g.) was boiled in dioxan (60 c.c.) with morpholine (0·74 c.c.) for 3 hr. The solution was evaporated and the residue taken up in a little ethanol. Colourless needles of cyaphenine slowly separated (0·1 g.; m. p. 229°) [Found: C, 81·6; H, 5·1%; *M* (Rast), 298. Calc. for $C_{21}H_{15}N_3$: C, 81·6; H, 4·9%; *M*, 309]; it gave no colour with ferric chloride and did not depress the m. p. of authentic cyaphenine.[7] The filtrate, on slow evaporation, gave acetone-1,1,3-tricarboxymorpholide (1 g.) as prismatic needles, m. p. 183°, raised to 185° on recrystallisation from ethanol (Found: C, 54·3; H, 7·0. Calc. for $C_{13}H_{27}N_3O_7$: C, 54·4; H, 6·85%): it gave a purple-red colour in aqueous ethanol with ferric chloride and did not depress the m. p. of a previous specimen (m. p. 181°).[3]

Degradation of 7-Chloro-4,5-dioxo-2-phenylpyrano[3,4-e]-[1,3]-oxazine with Aqueous Alkali.—The chloro-compound No. 1 (2·76 g.) was heated under reflux with sodium hydroxide (2 g.) in water (20 c.c.) for 1 hr., during which ammonia was evolved. The filtrate from the resin (possibly acetone resin) was acidified with hydrochloric acid. Benzoic acid then crystallised, with m. p. and mixed m. p. 118—119°.

7-Hydroxy-4,5-dioxo-2-phenylpyrano[3,4-e]-[1,3]-oxazine (X).—(*a*) *Formation.* The finely powdered chloro-oxopyrano-oxazine No. 1 (7·7 g.) and dioxan (50 c.c.) containing water (1·0 c.c.) were heated under reflux for 10 min., during which most of the solid dissolved and hydrogen chloride was evolved. The clarified solution was evaporated to a small bulk, and dry ether was added. The *7-hydroxy-compound* (2·58 g., 36%) crystallised from dioxan–ether as yellowish needles, m. p. 245° (decomp.) (Found: C, 60·8; H, 3·35; N, 5·4. $C_{13}H_7NO_5$ requires C, 60·7; H, 2·75; N, 5·45%). It gave an orange colour with aqueous-ethanolic ferric chloride and dissolved in sodium hydrogen carbonate solution without effervescence. Acidification of the latter solution reprecipitated the hydroxy-compound (mixed m. p.).

(*b*) *Interaction with morpholine.* The hydroxy-compound (X) (0·63 g.) was heated with morpholine (0·215 c.c.) in chloroform (10 c.c.), and the solution then evaporated. Trituration of the residue with ether and crystallisation of the solid from chlorobenzene yielded yellow laths, m. p. 205° (decomp.) of the *morpholinium salt* (Found: C, 59·15; H, 4·75; N, 8·1. $C_{17}H_{16}N_2O_6$ requires C, 59·3; H, 4·7; N, 8·15%) of the hydroxy-compound (X). This dissolved in sodium hydrogen carbonate solution without effervescence, and in aqueous ethanol gave a brownish colour with ferric chloride

Hydrolysis of 7-Chloro-4,5-dioxo-2-phenylpyrano[3,4-e]-[1,3]-oxazine.—The powdered chloro-compound No. 1 (3·1 g.) was suspended in dioxan containing water (0·22 c.c.). After 2 days, starting material (1·2 g.) was removed and the filtrate evaporated under reduced pressure. Trituration of the residue with ether afforded crude yellow 7-hydroxy-4,5-dioxo-2-phenylpyrano[3,4-*e*]-[1,3]-oxazine [0·15 g.; m. p. ~200° (decomp.); orange ferric colour] which was washed with chloroform. The combined filtrate and washings rapidly deposited an acid (0·3 g.), m. p. 136—137° (decomp.), which was chlorine-free, water-soluble, gave a deep red colour with ferric chloride, and depressed the m. p. of malonic acid and of 6-chloro-4-hydroxy-2-oxopyran-3-carboxylic acid.[2] From a small volume of dioxan, by addition of chloroform and light petroleum (b. p. 60—80°), *γ-(benzoylcarbamoyl)acetoacetic acid* (XI) crystallised as needles, m. p. 137° (decomp.) (Found: C, 57·9; H, 4·7; N, 5·6. $C_{12}H_{11}NO_5$ requires C, 57·8; H, 4·45; N, 5·6%).

[7] Beilstein, " Handbuch der organischen Chemie," 4th edn., Hauptwerk, Vol. XXVI, p. 97.

When this mixed imide (XI) (50 mg.) was boiled with water (0·5 c.c.) for several min. and the solution cooled, needles of benzamide (20 mg.; m. p. 125—126° and mixed m. p. 126—127°) separated.

Action of Alcohols on 7-Chloro-4,5-dioxo-2-phenylpyrano[3,4-e]-[1,3]-oxazine.—(*a*) *Hot ethanol* The chloro-compound No. 1 (0·4 g.) was heated under reflux with dioxan (5 c.c.) and ethanol (1 c.c.) for 2 hr. Next day, the solution (which smelt of benzoic ester) was evaporated, and the oil taken up in benzene. Benzamide (0·1 g.) separated, having m. p. and mixed m. p. 127—128°. The filtrate was evaporated, the oil taken up in dry ether, and a trace of a flocculent solid filtered off. The ether was evaporated, and the oily residue, in a little ethanol, was treated with aqueous copper acetate. After the mixture had been cooled in ice, stirred, and treated with ethanol (a few drops), the hydrated copper enolate of ethyl acetone-1,1,3-tricarboxylate separated as a very pale green crystalline precipitate (0·15 g.), m. p. and mixed m. p. 83—84°.[2]

(*b*) *Hot methanol.* The chloro-compound (0·7 g.) was heated under reflux with dioxan (10 c.c.) and methanol (0·3 c.c.) for 25 min. The solution then gave an orange-red colour with ferric chloride. The solution was evaporated and the residue triturated with benzene. Recrystallisation of the solid product (0·1 g.) from benzene afforded needles of benzamide, m. p. 127° (Found: C, 69·3; H, 6·0. Calc. for C_7H_7NO: C, 69·4; H, 5·8%).

(*c*) *Cold methanol.* The powdered chloro-compound (1·2 g.) was kept under methanol (10 c.c.) for 3 weeks, and the yellow solid then collected (0·6 g.) and washed with methanol. This product (Found: N, 5·2%) gave an orange colour with ferric chloride and had m. p. 243—245° (decomp.) undepressed on admixture with the 7-hydroxy-compound (X). The filtrate, on spontaneous evaporation, deposited some ammonium chloride and left an oil. The latter smelt of methyl benzoate and gave a deep red colour with aqueous-ethanolic ferric chloride, indicating the presence of acetoacetic ester.

We gratefully acknowledge a maintenance grant (to S. J. D.) from the Department of Scientific and Industrial Research.

Organic Chemistry Research Laboratories,
Imperial College of Science and Technology,
South Kensington, London, S.W.7.

[*Received, March 5th*, 1962.]