Heterocyclic Syntheses with Malonyl Chloride. Part XI.[1] Reactions of 2-Alkyl-(or -Aryl-)thio-7-chloropyrano[3,4-*e*][1,3]oxazine-4,5-diones with Water and with Alcohols

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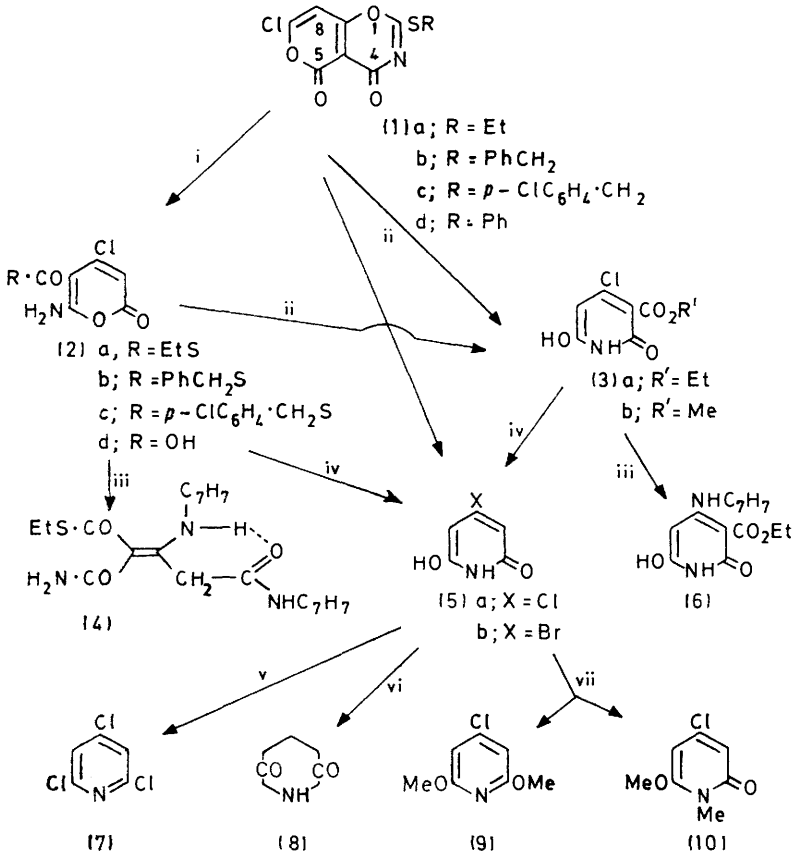
When heated with water in dioxan, the title compounds lost carbon dioxide and thiol in undergoing a complex degradation to 4-chloro-6-hydroxy-2-pyridone. Under milder conditions, *S*-alkyl (or -aryl) 6-amino-4-chloro-2-oxopyran-5-thiocarboxylates were obtained. With an excess of hydrogen chloride and 1 molar proportion of water in boiling dioxan, *S*-alkyl (4-halogeno-2-oxopyran-6-yl)thiocarbamates resulted. An excess of boiling ethanol produced ethyl 4-chloro-1,2-dihydro-6-hydroxy-2-oxopyridine-3-carboxylate, whilst under milder conditions there was addition to the 2,3-double bond or substitution of the 2-thio-group, or both, followed by elimination opening of the oxazine ring between the 1- and 2-positions. With 1 molar proportion of ethanol in boiling dioxan, *S*-alkyl (6-chloro-3-ethoxycarbonyl-2-oxopyran-4-yl)thiocarbamates resulted. Spectroscopic and chemical evidence for the constitutions of the products is described, and modes of formation are discussed.

THE 2-alkylthio-7-chloropyrano-oxazines obtained from alkyl thiocyanates and malonyl chloride underwent reactions with amines which were readily interpreted in terms of the bicyclic structure (1).[1] In related structural work, reactions with water and with alcohols had proved helpful.[2-4] However, the behaviour of the compounds (1) towards water at first seemed irrational because it led, not to 6-chloro-pyrone or -pyridone derivatives, but to 4-chloropyrones (2) and (12), the 4-chloropyridones (3) and (5a), and the β-chloroglutaconic acid derivatives (13a and b). These unexpected findings, and related reactions of the bicyclic system (1) with alcohols, are now discussed

Degradation with Water.—When the pyrano-oxazines (1a—c) were heated with a small excess of water (3 molar proportions) in boiling dioxan, carbon dioxide and thiol were evolved, and a chloro-dihydroxypyridine was formed, as indicated by its elemental composition, mass spectrum, light absorption, and other spectral

[1] Part X, J. M. A. Al-Rawi and J. A. Elvidge, *J.C.S. Perkin I*, 1973, 2432.
[2] M. A. Butt, J. A. Elvidge, and A. B. Foster, *J. Chem. Soc.*, 1963, 3069.
[3] S. J. Davis and J. A. Elvidge, *J. Chem. Soc.*, 1962, 3553.
[4] S. J. Davis and J. A. Elvidge, *J. Chem. Soc.*, 1952, 4109.

properties, and by its conversion with phosphoryl chloride into the known 2,4,6-trichloropyridine (7).[5] The compound was not, however, the expected 6-chloro-2,4-dihydroxy-compound [6] but was evidently the hitherto unknown 4-chloro-2,6-dihydroxypyridine (or pyridone tautomer) (5a), and this was confirmed by its reductive dehalogenation to glutarimide (8). When treated with an excess of diazomethane in ether, compound (5a) afforded 4-chloro-2,6-dimethoxypyridine (9) together with 4-chloro-6-methoxy-1-methyl-2(1*H*)-pyridone (10), 2-alkylthio-7-chloropyrano-oxazines (1a—c) were treated with 1 molar proportion of water in dioxan at 85 °C. These milder conditions still caused evolution of carbon dioxide but of little or no thiol, and yielded products, $C_6H_3ClNO_3(SR)$, for which structure (2) was eventually deduced. These products showed intense u.v. absorption at 330—340 nm reminiscent of a 6-aminopyrone [3] and of 7-aminopyranodioxins.[9] The i.r. spectra (Table) suggested the presence of a bonded primary amino-group,[10] a thiolester carbonyl (1 675 cm^{-1} in various



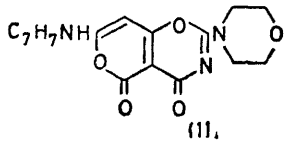
Reagents: i, H_2O at 85 °C; ii, boiling R'OH; iii, $PhCH_2{\cdot}NH_2$; iv, boiling H_2O–H^+; v, $POCl_3$; vi, H_2,Pd–C; vii, CH_2N_2

as indicated principally by the ^1H n.m.r. spectra. The u.v. spectrum of compound (9) closely resembled that of 2,6-diethoxypyridine,[7] as expected: that of the pyridone (10) closely resembled the u.v. spectrum of the parent compound (5a), indicating that the latter existed predominantly in the 2-pyridone form shown. That the chemical shifts of the 3- and 5-protons were the same meant that compound (5a) exhibited dynamic tautomerism.[8]

To find reasons for the formation of the unexpected 4-chloropyridone (5a), products of less extensive change were sought (but were not at first found). Thus the thiolesters),[11] and a hydrogen-bonded pyran-2-carbonyl group.[1,3,12] The presence of an ' acidic ' NH_2 group and of an EtS function was confirmed by the ^1H n.m.r. spectrum, which also revealed a ring proton, τ 4.3. In the dimethyl sulphoxide solution, hydrogen-bonding between functions was not obvious, as it was in chloroform.[2,3,12] However, the various observations suggested the formulation (2) and the i.r. data indicated intermolecular association between the amino and pyran-carbonyl functions, as found for compound (11).[1] This association was evidently favoured over internal

[5] R. Graf, *J. prakt. Chem.*, 1932, **133**, 36.
[6] G. Schroeter and E. Finck, *Ber.*, 1938, **71**, 671.
[7] E. Spinner and J. B. White, *J. Chem. Soc.*, 1966, 991.
[8] *Cf.* J. A. Elvidge and J. A. Pickett, *J.C.S. Perkin I*, 1972, 1483.
[9] S. J. Davis and J. A. Elvidge, *J. Chem. Soc.* (*B*), 1953, 2251.
[10] L. J. Bellamy, ' The Infrared Spectra of Complex Molecules,' Methuen, London, 1958, pp. 250—251.
[11] R. S. Rasmussen and R. R. Brattin, Shell Report, vol. 3, mentioned in ' The Chemistry of Penicillin,' eds. H. T. Clarke, J. R. Johnson, and R. Robinson, Princeton University Press, Princeton, 1949, p. 404.
[12] J. A. Elvidge, *J. Chem. Soc.*, 1962, 2606.

chelation between the amino and the thiolester carbonyl groups, which in ethyl thioanthranilate shifted the



(11)

carbonyl absorption to 1 645 cm^{-1}. That the amino and thiolester functions were nevertheless adjacent was indicated by the mass spectra of the products (2a and b) in that one of the significant fragmentation modes of the molecular ions was loss of RSH. This could arise, then, by a McLafferty type rearrangement. Degradation of compound (3a) did not undergo ring scission, in agreement with its 6-hydroxy-2-pyridone constitution,[14] but merely substitution of the 4-chlorine to give the 4-benzylaminopyridone (6). Hydrolysis of the pyridone esters (3) by prolonged boiling with aqueous acid was accompanied by decarboxylation and gave the 4-chloro-6-hydroxy-2-pyridone (5a). The same product (5a) resulted from similar hydrolysis of the aminopyrone esters (2a and c).

Mode of Formation of the Aminopyrones (2).—The conversion by water of the bicyclic compounds (1) into the aminopyrones (2) and the chlorohydroxypyridone (5a) appeared to involve attack by water at the 2-position (as with amines),[1] ring openings, and a reclosure,

Representative u.v. and i.r. absorptions

				$\nu_{max.}$(Nujol)/cm^{-1}			
Compound	Solvent	$\lambda_{max.}$/nm	$10^{-3}\varepsilon$	NH or OH	CO		
(2a)	MeCN	337.5	14.7	3 275	1 720s	1 610	1 550
		297	12.8	3 120	1 685sh	1 595s	
(3a)	MeCN	315 sh	6.9	2 900—2 600	1 656s	1 582	1 408s
		305 infl.	9.9				
		292 infl.	10.3				
		272.5	12.0				
(5a)	MeOH	316	9.2	2 700—2 400	1 690sh	1 637s	1 540
		235	5.2		1 660	1 600s	
(6)	MeCN	320	12.3	3 110w	1 660s, br	1 600s	1 560
		305	13.3	3 200—2 300			
		273	14.0				
(9)	95% EtOH	278	11.2			1 592s	1 585s
		230	8.3				
(10)	95% EtOH	308	8.1		1 658s	1 582	1 542
		233	4.2				
(12a)	95% EtOH	380 infl.	4.8	3 180	1 713s	1 617	1 550
		341	14.8		1 691s		
		242.5	9.2				
(12c)	95% EtOH	336	11.7		1 750s	1 606	1 535s
		223 infl.	9.4		1 674s	1 590	1 523s
(14)	MeCN	273.5	9.4	3 300—2 400	1 730s	1 600s	1 575sh
		226	7.5		1 647w		
(15)	$CHCl_3$	322	9.4		1 780s	1 595s	1 520
		282.5	11.4		1 750	1 545s	
		275	11.9				
(2d)	Dioxan	330	11.3	3 360	1 720	1 656sh	1 550s
		271	11.3	3 210	1 675s	1 610	
(17a)	MeCN	312	12.9	3 275	1 734s	1 622	1 524s
					1 662s		
(18a)	MeCN	347.5	17.0	3 160	1 740s	1 603	1 508
					1 710s	1 555	
					1 637s		
(19)	MeCN	337	13.8		1 783s	1 627	1 518s
		269	9.7		1 688s	1 593	
(20a)	MeCN	321	13.2	3 150	1 747s	1 570s	
		287	6.3		1 690s		
		245	12.1		1 640		

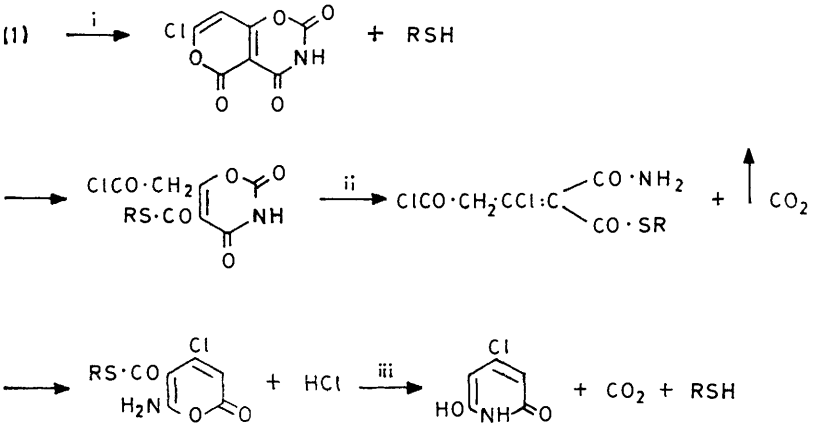
the pyrone *S*-ethyl ester (2a) with benzylamine afforded the α-(ethylthio)carbonyl-β-benzylaminoglutaconamide (4), for which the ^1H n.m.r. spectrum demonstrated the position of the double bond.

When the 6-aminopyrone thiolesters (2) were heated in dioxan with ethanol or methanol, products $C_6H_3ClNO_3$-(OR) were isolated. The reaction was not just an ester exchange, however, because the u.v. and i.r. characteristics of the products (Table) were similar to those of 6-chloro-5-ethoxycarbonyl-4-hydroxy-2(1*H*)-pyridone.[13] Evidently there had been alcoholysis of the pyrone ring in the compounds (2) and reclosure to give the 4-chloropyridone esters (3). When heated with benzylamine, as in Scheme 1. Yields were never high, as indeed would be expected. Support for the essential stages in the Scheme came from three further experiments. When the 7-chloropyrano-oxazine (1a) was heated with a slight excess of hydrobromic acid, a mixture of the 4-bromo- and -chloro-hydroxypyridones (5b and a) resulted, as demonstrated by mass spectrometry. The reaction course thus allowed halogen exchange. When pyrano-oxazine (1a) that had been labelled at C-2 with ^{13}C was heated with water, the aminopyrone product

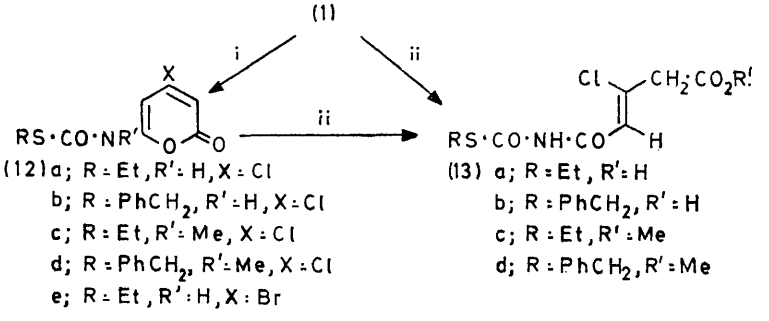
[13] S. J. Davis, J. A. Elvidge, and A. B. Foster, *J. Chem. Soc.*, 1962, 3638.
[14] J. F. Thorpe, *J. Chem. Soc.*, 1905, **87**, 1669.

(2a) was devoid of label, in accord with the loss of that carbon as dioxide. When the degradation of the 2-benzylthiopyrano-oxazine (1b) with water was conducted in the presence of an excess of *p*-chlorotoluene-α-thiol, a mixture of the aminopyrone 5-thiolesters (2b and c) was obtained in which the latter predominated (as shown by nm.r. spectroscopy), again as expected from Scheme 1. The recyclisation stage (on to oxygen rather than nitrogen) [15a] is considered to involve a glutaconoyl chloride because the glutaconic acid derivative (13a) was unchanged after being refluxed in dioxan for 1 h, or even after being melted for 5 min.

four compounds (12) absorbed light beyond 335 nm and so were aminopyrone derivatives [1,3] rather than isomeric pyridones.[16] Moreover the NH compounds showed i.r. carbonyl absorption at 1 713 (bonded pyran-2-carbonyl) [3] and 1 690 cm^{-1} (*S*-alkyl thiocarbamate carbonyl); [16] the NMe derivatives (which would not associate intermolecularly) absorbed at 1 750 and 1 674 cm^{-1}. Additional compelling evidence for the pyran-6-thiocarbamate structures (12) came from the hydrolysis of compounds (12a and b) with hydrochloric acid in acetic acid, which gave the β-chloroglutaconic acid derivatives (13a and b), converted by diazomethane into the methyl



SCHEME 1 Reagents: i, H_2O, 85 °C; ii, HCl from concomitant hydrolysis; iii, boiling aq. acid



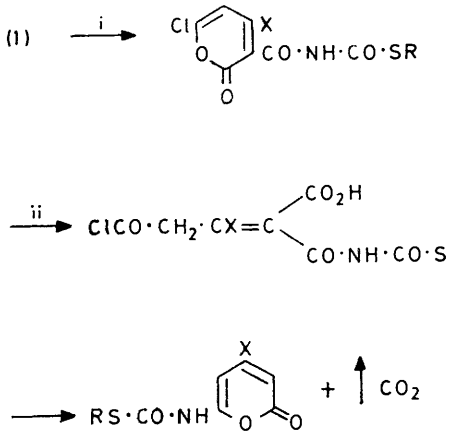
Reagents: i, H_2O–HX at 74 °C (R' = H); ii, boiling aq. HCl–HOAc

Degradation with Aqueous Acid.—With 2 molar proportions of water in dioxan at 74 °C in the presence of an excess of hydrogen chloride (no reaction occurred with *dry* hydrogen chloride), the pyrano-oxazines (1a and b) afforded the 4-chloro-2-oxopyran-6-thiocarbamates (12a and b). These products with diazomethane yielded the *N*-methyl derivatives (12c and d), as confirmed by the ^1H n.m.r. chemical shifts: the spectra also showed that two ring positions were unsubstituted. All esters (13c and d). The position of the double bond followed from the carbonyl frequencies of the carboxy and ester functions. In the acids, the carboxy was evidently hydrogen-bonded intermolecularly to the thiocarbamate carbonyl group, whereas in the esters there was bonding from the NH to the ester carbonyl. The glutaconic acids (13a and b) were also obtained directly from the pyrano-oxazines (1a and b), respectively, with an excess of water in acetone for 3 days, during which acidity developed from side reactions. A

[15] *Cf.* I. T. Millar and H. D. Springall, Sidgwick's 'Organic Chemistry of Nitrogen,' Clarendon Press, Oxford, 1966, (*a*) p. 429; (*b*) pp. 244—245.

[16] M. Hamer and E. P. Lira, *J. Heterocyclic Chem.*, 1972, **9**, 215.

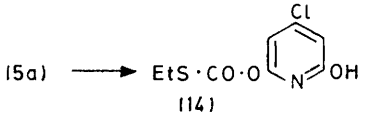
possible mode of formation of compounds (12) is shown in Scheme 2. Consistent with this was the formation



SCHEME 2 Reagents: i, HX; ii, H_2O

of the 4-bromo-analogue (12e) when the pyrano-oxazine (1a) was treated with water and hydrogen bromide. Also in agreement was the retention of the ^{13}C label in the 6-thiocarbamate carbonyl group (as shown by mass spectrometry and by n.m.r. spectroscopy) when the [2-^{13}C]pyrano-oxazine (1a) was used as starting material.

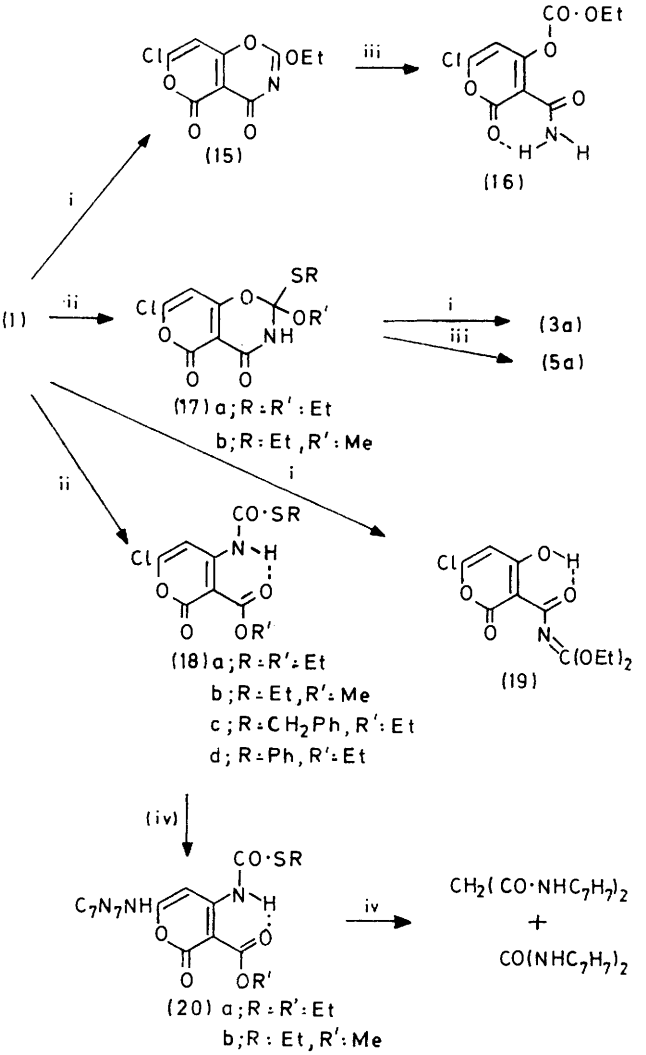
For comparison with the pyran-6-thiocarbamate structure (12a), the isomeric hydroxypyridyl thiocarbonate ester was sought. Acylation of 4-chloro-6-hydroxy-2-pyridone (5a) with *S*-ethyl chlorothioformate gave a product (14) which, as a 2,6-dihydroxypyridine



derivative [*cf.* compound (9)] absorbed light at 273 nm and did not show pyridone carbonyl i.r. absorption at 1 660 cm^{-1}.[2,17] The carbonyl group in the thiocarbonate side chain absorbed characteristically at 1 730 cm^{-1}.[16] Methylation with diazomethane gave a mixture of *N*- and *O*-methyl derivatives, as shown by ^1H n.m.r. spectroscopy, which confirmed that the compound (14) was indeed the *O*- and not the *N*-acyl compound. It was uncertain why compound (14) (as solid or in MeCN) preferred the pyridine tautomeric form (unlike its precursor). However, in ethanol the tautomeric equilibrium shifted slightly towards the pyridone form as indicated by the appearance of a weak band at 315 nm.

Action of Alcohols on Compounds (1).—With an excess of ethanol in chloroform at ambient temperature for some days, the pyrano-oxazine (1a) suffered mainly replacement of the 2-substituent by an ethoxy-group to give (15). Also formed in small yield, and possibly because of incomplete exclusion of moisture, was a sparingly soluble compound, $C_6H_4ClNO_4$, which had u.v. absorption very similar to that of compounds (2), suggesting the aminopyrone structure (2d). This was supported by the ^1H n.m.r. spectrum, and by the i.r. absorption (*cf.* that of anthranilic acid).[18] The data were not consistent[3,12] with a 6-chloro-3-carbamoyl-4-hydroxypyran-2-one constitution,[2] which at first seemed more likely.

By heating the pyrano-oxazine (1a) with 1 molar proportion of methanol or ethanol for 1.5 h, a pair of isomeric products, (17) and (18), was obtained in each case. The compositions of these products corresponded to an addition of the alcohol. The more soluble product of each pair had a u.v. absorption maximum near 310 nm, typical of the 6-chloro-4-hydroxypyran-2-one system[4,12] and showed i.r. bands attributable to a

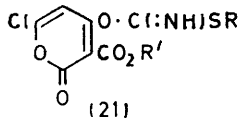


Reagents: i, EtOH; ii, R'OH; iii, H_2O; iv, $PhCH_2{\cdot}NH_2$

secondary amide and the pyran-2-carbonyl. Consistent with these findings and with the ^1H n.m.r. spectrum was

[17] A. R. Katritzky and R. A. Jones, *J. Chem. Soc.*, 1960, 2947.
[18] Sadtler Standard Spectra, No. 2703.

the bicyclic structure (17). As expected, when heated with water or ethanol, compounds (17) were degraded and converted into the pyridones (5a) and (3a), respectively. The less soluble pair of alcohol-addition products (18) from the earlier reaction absorbed at 347 nm and so were aminopyrone derivatives: similar compounds were also obtained from the pyrano-oxazines (1b and d) with ethanol (but in these two cases the more soluble products were discarded). The i.r. spectra indicated the presence of the expected pyran-2-carbonyl group, a bonded ester carbonyl, and a thiocarbamate group. The ^{1}H n.m.r. spectrum added support to these conclusions by showing resonances attributable to the alkyl ester and alkyl or aryl thiocarbamate functions. In addition there was a ring-proton signal near τ 3.1 which, to judge from the ring-proton shifts for compounds (2) and (12), indicated a free 5-position deshielded by an adjacent substituent carbonyl group. Hence structure (18) was deduced. As expected, the chlorine atom in compounds (18a and b) was readily replaced by benzylamine to give the 6-benzylaminopyrones (20), which had light absorption similar to those of the 4,6-diaminopyrones previously described.[1] More vigorous interaction with benzylamine destroyed the pyrone ring, showing that the compounds (20) were not pyridones,[14] and afforded a mixture of *NN'*-dibenzyl-malonamide and -urea.[1] Formation of compounds (18) possibly occurred *via* opening of the oxazine ring at the 4-position by



(21)

alcohol to give an intermediate iminocarbonic ester (21) and rearrangement.[15b] By an obvious extension, Schemes 1 and 2 could be modified to provide (in theory) positional isomers of compounds (2) and (12). However, the alternative structures are invalid because they would not explain the ready conversion of compounds (2) into the pyridones (3) or of compounds (12) into the β-chloroglutaconic acids (13).

The isolation of the products (17a and b) made it appear that the 2-ethoxy-compound (15) had arisen from the pyrano-oxazine (1a) by addition of ethanol followed by elimination of ethanethiol. A further addition to compound (15) would give a 2,2-diethoxy-compound (17) but this was not encountered in the present experiments. However, the isomeric product (19) was isolated, which is the product of an elimination ring-opening (alternative to loss of ethanol). Also, a product (16) was obtained which evidently resulted from addition of water to compound (15) followed by an elimination ring-opening between the 2- and 3-positions. Both products (16) and (19) showed the expected u.v. and i.r. absorptions.

EXPERIMENTAL

U.v. and i.r. spectra (Nujol) were measured with Unicam SP 800B and SP 200 spectrophotometers, respectively. ^{1}H and ^{13}C n.m.r. results are for solutions in deuteriochloroform unless otherwise specified.

4-Chloro-6-hydroxy-2(1H)-pyridone (5a).—The 7-chloro-2-ethylthiopyrano-oxazine [1] (1a) (2.6 g, 0.01 mol) in dioxan (30 ml) was heated under reflux with water (0.5 g, 0.03 mol) for 2 h. Carbon dioxide and ethanethiol were evolved. Evaporation, and washing of the residue with chloroform and ether, gave *4-chloro-6-hydroxy-2(1H)-pyridone* (0.5 g, 35%), m.p. 224° (decomp.) (from acetic acid) (Found: C, 41.4; H, 2.75; N, 9.6. $C_5H_4ClNO_2$ requires C, 41.2; H, 2.7; N, 9.6%), τ (dioxan) 4.25 (s, 3- and 5-H) and −0.2br (OH and NH). This pyridone (30%) (*m/e* 145/147; mixed m.p.) was also obtained by similar treatment of compounds (1b and d).

The pyridone (5a) (1 g) was heated with phosphoryl chloride (15 ml) in a sealed tube at 180 °C for 24 h. Treatment with water and steam-distillation yielded 2,4,6-trichloropyridine (0.5 g) as needles, m.p. 31—32° (lit.,[5] 33°), $\nu_{max.}$ 3 080w (CH), 1 555s, and 1 543s cm^{-1}, τ 2.73 (s, 3- and 5-H), *m/e* 181/183/185/187.

The pyridone (5a) (1 g) in 85% ethanol (100 ml) was shaken with 10% palladium–charcoal (50 mg) in hydrogen (uptake 2 molar proportions in 100 min). Filtration and evaporation gave glutarimide (0.7 g, 90%), m.p. 154° (lit.,[19] 154—155°), *m/e* 113, $\nu_{max.}$ 3 200w (NH), 1 702s, and 1 665s cm^{-1} (CO), τ 7.98 (m, β-H$_2$), 7.7–7.18 (m, 2 × CH$_2$), and 1.18br (NH).

A suspension of the pyridone (5a) (0.4 g) in ether (5 ml) was treated with an excess of ethereal diazomethane for 10 min; the solution was evaporated and the residue washed with light petroleum (b.p. 40—60°) (50 ml) to leave *4-chloro-6-methoxy-1-methyl-2(1H)-pyridone* (10) (0.2 g), m.p. 104° [after crystallisation from light petroleum (b.p. 60—80 °C) and sublimation at 74 °C and 16 mmHg] (Found: C, 48.1; H, 4.6; N, 8.0. $C_7H_8ClNO_2$ requires C, 48.4; H, 4.6; N, 8.1%), *m/e* 173/175, τ 6.6 (s, 1-Me), 6.1 (s, MeO), and 4.43 and 3.76 (d,d, 3- and 5-H, *J* 2 Hz). Evaporation of the washings, and crystallisation of the residue from ethanol–water gave *4-chloro-2,6-dimethoxypyridine* (9) (0.2 g), m.p. 64° (after sublimation at 58 °C and 16 mmHg) (Found: C, 48.25; H, 4.6; N, 8.0. $C_7H_8ClNO_2$ requires C, 48.4; H, 4.6; N, 8.0%), *m/e* 173/175, τ(CCl_4) 6.13 (s, 2 × MeO) and 3.73 (s, 3- and 5-H).

S-Alkyl (or -Aryl) 6-Amino-4-chloro-2-oxopyran-5-thiocarboxylates (2).—(i) The 2-ethylthiopyrano-oxazine (1a) (2.6 g, 0.01 mol) in dry dioxan (30 ml) was heated with water (0.18 g, 0.01 mol) at 80—85 °C for 1.5 h. The solution was evaporated to dryness under reduced pressure and the residue was washed with, and crystallised from, chloroform to afford pale yellow plates of the *S-ethyl ester* (2a) (0.83 g, 40%), m.p. 170° (decomp.) (Found: C, 41.5; H, 3.6; N, 6.1. $C_8H_8ClNO_2S$ requires C, 41.2; H, 3.4; N, 6.0%), *m/e* 233 and 235, τ [$(CD_3)_2SO$] 8.77 (t, Me, *J* 7.6 Hz), 7.07 (q, SCH_2), 4.3 (s, 3-H), and 0.77br (NH_2).

(ii) Similarly, the benzylthiopyrano-oxazine (1b) (3.21 g) gave the *S-benzyl ester* (2b) (1.3 g, 45%), m.p. 186° (decomp.) (Found: C, 52.6; H, 3.3; N, 4.7. $C_{13}H_{10}ClNO_2S$ requires C, 52.8; H, 3.4; N, 4.7%), *m/e* 295 and 297, $\lambda_{max.}$ (MeCN) 338 and 302.5 nm (10^{-3} ε 17.6 and 14.0), $\nu_{max.}$ 3 350, 3 250 (NH_2), 1 733s, and 1 685sh cm^{-1} (CO), τ [$(CD_3)_2SO$] 5.8 (s, CH_2), 4.28 (s, 3-H), 2.69 (Ph), and 0.68br (NH_2), and (iii) the 2-*p*-chlorobenzylthio-compound (1c) afforded the *S-p-chlorobenzyl ester* (2c) (42%), m.p. 200° (decomp.) (Found:

[19] J. A. Elvidge, R. P. Linstead, and A. M. Salaman, *J. Chem. Soc.*, 1959, 208.

C, 47.7; H, 2.65; N, 4.0. $C_{13}H_9Cl_2NO_3S$ requires C, 47.3; H, 2.7; N, 4.2%), *m/e* 329, 331, and 333, $\lambda_{max.}$ ($CHCl_3$) 331 and 308sh (10^{-3} ε 23 and 18.6), $\nu_{max.}$ 3 315, 3 150 (NH_2), and 1 720s and 1 668s cm^{-1} (CO). These esters in ethanol gave a purple colour with iron(III) chloride.

Repetition of experiment (ii) with added *p*-chlorotoluene-α-thiol (4.0 g, 0.025 mol) gave a crystalline mixture (1.6 g), m.p. *ca.* 169° (decomp.), of the *S*-benzyl (2b) and the *S*-*p*-chlorobenzyl (2e) esters (3 : 7 by ^1H n.m.r.), *m/e* (180 °C) 297 and 299, *m/e* (200 °C) 321, 323, and 325.

S-Ethyl thioanthranilate [20] had b.p. 172° at 15 mmHg, n_D^{25} 1.638 0, $\nu_{max.}$ (film) 3 500, 3 400 (NH_2), 1 645 (CO), 1 620, 1 590, and 1 560 cm^{-1}.

To the 6-amino-4-chloro-2-oxopyran 5-thiolester (2a) (1.1 g) in dry dioxan (25 ml), benzylamine (2 ml) was added, followed after 10 min by an excess of water. The precipitate was washed with water and light petroleum (b.p. 40—60 °C) to give S-*ethyl* 3-*benzylamino*-4-*benzylcarbamoyl*-2-*carbamoylbut*-2-*enethioate* (4) (1.2 g, 55%), m.p. 190° (decomp.) (from nitromethane) (Found: C, 64.5; H, 6.2; N, 10.2. $C_{22}H_{26}N_3O_3S$ requires C, 64.2; H, 6.1; N, 10.2%), *m/e* 411, τ 8.74 (t, Me, *J* 6.8 Hz), 7.12 (q, CH_2S), 6.61 (s, 4-H_2), 5.60 and 5.26 (d,d, 2 × CH_2, *J* 6 Hz), 4.05br (NH_2), 2.74 (s, 2 × Ph), 1.53br (4-CO·NH), and −1.01br (3 NH bonded).

Alkyl 4-*Chloro*-1,2-*dihydro*-6-*hydroxy*-2-*oxopyridine*-3-*carboxylates* (3).—The 6-amino-4-chloropyrone thiolester (2a) (1 g) was heated in dry dioxan (15 ml) with ethanol (0.5 ml) under reflux for 2.5 h. Evaporation gave the *ethyl ester* (3a) (0.8 g, 80%), decomp. at 222° after turning yellow at 184° [from acetic acid (charcoal)] (Found: C, 44.1; H, 3.65; N, 6.4. $C_8H_8ClNO_4$ requires C, 44.1; H, 3.9; N, 6.6%), *m/e* 217 and 219, τ [$(CD_3)_2SO$] 8.76 (t, Me, *J* 6.8 Hz), 5.78 (q, CH_2O), 4.25 (s, 5-H), and 1.75br (NH, OH). A similar reaction of the aminopyrone (2a) with methanol (0.4 ml) afforded the *pyridone methyl ester* (3b) (80%), m.p. >300° (decomp.) [from acetonitrile (charcoal) after being washed with carbon tetrachloride] (Found: C, 41.3; H, 2.9; N, 6.9. $C_7H_6ClNO_4$ requires C, 41.2; H, 3.0; N, 6.7%), *m/e* 203 and 205, $\lambda_{max.}$ (dioxan) 317sh, 303 infl, 292.5 infl, and 275 nm (10^{-3}ε 7.4, 11.1, 11.5, and 12.8), τ[$(CD_3)_2SO$] 6.25 (s, Me), 4.2 (s, 5-H), and 1.2br (NH, OH). The same pyridone esters (3a and b) (50%) were similarly obtained from the pyrano-oxazines (1a, b, and d) with ethanol and methanol (3 molar proportions) in boiling dioxan.

A mixture of the 4-chloropyridone ester (3a) (0.4 g), dry dioxan (10 ml), and benzylamine (0.4 ml, 3 molar proportions) was boiled for 1.5 h. The solution was evaporated under reduced pressure and the residue washed with water to give *ethyl* 4-*benzylamino*-1,2-*dihydro*-6-*hydroxy*-2-*oxopyridine*-3-*carboxylate* (6) as a dihydrate (0.32 g, 50%), m.p. 159° (decomp.) (from acetonitrile) (Found: C, 55.1; H, 5.3; N, 8.55. $C_{15}H_{16}N_2O_4,2H_2O$ requires C, 55.5; H, 6.1; N, 8.6%), τ [$(CD_3)_2SO$] 8.82 (t, Me, *J* 7 Hz), 5.99 (s, 4-CH_2), 5.95 (q, CH_2O), 4.99 (s, 5-H), 2.6 (s, Ph), and 1.8br (2 × NH and OH), *m/e* 288.

The pyridone ester (3a) (0.5 g) in dioxan (20 ml) was heated under reflux with concentrated hydrochloric acid (1.5 ml) for 1 h. Evaporation, extraction of the residue with acetone (50 ml), and concentration of the extract yielded 4-chloro-6-hydroxy-2-pyridone (0.2 g, 60%), m.p. and mixed m.p. 224° (decomp.), *m/e* 145 and 147. The same product was obtained by heating tha aminopyrones (1a—d) (1 g) in boiling dioxan (25 ml) with water (0.18 g) for 2—3 h, evaporating, washing the residue with chloroform, and then crystallising from acetic acid.

Treatment of the Pyrano-oxazine (1a) *with Hydrobromic Acid.*—The pyrano-oxazine (1a) (2.6 g) in dioxan (30 ml) was boiled with 64% hydrobromic acid (1.5 ml) for 2 h. Work-up (as in the preceding experiment) gave plates (0.9 g), m.p. *ca.* 222° (decomp.), of a mixture of 4-bromo-6-hydroxy-2-pyridone (5b) [*m/e* 189/191 (1 : 1), 161/163, and 146/148] and the 4-chloro-compound (5a) [*m/e* 145/147 (3 : 1), 117/119, and 102/104].

The [2-^{13}C]*Pyrano-dioxin* (1a).—Potassium [^{13}C]cyanide (1.5 g) (Prochem, 66% enriched) was heated in ethanol with sulphur to give potassium [^{13}C]thiocyanate [21] (100%). Dilution with an equal weight of potassium thiocyanate, conversion [22] into ethyl [^{13}C]thiocyanate, and then interaction with malonyl chloride [1] gave 7-chloro-2-ethylthio-[2-^{13}C]pyrano[3,4-*e*][1,3]oxazine-4,5-dione (72%; 33% enrichment), *m/e* 259/261 and 260/262 (M^+), δ 175.7 (2-^{13}C). Degradation of a portion with 1 molar proportion of water in dioxan, as in experiment (i) before, gave *S*-ethyl 6-amino-4-chloro-2-oxopyran-5-thiocarboxylate devoid of ^{13}C enrichment [*m/e* 233/235 (3 : 1); ^{13}C n.m.r. spectrum]. Degradation of a further portion with water and hydrogen chloride, as in the next experiment, gave *S*-ethyl *N*-(4-chloro-2-oxopyran-6-yl)[^{13}C]thiocarbamate (33% enrichment), *m/e* 233/235 and 234/236 (M^+), δ[$(CD_3)_2SO$] 164.3 (6-NH-^{13}CO).

4-*Chloro*-2-*oxopyran*-6-*thiocarbamates* (12).—With exclusion of external moisture, the pyrano-oxazine (1a) (2.59 g) in dioxan (30 ml) containing water (0.4 g, 0.02 mol) was kept at 74 °C for 1.5 h while hydrogen chloride was passed through the solution. Evaporation, and washing of the residue with carbon tetrachloride afforded S-*ethyl* N-(4-*chloro*-2-*oxopyran*-6-*yl*)*thiocarbamate* (12a) (0.72 g, 30%), m.p. 202° (decomp.) [from nitromethane (charcoal)] (Found: C, 41.1; H, 3.6; N, 6.0. $C_8H_8ClNO_3S$ requires C, 41.1; H, 3.4; N, 6.0%), *m/e* 233/235, τ[$(CD_3)_2SO$] 8.78 (t, Me, *J* 7 Hz), 7.11 (q, CH_2S), 3.83 and 3.33 (d,d, 3- and 5-H, *J* 1.5 Hz), and −1.97br (NH). Similarly, the pyrano-oxazine (1b) gave the S-*benzyl analogue* (12b) (30%), m.p. 197° (decomp.) (Found: C, 52.8; H, 3.3; N, 4.9. $C_{13}H_{10}ClNO_3S$ requires C, 52.8; H, 3.4; N, 4.7%), $\lambda_{max.}$ (EtOH) 378 infl., 341, and 241 nm (10^{-3} ε 9.0, 15.3, and 2.4), τ [$(CD_3)_2SO$] 5.83 (s, CH_2), 3.82 and 3.33 (d,d, 3- and 5-H, *J* 1.8 Hz), 2.68 (s, Ph), and −2.02br (NH).

From the pyrano-oxazine (1a), by using hydrogen bromide as above, S-*ethyl* N-(4-*bromo*-2-*oxopyran*-6-*yl*)*thiocarbamate* (12e) was obtained, m.p. 210° (decomp.) (Found: C, 35.0; H, 3.1; N, 5.05. $C_8H_8BrNO_3S$ requires C, 34.55; H, 2.9; N, 5.0%), *m/e* 277/279 (1 : 1), $\nu_{max.}$ 3 180 (NH), 1 713s [C(2)O], 1 691s (6-NH·CO), 1 617, and 1 550 cm^{-1}, τ[$(CD_3)_2SO$] 8.76 (t, Me, *J* 7 Hz), 7.13 (q, CH_2S), 3.64 and 3.19 (d,d, 3- and 5-H, *J* 1.2 Hz), and −1.92br (NH).

Treatment of a suspension of the thiocarbamate (12a) (0.2 g) in ether (5 ml) with an excess of ethereal diazomethane for 10 min, evaporation, and tritiation of the residue with light petroleum (b.p. 40—60 °C) gave S-*ethyl* N-(4-*chloro*-2-*oxopyran*-6-*yl*)-N-*methylthiocarbamate* (12c) (0.2 g, 96%), m.p. 102° [from light petroleum (b.p. 60—80 °C) (charcoal)] (Found: C, 43.7; H, 4.2; N, 5.6. $C_9H_{10}ClNO_3S$ requires C, 43.6; H, 4.0; N, 5.65%), *m/e* 247/249, τ(CCl_4) 8.67 (t, $MeCH_2$, *J* 7 Hz), 7.08 (q, CH_2S),

[20] U.S.P. 3,123,631/1964.
[21] M. Kucharski and R. Plejewski, *Kernenergi*, 1963, **6**, 649.
[22] P. Walden, *Ber.*, 1907, **40**, 3214.

6.62 (s, NMe), and 4.03 and 3.28 (d,d, 3- and 5-H, *J* 1.6 Hz). Similarly, the thiocarbamate (12b) yielded the *S-benzyl analogue* (12d), m.p. 74° (Found: C, 54.1; H, 3.8; N, 4.5. $C_{14}H_{12}ClNO_3S$ requires C, 54.3; H, 3.9; N, 4.5%), *m/e* 309/311, $\lambda_{max.}$ (EtOH) 337 nm (10^{-3} ε 9.0), $\nu_{max.}$ 1 736s [C(2)O], 1 678s (6-NH·CO), 1640w, 1610sh, 1598, 1537s, and 1530sh cm^{-1}, τ(CCl_4) 6.61 (s, NMe), 5.86 (s, CH_2), 3.99 and 3.27 (d,d, 3- and 5-H, *J* 1.7 Hz), and 2.74 (s, Ph).

Hydrolysis of the thiocarbamate (12a) (0.23 g) in boiling acetic acid (10 ml) containing 3N-hydrochloric acid (1.5 ml) for 20 min, cooling of the solution, and dilution with water provided *4-carboxy-3-chloro-N-[(ethylthio)carbonyl]but-2-enamide* (13a) (0.15 g, 60%), m.p. 140° [from nitromethane (charcoal)] (Found: C, 38.5; H, 4.0; N, 5.7. $C_8H_{10}ClNO_4S$ requires C, 38.2; H, 4.0; N, 5.6%), *m/e* 251/253, τ[$(CD_3)_2SO$] 8.79 (t, Me, *J* 7 Hz), 7.19 (q, CH_2S), 5.84 (s, 4-H_2), 3.71 (s, 2-H), 1.8br (NH), and −1.42br (CO_2H). This acid dissolved in 5% sodium hydrogen carbonate solution with effervescence.

Similarly, the thiocarbamate (12b) on hydrolysis gave the *glutaconic acid derivative* (13b) (58%), m.p. 166° (Found: C, 50.0; H, 3.9; N, 4.5. $C_{13}H_{12}ClNO_4S$ requires C, 49.8; H, 3.8; N, 4.5%), *m/e* 313/315, $\nu_{max.}$ 3 170 (NH), 3 060 (CH), 2220br (OH), 1 730 (sat. CO_2H), 1 675 (CO·NH), 1 627s (bonded CO·S, C=C), 1 585w, and 1 500 cm^{-1}, τ [$(CD_3)_2SO$] 5.92 (s, CH_2), 5.87 (s, 4-H_2), 3.73 (s, 2-H), 2.72 (s, Ph), 2.7br (NH), and −1.95br (CO_2H).

The same two acids (13a and b) were, respectively, obtained (*ca.* 40%, m.p.s 140 and 166°) from the pyrano-oxazines (1a and b) (2.6 and 3.2 g) in acetone (30 ml portions) containing water (10 ml) for 3 days; the products were isolated by evaporation of the solutions, washing of the residues with chloroform, and crystallisation of the remaining solids from nitromethane (charcoal).

Treatment of the preceding two acids with an excess of ethereal diazomethane for 10 min gave respectively *3-chloro-N-[(ethylthio)carbonyl]-4-methoxycarbonylbut-2-enamide* (13c) (96%), m.p. 112° [from light petroleum (b.p. 80—100 °C)] (Found: C, 40.7; H, 4.5; N, 5.15. $C_9H_{12}ClNO_4S$ requires C, 40.7; H, 4.5; N, 5.3%), *m/e* 265/267, $\nu_{max.}$ 3 175 (NH), 3 050 (CH), 1 710s (bonded CO_2Me), 1 672 (CO·NH and CO·SEt), 1 635 (C=C), and 1 525s cm^{-1}, $\lambda_{max.}$ (EtOH) 229 nm (10^{-3} ε 21.0), τ 8.7 (t, *Me*CH_2, *J* 7 Hz), 7.08 (q, CH_2S), 6.24 (s, MeO), 5.9 (s, 4-H_2), 3.68 (s, 2-H), and 1.00br (NH), and the corresponding *S-benzyl compound* (13d), m.p. 140° (Found: C, 51.3; H, 4.3; N, 4.1. $C_{14}H_{14}ClNO_4S$ requires C, 51.3; H, 4.3; N, 4.3%), *m/e* 327/329, $\nu_{max.}$ 3 245 (NH), 3 150 (bonded NH), 3 050 (CH), 1 718s (bonded CO_2Me), 1 680 (CO·NH and CO·S), 1 640 (C=C), and 1 536s cm^{-1}, τ 6.24 (s, MeO), 5.96 (s, CH_2), 5.89 and 5.85 (s,s, 4-H_2, total 2 H), 3.75 and 3.69 (s,s, 2-H, total 1 H), 2.71 (m, Ph), and 0.89br (NH).

S-Ethyl 4-Chloro-6-hydroxy-2-pyridyl Thiocarbonate (14).—4-Chloro-6-hydroxy-2(1*H*)-pyridone (5a) (0.5 g) and dry dioxan (10 ml) were heated with *S*-ethyl chlorothioformate [23] (3 ml) in a sealed tube at 140 °C for 4 h. Evaporation under reduced pressure, extraction with carbon tetrachloride, and evaporation of the extract gave the *thiocarbonate* (0.28 g, 60%), m.p. 108° [from light petroleum (b.p. 60—80 °C) (charcoal)] (Found: C, 41.2; H, 3.4; N, 6.0. $C_8H_8ClNO_3S$ requires C, 41.1; H, 3.4; N, 6.0%), *m/e* 233/235. With ethereal diazomethane, this compound afforded a mixture of *O*- and *N*-methyl derivatives, τ 8.62 (t, Me, *J* 7.5 Hz), 7.04 (q, CH_2S), 6.63 (s, MeN), 6.13 (s, MeO), 3.93 and 3.55 (d,d, 3- and 5-H, *J* 2.4 Hz), and 3.38 and 3.31 (d,d, 3- and 5-H, *J* 1.5 Hz).

Reactions of the Pyrano-oxazines (1) *with Alcohols*.—The 7-chloro-2-ethylthio-compound (1a) (2.6 g) in dry chloroform (20 ml) was mixed with an excess of dry ethanol (25 ml). After 4 days, the solution was evaporated under reduced pressure, and the residue triturated with light petroleum (b.p. 60—80 °C) to afford *7-chloro-2-ethoxypyrano[3,4-e][1,3]oxazine-4,5-dione* (15) (1.5 g, 62%), m.p. 130° (fractionally recrystallised from carbon tetrachloride) (Found: C, 44.1; H, 2.5; N, 5.5. $C_9H_6ClNO_5$ requires C, 44.35; H, 2.5; N, 5.7%), *m/e* 243/245, τ 8.51 (t, Me, *J* 7 Hz), 5.37 (q, CH_2), and 3.72 (s, 8-H). The solid insoluble in the carbon tetrachloride was crystallised from acetonitrile (charcoal) to give plates, m.p. 200° (decomp.) of *6-amino-4-chloro-2-oxopyran-5-carboxylic acid* (2d) (0.2 g; 10%) (Found: C, 37.9; H, 2.0; N, 7.4. $C_6H_4ClNO_4$ requires C, 38.0; H, 2.1; N, 7.3%), *m/e* 189/191, τ [$(CD_3)_2SO$)] 4.4 (s, 3-H) and 0.99br (NH_2,CO_2H).

Repetition of the preceding reaction, evaporation of the solution, and washing of the residue with chloroform afforded *ethyl 3-carbamoyl-6-chloro-2-oxopyran-4-yl carbonate* (16), m.p. 157° (from nitromethane) (Found: C, 41.6; H, 3.1; N, 5.35. $C_9H_8ClNO_6$ requires C, 41.4; H, 3.1; N, 5.4%), *m/e* 261/263, $\lambda_{max.}$ (MeCN) 328 and 274 nm (10^{-3} ε 8.7 and 15.9), $\nu_{max.}$ 3 200—2 400 (NH bonded), 1 760s (vinyl carbonate CO, intermolecularly bonded), 1 730 [C(2)O bonded], 1 705 (3-CO), 1 590, and 1 535 cm^{-1}.

The 2-ethylthiopyrano-oxazine (1a) (2.6 g, 0.01 mol) was heated in dry dioxan (35 ml) containing ethanol (0.57 ml; 0.01 mol) under reflux for 2 h. Evaporation and washing of the residue with carbon tetrachloride (50 ml) left *S-ethyl N-(6-chloro-3-ethoxycarbonyl-2-oxopyran-4-yl)thiocarbamate* (18a) (1.5 g, 50%), m.p. 173° (decomp.) (Found: C, 43.1; H, 3.95; N, 4.6. $C_{11}H_{12}ClNO_5S$ requires C, 43.3; H, 3.9; N, 4.6%), *m/e* 305/307, τ 8.65 (t, 2 × Me, *J* 7 Hz), 6.95 (q, CH_2S), 5.73 (q, CH_2O), 3.14 (s, 5-H), and −1.7br (NH). Evaporating the carbon tetrachloride washings gave an oil which, after extraction into hot light petroleum (b.p. 60—80 °C), yielded pale yellow crystals of *7-chloro-2-ethoxy-2-ethylthio-2,3-dihydropyrano[3,4-e][1,3]-oxazine-4,5-dione* (17a) (0.3 g, 10%), m.p. 106° [from light petroleum (b.p. 60—80 °C) (charcoal)] (Found: C, 43.5; H, 4.0; N, 4.4%), *m/e* 305/307, τ 8.68 (t, 2 × Me, *J* 7 Hz), 6.98 (q, CH_2S), 5.73 (q, CH_2O), 3.94 (s, 8-H), and −0.69br (NH).

Substitution of methanol (0.42 ml, 0.01 mol) for ethanol in the preceding reaction (similar work-up) afforded *S-ethyl N-(6-chloro-3-methoxycarbonyl-2-oxopyran-4-yl)thiocarbamate* (18b) (1.4 g), m.p. 153° (Found: C, 41.1; H, 3.6; N, 4.8. $C_{10}H_{10}ClNO_5S$ requires C, 41.2; H, 3.4; N, 4.8%), *m/e* 291 and 293, $\lambda_{max.}$ (MeCN) 346.5 nm, τ 8.67 (t, Me, *J* 7 Hz), 6.96 (q, CH_2S), 6.18 (s, MeO), 3.12 (s, 5-H), and −1.39br (NH), and *7-chloro-2-ethylthio-2,3-dihydro-2-methoxypyrano[3,4-e][1,3]oxazine-4,5-dione* (17b) (0.3 g) as pale yellow needles, m.p. 127° [from light petroleum (b.p. 60—80 °C) (charcoal)] (Found: C, 41.3; H, 3.5; N, 5.0%), *m/e* 291/293, $\lambda_{max.}$ (MeCN) 310 nm (10^{-3} ε 11.5), τ 8.68 (t, Me, *J* 7 Hz), 6.98 (q, CH_2S), 6.19 (s, MeO), 3.93 (s, 8-H), and −0.90br (NH).

The 2-benzylthiopyrano-oxazine (1b) (3.2 g, 0.01 mol), dry dioxan (50 ml), and dry ethanol (0.57 ml, 0.01 mol), were heated under reflux for 1 h. Evaporation left oily crystals, recrystallisation of which from ethyl acetate

[23] R. Riemschneider and O. Lorenz, *Monatsh.*, 1953, **84**, 518.

(charcoal) afforded S-*benzyl* N-(6-*chloro*-3-*ethoxycarbonyl*-2-*oxopyran*-4-*yl*)*thiocarbamate* (18c) (1.4 g, 40%), m.p. 180° (decomp.) (Found: C, 51.9; H, 3.8; N, 3.6. $C_{16}H_{14}ClNO_5S$ requires C, 52.2; H, 3.8; N, 3.8%), *m/e* 367/369, $\lambda_{max.}$ (MeCN) 372 nm (10^{-3} ε 17.9), $\nu_{max.}$ 3 150 (NH bonded), 3 095 (CH), 1 745 [C(2)O], 1 705 (4-NH·CO), 1 630 (3-CO, bonded), 1 600s, 1 550s, and 1 500s cm^{-1}, τ 8.71 (t, Me, *J* 6.8 Hz), 5.72 (q, CH_2O), 5.70 (s, CH_2S), 3.12 (s, 5-H), 2.71 (m, Ph), and −1.97br (NH). Similarly, the pyrano-oxazine (1d) gave, after washing away oil with carbon tetrachloride, the S-*phenyl ester* (18d) (1.3 g) as pale yellow needles, m.p. 182° (decomp.) [from carbon tetrachloride (charcoal)] (Found: C, 50.6; H, 3.4; N, 3.8. $C_{15}H_{12}ClNO_5S$ requires C, 50.9; H, 3.4; N, 3.7%), $\lambda_{max.}$ (MeCN) 356 nm (10^{-3} ε 16.4), $\nu_{max.}$ 3 150, 3 095, 1 740, 1 703, 1 650, 1 598s, and 1 550s cm^{-1}, τ 8.68 (t, Me, *J* 6.8 Hz), 5.76 (q, CH_2O), 3.10 (s, 5-H), 2.55 (s, Ph), and −1.76br (NH).

Dry benzylamine (0.2 ml, 2 equiv.) was added in drops during 15 min to the 6-chloro-pyrone derivative (18a) (0.33 g) in pure chloroform (15 ml). The solution was heated for 0.5 h and then evaporated, and the residue was washed with water to afford S-*ethyl* N-(6-*benzylamino*-3-*ethoxycarbonyl*-2-*oxopyran*-4-*yl*)*thiocarbamate* (20a) (0.25 g, 80%), m.p. 226° (decomp.) [from acetonitrile (charcoal)] (Found: C, 57.2; H, 5.4; N, 7.3. $C_{18}H_{20}N_2O_5S$ requires C, 57.4; H, 5.3; N, 7.4%), *m/e* 376, τ [$(CD_3)_2SO$] 8.83 and 8.80 (t,t, 2 × Me, *J* 7 Hz), 7.38 (q, CH_2S), 5.85 (q, CH_2O), 5.44 (d, CH_2N, *J* 5.1 Hz), 3.50 (s, 5-H), 2.66 (s, Ph), −0.82br (t, 6-NH), and −1.02br (NH·CO). Similarly, the 6-chloropyrone (18b) afforded the *analogue* (20b) (75%), m.p. 213° (decomp.) (Found: C, 56.2; H, 5.1; N, 7.9. $C_{17}H_{18}N_2O_5S$ requires C, 56.35; H, 5.0; N, 7.7%), *m/e* 362, $\lambda_{max.}$ (MeCN) 320.5 and 287.5 nm, τ [$(CD_3)_2SO$] 8.83 (t, Me, *J* 7 Hz), 7.25 (q, CH_2S), 6.32 (s, MeO), 5.43 (d, CH_2N, *J* 5 Hz), 3.47 (s, 5-H), 2.65 (s, Ph), −0.2br (NH·CO), and −0.8br (t, 6-NH).

The 6-chloropyrone derivative (18a) (0.3 g) was heated with dry benzylamine (10 ml) under reflux for 3 h. The excess of benzylamine was removed under reduced pressure, and the residue was washed with water and then with ethanol (50 ml). The residue was crystallised from ethanol to give *NN'*-dibenzylurea [1] (0.16 g, 80%), m.p. and mixed m.p. 169°. Evaporation of the ethanol washings gave *NN'*-dibenzylmalonamide [1] (0.45 g), m.p. and mixed m.p. 140°.

The 7-chloro-2-ethylthiopyrano-oxazine (1a) (2.6 g) was dissolved in dry dioxan (35 ml) and heated under reflux with ethanol (1.44 ml, 2.5 molar proportions) for 1.5 h. The solution was evaporated under reduced pressure, the residue was washed with hot carbon tetrachloride, and the remaining solid was crystallised from acetic acid (charcoal) to yield ethyl 4-chloro-1,2-dihydro-6-hydroxy-2-oxopyridine-3-carboxylate (0.88 g), m.p. and mixed m.p. 224° (decomp.). The carbon tetrachloride evaporated slowly and so afforded pale yellow 6-*chloro*-3-*diethoxymethylenecarbamoyl*-4-*hydroxy-pyran*-2-*one* (19) (0.5 g, 15%), m.p. 144° [from carbon tetrachloride (charcoal)] (Found: C, 45.3; H, 4.3; N, 4.6. $C_{11}H_{12}ClNO_6$ requires C, 45.6; H, 4.1; N, 4.8%), *m/e* 289/291, τ 8.57 (t, 2 × Me, *J* 7 Hz), 5.56 and 5.47 (q,q, 2 × CH_2O), 3.81 (s, 5-H), and −4.93br (chelated OH).

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