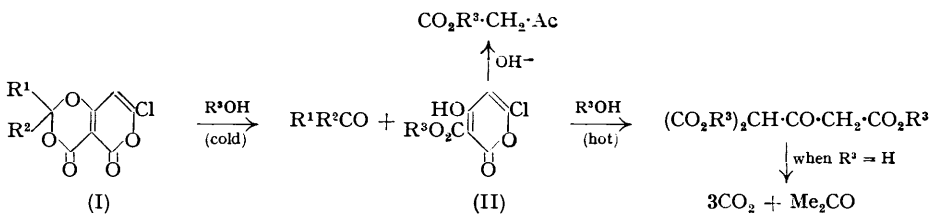
464. *Heterocyclic Syntheses with Malonyl Chloride. Part II.* 2 : 2-Disubstituted 6′-Amino-2′ : 4-diketopyrano(3′ : 4′-5 : 6)-1 : 3-dioxins and Simpler Derivatives of 4-Keto-1 : 3-dioxin.*

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

The chloropyronodioxins (I), prepared from malonyl chloride and ketones, react stepwise with primary and secondary amines to yield (non-basic) aminopyronodioxins (III) and thence, with fission of the pyrone ring, biscarboxyamide derivatives (IV) of 4-keto-1 : 3-dioxin. The unsaturated lactone-like ring of these compounds is stable to acid but not basic reagents. Sodium hydroxide or boiling water degrades the ketodioxins (IV) to acetone 1 : 3-dicarboxyamides, whilst amines yield acetone-1 : 1 : 3-tricarboxyamides; sodium methoxide with the dianilide (IV) afforded a monoester dianilide of acetone-tricarboxylic acid.

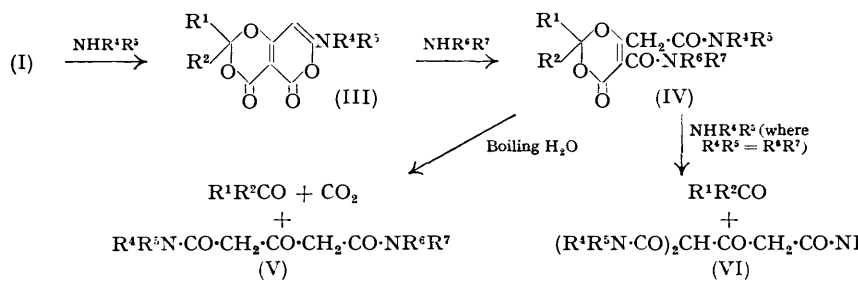
Light absorptions are recorded for the new heterocyclic series (III) and (IV).

6′-Chloro-2′ : 4-diketopyrano(3′ : 4′-5 : 6)-1 : 3-dioxin derivatives (I), which are formed by heating malonyl chloride with ketones, interact readily with alcohols and water (Part I*), according to the scheme :



(I) (II)

We have now examined the behaviour of compounds (I) towards primary and secondary amines. End-products analogous to the above are given, *viz.*, acetone-1 : 1 : 3-tricarboxyamides (VI) and the original ketone, but the intermediate reaction stages are different. First there is replacement of the chlorine atom then fission of the pyrone ring, and *lastly* fission of the ketodioxin ring :



The stages are clear-cut, and the products (III), (IV), (V), and (VI) are obtained in good yields.

6′-Amino-2 : 4′-diketopyrano(3′ : 4′-5 : 6)-1 : 3-dioxins.—Treatment of the chloropyronodioxins (I), $C_7HR^1R^2O_5Cl$, in chloroform with 2 mols. of various amines (NHR^4R^5) gave amine hydrochlorides and the 6′-substitution products (III), $C_7HR^1R^2O_5NR^4R^5$, which are listed in Table 1. These aminopyranodioxins absorbed light strongly in the 3300—3400-Å region and resembled in this respect the simpler pyrone derivative (VII), obtained from (II; R^3 = Et) with morpholine.

The aminopyronodioxins (III), unlike the parent chloro-compounds (I), were stable to water and alcohols. They lacked basic properties, simulating amides. In particular

* Part I, *J.*, 1952, 4109.

TABLE 1. *6'-Amino-2' : 4-diketopyrano(3' : 4'-5 : 6)-1 : 3-dioxins* (III) *and a related pyran.*

No.	Chloro-compound (I) R^1, R^2	(g.)	Base, c.c.	Method *	Product (III) NR^4R^5	Yield (%)	Form, solvent †
1	Me_2	0·5	Morpholine, 0·38	*a*	Morpholino	93	Needles, EtOH
2	,,	4·61	Piperidine, 3·95	,,	Piperidino	72	Needles, C_6H_6–Pet
3	,,	2·3	$NHEt_2$, 2·06	,,	NEt_2	91	Prisms, EtOH
4	,,	0·46	NHMePh, 0·435	,,	NMePh	73	Needles, EtOH
5	,,	5	NH_2Ph, 4	*b*	NHPh	98	EtOH
6	,,	4·61	$NH_2{\cdot}CH_2Ph$, 4·36	,,	$NH{\cdot}CH_2Ph$	98	EtOH
7	,,	2·04	Aq. NH_3 (*d* 0·88), 1·1	*c*	NH_2 [1]	38	EtOH
8	Ph_2	0·5	Morpholine, 0·5	*d* [2]	Morpholino	70	Plates, $CHCl_3$–Et_2O
9	,,	3·55	Piperidine, 2·05	*d*	Piperidino	70	Leaflets, *cyclo*hexanone
10	,,	3·55	NH_2Bu^n, 2	*a*	$NHBu^n$	85	Prisms, EtOH
11	,,	5	$NH_2{\cdot}CH_2Ph$, 3·08	,,	$NH{\cdot}CH_2Ph$	66	Needles, $H{\cdot}CO{\cdot}NMe_2$–EtOH
12	,,	5	NH_2Ph, 2·54	,,	NHPh	85	,, ,,
13	Me, Pr^n	1	Morpholine, 0·67	*a* [3]	Morpholino	66	C_6H_6–Pet
14	Me, Ph	1	,, 0·59	*a*	,,	51	Pr^nNO_2
15	Me, CO_2Et	0·98	$NHEt_2$, 0·7	*a* [2]	NEt_2	49	Needles, EtOH
16	$\cdot[CH_2]_5\cdot$	0·5	Morpholine, 0·32	*a* [2]	Morpholino	56	C_6H_6
17	Chloro-compound (II), R^3 = Et	0·33	Morpholine, 0·27	*a*	*Ethyl 4-hydroxy-2-keto-6-morpholinopyran-3-carboxylate* (VII)		Plates, EtOH

* (*a*) The base was added slowly with mixing to the chloro-compound in chloroform. The mixture was washed with water, and the chloroform solution evaporated under reduced pressure. (*b*) The mixture obtained as in (*a*) was filtered and the solid washed with water. (*c*) The aqueous base was mixed slowly with a cooled solution of the chloro-compound in dioxan; the mixture was filtered and the filtrate evaporated. (*d*) The reactants, separately dissolved in dry benzene, were mixed and warmed on the steam-bath for several minutes; the mixture was washed with dilute hydrochloric acid, and water, and the benzene solution dried (Na_2SO_4) and evaporated.

† Pet = light petroleum (b. p. 100—120°).

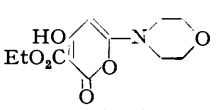
[1] Or (VIII). [2] The crude product was triturated with dry ether. [3] The crude product was triturated with light petroleum (b. p. 80—100°).

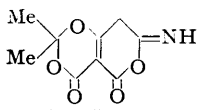
No.	M. p.	Formula	Found (%) C	H	N	Required (%) C	H	N	Light absorption in dioxan $\lambda_{max.}$ (Å)	ε
1	182° *	$C_{13}H_{15}O_6N$	55·4	5·4	5·3	55·5	5·4	5·0	2270	17,400
									3360	30,900
2	151·5 *	$C_{14}H_{17}O_5N$	60·0	5·95	5·55	60·2	6·15	5·0	—	—
3	145 *	$C_{13}H_{17}O_5N$	58·4	6·7	5·05	58·4	6·4	5·25	—	—
4	160	$C_{16}H_{15}O_5N$	63·65	5·15	4·9	63·8	5·0	4·65	—	—
5	192·5 *	$C_{15}H_{13}O_5N$	63·1	4·8	4·95	62·7	4·55	4·9	3400	33,000
6	176 *	$C_{16}H_{15}O_5N$	63·9	5·2	5·15	63·8	5·0	4·65	3300	28,300
7	>300 *	$C_9H_9O_5N$	50·9	4·55	6·65	51·2	4·3	6·65	2810	13,000
									3040	13,000 †
8	186 *	$C_{23}H_{19}O_6N$	67·9	4·95	3·4	68·1	4·7	3·5	2270	25,000
									3380	36,500
9	182 *	$C_{24}H_{21}O_5N$	71·55	5·5	3·1	71·45	5·25	3·5	—	—
10	167·5	$C_{23}H_{21}O_5N$	70·65	5·6	3·8	70·55	5·4	3·6	—	—
11	179 *	$C_{26}H_{19}O_5N$	73·2	4·65	3·4	73·4	4·5	3·3	—	—
12	173 *	$C_{25}H_{17}O_5N$	72·5	4·4	3·85	73·0	4·15	3·4	—	—
13	143 *	$C_{15}H_{19}O_6N$	58·15	6·3	4·45	58·2	6·2	4·55	2510	7,700
									2560	7,700
									3330	21,700
14	186 *	$C_{18}H_{17}O_6N$	62·5	5·15	4·1	62·9	5·0	4·1	2270	15,800
									2510	6,200
									2580	6,200
									3370	36,000
15	110·5	$C_{15}H_{19}O_7N$	55·75	5·95	4·65	55·4	5·9	4·3	3330	25,400
16	191 *	$C_{16}H_{19}O_6N$	60·4	6·15	4·1	59·8	5·95	4·35	—	—
17	165	$C_{12}H_{15}O_6N$	54·05	5·85	5·1	53·5	5·6	5·2	2270	14,800
									3250	31,800

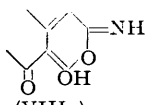
* With decomp. † Similar values in chloroform.

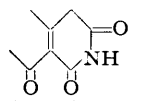
the anilino-compound (III; $R^1 = R^2 = Me$, $R^4 = H$, $R^5 = Ph$) was pseudo-acidic, and with the aqueous hydroxides of lithium, sodium, and potassium (though not with ammonia), it gave sparingly soluble crystalline metal derivatives. Reaction of the sodio-derivative with methyl iodide afforded an *N*-methyl compound. This was identical with (III;

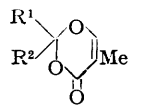
$R^1 = R^2 = R^4 = Me$, $R^5 = Ph$), prepared from the chloropyronodioxin (I; $R^1 = R^2 = Me$) and methylaniline.


(VII)


(VIII)


(VIII*a*)


(VIII*b*)


(IX*a*; $R^1 = R^2 = Me$)
(IX*b*; $R^1 = Me$, $R^2 = Ph$)

With ammonia, the chloropyronodioxin (I; $R^1 = R^2 = Me$) yielded a monosubstitution product as expected, but this had a different absorption spectrum from the previous amine products (III), with less intense maxima at shorter wave-lengths (see Table 1). The ammonia product may therefore exist in the form (VIII) rather than (III; $R^1 = R^2 = Me$, $R^4 = R^5 = H$). The alternative tautomeric form (VIII*a*) could be discounted because the compound lacked enol properties. Moreover the isomeric pyridone structure (VIII*b*) and its tautomeric forms were ruled out because of the ease with which the ring was split, *e.g.*, by morpholine (see below). This lability precluded the condensation of the compound with primary amines in the way possible with other imino-heterocycles (see Elvidge and Linstead, *J.*, 1952, 5000).

4-*Keto*-1 : 3-*dioxins*.—Treatment of the aminopyronodioxins (III) and (VIII) with a further mol. of a primary or secondary amine caused fission of the pyrone ring, and the diamide derivatives (IV) of 4-keto-1 : 3-dioxin were formed (see Table 2). Those derivatives (IV) having $R^4R^5 = R^6R^7$ were also obtained direct from the chloropyronodioxins (I) with the appropriate larger quantity of amine (excess of amine led to acetonetricarboxyamides). The structure of the morpholine product (IV; $R^1 = R^2 = Me$, $NR^4R^5 = NR^6R^7$ = morpholino) was confirmed by degradation with boiling water (or cold sodium hydroxide). Carbon dioxide and acetone were formed, together with enolic acetone-1 : 3-dicarboxymorpholide, the identity of which was verified by a synthesis from diethyl acetone-1 : 3-dicarboxylate and morpholine.

The only previous representatives of the simple 4-keto-1 : 3-dioxins seem to be the parent substance itself (Mejuto and Calvet, *Anal. Fis. Quim.*, 1934, **32**, 1168) and the two derivatives (IX*a* and *b*) (Carroll and Badger, *J. Amer. Chem. Soc.*, 1952, **74**, 6305). Hence the new members (IV) have been examined in some detail. These all absorb light in the 2500—2700-Å region but there are marked substituent effects (see Table 2) as is the case, *e.g.*, with *N*-substituted crotonamides (Crombie, *J.*, 1952, 2997). Qualitative chemical tests showed that the ring was stable to cold water and aqueous hydrochloric acid, and to boiling alcohols and dilute methanolic hydrogen chloride. At pH 9 the Légal and dichlorophenol–indophenol colour tests were negative, and ammoniacal silver nitrate was reduced only when hot. Rupture of the ring occurred with methanolic sodium methoxide, besides boiling water and cold sodium hydroxide, and also with primary and secondary amines.

In containing an enol ether link and an αβ-unsaturated lactone grouping, the 4-keto-1 : 3-dioxin ring system bears an interesting relation to both of the two main types of unsaturated lactone (see Kuehl, Linstead, and Orkin, *J.*, 1950, 2213; also pp. 2223, 2228, and *J.*, 1951, 1501). The properties of the compounds (IV) indicate that they are indeed composite in type. These ketodioxins resemble enol lactones in reacting easily with basic reagents and hot water, but differ from them and resemble αβ-unsaturated lactones in being stable to alcoholic acid and in lacking reducing properties. Carroll and Badger (*loc. cit.*) compared the reactions of ketodioxins with those of diketen.

However, the ease with which the ketodioxin ring reacts under given conditions may perhaps be influenced strongly by the nature of substituents. This is suggested by the differing reactivity of the fused ketopyrano(3′ : 4′-5 : 6)dioxin system to, *e.g.*, alcohols, when substituted by chlorine as in (I) or by amine residues as in (III) : the compounds (I) readily give (II), but the compounds (III) do not react with alcohols alone.

Acetonecarboxylic Acid Derivatives.—The reactions of the easily available chloropyronodioxins (I) and their pyrone (II) and ketodioxin (IV) degradation products with basic reagents provide routes to esters, amides, and mixed ester-amides of acetone-1 : 3-di- and

-1 : 1 : 3-tri-carboxylic acid, which hitherto have been largely inaccessible. The preparations from (I; $R^1 = R^2 = Me$) of triethyl acetone-1 : 1 : 3-tricarboxylate (Part I of this series) and acetone-1 : 3-dicarboxymorpholide (above) were the first examples. The following additional preparations illustrate the scope of the method.

TABLE 2. *Reaction of the aminopyronodioxins* (III) *with* 1 *mol. of various amines : 4-keto-*1 : 3*-dioxin-*6*-acetic-*5*-carboxyamides.*

	Aminopyronodioxin (III; $R^1 = R^2 = Me$)			Method,* reaction time	4-Keto-2 : 2-dimethyl-1 : 3-dioxin (IV)		Yield	Form,
No.	NR^4R^5	(g.)	Base (c.c.)	(min.)	NR^4R^5	NR^6R^7	(%)	solvent †
18	Morpholino	0·55	Morpholine, 0·2	*a*, 30	Morpholino	Morpholino	—	EtOAc–Et_2O
19	,,	1·1	$NHEt_2$, 0·45	*a*,[1] 30	Morpholino	NEt_2	52	Prisms, C_6H_6–Pet (b. p. 60—80°)
20	Piperidino	1·4	Morpholine, 0·435	*a*,[2] 25	Piperidino	Morpholino	80	,, ,,
21	NHPh	1	NH_2Ph, 0·32	*b*	NHPh	NHPh	—	Pet (b. p. 100—120°)
22	$NH{\cdot}CH_2Ph$	1	NH_2Bu^n, 0·33	*a*,[3] 40	$NH{\cdot}CH_2Ph$	$NHBu^n$	24	Laths, Pet (b. p. 60—80°)
23	NH_2	0·42	Morpholine, 0·18	*c*	NH_2	Morpholino	50	Needles, EtOH
	Aminopyronodioxin (III; $R^1 = R^2 = Ph$)				2 : 2-Diphenyl-4-keto-1 : 3-dioxin			
	NR^4R^5	(g.)			NR^4R^5	NR^6R^7		
24	Morpholino	1·24	Morpholine, 0·27	*a*, 10	Morpholino	Morpholino	73	EtOH
25	$NHBu^n$	7·1	Morpholine, 1·58	*d* [3]	$NHBu^n$	Morpholino	73	Leaflets, C_6H_6–Pet (b. p. 100—120°)

* (*a*) Heated under reflux in chloroform, and the solution evaporated. (*b*) Heated under reflux in dioxan for 1 hr. The mixture was filtered, the solution evaporated, and the residue triturated with light petroleum (b. p. 40—60°). (*c*) Kept in dioxan at room temperature overnight, and the solution evaporated. (*d*) Shaken in chloroform (50 c.c.) for 1 day at room temp. Unchanged pyronodioxin (1·05 g.) was collected and the filtrate washed with water and evaporated.

† Pet = light petroleum.

[1, 2, 3] The crude product was triturated with (1) light petroleum (b. p. 40—60°), or (2) ether, or (3) light petroleum (b. p. 60—80°).

			Found (%)			Required (%)			Light absorption, (i) in dioxan (ii) in $CHCl_3$	
No.	M. p.	Formula	C	H	N	C	H	N	$\lambda_{max.}$ (Å)	ε
18	134°	$C_{17}H_{24}O_7N_2$	55·8	6·7	7·8	55·4	6·6	7·6	(i) 2270	9,200
									2510	11,100
									2560	11,800
19	117	$C_{17}H_{26}O_6N_2$	57·3	7·3	8·2	57·65	7·4	7·9	—	—
20	131·5	$C_{18}H_{26}O_6N_2$	59·1	7·05	8·05	59·0	7·15	7·65	—	—
21	100	$C_{21}H_{20}O_5N_2$	66·55	5·6	7·25	66·3	5·3	7·35	(ii) 2400	20,900
									2510	17,100
									2900	14,000
22	86	$C_{20}H_{26}O_5N_2$	64·3	7·1	7·45	64·15	7·0	7·5	(ii) 2700	8,600 ‡
									2800	8,600
23	223 (decomp.)	$C_{13}H_{18}O_6N_2$	52·55	6·35	9·45	52·35	6·1	9·4	—	—
24	135	$C_{27}H_{28}O_7N_2$	65·6	6·0	5·6	65·85	5·75	5·7	(i) 2510	11,300
									2570	11,300
									3280	2,200
									3430	2,200
25	117·5	$C_{27}H_{30}O_6N_2$	67·55	6·5	6·35	67·75	6·3	5·85	(ii) 2580	6,900
									2660	7,900
									2760	4,800

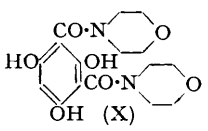
‡ Fluoresced strongly.

The ketodioxin derivative (IV; $R^1 = R^2 = Me$, $R^4 = R^6 = H$, $R^5 = CH_2Ph$, $R^7 = Bu^n$), prepared from (I; $R^1 = R^2 = Me$) by reaction with first benzylamine and then *n*-butylamine, was treated with boiling water. The mixed benzylamide *n*-butylamide (V) of acetone-1 : 3-dicarboxylic acid was thus obtained in good yield. Treatment of the dianilide (IV; $R' = R^2 = Me$) with methanolic sodium methoxide afforded the mixed methyl ester dianilide of acetone-1 : 1 : 3-tricarboxylic acid $NHPh{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}CH(CO_2Me){\cdot}CO{\cdot}NHPh$. The alternative reaction of aniline with the chloropyrone ester (II; $R^3 = Me$), obtained from

(I; $R^1 = R^2 = Ph$) with methanol, yielded an identical acetonetricarboxylic ester dianilide, so that the structure of this product is certain.

Treatment of the benzylaminopyronodioxin (III; $R^1 = R^2 = Ph$, $R^4 = H$, $R^5 = CH_2Ph$) with 2 mols. of benzylamine afforded enolic acetone-1 : 1 : 3-tricarboxybenzylamide (VI). From each of the chloropyronodioxins (I; $R^1 = R^2 = Me$ and $R^1 = R^2 = Ph$) with an excess of morpholine, enolic acetone-1 : 1 : 3-tricarboxymorpholide (VI) was readily prepared. Its formation from the diphenyl compound (I; $R^1 = R^2 = Ph$) was also carried out stepwise (I) ⟶ (III) ⟶ (IV) ⟶ (VI): benzophenone was a second product at the last stage. The structure of the trimorpholide was confirmed by fission with morpholine at 100°, over 1·4 mols. of malondimorpholide being obtained.

In contrast to the success of the above methods, attempts to synthesise, *e.g.*, acetone-1 : 1 : 3-tricarboxymorpholide by standard routes failed. Triethyl acetone-1 : 1 : 3-tricarboxylate with hot morpholine gave malondimorpholide only. As an alternative it had been hoped to condense malonic half-morpholide acid chloride with a metal derivative of malondimorpholide, but neither the magnesio- nor the sodio-derivative of the latter could be obtained. Dissolution of sodium in molten malondimorpholide caused a self-condensation. We suggest structure (X) for the hygroscopic enolic product, $C_{16}H_{20}O_7N_2$, by analogy with the production of diethyl phloroglucinol-1 : 3-dicarboxylate from malonic ester and sodium (Moore, *J.*, 1904, **85**, 165).



(X)

Experimental

General Properties of Aminopyronodioxins.—The aminopyronodioxins (III) were stable to water and boiling alcohol (no colour with ferric chloride) and did not yield salts with hydrogen chloride in chloroform, or picric acid in dioxan. The 6′-amino(or imino)-compound (No. 7) gave a deep blue-green colour with nitrous acid in aqueous dioxan; this solution afforded no azo-dye with sodium phenoxide. The benzylamino-compound (No. 6) was insoluble in aqueous sodium hydroxide, but the anilino-compound (No. 5) dissolved easily in aqueous lithium, sodium, potassium, and ammonium hydroxide; crystalline metal derivatives separated rapidly from the first three solutions.

Methylation of 6′-Anilino-2′ : 4-diketo-2 : 2-dimethylpyrano(3′ : 4′-5 : 6)-1 : 3-dioxin.—When stirred with sodium hydroxide (0·245 g., 2 mols.) in water (10 c.c.) the anilino-compound (No. 5) (0·88 g.) dissolved, and after a few minutes the sodio-derivative (0·95 g.) separated as needles. A portion (0·53 g.) in methanol was kept with excess of methyl iodide overnight. The solution was evaporated and the residue triturated with water to remove sodium iodide. From ethanol, the product (0·34 g., 66%) formed needles, m. p. 160° alone and when mixed with 2′ : 4-diketo-2 : 2-dimethyl-6′-methylanilinopyrano(3′ : 4′-5 : 6)-1 : 3-dioxin (No. 4).

General Properties of the 4-Keto-1 : 3-dioxin Derivatives (IV).—None of the compounds (IV) gave a colour with ferric chloride in aqueous dioxan. The dimorpholide (No. 18) and the morpholide amide (No. 23) were easily water-soluble. Their stability to various reagents was investigated by testing for enolic products with ferric chloride, after any excess of acid or alkaline reagent had first been neutralised. With dioxin No. 18 in the cold the test was negative after treatment with aqueous hydrochloric acid for 1 hr. or (also with Nos. 19 and 20) with water for 3 days, and under reflux with methanolic hydrogen chloride (1 hr.), methanol (10 min.), or butanol (5 min.); with boiling aqueous sodium hydroxide or methanolic sodium methoxide there was a purple and a deep red colour respectively after 5 min.; with boiling water, Nos. 18, 19, and 20 gave a purple colour in the test after 10 min.

Tests for reducing properties were performed on dioxin No. 20, by methods described by Kuehl, Linstead, and Orkin (loc. cit.) (see p. 2253).

Reaction of the Chloropyronodioxin (I; $R^1 = R^2 = Me$) *with 3 Mols. of Morpholine.*—Solutions of the chloro-compound (1 g.) in benzene (40 c.c.), and of morpholine (2·5 c.c.) in benzene (10 c.c.), were heated together under reflux for 5 min. The mixture was washed with dilute hydrochloric acid and water, the benzene layer was combined with three chloroform extracts of the aqueous washings, dried (Na_2SO_4), and evaporated, and the residue triturated with dry ether. The product (1·3 g., 81%) crystallised from ethyl acetate–ether and had m. p. 134° alone and in admixture with the dimorpholide of 4-keto-2 : 2-dimethyl-1 : 3-dioxin-6-acetic-5-carboxylic acid (No. 18).

Degradation of the Dimorpholide of 4-Keto-2 : 2-dimethyl-1 : 3-dioxin-6-acetic-5-carboxylic

Acid.—The preceding dioxin derivative (No. 18) (0·5 g.) was heated with water under reflux for 2 hr., during which carbon dioxide was evolved. The solution was distilled almost to dryness; the distillate with Brady's reagent gave acetone 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 125°. The residue in the distillation flask was dried under reduced pressure, then triturated with ether, affording acetone-1 : 3-dicarboxymorpholide (0·3 g., 78%), m. p. 132° undepressed by the authentic material described below.

Acetone-1 : 3-*dicarboxymorpholide.*—(*a*) Diethyl acetone-1 : 3-dicarboxylate (10 g.) was heated with morpholine (10·25 c.c.) at 75° for 19 hr., and the product (5·2 g., 37%) precipitated by addition of benzene. From ethanol, *acetone*-1 : 3-*dicarboxymorpholide* formed needles, m. p. 132° (Found: C, 54·85; H, 7·05; N, 10·0. $C_{13}H_{20}O_5N_2$ requires C, 54·9; H, 7·1; N, 9·85%). It gave a purple colour with aqueous ferric chloride. The m. p. was depressed to 110° by malondimorpholide.

(*b*) The foregoing dioxin-dimorpholide (No. 18) (1·1 g.) in water (10 c.c.) was heated with 2N-sodium hydroxide (1·5 c.c.) at 100° for 10 min. The cooled solution was neutralised with aqueous sulphuric acid (evolution of carbon dioxide), and extracted with chloroform (3 × 10 c.c.), evaporation of which gave acetone-1 : 3-dicarboxymorpholide (0·58 g., 68%), m. p. and mixed m. p. 131°.

Acetone-1-*carboxybenzylamide*-3-*carboxy*-n-*butylamide.*—6'-Benzylamino-2' : 4-diketo-2 : 2-dimethylpyrano(3' : 4'-5 : 6)-1 : 3-dioxin (No. 6) (1 g.) was heated with *n*-butylamine (0·33 c.c.) in chloroform (10 c.c.) under reflux for 1 hr. Evaporation of the chloroform afforded the crude oily ketodioxin derivative, which was boiled with water for 2·5 hr. From water, *acetone*-1-*carboxybenzylamide*-3-*carboxy*-n-*butylamide* (0·3 g., 31%) crystallised with m. p. 139° (Found: C, 65·9; H, 7·85; N, 9·55. $C_{16}H_{22}O_3N_2$ requires C, 66·2; H, 7·65; N, 9·65%).

1-*Carbomethoxyacetone*-1 : 3-*dicarboxyanilide.*—(*a*) 4-Keto-2 : 2-dimethyl-1 : 3-dioxin-6-acetanilide-5-carboxyanilide (No. 21) (150 mg.) in methanol was heated under reflux for 15 min. with sodium methoxide (from 9 mg. of sodium). The cooled solution was poured into aqueous hydrochloric acid, whereupon the acetonetricarboxylic ester dianilide (100 mg., 71%) separated, m. p. 214° (decomp.) undepressed by the specimen obtained in the following experiment.

(*b*) Methyl 6-chloro-4-hydroxy-2-ketopyran-3-carboxylate (Part I, *loc. cit.*) (0·5 g.) in chloroform was warmed with aniline (0·45 c.c.) for several minutes. The mixture was shaken with water, and the chloroform separated and evaporated. *Carbomethoxyacetone*-1 : 3-*dicarboxyanilide* (0·53 g., 64%) crystallised from benzene and had m. p. 213° (decomp.) (Found: C, 64·25; H, 4·95; N, 7·6. $C_{19}H_{18}O_5N_2$ requires C, 64·4; H, 5·1; N, 7·9%). It gave a deep red colour with ferric chloride in aqueous dioxan.

Acetone-1 : 1 : 3-*tricarboxybenzylamide.*—6'-Benzylamino-2' : 4-diketo-2 : 2-diphenylpyrano-(3' : 4'-5 : 6)-1 : 3-dioxin (No. 11) (0·5 g.) and benzylamine (0·26 c.c., 2 mols.) in dimethylformamide (7 c.c.) were kept for 15·5 hr. Evaporation of the solution under reduced pressure, and trituration of the residue with light petroleum (b. p. 60—80°) yielded *acetone*-1 : 1 : 3-*tricarboxybenzylamide* (0·44 g., 81%) which crystallised from benzene–light petroleum (b. p. 60—80°) and had m. p. 100° (Found: N, 9·55. $C_{27}H_{27}O_4N_3$ requires N, 9·2%). It gave a deep red colour with alcoholic ferric chloride.

Acetone-1 : 1 : 3-*tricarboxymorpholide.*—(*a*) 6'-Chloro-2' : 4-diketo-2 : 2-dimethylpyrano(3' : 4'-5 : 6)-1 : 3-dioxin (Part I) (0·41 g.) in chloroform was gradually treated with morpholine (0·31 c.c., 2 mols.). The solution was shaken with water, and the chloroform layer was dried (Na_2SO_4) and kept with morpholine (0·31 c.c.) overnight. Evaporation yielded *acetone*-1 : 1 : 3-*tricarboxymorpholide* which crystallised from ethanol as needles, m. p. 181° (Found: C, 54·9; H, 7·0; N, 10·4. $C_{18}H_{27}O_7N_3$ requires C, 54·4; H, 6·85; N, 10·55%). It gave a red-purple colour with aqueous ferric chloride.

(*b*) The tricarboxymorpholide was also obtained by keeping the chloro-2 : 2-diphenylpyronodioxin (I; $R^1 = R^2 =$ Ph) with an excess of morpholine in chloroform.

(*c*) 4-Keto-2 : 2-diphenyl-1 : 3-dioxin-6-acetomorpholide-5-carboxymorpholide (No. 24) (0·5 g.) was heated with morpholine (0·09 c.c.) in dioxan on the steam-bath for 15 min. The solution was evaporated, and the residue washed with ether, yielding acetone-1 : 1 : 3-tricarboxymorpholide (0·4 g.) with m. p. and mixed m. p. 181° after recrystallisation from ethanol. The ethereal washings contained benzophenone which was isolated as the 2 : 4-dinitrophenylhydrazone, m. p. and mixed m. p. 232°.

Fission to Malondimorpholide.—The tricarboxymorpholide (0·23 g.) was heated with morpholine (0·51 c.c., 10 mols.) on the steam-bath for 15 hr. Trituration with ether yielded malondimorpholide (0·2 g., 1·4 mols.), m. p. 132° undepressed by authentic material.

The latter was obtained in good yield by heating diethyl malonate (100 g.) with an excess of morpholine (135 g.) at 150° for 42 hr. *Malondimorpholide* crystallised from ethanol as plates, m. p. 137° (Found: C, 54·25; H, 7·45; N, 11·25. $C_{11}H_{18}O_4N_2$ requires C, 54·5; H, 7·5; N, 11·6%).

*Action of Morpholine on Triethyl Acetone-*1 : 1 : 3*-tricarboxylate.*—The triester (5·5 g.) was heated with morpholine (5·2 c.c.) at 75° for 22 hr. The product gave no colour with aqueous ferric chloride. Treatment with benzene yielded malondimorpholide (2·75 g.), m. p. 135° undepressed by authentic material.

Malonic Monoethyl Ester Morpholide.—Diethyl malonate (160 g.) and morpholine (87 g., 1 mol.) were heated at 150°.for 24 hr. Malondimorpholide (41 g.) was filtered off and washed with ether, and the filtrate was distilled under reduced pressure, yielding *malonic monoethyl ester morpholide* (84 g., 42%), b. p. 135—145°/1·5 mm., m. p. 59·5° [from light petroleum (b. p. 40—60°)] (Found: C, 53·55; H, 7·6; N, 6·45. $C_9H_{15}O_4N$ requires C, 53·7; H, 7·5; N, 6·95%).

Attempted Preparation of Metal Derivatives of Malondimorpholide.—The morpholide was treated with magnesium methoxide (1 mol.) in methanol and the solution evaporated to dryness. The residue was suspended in dry benzene and acetyl chloride added. Heat was evolved. Evaporation, treatment with aqueous acid, and extraction with chloroform gave malondimorpholide (recovery, 75%).

Repetition of the reaction, with sodium and formamide–dioxan, instead of magnesium methoxide in methanol, yielded only malondimorpholide.

Action of Sodium on Molten Malondimorpholide.—Malondimorpholide (4·84 g.) was heated with sodium (0·23 g.) until the metal had dissolved. Morpholine vapour was evolved. After being cooled, the product was treated with water (20 c.c.), and the solution was washed with chloroform (5 × 10 c.c.), acidified, clarified, and extracted with chloroform (5 × 25 c.c.). Evaporation of the latter and trituration of the residue with ether afforded *phloroglucinol-dicarboxymorpholide* which separated from dioxan–ether as a pale yellow powder, m. p. 227° (Found: C, 55·2; H, 5·75; N, 8·05. $C_{16}H_{20}O_7N_2$ requires C, 54·55; H, 5·7; N, 7·95%). It gave a deep red colour with aqueous ferric chloride.

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