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4-Substituted-2,3,5-pyrrolidinetriones

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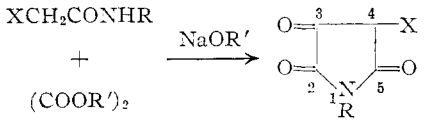
Pyrrolidinetriones containing electron-attracting groups such as cyano, alkoxycarbonyl, acyl and carbamoyl in the 4-position have been prepared by condensation of the appropriate α-substituted acetamides with oxalate esters. These compounds are strong acids and, in some cases, the sodium salts can be recrystallized from aqueous mineral acids. When the group in the 4-position is ammonium or sulfonium, the products are intramolecular salts of the ylide type.

Pyrrolidinetriones carrying hydrocarbon substituents on the 4-position and a variety of N-substituents have been prepared by the condensation of oxalate esters with substituted acetamides[1] and by the cyclization of *p*-alkyl-α-cyano-β-hydroxycinnamates.[2] Claims also have been made to their synthesis from oxalyl chloride and substituted acetamides,[3] but subsequent workers[2,4,5] have shown that most of these products are almost certainly oxazolidinediones. The known pyrrolidinetriones are characterized by their ease of hydrolysis, and, in the case of those having no 4-substituent, by the reactivity of the methylene group leading to bimolecular condensation and other complicating side reactions during synthesis and isolation.[1]

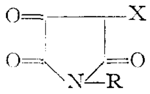
We have now found that pyrrolidinetriones having strong electron-attracting groups in the 4-position possess a number of remarkable properties including increased resistance to hydrolysis, strong acid character, and the ability to form stable salts or complexes with a variety of metal ions. These 4-substituted pyrrolidinetriones were prepared by the condensation of oxalate esters with acetamides appropriately substituted in the α-position.



Acetamides substituted with carbamoyl, alkoxycarbonyl, cyano, acyl, sulfonium and ammonium groups in the α-position were employed successfully, as was α-cyanothioacetamide. The amide also could be mono-N-substituted with a variety of hydrocarbon groups.

TABLE I

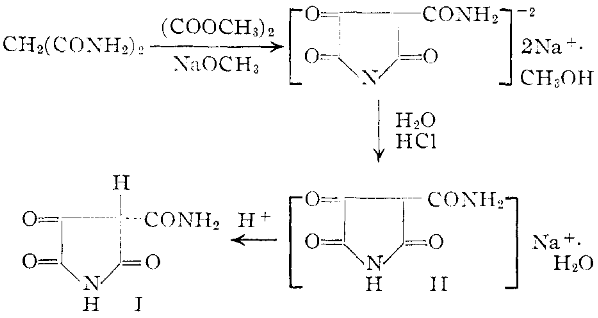
pK_A MEASUREMENTS OF PYRROLIDINETRIONES



X	R	Solvent	pK_A
$CONH_2$	H	H_2O	2.7
$CO_2C_2H_5$	H	H_2O	2.8
m-$CF_3C_6H_4NHCO$	*m*-$CF_3C_6H_4$	C_6H_6/C_2H_5OH	2.05
$CONHC_6H_5$	C_6H_5	C_6H_6/C_2H_5OH	2.25
$COCH_3$	C_6H_5	C_6H_6/C_2H_5OH	2.25
$CONHC_6H_{11}$[a]	$CONHC_6H_{11}$	C_6H_6/C_2H_5OH	3.10

[a] C_6H_{11} = cyclohexyl.

A typical example of these compounds, 4-carbamoyl-2,3,5-pyrrolidinetrione (I), was prepared from sodium methoxide, malonamide and dimethyl oxalate.



The disodium salt precipitated directly from the alcoholic medium and was converted to a hydrated monosodium salt II by treatment with dilute hydrochloric acid. The water of crystallization could be removed either by heating the salt under vacuum or by gently warming a solution of the salt in dimethylformamide until the anhydrous salt precipitated.

Attempts to remove the sodium from II by displacement with mineral acids were unsuccessful.[5a] In fact, the salt could be recrystallized from hot 25% sulfuric acid. The sodium-free product I was obtained by treating an aqueous solution of II with a sulfonic acid-type ion exchange resin. Large volumes of water were required because only 0.44 g. of the hydrated salt dissolves in 100 ml. of water at room temperature.

The structures of I and II were established by analyses, reaction of II with 2,4-dinitrophenylhydrazine to give a hydrazone, hydrolysis of I in warm aqueous ammonium hydroxide to oxalic acid and malonamide, and reaction with ferric chloride to give a positive enol test. The infrared spectrum of I showed strong bands at 5.8 and 5.95 μ and a weak one at 5.6 μ, in agreement with published spectra for similar compounds.[2,4,5]

Analogs of I having cyano, acetyl or ethoxycarbonyl groups in the 4-position also were produced only by use of acid exchange resins. The ease with which the free acids could be obtained was markedly altered by the presence of alkyl sub-

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(1) W. Wislicenus and W. Sattler, *Ber.*, **24**, 1245 (1891).

(2) G. S. Skinner and C. B. Miller, Jr., THIS JOURNAL, **75**, 977, 6359 (1953).

(3) G. S. Skinner and J. F. Perkins, *ibid.*, **72**, 5569 (1950).

(4) J. C. Sheehan and E. J. Corey, *ibid.*, **74**, 360 (1952).

(5) G. S. Skinner and R. E. Ludwig, *ibid.*, **78**, 4656 (1956).

(5a) NOTE ADDED IN PROOF.—Since the manuscript was submitted, R. H. Wiley and S. C. Slaymaker, THIS JOURNAL, **80**, 1385 (1958), have reported the isolation of 4-carbamoyl-2,3,5-pyrrolidinetrione by heating an aqueous suspension of the crude sodium salt to boiling and then acidifying with hydrochloric acid.

stituents on the ring nitrogen atom and by the presence of a thiocarbonyl group. For example, the sodium could be removed from the N-methyl analog of I and from the product obtained from α-cyanothioacetamide by treatment with aqueous hydrochloric acid.

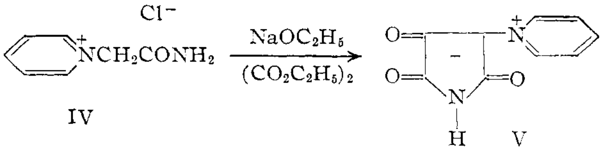
The pyrrolidinetriones form salts with a variety of other metals, and the solubilities of these salts are greatly affected by the presence of hydrocarbon substituents. For example, aqueous solutions of II form precipitates when mixed with dilute solutions of Cu^{++}, Hg^{++}, Pb^{++} and Ag^{+} ions. If each nitrogen atom of II is substituted with a methyl group, as in 1-methyl-4-N-methylcarbamoyl-2,3,5-pyrrolidinetrione (III), precipitates are also obtained with Ca^{++}, Ba^{++} and Zn^{++} ions. The corresponding allyl derivative also forms precipitates with Co^{++}, Ni^{++} and Fe^{+++}. Compound II is insoluble in most organic liquids. However, the alkali metal salts of the analog having a cyclohexyl group on each nitrogen are soluble even in aliphatic hydrocarbons. Table IV lists a number of metal derivatives which were prepared from II.

The acid strengths of several pyrrolidinetriones were measured in an effort to account for the stability of the sodium salts. As seen in Table I, the acid strengths of these compounds are comparable to that of chloroacetic acid (pK_A 2.8).

Ultraviolet absorption spectra of these pyrrolidinetriones resemble to a certain extent those of α,β-unsaturated ketones in that both possess peaks at approximately 240 and at 330 mμ. However, the second peak of the heterocycles is nearer the visible and about ten times as intense as that of the unsaturated ketones.

Some information on the hydrolytic stability of these compounds has been obtained by following changes in their ultraviolet absorption spectra in basic and acidic aqueous solutions. These solutions were prepared and examined spectrometrically immediately and again after the solution had been stored for 72 hours at room temperature. Compounds II and 1-methyl-4-N-methylcarbamoyl-2,3,5-pyrrolidinetrione (III) were unaffected in acid, and III was not appreciably affected in 0.01 *N* NaOH. However, as shown in Fig. 1, the spectrum of II is not recognizable after treatment with aqueous base. Thus, replacement of the imide hydrogen by a methyl group retards alkaline degradation.

In the general class of electron-attracting groups the most powerful are those which possess a unit positive charge, such as the sulfonium and quaternary ammonium groups. Accordingly, pyrrolidinetriones with such substituents have been prepared and examined briefly. Carbamoylmethylpyridinium chloride (IV) underwent smooth condensation with ethyl oxalate to give the internal salt of a pyrrolidinetrione (V). According to nomenclature suggested by Wittig,[6] V is named 4-pyridinium-2,3,5-trioxopyrrolidylide. Its infrared absorption spectrum has strong bands at 5.6, 5.81 and 6.05 μ and a weak one at 5.57 μ. It is remarkably stable and melts without decomposition above 300°. Similar, but less stable, products were prepared with dimethylsulfonium and trimethylammonium groups in the 4-position.



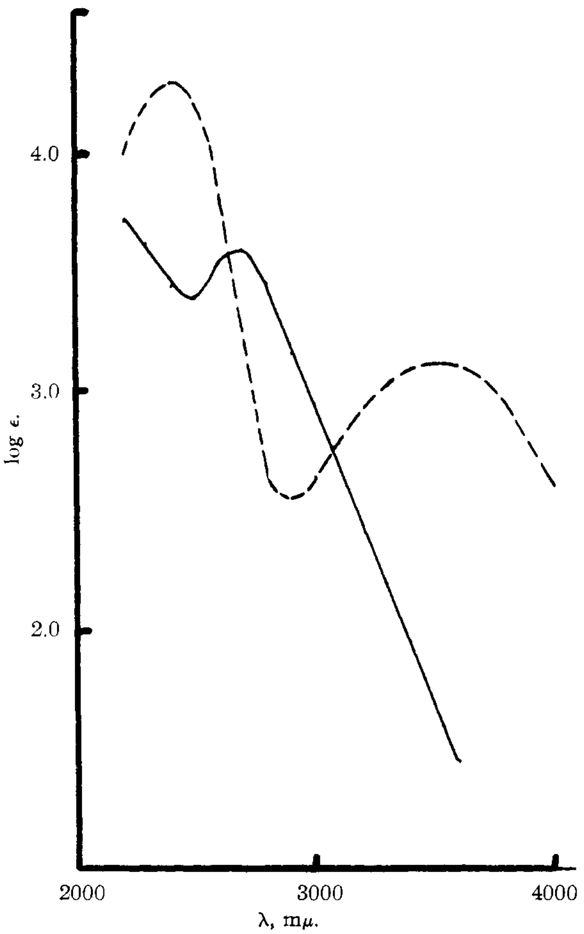


Fig. 1.—Absorption spectra of 4-carbamoyl-2,3,5-pyrrolidinetrione (I) in 0.01 *N* NaOH: --------, after mixing; ———, 72 hr. later.

Experimental

Materials.—The N,N′-disubstituted malonamides were prepared by reaction of ethyl malonate with methylamine,[7] cyclohexylamine[8] and dodecylamine.[8] Acetoacetamide was prepared from diketene and ammonium carbonate.[9] The addition of chloroacetamide to pyridine[10] and to trimethylamine[11] gave the corresponding carbamoylmethylammonium chlorides. The condensation of sodium *p*-toluenesulfinate and α-chloroacetamide gave α-(*p*-tolylsulfonyl)-acetamide.[12] Reaction of two moles of aqueous ammonia with ethyl benzoylacetate gave the imino amide from which benzoylacetamide was obtained by hydrolysis.[13] A standard procedure was used to obtain benzoylacetanilide.[14] Ethy

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(6) G. Wittig, *Angew. Chem.*, **63**, 15 (1951).

(7) M. A. Whiteley, *J. Chem. Soc.*, **83**, 33 (1903).

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(10) A. H. Cook, J. Downer and B. Hornung, *J. Chem. Soc.*, 502 (1941).

(11) R. R. Renshaw and H. T. Hotchkiss, Jr., THIS JOURNAL, **48**, 2698 (1926).

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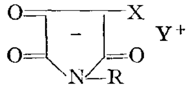
TABLE II

ULTRAVIOLET ABSORPTION MAXIMA

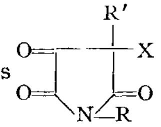


R	X	Y	$m\mu^1$	log	$m\mu^2$	log	Solvent
H	$CONH_2$	Na	235	4.25	345	2.26	H_2O
CH_3	$CONHCH_3$	Na	240	4.35	365	3.28	H_2O
C_6H_5	$COCH_3$	H	259	4.37	None		C_2H_5OH
C_6H_5	$CONHC_6H_5$	H	262	4.57	358	3.50	C_2H_5OH
C_6H_5	$CONHC_6H_5$	Na	261	4.54	367	3.38	C_2H_5OH
m-$CF_3C_6H_4$	m-$CF_3C_6H_4NHCO$	H	268	4.59	358	3.51	C_2H_5OH
C_6H_{11}[a]	$CONHC_6H_{11}$	H	241	4.30	342	3.31	C_2H_5OH
C_6H_{11}	$CONHC_6H_{11}$	Na	234	4.35	363	3.29	C_2H_5OH
$C_{10}H_{19}$[b]	$CONHC_{10}H_{19}$	H	238	4.36	353	3.25	C_2H_5OH
H	$C_5H_5N^+$		227	4.23	330	3.88	H_2O

[a] C_6H_{11} = cyclohexyl. [b] $C_{10}H_{19}$ = 2-methyl-5-isopropylcyclohexyl.

TABLE III

4-SUBSTITUTED-2,3,5-PYRROLIDINETRIONES



X	R	R'	Yield, %	M.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Metal, % Calcd.	Metal, % Found
$CONH_2$	H	Na	74		$C_5H_2N_2O_4Na_2 \cdot CH_3OH$	30.78	29.83	3.00	2.24	12.0	12.23	19.65	19.49
$CONH_2$	H	Na	64[e]		$C_5H_3N_2O_4Na$	33.72	33.48	1.70	2.29	15.73	15.50	12.91	12.24
$CONH_2$	H	H	63		$C_5H_4N_2O_4$	38.48	38.52	2.58	2.81	17.94	17.60		
$CONHCH_3$	CH_3	Na	85[f]	184–188	$C_7H_7N_2O_4Na \cdot H_2O$	37.50	37.49	4.05	4.07	12.50	12.25	10.36	10.34
$CONHCH_3$	CH_3	H		215 dec.	$C_7H_9N_2O_4$	45.60	45.53	4.38	4.31	15.20	14.76		
$CONHCH_2CH{=}CH_2$	$CH_2CH{=}CH_2$	H	50	98–100	$C_{11}H_{12}N_2O_4$	55.80	55.48	5.12	5.02	11.86	12.13		
$CONHC_6H_5$	C_6H_5	Na	80		$C_{17}H_{11}N_2O_4Na \cdot H_2O$	58.62	59.14	3.76	3.84	8.05	8.53	6.6	7.0
$CONHC_6H_5$	C_6H_5	H	59	168 dec.	$C_{17}H_{12}N_2O_4$	66.22	66.24	3.93	4.13	9.09	9.38		
$CONHC_6H_{11}$[a]	C_6H_{11}	H	86	188–189 d.	$C_{17}H_{24}N_2O_4$	63.74	63.84	7.55	7.66	8.75	8.50		
m-$CF_3C_6H_4NHCO$	m-$CF_3C_6H_4$	H	45	145–146	$C_{19}H_{10}F_6N_2O_4$	51.36	51.13	2.27	2.35	6.31	6.31	[b]	
$CONHC_{10}H_{19}$[c]	$C_{10}H_{19}$	H	61	98–102	$C_{25}H_{40}N_2O_4 \cdot H_2O$					6.22	6.24		
$CONH$-n-$C_{12}H_{25}$	n-$C_{12}H_{25}$	Na	86		$C_{29}H_{51}N_2O_4Na$	67.66	67.95	10.00	10.18	5.45	5.20		
CN	H	Na	61	Dec. at 325–330	$C_5HN_2O_3Na \cdot H_2O$	33.72	34.36	1.69	1.92	15.73	15.60	13.0	13.7
CO_2Et	H	Na	52	Dec. at 224–226	$C_7H_6NO_5Na \cdot H_2O$	37.34	37.22	3.55	3.04	6.22	6.37		
$COCH_3$	H	Na	90[f]		$C_6H_4NO_4Na \cdot H_2O$	36.93	37.31	3.10	3.18	7.18	7.38	11.8	12.0
$COCH_3$	C_6H_5	H	18	170–171 d.	$C_{12}H_9NO_4$	62.33	62.47	3.92	4.22	6.06	6.49		
COC_6H_5	C_6H_5	H	19	183–184	$C_{17}H_{11}NO_4$	69.60	69.69	3.78	3.79	4.79	5.14		
COC_6H_5	H	H	24	175–177	$C_{11}H_7NO_4$	60.90	61.33	3.25	3.33	6.45	6.42		
p-$CH_3C_6H_4SO_2$	H	Na	57	>300	$C_{11}H_9NO_4SNa$	45.70	45.69	2.79	2.91	4.85	4.83	7.96	8.07[d]

[a] C_6H_{11} = cyclohexyl. [b] F, calcd. 25.67, found 25.74. [c] $C_{10}H_{19}$ = 2-methyl-5-isopropylcyclohexyl. [d] S, calcd. 11.00, found 11.40. [e] From Na salt. [f] Crude.

TABLE IV

CHELATES AND SALTS OF 4-CARBAMOYL-2,3,5-PYRROLIDINETRIONE

Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Metal, % Calcd.	Metal, % Found
$(C_5H_3N_2O_4)_2Fe \cdot 4H_2O$	27.41	27.53	3.22	3.25	12.79	12.89	12.72	12.73
$(C_5H_3N_2O_4)_2Co \cdot 4H_2O$	27.22	27.24	3.20	3.34	12.69	12.57	13.33	12.41
$(C_5H_3N_2O_4)_2Ni \cdot 4H_2O$	27.20	27.25	3.20	3.31	12.68	12.70	13.30	12.76
$(C_5H_3N_2O_4)_3Al \cdot 3H_2O$	33.00	33.40	2.76	2.79	15.39	15.47	4.94	5.74
$(C_5H_3N_2O_4)_3Fe \cdot 2H_2O$	32.34	32.12	2.35	2.65	15.08	14.99	10.0	10.43
$(C_5H_3N_2O_4)Ag$	22.80	22.38	1.15	1.63	10.63	10.42	41.00	39.74
$(C_5H_3N_2O_4)_2Sn$	28.00	28.44	1.41	1.75	13.07	12.88	27.65	30.64
$(C_5H_3N_2O_4)_2Pb$	23.20	23.43	1.17	1.45	10.81	10.62	40.00	40.55
$(C_5H_3N_2O_4)_2Cu \cdot H_2O$					14.30	14.43	16.20	16.07

malonamate was prepared from the imino ester hydrochloride obtained from ethyl cyanoacetate, anhydrous hydrogen chloride and ethyl alcohol.[15] Consistently high yields of the imino ester hydrochloride were obtained by using equal molar quantities of the alcohol and nitrile with an inert solvent such as ethyl ether. The imino ester salt separated as a white crystalline solid which could be collected in a pure form by simply filtering, washing with ether and drying. Gentle heating of the salt gave the ester amide and ethyl chloride.

Several new malonamides were prepared by amidation of ethyl malonate with the appropriate amine. The yields and properties of these compounds are as follows:

N,N'-Diallylmalonamide[16]: 91% yield; recrystallized from ethyl alcohol, m.p. 144–145°. *Anal.* Calcd. for $C_9H_{14}N_2O_2$: N, 15.35. Found: N, 15.35.

3,3'-Bis-(trifluoromethyl)-malonanilide: 51% yield; recrystallized from benzene, m.p. 160–161°. *Anal.* Calcd. for $C_{17}H_{12}N_2F_6O_2$: C, 52.31; H, 3.10; N, 7.18; F, 29.21. Found: C, 52.43; H, 3.42; N, 7.34; F, 29.8.

N,N'-Bis-(2-methyl-5-isopropylcyclohexyl)-malonamide.—2-Methyl-5-isopropylcyclohexylamine was prepared by reducing 2-nitro-*p*-cymene at 1000–2500 lb./sq. in. hydrogen pressure at 100° with ruthenium dioxide catalyst, b.p. 91–93° (16 mm.), $n^{25}D$ 1.4620. *Anal.* Calcd. for $C_{10}H_{21}N$: C, 77.34; H, 13.63; N, 9.02. Found: C, 77.68, H, 13.41; N, 8.64. The amide, a waxy solid, was obtained in quantitative yield. Recrystallization from petroleum ether gave a product melting at 174–187°. *Anal.* Calcd. for $C_{23}H_{42}N_2O_2$: C, 72.98; H, 11.19; N, 7.40. Found: C, 72.96; H, 11.10; N, 7.25.

Synthesis of Pyrrolidinetriones.[17] **4-Carbamoyl-2,3,5-pyrrolidinetrione** (I).—This synthesis is typical of those pyrrolidinetriones which were obtained by use of acid exchange resins. Malonamide (61.2 g., 0.6 mole) was added to a solution of sodium methoxide prepared from 27.6 g. (1.2 g. atoms) of sodium and 1 l. of absolute methanol. A solution of 70.8 g. (0.6 mole) of dimethyl oxalate in 500 ml. of methanol was added immediately through a dropping funnel as rapidly as possible at reflux temperature. The reaction was not noticeably exothermic and appeared to be complete in a few minutes as indicated by precipitation of the yellow disodium salt. The solid was collected by filtration, washed with methanol, and dried under vacuum at 70°; weight 103 g. (74%). *Anal.* Calcd. for $C_5H_3O_4N_2Na_2 \cdot CH_3OH$: C, 30.90; H, 3.00; N, 12.00; Na, 19.7. Found: C, 29.83; H, 2.24; N, 12.23; Na, 19.49.

To obtain the monosodium salt, a 10-g. sample of the above product was recrystallized from 110 ml. of 5% hydrochloric acid. The orange solid was collected by filtration, washed with distilled water, and dried at 100° in a vacuum oven; weight 5.6 g. *Anal.* Calcd. for $C_5H_3O_4N_2Na$: C, 33.72; H, 1.70; N, 15.73; Na, 12.91. Found: C, 33.48; H, 2.29; N, 15.50; Na, 12.24. When 3 g. of this monosodium salt was dissolved in 25 g. of hot 25% sulfuric acid, one gram of the salt was recovered on cooling. That it was starting material was shown by the presence of sodium and a positive ferric chloride test.

The sodium-free pyrrolidinetrione was obtained by dissolving 2 g. of the monosodium salt in 400 ml. of water and passing the resulting solution through a column of Amberlite IR-120 cation exchange resin. The column was eluted until the washes were neutral. The water was removed by evaporation under vacuum at 30° to obtain 1.09 g. of a light tan solid which decomposed at 230–234°. The ultraviolet spectrum indicated that the original ring system had been retained during this treatment. *Anal.* Calcd. for $C_5H_4O_4N_2$: C, 38.48; H, 2.58; N, 17.94. Found: C, 38.52; H, 2.81; N, 17.60.

1-Phenyl-4-(N-phenylcarbamoyl)-2,3,5-pyrrolidinetrione.—The synthesis of this compound will serve as an example of the type which can be freed from sodium by treatment with strong mineral acid.

To a solution of sodium ethoxide prepared from 17.8 g. (0.774 mole) of sodium and 320 ml. of absolute alcohol was added 98 g. (0.386 mole) of malonanilide, m.p. 223–224°, as a slurry in 300 ml. of alcohol. When the mixture had cooled to 36°, 60 g. (0.41 mole) of diethyl oxalate in 16 ml. of alcohol was added in one portion. The temperature rose to 50° within two minutes, and the whole mixture formed a mush of yellow crystals. The product was collected, washed with alcohol, and dried in a vacuum oven to obtain a quantitative yield, 127 g. A 5.0-g. sample of the crude yellow sodium salt was recrystallized from 50% ethyl alcohol–water; yield 4.55 g. Analyses indicated the product to be the monosodium salt monohydrate. *Anal.* Calcd. for $C_{17}H_{11}O_4N_2Na \cdot H_2O$: C, 58.62; H, 3.76; N, 8.05; Na, 6.6. Found: C, 59.14; H, 3.84; N, 8.53; Na, 7.0.

The free pyrrolidinetrione was obtained by heating a 10-g. sample of the crude product on a steam-bath with 200 ml. of 5% hydrochloric acid. The solid was collected, washed with distilled water, and dried in a vacuum oven; yield 8.1 g. The product was recrystallized from 150 ml. of benzene to yield bright yellow needles, 5.5 g., m.p. 168° dec. *Anal.* Calcd. for $C_{17}H_{12}O_4N_2$: C, 66.22; H, 3.93; N, 9.09. Found: C, 66.24; H, 4.13; N, 9.38.

4-Cyano-2,3-dioxo-5-thionopyrrolidine.—The α-cyanothioacetamide used in this condensation was prepared as follows[18]: Hydrogen sulfide was passed through a porous glass disk into a mixture of 100 g. (1.51 moles) of malononitrile, 150 ml. of absolute ethyl alcohol and 15 g. of triethanolamine at 30°. The addition was stopped as soon as solid product no longer formed. The reaction mixture was cooled to 0° for 2 hours, and the solid was collected by filtration and recrystallized from alcohol, m.p. 118–120°, weight 70 g. (47%). *Anal.* Calcd. for $C_3H_4N_2S$: C, 35.98; H, 4.03; N, 27.98; S, 32.01. Found: C, 36.41; H, 4.01; N, 27.89; S, 32.03.

To a solution of sodium ethoxide prepared from 57.5 g. (2.5 g. atoms) of sodium and 1.3 l. of absolute alcohol was added 122.5 g. (1.25 moles) of cyanothioacetamide in one portion. Immediately, 190 g. (1.15 moles) of diethyl oxalate in 200 ml. of absolute ethyl alcohol was poured into the reaction mixture as rapidly as possible. A beaker is recommended for this step. The mixture turned orange and solidified in about 10 seconds. The combined product from two runs was broken up, vacuum filtered, and dried under vacuum at room temperature to obtain 530 g. of red solid. The product was purified by adding it to an ice-water–hydrochloric acid mixture in a Waring Blendor, allowing to stand for one hour at 0°, filtering, and drying; weight, 261 g. A small sample of the product was recrystallized quickly from hot water to give the monohydrate

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(15) B M. Gupta, *J. Chem. Soc.*, **119**, 303 (1921).

(16) E. A. Pauw, *Rec. trav. chim.*, **55**, 215 (1936).

(17) We are indebted to Dr. W. H. Wood who prepared many of the pyrrolidinetriones containing cyclohexyl groups.

(18) E. G. Howard, U. S. Patent 2,773,260 (1956).

of 4-cyano-2,3-dioxo-5-thionopyrrolidine, which decomposed at 247°. *Anal.* Calcd. for $C_5H_2N_2SO_2 \cdot H_2O$: N, 16.25; S, 18.62. Found: N, 16.11; S, 18.79.

2,4-Dinitrophenylhydrazones.—The following pyrrolidinetriones were treated with 2,4-dinitrophenylhydrazine to give the corresponding hydrazones:

From 4-carbamoyl-2,3,5-pyrrolidinetrione, m.p. 225–228°. *Anal.* Calcd. for $C_{11}H_8N_6O_7$: C, 39.39; H, 2.40; N, 25.00. Found: C, 39.33; H, 2.57; N, 25.22.

From 4-N-methylcarbamoyl-1-methyl-2,3,5-pyrrolidinetrione, m.p. 240° dec. *Anal.* Calcd. for $C_{13}H_{12}N_6O_7$: C, 42.86; H, 3.32; N, 23.07; mol. wt., 364. Found: C, 42.99; H, 3.37; N, 22.86; mol. wt., 304.

From 4-(*p*-tolylsulfonyl)-2,3,5-pyrrolidinetrione, m.p. 235–236°. *Anal.* Calcd. for $C_{17}H_{13}N_5SO_8$: C, 45.60; H, 2.93; N, 15.66; S, 7.16. Found: C, 45.82; H, 3.06; N, 15.94; S, 6.81.

Hydrolysis of the Sodium Salt of 4-Carbamoyl-2,3,5-pyrrolidinetrione (II).—The sodium salt of 4-carbamoyl-2,3,5-pyrrolidinetrione (0.179 g.) was dissolved in 200 ml. of water containing 1 g. of hydrated calcium nitrate and 1 ml. of concentrated aqueous ammonia and heated on the steam-bath for one hour to obtain 0.118 g. of calcium oxalate (92%). This solid was dissolved in dilute sulfuric acid and titrated with 14.4 ml. of 0.1065 *N* $KMnO_4$, which is 84% of the theoretical amount for oxidation of the oxalate to carbonate. Control experiments in which malonic acid and methyl oxaloacetate were substituted for II did not give precipitates.

When II was treated with *p*-chlorobenzenediazonium hydroxide in basic solution, a bright red precipitate formed. This red precipitate gave an intense blue coloration when dissolved in concentrated hydrochloric acid. An authentic sample of malonamide gave identical reactions, indicating that malonamide was present as one hydrolysis product. This behavior toward the diazonium hydroxide appears to be an excellent specific test for small quantities of malonamide. The presence of alkyl groups in the molecule diminishes the intensity of the blue color. Other compounds possessing an active methylene group, such as ethyl acetoacetate, acetylacetone, cyanoacetamide, etc., give the diazonium coupling products which form no blue color with strong acid.

Reactions of Pyrrolidinetriones with Metal Salts.—The general procedure used to prepare the metal derivatives of the pyrrolidinetriones is illustrated below.

A 1.96-g. (0.01 mole) sample of the orange monosodium salt of 4-carbamoyl-2,3,5-pyrrolidinetrione (I) was dissolved in 60 ml. of hot water and the solution was filtered. To this solution, which was stirred and heated on the steam-bath, was added a filtered solution of 1.5 g. (0.0055 mole) of $FeCl_3 \cdot 6H_2O$. The metal complex began to precipitate immediately. After the addition was complete, the mixture was allowed to cool to room temperature, and the solids were collected by filtration, washed with water, and dried overnight in a vacuum desiccator at room temperature over calcium chloride; weight 1.74 g. (94% based on II). *Anal.* Calcd. for $(C_5H_3N_2O_4)_3Fe \cdot 2H_2O$: C, 32.34; H, 2.35; N, 15.08; Fe, 10.0. Found: C, 32.12; H, 2.65; N, 14.99; Fe, 10.43.

4-Pyridinium-2,3,5-trioxo-4-pyrrolidylide (V).[19]—To a solution of 1.84 g. (0.08 g. atom) of sodium in 250 ml. of absolute methanol were added 10 g. (0.07 mole) of N-carbamoylmethylpyridinium chloride and 10.2 g. (0.07 mole) of diethyl oxalate. After a short induction period, a bright yellow solid began to precipitate. The mixture was stirred for 25 minutes and the solid was collected and dried to obtain 7.5 g. (56.5%) of 4-pyridinium-2,3,5-trioxo-4-pyrrolidylide. Recrystallization from hot water gave a bright yellow solid melting at 309–312°. *Anal.* Calcd. for $C_9H_6N_2O_3$: C, 56.78; H, 3.16; N, 14.73. Found: C, 56.99; H, 3.34; N, 14.57.

4-Trimethylammonium-2,3,5-trioxo-4-pyrrolidylide.—To a solution of sodium ethoxide prepared from 100 ml. of absolute ethyl alcohol and 4.6 g. (0.2 g. atom) of sodium was added 18.0 g. (0.18 mole) of dry powdered trimethylcarbamoylmethylammonium chloride at 40° with very rapid stirring. Some sodium chloride precipitated. Immediately, 17.3 g. (0.1118 mole) of diethyl oxalate was added in one portion to obtain an intensely yellow-colored mixture which was stirred at room temperature for one hour. The crude solid product was collected by filtration; yield 23 g. (85% taking into consideration the NaCl present).

A portion of the product was purified by dissolving in hot ethyl alcohol, neutralizing with concentrated hydrochloric acid, filtering, and cooling. The precipitated solid was recrystallized from absolute alcohol. When heated, the solid began to decompose at 240° and melted to a black liquid at 263°. *Anal.* Calcd. for $C_7H_{10}N_2O_3$: C, 49.40; H, 5.92; N, 16.47. Found: C, 49.49; H, 5.65; N, 16.30.

Dimethylcarbamoylmethylsulfonium Iodide.—A solution of 10.5 g. (0.1 mole) of methylcarbamoylmethyl sulfide, 14.2 g. (0.1 mole) of methyl iodide and 35 ml. of ethyl alcohol was heated at 50° for 0.5 hour to obtain a yellow crystalline product (17 g.) which was recrystallized from absolute ethyl alcohol. The product was soluble in water and gave a copious precipitate with silver nitrate solution. *Anal.* Calcd. for $C_4H_{10}NOSI$: N, 5.67; S, 12.97; I, 51.37. Found: N, 5.47; S, 13.43; I, 51.50.

4-Dimethylsulfonium-2,3,5-trioxo-4-pyrrolidylide.—To a stirred solution of sodium ethoxide prepared from 1.0 g. (0.041 g. atom) of sodium and 17 ml. of ethyl alcohol was added 7.30 g. (0.0285 mole) of dimethylcarbamoylmethylsulfonium iodide and 4.4 g. (0.03 mole) of diethyl oxalate at room temperature. The reaction mixture was stirred for two hours and the solid product was collected by filtration. The hygroscopic product was triturated with hot ethyl alcohol to which was added enough concentrated hydrochloric acid to neutralize the base present. The hot alcohol solution was filtered and cooled to obtain a white crystalline product which, after recrystallization from alcohol, melted with rapid decomposition at 205–210°. *Anal.* Calcd. for $C_6H_7NO_3S$: C, 41.60; H, 4.07; N, 8.09. Found: C, 41.00; H, 4.23; N, 8.03.

1-Hydroxymethyl-4-pyridinium-2,3,5-trioxopyrrolidylide.—To a mixture of 1.90 g. (0.01 mole) of V, two drops of pyridine and 25 ml. of water was added 3.2 g. (0.04 mole) of 37.8% aqueous formaldehyde. After a portion of the solid had dissolved, the hydroxymethyl derivative began to precipitate; 25 ml. of water was added and the mixture was heated to boiling to effect complete solution. The solution was filtered and cooled to obtain 1.5 g. of yellow solid which melted with decomposition at about 310°. The infrared spectrum of this compound closely resembled that of the starting material I. *Anal.* Calcd. for $C_{10}H_8N_2O_4$: C, 54.55; H, 3.66; N, 12.73. Found: C, 54.56; H, 3.93; N, 12.61. The gas evolved on heating was identified as formaldehyde by means of its 2,4-dinitrophenylhydrazone.

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(19) E. G. Howard, U. S. Patent 2,786,060 (1956).