Summary

The preparation of 3,3′,3″,3‴-tetranitro-, 3,3′,3″,3‴-tetraamino- and 3,3′,3″,3‴-tetra-(acetylamino)-tetraphenyldiarsyl has been described.

ANN ARBOR, MICH. RECEIVED AUGUST 3, 1933

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF KANSAS]

The Action of Amines on the Esters of Carboxy Substituted Ureas, Thioureas and Guanidines. III

BY J. ALDEN MURRAY AND F. B. DAINS

This is a continuation of the study of the action of amines on carbonyldiurethan and allophanic ester[1] together with their sulfur analogs and on the ethyl esters of guanidinecarboxylic acids. These latter can be regarded as derivatives of allophanic ester or carbonyldiurethan in which the carbonyl oxygen is replaced by S, CH_3S, NH or NH_2.

The experimental results have shown that with the sulfur derivatives the S or CH_3S was the first point of attack, while with the guanidinecarboxylic esters, as in carbonyldiurethan, the carbethoxy groups were first affected. In some cases ring closure occurred to form heterocyclic compounds.

Experimental

1. Urea Derivatives

Methyl and Ethyl Amines and Allophanic Ester.—On long standing the ester went into solution in the amines (33%) and from the residues, on evaporation, were isolated 1-methylbiuret (m. p. 175°) and 1-ethylbiuret (m. p. 159°) in 60% yields.[2]

Benzylamine and Allophanic Ester.—γ-Benzylallophanic ester[3] (I), $C_6H_5CH_2NHCONHCOOC_2H_5$, was the main product when the components were heated at 135° for three hours.

Heated at 150° for five hours, 1,5-dibenzylbiuret (II), $HN(CONHCH_2C_6H_5)_2$, (m. p. 169°) resulted, while at 200° the biuret dissociated to give cyanuric acid and *s*-dibenzylurea (m. p. 169°).[4]

Phenyl Isocyanate and Allophanic Ester.—The ester and isocyanate were heated at 125° for five hours.[5] The residue consisted of unchanged ester, carbanilide, and the addition product 1-phenyl-5-carbethoxybiuret (m. p. 175°).[6]

Phenylhydrazine and γ-Phenylallophanic Ester.—This mixture, when heated at 130° for five hours, gave aniline and 1-phenylurazole (m. p. 263°).[7]

Methyl and Ethyl Amines and Carbonyldiurethan.—The diurethan dissolved immediately in an excess of 33% ethylamine solution, but in a few minutes a deposit of allophanic ester appeared.[8] On two weeks standing this dissolved and the solution was found to contain 1-ethylbiuret and traces of an oil, the ethyl ester of ethylcarbamic acid.[9]

With methylamine, the diurethan gave, in thirty-six hours, 1-methylbiuret.

Benzylamine and Carbonyldiurethan.—In water solution on standing, and at 115° without water, the reactants formed allophanic ester and ethyl benzylcarbamate (m. p. 49°),[10] results due to simple aminolysis. At 135°, the products were ammonia, allophanic ester and ethyl γ-benzylallophanate (I); at 160°, 1,5-dibenzylbiuret (II); and at 200° *s*-dibenzylurea.

Hydrazine and Carbonyldiurethan.—On standing in alcoholic solution, allophanic ester alone was isolated.

Phenylhydrazine and Carbonyldiurethan.—When molar quantities were heated at 115 or 140°, 1-phenylurazole was the main product,[7] but at 160° iminodicarboxylic acid diphenylhydrazide (III), $HN(CONHNHC_6H_5)_2$, was formed. It is soluble in sodium hydroxide.

2. Thiourea Derivatives

Thioallophanic Ester, $H_2NCSNHCOOC_2H_5$.[11]—The ester was hydrolyzed to thiourea by aqueous ammonia and alkyl amines, and by alcoholic potassium hydroxide. Heated at 160° for an hour with aniline or *o*-toluidine, it yielded the *s*-diaryl oxygen ureas. Efforts to methylate the ester were fruitless.

Amines and the Methyl Ether of Thiocarbonyldiurethan, $CH_3SC(NCOOC_2H_5)NHCOOC_2H_5$.[12]—The primary amines react with the methyl thioether in alcoholic solution with the loss of mercaptan and the formation of substituted guanidines. The yields were very satisfactory. Thus, methylamine gave γ-methyl-β-dicarbethoxyguanidine (IV), $CH_3NHC(NCOOC_2H_5)NHCOOC_2H_5$. Analogous results were obtained with ethylamine (V), ethanolamine (VI), benzylamine (VII), aniline (VIII), *o*-toluidine (IX), phenylhydrazine (X), *o*-aminophenol (XI), *p*-aminobenzoic acid (XII), anthranilic acid (XIII), and methyl anthranilate (XIV).

(1) (a) Dains Greider, and Kidwell, THIS JOURNAL, **41**, 1004 (1919); (b) Dains and Wertheim, *ibid.*, **42**, 2303 (1920).

(2) Hofmann, *Ber.*, **4**, 265 (1871); Biltz and Jeltsch, *ibid.*, **56**, 1919 (1923).

(3) Prepared, for comparison, in 70% yield by heating benzylurea and ethyl chloroformate on the steam-bath for an hour.

(4) A mixture of the biuret and urea melted about 150°.

(5) Lakra and Dains, THIS JOURNAL, **51**, 2221 (1929).

(6) Ref. 1a, p. 1007.

(7) Ref. 1b, p. 2308.

(8) Ref. 1a, p. 1007.

(9) Basterfield, Woods and Whelen, THIS JOURNAL, **49**, 2848 (1927).

(10) Hantzsch, *Ber.*, **31**, 180 (1898).

(11) Doran, *J. Chem. Soc.*, **69**, 325, 331, 336 (1896); Dixon and Taylor, *ibid.*, **93**, 696 (1903); Dixon and Kennedy, *ibid.*, **117**, 80 (1920).

(12) Olin and Dains, THIS JOURNAL, **52**, 3326 (1930).

Glycine and the Methyl Ether of Thiocarbonyldiurethan. Dicarbethoxyguanidineacetic Acid (XV), $HOOCCH_2NHC(NCOOC_2H_5)NHCOOC_2H_5$.—The components were refluxed in water–alcohol solution. The compound was soluble in hot water. When boiled in alcoholic potassium hydroxide (5%) for twenty minutes, it gave potassium bicarbonate and the potassium salt of **monocarbethoxyguanidineacetic acid**. The free acid (XVI) was practically insoluble except in acids and bases.

On hydrolysis of XV with dilute hydrochloric acid carbonyldiurethan and glycine were formed.

The ethyl ester of dicarbethoxyguanidineacetic acid (XVII) was formed when an alcohol–water solution of the thio methyl ether and ethyl aminoacetate stood for six weeks.

Heterocyclic Compounds

Hydroxylamine and the Methyl Ether of Thiocarbonyl diurethan. Tetrahydro-3-carbethoxyimino-5-oxy-1,2,3,4-oxdiazole (XVIII), $\overset{1}{O}\overset{2}{N}\overset{3}{H}C(NCOOC_2H_5)\overset{4}{N}H\overset{5}{C}O$.—Hydroxylamine and the ester, on standing in alcohol solution, evolved mercaptan and gave the oxdiazole,[13] which was very soluble in acids or bases.

Hydrazine and the Methyl Ether of Thiocarbonyldiurethan. Tetrahydro-3-carbethoxyimino-5-oxy-1,2,4-triazole (XIX), $\overset{1}{N}H\overset{2}{N}H\overset{3}{C}(NCOOC_2H_5)\overset{4}{N}H\overset{5}{C}O$.—The hydrazine was allowed to react with the thioether in alcohol solution or the mixture heated gently until the evolution of mercaptan ceased. The precipitate, which was about 1% soluble in water, was readily soluble in ammonia or weak bases.

***o*-Phenylenediamine and the Methyl Ether of Thiocarbonyldiurethan. 2-Carbethoxyimino-2,3-dihydrobenzimidazole (XX)**, $C_6H_4\overset{1}{N}H\overset{2}{C}(NCOOC_2H_5)\overset{3}{N}H$.—Molar quantities were heated in alcohol solution. The difficultly soluble imidazole is a weak base, being precipitated from its solution in glacial acetic acid by water.

Anthranilic Acid Derivatives

2-Carbethoxyimino-4-oxy-1,2,3,4-tetrahydroquinazoline (XXI), $C_6H_4\overset{1}{N}H\overset{2}{C}(NCOOC_2H_5)\overset{3}{N}H\overset{4}{C}O$, was formed in small yield when the guanidine ester (XIV) was heated carefully.

It was also formed, in good yield, when either of the guanidine esters (XIII) or (XIV) was boiled for fifteen minutes in an alcoholic solution of an equivalent quantity of potassium hydroxide. The mixture was poured into water and acidified and the precipitate recrystallized from 15% alcohol.

o,o'-Dicarbomethoxycarbanilide (XXII), $CO(NHC_6H_4COOCH_3)_2$, was formed when the methyl thioether and methyl anthranilate were heated at 140° for three hours. It was identical with a specimen synthesized from phosgene and methyl anthranilate.

Amines and Thiocarbonyldiurethan, $SC(NHCOOC_2H_5)_2$.[12]—In contradiction to carbonyldiurethan, in which the carbethoxy groups are the points of attack, the thio analog is characterized by its especially active sulfur atom. It formed thio ethers and was easily desulfurized.

(13) Johnson and Menge, *Am. Chem. J.*, **32**, 370 (1904).

TABLE I

No.	Compound	Yield, %	M. p., °C.	Nitrogen, % Calcd.	Found
I	γ-Benzylallophanic ester ($C_{11}H_{14}N_2O_3$)	..	103	12.44	12.61
II	1,5-Dibenzylbiuret ($C_{16}H_{17}N_3O_2$)	..	169	14.82	14.84
III	Iminodicarboxylic acid diphenylhydrazide ($C_{14}H_{16}N_6O_2$)	..	291	24.67	24.55
	γ R-α,β-Dicarbethoxyguanidines				
IV	Methyl ($C_8H_{15}N_3O_4$)	(25) 70	71	19.33	19.14
V	Ethyl ($C_9H_{17}N_3O_4$)	75	(Oil)	18.18	18.33
VI	β-Hydroxyethyl ($C_9H_{17}N_3O_5$)	80	98	17.06	16.98
VII	Benzyl ($C_{14}H_{19}N_3O_4$)	(55) 85	(Oil)	14.33	14.40
VIII	Phenyl ($C_{13}H_{17}N_3O_4$)	70	71	15.05	15.17
IX	*o*-Tolyl ($C_{14}H_{19}N_3O_4$)	90	75	14.33	14.37
X	Anilino ($C_{13}H_{18}N_4O_4$)	(55) 85	192	19.05	19.05
XI	*o*-Hydroxyphenyl ($C_{13}H_{17}N_3O_5$)	50	135	14.23	14.18
XII	*p*-Carboxyphenyl ($C_{14}H_{17}N_3O_6$)	60	198	13.00	12.94
XIII	*o*-Carboxyphenyl ($C_{14}H_{17}N_4O_6$)	45	174	13.00	12.92
XIV	*o*-Carbomethoxyphenyl ($C_{15}H_{19}N_3O_6$)	40	67	12.45	12.49
XV	Acetic acid ($C_9H_{15}N_3O_6$)	40	210	16.09	16.16
XVI	Acetic (β-Carbethoxy) ($C_8H_{11}N_3O_4$)	65	Chars 250–275	22.22	22.17
XVII	Ethylaceto ($C_{11}H_{19}N_3O_6$)	30	56	14.52	14.50
XVIII	Tetrahydro-3-carbethoxyimino-5-oxy-1,2,4-oxdiazole ($C_5H_7N_3O_4$)	45	226	24.28	24.25
			C	34.66	34.92
			H	4.07	3.76
XIX	Tetrahydro-3-carbethoxyimino-5-oxy-1,2,4-triazole ($C_5H_8N_4O_3$)	60	Over 335	32.56	32.65
			C	34.88	34.85
			H	4.68	4.38
XX	2-Carbethoxyimino-2,3-dihydrobenzimidazole ($C_{10}H_{11}N_3O_2$)	97	320 (dec.)	20.49	20.43
			C	58.51	58.55
			H	5.41	5.31
XXI	2-Carbethoxyimino-4-oxy-1,2,3,4-tetrahydroquinazoline ($C_{11}H_{11}N_3O_3$)	(13) 85	163	18.02	18.03
			C	56.63	56.33
			H	4.76	4.76
XXII	o,o'-Dicarbomethoxycarbanilide ($C_{17}H_{16}N_2O_5$)	30	144	8.54	8.43
XXIII	Hexahydro-1-phenyl-2,6-dioxy-4-imino-*s*-triazine ($C_9H_8N_4O_2$)	30	Over 335	27.44	27.50
XXIV	α-Methyl-α,γ-dicarbethoxyguanidine ($C_8H_{15}N_3O_4$)	97	85	19.34	19.31
XXV	Carbethoxydicarboxanilidoguanidine ($C_{18}H_{19}N_5O_4$)	40	151 (dec.)	18.99	19.22
XXVI	Hexahydro-1-phenyl-2-thio-4-imino-6-oxy-*s*-triazine ($C_9H_8N_4OS$)	(50) 90	180 (dec.)	25.45	25.50
XXVII	1-Phenyl-2-methylthio-4-imino-6-oxy-1,4,5,6-tetrahydro-*s*-triazine ($C_{10}H_{10}N_4OS$)	40	247	23.91	23.84

Amines, on heating in alcoholic solution, eliminated hydrogen sulfide with the formation of the same guanidine derivatives that were obtained from its methyl ether.

3. Guanidine Derivatives

Aniline and Dicarbethoxyguanidine[14]

Hexahydro-1-phenyl-2,6-dioxy-4-imino-*s*-triazine (XXIII), $C_6H_5\overset{1}{N}\overset{2}{C}O\overset{3}{N}H\overset{4}{C}(NH)\overset{5}{N}H\overset{6}{C}O$.—Molar quantities of the ester and aniline were heated at 140° with the loss

(14) Ref. 12. Yield, 90–95%. The picrate melts at 199°.

of ammonia and ethyl alcohol. From the reaction mass were isolated carbanilide and the triazine, which was very insoluble in boiling alcohol but dissolved in cold sodium hydroxide (10%).

α-Methyl-α,γ-dicarbethoxyguanidine (XXIV), $HNC(N(CH_3)COOC_2H_5)NHCOOC_2H_5$, was obtained from the potassium salt of dicarbethoxyguanidine and dimethyl sulfate in dry acetone on five hours of refluxing. Its structure was proved by the fact that it is different from the isomeric methylimino compound (IV).

Hydrolysis of Dicarbethoxyguanidine.—A boiling saturated alcoholic solution of potassium hydroxide was treated with an equivalent weight of dicarbethoxyguanidine and boiled for a few minutes. The solution was evaporated on the steam-bath, the residue made up to the original volume with water and evaporated twice, and finally dissolved in an equal volume of water and cooled. An almost quantitative yield of monocarbethoxyguanidine hydrate[15] was obtained. The hydrochloride melted at 128–130° and the picrate at 227°.

Phenyl Isocyanate and Carbethoxyguanidine. Carbethoxydicarboxanilidoguanidine (XXV), $(C_6H_5NHCONH)_2C(NCOOC_2H_5)$.—Carbethoxyguanidine was treated with an excess of phenyl isocyanate and the reaction completed on the steam-bath. A little carbanilide was formed but the main product was the above diurea.[16]

(15) Pinck and Blair, THIS JOURNAL, **49**, 509 (1927); Basterfield and Paynter, *ibid.*, **48**, 2177 (1926); Nencki, *Ber.*, **7**, 1588 (1874); *J. prakt. Chem.*, [2] **17**, 237 (1878).

(16) Johnson, *Am. Chem. J.*, **29**, 482; **30**, 172 (1903); Ref. 5, p. 2224.

Phenyl Isothiocyanate and Carbethoxyguanidine. Hexahydro-1-phenyl-2-thio-4-imino-6-oxy-*s*-triazine (XXVI), $C_6H_5\overset{1}{N}\overset{2}{C}S\overset{3}{N}H\overset{4}{C}(NH)\overset{5}{N}H\overset{6}{C}O$.—The mustard oil and guanidine were warmed in alcohol solution for eight hours or, with better yield, heated without a solvent at 115° for two hours. The triazine was difficultly soluble except in acids and strong bases.

It gave a **methyl thio ether** (XXVII) with dimethyl sulfate in dry acetone solution.

Summary

1-Methyl and 1-ethyl biuret have been formed from allophanic ester and carbonyldiurethan by the action of methyl and ethyl amines. Amines have been found to easily hydrolyze thioallophanic ester to thiourea.

Thiocarbonyldiurethan and its methyl ether have been found to give with amines alkyl and aryl dicarbethoxyguanidines. With hydroxylamine, hydrazine, *o*-phenylenediamine, and anthranilic acid, heterocyclic compounds have been synthesized.

From dicarbethoxyguanidine, monocarbethoxyguanidine and α-methyl-α,γ-dicarbethoxyguanidine, were obtained, while with aniline and with phenyl isocyanate triazines were formed.

LAWRENCE, KANSAS RECEIVED AUGUST 7, 1933

[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY AT CORNELL UNIVERSITY]

The Preparation and Reactions of Some Furyl Isocyanates

BY A. T. BLOMQUIST[1] AND H. B. STEVENSON

A survey of the literature of the furan series affords relatively meager information regarding amines and their derivatives in which the nitrogen atom is directly attached to the furan nucleus. Only in those instances in which the furan nucleus has been substituted with negative groups, such as nitro, carboxyl and carbethoxyl, has it been possible to isolate aminofurans. Typical examples of amines which have been obtained in the furan series are 5-amino-2-furoic acid,[2] 3,4-diamino-5-nitro-2-furoic acid,[3] ethyl 5-amino-4-nitro-2-furoate[4] and ethyl 4-amino-5-acetamino-2-furoate.[5]

All attempts to isolate a simple amino derivative of furan, or of one of its homologs, have been unsuccessful. Marquis[2] attempted the preparation of α-aminofuran by decarboxylation of 5-amino-2-furoic acid and by hydrolysis of α-acetaminofuran. Freundler[6] and Leimbach[7] were also unsuccessful in preparing α-aminofuran by hydrolysis of the urethan obtained when furoyl azide was heated with methyl alcohol.

The more precise information now available concerning the behavior of furan compounds has made it seem possible that suitable conditions might be developed for the isolation of simple aminofurans. Indeed, several types of furan compounds (*e. g.*, α-furfuryl chloride[8] and 2-iodofuran[9]), which could not be obtained by earlier workers, have recently been isolated in the pure state. From a consideration of the behavior of

(1) National Research Fellow in Chemistry.

(2) Marquis, *Ann. chim.*, [8] **4**, 196 (1905).

(3) Traube and Lazar, *Ber.*, **46**, 3438 (1913).

(4) Rinkes, *Rec. trav. chim.*, **51**, 353 (1932).

(5) Gilman and Burtner, THIS JOURNAL, **55**, 2903 (1933).

(6) Freundler, *Bull. soc. chim.*, **17**, 424 (1897).

(7) Leimbach, *J. prakt. Chem.*, [2] **65**, 35 (1902).

(8) Kirner, THIS JOURNAL, **50**, 1955 (1928).

(9) Gilman, Mallory and Wright, *ibid.*, **54**, 733 (1932).