Table II

Salt Effect on Deamination of Oxidized Developing Agents

I		II		III	
μ	k,[a] sec.$^{-1}$	μ	k, sec.$^{-1}$	μ	k, sec.$^{-1}$ × 10^3
0.0104	5.56	0.0141	24.0	0.0077	0.280 ± 0.003
.0225	4.90	.0262	24.0	.0225	.287 ± .009
.0400	4.38	.0437	22.8	.0400	.294 ± .009
.0625	3.92	.0662	24.0	.0625	.287 ± .010
		.1141	22.0		

[a] k calculated as first-order rate constant since (OH^-) remained essentially unchanged during the reaction.

It should be pointed out that the salt effect is determined by the equilibrium and not the detailed mechanism which produces the critical complex. While we make the plausible assumption that the predominating species and reactive species are identical in representing the reaction by eq. c to e, any other pair of reactive species in rapid equilibrium with those shown would exhibit identical salt effects.[6]

Rochester, New York

(6) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 260.

[Contribution from the Research Department, Carbide and Carbon Chemicals Company]

N,N-Bis-(2-cyanoethyl)-carboxamic Acids and Esters

By John W. Lynn

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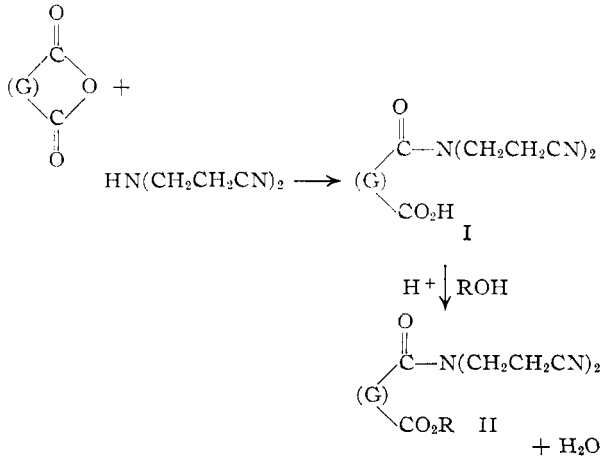
The syntheses of several N,N-bis-(2-cyanoethyl)-carboxamic acids and esters thereof are described starting with cyclic anhydrides, β,β'-iminodipropionitrile and alcohols.

The reaction of β,β'-iminodipropionitrile with cyclic anhydrides gives the corresponding N,N-bis-(2-cyanoethyl)-carboxamic acids (I) in good yield. The only amic acids of this type previously reported are the derivatives of phthalic[1] and succinic anhydrides[2]; the latter by name alone. Esters of N,N-bis-(2-cyanoethyl)-carboxamic acids are hitherto unreported. Several alkyl N,N-bis-(2-cyanoethyl)-carboxamates (II) are useful as plasticizers for vinyl chloride–acrylonitrile resins.

Several cyclic anhydrides were allowed to react with β,β'-iminodipropionitrile in an inert solvent. A slight excess of the anhydride generally resulted in better yields. Physical properties, analyses and yields of the products are given in Table I.

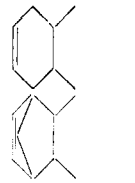
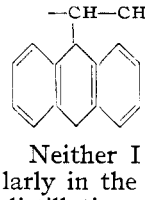
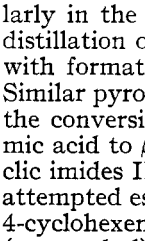
Alkyl N,N-bis-(2-cyanoethyl)-carboxamates (II) are readily prepared by esterification of purified carboxamic acids or, in some cases, by the direct esterification of crude acid reaction mixtures.



Purified esters were not obtainable, except in those cases where the product was a crystallizable solid, owing to thermal degradation during attempted distillations. The products were generally purified by steam distillation to remove volatile by-products. Data on these esters are given in Table II.

Table I

N,N-bis-(2-cyanoethyl)-carboxamic Acids HO_2C-(G)-$CON(CH_2CH_2CN)_2$

(G)	Formula	Yield, %	M.p., °C.	Nitrogen, % Calcd.	Found
$-CH_2CH_2-$	$C_{10}H_{12}N_4O_3$	92.6	118–119	18.83	18.73
$-CH{=}CH-$ (*cis*)	$C_{11}H_{14}N_4O_3$	91.0	140–141	19.0	18.91
$-(CH_2)_3-$	$C_{11}H_{16}N_4O_3$	69.6	85–87.5	17.71	18.10
$-C(CH_3){=}CH-$	$C_{11}H_{13}N_4O_3$	40.0	108–110	17.85	18.16
$-C(=CH_2)CH_2-$	$C_{11}H_{13}N_4O_3$	32.0	130–131	17.85	17.40
	$C_{14}H_{17}N_4O_3$	95.0	130–133	15.49	15.23
	$C_{15}H_{17}N_4O_3$	92.0	135–136	14.63	15.08
	$C_{23}H_{21}N_4O_3$	83.2	139–141	10.80	10.29

Neither I nor II is thermally stable, particularly in the presence of mineral acid. Attempted distillation of the esters resulted in decomposition, with formation of N-(2-cyanoethyl)-carboximides. Similar pyrolyses have been reported previously for the conversion of N,N-bis-(2-cyanoethyl)-phthalamic acid to β-phthalimidopropionitrile.[1,3] The cyclic imides III were also obtained as a result of the attempted esterification of N,N-bis-(2-cyanoethyl)-4-cyclohexene-1,2-carboxamic acid and N,N-bis-(cyanoethyl)-bicyclo[2.2.1]-5-heptene-2,3-carboxamic acid. The structures of these reaction products were proved by their independent synthesis by means of the cyanoethylation of the respective unsubstituted imides.

(1) S. Chodroff, R. Kapp and C. O. Beckman, This Journal, **69**, 256 (1947).

(2) R. O. Zerbe, U. S. Patent 2,582,732.

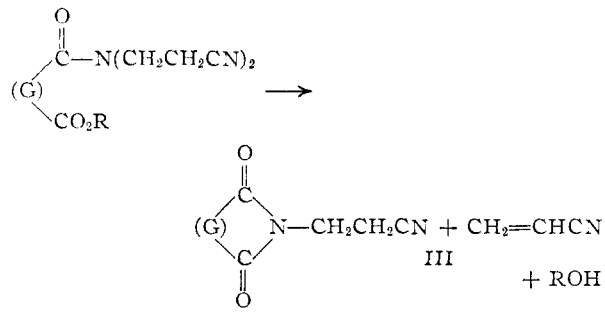
(3) F. E. Küng, U. S. Patent 2,401,429.

TABLE II

ALKYL N,N-BIS-(2-CYANOETHYL)-CARBOXAMATES $RO_2C-(G)-CON(CH_2CH_2CN)_2$

(G)	R	Formula	Yield, %	$n^{30}D$	M.p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
$-CH_2CH_2-$	$-CH_3$	$C_{11}H_{15}N_3O_3$	60	1.4832						17.7	17.4
$-CH_2CH_2-$	$-C_2H_5$	$C_{12}H_{17}N_3O_3$	81	1.4788						16.7	16.7
$-CH_2CH_2-$	$-i-C_3H_7$	$C_{13}H_{19}N_3O_3$	55	....	45–47					15.8	15.2
$-CH_2CH_2-$	$-n-C_4H_9$	$C_{14}H_{21}N_3O_3$	92	1.4767						15.0	15.4
$-CH_2CH_2-$	$-CH_2CH(C_2H_5)_2$	$C_{16}H_{25}N_3O_3$	99	1.4763						13.6	13.3
$-CH_2CH_2-$	$-CH_2CH(C_2H_5)-(C_4H_9)$	$C_{18}H_{29}N_3O_3$	70	1.4736						12.5	12.4
$-CH_2CH_2-$	$-CH_2CH=CH_2$	$C_{13}H_{17}N_3O_3$	60	1.4893						15.9	15.6
$-CH_2CH_2-$	$O(CH_2CH_2-)_2$	$C_{22}H_{32}N_6O_7$	25	....		55.8	55.4	6.2	6.2	16.3	15.8
$-CH=CH-$(*trans*)	$-C_2H_5$	$C_{12}H_{15}N_3O_3$	26	....	68–69	57.8	57.9	6.2	6.0	16.9	16.7
$-(CH_2)_3-$	$-n-C_4H_9$	$C_{15}N_{23}N_3O_3$	99	1.4700		62.9	62.5	7.6	7.7	13.7	14.2
$-(CH_2)_3-$	$-CH_2CH=CH_2$	$C_{14}H_{19}N_3O_3$	94	1.4873		60.6	60.3	6.9	6.9	15.1	15.3
$-C(CH_3)=CH-$	$-n-C_4H_9$	$C_{15}H_{21}N_3O_3$	83	....		61.8	61.6	7.2	7.5	..	..

Esterification of N,N-bis-(2-cyanoethyl)-phthalmic acid and N,N-bis-(2-cyanoethyl)-maleamic acid was not possible using ordinary methods, such as heating in a refluxing toluene–ethanol solution containing sulfuric acid as catalyst. This extreme



lack of reactivity is believed to be due to the nature of the carboxylic acid group as well as to some steric hindrance, caused by the cyanoethyl groups being held in a fixed *cis* configuration to the carboxy group under attack. Support for this view is provided by the observation that when anhydrous hydrogen chloride is used as a catalyst the maleamic acid reacts to produce ethyl N,N-bis-(2-cyanoethyl)-fumaramate. Presumably, hydrogen chloride catalyzed the isomerization of the *cis* to the *trans* form.

A very small amount of a solid by-product was obtained from several alkyl N,N-bis-(2-cyanoethyl)-succinamates. Analysis of the material proved it to be N,N,N′,N′-tetra-(2-cyanoethyl)-succinamide. Presumably, it was formed by aminolysis of the succinamates by a small amount of unreacted β,β′-iminodipropionitrile.

Experimental[4]

N,N-Bis-(2-cyanoethyl)-carboxamic Acids. (I).—β,β′-Iminodipropionitrile was added slowly to a mixture of the cyclic anhydride in refluxing dry benzene. Generally, solution was effected as the anhydride was consumed. The products crystallized from the reaction mixture on cooling. Purification by recrystallization from lower alcohols generally was employed.

Alkyl N,N-Bis-(2-cyanoethyl)-carboxamates (II).—In general, the carboxamic acids were esterified by refluxing in a solution consisting of an excess of the desired alcohol, benzene and 0.1% sulfuric acid based on the total charge. The water of reaction was removed as the benzene azeotrope to complete the esterification. After the reaction mixture had been washed with 20% sodium carbonate solution, the solvent was evaporated and the residual oil was steam distilled and dried under reduced pressure. The products were generally amber colored, viscous oils.

Methyl N,N-bis-(2-cyanoethyl)-succinamate was prepared by the ethylene dichloride method of Clinton and Laskowski.[5]

Ethyl N,N-Bis-(2-cyanoethyl)-fumarate.—β,β′-Iminodipropionitrile (2 moles) was added slowly to a stirred suspension of maleic anhydride (2 moles) in refluxing benzene, and the mixture was refluxed for 2 hr. Ethanol (4 moles) was added, and the mixture was refluxed for 11 hr. while passing dry hydrogen chloride in a very slow stream below the surface and removing the water formed azeotropically. The cooled reaction mixture was filtered and washed with 20% sodium carbonate solution and then concentrated. The residual oil crystallized on standing. Recrystallization from aqueous ethanol gave ethyl N,N-bis-(2-cyanoethyl)-fumarate in 26% yield as colorless crystals melting at 68–69°.

Anal. Calcd. for $C_{12}H_{15}N_3O_3$: C, 57.81; H, 6.02; N, 16.88. Found: C, 57.87; H, 5.98; N, 16.67.

The infrared spectrum had the following characteristic bands: 4.47 μ (cyano), 5.86 μ (conjugated ester), 6.1 μ (amide), 12.4 and 12.85 μ (*trans* configuration of fumarates).

N-(2-Cyanoethyl)-4-cyclohexene-1,2-carboximide.—The only product isolated from the attempted esterification of N,N-bis-(2-cyanoethyl)-4-cyclohexene-1,2-carboxamic acid with butanol-1, 2-ethylbutanol-1 or 2-ethylhexanol-1 was a colorless crystalline solid, melting at 108–109°.

A mixture of 4-cyclohexene-1,2-carboximide (1.8 moles, m.p. 134–136°) and acrylonitrile (9.4 moles) was refluxed while adding 19 g. of 40% sodium hydroxide. After refluxing for 1 hr., the reaction mixture was cooled and acidified with 50% sulfuric acid. On evaporation of the excess acrylonitrile crystallization occurred. Recrystallization from ethanol gave N-(2-cyanoethyl)-4-cyclohexene-1,2-carboximide as colorless crystals, melting at 108° in 68% yield.

Anal. Calcd. for $C_{11}H_{12}N_2O_2$: C, 64.68; H, 5.88; N, 13.72. Found: C, 64.51; H, 6.00; N, 13.45.

A mixed melting point with the product obtained in the attempted esterifications above showed no depression.

N-(2-Cyanoethyl)-bicyclo[2.2.1]-5-heptene-2,3-carboximide.—The only product isolated from the attempted esterification of N,N-bis-(2-cyanoethyl)-bicyclo[2.2.1]-5-heptene-2,3-carboxamic acid with 2-ethylbutanol-1 or 2-ethylhexanol-1 was a colorless crystalline solid melting at 113–114°. The reported melting point for the title compound is 113–115°.[6]

Anal. Calcd. for $C_{12}H_{12}N_2O_2$: N, 12.96. Found: N, 12.63.

A mixture of bicyclo[2.2.1]-5-heptene-2,3-carboximide (2 moles, m.p. 185°) and acrylonitrile (10 moles) was refluxed while adding 20 g. of 40% sodium hydroxide. After refluxing for 1 hr., the cooled solution was acidified with 50% sulfuric acid. Evaporation of the excess acrylonitrile left a solid residue, which was crystallized from ethanol to

(4) Melting points are uncorrected.

(5) R. O. Clinton and S. C. Laskowski, THIS JOURNAL, **70**, 3135 (1948).

(6) H. W. Arnold and N. E. Searle, U. S. Patent 2,462,835.

give N-(2-cyanoethyl)-bicyclo[2.2.1]-5-heptene-2,3-carboximide as colorless crystals, melting at 113–115°, in 75% yield.

Anal. Calcd. for $C_{12}H_{12}N_2O_2$: C, 66.62; H, 5.56; N, 12.96. Found: C, 66.83; H, 5.41; N, 13.05.

A mixed melting point with the product obtained from the attempted esterifications above showed no depression.

N,N,N',N'-Tetra-(2-cyanoethyl)-succinamide.—A small amount of solid filtered from several different alkyl N,N-bis-(2-cyanoethyl)-succinamates proved in each case to be the same material. It was flammable, neutral to litmus, very slightly soluble in organic solvents but could be crystallized from hot water to give a nicely crystalline solid, melting from 175–176°.

Anal. Calcd. for $C_{16}H_{20}N_6O_2$: C, 58.50; H, 6.19; N, 25.60. Found: C, 58.41; H, 6.27; N, 25.44.

Acknowledgments.—The author is grateful to Mr. H. C. Shue for technical assistance, Mr. Q. Quick for microanalyses and Mr. C. M. Lovell for infrared analyses.

SOUTH CHARLESTON, W. VA.

[CONTRIBUTION FROM THE DEPARTMENTS OF AGRICULTURAL CHEMISTRY, CHEMISTRY AND HORTICULTURE, MICHIGAN STATE UNIVERSITY]

The Synthesis of Several Acid Analogs of 2-Mercaptobenzimidazole[1,2]

BY THEODORE L. REBSTOCK, CHARLES D. BALL, CHARLES L. HAMNER AND HAROLD M. SELL

RECEIVED JULY 11, 1956

Twenty-three acid analogs of 2-mercaptobenzimidazoles were prepared by treating substituted 2-mercaptobenzimidazoles with monochloroacetic, α-bromopropionic or β-bromopropionic acid.

Several workers have reported that benzimidazole is an antagonist of purine compounds. Woolley[3] observed that benzimidazole inhibited the growth of several yeasts and bacteria and that the inhibition could be completely removed by the addition of aminopurines. Klotz and Mellody[4] demonstrated that yeast nucleic acid reversed the inhibitory effect of benzimidazole on the growth of the bacterium, *Escherichiacoli*. Gillespie, *et al.*,[5] showed that 4-methoxy-6-methylbenzimidazole inhibited growth of *Tetrahymena gelii*, a guanine-requiring protozoan and also of developing embryos of *Rani pipiens*. By using peas as the test plant, Galston, *et al.*,[6] noted that benzimidazole was a metabolic antagonist of adenine and hindered cell elongation. Recently Rebstock, *et al.*, reported that several acid analogs of 2-mercaptobenzimidazole arrested leaf and stem growth of Cranberry bean plants and root formation of cucumber seedlings.[7]

In the present work several new acid analogs of 2-mercaptobenzimidazole were synthesized to study the effect of chemical structure of derivatives of 2-mercaptobenzimidazole on growth inhibition of plants. Different chemical groups were substituted in the benzene ring of the benzimidazole nucleus and the thioether acid side chains were varied.

The acids were prepared by the Williamson synthesis by treating the appropriately substituted 2-mercaptobenzimidazoles with monochloroacetic, α-bromopropionic or β-bromopropionic acids. The 2-mercaptobenzimidazoles were synthesized from suitably substituted *o*-phenylenediamines by the method described by Van Allan and Deacon[8] using a mixture of potassium hydroxide dissolved in aqueous ethanol and carbon disulfide. Where the *o*-phenylenediamines were commercially unavailable, these compounds were prepared from the corresponding *o*-nitroaniline or *o*-dinitrobenzene derivative by either reducing the nitro compound with stannous chloride or tin in concentrated hydrochloric acid. The melting points, neutralization equivalents, yields and analyses for the (2-benzimidazolylthio) acid derivatives are summarized in Table I.

The results of the biological assay of these compounds will be reported elsewhere.

Experimental

Preparation of (2-Benzimidazolylthio) Acid Derivatives.—The acetic, α-propionic and β-propionic acid derivatives were synthesized by treating the appropriately substituted 2-mercaptobenzimidazole with monochloroacetic, α-bromopropionic or β-bromopropionic acids. Equal molar quantities of the monohalogenated acid and the 2-mercaptobenzimidazole were refluxed two hours in a 2 *N* aqueous sodium hydroxide solution. After cooling, the solution was filtered and made acid to congo red with dilute hydrochloric acid. The precipitated acid was collected on a filter, dissolved in a minimum volume of boiling ethanol and decolorized with Norite. The filtered hot alcohol solution was diluted with water until a permanent cloudiness was obtained and then placed in the refrigerator for crystallization. The acid derivatives were recrystallized until the melting points were constant.

Preparation of 2-Mercaptobenzimidazoles.—These compounds were prepared by the procedure of Van Allan and Deacon[8] using as the reactants the appropriately substituted *o*-phenylenediamine and a mixture of aqueous ethanolic potassium hydroxide and carbon disulfide.

Preparation of *o*-Phenylenediamines.—4-Chloro- and 4-nitro-*o*-phenylenediamine were secured from Distillation Products Industries. 4-Methoxy-1,2-diaminobenzene,[9] 4-phenyl-1,2-diaminobenzene,[10] 4-methyl-1,2-diaminobenzene[11] and 3,5-dimethyl-1,2-diaminobenzene[12] were prepared from

(1) From the Ph.D. thesis of Theodore L. Rebstock, Michigan State University, 1956.

(2) Journal Article No. 1932, Michigan Agricultural Experiment Station, East Lansing. Supported in part by the Horace H. Rackham Research Endowment of Michigan State University.

(3) D. W. Woolley, *J. Biol. Chem.*, **152**, 225 (1944).

(4) I. M. Klotz and M. Mellody, *J. Bact.*, **56**, 253 (1948).

(5) H. B. Gillespie, M. Engelman and S. Graff, THIS JOURNAL, **76**, 3531 (1954).

(6) A. W. Galston, R. S. Baker and J. W. King, *Physiol. Plantarum*, **6**, 863 (1953).

(7) T. L. Rebstock, C. D. Ball, C. L. Hamner and H. M. Sell, *Plant Physiol.*, **30**, 382 (1955).

(8) J. A. Van Allan and B. D. Deacon, *Org. Syntheses*, **30**, 56 (1950).

(9) F. H. S. Curd, D. G. Davey and G. J. Stacey, *J. Chem. Soc.*, 1271 (1949).

(10) F. Bell and J. Kenyon, *ibid.*, 2705 (1926).

(11) E. Noelting and L. Stoecklin, *Ber.*, **24**, 565 (1891).

(12) E. Noelting and G. Thesmar, *ibid.*, **35**, 640 (1902).