50 ml. of ether. There were no apparent signs of any reaction. After heating under reflux for a total of 6 hr., the reflux condenser was replaced by an inverted Friedrichs condenser and the ether removed. The viscous residue was cooled and treated with 100 ml. of 5*N* hydrochloric acid, thus forming a yellow oily layer. The mixture was warmed on a water bath for 20 min. to complete the hydrolysis of the acetal. The product was extracted with ether, and the extracts were washed successively with water, saturated sodium bicarbonate solution and water. After drying over sodium sulfate, distillation of the product gave two fractions: (*a*) 2 g. (17%) of b.p. 98–103° (9 mm.), which readily formed a yellow, crystalline derivative with 2,4-dinitrophenylhydrazine; and (*b*) 3.3 g. (20%) of b.p. 122–124° (9 mm.), which formed a 2,4-dinitrophenylhydrazone only after prolonged boiling. The residue (5.3 g.), a sweet-smelling, yellow, viscous liquid, was impure sebacaldehyde. Fraction (*b*), thought to be unhydrolyzed acetal, was boiled for 1 hr. with 7% sulfuric acid (25 ml.) and dioxane (12 ml.). Distillation of the hydrolyzate gave two fractions, which had boiling points identical to those of fractions (*a*) and (*b*) above. Combination of the two samples of b.p. 98–103° (9 mm.) followed by several fractionations gave pure 9-fluorononanal (2.9 g., 25%).

The *2,4-dinitrophenylhydrazone* was recrystallized from methanol as long yellow needles.

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LONDON, ONTARIO, CANADA

[CONTRIBUTION FROM THE WILLIAM H. NICHOLS CHEMICAL LABORATORY, NEW YORK UNIVERSITY]

Addition of Ethylenediamine to Methyl Methacrylate and to Acrylonitrile. Reactions of the Adducts

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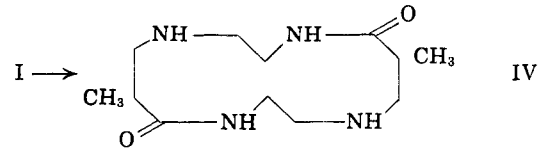
Ethylenediamine has been added to methyl methacrylate and to acrylonitrile. Several diamino esters, diamino acids, and derivatives of these have been prepared. Aged samples of one of the adducts have yielded a substance believed to be 1,5,8,12-tetraza-3,10-dimethyl-2,9-cyclotetradecanedione.

During the course of another investigation certain diamino acids were needed as reference compounds. The simplest representatives of this particular group might be prepared from ethylenediamine and derivatives of acrylic acid. Accordingly such reactions have been studied.

The accompanying flowsheet indicates that both 1:1 and 1:2 adducts, I and II, were obtained from ethylenediamine and methyl methacrylate. The proportions of these adducts were controlled by the ratio of reactants as illustrated in Table I. The formation of adducts which contain only one

$$NH_2CH_2CH_2NH_2 + CH_2{=}C(CH_3)CO_2CH_3 \begin{cases} \nearrow NH_2CH_2CH_2NHCH_2CH(CH_3)CO_2CH_3 & \text{I} \\ \searrow [-CH_2NHCH_2CH(CH_3)CO_2CH_3]_2 & \text{II} \end{cases}$$

$$\text{I} \longrightarrow NH_2CH_2CH_2NHCH_2CH(CH_3)CO_2H{\cdot}2HCl \quad \text{III}$$



IV

$$NH_2CH_2CH_2NH_2 + CH_2{=}CHCN \longrightarrow NH_2CH_2CH_2NHCH_2CH_2CN \quad \text{V}$$

$$\text{V} \longrightarrow NH_2CH_2CH_2NHCH_2CH_2CO_2C_2H_5{\cdot}2HCl \quad \text{VI}$$

$$\text{VI} \longrightarrow NH_2CH_2CH_2NHCH_2CH_2CO_2H{\cdot}2HCl \quad \text{VII}$$

molecule of methyl methacrylate per amino group has been observed previously.[1]

TABLE I
PRODUCTS FROM ETHYLENEDIAMINE AND METHYL METHACRYLATE

Run	Moles ED[a] / Moles MM	Yield, % I	Yield, % II
1	6.0	62	—
2	3.0	55, 61	—
3	1.1	47	24
4	1.0	37, 44	28, 28

[a] ED = ethylenediamine, MM = methyl methacrylate.

Several unsuccessful attempts were made to obtain the 1:1 adduct of ethylenediamine and methyl acrylate by identical procedures. However, these reaction mixtures could not be distilled without decomposition and appeared to be polymeric.[2] Presumably, an explanation of our diverse results with the two acrylates resides in their structural difference. The alpha methyl group would be expected to retard weakly addition by the inductive effect and to retard strongly aminolysis by both inductive and steric effects. The fact that many amines have been added in good yield to both acrylates demonstrates that addition is usually faster than aminolysis. Thus, it is probable that the 1:1 adduct of ethylenediamine and methyl acrylate was formed but that addition was followed by polymeric aminolysis. The observed instability of the adduct I may be offered as evidence for the latter conclusion. Finally, it is important to note that 1:1 adducts of ethylenediamine contain a primary amino group and, in that sense, an excess of amine. Thus, our results should be compared with those of Morsch[3] who showed that adducts of methylamine and methyl acrylate gave amides with excess methylamine.

The desired unsubstituted diamino acid was synthesized by an indirect method. Ethylenediamine was added to acrylonitrile to yield the adduct V which was converted by standard methods into the ester VI and acid VII. At the time these reactions were carried out the 1:2 adduct of ethylene diamine and acrylonitrile was not desired and experimental conditions were selected to minimize its formation. The preparation of both of these adducts has since been reported.[4]

An interesting phase of this work evolved from the observation that the diamino ester I is unstable. Samples of this material, a colorless mobile liquid, gradually thicken and partially crystallize. A colorless solid of m.p. 260–262° was isolated in 4% yield from such aged samples. This substance has been formulated as 1,5,8,12-tetraza-3,10-dimethyl-2,9-cyclotetradecanedione (IV) on the bases of analytical and chemical evidence. The formation of IV from I may be rationalized in terms of intermolecular and intramolecular aminolysis.

(1) D. R. Howton, *J. Org. Chem.*, **10**, 277 (1945).

(2) The preparation of resinous compounds from ethylenediamine and esters of acrylic and methacrylic acids has been reported by G. D. Graves in U. S. Patent 2,146,210.

(3) K. Morsch, *Monatsh.*, **63**, 220 (1933).

(4) A. P. Terent'ev and A. N. Kost, *Zhur. Obshchei Khim.*, **20**, 2069 (1950); *C. A.*, **45**, 5622 (1951).

EXPERIMENTAL[5]

Methyl 3-(2-aminoethylamino)-2-methylpropanoate (I) *and N,N'-di(2-methoxycarbonyl-2-methylethyl)ethylenediamine* (II). Methyl methacrylate[6] was added to 95–100% ethylenediamine with stirring over a period of 60 to 90 min. The temperature of the reaction mixture was maintained at 30–40° by intermittent cooling. After addition of the acrylate the reaction mixtures were allowed to remain at room temperature for 20 to 24 hr. prior to distillation. The amounts of reactants and the yields of I and II are recorded in Table I.[7] The diamino ester I was obtained as a colorless oil of b.p. 88° at 2.0 mm.

Anal. Calcd. for $C_7H_{16}N_2O_2$: C, 52.5; H, 10.0; N, 17.5. Found: C, 52.7; H, 9.9; N, 17.6.

The dihydrochloride of I was isolated as a colorless, microcrystalline, hygroscopic solid of m.p. 139–141°.

Anal. Calcd. for $C_7H_{18}Cl_2N_2O_2$: Cl, 30.4; N, 12.0. Found: Cl, 30.1; N, 12.1.

The 1:2 adduct II was obtained as a colorless oil of b.p. 125° at 0.1 mm.

Anal. Calcd. for $C_{12}H_{24}N_2O_4$: C, 55.3; H, 9.2; N, 10.8. Found: C, 55.7; H, 9.0; N, 11.0.

Dihydrochloride of II, m.p. 149–151°.

Anal. Calcd. for $C_{12}H_{26}Cl_2N_2O_4$: N, 8.4. Found: N, 8.2.

Treatment of II with benzenesulfonyl chloride yielded *N,N'-dibenzenesulfonyl-N,N'-di(2-methoxycarbonyl-2-methylethyl)ethylenediamine* of m.p. 140–142° after recrystallization from a mixture of benzene and ligroin.

Anal. Calcd. for $C_{24}H_{32}N_2O_8S_2$: N, 5.2. Found: N, 5.2.

3-(2-Aminoethylamino)-2-methylpropanoic acid dihydrochloride (III). The diamino ester I (3.00 g.) was dissolved in 15 ml. of 12% hydrochloric acid and the solution was heated on the steam bath for 3 hr. Evaporation under reduced pressure gave a syrup which was crystallized from ethanol to yield 2.00 g. (46%) of III. After recrystallization from the same solvent III was isolated as colorless needles of m.p. 179–181°.

Anal. Calcd. for $C_6H_{16}Cl_2N_2O_2$: Cl, 32.4; N, 12.8. Found: Cl, 32.3; N, 12.7.

The benzoyl derivative of III was prepared from I by a Schotten-Baumann reaction, which gave an oil, followed by refluxing for 2 hr. in 5% sodium carbonate solution. Acidification of the alkaline solution yielded a mixture of oil and solid. The solid, benzoic acid, was dissolved in ether leaving the oil which was dissolved in benzene and crystallized by the addition of petroleum ether. After recrystallization from a mixture of benzene and ethanol, *N,N'-dibenzoyl-3-(2-aminoethylamino)-2-methylpropanoic acid* was isolated as colorless needles of m.p. 122–124°.

Anal. Calcd. for $C_{20}H_{22}N_2O_4$: N, 7.9. Found: N, 7.9.

Stability of I. Formation of *1,5,8,12-tetraza-3,10-dimethyl-2,9-cyclotetradecanedione* (IV). Samples of I gradually thickened and began to crystallize after standing for about four days at laboratory temperatures. For about two weeks ethyl ether could be used to dissolve the oil but after that the oil was no longer soluble in ether and ice water or acetone was

(5) Melting points are uncorrected. Some of the microanalyses were performed by the Schwarzkopf Microanalytical Laboratory, New York.

(6) Samples of methyl acrylate and methyl methacrylate were generously contributed by the Rohm & Haas Co.

(7) The authors are indebted to Mr. Morton Rezak for repeating several of these reactions.

used. A sample of I (52 g.), which had remained at laboratory temperatures for two months, was stirred with 50 ml. of ice water and filtered to yield 2.1 g. (4%) of colorless needles. After recrystallization from water IV melted from 260–262° with decomposition.

Anal. Calcd. for $C_{12}H_{24}N_4O_2$: C, 56.2; H, 9.4; N, 21.9; neut. equiv., 128; mol. wt., 256. Found: C, 56.6; H, 9.2; N, 21.8; neut. equiv., 129; mol. wt., 234 (Rast), 284 (Barger).

A nitroso derivative of IV was prepared by treating an aqueous solution of the hydrochloride with sodium nitrite. After recrystallization from dimethylformamide the nitroso derivative of IV melted from 255–263° with decomposition.

Anal. Calcd. for $C_{12}H_{22}N_6O_4$: N, 26.7. Found: N, 26.9.

A benzoyl derivative of IV was prepared by the usual procedure and was recrystallized from acetic acid, m.p. 296–298° with decomposition.

Anal. Calcd. for $C_{26}H_{32}N_4O_4$: N, 12.1. Found: N, 11.9.

2-(2-Aminoethylamino)propanenitrile (V). Acrylonitrile (10.6 g., 0.20 mole) was added dropwise with stirring, over a period of 90 min., to 36.0 g. (0.60 mole) of ethylenediamine. The mixture was allowed to stand at room temperature overnight and was then distilled under reduced pressure to yield 13.4 g. (59%) of V, b.p. 124–127° at 10 mm. (reported[4] 101° at 1.5 mm.).

Anal. Calcd. for $C_5H_{11}N_3$: neut. equiv., 56.6. Found: neut. equiv., 57.9.

The dihydrochloride of V was prepared in ethanol by the addition of ethanolic hydrogen chloride. After recrystallization from ethanol the salt was isolated as colorless, hygroscopic needles of m.p. 129–131° (reported[4] only that this substance is a very hygroscopic solid).

Anal. Calcd. for $C_5H_{13}Cl_2N_3$: Cl, 38.1; N, 22.6. Found: C, 38.2; N, 22.9.

The benzoyl derivative of V was prepared in the usual manner and was obtained initially as an oil. A benzene solution of the oil was concentrated and the derivative crystallized by the addition of ligroin. After several recrystallizations from benzene, *N,N'-dibenzoyl-3-(2-aminoethylamino) propanenitrile* was isolated as a colorless solid of m.p. 96–98° (a monobenzoyl derivative has been reported[4]).

Anal. Calcd. for $C_{19}H_{19}N_3O_2$: N, 13.1. Found: N, 13.0.

Ethyl 3-(2-aminoethylamino) propanoate dihydrochloride (VI). The amino nitrile V (1.00 g.) was added dropwise to 10 ml. of absolute ethanol saturated with dry hydrogen chloride. After the addition of 0.2 ml. of water the mixture was tightly stoppered and left at room temperature overnight. After heating under reflux for 5 hr. the mixture was filtered hot and on cooling the filtrate deposited 0.79 g. (38%) of VI as very hygroscopic, colorless plates of m.p. 152–154° with previous softening.

Anal. Calcd. for $C_7H_{18}Cl_2N_2O_2$: N, 12.0. Found: N, 12.2.

3-(2-Aminoethylamino)propanoic acid dihydrochloride (VII). The ester dihydrochloride VI (1.000 g.) was dissolved in 10 ml. of dilute hydrochloric acid and the solution was refluxed for 90 min. Evaporation under reduced pressure gave a solid which was recrystallized from ethanol to yield 0.668 g. (76%) of VII as tiny, colorless plates, m.p. 153–155° with previous softening.

Anal. Calcd. for $C_5H_{14}Cl_2N_2O_2$: Cl, 34.6; N, 13.7. Found: Cl, 34.4; N, 13.8.

A sample of VII was converted to the dibenzoyl derivative in the usual manner. After recrystallization from a mixture of benzene and ethanol, *N,N'-dibenzoyl-3-(2-aminoethylamino)propanoic acid* was obtained as clusters of thin, colorless needles of m.p. 149–151° with previous softening at 145°.

Anal. Calcd. for $C_{19}H_{20}N_2O_4$: N, 8.2. Found: N, 8.1.

NEW YORK 53, N. Y.

[CONTRIBUTION NO. 443 FROM THE RESEARCH LABORATORIES OF HOFFMANN-LA ROCHE, INC.]

Pyridindene Derivatives. III. Synthesis from Arecoline

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Two racemic forms of 1-methyl-3-carbomethoxy-4-phenylpiperidine have been obtained from the reaction of phenylmagnesium bromide with arecoline. The two racemic acids were cyclized to the same 2-methyl-2,3,4,4a,9,9a-hexahydro-9-keto-1-pyridindene (VIII).

Treatment with lithium phenyl gave the 9-hydroxy-9-phenyl compound (IX), which was converted into the 9-chloro derivative. The latter was dehydrohalogenated to 2-methyl-9-phenyl-2,3,4,9-tetrahydro-1-pyridindene (XII).

Our earlier work on derivatives of pyridindene has been extended with the objective of devising a synthesis independent of the earlier route.[2] We hoped that this synthesis would allow us to prepare a larger number of derivatives and at the same time serve as an independent confirmation of the structure.

Accordingly, the preparation of 1-methyl-3-carboxy-4-phenyl-piperidine (IV) was investigated as a starting material for the compound XII. Koelsch[3] obtained compound IV by a series of reactions involving a Michael condensation of ethyl cyanoacetate and ethyl cinnamate, reduction over Raney nickel to give the piperidone I, reduction of the carbonyl group with sodium and butanol, and finally N-methylation with formaldehyde. Although the process is feasible, considerable technical difficulty is involved, especially in the reduction with sodium. Other methods of reduction were tried and some limited success was obtained with the copper chromite catalyst.[4] This catalyst in the presence of methanol not only reduced the carbonyl group but simultaneously led to the methylation of the nitrogen, resulting in the ester III (R = ethyl). Hydrolysis of this ester yielded a free acid, which proved to be identical with the acid obtained by the

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