steam-bath for eighteen hours. After adding water, the non-aqueous layer was separated, combined with the ether extracts of the water washings, dried and distilled. The forerun consisted of an almost theoretical recovery of the excess hexamethylene dibromide, b. p. 112–114° at 12 mm. The bromoester boiled at 204–205° at 4 mm., n^{24}D 1.5283. It weighed 126 g., an 82% yield.

Anal. Calcd. for $C_{19}H_{27}O_2Br$: Br, 21.76. Found: Br, 21.57.

ω-Morpholinohexyl 1-Phenylcyclohexanecarboxylate.—To 123.5 g. (0.34 mole) of the foregoing bromoester in 200 cc. of dry benzene, 59.0 g. (0.68 mole) of morpholine was added slowly. The reaction mixture was then stirred and refluxed five and one-half hours, after which the benzene layer was washed with water then extracted with acid. The base which was regenerated by the addition of alkali was extracted with ether and dried. Removal of the solvent, followed by distillation of the residue, gave 108 g. (86%) of the aminoester, b. p. 228–230° at 4 mm., n^{24}D 1.5166.

By method Ia, an 87% yield of this base was obtained.

The hydrochloride melted at 121–122° after crystallization from ethyl acetate.

γ-Bromopropyl 1-Phenylcyclopropanecarboxylate.—A solution of 25 g. (0.138 mole) of 1-phenylcyclopropanecarboxylic acid chloride in 20.5 g. (0.148 mole) of trimethylene bromohydrin was heated on the steam-bath overnight. The reaction mixture was washed successively with water and sodium bicarbonate, then dried and distilled. The main fraction weighed 25.2 g., (65%) and boiled at 151–153° at 3 mm., n^{26}D 1.5364.

Anal.[13] Calcd. for $C_{13}H_{15}O_2Br$: C, 55.12; H, 5.34. Found: C, 55.96; H, 5.42.

γ-Morpholinopropyl 1-Phenylcyclopropanecarboxylate.—The foregoing bromide, 11.3 g. (0.041 mole), was converted to the morpholino derivative as described above for the ω-morpholinohexyl ester. The product boiled at 173–175° at 2 mm., n^{26}D 1.5193. The yield was 8.5 g. or 73%.

The hydrochloride, m. p. 168–169°, was crystallized from absolute alcohol.

Acknowledgment.—The author is indebted to Mr. E. F. Shelberg and Mr. L. F. Reed of the Microanalytical Department of these laboratories for the microanalyses and to Mr. Wm. B. Brownell for his assistance in preparing some of the intermediates.

Summary

A series of basic esters derived from 1-phenylcyclopropanecarboxylic acid and 1-phenylcyclohexanecarboxylic acid has been described.

Preliminary pharmacological data indicate that several of these esters possess pronounced antispasmodic properties.

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[13] Fractionation of this material did not improve the analysis.

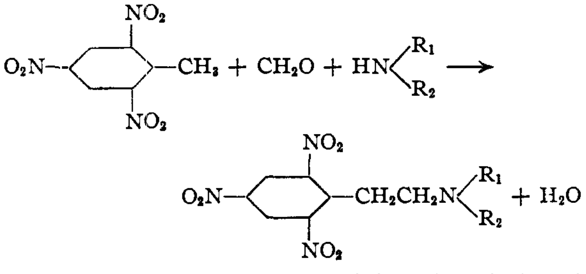
NORTH CHICAGO, ILLINOIS RECEIVED JULY 13, 1946

[CONTRIBUTION FROM ROHM AND HAAS CO., INC.]

Trinitro-phenylethyl Amines from TNT[1]

BY HERMAN A. BRUSON AND GEORGE B. BUTLER

While attempting to utilize 2,4,6-trinitrotoluene in the preparation of combustible plastics,[1a] it was found that this compound would undergo the Mannich reaction with formaldehyde and secondary amines to give 2,4,6-trinitrophenylethyl amines according to the reaction



Vender[2] prepared 2,4,5-trinitrophenylethanol by treating 2,4,5-trinitrotoluene with aqueous formaldehyde in the presence of potassium carbonate, but described no Mannich-type bases. McLeod and Robinson[3] described the formation of 2,4-dinitrophenylethyl-N-diethylamine as a yellow oil from the reaction of equivalent weights of 2,4-dinitrotoluene and the *i*-amyl ether of methylol diethylamine in boiling *i*-amyl alcohol, but could isolate no definite compounds from the reaction of these amine ethers with 2,4,6-trinitrotoluene.

Kermack and Muir[4] obtained 2,4-dinitrophenylethyl-N-diethylamine by treating equivalent quantities of 2,4-dinitrotoluene, diethylamine, and formaldehyde in boiling ethanol. They also described the formation of 1,3-dipiperidino-2-(2,4-dinitrophenyl)-propane[5] by the reaction of one mole of 2,4-dinitrotoluene with two moles each of piperidine and formaldehyde.

It also has been reported that the alkaloid berberine[6] condenses with TNT to give an orange red compound but its properties are not described. Berberine in its pseudo-base form contains an >N—CHOH— grouping, but whether this combines with TNT by loss of water or by the formation of a simple addition product is not clear.

The condensation of TNT with formaldehyde and secondary amines takes place readily at temperatures from about 0 to 100°, depending upon the amine, by mixing together equivalent weights of the reactants. In the cases of the lower, more reactive amines, low temperatures are suitable to complete the reaction, but in the cases of

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[1] This paper is based on work done for the Office of Scientific Research and Development under OSRD Contract No. OEM sr-643 with the Rohm and Haas Co.

[1a] Bruson and Butler, U. S. Patent 2,400,806 (1946).

[2] Vender, *Gazz. chim. ital.*, **45**, II, 97 (1915).

[3] McLeod and Robinson, *J. Chem. Soc.*, **119**, 1470 (1921).

[4] Kermack and Muir, *J. Chem. Soc.*, 300 (1933).

[5] Mannich and Stein, *Ber.*, **58**, 2659 (1925).

[6] Robinson and Robinson, *J. Chem. Soc.*, **111**, 958 (1917).

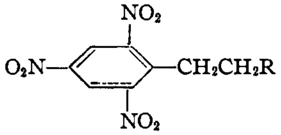
the higher, less reactive amines, higher temperatures are advantageous. Small amounts of alkali metal hydroxides accelerate the condensation. In view of the tendency for TNT to ignite in contact with free bases, it is necessary to carry out the condensation in an inert solvent or a liquid suspending medium for the reactants. Suitable liquids for this purpose are dioxane, benzene, alcohol or water.

The Mannich reaction with TNT as a component was applied to the following secondary amines.

Morpholine, piperidine, diethanolamine, N-methylaniline, dibenzylamine, dimethylamine, di-

TABLE I

PROPERTIES AND ANALYSES OF 2,4,6-TRINITROPHENYLETHYL AMINES



$O_2N-C_6H_2(NO_2)_2-CH_2CH_2R$

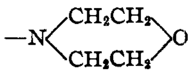
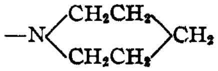
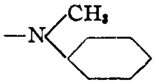
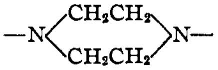
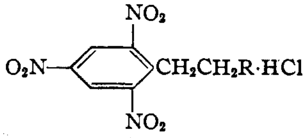
R =	M. p., °C.	Recrystallized from	Empirical formula	Analyses, % Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
	135	1:1 Benzene-ethanol	$C_{12}H_{14}O_7N_4$	44.2	4.30	17.18	44.3	4.41	17.00
	104	Ethanol	$C_{13}H_{16}O_6N_4$	48.2	4.94	17.29	48.3	5.06	17.15
$-N(C_2H_4OH)_2$	87	Benzene	$C_{12}H_{16}O_8N_4$	..	..	16.29	..	..	16.28
	175	Ethanol	$C_{15}H_{14}O_6N_4$	52.1	4.05	16.16	52.1	4.15	16.08
$-N(CH_2-C_6H_5)_2$	104	Ethanol	$C_{22}H_{20}O_6N_4$	60.5	4.60	12.83	60.5	4.85	12.86
	170	Xylene	$C_{20}H_{20}O_{12}N_8$	42.6	3.55	19.86	43.3	3.68	19.90

TABLE II

PROPERTIES AND ANALYSES OF 2,4,6-TRINITROPHENYLETHYL AMINE HYDROCHLORIDES



$O_2N-C_6H_2(NO_2)_2-CH_2CH_2R\cdot HCl$

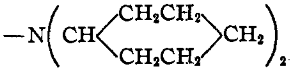
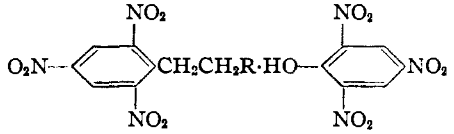
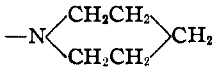
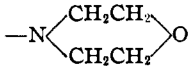
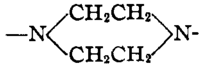
R =	M. p., °C.	Recryst. from	Empirical formula	Analyses, % Calcd. Ion. Cl	Calcd. N	Found Ion. Cl	Found N
$-N(CH_3)_2$	183	Ethanol	$C_{10}H_{13}O_6N_4Cl$	11.10	17.45	11.23	17.00
$-N(C_2H_5)_2$	136	Ethylene dichloride	$C_{12}H_{17}O_6N_4Cl$	10.20	16.10	10.18	15.61
$-N(n\text{-}C_4H_9)_2$	119	Benzene	$C_{16}H_{25}O_6N_4Cl$	8.78	13.85	9.14	13.34
	220 (dec.)	Ethanol	$C_{20}H_{29}O_6N_4Cl$	7.80	12.26	8.39	11.97

TABLE III

PROPERTIES AND ANALYSES OF PICRATES OF 2,4,6-TRINITROPHENYLETHYL AMINES

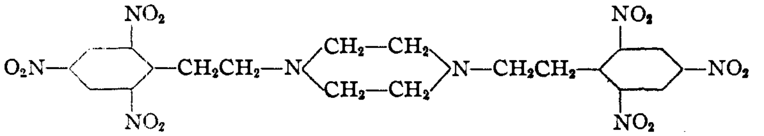


$O_2N-C_6H_2(NO_2)_2-CH_2CH_2R\cdot HO-C_6H_2(NO_2)_3$

R =	M. p., °C.	Empirical formula	Analyses, % Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
	171	$C_{19}H_{19}O_{13}N_7$	41.2	3.44	17.72	41.0	3.45	17.55
	161	$C_{18}H_{17}O_{14}N_7$	38.9	3.06	17.65	38.6	3.14	17.70
$-N(C_2H_4OH)_2$	128–130	$C_{18}H_{19}O_{15}N_7$	37.7	3.32	17.10	37.5	3.09	17.15
$-N(CH_2-C_6H_5)_2$	162	$C_{28}H_{23}O_{13}N_7$	50.5	3.46	14.74	50.3	3.48	14.79
	Dec. >200	$C_{32}H_{26}O_{26}N_{14}$	37.6	2.54	19.18	37.8	2.73	19.18

ethylamine, di-*n*-butylamine, dicyclohexylamine and piperazine.

The latter combined with two moles each of formaldehyde and TNT to give bis-(2,4,6-trinitrophenylethyl)-N_1N'-piperazine.



In general the reaction is applicable to secondary amines that readily form an N-methylol derivative with formaldehyde. Diphenylamine and similar very weakly basic amines which do not readily form N-methylol derivatives with formaldehyde fail to react. The formaldehyde used is preferably in the form of an aqueous 30–37% solution, but may also be used in the form of paraformaldehyde.

Experimental

2,4,6-Trinitrophenylethyl-N-morpholine.—The preparation of this compound is given as a typical example of the general procedure used for the preparation of these compounds.

To a stirred solution of 11.5 g. (0.05 mole) of 2,4,6-trinitrotoluene and 25 g. of dioxane cooled to 5°, there was gradually added 4.5 g. (0.05 mole) of morpholine, 1 g. of 2% sodium hydroxide solution, and 4.5 g. (0.05 mole) of 37% aqueous formaldehyde, the additions being made in the order given. The temperature of the reaction mixture was maintained between 5 and 10° while the various reagents were added and for a period of one hour thereafter. The mixture was warmed at 40–50° for one hour, then cooled to 10° and mixed with 100 g. of cold water containing 0.5 g. of concentrated hydrochloric acid. Stirring was continued and the mixture cooled until the product crystallized out. It was filtered, washed and dried in the air. The material thus obtained amounted to 15.5 g. (95% of theory) and melted at 125°. After recrystallization from a 1:1 mixture of benzene and ethanol, it formed tan-colored needles melting at 135°.

The picrate of the above compound melts at 161°. It was prepared by mixing equivalent quantities of the compound and picric acid in hot alcoholic solution. This procedure was typical of that used for the preparation of all picrates described.

In those cases in which the product obtained was an oil or was difficult to crystallize, the reaction product was taken up in ether, dried over anhydrous calcium chloride and the hydrochloride of the amine precipitated by passing dry hydrogen chloride into the solution. The salt was purified by recrystallization to obtain the pure hydrochloride of the tertiary amine.

In most cases, the theoretical yield of the crude reaction product was approached with little or no loss by decomposition or by-products. Dioxane was used as solvent in all the preparations.

Tables I, II and III include the compounds prepared, physical properties and analyses.

Acknowledgment.—The authors wish to express their appreciation to Mr. Clyde W. Nash of the Rohm and Haas Analytical Laboratories, Bristol, Pa., for the microanalyses reported here.

Summary

2,4,6-Trinitrotoluene (TNT) undergoes the Mannich reaction with formaldehyde and N-methylol-forming secondary amines to give 2,4,6-trinitrophenylethyl-N-*t*-amines. The following secondary amines were used: dimethylamine, diethylamine, dibutylamine, dicyclohexylamine, dibenzylamine, diethanolamine, N-methylaniline, morpholine, piperidine and piperazine. Piperazine condensed with two moles each of formaldehyde and TNT.

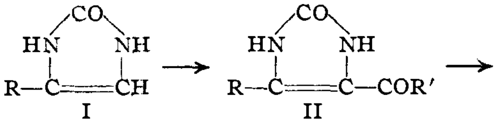
PHILADELPHIA, PA. RECEIVED JULY 26, 1946

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF HOFFMANN-LA ROCHE, INC.]

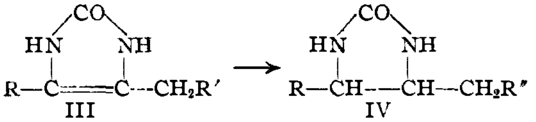
Studies in the Imidazolone Series. The Synthesis of a Lower and a Higher Homolog of Desthiobiotin and of Related Substances[1]

BY ROBERT DUSCHINSKY AND L. ALLEN DOLAN

In a previous paper,[1a] it was shown that Friedel–Crafts acylations of 4-methyl-2-imidazolone (I, R = CH_3), followed by hydrogenation of the obtained ketones (II), lead to imidazolidone compounds, the keto group being first reduced to methylene (III and IV).



I II



III IV

In the present paper it is reported that 2-imidazolone (I, R = H) and 4-ethyl-2-imidazolone (I, R = C_2H_5) react in a similar manner.

Curiously enough, compounds having different properties are described in the literature as 2-imidazolone. In 1892 Marckwald reported the synthesis of imidazolone from amino acetal (V) *via* ureido acetal (VI), and described it as a substance

$$H_2NCH_2CH(OC_2H_5)_2\ (V) \longrightarrow H_2NCONHCH_2CH(OC_2H_5)_2\ (VI) \longrightarrow I\ (R = H)$$

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(1) Presented before a session of the Division of Organic Chemistry, 109th Meeting of the American Chemical Society, Atlantic City, New Jersey, April 10, 1946.

(1a) Duschinsky and Dolan, THIS JOURNAL, 67, 2069 (1945).