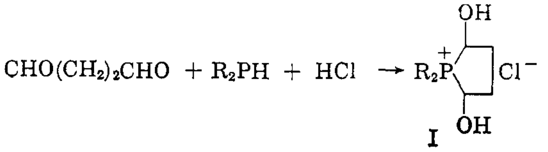
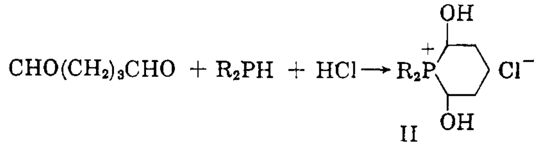
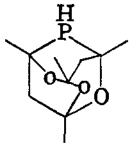

I

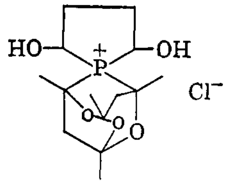
R = n-C_4H_9, i-C_4H_9

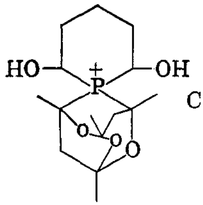

II

R = n-C_4H_9, i-C_4H_9, $cyclo$-C_6H_{11}, n-C_8H_{17}

in which the phosphorus atoms are parts of spiran as well as adamantane ring systems were also obtained readily by this method. The secondary phosphine (V) used in these cases is produced by the reaction of phosphine with 2,4-pentanedione.[2]


V


III


IV

In carrying out this heterocycle synthesis, the order of addition of reagents proved to be critical. The general method adopted after detailed study of the reactions of di-n-butylphosphine and di-i-butylphosphine with glutaraldehyde, was to add concentrated hydrochloric acid to an alcoholic solution of the phosphine and aldehyde reactants. This technique produced 30–50% yields of the crystalline heterocyclic phosphonium salts. Other modes of addition resulted in lower yields or complex mixtures of products.

Aside from correct analyses and reasonable infrared data, support for the proposed cyclic structures was obtained from molecular weight measurements (Table I). The results show that the salts are dissociated in aqueous solution. On the other hand, values obtained in the less polar solvents ethanol and chloroform are generally in good agreement with those calculated for the formula weight.

EXPERIMENTAL[3]

Materials. Di-n-octylphosphine, diisobutylphosphine and dicyclohexylphosphine were prepared by the method of Stiles, Rust and Vaughan.[4] Di-n-butylphosphine was obtained from Food Machinery and Chemical Corp. Glutaraldehyde and succinaldehyde (2,5-diethoxytetrahydrofuran) were Carbide and Carbon Chemicals Co. materials.

1,1-Diisobutyl-2,6-dihydroxyphosphoniacylcyclohexane chloride. To a solution of 9.0 g. (0.062 mole) of diisobutylphosphine, 24.7 g. (0.062 mole) of 25% aqueous glutaraldehyde, 50 ml. of methanol and 25 ml. of tetrahydrofuran under a nitrogen atmosphere was added dropwise 7 ml. of concentrated hydrochloric acid. The solution was heated under reflux for 2 hr. and then evaporated under reduced pressure. The residue was recrystallized from acetone to give 6.0 g. (34%) of product, m.p. 150–152°.

Other Heterocyclic Dihydroxy Phosphonium Salts. These were prepared using minor variations of the above procedure. The pertinent information is given in Table I.

American Cyanamid Co.
Central Research Div.
Chemical Research Dept.
Stamford, Conn.

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(2) M. Epstein and S. A. Buckler, *J. Am. Chem. Soc.*, **83**, 3279 (1961).

(3) Melting points are uncorrected. Analyses and molecular weight measurements were carried out under the supervision of Dr. J. A. Kuck.

(4) A. R. Stiles, F. F. Rust, and W. E. Vaughan, *J. Am. Chem. Soc.*, **74**, 3282 (1952).

Isomeric Hydroxyacetanilides by Reductive Acylation of Nitrophenols

Morris Freifelder

Received September 25, 1961

The need for some pure hydroxyacetanilides in this laboratory prompted an investigation into reductive acetylation of the isomeric nitrophenols. While aminophenols are readily acylated their well known propensity for darkening on storage leads to colored reaction products unless the starting materials are freshly prepared. It was thought therefore that reduction of the nitrophenols in the presence of acetic anhydride might lead to better products.

This procedure has been used for the *para* derivative employing platinum oxide catalyst.[1] In our hands the same reduction with this catalyst led to a colored product. The use of palladium-on-carbon, on the other hand, gave not only good yield, but also a product that required little purification. Similarly, excellent quality *o*- and *m*-hydroxyacetanilides were prepared from the corresponding nitrophenols.

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(1) J. H. Burckhalter *et al.*, *J. Am. Chem. Soc.*, **70**, 1363 (1948) obtained a 58% yield. Obviously since it was an intermediate in synthesis the authors reported no attempt to increase yield.

EXPERIMENTAL[2]

p-Hydroxyacetanilide. A mixture of 13.9 g. (0.1 mole) of *p*-nitrophenol, 75 cc. of glacial acetic acid, 10.2 g. (0.1 mole) of acetic anhydride, and 0.250 g. of 5%palladium-on-carbon was hydrogenated under 2 atm. pressure. The uptake of hydrogen was complete in about 1 hr. After filtration from the catalyst, the solution was concentrated under reduced pressure to a thick sirup. After addition of 100 cc. of water, the mixture was allowed to stand in the cold for several hours. It was then filtered and the product recrystallized from hot water containing about 0.5 g. of sodium hydrosulfite. A 79% yield of crystalline product melting at 170–171° was obtained; lit. 168°,[1] 168–169°.[3]

Anal. Calcd. for $C_8H_9N_2O_2$: C, 63.54; H, 5.99; N, 9.26. Found: C, 63.35; H, 5.70; N, 9.06.

In the preparation of *o*-hydroxyacetanilide the product crystallized during the course of reaction. It was necessary then to add the reaction mixture to 600 cc. of water and heat to dissolve. The hot solution was then filtered from the catalyst through a heated funnel. Beautifully crystalline colorless material was obtained on cooling; yield, 82.5%, m.p. 208–209°.[4]

Anal. Calcd. for $C_8H_9N_2O_2$: C, 63.54; H, 5.99; N, 9.26. Found: C, 63.38; H, 6.12; N, 9.25.

m-Hydroxyacetanilide was prepared in a similar manner from *m*-nitrophenol. However, since this product is somewhat water-soluble, the residue resulting from concentration of the reduction solution was treated with 100 cc. of water and cooled thoroughly until precipitation was complete. It was then filtered and drained thoroughly without washing. A 73% yield was obtained, m.p. 151–151.5°; lit.[5] 148–149°.

Anal. Calcd. for $C_8H_9N_2O_2$: C, 63.54; H, 5.99; N, 9.26. Found: C, 63.40; H, 6.21; N, 9.32.

Abbott Laboratories
Organic Research Dept.
North Chicago, Ill.

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(2) Microanalyses were carried out by Mr. E. F. Shelberg and Mr. O. Kolsto and their staff.

(3) L. Claisen and F. Kremers, *Ann.*, 418, 104 (1919).

(4) E. Bamberger, *Ber.*, 36, 2042 (1903), reports 209° with sintering beginning at 200°. N. N. Crounse and L. C. Raiford, *J. Org. Chem.*, 10, 419 (1945), give 207–208°.

(5) M. Ikuta, *Am. Chem. J.*, 15, 39 (1893).

N-Substituted Vanillamides

Harold Monsimer and Souren Avakian[1]

Received September 25, 1961

Recently, the preparation of a number of *N*-substituted vanillamides was reported.[2–4] The fact

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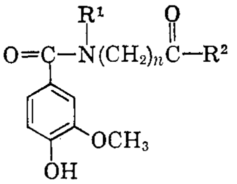
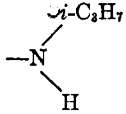
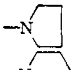
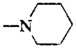
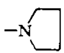
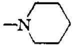
(1) Present address, Denver Chemical Co., Stamford, Conn.

(2)(a) K. Kratzl and E. Kvasnicka, *Monatsh.*, 83, 18 (1952); (b) U. S. Patent 2,641,612 (1953); (c) Austrian Patents 168,059 (1950) and 172,341 (1952).

TABLE I

Vanillamides with Two Carboxylic Functions[a]



n	R^1	R^2	M.P.[b]	Nitrogen, % Calcd.	Nitrogen, % Found	Yield, %
1	C_2H_5	$—N(CH_3)_2$	56–57	9.99	9.79	70
1	C_2H_5	$—N(C_2H_5)_2$	91–92	9.09	9.11	40
1	C_2H_5	$—N(CH_2CH{=}CH_2)_2$	112–113	8.43	8.43	30
1	C_2H_5		140–142	9.52	9.46	80
1	C_2H_5		144–145	9.15	8.93	40
1	C_2H_5		74–76	8.74	8.67	30
1	$CH_2CH{=}CH_2$	$—N(C_2H_5)_2$	94–95	8.74	8.69	40
1	$CH_2CH{=}CH_2$	$—N(CH_2CH{=}CH_2)_2$	88–89	8.19	8.08	55
1	$CH_2CH{=}CH_2$		149–150	8.80	8.71	40
1	$CH_2CH{=}CH_2$		133–134	8.43	8.42	46
2	H	$—N(C_2H_5)_2$	124–125	9.52	9.52	40
2	C_2H_5	$—N(C_2H_5)_2$	glass[c]	8.69	8.42	55

[a] The starting ω-aminocarboxylic amides were prepared from the corresponding ω-chlorocarboxylic acid chlorides and the appropriate amines. [b] Melting points are uncorrected. [c] This compound was purified by distillation in a "Rota Film" molecular still at a jacket temperature of 200°, 30 μ.