

Experimental

3,4-Dichlorobenzyl Cyanide.—This nitrile was prepared in the usual manner from 3,4-dichlorobenzyl chloride and was obtained as a colorless liquid, b. p. 170° (12 mm.).

Anal. Calcd. for C₈H₅Cl₂N: N, 7.50. Found: N, 7.37, 7.51.

2-(3,4-Dichlorophenyl)-4-diethylaminobutylamine.—A solution of 128 g. (0.45 mole) of α-(3,4-dichlorophenyl)-γ-diethylaminobutyronitrile in 600 cc. of 15% methanolic ammonia was reduced in the presence of 30 g. of Raney nickel under fifty atmospheres pressure of hydrogen at 50°. The catalyst was removed by filtration and the residue distilled to give 124 g. (95.5%) of product, b. p. 125° (1 mm.).

Anal. Calcd. for C₁₄H₂₂Cl₂N₂: N, 9.77. Found: N (Dumas), 9.90; N (titration), 9.77.

4-[2-(p-Chlorophenyl)-4-diethylaminobutylamino]-7-chloroquinoline.—A mixture of 19.8 g. (0.1 mole) of 4,7-dichloroquinoline, 54 g. (0.211 mole) of 2-(p-chlorophenyl)-4-diethylaminobutylamine, and a pinch of potassium iodide was heated in a bath kept at 180°. The temperature of the reaction mixture was allowed to rise spontaneously to 198° and then kept at 180° so that the total time of heating at 180° or higher was thirty-five minutes. A solution of the viscous oil in 125 cc. of 40% acetic acid was added to excess, dilute sodium hydroxide and the liberated oil dissolved in ether. The ether solution was dried by shaking with potassium carbonate and set aside to crystallize. The 25.5 g. of white crystalline product, m. p. 122–125°, was recrystallized from Skellysolve C to give 25 g. (60%), m. p. 127–129°.

Anal. Calcd. for C₂₃H₂₇Cl₂N₃: C, 66.4; H, 6.50; N, 10.10. Found: C, 66.12; H, 6.59; N, 9.79.

4-[2-(p-Chlorophenyl)-5-diethylaminopentylamino]-7-chloroquinoline.—A mixture of 30 g. of phenol, 34 g. (0.126 mole) of 2-(p-chlorophenyl)-5-diethylaminopentylamine, 19.8 g. (0.1 mole) of 4,7-dichloroquinoline, and a pinch of potassium iodide was kept at 130–140° for three hours, dissolved in 125 cc. of 40% acetic acid, and added to excess, dilute sodium hydroxide. An ether solution of the liberated oil was washed well with 10% sodium hydroxide and

then water, dried by shaking with potassium carbonate, and set aside to crystallize, yielding 29 g. of white crystalline product, m. p. 113–115°. Several recrystallizations from benzene-Skellysolve C gave 24.5 g. (57%), m. p. 119.5–121°.

Anal. Calcd. for C₂₄H₂₉Cl₂N₃: C, 66.98; H, 6.74; N, 9.77. Found: C, 66.98; H, 7.00; N, 9.89.

7-Chloro-4-[4-diethylamino-2-(p-hydroxyphenyl)-butylamino]-quinoline.—A solution of 30 g. (0.073 mole) of 7-chloro-4-[4-diethylamino-2-(p-methoxyphenyl)-butylamino]-quinoline in 450 cc. of 48% hydrobromic acid was refluxed for fifteen minutes and concentrated *in vacuo*. An aqueous solution of the residue was treated with charcoal and filtercel and added to excess ammonium hydroxide to precipitate a white solid weighing 26 g. (89.7%), m. p. 162–164°. Recrystallization from alcohol yielded 20 g., m. p. 163–164°. The product was soluble in dilute sodium hydroxide.

Anal. Calcd. for C₂₃H₂₅ClN₃O: C, 69.43; H, 7.04; N, 10.57. Found: C, 69.05; H, 7.12; N, 10.57.

Acknowledgment.—The authors wish to acknowledge, with appreciation, the advice of Drs. C. M. Suter and J. S. Buck. We wish to thank the Misses Bass, Rainey and Curran for the microanalyses recorded.

Summary

The preparation of a series of 4-dialkylaminoalkyl nitriles and amines is described in which a phenyl or substituted phenyl group is in the 2-position. These diamines have been condensed with 4,7-dichloroquinoline and 4,7-dichloro-3-methylquinoline to give a series of 7-chloro-4-substituted aminoquinolines and 7-chloro-3-methyl-4-substituted aminoquinolines. The preparation of an analogous series of 9-amino-6-chloro-2-methoxyacridine derivatives is reported.

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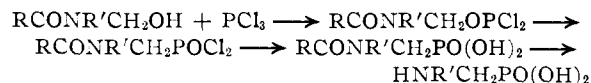
NOTES

The Preparation of β-Aminoethanephosphonic Acid

By JACOB FINKELSTEIN

During the course of an investigation in this Laboratory it was desirable to prepare β-aminoethanephosphonic acid: H₂NCH₂CH₂PO(OH)₂ (I). The only compounds of this type reported are aminomethanephosphonic acid and its N substituted derivatives.¹ These substances were prepared from methylolamides RCO—NR'CH₂OH which when treated with phosphorus trihalide produce intermediate dihalogen phosphorus esters, which rearrange spontaneously into phosphonic acid dihalides, and on hydrolyzing the phosphonic acids are obtained

(1) U. S. Patent 2,304,156 and 2,328,358.



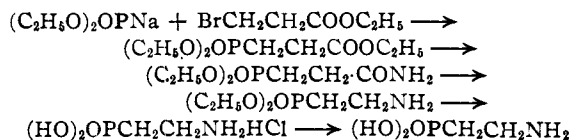
This method is possibly not applicable to the preparation of compounds of the type =N—(CH₂)_x—P^z where x > 1.

Nylen² has described the preparation of β-phosphonopropionic acid triethyl ester and its C-amide (β-carbamylethanephosphonic acid diethyl ester). This latter substance, when subjected to the Hofmann degradation, yielded the desired substance (I). The corresponding hydrazide was also prepared from the ester but would not undergo the Curtius rearrangement.

Nylen prepared the ester in 35% yield by the reaction of sodiodiethyl phosphite with ethyl β-

(2) Nylen, *Ber.*, **59**, 1119 (1926).

iodopropionate in ether. Upon distillation, it undergoes violent decomposition. For this investigation the ester was prepared in 78% yield from sodio-diethyl phosphite with ethyl β -bromopropionate in dry xylene. The product distilled very smoothly. The C-amide was obtained in the usual manner. The reactions may be summarized as follows



The amino acid is a colorless, crystalline substance freely soluble in water and insoluble in alcohol. It is stable to hot hydrochloric acid and possesses a characteristic titration curve with one sharp break, at pH 7.5, due to the zwitterion effect.

Experimental

β -Phosphonopropionic Acid Triethyl Ester.—To 68 g. of dry sodium ethoxide in 500 cc. of dry xylene, 138 g. of diethyl phosphite³ is added slowly while stirring. When completely reacted, 181 g. of ethyl β -bromopropionate is added dropwise with vigorous stirring while the reaction mixture is kept in an ice-salt bath. After permitting the mixture to stand overnight to reach room temperature, it is warmed for two hours in a water-bath. After cooling, the sodium bromide is removed by filtering, the xylene distilled off *in vacuo* and the residual oil fractionated *in vacuo*; b. p. 141–143° at 9 mm. The ester is a clear, colorless liquid; yield, 78%.

β -Aminoethanephosphonic Acid.—To a solution of 30.8 g. of potassium hydroxide and 8 g. of bromine in 200 cc. of water at 0°, 10.45 g. of β -carbamylethanephosphonic acid diethyl ester is added and the mixture stirred until complete solution has occurred. After allowing the solution to stand overnight, at room temperature, 90 cc. of 48% hydrobromic acid is added when about one liter of carbon dioxide is evolved. The solution is evaporated to dryness *in vacuo* from a warm water-bath. The residue is treated with 75 cc. of water and filtered. The filtrate, at about pH 1, is heated in a sealed tube at 150–190° for two hours. The reaction mixture is then evaporated to dryness *in vacuo*, the residual cake extracted with 100 cc. of warm alcohol and the extract filtered. The filtrate is treated with excess aniline while stirring to precipitate the amino acid. After two recrystallizations from 50% alcohol, the product is pure; m. p. 281–282° (cor.), yield, 71%.

Anal. Calcd. for $C_2H_5NPO_3$: C, 19.20; H, 6.45; N, 11.20. Found: C, 19.21; H, 6.51; N, 10.55.

(3) Milobendzki and Sachnowski, *C. A.*, **13**, 2865 (1919).

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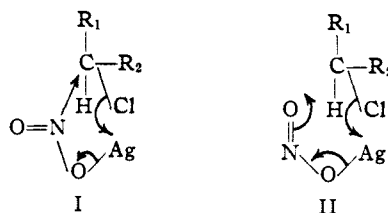
Reaction of *d*- α -Phenethyl Chloride with Silver Nitrite

BY RICHARD H. EASTMAN AND SIDNEY D. ROSS

The reaction of silver nitrite with optically active β -*n*-octyl bromide has been shown¹ to lead to optically active β -nitro-*n*-octane and β -*n*-octyl nitrite. In view of the heterogeneous nature of this reaction it occurred to us that reac-

(1) Shriner and Young, *THIS JOURNAL*, **53**, 3332 (1930).

tion complexes of the type I and II with the indicated electronic shifts would account for the retention of optical activity in the products



equally as does the assumption of a simple displacement of chloride ion by nitrite ion, the sense of the attack of the latter determining whether nitro compound or nitrite is the product. As a test of our hypothesis we have carried out the reaction of silver nitrite with *d*- α -phenethyl chloride in benzene, in which case a retention of optical activity would be expected if cyclic complexes of the type shown were intermediates. Our choice of the optically active halide was dictated by the observation that if activity were retained in this case, the experiment would constitute good evidence for the hypothetical mechanism, since it has been shown² that in the reaction of benzyl chloride with mercuric salts, the mercuric ion simply removes the halogen leaving the alkyl residue as a carbonium ion or its equivalent. If the silver ion of the silver nitrite operates in this latter sense rather than in the former in the case of *d*- α -phenethyl chloride, the formation of α -phenethyl nitrite and α -nitroethylbenzene should be attended with racemization.

Our experiments show that racemization is the predominant course of the reaction in question.

Experimental

***d*- α -Phenethyl Chloride.**—This material was obtained from *d*- α -phenethyl alcohol³ ($[\alpha]^{25}_D +29.8^\circ$) by the method of McKenzie and Clough.⁴ Our material had b. p. 85–86° at 29 mm., n^{25}_D 1.5250 and $[\alpha]^{25}_D +37.0^\circ$.

***d*- α -Phenethyl Nitrite.**—A mixture of 3.5 g. of sodium nitrite, 10 cc. of water and 6.1 g. *d*- α -phenethyl alcohol ($[\alpha]^{25}_D +29.8^\circ$) was cooled in an ice-bath and treated with 8.5 cc. of 6 *N* hydrochloric acid in portions during fifteen minutes with swirling. The layers were then separated, the product was diluted with ether, dried over sodium sulfate, freed from solvent and distilled through a two-foot Podbielniak column to yield 4.5 g. of *d*- α -phenethyl nitrite, a yellow oil of turpentine odor, of b. p. 70–71° at 16 mm.,⁵ of n^{25}_D 1.4912, and of $[\alpha]^{25}_D +39.9^\circ$.

Reaction of *d*- α -Phenethyl Chloride with Silver Nitrite.—Eight and one-half grams of *d*- α -phenethyl chloride ($[\alpha]^{25}_D +37.0^\circ$) and 12.2 g. of silver nitrite (dried *in vacuo* over phosphorus pentoxide) were shaken together in 100 cc. of dry benzene for twelve hours. The silver halide was filtered off, the benzene was removed *in vacuo*, and the product was distilled through a two-foot Podbielniak column. The following fractions were obtained:

(2) Roberts and Hammett, *ibid.*, **59**, 1063 (1937).

(3) We wish to express our appreciation to George DeLaMater of Harvard University for providing us with the active phenethyl alcohols.

(4) McKenzie and Clough, *J. Chem. Soc.*, **103**, 687 (1913).

(5) *d*- α -Phenethyl nitrite has been previously reported as a yellow oil of b. p. 72.5–73° at 19 mm. [Holmberg, *Ber.*, **45**, 999 (1912)].