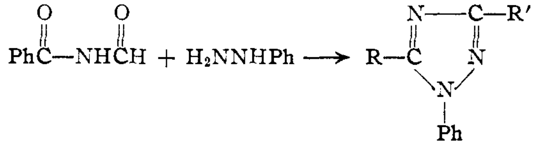
mide (II). In addition, II was insoluble in bicarbonate solution but soluble in dilute sodium hydroxide with concomitant hydrolysis to benzamide and sodium formate, thus exhibiting behavior fairly characteristic of unsymmetrical secondary amides.

Einhorn, Bischkopff and Szelinski[2] have reported the preparation of II but have described it as melting at 120° and forming a molecular compound with benzene, m.p. 84°. These characteristics do not agree with those observed by us, since our compound melted lower and was unchanged by recrystallization from benzene. In order to resolve these differences, we have repeated their synthesis of formalbenzamide; thus N-methylolbenzamide was prepared and oxidized according to their procedure. The material obtained did not correspond to the product which was previously described but melted at 112–113° and was identical in all respects with the formylbenzamide which we had obtained from I.

The previous workers reported that their formylbenzamide condensed with phenylhydrazine to give a disubstituted triazole, m.p. 96–97°, which was assumed to be 1,3-diphenyl-1,2,4-triazole (III). A picrate, m.p. 148°, was also reported for this triazole (III).



III, R = H, R′ = Ph
IV, R = Ph, R′ = H

We have found, however, that II condenses with phenylhydrazine to give a triazole, m.p. 90.5–91°, with a picrate, m.p. 138–139° (crude) and 140–141° (purified). Furthermore, we have established conclusively that this is the isomeric 1,5-diphenyl-1,2,-4-triazole (IV) by comparison with an authentic sample of IV prepared by the method of Young.[3] Both Young and Cleve[4] had prepared this triazole prior to the time of Einhorn, *et al.*, and had found the m.p. 91°, and picrate, m.p. 139° (crude).

Apparently the anomalous results reported by the earlier workers can be explained partly on the basis of incorrect melting point data, since their values were all 6–7° higher than those observed by us or by Cleve and Young. It was largely on the basis of these differences that they assumed their triazole to be III rather than the known compound IV. The formation of an addition compound with benzene is still unexplained.

Experimental

N-Formylbenzamide (II).—A solution of 8 g. of N-formyldibenzamide hydrate, m.p. 78–80°, in 100 ml. of xylene was refluxed for 2 hours, cooled, and shaken with four 50-ml. portions of saturated sodium bicarbonate solution to remove benzoic acid. After washing with 50 ml. of distilled water, the xylene solution was concentrated to about 25 ml., cooled, and the needles of N-formalbenzamide which separated were collected by filtration. Addition of petroleum ether to the filtrate caused the separation of more crystals making a total of 4.2 g. (95%), m.p. 108–111°. Recrystallization from petroleum ether gave pure needles, m.p. 112–113°. A mixed melting point with N-formylbenzamide, m.p. 112–113°, prepared by the method of Einhorn[2] and coworkers showed no depression.

Anal. Calcd. for $C_8H_7O_2N$: C, 64.40; H, 4.73; N, 5.53. Found: C, 64.58; H, 4.63; N, 5.69.

1,5-Diphenyl-1,2,4-triazole (IV).—Phenylhydrazine (0.75 g.) in 30 ml. of 30% acetic acid was treated with 1 g. of pure N-formylbenzamide in accordance with directions.[2] This procedure yielded 1.25 g. (84%) of crude, m.p. 70–80°, triazole which after two recrystallizations from petroleum ether, melted sharply at 90.5–91°. The compound crystallized in plates from petroleum ether or needles from water or dilute alcohol.

Anal. Calcd. for $C_{14}H_{11}N_3$: C, 75.99; H, 5.01; N, 18.99. Found: C, 75.68; H, 4.88; N, 19.02.

An authentic sample of IV, m.p. 90.5–91°, prepared by the method of Young,[3] showed no depression in a mixed melting point with this material.

1,5-Diphenyl-1,2,4-triazole Picrate.—About 50 mg. of triazole was heated for 10 minutes with 100 mg. of picric acid in 10 ml. of ethanol. The tiny yellow needles which separated on cooling were removed by filtration and, when dry, melted 138–139°; reported by Cleve,[4] 139° (crude). Recrystallization from dilute ethanol gave a pure product melting at 140–141°.

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[2] A. Einhorn, E. Bischkopff and B. Szelinski, *Ann.*, **343**, 227 (1905).

[3] G. Young, *J. Chem. Soc.*, **67**, 1069 (1895).

[4] A. Cleve, *Ber.*, **29**, 2679 (1896).

Solubilities of Quaternary Ammonium Salts in Methanol and *n*-Butanol

BY ARTHUR A. VERNON AND ROBERT E. WALCK, JR.

As part of a study of the effect of dielectric constant on solubility, the solubility of some quaternary ammonium salts was determined in two alcohols. Methanol, with a dielectric constant of 32.0, and *n*-butanol, whose dielectric constant is 17.8, were used as solvents.

Experimental

Materials.—Methanol was stored over Hydralo for several days and was then distilled over Hydralo in a fractionating column, discarding the first and last fifths. The refractive index at 14.5° was 1.3312 compared with the "International Critical Tables" value of 1.33118.

n-Butanol was purified by the method of Clarke, Robinson and Smith.[1] It was washed with dilute sulfuric acid, using 250 cc. of acid for each 800 cc. of alcohol and then with a 15% sodium bisulfite solution. The alcohol was then boiled with a 20% aqueous sodium hydroxide solution for 1.5 hours and dried, first with potassium carbonate and second with barium oxide. The *n*-butanol was then distilled in a fractionating column, discarding the first and last fifths. The refractive index at 20° was 1.3991 compared with the "International Critical Tables" value of 1.39909.

Tetramethylammonium bromide and iodide (Eastman Kodak Co.) were recrystallized from 95% ethanol and dried at 80° for 24 hours. The bromide analyzed 51.77% bromine by Volhard titration compared to the theoretical 51.87%. The iodide analyzed 62.91% iodine compared to the theoretical 63.16%.

Tetramethylammonium chloride (Eastman Kodak Co.) was recrystallized from 95% ethanol and dried at 120° in a vacuum oven for 36 hours. The product analyzed 32.35% chlorine as compared to the theoretical 32.42%.

Tetrapropylammonium iodide (Eastman Kodak Co.) was recrystallized from an ethanol–ether mixture and dried at 80° for 24 hours. Analysis showed 40.43% iodine as compared to the theoretical 40.55%.

All other salts were prepared by conventional methods of refluxing the amine with a slight excess of halide and recrystallizing the crude product from a suitable solvent or

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[1] J. Clarke, R. Robinson and J. C. Smith, *J. Chem. Soc.*, 2647 (1927).

solvent pair. Except for the tetrabutylammonium iodide, which was dried at 70°, these salts were dried at 80° for 24 hours.

ANALYSIS OF THE REMAINING SALTS

Salt	Theoretical, % halide	Actual, % halide
$(C_2H_5)_4NBr$	38.06	37.98
$(C_2H_5)_4NI$	49.39	49.19
$(C_3H_7)_4NBr$	30.05	29.93
$(C_4H_9)_4NI$	34.39	34.22

Procedure.—The method of saturation and the removal and analysis of samples was the same as reported by Vernon and Goldberg.[2]

Results.—The solubility results given in Table I are the averages of from three to five determinations.

SOLUBILITY OF QUATERNARY AMMONIUM SALTS IN METHANOL AND *n*-BUTANOL AT 25°

Salt	Moles per kg. solution Methanol	*n*-Butanol
$(CH_3)_4NCl$	3.71 ± 0.025	0.384 ± 0.0005
$(CH_3)_4NBr$	0.269 ± .0012	.0040 ± .0001
$(CH_3)_4NI$	0.0193 ± .00013	
$(C_2H_5)_4NBr$	2.85 ± .0025	.977 ± .0032
$(C_2H_5)_4NI$	0.429 ± .0005	.0076 ± .00016
$(C_3H_7)_4NBr$	2.74 ± .0033	1.72 ± .003
$(C_3H_7)_4NI$	1.83 ± .000	0.195 ± .002
$(C_4H_9)_4NI$	1.95 ± .006	1.04 ± .000

The average deviation of the individual determinations from the mean is no greater than 1% except for the tetramethylammonium bromide and tetraethylammonium iodide where the average deviation is no greater than 3%.

Tetramethylammonium iodide was not run in *n*-butanol because its solubility could not be determined within an experimental error of 5%.

Discussion.—The solubilities of all the salts are greater in methanol, whose dielectric constant is 32.0, than in *n*-butanol with a dielectric constant of 17.8. Within a given quaternary ammonium group the solubilities decrease in the order: chloride, bromide, iodide. The solubility of the iodides in both solvents increases as the quaternary ammonium ion becomes larger. The bromide solubilities in butanol increase with the size of the quaternary ammonium ion but the effect in methanol is not progressive.

(2) G. Goldberg and A. A. Vernon, THIS JOURNAL, **73**, 2845 (1951).

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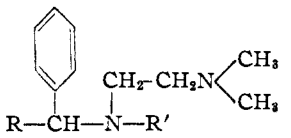
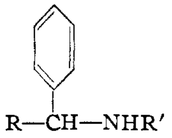
Substituted Tertiary Amines

BY FRANK J. VILLANI, MARY S. KING AND DOMENICK PAPA

According to a recent publication of Hall and Burckhalter,[1] the reaction of benzhydryl-2-aminopyridine (IIA) and dimethylaminoethyl chloride in the presence of sodamide yielded β-(dimethylaminoethyl)-2-aminopyridine, instead of the expected N-(β-dimethylaminoethyl)-N-benzhydrylamino-2-pyridine (IA). This observation has prompted us to report some work which was carried out in our



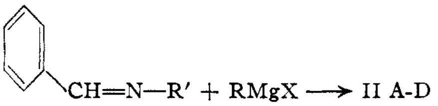
IA, R = phenyl; R' = 2-pyridyl
IB, R = methyl; R' = 2-pyridyl
IC, R = phenyl; R' = phenyl
ID, R = methyl; R' = methyl



IIA, R = phenyl; R' = 2-pyridyl
IIB, R = methyl; R' = 2-pyridyl
IIC, R = phenyl; R' = phenyl
IID, R = methyl; R' = phenyl

laboratories several years ago on the synthesis of IA and several related compounds (IB, IC and ID). This work was undertaken as part of a comprehensive program on the synthesis of potential histamine antagonists.[2] An examination of the structure of IA reveals that this compound contains the substituted tertiary nitrogen and benzhydryl moieties characteristic of the clinically effective antihistamines of the ethylenediamine and ethanolamine types, respectively.

The tertiary amine IA was prepared by the alkylation of the secondary amine IIA by adding two moles of sodamide, suspended in toluene, to a mixture of one mole each of IIA and dimethylaminoethyl chloride hydrochloride in toluene. This alkylation procedure differs from that previously described,[1] the latter procedure employing the addition of a benzene solution of dimethylaminoethyl chloride to the sodium salt of the amine. The requisite secondary amines of formula II (A to D) were prepared in good yields by the addition of a large excess of the appropriate Grignard reagent to the corresponding Schiff bases (III) according to the



III

procedure of Moffett and Hoehn.[3] Maximum yields of the secondary amines were obtained when the molar ratio of the Grignard reagent to the Schiff base was at least four to one.

The compounds of formula I were subjected to the previously described pharmacological tests[4] and showed $^1/_{40}$ to $^1/_{100}$ the antihistaminic potency of γ-phenyl-γ-(2-pyridyl)-N,N-dimethylpropylamine.[5]

Experimental

Benzalaniline was prepared in 92% yield by the method of Bigelow and Eatough,[6] m.p. 51–52°.

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(1) L. A. R. Hall and J. H. Burckhalter, THIS JOURNAL, **73**, 473 (1951).

(2 For the last paper of this series, see D. Papa, N. Sperber and M. Sherlock, *ibid.*, **73**, 1279 (1951).

(3) R. B. Moffet and W. M. Hoehn, *ibid.*, **69**, 1792 (1947).

(4) N. Sperber, D. Papa, E. Schwenk and M. Sherlock, *ibid.*, **71**, 887 (1949).

(5) N. Sperber, D. Papa, E. Schwenk, M. Sherlock and R. Fricano, *ibid.*, **73**, 5752 (1951).

(6) L. A. Bigelow and H. Eatough, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 80.