seems possible, however, that K for a single hydroxyl within the molecule will depend upon the nature of that group.

The correctness of $K = 0.65$ is most readily tested by calculation of n, on that basis. The values appear in the sixth column of the table and are in good agreement with the number of hydroxyl groups listed in the seventh column. The greatest deviation will be noticed for *d*-mannitol; possibly a different equilibrium constant applies for open chain polyhydric alcohols.

The close agreement between exchange number and hydroxyl groups, in the cases reported, makes it possible to develop such exchange experiments in a quantitative procedure for the determination of hydroxyl groups.[8] The results compare favorably with those obtained by means of conventional methods of OH determination. The reagent has become rather inexpensive and actual losses, due to exchange and manipulation, are slight. Substances analyzed can be recovered completely.

It remains to be seen, however, whether or not the method can be generally applied to hydroxy compounds using smaller samples than the ones reported in this paper. This we expect to answer in the near future.

Acknowledgment.—We are indebted to the Chemical Foundation for the loan of 25 g. of 99% D_2O, until our own supply had arrived from abroad.

Summary

1. Quantitative isotopic exchange reactions have been carried out with free hexoses, their methylglycosides and other derivatives in concentrations of 11–30 and 80–96% D_2O.

2. It is shown that consistent results can be obtained only if the equilibrium constant K for the expression $ROH + HOD \rightleftharpoons ROD + HOH$ is considered explicitly.

3. A common K, numerically 0.65, is used for the calculation of the exchange number of twenty-one samples.

4. The exchange number n agrees closely with the number of hydroxyl groups of the sample.

5. The possibility of adopting isotopic exchange reactions for the quantitative determination of hydroxyl groups is discussed.

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(8) *Cf.* A. Farkas, "Orthohydrogen, Parahydrogen and Heavy Hydrogen," Cambridge University Press, 1935, p. 200. This work came to our attention when this manuscript was being prepared.

[CONTRIBUTION FROM THE ORGANIC CHEMICAL LABORATORY OF THE UNIVERSITY OF FLORIDA]

Derivatives of Piperazine. V. Compounds from N-Phenylpiperazine and Derivatives of Monochloroacetic Acid

BY DAVID E. ADELSON AND C. B. POLLARD

In a recent publication[1] the preparation and properties of compounds arising from the reaction between piperazine and derivatives of monochloroacetic acid have been described. These reactions have been extended in the synthesis of similar derivatives of N-phenylpiperazine.

The resulting acetates (Table I) invariably contain small amounts of hydrochloride and free base in spite of the care with which the syntheses are effected. The former is removed as a sticky solid by dissolving the crude ester in ether and filtering; the latter by subsequent distillation *in vacuo*. Peculiarly enough, N-phenylpiperazino-*n'*-butyl acetate is a crystalline solid; the other esters of this series are pale yellow oils. They are all insoluble in water, whereas the piperazino-1,4-bis-(alkyl acetates) are water soluble. The members of both series of esters are soluble in the common organic solvents. The N-phenylpiperazino-N'-alkyl acetates possess higher boiling points, specific gravities and refractive indexes than the corresponding piperazino-1,4-bis-(alkyl acetates). Within each series the specific gravities and refractive indexes vary in a fashion that is normally encountered in homologous series of esters.

In the case of the other compounds studied the N-phenylpiperazine derivative always melts at a lower temperature than the corresponding piperazine compound. In general, the reactivity in the N-phenylpiperazine series of compounds is greater than that in the piperazine series. The purification of the liquid members of the N-phenylpiperazine series is more difficult than in the case of the

(1) Adelson and Pollard, THIS JOURNAL, 57, 1280 (1935).

TABLE I

PHYSICAL CONSTANTS AND ANALYSES OF THE N-PHENYLPIPERAZINO-N'-ALKYL ACETATES

Ester	M. p., °C. corr.	B. p., °C. corr.	Press., mm.	Bath, °C.	d^{20}_{20}	n^{25}	Analyses, % N — Free base Calcd.	Free base Found	Dihydrochloride[c] Calcd.	Dihydrochloride[c] Found
Methyl	Oil	175–177	4–5	245	1.121	1.548			9.12	9.09
Ethyl	Oil	194–195	7–8	235	1.112	1.543	8.09[a]	8.09[a]	8.72	8.56
n-Propyl	Oil	185–186	3–4	250	1.089	1.536			8.36	8.43
n-Butyl	54–54.5	218–220[b]	8–9	270	...	...	10.14	10.02		

[a] Sulfate. [b] Slight decomposition. [c] Oven-dried.

liquid members of the piperazine series. The solubilities of the compounds in the N-phenylpiperazine series are greater and include a wider range of solvents than those in the piperazine series.

Experimental

N - Phenylpiperazino - N' - alkyl Acetates.—(Table I.) These arise from the action of N-phenylpiperazine[2] on the appropriate chloroacetic ester in ethanol solution in the presence of sodium carbonate. The average yield is 65–75%.

N-Phenylpiperazino-N'-ethanamide.—(a) From N-phenylpiperazino-N'-ethyl acetate and concentrated ammonium hydroxide in 85% yield, m. p. 169–170°. Calcd. for $C_{12}H_{17}ON_3$: N, 19.17. Found: N, 19.22. (b) From N-phenylpiperazine, chloroethanamide and sodium carbonate in quantitative yield, m. p. 169–170°. Found: N, 19.12. Toluene is the best solvent for recrystallization.

N-Phenylpiperazino-N'-ethanenitrile.—(a) From N-phenylpiperazine, methanal and hydrogen cyanide in 40% yield, m. p. 65–65.5°. Calcd. for $C_{12}H_{15}N_3$: N, 20.89. Found: N, 20.70. (b) From N-phenylpiperazine, chloroethanenitrile and sodium carbonate in hexane in 70% yield, m. p. 65–65.5°. Found: N, 20.71. Purification is effected by recrystallization from hexane.

Reduction of N-Phenylpiperazino-N'-ethyl Acetate.—This is accomplished by means of sodium and *n*-butyl alcohol. After removal of the latter by steam distillation the strongly alkaline solution is extracted with hot benzene which is cooled and dried over sodium carbonate. Evaporation of the benzene yields N-phenylpiperazino-N'-β-ethanol (yield, 35%), purified by repeated crystallization from hexane, m. p. 82.5–83°. A mixed melting point with an authentic specimen[3] shows no depression. Although the products of these two independent syntheses prove to be identical, Prelog and Blazek[4] report a third synthesis of the alcohol with a melting point of 91°. Upon decolorization and filtration of the hot concentrated alkaline reduction solution, N-phenylpiperazino-N'-sodium acetate is obtained. Calcd. for $C_{12}H_{15}O_2N_2Na$: N, 11.57. Found: N, 11.39. A sample of the latter prepared by refluxing N-phenylpiperazine, sodium chloroacetate and sodium carbonate in aqueous solution and purified by crystallization from water shows similar properties and 11.48% N. The yield is quantitative.

Summary

1. The preparation and properties of compounds arising from the reaction between N-phenylpiperazine and derivatives of monochloroacetic acid have been described.

2. A comparison has been made between these compounds and those of the piperazine series.

(2) Pollard and MacDowell, THIS JOURNAL, **56**, 2199 (1934).

(3) Adelson, MacDowell and Pollard, unpublished work.

(4) Prelog and Blazek, *Collection Czechoslov. Chem. Communications*, **6**, 549 (1934).

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[CONTRIBUTION FROM THE DEPARTMENT OF COLLOID CHEMISTRY, D. J. MCCARTHY FOUNDATION, TEMPLE UNIVERSITY SCHOOL OF MEDICINE]

Physical Chemistry of Lipoids. II. The Protective Power of Cephalin[1]

BY MONA SPIEGEL-ADOLF

The protective power of colloids can be investigated in different ways. It can be tested, for instance, on colloidal gold in the manner used by Schulz and Zsigmondy[2] for the classification of protein fractions or protein derivatives.[3] Furthermore, the protective power of a colloid may be used with reference to other colloids. For the biologist especially the interaction between colloids of the human body is of interest.

Although lipoids are known to behave in aqueous solutions like lyophilic colloids, no figures for their protective power could be found. The results to be reported here were obtained with the intention of supplying this deficiency. Investigations of the interactions between lecithin and proteins have been reported previously;[4]

(1) Read before the Meeting of the American Chemical Society at New York, April 23, 1935.

(2) Fr. N. Schulz and R. Zsigmondy, *Hofmeister's Beitr.*, **3**, 137 (1902).

(3) E. Zunz, *Arch. int. d. Physiol.*, **1**, 427 (1904); M. Spiegel-Adolf, *Biochem. J.*, **28**, 1201 (1934).

(4) M. Spiegel-Adolf, *ibid.*, **26**, 2183 (1932).