TABLE I

PIPERIDINE AND PYRROLIDINE DERIVATIVES

Product from	Empirical formula	M.p., °C.[a]	Analyses, % Calcd.	Found[b]
Piperidine and:				
Glycerol-α,γ-dibromohydrin[c]	$C_{13}H_{28}Br_2N_2O$	273–274	41.17	41.18
Phenacyl bromide	$C_{13}H_{18}BrNO$	230–231	28.12	28.00
p-Phenylphenacyl bromide[d]	$C_{19}H_{22}BrNO$	244–246	22.18	21.96
β-Phenylethyl iodide	$C_{13}H_{20}IN$	197–198	40.01	39.95
N-Ethylpiperidine and:				
Phenacyl bromide[e]	$C_{15}H_{22}BrNO$	191–193	25.59	25.55
p-Fluorophenacyl bromide[f]	$C_{15}H_{21}BrFNO$	183	24.14	24.06
p-Chlorophenacyl bromide	$C_{15}H_{21}BrClNO$	190	23.08	22.88
p-Bromophenacyl bromide	$C_{15}H_{21}Br_2NO$	211	20.43	20.61
p-Iodophenacyl bromide	$C_{15}H_{21}BrINO$	232–233	18.28	18.31
p-Methoxyphenacyl bromide	$C_{16}H_{24}BrNO_2$	166–168	23.36	23.20
2-(α-Bromoaceto)-thiophene[g]	$C_{12}H_{20}BrNSO$	210–211	25.11	24.94
N-Phenylethylpiperidine and:				
Methyl iodide	$C_{14}H_{22}IN$	180–181	38.32	38.81
Ethyl iodide	$C_{15}H_{24}IN$	149–151	36.76	36.53
1-(2-Phenyl-2-hydroxyethyl)-piperidine and:				
Methyl iodide	$C_{14}H_{22}INO$	138–139	36.55	36.39
Phenacyl bromide	$C_{20}H_{25}BrNO_2$	230	19.77	19.61
Pyrrolidine and:				
Phenylethyl bromide[h]	$C_{12}H_{18}BrN$	161	31.24	31.02
Phenylethylene oxide	$C_{12}H_{17}NO$	58.5–59.5		
1-(2-Phenyl-2-hydroxyethyl)-pyrrolidine and:				
Methyl iodide	$C_{13}H_{20}INO$	130.5–131.0	38.09	37.84

[a] The salts melted with decomposition. [b] Average of two Volhard analyses for ionic halogen. [c] Prepared by Mr. Lilburn L. Norton. [d] *Cf.* B. R. Carpenter and E. T. Turner, *J. Chem. Soc.*, 869 (1934). [e] Prepared by Miss Emma Kite and Miss Frances Pierce. [f] Prepared by Mr. Harold Lyons. [g] Prepared by Mr. Clifford Myers. [h] Prepared by Miss Emma Kite and Mr. George Biggerstaff. [i] Calcd.: N, 7.33; found by Kjeldahl analysis, N, 7.18.

white crystals which weighed 4.0 g. (58%) after repeated recrystallization by dissolving in ethanol and adding ether.

1-(**2-Phenyl-2-hydroxyethyl**)-**pyrrolidine**.—A mixture of 24 g. of phenylethylene oxide and 21.3 g. of pyrrolidine refluxed 5 hours and distilled at 107–122° at 0.8–1.5 mm., yielded 24.1 g. (63%) of white crystals, m.p. 58.5–59.5°, after recrystallization from isohexane. A sample was submitted to the Malaria Testing Laboratories of the National Institutes of Health which reported the following results: MED (Q <0.1, MTD (Q =) 2.

Acknowledgments.—The authors wish to express their appreciation to Dr. M. J. Shear and Dr. J. L. Hartwell of the National Cancer Institute for their interest in this project and arranging screening tests against tumors in mice, to be reported elsewhere, to Dr. Erich Mosettig for arranging the anti-malarial tests, to the E. I. du Pont de Nemours and Company for a supply of pyrrolidine, and to Miss Betty Gay Walden and Miss Marguerite Close for Volhard halogen analyses of the products.

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An Observation on a Partial Resolution of Racemic Compounds[1]

BY MARVIN D. ARMSTRONG

Several texts contain excellent summaries of the methods which have been used for the resolution of racemic compounds. The most convenient chemical method in general use at present for the resolution of racemic acids or bases involves their combination with an optically active base or acid to form diastereoisomeric salts.[2] In the case of an acid, *dl*A, appropriate choice of an optically active base, *l*B results in the formation of salts *d*A·*l*B and *l*A·*l*B which may be separated by fractional crystallization from suitable solvents. The differences in the solubility of the salts makes possible the resolution and one or both of the crystalline salts may be obtained in a pure form.

The experiment reported here may be regarded as a variation of this procedure. One-half the theoretical amount of base, *l*B, is added to a solution of *dl*A under conditions where the salts are very soluble and A crystallizes as the solution is allowed to cool. If the salts are completely ionized, the solution should contain equal amounts of $d\text{A}^-$ and $l\text{A}^-$, hence equal amounts of *d*A and *l*A, along with $l\text{B}^+$, and no enrichment of either form of A should occur in the A which crystallizes. Actually, in the case reported, where A is S-carboxymethyl-DL-homocysteine and B is brucine, a considerable enrichment of the D form of the amino acid occurred in the carboxymethylhomocysteine that crystallized. A similar experiment involving DL-phenylalanine and *d*-camphorsulfonic acid (Reychler acid) resulted in a small but definite enrichment of the L-form in the phenylalanine that crystallized.

(1) This research was supported by a grant from the U. S. Public Health Service.

(2) Gilman, "Organic Chemistry," Vol. I, second ed., John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 254–264.

The most logical explanation for these results is the preferential formation of un-ionized salts in solution, with stereochemical specificity leading to the formation of a higher concentration of un-ionized LA·*l*B. This would result in a higher concentration of DA in solution and then in the solid phase that crystallized. These results might have been predicted from the fact that such salts have long been known to be partially undissociated in concentrated solutions.[3] The preferential *retention in solution* of one optically active form of the acid is to be emphasized as the factor leading to the enrichment of the crystallized material in the other form.

It is probable that variations in such experimental conditions as relative proportions of racemic and optically active compounds used, temperature at which crystallization is allowed to occur, solvents used, repeated treatments, etc., would result in more effective resolution. However, although hypothetical cases may be constructed where a use of this method of partial resolution might be of importance, no practical use is apparent at present. For this reason no further investigation of the phenomenon has been undertaken, and it is reported here as a matter of theoretical interest.

Experimental

To a solution of 1.5 g. of S-carboxymethyl-DL-homocysteine in 15 ml. of hot water was added a solution of 2.0 g. of brucine (0.55 mole) in 15 ml. of hot absolute ethanol. The resulting solution was diluted with 15 ml. of hot absolute ethanol and was allowed to cool slowly to room temperature. It was then cooled in the refrigerator for several days, the solid was collected, washed and dried; 0.47 g. was obtained. This product was dissolved in 8 ml. of hot water, treated with Norite and filtered, and the filtrate was diluted with 16 ml. of absolute ethanol and was cooled. The solid was collected on a filter, washed and dried: 0.31 g., m.p. 227–230° dec., $[\alpha]^{25}D$ −5.1° (*c* 1, *N* HCl); (carboxymethyl-L-homocysteine, m.p. 232–234° dec., $[\alpha]^{24}D$ +21.2° (*c* 1, *N* HCl); carboxymethyl-DL-homocysteine, m.p. 224–226 dec.).[4] This product had the sour taste characteristic of carboxymethylhomocysteine and no trace of brucine could be detected.

Anal. Calcd. for $C_6H_{11}O_4NS$: N, 7.25; S, 16.59. Found: N, 7.05; S, 16.24.

The mother liquor from the first filtration was heated, 4.3 ml. of 1 *N* HCl was added, and the solution was cooled to room temperature and allowed to stand overnight. The solid that separated was collected, washed and dried; 0.77 g. was obtained. It was recrystallized from a mixture of 15 ml. of water and 30 ml. of absolute ethanol yielding 0.65 g. of analytically pure material; m.p. 226–229° dec., $[\alpha]^{25}D$ +3.5° (*c* 1, *N* HCl). A test by tasting showed brucine to be absent.

Anal. Calcd. for $C_6H_{11}O_4NS$: N, 7.25; S, 16.59. Found: N, 7.17; S, 16.71.

(3) Ref. 2, p. 295.

(4) Armstrong and Lewis, *J. Org. Chem.*, **16**, 749 (1951).

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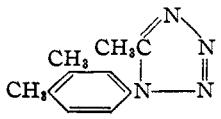
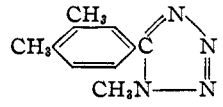
1-(3′,4′-Dimethylphenyl)-5-methyltetrazole

BY FREDERIC R. BENSON, LAWRENCE W. HARTZEL AND WALTER L. SAVELL

A by-product of the Schmidt reaction with 3,4-dimethylacetophenone was reported previously.[1] It was suggested that the substance was probably 1-(3′,4′-dimethylphenyl)-5-methyltetrazole (I) or possibly the isomer, 1-methyl-5-(3′,4′-dimethylphenyl)-tetrazole (II). Identity of the compound as I has now been established.



I



II

The procedure[2] for converting N-substituted aromatic amides through the imide chlorides to 1,5-disubstituted tetrazoles recently has been improved and extended to aliphatic and mixed aliphatic-aromatic amides.[3] This modification was applied to 3,4-dimethylacetanilide producing I of unequivocal constitution. Melting points, both individual and mixed, of this compound and that isolated from the Schmidt reaction were found to be the same. Ultraviolet absorption spectra (Fig. 1) of the substances are virtually identical, with a maximum at a wave length of 231 mμ. Finally the methiodides of the compounds from the two syntheses were prepared. Both methiodides had the same melting point with no depression for their mixture.

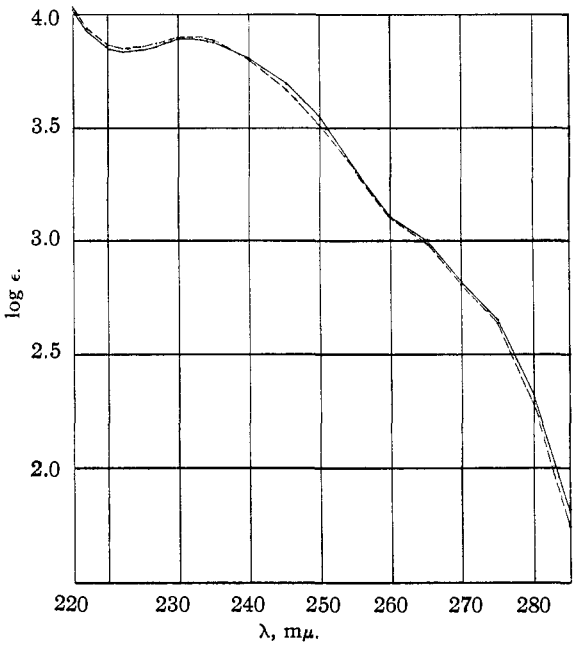


Fig. 1.—Absorption spectra of 1-(3′,4′-dimethylphenyl)-5-methyltetrazole: - - -, prepared from 3,4-dimethylacetanilide, and ——, prepared from 3,4-dimethylacetophenone.

Experimental

The isolation of the tetrazole derived from the Schmidt reaction with 3,4-dimethylacetophenone was carried out as previously described.[1]

1-(3′,4′-Dimethylphenyl)-5-methyltetrazole.—This compound was prepared in 72% yield following the method described by Harvill, *et al.*[3] The white solid after recrystallization first from heptane and then from water melted at 110.5° cor. A mixed melting point with the product isolated from the Schmidt reaction showed no depression. The

(1) F. R. Benson, L. W. Hartzel and W. L. Savell, THIS JOURNAL, **71**, 1111 (1949).

(2) J. v. Braun and W. Rudolph, *Ber.*, **74**, 264 (1941).

(3) E. K. Harvill, R. M. Herbst, E. C. Schreiner and C. W. Roberts, *J. Org. Chem.*, **15**, 662 (1950).