moved and more was recovered from the benzene layer. Recrystallized from benzene as clusters of minute needles; m. p. 177–177.5°; yield 88%. Compound XI is soluble in benzene, acetone, glacial acetic acid. It is recovered unchanged after boiling for several hours with aqueous alcoholic potassium hydroxide.

Anal. Calcd. for $C_{20}H_{17}O_2N$: C, 79.17; H, 5.65; N, 4.62. Found: C, 79.66; H, 5.72; N, 4.80.

Diphenylacetic Acid from XI.—A mixture of XI (1 g.), red phosphorus (1 g.), 1 cc. of hydriodic acid (57%), and 15 cc. of glacial acetic acid was kept at its boiling point for one hour. The mixture was then poured into water, and the solid which separated was crystallized from water; m. p. 145–146°; yield, 0.6 g. (85%). Melting point methods showed this product to be identical with a known sample of diphenylacetic acid.

3,3-Diphenyloxindole (XII) (from XI).—Benzilanilide (1.0 g.) was heated with freshly fused zinc chloride (1.0 g.) at 185–190° for one-half hour. The solid mass resulting after cooling was extracted several times with hot 75% ethyl alcohol. The residue was recrystallized from benzene as stubby needles; m. p. 225–226°; yield, 0.7 g.

For purposes of identification, XII was also prepared from 3,3-dichloro-oxindole and benzene (with aluminum chloride). The products obtained by the two methods were identical.

Anal. Calcd. for $C_{20}H_{15}ON$: C, 84.18; H, 5.30; N, 4.91. Found: C, 83.82; H, 5.54; N, 4.94.

Summary

1. N-Methyl- and N-ethyl-benzoylformanilide react with phenylmagnesium bromide to yield the respective N-alkylbenzilanilides. The latter, upon treatment with acid or dehydrating agents, form the corresponding 1-alkyl-3,3-diphenyloxindoles.

2. Methyl- and ethylaniline react with acetylbenzilyl chloride to produce the respective 1-alkyl-3,3-diphenyloxindoles.

3. N-Methylphenylglyoxylic acid *p*-phenetide and phenylmagnesium bromide yield a crude product which upon treatment with acids forms 3,3-diphenyl-5-ethoxy-1-methyloxindole.

4. 3,3-Diphenyl-1-methyl-β-naphthoxindole is formed through the action of N-methyl-β-naphthylamine with acetylbenzilyl chloride.

5. Benzilanilide upon treatment with zinc chloride yields 3,3-diphenyloxindole.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE CITY COLLEGE, THE COLLEGE OF THE CITY OF NEW YORK]

Alkanolamines. XI. Monoalkylamino Alcohols and their Esters

BY CHESTER B. KREMER AND E. WALDMAN

This is a continuation of the work dealing with esters of substituted amino alcohols.[1] Goldberg and his co-workers[2,3] have synthesized a number of these esters of monoalkylamino alcohols. In this present work we have prepared a series of monoalkylamino alcohols in which the carbon atom alpha to the amino group is substituted with two alkyl groups. The monoalkyl substituent on the amine nitrogen varied from ethyl to amyl in the normal series and from propyl to amyl in the iso series. The alcohols were low melting, white solids. While no regular relationship existed among the melting points of the solids, such a relationship was found to exist for the boiling points of the compounds. This is in keeping with the general rule that melting points of organic compounds do not show the same regular changes in an homologous series as do the boiling points. Further, the boiling point of an iso derivative approximated that of the next lower member of the normal series.

The monoalkyl derivatives were formed by refluxing 2-amino-2-methyl-propanol-1 with the appropriate alkyl bromide, employing ethanol as a solvent. The normal alkyl halides reacted readily. The iso alkyl halides reacted more slowly, and in the order: isoamyl>isobutyl>isopropyl. After ten to fifteen hours of refluxing the isoamyl bromide had reacted to the extent of 70% or better; the isobutyl bromide less than 40% and the isopropyl bromide approximately 20%. It was only after prolonged refluxing that the latter reacted to any appreciable extent. It is quite apparent that the iso grouping inhibits this reaction in proportion to its distance from the halide atom.

The *p*-nitrobenzoates of the amino alcohols were obtained by condensing them with *p*-nitrobenzoyl chloride, in pyridine. Temperature control is important, optimum conditions being between 30 and 40°. Formation of the esters in aqueous alkaline medium gave poor yields and

(1) C. B. Kremer, THIS JOURNAL, 61, 1321 (1939).
(2) S. D. Goldberg and W. F. Whitmore, *ibid.*, 59, 2280 (1937).
(3) S. D. Goldberg, W. F. Ringk and P. E. Spoerri, *ibid.*, 61, 3562 (1939).

TABLE I

R =	Monoalkylamino alcohols $(CH_3C(NHR)(CH_3)CH_2OH)$ M. p., °C.	B. p., °C.	Mol. formula	Nitrogen, % Calcd.	Found	*p*-Nitrobenzoates of monoalkylamino alcohols M. p., °C.	Mol. formula	Nitrogen, % Calcd.	Found
Ethyl	75.5–76.5	162–163	$C_6H_{15}ON$	11.95	11.91	206.5–207.0	$C_{13}H_{18}O_4N_2$	10.52	[a]
n-Propyl	59.5–60.5	183–185	$C_7H_{17}ON$	10.67	10.55	185.0–185.5	$C_{14}H_{20}O_4N_2$	9.99	9.75
i-Propyl	43.0–45.0	165–166	$C_7H_{17}ON$	10.67	10.64	140.0–141.0	$C_{14}H_{20}O_4N_2$	9.99	[a]
n-Butyl	69.5–70.0	195–196	$C_8H_{19}ON$	9.64	9.48	163.5–164.0	$C_{15}H_{22}O_4N_2$	9.52	9.22
i-Butyl	51.0–52.5	185–186	$C_8H_{19}ON$	9.64	9.70	165.0–166.0	$C_{15}H_{22}O_4N_2$	9.52	9.27
n-Amyl	60.0–60.5	216–217	$C_9H_{20}ON$	8.80	8.78	151.0–151.5	$C_{16}H_{24}O_4N_2$	9.09	9.03
i-Amyl	76.5–77.0	205–207	$C_9H_{20}ON$	8.80	8.76	168.0–168.5	$C_{16}H_{24}O_4N_2$	9.09	9.10

[a] Discordant results probably due to persistent impurities.

non-reproducible results. The nitro esters were very pale yellow solids.

The *p*-aminobenzoates can be obtained by reducing a paste of the nitro ester in concentrated hydrochloric acid with powdered tin. The temperature must not exceed 40–45°. The *p*-aminobenzoic acid ester hydrochlorides are then prepared by treating an ether solution of the free base with dry gaseous hydrogen chloride. The hydrochlorides are white, extremely hygroscopic solids.

The physiological effect of various derivatives of the anesthetic bases will be reported elsewhere.

Experimental

The 2-amino-2-methyl-propanol-1 was purchased from the Commercial Solvents Corporation, and the alkyl bromides from the Eastman Kodak Company. All of the materials were purified by redistilling.

Preparation of Monoalkylamino Alcohols.—Molar quantities of the alkyl bromide and 2-amino-2-methyl-propanol-1 were refluxed in ethanol solution from fifteen to forty-eight hours. The ethanol was then distilled off and the residue treated with 30% sodium hydroxide solution. The warm solution separated into two layers. The aqueous layer was drawn off and the oily layer transferred to a beaker, where it rapidly solidified. The monoalkylamino alcohols can be purified by recrystallization from petroleum ether. Melting points and analyses of the alcohols are given in Table I.

Preparation of the *p*-Nitrobenzoic Acid Esters.—To 14.5 g. (0.1 mole) of the monobutylamino alcohol dissolved in 50 ml. of freshly distilled pyridine, was added 18.6 g. (0.1 mole) of *p*-nitrobenzoyl chloride. The addition was made in small portions and with constant stirring. Care is necessary in maintaining the temperature between 30 and 40°. After addition of the *p*-nitrobenzoyl chloride was completed, the mixture was allowed to stand for twenty-four hours and then diluted with 400 ml. of water. A voluminous curdy yellow precipitate formed and was filtered off, washed with 50 ml. of 2% sodium carbonate solution and allowed to dry. The nitro ester thus obtained was purified by recrystallization from ethanol. Melting points and analyses of the nitro esters are given in Table I.

Summary

1. A series of new monoalkylamino alcohols is reported.

2. The *p*-nitrobenzoates of these amino alcohols have been prepared.

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The Effect of Urea on the Electrophoretic Patterns of Serum Proteins

BY DAN H. MOORE

The effect of urea on the electrophoretic patterns of serum proteins has been examined in the electrophoresis apparatus of Tiselius.[1] One of the important characteristics of the Tiselius method is its ability to reduce convection in the cell (U-tube) caused by heat generated by passage of current. This is done by submerging the apparatus in a bath which should be maintained at the temperature where the change of density with temperature is least, *i. e.*, about 4° for dilute aqueous solutions. The patterns depending upon refraction gradients at the protein boundaries were obtained by means of the scanning method of Longsworth.[2]

Normal human serum was diluted 1:4 with a 0.02 *M* phosphate buffer containing physiological saline and 2.8 *M* urea, and dialyzed against the same buffer containing the urea and saline. The electrophoretic pattern is illustrated in Fig. 1a. The albumin is *apparently* broken up into three

(1) A. Tiselius, *Trans. Faraday Soc.*, **33**, 524 (1937).

(2) L. G. Longsworth, THIS JOURNAL, **61**, 529 (1939).