reactions. Thus, the former may be more sensitive to bulk effect of substituents. On the other hand, the explanation may be as simple as stating that the canonical forms with positive charges in the ring are more important in the transition complex hybrid of electrophilic reactions than the corresponding negative charges in nucleophilic reactions. If either or both of these explanations are true, they focus attention on the importance of solvation forces in attempts to study influences of groups remote from the reaction center.[10]

TABLE I

DISSOCIATION CONSTANTS OF SUBSTITUTED BENZOIC ACIDS[a]

Benzoic Acid	$K' \times 10^5$ (Uncorrected)	$K \times 10^5$ (Corrected) ($K' \times 1.20/1.86$)
Unsubstituted	1.86	1.20
3,5-$(CH_3)_2$	1.15	0.741
3,5-$(C_2H_5)_2$	0.851	0.588
3,4,5-$(CH_3)_3$	0.759	0.490
3,4,5-$(C_2H_5)_3$	0.589	0.380
4-Nitro	49.0	31.6

[a] In 57.6% aqueous ethanol at 25°.

EXPERIMENTAL

Materials. Baker and Adamson benzoic acid was twice recrystallized from water. The alkyl substituted benzoic acids were prepared by hypobromite oxidation of the corresponding ketones,[10] the melting points of the purified acids being as follows: 3,5-diethyl, 129–129.5°; 3,5-dimethyl, 171.5–172.5°; 3,4,5-trimethyl, 220.5–221.5°; 3,4,5-triethyl, 142–143°; 4-nitro, 242°. The water and ethanol each were refluxed and distilled, and the distillates stored under a nitrogen atmosphere.

The standard sodium hydroxide was prepared by dilution of 3.6 ml. of saturated sodium hydroxide solution with 330 ml. of carbonate-free water and 570 ml. of 95% ethanol. The solution was approximately 0.1N in 57.6% (by weight) of alcohol. It was tested daily for carbonate by adding 5 drops of 0.5N barium chloride solution to a 10-ml. aliquot.

Apparatus. Titrations were followed with a Leeds and Northrup pH meter, Model 7663-Al, using glass and calomel electrodes. The saturated potassium chloride bridge was made from 57.6% aqueous alcohol, and the glass electrode stored in aqueous alcohol of the same concentration. The pH meter was calibrated by means of the known pK of benzoic acid in 57.6% aqueous ethanol,[6] and the correction applied to all the other acids as shown in the procedure.

The titration system consisted of storage delivery bottles for water, ethanol, and sodium hydroxide solution, titration jar, and a nitrogen inlet, all in a closed system under about 2.5 lb./sq. in. pressure. The solution was stirred with a magnetic stirrer at a temperature maintained at 25° ± 0.5°.

Procedure. The amount of acid added was always sufficient to make the concentration of the acid one tenth that of the strength of the base.[16] The pH meter was checked by buffers at pH 7 and 4, and the base added to the 10 ml. buret under nitrogen pressure. After the acid was dissolved in 22 ml. of ethanol, 13 ml. of water was added to make the solution 57.6% aqueous ethanol. The jar was sealed with a rubber stopper containing electrodes, burette tip, and pressure line while the system was swept with nitrogen. The system was then maintained under about 2.5 lbs. of nitrogen pressure.

(16) M. M. Davis and H. B. Hetzer, *J. Phys. Chem.*, 61, 123 (1957).

The pH of solution was recorded at 0.1-ml. intervals in the 40–60% neutralization range. Endpoints were also obtained to check the neutral equivalent of each acid. At two points on either side of the half-neutralization point and at the half-neutralization point itself, the five points averaging 0.1 ml. apart from each other, the pK was calculated from the formula

$$pK = pH - \log \frac{C_B + a_H^+}{C_A - a_H^+} + \frac{166\sqrt{\mu}}{1 + 1.65}$$

where C_B is concentration of base added, C_A is concentration of unneutralized acid, and a_H^+ is the hydrogen ion activity. The formula was used in lieu of extrapolation of the acid dissociation constant to zero concentration.[13] The five values of pK were averaged, and the average value shown in Table I as K′ (uncorrected). As the value of K for benzoic acid in 57.6% aqueous alcohol is 1.2×10^{-5} as reported,[6] the correction factor, 1.20/1.86, was applied to all the other uncorrected dissociation constants. These values are given in the column for K (corrected). As a further check, the pK values were determined about a month after the initial values were obtained using new solutions and new electrodes. No difference in K was noted for any acid except *p*-nitrobenzoic acid. The new value was used in the table. Standard deviations and correlation coefficients were calculated by regular procedures.[17]

(17) A. G. Worthing and J. Geffner, *Treatment of Experimental Data*, John Wiley and Sons, New York, 1948, p. 273.

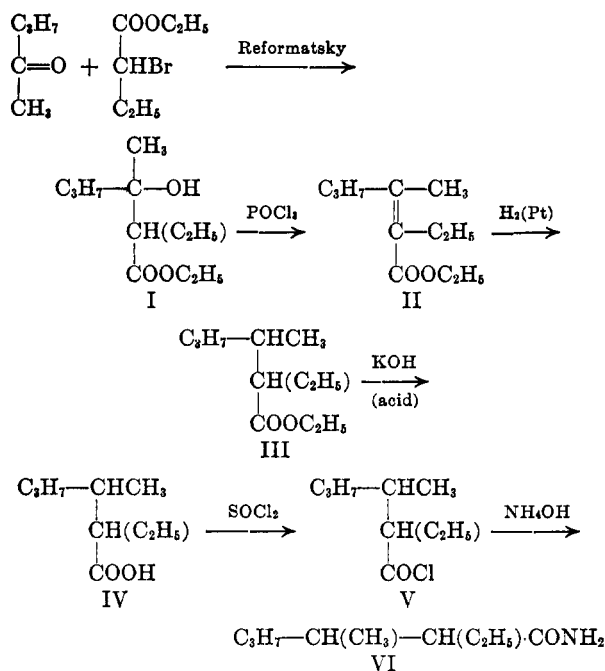
2-Ethyl-3-methylhexanamide

RICHARD E. STRUBE

Two different melting points are reported in the literature for 2-ethyl-3-methylhexanamide. Volwiler and Tabern[1] found 97–98° while Maynert and Washburn[2] gave a melting point of 91–93°. This compound was also synthesized in these laboratories by the sequence of reactions formulated below. Although the "purified" end-product (VI) gave the correct analytical values it melted at 95–109°. Since 2-ethyl-3-methylhexanamide has two asymmetric carbon atoms, it is likely that compound VI consisted of a mixture of racemates. The separation of the mixture into two racemic pairs was accomplished by chromatography on an aluminum oxide column. Two products were isolated, one melting at 89–90.5° and another at 123–124°. These melting points are uncorrected, and therefore, one may assume that the melting point of the lower melting product is in agreement with that reported by Maynert and Washburn.[2] The analytical

(1) E. H. Volwiler and D. L. Tabern, *J. Am. Chem. Soc.*, 58, 1353 (1936).
(2) E. W. Maynert and E. Washburn, *J. Org. Chem.*, 15, 261 (1950).

$$
\begin{array}{c}
\underset{\substack{| \\ C_3H_7 \\ | \\ C=O \\ | \\ CH_3}}{}
\quad + \quad
\underset{\substack{COOC_2H_5 \\ | \\ CHBr \\ | \\ C_2H_5}}{}
\quad \xrightarrow{\text{Reformatsky}}
\end{array}
$$

$$
\underset{I}{\underset{\substack{COOC_2H_5}}{\overset{\substack{CH_3 \\ |}}{C_3H_7-\overset{|}{C}-OH} \atop \underset{|}{CH(C_2H_5)}}}
\quad \xrightarrow{POCl_3} \quad
\underset{II}{\underset{\substack{COOC_2H_5}}{C_3H_7-\overset{\substack{CH_3 \\ \|}}{C}-CH_3 \atop \underset{|}{C}-C_2H_5}}
\quad \xrightarrow{H_2(Pt)}
$$

$$
\underset{III}{\underset{\substack{COOC_2H_5}}{C_3H_7-CHCH_3 \atop \underset{|}{CH(C_2H_5)}}}
\quad \xrightarrow[\text{(acid)}]{KOH}
$$

$$
\underset{IV}{\underset{\substack{COOH}}{C_3H_7-CHCH_3 \atop \underset{|}{CH(C_2H_5)}}}
\quad \xrightarrow{SOCl_2} \quad
\underset{V}{\underset{\substack{COCl}}{C_3H_7-CHCH_3 \atop \underset{|}{CH(C_2H_5)}}}
\quad \xrightarrow{NH_4OH}
$$

$$
\underset{VI}{C_3H_7-CH(CH_3)-CH(C_2H_5)\cdot CONH_2}
$$

values of the product melting at 123–124° are in agreement with those calculated for 2-ethyl-3-methylhexanamide and, as expected, the infrared absorption curves of the two racemates are almost identical. The significant differences are in the intensities of the bands at 1160 and 1117 cm.$^{-1}$ The possibility of the existence of different crystal forms was excluded by the observation that crystallization of the molten compounds caused no change in melting points.

EXPERIMENTAL

Ethyl-2-ethyl-3-hydroxy-3-methylhexanoate (I). To 75.0 g. (1.15 g.-atoms) of zinc dust was added 20–30 ml. of a solution of 115.0 g. (1.34 moles) of n-propyl methyl ketone, 225.0 g. (1.15 moles) of ethyl-α-bromobutyrate in 150 ml. of dry benzene. The mixture was stirred and heated until the reaction started. The rest of the solution was introduced at such a rate that gentle refluxing occurred. After the solution was added, refluxing was continued for 45 min. The cooled reaction mixture was poured into 600 ml. of ice-cold 10% sulfuric acid with vigorous stirring. The acid layer was separated and the benzene solution washed twice with 100-ml. portions of ice-cold 15% sulfuric acid. The benzene solution was washed once with 25 ml. of cold 10% aqueous sodium carbonate, then with 25 ml. of cold 5% sulfuric acid, and finally with two 25-ml. portions of water. The benzene solution was dried with anhydrous magnesium sulfate, filtered and distilled, yield 184.5 g. (83%); b.p. 85–95° at 8 mm. This crude product was used in the next reaction.

Ethyl 2-ethyl-3-methyl-2-hexenoate (II). Compound I (184.5 g.) was dissolved in 600 ml. of benzene and 75 g. of phosphorus oxychloride was added. The mixture was heated on the steam bath for 3 hr. After cooling to room temperature the solution was extracted successively with an aqueous solution of sodium bicarbonate and water until neutral to litmus paper. After drying over anhydrous sodium sulfate, there was obtained 108 g. (64%) of compound II, b.p. 97–102° at 22 mm.

Ethyl 2-ethyl-3-methylhexanoate (III). Compound II (88.4 g.) was catalytically (platinum oxide) hydrogenated at an initial pressure of 50 lb./sq. inch. There was obtained

70.8 g. (80%) of compound III; b.p. 87–91° at 13–14 mm. [lit.[3] b.p. 197–198°].

2-Ethyl-3-methylhexanoic acid (IV). Compound III (70.8 g.) was hydrolyzed by refluxing under vigorous stirring with a solution of 55.0 g. of potassium hydroxide in 200 ml. of water for a period of 80 hr. After this time the ester layer had disappeared. The solution was acidified with hydrochloric acid (1:1) and extracted with ether. After drying over anhydrous magnesium sulfate there was obtained 51.0 g. (60%) of compound IV; b.p. 127–132° at 14 mm. (lit.[3] b.p. 230–232°).

2-Ethyl-3-methylhexanoyl chloride (V). Compound IV (51.0 g.) was added dropwise to 51 g. of thionyl chloride at 10–15°. After 1 hr. at room temperature the flask was heated for another hour at 50°. Then the excess of thionyl chloride was removed by distillation and the acid chloride distilled under reduced pressure; yield 53.0 g. (93%); b.p. 80–82° at 14 mm. (lit.[4] b.p. 87–89° at 25 mm.).

2-Ethyl-3-methylhexanamide (VI). Compound V (53.0 g.) was added under vigorous stirring to 300 ml. of cold concd. aqueous ammonia at such a rate that the temperature did not rise above 15°. After the addition stirring was continued for 1 hr. The precipitate formed was removed by filtration and dried *in vacuo;* yield 40.4 g. (87%). The product was recrystallized twice from dilute ethanol (100 ml. of ethanol and 150 ml. of water) and once from methylcyclohexane; yield 27.0 g. (60%); m.p. 95–109°.

Anal. Calcd. for $C_9H_{19}NO$: C, 68.74; H, 12.18; N, 8.91. Found: C, 68.98; H, 12.14; N, 8.64.

The infrared absorption cruves supported the structure λ_{max}^{Nujol} in cm.$^{-1}$: 3180, 3350 (NH); 1655 (amide CO); 1635 sh (amide NH); other max. 1302, 1255, 1160, 1145, 1117 (sh).

Chromatography. Two grams of compound VI was chromatographed on 200 g. of aluminum oxide (Merck, acid washed) using a column of approximately 1 in. diameter. The elution was done as shown below. Most fractions had a wide melting range. Fractions 13–24 melted completely

Fractions	Solvents	Wt., mg.	Size of Fractions, ml.
1–12	Methylene chloride–Skelly-solve B (1:1)	193	100
13–24	Methylene chloride–Skelly-solve B (3:1)	321	100
25–36	Methylene chloride	123	100
37–41	Methylene chloride and 1% acetone	134	250
42–46	Methylene chloride and 5% acetone	268	250
47–51	Methylene chloride and 10% acetone	441	250
52–56	Methylene chloride and 20% acetone	219	250

below 100°; fraction 15 had a sharp melting point of 89–90.5°. Fractions 40–49 started to melt above 115°. These fractions were combined and recrystallized from dilute ethanol giving a product melting sharply at 123–124°.

Anal. Calcd. for $C_9H_{19}NO$: C, 68.74; H, 12.18; N, 8.91. Found: C, 68.42; H, 11.77; N, 9.09.

The infrared absorption curves of the two racemates were almost identical, the significant differences were the intensities of the bands at 1160 and 1117 cm.$^{-1}$

(3) A. C. Cope and S. M. McElvain, *J. Am. Chem. Soc.,* 54, 4323 (1932).

(4) G. S. Skinner and J. F. Perkins, *J. Am. Chem. Soc.,* 72, 5569 (1950).

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Synthesis of Some *N*-Benzyl-*N*-alkyl-*N*-*n*-octylamines

P. J. APICE[1]

A recent research program of this laboratory involved the preparation of some new tertiary amines from the intermediate *N*-benzyl-*N*-*n*-octylamine. In general, the intermediate *N*-benzyl-*N*-*n*-octylamine can be prepared *via* reduction of the corresponding Schiff base,[2] or by the reaction of

The scope of the project involved only the *n*-alkyl halides from one to seven carbon atoms. The *N*,*N*-di-*n*-octyl compound was isolated from the intermediate secondary amine when the latter was produced.

The elemental analyses and physical properties are given in Tables I and II. It is worthy to note confirmation of the atomic factor value for the methylene group (D line) for the series synthesized. Calculations from the observed molecular refractivities over the range of one to eight carbon atoms give an M_D value of 4.617, while the generally accepted value is 4.618.[4]

Several attempts to prepare the usual derivatives of the tertiary amines of this series have thus far been unsuccessful. This difficulty is probably due mainly to steric effects.

EXPERIMENTAL[5]

N-Benzyl-N-n-octylamine. This base was obtained as the main product by the following process: Benzylamine, 286 g. (2.67 moles), was mixed with *n*-octyl bromide, 257 g. (1.33

TABLE I

ELEMENTAL ANALYSES

Alkyl	Formula	Yield, %	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
H—	$C_{15}H_{25}N$	68	82.12	83.23	11.49	11.59	6.39	6.13
CH₃—	$C_{16}H_{27}N$	39	82.34	82.99	11.66	11.63	6.00	5.92
C₂H₅—	$C_{17}H_{29}N$	73	82.53	83.01	11.81	11.78	5.66	5.78
n-C₃H₇—	$C_{18}H_{31}N$	61	82.69	83.00	11.95	11.97	5.36	5.19
n-C₄H₉—	$C_{19}H_{33}N$	64	82.84	83.23	12.07	12.18	5.09	5.12
n-C₅H₁₁—	$C_{20}H_{35}N$	59	82.97	83.47	12.19	12.25	4.84	4.80
n-C₆H₁₃—	$C_{21}H_{37}N$	64	83.10	82.81	12.29	12.42	4.61	4.50
n-C₇H₁₅—	$C_{22}H_{39}N$	66	83.20	83.31	12.39	12.45	4.41	4.21
n-C₈H₁₇—	$C_{23}H_{41}N$	—	83.31	83.53	12.46	12.46	4.23	4.11

TABLE II

PHYSICAL PROPERTIES

Alkyl	B.P.,/Mm.	Sp. Gr. $\frac{20}{20}$	n_D^{20}	Molecular Refractivity Calcd.	Molecular Refractivity Obs.
H—	159–161.5/10	0.8914	1.4945	71.54	71.70
CH₃—	150–151.5/9	0.8825	1.4909	76.50	76.57
C₂H₅—	155.5–157/9	0.8796	1.4886	81.12	81.16
n-C₃H₇—	167–169/11	0.8758	1.4857	85.73	85.66
n-C₄H₉—	166–169/8	0.8722	1.4850	90.28	90.43
n-C₅H₁₁—	178.5–180.5/9	0.8702	1.4835	94.97	95.09
n-C₆H₁₃—	185–187.5/8	0.8688	1.4823	99.59	99.65
n-C₇H₁₅—	195–197/8	0.8682	1.4818	104.21	104.23
n-C₈H₁₇—	211–212/9	0.8679	1.4815	108.82	108.89

benzylamine with an *n*-oxtyl halide, or vice versa. In this work the second method was employed. This method is similar to that used by King and Work[3] in preparing various secondary and tertiary benzylamines.

moles), in a large beaker and allowed to stand at room temperature. The reaction is mildy exothermic, and after 45 min. benzylamine hydrobromide was deposited as a white slush. The mixture was heated on a boiling water bath for 1 hr., cooled, diluted with dry ether, and the benzylamine

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(1) Present address: Plastics and Coal Chemicals Division, Allied Chemical Corporation, Technical Department, Edgewater, N. J.

(2) R. E. Lutz, *et al.*, *J. Org. Chem.*, **12**, 760 (1947).

(3) H. King and T. S. Work, *J. Chem. Soc.*, 401 (1942).

(4) H. Gilman, *Organic Chemistry, An Advanced Treatise*, Vol. *II*, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 1751.

(5) All melting and boiling points are corrected.