was found to have a purity of 98.6 ± 0.2 mole per cent.[15]; its freezing point is 19.15 ± 0.06° and the f.p. calculated for zero impurity is 20.2 ± 0.3°.[16] Descamps[6] reported m.p. 20.1°.

Storage of the alcohol of 98.6 ± 0.2 mole per cent. purity in quartz without a drying agent (in a desiccator kept in the dark) for two months did not result in any change in the properties of this alcohol. In contrast, when a solution consisting of 4 ml. of the 98.6 ± 0.2 mole per cent. alcohol and 4 drops of distilled water ($n^{20}\mathrm{D}$ 1.5169) was placed in a brand new glass-stoppered Pyrex flask and the flask was stored in a desiccator kept on the desk-top out of direct sunlight, the solution soon underwent change. Thus after 15 days the $n^{20}\mathrm{D}$ had risen to 1.5193, the solution had become pale yellow, it had taken on a strong odor of acetophenone, and on treatment with 2,4-dinitrophenylhydrazine[13] it gave the 2,4-dinitrophenylhydrazone of acetophenone; m.p. and mixed m.p. 248–249° (uncor.). After 19 weeks $n^{20}\mathrm{D}$ had gone up to 1.5258 and the yellow color was much more pronounced.

Acknowledgment.—The authors are grateful to the Research Corporation for generous financial assistance.

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[15] The method of F. D. Rossini, *et al.*, as modified by K. L. Nelson of this Department was employed. This will be published shortly. We are indebted to Mr. Nelson for his assistance in the determination and interpretation of the cooling curve data.

[16] The relevant data are to be found in the doctoral dissertation of S. A. Herbert, Jr., Purdue University, 1952.

DEPARTMENT OF CHEMISTRY
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Ultrasonic Velocity in a Series of Alkyl Acetates

BY R. T. LAGEMANN,[1] E. G. MCLEROY AND O. MILNER

Measurements of ultrasonic velocity are being made on various homologous series of organic compounds. These measurements generally show an increase of ultrasonic velocity with increase in molecular weight from the first member of the series onward. Certain series, however, show a definite minimum in the velocity, as has been shown recently for some ketones,[2] and some series would seem to show a decrease of velocity with increase in molecular weight. It has been thought in the past that the alkyl acetates belong to the last-named class. In a review article, Parthasarathy[3] says "the esters show a diminution in velocity with increasing length of the alcohol radical," and in support of his contention he presents a table taken from an earlier paper[4] giving data on five alkyl acetates.

Upon repeating the measurements on these five compounds and extending the series further at three temperatures, it is found that actually there is only a decrease as one goes from the first to the second member of the series, and that for the ethyl through heptyl members of the *n*-alkyl acetates there is a steady increase in the velocity. This may be seen in Table I. It may also be noted, in agreement with what has been found elsewhere[5] for certain other compounds, that the iso-isomer has a lower velocity than the corresponding normal one. Indeed, it was the inclusion by Parthasarathy of his results on the *i*-amyl acetate with those for four normal ones, which no doubt was in part responsible for the enunciation of the erroneous rule. For all the compounds investigated the temperature coefficient of velocity is nearly the same, as is commonly found.

TABLE I

ULTRASONIC VELOCITY IN A SERIES OF ALKYL ACETATES

Acetate	Velocity of sound, m./sec. 10°	20°	30°	Density, g./cc. at 30°	Adiabatic compressibility, dyne^{-1} cm.^{2} at 30° ($\times 10^{12}$)
Methyl	1228	1181	1136	0.9207	84.16
Ethyl	1209	1164	1119	.8886	89.87
n-Propyl	1232	1189	1146	.8777	86.75
n-Butyl	1256	1214	1170	.8707	83.90
n-Amyl	1280	1238	1197	.8685	80.36
n-Hexyl	1300	1258	1220	.8642	77.74
n-Heptyl	1319	1280	1241	.8618	75.34
Isopropyl	1178	1144	1100	.8616	95.92
Isobutyl	1219	1175	1134	.8600	90.42
Isoamyl	1258	1218	1179	.8645	83.21

Experimental

The compounds were Eastman Kodak Co. chemicals freshly fractionated in a Todd column of 30–50 theoretical plates before the ultrasonic velocity was measured. The velocity measurements were made on a variable-path ultrasonic interferometer[6] operated at 500 kc. per second and with the liquid under study kept at the stated temperature to within ± 0.03° with a constant temperature water-bath. The densities were measured with a 3-ml. double-arm pycnometer of the kind described by Lipkin and his co-workers.[7]

The three iso-alkyl acetates were obtained from Dr. W. Joe Frierson, to whom we are grateful. The work was also assisted by a Grant-in-Aid from the Research Corporation.

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[1] Department of Physics, Vanderbilt University, Nashville, Tennessee.

[2] R. T. Lagemann, R. Gwin, C. T. Lester, J. R. Proffit and E. C. Suratt, THIS JOURNAL, **73**, 3213 (1951).

[3] S. Parthasarathy, *Current Sci.*, **6**, 322 (1938).

[4] S. Parthasarathy, *Proc. Ind. Acad. Sci.*, **3A**, 482 (1936).

[5] A. Weissler, THIS JOURNAL, **70**, 1634 (1948); S. Parthasarathy, *Proc. Ind. Acad. Sci.*, **4A**, 59 (1936); W. Schaaffs, *Z. physik. Chem.*, **196**, 413 (1951).

[6] D. R. McMillan, Jr., and R. T. Lagemann, *J. Acoust. Soc. Am.*, **19**, 956 (1947).

[7] M. R. Lipkin, J. A. Davison, W. T. Harvey and S. S. Kurtz, Jr., *Ind. Eng. Chem., Anal. Ed.*, **16**, 55 (1944).

DEPARTMENT OF PHYSICS
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N-Monosubstituted 2-Aminopyridines, 2-Aminopyrimidines and 2-Aminolepidines

BY IRVING ALLAN KAYE AND IRVING C. KOGON

In this investigation a number of N-monosubstituted 2-aminopyridines, 2-aminopyrimidines and 2-aminolepidines were prepared by two general methods as intermediates for the subsequent synthesis of compounds having possible chemotherapeutic application. Most of the pyridyl- and lepidylamines were obtained by heating a mixture of either 2-bromopyridine or 2-chlorolepidine and two or more equivalents of a primary amine at 170–180° for about 18 hours.[1] Yields were increased when a considerable excess of primary amine was employed. The remaining products were synthesized by alkylation of a heterocyclic amine with an alkyl halide in the presence of lithium amide.[1] Some reactions were conducted in the conventional two-step manner, *i.e.*, a lithium derivative of a heterocyclic amine was formed from

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[1] I. A. Kaye, THIS JOURNAL, **71**, 2322 (1949).

TABLE I

SECONDARY AMINES, R–R′–NH

R[a]	R′	Procedure	B.p. °C.	B.p. Mm.	Yield, %	M.p., °C.	Formula	Analyses, % Carbon Calcd.	Analyses, % Carbon Found	Analyses, % Hydrogen Calcd.	Analyses, % Hydrogen Found
C_5H_4N-	$2\text{-}(5\text{-}Cl\text{-}C_4H_2S)CH_2-$[a]	B-1			32[b]	84–86.5[b,c]					
C_5H_4N-	$2\text{-}(5\text{-}Br\text{-}C_4H_2S)CH_2-$[a]	B	136–140	0.07	37[d]	80–81[b,c]					
C_5H_4N-	$-CH_2-CH_2NMe_2$	B	123–132	10	50[e,f]						
C_5H_4N-	$-CH_2-CH_2NC_4H_8O$[g]	A-8-21[h]	176–181.5	19	63[d,f]	186–187[g,m]	$C_{11}H_{17}N_3O\cdot 2C_6H_3N_3O_7$[g]	19.03[i]	19.09[i]		
		C	105–109	0.04	34[d]						
C_5H_4N-	$-(CH_2)_3NEt_2$	A-4-15.5[h]	165	14	97[d,j]	165.5–166.5[j,k]	$C_{14}H_{12}N_3$	20.23[i]	20.07[i]		
		C	103–105	0.2	51[d]						
C_5H_4N-	$-(CH_2)_3N(n\text{-}Bu)_2$	A-4-17[h]	198–207	19	54[d]	150.5–152[l,m]	$C_{16}H_{29}N_3\cdot 2C_6H_3N_3O_7$[m]	46.60	46.40	4.89	4.79
C_5H_4N-	$-(CH_2)_3C_6H_5$	A-4-17[h]	204–207	19	94[d]	116–116.5[m,n]	$C_{14}H_{16}N_2\cdot C_6H_3N_3O_7$[m]	54.42	54.62	4.30	4.38
C_5H_4N-	$-CH(Me)-(CH_2)_3NEt_2$	A-2-18[h]	165–172	11	31[d,r]		$C_{14}H_{25}N_3$	71.44	71.58	10.71	10.76
$C_4H_3N_2-$	$2\text{-}(5\text{-}Br\text{-}C_4H_2S)CH_2-$	B-1			28[b]	102–103[b]	$C_9H_8BrN_3S$	15.56[i]	15.50[i]		
$C_4H_3N_2-$	$-CH_2C_6H_4Cl(4)$	B-1			30[o]	128–129[b]	$C_{11}H_{10}ClN_3$	19.13[i]	19.00[i]		
$C_{10}H_8N-$	$-CH_2-CH_2C_6H_5$	A-4-18[h]	132–142	0.04	96[d]	183–184[m,p]	$C_{18}H_{18}N_2\cdot C_6H_3N_3O_7$[m]	58.65	58.36	4.31	4.36
$C_{10}H_8N-$	$-(CH_2)_3N(n\text{-}Bu)_2$	A-2-18.5[h]	132–138	0.04	56[d]	187–188[m,q]	$C_{21}H_{33}N_3$	76.84	76.40	10.16	10.05
$C_{10}H_8N-$	$-CH(Me)-(CH_2)_3NEt_2$	A-2-17[h]	134	0.04	93[d]	193.5–194.5[m,p]	$C_{19}H_{29}N_3\cdot 2C_6H_3N_3O_7$[m]	49.14	48.92	4.66	4.79

[a] C_5H_4N-, $C_4H_3N_2-$ and $C_{10}H_8N-$ are 2-pyridyl, 2-pyrimidyl and 2-lepidyl, respectively. C_4H_2S is a substituted thiophene group. [b] Recrystallized from methanol. [c] This compound was prepared in a similar fashion, using sodium hydride in place of lithium amide, by J. H. Clark, R. C. Clapp, J. R. Vaughan, Jr., L. H. Sutherland, R. Winterbottom, G. W. Anderson, J. D. Forsyth, J. Blodinger, S. L. Eberlin and J. P. English, *J. Org. Chem.*, 14, 216 (1949). Their 2-(5-chloro-2-thenyl)-aminopyridine was obtained in a crude yield of 20%, m.p. 71–74°. The m.p. of their recrystallized product is given as 84–86°. In the same way they obtained a 33% yield of 2-(5-bromo-2-thenyl)-aminopyridine, the purest fraction of which melted at 81–83°. [d] Yield of distilled product. [e] Yield of redistilled product. [f] Huttrer and coworkers (ref. 3) reported a 67% yield. [g] NC_4H_8O is the morpholino grouping. Huttrer, *et al.* (ref. 3), prepared 2-(2-morpholinoethyl)-aminopyridine in 43% yield and reported a m.p. of 184.5–186° for the monopicrate. Calcd. for $C_{11}H_{17}N_3O\cdot C_6H_3N_3O_7$: N, 19.26. Huttrer's group found: N, 19.32. We have assumed that our salt is a dipicrate (its analysis is acceptable for either the mono- or the dipicrate), since the salts of other 2-(dialkylaminoalkyl)-aminopyridines (and lepidines) which we have prepared have all analyzed correctly for the dipicrates, dihydrochlorides and diacid oxalates. The salt was recrystallized from acetone. [h] The first number after the letter represents the molar ratio of primary amine to heterocyclic halide; the second number refers to the number of hours the reaction mixture was maintained at a bath temperature of 170–180°. [i] Nitrogen analysis. [j] F. C. Whitmore, H. S. Mosher, D. P. J. Goldsmith and A. W. Rytina, THIS JOURNAL, **67**, 393 (1945), using a method similar to our Method B but with a 100% excess of sodamide in place of lithium amide and a 100% excess of 2-aminopyridine, obtained an 87% yield. Their picrate melted at 163.5–164°. [k] Since the crude picrate was insoluble in most solvents, it was purified by washing with hot chloroform–ether. [l] Recrystallized from chloroform–ether. [m] Picrate. [n] Recrystallized from ethanol. [o] This reaction was carried out in xylene rather than benzene in which poorer yields resulted. The crude product was purified by decolorizing a dilute hydrochloric acid solution of the compound with charcoal. After the decolorized solution was rendered alkaline, the crude product, m.p. 121–124°, precipitated. [p] Recrystallized from chloroform. [q] Recrystallized from acetone. [r] J. N. Ashley and J. F. Grove, *J. Chem. Soc.*, 768 (1945), obtained a 28% yield by a similar method.

the amine and lithium amide and then brought into reaction with an alkyl halide. Subsequently it was found that comparable yields could be obtained, and a shorter reflux period employed, when a mixture of all three reactants was refluxed in an appropriate solvent.[2] While yields of secondary amines, prepared by this reaction, were generally fair, excellent yields of tertiary amines have almost invariably been obtained when a secondary heterocyclic amine was condensed with a small excess of an alkyl halide and lithium amide. For example, N,N - dimethyl - N′ - benzyl - N′ - (2 - pyridyl)-ethylenediamine (Pyribenzamine)[3] was prepared in 96 and 97% yields by the one- and two-step reactions, respectively.

Five of the products were tested for activity against sarcoma 180. None of the compounds [2-(5-bromo-2-thenyl)-aminopyridine, 2-(5-bromo-2-thenyl)-aminopyrimidine, 2-(5-chloro-2-thenyl)-aminopyridine, 2-(4-diethylamino-1-methylbutyl)-aminopyridine and 2-(4-diethylamino-1-methylbutyl)-aminolepidine] have shown any evidence of ability to retard the growth of the sarcoma in mice.[4]

Experimental[5]

Secondary Amines from a Heterocyclic Halide and a Primary Aliphatic Amine. Method A.—The procedure previously described[1] was followed. Results, using this method as well as Methods B and C, are summarized in Table I.

Lithium Amide Condensation. Two-step Reaction. Method B.—This was identical with the Method B of a pre-

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[2] A. Wohl and M. Lange, *Ber.*, **40**, 4727 (1907), used a similar technique in preparing N-phenylaminoacetal.

[3] C. P. Huttrer, C. Djerassi, W. L. Beears, R. L. Mayer and C. R. Scholz, THIS JOURNAL, **68**, 1999 (1946).

[4] These tests were conducted under the supervision of Dr. C. Chester Stock of the Sloan-Kettering Institute for Cancer Research.

[5] All melting points are corrected; boiling points are not.

vious communication[1] except that benzene was substituted for toluene as solvent. In a few cases products were purified by recrystallization without prior distillation (Method B-1).

Lithium Amide Condensation. One-step Reaction. Method C.—A mixture consisting of 0.1 mole of a heterocyclic amine, 0.1 mole of an alkyl halide and 0.1 mole of lithium amide[6] in 100 ml. of benzene was refluxed for 10–20 hours. (When a dialkylaminoalkyl chloride hydrochloride was one of the reactants, the amount of lithium amide was doubled.) The reaction mixture was filtered hot and the residue washed well with benzene. After removing the solvent, the residue which remained was distilled *in vacuo*.

In this manner there was obtained 24.4 g. (96%) of N,N-dimethyl-N'-benzyl-N'-(2-pyridyl)-ethylenediamine, b.p. 121–122° (0.02 mm.) by refluxing a mixture of 18.4 g. (0.10 mole) of 2-benzylaminopyridine, 5.4 g. (0.24 mole of 98% purity) of lithium amide, 17.3 g. (0.12 mole) of dimethylaminoethyl chloride hydrochloride and 200 ml. of benzene for 20 hours. When prepared on the same scale by the two-step reaction (Method B), the yield was 24.7 g. (97%).[3]

Acknowledgment.—The authors are indebted to Endo Products, Inc., for financial support of part of this investigation, and to Mr. David Regenbogen for bringing the procedure of Wohl and Lange[2] to their attention.

[6] The product obtained from Metalloy Corp. is of 98% purity. In the course of handling, the lithium amide content decreases considerably. The practice in our laboratory is to transfer the contents of the one- or two-pound tins to six-ounce amber bottles (narrow-neck and screw-cap) which are kept tightly stoppered and sealed with paraffin. If left open for a minimum of time during the weighing of the compound, the titer remains fairly constant.

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The Phase System BaO–$BaCO_3$

BY J. J. LANDER

In the system BaO–$BaCO_3$ Finkelstein[1] assumes the existence of a basic carbonate in the solid phase and assigns to it the composition BaO·$BaCO_3$. But Hackspill and Wolfe[2] assign the composition 2$BaCO_3$·BaO to the eutectic and report that they found no evidence for the existence of a basic carbonate in the solid phase. This note reports the results of a thermal analysis investigation of the system which agree with the conclusions of Hackspill and Wolfe.

A modification of the thermal analysis apparatus described by Smith[3] was used. An essential feature is an arrangement for obtaining a constant rate of heat flow into or out of the specimen by maintaining a constant temperature difference across a thermal insulator which surrounds the specimen. Materials were used which could be heated to temperatures as high as 1300°. The ceramic containers were made of alundum and the thermocouples were Pt, Pt + 10% Rh. Two other modifications were made. Heating elements were provided above and below the specimen in order to reduce the size of the equipment, and a number of series junctions were used in the differential thermocouple circuit in order to obtain increased sensitivity. Regulation was by automatic in-out switching of a resistance in the heater circuit.

In a typical run a measured amount of CO_2 was pumped from a known amount of $BaCO_3$ at a temperature of about 1000° in the early stages of decomposition, but as high as 1200° in the final stages. Temperature–time curves for heating and cooling in a closed system between 1100 and 600° were then obtained. Three arrests were usually observed, and these were due to the following transitions: (1) the orthorhombic to hexagonal transition of $BaCO_3$ at 806°; (2) the hexagonal to cubic transition at 968°; (3) the melting of the eutectic at 1030°.

The first two temperatures differ by a few degrees from those given in an earlier report,[4] and are considered more reliable. A typical set of results is shown in Fig. 1.

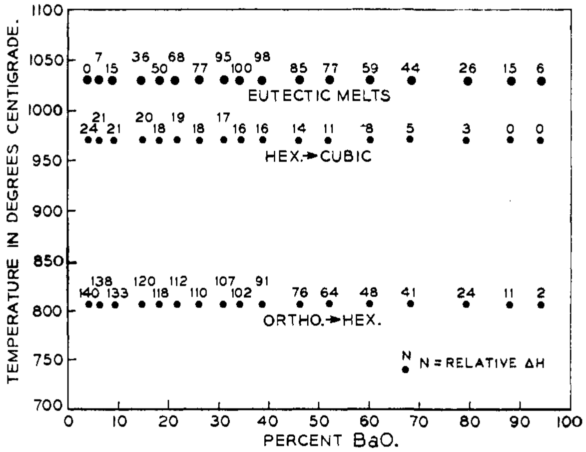

Fig. 1.—Observed relative heats of transitions as a function of temperature and composition.

The following phenomena were observed in a series of three separate sets of runs each started with fresh material: (1) The heat of transition at 806° decreased linearly with increasing BaO content and the temperature of transition remained unchanged (±1°). It is concluded that at 806° and throughout the composition range the separate phases $BaCO_3$ and BaO coexist. (2) The heat of the transition at 968° decreased linearly with increasing BaO content and the temperature of transition remained unchanged (±3°). Therefore, at 968° and throughout the composition range the separate phases $BaCO_3$ and BaO coexist. (3) The eutectic arrest did not appear until about 4% (±1%) decomposition was reached. The heat released increased linearly to a maximum at 33% (±1%) decomposition and decreased linearly to zero at about 98% (±2%) decomposition. The eutectic temperature remained constant at 1030° (±3°).

Quantitative thermal data may be obtained from Fig. 1 and known heats of transition for the reactions $BaCO_3$(ortho) → $BaCO_3$(hex.) and $BaCO_3$ (hex.) → $BaCO_3$(cubic).[5] In Fig. 1 the symbol N = relative ΔH is the heat evolved relative to the heat evolved at the eutectic point, which heat has been arbitrarily assigned the value 100.

The eutectic composition observed, 33% BaO,

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[1] A. Finkelstein, *Ber.*, **39**, 1585 (1906).

[2] L. Hackspill and G. Wolfe, *Compt. rend.*, **204**, 1820 (1937).

[3] C. S. Smith, *AIME*, **137**, 236 (1940).

[4] J. J. Lander, *J. Chem. Phys.*, **17**, 892 (1949).

[5] See J. J. Lander, THIS JOURNAL, **73**, 5794 (1951).