Binary Systems Containing Isoamyl Alcohol or Active Amyl Alcohol

Physical Properties and Azeotropic Properties

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ISOMERIC amyl alcohols, active amyl alcohol [(-)-2-methylbutanol] and isoamyl alcohol (3-methylbutanol) are the principal compounds in fusel oil (*25*). A by-product of normal alcoholic fermentation, fusel oil is produced to the extent of 0.1 to 0.7 per cent of the ethyl alcohol yield (*16*). The mixed amyl alcohols are used as solvents and extractives in large amounts in many industrial processes where a five-carbon branched-chain primary alcohol is needed. The purified active amyl alcohol might be used as a starting material for the synthesis of compounds having optical activity.

Le Bel (*30*) tried to purify the optically active isomer by chlorination, because isoamyl alcohol is more rapidly chlorinated. Pasteur (*33*) separated the amyl sulfates by their different solubilities. Isom and Hunt (*27*) found only a very slight separation of the alcohols on passing a mixture through a 50-foot column packed with activated carbon at 91° C., and Blessin, Kretschmer, and Wiebe (*5*) reported that separation of normal alcohols by thermal diffusion was virtually impossible.

Isoamyl and active amyl alcohols are difficult to separate by fractional distillation, as their boiling points are 132.0° and 128.7° C. (*2*, *6*), respectively, at atmospheric pressure. Whitmore and Olewine (*37*) reported that several fractionations on a 101-plate column were necessary to obtain 95% pure active amyl alcohol. Brauns reported (*6*) that fractional distillation seemed the only practicable method.

Separating the two branched-chain primary amyl alcohols by fractional distillation after addition of a third component which would azeotrope with one or both alcohols has never been investigated. Horsley (*23*) records several azeotropes involving isoamyl alcohol, but only one study of systems containing active amyl alcohol (*4*). The azeotroping agent should ideally form a low boiling azeotrope with active amyl and none with isoamyl, or a high boiling azeotrope with isoamyl and none with active amyl alcohol. Or, if it azeotropes with both alcohols, the boiling points should differ by considerably more than 3.3° C.

To determine whether or not an azeotrope had formed in the distillation fractions of binary mixtures containing either isoamyl or active amyl alcohol and another component, the physical properties of such mixtures had to be evaluated.

Possible azeotroping agents, chosen with consideration of the principles developed by Ewell, Harrison, and Berg (*11*), were mixed with pure isoamyl and active amyl alcohols to make known solutions for determinations of refractive indices, densities and, for active amyl solutions, optical activities. In nearly every case nine mixtures of each binary combination were prepared, successive samples differing by approximately 10 weight % in azeotroping agent content.

The amyl alcohols were obtained from grape brandy fusel oil by repeated fractional distillations. The active amyl alcohol was distilled until the optical rotation agreed with the values of Markwald and McKenzie (*32*), who used fractional crystallization of the 1-amyl-3-nitrophthalate acid esters to separate the last traces of isoamyl from the active amyl derivative. After saponification, distillation, drying, and redistillation, the physical constants of the active amyl alcohol were measured. The possibility of some (+) isomer of active amyl alcohol being present was not considered in the research reported. Cohen, Marshall, and Woodman (*8*) attempted resolution of the 3-nitrophthalic acid 2-monoester of active amyl alcohol by conversion to the brucine salts, but obtained active amyl alcohol of decreased optical activity. This they attributed to racemization by the hot base during hydrolysis of the ester-salt which seems unlikely, as the center of optical activity is not involved directly in the hydrolysis reaction. It was desirable, therefore, to attempt resolution of the active amyl nitrophthalate monoester using other optically active bases, to be certain that Markwald and McKenzie's value was that of the single pure optical isomer.

Physical Properties of Binary Mixtures of Isoamyl or Active Amyl Alcohol and Other Compounds

EXPERIMENTAL

Equipment. Refractive index measurements were made on a Zeiss Abbe refractometer with prisms thermostated at 25° ±0.05° C.

Density determinations were made using 0.7- and 1.8-ml. pycnometers suspended in a thermostat controlled at 25° ±0.05° C. The pycnometers were made from serological pipets and could be read with an accuracy which permitted determination of densities within ±0.0002 gram per ml. The densities as reported are corrected for air buoyancy.

The optical rotation measurements were made on a Model 8 Rudolph polarimeter equipped with a sodium light source and using a 2-dm. capillary tube (not thermostated), and were corrected from room temperature to 25° C. by measuring the rotation of pure active amyl alcohol at the same time and temperature. The correction factor to convert the rotation of active amyl alcohol at room temperature to α_D^{25} −9.50° was applied to the rotations of any mixtures obtained under the same conditions. Correction factors varied from 1.013 to 0.998. The polarimeter could be read with a precision of ±0.02°.

The fractional distillations were carried out with a Heli-grid Podbielniak column, 48 inches long and 8 mm. in diameter, equipped as described by Ikeda, Webb, and Kepner (*25*). The piperidine derivatives were distilled with a Wheeler center-rod column 30 cm. long with an inside diameter of 8 mm. Head temperatures were measured by a thermocouple in the Podbielniak column and a mercury thermometer in the Wheeler column. Distillation flasks were heated by Glas-Col heating mantles or external heating coils set in Dewar flasks. The heat input was precisely controlled by Powerstats connected to a constant voltage line. Take-off rates were controlled by solenoids activated by electronic or clock timers. Rated efficiencies under total reflux were over 200 theoretical plates for the Podbielniak and approximately 75 for the Wheeler column.

Purification of Reagents. Isoamyl and active amyl alcohols were obtained from grape brandy fusel oil. An excess of solid sodium chloride was added to the fusel oil to salt out as much water as possible. The organic phase was separated, dried for several weeks over several changes of freshly dehydrated magnesium sulfate, then fractionally distilled using the 4-foot Heli-grid Podbielniak column with timer ratios of approximately 200 to 1 and a throughput which permitted collection of approximately 130 ml. in 24 hours. The distillate receiver was changed daily and the per cent of activity amyl alcohol determined on a polarimeter. The distillation fractions obtained from many batches of fusel oil were combined according to their active amyl alcohol content. Samples were repeatedly redistilled to increase the per cent of active amyl alcohol with the ultimate isolation of constant boiling material with constant physical properties: b.p. 128.5° C., n_{D}^{25} 1.4088, d_4^{25} 0.8154, $\alpha_{\mathrm{D}}^{25} - 9.50°$ (2-dm. tube). The pot residue remaining from the initial fusel oil charges after removal of all the active amyl alcohol was further distilled through the Podbielniak column to give pure isoamyl alcohol: b.p. 132.0° C., n_{D}^{25} 1.4048, d_4^{25} 0.8059. These constants agreed with values previously published (*24*) and with the rotation of active amyl alcohol reported by Markwald and McKenzie (*32*).

n-Octane (500 grams, Eastman technical grade) was shaken with three 200-ml. portions of fuming sulfuric acid for 7 hours, washed twice with dilute sodium hydroxide solution, twice with water, then dried overnight over anhydrous magnesium sulfate. After removal of the drying agent, the *n*-octane was fractionally distilled to give material boiling at 125.3–6.3° C.: n_{D}^{25} 1.3945, d_4^{25} 0.6985. Literature values (*35*): n_{D}^{25} 1.39534, d_4^{25} 0.69882.

Chlorobenzene (Eastman White Label) was redistilled to give material boiling at 131.5–2.0° C.: n_{D}^{25} 1.5219, d_4^{25} 1.1010. Literature values (*34*): n_{D}^{25} 1.5246, d_4^{25} 1.1010.

Ethylbenzene (Eastman White Label) was used without further purification: n_{D}^{25} 1.4930, d_4^{25} 0.8625. Literature values (*13*): n_{D}^{25} 1.49320, d_4^{25} 0.86264.

Toluene (Eastman White Label) was used without further purification: n_{D}^{25} 1.4930, d_4^{25} 0.8604. Literature values (*13*): n_{D}^{25} 1.49414, d_4^{25} 0.8623.

2,2,5-Trimethylhexane (Phillips pure grade, 99^+ mole %) was used without further purification: n_{D}^{25} 1.3971, d_4^{25} 0.7031. Literature values (*13*): n_{D}^{25} 1.39728, d_4^{25} 0.70322.

2,6-Lutidine (Eastman White Label) was dried over solid potassium hydroxide and redistilled to give a fraction boiling at 140.5–2.0° C.: n_{D}^{25} 1.4953, d_4^{25} 0.9187. Literature values (*7*): n_{D}^{25} 1.4953, d_4^{25} 0.9183.

2-Picoline (Eastman prictical grade) was redistilled to give material boiling at 127.5–8.5° C.: n_{D}^{25} 1.4982, d_4^{25} 0.9391. Literature values (*14*): n_{D}^{20} 1.50105, n_{D}^{30} 1.49592, d_4^{20} 0.94432, d_4^{30} 0.93491.

2,6-Dimethylpiperidine (Eastman White Label) was redistilled to give material boiling at 127.5–8.0° C.: n_{D}^{25} 1.4368, d_4^{25} 0.8156. Literature values (*19*): n_{D}^{25} 1.4366, d_4^{25} 0.8158.

1,2-Dimethylpiperidine was prepared by methylation of 2-methylpiperidine with methyl iodide in ether by a procedure adapted from Flaschner (*12*) in 20% yield: b.p. 127.5–8.5° C., n_{D}^{25} 1.4388, d_4^{25} 0.8180. Literature values (*21*): n_{D}^{20} 1.4395, d_4^{15} 0.824.

o-Fluorotoluene (Eastman White Label) was used without further purification: n_{D}^{25} 1.4710, d_4^{25} 0.9981. Literature values (*36*): $n_{\mathrm{D}}^{17.3}$ 1.47161, $d_4^{17.3}$ 1.00142.

Diisopropyl ketone (Eastman practical grade) was dried over anhydrous magnesium sulfate and distilled to give material boiling at 123.5–4.5° C.: n_{D}^{25} 1.3872, d_4^{25} 0.7986. Literature values (*18*): n_{D}^{20} 1.4001, d_4^{20} 0.8108.

Samples for Analysis. Mixtures for experimental measurements were prepared by weighing the purified components into weighing bottles on a standard analytical balance to give weight fractions at intervals of approximately 10 weight %. The data obtained from these binary mixtures are presented in Tables I and II and summarized in Figures 1 to 5.

RESOLUTION OF ACTIVE AMYL ALCOHOL FROM FUSEL OIL

Synthesis of 3-Nitrophthalic Acid 2-Monoester of Active Amyl Alcohol. 3-Nitrophthalic anhydride was prepared from 3-nitrophthalic acid by the method of Nicolet and Bender (*15*). The 3-nitrophthalic acid 2-monoester of active amyl alcohol was synthesized by an adaptation of the methods of Cohen, Marshall, and Woodman (*8*) and Henze (*22*).

A mixture of 200 ml. of dry toluene and 70 grams of 3-nitrophthalic anhydride was placed in a 500-ml. three-necked flask fitted with a stirrer, dropping funnel, and reflux condenser with a calcium chloride drying tube. It was brought to a boil and 35 ml. of active amyl alcohol were added slowly with stirring. The stirrer was removed and the mixture was refluxed overnight. When it had cooled, the crystalline material was filtered with suction and dissolved in 5% sodium bicarbonate solution. The toluene filtrate was extracted with 200 ml. of 5% sodium bicarbonate solution. The combined sodium bicarbonate solutions were adjusted to pH 8 with solid sodium bicarbonate and a small amount of insoluble material was removed by filtration. The basic solution was acidified with concentrated hydrochloric acid stepwise to pH 2. The successive precipitates were filtered by suction, air-dried, ground in a mortar, and extracted with acetone. Insoluble material was removed by filtration and the combined acetone solutions were evaporated to dryness. The residues were dissolved in boiling benzene, filtered hot, and repeatedly recrystallized from benzene to give 42 grams (46% yield) of the monoester with a constant melting point of 157.5–58.5° C.

Preparation of Cinchonidine Salt. A mixture of 50 grams of 3-nitrophthalic acid 2-monoester of active amyl alcohol, 52.5 grams of cinchonidine, and 300 ml. of actone was refluxed for 1 hour. The acetone was then removed under reduced pressure at room temperature. The salt was dissolved in chloroform and *n*-pentane added until the solution just remained clear. The salt crystallized slowly at room temperature and was collected by suction filtration after several hours. Addition of more *n*-pentane to the filtrate gave additional crystalline material. Repeated recrystallizations from chloroform and pentane gave 92 grams (90% yield) of the cinchonidine salt with a constant melting point of 101–3° C.

Attempts to purify the cinchonidine salt by recrystallization from dilute ethyl alcohol or ethyl acetate–*n*-pentane mixtures were not successful, as the melting point of the crystals steadily decreased.

Saponification of Cinchonidine Salt. A mixture of 93 grams of the recrystallized cinchonidine salt and 600 ml. of 20% potassium hydroxide solution was refluxed for 2 hours. The reaction mixture was steam-distilled until all the active amyl alcohol had gone over (about 75 ml. of solution), and the distillate was extracted with three 30-ml. portions of diethyl ether. Completeness of saponification was checked by filtering the insoluble cinchonidine from the basic steam distillation residue, adding 60 grams of sodium hydroxide, and resaponifying. No formation of further active amyl alcohol was observed. The combined ether extracts were dried over anhydrous magnesium sulfate, filtered, and added to 35 ml. of absolute ethyl alcohol. This mixture was distilled through a Wheeler GE-118-L center-rod column using a timer ratio of about 30 to 1 until the head temperature rose to 80° C. and a ratio of about 480 to 1 at higher temperatures. Approximately 6 ml. of active amyl alcohol, collected in six fractions, was obtained, which had constant properties: b.p. 128.5° C., n_{D}^{25} 1.4082, d_4^{25} 1.8161, $\alpha_{\mathrm{D}}^{25} - 9.50°$. The average of 10 polarimeter readings was −9.495 with average deviation of ±0.012. Fusel oil active amyl alcohol purified by distillation only showed $\alpha_{\mathrm{D}}^{25} -9.492° \pm 0.010$.

The stability of active amyl alcohol to racemization under

Table I. Binary Mixtures Containing Isoamyl Alcohol

Isoanyl Alcohol with			
Mole %	Wt. %	n_D^{25}	d_4^{25}
n-Octane			
100.00	100.00	1.4048	0.8059
92.01	89.89	1.4035	0.7938
83.84	80.01	1.4023	0.7818
75.18	70.04	1.4011	0.7698
66.04	60.01	1.3999	0.7586
56.53	50.09	1.3989	0.7474
46.42	40.07	1.3978	0.7364
35.67	29.97	1.3969	0.7263
24.76	20.26	1.3961	0.7168
12.67	10.07	1.3953	0.7070
0.00	0.00	1.3945	0.6985
Chlorobenzene			
100.00	100.00	1.4048	0.8059
91.90	89.85	1.4134	0.8285
83.40	79.80	1.4225	0.8522
73.78	69.84	1.4322	0.8767
65.20	59.59	1.4430	0.9034
56.20	50.08	1.4536	0.9309
46.00	40.02	1.4652	0.9600
35.67	29.97	1.4779	0.9917
24.22	20.04	1.4910	1.0249
12.57	10.13	1.5053	1.0606
0.00	0.00	1.5219	1.1010
Ethylbenzene			
100.00	100.00	1.4048	0.8059
91.48	89.92	1.4128	0.8111
82.72	79.90	1.4210	0.8164
73.75	70.00	1.4292	0.8214
64.32	59.95	1.4375	0.8268
54.62	49.99	1.4462	0.8321
44.50	39.97	1.4550	0.8377
33.99	29.95	1.4640	0.8435
23.17	20.03	1.4734	0.8495
11.88	10.07	1.4830	0.8558
0.00	0.00	1.4930	0.8625
Toluene			
100.00	100.00	1.4048	0.8059
90.30	89.91	1.4123	0.8112
80.55	79.85	1.4203	0.8159
70.75	69.83	1.4282	0.8206
60.99	59.93	1.4361	0.8256
51.11	50.01	1.4451	0.8308
Isoamyl Alcohol with			
Mole %	Wt. %	n_D^{25}	d_4^{25}
Toluene (*continued*)			
41.01	39.95	1.4539	0.8362
31.00	30.06	1.4632	0.8415
20.74	20.02	1.4728	0.8475
10.51	10.10	1.4828	0.8537
0.00	0.00	1.4930	0.8604
2,2,5-Trimethylhexane			
100.00	100.00	1.4048	0.8059
92.86	89.94	1.4040	0.7958
85.33	79.99	1.4031	0.7831
77.26	70.01	1.4021	0.7722
68.59	60.01	1.4012	0.7618
59.31	50.05	1.4003	0.7504
49.25	40.01	1.3995	0.7400
38.40	30.00	1.3988	0.7299
26.77	20.08	1.3981	0.7208
13.93	10.01	1.3976	0.7116
0.00	0.00	1.3971	0.7031
2,6-Lutidine			
100.00	100.00	1.4048	0.8059
91.52	89.86	1.4143	0.8191
82.82	79.86	1.4238	0.8313
73.89	69.96	1.4331	0.8432
64.55	59.97	1.4423	0.8551
54.89	50.03	1.4514	0.8664
44.77	40.01	1.4602	0.8781
34.30	30.04	1.4691	0.8887
23.50	20.17	1.4779	0.8990
11.92	10.02	1.4867	0.9090
0.00	0.00	1.4953	0.9187
2-Picoline			
100.00	100.00	1.4048	0.8059
90.34	89.85	1.4140	0.8193
80.83	79.97	1.4231	0.8323
71.17	70.03	1.4322	0.8455
61.29	59.98	1.4412	0.8588
51.32	49.95	1.4502	0.8718
41.29	39.97	1.4596	0.8849
31.22	30.05	1.4689	0.8979
20.95	20.05	1.4784	0.9117
10.61	10.10	1.4882	0.9253
0.00	0.00	1.4982	0.9396
Isoamyl Alcohol with			
Mole %	Wt. %	n_D^{25}	d_4^{25}
2,6-Dimethylpiperidine			
100.00	100.00	1.4048	0.8059
92.02	89.98	1.4100	0.8114
83.63	79.91	1.4150	0.8162
74.97	69.99	1.4196	0.8199
65.74	59.91	1.4238	0.8231
56.20	49.98	1.4272	0.8246
46.15	40.03	1.4301	0.8250
35.50	30.00	1.4326	0.8244
24.39	20.08	1.4345	0.8229
12.63	10.12	1.4359	0.8202
0.00	0.00	1.4368	0.8156
1,2-Dimethylpiperidine			
100.00	100.00	1.4048	0.8059
91.95	89.89	1.4096	0.8118
83.62	79.90	1.4142	0.8157
75.01	70.04	1.4185	0.8186
65.83	60.00	1.4221	0.8208
56.09	49.87	1.4259	0.8220
0.00	0.00	1.4388	0.8180
o-Fluorotoluene			
100.00	100.00	1.4048	0.8059
91.70	89.85	1.4100	0.8218
83.35	80.02	1.4152	0.8372
74.38	69.91	1.4210	0.8543
65.17	59.96	1.4269	0.8718
55.48	49.93	1.4336	0.8906
45.41	39.99	1.4400	0.9098
34.93	30.06	1.4471	0.9298
23.87	20.06	1.4543	0.9508
12.21	10.01	1.4625	0.9740
0.00	0.00	1.4710	0.9981
Diisopropyl Ketone			
100.00	100.00	1.4048	0.8059
92.02	89.90	1.4041	0.8053
83.80	79.97	1.4035	0.8047
75.13	69.99	1.4029	0.8040
66.05	60.03	1.4021	0.8033
56.50	50.07	1.4015	0.8025
46.35	40.01	1.4009	0.8018
35.68	29.99	1.4000	0.8011
24.56	20.08	1.3992	0.8002
12.71	10.10	1.3982	0.7994
0.00	0.00	1.3972	0.7986

the saponification conditions used was demonstrated on a sample of purified alcohol, with subsequent isolation of the alcohol. No change in rotation was observed.

Other Attempted Resolutions. The brucine salt of the 3-nitrophthalic acid 2-monoester of active amyl alcohol was prepared as described above. In contast to the report of Cohen, Marshall, and Woodman (*8*) all attempts to recrystallize the salt from dilute ethyl alcohol under a variety of concentration and temperature conditions in this laboratory were unsuccessful. Other solvent systems were tried without success. Attempts to prepare the cinchonine salt by this technique were not successful.

RESULTS AND DISCUSSION

Active amyl alcohol recovered from saponification of the purified cinchonidine salt of the 3-nitrophthalic acid 2-monoester of active amyl alcohol had the same optical activity as that from fusel oil purified only by repeated fractional distillations. This proves that only the single (−) isomer occurs in fusel oils. This was probably to be expected, but as all the details of the biosynthesis of active amyl alcohol have not been elucidated, some of the (+) isomer might have been formed. Since only the (−) optical isomer of active amyl alcohol is present, all the steps in the biosynthesis of the carbon skeleton of the alcohol must be stereospecific and therefore enzymatic in nature.

The lowered optical activity value attributed by Cohen, Marshall, and Woodman to racemization of active amyl alcohol during saponification of the brucine salt of its 3-nitrophthalate 2-monoester could not be duplicated in this laboratory. In the research reported, the cinchonidine salt of this ester was hydrolyzed with hot base to yield the alcohol with unlowered optical activity. Preliminary experiments also demonstrated that the alcohol itself, when heated in the presence of base, did not lose optical activity. Possibly Cohen, Marshall, and Woodman's sample was insufficiently dried before rotation was measured.

While the presence of some (+) active amyl alcohol in the (−) active amyl alcohol normally found in fusel oils would not affect the densities and refractive indices of mixtures of the alcohols and possible azeotroping agents, optical activities would be affected. The finding that only pure (−) active amyl alcohol is present in fusel oil, places a firm foundation under the value determined by Markwald and McKenzie.

Physical properties of binary mixtures of isoamyl alcohol and possible azeotrope-forming substances are listed in Table I; properties of active amyl alcohol binary mixtures, in Table II. These data are important in determining the compositions of unknown mixtures of the components with isoamyl or active amyl alcohol. Figures 1 and 2 show the data for some isoamyl alcohol systems; Figures 3 and 4 show the corresponding active amyl alcohol systems. Figure

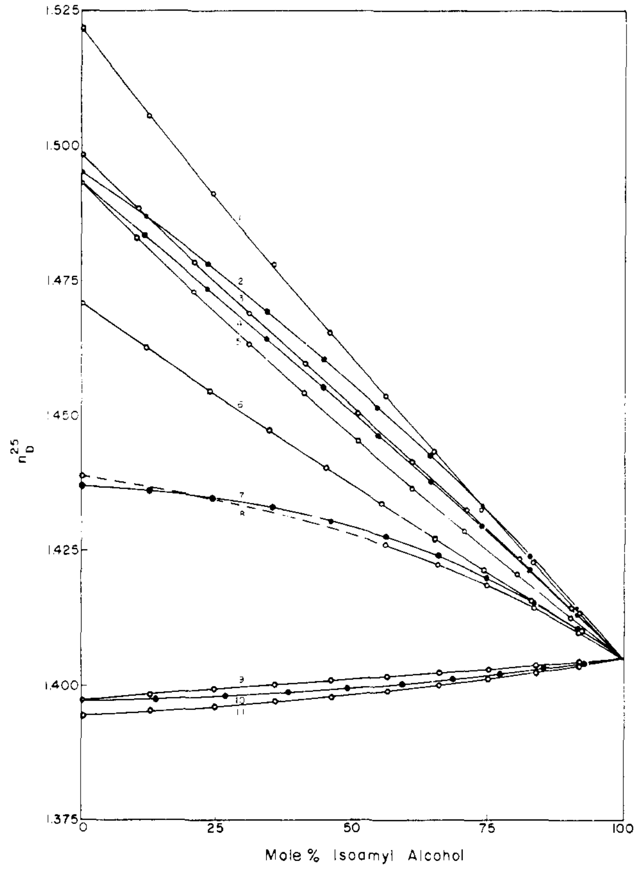

Figure 1. Refractive indices of binary mixtures containing isoamyl alcohol

1. Chlorobenzene. 2. 2,6-Lutidine. 3. 2-Picoline. 4. Ethylbenzene. 5. Toluene. 6. o-Fluorotoluene. 7. 2,6-Dimethylpiperidine. 8. 1,2-Dimethylpiperidine. 9. Diisopropyl ketone. 10. 2,2,5-Trimethylhexone. 11. *n*-Octane

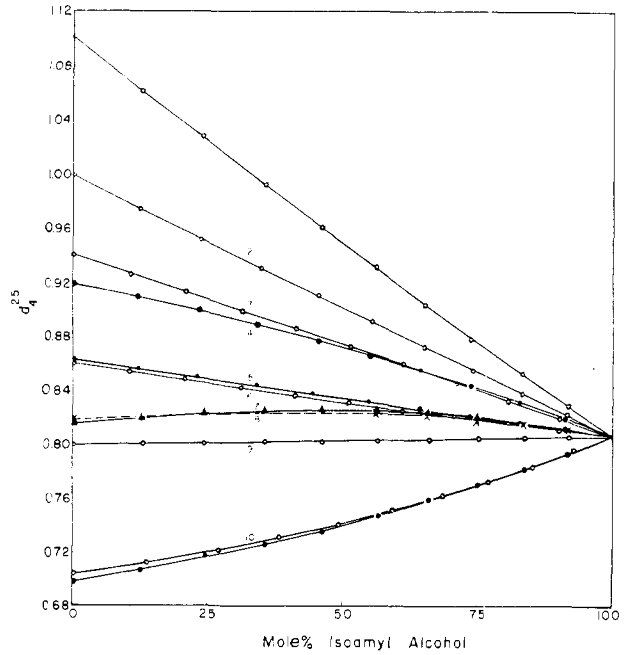

Figure 2. Densities of binary mixtures containing isoamyl alcohol

1. Chlorobenzene. 2. o-Fluorotoluene. 3. 2-Picoline. 4. 2,6-Lutidine. 5. Ethylbenzene. 6. Toluene. 7. 2,6-Dimethylpiperidine. 8. 1,2-Dimethylpiperidine. 9. Diisopropyl ketone. 10. 2,2,5-Trimethylhexane. 11. n-Octane

5 shows the relationship between composition and optical activity for the active amyl alcohol systems.

The figures show that for mixtures of unknown composition there are significant differences in the slopes of the functions plotted and therefore in the precision of the analytical values that can be obtained. The precisions with which the properties can be measured also vary, so that the error in a composition analysis value will be proportional to the error in the instrument reading and inversely proportional to the slope of the plotted function.

For systems containing isoamyl alcohol the plots of density *vs.* composition show variations from functions of positive curvature through essentially straight lines to functions of negative curvature. In the concave density-composition functions such as those of the octane-isoamyl, chlorobenzene-isoamyl, and 2,2,5-trimethylhexane-isoamyl systems, the decreased density with respect to that of an ideal mixture is probably best interpreted as resulting from a breaking up of the compact hydrogen-bonded structure of the pure alcohol upon addition of the second component. The corresponding active amyl alcohol systems have almost identically shaped density-composition curves.

Ewell and others (*11*) classified organic liquids according to their ability to form hydrogen bonds.

CLASS I. Liquids capable of forming three-dimensional networks of strong hydrogen bonds—e.g., water, glycol, glycerol.

CLASS II. Other liquids whose molecules contain both active hydrogen atoms and donor atoms (oxygen, nitrogen, fluorine)—e.g., alcohols, acids, phenols, primary and secondary amines.

CLASS III. Liquids containing donor atoms, but no active hydrogen atoms—e.g., ethers, ketones, aldehydes, esters, tertiary amines.

CLASS IV. Liquids composed of molecules containing active hydrogen atoms, but no donor atoms—e.g., chloroform, 1,1-dichloroethane.

CLASS V. All other liquids which cannot form hydrogen bonds—e.g., hydrocarbons, sulfides, carbon disulfide, halohydrocarbons not in Class IV.

According to Ewell, Harrison, and Berg (*11*) mixtures of alcohols and hydrocarbons or chlorobenzene should show positive deviations from Raoult's law. The observed decreases in density upon mixing in these systems, if due to a net decrease in hydrogen bonds, would result in enhanced vapor pressures for the mixtures and therefore positive deviations from Raoult's law.

Plots of the index of refraction *vs.* composition for the amyl alcohols-Class V compounds also show concave curves of shapes analogous to those of the corresponding density-composition functions. This suggests that the deviations from ideality in the refractive index-composition functions reflect primarily the departures from ideality of the densities of the solution at the liquid-prism interface in the refractometer.

The density-composition plots for the systems amyl alcohols-1,2-dimethylpiperidine and amyl alcohols-2,6-dimethylpiperidine show that these functions are convex with respect to the composition axis. This departure from linearity indicates an increase in density or a contraction in volume upon mixing. Such contractions are probably most rationally accounted for by assuming a net increase in hydrogen bonding within the solution mixture. An increase should decrease vapor pressure with respect to that calculated from Raoult's law.

Plots of refractive index *vs.* composition for the alcohol-dimethylpiperidine systems also show the convex form in analogy with the density-composition plots of these systems. Here also the density changes are probably the principal factor in causing deviations from linearity in the refractive index-composition functions.

2-Picoline, ethylbenzene, and diisopropyl ketone give essentially straight-line plots for the density-composition function when mixed with isoamyl or active amyl alcohol. The 2-picoline and diisopropyl ketone–alcohol systems represent mixtures of Classes II and III and can be expected to show positive or negative deviations from ideality, depending upon net decrease or increase in hydrogen bonding upon mixing of the two components. The density-composition functions would indicate very little net change in the hydrogen bond total on mixing. Ethylbenzene, a Class V substance, should show a positive deviation from Raoult's law, according to Ewell. Berg, Harrison, and Montgomery (*4*) have reported the formation of a minimum boiling azeotrope for the ethylbenzene–isoamyl alcohol system which necessitates a positive deviation from Raoult's law. Therefore, departures from ideality in the vapor pressure–composition functions are not always reflected in a corresponding curvature in the density-composition function.

The plots of refractive index *vs.* composition for the alcohols-2-picoline, ethylbenzene, and diisopropyl ketone systems show a slight curvature, but are very close to straight lines.

Observed rotation *vs.* composition for the binary systems containing active amyl alcohol is plotted in Figure 5. The high degree of concave curvature with respect to the composition axis is probably the most significant feature of these plots. The observed rotation should be influenced by density. However, as all the lines are of negative curvature, factors other than density anomalies are predominant, because the density-composition functions had both positive and negative curvature. Trial plots of calculated specific rotations *vs.* composition for the active amyl alcohol systems were also curves. The specific rotation values, being calculated to unit density, would not show the effect of **density** anomalies on the rotation-composition plots.

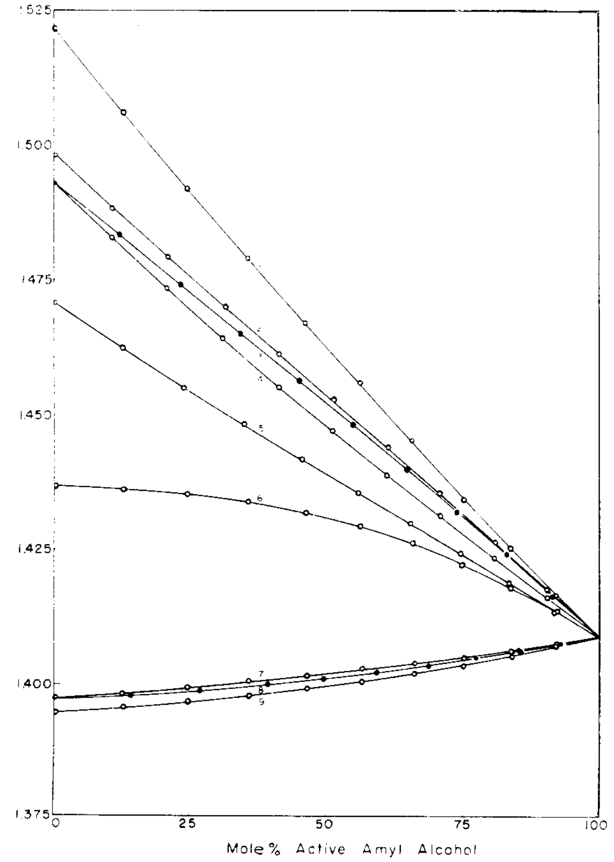

Figure 3. Refractive indices of binary mixtures containing active amyl alcohol

1. Chlorobenzene. 2. 2-Picoline. 3. Ethylbenzene. 4. Toluene. 5. o-Fluorotoluene. 6. 2,6-Dimethylpiperidine. 7. Diisopropyl ketone. 8. 2,2,5-Trimethylhexane. 9. *n*-Octane

AZEOTROPIC PROPERTIES

The binary systems used in the work reported above were further investigated for azeotropic data. A limited amount of work on azeotropes of isoamyl alcohol or of active amyl alcohol is presented in the literature.

EXPERIMENTAL

The same type of equipment was used as for the measurement of physical properties.

Purification of Reagents. The following compounds were also used: 1-Ethylpiperidine (Eastman White Label) was purified by redistillation: b.p. 130.5–1.0° C., n_D^{25} 1.4412. Literature value (*31*): n_D^{25} 1.4440.

o-Fluorophenol (Matheson) was purified by redistillation: b.p. 151–2° C., n_D^{25} 1.5130, d_4^{25} 1.2140. Literature values (*1*): n_D^{25} 1.5107, d_4^{25} 1.2108.

Mesityl oxide (Eastman White Label) was purified by redistillation: b.p. 130–1° C., n_D^{25} 1.4421. Literature value (*20*): n_D^{13} 1.44840.

Cyclopentanone (Eastman White Label) was purified by redistillation: b.p. 129.5–30.5° C., n_D^{25} 1.4343. Literature value (*17*): n_D^{20} 1.4366.

2,2,3,3,4,4,5,5-Octafluoro-1-pentanol (1*H*,1*H*,5*H*-octafluoro-1-pentanol) from the Du Pont Co., was purified by redistillation: b.p. 140–1° C., n_D^{25} 1.3158, d_4^{25} 1.6583. Literature values (*10*): n_D^{20} 1.3178, d_4^{20} 1.6647.

Distillation of Binary Azeotropic Mixtures. In general the mixtures were distilled through the 4-foot Podbielniak column using 100-gram pot charges. The column was equilibrated under total reflux for several hours before removal of the distillate was started. The boil-up rate was controlled so that with a timer ratio of 150 to 1 the take-off rate was approximately 6 ml. per hour. As long as the head temperature remained constant, fractions of 6 to 12 ml. were collected to establish constancy of composition. Because less than 8 ml. of distillate would normally come over during any transition temperature, only one transition cut was usually taken.

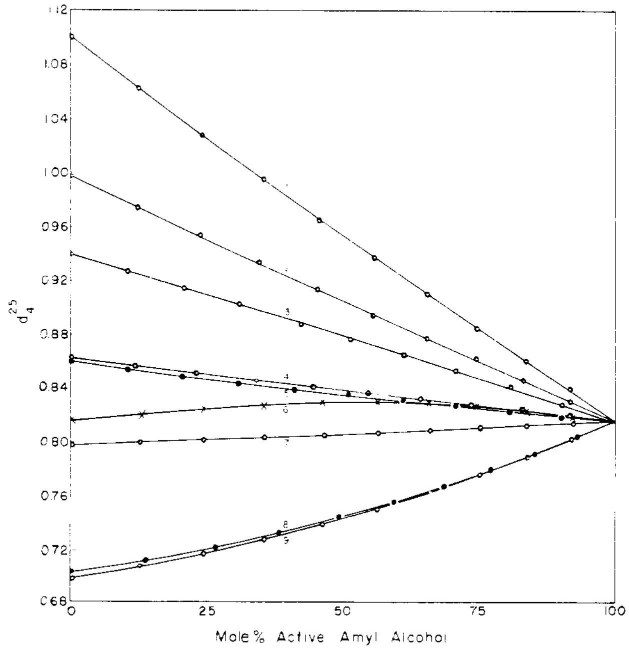

Figure 4. Densities of binary mixtures containing active amyl alcohol

1. Chlorobenzene. 2. o-Fluorotoluene. 3. 2-Picoline. 4. Ethylbenzene. 5. Toluene. 6. 2,6-Dimethylpiperidine. 7. Diisopropyl ketone. 8. 2,2,5-Trimethylhexane. 9. *n*-Octane

Table II. Binary Mixtures Containing Active Amyl Alcohol

Active Amyl Alcohol with				
Mole %	Wt. %	n_D^{25}	d_4^{25}	α_D^{25}
n-Octane				
100.00	100.00	1.4088	0.8154	−9.50
92.12	90.02	1.4070	0.8023	−8.27
83.87	79.94	1.4051	0.7894	−7.19
75.09	69.94	1.4034	0.7766	−6.20
66.02	59.99	1.4019	0.7634	−5.22
56.42	49.98	1.4006	0.7514	−4.36
46.40	40.05	1.3990	0.7396	−3.47
35.76	30.05	1.3978	0.7285	−2.52
24.56	20.08	1.3968	0.7180	−1.65
12.76	10.15	1.3956	0.7079	−0.88
0.00	0.00	1.3945	0.6985	−0.00
Chlorobenzene				
100.00	100.00	1.4088	0.8154	−9.50
91.78	89.74	1.4163	0.8393	−8.46
83.55	79.91	1.4253	0.8606	−7.50
74.87	70.00	1.4340	0.8843	−6.49
65.63	59.93	1.4452	0.9100	−5.52
55.99	49.91	1.4561	0.9367	−4.63
45.93	39.95	1.4671	0.9652	−3.83
35.45	30.08	1.4790	0.9955	−2.87
24.20	20.00	1.4919	1.0281	−2.02
12.56	10.11	1.5059	1.0623	−1.07
0.00	0.00	1.5219	1.1010	0.00
Ethylbenzene				
100.00	100.00	1.4088	0.8154	−9.50
91.43	89.86	1.4161	0.8198	−8.30
82.75	79.94	1.4240	0.8241	−7.20
73.67	69.91	1.4318	0.8277	−6.19
64.41	60.04	1.4396	0.8321	−5.26
54.60	49.97	1.4480	0.8362	−4.31
44.80	40.05	1.4565	0.8411	−3.45
34.14	30.09	1.4650	0.8459	−2.57
23.13	19.99	1.4741	0.8509	−1.75
11.94	10.12	1.4831	0.8563	−0.93
0.00	0.00	1.4930	0.8625	0.00
Toluene				
100.00	100.00	1.4088	0.8154	−9.50
90.25	89.86	1.4160	0.8193	−8.25
80.70	80.00	1.4234	0.8233	−7.13
70.81	69.89	1.4311	0.8269	−6.07
61.05	60.00	1.4389	0.8311	−5.12
51.14	50.04	1.4471	0.8351	−4.26
41.11	40.06	1.4552	0.8394	−3.35
30.93	30.00	1.4643	0.8440	−2.52
20.83	20.11	1.4735	0.8489	−1.69
10.46	10.06	1.4829	0.8543	−0.92
0.00	0.00	1.4930	0.8604	0.00
2,2,5-Trimethylhexane				
100.00	100.00	1.4088	0.8154	−9.50
92.85	89.92	1.4074	0.8039	−8.45
85.27	79.91	1.4060	0.7915	−7.30
77.26	70.02	1.4047	0.7788	−6.30
68.61	60.04	1.4034	0.7671	−5.33
59.31	50.05	1.4021	0.7546	−4.41
2,2,5-Trimethylhexane (continued)				
49.34	40.10	1.4009	0.7433	−3.44
38.40	30.00	1.3997	0.7324	−2.60
26.71	20.03	1.3987	0.7218	−1.71
14.03	10.08	1.3978	0.7120	−0.88
0.00	0.00	1.3971	0.7031	0.00
2-Picoline				
100.00	100.00	1.4088	0.8154	−9.50
90.39	89.91	1.4174	0.8287	−8.26
80.73	79.86	1.4264	0.8407	−7.07
70.93	69.79	1.4352	0.8530	−6.01
61.29	59.98	1.4439	0.8654	−5.03
51.38	50.01	1.4527	0.8776	−4.04
41.32	39.99	1.4612	0.8896	−3.23
31.14	29.97	1.4702	0.9021	−2.32
20.88	19.99	1.4792	0.9141	−1.55
10.56	10.06	1.4882	0.9271	−0.75
0.00	0.00	1.4982	0.9396	−0.00
2,6-Dimethylpiperidine				
100.00	100.00	1.4088	0.8154	−9.50
92.00	89.96	1.4134	0.8199	−8.24
83.63	79.92	1.4179	0.8239	−7.03
74.71	69.70	1.4219	0.8269	−5.86
65.81	59.98	1.4260	0.8287	−4.91
56.14	49.92	1.4291	0.8292	−3.94
46.14	40.02	1.4319	0.8290	−3.03
35.59	30.09	1.4339	0.8270	−2.20
24.28	19.98	1.4351	0.8245	−1.43
12.60	10.09	1.4360	0.8206	−0.67
0.00	0.00	1.4368	0.8156	0.00
o-Fluorotoluene				
100.00	100.00	1.4088	0.8154	−9.50
91.77	89.92	1.4134	0.8304	−8.41
83.33	80.00	1.4188	0.8457	−7.40
74.45	69.99	1.4241	0.8613	−6.41
65.26	60.06	1.4297	0.8780	−5.46
55.60	50.06	1.4354	0.8950	−4.62
45.46	40.02	1.4418	0.9136	−3.69
34.87	30.00	1.4482	0.9330	−2.80
23.92	20.11	1.4550	0.9531	−1.98
12.50	10.26	1.4624	0.9743	−1.03
0.00	0.00	1.4710	0.9981	0.00
Diisopropyl Ketone				
100.00	100.00	1.4088	0.8154	−9.50
92.02	89.91	1.4073	0.8139	−8.55
83.71	79.87	1.4060	0.8122	−7.86
75.12	69.98	1.4049	0.8105	−6.86
66.07	60.02	1.4038	0.8087	−5.97
56.54	50.05	1.4028	0.8070	−5.01
46.39	40.05	1.4015	0.8052	−4.11
35.76	30.06	1.4005	0.8035	−3.12
24.48	20.02	1.3993	0.8020	−2.18
12.68	10.08	1.3983	0.8003	−1.11
0.00	0.00	1.3972	0.7972	0.00

Distillations involving the piperidine derivatives and *o*-fluorophenol were run on the all-glass Wheeler column with a boil-up rate adjusted so that about one drop per second of the reflex liquid dropped back into the pot. Use of timer ratios of about 900 to 1 resulted in a take-off rate of 0.20 to 0.25 ml. per hour. Consequently, pot charges on this column were seldom more than 15 ml. and cuts of 0.7 to 2.5 ml. were usually taken during distillation. The column was normally equilibrated under total reflux overnight before removal of distillate was started.

Pot charges of known composition by weight were used. It was desirable, for the low-boiling azeotropes, to have a pot charge which would give several cuts of the pure azeotrope, then a clear transition to a pure component. Usually a preliminary run was made to determine the approximate composition of the azeotrope; then the composition of the pot charge was determined. In the high-boiling azeotropic systems, most of which were distilled through the Wheeler column using very small boil-up rates and high reflux ratios, selection of the proper composition of the pot charge was extremely important. The most satisfactory method was to make two preliminary runs, with the pot charge (1) mainly amyl alcohol, and (2) mainly the azeotropic agent. The refractive indices of the distillation cuts were determined. A convergence of these values from the two preliminary runs indicated the presence and approximate composition of the high boiling azeotrope. A binary mixture with the refractive index estimated to be approximately that of the azeotrope was used for the pot charge in the final fractional distillation.

The distillation fractions were analyzed by measurement of refractive index, density, and optical rotation. The physical constants listed in Table VI for the azeotropic mixtures were essentially constant for several distillation fractions. Compositions corresponding to the observed physical properties were determined from plots of physical properties *vs.* composition for each binary mixture.

Detailed experimental results for the isoamyl alcohol-*n*-octane system, as a typical example of a low boiling azeotrope, and for the active amyl alcohol-2,6-dimethylpiperidine system, as an example of a high boiling azeotrope, are presented below.

ISOAMYL ALCOHOL AND *n*-OCTANE. A pot charge of 10 grams of isoamyl alcohol and 90 grams of *n*-octane, purified as described, was refluxed overnight in the Podbielniak column, and distilled (Table III).

From the constant composition of cuts 2 to 5 and plots of physical properties *vs.* composition, the boiling point and composition of the isoamyl alcohol-*n*-octane azeotrope were determined: $n_D^{25} = 1.3970$ and $d_4^{25} = 0.7270$ correspond to 30.5 weight % or 36.3 mole % of isoamyl alcohol.

ACTIVE AMYL ALCOHOL AND 2,6-DIMETHYLPIPERIDINE. All distillations were carried out in the Wheeler column. In the first preliminary run 5 grams each of active amyl alcohol and 2,6-dimethylpiperidine, purified as described, were refluxed overnight and then fractionated. In the second preliminary run 6 grams of active amyl alcohol and 4 grams of 2,6-dimethylpiperidine were refluxed for 8 hours and then fractionated (Table IV).

Table III. Distillation of Isoamyl Alcohol-*n*-Octane Mixture

Distn. Cut	B.P., ° C.	Pressure, Mm. Hg	Ml.	n_D^{25}	d_4^{25}
1	<116.5	760.4	6	1.3963	0.7245
2	117.2	760.6	8	1.3972	0.7270
3	117.2	760.6	6	1.3971	0.7271
4	117.2	761.0	15	1.3970	0.7265
5	117.2	760.8	6	1.3969	0.7265
6	125.0	760.6	2	1.3954	0.7082
7	125.3	760.1	8	1.3952	0.6995
8	125.3	760.0	10	1.3951	0.6991
Pot res.	...	...	45	1.3952	0.6994

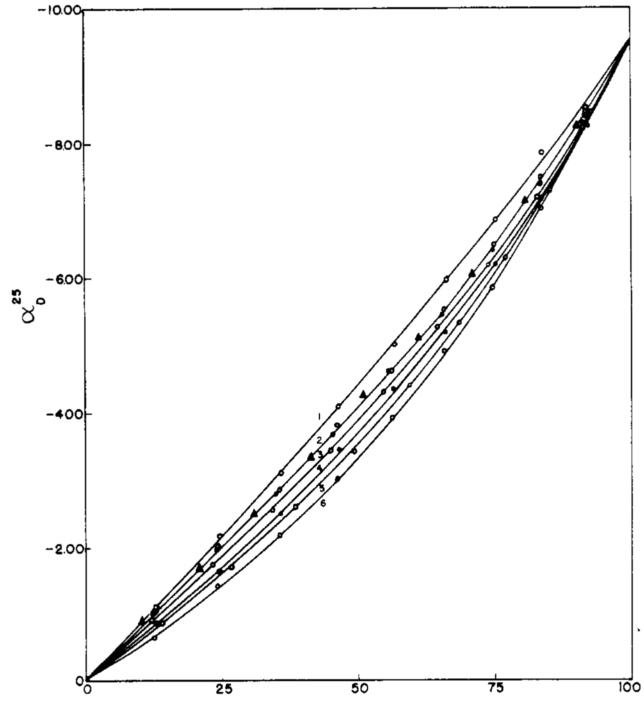

Figure 5. Rotations of binary mixtures containing active amyl alcohol

1. Diisopropyl ketone. 2. o-Chlorobenzene. 3. Ethylbenzene. 4. *n*-Octane. 5. 2,2,5-Trimethylhexane. 6. 2,6-Dimethylpiperidine.
o-Fluorotoluene. Toluene.

A mixture of active amyl alcohol and 2,6-dimethylpiperidine was prepared to have n_D^{25} 1.4275; 17 ml. were refluxed overnight in the Wheeler column and then fractionally distilled (Table V).

From the constant composition of cuts 4 to 8 and the pot residue in Table IV and plots of physical properties *vs.* composition, the boiling point and composition of the active amyl alcohol-2,6-dimethylpiperidine azeotrope were determined. The plot of density *vs.* composition goes through a maximum. The composition in best agreement with the compositions determined from the refractive index and rotation measurements is listed below.

n_D^{25} = 1.4278. 54.5 weight % or 60.5 mole % active amyl alcohol
d_4^{25} = 0.8290. 54.3 weight % or 60.4 mole % active amyl alcohol
α_D^{25} = -4.26. 53.8 weight % or 59.9 mole % active amyl alcohol

RESULTS AND DISCUSSION

The physical properties and compositions of the binary azeotropic mixtures studied are summarized in Table VI. The boiling points of the active amyl and isoamyl alcohols are listed the first time they appear, and the approximate boiling points of the second components in the binary mixtures are listed for comparison with the boiling points of the azeotropic mixtures. Atmospheric pressure varied from approximately 758 to 770 mm. of mercury for the various azeotropic distillations but was essentially constant for any one distillation. To facilitate comparisons, the listed boiling points of the azeotropes have been calculated for a pressure of 760 mm. of mercury (*26*). The average correction was 0.043° C. per mm. and the maximum correction was less than 0.5° C.

The composition of each azeotropic mixture was determined from the constant properties (refractive index, density and, in the case of active amyl alcohol mixtures, optical rotation) of the azeotropic cuts by plots of physical constants *vs.* composition reported above for the binary mixtures and is reported to the nearest whole per cent. In selecting the final value, more consideration was given to the value obtained from the physical constants that varied most with composition for a given system. For example, the experimental results for the active amyl alcohol-*n*-octane azeotrope were n_D^{25} 1.3981, d_4^{25} 0.7327, and α_D^{25} -2.89°, which corresponded to 38.7, 39.9, and 40.1 mole % active amyl alcohol. The differences between the physical constants for the pure components, active amyl alcohol and *n*-octane, are refractive index 0.0143 unit, density

Table IV. Preliminary Distillations of Active Amyl Alcohol-2,6-Dimethylpiperidine System

Distn. Cut	n_D^{25} First run	n_D^{25} Second run
1	1.4296	1.4242
2	1.4296	1.4247
3	1.4295	1.4249
4	1.4294	1.4251
5	1.4290	1.4257
6	1.4285	1.4261

Table V. Distillation of Active Amyl Alcohol-2,6-Dimethylpiperidine System

Distn. Cut	B.P., ° C.	Pressure, Mm. Hg	Ml.	n_D^{25}	d_4^{25}	α_D^{25}
1	< 131.0	768.5	0.8	1.4221	...	...
2	131.0	766.6	0.7	1.4269	...	...
3	131.0	767.4	0.7	1.4272	...	...
4	131.0	768.5	1.5	1.4277	0.8288	...
5	131.0	767.0	2.0	1.4278	0.8291	-4.23
6	131.0	767.4	1.5	1.4278	...	...
7	131.2	769.2	2.3	1.4279	0.8290	-4.26
8	131.0	767.8	3.7	1.4278	0.8290	-4.32
Pot. res.	...	...	1.6	1.4280	0.8290	-4.25

0.1169 unit, and optical rotation 9.50 units. These differences coupled with a precision of ±0.0002 in the density or refractive index measurements and ±0.02 in the optical rotation measurements permit determination of the composition of a *n*-octane–active amyl alcohol mixture with accuracies of the order of ±1.4, ±0.17, and ±0.21% from measurements of the refractive index, density, or optical rotation, respectively. The compositions obtained from the density and optical rotation measurements were thus given the most weight, and the composition of the *n*-octane–active amyl alcohol azeotrope is listed in Table VI as 40 mole %.

Azeotropes of active amyl alcohol with styrene and ethylbenzene at 60 mm. pressure are listed by Horsley (*23*). In the present work an azeotrope of isoamyl alcohol and ethylbenzene boiling at 125.7° C. at 760 mm. and containing 49 weight % of isoamyl alcohol was observed, in excellent agreement with the values reported by Berg, Harrison, and Montgomery (*4*), 125.9° C. at 760 mm. of mercury and 49 weight % of isoamyl alcohol. Lecat (*28*) reported an isoamyl alcohol-chlorobenzene azeotrope boiling at 124.35° C. at 760 mm. and containing 34 weight % of isoamyl alcohol. In the present work values of 123.9° C. at 760 mm. and 38 weight % of isoamyl alcohol were observed for the isoamyl alcohol–chlorobenzene system. Lecat (*29*) reported a boiling point higher than 132.5° C. at 760 mm. for the isoamyl alcohol-2-picoline system, but no composition for the azeotrope. In the present investigation the boiling point of the azeotrope was found to be 132.8° C., and the composition was 61 weight % isoamyl alcohol. Berg and Harrison (*2*) list the isoamyl alcohol–toluene system as nonazeotropic. The present article shows data for an azeotrope for this system boiling at 109.7° C. at 760-mm. pressure, approximately 1° below the boiling point of toluene, and containing 10 weight % of isoamyl alcohol. This discrepancy is undoubtedly due to the greatly increased efficiency of the fractional distillation equipment and the much larger reflux ratios used in the present work.

The formation of maximum or minimum boiling azeotropes is dependent on variations from ideality in the vapor pressures of solutions from those predicted by Raoult's law. Ewell and Berg (*3, 11*) attribute these deviations almost entirely to hydrogen bonding and consider other forces of attraction between molecules relatively unimportant. From the Ewell system of classification and the strength of the hydrogen bonds present, it is possible to predict the nature and approximate extent of these deviations (*3, 11*). If after two components are mixed there is a total net decrease in the amount of hydrogen bonding, there should be a positive deviation from Raoult's law, with the possibility of forming a minimum boiling azeotrope. If the net result is an increase in the amount of hydrogen bonding, there should be a negative deviation with the possibility of forming a maximum boiling azeotrope. Whether or not the deviation from ideality in a homogeneous solution is sufficient for the formation of azeotropes is also dependent on the relative boiling points of the pure components. If the boiling points are nearly the same, a relatively small deviation from ideality can result in formation of a maximum or minimum boiling azeotrope; if they are widely separated, a much greater deviation from ideality is necessary.

The two amyl alcohols investigated in this work are in Ewell's Class II; they have both active hydrogen atoms and donor atoms. The two compounds boil only 3.3° C. apart at atmospheric pressure and differ only in the position of the branch methyl group on the chain. The extreme

Table VI. Summary of Azeotropic Investigations

System	B.P. of Component, ° C.	Binary Azeotropic Mixtures					
		B.P. (760 mm.), ° C.	n_D^{25}	d_4^{25}	α_D^{25}	Alcohol, wt. %	Alcohol, mole %
n-Octane	126	...	...	...	...	...	...
Active amyl alcohol	128.5	117.0	1.3981	0.7327	−2.89	34	40
Isoamyl alcohol	132.0	117.0	1.3970	0.7265	...	30	36
Chlorobenzene	132	...	...	...	...	...	...
Active amyl alcohol		124.4	1.4630	0.9553	−4.12	43	49
Isoamyl alcohol		123.9	1.4671	0.9641	...	38	44
Ethylbenzene	136	...	...	...	...	...	...
Active amyl alcohol		125.0	1.4452	0.8360	−4.60	53	57
Isoamyl alcohol		125.7	1.4471	0.8326	...	49	53
Toluene	111	...	...	...	...	...	...
Active amyl alcohol		109.9	1.4811	0.8535	−1.10	12	12
Isoamyl alcohol		109.7	1.4821	0.8538	...	10	10
2,2,5-Trimethylhexane	124	...	...	...	...	...	...
Active amyl alcohol		115.5	1.3996	0.7310	−2.44	29	37
Isoamyl alcohol		116.0	1.3985	0.7270	...	26	34
o-Fluorotoluene	114	...	...	...	...	...	...
Active amyl alcohol		112.0	1.4580	0.9168	−1.54	16	19
Isoamyl alcohol		112.1	1.4588	0.9632	...	14	17
Diisopropyl ketone	125	...	...	...	...	...	...
Active amyl alcohol		124.1	1.3993	0.8020	−2.38	21	26
Isoamyl alcohol		124.5	1.3980	0.7992	...	8	10
2-Picoline	129	...	...	...	...	...	...
Active amyl alcohol		132.8	1.4540	0.8794	−4.00	49	50
Isoamyl alcohol		132.8	1.4402	0.8581	...	61	62
2,6-Dimethylpiperidine	128	...	...	...	...	...	...
Active amyl alcohol		130.7	1.4278	0.8290	−4.26	54	60
Isoamyl alcohol		132.6	1.4169	0.8177	...	76	80
1,2-Dimethylpiperidine	128	...	...	...	...	...	...
Active amyl alcohol		130.3	...	...	...	Undetd.	...
Isoamyl alcohol		132.5	1.4133	0.8158	...	81	85

similarity in structure greatly limits the possibility of any third component acting as an entrainer and forming a minimum boiling azeotrope with one alcohol but not the other. The greatest possibility of success in separating the alcohols by azeotropic techniques lies in finding a third component which will form azeotropes differing in boiling point by a considerably greater margin than the alcohols themselves. This, in the case of minimum boiling azeotropes, would be most likely if the boiling point of the azeotropic agent were of the same order as that of the active amyl alcohol or slightly lower.

The addition of Class V compounds to Class II amyl alcohols can result only in breaking hydrogen bonds with a resultant positive deviation from ideality. If the boiling points and other factors are favorable, such a combination could only form a minimum boiling azeotrope, if any. Minimum boiling azeotropes were observed for binary mixtures of isoamyl alcohol and active amyl alcohol with each of the Class V compounds, *n*-octane, chlorobenzene, ethylbenzene, toluene, and 2,2,5-trimethylhexane. However, in the case of each Class V compound tried, the boiling points of the amyl alcohol azeotropes were closer together than the boiling points of the amyl alcohols themselves. According to the principles discussed, *n*-octane (b.p. 126° C.) appeared to be an ideal substance for azeotropic separation of the two amyl alcohols, but the boiling points of the two azeotropes were identical. Chlorobenzene has a boiling point of 132° C., identical with that of isoamyl alcohol. Here the greater boiling point depression of the chlorobenzene-isoamyl alcohol system only brought the boiling points of the two azeotropes closer together. The choice of a Class V azeotropic agent with the theoretical optimum boiling point was apparently not a sufficient criterion for azeotropic separation of the two amyl alcohols. The variations in structure of the five Class V compounds investigated did not result in differentiation in the ability of these compounds to decrease hydrogen bonding in the isoamyl or active amyl alcohol which might reflect the difference in position of the branch methyl group.

Low boiling azeotropes are much more numerous than high boiling azeotropes. A high boiling azeotrope will result when, on mixing two liquids, increase in the total amount of hydrogen bonding gives a large enough negative deviation from Raoult's law. The extent of deviation would be dependent on the difference in boiling point between the liquids. Because the formation of a high boiling azeotrope is thus dependent on the net formation of more hydrogen bonds on mixing two liquids, the structural differences of the two amyl alcohols under investigation would seem to offer a greater chance of having a differentiating effect than in the case of minimum boiling azeotropes. In other words, active amyl alcohol, with a methyl group on the 2-carbon, should provide more steric hindrance to increased hydrogen bond formation with an azeotroping agent than isoamyl alcohol, with a methyl group on the 3-carbon. By proper choice of azeotropic agent, as to both structure and boiling point, it would seem possible to form a high boiling azeotrope with isoamyl alcohol and not with active amyl alcohol and thus spread the boiling points sufficiently to permit easy separation.

Mixtures of alcohols with compounds containing only donor atoms (Class III) will result in both making and breaking hydrogen bonds, but usually a net decrease in hydrogen bonds with the formation of a minimum boiling azeotrope. However, such a mixture may result in a negative deviation from Raoult's law with the formation of a maximum boiling azeotrope. In a series of ketones investigated, mesityl oxide (b.p. 130° C.), cyclopentanone (b.p. 130° C.), and diisopropyl ketone (b.p. 125° C.), only the diisopropyl ketone formed azeotropes with the two amyl alcohols. In the cases of the mesityl oxide and cyclopentanone, compounds with optimum boiling points for the formation of azeotropes with the amyl alcohols, the oxygen donor atom apparently caused formation of about as many new hydrogen bonds as were broken on mixing the ketones with the alcohols. With the diisopropyl ketone mixing caused a net decrease in hydrogen bonds with the formation of minimum boiling azeotropes with boiling points of 124.1° and 124.5° C. at 760 mm. for the active amyl and isoamyl alcohols, respectively. The steric factors associated with the branched alkyl groups of the diisopropyl ketone permitted a somewhat greater deviation from ideality in the case of the isoamyl alcohol than in the active amyl alcohol. However, as minimum boiling azeotropes were formed, this only brought the boiling points of the two azeotropes closer together. The deviations from ideality using diisopropyl ketone were much smaller than those observed for 2,2,5-trimethylhexane (b.p. 124° C.) which formed azeotropes with active and isoamyl alcohols boiling at 115.5° and 116.0° C., respectively. The hydrocarbon could only break hydrogen bonds, whereas the ketone could also make new hydrogen bonds.

o-Fluorotoluene, in which the fluorine attached to the aromatic nucleus might act as a weak donor atom at best, formed low boiling azeotropes with almost identical boiling points with both alcohols. The deviation from ideality was thus somewhat greater in the binary mixture containing isoamyl alcohol than in the one containing active amyl alcohol. The other two fluorine-containing compounds—*o*-fluorophenol and 2,2,3,3,4,4,5,5-octafluoro-1-pentanol—did not form azeotropic systems with either amyl alcohol. Each compound contained active hydrogens and oxygen as well as fluorine as potential donor atoms (Class II). Phenols are known to form high boiling azeotropes with alcohols when the boiling points of the compounds are of the right order of magnitude. In the present case, *o*-fluorophenol, the lowest boiling phenol available, was apparently still far too high boiling (151.5° C.) for any deviations from ideality when mixed with either amyl alcohol to permit formation of an azeotropic mixture. The multiplicity of fluorine atoms as potential donor atoms in the octafluoropentanol (b.p. 140° C.) apparently did not sufficiently increase hydrogen bonding when mixed with either amyl alcohol to overcome the large boiling point differences between the compounds and give maximum boiling azeotropes.

Amines, with the nitrogen atom acting as a donor atom of varying strength depending on the structure, often form high boiling azeotropes with alcohols. Tertiary amines have only donor atoms (Class III), whereas primary and secondary amines have active hydrogens as well as the nitrogen donor atom (Class II). Mixtures of 2-picoline with active amyl and isoamyl alcohols formed maximum boiling azeotropes which had identical boiling points of 132.8° C., but differed considerably in composition. The single methyl group ortho to the tertiary nitrogen of 2-picoline apparently did not result in sufficient steric inhibition of the formation of new hydrogen bonds when mixed with the amyl alcohols to differentiate between them as to formation of the maximum boiling azeotropes. Deviation from ideality was greater in the 2-picoline-active amyl alcohol mixture, where the boiling points of the two components were almost identical, than in the 2-picoline-isoamyl alcohol mixture.

Preliminary distillations at atmospheric pressure of mixtures of isoamyl alcohol and 2,6-lutidine, which contains two methyl groups ortho to the tertiary nitrogen atom, did not indicate formation of an azeotropic mixture. The boiling point (141° C.) of 2,6-lutidine was somewhat above the optimum boiling point for the formation of an azeotrope with isoamyl alcohol at atmospheric pressure. Nutting and Horsley (*23*) have published a graphical method based on the use of the Cox vapor pressure chart (*9*) for predicting the effect of pressure on an azeotropic system. Determination of the boiling points of 2,6-lutidine and isoamyl alcohol at various pressures and a plot of the results on a Cox vapor pressure chart indicated that the boiling points of isoamyl alcohol and 2,6-lutidine would be essentially identical at 70-mm. pressure. Distillation of a mixture of these two components at 70-mm. pressure using the Podbielniak column indicated the possibility of a maximum boiling azeotrope. The data were not entirely conclusive. The reduction in pressure also resulted in convergence of the boiling points of the active amyl and isoamyl alcohols, so that the possibility of separating the two alcohols by azeotropic techniques under these conditions appeared too slight to warrant further investigation. The 2,6-lutidine–active amyl alcohol system was not investigated at atmospheric pressure, because the boiling point difference was greater and the steric inhibition of the formation of new hydrogen bonds would be greater than in the case of the 2,6-lutidine–isoamyl alcohol system.

2,6-Dimethylpiperidine formed maximum boiling azeotropes with both active amyl and isoamyl alcohols. Piperidine derivatives, as azeotropic agents, contain donor nitrogen atoms which are considerably stronger than in the pyridine derivatives first discussed. The 2,6-dimethylpiperidine, which has two methyl groups ortho to the donor nitrogen as well as an active hydrogen atom attached to the nitrogen, caused a sufficient increase in hydrogen bond formation when mixed with either amyl alcohol to give a maximum boiling azeotrope, although its boiling point was slightly below that of active amyl alcohol. The results indicate that the relative boiling points of the two components of each mixture were of more importance in the formation of the azeotrope than any differentiating effect of the possible steric inhibition of hydrogen bonding, because of the two ortho methyl groups in the 2,6-dimethylpiperidine. 1,2-Dimethylpiperidine, which has no active hydrogen, has a slightly stronger nitrogen donor atom and a somewhat greater steric inhibition of hydrogen bonding on the nitrogen than 2,6-dimethylpiperidine. The boiling points of the maximum boiling azeotropes for the binary mixtures of 1,2-dimethylpiperidine with isoamyl and active amyl alcohols were, however, essentially identical with the boiling points for mixtures involving 2,6-dimethylpiperidine. The increase in steric hindrance associated with the presence of a methyl group on the nitrogen in 1,2-dimethylpiperidine apparently did not affect formation of azeotropes with respect to the differences in position of the branch methyl group in isoamyl and active amyl alcohol. The presence of the ethyl group on the nitrogen atom of 1-ethylpiperidine affectively prevented formation of sufficient new hydrogen bonds for azeotrope formation. The 1-ethylpiperidine, which had a boiling point of 131° C., ideal for differentiation between the two amyl alcohols by azeotrope formation, did not form azeotropic mixtures with isoamyl or active amyl alcohol.

CONCLUSIONS

The strong hydrogen bonding of both pure amyl alcohols and the similarities in structure and properties make separation of active amyl and isoamyl alcohols by azeotropic distillation extremely difficult. The position of the branch methyl group results in slightly greater hindrance to hydrogen bonding with an azeotropic agent in active amyl alcohol. The steric configuration of the azeotropic agent does not appear significant in the formation of minimum boiling azeotropes. In the formation of maximum boiling azeotropes the steric configuration of the azeotropic agent affected mainly its own ability to form new hydrogen bonds. The slight difference in deviation from Raoult's law could be correlated with the structure of the azeotropic agent and the position of the branch methyl group in the amyl alcohol. The difference between the boiling point of the azeotropic agent and the amyl alcohol was extremely important in azeotrope formation, more so for maximum boiling than for minimum boiling azeotropes. Minimum boiling azeotropes were observed when the difference in boiling point of the components was over 20° C.; no maximum boiling azeotropes were observed where it was over 5° C. Separation of the two amyl alcohols by azeotropic distillation at reduced pressures does not appear likely, because the boiling points of active amyl alcohol and isoamyl alcohol converge with reduction in the pressure. Successful azeotropic separation of active amyl and isoamyl alcohol will require somewhat different properties in the azeotropic agent than those reported here.

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