864. *Physical Properties and Chemical Constitution. Part XXVIII.* Pyridine Derivatives.*

By COLIN T. KYTE, GEORGE H. JEFFERY, and ARTHUR I. VOGEL.

Pure samples of pyridine, α-, β-, and γ-picoline, 2-, 3-, and 4-alkylpyridines (ethyl to n-heptyl), 2,3-, 2,6-, 2,4-, 2,5-, and 3,5-lutidine, 2-, 3-, and 4-acetylpyridine, and the alkyl (methyl to n-heptyl) esters of picolinic, nicotinic, and isonicotinic acid have been prepared and their physical properties (refractive indices at 20° and densities and surface tensions over a range of temperatures) have been determined: representative ultraviolet and infrared spectra were also measured. The CH_2 differences for parachors, molecular refractions, and molecular refraction coefficients for the 2-, 3-, and 4-alkylpyridines and for the n-alkyl esters, as well as the corresponding constants for the 2-, 3-, and 4-pyridyl group, have been evaluated.

Subsidiary measurements on formyl-, hydroxymethyl-, and acetylpyridines, dialkyl oxalates, and aliphatic aldehydes have also been made.

No systematic investigation of the physical properties of pure pyridine derivatives was available when the work described in this paper began, in September 1953.[1] After completion of our experiments on pyridine and alkylpyridines, an exhaustive study at the National Chemical Laboratory, Teddington, of the purification of pyridine, the isomeric picolines, and 2,6-lutidine and some of their salient physical properties was published:[2] although we worked with small quantities of commercial starting materials and by simpler procedures, our results agree excellently with these, even to identity of ultraviolet and infrared spectra.

Pyridine and Alkylpyridines.—The purification of pyridine and α-, β-, and γ-picoline is described in the Experimental section. We find, contrary to the experience of Heap,

* Part XXVII, *J.*, 1959, 3521.

[1] Kyte, Ph.D. Thesis, London, September, 1956.

[2] Biddiscombe, Coulson, Handley, and Herington, *J.*, 1954, 1957.

Jones, and Speakman,[3] that each of these bases gives two zinc chloride complexes $(Base)_2,ZnCl_2$ and $(Base)_2,HCl,ZnCl_2$; these are readily separated by their differing solubilities in hot ethanol and can be recrystallised to sharp and constant melting points (the former salts have the higher melting points). The complexes $(Base)_2,HCl,ZnCl_2$ are preferred for purifications. For β-picoline, the γ-picoline and 2,6-lutidine are conveniently removed by utilising their greater reactivity with a mixture of phthalic anhydride and acetic anhydride.[4] γ-Picoline, regenerated from the " acid " zinc chloride complex, was treated with urea to remove 2,6-lutidine: the pure compound is obtained by fractional freezing in a special apparatus (see Appendix).

Five lutidines were investigated. Purification of 2,3- and 2,6-lutidine was effected *via* the insoluble urea complexes; 2,5-lutidine *via* the phenol complex, which is solid at room temperature; 2,4-lutidine *via* the hydrochloride prepared in benzene solution; and 3,5-lutidine was a synthetic product.

In all cases purification was effected in three stages: (i) fractional distillation, (ii) conversion into a solid derivative, followed by regeneration of the base until the physical properties (density, refractive index, and ultraviolet spectrum) were constant, and (iii) fractional freezing.

2-, 3-, and 4-Alkylpyridines were prepared by alkylation of the corresponding picolines in the presence of sodamide: [5]

$$C_5H_4N\cdot CH_3 + NaNH_2 \rightleftharpoons C_5H_4N\cdot CH_2^-Na^+ + NH_3$$
$$C_5H_4N\cdot CH_2^-Na^+ + RX \longrightarrow C_5H_4N\cdot CH_2R + Na^+X^-$$

Alkyl chlorides are the preferred alkylating reagents. The experimental conditions for reaction depend on the picoline and the physical state of the sodamide. With α-picoline and a colloidal suspension of sodamide in xylene, only monoalkylation ensued at 140° (cf. Brown and Murphy [6] who found it necessary to keep the temperature below 15° in order to prevent disubstitution with sodamide freshly prepared in liquid ammonia). γ-Picoline reacted more vigorously with colloidal sodamide in xylene and an alkyl chloride: the optimum yield of n-alkylpyridine $C_5H_4N\cdot CH_2R$ (*ca.* 36%) was obtained at 0° but this was usually accompanied by 19—20% of dialkylated product $C_5H_4N\cdot CHR_2$ together with unchanged γ-picoline; formation of the dialkylated product can be avoided by alkylation in liquid ammonia. Satisfactory monoalkylation of β-picoline requires use of liquid ammonia solutions and sodamide prepared in this solvent. It is interesting that the carbanions $X\cdot CH_2^-$ formed by interaction of sodamide and monomethylpyridines are coloured: that from α-picoline is red, γ-picoline green, and β-picoline yellowish-brown. This colour is completely discharged when the equivalent quantity of alkyl halide is added. In liquid ammonia solution there is some competition between the carbanion and the amide ion for the alkyl halide, and some of the latter is converted into the alkylamine. The best yields of n-alkylpyridines are obtained by using a small excess of alkyl halide and sodamide to allow for this side reaction. Alkylamine formation interfered most seriously when the lower alkyl halides (particularly iodides) were involved; thus the yield of 3-ethylpyridine was only 5—10% with β-picoline and methyl bromide or iodide, but was improved appreciably by using a large excess of both sodamide and alkyl halide. No difficulty was experienced in preparing 2- and 4-ethylpyridine by this method, but the b. p. of the 4-ethylpyridine was not altogether satisfactory. The preferred method for preparation of the pure monoethylpyridines was Wolff–Kishner reduction of the methyl ketones.

Secondary alkylpyridines were readily prepared in liquid ammonia by using two equivalents each of sodamide and alkyl halide, or by alkylation in two stages: $X\cdot CH_3 \longrightarrow X\cdot CH_2R \longrightarrow X\cdot CHRR'$.

[3] Heap, Jones, and Speakman, *J. Amer. Chem. Soc.*, 1921, **43**, 1936.
[4] Reithoff, Savitt, Richards, and Othmer, *Ind. Eng. Chem. Analyt.*, 1946, **18**, 458.
[5] Cf. Tchitchibabin, *Bull. Soc. chim. France*, 1936, **3**, 1607; 1938, **5**, 429, 436.
[6] Brown and Murphy, *J. Amer. Chem. Soc.*, 1951, **73**, 3308.

4-Alkylpyridines (ethyl to n-butyl) were also prepared from pyridine by a slight modification of Wibaut and Arens's method.[7] The physical properties of the purified products were in good agreement with those obtained by the alkylation of γ-picoline.

n-Alkyl Pyridinemonocarboxylates.—Pure picolinic, nicotinic, and isonicotinic acid were prepared by oxidation of the pure picolines with potassium permanganate.[8] The esters of picolinic acid (methyl to n-pentyl) were prepared by the hydrogen chloride method, as were n-butyl nicotinate and ethyl and n-propyl isonicotinate. The sulphuric acid method was employed for methyl, ethyl, n-propyl, and isopropyl nicotinate and for methyl, n-propyl and isopropyl isonicotinates. The higher esters (and also s-butyl and t-butyl nicotinate) are readily obtained by conversion of the acid with thionyl chloride into the acid chloride hydrochloride, followed by reaction with the appropriate alcohol; they were purified by conversion in ether solution into the insoluble hydrochlorides, a procedure which removes traces of sulphur compounds.

Physical Data.—The results for parachors (P), molecular refractivities (R), and

TABLE 1. *Mean values for* CH_2.

Compounds	P	R_C	R_D	R_F	$R_{G'}$	Mn_D^{20}
2-Alkylpyridines	39·2	4·63	4·65	4·70	4·76	20·59
s	0·6	$0·00_3$	$0·00_2$	0·02	0·06	0·04
3-Alkylpyridines	38·8	4·63	4·65	4·70	4·75	20·55
s	0·7	$0·00_2$	0·00	0·01	$0·00_2$	0·05
4-Alkylpyridines	39·4	4·63	4·65	4·70	4·76	20·60
s	0·6	$0·00_2$	0·00	$0·00_2$	0·02	0·09
Alkyl picolinates	37·7	4·62	4·64	4·69	4·75	20·52
s	0·7	0·01	$0·00_{44}$	0·01	0·04	0·09
Alkyl nicotinates	38·4	4·62	4·63	4·69	4·74	20·52
s	0·6	0·02	0·02	0·03	0·04	0·34
Alkyl isonicotinates	39·0	4·62	4·64	4·70	4·75	20·50
s	0·7	0·01	0·01	0·01	0·04	0·09

molecular refraction coefficients (Mn_D^{20}) for all the compounds investigated are collected in Tables 5 and 6 (pp. 4467 and 4468). The mean values of the CH_2 increments for the various series were calculated by the method of least squares, and are given in Table 1: the data for the methyl compounds (for P) and for the methyl and ethyl compounds (which appear to be anomalous for R and Mn_D^{20}) were not used in the calculations; s is the standard deviation. The mean values for the CH_2 increments agree well with those found from normal aliphatic hydrocarbons [9] and other series; the parachor values seem somewhat low.

It is of interest to compute the constants for the pyridyl group (C_5H_4N). The following expressions may be used:

Alkylpyridines: $$(C_5H_4N) = (C_5H_4N)R - (R) - (C{-}C) \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where (R) is the constant for the alkyl group: [10]

Pyridinecarboxylic esters:

$$(C_5H_4N) = (C_5H_4N)CO_2R - \tfrac{1}{2}(CO_2R)_2 - \tfrac{1}{2}(C{-}C) \quad . \quad . \quad . \quad . \quad (2)$$

where $(CO_2R)_2$ is the corresponding di-n-alkyl oxalate; [10] or

$$(C_5H_4N) = (C_5H_4N)CO_2R - (R) - (C{=}O) - (C{-}O) - (C{-}C) \quad . \quad . \quad . \quad (3)$$

Expression (2) is preferred to (3) since some allowance is thereby made for the effect of conjugation of the carbonyl group with the pyridine ring. The mean results for the pyridyl group are collected in Table 2; in the deduction of the mean values, methyl has

[7] Wibaut and Arens, *Rec. Trav. chim.*, 1941, **60**, 119; 1942, **61**, 59; cf. Frank and Smith, *Org. Synth.*, 1947, **27**, 38.
[8] Black, Depp, and Corson, *J. Org. Chem.*, 1949, **14**, 14.
[9] Vogel, Part IX, *J.*, 1946, 133.
[10] Some new experimental data for di-n-alkyl oxalates are given in the Experimental section; see also Part XIII, *J.*, 1948, 631. For constants used in the calculations, see Part XXIV, *J.*, 1952, 514.

been neglected for the parachor, and both methyl and ethyl for the refractivities; s is the standard deviation. The constants derived from the monoalkylpyridines for the pyridyl group are regarded as the most trustworthy; it is doubtful whether adequate allowance for conjugation is made in the method of calculation used for the esters. The mean values are compared below with those deduced from the experimental data for pyridine: $(C_5H_4N) = C_5H_5N - (C{-}H)$. The small differences found in the constants derived from the 2-, 3-, and 4-alkylpyridines are regarded as outside the limits of experimental error, but for most purposes a mean value is sufficiently accurate.

(C_5H_4N)	P	R_C	R_D	R_F	$R_{G'}$	Mn_D^{20}
From alkylpyridines	174·1	22·59	22·77	23·32	22·74	115·54
From pyridine	180·5	22·15	22·40	22·85	23·13	115·59

TABLE 2. *Mean constants for pyridyl groups from alkylpyridines and esters of pyridinecarboxylic acids.*

Compound	P	R_C	R_D	R_F	$R_{G'}$	Mn_D^{20}
			2-Pyridyl group			
2-Alkylpyridine	173·9	22·67	22·84	23·41	23·85	115·23
s	1·5	0·01	0·00	0·03	0·06	0·02
Alkyl picolinates	171·0	22·31	23·01	23·08	23·60	118·51
s	3·0	0·02	0·02	0·02	0·05	0·19
			3-Pyridyl group			
3-Alkylpyridines	173·2	22·56	22·74	23·29	23·70	115·68
s	3·3	0·01	0·00	0·03	0·02	0·07
Alkyl nicotinates	172·6	22·26	22·96	23·03	23·54	117·63
s	2·5	0·01	0·02	0·02	0·03	0·24
			4-Pyridyl group			
4-Alkylpyridines	175·2	22·55	22·72	23·27	23·68	115·72
s	0·9	0·01	0·00	0·03	0·04	0·05
Alkyl nicotinates	173·0	22·20	22·90	22·96	23·47	117·12
s	1·7	0·02	0·02	0·02	0·05	0·25

A comparison of the calculated values of some physical properties of the lutidines with those deduced from the actual experimental observations is of some interest. The calculated values were obtained by evaluating the contribution of the CH_2 group in the α-, β-, and γ-positions of the picolines ($C_5H_4N{\cdot}CH_3 - C_5H_4NH$) and adding this to the experimental values of the appropriate picoline. The results are collected in Table 3.

TABLE 3. *Lutidines: observed and calculated results.*

	P		R_D		Mn_D^{20}	
Lutidine	Obs.	Calc.	Obs.	Calc.	Obs.	Calc.
2,6-	275·4	276·2	34·03	34·04	160·45	160·10
2,4-	276·4	274·8	33·92	33·96	160·82	160·55
2,5-	274·2	275·5	33·92	33·95	160·78	160·64
2,3-	271·8	275·5	33·78	33·96	161·64	160·64
3,5-	274·3	277·1	33·80	33·86	161·38	161·18

Measurements have also been made on hydroxymethylpyridines, pyridinealdehydes, and methyl pyridyl ketones. The constants for the pyridyl group (Table 4) were calculated from the following relations:

$$(C_5H_4N) = C_5H_4N{\cdot}CH_2{\cdot}OH - 2(C{-}H) - (C{-}C) - (C{-}O)_{\text{ethers}} - (O{-}H)_{\text{alcohols}}$$

$$(C_5H_4N) = C_5H_4N{\cdot}CHO - (CHO) - (C{-}C)$$

$$(C_5H_4N) = C_5H_4N{\cdot}COCH_3 - (C{=}O)_{\text{Me ketones}} - 2(C{-}C) - (CH_3)$$

Most of the constants are given in Part XXIV.[11] The mean values for (CHO), derived

[11] Vogel, Cresswell, Jeffery, and Leicester, Part XXIV, *J.*, 1952, 514.

from new measurements on a number of aliphatic aldehydes [(CHO) = R·CHO — (R) — (C–C)], are as follows: P, 60·5; R_C, 5·15; R_D, 5·16; R_F, 5·28; $R_{G'}$, 5·32; Mn_D^{20}, 33·79. The hydroxymethylpyridines and pyridinealdehydes were purified commercial samples and the results, particularly for pyridine-3-aldehyde, are not as trustworthy as those deduced from the alkyl pyridines.

TABLE 4. *Constants for pyridyl group* (C_5H_4N) *from pyridine alcohols, aldehydes, and ketones.*

	P	R_D	Mn_D^{20}		P	R_D	Mn_D^{20}
2-C_5H_4N·CH_2·OH...	180·8	22·62	117·08	2-C_5H_4N·$COCH_3$ ...	176·9	23·05	117·57
3-C_5H_4N·CH_2OH ...	182·5	22·60	117·30	3-C_5H_4N·$COCH_3$ ...	178·9	22·94	119·41
				4-C_5H_4N·$COCH_3$ ...	178·9	22·82	118·43
2-C_5H_4N·CHO	178·5	23·38	117·52				
3-C_5H_4N·CHO	180·5	23·43	119·32				
4-C_5H_4N·CHO	184·8	23·29	118·73				

Some new measurements on dialkyl oxalates have been made. The mean constants for 2(CO_2) in oxalates, calculated from 2(CO_2) = $(CO_2R)_2$ — 2(R) — 2(C–C), are: P, 64·9; R_C, 6·45; R_D, 6·47; R_F, 6·60; $R_{G'}$, 6·65; Mn_D^{20}, 64·18. These constants are higher, owing to conjugation, than the values derived from aliphatic esters.[10]

EXPERIMENTAL

Physical Measurements.—Surface tensions were measured by the maximum bubble pressure method (for apparatus, see Part XXIV [11]). The tubes comprising the bubbler were of precision bore with the narrow-bore capillary of 0·1—0·2 mm. diameter and the wider-bore capillary of 2—3 in diameter. The difference in heights of the two arms of the U-tube was determined by means of a Precision Tool and Instrument Co. cathetometer, reading to 0·01 mm. The four apparatuses used were calibrated with pure benzene.

Densities were determined with a Pyrex glass pycnometer (cf. Part III [12]) of about 1 ml. capacity at 20° (thermostat maintained at 20° ± 0·01°), about 41° (methylene chloride vapour), about 61° (chloroform vapour) and about 86° (trichloroethylene vapour), the exact temperature being read on a small Anschütz thermometer placed in the vapour-jacket with the pycnometer. The density at $t°$ (d_4^t) was calculated from the observed densities by assuming a linear variation with temperature. The parachor P was calculated in the usual manner; allowance was made for the density of the vapour (computed as described by Sugden, Reed, and Wilkins [13]) where the temperature of measurement was within 50° of the b. p. of the sample. Only the values of the density and surface tension at rounded temperatures (20°, 40°, 60°, and 85°) and the mean values of the parachor are recorded.

The refractive index measurements were made at 20° ± 0·05° in a Hilger–Chance refractometer (precision model) for liquids. The light sources were an electric sodium lamp for the D line, and a Guild hydrogen tube for the C, F, and G′ lines. The G′ line was sometimes rather faint and in consequence $n_{G'}$ is slightly less trustworthy than the other refractive indices.

Unless otherwise stated, b. p.s are corrected. All the compounds were re-fractionated immediately before measurement. The purity of every compound was established by vapour-phase chromatography (a Griffin & George VPC apparatus Mark II was employed) and by infrared spectroscopy. A modified Claisen flask with 4″ or 6″ fractionating side-arm packed with Fenske helices or with 1/16″ Dixon gauze rings was used for this purpose: if this proved inefficient, a larger column 8″ or 12″ in length, 14 mm. in diameter, packed with 1/16″ Dixon gauze rings and fitted with a variable take-off head, was employed.

Pyridine.—Four methods of purification of " AnalaR " pyridine were used.

(i) The sample was dried over powdered barium oxide, filtered, and distilled through an 8″ Widmer column. After a small fore-run, the main fraction, b. p. 114·9°/768 mm., was collected: it had d_4^{20} 0·9819, n_D^{20} 1·50987.

(ii) Pyridine (80 ml.) was added with stirring to a solution of anhydrous zinc chloride (68 g.) and concentrated hydrochloric acid (42 ml.) in absolute ethanol (200 ml.) After cooling, the precipitate, $(C_5H_5N)_2,ZnCl_2,HCl$, was filtered off, washed with a little alcohol, and dried in the air. The yield was 136 g., and the m. p. 151—152°; two recrystallisations from absolute

[12] Vogel, *J.*, 1938, 1325.
[13] Sugden, Reed, and Wilkins, *J.*, 1925, **125**, 1540.

ethanol raised the m. p. to 153°. The free base was liberated by addition of an excess of sodium hydroxide solution and steam-distilled until the distillate was no longer alkaline to litmus; solid sodium hydroxide (*ca.* 20 g.) was then added to the distillate, and the upper layer dried by shaking it with potassium hydroxide pellets, followed by storage for several days over powdered barium oxide. On fractionation through an 8″ Widmer column most distilled at 115·0°/771 mm. and had d_4^{20} 0·9828, n_D^{20} 1·51007.

The zinc chloride complex produced by adding pyridine to a solution of zinc chloride and hydrochloric acid in 50% aqueous ethanol [3] melts over the range 150—210°, which is unaffected by recrystallisation from absolute alcohol. Recrystallisation from 60% alcohol yields a salt of m. p. 203—208°; the m. p. is raised to 208° by further recrystallisation. Extraction of the crude product with a small volume of boiling absolute ethanol so that only a small portion of the solid dissolves gives a residue of m. p. 200—208°; the alcoholic solution deposits a solid of m. p. 150—162°, which melts at 152° after recrystallisation from absolute ethanol. Recrystallisation of the last material from aqueous solvents leads to a product of m. p. 208°. Analysis shows that the complex, m. p. 153°, is the " acid " salt $(C_5H_5N)_2,ZnCl_2,HCl$, whilst that of m. p. 208° is $(C_5H_5N)_2,ZnCl_2$.

(iii) A solution of pyridine (60 ml.) in 10% (w/v) hydrochloric acid (300 ml.) was added to a solution of mercuric chloride (405 g.) in hot water (2·3 l.), and the mixture was allowed to cool. The white crystals of the complex $(C_5H_5N)_2,2HgCl_2$ were filtered off, washed with a little alcohol, and dried at 110°: the m. p. (178—178·5°) was raised by two recrystallisations from 1% hydrochloric acid to 178·5—179°. The base was liberated, dried, and distilled as under (ii). The main fraction, b. p. 115·8°/777 mm., had d_4^{20} 0·9832, n_D^{20} 1·51021.

(iv) Pyridine (250 ml.) was dissolved in 17% hydrochloric acid (600 ml.), and steam was passed through the boiling solution until about 2 l. of distillate were collected; the first few ml. of distillate contained oily drops of an evil-smelling liquid. The free base was isolated by rendering the residue strongly alkaline with sodium hydroxide, steam-distillation, and addition of solid sodium hydroxide (200 g.) to the steam-distillate; the upper layer was dried (KOH, folllowed by powdered BaO) and distilled through an 8″ Widmer column. The main fraction boiled at 115·0°/759 mm. and had d_4^{20} 0·9831, n_D^{20} 1·51021. These physical constants may be compared with those of Timmermans [14] (d_4^{20} 0·9830, n_D^{20} 1·5102) and Biddiscombe *et al.*[2] (d_4^{20} 0·98310, n_D^{20} 1·51020).

A sample prepared by method (iv) was used for the detailed measurements of the physical properties.

α-Picoline.—The starting material was α-picoline of 99% purity (Yorkshire Tar Distillers). Four methods of purification were used and are similar to those described for pyridine.

(i) A sample, dried over powdered barium oxide and fractionated, had b. p. 129·7—129·8°/777 mm., d_4^{20} 0·9443, n_D^{20} 1·50109.

(ii) α-Picoline (90 ml.) was added to a solution of anhydrous zinc chloride (168 g.) and of concentrated hydrochloric acid (42 ml.) in absolute ethanol (200 ml.). The resulting white crystals were filtered off and recrystallised twice from absolute ethanol (m. p. 118·5—119·5°). This was the acid salt $(C_6H_7N)_2,ZnCl_2,HCl$. The α-picoline, liberated as described for pyridine and fractionated through a 6″ Dufton column, had b. p. 129·7—129·8°/778 mm., d_4^{20} 0·9443, n_D^{20} 1·50102.

In presence of a larger proportion of water, the complex $(Base)_2,ZnCl_2$, m. p. 166—168°, is also formed and can be separated as described for pyridine. The " acid " zinc chloride salt is preferred in all cases for purification because of the ease with which it is recrystallised from absolute ethyl alcohol.

(iii) α-Picoline (80 ml.) was added to a solution of mercuric chloride (430 g.) in hot water (2·4 l.), and the solution allowed to cool. The resulting white crystals, $(C_6H_7N)_2,HgCl_2$, were filtered off, washed with a little alcohol, and when dried at 110° melted at 153—154°; two recrystallisations from 1% hydrochloric acid raised the m. p. to 156—157°. The α-picoline, isolated as described for pyridine and distilled through a 6″ Dufton column, had b. p. 129·5°/768 mm., d_4^{20} 0·9444, n_D^{20} 1·50106.

(iv) A solution of the base in 17% hydrochloric acid was treated with steam (only a minute amount of non-basic impurity was separated), the solution rendered strongly alkaline, and the liberated base distilled in steam and isolated as for pyridine. It had b. p. 129·5°/770 mm., d_4^{20}

[14] Timmermans, " Physico-Chemical Constants of Pure Organic Compounds," Elsevier Publ. Co., 1950, p. 568.

0·9443, n_D^{20} 1·50102. This sample was employed for the detailed measurements of the physical properties. Freiser and Glowacki [15] give d_4^{20} 0·9443, n_D^{20} 1·50102. Biddiscombe *et al.*[2] give d_4^{20} 0·94432, n_D^{20} 1·50101.

β-*Picoline.*—The starting material was a commercial product of 95% purity (Yorkshire Tar Distillers). The likely impurities, γ-picoline and 2,6-lutidine, cannot be removed by distillation because of the proximity of their b. p.s to that of β-picoline; furthermore d_4^{20} and n_D for β- and γ-picoline are so close that these cannot be used for detecting the γ-isomer in β-picoline, but density and refractive-index measurements are useful for the detection of the presence of 2,6-lutidine.

The following methods of purification were investigated.

(i, ii) Drying and fractionation, or purification by way of the $(C_6H_7N)_2,ZnCl_2,HCl$ complex, gave impure products.

(iii) For removal of γ-picoline and of 2,6-lutidine by acetic and phthalic anhydride (to yield highly coloured compounds). The claims of the original authors [4] are optimistic (cf. Biddiscombe *et al.*[2]) since a very pale yellow colour is produced by repeated treatment with the anhydride mixture, presumably owing to the slow reaction of β-picoline. Nevertheless, a modified procedure ultimately gave a very pure product.

Dry commercial β-picoline (125 ml.), acetic anhydride (31 g.), and phthalic anhydride (31 g.) were refluxed for 5 hr. When cold, the product was treated with sodium hydroxide (50 g.) in water (100 ml.); the liberated base was isolated by steam-distillation and dried. A 10 ml. portion of the partially purified base was refluxed with 10 g. of the anhydride mixture: a deep orange colour developed after 10 min. All the base was accordingly refluxed with 62 g. of the anhydride mixture for a further 5 hr. This procedure was repeated until a test sample gave only a pale yellow colour when refluxed with the anhydride mixture, and further refluxing of the main bulk with fresh anhydride mixture for 5 hr. did not yield a more intense colour than the test sample. A total reflux period of at least 15 hr. was required.

The preferred procedure for purifying β-picoline (*e.g.*, for use in the preparation of nicotinic acid) was to reflux the base (500 ml.) with the anhydride mixture (250 g.) for 20—24 hr. and then distil the whole until oily drops of phthalic anhydride formed in the still-head. The distillate was treated with sodium hydroxide (250 g. in 1·5 l. of water) contained in a three-necked flask and steam-distilled. Sodium hydroxide (250 g.) was added to the distillate (about 2 l.), and the β-picoline which separated was removed, dried (K_2CO_3, followed by powdered barium oxide), and fractionated, then having b. p. 144·0°/767 mm., d_4^{20} 0·9566, n_D^{20} 1·50685 (Biddiscombe *et al.*[2] give d_4^{20} 0·95658, n_D^{20} 1·50682). The infrared spectrum was identical with that obtained by Biddiscombe *et al.*

γ-*Picoline.*—The starting material was a commercial product of 95% purity (Yorkshire Tar Distillers). Four methods of purification were investigated.

(i) The sample, dried over barium oxide and fractionated, had b. p. 145—145·5°/760 mm., d_4^{20} 0·9540, n_D^{20} 1·50567.

(ii) The "acid" zinc chloride complex $(C_6H_7N)_2,ZnCl_2,HCl$, prepared as described for α-picoline, had m. p. 125—129°; four recrystallisations from absolute ethanol raised the m. p. to 130—130·5°. The base liberated, after drying and fractionation, had b. p. 145·2—145·4°/764 mm., d_4^{20} 0·9541, n_D^{20} 1·50571.

(iii) Commercial γ-picoline (100 g.) was warmed to 45° and anhydrous oxalic acid (100 g.) was added in small portions at such a rate that the temperature did not rise above 70°. The mixture, which solidified on cooling, was dissolved in hot ethanol (100 ml.) and, after cooling, the γ-picoline hydrogen oxalate filtered off: it melted at 139—141° and at 139—140·5° after recrystallisation from absolute ethanol (lit.,[16] m. p. 139—140°). The base, liberated by an excess of sodium hydroxide solution, dried and, distilled through a 6″ Dufton column, had b. p. 144·8—145·0°/763 mm., d_4^{20} 0·9540, n_D^{20} 1·50550.

(iv) This procedure is based upon fractional freezing after the removal of the 2,6-lutidine impurity by a chemical method. The usual method for removing the 2,6-lutidine *via* the urea complex (cf. Biddiscombe *et al.*[2,17]) was not effective for the small amount present in commercial γ-picoline.

[15] Freiser and Glowacki, *J. Amer. Chem. Soc.*, 1948, **70**, 2575.
[16] Lidstone, *J.*, 1940, 241.
[17] Yorkshire Tar Distillers Ltd., B.P. 584,148: Riethoff and Pittsburgh Coke and Iron Co., B.P. 592,384; U.S.P. 2,383,016, 2,295,606.

2,6-Lutidine exhibits strong absorption at 270 mμ; γ-picoline does not absorb at this wavelength. After preliminary trials in which the removal of 2,6-lutidine was followed by comparison of the absorption of fractions at 253 and 270 mμ, the following procedure was evolved.

Commercial γ-picoline (500 ml.) was added to a solution of zinc chloride (400 g.) in water (2 l.) containing a few drops of hydrochloric acid. Steam was passed through the suspension until 1·5 l. of distillate were collected. The residue was treated with sodium hydroxide (200 g.), and the base isolated by steam-distillation, followed by addition of solid sodium hydroxide, ether-extraction, drying, and distillation. The partly purified base, in 100 ml. quantities, was subjected to slow fractional freezing, with intermittent gas stirring (the apparatus is described in the Appendix) until the initial freezing temperature rose to 4·25° and remained constant; five freezings sufficed. In the first experiment 80% was frozen and the initial f. p. was 2·6°; in the subsequent four experiments 90% was frozen and the respective initial f. p. were 3·5°, 4·0°, 4·25°, and 4·25° respectively. Finally the purified γ-picoline was distilled to remove traces of moisture: it had b. p. 145·0°/765 mm., d_4^{20} 0·9548, n_D^{20} 1·50584 (cf. lit.,[2] d_4^{20} 0·95478, n_D^{20} 1·50584), and the infrared absorption was identical with that reported.[2]

Dimethylpyridines.—The following general methods of purification were used. The purest commercial products were subjected to (*a*) efficient fractional distillation, (*b*) conversion into a solid derivative, and (*c*) fractional freezing to a constant initial f. p. Purification was followed in (*a*) and (*b*) by measurement of the density, refractive index, and ultraviolet absorption. The *d* and n_D measurements were useful for 2,3- and 2,6-lutidine since these properties differ appreciably from those of the likely impurities: for 2,4- and 2,5-lutidine, only the ultraviolet absorption spectrum is of value. Traces of moisture were removed from the final products by fractional distillation.

2,3-*Lutidine.* A commercial sample (Eastman Kodak; 100 g.) was dried over barium oxide and fractionated through a 20″ column filled with 1/16″ Dixon gauze rings and operated at a reflux ratio of 35 : 1; 80% distilled at 160·0—160·9°/760 mm. (sample 1). The redistilled base (68 g.) was treated, with stirring, with urea (27 g.) in water (50 ml.), then cooled to 5°, and the paste was filtered at the pump and washed with water (50 ml.). The solid was dissolved in water (200 ml.) and steam-distilled until the distillate yielded no turbidity when treated with a little solid sodium hydroxide. The base was isolated from the steam-distillate by the addition of excess of solid sodium hydroxide, the upper layer being removed and the aqueous layer extracted with ether (50 ml.). The combined upper layers were dried (K_2CO_3) and distilled through a short column: they had b. p. 160·5—161°/760 mm. (sample 2). Repetition of the urea treatment improved the purity slightly (sample 3). Final purification was by slow fractional freezing; each freezing occupied about 3 hr. During the first freezing about 77% was frozen and the liquid poured off; the crystals were melted and the process repeated until about 90% was frozen. The initial and final f. p.s were −14·8°; this product boiled at 161·0°/765 mm. (sample 4). The physical properties of the various samples were as tabulated.

Sample	d_4^{20}	n_D^{20}	$\lambda_{max.}$	$10^{-3}E$	Sample	d_4^{20}	n_D^{20}	$\lambda_{max.}$	$10^{-3}E$
1	0·9453	1·50785	266·5—270·0	7·34	3	0·9461	1·50862	267·0	7·57
2	0·9455	1·50831	266·7—267·0	7·46	4	0·9464	1·50857	267·0	7·55

The ultraviolet spectra were measured in 0·1N-sulphuric acid with a Unicam S.P. 500 spectrophotometer. About 0·1 g., accurately weighed, was dissolved in 100 ml. of 0·1N-sulphuric acid, and 1 ml. of this solution was diluted to 100 ml.; it had an optical density of about 0·600 (25% transmission) at the peak. Andon *et al.*[18] give for 2,3-lutidine: $\lambda_{max.}$ 267, *E* 7250.

2,6-*Lutidine.*—A commercial sample (Yorkshire Tar Distillers) of 95% purity was dried and distilled: the main fraction boiled at 144·0—144·3°/758 mm. and had d_4^{20} 0·9540, n_D^{20} 1·50567. The redistilled base (480 ml.) was slowly added, with stirring, to a cold solution of urea (340 g.) in water (500 ml.). After being kept overnight, the solid was filtered off and washed with cold water. The urea complex was suspended in about an equal weight of water, and steam was passed through the suspension; the solid dissolved and subsequently two layers were formed. Most of the organic layer passed over into the steam-distillate (about 2 l.). The regenerated 2,6-lutidine was isolated by addition of an excess of solid sodium hydroxide, and the upper layer removed, dried (KOH, followed by BaO), and distilled: 456 ml. of the base were recovered. The purification through the urea complex was repeated twice, about 94% being recovered on each occasion. The final product had b. p. 144·0°/758 mm., d_4^{20} 0·9224, n_D^{20} 1·49765. The

[18] Andon, Cox, and Herington, *Trans. Faraday Soc.*, 1954, **50**, 925.

purified 2,6-lutidine (110 ml.) was fractionally frozen: in the first and second experiments 80% was frozen and the initial f. p.s were −5·7° and −5·8° respectively. When dried and distilled, the product had d_4^{20} 0·9225, n_D^{20} 1·49779 (lit.,[2] d_4^{20} 0·92257, n_D^{20} 1·49767).

2,4-*Lutidine*. A commercial product (Eastman Kodak; 250 g.) of 85% purity was fractionated as described for 2,3-lutidine. About 72% distilled at 156·4—157·4°/760 mm. (sample 1). The redistilled base (200 g.), benzene (500 ml.), and concentrated hydrochloric acid (150 ml.) were heated (Dean and Stark separator) on a water-bath until water no longer collected in the separator and the temperature reached 80° (thermometer-bulb just above the liquid). When cold, the supernatant benzene was decanted and the 2,4-lutidine hydrochloride was washed with a little benzene. The hydrochloride was dissolved in water (350 ml.) and any benzene present was removed in steam; a solution of sodium hydroxide (80 g.) was added, and the liberated base distilled in steam and isolated as usual. Distillation through a short column gave 2,4-lutidine (165 g.), b. p. 156·8—157·0°/762 mm. (sample 2). The regenerated base, reprecipitated as the hydrochloride in benzene and isolated as before, had b. p. 158·4—158·5°/757 mm. (sample 3). Fractional freezing of the resulting 2,4-lutidine led to small crystals which rendered decantation impossible: the residual liquid was separated by suction through a filter-stick. The base was placed in the special f. p. apparatus and immersed in acetone–carbon dioxide; the temperature of freezing remained constant at −67·8° for 2 hr. and fell to −68·5° during a further hour; the liquid (about 40%) was removed, and the crystals were melted and distilled through a 4″ column filled with Fenske helices, then having b. p. 158°/771 mm. (sample 4). The physical properties of the various samples are tabulated below (Andon *et al.*[18] give $\lambda_{max.}$ 259, E 5990).

Sample	d_4^{20}	n_D^{20}	$\lambda_{max.}$	$10^{-3}E$	Sample	d_4^{20}	n_D^{20}	$\lambda_{max.}$	$10^{-3}E$
1	0·9309	1·50105	260—260·5	5·70	3	0·9305	1·50092	259	6·09
2	0·9305	1·50095	259	6·06	4	0·9305	1·50087	259	6·07

2,5-*Lutidine*. A commercial 2,4/2,5-lutidine fraction (Midland Tar Distillers) was fractionated through a 20″ column packed with Fenske helices and at a reflux ratio of 10 : 1, the fraction of b. p. 155—165°/760 mm. (60% of the whole) being separated for the isolation of the 2,5-lutidine. The redistilled base (300 g.) was treated with phenol (450 g.) and distilled through a 20″ column packed with 1/16″ Dixon gauze rings at 212 mm. (pressure controlled by a Cartesian manostat) at a reflux ratio of 4 : 1. The fraction (137 ml.) of b. p. 152·6—153·6° deposited a solid phenol complex at −25°; recrystallisation from light petroleum (b. p. 40—60°) gave 25 g. of a solid, m. p. 47—48°. The phenol complex (75 g.) was recrystallised from light petroleum (150 ml.) and yielded the pure 2,5-lutidine–phenol complex (55 g.), m. p. 57·5°. This was suspended in water (100 ml.), sodium hydroxide (40 g.) in water (100 ml.) was added, and the mixture was steam-distilled. The distillate was treated with sodium hydroxide (25 g.), the upper layer separated, and the aqueous layer extracted with ether (2 × 25 ml.). The combined upper layers were dried (K_2CO_3) and distilled: 28 g. of 2,5-lutidine, b. p. 156·5—157·0°/758 mm., d_4^{20} 0·9297, n_D^{20} 1·50060, $\lambda_{max.}$ 270·0 (E 6640) were obtained. Finally the 2,5-lutidine was subjected to two fractional freezings (75% solid, f. p. −16·0°; 50% solid, f. p. −16·0°). The melted solid was distilled through a short column and had b. p. 157·8°/768 mm., d_4^{20} 0·9298, n_D^{20} 1·50050, $\lambda_{max.}$ 270·0 (E 6640) (Andon *et al.*[18] give $\lambda_{max.}$ 270, E 6710). No 2,4- or 3,5-lutidine was revealed by the infrared spectrum.

3,5-*Lutidine*. A synthetic product, b. p. 170—175°/763 mm., was kindly supplied by Messrs. Robinson Bros. The base (100 ml.) was dissolved in dilute hydrochloric acid (1 : 4) and steam was passed through the solution until 1 l. of distillate was collected. The residue was rendered alkaline with excess of concentrated sodium hydroxide solution and steam-distilled: the base was extracted with ether, dried (K_2CO_3), and distilled through a short column: it had b. p. 171·5—172·5°/763 mm., d_4^{20} 0·9418, n_D^{20} 1·50605. Fractional distillation through a 20″ column charged with 1/16″ Dixon gauze rings with a reflux ratio of 40 : 1 gave a middle fraction of b. p. 172·3—172·4°/773 mm. (61 ml.) with d_4^{20} 0·9419, n_D^{20} 1·50606. Three fractional freezings (75% frozen) gave a product of f. p. −6·3°, b. p. 172·0°/767 mm., d_4^{20} 0·9419, n_D^{20} 1·50613, $\lambda_{max.}$ 268·0 (E 6100) (Andon *et al.*[18] give $\lambda_{max.}$ 268, E 5820). The physical properties were unchanged when this product (25 g.) was refluxed with a mixture of acetic anhydride (7 g.) and phthalic anhydride (7 g.) for 6 hr. and the base recovered as described for β-picoline.

Preparation of Alkylpyridines with Finely Divided Sodamide in Xylene.—General procedure. Commercial sodamide (May and Baker) was ground under anhydrous xylene to a finely divided

(" colloidal ") state, in a 500 ml. reagent bottle charged with porcelain spheres (3/8" diameter) and carrying a soda-lime guard tube. Sodamide (50 g.) and sodium-dried xylene (100 ml.) gave, in 2—3 hr., a suspension that did not settle for 30 min. Into the whole, pure α-picoline (usually 38·2 g.) was introduced. The mixture was stirred and pure, freshly distilled alkyl chloride (10% excess for monoalkylation) added during 15 min. After 2—3 hours' refluxing the mixture was cooled in ice, and the excess of sodamide was decomposed by water (100 ml.), two layers being formed. The upper layer was removed and the aqueous layer extracted with benzene (2 × 50 ml.); the combined organic layers were extracted with 2·5N-hydrochloric acid (2 × 50 ml.), and steam passed through the acid extracts until 1 l. of distillate was collected (discarded); sodium hydroxide (60 g.) was added to the residual liquid and the liberated base isolated in steam. Sodium hydroxide (20 g.) was added to the distillate, the upper layer removed, and the aqueous layer extracted with ether (3 × 50 ml.). The combined upper layer and ether extracts were dried (K_2CO_3) and distilled in a modified Claisen flask with a 4" side arm charged with glass helices; the low-boiling fraction consists of 10—20% of the α-picoline, after which the n-alkylpyridine distils. There was no high-boiling residue.

2-*Propylpyridine*. Ethyl chloride (50 ml.) was added during 15 min. to a stirred mixture of colloidal sodamide (50 g.) in xylene (150 ml.) and α-picoline (53 ml.) under a condenser containing solid carbon dioxide. The mixture was stirred at room temperature for 15 min., then heated on a water-bath at 40°; a vigorous reaction ensued and the flask was cooled occasionally. After 1 hr., the flask was heated in an electric heating-mantle to maintain the temperature of the mixture at 75° for 1 hr. The yield of 2-propylpyridine, b. p. 170—170·5°/761 mm., was 45 g.

2-*Butylpyridine*. Colloidal sodamide (50 g.) in xylene (150 ml.), α-picoline (40 ml.), and propyl chloride (36 ml.), refluxed for 3 hr., gave 2-butylpyridine, b. p. 77·5°/15 mm. (38 g.).

2-*Pentylpyridine*. Colloidal sodamide (40 g.) in xylene (150 ml.), α-picoline (40 ml.), and butyl chloride (42·5 ml.), refluxed for 2 hr., gave 2-pentylpyridine, b. p. 104·5°/17 mm. (41 g.).

2-*Hexylpyridine*. Sodamide (40 g.) in xylene (150 ml.), α-picoline (40 ml.), and pentyl chloride (54 ml.), in 3 hr., gave 2-*hexylpyridine*, b. p. 111—111·5°/15 mm. (49 g.) (Found: C, 81·1; H, 10·2; N, 8·2. $C_{11}H_{17}N$ requires C, 81·0; H, 10·4; N, 8·6%).

2-*Heptylpyridine*. Sodamide (40 g.), xylene (150 ml.), α-picoline (40 ml.), and hexyl chloride (61 ml.), in 3 hr., gave 2-*heptylpyridine*, b. p. 122·5°/13 mm. (55 g.) (Found: C, 81·5; H, 10·6; N, 8·0. $C_{12}H_{19}N$ requires C, 81·3; H, 10·7; N, 8·0%).

Preparation of Alkylpyridines with Sodamide in Liquid Ammonia.—General procedure. A 1·5-l. three-necked flask, surrounded by a 5-l. beaker and equipped with a glycerol-sealed stirrer, a dropping funnel, and a wide-bore air-condenser, was charged with *ca.* 750 ml. of liquid ammonia and 1—2 g. of finely powdered ferric nitrate. Sodium (10% excess), in small pieces, was added to the stirred solution (about 10 g. in 20—30 min.) and stirring was continued until the blue colour disappeared (lamp behind flask; formation of frost on flask prevented by occasional spraying with alcohol). Sufficient liquid ammonia was then added (if necessary) to restore the volume to 600—700 ml. The weighed quantity of picoline was introduced through the condenser, the mixture stirred, and, after 5 min., the alkyl halide was added as rapidly as the vigour of the reaction permitted. The colour of the solution was discharged immediately after the addition of all the halide. The ammonia was allowed to evaporate overnight, water added (to decompose sodamide), and the base isolated as detailed for 2-alkylpyridines.

3-*Propylpyridine*. Sodamide (from 10·1 g. of sodium) in liquid ammonia (700 ml.), β-picoline (37·2 g.), and ethyl chloride (50 ml.) gave 3-*propylpyridine* (28·5 g.) which after two fractionations through a 4" column of 1/16" Dixon gauze rings, boiled at 66—66·5°/8 mm. (Found: C, 79·6; H, 9·1; N, 11·2. $C_8H_{11}N$ requires C, 79·3; H, 9·1; N, 11·6%).

3-*Butylpyridine*. Sodamide (12·6 g. of sodium) in liquid ammonia (700 ml.), β-picoline (46·6 g.), and propyl chloride (43·2 g.) yielded 3-*butylpyridine* (36 g.), b. p. 82°/7 mm. (Found: C, 80·2; H, 9·6; N, 10·2. $C_9H_{13}N$ requires C, 80·0; H, 9·6; N, 10·4%).

3-*Pentylpyridine*. Sodamide (13·8 g. of sodium) in liquid ammonia (750 ml.), β-picoline (46·6 g.), and butyl chloride (75·3 g.) yielded 3-*pentylpyridine* (41 g.), b. p. 100°/9 mm. (Found: C, 80·6; H, 10·2; N, 9·2. $C_{10}H_{15}N$ requires C, 80·5; H, 10·1; N, 9·4%).

Similarly were prepared 3-*hexyl*-, b. p. 113°/7 mm. (Found: C, 80·8; H, 10·5; N, 8·3. $C_{11}H_{17}N$ requires C, 81·0; H, 10·4; N, 8·6%), 3-*heptyl*-, b. p. 139·5—140°/7 mm. (Found: C, 81·5; H, 10·8; N, 7·8. $C_{12}H_{19}N$ requires C, 81·3; H, 10·7; N, 8·0%), 4-ethyl-, b. p. 165·5—166·5°/753 mm. (insufficiently pure for measurement of the physical properties), and 4-propylpyridine, b. p. 70°/10 mm.

4-*Isopropylpyridine*. The crude product from sodamide (28·8 g. of sodium) in liquid ammonia (1200 ml.), γ-picoline (50 ml.), and methyl iodide (187 g.), upon distillation through a 20″ column packed with 1/16″ Dixon gauze rings at a reflux ratio of 35 : 1, gave three main fractions: (i) b. p. 166—182°/764 mm. (21 g.; largely 4-ethylpyridine); (ii) b. p. 182—186°/764 mm. (22 g.; 4-isopropylpyridine); and (iii) b. p. 186—196°/764 mm. (15 g.; largely 4-t-butylpyridine). Refractionation of fraction (ii) gave pure 4-isopropylpyridine, b. p. 182·5°/763 mm.

4-*s-Butylpyridine*. Methyl bromide was added to a mixture prepared from sodamide (6·7 g. of sodium) in liquid ammonia (1 l.) and 4-propylpyridine (29 g.) until the green colour of the solution was discharged. Fractionation of the product through a 6″ column packed with 1/16″ Dixon gauze rings yielded pure 4-s-butylpyridine (18 g.), b. p. 197°/765 mm.

4-*t-Butylpyridine*. Methyl bromide was added to a stirred mixture prepared from sodamide (15·3 g. of sodium) in liquid ammonia (1 l.) and 4-ethylpyridine (40·8 g.) until the green colour was discharged. Isolation, as for 4-isopropylpyridine, gave a fraction, b. p. 180—196°/765 mm. (20 ml.), and another of b. p. 197°/765 mm. (26 g.). Refractionation of the latter gave pure 4-t-butylpyridine, b. p. 197°/765 mm.

4-1′-*Ethylpropylpyridine*. Ethyl chloride was added to a mixture prepared from sodamide (22·1 g. of sodium) in liquid ammonia (700 ml.) and γ-picoline (40 ml.) until the green colour was discharged. Fractionation yielded 38 g. of pure 4-1′-ethylpropylpyridine, b. p. 112·5°/20 mm.

Preparation of Alkylpyridines with Sodamide in the Absence of a Solvent.—General procedure. Commercial sodamide (40 g.) (May and Baker) and pure γ-picoline (39·2 ml.) were stirred at 0° for 10—20 min. The alkyl chloride (usually 0·40 mol.) was added, with stirring, during 2—3 hr. at 0°, and stirring continued for 2 hr. longer. The excess of sodamide was decomposed at 0° by water (100 ml.). The upper layer was dissolved in 2·5N-hydrochloric acid (200 ml.); the aqueous layer was extracted with benzene (2 × 50 ml.), and the combined benzene extracts were treated with 2·5N-hydrochloric acid (2 × 50 ml.). Steam was passed through the combined acid extracts until 1 l. of distillate was collected (discarded). Sodium hydroxide (60 g.) was added to the residue, and the base isolated by steam-distillation, the distillate being treated with sodium hydroxide (20 g.), the organic layer removed, and the aqueous layer extracted with ether (3 × 50 ml.). The combined basic extracts were dried (K_2CO_3) and distilled from a modified Claisen flask with a side arm incorporating a 4″ column packed with glass helices. Three fractions were collected: (i) unchanged γ-picoline (10—20%), (ii) monosubstituted γ-picoline $C_5H_4N{\cdot}CH_2R$, and (iii) disubstituted γ-picoline $C_5H_4N{\cdot}CHR_2$.

4-*Butylpyridine*. The product from sodamide (40 g.), pure γ-picoline (39·2 ml.) and propyl chloride (40 ml.), on fractionation, gave fractions: (i) b. p. up to 84°/8 mm. (3 ml.); (ii) b. p. 84—87°/8 mm. (19 g.); and (iii) 115—117·5°/8 mm. (14 g.). Redistillation of fraction (ii) yielded pure 4-butylpyridine, b. p. 84°/8 mm. Redistillation of fraction (iii) afforded 4-1′-*propylbutylpyridine*, b. p. 110—110·5°/8 mm. (Found: C, 81·4; H, 10·5; N, 7·6. $C_{12}H_{19}N$ requires C, 81·3; H, 10·7; N, 8·0%).

4-*Pentylpyridine*. Fractionation of the product from sodamide (40 g.), γ-picoline (39·2 ml.), and butyl chloride (42 ml.) gave fractions: (i) b. p. 21—60°/20 mm. (4 ml.); (ii) b. p. 117—120°/23 mm. (21 g.); and (iii) b. p. 150—163°/23 mm. (mainly 157°/23 mm.) (16 g.); and thence, by redistillation, 4-pentylpyridine, b. p. 95°/6 mm. (Found: C, 80·7; H, 10·2; N, 8·8. Calc. for $C_{10}H_{15}N$: C, 80·5; H, 10·1; N, 9·4%), and 4-1′-*butylpentylpyridine*, b. p. 157°/23 mm. (Found: C, 81·6; H, 11·5; N, 6·4. $C_{14}H_{23}N$ requires C, 81·9; H, 11·3; N, 6·8%).

Similarly were prepared 4-hexyl-, b. p. 110—110·5°/5 mm., 4-1′-pentylhexyl-, b. p. 140—170°/7 mm., 4-heptyl-, b. p. 119°/4 mm., and 4-1′-*hexylheptyl-pyridine*, b. p. 165—166°/5 mm. (Found: C, 83·0; H, 11·7; N, 5·3. $C_{18}H_{31}N$ requires C, 82·8; H, 11·9; N, 5·4%).

Syntheses by Modified Wibaut–Arens Method.—4-Ethylpyridine. Activated " AnalaR " zinc powder [19] (60 g.) was added in portions (10 g.) during 40—50 min. to a stirred mixture of pure pyridine (61·2 ml.) and acetic anhydride (300 ml.); stirring was continued for 2 hr. at 30—40°. Acetic acid (60 ml.) was added, followed by zinc powder (25 g.) in 4 portions during 15 min., and finally zinc powder (26 g.) all at once. The heat evolved caused the mixture to reflux: refluxing was continued for 30 min. The mixture was then made alkaline with concentrated sodium hydroxide solution and steam-distilled until the distillate was neutral to litmus (*ca.* 1·2 l.). Sodium hydroxide (200 g.) was added to the distillate, and the base extracted

[19] Frank and Smith, *Org. Synth.*, 1947, **27**, 39.

with ether, dried (K_2CO_3), and distilled through a 8″ Dufton column: crude 4-ethylpyridine (30 g.), b. p. 155—161°/741 mm., was obtained. Two redistillations through a 4″ Fenske-type column packed with glass helices gave a fairly pure product, b. p. 166—166·5°/759 mm., d_4^{20} 0·9413, n_D^{20} 1·50225; this sample acquired a pale yellow colour in 2 weeks.

4-*Propylpyridine*. The procedure was similar to that described for 4-ethylpyridine, with propionic anhydride (250 ml.), pyridine (62·5 ml.), activated zinc powder (62·5 g.) added during 2·5 hr. at 40°, then propionic acid (88 ml.) with zinc powder (25 g.) in 5 portions during 30 min. and 25 g. in one lot, and final refluxing for 30 min. Crude 4-propylpyridine, b. p. 185—186°/759 mm. (31 g.) was dissolved in 5N-hydrochloric acid (250 ml.) and steam-distilled until the distillate (500 ml.) was odourless; the base, isolated by addition of excess of sodium hydroxide solution and steam-distillation, had b. p. 186—186·5°/759 mm., 69·5°/10 mm.

4-Butylpyridine, obtained similarly and redistilled, boiled at 84—84·5°/17 mm.

4-*Ethyl*-3-*methylpyridine*. The quantities employed were: redistilled acetic anhydride (430 ml.); pure β-picoline (150 ml.); activated zinc powder (170 g.) added during 6 hr. at 30°; glacial acetic acid (100 ml.); zinc powder (40 g.) added during 2 hr., 45 g. in one lot; final refluxing 30 min. Crude 4-ethyl-3-methylpyridine, b. p. 198—199°/760 mm. (76 g.), on purification and redistillation, gave the pure base, b. p. 201°/771 mm.

Preparation of Pyridine Ketones.—The three methyl pyridine ketones were prepared by the condensation of the *pure* ethyl pyridinemonocarboxylate with ethyl acetate, followed by acid hydrolysis of the resulting keto-esters (which were not isolated). The condensation reagents were: for 4-acetylpyridine, sodium ethoxide suspended in dry xylene (71% yield); for 3-acetylpyridine, sodium ethoxide in dry xylene (55% yield), or sodium hydride (73% yield); for 2-acetylpyridine, triphenylmethylsodium (49% yield) or sodium hydride (77% yield). Sodium ethoxide alone and in the absence of a solvent had previously been employed in the initial condensation of the alkyl pyridinecarboxylate and ethyl acetate;[20,21,22,23] the conditions given below are more satisfactory.

4-*Acetylpyridine*. In a 500 ml. three-necked flask fitted with a dropping funnel, mercury-sealed stirrer and reflux condenser, were placed " molecular " sodium (16·6 g.) and dry xylene (200 ml.); absolute ethanol (41·0 ml.) was added with stirring, at such a rate that the reaction was not too vigorous, after which stirring was continued for 1 hr. A mixture of dry, redistilled ethyl acetate (95 ml.) and ethyl isonicotinate (71 g.) was added to the suspension of sodium ethoxide during 3 hr., and the mixture refluxed for 8 hr.; a yellow precipitate of the sodio-β-keto-ester was formed. Most of the xylene was removed by distillation (water-pump) and the yellow residue was dissolved in warm water (500 ml.). The xylene layer was separated and the aqueous layer extracted with ether (2 × 40 ml.). The remaining aqueous layer was treated with concentrated hydrochloric acid (180 ml.: final concentration 10% w/v), and the mixture refluxed for 3 hr.; the cold solution was made alkaline with sodium carbonate and extracted with ether (8 × 50 ml.), and the extracts were dried (K_2CO_3) and distilled through a 4″ Fenske-type column filled with glass helices. The yield of 4-acetylpyridine, b. p. 101°/12 mm., was 40·1 g. (cf. Kolloff and Hunter[21] who give b. p. 211—212°; Burrus and Powell[22] give b. p. 77°/5 mm.).

3-*Acetylpyridine*. (*a*) Condensation of sodium ethoxide [from sodium (7·3 g.) and absolute ethanol (34·5 g.)] in dry xylene (200 ml.), ethyl nicotinate (60·5 g.), and ethyl acetate (78·5 g.), and subsequent treatment with concentrated hydrochloric acid (180 ml.) as for 4-acetylpyridine, yielded 3-acetylpyridine, b. p. 102·5—103·5°/8 mm. (26·4 g.).

(*b*) Sodium hydride (7·7 g., weighed in dry nitrogen in a " dry " box) was covered with dry xylene (200 ml.) under nitrogen. A mixture of ethyl nicotinate (35 g.) and dry ethyl acetate (28·2 g.) was added, with stirring, during 1 hr. in a slow stream of nitrogen; stirring was continued for 1 hr. and the mixture refluxed for 5 hr., then cooled. Water (500 ml.) was added with stirring to the thick yellow sludge, and stirring was continued until all the solid had dissolved. The aqueous layer was separated and the xylene layer shaken with water (2 × 50 ml.); the combined aqueous layers were extracted with ether (2 × 40 ml.), and then sufficient concentrated hydrochloric acid (215 ml.) was added to the residual aqueous solution to give a concentration of 10% w/v. The mixture was refluxed for 3 hr. The ketone was

[20] Strong and McElvain, *J. Amer. Chem. Soc.*, 1933, **55**, 818.
[21] Kolloff and Hunter, *J. Amer. Chem. Soc.*, 1941, **63**, 492.
[22] Burrus and Powell, *J. Amer. Chem. Soc.*, 1945, **67**, 1468.
[23] Brown and Murphy, *J. Amer. Chem. Soc.*, 1951, **73**, 3312.

isolated as for 4-acetylpyridine; it boiled at 112—114°/16 mm. (20·3 g.). The products from the two preparations were combined and distilled through a 4″ Fenske-type column: pure 3-acetylpyridine, b. p. 113°/16 mm., was obtained [cf. lit., b. p. 217—218° (ref. 21), 90—92°/5 mm. (ref. 20), 80°/5 mm. (ref. 22), b. p. 66°/1 mm. (ref. 23)].

2-*Acetylpyridine.* (*a*) To sodium hydride (12·0 g.) suspended in dry xylene (200 ml.) was added a mixture of ethyl picolinate (60·4 g.) and dry ethyl acetate (36·5 g.) during 1 hr.; the mixture was stirred for 1·5 hr. and refluxed for 2 hr. The paste that resulted on cooling was treated with ethanol (25 ml.), followed by water (200 ml.) to dissolve the solid. Sufficient concentrated hydrochloric acid was added to give a final concentration of 10% w/v. Isolation as for 3-acetylpyridine gave 2-acetylpyridine, b. p. 92°/17 mm. (37·2 g.).

(*b*) Triphenylmethylsodium (0·086 mol.) in ether (700 ml.) [24] was treated with ethyl picolinate (11·9 g.) and dry ethyl acetate (8·8 g.) rapidly in a stream of nitrogen. Stirring was continued for 1 hr. then water (50 ml.) was added. The lower layer was separated, the ether layer was extracted with water (2 × 30 ml.), and the combined aqueous layers were treated with concentrated hydrochloric acid to give a final concentration of 10% w/v, and refluxed for 3 hr. The yield of 2-acetylpyridine, b. p. 92—93°/17 mm., isolated as above, was 4·5 g. (lit., b. p. 187—190°/1 atm.,[21] b. p. 53°/5 mm.[22]).

Reduction of Methyl Pyridyl Ketones.—*4-Ethylpyridine.* 4-Acetylpyridine (22·9 g.), 99—100% hydrazine hydrate (15 ml.), and solid potassium hydroxide (23 g.) in trimethylene glycol (30 ml.) (dried over $MgSO_4$) were heated under reflux at 100°, a vigorous reaction ensuing.[25] The bath-temperature was raised during 3 hr. to 160° and kept at 160° for 3 hr. The mixture was distilled until no more base passed over, water (25 ml.) was added to the residue in the flask, and distillation was continued. Solid sodium hydroxide was added to the distillate, the upper layer separated, the aqueous layer extracted with ether, and the combined extracts and upper layer were dried (K_2CO_3) and fractionated twice through a 4″ Fenske-type column filled with glass helices: pure 4-ethylpyridine, b. p. 166·5°/754 mm. (16 g.), was obtained.

Similarly were prepared 3-, b. p. 166°/758 mm. (15·8 g. from 22·8 g. of ketone), and 2-ethylpyridine, b. p. 150°/760 mm. (11·3 g. from 18·3 g. of ketone).

Esters of Pyridinemonocarboxylic Acids.—No detailed study of the physical properties of the pure esters has been made.[26] To ensure purity, the acids were prepared by oxidation of the pure picolines with potassium permanganate; [8] they were esterified (i) with hydrogen chloride as catalyst, (ii) with sulphuric acid as catalyst, or (iii) by reaction of the acid chloride hydrochloride with the appropriate alcohol. Method (i) was used for the lower alkyl esters whilst (ii) and (iii) were preferred for the higher alkyl esters.

Pyridinealdehydes.—The "pure" commercial aldehydes (Raschig, Ludwigshafen) were purified as follows. The aldehyde (50 g.) was added to boiled-out water (250 ml.) at 0° under nitrogen. Sulphur dioxide was passed into the solution until precipitation was complete. The addition compound was filtered off rapidly, washed with a little water, and refluxed in 17% hydrochloric acid (200 ml.) under nitrogen until the solid disssolved; the solution was neutralised with sodium hydrogen carbonate and extracted with ether (5 × 30 ml.), and the extracts were dried in a nitrogen atmosphere and distilled twice in nitrogen. The b. p.s were: pyridine-2-, 81·5°/25 mm., -3-, 89·5°/14 mm., and -4-aldehyde, 79·5°/12 mm. The purified aldehydes were stored under nitrogen; a fresh sample was used for each physical measurement. Surface tensions were also measured in nitrogen.

Hydroxymethylpyridines.—The pure commercial alcohols (Raschig) were fractionated twice. 2-Pyridylmethanol had b. p. 102·5°/8 mm.; the 3-isomer had b. p. 120°/12 mm.; the 4-isomer had m. p. 67·5° and was not investigated.

Dialkyl Oxalates.—These were prepared, as described in Part XIII,[27] by A. Watling, B.Sc. The surface tension measurements recorded in Part XIII were made by the method of capillary rise.

Aliphatic Aldehydes.—Butyraldehyde. Commercial butyraldehyde was purified through the bisulphite compound. This was decomposed by steam-distillation with excess of sodium

[24] Vogel, "A Text Book of Practical Organic Chemistry," Longmans, Green & Co., London, 1957, p. 479.
[25] Cf. Fand and Lutomski, *J. Amer. Chem. Soc.*, 1949, **71**, 2931.
[26] Cf. alkyl nicotinates: Badgett, Provost, Ogg, and Woodward, *J. Amer. Chem. Soc.*, 1945, **67**, 1135; Huber, Boehme, and Laskowski, *ibid.*, 1946, **68**, 187.
[27] Vogel, *J.*, 1948, 631.

TABLE 5.

Ref. no.	Compound	B. p.°/mm.	d_4^{20}	d_4^{40}	d_4^{60}	d_4^{85}	γ_{20}	γ_{40}	γ_{60}	γ_{85}	P
670	Pyridine [a]	115°	0·9831	0·9637	0·9438	0·9194	36·94	34·20	33·40	27·97	198·3
					Alkylpyridines						
671	2-Methyl [a]	129·5	0·9443	0·9268	0·9077	0·8852	33·66	31·09	28·63	25·57	237·2
672	2-Ethyl	150	0·9319	0·9151	0·8995	0·8732	32·08	29·66	27·37	24·65	273·2
673	2-Propyl	170	0·9158	0·8994	0·8830	0·8625	31·48	29·07	27·01	24·47	312·9
674	2-Butyl	77·5/15	0·9071	0·8909	0·8747	0·8544	31·03	29·02	27·03	24·57	352·0
675	2-Pentyl	104·5/17	0·9009	0·8861	0·8705	0·8502	30·97	29·02	27·07	24·60	391·9
676	2-Hexyl	111/15	0·8952	0·8805	0·8656	0·8463	30·65	28·86	27·06	24·90	430·2
677	2-Heptyl	122·5/13	0·8906	0·8766	0·8616	0·8431	30·85	29·13	27·43	25·31	470·4
678	3-Methyl	144	0·9565	0·9389	0·9195	0·8995	35·06	32·71	30·44	27·55	237·4
679	3-Ethyl	166	0·9404	0·9242	0·9088	0·8877	33·77	31·58	29·37	26·63	274·5
680	3-Propyl	66/8	0·9254	0·9089	0·8950	0·8738	32·52	30·43	28·41	25·95	312·9
681	3-Butyl	82/7	0·9150	0·9002	0·8860	0·8669	31·97	29·88	28·04	25·64	351·2
682	3-Pentyl	100/9	0·9077	0·8935	0·8785	0·8602	31·60	29·79	27·98	25·67	390·3
683	3-Hexyl	113/7	0·9012	0·8879	0·8741	0·8555	31·13	29·45	27·77	25·77	428·8
684	3-Heptyl	139·5/7	0·8954	0·8822	0·8670	0·8498	31·26	29·56	27·87	25·80	468·2
685	4-Methyl [a]	145	0·9548	0·9372	0·9186	0·8963	35·45	33·12	30·85	28·03	238·6
686	4-Ethyl [b]	166·5	0·9410	0·9243	0·9070	0·8864	33·72	31·53	29·32	26·58	274·6
687	4-Propyl [c]	69·5/10	0·9255	0·9095	0·8934	0·8733	32·13	30·03	27·94	25·52	311·8
688	4-Isopropyl	182·5	0·9258	0·9095	0·8936	0·8736	33·75	31·50	29·41	26·82	315·5
689	4-Butyl [d]	84·0/8	0·9155	0·9008	0·8851	0·8652	32·38	30·47	28·54	26·20	352·9
690	4-s-Butyl	197	0·9197	0·9048	0·8890	0·8700	34·72	32·75	30·80	28·37	352·5
691	4-t-Butyl	197	0·9219	0·9066	0·8912	0·8724	33·59	31·67	29·77	27·40	351·3
692	4-Pentyl	95/6	0·9089	0·8938	0·8784	0·8590	32·43	30·43	28·47	26·05	392·2
693	4-$CHEt_2$	112·5/20	0·9122	0·8980	0·8837	0·8652	33·22	31·09	28·95	26·29	391·8
694	4-Hexyl	110/5	0·9014	0·8868	0·8720	0·8529	31·67	30·07	28·48	26·52	431·9
695	4-Heptyl	119/4	0·8965	0·8818	0·8679	0·8497	32·20	30·45	28·75	26·62	472·6
696	4-$CHPr^n_2$	110/8	0·8994	0·8860	0·8721	0·8552	31·47	29·67	27·90	25·68	467·4
697	4-$CH(C_6H_{13})_2$	165/5	0·8809	0·8679	0·8548	0·8378	31·27	29·54	27·82	25·67	702·2
698	2,3-Me_2	161	0·9464	0·9316	0·9146	0·8924	33·27	31·08	28·96	26·30	271·9
699	2,4-Me_2	158	0·9305	0·9142	0·8963	0·8740	33·18	30·75	28·34	25·40	276·1
700	2,5-Me_2	157	0·9298	0·9138	0·8978	0·8778	32·34	30·02	27·77	24·98	274·1
701	2,6-Me_2	144·5	0·9226	0·9055	0·8871	0·8646	31·65	29·18	26·97	24·08	275·2
702	3,5-Me_2	172	0·9419	0·9277	0·9095	0·8900	33·83	31·64	29·48	26·80	274·2
703	4-Et-3-Me	201	0·9477	0·9327	0·9168	0·8980	36·05	33·70	31·36	28·50	312·9
					Alkyl picolinates						
704	Methyl	95/1	1·1711	1·1531	1·1354	1·1121	43·47	41·32	39·16	36·42	301·8
705	Ethyl	108/6	1·1193	1·1014	1·0837	1·0609	39·73	37·56	35·42	32·76	340·0
706	Propyl	117/5	1·0841	1·0681	1·0507	1·0284	37·04	34·98	33·07	30·72	376·8
707	Butyl	118/2	1·0611	1·0451	1·0289	1·0089	35·87	33·94	32·03	29·67	414·0
708	Pentyl	136/4	1·0417	1·0257	1·0089	0·9894	34·63	32·89	31·17	29·03	451·8
709	Hexyl	144/3	1·0250	1·0094	0·9932	0·9731	34·13	32·31	30·53	28·30	490·0
710	Heptyl	146/2	1·0110	0·9853	0·9794	0·9599	33·38	31·62	29·94	27·86	527·9
					Alkyl nicotinates						
711	Methyl	85·7/5	—	1·1467	1·1273	1·1034	—	39·03	36·66	33·72	298·9
712	Ethyl [g]	84/5	1·1084	1·0901	1·0716	1·0492	37·82	35·54	33·30	30·54	338·9
713	n-Propyl [h]	113/6	1·0748	1·0573	1·0394	1·0179	36·13	34·14	32·18	29·77	377·8
714	Isopropyl	92·5/5	1·0624	1·0447	1·0267	1·0036	33·87	31·57	29·35	26·66	374·8
715	Butyl [h]	120/2	1·0519	1·0351	1·0181	0·9960	35·23	33·33	31·46	29·14	416·2
716	Bu^s	104·5/2	1·0433	1·0271	1·0103	0·9909	34·83	31·49	29·42	26·82	417·7
717	Bu^t	99/2	1·0393	1·0232	1·0061	0·9844	33·53	32·78	30·76	28·28	415·4
718	Pentyl	133/2	1·0357	1·0188	1·0024	0·9815	34·26	32·57	30·89	28·82	453·7
719	Hexyl [h]	147/2	1·0163	1·0006	0·9845	0·9647	33·72	31·94	30·19	28·02	492·3
720	Heptyl [h]	147/1	1·0050	0·9890	0·9730	0·9531	33·28	31·59	29·88	27·77	531·0
					Alkyl isonicotinates						
721	Methyl	84/3	1·1610	1·1416	1·1222	1·0977	40·82	38·50	36·12	33·17	299·2
722	Ethyl	84/6	1·1049	1·0858	1·0681	1·0436	37·16	35·02	32·87	30·24	338·3
723	Propyl	95/3	1·0721	1·0536	1·0350	1·0124	35·23	33·22	31·22	28·74	376·6
724	Butyl	119/2	1·0488	1·0326	1·0147	0·9931	34·78	32·87	30·98	28·64	416·3
725	Pentyl	139/4	1·0306	1·0128	0·9961	0·9755	33·93	32·23	30·52	28·47	454·9
726	Hexyl	142/1	1·0140	0·9978	0·9818	0·9617	33·48	31·72	29·98	27·84	493·2
727	Heptyl	147/1	1·0015	0·9878	0·9718	0·9506	33·76	32·02	30·32	27·86	533·0

TABLE 5. (*Continued.*)

Ref. no.	Compound	B. p.°/mm.	d_4^{20}	d_4^{40}	d_4^{60}	d_4^{85}	γ_{20}	γ_{40}	γ_{60}	γ_{85}	P
					Methyl pyridyl ketones						
728	2-Pyridyl	92/17	1·0818	1·0624	1·0456	1·0192	39·68	37·27	34·94	32·03	281·6
729	3-Pyridyl	113/16	1·1065	1·0897	1·0717	1·0497	44·72	42·22	39·78	36·92	283·6
730	4-Pyridyl	101/12	1·1009	1·0845	1·0662	1·0441	44·03	41·48	38·98	35·90	283·6
					Pyridinealdehydes						
731	2-Aldehyde	81·5/25	1·1201	1·1007	1·0847	1·0599	41·53	39·22	36·94	34·07	243·2
732	3-Aldehyde	89·5/14	1·1415	1·1255	1·1071	1·0802	46·57	43·98	41·46	38·37	245·4
733	4-Aldehyde	79·5/12	1·1371	1·1170	1·1018	1·0759	48·71	46·02	43·43	40·25	249·5
					Hydroxymethylpyridines						
734	2-	102·5/8	1·1317	1·1166	1·1008	1·0816	47·30	45·03	42·78	40·03	253·5
735	3-	120/12	1·1357	1·1227	1·1093	1·0714	49·78	47·36	45·02	42·18	255·2
					Dialkyl oxalates						
736	Et_2	63·5/5	1·0783	1·0582	1·0366	1·0041	32·43	30·22	28·07	25·43	323·9
737	$Pr^n{}_2$ [j]	84·5/6	1·0189	1·0001	0·9801	0·9526	29·96	28·07	26·22	23·93	401·6
738	$Bu^n{}_2$ [j]	108·5/5	0·9879	0·9712	0·9524	0·9286	29·92	28·03	26·23	23·96	479·9
739	$(C_5H_{11})_2$ [j]	143·0/10	0·9655	0·9489	0·9333	0·9156	29·37	27·63	25·92	23·80	557·1
740	$(C_6H_{13})_2$	158·5/5	0·9502	0·9342	0·9180	0·8982	30·45	28·73	27·03	24·88	640·6
741	$(C_7H_{13})_2$	147·5/1	0·9386	0·9236	0·9076	0·8903	31·33	29·27	27·32	24·90	721·1
					Aliphatic aldehydes, R·CHO						
	R										
742	Pr^n [k]	75	0·8027	0·7871	—	—	24·28	—	—	—	199·5
743	Bu^n [k]	103	0·8112	0·7945	—	—	24·82	22·97	—	—	237·4
744	C_5H_{11}	51/40	0·8162	0·8012	0·7836	—	25·94	23·92	21·90	—	276·4
745	C_6H_{13}	40·5/12	0·8174	0·8005	0·7817	0·7667	26·93	24·90	22·85	20·28	318·4

TABLE 6.

Ref. no.	n_C^{20}	n_D^{20}	n_F^{20}	$n_{G'}^{20}$	$[R]_C$	$[R]_D$	$[R]_F$	$[R]_G$	Mn_D^{20}
670 [a]	1·50547	1·51021	1·52206	1·52960	23·823	24·071	24·539	24·832	119·46
					Alkylpyridines				
671 [a]	1·49662	1·50102	1·51251	1·52230	28·839	29·057	29·617	30·092	139·78
672	1·49369	1·49783	1·50864	1·51791	33·46	33·69	34·31	34·84	160·49
673	1·48912	1·49314	1·50325	1·51202	38·20	38·46	39·13	39·71	180·93
674	1·48647	1·48023	1·49999	1·50848	42·83	43·11	43·84	44·47	201·48
675	1·48473	1·48843	1·49789	1·50591	47·45	47·76	48·54	49·21	222·12
676	1·48290	1·48645	1·49542	1·50437	52·09	52·41	53·23	54·05	242·68
677	1·48165	1·48515	1·49398	1·50202	56·71	57·07	57·95	58·95	263·30
678 [a]	1·50224	1·50685	1·51834	1·52826	28·743	28·967	29·519	29·992	140·32
679	1·49817	1·50231	1·51320	1·52261	33·41	33·64	34·26	34·79	160·97
680	1·49343	1·49745	1·50770	1·51656	38·08	38·35	39·01	39·59	181·46
681	1·48995	1·49380	1·50359	1·51198	42·72	43·00	43·71	44·34	201·96
682	1·48785	1·49146	1·50071	1·50888	47·35	47·65	48·41	49·08	222·57
683	1·48566	1·48920	1·49828	1·50602	51·98	52·30	53·13	53·83	243·13
684	1·48356	1·48698	1·49575	1·50317	56·61	56·95	57·82	58·58	263·63
685 [a]	1·50144	1·50584	1·51719	1·52700	28·756	28·971	29·517	29·984	140·23
686 [b]	1·49798	1·50211	1·51271	1·52185	33·37	33·61	34·21	34·72	160·95
687 [c]	1·49331	1·49729	1·50735	1·51608	38·07	38·33	38·99	39·55	181·44
688	1·49285	1·49673	1·50677	1·51542	38·05	38·30	38·96	39·52	181·37
689 [d]	1·49014	1·49387	1·50355	1·51174	42·71	42·98	43·69	44·30	201·79
690	1·49135	1·49515	1·50483	1·51317	42·60	42·88	43·59	44·20	202·14
691	1·49238	1·49616	1·50581	1·51405	42·58	42·85	43·56	44·17	202·28
692	1·48841	1·49196	1·50127	1·50926	47·34	47·63	48·39	49·05	222·65
693	1·48914	1·49278	1·50209	1·50737	47·12	47·53	48·40	48·72	222·25
694	1·48568	1·48917	1·49818	1·50657	51·97	52·28	53·10	53·83	243·12
695	1·48420	1·48759	1·49631	1·50439	56·60	56·93	57·80	58·58	263·74
696	1·48504	1·48846	1·49718	1·50460	56·50	56·70	57·70	58·43	263·89
697	1·47950	1·48260	1·49144	1·49688	84·24	84·70	86·03	86·83	387·61

TABLE 6. (*Continued.*)

Ref. no.	n_C^{20}	n_D^{20}	n_F^{20}	$n_{G'}^{20}$	$[R]_C$	$[R]_D$	$[R]_F$	$[R]_{G'}$	Mn_D^{20}
698	1·50418	1·50857	1·52003	1·52890	33·538	33·783	34·421	34·970	161·64
699	1·49653	1·50085	1·51198	1·52166	33·706	33·920	34·544	35·104	160·82
700	1·49612	1·50050	1·51182	1·52171	33·670	33·923	34·570	35·130	160·78
701	1·49346	1·49779	1·50908	1·51889	33·783	34·032	34·675	35·249	160·45
702	1·50184	1·50613	1·51755	1·52749	33·562	33·803	34·447	34·996	161·38
703 [e]	1·50617	1·51026	1·52100	1·53033	38·00	38·26	38·93	39·52	183·01
					Alkyl picolinates				
704	1·51654	1·52107	1·53334	1·54413	35·35	35·65	36·34	36·93	208·61
705	1·50622	1·51063	1·52200	1·53194	40·14	40·44	41·20	41·86	227·83
706	1·49996	1·50404	1·51479	1·52425	44·81	45·12	45·93	46·64	248·45
707	1·49745	1·501.2	1·51167	1·52062	49·43	49·77	50·62	51·37	269·05
708	1·49423	1·49821	1·50805	1·51668	54·04	54·41	55·32	56·10	289·56
709	1·49198	1·49562	1·50524	1·51354	58·68	59·04	60·01	60·84	309·97
710	1·48986	1·49347	1·50273	1·51156	63·30	63·68	64·69	65·65	330·54
					Alkyl nicotinates				
711	—	—	—	—	—	—	—	—	—
712 [g]	1·49989	1·50423	1·51532	1·52497	40·10	40·39	41·14	41·79	227·35
713 [h]	1·49488	1·49838	1·50908	1·51842	44·78	45·09	45·90	46·61	247·55
714	1·48857	1·49262	1·50302	1·52102	44·84	45·13	45·96	46·66	246·56
715 [h]	1·49148	1·49540	1·50549	1·51425	49·39	49·73	50·58	51·32	268·04
716	1·48709	1·49099	1·50098	1·50974	49·42	49·75	50·61	51·36	267·22
717	1·48506	1·48894	1·49887	1·50751	49·43	49·77	50·62	51·37	266·86
718	1·49032	1·49432	1·50390	1·51253	53·99	54·36	55·25	56·05	288·80
719 [h]	1·48654	1·49018	1·49950	1·50773	58·61	58·97	59·93	60·76	308·87
720 [h]	1·48614	1·48968	1·49888	1·50717	63·25	63·63	64·66	65·57	329·71
					Alkyl isonicotinates				
721	1·50918	1·51373	1·52511	1·53533	35·28	35·54	36·19	36·79	207·59
722	1·49692	1·50112	1·51222	1·52168	40·03	40·31	41·07	41·71	226·91
723	1·49185	1·49590	1·50629	1·51548	44·69	45·00	45·80	46·50	247·11
724	1·48883	1·49269	1·50270	1·51145	49·32	49·65	50·50	51·24	267·56
725	1·48708	1·49089	1·50045	1·50900	53·94	54·29	55·19	55·99	288·10
726	1·48497	1·48856	1·49784	1·50657	58·58	58·95	59·90	60·78	308·51
727	1·48367	1·48722	1·49633	1·50419	63·18	63·57	64·58	65·45	329·11
					Methyl pyridyl ketones				
728	1·51721	1·52224	1·53543	1·54717	33·89	34·16	34·88	35·52	184·40
729	1·52925	1·53442	1·54781	1·55995	33·78	34·05	34·76	35·34	185·97
730	1·52425	1·52931	1·54241	1·55423	33·68	33·92	34·65	35·28	185·26
					Pyridinealdehydes				
731	1·53075	1·53653	1·55185	1·56572	29·57	29·84	30·55	31·18	164·20
732	1·54372	1·54983	1·56584	1·58038	29·61	29·89	30·60	31·25	166·00
733	1·53813	1·54403	1·55961	1·57386	29·47	29·75	30·44	31·08	165·41
					Hydroxymethylpyridines				
734	1·53972	1·54442	1·55660	1·56718	30·24	30·46	31·02	31·51	168·54
735	1·54168	1·54649	1·55866	1·56933	30·23	30·45	31·01	31·49	168·76
					Dialkyl oxalates				
736 [j]	1·40812	1·41024	1·41547	1·41979	33·44	33·60	33·97	34·28	206·1
737 [j]	1·41431	1·41646	1·42178	1·42613	42·75	42·94	43·43	43·82	246·73
738 [j]	1·42119	1·42337	1·42881	1·43316	51·94	52·17	52·76	53·22	287·87
739 [j]	1·42661	1·42883	1·43425	1·43867	61·20	61·48	62·15	62·70	329·06
740	1·43132	1·43361	1·43908	1·44352	70·42	70·75	71·53	72·15	370·37
741	1·43524	1·43752	1·44304	1·44750	79·67	80·03	80·91	81·62	411·72
					Aliphatic aldehydes				
742 [k]	1·37797	1·37995	1·38488	1·38903	20·72	20·81	21·05	21·25	99·49
743 [k]	1·39237	1·39429	1·39937	1·40360	25·31	25·42	25·70	25·99	120·10
744	1·40241	1·40450	1·40966	1·41399	29·91	30·04	30·38	30·67	140·67
745	1·40950	1·41163	1·41692	1·42131	34·57	34·73	35·12	35·44	161·18

[a] Cf. Biddiscombe *et al.*[2] [b] Sample prepared by reduction of 4-acetylpyridine. [c] Sample prepared from pyridine and propionic anhydride. [d] Sample prepared from pyridine and butyric anhydride. [e] Cf. Wibaut and Arens, *Rec. Trav. chim.*, 1943, **62**, 549. [f] M. p. 38°. [g] Cf. Badgett *et al.*[26] [h] Cf. Badgett *et al.*[26] [j] Cf. Vogel.[27] [k] Cf. Coomber and Partington, *J.*, 1938, 1444.

hydrogen carbonate solution, the distillate was collected and ether-extracted in nitrogen, and the dried extract distilled through a 4″ Fenske-type column filled with glass helices; the product had b. p. 75°/764 mm.

Heptaldehyde, purified as above, had b. p. 40·5°/12 mm.

Valeraldehyde and hexanaldehyde. These were prepared by passing pure pentyl and hexyl alcohol respectively through a copper–chromium oxide catalyst deposited on pumice (3—8 mesh) [28] contained in a copper tube heated at 320°.[29] The crude products were dried ($MgSO_4$) and distilled through a 6″ Fenske-type column (packed with glass helices) with a variable take-off head at a reflux ratio of 10 : 1. Valeraldehyde had b. p. 102·5—103·5°/768 mm.; hexanaldehyde had b. p. 50·5—51°/40 mm.

Physical Properties.—Tables 5 and 6 summarise the physical properties. The numbering of compounds in bold type follows from Part XXIV.[11] B. p.s in Table 5 are at 760 mm. unless otherwise indicated.

Ultraviolet Spectra.—Measurements were made in matched 1 cm. silica cells on a Unicam spectrophotometer S.P. 500. Hexane " free from aromatic hydrocarbons " was purified by percolation through a 40″ column of silica gel (14—20 mesh). Solutions were prepared by dissolving an accurately weighed amount (12—15 mg.) of the sample in 10·0 ml. of purified hexane: 1·00 ml. of this solution was diluted to 25·0 ml. with purified hexane.

TABLE 7. *Absorption maxima.*

Alkyl	*c*	$\lambda_{max.}$	*E*	$\lambda_{max.}$	*E*	$\lambda_{max.}$	*E*
		2-Alkylpyridines					
Methyl	0·50	256·0	2450	261·5	2450	268·0	1800
Butyl	0·57	256·0	2400	261·5	2400	268·0	1800
Heptyl	0·48	256·0	2500	261·5	2500	268·0	1900
		3-Alkylpyridines					
Methyl	0·95	258·0	2200	262·5	2200	267·0	1650
Butyl	0·71	258·0	2350	262·5	2350	267·0	1750
Heptyl	0·51	258·0	2400	262·5	2400	267·0	1800
		4-Alkylpyridines					
Methyl	0·57	255·0	1600				
Butyl	0·37	255·0	1700				
t-Butyl	0·38	255·0	1700				
Heptyl	0·27	255·0	1700				
		Dialkylpyridines					
2,6-Me_2	0·45	261·0	2950	265·5	3150	272·5	2300
2,5-Me_2	0·29	264 *	2750	269·0	2900	275·5	2150
2,4-Me_2	0·25	—	—	260·5	2050	267·5	1850
2,3-Me_2	0·23	260 *	2800	265·5	2950	271 *	2300
2,5-Me_2	0·25	266 *	2650	269·0	2800	275·0	2150
4-Et-3-Me	0·32	256 *	1950	260·0	2050	268 *	1600
		Alkyl picolinates					
Methyl	0·49	263·5	3300	259·0	3300		
Ethyl	0·43	263·5	3250	259·0	3200		
Butyl	0·39	263·5	3300	259·0	3300		

Alkyl	*c*	$\lambda_{max.}$	*E*	$\lambda_{max.}$	*E*
	Alkyl nicotinates				
Methyl	0·43	262·5	2650	257·5	2650
Ethyl	0·41	262·5	2550	257·5	2500
Butyl	0·32	262·5	2650	257·5	2650
	Alkyl isonicotinates				
Methyl	0·39	273·5	2600		
Ethyl	0·38	273·5	2550		
Butyl	0·34	273·5	2600		
Solvent	*c*	$\lambda_{max.}$	*E*	$\lambda_{max.}$	*E*
	2-Acetylpyridine				
Hexane	0·33	267·5	3150	227·5	6850
0·1N-H_2SO_4	0·10	269·5	6800	224·0	2800
0·1N-NaOH	0·10	270·0	4950	230·0	7400
	3-Acetylpyridine				
Hexane	0·38	266·0	2400	227·5	8550
0·1N-H_2SO_4	0·14	264·0	4550	222·5	5200
0·1N-NaOH	0·14	267·5	3000	230·0	8250
	4-Acetylpyridine				
Hexane	0·41	279·0	2050	221·0	7400
0·1N-H_2SO_4	0·15	275·0	3650	222·0	7050
0·1N-NaOH	0·15	282·0	2550	222·0	9050

* Inflexion.

The results are in Table 7. λ are in mμ. Concentrations *c* are in millimoles per l. Our values for $\lambda_{max.}$ and for *E* for the three picolines are in excellent agreement with those of Herington [30] for cyclohexane solutions. Agreement was satisfactory with the published data on methyl 3-pyridyl ketone [31] in 2,2-dimethylbutane and acidified ethanol.

Infrared Spectra.—The infrared absorption spectra (capillary film) were kindly measured

[28] Ref. 24, p. 321.

[29] Linstead, Elvidge, and Whalley, " Modern Techniques of Organic Chemistry," Butterworths, London, 1955, p. 100.

[30] Herington, *Discuss. Faraday Soc.*, 1950, **9**, 31; only curves of the absorption spectra are given.

[31] Swain, Eisner, Woodward, and Brice, *J. Amer. Chem. Soc.*, 1949, **71**. 1342.

by Mr. R. F. Branch, B.Sc. of the Ministry of Supply, Woolwich, using a Perkin–Elmer double-beam instrument with a rock-salt prism. The compounds were sealed into glass vials immediately after distillation, and exposure to the atmosphere was reduced to a minimum in transfer to the cell of the instrument. However, sufficient water was absorbed to give O–H association bands at 3030—2860 cm.$^{-1}$.

The spectra for the three picolines and for 2,6-lutidine were identical with those obtained by Biddiscombe *et al.*[2] except that our spectra contained the water absorption band at 3030—2860 cm.$^{-1}$. See also Coulson, *J.*, 1959, 1934.

Lists of the main frequencies and rough estimates of the intensities of the stronger absorption bands are presented in Table 8 (vs = very strong, s = strong, and m = medium).*

TABLE 8. *Infrared spectra: main peaks (cm.$^{-1}$).*

Key: (1) 2,3-Lutidine. (2) 2,4-Lutidine. (3) 2,5-Lutidine. (4) 3,5-Lutidine. (5) 2-Acetylpyridine. (6) 3-Acetylpyridine. (7) 4-Acetylpyridine. (8) Et picolinate. (9) Et nicotinate. (10) Et isonicotinate.

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)
680s	727s	710m	710vs	742s	704vs	817vs	695vs	703vs	677vs
727vs	754m	725s	723s	780vs	748m	960s	707vs	743vs	707vs
788vs	817vs	815vs	856vs	953s	810vs	991s	747vs	786m	758vs
852m	912s	856m	928m	995s	956vs	1018m	783m	833m	853vs
970s	996m	1028s	943m	1042s	1021vs	1061s	824s	853s	874s
991s	1032s	1130m	1007m	1100s	1090m	1080m	856s	872m	992s
1020s	1131m	1237m	1032vs	1145m	1117s	1213s	872m	1025vs	1020vs
1067m	1137m	1287m	1089vs	1245vs	1191s	1260vs	993vs	1037vs	1063vs
1120vs	1163m	1368vs	1137vs	1278vs	1238s	1316m	1020s	1109vs	1115vs
1172s	1243m	1440s	1162vs	1291s	1267vs	1353vs	1044vs	1169vs	1170s
1231s	1287s	1480vs	1227s	1353vs	1353vs	1401vs	1086vs	1190vs	1210s
1267m	1372s	1560s	1267m	1415m	1412vs	1543s	1126vs	1290vs	1214vs
1361s	1395s	1590s	1313s	1430s	1467m	1588m	1169s	1320vs	1277vs
1373s	1444vs	2890s	1370vs	1456m	1581vs	1684vs	1239vs	1361vs	1316vs
1422vs	1482vs	2960m	1413vs	1581s	1682vs	3000m	1275vs	1386vs	1361vs
1430vs	1560vs	3370m	1450vs	1692vs	2980m	3330m	1287vs	1415vs	1404vs
1450vs	1600vs		1570vs		3390m		1300vs	1440s	1440s
1570vs	2930s		1590s				1361vs	1464vs	1460s
1620m	2990s		1620m				1384s	1588vs	1487s
1638m	3450m		1650m				1430vs	1720vs	1558vs
1650m			1770m				1460s	2970vs	1592m
2900vs			1850m				1575vs		1720vs
3020s			2880vs				1636m		2970s
3370s			2940vs				1710vs		3430m
			2980vs				1730vs		
			3370s				2960s		
							3040m		
							3430m		

The stretching vibration frequencies of the carbonyl links in the pyridinemonocarboxylic esters and the acetylpyridines are at slightly lower frequencies than those of aliphatic compounds,[32] *viz.*: Et picolinate 1708, Et nicotinate 1717, Et isonicotinate 1720, aliphatic esters [32] 1740—1738, 2-acetylpyridine 1693, 3-acetylpyridine 1680, 4-acetylpyridine 1686, and aliphatic ketones 1710 cm.$^{-1}$.

APPENDIX. *Apparatus for fractional freezing.*

The apparatus used for the purification of γ-picoline and various lutidines by fractional freezing is shown in Figs. 1 and 2. It consists of a test-tube (20 × 4 cm.) held by a cork in a larger tube (20 × 7 cm.) immersed in a Dewar vessel containing, usually, acetone and carbon dioxide. The liquid to be frozen is placed in the inner tube, which is closed by a cork holding a gas-inlet tube (4—5 mm. diameter; bent and drawn out at the lower end to 1 mm. diameter), a long-stem alcohol thermometer, and an outlet tube (with a calcium chloride guard-tube, not illustrated). The apparatus for intermittent gas stirring (Fig. 2) consists of: *A*, the inlet tube

* The complete spectra are given in C. T. Kyte, Ph.D. Thesis, London, September, 1956.

[32] Thompson and Torkington, *J.*, 1945, 640.

for pure nitrogen; *B*, the gas outlet tube, connected by rubber " pressure " tubing through a wash-bottle containing concentrated sulphuric acid to the gas inlet tube in Fig. 1; *G*, a B24 ground-glass joint; *C*, a mercury reservoir; *D*, a glass needle-valve, constructed of tubing with the same internal diameter as tube *B* (5 mm.), ground in at *E*, the upper end being of 3 mm. glass rod; to ensure that the glass " needle " moves vertically, two sets of " pips " are fused on to the glass " needle." The glass " needle " is mounted on a cork float *F*. When *C* is raised the pressure of mercury on the float forces the " needle " upwards and closes the gas outlet *B*. *C* is raised so that the float is immersed in mercury to a depth of about 1″. A slow stream of nitrogen is allowed to pass into the gas-chamber through *A*: the resulting pressure gradually

FIG. 1.

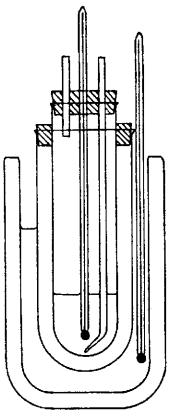
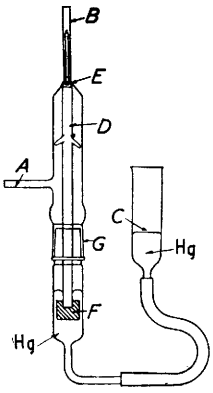


FIG. 2.



forces the mercury back into the reservoir *C* and ultimately the level of the mercury falls below that of the cork float *F*, the glass " needle " then falls, releasing the gas pressure through the outlet *B*; the mercury simultaneously rises to its original level, closing the glass valve. The height of the mercury in *C* and the rate of flow of gas from the cylinder are adjusted to give 0·5 sec. bursts of gas every 10—20 sec.; the rate of bubbling is indicated by the sulphuric acid wash-bottle.

Stirring with a slow and continuous stream of gas was unsatisfactory because, when about half of the liquid was frozen, channelling occurred which led to supercooling. The vigorous intermittent stirring produced very efficient agitation in the suspension and distintegrated small aggregates of crystals.

The cooling-bath was maintained at 5—6° below the f. p. of the liquid by the occasional addition of solid carbon dioxide: a sample of about 50 ml. could thus be frozen in 4—8 hr. A cooling curve was plotted for each sample and the freezing was continued until the temperature began to fall rapidly. The gas supply was then discontinued, the thermometer and inlet tube were removed, and the supernatant liquid was decanted into a measuring cylinder. The " freezing " tube was then closed, the solid allowed to melt, and the process repeated.

If seeding of the liquid was required in order to prevent supercooling, crystals were introduced on a glass rod through the outlet tube.

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DEPARTMENT OF CHEMISTRY, WOOLWICH POLYTECHNIC,
LONDON, S.E.18.

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