

CHROM. 4118

SORBATE-SORBENT INTERACTIONS OF NITROGEN HETEROCYCLES IN
GAS CHROMATOGRAPHY

PYRIDINE DERIVATIVES

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(Received April 8th, 1969)

SUMMARY

The gas chromatography of a wide variety of pyridine and benzene derivatives was carried out. The sorbate-sorbent interactions of 3-substituted pyridines and 4-alkylpyridines were similar to those in the benzene derivatives; the retention times of the more readily available benzene compounds could accurately predict the retention times of 3-substituted pyridines. Similar relations with other pyridines were complicated by steric effects and by direct resonance interactions between substituents and the ring nitrogen.

INTRODUCTION

Recent reports¹⁻³ suggested that the π -electrons in benzenoid compounds were responsible for a greater part of the sorbate-sorbent interactions in gas chromatography and there were correlations between retention times and substituent constants (σ). For our studies in heterocyclic chemistry and in water pollution problems we used gas chromatography to analyze and identify a wide variety of 2-, 3-, and 4-substituted pyridines. Although there have been several reports⁴⁻⁹ on the analysis of pyridines, these chromatographic data were limited to a small number of compounds and were obtained under different analytical conditions. Since a comprehensive listing of such information is not available and since little is known concerning the sorbate-sorbent interactions with nitrogen heterocycles, we wish to present our observations.

EXPERIMENTAL

Most of the compounds referred to in this paper were obtained commercially or kindly donated to us. 3-Fluoropyridine was prepared by Mr. JAMES SALITROS via

the Schieman reaction¹⁰. The boiling points were obtained from the Handbook of Chemistry or the references cited (Table I).

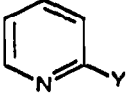
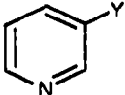
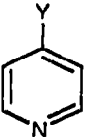
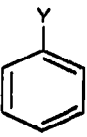
The gas chromatographic analysis was carried out with a Varian Aerograph Model 1200, fitted with a flame-ionization detector. The injector and detector temperatures were kept at 240 and 250°, respectively, but the column temperatures were maintained at 73, 100, or 150°. A 1/8 in. × 5 ft. stainless steel column packed with 5% SE-30 on 60/80 Chromosorb W was used. The response was set at 16×10^2 and the nitrogen flow was 22.5 ml/min.

One microliter sample was injected; the samples were prepared by dissolving 0.1 g of a solid (or 0.1 ml, in the case of a liquid) in 4.9 ml of anhydrous ether. 2-*n*-Propylpyridine (retention time 1.26 min at 100°) was used to check the reproducibility of the system. (Retention times observed were independent of sample size up to 3 μ l).

TABLE I

BOILING POINTS (b.p.) AND RETENTION TIMES (t_r) OF THE MONOSUBSTITUTED BENZENES AND PYRIDINES CHROMATOGRAPHED AT 100°

All the boiling points were obtained from the Handbook of Chemistry and Physics¹⁴.

Y								
	b.p. (°C)	t_r (min)	b.p. (°C)	t_r (min)	b.p. (°C)	t_r (min)	b.p. (°C)	t_r (min)
H	115	0.42	115	0.42	115	0.42	80	0.34
CH ₃	128	0.56	143	0.67	143	0.67	111	0.49
C ₂ H ₅	149	0.80	165	1.01	164	1.03	136	0.70
<i>n</i> -C ₃ H ₇	168	1.26	—	—	186	1.73	159	1.06
F	128 ^a	0.46	105 ^a	0.41	—	—	85	0.37
Cl	170	0.93	148	0.77	148 ^b	0.75	132	0.64
Br	192 ^a	1.45	169	1.16	125 ^b	0.92	155	0.94
CN	212	1.67	201 ^a	1.26	195 ^a	1.01	191	1.12
COCH ₃	192	1.51	220	2.17	212	1.78	202	1.78
CHO	181 ^a	1.01	203 ^a	1.24	—	—	178	1.04
OCH ₃	167	0.73	—	—	—	—	154	0.87
NH ₂	204	1.49	273	2.32	273 ^a	3.36	184	1.08
CH ₂ NH ₂	—	—	—	—	230	2.54	185	1.44
NMe ₂	196	2.18	—	—	(114) ^c	6.30	194	2.02
Benzoyl	315 ^a	5.07 ^d	—	—	—	—	306	4.14 ^e

^a Boiling points were obtained from ref. 15.

^b At 515 mm.

^c Melting point.

^d At 0.3 mm.

^e Chromatographed at 150°.

RESULTS AND DISCUSSION

Tables I and II are summaries of the various pyridine and benzene derivatives chromatographed; SE-30, a common liquid substrate, was used as the sorbent. Most of the compounds were analyzed at 100°, but a temperature of 73 or 150° was also

TABLE II

RETENTION TIMES OF VARIOUS COMPOUNDS CHROMATOGRAPHED AT 73, 100, AND 150° RESPECTIVELY

No.	Compound	Retention times (min)		
		73°	100°	150°
1	Pyridine	0.77	0.42	—
2	3-Picoline	1.53	0.67	—
3	4-Picoline	1.56	0.67	—
4	2,6-Lutidine	1.76	0.76	—
5	2-Ethylpyridine	1.96	0.80	—
6	2,5-Lutidine	2.40	0.95	—
7	2,4-Lutidine	2.43	0.96	—
8	4-Cyanopyridine	—	1.01	0.45
9	Benzylchloride	—	1.32	0.50
10	2-Amino-5-picoline	—	2.39	0.71
11	Methylnicotinate	—	2.63	0.74
12	2-Ethanolpyridine	—	2.85	0.76
13	3-Pyridylcarbinol	—	2.90	0.73
14	2-Chloro-5-nitropyridine	—	4.18	0.99
15	2-Methoxy-5-nitropyridine	—	5.31	1.11
16	Isoquinoline	—	5.25	1.07
17	2-Methoxy-3-nitropyridine	—	5.50	1.12
18	2-Methylquinoline	—	6.57	1.26
19	3-Pyridylpropanol	—	8.70	1.46

employed so that suitable retention times and symmetrical peaks were obtained. The retention times at 73° (or 150°) may be converted to the retention times at 100° using Fig. 1. These linear relationships allowed comparisons of retention times of compounds having widely different vapor pressures and boiling points (from 60 to 350°) on a common scale (100°). The relationships can also be used to predict retention times at 73 or 150°, once the retention time at 100° of a compound is known.

A linear relationship between retention times (or $\log t_r$) and boiling points expected^{11, 12} of SE-30 was not observed, though a general trend was evident (Fig. 2).

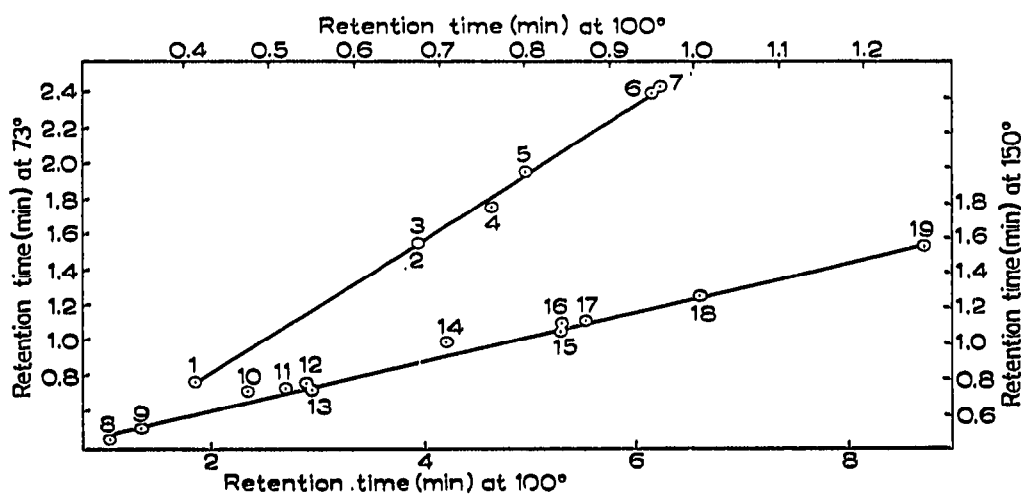


Fig. 1. Correlations of retention times at different temperatures. For explanation of the numbers see Table II.

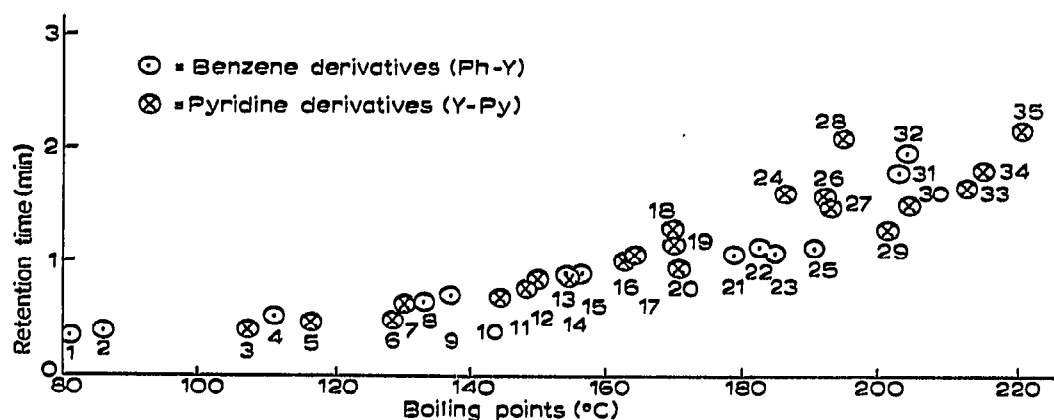


Fig. 2. Plot of retention times *versus* boiling points. (1) = Benzene, (2) = PhF, (3) = 3-F-Py, (4) = PhCH₃, (5) = Pyridine, (6) = 2-F-Py, (7) = 2-CH₃-Py, (8) = PhCl, (9) = PhEt, (10) = 4-CH₃-Py, (11) = 4-Cl-Py, (12) = 2-Et-Py, (13) = PhOCH₃, (14) = 3-Cl-Py, (15) = PhBr, (16) = 3-Et-Py, (17) = 4-Et-Py, (18) = 2-*n*Pr-Py, (19) = 3-Br-Py, (20) = 2-Cl-Py, (21) = PhCHO, (22) = PhOH, (23) = PhNH₂, (24) = 4-*n*Pr-Py, (25) = PhCN, (26) = 2-CH₃CO-Py, (27) = 2-Br-Py, (28) = 2-(CH₃)₂N-, (29) = 3-CN-Py, (30) = 2-NH₂-Py, (31) = PhCOCH₃, (32) = PhN(CH₃)₂, (33) = 2-CN-Py, (34) = 4-COCH₃-Py, (35) = 3-COCH₃-Py.

Better correlations were obtained for families of similar compounds, *e.g.*, benzene derivatives fall on one line and pyridine derivatives on another.

Mono-substituted benzenes (1) and their nitrogen analogues, the 2-, 3-, and 4-substituted pyridines (2-4), have similar π -electron systems. In addition, the

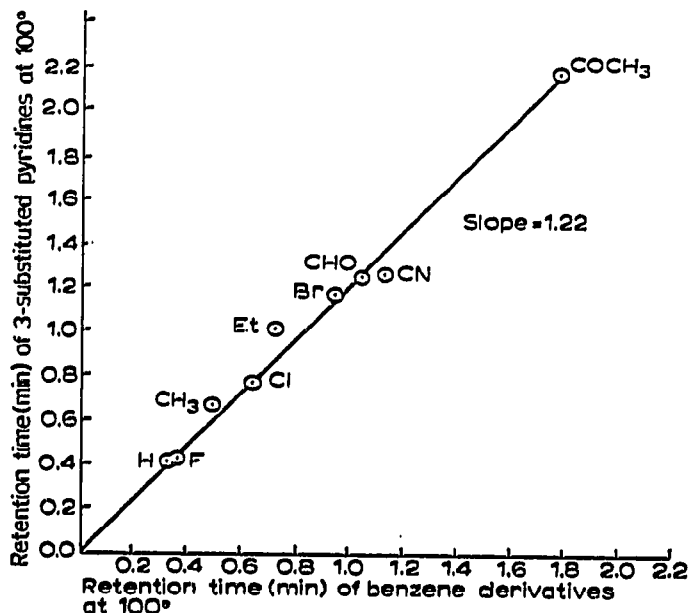
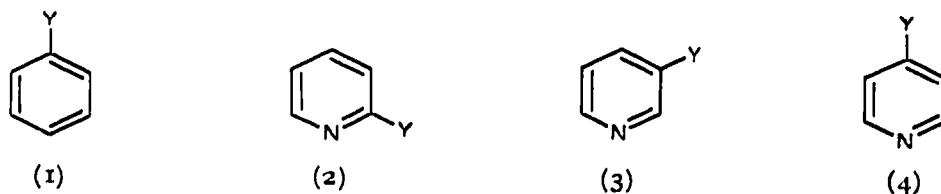


Fig. 3. Plots of retention times of 3-substituted pyridines *versus* the corresponding benzene derivatives.

TABLE III

PREDICTION OF RETENTION TIMES OF 3-SUBSTITUTED PYRIDINES (t_{Py}) FROM THE RETENTION TIMES OF THE CORRESPONDING BENZENE DERIVATIVES (t_{Bz})^a

Substituent	Predicted t_{Py}	Observed t_{Py}	Δ
H	0.43	0.43	0.00
F	0.44	0.41	0.03
CH ₃	0.63	0.67	0.04
Cl	0.77	0.77	0.00
Et	0.91	1.01	0.10
Br	1.15	1.16	0.01
CHO	1.27	1.24	0.03
CN	1.34	1.26	0.08
COCH ₃	2.17	2.17	0.00

$${}^a t_{Py} = 1.22 t_{Bz}$$

pyridine series have a ring nitrogen which would be expected to enhance sorbate-sorbent interactions and therefore influence retention times. The nature and extent of this interaction may be evaluated by Figs. 3-5. Except for 3-aminopyridine in which the substituent (NH₂) was expected to interact very strongly, there was a linear relationship between the retention times of various 3-substituted pyridines (t_{Py}) and the corresponding mono-substituted benzenes (t_{Bz}) respectively (Fig. 3): $t_{Py} = 1.22 t_{Bz}$.

Table III shows the excellent agreement between observed and predicted values. From the practical point of view, we suggest that laboratories which do not carry a large stock of pyridines use the readily available 3-alkylpyridines and alkylbenzenes to derive a similar relationship for their particular system.

The excellent linear relationship between 3-substituted pyridines and the corresponding benzenes derivatives indicates that these two series have similar sorbent-sorbate interactions, due to the similar geometry, π -electron systems, and mechanisms for the transmission of substituent effects. It is interesting to note that

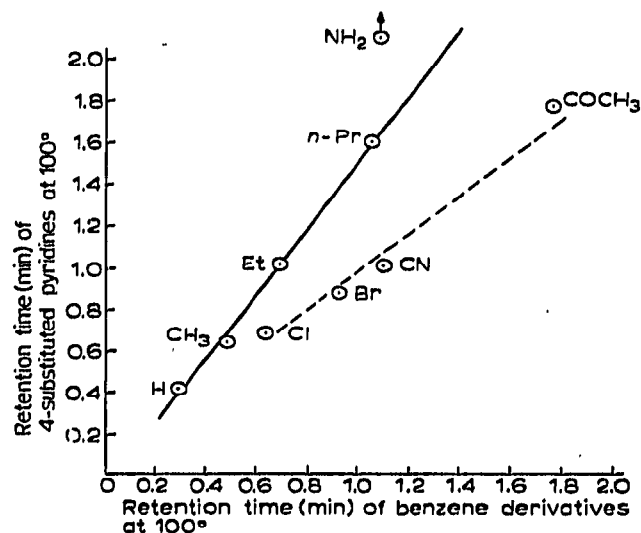


Fig. 4. Plots of retention times of 4-substituted pyridines versus the corresponding benzene derivatives.

TABLE IV

EFFECT OF REPLACING A METHYLENE GROUP BY A CARBONYL GROUP ON RETENTION TIMES

Substituted pyridine	Retention time (min)	Ratio of retention times
$\begin{array}{c} \text{O} \\ \\ 2\text{-C-H} \end{array}$	1.01	1.8
2-CH ₃	0.56	
$\begin{array}{c} \text{O} \\ \\ 3\text{-C-H} \end{array}$	1.24	1.8
3-CH ₃	0.67	
$\begin{array}{c} \text{O} \\ \\ 2\text{-C-CH}_3 \end{array}$	1.51	1.9
2-CH ₂ -CH ₃	0.80	
$\begin{array}{c} \text{O} \\ \\ 3\text{-CCH}_3 \end{array}$	2.17	3.2
3-CH ₂ CH ₃	0.67	
$\begin{array}{c} \text{O} \\ \\ 4\text{-C-CH}_3 \end{array}$	1.78	1.7
4-CH ₂ -CH ₃	1.03	
* C ₆ H ₅ $\begin{array}{c} \text{O} \\ \\ \text{CH}^a \end{array}$	1.04	2.1
C ₆ H ₅ $\begin{array}{c} \text{O} \\ \\ \text{CH}_3^a \end{array}$	0.49	
C ₆ H ₅ $\begin{array}{c} \text{O} \\ \\ \text{CCH}_3^a \end{array}$	1.78	2.5
C ₆ H ₅ CH ₂ CH ₃ ^a	0.70	

^a Benzene derivative.

the retention times of *all* these pyridine compounds were 22% longer than those of the corresponding benzene derivatives, thus suggesting that the ring nitrogen-sorbent interaction was independent of steric or strong resonance effects (*cf.* below).

The importance of the contribution by the ring nitrogen is again observed in Figs. 4 and 5. A linear relationship was obtained between 4-alkylpyridines and alkylbenzenes; however, compounds with substituents (*e.g.*, NH₂, COCH₃, Br) which could conjugate directly and strongly with the ring nitrogen deviated from this line (Fig. 4). However, the direction of the deviation from the alkyl derivatives line agreed with the values of σ_p^0 , the so-called normal substituent constant¹³, which were measures of *p*-substituent effects. Thus, the point for the NH₂-derivative ($\sigma_p^0 = -0.038$) fell to the left of the solid line, but that of COCH₃-derivative ($\sigma_p^0 = +0.46$) was on the right.

Fig. 5 shows the plot of the retention times of 2-substituted pyridines and the

corresponding substituted benzenes. As expected, steric and electronic (resonance) effects were too complex to allow simple interpretation of the interactions.

Finally, two general trends should be mentioned. The 2-substituted pyridines chromatographed faster than the corresponding 3- or 4-substituted pyridines, indicating steric inhibition of the interaction of the ring nitrogen with the sorbent. The replacement of a methylene group (CH_2) by a carbonyl moiety ($\text{C}=\text{O}$) caused the increase (2-3 fold) of retention times (Table IV), due primarily to an added interaction of the carbonyl π -system with the sorbent.

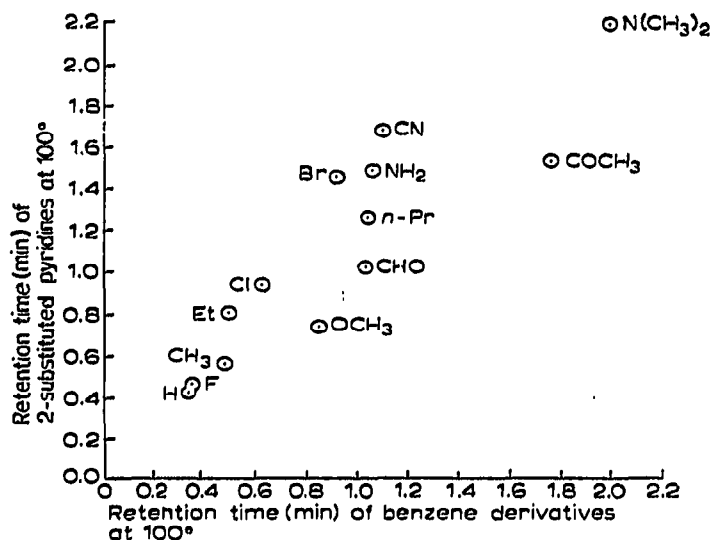


Fig. 5. Plots of retention times of 2-substituted pyridines *versus* the corresponding benzene derivatives.

ACKNOWLEDGEMENTS

Funds for this study were provided in part by Grant No. WP-01312, FWPCA, Department of Interior. The additional financial assistance from the Welch Research Foundation in the form of supplies and a scholarship for this project is gratefully acknowledged. The authors wish to thank Reilly Tar and Chemical Corporation for samples of pyridines.

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