

GAS-LIQUID CHROMATOGRAPHY OF SOME TYPES OF HETEROCYCLIC COMPOUNDS

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INTRODUCTION

The importance of gas-liquid chromatography is quite extensively recognised, at present, for solving not only analytical problems in the broad sense, but also as a method permitting the resolution of some of the questions related to the characteristic parameters of a molecule. The number of investigations in which the behaviour of a substance under conditions of gas-liquid chromatography is linked with the structure and spatial image of a molecule, is, however, still quite limited.

In this respect, heterocyclic compounds hold a prominent place. In most cases these are polar substances in which, when passing from one compound to another (as, for instance, in the thiophene, furan and pyrrole series), it is possible to trace by the chromatographic behaviour the peculiarities due to the heteroatom as long as it conserves, at first approximation, the geometry of the ring. In addition, the analytical aspect of the matter has not, in the main, been investigated either.

This work describes the basic results of studying the gas-liquid chromatographic behaviour of heterocyclic compounds; these were mostly synthesized first at the Zelinsky Institute of Organic Chemistry of the U.S.S.R. Academy of Sciences. The results illustrate the complex of problems which can be solved by gas-liquid chromatography, for instance:

- (1) Qualitative and quantitative analyses of multicomponent mixtures, including high-boiling mixtures (with a boiling point up to 450°) and highly polar (e.g. pyridine) compounds;
- (2) Determination of thermodynamic parameters of interaction between a substance and a stationary phase, and interpretation of the thermodynamic data as a function of the structure of a molecule.

EXPERIMENTAL

The investigation was carried out on a gas-liquid chromatograph made at the Zelinsky Institute of Organic Chemistry of the U.S.S.R. Academy of Sciences. The chromatograph is equipped with a heat conductivity detector, a 2 mV recorder with a time range of 1-2 sec, and an air thermostat which makes it possible to maintain a temperature in the column and in the heat conductivity detector up to 300°. Helium was used as carrier gas.

In every case, except when specially stipulated, copper spiral columns were used, with an inner diameter of 4–6 mm. To distribute the filling evenly, it was charged into the columns with periodic tapping.

PYRIDINE BASES

Gas-liquid chromatography of polar substances is generally complicated by the fact that the substance to be chromatographed interacts with the solid support, producing sharp non-symmetrical peaks on the chromatogram. Such interaction is particularly marked when acids or bases are chromatographed; the separation of pyridine bases entails just such complications. Acid-base interaction with the solid support is superimposed on the process of dissolution in the stationary phase. To eliminate such interaction, we used as a solid support either diatomite brick treated beforehand with 5 % alcoholic caustic soda with subsequent decantation¹, or sodium chloride for which acid-base interaction is practically precluded². Either way has

TABLE I

RELATIVE RETENTION VOLUMES OF NITROGEN-CONTAINING HETEROCYCLIC COMPOUNDS

Item No.	Compound	Mol. wt.	Boiling point (°C)	$V_{R^{rel.}}$					
				PEGA/diatomite brick			PEGA/NaCl		
				150°	180°	210°	150°	180°	210°
1	Pyridine	79.1	115.3	1.0	1.0	1.0	1.0	1.0	1.0
2	α -Picoline	93.1	128.8	1.2	1.08	1.0	1.19	1.05	1.0
3	β -Picoline	93.1	143.8	1.72	1.43	1.16	1.75	1.4	1.2
4	γ -Picoline	93.1	145.4	1.85	1.42	1.16	1.9	1.4	1.2
5	2-Ethylpyridine	107.1	149.0	1.4	1.1	1.0	1.2	1.05	1.0
6	4-Ethylpyridine	107.1	165.0	3.3	2.1	1.2	3.2	2.0	1.1
7	4-Vinylpyridine	105.1	170.0	—	2.2	1.3	—	—	—
8	2,4-Lutidine	107.1	158.4	2.0	1.5	—	1.9	1.5	1.2
9	2,6-Lutidine	107.1	144.0	1.1	1.0	1.0	1.0	1.0	—
10	2,4,6-Trimethylpyridine	121.1	171.0	2.06	1.4	1.03	1.7	—	—
11	Ethyl nicotinate	151.2	223–224	—	3.9	2.6	3.14	2.4	1.63
12	Ethyl isonicotinate	151.2	216–217	—	3.44	2.38	2.82	2.2	1.55
13	3-Acetylpyridine	121.1	225	—	4.72	3.14	4.4	2.9	1.98
14	4-Acetylpyridine	121.1	215	—	4.0	2.6	4.08	2.8	1.8
15	3-Propionylpyridine	135.2	233	—	5.3	3.48	5.70	3.33	2.03
16	4-Propionylpyridine	135.2	225	—	4.98	—	—	—	—
17	3-Butyrylpyridine	149.2	240	—	6.35	3.8	7.3	3.94	2.33
18	4-Butyrylpyridine	149.2	230	—	5.66	3.4	6.7	3.7	2.2
19	3-Valerylpyridine	163	255	—	8.87	5.12	—	4.87	2.8
20	4-Valerylpyridine	163	240	—	7.7	—	—	—	—
21	α -Aminopyridine	94.1	210	—	4.26	3.74	—	—	3.0
22	Diethylamide of nicotinic acid	—	280	—	—	—	—	—	5.4
23	Piperidine	85.2	106	—	1.16	1.0	1.4	1.14	1.0
24	N-Acetylpiperidine	127.2	226–7	—	5.3	3.83	2.6	2.3	1.67
25	Quinoline	129.2	238	—	6.1	3.5	—	4.77	2.3
26	Isoquinoline	129.2	243	—	7.3	4.66	—	8.5	3.8
27	Quinaldine	143.1	247	—	6.35	3.6	—	5.7	2.46
28	Indole	117.1	223–4	—	14.8	8.9	—	7.65	4.1
	V_0 (pyridine)						29.0	8.62	4.78

proved quite justifiable³ (see Table I*). For example, an analysis was made in less than 10 min of a seven-component mixture of nitrogen-containing compounds on polyethyleneglycol adipate (PEGA) (Fig. 1). The latter, a stationary phase possessing high thermal stability and selectivity, was obtained by conventional methods⁴. A multicomponent mixture consisting, in the main, of pyridine derivatives could also be separated on a sodium chloride support (Fig. 2).

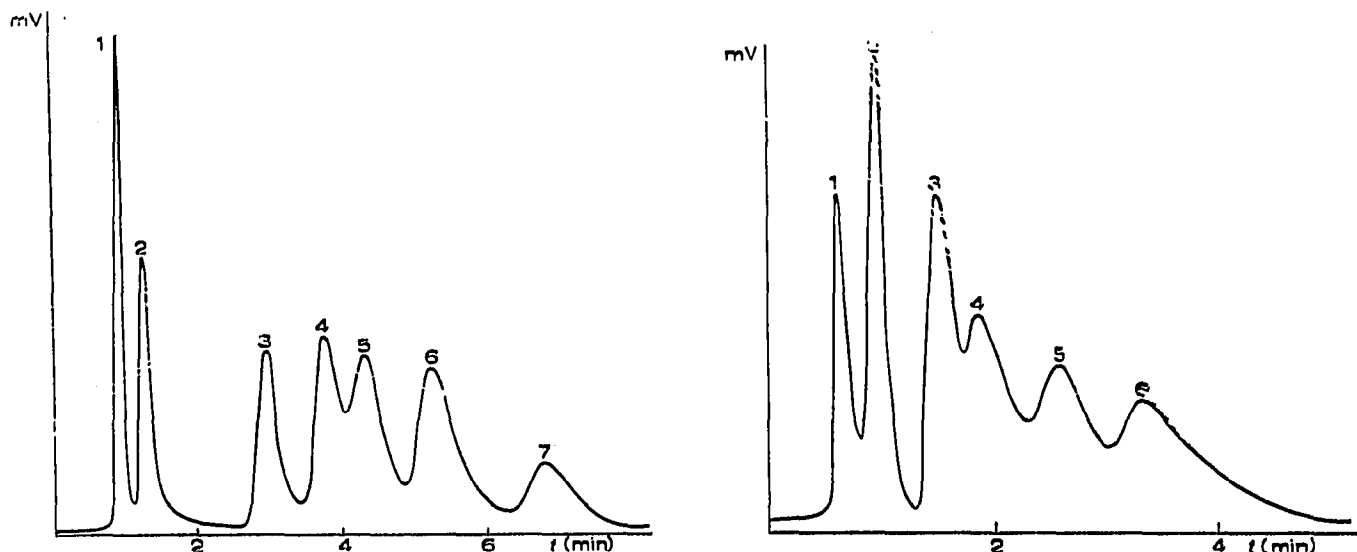


Fig. 1. Chromatogram of a mixture of nitrogen-containing compounds. Column: 20% of polyethyleneglycol adipate on diatomite brick treated with a 5% alcoholic solution of caustic soda; 2.6 m long; I.D., 6 mm; material, copper. Experimental conditions: temperature of the column and of the heat conductivity detector, 180°; helium flow rate, 67 ml/min. Notations of the peaks: 1 = pyridine; 2 = 2,4,6-trimethylpyridine; 3 = aniline; 4 = ethyl nicotinate; 5 = ethyl isonicotinate; 6 = 3-acetylpyridine; 7 = quinoline.

Fig. 2. Chromatogram of a mixture of nitrogen-containing compounds. Column: 1.0% polyethyleneglycol adipate on sodium chloride; 2.6 m long; I.D., 6 mm; material, copper. Experimental conditions: temperature of the column and of the heat conductivity detector, 180°; helium flow rate, 55 ml/min. Notations of the peaks: 1 = pyridine; 2 = aniline; 3 = ethyl nicotinate; 4 = 3-acetylpyridine; 5 = 3-butyrylpyridine; 6 = 3-valerylpyridine.

Polyethyleneglycol, when used on sodium chloride, possesses a lower selectivity than PEGA. Even at comparatively low temperatures (of the order of 150°), it is not possible to separate ethyl nicotinate and 3-acetylpyridine, which have similar boiling points, on it.

Pyridine, ethyl nicotinate and 3-acetylpyridine were chosen for the investigation of quantitative methods of analysis of compounds of the pyridine series. Aniline can be successfully used as an internal standard for analysis. The resultant method for the quantitative separation of various pyridine derivatives has made it possible to choose rapidly the optimal conditions in the catalytic synthesis of alkyl pyridyl ketones from aliphatic acids and esters of pyridinecarboxylic acids⁵.

Reaction mixtures containing pyridine, a ketone of the aliphatic series, the products of its condensation, an ester of pyridinecarboxylic acid and alkyl pyridyl

* The boiling points given in the tables and figures were obtained by bringing the boiling point in a vacuum to normal conditions.

ketone were analysed in about 10 min (Fig. 3). The quantity of polymeric products formed in the course of the reaction, without leaving the column, was determined by adding aniline as internal standard. Information was obtained as to whether ketonization reaction takes place, and to what extent, without any preliminary treatment of the reaction mixture. Thus, there was no necessity to accumulate any catalysate, the stability of the catalyst was strictly and rapidly controlled, and all the components of the mixture were determined quantitatively.

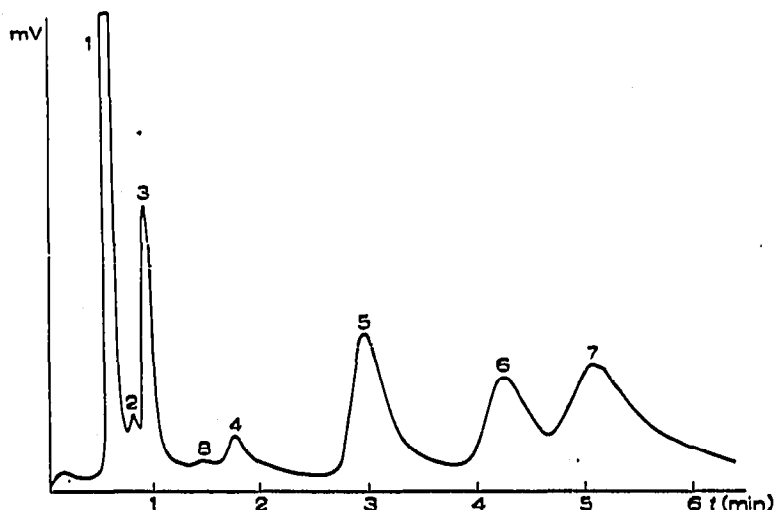


Fig. 3. Chromatogram of a catalysate in the ketonization reaction of ethyl nicotinate with acetic acid over an oxide aluozirconium catalyst. See legend of Fig. 1 for the column and the experimental conditions. Notations of the peaks: 1 = acetone; 2 = mesityl oxide; 3 = pyridine; 4 = non-identified peak; 5 = aniline; 6 = ethyl nicotinate; 7 = 3-acetylpyridine; 8 = diacetone alcohol.

Treatment of the solid support, diatomite brick, with an alkali leads to a reduction in the surface area of the brick from 20 m²/g (before treatment) to 1 m²/g (after treatment) and also apparently to partial suppression of the acid centres. Reduction of the surface area of the brick accounts for a shorter retention time, and suppression of the acid centres results in a decrease in "tailing". It was not possible, however, to completely eliminate "tailing". As can be seen from the above, a shorter retention time does not interfere with either qualitative or quantitative analysis. Complete symmetry of the peak was not observed even when sodium chloride was used as a solid support (Fig. 2). The existence of some interaction with the solid support (sodium chloride or diatomite brick after treatment with an alkali) is also corroborated by the relationship between the retention time (t_R) and the size of the sample (the greater the size of the sample, the smaller t_R).

We will now consider the possible modes of interaction of nitrogen-containing heterocyclic compounds (see Table I) with the stationary phase:

(a) acid-base (pyridine base: donor of electrons; stationary phase: acceptor of electrons);

(b) through the formation of a hydrogen bond.

Such interactions naturally depend on steric obstacles set up by the introduction of substituents into the molecule of the pyridine base.

The existence of a relationship between the retention volumes and the boiling points of nitrogen-containing heterocyclic compounds allows the establishment of a

number of rules (Fig. 4). By the nature of the interaction, the compounds under investigation may be classified into three groups: (1) alkyl derivatives of pyridine, (2) oxygen-containing compounds, and (3) derivatives with two nitrogen atoms in the molecule. Typical of the oxygen-containing pyridine bases is a larger angle of incline ($0.01 \Delta \log V_R^{\text{rel.}}$ per 1°) than that for alkylpyridines (0.005 per 1°). Hence, the coefficient of selectivity⁶ for a pair of oxygen-containing alkyl derivatives on

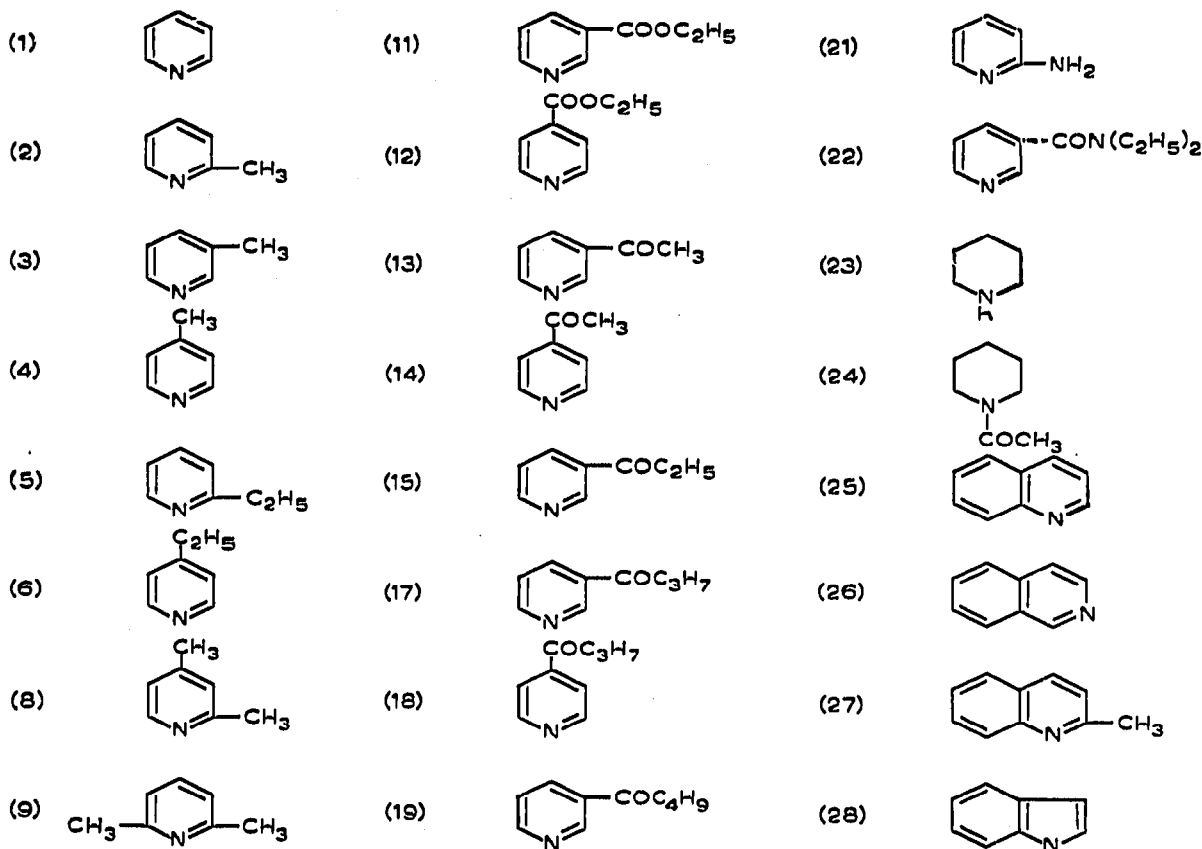
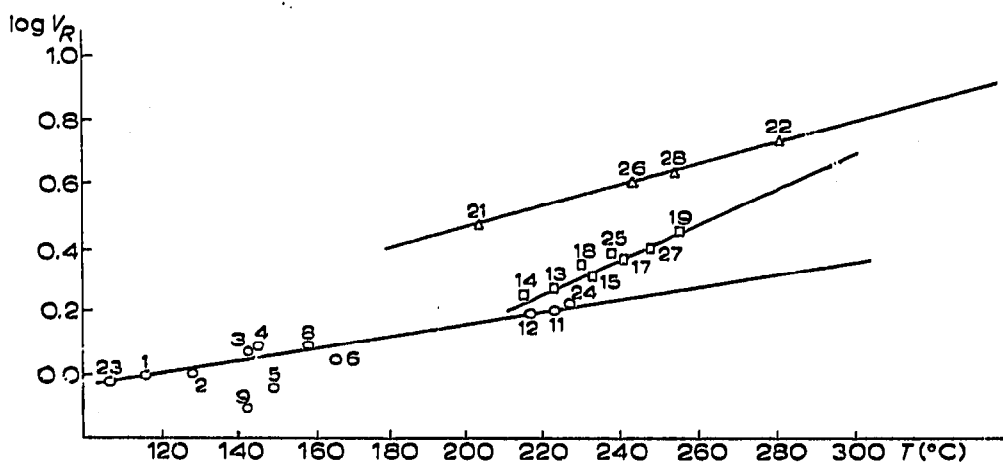


Fig. 4. Relationship between relative retention volumes (internal standard of pyridine $V_R^{\text{rel.}} = 1$) and boiling points. See legend of Fig. 2 for the column and the experimental conditions. Temperature: 210° . For compounds 7, 10, 16 and 20 no V_R data were determined at 210° .

polyethyleneglycol adipate equals 2. The addition of one more nitrogen atom to a pyridine molecule entails a sharp increase in the retention volume. The increase in $V_R^{\text{rel.}}$ for isoquinoline as compared with quinoline can be explained by an intensification of the basic properties in the case of isoquinoline. A larger $V_R^{\text{rel.}}$ for indole than for pyridine bases with approximately the same boiling points appears to be related to the formation of hydrogen bonding between the hydrogen of the indole NH and the oxygen of polyethyleneglycol adipate. Piperidine is a stronger base than pyridine, and, apart from this, is capable of forming a hydrogen bond with the stationary phase; for this reason its retention volume is greater than the one anticipated from its boiling point. Substitution of an acetyl group for hydrogen in piperidine precludes the possible formation of a hydrogen bond and sharply reduces the basicity; the retention volume begins to conform to the boiling point of an N-acylated derivative. The magnitude of the retention volume is also greatly influenced by steric effects in the molecule of the chromatographed substance.

As the nitrogen atom is the centre of basicity of pyridine bases, anything which impedes its interaction with the stationary phase will lead to a decrease in the retention volume. Such effects arise as a result of introducing substituents in the α -position of a pyridine ring. For instance, such steric hindrance is encountered in α -picoline only to a slight extent, is greater in 2-ethylpyridine owing to a more voluminous substituent, and increases still further with 2,6-dimethylpyridine, where both α -positions are occupied. As a result, the values of the retention volumes are below the curve $\log V_R^{\text{rel.}}$ -boiling point (Fig. 4). These differences cannot be attributed to a change in basicity since with an increase of the number of alkyl groups in substituted pyridines the basicity increases⁷. In the case of alkyl 3- or 4-pyridyl ketones, a linear relationship is observed between the retention volume and the number of carbon atoms in the side chain (Fig. 5); underlying this effect is the connection between the change in the logarithm of the retention volume and the increased work to transport a molecule of a substance from a solution to the gaseous phase on lengthening the carbon chain by one methylene group⁸.

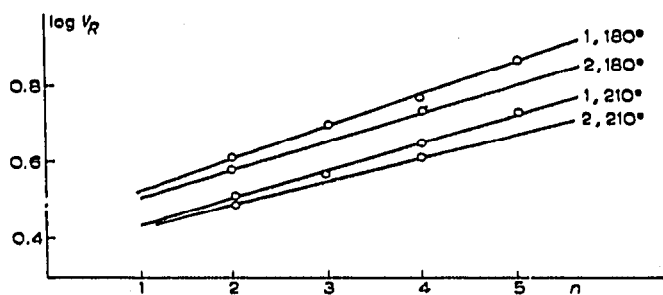


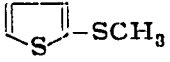
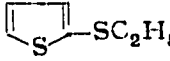
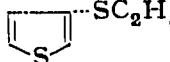
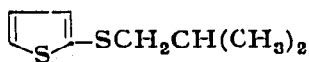
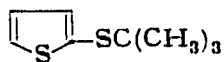
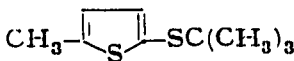
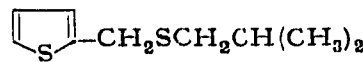
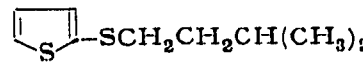
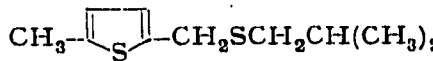
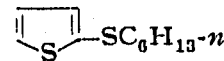
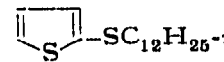
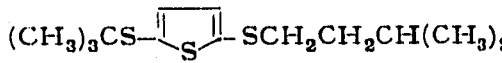
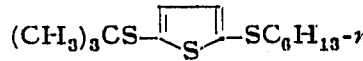
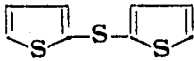
Fig. 5. Relationship between $\log V_R^{\text{rel.}}$ (internal standard aniline) and the number of carbon atoms in the side chain of alkyl pyridyl ketones. 1 = Alkyl 3-pyridyl ketones; 2 = Alkyl 4-pyridyl ketones.

SULPHIDES OF THE THIOPHENE SERIES

Gas-liquid chromatography of high-boiling compounds represents a complex problem since the retention time at temperatures generally used in chromatography is so long that the substance does not even leave the column. At the same time a rise in temperature is undesirable and often impossible. The shorter retention time of



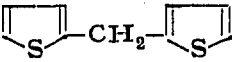



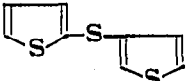

TABLE II

HEATS OF EVAPORATION AND SOLUTION OF THIOPHENE DERIVATIVES IN POLYETHYLENEGLYCOL ADIPATE AND SILICONE RUBBER SKTV

Thiophene derivatives	Heat of evaporation at boiling point, ΔH_V (kcal/mole)	Heat of evaporation at 200°, ΔH_V^{200} (kcal/mole)	Polyethyleneglycol adipate on diatomite brick		Silicone rubber on sodium chloride	
			Heat of solution, ΔH_S (kcal/mole)	Excess heat of solution, $\Delta \bar{H}_S^E$ (kcal/mole)	Heat of solution, ΔH_S (kcal/mole)	Excess heat of solution, $\Delta \bar{H}_S^E$ (kcal/mole)
	9.52	—	11.0	-2.40	9.60	-1.02
	9.85	—	11.4	-2.47	—	—
	10.16	10.3	12.0	-2.48	11.0	-1.64
	10.68	11.15	12.2	-1.83	12.6	-2.39
	9.93	9.93	11.7	-2.53	11.0	-1.83
	10.57	10.93	11.8	-1.30	12.9	-2.91
	10.91	11.41	13.2	-2.29	13.6	-3.13
	10.74	11.25	12.6	-2.46	13.5	-3.19
	11.87	13.08	—	—	13.4	-1.26
	11.49	12.48	14.05	-2.68	14.2	-2.66
	14.13	16.64	15.65	-0.19	19.5	-3.80
	14.84	17.77	—	—	16.0	+0.83
	15.07	18.11	—	—	17.6	-0.43
	12.01	13.17	13.95	-1.87	15.1	-2.87

(continued on p. 74)

TABLE II (continued)

Thiophene derivatives	Heat of evaporation at boiling point, ΔH_V (kcal/mole)	Heat of evaporation at 200°, ΔH_V^{200} (kcal/mole)	Polyethyleneglycol adipate on diatomite brick		Silicone rubber on sodium chloride	
			Heat of solution, ΔH_S (kcal/mole)	Excess heat of solution, $\Delta \bar{H}_{SE}$ (kcal/mole)	Heat of solution, ΔH_S (kcal/mole)	Excess heat of solution, $\Delta \bar{H}_{SE}$ (kcal/mole)
$n\text{-H}_0\text{C}_4\text{-}$  $\text{-C}_4\text{H}_0\text{-}n$	10.96	—	12.8	—1.98	19.4	—2.74
$(\text{CH}_3)\text{C-}$  $\text{-C}(\text{CH}_3)_3$	10.46	10.78	11.0	—1.0	12.6	—2.76
	11.2	12.00	13.6	—2.71	13.2	—2.15
$\text{CH}_3\text{-}$  $\text{-CH}_2\text{-}$  -CH_3	11.87	13.08	15.6	—3.62	—	—
	12.36	13.84	14.95	—2.21	12.7	+0.20
	12.36	13.84	15.00	—2.26	14.0	—1.0
	7.52	—	6.83	—1.96	—	—

pyridine bases found after treatment of the solid support with an alkali (notably, as a result of its reduced surface) induced us to use it also for separating high-boiling sulphides of the thiophene series^{3*} (Table II). At a temperature as low as 210° it was possible to elute sulphides of the thiophene series with a boiling point up to 460° on polyethyleneglycol adipate on diatomite brick treated with alkali (Fig. 6).

In this class of compounds, treatment of the solid carrier with alkali leads to a decrease in the retention volume by several magnitudes, to an extension of the band and the appearance of non-symmetry in the peak. The last two effects impair separation.

However, the temperature relationship of the logarithm of the corrected retention volume is the same for brick treated or untreated with alkali; in the case of methyl 2-thienyl sulphide, the heat of dissolution in polyethyleneglycol adipate is equal to 11 kcal/mole. Treatment of the solid support with an alkali does not tell either on the temperature relationship of other alkyl 2-thienyl sulphides and does not, consequently, affect the specific interaction of sulphides with the stationary phase. It was possible to separate a 12-component mixture of thiophene derivatives on untreated brick with polyethyleneglycol adipate as the stationary phase; the list

* Preparation of most sulphides of the thiophene series is described in refs. 9-12.

of the derivatives is given in the legend of Fig. 7. It is also possible to separate isomeric dithienyl sulphides, α -*tert.*-butylmercapto- and α -isobutylmercaptothiophenes and other compounds of a similar structure. The term θ (ref. 13) equals 0.7 or more. The method of separation developed has made it possible to demonstrate, notably, that *tert.*-butyl 2-thienyl sulphide obtained by addition of 2-mercaptothiophene to isobutylene does not contain an admixture of isobutyl 2-thienyl sulphide and that, likewise, α,β' - and β,β' -dithienyl sulphides obtained by reaction of the corresponding lithium thiophenes with dithienyl disulphides are free of any other isomers.

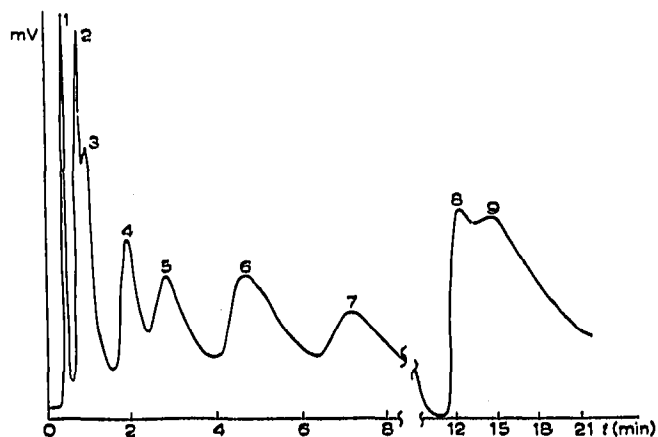


Fig. 6. Chromatogram of a mixture of the thiophene series sulphides. See legend of Fig. 1 for the column. Experimental conditions: temperature of the column and of the heat conductivity detector, 210°; helium flow rate, 60 ml/min. Notations of the peaks: 1 = solvent; 2 = methyl 2-thienyl sulphide; 3 = *tert.*-butyl (5-methyl-2-thienyl) sulphide; 4 = *n*-hexyl 2-thienyl sulphide; 5 = 2,5-bis-(*tert.*-butylmercapto)-thiophene; 6 = 2-*tert.*-butylmercapto-5-(isoamylmercapto)-thiophene; 7 = 2-*tert.*-butylmercapto-5-(*n*-hexylmercapto)-thiophene; 8 = 5-ethylmercapto-2,2'-dithienyl sulphide; 9 = 5-isobutylmercapto-2,2'-dithienyl sulphide.

In the case of some of the above-mentioned sulphides it was possible to observe a so-called "reaction chromatography", expressed by the fact that the compound underwent a transformation before entering the column; this occurred with a copper evaporator. The presence of a *tert.*-butyl group at the sulphide sulphur bound with the thiophene ring, or a bond of sulphide sulphur with this ring through a methylene group is common to all such compounds. If the *tert.*-butyl group is bound directly with the thiophene ring, the compound is not destroyed. This interesting fact may be used to confirm the structure of sulphides of the above-mentioned types.

There is a linear relationship between the retention volume and the boiling point of sulphides of the thiophene series by which it is possible to trace, as in the case of pyridine bases, the effect of the structure of the sulphide on the retention volume (Fig. 8). Typical of sulphides with two thiophene rings is the larger angle of incline than that for sulphides with one thiophene ring, and, consequently, a greater selectivity of the stationary phase. A comparison between the retention volumes of 2,2'-dithienylmethane and 2,2'-dithienyl sulphide indicates that substitution of a sulphur atom for a methylene group does not affect the interaction with the stationary phase, and both substances chromatograph in accordance with their boiling points (Fig. 8). In the case of 1,2-bis-(thienyl-2-mercapto)-ethane, *i.e.* when the thiophene rings are disrupted by two sulphur atoms and two methylene groups, interaction between the

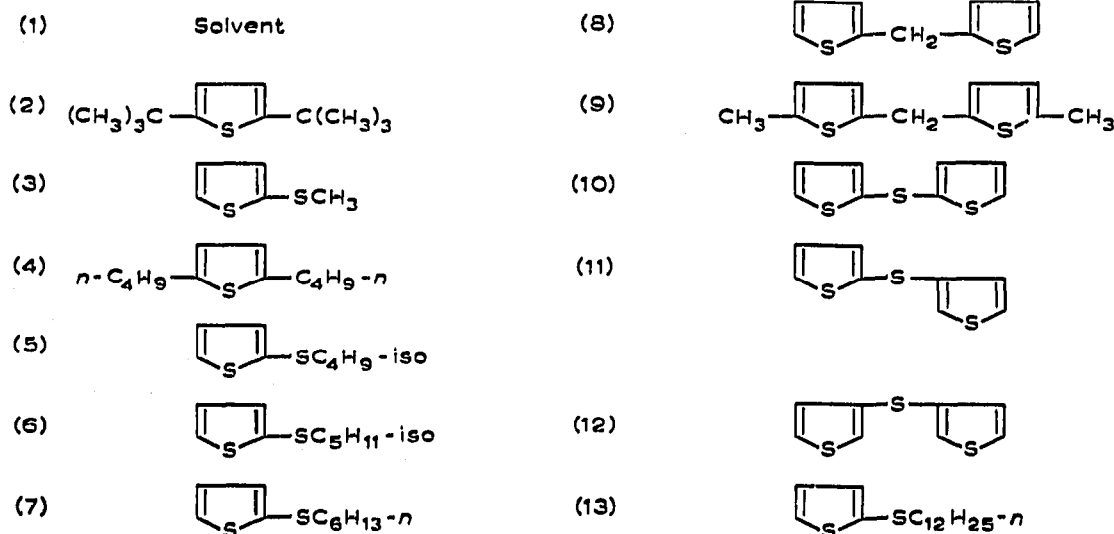
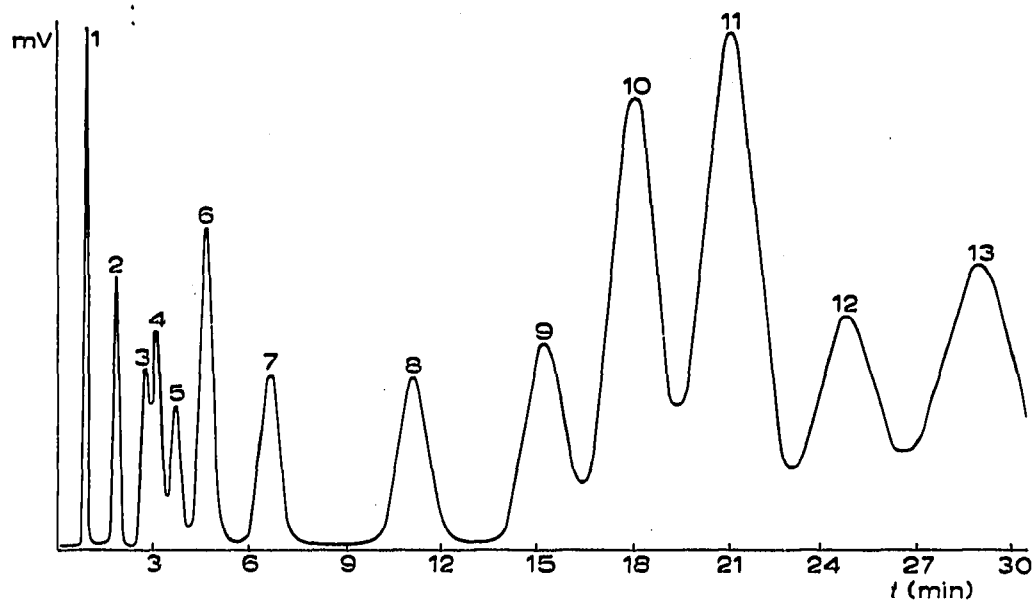


Fig. 7. Chromatogram of a mixture of sulphur-containing compounds (in the main, thiophene series sulphides). Column: 20% polyethyleneglycol adipate on diatomite brick; 2.6 m long; I.D., 6 mm; fraction of the solid support: 0.25–0.5 mm. Experimental conditions: temperature of the column and of the heat conductivity detector, 220°. Notations of the peaks: 1 = solvent; 2 = 2,5-di-*tert.*-butyl-thiophene; 3 = methyl 2-thienyl sulphide; 4 = 2,5-di-*n*-butyl thiophene; 5 = isobutyl 2-thienyl sulphide; 6 = isoamyl 2-thienyl sulphide; 7 = *n*-hexyl 2-thienyl sulphide; 8 = 2,2'-dithienylmethane; 9 = 5,5'-dimethyl-2,2'-dithienylmethane; 10 = 2,2'-dithienyl sulphide; 11 = 2,3'-dithienyl sulphide; 12 = 3,3'-dithienyl sulphide; 13 = *n*-dodecyl 2-thienyl sulphide.

substance and the stationary phase is governed by the same rule. If an alkyl mercapto group is introduced into one of the α -positions of 2,2'-dithienyl sulphide, one thiophene ring is immediately substituted in the two α -positions and, as a result, shielded. The sharp decrease in the retention volume, recorded in this case, is, of course, a consequence of the difficulty of interaction with the stationary phase. Such an effect can be traced by the derangement of the relationship $\log V_R^{\text{rel.}}$ –boiling point (dotted line

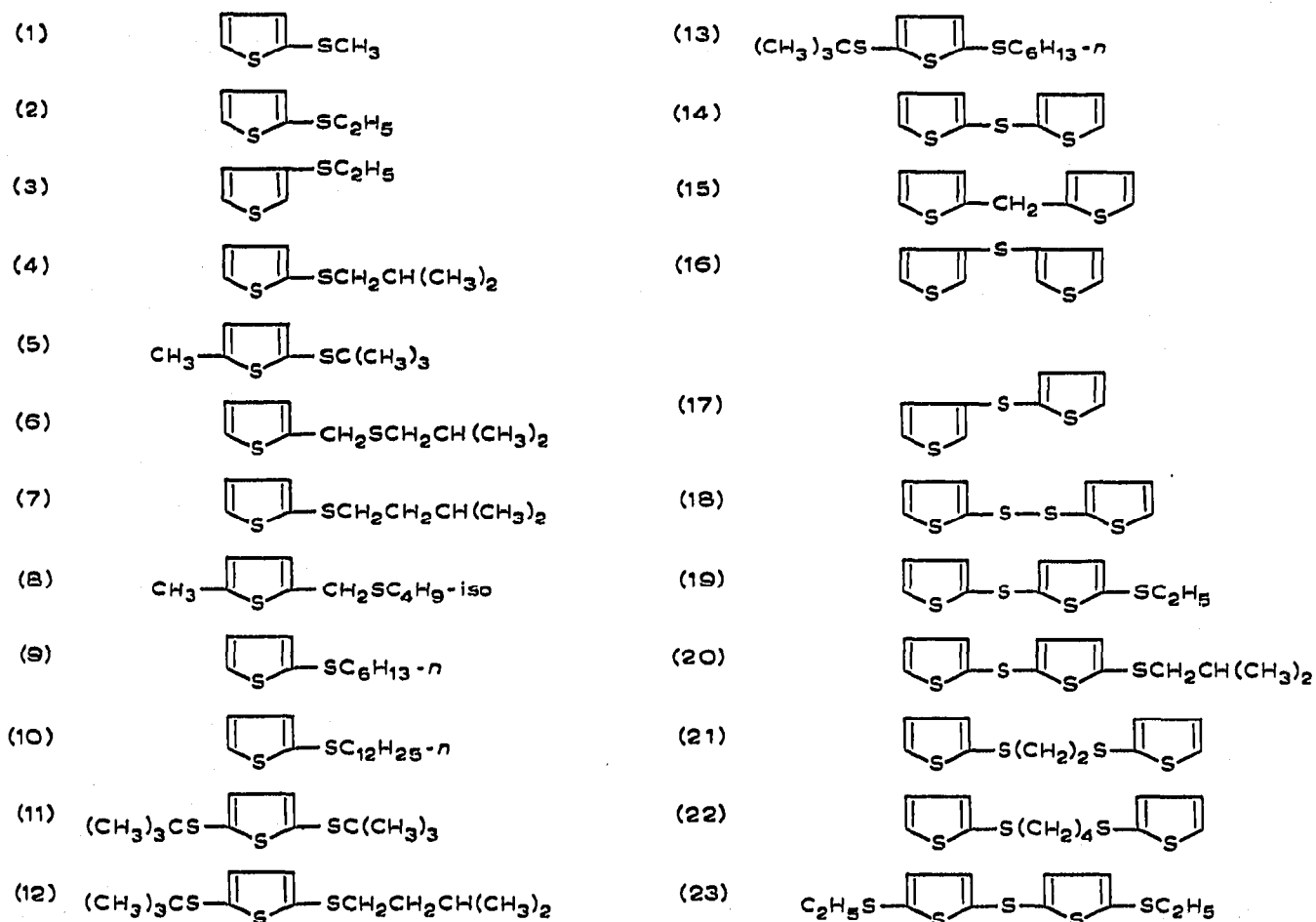
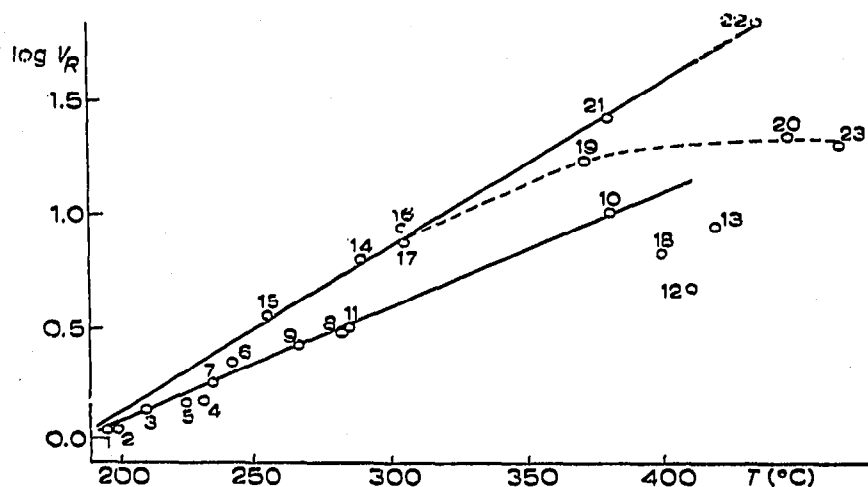


Fig. 8. Relationship between the logarithm of relative retention volumes of thiophene sulphides (internal standard methyl 2-thienyl sulphide) and their boiling points. Column: polyethyleneglycol adipate applied to diatomite brick treated with an alkali. Temperature of the column and of the heat conductivity detector 210° .

in Fig. 8), which becomes greater as the size of the alkyl mercapto group increases. Similar effects are also observed in the series of sulphides with one thiophene ring (Fig. 8). In this case, it is necessary that two voluminous alkyl substituents should be present in both α -positions to reduce interaction with the stationary phase. The resultant relationships between the logarithm of the retention volume and the boiling point of the sulphide permit definite conclusions to be drawn regarding the structure of the compound under investigation.

Accurate and detailed information on interaction with the stationary phase and on the nature of the structural elements in the substances under investigation can be gained by considering the thermodynamics of solution. As is well known, the retention volume is linked with the free energy of solution and depends on the enthalpic and entropic terms^{14,15}. The temperature relationship of the logarithm of the corrected retention volume allows the enthalpic component to be determined, *i.e.* the heat of solution (ΔH_S). The heat of solution determined experimentally includes the heat of evaporation (ΔH_V) and the excess heat of solution ($\Delta \bar{H}_{S^E}$)^{14,15}. When solutions close to ideal ones are formed, the heat of solution equals that of evaporation and $\Delta \bar{H}_{S^E} = 0$. By determining the magnitude of $\Delta \bar{H}_{S^E}$, it is possible to assess the degree of interaction between the stationary phase and the substance under investigation. The relationship connected with the difference in the heats of evaporation is then precluded. At boiling point the former was calculated by Kistyakovsky's equation¹⁶:

$$\Delta H_V/T_{b.p.} = 8.75 + 4.576 \log T_{b.p.}$$

At a temperature differing from the boiling point (*e.g.* the temperature of the chromatogram), the heat of evaporation was calculated by Watson's equation¹⁶:

$$\frac{(\Delta H_V)_1}{(\Delta H_V)_2} = \left[\frac{1-(T_r)_1}{1-(T_r)_2} \right]^{0.37}$$

where $(\Delta H_V)_1$ and $(\Delta H_V)_2$ are the heats of evaporation at boiling point, T_1 , and the temperature of the experiment, T_2 ; $(T_r)_1 = T_1/T_c$, where T_c is the critical temperature and $(T_r)_2 = T_2/T_c$. The critical temperature, T_c , for sulphur-containing compounds was determined according to the formula¹²:

$$T_c = 1.41 \cdot T_{b.p.} + 66$$

For thiophene, the value of ΔH_V calculated by Kistyakovsky's equation (7.29 kcal/mole) differs from the one calculated experimentally¹⁷ (7.52 kcal/mole) by 3%. The values of ΔH_V , ΔH_S and $\Delta \bar{H}_{S^E}$ obtained for thiophene derivatives are summarized in Table II (within ± 0.05). In practically every case the term $\Delta \bar{H}_{S^E}$ is negative (exothermic effect in solution), which corresponds to the deviations in Raoult's law. Such deviations confirm the interaction between the compound to be chromatographed and the stationary phase.

Let us follow the change in the value of $\Delta \bar{H}_{S^E}$ when passing from one compound to another (Table II). The addition of an alkylmercapto group to a thiophene ring leads to an increase in the degree of interaction between the substance and the

stationary phase. Substitution of an ethylmercapto for a methylmercapto group does not markedly affect the magnitude of the excess heat of solution. An increase in the length of the alkyl chain or the presence of another α -substituent sharply reduces the interaction. Apparently there is not much difference when the alkylmercapto group is in either the α - or the β -position or when the sulphur atom is linked with the thiophene ring either directly or through the methylene group. The excess heat of solution is approximately the same for non-substituted thiophene and a compound with two thiophene rings bound by sulphur sulphide in an α -position. For alkyl-substituted thiophenes with an unbranched side chain the excess heat of solution is of the same magnitude as that for thiophene; it diminishes when the alkyl chain is branched (for 2,5-di-*tert.*-butylthiophene it amounts to -1.0) as a result of steric hindrance and the interaction between the substance and the stationary phase. The influence of steric hindrance on $\Delta\bar{H}_s^E$ should be distinguished from the reduction in the excess heat of solution upon an increase in the size of a molecule owing to the greater work required for drawing apart the molecules of the stationary phase¹⁸. The conclusion may be drawn that the thiophene ring and sulphur sulphide do not exercise such a reciprocal influence which would be expressed in a stronger interaction between sulphides of the thiophene series and the stationary phase.

A principal role in the interaction with the stationary phase is played by the thiophene ring whose shielding sharply reduces the interaction with the stationary phase. In a non-polar solvent (silicone rubber, Table II) the major part in the interaction with the stationary phase will be played by dispersion forces (and not a dipole-dipole interaction as in the case of the above-mentioned example with polyethyleneglycol adipate) which increase in proportion to the number of groups which come into direct contact with the stationary phase¹⁹. It is natural that there, too, steric hindrance will play a substantial part. But in general, as the hydrocarbon chain grows, interaction with the stationary phase increases. As can be seen from Table II, the nature of the change in $\Delta\bar{H}_s^E$ in the case of silicone rubber is opposite to that in $\Delta\bar{H}_s^E$ in the case of polyethyleneglycol adipate. The above leads to the assumption that comparative chromatographic characteristics permit the measurement of polarity of a substance and the peculiarities of its structure to be assessed with some reliability.

FURAN DERIVATIVES*

It was of considerable interest to compare the chromatographic features of similar thiophene and furan derivatives. A manifestation of the substitution of an oxygen atom for an atom of the sulphur in the ring, which leads to some increase in the dipole moment of the molecule, might be anticipated in such a comparison. Tables III and IV show the compounds under investigation.


In the case of derivatives with one furan ring, a linear relationship is observed between $\log V_R^{\text{rel.}}$ and the $T_{b.p.}$ of the substance (Fig. 9). A comparison of the chromatographic behaviour of furan and furylthienylmethane indicates that addition to the furan molecule of a thiophene ring linked through a methylene bridge with the furyl residue doubles the selectivity of separation. In this case both dithienylmethanes

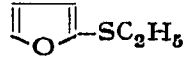
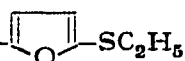
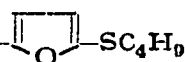
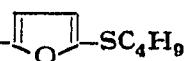

* Synthesis of the substances is described in refs. 20-22.

TABLE III

RELATIVE RETENTION VOLUMES ($V_R^{rel.}$), HEATS OF EVAPORATION (ΔH_V) AND HEATS OF SOLUTION (ΔH_S) OF SULPHIDES OF THE FURAN SERIES

Stationary phase: 20% polyethyleneglycol adipate on diatomite brick treated with an alkali.

For CH_3 -- SC_2H_5 , the retention time is 2.55 min at 137°, 1.05 min at 180°, and 0.6 min at 210°.

Item No.	Compound	$T_{b.p.}$ at 760 mm Hg (°C)	$V_R^{rel.}$			ΔH_S (kcal/mole)	ΔH_V (kcal/mole)
			137°	180°	210°		
1		158-160	0.78	0.88	—	11.0	9.0
2	CH_3 - 	179-180	1.0	1.0	1.0	12.2	9.5
3	CH_3 - 	218-219	1.96	1.46	1.41	13.6	10.4
4	CH_3 - 	209-210	1.53	1.28	—	—	—
5	CH_3 - 	65	0.22	—	0.71	—	—


and furylthienylmethanes are subordinated to one linear relationship. Mobile π -electrons in the ring, and not the alkylmercapto group, seem to play a major part in the interaction with the stationary phase in this case. The degree of interaction between the stationary phase and the thiophene and furan ring is practically the same. Interaction between diphenylmethane and the stationary phase is considerably less than in the corresponding furan and thiophene derivatives. As in the case of alkyl 2-thienyl sulphides, the excess heat of solution of sulphides of the furan series in the stationary phase (in polyethyleneglycol adipate) is negative, *i.e.* there is an exothermic effect and negative deviations from Raoult's law during solution.
















Low-boiling sulphides of the furan series with one furan ring are separated at 137° (Table III and Fig. 10); the last component has a boiling point of 220°. All separations of a five-component mixture take eight minutes. The retention time increases with the number of carbon atoms in a molecule. For compounds of the furan series which have branched alkyl substituents and lower boiling points, the retention time diminishes correspondingly. Fig. 11 shows a chromatogram of a seven-component mixture of higher-boiling furan and thiophene derivatives. The last component has a boiling point of 305°; the whole separation takes seven minutes at 210°. Introduction of methyl groups into the molecule of heterocyclic diarylmethane proves to be insufficient for its separation from non-substituted homologues; for this reason 2-methyl-5-(2-furyl)-thiophene appears on the chromatogram as a bend on the 2-furyl-2-thienylmethane peak (Fig. 11). In view of the fact that the boiling point of di-(2-thienyl)-methane is higher than of 2-thienyl-2-furylmethane, it is eluted later. The boiling points of 5-*n*-butylmercapto-2-methylfuran and 2-furyl-2-thienyl-

TABLE IV

RELATIVE RETENTION VOLUMES (V_R^{rel}) OF SULPHIDES OF THE FURAN SERIES AND OF DITHIENYL- AND FURYLTHIENYLMETHANE

Stationary phase: 20% of polyethyleneglycol adipate on diatomite brick treated with an alkali.

For CH_3 -- SC_2H_5 , the retention time is 0.6 min.

Item No.	Compound	$T_{b.p.}$ at 760 mm Hg	$V_R^{rel.}$ at 210°
1	CH_3 -  - SC_2H_5	179-180	1.0
2	C_2H_5 -  - SC_2H_5	195	1.05
3	$\text{H}_5\text{C}_2\text{S}$ -  - SC_2H_5	240-245	2.42
4	 - CH_2 -  - SC_2H_5	305	8.7
5	$\text{H}_5\text{C}_2\text{S}$ -  - CH_2 - 	305	8.3
6	 - CH_2 -  - CH_3	230	2.67
7	 - CH_2 - 	215	2.50
8	 - CH_2 - 	260	4.42
9	CH_3 -  - CH_2 -  - CH_3	285	7.0

methane are nearly the same (215-218°). Nevertheless, the latter appears later, thereby corroborating the previous conclusion that the degree of interaction of the stationary phase with the thiophene of furan ring is higher than with the alkylmercapto group. A similar conclusion can be drawn by comparing the retention time of 2,5-bis-(ethylmercapto)-furan ($t_R^{210^\circ}$, 1.45 min, $T_{b.p.}$ 240-245°) with the retention time of 2-methyl-5-(2-furfuryl)-thiophene ($t_R^{210^\circ}$, 1.6 min, $T_{b.p.}$ 230°).

THIENOTHIOPHENES

Investigation into the chromatographic behaviour of thienothiophene derivatives was of special interest. On the one hand, it was possible to explain the behaviour of condensed thiophene systems, and on the other, to resolve questions of identification of compounds since thienothiophenes can be obtained in different

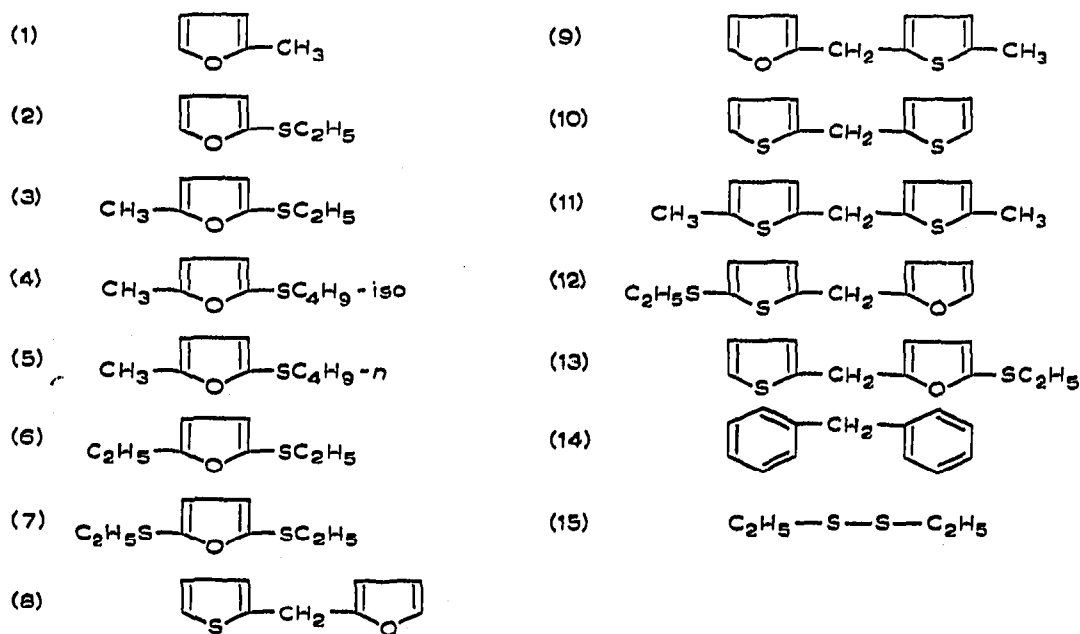
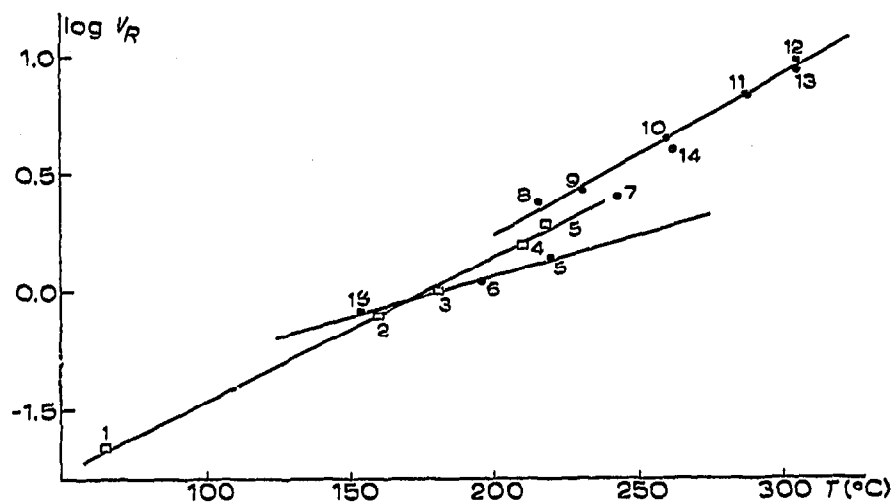


Fig. 9. Relationship between relative retention volumes and boiling points. Column: 20% polyethyleneglycol adipate on diatomite brick treated with an alkali. Temperature: (□) 137°, (●) 210°. Notations of the points: 1 = sylvan; 2 = 2-ethylmercaptofuran; 3 = 5-ethylmercapto-2-methylfuran; 4 = 5-isobutylmercapto-2-methylfuran; 5 = 5-n-butylmercapto-2-methylfuran; 6 = 5-ethylmercapto-2-ethylfuran; 7 = 2,5-bis(ethylmercapto)-furan; 8 = 2-furyl-2'-thienylmethane; 9 = 2-methyl-5-(2-furfuryl)-thiophene; 10 = di-(2-thienyl)-methane; 11 = bis-(5-methyl-2-thienyl)-methane; 12 = ethyl (5-furfuryl-thienyl-2) sulphide; 13 = ethyl (5-thienyl-furyl-2) sulphide; 14 = diphenylmethane; 15 = diethyl disulphide.

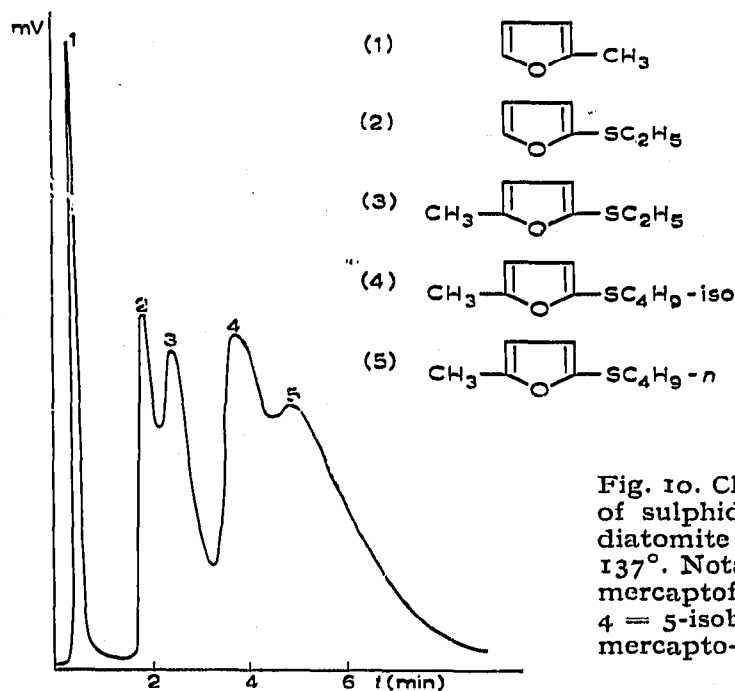


Fig. 10. Chromatogram of a mixture of the furan series of sulphides. Column: polyethyleneglycol adipate on diatomite brick treated with an alkali. Temperature: 137°. Notations of the peaks: 1 = sylvan; 2 = 2-ethylmercaptofuran; 3 = 5-ethylmercapto-2-methylfuran; 4 = 5-isobutylmercapto-2-methylfuran; 5 = 5-*n*-butylmercapto-2-methylfuran.

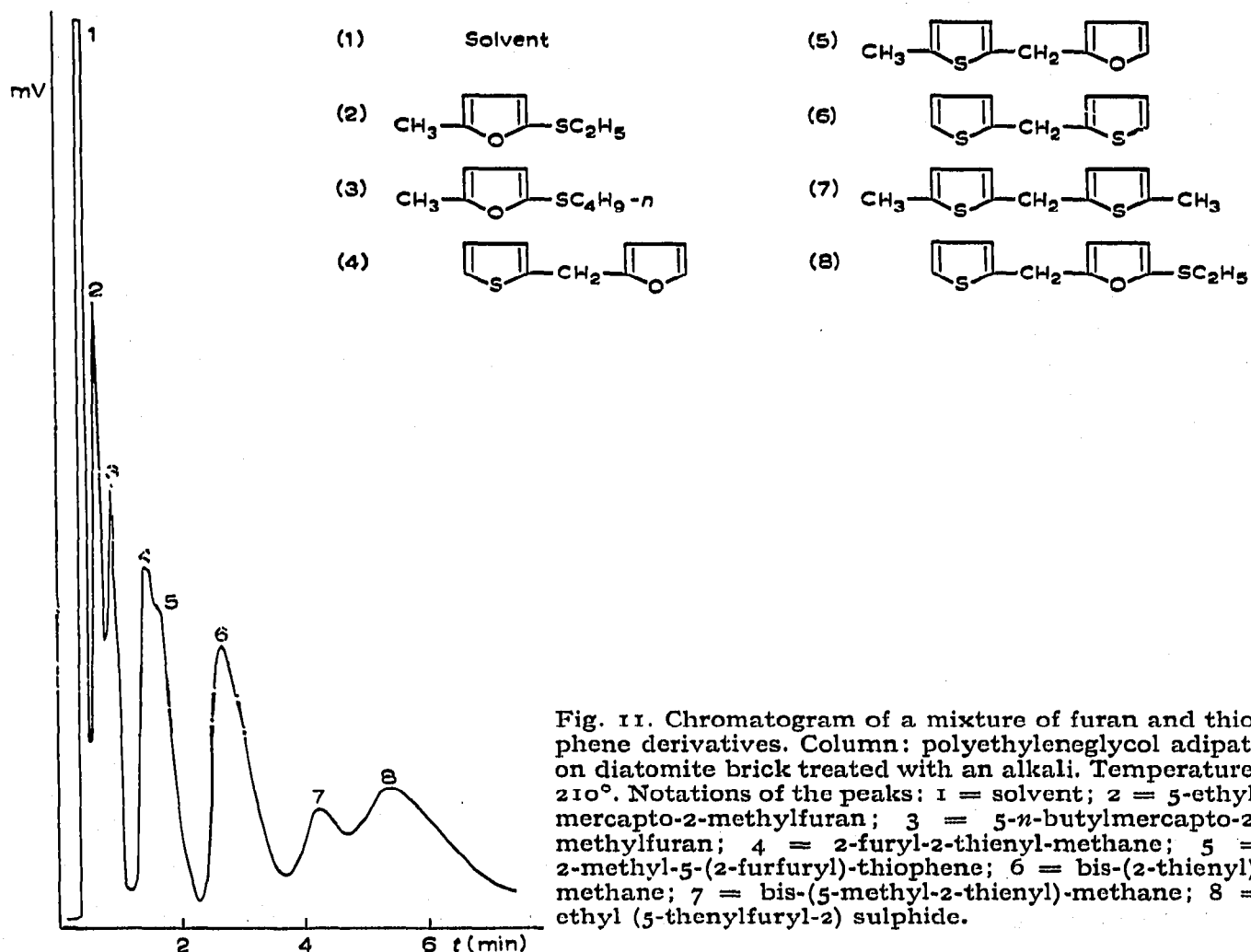


Fig. 11. Chromatogram of a mixture of furan and thiophene derivatives. Column: polyethyleneglycol adipate on diatomite brick treated with an alkali. Temperature: 210°. Notations of the peaks: 1 = solvent; 2 = 5-ethylmercapto-2-methylfuran; 3 = 5-*n*-butylmercapto-2-methylfuran; 4 = 2-furyl-2-thienyl-methane; 5 = 2-methyl-5-(2-furfuryl)-thiophene; 6 = bis-(2-thienyl)-methane; 7 = bis-(5-methyl-2-thienyl)-methane; 8 = ethyl (5-thienylfuryl-2) sulphide.

TABLE V

RELATIVE RETENTION VOLUMES AND COEFFICIENTS OF SEPARATION OF THIENOTHIOPHENE DERIVATI

Item No.	Compound	Boiling point at 760 mm Hg (°C)	20% PEGA-diatomite brick + alkali, 2 m column		
			150° $V_R^{rel.}$	170° $V_R^{rel.}$	211° $V_R^{rel.}$
1	3-Methyl-5-ethylthieno(3,2b)-thiophene	248	1.0 ($V_R = 1565$ ml) ($t_R = 23.7$ min)	1.0 ($V_R = 660$ ml) ($t_R = 12$ min)	1.0 ($V_R = 263$ ml) ($t_R = 2.5$ min)
2	3-Methyl-5-ethyl-thieno(2,3b)-thiophene	258	1.05	1.08	1.0
3	3-Methylthieno(3,2b)thiophene	230	0.47	0.647	0.647
4	3-Methylthieno(2,3b)thiophene	245		0.88	
5	3-Acetylmercaptothiophene	257		0.556	
6	2-Acetylmercaptothiophene	265		1.88	
7	Thieno(3,2b)thiophene	221-224		0.526	
8	2-Ethylthieno(3,2b)thiophene	250			
9	2-Ethylthieno(2,3b)thiophene	245			

* For the pair thieno(3,2b)thiophene and 3-methylthieno(2,3b)thiophene.

** θ is given for the following pairs: 3-methyl-5-ethylthieno(3,2b)thiophene and 3-methylthieno(3,2b)thiophene; 3-methyl-5-ethylthieno(2,3b)thiophene and 2-ethylthieno(2,3b)thiophene; 3-methylthieno(3,2b)thiophene and 2-ethylthieno(3,2b)thiophene.

ways. Thieno(2,3b)thiophene derivatives (I) are characterized by greater retention volumes than derivatives of thieno(3,2b)thiophene (II) (Table V, Fig. 12). This is



in agreement with the higher boiling points and the presence of a dipole moment in (I) (ref. 23). Introduction of an alkyl group raises the boiling point of the substance and, correspondingly, its retention time. Treatment of diatomite brick, the solid support, with an alkali results in a reduced retention time and in the appearance of "tailing". The latter effect is directly opposite to the one resulting from treat-

TABLE VI

QUANTITATIVE ANALYSIS OF A MIXTURE OF 3-METHYL-5-ETHYLTHIENO(2,3b)THIOPHENE (III) AND 3-METHYL-5-ETHYLTHIENO(3,2b)THIOPHENE (IV)

Standard mixture (%)		Per cent determined			
		By the area of the peak*		By the product height × retention time**	
III	IV	III	IV	III	IV
50	50	49.5	50.5	49	51
40	60	43	57	44	56
30	70	30	70	30	70

* On a column of polyethyleneglycol adipate applied to coated tile.

** On a column of polyethyleneglycol adipate applied to diatomite brick treated with alkali.

% PEGA-diatomite brick + sali, 2.6 m column		15% PEGA-coated tile, 3 m column		1% silicone rubber SKTV-NaCl, 2 m column	
5° rel.	θ	153° V _R rel.	θ	200° V _R rel.	θ
<i>t_R</i> = 29.00 ml) <i>t</i> = 44.5 min)	0.36	1.0 (V _R = 3560 ml) (<i>t_R</i> = 59.4 min)	0.42	1.0 (<i>t_R</i> = 5.1 min)	1.00
11	1.0	1.13		1.09	1.00**
50				0.59	1.0**
58					
405					
503	0.82*			0.79	1.0**
				0.79	1.0**

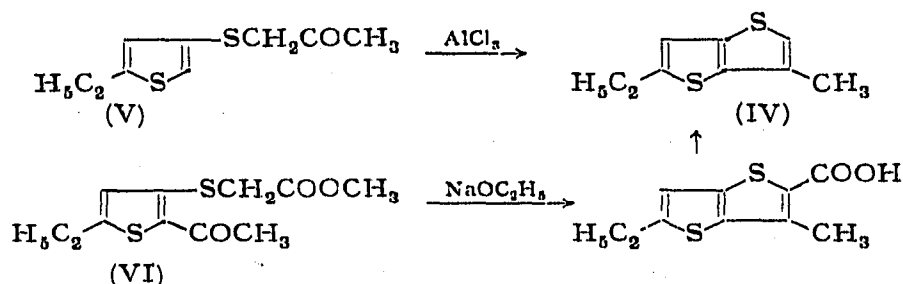
ment of the solid carrier with an alkali when pyridine bases are separated. This naturally impedes separation of isomeric thienothiophenes: instead of maxima, "shoulders" and bends appear on the chromatogram. Nevertheless, as shown in Table VI, this hardly interferes with the determination of the contents of isomers in the mixture.

After treatment of the support with an alkali, the retention time becomes even shorter than that on a column with 1% of silicone rubber applied to sodium chloride.

The methods developed for the chromatographic separation of isomeric thienothiophenes have made it possible to resolve the following questions:

(a) identity of thienothiophene derivatives obtained in various ways;

(b) the route of the transformation upon cyclization of derivatives of acetylmercaptothiophene. (IV), obtained by cyclization of 5-ethyl-3-acetylmercaptothiophene (V) with aluminium chloride proved to be identical to the product obtained from methyl (5-ethyl-2-acetyl-3-thienylmercapto)-acetate (VI) (ref. 24).



No isomeric thienothiophene is formed in the reaction, *i.e.* there is no migration of the acetylmercapto group from the 3- into the 2-position of the thiophene ring in the course of the reaction with aluminium chloride. 3-Methylthieno-(3,2b)thio-

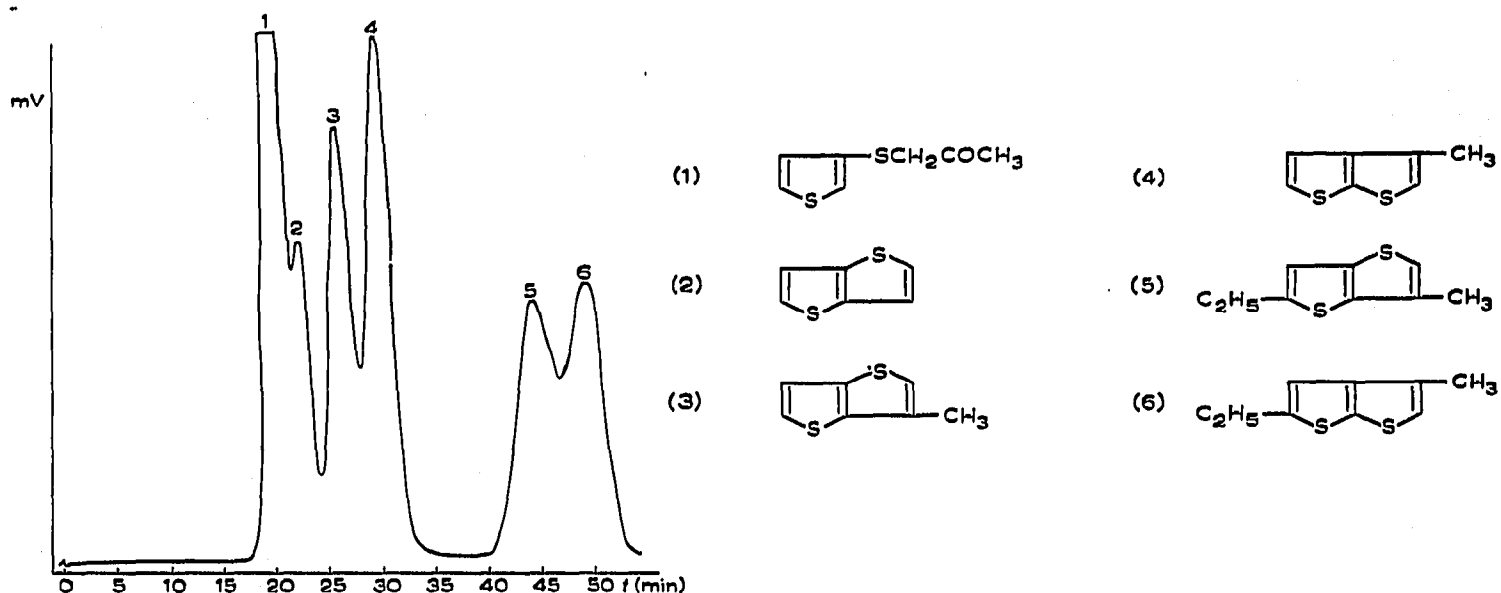
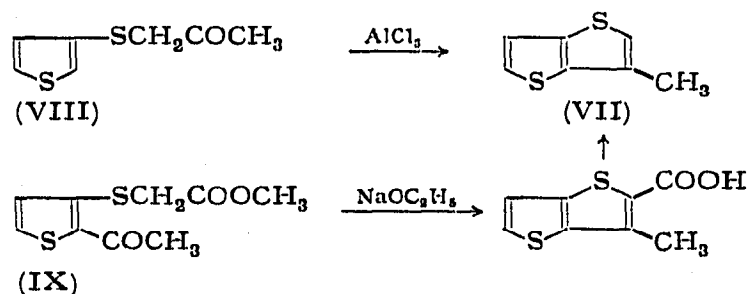


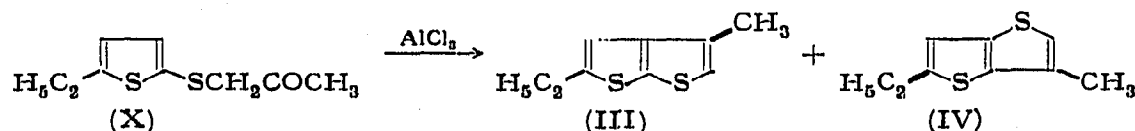
Fig. 12. Chromatogram of a mixture of isomeric thienothiophenes. Column: 20% polyethylene-glycol adipate on diatomite brick, 2.6 m long, I.D. 6 mm. Fraction of the solid support: 0.25–0.50 mm. Experimental conditions: temperature of the column and of the heat conductivity detector, 175°; helium flow rate, 66 ml/min; pressure at inlet, 0.45 kg/cm². Notations of the peaks: 1 = 3-acetylmercaptothiophene; 2 = thieno(3,2b)thiophene; 3 = 3-methylthieno(3,2b)thiophene; 4 = 3-methylthieno(2,3b)thiophene; 5 = 3-methyl-5-ethylthieno(3,2b)thiophene; 6 = 3-methyl-5-ethylthieno(2,3b)thiophene.

phene (VII) synthesized by cyclization of 3-acetylmercaptothiophene (VIII) with aluminium chloride, is identical to the product obtained from methyl (2-acetyl-3-thienylmercapto)-acetate (IX) (ref. 24).



In this case, there is no migration of the acetylmercapto group either.

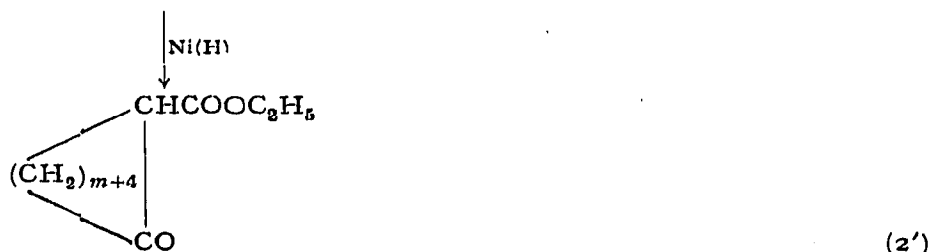
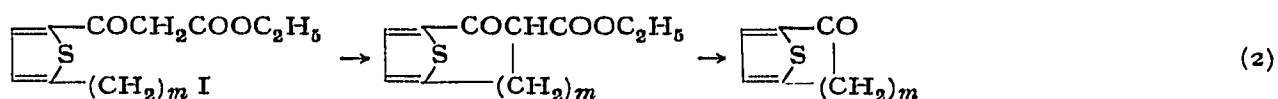
However, on cyclization of 5-ethyl-2-acetylmercaptothiophene (X) in the presence of aluminium chloride, the acetylmercapto group shifts to a 3-position, forming a mixture of isomeric dialkyl-substituted thienothiophenes (III) and (IV):



It was also shown by gas-liquid chromatography, that no migration of alkyl groups occurs in any of the above cases.

MACROCYCLIC COMPOUNDS INCLUDING A THIOPHENE RING

In recent years the Institute of Organic Chemistry developed a new method of synthesizing macrocyclic compounds based on thiophene²⁵, consisting in intramolecular acylation (Diagram 1) or alkylation (Diagram 2) of compounds of the thiophene series:



The macrocyclic compounds so formed, which include a thiophene ring, can be easily transformed into macrocyclic ketones by reducing desulphurization on Raney nickel (Diagram 3).



Several highly interesting points arise from the viewpoint of chromatography:

(a) The possibility of analytically separating macrocyclic ketones which include a thiophene ring and alicyclic ketones. The complexity of separation is connected in this case with the high boiling point and the strong polarity of the substance to be separated, and apart from this, there is a difficulty here owing to the fact that the substances to be analysed must be prevented from contact with material such as copper, which is generally used in making the columns, the evaporator, and the heat conductivity detector.

(b) The nature of interaction between ketones, which include a thiophene ring, and alicyclic ketones with the stationary phase, and the change in such interactions on a change in the size of the ring. As in previous cases, separations were carried out on a laboratory chromatograph made at the Institute of Organic Chemistry, U.S.S.R. Academy of Sciences, but in this case the heat conductivity detector was made of stainless steel with a tungsten filament; the evaporator and the U-shaped tubes were likewise made of stainless steel. Chromosorb W was used as solid support and coated with 15% polyethyleneglycol succinate as the stationary phase. The data on the relative retention volumes are given in Table VII. Fig. 13 shows a chromatogram of an eight-component mixture of alicyclic C₁₄-C₁₇ ketones and of corre-

TABLE VII

RELATIVE RETENTION VOLUMES AND COEFFICIENTS OF SEPARATION (θ) OF α -CYCLOTHIENONES AND ALICYCLIC KETONES

Compound	Boil- ing point at 760 mm Hg (°C)	15% polyethyleneglycol succinate-Chromosorb W						PEGA-diatomite brick + alkali		
		180°		200°		217.5°		180°	200°	210°
		$V_{Rrel.}$	θ	$V_{Rrel.}$	θ	$V_{Rrel.}$	θ	$V_{Rrel.}$	$V_{Rrel.}$	$V_{Rrel.}$
Cyclotetradecanone	288	0.778		0.807		0.826		0.746		0.71
			0.90		0.86		0.8			
Cyclopentadecanone	330	1.00 ($V_{R'} = 30$ ml) ($t_R = 11.4$ min)	0.85 ($V_{R'} = 170$ ml) ($t_R = 6.5$ min)	1.00 ($V_{R'} = 98.2$ ml) ($t_R = 4.1$ min)	0.82	0.75 ($V_{R'} = 836$ ml) ($t_R = 15.2$ min)	1.00 ($V_{R'} = 445$ ml) ($t_R = 8.1$ min)	1.00 ($V_{R'} = 396$ ml) ($t_R = 7.2$ min)		
Cyclohexadecanone	345	1.26		1.23		1.20		1.38		1.19
			0.90		0.87		0.83			
Cycloheptadecanone	365	1.61		1.51		1.45		1.85	1.82	1.52
			1.0		1.0		1.0			
(10)- α -Cyclo- thienone-I	330	5.01		4.60		4.16		4.23		3.68
			1.0		1.0		0.97			
(11)- α -Cyclo- thienone-I	360	6.64		5.85		5.17				4.8
			1.0		1.0		0.94			
(12)- α -Cyclo- thienone-I	380	8.62		7.37		6.38				6.2
			1.0		1.0		0.98			
(13)- α -Cyclo- thienone-I	410	11.5		9.45		7.98				

spending α -cyclothienones with boiling points ranging from 290 to 410°. A practically complete separation of the components of the mixture was recorded. With a rise in temperature from 180° to 220°, the time of analysis is shortened to 30 min, while separation does not deteriorate markedly. It is worth noting that the temperature at which separation was carried out was about 200° below the boiling point of the highest-boiling component. As can be seen from the graph of the relationship between logarithm of the retention volume and the number of carbon atoms in the ring (Fig. 14), the selectivity of the stationary phase for the ketones which include a thiophene ring is higher than that for the alicyclic ketones (the change in $\log V_{R^{rel}}$ for one carbon atom amounts to 0.125 in the first case, and to 0.1 in the second). This is possibly connected with the fact that the thiophene ring contributes additionally to the interaction with the stationary phase.

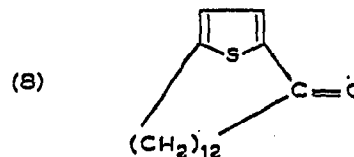
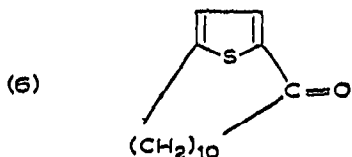
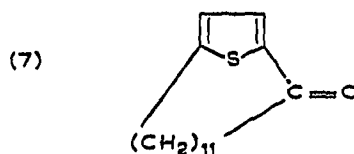
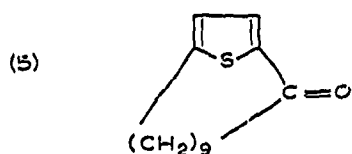
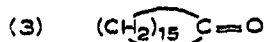
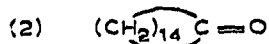
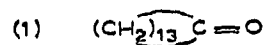
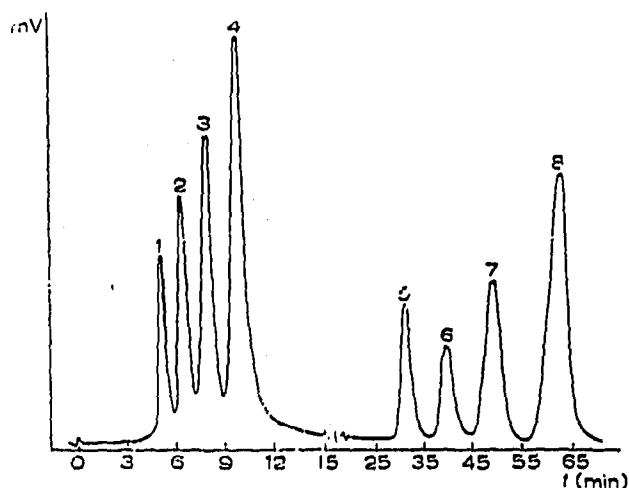


Fig. 13. Chromatogram of an 8-component mixture of alicyclic ketones and α -cyclothienones. Column: 15% polyethyleneglycol succinate on Chromosorb W, U-shaped stainless steel, 2 m long; I.D., 4 mm. Fraction of the solid support: 60-80 mesh. Experimental conditions: temperature of the column and of the heat conductivity detector, 200.6°; helium flow rate, 50 ml/min; pressure at the inlet, 1.15 kg/cm². Notations of the peaks: 1 = cyclotetradecanone; 2 = cyclopentadecanone; 3 = cyclohexadecanone; 4 = cycloheptadecanone; 5 = (10)- α -cyclothienone-1; 6 = (11)- α -cyclothienone-1; 7 = (12)- α -cyclothienone-1; 8 = (13)- α -cyclothienone-1.

The heats of solution of alicyclic ketones and of α -cyclothienones in polyethyleneglycol succinate were determined by the temperature relationship of the corrected retention volumes within the range of 180-220°. ΔH_S is greater for α -

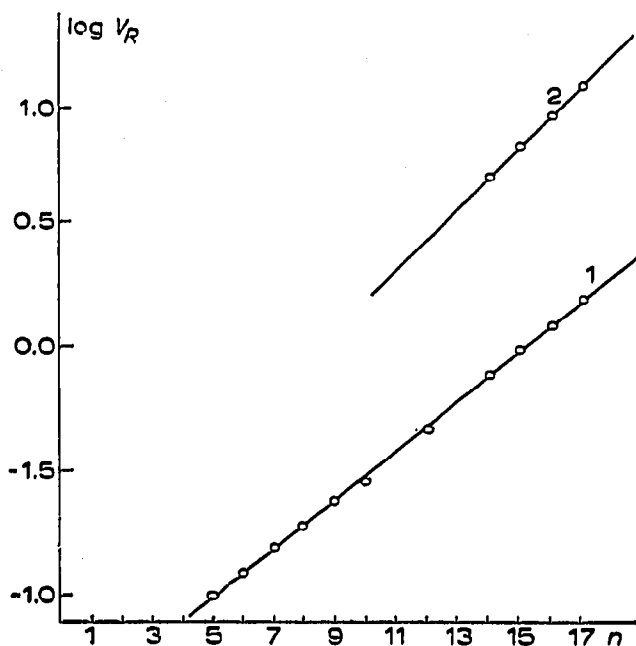


Fig. 14. Relationship between relative retention volumes (V_R^{rel} , of cyclopentadecanone = 1) and the number of carbon atoms in a molecule at 180° on the polyethyleneglycol succinate-Chromosorb column. 1 = Alicyclic ketones; 2 = α -cyclotrienones.

cyclotrienones than for alicyclic ketones by 2.2 kcal/mole. In both series, ΔH_S grows linearly with the number of carbon atoms in a molecule. The change in ΔH_S for one methylene group amounts to 0.65 kcal/mole for both types of ketone. The resultant linear relationship between ΔH_S and the number of carbon atoms in a

TABLE VIII

HEAT OF EVAPORATION AND OF SOLUTION AND EXCESS HEAT OF SOLUTION OF ALICYCLIC KETONES A

	C_4	C_5	C_6	C_7	C_8	C_9
<i>Alicyclic ketones</i>						
Heat of solution at $180-220^\circ$	5.91	6.56	7.21	7.86	8.51	9.16
Heat of evaporation at boiling point	7.63	8.33	8.90	9.47	9.84	10.16
Heat of evaporation at 200°	5.40	6.81	7.92	9.03	9.75	10.38
	(9.09*)	(10.17**)	(10.96***)			
Excess heat of solution at 200°	- 1.45	- 0.69	- 0.23	+ 0.23	+ 0.30	+ 0.2
<i>α-Cyclotrienones</i>						
Heat of solution at $180-220^\circ$						
Heat of evaporation at boiling point						
Heat of evaporation at 200°						
Excess heat of solution at 200°						

* Heat of evaporation at 0° ; according to published data, the heat of evaporation at 0° amounts to 9.18 kcal/mole (ref. 26).

** Heat of evaporation at 10° ; according to published data, the heat of evaporation at 10° amounts to 10.41 kcal/mole (ref. 26).

*** Heat of evaporation at 30° ; according to published data, the heat of evaporation at 30° amounts to 10.71 kcal/mole (ref. 26).

ring enables the determination of ΔH_S for any term of the series according to the formula:

$$\Delta H_S = 3.31 + 0.65 n \text{ kcal/mole (acyclic ketones),}$$

$$\Delta H_S = 5.5 + 0.65 n \text{ kcal/mole (\alpha-cyclothienones),}$$

where n is the number of carbon atoms in the molecule.

Table VIII gives the heat of evaporation at the boiling point of ketone, calculated by the Kistyakovsky equation¹⁶, the heat of evaporation at the average temperature of the chromatogram (200°), computed by Watson's equation¹⁶, the experimentally determined heat of solution within a range of 180° to 220° for C₁₄-C₁₇ ketones, and the heat of solution for alicyclic ketones C₄-C₁₃, found from the above linear relationship. Wherever possible, the calculated heat of evaporation was compared with published data. The maximum deviation did not exceed 2.5 %. From the excess heat of solution it was possible to appraise the nature of the interaction between the ketones and the stationary phase. In the case of alicyclic ketones, the nature of the interaction changes with an increase in the size of the ring. Typical of alicyclic C₄-C₆ ketones are the negative $\Delta \bar{H}_{S^E}$ values (Table VIII) (exothermic effect upon solution) and a negative deviation from the ideal state of a solution. In this case there is an interaction between the ketone molecules and the stationary phase molecules, the strength of the interaction dropping from the C₄-ketone to the C₆-ketone. Already with the C₇-ketone, $\Delta \bar{H}_{S^E}$ becomes positive (endothermic effect upon solution), which confirms the positive deviations from the ideal state of a solution. The ketone molecules are ejected, as it were, from the solution. However, when passing over to C₉-C₁₁-ketones, such a "negative" interaction between ketone and the stationary phase diminishes and $\Delta \bar{H}_{S^E}$ becomes again negative at C₁₁. Further on, up to C₁₈,

ALICYCLIC KETONES IN POLYETHYLENEGLYCOL SUCCINATE (kcal/mole)

	C ₁₁	C ₁₂	C ₁₃	C ₁₄	C ₁₅	C ₁₆	C ₁₇	C ₁₈	C ₁₉	C ₂₀
10.81	10.46	11.11	11.76	12.46	13.14	13.95	14.36	15.01	15.66	16.31
10.39	10.62	11.08	11.43	11.97	12.95	13.30	13.77	14.24	—	—
10.83	11.28	12.20	12.90	13.98	16.0	16.72	17.70	18.69	—	—
10.08	— 0.12	+ 0.15	+ 0.20	+ 0.58	+ 1.92	+ 1.83	+ 2.40	+ 2.74	—	—
		13.30†	13.95†	14.55	15.23	16.00	16.55	17.20	17.85	18.50
				12.95	13.65	14.13	14.84			
				14.78	15.89	16.65	17.77			
				— 0.71	— 0.28	— 0.29	+ 0.28			

† This value was obtained by extrapolation.

$\Delta\bar{H}_S^E$ is positive and rises continuously. Such a pattern of changes in the excess heat of solution with an increase in the size of the ring leads to the following conclusion. In homologues of a series with a small-sized ring, the work consumed in moving apart the molecules of the stationary phase is small, and the interaction between the dipole molecule of a ketone and the phase molecules is fairly large. As the size of the ring grows, the work required for moving apart the stationary phase molecules increases and the gain in energy diminishes. Somewhere in the region of C₁₀ these two factors compensate each other and the solution approximates an ideal one. However, further on, up to C₁₈, the energy consumed by moving apart the stationary phase molecules becomes the fundamental magnitude, *i.e.* the energy required for a molecule of an alicyclic macroketone to find its place there. In the case of α -cyclohexenones with the same size of ring, there appears an additional source of interaction: between the liquid phase and system of π -electrons of the thiophene ring. The work consumed for moving apart the stationary phase molecules is overlapped for C₁₄-C₁₀ ketones by interaction with the ketone group and the thiophene ring. It is only at C₁₇ that the size of the ring reaches such a magnitude that the interaction is accompanied by an endothermal, and not by an exothermal effect.

It appears that the relationships found should be regarded as preliminary since steric interactions in the molecule of a cyclic ketone were not taken into account in the discussion. This point merits special consideration, especially in view of the fact that anomalous values of $\Delta\bar{H}_S^E$ are to be found in the region of the middle-sized rings (C₉-C₁₂). This demonstrates once more the relationships existing between chromatographic behaviour of a substance and its structure.

SUMMARY

Gas-liquid chromatography, when used for heterocyclic compounds, opens up wide prospects for its analytical application. Highly polar and high-boiling substances can be chromatographed by using either diatomite brick treated with an alkali (content of the stationary phase 15-20%), or sodium chloride with a small amount of the stationary phase (about 1%). Proceeding from the thermodynamics of the interaction between the investigated substances and the stationary phase, it is possible to reveal the fine effects related to the structure of a molecule.

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