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GAS–LIQUID CHROMATOGRAPHY ON FLUORINATED STATIONARY PHASES

II. FLUORINATED COMPOUNDS CONTAINING A FUNCTIONAL GROUP

F. VERNON and G. T. EDWARDS
The Ramage Laboratories, Department of Chemistry and Applied Chemistry, University of Salford, Salford M5 4WT, Lancs. (Great Britain)
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SUMMARY

The retention of fluorinated organic compounds containing a functional group has been studied and compared with the parent compounds. On fluorinated stationary phases it is found that the influence of fluorine in the solute is a major factor in retention. The solute–stationary phase interactions and solute functional group–stationary phase interactions are examined in terms of retention index increments and reveal that a new gas–liquid chromatographic stationary phase, Krytox fluorinated polyether, shows an exceptional ability to separate fluorinated from non-fluorinated compounds due to the very small degree of stationary phase interaction with the latter.

INTRODUCTION

In Part I the properties of four fluorinated stationary phases suitable for gas–liquid chromatography (GLC) were described[1]. The four phases were of low polarity and were, in order of increasing polarity as determined from McReynolds' constants[2], Krytox AC, Kel F 90 oil, Fluorolube 2000 oil, and silicone QF-1.

For the GLC separation of fluorinated solutes, it was found that the degree of fluorination was the most important factor when separations on Krytox and Fluorolube were carried out. Krytox was the most efficient phase for hydrocarbon–fluorohydrocarbon separations, whilst Fluorolube was slightly better for separations of fluorocompounds with varying degrees of fluorination. For those compounds with the same degree of fluorination but having substantially different boiling points, such as fluorobenzene and fluorotoluene, Kel F oil proved to be the best stationary phase for separations. The importance of the degree of fluorination is apparent from the study which was carried out on hydrocarbons and their fluoro derivatives.

It could be expected that when, in addition to fluorine, a second and possibly highly polar functional group is present in the molecule, the degree of fluorination would have a reduced effect on the retention index. Forces of attraction between solutes and stationary phase could then be primarily of the dipole-induced dipole type with the fluorine atom in the solutes exerting only a small effect on solute dipole. To test this, a series of compounds containing functional groups together with their fluoro derivatives have been examined on the four fluorinated phases and on a reference phase. As many of the disubstituted benzenes examined had high boiling points, it was not possible to use squalane as the reference. Apiezon L grease was therefore chosen for obtaining reference GLC retention data at a column temperature of 180°. Brown *et al.*[3] have published retention data on fluoroalcohols on two fluorinated electron acceptor stationary phases and Gvosdovich and Jashin[4] have described the gas chromatographic separations of fluoroesters, fluoroalcohols and fluoroacetophenone from the parent compounds on porous polymers. However, published work on fluorinated solute separations is mostly confined to fluorocarbon analysis and a comprehensive examination of the GLC behaviour of fluoro compounds is overdue.

EXPERIMENTAL

All measurements were made on a Pye Series 104 gas chromatograph with flame ionization detector. Columns were 1 M × 6 mm O.D. tubing packed with 20% w/w of stationary phase coated on acid-washed, DCMS-treated Celite, 80–100 mesh particle size. The carrier gas was nitrogen at a flow-rate of 20 ml/min. Kováts[5] retention indices were obtained using the two appropriate *n*-paraffins and calculated from adjusted retention volumes. The dead volume of each column was found using the method of Peterson and Hirsch[6].

Phases

The following stationary phases were used: (1) Kel F 90 oil, a poly(chlorotrifluoroethylene), obtained from Phase Separations, Queensferry, Great Britain; (2) Fluorolube 2000 oil, a chlorofluorocarbon polymer, obtained from Phase Separations; (3) Silicone QF-1, poly(methyl-3,3,3-trifluoropropylsiloxane), obtained from Phase Separations; (4) Krytox 240 AC[7], a perfluoroalkyl polyether oil thickened with Vydax 1000 fluorocarbon telomer solids, obtained from DuPont, Wilmington, Del., U.S.A.

RESULTS AND DISCUSSION

The retention data for acetylacetone and hexafluoroacetylacetone at 100° are given in Table I. The retention index values for the two solutes on the five stationary phases studied (Table I(a)) clearly demonstrate the high selectivity of silicone QF-1 for ketones, in agreement with the McReynolds Y' constant[1] of 225. The large difference in boiling point between acetylacetone (139°) and its hexafluoro derivative (70°) is seen in the retention index values on squalane but the effect of extensive fluorination is to greatly enhance the interaction of the hexafluoro derivatives with Krytox and Kel F oil. The figures in Table I(b) are a measure of the solute–stationary phase interaction, being the retention increment (ΔI) of the solute on the fluorinated stationary phase over the solute on squalane. The high degree of interaction between the trifluoropropyl groups of silicone QF-1 and the carbonyl groups of acetylacetone is reduced considerably upon the incorporation of fluorine atoms onto adjacent carbon

TABLE I

RETENTION DATA FOR ACETYLACETONE AND HEXAFLUOROACETYLACETONE AT 100°

	Krytox AC	*Silicone QF-1*	*Kel F 90*	*Fluorolube 2000*	*Squalane*
(a) I values*					
Acetylacetone	858	1080	887	907	771
Hexafluoro derivative	727	682	605	520	404
(b) ΔI values**					
Acetylacetone	87	309	116	136	
Hexafluoro derivative	323	278	201	116	
(c) $\delta\Delta I$ values***	236	−31	85	−20	

* Retention index (I) values.

** Solute–stationary phase interaction ΔI. $\Delta I = I_{\text{stationary phase}} - I_{\text{squalane}}$.

*** Retention increment ($\delta\Delta I$) for the replacement of hydrogen atoms by fluorine. $\delta\Delta I = \Delta I_{\text{hexafluorodiketone}} - \Delta I_{\text{diketone}}$.

atoms. The strong inductive effect reduces the availability of electrons at the carbonyl oxygens thereby reducing dipole–dipole interaction by an increment of 31 units, as seen in Table I(c). A similar, though somewhat smaller effect is seen for the Fluorolube column, where the degree of interaction has been reduced by twenty units upon the introduction of the six fluorines.

The work on hydrocarbons and fluorocarbons in Part I led to the conclusion that the presence of fluorine in the solute molecule could be the major factor in separations on Krytox. On studying the diketones, this conclusion is verified. The retention index of acetylacetone on Krytox is less than 100 units higher than the value on squalane, showing that the degree of interaction with this phase is quite small. Solute–stationary phase interaction for the hexafluoro derivative, however, is over 300 units with an enhanced retention of 236 units due to the presence of the six fluorine atoms. Kel F oil also shows selective retention for the fluoro compound to a smaller extent with an enhanced retention increment of 85 units.

Table II gives the retention index values of substituted benzenes and their monofluoro derivatives on the four fluorinated phases and an Apiezon L reference phase at 180°. From a consideration of solute boiling points and retention indices on Apiezon L for the parent compound and its *p*-fluoro derivative it can be seen that a reduction in retention index occurs upon the introduction of the fluorine although the boiling point remains constant or increases slightly. The polarizabilities of hydrogen and fluorine exhibit only a small difference but the Van der Waals radius of hydrogen is less than that of fluorine. Consequently, the value of α/r^6, characterising the dispersion interaction, is less for fluorine than for hydrogen. When considering a hydrocarbon phase, such as squalane or Apiezon L, therefore, a decrease in retention time should result when substituting fluorine atoms for hydrogen atoms in the molecule due to the decrease in dispersion interaction. Kováts and Weisz[8] have suggested that the retention index on a non-polar, reference phase is a measure of the contribution to the free energy of transfer from gas to liquid phase, ΔG, for the creation of a "hole" in the solvent cage plus ΔG due to dispersion forces. The reduced dispersion interaction on substituting fluorine will lead to a reduction in the free energy of transfer

TABLE II

RETENTION INDEX (*I*) VALUES OF AROMATIC COMPOUNDS AND MONOFLUORO-DERIVATIVES AT 180°

Compound	*I*					
	Krytox AC	*Silicone QF-1*	*Kel F 90*	*Fluorolube 2000*	*Apiezon L*	*B.p. (°C)*
Phenol	1000	1209	1088	1088	955	185
p-Fluorophenol	1067	1259	1100	1113	955	182
Aniline	1059	1263	1193	1168	999	183
p-Fluoroaniline	1134	1318	1205	1211	996	188
Anisole	967	1100	1016	1026	940	154
o-Fluoroanisole	1036	1198	1059	1053	934	154
m-Fluoroanisole	1000	1129	1043	1047	925	154
p-Fluoroanisole	1019	1160	1043	1042	925	157
Methyl benzoate	1163	1416	1252	1237	1109	199
Methyl *o*-fluorobenzoate	1200	1416	1285	1261	1097	209
Methyl *m*-fluorobenzoate	1185	1405	1279	1214	1074	197
Methyl *p*-fluorobenzoate	1185	1408	1278	1215	1074	198
Nitrobenzene	1243	1562	1273	1289	1128	211
m-Fluoronitrobenzene	1225	1573	1229	1238	1067	205

of the solute and therefore to a reduced retention index. The Apiezon L results for *p*-fluoro substitution into aniline, anisole and methyl benzoate confirm this; for instance, with a 3° rise in boiling point from anisole to *p*-fluoroanisole there is nevertheless a fall of 15 units in the retention index. Phenol is anomalous in this respect, for although the boiling point falls 3° on substitution in the *para* position, this, together with reduced dispersion, should lead to a considerable reduction in retention index, but the values for phenol and its *p*-fluoro derivative are identical.

For all fluorinated stationary phases, the retention index for the fluoro compound is higher than that for the parent when an activating group, hydroxy, methoxy, or amino, is present. The small decreases on fluorination of methyl benzoate and nitrobenzene are, in fact, due to dispersion effects, as can be seen from Table III, where retention increments representing the contribution to ΔG from dipole interactions, plus specific interactions such as hydrogen bond formation, are listed. Table III shows that in all cases there is enhanced interaction between solute and fluorinated stationary phase upon the introduction of fluorine into the solute, irrespective of the position in the ring at which the fluorine is introduced. As before, this effect is the greatest on Krytox, where very low degrees of interaction are observed for phenol, anisole, aniline and methyl benzoate. By comparison with Kel F oil, which it often resembles in its retention behaviour, Krytox shows a normal degree of interaction with only one non-fluoro compound studied; with nitrobenzene the interaction contributes 115 units to the retention index compared with a contribution of 145 units for this solute on Kel F oil.

From Table III, the "*ortho* effect" of the fluorine can be seen where, in the case of an activating functional group such as methoxy, the *o*-fluoro isomer has the greatest degree of interaction with three of the stationary phases whilst when the functional group is the deactivating carboxymethoxy, a fluorine in the *ortho* position leads to the minimum degree of interaction with these phases. Fluorolube oil behaves anomal-

TABLE III

SOLUTE–STATIONARY PHASE INTERACTIONS (ΔI) FOR AROMATIC COMPOUNDS AND MONOFLUORO DERIVATIVES AT 180°

Compound	ΔI			
	Krytox AC	*Silicone QF-1*	*Kel F 90*	*Fluorolube 2000*
Phenol	45	254	133	133
p-Fluorophenol	112	304	145	158
Aniline	60	264	194	169
p-Fluoroaniline	138	322	209	215
Anisole	27	160	76	86
o-Fluoroanisole	102	264	125	119
m-Fluoroanisole	75	204	118	122
p-Fluoroanisole	94	235	118	117
Methyl benzoate	54	307	143	128
Methyl *o*-fluorobenzoate	103	319	188	164
Methyl *m*-fluorobenzoate	111	331	205	140
Methyl *p*-fluorobenzoate	111	334	204	141
Nitrobenzene	115	434	145	161
m-Fluoronitrobenzene	158	506	162	171

ously in this respect with the interaction magnitude being independent of the fluorine position in the fluoroanisole and the methyl *o*-fluorobenzoate actually showing the highest degree of interaction of the three isomers with this phase.

Table IV shows the extent to which the functional group contributes to solute–stationary phase interaction, $\delta\Delta I$, the values being derived from Table III thus:

Parent compound, $\delta\Delta I = \Delta I_{\text{parent}} - \Delta I_{\text{benzene}}$
Fluoro compound, $\delta\Delta I = \Delta I_{\text{fluoro}} - \Delta I_{\text{fluorobenzene}}$

TABLE IV

FUNCTIONAL GROUP INTERACTION ($\delta\Delta I$) WITH STATIONARY PHASE AND DIFFERENCE IN INTERACTION BETWEEN A COMPOUND AND ITS FLUORO DERIVATIVE

Compound	*Krytox AC*		*Silicone QF-1*		*Kel F 90*		*Fluorolube 2000*	
	$\delta\Delta I$	*Diff.*	$\delta\Delta I$	*Diff.*	$\delta\Delta I$	*Diff.*	$\delta\Delta I$	*Diff.*
Phenol	27		122		85		53	
p-Fluorophenol	39	12	130	8	63	−22	49	−4
Aniline	42		132		146		89	
p-Fluoroaniline	65	23	148	16	127	−19	106	17
Anisole	9		28		28		6	
o-Fluoroanisole	29	20	90	62	43	15	10	4
m-Fluoroanisole	2	−7	30	2	36	8	13	7
p-Fluoroanisole	21	12	61	33	36	8	8	2
Methyl benzoate	36		175		95		48	
Methyl *o*-fluorobenzoate	30	−6	145	−30	106	11	55	7
Methyl *m*-fluorobenzoate	38	2	157	−18	123	28	31	−17
Methyl *p*-fluorobenzoate	38	2	160	−15	122	27	32	−16
Nitrobenzene	97		302		97		81	
m-Fluoronitrobenzene	85	−12	332	30	80	−17	62	−19

and the second column lists the influence which the fluorine exerts on the functional group–stationary phase interaction and is derived from:

Influence of F $= \delta\Delta I_{\text{fluoro}} - \delta\Delta I_{\text{parent}}$

From Table IV, maximum $\delta\Delta I$ values are seen for silicone QF-1, where the interactions between the trifluoropropyl groups of the phase and the carbonyl and nitro oxygens in the benzoates and the nitro compounds, respectively, are considerable. This silicone phase demonstrates an unexpectedly high degree of interaction with phenolic hydroxyl groups but not with their methoxy derivatives. This is unusual in that it may not be predicted from the McReynolds constants[1]. The values for Z' and U' at 336 and 432, respectively, support the prediction of a high degree of interaction with carbonyl and nitro compounds. The S' value of 281 could be in agreement with the interaction of the silicone phase with amines but a Y' value of 225 suggests that phenolic interaction with silicone would be only slightly higher than with Fluorolube, where Y' is 192.

The difference values in Table IV represent the effect of the fluorine on the functional group–stationary phase interaction. The "*ortho* effect" is clearly seen with enhancement of methoxy interaction and suppression of carboxymethoxy interaction, the effect being, of course, electronic in nature as fluorine is too small to exert a steric effect in the *ortho* position. On Krytox and silicone QF-1 the *para*-substituted phenol, anisole and aniline show increased differences on fluorine substitution due to the increased dipole of the solute molecule, with the largest effect being on the nitro group. Substitution of fluorine into a molecule carrying the carboxymethoxy deactivating group has very little effect with the Krytox phase and reduces the functional group–stationary phase interaction considerably with silicone and Fluorolube phases. This reduction probably arises from the reduction in dipole moment when the electronegative fluorine is introduced *para* to the electronegative carbonyl group. The decrease in nitro group interaction is considerable on three of the phases again due to a decrease in the solute dipole. Only with silicone, with its bonding potential of the trifluoropropyl groups to solute oxygen, is an enhanced functional group interaction found on introduction of fluorine. For most of the interactions studied, it is found that Kel F oil interacts in the opposite way to silicone QF-1. Thus, whilst fluorine gives a positive effect on phenol and amine interactions with Krytox and QF-1, the effect is negative, *i.e.* reduced interaction of these groups, with Kel F. The deactivating carboxymethoxy group suffers a reduction of interaction with QF-1, whereas its interaction with Kel F is enhanced, whilst the reverse is true for both phases and the nitro group.

CONCLUSIONS

The supposition that when a polar functional group was present in the molecule this would have a significant effect upon the retention index and reduce the importance of the presence and extent of fluorine substitution is not supported by the evidence obtained on the fluorinated stationary phases studied. In Part I it was concluded that fluorination caused an average increase in retention index per fluorine atom of approximately 45, 20, 25 and 5 units for Krytox, silicone QF-1, Kel F 90 and Fluorolube 2000, respectively. The comparable values, obtained by dividing the figures in Table I(c) by the number of fluorine atoms in hexafluoroacetylacetone, are 40, −5, 14 and

—4 units, respectively. This means that only on Krytox is the retention index of hexafluoroacetylacetone determined primarily by the fluorine content rather than by the presence of the two carbonyl groups. Kel F 90 is the only other stationary phase upon which the extent of fluorination exceeds the presence of the carbonyl groups in determining the retention index. For the substituted benzenes studied, the retention increments due to the fluorine for Krytox, silicone QF-1, Kel F 90 and Fluorolube 2000 are approximately 55, 40, 30 and 30 units, respectively, for the fluoro derivatives. The increments for substituted benzenes on Krytox vary from 40 units on the nitro derivative to 80 units on the amino substituent so the effect of fluorine substitution is large on this stationary phase irrespective of the nature of the functional group present. The silicone phase shows an average increase in the contribution of the fluorine towards retention, the only anomaly being for the carboxymethoxy compounds, where an average increment of around 20 units is found. Kel F shows its highest effect with this solute, however —a 50 unit enhancement— whereas for phenol and aniline the presence of fluorine is a minor effect, increasing the interactions by only 12 and 15 units, respectively. Fluorolube oil shows an increased effect for fluorine in substituted benzenes over that of benzene irrespective of the nature of the substituent. The minimum increment on this phase is 10 units for the nitro compounds and the maximum 45 units for the amines.

In general, the most useful phase for fluoro compound separations would appear to be Krytox AC. The largest effects due to the presence of fluorine in an organic molecule are found with this phase and those effects, when studied by the retention index system, often approach ideality. Silicone QF-1 is an extremely useful stationary phase for fluoro compounds but is of much more restricted application, being effective when the solute is of an electron-donor species.

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