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Liquid Crystals as Solvents. I. The Use of Nematic and Smectic Phases in Gas–Liquid Chromatography[1]
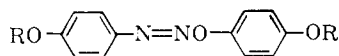
By Michael J. S. Dewar and J. P. Schroeder

This paper, the first in a series dealing with applications of liquid crystals as solvents, describes studies of such materials as stationary phases in gas–liquid chromatography. The use of the nematic phase of 4,4′-dimethoxyazoxybenzene has led to excellent separations of a number of *meta–para* pairs of disubstituted benzene derivatives; mixtures of *m*- and *p*-xylene were easily separated using the smectic phases of the corresponding dihexyloxy- and diheptyloxyazoxybenzenes. The retention times vary in an interesting manner with temperature, showing a marked increase at the transition point to normal liquid; as anticipated, this effect is less for the more nearly linear *para* isomers.

Introduction

Liquid crystals[2] form a curiously neglected state of matter, intermediate between crystalline solids and "normal" isotropic liquids. They are formed by certain compounds with elongated, relatively polar molecules whose mutual attraction tends to orient them with their long axes parallel. Such materials first melt to an anisotropic liquid in which the molecules are free to move about only so long as they remain parallel to one another; at a higher temperature the melt undergoes a sharp transition to a normal liquid. Certain substances exist in not one but two distinct liquid crystalline phases. These on fusion give first a smectic phase in which the molecules are not only constrained to be parallel, but are also arranged in layers; at a higher temperature they undergo transition to the nematic phase when this extra constraint is lost; and then at a still higher temperature the nematic phase changes to a normal liquid. Certain substances are even claimed to exist in two or more distinct smectic phases.[2]

Liquid crystals therefore behave mechanically as liquids, but they preserve some of the order of crystalline solids. If a material whose molecules are rod-shaped is dissolved in a liquid crystal, we may expect the solute molecules to be oriented parallel to the molecules of the solvent. The resulting geometrical constraint should have obvious and interesting physical and chemical consequences, and so liquid crystals should show very unusual solvent properties. This paper is the first of a series describing a general study of liquid crystals as solvents.

First of course it is necessary to know the conditions under which binary mixtures will behave as liquid crystals; a survey of this kind was carried out some time ago by Dr. J. S. Dave and one of us[3]; addition of a second component depresses the (nematic → liquid) transition temperature of *p*-azoxyanisole (Ia) and re-

RO—⟨ ⟩—N=NO—⟨ ⟩—OR

Ia, R = CH₃
b, R = *n*-C₆H₁₃
c, R = *n*-C₇H₁₅

duces the range over which the mixture is anisotropic. As might have been expected, the effect was smaller[3a]

the more nearly the solute molecules resembled those of *p*-azoxyanisole in size, shape, and polarity. Evidently the energetically favorable arrangement of molecules in the nematic phase is disturbed by a foreign material, but to a lesser extent the more closely the two resemble one another.

One obvious and straightforward application of liquid crystals would be their use as stationary phases in gas–liquid chromatography. The relative retention times of different samples on a given column depend mainly on their partition coefficients between the gaseous and liquid phases; these depend primarily on the boiling point of the sample, and secondarily on specific interactions between its molecules and those of the liquid phase. Existing column packings therefore discriminate mainly on the basis of boiling point, and, secondarily, in the case of packings such as Carbowax, on specific solvent–solute interactions. It is therefore often very difficult to separate position isomers that differ little in polarity, a classic—and technically important—example being provided by *m*- and *p*-xylene. Liquid crystals might provide a solution to this impasse, for one might expect their relative affinities for a series of isomers to depend on the shapes of the latter. Moreover, by an obvious extension of this reasoning, one might expect optically active liquid crystals to provide a method of resolution of *dl*-mixtures by gas–liquid chromatography, a sofar unsolved problem.

In this paper we describe a study of the separation of various isomeric disubstituted benzenes on *p*-azoxyanisole (Ia). This is by no means an ideal substrate for the length[4] of its nematic phase is small, implying that the tendency to order in it is easily overcome. However, our results demonstrate the potential usefulness of liquid crystals in this connection and they also have implications of general interest concerning the nature of the (nematic → liquid) transition. We also carried out some experiments with the smectic phase of 4,4′-di-*n*-hexyloxy- (Ib) and 4,4′-di-*n*-heptyloxyazoxybenzene (Ic) which indicate that one can obtain solutions in them which are still smectic. To our knowledge, no binary smectic systems have been reported; their existence is of interest, since smectic phases have a layer structure equivalent to the superposition of two-dimensional liquids and study of the thermodynamic properties of solutions in them would be of value in connection with the theory of liquids.

(2) G. W. Gray, "Molecular Structure and the Properties of Liquid Crystals," Academic Press, Inc., New York, N. Y., 1962.

(3) J. S. Dave and M. J. S. Dewar, (a) *J. Chem. Soc.*, 4616; (b) *ibid.*, 4305 (1955).

(4) The length of a smectic or nematic phase is defined[2] as the range in °C. over which it exists.

Experimental[5]

Materials.—p-Azoxyanisole (Ia) was prepared in 97% yield by reduction of p-nitroanisole with methanolic sodium methoxide.[6] After one recrystallization from benzene it had m.p. 120–121°, (nematic → liquid) transition temp. 135° (lit.[7] 118.5°, 135°). The homologous ethers Ib and Ic were prepared likewise; after recrystallization twice from 95% ethanol, Ib had m.p. 71°, transitions (smectic → nematic) 80°, (nematic → liquid) 130° (lit.[8] 72°, 81°, 127°); corresponding values for Ic, 75°, 95°, 127° (lit.[8] 74°, 92°, 122.5°). Weygand and Gabler[8] reported that Ib melts at 81° to a nematic phase, the (solid → smectic) transition being observed only as a monotropic transition on cooling. We could not confirm this; in our hands Ib invariably melted at 71° to smectic liquid.

The substituted benzenes were commercial samples and were not purified further. In only one case (methyl m-toluate) did gas chromatography show a major contaminant (ca. 10%); in the other compounds only very small amounts of impurity were present.

Apparatus.—Transition temperatures were determined with a Nalge–Axelrod hot-stage melting point apparatus, which has a viewing microscope and provision for observing birefringence. The chromatograms were obtained with an Aerograph Hy-Fi gas chromatograph, Model 600-C, using nitrogen as carrier gas. The oven temperatures were measured with a calibrated mercury thermometer; temperature variations of ±1° existed between different parts of the oven. The liquid crystal chromatographic columns were made from 3.2 mm. o.d. annealed copper tubing.

TABLE I

CHROMATOGRAPHIC COLUMNS

Column	Length, m.	Stationary phase	Wt. of packing, g.
1	1.5	Ia	0.9
2	8.8	Ia	5.1
3	7.6	Ib	5.0
4	7.6	Ic	5.0
5[a]	1.5	Silicone[b]	...

[a] Wilkens Instrument and Research, Inc., 3.2 mm. o.d. stainless steel. [b] Silicone SE-30, 5% on Chromosorb-W.

TABLE II

RELATIVE RETENTION TIMES FOR BENZENE POSITION ISOMERS IN GAS CHROMATOGRAPHIC COLUMNS EMPLOYING (1) A SILICONE POLYMER AND (2) A NEMATIC COMPOUND AS LIQUID PHASES

Compound	Rel. retention times[a] (meta isomer = 1.00) Silicone polymer[b]	4,4'-Dimethoxyazoxybenzene[c]
p-CH₃OC₆H₄OCH₃	0.99	1.17
		1.16 (col. 1)
p-CH₃C₆H₄CH₃	1.00	1.03
p-BrC₆H₄CH₃	1.01	1.10
o-BrC₆H₄CH₃	1.02	0.92
p-BrC₆H₄Br	1.02	1.17
		1.17 (col. 1)
p-ClC₆H₄CH₃	1.02	1.09
p-ClC₆H₄Cl	1.03	1.16
p-CH₃C₆H₄OCH₃	1.03	1.10
p-BrC₆H₄Cl	1.03	1.16
p-ClC₆H₄COCH₃	1.06	1.28
p-CH₃C₆H₄COOCH₃	1.07	1.26
o-CH₃C₆H₄CH₃	1.14	1.20

[a] Retention times were corrected for gas hold-up. [b] Column 5 is described in the Experimental section. Chromatograms were determined at 100° with N₂ as carrier gas, flow rate 22 ml./min. [c] Columns 1 and 2 are described in the Experimental section. Except where indicated otherwise, column 2 was used. Chromatograms were determined at 124–127° with N₂ as carrier gas, flow rate 30–40 ml./min. except for the xylenes (20 ml./min.).

(5) Temperatures are corrected.
(6) B. M. Bogoslovskii, Akad. Nauk S.S.S.R., Inst. Org. Khim., Sintezy Org. Soedinenii, Sbornik, **2**, 5 (1952).
(7) W. Davies and R. A. R. Down, J. Chem. Soc., 586 (1929); R. S. Porter and J. F. Johnson, J. Phys. Chem., **66**, 1826 (1962).
(8) C. Weygand and R. Gabler, J. prakt. Chem., **155**, 332 (1940).

TABLE III

RETENTION TIMES OF BENZENE POSITION ISOMERS IN COLUMN 1 (STATIONARY LIQUID PHASE: 4,4'-DIMETHOXYAZOXYBENZENE)[a,b,c]

Column temp., °C.	CH₃OC₆H₄OCH₃ meta	para	BrC₆H₄Br meta	para	CH₃C₆H₄COOCH₃ meta	para	ClC₆H₄COCH₃ meta	para
115[d]					10.52	13.55		
120[d]					9.20	11.75		
125					8.29	10.38	15.90	20.25
126	6.80	7.85	6.03	7.03				
129	6.38	7.23	5.72	6.55				
130					7.46	9.18	13.96	17.45
133	6.02	6.75	5.45	6.20				
134					6.85	8.28	12.90	15.85
135	5.87	6.52	5.38	6.08				
136	5.83	6.45	5.35	6.03	6.70	8.00	12.60	15.22
137	5.80	6.40	5.40	6.00	6.75	8.00	12.50	14.90
138	5.93	6.42	5.50	6.12	6.83	8.05	12.60	15.00
139	5.90	6.42	5.60	6.08	7.08	8.15	12.90	15.11
140	6.05	6.47	5.73	6.25	7.00	8.06	12.90	15.10
141	5.93	6.22	5.55	6.12	6.84	7.88	12.38	14.43

[a] Column 1 is described in the Experimental section. [b] Injection chamber temperature was 245° for all runs. [c] Carrier gas (N₂) flow rate was 40 ml./min. for the dibromo- and dimethoxybenzenes, 35 ml./min. for the chloroacetophenones and methyl toluates. [d] These temperatures are below the (solid → nematic) transition point of 4,4'-dimethoxyazoxybenzene. The runs were made after cooling from above the transition temperature. The data indicate that the stationary liquid phase had supercooled and was still in the nematic form.

The packings were prepared from Chromosorb-W (60–80 mesh) using solutions of I in acetone or dichloromethane; the packings were all 15% liquid phase by weight. The characteristics of the four columns used are listed in Table I, together with those of a commercial silicone column.

Procedure.—Since solutes lower[8] the (nematic → liquid) transition temperature of Ia and also reduce the range over which Ia is nematic, we used small samples (0.05–0.2 μl. of a 1% solution in carbon disulfide for column 1, 0.3–0.5 μl. for the longer columns). The injection chamber was maintained 100° above the temperature of the column.

Results

Table II compares relative retention times for various benzene position isomers on Ia and on silicone.

Table III lists retention times for the benzene derivatives on column 1 at various temperatures, while Table IV shows similar results for column 2.

Figure 1 shows typical chromatograms of mixtures of isomeric chlorotoluenes, bromotoluenes, and methylanisoles at various temperatures.

Note that the separations deteriorate above 135°, the temperature of the (nematic → liquid) transition. Equally good separations were obtained in the case of the other meta-para pairs, except for the xylenes; these could not be separated on Ia.

Mixtures of m- and p-xylene could be separated on columns 3 and 4, packed with Ib and Ic, respectively, in the smectic region. Figures 2a and 2b show typical chromatograms on the two substrates, while Fig. 3 is a plot of retention time vs. temperature for the three isomers on column 3 (Ib).

Discussion

A nematic liquid crystal would be expected to show a selective affinity for linear molecules, since these should be able to fit better into its "lattice"; on this basis one might expect columns of nematic I to retain selectively p-disubstituted benzenes, relative to the
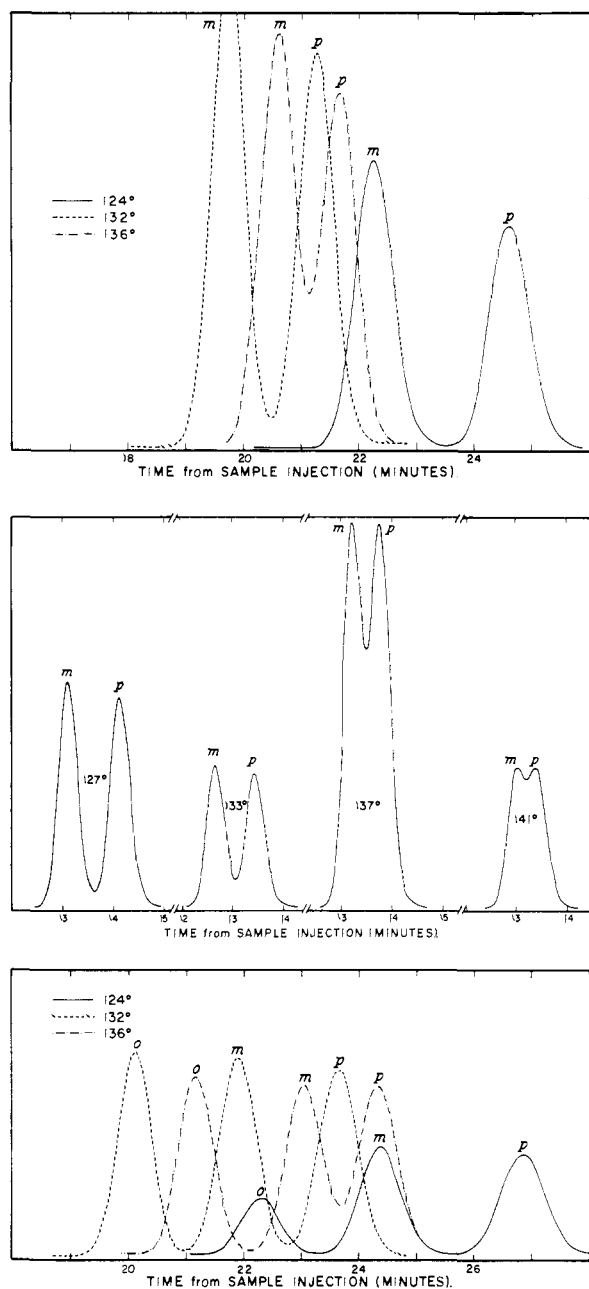
Fig. 2.—Chromatogram of a mixture of m- and p-xylene: (a) upper, on column 3 (Ib); (b) lower, on column 4 (Ic).

Fig. 3.—Plot of retention time vs. temperature for o-, m-, and p-xylene on column 3 (Ib).

Fig. 1.—Chromatograms on Ia at various temperatures of mixtures of: (a, top) m- and p-methylanisole; (b, middle) m- and p-chlorotoluene; (c, lower) o-, m-, and p-bromotoluene.

ortho and meta isomers. Table I shows that this is in fact the case; the ratio of retention times is much greater on columns of Ia than on a "normal" liquid silicone packing. Consequently we were able to obtain excellent separations of the sets of position isomers listed in Tables II and III, as the typical chromatograms in Fig. 1 indicate. We deliberately chose disubstituted benzenes whose m- and p-isomers were known to be difficult to separate, or were likely to be so in view of their similar boiling points; indeed the meta and para isomers of methylanisole, dibromobenzene, dimethoxybenzene, methyl toluate, and chloroacetophenone have not, as far as we know, previously been separated by gas chromatography. These results are the more striking in that p-azoxyanisole is by no means an ideal substrate for this purpose, as we pointed out above; compounds are known[2] which remain nematic over ranges of 200° or more, and these would
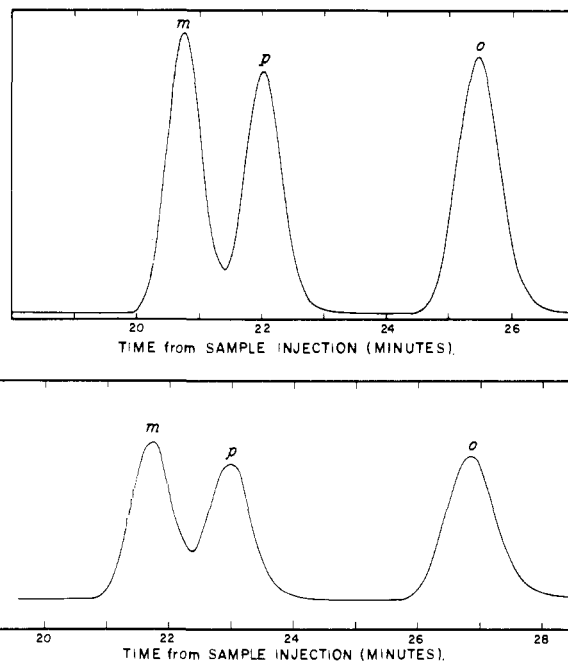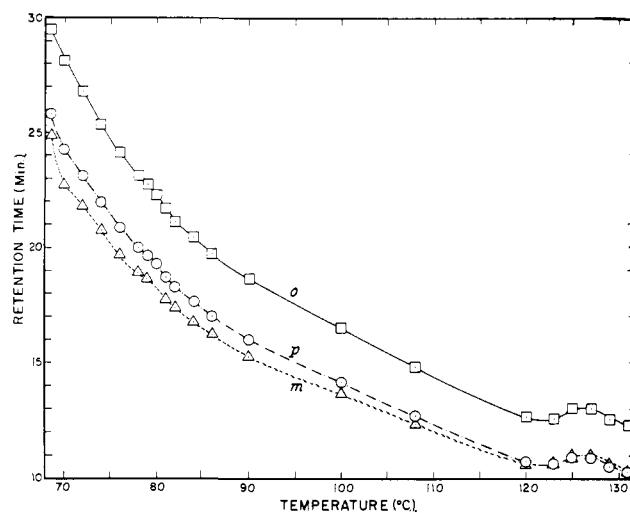
be expected to show a much greater discrimination between position isomers than Ia.

Such materials would of course have the further advantage of allowing a wider range of column temperatures; as one would expect, and as the chromatograms in Fig. 1 indicate, the separation of meta and para isomers deteriorates above the temperature (135°) of the (nematic → liquid) transition for Ia.

The retention times show an interesting variation with temperature, shown very clearly in the plots of Fig. 4 and 5. Normally retention times decrease with increasing column temperature, attributed partly to the decrease in the gas–liquid partition constant and partly to decreased viscosity of the stationary phase (which facilitates diffusion of the sample through it). However, on columns of Ia the retention times increase over a range of 2–4° in the region of the (nematic → liquid) transition (135°). It seems likely that the rise is caused by a decrease in the free energy of solution of the sample on passing from nematic to

TABLE IV

RETENTION TIMES OF BENZENE POSITION ISOMERS IN COLUMN 2 (STATIONARY LIQUID PHASE: 4,4'-DIMETHOXYAZOXYBENZENE)[a,b,c]

Column temp., °C.	$BrC_6H_4CH_3$			$CH_3OC_6H_4CH_3$		$ClC_6H_4CH_3$		ClC_6H_4Cl		BrC_6H_4Cl		BrC_6H_4Br		$CH_3OC_6H_4CH_3$	
	ortho	meta	para	meta	para	meta	para	meta	para	meta	para	meta	para	meta	para
124						13.61	14.75	20.05	23.10	37.00	42.85				
125	23.13	25.20	27.75	22.20	24.45							72.00	84.00	81.55	95.00
127						13.11	14.12	19.10	21.83	34.90	40.10				
129	21.72	23.55	25.65	21.30	23.05										83.00
130						12.77	13.67	18.38	20.86	33.60	38.25				
132	21.32	23.25	24.88	20.80	22.27	12.47	13.25	18.08	20.35	32.93	37.23				
133	21.25	23.10	24.90	20.80	22.27	12.68	13.45	18.07	20.28	33.00	37.12	64.15	72.70	70.50	78.00
134	22.20	24.05	25.40	21.50	22.60	12.90	13.58	18.39	20.42	33.10	37.20				
135	22.65	24.75	25.97	21.80	22.70										
136	23.30	24.95	26.15	22.30	23.25	13.11	13.72	18.90	20.85	34.33	37.93				
137	23.20	25.27	26.43	22.47	23.12	13.23	13.78	18.94	20.75	34.77	38.18				
138	22.88	24.78	25.83	22.05	22.85	13.30	13.72	19.07	20.83	34.70	37.90				
139	22.35	24.10	25.40	21.40	22.32	13.21	13.60	18.95	20.65	34.25	37.30	67.70	72.10	71.25	74.40
141						13.03	13.39	18.58	20.19						

[a] Column 2 is described in the Experimental section. [b] Carrier gas (N_2) flow rate was 30 ml./min. for the methylanisoles, bromotoluenes, dibromobenzenes, and dimethoxybenzenes; 35 ml./min. for the chlorotoluenes, dichlorobenzenes, and bromochlorobenzenes. [c] Injection chamber temperature was 245° for all runs.

normal liquid, owing to the disturbance of the nematic "lattice"; if so, the effect should be less for the linear para isomers, as is observed. It would be interesting to study the change in free energy of solution of various materials in Ia over the transition region, and, if possible, to determine the corresponding change in heat and entropy of solution; experiments along these lines are in progress.
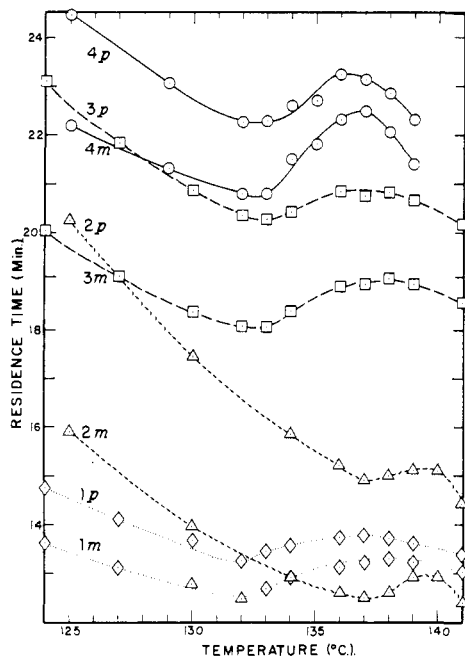
viscosity and volume[10] over the transition region. This would also agree with the views of Tolstoï[11] who regards the transition as involving a gradual loss in molecular order, some small scale order being retained above the "transition temperature." Our results would be in accord with this though in our case part at least of the effect was probably caused by inadequate temperature control.
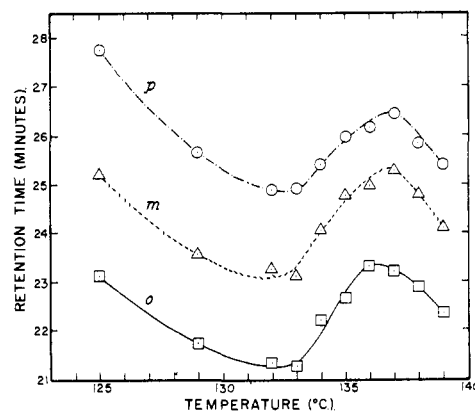

Fig. 4.—Plots of retention time vs. temperature for m- (1m) and p-chlorotoluene (1p), m- (2m) and p-chloroacetophenone (2p), m- (3m) and p-dichlorobenzene (3p), and m- (4m) and p-methylanisole (4p).

The plots of Fig. 4 and 5 raise two other points. First, the rises in the retention times take place over a range of temperature, rather than sharply; second, the maxima occur at a higher temperature than the (nematic → liquid) transition in pure Ia. Dave and Dewar[3] suggested from their study of phase diagrams that the (nematic → liquid) transition might be a second-order one, and this idea gains some support from measurements of specific heat,[9] and of changes in

Fig. 5.—Plots of retention time vs. temperature for o- (———), m- (– – – –), and p-bromotoluene (— · —).

The fact that the maxima in the plots occurred above the normal transition temperature may also not be significant; on the other hand, it might indicate that the transition temperature is raised when Ia is spread in a thin film over the chromatographic support, for surfaces have a profound orienting effect on liquid crystals.[2] Martin and Müller[9] claimed that the transition temperature of Ia, measured by specific heat change in bulk samples, was 132°, and they attribute the higher value (135°) commonly reported to orientation by the glass surface of the capillaries or microscope slides used to contain the sample in optical determinations of the transition point. On the other hand, Porter and Johnson[10] found the normal value by measurement of changes in viscosity and volume, and Dave and Dewar[3] found identical transition tempera-

(9) H. Martin and F. H. Müller, Kolloid-Z., 187, 107 (1963).
(10) R. S. Porter and J. F. Johnson, J. Appl. Phys., 34, 51 (1963).
(11) N. A. Tolstoï, J. Exptl. Theoret. Phys. (USSR), 17, 724 (1947).

tures for a variety of binary mixtures of Ia with other compounds by observation of birefringence in glass capillaries, and by cooling curve studies with larger samples (5–10 g.).

The separation of *m*- and *p*-xylene has been a classic problem in gas–liquid chromatography, being both difficult and of practical importance. The isomers cannot be separated on normal packings; partial separations have been reported using as the stationary phase benzylbiphenyl,[12a] dialkyl tetrachlorophthalates,[12b] 1-chloronaphthalene,[12c] dimethyl sulfolane,[12c] or mixtures[12c] of 1-nitronaphthalene with ethylene carbonate, while better separations (relative retention values 1.06–1.08) have been reported on benzo[*h*]quinoline,[12d,e,f] phenanthrene,[12d] or primary aromatic amines.[12g,h,i] The best separations have been obtained by using a commercially available clay, Bentone 34,[13] either alone,[14] when the relative retention value is a phenomenal 1.5 but tailing is severe; or as a support for silicone oil,[15a] squalane,[15b] polyethylene glycol,[15b] dialkyl phthalates,[15c] or Apiezon L,[15d] when the relative retention values are smaller (1.09–1.13) but sharp symmetrical peaks are obtained.

The special role of Bentone 34 can be attributed to its layer structure; the ease of adsorption of a foreign material between the layers of the expanded clay presumably depends on the geometrical shape of the adsorbed molecules, and this enables the clay to discriminate between benzene position isomers.

We were unable to separate *m*- and *p*-xylene on *p*-azoxyanisole; however, the relative retention times

(12) (a) A. Zlatkis, L. O'Brien, and P. R. Schooly, *Nature*, **181**, 1794 (1958); (b) S. H. Langer, C. Zahn, and G. Pantazoplos, *Chem. Ind.* (London), 1145 (1958); (c) A. Zlatkis, S. Y. Ling, and H. R. Kaufman, *Anal. Chem.*, **31**, 945 (1959); (d) D. H. Desty, A. Goldup, and W. T. Swanton, *Nature*, **183**, 107 (1959); (e) D. H. Desty, A. Goldup, and B. H. F. Whyman, *J. Inst. Petroleum*, **45**, 287 (1959); (f) S. M. Csicsery and H. Pines, *J. Chromatog.*, **9**, 34 (1962); (g) T. Araki and R. Goto, *Bull. Chem. Soc. Japan*, **33**, 115 (1960); (h) V. M. Nabivach, *Neftekhimiya*, **2**, 906 (1962); (i) L. C. Case, *J. Chromatog.*, **6**, 381 (1961).

(13) Bentone 34 is a montmorillonite clay in which the naturally occurring cations have been exchanged for dimethyldioctadecylammonium ions.

(14) M. A. Hughes, D. White, and A. L. Roberts, *Nature*, **184**, 1796 (1959); J. van Rysselberge and M. van der Stricht, *ibid.*, **193**, 1281 (1962).

(15) (a) J. V. Mortimer and P. L. Gent, *ibid.*, **197**, 789 (1963); (b) *J. Gas Chromatog.*, **1**, No. 5, 28 (1963); (c) *Anal. Chem.*, **36**, 754 (1964); S. F. Spencer, *ibid.*, **35**, 592 (1963); (d) M. van der Stricht and J. van Rysselberge, *J. Gas Chromatog.*, **1**, No. 8, 29 (1963).

showed an interesting variation with temperature. In the normal liquid region, the retention time for the *para* isomer was less than for the *meta* isomer, as has been observed for other liquids as stationary phases[12,15]; however, this order was reversed in the nematic region, owing presumably to selective adsorption of the linear isomer by the mesophase. It seemed likely that a complete separation could be effected if the temperature of the column could be lowered. This of course was impossible using *p*-azoxyanisole; we therefore tried the higher homologs Ib and Ic which have lower melting points (71 and 75°, respectively). These compounds also differ from Ia in melting first to smectic phases; nothing whatever seems to have been reported on binary smectic systems, but one might expect smectic liquid crystals to show even greater discrimination to solutes than do the less ordered nematic forms. Indeed, we found that excellent separations of the xylenes could be effected (Fig. 2) by operating at 75° or lower, *i.e.*, in the smectic region.

Figure 3 shows a plot of relative retention times *vs.* temperature for the three xylenes on a column of Ib; note the decrease in retention time at the (smectic → nematic) transition temperature (80°). This is unexpected, for the decrease in order in passing from a smectic to a nematic phase should lead to an increase in solubility and so in retention time.

A possible explanation of this seems to be that smectic stationary phases may not, like normal liquids, operate under equilibrium conditions. The viscosity of a smectic liquid crystal is extremely anisotropic, being very great for shear across the planes of two-dimensional liquid.[2] This is a consequence of the layer structure, the mechanical properties of a smectic phase being similar to those of graphite. It therefore seems possible that diffusion through a smectic stationary phase may be slow enough to affect the residence time. In this case two factors could operate in the transition from smectic to nematic; the decrease in order would lead to an increase in retention time, while the viscosity effect should lead to a decrease. The observed result, a small decrease in retention time, could then be explained as a sum of these opposing effects, the latter predominating.