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# Quantitative structure–retention relationships (QSRR) of congeneric aromatics series studied on phenyl OV phases in gas chromatography

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**Abstract**

Quantitative structure–retention relationships (QSRR) were established for three congeneric aromatic series of substituted benzene, benzaldehyde and acetophenone compounds which had been studied, previously, in gas chromatography, on six OV stationary phases with different phenyl percentages. Correspondence factor analysis (CFA) establishes the influences of temperature and phenyl percentage of the stationary phases on the retention indices. Topological analysis quantifies the contributions of molecular structure and phenyl content of the stationary phase on the chromatographic retention. The validity of the global linear model used in topological analysis is confirmed by CFA of the different set of topological parameters calculated for the retention of the compounds on the six OV stationary phases.

## 1. Introduction

The quantitative structure–retention relationship (QSRR) [1] is a powerful concept in chromatography. Owing to the potentially infinite number of chromatographic systems and solutes, rationalization of the study of the chromatographic behaviour of solutes becomes a necessity. QSRR is particularly useful to chromatographers in order to prepare experimental designs [2], to optimize the separation of complex mixtures or to elucidate retention mechanisms. The quality and the precision of the experimental data constitute an important and general problem which arises in QSRR. In gas chromatography, the Kováts indices (K.I.) fulfil this requirement. They are a valuable source of information for the chemometrician to develop and test new procedures of data processing. The K.I. data can be much more precise than many sources of physico-chemical data, and especially more precise than biological data, mainly when they result from in vivo tests. A factor of 100 in precision is not unusual.

The QSRR strategy is useful for the chromatographer, but also for the chemometrician, to transfer knowledge to other areas, such as in drug design, where the conventional acronym QSAR is used [3], the word retention (R) being replaced by activity (A). Previously, topological

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analysis (TA) [4,5] and factor analysis [6–8] chiefly used retention data for their first applications in chemistry. Now, retention data are also used to test the new neural networks [9,10] procedures and software, even if drug design is the long-term target.

The problem with which one is faced in QSRR is to exploit the complexity and the richness of the information content of raw chromatographic data. QSRR aims at obtaining the simplest models to explain and quantify the chromatographic behaviour of the solutes and/or the role of the chromatographic systems. With a large data set, generally in the form of a data matrix, different chemometric procedures are now used. These procedures could be divided into two groups according to the target.

The first group of procedures includes the "analysis of relative distances", such as hierarchical ascending classification (HAC), factor analysis with principal component analysis (PCA) or correspondence factor analysis (CFA). They are based on strictly different mathematical procedures for the analysis of the relative distances between the solutes or between the chromatographic systems. Nevertheless, their practical interest is to provide an analysis of trends. They help to reveal nested factors in the raw data matrix and to specify the chromatographic mechanism.

The second group of procedures are chiefly concerned with "explicative procedures". Most often these procedures are based on multilinear relationships (MLR). They aim at explaining the chromatographic behaviour or some of the above-revealed nested factors by using chemical descriptors. These descriptors may be some physico-chemical or electronic properties (boiling point, partition coefficient, Hammett–Taft electronic parameter, etc.), topological indices (Kier [11], Wiener [12], etc.) or the DARC [13] topological descriptors which have the advantage of a non-previous degenerescency of the structural information content.

Currently in QSRR, the most important problems are to develop new methods, to push the limits of applicability of the known methods and to exploit their complementarity. Factor analysis is often used for clustering to study heterogeneous series of compounds, and fine and deeper information can be revealed when homogeneous series of compounds are used. Then, more subtle structural, steric or electronic effects can be detected. In this direction, a useful approach has been found by progressively increasing the degree of homogeneity of the solutes: various hydrocarbons [8] or esters [14]. Nevertheless, for these cases a large variety of stationary phases were used. They could induce large variations of the type and strength of physico-chemical interactions between solutes and the stationary phase. More recently, an analysis of trends with the help of CFA was presented for a homogeneous series of aromatic compounds studied on a homogeneous series of OV methylphenylsilicones at different temperatures [15]. However, a fundamental question remains dealing with QSRR: what are the limits of the homogeneity of the chromatographic data set to apply the above first and second groups of procedures?

This paper aims at exploring the sensitivity and limits of two complementary statistical procedures, CFA and TA, in the case of a high degree of homogeneity of the solute and stationary phase series. Instead of the previous aromatic solute series, three congeneric series have been considered independently, namely monosubstituted benzenes, disubstituted benzaldehydes and acetophenones. They were studied at one temperature (120°C), in gas chromatography, on a homogeneous series of OV methylphenylsilicone stationary phases with a phenyl content varying in the range 0–75%. In the first step, CFA will be used to delineate the observed structural effects. In the second step, quantification of the structural effects with TA will be performed. The possibilities and limits of such approaches will be discussed.

## 2. Data processing

### 2.1. Correspondence factor analysis (CFA)

Among the various methods of factor analysis, the CFA method, developed by Benzécri [16], is

most suitable for the analysis of fine structural effects in congeneric series of compounds. As described elsewhere [8], in CFA first the row and column margin values are calculated from the experimental data matrix. Then the combination of the margin values divided by the sum of the experimental data matrix gives rise to the independence matrix. The difference between the experimental data matrix and the independence matrix leads to the residual matrix. Then eigenvalues and eigenvectors are derived from the latter matrix. The abscissas of row and column designees, the column points after their projection in a two-dimensional space, i.e., of compounds and chromatographic systems, are recalculated in this reduced hyperspace and simultaneous projections are drawn [19].

### 2.2. Topological analysis

In accordance with the DARC (description, acquisition, retrieval and computer-aided design) [13] topological system and the DARC/PELCO (perturbation of an environment which is limited, concentric and ordered) [4] procedure, the environment of each compound is described starting from an origin taken as the focus. Each substituent is localized in an environment which is limited, concentric and ordered (ELCO). The influence of each substituent on the retention index is calculated in the form of a perturbation term corresponding to the formal replacement of an hydrogen atom by this substituent. The evaluation of the perturbation term is done on statistical bases and is an average one, taking into account all the compounds in which it is found. For the three congeneric sub-series studied the phenyl group is taken as the focus; only the first concentric environment, with two layers of heavy atoms or of sub-groups, is necessary to regroup and to organize all the compounds in a large congeneric series.

## 3. Data

### 3.1. Correspondence factor analysis

The 43 compounds considered, presented in Table 1, include monosubstituted benzenes (B series), *o*-, *m*-, *p*-substituted benzaldehydes (A series) and acetophenones (C series). These compounds were studied on seven OV methylphenylsilicone phases. The monosubstituted phenyl compounds (B) were studied in the range 80–140°C and the disubstituted phenyl compounds (A and C) in the range 120–160°C [17].

Three different data matrices of the Kováts indices will be studied corresponding to the three congeneric series (Table 2). The experimental design is shown in Tables 2–7.

Table 1
Presentation of the compounds studied

| *Substituents* | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| X | H | F | $CH_3$ | Cl | $OCH_3$ | Br | OH | $OC_2H_5$ | $NO_2$ |
| Label | H | F | M | Cl | OM | Br | OH | OE | N |
| *Compounds*[a] | | | | | | | | | |
| B | BH | BF | BM | BCl | BOM | BBr | BOH | BOE | BNO2 |
| A | AH | AoF | AoM | AoCl | AoOM | AoBr | AoOH[b] | AoOE[b] | AoN[b] |
| | | AmF | AmM | AmCl | AmOM | AmBr | AmOH[b] | | AmN[b] |
| | | ApF | ApM | ApCl | ApOM | ApBr[b] | ApOH[b] | | ApN[b] |
| C | CH | CoF | CoM | CoCl | | | CoOH | | |
| | | | CmM | | | | | | |
| | | CpF | CpM | CpCl | CpOM | CpBr | | | |

[a] $B = XC_6H_5$; $A = XC_6H_4CHO$; $C = XC_6H_4COCH_3$.
[b] These compounds were not included in the topological analysis.

Table 2
Experimental design: three data matrices, B, A and C, studied with CFA[a]

| T (°C) | OV-101 | OV-3 | OV-7 | OV-11 | OV-17 | OV-22 | OV-25 |
|---|---|---|---|---|---|---|---|
| 80 | B | | | | | | |
| 90 | B | | | | | | |
| 100 | B | | B | B | | B | B |
| 110 | B | | | | | | |
| 120 | B C | B C | B C | B C | B C | C | B C |
| 130 | C | C | C | B C | C | C | B C |
| 140 | A C | C | A C | B A C | A C | A C | B |
| 160 | A C | C | A C | A C | A C | A C | A |

[a] B = benzene series; A = benzaldehyde series; C = acetophenone series.

### 3.2. Topological analysis

The selected set of standard data correspond to the stationary phases OV-101, OV-3, OV-7, OV-11, OV-17 and OV-25 and to a temperature of 120°C. The weighted perturbation term of the stationary phase is taken into account as a disjoint ELCO which defines a second concentric environment limited to the phenyl content of the stationary phase. The evaluation of the interactions between the molecular phenyl group of the three series and the stationary phase are modelled by the contribution of the focus to the considered series. The organization of the molecular and stationary phase environments by the ELCO concept gives rise to the 27 topological sites plus the focus shown in Fig. 4. The 28 perturbation terms are calculated from the experimental data matrix corresponding to the 35 compounds studied on the six stationary phases (Tables 1 and 3).

## 4. Results and discussion

### 4.1. Correspondence factor analysis

The CFA of the first data matrix corresponding to the monosubstituted benzenes series gives rise to the first factorial plane presented in Fig. 1. This plane includes 86% of the information content, 54% according to the first axis and 32% according to the second axis. The first axis is determined principally by methylbenzene and benzaldehyde, for the compounds, and by the non-polar OV-101 stationary phase, used at five different temperatures, and by the polar OV-25 phase at 100 and 120°C working temperatures.

Compounds with strong electron-acceptor substituents are projected on the right side of the factorial plane and compounds with electron-donor or weak acceptor substituents are projected on the left side.

Table 3
Experimental design: data studied with topological information[a]

| T (°C) | OV-101 (0% Ph) | OV-3 (10% Ph) | OV-7 (20% Ph) | OV-11 (35% Ph) | OV-17 (50% Ph) | OV-22 (60% Ph) | OV-25 (75% Ph) |
|---|---|---|---|---|---|---|---|
| 110 | | | | | | | |
| 120 | B A C | B A C | B A C | B A C | B A C | | B A C |
| 130 | | | | | | | |
| 140 | | | | | | | |
| 160 | | | | | | | |

[a] B = benzene series; A = benzaldehyde series; C = acetophenone series.

Table 4
Experimental design: Kováts indices determined at various temperatures for the benzene series

| Compound | OV-101 | | | | | OV-3 | OV-7 | |
|---|---|---|---|---|---|---|---|---|
| | 80°C | 90°C | 100°C | 110°C | 120°C | 120°C | 100°C | 120°C |
| BH | 654.70 | 660.20 | 663.20 | 667.40 | 669.90 | 689.80 | 696.40 | 711.40 |
| BF | 663.20 | 668.00 | 671.50 | 672.60 | 673.90 | 697.90 | 717.40 | 720.90 |
| BM | 761.80 | 763.00 | 765.50 | 768.40 | 771.60 | 792.80 | 811.80 | 815.70 |
| BCl | 836.00 | 838.80 | 842.00 | 850.00 | 850.30 | 886.60 | 900.30 | 908.10 |
| BOM | 898.10 | 901.00 | 903.80 | 908.80 | 910.10 | 945.40 | 972.90 | 979.70 |
| BBr | 914.70 | 923.70 | 924.00 | 932.00 | 934.80 | 973.70 | 990.60 | 1001.80 |
| AH | 924.90 | 926.60 | 930.50 | 948.90 | 950.70 | 1005.50 | 1035.10 | 1043.50 |
| BOH | 944.70 | 945.20 | 950.20 | 950.70 | 952.50 | 1014.40 | 1026.30 | 1029.00 |
| BOE | 971.60 | 973.30 | 976.30 | 981.30 | 980.50 | 1032.50 | 1042.80 | 1046.80 |
| CH | 1028.30 | 1030.50 | 1033.40 | 1040.20 | 1043.10 | 1109.10 | 1138.00 | 1152.20 |
| BNO2 | 1049.20 | 1057.40 | 1058.30 | 1066.70 | 1068.50 | 1133.30 | 1165.20 | 1177.00 |

| | OV-11 | | | | OV-17 | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 100°C | 120°C | 130°C | 140°C | 80°C | 90°C | 100°C | 110°C | 120°C |
| BH | 723.30 | 737.80 | 748.80 | 759.70 | 752.00 | 753.40 | 755.40 | 760.20 | 763.80 |
| BF | 724.10 | 740.50 | 753.00 | 776.30 | 760.30 | 763.40 | 763.50 | 766.10 | 780.10 |
| BM | 843.10 | 845.40 | 846.60 | 863.00 | 855.10 | 857.90 | 860.00 | 862.90 | 872.00 |
| BCl | 930.80 | 941.10 | 947.20 | 954.40 | 953.10 | 956.20 | 960.40 | 963.90 | 987.20 |
| BOM | 1012.60 | 1019.90 | 1022.30 | 1026.80 | 1042.20 | 1043.90 | 1046.70 | 1049.20 | 1074.80 |
| BBr | 1028.60 | 1039.90 | 1046.60 | 1052.70 | 1050.90 | 1055.20 | 1060.90 | 1067.30 | 1080.70 |
| AH | 1085.90 | 1094.10 | 1097.20 | 1101.30 | 1118.20 | 1120.30 | 1125.30 | 1130.20 | 1134.30 |
| BOH | 1071.50 | 1076.40 | 1077.80 | 1080.50 | 1108.00 | 1110.00 | 1112.70 | 1115.30 | 1127.00 |
| BOE | 1080.60 | 1085.90 | 1088.10 | 1090.70 | 1109.80 | 1110.30 | 1113.10 | 1115.80 | 1144.10 |
| CH | 1190.70 | 1199.70 | 1204.20 | 1234.90 | 1138.00 | 1140.90 | 1144.60 | 1150.10 | 1234.60 |
| BNO2 | 1217.20 | 1231.00 | 1237.80 | 1242.40 | 1239.20 | 1256.50 | 1263.90 | 1271.10 | 1291.40 |

| | OV-25 | | | | OV-22 |
|---|---|---|---|---|---|
| | 100°C | 120°C | 130°C | 140°C | 100°C |
| BH | 807.40 | 812.00 | 832.70 | 867.10 | 784.20 |
| BF | 809.40 | 817.20 | 878.00 | 893.90 | 785.40 |
| BM | 908.50 | 916.30 | 931.20 | 935.90 | 892.80 |
| BCl | 1018.50 | 1026.20 | 1028.80 | 1046.20 | 995.30 |
| BOM | 1115.50 | 1122.60 | 1124.00 | 1157.60 | 1087.20 |
| BBr | 1129.00 | 1138.10 | 1146.20 | 1190.80 | 1100.50 |
| AH | 1197.30 | 1206.80 | 1214.80 | 1234.30 | 1168.40 |
| BOH | 1178.30 | 1189.70 | 1204.30 | 1211.10 | 1148.40 |
| BOE | 1192.60 | 1199.70 | 1207.70 | 1216.80 | 1151.00 |
| CH | 1312.60 | 1325.60 | 1328.20 | 1347.50 | 1269.70 |
| BNO2 | 1341.20 | 1351.20 | 1363.10 | 1475.70 | 1308.30 |

The temperature effects relative to the non-polar OV-101 stationary phase are projected into the same cluster, on the left side of Fig. 1 (0108 up to 0112). This indicates regular variations of the behaviour of the compounds, governed principally here by the partition coefficient,

Table 5
Experimental design: Kováts indices determined at various temperatures for the benzaldehyde series

| Compound | OV-101 | | OV-7 | | OV-11 | |
|---|---|---|---|---|---|---|
| | 140°C | 160°C | 140°C | 160°C | 140°C | 160°C |
| AH | 953.40 | 964.40 | 1050.60 | 1081.90 | 1101.30 | 1113.90 |
| ApM | 1073.90 | 1083.60 | 1169.70 | 1199.70 | 1230.30 | 1234.40 |
| AmM | 1060.60 | 1070.40 | 1156.50 | 1185.90 | 1214.60 | 1218.00 |
| AoM | 1065.60 | 1070.90 | 1159.20 | 1190.10 | 1216.30 | 1221.70 |
| ApOM | 1230.60 | 1239.60 | 1352.60 | 1381.50 | 1427.10 | 1430.00 |
| AmOM | 1178.60 | 1187.80 | 1293.60 | 1321.90 | 1361.80 | 1364.20 |
| AoOM | 1222.50 | 1227.90 | 1345.10 | 1367.80 | 1404.00 | 1408.80 |
| ApOE | 1301.40 | 1310.60 | 1447.90 | 1451.70 | 1459.40 | 1489.00 |
| AoOE | 1283.00 | 1286.40 | 1398.00 | 1418.40 | 1451.60 | 1457.30 |
| ApCl | 1116.00 | 1122.60 | 1223.00 | 1252.80 | 1288.70 | 1292.00 |
| AmCl | 1108.40 | 1118.90 | 1217.40 | 1246.40 | 1280.40 | 1283.00 |
| AoCl | 1112.70 | 1122.40 | 1215.20 | 1244.40 | 1273.30 | 1277.20 |
| ApF | 942.50 | 948.30 | 1038.60 | 1069.90 | 1094.50 | 1102.30 |
| AmF | 937.60 | 939.10 | 1035.70 | 1057.20 | 1080.10 | 1086.20 |
| AoF | 941.50 | 947.30 | 1025.70 | 1061.10 | 1079.40 | 1085.40 |
| ApBr | 1207.10 | 1216.50 | 1319.30 | 1349.30 | 1391.40 | 1392.80 |
| AmBr | 1193.50 | 1207.80 | 1314.30 | 1344.20 | 1384.40 | 1384.80 |
| AoBr | 1204.70 | 1211.60 | 1311.90 | 1340.40 | 1375.10 | 1377.50 |
| ApOH | 1318.60 | 1320.80 | 1457.50 | 1458.90 | 1529.80 | 1531.80 |
| AmOH | 1262.40 | 1267.00 | 1396.50 | 1401.40 | 1437.40 | 1468.00 |
| AoOH | 1041.40 | 1047.60 | 1135.40 | 1167.70 | 1193.70 | 1199.10 |
| ApN | 1291.80 | 1302.20 | 1469.10 | 1481.90 | 1509.50 | 1541.50 |
| AmN | 1304.20 | 1314.50 | 1474.80 | 1482.90 | 1524.00 | 1556.30 |
| AoN | 1271.00 | 1277.00 | 1428.50 | 1446.80 | 1492.00 | 1496.20 |

| | OV-17 | | OV-22 | | OV-25 |
|---|---|---|---|---|---|
| | 140°C | 160°C | 140°C | 160°C | 160°C |
| AH | 1144.90 | 1152.70 | 1187.10 | 1203.10 | 1249.30 |
| ApM | 1265.90 | 1274.80 | 1307.20 | 1320.40 | 1367.80 |
| AmM | 1249.40 | 1252.10 | 1289.90 | 1300.30 | 1348.90 |
| AoM | 1252.30 | 1257.60 | 1296.00 | 1311.00 | 1361.40 |
| ApOM | 1475.60 | 1485.20 | 1527.00 | 1537.00 | 1597.70 |
| AmOM | 1405.60 | 1411.70 | 1454.40 | 1462.00 | 1521.90 |
| AoOM | 1448.90 | 1456.50 | 1502.10 | 1509.80 | 1576.10 |
| ApOE | 1537.20 | 1543.60 | 1587.10 | 1596.80 | 1652.00 |
| AoOE | 1495.00 | 1502.00 | 1543.00 | 1569.60 | 1606.10 |
| ApCl | 1327.00 | 1336.80 | 1370.30 | 1383.00 | 1433.50 |
| AmCl | 1317.60 | 1323.30 | 1360.00 | 1370.10 | 1423.20 |
| AoCl | 1309.00 | 1317.80 | 1351.10 | 1366.40 | 1417.30 |
| ApF | 1125.90 | 1135.50 | 1167.00 | 1183.10 | 1219.00 |
| AmF | 1111.10 | 1107.70 | 1152.30 | 1160.30 | 1200.10 |
| AoF | 1110.60 | 1109.40 | 1146.00 | 1167.90 | 1201.50 |
| ApBr | 1433.70 | 1446.60 | 1481.60 | 1494.00 | 1570.70 |
| AmBr | 1425.40 | 1436.00 | 1471.80 | 1483.70 | 1552.60 |
| AoBr | 1414.50 | 1428.00 | 1465.80 | 1479.10 | 1544.00 |
| ApOH | 1590.50 | 1596.20 | 1651.00 | 1658.90 | 1729.50 |
| AmOH | 1521.50 | 1528.90 | 1581.20 | 1582.80 | 1662.30 |
| AoOH | 1229.00 | 1234.70 | 1273.10 | 1289.90 | 1338.40 |
| ApN | 1598.60 | 1609.00 | 1657.10 | 1662.10 | 1721.90 |
| AmN | 1610.50 | 1621.70 | 1672.10 | 1671.70 | 1734.40 |
| AoN | 1548.40 | 1560.20 | 1610.40 | 1611.10 | 1674.20 |

Table 6
Experimental design: Kováts indices determined at various temperatures for the acetophenone series

| Compound | OV-101 | | | | OV-3 | | | |
|---|---|---|---|---|---|---|---|---|
| | 120°C | 130°C | 140°C | 160°C | 120°C | 130°C | 140°C | 160°C |
| CH | 1043.10 | 1044.70 | 1058.50 | 1066.10 | 1109.10 | 1112.40 | 1115.40 | 1117.40 |
| CpM | 1162.70 | 1163.60 | 1178.20 | 1181.70 | 1226.40 | 1228.20 | 1231.90 | 1235.30 |
| CmM | 1148.30 | 1149.50 | 1161.70 | 1168.90 | 1213.30 | 1215.00 | 1218.20 | 1221.50 |
| CoM | 1112.40 | 1113.10 | 1124.70 | 1133.70 | 1174.60 | 1177.70 | 1181.20 | 1184.10 |
| CpOM | 1310.90 | 1314.30 | 1325.80 | 1333.40 | 1392.40 | 1394.00 | 1398.30 | 1402.20 |
| CpCl | 1204.40 | 1204.50 | 1220.10 | 1226.30 | 1276.50 | 1278.70 | 1282.90 | 1285.50 |
| CoCl | 1167.30 | 1170.60 | 1183.50 | 1193.80 | 1236.60 | 1240.70 | 1245.40 | 1251.10 |
| CpF | 1029.00 | 1029.70 | 1040.70 | 1047.60 | 1098.60 | 1099.80 | 1102.00 | 1105.50 |
| CoF | 1005.00 | 1006.40 | 1019.60 | 1026.40 | 1065.70 | 1068.40 | 1071.60 | 1073.40 |
| CoOH | 1135.60 | 1139.10 | 1152.50 | 1162.70 | 1204.40 | 1208.50 | 1212.80 | 1218.80 |
| CpBr | 1286.30 | 1296.70 | 1308.00 | 1315.10 | 1365.90 | 1369.00 | 1374.50 | 1381.60 |
| | OV-7 | | | | OV-11 | | | |
| | 120°C | 130°C | 140°C | 160°C | 120°C | 130°C | 140°C | 160°C |
| CH | 1152.20 | 1153.90 | 1155.40 | 1162.50 | 1199.70 | 1204.20 | 1234.90 | 1216.30 |
| CpM | 1265.60 | 1266.80 | 1271.80 | 1278.60 | 1313.20 | 1319.60 | 1325.90 | 1335.00 |
| CmM | 1251.90 | 1252.90 | 1258.20 | 1265.40 | 1285.70 | 1305.60 | 1311.80 | 1318.50 |
| CoM | 1213.40 | 1215.10 | 1219.50 | 1226.40 | 1254.30 | 1264.20 | 1269.80 | 1278.20 |
| CpOM | 1442.50 | 1443.20 | 1448.40 | 1456.60 | 1502.90 | 1510.40 | 1516.00 | 1526.50 |
| CpCl | 1321.10 | 1321.40 | 1327.90 | 1335.60 | 1371.40 | 1377.70 | 1384.90 | 1395.60 |
| CoCl | 1281.40 | 1281.80 | 1288.50 | 1299.00 | 1322.80 | 1336.80 | 1343.60 | 1355.20 |
| CpF | 1135.60 | 1139.30 | 1141.10 | 1143.80 | 1182.90 | 1186.90 | 1191.50 | 1198.20 |
| CoF | 1100.90 | 1103.10 | 1106.40 | 1113.00 | 1142.70 | 1146.50 | 1151.80 | 1159.80 |
| CoOH | 1247.90 | 1248.30 | 1254.80 | 1265.10 | 1301.20 | 1308.20 | 1311.40 | 1319.40 |
| CpBr | 1413.70 | 1414.70 | 1422.10 | 1433.30 | 1468.70 | 1477.40 | 1485.00 | 1498.80 |
| | OV-17 | | | | OV-22 | | | |
| | 120°C | 130°C | 140°C | 160°C | 120°C | 130°C | 140°C | 160°C |
| CH | 1234.60 | 1252.90 | 1255.60 | 1264.70 | 1289.70 | 1294.70 | 1295.80 | 1336.60 |
| CpM | 1349.40 | 1366.40 | 1370.00 | 1382.40 | 1403.20 | 1407.30 | 1409.70 | 1441.10 |
| CmM | 1336.10 | 1353.50 | 1357.00 | 1369.70 | 1390.20 | 1395.30 | 1396.60 | 1439.80 |
| CoM | 1294.60 | 1311.30 | 1314.50 | 1329.00 | 1349.00 | 1353.20 | 1354.80 | 1397.00 |
| CpOM | 1551.80 | 1569.30 | 1573.90 | 1587.60 | 1616.00 | 1621.40 | 1622.30 | 1652.90 |
| CpCl | 1408.70 | 1426.60 | 1431.40 | 1445.20 | 1463.90 | 1469.60 | 1470.90 | 1497.90 |
| CoCl | 1370.20 | 1388.40 | 1393.10 | 1411.00 | 1428.50 | 1435.70 | 1436.10 | 1480.50 |
| CpF | 1214.70 | 1230.60 | 1231.30 | 1239.60 | 1263.40 | 1268.40 | 1278.50 | 1298.90 |
| CoF | 1172.80 | 1190.10 | 1192.50 | 1205.50 | 1220.50 | 1225.90 | 1233.60 | 1272.50 |
| CoOH | 1332.30 | 1350.40 | 1355.00 | 1372.40 | 1387.70 | 1394.90 | 1395.20 | 1440.60 |
| CpBr | 1512.00 | 1530.70 | 1536.90 | 1554.60 | 1571.50 | 1579.60 | 1594.20 | 1616.10 |
| | OV-25 | | | | | | | |
| | 120°C | 130°C | | | | | | |
| CH | 1325.60 | 1328.20 | | | | | | |
| CpM | 1439.20 | 1446.80 | | | | | | |
| CmM | 1425.80 | 1432.40 | | | | | | |
| CoM | 1392.50 | 1393.40 | | | | | | |
| CpOM | 1663.60 | 1669.80 | | | | | | |
| CpCl | 1500.60 | 1509.20 | | | | | | |
| CoCl | 1476.00 | 1478.40 | | | | | | |
| CpF | 1293.60 | 1300.00 | | | | | | |
| CoF | 1258.00 | 1258.20 | | | | | | |
| CoOH | 1432.20 | 1434.50 | | | | | | |
| CpBr | 1613.40 | 1622.30 | | | | | | |

Table 7
Experimental design: regrouped data of topological analysis at 120°C

| Compound | Acetophenone series | | | | | |
|---|---|---|---|---|---|---|
| | OV-101 | OV-3 | OV-7 | OV-11 | OV-17 | OV-25 |
| CH | 1043.10 | 1109.10 | 1152.20 | 1199.70 | 1234.60 | 1325.60 |
| CpM | 1162.70 | 1226.40 | 1265.60 | 1313.20 | 1349.40 | 1439.20 |
| CmM | 1148.30 | 1213.30 | 1251.90 | 1285.70 | 1336.10 | 1425.80 |
| CoM | 1112.40 | 1174.60 | 1213.40 | 1254.30 | 1294.60 | 1392.50 |
| CpOM | 1310.90 | 1392.40 | 1442.50 | 1502.90 | 1551.80 | 1663.60 |
| CpCl | 1204.40 | 1276.50 | 1321.10 | 1371.40 | 1408.70 | 1500.60 |
| CoCl | 1167.30 | 1236.60 | 1281.40 | 1322.80 | 1370.20 | 1476.00 |
| CpF | 1029.00 | 1098.60 | 1135.60 | 1182.90 | 1214.70 | 1293.60 |
| CoF | 1005.00 | 1065.70 | 1100.90 | 1142.70 | 1172.80 | 1258.00 |
| CoOH | 1135.60 | 1204.40 | 1247.90 | 1301.20 | 1332.30 | 1432.20 |
| CpBr | 1286.30 | 1365.90 | 1413.70 | 1468.70 | 1512.00 | 1613.40 |
| | Benzaldehyde series | | | | | |
| | OV-101 | OV-3 | OV-7 | OV-11 | OV-17 | OV-25 |
| AH | 950.70 | 1005.50 | 1043.50 | 1094.10 | 1134.30 | 1206.80 |
| ApM | 1067.30 | 1124.70 | 1165.90 | 1195.20 | 1254.10 | 1325.30 |
| AmM | 1055.60 | 1110.90 | 1148.30 | 1188.00 | 1228.20 | 1308.10 |
| AoM | 1056.00 | 1111.70 | 1151.70 | 1188.10 | 1230.80 | 1313.40 |
| ApOM | 1224.10 | 1296.80 | 1348.60 | 1391.00 | 1463.00 | 1556.50 |
| AmOM | 1172.90 | 1236.90 | 1289.30 | 1335.00 | 1385.10 | 1480.20 |
| AoOM | 1212.90 | 1278.50 | 1329.60 | 1377.00 | 1428.80 | 1509.10 |
| ApCl | 1107.40 | 1171.90 | 1218.70 | 1251.70 | 1314.20 | 1389.80 |
| AmCl | 1102,30 | 1162.50 | 1212.20 | 1251.20 | 1295.50 | 1379.40 |
| AoCl | 1104.90 | 1159.50 | 1201.10 | 1239.50 | 1285.30 | 1369.50 |
| ApF | 935.50 | 991.70 | 1035.00 | 1069.00 | 1120.20 | 1182.50 |
| AmF | 926.80 | 980.80 | 1021.20 | 1060.10 | 1091.90 | 1161.70 |
| AoF | 931.30 | 983.20 | 1019.40 | 1056.10 | 1089.90 | 1160.60 |
| AmBr | 1186.30 | 1248.90 | 1307.80 | 1348.10 | 1400.80 | 1493.90 |
| AoBr | 1186.60 | 1240.30 | 1294.20 | 1335.00 | 1388.30 | 1484.30 |
| | Benzene series | | | | | |
| | OV-101 | OV-3 | OV-7 | OV-11 | OV-17 | OV-25 |
| BH | 669.90 | 689.80 | 711.40 | 737.80 | 763.80 | 812.00 |
| BF | 673.90 | 697.90 | 720.90 | 740.50 | 780.10 | 817.20 |
| BM | 771.60 | 792.80 | 815.70 | 845.40 | 872.00 | 916.30 |
| BCl | 850.30 | 886.60 | 908.10 | 941.10 | 987.20 | 1026.20 |
| BOM | 910.10 | 945.40 | 979.70 | 1019.90 | 1074.80 | 1122.60 |
| BBr | 934.80 | 973.70 | 1001.80 | 1039.90 | 1080.70 | 1138.10 |
| BOH | 952.50 | 1014.40 | 1029.00 | 1076.40 | 1127.00 | 1189.70 |
| BOE | 980.50 | 1032.00 | 1046.80 | 1085.90 | 1144.10 | 1199.70 |
| BNO2 | 1068.50 | 1133.30 | 1177.00 | 1231.00 | 1291.40 | 1351.20 |

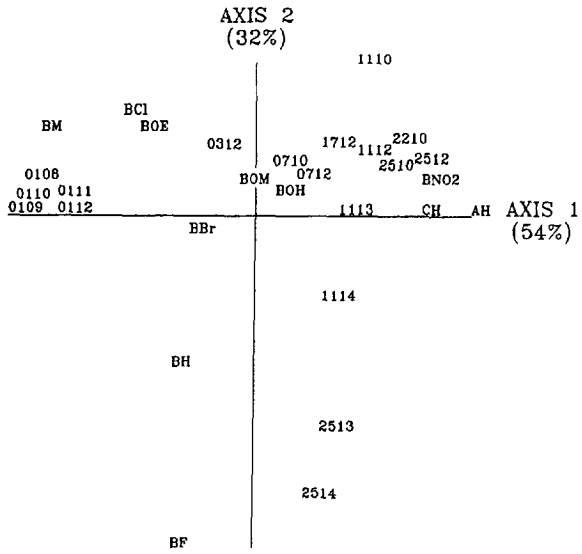


Fig. 1. Correspondence factor analysis of the monosubstituted benzene series. The first factorial plane includes 86% of the information content. The compounds with electron-donor groups are located on the left side and compounds with electron-acceptor groups on the right side. The chromatographic system designee is composed of four characters. The first two characters indicate the stationary phase and correspond to the value *n* taken from the name OV-*n*, i.e., 01, 03, 07, 11, 17, 22, 25 for OV-101, OV-3, . . . , up to OV-25, respectively. The two last characters indicate the temperature and correspond to the number of 10°C steps; i.e., 08, 09, 10, 11, 12, 13, 14 and 16 for 80, 90, 100, . . . , up to 160°C, respectively.

despite the temperature effects which remain proportional between each other. From the mathematical point of view this indicates a proportionality between the corresponding column of the data matrix. For the more polar OV-11 great variations of the temperature effects are observed according to axis 2. In a similar manner, the influence of the temperature is not proportional for OV-25; 2510 and 2512, which are close together, are far from 2513 and 2514. The projections of the polar phases show that the physico-chemical interactions are evolving regularly with temperature for the polar phases, but in a non-proportional way. The special behaviour of fluorobenzene (BF) must be emphasized. This point will be discussed later with the topological analysis.

In this first factorial plane, the first axis is related to the polarity of the compounds and the stationary phases. The non-polar OV-101, with 0% phenyl groups, and the slightly more polar OV-3, with 10% phenyl groups, have McReynold's indices of 227 and 423, respectively. They are located on the left side of the factorial plane. The other phases with a higher phenyl content, from 20% up to 75%, are located on the right side of the factorial plane. Their polarity ranges from 592 to 1175 on the McReynolds scale. At a constant temperature, e.g., 120°C, the representative points of the stationary phases are scattered according to axis 1.

In the monosubstituted benzene series, no correlation between the abcissa ordinates and the Hammett–Taft $\sigma$ electronic parameters are observed. Only trends are observed for a rough classification of the compounds on this first axis, according to their polarity, from the non-polar benzene up to the more polar nitrobenzene, aceto-
phenone and benzaldehyde.

The CFA of the benzaldehyde series is presented in Fig. 2. This factorial plane includes 86% of the information content, 76% for axis 1 and 10% for axis 2. The most deactivated compounds, such as the three positional isomers *o*-, *m*- and *p*-nitrobenzaldehyde (AoN, AmP and ApN), are on the left part of the diagram. The less polar compounds with donor or weakly acceptor substituents are on the right side. Once again, the first axis is related to increasing polarity, here from the right towards the left. The inversion of the direction of this first axis, related to the corresponding increase in the polarity of the chromatographic systems involved, is just a mathematical artefact which must not be related to any physico-chemical meaning.

For the three positional isomers of the disubstituted compounds, a clear separation of the *ortho* isomers is observed. These *ortho* isomers are located on the right side of their analogues despite their relatively higher dipolar moments, as is observed more particularly for the halo, hydroxy and nitro derivatives. This suggests that

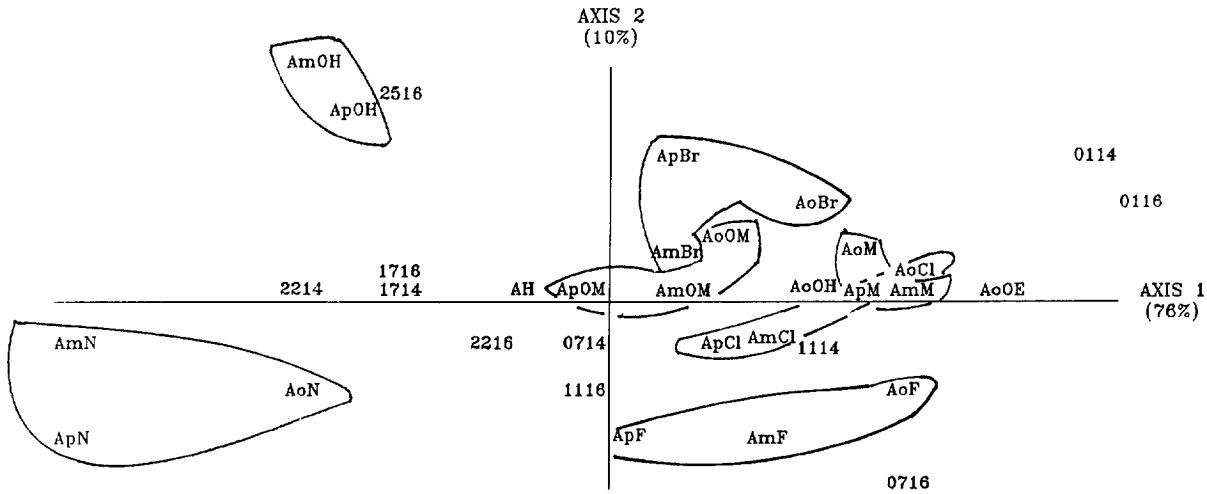


Fig. 2. Correspondence factor analysis of the benzaldehyde series. The first factorial plane includes 86% of the information content. The greater part of this information content, i.e., 76%, is taken into account by axis 1, which indicates the average variation of polarity of the stationary phases and compounds.

the *ortho* substituent partially hides the polarity of the compounds owing to the aldehyde group.

The acetophenone series corresponds to a set of eleven compounds studied under 26 different chromatographic conditions, i.e., seven OV stationary phases and four different temperatures, as indicated Table 6. Projection on the first factorial plane is given Fig. 3. This plane

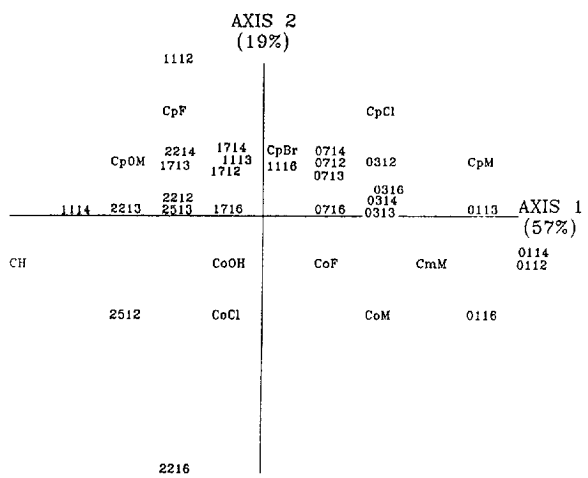


Fig. 3. Correspondence factor analysis of the acetophenone series. The first factorial plane includes 76% of the information. The first factorial axis corresponds to 57% of the information content. It indicates the average variation of polarity. The second axis contributes to 19% of the information content and separates *ortho* and *para* isomers.

includes 76% of the information content, 57% according to the first axis and 19% according to the second axis. The absence of the polar nitroacetophenonone compounds explains why a qualitative relationship between the first axis and the polarity of the compounds and stationary phases seems slightly less evident here. In contrast, axis 2 introduces a clear separation between *ortho* and *para* isomers. Most of the *ortho* derivatives have negative coordinates according to axis 2. It must be noted that *ortho* derivatives have greater dipolar moments but lower boiling points than the *para* homologues. This explains their lower chromatographic retention. This would certainly be related to steric hindrance of the polar carbonyl group with the *ortho* substituent, which induces the systematic trends seen in Fig. 3.

### 4.2. Topological analysis

The results of the simultaneous topological analysis of all the Kováts indices of the three compound series, studied at 120°C, are given in Fig. 4. The perturbation term of each substituent, located on the first concentric environment, represents its contribution to the Kováts index. The focus, i.e., the benzene group, has a

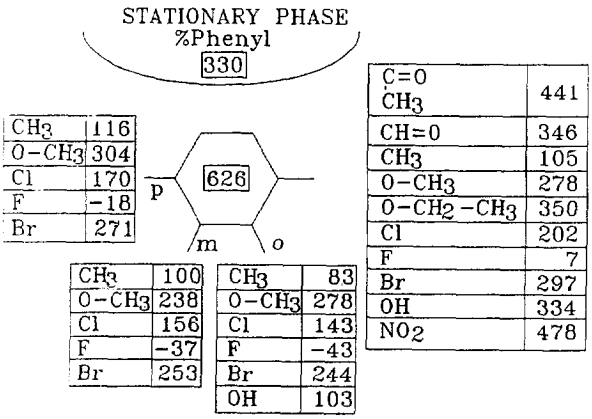


Fig. 4. Global topological analysis of the Kováts indices. Perturbation terms for the three aromatic congeneric series studied on the seven OV stationary phases. The contribution of the stationary phase is given by the perturbation term 330 multiplied by its percentage phenyl content.

contribution of 626. The square multiple regression coefficient $R^2$ equals 0.99.

Let us consider the influence of the substituent position. The perturbation terms decreases from the *para* to the *ortho* position for all compounds except for the methoxy group. With the methyl group the perturbation ranges from 116 to 83, with an average value of 100. This result agrees with the definition of the Kováts index, i.e., the contribution to the retention index of one carbon atom of an *n*-alkane equals 100. The contribution of the aromatic focus is not far from six linear linked carbon atoms. Outside the methoxy group, the modifications of the perturbation terms from the *para* to the *meta* position or to the *ortho* position are similar for all the substituents, namely ca. −17 and −28, respectively.

The perturbation term of the methyl substituent in the monosubstituted series is around 100 Kováts index units. Considering methyl, methoxy and ethoxy groups and assuming that the perturbation term of a carbon atom is constant whatever the level of the concentric environment, the perturbation of the oxygen atom may be evaluated at a value around 170. In the same way, the perturbation of the oxygen atom on the second concentric environment may be evaluated, from acetophenone and benzaldehyde, at 240. The fluoro, chloro and bromo groups have perturbation terms in accordance to the values obtained with *para*, *meta* and *ortho* positions. These values are higher than 26 Kováts index units. The hydroxy group has a particular high perturbation term, 334, introduced by phenol. The hydroxy group in the *ortho* position has a much lower perturbation term, equal to 103. The large difference between the two values, $\Delta = 231$, is related to the chelation of the OH substituent with the carbonyl group of the benzaldehyde or acetophenone organic function.

The stationary phase has a perturbation term equal to 330 multiplied by the phenyl percentage. For example, the perturbation term of OV-25 is $0.75 \cdot 330 = 247$ Kováts index units. This term represents the contribution to the Kováts indices which increases with increasing polarity of the stationary phase, whatever the nature of the compounds. The phenyl group of the stationary phase has a lower perturbation term than the phenyl group of the compounds. It may be assumed that this term is a combination of the temperature and phenyl effects. These two effects are antagonistic. The phenyl percentage has a positive contribution to the Kováts indices and the temperature has a negative contribution.

### *4.3. Interpretation of topological analysis using correspondence factor analysis*

Topological analysis is based on an additive model. The perturbation term, corresponding to a particular topological site, is calculated as an average one. Nevertheless, finer analysis may be organized to take into account interaction terms which correspond in fact to supplementary terms, when two particular sites are present simultaneously and introduce deviations from a simple additive model. These interaction terms have been related to steric effects in gas–solid chromatography [5], and their interest must not be limited to a pure mathematical device. To test the quality of the chosen additive topological model, with or without interaction terms, CFA can also be used. The deviation from an additive model when the polarity of the stationary phase increases may be presented clearly by CFA mapping.

Six new sets of perturbation terms were calculated separately for all the six series of Kováts

indices corresponding to the above-mentioned compounds studied on the six stationary phases at 120°C (Table 8). These sets give rise to a perturbation term matrix with column designees corresponding to the six chromatographic stationary phases and with row designees corresponding to the 27 substituents.

This derived matrix was analysed by CFA projections of the substituent and phase designees on the first factorial plane are given in Fig. 5. This plane contributes 94% of the information content, 88% for the first axes and 6% for the second. The first axis is defined by the variation of the phenyl percentage ranging from 0% (OV-101) to 75% (OV-25), and by the projection of the fluoro substituents. The polarity of the stationary phase increases from the right to the left. The projections of the substituents range approximately from the least polar methyl group to the most polar $NO_2$ group. All the substituents are projected between OV-101 and OV-25 phases, excepted for the *ortho*-, *meta*- and *para*-fluoro substituents.

In first approximation, the central cluster in Fig. 5 shows that the $\Delta I$ topological indices may be considered to be proportional to the polarity of the stationary phase. Nevertheless, in the second approximation, some regularities may be

Table 8
Topological analysis of the Kováts indices on the OV stationary phases at 120°C

| Substituent | Global analysis | OV-101 (0% Ph) | OV-3 (10% Ph) | OV-7 (20% Ph) | OV-11 (35% Ph) | OV-17 (50% Ph) | OV-25 (75% Ph) |
|---|---|---|---|---|---|---|---|
| Phase | 330.67 | | | | | | |
| Focus | 626.07 | 669.90 | 689.80 | 711.40 | 737.80 | 763.80 | 812.00 |
| COCH3 | 441.36 | 368.68 | 414.02 | 432.69 | 459.26 | 465.81 | 507.67 |
| CHO | 346.94 | 285.32 | 320.98 | 340.21 | 358.94 | 375.49 | 400.73 |
| pCH3 | 115.82 | 118.10 | 118.25 | 117.90 | 107.30 | 117.30 | 116.05 |
| mCH3 | 100.08 | 105.05 | 104.80 | 102.25 | 89.95 | 97.70 | 100.75 |
| oCH3 | 82.86 | 87.30 | 85.85 | 84.70 | 74.30 | 78.25 | 86.75 |
| pOCH3 | 303.74 | 270.60 | 287.30 | 297.70 | 300.05 | 322.95 | 343.85 |
| mOCH3 | 238.84 | 217.68 | 226.12 | 237.69 | 238.26 | 245.81 | 267.47 |
| oOCH3 | 278.26 | 257.68 | 267.72 | 277.99 | 280.26 | 289.51 | 296.37 |
| pCl | 169.77 | 159.00 | 166.90 | 172.05 | 164.65 | 177.00 | 179.00 |
| mCl | 156.12 | 147.08 | 151.72 | 160.59 | 154.46 | 156.21 | 166.67 |
| oCl | 142.91 | 139.20 | 140.75 | 143.40 | 134.25 | 143.30 | 156.55 |
| pF | −17.58 | −14.65 | −12.15 | −12.55 | −20.95 | −17.00 | −28.15 |
| mF | −37.31 | −28.42 | −29.98 | −30.41 | −36.64 | −47.39 | −51.03 |
| oF | −42.80 | −28.75 | −32.85 | −37.70 | −47.50 | −53.10 | −56.90 |
| pBr | 271.19 | 247.72 | 262.08 | 269.61 | 271.64 | 282.39 | 293.73 |
| mBr | 253.24 | 231.08 | 238.12 | 256.19 | 251.36 | 261.51 | 281.17 |
| oBr | 243.72 | 231.38 | 229.52 | 242.59 | 238.26 | 249.01 | 271.57 |
| oOH | 103.46 | 97.02 | 100.58 | 103.81 | 104.14 | 102.69 | 112.53 |
| CH3 | 104.85 | 101.70 | 103.00 | 104.30 | 107.60 | 108.20 | 104.30 |
| OCH3 | 277.97 | 240.20 | 255.60 | 268.30 | 282.10 | 311.00 | 310.60 |
| Cl | 202.47 | 180.40 | 196.80 | 196.70 | 203.30 | 223.40 | 214.20 |
| F | 7.63 | 4.00 | 8.10 | 9.50 | 2.70 | 16.30 | 5.20 |
| Br | 297.38 | 264.90 | 283.90 | 290.40 | 302.10 | 316.90 | 326.10 |
| OH | 334.05 | 282.60 | 324.60 | 317.60 | 338.60 | 363.20 | 377.70 |
| OCH2CH3 | 350.72 | 310.6 | 342.2 | 335.4 | 348.1 | 380.3 | 387.7 |
| NO2 | 477.95 | 398.6 | 443.5 | 465.6 | 493.2 | 527.6 | 539.2 |

The first column gives perturbation term of each substituent on the six OV stationary phases considering the perturbation term of the stationary phase as a second concentric environment as presented in Fig. 4. The next six columns are perturbation terms of each substituent on each stationary phase. The focus then includes the perturbation term of the phenyl group plus that of the stationary phase.

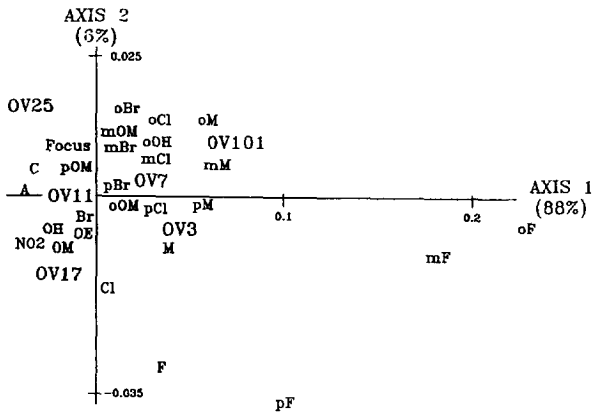


Fig. 5. Correspondence factor analysis of the matrix of perturbation terms derived independently on six stationary phases. The fluoro compounds exhibit the greatest deviation from an ideal model based on a linear influence of the increase of the phenyl content of the stationary phases.

noticed within this cluster. The variation of the $\Delta I$ topological indices slowly increases with increasing polarity of the stationary phase, in other words, the effect of the increasing polarity of the stationary phases is not completely taken into account by the focus.

The projections of the fluoro substituents show the particular behaviour of the corresponding compounds. The contributions of the fluoro substituents are negative and the variation of their $\Delta I$ topological indices decreases as the polarity of the stationary phase increases. The distance of the projection from the origin increases from the mono to the *para*, *meta* and *ortho* substituents. This remains in accordance with the CFA map (Fig. 2).

To explain the projection of the stationary phases on Fig. 5, a relative variation of the perturbation terms from the least polar to the most polar stationary phases is used. This relative variation is calculated in the following way. The apolar OV-101 stationary phase is taken as a reference. The difference between the perturbation term obtained on a given stationary phase minus its corresponding value on the OV-101 stationary phase is divided by the percentage of phenyl groups in the polar stationary phase. These relative perturbation terms are plotted versus the relative perturbation terms determined on the two less polar phases OV-101 and OV-3. The corresponding graph (Fig. 6) shows clearly that the relative perturbation terms vary clockwise from the first bisector towards the $x$ axis. The less polar phases are near the first bisector and the more polar phases are near the $x$ axis. This variation indicates that the increase of each perturbation term with increasing polarity of the stationary phase decreases from the less to the more polar phases. This observation emphasizes that the polarity is not directly proportional with the phenyl percentage of the stationary phases at the ultimate and available level of precision.

## 5. Conclusion

Even with the chosen homogeneous series of OV stationary phases, with various phenyl percentages, the retention mechanism of these congeneric aromatic compound series is not simple. Correlations between the Kováts indices and the Hammett constants have not been detected here for any of the three compounds series. Only a qualitative relationship between Hammett constants and the coordinates on the first factorial axis of the compound may be observed, in contrast to what it has been possible to observe previously in liquid chromatography [18].

From the experiment design point of view, this work emphasizes that an apparently simple experimental model, for example a homogeneous series of aromatic compounds studied on a homogeneous series of OV stationary phases, does not automatically imply a simple chromatographic retention mechanism! In fact, to obtain a purer mechanism a sufficient levelling effect of the various stationary phases must be obtained to counterbalance the large variation of electronic effects and polarities of this aromatic series. The above results show that, relative to the solute polarities, such a goal cannot be reached within the range of polarities of commercially available phenyl OV phases.

CFA and TA are sensitive methods for statistical analyses of the main factors which govern the

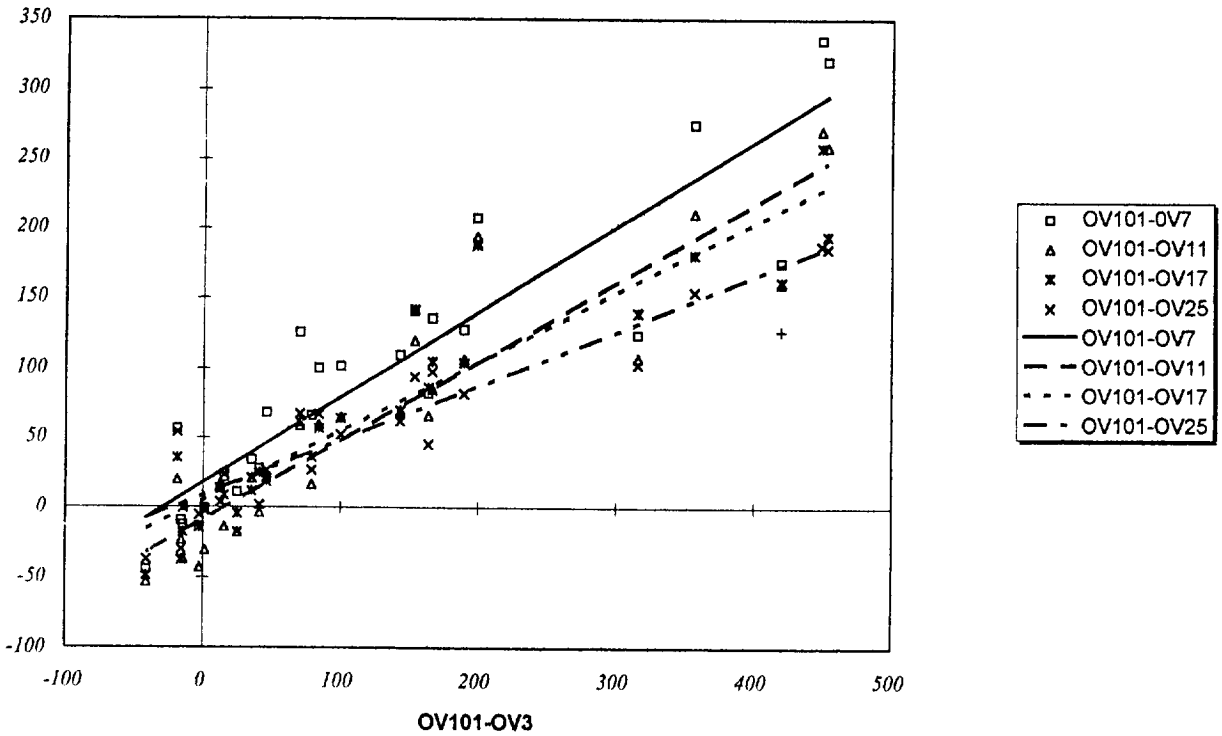


Fig. 6. Topological analysis of the Kováts indices. Relative variation of the perturbation term from OV-7 up to OV-25 stationary phases. The apolar OV-101 stationary phase is taken as a reference. This figure emphasizes the slight deviations from a proportional model in which the contribution of the structural parameters of the solutes would be directly proportional of the phenyl percentage of the stationary phase.

chromatographic process. These statistical analyses suggest that the possible charge-transfer complexes with the phenyl groups of the stationary phase are not the driving force of this mechanism. This mechanism of polar interactions certainly matches the partition one, depending on the substituents of the compounds and on the polarity of the stationary phase. These dual effects contribute to the scattering of the projections of the row and column designees and prevent any quantitative relationships between retention indices and physico-chemical parameters.

From the chemometrics point of view, this work also emphasizes that to model complex retention behaviour, whatever the mechanism, CFA and/or TA reveal themselves to be complementary valuable statistical methods in QSRR. To reveal nested structural or physico-chemical parameters, acting at a second-order level, CFA is very sensitive. It offers an analysis of the relative chromatographic behaviour of the compounds and/or of the stationary phases. When congeneric series are used, as a probe, to gain a deeper insight into the chromatographic mechanism, or to evaluate the weight of solute structural parameters, TA has the advantage of allowing a quantitative discussion directly of group contributions. Such models, and chiefly the TA one, may be used as an explicative but also as a predictive tool, to estimate the retention of new compounds. This is particularly interesting in petrochemistry and in medicinal chemistry to optimize, for example, the separation of various type of isomers in congeneric series of potent new drugs.

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## References

[1] R. Kaliszan, Quantitative Structure–Chromatographic Retention Relationships (Chemical Analysis, Vol. 93), Wiley, New York, 1987.
[2] S.N. Deming and S.L. Morgan, Experimental Design: a Chemometric Approach, Elsevier, Amsterdam, 1987.
[3] H. Kubinyi, 3D QSAR in Drug Design: Theory, Method and Application, ESCOM, Leiden, 1993.
[4] J.R. Chrétien and J.E. Dubois, Anal. Chem., 49 (1977) 747–756.
[5] J.R. Chétien, J.E. Dubois, R.F. Hirsch and R.J. Gaydosh, J. Chromatogr., 207 (1981) 115–130.
[6] P.H. Weiner, C.J. Dack and D.G. Howery, J. Chromatogr., 69 (1972) 249.
[7] M.J. Chastrette, J. Chromatogr. Sci., 14 (1976) 357.
[8] R.F. Hirsch, R.J. Gaydosh and J.R. Chrétien, Anal. Chem., 52 (1980) 723–728.
[9] K.L. Petterson, Anal. Chem., 64 (1992) 379–386.
[10] D.B. Kireev, J. Chem. Inf. Comput. Sci., in press.
[11] L.B. Kier and L.H. Hall, Molecular Connectivity in Chemistry and Drug Research, Academic Press, New York, 1976.
[12] H. Wiener, J. Am. Chem. Soc., 69 (1947) 17.
[13] J.E. Dubois, in W.T. Wipke, S. Heller, R. Feldmann and E. Hyde (Editors), Computer Representation and Manipulation of Chemical Information, Wiley, New York, 1974, p. 239.
[14] K. Szymoniak and J.R. Chrétien, J. Chromatogr., 404 (1987) 11–22.
[15] J.R. Chrétien, M. Righezza, A. Hassani and B.Y. Meklati, J. Chromatogr., 609 (1992) 261–267.
[16] J.P. Benzécri, L'Analyse des Données, Vol. 2, Dunod, Paris, 1973.
[17] A. Hassani and B.Y. Meklati, Chromatographia, 33 (1992) 267–271.
[18] B. Walczak, L. Morin-Allory, J.R. Chrétien, M. Lafosse and M. Dreux, J. Chemometr. Intell. Lab. Syst., 1 (1986) 79–90.
[19] E.R. Malinowski and D.G. Howery, Factor Analysis in Chemistry, Wiley, 1980.