Reference GLC Data for the Analysis of Phenolic Compounds as Trimethylsilyl Derivatives*

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Abstract

Comprehensive reference GLC data are given for trimethylsilyl (Me_3Si) derivatives of about 130 aromatic compounds grouped as phenols and naphthols, alcohols, carboxylic acids, aldehydes and ketones, and chloro compounds. The aldehydes and ketones were analysed as both oxime and *O*-methyl oxime derivatives.

Retention data on methyl and phenyl (50%) silicone columns are given as MU (MU^{Me} and MU^{Ph}) values in temperature-programmed analysis. Correlations between structure and retention are interpreted in terms of MU^{Me} and ΔMU ($MU^{Ph} - MU^{Me}$) increments of structural elements. Methods for predicting MU values are proposed. Diagrams of MU^{Me} versus ΔMU are shown to be an efficient aid in qualitative analysis.

Approximate FID relative molar response values are estimated from the atomic composition of the derivatives.

Introduction

Gas chromatography of Me_3Si derivatives has developed into a standard technique for the analysis of phenolic as well as many other types of hydrophilic organic compounds. This is true in all important fields of application from medicine to industrial pollution.

The purpose of the present investigation is to give comprehensive reference data adapted to efficient use for qualitative and quantitative analysis. The qualitative approach is partly based on that recently used for Me_3Si derivatives of carbohydrate-related carboxylic acids (1). Special emphasis is given to compounds of interest as possible waste products from the cellulose industry.

The advantages of simultaneous analysis of many compounds has led to the use of temperature programming (2-6) more often than isothermal analysis (7) in studies comprising a wide range of phenolic compounds. The MU (4) and ΔMU (2) concepts are suitable for retention measurements as a substitute for the retention index data used in isothermal analysis. The possibility of simultaneous silylation of several functional groups further extends the range of compounds which can be analysed simultaneously and is a major reason for the predominant use (5) of Me_3Si derivatives for phenolic compounds. Actually, the silylation technique previously used with carbohydrate-related compounds (8) was found to be appropriate in the present study as well.

Experimental

The bulk of the compounds studied were commercial samples. However, many of the arylalkanols were prepared by reduction of the corresponding carboxylic acids with $LiAlH_4$ in diethyl ether or of the corresponding aldehydes or ketones with KBH_4 in ethanol/water. A few compounds were isolated and identified from kraft black liquor (9). Mass spectrometry was used for structural confirmations of the derivatives.

Oximes and *O*-methyl oximes of aldehydes and ketones were prepared with $HONH_2$,HCl and $MeONH_2$,HCl in pyridine. Silylation of hydroxyl, carboxyl or carboxylate, and oxime groups was performed with BSTFA + TMCS (2:1) in the same solvent at ambient temperature on sample amounts in the mg range. Most derivatives were transferred to cyclohexane (~1 ml) containing a small amount of BSTFA before GLC analysis or storage in flame-sealed glass capillaries. Other precautions and experimental details were the same as previously described with corresponding aliphatic compounds (8).

The retention data were obtained on a Perkin-Elmer Model 3920 Gas Chromatograph equipped with two parallel columns coupled to one injector but with separate detection devices. Injection: ~1 μl manually or automatically with the Perkin-Elmer Model 4900 Autosampler. Detection: Dual flame ionization detectors with separate amplifiers and recording integrators (Hewlett-Packard 3380 A and 3380 S) giving retention in minutes to two decimal places. Columns: 2 m × 0.2 cm i.d. stainless steel. Packings: 3% OV-101 on 100/120 mesh Gas-Chrom Q and 3% SP-2250 on 100/120 mesh Supelcoport. Carrier gas: Purified nitrogen, ~30 ml/min (OV-101) and ~20 ml/min (SP-2250). Initial temperature: 80°C. Programming: 4°/min to 240°C, linearly from the injection.

The MU values were determined relative to the even-numbered *n*-alkanes as previously described (1) with the derivatives of *myo*-inositol and phenol as dual markers. In routine applications, *myo*-inositol was used as internal standard and simultaneously as marker, alone or together with reagent peaks. The retention time correction for the marker could be applied to all components of a sample with good results because most deviations occur in the initial stage of the temperature program. The retention time differences between different samples on use of the autosampler with over-night automatic operation were only a few seconds, however.

Tabulated and Diagrammatic Data

Reference data are given for genuine phenols and naphthols (Table I) and for aromatic, mainly phenolic, alcohols (Table II), carboxylic acids (Table III), aldehydes and ketones (Table IV), and chloro compounds (Table V). With the aldehydes and ketones, data are given for both *O*-Me_3Si and *O*-methyl oxime derivatives.

The parameters given are the same in Tables I-V. The meaning of the corresponding symbols is explained under Table I. The first column gives the number of Me_3Si groups intro-

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Table I. Phenols and naphtols

Compound	[Si]	M	MU^{Me}	[C+O]	MU^{Ph}	ΔMU	0.3[π+OMe]	RMR	M_0
myo-Inositol (marker and int. standard)	6	612	21.53	30	20.41	-1.12	0.0	21.0	180
Phenols									
Phenol	1	166	10.33	10	11.16	0.83	0.9	8.5	94
2-Methylphenol (o-cresol)	1	180	11.08	11	12.03	0.95	0.9	9.5	108
3-Methylphenol (m-cresol)	1	180	11.17	11	12.17	1.00	0.9	9.5	108
4-Methylphenol (p-cresol)	1	180	11.29	11	12.29	1.00	0.9	9.5	108
2,4-Dimethylphenol	1	194	12.15	12	12.93	0.78	0.9	10.5	122
2,6-Dimethylphenol	1	194	12.23	12	13.08	0.85	0.9	10.5	122
3,4-Dimethylphenol	1	194	12.44	12	13.43	0.99	0.9	10.5	122
2-Ethylphenol	1	194	11.85	12	12.65	0.80	0.9	10.5	122
3-Ethylphenol	1	194	12.11	12	12.98	0.87	0.9	10.5	122
4-Ethylphenol	1	194	12.25	12	13.10	0.85	0.9	10.5	122
2,4,5-Trimethylphenol	1	208	13.14	13	14.08	0.94	0.9	11.5	136
2-Propylphenol	1	208	12.57	13	13.33	0.76	0.9	11.5	136
4-Propylphenol	1	208	13.09	13	14.03	0.94	0.9	11.5	136
2-Isopropyl-5-methylphenol (thymol)	1	222	13.01	14	13.80	0.79	0.9	12.5	150
4-tert-Butylphenol	1	222	13.41	14	14.32	0.91	0.9	12.5	150
2-Methoxyphenol (guaiacol)	1	196	12.10	12	13.37	1.27	1.2	9.0	124
3-Methoxyphenol	1	196	12.64	12	14.08	1.44	1.2	9.0	124
4-Methoxyphenol	1	196	12.71	12	14.12	1.41	1.2	9.0	124
2-Methoxy-4-propylphenol	1	238	14.63	15	15.88	1.25	1.2	12.0	166
4-Allyl-2-methoxyphenol (eugenol)	1	236	14.58	15	16.01	1.43	1.5	12.0	164
2,6-Dimethoxyphenol	1	226	13.79	14	15.56	1.77	1.5	9.5	154
4-Phenylphenol	1	242	17.46	16	19.49	2.03	1.8	14.5	170
1,2-Benzenediol (pyrocatechol)	2	254	13.09	14	13.78	0.69	0.9	11.0	110
1,3-Benzenediol (resorcinol)	2	254	13.78	14	14.54	0.76	0.9	11.0	110
1,4-Benzenediol (hydroquinone)	2	254	14.00	14	14.68	0.68	0.9	11.0	110
4-Methyl-1,2-benzenediol	2	268	13.88	15	14.56	0.68	0.9	12.0	124
5-Methyl-1,3-benzenediol (orcinol)	2	268	14.46	15	15.27	0.81	0.9	12.0	124
1,2,3-Benzenetriol (pyrogallol)	3	342	15.48	18	15.99	0.51	0.9	13.5	126
1,3,5-Benzenetriol (phloroglucinol)	3	342	16.54	18	17.22	0.68	0.9	13.5	126
Naphthols									
1-Naphthol	1	216	15.17	14	16.89	1.72	1.5	12.5	144
2-Naphthol	1	216	15.36	14	17.12	1.76	1.5	12.5	144
1,3-Naphthalenediol	2	304	18.29	18	19.79	1.50	1.5	15.0	160
2,7-Naphthalenediol	2	304	18.92	18	20.42	1.50	1.5	15.0	160

Symbols:

[Si] : Number of trimethylsilyl groups.

M : Mass of molecular ion in mass spectrometry.

MU^{Me} : Methylene units on a 100% methyl silicone.

[C+O]: Number of carbon + oxygen atoms of the derivative.

MU^{Ph} : Methylene units on a 50% phenyl, 50% methyl silicone.

ΔMU : $MU^{Ph} - MU^{Me}$.

[π+OMe]: Number of formal unsaturations + methoxyl groups.

RMR : Approximate relative molar response calculated as [C] - 0.5[O+N+Cl].

M_0 : Molecular mass of underivatized compound.

duced, and the second gives the molecular weight of the derivative as obtained by mass spectrometry. The third column gives the retention (MU^{Me}) on the non-polar 100% methyl silicone. With the non-chloro compounds, the number of carbon + oxygen (+ nitrogen) atoms given in the fourth column approximately equals MU^{Me}. The retention (MU^{Ph}) on the medium-polar 50% phenyl, 50% methyl silicone is given in the central column. The two types of stationary phases studied may be regarded as standard phases for GLC of aromatic compounds. As shown in the next two columns, the difference, ΔMU, between the two MU values is related to the number of formal double bonds plus methoxyl groups. When this number is multiplied by 0.3, approximate coincidence with the ΔMU value is observed. The last but one column gives an estimated relative molar response (RMR) for use in quantitative analysis. Division with the molecular weight given in the

Table II. Aromatic alcohols

Compound	[Si]	M	MU^{Me}	[C+O]	MU^{Ph}	ΔMU	0.3[π+OMe]	RMR	M_0
Arylalkanols									
Phenylmethanol (benzyl alcohol)	1	180	11.32	11	12.34	1.02	0.9	9.5	108
1-Phenylethanol	1	194	11.18	12	12.10	0.92	0.9	10.5	122
2-Phenylethanol	1	194	12.14	12	13.03	0.89	0.9	10.5	122
1-Phenyl-1-propanol	1	208	12.01	13	12.67	0.66	0.9	11.5	136
3-Phenyl-1-propanol	1	208	13.20	13	14.19	0.99	0.9	11.5	136
4-Methoxyphenylmethanol	1	210	13.77	13	15.30	1.53	1.2	10.0	138
4-Hydroxyphenylmethanol	2	268	15.00	15	15.88	0.88	0.9	12.0	124
Phenyl-1,2-ethanediol	2	282	14.30	16	14.96	0.66	0.9	13.0	138
2-(4-Hydroxyphenyl)ethanol	2	282	15.66	16	16.51	0.85	0.9	13.0	138
1-(4-Hydroxyphenyl)-1-propanol	2	296	15.39	17	15.88	0.49	0.9	14.0	152
3-(4-Hydroxyphenyl)-1-propanol	2	296	16.80	17	17.62	0.82	0.9	14.0	152
4-Hydroxy-3-methoxyphenylmethanol	2	298	16.33	17	17.54	1.21	1.2	12.5	154
3-Hydroxy-4-methoxyphenylmethanol	2	298	16.26	17	17.52	1.26	1.2	12.5	154
1-(4-Hydroxy-3-methoxyphenyl)ethanol	2	312	15.99	18	16.94	0.95	1.2	13.5	168
2-(4-Hydroxy-3-methoxyphenyl)ethanol	2	312	17.05	18	18.22	1.17	1.2	13.5	168
3-(4-Hydroxy-3-methoxyphenyl)-1-propanol	2	326	18.13	19	19.31	1.18	1.2	14.5	182
1-(4-Hydroxy-3,5-dimethoxyphenyl)ethanol	2	342	17.25	20	18.52	1.27	1.5	14.0	198
3-(4-Hydroxyphenyl)-1,2-propanediol	3	384	18.64	21	19.03	0.39	0.9	16.5	168
3-(3,4-Dihydroxyphenyl)-1-propanol	3	384	18.76	21	19.31	0.55	0.9	16.5	168
4-Hydroxy-3-methoxyphenyl-1,2-ethanediol	3	400	18.50	22	19.19	0.69	1.2	16.0	184
3-(4-Hydroxy-3-methoxyphenyl)-1,2-propanediol	3	414	19.81	23	20.49	0.68	1.2	17.0	198
3,4-Dihydroxyphenyl-1,2-ethanediol	4	458	19.09	24	19.28	0.19	0.9	18.0	170
Arylalkenols (trans-)									
3-(4-Hydroxy-3-methoxyphenyl)-2-propen-1-ol	2	324	19.35	19	20.82	1.47	1.5	14.5	180

last column provides a corresponding weight response factor related to the underivatized compounds.

Diagrams of MU^{Me} versus ΔMU are given in Figures 1-2 for the main categories of compounds studied. Different structural classes fall into characteristic areas as indicated by the dashed lines. A study of the diagrammatic and tabulated data demonstrates that the structural units of interest can be attributed increments in MU^{Me} and ΔMU as well as in RMR. Observed typical values of such increments are given in Table VI.

Relationships between Structure and Retention

The MU concept, which is analogous to the retention index concept, expresses retention as the chain length of an equally retained hypothetical *n*-alkane (4). The molecular cohesive forces between an *n*-alkane and a stationary phase are very nearly proportional to the chain length. Since the retention is caused by molecular forces between solute and stationary phase, the direct correspondence between MU and the magnitude of these forces is easily understood. This correspondence provides the basis for interpretations of relations between MU values and solute structure (1).

On a non-polar stationary phase, retention is due to the non-polar dispersion forces. These may be regarded as proportional to the outer surface area of the solute molecule. Differences in MU^{Me} values can therefore be interpreted in terms of differences in this area. With the phenolic compounds the MU^{Me} increments given in Table VI are illustrative. Addition of a methylene group increases MU by roughly one unit as in *n*-alkanes. Detailed relations between structure and retention index for alkylbenzenes have been discussed by Engewald and Wennrich (10). The methoxy, chloro, and *O*-methyl oxime groups also increase MU^{Me} according to the size of the atoms involved. The introduction of two carbon atoms as a *trans*-ethylene unit between two large groups causes a relatively large increase of area and MU^{Me}. The Me_3Si-containing groups, however, contribute less than the atoms and masses involved would suggest. This is ascribed to the spherical shape of the $OSiMe_3$ group which results in a comparatively small contribution to the outer surface area (1). The anomalously small MU^{Me} increments from the Me_3Si groups is the major reason why the number of C + O (+ N) atoms affords a better estimate of MU^{Me} than the molecular weight of the derivatives (Tables I-IV).

An *ortho* position of two large substituents on the aromatic ring results in a smaller outer surface area and consequently a smaller MU^{Me} value than a *meta* and particularly a *para* position of the same substituents. With more than two substituents the MU^{Me} value is reduced in proportion to the number of *ortho* positions. Anomalously low MU^{Me} increments are also observed with structural changes which introduce a secondary or a tertiary $OSiMe_3$ group into the aliphatic portion of the molecules. This is explained by an increased compactness imposed on the molecule by the bulky $OSiMe_3$ group.

Table III. Aromatic carboxylic acids

Compound	[Si]	M	MU^{Me}	[C+O]	MU^{Ph}	ΔMU	0.3[π+OMe]	RMR	M_0
Benzoic acids									
Benzoic	1	194	12.29	12	13.54	1.25	1.2	9.0	122
3,4-Dimethoxybenzoic	1	254	16.84	16	19.34	2.50	1.8	10.0	182
2-Hydroxybenzoic (salicylic)	2	282	15.02	16	16.20	1.18	1.2	11.5	138
3-Hydroxybenzoic	2	282	15.59	16	16.72	1.13	1.2	11.5	138
4-Hydroxybenzoic	2	282	16.22	16	17.27	1.05	1.2	11.5	138
4-Hydroxy-3-methoxybenzoic	2	312	17.55	18	19.05	1.50	1.5	12.0	168
4-Hydroxy-3,5-dimethoxybenzoic	2	342	18.84	20	20.78	1.94	1.8	12.5	198
2,3-Dihydroxybenzoic	3	370	17.43	20	18.42	0.99	1.2	14.0	154
2,5-Dihydroxybenzoic	3	370	17.83	20	18.73	0.90	1.2	14.0	154
3,4-Dihydroxybenzoic	3	370	18.26	20	19.14	0.88	1.2	14.0	154
3,5-Dihydroxybenzoic	3	370	18.28	20	19.20	0.92	1.2	14.0	154
2,3,4-Trihydroxybenzoic	4	458	19.32	24	19.95	0.63	1.2	16.5	170
2,4,6-Trihydroxybenzoic	4	458	20.03	24	20.90	0.87	1.2	16.5	170
3,4,5-Trihydroxybenzoic (gallic)	4	458	19.76	24	20.48	0.72	1.2	16.5	170
Benzenedicarboxylic acids									
1,2-Benzenedicarboxylic (phtalic)	2	310	16.75	18	18.56	1.81	1.5	12.0	166
1,3-Benzenedicarboxylic	2	310	17.48	18	18.86	1.38	1.5	12.0	166
1,4-Benzenedicarboxylic	2	310	17.88	18	18.94	1.06	1.5	12.0	166
Arylalkanoic acids [a]									
$C_6H_5CH_2COOH$	1	208	12.75	13	14.28	1.53	1.2	10.0	136
$C_6H_5CH_2CH_2COOH$	1	222	13.97	14	15.44	1.47	1.2	11.0	150
$C_6H_5CH(OH)COOH$	2	296	14.70	17	15.90	1.20	1.2	12.5	152
$(4\text{-}OH)C_6H_4CH_2COOH$	2	296	16.29	17	17.62	1.33	1.2	12.5	152
$C_6H_5CH_2CH(OH)COOH$	2	310	15.81	18	16.84	1.03	1.2	13.5	166
$(4\text{-}OH)C_6H_4CH_2CH_2COOH$	2	310	17.50	18	18.80	1.30	1.2	13.5	166
$(4\text{-}OH,3\text{-}OCH_3)C_6H_3CH_2COOH$	2	326	17.61	19	19.27	1.66	1.5	13.0	182
$(4\text{-}OH)C_6H_4CH(OH)COOH$	3	384	17.90	21	18.86	0.96	1.2	15.0	168
$(3\text{-}OH,4\text{-}OH)C_6H_3CH_2COOH$	3	384	18.33	21	19.35	1.02	1.2	15.0	168
$(4\text{-}OH)C_6H_4CH_2CH(OH)COOH$	3	398	19.12	22	19.90	0.78	1.2	16.0	182
$(3\text{-}OH,4\text{-}OH)C_6H_3CH_2CH_2COOH$	3	398	19.50	22	20.42	0.92	1.2	16.0	182
$(4\text{-}OH,3\text{-}OCH_3)C_6H_3CH(OH)COOH$	3	414	18.90	23	20.16	1.26	1.5	15.5	198
$(4\text{-}OH,3\text{-}OCH_3)C_6H_3CH_2CH(OH)COOH$	3	428	20.28	24	21.37	1.09	1.5	16.5	212
$(4\text{-}OH,3\text{-}OCH_3)C_6H_3CH_2CH_2CH(OH)COOH$	3	442	21.47	25	22.67	1.20	1.5	17.5	226
$(4\text{-}OH,3\text{-}OCH_3)C_6H_3CH_2C(CH_3)(OH)COOH$	3	442	20.30	25	21.15	0.85	1.5	17.5	226
$(3\text{-}OH,4\text{-}OH)C_6H_3CH(OH)COOH$	4	472	19.50	25	20.20	0.70	1.2	17.5	184
Arylalkenoic acids (trans-)									
$C_6H_5CH{=}CHCOOH$	1	220	15.22	14	17.01	1.79	1.5	11.0	148
$(4\text{-}OH)C_6H_4CH{=}CHCOOH$	2	308	19.25	18	20.76	1.51	1.5	13.5	164
$(4\text{-}OH,3\text{-}OCH_3)C_6H_3CH{=}CHCOOH$	2	338	20.77	20	22.63	1.86	1.8	14.0	194
$(4\text{-}OH,3\text{-}OCH_3,5\text{-}OCH_3)C_6H_2CH{=}CHCOOH$	2	368	22.21	22	24.50	2.29	2.1	14.5	224
$(3\text{-}OH,4\text{-}OH)C_6H_3CH{=}CHCOOH$	3	396	21.43	22	22.44	1.01	1.5	16.0	180

[a] Formulas are given because some systematic names may be confusing.

The C + O (+ N) estimate of MU^{Me} does not account for the isomeric effects of *ortho* substitution and secondary (or tertiary) aliphatic $OSiMe_3$ substitution and tends to predict correspondingly too high values. Even after correction for these effects (Table VI), too high MU^{Me} values are predicted for the largest molecules because the contribution of central atoms to the dispersion forces gradually decreases as the molecular size increases.

With somewhat more polar stationary phases like the phenyl silicones, the dispersion forces are of the same order of magnitude as with non-polar phases. However, except with non-polar solutes like the *n*-alkanes, dipole and induced dipole

Table IV. Aromatic aldehydes and ketones

Compound	[Si]	M	MU^{Me}	[C+O+N]	MU^{Ph}	ΔMU	0.3[π+OMe]	RMR	M_0
Hydroxylamine (reagent and marker)	3	249	11.11	11	10.89	-0.22	0.0	8.0	33
Benzaldehydes (O-Me_3Si oximes)									
Benzaldehyde	1	193	12.57	12	13.92	1.35	1.2	9.0	106
4-Methoxybenzaldehyde	1	223	15.15	14	17.07	1.92	1.5	9.5	136
2-Hydroxybenzaldehyde	2	281	15.50	16	16.64	1.14	1.2	11.5	122
3-Hydroxybenzaldehyde	2	281	15.88	16	16.91	1.03	1.2	11.5	122
4-Hydroxybenzaldehyde	2	281	16.42	16	17.51	1.09	1.2	11.5	122
2-Hydroxy-3-methoxybenzaldehyde	2	311	17.19	18	18.70	1.51	1.5	12.0	152
3-Hydroxy-4-methoxybenzaldehyde	2	311	17.72	18	19.24	1.52	1.5	12.0	152
4-Hydroxy-3-methoxybenzaldehyde	2	311	17.71	18	19.18	1.47	1.5	12.0	152
4-Hydroxy-3,5-dimethoxybenzaldehyde	2	341	19.16	20	20.99	1.83	1.8	12.5	182
2,4-Dihydroxybenzaldehyde	3	369	18.64	20	19.55	0.91	1.2	14.0	138
3,4-Dihydroxybenzaldehyde	3	369	18.50	20	19.21	0.71	1.2	14.0	138
Arylalkanones (O-Me_3Si oximes)									
Acetophenone	1	207	13.13	13	14.51	1.38	1.2	10.0	120
Propiophenone	1	221	13.57	14	14.86	1.29	1.2	11.0	134
4-Hydroxypropiophenone	2	309	17.21	18	18.13	0.92	1.2	13.5	150
4-Hydroxy-3-methoxyacetophenone	2	325	18.05	19	19.48	1.43	1.5	13.0	166
4-Hydroxy-3,5-Dimethoxyacetophenone	2	355	19.34	21	21.09	1.75	1.8	13.5	196
Benzaldehydes (O-methyl oximes)									
Benzaldehyde	0	135	10.71	10	12.45	1.74	1.5	7.0	106
4-Methoxybenzaldehyde	0	165	13.39	12	15.70	2.31	1.8	7.5	136
2-Hydroxybenzaldehyde	1	223	14.10	14	15.57	1.47	1.5	9.5	122
3-Hydroxybenzaldehyde	1	223	14.33	14	15.85	1.52	1.5	9.5	122
4-Hydroxybenzaldehyde	1	223	14.75	14	16.24	1.49	1.5	9.5	122
2-Hydroxy-3-methoxybenzaldehyde	1	253	15.83	16	17.81	1.98	1.8	10.0	152
3-Hydroxy-4-methoxybenzaldehyde	1	253	16.23	16	18.28	2.05	1.8	10.0	152
4-Hydroxy-3-methoxybenzaldehyde	1	253	16.24	16	18.23	1.99	1.8	10.0	152
4-Hydroxy-3,5-dimethoxybenzaldehyde	1	283	17.76	18	20.22	2.46	2.1	10.5	182
2,4-Dihydroxybenzaldehyde	2	311	17.40	18	18.71	1.31	1.5	12.0	138
3,4-Dihydroxybenzaldehyde	2	311	17.04	18	18.29	1.25	1.5	12.0	138
Arylalkanones (O-methyl oximes)									
Acetophenone	0	149	11.71	11	13.52	1.81	1.5	8.0	120
Propiophenone	0	163	12.30	12	14.06	1.76	1.5	9.0	134
4-Hydroxypropiophenone	1	251	16.10	16	17.64	1.54	1.5	11.5	150
4-Hydroxy-3-methoxyacetophenone	1	267	17.03	17	19.07	2.04	1.8	11.0	166
4-Hydroxy-3,5-dimethoxyacetophenone	1	297	18.42	19	20.86	2.44	2.1	11.5	196

forces between a solute and the polar phase add to the cohesive forces. As a consequence, the ΔMU values essentially represent the magnitude of polar interactions between solute and phase. Because of the moderately polar nature of the phenyl silicones and the non-polar character of the Me_3Si groups, the polar contributions to retention (ΔMU) are very small compared to the non-polar contributions (MU^{Me}).

From Table VI, it is seen that all double bonds, including those of the aromatic nucleus, and methoxyl groups cause similar increments in ΔMU. These increments of approximately 0.3 units permit an estimation of ΔMU from the number of these structural elements (Tables I-IV). The effects are explained by π-electron and dipole interactions with the phenyl groups of the stationary phase. Chlorine atoms contribute less than double bonds and methoxyl groups.

The polar contributions depend not only on the presence of polar groups in the solute structure but also on whether these groups can develop an intimate contact with the appropriate groups in the stationary phase (1). The bulky, non-polar Me_3Si group protects neighbouring polar bonds partly or completely from interactions with the stationary phase as demonstrated by the effect of Me_3Si ether, ester and oxime groups on ΔMU. The negative contribution to ΔMU from silyl ether groups (secondary and tertiary in particular) indicates a shielding effect not only on the ether linkages but also on other polar groups in the molecule.

Table V. Aromatic chloro compounds

Compound	[Si]	M	MU^{Me}	[C+O]	MU^{Ph}	ΔMU	0.3[π+OMe]	RMR	M_0
Phenols									
3-Chlorophenol	1	200	12.05	10	12.94	0.89	0.9	8.0	128
4-Chlorophenol	1	200	12.18	10	13.14	0.96	0.9	8.0	128
2,3-Dichlorophenol	1	234	13.71	10	15.04	1.33	0.9	7.5	162
2,4-Dichlorophenol	1	234	13.45	10	14.63	1.18	0.9	7.5	162
2,5-Dichlorophenol	1	234	13.24	10	14.42	1.18	0.9	7.5	162
2,6-Dichlorophenol	1	234	13.26	10	14.51	1.25	0.9	7.5	162
2,4,5-Trichlorophenol	1	268	14.95	10	16.11	1.16	0.9	7.0	196
2,4,6-Trichlorophenol	1	268	14.66	10	15.88	1.22	0.9	7.0	196
3,4,5-Trichlorophenol	1	268	15.37	10	16.56	1.19	0.9	7.0	196
2,3,4,5-Tetrachlorophenol	1	302	16.83	10	18.26	1.43	0.9	6.5	230
2,3,4,6-Tetrachlorophenol	1	302	16.56	10	18.03	1.47	0.9	6.5	230
2,3,5,6-Tetrachlorophenol	1	302	16.45	10	17.90	1.45	0.9	6.5	230
Pentachlorophenol	1	336	18.40	10	20.05	1.65	0.9	6.0	264
4-Chloro-3-methylphenol	1	214	13.07	11	14.15	1.08	0.9	9.0	142
2-Chloro-5-methoxyphenol	1	230	14.10	12	15.73	1.63	1.2	8.5	158
3-Chloro-5-methoxyphenol	1	230	14.21	12	15.64	1.43	1.2	8.5	158
4-Chlorobenzene-1,3-diol	2	288	15.21	14	16.13	0.92	0.9	10.5	144
4,6-Dichlorobenzene-1,3-diol	2	322	16.48	14	17.34	0.86	0.9	10.0	178
Benzoic acids									
2-Chlorobenzoic	1	228	13.88	12	15.54	1.66	1.2	8.5	156
3-Chlorobenzoic	1	228	13.85	12	15.17	1.32	1.2	8.5	156
4-Chlorobenzoic	1	228	13.88	12	15.20	1.32	1.2	8.5	156
3-Chloro-4-hydroxybenzoic	2	316	17.49	16	18.66	1.17	1.2	11.0	172
3,5-Dichloro-4-hydroxybenzoic	2	350	18.65	16	19.66	1.01	1.2	10.5	206

Qualitative Analysis

The commonplace use of reference retention data is for table-matching with data of samples to be analysed. The influence of experimental parameters on the retention data is of great interest in such applications. When temperature programming is used for analysis, MU values are likely to be preferable to retention indices as reference data (1). The magnitude of the deviations to be expected between MU values determined on the same structural type of stationary phase but under other differing conditions is illustrated by comparison with previously published data for phenolic acids on the OV-1 and OV-17 stationary phases (2). The column dimensions, supports, temperature program, carrier gas, etc., were much different from what is used in this study. In spite of that, the MU^{Me} deviations were typically only ±0.02 units whereas the MU^{Ph} (and ΔMU) values were typically 0.05-0.10 units higher on OV-17 than on SP-2250. A few determinations of MU^{Ph} made on a OV-17 column indicate that the latter deviations are due mainly to the different stationary phases. Reported MU values (3) for derivatives of some non-carboxylic compounds also differ very little from the tabulated data. Deviating (too low) MU values for early eluted compounds may be due to a high initial temperature which causes a non-linear interpolation curve for the early eluted *n*-alkanes. From the comparisons made, it is concluded that the reference MU data reported are adequate for use in qualitative analysis even if widely different experimental conditions are used and even with different trade marks of methyl and 50% phenyl silicones.

Two-column analysis increases the versatility of GLC as a technique for qualitative analysis much beyond the table-matching level (1). The MU^{Me} versus ΔMU approach permits diagrammatic representations which reflect molecular size along one axis and molecular polarity along the other. As illustrated by Figures 1-2, such diagrams can be used not only for efficient exclusion of structural alternatives but also for predicting structural features of an unknown compound. With a phenyl silicone as the polar stationary phase, phenolic compounds differ from aliphatic compounds with the same functional groups (1) by higher ΔMU values. This is ascribed to the effect of the aromatic ring and normally permits phenolic Me_3Si derivatives to be distinguished from aliphatic Me_3Si derivatives. Similarly, phenolic carboxylic acid and oxime derivatives (Figure 2) appear to the right of phenols and arylalkanols (Figure 1). An additional methoxyl group is revealed by a rightward shift of about the same magnitude. The number of Me_3Si groups can usually be deduced because of the large contribution to MU^{Me} from each of these groups. The sub-positions relative to the corresponding borderlines reflect primarily different numbers of carbon atoms (cf. alkylphenols) and *ortho* positions in the structures. Similarly, the sub-positions along the ΔMU axis may indicate the presence of secondary $OSiMe_3$ groups in the aliphatic portion of arylalkanols and arylalkanoic acids. With the chlorophenols the number of chlorine atoms can be deduced. Chlorobenzenediols and chloromethoxyphenols (not marked) tend to appear to the

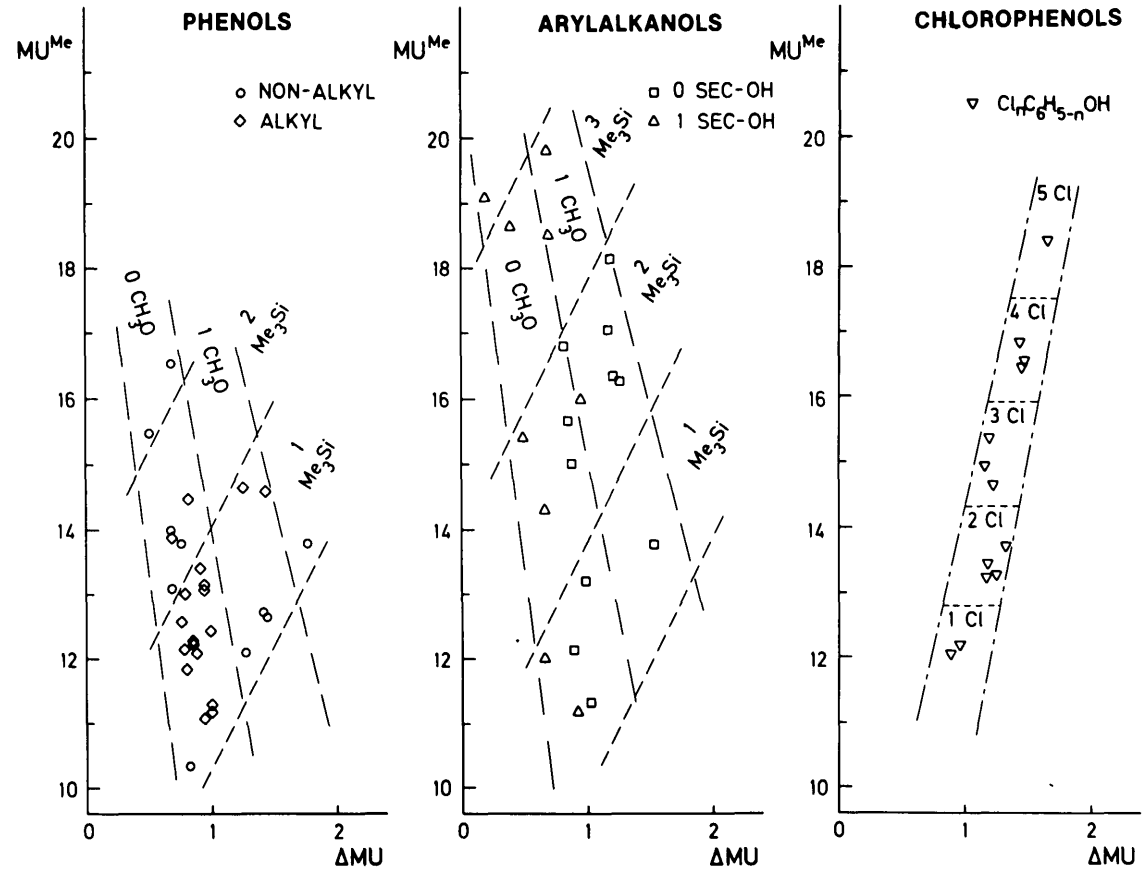

Figure 1. Diagrams of MU^{Me} versus ΔMU (MU^{Ph}-MU^{Me}) illustrating retention characteristics of Me_3Si derivatives of phenols, arylalkanols, and chlorophenols on methyl and phenyl (50%) silicone stationary phases.

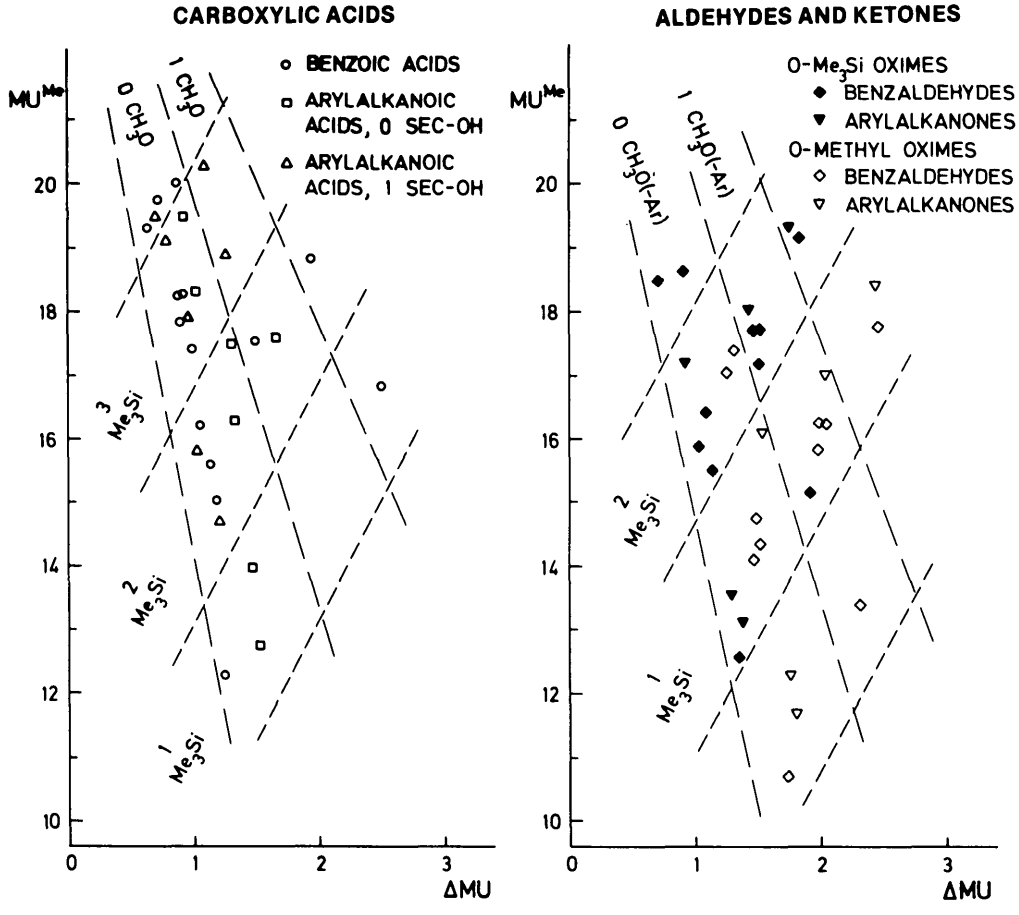

Figure 2. Diagrams of MU^{Me} versus ΔMU illustrating retention characteristics of Me_3Si derivatives of aromatic carboxylic acids and of oxime/Me_3Si derivatives of aromatic aldehydes and ketones.

Table VI. Approximate retention and response increments caused by addition of structural units

Structural unit [a]	MU^{Me}	[C + O + N] [b]	ΔMU	0.3 [π + OMe] [b]	RMR [b]
$-CH_2-$	1.0	1	0.0	0.0	1
$(Ar)-OCH_3$	2.0	2	0.4	0.3	0.5
$(R,Ar)-OSiMe_3$	3.5	4	-0.2	0.0	2.5
$(R,Ar)-COOSiMe_3$	5.0	6	0.3	0.3	3
$(Ar)-CH{=}NOSiMe_3$	5.5	6	0.2	0.3	3
$(Ar)-CH{=}NOCH_3$	4.0	4	0.6	0.6	1
(Ar)-CH=CH-(R) (trans)	3.0	2	0.4	0.3	2
(Ar)-Cl	1.5	--	0.2	--	-0.5
o-position [c]	-0.5	--	0.0	--	0
sec.-pos. of $(R)-OSiMe_3$ [d]	-1.0	--	-0.3	--	0

[a] Terminal units replace a hydrogen atom. [b] Predicted MU, ΔMU, and RMR values (cf. Tables I-V). [c] Except with chloro and small alkyl substituents. [d] Resulting from introduction of $(R)-OSiMe_3$, $(R)-COOSiMe_3$, or alkyl groups.

left and to the right, respectively, of the genuine chlorophenols. A few compounds (not marked), e.g., the arylalkenoic acids, fall outside the patterns indicated in Figures 1-2 because they contain exceptional structural elements with special effects on MU^{Me} and ΔMU.

Tentatively deduced structures should be checked by calculating approximate MU^{Me} and ΔMU values. This can be done from reference data of related compounds by adding increments according to Table VI or according to increments observed with related structural changes. Thus, retention differences such as those caused by changes between the three frequently occurring 4-hydroxy, 4-hydroxy-3-methoxy, and 3,4-dihydroxy substitution patterns can be predicted with a very high accuracy because of the low mutual effects between these substituents and an aliphatic side-chain. Previously, methods for calculating similar retention index data have been described for both aliphatic (11) and aromatic (12) compounds.

With the aldehydes and ketones, *O*-methyl oxime as well as *O*-Me_3Si oxime protecting groups improve analytical results and prevent ambiguous formation of enol derivatives from ketones. Both *syn* and *anti* isomers of the oximes are formed, but data are given only for the predominant isomer. The amount of the other isomer is very small with the aldehydes but may amount to 10% for the ketone *O*-Me_3Si oximes and at least twice as much for the ketone *O*-methyl oximes. The MU values are typically 0.4-0.8 units lower than those of the major isomer on both columns. This fact as well as the relation between isomer ratio and steric strain demonstrate that the major isomer has the phenyl moiety and the OMe or $OSiMe_3$ group on the opposite sides of the double bond. The lower amount of the minor isomer, the favourable combination with analysis of carbohydrate-related compounds (8), and the higher molar response speak in favour of the use of *O*-Me_3Si oximes. The *O*-methyl oximes may well provide better separations for special applications, however, as can be predicted by the data given. Analysis by both methods is very useful for sorting out compounds containing aldehydo and keto groups.

For final identifications of phenolic compounds, mass spectrometry in combination with gas chromatography is extremely useful. The molecular weight is easily obtained and several specific fragmentations exist (9,13). However, as demonstrated above, GLC alone is a powerful and readily accessible tool for qualitative analysis.

Quantitative Analysis

The reliability of quantitative determinations was found to depend on several factors. Losses of phenolic acids before silylation by formation of intermolecular esters during drying of isolated samples are avoided by initial conversion of the acids to sodium salts. All derivatives prepared were protected against moisture as previously described (8). On gas chromatography, Me_3Si ethers and oximes were more stable than Me_3Si esters. The esters having a methylene group adjacent to the ester group and particularly the esters of the 3-arylpropenoic (cinnamic) acids were the most labile derivatives. Previous studies (14) have demonstrated that even the cinnamic acids in very small amounts can be satisfactorily determined on packed columns. On routine analysis, progressively greater percent losses were observed when the amount of sample was decreased in the 0.1 mg range, particularly with the least stable derivatives and with impure samples. Indications of impaired quantitative results on analysis of impure samples and pyridine solutions were obtained. The low-viscosity OV-101 and SP-2250 stationary phases were chosen for good performance with early eluted compounds. When programming to as much as 240°, the OV-17 phenyl silicone was preferred to SP-2250 for routine applications because of an observed somewhat slower deterioration on prolonged use. Compared to isothermal analysis, particular attention had to be paid to septum bleeding and decompositions in the heated (~240°C) injector.

If losses during derivatization and chromatography are avoided, the quantitative results depend primarily on the response factors used. Accurate experimental determinations of such factors are often difficult and laborious because the degree of purity of the reference samples must be determined. The value of these factors is also questionable since experimental conditions influence the response of the flame ioniza-

tion detector. Hence, relative molar response (RMR) values which can be estimated empirically from molecular structure offer an attractive alternative. The molecular weight or the number of carbon atoms gives a good approximation of RMR when the content of heteroatoms is low. The effect of added oxygen (15), nitrogen (16), and chlorine (17) atoms is to reduce RMR whereas the effect of silicon in Me_3Si derivatives (18) is small. Estimation of RMR as the number of carbon atoms minus half the number of oxygen, nitrogen, and chlorine atoms (Tables I-V) was considered to be the best compromise between accuracy and simplicity for the compounds included in this study. Experimental determinations of RMR values for a few compounds belonging to different structural categories indicated values within ±5% of those predicted. All Me_3Si groups should contribute similarly to RMR and reduce the relative importance of irregular contributions to RMR from individual structural features. It is also emphasized that the large contribution to RMR from the Me_3Si groups results in a high detection sensitivity for the phenolic compounds studied.

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