

PAPER CHROMATOGRAPHY AND CHEMICAL STRUCTURE

IV. INTRAMOLECULAR HYDROGEN BONDING

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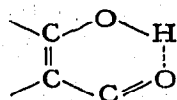
INTRODUCTION

In a previous communication¹, we discussed some of the structural factors in molecules that are responsible for constitutive effects on R_M . One of these was considered to be internal hydrogen bonding and in this communication we wish to present a more detailed study of this phenomenon. The fact that hydrogen bonding or chelation influences chromatographic behaviour was observed for the first time by BATE-SMITH AND WESTALL², who noted that, where it occurred, there was a deviation from MARTIN'S equation³. We have already discussed¹ the relation of internal hydrogen bonding to the *ortho*-effect, in which it may play a prominent part. Such *ortho*-effects, predominantly of the hydrogen bond type, can be observed in the chromatographic data of many workers: it is sufficient to quote FRANC⁴ on the amino-anthraquinones and hydroxy-anthraquinones and LATINAK⁵ on hydroxy-naphthalene derivatives, whose work gives many illustrations of the phenomenon.

Although, therefore, there are many empirical observations on the effect of internal hydrogen bond on R_M , there does not appear to have been any more theoretical or quantitative approach to the subject. In order to study the effect of internal hydrogen bonding it is essential—as in other types of chromatographic study—to isolate it from other simultaneous and complicating factors. This is not always easy, as hydrogen bonding between two groups must partly depend on their steric interaction. In aromatic systems in particular, internal hydrogen bonding may affect and be affected by electronic factors. If it were possible, however, to isolate the effect of hydrogen bonding in a series of compounds in which the strength of the bond is known to vary in a predictable manner, it might then be possible to study the quantitative relationship between the degree of bonding and R_M . Since internal hydrogen bonding increases the solubility of organic compounds in non-polar solvents and decreases their solubility in polar solvents the relationship can be studied to advantage in a reversed phase system, where problems of adsorption (which might profoundly influence hydrogen bonding) are minimized.

The classic, and in many ways the simplest and definitive, case of hydrogen bonding occurs in the 6-atom system shown schematically below (I). This system is present in the enolic form of β -diketones and in *o*-substituted aromatic hydroxy-aldehydes and hydroxy-esters. It has been shown by several workers that the strength of chelation in such a system is dependent on the existence of a high degree of conju-

gation in the chelate ring. Under these conditions, stabilization of the chelate ring through resonance forms is possible—a concept first put forward in different terms by ROBINSON⁶ and confirmed and illustrated by the work of BAKER⁷ on the resacetophenones. More recently, HUNSBERGER and his co-workers⁸⁻¹¹ were able to demonstrate that a roughly quantitative correlation exists between the degree of hydrogen



(I)

bonding in *o*-substituted hydroxy-aldehydes, hydroxy-ketones and hydroxy-esters and the double bond character of the double bond bearing the two chelated groups. They did this by studying the relative shift of the (C=O) bond in the infra-red spectra of the hydroxy compounds, with and without the second *ortho*-substituent. They found that the magnitude of this shift, $\Delta\nu(\text{C}=\text{O})$, increased as the double bond character of the double bond increased. One way, therefore, of investigating the quantitative effect of internal hydrogen bonding on R_M would be to study a series of compounds such as was used by HUNSBERGER, in which the constitutive ΔR_M effects could be related to the double bond character of the double bond bearing the chelated groups. A series of hydroxy-aldehydes, hydroxy-esters, and parent phenols and aldehydes were chromatographed for this investigation.

EXPERIMENTAL

Compounds

These were either obtained commercially or prepared according to the methods of HUNSBERGER⁸⁻¹¹.

Chromatography

Sheets of Whatman No. 4 paper, 23 × 57 cm, were impregnated with a 10% (v/v) solution of olive oil in light petroleum (40–60°). The mobile phase was dry methanol. The chromatograms were developed by the descending technique for 4 h, during which time the front migrated about 42 cm. Chromatography was also carried out by the tankless horizontal method of GREEN AND MARCINKIEWICZ¹², which gave rather better results with volatile compounds such as salicylaldehyde. The R_M values obtained by the two methods did not differ by more than ± 0.01 and the results in Table I represent mean values from three runs by the descending method and one run by the horizontal method.

Visualization

Phenols were located by spraying with aqueous sodium carbonate (5% w/v) and then diazotised *o*-dianisidine.

RESULTS AND DISCUSSION

Table I gives the R_F and R_M values of a series of phenols and the corresponding *o*-hydroxy-aldehydes derived from them. Table II gives results for three hydroxy-esters. $\Delta R_M(\text{CHO})$ and $\Delta R_M(\text{COOCH}_3)$ are the increments due to the introduction of either

TABLE I
 R_F^* AND R_M VALUES OF PHENOLS AND *o*-HYDROXY-ALDEHYDES AND
 CALCULATED $\Delta R_M(\text{CHO})$ INCREMENTS

Parent phenol and <i>o</i> -hydroxy-aldehyde	R_F	R_M	$\Delta R_M(\text{CHO})$	Relevant bond in corresponding hydrocarbon
Phenol	0.81	-0.628		
Salicylaldehyde	0.77	-0.523	+ 0.105	Benzene
1-Naphthol**	0.73	-0.420		
1-Hydroxy-2-naphthaldehyde	0.54	-0.074	+ 0.346	1,2 in naphthalene
2-Naphthol**	0.73	-0.420		
2-Hydroxy-1-naphthaldehyde	0.51	-0.020	+ 0.400	1,2 in naphthalene
2-Naphthol**	0.73	-0.420		
2-Hydroxy-3-naphthaldehyde	0.69	-0.347	-0.073	2,3 in naphthalene
9-Phenanthrol	0.62	-0.208		
9-Hydroxy-10-phenanthraldehyde	0.27	+ 0.438	+ 0.646	9,10 in phenanthrene
3,4-Xylenol	0.75	-0.486		
6-Hydroxy-3,4-xylaldehyde	0.66	-0.290	+ 0.196	4,5 in <i>o</i> -xylene
5-Indanol	0.73	-0.420		
6-Hydroxy-5-indanecarboxaldehyde	0.62	-0.202	+ 0.218	5,6 in indane
6-Tetralol	0.69	-0.342		
3-Hydroxy-5,6,7,8-tetrahydro-2-naphthaldehyde	0.59	-0.156	+ 0.186	6,7 in tetralin

* R_F values were calculated from the R_M values¹.

** No *ortho*-effect in the naphthols was observed in this system.

the CHO group or the COOCH₃ group into each phenol. It will be seen that these ΔR_M values vary greatly, depending on the nature of the phenol and, in particular, the nature of the double bond bearing the chelate ring. In Fig. 1, therefore, $\Delta R_M(\text{CHO})$ and $\Delta R_M(\text{COOCH}_3)$ are plotted against $\Delta\nu(\text{C}=\text{O})$ as determined for the infra-red shift of the carbonyl band in the same series of compounds by HUNSBERGER and co-workers⁸⁻¹¹.

TABLE II
 R_F^* AND R_M VALUES OF AROMATIC HYDROXY-ESTERS AND PHENOLS
 AND CALCULATED $\Delta R_M(\text{COOCH}_3)$ INCREMENTS

Compound	R_F	R_M	$\Delta R_M(\text{COOCH}_3)$	Relevant bond in corresponding hydrocarbon
Phenol	0.81	-0.628		
Methyl salicylate	0.50	0.000	+ 0.628	Benzene
1-Naphthol	0.73	-0.420		
Methyl 1-hydroxy-2-naphthoate	0.32	+ 0.335	+ 0.755	1,2 in naphthalene
2-Naphthol	0.73	-0.420		
Methyl 2-hydroxy-3-naphthoate	0.425	+ 0.133	+ 0.553	2,3 in naphthalene

* R_F values were calculated from the R_M values¹.

With the exception of the $\Delta R_M(\text{CHO})$ values for 6-tetralol and 3,4-xylenol, the chromatographic data fit the infra-red data well, and this applies not only to the hydroxy-aldehydes (Fig. 1a) but also to the three aromatic hydroxy-esters (Fig. 1b). The $\Delta R_M(\text{CHO})$ values for 6-tetralol, 5-indanol and 3,4-xylenol are in fact all similar and the difference between them is not much greater than experimental error. These results are remarkably similar to those for the infra-red shift, as shown by HUNSBERGER *et al.*¹¹, leaving little doubt that essentially the same phenomenon is under study. Their conclusions, in agreement with ours, were that there is a negligible amount of bond fixation in the ground-state of either indane or tetralin, indicating that there is no appreciable MILLS-NIXON effect in these molecules. However, the $\Delta R_M(\text{CHO})$ values for 6-tetralol, 5-indanol and 3,4-xylenol are somewhat greater than $\Delta R_M(\text{CHO})$ for phenol itself. This seems to indicate that the intramolecular hydrogen bond may

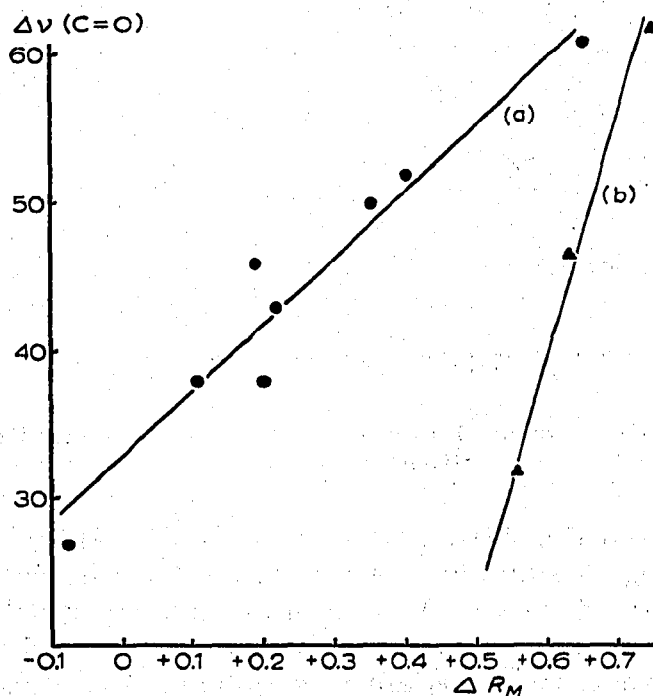


Fig. 1. Relationship between (a) $\Delta R_M(\text{CHO})$ and (b) $\Delta R_M(\text{COOCH}_3)$ and $\Delta\nu(\text{C}=\text{O})$ in the infra-red spectra of *o*-substituted hydroxy-aldehydes and hydroxy-esters.

be at least slightly affected by alkyl substitution in the aromatic ring (the two methyl groups in *o*-xylene are formally similar to the $\alpha\text{-CH}_2$ groups in tetralin). On the basis of chromatographic and infra-red evidence, however, it is not possible to decide whether this difference is due to different bond orders and free valencies in alkylated benzenes or to a difference in charge distribution (inductive effect of alkyl groups).

In Fig. 2 we have plotted the $\Delta R_M(\text{CHO})$ and $\Delta R_M(\text{COOCH}_3)$ values against the bond order of the relevant individual bond in the corresponding hydrocarbon (given in Tables I and II), calculated by the molecular orbital method (L.C.A.O. approximation¹³). The values for indane, tetralin and *o*-xylene are not included, as their bond orders cannot be calculated. The close approach to linearity in both series of compounds provides the strongest evidence (a) that the partition coefficient of these *o*-hydroxy compounds varies directly with the bond order of the bond bearing the

chelate ring, and (b) *in extenso*, that intramolecular hydrogen bonding is directly related in such compounds to relevant bond order. It will be observed that the slope of the plot for the hydroxy-esters is greater than that for the aldehydes. This indicates that chelation is rather stronger in the aldehydes: this could be expected, in view of the greater electronic density on the carbonyl oxygen in these compounds.

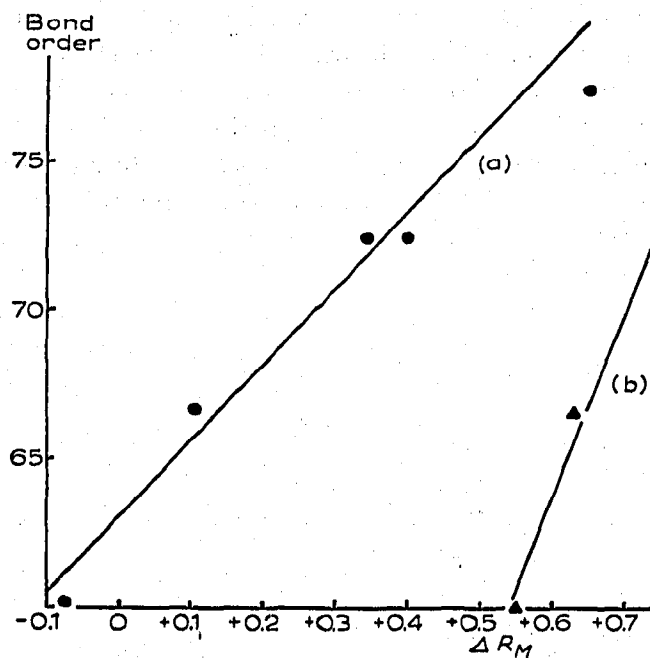
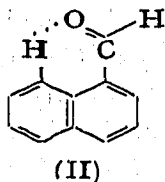


Fig. 2. Relationship between (a) $\Delta R_M(\text{CHO})$ and (b) $\Delta R_M(\text{COOCH}_3)$ and relevant bond order in corresponding hydrocarbon for *o*-substituted hydroxy-aldehydes and hydroxy-esters.

The difference between the $\Delta R_M(\text{CHO})$ values for 1-naphthol and 2-naphthol is 0.054. A somewhat analogous difference was also observed in the infra-red studies of HUNSBERGER⁸, who obtained $\Delta\nu(\text{C}=\text{O}) = 50$ and 52 respectively for the two compounds. What accounts for the chromatographic difference (and hence the difference in hydrogen bonding) in these two substances, which are both substituted on the same double bond? HUNSBERGER *et al.*¹¹ postulated that a slight difference in hydrogen bonding was produced by "a steric facilitation of chelation due to the proximity of the *peri*-CH in the naphthalene nucleus". On this hypothesis, the *peri*-CH group is assumed to exert a greater steric effect on the bulkier CHO group in the 1-position than it does when the OH group is in this position. MARCINKIEWICZ AND GREEN¹⁴ showed by a molecular orbital treatment that the difference might be due, not to a steric factor,



but to the different free valencies in positions 1 and 2 of the naphthalene nucleus. That this might be so is further supported by the chromatographic data. 1-Naphthal-

dehyde and 2-naphthaldehyde were run in the same system as the hydroxy-aldehydes and had R_M values of -0.143 and -0.217 , respectively. The difference between them is almost identical with that between the two hydroxy-aldehydes. Now, since in this system the steric *ortho*-effect seems to be negligible (*cf.* the two naphthols, which have identical R_F values), the R_M difference between 1- and 2-naphthaldehydes seems to be due to another reason. This may be competitive intramolecular hydrogen bond formation between the CHO group and the *peri*-CH group, as shown above (II), a process that would be facilitated by the difference in the free valencies of the carbon atoms at positions 1 and 2 in naphthalene.

SUMMARY

The constitutive effects of intramolecular hydrogen bonding on the chromatography of aromatic *o*-hydroxy-aldehydes and *o*-hydroxy-esters have been studied. It is shown that the degree of hydrogen bonding between the two *ortho*-groups as indicated by the shifts $\Delta\nu(\text{C}=\text{O})$ in the infra-red spectra of the compounds can be quantitatively correlated with the values of $\Delta R_M(\text{CHO})$ or $\Delta R_M(\text{COOCH}_3)$ found by comparing the R_M values of the compounds with those of the parent phenols. Both the chromatographic and infra-red effects can be related to the bond order of the double bond (in the parent hydrocarbon) bearing the two chelating groups. Intramolecular hydrogen bonding is an important factor affecting the precise theoretical calculation of R_M . This study provides an example of how such a constitutive effect can be evaluated.

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