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CHEMICAL CONSTITUTION AND CHROMATOGRAPHIC BEHAVIOR

INFLUENCE OF ISOMERIC AND STEREOISOMERIC CONSTITUTIONS
ON THE CHROMATOGRAPHIC MIGRATION

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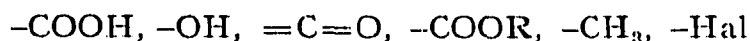
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SUMMARY

The thin-layer chromatographic behavior of an organic compound is not only determined by the size of the molecule, nature and number of functional groups, and number of double bonds, but it is also influenced by the geometric arrangement of the atoms, the functional groups, etc. within the molecule. It is therefore possible to separate *cis/trans* isomers from each other. Compounds with a *syn* and *anti* configuration are also separable. Another example of this is the thin-layer chromatographic separation of compounds with *endo/exo* arrangements and molecules which have functional groups either in an equatorial or axial position.

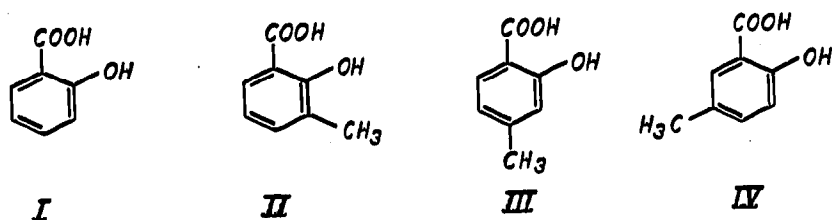
INTRODUCTION

The adsorption chromatographic behavior of organic compounds is determined by a series of factors such as the number, type and position of the substituents in the molecule, the presence of double bonds and the conformation of the molecules. BROCKMANN AND VOLPERS¹ discovered that the more conjugated double bonds present in a compound the more strongly is it adsorbed, and that the functional groups contained in a molecule can be arranged in the following order of decreasing adsorption:



Similar to these observations made by BROCKMANN AND VOLPERS on mono-substituted aromatics (BROCKMANN rules) a certain order has been noted in the adsorption behavior of pyridine compounds² and sulfur heterocycles³. The α -, β - and γ -substituted pyridines react differently, as can be gathered from Table I.

When aromatic compounds contain two or more strongly polar groups, these determine their chromatographic behavior; further addition of a methyl group has no effect. So the R_f value (73) of salicylic acid (I) obtained by thin-layer chromatography (TLC) on silica gel with methyl alcohol as the solvent does not differ from those



of the isomeric cresotic acids (II–IV) formed by methyl substitution (R_F values 72, 73 and 73, respectively)⁴.

However, the case is different with phenols. For example, with isomeric xylenols (dimethylphenols) the neighboring positions of the methyl groups and the phenolic hydroxyl group influences the adsorption affinity due to steric hindrance⁵. When both positions adjacent to the hydroxyl group in the molecule are substituted, this isomer travels further than those isomers that have only one substituent in the position *ortho* to the hydroxyl group. When finally the positions adjacent to the hydroxyl are not substituted, the adsorption is further intensified.

TABLE I

ADSORPTION OF PYRIDINE DERIVATIVES
Solvent: ethyl acetate.

<i>Position of substituents</i>	<i>Decreasing adsorption</i>
	α $-\text{COOH}$, $-\text{OH}$, $-\text{CH}_2\text{OH}$, $-\text{NH}_2$, $-\text{CH}_3$, $-\text{CHO}$, $-\text{Hal}$
	β $-\text{COOH}$, $-\text{CH}_2\text{OH}$, $-\text{NH}_2$, $-\text{OH}$, $-\text{CHO}$, $-\text{CH}_3$, $-\text{Hal}$
	γ $-\text{OH}$, $-\text{COOH}$, $-\text{NH}_2$, $-\text{CH}_2\text{OH}$, $-\text{CH}_3$, $-\text{CHO}$

On the other hand, a hydroxyl group with an *ortho* nitro group may form hydrogen bondings which profoundly reduce the adsorption affinity of these compounds (*ortho* effect). This means that the R_F value rises conspicuously in comparison with the *para*-substituted compound. The amino group can also form hydrogen bondings; this is obviously the case in *o*-nitraniline⁶.

THE INFLUENCE OF HYPERCONJUGATION

The TLC behavior of isomeric picolines (methylpyridines) is quite interesting. With ethyl acetate as a solvent they travel in the order β -, α - and γ -picoline. The

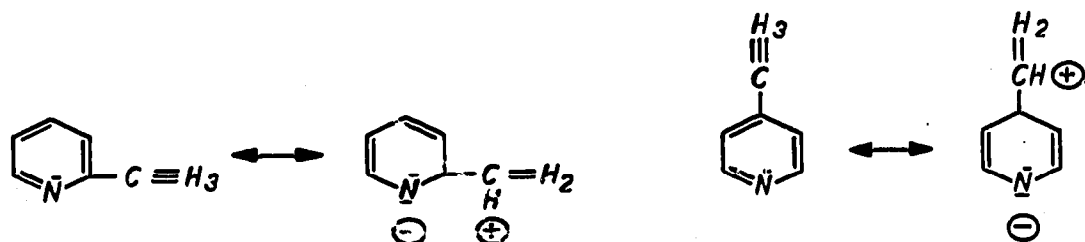


Fig. 1. Hyperconjugation of α - and γ -picoline.

compounds substituted with a methyl group in the α - or γ -positions thus have a higher adsorption affinity. Compared with β -picoline they also show a better reactivity. The reason for this behavior is the occurrence of hyperconjugation which obviously influences the chromatographic adsorption (Fig. 1). The bond between the alkyl carbon and the ring carbon assumes the character of a double bond⁷.

BEHAVIOR OF ISOMERIC UNSATURATED COMPOUNDS

Silica gel layers impregnated with silver nitrate yield good separations of isomeric unsaturated hydrocarbons. As shown by Fig. 2 the isomeric safrol(V) and isosafrol(VI) can likewise be separated⁸. The different position of the double bond located in the side chain of the isomers results in different complex bonds with the silver ions.

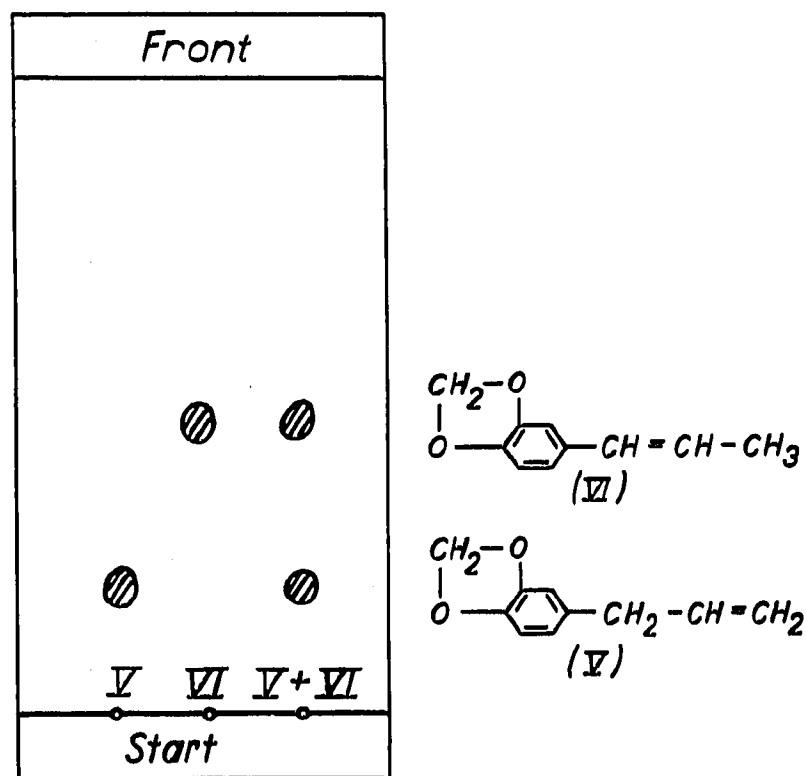


Fig. 2. TLC of safrol (V) and isosafrol (VI) on silica gel impregnated with AgNO_3 . Solvent system: benzene-cyclohexane (1:1).

LAWRENCE⁹ studied the ability of unsaturated terpene hydrocarbons to form π -complexes with silver ions and drew the following possible conclusions:

(1) Cyclic terpenes with single internal double bonds do not readily form π -complexes.

(2) Cyclic or acyclic terpenes with two non-terminal double bonds do not readily form π -complexes unless the double bonds are *cis* conjugated.

(3) Cyclic or acyclic terpenes with *exo*-cyclic or terminal double bonds do form π -complexes.

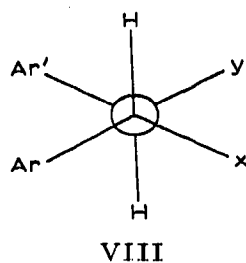
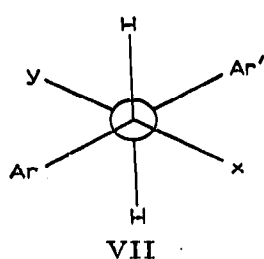
INFLUENCE OF DIFFERENT KINDS OF ISOMERISM

We have studied the different chromatographic behavior of *cis/trans* isomeric compounds^{6,10,11} on thin layers and found that the *trans* compounds always migrate faster than the *cis* compounds, *viz.* maleic acid < fumaric acid, *cis*-stilbene < *trans*-stilbene, and *cis*-azobenzene < *trans*-azobenzene.

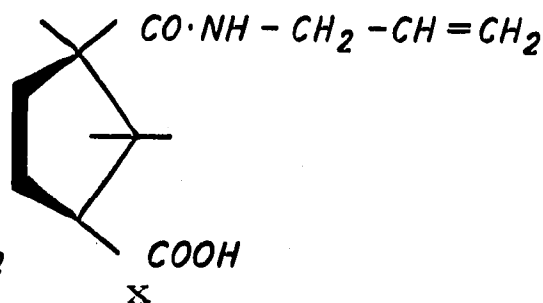
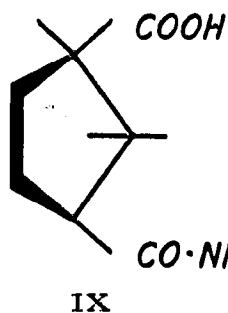
Good separations of the inorganic *cis/trans* isomeric cobalt complexes are possible¹². Here the *cis* forms always migrate faster than the corresponding *trans* forms.

Analogously to the *cis/trans* isomerism of the C=C double bond, the two possible stereoisomeric compounds with C=N double bonds are called the *syn* and *anti* forms. The reaction between aldehydes and asymmetrical ketones and hydroxylamine forms such isomers, called oximes, which can be separated by TLC¹³. In the case of benzaldehyde and its derivatives all *syn* isomers had higher R_F values than the *anti* isomers. On the other hand, with the condensation derivatives of benzaldehyde (*i.e.*, "oin"-oximes, benzoin oximes, anisoin oximes) all *syn* isomers displayed smaller R_F values than the *anti* isomers.

PALAMAREVA *et al.*¹⁴ used TLC as a method for assigning the relative configurations to various pairs of aliphatic diastereoisomeric compounds of the type Ar-CH(X)-CH(Y)-Ar', where X and Y are polar groups, and Ar and Ar' are phenyl- or *m*- or *p*-alkoxy-substituted phenyl groups. In all cases they found that the *erythro* isomers (VII) have higher R_F values than the corresponding *threo* isomers (VIII), irrespective of the polarity of the developing solvents and of the formation of an intramolecular hydrogen bond between X and Y.

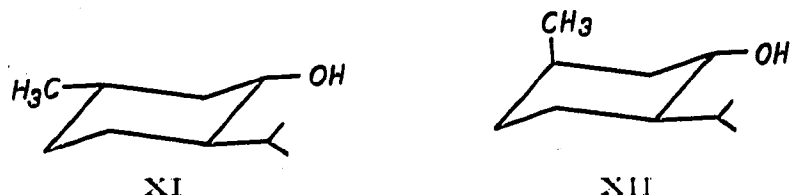


HENEIN AND DAVID¹⁵ succeeded in separating the α - and β -structural isomers of N-alkyl-*dl*-camphoric acid (IX and X, respectively). The β -structure showed a higher adsorption affinity. This example again demonstrates the importance of the carboxyl group with regard to adsorption affinity. In the case of the β -isomer the carboxyl group has no other substituent on the carbon atom in the neighboring position.



INFLUENCE OF CONFORMATION

The TLC behavior of the stereoisomeric menthols is fundamentally influenced by the position of the hydroxyl group, which is equatorial in menthol (XI) and isomenthol (XII) and axial in neomenthol (XIII) and neoisomenthol (XIV). The molecules with equatorial hydroxyl groups showed a higher adsorption affinity with benzene as a solvent. The effect of the methyl group which is equatorial in menthol and neomenthol and axial in isomenthol and neoisomenthol is of less importance. The influence of the hydroxyl group can be eliminated by letting it react with 3,5-



dinitrobenzoic acid to form the respective dinitrobenzoate. This then increases the influence of the methyl group on the chromatographic behavior^{10,17}.

The chlorinated stereoisomeric hydrocarbons aldrin (XV) and isodrin (XVI) also behave very differently on being chromatographed due to their different conformation (Fig. 3)¹⁸. The difference exists in the position of the methylene bridge, which has an *endo-exo* position in aldrin and an *endo-endo* position in isodrin. It could be

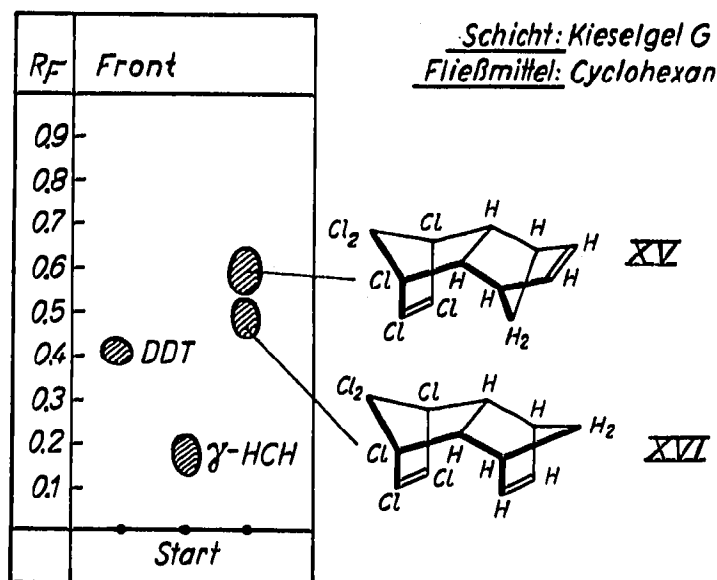


Fig. 3. TLC of aldrin (XV) and isodrin (XVI) on Kieselgel G. Solvent: cyclohexane.

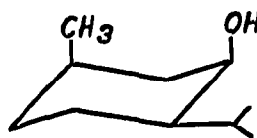
said that the C=C double bonds in aldrin have a *trans* position, thus aldrin has a higher R_F value than isodrin.

The uniplanar arrangement of the rings is typical of all polycyclic aromatics. When such compounds are partially hydrogenated, this uniplanar structure of the ring carbon atoms is upset. As can be gathered from the structural formula (XVII) one of the aromatic rings is distorted out of the uniplanar level when the C=C

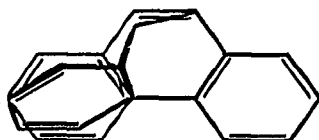
double bond in the 9,10-position of phenanthrene is hydrogenated. 9,10-Dihydroanthracene (XVIII) also assumes a conformation which places the aromatic rings at angles to each other. Two independent aromatic systems are formed as a result of hydrogenation. The adsorption affinity of the dihydro compounds is additionally influenced by the resulting conformation of the molecules¹⁰.



XIII



XIV



XVII



XVIII

This influence can clearly be revealed by the chromatographic analysis of the pair anthracene/dihydroanthracene. Anthracene has the higher R_F value and can easily be separated from the dihydro compound. A corresponding test with phenanthrene/dihydrophenanthrene showed a similar result, the difference in the R_F values, however, being less pronounced.

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