

RELATION BETWEEN THE STRUCTURE AND THE CHROMATOGRAPHIC BEHAVIOUR OF FURAN, PYRROLE AND THIOPHENE DERIVATIVES

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A comparison of the number of papers concerned with the paper chromatography of aromatic and heterocyclic compounds, shows that those dealing with heterocyclic compounds are decidedly in the minority. The same fact applies to studies of the chromatographic behaviour of these compounds in relation to their structure. The situation is, in general, rendered more difficult by the circumstance that no profound conclusions can be drawn from a study of the chromatographic behaviour of arbitrarily chosen compounds, the structures of which are only similar to a limited extent.

Recently we had the opportunity of studying the chromatographic behaviour of several mono- and dicarboxylic acids derived from furan, pyrrole and thiophene and in the present paper we have attempted to explain some of the phenomena and relations observed.

EXPERIMENTAL PART

The chromatographic separation of the acids given in Table I was effected by the descending technique on Schleicher & Schüll paper 2045b (very slow). The acids were applied on the starting point as pyridine solution, quantities of about 25 μg being

TABLE I

R_F VALUES OF MONO- AND DICARBOXYLIC ACIDS

Solvent system: *n*-butanol-ethanol-pyridine-water (3:1:1:1). Paper: Schleicher & Schüll 2045b.
Temp.: 20° \pm 0.5°.

<i>Acid</i>	<i>R_F</i>	<i>(R_F)_{BA} - R'_F*</i>	<i>(R_F)_{MA} - (R_F)_{DA}*</i>
Benzoic	0.59		
Terephthalic	0.215		0.375
Furan-2-carboxylic	0.30	0.21	
Furan-2,5-dicarboxylic	0.063		0.42**
Thiophene-2-carboxylic	0.46	0.05	
Thiophene-2,5-dicarboxylic	0.10		0.44**
Pyrrole-2-carboxylic	0.41	0.10	
2,5-Dimethylpyrrole-3,4-dicarboxylic	0.17		0.40***

* BA = benzoic acid; MA = monocarboxylic acid; DA = dicarboxylic acid.

** For all differences between the *R_F* values, which lie outside an *R_F* range of 0.16-0.84, the calculation of the *R_M* function was used.

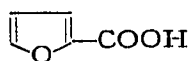
*** = CH- increments (+ 0.08) added.

used. The chromatograms were developed with a butanol-ethanol-pyridine-water mixture (3:1:1:1) for a period of 16-17 hours. Detection was carried out by spraying the chromatograms with a saturated aqueous solution of 2,6-dichlorophenol-indophenol; the acids give pink spots on a blue background.

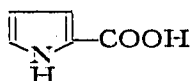
In order to prevent variations in the R_F values, the chromatographic procedure was performed in a room where the temperature was kept constant. The R_F values given in Table I are averages of the values obtained from 10 selected chromatograms.

RESULTS AND DISCUSSION

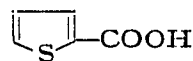
As can be seen in Table I two aromatic acids—benzoic acid and terephthalic acid—were also chromatographed besides the heterocyclic acids. This was done in order to study the differences between the heterocyclic and aromatic nucleus. First, the monocarboxylic acids were compared. The R_F values of these acids increased in the following order: furan-2-carboxylic acid (I), pyrrole-2-carboxylic acid (II), thiophene-2-carboxylic acid (III), benzoic acid.



I



II



III

All the above-mentioned heterocyclic acids have one =CH- group less than benzoic acid. Previously we had computed¹ that each additional =CH- group causes an increase in the R_F value of about 0.08 unit in the solvent system used. Therefore, for an adequate comparison this increment should be added to the R_F values of all the heterocyclic acids. In this way a modified value R'_F , is obtained:

	R'_F
Thiophene-2-carboxylic acid	0.54
Pyrrole-2-carboxylic acid	0.49
Furan-2-carboxylic acid	0.38

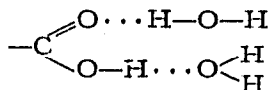
On comparing these calculated values with the R_F value of benzoic acid (0.59), it is evident that thiophene-2-carboxylic acid exhibits the most pronounced "aromatic" character. This observation is in full agreement with the data of other authors^{2,3}, who have studied the electron structure of thiophene derivatives. The R_F values of the other acids decrease in a certain order. This decrease in the R_F value can be explained in the same way as the chromatographic separation of similar derivatives, which differ in that they form intermolecular hydrogen bonds of various energy content with the stationary phase. It is known that bonds of the type O-H...O have the highest energy levels; those of the O-H...N type come next and those of the O-H...S type have the lowest energy. On comparing the differences $(R_F)_{\text{benzoic acid}} - R'_F$ (given in Table I), it is evident that they can be arranged in the same order as the energy levels of the hydrogen bonds of these different types. If the previously calculated chromatographic equivalent of the hydrogen bond $R_E = 1.3 \pm 0.1$ kcal/mol (this value corresponds to the change in R_M that occurs if the

chelate-bond energy is varied by 1.3 ± 0.1 kcal/mol)⁴ is used in the calculation of these energy levels, the following values of the bond energy are obtained:

O-H...O	5.5 ± 0.5 kcal/mol
O...H-N	2.6 ± 0.3 kcal/mol
O-H...S	1.3 ± 0.1 kcal/mol

These values are in good agreement with the data obtained by another method⁵.

Next, the behaviour of the dicarboxylic acids was studied. The introduction of another -COOH group into the molecule gives rise to a considerable decrease in the R_F value. Calculation of the differences between the R_F values of mono- and dicarboxylic acids (see Table I) shows that these differences are practically constant. The average difference (0.41) is in very good agreement with prior observations for another group of aromatic acids¹. If we examine this value more closely, we find that it is nearly twice as great as that computed for the difference between the R'_F value of furan-2-carboxylic acid and the R_F of benzoic acid, *i.e.* it corresponds to two hydrogen bonds of the O-H...O type:



It is possible to make a further comparison, namely between dicarboxylic acids. For purposes of calculation the increment for one =CH- group (+ 0.08) is again added to the R_F values; thus the following values are obtained:

	R'_F
Furan-2,5-dicarboxylic acid	0.09
2,5-Dimethylpyrrole-3,4-dicarboxylic acid	0.12
Thiophene-2,5-dicarboxylic acid	0.14

The same calculation as in the case of the monocarboxylic acids (*i.e.* comparing these data with the R_F value of terephthalic acid) leads to the following results:

O-H...O	ΔR_F 0.23	5.95 ± 0.6 kcal/mol
O...H-N	ΔR_F 0.14	3.6 ± 0.4 kcal/mol
O-H...S	ΔR_F 0.11	2.8 ± 0.3 kcal/mol

Whereas the energy of an intermolecular hydrogen bond O-H...O of furan-2,5-dicarboxylic acid is, on the whole, the same as that of the monocarboxylic acid, this value is somewhat increased in the case of pyrroledicarboxylic acid. In the case of thiophene-2,5-dicarboxylic acid, however, a substantial increase is observed (to approximately twice the value). The only explanation for this phenomenon would seem to be the same that KESWANI AND FREISER⁶ suggested for the fact that the observed dipole moments of thiophenealdehyde and acetylthiophene were greater than the values calculated by the vector method. According to these authors the difference is caused by the resonance effect. In this case, the negative electrical charge at the sulphur atom increases as well, so that the energy of the intermolecular hydrogen bond rises.

Further, we shall discuss the possibility of making a rough estimation of the

bond angles of carboxylic groups. In one of our preceding papers we deduced a relation between the chromatographic behaviour and the dipole moments of aromatic isomers⁷:

$$R_F = K - 0.1 \mu \quad \text{for an } R_F \text{ range of } 0.16 - 0.84$$

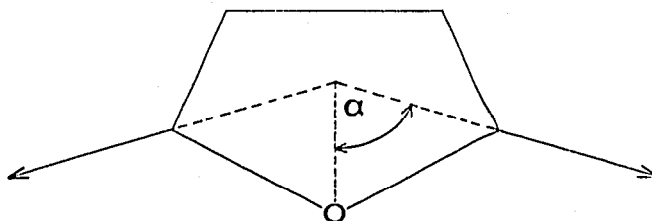
and

$$R_M = C + 2.3 \log \frac{1 + 0.1 \mu}{1 - 0.1 \mu}$$

If we assume that the two carboxyl groups of terephthalic acid are so arranged that they form an angle of 180° , then if the angle between the carboxyl groups of furan-2,5-dicarboxylic acid were also 180° , the difference between the dipole moments of furan-2-carboxylic acid and furan-2,5-dicarboxylic acid would be the same as that between benzoic acid and terephthalic acid. In the case of furan-2,5-dicarboxylic acid, however, this angle must evidently have another value and, consequently, the difference between the dipole moments cannot be the same. The dipole moment of furan-2,5-dicarboxylic acid can be calculated as the vector sum of the dipole moments of the functional groups, with the formula

$$\mu = 2 \cos \alpha \cdot \mu'$$

in which μ' designates the contribution of the group dipole moments to the total dipole moment of the molecule.



By calculating μ from the equation $R_F = K - 0.1 \mu$ and substituting for μ' the value 1.7, we find that $2\alpha = 144^\circ$. If we assume that the R_F value is determined with an accuracy of ± 0.01 , then the error in the estimation of the angle will be $\pm 7^\circ$.

If we assume that the carboxyl group divides the corresponding $-O-C=C-$ angle into two equal parts and use the data obtained by SCHOMAKER AND PAULING⁸, for the calculation of the furan angle, the same value for 2α is obtained. A similar calculation can also be made for thiophene-2,5-dicarboxylic acid. The dipole moment calculated in this case is lower than the one found; this fact can also be explained by the above-mentioned resonance effect.

With this example we have attempted to show what relations may be revealed by comparing a few R_F values if suitable series of similar compounds are chosen. However, it need not be pointed out that the accuracy in determining the R_F values should be as high as possible.

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SUMMARY

The chromatographic behaviour of mono- and dicarboxylic acids derived from benzene, furan, pyrrole, and thiophene has been studied. The energy levels of intermolecular hydrogen bonds of heterocyclic acids have been estimated and an attempt has been made to calculate the bond angles of furan-2,5-dicarboxylic acid.

REFERENCES

- ¹ J. FRANC, *Collection Czechoslov. Chem. Commun.*, 23 (1958) 655.
- ² H. C. LONGUET-HIGGINS, *Trans. Faraday Soc.*, 45 (1949) 173.
- ³ H. D. HARTOUGH, *Thiophene and its Derivatives*, Interscience Publishers, Inc., New York, 1952.
- ⁴ J. FRANC, *Collection Czechoslov. Chem. Commun.*, 22 (1957) 995; *Z. Elektrochem.*, 61 (1957) 1069.
- ⁵ L. PAULING, *The Nature of the Chemical Bond*, Cornell University Press, New York, 1948.
- ⁶ R. KESWANI AND H. FREISER, *J. Am. Chem. Soc.*, 71 (1949) 1789; *J. Am. Chem. Soc.*, 71 (1949) 218.
- ⁷ J. FRANC AND J. LATINÁK, *Collection Czechoslov. Chem. Commun.*, 20 (1955) 817, 826, 830.
- ⁸ K. SCHOMAKER AND L. PAULING, *J. Am. Chem. Soc.*, 61 (1939) 1769.

J. Chromatog., 3 (1960) 317-321