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Separation of carbethoxymethylpyrroles by thin-layer chromatography

The separation by thin-layer chromatography (TLC) of alkyl carbethoxypyrroles and carboxylic acid pyrroles has received little attention[1,2]. During a study on alkylation[3] and Hantzsch synthesis[4] of pyrroles a large number of α- and β-carbetoxyalkylpyrroles were prepared. In this paper we report a TLC procedure which allows the separation of α- and β-carbethoxymethylpyrroles.

Material and methods

The details of the preparation and structural identification of various methylcarbethoxypyrroles used in this investigation are reported elsewhere[3-6]. A suspension of 30 g of Silica Gel G (E. Merck, Darmstadt) in 60 ml water was spread on glass plates 20 × 20 cm to a thickness of 250 μ with a Desaga applicator. The plates were dried at 105–110° for 30 min and stored in a desiccator. A 0.1% solution of the compounds in methanol was prepared and 2 μg of each compound was spotted 2 cm from the edge of the plate. The plate was then developed with 150 ml of the solvent system ether–*n*-hexane containing 2% glacial acetic acid (1:1). Usually 45 min were required for the solvent to travel a distance of 12–15 cm. The plates were then dried, sprayed with Ehrlich reagent[7] and after keeping for 5 min at 100° the pyrroles appeared as red, pink, brown, blue and violet spots.

Results and discussion

Several solvent systems such as ethyl acetate–benzene, benzene–methanol, chloroform–acetone, chloroform–ethyl acetate and ether–*n*-hexane containing 2% glacial acetic acid, in various proportions were tried. Also many supports such as Silica Gel G, alumina, kieselguhr and cellulose were tried. Only the mixture ether–*n*-hexane containing 2% glacial acetic acid (1:1) on Silica Gel G gave good separation.

Three main groups of compounds were studied, namely: monomethyl carbethoxypyrroles; dimethyl carbethoxypyrroles; and trimethyl carbethoxypyrroles.

Monomethyl carbethoxypyrroles. The R_F values of monomethyl carbethoxy-

TABLE I

SEPARATION OF MONOMETHYL CARBETHOXYPYRROLES BY TLC

Solvent system used: ether–*n*-hexane containing 2% glacial acetic acid (1:1).

Compounds		$R_F \times 100$	*Colour with Ehrlich*
No.	*Name*		
1	2-Methyl-3-carbethoxypyrrole	54	violet
2	3-Methyl-4-carbethoxypyrrole	54	blue
3	2-Methyl-5-carbethoxypyrrole	70	pink
4	3-Methyl-2-carbethoxypyrrole	70	violet
5	2-Methyl-3,5-dicarbethoxypyrrole	62	pink
6	3-Methyl-2,5-dicarbethoxypyrrole	70	pink
7	2-Methyl-3-carbmethoxypyrrole	54	violet
8	2-Methyl-3-carbobenzoxypyrrole	54	blue
9	2-Methyl-3-*tert.*-carbutoxypyrrole	66	violet

pyrroles are shown in Table I. The α-carbethoxy monomethylpyrroles are readily separated from the corresponding β-carbethoxy monomethylpyrroles in this system. Thus the α-carbethoxy compounds (3 and 4) are readily separated from the β-carbethoxy compounds (1 and 2). Separations are not possible between the individual α-carbethoxy monomethylpyrroles nor between individual β-carbethoxy monomethylpyrroles. Among the monomethyl dicarbethoxypyrroles, 2-methyl-3,5-dicarbethoxypyrrole(5) has an R_F value intermediate between α-carbethoxy monomethyl- and β-carbethoxy monomethylpyrroles. The α-dicarbethoxymonomethylpyrrole (6) has an R_F value similar to α-carbethoxy monomethylpyrrole. Replacement of a 3-carbethoxy substituent (1) by a *tert.*-butoxyester (9) decreases the polarity of the compound and results in an increased R_F value. The 3-carbmethoxy monomethyl- (7) and 3-carbobenzoxy monomethylpyrrole (8) have the same R_F values as 3-carbethoxy monomethylpyrrole (1).

Dimethyl carbethoxypyrroles. The α-carbethoxy dimethylpyrroles (10–12) have higher R_F values than the β-carbethoxy dimethylpyrroles (14,15) (Table II) and are readily separable. Individual α-carbethoxy dimethyl isomers are not separable.

TABLE II

SEPARATION OF DIMETHYL CARBETHOXYPYRROLES BY TLC

Solvent system used: ether–*n*-hexane containing 2% glacial acetic acid (1:1).

Compounds		$R_F \times 100$	*Colour with Ehrlich*
No.	*Name*		
10	2,3-Dimethyl-5-carbethoxypyrrole	70	brown
11	2,4-Dimethyl-5-carbethoxypyrrole	70	pink
12	3,4-Dimethyl-5-carbethoxypyrrole	70	blue
13	3,4-Dimethyl-2,5-dicarbethoxypyrrole	70	pink
14	2,4-Dimethyl-3-carbethoxypyrrole	62	red
15	2,5-Dimethyl-3-carbethoxypyrrole	54	brown
16	2,4-Dimethyl-3,5-dicarbethoxypyrrole	62	pink

Among β-carbethoxy dimethylpyrroles, 2,4-dimethyl-3-carbethoxypyrrole (14) has a higher R_F value than 2,5-dimethyl-3-carbethoxypyrrole (15), and the compounds are separable. Among dimethyl dicarbethoxypyrroles, compounds with carbethoxy groups in the α- and β-positions (16) have R_F values intermediate between α-carbethoxy dimethyl- and β-carbethoxy dimethylpyrroles. On the other hand dimethyl dicarbethoxypyrroles with two carbethoxy groups in the α-position (13) have similar R_F values to dimethylpyrroles with one α-carbethoxy substituent (10–12).

Trimethyl carbethoxypyrroles. In this series there are only two isomers (Table III) the α- and β-carbethoxy trimethylpyrroles. The α-carbethoxy trimethylpyrrole (17) has a higher R_F value than the β-carbethoxy trimethylpyrrole (18).

The α-carbethoxy group is more strongly conjugated with the pyrrole ring than the β-carbethoxy group[8], which makes the former less polar and hence move faster. This is the reason why the methyl substituted pyrroles with α-carbethoxy substituents can be separated from the corresponding β-carbethoxy methylpyrroles. Replacement of a 3-carbethoxy group (1) by a *tert.*-butylester group (9) makes the compound less polar and hence move faster. Pyrroles with one β-carbethoxy group containing one

TABLE III

SEPARATION OF TRIMETHYL CARBETHOXYPYRROLES BY TLC

Solvent system used: ether–*n*-hexane containing 2% glacial acetic acid (1:1).

Compounds		$R_F \times 100$	*Colour with Ehrlich*
No.	*Name*		
17	2,3,4-Trimethyl-5-carbethoxypyrrole	70	pink
18	2,4,5-Trimethyl-3-carbethoxypyrrole	62	pink

methyl group in position 2 or 3 can be separated from pyrroles with one β-carbethoxy group containing two methyl substituents in position 2, 4 or three methyl groups in position 2,4,5. Methyl pyrroles with carbethoxy groups in α- and α'-positions have the same R_F value as mono α-carbethoxy methylpyrroles. Methylpyrroles with carbethoxy groups in both α- and β-positions have R_F values intermediate between α-carbethoxy methyl and β-carbethoxy methylpyrroles.

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1 L. CHIERICI AND M. PERANI, *Ric. Sci., Sez. A.*, 6 (1964) 168.
2 M. PIATTELLI, E. FALTORUSSO AND S. MAGNO, *Rend. Accad. Sci. Fis. Mat. Naples*, 28 (1961) 165.
3 M. W. ROOMI AND S. F. MACDONALD, *Can. J. Chem.*, 48 (1970) 139.
4 M. W. ROOMI AND S. F. MACDONALD, *Can. J. Chem.*, 48 (1970) 1689.
5 H. FISCHER AND H. ORTH, *Die Chemie des Pyrroles*, Vol. 1, Akad. Verlag, Leipzig, 1934.
6 M. W. ROOMI AND H. DUGAS, *Can. J. Chem.*, 48 (1970) 2303.
7 J. E. FALK, *Porphyrins and Metalloporphyrins*, Elsevier, Amsterdam, 1964, p. 160.
8 R. A. JONES, *Advan. Heterocycl. Chem.*, 11 (1970) 383.

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