Comparative Study On Chiral Separation Of Pyrethroic Acids with Amino and Neutral Cyclodextrine Derivatives

Cârje Anca Gabriela[1], Juvancz Z.[2], Iványi R.[3], Schurig V.[4], Tőkés B.[1]

[1] Departament of Physical Chemistry, Faculty of Pharmacy, University of Medicine and Pharmacy, Târgu Mureş
[2] Departament of Environmental Engineering Tech Polytehnical Institution, Budapest, Hungary
[3] Cyclolab cyclodextrin R&D, Budapest, Hungary
[4] University of Tübingen, Institute of Organic Chemistry, Germany

Background: Pyrethroids are used as synthetic insecticides. They have more intensive effects than pyrethrum acid, or natural analogues found in the flowers of Chrysanthenum cinerariaefolium (Fam. Asteraceae). In the pyrethroic acids, both the geometric and chiral isomerisms appear as cumulated, therefore these compounds can be successfully used to study chiral separation.
The **aim** of the study was to separate by means of positively ionizable selector: permethyl- monoamino-β-cyclodextrin (PMMAβCD), monoamino-β-cyclodextrin (MAβCD) and other neutral β-cyclodextrin derivatives, the enatiomers and diastereomers of permethrinic, deltamethrinic and chrysanthemic pyrethroic acids.
Methods: Pyrethroic acids studied were chrysanthenum, permethrynic and deltamethrinic with pKa values 5,1±0,4. As chiral selectors, we used cyclodextrins: permethyl-monoamino-β-cyclodextrin(PMMAβCD) and monoamino-β-cyclodextrin(MAβCD) particularly the positively charged cyclodextrins. Experiments were carried out on a Hewlett Packard ^{3D}CE system (Hewlett Packard, Waldbronn, Germany) with diode array UV detector at 25 °C. To characterise the separation of enantiomers we used resolution values R_s (calculated by half-width method).
Results: The PMMAβCD at 15 mM is an effective chiral separation agent for pyrethroic acids as it can fully separate all isomers of chrysanthemic, permethrinic and deltamethrinic acids with the exception of trans chrysanthemic acid which was only partially separated.
Conclusion: The best chiral separation agent toward pyrethroic acids studied was found to be permethyl-momoamino-β-cyclodextrin (PMMAβCD). The cis isomers show higher selectivity than trans isomers in the ionized form of acids. Our results show that dissociation alone can not fully explain the appearance of experimental curves, should take into consideration stereochemistry contributions.

Keywords: pyrethroic acids, chiral selector, permethyl-momoamino-β-cyclodextrin (PMMAβCD), monoamino-β-cyclodextrin (MAβCD)

Introduction

Pyrethroic acids used as synthetic insecticide have more intensive effect than pyrethrum acid, or natural analogues derived from chrysanthemum flowers. They have high toxicity to bees and fish, but low to mammalians [1]. In their structure there are two chiral centers (1, 3), and the cis(Z) and trans (E) isomerisms mean the steric arrangement of groups introduced in positions 1 and 3 relative to the cyclopropane plane. Of course, both the chiral centers can adopt R or S configuration (Figure 1).

Diastereomers are called cis/trans isomers according to the relative configuration of the carboxyl and substituted alkene (e.g. dimethyl-, dichloro-, dibromo-vinyl) groups on the cyclopropane ring. These acids are frequently esterified with optically active alcohols, like cypermethrin, cyfluthrin, creating additional stereoisomers. The 1R-cis and 1R-trans isomers of acids show much more effective insecticidal activity than the other isomers. The acidic and alcoholic mixture are frequently analyzed separately because the large number of enantiomers which makes difficult to separate every isomer in ester form. Capillary electrophoresis seems to be an ideal method for the chiral analysis of pyrethroic acids due to its high efficiency and good compatibility to ionic analytes in the chiral analysis of these multicomponent acids. Cyclodextrins were used as chiral selectors and particularly the positively charged cyclodextrins showed good results. When the selectors and selectands are oppositely charged, their mobility difference is higher than if only one partner would have a charge and the other would be neutral, or if both had the same increment in their charges [2,3].

Material and methods

The chemicals were purchased from Sigma-Aldrich Chemie Gmbh (Steinheim, Germany) and used without any further purification. Pyrethroic acids (chrysanthemum, permethrynic and deltamethrinic acids) were donated by Department of Organic Chemical Technology, Budapest University of Technology and Economics. The pK_a values of these acids ranged 5,1±0,4 [2].

CE experiments were carried out on a Hewlett Packard ^{3D}CE system (Hewlett Packard, Waldbronn, Germany) with diode array UV detector at 25 °C. Uncoated fused-silica capillaries (FSOT) 58.5 cm (50 effective length) x 50 μm I.D. (375 μm O.D.) (Composite Metal Services Ltd., Worcestershire, UK) were used within this study.

Capillary was flushed with water before every analysis, then with 0,1 M NaOH, and again with water for 2 minutes and finally with the running buffer for 5 min.

For all CE experiments, the initial background electrolyte (BGE) consisted of 40 mM boric, acetic and phos-

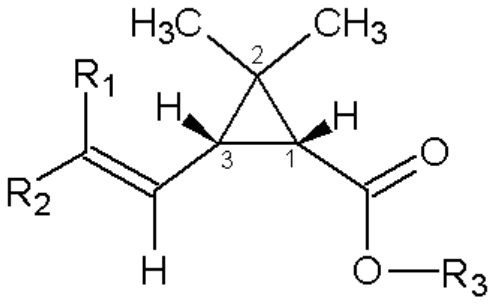

Fig. 1. Chemical structure of pyrethroid acids

phoric acid buffers in ratio of 1:2:2 (Britton-Robinson). The exact pH values of BGEs were adjusted with 0,1 m NaOH solution. 15 mM of PMMAβCD was dissolved in the BGE. The final running buffers and sample solutions were filtered through a 0.22 µm Millex-GV syringe filter (Millipore, Bedford, USA) and sonicated for 10 minutes. Methanolic solution (1 mg/ml of samples) was dissolved in the running buffer. Injections was made in the anodic end of capillary using 150 mbar*s, the separation potential was 30 kV, and the analytes were recorded at 202 and 220 nm.For characterization of the separation of enantiomers we used resolution values (Rs) [1].

Results

The best chiral separation agent toward pyrethroic acids studied was found to be permethyl-momoamino-β-cyclodextrin (PMMAβCD). The apolar character and amino group in its structure PMMβCD offers a stable EOF in cathodic direction. The best efficiency values were found to be at high pH values, where the analytes are ionized and the PMMAβCD is neutral. Efficiency decreases slightly when both analytes and selectors are ionized. The lowest efficiency values were observed when the analytes are neutral and selectors are ionized, at low pH values because of the apolar character of protonated pyrethroic acids. The wall adsorption was avoided because of good solubilizing character of methoxy mixture of PMMAβCD even in protonated form of acids [1].

Enantiomers with low selectivity show high efficiency of the system and also good resolution values. The high selectivity of PMMAbCD gives higher resolution in several cases [4].

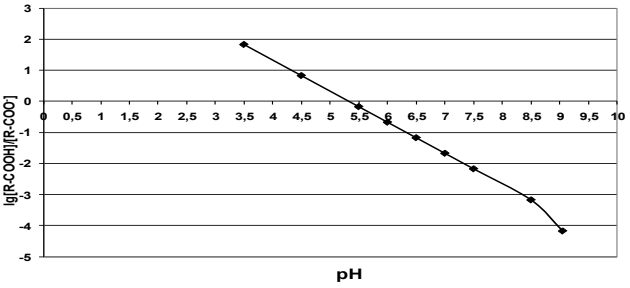

Fig. 3. The (pH, lg[R-COOH]/lg[R-COO-]) of cis-permethrinic acid (0.34 mM) with PMMAβCD selector (15 mM)

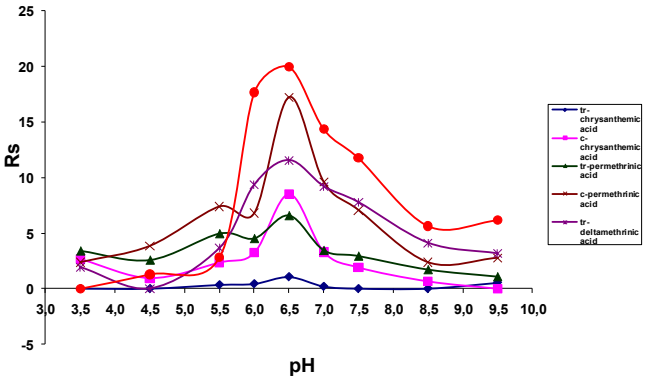

Fig. 2. The (pH, Rs) curves of pyrethroid acids with PMMβCD selector (15 mM)

We noticed that the resolution optimum was found at pH 6.5 for a mixture which contained all studied pyrethroic acids at 15 mM concentration of chiral selector PMMAbCD.

The best resolution was obtained in case of cis-deltamethrinic acid, Rs = 20.0 and the worst was trans chrysantemic acid Rs = 1.10. It is clear that cis isomers show higher selectivity than trans isomers in the ionized form of acids (Figure 2).

Since the best separation occurred at 15 mM PMMAbCD we calculated protonated form/deprotonated form ratio for cis-permethrinic acid 0.34 mM (Figure 3).

$$R - COOH \Longleftrightarrow H^+ + R - COO^-$$

$$Ka = \frac{[R - COO^-][H^+]}{[R - COOH]}$$

$$\lg \frac{[R - COOH]}{[R - COO^-]} = pKa - pH$$

We calculated following the same reasoning, the protonated form/deprotonated form ratio for the two cyclodextrins studied: PMMAβCD (pKa = 9.05) and MAβCD (pKa = 8.70) both at 15 mM concentration at all pH values (Figure 4-5).

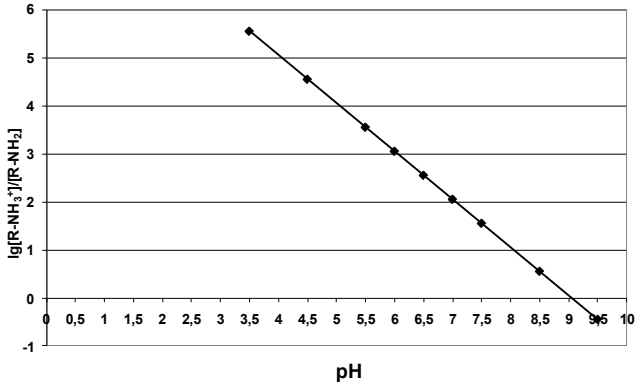

Fig. 4. The (pH,lg[R-NH3+]/lg[R-NH2]) of cis permethrinic acid (0.34 mM) with PMMAβCD selector (15 mM)

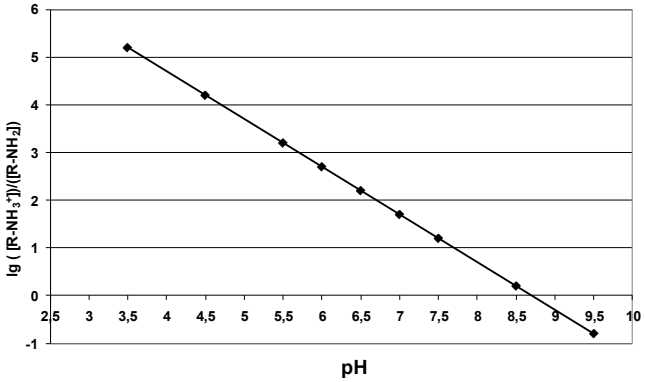

Fig. 5. The (pH, lg[R-NH_3+]/lg[R-NH_2]) of cis permethrinic acid (0.34 mM) with MAβCD selector (15 mM)

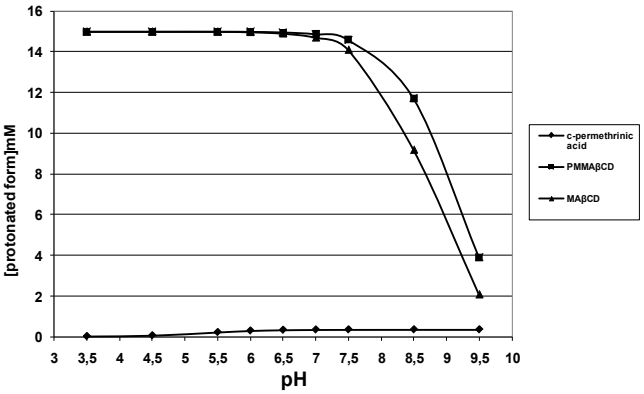

Fig. 6. The (pH, [protonated form]mM) of cis permethrinic acid (0.34 mM), PMMAβCD selector (15 mM) and MAβCD selector (15 mM)

Discussions

Knowing the value of $\frac{[R-COOH]}{[R-COO^-]}$ and [R-COOH]+[R-COO-] = 0.34 mM we calculated [R-COO-] at all pH values for cis-permethrimic acid, pKa = 5.32 [1,5]. Following the same reasoning we calculated for both the chiral selectors used (PMMAβCD and MAβCD) the concentration of protonated form [R-NH_3^+] [1,3].

Figure 6 shows that the charged forms reach their limit values (higher, respectively lower) between pH 6–7. At 6.5 pH value, the amount of protonated form of the amino groups decreases abruptly, but there remains enough for the quantities of dissociated acid interact with cations. The graphs show that dissociation alone can not fully explain the appearance of experimental curves, therefore one stereochemistry contributions should be taken into consideration.

Conclusions

The PMMAβCD at 15 mM is an effective chiral separation agent for pyrethroic acids. It can fully separate all isomers of chrysanthemic, permethrinic and deltamethrinic acids with the exception of trans chrysanthemic acid which was only partially separated.

In the acid dissociation of pyrethroids a very important role is played by steric factors, confirmed by low values of resolution obtained in the case of MAβCD, athough it dissociates similarly to PMMAβCD.

References

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