

Short Communication

Determination of dissociation constants of aromatic carboxylic acids by ion chromatography

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ABSTRACT

The method for the numerical analysis of the substituent effect on the retention times of substituted benzoate anions in ion chromatography was applied to that of substituted naphthoate anions in order to determine the dissociation constants of several aromatic carboxylic acids. The C-5–C-8 part of naphthalene was postulated as a substituent of benzoate, and the *steric effect index* and the *positional effect correction index* of the substituent were determined. Finally, the dissociation constants of substituted naphthoic acids were determined.

INTRODUCTION

The determination of the dissociation constants of large aromatic carboxylic acids, such as substituted naphthoic acids, by using titrimetric or electrochemical methods is very difficult because these acids have a hydrophobic naphthalene structure and low solubility in water.

In high-performance liquid chromatography (HPLC), it is well known that the elution behaviours of monoprotic acidic or basic sample species can be expressed as functions of the dissociation constants (K_a) of the respective species [1–5], and this relationship is often used for the optimization of chromatographic conditions or the determination of the pK_a values of sample species [2,5–8]. In ion chromatography

(IC), similar relationships and applications have been reported [9,10]. However, in these methods, the pK_a values cannot be determined without many chromatographic measurements using different eluent pH conditions.

In a previous paper [11], we investigated numerically the elution behaviours of substituted benzoate anions in IC. It was found that the analysis of the substituent effect on the retention times of these anions can be performed by dividing the effect into three terms: an “LFER-applicable effect term”, a “steric effect term” and a “positional effect correction term”. The first is expressed as a function of pK_a , the second as a function of the kind and number of substituents and the third as a function of the position of the substituents.

In this work, the numerical analysis method was applied to the interpretation of the elution behaviours of substituted naphthoate anions in IC by postulating $-(CH)_4-$, which is shown in

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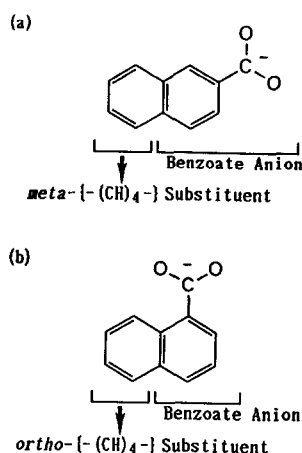


Fig. 1. Definition of $-(CH)_4-$. (a) 2-Naphthoic acid [m - $-(CH)_4-$]; (b) 1-naphthoic acid [o - $-(CH)_4-$].

Fig. 1, as a *substituent* of benzoate. Also, the dissociation constants of substituted naphthoic acids and anthracene-9-carboxylic acid were determined by the numerical analysis methods and by measurement under only a single eluent condition.

TABLE I

SUBSTITUTED BENZOIC AND NAPHTHOIC ACIDS USED IN THIS STUDY AND THEIR RETENTION TIMES

Eluent: 100 mM Tris-HCl (pH 7.0).

| No. | Compound | pK_a (25°C) [12] | IC-Anion-PW column | | IC-Anion-SW column | |
|-----|------------------------------|--------------------------|--------------------|------------|--------------------|------------|
| | | | t'_R (min) | Log t'_R | t'_R (min) | Log t'_R |
| 1 | Benzoic acid | 4.20 | 1.35 | 0.130 | 3.28 | 0.516 |
| 2 | <i>o</i> -Chlorobenzoic acid | 2.88 | 1.16 | 0.064 | 2.45 | 0.389 |
| 3 | <i>m</i> -Chlorobenzoic acid | 3.83 | 5.30 | 0.724 | 6.79 | 0.832 |
| 4 | <i>p</i> -Chlorobenzoic acid | 3.99 | 5.13 | 0.710 | 5.91 | 0.772 |
| 5 | 2,4-Dichlorobenzoic acid | 2.68 ^a | 3.89 | 0.590 | 4.20 | 0.623 |
| 6 | 2,5-Dichlorobenzoic acid | 2.47 ^a | 3.66 | 0.563 | 4.13 | 0.616 |
| 7 | 2,6-Dichlorobenzoic acid | 1.59 ^a | 1.46 | 0.164 | 2.47 | 0.393 |
| 8 | 3,4-Dichlorobenzoic acid | 3.64 ^b | 18.81 | 1.274 | 12.37 | 1.092 |
| 9 | 1-Naphthoic acid | 3.70 | 5.40 | 0.732 | 9.59 | 0.982 |
| 10 | 2-Naphthoic acid | 4.16 | 16.14 | 1.208 | 27.34 | 1.437 |
| 11 | Anthracene-9-carboxylic acid | 3.65 | 25.54 | 1.407 | 40.17 | 1.604 |
| 12 | 2-Hydroxy-1-naphthoic acid | 3.29 | 96.88 | 1.986 | 72.41 | 1.860 |
| 13 | 1-Hydroxy-2-naphthoic acid | — | 169.52 | 2.229 | 129.07 | 2.111 |
| 14 | 3-Hydroxy-2-naphthoic acid | 2.71 ^c | 124.40 | 2.095 | 88.56 | 1.947 |
| 15 | 3-Amino-2-naphthoic acid | — | 19.11 | 1.281 | 27.91 | 1.446 |

^a Ref. 13.

^b Ref. 14.

^c Ref. 15.

EXPERIMENTAL

Apparatus

A Tosoh HLC-601 ion chromatography system was used. For the retentions of the anions, a column (50 mm × 4.6 mm I.D.) packed with Tosoh TSKgel IC-Anion-PW (polymethacrylate gel base, particle size 10 μm, capacity 0.03 mequiv./g) or Tosoh TSKgel IC-Anion-SW (silica gel base, particle size 5 μm, capacity 0.4 mequiv./g) was used. The flow-rate was maintained at 1.0 ml/min under a pressure of 20–50 kg/cm². The column was placed in an oven set at 30°C. The peaks were detected with a Tosoh UV-8 Model II ultraviolet detector at a wavelength of 254 nm and recorded with a Shimadzu Chromatopack C-R1A recorder.

Eluents

A stock solution of 1 M hydrochloric acid was prepared by diluting the concentrated acid and a stock solution of 1 M tris(hydroxymethyl)-aminomethane (Tris) was prepared by dissolving

the reagent in distilled water. The eluent (100 mM Tris–HCl, pH 7.0) was prepared by mixing these stock solutions with distilled water and deaerating the mixture.

Sample solutions

The substituted benzoates and naphthoates used in this study are shown in Table I [12–15]. Each stock solution (20 mM) of these sodium salts was prepared by dissolving the compound in distilled water or by neutralizing the acid with aqueous sodium hydroxide solution. Working solutions (0.2 mM) were prepared by diluting the stock solutions with distilled water.

Calculation of retention indices and determination of dissociation constants

In a previous paper [11], we reported that the retention times [$t'_R(\text{R})$] of substituted benzoates (RCOO^-) can be expressed as follows:

$$\begin{aligned} \log t'_R(\text{R}) &= A + (-\rho')\text{p}K_a(\text{R}) \\ &+ \left(\sum_j n_{X_j} i'_{X_j} + \sum_j n_{o-X_j} i''_{o-X_j} \right. \\ &+ \left. \sum_j n_{p-X_j} i''_{p-X_j} + \sum_j n_{X_j X_j} i''_{X_j X_j} \right) \\ &= A + (-\rho')\text{p}K_a(\text{R}) \\ &+ i'_{\text{Cl}} \left(\sum_j n_{X_j} j'_{X_j} + \sum_j n_{o-X_j} j''_{o-X_j} \right. \\ &+ \left. \sum_j n_{p-X_j} j''_{p-X_j} + \sum_j n_{X_j X_j} j''_{X_j X_j} \right) \quad (1) \end{aligned}$$

where

A = a constant determined by the experimental conditions;

$-\rho'$ = an “LFER-applicable effect constant”;

i'_{X_j} = an “adjusted steric effect factor” of substituent X_j ;

i''_{o-X_j} , i''_{p-X_j} , $i''_{X_j X_j}$ = “adjusted positional effect correction factors” of *ortho*- X_j , *para*- X_j and neighbouring X_j and X_j substituent(s), respectively;

n_{X_j} , n_{o-X_j} , n_{p-X_j} , $n_{X_j X_j}$ = the number of respective substituent(s);

j'_{X_j} ($= i'_{X_j}/i'_{\text{Cl}}$) = a “steric effect index” of X_j ;
 j''_{o-X_j} , j''_{p-X_j} , $j''_{X_j X_j}$ ($= i''_{o-X_j}/i'_{\text{Cl}}$, $i''_{p-X_j}/i'_{\text{Cl}}$, $i''_{X_j X_j}/i'_{\text{Cl}}$) = “positional effect correction indices” of the respective substituent(s).

We consider that this equation should also be applicable to the determination of the retention times of substituted naphthoates by using $i'_{-(\text{CH})_4-}$, $i''_{o-(\text{CH})_4-}$, $j'_{-(\text{CH})_4-}$ and $j''_{o-(\text{CH})_4-}$.

The values of A , $-\rho'$ and i'_{Cl} were regressively calculated from the retention times of Cl-substituted benzoate by using eqn. 1 and by neglecting $i''_{o-\text{Cl}}$, $i''_{p-\text{Cl}}$ and $i''_{\text{Cl}-\text{Cl}}$. The values of $i'_{-(\text{CH})_4-}$, $i''_{o-(\text{CH})_4-}$, $j'_{-(\text{CH})_4-}$ and $j''_{o-(\text{CH})_4-}$ were calculated from the retention times of 2- and 1-naphthoates by substituting the above-calculated values into eqn. 1. The method of calculation is detailed under Experimental in ref. 11. The $\text{p}K_a$ values of substituted naphthoates were determined by substituting these indices into eqn. 1.

RESULTS AND DISCUSSION

Calculation of $j'_{-(\text{CH})_4-}$ and $j''_{o-(\text{CH})_4-}$

Table I shows the retention times of the

TABLE II

THE CALCULATED VALUES OF THE FACTORS AND INDICES

Eluent: 100 mM Tris–HCl (pH 7.0).

| Factor or index | IC-Anion-PW column ^a | IC-Anion-SW column ^b |
|--------------------------|---------------------------------|---------------------------------|
| i'_{Cl} | 0.705 | 0.363 |
| $i'_{(\text{CH})_4-}$ | 1.087 | 0.932 |
| $i''_{o-(\text{CH})_4-}$ | -0.217 | -0.293 |
| j'_{Cl} | 1.000 ^c | 1.000 ^c |
| $j'_{-(\text{CH})_4-}$ | 1.542 | 2.567 |
| $j''_{o-(\text{CH})_4-}$ | -0.308 | -0.807 |
| j''_{OH} | 0.265 ^d | 0.446 ^d |
| $j''_{o-\text{OH}}$ | 1.945 ^d | 2.185 ^d |
| j''_{NH_2} | -0.700 ^d | -0.723 ^d |
| $j''_{o-\text{NH}_2}$ | 0.345 ^d | 0.257 ^d |

^a $A = -2.217$, $-\rho' = 0.562$.

^b $A = -0.959$, $-\rho' = 0.352$.

^c Defined as unity.

^d Ref. 11.

TABLE III

COMPARISON BETWEEN THE pK_a VALUES OF THE SUBSTITUTED NAPHTHOIC ACIDS DETERMINED BY THIS METHOD AND THOSE IN THE LITERATURE

| No. | Compound | This method | | | Literature |
|-----|------------------------------|--------------------|--------------------|-----------------|------------------------|
| | | IC-Anion-PW column | IC-Anion-SW column | Mean value | |
| 11 | Anthracene-9-carboxylic acid | 3.35 | 3.65 | 3.50 ± 0.15 | 3.65 [12] |
| 12 | 2-Hydroxy-1-naphthoic acid | 3.16 | 3.48 | 3.32 ± 0.16 | 3.29 [12] |
| 13 | 1-Hydroxy-2-naphthoic acid | 3.20 | 3.36 | 3.28 ± 0.08 | — |
| 14 | 3-Hydroxy-2-naphthoic acid | 2.97 | 2.89 | 2.93 ± 0.04 | 2.71 [15] |
| 15 | 3-Amino-2-naphthoic acid | 4.74 | 4.67 | 4.71 ± 0.04 | 4.56 [10] ^a |

^a Determined by ion chromatography with change of eluent pH [10]. Eluent: 50 mM Tris-HBr (pH 3.00-7.00). Column: IC-Anion-SW. Standard sample: γ -resorcylic acid ($pK_a = 1.30$ [12]).

substitution benzoate and naphthoate anions. By using the data for entries 1-8 in Table I, the values of A , $-\rho'$ and i'_{Cl} were regressively calculated as -2.217 , 0.562 and 0.705 , respectively, on IC-Anion-PW and -0.959 , 0.352 and 0.363 , respectively, on IC-Anion-SW. By using these values and the data for entries 9 and 10 in Table I, the values of $i'_{-(CH)_4-}$, $i''_{o-(CH)_4-}$, $j'_{-(CH)_4-}$ and $j''_{o-(CH)_4-}$ were calculated and are given in Table II with several previously reported indices [11].

Determination of the dissociation constants

By substituting the constants and indices shown in Table II into eqn. 1, the dissociation constants of several substituted naphthoic acids were calculated. Table III compares the dissociation constants of the acids determined by this method and those in the literature [10,12,15]. The pK_a values were similar to each other. Some discrepancies between the values obtained from the indices for IC-Anion-PW and those for IC-Anion-SW seem to be due to errors caused by the regressive calculations. From the results, it was concluded that this method is very effective for determining the pK_a values of large aromatic carboxylic acids, such as substituted naphthoic acids. The pK_a values of 1-hydroxy-2-naphthoic acid and 3-amino-2-naphthoic acid were determined as 3.28 ± 0.08 and 4.71 ± 0.04 , respectively.

This method is very useful because the pK_a values can be determined by measuring the t'_R values under any eluent conditions, and it is effective for the simultaneous determination of the pK_a values of many compounds having similar structures.

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