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# Resolution prediction and optimization of temperature programme in comprehensive two-dimensional gas chromatography

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**Abstract**

A model is developed for predicting the resolution of interested component pair and calculating the optimum temperature programming condition in the comprehensive two-dimensional gas chromatography (GC × GC). Based on at least three isothermal runs, retention times and the peak widths at half-height on both dimensions are predicted for any kind of linear temperature-programmed run on the first dimension and isothermal runs on the second dimension. The calculation of the optimum temperature programming condition is based on the prediction of the resolution of "difficult-to-separate components" in a given mixture. The resolution of all the neighboring peaks on the first dimension is obtained by the predicted retention time and peak width on the first dimension, the resolution on the second dimension is calculated only for the adjacent components with un-enough resolution on the first dimension and eluted within a same modulation period on the second dimension. The optimum temperature programming condition is acquired when the resolutions of all components of interest by GC × GC separation meet the analytical requirement and the analysis time is the shortest. The validity of the model has been proven by using it to predict and optimize GC × GC temperature programming condition of an alkylpyridine mixture.


*Keywords:* Comprehensive two-dimensional gas chromatography; Resolution prediction; Optimization; Temperature program

## 1. Introduction

Comprehensive two-dimensional gas chromatography (GC × GC) is a multidimensional chromatographic technique, which was pioneered by Phillips and co-workers [1,2]. It has been demonstrated as a powerful tool for complex mixtures analysis [3–9]. The GC × GC separation is obtained by combining two columns with different separation mechanisms in series by means of a modulator. Compounds are first separated on a high-resolution capillary column under temperature programming conditions. The effluent of the first column is then focused in very small fractions and re-injected into the second column in very short time intervals. This second column is shorter and narrower to realize fast GC separation. The separation speed of the second column is so high that it is effectively operated under isothermal conditions. In general, both columns are located in one GC oven, and the temperature influences the separations in both dimensions simultaneously.

The purpose of optimizing chromatographic parameters is to achieve acceptable resolution in the shortest possible analysis time. The optimization of GC × GC separation is often a tedious and time-consuming task and is usually performed by trial-and-error methods. Some authors [6,10] presented the optimization results by multiple GC × GC runs under different kinds of conditions. A model used for prediction and optimization of GC × GC separation, especially for the important targeted compounds, is very essential. Numerous methods [11–15] have been described to predict retention time and peak widths in isothermal or temperature-programmed one-dimensional gas chromatography (1D-GC), but these methods are unsuitable for the GC × GC. Beens et al. [16] developed a model to predict the eventual chromatogram of GC × GC for a given separation problem. The model is based on calculating retention times and peak widths of the compounds to be separated, on both columns, thus predicting the eventual chromatogram. It starts

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from estimating the retention factors ($k$) of the compounds at their elution temperature. It is performed with the help of the (calculated) vapor pressures and the enthalpic contribution to the activity coefficient as obtained from the Kovats retention indices. The main aim of this work is to develop a model for predicting the resolution of target compounds and calculating the optimum temperature programming condition of comprehensive two-dimensional gas chromatography.

## 2. Theory

In order to optimize the GC × GC temperature conditions, retention times and peak widths on two dimensions should be obtained. In capillary gas chromatography, the isothermal retention of a solute $i$ in a GC column of phase ratio $\beta$ can be assumed to be given by:

$$\ln k_i = -\frac{\Delta H_{v,i}}{RT} + (\Delta S_{v,i}) + \ln \beta \tag{1}$$

or

$$\ln k = a_1 + \frac{b_1}{T} \tag{2}$$

where $T$ is the column temperature in degrees K, $k_i$ or $k$ is the capacity factor of the solute $i$, and $\Delta H_{v,i}$ and $\Delta S_{v,i}$ are the vaporization enthalpy and entropy of $i$ from the stationary phase to the mobile phase. Values of $\Delta H_{v,i}$, $\Delta S_{v,i}$, $a_1$ and $b_1$ are usually assumed to be temperature independent. In capillary GC the basic equation of the retention time, $t_R$, of a solute is given by:

$$t_R = t_M(1 + k) \tag{3}$$

where $t_M$ is the column dead time. In isothermal GC, the retention time can be calculated directly from Eqs. (2) and (3), when $t_M$, $a_1$ and $b_1$ are known.

As is well known, d$x$/d$t$ is the rate of solute traveling along the column and is determined by the linear velocity of carrier gas $u$ and $k$ as shown in Eq. (4):

$$\frac{dx}{dt} = \frac{u}{1 + k} \tag{4}$$

For the isothermal step, the distance traveling along the column $\Delta x_i$ in time interval $t_{i+1} - t_i$ is determined by Eq. (5):

$$\Delta x_i = \frac{(t_{i+1} - t_i)L}{t_M(1 + k')} \tag{5}$$

For linear or segmented temperature programs

$$\Delta x_i = \frac{1}{\gamma_i} \int_{t_i}^{t_{i+1}} \frac{L}{t_M(T)[1 + k(T)]} dt \tag{6}$$

where $\gamma_i$ is the heating rate. In the constant pressure GC mode, the column dead time is the function of temperature. A linear relationship exists between dead time and oven temperature within a certain range of temperature,

$$t_M = a_2 + b_2 T \tag{7}$$

At constant flow-rate mode $t_M$ is almost constant and is hardly influenced by the oven temperature.

For the gas–liquid chromatography, the column dead time can be deduced by the retention time of methane or calculated theoretically based on the retention values of homologues series.

To optimize the GC × GC operation condition, it is necessary to predict the peak width at half height $w_{1/2}$ for both isothermal and temperature-programmed modes. There is a well-known relationship between $w_{1/2}$ and retention time, $t_R$, in isothermal separation [17,18].

$$w_{1/2} = a_3 + b_3 t_R \tag{8}$$

As for temperature-programmed gas chromatography, the spreading of peaks is related to the retention temperature. If $T_{ei}$ is the elution temperature of component $i$,

$$k_i = \exp\left(a_1 + \frac{b_1}{T_{ei}}\right) \tag{9}$$

let

$$t_R^* = (1 + k)t_M = \left(1 + \exp\left(a_1 + \frac{b_1}{T_{ei}}\right)\right) t_M \tag{10}$$

where $t_R^*$ is the retention time of solute eluted isothermally at the retention temperature $T_{ei}$ and is named the "invented retention time" [18]. It has been proven [18] that the relationship described by Eq. (8) is still compatible with that between $t_R^*$ and $w_{1/2}$. Thus it is possible to approximate the peak width in temperature-programmed gas chromatography by means of the concept of invented retention time. In GC × GC separation, the components were separated by temperature-programmed mode on the first dimension and isothermal mode on the second dimension. According to above equation, the isothermal or temperature-programmed retention time and peak width on two dimensions can be predicted through several isothermal operations.

Under the optimum GC × GC separation condition, peak resolution $R_s$ of any solutes of interest eluted at the end of the column is no less than required one $(R_s)_{req}$, and analysis time should be as short as possible,

$$R_s \geq (R_s)_{req} \tag{11}$$

where $(R_s)_{req}$ is the resolution that meets the requirement of quantitative analysis. In GC × GC, peak resolution on two dimensions must be taken into account, defined as ${}^1R_s$ and ${}^2R_s$, respectively. The resolution of all the neighboring peaks on the first dimension is calculated by the predicted ${}^1t_R$ and ${}^1w_{1/2}$ on the first dimension in the given conditions. The resolution on the second dimension is calculated only for the components whose resolution on the first dimension is less than the required one and eluted on the second dimension within the same modulation period. According to the above discussion, ${}^1R_s$ can be calculated as:

$${}^1R_s = \frac{{}^1t_R(i) - {}^1t_R(i-1)}{({}^1w_{1/2}(i) + {}^1w_{1/2}(i-1)) \times 1.7} \times 2 \tag{12}$$

where ${}^1w_{1/2}(i)$ and ${}^1w_{1/2}(i-1)$ are the peak widths at half height of component $i$ and $i-1$ on the first dimension, the retention time of component $i$ is larger than that of component $i-1$. The values of ${}^1w_{1/2}$ can be predicted by their "invented retention times" on the first column.

Using the similar method, co-eluted components at the end of the first column simultaneously enter into the second column for the further separation. The temperature on the second column within the same modulation cycle was considered as isothermal. ${}^2R_s$ can be calculated by:

$$ {}^2R_s = \frac{{}^2t_R(i) - {}^2t_R(i-1)}{({}^2w_{1/2}(i) + {}^2w_{1/2}(i-1)) \times 1.7} \times 2 \quad (13) $$

where ${}^2w_{1/2}(i)$ and ${}^2w_{1/2}(i-1)$ are peak widths at half height of components $i$ and $i-1$ on the second dimension. Component $i$ and $i-1$ are eluted in the same modulation cycle and the retention time of component $i$ is larger than that of component $i-1$. The ${}^2w_{1/2}$ can be calculated according to their retention time on the second column. The final flow chart of the optimization algorithm for temperature programming is presented in Fig. 1.

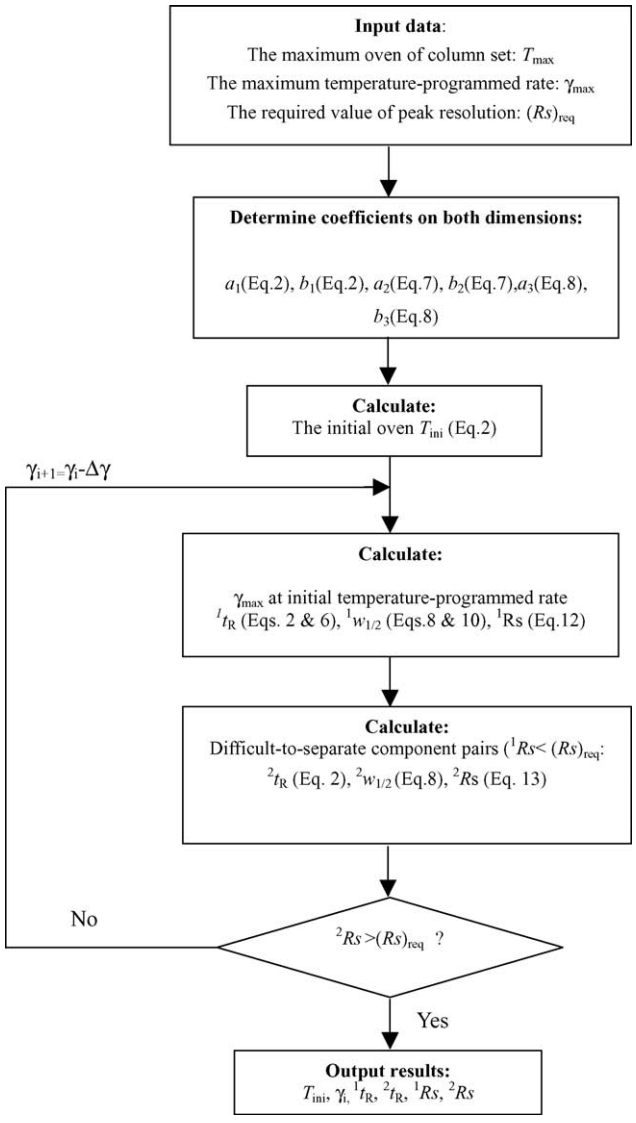


Fig. 1. Algorithm for the calculation steps to optimize a GC × GC separation.

## 3. Experimental

### 3.1. GC × GC conditions

The GC × GC system consisted of an Agilent 6890 (Agilent Technologies, Wilmington, DE, USA) gas chromatograph equipped with a cryogenic jet modulator (prototype KT2001 Retrofit kit; Zoex, Lincoln, NE, USA) for modulation and injection in the second dimension column. The setup and operation of the modulator were described elsewhere [7]. A 6.0 m × 0.18 mm × 3.5 μm VB-5 column (Valco instruments. Co., USA) was used as the first dimension column, and a 2.0 m × 0.1 mm × 0.1 μm 007-17 column (Quadrex, USA) as the second dimension column. The columns were connected by means of a press-fit connector. Both columns were installed in the same oven. The injected volume was 0.1 μL at a split ratio of 1:100. The carrier gas was helium. The constant flow-rate was used during both isothermal and programmed temperature analysis. The column flow rate was 0.6 ml/min. The prediction of retention time, peak width at half-height and peak resolution of both dimensions was carried out by homemade software.

### 3.2. Chemicals

Pyridine, 2-methylpyridine, 4-methylpyridine, 2,6-dimethylpyridine, 2-ethylpyridine, 2,5-dimethylpyridine, 2,4,6-trimethylpyridine and 2,3,5-trimethylpyridine were purchased from Sigma–Aldrich. Five *n*-alkanes in the range *n*-$C_6$ through *n*-$C_{10}$ were obtained from Shanghai Chemical Reagent Corporation (Shanghai, China). To test the developed method presented above, a mixture containing thirteen components was prepared. For the determination of the dead time of both dimensions, a mixture was compiled containing *n*-alkanes in the range *n*-$C_6$ through *n*-$C_{12}$. The purity of all analytes was at least 98%.

## 4. Results and discussion

### 4.1. Determination of the column dead time on two dimensions

As described in the theory section, the linear relationship exists between dead time and oven temperature within a certain range of temperature under constant pressure mode. In this study, the constant flow-rate mode was used for both isothermal and temperature-programmed analysis, and the dead time was approximately considered as constant. On a single column system $t_M$ is readily measured, but for the

second column of a GC × GC column set, direct measurement of $t_M$ is not possible. Marker compounds (methane, butane, etc.) are not retained in the modulating cryo-trap, so an indirect method must be used. In the meantime, the phase ratio of the first column used in this experiment was low, methane had significant retention. So the dead time of both dimensions were to be calculated.

A method has been suggested using measurements of retention times of homologous series (alkanes) under isothermal conditions [19,20]. From a plot of carbon number versus logarithm of adjusted retention time, $t_M$ can be estimated,

$$n = m \ln t'_R + q = m \ln(t_R - t_M) + q \quad (14)$$

where $n$ is the carbon number of the $n$-alkane, and $t'_R$ is adjust retention time.

Using this method, $n$-alkanes in the range of $n$-$C_6$ through $n$-$C_{10}$ were measured under three temperatures 100 °C, 120 °C and 140 °C, with three injections at each temperature without modulation. The calculation found that the dead times of first column at three different oven temperatures were almost same, 0.45 min. Similarly, the dead time of second dimension column was deduced from Eq. (14) by measuring $n$-alkanes in the range of $n$-$C_8$ through $n$-$C_{12}$ at oven temperature 100 °C with modulation, was 1.52 s.

### 4.2. Prediction of GC × GC separation

For the prediction of retention time of the first column, three isothermal runs covering the expected temperature range of the temperature-programmed analysis were carried out. The test mixture containing 13 analytes was measured on the GC × GC column set under three temperatures 100 °C, 120 °C and140 °C, with three injections at each temperature, and the modulator was not used. Compared with the retention time of the first column, that of the second column was too short to be considered. The total retention time value of whole column set without modulation was approximately considered as the retention time value of the first column. The averaged isothermal retention time values at the three temperatures were used to solve the Eq. (2) in order to calculate the coefficients $a_1$ and $b_1$. The results are shown in Table 1. The coefficients of retention time versus peak width at half-height, $a_3$ and $b_3$ are also calculated and shown in Table 1. It can be observed from Table 1 that good linearity of $\ln k$ versus $1/T$ plot is obtained, and the correlation coefficients of thirteen compounds are no less than 0.9998. Similarly, good linearity is also obtained between $w_{1/2}$ versus $t_R$ plot.

The coefficients of $\ln k$ versus $1/T$ plot on the second dimension was determined using GC × GC column set with modulation. The retention time values of $n$-$C_6$–$n$-$C_{10}$ on the second dimension were determined at 80 °C, 90 °C and 100 °C. The retention time values of the rest eight compounds on the second dimension were determined at 100 °C, 120 °C and 140 °C. The results are shown in Table 2. It can be observed from Table 2 that good linearity also existed between $\ln k$ and $1/T$ on second dimension.

Using the coefficients from Table 1, the linear temperature-programmed retention time values of the first column are deduced from Eq. (6). The values of elution temperature of every compound on the first dimension are obtained at the different heating rate $\gamma$ and the initial temperature $T_i$, permit the calculation of the retention time. Because both columns were located in the same oven, the elution temperatures of components on the first dimension are also their separated temperatures on the second dimension. The retention time values on the second dimension can be calculated according to Eq. (2). The predicted values and experimental values on two dimensions under four different temperature-programmed rates are shown in Tables 3 and 4.

Table 1
Basic data of compounds on first dimension in isothermal processes[a]

| Component | $\ln k$ | | | $\ln k = a_1 + b_1/T$ | | Correlation coefficient |
|---|---|---|---|---|---|---|
| | $T$ = 373 K | $T$ = 393 K | $T$ = 413 K | $b_1$ | $a_1$ | |
| $n$-$C_6$ | 0.537 | 0.124 | −0.225 | 2936.43 | −7.3394 | 0.9998 |
| $n$-$C_7$ | 1.183 | 0.701 | 0.291 | 3434.32 | −8.0288 | 0.9999 |
| $n$-$C_8$ | 1.831 | 1.282 | 0.813 | 3925.48 | −8.6970 | 0.9999 |
| $n$-$C_9$ | 2.479 | 1.863 | 1.334 | 4412.20 | −9.3541 | 0.9999 |
| $n$-$C_{10}$ | 3.127 | 2.443 | 1.855 | 4899.66 | −10.0139 | 0.9999 |
| Pyridine | 1.536 | 1.056 | 0.629 | 3492.18 | −7.8274 | 0.9999 |
| 2-Methylpyridine | 1.985 | 1.455 | 0.986 | 3848.24 | −8.3333 | 1.0000 |
| 4-Methylpyridine | 2.295 | 1.741 | 1.252 | 4015.43 | −8.4721 | 1.0000 |
| 2,6-Dimethylpyridine | 2.404 | 1.825 | 1.313 | 4203.34 | −8.8667 | 1.0000 |
| 2-Ethylpyridine | 2.554 | 1.967 | 1.450 | 4252.92 | −8.8500 | 1.0000 |
| 2,5-Dimethylpyridine | 2.715 | 2.113 | 1.582 | 4364.76 | −8.9889 | 1.0000 |
| 2,4,6-Trimethylpyridine | 3.096 | 2.446 | 1.875 | 4706.41 | −9.5238 | 1.0000 |
| 2,3,5-Trimethylpyridine | 3.523 | 2.844 | 2.248 | 4910.59 | −9.6451 | 1.0000 |

| | $b_3$ | $a_3$ | Correlation coefficient |
|---|---|---|---|
| $w_{1/2} = a_3 + b_3 t_R$ | 0.01291 | 0.02072 | 0.999 |

[a] $^1t_M$ = 0.45 min.

Table 2
Basic data of compounds on second dimension at different temperatures[a]

| | $\ln k$ | | | $\ln k = a_1 + b_1/T$ | | Correlation coefficient |
|---|---|---|---|---|---|---|
| | $T = 353$ K | $T = 363$ K | $T = 373$ K | $b_1$ | $a_1$ | |
| *n*-$C_6$ | −2.079 | −2.721 | −3.638 | 10238.79 | −31.03 | 0.9931 |
| *n*-$C_7$ | −1.498 | −1.933 | −2.385 | 5839.03 | −18.03 | 0.9996 |
| *n*-$C_8$ | −0.865 | −1.073 | −1.692 | 4419.10 | −13.43 | 0.9990 |
| *n*-$C_9$ | −0.204 | −0.617 | −0.999 | 4927.57 | −14.18 | 0.9993 |
| *n*-$C_{10}$ | 0.448 | 0.088 | −0.342 | 4902.28 | −13.45 | 0.9993 |

| | $\ln k$ | | | $\ln k = a_1 + b_1/T$ | | Correlation coefficient |
|---|---|---|---|---|---|---|
| | $T = 373$ K | $T = 393$ K | $T = 413$ K | $b_1$ | $a_1$ | |
| Pyridine | −0.733 | −1.440 | −2.134 | 5388.30 | −15.17 | 0.9997 |
| 2-Methylpyridine | −0.399 | −1.112 | −1.692 | 4983.14 | −13.77 | 0.9995 |
| 4-Methylpyridine | −0.020 | −0.693 | −1.335 | 5062.30 | −13.59 | 0.9999 |
| 2,6-Dimethylpyridine | −0.061 | −0.747 | −1.335 | 4908.52 | −13.23 | 0.9999 |
| 2-Ethylpyridine | 0.118 | −0.593 | −1.195 | 5059.48 | −13.45 | 0.9998 |
| 2,5-Dimethylpyridine | 0.294 | −0.399 | −1.035 | 5118.12 | −13.43 | 1.0000 |
| 2,4,6-Trimethylpyridine | 0.593 | −0.141 | −0.775 | 5271.50 | −13.54 | 0.9999 |
| 2,3,5-Trimethylpyridine | 1.116 | 0.365 | −0.305 | 5474.59 | −13.56 | 1.0000 |

| | $b_3$ | $a_3$ | Correlation coefficient |
|---|---|---|---|
| $w_{1/2} = a_3 + b_3 t_r$ | 0.04394 | −0.03256 | 0.996 |

[a] $^2t_M = 1.52$ s.

Table 3
Comparison of predicted and experimental retention time values of the first column

| Compounds | 2 °C/min | | | 5 °C/min | | | 8 °C/min | | | 15 °C/min | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $^1t_{R(exp)}$ (min) | $^1t_{R(pre)}$ (min) | $e_{abs}$ (min)[a] | $^1t_{R(exp)}$ (min) | $^1t_{R(pre)}$ (min) | $e_{abs}$ (min)[a] | $^1t_{R(exp)}$ (min) | $^1t_{R(pre)}$ (min) | $e_{abs}$ (min)[a] | $^1t_{R(exp)}$ (min) | $^1t_{R(pre)}$ (min) | $e_{abs}$ (min)[a] |
| *n*-$C_6$ | 1.20 | 1.20 | 0.00 | 1.16 | 1.17 | 0.01 | 1.14 | 1.15 | 0.01 | 1.09 | 1.10 | 0.01 |
| *n*-$C_7$ | 1.86 | 1.85 | 0.01 | 1.75 | 1.76 | 0.01 | 1.69 | 1.69 | 0.00 | 1.56 | 1.55 | 0.01 |
| Pyridine | 2.42 | 2.42 | 0.00 | 2.27 | 2.26 | 0.01 | 2.15 | 2.14 | 0.01 | 1.94 | 1.92 | 0.02 |
| *n*-$C_8$ | 3.04 | 3.02 | 0.02 | 2.76 | 2.76 | 0.00 | 2.57 | 2.55 | 0.02 | 2.24 | 2.21 | 0.03 |
| 2-Methylpyridine | 3.43 | 3.43 | 0.00 | 3.11 | 3.09 | 0.02 | 2.86 | 2.84 | 0.02 | 2.47 | 2.44 | 0.03 |
| 4-Methylpyridine | 4.38 | 4.38 | 0.00 | 3.85 | 3.83 | 0.02 | 3.47 | 3.45 | 0.02 | 2.91 | 2.87 | 0.04 |
| 2,6-Dimethylpyridine | 4.76 | 4.76 | 0.00 | 4.12 | 4.10 | 0.02 | 3.68 | 3.65 | 0.03 | 3.04 | 2.99 | 0.05 |
| *n*-$C_9$ | 5.04 | 5.01 | 0.03 | 4.28 | 4.26 | 0.02 | 3.80 | 3.77 | 0.03 | 3.11 | 3.05 | 0.06 |
| 2-Ethylpyridine | 5.35 | 5.35 | 0.00 | 4.55 | 4.53 | 0.02 | 4.03 | 3.99 | 0.04 | 3.28 | 3.23 | 0.05 |
| 2,5-Dimethylpyridine | 6.06 | 6.05 | 0.01 | 5.04 | 5.02 | 0.02 | 4.41 | 4.37 | 0.04 | 3.54 | 3.47 | 0.07 |
| 2,4,6-Trimethylpyridine | 8.01 | 8.00 | 0.01 | 6.30 | 6.26 | 0.04 | 5.34 | 5.27 | 0.07 | 4.12 | 4.00 | 0.12 |
| *n*-$C_{10}$ | 8.15 | 8.10 | 0.05 | 6.33 | 6.28 | 0.05 | 5.35 | 5.28 | 0.07 | 4.10 | 4.03 | 0.07 |
| 2,3,5-Trimethylpyridine | 10.79 | 10.79 | 0.00 | 7.98 | 7.92 | 0.06 | 6.57 | 6.47 | 0.10 | 4.89 | 4.75 | 0.14 |

| Compounds | 2 °C/min | | | 5 °C/min | | | 8 °C/min | | | 15 °C/min | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $^1w_{1/2(exp)}$ (s) | $^1w_{1/2(pre)}$ (s) | $e_{abs}$[a] (s) | $^1w_{1/2(exp)}$ (s) | $^1w_{1/2(pre)}$ (s) | $e_{abs}$[a] (s) | $^1w_{1/2(exp)}$ (s) | $^1w_{1/2(pre)}$ (s) | $e_{abs}$[a] (s) | $^1w_{1/2(exp)}$ (s) | $^1w_{1/2(pre)}$ (s) | $e_{abs}$[a] (s) |
| *n*-$C_6$ | 1.80 | 2.10 | 0.30 | 1.80 | 2.11 | 0.31 | 1.66 | 2.08 | 0.42 | 1.75 | 2.18 | 0.43 |
| *n*-$C_7$ | 2.32 | 2.58 | 0.26 | 2.30 | 2.51 | 0.21 | 2.08 | 2.41 | 0.33 | 1.81 | 2.25 | 0.44 |
| Pyridine | 3.01 | 3.02 | 0.01 | 2.89 | 2.80 | 0.09 | 2.30 | 2.66 | 0.36 | 2.03 | 2.42 | 0.39 |
| *n*-$C_8$ | 3.26 | 3.43 | 0.17 | 2.92 | 3.08 | 0.16 | 2.54 | 2.84 | 0.30 | 2.00 | 2.51 | 0.51 |
| 2-Methylpyridine | 3.60 | 3.69 | 0.09 | 3.14 | 3.27 | 0.13 | 2.57 | 2.99 | 0.42 | 2.18 | 2.60 | 0.42 |
| 4-Methylpyridine | 4.16 | 4.28 | 0.12 | 3.40 | 3.63 | 0.23 | 2.77 | 3.23 | 0.46 | 2.18 | 2.72 | 0.54 |
| 2,6-Dimethylpyridine | 4.37 | 4.50 | 0.13 | 3.45 | 3.73 | 0.28 | 2.81 | 3.29 | 0.48 | 2.26 | 2.74 | 0.48 |
| *n*-$C_9$ | 4.40 | 4.63 | 0.23 | 3.56 | 3.77 | 0.21 | 2.83 | 3.30 | 0.47 | 2.19 | 2.72 | 0.53 |
| 2-Ethylpyridine | 4.64 | 4.84 | 0.20 | 3.59 | 3.80 | 0.21 | 2.95 | 3.50 | 0.55 | 2.30 | 2.80 | 0.50 |
| 2,5-Dimethylpyridine | 5.26 | 5.23 | 0.03 | 3.87 | 4.10 | 0.23 | 3.07 | 3.52 | 0.45 | 2.34 | 2.84 | 0.50 |
| 2,4,6-Trimethylpyridine | 6.01 | 6.17 | 0.16 | 4.15 | 4.49 | 0.34 | 3.29 | 3.72 | 0.43 | 2.36 | 2.92 | 0.56 |
| *n*-$C_{10}$ | 5.70 | 6.17 | 0.47 | 4.23 | 4.44 | 0.21 | 3.37 | 3.67 | 0.30 | 2.59 | 2.87 | 0.28 |
| 2,3,5-Trimethylpyridine | 7.00 | 7.33 | 0.33 | 4.38 | 4.92 | 0.54 | 3.38 | 3.95 | 0.57 | 2.39 | 3.01 | 0.62 |

[a] The initial temperature is 100 °C, $e_{abs} = |value_{(pre)} - value_{(exp)}|$.

Table 4
Comparison of predicted and experimental retention time of the second column

| Component | 2 °C/min | | | | 5 °C/min | | | | 8 °C/min | | | | 15 °C/min | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $T_{pre}$ (K) | $^2t_{R(exp)}$ (s) | $^2t_{R(pre)}$ (s) | $e_{abs}$[a] (s) | $T_{pre}$ (K) | $^2t_{R(exp)}$ (s) | $^2t_{R(pre)}$ (s) | $e_{abs}$[a] (s) | $T_{pre}$ (K) | $^2t_{R(exp)}$ (s) | $^2t_{R(pre)}$ (s) | $e_{abs}$[a] (s) | $T_{pre}$ (K) | $^2t_{R(exp)}$ (s) | $^2t_{R(pre)}$ (s) | $e_{abs}$[a] (s) |
| *n*-$C_6$ | 375.4 | 1.56 | 1.56 | 0.00 | 378.8 | 1.55 | 1.56 | 0.01 | 382.1 | 1.54 | 1.56 | 0.02 | 389.4 | 1.53 | 1.56 | 0.03 |
| *n*-$C_7$ | 376.7 | 1.64 | 1.68 | 0.04 | 381.8 | 1.62 | 1.62 | 0.00 | 386.5 | 1.60 | 1.56 | 0.04 | 396.4 | 1.58 | 1.56 | 0.02 |
| Pyridine | 377.8 | 2.13 | 2.13 | 0.00 | 384.3 | 2.00 | 2.00 | 0.00 | 390.1 | 1.91 | 1.98 | 0.07 | 401.8 | 1.78 | 1.86 | 0.08 |
| *n*-$C_8$ | 379.0 | 1.78 | 1.80 | 0.02 | 386.8 | 1.72 | 1.74 | 0.02 | 393.5 | 1.69 | 1.68 | 0.01 | 406.6 | 1.64 | 1.62 | 0.02 |
| 2-Methylpyridine | 379.9 | 2.31 | 2.35 | 0.04 | 388.4 | 2.11 | 2.15 | 0.04 | 395.7 | 1.99 | 2.04 | 0.05 | 409.6 | 1.83 | 1.92 | 0.09 |
| 4-Methylpyridine | 381.8 | 2.62 | 2.63 | 0.01 | 392.1 | 2.29 | 2.32 | 0.03 | 400.6 | 2.11 | 2.16 | 0.05 | 416.0 | 1.89 | 1.95 | 0.06 |
| 2,6-Dimethylpyridine | 382.5 | 2.55 | 2.57 | 0.02 | 393.5 | 2.24 | 2.27 | 0.03 | 402.2 | 2.07 | 2.10 | 0.03 | 417.8 | 1.87 | 1.92 | 0.05 |
| *n*-$C_9$ | 383.0 | 1.93 | 1.98 | 0.05 | 394.4 | 1.80 | 1.80 | 0.00 | 403.4 | 1.73 | 1.74 | 0.01 | 419.6 | 1.65 | 1.62 | 0.03 |
| 2-Ethylpyridine | 383.7 | 2.68 | 2.72 | 0.04 | 395.6 | 2.30 | 2.32 | 0.02 | 404.9 | 2.10 | 2.13 | 0.03 | 421.4 | 1.88 | 1.92 | 0.04 |
| 2,5-Dimethylpyridine | 385.1 | 2.85 | 2.94 | 0.09 | 398.1 | 2.38 | 2.44 | 0.06 | 408.0 | 2.15 | 2.19 | 0.04 | 425.0 | 1.90 | 1.95 | 0.05 |
| 2,4,6-Trimethylpyridine | 389.0 | 3.05 | 3.14 | 0.09 | 404.3 | 2.44 | 2.48 | 0.04 | 415.2 | 2.17 | 2.22 | 0.05 | 433.0 | 1.91 | 1.92 | 0.01 |
| *n*-$C_{10}$ | 389.2 | 2.16 | 2.19 | 0.03 | 404.7 | 1.92 | 1.92 | 0.00 | 415.8 | 1.81 | 1.80 | 0.01 | 434.5 | 1.69 | 1.62 | 0.07 |
| 2,3,5-Trimethylpyridine | 394.6 | 3.60 | 3.63 | 0.03 | 412.6 | 2.65 | 2.72 | 0.07 | 424.8 | 2.29 | 2.34 | 0.05 | 444.2 | 1.96 | 1.98 | 0.02 |

| Component | 2 °C/min | | | 5 °C/min | | | 8 °C/min | | | 15 °C/min | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $^2w_{1/2(exp)}$ (s) | $^2w_{1/2(pre)}$ (s) | $e_{abs}$[a] (s) | $^2w_{1/2(exp)}$ (s) | $^2w_{1/2(pre)}$ (s) | $e_{abs}$[a] (s) | $^2w_{1/2(exp)}$ (s) | $^2w_{1/2(pre)}$ (s) | $e_{abs}$[a] (s) | $^2w_{1/2(exp)}$ (s) | $^2w_{1/2(pre)}$ (s) | $e_{abs}$[a] (s) |
| *n*-$C_6$ | 0.038 | 0.036 | 0.002 | 0.042 | 0.035 | 0.007 | 0.039 | 0.035 | 0.004 | 0.038 | 0.035 | 0.003 |
| *n*-$C_7$ | 0.041 | 0.040 | 0.001 | 0.042 | 0.039 | 0.003 | 0.039 | 0.038 | 0.001 | 0.038 | 0.037 | 0.001 |
| Pyridine | 0.061 | 0.061 | 0.000 | 0.063 | 0.055 | 0.008 | 0.052 | 0.051 | 0.001 | 0.045 | 0.046 | 0.001 |
| *n*-$C_8$ | 0.048 | 0.046 | 0.002 | 0.044 | 0.043 | 0.001 | 0.039 | 0.042 | 0.003 | 0.043 | 0.039 | 0.004 |
| 2-Methylpyridine | 0.064 | 0.069 | 0.005 | 0.060 | 0.060 | 0.000 | 0.059 | 0.055 | 0.004 | 0.045 | 0.048 | 0.003 |
| 4-Methylpyridine | 0.079 | 0.082 | 0.003 | 0.069 | 0.068 | 0.001 | 0.063 | 0.060 | 0.003 | 0.051 | 0.050 | 0.001 |
| 2,6-Dimethylpyridine | 0.078 | 0.079 | 0.001 | 0.062 | 0.066 | 0.004 | 0.060 | 0.058 | 0.002 | 0.051 | 0.049 | 0.002 |
| *n*-$C_9$ | 0.055 | 0.052 | 0.003 | 0.046 | 0.047 | 0.001 | 0.042 | 0.044 | 0.002 | 0.044 | 0.040 | 0.004 |
| 2-Ethylpyridine | 0.083 | 0.085 | 0.002 | 0.070 | 0.069 | 0.001 | 0.060 | 0.060 | 0.000 | 0.051 | 0.050 | 0.001 |
| 2,5-Dimethylpyridine | 0.087 | 0.093 | 0.006 | 0.070 | 0.072 | 0.002 | 0.063 | 0.062 | 0.001 | 0.047 | 0.051 | 0.004 |
| 2,4,6-Trimethylpyridine | 0.094 | 0.101 | 0.007 | 0.065 | 0.074 | 0.009 | 0.066 | 0.063 | 0.003 | 0.052 | 0.051 | 0.001 |
| *n*-$C_{10}$ | 0.060 | 0.063 | 0.003 | 0.041 | 0.052 | 0.011 | 0.045 | 0.047 | 0.002 | 0.042 | 0.042 | 0.000 |
| 2,3,5-Trimethylpyridine | 0.121 | 0.125 | 0.004 | 0.078 | 0.084 | 0.006 | 0.062 | 0.068 | 0.006 | 0.055 | 0.054 | 0.001 |

[a] $e_{abs} = |value_{(pre)} - value_{(exp)}|$.

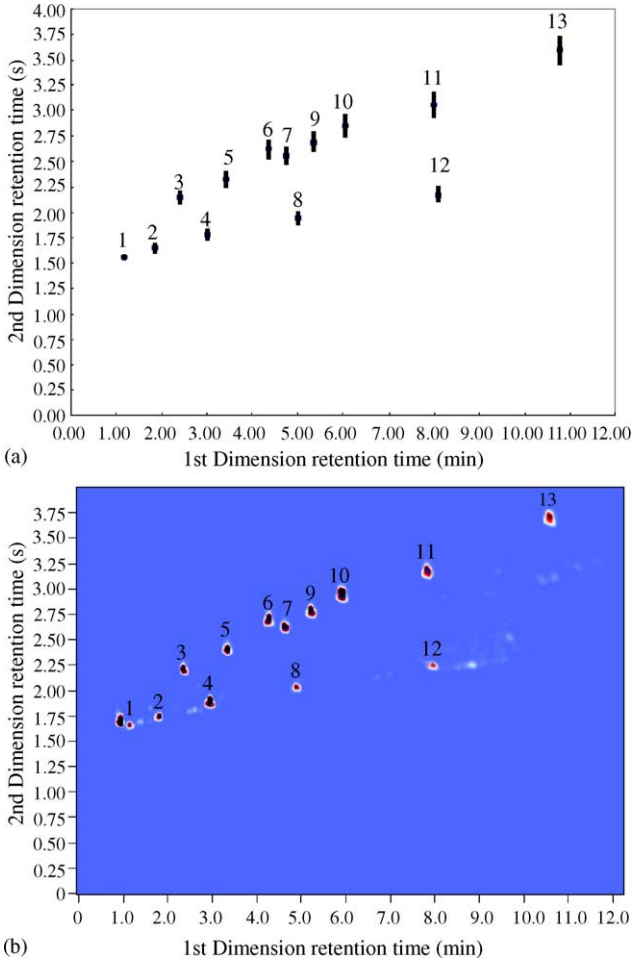


Fig. 2. (a) Predicted GC × GC chromatogram of 13 components. (b) Experimental GC × GC chromatogram of the same components. Chromatographic conditions: initial temperature at 100 °C, the heating rate of 2 °C/min and modulation period 4 s. Compound identification: (1) *n*-$C_6$; (2) *n*-$C_7$; (3) pyridine; (4) *n*-$C_8$; (5) 2-methylpyridine; (6) 4-methylpyridine; (7) 2,6-dimethylpyridine; (8) *n*-$C_9$; (9) 2-ethylpyridine; (10) 2,5-dimethylpyridine; (11) 2,4,6-trimethylpyridine; (12) *n*-$C_{10}$; and (13) 2,3,5-trimethylpyridine.

A good agreement between experimental and predicted data is observed from the tables. The prediction accuracy of retention times of the second dimension is slightly worse than that of the first dimension. The predicted and experimental GC × GC chromatograms under heating rate of 2 °C/min are given in Fig. 2. It can be seen that the accuracy of predicted chromatogram is very good.

### 4.3. Optimization of GC × GC separation

At the optimized conditions, all the compounds of interest have a good resolution, and the total analytical time should be the shortest. It is well-known that higher temperature can achieve a short analytical time, but leading to the possible loss of resolution. Generally, a higher initial temperature is helpful for shorting the analytical time, but too small retention factor will result in a higher required column efficiency to achieve the required resolution. Therefore, the initial temperature should be limited to a suitable value. In this research, temperature of the first eluted peak when its retention factor was approximately equal to 2.0 was selected as the initial oven temperature of temperature program. For the test sample, the initial oven temperature was 90 °C.

For the given column set, the maximum allowed oven temperature was 320 °C, and the maximum allowed heating rate of the instrument was 30 °C/min. The required peak resolution $(R_s)_{req}$ was assigned to 1.3. Using the maximum allowed heating rate as the initial heating rate, the predicted retention time, peak width at half-height and peak resolution on the first dimension $^1R_s$ are shown in Table 5. A total of three pairs components whose $^1R_s$ are less than $(R_s)_{req}$ are shown under the initial condition in Table 5. They are 4-methylpyridine and 2,6-dimetylpyridine, 2,6-dimethylpyridine and *n*-nonane, 2,4,6-trimethylpyridine and *n*-decane. The resolutions of these difficult-to-separate component pairs on the second dimension are further calculated. Using the elution temperature of each difficult-to-separate pair on the first dimension as their separation temperature on second dimension, the retention time, peak widths at half-height and peak resolution on the second dimension of three difficult-to-separate pairs are predicted. It was found that after the separation of the second dimension, the $^2R_s$ value of 4-methylpyridine and 2,6-dimethylpyridine on second dimension is 0.01, which is still less than the $(R_s)_{req}$ value. Therefore, the temperature rate had to be decreased.

The step width $\Delta\gamma$ was assigned 0.5 °C/min, then the next heating rate ($\gamma_2$) was 29.5 °C/min. A series of predictions were carried out with decreasing values of $\gamma$ until peak resolution of all the 13 components met the required value. The final optimum heating rate was found to be 20 °C/min. Two-dimensional resolutions under this optimum heating rate are shown in Table 6. Two pairs of difficult-to-separate components are found by the first column separation. They are 2,6-dimethylpyridine and *n*-nonane, 2,4,6-trimethylpyridine and *n*-decane. After the further separation of the second dimension, the $^2R_s$ values of 2,6-dimethylpyridine and *n*-nonane, 2,4,6-trimethylpyridine and *n*-decane are 2.4 and 2.1, respectively. All the components meet the resolution requirement through two-dimensional separation.

At the above optimized conditions, the retention times and peak widths at half-height of thirteen compounds on two dimensions predicted are given in Table 7. The predicted and experimental GC × GC chromatograms are shown in Fig. 3. It can be observed that the predicted chromatogram is in good agreement with experimental one. All the thirteen components are completely separated within 5 min. It can be further found from Fig. 3 that to keep the peak resolution of the first dimension, the final modulation period could be defined at 1 s.

To compare the separation power of GC × GC and 1D-GC methods, the first column of GC × GC column set was used as the 1D-GC column. The 1D-GC separation of the test mixture was also optimized by application of multi-step temperature programming [18]. The chromatogram with

Table 5
Two-dimensional separations using an initial heating rate of 30 °C/min

| No. | Compounds | $^1t_{R(pre)}$ (min) | $^1w_{1/2(pre)}$ (min) | $^1R_s$ | $T_{e(pre)}$ (°C) | $^2t_{R(pre)}$ (s) | $^2w_{1/2(pre)}$ (s) | $^2R_s$ |
|---|---|---|---|---|---|---|---|---|
| 1 | *n*-$C_6$ | 1.117 | 0.0325 | | | | | |
| 2 | *n*-$C_7$ | 1.518 | 0.0362 | 6.9 | | | | |
| 3 | Pyridine | 1.809 | 0.0387 | 4.6 | | | | |
| 4 | *n*-$C_8$ | 2.110 | 0.0392 | 3.2 | | | | |
| 5 | 2-Methylpyridine | 2.184 | 0.0405 | 2.4 | | | | |
| 6 | 4-Methylpyridine | 2.472 | 0.0418 | 4.1 | 164.1 | 1.715 | 0.0430 | |
| 7 | 2,6-Dimethylpyridine | 2.544 | 0.0415 | 1.0 | 166.2 | 1.716 | 0.0431 | 0.01 |
| 8 | *n*-$C_9$ | 2.569 | 0.0410 | 0.4 | 167.1 | 1.599 | 0.0378 | 1.69 |
| 9 | 2-Ethylpyridine | 2.694 | 0.0421 | 1.8 | | | | |
| 10 | 2,5-Dimethylpyridine | 2.840 | 0.0424 | 2.1 | | | | |
| 11 | 2,4,6-Trimethylpyridine | 3.122 | 0.0427 | 3.9 | 183.6 | 1.720 | 0.043 | |
| 12 | *n*-$C_{10}$ | 3.159 | 0.0418 | 0.5 | 184.8 | 1.620 | 0.038 | 1.55 |
| 13 | 2,3,5-Trimethylpyridine | 3.572 | 0.0435 | 5.6 | | | | |

The initial temperature is 90 °C. Underlined data indicate the values that are less than the value of $(R_s)_{req}$.

Table 6
Two-dimensional separations under an optimum heating rate of 20 °C/min

| No. | Compounds | $^1t_{R(pre)}$ (min) | $^1w_{1/2(pre)}$ (min) | $^1R_s$ | $^1T_{e(pre)}$ (°C) | $^2t_{R(pre)}$ (s) | $^2w_{1/2(pre)}$ (s) | $^2R_s$ |
|---|---|---|---|---|---|---|---|---|
| 1 | *n*-C6 | 1.187 | 0.0346 | | 113.74 | | | |
| 2 | *n*-C7 | 1.681 | 0.0402 | 7.8 | 123.62 | | | |
| 3 | Pyridine | 2.046 | 0.0439 | 5.1 | 130.92 | | | |
| 4 | *n*-C8 | 2.341 | 0.0453 | 3.9 | 136.82 | | | |
| 5 | 2-Methylpyridine | 2.551 | 0.0473 | 2.6 | 141.02 | | | |
| 6 | 4-Methylpyridine | 2.943 | 0.0495 | 4.8 | 148.86 | | | |
| 7 | 2,6-Dimethylpyridine | 3.055 | 0.0494 | 1.4 | 151.10 | 1.81 | 0.047 | |
| 8 | *n*-C9 | 3.106 | 0.0489 | 0.6 | 152.12 | 1.63 | 0.039 | 2.4 |
| 9 | 2-Ethylpyridine | 3.260 | 0.0505 | 1.8 | 155.20 | | | |
| 10 | 2,5-Dimethylpyridine | 3.469 | 0.0511 | 2.4 | 159.38 | | | |
| 11 | 2,4,6-Trimethylpyridine | 3.937 | 0.0518 | 5.0 | 168.74 | 1.82 | 0.047 | |
| 12 | *n*-C10 | 3.905 | 0.0508 | 0.4 | 168.10 | 1.67 | 0.040 | 2.1 |
| 13 | 2,3,5-Trimethylpyridine | 4.531 | 0.0534 | 6.6 | 180.62 | | | |

The initial temperature is 90 °C. Underlined data indicate the value that are less than the value of $(R_s)_{req}$.

Table 7
Retention times and half-widths on the two columns under optimum temperature programming condition

| No. | Compounds | $^1w_{1/2(pre)}$(min) | $^1t_{R(pre)}$(min) | $^1t_{R(exp)}$(min) | $^1e_{abs}$[a] | $^2w_{1/2(pre)}$(s) | $^2t_{R(pre)}$(s) | $^2t_{R(exp)}$(s) | $^2e_{abs}$[b] |
|---|---|---|---|---|---|---|---|---|---|
| 1 | *n*-$C_6$ | 0.0346 | 1.187 | 1.150 | 0.037 | 0.035 | 1.54 | 1.56 | 0.02 |
| 2 | *n*-$C_7$ | 0.0402 | 1.681 | 1.700 | 0.019 | 0.037 | 1.58 | 1.62 | 0.04 |
| 3 | Pyridine | 0.0439 | 2.046 | 2.100 | 0.054 | 0.045 | 1.76 | 1.80 | 0.04 |
| 4 | *n*-$C_8$ | 0.0453 | 2.341 | 2.350 | 0.009 | 0.039 | 1.63 | 1.62 | 0.01 |
| 5 | 2-Methylpyridine | 0.0473 | 2.551 | 2.550 | 0.001 | 0.046 | 1.79 | 1.86 | 0.07 |
| 6 | 4-Methylpyridine | 0.0495 | 2.943 | 3.000 | 0.057 | 0.048 | 1.83 | 1.92 | 0.09 |
| 7 | 2,6-Dimethylpyridine | 0.0494 | 3.055 | 3.100 | 0.045 | 0.047 | 1.81 | 1.86 | 0.05 |
| 8 | *n*-$C_9$ | 0.0489 | 3.106 | 3.150 | 0.044 | 0.039 | 1.63 | 1.62 | 0.01 |
| 9 | 2-Ethylpyridine | 0.0505 | 3.260 | 3.300 | 0.040 | 0.047 | 1.82 | 1.86 | 0.04 |
| 10 | 2,5-Dimethylpyridine | 0.0511 | 3.469 | 3.550 | 0.081 | 0.048 | 1.83 | 1.86 | 0.03 |
| 11 | 2,4,6-Trimethylpyridine | 0.0518 | 3.937 | 4.050 | 0.113 | 0.048 | 1.82 | 1.86 | 0.04 |
| 12 | *n*-$C_{10}$ | 0.0508 | 3.905 | 4.050 | 0.145 | 0.041 | 1.67 | 1.68 | 0.01 |
| 13 | 2,3,5-Trimethylpyridine | 0.0534 | 4.531 | 4.700 | 0.169 | 0.049 | 1.86 | 1.92 | 0.06 |

[a] $^1e_{abs} = |^1t_{R(pre)} - {}^1t_{R(exp)}|$.
[b] $^2e_{abs} = |^2t_{R(pre)} - {}^2t_{R(exp)}|$.

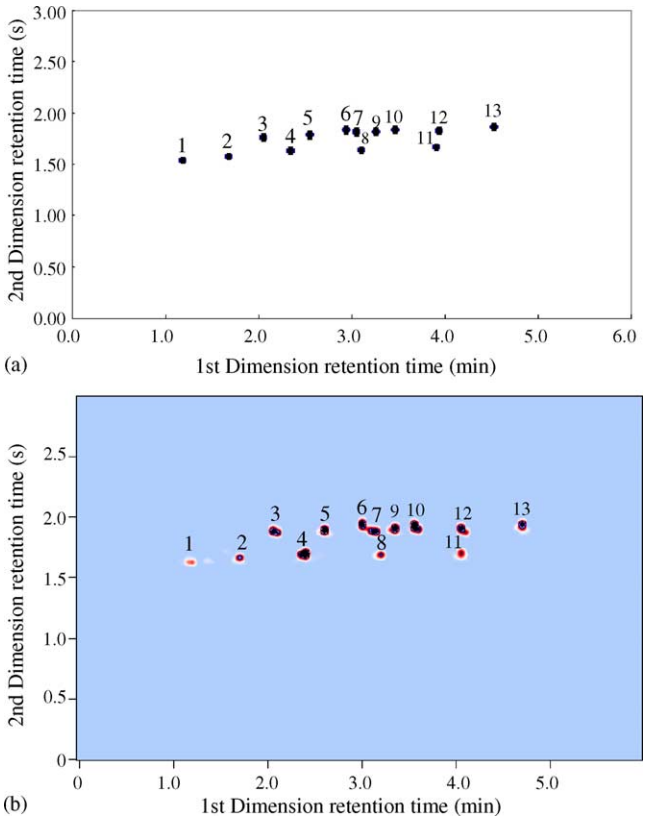


Fig. 3. Predicted (a) and experimental (b) chromatograms of GC × GC separation under optimum temperature programming condition. Chromatographic conditions: initial temperature at 90 °C, the heating rate of 20 °C/min and modulation period 3 s. Compound identification is shown in Fig. 2.

predicted optimum temperature programming is shown in Fig. 4. It can be seen that a good separation of thirteen components was also obtained within 20 min. Comparing Fig. 3 with Fig. 4, the analysis time of GC × GC is about one quarter of that using 1D-GC method.

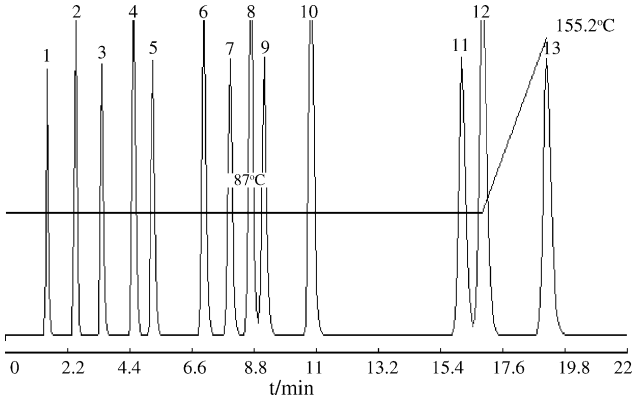


Fig. 4. The 1D-GC chromatogram with optimum temperature. Chromatographic condition: column 6.0 m × 0.18 mm × 3.5 μm VB-5, oven temperature program 87 °C (16.8 min), 30 °C/min to 155.2 °C. Compound identification is shown in Fig. 2.

## 5. Conclusions

This study suggests an optimization method for oven temperature program in comprehensive two-dimensional chromatography based on the retention value prediction. The predicted values of two-dimensional retention times on both dimensions are in good agreement with the experimental ones. By predicted retention times and peak widths, the resolution of neighboring peaks on two dimensions was calculated. In turn, optimum linear temperature programming condition in GC × GC was suggested by taking the two-dimensional resolution of difficult-to-separated component pairs into account. Using the developed model, a GC × GC chromatogram can be accurately predicted.

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