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Accuracy of computer-simulated gas chromatographic separations based on a linear elution strength model

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ABSTRACT

Computer simulation using commercially available software (DryLab GC) for temperature–programmed gas chromatography was investigated for accuracy of predicted retention and resolution. The simulations, based on a linear elution strength model, were evaluated for a variety of samples, temperature programming rates and stationary phases. Reliable simulations were obtained for both linear and segmented temperatures programs. Predicted retention times were accurate to within ±4% and the resolution of adjacent bands was generally accurate to within ±12%.

INTRODUCTION

Temperature programming is widely used in the development of gas chromatographic (GC) separations and is especially useful for the analysis of mixtures covering a wide range of volatilities. Increasing the column temperature has a predominant effect of reducing retention, but the selectivity of a column can also be affected [1–6]. The influence of temperature on selectivity can be exploited in the development of GC separations; however, optimizing the selectivity by varying the temperature program can be difficult, especially for complex mixtures. Changing a programming rate to improve the resolution of a given solute pair may reduce the separation of other solute pairs. The choice of temperature programming rate is often achieved through trial and error, but the difficulty of applying this approach to optimization increases as the number of peaks present in a chromatogram increases.

A number of approaches to the systematic optimization of temperature in GC have been described [7–17], including the use of computer simulation [18–20]. Although the utility of systematic approaches has been clearly documented, the widespread use of computer-assisted optimization techniques has not occurred. Software designed for the optimization of temperature-programmed GC separations has not been readily available, and many chromatographers lack the expertise needed to develop computer programs to perform the required calculations. Software (DryLab GC) for GC simulations based on a linear elution strength (LES) model has recently been described by Bautz *et al.* [21]. Data from two experimental runs carried out at different linear temperature programming rates are used as input for the LES model. Computer simulations can then be predicted for other linear temperature programming rates, isothermal runs or multi-segment temperature programs. Accuracy of

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computer simulations was reported for the separation of a mixture of phenols on a non-polar column.

In this study we investigated the accuracy of computer simulations using DryLab GC for a variety of experimental conditions. The effect of column polarity on the accuracy of predicted retention times and resolution was studied. We also investigated the accuracy of separations optimized with the use of computer-simulated relative resolution maps and multiple-ramp temperature programs.

EXPERIMENTAL

Equipment

The gas chromatograph was an HP5890 equipped with a split–splitless injector port, flame ionization detector and an HP7673A automatic sampler (Hewlett-Packard, Avondale, PA, USA). Data collection was accomplished with a Model 6000 Laboratory Data System (PE/Nelson Analytical, Palo Alto, CA, USA). Fused-silica capillary columns used in this study included DB-1 (30 m × 0.32 mm I.D.), DB-1 (15 m × 0.25 mm I.D.) and DB-1701 (15 m × 0.32 mm I.D.) (J & W Scientific, Folsom, CA, USA) and Supelcowax (15 m × 0.25 mm I.D.) (Supelco, Bellefonte, PA, USA). The film thickness for each column was 0.25 μm. Hydrogen was used as the carrier gas for all separations. Sample injections were made in the split mode using injection volume of 1 μl with a splitting ratio of 100:1.

Software

Simulations were calculated using the computer program DryLab GC (LC Resources, Lafayette, CA, USA) run on an IBM 3270-PC (XT) computer equipped with a math coprocessor.

Samples

Aliphatic hydrocarbon standards ranging from C_{10} to C_{26} were obtained from Sadtler Research Labs. (Philadelphia, PA, USA). The hydrocarbon mixture contained *ca.* 0.5 mg/ml of each hydrocarbon in hexane. A "pesticide test mix" containing α-BHC, β-BHC, aldrin, *o,p'*-DDD, *p,p'*-DDD, *p,p'*-DDE, *o,p'*-DDT, *p,p'*-DDT, dieldrin, endrin, heptachlor, heptachlor epoxide and lindane was purchased from Supelco. The concentration of each pesticide ranged from 0.025 to 0.26 mg/ml in isooctane. Salicylaldehyde, N-methylaniline, decanol, methyl decanoate and 1-bromodecane were obtained from Aldrich (Milwaukee, WI, USA). These solutes were dissolved in acetone at concentrations of *ca.* 0.5 mg/ml.

RESULTS AND DISCUSSION

The accuracy of predicted retention times was evaluated for the separation of a homologous series of straight-chain aliphatic hydrocarbons on a non-polar (DB-1) column. Experimental data were collected at three linear temperature programming rates (10, 20 and 30°C/min from 35 to 300°C). Predicted retention times for each programming rate were calculated using experimental data from the remaining two runs as input for the DryLab GC program (*e.g.*, data from the 10 and 20°C/min runs were used as input to predict retention times for 30°C/min).

Experimental and predicted retention times for C_{10}–C_{26} *n*-alkanes are compared in Table I. The average error of calculated retention times is less than ±3% for each of the three programming rates. This degree of accuracy should be acceptable for most GC method development purposes. Predicted retention times for the 20°C/min programming rate are the most accurate. These retention times were calculated by interpolation of the 10 and 30°C/min data and are consistently greater than the experimental retention times. Larger errors are observed when simulations are made by extrapolation of experimental data. Predicted retention times for the 10 and 30°C/min programming rates were obtained by extrapolation and have slightly larger average errors than the 20°C/min data. The magnitude of the retention time error depends not only on whether the calculations involve interpolation or extrapolation but also on the degree of difference between the experimental retention times and predicted retention. A plot of relative error *versus* experimental retention time for the 20°C/min run is shown in Fig. 1A. The errors are systematic and correlate with the experimental retention time. Similar correlations are observed for the 10 and 30°C/min predictions.

The usual aim of chromatographic method development is to obtain acceptable resolution in a minimum amount of time. Although the accurate prediction of retention time is desirable, it is also neces-

TABLE I

COMPARISON OF EXPERIMENTAL AND CALCULATED RETENTION TIMES FOR *n*-ALKANE MIXTURE ON A 30-m DB-1 COLUMN

n-Alkane	Retention time (min)					
	10°C/min[a]		20°C/min[a]		30°C/min[a]	
	Expt.	Calc.	Expt.	Calc.	Expt.	Calc.
C_{10}	3.17	3.07	2.32	2.34	1.91	1.88
C_{11}	4.54	4.40	3.08	3.11	2.44	2.40
C_{12}	5.95	5.73	3.83	3.86	2.95	2.90
C_{13}	7.34	7.12	4.55	4.59	3.45	3.40
C_{14}	8.67	8.45	5.24	5.27	3.91	3.86
C_{15}	9.93	9.69	5.89	5.93	4.36	4.30
C_{16}	11.13	10.84	6.50	6.54	4.77	4.72
C_{17}	12.27	11.99	7.09	7.13	5.17	5.12
C_{18}	13.36	13.08	7.65	7.69	5.55	5.49
C_{19}	14.40	14.09	8.18	8.22	5.91	5.85
C_{20}	15.39	15.08	8.69	8.74	6.26	6.19
C_{21}	16.34	15.98	9.17	9.23	6.59	6.52
C_{22}	17.25	16.91	9.64	9.70	6.91	6.84
C_{23}	18.12	17.78	10.09	10.14	7.12	7.14
C_{24}	18.96	18.62	10.52	10.57	7.50	7.43
C_{25}	19.77	19.40	10.93	10.98	7.78	7.71
C_{26}	20.54	20.17	11.33	11.38	8.05	7.98
Av. error (%)[b]	−2.39 ± 0.56		0.64 ± 0.16		−1.19 ± 0.28	

[a] Temperature programming rate.

[b] Errors in retention time are calculated as the average error divided by the average retention time × 100. Uncertainties are reported as ± 1 standard deviation.

sary to obtain accurate predictions of resolution as a function of separation conditions. The retention time difference (Δt_r) of adjacent bands is proportional to resolution and can be used to judge the accuracy of computer simulations [21]. Predicted and experimental retention time differences for adjacent bands were calculated for the hydrocarbon data and the average errors are summarized in Table II. Predicted retention time differences are generally accurate to within 5%. As a result of the correlation between the percentage error in predicted retention time and the experimental retention time, adjacent peaks in a computer simulation will have retention time errors of similar magnitude. In the calculation of Δt_r of adjacent peaks the retention time errors will tend to be offset, resulting in predicted resolutions that are relatively unaffected by the magnitude of retention time errors. In contrast to retention time errors, predicted resolution errors should therefore be independent of retention time in any given computer simulation. This is confirmed by the 20°C/min data shown in Fig. 1B, in which the error of retention time differences exhibits no correlation with retention time.

To be generally useful as an aid for GC method development, the LES model should be capable of providing accurate simulations for separations obtained with both polar and non-polar stationary phases. The effect of stationary phase polarity on the accuracy of computer simulations was investigated using a test mixture of randomly selected compounds spanning a wide range of polarity: salicylaldehyde, N-methylaniline, decanol, methyl decanoate, 1-bromodecane and hexadecane). This mixture was separated using columns of low polarity (DB-1), intermediate polarity (DB-1701) and high polarity (Supelcowax). Linear temperature programming rates of 2 and 25°C/min from 35 to

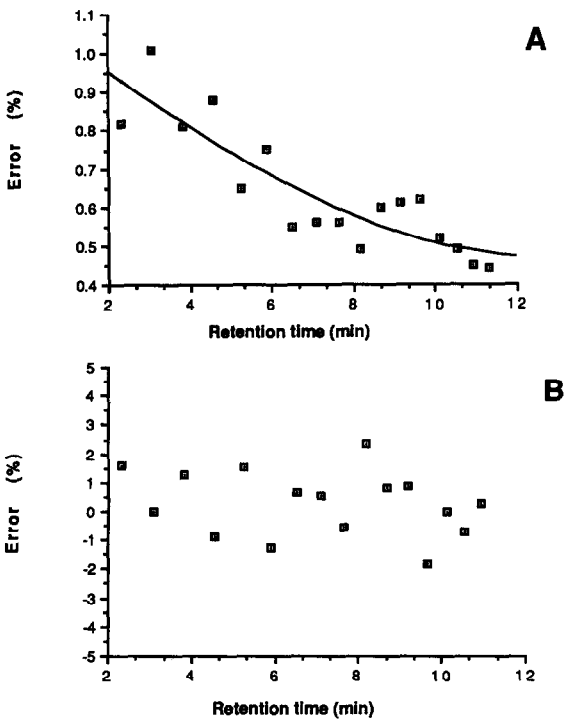

Fig. 1. Comparison of percentage error *vs.* retention time for *n*-alkanes separated on a 30-m DB-1 column with a programming rate of 20°C/min from 35 to 300°C. (A) Predicted retention times and (B) predicted retention time difference of adjacent bands.

TABLE II

SUMMARY OF ERRORS IN PREDICTED RETENTION TIME DIFFERENCES FOR *n*-ALKANE MIXTURE

Heating rate (°C/min)	Av. error, Δt_r(%)[a]
10	−1.5 ± 2.4
20	0.29 ± 1.1
30	−0.64 ± 1.2

[a] Errors in Δt_r are calculated as the average retention time difference of adjacent bands divided by the average difference in retention times for all adjacent bands × 100.

275°C were used to generate input data. Simulated and experimental runs were then carried out at intermediate rates of 12 or 13.5°C/min. Relative errors for predicted retention times and retention time differences are presented in Table III. The retention time errors for the non-polar column are slightly larger than those for either the polar or intermediate-polarity columns, but for all three columns the errors are less than 4%. The difference between the polar and intermediate-polarity columns is not significant. Owing to the relatively large variability in the errors of predicted retention time differences, no significant differences are observed between the three columns. The predicted retention time differences are accurate to within ±12% for all three

TABLE III

COMPARISON OF EXPERIMENTAL AND CALCULATED RETENTION TIMES FOR TEST MIXTURE ON COLUMNS OF DIFFERENT POLARITY

Compound	Retention time (min)					
	DB-1[a]		DB-1701[b]		Supelcowax[c]	
	Expt.	Calc.	Expt.	Calc.	Expt.	Calc.
Salicylaldehyde	5.27	5.46	4.78	4.88	1.91	1.88
N-Methylaniline	5.57	5.77	5.28	5.40	2.44	2.40
Decanol	8.16	8.44	7.38	7.49	9.69	9.88
Methyl decanoate	8.74	9.01	7.51	7.63	8.19	8.35
1-Bromodecane	9.04	9.34	7.63	7.76	8.00	8.18
Hexadecane	11.65	11.99	9.70	9.87	8.22	8.38
Av. error, t_r (%)[c]	3.33 ± 0.26		1.82 ± 0.30		2.15 ± 0.22	
Av. error, Δt_r (%)[c]	0.26 ± 3.87		4.30 ± 3.74		−2.96 ± 7.97	

[a] Programming rate 13.5°C/min, 14-m column.
[b] Programming rate 12.0°C/min.
[c] See footnote to Tables I and II.

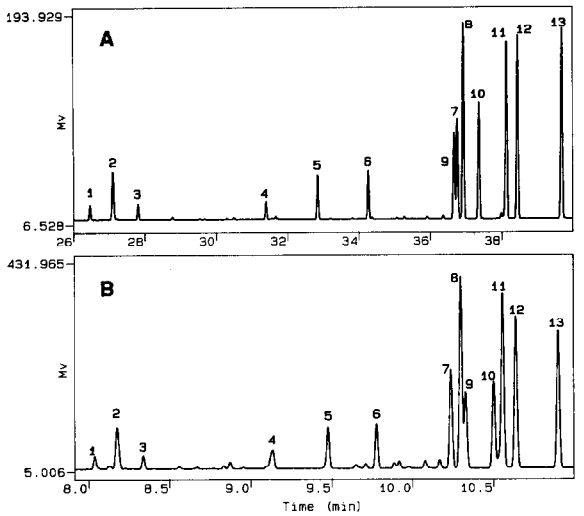

Fig. 2. Comparison of chromatograms for pesticide sample demonstrating the change in relative retention with programming rate. Conditions: 30-m DB-1 column programmed at (A) 5°C/min and (B) 25°C/min from 35 to 330°C. Peaks 1 = α-BHC; 2 = β-BHC; 3 = lindance; 4 = heptachlor; 5 = aldrin; 6 = heptachlor epoxide; 7 = *p,p'*-DDE; 8 = *o,p'*-DDD; 9 = dieldrin; 10 = endrin; 11 = *p,p'*-DDD; 12 = *o,p'*-DDT; 13 = *p,p'*.DDT.

columns. These results suggest that column polarity does not significantly affect the accuracy of simulations based on the LES model.

Computer simulation is very useful for optimizing separations in which the relative retentions of peaks change at different temperature programming rates. A practical feature of this computer program is the ability to calculate and plot relative resolution maps (similar to window diagrams [19]). The utility of relative resolution maps is demonstrated for the separation of thirteen pesticides. Input data for computer simulations were obtained at temperature programming rates of 5 and 25°C/min from 35 to 330°C. A comparison of the two chromatograms (Fig. 2) shows that the relative retention of peaks 7–11 changes significantly. A relative resolution map for the pesticide mixture (Fig. 3) displays the predicted resolution between the worst-resolved pair of peaks over a broad range of temperature programming rates. Three significant maxima are present at programming rates of 3.9, 9.2 and 31°C/min. (Accurate programming rates for these resolution maxima were obtained using tabulated values of predicted resolution *vs.* programming rate.) The highest achievable resolution predicted by the relative resolution map occurs at a rate of 3.9°C/min. The minimum resolution at this rate is predicted to be 1.8, which would indicate baseline resolution of all components. Computer-simulated and experimental chromatograms at 3.9°C/min are shown in Figure 4. Excellent agreement is observed between the predicted and experimental values. Baseline resolution was achieved, but the separation required nearly 50 min for completion.

An advantage of using relative resolution maps is that they allow the chromatographer to select con-

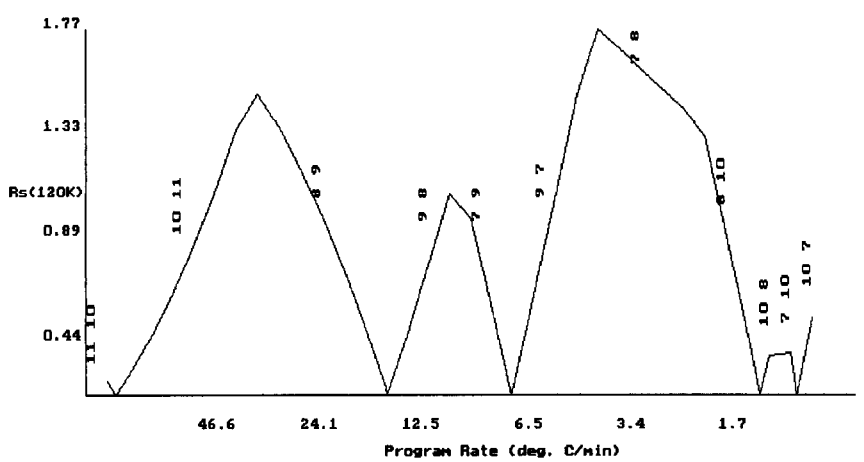

Fig. 3. Relative resolution (R_s) map for pesticide sample. Separation conditions as in Fig. 2. 120 K is the calculated number of theoretical plates (120 000).

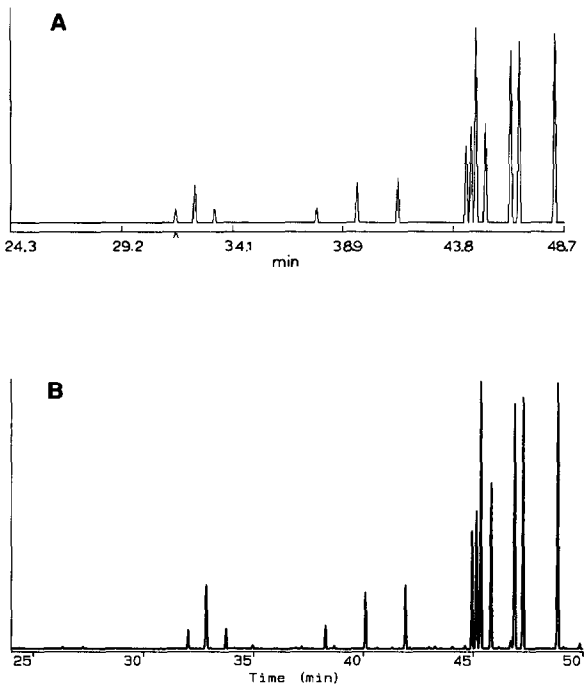

Fig. 4. Comparison of predicted *vs.* experimental chromatograms for pesticide mixture with a programming rate of 3.9°C/min. Other conditions as in Fig. 2. (A) Computer simulation; (B) experimental separation.

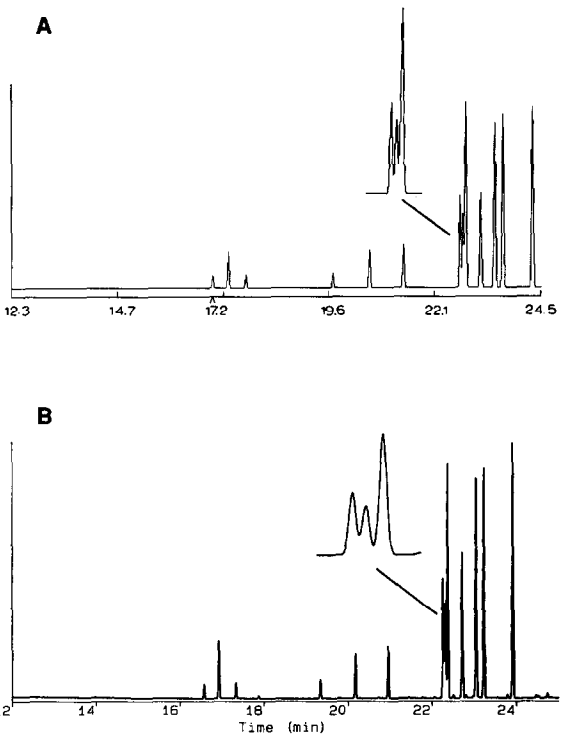

Fig. 5. Comparison of predicted *vs.* experimental chromatograms for pesticide sample with a programming rate of 9.2°C/min. Other conditions as in Fig. 2. (A) Computer simulation; (B) experimental separation.

ditions that, although not providing maximum resolution, allow other factors such as speed and sensitivity to be taken into consideration. If less than baseline resolution is acceptable, two other maxima in the relative resolution map predict that adequate separation can be achieved in much less time. Temperature programming rates in the range 8–10°C/min are commonly used for GC method development. The resolution maximum at 9.2°C/min falls in this range, but it is a local optimum and is predicted to provide neither the best resolution nor the fastest separation time. A chromatographer who explores a limited range of temperature programming rates during method development could mistakenly conclude that this local optimum gives the "best" separation.

A comparison of computer-simulated and experimental chromatograms at 9.2°C/min is shown in Fig. 5. Although baseline resolution of all peaks has not been achieved (as predicted), the separation time has been reduced to 24 min. A further reduction in separation time is predicted by the resolution maximum corresponding to a programming rate of 31°C/min. Computer-simulated and experimental chromatograms at this rate are compared in Fig. 6. The experimental and predicted retention times show excellent agreement. The observed resolution for the two critical band pairs is slightly less than predicted because the computer simulation does not take into asccount the effect of temperature on column efficiency. At the expense of resolution, the separation time and sensitivity have been substantially improved over the 3.9°C/min run. The separation time has been reduced to less than 10 min (five-fold decrease) and the sensitivity increased by a factor of 3.

The accuracy of computer simulations of multiple-ramp temperature programs was also investigated. Manual optimization of multiple-ramp programs can be extremely tedious and time consum-

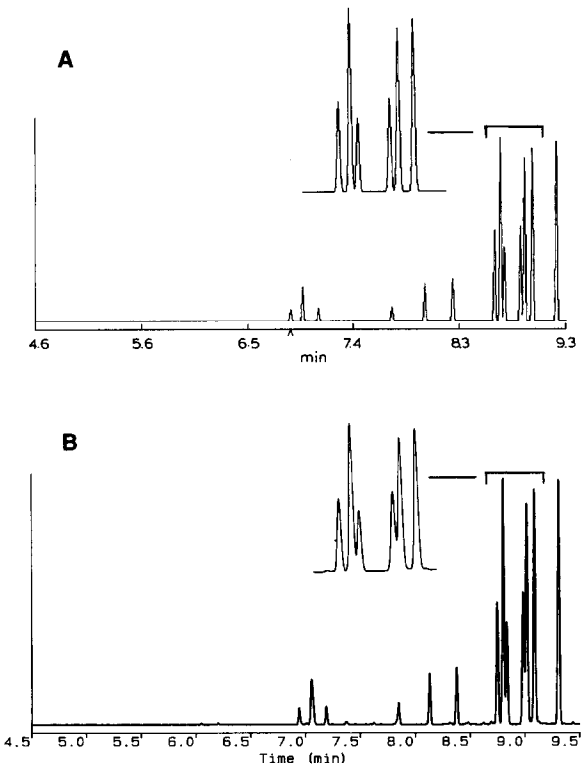

Fig. 6. Comparison of predicted *vs.* experimental chromatograms for pesticide sample with a programming rate of 31°C/min. Other conditions as in Fig. 2. (A) Computer simulation; (B) experimental separation.

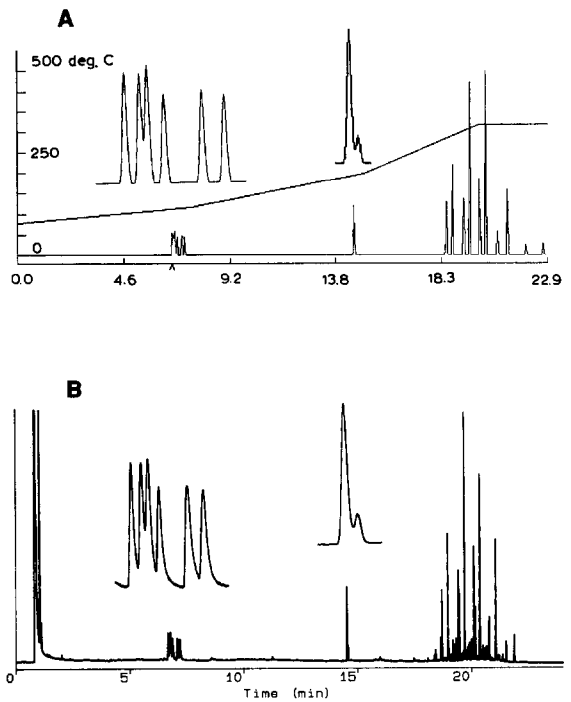

Fig. 7. Comparison of predicted *vs.* experimental chromatograms for an unknown sample using a four-segment temperature programme. Conditions: DB-1701 column programmed at 80, 120, 200 and 320°C at 0, 7.5, 15 and 20 min, with a final isothermal segment at 320°C for 4 min. (A) Computer simulation; (B) experimental separation.

ing, but using computer simulation a large number of multiple-ramp programs can be quickly evaluated. The chromatographic analysis of a sample containing a mixture of unknown components was optimized in preparation for analysis by mass spectrometry. This example illustrates that the identity of chromatographic peaks need not be known for optimization provided that corresponding peaks in the two chromatograms used for input data can be matched. Experimental and simulated chromatograms for a four-segment temperature program are shown in Fig. 7. Programming rates of 5, 11 and 24°C/min were used in succession, followed by a final isothermal segment. Retention times were accurately predicted to within ± 1% and the predicted resolutions of adjacent bands (measured as retention time differences) were accurate to within ± 9%.

CONCLUSIONS

Computer simulations based on a linear elution strength model were found to be reliable for the optimization of GC temperature programs. Retention times and retention time differences were accurately predicted for separations involving a variety of samples and column types. Predicted retention times were accurate to within ± 4% and resolution was generally accurate to within ± 12%.

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