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MOLECULAR INTERCONVERSION BEHAVIOUR IN COMPREHENSIVE TWO-DIMENSIONAL GAS CHROMATOGRAPHY

BY

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ABSTRACT

Comprehensive two-dimensional gas chromatography (GC×GC) is shown to provide information on dynamic molecular behaviour (interconversion), with the interconversion process occurring on both columns in the coupled-column experiment. The experiment requires suitable adjustment of both experimental conditions and relative dimensions of each of the columns. In this case, a longer column than normally employed in GC×GC allows sufficient retention duration on the second column, which permits the typical plateau-shape recognised for the interconversion process to be observed. The extent of interconversion depends on prevailing temperature, retention time, and the phase type. Polyethylene glycol-based phases were found to result in high interconversion kinetics, although terephthalic-acid terminated PEG had a lesser extent of interconversion. Much less interconversion was seen for phenyl-methyl polysiloxane and cyclodextrin phases. This suggests that for the oximes, interconversion largely occurs in the stationary phase. Examples of different extents of interconversion in both dimensions are shown, including peak coalescence on the first column with little interconversion on second column.

INTRODUCTION

Dynamic chromatography refers to a specific observation in chromatographic separations where molecular transformations (chemical structural change) lead to non-linear chromatographic peak shapes. In addition to the primary equilibria controlled by chromatographic distribution processes, it is secondary processes (secondary equilibria) of molecules which lead to dynamic chromatography. The general processes which are encompassed dynamic chromatography have been recently reviewed by Trapp et al. [1], and Krupcik et al [2]. **Figure 1** presents the general equilibria of concern here based upon the usual single dimension schematic [3-5], but extended by the presence of the second column. Molecules are resolved according to their distribution constant and retention differences (K_A, K_B, t_{RA}, t_{RB}). If molecule A undergoes change to B at some position along the column, then it will have an elution time between t_{RA} and t_{RB}. This leads to a plateau region between the two terminal peaks (**Figure 2**) depending upon the interconversion kinetics (i.e. temperature and time determine the extent of the 'reaction'). Throughout this study, A and B will be used to refer to the first- and second-eluting isomers of the respective compounds, which for oximes are *E*- and *Z*-isomers. If interconversion is fast enough, only a smooth overall peak shape is obtained without any evidence of the terminal (unconverted) peaks, according to the peak distribution trend seen **Figure 3(A)-(C)**.

Whilst this behaviour may be recognised in GC, HPLC [6,7] and in TLC [8], the present work will focus on GC separations. Schurig [9] investigated enantiomeric interconversions, where the separation column incorporates a chiral selector such as a metal complex or cyclodextrin to effect the necessary enantiomer resolution. The 'reaction' may be a flipping-type process, with inversion of chirality [10], sterically-hindered rotations of polyaromatic molecules [11], twisting behaviour of octahedral metal complexes of Cr [12], molecular migrations of a chromium tricarbonyl moiety on a planar methyl naphthalene molecule [12], and *E*-*Z* isomerisation about partial-double bonds of oximes [13]. Haglund, and the König and Schurig groups have reported [14-18] observations on atropisomerisation arising from sterically-hindered rotations in chlorinated biphenyls, leading to the same general dynamic GC behaviour. Langer and Patton [19] studied irreversible thermal decomposition of dicyclopentadiene to the monomer, and calculated kinetic data for the process.

All of the above studies used single column GC for the separation process. The chromatographic band shape is very similar in all cases of reversible processes, but as the energy of the process varies for the different molecular systems, the temperatures at which the processes are apparent will vary. Additionally, this temperature must be compatible with the elution temperature of the molecules, and therefore compatibility between the energy of the chromatographic separation, and the energy of the interconversion. For instance, if an interconversion energy barrier is very small, and a high temperature is required for the analysis of the compounds on a GC column in order to obtain elution, then most probably the individual A and B isomers will not be observed, and the rapidly interconverting compound will yield only one peak (i.e. they will coalesce); a broadened peak width compared to the peak of a simple molecule will arise if the rate of interconversion is moderately fast.

Interrogation of the interconversion process to obtain kinetic and activation data normally is based on the total peak envelope shape, and often mathematical modelling of the process is used to fit the shape to a model that can be used to predict the relative rates, activation parameters and interconversion energies of the process [2,20,21]. Estimation of the degree of injected isomer that has not undergone a change in structure (e.g. by comparison with inert internal standard), at both different times of reaction (eg flow rate changes) and temperatures, allows the activation energy to be derived. Deconvolution, or separate isomer identification, of the peak envelope has not been possible previously, due to the fact that the isomers will often have the same mass spectra (note that spectroscopic detectors sensitive to molecular shape such as FTIR have not been reported in this application area to this time). The first successful study to demonstrate physical deconvolution of the isomers was reported by Marriott *et.al*. by using comprehensive two-dimensional gas chromatography (GC×GC) [22]. In the coupled two-column method, the second column was able to resolve unresolved solutes from the first column. The second column was designed to give very fast elution, with sufficient resolution of the isomers, so that the extent of interconversion was either minimal or negligible on the second column (^{2}D), although there will have existed a small finite extent of interconversion. The GC×GC method allowed novel presentation of the isomerisation process, with complete resolution of the interconverting molecules. Subsequent to this, a temperature dependent study

permitted extraction of kinetic data by simulation of the dynamic GC×GC method (termed dynamic comprehensive two-dimensional gas chromatography, or DGC×DGC) [23]. Where negligible interconversion occurs on ^{2}D, it may be acceptable to refer to the system as DGC×GC. All above studies and interpretative models appear to have used isothermal conditions.

Molecular structural changes may occur in either or both phases of the separation medium. In some enantiomerisation processes, it is possible that the stationary phase, which incorporates the chiral selector, can have a catalytic or inhibitive effect on the interconversion process, in addition to its primary role in providing enantioseparation. In processes such as the molecular migration of the $Cr(CO)_3$ group over the surface of the naphthalene molecule, this may occur in either phase – and possibly more likely in the gas phase. The stationary phase will be involved in (possibly catalytically) promoting the interconversion if it activates the interconversion process. In such cases, it will become apparent whether the stationary phase has some effect by investigating chemically different phases.

Observation of the interconversion process requires the isomers to be chromatographically separated. The plateau between the peaks of the two interconverting species becomes less well defined as the resolution of the terminal compounds decreases, or as the interconversion kinetics increase, with the distribution collapsing into a single, broad peak, and then progressively to a much narrower peak as the rate further increases (**Figure 3**). The time duration (width) of the total peak distribution may be compared with that of an 'inert' internal standard (IS). In Figure 3(A), peaks A and B have similar widths to the IS peak, but the A↔B distribution duration is much greater. As interconversion occurs more rapidly (Figure 3(B)), A and B are no longer independently seen, and the peak envelope duration becomes narrower, and eventually approaches the width of the IS peak (Figure 3(C)). Thus peak coalescence of the two participating isomers may arise from either insufficient resolution or increased rate of reaction. Schurig discussed these effects with respect to enantiomerisation processes [24]. Of the six types mentioned, two are perhaps more relevant to the present situation. Thus peak coalescence of the first type arises from using a chromatographic column which is incapable of resolving the isomers (eg. for

enantiomers, using a stationary phase which is racemic or has little selectivity difference towards the isomers). Peak coalescence of the third type arises from employing a condition where the interconversion occurs so rapidly that no resolution of the two isomers is achieved even though in a structurally inert system one may (expect to) obtain resolved peaks. Note that in a two-dimensional system, it may be possible to obtain peak coalescence of both the first and second types on ^{1}D, but to still achieve peak resolution on the ^{2}D column.

In the present study, the effects of use of different temperature operation, including temperature programming, which has not previously been reported for dynamic GC×GC studies, and the use of different column stationary phase types on the extent of interaction, were investigated. In addition, previous work is extended by employing longer ^{2}D columns on which some degree of interconversion is sought. It was of interest to see if coalescence processes on the first column, or use of phases that do not promote interconversion in the first dimension, might offer insight into different chemical processes, or ways to study such processes.

EXPERIMENTAL

Chemical standards

Acetaldoxime and butyraldoxime standards were obtained from Aldrich and Tokyo Kasei respectively, and used as received. The *E* and *Z* isomers are in different proportions in these two samples; thus the first eluting isomer of acetaldoxime (*E*-isomer) is in lesser abundance than the later eluting isomer. They were diluted in solvent acetone to nominal concentrations of 1%, which gave suitable peak responses in the GC analysis.

Various internal standards of n-alcohols were used to compare peak widths of the inert internal standard with the peak envelopes of the interconverting compounds.

Instrumentation

Hewlett-Packard model 5890 (Hewlett-Packard, Little Falls, DE) and Shimadzu model GC-17A (Mount Waverley, Vic, Australia) GC instruments were used for single column analysis of standard solutions, in order to evaluate various columns for their effect on stimulating interconversion. An Agilent Technologies model 6890 GC (Burwood, Vic, Australia) was used for GC×GC studies, in which an Everest model cryogenic modulation system (Chromatography Concepts, Doncaster, Australia) retrofitted to the GC was used to effect the GC×GC modulation process between the two columns. The schematic diagram of the arrangement is shown in Figure 1.

Capillary columns

The column types used are listed in Table 1. Only one type of phase type was used for ^{2}D, with different column lengths investigated, as indicated. Column sets are described in the text as [column 1, column 2 (length)].

Software

GC×GC were exported and converted into matrix form for presentation as 2D contour or surface plots, using Transform (Fortner Research, VA, USA).

RESULTS AND DISCUSSION

GC×GC for study of dynamic GC

By employing a fast GC separation step at the end of the primary column, and especially by decoupling the two dimensions through the use of the modulation process in GC×GC, it is possible to provide discrete separation on ^{2}D, of the overlapping peaks on ^{1}D. The formal GC×GC technique normally employs about 4 individual or discrete analyses per chromatographic peak, which elutes from ^{1}D. The role of GC×GC in the study of dynamic GC is to provide quantitative measurement of the two interconverting isomers, that lead to the observed unresolved dynamic GC peak on the first column, over the whole distribution. The use of spectroscopic detection will also give a unique measurement of each isomer only if the detection mechanism is capable of distinguishing the isomers. Probably the only technique that can do this during GC is FTIR detection, with its geometrical isomer specificity [25,26]. More common methods such as mass spectrometry cannot readily distinguish isomers of the sort described here, where molecular ions and fragmentation patterns will be essentially the same. NMR is capable of uniquely identifying isomerisation of oximes in solution [27], but this has not been used for the GC experiment.

Thus provided ^{2}D conditions permit only negligible interconversion of A and B isomers, and can adequately resolve them, then it is possible to obtain the instantaneous relative proportions of A and B over the total dynamic GC envelope. The question can be posed as to what are the constraints of conditions and dimensions of ^{2}D which prevent interconversion on ^{2}D. Clearly this should effectively be a short retention time to minimise the extent of interconversion. This can be achieved by using a short, narrow bore, thin film coated column, to give $^{2}t_{R}$ of a few seconds. This is precisely the same condition required in general GC×GC analysis. Temperature must also be considered.

Isothermal *vs* temperature programming operation

The previous study employed isothermal analysis for DGCxGC [22]. This produced separation of components on ^{1}D, via different $^{1}t_{R}$ values, an interconversion region where A and B coexist in an appropriate ratio, and separation of A and B on ^{2}D

according to their specific ^2t_R values. The 2D GC×GC plot produced in isothermal analysis is shown in **Figure 4A**. Contrasting this is the plot from temperature programming analysis (Figure 4B). As the oven temperature increases, the ^2t_R value will decrease. Hence the retention plot for each of components A and B will tend to a shorter ^2t_R as the total time increases. This is recognisable as similar to "isovolatile'" plots demonstrated in a recent method for estimating retention indices on ^{2}D [28]. There is a second consideration to apply to the 2D plot with respect to the interconversion process. Under isothermal conditions, each ^{2}D chromatogram is at exactly the same temperature, but the greater ^{1}D retention time means that there is a progressively greater extent of reaction of either A $\rightarrow$ B or B $\rightarrow$ A from the resolved components on ^{1}D. However the rate constant and equilibrium constant will be constant throughout the analysis. Since the interconversion process is defined by the activation enthalpy and entropy, and for isomers, by the isomeric ratio, using temperature program conditions for such a process means that the temperature and therefore the reaction rate constants must be defined at all points in time during elution. As the final temperature is defined at the elution time, it should be possible to derive information from the change in conditions starting with the elution of the less strongly retained isomer and ending with the stronger retained isomer. There are two unknown variables, but with GC×GC a larger number of equations (>2) will be required to derive the values. This will require further study to decide if the process can be suitably modelled. Note that the difference in temperature over the elution time of the compounds is not great, and may be about 10 – 20^{o}C. The effect of the temperature program on rate of interconversion can be seen from its effect on the plateau region between A and B. In **Figure 5(A)** (isothermal), the plateau has a slight increase in slope from isomer A to B. With temperature programming, the plateau has a more pronounced increase in slope towards the B isomer, such as that in Figure 5(C) at 25^{o}C/min, suggesting that isomer B progressively undergoes greater conversion with the increase in program rate since it experiences increased temperature in the column. The sequence of chromatograms in Figure 5 shows only a subtle change, because there is only a small elevated temperature environment for isomer B compared with that of isomer A. However the effect on kinetics of the process will be real. By calculating the areas of unconverted isomer A and B, it would be expected that the area ratio of A/B would increase as temperature program rate increases (i.e. B

reacts more than A). However whilst the trend in this ratio appears to agree with that expected, there is considerable uncertainty in correctly measuring the amount of unconverted isomers in this experiment due to underlying interference arising from the interconversion process.

Effect of different column phases on interconversion

Previous study on dynamic GC of oximes almost invariably used the polyethylene glycol phase (or its terephthalic acid treated analogue) for generation of the interconversion process. It is not clear whether a definitive estimation of interconversion can be derived from separate contributions for the gas and stationary phases. Since oximes may isomerise in the absence of the stationary phase, the GC stationary phase may have catalytic or inhibitive effect on the process. This may be represented by the stationary phase effect on the energy barrier of the interconversion, shown in **Figure 6**. As part of the present study, additional phases were chosen, especially as a search for those that might lead to peak coalescence of the first kind, or might inhibit interconversion. These will then allow an interpretation of the role of the gas phase in the dynamic process. Note that if A and B are not resolved on ^{1}D, then provided ^{2}D can give resolution of A and B, it should still be possible to obtain kinetic data from the system. Simply operating a given column at a very high temperature would also lead to peak coalescence, but it may be too high to permit ^{2}D to achieve resolution.

For a column phase that gives no peak interconversion on ^{1}D, it may still be possible to observe some peak shape asymmetry typical of dynamic behaviour on ^{2}D. In this case, A and B will elute at their respective peak retention positions, and the peak shapes of the individual peaks on ^{2}D will resemble that arising from an A→B or B→A process rather than a shape arising from either dynamic interconversion (ie. showing the two isomer peaks) or the simple symmetric shape of an inert compound.

In this work it was observed that the interconversion rate proceeded in the following order:

BP20 > BP21 > BP10 > BPX5 ~ enantioselective column (note that this column has the cyclodextrin selector supported within a dimethylpolysiloxane base polymer).

This is in accordance with the polarity of the column stationary phase, and so the interconversion may be associated with the lone-pair of the nitrogen interacting with the stationary phase to permit (activate) the isomerisation process at the 'partial double' bond C=N. The gas phase contribution to isomerisation appears to be minor, since on the low-polarity phases little evidence of plateau occurs. A recent report on matrix isolation FTIR and molecular orbital studies [26] supports this conclusion where there was no evidence of gaseous phase isomerization. In addition, torsional motion about the C=N bond was not favoured over an inversion of substituents at the imino group. The energy barrier for each of these processes was calculated to be 413.4 and 256.5 kJ mol^{-1} respectively, using molecular mechanics methods.

Chromatographically, the effect may be demonstrated by the extent of peak interconversion on ^{1}D for a range of stationary phase types (see **Figure 7**). It can be seen that BP20 (Figure 7(A)) gives almost unrecognisable A and B peaks even at oven temperatures as low as 40^{o}C, whereas BP10 (Figure 7(C)) gave much less interconversion, and significant unconverted A and B. BP21 (Figure 7(B)) was somewhat intermediate between these two, and BPX5 (Figure 7(D)) less than BP10. Whilst different conditions have been used, these trends can still be drawn. Thus whilst (B) and (C) are recorded at 70 and 60^{o}C respectively, the increased plateau for (B) is more than can be simply expected from a 10^{o}C change in temperature. Both (C) and (D) were at the same temperature, and have similar total elution times, but there is a less evident plateau for both acetaldoxime and butyraldoxime in (D).

Generating dynamic behaviour on ^{2}D

There exists a further ^{2}D plot type which can be generated. By increasing the extent of interaction on ^{2}D it is possible to observe the classic plateau between the resolved peaks on ^{2}D. This should allow a rather unusual 2D plot to be obtained, where the basic shape shown in Figure 4(A) would also exhibit interconversion along the $^{2}t_{R}$ axis. It might be then expected that the 2D plot would show a zone (as a maximum) of unconverted A and B, and a raised response in both ^{1}D and ^{2}D directions – almost like a saddle response surface. Unfortunately, in order to obtain conditions which gave ^{2}D interconversion, it was found that on ^{1}D peak coalescence was substantial. Since again ^{2}D is short, it would be required that ^{2}D should have an enhanced interconversion kinetics, with ^{1}D a reduced kinetics, for the two dynamic processes to be adequately

observed. This suggests a column set combination of BP10/BP20. **Figure 8** demonstrates the interconversion behaviour found in the column set combination [2, 6 (4.0)] at the conditions listed in the Figure caption. The conditions employed reasonably high flow rate and so a narrow total peak duration was obtained on ^{1}D with only 2 or 3 modulations (denoted M1 and M2 in Figure 8(A)) generated. Between the two resolved isomers on ^{2}D, shown as the pairs A and B for a single modulation, a small increased baseline is seen, corresponding to the interconversion plateau. Because A and B are of similar responses in each modulation, this implies that there is little resolution between the isomers on ^{1}D, and is interpreted as due to rapid interconversion on that column. In Figure 8(B), the higher oven temperature leads to a higher plateau, but the phase of modulation [29] also changes due to the altered retention time of the compounds on ^{1}D. Thus three modulations are seen with one major central peak.

The column set was changed to [1, 6 (4.0 m)] (**Figure 9**). Greater modulation times were used since peaks on ^{2}D become broader on the longer column, and also the higher temperatures used should promote more interconversion on ^{2}D. The difficulty in adjustment of conditions to achieve the desired result can be seen for acetaldoxime in Figure 9(A). Greater interconversion and hence a more substantial plateau will be found at higher temperature, but a higher temperature will further reduce resolution, which is only just sufficient to identify the plateau in this example. For butyraldoxime (Figure 9(B)), the resolution is much better than for acetaldoxime and so 100^{o}C can be used. The plateau between A and B on the second dimension can be readily recognised here, with the response returning to baseline after the second peak (B) for each modulation has eluted. Again, adjusting conditions to get even more interconversion on ^{2}D will only serve to diminish resolution of the isomers. The extent of interconversion on ^{1}D is fast enough to present only a smooth envelope, with no evidence of unconverted A and B on the first column. Hence again ^{1}D shows much greater extent of interconversion than ^{2}D in this example. Clearly, careful column choice, their dimensions and conditions are required to observed DGCxDGC, as opposed to DGCxGC. Note also that it is difficult to use an even longer column for ^{2}D, because although it will give greater dynamic GC effects, it is important to have peaks which are sufficiently narrow, since this aids their separation and presentation within the modulation period required of GC×GC, which in turn is used as the time-

basis for data conversion. Figure 9(C) is the 2D contour plot for the result shown in Figure 9(B). By plotting the lowest contour lines at a level less than the plateau (eg 15pA, 20pA) the saddle response between the A and B peaks is generated on the 2D Figure. The maximum 'pulse' of the A and B isomers do not exactly coincide at the same ^{1}D time, being at about 7.25 and 7.40 min respectively, and so the interconversion rate on ^{1}D is still not rapid enough to give equivalent ^{1}D times.

CONCLUSIONS

Interconversion effects of structurally dynamic oxime compounds were investigated by using single column and comprehensive two-dimensional gas chromatography analysis. The effect that temperature programming has on the 2D contour plot is consistent with the expected variation in $^{2}t_{R}$ from isovolatility considerations, with an approximately exponential decay shape in the contour line. Temperature programming should also result in kinetics of the interconversion process varying for the two isomers as they pass down the column. It is possible that suitable modelling of the dynamic process under temperature programmed conditions will permit determination of various activation parameters for the isomer interconversion, not directly obtained from a single isothermal analysis result.

Different stationary phase columns appear to have different rates of interconversion, approximately correlated with phase polarity. Thus extents of interconversion, as evidenced by the magnitude of the plateau between the isomers, appears to be in the order of BP20 > BP21 > BP10 > BPX5 ~ chiral column.

By using conditions that increase kinetics of interconversion in the second dimension column (longer ^{2}D column, higher temperature), it is possible to increase the interconversion on the second column, and so observe the plateau between the two isomers on ^{2}D. Under these conditions, the much longer first column gave substantial interconversion, and so peak coalescence is almost achieved on this column under these conditions. It was not possible, on the columns used, to either suppress or only have a small extent of interconversion on ^{1}D whilst having interconversion on ^{2}D. Such conditions would generate a range of different contour plots, indicative of the kinetics in each phase.

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Table 1

Column types used in this study

Col #	Phase type / name	Column length	Position
1	BP21; Polyethylene glycol acid treated (SGE International)	25 m x 0.22 mm ID x 0.25 μm df	^{1}D column
2	BP20; Polyethylene glycol (SGE)	12 m x 0.22 mm ID x 0.25 μm df	^{1}D column
3	BP10; 14% cyanopropylphenyl dimethyl polysiloxane (SGE)	12 m x 0.22 mm ID x 0.25 μm df	^{1}D column
4	BPX5; 5% phenyl polysilphenylene siloxane (SGE)	30 m x 0.25 mm ID x 0.25 μm df	^{1}D column
5	CP-Chirasil-Dex CB (Varian)	25m x 0.32 mm ID x 0.25 μm df	^{1}D column
6	BP20; Polyethylene glycol (SGE)	(0.8, 2.0, 4.0) m x 0.1 mm ID x 0.1 μm df	^{2}D column

Figure Legends

Figure 1

Illustration of the dynamic interconversion system A $\rightleftharpoons$ B for isomers A and B. K are chromatographic distribution constants; k is the interconversion rate constant for A→B and k_- is for the reverse process; subscripts M and S refer to mobile phase and stationary phase respectively. In a two-dimensional system, the first (^{1}D) and second (^{2}D) columns may be different phases, and so have different kinetic parameters indicated by superscript ^{1} and ^{2} respectively. The cryogenic modulator M provides the mechanism for modulating the first dimension peak to the second column.

Figure 2

The classic dynamic chromatogram has original injected peaks A and B, and an interconversion or plateau region arising from molecular structural change during chromatographic elution. (I) is for acetaldoxime and (II) is for butyraldoxime, where the initial amount of A isomer is less for acetaldoxime (the *E* isomer) and more for butyraldoxime.

Figure 3

As the rate or extent of interconversion increases, the two isomer peaks, which are originally well resolved (A: 70^{o}C; 20 psi), progressively collapse into a single peak whose extremities are determined by the retention properties of the individual isomers (B: 90^{o}C; 5 psi), and then into a much narrower peak which now will have width much more like a normal GC peak (C: 110^{o}C; 5 psi). Note that since these conditions are brought about by increases in temperature or reduced flow rate, the relative peak retentions will change: they are shown here approximately normalised to the retention of the peak set.

Figure 4

Comparison of the effect of isothermal oven operation, against temperature programmed operation, for the comprehensive two-dimensional gas chromatography experiment in DGCxDGC. Column set [1, 6(0.8)].

A. Acetaldoxime with n-hexanol (IS) at 70ºC, 20 psi, 3 s modulation

B. Acetaldoxime and butyraldoxime with n-hexanol (IS) at 70°C for 2.5 min heated to 100°C at 5°C/min, 20 psi, 3 s modulation.
imp = impurity in the starting materials

Figure 5

Effect of temperature programming on the interconversion plateau for acetaldoxime (A). isothermal 60°C; (B). 60°C for 3 min, followed by temperature programming at 15°C/min; (C). 60°C for 3 min, followed by temperature programming at 25°C/min.

Figure 6

Effect of stationary phase catalytic or inhibitive effect on the energy barrier and hence kinetics of interconversion of molecules A and B. (A) indicates a process with similar ground state energies of the two molecules. (B) illustrates a situation where the forward and reverse reactions can have different energy and kinetics. (C) shows the possible effect of the stationary phase in altering the kinetics by increasing or decreasing the energy of the interconversion.

Figure 7

Comparison of extents of interconversion on a selection of different stationary phases, under different experimental conditions of temperature and pressure.

(A). BP20 at 40°C, 25 psi; (B). BP21 at 70°C, 20 psi; (C). BP10 at 60°C, 15 psi; (D). BPX5 at 60°C, 20 psi

Figure 8

Interconversion of butyraldoxime on the ^{2}D column using column set [2, 6 (4.0)] under differing temperature conditions. (A). 80°C; 8.0 s modulation; (B). 90°C, 5.5 s modulation. A and B denote the two isomers, and M1 and M2 denote two successive modulation events over the first column peak elution. For (B), three modulations can be seen. Since there are few modulations, it is apparent that the peak elution from the first column is both rather narrow, and that also there is fast interconversion on this column.

Figure 9

Illustration of effect fast interconversion, giving only one apparent peak on ^{1}D, and with interconversion on ^{2}D using column set [1, 6 (4.0 m)].

(A). Acetaldoxime; oven 90^{o}C, 8 s modulation

(B). Butyraldoxime; oven 100^{o}C, 4 s modulation

FIGURE 1

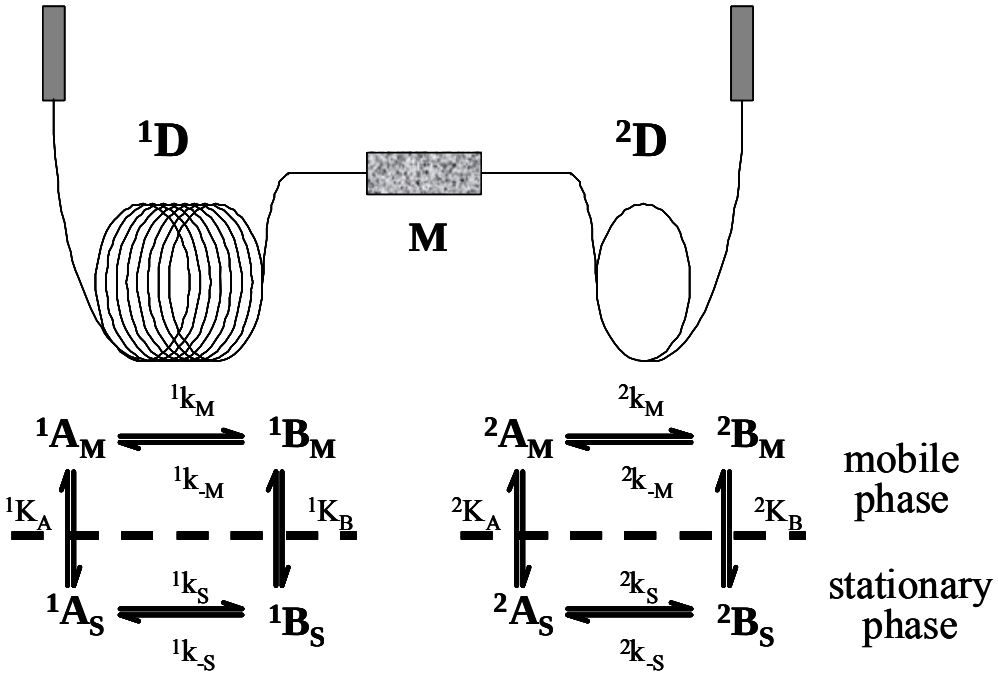

^1D
^2D
M
^1k_M
$^1k_{-M}$
^1A_M
^1B_M
^1K_A
^1K_B
^1k_S
$^1k_{-S}$
^1A_S
^1B_S
^2k_M
$^2k_{-M}$
^2A_M
^2B_M
^2K_A
^2K_B
^2k_S
$^2k_{-S}$
^2A_S
^2B_S
mobile phase
stationary phase

FIGURE 2

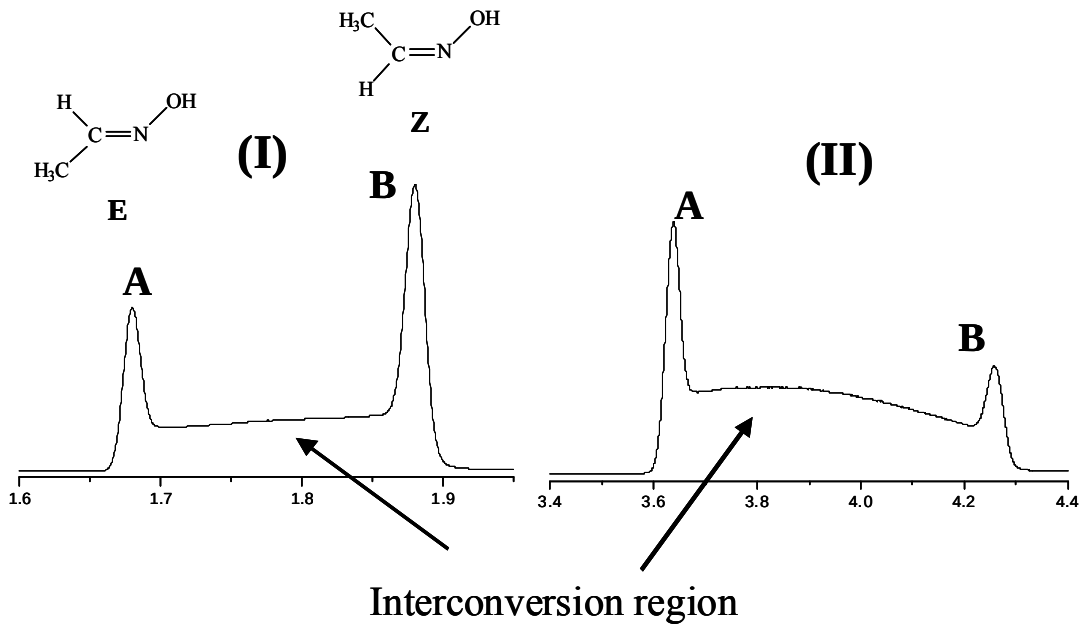

H3C
OH
C=N
H
Z
H
OH
C=N
H3C
E
(I)
B
A
(II)
A
B
1.6
1.7
1.8
1.9
3.4
3.6
3.8
4.0
4.2
4.4
Interconversion region

FIGURE 3

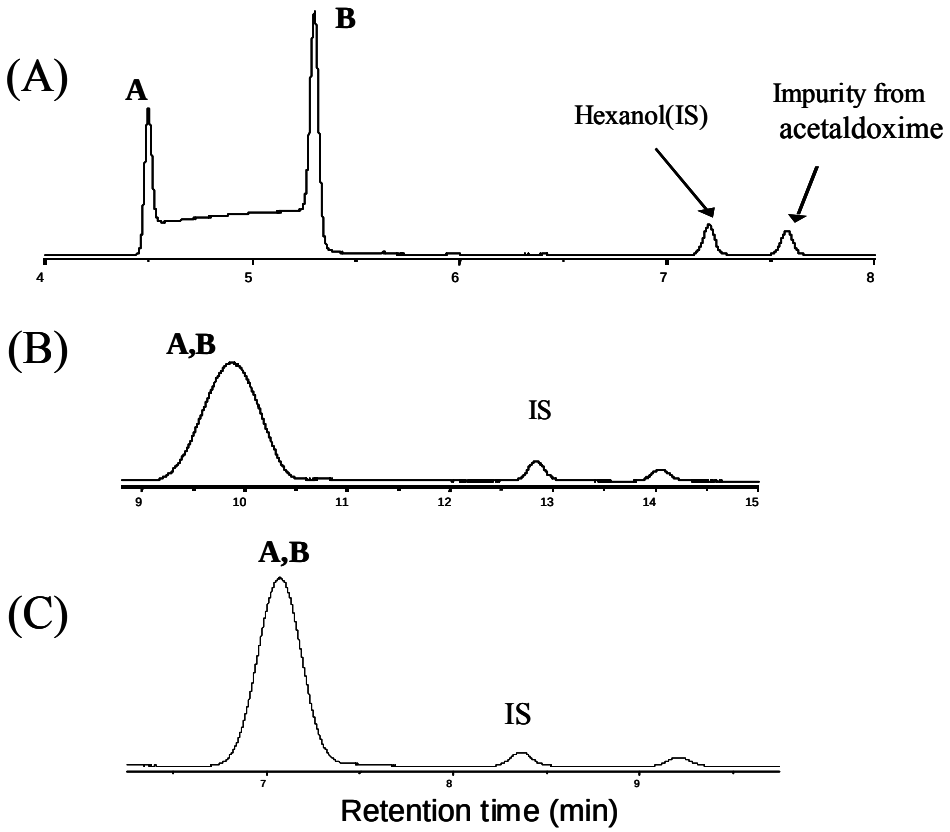

(A)
A
B
Hexanol(IS)
Impurity from
acetaldoxime
4
5
6
7
8
(B)
A,B
IS
9
10
11
12
13
14
15
(C)
A,B
IS
7
8
9
Retention time (min)

FIGURE 3

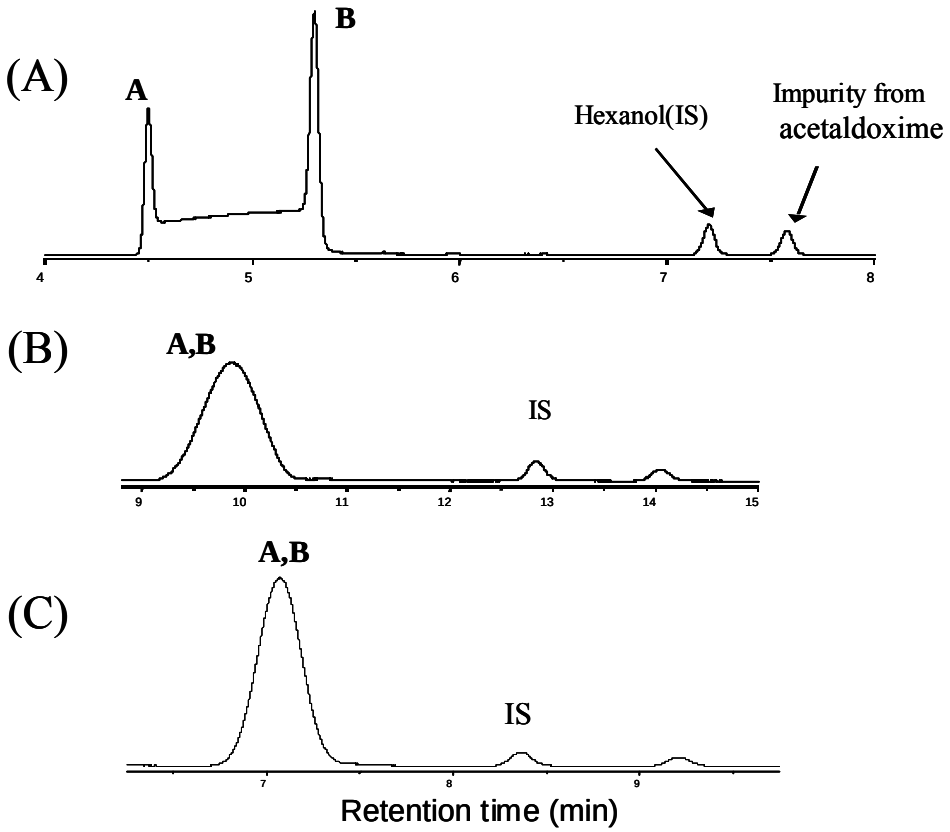

(A)
A
B
Hexanol(IS)
Impurity from
acetaldoxime
4
5
6
7
8
(B)
A,B
IS
9
10
11
12
13
14
15
(C)
A,B
IS
7
8
9
Retention time (min)

FIGURE 4B

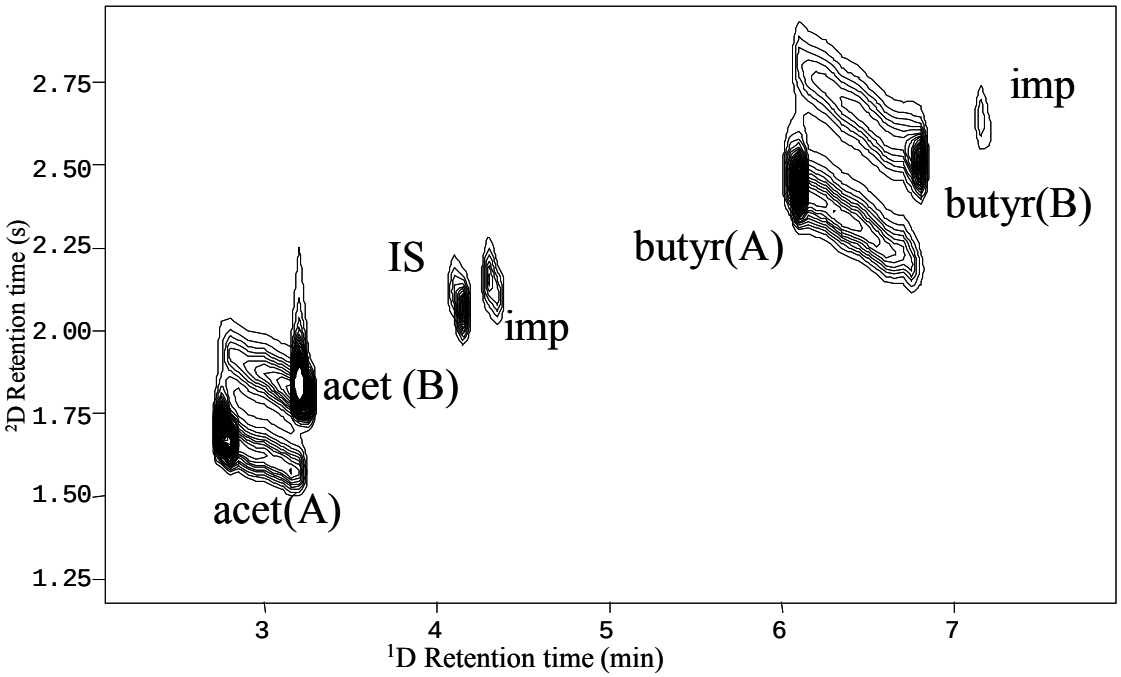

2.75
2.50
2.25
2.00
1.75
1.50
1.25
2D Retention time (s)
3
4
5
6
7
1D Retention time (min)
imp
butyr(B)
butyr(A)
IS
imp
acet (B)
acet(A)

FIGURE 5

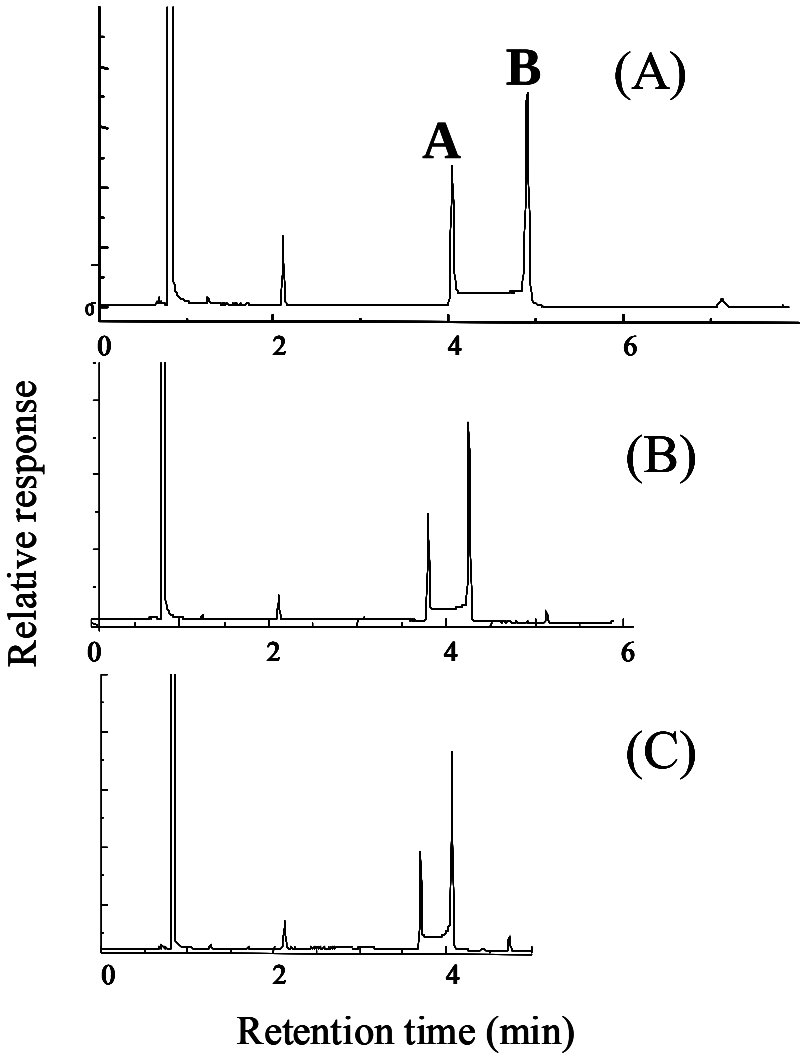


FIGURE 6

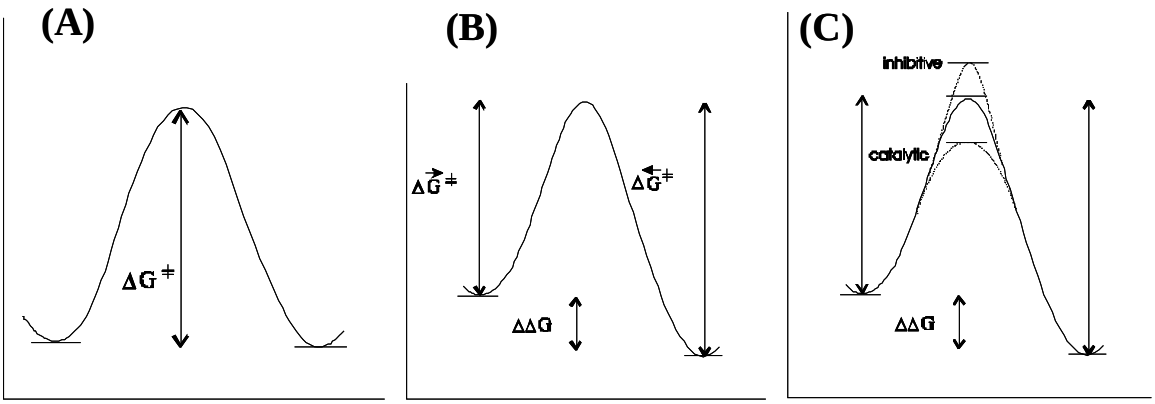


FIGURE 7

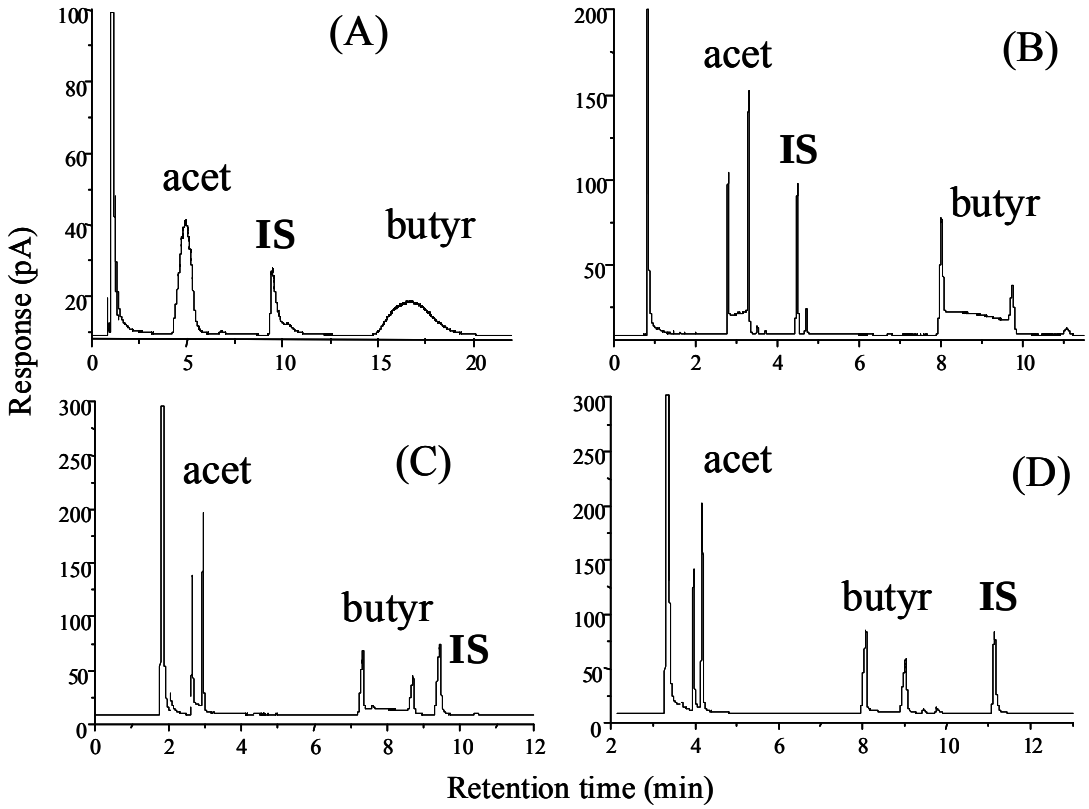

(A)
acet
IS
butyr
(B)
acet
IS
butyr
(C)
acet
butyr
IS
(D)
acet
butyr
IS
Response (pA)
Retention time (min)

Figure 8

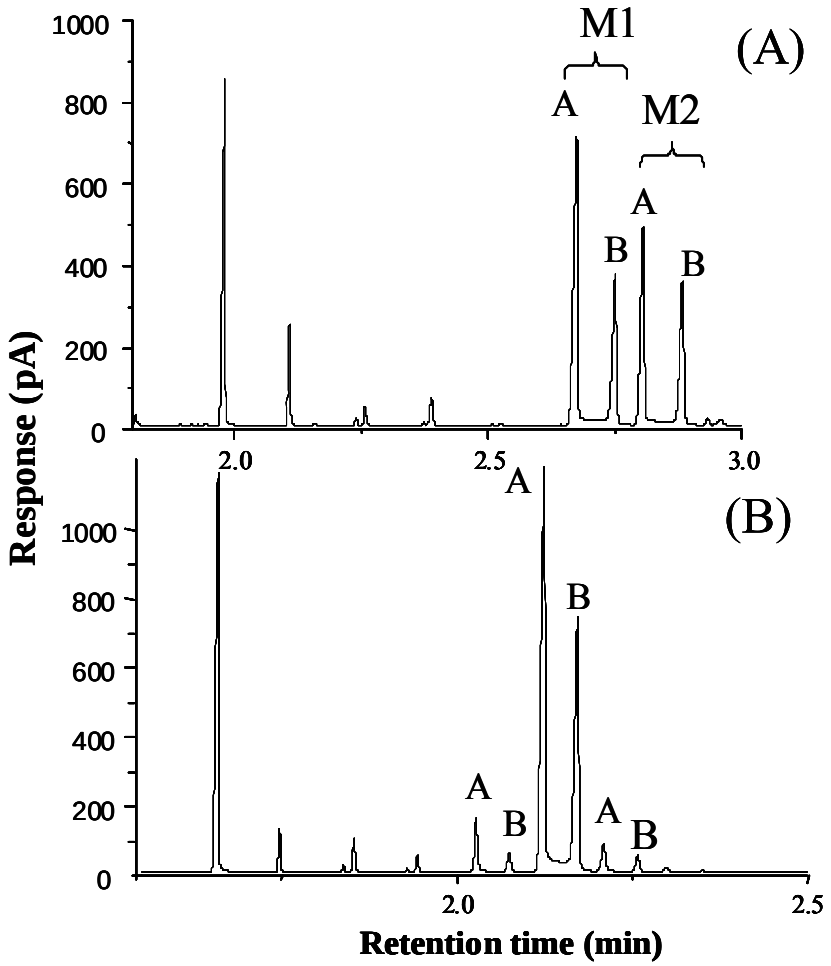
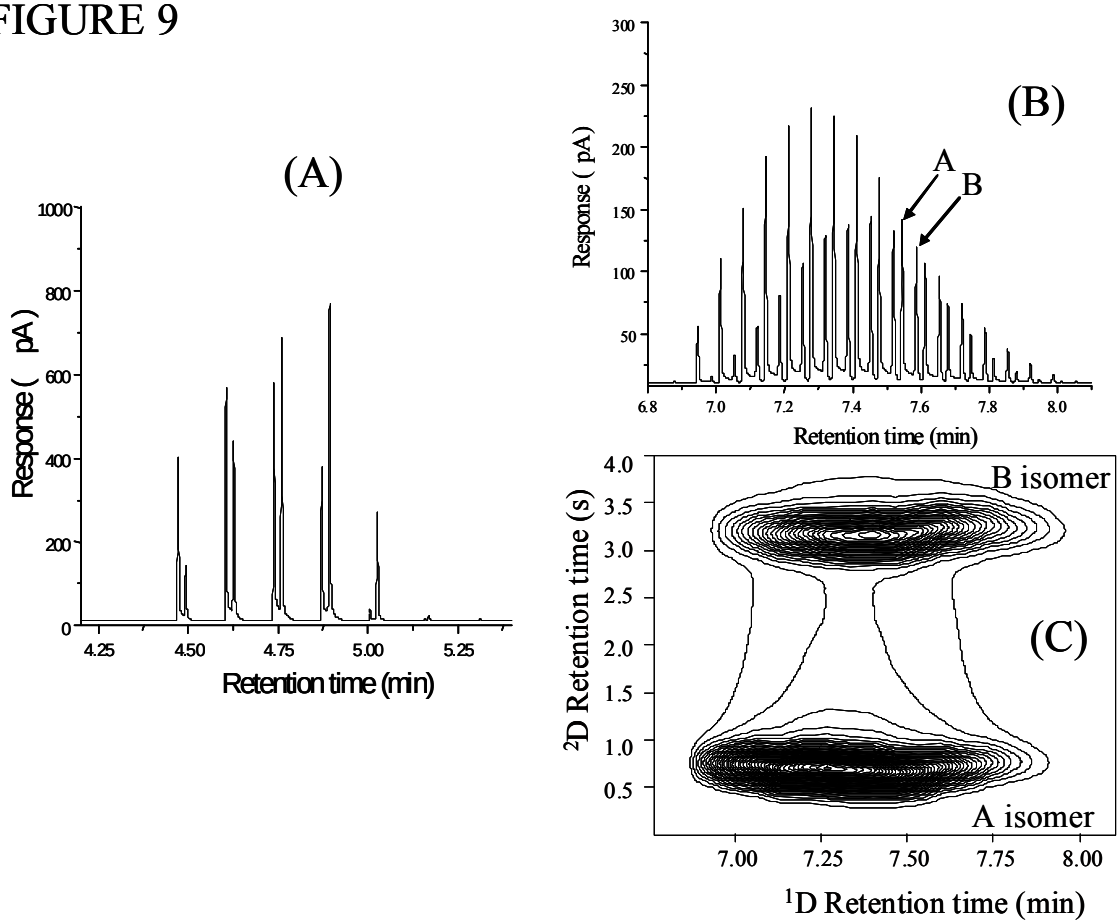

M1
(A)
A
M2
A
B
B
1000
800
600
400
200
0
2.0
2.5
3.0
A
(B)
B
A
B
A
B
1000
800
600
400
200
0
2.0
2.5
Response (pA)
Retention time (min)

FIGURE 9


(A)
Response (pA)
Retention time (min)
(B)
A
B
Response (pA)
Retention time (min)
(C)
B isomer
A isomer
2D Retention time (s)
1D Retention time (min)