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The solvolysis mechanism of simple secondary tosylates in 50% aqueous TFE†

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Abstract

The solvolysis of simple secondary tosylates in 50% trifluoethanol has been investigated using stereochemical and isotopic labels. 2-butyl, 2-pentyl and 2-octyl tosylate all solvolyse at very similar rates (~ 1×10^{-5} s^{-1}) at 30 °C. Slow racemization of *S*-2-butyl tosylate (~ 4.6×10^{-7} s^{-1}) was observed during solvolysis, but *R*-2-octyl tosylate did not show any significant racemization. Competing rearrangement of 3-pentyl tosylate to 2-pentyl tosylate was observed during solvolysis and is attributed to 1,2-hydride transfer, which occurs at a rate sufficient to account for the difference in the rates of racemisation of 2-butyl and 2-octyl tosylate. The stereochemistry of the alcohol product was studied for the reaction of *R*-2-octyl tosylate by derivatizing the corresponding alcohol to 4-nitrobenzoate, and showed high but not complete stereoselectivity (92:8 inversion:retention of configuration). ^{18}O isotope exchange at the leaving group tosylate showed that both 2-butyl and 2-octyl tosylates exchange at similar rates (~ 1.6×10^{-7} s^{-1}). Partitioning of a common intermediate carbenium ion cannot account for all these data, so a series of parallel concerted mechanisms (solvolysis, 1,2-hydride transfer and isotope exchange) is proposed as the best explanation.

Keywords: Solvolysis; Carbocation; Isotope exchange; 1,2-hydride transfer

INTRODUCTION

Whether simple secondary carbenium ions can be formed as intermediates in polar but weakly nucleophilic solvents or not has been the subject of debate for a long time. No clear-cut conclusion has been reached despite a series of mechanistic studies with 2-propyl and 2-butyl substrates.[1,2,3,4]

Tidwell[3], Dannenberg[4] and Farcaşiu[6] studied the solvolysis of 2-butyl tosylate in trifluoroacetic acid (TFA). As a 1,2 hydride shift was observed during the reaction, these authors all agreed that a simple secondary substrate in TFA should react by a stepwise substitution mechanism with a true intermediate rather than through a concerted pathway. However, they did not reach a consensus on whether the intermediate was a bridged cation or an "open" carbenium ion. Furthermore, the reaction in TFA is complicated by the reversible addition of trifluoroacetate and tosylate to the alkene product that also forms.

On the other hand, Dietze[1] correlated the rates of reaction of 2-propyl nosylate in pure hexafluoroisopropanol (HFIP) with different nucleophiles against the same reactions with methyl iodide. Since the second order rate constant for HFIP was on the same straight line generated by other nucleophiles known to react by S_N2 mechanisms for both substrates, the solvolysis of 2-propyl substrates in HFIP was proposed to follow the same mechanism. A change in mechanism would be expected to give a positive deviation from the correlation.

Jencks and Dietze[2] had previously applied the same correlation method to the solvolysis reaction of 1-(4-nitrophenyl)-2-propyl derivatives in trifluoroethanol (TFE) and water/TFE mixtures[1]. Their conclusion was that these simple secondary substrates react through a concerted solvolysis pathway, even in these weakly nucleophilic solvents, with an "open" transition state. The

mechanistic pathway was described as a forced uncoupled concerted mechanism[5] with a transition state that has similar properties to a true carbenium intermediate.

Thus, the evidence for either mechanism is not unambiguous and compelling, so we have investigated this reaction in 50% aqueous TFE by studying of the stereochemistry of both starting material and solvolysis products, and through selective isotope labelling[7] in the tosylate group. Overall, the mechanism of solvolysis of secondary tosylates in 50% TFE is best regarded as a concerted pathway without forming a discrete intermediate.[1,2] The changes in stereochemistry and labeling that apparently signal an intermediate (carbenium) species are best explained through competing concerted pathways.

EXPERIMENTAL SECTION

General

The alkyl tosylates, 4-nitrobenzoate ester and ^{18}O labeled tosyl chloride were synthesized as described below. All other chemicals were purchased from Sigma-Aldrich, Alfa Aesar, Acros Organics or Santa Cruz Biotechnology. TFE was distilled from P_2O_5 and stored over 4Å molecular sieves. UHQ water was obtained from an ELGA PURELAB Option S-R 7-15 system. All other chemicals were used directly without further purification.

^1H NMR and ^{13}C NMR spectra were recorded on Bruker AV-HD 400 and AV-HD 500 instruments. HPLC analysis to monitor reaction progress was carried out on a Waters 2690 (486 Tunable Absorbance Detector) and 2695 (2487 Dual λ Absorbance Detector) system with a Waters C8 column and UV detection at 265 nm. A gradient elution was used, changing from 95% water (containing 0.1% TFA) and 5% acetonitrile to 5% water (containing 0.1% TFA) and 95% acetonitrile over 20 mins followed by a further 10 mins of the final eluent mixture. Chiral HPLC analysis of the reactants and alcohol derivatives was recorded on a Gilson 805 manometric

model (Gilson 811B Dynamic Mixer, Gilson 305 + 306 Pump and Applied Biosystems 757 Absorbance Detector) with a Phenomenex® Cellulose-2 chiral column and UV detection at 226 nm (for tosylates) and 265 nm (for 4-nitrobenzoates). The eluent for tosylate substrates was 12% isopropanol-88% hexane with a flow rate 0.8 mL/min, except for 2-octyl tosylate where 1% isopropanol-99% hexane was used with a flow rate of 1.0 mL/min. For 4-nitrobenzoate, 0.3% isopropanol-99.7% hexane was used with a flow rate 1.0 mL/min. GC analysis of 2-butanol, 2-octanol and 2-octene was determined with a Perkin Elmer ARNEL Auto System XL GC model. 2-butanol was analysed isothermally at 40 ℃ with a split ratio of 20. 2-octanol and 2-octene were analysed isothermally at 90 ℃ with a split ratio of 20.

Syntheses

2-butyl tosylate was synthesised following a published procedure[8]. 0.74 g (10 mmol) 2-butanol was dissolved in 10 mL anhydrous pyridine in an ice-water bath. 2.29 g (12 mmol) tosyl chloride was added portion wise within 10 mins. The solution was stirred in the ice-water bath for another 6 hrs before quenching with cold 3 M HCl solution (25 mL). After extracting with DCM (25 mL), the organic phase was washed with another 25 mL of 3 M HCl and the water phase was extracted with DCM (3 × 5 mL). The combined organic phase was washed with saturated $NaHCO_3$ and dried over Na_2SO_4 before removing the solvent under vacuum. The crude product was purified by flash chromatography using hexane: ethyl acetate (4:1), yielding 1.59 g (70%) of **2-butyl tosylate** as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): 7.81 (2H, d, J = 8.8 Hz), 7.35 (2H, d, J = 8.7 Hz), 4.51 – 4.60 (1H, m), 2.48 (3H, s), 1.52 – 1.78 (2H, m), 1.35 (3H, d, J = 6.5 Hz) and 0.82 (3H, t, J = 7.5 Hz). ^{13}CNMR (100 MHz, $CDCl_3$): 144.37, 134.64, 129.70, 127.70, 81.79, 29.48, 21.62, 20.30 and 9.30.[8,9]

***S*-2-butyl tosylate** (ee 91%), **2-pentyl tosylate**, **3-pentyl tosylate**, **2-octyl tosylate** and ***R*-2-octyl tosylate** (ee 99.5%) were all synthesized by the same procedure[8] and purified by flash chromatography with the same eluent as above.

2-pentyl tosylate[9]: 65% yield as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): 7.81 (2H, d, J = 8.8 Hz), 7.35 (2H, d, J = 8.8 Hz), 4.59 – 4.74 (1H, m), 2.48 (3H, s), 1.51 – 1.76 (2H, m), 1.35 (3H, d, J = 6.6 Hz) and 0.67 (3H, t, J = 7.4 Hz). ^{13}CNMR (100 MHz, $CDCl_3$): 144.33, 134.74, 129.66, 127.67, 80.36, 38.63, 21.56, 20.76, 18.14 and 13.58.

3-pentyl tosylate[10,11]: 50% yield as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): 7.81 (2H, d, J = 8.3 Hz), 7.34 (2H, d, J = 8.2 Hz), 4.42 – 4.73 (1H, m), 2.47 (3H, s), 1.67 – 1.80 (4H, m) and 0.85 (3H, t, J = 7.4 Hz). ^{13}CNMR (100 MHz, $CDCl_3$): 144.30, 135.16, 129.66, 128.67, 66.84, 21.56, 20.26 and 11.08.

***R*-2-octyl tosylate**[12,13]: 60% yield as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): 7.79 (2H, d, J = 8.7 Hz), 7.35 (2H, d, J = 8.8 Hz), 4.52 – 4.67 (1H, m), 2.46 (3H, s), 1.65 – 1.08 (15H, m) and 0.85 (3H, t). ^{13}CNMR (100 MHz, $CDCl_3$): 144.33, 134.71, 129.66, 127.70, 80.67, 36.49, 31.57, 28.78, 24.80, 22.45, 21.57, 20.84 and 13.99.

2-octyl-4-nitrobenzoate: After the solvolysis reaction of *R*-2-octyl tosylate was complete (at least 7 half-lives), the TFE was removed under vacuum and the aqueous solution extracted with 30 mL diethyl ether. After washing with brine, the ether solution was concentrated under vacuum and the residue dissolved in 10 mL DCM charged with 2 eq DMAP in a water-ice bath. 1.5 equivalents of 4-nitrobenzoyl chloride was added portion wise within 5 mins and the reaction was kept in the ice bath for 2 hrs before slowly warming to room temperature. The mixture was stirred at room temperature overnight before the solvent was removed under vacuum. The residue was dissolved in 1.5 mL hexane and diluted to a suitable concentration for chiral HPLC

analysis. HPLC analysis gave two peaks with retention times of 20.2 and 22.1 minutes in a ratio of 92:8 that correspond to the 4-nitrobenzoate enantiomers as determined by analysis of racemic 2-octyl-4-nitrobenzoate by the same method.

^{18}O-tosyl chloride was synthesis by modifying a published procedure[14]. To a 100 mL round bottom flask charged with 30 mL anhydrous acetonitrile, 1.86g (15 mmol) p-thiocresol and 1 mL $H_2{}^{18}O$ (97% isotope labelled, Santa Cruz Biotechnology) was added and stirred in an ice-water bath for 15 mins. 4.18g (18 mmol) trichloroisocyanuric acid was added portion-wise to the cooled solution within 15 mins and the reaction was kept at 0 ℃ for 1 h, then allowed to warm to room temperature and stirred overnight before removing the solvent under vacuum. 30 mL diethyl ether was added and the mixture shaken violently. The solid was filtered off and washed with 5 × 2 mL diethyl ether; the combined filtrate was concentrated under vacuum to afford 2.86 g (14.7 mmol) of the **^{18}O-tosyl chloride** (98%). The extent of labelling by ^{18}O was been determined by GC-MS which showed that the tosyl chloride contained 93.5% doubly labelled ^{18}O-tosyl chloride and 6.5% singly labelled ^{18}O-tosyl chloride. The crude ^{18}O-tosyl chloride was used to synthesise the tosylate esters immediately it was isolated, using the same synthetic and purification methods described above.

Kinetic analysis

The solvolysis reactions of all the tosylate esters were carried out under the same conditions: 5 mM tosylate, 5 mM 2,6-dimethyl pyridine, 1 mM 2,6-dimethyl-3-hydroxy pyridine (as an internal standard) and 1 M sodium perchlorate in 50% aqueous TFE (v/v) at 30 ℃. The solutions were immersed in a thermostated water bath, and the progress of the reactions was monitored by analyzing aliquots of the reactions mixture using HPLC as described above for 72 hrs. The peak

areas in the chromatograms were integrated and a first order equation fit to these data; in all cases, $R^2 > 0.99$.

Stereochemical analysis

2-*S*-butyl tosylate (100 mM and 10 mM; initial ee 91%): At various time intervals, an appropriate volume of the reaction mixture (100 or 10 mM 2-*S*-butyl tosylate; 1.2 equivalents 2,6-dimethylpyridine; 1 M sodium perchlorate) was withdrawn and extracted with hexane. As the reaction proceeded, increasing volumes of the solution were required to ensure sufficient reactant was present for the analysis. The hexane layer was analyzed directly by chiral HPLC to measure the ratio of the tosylate enantiomers, and by chiral GC to measure the ratio of the 2-butanol enantiomers. Solutions with varying concentrations of tosylate anion present (5 mM 2-*S*-butyl tosylate; 6 mM 2,6-dimethylpyridine; 0.1, 0.5 or 1.0 M sodium tosylate, with the total salt concentration made up to 1 M with sodium perchlorate; 1 M 15-crown-5) were analysed the same way.

2-*R*-octyl tosylate (5 mM (initial ee 99.5%); 6 mM 2,6-dimethylpyridine; 1 M sodium perchlorate) was analysed as above to determine the stereochemical changes in the reactant as the reaction progressed. To monitor the stereochemical changes in the alcohol product 2-*R*-octyl tosylate (10 mM; 12 mM 2,6-dimethylpyridine; 1 M sodium perchlorate) was allowed to proceed to completion (7 half lives), and the 2-octanol isolated as above and converted to 4-nitrobenzoate ester before being analyzed by chiral HPLC.

Isomerisation of 3-pentyl tosylate and 2-pentyl tosylate: At various time intervals, an appropriate volume of the reaction mixture was withdrawn and extracted with hexane, which was directly analyzed by chiral HPLC. The signals for 3-pentyl tosylate and both enantiomers of 2-

pentyl tosylate were completely resolved in the chromatogram, and the ratio was determined by integrating these peaks.

Product analysis

The products from the solvolysis of 2-butyl tosylate and 2-pentyl tosylate were analyzed by ^{13}C NMR. These reactions was carried out in 1:1 TFE:D_2O (v/v), with all other conditions the same as for the kinetic measurements. The ratio of the alcohol and ether products were measured by integrating peaks for the carbon at position 2. The products from the solvolysis of 2-octyl tosylate were directly analyzed by GC, using authentic 2-octene and 2-octanol as external standards to calibrate the yield of respective products. 2-octene was observed as a mixture of E/Z isomers, but 1-octene was not detected.

Product stability

When 2-octene was incubated under the solvolysis conditions (10 mM in 50% aqueous TFE with 20 mM pyridinium tosylate, 10 mM 2,6-dimethyl pyridine and 1 M sodium perchlorate) for 5 days and then analysed by GC, no new peaks could be identified. When *R*-2-octanol was incubated under the solvolysis conditions (10 mM in 50% aqueous TFE with 20 mM pyridinium tosylate, 10 mM 2,6-dimethyl pyridine and 1 M sodium perchlorate) for 2 weeks, then derivatized to the 4-nitrobenzoate ester, chiral HPLC analysis showed the ee had not changed.

^{18}O isotope exchange analysis[7]

^{18}O-labelled-2-butyl tosylate (5 mmol) and **^{18}O-labelled-2-octyl tosylate** (5 mmol) were individually subjected to solvolysis under the conditions described above (with an initial reactant concentration of 10 mM). At different time intervals, an appropriate volume of solution (to be able to extract about 50 mg of the unreacted tosylate) was withdrawn and extracted with diethyl ether. The organic layer was separated and dried over Na_2SO_4 and the solvent removed under

vacuum. The residues were combined and dissolved in 1 ml $CDCl_3$ and analysed by ^{13}C NMR at 125 MHz (pulse angle 45°, 10000 transients at 25 °C acquired with a 250 Hz sweep width, 8000 data points (0.031 Hz/pt) and a 16s relaxation delay time) to determine the relative concentrations of tosylate esters with ^{18}O in the bridging and nonbridging positions. The ^{13}C signals at the 2-position were centred at 81.8 (2-butyl tosylate) and 80.8 (2-octyl tosylate) ppm, respectively. The peaks were sufficiently resolved (0.045 ppm difference) to allow the ratio of ^{13}C bonded to ^{18}O or ^{16}O to be calculated by integration of the signals.

RESULTS

The first order rate constants for solvolysis of 2-butyl tosylate, 2-pentyl tosylate and 2-octyl tosylate are $1.15\pm0.05 \times 10^{-5}$ s^{-1}, $1.05\pm0.05 \times 10^{-5}$ s^{-1} and $1.20\pm0.0.06 \times 10^{-5}$ s^{-1} respectively (at 30 ℃ in 50% aqueous TFE). Within experimental error, these secondary tosylates all solvolyse at the same rate whereas 3-pentyl tosylate reacts about twice as fast and has a rate constant for solvolysis of $1.95\pm0.05 \times 10^{-5}$ s^{-1}, consistent with earlier reports.[15]

The substitution products from solvolysis of 2-butyl tosylate are 2-butanol and 2-trifluoroethoxy butyl ether in a ratio of 5:1. As the molar ratio of water to TFE in the reaction mixture is about 4:1, the selectivity for water over TFE is about 1.25:1, which is slightly larger than a simple tertiary substrate solvolysis[16] or a secondary substrate by a concerted pathway with a cation-like transition state[5]. Under our reaction conditions, potential elimination products could not be identified with confidence due to their volatility. GC analysis of the solvolysis products of 2-octyl tosylate, where the potential elimination products are less volatile, showed that the ratio of alcohol:trifluoroethyl ether:2-octene is about 5:1:4. The yield of each product was deduced by using authentic samples (2-octanol and 2-octene) to calibrate the instrument, and demonstrated a mass balance. Thus, the solvolysis reaction under neutral condition still produced a significant

amount of elimination products. Both *E* and *Z* isomers (*E*:*Z* about 4:1) of 2-octene were observed, but 1-octene was not detected.

During the solvolysis of 0.01 M *S*-2-butyl tosylate in 50% aqueous TFE, partial racemization of the reactant occurred, with an observed first order rate constant for racemization of $4.6\pm0.1 \times 10^{-7}$ s^{-1} (Figure 1A), corresponding to a first rate constant of $2.3\pm0.1 \times 10^{-7}$ s^{-1} for the interconversion of the enantiomers.

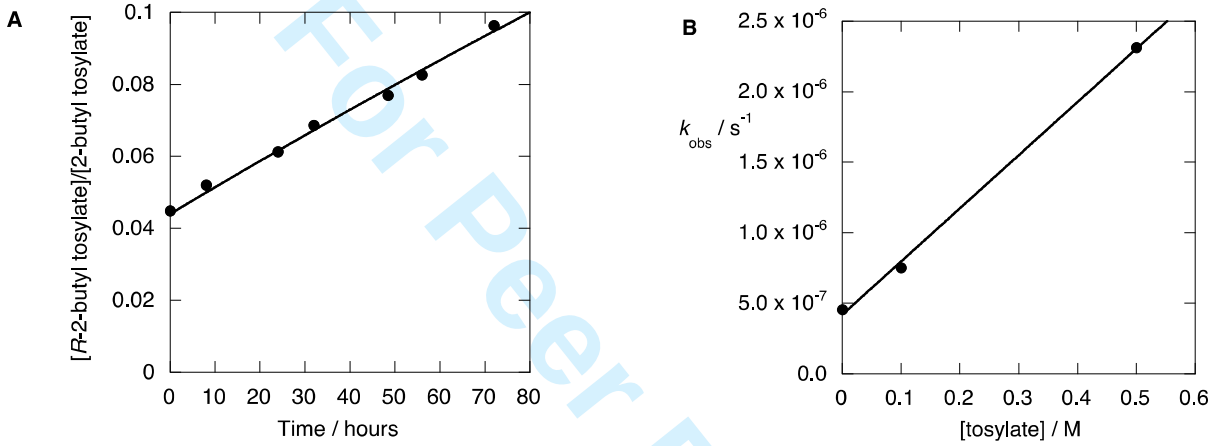
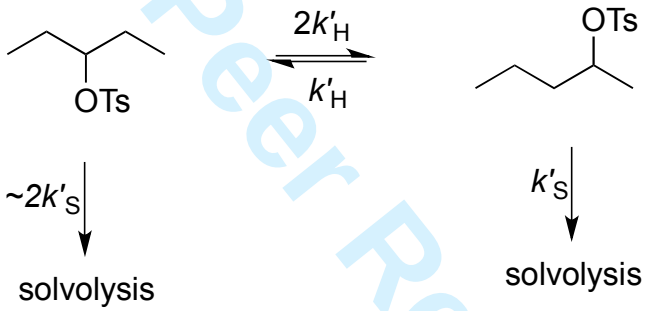


Figure 1. A: Change in the ratio [*R*-2-butyl tosylate] / [2-butyl tosylate] with reaction time when the initial concentration of reactant is 0.01 M. The solid line is the best fit of the equation [*R*-2-butyl tosylate] / [2-butyl tosylate] = $0.5 - 0.455e^{-kt}$ with $k = 4.6\pm0.1 \times 10^{-7}$ s^{-1} B: Variation in observed rate constant for racemization with concentration of tosylate. The solid line is the linear least squares fit, and has the equation $4.2\pm0.1 \times 10^{-7} + 3.8\pm0.2 \times 10^{-6}$[tosylate] s^{-1}.

This could be due to reaction between the reactant and the tosylate leaving group (generated in the course of the reaction), inverting the stereogenic centre in the reactant. To quantify its significance, the tosylate anion concentration was varied from 0.1 to 0.5 M (in the presence of 1 M 15-crown-5 to avoid ion pairing at high concentrations). The racemization rate increased linearly over this concentration range (Figure 1B), giving a second order rate constant of $3.8\pm0.2 \times 10^{-6}$ M^{-1} s^{-1}, which corresponds to a second order rate constant of for the substitution $1.9\pm0.1 \times 10^{-6}$ M^{-1} s^{-1} reaction.

In contrast, *R*-2-octyl tosylate only generated ~1% *S*-2-octyl tosylate after 72 hrs reaction (corresponding to a first rate constant for racemisation of ~3.9×10^{-8} s^{-1}).

During the solvolysis of 3-pentyl tosylate, 2-pentyl tosylate appears transiently in the reaction mixture. This can be explained by the occurrence of a 1,2 hydride shift mechanism (scheme 1). By measuring the ratio of [2-pentyl tosylate] : [3-pentyl tosylate] at different time intervals and using numerical integration (Berkeley Madonna®) to fit scheme 1 to these data, k'_H (the 1,2-hydride transfer rate constant) was evaluated as ~9×10^{-7} s^{-1}. Scheme 1 assumes that hydride transfer to the C_3 position in 3-pentyl tosylate is twice as fast as to the C_2 position in 2-pentyl tosylate for statistical reasons.

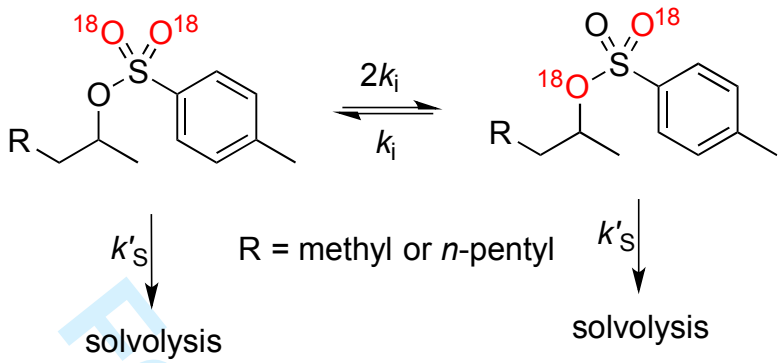


Scheme 1

After solvolysis of *R*-2-octyl tosylate, 2-octanol was isolated and derivatized to the corresponding 4-nitrobenzoate ester to allow analysis by chiral HPLC using UV detection. The ratio of retention to inversion at the stereogenic carbon is 8:92. This is much greater than the fraction of reactant inversion noted above and represents the facial selectivity in the hydrolysis reaction.

During the solvolysis of ^{18}O labelled 2-butyl tosylate and labelled 2-octyl tosylate, scrambling of the isotopically labeled positions was detected by ^{13}C NMR analysis of the residual reactant (Figure 2). The extent of scrambling was similar in both cases (~8% after 4 half lives), indicating similar ^{18}O scrambling rate constants (k_i Scheme 2); the ratio of the two isotopomers at various

time intervals is given in table 1. Fitting with a first order equation gives $k_i = 5.4 \pm 0.3 \times 10^{-7}$ s^{-1} for 2-butyl tosylate, and $k_i = 4.2 \pm 0.2 \times 10^{-7}$ s^{-1} for 2-octyl tosylate.



Scheme 2

Table 1. Results of isotope exchange for labelled 2-butyl tosylate and labelled 2-octyl tosylates

Time/s	C-^{18}O:C-^{16}O	C-^{18}O:C-^{16}O
0	0:100	0:100
57600	1.6:98.4	1.2:98.8
144000	4.6:95.4	3.8:96.2
239400	8.5:91.5	6.6:93.4

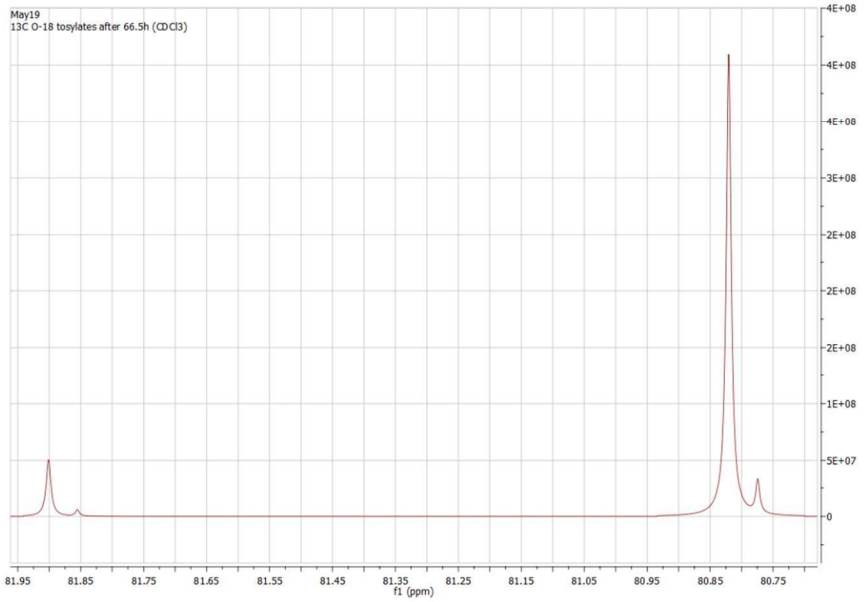


Figure 2. ^{13}C NMR spectrum of labelled 2-butyl tosylate and 2-octyl tosylate recovered after 66.5 hours

DISCUSSION

Classical signs of the capacity of a secondary tosylate to form a stable carbenium ion intermediate are: the loss of stereochemical integrity at the stereogenic centre; that the non-equivalent oxygens in the tosylate group can exchange position; and that substitution of the tosylate does not occur with complete inversion of configuration. These observations are all apparent in the data reported here. The products of the reaction are stable under the reaction conditions, and neither revert to reactant nor change their stereochemistry once formed, unlike solvolysis in TFA.[3,4,6] Thus, these observations must be explained by the mechanistic pathway of the solvolysis reaction.

Racemisation of both 2-butyl and 2-octyl tosylate is observed under the solvolysis conditions. It is possible that tosylate released in the course of the reaction can act as a competitive nucleophile and invert the stereochemistry of the reactant. This process would also provide a route for scrambling of the isotopic label in the alkyl tosylate. Measuring the rate of reaction between tosylate and 2-butyl tosylate gives a second order rate constant of $1.9 \pm 0.1 \times 10^{-6}$ M^{-1} s^{-1} for the bimolecular substitution reaction. If this figure is combined with the rate of solvolysis, the fraction of the minor enantiomer can be calculated from equation 1

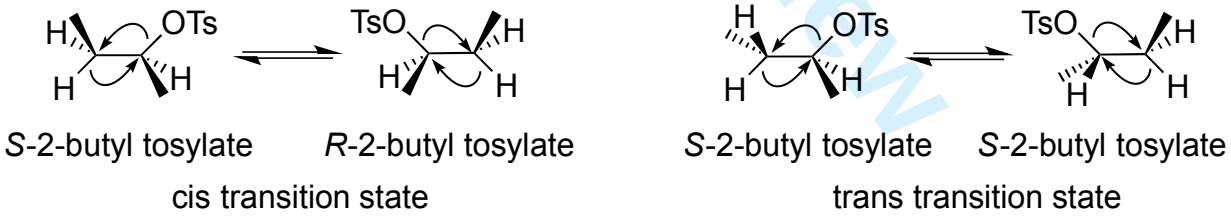
$$\frac{[R\text{-2-butyl tosylate}]}{[2\text{-butyl tosylate}]} = 0.5 - \frac{ee}{2} exp(-2k_N[A_0](t - \frac{\left(1-e^{(-k'_S t)}\right)}{k'_S})) \quad (1)$$

in which k_N is the second order rate constant for the incorporation of tosylate from solution, k'_S is the rate constant for solvolysis, $[A]_0$ is the initial concentration of the reactant, and ee is the initial enantiomeric excess. Over 72 hours, equation 1 predicts that the remaining substrate from 10 mM *R*-2-octyl tosylate (initially 0.25% *S*) will contains ~0.6% S, close to the observed vaue of ~1%. However, for 10 mM *S*-2-butyl tosylate (initially 4.5% *R*), the prediction is that the remaining substrate will contains 4.8% *R*, significantly different from the observed value of ~10%

R. It is evident that a significant additional pathway for racemization is required for 2-butyl tosylate.

A second process that can lead to racemization is a 1,2 hydride shift, coupled with 1,2 leaving group migration. In 2-butyl tosylate, each migration still gives 2-butyl tosylate but can lead to a change in stereochemistry. In 2-octyl tosylate, racemization requires two migrations – to the 3 position, then back to the 2 position. The rate constant for the 1,2 migration between secondary centres was measured by studying the simultaneous solvolysis and isomerization of 3-pentyl tosylate. As 2-pentyl tosylate is significantly less reactive than 3-pentyl tosylate to solvolysis, and because the rate of isomerization to the 2-pentyl tosylate is benefits from a statistical factor of 2, appreciable concentrations of 2-pentyl tosylate accumulate in the reaction mixture. Analysis of this accumulation using numerical integration gives a rate constant for the 1,2 shift of 9×10^{-7} s^{-1}.

Considering the stereochemistry of the reaction of 2-butyl tosylate, the 1,2 transfer could happen through two transition states: cis and trans (Scheme 3). Both will contribute to the observed rate constant for the 1,2 shift of 9×10^{-7} s^{-1}, but only the cis transition state will cause racemization.



Scheme 3

The ratio of the two transition states can be estimated to be about 4:1 by using cis and trans 2-butene as a model,[3] leading to a predicted rate constant of 1.8×10^{-7} s^{-1} for the interconversion of the 2-butyl tosylate isomers through this pathway. This value is similar to the observed rate constant for the interconversion of the 2-butyl tosylate enantiomers (Figure 1). Fitting equation 2

to the best fit for the 1,2 shift rate constant (k'_H) using the independently measured rate constants for tosylate exchange and solvolysis leads to the solid line given in figure 2, and $k'_H = 2.1 \pm 0.1 \times 10^{-7}$ s^{-1} in good agreement with the behavior of 3-pentyl tosylate.

$$\frac{[R-2-\text{butyl tosylate}]}{[2-\text{butyl tosylate}]} = 0.5 - \frac{ee}{2} exp(-2k_N[A_0]\left(t - \frac{\left(1-e^{(-k'_S t)}\right)}{k'_S}\right) - 2k'_H t) \quad (2)$$

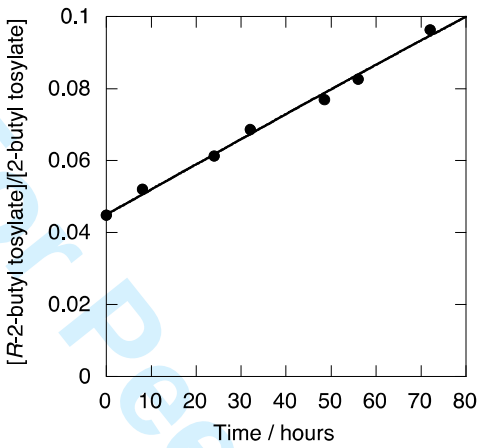
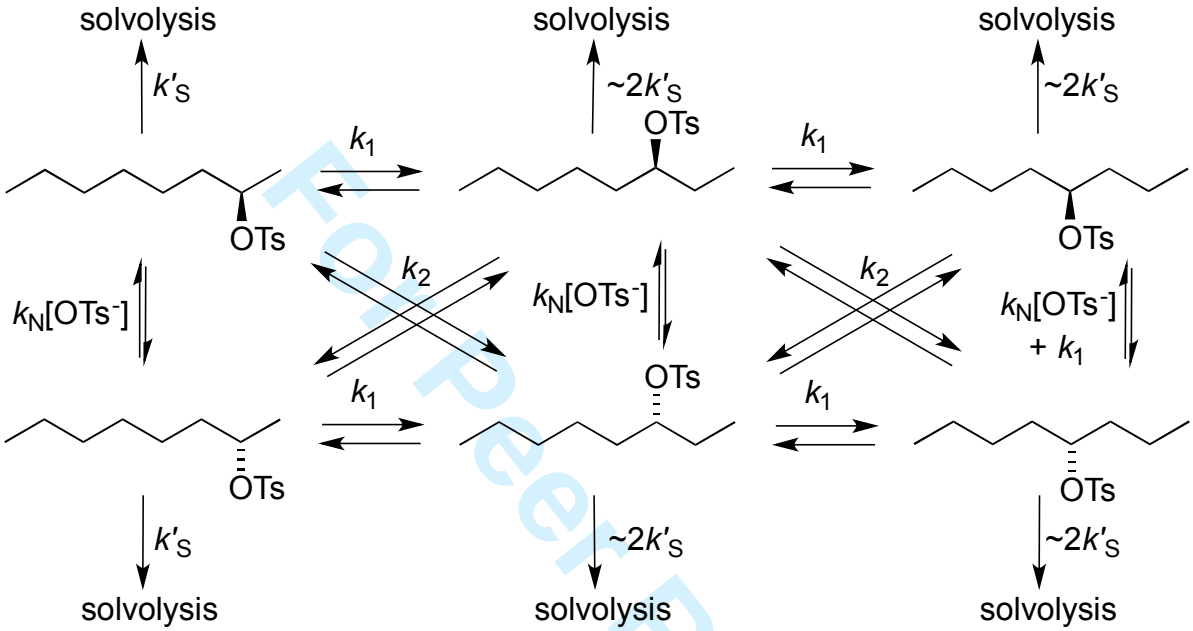


Figure 3. Racemization of 10mM *S*-2-butyl tosylate. The solid line is the best fit of equation 2, accounting for racemization through tosylate anion incorporation and 1,2 shifts.

Similarly, the behavior of 2-octyl tosylate due to these factors can be predicted. In this case, the effect of 1,2 shifts on racemization is much reduced because (i) migration from the 3 position is partitioned between the 2 and 4 positions and (ii) the competing rate of solvolysis in the 3 and 4 positions is faster than from the 2 position. We assume that 3-octyl tosylate and 4-octyl tosylate undergo solvolysis two times faster than 2-octyl tosylate (i.e. at the same rate as 3-pentyl tosylate, which is a conservative estimate[15]). Numerical modeling of scheme 4 (using Berkeley Madonna®) was used to predict the variation in the ratio of the two enantiomers with time, with $k_1 = 0.8k'_H = 7.2 \times 10^{-7}$ s^{-1} and $k_2 = 0.2k'_H = 1.8 \times 10^{-7}$ s^{-1}, and $k'_S = 1.1 \times 10^{-5}$ s^{-1} and $k_N = 2.2 \times 10^{-6}$ M^{-1} s^{-1}. Each arrow is associated with the rate constant shown near it (i.e. forward and reverse reactions have the same rate constant, shown once for clarity). This predicts that 1,2 migrations lead to ~0.4% racemization. In contrast to 2-butyl tosylate, migration away from the 2 position and more

rapid solvolysis of these isomers suppresses the observation of racemisation through the 1,2 migration pathway. In combination with the incorporation of tosylate formed during the solvolysis reaction, the ~1% fraction of *S*-2-octyl tosylate observed after 72 hours is satisfactorily accounted for.



Scheme 4

From these data, the dominant process that competes with solvolysis to affect the structure of 2-butyl tosylate in dilute solution is 1,2-migration. When analysed through the stereochemical changes in the substrate, most of the migrations (~80%) are invisible as they lead to the same enantiomer. These migrations do not affect the structure of 2-octyl tosylate to any significant extent. During this process, the bridging and non-bridging oxygen atoms of the tosylate can potentially change position. Selective isotopic labeling of the non-bridging oxygens in the reactant was used to reveal the extent of this process, and showed that both 2-butyl and 2-octyl tosylates scramble the position of ^{18}O introduced into the non-bridging positions to a similar extent (7% and 9% after 72 hours, with slightly greater exchange occurring in the 2-butyl tosylate). Taking into account the statistical factors and assuming heavy atom isotope effects are

negligible, the rate constants for isotopic exchange are $1.8\pm0.1 \times 10^{-7}$ s^{-1} (2-butyl tosylate) and $1.4\pm0.1 \times 10^{-7}$ s^{-1} (2-octyl tosylate).

Residual 2-octyl tosylate is not significantly affected by 1,2-hydride transfer or incorporation of tosylate released during solvolysis, so ^{18}O scrambling at the C_2 position of labelled 2-octyl tosylate requires a pathway independent of these processes. ^{18}O scrambling in labelled 2-butyl tosylate will also include this pathway, plus a possible contribution from isotope exchange associated with 1,2-migration.

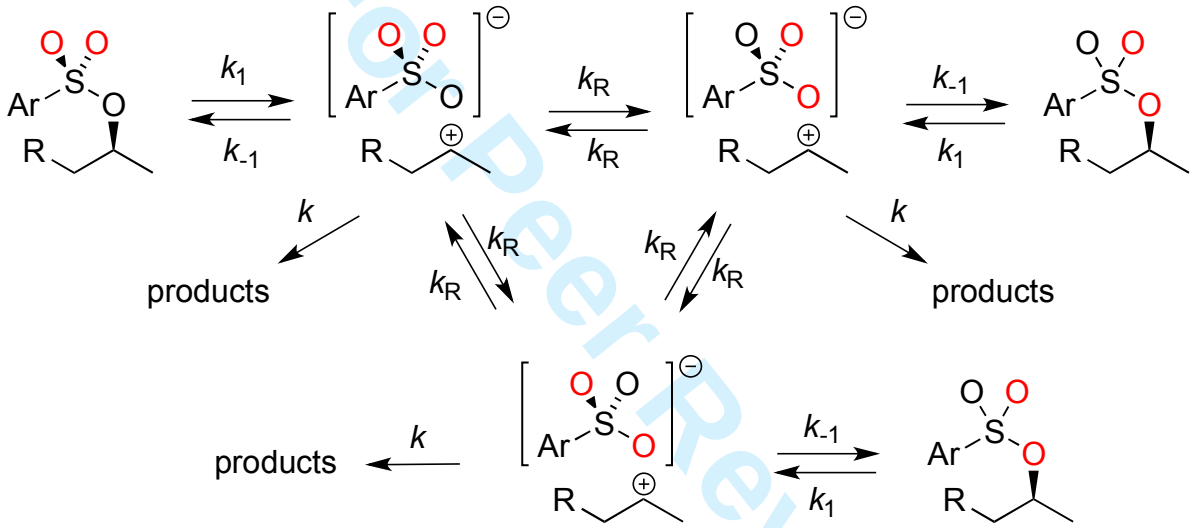
If 1,2-migration in 2-butyl tosylate occurs by a pathway that selectively involves a non-bridging oxygen in the tosyl group, then the rate constant for isotopic exchange through this pathway would be the same as for 1,2 migration ($\sim 9 \times 10^{-7}$ s^{-1}). If migrations occur selectively through the bridging oxygen, then 1,2-transfer will not cause any isotope exchange. As the rate constant for isotopic exchange in 2-butyl tosylate is greater by only $\sim 0.5 \times 10^{-7}$ s^{-1} than for 2-octyl tosylate, isotopic exchange through the 1,2 migration must be strongly selective (~95%) for the bridging oxygen, assuming that the contribution from direct exchange at the 2 position is similar for both compounds.

The simplest detailed mechanism to potentially account for all these data is the formation of a carbenium ion that can partition between solvolysis, reversion back to reactant and a 1,2 hydride shift (followed by either solvolysis or reversion back to reactant for 2-butyl tosylate). For reversion back to reactant to be accompanied by an exchange of oxygen atoms, rotation of the tosylate is required. This process has a rate constant of 5×10^{10} s^{-1},[5,7] slightly slower than the solvent reorganization rate constant of 10^{11} s^{-1} that limits solvolysis of the carbenium ion.[17]

The 1,2-hydride transfer and isotope exchange could also occur in a coupled process, with 1,2-hydride transfer accompanying isotope exchange. This must be a minor pathway, as shown by

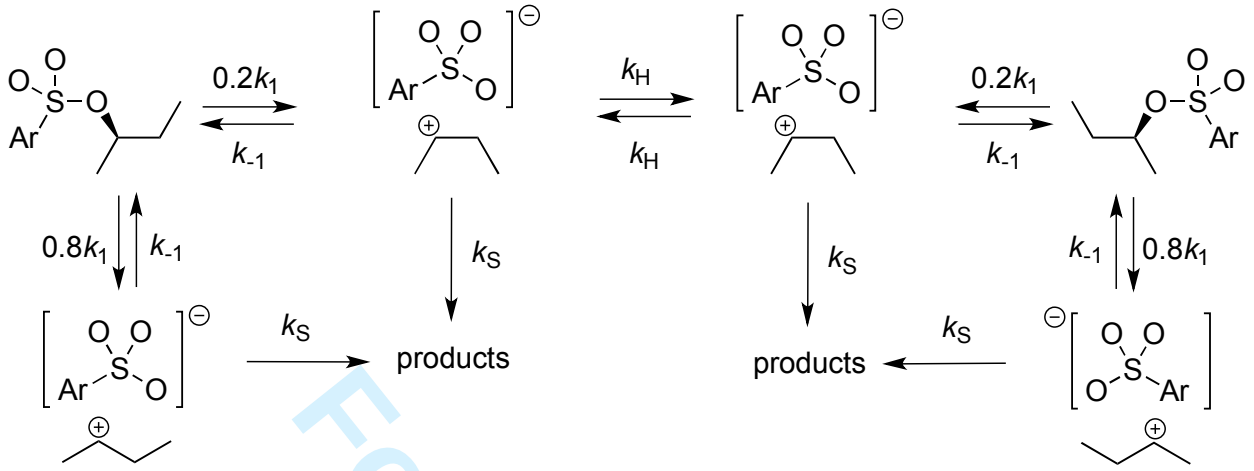
the similarity in isotope scrambling rates in 2-butyl and 2-octyl tosylate, and is not included in this mechanism (but see below).

Scheme 5 shows this proposal as applicable to the data for the isotope scrambling in the reactant. For 2-octyl tosylate, 1,2 hydride shift contributes to formation of products, but in 2-butyl tosylate this an identity reaction that does not affect the rate of solvolysis. The potential effect of 1,2-hydride shift on oxygen exchange is small (see above) and is not included in this scheme (see below).



Scheme 5

Scheme 6 shows this proposal as applicable to the data for racemization of 2-butyl tosylate. The overall rate constant for formation of the ion pair with the correct geometry is $0.2k_1$ based on the different energies of the trans and gauche forms. The trans cation can also undergo 1,2 hydride transfer, but this does not change the sense of the stereogenic centre. The trans cation contributes to solvolysis and oxygen exchange, but not to racemization. We assume that hydride transfer and ion recombination are not significantly affected by the different geometry.



Scheme 6

These schemes lead to these expressions for the observed rate constant for solvolysis:

2-butyl tosylate: $k_{obs} = k_1\, k_S / (k_{-1} + k_S) = 1.15 \times 10^{-5}\ s^{-1}$ (3)

2-octyl tosylate: $k_{obs} = k_1\, (k_S + k_H\ ) / (k_{-1} + k_S + k_H) = 1.20 \times 10^{-5}\ s^{-1}$ (4)

The rate of isotope exchange is described by the expression:

$[^{18}OTs]/\{[^{16}OTs]+[^{18}OTs]\} = 2/3(1-e^{-at})$, where a is:

2-butyl tosylate: $3k_1k_R\, k_{-1}/[(k_{-1} + k_S)\ (k_{-1} + k_S + 3k_R)] = 5.4 \times 10^{-7}\ s^{-1}$ (5)

2-octyl tosylate: $3k_1k_R\, k_{-1}/[(k_{-1} + k_S + k_H)(\ k_{-1} + k_S + k_H + 3k_R)] = 4.2 \times 10^{-7}\ s^{-1}$ (6)

Finally, the racemization of S-2-butyl tosylate induced by 1,2-hydride transfer is described by the expression:

[R-OTs]/{[R-OTs]+[S-OTs]} = 0.5 - 0.455e^{-bt}, where b is:

$0.4\ k_1\ k_{-1}\ k_H/[(k_{-1} + k_S)(k_{-1} + k_S + 2k_H)] = 4.2 \times 10^{-7}\ s^{-1}$ (7)

These equations cannot be solved with a consistent set of values for the rate constants.

For example, using $k_R = 5 \times 10^{10}\ s^{-1}$,[5,7] and assuming k_S is limited to the solvent reorganization rate constant of $k_S = 10^{11}\ s^{-1}$ if the carbenium ion is a true intermediate,[17] we can combine

equations 3 and 5 to obtain a value for k_{-1} of 8×10^9 s^{-1}. However, using this value and combining 3 and 7 leads to a negative value for k_H. If k_S is assumed to be greater than 10^{11} s^{-1}, to avoid this problem, the mechanism now becomes at least a pre-association enforced concerted mechanism, and is not consistent with the scheme. Combining equations 3 and 4 shows that k_{-1} must be at least $0.04k_S$ to avoid k_H being negative. If k_{-1} approaches this limit, then k_H becomes large relative to k_S which is inconsistent as then 2-octyl tosylate should solvolyse significantly faster than 2-butyl tosylate; however, the observed solvolysis rates for both substrates are virtually the same. If k_{-1} is comparable or much much larger than k_S, then k_H becomes insignificant relative to k_S. However, this is incompatible with the observation that oxygen exchange is observed in a partitioning process that involves k_R, which has to be comparable with k_H, and which itself is comparable to k_S. Generally, these set of equations are not self consistent, and so the scheme involving a common carbenium ion intermediate cannot be valid.

According to this analysis, the pathway for solvolysis of simple secondary tosylates in 50% TFE is a true concerted mechanism without forming any intermediates. Similarly, the oxygen exchange and 1,2 hydride shift must follow parallel concerted pathways.

CONCLUSION

The data presented here is best explained by competing concerted pathways for solvolysis, 1,2 hydride migration and oxygen exchange, rather than the formation of a carbenium ion. The substitution reactions must proceed through a concerted pathway, likely an enforced concerted, uncoupled pathway as previously suggested for similar substitution reactions.

Since 1,2-hydride migration and oxygen exchange at the tosylate are observed, the transition state is expected to be similar in character to a true carbenium intermediate as would be expected in the uncoupled concerted process. The stereochemistry of the product-alcohol has a significant

level of retained configuration (8%) which requires an open transition state to allow enough space for front-side attack at the substituted carbon, presumably via the solvation shell of the leaving group, as observed in the solvolysis reaction of *S*-1-(3-nitrophenyl)ethyl tosylate in 50% TFE[5]. An important observation is that oxygen scrambling within the reactant can be achieved without forming an intermediate ion pair, and so isotope exchange cannot be used to infer the presence of such an intermediate.[5,18,19] Presumably the transition state resembles a true carbenium ion intermediate, but leaving group departure can be coupled with leaving group rotation to. As this concerted exchange is slow compared with other substrates that can form cation intermediates[7], this suggests that the energy barrier for a concerted exchange is higher than for the step-wise pathway.

Acknowledgements

We acknowledge the Department of Chemistry, The University of Sheffield for generous support of this work.

REFERENCES

[1] P. E. Dietze, R. Hariri, J. Khattak, *J. Org. Chem.* **1989**, *54*, 3317.

[2] P. E. Dietze, W. P. Jencks, *J. Am. Chem. Soc.* **1986**, *108*, 4549.

[3] A. D. Allen, I. C. Ambidge, T. T. Tidwell, *J. Org. Chem.* **1983**, *48*, 4527.

[4] J. J. Dannenberg, J. K. Barton, B. Bunch, B. J. Goldberg, T. Kowalski, *J. Org. Chem.* **1983**, *48*, 4524.

[5] Y. Tsuji, M. M. Toteva, T. L. Amyes, J. P. Richard, *Org. Lett*. **2004**, *6*, 3633.

[6] D. Farcaşiu, *J. Chem. Soc., Chem. Commun.* **1994**, *22*, 2611.

[7] a) Y. Tsuji, T. Mori, J. P. Richard, T. L. Amyes, M. Fujio, Y. Tsuno, *Org. Lett*. **2001**, *3*, 1237. b) Y. Tsuji, M. M. Toteva, T. L. Amyes, J. P. Richard, *Org. Lett*. **2004**, *6*, 3633. c) M. Teshima, Y. Tsuji, J. P. Richard, *J. Phys. Org. Chem.* **2010**, *23*, 730.

[8] D. H. Burns, J. D. Miller, H. K. Chan, M. O. Delaney, *J. Am. Chem. Soc.* **1997**, *119*, 2125.

[9] Y. Muraki, T. Taguri, R. Yamakawa, T. Ando, *J. Chem. Ecol*. **2014**, *40*, 250

[10] X. Ma, Y. Zhang, Y. Zhang, C. Peng, Y. Che, J. Zhao, *Adv. Mater*. **2015**, *27*, 7746.

[11] M. Pohmakotr, W. Ieawsuwan, P. Tuchinda, P. Kongsaeree, S. Prabpai, V. Reutrakul, *Org. Lett*. **2004**, *6*, 4547

[12] Y. Nitta, Y. Arakawa, N. Ueyama, *Chem. Pharm. Bull.* **1986**, *34*, 2710.

[13] C. Chiappe, D. Pieraccini, *Green Chem*. **2003**, *5*, 193.

[14] a) H. Veisi, R. Ghorbani-Vaghei, J. Mahmoodi, *Bull. Korean Chem. Soc.* **2011***, 32*, 3692. b) H. Veisi, A. Sedrpoushan, S. Hemmati, D. Kordestani, *Phosphorus, Sulfur, Silicon Relat. Elem.* **2012**, *187*, 769.

[15] a) T. W. Bentley, C. T. Bowen, D. H. Morten, P. V. R. Schleyer, *J. Am. Chem. Soc.* **1981**, *103*, 5466. b) P. E. Peterson, R. E. Kelley Jr, R. Belloli, K. A. Sipp, *J. Am. Chem. Soc.* **1965**, *87*, 5169. c) T. W. Bentley, P. V. R. Schleyer, *J. Am. Chem. Soc.* **1976**, *98*, 7658.

[16] M. M. Toteva, J. P. Richard, *J. Am. Chem. Soc.* **1996**, *118*, 11434.

[17] U. Kaatze, R. Pottel, A. Schumacher, *J. Phys. Chem.* **1992**, *96*, 6017.

[18] Y. Tsuji, J. P. Richard, *J. Am. Chem. Soc.* **2006**, *128*, 17139.

[19] P. E. Dietze, M. Wojciechowski, *J. Am. Chem. Soc.* **1990**, *112*, 5240.

Supporting Information

The solvolysis mechanism of simple secondary tosylates in 50% TFE

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Table S1. Racemization of **S-2-butyl tosylate** (0.1 mol/L) in 50% TFE at different time intervals

Reaction time/h	Peak area for **S-2-butyl tosylate**/mV·s	Peak area for **R-2-butyl tosylate**/mV·s	Ratio ([S]+[R]) / [R]
0	790.416	37.143	22.28:1
17	605.824	35.487	18.07:1
24.5	526.297	36.283	15.50:1
41	342.526	28.671	12.95:1
48.5	257.423	24.804	11.38:1
65	128.900	14.745	9.74:1
73.5	183.281	20.816	9.6:1

Table S2. Racemization rate of **S-2-butyl tosylate** (0.1 mol/L) against the tosylate anion presented

Concentration of toyslate anion (mol/L)	k_i in [R] / {[R]+[S]} = 0.5 – aexp(-k_i × t)
0.1	0.752×10^{-6} s^{-1}
0.5	2.312×10^{-6} s^{-1}
1.0	5.743×10^{-6} s^{-1}

Table S3. Racemization of **S-2-butyl tosylate** (0.01 mol/L) in 50% TFE at different time intervals

Reaction time/h	Peak area for **S-2-butyl tosylate**/mV·s	Peak area for **R-2-butyl tosylate**/mV·s	Ratio ([S]+[R]) / [R]
0	790.416	37.143	22.3:1
8	240.144	13.173	19.2:1
24	178.725	11.666	16.3:1
32	187.067	13.781	14.6:1
48.5	123.362	10.286	13.0:1
56	359.099	32.359	12.1:1
72	202.228	21.561	10.3:1

Table S4. Ratio of **2-pentyl tosylate** to **3-pentyl tosylate** under solvolysis conditions

Time/s	[**2-pentyl tosylate**]$_t$ / [**3-pentyl tosylate**]$_t$
0	0.00
165600	0.39
180000	0.56
194400	0.84
252000	1.48
280800	2.01
340200	6.98

Table S5. 2-butanol generated from **S-2-butyl tosylate** at different time intervals by chiral GC determination

Reaction time/h	Peak area of R-2-butanol/ uV·s	Peak area of S-2-butanol/ uV·s	Ratio ([R] / [S])
17	576.41	92.97	6.2:1
24.5	712.39	122.79	5.9:1
41	910.59	150.73	6.0:1
48.5	922.88	146.48	6.3:1
65	1176.41	176.86	6.4:1
73.5	808.71	126.21	6.3:1

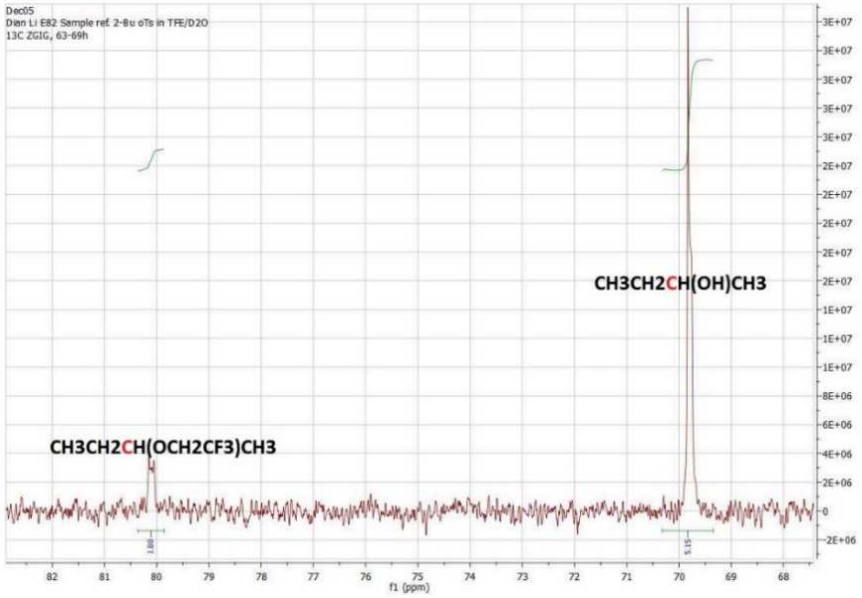


Figure S1. ^{13}CNMR spectrum of 2-butanol and 2-butyl trifluoroethyl ether from **2-butyl tosylate**

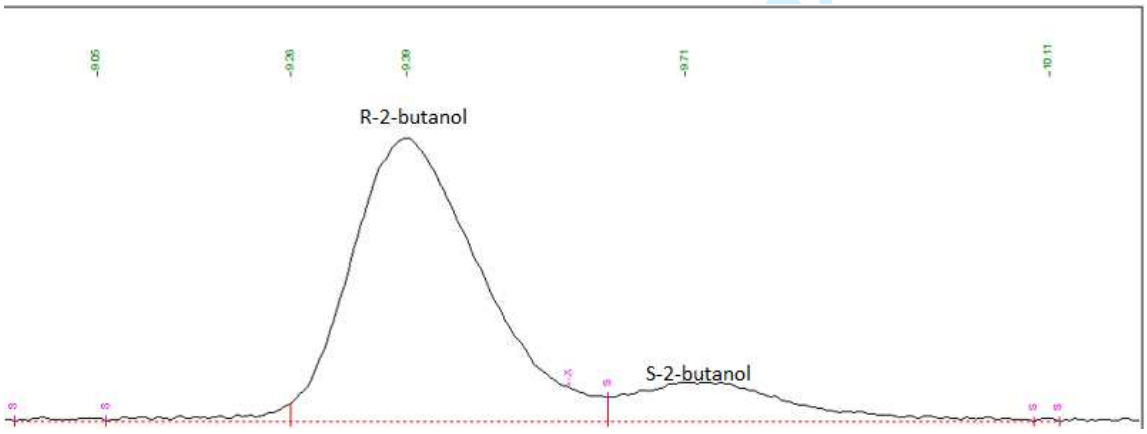
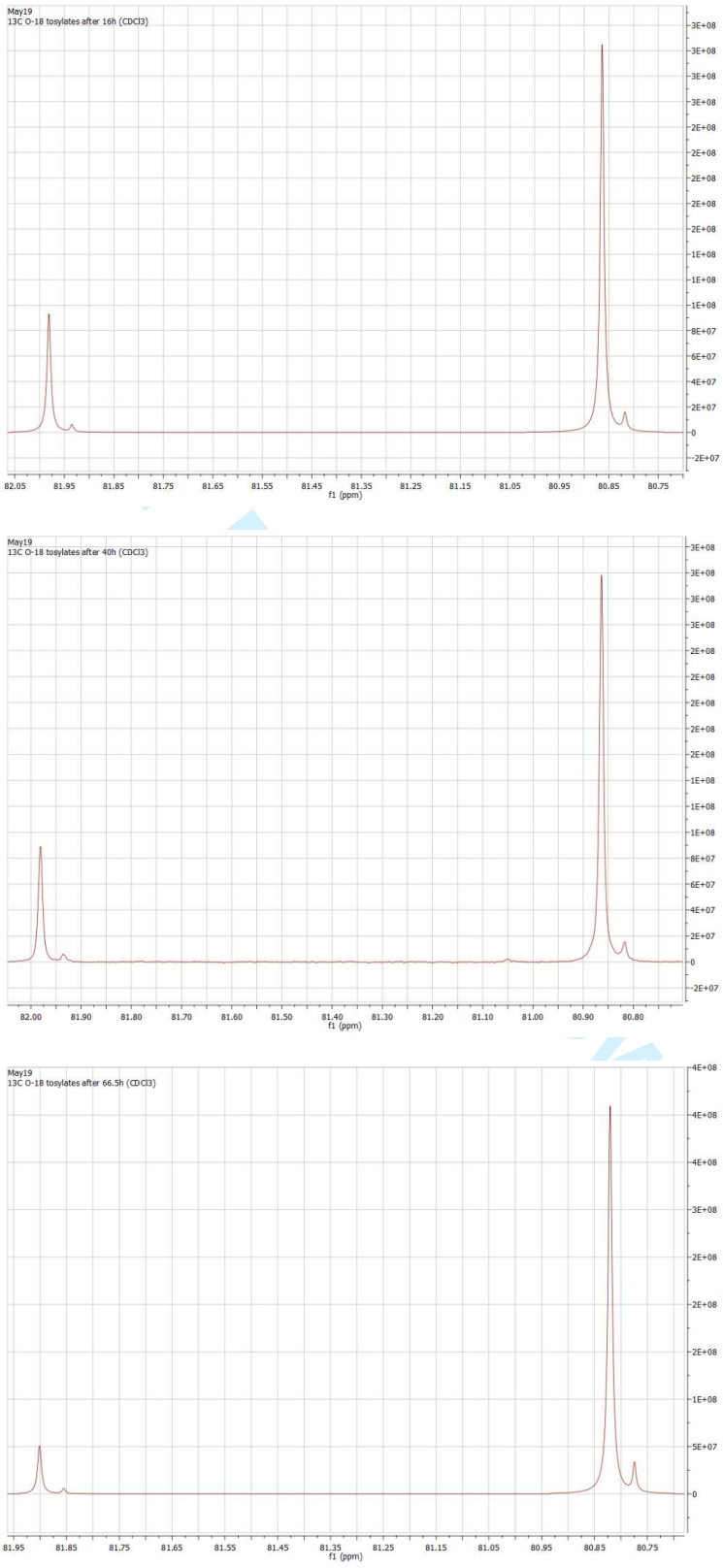


Figure S2. Chiral GC spectrum of 2-butanol generated from **S-2-butyl tosylate**

Figure S3. ^{13}CNMR spectrum of labelled 2-butyl tosylate and 2-octyl tosylate recovered after 16, 40 and 66.5 hours



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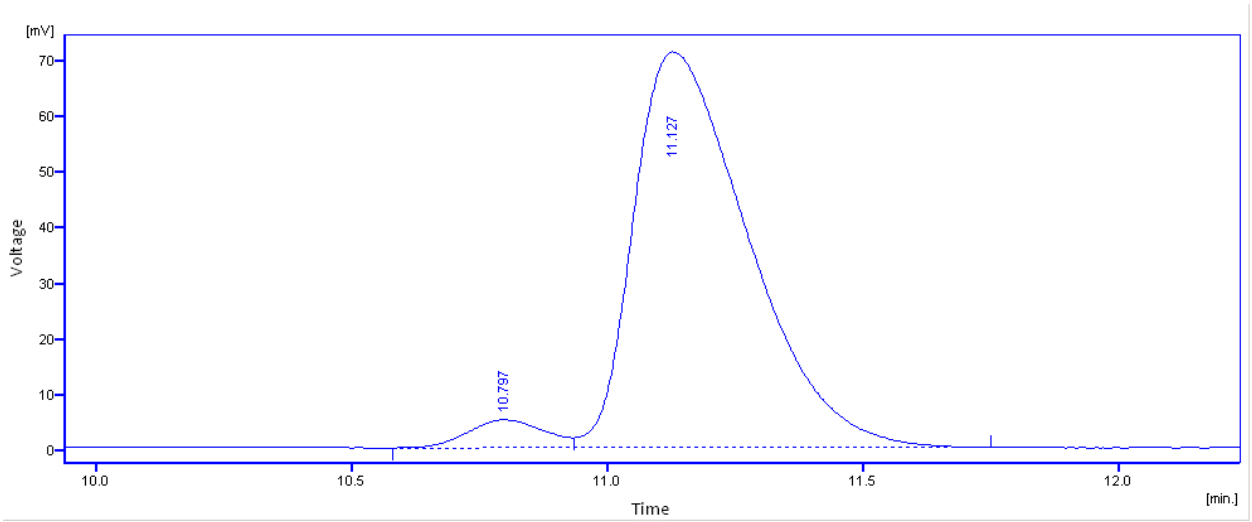
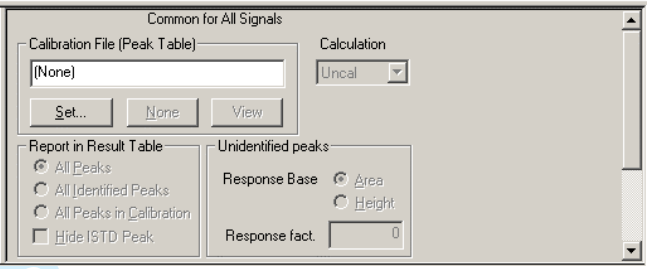
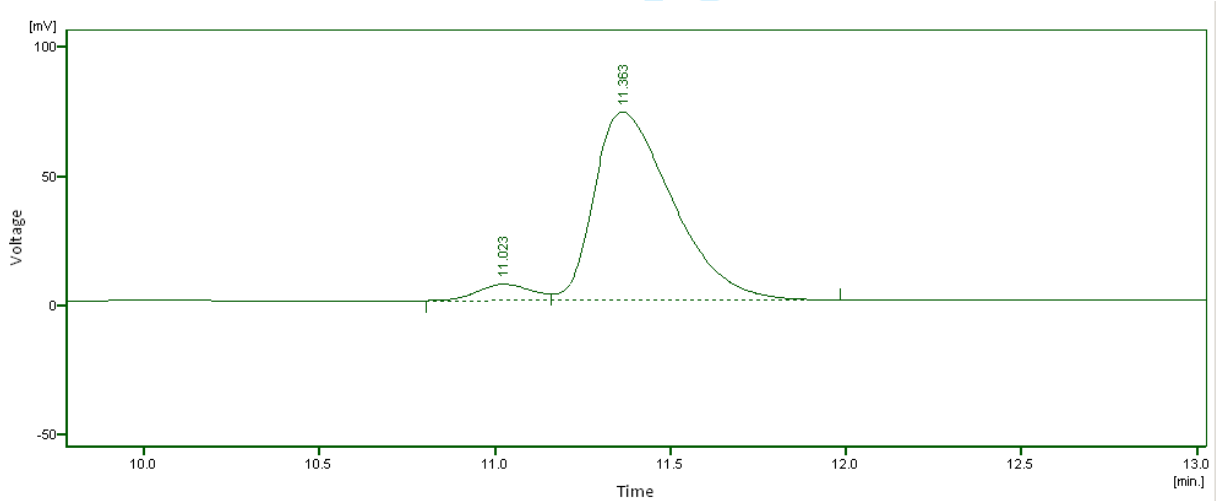
Chiral HPLC spectrum of S-2-butyl tosylate (starting material)



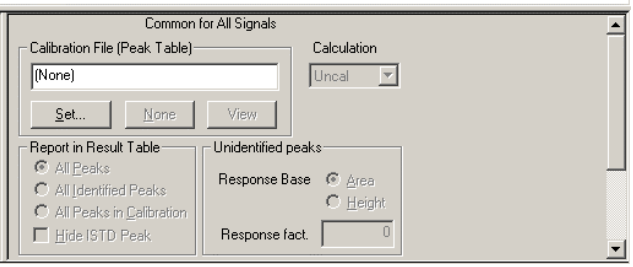
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	10.797	52.281	5.013	4.5	6.6	0.18
2	11.127	1103.598	71.067	95.5	93.4	0.24
	Total	1155.879	76.080	100.0	100.0	



Chiral HPLC spectrum of solvolysis of S-2-butyl tosylate (0.1 mol/L) after 17, 24.5, 41, 65 and 73.5 hours



	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	11.023	67.552	6.267	5.6	7.9	0.19
2	11.363	1132.788	73.115	94.4	92.1	0.24
	Total	1200.341	79.382	100.0	100.0	



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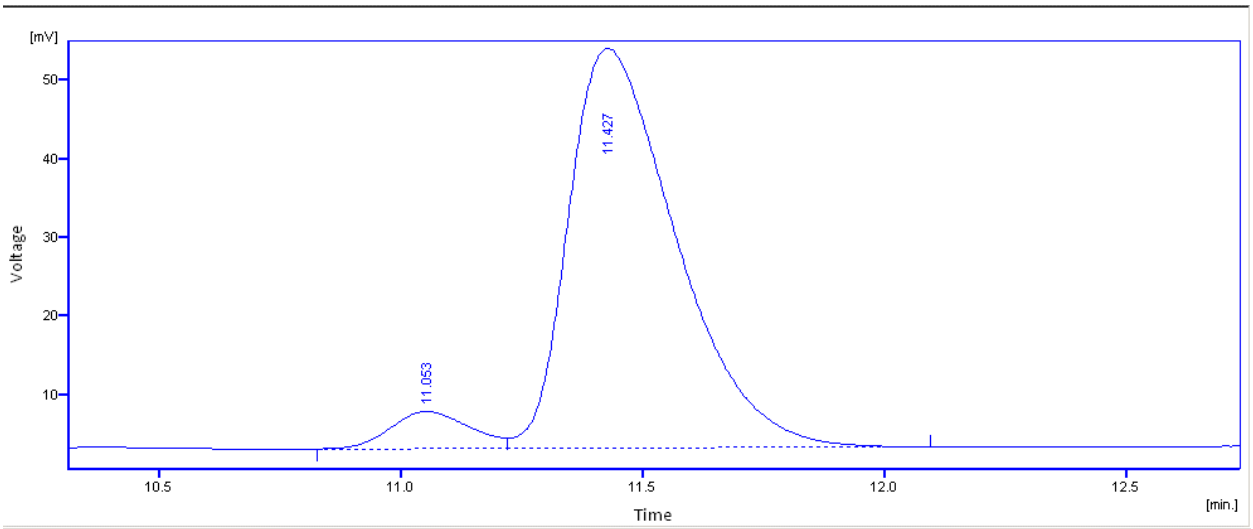

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1	11.053	53.612	4.702	6.4	8.5	0.19
2	11.427	787.871	50.874	93.6	91.5	0.24
	Total	841.483	55.576	100.0	100.0	

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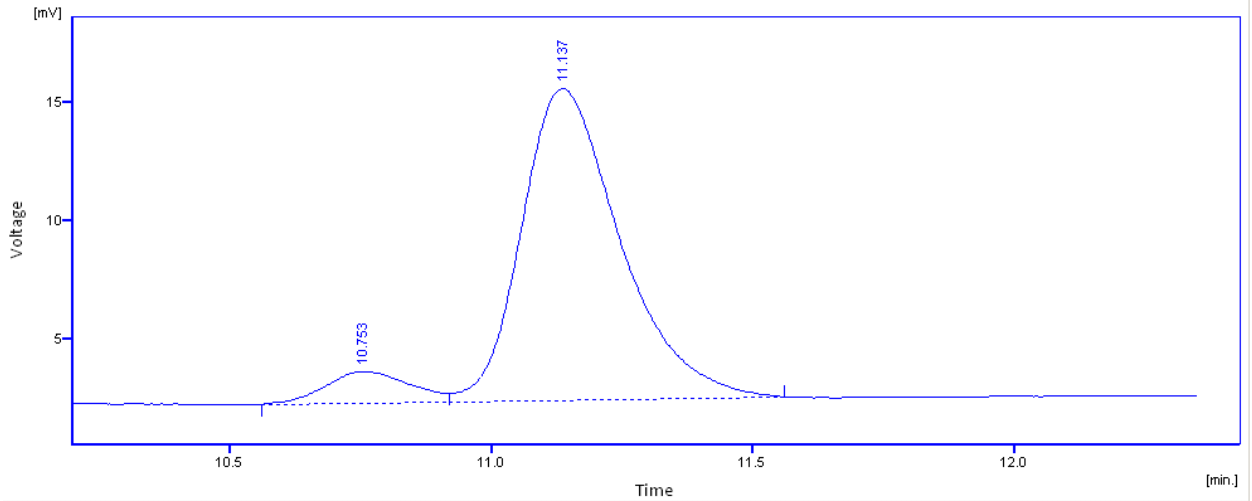

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	10.753	14.655	1.329	7.8	9.2	0.18
2	11.137	173.141	13.194	92.2	90.8	0.20
	Total	187.796	14.523	100.0	100.0	

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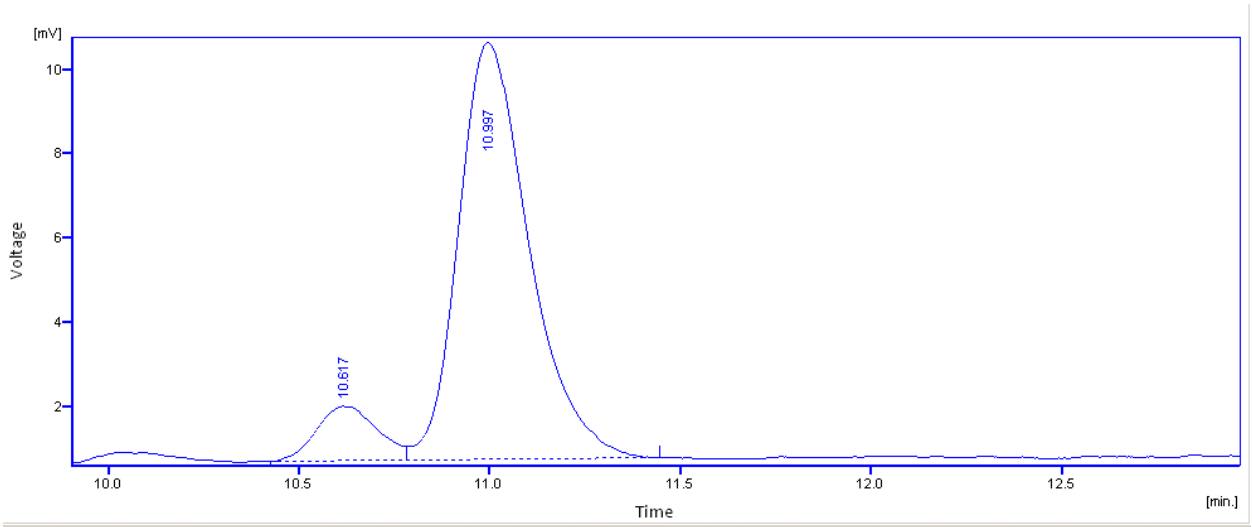

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	10.617	14.252	1.291	10.1	11.6	0.18
2	10.997	127.022	9.875	89.9	88.4	0.20
	Total	141.274	11.167	100.0	100.0	

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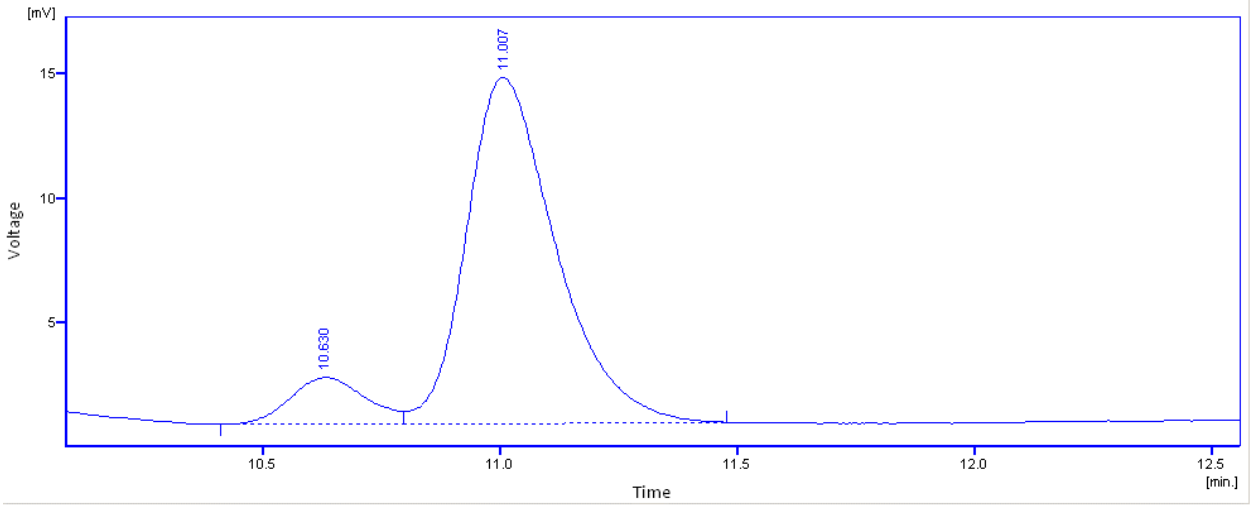

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	10.630	20.596	1.857	10.2	11.8	0.18
2	11.007	181.361	13.844	89.8	88.2	0.20
	Total	201.957	15.701	100.0	100.0	

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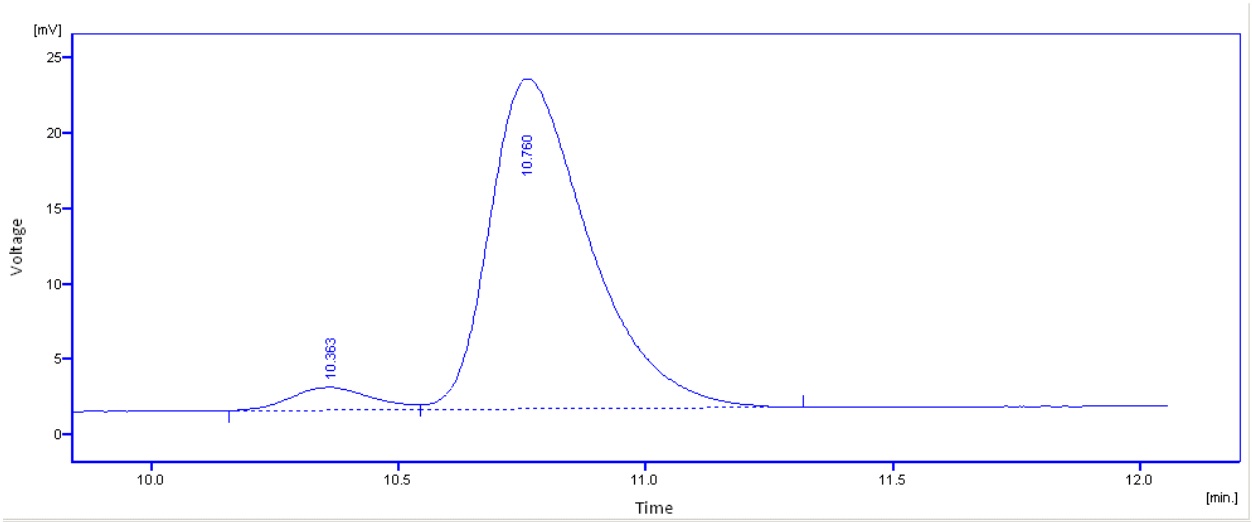
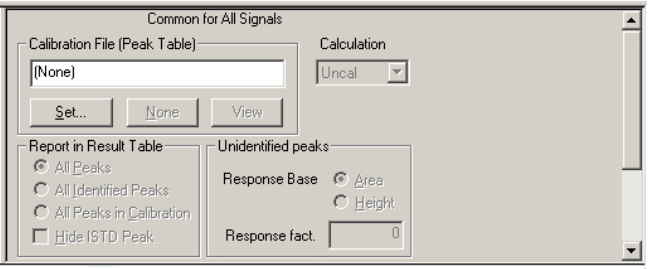
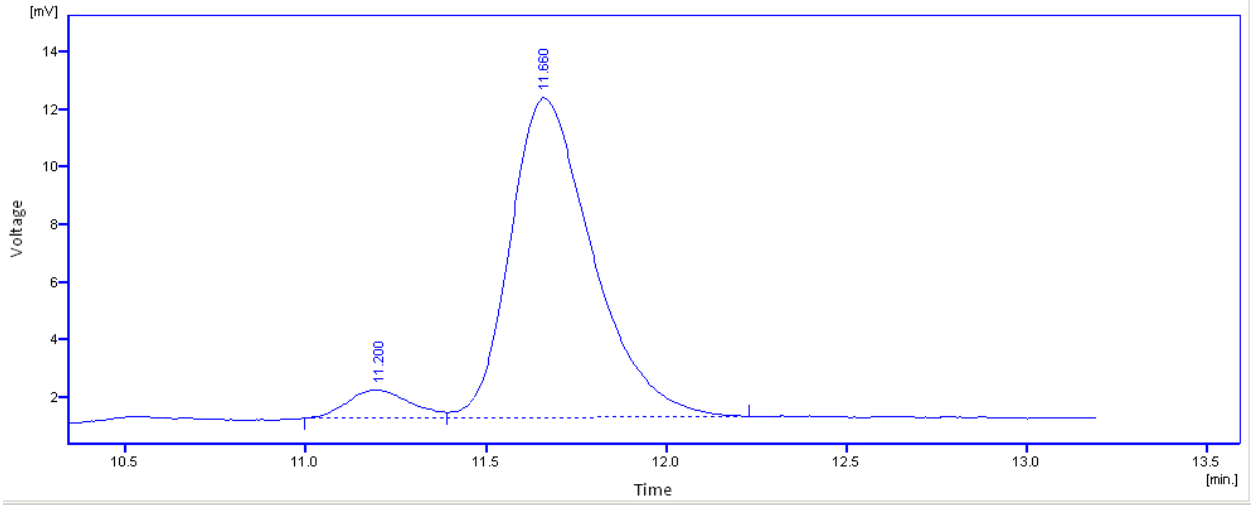
Chiral HPLC spectrum of solvolysis of S-2-butyl tosylate (0.01 mol/L) after 8, 24, 32, 48.5, 56 and 72 hours

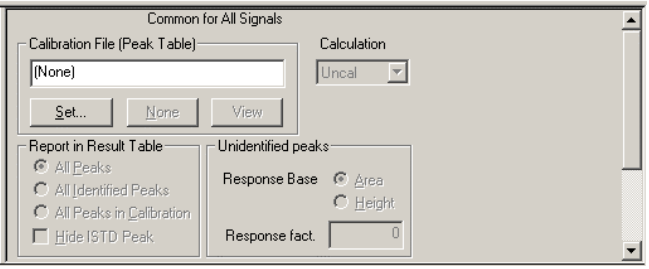


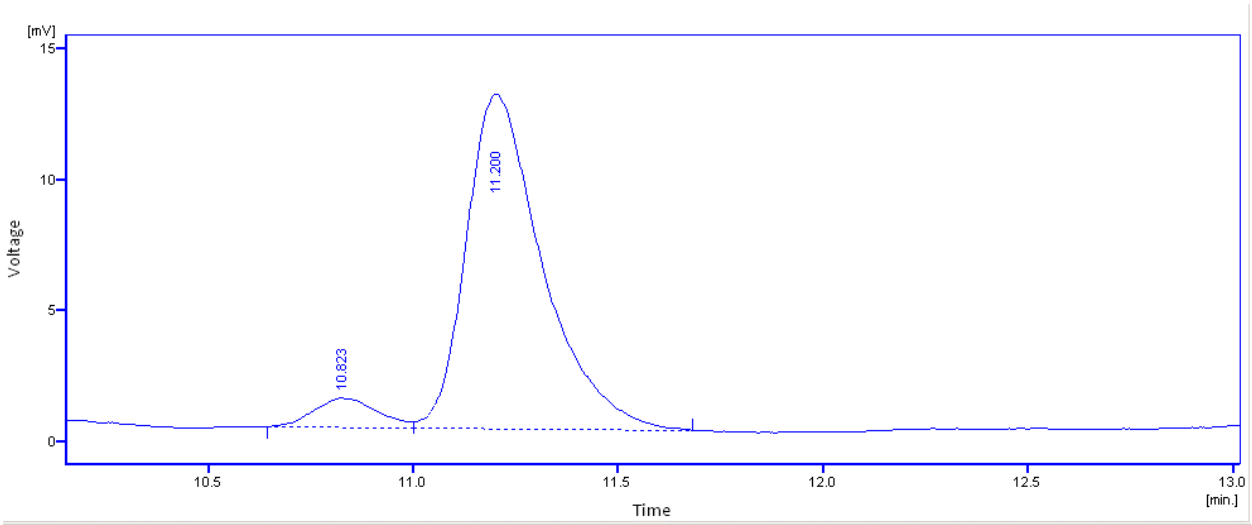
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	10.363	16.998	1.504	5.3	6.4	0.18
2	10.760	306.298	21.884	94.7	93.6	0.21
	Total	323.296	23.388	100.0	100.0	



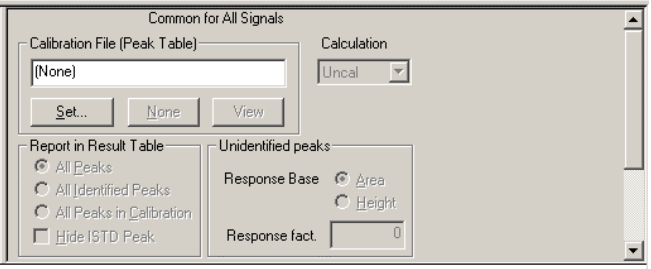


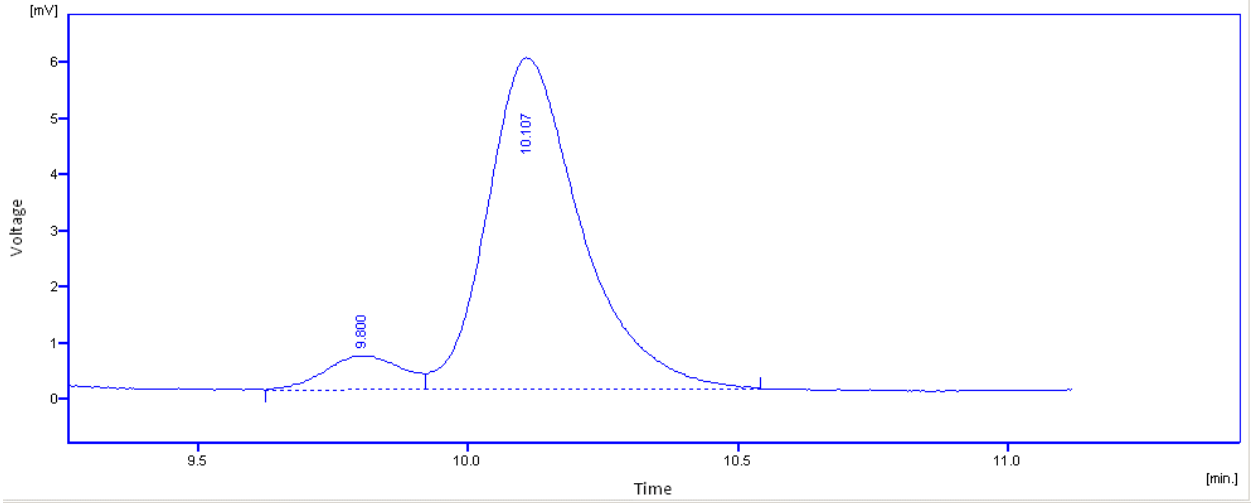
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	11.200	11.705	0.963	6.2	8.0	0.20
2	11.660	175.846	11.086	93.8	92.0	0.24
	Total	187.552	12.049	100.0	100.0	



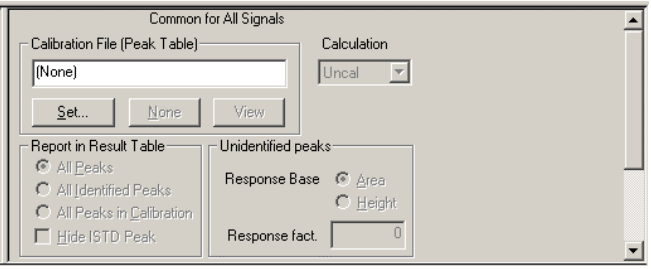


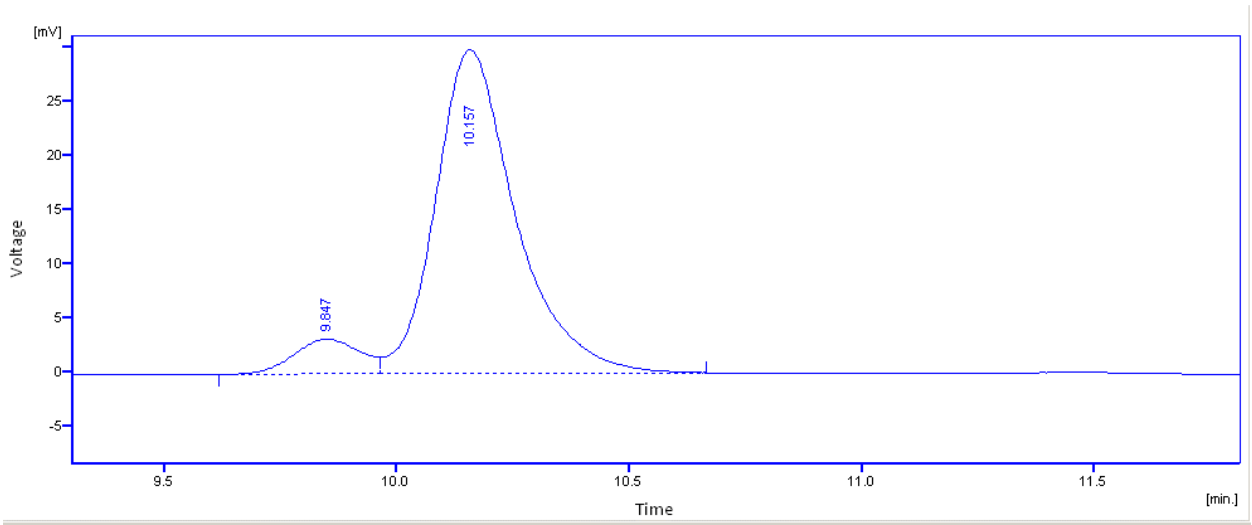
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	10.823	11.838	1.106	6.7	8.0	0.17
2	11.200	164.845	12.763	93.3	92.0	0.19
	Total	176.683	13.869	100.0	100.0	



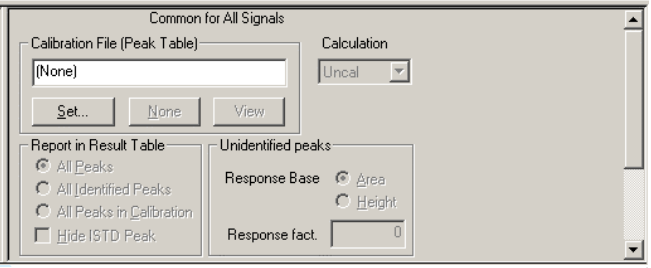


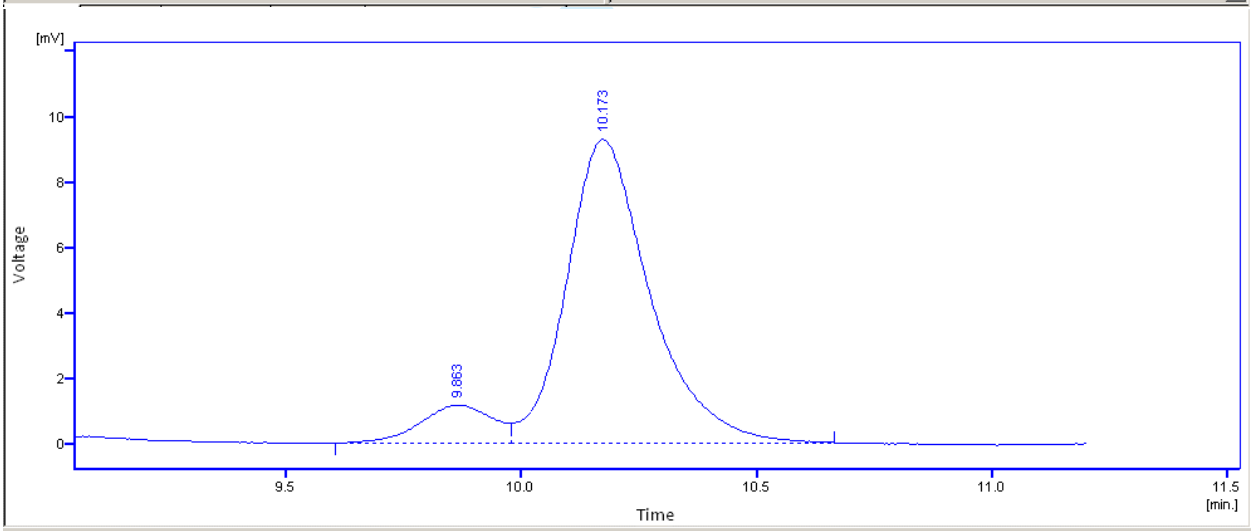
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	9.800	5.931	0.599	7.7	9.2	0.18
2	10.107	71.245	5.915	92.3	90.8	0.18
	Total	77.176	6.513	100.0	100.0	



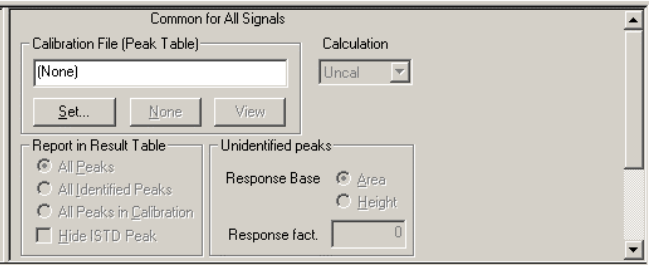


	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	9.847	31.854	3.221	8.2	9.7	0.18
2	10.157	357.250	29.909	91.8	90.3	0.18
	Total	389.104	33.130	100.0	100.0	

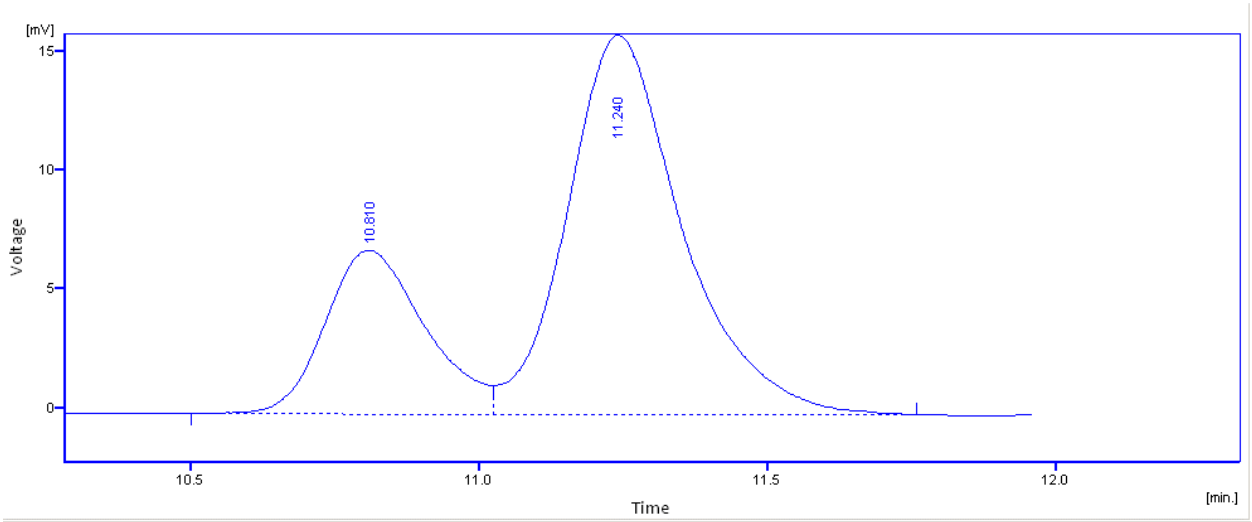




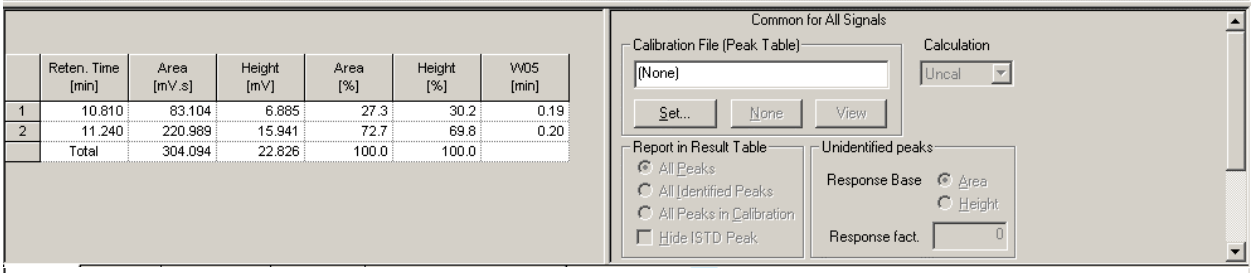
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	9.863	12.337	1.162	9.8	11.1	0.20
2	10.173	114.057	9.266	90.2	88.9	0.18
	Total	126.394	10.428	100.0	100.0	

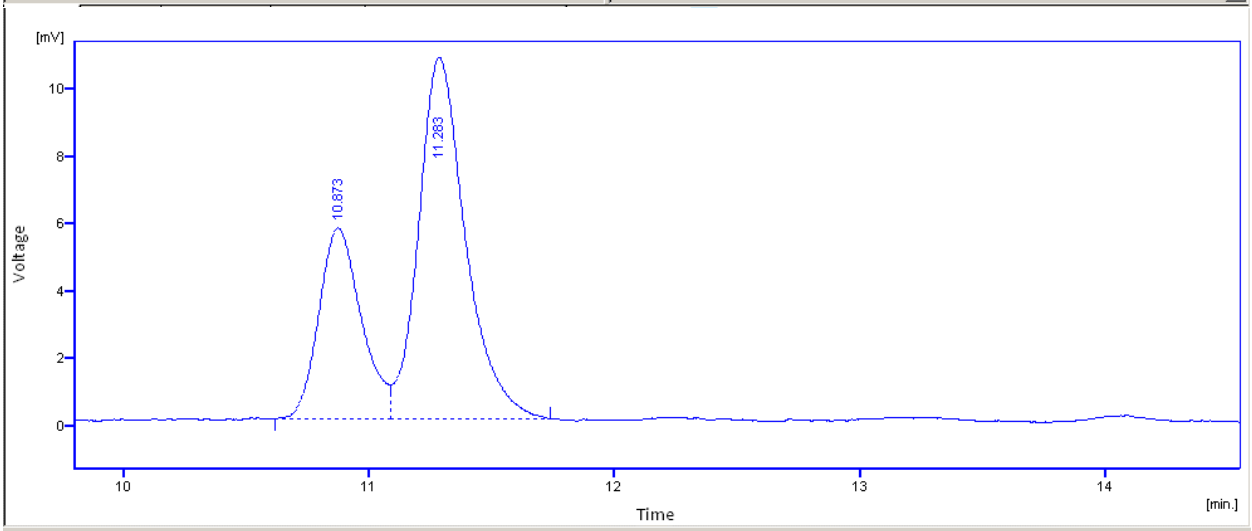


Chiral HPLC spectrum of solvolysis of S-2-butyl tosylate (0.01 mol/L) with 1 mol/L sodium tosylate after 55 and 72 hours

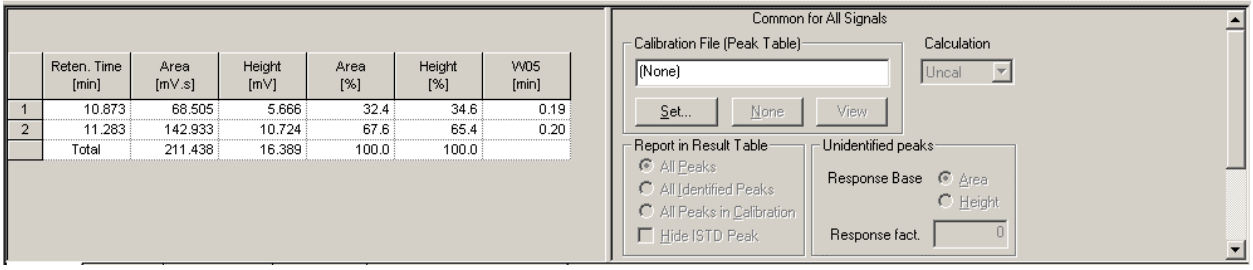


	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	10.810	83.104	6.885	27.3	30.2	0.19
2	11.240	220.989	15.941	72.7	69.8	0.20
	Total	304.094	22.826	100.0	100.0	

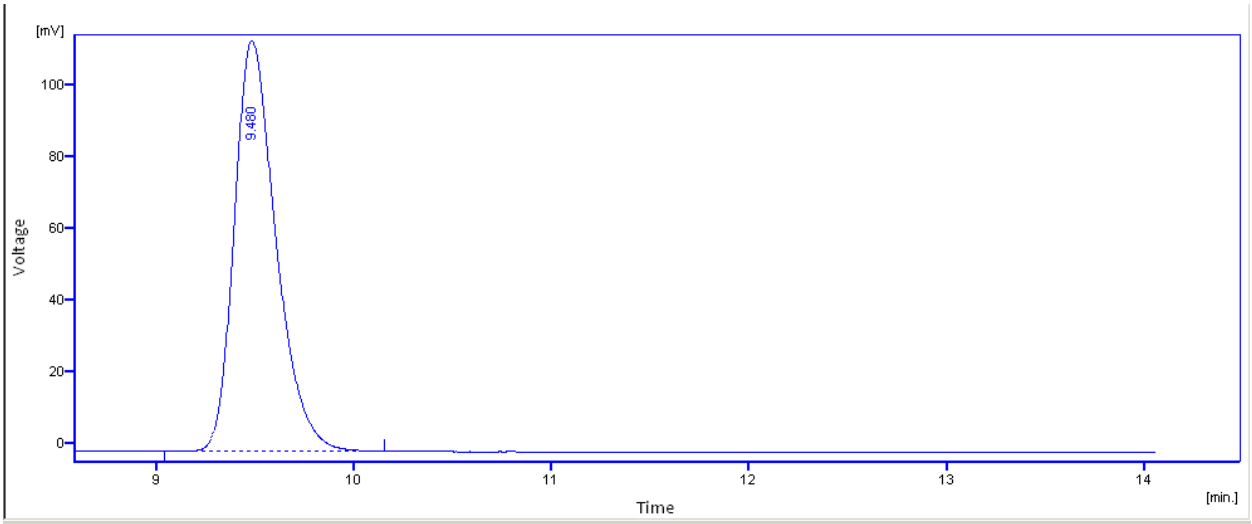




	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	10.873	68.505	5.666	32.4	34.6	0.19
2	11.283	142.933	10.724	67.6	65.4	0.20
	Total	211.438	16.389	100.0	100.0	



HPLC spectrum of 3-pentyl tosylate (starting material)

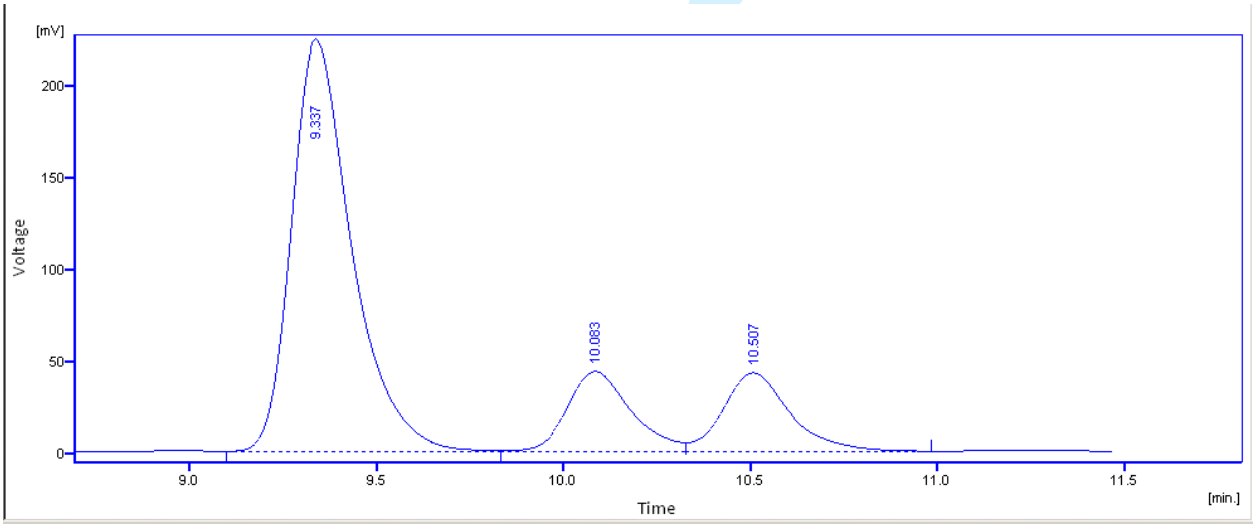


Result Table (test initial rearranged value of 3-pentyl tosylate in acetonitrile dian li) <-- Uncal

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	9.480	1683.545	114.779	100.0	100.0	0.22
	Total	1683.545	114.779	100.0	100.0	

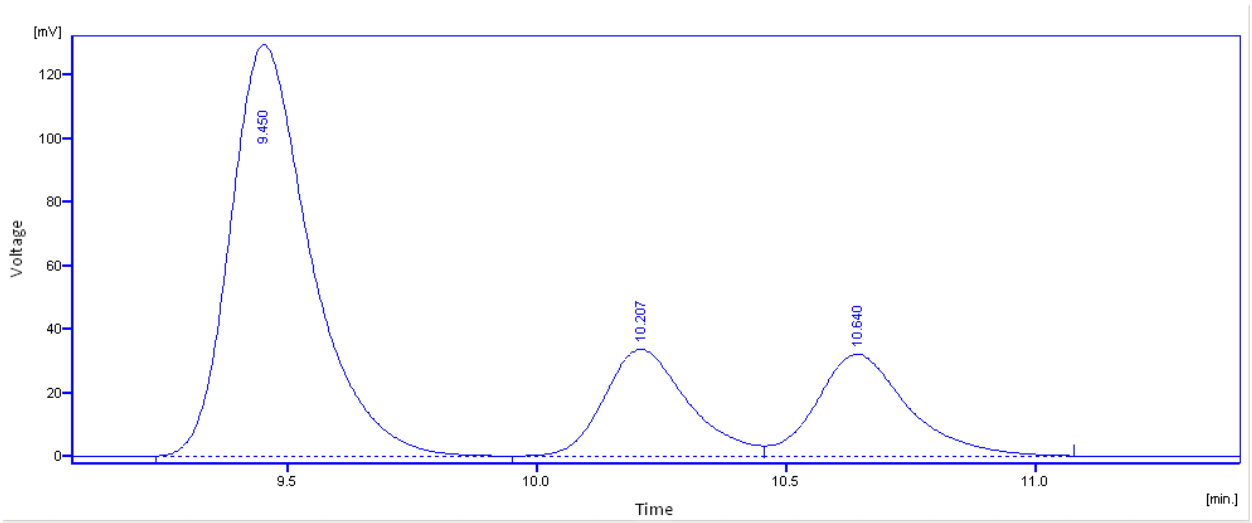
Common for All Signals
Calibration File (Peak Table): (None) Set... None View
Calculation: Uncal
Report in Result Table: All Peaks / All Identified Peaks / All Peaks in Calibration / Hide ISTD Peak
Unidentified peaks: Response Base: Area / Height; Response fact.: 0

HPLC spectrum of solvolysis of 3-pentyl tosylate (0.01 mol/L) after 46, 50, 54, 70 and 78 hours



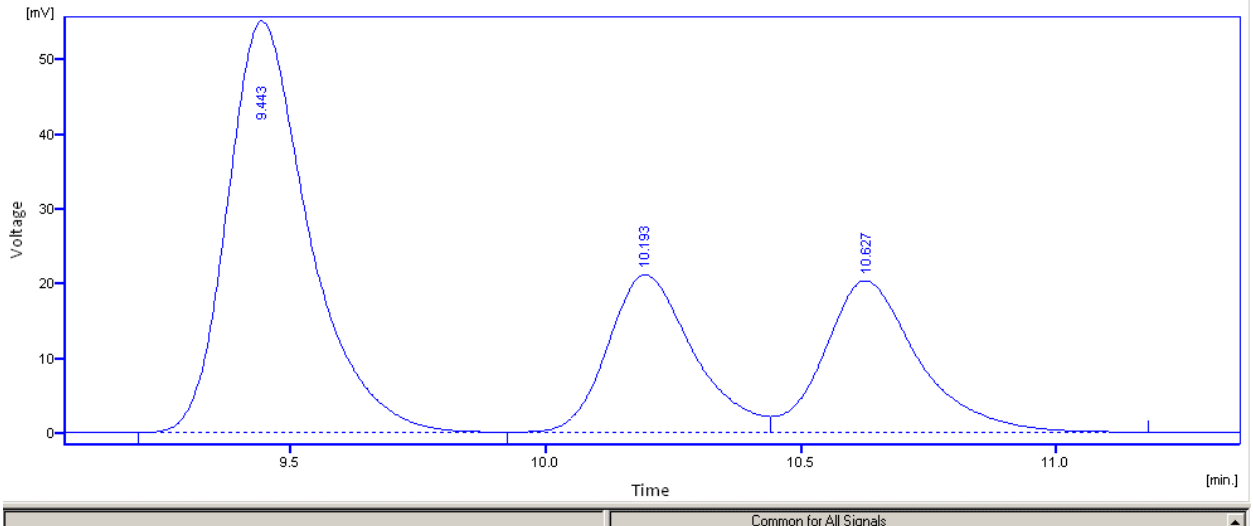
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	9.337	2516.576	223.729	71.0	72.3	0.17
2	10.083	506.393	43.267	14.3	14.0	0.18
3	10.507	523.567	42.521	14.8	13.7	0.18
	Total	3546.536	309.517	100.0	100.0	

Common for All Signals
Calibration File (Peak Table): (None) Set... None View
Calculation: Uncal
Report in Result Table: All Peaks / All Identified Peaks / All Peaks in Calibration / Hide ISTD Peak
Unidentified peaks: Response Base: Area / Height; Response fact.: 0



	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	9.450	1444.390	129.566	64.5	66.4	0.17
2	10.207	390.096	33.523	17.4	17.2	0.18
3	10.640	405.733	32.041	18.1	16.4	0.19
	Total	2240.219	195.130	100.0	100.0	

Common for All Signals
Calibration File (Peak Table)
(None)
Set... None View
Calculation
Uncal
Report in Result Table
All Peaks
All Identified Peaks
All Peaks in Calibration
Hide ISTD Peak
Unidentified peaks
Response Base Area Height
Response fact. 0



	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	9.443	608.457	54.962	54.6	57.1	0.17
2	10.193	245.430	21.055	22.0	21.9	0.18
3	10.627	259.491	20.264	23.3	21.0	0.19
	Total	1113.378	96.281	100.0	100.0	

Common for All Signals
Calibration File (Peak Table)
(None)
Set... None View
Calculation
Uncal
Report in Result Table
All Peaks
All Identified Peaks
All Peaks in Calibration
Hide ISTD Peak
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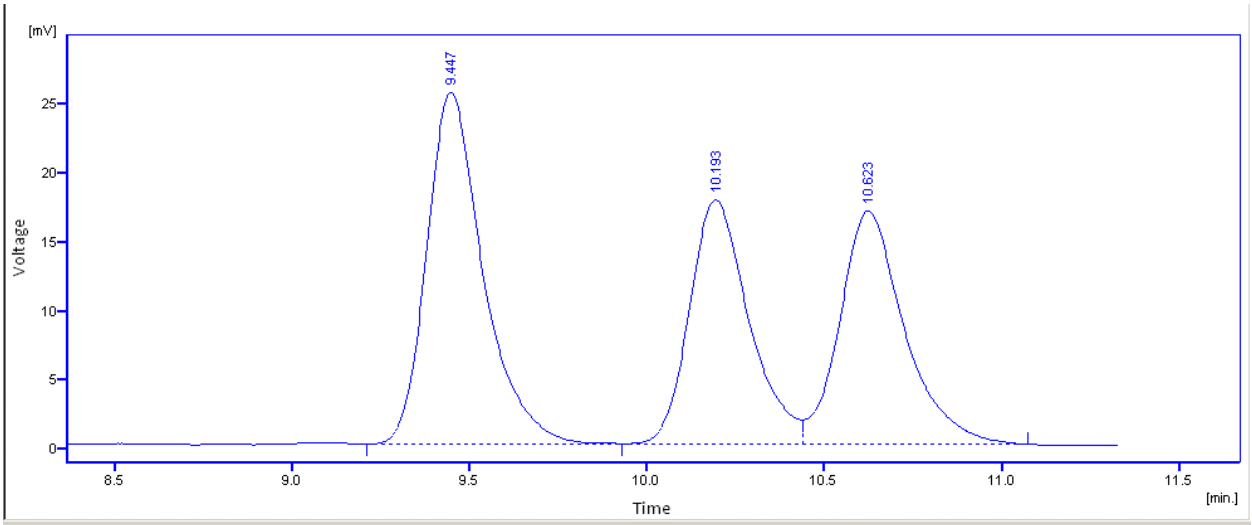
Response Base Area Height
Response fact. 0



	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	9.447	280.973	25.398	40.1	42.4	0.17
2	10.193	205.863	17.646	29.3	29.4	0.18
3	10.623	214.659	16.888	30.6	28.2	0.19
	Total	701.495	59.932	100.0	100.0	

Common for All Signals
Calibration File (Peak Table)
(None)
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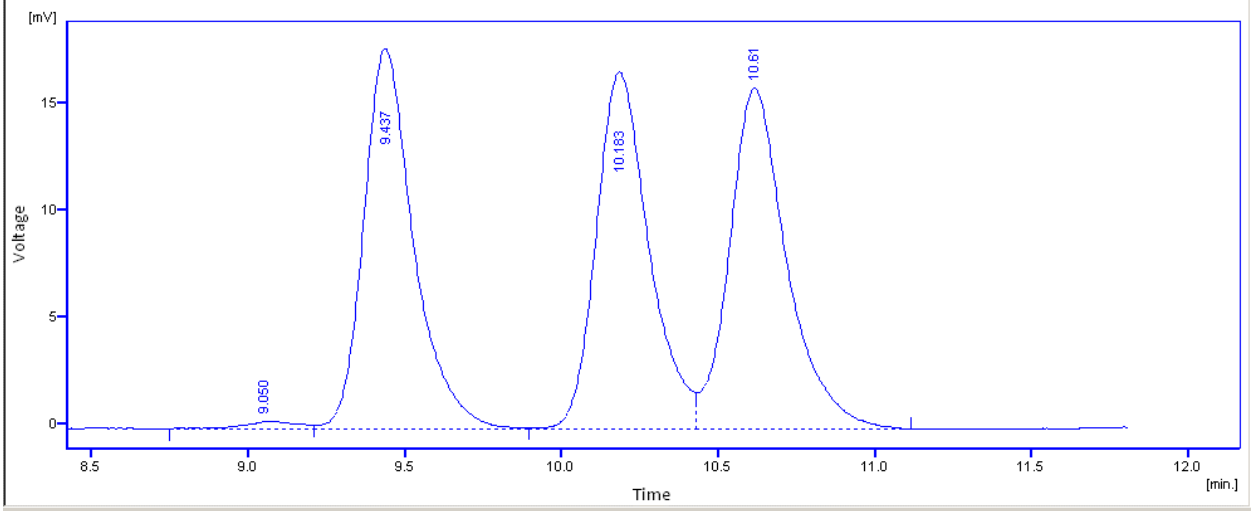
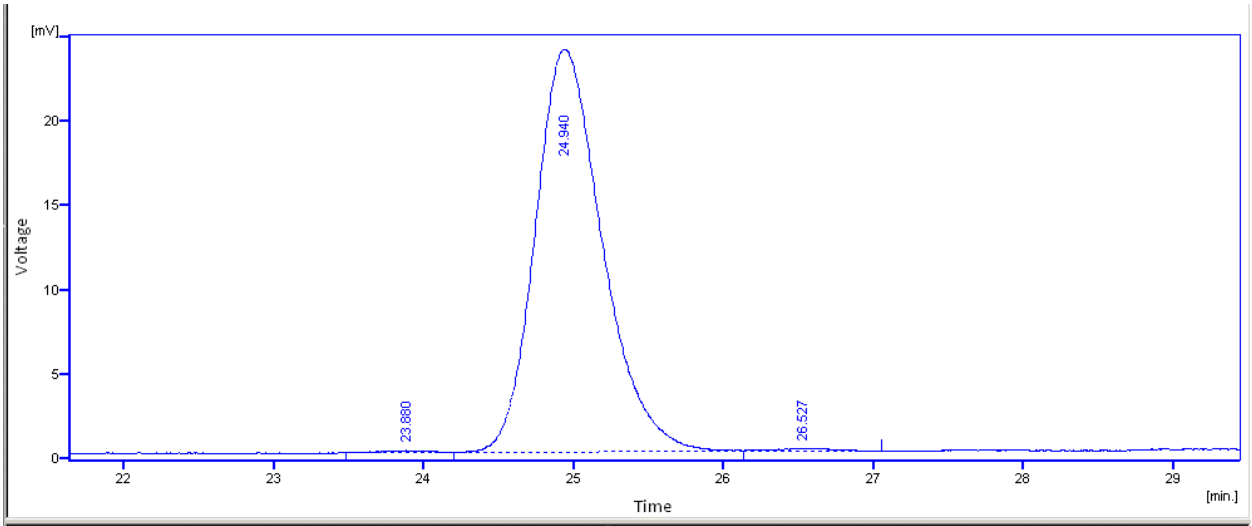
Calculation
Uncal
Report in Result Table
All Peaks
All Identified Peaks
All Peaks in Calibration
Hide ISTD Peak
Unidentified peaks
Response Base Area Height
Response fact. 0



	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	9.050	4.304	0.330	0.7	0.7	0.23
2	9.437	197.758	17.778	32.9	35.1	0.16
3	10.183	195.438	16.679	32.5	32.9	0.18
4	10.613	203.908	15.932	33.9	31.4	0.19
	Total	601.407	50.720	100.0	100.0	

Common for All Signals
Calibration File (Peak Table)
(None)
Set... None View
Calculation
Uncal
Report in Result Table
All Peaks
All Identified Peaks
All Peaks in Calibration
Hide ISTD Peak
Unidentified peaks
Response Base Area Height
Response fact. 0

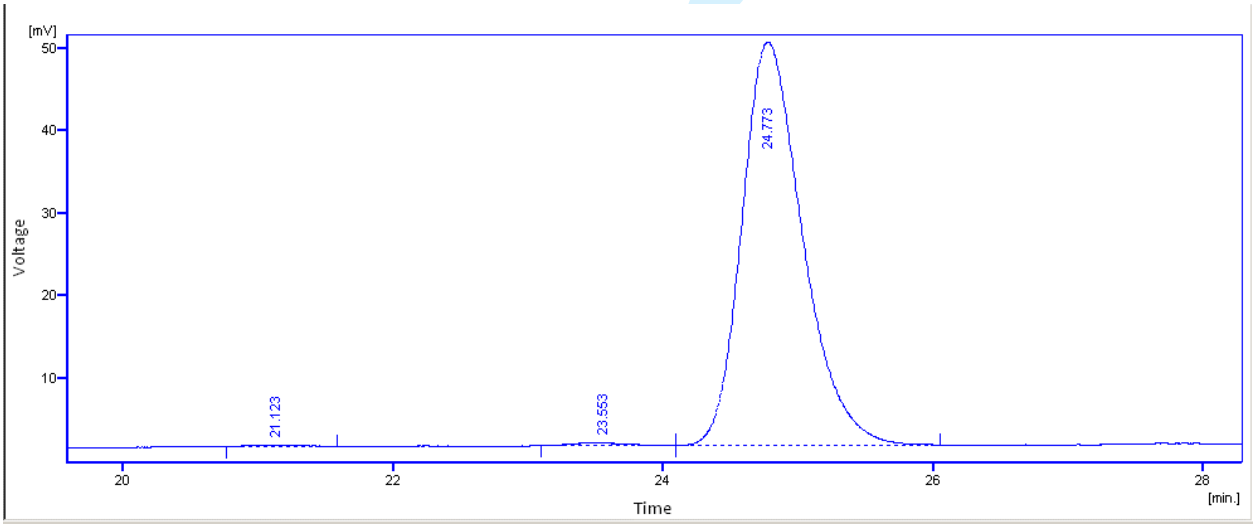
Chiral HPLC spectrum of R-2-octyl tosylate (starting material)



	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	23.880	2.739	0.134	0.4	0.6	0.33
2	24.940	747.300	23.947	98.9	98.7	0.48
3	26.527	5.585	0.172	0.7	0.7	0.56
	Total	755.625	24.253	100.0	100.0	

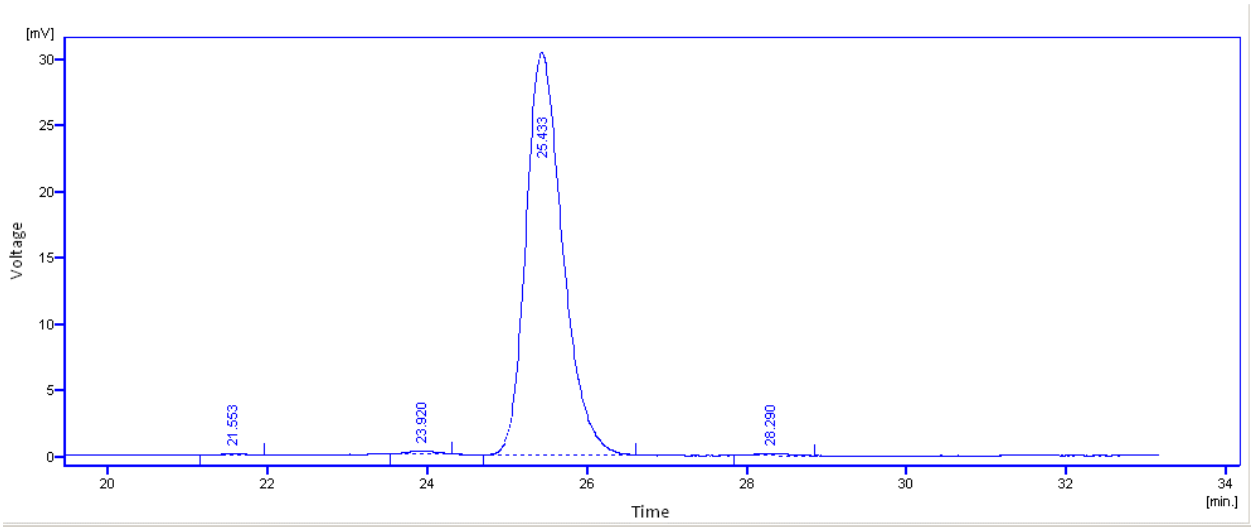
Common for All Signals
Calibration File (Peak Table)
(None)
Set... None View
Calculation
Uncal
Report in Result Table
All Peaks
All Identified Peaks
All Peaks in Calibration
Hide ISTD Peak
Unidentified peaks
Response Base Area Height
Response fact. 0

Chiral HPLC spectrum of solvolysis of R-2-octyl tosylate (0.01 mol/L) after 16.1, 24, 40, 48, 64 and 72 hours

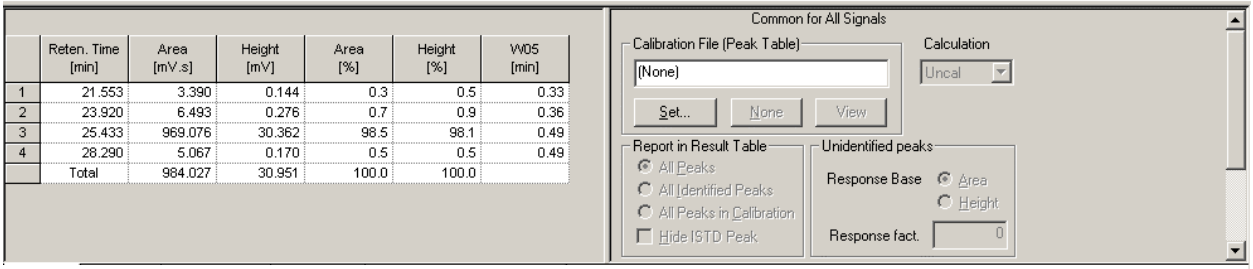


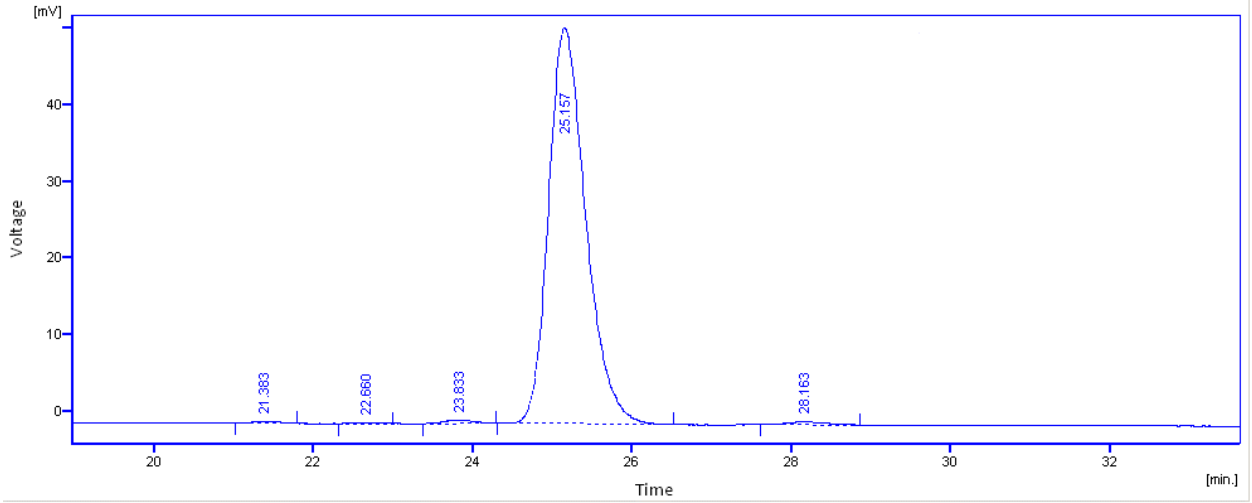
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	21.123	4.890	0.204	0.3	0.4	0.39
2	23.553	10.300	0.357	0.7	0.7	0.46
3	24.773	1528.720	48.907	99.0	98.9	0.48
	Total	1543.910	49.468	100.0	100.0	

Common for All Signals
Calibration File (Peak Table)
(None)
Set... None View
Calculation
Uncal
Report in Result Table
All Peaks
All Identified Peaks
All Peaks in Calibration
Hide ISTD Peak
Unidentified peaks
Response Base Area Height
Response fact. 0

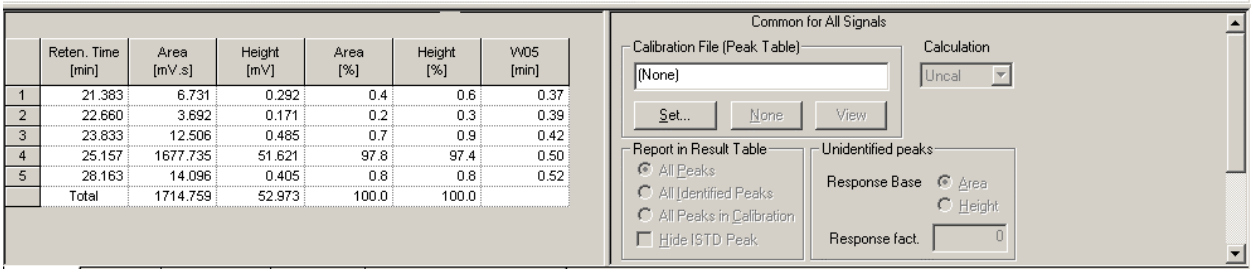


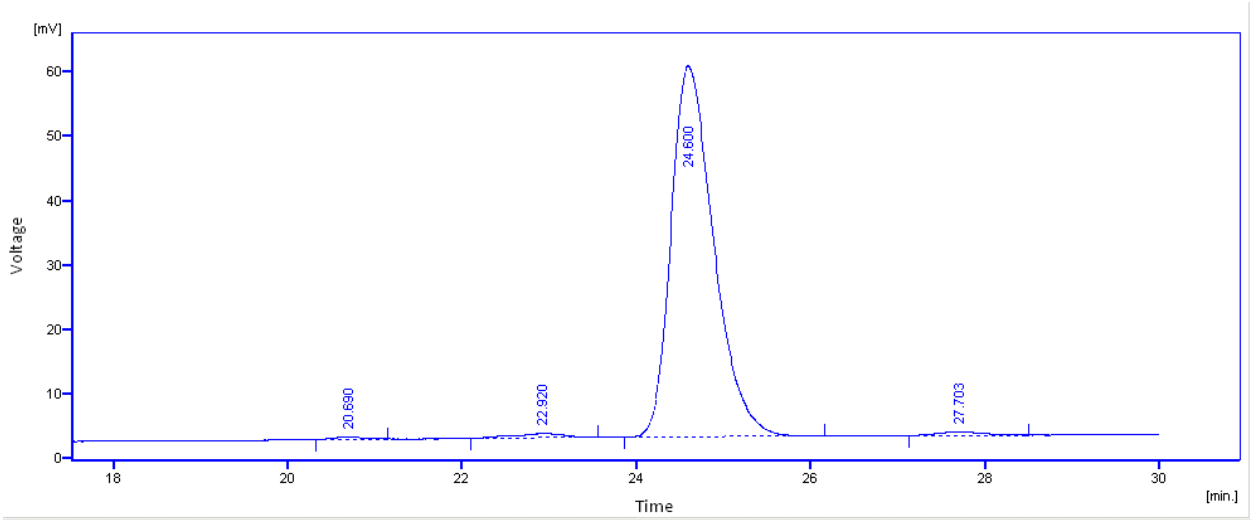
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	21.553	3.390	0.144	0.3	0.5	0.33
2	23.920	6.493	0.276	0.7	0.9	0.36
3	25.433	969.076	30.362	98.5	98.1	0.49
4	28.290	5.067	0.170	0.5	0.5	0.49
	Total	984.027	30.951	100.0	100.0	





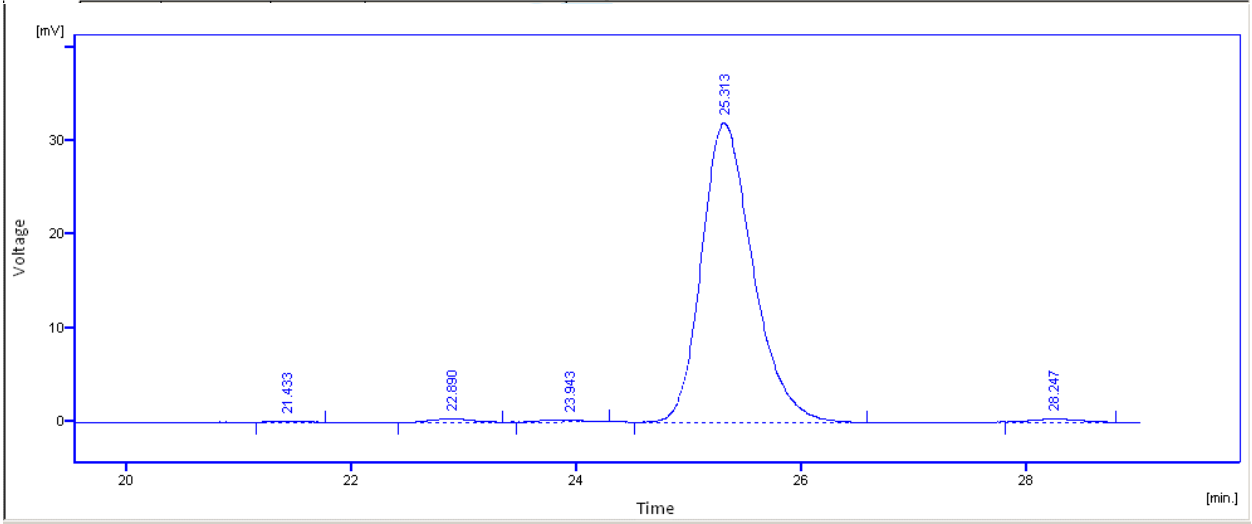
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	21.383	6.731	0.292	0.4	0.6	0.37
2	22.660	3.692	0.171	0.2	0.3	0.39
3	23.833	12.506	0.485	0.7	0.9	0.42
4	25.157	1677.735	51.621	97.8	97.4	0.50
5	28.163	14.096	0.405	0.8	0.8	0.52
	Total	1714.759	52.973	100.0	100.0	





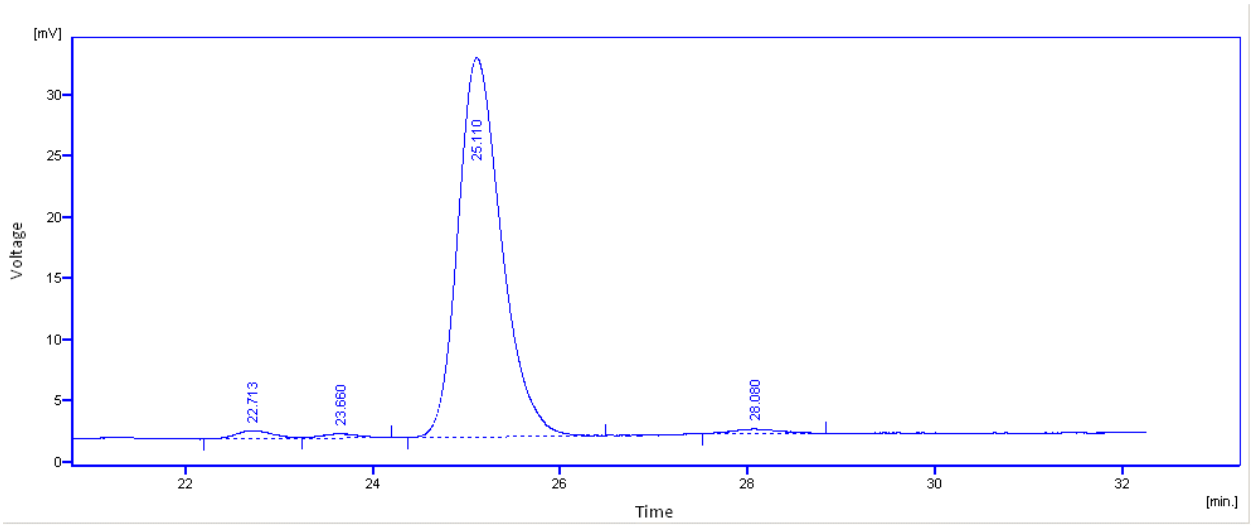
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	20.690	8.210	0.336	0.4	0.6	0.41
2	22.920	26.351	0.673	1.3	1.1	0.53
3	24.600	1961.225	57.702	97.3	97.3	0.52
4	27.703	19.716	0.567	1.0	1.0	0.56
	Total	2015.501	59.278	100.0	100.0	

Common for All Signals
Calibration File (Peak Table)
(None)
Set... None View
Calculation
Uncal
Report in Result Table
All Peaks
All Identified Peaks
All Peaks in Calibration
Hide ISTD Peak
Unidentified peaks
Response Base Area Height
Response fact. 0



	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	21.433	3.261	0.169	0.3	0.5	0.34
2	22.890	9.814	0.383	0.9	1.2	0.41
3	23.943	6.143	0.254	0.6	0.8	0.40
4	25.313	1013.472	31.906	97.2	96.5	0.48
5	28.247	10.110	0.336	1.0	1.0	0.47
	Total	1042.801	33.047	100.0	100.0	

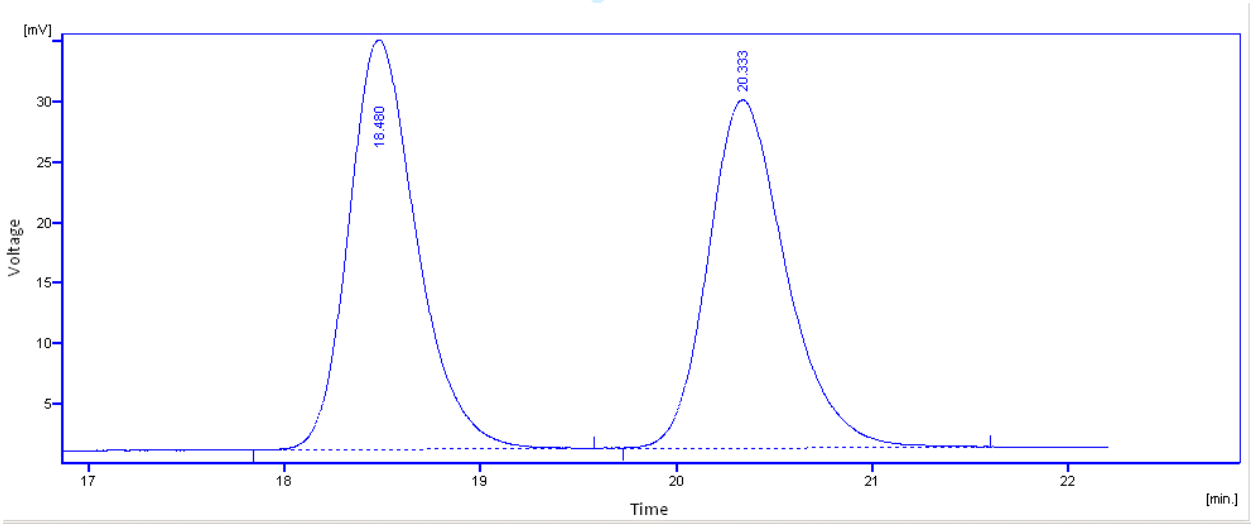
Common for All Signals
Calibration File (Peak Table)
(None)
Set... None View
Calculation
Uncal
Report in Result Table
All Peaks
All Identified Peaks
All Peaks in Calibration
Hide ISTD Peak
Unidentified peaks
Response Base Area Height
Response fact. 0



	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	22.713	19.060	0.682	1.8	2.1	0.43
2	23.660	9.938	0.358	1.0	1.1	0.42
3	25.110	990.903	30.994	95.9	95.6	0.49
4	28.080	13.320	0.375	1.3	1.2	0.54
	Total	1033.221	32.410	100.0	100.0	

Common for All Signals
Calibration File (Peak Table)
(None)
Set... None View
Calculation
Uncal
Report in Result Table
All Peaks
All Identified Peaks
All Peaks in Calibration
Hide ISTD Peak
Unidentified peaks
Response Base Area Height
Response fact. 0

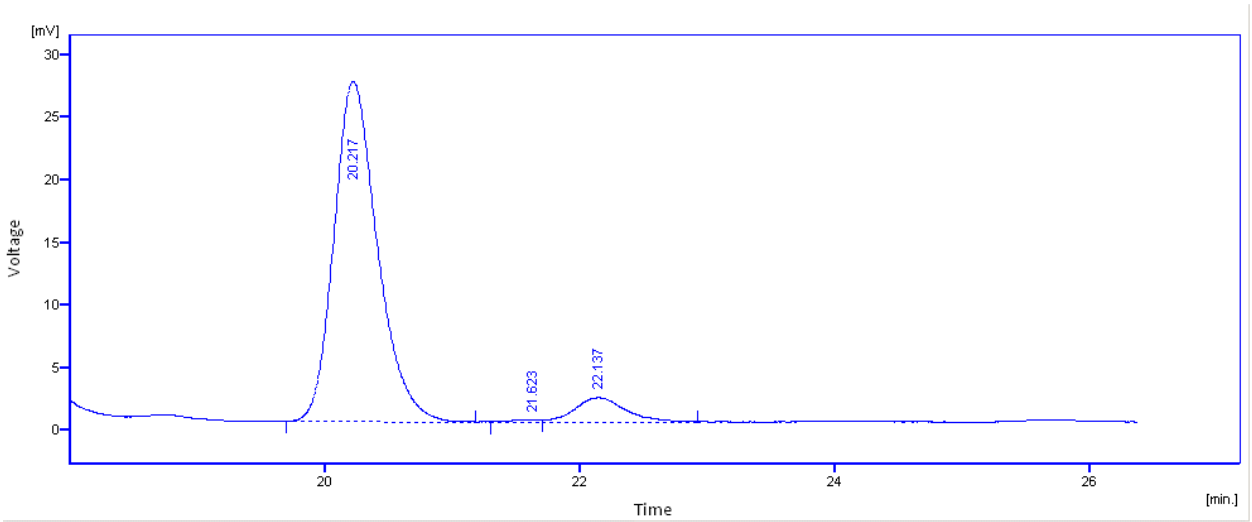
Chiral HPLC spectrum of racemic 2-octyl PNB



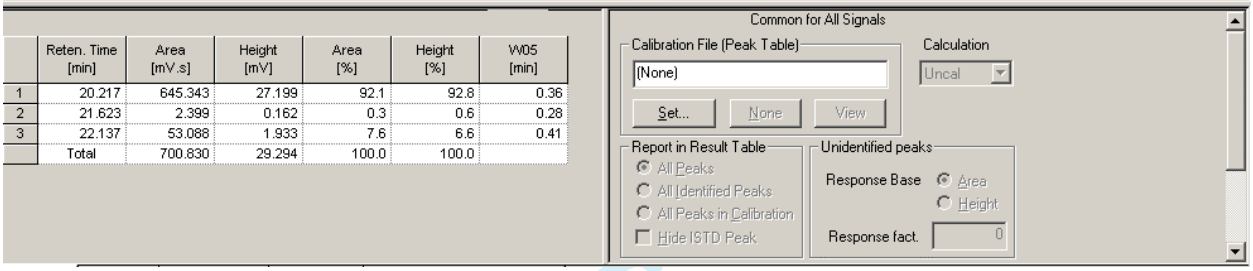
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	18.480	818.547	33.936	50.7	54.1	0.37
2	20.333	794.674	28.788	49.3	45.9	0.42
	Total	1613.222	62.724	100.0	100.0	

Common for All Signals
Calibration File (Peak Table)
(None)
Set... None View
Calculation
Uncal
Report in Result Table
All Peaks
All Identified Peaks
All Peaks in Calibration
Hide ISTD Peak
Unidentified peaks
Response Base Area Height
Response fact. 0

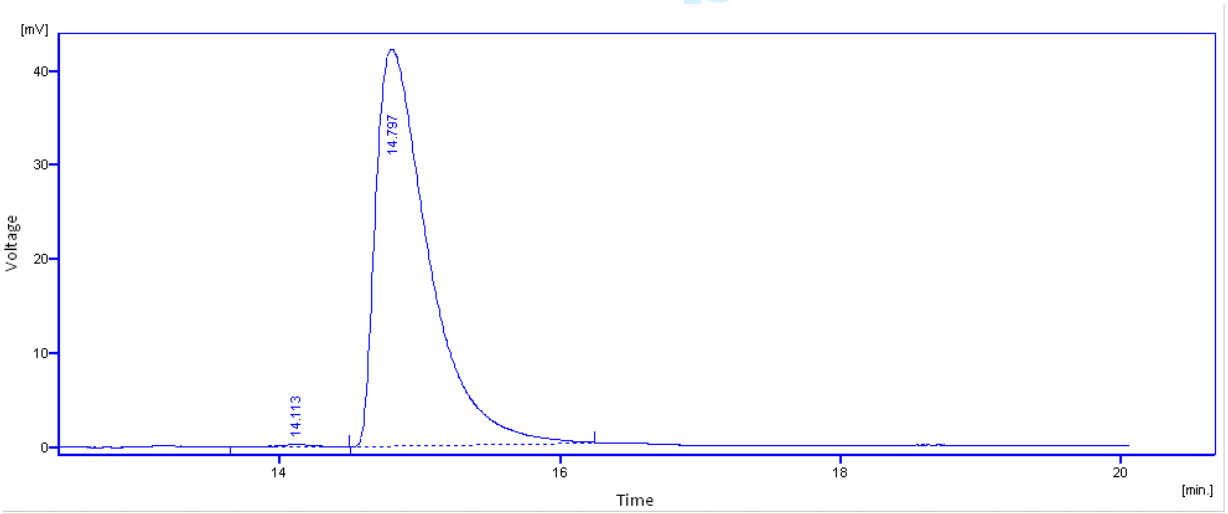
Chiral HPLC spectrum of 2-octyl PNB from R-2-octyl tosylate solvolysis



	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	20.217	645.343	27.199	92.1	92.8	0.36
2	21.623	2.399	0.162	0.3	0.6	0.28
3	22.137	53.088	1.933	7.6	6.6	0.41
	Total	700.830	29.294	100.0	100.0	



Chiral HPLC spectrum of 2-octyl PNB from R-2-octanol after 2 weeks under the same solvolysis conditions



	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	14.113	3.775	0.228	0.3	0.5	0.23
2	14.797	1106.248	42.203	99.7	99.5	0.39
	Total	1110.023	42.431	100.0	100.0