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Secondary Isotope Effects on the Deslipping Reaction of Rotaxanes: High-Precision Measurement of Steric Size

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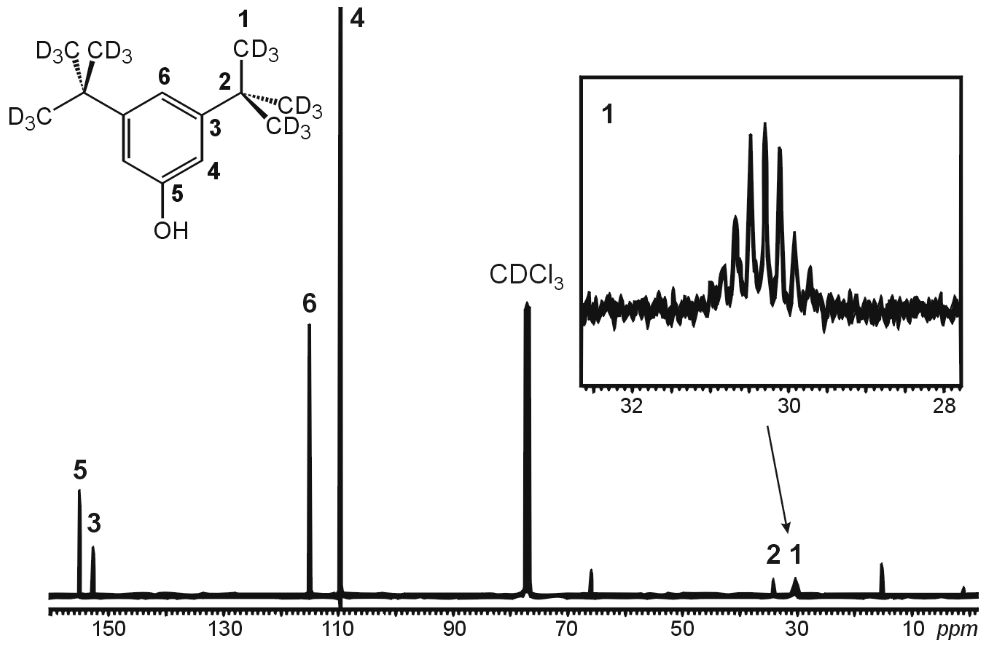
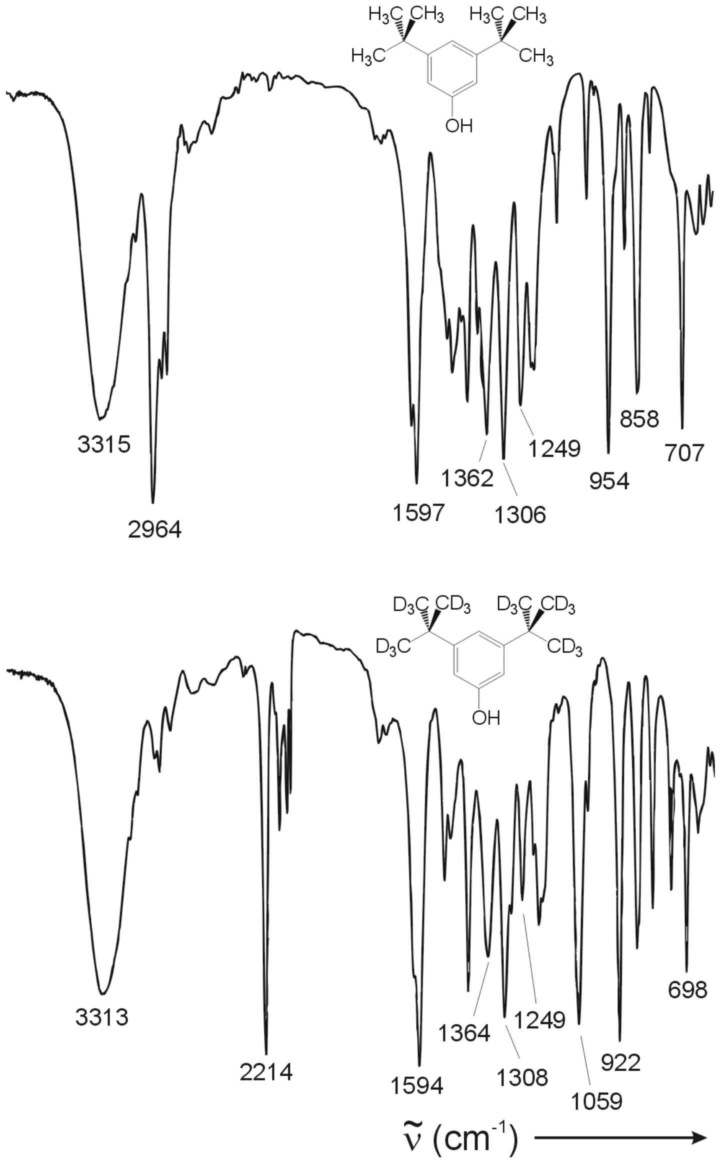
Selected analytical data

a) 3,5-Di-[D_9]-*t*-butylphenol 5b

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ = 6.68 (d, 2H, $^4J_{HH}$ = 1.6 Hz), 6.98 (t, 1H, $^4J_{HH}$ = 1.6 Hz); ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ = 30.3 (sept, $^1J_{CD}$ = 19.0 Hz, CD_3), 34.2 (C_q), 109.6 (C-H), 114.9 (C-H), 152.7 (C_q), 154.9 (C-OH); MS (EI, 70 eV): m/z = 224 ($M^{+\bullet}$, 26 %), 206 ($[M-CD_3]^+$, 100 %), 66 ($C_4D_9^+$, 46 %).



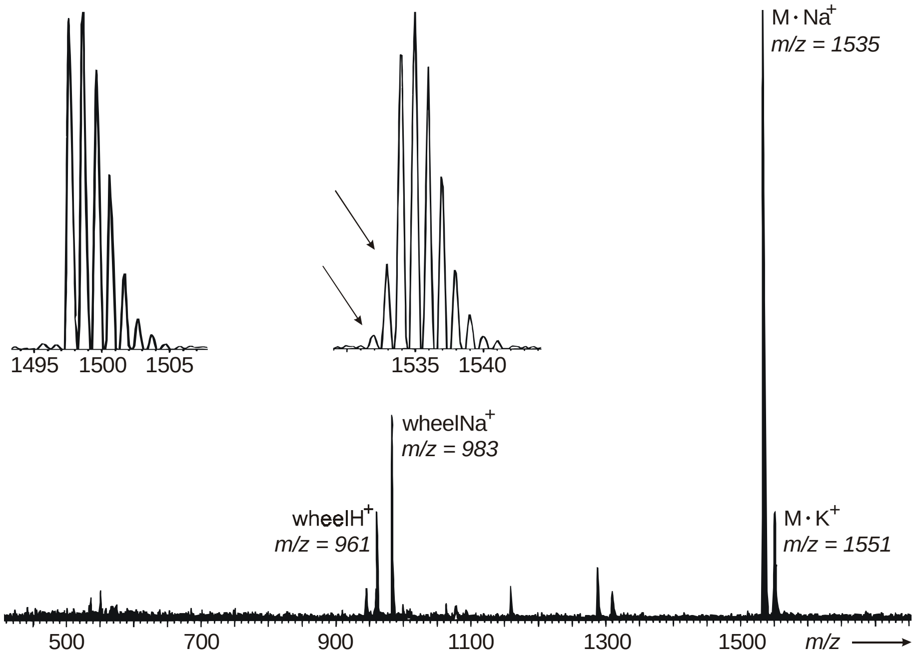
*^{13}C NMR spectrum of stopper **5b**. The inset shows the signal for the CD_3 groups which is split into seven lines with a $^1J_{CD}$ coupling constant of 19 Hz.*



IR spectra of unlabeled stopper ***5a*** *(top) and labeled stopper* ***5b*** *(bottom). The bands for the C-D stretching vibrational modes appear at the expected positions around 2200 cm^{-1}.*

b) [2]{1,4-Bis(3,5-di-[D$_9$]-*tert*-butylphenyloxymethyl)-benzene}-{11'-*tert*-butyl-5',17',23',35',38',40',43',45'-octamethyldispiro[cyclohexane-1,2'-7',15',25',33'-tetraazahepta-cyclo[32.2.2.2$^{3'.6'}$.2$^{16'.19'}$.2$^{21'.24'}$.1$^{9'.13'}$. 1$^{27'.31'}$]hexatetraconta-3',5',9',11',13'(44'),16',18',21',23',27',29',31'(39'),34',36',37',40',42',45'-octadecaene-20´,1´´-cyclohexane]-8´,14´,26´,32´-tetrone}rotaxane 9b.

R_f = 0.20 (CH_2Cl_2/MeOH = 30:1); yield: 37 %; ^{1}H-NMR (400.1 MHz, $C_2D_2Cl_4$): δ(ppm) = 1.33 (s, 36H, wheel-C(CH_3)$_3$), 1.42-1.56 (br, 4H, wheel-CH_2), 1.60-1.70 (br, 8H, wheel-CH_2), 1.78 (s, 12H, wheel-CH_3), 1.81 (s, 12H, wheel-CH_3), 2.22-2.44 (br, 8H, wheel-CH_2), 4.25 (s, 4H, axle-OCH_2), 5.72 (s, 4H, axle-ArH), 6.41 (s, 4H, axle-ArH), 6.98 (m, 10H, ArH), 7.31 (s, 2H, NH), 7.34 (s, 2H, NH), 7.61 (t, ^3J = 7.7 Hz, 1H, wheel-ArH), 7.63 (s, 1H, wheel-ArH), 7.78 (s, 1H, wheel-ArH), 8.10 (d, ^3J = 7.7 Hz, 2H, wheel-ArH), 8.11 (s, 2H, wheel-ArH); ^{13}C-NMR (100.6 MHz, $CDCl_3$): δ(ppm) = 18.6, 23.1, 26.4, 30.2 ($^1J_{CD}$ = 19.0 Hz), 31.2, 34.2, 35.4, 35.8, 45.3, 71.5, 108.8, 116.7, 122.1, 124.7, 126.8, 127.0, 128.0, 129.7, 130.4, 131.1, 131.4, 132.5, 134.2, 134.5, 135.2, 135.3, 136.0, 149.1, 149.2, 153.0, 154.1, 157.8, 165.3, 165.7; MALDI-MS: m/z (%) = 1550.8 (18) [M+K^+], 1535.0 (100) [M+Na^+], 983.3 (37) [wheelNa^+], 961.3 (18) [wheelH^+].



*MALDI mass spectrum of rotaxane **9b**. The insets show the experimental isotope patterns determined for rotaxanes **9a** (left) and **9b** (right). The two arrows point to signals for **9b**-[H_1D_{35}] and **9b**-[H_2D_{34}] from which the degree of deuteration can be estimated to be >96%. These signals are not due to hydrogen losses as indicated by their virtual absence in the pattern of **9a**.*

The degree of deuteration is >95% according to the ^{1}H-NMR in good agreement with the isotope pattern obtained by MALDI-MS, which results in a degree of deuteration of >96%.

c) [2]{4,4'-Bis(3,5-di-[D_9]-*tert*-butylphenyloxymethyl)-1,1'-bibenzyl}-{11'-*tert*-butyl-5', 17',23',35',38',40',43',45'-octamethyldispiro[cyclohexane-1,2'-7',15',25',33'-tetraaza-heptacyclo[32.2.2.2$^{3'.6'}$.2$^{16'.19'}$.2$^{21'.24'}$.1$^{9'.13'}$.1$^{27'.31'}$]hexatetraconta-3',5',9',11',13'(44'),16', 18',21',23',27',29',31'(39'),34',36',37',40',42',45'-octadecaene-20´,1´´-cyclohexane]-8´,14´,26´, 32´-tetrone}rotaxane 10b.

R_f = 0.89 (CH_2Cl_2/MeOH = 20:1); yield: 57 %; m.p. = 206-208°C; ^{1}H-NMR (400.1 MHz, $CDCl_3$): δ(ppm) = 1.32 (s, 9H, wheel-$C(CH_3)_3$), 1.43-1.58 (br, 4H, wheel-CH_2), 1.60-1.73 (br, 8H, wheel-CH_2), 1.86 (s, 12H, wheel-CH_3), 1.88 (s, 12H, wheel-CH_3), 2.27-2.38 (br, 8H, wheel-CH_2), 2.40 (s, 4H, axle-CH_2), 4.48 (s, 4H, axle-OCH_2), 6.45 (d, ^3J = 7.7 Hz, 4H, axle-ArH), 6.54 (d, 4H, ^4J = 1.5 Hz, axle-ArH), 6.61 (d, ^3J = 7.7 Hz, 4H, axle-ArH), 6.92 (t, ^4J = 1.5 Hz, axle-ArH), 6.96 (s, 4H, NH), 7.02 (s, 4H, wheel-ArH), 7.03 (s, 4H, wheel-ArH), 7.46 (s, 1H, wheel-ArH), 7.59 (t, ^3J = 7.7 Hz, 1H, wheel-ArH), 7.62 (s, 1H, wheel-ArH), 8.08 (d, ^3J = 7.7 Hz, 2H, wheel-ArH), 8.09 (s, 2H, wheel-ArH); ^{13}C-NMR (100.6 MHz, $CDCl_3$) δ(ppm) = 18.8, 23.0, 26.4, 30.2 (sept, $^1J_{CD}$ = 19.0 Hz), 31.6, 31.9, 35.3, 35.7, 36.1, 37.9, 45.8, 70.5, 109.3, 116.1, 124.6, 127.1, 127.3, 128.3, 128.4, 129.1, 129.9, 130.7, 131.5, 131.7, 132.4, 134.9, 135.0, 135.1, 141.2, 149.2, 149.3, 153.1, 154.6, 158.4, 165.5, 165.8; MALDI-MS: m/z (%) = 1654.6 (11) [$M+K^+$], 1638.6 (100) [$M+Na^+$], 983.2 (47) [wheelNa^+], 961.2 (18) [wheelH^+].

The degree of deuteration is >95% according to the ^{1}H-NMR and the isotope pattern obtained by MALDI-MS.

Kinetic measurements

For each of the rotaxanes, the rate constants of the deslipping reaction have been measured at several different temperatures by ^{1}H-NMR experiments. The temperature range was chosen such that deslipping occurred with a half life between 10 min and ca. 100 hours. The NMR samples were kept in an oil or - at lower temperatures - a water bath at constant temperature (± 0.1 K). Each pair of deuterated and non-labeled rotaxane was treated exactly the same way so that systematic errors cancel more or less completely in the determination of kinetic isotope effects. Measurements at 383 K were carried out inside the NMR instrument by heating the sample with the high temperature unit. This was necessary due to the short time intervals caused by the short half life of rotaxanes **9a,b** at these temperatures. In each experiment except for the two lowest temperatures, the deslipping was followed until ca. 75% of the rotaxane was converted into the free components. For the evaluation of the data, the integration of as many signals as possible were averaged in order to reduce experimental error. In order to further reduce the error margins, we used the serial processing routines of the Bruker WinNMR program package so that all spectra of each rotaxane were integrated exactly the same way. This averages the data for as many protons as possible (some signals of the rotaxanes are superimposed by signals for the free components and could thus not be used for analysis) and further reduces the errors of the integrations. A closer inspection of the signals increasing over time confirmed that they correspond to the intact free components and thus exclude decomposition of the axle or wheel rather than deslipping as the reason for rotaxane degradation. All measurements were carried out in [D_2]-tetrachloroethane as the solvent.

Plots of $ln(c/c_0)$ versus t (s)

The following pages show plots of $ln(c/c_0)$ versus time *t (s)* for each temperature and pair of rotaxanes. In all cases, the correlation coefficient is excellent and linear relationships provide evidence for the unimolecular nature of the deslipping reaction. It is clearly visible that the differences between the deuterated and non-labeled rotaxanes are far beyond experimental error. The isotope effects are determined as

$$KIE = \frac{k_H}{k_D} = e^{-\frac{\Delta\Delta G^{\neq}}{RT}} \qquad (1)$$

which follows from the *Eyring* equation through:

$$k_H = \frac{k_B T}{h} e^{-\frac{\Delta G_H^{\neq}}{RT}} \qquad (2)$$

$$k_D = \frac{k_B T}{h} e^{-\frac{\Delta G_D^{\neq}}{RT}} \qquad (3)$$

$$\Delta\Delta G^{\neq} = \Delta G_H^{\neq} - \Delta G_D^{\neq} \qquad (4)$$

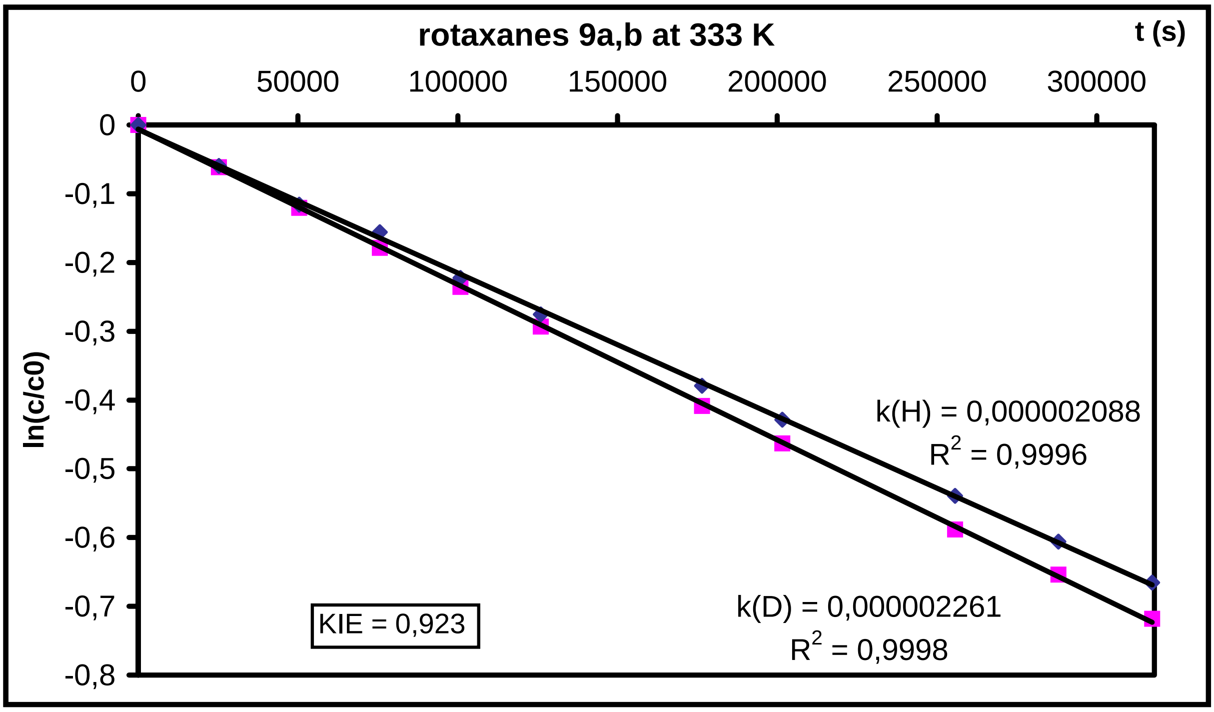
All KIE values are < 1 indicating the operation of a secondary, inverse isotope effect. No significant change of the KIE with temperature is observed. Substitution of $\Delta\Delta G^{\neq}$ according to eq. (5) leads to eqs. (6) and (7):

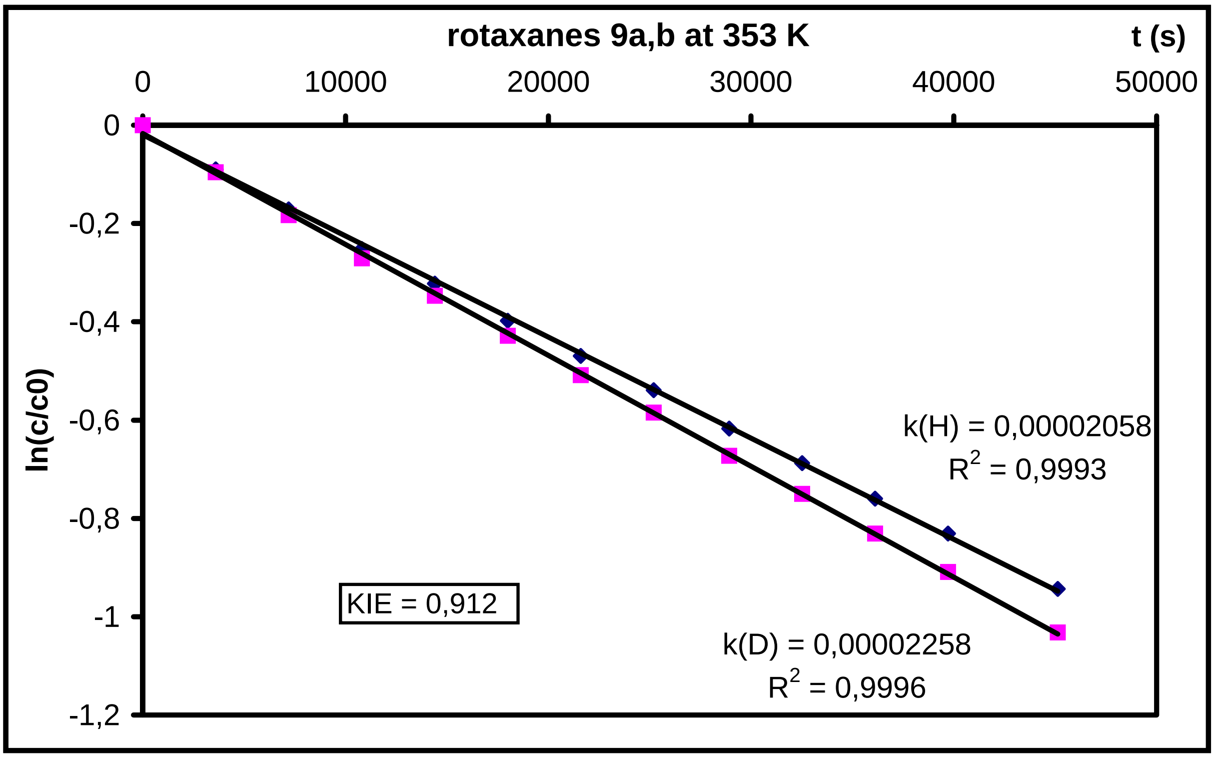
$$\Delta\Delta G^{\neq} = \Delta\Delta H^{\neq} - T\Delta\Delta S^{\neq} \qquad (5)$$

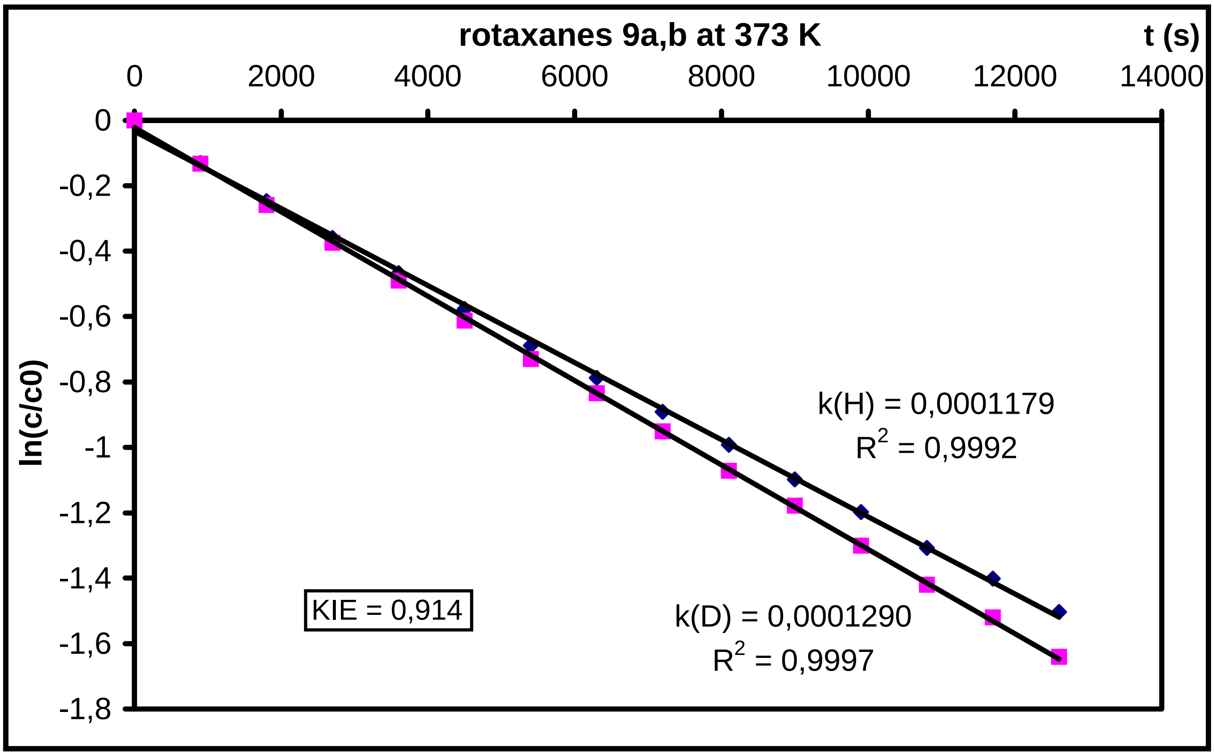
$$KIE = e^{-\frac{\Delta\Delta G^{\neq}}{RT}} = e^{-\frac{\Delta\Delta H^{\neq}}{RT}+\frac{\Delta\Delta S^{\neq}}{R}} \qquad (6)$$

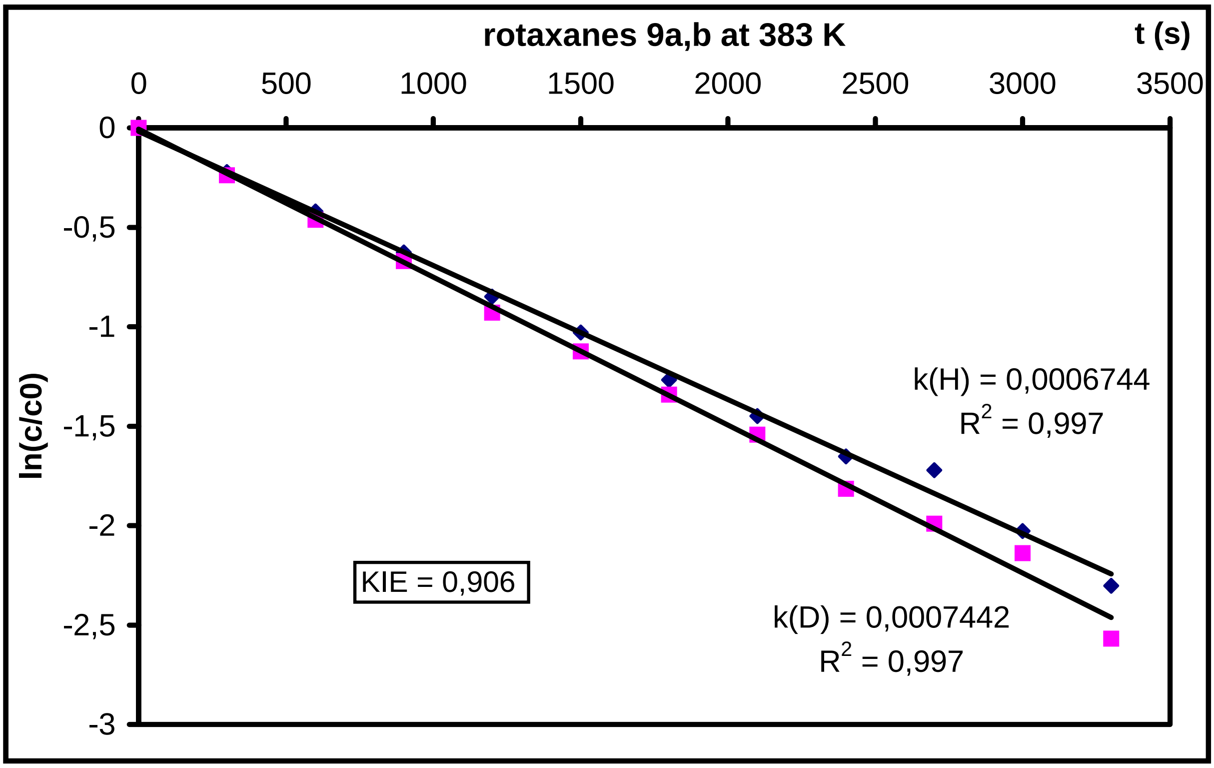
$$\ln KIE = -\frac{\Delta\Delta H^{\neq}}{RT} + \frac{\Delta\Delta S^{\neq}}{R} \qquad (7)$$

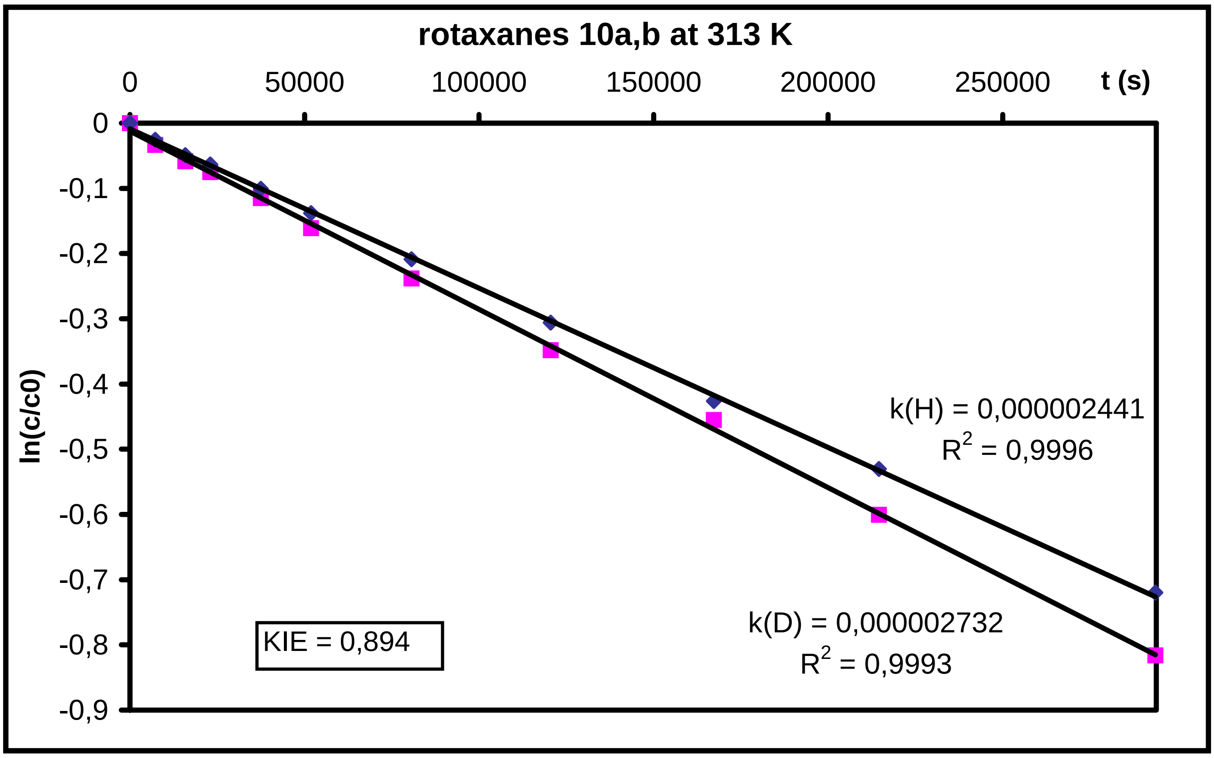
The virtual absence of a temperature dependence of the KIE thus provides evidence that the isotope effect is mainly due to entropic effects, since equation (7) implies that $\Delta\Delta H^{\neq}$ must be close to zero in this case.

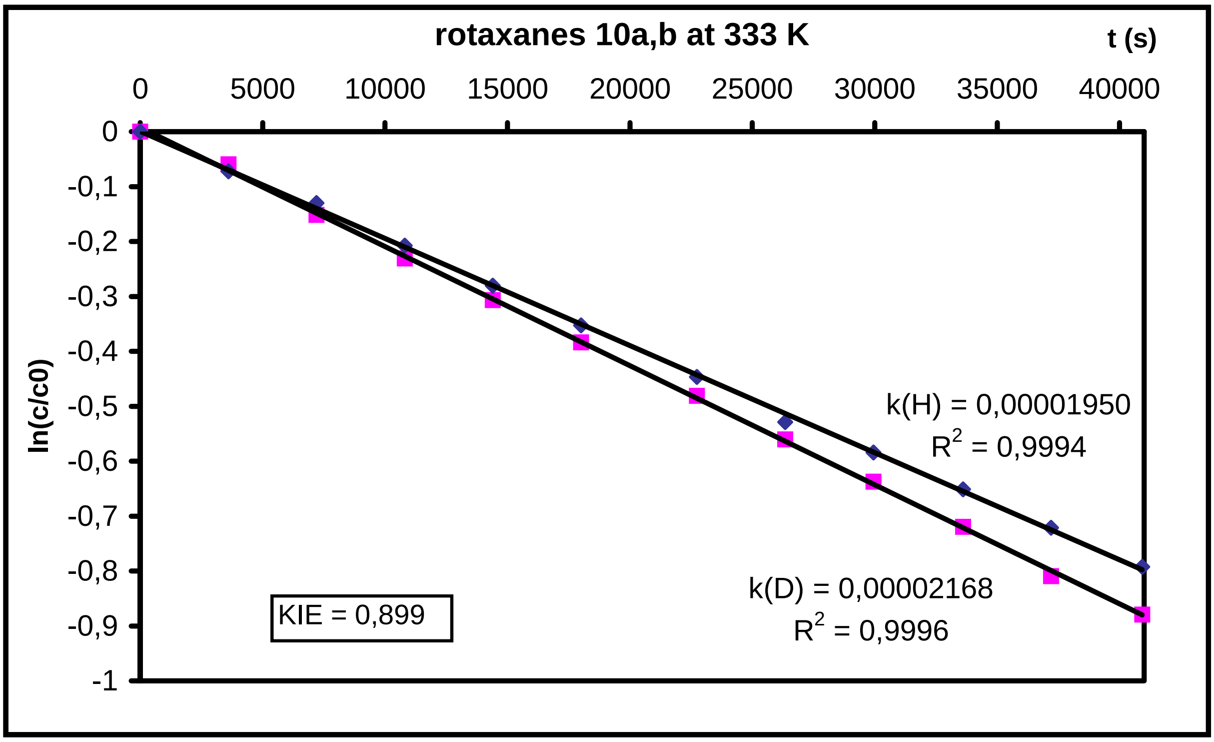

rotaxanes 9a,b at 333 K
t (s)
0
50000
100000
150000
200000
250000
300000
0
-0,1
-0,2
-0,3
-0,4
-0,5
-0,6
-0,7
-0,8
ln(c/c0)
k(H) = 0,000002088
R2 = 0,9996
KIE = 0,923
k(D) = 0,000002261
R2 = 0,9998

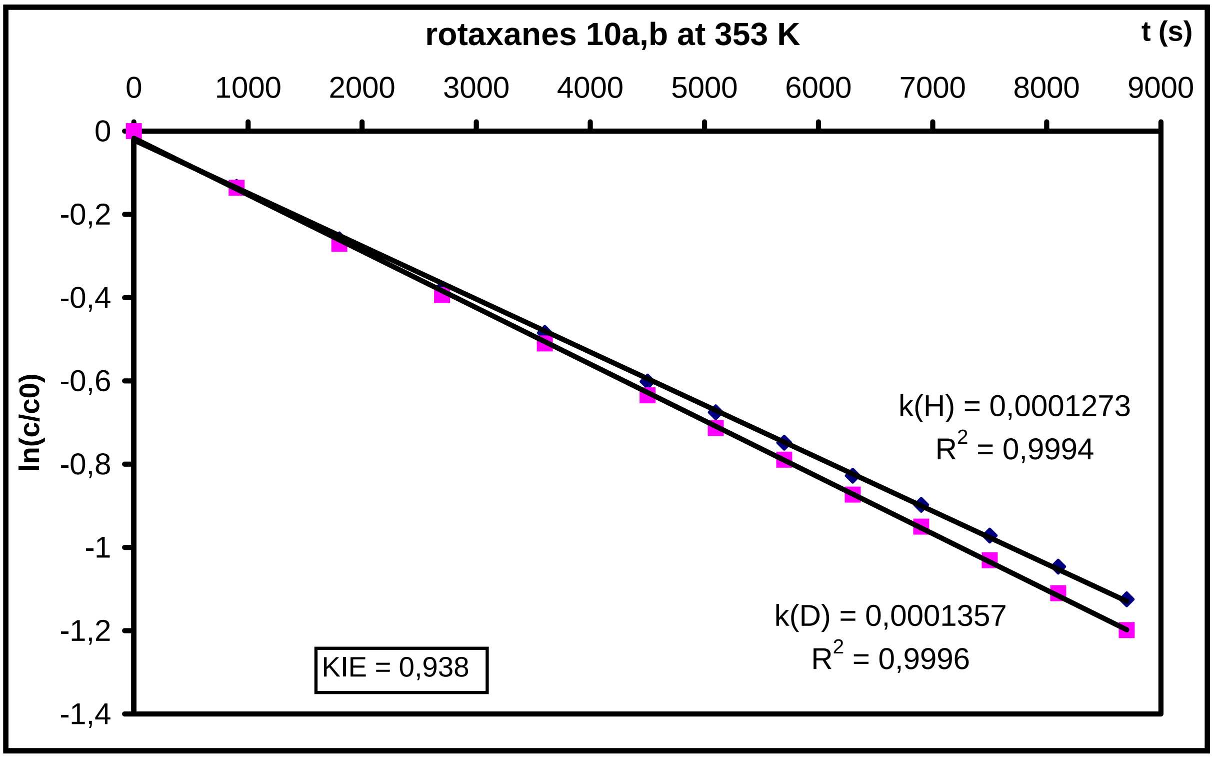

rotaxanes 9a,b at 353 K
t (s)
0
10000
20000
30000
40000
50000
0
-0,2
-0,4
-0,6
-0,8
-1
-1,2
ln(c/c0)
k(H) = 0,00002058
R2 = 0,9993
KIE = 0,912
k(D) = 0,00002258
R2 = 0,9996


rotaxanes 9a,b at 373 K
t (s)
0
2000
4000
6000
8000
10000
12000
14000
0
-0,2
-0,4
-0,6
-0,8
-1
-1,2
-1,4
-1,6
-1,8
ln(c/c0)
k(H) = 0,0001179
R2 = 0,9992
KIE = 0,914
k(D) = 0,0001290
R2 = 0,9997

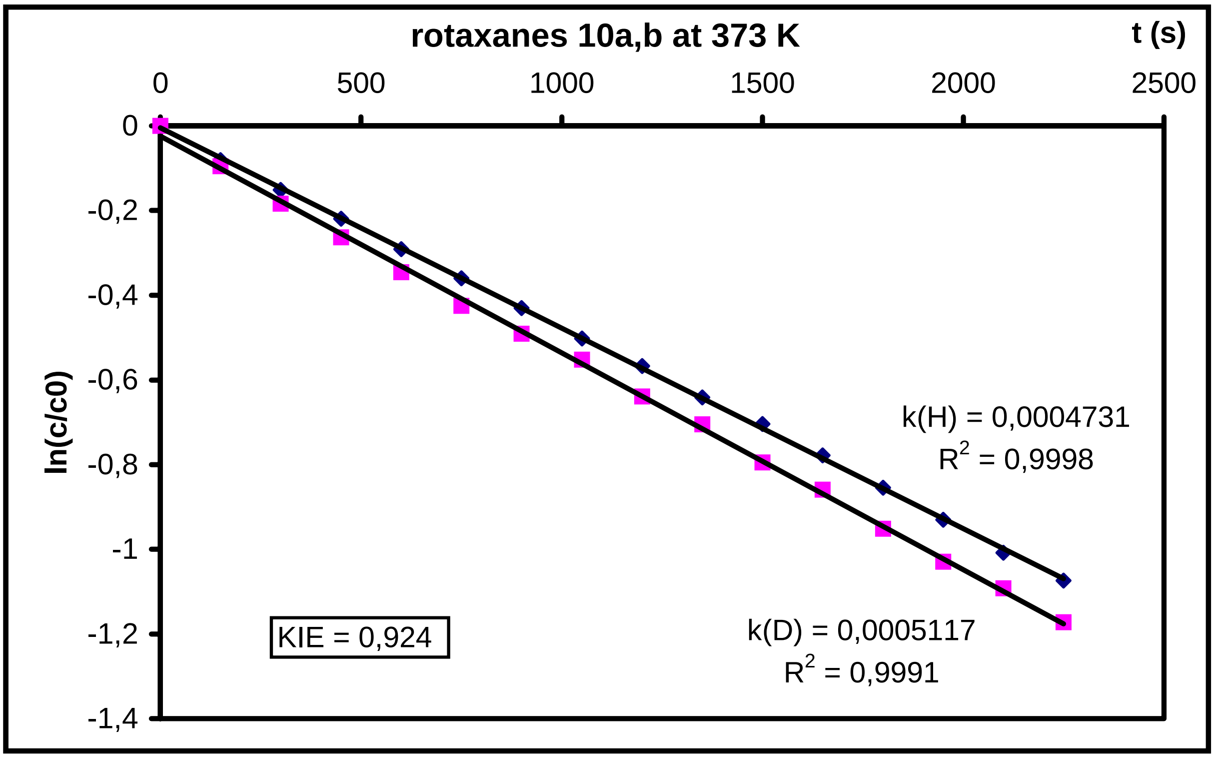

rotaxanes 9a,b at 383 K
t (s)
0
500
1000
1500
2000
2500
3000
3500
0
-0,5
-1
-1,5
-2
-2,5
-3
ln(c/c0)
k(H) = 0,0006744
R2 = 0,997
KIE = 0,906
k(D) = 0,0007442
R2 = 0,997


rotaxanes 10a,b at 313 K
t (s)
0
50000
100000
150000
200000
250000
0
-0,1
-0,2
-0,3
-0,4
-0,5
-0,6
-0,7
-0,8
-0,9
ln(c/c0)
k(H) = 0,000002441
R2 = 0,9996
k(D) = 0,000002732
R2 = 0,9993
KIE = 0,894


rotaxanes 10a,b at 333 K
t (s)
0
5000
10000
15000
20000
25000
30000
35000
40000
0
-0,1
-0,2
-0,3
-0,4
-0,5
-0,6
-0,7
-0,8
-0,9
-1
ln(c/c0)
k(H) = 0,00001950
R2 = 0,9994
k(D) = 0,00002168
R2 = 0,9996
KIE = 0,899



rotaxanes 10a,b at 353 K
t (s)
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
0
-0,2
-0,4
-0,6
-0,8
-1
-1,2
-1,4
ln(c/c0)
k(H) = 0,0001273
R^2 = 0,9994
k(D) = 0,0001357
R^2 = 0,9996
KIE = 0,938



rotaxanes 10a,b at 373 K
t (s)
0
500
1000
1500
2000
2500
0
-0,2
-0,4
-0,6
-0,8
-1
-1,2
-1,4
ln(c/c0)
k(H) = 0,0004731
R^2 = 0,9998
k(D) = 0,0005117
R^2 = 0,9991
KIE = 0,924