Electronic supporting information for

"The effects of an ionic liquid on azide-alkyne cycloaddition reactions"

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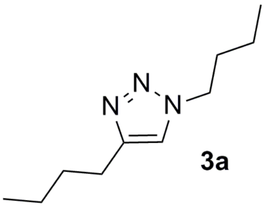
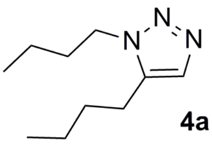
Spectral assignments for the regioisomeric mixtures of the triazoles 3 and 4



3a

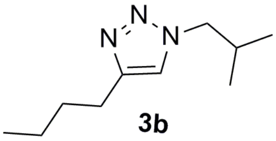


4a

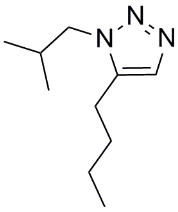
1,4-Dibutyl-1,2,3-triazole ***3a*** *and 1,5-dibutyl-1,2,3-triazole* ***4a***. Butylazide **2a**, 0.524h, 5.3 mmol. 1-Hexyne **1a**, 2.03 g, 25 mmol. Reaction time, 48 hours. Yield, 0.614 g, 64%, yellow liquid. Signals monitored: δ 4.30 vs 4.22. Intensities, 1.2:1.

^{1}H NMR (300 MHz, $CDCl_3$) Isomer **3a**: δ 0.78-0.92 (m, 6H, $C\underline{H}_3$), 1.20-1.36 (m, 4H, $C\underline{H}_2CH_3$), 1.49-1.62 (m, 2H, Ar-$CH_2C\underline{H}_2$), 1.70-1.85 (m, 2H, $NCH_2C\underline{H}_2$), 1.70-1.85 (m, 2H, $NCH_2C\underline{H}_2$), 2.70 (m, 2H, $CC\underline{H}_2$), 4.30 (m, 2H, $NC\underline{H}_2$), 7.42 (s, 1H, HetAr-H).

^{1}H NMR (300 MHz, $CDCl_3$) Isomer **4a**: δ 0.78-0.92 (m, 6H, $C\underline{H}_3$), 1.20-1.36 (m, 4H, $C\underline{H}_2CH_3$), 1.49-1.62 (m, 2H, HetAr-$CH_2C\underline{H}_2$), 1.70-1.85 (m, 2H, $NCH_2C\underline{H}_2$), 1.70-1.85 (m, 2H, $NCH_2C\underline{H}_2$), 2.61 (m, 2H, $CC\underline{H}_2$), 4.22 (m, 2H, $NC\underline{H}_2$), 7.26 (s, 1H, HetAr-H).



3b

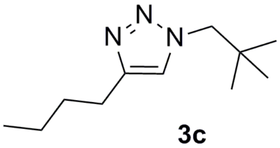


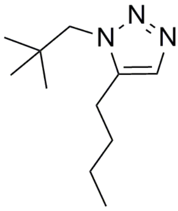
4b

4-Butyl-1-(2-methylpropyl)-1,2,3-triazole ***3b*** *and 5-butyl-1-(2-methylpropyl)- 1,2,3-triazole* ***4b***. Isobutyl azide **2b**, 0.559 g, 5.6 mmol. 1-hexyne **1a**, 2.06 g, 25 mmol. Reaction time, 48 hours. Yield, 0.905 g, 89%, yellow liquid. Signals monitored: δ 4.12 vs 4.04. Intensities, 1.2:1.

^{1}H NMR (300 MHz, $CDCl_3$) Isomer **3b**: δ 0.93-0.97 (m, 9H, $(C\underline{H}_3)_2$ and $C\underline{H}_3$), 1.18-1.33 (m, 2H, $C\underline{H}_2CH_3$), 1.45-1.58 (m, 2H, HetAr-$CH_2C\underline{H}_2$), 1.99-2.12 (m, 2H, $C\underline{H}$), 2.72 (t, J = 7.7 Hz, 2H, HetAr-$C\underline{H}_2$), 4.12 (d, J = 7.3 Hz, 2H, **3b** $NC\underline{H}_2$), 7.45 (s, 1H, HetAr-H).

^{1}H NMR (300 MHz, $CDCl_3$) Isomer **4b**: δ 0.93-0.97 (m, 9H, $(C\underline{H}_3)_2$ and $C\underline{H}_3$), 1.18-1.33 (m, 2H, $C\underline{H}_2CH_3$), 1.45-1.58 (m, 2H, HetAr-$CH_2C\underline{H}_2$), 1.99-2.12 (m, 2H, $C\underline{H}$), 2.61 (t, J = 7.7 Hz, 2H, HetAr-$C\underline{H}_2$), 4.04 (d, J = 7.31 Hz, 2H, $NC\underline{H}_2$), 7.25 (s, 1H, HetAr-H).

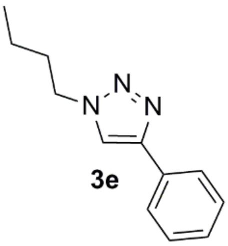

3c

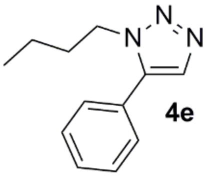

4c

4-Butyl- 1-(2,2-dimethylpropyl)-1,2,3-triazole ***3c*** *and 5-butyl-1-(2,2-dimethylpropyl)-1,2,3-triazole* ***4c***. Neopentyl azide **2c**, 0.296 g, 2.6 mmol. 1-Hexyne **1a**, 2.01 g, 25 mmol. Reaction time, 7 days. Crude yield, 0.512 g, yellow liquid. Signals monitored: δ 4.12 vs 4.04. Intensities, 3.1:1.

^{1}H NMR (300 MHz, $CDCl_3$) Isomer **3c**: δ 0.80-0.96 (m, 12H, $(C\underline{H}_3)_3$ and $CH_2C\underline{H}_3$), 1.21-1.38 (m, 2H, $C\underline{H}_2CH_3$), 1.66-1.83 (m, 2H, Ar-$CH_2C\underline{H}_2$), 3.02 (t, J = 7.6 Hz, 2H, **3c** HetAr-$C\underline{H}_2$), 4.12 (s, 2H, **3c** $NC\underline{H}_2$), 8.03 (s, 1H, **3c** HetAr-H).

Isomer **4c**: δ 0.80-0.96 (m, 12H, $(C\underline{H}_3)_3$ and $CH_2C\underline{H}_3$), 1.21-1.38 (m, 2H, $C\underline{H}_2CH_3$), 1.66-1.83 (m, 2H, Ar-$CH_2C\underline{H}_2$), 2.72 (t, J = 7.2 Hz, 2H, HetAr-$C\underline{H}_2$), 3.02 (t, J = 7.6 Hz, 2H, Ar-$C\underline{H}_2$), 4.04 (s, 2H, **4c** $NC\underline{H}_2$), 8.18 (s, 1H, **4c** HetAr-H).

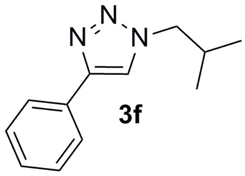

3e


4e

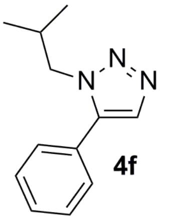
*1-Butyl-4-phenyl-1,2,3-*triazole[60] ***3e*** *and 1-butyl-5-phenyl-1,2,3-triazole* ***4e***. Butyl azide **2a**, 0.517 g, 5.2 mmol. phenylacetylene **1b**, 2.01 g, 20 mmol. Reaction time, 48 hours. Yield, 0.690 g, 66%, yellow liquid. Signals monitored: δ 4.36 vs 4.42. Intensities, 1:1.

^{1}H NMR (300 MHz, $CDCl_3$) Isomer **3e**: 0.99 (t, J = 7.4 Hz, 3H, $C\underline{H}_3$), 1.41 (sext, J = 7.4 Hz, 2H, $C\underline{H}_2CH_3$), 1.96 (qn, J = 7.4 Hz, 2H, $NCH_2C\underline{H}_2$), 4.36 (t, J = 7.4 Hz, 2H, $NC\underline{H}_2$), 7.3-7.5 (m, 3H, Ar-H), 7.78 (s, 1H, HetAr-H), 7.86 (m, 2H, **3e** Ar-H).

Isomer **4e**: δ 0.87 (t, J = 7.4 Hz, 3H, $C\underline{H}_3$), 1.29 (sext, J = 7.4 Hz, 2H, $C\underline{H}_2CH_3$), 1.83 (qn, J = 7.4 Hz, 2H, $NCH_2C\underline{H}_2$), 4.42 (t, J = 7.4 Hz, 2H, $NC\underline{H}_2$), 7.3-7.5 (m, 5H, **3e** and **4e** Ar-H), 7.70 (s, 1H, **4e** HetAr-H).



3f

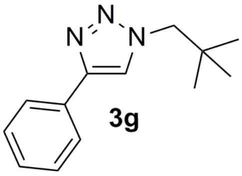


4f

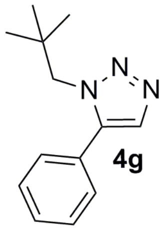
1-(2-Methylpropyl)-4-phenyl-1,2,3-triazole ***3f*** *and 1-(2-Methylpropyl)-5-phenyl-1,2,3-triazole* ***4f****.* Isobutyl azide **2b**, 0.539 g, 5.4 mmol. phenylacetylene **1b**, 2.56 g, 25 mmol. Reaction time, 48 hours. Yield, 0.512 g, 47%, yellow liquid. Signals monitored: δ 4.18 vs 4.15. Intensities, 1:1.

^{1}H NMR (300 MHz, $CDCl_3$) Isomer **3f**: δ 0.94 (d, J=6.7 Hz, 6H, $(C\underline{H}_3)_2$), 2.34 (sept, J=6.8 Hz, 2H, $C\underline{H}$), 4.18 (m, 2H, $C\underline{H}_2$), 7.27-7.52 (m, 3H, Ar-H), 7.79 (s, 1H, HetAr-H), 7.83 (m, 2H, Ar-H).

^{1}H NMR (300 MHz, $CDCl_3$) Isomer **4f**: δ 0.79 (d, J=6.7 Hz, 6H, $(C\underline{H}_3)_2$), 2.13 (sept, J=6.8 Hz, 2H, $C\underline{H}$), 4.15 (m, 2H, $C\underline{H}_2$), 7.27-7.52 (m, 5H, Ar-H), 7.66 (s, 1H, HetAr-H).



3g

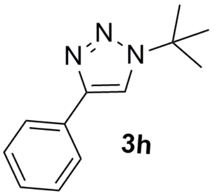


4g

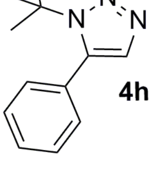
1-(2,2-Dimethylpropyl)-4-phenyl-1,2,3-triazole ***3g*** *and 1-(2,2-dimethylpropyl)-5-phenyl-1,2,3-triazole* ***4g****.* Neopentyl azide **2c**, 0.289 g, 2.9 mmol. phenylacetylene **1b**, 2.06 g, 20 mmol. Reaction time, 48 hours. Yield, 0.817 g, 85%, yellow solid. Signals monitored: δ 4.15 vs 4.19. Intensities, 1.2:1.

^{1}H NMR (300 MHz, $CDCl_3$) Isomer **3g**: δ 0.99 (s, 9H, $(C\underline{H}_3)_3$), 4.15 (s, 2H, $NC\underline{H}_2$), 7.27-7.48 (m, 3H, Ar-H), 7.71 (s, 1H, HetAr-H), 7.80-7.85 (m, 2H, Ar-H).

^{1}H NMR (300 MHz, $CDCl_3$) Isomer **4g**: δ 0.78 (s, 9H, $(C\underline{H}_3)_3$), 4.19 (s, 2H, $NC\underline{H}_2$), 7.27-7.48 (m, 5H, HetAr-H), 7.64 (s, 1H, Ar-H).



3h



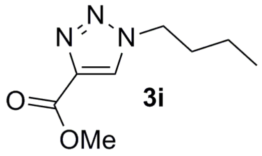
4h

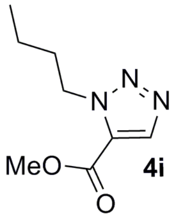
1-(1,1-Dimethylethyl)-4-phenyl-1,2,3-triazole ***3h*** *and 1-(2,2-dimethylethyl)-5-phenyl-1,2,3-triazole* ***4h****.* *tert*-Butyl azide **2d**, 0.554 g, 5.6 mmol. phenylacetylene **1b**, 2.18 g, 21 mmol. Reaction time, 7 days. Yield, 0.241 g, 21%, yellow solid.

Signals monitored: δ 1.72 vs 1.56. Intensities, 3.6:1.

^{1}H NMR (300 MHz, CDCl$_3$) Isomer **3h**: δ 1.72 (s, 9H, (C$\underline{H}_3$)$_3$), 7.28-7.46 (m, 3H, Ar-H), 7.82 (s, 1H, HetAr-H), 7.84 (m, 2H, Ar-H).

^{1}H NMR (300 MHz, CDCl$_3$) Isomer **4h**: δ 1.56 (s, 9H, (C$\underline{H}_3$)$_3$), 7.28-7.46 (m, 5H, Ar-H), 7.55 (s, 1H, HetAr-H).


3i


4i

1-Butyl-4-(carbomethoxy)-1,2,3-triazole ***3i*** *and 1-butyl-5-(carbomethoxy)-1,2,3-triazole* ***4i****.* Butyl azide **2a**, 0.567 g, 5.7 mmol. Methyl propiolate **1c**, 2.02 g, 24 mmol. Reaction time, 48 hours. Yield, 0.912 g, 79%, brown solid. Signals monitored: δ 3.98 vs 3.96. Intensities, 7.5:1.

^{1}H NMR (300 MHz, CDCl$_3$) Isomer **3i**: δ 0.99 (m, 3H, CH$_2$C$\underline{H}_3$), 1.39 (m, 2H, C$\underline{H}_2$CH$_3$), 1.95 (m, 2H, NCH$_2$C$\underline{H}_2$), 3.98 (s, 3H, OMe), 4.75 (t, J = 7.4 Hz, 2H, **3i** NC$\underline{H}_2$), 8.14 (s, 1H, HetAr-H).

^{1}H NMR (300 MHz, CDCl$_3$) Isomer **4i**: δ 0.99 (m, 3H, CH$_2$C$\underline{H}_3$), 1.39 (m, 2H, C$\underline{H}_2$CH$_3$), 1.95 (m, 2H, NCH$_2$C$\underline{H}_2$), 3.96 (s, 3H, OMe), 3.98 (s, 3H, OMe), 4.45 (t, J = 7.3 Hz, 2H, NC$\underline{H}_2$), 8.11 (s, 1H, HetAr-H).

Table S1 - The ratios of the triazoles **3c** and **4c** resulting from the reaction between neopentyl azide **2c** and 1-hexyne **1a** in the noted solvents. The results are the averages of triplicate experiments.

Solvent	**Ratio of the triazoles 3c:4c**[a]
heptane	1.6 ± 0.2 : 1
acetonitrile	10.0 ± 0.6 : 1
ethanol	12 ± 1 : 1

[a] Uncertainties quoted are 95% confidence intervals.

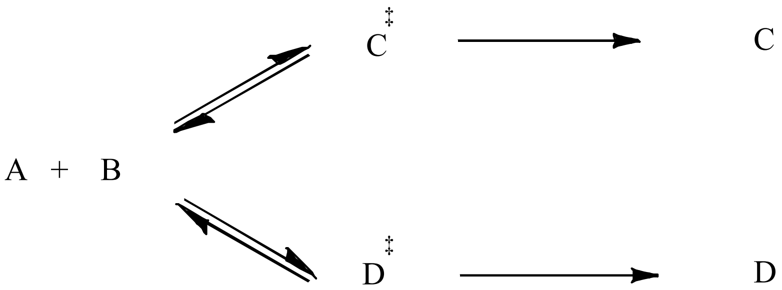
Table S2 - Activation parameters for the formation of each of the isomers **3i** and **4i** in reaction of compounds **1c** and **2a**.

Isomer	**$\Delta H^{\ddagger}$ / kJ^{-1} mol^{-1}**[a]	**$\Delta S^{\ddagger}$ / J^{-1} K^{-1} mol^{-1}**[a]
3i	69.6 ± 8.8	-179 ± 26
4i	76.4 ± 0.7	-178 ± 2

[a] Uncertainties quoted are 95% confidence intervals.

Comparison of observed activation parameters to those for individual processes in parallel reactions.

Assume two reagents can proceed through different transition states, as below, giving rise to two separate products. The observed rate is k, whilst the actual rates of formation are k_C and k_D, for the species C and D, respectively.



Given the bimolecular Eyring equation (1):

$$\ln\left(\frac{kh}{k_B RT^2}\right)=\frac{\Delta S^{\ddagger}}{R}-\frac{\Delta H^{\ddagger}}{RT}$$

and applying this to consumption of the starting material:

$$\ln\left(\frac{k_{obs}h}{k_B RT^2}\right)=\frac{\Delta S^{\ddagger}_{obs}}{R}-\frac{\Delta H^{\ddagger}_{obs}}{RT}$$

Given k_{obs} arises from both k_C and k_D:

$$\ln\left(\frac{(k_C+k_D)h}{k_B RT^2}\right)=\frac{\Delta S^{\ddagger}_{obs}}{R}-\frac{\Delta H^{\ddagger}_{obs}}{RT}$$

$$\ln\left(\frac{hk_C}{k_B RT^2}+\frac{hk_D}{k_B RT^2}\right)=\frac{\Delta S^{\ddagger}_{obs}}{R}-\frac{\Delta H^{\ddagger}_{obs}}{RT}$$

$$\frac{hk_C}{k_B RT^2}+\frac{hk_D}{k_B RT^2}=e^{\frac{\Delta S^{\ddagger}_{obs}}{R}-\frac{\Delta H^{\ddagger}_{obs}}{RT}}$$

Using the exponential form of (1) for k_C and k_D and simplifying:

$$e^{\frac{\Delta G^{\ddagger}_C}{RT}}+e^{-\frac{\Delta G^{\ddagger}_D}{RT}}=e^{-\frac{\Delta G^{\ddagger}_{obs}}{RT}}$$

$$\frac{e^{\frac{\Delta G^{\ddagger}_C}{RT}}}{e^{-\frac{\Delta G^{\ddagger}_D}{RT}}}+\frac{e^{-\frac{\Delta G^{\ddagger}_D}{RT}}}{e^{-\frac{\Delta G^{\ddagger}_D}{RT}}}=\frac{e^{-\frac{\Delta G^{\ddagger}_{obs}}{RT}}}{e^{-\frac{\Delta G^{\ddagger}_D}{RT}}}$$

$$e^{\frac{\Delta G_D^\ddagger}{RT}-\frac{\Delta G_C^\ddagger}{RT}}+1=e^{\frac{\Delta G_D^\ddagger}{RT}-\frac{\Delta G_{obs}^\ddagger}{RT}}$$

$$\ln(e^{\frac{\Delta G_D^\ddagger}{RT}-\frac{\Delta G_C^\ddagger}{RT}}+1)=\ln(e^{\frac{\Delta G_D^\ddagger}{RT}-\frac{\Delta G_{obs}^\ddagger}{RT}})$$

If we assume that there is a high selectivity for the formation of product C then:

$$k_C \gg k_D$$

$$\Delta G_C^\ddagger \ll \Delta G_D^\ddagger$$

$$\Delta G_D^\ddagger - \Delta G_C^\ddagger > 0$$

$$\frac{\Delta G_D^\ddagger}{RT}-\frac{\Delta G_C^\ddagger}{RT} > 0$$

Since ln(x+1) approaches ln(x) for large positive x values:*

$$\ln(e^{\frac{\Delta G_D^\ddagger}{RT}-\frac{\Delta G_C^\ddagger}{RT}}+1)=\ln(e^{\frac{\Delta G_D^\ddagger}{RT}-\frac{\Delta G_{obs}^\ddagger}{RT}})$$

$$\ln(e^{\frac{\Delta G_D^\ddagger}{RT}-\frac{\Delta G_C^\ddagger}{RT}})\approx\ln(e^{\frac{\Delta G_D^\ddagger}{RT}-\frac{\Delta G_{obs}^\ddagger}{RT}})$$

$$\frac{\Delta G_D^\ddagger}{RT}-\frac{\Delta G_C^\ddagger}{RT}\approx\frac{\Delta G_D^\ddagger}{RT}-\frac{\Delta G_{obs}^\ddagger}{RT}$$

$$\Delta G_C^\ddagger \approx \Delta G_{obs}^\ddagger$$

$$\Delta H_C^\ddagger - T\Delta S_C^\ddagger \approx \Delta H_{obs}^\ddagger - T\Delta S_{obs}^\ddagger$$

Hence, the observed activation parameters are comparable to the C isomer alone (since this correlation is over a range of temperatures). In our case, compound C is the 4-substitued triazole **29*i*** in the above argument.

[*] Clearly the validity of this assumption needs to be considered:

Say ln(x+1) = ln(x) for x > a then it is necessary for

$$e^{\frac{\Delta G_D^{\ddagger}}{RT}-\frac{\Delta G_C^{\ddagger}}{RT}} > a$$

$$e^{\frac{\Delta G_D^{\ddagger}}{RT}-\frac{\Delta G_C^{\ddagger}}{RT}} > a$$

$$\frac{e^{\frac{\Delta G_D^{\ddagger}}{RT}}}{e^{\frac{\Delta G_C^{\ddagger}}{RT}}} > a$$

Using the exponential form of equation (1) gives:

$$\frac{\frac{k_C h}{k_B T}}{\frac{k_D h}{k_B T}} > a$$

$$\frac{k_C}{k_D} > a$$

Hence, we can monitor the validity of the assumption by considering the ratios of the rates of formation. Noting the regioselectivity to be approximately 8 : 1 we are effectively assuming that Ln(9)=Ln(8). This introduces an absolute error of 0.12 in the natural logarithm, but a 12% error in the component including activation parameters since:

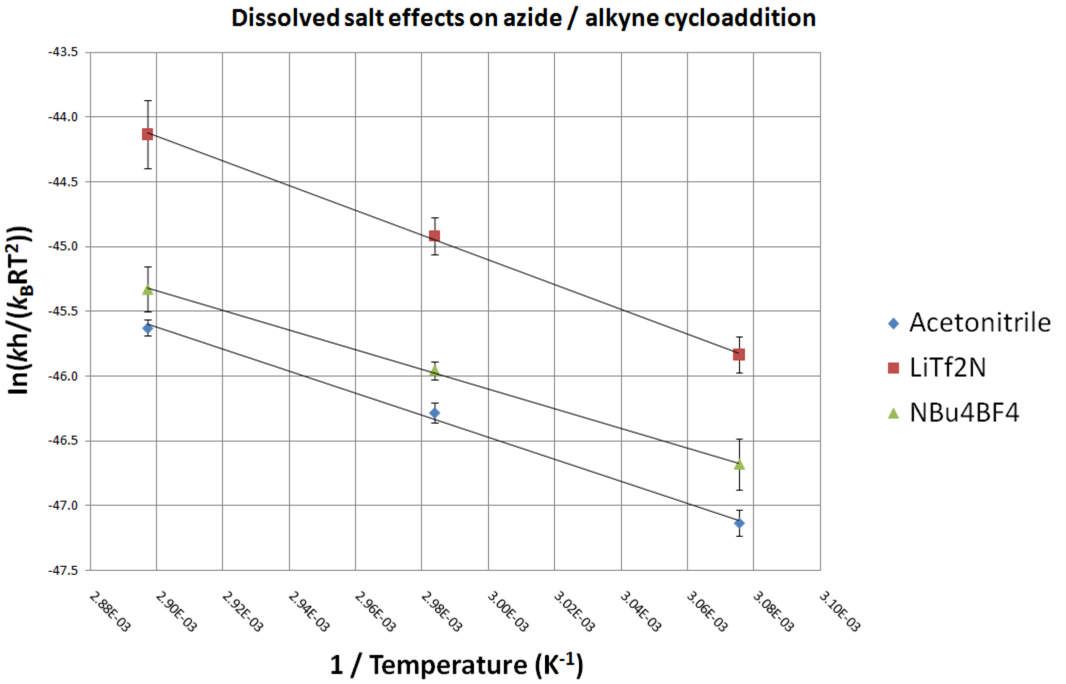
$$y = e^{x}$$

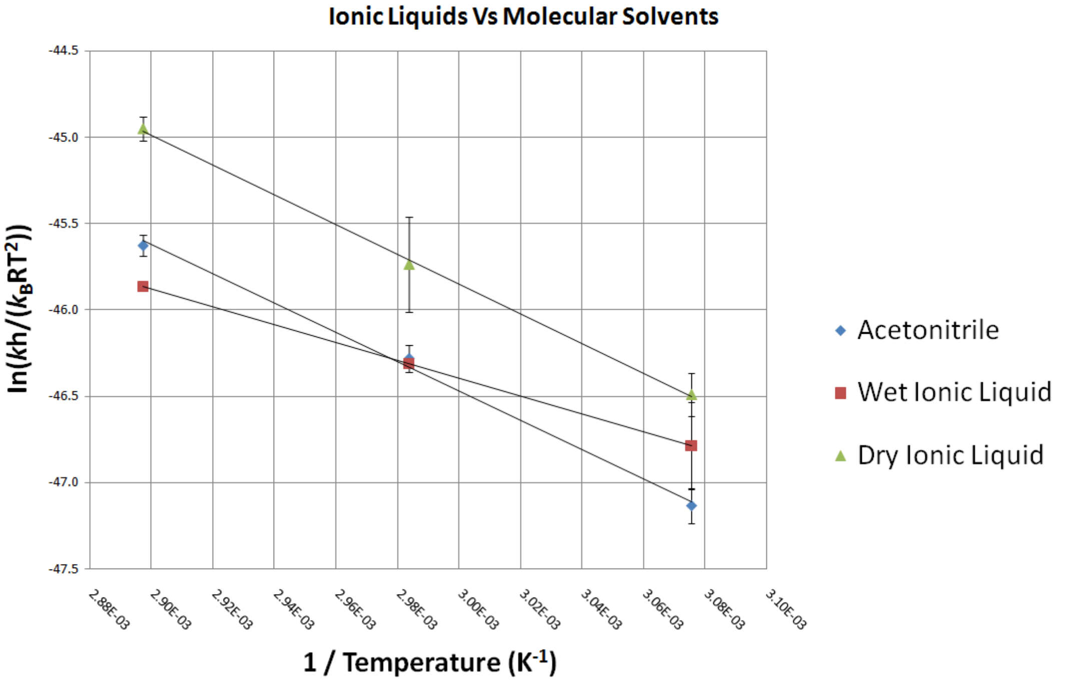
$$\frac{\sigma_y}{y} = \sigma_x$$

(The relative error in y is the absolute error in x.)

Now whilst this is relatively large, it would be expected to be of approximately the same magnitude in each case *plus* in the same direction. **That is, it is a systematic error introduced by this assumption which is effectively the same in each case.**

Eyring plots for the reaction of compounds 1c and 2a in various solvent systems.





Rates used are the average of at least three and up to six replicate experiments, with the exception of the 'wet' ionic liquid (χ_{H_2O} *ca.* 0.05) case where a total of six experiments were conducted. Uncertainties shown are 95% confidence intervals.

Table S3 – Second order rate constants for the reaction of compounds **1c** and **2a** at various temperatures, along with calculated activation parameters, in various solvent systems

Solvent	**Temperature / K**	k'' / M^{-1} s^{-1} [a]	$\ln(k''h/k_BRT^2)$ [a]	$\Delta H^‡$ / [a] kJ^{-1} mol^{-1}	$\Delta S^‡$ / [a] J $K^{-1}mol^{-1}$
	325.15	$(6.05 \pm 0.63) \times 10^{-5}$	-47.1(1)		
CH_3CN	335.15	$(1.55 \pm 0.12) \times 10^{-4}$	-46.3(1)	70(2)	177(6)
	345.15	$(3.16 \pm 0.19) \times 10^{-4}$	-45.6(1)		
$Li[Tf_2N]$	325.15	$(2.28 \pm 0.32) \times 10^{-4}$	-45.8(1)		
solution	335.15	$(6.07 \pm 0.86) \times 10^{-4}$	-44.9(1)	79(3)	138(10)
	345.15	$(1.41 \pm 0.38) \times 10^{-3}$	-44.1(3)		
$NBu_4[BF_4]$	325.15	$(9.78 \pm 1.97) \times 10^{-5}$	-46.7(2)		
solution	335.15	$(2.14 \pm 0.15) \times 10^{-4}$	-46.0(1)	63(2)	194(7)
	345.15	$(4.27 \pm 0.75) \times 10^{-4}$	-45.3(2)		
‘Wet’	325.15	$(8.28 \pm 2.28) \times 10^{-5}$	-46.8(3)		
$Bmim[Tf_2N]$	335.15	$(1.50 \pm 0.17) \times 10^{-4}$	-46.3(0)	43(3)	256(10)
	345.15	$(2.83 \pm 0.31) \times 10^{-4}$	-45.7(0)		
‘Dry’	325.15	$(1.19 \pm 0.15) \times 10^{-5}$	-46.5(1)		
$Bmim[Tf_2N]$	335.15	$(2.72 \pm 0.46) \times 10^{-4}$	-45.7(3)	72(4)	-166(11)
	345.15	$(6.22 \pm 0.45) \times 10^{-4}$	-44.9(2)		

[a] Uncertainties quoted are 95% confidence intervals.