Supporting Information: Probing the Mechanism of Thermally Driven thiol-Michael Dynamic Covalent Chemistry

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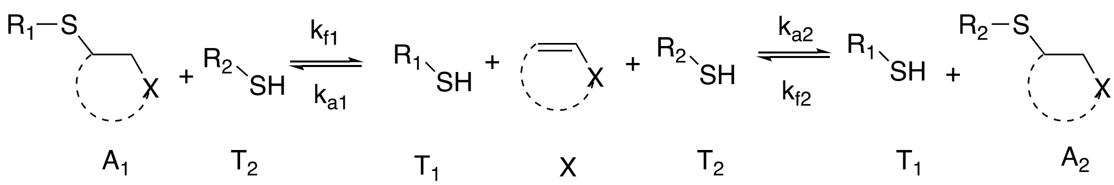
Kinetic Model

The dynamic thiol-Michael equilibrium is modeled using the following system of differential equations:



Here species A_1 and A_2 represent the TM adducts of thiol-1 (T_1) and thiol-2 (T_2) respectively, and X represents the free, unreacted, Michael acceptor. The rate coefficients k_{a1} and k_{a2} represent the addition rate coefficients of thiol-1 and thiol-2 to the Michael acceptor respectively, and rate coefficients k_{f1} and k_{f2} represent the fragmentation rate coefficients of adduct-1 and adduct-2.

The overall equilibrium between the measurable A_1, T_1, A_2 and T_2 species is given below:

$$K_o = \frac{k_{f1}}{k_{f2}}\frac{k_{a2}}{k_{a1}} = \frac{[A_2][T_1]}{[A_1][T_2]}$$

Note that the concentration of the Michael acceptor, X, is below the detection limit of the NMR spectrometer therefore it is not explicitly included in the analysis of experimental data, but it is included in simulations

This dynamic equilibrium can be simulated using the following system of time dependent differential equations:

$$\frac{d[A_1]}{dt} = k_{a1}[X][T_1] - k_{f1}[A_1] \quad (1)$$

$$\frac{d[T_1]}{dt} = -k_{a1}[X][T_1] + k_{f1}[A_1] \quad (2)$$

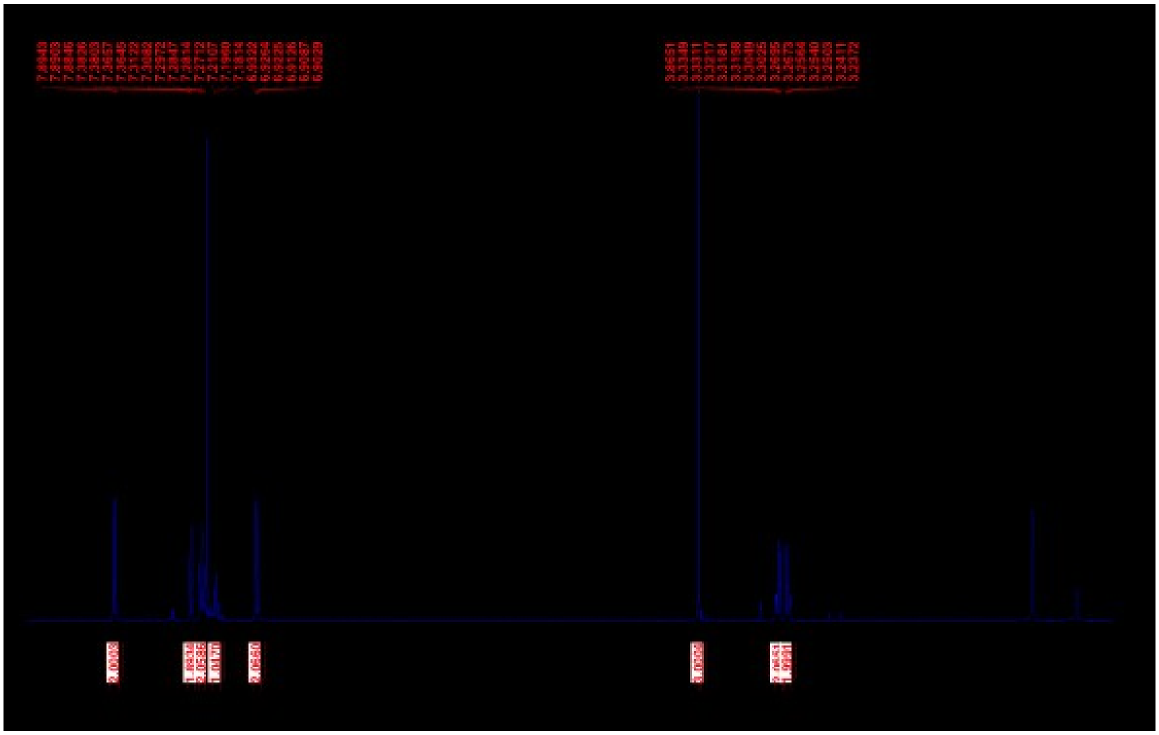
$$\frac{d[A_2]}{dt} = k_{a2}[X][T_2] - k_{f2}[A_2] \quad (3)$$

$$\frac{d[T_2]}{dt} = -k_{a2}[X][T_2] + k_{f2}[A_2] \quad (4)$$

$$\frac{d[X]}{dt} = -k_{a1}[X][T_1] - k_{a2}[X][T_2] + k_{f1}[A_1] + k_{f2}[A_2] \quad (5)$$

These equations were coded and solved numerically in MATLAB_R2017a.

Results



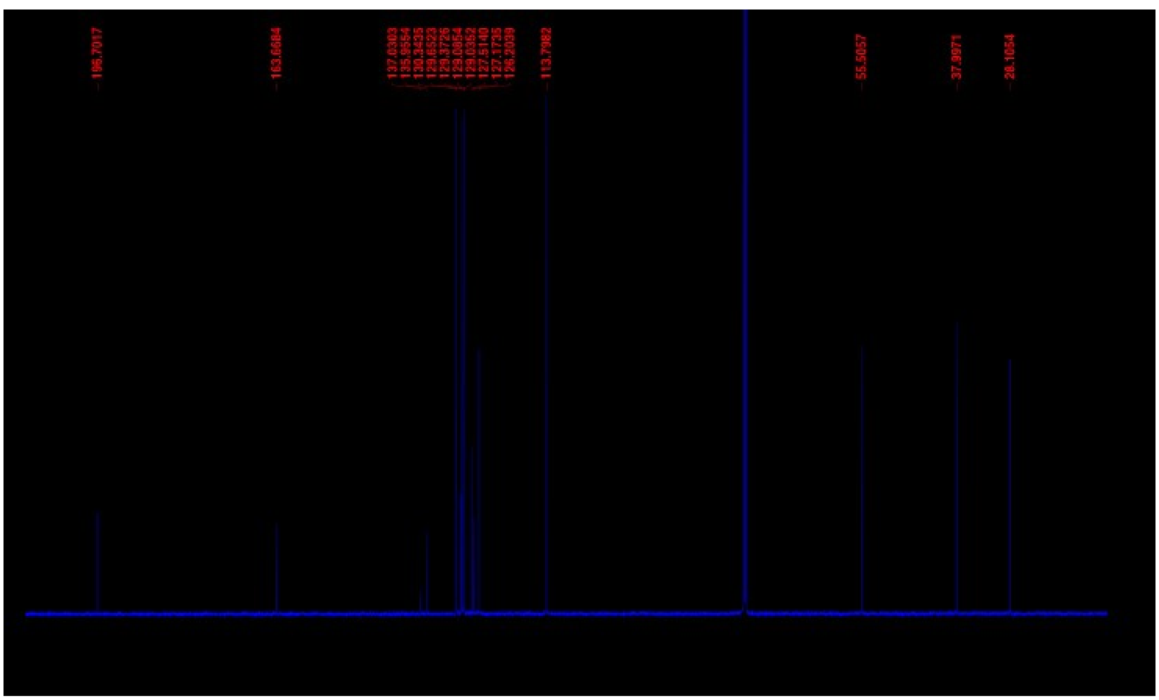
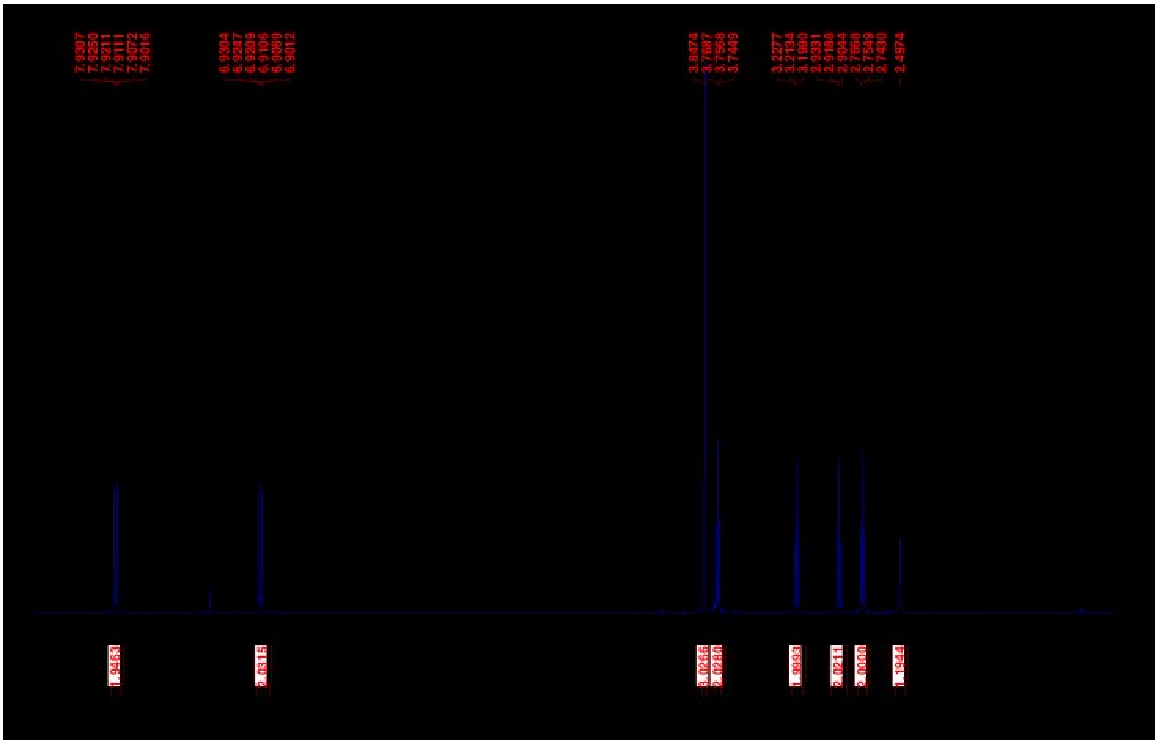


Figure S1: Top: ^{1}H-NMR spectrum (500 MHz) and Bottom: ^{13}C-NMR spectrum (126 MHz) of TP-PVK-OMe in $CDCl_3$.



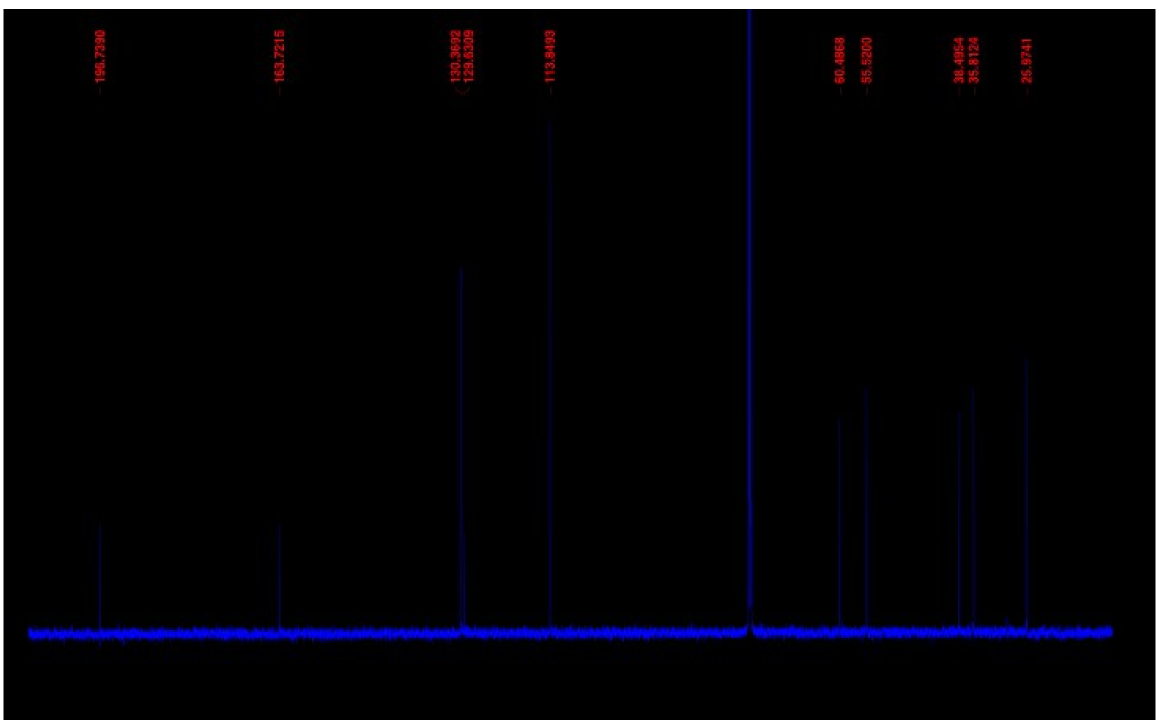
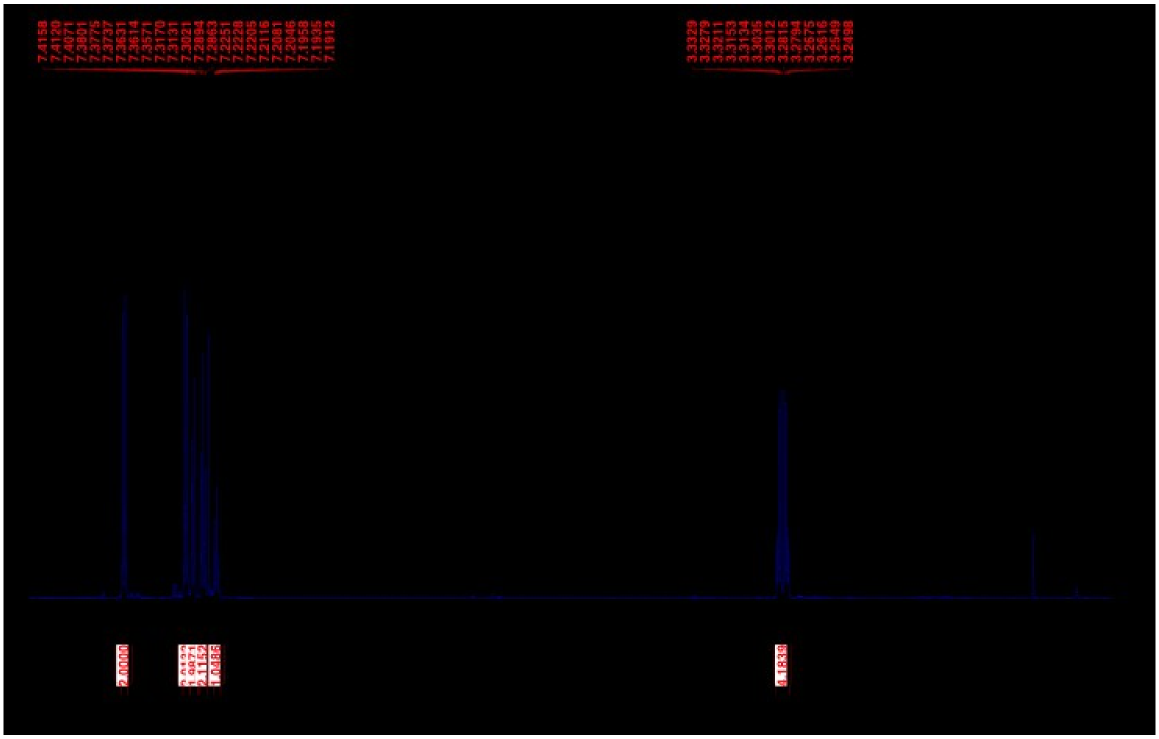


Figure S2: Top: ^{1}H-NMR spectrum (500 MHz) and Bottom: ^{13}C-NMR spectrum (126 MHz) of ME-PVK-OMe in $CDCl_3$.



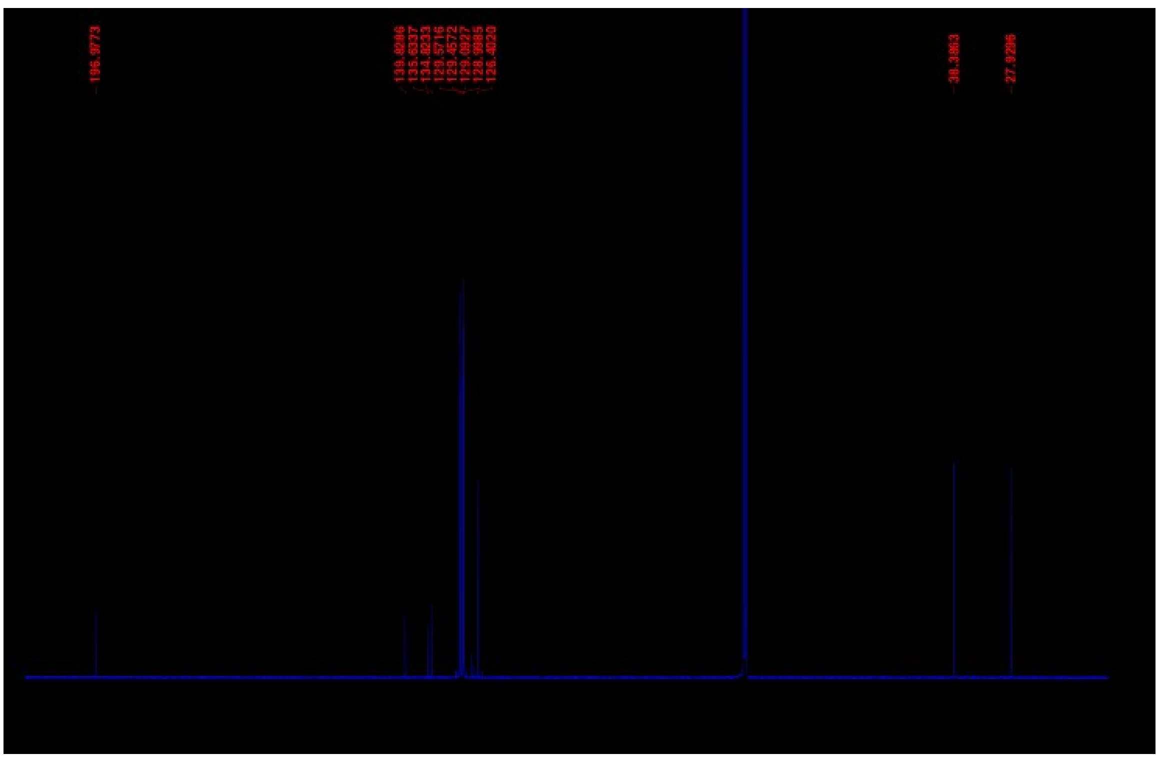
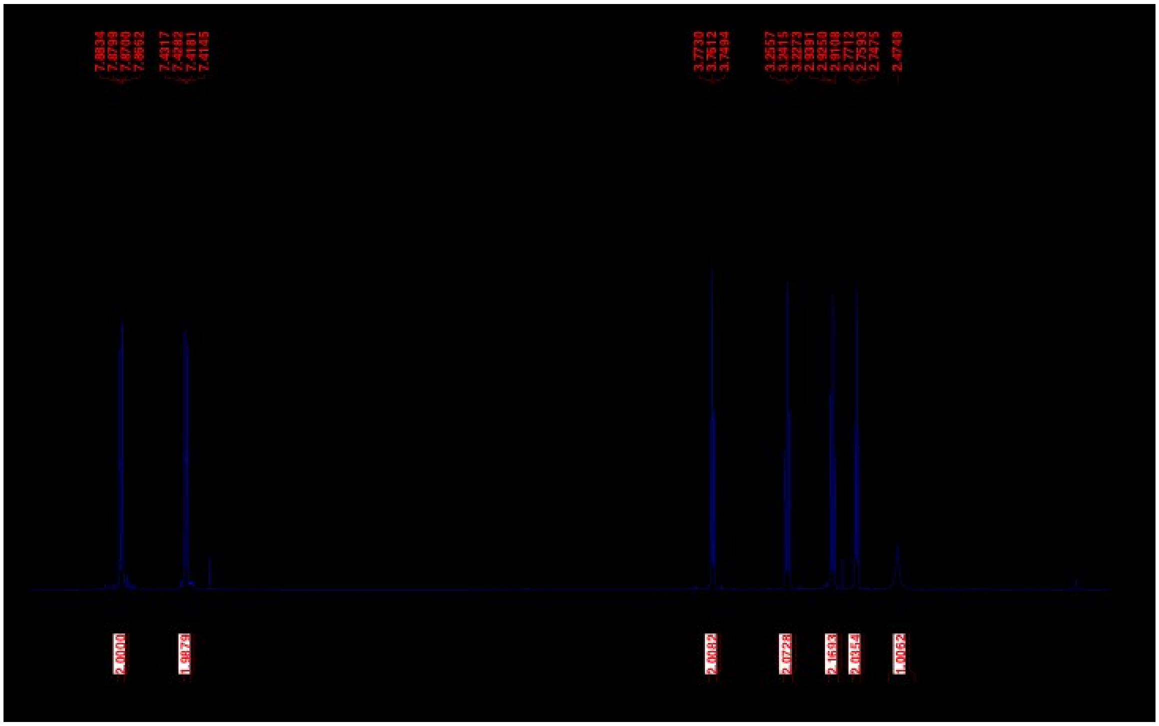


Figure S3: Top: ^{1}H-NMR spectrum (500 MHz) and Bottom: ^{13}C-NMR spectrum (126 MHz) of TP-PVK-Cl in $CDCl_3$.



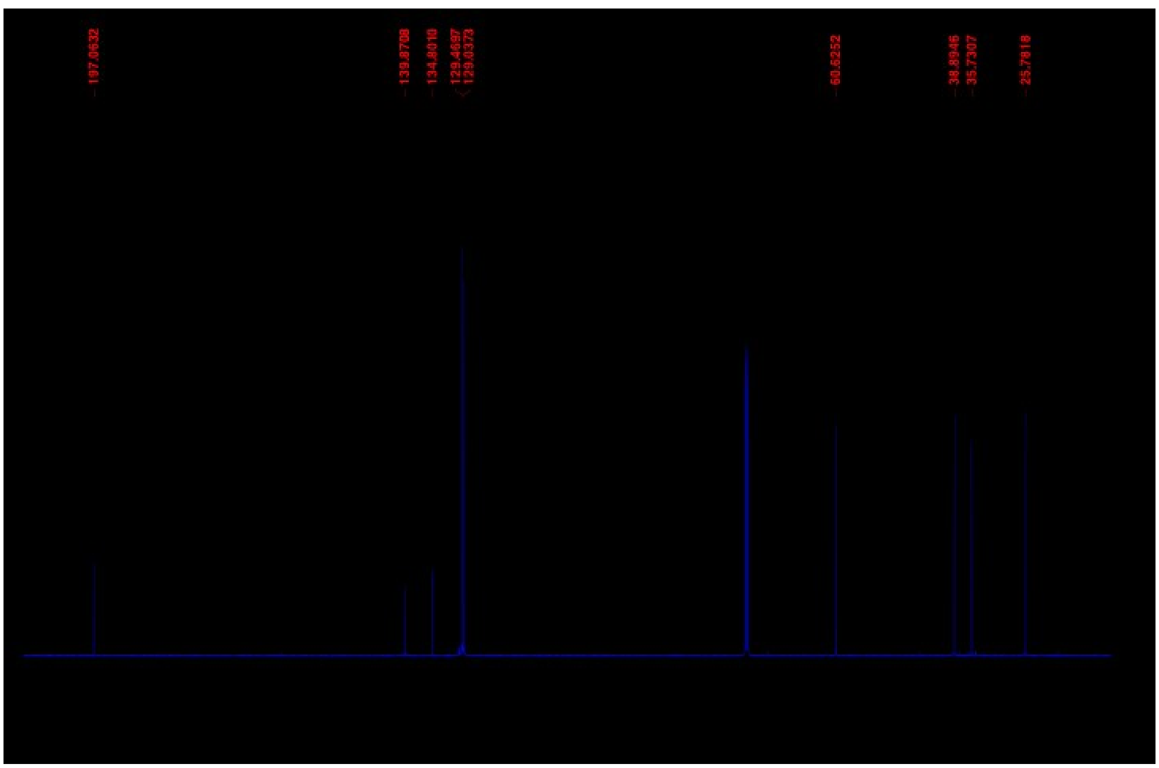


Figure S4: Top: ^{1}H-NMR spectrum (500 MHz) and Bottom: ^{13}C-NMR spectrum (126 MHz) of ME-PVK-Cl in $CDCl_3$.

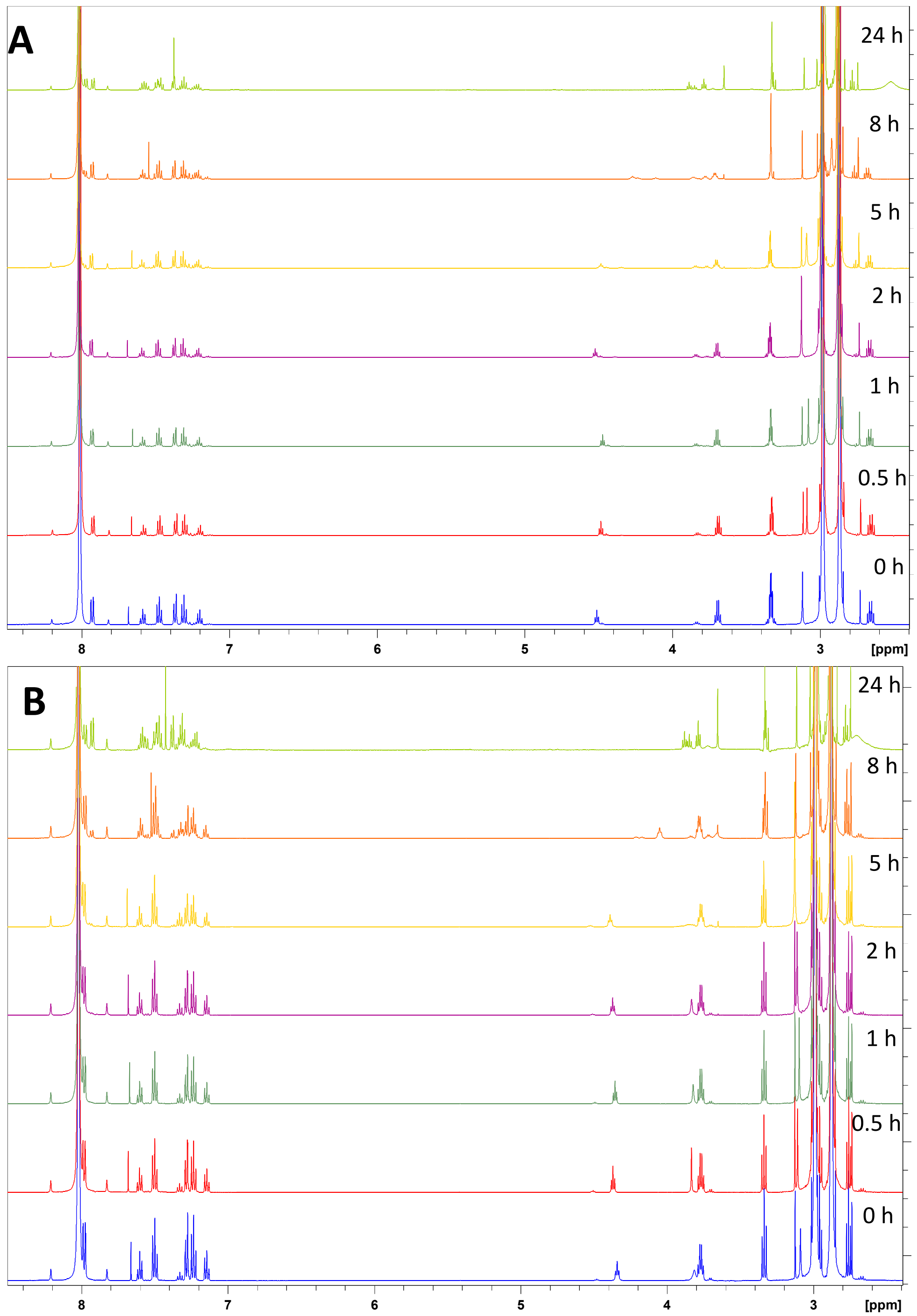


Figure S5: Typical kinetics of exchange for TP-ME-PVK system. A) Gives kinetic data initialized from the TP-PVK adduct with 1 equivalent of MESH. B) Gives kinetic data initialized from the ME-PVK adduct with 1 equivalent of TPSH.

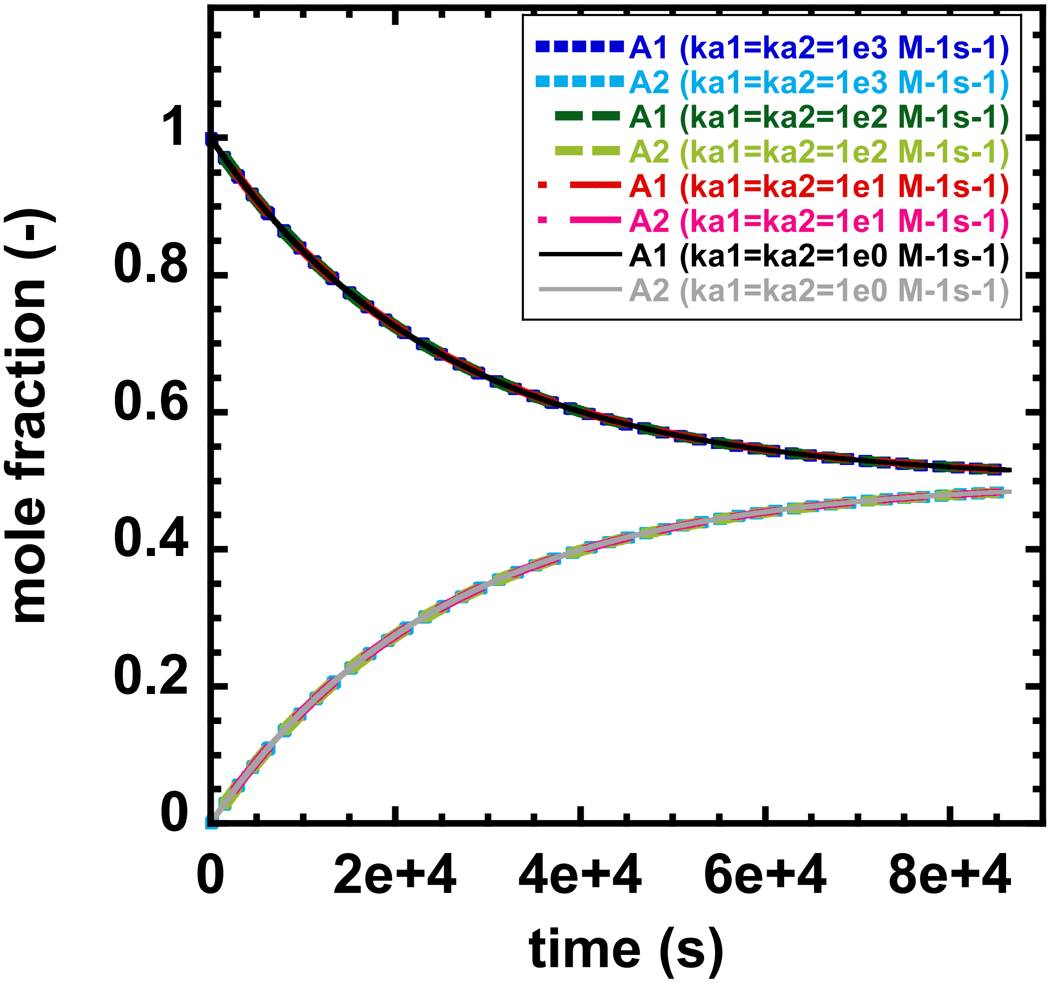


Figure S6: Sensitivity analysis, simultaneous variation of k_{a1} and k_{a2} . Conditions k_{f1}=k_{f2}=2e-5 s^{-1}, $K_{overall}$= 1. Initial conditions $[A_2]_0$=$[T_1]_0$ = 0 M, $[A_1]_0$=$[T_2]_0$ = 1 M.

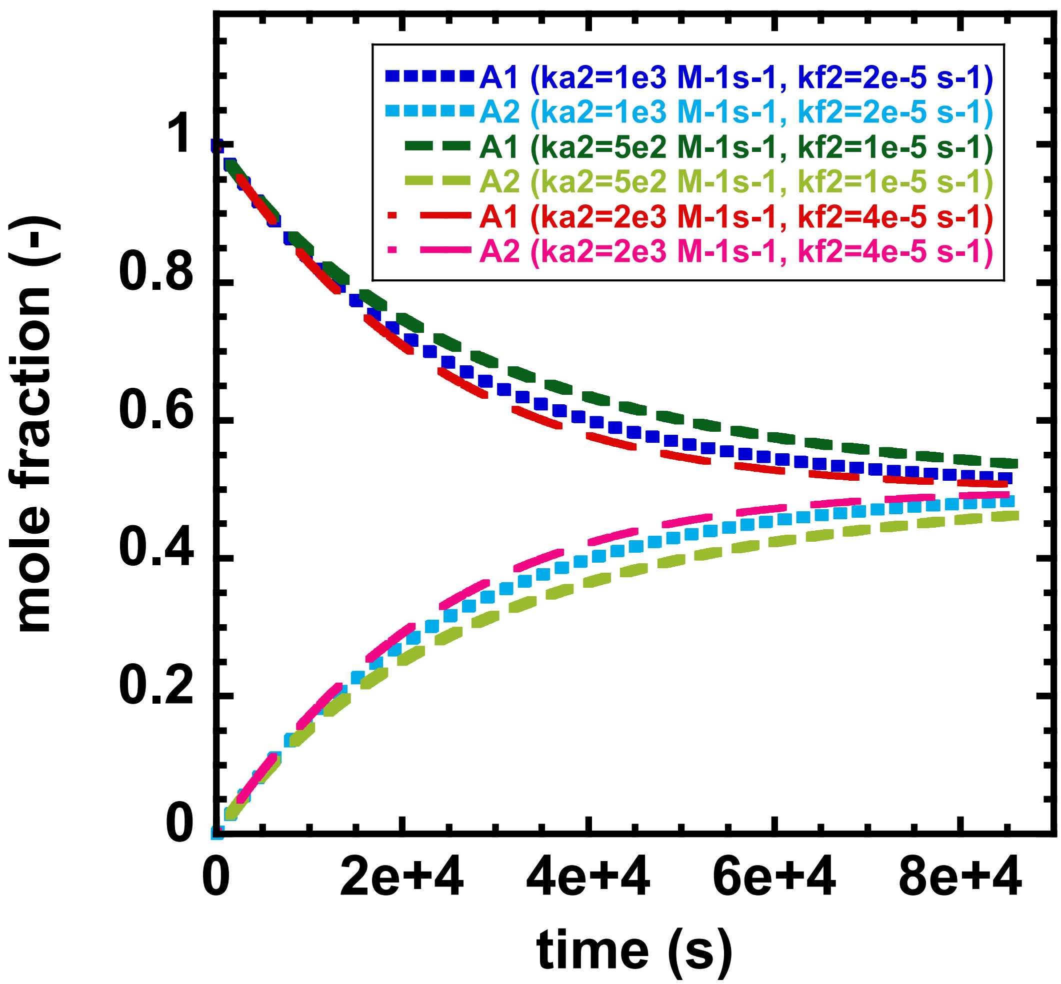


Figure S7: Sensitivity analysis, simultaneous variation of k_{a2} and k_{f2} . Conditions k_{f1}=2e-5 s^{-1}, k_{a1}=1e3 $M^{-1}s^{-1}$, $K_{overall}$= 1. Initial conditions $[A_2]_0=[T_1]_0$ = 0 M, $[A_1]_0=[T_2]_0$=1 M.

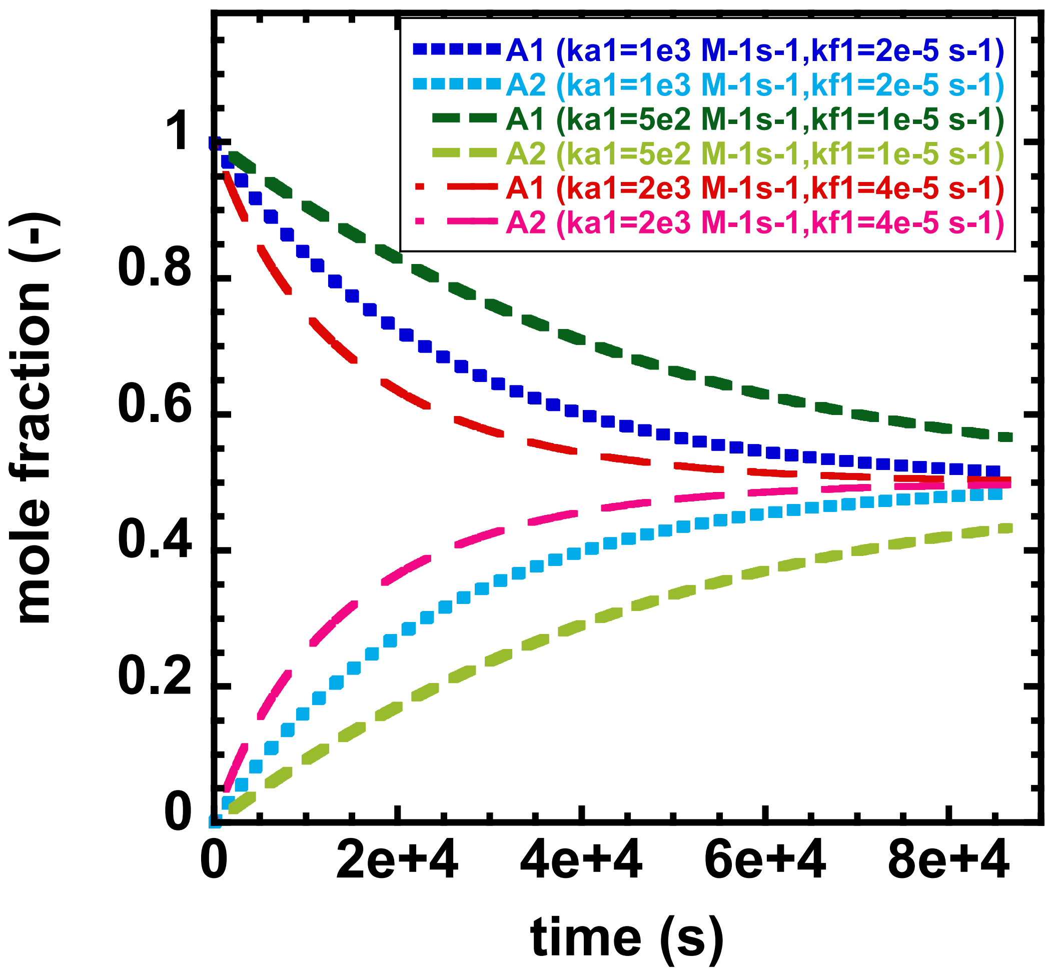


Figure S8: Sensitivity analysis, simultaneous variation of k_{a1} and k_{f1} . Conditions k_{f2}=2e-5 s^{-1}, k_{a2}=1e3 $M^{-1}s^{-1}$, $K_{overall}$= 1. Initial conditions $[A_2]_0=[T_1]_0$ = 0 M, $[A_1]_0=[T_2]_0$=1 M.

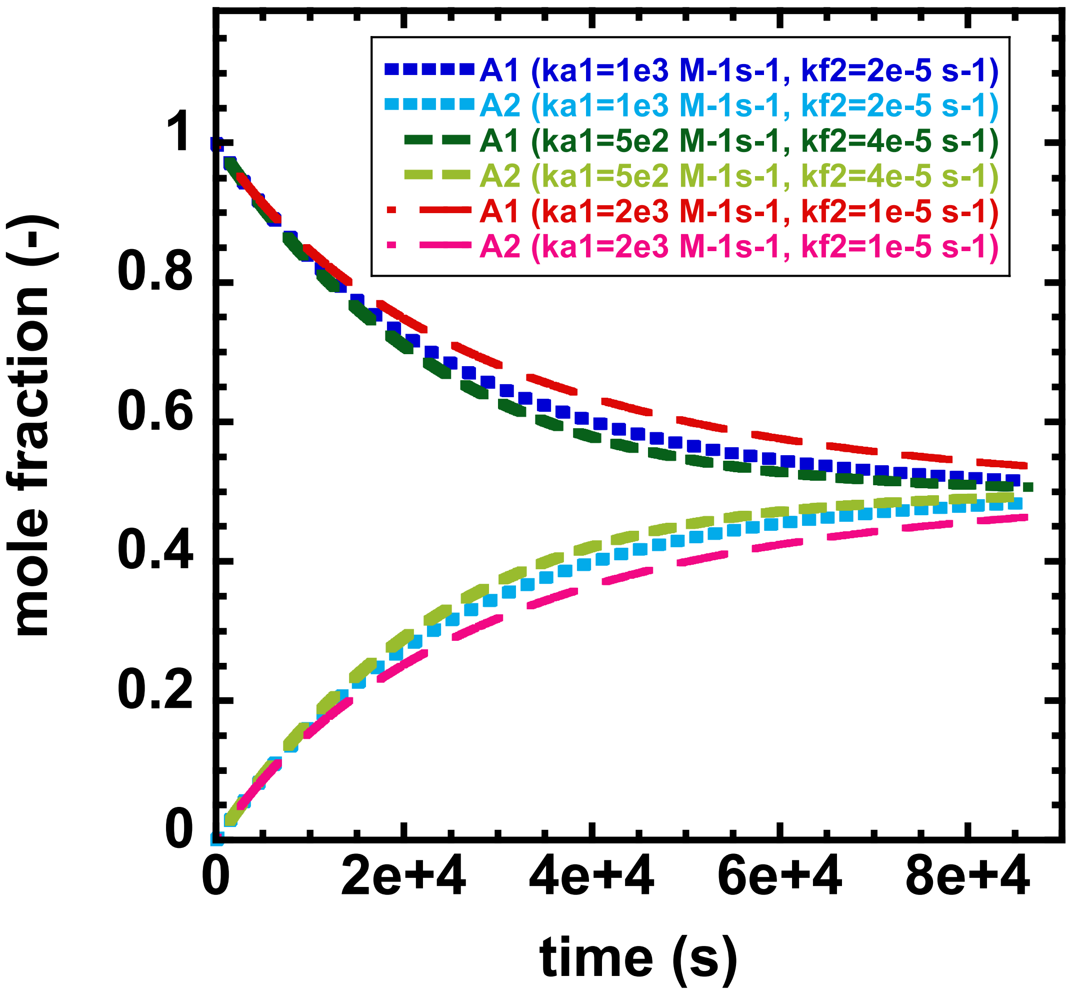


Figure S9: Sensitivity analysis, simultaneous variation of k_{a1} and k_{f2} . Conditions k_{f1}=2e-5 s^{-1}, k_{a2}=1e3 $M^{-1}s^{-1}$, $K_{overall}$= 1. Initial conditions $[A_2]_0=[T_1]_0$ = 0 M, $[A_1]_0=[T_2]_0$=1 M.

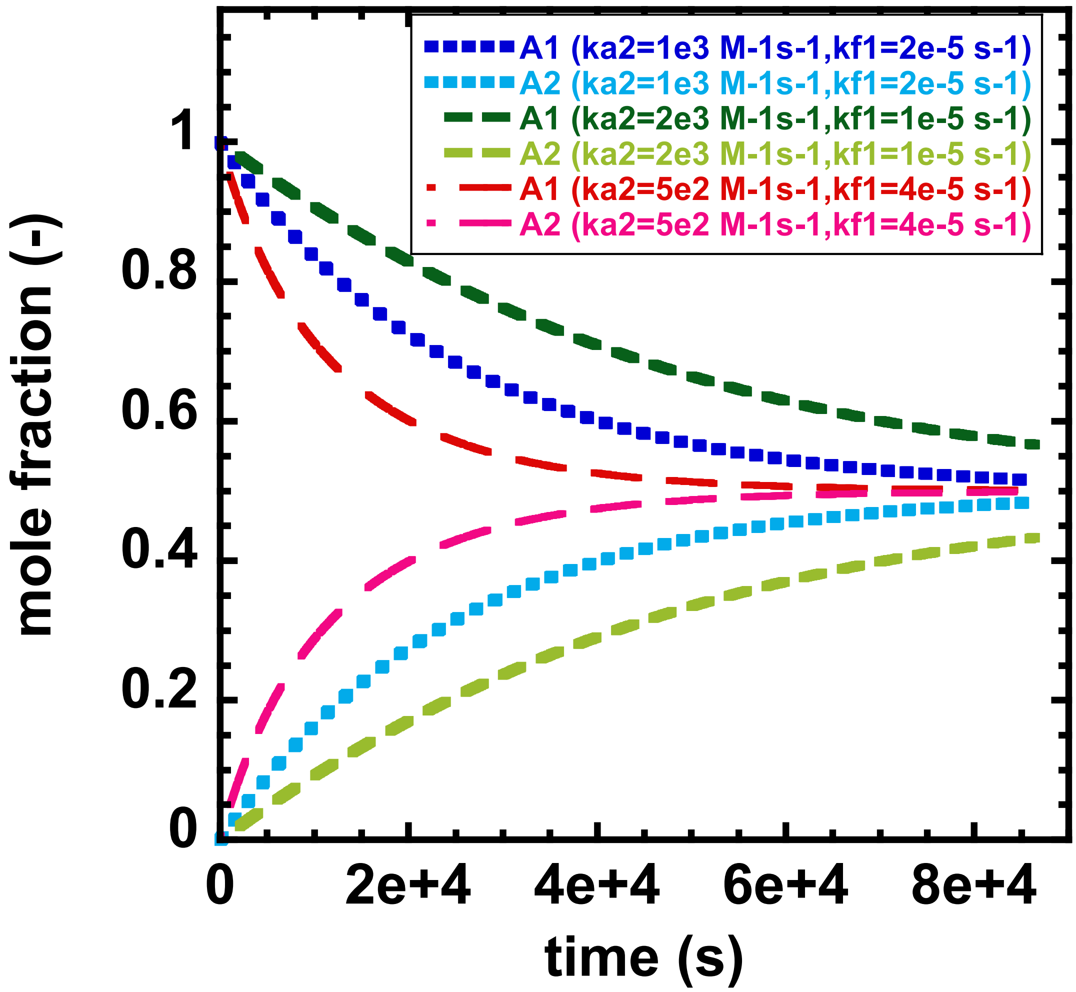


Figure S10: Sensitivity analysis, simultaneous variation of k_{a2} and k_{f1} . Conditions k_{f2}=2e-5 s^{-1}, k_{a1}=1e3 $M^{-1}s^{-1}$, $K_{overall}$= 1. Initial conditions $[A_2]_0=[T_1]_0$ = 0 M, $[A_1]_0=[T_2]_0$=1 M.

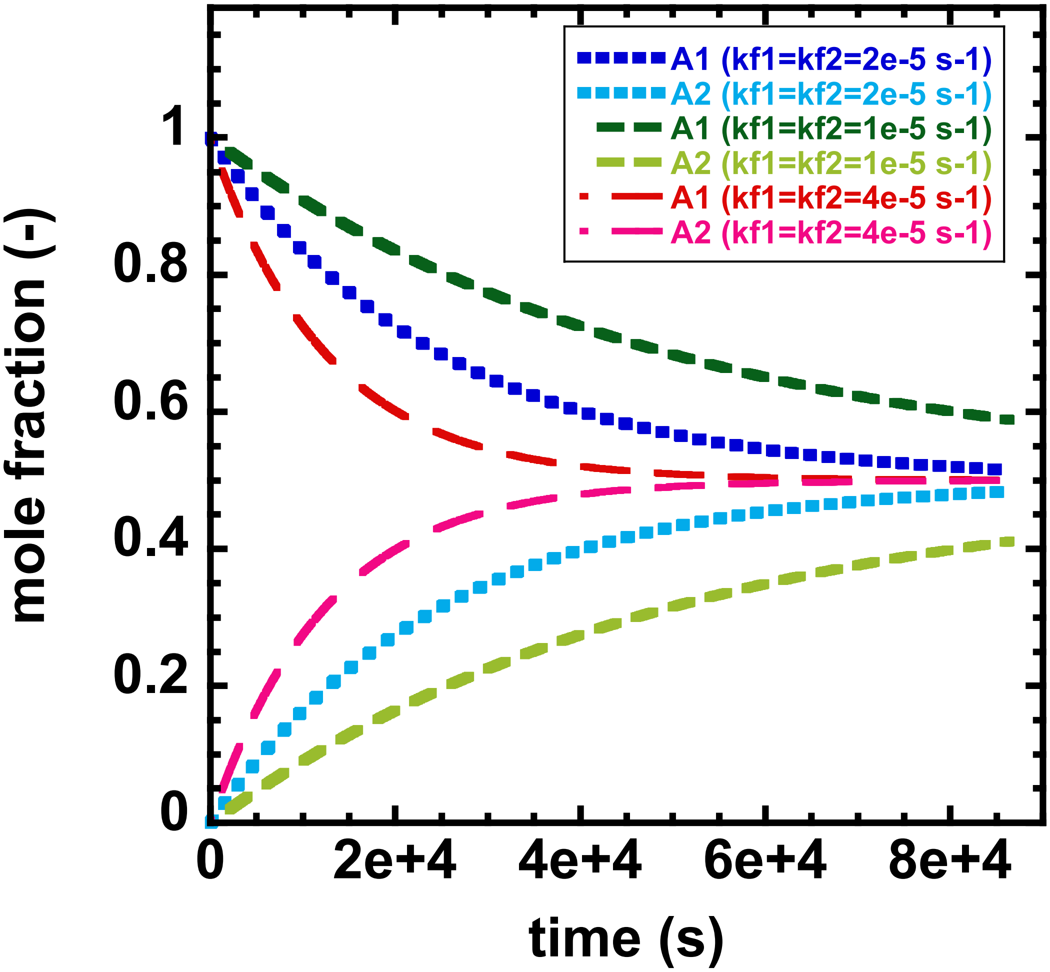


Figure S11: Sensitivity analysis, simultaneous variation of k_{f1} and k_{f2} . Conditions:

k_{a1}=k_{a2}=1e3 $M^{-1}s^{-1}$, $K_{overall}$= 1. Initial conditions $[A_2]_0$=$[T_1]_0$ = 0 M, $[A_1]_0$=$[T_2]_0$ = 1 M.

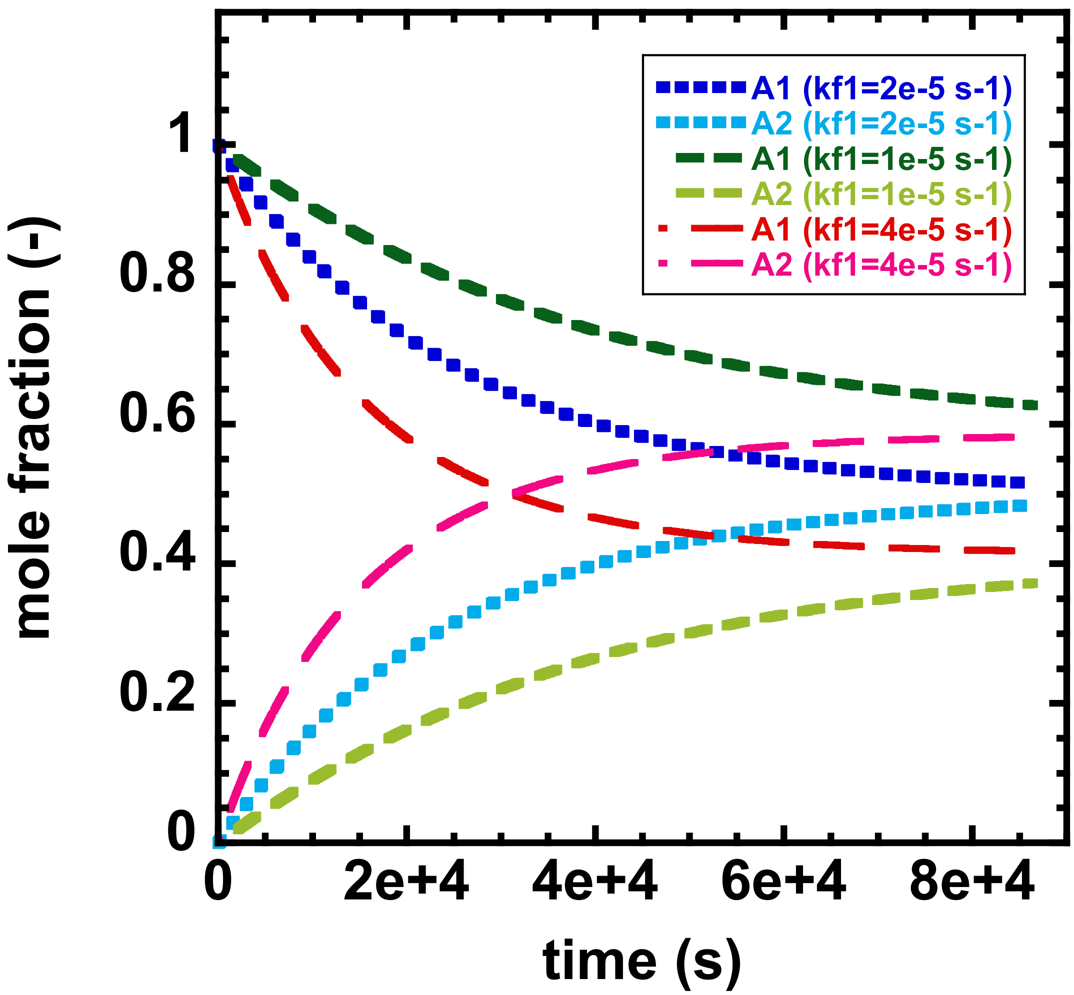


Figure S12: Sensitivity analysis, simultaneous variation of k_{f1} . Conditions:

k_{a1}=k_{a2}=1e3 $M^{-1}s^{-1}$, k_{f2}=2e-5s^{-1}. Initial conditions $[A_2]_0$=$[T_1]_0$ = 0 M, $[A_1]_0$=$[T_2]_0$ = 1 M.

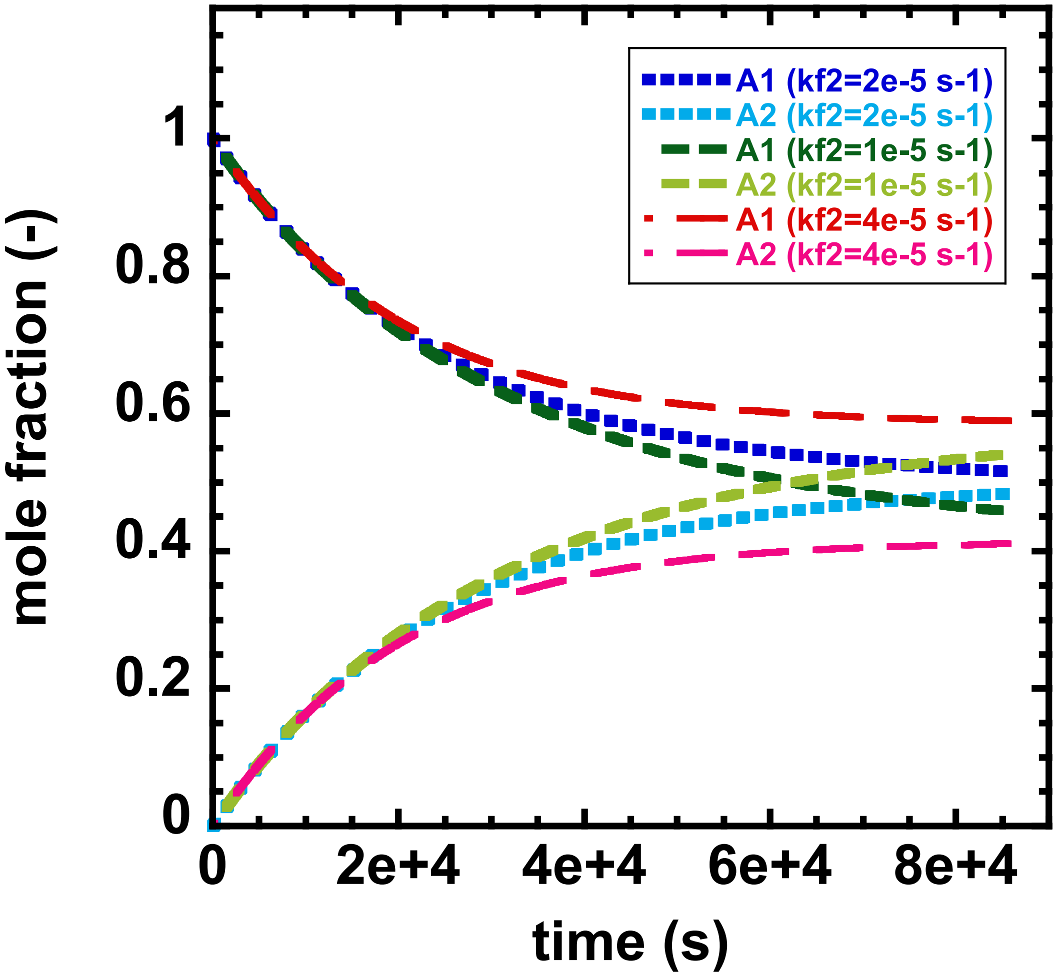


Figure S13: Sensitivity analysis, simultaneous variation of k_{f2} . Conditions:

k_{a1}=k_{a2}=1e3 $M^{-1}s^{-1}$, k_{f1}=2e-5s^{-1}. Initial conditions $[A_2]_0$=$[T_1]_0$ = 0 M, $[A_1]_0$=$[T_2]_0$ = 1 M.