SUPPLEMENTARY INFORMATION

Amplification of enantiomeric excess, mirror-image symmetry breaking and kinetic proofreading in Soai reaction models with different oligomeric orders

Jean-Claude Micheau*[,a], Christophe Coudret[a], José-Manuel Cruz[b] and Thomas Buhse*[,b]

[a)] Laboratoire des IMRCP, UMR au CNRS No. 5623, Université Paul Sabatier, 118, Route de Narbonne, 31062 Toulouse Cedex, France (micheau@chimie.ups-tlse.fr)

[b)] Centro de Investigaciones Químicas, Universidad Autónoma del Estado de Morelos, Avenida Universidad 1001, 62209 Cuernavaca, Morelos, Mexico (buhse@uaem.mx)

1. Implementation of the models

The models M1, M2 and M3 are based on a unique skeleton. The main difference between them is the number of processes that were taken into account. The number of species and processes are 9 and 16 (M1), 14 and 32 (M2), 20 and 48 (M3), respectively (see also Table S4).

1.1 Processes and rates

Uncatalyzed reactions

$A + Z \rightarrow R$	$v0 = k_0[A][Z]$
$A + Z \rightarrow S$	$v1 = k_0[A][Z]$

Monomer activation and de-activation

$R + Z \rightarrow RZ$	$v2 = k_3[R][Z]$
$RZ \rightarrow R + Z$	$v3 = k_4[RZ]$
$S + Z \rightarrow SZ$	$v4 = k_3[S][Z]$
$SZ \rightarrow S + Z$	$v5 = k_4[SZ]$

Dimerization and dimer splitting

$R + R \rightarrow RR$	$v6 = k_1[R][R]$
$RR \rightarrow R + R$	$v7 = k_2[RR]$
$R + S \rightarrow RS$	$v8 = k_1[R][S]$
$RS \rightarrow R + S$	$v9 = p_{RS}k_2[RS]$
$S + S \rightarrow SS$	$v10 = k_1[S][S]$
$SS \rightarrow S + S$	$v11 = k_2[SS]$

with $p_{RS} = exp(-\Delta E_{RS}/RT)$

Dimer activation

$RR + \mathrm{Z} \rightarrow \mathrm{Z}RR$	$\mathrm{v}12 = k_6[RR][\mathrm{Z}]$
$\mathrm{Z}RR \rightarrow RR + \mathrm{Z}$	$\mathrm{v}13 = k_7[\mathrm{Z}RR]$
$RS + \mathrm{Z} \rightarrow \mathrm{Z}RS$	$\mathrm{v}14 = k_6[RS][\mathrm{Z}]$
$\mathrm{Z}RS \rightarrow RS + \mathrm{Z}$	$\mathrm{v}15 = k_7[\mathrm{Z}RS]$
$SS + \mathrm{Z} \rightarrow \mathrm{Z}SS$	$\mathrm{v}16 = k_6[SS][\mathrm{Z}]$
$\mathrm{Z}SS \rightarrow SS + \mathrm{Z}$	$\mathrm{v}17 = k_7[\mathrm{Z}SS]$

Trimerization and trimer splitting

$RR + R \rightarrow RRR$	$\mathrm{v}18 = k_8[RR][R]$
$RRR \rightarrow RR + R$	$\mathrm{v}19 = k_9[RRR]$
$RR + S \rightarrow RRS$	$\mathrm{v}20 = k_8[RR][S]$
$RRS \rightarrow RR + S$	$\mathrm{v}21 = k_9 p_{RS}^2[RRS]$
$RS + R \rightarrow RRS$	$\mathrm{v}22 = k_8[RS][R]$
$RRS \rightarrow RS + R$	$\mathrm{v}23 = k_9 p_{RS}[RRS]$
$RS + S \rightarrow SSR$	$\mathrm{v}24 = k_8[RS][S]$
$SSR \rightarrow RS + S$	$\mathrm{v}25 = k_9 p_{RS}[SSR]$
$SS + R \rightarrow SSR$	$\mathrm{v}26 = k_8[SS][R]$
$SSR \rightarrow SS + R$	$\mathrm{v}27 = k_9 p_{RS}^2[SSR]$
$SS + S \rightarrow SSS$	$\mathrm{v}28 = k_8[SS][S]$
$SSS \rightarrow SS + S$	$\mathrm{v}29 = k_9[SSS]$

Trimer activation

$RRR + \mathrm{Z} \rightarrow \mathrm{Z}RRR$	$\mathrm{v}30 = k_{11}[RRR][\mathrm{Z}]$
$\mathrm{Z}RRR \rightarrow RRR + \mathrm{Z}$	$\mathrm{v}31 = k_{12}[\mathrm{Z}RRR]$
$RRS + \mathrm{Z} \rightarrow \mathrm{Z}RRS$	$\mathrm{v}32 = k_{11}[RRS][\mathrm{Z}]$
$\mathrm{Z}RRS \rightarrow RRS + \mathrm{Z}$	$\mathrm{v}33 = k_{12}[\mathrm{Z}RRS]$
$SSR + \mathrm{Z} \rightarrow \mathrm{Z}SSR$	$\mathrm{v}34 = k_{11}[SSR][\mathrm{Z}]$
$\mathrm{Z}SSR \rightarrow SSR + \mathrm{Z}$	$\mathrm{v}35 = k_{12}[\mathrm{Z}SSR]$
$SSS + \mathrm{Z} \rightarrow \mathrm{Z}SSS$	$\mathrm{v}36 = k_{11}[SSS][\mathrm{Z}]$
$\mathrm{Z}SSS \rightarrow SSS + \mathrm{Z}$	$\mathrm{v}37 = k_{12}[\mathrm{Z}SSS]$

Monomer catalysis

$\mathrm{A} + R\mathrm{Z} \rightarrow RR$	$\mathrm{v}38 = [(1+ p_{st})/2]k_5[\mathrm{A}][R\mathrm{Z}]$
$\mathrm{A} + R\mathrm{Z} \rightarrow RS$	$\mathrm{v}39 = [(1- p_{st})/2]k_5[\mathrm{A}][R\mathrm{Z}]$
$\mathrm{A} + S\mathrm{Z} \rightarrow SS$	$\mathrm{v}40 = [(1+ p_{st})/2]k_5[\mathrm{A}][S\mathrm{Z}]$
$\mathrm{A} + S\mathrm{Z} \rightarrow RS$	$\mathrm{v}41 = [(1- p_{st})/2]k_5[\mathrm{A}][S\mathrm{Z}]$

with $p_{st} = 1 - exp(-\Delta E_a/RT)$

Dimer catalysis

$\mathrm{A} + \mathrm{Z}R2 \rightarrow RRR$	$\mathrm{v}42 = [(1+ p_{st})/2]k_{10}[\mathrm{A}][\mathrm{Z}RR]$
$\mathrm{A} + \mathrm{Z}RR \rightarrow RRS$	$\mathrm{v}43 = [(1- p_{st})/2]k_{10}[\mathrm{A}][\mathrm{Z}RR]$
$\mathrm{A} + \mathrm{Z}RS \rightarrow RRS$	$\mathrm{v}44 = k_{10}[\mathrm{A}][\mathrm{Z}RS]$
$\mathrm{A} + \mathrm{Z}RS \rightarrow SSR$	$\mathrm{v}45 = k_{10}[\mathrm{A}][\mathrm{Z}RS]$

$\mathrm{A} + \mathrm{Z}SS \rightarrow SSS$	$\mathrm{v46} = [(1+p_{st})/2]k_{10}[\mathrm{A}][\mathrm{Z}SS]$
$\mathrm{A} + \mathrm{Z}SS \rightarrow SSR$	$\mathrm{v47} = [(1-p_{st})/2]k_{10}[\mathrm{A}][\mathrm{Z}SS]$

Trimer catalysis

$\mathrm{A} + \mathrm{Z}RRR \rightarrow RRRR$	$\mathrm{v48} = [(1+p_{st})/2]k_{13}[\mathrm{A}][\mathrm{Z}RRR]$
$\mathrm{A} + \mathrm{Z}RRR \rightarrow RRRS$	$\mathrm{v49} = [(1-p_{st})/2]k_{13}[\mathrm{A}][\mathrm{Z}RRR]$
$\mathrm{A} + \mathrm{Z}RRS \rightarrow RRRS$	$\mathrm{v50} = [(1+p_{st})/2]k_{13}p_{RS}[\mathrm{A}][\mathrm{Z}RRS]$
$\mathrm{A} + \mathrm{Z}RRS \rightarrow RRSS$	$\mathrm{v51} = [(1-p_{st})/2]k_{13}p_{RS}[\mathrm{A}][\mathrm{Z}RRS]$
$\mathrm{A} + \mathrm{Z}SSR \rightarrow SSSR$	$\mathrm{v52} = [(1+p_{st})/2]k_{13}p_{RS}[\mathrm{A}][\mathrm{Z}SSR]$
$\mathrm{A} + \mathrm{Z}SSR \rightarrow RRSS$	$\mathrm{v53} = [(1-p_{st})/2]k_{13}p_{RS}[\mathrm{A}][\mathrm{Z}SSR]$
$\mathrm{A} + \mathrm{Z}SSS \rightarrow SSSS$	$\mathrm{v54} = [(1+p_{st})/2]k_{13}[\mathrm{A}][\mathrm{Z}SSS]$
$\mathrm{A} + \mathrm{Z}SSS \rightarrow SSSR$	$\mathrm{v55} = [(1-p_{st})/2]k_{13}[\mathrm{A}][\mathrm{Z}SSS]$

Tetramer splitting to dimers

$RRRR \rightarrow RR + RR$	$\mathrm{v56} = k_{14}[RRRR]$
$RR + RR \rightarrow RRRR$	$\mathrm{v57} = k_{15}[RR][RR]$
$RRRS \rightarrow RR + RS$	$\mathrm{v58} = k_{14}p_{RS}[RRRS]$
$RR + RS \rightarrow RRRS$	$\mathrm{v59} = k_{15}[RR][RS]$
$RRSS \rightarrow RS + RS$	$\mathrm{v60} = k_{14}p_{RS}[RRSS]$
$RS + RS \rightarrow RRSS$	$\mathrm{v61} = k_{15}[RS][RS]$
$RRSS \rightarrow RR + SS$	$\mathrm{v62} = k_{14}p_{RS}^{\,3}[RRSS]$
$RR + SS \rightarrow RRSS$	$\mathrm{v63} = k_{15}[RR][SS]$
$SSSR \rightarrow SS + RS$	$\mathrm{v64} = k_{14}p_{RS}[SSSR]$
$SS + RS \rightarrow SSSR$	$\mathrm{v65} = k_{15}[SS][RS]$
$SSSS \rightarrow SS + SS$	$\mathrm{v66} = k_{14}[SSSS]$
$SS + SS \rightarrow SSSS$	$\mathrm{v67} = k_{15}[SS][SS]$

1.2 Differential equations

$\mathrm{d[A]/dt} = -\mathrm{v0} - \mathrm{v1} - \mathrm{v38} - \mathrm{v39} - \mathrm{v40} - \mathrm{v41} - \mathrm{v42} - \mathrm{v43} - \mathrm{v44} - \mathrm{v45} - \mathrm{v46} - \mathrm{v47} - \mathrm{v48} - \mathrm{v49} - \mathrm{v50} - \mathrm{v51} - \mathrm{v52} - \mathrm{v53} - \mathrm{v54} - \mathrm{v55};$

$\mathrm{d[Z]/dt} = -\mathrm{v0} - \mathrm{v1} - \mathrm{v2} + \mathrm{v3} - \mathrm{v4} + \mathrm{v5} - \mathrm{v12} + \mathrm{v13} - \mathrm{v14} + \mathrm{v15} - \mathrm{v16} + \mathrm{v17} - \mathrm{v30} + \mathrm{v31} - \mathrm{v32} + \mathrm{v33} - \mathrm{v34} + \mathrm{v35} - \mathrm{v36} + \mathrm{v37};$

$\mathrm{d}[R]/\mathrm{dt} = \mathrm{v0} - \mathrm{v2} + \mathrm{v3} - 2{*}\mathrm{v6} + 2{*}\mathrm{v7} - \mathrm{v8} + \mathrm{v9} - \mathrm{v18} + \mathrm{v19} - \mathrm{v22} + \mathrm{v23} - \mathrm{v26} + \mathrm{v27};$

$\mathrm{d}[S]/\mathrm{dt} = \mathrm{v1} - \mathrm{v4} + \mathrm{v5} - \mathrm{v8} + \mathrm{v9} - 2{*}\mathrm{v10} + 2{*}\mathrm{v11} - \mathrm{v20} + \mathrm{v21} - \mathrm{v24} + \mathrm{v25} - \mathrm{v28} + \mathrm{v29};$

$\mathrm{d}[R\mathrm{Z}]/\mathrm{dt} = \mathrm{v2} - \mathrm{v3} - \mathrm{v38} - \mathrm{v39};$

$\mathrm{d}[S\mathrm{Z}]/\mathrm{dt} = \mathrm{v4} - \mathrm{v5} - \mathrm{v40} - \mathrm{v41};$

$\mathrm{d}[RR]/\mathrm{dt} = \mathrm{v6} - \mathrm{v7} - \mathrm{v12} + \mathrm{v13} - \mathrm{v18} + \mathrm{v19} - \mathrm{v20} + \mathrm{v21} + \mathrm{v38} + 2{*}\mathrm{v56} - 2{*}\mathrm{v57} + \mathrm{v58} - \mathrm{v59} + \mathrm{v62} - \mathrm{v63};$

$\mathrm{d}[RS]/\mathrm{dt} = \mathrm{v8} - \mathrm{v9} - \mathrm{v14} + \mathrm{v15} - \mathrm{v22} + \mathrm{v23} - \mathrm{v24} + \mathrm{v25} + \mathrm{v39} + \mathrm{v41} + \mathrm{v58} - \mathrm{v59} + 2{*}\mathrm{v60} - 2{*}\mathrm{v61} + \mathrm{v64} - \mathrm{v65};$

$\mathrm{d}[SS]/\mathrm{dt} = \mathrm{v10} - \mathrm{v11} - \mathrm{v16} + \mathrm{v17} - \mathrm{v26} + \mathrm{v27} - \mathrm{v28} + \mathrm{v29} + \mathrm{v40} + \mathrm{v62} - \mathrm{v63} + \mathrm{v64} - \mathrm{v65} + 2{*}\mathrm{v66} - 2{*}\mathrm{v67};$

$\mathrm{d}[\mathrm{Z}RR]/\mathrm{dt} = \mathrm{v12} - \mathrm{v13} - \mathrm{v42} - \mathrm{v43};$

$\mathrm{d}[\mathrm{Z}RS]/\mathrm{dt} = \mathrm{v14} - \mathrm{v15} - \mathrm{v44} - \mathrm{v45};$

$\mathrm{d}[\mathrm{Z}SS]/\mathrm{dt} = \mathrm{v16} - \mathrm{v17} - \mathrm{v46} - \mathrm{v47};$

$\mathrm{d}[RRR]/\mathrm{dt} = \mathrm{v18} - \mathrm{v19} - \mathrm{v30} + \mathrm{v31} + \mathrm{v42};$

$\mathrm{d}[RRS]/\mathrm{dt} = \mathrm{v20} - \mathrm{v21} + \mathrm{v22} - \mathrm{v23} - \mathrm{v32} + \mathrm{v33} + \mathrm{v43} + \mathrm{v44};$

$\mathrm{d}[SSR]/\mathrm{dt} = \mathrm{v24} - \mathrm{v25} + \mathrm{v26} - \mathrm{v27} - \mathrm{v34} + \mathrm{v35} + \mathrm{v45} + \mathrm{v47};$

$\mathrm{d}[SSS]/\mathrm{d}t = \mathrm{v}28 - \mathrm{v}29 - \mathrm{v}36 + \mathrm{v}37 + \mathrm{v}46$;

$\mathrm{d}[\mathrm{Z}RRR]/\mathrm{d}t = \mathrm{v}30 - \mathrm{v}31 - \mathrm{v}48 - \mathrm{v}49$;

$\mathrm{d}[\mathrm{Z}RRS]/\mathrm{d}t = \mathrm{v}32 - \mathrm{v}33 - \mathrm{v}50 - \mathrm{v}51$;

$\mathrm{d}[\mathrm{Z}SSR]/\mathrm{d}t = \mathrm{v}34 - \mathrm{v}35 - \mathrm{v}52 - \mathrm{v}53$;

$\mathrm{d}[\mathrm{Z}SSS]/\mathrm{d}t = \mathrm{v}36 - \mathrm{v}37 - \mathrm{v}54 - \mathrm{v}55$;

$\mathrm{d}[RRRR]/\mathrm{d}t = \mathrm{v}48 - \mathrm{v}56 + \mathrm{v}57$;

$\mathrm{d}[RRRS]/\mathrm{d}t = \mathrm{v}49 + \mathrm{v}50 - \mathrm{v}58 + \mathrm{v}59$;

$\mathrm{d}[RRSS]/\mathrm{d}t = \mathrm{v}51 + \mathrm{v}53 - \mathrm{v}60 + \mathrm{v}61 - \mathrm{v}62 + \mathrm{v}63$;

$\mathrm{d}[SSSR]/\mathrm{d}t = \mathrm{v}52 + \mathrm{v}55 - \mathrm{v}64 + \mathrm{v}65$;

$\mathrm{d}[SSSS]/\mathrm{d}t = \mathrm{v}54 - \mathrm{v}66 + \mathrm{v}67$;

1.3 Calculation of the enantiomeric excess (*ee*)

Total optical rotation = $([R] + [R\mathrm{Z}] + 2[RR] + 2[\mathrm{Z}RR] + 3[RRR] + [RRS] + 3[\mathrm{Z}RRR] + [\mathrm{Z}RRS] + 4[RRRR] + 2[RRRS]) - ([S] + [S\mathrm{Z}] + 2[SS] + 2[\mathrm{Z}SS] + [SSR] + 3[SSS] + [\mathrm{Z}SSR] + 3[\mathrm{Z}SSS] + 2[SSSR] + 4[SSSS])$

Total chiral matter = $[R] + [R\mathrm{Z}] + 2[RR] + 2[RS] + 2[\mathrm{Z}RR] + 2[\mathrm{Z}RS] + 3[RRR] + 3[RRS] + 3[\mathrm{Z}RRR] + 3[\mathrm{Z}RRS] + 4[RRRR] + 4[RRRS] + 4[RRSS] + [S] + [S\mathrm{Z}] + 2[SS] + 2[\mathrm{Z}SS] + 3[SSR] + 3[SSS] + 3[\mathrm{Z}SSR] + 3[\mathrm{Z}SSS] + 4[SSSR] + 4[SSSS]$

ee (absolute value) = $|\,\textit{Total optical rotation}\,| \,/\, \textit{Total chiral matter}$

2. Correspondence between models M1, M2 and M3 and kinetic parameters

Table S1. List of processes with their rate constants as used in models M1, M2 and M3.

a) homochiral side (here shown only as the "R-side, the term "right" is reserved to the stereospecific self-reproduction of "R").

process name	process	M1	M2	M3	notes
non catal. react.	$\mathrm{A} + \mathrm{Z} \rightarrow R$ or S	k_0	k_0	k_0	
monomer activ.	$R + \mathrm{Z} \rightarrow RZ$	k_3	0	0	
monomer deactiv.	$RZ \rightarrow R + \mathrm{Z}$	k_4	0	0	
dimerization	$R + R \rightarrow RR$	k_1	k_1	k_1	
dimer split.	$RR \rightarrow R + R$	k_2	k_2	k_2	
dimer activ.	$RR + \mathrm{Z} \rightarrow ZRR$	0	k_6	0	
dimer deactiv.	$ZRR \rightarrow RR + \mathrm{Z}$	0	k_7	0	
trimerization	$RR + R \rightarrow RRR$	0	k_8	k_8	
trimer split.	$RRR \rightarrow RR + R$	0	k_9	k_9	
trimer activ.	$RRR + \mathrm{Z} \rightarrow ZRRR$	0	0	k_{11}	
trimer deactiv.	$ZRRR \rightarrow \mathrm{Z} + RRR$	0	0	k_{12}	
monomer catalysis (right)	$\mathrm{A} + RZ \rightarrow RR$	$[(1+p_{ST})/2]k_5$	0	0	*(1)*
dimer catal.	$\mathrm{A} + ZRR \rightarrow RRR$	0	k_{10}	0	
trimer. catal.	$\mathrm{A} + ZRRR \rightarrow RRRR$	0	0	k_{13}	
tetramer split. (sym.)	$RRRR \rightarrow RR + RR$	0	0	k_{14}	
tetramerization (sym)	$RR + RR \rightarrow RRRR$	0	0	k_{15}	

b)- heterochiral processes. *(the term "wrong" is reserved to the self-reproduction with inversion of configuration i.e. when "R" gives "S"; S-rich heterooligomers are not shown).*

process name	process	M1	M2	M3	notes
dimerization	$R + S \rightarrow RS$	k_1	k_1	k_1	
dimer splitting	$RS \rightarrow R + S$	$p_{RS}k_2$	$p_{RS}k_2$	$p_{RS}k_2$	(2)
dimer activ.	$RS + \mathrm{Z} \rightarrow ZRS$	0	k_6	0	
dimer deactiv.	$ZRS \rightarrow RS + \mathrm{Z}$	0	k_7	0	
trimerization	$RS + R \rightarrow RSR$	0	k_8	k_8	
trimer split (hetero)	$RSR \rightarrow RS + R$	0	$p_{RS}k_9$	$p_{RS}k_9$	(3)
trimer split.(homo)	$RSR \rightarrow RR+S$	0	$p_{RS}{}^2k_9$	$p_{RS}{}^2k_9$	(4)
trimer activ.	$RSR + \mathrm{Z} \rightarrow ZRSR$	0	0	k_{11}	
trimer deactiv.	$ZRSR \rightarrow \mathrm{Z} + RSR$	0	0	k_{12}	
monom. cat. (wrong)	$\mathrm{A} + RZ \rightarrow RS$	$[(1-p_{ST})/2]k_5$	0	0	(5)
dimer cat. (wrong)	$\mathrm{A}+ZRR \rightarrow RSR$	*0*	$[(1-p_{ST})/2]k_{10}$	0	(6)
dimer cat. (hetero)	$\mathrm{A} + ZRS \rightarrow RSR$	0	k_{10}	0	
trimer cat. (wrong)	$\mathrm{A}+ZRRR \rightarrow RRRS$	0	0	$[(1-p_{ST})/2]k_{13}$	(7)
trimer cat. (hetero-right)	$\mathrm{A}+ZRSR \rightarrow RRRS$	0	0	$[(1+p_{ST})/2]p_{RS}k_{13}$	(8)
trimer cat. (hetero-wrong)	$\mathrm{A}+ZRSR \rightarrow RSRS$	0	0	$[(1-p_{ST})/2]p_{RS}k_{13}$	(9)
tetram. split. (hetero)	$RRRS \rightarrow RR + RS$	0	0	$p_{RS}{}^nk_{14}$	(10)
tetramerization	$RR + RS \rightarrow RRRS$	0	0	k_{15}	
tetram. split. (meso-hetero)	$RRSS \rightarrow RS + RS$	0	0	$p_{RS}{}^pk_{14}$	(11)
tetramerization	$RS + RS \rightarrow RRSS$	0	0	k_{15}	
tetram. split. (meso-homo)	$RRSS \rightarrow RR + SS$	0	0	$p_{RS}{}^qk_{14}$	(12)
tetramerization	$RR + RS \rightarrow RRRS$	0	0	k_{15}	

Notes:

(1): As $p_{st} = 1 - \exp(-\Delta E_a/RT)$*, the rate of the right process is proportional to* $[1 - 0.5^* \exp(-\Delta E_a/RT)]$*. Wrong processes are shown in notes (5) to (7), their rates are proportional to* $[0.5^* \exp(-\Delta E_a/RT)]$*. Classical calculation of % stereoselectivity under the form of (100-X)/X corresponds to* $X = 50^*\exp(-\Delta E_a/RT)$*. For instance, a 80:20 stereoselectivity corresponds to* $X = 20$ *i.e. to* $\Delta E_a/RT = 0.92$ *or* $\Delta E_a = 0.55$ *Kcal/mol at 300K;*

(2): $p_{RS} = \exp(-\Delta E_{RS}/RT)$*; stability parameter of the heterodimer, if pRS <1, i.e.* $\Delta E_{RS} > 0$*, the hetero-dimer is more stable than the homo-dimer;*

(3): As shown on scheme 4d, there is one RS splitting, hence the exponent of p_{RS} *is 1;*

(4): As shown on scheme 4c, there is two RS splittings, hence the exponent of p_{RS} *is 2;*

(5), (6) and (7): processes corresponding to the wrong selectivity i.e. the configuration of the newly synthesized chiral center is inverse, (see note (1);

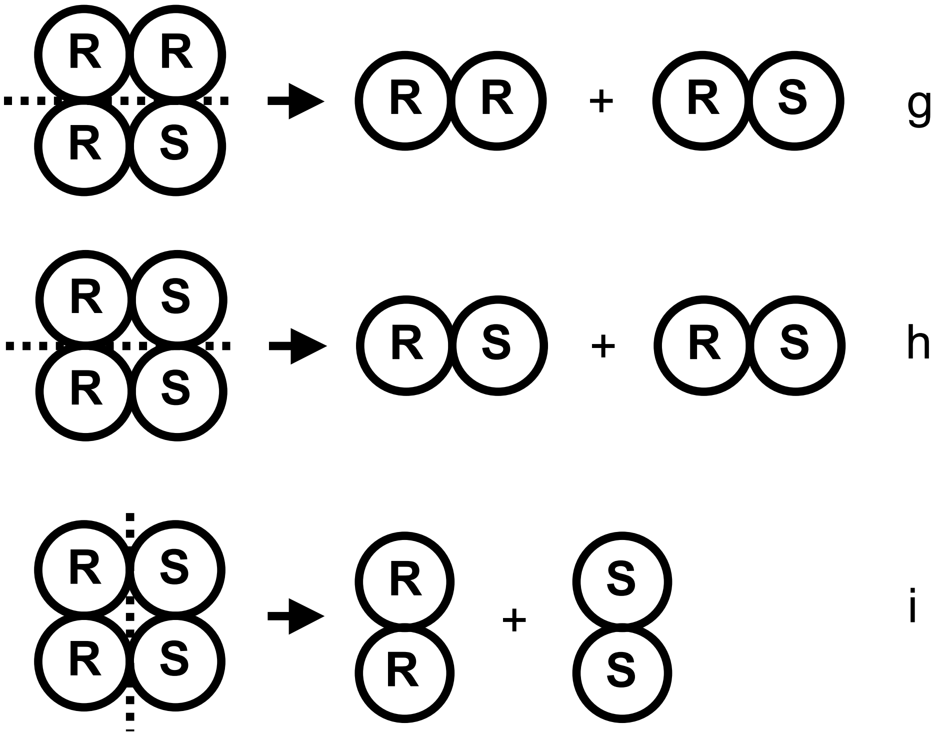
(8), (9): factor p_{RS} *takes into account the higher stability of the heterotrimers;*

(10): exponent "n" depends on geometry of the assumed tetramer, n= 2 if tetrahedral, n= 1 if planar (see scheme S1);

(11): exponent "p" depends on geometry of the assumed tetramer, n= 2 if tetrahedral, n= 0 or 2 if planar (see scheme S1);

(12): exponent "q" depends on geometry of the assumed tetramer, n= 4 if tetrahedral, n = 2 if planar (see scheme S1);

3. Details of RS splittings in planar tetramers



Scheme S1. Competitive planar hetero-tetramer R$_3$S splitting showing 1 R—S split in (g) (dashed bold lines). Meso-tetramer R$_2$S$_2$ splitting exhibiting 0 RS split in (h) and two and 2 R-S splits (dashed bold lines) in (i).

4. Generation of random parameter values for the exploration of model M1

4.1. M1 model parameters

Order of magnitude of parameter values were chosen randomly within Table S1 (order of magnitude = average ± 4). Average values have been selected to give rise to a slight chiral attenuation (from *ee* = 0.44 to *ee* = 0.42), i.e. neither MISB nor chiral amplification.

Table S2. List of parameters used in model M1 and their range of variation. Otherwise mentioned, the parameter values are shown from their exponents, i.e. 10^{m} is displayed as “m”.

name of the parameter	symbol	average value	range
non-catalytic step	k_0	-7	-11 to -3
activation	k_3	4	0 to +8
de-activation	k_4	-2	-6 to +3
dimerization	k_1	+5	+1 to +9
dimer split	k_2	+1	-3 to +5
catalytic step	k_5	3	-1 to +7
ΔE_{RS} (kcal/mol)	-	5	0 to 9
ΔE_a (kcal/mol)	-	2.5	0.5 to 4.5

4.2. Variation of the parameters

The various parameters have been varied using the following way:
A random number ranging between 1 and 9 is generated then the corresponding order of magnitude from 10^{-4} to 10^{+4} is used to shift the average value of the parameter to be varied according to Table S2.

Table S3. Correspondence between the generated random numbers (from 1 to 9) and the parameter variations within eight orders of magnitude.

random number	1	2	3	4	5	6	7	8	9
order of magnitude by which the parameters will be varied	-4	-3	-2	-1	0	+1	+2	+3	+4

4.3 Numerical simulations of model M1 using randomly generated parameters

The procedure is repeated for each M1 parameter. Table S3 gathers all 40 randomly generated runs and their corresponding outputs.

Table S4. Randomly generated runs of M1. ee amplification (amplif) was tested after initial addition of 0.5% of optically active carbinols (ee_0 = 0.44). MISB is occurring without any additive.

run		**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
non-cat.	k_0	-8	-6	-10	-11	-10	-3	-3	-8	-8	-7
activation	k_3	+3	0	+6	-1	0	+8	-1	0	-1	+3
de-activation	k_4	-3	-4	0	-6	-4	-4	+1	0	-6	-2
dimerization	k_1	+3	+4	+2	+9	+2	+8	+3	+9	+8	+5
dimer split	k_2	0	+2	+2	+3	+5	+2	+3	-1	+2	+2
catal. step	k_5	0	+2	+1	+5	+1	+3	+7	+1	+6	+4
ΔE_{RS} (kcal/mol)		1	9	6	6	2	7	4	5	9	2
ΔE_a (kcal/mol)		3	3.5	4	1	.5	1	4.5	2	.5	4
amplif		no	yes	no	yes	no	no	no	yes	no	yes
MISB		no	yes	no	yes	no	no	no	yes	yes	no
half-time (cat.)		34.6	32.6	2.73	27000	17.3	0.10	910	3.9e+5	3.5e+4	0.12
half-time (no cat.)		113	144	12.4	31000	73.8	0.23	910	4.4e+5	4.4e+7	0.35

run		**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**
non-catal.	k_0	-2	-8	-4	-5	-5	-10	-10	-7	-6	-5
activation	k_3	+8	+1	+8	+3	+6	+1	+6	+6	+2	+1
de-activat.	k_4	-3	+1	+2	+1	-3	+1	+3	-1	-2	-3
dimerization	k_1	0	0	+6	+8	0	+4	+8	+8	+5	+4
dimer split	k_2	+4	+1	-2	+6	0	-3	-3	+4	+4	+6
catal. step	k_5	-1	-2	+5	+4	-2	-2	+5	-2	+6	+2
ΔE_{RS} (kcal/mol)		4.1	2.8	5.5	2.8	8.3	5.5	2.8	9.7	2.8	9.7
ΔE_a (kcal/mol)		0.3	0.7	2.3	2.3	4.7	4.7	0.7	.97	4.7	2.3
amplif		no	no	no	yes	no	yes	no	no	yes	yes
MISB		no	no	no	no	no	yes	no	no	no	no
half-time (cat.)		61	10000	309	0.097	2350	4.6e+6	5400	2700	0.18	2
half-time (no cat.)		192	21000	356	0.17	2770	3.5e+7	20000	5200	0.73	17

run		**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**	**29**	**30**
non-catal.	k_0	-9	-5	-8	-9	-5	-7	-9	-9	-11	-10
activation	k_3	+6	+5	+6	+7	+2	+4	+5	+1	+1	0
de-activat.	k_4	+1	0	+1	-3	+3	-3	-3	+2	-6	-3
dimerization	k_1	+7	+8	+6	+4	+9	2	+1	+2	+2	+9
dimer split	k_2	+5	+6	+5	+3	+5	2	-1	+1	-3	-3
catal. step	k_5	+1	+2	+5	0	+2	0	+3	+1	+2	+2
ΔE_{RS} (kcal/mol)		5.5	8.3	9.7	6.9	6.9	0	0	6.9	8.3	1.4
ΔE_a (kcal/mol)		4.7	0.3	1.7	1.9	4.7	3.1	3.1	2.3	3.7	2.3
amplif		yes	no	no	no	yes	no	no	yes	no	yes
MISB		no	no	no	no	yes	no	no	yes	no	no
half-time (catal.)		2.64	0.53	3.8e-4	27.2	154	26.5	39.2	113	3920	2.3e+6
half-tim (no cat.)		18.4	1.45	2.1e-3	100	220	73.8	174	845	17000	4.2e+6

Table S4 (continued).

run		**31**	**32**	**33**	**34**	**35**	**36**	**37**	**38**	**39**	**40**
non-catal.	k_0	-6	-7	-6	-8	-4	-5	-3	-2	-4	-11
activation	k_3	+5	+6	-1	6	-1	+4	+6	+4	+4	+1
de-activat.	k_4	+3	-2	-4	-5	-6	-1	-1	-2	-6	0
dimerization	k_1	+7	0	+7	7	+3	+3	+3	+9	+5	+1
dimer split	k_2	0	+2	+2	-3	+1	0	+2	+3	-1	+5
catal. step	k_5	+4	+3	+5	3	-1	0	+1	+6	-2	-1
ΔE_{RS} (Kcal/mol)		0	0	5.5	8.3	5.5	9.7	9.7	5.5	8.3	4.1
ΔE_a (Kcal/mol)		4.7	1.9	1.1	1.9	1.7	1.9	1.9	1.1	1.7	3.7
amplif		no	no	yes	no	yes	yes	no	yes	no	no
MISB		no	no	yes	no	yes	no	no	yes	no	no
half-time (catal.)		4	8.2e-2	3.9e+5	4.1e+3	700	35.3	2.77	0.25	1620	1050
half-tim (no cat.)		12.7	3.5e-1	4.4e+5	1.1e+4	4300	66.7	4.15	0.46	1700	1350

4. Definition of other parameters

Table S5. Relationship at 300K between the diatereoisomeric energy difference ΔE_{RS} (in kcal/mol) and the diastereoisomeric parameter p_{RS}.

ΔE_{RS}	p_{RS}
0.50000	4.35e-01
1.0000	1.89e-01
1.5000	8.21e-02
2.0000	3.57e-02
3.0000	6.74e-03
4.0000	1.27e-03
5.0000	2.40e-04
6.0000	4.54e-05
7.0000	8.57e-06
8.0000	1.62e-06
9.0000	3.06e-07

Table S6. Relationship between the activation energy difference ΔE_a (in kcal/mol), the stereoselectivity p_{st} *and the stereoselectivity ”s”*.

ΔE_a	p_{st}	*s*
0.0000	0.00000	50/50
0.25	0.341	67/33
0.50000	0.565	78/22
1.0000	0.811	91/9
1.5000	0.918	96/4
2.0000	0.964	98/2
3.0000	0.993	99/1
4.0000	0.999	99.9/0.1
4.5	0.9995	99.97/0.03

5. Generation of a typical MISB scenario using M2

A typical MISB *ee* vs. time step-like curve has been generated using model M2 provided with the arbitrarily chosen parameters given in Figure S1.

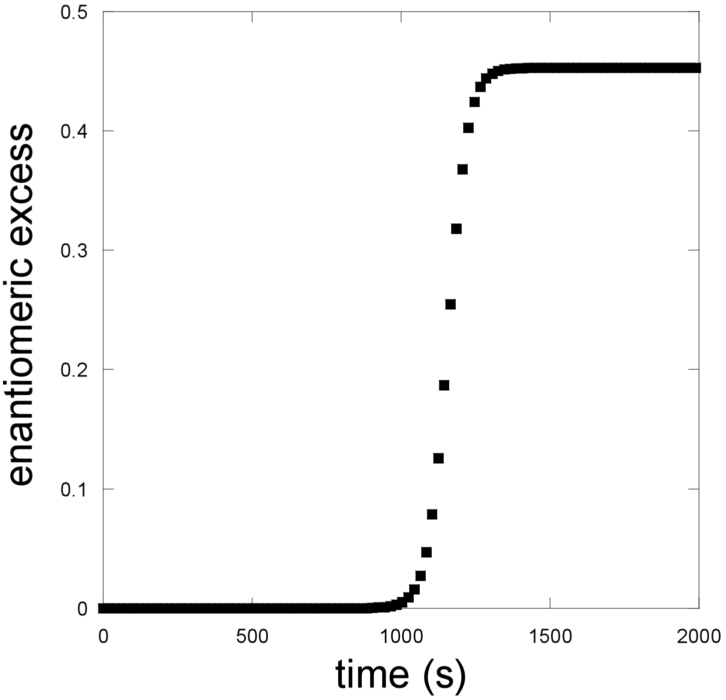


Figure S1. Step-like evolution of the *ee* after MISB in model M2. $[A]_0 = 0.2$ M; $[Z]_0 = 0.4$ M; $[R]_0 = 7.22e\text{-}4$; $[S]_0 = 2.78e\text{-}4$; $k_0 = 1.0e\text{-}03$; $k_1 = 7.3e{+}04$; $k_2 = 4.6e{+}02$; $k_6 = 7.7e{+}01$; $k_7 = 1.2e\text{-}05$; $k_8 = 5.0e{+}00$; $k_9 = 9.8e{+}00$; $k_{10} = 6.8e\text{-}01$; $\Delta E_{RS} = 4.1$; $\Delta E_a = 3.7$ kcal/mol.

6. Fitting of the step-like evolution curve using models M1, M2 and M3

6.1 Example of adjusted parameters for the reproduction of the step-like diagram

Table S7 shows some examples of optimized parameters set that are able to reproduce the step-like evolution of the *ee* with the models M1, M2 or M3.

Table S7. Examples of model parameters giving rise to an *ee* evolution fitting the step-like diagram. To limit the calculation instabilities, an infinitesimal amount of catalyst ($[R]_0$ = 1e-20 M) has been added for the M2 and M3 simulations.

process name	const.	process	M1	M2	M3
non catal. react.	k_0	$\mathrm{A} + \mathrm{Z} \rightarrow R$ or S	1.28e-6	3.81e-4	5.48e-6
monomer activ.	k_3	$R + \mathrm{Z} \rightarrow RZ$	4.76	0	0
monomer deactiv.	k_4	$RZ \rightarrow R + \mathrm{Z}$	1.54e-2	0	0
dimerization	k_1	$R + R \rightarrow RR$	2.48e+4	2.39e+3	9.87e+4
dimer split.	k_2	$RR \rightarrow R + R$	1.67e+2	2.24e+3	1.72e+1
dimer activ.	k_6	$RR + \mathrm{Z} \rightarrow ZRR$	0	4.93e+3	0
dimer deactiv.	k_7	$ZRR \rightarrow RR + \mathrm{Z}$	0	7.61e-6	0
trimerization	k_8	$RR + R \rightarrow RRR$	0	8.22e-2	1.59e+3
trimer split.	k_9	$RRR \rightarrow RR + R$	0	1.20e+3	4.66e-2
trimer activ.	k_{11}	$RRR + \mathrm{Z} \rightarrow ZRRR$	0	0	2.63e+4
trimer deactiv.	k_{12}	$ZRRR \rightarrow \mathrm{Z} + RRR$	0	0	6.75e+4
monomer catal.	k_5	$\mathrm{A} + RZ \rightarrow RR$	2.89e-1	0	0
dimer catal.	k_{10}	$\mathrm{A} + ZRR \rightarrow RRR$	0	6.13e-1	0
trimer. catal.	k_{13}	$\mathrm{A} + ZRRR \rightarrow RRRR$	0	0	1.45e+5
tetramer split. (sym.)	k_{14}	$RRRR \rightarrow RR + RR$	0	0	8.80e+1
tetrameriz. (sym.)	k_{15}	$RR + RR \rightarrow RRRR$	0	0	2.99e+4
diatereo. param.	ΔE_{RS}	(kcal/mol)	7.96	4.57	2.37
stereoselect. param.	ΔE_a	(kcal/mol)	1.70	4.38	4.66

The optimized numerical values are not unique and are given here as an example (see Table S8 for the explored parameters range).

6.2 Explored parameter range for the three models

Forty independent curve fittings have been performed for each model. The extreme values observed for each model are gathered on Table S8.

Table S8. Orders of magnitude of the explored parameters range for each model. This table takes into account all the sets of parameters that have been explored during the fitting of the MISB step-like *ee* evolution curve shown on figure S1.

		M1 *(a)*	M1*(a)*	M2	M2	M3	M3
parameters	*processes*	lo	hi	lo	hi	lo	hi
k_0	A + Z → *R* or *S*	-10	-4	-8	-3	-8	-4
k_3	*R* + Z → *RZ*	-1	0	-	-	-	-
k_4	*RZ* → *R* + Z	-5	+3	-	-	-	-
k_1	*R* + *R* → *RR*	+1	+4	+2	+8	+2	+6
k_2	*RR* → *R* + *R*	0	+3	-2	+4	-2	+2
k_6	*RR* + Z → *ZRR*	-	-	0	+4	-	-
k_7	*ZRR* → *RR* + Z	-	-	-7	0	-	-
k_8	*RR* + *R* → *RRR*	-	-	-3	+4	+1	+6
k_9	*RRR* → *RR* + *R*	-	-	-1	+4	+1	+5
k_{11}	*RRR* + Z → *ZRRR*	-	-	-	-	+1	+7
k_{12}	*ZRRR* → Z + *RRR*	-	-	-	-	-2	+3
k_5	A + *RZ* → *RR*	-1	+6	-	-	-	-
k_{10}	A + *ZRR* → *RRR*	-	-	-1	0	-	-
k_{13}	A + *ZRRR* → *RRRR*	-	-	-	-	+1	+4
k_{14}	*RRRR* → *RR* + *RR*	-	-	-	-	0	+3
k_{15}	*RR* + *RR* → *RRRR*	-	-	-	-	+2	+7
ΔE_{RS}	(kcal/mol)	4	8.6	2.1	8.4	1.3	5
ΔE_a	(kcal/mol)	0.3	5	0.3	5	0.3	4

(a): *low activation rate constant k_3 is in agreement with results gathered in figure 7 (see main text). All other parameters lie within similar ranges than in table S4.*

7. Robustness of the MISB to low ΔE_{RS}

In order to check that the relative values of ΔE_{RS} observed in models M1, M2 and M3 do not depend on the step-like fitted curve shown in Fig. S1, the corresponding values of ΔE_{RS} have been lowered until the *ee* after MISB was only 1%. The probability analysis of the lowered ΔE_{RS} given on Fig. S2 shows the same pattern as on Fig. 9 of the main text.

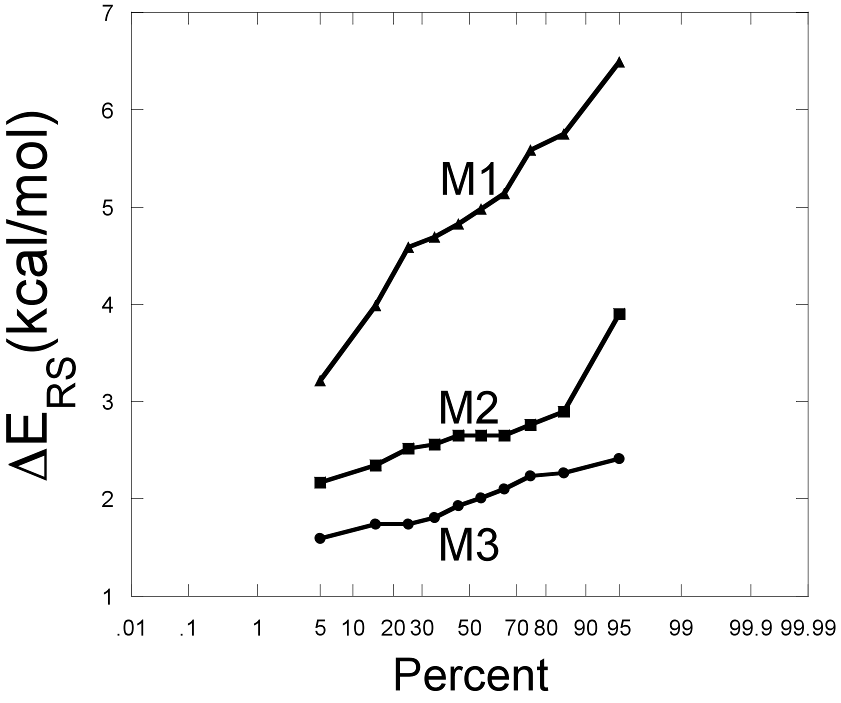


Figure S2. Probability analysis of ΔE_{RS} on M1 (triangles), M2 (squares) and M3 (filled circles) showing that M3 accepts lower ΔE_{RS} than the other models to perform MISB whatever the values of the other parameters.

8. Computation techniques

The model calculations were carried out with the simulation-adjustment software package *Sa3* written by D. Lavabre, Laboratoire des IMRCP, Université Paul Sabatier, Toulouse, France that is freely available at http://cinet.chim.pagesperso-orange.fr/index.html#.

The general algorithm for the numerical integration of the differential equations was based on a semi-implicit fourth-order Runge-Kutta method with stepwise control for stiff ordinary differential equations. One remarkable effect of the automatic step-size adaptation is the introduction of arithmetical rounding giving rise to numerical noise. The minimization algorithms for the curve fitting procedures were either of the Powell type or random walk simulated annealing. Fitted rate parameters were automatically and iteratively returned to the numerical integration until a minimum in the residual error was reached.