Mechanistic Basis for High Reactivity of (salen)Co–OTs in the Hydrolytic Kinetic Resolution of Terminal Epoxides

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Supporting Information

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1. Procedures, materials, and instrumentation

General experimental procedures. Reactions were carried out in oven-dried round bottomed flasks, unless otherwise noted. The flasks were fitted with rubber septa and reactions were conducted under a positive pressure of nitrogen. Kinetic experiments were performed in oven-dried glass mixing vessels charged with 12.5 mm x 3 mm PTFE-coated stir bars. These vessels were 16-mL, 21 mm x 70 mm borosilicate screw-thread vials fitted with open-top black phenolic screw caps and PTFE septa. Stainless steel syringes or cannulae were used to transfer air- and moisture-sensitive liquids. Flash chromatography was performed using silica gel 60 (230-400 mesh).

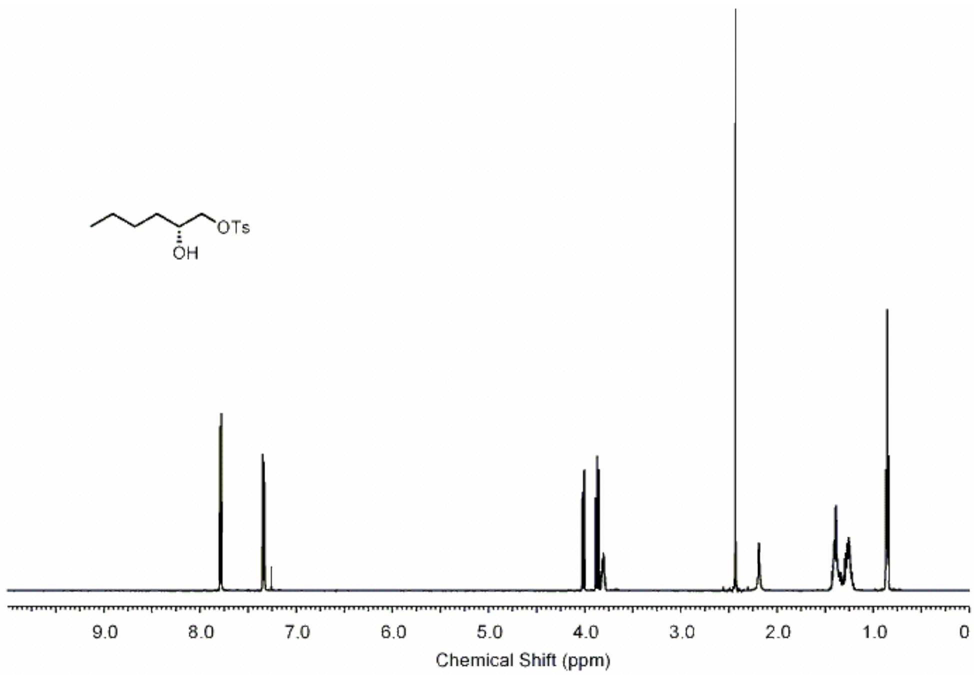
Materials. Commercial reagents were used as received with the following exceptions: dichloromethane was dried by passing through a column of activated alumina. (*R*)- and (*S*)-1,2-epoxyhexane were prepared using HKR technology in at least 99.5% enantiomeric excess, and were distilled from CaH_2 before use.

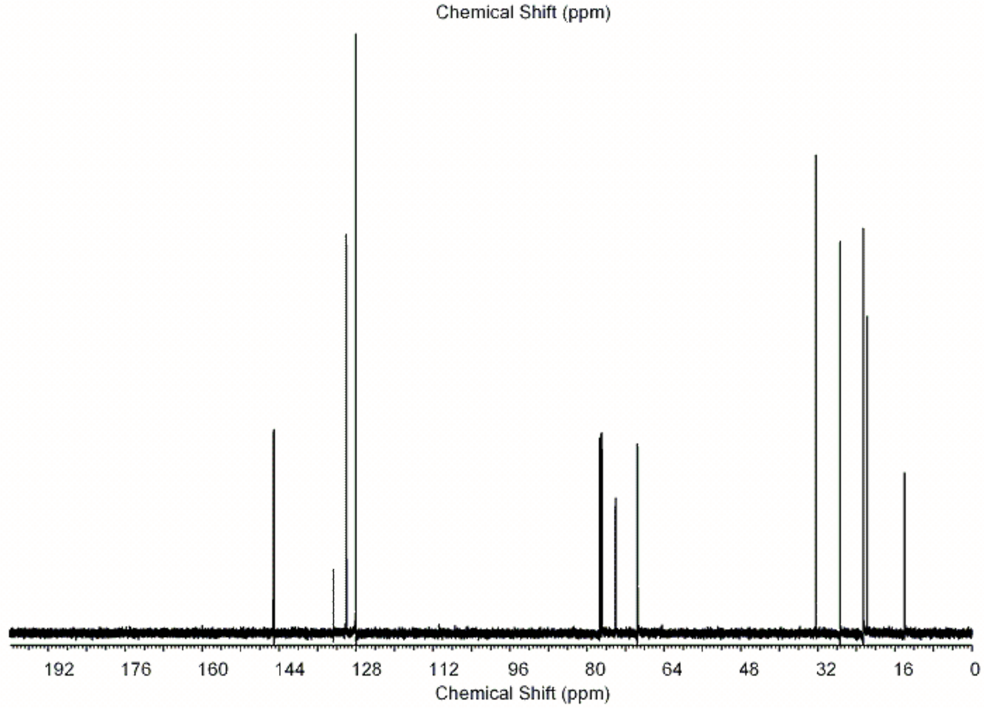
Instrumentation. Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on 400 or 500 MHz (^{1}H resonance) spectrometers. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$: δ 7.26) Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent ($CDCl_3$: δ 77.16). Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz). Infrared (IR) spectra were obtained using an ATR FTIR spectrometer. Data are represented as follows: frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak, br = broad). Optical rotations were measured using a 2-mL cell with a 10-cm path length on a digital polarimeter. The mass spectral data were obtained with a Quadrupole LC/MS operating in positive electrospray ionization mode. Samples were injected in 0.1% formic acid in methanol and bypassed the LC column on their way to the detector. Reaction calorimetry experiments were carried out as described previously.[1]

[1] Nielsen, L. P. C.; Stevenson, C. P.; Blackmond, D. G.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2004**, *126*, 1360–1362.

2. Synthesis of tosylate addition product

(*R*)-2-hydroxyhexyl 4-methylbenzenesulfonate (**3d**):





3. Analysis of (salen)Co–OTs deactivation at long delay times

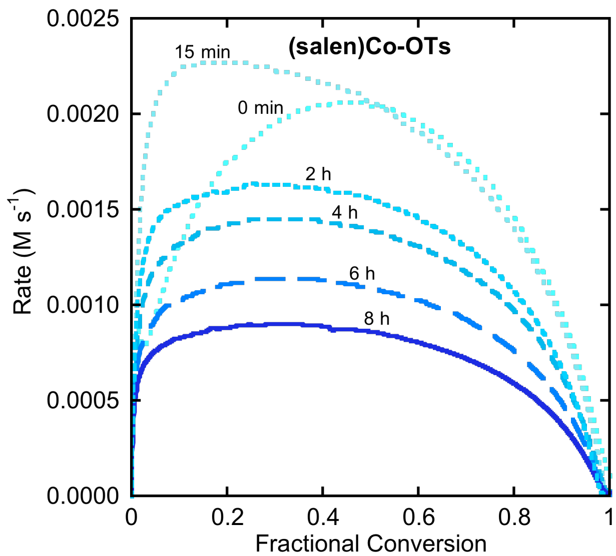


Figure S1. Loss of catalytic activity when (salen)Co–OTs is aged with epoxide for extended periods of time. Plot of the rates of hydrolysis of (*S*)-1,2-epoxyhexane ($[epoxide]_i$ = 6.0 M) in 1,2-hexanediol versus conversion of water ($[H_2O]_i$ = 3.4 M) in 1,2-hexanediol. In each experiment, (*R*,*R*)-(salen)Co–OTs (0.15 mol %) was added to the reaction mixture as an 83 mM CH_2Cl_2 solution; water was added subsequently after the indicated delay time. These mixtures remain homogeneous throughout the course of the reaction. An 8 h delay results in a reaction that reaches 95% conversion after 1.2 hours.

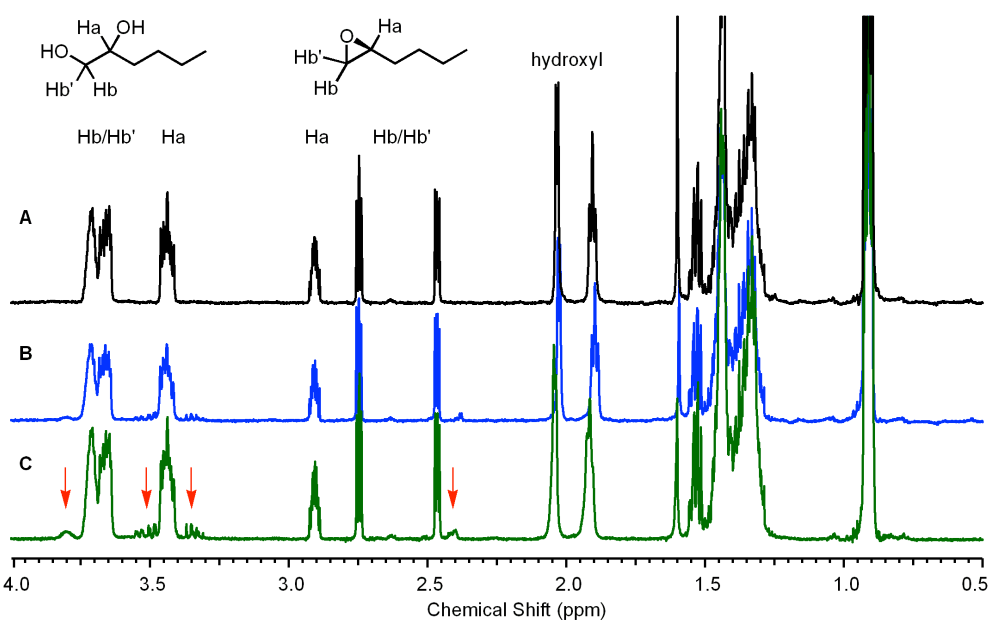


Figure S2. ^{1}H NMR spectra of completed hydrolysis reactions of (*S*)-1,2-epoxyhexane under the conditions used for the "delayed addition" experiment. All spectra were acquired in chloroform-*d* at a 500 MHz ^{1}H frequency. (A) HKR reaction catalyzed by (salen)Co–Cl after full conversion of water. (B) HKR reaction catalyzed by (salen)Co–OTs after full conversion of water. (C) HKR reaction catalyzed by (salen)Co–OTs and allowed to stir at 25 ºC overnight after full conversion of water. Red arrows denote ^{1}H NMR resonances that appear when catalyst is aged with epoxide (both in the presence and absence of water), and are presumably oligo(epoxyhexane).

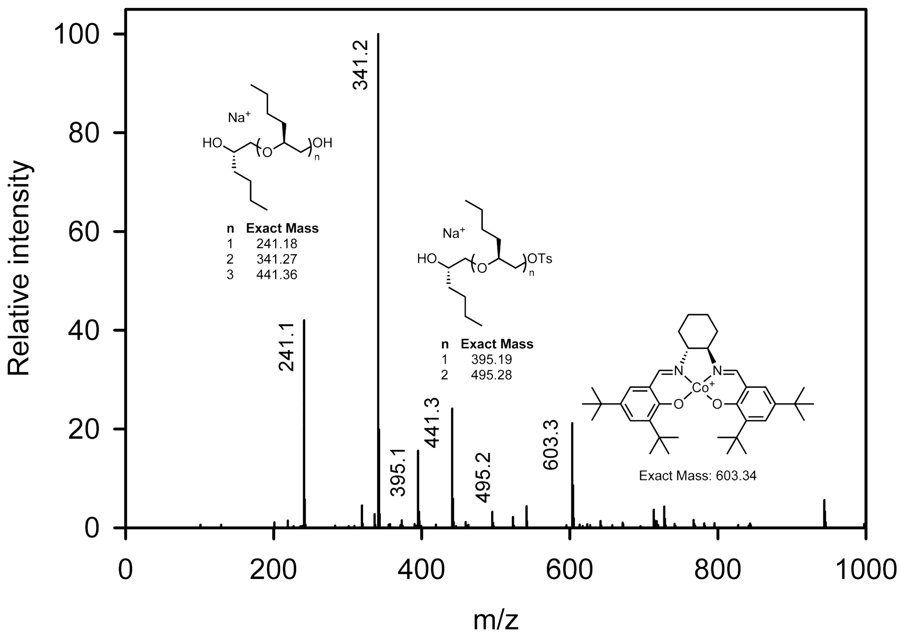


Figure S3. ESI-MS analysis of a mixture of (*S*)-1,2-epoxyhexane and (*R,R*)-(salen)Co–OTs (0.15 mol %) aged for 18 h at room temperature. Little oligomerization—less than 1% relative to epoxide—is observed by ^{1}H NMR spectroscopy under these conditions; much more is observed when 1,2-hexanediol or water is also present. We propose that the formation of tosylated oligoepoxides results in the irreversible conversion of (salen)Co–OTs to (salen)Co–OH under the reaction conditions. When a solution of 1,2-epoxyhexane and 1,2-hexanediol is analyzed by MS under these ionization conditions, only small amounts of epoxide dimer- and trimerization are observed.

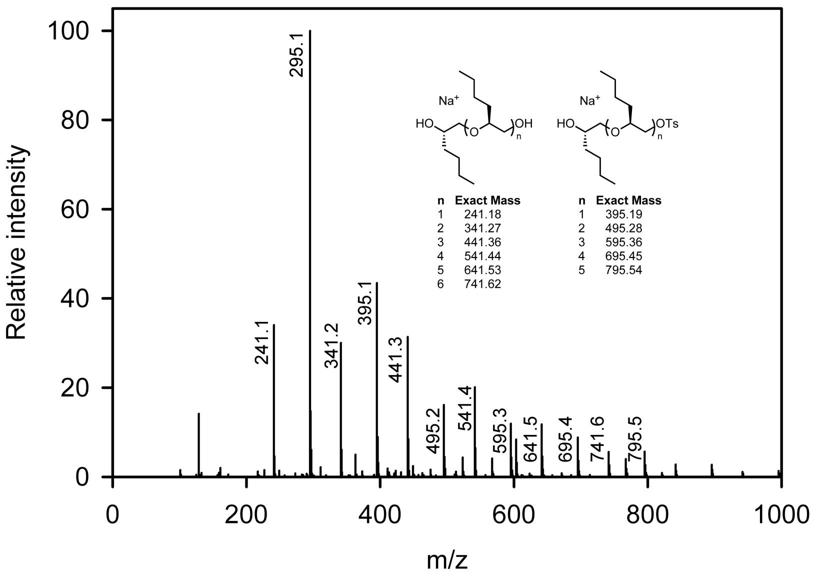


Figure S4. ESI-MS analysis of a mixture of (*R*)-1,2-epoxyhexane (1 equiv), tosylate addition product **3d** (0.4 equiv) and (*S,S*)-(salen)Co–OAc (0.15 mol %) aged for 3 h at room temperature.

4. Kinetics Data

Experiment: 1.00 mL (*S*)-1,2-epoxyhexane, 300 µL 1,2-hexanediol. Add 150 µL of an 83 mM solution of (*R*,*R*)-(salen)Co–OAc in CH_2Cl_2. Add 85 µL of water after indicated delay time.

Conversion (%)	Rate x 10^4 (M s^{-1})					
	0 min	15 min	30 min	60 min	120 min	180 min
2	9.89	7.13	11.21	3.44	1.69	1.52
4	9.29	9.92	12.52	3.12	1.57	1.44
6	9.40	11.47	12.33	2.73	1.46	1.35
8	9.60	12.51	11.69	2.44	1.36	1.27
10	9.86	13.31	10.76	2.08	1.25	1.20
12	10.10	13.89	9.88	1.79	1.19	1.13
14	10.38	14.23	9.00	1.62	1.11	1.07
16	10.65	14.46	8.17	1.44	1.06	1.01
18	10.94	14.53	7.38	1.29	0.99	0.96
20	11.19	14.53	6.60	1.16	0.94	0.91
22	11.43	14.42	5.89	1.06	0.91	0.86
24	11.64	14.24	5.31	1.01	0.86	0.82
26	11.80	13.95	4.76	0.94	0.81	0.80
28	11.90	13.64	4.27	0.88	0.78	0.76
30	11.94	13.21	3.80	0.82	0.74	0.72
32	12.00	12.72	3.35	0.79	0.71	0.71
34	11.93	12.20	2.93	0.75	0.70	0.68
36	11.84	11.58	2.54	0.70	0.66	0.66
38	11.62	10.94	2.18	0.68	0.63	0.64
40	11.35	10.24	1.84	0.67	0.62	0.62
42	10.95	9.55	1.57	0.63	0.60	0.59
44	10.47	8.76	1.35	0.60	0.57	0.58
46	9.94	8.02	1.20	0.58	0.56	0.57
48	9.30	7.22	1.03	0.57	0.54	0.54
50	8.63	6.44	0.92	0.55	0.52	0.54
52	7.92	5.66	0.83	0.52	0.51	0.52
54	7.16	4.88	0.76	0.50	0.50	0.49
56	6.39	4.16	0.71	0.49	0.46	0.47
58	5.58	3.51	0.66	0.46	0.47	0.45
60	4.79	2.92	0.62	0.45	0.43	0.44
62	4.03	2.38	0.59	0.43	0.43	0.43
64	3.33	1.92	0.56	0.41	0.41	0.42
66	2.68	1.51	0.53	0.39	0.39	0.40
68	2.14	1.19	0.50	0.38	0.39	0.39
70	1.70	0.94	0.48	0.37	0.37	0.37
72	1.34	0.75	0.45	0.34	0.35	0.35
74	1.01	0.63	0.44	0.32	0.34	0.34
76	0.76	0.53	0.40	0.30	0.32	0.33
78	0.59	0.46	0.38	0.29	0.30	0.31
80	0.46	0.41	0.36	0.27	0.29	0.30
82	0.37	0.36	0.34	0.25	0.29	0.28
84	0.30	0.32	0.31	0.23	0.26	0.26
86	0.25	0.29	0.30	0.21	0.23	0.24
88	0.21	0.26	0.27	0.20	0.23	0.23
90	0.17	0.23	0.25	0.19	0.22	0.22
92	0.14	0.20	0.23	0.16	0.20	0.21
94	0.11	0.18	0.22	0.14	0.18	0.18
96	0.08	0.14	0.18	0.12	0.17	0.16
98	0.05	0.12	0.16	0.11	0.15	0.15

Experiment: 1.00 mL (*S*)-1,2-epoxyhexane, 300 μL 1,2-hexanediol. Add 150 μL of an 83 mM solution of (*R,R*)-(salen)Co–OTs in CH_2Cl_2. Add 85 μL of water after indicated delay time.

Conversion (%)	Rate x 10^4 (M s^{-1})								
	0 min	15 min	30 min	60 min	120 min	180 min	240 min	360 min	480 min
2	7.72	15.70	14.29	12.18	11.93	10.36	9.70	7.87	6.53
4	8.60	19.47	17.25	14.57	13.86	12.29	11.47	8.93	7.40
6	10.24	21.26	18.38	15.55	14.76	13.23	12.31	9.68	7.82
8	11.85	21.90	19.11	16.06	15.26	13.82	12.82	10.01	8.10
10	13.11	22.49	19.51	16.42	15.54	14.12	13.18	10.21	8.30
12	14.25	22.66	19.71	16.63	15.79	14.49	13.40	10.48	8.42
14	15.31	22.75	19.89	16.84	15.92	14.65	13.75	10.69	8.53
16	16.19	22.86	20.07	17.01	16.08	14.80	13.97	10.87	8.70
18	16.94	22.86	20.15	17.13	16.25	14.97	14.03	11.01	8.78
20	17.56	22.85	20.33	17.22	16.19	15.12	14.21	11.12	8.84
22	17.95	22.82	20.34	17.31	16.36	15.18	14.28	11.19	8.93
24	18.50	22.83	20.38	17.38	16.51	15.19	14.42	11.26	8.98
26	18.84	22.68	20.48	17.42	16.65	15.30	14.47	11.35	8.97
28	19.34	22.62	20.48	17.45	16.57	15.41	14.51	11.38	8.99
30	19.66	22.46	20.54	17.47	16.56	15.61	14.52	11.37	9.02
32	19.86	22.33	20.51	17.48	16.60	15.34	14.50	11.43	9.02
34	20.16	22.30	20.47	17.48	16.56	15.57	14.53	11.32	9.03
36	20.35	22.11	20.34	17.38	16.45	15.30	14.51	11.36	8.99
38	20.53	21.97	20.23	17.37	16.44	15.39	14.49	11.37	8.97
40	20.60	21.78	20.19	17.32	16.40	15.40	14.43	11.32	8.92
42	20.68	21.67	19.99	17.17	16.31	15.22	14.33	11.21	8.73
44	20.71	21.51	19.98	17.09	16.21	15.22	14.24	11.18	8.78
46	20.67	21.35	19.79	17.02	16.15	15.13	14.19	11.08	8.76
48	20.67	21.28	19.68	16.84	16.04	15.02	14.10	11.00	8.71
50	20.50	20.86	19.44	16.68	15.93	14.93	13.93	10.93	8.64
52	20.47	20.64	19.17	16.54	15.74	14.77	13.79	10.82	8.55
54	20.38	20.31	19.04	16.38	15.55	14.64	13.66	10.69	8.44
56	20.15	19.95	18.73	16.16	15.38	14.44	13.47	10.53	8.33
58	19.89	19.53	18.49	15.94	15.17	14.12	13.28	10.42	8.18
60	19.66	19.25	18.15	15.69	14.97	13.92	13.06	10.28	8.07
62	19.29	18.97	17.84	15.47	14.68	13.74	12.87	10.09	7.91
64	18.96	18.54	17.51	15.19	14.42	13.41	12.60	9.88	7.75
66	18.56	18.12	17.18	14.86	14.15	13.11	12.35	9.69	7.59
68	18.15	17.69	16.82	14.53	13.86	12.85	12.07	9.57	7.40
70	17.64	17.22	16.39	14.17	13.50	12.54	11.75	9.26	7.23
72	17.23	16.75	16.01	13.80	13.17	12.25	11.40	8.97	7.01
74	16.65	16.11	15.43	13.32	12.75	11.79	11.05	8.67	6.78
76	16.02	15.57	14.84	12.86	12.29	11.36	10.64	8.39	6.50
78	15.26	14.92	14.21	12.34	11.85	10.91	10.24	8.01	6.23
80	14.49	14.24	13.62	11.75	11.32	10.37	9.73	7.63	5.91
82	13.54	13.44	12.86	11.11	10.71	9.79	9.19	7.18	5.58
84	12.70	12.58	12.18	10.47	10.07	9.16	8.61	6.70	5.20
86	11.59	11.70	11.29	9.61	9.39	8.43	7.93	6.19	4.77
88	10.44	10.59	10.23	8.77	8.56	7.70	7.15	5.59	4.29
90	9.23	9.45	9.07	7.74	7.62	6.77	6.31	4.90	3.76
92	7.67	8.08	7.80	6.63	6.53	5.70	5.32	4.11	3.14
94	5.98	6.56	6.27	5.26	5.32	4.52	4.14	3.14	2.39
96	3.90	4.59	4.33	3.67	3.76	3.07	2.73	2.02	1.52
98	1.48	2.39	2.09	1.89	1.92	1.36	1.07	0.65	0.56

Experiment: 1.00 mL (*S*)-1,2-epoxyhexane, 300 μL 1,2-hexanediol. Add 150 μL of an 83 mM solution of (*R*,*R*)-(salen)Co–Cl in CH_2Cl_2. Add 85 μL of water after indicated delay time.

Conversion (%)	Rate x 10^4 (M s^{-1})					
	0 min	15 min	30 min	60 min	120 min	180 min
2	16.44	3.98	3.20	2.51	2.10	1.94
4	18.18	3.64	2.92	2.33	1.99	1.85
6	13.50	3.36	2.71	2.22	1.83	1.75
8	8.55	3.09	2.53	2.10	1.74	1.68
10	6.02	2.85	2.36	2.00	1.65	1.62
12	4.91	2.63	2.21	1.90	1.59	1.57
14	4.29	2.43	2.07	1.81	1.54	1.49
16	3.83	2.23	1.96	1.73	1.47	1.45
18	3.44	2.08	1.85	1.65	1.42	1.39
20	3.11	1.93	1.72	1.58	1.36	1.35
22	2.81	1.81	1.62	1.52	1.32	1.30
24	2.54	1.67	1.54	1.46	1.28	1.26
26	2.33	1.59	1.47	1.39	1.23	1.21
28	2.12	1.49	1.39	1.34	1.19	1.16
30	1.94	1.41	1.33	1.28	1.16	1.12
32	1.81	1.34	1.26	1.23	1.12	1.08
34	1.68	1.26	1.22	1.18	1.07	1.03
36	1.56	1.19	1.15	1.13	1.03	0.99
38	1.44	1.13	1.10	1.09	0.98	0.95
40	1.35	1.08	1.05	1.05	0.93	0.93
42	1.25	1.04	1.00	1.01	0.91	0.88
44	1.15	0.99	0.96	0.97	0.88	0.85
46	1.08	0.94	0.92	0.93	0.86	0.83
48	1.02	0.90	0.88	0.89	0.82	0.80
50	0.96	0.85	0.84	0.86	0.79	0.77
52	0.91	0.82	0.80	0.82	0.76	0.74
54	0.85	0.78	0.77	0.79	0.72	0.71
56	0.81	0.75	0.74	0.76	0.70	0.68
58	0.77	0.71	0.71	0.74	0.67	0.65
60	0.72	0.68	0.67	0.71	0.64	0.63
62	0.68	0.63	0.64	0.68	0.61	0.60
64	0.64	0.61	0.62	0.65	0.59	0.57
66	0.61	0.57	0.58	0.62	0.56	0.54
68	0.57	0.54	0.56	0.59	0.54	0.52
70	0.53	0.51	0.52	0.56	0.51	0.49
72	0.49	0.49	0.49	0.53	0.50	0.47
74	0.47	0.46	0.46	0.51	0.46	0.45
76	0.44	0.43	0.44	0.48	0.44	0.41
78	0.40	0.40	0.41	0.45	0.41	0.39
80	0.36	0.36	0.37	0.42	0.38	0.36
82	0.33	0.33	0.34	0.39	0.36	0.33
84	0.30	0.31	0.32	0.36	0.32	0.30
86	0.27	0.29	0.28	0.33	0.30	0.28
88	0.23	0.25	0.25	0.30	0.27	0.24
90	0.21	0.21	0.23	0.27	0.24	0.21
92	0.17	0.19	0.20	0.25	0.21	0.19
94	0.15	0.16	0.17	0.21	0.18	0.14
96	0.11	0.13	0.14	0.18	0.15	0.13
98	0.09	0.10	0.10	0.15	0.13	0.08

Experiment: 1.00 mL (*R*)-1,2-epoxyhexane, 300 µL 1,2-hexanediol, 8.2 mg (*S*,*S*)-(salen)Co–Cl. Add 85 µL of water. Then add 150 µL of an 83 mM solution of **3d** in CH_2Cl_2 after indicated delay time.

Conversion (%)	Rate x 10^4 (M s^{-1})		
	No **3d**	1 min	40 min
2	3.03	5.10	3.01
4	2.94	8.24	2.91
6	2.83	10.43	2.75
8	2.73	12.23	2.60
10	2.61	13.72	2.47
12	2.50	14.81	2.36
14	2.40	15.78	2.23
16	2.30	16.75	2.12
18	2.20	17.46	2.02
20	2.12	18.15	3.56
22	2.02	18.69	6.39
24	1.95	19.17	8.77
26	1.87	19.55	10.42
28	1.79	19.93	11.72
30	1.71	20.27	12.78
32	1.64	20.50	13.77
34	1.57	20.70	14.47
36	1.51	20.93	15.02
38	1.45	21.07	15.60
40	1.39	21.15	16.00
42	1.33	21.17	16.28
44	1.27	21.12	16.68
46	1.22	21.13	16.94
48	1.16	21.19	17.11
50	1.11	21.14	17.24
52	1.06	21.03	17.30
54	1.00	20.84	17.33
56	0.96	20.70	17.32
58	0.91	20.52	17.25
60	0.87	20.22	17.19
62	0.82	19.90	17.04
64	0.77	19.65	16.80
66	0.73	19.26	16.54
68	0.68	18.89	16.28
70	0.64	18.45	16.01
72	0.59	18.08	15.59
74	0.56	17.52	15.18
76	0.50	16.88	14.68
78	0.47	16.18	14.07
80	0.42	15.40	13.51
82	0.38	14.57	12.82
84	0.33	13.69	12.07
86	0.29	12.62	11.14
88	0.25	11.38	10.14
90	0.21	9.99	8.97
92	0.16	8.42	7.60
94	0.12	6.41	6.05
96	0.08	4.17	4.20
98	0.05	1.42	1.99

Experiment: 1.00 mL (*R*)-1,2-epoxyhexane, 300 µL 1,2-hexanediol, 8.2 mg (*S*,*S*)-(salen)Co–Cl. Add 150 µL of an 83 mM solution of **3d** in CH_2Cl_2. Add 85 µL of water after indicated delay time.

Conversion	Rate x 10^4 (M s^{-1})								
(%)	No **3d**	0 min	2 min	5 min	10 min	30 min	60 min	120 min	180 min
2	2.33	5.10	10.32	13.60	13.81	15.33	12.71	12.30	11.51
4	2.26	8.24	12.90	16.93	18.19	19.22	16.83	15.38	13.75
6	2.15	10.43	14.65	18.62	20.23	21.21	18.55	16.85	15.00
8	2.04	12.23	16.26	19.81	21.68	22.27	19.71	17.76	15.53
10	1.95	13.72	17.17	20.72	22.61	22.88	20.37	18.39	16.01
12	1.85	14.81	17.93	21.47	23.13	23.20	20.87	18.71	16.33
14	1.77	15.78	18.91	21.90	23.44	23.40	21.20	18.98	16.57
16	1.69	16.75	19.49	22.42	23.98	23.67	21.47	19.13	16.65
18	1.62	17.46	19.98	22.74	24.21	23.80	21.73	19.27	16.83
20	1.53	18.15	20.49	23.10	24.37	23.84	21.94	19.53	16.86
22	1.48	18.69	20.88	23.42	24.49	24.02	22.08	19.63	17.16
24	1.43	19.17	21.26	23.62	24.55	24.14	22.20	19.70	17.27
26	1.36	19.55	21.61	23.80	24.67	24.05	22.30	19.75	17.21
28	1.31	19.93	21.86	23.93	24.80	24.04	22.35	19.81	17.23
30	1.25	20.27	22.04	24.03	24.83	24.01	22.36	19.75	17.26
32	1.20	20.50	22.21	24.12	24.79	23.92	22.37	19.78	17.31
34	1.16	20.70	22.34	24.18	24.71	23.93	22.36	19.79	17.20
36	1.10	20.93	22.42	24.20	24.51	23.70	22.32	19.73	17.19
38	1.06	21.07	22.48	24.17	24.32	23.78	22.23	19.69	17.12
40	1.02	21.15	22.52	24.11	24.26	23.72	22.15	19.58	17.05
42	0.98	21.17	22.51	24.01	24.18	23.60	22.05	19.46	17.01
44	0.95	21.12	22.47	23.93	24.08	23.38	21.87	19.35	16.93
46	0.91	21.13	22.36	23.84	23.50	23.13	21.73	19.24	16.88
48	0.88	21.19	22.28	23.67	23.49	22.95	21.57	19.06	16.70
50	0.84	21.14	22.13	23.51	23.44	22.86	21.35	18.92	16.49
52	0.80	21.03	21.96	23.25	23.05	22.57	21.13	18.63	16.33
54	0.77	20.84	21.81	23.04	22.62	22.28	20.89	18.43	16.20
56	0.74	20.70	21.53	22.82	22.54	21.90	20.59	18.20	15.92
58	0.71	20.52	21.26	22.76	22.48	21.54	20.30	17.94	15.76
60	0.68	20.22	20.98	22.14	21.93	21.26	19.98	17.75	15.62
62	0.64	19.90	20.65	21.52	21.36	20.88	19.64	17.41	15.36
64	0.62	19.65	20.28	21.18	20.92	20.45	19.21	17.07	15.01
66	0.59	19.26	19.88	20.81	20.45	20.00	18.81	16.69	14.67
68	0.55	18.89	19.48	20.36	19.94	19.46	18.32	16.23	14.35
70	0.53	18.45	19.02	19.87	19.45	18.90	17.90	15.81	13.93
72	0.49	18.08	18.25	19.20	18.78	18.33	17.37	15.34	13.59
74	0.46	17.52	17.72	18.59	18.18	17.79	16.82	14.83	13.09
76	0.43	16.88	17.13	17.86	17.46	17.12	16.12	14.27	12.69
78	0.40	16.18	16.42	17.09	16.71	16.29	15.49	13.67	12.08
80	0.37	15.40	15.73	16.24	15.91	15.56	14.74	13.00	11.63
82	0.34	14.57	14.79	15.25	14.85	14.66	13.94	12.31	10.98
84	0.30	13.69	13.70	14.22	13.78	13.77	12.99	11.46	10.22
86	0.28	12.62	12.58	13.15	12.78	12.65	11.95	10.59	9.56
88	0.24	11.38	11.44	11.75	11.47	11.37	10.77	9.50	8.66
90	0.20	9.99	9.94	10.34	9.97	9.97	9.51	8.40	7.70
92	0.17	8.42	8.24	8.45	8.22	8.42	8.03	7.00	6.59
94	0.14	6.41	6.37	6.46	6.32	6.47	6.26	5.39	5.28
96	0.11	4.17	3.91	4.09	3.88	4.26	4.23	3.41	3.64
98	0.07	1.42	1.26	1.28	1.24	1.67	1.72	1.13	1.71