

Topic Review Group meeting

Memory of chirality

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Based on: Zhao, H.; Hsu, D. C.; Carlier, P.R. *Synthesis* **2005**, 1, 1.

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- > Types of chirality
- > Requirements for memory of chirality
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Definitions of memory of chirality

- > Central chirality at a carbon alpha to a carbonyl group is preserved as transient axial chirality of the intermediate enolate and is then regenerated as central chirality in the reaction product (memory of chirality).¹
- > The chirality of the starting material is preserved in a reactive intermediate for a limited time.²
- > The chirality of a starting material having a chiral sp³-carbon is preserved in the reaction product even though the reaction proceeds at the chiral carbon as a reaction center through reactive intermediates such as carbanion, singlet monoradicals, biradicals, or carbenium ions.³

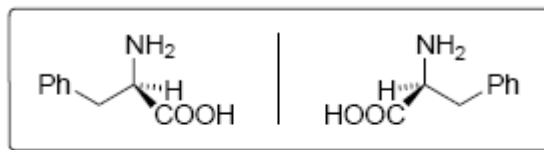
¹ Kawabata, T.; Yahiro, K.; Fuji, K. *J. Am. Chem. Soc.* **1991**, *113*, 9694.

² Fuji, K.; Kawabata, T. *Chem.–Eur. J.* **1998**, *4*, 373.

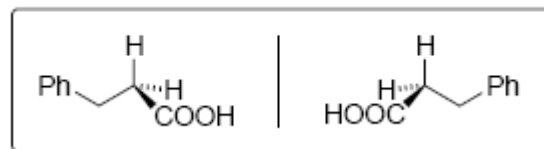
³ Wanyoike, G. N.; Onomura, O.; Maki, T.; Matsumura, Y. *Org. Lett.* **2002**, *4*, 1875.

Types of Chirality

a) Static chirality



b) Dynamic chirality

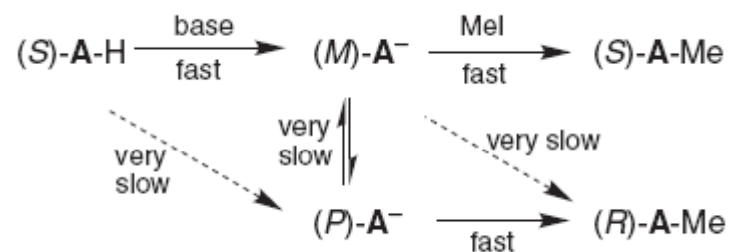


- > Dynamic chirality is not a sufficient condition for MOC since the intermediate has to be formed enantioselectively.

¹ Fuji, K.; Kawabata, T. *Chem.–Eur. J.* **1998**, *4*, 373.

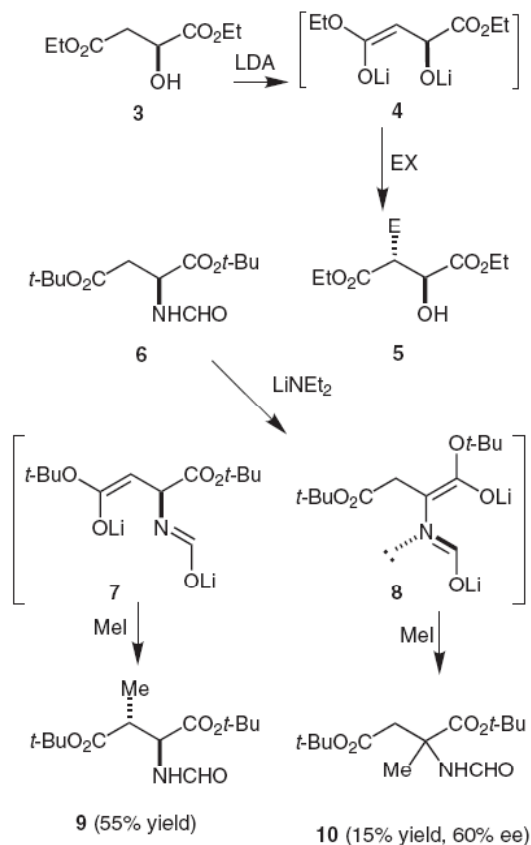
Requirements for memory of chirality

- > The three requirements for memory of chirality are:¹



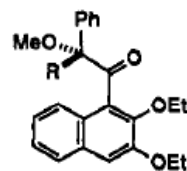
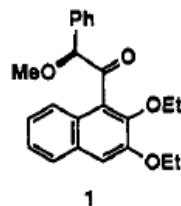
¹ Zhao, H.; Hsu, D.C.; Carlier, P.R. *Synthesis* **2005**, 1, 1.

Memory of chirality in enolate chemistry



- > Seebach, D.; Wasmuth, D. *Angew. Chem.* **1981**, 93, 1007.
- > Zhao, H.; Hsu, D. C.; Carlier, P.R. *Synthesis* **2005**, 1, 1.

Memory of chirality in enolate chemistry



4 a : R = Me
 b : R = Et
 c : R = CH₂Ph
 d : R = CH₂CH=CH₂

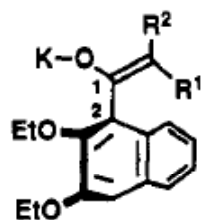
Table I. Enantioselective Alkylation of **1**^a

entry	RX	product ^b	yield, %	ee, ^c %	[α] _D ²⁰ (c) ^d	confign
1	MeI	4a	48	66	-15.8° (2.3)	<i>R</i>
2	EtI	4b	27	65	+18.5° (1.3)	<i>R</i>
3	PhCH ₂ Br	4c	31	67	+25.6° (2.3)	<i>e</i>
4	CH ₂ =CHCH ₂ Br	4d	36	48	+13.9° (1.8)	<i>e</i>

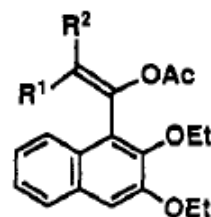
^a Chiral ketone **1** of 93% ee was used. For the experimental procedure, see ref 9. ^b Enol ethers were also obtained in 12–30% yield. ^c Determined by HPLC analysis (CHIRALPAK AD, hexane:2-propanol = 95:5). ^d Measured in chloroform. ^e Not determined.

> Kawabata, T.; Yahiro, K.; Fuji, K. *J. Am. Chem. Soc.* **1991**, *113*, 9694.

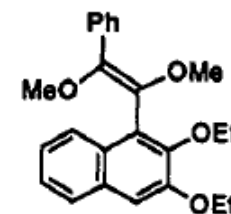
Memory of chirality in enolate chemistry



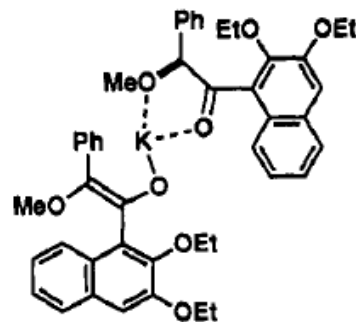
7 : $R^1 = \text{OMe}$, $R^2 = \text{Ph}$
 8 : $R^1 = \text{Ph}$, $R^2 = \text{OMe}$



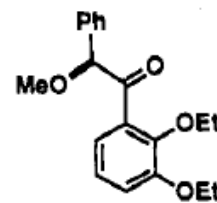
9 : $R^1 = \text{OMe}$, $R^2 = \text{Ph}$
 10 : $R^1 = \text{Ph}$, $R^2 = \text{OMe}$



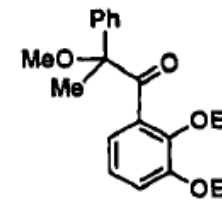
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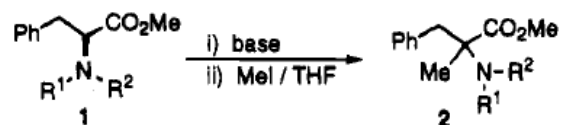
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> Kawabata, T.; Yahiro, K.; Fuji, K. *J. Am. Chem. Soc.* **1991**, *113*, 9694.

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compd	R ¹	R ²	base	product	yield, %	% ee ^b
1a	Me	CH ₂ Ph	LDA	2a	45	~0 ^c
1b	Me	CHO	LHMDS ^d	2b	66	~0
1c	Me	COPh	LDA	2c	50	12
1d	Me	CO ₂ CH ₂ Ph	LHMDS ^e	2d	40 ^f	26
1e	Me	CO ₂ Ad ^g	LHMDS	2e	38	35
1f	Me	CO ₂ ^t Bu	LHMDS	2f	30 ^f	36
1g	H	CO ₂ ^t Bu	LDA ^h	2g	57	~0

^a Substrate **1** of >84% ee was treated with the base (1.1–1.8 equiv) at –78 °C for 30–60 min followed by methyl iodide at –78 °C to room temperature. Reactions were run in THF unless otherwise indicated. ^b Ee was determined by HPLC analysis using Daicel CHIRALCEL OD (5% ⁱPrOH–hexane) after conversion to **2c** unless otherwise indicated. ^c Determined on **2a** using Daicel CHIRALCEL OJ (1% ⁱPrOH–hexane). ^d Lithium hexamethyldisilazide. ^e Run in THF–DMF (10:1). ^f Overall yield of **2c**. ^g 1-Adamantyl ester. ^h The amount of base used was 2.4 equiv.

Table 2. Asymmetric α -Methylation of **3**^a

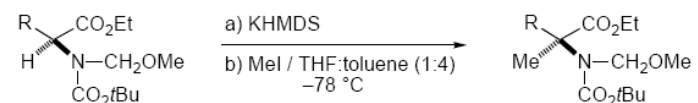
entry	base	equiv of base	yield of 5 , %	ee of 6 , ^b %	recovery of 3 , %	ee of recovered 3 , ^c %
1	LTMP	1.1	38	79 (<i>S</i>)	23	87
2	LDA	1.2	57	22 (<i>S</i>)	25	<i>d</i>
3	LHMDS	1.2	0 ^e		<i>d</i>	<i>d</i>
4	KHMDS	1.2	79	20 (<i>R</i>)	0	
5	LTMP	1.0	40	82 (<i>S</i>)	36	92
6	LTMP	1.5	42	77 (<i>S</i>)	17	73
7	LTMP	2.0	42	73 (<i>S</i>)	13	48
8	LTMP	4.0	36	66 (<i>S</i>)	13	54
9	LTMP	6.0	37	55 (<i>S</i>)	22	48

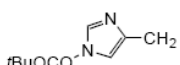
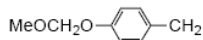
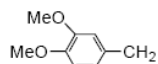
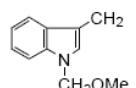
^a **3** (98% ee) was treated with the base in THF at –78 °C for 15 min followed by methyl iodide at –78 °C for 4 h. ^b Determined by HPLC analysis using Daicel CHIRALPAK AS (3% EtOH–hexane). The letter in the parentheses indicates the absolute configuration. ^c The absolute configuration was *S* in each entry. Ee was determined by HPLC analysis using Daicel CHIRALPAK AS (3% EtOH–hexane). ^d Not determined. ^e This result was in sharp contrast to that from **1** (Table 1, **1f**). Reproducibility of the results was confirmed by repeated experiments.

> Kawabata, T.; Yahiro, K.; Fuji, K. *J. Am. Chem. Soc.* **1991**, *113*, 9694.

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Table 1. Asymmetric α -methylation of α -amino acid derivatives.^[a]

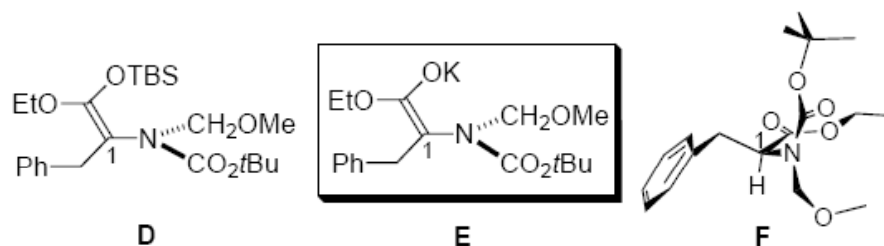
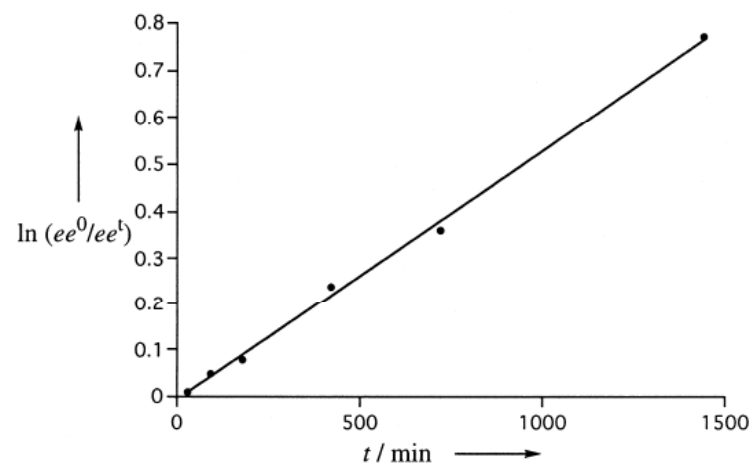
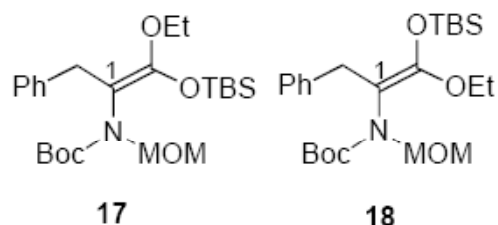


Entry	R	Substrate ^[b]	Product	Yield [%]	<i>ee</i> [%] ^[c]	$[\alpha]_D^{20}$ (c in CHCl ₃)	Configuration ^[d]
1	PhCH ₂	3	4	96	81	− 89 (1.2)	<i>S</i>
2		5	6	83	93	− 43 (1.1)	[e]
3		7	8	94	79	− 81 (1.0)	<i>S</i>
4		9	10	95	80	− 96 (1.0)	<i>S</i>
5		11	12	88	76	− 64 (0.9)	[e]
6	Me ₂ CH	13	14 ^[f]	81	87	+ 8.5 (1.2) ^[g]	<i>S</i>
7	Me ₂ CHCH ₂	15	16 ^[f]	78	78	+ 20 (0.5) ^[g]	<i>S</i>

[a] The substrate was treated with 1.1 equiv of KHMDS at $-78\text{ }^\circ\text{C}$ for 30 min (for **3**, **5**, **7**, **9**, and **11**) or 60 min (for **13** and **15**) followed by 10 equiv of methyl iodide for 16–17 h at $-78\text{ }^\circ\text{C}$. See the Supporting Information for the experimental procedure and physical data. [b] The *ee* value of each substrate is $>99\%$. [c] Determined by HPLC using columns with chiral stationary phases: **4**: Chiralpack AD, 2% *i*PrOH in hexane; **6**, **8**: Chiralpack AD, 5% EtOH in hexane; **10**, **12**: Chiralpack AD, 5% *i*PrOH in hexane; **14** (benzoate): Chiralpack AS, 3% *i*PrOH in hexane; **16** (benzoate): Chiralpack AD, 1% *i*PrOH in hexane. [d] Absolute configuration of the corresponding α -methyl- α -amino acid. [e] Not determined. [f] Obtained as an inseparable mixture with the substrate. The yield was determined on the basis of the ratio of signals observed in the 400 MHz ¹H NMR spectra. Complete separation was achieved with the corresponding *N*-benzoyl derivative. [g] Optical rotation of the corresponding *N*-benzoyl derivative.

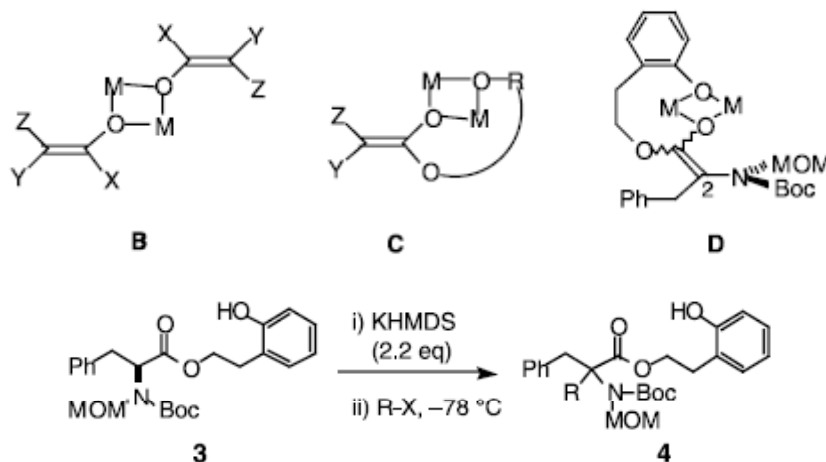
> Kawabata, T.; Suzuki, H.; Nagae, Y.; Fuji, K. *Angew. Chem. Int. Ed.* **2000**, *39*, 2155.

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> Kawabata, T.; Suzuki, H.; Nagae, Y.; Fuji, K. *Angew. Chem. Int. Ed.* **2000**, *39*, 2155.

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Entry	R-X	Solvent	Yield (%)	Ee (%) ^a
1	MeI	Toluene:THF = 4:1	81	88 ^b (81) ^c
2	MeI	THF	83	75 ^b (35) ^c
3	CH ₂ =CHCH ₂ I	Toluene:THF = 4:1	71	82 (55) ^c
4	(CH ₃) ₂ C=CHCH ₂ Br	Toluene:THF = 4:1	47	87 (69) ^c
5	<i>trans</i> -PhCH=CHCH ₂ I	Toluene:THF = 4:1	89	83 (48) ^c

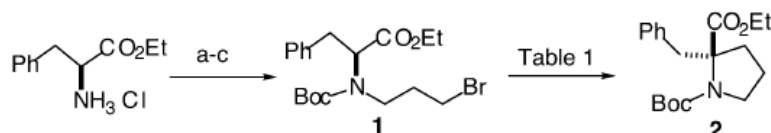
^a Ee was determined by HPLC analysis with a chiral stationary phase.

^b (*S*)-Isomer.

^c % Ee of the corresponding product from 1.

> Kawabata, T.; Kawakami, S.; Fuji, K. *Tetrahedron Lett.* **2002**, 43, 1465.

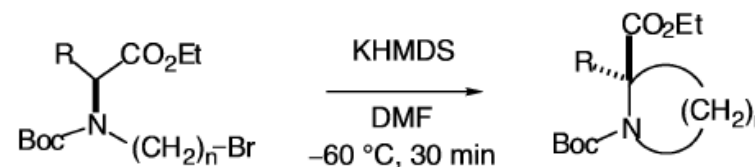
Memory of chirality in enolate chemistry



(a) 3-bromo-1-propanol, K₂CO₃, DMF, (b) (Boc)₂O, *i*-Pr₂NEt, (c) CBr₄, PPh₃ (63% overall)

entry	base ^a	solvent	temp, time	2, yield (%)	2 ^b , ee ^c (%)
1	KHMDS ^d	THF	-78 °C, 30 min	92	89
2	KHMDS ^d	toluene	-78 °C, 2 h	92	47
3	KHMDS ^d	DMF	-60 °C, 30 min	94	98
4	LHMDS ^e	DMF	-60 °C, 30 min	60	77
5	LTMP ^f	DMF	-60 °C, 30 min	~0	

^a 1.2 equiv of base was used. ^b The (*S*)-isomer was obtained in every entry. See the Supporting Information. ^c Determined by HPLC analysis. ^d Potassium hexamethyldisilazide. ^e Lithium hexamethyldisilazide. ^f Lithium 2,2,6,6-tetramethylpiperidide.

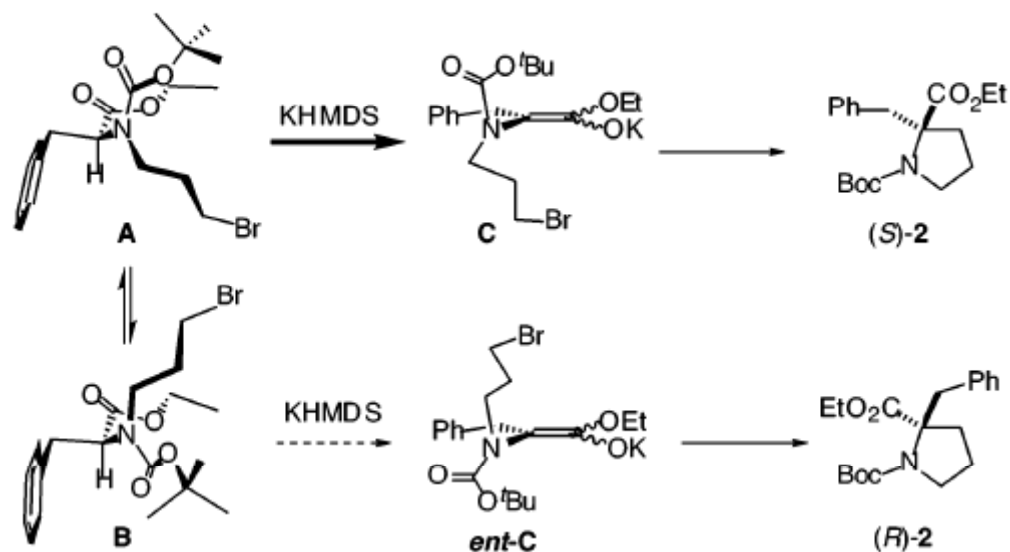


entry	substrate	n	R	product	yield (%)	ee (%) ^b
1	1 ^c	3	PhCH ₂	2	94	98 (<i>S</i>)
2	3	3	4-EtO-C ₆ H ₄ -CH ₂	4	95	97
3	5	3	MeSCH ₂ CH ₂	6	92	97
4	7	3	Me ₂ CH	8	78	94
5	9	3	CH ₃	10	91	95 (<i>R</i>)
6	11	2	PhCH ₂	12	61	95
7	13 ^c	4	PhCH ₂	14	84	97
8	15 ^c	5	PhCH ₂	16	31 ^e	83 (<i>S</i>)
9 ^d	15 ^c	5	PhCH ₂	16	61 ^f	72 (<i>S</i>)

^a A solution of substrate (0.25 mmol) in dry DMF (2.4 mL) was treated with 1.2 mol equiv of KHMDS (0.50 M in THF) for 30 min at -60 °C, unless otherwise mentioned. ^b The ee was determined by HPLC analysis. The letter in the parentheses indicates the absolute configuration. See the Supporting Information. ^c >99% ee. ^d The reaction was run for 2 h. ^e 15 (70% ee) was recovered in 52% yield. ^f 15 (54% ee) was recovered in 17% yield.

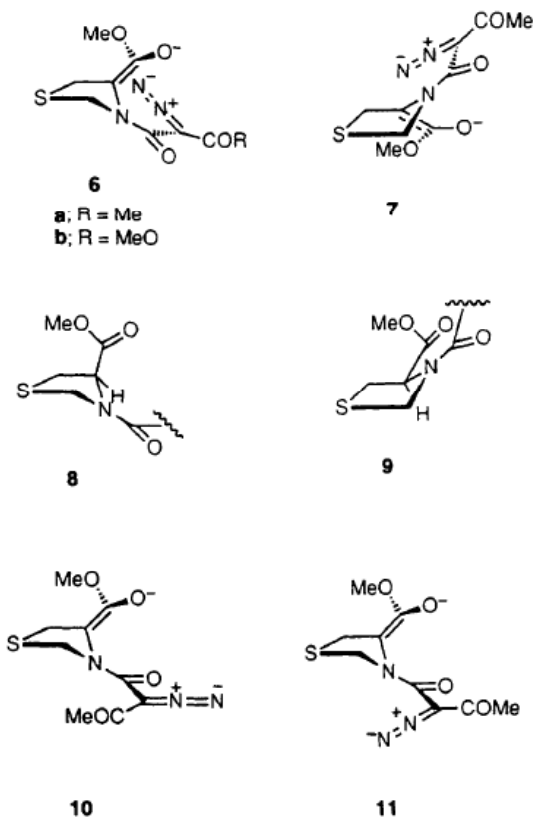
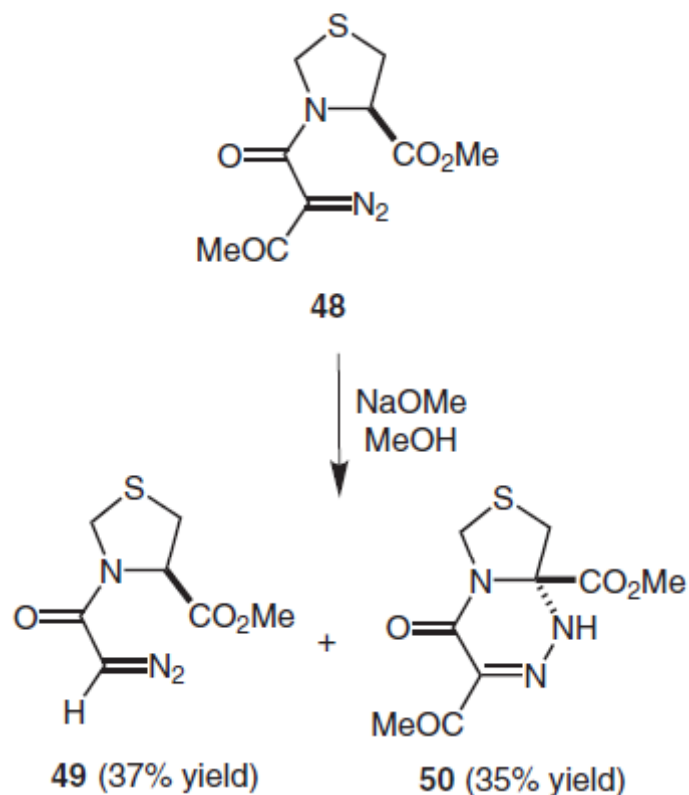
> Kawabata, T.; Kawakami, S.; Majumdar, S. *J. Am. Chem. Soc.* **2003**, *125*, 13012.

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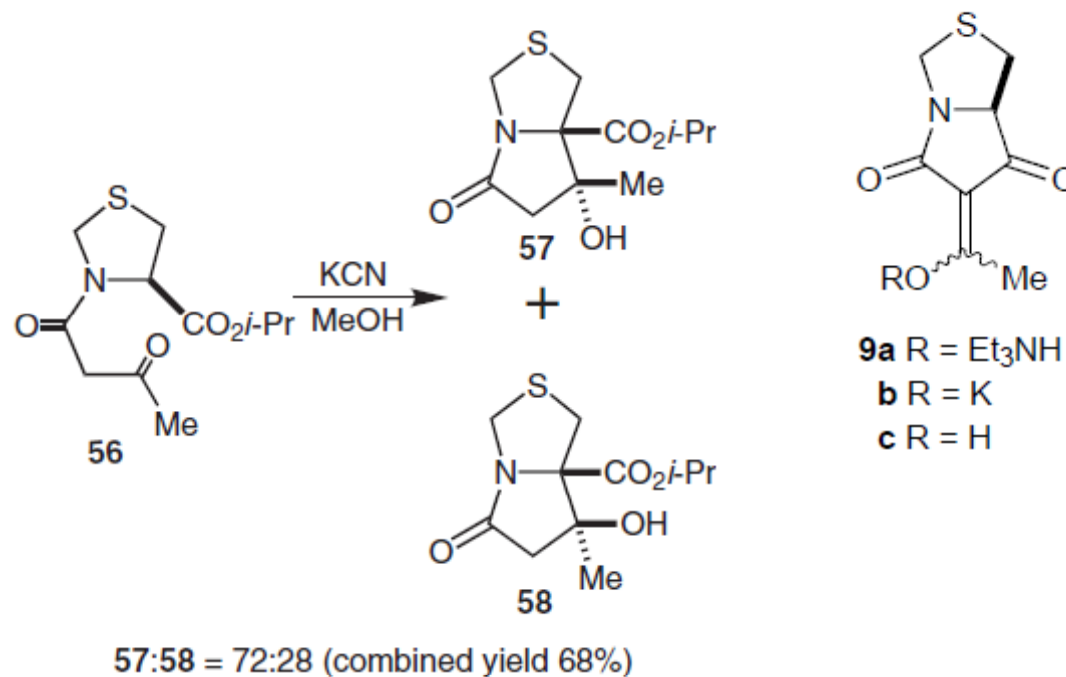
> Kawabata, T.; Kawakami, S.; Majumdar, S. *J. Am. Chem. Soc.* **2003**, *125*, 13012.

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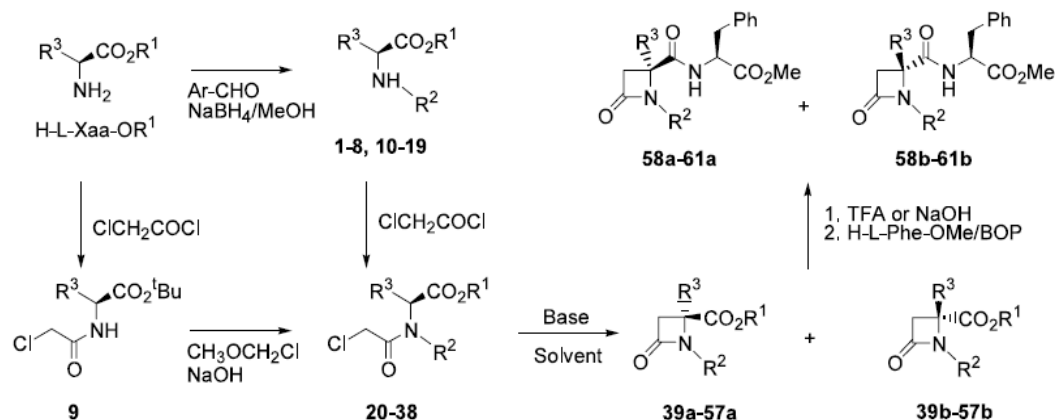
- > Zhao, H.; Hsu, D. C.; Carrier, P.R. *Synthesis* **2005**, 1, 1.
- > Vohra, S. et al. *J. Chem. Soc. Perkin Trans. 1* **1993**, 1761.

Memory of chirality in enolate chemistry



- > Zhao, H.; Hsu, D. C.; Carlier, P.R. *Synthesis* **2005**, 1, 1.
- > Vohra, S. et al. *Chem. Commun.* **1998**, 299.

Memory of chirality in enolate chemistry



Compd.	R ¹	R ²	R ³	Compd.	R ¹	R ²	R ³
1, 20, 39	^t Bu	Pmb	CH ₂ Ph	10, 29, 48	Me	Pmb	CH ₂ C ₆ H ₄ (p-O-di-Cl-Bzl)
2, 21, 40	Me	Pmb	CH ₂ Ph	11, 30, 49	^t Bu	Pmb	CH ₂ In(<i>N</i> -Boc)
3, 22, 41	Bzl	Pmb	CH ₂ Ph	12, 31, 50	^t Bu	Bzl	CH ₂ In
4, 23, 42	Bzl	2,4-Dmb	CH ₂ Ph	13, 32, 51	Me	Pmb	(CH ₂) ₃ -NHZ
5, 24, 43	Me	2,3,4-Tmb	CH ₂ Ph	14, 33, 52	Me	Pmb	(CH ₂) ₄ -NHZ
6, 25, 44	Bzl	2,4,6-Tmb	CH ₂ Ph	15, 34, 53, 58	Me	Pmb	CH ₂ CO ₂ ^t Bu
7, 26, 45	Me	3,4,5-Tmb	CH ₂ Ph	16, 35, 54, 59	Me	Pmb	(CH ₂) ₂ CO ₂ ^t Bu
8, 27, 46	^t Bu	Nph	CH ₂ Ph	17, 36, 55, 60	Me	Pmb	CH ₂ CH(CH ₃) ₂
9, 28, 47	^t Bu	Mom	CH ₂ Ph	18, 37, 56, 60	^t Bu	Pmb	CH ₂ CH(CH ₃) ₂
				19, 38, 57, 61	^t Bu	Bzl	CH ₃

> Bonache, M^a, A. Et al. *Tetrahedron Asymmetry* **2003**, *14*, 2161.

Memory of chirality in enolate chemistry

Table 1. Influence of the R¹ group on the selectivity of the cyclization of L-Phe derivatives.

Entry	Starting compd	R ¹	Base	Solvent	Final compd	Yield (%) ^a	a:b ^b	e.e.
1	20	^t Bu	Cs ₂ CO ₃	MeCN	39	71	78:22 ^c	56
2	21	Me	Cs ₂ CO ₃	MeCN	40	74	78:22 ^d	56
3	22	Bzl	Cs ₂ CO ₃	MeCN	41	75	79:21 ^e	58
4	20	^t Bu	BTPP	MeCN	39	73	76:24 ^c	52
5	21	Me	BTPP	MeCN	40	68	67:33 ^d	34
6	22	Bzl	BTPP	MeCN	41	58	57:43 ^e	14
7	20	^t Bu	BEMP	MeCN	39	81	76:24 ^c	52
8	20	^t Bu	BTPP	DCM	39	58	74:26 ^c	48
9	21	Me	BTPP	DCM	40	65	67:33 ^d	34
10	20	^t Bu	BEMP	DCM	39	65	75:25 ^c	50
11	21	Me	BEMP	DCM	40	68	68:32 ^d	36
12	20	^t Bu	BTPP	NMP	39	56	43:57 ^c	14 ^f
13	21	Me	BTPP	NMP	40	79	34:66 ^d	32 ^f
14	20	^t Bu	BEMP	NMP	39	52	51:49 ^c	2
15	21	Me	BEMP	NMP	40	81	43:57 ^d	14 ^f

^a Isolated yield.

^b Measured by chiral HPLC (Column: OL-389).

^c Hexane/acetone (96:4), 1.5 ml/min.

^d Hexane/EtOH (95:5), 1 ml/min.

^e OL-321, hexane/EtOH (97:3), 1 ml/min.

^f Major isomer has *R* configuration.

> Bonache, M^a, A. et al. *Tetrahedron Asymmetry* **2003**, *14*, 2161.

Memory of chirality in enolate chemistry

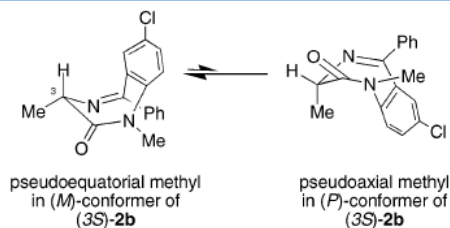
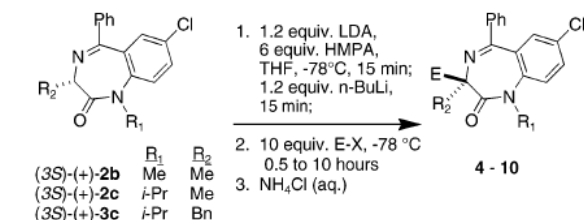


Table 1. Racemizing (**2b**) and Enantioselective (**2c**, **3c**)
Deprotonation/Trapping Reactions of 1,4-Benzodiazepin-2-ones

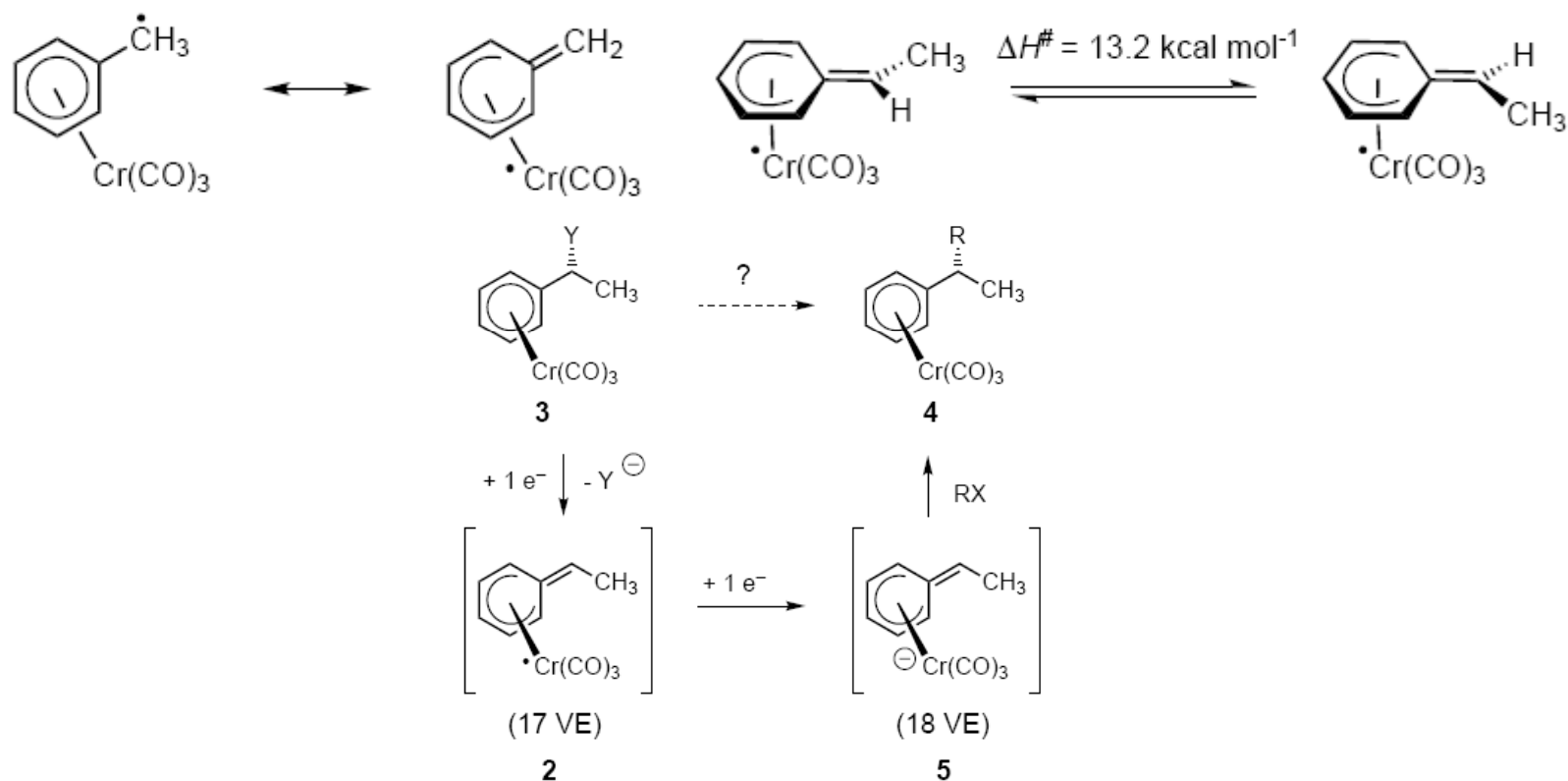


entry	R ₁	R ₂	E ^a	product	% yield	% ee ^b
1	Me	Me	Bn	(+)- 4	72	0 ^c
2	<i>i</i> -Pr	Me	Bn	(+)- 5	74	97 (3 <i>R</i>)
3	<i>i</i> -Pr	Me	4-MeC ₆ H ₄ CH ₂	(+)- 6	68	95 (3 <i>R</i>)
4	<i>i</i> -Pr	Me	2-PhC ₆ H ₄ CH ₂	(+)- 7	70	99
5	<i>i</i> -Pr	Me	allyl	(+)- 8	76	94
6	<i>i</i> -Pr	Me	D	(+)- 9	85 ^d	99 (3 <i>S</i>)
7	<i>i</i> -Pr	Bn	Me	(-)- 5	64	95 (3 <i>S</i>)
8	<i>i</i> -Pr	Bn	allyl	(+)- 10	57	86

^a Electrophiles used: BnBr, 4-MeC₆H₄CH₂Br, 2-PhC₆H₄CH₂Br, allyl bromide, D-OTFA, MeI. ^b % ee measured by chiral stationary phase HPLC (Chiralcel OD, AD). ^c Racemic **4** is also obtained if BnBr is added only 10 s after deprotonation by LDA. ^d The extent of deuteration is 96%.

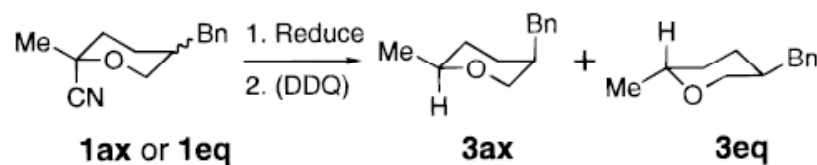
> Carlier, P. R. et al. *JACS* **2003**, *125*, 11482.

Memory of chirality in complex chemistry



- > Schmalz, H.-G.; Koning, C.B.S.; Bernicke, D.; Siegel, S.; Pfletschinger, A. *Angew. Chem. Int. Ed.* **1999**, 38, 1620.

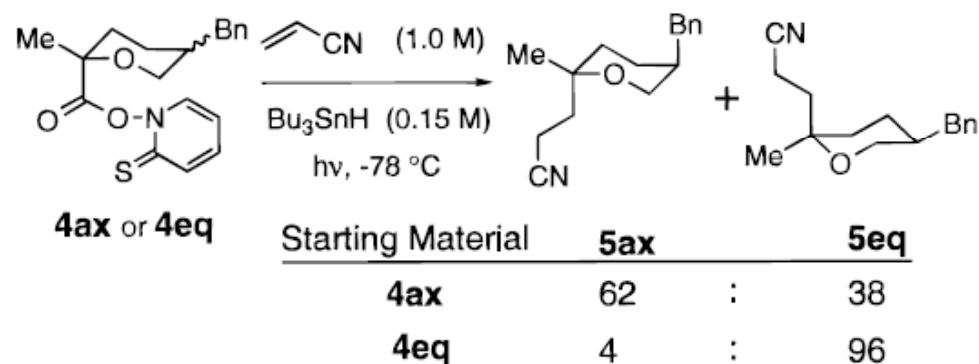
Retentive radical trapping controlled by a slow ring inversion



entry	substrate	conditions ^a	ratio (3ax:3eq) ^b
1	1ax	Li/NH ₃ (-78 °C)	66:34
2	1eq	Li/NH ₃ (-78 °C)	4:96
3	1ax	LiDBB (-78 °C)	66:34
4	1eq	LiDBB (-78 °C)	5:95
5	1ax	Li/NH ₃ (-33 °C)	39:61
6	1eq	Li/NH ₃ (-33 °C)	5:95
7	1ax	LiDBB (-95 °C)	71:29

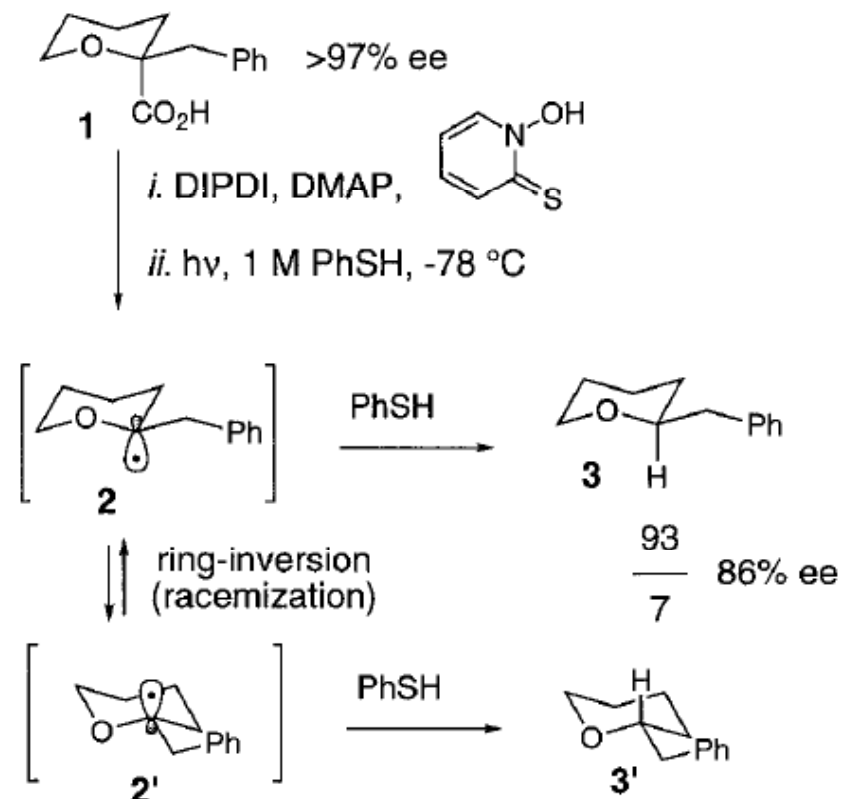
> Buckmelter, A.J.; Powers, J.P.; Rychnovsky, S.D. *J. Am. Chem. Soc.* **1998**, *120*, 5589

Retentive radical trapping controlled by a slow ring inversion



> Buckmelter, A.J.; Powers, J.P.; Rychnovsky, S.D. *J. Am. Chem. Soc.* **1998**, *120*, 5589

Retentive radical trapping controlled by a slow ring inversion



- > Buckmelter, A.J.; Kim, A.I.; Rychnovsky, S.D. *J. Am. Chem. Soc.* **2000**, 122, 9386

Retentive radical trapping controlled by a slow ring inversion

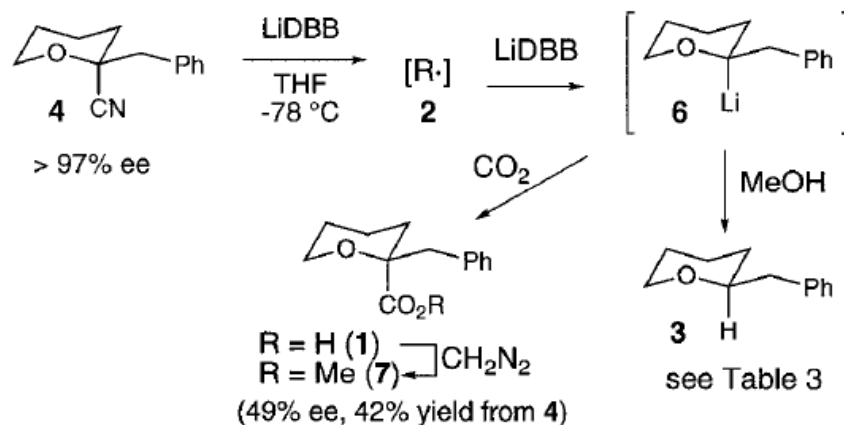


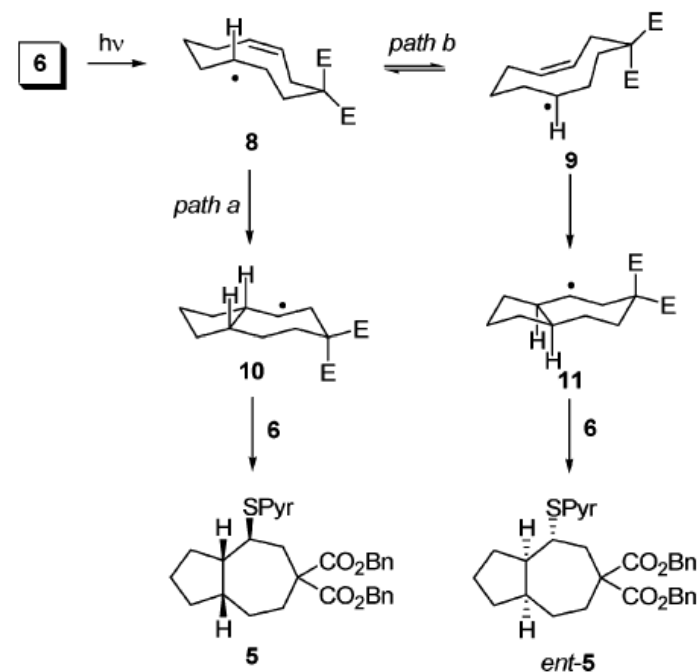
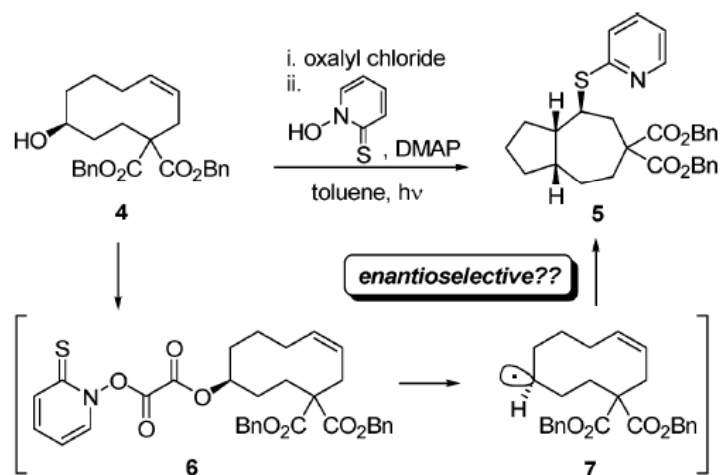
Table 3. Reductive Decyanations of **4** with LiDBB in THF

conditions ^a	optical purity of 3
0.12 M LiDBB, $-78\text{ }^\circ\text{C}$	26% ee
0.31 M LiDBB, $-78\text{ }^\circ\text{C}$	30% ee
0.47 M LiDBB, $-78\text{ }^\circ\text{C}$	39% ee
0.63 M LiDBB, $-78\text{ }^\circ\text{C}$	40% ee
Inverse addition, $-78\text{ }^\circ\text{C}$	9% ee

^a The nitrile in THF was added to the solution of Li in NH_3 unless otherwise noted.

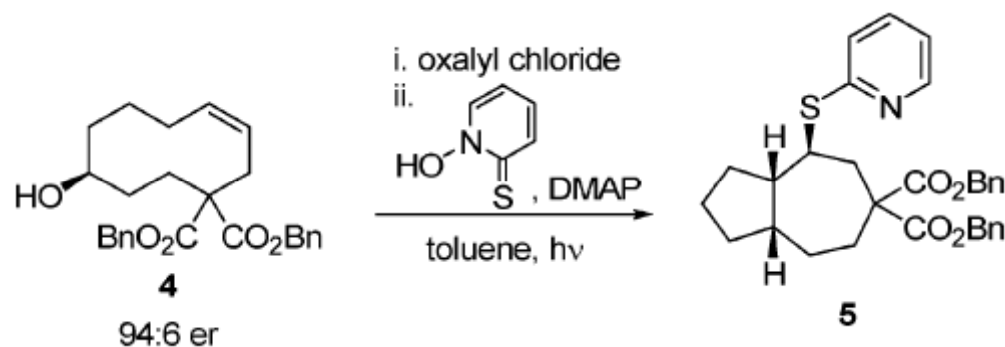
- > Buckmelter, A.J.; Kim, A.I.; Rychnovsky, S.D. *J. Am. Chem. Soc.* **2000**, *122*, 9386

Memory of chirality in radical cyclisation



> Dalgard, J.E.; Rychnovsky, S.D. *Org. Lett.* **2004**, 6, 2713

Memory of chirality in radical cyclisation



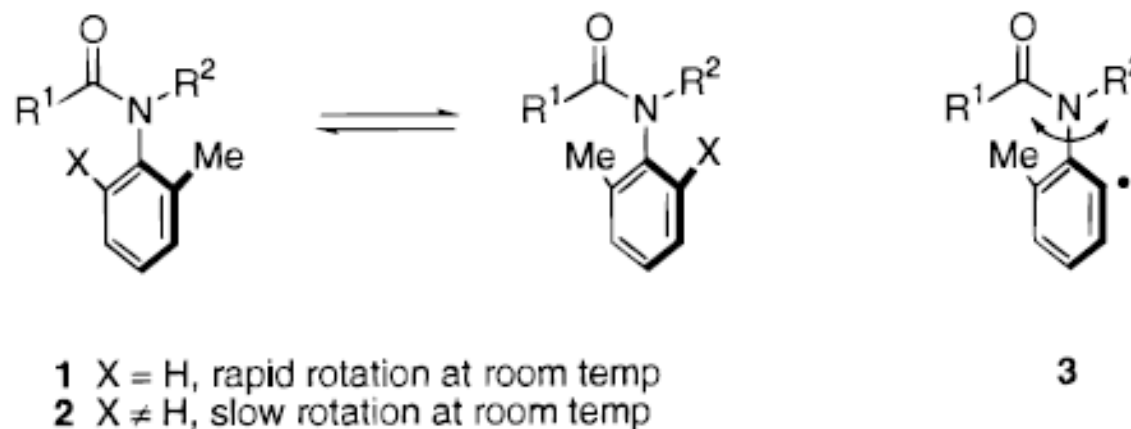
entry ^a	temp (°C)	yield (%)	er ^b
1	23	88	63:37
2	0	67	79:21
3	-15	51	84:16
4	-35	43	84:16

^a Reaction mixtures were photolyzed with a 500-W tungsten lamp.

^b Enantiomeric ratio determined by chiral HPLC analysis (Diacel OD-H column), 90:10 hexanes/IPA, 0.9 mL/min.

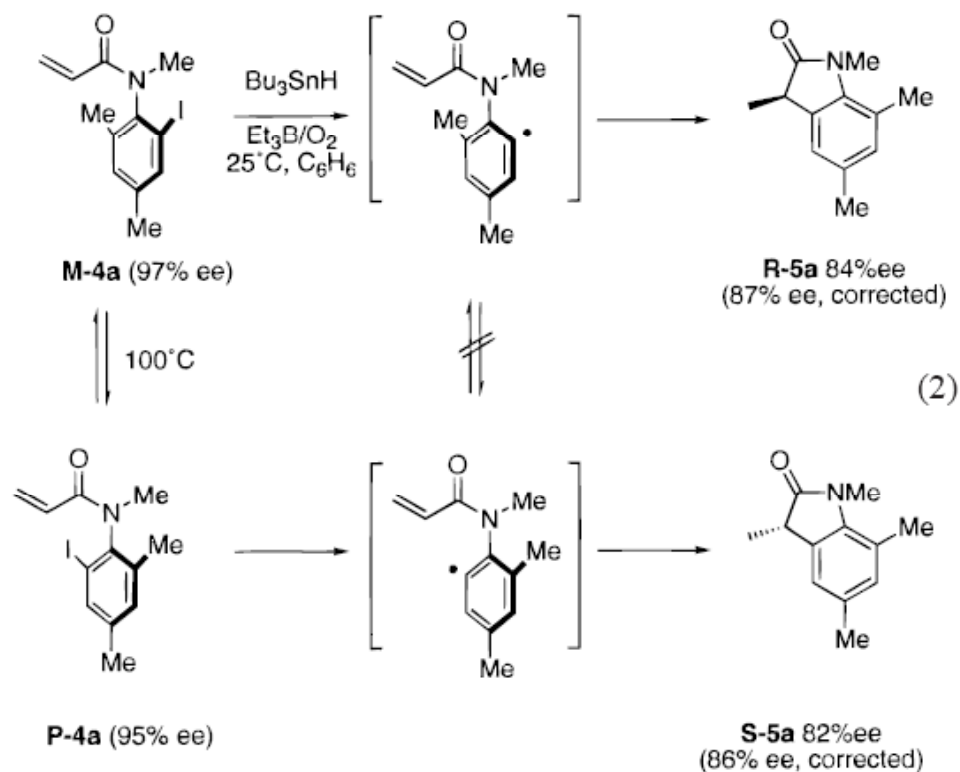
> Dalgard, J.E.; Rychnovsky, S.D. *Org. Lett.* **2004**, *6*, 2713

Memory of chirality in radical cyclisation



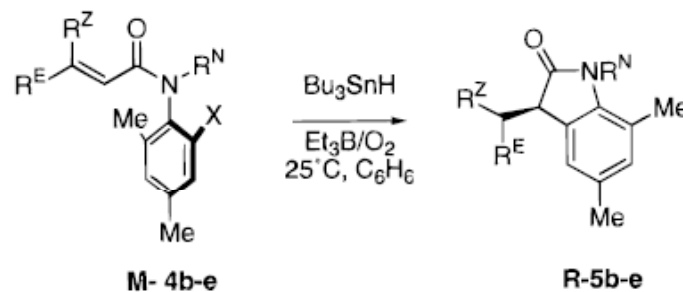
> Curran, D.P.; Liu, W.; Chen, C.H.-T. *J. Am. Soc.* **1999**, *121*, 11012.

Memory of chirality in radical cyclisation



> Curran, D.P.; Liu, W.; Chen, C.H.-T. *J. Am. Soc.* **1999**, *121*, 11012.

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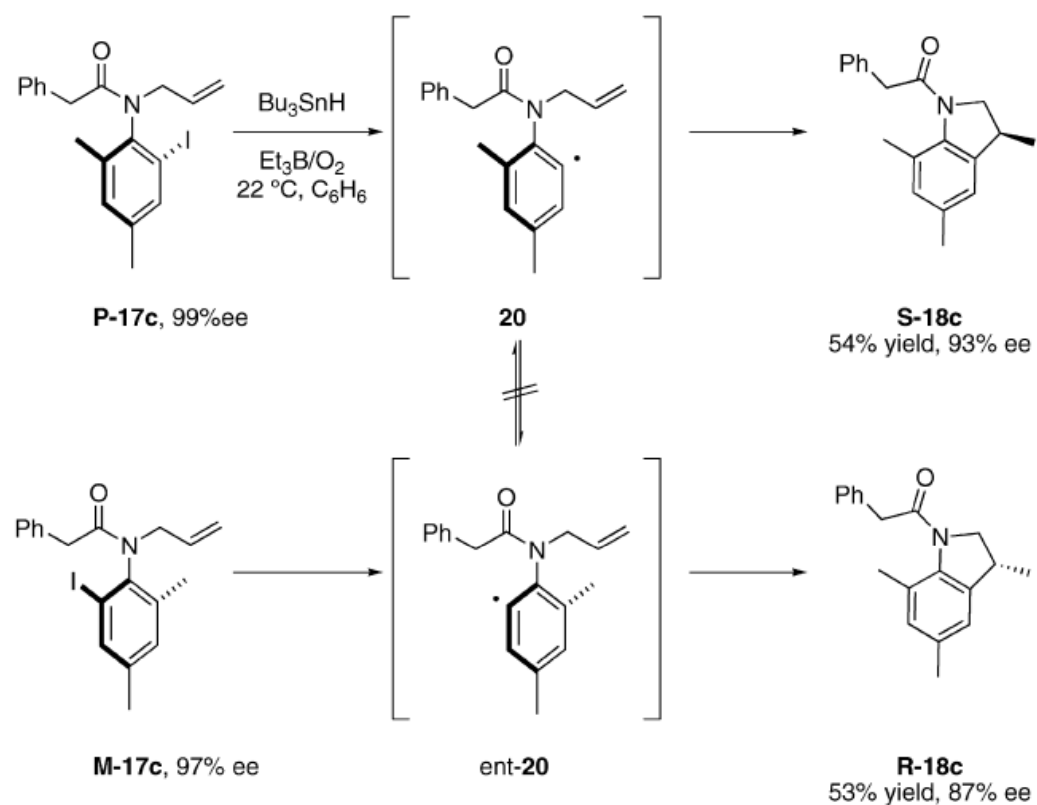


entry	precursor	R ^N	R ^E	R ^Z	X	product	yield, ^a %	ee, ^b %
1	M-4b-I	Me	Me	H	I	R-5b	73	89
2	P-4b-I	Me	Me	H	I	S-5b	70	85
3	M-4b-Br	Me	Me	H	Br	R-5b	60	92
4	P-4b-Br	Me	Me	H	Br	S-5b	60	87
5	M-4c	Me	Ph	H	I	R-5c	75	94
6	P-4c	Me	Ph	H	I	S-5c	73	92
7	M-4d	Me	Me	Me	I	R-5d	91	49
8	P-4d	Me	Me	Me	I	S-5d	88	50
9	M-4e	Et	Me	H	I	R-5e	93	90
10	P-4e	Et	Me	H	I	S-5e	86	90

^a Determined by NMR against an internal standard. ^b Corrected for ee of **4**, which was 95–98%.

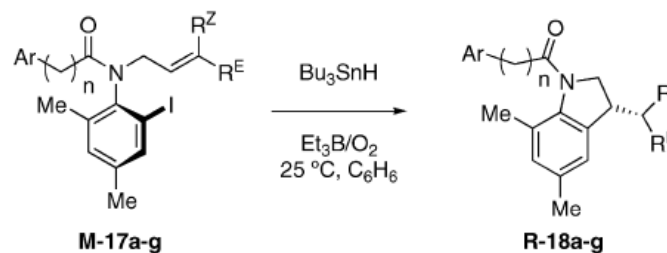
- > Curran, D.P.; Liu, W.; Chen, C.H.-T. *J. Am. Soc.* **1999**, *121*, 11012.

Memory of chirality in radical cyclisation



> Curran, D.P.; Chen, C.H.-T.; Geib, S.J.; Lapierre, A.J.B. *Tetrahedron* **1999**, *60*, 4413.

Memory of chirality in radical cyclisation



Entry	Precursor ^a	Ar	n	R ^Z	R ^E	Product	Yield ^b	%ee _{SM} ^c	%ee _P ^d	Chirality transfer ^e (%)
1	P-17a	Ph	0	H	H	S-18a	95	99	86	93
2	M-17a	Ph	0	H	H	R-18a	92	>99	87	93
3	P-17b	4-BrC ₆ H ₄	0	Me	Me	S-18b	72	99	48	72
4	M-17b	4-BrC ₆ H ₄	0	Me	Me	R-18b	95	98	47	72
5	P-17c	Ph	1	H	H	S-18c	54	>99	93	97
6	M-17c	Ph	1	H	H	R-18c	53	97	87	95
7	P-17d	Ph	1	H	Ph	S-18d	40	>99	74	87
8	M-17d	Ph	1	H	Ph	R-18d	50	98	76	88
9	P-17e	Ph	1	H	Me	S-18e	77	>99	79	89
10	M-17e	Ph	1	H	Me	R-18e	71	>99	83	91
11	P-17f	Ph	1	Me	Me	S-18f	79	>99	63	81
12	M-17f	Ph	1	Me	Me	R-18f	81	>99	57	78
13	P-17g	Ph	2	H	H	S-18g	67	96	85	94
14	M-17g	Ph	2	H	H	R-18g	74	>99	90	95

^a The P configuration is assigned to the dextrorotatory enantiomers and M to levorotatory.

^b Isolated yield after chromatography.

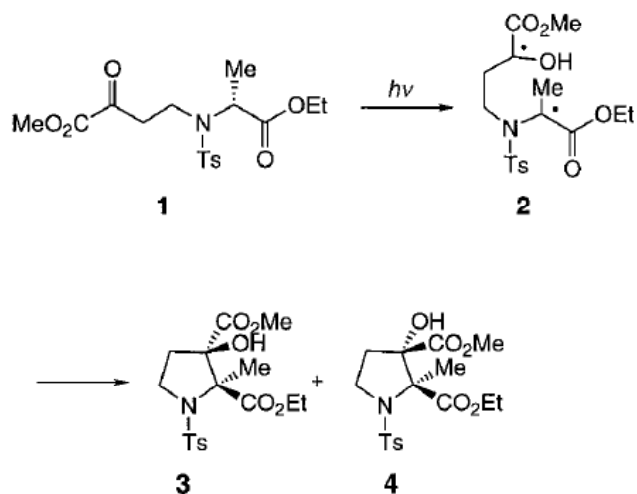
^c ee of precursor.

^d ee of product **18**.

^e Yield (not excess) of the major enantiomer of **18** expected from an enantiopure sample of **17**.

> Curran, D.P.; Chen, C.H.-T.; Geib, S.J.; Lapierre, A.J.B. *Tetrahedron* **1999**, *60*, 4413.

Memory of chirality in radical cyclisation

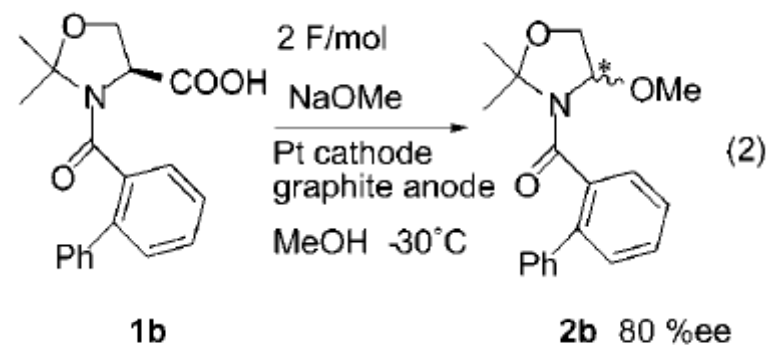
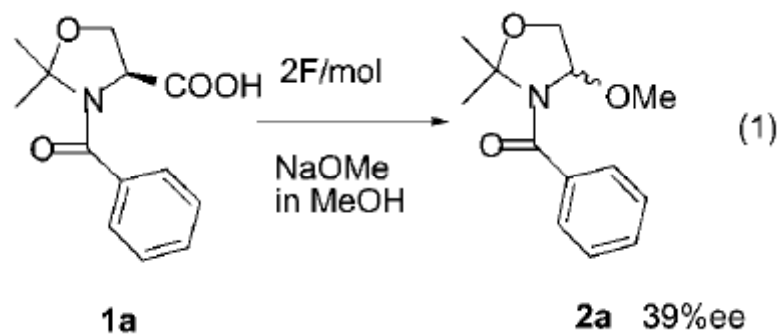


Conditions	3:ent-3	4:ent-4	<i>cis:trans</i>	Overall yield [%] ^[a]
$h\nu$ /naphthalene (1M)	24	16	5.7	47 ^[b]
$h\nu$ /naphthalene (0.5 M)	18	13	5.3	50 ^[b]
$h\nu$ /isoprene (0.5 M)	9.4	3.0	2.9	47 ^[b]
$h\nu$ /O ₂	9.6	3.6	2.6	48 ^[c]
$h\nu$ /Ar	2.4	1.6	0.9	35 ^[c]
$h\nu$ /benzophenone (1M)/Ar	1.4	1.4	0.8	10 ^[d]

[a] Based on the conversion (80–90%). [b] Irradiation time 10 h.
[c] Irradiation time 2 h. [d] Irradiation time 20 min.

> Giese, B. et al. *Angew. Chem. Int. Ed.* **1999**, *38*, 2586.

Memory of chirality involving carbocation intermediates



> Wanyoike, G. N.; Onomura, O.; Maki, T.; Matsumura, Y. *Org. Lett.* **2002**, *4*, 1875.

Memory of chirality involving carbocation intermediates

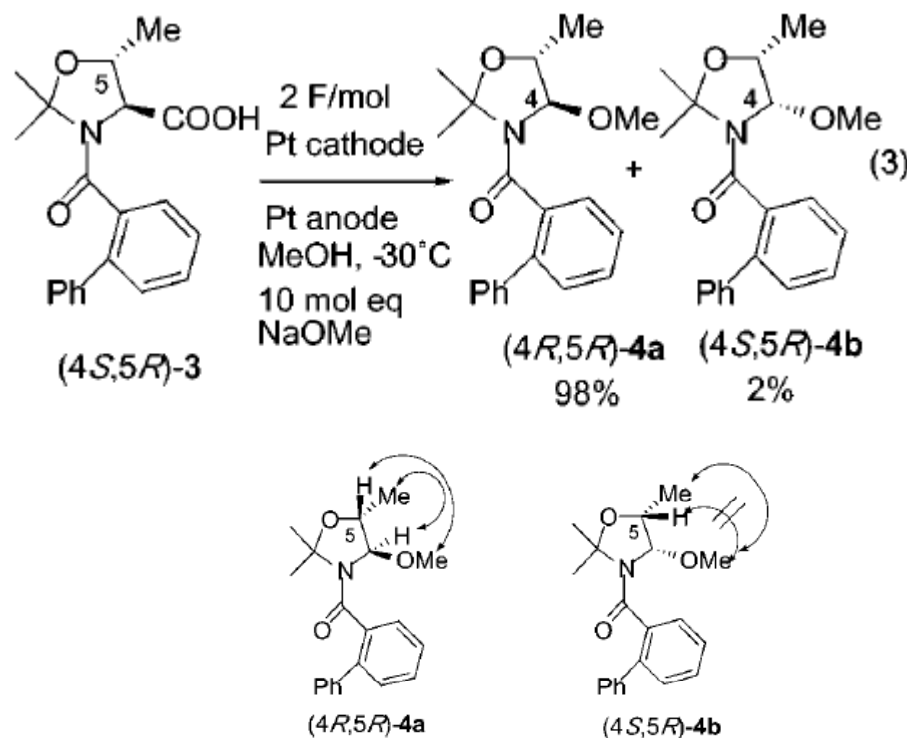
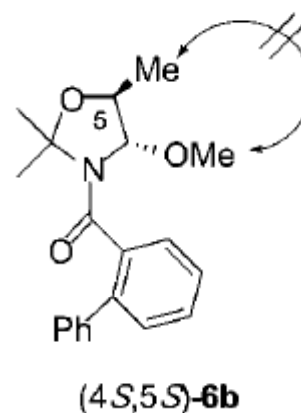
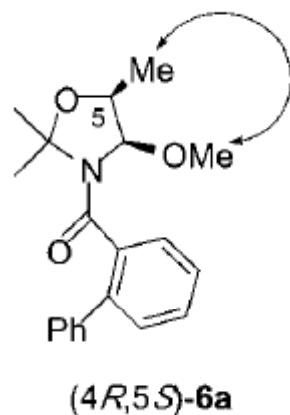
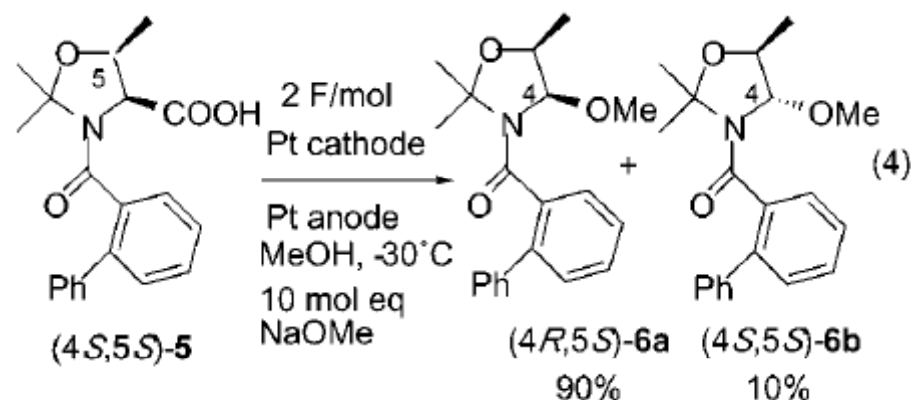


Figure 1. NOESY for 4a and 4b

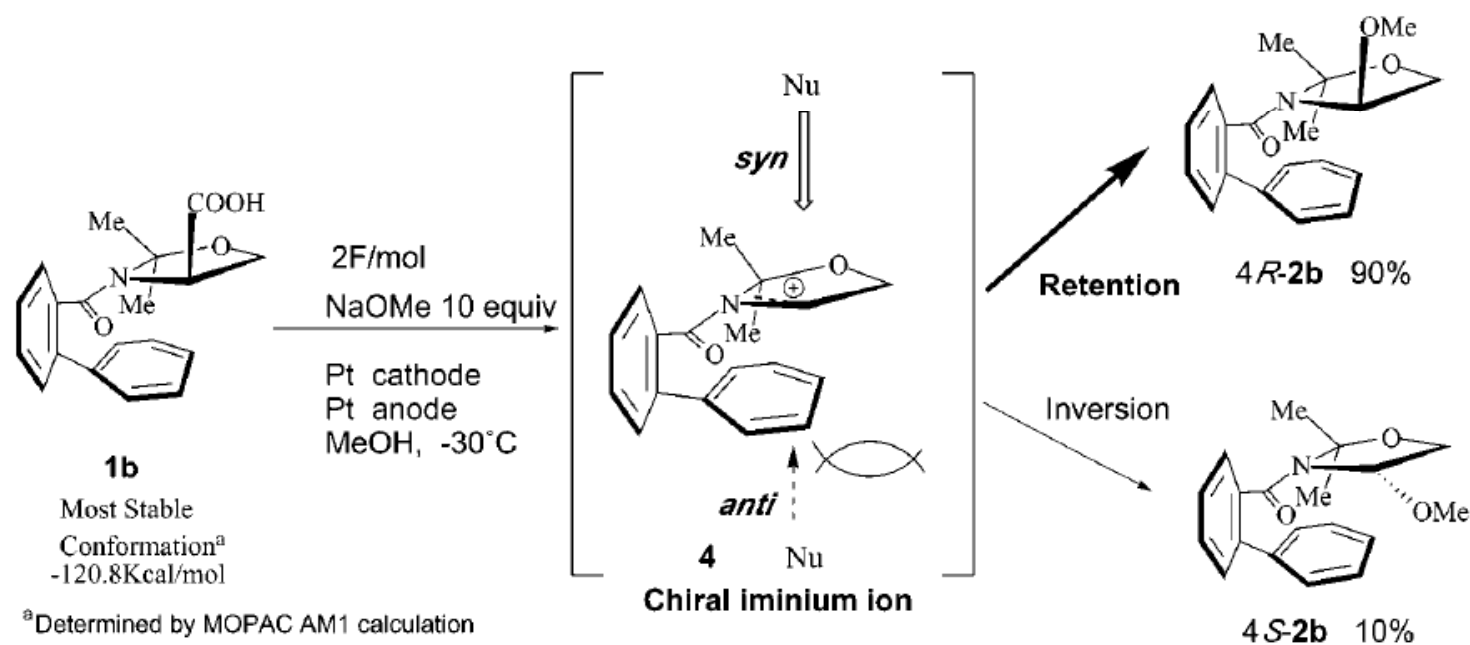
- > Wanyoike, G. N.; Onomura, O.; Maki, T.; Matsumura, Y. *Org. Lett.* **2002**, *4*, 1875.

Memory of chirality involving carbocation intermediates



- > Wanyoike, G. N.; Onomura, O.; Maki, T.; Matsumura, Y. *Org. Lett.* **2002**, *4*, 1875.

Memory of chirality involving carbocation intermediates



- > Wanyoike, G. N.; Onomura, O.; Maki, T.; Matsumura, Y. *Org. Lett.* **2002**, *4*, 1875.

Conclusion

- > Memory of chirality is an emerging strategy for enantioselective synthesis
- > To date, most MOC experiments were carried out in enolate chemistry, but MOC is also performed in radical chemistry and with involvement of carbocations as reactive intermediates.
- > Three conditions have to be fulfilled for MOC:
 - > The chiral starting material must be transformed in a conformationally chiral intermediate
 - > The intermediate must not racemize during the timescale of the reaction
 - > The reaction from the reactive intermediate has to work with a high ee.