

A Diastereomer Method for Determining % EE by ^1H NMR and/or MS Spectrometry with Complete Removal of the Kinetic Resolution Effect

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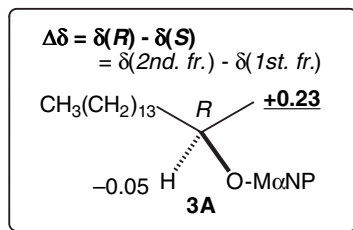
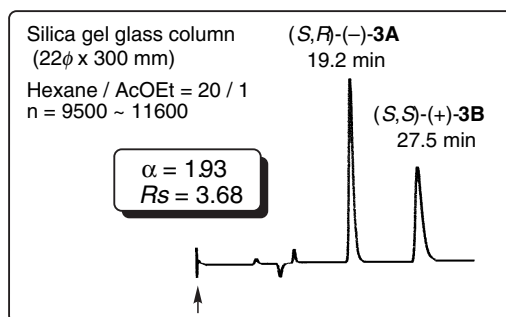
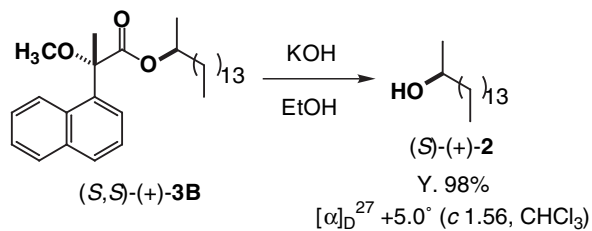
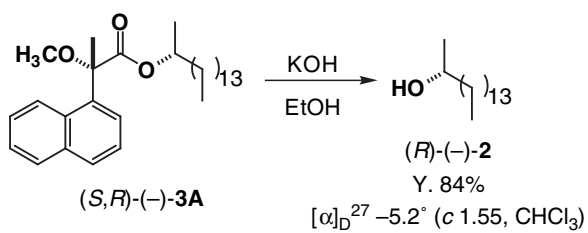
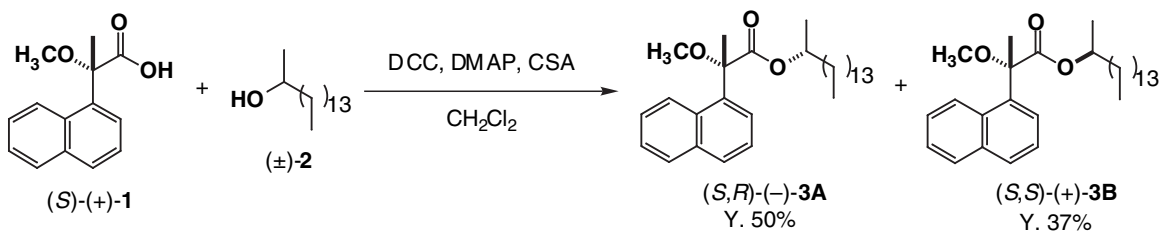
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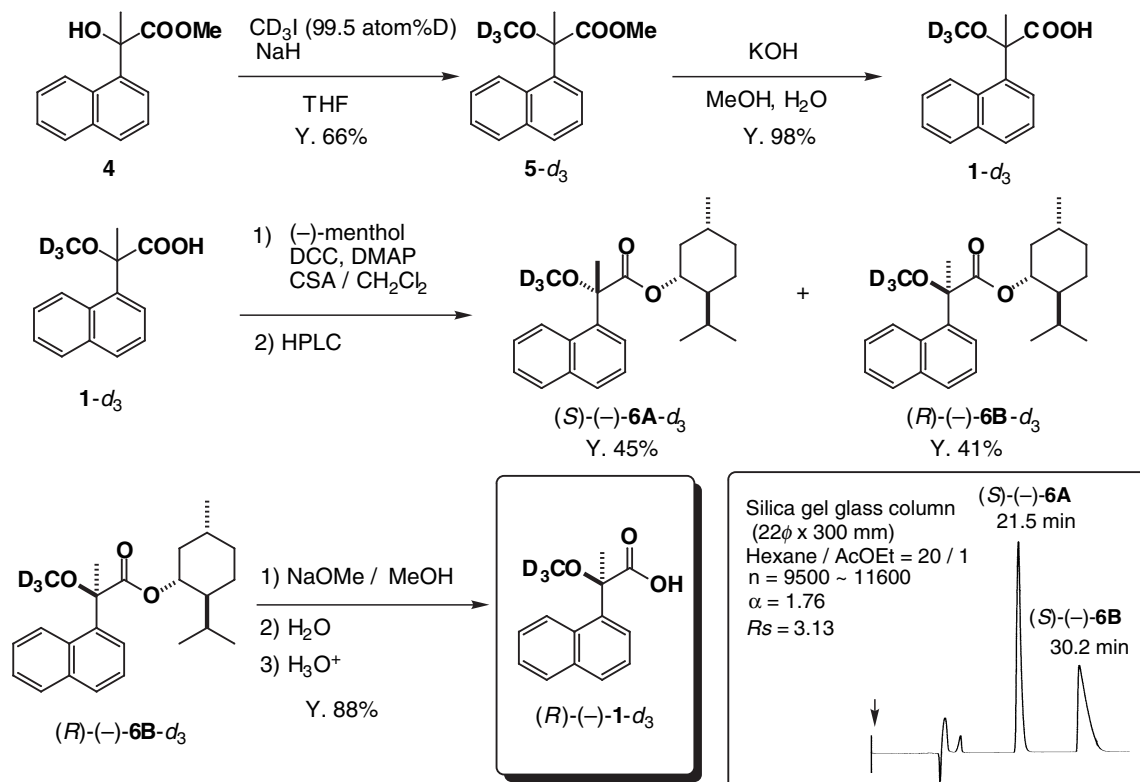
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Supporting Information Available: Synthetic schemes, preparation procedure of M α NP ester, ^1H NMR spectra, and tables of ^1H NMR and MS spectroscopic data. This material is available free of charge via the Internet at <http://pubs.acs.org>

Scheme 2. Preparation of Enantiopure 2-Hexadecanol



Scheme 3. Synthesis of (*R*)-(-)-**1-d₃**



Preparation of M α NP esters. A mixture of M α NP acids (*S*)-(+)-**1** and (*R*)-(-)-**1-d**₃ (ratio, 1:0.987, total 8.1 mg, 0.0349 mmol), partially enriched chiral 2-hexadecanol (*R*)-**2** (60.87% ee, 9.237 mg, 0.0381 mmol), 1,3-dicyclohexylcarbodiimide (DCC, 40.4 mg, 0.196 mmol), 4-dimethyl-aminopyridine (DMAP, 8.4 mg, 0.069 mmol), and 10-camphorsulfonic acid (CSA, 7.8 mg, 0.034 mmol) in CH₂Cl₂ (1.0 mL) was stirred at 20–40 °C overnight. After water (0.5 mL) and diethyl ether (5.9 mL) were added, the mixture was stirred for 1 h to decompose excess DCC. The mixture was stirred with anhydrous MgSO₄ for 10 min and then filtered. The filtrate was evaporated to dryness in vacuo and the residue was subjected to short column chromatography on silica gel (hexane/EtOAc 20:1). The diastereomeric mixture obtained was separated by HPLC on silica gel (hexane/EtOAc 20:1): separation factor $\alpha = 1.96$; resolution factor $R_s = 4.15$. The first eluted ester **3a** was obtained as colorless syrup (6.0 mg, 37%): ¹H NMR (600 MHz, CDCl₃) δ 0.88 (3 H, dd, $J = 7.2, 6.7$ Hz), 0.88 (3 H, d, $J = 6.2$ Hz), 1.00–1.45 (26 H, m), 1.97 (3 H, s), 3.12 (2.46 H, s), 4.91 (1 H, dqd, $J = 6.7, 6.2, 5.3$ Hz), 7.43–7.47 (3 H, m), 7.62 (1 H, br d, $J = 7.3$ Hz), 7.80–7.85 (2 H, m), 8.37–8.40 (1 H, m).

The second eluted ester **3b** was obtained as colorless syrup (5.2 mg, 32%): ¹H NMR (600 MHz, CDCl₃) δ 0.50 (2 H, m), 0.83 (2 H, m), 0.89 (3 H, dd, $J = 7.1, 7.0$ Hz), 1.03 (2 H, m), 1.11 (3 H, d, $J = 6.2$ Hz), 1.09–1.36 (20 H, m), 1.98 (3 H, s), 3.09 (0.60 H, s), 4.86 (1 H, dqd, $J = 6.4, 6.2, 4.8$ Hz), 7.43–7.47 (3 H, m), 7.58 (1 H, br d, $J = 7.3$ Hz), 7.81–7.84 (2 H, m), 8.43–8.45 (1 H, m).

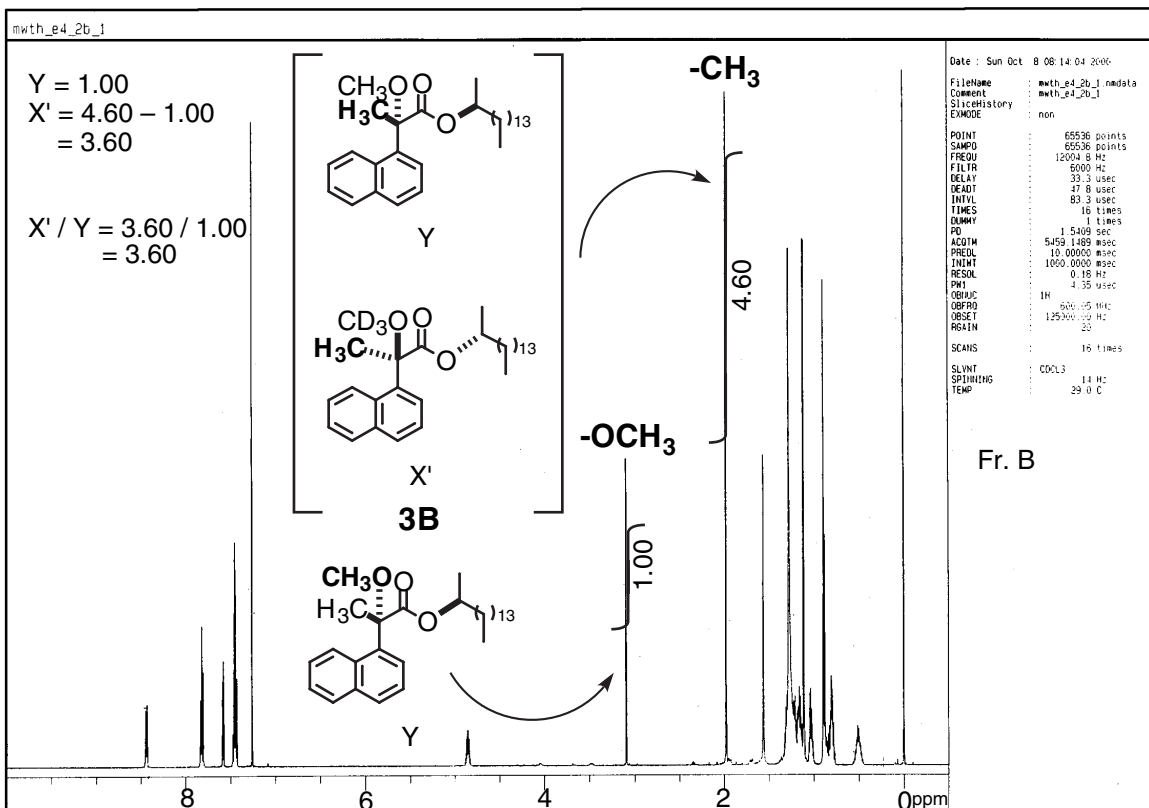
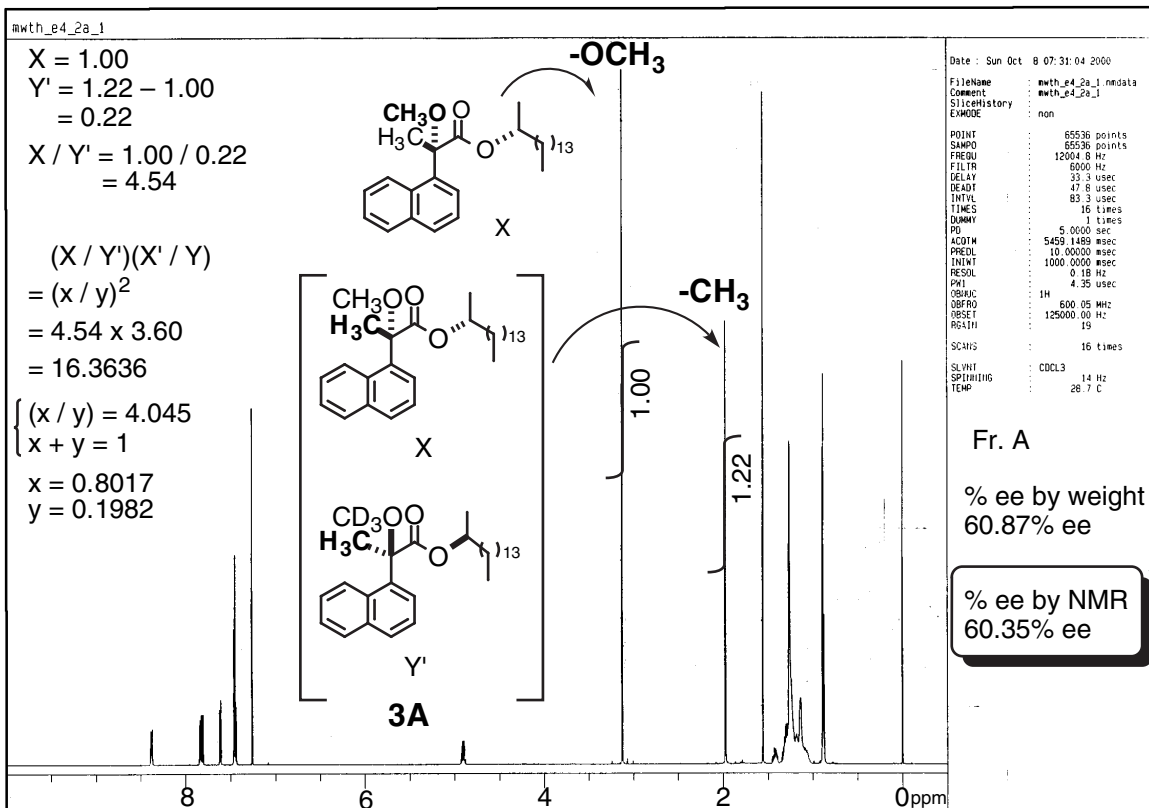
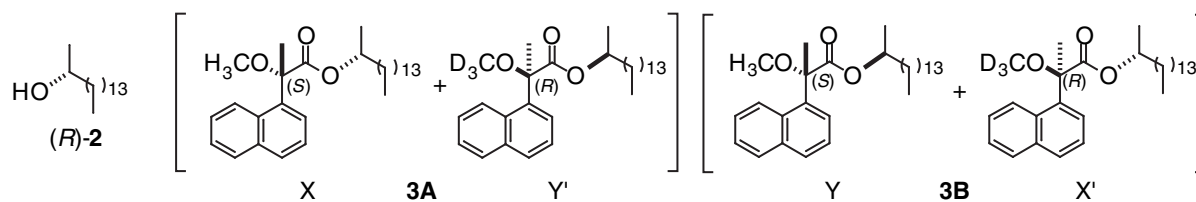


Figure 5. ¹H NMR spectra of diastereomeric MoαNP esters.

Table 1. Determination of % ee by ^1H NMR spectroscopy using $\text{Mo}\alpha\text{NP-}d_3$ acid.

entry	Weight					NMR							%ee weight	%ee NMR
	<i>rac</i> -2 (mg)	(<i>R</i>)-2 (mg)	x: (<i>R</i>)-2 (mg)	y: (<i>S</i>)-2 (mg)	x/y	X	Y	X'	Y'	X/Y'	X'/Y	x/y		
1	11.5000	0.0000	5.7500	5.7500	1.000	1.00	1.00	1.00	1.00	1.00	1.00	1.000	0.00	0.00
2	8.2535	1.0210	5.1477	4.1267	1.247	1.00	1.00	1.02	0.65	1.54	1.02	1.253	11.0	11.2
3	7.5004	1.8329	5.5831	3.7502	1.489	1.00	1.00	1.22	0.58	1.72	1.22	1.450	19.6	18.4
4	6.4093	2.7033	5.9079	3.2046	1.844	1.00	1.00	1.50	0.44	2.27	1.50	1.846	29.8	29.7
5	5.4922	3.6183	6.3644	2.7461	2.317	1.00	1.00	2.12	0.42	2.38	2.12	2.247	39.7	38.4
6	4.7658	4.6908	7.0737	2.3829	2.968	1.00	1.00	2.54	0.29	3.45	2.54	2.960	49.6	49.5
7	3.6144	5.6225	7.4297	1.8072	4.111	1.00	1.00	3.60	0.22	4.54	3.60	4.045	60.9	60.4
8	2.7561	6.4306	7.8086	1.3780	5.667	1.00	1.00	4.42	0.13	7.69	4.42	5.831	70.0	70.7
9	1.8202	7.3509	8.2610	0.9101	9.077	2.64	1.00	7.55	0.24	11.00	7.55	9.113	80.2	80.2
10	0.9864	8.2779	8.7711	0.4932	17.784	1.00	1.00	15.58	0.05	20.00	15.58	17.652	89.4	89.3
11	0.7024	8.4420	8.7932	0.3512	25.038	2.76	0.13	2.70	0.16	17.25	20.77	18.928	92.3	90.0
12	0.5993	8.6381	8.9378	0.2996	29.827	2.90	0.05	1.35	0.03	96.67	27.00	51.088	93.5	96.2
13	0.3694	8.8575	9.0422	0.1847	48.956	2.86	0.07	2.71	0.04	71.50	38.71	52.612	96.0	96.3
14	0.1431	9.1803	9.2518	0.0716	129.31	2.77	0.04	2.85	0.08	34.62	71.25	49.669	98.5	96.1
15	0.0801	9.1467	9.1868	0.0400	229.38	2.55	0.03	2.84	0.34	7.50	94.67	26.646	99.1	92.8



Scheme 4. Synthesis of (*R*)-(-)-1-*d*₆

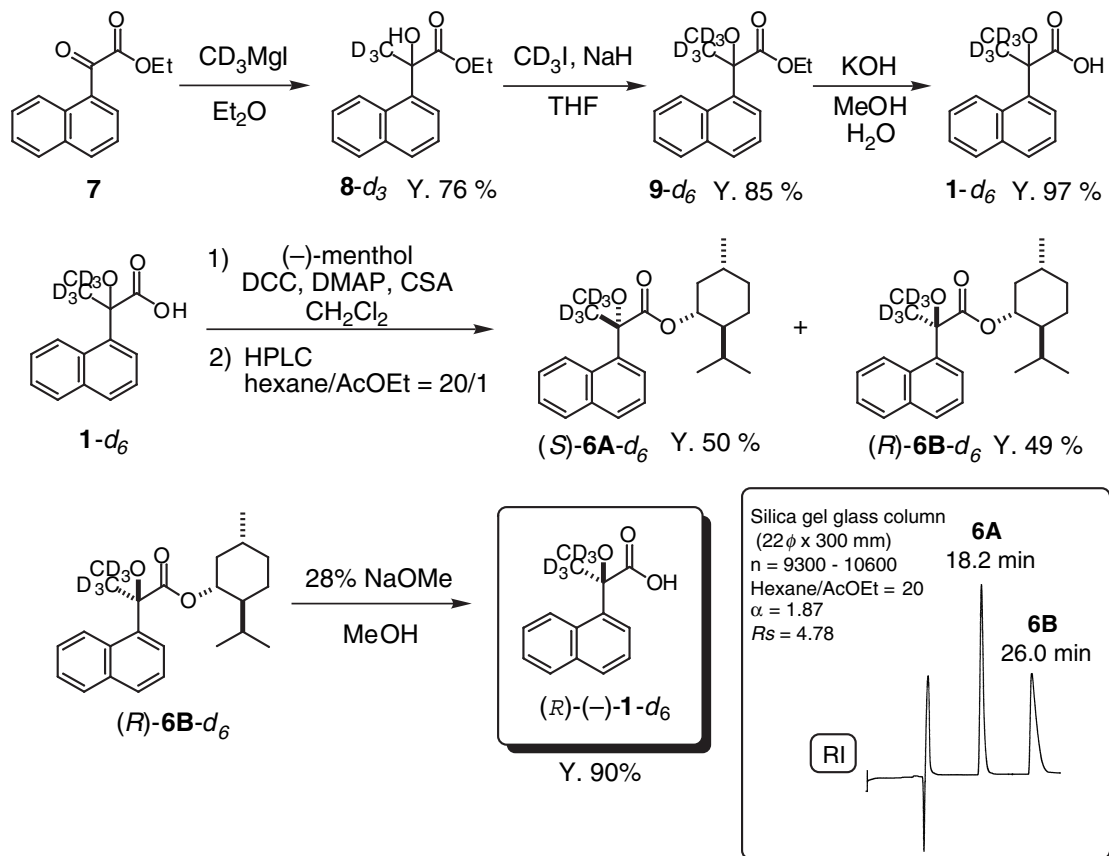


Table 2. Determination of % ee by MS spectrometry using M α NP-*d*₆ acid (background correction).

entry	weight					ion intensity							%ee weight	%ee EI-MS
	<i>rac</i> -2 (mg)	(<i>R</i>)-2 (mg)	x: (<i>R</i>)-2 (mg)	y: (<i>S</i>)-2 (mg)	x/y	[M] _A ⁺	[M+6] _A ⁺	[M] _B ⁺	[M+6] _B ⁺	$\frac{[M]_A^+}{[M+6]_A^+}$	$\frac{[M+6]_B^+}{[M]_B^+}$	x/y		
1	12.1000	0.0000	6.0500	6.0500	1.000	35.506	34.984	35.131	35.368	1.0149	1.0067	1.0108	0.00	0.54
2	10.8184	1.2816	6.6908	5.4092	1.237	34.051	29.022	26.077	35.725	1.1733	1.3700	1.2678	10.59	11.81
3	9.6350	2.4937	7.3112	4.8175	1.518	39.060	27.425	23.397	38.550	1.4242	1.6476	1.5319	20.56	21.01
4	8.3972	3.5910	7.7896	4.1986	1.855	42.510	24.491	23.487	44.146	1.7357	1.8062	1.8062	29.95	28.73
5	7.2305	4.8407	8.4560	3.6152	2.339	45.060	21.549	18.373	47.441	2.0911	2.5821	2.3236	40.10	39.82
6	5.9939	6.0377	9.0346	2.9970	3.015	47.436	18.760	15.403	50.359	2.5285	3.2694	2.8752	50.18	48.39
7	4.8817	7.2567	9.6976	2.4408	3.973	50.662	14.668	12.406	54.253	3.4540	4.3732	3.8865	59.78	59.07
8	3.6670	8.4631	10.2966	1.8335	5.616	52.284	11.221	8.607	55.278	4.6594	6.4224	5.4703	69.77	69.09
9	2.4389	9.6222	10.8416	1.2195	8.891	59.405	8.067	6.533	59.819	7.3638	9.1563	8.2113	79.78	78.29
10	1.2583	10.7584	11.3876	0.6291	18.100	61.421	4.589	3.245	62.721	13.3855	19.3262	16.0839	89.53	88.29
11	0.9682	11.0236	11.5077	0.4841	23.771	63.353	3.647	2.550	63.680	17.3702	24.9730	20.8275	91.93	90.84
12	0.7203	11.2910	11.6511	0.3602	32.351	62.540	2.736	2.022	60.419	22.8551	29.8871	26.1356	94.00	92.63
13	0.4835	11.5085	11.7502	0.2418	47.429	63.353	2.076	1.651	66.292	30.5172	40.1458	35.0020	95.97	94.44
14	0.2396	11.7726	11.8924	0.1198	99.269	62.829	1.188	0.897	61.577	52.8972	68.6151	60.2457	98.01	96.73
15	0.1275	11.8630	11.9268	0.0637	187.09	60.621	0.806	0.663	57.728	75.2158	87.1145	80.9468	98.94	97.56

