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TETRAHEDRON: *ASYMMETRY*

Preparation of highly optically active substituted 2,3-methanocinnamyl alcohols

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Abstract—Cyclopropanation of a variety of substituted cinnamyl alcohols with Et_2Zn and CH_2I_2 proceeded in the presence of a catalytic amount of (*S*)-2-(methanesulfonyl)amino-1-(*p*-toluenesulfonyl)amino-3-phenylpropane to afford the corresponding cyclopropylmethanols in excellent yields and with moderate to high enantioselectivity (51–86% ee). Highly enantiomerically enriched substituted 2,3-methanocinnamyl alcohols (84–97% ee) were obtained by conversion of the corresponding 2,3-methanocinnamyl alcohols produced in the enantioselective cyclopropanation to the 3,5-dinitrobenzoyl ester derivatives, followed by recrystallization and hydrolysis.

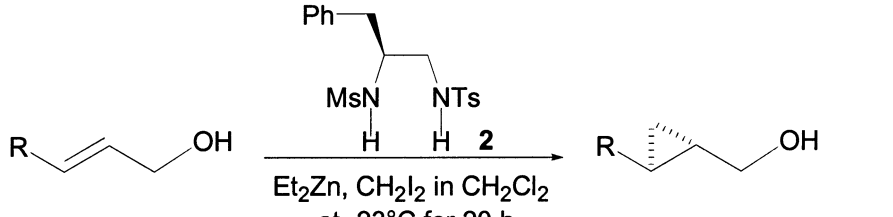
1. Introduction

Since Kobayashi developed the first enantioselective Simmons–Smith cyclopropanation catalyzed by a C_2-symmetrical disulfonamide–zinc or aluminum complex, Denmark's and our research group have optimized conditions for Kobayashi's method, and reported enantioselective cyclopropanations using a catalytic amount of a new type of disulfonamide derived from an α-amino acid, respectively.[1,2] Herein, we describe a method for catalytic enantioselective Simmons–Smith cyclopropanation of substituted cinnamyl alcohols **1** using (*S*)-2-(methanesulfonyl)amino-1-(*p*-toluenesulfonyl)amino-3-phenylpropane **2** and the preparation of highly optically active substituted 2,3-methanocinnamyl alcohols **3**.

2. Results and discussion

In a preliminary investigation, the reaction of cinnamyl alcohol **1a** with Et_2Zn and CH_2I_2 in the presence of a catalytic amount of **2** afforded the cyclopropane product **3a** with 82% ee, which was slightly lower than that obtained (85% ee) when the reaction was completed in the presence of (*S*)-2-(methanesulfonyl)amino-1-(*p*-nitrobenzenesulfonyl)amino-3-phenyl-propane **2′**.[2] On the other hand, enantiomeric excesses (89% ee each) of the products from the reactions of *trans*-5-phenyl-2-penten-1-ol **1b** and *trans*-4-(triphenyl)methoxy-2-butene-1-ol **1c** in the presence of **2** were higher than those obtained in analogous reactions in the presence of **2′** (54 and 65% ee, respectively).

The cyclopropanation of cinnamyl alcohols substituted on the aromatic ring by electron-donating or electron-withdrawing groups was then examined: the results from the cyclopropanation of various substituted cinnamyl alcohols **1d**–**1t** with Et_2Zn and CH_2I_2 in the presence of 10 mol% of **2** are summarized in Table 1. We chose methoxy and methyl substituents as representative electron-donating groups (see entries 1–8) and trifluoromethyl, chloro, and bromo substituents as electron-withdrawing groups (see entries 9–17). In the case



1a: R = Ph
1b: R = $PhCH_2CH_2$
1c: R = $TrOCH_2$

3a: 93% yield, 82% ee
3b: quant. yield, 89% ee
3c: 98% yield, 89% ee

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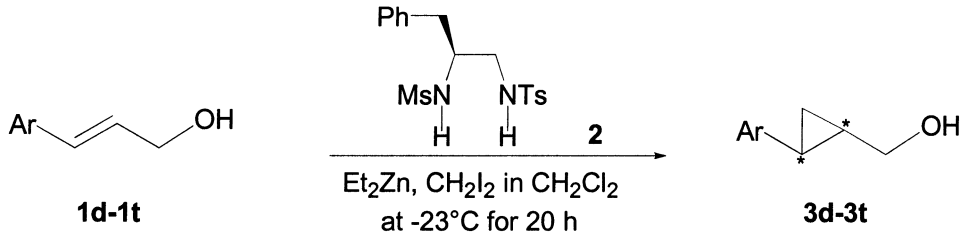
Table 1. Cyclopropanation of substituted cinnamyl alcohols **1d**–**1t** in the presence of **2**[a]

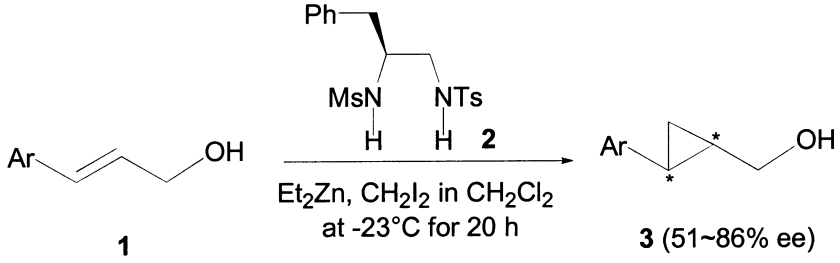


Entry	1	Ar	Yield (%)	ee (%)	Eluent (%)[b]	$[\alpha]_D$[c]
1	**1d**	*p*-$MeOC_6H_4$	98	76[d]	5	+54.2
2	**1e**	*m*-$MeOC_6H_4$	99	78[e]	5	+52.1
3	**1f**	*o*-$MeOC_6H_4$	96	56[f]	5	−23.0
4	**1g**	3,5-$(MeO)_2C_6H_3$	86	82[e]	10	+43.3
5	**1h**	*p*-MeC_6H_4	93	80[d]	5	+66.1
6	**1i**	*m*-MeC_6H_4	88	70[e]	5	+52.5
7	**1j**	*o*-MeC_6H_4	95	78[e]	5	+55.1
8	**1k**	2,4,6-$Me_3C_6H_2$	96	51[d]	5	+45.4
9	**1l**	*p*-$CF_3C_6H_4$	96	84[g]	1	+53.4
10	**1m**	*m*-$CF_3C_6H_4$	98	78[h]	1	+35.9
11	**1n**	*o*-$CF_3C_6H_4$	99	86[h]	1	+53.8
12	**1o**	*p*-BrC_6H_4	98	80[g]	1	+55.1
13	**1p**	*p*-ClC_6H_4	97	82[g]	1	+64.0
14	**1q**	*m*-ClC_6H_4	Quant.	77[i]	1	+57.8
15	**1r**	*o*-ClC_6H_4	Quant.	74[f]	5	0.0
16	**1s**	3,5-$Cl_2C_6H_3$	99	74[d]	5	+49.5
17	**1t**	2,6-$Cl_2C_6H_3$	Quant.	74[f]	5	+62.6

[a] All reactions were carried out with 1 equiv. of an allylic alcohol **1**, 0.1 equiv. of **2**, 2 equiv. of Et_2Zn, and 3 equiv. of CH_2I_2 in anhydrous CH_2Cl_2.
[b] The number indicates concentration of *i*-PrOH in hexane as an eluent on HPLC analysis for determination of enantiomeric excess of the product.
[c] Measured in $CHCl_3$.
[d] Determined by HPLC analysis using Chiralcel OD.
[e] Determined by HPLC analysis using Chiralcel OJ.
[f] Determined by HPLC analysis using Chiralcel AD.
[g] Determined by HPLC analysis using Chiralcel AD after acetylation.
[h] Determined by HPLC analysis using Chiralcel OJ after acetylation.
[i] Determined by HPLC analysis using Chiralcel OD after acetylation.

of cinnamyl alcohols substituted with a methoxy group (entries 1–4), the *meta*- and *para*-substituted alcohols **1d**, **1e**, and **1g** afforded higher enantioselectivities (76–82% ee) than the *ortho* substituted alcohol **1f**. In the case of the cinnamyl alcohols substituted with a methyl group, the *para*-monosubstituted alcohol gave the corresponding cyclopropylmethanol **3h** with the highest ee of 80% (see entries 5–8). The reactions of cinnamyl alcohols substituted at the *ortho*-position with an electron-donating group afforded lower enantioselectivities (51–56% ee), as indicated in entries 3 and 8. Good enantioselectivites (74–86% ee) were obtained in the reactions of cinnamyl alcohols substituted with electron-withdrawing groups (**1l**–**1t**), as shown in entries 9–17.

Highly enantiomerically enriched substituted 2,3-methanocinnamyl alcohols **3** were prepared by conversion of the corresponding 2,3-methanopropanols **3** (70–86% ee) to their 3,5-dinitrobenzoyl ester derivatives, followed by recrystallization[3] and hydrolysis: alcohols **3** were reacted with 3,5-dinitrobenzoyl chloride and Et_3N in CH_2Cl_2 to afford, after silica gel column chromatography, the corresponding esters **4**. The esters **4** were recrystallized from EtOAc–hexane (1:3) twice to give a constant specific rotation for **4** from the mother solution. The recrystallized esters **4** were hydrolyzed with 2 M aq. NaOH in MeOH to afford the corresponding alcohols **3** in 82–100% yields with ee of 84 ~ 97%, as shown in Table 2.



3. Conclusions

In summary, (*S*)-2-(methanesulfonyl)amino-1-(*p*-toluenesulfonyl)-amino-3-phenylpropane **2** works catalytically in the Simmons–Smith cyclopropanation of substituted cinnamyl alcohols **1d**–**1t**. The presence of electron-donating or electron-withdrawing groups on the aromatic ring of the cinnamyl alcohol has little effect on the catalytic performance of this ligand. Highly enantiomerically enriched substituted 2,3-methanocinnamyl alcohols **3** can be obtained by recrystallization of the corresponding 3,5-dinitrobenzoyl ester derivatives **4**, followed by hydrolysis.

We are currently working on the optimization of α-amino acid-derived chiral disulfonamides for the catalytic enantioselective cyclopropanation of various allylic alcohols. Further investigations on this type of chiral controller ligands for catalytic reactions such as Diels–Alder reaction, alkylation, etc. are also in progress.

4. Experimental

4.1. General

Optical rotations were measured with a JASCO DIP-370 digital polarimeter. ^{1}H NMR spectra were measured with a JEOL JNM-GSX400 (400 MHz). The chemical shifts are expressed in ppm downfield from tetramethylsilane, using tetramethylsilane ($\delta = 0$) and/or residual chloroform ($\delta = 7.25$) as an internal standard. Splitting patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad signal. Unless otherwise noted, all experiments were carried out under an argon atmosphere. For thin layer chromatographic (TLC) analyses, Merck precoated TLC aluminum plates (silica gel 60 F254, Art 5554) were used.

4.2. Typical procedure for Simmons–Smith cyclopropanations

To a colorless clear solution of the disulfonamide **2** (38 mg, 0.1 mmol, 0.1 equiv.) and **1** (1 mmol, 1 equiv.) in anhydrous CH_2Cl_2 (15 mL) was added dropwise at −78°C a solution of Et_2Zn in hexane (1.0 M, 2.0 mL, 2 mmol, 2 equiv.) and CH_2I_2 (242 μL, 3 mmol, 3 equiv.). After stirring for 20 h at −23°C, the colorless suspension was quenched at the temperature with 0.5 mL of Et_3N, diluted with 70 mL of Et_2O, washed with 20 mL of brine, and dried over $MgSO_4$. The crude product was chromatographed on silica gel with a mixture of EtOAc and hexane to afford **3**.

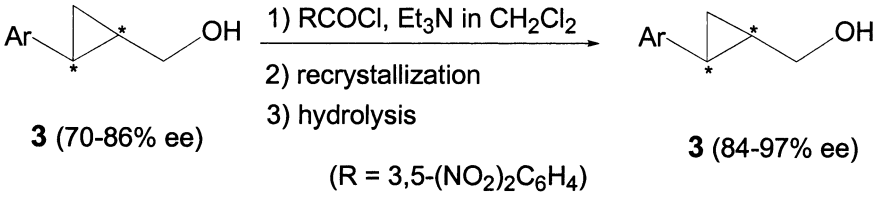
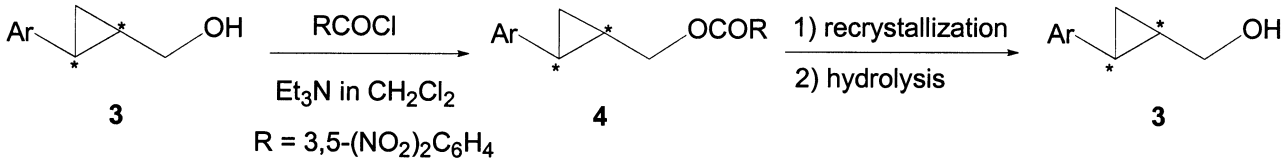


Table 2. Preparation of highly optically active substituted 2,3-methanocinnamyl alcohols **3**



Entry	**3** (% ee)	Ar	Esterification[a]		Recrystallization[b]		Hydrolysis[c]	
			Yield (%)	$[\alpha]_D$[d]	Recovery (%)	$[\alpha]_D$[d]	Yield (%)	ee (%)
1	**3a** (82)	Ph	Quant.	+38.8	72	+48.0	Quant.	95[e]
2	**3h** (80)	*p*-MeC_6H_4	61	+40.0	21	+52.2	90	95[e]
3	**3i** (70)	*m*-MeC_6H_4	85	+37.8	89	+40.4	82	84[f]
4	**3j** (78)	*o*-MeC_6H_4	62	+13.1	69	+20.8	Quant.	96[f]
5	**3*l*** (84)	*p*-$CF_3C_6H_4$	90	+39.5	17	+47.3	86	97[g]
6	**3m** (78)	*m*-$CF_3C_6H_4$	81	+32.0	46	+36.8	Quant.	97[h]
7	**3n** (86)	*o*-$CF_3C_6H_4$	57	+16.0	30	+16.4	Quant.	93[h]
8	**3o** (80)	*p*-BrC_6H_4	87	+37.4	74	+43.3	96	92[g]
9	**3p** (82)	*p*-ClC_6H_4	96	+38.0	73	+43.1	94	93[g]

[a] All reactions were carried out with 1 equiv. of an alcohol **3**, 1.1 equiv. of 3,5-dinitrobenzoyl chloride, 2 equiv. of Et_3N in anhydrous CH_2Cl_2.
[b] Recrystallized from EtOAc and hexane twice and obtained from the mother solution.
[c] All reactions were carried out with 1 equiv. of **4** and 2 equiv. of 2 M aq. NaOH in MeOH.
[d] Measured in $CHCl_3$.
[e] Determined by HPLC analysis using Chiralcel OD.
[f] Determined by HPLC analysis using Chiralcel OJ.
[g] Determined by HPLC analysis using Chiralcel AD after acetylation.
[h] Determined by HPLC analysis using Chiralcel OJ after acetylation.

4.2.1. 3-(4-Methoxy)phenyl-2,3-methano-1-propanol, 3d. $[\alpha]_D^{19}$ +54.2 (*c* 1.07, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 0.82–0.97 (2H, m, CH_2 of cyclopropane), 1.32–1.47 (1H, m, C*H*CH_2O), 1.57 (1H, brs, OH), 1.74–1.86 (1H, m, ArC*H*), 3.58 (1H, dd, $J=5.2$, 9.7 Hz, CH_AO), 3.64 (1H, dd, $J=5.3$, 9.7 Hz, CH_BO), 3.78 (3H, s, CH_3), 6.81, 7.01 (2H, 2H, d, d, $J=8.7$, 8.7 Hz, C_6H_4).

4.2.2. 3-(3-Methoxy)phenyl-2,3-methano-1-propanol, 3e. $[\alpha]_D^{19}$ +52.1 (*c* 1.19, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 0.88–0.98 (2H, m, CH_2 of cyclopropane), 1.38–1.49 (1H, m, C*H*CH_2O), 1.76–1.82 (1H, m, ArC*H*), 1.89 (1H, brs, OH), 3.59 (2H, d, $J=8.8$ Hz, CH_2O), 3.78 (3H, s, CH_3), 6.61–6.71, 7.17 (3H, 1H, m, t, $J=7.9$ Hz, C_6H_4).

4.2.3. 3-(2-Methoxy)phenyl-2,3-methano-1-propanol, 3f. $[\alpha]_D^{19}$ −23.0 (*c* 1.00, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 0.79–0.92 (1H, m, CH_A of cyclopropane), 1.00–1.12 (1H, m, CH_B of cyclopropane), 1.13–1.30 (1H, m, C*H*CH_2O), 1.82–1.96 (1H, m, ArC*H*), 2.30 (1H, brs, OH), 3.20–3.33 (1H, m, CH_AO), 3.78–3.94 (1H, m, CH_BO), 3.88 (3H, s, CH_3), 6.89–7.00, 7.25 (3H, 1H, m, t, $J=4.4$ Hz, C_6H_4).

4.2.4. 3-(3,5-Dimethoxy)phenyl-2,3-methano-1-propanol, 3g. $[\alpha]_D^{15}$ +43.3 (*c* 1.04, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 0.87–1.02 (2H, m, CH_2 of cyclopropane), 1.39–1.53 (1H, m, C*H*CH_2O), 1.67 (1H, brs, OH), 1.73–1.82 (1H, m, ArC*H*), 3.61 (2H, d, $J=6.8$ Hz, CH_2O), 3.77 (6H, s, $CH_3\times2$), 6.24, 6.27 (2H, 1H, d, d, $J=2.3$, 2.3 Hz, C_6H_3).

4.2.5. 3-(4-Methyl)phenyl-2,3-methano-1-propanol, 3h. $[\alpha]_D^{18}$ +66.1 (*c* 1.24, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 0.85–0.95 (2H, m, CH_2 of cyclopropane), 1.35–1.48 (1H, m, C*H*CH_2O), 1.68 (1H, brs, OH), 1.75–1.82 (1H, m, ArC*H*), 2.30 (3H, s, CH_3), 3.57 (1H, dd, $J=6.8$, 11.2 Hz, CH_AO), 3.62 (1H, dd, $J=6.8$, 11.2 Hz, CH_BO), 6.96, 7.07 (2H, 2H, d, d, $J=8.1$, 8.1 Hz, C_6H_4).

4.2.6. 3-(3-Methyl)phenyl-2,3-methano-1-propanol, 3i. $[\alpha]_D^{26}$ +52.5 (*c* 0.40, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 0.87–0.98 (2H, m, CH_2 of cyclopropane), 1.38–1.51 (1H, m, C*H*CH_2O), 1.67 (1H, brs, OH), 1.75–1.81 (1H, m, ArC*H*), 2.31 (3H, s, CH_3), 3.60 (2H, d, $J=6.8$ Hz, CH_2O), 6.86, 6.89, 6.97, 7.15 (1H, 1H, 1H, 1H, d, s, d, t, $J=7.6$, 7.6, 7.6 Hz, C_6H_4).

4.2.7. 3-(2-Methyl)phenyl-2,3-methano-1-propanol, 3j. $[\alpha]_D^{22}$ +55.1 (*c* 1.18, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 0.86–0.96 (2H, m, CH_2 of cyclopropane), 1.34–1.43 (1H, m, C*H*CH_2O), 1.62 (1H, brs, OH), 1.79–1.84 (1H, m, ArC*H*), 2.94 (3H, s, CH_3), 3.62 (1H, dd, $J=5.3$, 8.6 Hz, CH_AO), 3.73 (1H, dd, $J=5.0$, 8.6 Hz, CH_BO), 6.97–6.99, 7.08–7.15 (1H, 3H, m, m, C_6H_4).

4.2.8. 3-(2,4,6-Trimethyl)phenyl-2,3-methano-1-propanol, 3k. $[\alpha]_D^{15}$ +45.4 (*c* 0.97, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 0.72–0.78 (1H, m, CH_A of cyclopropane), 0.93–0.99 (1H, m, CH_B of cyclopropane), 1.24–1.38 (1H, m, C*H*CH_2O), 1.49 (1H, brs, OH), 1.56–1.64 (1H, m, ArC*H*), 2.25, 2.37 (3H, 6H, s, s, $CH_3\times3$), 3.48 (1H, dd, $J=7.8$, 11.3 Hz, CH_AO), 4.01 (1H, dd, $J=5.4$, 11.3 Hz, CH_BO), 6.83 (2H, s, C_6H_2).

4.2.9. 3-(4-Trifluoromethyl)phenyl-2,3-methano-1-propanol, 3l. $[\alpha]_D^{22}$ +53.4 (*c* 1.03, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 1.00–1.05 (2H, m, CH_2 of cyclopropane), 1.47–1.53 (1H, m, C*H*CH_2O), 1.65 (1H, brs, OH), 1.87–1.91 (1H, m, ArC*H*), 3.62 (1H, dd, $J=6.6$, 11.4 Hz, CH_AO), 3.66 (1H, dd, $J=6.6$, 11.4 Hz, CH_BO), 7.15, 7.50 (2H, 2H, d, d, $J=8.4$, 8.4 Hz, C_6H_4).

4.2.10. 3-(3-Trifluoromethyl)phenyl-2,3-methano-1-propanol, 3m. $[\alpha]_D^{26}$ +35.9 (*c* 1.29, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 0.95–1.11 (2H, m, CH_2 of cyclopropane), 1.42–1.57 (1H, m, C*H*CH_2O), 1.62 (1H, brs, OH), 1.85–1.99 (1H, m, ArC*H*), 3.57–3.75 (2H, m, CH_2O), 7.19–7.46 (4H, m, C_6H_4).

4.2.11. 3-(2-Trifluoromethyl)phenyl-2,3-methano-1-propanol, 3n. $[\alpha]_D^{26}$ +53.8 (*c* 0.99, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 0.94–1.07 (1H, m, CH_A of cyclopropane), 1.07–1.20 (1H, m, CH_B of cyclopropane), 1.38–1.54 (1H, m, C*H*CH_2O), 1.68 (1H, brs, OH), 2.08–2.23 (1H, m, ArC*H*), 3.60 (1H, dd, $J=6.8$, 11.4 Hz, CH_AO), 3.74 (1H, dd, $J=6.4$, 11.4 Hz, CH_BO), 7.08, 7.26, 7.44, 7.62 (1H, 1H, 1H, 1H, d, t, t, d, $J=7.6$, 7.6, 7.6, 7.6 Hz, C_6H_4).

4.2.12. 3-(4-Bromo)phenyl-2,3-methano-1-propanol, 3o. $[\alpha]_D^{17}$ +55.1 (*c* 1.98, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 0.87–1.00 (2H, m, CH_2 of cyclopropane), 1.33–1.47 (1H, m, C*H*CH_2O), 1.75–1.81 (1H, m, ArC*H*), 1.83 (1H, brs, OH), 3.60 (2H, d, $J=6.7$ Hz, CH_2O), 6.93, 7.36 (2H, 2H, d, d, $J=8.4$, 8.4 Hz, C_6H_4).

4.2.13. 3-(4-Chloro)phenyl-2,3-methano-1-propanol, 3p. $[\alpha]_D^{17}$ +64.0 (*c* 1.11, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 0.85–1.03 (2H, m, CH_2 of cyclopropane), 1.33–1.51 (1H, m, C*H*CH_2O), 1.62 (1H, brs, OH), 1.78–1.82 (1H, m, ArC*H*), 3.62 (2H, d, $J=6.7$ Hz, CH_2O), 6.99, 7.21 (2H, 2H, d, d, $J=8.4$, 8.4 Hz, C_6H_4).

4.2.14. 3-(3-Chloro)phenyl-2,3-methano-1-propanol, 3q. $[\alpha]_D^{14}$ +57.8 (*c* 1.35, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 0.96 (2H, t, $J=7.1$ Hz, CH_2 of cyclopropane), 1.37–1.51 (1H, m, C*H*CH_2O), 1.69 (1H, brs, OH), 1.77–1.83 (1H, m, ArC*H*), 3.61 (2H, d, $J=8.4$ Hz, CH_2O), 6.94, 7.04, 7.10–7.20 (1H, 1H, 2H, dd, s, m, $J=1.6$, 7.3 Hz, C_6H_4).

4.2.15. 3-(2-Chloro)phenyl-2,3-methano-1-propanol, 3r. $[\alpha]_D^{15}$ 0.0 (*c* 1.08, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 0.92–0.99 (1H, m, CH_A of cyclopropane), 1.03–1.09 (1H, m, CH_B of cyclopropane), 1.29–1.43 (1H, m, C*H*CH_2O), 1.73 (1H, brs, OH), 2.04–2.10 (1H, m, ArC*H*), 3.63 (1H, dd, $J=7.1$, 11.3 Hz, CH_AO), 3.72 (1H, dd, $J=6.4$, 11.3 Hz, CH_BO), 6.99, 7.10–7.21, 7.35 (1H, 2H, 1H, dd, m, dd, $J=2.1$, 7.4 Hz, $J=1.6$, 7.3 Hz, C_6H_4).

4.2.16. 3-(3,5-Dichloro)phenyl-2,3-methano-1-propanol, 3s. $[\alpha]_D^{24}$ +49.5 (*c* 1.01, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 0.95–1.01 (2H, m, CH_2 of cyclopropane), 1.38–1.50 (1H, m, C*H*CH_2O), 1.58 (1H, brs, OH), 1.76–1.82 (1H, m, ArC*H*), 3.59 (1H, dd, $J=6.8$, 11.2 Hz, CH_AO), 3.66 (1H, dd, $J=6.4$, 11.2 Hz, CH_BO), 6.94, 7.14 (2H, 1H, d, t, $J=1.9$, 1.9 Hz, C_6H_3).

4.2.17. 3-(2,6-Dichloro)phenyl-2,3-methano-1-propanol, 3t. $[\alpha]_D^{17}$ +62.6 (*c* 1.07, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 1.00–1.06 (1H, m, CH_A of cyclopropane), 1.12–1.19 (1H, m, CH_B of cyclopropane), 1.47–1.60 (1H, m, C*H*CH_2O), 1.60–1.73 (1H, m, ArC*H*), 1.65 (1H, brs, OH), 3.60 (1H, dd, $J=7.1$, 11.3 Hz, CH_AO), 3.97 (1H, dd, $J=5.8$, 11.3 Hz, CH_BO), 7.09, 7.28 (1H, 2H, t, d, $J=8.2$, 8.2 Hz, C_6H_3).

4.3. Typical procedure for esterifications

To a solution of **3** (1 equiv.) and DMAP (0.2 equiv.) in anhydrous CH_2Cl_2 was added 3,5-dinitrobenzoyl chloride (1.1 equiv.), then Et_3N (2.2 equiv.) was added dropwise at 0°C. After stirring for 3 h at rt, the reaction mixture was quenched with water, extracted with EtOAc, washed with brine, and dried over $MgSO_4$. The crude product was chromatographed on silica gel with a mixture of EtOAc and hexane to afford **4**.

4.3.1. 3,5-Dinitrobenzoyl 3-phenyl-2,3-methano-1-propanate, 4a. $[\alpha]_D^{23}$ +38.8 (*c* 1.18, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 1.08–1.17 (2H, m, CH_2 of cyclopropane), 1.62–1.70 (1H, m, C*H*CH_2O), 2.02–2.07 (1H, m, ArC*H*), 4.46 (2H, d, $J=7.2$ Hz, CH_2O), 7.09–7.30 (5H, m, C_6H_5), 9.18, 9.22 (2H, 1H, d, t, $J=2.0$, 2.0 Hz, C_6H_3).

4.3.2. 3,5-Dinitrobenzoyl 3-(4-methyl)phenyl-2,3-methano-1-propanate, 4h. $[\alpha]_D^{21}$ +40.0 (*c* 1.00, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 1.03–1.16 (2H, m, CH_2 of cyclopropane), 1.54–1.68 (1H, m, C*H*CH_2O), 1.96–2.04 (1H, m, ArC*H*), 2.31 (3H, s, CH_3), 4.44 (2H, d, $J=7.3$ Hz, CH_2O), 6.99, 7.09 (2H, 2H, d, d, $J=8.0$, 8.0 Hz, C_6H_4), 9.19, 9.23 (2H, 1H, d, t, $J=2.1$, 2.1 Hz, C_6H_3).

4.3.3. 3,5-Dinitrobenzoyl 3-(3-methyl)phenyl-2,3-methano-1-propanate, 4i. $[\alpha]_D^{23}$ +37.8 (*c* 0.98, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 1.03–1.19 (2H, m, CH_2 of cyclopropane), 1.53–1.72 (1H, m, C*H*CH_2O), 1.96–2.07 (1H, m, ArC*H*), 2.32 (3H, s, CH_3), 4.45 (2H, d, $J=7.3$ Hz, CH_2O), 6.90, 6.91, 7.00, 7.17 (1H, 1H, 1H, 1H, d, s, d, t, $J=7.3$, 7.3, 7.3 Hz, C_6H_4), 9.19, 9.23 (2H, 1H, d, t, $J=2.1$, 2.1 Hz, C_6H_3).

4.3.4. 3,5-Dinitrobenzoyl 3-(2-methyl)phenyl-2,3-methano-1-propanate, 4j. $[\alpha]_D^{24}$ +13.1 (*c* 0.99, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 1.02–1.10 (1H, m, CH_A of cyclopropane), 1.10–1.20 (1H, m, CH_B of cyclopropane), 1.50–1.64 (1H, m, C*H*CH_2O), 1.98–2.08 (1H, m, ArC*H*), 2.44 (3H, s, CH_3), 4.44 (1H, dd, $J=7.8$, 11.5 Hz, CH_AO), 4.58 (1H, dd, $J=6.9$, 11.5 Hz, CH_BO), 6.97–7.05, 7.08–7.20 (1H, 3H, m, m, C_6H_4), 9.21, 9.24 (2H, 1H, d, t, $J=2.1$, 2.1 Hz, C_6H_3).

4.3.5. 3,5-Dinitrobenzoyl 3-(4-trifluoromethyl)phenyl-2,3-methano-1-propanate, 4l. $[\alpha]_D^{23}$ +39.5 (*c* 0.97, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 1.19 (2H, t, $J=7.2$ Hz, CH_2 of cyclopropane), 1.67–1.75 (1H, m, C*H*CH_2O), 2.08–2.13 (1H, m, ArC*H*), 4.47 (2H, d, $J=8.4$ Hz, CH_2O), 7.19, 7.52 (2H, 2H, d, d, $J=8.1$, 8.1 Hz, C_6H_4), 9.18, 9.23 (2H, 1H, d, t, $J=2.2$, 2.2 Hz, C_6H_3).

4.3.6. 3,5-Dinitrobenzoyl 3-(3-trifluoromethyl)phenyl-2,3-methano-1-propanate, 4m. $[\alpha]_D^{21}$ +32.0 (*c* 1.01, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 1.19 (2H, t, $J=7.2$ Hz, CH_2 of cyclopropane), 1.64–1.80 (1H, m, C*H*CH_2O), 2.09–2.13 (1H, m, ArC*H*), 4.45 (1H, dd, $J=7.2$, 11.6 Hz, CH_AO), 4.49 (1H, dd, $J=7.4$, 11.6 Hz, CH_BO), 7.23–7.49 (4H, m, C_6H_4), 9.19, 9.24 (2H, 1H, d, t, $J=2.0$, 2.0 Hz, C_6H_3).

4.3.7. 3,5-Dinitrobenzoyl 3-(2-trifluoromethyl)phenyl-2,3-methano-1-propanate, 4n. $[\alpha]_D^{21}$ +16.0 (*c* 1.08, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 1.10–1.21 (1H, m, CH_A of cyclopropane), 1.21–1.38 (1H, m, CH_B of cyclopropane), 1.52–1.75 (1H, m, C*H*CH_2O), 2.28–2.43 (1H, m, ArC*H*), 4.49 (2H, d, $J=7.6$ Hz, CH_2O), 7.12, 7.31, 7.47, 7.64 (1H, 1H, 1H, 1H, d, t, t, d, $J=7.6$, 7.6, 7.6, 7.6 Hz, C_6H_4), 9.20, 9.23 (2H, 1H, d, t, $J=2.0$, 2.0 Hz, C_6H_3).

4.3.8. 3,5-Dinitrobenzoyl 3-(4-bromo)phenyl-2,3-methano-1-propanate, 4o. $[\alpha]_D^{19}$ +37.4 (*c* 1.07, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 1.12 (2H, t, $J=7.0$ Hz, CH_2 of cyclopropane), 1.53–1.69 (1H, m, C*H*CH_2O), 1.97–2.07 (1H, m, ArC*H*), 4.44 (2H, d, $J=7.3$ Hz, CH_2O), 6.97, 7.39 (2H, 2H, d, d, $J=8.4$, 8.4 Hz, C_6H_4), 9.18, 9.24 (2H, 1H, d, t, $J=2.1$, 2.1 Hz, C_6H_3).

4.3.9. 3,5-Dinitrobenzoyl 3-(4-chloro)phenyl-2,3-methano-1-propanate, 4p. $[\alpha]_D^{19}$ +38.0 (*c* 1.21, $CHCl_3$). ^1H NMR ($CDCl_3$) δ 1.12 (2H, t, $J=7.0$ Hz, CH_2 of cyclopropane), 1.52–1.68 (1H, m, C*H*CH_2O), 1.97–2.07 (1H, m, ArC*H*), 4.45 (2H, d, $J=7.3$ Hz, CH_2O), 7.02, 7.24 (2H, 2H, d, d, $J=8.4$, 8.4 Hz, C_6H_4), 9.19, 9.23 (2H, 1H, d, t, $J=2.1$, 2.1 Hz, C_6H_3).

4.4. Typical procedure for recrystallizations

The ester **4** was recrystallized twice from EtOAc–hexane and the resulting **4** was collected from the mother liquor solution.

4.5. Typical procedure for hydrolyses

To a solution of **4** (1 equiv.) in a 1:1 mixture of MeOH and water was added 2 M aq. NaOH (5 equiv.). After stirring for 15 h at rt, the reaction mixture was quenched with 2 M aq. NH_4Cl, extracted with EtOAc, washed with brine, and dried over $MgSO_4$. Purification was performed by silica gel chromatography to afford **3**.

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