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Tetrahedron: *Asymmetry* 14 (2003) 305–315

TETRAHEDRON: *ASYMMETRY*

Stereoselective conjugate addition of diethylzinc to enones and nitroalkenes

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Received 22 October 2002; revised 6 December 2002; accepted 9 December 2002

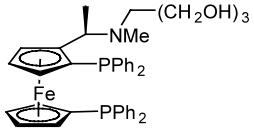
Abstract—Bidirectionally directed conjugate addition of diethylzinc to enones and nitroalkene was achieved with good enantioselectivity.

1. Introduction

Design of catalytic asymmetric reactions is usually centered around the development of optically active catalysts that will bind substrates unambiguously before reaction, direct the reactant to the reaction center, and finally exchange the coordinated guests from the product molecule for an unreacted substrate, thus affording a catalytic cycle. However, it would be preferable to have the ability to deliver a reactant that is already bound to a certain part of the catalyst, especially to the coordinated substrate. In this way the direction of attack can be closely controlled. This concept is not new—in the 1980s Hayashi et al. utilized hydrogen bonding of stabilized carbanions with the hydroxyl group of the ligand for enantioselective Pd-catalyzed allylation.[1] CBS reduction,[2] amino alcohol (or thiol)-catalyzed addition of organozinc reagents to aldehydes,[3] and Shibasaki's cyanosilylation[4] and Reissert reactions[5] are noteworthy among other examples of this type of stereocontrol.

The enantioselective conjugate addition of organometallic reagents to α,β-unsaturated substrates, such as enone[6] and nitroolefin,[7] is of considerable synthetic interest. In many cases, phosphorus-containing ligands such as phosphorus amidite, oxazoline-phosphite and phosphite ligands showed excellent enantioselectivities in the copper-catalyzed Michael addition of organozinc or organomagnesium reagents to enones and other α,β-unsaturated carbonyl compounds. Feringa et al. reported on the highly enantioselective conjugate addition of dialkylzinc catalyzed by Cu-chiral phosphorus amidite complexes,[8] and Alexakis et al. reported on the conjugate addition of diethylzinc to several nitroolefins catalyzed with trivalent phosphorus ligands including phosphorus amidite.[9] Recently, Hoveyda et al. reported on the highly enantioselective conjugate addition of diethylzinc to acyclic enones.[10]

Previously, we examined thianickelolidine ligands for conjugate addition of dialkylzinc reagents to enones, where a sulfur centre was used as an anchor for diethylzinc. The enantioselectivity was found to be only moderate (62–74%) in the case of chalcone (Fig. 1).[11]



Nucleophile steering to allyl-Pd species

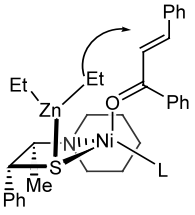


Figure 1.

2. Results and discussion

2.1. Synthesis of ligands

Herein, we report an extension of this concept to BINOL derivatives, which simultaneously provide a Lewis acidic site (for activation of enone) and the anchoring site(s) for organo copper species formed

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0957-4166/03/$ - see front matter
PII: S0957-4166(02)00838-8

during the reactions (Fig. 2). The primary concern here is that Lewis acid coordination to enones is usually nonselective since the two lone pairs of the carbonyl oxygen are in similar steric and electronic environments, which eventually leads to poor levels of enantiocontrol (Fig. 2).

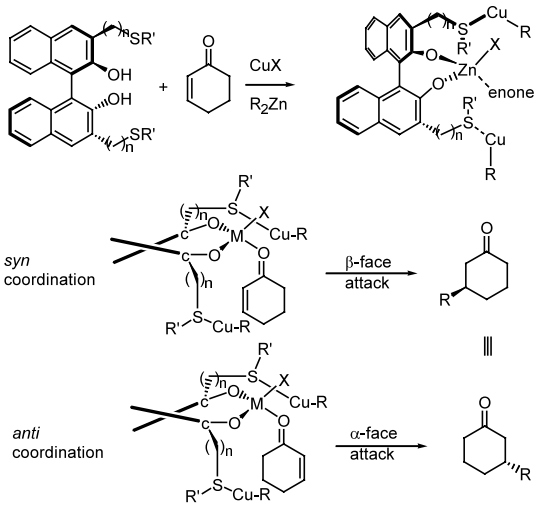


Figure 2.

Our theory was that, irrespective of the coordination mode of the enone (i.e. metal *syn* or *anti* to the C=C double bond), it may be possible to selectively attack the double bond of the enone from different arms of a binaphthyl skeleton. During this study, Woodward and co-workers have published several papers on a conceptually similar approach using the sulfide complex **5**,[12] which, we believe, is operationally different from our ligands.

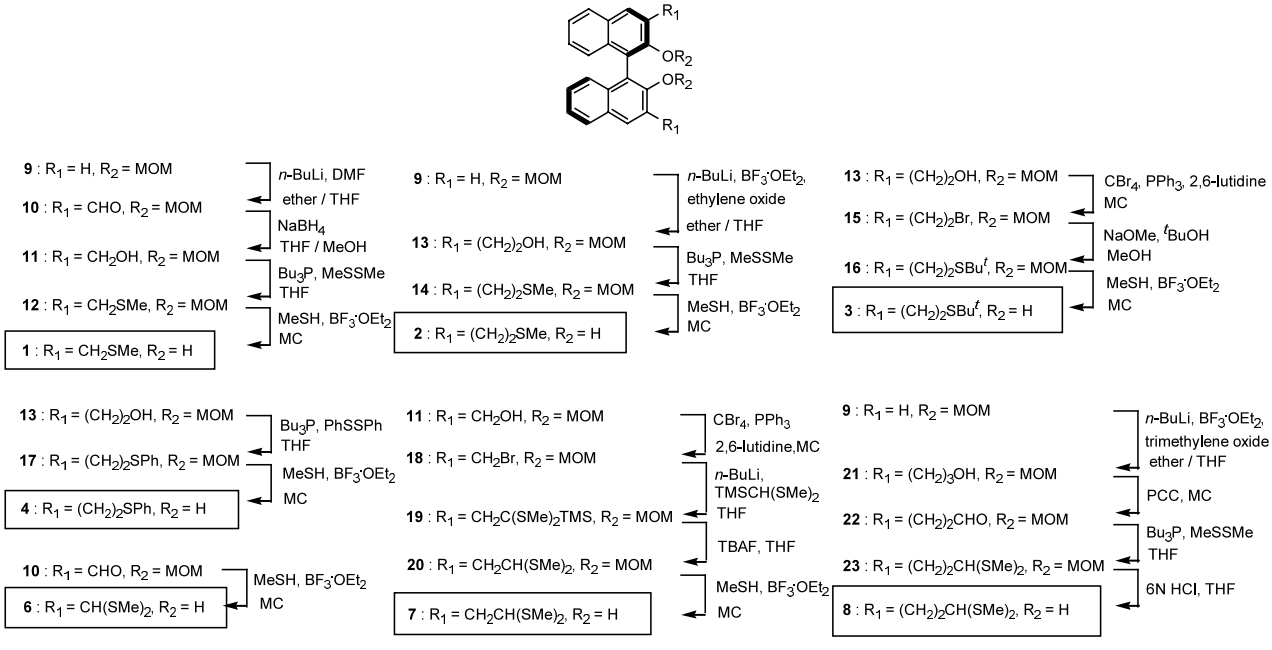
With this in mind, binaphthols modified by varying the chain length between the binaphthol core and the Cu-binding site were prepared from bis(methoxymethyl) ethers and used in the conjugate addition of diethylzinc to enones and nitroalkenes.

We synthesized these ligands from the MOM-protected BINOL (**9** in Scheme 1), which could introduce many electrophiles to the α-position to the hydroxy group of BINOL.[13] The route for the synthesis of these ligands is described in Scheme 1.

2.2. Asymmetric 1,4-addition reactions

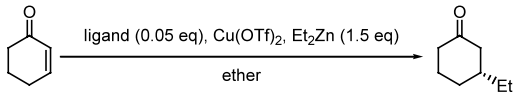
With these bissulfides in hand, extensive optimization studies were carried out. Initially, optimization experiments on the ligand structure was conducted with 2-cyclohexen-1-one as a model substrate, copper triflate ($Cu(OTf)_2$) as a catalyst metal salt, and diethyl ether as a solvent. Thus, a solution of the ligand in ether at rt was added to a stirred suspension of $Cu(OTf)_2$ in ether and the mixture was stirred for 30 min. Et_2Zn (neat; 1.5 equiv.) was added dropwise at 0°C, and the mixture was stirred for a further 5 min. Subsequently, the reaction mixture was cooled to the temperature indicated, and 2-cyclohexen-1-one was added at the required temperature. After the reaction was complete, the mixture was worked up, and the product was converted to the corresponding ketal with (2*R*,4*R*)-(−)-pentanediol in the presence of a catalytic amount of acid. Thus, sulfide ligands were shown to be better than dithioacetals even though dithioacetals **8** with long tethers did show some enantioselectivity (Table 1).

The *prior* formation of aluminum binolate by adding the exact amount of an alkylaluminum reagent such as Me_3Al and Me_2AlCl (to increase the Lewis acidity) did,



Scheme 1. Synthesis of ligands.

Table 1. Effect of side chain functionality (sulfide versus dithioacetal) in the Cu-catalyzed conjugate addition



Entry	Ligand	$Cu(OTf)_2$ (equiv.)	Condition	Yield (%)[a]	ee (%)[b]	Conf.[c]
1	**1**	0.10	0°C/16 h	86	0	–
2	**6**	0.10	0°C/2 h	12	0	–
3	**2**	0.10	0°C/2 h	95	69	*R*
4	**3**	0.05	0°C/1 h	91	65	*R*
5	**7**	0.05	0°C/2 h	16	11	*R*
6	**8**	0.05	−15°C/2 h	41	56	*R*

[a] Isolated yield by flash column chromatography on silica gel.
[b] Enantiomeric excess was determined by GC analysis of the chiral acetal derived from (2*R*,4*R*)-(−)-pentanediol (HP-FFAP (25 m×0.32 mm); t_R: 7.69 min (*R*), 8.05 min (*S*)).
[c] Absolute configuration was determined by comparison of the specific rotation with that reported in the literature.[14]

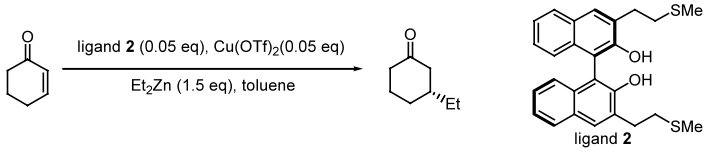
in fact, lead to lower enantioselectivity. Another fundamental question was whether the sequence of addition of the reagents would affect the outcome of the reaction. In fact, the order of addition did not affect the enantioselectivity of the reaction (Table 2).

Among the sulfides **1**–**4**, the best ligands were the C2-bridged ligands with stronger affinity for Cu, **2** and **3** (but not phenyl-substituted ligand **4**). Between the C2-bridged ligands, **2** and **3**, the choice was ambiguous since with cyclic enones the methylthio ligand **2** was better than the *t*-butylthio ligand **3**, but the trend was reversed with acyclic enones (vide infra). And the optimal mole ratio of the ligand to Cu salt was shown to be <2. At ratios of >2 the enantioselectivity dropped significantly, presumably because uncoordinated Cu salt present in the reaction mixture would trigger the formation of racemic products via competitive non-enantioselective reaction.

Initially, it was conceived that non-polar solvents were preferable since coordinating solvents could disturb both the interaction of the Lewis acidic Zn centre with the Lewis basic carbonyl oxygen and the coordination of copper salts with the sulfide ligand, eventually showing considerable solvent effects on enantioselectivity. However, the use of highly polar and non-polar solvents gave lower enantioselectivities. Thus, MTBE (methyl *tert*-butyl ether) was found to be *universally* optimum (Table 3).

With these facts in hand, the effect source of Cu(I) was studied using several salts, such as the commonly used $Cu(OTf)_2$, $[Cu(MeCN)_4]BF_4$, $Cu(acac)_2$, CuO-*t*-Bu, Cu(I) halides (Br or I) and several Cu(II) carboxylates. Unfortunately, however, the effect of Cu salts was substrate-dependent (vide infra). It is generally believed that the reactive copper is, irrespective of the initial form of Cu salt employed, Cu(I), which could be generated by reduction of Cu(II) in the reaction media. It is interesting to note that near the completion of our study, Alexakis also reported the dramatic effects of Cu(II) acetate on the enantioselectivity of the conjugate addition of diethylzinc in the presence of biphenol-

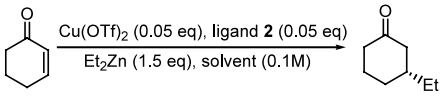
Table 2. Mode of addition of reagents in the Cu-catalyzed conjugate addition of Et_2Zn



Entry	Conditions	Yield (%)[a]	ee (%)[b]	Config.[c]
1	(1) Me_2AlCl (0.05 equiv., rt, 1.6 h). (2) $Cu(OTf)_2$ (rt, 1 h). (3) Substrate (−20°C). (4) Et_2Zn[d] (−20°C to rt)	76	24	*R*
2	(1) $Cu(OTf)_2$ (rt/1 h). (2) Et_2Zn[d] (−15°C/15 min). (3) −15°C/2 h	73	50	*R*
3	(1) Et_2Zn[d] (0°C/1 h). (2) $Cu(OTf)_2$ (−15°C/10 min). (3) −15°C/2 h	56	49	*R*

[a] Isolated yield by flash column chromatography on silica gel.
[b] Enantiomeric excess was determined by GC analysis of the chiral acetal derived from (2*R*,4*R*)-(−)-pentanediol (HP-FFAP (25 m×0.32 mm); t_R: 7.69 min (*R*), 8.05 min (*S*)).
[c] Absolute configuration was determined by comparison of the specific rotation value with that reported in the literature.[14]
[d] Et_2Zn (1.0 M in hexane) was used.

Table 3. Effect of solvent in the Cu-catalyzed conjugate addition



Entry[a]	Solvent	Condition	Yield (%)[b]	ee (%)[c]	Config.[d]
1	Toluene	−15°C/2 h	73	50	*R*
2	MC	0°C/2 h	75	16	*R*
3	Ether	0°C/2 h	95	69	*R*
4	MTBE	0°C/2 h	95	72	*R*

[a] Et_2Zn (1.0 M in hexane) was used.
[b] Isolated yield by flash column chromatography on silica gel.
[c] Enantiomeric excess was determined by GC analysis of the chiral acetal derived from (2*R*,4*R*)-(−)-pentanediol (FFAP (25 m×0.32 mm); t_R: 7.69 min (*R*), 8.05 min (*S*)).
[d] Absolute configuration was determined by comparison of the specific rotation value with that reported in the literature.[14]

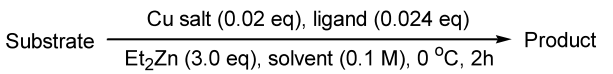
derived phosphoramidites,[15] although the substrate-specificity in their case is somewhat opposite from that seen in this study: In our case $Cu(OAc)_2$ gave the best enantioselectivity where applicable of the Cu(II) carboxylates employed (acetate, benzoate, and 2-ethylhexanoate).

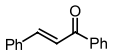
From this rather crude optimization (due to the unfortunate non-generality of this type of reaction), the following method was developed: to a stirred suspension of the Cu salt (2 mol%) in an inert solvent was added a ligand (2.4 mol%, 20% excess to eliminate the possibility of uncomplexed Cu salt) in the same solvent at rt. The amount of solvent was adjusted so that the final concentration of the substrate was 0.1 M. And the mixture was stirred for 30 min. Et_2Zn (neat; 3.0 equiv.) was added dropwise at 0°C and the mixture was stirred for a further 5 min. Subsequently, the reaction mixture was cooled to the temperature indicated (0°C for enones and −30°C for nitroolefins), and the enone (or nitroolefin) was added. Usually, reaction times of 2 h were sufficient for complete consumption of the starting materials in both cases. As can be seen from Table 4, the MTBE solvent gave the best enantioselectivity and reactivity. The salt effect was rather dramatic: for cyclic enones such as 2-cyclohexenone and 2-cycloheptenone, a combination of ligand **2** and $Cu(OTf)_2$ gave better enantioselectivity while the ligand 3-$Cu(OAc)_2$ combination gave better enantioselectivity with an acyclic enone (chalcone). Additionally, the enantioselectivity with chalcone (96% ee) using the ligand 3-$Cu(OAc)_2$ system was much better than the much heralded binol phosphorimidite protocol of Feringa and Alexakis (71% ee), while the enantioselectivity with our system was inferior. (85% ee versus 99% ee in case of 2-cyclohexenone.) In the case of chalcone, the arylsulfide ligand (**4** in Fig. 3) showed moderate enantioselectivity under the reaction conditions described above (74% yield, 22% ee).

Exactly the same trend was observed with acyclic nitroolefins: The *t*-butylthio ligand **3** and $Cu(OAc)_2$ combination gave better enantioselectivity than the methylthio ligand **2** (Table 5).

As for the mechanism of this reaction, nothing is clear yet. In view of the strange preference of cyclic substrates towards the methylthio ligand 2-$Cu(OTf)_2$ combination and that of acyclic substrates towards the

Table 4. Cu-catalyzed conjugate addition of Et_2Zn to various enones (at 0°C for 2 h)



Entry[a]	Substrate	Ligand	Cu salt	Yield (%)[c]	ee (%)	Conf.
1		**2**	**$Cu(OTf)_2$**	95	**85**[d]	*R*
2			$Cu(OAc)_2$	86	22[d]	*R*
3			$Cu(acac)_2$	58	8[d]	*R*
4		**3**	$Cu(OTf)_2$	93	77[d]	*R*
5			$Cu(OAc)_2$	49	13[d]	*R*
6		**2**	**$Cu(OTf)_2$**	96	**81**[e]	*R*[f]
7			$Cu(OAc)_2$	23	21[e]	*R*[f]
8		**3**	$Cu(OTf)_2$	86	76[e]	*R*[f]
9			$Cu(OAc)_2$	10	44[e]	*R*[f]
10		**2**	$Cu(OTf)_2$	22	17[g]	*R*
11			$Cu(OAc)_2$	53	44[g]	*S*
12			$Cu(acac)_2$	24	40[g]	*S*
13			$Cu(OTf)_2$	72	92[g]	*S*
14		**3**	**$Cu(OAc)_2$**	91	**96**[g,h]	*S*
15[b]			**$Cu(OAc)_2$**	85	**96**[g,h]	*S*

[a] solvent: MTBE, Et_2Zn: 3.0 eq. [b] solvent: toluene, Et_2Zn: 3.0 eq. [c] Isolated yield after flash column chromatography on silica gel. [d] Enantiomeric excess was determined by GC analysis of the chiral acetal derived from (2*R*,4*R*)-(-)-pentanediol (HP-FFAP (25m x 0.32mm); t_R: 7.69 min (*R*), 8.05 min (*S*)). [e] Enantiomeric excess was determined by GC analysis (CP-Cyclodextrin-B-2,3,6-M-19; t_R: 23.43 min (*S*), 24.09 min (*R*)). [f] Absolute configuration was determined by comparison of the specific rotation with the literature value.[16] [g] Enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 0.3% ^{i}PrOH/*n*-hexane, 0.5mL/min ; t_R: 44.67 min (*S*), 50.98 min (*R*)).[17] [h] The reaction was carried out at -10 °C for 2 h.

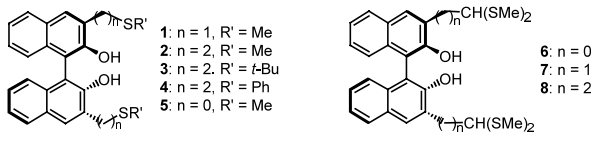


Figure 3.

Table 5. Cu-catalyzed conjugate addition of Et_2Zn to various nitroolefins (at −30°C, 2 h)

Substrate —[Cu salt (0.02 eq), ligand (0.024 eq); Et_2Zn (3.0 eq), solvent (0.1 M), -30 °C, 2h]→ Product

Entry [a]	Substrate	Ligand	Cu salt	Yield (%)[c]	ee (%)	Conf.
1	Ph–CH=CH–NO_2	**2**	$Cu(OAc)_2$	84	35[d]	*S*
2			$Cu(OTf)_2$	84	15[d]	*S*
3[b]			$Cu(OAc)_2$	69	32[d]	*S*
4			**$Cu(OAc)_2$**	74	**70**[d]	*S*
5		**3**	$Cu(OTf)_2$	67	23[d]	*S*
6[b]			$Cu(OAc)_2$	69	27[d]	*S*
7[b]			$Cu(OTf)_2$	67	35[d]	*S*
8	*p*-MeOPh–CH=CH–NO_2	**2**	$Cu(OAc)_2$	82	47[e]	*S*
9			$Cu(OTf)_2$	68	24[e]	*S*
10			**$Cu(OAc)_2$**	86	**68**[e]	*S*
11		**3**	**$Cu(OTf)_2$**	97	**79**[e]	*S*
12[b]			$Cu(OAc)_2$	88	53[e]	*S*

[a] solvent: MTBE, Et_2Zn: 3.0 eq. [b] solvent: toluene, Et_2Zn: 3.0 eq. [c] Isolated yield by flash column chromatography on silica gel. [d] Enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 5.0% ^{i}PrOH/*n*-hexane, 0.5mL/min; t_R: 23.82 min (*R*), 30.10 min (*S*)).[18] [e] Enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, 5.0% ^{i}PrOH/*n*-hexane, 0.7mL/min; t_R: 20.75 min (*R*), 32.32 min (*S*)).[18]

t-butylthio ligand 3-$Cu(OAc)_2$ combination, the Cu salt effect is approximately opposite to the Alexakis' results.[9] However, we are pleased to present evidence that supports our initial hypothesis that the ligands were designed in such a way that the enones and alkylcopper species were brought together: with 2-cyclohexenone itself in the presence of $Cu(OTf)_2$, unsubstituted binol itself gave only 7% ee of (3*R*)-ethylcyclohexanone, and the monosubstituted binol sulfide (Fig. 4), which was prepared analogously, gave (3*R*)-ethylcyclohexanone with ee of only 74%.

3. Conclusion

In conclusion, new BINOL-based thioether ligands were developed for the enantioselective conjugate addition of alkylzinc reagents to acyclic, cyclic unsaturated ketones and nitroolefins. The last few decades have witnessed the proliferation of the development of phosphorus ligands for asymmetric conjugate addition reactions of organocopper reagents. We reported herein some new thioether ligands based on the sulfur-copper affinity, especially, the reaction with *trans*-chalcone, which gave rise to excellent results (96.3% ee and 91% yield).

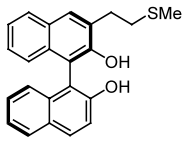


Figure 4.

4. Experimental

4.1. Preparation of (*R*)-2,2′-bis(methoxymethoxy)-(1,1′)-binaphthalenyl-3,3′-dicarboxaldehyde, 10

To a stirred solution of (*R*)-2,2′-bis(methoxymethoxy)-(1,1′)-binaphthalenyl (3.50 g, 9.35 mmol in 156 mL ether) was added *n*-BuLi (12.5 mL, 28.1 mmol, 2.23 M in hexane) at 0°C and stirred for 3 h at room temperature. The resulting mixture was cooled to 0°C and diluted with anhydrous THF (93.5 mL). To the resulting dark brown solution was added *N*,*N*-dimethylformamide (2.75 mL, 37.4 mmol) at 0°C and the resulting solution was warmed to room temperature. The reaction mixture was quenched by addition of a saturated $NaHCO_3$ solution and extracted with diethyl ether. The combined organic phase was dried with Na_2SO_4, filtered and concentrated under reduced pressure. The product was purified with flash column chromatography using 20% EtOAc/*n*-hexane as yellow solid (2.857 g). Yield 71%. $[\alpha]_D^{25}$ −51.7 (*c* 1.0, $CHCl_3$). Mp 114–118°C. IR (KBr) 2988, 2904, 2824, 1691, 1618, 1582, 1497, 1448, 1346, 1154, 952 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 2.88 (s, 6H, OCH_3), 4.69 (d, $J=6.2$ Hz, 2H, OCH_2O), 4.73 (d, $J=6.2$ Hz, 2H, OCH_2O), 7.22 (dd, $J=8.5$ Hz, $J'=0.8$ Hz, 2H, aromatic), 7.41–7.45 (m, 2H, aromatic), 7.51–7.54 (m, 2H, aromatic), 8.08 (d, $J=8.2$ Hz, 2H, aromatic), 8.62 (s, 2H, aromatic), 10.5 (s, 2H, CHO). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 56.99, 100.59, 126.08, 126.26, 128.89, 129.61, 130.06, 130.29, 132.28, 136.69, 154.03, 190.63. MS (EI, 70 eV) *m*/*z*: 430 (M^+), 354 ($M-C_3H_8O_2$). Anal. calcd for $C_{26}H_{22}O_6$: C, 72.55; H, 5.15. Found: C, 72.56; H, 5.28%.

4.2. Preparation of (*R*)-3,3′-bis(hydroxymethyl)-2,2′-bis(methoxymethoxy)-(1,1′)-binaphthalenyl, 11

To a stirred solution of **10** (1.82 g, 4.22 mmol in 10.6 mL THF and 10.6 mL MeOH) was added sodium borohydride (0.959 g, 25.3 mmol) portionwisely at 0°C and stirred at rt for 12 h. After completion of reaction the resulting mixture was cooled to 0°C. The solution was quenched by addition of cold water (1.06 mL) and the solvent was removed under reduced pressure. The aqueous phase was extracted with ethyl acetate. The combined solution was dried with Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash column chromatography using 50% EtOAc/*n*-hexane (1.83 g). Yield 100%. $[\alpha]_D^{25}$ −159.3 (*c* 1.0, $CHCl_3$). IR (neat) 3423, 3055, 2837, 1357, 1265, 1151, 976 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 3.12 (s, 6H, OCH_3), 3.39 (br s, 2H, OH), 4.39 (dd, $J=14.2$ Hz, $J'=6.2$ Hz, 4H, CH_2OH), 4.77 (d, $J=12.6$ Hz, 2H, OCH_2O), 7.94 (s, 2H, aromatic), 4.91 (d, $J=12.6$ Hz, 2H, OCH_2O), 7.07–7.09 (m, 2H, aromatic), 7.17–7.21 (m, 2H, aromatic), 7.34–7.38 (m, 2H, aromatic), 7.83 (d, $J=8.1$ Hz, 2H, aromatic). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 57.12, 61.87, 99.32, 125.15, 125.44, 125.73, 126.85, 128.19, 129.75, 130.96, 133.75, 134.54, 153.13. MS (EI, 70 eV) *m*/*z*: 432 (M^+-2), 406 ($M-CH_3O$), 391 ($M-C_2H_5O$). Anal. calcd for $C_{26}H_{26}O_6$: C, 71.87; H, 6.03. Found: C, 70.79; H, 6.35%.

4.3. Preparation of (*R*)-2,2′-bis(methoxymethoxy)-3,3′-bis(methylsulfanylmethyl)-(1,1′)-binaphthalenyl, 12

In a 50 mL round-bottomed flask was placed **11** (1.83 g, 4.21 mmol), dissolved with THF (21.1 mL) and cooled to 0°C. To that reaction mixture were added tributylphosphine (3.15 mL, 12.6 mmol) and dimethyl disulfide (1.14 mL, 12.6 mmol) successively. Finally the solution was heated under reflux for 40 h. The reaction mixture was treated with H_2O and the aqueous phase was extracted ether. The combined organic phase was dried with Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified with flash column chromatography using 10% EA/*n*-hexane (1.22 g). Yield 59%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.90 (s, 2H, aromatic), 2.15 (s, 6H, SCH_3), 2.92 (s, 6H, OCH_3), 4.04 (dd, $J=13.5$ Hz, $J'=26.9$ Hz, 4H, CH_2SCH_3), 4.50 (d, $J=5.5$ Hz, 2H, OCH_2O), 4,65 (d, $J=5.8$ Hz, 2H, OCH_2O), 7.15–7.24 (m, 2H, aromatic), 7.34–7.40 (m, 2H, aromatic), 7.85 (d, $J=8.2$ Hz, 2H, aromatic). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 15.59, 33.76, 56.71, 99.28, 125.18, 125.66, 126.01, 126.36, 127.71, 129.80, 130.59, 131.67, 133.49, 152.69.

4.4. Preparation of (*R*)-3,3′-bis(methylsulfanylmethyl)-(1,1′)-binaphthalenyl-2,2′-diol, 1

In a 50 mL round-bottomed flask were placed **12** (1.22 g, 2.46 mmol) and MC (14.6 mL). This resulting mixture was cooled to −78°C and MeSH (1.19 g, 24.6 mmol in 10.0 mL MC) and $BF_3{\cdot}OEt_2$ (0.094 mL, 0.74 mmol) were added successively. The cooling bath was removed and the reaction mixture was stirred for 12 h at rt. After the completion of reaction, saturated $NaHCO_3$ solution was added to that solution. The organic phase was extracted with MC and the combined organic phase was washed with brine. The crude product was purified with flash column chromatography using 10% EA/*n*-hexane (0.926 g). Yield 92%. $[\alpha]_D^{25}$ +105.5 (*c* 1.0, $CHCl_3$). Mp: 103–105°C. IR (KBr) 3354, 3058, 2920, 1624, 1455, 1208, 1142, 753 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.11 (s, 6H, SCH_3), 3.96 (s, 4H, CH_2SCH_3), 5.58 (s, 2H, OH), 7.06 (d, 2H, $J=8.4$ Hz, aromatic), 7.22–7.25 (m, 2H, aromatic), 7.31–7.35 (m, 2H, aromatic), 7.83 (d, $J=7.7$ Hz, aromatic), 7.87 (s, 2H, aromatic). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 15.31, 33.73, 112.47, 124.20, 124.19, 126.39, 127.06, 128.04, 129.04, 130.67, 132.84, 151.24. MS (EI, 70 eV) *m*/*z*: 406 (M^+), 358 (M–CH_4S), 311 (M–$C_2H_7S_2$). Anal. calcd for $C_{24}H_{22}O_2S_2$: C, 70.90; H, 5.45; S, 15.77. Found: 70.96, H, 5.47; S, 15.70%.

4.5. Preparation of (*R*)-3,3′-bis(2-hydroxyethyl)-2,2′-bis(methoxymethoxy)-(1,1′)-binaphthalenyl, 13

To a stirred solution of (*R*)-2,2′-bis(methoxymethoxy)-(1,1′)-binaphthalenyl (3.000 g, 8.012 mmol in 133.5 mL ether) was added *n*-BuLi (11.1 mL, 24.04 mmol, 2.17 M in hexane) at 0°C and stirred for 3 h at room temperature. The resulting mixture was cooled to −78°C and diluted with anhydrous THF (80.12 mL). To the resulting dark brown solution was added ethylene oxide (5.83 mL, 32.04 mmol, 5.50 M in ether), followed by $BF_3{\cdot}OEt_2$ (3.05 mL, 24.03 mmol) and stirred for 1 h at −78°C. The reaction mixture was quenched by addition of saturated $NaHCO_3$ solution and extracted with diethyl ether. The combined organic phase was dried with Na_2SO_4, filtered and concentrated under reduced pressure. The product was purified with flash column chromatography using 70% EtOAc/*n*-hexane (1.68 g). Yield 45%. IR (neat) 3384, 3057, 2935, 2884, 1497, 1356, 1236, 1156, 921, 752 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.15 (br s, 2H, OH), 2.99 (s, 6H, OCH_3), 3.11–3.30 (m, 4H, CH_2OH), 4.03 (t, $J=6.3$ Hz, 4H, $ArCH_2$), 4.40 (d, $J=5.8$ Hz, 2H, OCH_2O), 4.54 (d, $J=5.8$ Hz, 2H, OCH_2O), 7.13–7.26 (m, 4H, aromatic), 7.39–7.42 (m, 2H, aromatic), 7.83–7.87 (m, 4H, aromatic). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 34.41, 56.70, 63.22, 99.01, 125.14, 125.27, 125.91, 126.14, 127.52, 129.99, 130.86, 132.37, 133.17, 153.21. MS (EI, 70 eV) *m*/*z*: 462 (M^+), 398 (M–$C_2H_4O_2$), 338 (M–$C_4H_{12}O_4$). Anal. calcd for $C_{28}H_{30}O_6$: C, 72.71; H, 6.54. Found: C, 72.74; H, 6.62%.

4.6. Preparation of (*R*)-2,2′-bis(methoxymethoxy)-3,3′-bis(2-methylsulfanylethyl)-(1,1′)binaphthalenyl, 14

In a 50 mL round-bottomed flask was placed **13** (0.409 g, 0.884 mmol), dissolved with THF (8.84 mL) and cooled to 0°C. To that reaction mixture were added tributylphosphine (0.661 mL, 2.65 mmol) and dimethyl disulfide (0.239 mL, 2.65 mmol) successively. Finally the solution was heated under reflux for 40 h. The reaction mixture was treated with H_2O and the aqueous phase was extracted ether. The combined organic phase was dried with Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified with flash column chromatography using 10% EA/*n*-hexane (0.240 g). Yield 52%. $[\alpha]_D^{25}$ −130.0 (*c* 0.34, $CHCl_3$). IR (neat) 3056, 2915, 2826, 1594, 1497, 1430, 1356, 1236, 1157, 1068, 978, 753 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83–7.85 (m, 4H, aromatic), 7.35–7.41 (m, 2H, aromatic), 7.11–7.39 (m, 4H, aromatic), 4.52 (d, $J=5.8$ Hz, 2H, OCH_2O), 4.41 (d, $J=5.8$ Hz, 2H, OCH_2O), 3.10–3.35 (m, 4H, $ArCH_2$), 2.85–3.06 (m, 4H, CH_2SMe), 2.98 (s, 6H, OCH_3), 2.20 (s, 6H, SCH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 153.18, 134.03, 133.24, 130.78, 129.44, 127.51, 126.05, 125.96, 125.22, 125.03, 99.06, 56.76, 34.60, 31.52, 15.64. MS (EI, 70 eV) *m*/*z*: 522 (M^+), 446 (M–$C_3H_8O_2$). Anal. calcd for $C_{30}H_{34}O_4S_2$: C, 68.93; H, 6.56; S, 12.27. Found: C, 68.64; H, 6.77, S, 12.21.

4.7. Preparation of (*R*)-3,3′-bis(2-methylsulfanylethyl)-(1,1′)-binaphthalenyl-2,2′-diol, 2

In a 25 mL round-bottomed flask was charged 14 (0.120 g, 0.230 mmol) and dissolved with THF (2.30 mL). To that solution was added catalytic amount of 6N HCl and heated under reflux for 12 h. The resulting solution was evaporated under reduced pressure and extracted with Et_2O. The combined organic phase was dried with Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified with flash column chromatography using 10% EA/*n*-hexane (0.097 g). Yield 96%. $[\alpha]_D^{25}$ +66.5 (*c* 1.0, $CHCl_3$). Mp:

122°C–124°C. IR (KBr) 3399, 3058, 2945, 2917, 1624, 1504, 1449, 1414, 1392,1211, 1131, 1016 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.84–7.87 (m, 4H, aromatic), 7.32–7.39 (m, 2H, aromatic), 7.22–7.29 (m, 2H, aromatic), 7.05–7.09 (m, 2H, aromatic), 5.22 (s, 2H, OH), 3.16–3.22 (m, 4H, $ArCH_2$), 2.89–2.94 (m, 4H, CH_2SCH_3), 2.17 (s, 6H, SCH_3). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 151.61, 132.40, 130.73, 129.34, 129.20, 127.91, 126.84, 124.10, 124.00, 110.98, 34.02, 31.36, 15.36. MS (EI, 70 eV) m/z: 434 (M^+), 373 ($M-C_2H_5S$), 325 ($M-C_3H_9SO_2$). Anal. calcd for $C_{26}H_{26}O_2S_2$: C, 71.85; H, 6.03; S, 14.76. Found: C, 71.81; H, 6.02, S, 14.49%.

4.8. Preparation of (*R*)-3,3′-bis(2-bromoethyl)-2,2′-bis-(methoxymethoxy)-(1,1′)-binaphthalenyl, 15

To a 50 mL round-bottomed flask were charged **13** (0.759 g, 1.64 mmol), CBr_4 (1.632 g, 4.92 mmol), and 2,6-lutidine (0.955 mL, 8.20 mmol) in 16.4 mL MC was added triphenylphosphine (1.075 g, 4.10 mmol) at 0°C and stirred at rt for 12 h. After completion of reaction, reaction mixture was quenched with water and extracted with methylene chloride. The combined organic phase was dried with Na_2SO_4, filtered and concentrated under reduced pressure. The resulting solid was dissolved with cold diethyl ether and insoluble solid was filtered off. The product was purified with flash column chromatography using 10% EtOAc/*n*-hexane (0.846 g). Yield 88%. $[\alpha]_D^{25}$ +116.3 (*c* 0.27, $CHCl_3$). IR (KBr) 3055, 2955, 2824, 1497, 1358, 1203, 969, 754, 555 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 3.07 (s, 6H, OCH_3), 3.34–3.62 (m, 4H, CH_2Br), 3.73–3.84 (m, 4H, $ArCH_2$), 4.38 (d, $J=5.8$ Hz, 2H, OCH_2O), 4.46 (d, $J=5.8$ Hz, 2H, OCH_2O), 7.12–7.15 (m, 2H, aromatic), 7.21–7.27 (m, 2H, aromatic), 7.37–7.44 (m, 2H, aromatic), 7.84–7.88 (m, 4H, aromatic). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 32.24, 35.28, 56.95, 99.26, 125.12, 125.24, 125.87, 126.48, 127.72, 130.26, 130.65, 132.32, 133.45, 153.33. MS (EI, 70 eV) m/z: 514 ($M^+-C_3H_8O_2+4$), 512 ($M^+-C_3H_8O_2+2$), 510 ($M^+-C_3H_8O_2$). Anal. calcd for $C_{28}H_{28}Br_2O_4$: C, 57.16; H, 4.80. Found: C, 57.13; H, 4.84%.

4.9. Preparation of (*R*)-3,3′-bis(2-*t*-butylsulfanylethyl)-2,2′-bis(methoxymethoxy)-(1,1′)-binaphthalenyl, 16

In a 25 mL round-bottomed flask sodium (0.070 g, 3.06 mmol) was dissolved in 10.2 mL MeOH and *t*-BuSH (0.402 mL, 3.57 mmol) was added at rt dropwisely. To this resulting solution was added **15** (0.600 g, 1.02 mmol) dissolved in THF as one portion at rt and stirred for 18 h. After the completion of reaction was added water to the reaction mixture and the solvent was removed under reduced pressure. The aqueous phase was extracted with ethyl ether and the combined organic phase was dried with Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified with flash column chromatography using 5% EA/*n*-hexane (0.581 g). Yield 94%. IR (neat) 3055, 2899, 2863, 2825, 1457, 1362, 1069, 922, 750 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.37 (s, 18H, *t*-Bu), 2.99 (s, 6H, OCH_3), 2.90–3.10 (m, 4H, CH_2SBu^t), 3.10–3.30 (m, 4H, $ArCH_2$), 4.43 (d, $J=5.8$ Hz, 2H, OCH_2O), 4.52 (d, $J=5.8$ Hz, 2H, OCH_2O), 7.12–7.26 (m, 4H, aromatic), 7.35–7.41 (m, 2H, aromatic), 7.82–7.86 (m, 4H, aromatic). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 28.84, 31.06, 31.92, 42.20, 56.78, 99.03, 124.96, 127.53, 125.98, 129.31, 130.77, 133.22, 134.44, 153.20. MS (EI, 70 eV) m/z: 606 (M^+), 474 ($M-C_6H_{12}SO$), 430 ($M-C_{10}H_{24}O_2$). Anal. calcd for $C_{36}H_{46}O_4S_2$: C, 71.25; H, 7.64; S, 10.57. Found: C, 69.27; H, 8.06, S, 9.44%.

4.10. Preparation of (*R*)-3,3′-bis(2-*t*-butylsulfanylethyl)-(1,1′)-binaphthalenyl-2,2′-diol, 3

In a 25 mL round-bottomed flask were placed **16** (0.581 g, 0.957 mmol) and MC (6.00 mL). This resulting mixture was cooled to −78°C and MeSH (0.460 g, 9.57 mmol in 3.57 mL MC) and $BF_3{\cdot}OEt_2$ (0.036 mL, 0.287 mmol) were added successively. The cooling bath was removed and the reaction mixture was stirred for 12 h at rt. After the completion of reaction, saturated $NaHCO_3$ solution was added to that solution. The organic phase was extracted with MC and the combined organic phase was washed with brine. The crude product was purified with flash column chromatography using 10% EA/*n*-hexane (0.464 g). Yield 94%. $[\alpha]_D^{25}$ +60.2 (*c* 1.0, $CHCl_3$). Mp: 129–132°C. IR (KBr) 3528, 3320, 2960, 2938, 2897, 1624, 1210, 750 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.34 (s, 18H, *t*-Bu), 2.95 (t, $J=7.7$ Hz, 4H, CH_2SBu^t), 3.16 (t, $J=7.7$ Hz, 4H, $ArCH_2$), 5.23 (s, 2H, OH), 7.06–7.10 (m, 2H, aromatic), 7.22–7.28 (m, 2H, aromatic), 7.32–7.38 (m, 2H, aromatic), 7.84–7.87 (m, 4H, aromatic). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 28.21, 31.04, 32.42, 42.33, 111.04, 124.03, 124.05, 126.74, 127.92, 129.32, 129.50, 130.69, 132.41, 151.65. MS (EI, 70 eV) m/z: 518 (M^+), 406 ($M-C_8H_{16}$), 359 ($M-C_9H_{19}S$). Anal. calcd for $C_{32}H_{28}O_2S_2$: C, 74.09; H, 7.38; S, 12.36. Found: C, 74.01; H, 7.38, S, 12.36%.

4.11. Preparation of (*R*)-2,2′-bis(methoxymethoxy)-3,3′-bis(2-phenylsulfanylethyl)-(1,1′)-binaphthalenyl, 17

In a 25 mL round-bottomed flask was charged **13** (0.300 g, 0.649 mmol) and dissolved with THF (6.46 mL). To that resulting solution were added tributylphosphine (0.485 mL, 1.95 mmol) and diphenyldisulfide (0.426 g, 1.95 mmol) at rt and heated under reflux for 12 h. The reaction mixture was treated with H_2O and the aqueous phase was extracted ether. The combined organic phase was dried with Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified with flash column chromatography using 10% EA/*n*-hexane (0.362 g). Yield 86%. ^1H NMR (300 MHz, $CDCl_3$): δ 2.91 (s, 6H, OCH_3), 3.14–3.45 (m, 8H, $ArCH_2CH_2Ph$), 4.36 (d, $J=5.8$ Hz, 2H, OCH_2O), 4.45 (d, $J=5.8$ Hz, 2H, OCH_2O), 7.11–7.52 (m, 16H, aromatic), 7.79–7.85 (m, 4H, aromatic). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 31.57, 33.96, 56.72, 99.04, 125.07, 125.16, 125.96, 126.14, 127.53, 128.91, 129.36, 129.63, 130.72, 133.28, 133.66, 136.40, 153.21. MS (EI, 70 eV) m/z: 646 (M^+), 570 ($M-C_3H_8O_2$). Anal. calcd for $C_{40}H_{38}O_4S_2$: C, 74.27; H, 5.92; S, 9.91. Found: C, 66.01; H, 5.82, S, 8.50%.

4.12. Preparation of (*R*)-3,3′-bis(2-phenylsulfanylethyl)-(1,1′)-binaphthalenyl-2,2′-diol, 4

In a 10 mL round-bottomed flask were placed **17** (0.100 g, 0.155 mmol) and MC (1.00 mL). This resulting mixture was cooled to −78°C and MeSH (0.0746 g, 1.55 mmol in 0.55 mL MC) and $BF_3{\cdot}OEt_2$ were added successively. The cooling bath was removed and the reaction mixture was stirred for 12 h at rt. After the completion of reaction, saturated $NaHCO_3$ solution was added to that solution. The organic phase was extracted with MC and the combined organic phase was washed with brine. The crude product was purified with flash column chromatography (10% EA/*n*-hexane). Yield 81%. $[\alpha]_D^{25}$ +67.3 (*c* 1.0, $CHCl_3$). IR (KBr) 3508, 3057, 2927, 1624, 1480, 1387, 1212, 1093, 1024, 739 cm^{-1} ^1H NMR (300 MHz, $CDCl_3$): δ 3.19–3.26 (m, 4H, CH_2SPh), 3.31–3.38 (m, 4H, $ArCH_2$), 5.14 (s, 2H, OH), 7.03–7.41 (m, 16H, aromatic), 7.81–7.85 (m, 4H, aromatic). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 24.69, 26.08, 103.86, 116.96, 117.17, 118.80, 119.96, 120.94, 121.74, 121.87, 121.92, 121.98, 122.33, 124.09, 125.41, 144.57. MS (EI, 70 eV) *m*/*z*: 558 (M^+), 448 ($M-C_6H_6S$), 325 ($M-C_{13}H_{13}S_2$). Anal. calcd for $C_{36}H_{30}O_2S_2$: C, 77.38; H, 5.41; S, 11.48. Found: C, 74.67; H, 5.73, S, 12.91%.

4.13. Preparation of (*R*)-3,3′-bis(bis(methylsulfanyl)-methyl)-(1,1′)-binaphthalenyl-2,2′-diol, 6

In a 100 mL round-bottomed flask were placed **10** (1.88 g, 4.37 mmol) and methylene chloride (33.7 mL). This resulting mixture was cooled to −78°C and MeSH (2.10 g, 43.7 mmol in 10.0 mL MC) and $BF_3{\cdot}OEt_2$ (0.166 mL, 1.31 mmol) were added successively. The cooling bath was removed and the reaction mixture was stirred for 12 h at rt. After the completion of reaction, saturated $NaHCO_3$ solution was added to that solution. The organic phase was extracted with MC and the combined organic phase was washed with brine. The crude product was purified with flash column chromatography using 10% EA/*n*-hexane (1.36 g). Yield 62%. $[\alpha]_D^{25}$ +61.5 (*c* 1.0, $CHCl_3$). Mp: 98°C. IR (KBr) 3489, 3057, 2913, 1620, 1434, 1145, 961, 751 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 2.22 (s, 12H, SCH_3), 5.44 (s, 2H, $CH(SCH_3)_2$), 5.55 (s, 2H, OH), 7.06–7.08 (m, 2H, aromatic), 7.27–7.31 (m, 2H, aromatic), 7.37–7.40 (m, 2H, aromatic), 7.91 (d, $J=8.1$ Hz, 2H, aromatic), 8.15 (s, 2H, aromatic). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 14.87, 50.06, 112.14, 124.05, 124.42, 127.60, 128.41, 128.56, 129.36, 132.73, 149.79. MS (EI, 70 eV) *m*/*z*: 451 ($M-CH_3S$), 403 ($M-C_2H_7S_2$), 389 ($M-C_3H_{10}S_2$). Anal. calcd for $C_{26}H_{26}O_2S_4$: C, 62.61; H, 5.25; S, 25.72. Found: C, 62.67; H, 6.57; S, 25.19%.

4.14. Preparation of (*R*)-3,3′-bis(2,2-bis(methylsulfanyl)-2-trimethylsilanylethyl)-2,2′-bis(methoxymethoxy)-(1,1′)-binaphthalenyl, 19

In a 50 mL round-bottomed flask were charged **11** (0.150 g, 0.345 mmol), CBr_4 (0.345 g, 1.03 mmol), 2,6-lutidine (0.202 mL, 1.73 mmol) and 3.45 mL MC and to this solution was added triphenylphosphine (0.226 g, 0.863 mmol) at 0°C and stirred at rt for 2 h. After completion of reaction, reaction mixture was quenched with water and extracted with methylene chloride. The combined organic phase was dried with Na_2SO_4, filtered and concentrated under reduced pressure. The resulting solid was dissolved with cold diethyl ether and insoluble solid was filtered off. The product was used for the next step without further purification. To a stirred solution of (bismethylsulfanylmethyl)trimethylsilane (0.249 g, 1.38 mmol) in 3.45 mL of THF was added *n*-BuLi (2.31 mL, 2.23 M in hexane, 1.04 mmol) at −78°C and slowly warmed to 0°C. The solution was stirred for 10 min at that temperature and cooled again to −78°C. To the resulting solution was added the product (dissolved in THF) obtained above. The reaction was quenched with H_2O and extracted with ether. The organic phase was dried with Na_2SO_4 and filtered. The solution was concentrated under reduced pressure and the crude product was purified with flash column chromatography using 5% EtOAc/*n*-hexane (0.225 g). Yield 74%. ^1H NMR (300 MHz, $CDCl_3$): δ 0.04 (s, 18H, TMS), 1.93 (s, 6H, SCH_3), 2.01 (s, 6H, SCH_3), 2.17 (s, 6H, OCH_3), 3.02 (s, 4H, CH_2) 4.27–4.36 (m, 4H, OCH_2O), 6.92–6.95 (m, 2H, aromatic), 7.02–7.08 (m, 2H, aromatic), 7.20–7.26 (m, 2H, aromatic), 7.74 (d, $J=6.9$ Hz, 2H, aromatic) 8.31 (s, 2H, aromatic).

4.15. Preparation of (*R*)-3,3′-bis(2,2-bis(methylsulfanylethyl))-2,2′-bis(methoxymethoxy)-(1,1′)-binaphthalenyl, 20

To a stirred solution **19** (0.070 g, 0.092 mmol) in 0.922 mL of THF was added TBAF (0.922 mL, 1.0 M in THF) at rt and stirred for 30 min. 6N HCl was added and stirred. The aqueous phase was extracted with ethyl acetate. The organic phase was dried with Na_2SO_4 and filtered. The solution was concentrated under reduced pressure and the crude product was purified with flash column chromatography using 10% EtOAc/*n*-hexane (0.050 g). Yield 88%. ^1H NMR (300 MHz, $CDCl_3$): δ 2.15 (s, 6H, SCH_3), 2.18 (s, 6H, SCH_3), 3.10 (s, 6H, OCH_3), 3.28 (dd, $J=8.5$ Hz, $J=14.0$ Hz, 2H, CH_2) 3.50 (dd, $J=6.9$ Hz, $J=14.0$ Hz, 2H, CH_2), 4.34 (dt, $J=7.0$ Hz, $J=8.3$ Hz, 2H, CH), 4.44 (dd, $J=5.8$ Hz, $J=10.7$ Hz, 4H, OCH_2O), 7.13–7.24 (m, 4H, aromatic), 7.35–7.41 (m, 2H, aromatic), 7.83–7.86 (m, 2H, aromatic).

4.16. Preparation of (*R*)-3,3′-bis-(2,2-bis(methylsulfanyl)ethyl)-(1,1′)-binaphthalenyl-2,2′-diol, 7

In a 25 mL round-bottomed flask were placed **20** (0.147 g, 0.239 mmol) and MC (1.4 mL). This resulting mixture was cooled to −78°C and MeSH (0.115 g, 2.39 mmol in 1.0 mL MC) and $BF_3{\cdot}OEt_2$ were added successively. The cooling bath was removed and the reaction mixture was stirred for 12 h at rt. After the completion of reaction, saturated $NaHCO_3$ solution was added to that solution. The organic phase was extracted with MC and the combined organic phase was washed with brine. The crude product was purified with flash

column chromatography using 10% EA/*n*-hexane (0.101 g). Yield 80%. $[\alpha]_D^{25}$ +60.8 (*c* 0.12, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ 2.16 (m, 12H, SCH_3), 3.37 (qd, $J=7.6$ Hz, $J=13.7$ Hz, 4H, CH_2), 4.24 (t, $J=7.5$ Hz, 2H, CH), 5.39 (s, 2H, OH) 7.09–7.11 (m, 2H, aromatic), 7.25–7.28 (m, 2H, aromatic), 7.34–7.38 (m, 2H, aromatic), 7.83–7.86 (m, 4H, aromatic).

4.17. Preparation of (*R*)-3,3′-bis(3-hydroxypropyl)-2,2′-bis (methoxymethoxy)-(1,1′)-binaphthalenyl, 21

To a stirred solution of (*R*)-2,2′-bis(methoxymethoxy)-(1,1′)-binaphthalenyl (0.150 g, 0.400 mmol in 6.67 mL ether) was added *n*-BuLi (0.597 mL, 1.20 mmol, 2.01 M in hexane) at 0°C and stirred for 3 h at room temperature. The resulting mixture was cooled to −78°C and diluted with anhydrous THF (4.00 mL). To the resulting dark brown solution was added trimethylene oxide (0.104 mL, 1.60 mmol), followed by $BF_3{\cdot}OEt_2$ (0.152 mL, 1.20 mmol) and stirred for 1 h at −78°C. The reaction mixture was quenched by addition of saturated $NaHCO_3$ solution and extracted with diethyl ether. The combined organic phase was dried with Na_2SO_4, filtered and concentrated under reduced pressure. The product was purified with flash column chromatography using 70% EtOAc/*n*-hexane (0.101 g). Yield 51%. $[\alpha]_D^{25}$ −136.9 (*c* 0.84, $CHCl_3$). IR (neat) 3406, 2936, 2876, 1497, 1431, 1236, 1157, 753 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 1.95 (br s, 2H, OH), 2.02–2.07 (m, 4H, $CH_2CH_2CH_2$), 2.95 (s, 6H, OCH_3), 2.90–3.15 (m, 4H, $ArCH_2$), 3.70–3.80 (br m, 4H, CH_2OH), 4.38 (d, $J=5.5$ Hz, 2H, OCH_2O), 4.53 (d, $J=5.5$ Hz, 2H, OCH_2O), 7.13–7.26 (m, 4H, aromatic), 7.36–7.41 (m, 2H, aromatic), 7.81 (m, 4H, aromatic). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 27.00, 33.74, 56.81, 61.89, 77.46, 99.08, 125.05, 125.28, 125.94, 127.43, 129.25, 131.01, 132.97, 135.23, 153.06. MS (EI, 70 eV) *m*/*z*: 430 ($M^+-C_3H_7O$). Anal. calcd for $C_{30}H_{34}O_6$: C, 73.45; H, 6.99. Found: C, 73.40; H, 7.01%.

4.18. Preparation (*R*)-3,3′-bis(3,3-bis(methylsulfanyl)-propyl)-2,2′-bis(methoxymethoxy)-(1,1′)-binaphthalenyl, 23

To a stirred solution of pyridinium chlorochromate (11.0 g, 51.0 mmol) and Celite in 20.0 mL MC was added **21** (1.47 g, 3.00 mmol in MC) at room temperature and the resulting mixture was heated under reflux for 30 min. After completion of reaction the resulting mixture was diluted with diethyl ether and the resulting solid was filtered off. The filtrate was concentrated under reduced pressure. The crude product was used for the next reaction. In another round-bottomed flask were charged the crude product and dimethyl disulfide (0.707 g, 7.50 mmol) and tributylphosphine (2.24 mL, 9.00 mmol) was added. The reaction mixture was stirred for 2 h and purified with flash column chromatography using 10% EtOAc/*n*-hexane (0.617 g). Yield 32% (two step). ^1H NMR (300 MHz, $CDCl_3$): δ 2,15 (s, 12H, SCH_3), 2.20–2.40 (m, 4H, $ArCH_2CH_2$), 2.94 (s, 6H, OCH_3), 3.05–3.30 (m, 4H, $ArCH_2$), 3.73 (t, $J=7.1$ Hz, 2H, $CH(SCH_3)_2$), 4.43 (d, $J=5.5$ Hz, 2H, OCH_2O), 4.54 (d, $J=5.7$ Hz, 2H, OCH_2O), 7.11–7.24 (m, 4H, aromatic), 7.34–7.41 (m, 2H, aromatic), 7.81–7.84 (m, 4H, aromatic). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 13.90, 24.75, 35.38, 53.66, 54.37, 99.19, 125.22, 126.14, 127.65, 129.36, 134.90, 153.09. MS (EI, 70 eV) *m*/*z*: 550 ($M^+-C_3H_8O_3$).

4.19. Preparation of (*R*)-3,3′-bis(3,3-bis(methylsulfanyl)-propyl)-(1,1′)-binaphthalenyl-2,2′-diol, 8

In a 25 mL round-bottomed flask was charged **23** (0.220 g, 0.342 mmol) and dissolved with THF (3.42 mL). To that solution was added catalytic amount of 6N HCl and heated to 70°C for 1 h. The resulting solution was evaporated under reduced pressure and extracted with Et_2O. The combined organic phase was dried with Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified with flash column chromatography using 10% EA/*n*-hexane (0.181 g). Yield 95%. $[\alpha]_D^{25}$ +57.7 (*c* 0.18, $CHCl_3$). Mp: 106°C. IR (KBr) 3423, 2915, 1625, 1438, 1389, 1211, 1143, 750 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 2.13 (s, 12H, SCH_3), 2.19–2.27 (m, 4H, $ArCH_2CH_2$), 3.16 (t, $J=7.7$ Hz, 4H, $ArCH_2$), 3.74 (t, $J=7.1$ Hz, 2H, $CH(SCH_3)_2$), 5.18 (s, 2H, OH), 7.82–7.86 (m, 4H, aromatic), 7.05–7.07 (m, 2H, aromatic), 7.22–7.28 (m, 2H, aromatic), 7.32–7.38 (m, 2H, aromatic). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 12.58, 29.34, 34.19, 54.06. 110.98, 123.98, 124.07, 126.73, 127.81, 129.36, 129.80, 130.51, 132.25, 151.68. MS (EI, 70 eV) *m*/*z*: 446 ($M^+-C_3H_7S_2$). Anal. calcd for $C_{30}H_{34}O_2S_4$: C, 64.94; H, 6.18; S, 23.12. Found: C, 64.72; H, 6.02, S, 23.22%.

4.20. General procedure for 1,4-addition to α,β-unsaturated cyclic ketones

In a 25 mL round-bottomed flask was charged Cu salt and diluted with solvent (half amount of total solvent volume). To that solution was added ligand (diluted with solvent) and stirred for 30 min at rt. Et_2Zn (neat) was added to the resulting solution at 0°C and stirred for 5 min. The resulting yellowish brown solution was immersed in bath for reaction temperature and enone was added at reaction temperature dropwisely. The reaction was monitored with TLC. After the completion of reaction 6N HCl was added to the reaction mixture very carefully and warmed to room temperature. The aqueous phase was extracted with diethyl ether and the combined organic phase was dried with Na_2SO_4, filtered and evaporated. The crude product was purified with flash column chromatography. The enantiomeric excess of 3-ethylcyclohexan-1-one was determined by GC analysis after conversion to the chiral acetal; 8-ethyl-(2*R*,4*R*)-2,4-dimethyl-1,5-dioxaspiro[5.5] undecane, which was prepared as described below.

4.20.1. (*R*)-3-Ethylcyclohexanone. ^1H NMR (300 MHz, $CDCl_3$): δ 0.90 (t, $J=7.4$ Hz, 3H, CH_3), 1.25–1.50 (m, 3H), 1.50–1.80 (m, 2H), 1.80–2.50 (m, 6H). MS (EI, 70 eV) *m*/*z*: 126 (M^+), 97 ($M-C_2H_5$).

4.21. Preparation of 8-ethyl-(2*R*,4*R*)-2,4-dimethyl-1,5-dioxaspiro[5.5]undecane

In a 25 mL round-bottomed flask were charged 3-ethylcyclohexan-1-one (0.269 g, 2.13 mmol), (2*R*,4*R*)-(−)-pentanediol (0.310 g, 2.98 mmol), catalytic amount of *p*-toluenesulfonic acid and benzene (7.1 mL). To that resulting mixture was added triethylorthoformate at room temperature and stirred for 1 h. After the completion of reaction water was added to that solution and the organic phase was extracted with diethyl ether. The combined organic phase was dried with Na_2SO_4 and filtered through the Celite pad. The crude product was purified with flash column chromatography (10% ether/*n*-hexane). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.87 (t, $J=7.4$ Hz, 3H, CH_3), 1.17–1.25 (m, 10H), 1.40–1.75 (m, 7H), 2.00–2.10 (m, 2H), 3.85–4.13 (m, 2H). MS (EI, 70 eV) m/z: 212 (M^+), 183 ($M-C_2H_5$). GC resolution: HP-FFAP (25 m×0.32 mm); oven temp.: 140°C, inj. temp.: 250°C, det. temp.: 250°C, flow rate: 1.0 mL/min; retention time: 7.69 min (*R*), 8.05 min (*S*).

4.21.1. (*R*)-3-Ethylcycloheptanone. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.93 (t, $J=7.1$ Hz, 3H, CH_3), 1.26–1.50 (m, 5H), 1.55–1.65 (m, 3H), 1.86–1.95 (m, 3H), 2.47–2.52 (m, 2H). MS (EI, 70 eV) m/z: 140 (M^+), 125 ($M-CH_3$), 111 ($M-C_2H_5$). GC resolution: CP-Cyclodextrin-B-2,3,6-M-19; oven temp.: 100°C, inj. temp.: 200°C, det. temp.: 200°C, Flow pressure: 70 kPa; retention time: 23.43 min (*S*), 24.09 min (*R*).

4.22. General procedure for 1,4-addition to α,β-unsaturated acyclic ketones

In a 25 mL round-bottomed flask was charged Cu salt and diluted with solvent (half amount of total solvent volume). To that solution was added ligand (diluted with solvent) and stirred for 30 min at rt. Et_2Zn (neat) was added to the resulting solution at 0°C and stirred for 5 min. The resulting yellowish brown solution was immersed in bath for reaction temperature and enone (diluted in small amount of solvent) was added at reaction temperature dropwisely. The reaction was monitored with TLC. After the completion of reaction 6N HCl was added to the reaction mixture very carefully and warmed to room temperature. The aqueous phase was extracted with diethyl ether and the combined organic phase was dried with Na_2SO_4, filtered and evaporated. The crude product was purified with flash column chromatography.

4.22.1. (3*S*)-1,3-Diphenylpentan-1-one. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.81 (t, $J=7.2$ Hz, 3H, CH_3), 1.61–1.82 (m, 2H, CH_2CH_3), 3.21–3.29 (m, 3H, $CHCH_2CO$), 7.14–7.40 (m, 5H, Ph), 7.38–7.45 (m, 2H, Ph), 7.50–7.56 (m, 1H, Ph), 7.88–7.92 (m, 2H, Ph). MS (EI, 70 eV) m/z: 209 ($M-C_2H_5$), 77 (Ph). HPLC resolution: Chiralcel OD-H; eluent 0.3% IPA/*n*-hexane; flow rate: 0.5 mL/min; retention time: 44.67 min (*S*), 51.0 min (*R*).

4.23. General procedure for 1,4-addition to nitroolefins

In a 25 mL round-bottomed flask was charged Cu salt and diluted with solvent (half amount of total solvent volume). To that solution was added ligand (diluted with solvent) and stirred for 30 min at rt. Et_2Zn (neat) was added to the resulting solution at 0°C and stirred for 5 min. The resulting yellowish brown solution was immersed in bath for reaction temperature and nitroolefin (diluted in small amount of solvent) was added at reaction temperature dropwisely. The reaction was monitored with TLC. After the completion of reaction 1:1 mixture of sat. $NH_4Cl_{(aq)}$ and 10% NH_4OH was added to the reaction mixture very carefully and warmed to room temperature. The aqueous phase was extracted with diethyl ether and the combined organic phase was dried with Na_2SO_4, filtered and evaporated. The crude product was purified with flash column chromatography.

4.23.1. (2*S*)-1-Nitro-2-phenylbutane. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.82 (t, $J=7.2$ Hz, 3H, CH_2CH_3), 1.57–1.80 (m, 2H, CH_2CH_3), 3.29–3.40 (m, 1H, CH), 4.52–4.57 (m, 2H, CH_2NO_2), 7.15–7.35 (m, 5H, Ph). MS (EI, 70 eV) m/z: 179 (M^+), 132 ($M-NO_2$), 104 ($M-C_2H_5NO_2$), 77 (Ph). GC resolution: Chirasil-dex CB (25 m×0.2 mm); oven temp.: 120°C, inj. temp.: 200°C, det. temp.: 200°C, flow rate: 1.0 mL/min; retention time: 29.28 min (*S*), 30.48 min (*S*). HPLC resolution: Chiralcel OD-H; Eluent 5% IPA/*n*-hexane; flow rate: 0.5 mL/min; retention time: 23.82 min (*R*), 30.10 min (*S*).

4.23.2. (2*S*)-1-Nitro-2-(4-methoxyphenyl)butane. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.83 (t, $J=7.4$ Hz, 3H, CH_2CH_3), 1.60–1.80 (m, 2H, CH_2CH_3), 3.20–3.40 (m, 1H, CH), 3.79 (s, 3H, OCH_3), 4.45–4.60 (m, 2H, CH_2NO_2), 6.86 (d, $J=8.8$ Hz, 2H, Ph), 7.10 (d, $J=8.8$ Hz, 2H, Ph). MS (EI, 70 eV) m/z: 209 (M^+). HPLC resolution: Chiralcel OD-H; eluent 5% IPA/*n*-hexane; flow rate: 0.7 mL/min; retention time: 20.75 min (*R*), 32.32 min (*S*).

Acknowledgements

This research was supported by a Sogang University Research Grant in 2002.

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