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Highly diastereoselective N-nitrosation of chiral (*E*)-2-(benzylidene-amino)ethanols with nitric oxide

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ABSTRACT

N-Nitrosation of (*E*)-(*S*)-2-(benzylidene-amino)ethanols **2** with nitric oxide occurred highly diastereoselectively, to give the (2*S*,4*S*)-diastereomer dominant *N*-nitroso-(2*S*,4*S*)-1,3-oxazolidines in good yield. Intermediate **2** was prepared from the reaction of benzaldehyde **1** with (*S*)-2-aminoethanol.

1. Introduction

N-Nitroso compounds have been considered to cause mutagenesis and carcinogenesis,[1] in addition to being utilized for enzyme inhibition and active site mapping.[2] As such, suppressing the formation of nitrosamines has been thought to protect biological tissues from cancer. Meanwhile, some nitrosamines have been widely used as nitric oxide (NO) releasing drugs in biomedicine.[3] Therefore, nitrosation studies may mimic interactions between biological tissues and nitrosating species, such as NO, N_2O_3, NO^+, NO_2/N_2O_4, and NOSCN, which generate mutagenic nitrosamines/peptides and nitrosate and deaminate DNA.[4]

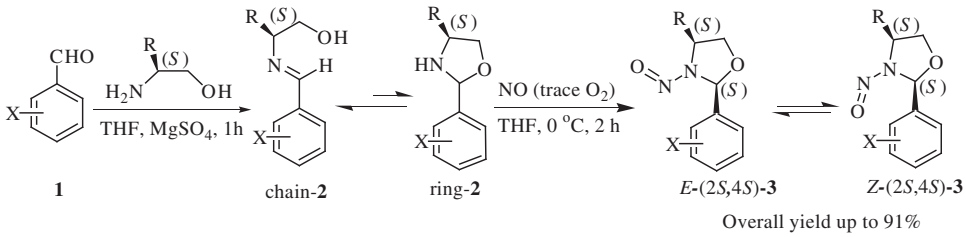
In our previous work,[5] we reported the reaction of NO with (*E*)-2-(benzylidene-amino)ethanol, which afforded an (*E*)-rotamer dominant mixture of (*E*)- and (*Z*)-*N*-nitroso-2-aryl-1,3-oxazolidine, wherein a tertiary carbon center was newly established. In conjunction with our continuing interest in the N-nitrosation of amines,[5] further studies were carried out to extend the 2-aminoethanol scope for chiral (*S*)-2-aminoethanols. It was found that the construction of a new tertiary carbon center in *N*-nitroso-2-aryl-1,3-oxazolidines occurred highly diastereoselectively.

2. Results and discussion

The reaction of benzaldehydes **1** with enantiopure (*S*)-2-aminoethanols afforded (*E*)-(*S*)-2-(benzylidene-amino) ethanols **2** in the primary steps. The resulting **2** reacted with NO in high diastereoselectivity to give (2*S*,4*S*)-diastereomer dominant *N*-nitroso-(2*S*,4*S*)-1,3-oxazolidines **3** in good yield with various ratios of (*E*)-(2*S*,4*S*)-**3** to (*Z*)-(2*S*,4*S*)-**3** (Scheme 1). The newly established tertiary carbon center was constructed highly diastereoselectively with an (*S*)-configuration.

Initial experiments using **2b** as a representative were concentrated on finding a suitable temperature, at which the reaction occurred with higher stereoselectivity. It was found that the ratio of (2*S*,4*S*)-**3b** to (2*R*,4*S*)-**3b** reached up to 95/5 at room temperature and up to 99/1 at 0 °C. It seemed that lower temperatures favored the stereochemistry more.

In a representative experiment, treatment of 1 mmol of *o*-chlorobenzaldehyde **1b** with 1 mmol of (*S*)-2-amino-3-phenylpropan-1-ol {$[\alpha]_D^{20} = -23$ (*c* 3.0, ethanol)} and 3 mmol of $MgSO_4$ in 30 mL of anhydrous tetrahydrofuran (THF) for 1 h gave rise to a mixture of chain- and ring-**2b** with an (*S*)-configuration. Purified NO was



Scheme 1.

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bubbled through the above-mentioned stirred solution at 0 °C for ca. 2 h. The stock solution was kept at a pressure of up to +10 mm H_2O column over local atmospheric pressure. After completion of the reaction, as indicated by TLC, the mixture was concentrated under vacuum, isolated and purified by column chromatography on silica gel (200–300 mesh, ethyl acetate-petroleum ether), and recrystallized from ethyl acetate, yielding colorless crystal **3b** (278 mg, 92% yield), *N*-nitroso-4-benzyl-2-(4′-chlorophenyl)-1,3-oxazolidine.

The two isomers of **3b**, major **3b** (99%) and minor **3b** (1%), were isolated. They were characterized by ^1H and ^{13}C NMR, MS, HRMS, and X-ray crystallography diffraction. X-ray analysis carried out on single crystals of major **3b** slowly grown in a mixed solvent of ethyl acetate and petroleum ether (1:20, v/v) (Fig. 1, the deposition number: CCDC 630583) clearly shows that major **3b** has a (2*S*,4*S*)-configuration with an (*E*)-conformation in the solid, where the (4*S*)-configuration of (*S*)-2-amino-3-phenylpropan-1-ol is known. As such, major **3b** is termed (2*S*,4*S*)-**3b** {$[\alpha]_D^{20} = -49$ (*c* 0.90, $CHCl_3$)}. It is present in a single (*E*)-conformation in the solid. ^1H NMR data for (2*S*,4*S*)-**3b** indicate that its two rotamers, (*E*)-(2*S*,4*S*)-**3b** and (*Z*)-(2*S*,4*S*)-**3b**, are in equilibrium with a ratio of 1.4:1 in solution. Minor **3b** was characterized to possess a (2*R*,4*S*)-configuration {$[\alpha]_D^{20} = +144$ (*c* 0.4, $CHCl_3$)}, a diastereomer of (2*S*,4*S*)-**3b**, and termed (2*R*,4*S*)-**3b**. X-ray crystallography

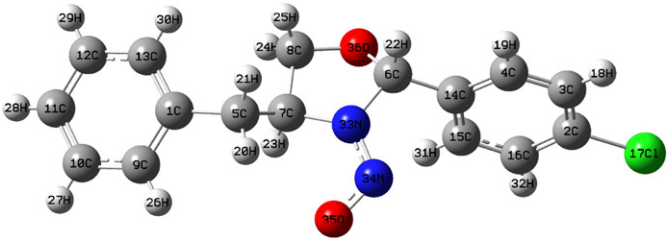


Figure 2. Molecular structure of (2*R*,4*S*)-**3b** (CCDC 632602).

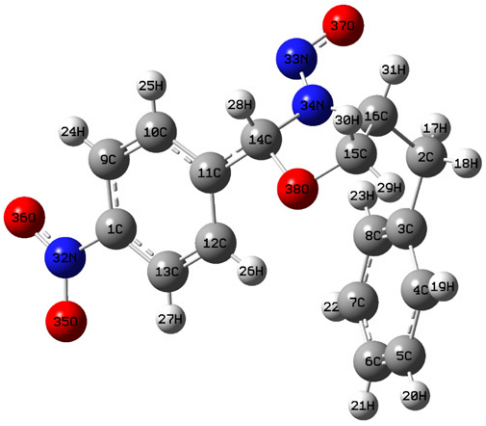


Figure 3. Molecular structure of (2*S*,4*S*)-**3d** (CCDC 632025).

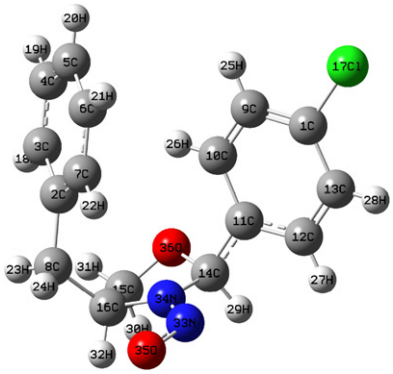


Figure 1. Molecular structure of (2*S*,4*S*)-**3b** (CCDC 630583).

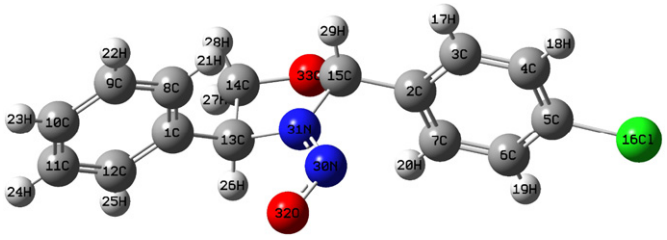
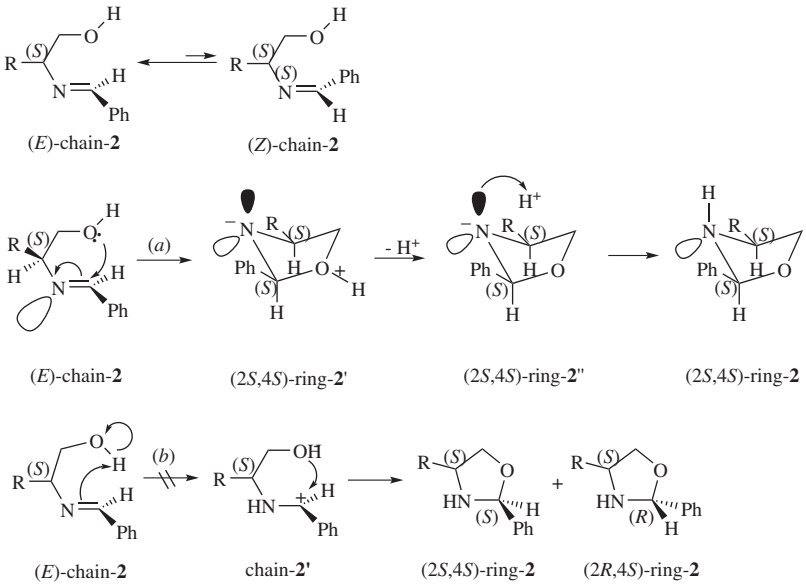


Figure 4. Molecular structure of (2*R*,4*S*)-**3i** (CCDC 630584).



Scheme 2.

Table 1
N-Nitrosation of (*E*)-(*S*)-2-(benzylidene-amino)ethanols with NO in THF

Entry	Benzaldehyde	X	R	Chain-**2**/ring-**2**[a]	Yield of **3**[b] (%)	(2*S*,4*S*)-**3**/(2*R*,4*S*)-**3**[c]	(*E*)-(2*S*,4*S*)-**3**/(*Z*)-(2*S*,4*S*)-**3**[d]	(*E*)-(2*R*,4*S*)-**3**/(*Z*)-(2*R*,4*S*)-**3**[d]
1	**1a**	H	Bn	98:2	87	98:2	1.9:1	1:1
2	**1b**	*p*-Cl	Bn	96:4	92	99:1	1.4:1	1:1
3	**1c**	*o*-Cl	Bn	95:5	91	99:1	1.5:1	1:1
4	**1d**	*p*-NO_2	Bn	90:10	91	92:8	1.4:1	1:1
5	**1e**	*p*-OCH_3	Bn	87:13	85	97:3	1.5:1	1:1
6	**1f**	*o*-OCH_3	Bn	90:10	83	95:5	1.6:1	1:1
7	**1g**	*p*-CH_3	Bn	94:6	87	95:5	2.3:1	1:1
8	**1h**	H	Ph	99:1	90	93:7	2.2:1	1:1
9	**1i**	*p*-Cl	Ph	98:2	91	98:2	2.3:1	1:1
10	**1j**	*o*-Cl	Ph	95:5	89	99:1	2.0:1	1:1
11	**1k**	*p*-NO_2	Ph	92:8	90	93:7	1.7:1	1:1
12	**1l**	*p*-OCH_3	Ph	95:5	84	96:4	1.9:1	1:1
13	**1m**	*o*-OCH_3	Ph	93:7	83	95:5	2.3:1	1:1
14	**1n**	*p*-CH_3	Ph	94:6	88	93:7	1.4:1	1:1

[a] The ratio of chain-**2** to ring-**2** was evaluated using the characteristic ^{1}H NMR peaks at 8.69–8.14 (N=CH) and 5.69–5.30 ppm (N–CH–O).
[b] Isolated yields after column chromatography.
[c] The ratio was estimated using individual isolated yields.
[d] The ratios were evaluated using the characteristic ^{1}H NMR peaks at 6.516–6.917 ((*E*)-**3**, N–CH–O) and 6.293–6.541 ppm ((*Z*)-**3**, N–CH–O).

diffraction (Fig. 2, the deposition number: CCDC 632602) showed the presence of a single (*E*)-conformation in solid. In solution, (2*R*,4*S*)-**3b** exists in both (*E*)-(2*R*,4*S*)-**3b** and (*Z*)-(2*R*,4*S*)-**3b** conformations with a ratio of 1:1. Similarly, Figures 3 and 4 show that both (2*S*,4*S*)-**3d** and (2*R*,4*S*)-**3i** are present in a single (*E*)-conformation in the solid.

It is assumed that the N-nitrosation would not significantly influence the chiral configuration of C-2 in ring-**2**. Hence, the stereochemistry occurs in the cycloaddition of chain-**2** during the tautomerism of **2**. The observed diastereoselectivity maybe attributed to three effects: (a) The imine moiety in chain-**2** is in a more stable (*E*)-conformation, (b) its N=C double bond is polarized to result in most δ^+ on the carbon atom. This favors an intramolecular nucleophilic attack of the Lewis basic oxygen on the carbon atom with δ^+ to undergo a cycloaddition (path *a* in Scheme 2), giving an intermediate (2*S*,4*S*)-ring-**2**′ with an (*S*)-configuration at C-2. Path *b* via a secondary carbocation chain-**2**′ formed from protonation by the hydroxyl group is obviated from the guess mechanisms because it will lead to a final 50:50 mixture of (2*S*,4*S*)- and (2*R*,4*S*)-**3b**, and (c) a stereoelectronic effect strongly influences the stereochemistry of the (2*S*,4*S*)-ring-**2**′ in the cycloaddition reaction. This stereoelectronic effect is caused by the nitrogen electron pair, which is oriented anticlinal to both the R (benzyl or phenyl) and phenyl groups on the five-membered ring during the cycloaddition reaction.[6] Such a stereoelectronic effect lowers the energy of (2*S*,4*S*)-ring-**2**′, accordingly. Only an (*S*)-configuration at C-4 can lead to these favorable orientations.

Table 2
^{1}H NMR data for –N–CH–O protons of **3**

Product	X	R	(*E*)-(2*S*,4*S*)-**3** (ppm)	(*Z*)-(2*S*,4*S*)-**3** (ppm)	$\delta_{(E)-(Z)}$ (ppm)
3a	H	Bn	6.67	6.36	0.31
3b	*p*-Cl	Bn	6.68	6.34	0.34
3c	*o*-Cl	Bn	6.95	6.54	0.41
3d	*p*-NO_2	Bn	6.82	6.42	0.40
3e	*p*-OCH_3	Bn	6.60	6.33	0.27
3f	*o*-OCH_3	Bn	6.92	6.54	0.38
3g	*p*-CH_3	Bn	6.65	6.33	0.32
3h	H	Ph	6.77	6.70	0.07
3i	*p*-Cl	Ph	6.73	6.64	0.09
3j	*o*-Cl	Ph	6.95	6.81	0.14
3k	*P*-NO_2	Ph	6.86	6.69	0.17
3l	*p*-OCH_3	Ph	6.69	6.52	0.17
3m	*o*-OCH_3	Ph	6.92	6.82	0.10
3n	*p*-CH_3	Ph	6.64	6.59	0.05

The diastereomeric nature of all the –N–CH–O protons of product **3** in their ^{1}H NMR spectra, due to the bent nature of the N=O bond and its mutual exchange, was clearly observed.[5,7] The ^{1}H NMR peak separation seems to be strongly dependent on the 4-substituent. A benzyl group leads to a bigger separation of 0.27–0.42 ppm, whereas a phenyl group causes a smaller separation of less than 0.1 ppm (Table 2). The ratio of (*E*)-(2*S*,4*S*)-**3** to (*Z*)-(2*S*,4*S*)-**3** in Table 1 was determined from the ^{1}H NMR peak area ratio of –N–CH–O corresponding to these two compounds.

Otherwise, the electronic feature of substituents on the benzene ring of the benzaldehyde affects more or less the product yield. An OCH_3 substituent on the benzene ring of benzaldehyde seems to give rise to a lower yield, as in the case of **1e**, **1f**, **1l**, and **1m**.

3. Conclusion

We have demonstrated that NO-mediated N-nitrosation converts (*E*)-(*S*)-2-(benzylidene-amino)ethanols to *N*-nitroso-(2*S*,4*S*)-1,3-oxazolidines, and the reaction occurs efficiently and highly diastereoselectively. The resulting oxazolines are present in a single (*E*)-conformation in solid, but they exist in both (*E*)- and (*Z*)-conformations with various ratios in solution. The products maybe used as potential NO donors. The homolytic dissociation energy of N–NO bonds has been estimated to be 28 kcal mol^{-1}.[8]

4. Experimental

4.1. General

All reagents were purchased from Alfa Aesar, and used as received. Solvents for reaction were treated by standard procedures prior to use.[9] Analytical thin-layer chromatography (TLC) was performed on silica gel precoated glass plates (0.25 mm thickness, 60F-254, E. Merck). Visualization was accomplished by an irradiation with a UV light at 254 nm. Flash chromatography was carried out using silica gel (200–300 mesh). NO was produced by the reaction of a 1 M H_2SO_4 solution with a saturated aqueous solution of $NaNO_2$ under an argon atmosphere. H_2SO_4 was added dropwise. NO was carried by argon and purified by passing through a series of scrubbing flasks containing 4 M NaOH, distilled water, and $CaCl_2$ in this order.

^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Varian MercuryPlus 300 or a Varian Avance 600 MHz NMR spectrometer. MS data were obtained with EI (70 eV) on an HP 5988 spectro-

meter by a direct inlet at 70 eV. High-resolution mass spectral analysis (HRMS) data were obtained on a Bruker Daltonics Apex II FT-ICR using an electrospray ionization technique. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer, and are reported in cm^{-1}. X-ray crystallography diffractions were carried out on a Bruker SMART APEX II Single-Crystal Diffractometer.

4.2. Characterization data for *N*-nitroso-1,3-oxazolidines (3)

4.2.1. Compound (*E*)-(2*S*,4*S*)-3a and (*Z*)-(2*S*,4*S*)-3a

Colorless crystals, mp 62–63 °C; $[\alpha]_D^{20} = -45$ (*c* 0.85, $CHCl_3$); IR (KBr) ν_{max} 3434 (vs), 3010 (vs), 2892 (s), 1904 (s), 1558 (s, ν_{sym} NO) cm^{-1}; MS (EI, 70 eV) *m/z* 268 (M^+, 25), 238 (50), 208 (65), 105 (100), 91 (90); HR-MS-ESI *m/z* calcd for $C_{16}H_{16}N_2O_2$ + Na 291.1205, found 291.1207, error −1.8 ppm. (*E*)-(2*S*,4*S*)-**3a**: ^1H NMR (600 MHz, $CDCl_3$) δ 7.35–7.46 (m, 10H, –Ph), 6.67 (s, 1H, –N–CH–O), 4.75–4.77 (m, 1H, –N–CH), 4.06–4.18 (m, 2H, –O–CH_2), 3.19–3.21 (dd, *J* = 4.2, 14.6 Hz, 1H, –CH_2–Ph), 2.60–2.65 (dd, *J* = 9.6, 14.6 Hz, 1H, –CH_2–Ph); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.5, 134.2, 133.6, 129.5 (2C), 128.4 (2C), 127.9 (2C), 127.3 (2), 126.9, 91.0, 69.5, 56.3, 36.2. (*Z*)-(2*S*,4*S*)-**3a**: ^1H NMR (600 MHz, $CDCl_3$) δ 7.35–7.46 (m, 10H, –Ph), 6.36 (s, 1H, –N–CH–O), 5.20–5.22 (m, 1H, –N–CH), 4.06–4.18 (m, 2H, –O–CH_2), 3.40–3.44 (dd, *J* = 6.2, 13.8 Hz, 1H, –CH_2–Ph), 3.10–3.13 (dd, *J* = 9.4, 13.2 Hz, 1H, –CH_2–Ph); ^{13}C NMR (150 MHz, $CDCl_3$) δ 135.8, 138.0, 135.0, 131.1, 129.3 (2C), 128.4 (2C), 128.0 (2C), 127.6 (2C), 88.7, 69.1, 60.3, 39.4.

4.2.2. Compound (*E*)-(2*S*,4*S*)-3b and (*Z*)-(2*S*,4*S*)-3b

Colorless crystals, mp 63.4 °C; $[\alpha]_D^{20} = -49$ (*c* 0.90, $CHCl_3$); IR (KBr) ν_{max} 3427 (vs), 3024 (vs), 2892 (s), 1914 (s), 1582 (s, ν_{sym} NO) cm^{-1}; MS (EI, 70 eV) *m/z* 302 (M^+, 18), 272 (65), 192 (70), 118 (100), 91 (90), 89 (30); HR-MS-ESI *m/z* calcd for $C_{16}H_{15}N_2O_2Cl$ + Na 325.0818, found 325.0826, error −2.4 ppm. (*E*)-(2*S*,4*S*)-**3b**: ^1H NMR (600 MHz, $CDCl_3$) δ 7.16–7.43 (m, 9H, –Ph-*p*-Cl, –Ph), 6.68 (s, 1H, –N–CH–O), 4.69–4.73 (m, 1H, –N–CH), 4.05–4.16 (m, 2H, –O–CH_2), 3.17–3.19 (dd, *J* = 3.6, 13.2 Hz, 1H, –CH_2–Ph), 2.59–2.63 (dd, *J* = 9.6, 13.2 Hz, 1H, –CH_2–Ph); ^{13}C NMR (150 MHz, $CDCl_3$) δ 136.2, 135.7, 134.9, 129.3, 129.0 (2C), 128.8 (2C), 128.3 (2C), 127.1 (2C), 91.6, 69.8, 56.7, 36.8. (*Z*)-(2*S*,4*S*)-**3b**: ^1H NMR (600 MHz, $CDCl_3$) δ 7.16–7.43 (m, 9H, –Ph-*p*-Cl, –Ph), 6.34 (s, 1H, –N–CH–O), 5.17–5.19 (m, 1H, –N–CH), 4.05–4.16 (m, 2H, –O–CH_2), 3.41–3.45 (dd, *J* = 6.0, 13.8 Hz, 1H, –CH_2–Ph), 3.08–3.12 (dd, *J* = 9.6, 13.2 Hz, 1H, –CH_2–Ph); ^{13}C NMR (150 MHz, $CDCl_3$) δ 135.8, 135.0, 134.0, 129.2, 129.0 (2C), 128.2 (2C), 128.0 (2C), 127.3(2C), 89.3, 69.4, 60.7, 38.6.

4.2.3. Compound (*E*)-(2*S*,4*S*)-3c and (*Z*)-(2*S*,4*S*)-3c

Colorless crystals, mp 62 °C; $[\alpha]_D^{20} = -48$ (*c* 1.00, $CHCl_3$); IR (KBr) ν_{max} 3430 (vs), 3028 (vs), 2890 (s), 1930 (s), 1581 (s, ν_{sym} NO) cm^{-1}; MS (EI, 70 eV) *m/z* 302 (M^+, 20), 272 (65), 192 (66), 118 (100), 91 (80), 89 (40); HR-MS-ESI *m/z* calcd for $C_{16}H_{15}N_2O_2Cl$ + Na 325.0818, found 325.0826, error −2.2 ppm. (*E*)-(2*S*,4*S*)-**3c**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.33–7.53 (m, 9H, –Ph-*o*-Cl, –Ph), 6.95 (s, 1H, –N–CH–O), 4.71–4.75 (m, 1H, –N–CH), 4.25–4.32 (m, 2H, –O–CH_2), 3.27–3.30 (dd, *J* = 3.2, 13.6 Hz, 1H, –CH_2–Ph), 2.63–2.68 (dd, *J* = 9.2, 13.8 Hz, 1H, –CH_2–Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.7, 135.2, 134.9, 129.1 (2C), 128.8, 128.5, 128.3, 127.8, 127.6 (2C), 127.0, 90.7, 68.2, 59.2, 36.4. (*Z*)-(2*S*,4*S*)-**3c**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.33–7.53 (m, 9H, –Ph-*o*-Cl, –Ph), 6.54 (s, 1H, –N–CH–O), 5.20–5.22 (m, 1H, –N–CH), 4.12–4.20 (m, 2H, –O–CH_2), 3.46–3.50 (dd, *J* = 5.8, 13.8 Hz, 1H, –CH_2–Ph), 3.12–3.16 (dd, *J* = 9.0, 13.0 Hz, 1H, –CH_2–Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.2, 136.5, 135.1, 130.5 (2C), 129.8, 128.4, 128.1, 128.0, 127.5 (2C), 127.3, 88.7, 67.4, 60.2, 39.6.

4.2.4. Compound (*E*)-(2*S*,4*S*)-3d and (*Z*)-(2*S*,4*S*)-3d

Colorless crystals, mp 69 °C; $[\alpha]_D^{20} = -52$ (*c* 1.00, $CHCl_3$); IR (KBr) ν_{max} 3440 (vs), 3078 (vs), 2926 (s), 1952 (s), 1523 (s, ν_{sym} NO) cm^{-1}; MS (EI, 70 eV) *m/z* 313 (M^+, 35), 283 (70), 191 (75), 150 (100), 91 (90), 89 (30); HR-MS-ESI *m/z* calcd for $C_{16}H_{15}N_3O_4$ + Na 336.0954, found 336.0959, error −2.0 ppm. (*E*)-(2*S*,4*S*)-**3d**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.10–8.27 (m, 9H, –Ph-*p*-NO_2, –Ph), 6.82 (s, 1H, –N–CH–O), 4.71–4.75 (m, 1H, –N–CH), 4.12–4.25 (m, 2H, –O–CH_2), 3.06–3.15 (m, 1H, –CH_2–Ph), 2.64–2.72 (dd, *J* = 9.0, 13.2 Hz, 1H, –CH_2–Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.9, 135.7, 134.2 (2C), 128.5 (2C), 128.3 (2C), 127.7 (2C), 123.0, 90.8, 69.9, 60.6, 55.4, 36.6. (*Z*)-(2*S*,4*S*)-**3d**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.10–8.27 (m, 9H, –Ph-*p*-NO_2, –Ph), 6.42 (s, 1H, –N–CH–O), 5.22–5.27 (m, 1H, –N–CH), 4.12–4.25 (m, 2H, –O–CH_2), 3.35–3.42 (m, 1H, –CH_2–Ph), 3.06–3.15 (m, 1H, –CH_2–Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.3, 135.4, 134.0 (2C), 128.4 (2C), 128.0 (2C), 127.1 (2C), 123.3, 88.6, 69.6, 60.6, 55.8, 39.6.

4.2.5. Compound (*E*)-(2*S*,4*S*)-3e and (*Z*)-(2*S*,4*S*)-3e

Colorless crystals, mp 62 °C; $[\alpha]_D^{20} = -43$ (*c* 1.00, $CHCl_3$); IR (KBr) ν_{max} 3442 (vs), 3051 (vs), 2944 (s), 1964 (s), 1528 (s, ν_{sym} NO) cm^{-1}; MS (EI, 70 eV) *m/z* 298 (M^+, 85), 267 (25), 238 (30), 136 (100), 117 (55), 91 (80); HR-MS-ESI *m/z* calcd for $C_{17}H_{18}N_2O_3$ + H 299.1393, found 299.1395, error −1.2 ppm. (*E*)-(2*S*,4*S*)-**3e**: ^1H NMR (300 MHz, $CDCl_3$) δ 6.86–7.46 (m, 9H, –Ph-*p*-OCH_3, –Ph), 6.60 (s, 1H, –N–CH–O), 4.68–4.73 (m, 1H, –N–CH), 4.13–4.23 (m, 2H, –O–CH_2), 3.84 (s, 3H, –O–CH_3), 3.02–3.13 (m, 1H, –CH_2–Ph), 2.64–2.72 (dd, *J* = 8.9, 12.8 Hz, 1H, –CH_2–Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.5, 135.2, 129.6, 128.6 (2C), 128.3 (2C), 128.0 (2C), 127.7 (2C), 123.0, 92.8, 69.9, 60.6, 58.1, 36.6. (*Z*)-(2*S*,4*S*)-**3e**: ^1H NMR (300 MHz, $CDCl_3$) δ 6.86–7.46 (m, 9H, –Ph-*p*-OCH_3), 6.33 (s, 1H, –N–CH–O), 5.22–5.27 (m, 1H, –N–CH), 4.12–4.25 (m, 2H, –O–CH_2), 3.784(s, 3H, –O–CH_3), 3.35–3.42 (m, 1H, –CH_2–Ph), 3.06–3.15 (m, 1H, –CH_2–Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.1, 134.8, 129.1, 128.1 (2C), 127.9 (2C), 127.1 (2C), 126.9 (2C), 123.3, 89.6, 69.0, 60.6, 58.7, 39.4.

4.2.6. Compound (*E*)-(2*S*,4*S*)-3f and (*Z*)-(2*S*,4*S*)-3f

Colorless crystals, mp 60 °C; $[\alpha]_D^{20} = -40$ (*c* 1.20, $CHCl_3$); IR (KBr) ν_{max} 3442 (vs), 3051 (vs), 2944 (s), 1964 (s), 1528 (s, ν_{sym} NO) cm^{-1}; MS (EI, 70 eV) *m/z* 298 (M^+, 70), 267 (45), 238 (40), 136 (100), 117 (65), 91 (70); HR-MS-ESI *m/z* calcd for $C_{17}H_{18}N_2O_3$ + H 299.1388, found 299.1395, error −3.6 ppm. (*E*)-(2*S*,4*S*)-**3f**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.46–8.34 (m, 9H, –Ph-*o*-OCH_3, –Ph), 6.92 (s, 1H, –N–CH–O), 4.64–4.70 (m, 1H, –N–CH), 4.11–4.20 (m, 2H, –O–CH_2), 3.72 (s, 3H, –O–CH_3), 3.01–3.12 (m, 1H, –CH_2–Ph), 2.63–2.71 (m, 1H, –CH_2–Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.3, 132.4, 129.3, 129.0 (2C), 128.8, 128.5, 128.3, 128.0, 127.9 (2C), 123.0, 91.8, 69.9, 60.6, 55.8, 36.6. (*Z*)-(2*S*,4*S*)-**3f**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.46–8.34 (m, 9H, –Ph-*o*-OCH_3, –Ph), 6.54 (s, 1H, –N–CH–O), 5.13–5.18 (m, 1H, –N–CH), 4.11–4.25 (m, 2H, –O–CH_2), 3.68 (s, 3H, –O–CH_3), 3.31–3.42 (m, 1H, –CH_2–Ph), 3.03–3.11 (m, 1H, –CH_2–Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.1, 132.6, 129.1, 128.9 (2C), 128.4, 128.1, 128.0, 127.3, 126.9 (2C), 123.3, 90.4, 69.0, 60.6, 55.7, 39.6.

4.2.7. Compound (*E*)-(2*S*,4*S*)-3g and (*Z*)-(2*S*,4*S*)-3g

Colorless crystals, mp 55 °C; $[\alpha]_D^{20} = -38$ (*c* 1.00, $CHCl_3$); IR (KBr) ν_{max} 3438 (vs), 3032 (vs), 2925 (s), 1935(s), 1520(s, ν_{sym} NO) cm^{-1}; MS (EI, 70 eV) *m/z* 282 (M^+, 40), 252 (55), 222 (60), 119 (100), 91 (70); HR-MS-ESI *m/z* calcd for $C_{17}H_{18}N_2O_3$ + H 283.1434, found 283.1446, error −4.2 ppm. (*E*)-(2*S*,4*S*)-**3g**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–8.14 (m, 9H, –Ph-*p*-CH_3, –Ph), 6.65 (s, 1H, –N–CH–O), 4.54–4.60 (m, 1H, –N–CH), 4.05–4.16 (m, 2H, –O–CH_2), 3.01–3.12 (m, 1H, –CH_2–Ph), 2.63–2.71 (m, 1H, –CH_2–Ph), 2.36 (s, 3H, –CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.3, 130.4, 129.3, 128.8

(2C), 128.3 (2C), 128.1 (2C), 127.2 (2C), 123.4, 91.5, 69.9, 60.5, 36.5, 21.3. (*Z*)-(2*S*,4*S*)-**3g**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36–8.14 (m, 9H, –Ph-*p*-CH_3, –Ph), 6.33 (s, 1H, –N–CH–O), 5.12–5.14 (m, 1H, –N–CH), 4.11–4.23 (m, 2H, –O–CH_2), 3.30–3.45 (m, 1H, –CH_2–Ph), 3.05–3.13 (m, 1H, –CH_2–Ph), 2.32 (s, 3H, –CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.4, 130.2, 129.1, 128.2 (2C), 128.0 (2C), 127.3 (2C), 126.4 (2C), 123.3, 90.2, 69.3, 60.6, 39.6, 29.5.

4.2.8. Compound (*E*)-(2*S*,4*S*)-3h and (*Z*)-(2*S*,4*S*)-3h

Colorless crystals, mp 53 °C; $[\alpha]_D^{20} = -35$ (*c* 0.40, $CHCl_3$); IR (KBr) ν_{max} 3428 (vs), 3005 (vs), 2834 (s), 1924 (s), 1553 (s, ν_{sym} NO) cm^{-1}; MS (EI, 70 eV) *m/z* 254 (M$^+$, 20), 223 (15), 194 (65), 104 (100), 91 (60); HR-MS-ESI *m/z* calcd for $C_{15}H_{14}N_2O_2$ + Na 277.0960, found 277.0950, error +3.6 ppm. (*E*)-(2*S*,4*S*)-**3h**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30–7.60 (m, 10H, –Ph), 6.77 (s, 1H, –N–CH–O), 5.34–5.39 (q, *J* = 6.9 Hz, 1H, –N–CH), 4.61–4.69 (dd, *J* = 7.5, 9.0 Hz, 1H, –O–CH_2), 4.07–4.12 (dd, *J* = 6.6, 9.3 Hz, 1H, –O–CH_2); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.5, 137.2, 135.6, 130.5, 128.4 (2C), 128.0 (2C), 127.9 (2C), 126.9 (2C), 91.0, 71.5, 61.3. (*Z*)-(2*S*,4*S*)-**3h**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30–7.60 (m, 10H, –Ph), 6.70 (s, 1H, –N–CH–O), 5.68–5.72 (q, *J* = 6.0 Hz, 1H, –N–CH), 4.53–4.61 (dd, *J* = 6.9, 9.0 Hz, 1H, –O–CH_2), 4.20–4.24 (dd, *J* = 6.6, 9.3 Hz, 1H, –O–CH_2); ^{13}C NMR (150 MHz, $CDCl_3$) δ 137.8, 137.0, 134.0, 131.0, 128.7 (2C), 128.5 (2C), 128.3 (2C), 127.6 (2C), 90.0, 72.7, 62.3.

4.2.9. Compound (*E*)-(2*S*,4*S*)-3i and (*Z*)-(2*S*,4*S*)-3i

Colorless crystals, mp 57 °C; $[\alpha]_D^{20} = -37$ (*c* 0.50, $CHCl_3$); IR (KBr) ν_{max} 3402 (vs), 3041 (vs), 2880 (s), 1918 (s), 1564 (s, ν_{sym} NO) cm^{-1}; MS (EI, 70 eV) *m/z* 288 (M$^+$, 18), 257 (10), 228 (40), 165 (90), 104 (100); HR-MS-ESI *m/z* calcd for $C_{15}H_{13}N_2O_2Cl$ + Na 311.0550, found 311.0558, error −2.4 ppm. (*E*)-(2*S*,4*S*)-**3i**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22–7.51 (m, 9H, –Ph-*p*-Cl, –Ph), 6.73 (s, 1H, –N–CH–O), 5.32–5.37 (q, *J* = 6.6 Hz, 1H, –N–CH), 4.62–4.68 (dd, *J* = 7.5, 9.3 Hz, 1H, –O–CH_2), 4.05–4.11 (dd, *J* = 6.6, 9.0 Hz, 1H, –O–CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.2, 136.0, 133.7, 129.1, 128.9 (2C), 128.3 (2C), 128.1 (2C), 126.1 (2C), 91.8, 72.5, 59.3. (*Z*)-(2*S*,4*S*)-**3i**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22–7.51 (m, 9H, –Ph-*p*-Cl, –Ph), 6.64 (s, 1H, –N–CH–O), 5.66–5.70 (q, *J* = 6.3 Hz, 1H, –N–CH), 4.53–4.58 (dd, *J* = 6.9, 9.3 Hz, 1H, –O–CH_2), 4.19–4.23 (dd, *J* = 6.0, 9.0 Hz, 1H, –O–CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.3, 135.2, 135.4, 129.8, 129.5 (2C), 129.0 (2C), 128.0 (2C), 127.3 (2C), 90.0, 72.7, 62.9.

4.2.10. Compound (*E*)-(2*S*,4*S*)-3j and (*Z*)-(2*S*,4*S*)-3j

Colorless crystals, mp 55 °C; $[\alpha]_D^{20} = -32$ (*c* 0.70, $CHCl_3$); IR (KBr) ν_{max} 3434 (vs), 3058 (vs), 2885 (s), 1925 (s), 1547 (s, ν_{sym} NO) cm^{-1}; MS (EI, 70 eV) *m/z* 288 (M$^+$, 23), 258 (40), 228 (55), 165 (70), 104 (100); HR-MS-ESI *m/z* calcd for $C_{15}H_{13}N_2O_2Cl$ + Na 311.0562, found 311.0558, error +1.2 ppm. (*E*)-(2*S*,4*S*)-**3j**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33–7.64 (m, 9H, –Ph-*o*-Cl, –Ph), 6.95 (s, 1H, –N–CH–O), 5.42–5.47 (q, *J* = 7.5 Hz, 1H, –N–CH), 4.68–4.72 (dd, *J* = 7.5, 9.3 Hz, 1H, –O–CH_2), 4.09–4.15 (dd, *J* = 7.2, 9.6 Hz, 1H, –O–CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.5, 136.4, 133.2, 129.8 (2C), 129.3, 129.3, 128.5, 128.1, 128.0, 126.5 (2C), 91.3, 72.2, 59.2. (*Z*)-(2*S*,4*S*)-**3j**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22–7.51 (m, 9H, –Ph-*o*-Cl, –Ph), 6.81 (s, 1H, –N–CH–O), 5.77–5.82 (q, *J* = 6.0 Hz, 1H, –N–CH), 4.60–4.64 (dd, *J* = 6.3, 9.0 Hz, 1H, –O–CH_2), 4.21–4.25 (dd, *J* = 6.9, 9.0 Hz, 1H, –O–CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.8, 136.2, 135.8, 130.1 (2C), 129.7, 129.4, 129.2, 129.0, 128.5, 127.2 (2C), 89.7, 72.4, 62.5.

4.2.11. Compound (*E*)-(2*S*,4*S*)-3k and (*Z*)-(2*S*,4*S*)-3k

Colorless crystals, mp 55 °C; $[\alpha]_D^{20} = -39$ (*c* 1.20, $CHCl_3$); IR (KBr) ν_{max} 3480 (vs), 3014 (vs), 2836 (s), 1931 (s), 1526(s, ν_{sym} NO) cm^{-1}; MS (EI, 70 eV) *m/z* 299 (M$^+$, 40), 268 (56), 239 (70), 150 (100), 91 (70); HR-MS-ESI *m/z* calcd for $C_{15}H_{13}N_3O_4$ + Na 322.0795, found 322.0801, error −2.2 ppm. (*E*)-(2*S*,4*S*)-**3k**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24–8.31 (m, 9H, –Ph-*p*-NO_2, –Ph), 6.86 (s, 1H, –N–CH–O), 5.35–5.39 (q, *J* = 6.9 Hz, 1H, –N–CH), 4.66–4.71 (dd, *J* = 6.9, 9.0 Hz, 1H, –O–CH_2), 4.12–4.17 (dd, *J* = 7.2, 9.3 Hz, 1H, –O–CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.5, 136.7, 129.2, 129.0, 128.7 (2C), 127.8 (2C), 126.1 (2C), 123.9 (2C), 91.0, 72.8, 59.4. (*Z*)-(2*S*,4*S*)-**3k**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24–8.31 (m, 9H, –Ph-*p*-NO_2, –Ph), 6.69 (s, 1H, –N–CH–O), 5.70–5.73 (q, *J* = 6.0 Hz, 1H, –N–CH), 4.57–4.62 (dd, *J* = 6.0, 9.3 Hz, 1H, –O–CH_2), 4.24–4.29 (dd, *J* = 6.6, 9.0 Hz, 1H, –O–CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.8, 136.2, 129.4, 128.5, 128.2 (2C), 127.5 (2C), 127.1 (2C), 123.8 (2C), 89.5, 73.2, 63.0.

4.2.12. Compound (*E*)-(2*S*,4*S*)-3l and (*Z*)-(2*S*,4*S*)-3l

Colorless crystals mp 50 °C; $[\alpha]_D^{20} = -41$ (*c* 1.10, $CHCl_3$); IR (KBr) ν_{max} 3424 (vs), 3068 (vs), 2932 (s), 1955 (s), 1574 (s, ν_{sym} NO) cm^{-1}; MS (EI, 70 eV) *m/z* 284 (M$^+$, 60), 254 (20), 224 (40), 136 (100), 117 (75), 91 (50); HR-MS-ESI *m/z* calcd for $C_{16}H_{16}N_2O_3$ + H 285.1232, found 285.1237, error −2.2 ppm. (*E*)-(2*S*,4*S*)-**3l**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.82–7.56 (m, 9H, –Ph-*p*-OCH_3, –Ph), 6.69 (s, 1H, –N–CH–O), 5.30–5.35 (q, *J* = 6.3 Hz, 1H, –N–CH), 4.61–4.66 (dd, *J* = 6.9, 9.0 Hz, 1H, –O–CH_2), 4.04–4.10 (dd, *J* = 6.6, 9.0 Hz, 1H, –O–CH_2), 4.03 (s, 3H, –O–CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.5, 135.2, 129.3, 128.6, 128.2 (2C), 128.0 (2C), 127.4 (2C), 123.2 (2C), 91.2, 71.8, 61.7, 55.2. (*Z*)-(2*S*,4*S*)-**3l**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.82–7.56 (m, 9H, –Ph-*p*-OCH_3, –Ph), 6.52 (s, 1H, –N–CH–O), 5.68–5.72 (q, *J* = 6.0 Hz, 1H, –N–CH), 4.53–4.57 (dd, *J* = 6.6, 9.0 Hz, 1H, –O–CH_2), 4.17–4.21 (dd, *J* = 6.0, 9.0 Hz, 1H, –O–CH_2), 3.83 (s, 3H, –O–CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.2, 134.8, 129.7, 128.5, 128.1 (2C), 127.3 (2C), 126.1 (2C), 123.3 (2C), 90.2, 73.0, 62.7, 55.2.

4.2.13. Compound (*E*)-(2*S*,4*S*)-3m and (*Z*)-(2*S*,4*S*)-3m

Colorless crystals, mp 46 °C; $[\alpha]_D^{20} = -39$ (*c* 1.00, $CHCl_3$); IR (KBr) ν_{max} 3447 (vs), 3065 (vs), 2938 (s), 1949 (s), 1570 (s, ν_{sym} NO) cm^{-1}; MS (EI, 70 eV) *m/z* 284 (M$^+$, 60), 254 (55), 224 (60), 136 (100), 117 (50), 91 (34); HR-MS-ESI *m/z* calcd for $C_{16}H_{16}N_2O_3$ + H 285.1238, found 285.1237, error +1.0 ppm. (*E*)-(2*S*,4*S*)-**3m**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.90–7.65 (m, 9H, –Ph-*o*-OCH_3, –Ph), 6.92 (s, 1H, –N–CH–O), 5.34–5.39 (q, *J* = 6.6 Hz, 1H, –N–CH), 4.64–4.69 (dd, *J* = 6.6, 9.0 Hz, 1H, –O–CH_2), 4.09–4.15 (dd, *J* = 6.3, 9.3 Hz, 1H, –O–CH_2), 4.23 (s, 3H, –O–CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.2, 135.0, 129.8, 129.7, 129.1 (2C), 128.3, 128.1, 128.0, 127.3 (2C), 123.2, 91.2, 71.6, 61.5, 55.4. (*Z*)-(2*S*,4*S*)-**3m**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.82–7.56 (m, 9H, –Ph-*o*-OCH_3, –Ph), 6.82 (s, 1H, –N–CH–O), 5.68–5.72 (q, *J* = 6.0 Hz, 1H, –N–CH), 4.53–4.57 (dd, *J* = 6.6, 9.0 Hz, 1H, –O–CH_2), 4.17–4.21 (dd, *J* = 6.0, 9.0 Hz, 1H, –O–CH_2), 3.83 (s, 3H, –O–CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.0, 134.5, 129.3, 129.0, 128.7 (2C), 128.5, 128.2, 127.5, 125.8 (2C), 123.3, 90.1, 72.8, 62.7, 55.2.

4.2.14. Compound (*E*)-(2*S*,4*S*)-3n and (*Z*)-(2*S*,4*S*)-3n

Colorless crystals, mp 43 °C; $[\alpha]_D^{20} = -32$ (*c* 0.90, $CHCl_3$); IR (KBr) ν_{max} 3447 (vs), 3065 (vs), 2938 (s), 1949 (s), 1570 (s, ν_{sym} NO) cm^{-1}; MS (EI, 70 eV) *m/z* 268 (M$^+$, 30), 238 (65), 208 (44), 119 (100), 91 (80); HR-MS-ESI *m/z* calcd for $C_{16}H_{16}N_2O_2$ + H 269.1286, found 269.1288, error −1.5 ppm. (*E*)-(2*S*,4*S*)-**3n**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.78–7.52 (m, 9H, –Ph-*p*-CH_3, –Ph), 6.64 (s, 1H, –N–CH–O), 5.31–5.36 (q, *J* = 6.3 Hz, 1H, –N–CH), 4.62–4.67 (dd, *J* = 6.3, 9.3 Hz, 1H, –O–CH_2), 4.08–4.14 (dd, *J* = 6.0, 9.3 Hz, 1H, –O–CH_2), 2.43 (s, 3H, –CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.4, 135.3, 129.3, 128.6, 128.4 (2C), 128.0 (2C), 127.3 (2C), 123.0 (2C), 91.4, 71.3, 61.3, 21.3. (*Z*)-(2*S*,4*S*)-**3n**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.78–7.52 (m, 9H, –Ph-*p*-CH_3, –Ph), 6.59 (s, 1H, –N–CH–O), 5.64–5.68 (q, *J* = 6.3 Hz, 1H, –N–CH), 4.52–4.56 (dd, *J* = 6.3, 9.3 Hz, 1H,

–O–CH_2), 4.18–4.22 (dd, J = 6.3, 9.0 Hz, 1H, –O–CH_2), 2.38 (s, 3H, –CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.2, 134.3, 129.5, 128.3, 128.1 (2C), 127.2 (2C), 125.4 (2C), 123.3 (2C), 90.2, 72.4, 62.3, 29.2.

4.2.15. Crystal data for (2*S*,4*S*)-3b

$C_{16}H_{15}N_2O_2Cl$, Mr = 302.75, space group $P21$ with cell parameters: a = 6.5605(3) Å, b = 0034(4) Å, c = 16.4669(9) Å, α = 90.00°, β = 100.873(2)°, γ = 90.00°, V = 743.00(7) Å^3, ρ_{calcd} = 1.353 mg/m^3, Z = 2, T = 294(2) K, μ=0.263 cm^{-1}, F_{000} = 316, $-7 \leqslant h \leqslant 7$, $-8 \leqslant k \leqslant 8$, $-16 \leqslant l \leqslant 19$, $5.04° \leqslant 2\theta \leqslant 50.98°$, 2718 data collected, 2181 unique data (R_{int} = 0.0186), 128 refined parameters. GOF(F^2) = 1.025, R_1 = 0.0406, wR_2 = 0.0792. The X-ray crystallographic structure of (2*S*,4*S*)-**3b** is shown in Figure 1. The crystallographic data have been deposited at the Cambridge Crystallographic Data Center as supplementary publication No. CCDC 630583.

4.2.16. Crystal data for (2*R*,4*S*)-3b

$C_{16}H_{15}N_2O_2Cl$, Mr = 302.75, space group $P212121$ with cell parameters: a = 5.7523(14) Å, b = 9.054(2) Å, c = 28.648(7) Å, α = 90.00°, β = 90.00°, γ = 90.00°, V = 1492.1(6) Å^3, ρ_{calcd} = 1.348 mg/m^3, Z = 4, T = 294(2) K, μ = 0.262 cm^{-1}, F_{000} = 632, $-6 \leqslant h \leqslant 6$, $-8 \leqslant k \leqslant 10$, $-34 \leqslant l \leqslant 34$, $4.72° \leqslant 2\theta \leqslant 50.98°$, 2750 data collected, 1531 unique data (R_{int} = 0.0543), 128 refined parameters. GOF(F^2) = 1.038, R_1 = 0.0446, wR_2 = 0.0741. The X-ray crystallographic structure of (2*R*,4*S*)-**3b** is shown in Figure 2. The crystallographic data have been deposited at the Cambridge Crystallographic Data Center as supplementary publication No. CCDC 632602.

4.2.17. Crystal data for (2*S*,4*S*)-3d

$C_{16}H_{15}N_3O_4$, Mr = 313.31, space group $P21$ with cell parameters: a = 6.7170(3) Å, b = 13.5145(7) Å, c = 8.2169(4) Å, α = 90.00°, β = 96.578(2)°, γ = 90.00°, V = 740.99(6) Å^3, ρ_{calcd} = 1.404 mg/m^3, Z = 2, T = 294(2) K, μ = 0.103 cm^{-1}, F_{000} = 328, $-7 \leqslant h \leqslant 8$, $-16 \leqslant k \leqslant 13$, $-9 \leqslant l \leqslant 9$, $5.00° \leqslant 2\theta \leqslant 50.98°$, 2071 data collected, 1617 unique data (R_{int} = 0.0309), 128 refined parameters. GOF(F^2) = 1.040, R_1 = 0.0420, wR_2 = 0.0855. The X-ray crystallographic structure of (2*S*,4*S*)-**3d** is shown in Figure 3. The crystallographic data have been deposited at the Cambridge Crystallographic Data Center as supplementary publication No. CCDC 632025.

4.2.18. Crystal data for (2*R*,4*S*)-3i

$C_{15}H_{13}N_2O_2Cl$, Mr = 288.72, space group $P212121$ with cell parameters: a = 7.5655(2) Å, b = 12.6030(3) Å, c = 14.4639(3) Å, α = 90.00°, β = 90.00°, γ = 90.00°, V = 1379.10(6) Å^3, ρ_{calcd} = 1.391 mg/m^3, Z = 4, T = 294(2) K, μ = 0.279 cm^{-1}, F_{000} = 600, $-9 \leqslant h \leqslant 6$, $-16 \leqslant k \leqslant 16$, $-16 \leqslant l \leqslant 18$, $4.28° \leqslant 2\theta \leqslant 54.52°$, 3084 data collected, 2294 unique data (R_{int} = 0.0270), 128 refined parameters. GOF(F^2) = 1.046, R_1 = 0.0401, wR_2 = 0.0699. The X-ray crystallographic structure of (2*R*,4*S*)-**3i** is shown in Figure 4. The crystallographic data have been deposited at the Cambridge Crystallographic Data Center as supplementary publication No. CCDC 630584.

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