A Practical Route to Regiospecifically Substituted (*R*)- and (*S*)-Oxazolylphenols

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Dedicated to Professor Dr. Horst Kunz on the occasion of his 60th birthday

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New, diversely substituted phenolic oxazolines **14a–d** and **15a–d** were prepared by two complementary routes A and B, starting from salicylic derivatives **4**–**7** and various enantiomerically pure 1,2-amino alcohols **13a–d**. In route A, the 1,2-amino alcohols **13a–d** were directly condensed with the salicylic acids **5** and **7**, using the Appel reaction, whereas in route B the amino alcohols **13b–d** were treated with the 2-hydroxybenzonitriles **4** and **6**, under Witte–Seeliger conditions. The latter route was advantageous for L-valinol **13b** and L-*tert*-leucinol **13c**, while route A was the method of choice for the new, sterically demanding amino alcohol **13a**, prepared from D- and L-serine. The nitro group in the salicylic derivatives **5** and **6** was introduced by means of a regiospecific *ipso* substitution of a *tert*-butyl group by nitric acid. The structure of the nitro product **5** was unambiguously assigned by NOE spectroscopy on the basis of the recently developed DPFGSE-ROE pulse sequence.

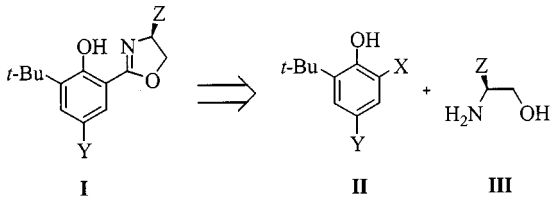
Introduction

The design of catalytic, asymmetric reactions that proceed with high enantioselectivity is an important goal in organic synthesis. An exponential increase in research in this area has resulted in substantial progress, particularly in the field of the metal-catalyzed epoxidation of nonfunctionalized alkenes (Jacobsen, Katsuki, and others).[1] Transition metal complexes derived from C_2-symmetric semicorrine (Pfaltz[2]) and bis(oxazoline) (Masamune, Evans, Nishiyama, and others[2d,2e,3]) have proven to be excellent catalysts for enantioselective cyclopropanation and aziridination. Chiral, enantiomerically pure oxazolines were readily available as both enantiomers, starting from D- and L-α-amino acids.[4] Besides bis(oxazolines), several monooxazolines joined to phosphanes,[5] pyridines,[6] and sulfides[7] have recently proven to be excellent ligands for the synthesis of asymmetric catalysts. In contrast, monooxazolines tethered to phenols have received far less attention. This situation was to change, however, when a phenolic oxazoline copper complex turned out to be a suitable catalyst for aerobic enantioselective (69% *ee*) Baeyer–Villiger oxidation (Bolm).[8] A salicyloxazoline derived from (1*S*,2*S*)-(+)-2-amino-1-phenyl-1,3-propanediol was reported to catalyze the addition of diethylzinc to arenecarbaldehydes with a reasonable enantiomeric excess (Williams).[9] Moderate enantioselectivities (60% *ee*) were achieved for cyclopropanation of styrene with chiral (salicyloxazoline)copper catalysts (Brunner),[10] while the enantioselective allylation of benzaldehyde (37% *ee*) was accomplished with chiral allylic (salicyloxazoline)chromium(III) catalysts (Kibayashi).[11] In addition, *O*-methyl-protected enantiomerically pure salicyloxazolines have been applied for the enantioselective (68% *ee*) Cu-catalyzed conjugate addition of Me_3Al to cross-conjugated dienones (Iwata).[12]

In order to obtain better enantioselectivities, new salicyloxazoline catalysts are needed. In this paper we present an efficient synthesis of a series of salicyloxazolines with sterically demanding phenyl substituents.

Results and Discussion

From retrosynthetic analysis and the synthon approach, chiral, nonracemic phenolic oxazolines such as **I** should be readily accessible from aromatic *ortho*-hydroxy acids or *ortho*-hydroxy nitriles **II** and enantiomerically pure 1,2-amino alcohols **III** (Scheme 1).[4] The bulky substituents (*t*Bu and



I **II** **III**

X = CO_2H, CN
Y = *t*-Bu, NO_2
Z = *i*-Pr, *t*-Bu, $CMe_2(OSiMe_3)$

Scheme 1

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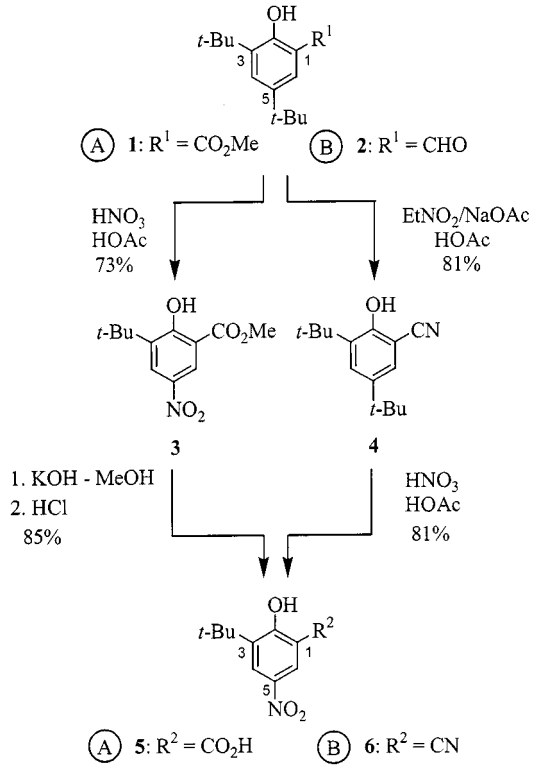
NO_2) on the aromatic substrates **II** were chosen for their opposite electronic properties. All optically active amino alcohols **III** were derived from α-amino acids. These amino alcohols **III** featured increasing steric demand on the aliphatic carbons that would form the oxazoline unit.

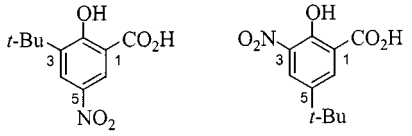
Salicylic Acid Derivatives

Methyl 3,5-di-*tert*-butyl-2-salicylate (**1**) was prepared from methyl salicylate according to a literature procedure[13]. Regiospecific *ipso* substitution of the *tert*-butyl group in the 5-position of **1** by NO_2, using fuming nitric acid in the presence of acetic acid, afforded nitro ester **3** (Scheme 2; route A).[14] Saponification of **3** with potassium hydroxide in methanol and subsequent acidification with hydrochloric acid yielded 3-*tert*-butyl-5-nitrosalicylic acid (**5**). Transformation of the aldehyde group of commercially available 3,5-di-*tert*-butylsalicylaldehyde (**2**) into a cyano group was performed in a one-step reaction, using nitroethane in the presence of sodium acetate and acetic acid, to give 3,5-di-*tert*-butyl-2-hydroxybenzonitrile (**4**) (Scheme 2; route B).[15] Regiospecific *ipso* substitution of the *tert*-butyl group in the 5-position of **4** by NO_2, again using concentrated nitric acid in the presence of acetic acid, afforded 3-*tert*-butyl-2-hydroxy-5-nitrobenzonitrile (**6**) (Scheme 2).[14]



Scheme 2

There was no evidence for the formation of 5-*tert*-butyl-3-nitrosalicylic acid (**5′**) (Scheme 3), indicating that the *ipso* substitution of the *tert*-butyl group in the 3-position of **1** does not take place. Compound **5** could easily be distinguished from **5′** by NMR (Figure 1), NOE spectroscopy being the method of choice. We therefore applied the recently developed DPFGSE-ROE pulse sequence[16] for structure analysis, employing a degassed solution of the reaction product in [D_6]DMSO. Irradiation of the signal at the lowest field in the ^{1}H NMR spectrum (δ = 8.5), assigned to 6-H, resulted in no enhancement of the signal of the *tert*-butyl group in the 3-position (Figure 1: B). Clearly, an enhanced signal for this group should be observed in the case of **5′**. Irradiation of the signal of 4-H (δ = 8.05) resulted in an intense enhancement of the *tert*-butyl signal, compatible



Scheme 3

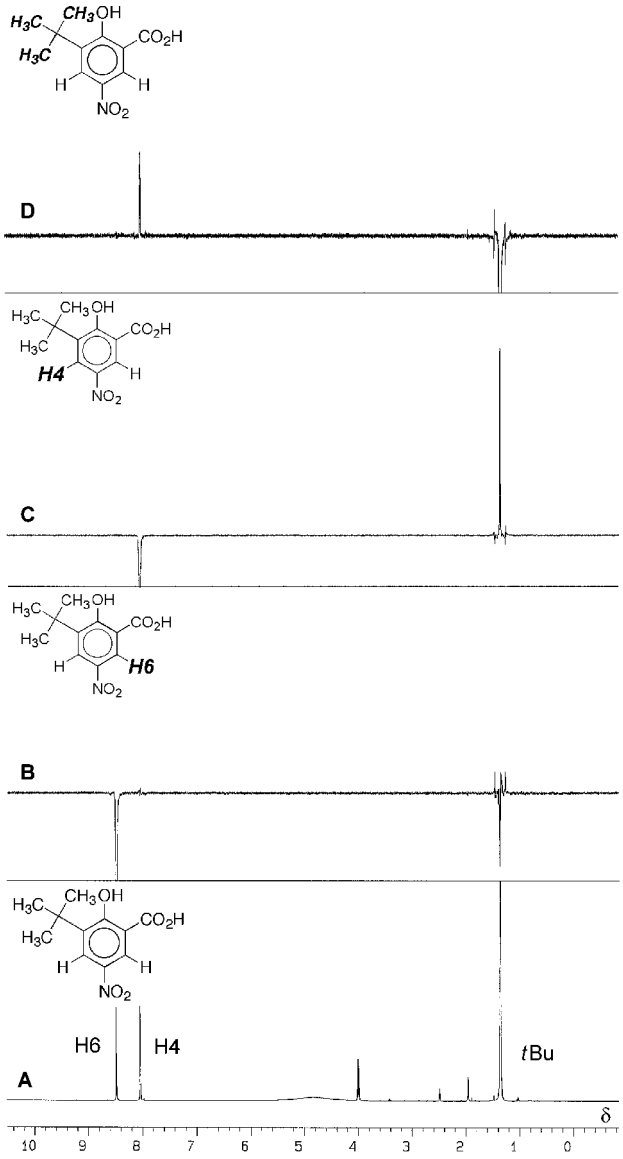
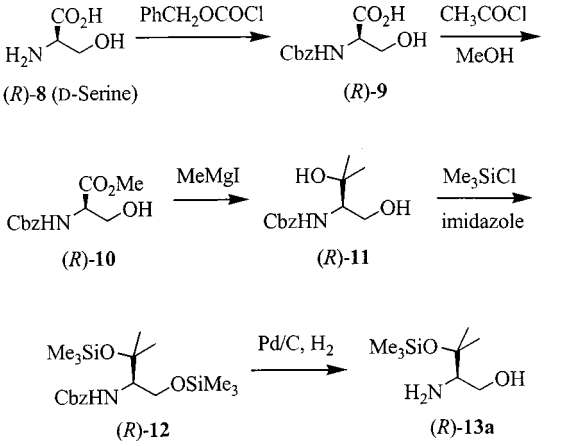


Figure 1. NOE spectra of **5** ([D_6]DMSO, 500 MHz, +24 °C)

with both **5** and **5′** (Figure 1: C). Irradiation at the signal of the *tert*-butyl group in the 3-position, however, produced strong enhancement of the 4-H signal, and no enhancement of the 6-H signal, which is incompatible with structure **5′** (Figure 1: D). This definitely rules out regioisomer **5′** as the reaction product. Further evidence for **5** is provided by the estimated chemical shifts for the aromatic ring protons 4- and 6-H. By application of the usual incremental rules, 4-H and 6-H in **5** should exhibit chemical shifts of δ = 8.64 and 8.29, respectively; that is, a shift difference of 0.35 ppm, compatible with the observed data (Figure 1: A). In the case of **5′**, however, 4-H and 6-H should resonate at δ = 8.27 and 8.29, respectively; i.e., with nearly identical chemical shifts. This was not observed.

Amino Alcohols

In analogy with ref.[17] the new trimethylsilyloxy-substituted amino alcohol (*R*)-**13a** was produced from D-serine [(*R*)-**8**] (Scheme 4). The first step in this sequence was the protection of the amino group of D-serine [(*R*)-**8**] to give carbamate (*R*)-**9**,[18] which was esterified with acetyl chloride and methanol to give D-serine ester (*R*)-**10**.[19] Treatment of (*R*)-**10** with methylmagnesium iodide yielded 1,3-diol (*R*)-**11**, the alcohol functionalities of which were then protected to give the bis(trimethylsilyloxy) derivative (*R*)-**12**. Removal of the Cbz protecting group by hydrogenolysis occurred with selective cleavage of the primary silyloxy group to afford amino alcohol (*R*)-**13a** (overall yield 49%).[20] Amino alcohol (*S*)-**13a** was also synthesized, starting from L-serine (overall yield 54%).



Starting material	Product yield (%)				
	9	**10**	**11**	**12**	**13a**
(*R*)-**8**	91	82	79	93	89
(*S*)-**8**	90	80	83	96	94

Scheme 4

Oxazolylphenols

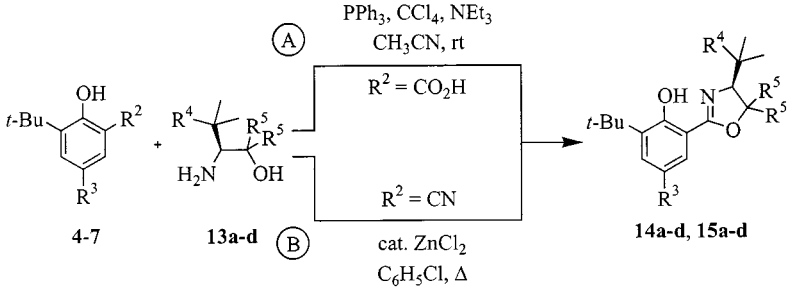
Oxazolines are accessible by direct condensation of 1,2-amino alcohols with either nitriles or carboxylic acids.[21] Condensation of salicylic acids **5** and **7** (produced from **1** according to ref.[13]) and 1,2-amino alcohols **13a–d**[22] using the Appel reaction[23] (Scheme 5; route A) afforded enantiomerically pure phenolic oxazolines **14a–d** and **15a–d** (yields: 38–62%).

Treatment of 2-hydroxybenzonitriles **4** and **6** with the 1,2-amino alcohols **13b–d**[22] under Witte–Seeliger conditions[24] (Scheme 5; route B) furnished the chiral phenolic oxazolines **14b–d** and **15b–d** (yields: 8–83%). Route A was the method of choice for the preparation of **14a**, **14d**, and **15a**, whereas route B was advantageous for the synthesis of **14b**, **14c**, and **15b–d** (Table 1). It is noteworthy that when route B was followed, the thermally fairly unstable 1,2-amino alcohol **13a** did not produce detectable amounts of **14a** and **15a**. Consequently, these two routes are

Table 1. Comparison of routes A and B for the synthesis of oxazolylphenols **14a–d** and **15a–d**

Route	Product yield (%)							
	14a	**14b**	**14c**	**14d**	**15a**	**15b**	**15c**	**15d**
A	58 (61)[a]	62	54	38	54 (56)[a]	49	48	52
B	n. r.[b]	79	83	8[c]	–	76	81	83

[a] Yields in brackets are for enantiomeric products starting from L-serine. – [b] No oxazoline was formed and 63% of starting nitrile was recovered. – [c] 80% of the starting nitrile was recovered.



	4	**5**	**6**	**7**	**14**	**15**	**13–15**	**a**	**b**	**c**	**d**
R^2	CN	CO_2H	CN	CO_2H	–	–	R^4	$OSiMe_3$	H	Me	H
R^3	*t*-Bu	NO_2	NO_2	*t*-Bu	*t*-Bu	NO_2	R^5	H	H	H	Ph

Scheme 5

complementary. Application of these chiral oxazolylphenols should result in interesting catalysts for asymmetric syntheses.[17]

Conclusion

In summary, we report two efficient, complementary synthetic routes for the preparation of a series of new, diversely substituted phenolic oxazolines derived from various enantiomerically pure 1,2-amino alcohols. In particular, regiospecific *ipso* substitution of a *tert*-butyl group of salicylic derivatives by a nitro group was carried out using nitric acid. The nitro product was unequivocally distinguished from its alternative regioisomer by NOE spectroscopy by application of our recently reported DPFGSE-ROE pulse sequence. Starting from D- and L-serine, both enantiomers of the new sterically demanding 2-amino-3-methyl-3-(trimethylsilyloxy)butan-1-ol were produced. Application of these new, diversely substituted phenolic oxazolines should produce efficient enantioselective catalysts.

Experimental Section

General: All solvents were stored over molecular sieves or CaH_2 and distilled before use. All moisture-sensitive and oxygen-sensitive reactions were conducted under nitrogen. − Flash chromatography was carried out using silica gel 60 (70−230 mesh). − Melting points are not corrected. − IR spectra were recorded for liquid films between NaCl plates. − NMR spectra were obtained in dilute $CDCl_3$ solutions except when otherwise stated, using Me_4Si as an internal standard at 400 MHz for ^1H and 100 MHz for ^{13}C; δ values are given in ppm. − Low-resolution mass spectra were carried out at the Institut für Organische Chemie in Erlangen. High-resolution mass spectra (HRMS) were obtained using 70 eV electron impact at the Centre Régional de Mesures Physiques de l'Ouest (Rennes). − Elemental analyses were carried out at the ICSN in Gif-Sur-Yvette or at the Institut für Organische Chemie in Erlangen. − Detailed lists of characterization data for all compounds, as well as ^1H and ^{13}C NMR spectra (including expansions) for most of them, are given in the Supporting Information (see footnote on the first page).

Methyl 3,5-Di-*tert*-butyl-2-hydroxybenzoate (1): A three-necked, round-bottomed flask equipped with a dropping funnel, a thermometer, and a reflux condenser was charged with methyl salicylate (10.65 g, 70 mmol) and 2-methyl-2-propanol (12.3 g, 166 mmol) in methanol (7 mL). Conc. H_2SO_4 (24 mL) was added dropwise to this solution, with vigorous stirring and cooling (0 to 5 °C). The resulting pink reaction mixture was stirred at ca. 20 °C for 5 h. The white precipitate was filtered off, washed with distilled water, dissolved in hot methanol, and crystallized by progressive cooling in the refrigerator. The colorless crystals of **1** were isolated by filtration and dried in a desiccator. Yield 16.09 g (87%); m.p. 72−73 °C. − IR (Nujol): $\tilde{\nu}$ = 1675 (C=O), 1440, 1247, 1115, 985, 802 cm^{-1}. − ^1H NMR: δ = 1.30 (s, 9 H), 1.43 (s, 9 H), 3.94 (s, 3 H), 7.52 (d, J = 2.6 Hz, 1 H), 7.71 (d, J = 2.6 Hz, 1 H), 11.35 (s, 1 H). − ^{13}C NMR: δ = 29.4 (3 C), 31.4 (3 C), 34.3, 35.1, 52.2, 111.3, 123.6, 130.4, 137.2, 140.4, 159.0, 171.7. − MS (EI): m/z = 264 [M^+ + H], 249, 232, 217 (base peak), 175, 87, 57, 41.

3,5-Di-*tert*-butyl-2-hydroxybenzoic Acid (7): A three-necked, round-bottomed flask equipped with a reflux condenser, a thermometer, and a septum was charged with **1** (6.6 g, 25 mmol), methanol (12.5 mL), and water (2.5 mL). KOH was added (2.8 g, 50 mmol) and the heterogeneous mixture was heated at reflux for 5 h. After cooling to 0 °C, the reaction mixture was acidified with HCl (10%). The precipitate was filtered off, washed with distilled water, and dried in a desiccator to afford **7** as a white solid. Yield 5.01 g (80%); m.p. 164−165 °C. − IR (Nujol, NaCl): $\tilde{\nu}$ = 3425 (broad, OH), 1649 (C=O), 1606 (C=C), 1234, 1190, 709 cm^{-1}. − ^1H NMR: δ = 1.32 (s, 9 H), 1.44 (s, 9 H), 5.40−6.90 (broad s, 1 H), 7.59 (d, J = 2.5 Hz, 1 H), 7.80 (d, J = 2.5 Hz, 1 H), 11.05 (broad s, 1 H). − ^{13}C NMR: δ = 29.4 (3 C), 31.3 (3 C), 34.3, 35.2, 110.3, 124.6, 131.7, 137.4, 140.9, 159.7, 175.8. − MS (EI): m/z = 250 [M^+], 235, 217 (base peak), 175, 87, 57, 41.

Methyl 3-*tert*-Butyl-2-hydroxy-5-nitrobenzoate (3): A three-necked, round-bottomed flask equipped with a dropping funnel, a thermometer, and a septum was charged with **1** (6.4 g, 24 mmol) and glacial acetic acid (300 mL). The solution was cooled to 0 °C and fuming HNO_3 (38.4 mL) was added dropwise, while the reaction temperature rose to 5 °C. The yellow solution was stirred for a further 15 min. at 0 °C and then poured onto ice. After the mixture had stood overnight in the refrigerator, the pale yellow precipitate was filtered off, washed with distilled water, and dried in a desiccator to afford **3**, which can be used directly for the next step. Chromatography over silica gel [gradient elution with ether/petroleum ether from 2:98 to 1:9, R_f = 0.36 (ether/petroleum ether, 1:4)] afforded slightly yellow crystals. Yield 4.44 g (73%); m.p. 110−111 °C. − IR (Nujol): $\tilde{\nu}$ = 1687 and 1674 (C=O), 1453, 1336, 1249, 805 cm^{-1}. − ^1H NMR: δ = 1.45 (s, 9 H), 4.03 (s, 3 H), 8.34 (d, J = 2.5 Hz, 1 H), 8.70 (d, J = 2.5 Hz, 1 H), 12.26 (s, 1 H). − ^{13}C NMR: δ = 28.9 (3 C), 35.4, 53.1, 111.9, 124.5, 127.5, 139.2, 139.9, 165.9, 170.4. − MS (EI): m/z = 253 [M^+], 238, 206 (base peak), 160. − $C_{12}H_{15}NO_5$ (253.3): calcd. C 56.91, H 5.97, N 5.53; found C 57.28, H 6.17, N 5.46.

3-*tert*-Butyl-2-hydroxy-5-nitrobenzoic Acid (5): A three-necked, round-bottomed flask equipped with a reflux condenser, a thermometer, and a septum was charged with **3** (3.8 g, 15 mmol), methanol (7.5 mL), and water (1.5 mL). KOH was added (1.68 g, 30 mmol) and the heterogeneous mixture was heated at reflux for 5 h. After cooling to 0 °C, the reaction mixture was acidified with HCl (10%) and the precipitate was filtered off, washed with distilled water and dried in a desiccator, to afford **5** as a yellow solid. Yield 3.05 g (85%); m.p. > 270 °C. − IR (HCB): $\tilde{\nu}$ = 2965, 1742, 1453, 1442, 1341, 697, 654 cm^{-1}. − ^1H NMR (CD_3OD): δ = 1.44 (s, 9 H), 8.24 (d, J = 2.9 Hz, 1 H), 8.67 (d, J = 2.9 Hz, 1 H). − ^{13}C NMR (CD_3OD): δ = 29.4 (3 C), 36.1, 116.7, 126.0, 126.8, 139.8, 140.0, 167.9, 173.9. − MS (EI): m/z = 239 [M^+], 224, 206 (base peak), 160.

3,5-Di-*tert*-butyl-2-hydroxybenzonitrile (4): A mixture of **2** (4.69 g, 20 mmol), nitroethane (2.87 mL, 3.0 g, 40 mmol), anhydrous (fused) sodium acetate (3.3 g, 40 mmol), and glacial acetic acid (4 mL) was refluxed for 6 h. After cooling, the reaction mixture was poured onto ice (40 g) and extracted with ethyl acetate (3 × 40 mL). The organic phase was washed with saturated aqueous sodium hydrogen carbonate solution (2 × 20 mL), dried with magnesium sulfate, and concentrated. The crude reaction product was crystallized in petroleum ether by progressive cooling in the refrigerator to afford light yellow crystals (3.20 g). Additional product was isolated by chromatography of the mother liquor on silica gel [R_f = 0.37 (10% ethyl acetate/petroleum ether); compound **4** was identified using alcoholic phosphomolybdic acid solution].

Yield (overall): 3.80 g (82%); m.p. 120−121 °C. − IR (Nujol): $\tilde{\nu}$ = 3300 (OH), 2233 (C≡N), 1603 (C=C), 1480, 1364, 1252, 1220, 1202 cm^{-1}. − ^1H NMR: δ = 1.29 (s, 9 H), 1.41 (s, 9 H), 6.12 (broad s, 1 H), 7.30 (d, *J* = 2.4 Hz, 1 H), 7.52 (d, *J* = 2.4 Hz, 1 H). − ^{13}C NMR: δ = 29.3 (3 C), 31.2 (3C), 34.4, 35.2, 99.5, 117.4, 126.1, 129.8, 137.2, 143.5, 155.0. − MS (EI): *m*/*z* = 231 [M^+], 216 (base peak), 188, 57. − $C_{15}H_{21}NO$ (231.3): calcd. C 77.88, H 9.12, N 6.06; found C 80.84, H 9.45, N 6.18.

3-*tert*-Butyl-2-hydroxy-5-nitrobenzonitrile (6): A three-necked, round-bottomed flask equipped with a dropping funnel, a thermometer, and a septum was charged with **4** (0.925 g, 4 mmol) and glacial acetic acid (13.5 mL). Conc. HNO_3 (1.6 mL; use of fuming HNO_3 in this case resulted in complete degradation) was added dropwise at 0 °C to the solution, while the reaction temperature rose to 5 °C. The yellow solution was stirred for a further 15 min at 0 °C and then poured onto ice. After the mixture had stood for 2 h in the refrigerator, the pale yellow precipitate was filtered off, washed with distilled water and dried in a dessicator. Purification was achieved by recrystallization from petroleum ether/toluene, affording pale yellow crystals of **6**. Yield 0.714 g (81%); m.p. 138−139 °C. − IR (Nujol): $\tilde{\nu}$ = 3300 (broad, OH), 2243 (C≡N), 1527, 1347 cm^{-1}. − ^1H NMR: δ = 1.46 (s, 9 H), 7.52 (broad s, 1 H), 8.32 (d, *J* = 2.7 Hz, 1 H), 8.40 (d, *J* = 2.7 Hz, 1 H). − ^{13}C NMR: δ = 28.9 (3 C), 35.6, 100.5, 114.9, 126.3, 127.7, 140.0, 140.9, 162.1. − MS (EI): *m*/*z* = 220 [M^+], 205 (base peak), 177, 159, 131. − $C_{11}H_{12}N_2O_3$ (220.2): calcd. C 59.99, H 5.49, N 12.72; found C 60.22, H 5.69, N 12.47.

***N*-(Benzyloxycarbonyl)-D-serine [(*R*)-9]:** Benzyl chloroformate (50 mL, 50 wt-% solution in toluene, 148 mmol) was added to a solution of (*R*)-**8** (10.5 g, 100 mmol) in saturated aqueous sodium hydrogen carbonate (400 mL). The mixture was stirred vigorously for 4 h at ca. 20 °C and the aqueous phase was extracted with ether (2 × 400 mL). The aqueous solution was acidified with conc. hydrochloric acid and extracted with ethyl acetate (3 × 400 mL), and the organic phase was dried with sodium sulfate and concentrated to afford crude (*R*)-**9**, which was used without further purification. Yield 21.77 g (91%); m.p. 114−115 °C. Starting from L-serine: Yield 21.62 g (90%); m.p. 118−119 °C. − IR (Nujol): $\tilde{\nu}$ = 3443 (broad, OH), 3338 (NH), 3318 (NH), 3205 (broad, NH), 1748 (C=O), 1691 (C=O), 1537, 1249, 1061, 1030, 750, 731, 697 cm^{-1}. − ^1H NMR (CD_3COCD_3): δ = 3.89 (dd, *J* = 11.1, 3.9 Hz, 1 H), 3.97 (dd, *J* = 11.1, 4.6 Hz, 1 H), 4.34 (ddd, *J* = 8.1, 4.6, 3.9 Hz, 1 H), 5.10 (s, 2 H), 4.20−5.90 (broad s, 2 H), 6.42 (d, *J* = 8.1 Hz, 1 H), 7.26−7.42 (m, 5 H). − ^{13}C NMR (CD_3COCD_3): δ = 57.2, 62.9, 66.8, 128.62 and 128.63 (3 C), 129.2 (2 C), 138.0, 157.0, 172.3. − MS (EI): *m*/*z* = 239 [M^+], 148, 108, 91 (base peak), 86, 79, 77, 65, 42.

***N*-(Benzyloxycarbonyl)-D-serine Methyl Ester [(*R*)-10]:** Acetyl chloride (16.05 mL, 225 mmol) was added dropwise to a solution of (*R*)-**9** (18.0 g, 75 mmol) in methanol (100 mL) at 0 °C. The mixture was heated at reflux for 16 h and then cooled to ca. 20 °C. The solvent was removed under reduced pressure. The residue was dissolved in dichloromethane (190 mL) and washed with saturated aqueous sodium hydrogen carbonate (2 × 75 mL). The organic phase was dried with magnesium sulfate and concentrated to afford (*R*)-**10** as a colorless oil. Yield 15.57 g (82%); m.p. 31−33 °C. Starting from L-serine: Yield 18.32 g (80%); m.p. 35−36 °C. − IR (Nujol): $\tilde{\nu}$ = 3390 (broad, OH, NH), 1715 with a shoulder at 1750 (C=O), 1215, 1063 cm^{-1}. − ^1H NMR: δ = 2.98 (broad s, 1 H), 3.74 (s, 3 H), 3.86 (dd, *J* = 11.3, 3.4 Hz, 1 H), 3.96 (dd, *J* = 11.3, 3.6 Hz, 1 H), 4.42 (ddd, *J* = 7.9, 3.6, 3.4 Hz, 1 H), 5.10 (s, 2 H), 5.93 (d, *J* = 7.9 Hz, 1 H), 7.26−7.40 (m, 5 H). − ^{13}C NMR: δ = 52.7, 56.1, 63.0, 67.2, 128.1 and 128.2 (3 C), 128.5 (2 C), 136.1, 156.3, 171.2. − MS (EI): *m*/*z* = 253 [M^+], 223, 194, 162, 150, 132, 108, 91 (base peak), 65. − $[\alpha]_D^{23}$ = −5.4, $[\alpha]_{578}^{23}$ = −5.7, $[\alpha]_{546}^{23}$ = −6.6, $[\alpha]_{436}^{23}$ = −12.1, $[\alpha]_{365}^{23}$ = −20.9 (*c* = 6.0, $CHCl_3$), starting from L-serine: $[\alpha]_D^{24}$ = +6.3, $[\alpha]_{578}^{24}$ = +6.4, $[\alpha]_{546}^{24}$ = +7.4, $[\alpha]_{436}^{24}$ = +12.9, $[\alpha]_{365}^{24}$ = +22.0 (*c* = 6.0, $CHCl_3$).

(*R*)-2-*N*-(Benzyloxycarbonylamino)-3-methyl-1,3-butanediol [(*R*)-11]: A three-necked, round-bottomed flask equipped with a reflux condenser and a dropping funnel was charged with magnesium turnings (6.5 g, 267 mmol) and anhydrous ethyl ether (60 mL). A solution of iodomethane (15.3 mL, 246 mmol) in anhydrous ethyl ether (120 mL) was added dropwise to this suspension, maintaining slight boiling, and the suspension was stirred for an additional 90 min at ca. 20 °C. A solution of (*R*)-**10** (10.5 g, 41.5 mmol) in anhydrous THF (60 mL) was added dropwise at 0 °C to the Grignard reagent. The dropping funnel was rinsed with THF (30 mL) and the white suspension was stirred at ca. 20 °C for a further 90 min. The reaction mixture was cooled to 0 °C, cautiously quenched by addition of ether (90 mL) and 1 N HCl (200 mL), and poured into a separating funnel. The aqueous phase was extracted with ethyl ether (3 × 200 mL), and the combined organic phases were dried with magnesium sulfate and concentrated under reduced pressure. The crude reaction product was purified by chromatography on silica gel to afford (*R*)-**11** as a colorless oil. Yield 8.30 g (79%); R_f = 0.07 (40% ethyl acetate/petroleum ether). Starting from L-serine: Yield 8.72 g (83%); m.p. 39−40 °C. − IR (neat): $\tilde{\nu}$ = 3404 (broad, OH), 3330 (broad, NH), 2977, 1700 (C=O), 1534, 1258, 1057 cm^{-1}. − ^1H NMR: δ = 1.21 (s, 3 H), 1.32 (s, 3 H), 3.27 (s, 1 H), 3.34−3.40 (broad s, 1 H), 3.51 (ddd, *J* = 9.1, 2.8, 2.3 Hz, 1 H), 3.78 (dd, *J* = 11.4, 2.3 Hz, 1 H), 3.96 (dd, *J* = 11.4, 2.8 Hz, 1 H), 5.09 (d, *J* = 12.5 Hz, 2 H), 5.10 (d, *J* = 12.5 Hz, 2 H), 5.80 (d, *J* = 9.1 Hz, 1 H), 7.28−7.39 (m, 5 H). − ^{13}C NMR: δ = 27.3, 27.4, 58.3, 63.1, 66.9, 73.5, 128.0 and 128. 2 (3 C), 128.5 (2 C), 136.4, 156.9. − MS (EI): *m*/*z* = 253 [M^+], 235, 222, 194, 177, 132, 91 (base peak), 65, 60. − $[\alpha]_D^{23}$ = −28.8, $[\alpha]_{578}^{23}$ = −30.0, $[\alpha]_{546}^{23}$ = −34.1, $[\alpha]_{436}^{23}$ = −58.5, $[\alpha]_{365}^{23}$ = −92.6 (*c* = 6.0, $CHCl_3$), starting from L-serine: $[\alpha]_D^{24}$ = +29.1, $[\alpha]_{578}^{24}$ = +30.4, $[\alpha]_{546}^{24}$ = +34.4, $[\alpha]_{436}^{24}$ = +59.0, $[\alpha]_{365}^{24}$ = +93.4 (*c* = 6.0, $CHCl_3$).

(*R*)-2-*N*-(Benzyloxycarbonylamino)-3-methyl-1,3-bis(trimethylsilyloxy)butane [(*R*)-12]: Chlorotrimethylsilane (2.28 mL, 18 mmol) was added dropwise to a solution of (*R*)-**11** (1.52 g, 6 mmol) and imidazole (2.45 g, 36 mmol) in anhydrous THF (33 mL) at 0 °C. After 16 h at 0 °C, without stirring, a mixture of ether/petroleum ether/triethylamine (2:98:5) (50 mL) was added to this suspension. Filtration through a pad of silica gel (15 g), washing with ether/petroleum ether/triethylamine (50:50:5) (75 mL), and removal of the organic solvents under vacuum afforded (*R*)-**12** as a colorless liquid. Yield 2.22 g (93%); R_f = 0.30 (ether/petroleum ether, 1:4). Starting from L-serine: Yield 4.30 g (96%). Because of migration of silyl functions during prolonged storage at 0 °C, (*R*)-**12** was stored at −27 °C and used within two weeks. − IR (neat): $\tilde{\nu}$ = 3446, 3342 (broad), 2958, 1726 (C=O), 1504, 1252, 1037, 842 cm^{-1}. − ^1H NMR: δ = 0.09 (broad s, 9 H), 0.11 (s, 9 H), 1.22 (s, 3 H), 1.29 (broad s, 3 H), 3.54 (ddd, *J* = 10.1, 5.8, 5.0 Hz), 3.65 (dd, *J* = 10.5, 5.8 Hz, 1 H), 3.77 (dd, *J* = 10.5, 5.0 Hz, 1 H), 5.03 (d, *J* = 10.1 Hz, 1 H), 5.10 (d, *J* = 12.1 Hz, 1 H), 5.13 (d, *J* = 12.1 Hz, 1 H), 7.28−7.40 (m, 5 H). − ^{13}C NMR: δ = −0.6 (3 C), 2.4 (3 C), 27.6, 27.8, 60.6, 61.4, 66.6, 75.4, 128.05 and 128.13 (3 C), 128.5 (2 C), 136.8, 156.6. − HRMS (EI): *m*/*z* = calcd. 382.1870 [M^+ − Me], found 382.1869. − MS (FAB): *m*/*z* = 470 [M^+ + $SiMe_3$], 398 [M^+ + H], 382 [M^+ − Me], 308 [M^+ − $OSiMe_3$] (base peak). − $[\alpha]_D^{27}$ = −3.0, $[\alpha]_{578}^{27}$ = −3.1, $[\alpha]_{546}^{27}$ = −3.4, $[\alpha]_{436}^{27}$ = −6.8, $[\alpha]_{365}^{27}$ = −11.9

(c = 4.4, $CHCl_3$), starting from L-serine: $[\alpha]_D^{23}$ = +3.2, $[\alpha]_{578}^{23}$ = +3.3, $[\alpha]_{546}^{23}$ = +3.9, $[\alpha]_{436}^{23}$ = +7.3, $[\alpha]_{365}^{23}$ = +13.2 (c = 4.3, $CHCl_3$). − $C_{19}H_{35}NO_4Si_2$ (397.7): calcd. C 57.39, H 8.87, N 3.52; found C 56.96, H 8.32, N 3.62.

(*R*)-2-Amino-3-methyl-3-(trimethylsilyloxy)butan-1-ol [(*R*)-13a]: Pd/C (10%, 0.60 g) was added to a solution of (*R*)-**12** (0.60 g, 1.5 mmol) in anhydrous ethanol (6 mL). The mixture was hydrogenated at ca. 20 °C and at atmospheric pressure for 18 h. The catalyst was removed by filtration through Celite and, after washing of the solid with 95% ethanol (3 mL), the filtrate was concentrated under vacuum to afford (*R*)-**13a** as a colorless oil. Yield 0.256 g (89%); m.p. < 0 °C. Starting from L-serine: Yield 0.453 g (94%). Because of migration of the silyl function during prolonged storage at 0 °C, (*R*)-**13a** was stored at −27 °C and used within two weeks. − IR (neat): $\tilde{\nu}$ = 3360 (broad, OH), 3296 (broad, NH), 2960, 1251, 1033, 840, 754 cm^{-1}. − ^1H NMR: δ = 0.13 (s, 9 H), 1.24 (s, 3 H), 1.27 (s, 3 H), 2.61 (dd, J = 8.2, 4.3 Hz, 1 H), 2.77 (broad s, 3 H), 3.44 (dd, J = 10.6, 8.2 Hz, 1 H), 3.69 (dd, J = 10.6, 4.3 Hz, 1 H). − ^{13}C NMR: δ = 2.4 (3 C), 26.5, 27.4, 61.5, 62.4, 75.6. − MS (EI): m/z = 192 [M^+ + H], 176, 160, 131 (base peak), 116, 105, 85, 73, 60. − $[\alpha]_D^{23}$ = +14.8, $[\alpha]_{578}^{23}$ = +15.3, $[\alpha]_{546}^{23}$ = +17.3, $[\alpha]_{436}^{23}$ = +28.3, $[\alpha]_{365}^{23}$ = +42.4 (c = 3.4, $CHCl_3$), starting from L-serine: $[\alpha]_D^{24}$ = −15.3, $[\alpha]_{578}^{24}$ = −15.8, $[\alpha]_{546}^{24}$ = −17.6, $[\alpha]_{436}^{24}$ = −28.3, $[\alpha]_{365}^{24}$ = −41.7 (c = 2.5, $CHCl_3$).

General Procedures for the Preparation of Phenolic 1,3-Oxazolines 14 and 15. − Method A: Salicylic acid **5** or **7** (1 mmol), amino alcohol **13** (1 mmol), triethylamine (0.56 mL, 4 mmol), and carbon tetrachloride (0.49 mL, 5 mmol) were added to either (for **5**) acetonitrile (6 mL) and pyridine (3 mL), or (for **7**) acetonitrile (9 mL). Triphenylphosphane (0.790 g, 3.0 mmol) was added (5 portions) over 3 h at ca. 20 °C under nitrogen. The light yellow solution (deep brown at the end in the case of **5**) was kept for 18 h at ca. 20 °C and concentrated under vacuum. The solid residue was treated with petroleum ether (15 mL) and saturated aqueous sodium hydrogen carbonate (4 mL) with vigorous stirring for 30 min. The organic phase was decanted. Petroleum ether (15 mL) was added and the slurry was vigorously stirred for 30 min. After decanting of the organic phase, this procedure was repeated twice more. The combined organic phases were dried with sodium sulfate and concentrated. The crude reaction product was purified (*solid transfer*) by flash chromatography [silica gel (40 g)/product (1 g)] to afford **14** and **15**, respectively. − **Method B:** Zinc chloride (5−8 mg, ca. 4−6 mol %) was melted under vacuum in a two-necked flask, and chlorobenzene (4 mL) was added under nitrogen at room temperature, followed by 2-hydroxybenzonitrile **4** or **6** (1 mmol) and amino alcohol **13** (1.25 mmol). The colorless solution (yellow suspension in the case of **6**) was heated at reflux for 16 h. The solvent was removed under reduced pressure and the oily residue dissolved in dichloromethane (8 mL). The solution was washed with saturated aqueous sodium hydrogen carbonate (2 mL), dried with sodium sulfate, and concentrated under vacuum. The residue was purified by flash chromatography to afford **14** and **15**, respectively.

(*R*)-2,4-Di-*tert*-butyl-6-[4-(1-methyl-1-trimethylsilyloxyethyl)-4,5-dihydro-2-oxazolyl]phenol [(*R*)-14a]. − Method A: Yield 0.235 g (58%). Starting from L-serine: Yield [(*S*)-**14a**]: 0.247 g (61%). − **Method B:** No product formation was observed and 63% of the starting nitrile derivative was recovered; colorless syrup; R_f = 0.19 (petroleum ether); elution with petroleum ether. − IR (Nujol): $\tilde{\nu}$ = 1635 (C=N), 1252, 1059, 840 cm^{-1}. − ^1H NMR: δ = 0.10 (s, 9 H), 1.21 (s, 3 H), 1.31 (s, 9 H), 1.37 (s, 3 H), 1.44 (s, 9 H), 4.23 (dd, J = 9.8, 7.3 Hz, 1 H), 4.32 (dd, J = 9.8, 8.5 Hz, 1 H), 4.44 (dd, J = 8.5, 7.3 Hz, 1 H), 7.44 (d, J = 2.5 Hz, 1 H), 7.53 (d, J = 2.5 Hz, 1 H), 12.66 (broad s, 1 H). − ^{13}C NMR: δ = 2.4 (3 C), 24.5, 28.7, 29.4 (3 C), 31.5 (3 C), 34.2, 35.1, 68.1, 74.9, 75.2, 109.8, 122.1, 127.9, 136.3, 139.8, 157.0, 166.9. − HRMS (EI): m/z = calcd. 405.2699 [M^+]; found 405.2676. − MS (FAB): m/z = 405 [M^+] (base peak), 390, 316. − $[\alpha]_D^{24}$ = +6.7, $[\alpha]_{578}^{24}$ = +7.6, $[\alpha]_{546}^{24}$ = +9.3, $[\alpha]_{436}^{24}$ = +30.8 (c = 2.7, $CHCl_3$), starting from L-serine: $[\alpha]_D^{27}$ = −6.8, $[\alpha]_{578}^{27}$ = −7.4, $[\alpha]_{546}^{27}$ = −9.3, $[\alpha]_{436}^{27}$ = −32.0 (c = 1.0, $CHCl_3$). − $C_{23}H_{39}NO_3Si$ (405.7): calcd. C 68.10, H 9.69, N 3.45; found C 68.16, H 9.48, N 3.56.

(*S*)-2,4-Di-*tert*-butyl-6-(4-isopropyl-4,5-dihydro-2-oxazolyl)phenol [(*S*)-14b]. − Method A: Yield 0.197 g (62%). − **Method B:** Yield 0.251 g (79%); colorless oil which crystallized after storage in the refrigerator; m.p. 95−97 °C, R_f = 0.54 (5% ethyl acetate/petroleum ether); gradient elution from petroleum ether to *tert*-butyl methyl ether/petroleum ether (1:99). − IR (neat): $\tilde{\nu}$ = 2960, 1637 (C=N), 1598 (C=C), 1255, 1103, 979 cm^{-1}. − ^1H NMR: δ = 0.95 (d, J = 6.7 Hz, 1 H), 1.03 (d, J = 6.7 Hz, 1 H), 1.31 (s, 9 H), 1.45 (s, 9 H), 1.79 (dqq, J = 6.9, 6.7, 6.7 Hz, 1 H), 4.05−4.14 (m, 2 H), 4.34−4.44 (m, 1 H), 7.44 (d, J = 2.5 Hz, 1 H), 7.53 (d, J = 2.5 Hz, 1 H), 12.71 (broad s, 1 H). − ^{13}C NMR: δ = 165.9, 156.9, 139.9, 136.3, 127.9, 122.1, 109.8, 71.6, 69.6, 35.1, 34.2, 33.1, 31.5 (3 C), 29.4 (3 C), 18.9, 18.7. − MS (EI): m/z = 317 [M^+], 302, 274, 260, 216, 57, 41, 28 (base peak). − $[\alpha]_D^{24}$ = −24.9, $[\alpha]_{578}^{24}$ = −26.0, $[\alpha]_{546}^{24}$ = −29.5, $[\alpha]_{436}^{24}$ = −44.0 (c = 1.4, $CHCl_3$). − $C_{20}H_{31}NO_2$ (317.5): calcd. C 75.67, H 9.84, N 4.41; found C 75.79, H 9.87, N 4.45.

(*S*)-2,4-Di-*tert*-butyl-6-(4-*tert*-butyl-4,5-dihydro-2-oxazolyl)phenol [(*S*)-14c]. − Method A: Yield 0.180 g (54%). − **Method B:** Yield 0.275 g (83%); colorless crystals; m.p. 155−156 °C, R_f = 0.52 with 2% ethyl acetate/petroleum ether (elution with petroleum ether). − IR (Nujol): $\tilde{\nu}$ = 1635 (C=N), 1255, 1106, 981, 786 cm^{-1}. − ^1H NMR: δ = 0.95 (s, 9 H), 1.31 (s, 9 H), 1.45 (s, 9 H), 4.11 (dd, J = 9.8, 8.1 Hz, 1 H), 4.19 (dd, J = 8.5, 8.1 Hz, 1 H), 4.33 (dd, J = 9.8, 8.5 Hz, 1 H), 7.44 (d, J = 2.5 Hz, 1 H), 7.52 (d, J = 2.5 Hz, 1 H), 12.74 (broad s, 1 H). − ^{13}C NMR: δ = 25.9 (3 C), 29.4 (3 C), 31.5 (3 C), 33.8, 34.2, 35.1, 67.7, 75.1, 109.7, 122.1, 127.9, 136.3, 139.8, 157.0, 165.9. − MS (EI): m/z = 331 [M^+], 316, 288, 274, 216, 57, 28 (base peak). − $[\alpha]_D^{24}$ = −13.7, $[\alpha]_{578}^{24}$ = −14.0, $[\alpha]_{546}^{24}$ = −15.5, $[\alpha]_{436}^{24}$ = −18.6 (c = 2.6, $CHCl_3$). − $C_{21}H_{33}NO_2$ (331.5): calcd. C 76.09, H 10.03, N 4.23; found C 76.01, H 10.11, N 4.14.

(*S*)-2,4-Di-*tert*-butyl-6-(4-isopropyl-5,5-diphenyl-4,5-dihydro-2-oxazolyl)phenol [(*S*)-14d]. − Method A: Yield 0.178 g (38%). − **Method B:** Yield 0.038 g (8%); white foam; m.p. 75−76 °C, R_f = 0.42 (2% ethyl acetate/petroleum ether); gradient elution from petroleum ether to *tert*-butyl methyl ether/petroleum ether (1:99). − IR (neat, NaCl): $\tilde{\nu}$ = 2959, 1644 (C=N), 1467, 1440, 1369, 1254, 700 cm^{-1}. − ^1H NMR: δ = 0.67 (d, J = 6.5 Hz, 3 H), 0.97 (d, J = 6.7 Hz, 3 H), 1.35 (s, 9 H), 1.45 (s, 9 H), 1.85 (qqd, J = 6.7, 6.5, 5.4 Hz, 1 H), 4.78 (d, J = 5.4 Hz, 1 H), 7.21−7.40 (m, 8 H), 7.48 (d, J = 2.5 Hz, 1 H), 7.55−7.60 (m, 2 H), 7.78 (d, J = 2.5 Hz, 1 H), 12.68 (s, 1 H). − ^{13}C NMR: δ = 17.7, 21.7, 29.4 (3 C), 30.3, 31.6 (3 C), 34.3, 35.2, 79.4, 91.7, 109.8, 122.1, 126.3 (2 C), 127.1 (2 C), 127.5, 127.8 (2 C), 127.9, 128.1, 128.4 (2 C), 136.5, 140.0, 140.2, 144.8, 157.3, 164.2. − HRMS (EI): m/z = calcd. 469.2981 [M^+]; found 469.2982. − MS (FAB): m/z = 469.3 [M^+], 302, 260, 237 (base peak). − $[\alpha]_D^{28}$ = −206.6, $[\alpha]_{578}^{28}$ = −216.4, $[\alpha]_{546}^{28}$ = −249.5, $[\alpha]_{436}^{28}$ = −460.0, $[\alpha]_{365}^{28}$ = −809.4 (c = 1.0, $CHCl_3$). − $C_{32}H_{39}NO_2$ (469.7): calcd. C 81.84, H 8.37, N 2.98; found C 81.75, H 8.17, N 2.91.

(*R*)-2-*tert*-Butyl-6-[4-(1-methyl-1-trimethylsilyloxyethyl)-4,5-dihydro-2-oxazolyl]-4-nitrophenol [(*R*)-15a]. − Method A: Yield

0.213 g (54%). Starting from L-serine: Yield [(*S*)-**15a**]: 0.220 g (56%). – **Method B:** No product formation; yellow syrup; R_f = 0.21 (2% ethyl acetate/petroleum ether); gradient elution from petroleum ether to *tert*-butyl methyl ether/petroleum ether (2:98). – IR (neat): $\tilde{\nu}$ = 2964, 1642 (C=N), 1337, 1246, 1056, 842 cm^{-1}. – ^1H NMR: δ = 0.07 (s, 9 H), 1.30 (s, 3 H), 1.34 (s, 3 H), 1.46 (s, 9 H), 4.26 (dd, *J* = 9.9, 7.3 Hz, 1 H), 4.42 (dd, *J* = 9.9, 8.6 Hz, 1 H), 4.55 (dd, *J* = 8.6, 7.3 Hz, 1 H), 8.28 (d, *J* = 2.8 Hz, 1 H), 8.51 (d, *J* = 2.8 Hz, 1 H), 14.02 (broad s, 1 H). – ^{13}C NMR: δ = 2.3 (3 C), 25.2, 28.4, 29.0 (3 C), 35.4, 68.8, 74.5, 75.2, 110.3, 122.8, 125.7, 138.82, 138.83, 164.7, 165.6. – HRMS (EI): *m*/*z* = calcd. 394.1924 [M^+], found 394.1929. – MS (FAB): *m*/*z* = 467 [M^+ + $SiMe_3$], 395 [M^+ + H] (base peak), 389, 336, 305. – $[\alpha]_D^{24}$ = −12.2, $[\alpha]_{578}^{24}$ = −12.9, $[\alpha]_{546}^{24}$ = −14.6 (*c* = 3.8, $CHCl_3$), starting from L-serine: $[\alpha]_D^{27}$ = +12.6, $[\alpha]_{578}^{27}$ = +13.2, $[\alpha]_{546}^{27}$ = +15.1 (*c* = 3.6, $CHCl_3$). – $C_{19}H_{30}N_2O_5Si$ (394.5): calcd. C 57.84, H 7.66, N 7.10; found C 57.93, H 7.78, N 7.17.

(*S*)-2-*tert*-Butyl-6-(4-isopropyl-4,5-dihydro-2-oxazolyl)-4-nitrophenol [(*S*)-15b]. – Method A: Yield 0.150 g (49%). – **Method B:** Yield 0.233 g (76%); pale yellow crystals; m.p. 85–87 °C; R_f = 0.31 (5% ethyl acetate/petroleum ether); gradient elution from petroleum ether to *tert*-butyl methyl ether/petroleum ether (2:98). – IR (Nujol): $\tilde{\nu}$ = 1640 (C=N), 1335, 1132, 867, 705 cm^{-1}. – ^1H NMR: δ = 0.99 (d, *J* = 6.7 Hz, 3 H), 1.07 (d, *J* = 6.7 Hz, 3 H), 1.46 (s, 9 H), 1.85 (qqd, *J* = 6.7, 6.7, 6.3 Hz, 1 H), 4.14–4.23 (m, 2 H), 4.48–4.55 (m, 1 H), 8.28 (d, *J* = 2.8 Hz, 1 H), 8.50 (d, *J* = 2.8 Hz, 1 H), 14.00 (broad s, 1 H). – ^{13}C NMR: δ = 18.6, 18.8, 29.0 (3 C), 33.0, 35.4, 70.4, 71.7, 110.3, 122.8, 125.6, 138.80, 138.83, 164.6, 164.8. – MS (EI): *m*/*z* = 306 [M^+], 291 (base peak), 264, 263, 221, 206, 177, 160, 131, 85, 73, 57, 41. – $[\alpha]_D^{24}$ = −44.8, $[\alpha]_{578}^{24}$ = −47.1, $[\alpha]_{546}^{24}$ = −54.7 (*c* = 2.6, $CHCl_3$). – $C_{16}H_{22}N_2O_4$ (306.4): calcd. C 62.73, H 7.24, N 9.14; found C 62.69, H 7.33, N 9.13.

(*S*)-2-*tert*-Butyl-6-(4-*tert*-butyl-4,5-dihydro-2-oxazolyl)-4-nitrophenol [(*S*)-15c]. – Method A: Yield 0.154 g (48%). – **Method B:** Yield 0.259 g (81%); pale yellow crystals; m.p. 146–148 °C; R_f = 0.34 (5% ethyl acetate/petroleum ether); gradient elution from petroleum ether to *tert*-butyl methyl ether/petroleum ether (2:98). – IR (Nujol): $\tilde{\nu}$ = 1642 (C=N), 1333, 1136, 977, 840, 705 cm^{-1}. – ^1H NMR: δ = 0.98 (s, 9 H), 1.46 (s, 9 H), 4.18 (dd, *J* = 10.0, 8.1 Hz, 1 H), 4.30 (dd, *J* = 8.8, 8.1 Hz, 1 H), 4.44 (dd, *J* = 10.0, 8.8 Hz, 1 H), 8.50 (d, *J* = 2.8 Hz, 1 H), 8.28 (d, *J* = 2.8 Hz, 1 H), 14.01 (broad s, 1 H). – ^{13}C NMR: δ = 25.8 (3 C), 29.0 (3 C), 33.8, 35.4, 68.5, 75.1, 110.2, 122.8, 125.6, 138.78, 138.82, 164.7, 164.8. – MS (EI): *m*/*z* = (%) 320 [M^+], 305 (base peak), 277, 263, 247, 235, 221, 206, 177, 160, 85, 57, 41. – $[\alpha]_D^{27}$ = −32.4, $[\alpha]_{578}^{27}$ = −34.0, $[\alpha]_{546}^{27}$ = −39.5 (*c* = 2.2, $CHCl_3$). – $C_{17}H_{24}N_2O_4$ (320.4): calcd. C 63.73, H 7.55, N 8.74; found C 63.95, H 7.36, N 8.87.

(*S*)-2-*tert*-Butyl-6-(4-isopropyl-5,5-diphenyl-4,5-dihydro-2-oxazolyl)-4-nitrophenol [(*S*)-15d]. – Method A: Yield 0.258 g (53%). – **Method B:** Yield 0.381 g (83%); pale yellow foam; m.p. 49–52 °C, R_f = 0.35 (5% ethyl acetate/petroleum ether); gradient elution from petroleum ether to *tert*-butyl methyl ether/petroleum ether (2:98). – IR (Nujol): $\tilde{\nu}$ = 1648 (C=N), 1336, 1144, 972, 918, 749, 701 cm^{-1}. – ^1H NMR: δ = 0.68 (d, *J* = 6.5 Hz, 3 H), 1.01 (d, *J* = 6.7 Hz, 3 H), 1.47 (s, 9 H), 1.90 (qqd, *J* = 6.7, 6.5, 5.4 Hz, 1 H), 4.88 (d, *J* = 5.4 Hz, 1 H), 7.26–7.36 (m, 6 H), 7.37–7.43 (m, 2 H), 7.54–7.60 (m, 2 H), 8.32 (d, *J* = 2.8 Hz, 1 H), 8.73 (d, *J* = 2.8 Hz, 1 H), 13.99 (broad s, 1 H). – ^{13}C NMR: δ = 17.6, 21.6, 29.0 (3 C), 30.2, 35.4, 78.9, 93.1, 110.3, 122.7, 125.8, 126.2 (2 C), 126.9 (2 C), 127.9, 128.0 (2C), 128.4, 128.6 (2C), 138.9, 139.0, 139.3, 143.9, 163.1, 164.9. – HRMS (EI): *m*/*z* = calcd. 458.2205 [M^+]; found 458.2184. – MS (FAB): *m*/*z* = 458 [M^+] (base peak), 276, 237; $[\alpha]_D^{28}$ = −219.3, $[\alpha]_{578}^{28}$ = −229.6, $[\alpha]_{546}^{28}$ = −264.2 (*c* = 3.3, $CHCl_3$). – $C_{28}H_{30}N_2O_4$ (458.6): calcd. C 73.34, H 6.59, N 6.11; found C 73.56, H 6.66, N 5.97.

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