Diastereoselective intermolecular addition of the 1,3-dioxolanyl radical to *N*-acyl aldohydrazones. Asymmetric synthesis of α -amino acid derivatives

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General: PYREX® vessels were used for all the photochemical reactions. All dry solvents were freshly distilled under argon from the appropriate drying agent before use. THF and toluene were distilled from sodium/benzophenone. Purchased reagents, as well some solvents: methanol, isopropanol and 1,3-dioxolane ($\geq 99\%$, GC), were used as received without further purification. Thin-layer chromatography (TLC) was performed on precoated silica gel aluminium plates and components were visualized by observation under UV light, or by treating the plates with a solution of $(\text{NH}_4)_6\text{Mo}_7\text{O}_{24} \cdot 4 \text{H}_2\text{O}$ (12.5 g) and $\text{Ce}(\text{SO}_4)_2 \cdot 4 \text{H}_2\text{O}$ (5 g) in 10% aqueous H_2SO_4 (500 mL), followed by heating. Flash column chromatography was performed on 230-400 mesh silica gel. Anhydrous Na_2SO_4 was used to dry organic solutions during workups. Concentrations were carried out in a rotary evaporator. ^1H NMR were recorded at 250, 300, 400 or 500 MHz as indicated; ^{13}C NMR at 63, 75, 100 or 125 MHz. Carbon types were determined from DEPT ^{13}C NMR experiments. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br s, broad signal.

Preparation of radical adducts **5a,b,d,e** from aldehydes **6**

General Procedure for the one-pot 1,3-dioxolanyl radical additions to aldehydes **6**

Aldehyde **6** (**a**, **b**, **d** or **e**) and *p*-TsOH (6 mol %) were added to a solution of **7S** (120 mol%) in the required volume of 1,3-dioxolane to make the solution 0.09 M in **6**. After 1h at room temperature, benzophenone (100 mol%) and InCl_3 (200 mol%) were added, and argon was bubbled for 20 min. The mixture was cooled (-78°C , acetone-dry ice bath) and then externally irradiated with a 450 W Hanovia medium-pressure mercury lamp. After complete conversion (1-3.8 h, TLC, GC-MS), the mixture was partitioned between H_2O and EtOAc, and the organic extracts dried. Solvent removal followed by flash chromatography using mixtures of EtOAc/hexanes afforded the corresponding *N*-acylhydrazines **5** as diastereomeric mixtures. The diastereomeric ratio was determined by ^1H NMR analysis of appropriate proton signals.

(*S*)-3-amino-4-benzyl-1,3-oxazolan-2-one (7*S*)¹

To a cold (-78 °C) solution of (*S*)-4-benzyl-1,3-oxazolan-2-one (3.89 g, 21.74 mmol) in dry THF (380 mL), *n*-BuLi (1.6 M in hexanes, 17.8 mL, 28.54 mmol) was added. After stirring for 1 h, *O*-(diphenylphosphinyl)hydroxylamine² (6.66 g, 28.54 mmol) was added and the reaction mixture stirred for additional 6 h at room temperature. Filtration (to eliminate diphenylphosphinic acid), solvent evaporation and purification by gradient flash chromatography (EtOAc/hexane 2:3 → 3:2) afforded **7*S*** as a pale yellow oil (3.39 g, 80%).

(4*S*)-4-Benzyl-3-{[1-(1,3-dioxolan-2-yl)-propyl]amino}-1,3-oxazolan-2-one (5*a*, Table 2, entry 1 in the article)

Prepared from propionaldehyde (**6a**, 57 μL, 0.76 mmol) according to the general procedure. Irradiation time: 1 h. Flash chromatography (EtOAc/hexane 1:4 → 1:3) afforded **5a** (241 mg, 99%, dr = 98.5:1.5) as a pale yellow oil. The diastereomeric ratio was determined by integration of the signals corresponding to the acetalic proton: at δ 4.95 for the major diastereoisomer and at δ 4.89 for the minor diastereoisomer in the 500 MHz ¹H NMR spectra. For the major (4*S*,1*R*) isomer: ¹H NMR (CDCl₃, 250 MHz) δ: 7.36-7.22 (m, 3H), 7.18-7.15 (m, 2H), 4.95 (d, *J* = 4.7 Hz, 1H), 4.38 (br s, 1H), 4.13 (dd, *J* = 16.0 Hz, *J* = 7.5 Hz, 1H), 4.06-3.85 (m, 6H), 3.35 (dd, *J* = 13.5 Hz, *J* = 3.4 Hz, 1H), 3.12 (m, 1H), 2.63 (dd, *J* = 13.5 Hz, *J* = 9.7 Hz, 1H), 1.61 (m, 2H), 1.05 (t, *J* = 7.5 Hz, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 158.6, 136.4, 129.5, 129.3, 127.4, 104.3, 66.0, 65.5, 65.4, 62.2, 59.5, 37.1, 21.7, 10.3; LRMS *m/z* (%) 307 [10.4, (M+H)⁺]; HRMS calcd for C₁₆H₂₃N₂O₄ (M+H)⁺ 307.165782, found 307.165310.

¹ Friestad, G. K.; Qin, J. *J. Am. Chem. Soc.* **2000**, *122*, 8329-8330. For a comparison of electrophilic amination reagents for *N*-amination of 2-oxazolidinones, see: Shen, Y.; Friestad, G. K. *J. Org. Chem.* **2002**, *67*, 6236-6239.

² Prepared according to: Colvin, E. W.; Kirby, G. W.; Wilson, A. C. *Tetrahedron Lett.* **1982**, *23*, 3835-3836.

(4*S*)-4-Benzyl-3-[[1-cyclopropyl-1-(1,3-dioxolan-2-yl)-methyl]amino]-1,3-oxazolan-2-one (5b, Table 2, entry 2 in the article)

Prepared from cyclopropanecarbaldehyde (**6b**, 38 μ L, 0.50 mmol) according to the general procedure. Irradiation time: 2.25 h. Flash chromatography (EtOAc/hexane 15:85 $\rightarrow$ 20:80) afforded **5b** (136 mg, 85%, dr = 97:3) as a pale yellow oil. The diastereomeric ratio was determined by integration of the signals corresponding to the methine proton α to the NH group: at δ 2.53 for the major diastereoisomer and at δ 2.45 for the minor diastereoisomer in the 300 MHz ^1H NMR spectra. For the major (4*S*,1*R*) isomer: ^1H NMR (CDCl_3 , 250 MHz) δ 7.36-7.22 (m, 3H), 7.19-7.15 (m, 2H), 5.02 (d, J = 4.4 Hz, 1H), 4.58 (br s, 1H), 4.21-3.84 (m, 7H), 3.35 (dd, J = 13.4 Hz, J = 3.0 Hz, 1H), 2.67 (dd, J = 13.4 Hz, J = 9.1 Hz, 1H), 2.53 (dd, J = 9.7 Hz, J = 4.4 Hz, 1H), 0.95-0.81 (m, 1H), 0.64-0.51 (m, 2H), 0.38-0.29 (m, 2H); ^{13}C NMR (CDCl_3 , 63 MHz) δ 157.7, 135.9, 129.0, 128.7, 126.8, 104.4, 65.9, 65.2, 64.9, 64.8, 59.3, 37.2, 10.3, 3.0, 1.5; LRMS m/z (%) 319 [17.5, ($\text{M}+\text{H}$) $^+$], 245 [19.2, (M -dioxolanyl) $^+$]; HRMS calcd for $\text{C}_{17}\text{H}_{23}\text{N}_2\text{O}_4$ ($\text{M}+\text{H}$) $^+$ 319.165782, found 319.165730.

(4*S*)-4-Benzyl-3-[[1-(1,3-dioxolan-2-yl)-1-(4-methoxyphenyl)methyl]amino]-1,3-oxazolan-2-one (5d, Table 2, entry 4 in the article)

Prepared from 4-methoxy-benzaldehyde (**6d**, 54 μ L, 0.43 mmol) according to the general procedure. Irradiation time: 3.8 h. Flash chromatography (EtOAc/hexane 1:3) afforded **5d** (148 mg, 88%, dr = 1:1) as a pale yellow oil. The diastereomeric ratio was determined by integration of the signals corresponding to one of the benzylic protons: at δ 2.54 for one diastereoisomer (5d') and at δ 2.16 for the other diastereoisomer (5d'') in the 300 MHz ^1H NMR spectra. For the 1:1 mixture of diastereoisomers: ^1H NMR

(CDCl₃, 300 MHz) δ 7.40-7.34 (m, 2H), 7.28-7.20 (m, 3H), 7.07-7.00 (m, 2H), 6.91-6.86 (m, 2H), 5.15 (dd, $J = 6.1$ Hz, $J = 1.7$ Hz, 1H'), 5.07 (dd, $J = 6.1$ Hz, $J = 1.7$ Hz, 1H'), 4.82 (br s, 1H'), 4.54 (br s, 1H'), 4.28 (d, $J = 6.1$ Hz, 1H'), 4.22 (d, $J = 6.1$ Hz, 1H'), 4.12-3.77 (m, 10H), 3.23 (m, 1H'), 3.07 (dd, $J = 13.1$ Hz, $J = 2.6$ Hz, 1H'), 2.54 (dd, $J = 13.1$ Hz, $J = 10.5$ Hz, 1H'), 2.16 (dd, $J = 13.1$ Hz, $J = 9.6$ Hz, 1H'); ¹³C NMR (CDCl₃, 75 MHz) δ 159.3, 159.2, 158.1, 157.2, 135.7, 135.6, 129.9, 129.6, 129.0, 128.8, 128.6, 128.5, 128.4, 126.6, 113.6, 113.5, 104.8, 104.4, 66.3, 65.5, 65.0, 64.9, 64.6, 58.3, 58.1, 55.1, 55.0, 37.4, 36.5; LRMS m/z (%) 385 [3.5, (M+H)⁺], 311 [11.3, (M-dioxolanyl)⁺]; HRMS calcd for C₂₁H₂₅N₂O₅ (M+H)⁺ 385.176347, found 385.174940.

(4S)-4-Benzyl-3-[[1-(1,3-dioxolan-2-yl)-1-(furan-2-yl)methyl]amino]-1,3-oxazolan-2-one (5e, Table 2, entry 5 in the article)

From furfural (**6e**, 37 μ L, 0.44 mmol) according to the general procedure. Irradiation time: 2.8 h. Flash chromatography (EtOAc/hexane 1:4 $\rightarrow$ 1:3) afforded **5e** (142 mg, 93%, dr = 4:1) as a pale yellow oil. The diastereomeric ratio was determined by integration of the signals corresponding to one of the benzylic protons: at δ 2.55 for the major diastereoisomer and at δ 1.97 for the minor diastereoisomer in the 300 MHz ¹H NMR spectra. For the 1*R*-1*S* isomeric mixture: ¹H NMR (CDCl₃, 300 MHz) δ 7.48 (d, $J = 0.9$ Hz, 1H_R), 7.44 (d, $J = 1.1$ Hz, 1H_S), 7.32-7.19 (m, 3H), 7.06 (m, 2H), 6.46-6.37 (m, 2H), 5.36 (d, $J = 6.2$ Hz, 1H_S), 5.32 (d, $J = 6.5$ Hz, 1H_R), 4.76 (d, $J = 2.9$ Hz, 1H_R), 4.72 (d, $J = 2.6$ Hz, 1H_S), 4.44 (dd, $J = 6.5$ Hz, $J = 2.9$ Hz, 1H_R), 4.42 (m, 1H_S), 4.12-3.85 (m, 7H), 3.24 (dd, $J = 13.0$ Hz, $J = 2.7$ Hz, 1H_R), 3.02 (dd, $J = 13.4$ Hz, $J = 2.9$ Hz, 1H_S), 2.55 (dd, $J = 13.0$ Hz, $J = 9.4$ Hz, 1H_R), 1.97 (dd, $J = 13.4$ Hz, $J = 9.1$ Hz, 1H_S); ¹³C NMR (CDCl₃, 63 MHz) δ 158.8, 157.4, 150.4, 150.1, 142.7, 135.9, 135.8, 129.1, 128.8, 128.8, 128.7, 126.9, 110.7, 110.6, 110.5, 110.3, 102.9, 102.7, 66.9, 65.9, 65.3, 65.2, 65.1, 59.6, 59.3, 59.1, 57.9, 37.1, 36.7; LRMS m/z (%) 345 [2.1, (M+H)⁺], 271 [4.6, (M-dioxolanyl)⁺]; HRMS calcd for C₁₈H₂₁N₂O₅ (M+H)⁺ 345.145047, found 345.143759.

Preparation of *N*-benzoyl amino acid **10** from adduct **5a**

(4*S*)-4-Benzyl-3{[(1*R*)-1-(1,3-dioxolan-2-yl)propyl](phenyl)carboxamido}-2-oxo-1,3-oxazolane (8**, Scheme 1 in the article)**

To a cold (−78 °C) solution of **5a** (278 mg, 0.91 mmol) in dry THF (9 mL, 0.1 M) *n*-BuLi (1.6 M in hexanes, 1.12 mL, 1.79 mmol) was added. After stirring for 40 min, addition of benzoyl chloride (0.21 mL, 1.79 mmol) and refluxing for 4 hours, the reaction mixture was quenched (brine) and extracted with CH₂Cl₂. The organic extracts were dried, concentrated and purified by gradient flash chromatography (EtOAc/hexane 15:85 → 25:75) to afford **8** as a white solid (309 mg, 83% yield). ¹H NMR is highly complex due to the presence of rotamers. ¹³C NMR (CDCl₃, 63 MHz) δ 170.8, 155.9, 136.4, 134.8, 129.9, 129.0, 128.7, 128.3, 127.2, 126.7, 103.4, 66.1, 65.7, 65.4, 64.9, 60.0, 36.2, 20.9, 10.7; LRMS *m/z* (%) 411 [4.9 (M+H)⁺]; Anal. Calcd for C₂₃H₂₆N₂O₅: C, 67.30; H, 6.38; N, 6.82. Found: C, 66.95; H, 6.46; N, 6.88.

One crystallization from Et₂O afforded crystalline **8** (mp = 166-169 °C) which was then converted to **9** and **10** as follows.

2-Hydroxyethyl (2*R*)-2-(phenylcarboxamido) butanoate (9**, Scheme 1 in the article)**

SmI₂ (0.1 M in THF) was added dropwise at room temperature to a solution of **8** (203 mg, 0.494 mmol) in dry THF (6 mL) and HMPA (0.26 mL, 1.479 mmol) until the reaction mixture remained deep blue. After 15 min (complete conversion by thin-layer chromatography), the solvent was concentrated to a small volume and the mixture partitioned between brine and EtOAc. Drying of the organic extracts, solvent removal, and gradient flash chromatography of the residue (EtOAc/hexane 1:4 → 1:1) afforded 2-[(1*R*)-1-(phenylcarboxamido)propyl]-1,3-dioxolane (105 mg, 90% yield) as a white

solid.³ ¹H NMR (CDCl₃, 300 MHz) δ 7.80-7.77 (m, 2H), 7.51-7.41 (m, 3H), 6.16 (d, J = 9.4 Hz, 1H), 4.97 (d, J = 1.9 Hz, 1H), 4.43-4.36 (m, 1H), 4.05-3.85 (m, 4H), 1.83-1.73 (m, 1H), 1.60-1.49 (m, 1H), 1.01 (t, J = 7.4 Hz, 3H); ¹³C NMR (CDCl₃, 63 MHz) δ 167.4, 134.6, 131.3, 128.5, 126.9, 103.9, 65.4, 65.2, 52.2, 23.2, 10.4. Ozone was bubbled through a solution of 2-[(1*R*)-1-(phenylcarboxamido)propyl]-1,3-dioxolane (90.5 mg, 0.38 mmol) in EtOAc (25 mL) at -78 °C for 7 minutes. Argon was bubbled for 10 min and the solvent removed. Flash chromatography (EtOAc/hexane 3:7 $\rightarrow$ 3:2), afforded **9** (90.9 mg, 94%) as a white solid. (mp = 61-63.5 °C, EtOAc/hexane). ¹H NMR (CDCl₃, 250 MHz) δ 7.82-7.78 (m, 2H), 7.55-7.39 (m, 3H), 6.75 (d, J = 7.5 Hz, 1H), 4.73 (m, 1H), 4.40-4.24 (m, 2H), 3.85 (t, J = 4.7 Hz, 2H), 2.67 (br s, 1H), 2.13-1.98 (m, 1H), 1.98-1.78 (m, 1H), 1.01 (t, J = 7.5 Hz, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 172.4, 167.4, 133.5, 131.6, 128.4, 126.9, 66.8, 60.5, 54.1, 25.4, 9.8; Anal. Calcd for C₁₃H₁₇NO₄: C, 62.20; H, 6.92; N, 5.61. Found: C, 62.14; H, 6.82; N, 5.57.

(*R*)-2-(phenylcarboxamido)butanoic acid (**10**)

LiOH·H₂O (15.3 mg, 0.36 mmol) was added to a solution of **9** (30.7 mg, 0.12 mmol) in dioxane/H₂O (3:1, 0.6 mL) at 0 °C. After 2.5 h, brine was added and the reaction mixture was first acidified to pH=3 by adding cool 5% aqueous HCl and then extracted with CH₂Cl₂. The organic extracts were dried, filtered and concentrated to afford chromatographically and spectroscopically pure **10** (23.5 mg, 92%) as a white solid with identical properties to an authentic sample independently prepared from commercial (*R*)-2-(phenylcarboxamido)butanoic acid (>99%).⁴ ¹H NMR (CDCl₃, 300 MHz) δ 10.42 (br s, 1H), 7.79 (m, 2H), 7.53-7.39 (m, 3H), 6.91 (d, J = 7.8 Hz, 1H), 4.78 (m, 1H), 2.15-2.01 (m, 1H), 1.97-1.83 (m, 1H), 1.01 (t, J = 7.4 Hz, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 175.7, 167.7, 133.4, 131.8, 128.5, 127.0, 53.9, 25.4, 9.6. The optical rotation of **10** (prepared from **9** and crystallized from CH₂Cl₂-hexane, mp = 106-108 °C): [α]_D²⁰ +4.28 (c = 0.7, CH₃OH) was sensibly higher than that of the sample prepared

³ *N*-acyl hydrazine **7S** (79 mg, 90% yield) was also separated in the column.

⁴ Both (*R*)- and (*S*)-2-aminobutanoic acids (>99%) are commercially available. They were converted into **10** and its enantiomer, respectively, according to Noshio, Y.; Seki, T.; Kondo, M.; Ohfuchi, T.; Tamura, M.; Okai, H. *J. Agric. Food Chem.* **1990**, *38*, 1368-1373.

from (*R*)-2-aminobutanoic acid (>99%): $[\alpha]_D^{20} +4.0$ ($c = 0.7$, CH_3OH). All our attempts to determine the enantiomeric purity of **10** using GC-MS (beta-DEXTM 120 and gamma-DEXTM 120 columns, $25\text{m} \times 0.25\text{mm}$) and HPLC (Chiralpack WH column, 0.25 mM $\text{CuSO}_4(\text{aq})$; and Chiralcel OJ, hexanes/isopropanol 95/5, 90/10, 85/15) failed so far, because under the conditions tried the (*S*)- and the (*R*)-2-(phenylcarboxamido)butanoic acids (from mixtures independently prepared),⁴ coeluted.

Preparation of radical adducts **3a-c** (and **5a** and **5c**) from *N*-acylhydrazones **1** (and **4 R = Et**, and **4 R = -CH(CH₃O)₂)**

Ethyl 2-{[(4*S*)-4-Benzyl-2-oxo-1,3-oxazolan-3-yl]imino}acetate (**1**)

p-TsOH·H₂O (6 mg, 0.06 mmol) and ethyl glyoxylate (118 μL , 0.59 mmol, ~ 50% in toluene) were added to a solution of **7S** (102 mg, 0.53 mmol) in dry toluene (0.15 M) at rt. After refluxing for 3 h and removal of the solvent, flash chromatography (EtOAc/hexane 1:3) afforded **1** (128 mg, 87%) as a pale yellow oil. ¹H NMR (CDCl_3 , 250 MHz) δ 8.40 (s, 1H), 7.37-7.27 (m, 3H), 7.19-7.15 (m, 2H), 4.56-4.46 (m, 1H), 4.36 (q, $J = 7.1\text{ Hz}$, 2H), 4.33 (dd, $J = 9.0\text{ Hz}$, $J = 2.8\text{ Hz}$, 1H), 4.21 (dd, $J = 9.0\text{ Hz}$, $J = 4.9\text{ Hz}$, 1H), 3.32 (dd, $J = 13.8\text{ Hz}$, $J = 3.7\text{ Hz}$, 1H), 2.89 (dd, $J = 13.8\text{ Hz}$, $J = 8.8\text{ Hz}$, 1H), 1.37 (t, $J = 7.1\text{ Hz}$, 3H); ¹³C NMR (CDCl_3 , 75 MHz) δ 163.0, 152.2, 139.0, 134.2, 129.1, 128.8, 127.3, 65.8, 61.6, 57.6, 37.4, 14.2.

(4*S*)-4-Benzyl-3-[(*E*)-propylideneamino]-1,3-oxazolan-2-one (**4a**)⁵

¹H NMR (CDCl_3 , 250 MHz) δ 8.05 (dd, $J = 5.2\text{ Hz}$, $J = 5.2\text{ Hz}$, 1H), 7.36-7.27 (m, 3H), 7.18-7.14 (m, 2H), 4.40-4.30 (m, 1H), 4.25 (dd, $J = 8.7\text{ Hz}$, $J = 8.7\text{ Hz}$, 1H), 4.08 (dd, J

⁵ Prepared according to: Friestad, G. K.; Qin, J. *J. Am. Chem. Soc.* **2001**, *123*, 9922-9923.

= 8.7 Hz, J = 5.5 Hz, 1H), 3.23 (dd, J = 13.8 Hz, J = 3.6 Hz, 1H), 2.79 (dd, J = 13.8 Hz, J = 8.7 Hz, 1H), 2.47-2.35 (m, 2H), 1.15 (dd, J = 7.5 Hz, J = 7.5 Hz, 3H); ^{13}C NMR (CDCl_3 , 63 MHz) δ 157.0, 154.3, 135.1, 129.1, 128.7, 127.0, 65.5, 57.3, 36.8, 26.5, 10.5.

(4*S*)-4-Benzyl-3-[(*E*)-2,2-dimethoxyethylidene]amino-1,3-oxazolan-2-one (4c)

7S (209 mg, 1.09 mmol) and *p*-TsOH·H₂O (10 mg, 0.05 mmol) were added at rt to a solution of dimethoxyacetaldehyde (175 μL , 0.91 mmol) in methanol (6 mL, 0.15 M in the aldehyde) in the presence of molecular sieves (242 mg). After refluxing for 3 h, the mixture was filtered, concentrated and purified by flash chromatography (EtOAc/hexane 3:7) to afford hydrazone **4c** as an oil (242 mg, 95%) containing <5% of (*S*)-(4-Benzyl-2-oxo-oxazolidin-3-ylimino) acetaldehyde. ^1H NMR (CDCl_3 , 250 MHz) δ : 7.88 (d, J = 5.3 Hz, 1H), 7.37-7.27 (m, 3H), 7.18-7.14 (m, 2H), 4.89 (d, J = 5.3 Hz, 1H), 4.45-4.35 (m, 1H), 4.27 (dd, J = 8.8 Hz, J = 8.8 Hz, 1H), 4.15 (dd, J = 8.8 Hz, J = 4.7 Hz, 1H), 3.46 (s, 6H), 3.25 (dd, J = 13.8 Hz, J = 3.4 Hz, 1H), 2.80 (dd, J = 13.8 Hz, J = 8.9 Hz, 1H); ^{13}C NMR (CDCl_3 , 63 MHz) δ 153.5, 147.6, 134.7, 129.1, 128.9, 127.3, 102.6, 65.7, 56.6, 55.9, 54.0, 53.9, 36.4.

General Procedure for the radical addition to *N*-acyl hydrazones **1 and **4a** and **4c****

A 0.02 M solution of the hydrazone (**1** for **3a-c**, **4a** for **5a**, **4c** for **5c**), benzophenone (100 mol%) and any other additive (where indicated) in the appropriate solvent (methanol for **3a**, isopropanol for **3b**, or 1,3-dioxolane for **3c** and **5a,c**) was deoxygenated by bubbling argon for 20 min. The mixture, kept at rt with the aid of circulating water (or at low temperature, where indicated, using an appropriate cooling bath), was externally irradiated with a 450 W Hanovia medium-pressure mercury lamp until the substrate was consumed (TLC and GC-MS). Solvent removal followed by flash chromatography, afforded adducts **3a-c**, **5a** and **5c** as mixtures of diastereoisomers. The diastereomeric ratio was determined by ^1H NMR analysis of appropriate proton signals.

Ethyl-2-{[(4*S*)-4-Benzyl-2-oxo-1,3-oxazolan-3-yl]amino}-3-hydroxypropanoate (3a**, Figure 1 in the article)**

Prepared from hydrazone **1** (79 mg, 0.28 mmol) in methanol according to the general procedure. Irradiation time: 0.5 h. Flash chromatography (EtOAc/hexane 15:85 → 35:65) afforded **3a** (28 mg, 31%) as a pale yellow oil. ^1H NMR (CDCl_3 , 400 MHz) δ 7.37-7.28 (m, 3H), 7.20-7.17 (m, 2H), 4.75 (d, $J = 5.7$ Hz, 1H), 4.26 (q, $J = 7.2$ Hz, 2H), 4.18-4.01 (m, 2H), 3.88 (m, 1H), 3.80 (m, 1H), 3.37 (dd, $J = 13.5$ Hz, $J = 3.4$ Hz, 1H), 2.68 (dd, $J = 13.5$ Hz, $J = 9.4$ Hz, 1H), 1.31 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 170.3, 159.4, 135.3, 129.1, 129.0, 127.2, 66.3, 63.2, 61.5, 60.8, 58.1, 36.8, 14.1; LRMS m/z (%) 309 [1.4, $(\text{M}+\text{H})^+$]; HRMS calcd for $\text{C}_{15}\text{H}_{21}\text{N}_2\text{O}_5$ $(\text{M}+\text{H})^+$ 309.145047, found 309.143779.

Ethyl 2-{[(4*S*)-4-Benzyl-2-oxo-1,3-oxazolan-3-yl]amino}-3-hydroxy-3-methylbutanoate (3b**, Figure 1 in the article)**

Prepared from hydrazone **1** (80 mg, 0.29 mmol) in isopropanol according to the general procedure. Irradiation time: 2 h. Flash chromatography (EtOAc/hexane 1:3 → 3:7) afforded **3b** (54 mg, 55%, dr = 2.3:1) as a pale yellow oil. The diastereomeric ratio was determined by integration of the signals corresponding to the methine proton α to the NH group: at δ 4.85 for the major diastereoisomer (2*S*) and at δ 4.92 for the minor diastereoisomer in the 250 MHz ^1H NMR spectra. For the diastereomeric mixture: ^1H NMR (CDCl_3 , 250 MHz) δ 7.35-7.20 (m, 3H), 7.17-7.15 (m, 2H), 4.92 (d, $J = 6.9$ Hz, 1H_R), 4.85 (d, $J = 6.3$ Hz, 1H_S), 4.38-3.94 (m, 5H), 3.52 (d, $J = 6.3$ Hz, 1H_S), 3.49 (d, $J = 6.9$, 1H_R), 3.37 (m, 1H_S), 3.26 (dd, $J = 13.1$ Hz, $J = 3.5$ Hz, 1H_R), 2.74-2.62 (m, 1H), 1.40 (s, 3H), 1.34 (t, $J = 6.1$ Hz, 3H), 1.27 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 172.0, 158.0, 135.6_R, 135.3_S, 128.9, 128.8, 128.7, 127.0, 71.7_R, 71.3_S, 71.1_S, 71.0_R, 66.3_R,

66.3_R, 61.5_R, 61.4_S, 58.4_S, 58.2_R, 37.8_R, 37.2_S, 27.1_S, 26.5_R, 25.6_R, 25.3_S, 14.2_S, 14.2_R; LRMS m/z (%) 337 [3.9, (M+H)⁺], 319 [3.7, (M-OH)⁺], 245 [5.0, (M-Bn)⁺]; HRMS calcd for C₁₇H₂₅N₂O₅ (M+H)⁺ 337.176347, found 337.177979.

Ethyl 2-{[(4*S*)-4-Benzyl-2-oxo-1,3-oxazolan-3-yl]amino}-2-(1,3-dioxolan-2-yl)ethanoate (3c**, Table 1 in the article)**

3c

Prepared from hydrazone **1** (65 mg, 0.23 mmol) in 1,3-dioxolane according to the general procedure. Irradiation time: 1 h. Flash chromatography (EtOAc/hexane 20:80 → 35:65) afforded **3c** (73 mg, 88%, dr = 1.5:1) as a pale yellow oil. The diastereomeric ratio was determined by integration of the signals corresponding to the acetalic proton: at δ 4.73 for the major diastereoisomer and at δ 4.90 for the minor diastereoisomer in the 250 MHz ¹H NMR spectra. For the 2*R*-2*S* mixture: ¹H NMR (CDCl₃, 250 MHz) δ 7.35-7.14 (m, 5H), 5.27 (d, J = 4.4 Hz, 1H_R), 5.26 (d, J = 4.7 Hz, 1H_S), 4.90 (d, J = 3.4 Hz, 1H_R), 4.73 (d, J = 3.4 Hz, 1H_S), 4.29 (q, J = 7.2 Hz, 2H_R), 4.28 (q, J = 7.2 Hz, 2H_S), 4.14-3.87 (m, 8H), 3.44 (dd, J = 15.3 Hz, J = 2.8 Hz, 1H_S), 3.36 (dd, J = 13.7 Hz, J = 3.0 Hz, 1H_R), 2.67-2.54 (m, 1H), 1.32 (t, J = 7.2 Hz, 3H_S) 1.24 (t, J = 7.2 Hz, 3H_R); ¹³C NMR (CDCl₃, 75 MHz) δ 169.4, 169.1, 157.9, 135.8, 129.1, 128.9, 128.8, 128.7, 126.9, 126.8, 102.6, 102.0, 66.3, 66.0, 65.7, 65.5, 65.2, 65.0, 61.7, 61.4, 58.7, 58.4, 37.2, 36.7, 14.0; LRMS m/z (%) 351 [2.7, (M+H)⁺]; HRMS calcd for C₁₇H₂₃N₂O₆ (M+H)⁺ 351.155612, found 351.157198.

(4*S*)-4-Benzyl-3-[[*(1R)*-1-(1,3-dioxolan-2-yl)-2,2-dimethoxyethyl]amino]-1,3-oxazolan-2-one (5c, Table 3, entry 3 in the article)

5c

Prepared from hydrazone **4c**⁶ (71mg, 0.24 mmol), benzophenone (47 mg, 0.25 mmol), and InCl₃ (115 mg, 0.50 mmol) in 1,3-dioxolane (3 mL), according to the general procedure. Irradiation time: 2 h at −78 °C. Flash chromatography (EtOAc/hexane 1:3 → 3:7) afforded **5c** (65 mg, 75%, dr = 95:5) as pale yellow oil. The diastereomeric ratio was determined by integration of the signals corresponding the dimethylacetalic proton (and the NH proton): at δ 4.54 (4.63) for the major diastereoisomer and at δ 4.56 (4.68) for the minor diastereoisomer in the 500 ¹H NMR spectra. For the major (4*S*,1*S*) isomer: ¹H NMR (CDCl₃, 300 MHz) δ 7.33-7.20 (m, 3H), 7.17-7.14 (m, 2H), 5.08 (d, *J* = 3.4 Hz, 1H), 4.63 (br s, 1H), 4.54 (d, *J* = 5.5 Hz, 1H), 4.15-3.85 (m, 7H), 3.48 (s, 3H), 3.47 (s, 3H), 3.44-3.35 (m, 2H), 2.66-2.57 (m, 1H); ¹³C NMR (CDCl₃, 63 MHz) δ 157.8, 136.1, 129.0, 128.7, 126.8, 104.4, 102.1, 66.0, 65.1, 64.9, 60.5, 58.2, 55.4, 55.1, 36.9; LRMS *m/z* (%) 353 [~0.6, (M+H)⁺], 321 [5.9, (M-OMe)⁺]; HRMS calcd for C₁₇H₂₅N₂O₆ (M+H)⁺ 353.171262, found 353.171549.

⁶ Chromatographed hydrazone **4c** containing <5% of 2-[[*(4S)*-4-benzyl-2-oxo-1,3-oxazolan-3-yl]imino]acetaldehyde: see the experimental procedure for **4c**.

3c, dr = 4.1:1
table 1, entry 3 in the article

5a, dr = 1.8:1
table 1, entry 4 in the article

5a, dr = 98:2
table 2, entry 1 in the article

5b, dr = 2.1:1

obtained from **6b** by irradiation at rt
(benzophenone, 1,3-dioxolane)

5b, dr = 97:3
table 2, entry 2 in the article

5c, dr =4:1
obtained by irradiation of **4c** at rt with
benzophenone in 1,3-dioxolane

5c, dr = 95:5
table 2, entry 3 in the article

5d, dr = 1:1
table 2, entry 4 in the article

5e, dr = 4:1
table 2, entry 5 in the article