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SPECIAL ISSUE

VIP

# Synthesis of Chiral Tetrahydrofurans and Pyrrolidines by Visible-Light-Mediated Deoxygenation

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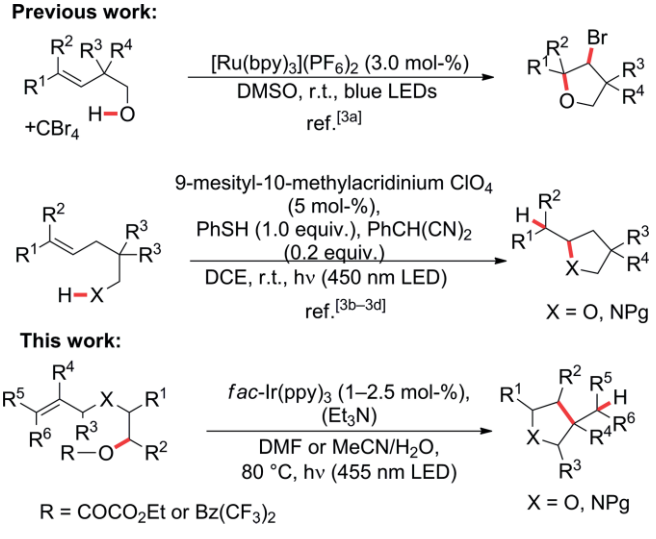
**Abstract:** The synthesis of chiral tetrahydrofurans and pyrrolidines starting from 1,2-diols or β-amino alcohols, respectively, by visible-light-mediated deoxygenation is described. Easily accessible monoallylated/propargylated substrates were activated either as inexpensive ethyl oxalates or as recyclable 3,5-bis(trifluoromethyl)benzoates to generate alkyl radicals suitable for 5-*exo-trig*/5-*exo-dig* cyclizations under visible-light irradiation.

## Introduction

Tetrahydrofurans and pyrrolidines represent important classes of heterocycles due to their diverse biological activities, and numerous natural products and pharmaceuticals incorporate chiral tetrahydrofuran[1] and pyrrolidine[2] rings. Many synthetic routes have been developed to these compound classes, among them methodologies making use of visible-light photocatalysis (Scheme 1).[3]

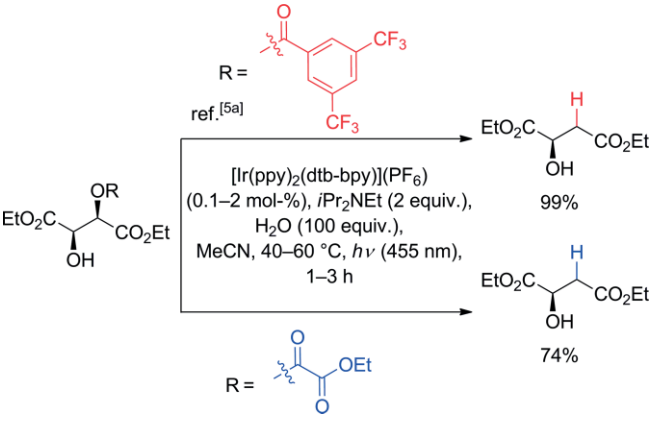



Scheme 1. Strategies towards photochemical tetrahydrofurans and pyrrolidines by visible-light-mediated transformations.[3]

These routes involve the formation of a C–X (X = O, NPg; Pg = protecting group) bond in the cyclization step starting from appropriately substituted alcohols or amines, in contrast to the approach reported here that features cyclization through C–C bond-forming reactions starting from monoallylated 1,2-diols or *N*-allylated amino alcohols, being readily available either from the chiral pool or by various synthetic routes such as the Sharpless asymmetric aminohydroxylation or dihydroxylation or epoxide ring-opening reactions.

## Results and Discussion

Following our interest in the catalytic conversion of renewable resources,[4] we recently reported a photoredox-catalyzed radical deoxygenation of alcohols via 3,5-bis(trifluoromethyl)benzoates.[5a] In the current study, we additionally evaluated ethyl oxalate as activating group, being pioneered by Utley and coworkers for electrochemical deoxygenations,[6] and which we find also allows efficient C–O bond activation under photochemical conditions (Scheme 2). However, rather than perform-




Scheme 2. Activation groups for the photoredox-catalyzed deoxygenation reaction of alcohols.

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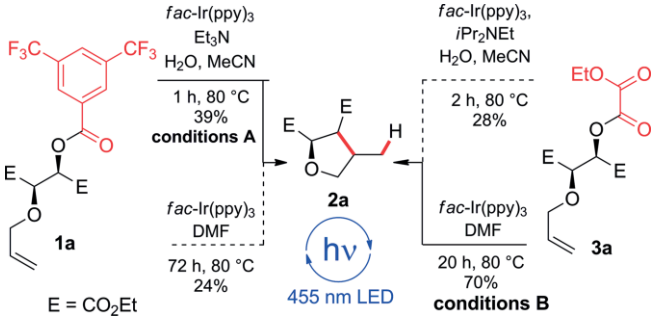
ing just simple reductive deoxygenations, we investigated horizontal functionalizations aiming at the synthesis of chiral tetrahydrofurans and pyrrolidines.

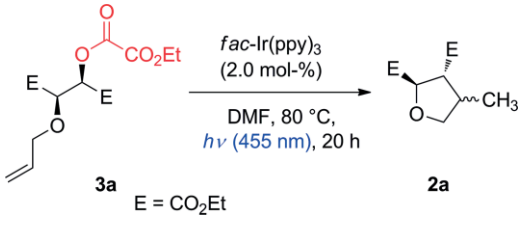
We started our investigation by exploring the deoxygenative, intramolecular cyclization reactions of modified tartrate derivatives, readily available in either enantiomerically pure form (Scheme 3). A 5-*exo*-*trig* cyclization to a tetrahydrofuran would be conceivable if one of the hydroxy groups is allylated and the other is activated for deoxygenation. Testing **1a**, in which deoxygenative radical formation was envisioned with 3,5-bis(trifluoromethyl)benzoate as activating group, indeed gave rise to tetrahydrofuran **2a**, albeit only in moderate yield.[7] As an alternative, we tested **3a**, in which radical deoxygenation was envisioned to occur with ethyl oxalate as activating group.[8] Indeed, **2a** could be obtained in considerably improved yields under optimized reaction conditions. The transformations of both **1a** and **3a** can be carried out in either the presence of a sacrificial amine (Scheme 3, top part: reductive quenching cycle) or in the absence of such an agent (Scheme 3, bottom part: oxidative quenching cycle). Although longer irradiation times are required when amines are omitted, the cyclizations typically proceed much more cleanly. Also, from an economic point of view, it is more attractive to avoid the use of relatively costly amines (*i*$Pr_2$NEt).




Scheme 3. Activation groups and reaction conditions tested for the construction of tetrahydrofurans through deoxygenative cyclization.

Low-priced ethyl oxalate activation[9] without sacrificial amines (conditions B) therefore seemed to be the parameters of choice for this transformation. However, ethyl oxalate esters are sometimes unstable and tend to decompose or hydrolyze quite easily, making the employment of 3,5-bis(trifluoromethyl)benzoyl derivatives a valid alternative (see below). In combination with sacrificial electron donors, very short reaction times for challenging substrates were achieved in this manner (conditions A). Cost aspects with respect to the benzoate group are mitigated as the auxiliary can easily be recycled and reused after activation and deoxygenation.[5] The highly reductive photocatalyst *fac*-[Ir(ppy)$_3$] [$E_{Red}(Ir^{4+}/Ir^{3+*})$ = –1.73 V vs. SCE][10] was crucial for transforming ethyl oxalate activated **3a** into cyclized compound **2a** (Table 1, Entry 1) without employing a sacrificial amine. Less-reducing iridium-based photocatalysts, such as [Ir(ppy)$_2$(dtb-bpy)]$PF_6$ [(dtb-bpy) = 2-(2,4-difluorophenyl)-5-(trifluoromethyl)pyridine, $E_{Red}(Ir^{3+}/Ir^{2+})$ = –1.51 V vs. SCE] or [Ir{dF(CF$_3$)ppy}$_2$(dtb-bpy)]$PF_6$ {dF(CF$_3$)ppy = 3,5-difluoro-2-[5-(trifluoromethyl)-2-pyridyl]phenyl} [$E_{Red}(Ir^{4+}/Ir^{3+*})$ = –1.21 V vs. SCE][11] were not capable of reducing oxalate tartrate **3a** ($E_{Red}$ = –1.65 V vs. SCE) and yielded only negligible amounts of product (Entries 2 and 3).[7] Likewise, [Ru(bpy)$_3$]$Cl_2$ [$E_{Red}(Ru^{2+}/Ru^{+})$ = –1.28 V vs. SCE][12] and [Cu(dap)$_2$]Cl [dap = 2,9-bis(4-anisyl)-1,10-phenanthroline, $E_{Red}(Cu^{2+}/Cu^{+*})$ = –1.43 V vs. SCE][13] were not suitable catalysts for promoting the formation of **2a** (Entries 4 and 5). Attempts to perform the reaction at ambient temperature or at 40 °C (Entry 6) gave no conversion of starting material **3a** at all. Applying higher temperatures was key for the photoinduced cyclization; higher temperatures should increase the rotational freedom in the substrate and thus may lead to a more favorable conformation for cyclization. Indeed, 89 % conversion and 51 % yield were achieved at 60 °C (Entry 7) and 100 % conversion and 70 % yield at 80 °C (Entry 1).[14]

Table 1. Catalyst screening, temperature dependence, and control experiments for the cyclization of compound **3a**.[a]




| Entry | Modifications to conditions | Conversion [%][b] | Yield [%][b] |
|---|---|---|---|
| 1 | none | 100 | 70 |
| 2 | [Ir(ppy)$_2$(dtb-bpy)]$PF_6$ | 22 | 0 |
| 3 | [Ir{dF(CF$_3$)ppy}$_2$(dtb-bpy)]$PF_6$ | 44 | 5 |
| 4 | [Ru(bpy)$_3$]$Cl_2$ | 6 | 0 |
| 5 | [Cu(dap)$_2$]Cl | 2 | 0 |
| 6 | room temperature or 40 °C | 0 | 0 |
| 7 | 60 °C | 89 | 51 |
| 8 | no light or no catalyst | < 5 | 0 |

[a] Reagents and conditions: Oxalate ester **3a** (0.1 mmol), *fac*-[Ir(ppy)$_3$] (2.0 mol-%), and DMF (0.1 M) at 80 °C and 455 nm LED irradiation under $N_2$ for 20 h. [b] Determined by GC-FID integration over all diastereomers with an internal standard.

Control experiments corroborated our assumption that the deoxygenation of **3a** is nevertheless a photochemically induced process; when either light or the photocatalyst (Entry 8) was absent, no reaction was observed (for full optimization of oxalates as well as benzoates, see the Supporting Information).

Because the reaction time for the batch setup on a 0.1 mmol scale was in the range of 1 d, it would take considerably longer to reach full conversion on a larger scale. Indeed, when we scaled up the reaction to 1.0 mmol keeping the substrate concentration constant, a prolonged reaction time of 7 d was required to achieve full conversion and 54 % isolated yield of **2a** with a batch setup (Table 2, Entry 1). Setting up the reaction in a microreactor should therefore be advantageous, as demonstrated previously for photoredox processes.[15]

Owing to the higher surface/volume ratio in the microreactor and improved miscibility, the continuous-flow mode typically offers shorter reaction times, higher yields, lower catalyst loadings, and facile upscaling. This was also true for the cyclization reaction of **3a**. By using a microreactor, full conversion was achieved after only 28 h and gave **2a** in 73 % yield (Entry 2).

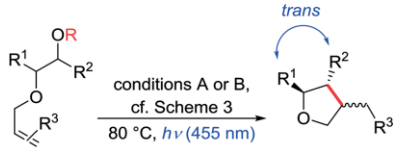
Table 2. Comparison of yield and reaction time for the cyclization of **3a** in a batch reaction and microreactor.[a]

| Entry | Setup | Time | Conversion [%][b] | Yield [%][c] |
|---|---|---|---|---|
| 1 | batch | 7 d | 100 | 54 |
| 2 | flow[d] | 28 h | 100 | 73 |

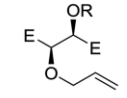
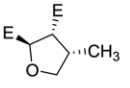
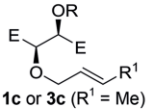
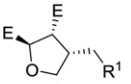
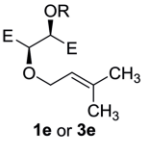
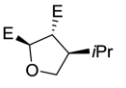
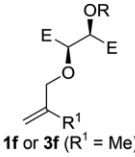
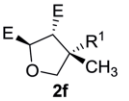
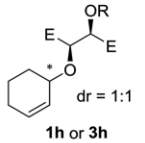
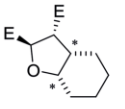
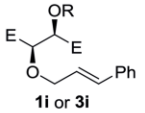
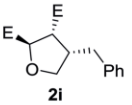
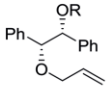
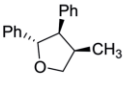
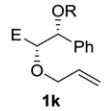
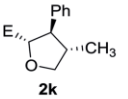
[a] Reagents and conditions: Oxalate ester **3a** (1.0 mmol), *fac*-[Ir(ppy)$_3$] (1.0 mol-%), and DMF (0.1 M) at 80 °C and 455 nm LED irradiation under $N_2$. [b] Determined by GC-FID with an internal standard. [c] Isolated yield. [d] Flow rate 0.35 mL/h, 35 µmol/h.

To explore the scope of the synthesis of tetrahydrofurans by deoxygenative cyclization, a number of tartrate derivatives were synthesized and subjected to the optimized reaction conditions (Table 3). Reactions with 3,5-bis(trifluoromethyl)benzoate-activated substrates **1** were allowed to react in a batch setup (conditions A), and substrates with ethyl oxalate as the activation group **3** were performed in a flow setup (see above, conditions B). Procedure B generally gave cleaner reactions and higher yields than procedure A, for which often minor amounts of simple reductive deoxygenation products were formed.[5] The diastereomeric ratios are typically similar for both procedures, because the reactions were run at identical temperatures. In all cases, high *anti* selectivity was obtained with respect to the stereocenters in the diol backbone, whereas the new stereocenter formed through the cyclization involving the allyl side-chain gave rise to epimers (see below). The asymmetric center at the allylated hydroxy center during the photoredox process is preserved, as is evident from the comparison between **2a** and *ent*-**2a** (Entries 1 and 2). A switch from the diethyl tartrate **3a** to the more bulky isopropyl derivative **3b** resulted in a slightly decreased product yield; however, a higher diastereomeric ratio of the products could not be achieved (Entries 1 and 3). The introduction of an additional methyl group at the γ position of the allyl system had only a minor influence on both the reaction yield and the diastereomeric ratio (*dr*; Entry 4). A further increase in the steric bulk at the γ position with a second methyl group (Entry 6) diminished the product yield from 38 to 31 % under conditions A and from 75 to 53 % under conditions B, but exclusively gave rise to the all-*trans*-configured tetrahydrofuran derivative **2e**. In the case of oxalate activation using **3e**, major amounts of the alkene were also observed that originate from elimination of a hydrogen atom from one of the methyl groups rather than reduction by abstraction from an external hydrogen source after cyclization. This mixture could be hydrogenated with $H_2$ and Pd/C to give **2e** in 53 % overall yield. Methyl substitution at the β position in **1f** and **3f** again gave good yields of the cyclization product with excellent diastereomeric induction (Entry 7). By employing cyclohexenyl-substituted **1h** and **3h** as substrates, the synthesis of cyclohexyl-annulated tetrahydrofuran **2h** was possible in acceptable yields but with high stereoselectivity (Entry 9); the product diastereomeric ratio mirrors the ratio in the starting materials (1:1). Neither procedure A nor B tolerates α,β-unsaturated esters (Entries 5 and 8); decomposition of the starting materials was observed. Attempting the cyclization with oxalyl-containing **3i** gave no conversion, but the corresponding 3,5-bis(trifluoromethyl)benzoate-activated derivative **1i** resulted in the forma-

Table 3. Substrate scope of the photoredox-catalyzed synthesis of chiral tetrahydrofurans **2**.[a]




**1** [R = 3,5-(CF$_3$)$_2$C$_6$H$_4$(CO)]
**3** [R = EtO$_2$C(CO)]
**2**

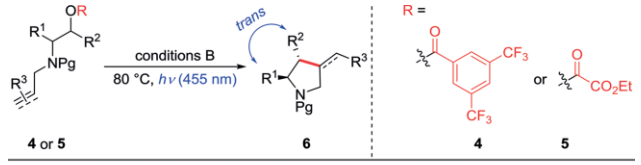
| Entry | Substrate | Product | Yield and *dr*[b] |
|---|---|---|---|
| 1 |  **1a** or **3a** |  **2a** | A, 39% (61:30:9) B, 73% (62:28:8:2) |
| 2 | *ent*-**3a** | *ent*-**2a** | B, 71% (57:37:6) |
| 3 | **3b** (E = CO$_2$*i*Pr) | **2b** | B, 65% (60:32:5:3) |
| 4 |  **1c** or **3c** (R$^1$ = Me) |  **2c** | A, 38% (65:21:14) B, 75% (60:34:5:1) |
| 5 | **1d** (R$^1$ = CO$_2$Me) | – | A, 0%[c] |
| 6 |  **1e** or **3e** |  **2e** | A, 31% (>95:5) B, 53%[d] (>95:5) |
| 7 |  **1f** or **3f** (R$^1$ = Me) |  **2f** | A, 46% (>95:5) B, 70% (>95:5) |
| 8 | **3g** (R$^1$ = CO$_2$Me) | – | B, 0%[c] |
| 9 |  dr = 1:1 **1h** or **3h** |  **2h** | A, 32% (53:47) B, 63% (57:43) |
| 10 |  **1i** or **3i** |  **2i** | A, 48% (78:22) B, 0% |
| 11 |  **1j** |  **2j** | A, 42% (49:42:9) |
| 12 |  **1k** |  **2k** | A, 57% (67:19:14) |

[a] E = CO$_2$Et unless otherwise noted. Reagents and conditions A: 3,5-bis(trifluoromethyl)benzoate ester (0.2–0.5 mmol), Et$_3$N (2.0 equiv.), *fac*-[Ir(ppy)$_3$] (2.0 mol-%), $H_2O$ (100 equiv.), and MeCN (0.04 M) at 80 °C under 455 nm LED irradiation under $N_2$ for 1 h in a batch setup. Reagents and conditions B: Oxalate ester (0.4–1.0 mmol), *fac*-[Ir(ppy)$_3$] (1.0 mol-%), and DMF (0.1 M) at 80 °C under 455 nm LED irradiation under $N_2$ in a flow setup (flow rate 0.30–0.35 mL/h, 29–33 h). [b] Isolated yield and *dr* determined by $^1$H NMR integration. [c] Decomposition of the starting material. [d] An alkane/alkene mixture (25:75) was initially formed, which was quantitatively hydrogenated ($H_2$, Pd/C).

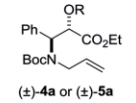
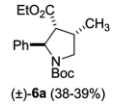
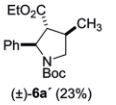
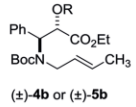
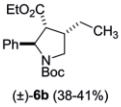
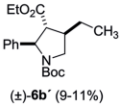
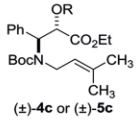
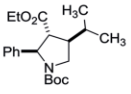
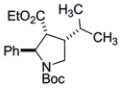
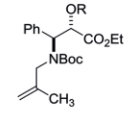
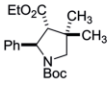
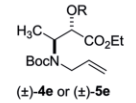
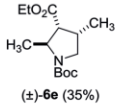
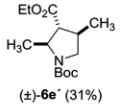
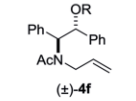
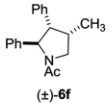
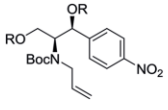
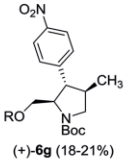
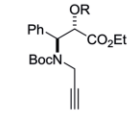
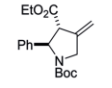
tion of benzyl-substituted tetrahydrofuran **2i** (Entry 10) in 48 % yield. Tetrahydrofuran products were also obtained when either only one or both of the ester groups in the tartrate backbone were substituted with phenyl groups (Entries 11 and 12).

A series of pyrrolidines were also synthesized by using this methodology by switching from 1,2-diols to the corresponding amino alcohol derivatives **4** and **5** (Table 4). Optimizing the reaction conditions (conditions B) for the pyrrolidine synthesis revealed that the oxidative quenching cycle was the best choice for both activation groups. The yields and diastereomeric ratios are typically similar for both benzoates **4** and oxalates **5**, and for the cases in which diastereomers are formed, they can be readily separated. Using (±)-**4a** or (±)-**5a** as substrate led to the formation of two separable diastereomers (±)-**6a** and (±)-**6a′** in yields of 61–62 % (Entry 1). The introduction of an additional methyl group at the γ position of the allyl system had a significant influence on the yield and diastereoselectivity. Although the yield dropped from 62 to 47 % for the oxalates and from 61 to 52 % for the benzoates, a higher diastereoselectivity was observed (Entry 2). A further increase in the steric bulk at the γ position with a second methyl group (Entry 3) caused no further decrease in the reaction yield but a reduction in the stereocontrol at the isopropyl-bearing stereocenter. Major amounts of the alkene were observed, similarly to the synthesis of the analogous tetrahydrofuran (see above). Subsequent hydrogenation with $H_2$ and Pd/C gave the desired product (±)-**6c** in yields of 48–53 %. Methyl substitution at the β position in (±)-**4d** and (±)-**5d** gave moderate yields of the cyclization product with excellent diastereomeric induction (Entry 4). Exchanging the phenyl group at the 1-position with a methyl group caused only a slightly higher yield and low diastereoselectivity (Entry 5), whereas exchanging the ester moiety for an additional phenyl group had a moderate influence on diastereoselectivity and allowed (±)-**6f** to be obtained in 50 % yield (Entry 6). Employing substrates (+)-**4g** or (+)-**5g**, synthesized from a commercially available, enantiopure amino diol, led to low yields of 28–30 % and slightly higher diastereoselectivity. Furthermore, 5-*exo-dig* cyclization with (±)-**4h** or (±)-**5h** was possible, giving a slightly lower yield compared with the corresponding 5-*exo-trig* reaction (Entry 1), but excellent diastereoselectivity (Entry 8).

Table 4. Substrate scope of the photoredox-catalyzed synthesis of pyrrolidines **6**.[a]



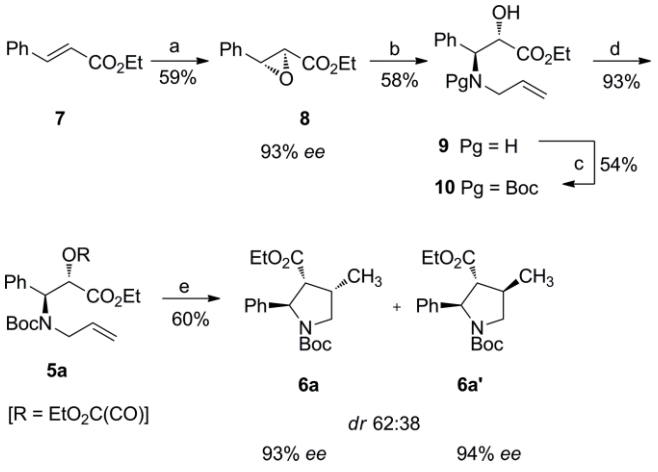

4 or 5 — 6 — 4 — 5

| Entry | Substrate | Major product | Minor product | Total yield and *dr*[b] |
|---|---|---|---|---|
| 1 |  (±)-**4a** or (±)-**5a** |  (±)-**6a** (38-39%) |  (±)-**6a′** (23%) | (±)-**4a**: 61% (61:39)<br>(±)-**5a**: 62% (63:37) |
| 2 |  (±)-**4b** or (±)-**5b** |  (±)-**6b** (38-41%) |  (±)-**6b′** (9-11%) | (±)-**4b**: 52% (79:21)<br>(±)-**5b**: 47% (81:19) |
| 3 |  (±)-**4c** or (±)-**5c** |  (±)-**6c** (25-28%) |  (±)-**6c′** (23-25%) | (±)-**4c**: 53%[c] (53:47)<br>(±)-**5c**: 48%[c] (52:48) |
| 4 |  (±)-**4d** or (±)-**5d** |  (±)-**6d** (38-45%) | – | (±)-**4d**: 45% (>99:1)<br>(±)-**5d**: 38% (>99:1) |
| 5 |  (±)-**4e** or (±)-**5e** |  (±)-**6e** (35%) |  (±)-**6e′** (31%) | (±)-**4e**: 66%[d] (53:47)<br>(±)-**5e**: 66% (53:47) |
| 6 |  (±)-**4f** |  (±)-**6f** | not isolated | (±)-**4f**: 50% (74:26)[e] |
| 7 |  (+)-**4g** or (+)-**5g** |  (+)-**6g** (18-21%) | not isolated | (+)-**4g**: 28%[d] (68:32)<br>(+)-**5g**: 30%[d] (73:27) |
| 8 |  (±)-**4h** or (±)-**5h** |  (±)-**6h** (45-47%) | – | (±)-**4h**: 45% (>99:1)<br>(±)-**5h**: 47% (>99:1) |

[a] Reagents and conditions B: 3,5-bis(trifluoromethyl)benzoate ester **4** or oxalate ester **5** (0.4–1.0 mmol), *fac*-[Ir(ppy)$_3$] (1.0 mol-%), and DMF (0.1 M) at 80 °C under 455 nm LED irradiation under $N_2$ in a flow setup (flow rate 0.30–1.0 mL/h, 10–33 h). [b] Given as the sum of the isolated yield of both diastereomers; *dr* is based on the isolated yields of the diastereomers. [c] After hydrogenation, initial alkane/alkene ratio = 23:77 for (±)-**6c**, 15:85 for (±)-**6c′**. [d] Flow rate 0.15 mL/h. [e] *dr* determined by $^1$H NMR integration, inseparable diastereomers.

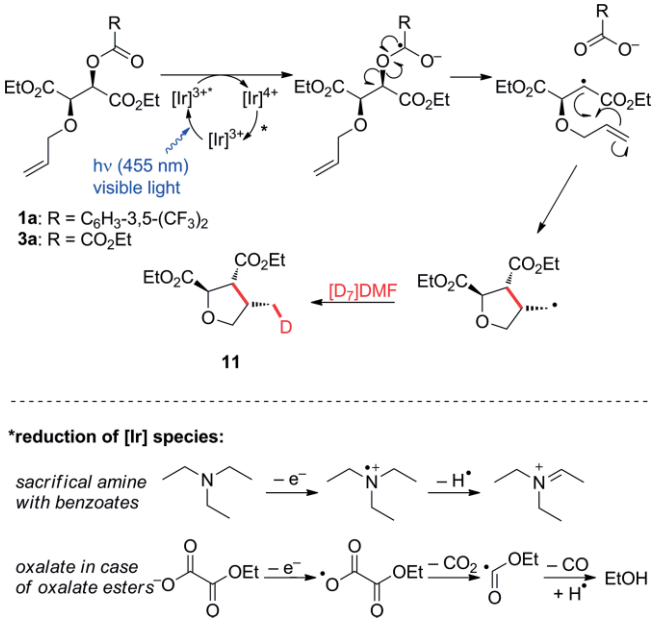
Although the method presented here produces epimers with respect to the stereocenter formed when cyclization at a prochiral allyl group takes place, enantiomeric and diastereomeric pyrrolidines with biologically relevant cores, that is, α- and β-prolines, can be readily prepared as pure stereoisomers that would otherwise be difficult to obtain. For example, the asymmetric epoxidation of ethyl cinnamate **7**[16] followed by ring-opening with allylamine,[17] *N*-Boc protection, and oxalyl activation readily gave rise to **5a** in good yield and in 93 % *ee* (Scheme 4). Photocyclization as described above gave rise to the readily separable diastereomers **6a** and **6a′**.

The mechanism for both deoxygenation protocols likely involves electron uptake by the activating group from excited $Ir^{3+*}$ species[18] followed by carbon–oxygen bond mesolysis giving rise to a carbon-centered radical. This can then be trapped either by hydrogen atom abstraction leading to undesired simple deoxygenation (not depicted) or in a 5-*exo-trig* fashion to give the tetrahydrofuran or pyrroldiine core structure. The primary radical thus formed undergoes hydrogen abstraction from the solvent or from a sacrificial amine radical cation (only when present, conditions A). Regeneration of the photocatalyst is accomplished by reduction with either ethyl oxalate,[19] solvent (conditions B), or sacrificial triethylamine (conditions A).



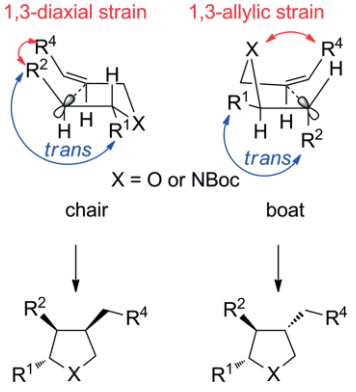

Scheme 4. Strategy for the enantioselective synthesis of substituted β-proline esters. Reagents and conditions: (a)[16] Shi catalyst (0.3 equiv.), $Na_2(EDTA)$ ($4 \times 10^{-5}$ M), $Bu_4NHSO_4$ (0.06 equiv.), Oxone (5.0 equiv.), $NaHCO_3$ (15.5 equiv.), $CH_3CN/H_2O$, 0 °C to room temp., 24 h, 59 %; (b)[17] allylamine (1.0 equiv.), EtOH, reflux, 24 h, 58 %; (c) $Boc_2O$ (1.2 equiv.), $Et_3N$ (1.2 equiv.), $CH_2Cl_2$, room temp., 24 h, 54 %; (d) ethyl oxalyl chloride (1.5 equiv.), pyridine (1.5 equiv.), $CH_2Cl_2$, 0 °C to room temp., 20 h, 93 %; (e) *fac*-[Ir(ppy)$_3$] (1.0 mol-%), LED (455 nm), DMF, 80 °C, 1.0 mL/h, 60 %.

Hydrogen abstraction from the solvent could be verified through a deuteriation experiment (Scheme 5): The cyclization of **3a** using [$D_7$]DMF gave compound **11** with single deuteriation at the terminal methyl group.




Scheme 5. Proposed mechanism for visible-light-mediated deoxygenation of **1** and **3** following a 5-*exo-trig* cyclization. Trapping of the radical species by deuterium abstraction from [$D_7$]DMF is shown.

The stereochemistry observed can be rationalized by competing chair- or boat-type transition states (Scheme 6), as has been discussed for analogous radical cyclizations to cyclopentanes.[20] A high preference for *anti* orientation of the substituents $R^1$ and $R^2$ at the diol or amino alcohol core appears to be the dominating control element, whereas the two possible conformations of the allyl side-chain suffer from 1,3-interactions with $R^2$ in the chair orientation and with X in the boat orientation.




Scheme 6. Proposed stereochemical model for the radical cyclization process.

## Conclusions

A protocol for the visible-light-mediated deoxygenation of monoallylated diols and β-amino alcohols followed by an intramolecular 5-*exo-trig*/5-*exo-dig* cyclization has been developed for the synthesis of chiral tetrahydrofuran and pyrrolidine derivatives. The method features inexpensive, readily available starting materials, and a sustainable, halogen-free activation of the hydroxy group towards radical reactions was realized by its transformation into either recyclable 3,5-bis(trifluoromethyl)-benzoate or inexpensive ethyl oxalate esters. Ethyl oxalate activated tartrates and ethyl oxalate or 3,5-bis(trifluoromethyl)-benzoate activated amino alcohols only require heat, a photoredox catalyst, and visible light to form chiral tetrahydrofuran or pyrrolidine derivatives in reasonable to good yields.

## Experimental Section

**General:** All chemicals were used as received or purified according to standard procedures[21] if necessary. Glassware was dried in an oven at 110 °C or flame-dried and cooled under a dry atmosphere prior to use. All reactions were performed using Schlenk techniques. Blue-light irradiation in batch processes was performed by using a CREE XLamp XP-E D5-15 LED ($\lambda$ = 450–465 nm). In microreactor processes, eight OSRAM OSLON Black Series LD H9GP LEDs ($\lambda$ = 455 ± 10 nm) were employed. Analytical TLC was performed on Merck TLC aluminium sheets coated with silica gel 60 F254. Reactions were monitored by TLC and visualized by a short-wave UV lamp and stained with a solution of potassium permanganate, *p*-anisaldehyde, ninhydrin, or Seebach's stain. Column flash chromatography was performed by using Merck flash silica gel 60 (0.040–0.063 mm). Melting points were measured with an automated melting-point system (MPA 100) with digital image processing technology by Stanford Research Systems. ATR-IR spectroscopy was carried out with a Cary 630 FTIR spectrometer or a Biorad Excalibur FTS 3000 spectrometer, equipped with a Specac Golden Gate Diamond Single Reflection ATR System. NMR spectra were recorded with Bruker Avance 300 and 400 spectrometers. Chemical shifts ($\delta$) for $^1$H NMR are reported in parts per million (ppm) relative to the signal of $CHCl_3$ at $\delta$ = 7.26 ppm, the DMSO quintet at $\delta$ = 2.50 ppm, or

the water signal at $\delta$ = 4.79 ppm. Chemical shifts ($\delta$) for $^{13}C$ NMR are reported in parts per million (ppm) relative to the center-line signal of the $CDCl_3$ triplet at $\delta$ = 77.2 ppm and the [$D_6$]DMSO septet at $\delta$ = 39.5 ppm. Coupling constants *J* are given in Hz. The following notations indicate the multiplicity of the signals: s = singlet, br. s = broad singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sept = septet, and m = multiplet, and combinations thereof. DEPT-135 analysis for the Avance 400 spectrometer shows $CH_3$ and CH peaks down and $CH_2$ peaks up. DEPT-135 analysis for the Avance 300 spectrometer shows $CH_3$ and CH peaks up and $CH_2$ peaks down. Mass spectra were recorded at the Central Analytical Laboratory at the Department of Chemistry of the University of Regensburg with a Varian MAT 311A, Finnigan MAT 95, Thermoquest Finnigan TSQ 7000, or Agilent Technologies 6540 UHD Accurate-Mass Q-TOF LC/MS spectrometer. Gas chromatographic analyses were performed with a Fisons Instruments gas chromatograph equipped with a capillary column (30 m × 250 µm × 0.25 µm) and a flame ionization detector. Enantiomeric excesses were determined by chiral HPLC (Phenomenex Lux Cellulose-2, 4.6 × 250 mm, particle size 5 µm). The yields reported refer to the isolated compounds unless otherwise stated.

**General Procedure for Reactions with Oxalates without a Sacrificial Electron Donor:** A Schlenk tube equipped with a magnetic stirring bar was charged with ethyl oxalate ester (1.0 mmol, 1.0 equiv.) and *fac*-[Ir(ppy)$_3$] (6.55 mg, 10.0 µmol, 1.0 mol-%), dissolved in DMF (10 mL, 0.1 M), sealed with a screw cap, and subsequently evacuated for 15 min and backfilled with $N_2$. The screw cap was replaced with a Teflon-sealed inlet for a glass rod, through which irradiation with a 455 nm high-power LED took place from above while the reaction mixture was magnetically stirred and heated in an aluminium block at 80 °C from below. The reaction was monitored by TLC. Afterwards, the reaction mixture was diluted with EtOAc (300 mL) and extracted with water (5 × 100 mL). The combined organic layers were dried with $Na_2SO_4$, the solvent was evaporated under reduced pressure, and the residue purified by flash column chromatography.

**General Procedure for Reactions with 3,5-Bis(trifluoromethyl)benzoates with a Sacrificial Electron Donor:** A Schlenk tube equipped with a magnetic stirring bar was charged with 3,5-bis(trifluoromethyl)benzoate ester (0.50 mmol, 1.00 equiv.) and *fac*-[Ir(ppy)$_3$] (6.6 mg, 10 µmol, 2.0 mol-%), sealed with a screw cap, and subsequently evacuated and backfilled with $N_2$ (3 ×). MeCN (12.5 mL), $Et_3N$ (0.35 mL, 0.25 g, 2.5 mmol, 5.0 equiv.), and degassed water (0.90 mL, 0.90 g, 50 mmol, 100 equiv.) were added, and the reaction mixture was magnetically stirred until a homogeneous solution was obtained. The reaction mixture was degassed by using the freeze-pump-thaw method (5 ×), and the screw cap was replaced with a Teflon-sealed inlet for a glass rod, through which irradiation with a 455 nm high-power LED took place from above while the reaction mixture was magnetically stirred and heated at 80 °C in an aluminium block from below. After completion of the reaction, as judged by TLC (typically 1 h), the mixture was concentrated under reduced pressure and the residue purified by flash silica gel column chromatography.

**General Procedure for the Reaction of Ethyl Oxalyl Esters and 3,5-Bis(trifluoromethyl)benzoate Esters in a Microreactor Setup:** A Schlenk tube equipped with a magnetic stirring bar was charged with ethyl oxalate ester (Reaction B, 1.0 equiv.) or 3,5-bis(trifluoromethyl)benzoate ester (Reaction A; 1.0 equiv.), *fac*-[Ir(ppy)$_3$] (1.0 mol-%), and DMF (0.1 M). The reaction mixture was degassed by sparging with $N_2$ through a needle and a septum for 30 min or by the freeze-pump-thaw method (3 ×) and pumped through a microreactor (which was also sparged with $N_2$) equipped with eight LEDs at a flow rate of 0.15–1.00 mL/h through a syringe pump while heated at 80 °C. Afterwards, the reaction mixture was diluted with diethyl ether (150 mL) or EtOAc (300 mL) and washed with brine (3 × 100 mL) or water (5 × 100 mL). The combined organic layers were dried with anhydrous $Na_2SO_4$, the solvent was evaporated under reduced pressure, and the residue purified by flash column chromatography.

**Compound 2a:** Elution with hexanes/EtOAc (6:1); colorless oil; yield: 45 mg (39 % with **1a**, *dr* = 61:30:9) and 167 mg (73 % with **3a**, *dr* = 62:28:8:2); $R_f$ (hexanes/EtOAc, 1:1) = 0.81. $^1H$ NMR (major diastereomer, 400 MHz, $CDCl_3$): $\delta$ = 4.80 (d, *J* = 6.1 Hz, 1 H), 4.26–4.16 (m, 4 H), 4.16–4.08 (m, 1 H), 3.63 (dd, *J* = 8.3, 6.2 Hz, 1 H), 3.24 (dd, *J* = 8.3, 6.1 Hz, 1 H), 2.67 (dquint, *J* = 13.4, 6.8 Hz, 1 H), 1.32–1.23 (m, 6 H), 1.01 (d, *J* = 7.0 Hz, 3 H) ppm. $^1H$ NMR (minor diastereomer 1, 400 MHz, $CDCl_3$): $\delta$ = 4.72 (d, *J* = 7.4 Hz, 1 H), 4.26–4.16 (m, 4 H), 4.16–4.08 (m, 1 H), 3.58 (t, *J* = 8.7 Hz, 1 H), 2.77 (dt, *J* = 11.1, 5.6 Hz, 1 H), 2.62–2.51 (m, 1 H), 1.32–1.23 (m, 6 H), 1.16–1.10 (m, 3 H) ppm. $^1H$ NMR (minor diastereomer 2, 400 MHz, $CDCl_3$): $\delta$ = 4.65 (d, *J* = 8.3 Hz, 1 H), 4.26–4.16 (m, 4 H), 4.16–4.08 (m, 1 H), 3.48 (t, *J* = 8.0 Hz, 1 H), 2.95 (t, *J* = 8.4 Hz, 1 H), 2.67 (dquint, *J* = 13.4, 6.8 Hz, 1 H), 1.32–1.23 (m, 6 H), 1.01 (d, *J* = 7.0 Hz, 3 H) ppm. $^1H$ NMR (minor diastereomer 3, 400 MHz, $CDCl_3$): $\delta$ = 4.59 (d, *J* = 2.3 Hz, 1 H), 4.26–4.16 (m, 4 H), 4.16–4.08 (m, 1 H), 3.41 (d, *J* = 7.3 Hz, 1 H), 2.77 (dt, *J* = 11.1, 5.6 Hz, 1 H), 2.62–2.51 (m, 1 H), 1.32–1.23 (m, 6 H), 1.01 (d, *J* = 7.0 Hz, 3 H) ppm. $^{13}C$ NMR (major diastereomer, 101 MHz, $CDCl_3$): $\delta$ = 172.0, 171.2, 78.7, 75.7, 61.5, 61.1, 52.3, 36.9, 14.4, 14.3, 13.4 ppm. $^{13}C$ NMR (minor diastereomer 1, 101 MHz, $CDCl_3$): $\delta$ = 172.2, 171.9, 79.9, 76.0, 61.4, 61.4, 55.8, 39.8, 15.9, 14.3, 14.3 ppm. IR(neat): $\tilde{\nu}$ = 2979, 2939, 2877, 2190, 1731, 1464, 1372, 1275, 1180, 1095, 1027, 939, 858, 462 $cm^{-1}$. HRMS (ESI): calcd. for $C_{11}H_{19}O_5$ [M + H]$^+$ 231.1227; found 231.1230.

**Compound *ent*-2a:** Elution with hexanes/EtOAc (6:1); colorless oil; yield: 163 mg (71 % with *ent*-**3b**, *dr* = 57:37:6); $R_f$ (hexanes/EtOAc, 1:1) = 0.81. $^1H$ NMR (major diastereomer, 300 MHz, $CDCl_3$): $\delta$ = 4.75 (d, *J* = 6.1 Hz, 1 H), 4.23–4.02 (m, 5 H), 3.63–3.48 (m, 1 H), 3.20 (dd, *J* = 8.3, 6.1 Hz, 1 H), 2.68–2.44 (m, 1 H), 1.30–1.17 (m, 6 H), 0.96 (d, *J* = 7.0 Hz, 3 H) ppm. $^1H$ NMR (minor diastereomer 1, 300 MHz, $CDCl_3$): $\delta$ = 4.68 (d, *J* = 7.4 Hz, 1 H), 4.23–4.02 (m, 5 H), 3.63–3.48 (m, 1 H), 2.73 (dd, *J* = 8.8, 7.4 Hz, 1 H), 2.68–2.44 (m, 1 H), 1.30–1.17 (m, 6 H), 1.08 (dd, *J* = 6.6 Hz, 3 H) ppm. $^1H$ NMR (minor diastereomer 2, 300 MHz, $CDCl_3$): $\delta$ = 4.61 (d, *J* = 8.3 Hz, 1 H), 4.23–4.02 (m, 5 H), 3.44 (t, *J* = 8.0 Hz, 1 H), 2.91 (t, *J* = 8.4 Hz, 1 H), 2.68–2.44 (m, 1 H), 1.30–1.17 (m, 6 H), 1.07 (d, *J* = 6.7 Hz, 3 H) ppm. $^{13}C$ NMR (major diastereomer, 75 MHz, $CDCl_3$): $\delta$ = 172.0, 171.2, 78.7, 75.7, 61.5, 61.2, 52.3, 36.9, 14.4, 14.3, 13.4 ppm. $^{13}C$ NMR (minor diastereomer 1, 75 MHz, $CDCl_3$): $\delta$ = 172.2, 171.9, 79.8, 76.0, 61.5, 61.4, 55.8, 39.8, 15.8, 14.4, 13.4 ppm. HRMS (ESI): calcd. for $C_{11}H_{19}O_5$ [M + H]$^+$ 231.1227; found 231.1230.

**Compound 2b:** Elution with hexanes/EtOAc (3:1); colorless oil; yield: 168 mg (65 % with **3b**, *dr* = 60:32:5:3); $R_f$ (hexanes/EtOAc, 1:1) = 0.83. $^1H$ NMR (major diastereomer, 300 MHz, $CDCl_3$): $\delta$ = 5.10–4.91 (m, 2 H), 4.69 (d, *J* = 6.3 Hz, 1 H), 4.07 (ddd, *J* = 8.3, 6.7, 4.3 Hz, 1 H), 3.64–3.47 (m, 1 H), 3.11 (dd, *J* = 8.4, 6.3 Hz, 1 H), 2.71–2.55 (m, 1 H), 1.25–1.13 (m, 12 H), 0.96 (d, *J* = 7.0 Hz, 3 H) ppm. $^1H$ NMR (minor diastereomer 1, 300 MHz, $CDCl_3$): $\delta$ = 5.10–4.91 (m, 2 H), 4.61 (d, *J* = 7.6 Hz, 1 H), 4.07 (ddd, *J* = 8.3, 6.7, 4.3 Hz, 1 H), 3.64–3.47 (m, 1 H), 2.71–2.55 (m, 1 H), 2.55–2.40 (m, 1 H), 1.25–1.13 (m, 12 H), 0.96 (d, *J* = 7.0 Hz, 3 H) ppm. $^1H$ NMR (minor diastereomer 2, 300 MHz, $CDCl_3$): $\delta$ = 5.10–4.91 (m, 2 H), 4.54 (d, *J* = 8.2 Hz, 1 H), 4.07 (ddd, *J* = 8.3, 6.7, 4.3 Hz, 1 H), 3.42 (t, *J* = 8.0 Hz, 1 H), 2.85 (t, *J* = 8.3 Hz, 1 H), 2.71–2.55 (m, 1 H), 2.85 (t, *J* = 8.3 Hz, 1 H), 1.25–

1.13 (m, 12 H), 0.96 (d, $J$ = 7.0 Hz, 3 H) ppm. $^1$H NMR (minor diastereomer 3, 300 MHz, $CDCl_3$): $\delta$ = 5.10–4.91 (m, 2 H), 4.49 (d, $J$ = 3.3 Hz, 1 H), 4.07 (ddd, $J$ = 8.3, 6.7, 4.3 Hz, 1 H), 3.64–3.47 (m, 1 H), 2.71–2.55 (m, 2 H), 1.25–1.13 (m, 12 H), 0.96 (d, $J$ = 7.0 Hz, 3 H) ppm. $^{13}$C NMR (major diastereomer 1, 75 MHz, $CDCl_3$): $\delta$ = 171.4, 170.5, 78.7 75.6, 68.8, 68.6, 52.3, 36.7, 21.9, 21.9, 21.8, 21.7, 13.3 ppm. $^{13}$C NMR (major diastereomer 2, 75 MHz, $CDCl_3$): $\delta$ = 171.5, 171.4, 79.8, 75.9, 68.8, 68.6, 56.1, 39.8, 21.9, 21.8, 21.8, 21.7, 15.5 ppm. IR (neat): $\tilde{\nu}$ = 2980, 2940, 2879, 1727, 1469, 1375, 1273, 1180, 1145, 1103, 989, 944, 902, 829 cm$^{-1}$. HRMS (ESI): calcd. for $C_{13}H_{23}O_5$ [M + H]$^+$ 259.1540; found 259.1545.

**Compound 2c:** Elution with hexanes/EtOAc (6:1 to 2:1); colorless oil; yield: 28 mg (38 % with **1c**, *dr* = 65:21:14) and 183 mg (75 % with **3c**, *dr* = 60:34:5:1); $R_f$ (hexanes/EtOAc, 1:1) = 0.92. $^1$H NMR (major diastereomer, 300 MHz, $CDCl_3$): $\delta$ = 4.71 (d, $J$ = 5.0 Hz, 1 H), 4.18–4.08 (m, 5 H), 3.64 (dt, $J$ = 13.8, 8.2 Hz, 1 H), 3.21 (dd, $J$ = 8.4, 5.0 Hz, 1 H), 2.48–2.32 (m, 1 H), 1.66–1.28 (m, 2 H), 1.27–1.20 (m, 6 H), 0.88 (ddd, $J$ = 7.5, 6.1, 3.9 Hz, 3 H) ppm. $^{13}$C NMR (major diastereomer 1, 75 MHz, $CDCl_3$): $\delta$ = 171.9, 171.4, 79.1, 73.3, 61.4, 61.0, 51.6, 44.1, 21.0, 14.3, 14.2, 12.8 ppm. $^{13}$C NMR (major diastereomer 2, 75 MHz, $CDCl_3$): $\delta$ = 172.5, 171.6, 79.9, 74.3, 61.3, 61.3, 54.2, 46.5, 25.1, 14.3, 14.2, 12.4 ppm. IR (neat): $\tilde{\nu}$ = 2970, 2938, 2878, 1729, 1464, 1372, 1266, 1179, 1135, 1095, 1028, 943, 857, 433 cm$^{-1}$. HRMS (ESI): calcd. for $C_{12}H_{21}O_5$ [M + H]$^+$ 245.1384; found 245.1388.

**Compound 2e:** Elution with hexanes/EtOAc (5:1); colorless oil; yield: 41 mg (31 % with **1e**, *dr* ≥ 95:5) and 137 mg (53 % with **3e**, *dr* ≥ 95:5); $R_f$ (hexanes/EtOAc, 3:1) = 0.48. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 4.62 (d, $J$ = 7.2 Hz, 1 H), 4.28–4.16 (m, 4 H), 4.13 (t, $J$ = 8.2 Hz, 1 H), 3.76 (t, $J$ = 8.7 Hz, 1 H), 2.90 (t, $J$ = 7.8 Hz, 1 H), 2.40 (q, $J$ = 8.2 Hz, 1 H), 1.73–1.61 (m, 1 H), 1.28 (t, $J$ = 7.1 Hz, 6 H), 0.94 (d, $J$ = 6.7 Hz, 3 H), 0.89 (d, $J$ = 6.7 Hz, 3 H) ppm. $^{13}$C NMR (101 MHz, $CDCl_3$): $\delta$ = 173.1, 171.4, 80.7, 73.0, 61.3, 61.2, 52.6, 51.6, 30.7, 20.9, 20.7, 14.2, 14.1 ppm. IR (neat): $\tilde{\nu}$ = 2963, 2876, 1732, 1468, 1447, 1372, 1263, 1221, 1192, 1106, 1026, 969, 861, 715, 575 cm$^{-1}$;HRMS (ESI): calcd. for $C_{13}H_{23}O_5$ [M + H]$^+$ 259.1540; found 259.1548.

**Compound 2f:** Elution with hexanes/EtOAc (6:1); colorless oil; yield: 56 mg (46 % with **1f**, *dr* > 95:5) and 68 mg (70 % with **3f**, *dr* ≥ 95:5); $R_f$ (hexanes/EtOAc, 1:1) = 0.80. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 4.89 (d, $J$ = 8.0 Hz, 1 H), 4.27–4.12 (m, 4 H), 3.69 (s, 2 H), 2.89 (d, $J$ = 8.0 Hz, 1 H), 1.31–1.23 (m, 6 H), 1.20 (s, $J$ = 3.9 Hz, 3 H), 1.02 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 172.3, 170.6, 81.6, 78.8, 61.4, 61.1, 58.1, 43.7, 24.9, 22.0, 14.4, 14.3 ppm. IR (neat): $\tilde{\nu}$ = 2978, 2874, 1729, 1466, 1371, 1337, 1264, 109, 1179, 1093, 1028, 968, 940, 860, 716, 441 cm$^{-1}$. HRMS (ESI): calcd. for $C_{12}H_{21}O_5$ [M + H]$^+$ 245.1384; found 245.1388.

**Compound 2h:** Elution with hexanes/EtOAc (6:1); colorless oil; yield: 35 mg (32 % with **1h**, *dr* = 53:47) and 170 mg (63 % with **3h**, *dr* = 57:43); $R_f$ (hexanes/EtOAc, 3:1) = 0.60. $^1$H NMR (major diastereomer, 300 MHz, $CDCl_3$): $\delta$ = 4.91 (d, $J$ = 8.4 Hz, 1 H), 4.23–4.14 (m, 4 H), 3.36 (dd, $J$ = 8.3, 6.5 Hz, 1 H), 2.37–2.27 (m, 1 H), 2.15–2.05 (m, 1 H), 1.75–1.29 (m, 7 H), 1.28–1.22 (m, 6 H) ppm. $^1$H NMR (minor diastereomer, 300 MHz, $CDCl_3$): $\delta$ = 4.72 (d, $J$ = 5.9 Hz, 1 H), 4.23–4.14 (m, 4 H), 3.01 (dd, $J$ = 5.7, 4.9 Hz, 1 H), 2.37–2.27 (m, 1 H), 1.91–1.79 (m, 1 H), 1.75–1.29 (m, 7 H), 1.28–1.22 (m, 6 H) ppm. $^{13}$C NMR (major diastereomer, 75 MHz, $CDCl_3$): $\delta$ = 173.0, 170.3, 79.2, 76.4, 61.3, 61.1, 53.3, 41.3, 27.7, 24.2, 23.2, 19.8, 14.4, 14.3 ppm. $^{13}$C NMR (minor diastereomer, 75 MHz, $CDCl_3$): $\delta$ = 172.9, 172.0, 78.7, 78.3, 61.4, 61.3, 53.2, 42.7, 28.1, 27.0, 23.3, 21.0, 14.3, 14.3 ppm. IR (neat): $\tilde{\nu}$ = 2970, 2938, 2878, 1729, 1464, 1372, 1266, 1179, 1135, 1095, 1028, 943, 857, 433 cm$^{-1}$. HRMS (ESI): calcd. for $C_{14}H_{23}O_5$ [M + H]$^+$ 271.1540; found 271.1543.

**Compound 2i:** Elution with hexanes/EtOAc (10:0 to 8:2); colorless oil; yield: 70 mg (48 % with **1i**, *dr* = 78:22); $R_f$ (hexanes/EtOAc, 4:1) = 0.27. $^1$H NMR (major diastereomer, 400 MHz, $CDCl_3$): $\delta$ = 7.34–7.10 (m, 5 H), 4.84 (d, $J$ = 5.9 Hz, 1 H), 4.28–4.15 (m, 4 H), 3.95 (dd, $J$ = 8.5, 6.1 Hz, 1 H), 3.78 (dd, $J$ = 8.5, 6.2 Hz, 1 H), 3.35 (dd, $J$ = 8.0, 5.8 Hz, 1 H), 2.84–2.76 (m, 2 H), 2.53 (dd, $J$ = 13.5, 10.3 Hz, 1 H), 1.29 (t, $J$ = 7.1 Hz, 3 H), 1.27 (t, $J$ = 7.1 Hz, 3 H) ppm. $^1$H NMR (minor diastereomer, 400 MHz, $CDCl_3$): $\delta$ = 7.34–7.10 (m, 5 H), 4.69 (d, $J$ = 6.9 Hz, 1 H), 4.28–4.15 (m, 2 H), 4.15–4.00 (m, 3 H), 3.78–3.71 (m, 1 H), 2.84–2.76 (m, 4 H), 1.28 (t, $J$ = 7.2 Hz, 3 H), 1.21 (t, $J$ = 7.0 Hz, 3 H) ppm. $^{13}$C NMR (major diastereomer, 101 MHz, $CDCl_3$): $\delta$ = 171.7, 171.0, 139.3, 128.7, 128.6, 126.5, 78.9, 73.1, 61.4, 61.2, 51.5, 43.7, 34.1, 14.3, 14.2 ppm. $^{13}$C NMR (minor diastereomer, 101 MHz, $CDCl_3$): $\delta$ = 172.0, 171.5, 138.9, 128.8, 128.6, 126.5, 79.9, 74.1, 61.4, 61.3, 53.8, 46.0, 37.9, 14.2, 14.1 ppm. IR (neat): $\tilde{\nu}$ = 2983, 2942, 1729, 1455, 1372, 1262, 1178, 1097, 1027, 951, 860, 746, 700, 493 cm$^{-1}$. HRMS (ESI): calcd. for $C_{17}H_{23}O_5$ [M + H]$^+$ 307.1540; found 307.1543.

**Compound 2j:** Elution with hexanes/EtOAc (25:1); colorless oil; yield: 20 mg (42 % with **1j**, *dr* = 49:42:9); $R_f$ (hexanes/EtOAc, 6:1) = 0.55. $^1$H NMR (major diastereomer, 400 MHz, $CDCl_3$): $\delta$ = 7.38–7.20 (m, 10 H), 5.34 (d, $J$ = 5.4 Hz, 1 H), 4.36 (dd, $J$ = 8.3, 7.1 Hz, 1 H), 3.75 (t, $J$ = 8.0 Hz, 1 H), 3.34 (dd, $J$ = 7.6, 5.3 Hz, 1 H), 2.68 (sept, $J$ = 7.3 Hz, 1 H), 0.72 (d, $J$ = 7 Hz, 3 H) ppm. $^{13}$C NMR (major diastereomer, 101 MHz, $CDCl_3$): $\delta$ = 143.6, 139.7, 128.9, 128.4, 128.3, 127.1, 126.6, 125.4, 85.1, 74.8, 57.4, 37.4, 13.5 ppm. IR (neat): $\tilde{\nu}$ = 2968, 2930, 2874, 1742, 1603, 1495, 1453, 1382, 1279, 1245, 1182, 1140, 1069, 1047, 1027, 925, 803, 748, 698, 611, 580, 528 cm$^{-1}$. HRMS (ESI): calcd. for $C_{17}H_{18}O$ [M + H]$^+$ 238.1352; found 238.1352.

**Compound 2k:** Elution with hexanes/EtOAc (10:1); colorless oil; yield: 26 mg (57 % with **1k**, *dr* = 67:19:14); $R_f$ (hexanes/EtOAc, 6:1) = 0.25. $^1$H NMR (major diastereomer, 300 MHz, $CDCl_3$): $\delta$ = 7.41–7.14 (m, 5 H), 4.46 (d, $J$ = 8.5 Hz, 1 H), 4.32–4.25 (m, 1 H), 4.23–4.09 (m, 2 H), 3.72 (dd, $J$ = 10.1, 8.4 Hz, 1 H), 2.93 (dd, $J$ = 10.1, 8.5 Hz, 1 H), 2.57–2.39 (m, 1 H), 1.18 (t, $J$ = 7.2 Hz, 3 H), 0.99 (d, $J$ = 6.5 Hz, 3 H) ppm. $^{13}$C NMR (major diastereomer, 75 MHz, $CDCl_3$): $\delta$ = 172.7, 139.6, 128.8, 127.8, 127.2, 84.1, 76.3, 60.9, 58.3, 43.5, 14.2, 14.2 ppm. $^{13}$C NMR (minor diastereomer 1, 75 MHz, $CDCl_3$): $\delta$ = 172.5, 142.4, 128.4, 127.2, 125.0, 83.6, 75.5, 61.2, 55.8, 36.5, 15.5, 14.3 ppm. $^{13}$C NMR (minor diastereomer 2, 75 MHz, $CDCl_3$): $\delta$ = 171.4, 137.4, 128.3, 127.7, 124.7, 82.0, 76.0, 60.4, 56.4, 42.4, 38.2, 13.6 ppm. IR (neat): $\tilde{\nu}$ = 2962, 2873, 1745, 1603, 1456, 1377, 1270, 1187, 1108, 1083, 1029, 965, 939, 864, 754, 700, 520 cm$^{-1}$. HRMS (ESI): calcd. for $C_{14}H_{19}O_3$ [M + H]$^+$ 235.1329; found 235.1331.

**Compounds (±)-6a and (±)-6a′:** Elution with *n*-pentane/diethyl ether (20:1 to 3:1); colorless oils; yield: 131 mg (39 %) of **6a** and 79 mg (23 %) of **6a′** using **5a**; 126 mg (38 %) of **6a** and 76 mg (23 %) of **6a′** using **4a**; $R_f$ (**6a**, *n*-pentane/EtOAc, 3:1) = 0.20; $R_f$ (**6a′**, *n*-pentane/EtOAc, 3:1) = 0.25. $^1$H NMR (**6a**, 400 MHz, $CDCl_3$): $\delta$ = 7.33–7.14 (m, 5 H), 5.06 (m, 1 H), 4.25–3.98 (m, 2 H), 3.84–3.66 (m, 1 H), 3.58–3.33 (m, 1 H), 3.06–2.82 (m, 1 H), 2.71–2.54 (m, 1 H), 1.45 (br. s, 3 H), 1.26 (t, $J$ = 7.2 Hz, 3 H), 1.12 (m, 6 H), 1.01 (d, $J$ = 7.0 Hz, 3 H) ppm. $^1$H NMR (**6a′**, 400 MHz, $CDCl_3$): $\delta$ = 7.35–7.11 (m, 5 H), 5.16–4.85 (m, 1 H), 4.24–3.98 (m, 3 H), 3.18 (t, $J$ = 10.7 Hz, 1 H), 2.63–2.40 (m, 2 H), 1.46–1.01 (m, 15 H) ppm. $^{13}$C NMR (**6a**, 101 MHz, $CDCl_3$): $\delta$ = 171.6, 154.6, 143.8, 128.4, 127.1, 127.1, 126.0, 79.6, 62.3, 60.8, 57.9, 53.5, 33.9, 28.6, 28.2, 14.6, 14.4 ppm. $^{13}$C NMR (**6a′**, 101 MHz, $CDCl_3$): $\delta$ = 172.3, 154.1, 143.9, 128.4, 127.1, 125.9, 79.7, 65.2, 61.9, 61.0, 54.6, 37.4, 28.1, 16.0, 14.4. IR (**6a**, neat): $\tilde{\nu}$ = 2974, 2930, 1730, 1685, 1480, 1398, 1282, 1256, 1230, 1185, 1141, 1036, 1006, 887, 760, 701 cm$^{-1}$. IR (**6a′**, neat): $\tilde{\nu}$ = 2978, 2933, 1733, 1692, 1480, 1394, 1279, 1163, 1126, 1025, 951, 895, 861, 760, 701 cm$^{-1}$. HRMS (**6a**, ESI): calcd. for $C_{19}H_{28}NO_4$ [M + H]$^+$ 334.2013; found

334.2020. HRMS (**6a′**, ESI): calcd. for $C_{19}H_{27}NNaO_4$ $[M + Na]^+$ 356.1832; found 356.1838.

**Compounds (±)-6b and (±)-6b′:** Elution with *n*-pentane/diethyl ether (20:1 to 3:1); colorless oils; yield: 128 mg (38 %) of **6b** and 32 mg (9 %) of **6b′** using **5b**; 106 mg (41 %) of **6b** and 27 mg (11 %) of **6b′** using **4b**; $R_f$ (**6b**, *n*-pentane/EtOAc, 3:1) = 0.33; $R_f$ (**6b′**, *n*-pentane/EtOAc, 3:1) = 0.40. $^1$H NMR (**6b**, 400 MHz, $CDCl_3$): $\delta$ = 7.34–7.16 (m, 5 H), 5.29–4.93 (m, 1 H), 4.18 (m, 2 H), 3.84–3.61 (m, 1 H), 3.58–3.29 (m, 1 H), 3.09–2.81 (m, 1 H), 2.38 (q, $J$ = 7.2 Hz, 1 H), 1.53–1.08 (m, 14 H), 0.98–0.84 (m, 3 H) ppm. $^1$H NMR (**6b′**, 400 MHz, $CDCl_3$): $\delta$ = 7.36–7.12 (m, 5 H), 5.08–4.81 (m, 1 H), 4.22–4.02 (m, 3 H), 3.20 (t, $J$ = 10.7 Hz, 1 H), 2.63 (t, $J$ = 10.0 Hz, 1 H), 2.47–2.31 (m, 1 H), 1.74–1.53 (m, 2 H), 1.51–1.30 (m, 3 H), 1.21 (t, $J$ = 7.1 Hz, 3 H), 1.10 (s, 6 H), 0.92 (t, $J$ = 7.5 Hz, 3 H) ppm. $^{13}$C NMR (**6b**, 101 MHz, $CDCl_3$): $\delta$ = 172.2, 154.6, 143.6, 142.5, 128.6, 128.4, 127.1, 125.8, 125.6, 79.6, 63.7, 63.3, 60.7, 56.7, 55.2, 51.4, 50.8, 41.2, 40.8, 28.6, 28.2, 22.2, 14.4, 14.3, 12.7, 12.2 ppm. $^{13}$C NMR (**6b′**, 101 MHz, $CDCl_3$): $\delta$ = 172.7, 154.2, 143.9, 128.5, 127.1, 125.8, 79.8, 65.5, 61.0, 60.4, 52.9, 44.0, 28.2, 25.0, 14.4, 12.2 ppm. IR (**6b**, neat): $\tilde{\nu}$ = 2989, 2930, 2863, 1733, 1681, 1480, 1405, 1279, 1163, 1074, 1014, 928, 898, 865, 768, 705 cm$^{-1}$. IR (**6b′**, neat): $\tilde{\nu}$ = 3034, 2989, 2930, 2866, 1733, 1685, 1480, 1405, 1279, 1163, 1107, 1070, 1010, 961, 928, 895, 764, 705 cm$^{-1}$. HRMS (**6b**, ESI): calcd. for $C_{20}H_{29}NNaO_4$ $[M + Na]^+$ 370.1989; found 370.1992. HRMS (**6b′**, ESI): calcd. for $C_{20}H_{29}NNaO_4$ $[M + Na]^+$ 370.1989; found 370.1991.

**Compounds (±)-6c and (±)-6c′:** Elution with *n*-pentane/diethyl ether (20:1 to 1:1); colorless oils; yield: 49 mg (25 %) of **6c** and 45 mg (23 %) of **6c′** using **5c**; 57 mg (28 %) of **6c** and 51 mg (25 %) of **6c′** using **4c**; $R_f$ (**6c**, *n*-pentane/EtOAc, 3:1) = 0.35; $R_f$ (**6b′**, *n*-pentane/EtOAc, 3:1) = 0.40. $^1$H NMR (**6c**, 400 MHz, $CDCl_3$): $\delta$ = 7.36–7.14 (m, 5 H), 5.11 (d, $J$ = 65.5 Hz, 1 H), 4.30–4.07 (m, 2 H), 3.76 (dt, $J$ = 45.3, 9.5 Hz, 1 H), 3.44 (td, $J$ = 10.7, 4.0 Hz, 1 H), 2.91 (dd, $J$ = 14.8, 6.6 Hz, 1 H), 2.17–2.00 (m, 1 H), 1.64–1.51 (m, 1 H), 1.47 (s, 3 H), 1.29 (t, $J$ = 7.1 Hz, 3 H), 1.22 (s, 6 H), 0.91 (d, $J$ = 6.6 Hz, 3 H), 0.89 (d, $J$ = 7.2 Hz, 3 H) ppm. $^1$H NMR (**6c′**, 400 MHz, $CDCl_3$): $\delta$ = 7.81–6.80 (m, 5 H), 4.98–4.77 (m, 1 H), 4.13 (ddq, $J$ = 10.8, 7.2, 3.7 Hz, 2 H), 4.07–3.91 (m, 1 H), 3.29 (t, $J$ = 10.9 Hz, 1 H), 2.71 (t, $J$ = 9.9 Hz, 1 H), 2.40 (tt, $J$ = 10.9, 7.6 Hz, 1 H), 1.68 (dd, $J$ = 13.7, 6.6 Hz, 1 H), 1.50–1.35 (m, 2 H), 1.20 (t, $J$ = 7.1 Hz, 3 H), 1.09 (s, 7 H), 0.93 (d, $J$ = 6.7 Hz, 3 H), 0.89 (d, $J$ = 6.8 Hz, 3 H) ppm. $^{13}$C NMR (**6c**, 101 MHz, $CDCl_3$): $\delta$ = 172.9, 172.8, 154.7, 154.5, 143.2, 142.3, 128.6, 128.4, 128.4, 127.2, 127.1, 125.6, 125.5, 64.7, 64.5, 60.7, 60.7, 55.0, 54.0, 50.7, 50.1, 47.0, 46.1, 28.9, 28.9, 28.7, 28.3, 22.0, 21.8, 21.6, 21.6, 14.4 ppm. $^{13}$C NMR (**6c′**, 101 MHz, $CDCl_3$): $\delta$ = 173.4, 154.2, 143.8, 128.5, 127.2, 125.7, 79.7, 66.5, 61.0, 58.8, 50.8, 48.4, 30.3, 28.1, 21.0, 19.9, 14.3 ppm. IR (**6c**, neat): $\tilde{\nu}$ = 3034, 2967, 1733, 1696, 1476, 1390, 1275, 1163, 1126, 1018, 951, 898, 865, 768, 701 cm$^{-1}$. IR (**6c′**, neat): $\tilde{\nu}$ = 2967, 2937, 1730, 1696, 1476, 1390, 1256, 1215, 1163, 1115, 1040, 943, 902, 772, 701 cm$^{-1}$. HRMS (**6c**, ESI): calcd. for $C_{21}H_{31}NNaO_4$ $[M + Na]^+$ 384.2145; found 384.2153. HRMS (**6c′**, ESI): calcd. for $C_{21}H_{31}NNaO_4$ $[M + Na]^+$ 384.2145; found 384.2151.

**Compound (±)-6d:** Elution with *n*-pentane/diethyl ether (7:1 to 1:1); colorless oil; yield: 61 mg (38 % with **5d**) and 59 mg (45 % with **4d**); $R_f$ (*n*-pentane/EtOAc, 3:1) = 0.29. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.40–7.09 (m, 5 H), 5.11 (d, $J$ = 9.5 Hz, 1 H), 4.30–3.98 (m, 2 H), 3.69 (d, $J$ = 10.8 Hz, 1 H), 3.38 (d, $J$ = 10.7 Hz, 1 H), 2.74 (d, $J$ = 9.5 Hz, 1 H), 1.41 (s, 2 H), 1.26–1.19 (m, 6 H), 1.09 (s, 7 H), 1.03 (s, 3 H) ppm. $^{13}$C NMR (101 MHz, $CDCl_3$): $\delta$ = 170.5, 154.4, 144.1, 128.3, 127.0, 126.1, 79.6, 64.0, 62.8, 61.0, 60.7, 40.6, 28.5, 28.1, 25.3, 22.4, 14.4 ppm. IR (neat): $\tilde{\nu}$ = 3034, 2974, 2933, 2874, 1730, 1692, 1457, 1394, 1364, 1297, 1264, 1226, 1185, 1156, 1007, 1028, 898, 861, 757, 701 cm$^{-1}$. HRMS (ESI): calcd. for $C_{20}H_{29}NNaO_4$ $[M + Na]^+$ 370.1989; found 370.1995.

**Compounds (±)-6e and (±)-6e′:** Elution with *n*-pentane/diethyl ether (20:1 to 3:1); colorless oils; yield: 80 mg (35 %) of **6e** and 71 mg (31 %) of **6e′** using **5e**; 48 mg (35 %) of **6e** and 43 mg (31 %) of **6e′** using **4e**; $R_f$ (**6e**, *n*-pentane/EtOAc, 3:1) = 0.29; $R_f$ (**6e′**, *n*-pentane/EtOAc, 3:1) = 0.40. $^1$H NMR (**6e**, 400 MHz, $CDCl_3$): $\delta$ = 4.11 (m, 3 H), 3.44 (dd, $J$ = 10.6, 6.7 Hz, 1 H), 3.21 (s, 1 H), 2.55 (m, 2 H), 1.43 (s, 9 H), 1.29–1.19 (m, 6 H), 0.94 (d, $J$ = 6.7 Hz, 3 H) ppm. $^1$H NMR (**6e′**, 400 MHz, $CDCl_3$): $\delta$ = 4.15 (q, $J$ = 7.1 Hz, 2 H), 3.89 (s, 1 H), 3.80 (s, 1 H), 2.82 (t, $J$ = 10.7 Hz, 1 H), 2.31 (tt, $J$ = 10.6, 6.6 Hz, 1 H), 2.20 (dd, $J$ = 10.8, 8.4 Hz, 1 H), 1.42 (s, 9 H), 1.30 (d, $J$ = 6.0 Hz, 3 H), 1.24 (t, $J$ = 7.1 Hz, 3 H), 1.03 (d, $J$ = 6.4 Hz, 3 H) ppm. $^{13}$C NMR (**6e**, 101 MHz, $CDCl_3$): $\delta$ = 172.4, 154.6, 79.2, 60.5, 55.0, 52.6, 33.8, 28.6, 20.7, 14.4, 14.1 ppm. $^{13}$C NMR (**6e′**, 101 MHz, $CDCl_3$): $\delta$ = 172.8, 154.2, 79.4, 60.9, 59.8, 57.0, 53.2, 36.5, 28.6, 21.03, 16.2, 14.4 ppm. IR (**6e**, neat): $\tilde{\nu}$ = 2974, 2937, 2876, 1733, 1692, 1457, 1390, 1282, 1252, 1174, 1107, 1062, 1029, 954, 869, 775 cm$^{-1}$. IR (**6e′**, neat): $\tilde{\nu}$ = 2974, 2933, 2876, 1733, 1692, 1457, 1394, 1290, 1256, 1163, 1096, 1033, 910, 869, 772 cm$^{-1}$. HRMS (**6e**, ESI): calcd. for $C_{14}H_{25}NNaO_4$ $[M + Na]^+$ 294.1676; found 294.1678. HRMS (**6e′**, ESI): calcd. for $C_{14}H_{25}NNaO_4$ $[M + Na]^+$ 294.1676; found 294.1683.

**Compound (±)-6f:** Elution with *n*-pentane/diethyl ether (1:1); colorless oil; yield: 82 mg (50 % with **4f**, *dr* = 74:26); $R_f$ (*n*-pentane/diethyl ether, 1:1) = 0.13. $^1$H NMR (major diastereomer, 400 MHz, $CDCl_3$): $\delta$ = 7.40–7.08 (m, 10 H), 5.12 (s, 1 H), 3.99 (dd, $J$ = 12.1, 7.9 Hz, 1 H), 3.41 (dd, $J$ = 12.1, 10.2 Hz, 1 H), 3.25–3.18 (m, 1 H), 2.82–2.62 (m, 1 H), 1.91 (s, 3 H), 0.68 (d, $J$ = 6.8 Hz, 3 H) ppm. $^1$H NMR (minor diastereomer, 400 MHz, $CDCl_3$): $\delta$ = 7.40–7.08 (m, 10 H), 5.50 (s, 1 H), 3.89 (dd, $J$ = 9.9, 7.6 Hz, 1 H), 3.32 (t, $J$ = 10.0 Hz, 1 H), 3.25–3.18 (m, 1 H), 2.82–2.62 (m, 1 H), 2.24 (s, 3 H), 0.70 (d, $J$ = 6.8 Hz, 3 H) ppm. $^{13}$C NMR (major diastereomer, 101 MHz, $CDCl_3$): $\delta$ = 170.6, 142.8, 140.4, 129.1, 128.9, 128.1, 127.7, 127.2, 125.6, 69.1, 58.7, 52.4, 33.2, 22.5, 13.9 ppm. $^{13}$C NMR (minor diastereomer, 101 MHz, $CDCl_3$): $\delta$ = 169.5, 142.6, 139.9, 128.7, 128.6, 128.2, 127.1, 127.0, 125.5, 66.5, 56.5, 53.9, 35.0, 23.0, 13.9 ppm. IR (neat): $\tilde{\nu}$ = 3063, 3030, 2963, 2930, 2874, 1722, 1648, 1495, 1454, 1409, 1357, 1279, 1245, 1178, 1137, 1081, 1029, 973, 913, 865, 801, 749, 701 cm$^{-1}$. HRMS (APCI): calcd. for $C_{19}H_{22}NO$ $[M + H]^+$ 280.1696; found 280.1702.

**Compound (+)-6gA:** Elution with *n*-pentane/diethyl ether (2:1); colorless oil; yield: 132 mg (30 % with **5g**, *dr* = 73:27); isolation of major diastereomer by additional column chromatography, yield: 96 mg (22 %); $R_f$ (*n*-pentane/diethyl ether, 1:1) = 0.33; $[\alpha]_D^{25}$ = +1.7 ($c$ = 1.0, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.20 (d, $J$ = 8.6 Hz, 1 H), 7.42 (d, $J$ = 8.7 Hz, 1 H), 4.76–4.51 (m, 1 H), 4.37 (d, $J$ = 10.9 Hz, 1 H), 4.28 (q, $J$ = 7.1 Hz, 2 H), 4.23–3.87 (m, 2 H), 3.06–2.81 (m, 2 H), 2.27 (s, 1 H), 1.49 (s, 9 H), 1.33 (t, $J$ = 7.1 Hz, 3 H), 0.93 (d, $J$ = 6.4 Hz, 3 H) ppm. $^{13}$C NMR (101 MHz, $CDCl_3$): $\delta$ = 157.7, 154.3, 151.6, 147.6, 147.4, 129.3, 129.1, 125.6, 124.2, 80.9, 80.4, 66.0, 65.4, 63.3, 56.9, 55.7, 54.5, 53.9, 41.5, 41.0, 40.4, 34.4, 32.0, 31.6, 30.5, 29.8, 28.6, 14.9, 14.0 ppm. IR (neat): $\tilde{\nu}$ = 2967, 2930, 2874, 1771, 1745, 1692, 1603, 1521, 1394, 1346, 1305, 1252, 1159, 1129, 1014, 853, 753, 701 cm$^{-1}$. HRMS (ESI): calcd. for $C_{13}H_{16}N_2O_5$ $[M + H - C_4H_8]^+$ 381.1292; found 381.1293.

**Compound (+)-6gB:** Elution with *n*-pentane/diethyl ether (2:1); colorless oil; yield: 88 mg (28 % with **4g**, *dr* = 68:32); isolation of major diastereomer by additional column chromatography, yield: 56 mg (18 %); $R_f$ (*n*-pentane/diethyl ether, 1:1) = 0.61; $[\alpha]_D^{25}$ = +2.5 ($c$ = 1.0, $CHCl_3$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.23–8.08 (m, 4 H), 8.01 (s, 1 H), 7.40 (d, $J$ = 8.7 Hz, 2 H), 4.71 (dd, $J$ = 10.9, 3.6 Hz, 1 H), 4.65–4.43 (m, 1 H), 4.42–4.19 (m, 1 H), 4.19–3.97 (m, 1 H), 3.07–2.72 (m, 2 H), 2.34–2.19 (m, 1 H), 1.50 (s, 9 H), 0.92 (d, $J$ = 6.4 Hz, 3 H) ppm. $^{13}$C NMR (101 MHz, $CDCl_3$): $\delta$ = 163.5, 154.5, 153.9, 147.7, 147.3, 132.8, 132.5, 132.1, 131.8, 129.6, 128.9, 126.6, 124.2, 121.5, 81.1, 80.6,

66.7, 66.1, 63.1, 58.5, 57.6, 54.6, 54.0, 42.0, 41.6, 28.6, 14.9 ppm. $^{19}F$ NMR (282 MHz, $CDCl_3$): $\delta$ = –63.59 ppm. IR (neat): $\tilde{\nu}$ = 2971, 2930, 2874, 1733, 1692, 1603, 1525, 1457, 1394, 1349, 1279, 1249, 1170, 1133, 984, 913, 846, 753 $cm^{-1}$. HRMS (ESI): calcd. for $C_{26}H_{26}F_6N_2NaO_6$ $[M + Na]^+$ 599.1587; found 599.1587.

**Compound (±)-6h:** Elution with *n*-pentane/diethyl ether (7:1 to 1:1); colorless oil; yield: 140 mg (47 % with **5h**) and 97 mg (45 % with **4h**); $R_f$ (*n*-pentane/EtOAc, 3:1) = 0.34. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 7.40–7.04 (m, 5 H), 5.39–5.13 (m, 3 H), 4.36 (dq, *J* = 15.0, 2.2 Hz, 1 H), 4.28–4.12 (m, 3 H), 3.46 (s, 1 H), 1.56–1.13 (m, 12 H) ppm. $^{13}C$ NMR (101 MHz, $CDCl_3$): $\delta$ = 171.2, 154.1, 143.1, 142.0, 128.5, 127.3, 125.7, 111.2, 79.9, 65.9, 63.9, 61.4, 58.4, 51.2, 28.3, 14.2 ppm. IR (neat): $\tilde{\nu}$ = 3064, 2978, 2933, 2870, 1733, 1696, 1454, 1390, 1320, 1252, 1159, 1111, 1033, 898, 753, 701 $cm^{-1}$. HRMS (APCI): calcd. for $C_{19}H_{26}NO_4$ $[M + H]^+$ 332.1856; found 332.1861.

**Compound 11:** Elution with hexanes/EtOAc (6:1); colorless oil; yield: 167 mg (73 % with **3a**, *dr* = 59:32:9); $R_f$ (hexanes/EtOAc, 1:1) = 0.81. $^1H$ NMR (major diastereomer, 400 MHz, $CDCl_3$): $\delta$ = 4.80 (d, *J* = 6.1 Hz, 1 H), 4.26–4.16 (m, 4 H), 4.16–4.08 (m, 1 H), 3.63 (dd, *J* = 8.3, 6.2 Hz, 1 H), 3.24 (dd, *J* = 8.3, 6.1 Hz, 1 H), 2.67 (dquint, *J* = 13.4, 6.8 Hz, 1 H), 1.32–1.23 (m, 6 H), 1.04–0.98 (m, 2 H) ppm. $^1H$ NMR (minor diastereomer 1, 400 MHz, $CDCl_3$): $\delta$ = 4.72 (d, *J* = 7.4 Hz, 1 H), 4.26–4.16 (m, 4 H), 4.16–4.08 (m, 1 H), 3.58 (t, *J* = 8.7 Hz, 1 H), 2.77 (dt, *J* = 11.1, 5.6 Hz, 1 H), 2.62–2.51 (m, 1 H), 1.32–1.23 (m, 6 H), 1.15–1.10 (m, 2 H) ppm. $^1H$ NMR (minor diastereomer 2, 400 MHz, $CDCl_3$): $\delta$ = 4.65 (d, *J* = 8.3 Hz, 1 H), 4.26–4.16 (m, 4 H), 4.16–4.08 (m, 1 H), 3.48 (t, *J* = 8.0 Hz, 1 H), 2.95 (t, *J* = 8.4 Hz, 1 H), 2.67 (dquint, *J* = 13.4, 6.8 Hz, 1 H), 1.32–1.23 (m, 6 H), 1.15–1.10 (m, 2 H) ppm. $^{13}C$ NMR (major diastereomer, 75 MHz, $CDCl_3$): $\delta$ = 172.0, 171.2, 78.7, 75.7, 61.5, 61.2, 52.3, 36.8, 14.5, 14.3, 13.4 ppm. HRMS (ESI): calcd. for $C_{11}H_{18}DO_5$ $[M + H]^+$ 232.1290; found 232.1288.

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[1] a) M. J. S. Dobner, S. S. Schwaiger, G. Altinier, R. Della Loggia, N. C. Kaneider, H. Stuppner, *Planta Med.* **2004**, *70*, 502–508; b) E. Speroni, S. Schwaiger, P. Egger, A. T. Berger, R. Cervellati, P. Govoni, M. C. Guerra, H. Stuppner, *J. Ethnopharmacol.* **2006**, *105*, 421–426.

[2] D. O'Hagan, *Nat. Prod. Rep.* **2000**, *17*, 435–446.

[3] a) R. Lin, H. Sun, C. Yang, Y. Yang, X. Zhao, W. Xia, *Beilstein J. Org. Chem.* **2015**, *11*, 31–36; b) J.-M. M. Grandjean, D. A. Nicewicz, *Angew. Chem. Int. Ed.* **2013**, *52*, 3967–3971; *Angew. Chem.* **2013**, *125*, 4059; c) D. A. Nicewicz, D. S. Hamilton, *Synlett* **2014**, *25*, 1191–1196; d) T. M. Nguyen, D. A. Nicewicz, *J. Am. Chem. Soc.* **2013**, *135*, 9588–9591.

[4] a) K. Ulbrich, P. Kreitmeier, O. Reiser, *Synlett* **2010**, 2037–2040; b) K. Ulbrich, P. Kreitmeier, T. Vilaivan, O. Reiser, *J. Org. Chem.* **2013**, *78*, 4202–4206; c) S. Kalidindi, W. B. Jeong, A. Schall, R. Bandichhor, B. Nosse, O. Reiser, *Angew. Chem. Int. Ed.* **2007**, *46*, 6361–6363; *Angew. Chem.* **2007**, *119*, 6478; d) A. Bergmann, O. Reiser, *Chem. Eur. J.* **2014**, *20*, 7613–7615; e) N. Arisetti, O. Reiser, *Org. Lett.* **2015**, *17*, 94–97.

[5] a) D. Rackl, V. Kais, P. Kreitmeier, O. Reiser, *Beilstein J. Org. Chem.* **2014**, *10*, 2157–2165; see also: b) E. Speckmeier, C. Padié, K. Zeitler, *Org. Lett.* **2015**, *17*, 4818–4821.

[6] a) J. H. P. Utley, *ARKIVOC* **2003**, *7*, 18–26; b) D. W. Sopher, J. H. P. Utley, *J. Chem. Soc., Chem. Commun.* **1981**, 134–136; c) Nazar-ul-Islam, D. W. Sopher, J. H. P. Utley, *Tetrahedron* **1987**, *43*, 959–970; d) Nazar-ul-Islam, D. W. Sopher, J. H. P. Utley, *Tetrahedron* **1987**, *43*, 2741–2748.

[7] Minor amounts of simple deoxygenated material were observed as by-product.

[8] Overman and co-workers recently demonstrated that tertiary carbon-centered radicals can be generated from hydroxy functionalities via *tert*-alkyl *N*-phthalimidoyl oxalates under visible-light irradiation and subsequently trapped by electron-deficient alkenes to construct quaternary carbon centers: G. L. Lackner, K. W. Quasdorf, L. E. Overman, *J. Am. Chem. Soc.* **2013**, *135*, 15342–15345.

[9] Sigma–Aldrich prices (August **2015**): ethyl oxalyl chloride 66 €/mol, 3,5-bis(trifluoromethyl)benzoyl chloride 2489 €/mol.

[10] J. D. Nguyen, E. M. D'Amato, J. M. R. Narayanam, C. R. J. Stephenson, *Nat. Chem.* **2012**, *4*, 854–859.

[11] M. S. Lowry, J. I. Goldsmith, J. D. Slinker, R. Rohl, R. A. Pascal, G. G. Malliaras, S. Bernhard, *Chem. Mater.* **2005**, *17*, 5712–5719.

[12] A. Juris, V. Balzani, F. Barigelletti, S. Campagna, P. Belser, A. von Zelewsky, *Coord. Chem. Rev.* **1988**, *84*, 85–277.

[13] a) J.-M. Kern, J.-P. Sauvage, *J. Chem. Soc., Chem. Commun.* **1987**, 546–548; b) M. Pirtsch, S. Paria, T. Matsuno, H. Isobe, O. Reiser, *Chem. Eur. J.* **2012**, *18*, 7336–7340; c) O. Reiser, *Acc. Chem. Res.* **2016**, *49*, 1990–1996.

[14] No simple reductive deoxygenation products were observed in the absence of sacrificial amines.

[15] For a leading review, see: Z. J. Garlets, J. D. Nguyen, C. R. J. Stephenson, *Isr. J. Chem.* **2014**, *54*, 351–360.

[16] X. W. She, X. Y. Shi, *J. Am. Chem. Soc.* **2002**, *124*, 8792–8793.

[17] J. Limberger, M. Mottin, F. F. Nachtigall, E. E. Castellano, R. G. da Rosa, *J. Mol. Catal. A* **2008**, *294*, 82–92.

[18] In the presence of sacrificial amine also a reductive quenching pathway would be conceivable.

[19] S. Nishida, Y. Harima, K. Yamashita, *Inorg. Chem.* **1989**, *28*, 4073–4077.

[20] D. C. Spellmeyer, K. N. Houk, *J. Org. Chem.* **1987**, *52*, 959–974.

[21] W. L. F. Armarego, C. L. L. Chai, in *Purification of Common Laboratory Chemicals*, 7th ed., Butterworth-Heinemann, Oxford, **2012**.

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