Highly Stereoselective and Efficient Synthesis of Functionalized Cyclohexanes with Multiple Stereocenters

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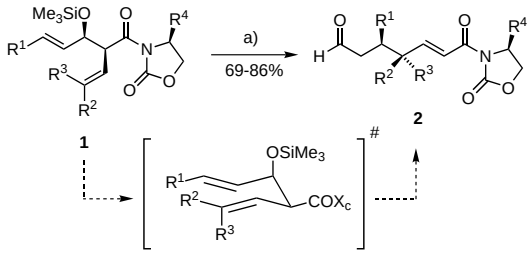
Dedicated to Professor Lutz F. Tietze on the occasion of his 60th birthday

Abstract: Chiral 7-oxo-2-enimides **2**, which were readily obtained through a silyloxy-Cope rearrangement of *syn*-aldol products **1**, have proved to be versatile substrates for a one-step, highly efficient and stereoselective synthesis of functionalized cyclohexanes. Organocopper and organoaluminum reagents have been employed as nucleophiles that underwent a conjugate addition to the enimide structure of the Cope products. The enolates formed in situ attacked the aldehyde or iminium ion in an intramolecular aldol or Mannich reaction, respectively, to directly yield cyclohexanols **3** and **4** and cyclohexylamines **5**, respectively, in moderate to good yields and with excellent stereocontrol.

Keywords: aldol reaction · asymmetric synthesis · Cope rearrangement · cyclohexanes · Mannich bases

Introduction

The thermal silyloxy-Cope rearrangement of aldol products **1** has been developed into a useful method in stereoselective synthesis (Scheme 1). Convergent and asymmetric synthesis of the substrates as well as good yields and excellent stereocontrol for the rearrangement are notable features of this process.[1]



Scheme 1. The silyloxy-Cope rearrangement of aldol products **1**. a) toluene, 180 °C, 1 – 2 h, then *p*TsOH · H_2O, rt, 15 min.

Furthermore, the Cope products **2** have proved to be versatile substrates for the straightforward synthesis of various complex organic structures, for example polyalkyl-substituted tetrahydropyrans,[2] piperidines,[3] terpenols,[4] and 1,3,5,... polyol chains[5] commonly found in the antifungal polyene macrolide antibiotics. We subsequently discovered that highly functionalized and enantiopure cyclohexanes may be obtained in one step from the Cope products using organocopper and organoaluminum reagents.[6] In this article, we detail our observations on this powerful approach towards the assembly of six-membered carbocycles with various functional groups and substituents attached to the ring.

In the synthesis of tetrahydropyrans and piperidines using the Cope products **2** as substrates, we took advantage of the ideal distance between the carbonyl group at C-7 and the conjugate double bond at C-2 of **2** to develop the following two-step sequence towards the oxygen and nitrogen-based heterocycles: 1) a chemoselective, nucleophilic addition to the aldehyde moiety, and subsequently 2) an intramolecular hetero-conjugate addition towards the conjugate double bond of **2** (Figure 1, top). The latter reaction furnished either stereoisomer at will, with high stereoselectivity depending on the carboxylic acid derivative.[2]

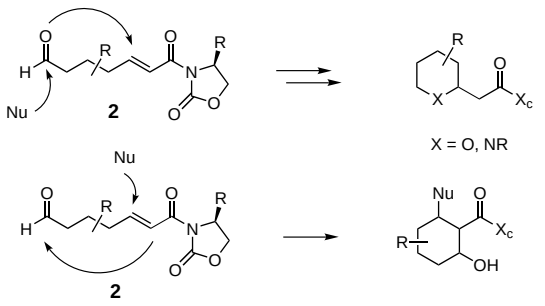


Figure 1. The two cyclization modes of the 7-oxo-2-enimides **2** to yield six-membered heterocycles (above) and carbocycles (below).

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We wondered whether we were able to reverse the order of addition and 1) add a nucleophile to the conjugate double bond of **2**, and subsequently 2) trap the resultant enolate in situ with the aldehyde moiety at C-7 to close the ring (Figure 1).

Results and Discussion

There is a significant amount of precedence in the literature for sequential Michael–aldol reactions,[7] but most of the work reported involves reactions with Michael acceptors and aldehydes in two different substrates. This scenario has the advantage that the conjugate addition step can be completed before the aldehyde, an even more reactive electrophile, is introduced into the reaction mixture. Relatively few reports, however, dealt with true domino Michael–aldol reactions in which both functional groups are in the same molecule. For example, Näf et al.[8] reported cuprate additions to ω-keto enones, and Nozaki et al.[9] introduced dialkylaluminum thiolates as powerful nucleophiles in reactions with ω-oxo enones and enoates.

Two selectivity issues were of concern to us. Firstly, we had to make sure that the nucleophile predominantly added to the conjugate double bond and left the aldehyde moiety mainly untouched. Secondly, since a new stereogenic center is generated, the stereoselectivity of the conjugate addition is crucial to the success of the whole process. In preliminary experiments, we discovered that the *tert*-leucine-derived oxazolidinone with a *t*Bu substituent served this purpose much better than the standard benzyl-substituted oxazolidinone.[10] With regard to the reagent choice, we concentrated on the use of cuprate and aluminum reagents in accordance with the results of Näf and Nozaki.

We synthesized the 7-oxo-2-enimides **2a–d** as substrates for the envisioned process in 69–86% yield as homogenous stereoisomers after chromatographic purification by using the silyloxy-Cope rearrangement of *syn*-aldols (Figure 2). Among

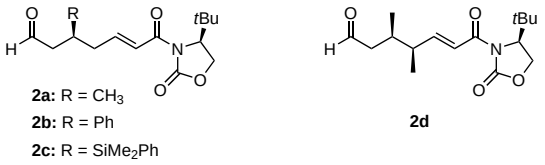
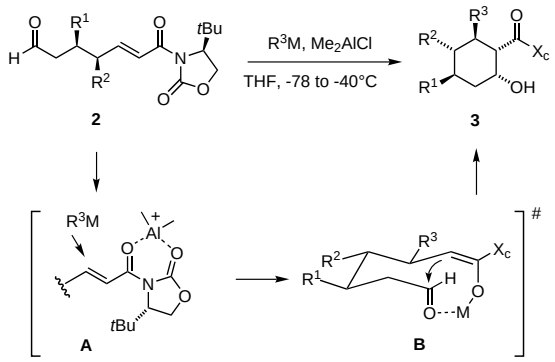


Figure 2. 7-Oxo-2-enimides **2a–d** used as substrates for the domino process.

the cuprate reagents tested in this study, the mono-organocuprates (RCu-LiI) introduced by Yamamoto et al.[11] in combination with the bidentate Lewis acid Me_2AlCl turned out to be the most satisfactory. Thus, reaction of **2a** with three equivalents of BuCu-LiI/Me_2AlCl in THF at $-78 \rightarrow -40\,^{\circ}C$ gave rise to 41% of the desired cyclohexanol **3a** as a single stereoisomer (Scheme 2 and Table 1). The principal side product (obtained in up to 20% yield) resulted from a double nucleophilic addition of the cuprate reagent to the aldehyde and the conjugate double bond. Lowering the number of equivalents of cuprate did not increase the proportion of



Scheme 2. Domino Michael–aldol reaction of 7-oxo-2-enimides **2**.

Table 1. Domino Michael–aldol reactions of 7-oxo-2-enimides **2a–d**.[a]

Entry	Substrate	Product	R^1	R^2	R^3	Yield [%]
1	**2a**	**3a**	CH_3	H	*n*Bu[b]	41
2	**2b**	**3b**	Ph	H	*n*Bu[b]	42
3	**2a**	**3c**	CH_3	H	SEt[c]	57
4	**2a**	**3d**	CH_3	H	SPh[c]	77
5	**2b**	**3e**	Ph	H	SPh[c]	65
6	**2c**	**3f**	$SiMe_2Ph$	H	SPh[c]	61
7	**2d**	**3g**	CH_3	CH_3	SPh[c]	59

[a] The stereoselectivity of the reaction was estimated to be >95:5, since no other stereoisomer was detected in the crude product by NMR. [b] A Yamamoto-type cuprate (*n*BuCu-LiI) was employed as nucleophile. [c] The Nozaki-type ate-complex (Me_3Al-SRLi) was employed as nucleophile.

cyclohexanol **3a**, and only resulted in a decrease in yield. Likewise, the cyclohexanol **3b** with a phenyl-substituent at C-5 was prepared from the 7-oxo-2-enimide **2b** in 42% yield with complete stereocontrol.

Although the yield of this domino process[12] was only moderate at best, the stereoselectivity of the overall reaction was surely remarkable considering the formation of two new σ-bonds and three new contiguous chiral centers. In accordance with our previous observations on the conjugate additions of organocuprates to enimides,[10] it is reasonable to assume that the addition took place on the Al-chelated imide complex **A** (Scheme 2); the lower face of the double bond is shielded by the bulky *t*Bu group that directs the conjugate addition towards the upper side. A directly related Al-chelate complex has been proposed by Evans et al. for the Me_2AlCl-mediated Diels–Alder reaction of unsaturated *N*-acyl oxazolidinones and was later confirmed experimentally by Castellino et al.[13] The enolate formed subsequently attacked the aldehyde in an intramolecular aldol reaction. The homogenous *syn*-stereochemistry of the aldol structure resulted from the intramolecular transposition of the metal ion from the enolate oxygen to the aldehyde oxygen in transition structure **B**, which was presumably essential for aldehyde activation (Scheme 2).

The assignment of product configuration was based on the homonuclear ^1H NMR coupling constants of the cyclohexane ring protons; the correct assignment of each signal was ascertained by $^1H-^{13}C$ two-dimensional spectra. The coupling constants J(1-H,2-H) = 2.0 Hz and J(2-H,3-H) = 11.5 Hz in compound **3b** were fully consistent with an equatorial

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position of the C-2- and C-3-substituents and the axial orientation of the C-1 OH-group (Figure 3). The coupling constants $J(4\text{-}H_{ax},5\text{-}H) = J(5\text{-}H,6\text{-}H_{ax}) = 13.0$ Hz were both indicative of the equatorial position of the C-5 phenyl group. Since we had previously proven that full chirality transfer within the sigmatropic process gives rise to a homogenous (5*S*)-configuration,[1] the deduction of the relative configuration also constituted a reliable proof of absolute configuration.

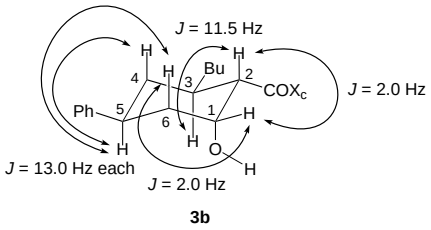


Figure 3. Assignment of product configuration for cyclohexanol **3b**.

To improve the yield of the reaction we attempted the in situ protection of the aldehyde moiety, because we suspected that competing nucleophilic addition at C-7 deteriorated the efficiency of the whole process. In this respect, various highly oxophilic organometallic reagents such as Me_2AlNR_2,[14] Me_2AlSPh,[9] and $Ti(NEt_2)_4$[15] were employed in sub-stoichiometric and stoichiometric amounts with the intention of converting the aldehyde reversibly into a N,O- or S,O-hemiacetal, thereby blocking its electrophilic nature (Figure 4). The best result was obtained in the reaction of **2a** with

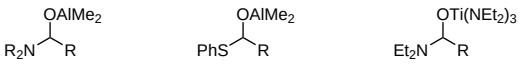
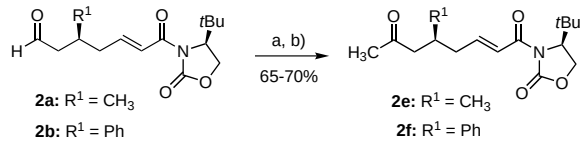


Figure 4. Attempted formation of metal-substituted N,O- and S,O-hemiacetals as in situ protecting groups for the aldehyde moiety of **2**.

0.5 equivalents of Me_2AlSPh in combination with three equivalents of BuCu-LiI/Me_2AlCl, which gave 48% yield of the desired cyclohexanol **3a** after 4 h at $-78\,^{\circ}C$. This material was, however, contaminated with small and irremovable amounts of the phenylthio-substituted cyclohexanol **3d** (see below) resulting from conjugate addition of the thiolate to the enimide. Hence, no further attempts were made in this direction.

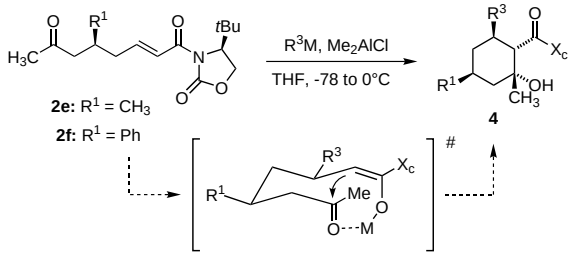
Hetero substituents were incorporated into the cyclohexanols by employing aluminum heteronucleophiles such as thiolates according to Nozaki (Scheme 2 and Table 1).[9] Initially we used dimethylaluminum thiolates prepared in situ from trimethylaluminum and a thiol, but later we discovered that the ate-complex $Me_3Al\text{-}SRLi$[9] was a superior reagent furnishing the thio-substituted cyclohexanols **3c–g** in good yields and with high stereocontrol. Considering the high oxophilicity of aluminum, it is very likely that these reagents initially added to the aldehyde to reversibly form an Al-S,O-hemiacetal that served as an in situ protecting group for the aldehyde. Yamamoto et al.[14] have previously introduced dimethylaluminum amides as in situ protecting groups for aldehydes that work by the same mechanism. Subsequently, the actual domino Michael–aldol process commenced and furnished the desired cyclohexanols.

Not unexpectedly, the Michael–aldol process proceeded in substantially higher yields when performed on the 7-keto-2-enimides **2e** and **2f** (Scheme 4 and Table 2). Here, the carbonyl activity was attenuated and hence the chemoselectivity in favor of the nucleophilic attack at the conjugate double bond was more pronounced. The ketones **2e** and **2f** were obtained in good yields from the aldehydes **2a** and **2b** through a chemoselective CH_3TiCl_3 addition,[16] and Swern oxidation[17] of the resulting secondary alcohols (Scheme 3).



Scheme 3. Synthesis of the 7-keto-2-enimides **2e**,**f**. a) CH_3TiCl_3, CH_2Cl_2, $-30\,^{\circ}C$, 45 min; b) DMSO, $(COCl)_2$, $-78\,^{\circ}C$, 30 min, then NEt_3, $-78 \rightarrow 0\,^{\circ}C$.

Various types of cuprate reagents were subsequently added to the 7-keto-2-enimides **2e** and **2f** and gave rise to the tertiary cyclohexanols **4a–g** in satisfactory to very good overall yields. Again, the stereoselectivity of the domino process was excellent furnishing the products as essentially single stereoisomers, presumably through the same kind of transition structure as discussed earlier. More importantly, Grignard reagents could be employed as cuprate precursors thus broadening the scope of the process. In these cases, the



Scheme 4. Domino Michael–aldol reactions on the 7-keto-2-enimides **2e**,**f**.

Table 2. Domino Michael–aldol reactions of 7-keto-2-enimides **2e–f**.[a]

Entry	Substrate	Product	R^1	R^3	M[b]	Yield [%]
1	**2e**	**4a**	CH_3	CH_3	Cu-LiI	54
2	**2e**	**4b**	CH_3	Et	Cu-$MgBr_2$	71
3	**2e**	**4c**	CH_3	*n*Bu	Cu-LiI	83
4	**2e**	**4d**	CH_3	*n*Hex	Cu-LiI	62
5	**2e**	**4e**	CH_3	allyl	Cu-$MgBr_2$	81
6	**2e**	**4f**	CH_3	Ph	Cu-$MgBr_2$	53
7	**2f**	**4g**	Ph	*n*Bu	Cu-LiI	51
8	**2e**	**4h**	CH_3	SPh	Me_3Al-Li	76
9	**2f**	**4i**	Ph	SPh	Me_3Al-Li	60
10	**2e**	**4k**	CH_3	N_3	Me_2Al	59
11	**2e**	**4l**	CH_3	NC_5H_{10}	Me_2Al	40

[a] The stereoselectivity of the reaction was estimated to be >95:5, since no other stereoisomer was detected in the crude product by NMR. [b] In the case of the Grignard-derived cuprates and the aluminum reagents, the external Lewis acid Me_2AlCl was omitted.

external Lewis acid (Me_2AlCl) could be omitted without a decrease in yield or selectivity. We assume that $MgBr_2$, formed in situ from the Grignard reagent and $CuBr \cdot SMe_2$, was able to act as a bidentate Lewis acid with formation of a chelated-imide complex like the one formed with Me_2AlCl.[18]

The addition of sulfur and nitrogen nucleophiles was again accomplished in moderate to good yields using aluminum thiolates, azides, and amides which gave rise to the cyclohexanols **4h–l**. It should be noted at this point that dimethylaluminum piperidide cleanly furnished the tertiary cyclohexanol **4l** in moderate yield (see below).

The assignment of product configuration for the tertiary cyclohexanols **4** was complicated by the fact that the proton at C-3 was lacking and is described here explicitly for **4i** (Figure 5). The configuration at C-1, C-2, and C-5 was again ascertained by the large *trans*-diaxial coupling constants J(1-H,2-H), J(4-H_{ax},5-H), and J(5-H,6-H_{ax}) which were each 12.5 Hz indicating the equatorial position of the C-1-, C-2-, and C-5-substituents. The configuration at C-3 was proven by a NOESY spectrum that revealed strong NOE effects between the axial protons at C-1, C-5, and the OH proton, which was consistent with the axial orientation of the C-3 OH group. In addition, a characteristic W coupling of $J = 2.5$ Hz between the OH proton and the axial proton at C-4 was observed, which could only occur in the case of an axial orientation of the hydroxyl group.

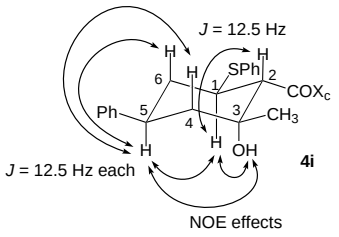
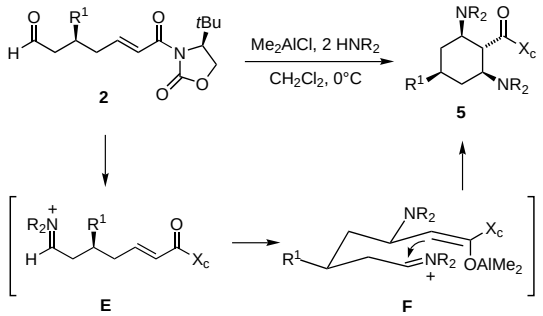


Figure 5. Assignment of the product configuration for the cyclohexanol **4i**.

When we attempted the synthesis of amino-substituted cyclohexanols from the 7-oxo-2-enimides **2a–c** in close analogy to the Nozaki protocol, we surprisingly isolated the cyclohexyldiamines **5a–g** in satisfactory yields instead (Scheme 5 and Table 3). Here, a nucleophilic addition of Me_2AlNR_2 or the free amine to the aldehyde moiety of **2** preceded the conjugate addition, presumably forming either an Al-N,O-hemiacetal[14] or the enamine. Either one may then



Scheme 5. Domino Michael–Mannich reactions on the 7-oxo-2-enimides **2**.

Table 3. Domino Michael–Mannich reactions of the 7-oxo-2-enimides **2a–c**.[a]

Entry	Substrate	Product	R^1	Amine	Yield [%]
1	**2a**	**5a**	CH_3	morpholine	69
2	**2a**	**5b**	CH_3	Et_2NH	46
3	**2a**	**5c**	CH_3	Bn_2NH	70
4	**2a**	**5d**	CH_3	Bu_2NH	65
5	**2b**	**5e**	Ph	piperidine	57
6	**2c**	**5f**	$SiMe_2Ph$	piperidine	59
7	**2c**	**5g**	$SiMe_2Ph$	morpholine	53

[a] The stereoselectivity of the reaction was estimated to be >95:5, since no other stereoisomer was detected in the crude product by NMR.

produce the iminium ion **E** that is then attacked by the enolate, formed by the conjugate addition of a second amine equivalent, in an intramolecular Mannich reaction.[19]

The *anti*-stereochemistry found in the Mannich products **5** was indicative of the proposed reaction path. Owing to a lack of vacant coordination sites at the iminium nitrogen, an intramolecular transposition of the metal cation was not possible here. Hence, the large iminium group assumed the sterically more favorable *pro*-equatorial position in transition structure **F** giving rise to the *anti*-stereochemistry between the COX_c- and NR_2-groups. The observed Michael–Mannich reaction pathway nicely supports the assumption that the Nozaki reagents Me_3Al-SRLi formed in fact in situ protecting groups for the aldehyde moiety (Al-*S*,*O*-hemiacetals). This behavior may also explain the exceptionally good yields when the aldehydes **2a**,**b** were treated with Me_3Al-SRLi (Table 1, entries 3–7).

The configuration of the Mannich products **5** was again assigned on the basis of the large *trans*-diaxial coupling constants between the respective ring protons (Figure 6). Here, all substituents adopted equatorial positions according to J(1-H,2-H), J(2-H,3-H), J(4-H_{ax},5-H), and J(5-H,6-H_{ax}) which were in the range of 10.5–12.0 Hz.

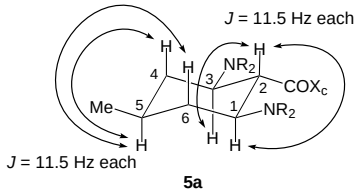


Figure 6. Assignment of the product configuration for the cyclohexylamine **5a**.

The domino Michael–Mannich reaction may be performed in two ways: 1) with preformed Me_2AlNR_2 (from Me_3Al and HNR_2), or 2) with a mixture of Me_2AlCl and the secondary amine. Both procedures furnished the desired products, the latter reaction, however, proceeded much faster giving rise to the product within 1–2 h at 0 °C in yields given in the table, whereas the former reaction required 24 h at room temperature and gave the products in lower yields. This result points to the Me_2AlCl/amine mixture being the more powerful reagent.

This observation also suggested that an enamine formed separately through reaction of **2** with a secondary amine

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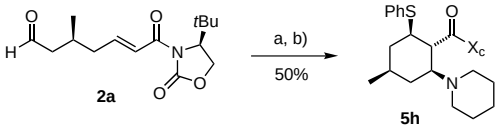
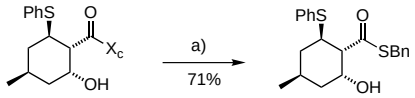
should be a good substrate for the same sequence, thereby offering the possibility of introducing two different substituents into the cyclohexane ring. Accordingly, reaction of **2a** with piperidine and $MgSO_4$ in toluene at 0 °C cleanly furnished the enamine which was then subjected to Nozaki's ate-complex (Me_3Al-SPhLi) to give rise to the phenylthio-substituted cyclohexylamine **5h** in 50% overall yield as a single stereoisomer (Scheme 6).



Scheme 6. Synthesis of phenylthio-substituted cyclohexylamine **5h**. a) Piperidine, $MgSO_4$, CH_2Cl_2; b) Me_3Al-SPhLi, THF, $-78\,^{\circ}C \rightarrow$ rt.

Finally, cleavage of the auxiliary was addressed. After some experimentation we found the Damon reagent, lithium benzylthiolate,[20] most suitable for this purpose. Thus, cyclohexanol **3d** was treated with lithium benzylthiolate in THF at room temperature for 15 h to furnish thioester **6** in 71% yield (Scheme 7).



Scheme 7. Cleavage of the chiral auxiliary. a) $LiSCH_2Ph$, THF, rt.

Conclusion

A highly stereoselective and efficient process has been developed for the de novo synthesis of enantiopure and multiply substituted cyclohexanols and cyclohexylamines. Acyclic 7-oxo-2-enimides **2**, readily obtained through the silyloxy-Cope rearrangement of aldol products **1**, were treated with carbon and heteronucleophiles in a domino Michael–aldol reaction and gave rise to highly substituted cyclohexanols **3** and **4**. This process resulted in the stereoselective formation of two new single bonds and three new stereogenic centers and eventually in the ring-closure. With secondary amines as nucleophiles, an iminium formation preceded the conjugate addition and gave rise to a domino Michael–Mannich reaction and the synthesis of highly substituted cyclohexylamines **5**. Based upon these results, the synthetic value of the bifunctional 7-oxo-2-enimides **2** for stereoselective synthesis has been once again demonstrated.

Experimental Section

General: Air and/or moisture sensitive reactions were carried out under N_2 using flame-dried glassware and standard syringe/septa techniques. Solvents were distilled directly prior to use from the appropriate drying agents: THF ($LiAlH_4$), CH_2Cl_2 and NEt_3 (CaH_2), Et_2O and toluene (Na). All reactions were monitored by thin-layer chromatography (TLC) carried out on pre-coated silica gel SIL G/UV_{254} plastic plates (Machery & Nagel) and visualized with UV light and 1% aqueous $KMnO_4$. Commercial reagents were used directly as received, unless otherwise stated. Products were purified by flash chromatography on Machery & Nagel silica gel 32–63 (particle size 0.032–0.063 mm). ^1H and ^{13}C NMR spectra were recorded on a Varian VXR 200 (200 MHz), Bruker AMX 300, (300 MHz) and Varian VXR 500 (500 MHz) in $CDCl_3$ at 25 °C with TMS as internal standard. IR spectra of evaporated films were recorded on a Bruker IFS 25 FT-IR instrument, and UV spectra on a Perkin–Elmer Lambda 9 spectrometer. Optical rotations were measured on a Perkin–Elmer 241 polarimeter. Mass spectra were taken at 70 eV (EI) or 200 eV (DCI/NH_3) on a Finnigan MAT 95A spectrometer. Microanalyses were performed by the microanalytical laboratory at the Institut für Organische Chemie der Universität Göttingen.

7-Oxo-2-enimide 2a: The Cope product **2a** was prepared from the corresponding silylated aldol adduct as published.[1b] Yield: 81%. $[\alpha]_D^{20} = +57.0$ ($c = 0.51$ in $CHCl_3$); IR (film): $\tilde{\nu} = 2988, 2934, 2884$ (CH), 1780 (imide), 1722 (aldehyde), 1688 (imide), 1638 cm^{-1} (C=C); ^1H NMR (200 MHz, $CDCl_3$): $\delta = 0.94$ (s, 9H; *t*Bu), 1.02 (d, $J = 6.5$ Hz, 3H; CH_3), 2.15–2.45 (m, 5H; 4′-H_2, 5-H, 6′-H_2), 4.17–4.32 (m, 2H; 5-H_2), 4.51 (dd, $J = 6.5$, 2.0 Hz, 1H; 4-H), 7.05 (dt, $J = 15.5$, 7.0 Hz, 1H; 3′-H), 7.28 (d, $J = 15.5$ Hz, 1H; 2′-H), 9.64 (t, $J = 1.0$ Hz, 1H; 7′-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 20.0$ (CH_3), 25.6 (*t*Bu), 27.5 (C-5′), 35.85 (*t*Bu), 39.5, 50.2 (C-4′, C-6′), 60.79 (C-4), 65.19 (C-5), 122.4 (C-2′), 148.3 (C-3′), 154.6 (C-2), 164.9 (C-1′), 201.7 (C-7′); MS (200 eV, DCI/NH_3): *m*/*z* (%): 299 (100) [M^++NH_4]; elemental analysis calcd (%) for $C_{15}H_{23}NO_4$ (281.35): C 64.06, H 8.19; found: C 64.35, H 8.19.

7-Oxo-2-enimide 2b: The Cope product **2b** was prepared from the corresponding silylated aldol adduct as published.[1b] Yield: 69%. M.p. 95 °C; $[\alpha]_D^{20} = +36.4$ ($c = 1.0$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 2972$ (CH), 1764 (imide), 1716 (aldehyde), 1684 (imide), 1632 cm^{-1} (C=C); ^1H NMR (200 MHz, $CDCl_3$): $\delta = 0.90$ (s, 9H; *t*Bu), 2.63 (td, $J = 7.0$, 1.0 Hz, 2H; 4′-H_2), 2.80 (dd, $J = 7.0$, 1.5 Hz, 2H; 6′-H_2), 3.41 (pent, $J = 7.0$ Hz, 1H; 5′-H), 4.22 (dd, $J = 9.0$, 7.0 Hz, 1H; 5-H), 4.29 (dd, $J = 9.0$, 2.5 Hz, 1H; 5-H), 4.47 (dd, $J = 7.0$, 2.5 Hz, 1H; 4-H), 6.95 (dt, $J = 15.5$, 7.0 Hz, 1H; 3′-H), 7.15–7.37 (m, 6H, 2′-H, phenyl-H), 9.66 (t, $J = 1.5$ Hz, 1H; 7′-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 25.6$ (*t*Bu), 35.9 (*t*Bu), 39.05 (C-5′), 39.5, 49.4 (C-4′, C-6′), 60.8 (C-4), 65.2 (C-5), 122.6 (C-2′), 127.0, 127.3, 128.8, 142.4 (phenyl-C), 147.7 (C-3′), 154.6 (C-2), 164.9 (C-1′), 200.9 (C-7′); MS (70 eV, EI): *m*/*z* (%): 343 (100) [M^+], 299 (12), 211 (71) [crotonoylimide$^+$], 182 (33), 157 (44), 144 (60) [oxazolidinone$^+$+2H], 105 (100); elemental analysis calcd (%) for $C_{20}H_{25}NO_4$ (343.42): C 69.95, H 7.34; found: C 69.87, H 7.43.

7-Oxo-2-enimide 2c: The Cope product **2c** was prepared from the corresponding silylated aldol adduct as published.[1b] Yield: 72%. $[\alpha]_D^{20} = +34.0$ ($c = 0.5$ in $CHCl_3$); IR (film): $\tilde{\nu} = 2966, 2874, 2726$ (CH), 1782 (C=O), 1684 (C=O), 1634 cm^{-1} (C=C); ^1H NMR (200 MHz, $CDCl_3$): $\delta = 0.33$ (s, 6H; $SiMe_2$), 0.92 (s, 9H; *t*Bu), 1.72 (m, 1H; 5′-H), 2.07–2.55 (m, 4H; 4′-H_2, 6′-H_2), 4.23 (dd, $J = 9.0$, 6.5 Hz, 1H; 5-H), 4.29 (dd, $J = 9.0$, 2.5 Hz, 1H; 5-H), 4.49 (dd, $J = 6.5$, 2.5 Hz, 1H; 4-H), 6.95 (ddd, $J = 14.5$, 8.5, 6.0 Hz, 1H; 3′-H), 7.15 (d, $J = 14.5$ Hz, 1H; 2′-H), 7.30–7.54 (m, 5H; phenyl-H), 9.64 (t, $J = 1.5$ Hz, 1H; 7′-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = -4.7, -4.6$ ($SiMe_2$), 18.5 (C-5′), 25.3 ($C(CH_3)_3$), 33.1, 43.5 (C-4′, C-6′), 35.5 ($C(CH_3)_3$), 60.4 (C-4), 64.9 (C-5), 121.5 (C-2′), 127.7, 129.1, 133.6, 136.3 (phenyl-C), 149.8 (C-3′), 154.3 (C-2), 164.5 (C-1′), 201.6 (C-7′); MS (70eV, EI): *m*/*z* (%): 401 (11) [M^+], 386 (18) [$M^+ - CH_3$], 345 (14) [$M^+ - t$Bu], 324 (21), 278 (100), 191 (19) [retro-aldol-cleavage, aldehyde$^+$], 135 (71) [$PhMe_2Si^+$], 57 (8) [*t*Bu$^+$]; elemental analysis calcd (%) for $C_{22}H_{31}NO_4Si$ (401.58): C 65.80, H 7.78; found: C 65.92, H 8.05.

7-Oxo-2-enimide 2d: The Cope product **2d** was prepared from the corresponding silylated aldol adduct as published.[1b] Yield: 86%. M.p. 70 °C; $[\alpha]_D^{20} = +93.0$ ($c = 1.0$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 2966, 2883$ (CH), 1783 (imide), 1716 (C=O, aldehyde), 1680 (imide), 1632 cm^{-1} (C=C); ^1H NMR (200 MHz, $CDCl_3$): $\delta = 0.95$ (s, 9H; *t*Bu), 0.97, 1.04 (2d, $J = 6.5$ Hz, 6H; $2CH_3$), 2.10–2.58 (m, 4H; 4′-H, 5′-H, 6′-H_2), 4.25 (dd, $J = 9.0$, 2.5 Hz, 1H; 5-H), 4.31 (dd, $J = 9.0$, 2.5 Hz, 1H; 5-H), 4.52 (dd, $J = 7.0$, 2.5 Hz, 1H; 4-H), 6.99 (dd, $J = 15.5$, 8.5 Hz, 1H; 3′-H), 7.25 (dd, $J = 15.5$, 1.0 Hz, 1H; 2′-H), 9.74 (t, $J = 1.5$ Hz, 1H; 7′-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 15.9, 17.1$ ($2CH_3$), 25.6 (*t*Bu), 32.35 (C-5′), 35.9 (*t*Bu), 41.75 (C-4′), 48.45 (C-6′), 60.9 (C-4), 65.2 (C-5), 120.6 (C-2′), 153.9 (C-3′), 154.7 (C-2), 165.2 (C-1′), 202.0 (C-7′); MS (70 eV, EI): *m*/*z* (%): 295 (9) [M^+], 252 (31), 225 (48), 153 (94) [M^+ – oxazolidinone], 144 (77)

[oxazolidinone$^+$+2H], 109 (85), 82 (100); elemental analysis calcd (%) for $C_{16}H_{25}NO_4$ (295.37): C 65.06, H 8.53; found: C 65.32, H 8.31.

7-Keto-2-enimide 2e: A solution of CH_3TiCl_3 in CH_2Cl_2 was prepared in situ from a 5% solution of methyllithium in diethyl ether (4.49 mL, 7.18 mmol) and a 1M solution of $TiCl_4$ in CH_2Cl_2 (7.18 mL, 7.18 mmol) at $-30\,^\circ C$. Subsequently, the 7-oxo-2-enimide **2a** (1.01 g, 3.59 mmol) was added to this solution at $-45\,^\circ C$ and the reaction mixture was stirred at this temperature for another 30 min. The reaction was stopped by the addition of pH 7 buffer, the phases were separated, and the aqueous layer was extracted twice with diethyl ether. The combined organic extracts were dried over $MgSO_4$, filtered, and evaporated. The crude product was directly subjected to a Swern oxidation: Oxalylchloride (3.09 mL, 3.60 mmol) was dissolved in CH_2Cl_2 (50 mL) and treated with DMSO (5.54 mL, 7.80 mmol) at $-78\,^\circ C$. After 30 min of stirring, the crude alcohol was added, and the solution was stirred for an additional 30 min at $-78\,^\circ C$. Subsequently, triethylamine (2.09 mL, 15.0 mmol) was added at $-78\,^\circ C$, and the reaction mixture was warmed to RT whereupon water was added. The layers were separated, the aqueous phase was extracted twice with diethyl ether and the combined organic extracts were dried over $MgSO_4$. After filtration and evaporation of the solvent, the crude product was purified by flash chromatography over silica gel (diethyl ether/pentane 1:1) to give the methylketone **2e** (690 mg, 65% yield over 2 steps) as a viscous oil. $[\alpha]_D^{20} = +66.6$ ($c = 0.5$ in $CHCl_3$); IR (film): $\tilde{\nu} = 2965$ (CH), 1778, 1689 (imide), 1636 cm^{-1} (C=C); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.95-0.96$ (m, 12H; *t*Bu, CH_3), 2.13 (s, 3H; CH_3), 2.14–2.55 (m, 5H; 4′-H_2, 5′-H, 6′-H_2), 4.24 (dd, $J = 9.0$, 7.0 Hz, 1H; 5-H), 4.30 (dd, $J = 9.0$, 2.0 Hz, 1H; 5-H), 4.52 (dd, $J = 7.0$, 2.0 Hz, 1H; 4-H), 6.98–7.32 (m, 2H; 2′-H, 3′-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 19.9$ (5′-CH_3), 25.6 (*t*Bu), 28.5, 30.5 (C-8′, C-5′), 35.9 (*t*Bu), 39.6, 50.0 (C-4′, C-6′), 60.8 (C-4), 65.2 (C-5), 122.2 (C-2′), 149.0 (C-3′), 154.6 (C-2), 165.1 (C-1′), 208.0 (C-7′); MS (70 eV, EI): *m*/*z* (%): 295 (16) [M^+], 238 (74), 211(24) [crotonoylimide$^+$], 153 (34) [M^+ – oxazolidinone], 95 (100); elemental analysis calcd (%) for $C_{16}H_{25}NO_4$ (295.37): C 65.06, H 8.53; found: C 65.24, H 8.56.

7-Keto-2-enimide 2f: 7-Oxo-2-enimide **2b** (1.28 g, 3.71 mmol) was converted into the title compound **2f** as described above. Yield: 70% (over 2 steps). $[\alpha]_D^{20} = +46.0$ ($c = 0.5$ in $CHCl_3$); IR (film): $\tilde{\nu} = 2967$ (CH), 1777, 1688 (imide), 1632 cm^{-1} (C=C); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.90$ (s, 9H; *t*Bu), 2.03 (s, 3H; 8′-H_3), 2.50–2.67 (m, 2H; 4′-H_2), 2.70–2.86 (m, 2H; 6′-H_2), 3.36 (pent, $J = 7.0$ Hz, 1H; 5′-H), 4.22 (dd, $J = 9.0$, 7.0 Hz, 1H; 5-H), 4.28 (dd, $J = 9.0$, 2.0 Hz, 1H; 5-H), 4.47 (dd, $J = 7.0$, 2.0 Hz, 1H; 4-H), 6.95 (dt, $J = 15.0$, 7.0 Hz, 1H; 3′-H), 7.15–7.35 (m, 6H; 2′-H, phenyl-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 25.6$ (*t*Bu), 30.6 (C-8′), 35.8 (*t*Bu), 39.4 (C-4′), 40.0 (C-5′), 49.4 (C-6′), 60.8 (C-4), 65.2 (C-5), 122.3 (C-2′), 126.7, 127.4, 128.6, 143.2 (phenyl-C), 148.3 (C-3′), 154.6 (C-2), 164.9 (C-1′), 207.0 (C-7′); MS (70 eV, EI): *m*/*z* (%): 357 (17) [M^+], 300 (39), 211 (100) [crotonoylimide$^+$], 157 (85), 144 (61) [oxazolidinone$^+$+2H], 105 (27); elemental analysis calcd (%) for $C_{21}H_{27}NO_4$ (357.44): C 70.56, H 7.61; found: C 70.26, H 7.37.

Cyclohexanol 3a: CuI (125 mg, 0.66 mmol) was suspended in dry THF (3 mL), and butyllithium (2.5M in hexane, 0.26 mL, 0.66 mmol) was added at $-30\,^\circ C$ whereupon the mixture immediately turned black. After 20 min, the solution was cooled to $-78\,^\circ C$, and a 1M solution of Me_2AlCl in hexane (0.66 mL, 0.66 mmol) and then **2a** (62 mg, 0.22 mmol) dissolved in THF (1 mL) were added. The solution was allowed to warm to $-40\,^\circ C$ over 3 h. At that temperature, saturated NH_4Cl solution was added, the layers were separated, and the aqueous phase was extracted twice with diethyl ether. The combined organic extracts were dried over $MgSO_4$, filtered, and evaporated. The crude product was purified by flash chromatography over silica gel (diethyl ether/pentane 1:1) to give cyclohexanol **3a** (30 mg, 41%) as a colorless oil. $[\alpha]_D^{20} = +6.6$ ($c = 1.67$ in $CHCl_3$); IR (film): $\tilde{\nu} = 3515$ (OH), 2927 (CH_3), 1779, 1704 (imide), 1183, 1101, 1058 cm^{-1} (C–O); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.73$ (q, $J = 12.5$ Hz, 1H; 4′-H), 0.80–0.95 (m, 6H; 2CH_3), 0.97 (s, 9H; *t*Bu), 0.98–1.41 (m, 7H; 4′-H, 6′-H_2, 2″-H_2, 3″-H_2), 1.80–2.20 (m, 4H; 3′-H, 5′-H, 1″-H_2), 3.05 (s, 1H; OH), 3.79 (dd, $J = 11.5$, 2.0 Hz, 1H; 2′-H), 4.00 (br s, 1H, 1′-H), 4.20 (dd, $J = 9.0$, 7.0 Hz, 1H; 5-H), 4.27 (dd, $J = 9.0$, 2.0 Hz, 1H; 5-H), 4.46 (dd, $J = 7.0$, 2.0 Hz, 1H; 4-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 14.0$ (CH_3), 22.1 (CH_3), 22.9 (butyl side chain), 25.2 (C-5′), 25.8 (*t*Bu), 28.4, 33.7 (butyl side chain), 33.85 (C-3′), 35.9 (*t*Bu), 40.0, 40.3 (C-4′, C-6′), 49.6 (C-2′), 61.5 (C-4), 65.1 (C-5), 67.3 (C-1′), 154.4 (C-2), 176.7 (C=O); MS (200 eV, DCI/NH_3): *m*/*z* (%): 357 (100) [M^++NH_4], 340 (42) [M^++H], 161 (70); elemental analysis calcd (%) for $C_{19}H_{33}NO_4$ (339.47): C 67.22, H 9.80; found: C 66.97, H 9.80.

Cyclohexanol 3b: 7-Oxo-2-enimide **2b** (200 mg, 0.58 mmol) was dissolved in THF (5 mL), and CuI (333 mg, 1.75 mmol), butyllithium (2.5M in hexane, 0.70 mL, 1.75 mmol), and a 1M solution of Me_2AlCl in hexane (1.75 mL, 1.75 mmol) were added as described above. Flash chromatography over silica gel (diethyl ether/pentane 1:1) gave **3b** (98 mg, 42%) as a white solid. M.p. 133 °C; $[\alpha]_D^{20} = +8.2$ ($c = 1.0$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 3549$ (OH), 2933 (CH_3), 1775, 1701 (imide), 1216, 1187, 1100 cm^{-1} (C–O); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.85$ (t, $J = 7.0$ Hz, 1H; CH_3), 0.98 (s, 9H; *t*Bu), 1.18–1.44 (m, 7H), 1.65 (td, $J = 13.0$, 2.0 Hz, 1H; 6′-H), 2.05–2.12 (m, 2H; 4′-H, 6′-H), 2.27–2.36 (m, 1H; 3′-H), 3.16 (tt, $J = 13.0$, 3.5 Hz, 1H; 5′-H), 3.30 (s, 1H; OH), 4.00 (dd, $J = 11.5$, 2.0 Hz, 1H; 2′-H), 4.17 (m, 1H; 1′-H), 4.26 (dd, $J = 9.0$, 7.5 Hz, 1H; 5-H), 4.32 (dd, $J = 9.0$, 1.5 Hz, 1H; 5-H), 4.52 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H), 7.15–7.33 (m, 5H; phenyl-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 14.0$ (CH_3), 22.9, 28.4, 33.7 (butyl side chain), 25.9 (*t*Bu), 34.4 (C-3′), 35.85 (*t*Bu), 36.7 (C-5′), 38.6, 39.2 (C-4′, C-6′), 49.4 (C-2′), 61.6 (C-4), 65.2 (C-5), 67.25 (C-1′), 126.2, 127.0, 128.4, 146.3 (phenyl-C), 154.4 (C-2), 176.8 (C=O); MS (70 eV, EI): *m*/*z* (%): 401 (17) [M^+], 383 (59), 240 (100), 212 (75); HRMS: *m*/*z* calcd for $C_{24}H_{35}NO_4$: 410.2566; found: 401.2566.

Cyclohexanol 3c: Thioethanol (13 μL, 0.17 mmol) was dissolved in THF (2 mL), and butyllithium (2.5M in hexane, 67 μL, 0.17 mmol) was added at 0 °C. After for 5 min, Me_3Al (2M in hexane, 84 μL, 0.17 mmol) was added to the reaction mixture at 0 °C. After stirring for 1 h at 0 °C, the solution was cooled to $-78\,^\circ C$, and 7-oxo-2-enimide **2a** (43 mg, 0.15 mmol) in THF (1 mL) was added. After stirring the solution for 1 h at $-78\,^\circ C$, the reaction was quenched with water, and the layers were separated. The aqueous phase was extracted twice with diethyl ether and the combined organic extracts were dried over $MgSO_4$. After filtration and evaporation of the solvents, the crude product was purified by flash chromatography over silica gel (diethyl ether/pentane 1:1) to give **3c** (30 mg, 57%) as a colorless oil. $[\alpha]_D^{20} = -16.0$ ($c = 0.35$ in $CHCl_3$); IR (film): $\tilde{\nu} = 3477$ (OH), 2960 (CH_3), 1778, 1705 (imide), 1187, 1119, 1100 cm^{-1} (C–O); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.85-1.40$ (m, 2H; 4′-H, 6′-H), 0.87 (d, $J = 6.0$ Hz, 3H; CH_3), 1.00 (s, 9H; *t*Bu), 1.19 (t, $J = 7.5$ Hz, 3H; CH_3), 1.80–2.20 (m, 3H; 4′-H, 5′-H, 6′-H), 2.59 (m, 2H; 1″-H_2), 3.18 (td, $J = 12.0$, 4.0 Hz, 1H; 1′-H), 3.25 (s, 1H; OH), 4.05–4.39 (m, 2H; 2′-H, 3′-H), 4.23 (dd, $J = 9.0$, 7.0 Hz, 1H; 5-H), 4.31 (dd, $J = 9.0$, 2.0 Hz, 1H; 5-H), 4.49 (dd, $J = 7.0$, 2.0 Hz, 1H; 4-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.8$ (C-2″), 21.9 (C-1″), 24.5 (C-1′), 25.8 (*t*Bu), 26.1 (C-5′), 36.2 (*t*Bu), 39.4, 42.9 (C-4′, C-6′), 40.5 (C-1′), 49.3 (C-2′), 61.5 (C-4), 65.1 (C-5), 67.5 (C-3′), 154.3 (C-2), 175.5 (C=O, amide); MS (70 eV, EI): *m*/*z* (%): 343 (30) [M^+], 264 (34), 182 (90), 144 (100) [oxazolidinone$^+$+2H]; HRMS: *m*/*z*: calcd for $C_{17}H_{29}NO_4S$: 343.1817; found: 343.1817.

Cyclohexanol 3d: 7-Oxo-2-enimide **2a** (49 mg, 0.17 mmol) was dissolved in THF (3 mL), and thiophenol (20 μL, 0.19 mmol), butyllithium (2.5M in hexane, 77 μL, 0.19 mmol), and Me_3Al (2M in hexane, 96 μL, 0.19 mmol) were added as described above. Flash chromatography over silica gel (diethyl ether/pentane 1:1) gave **3d** (51 mg, 77%) as a colorless oil. $[\alpha]_D^{20} = +3.3$ ($c = 1.21$ in $CHCl_3$); IR (film): $\tilde{\nu} = 3471$ (OH), 2960 (CH_3), 1779, 1705 (imide), 1187, 1118, 1057 cm^{-1} (C–O); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.85$ (d, $J = 6.5$ Hz, 3H; 5′-CH_3), 1.02 (s, 9H; *t*Bu), 1.08 (ddd, $J = 13.5$, 12.0, 2.0 Hz, 1H; 4′-H), 1.18 (dt, $J = 13.5$, 12.0 Hz, 1H; 6′-H), 1.85 (dtd, $J = 13.5$, 3.5, 2.0 Hz, 1H; 4′-H), 1.90–2.02 (m, 1H; 5′-H), 2.07 (dtd, $J = 13.5$, 3.5, 2.0 Hz, 1H; 6′-H), 3.22 (br s, 1H; OH), 3.61 (td, $J = 12.0$, 3.5 Hz, 1H; 1′-H), 4.13 (br s, 1H; 3′-H), 4.22 (dd, $J = 12.0$, 2.0 Hz, 1H; 2′-H), 4.26 (dd, $J = 9.0$, 7.5 Hz, 1H; 5-H), 4.32 (dd, $J = 9.0$, 1.5 Hz, 1H; 5-H), 4.52 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H), 7.22–7.45 (m, 5H; phenyl-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 21.5$ (C-1″), 25.8 (C-5′), 25.8 (*t*Bu), 36.2 (*t*Bu), 39.4, 42.6 (C-4′, C-6′), 45.0 (C-1′), 48.9 (C-2′), 61.6 (C-4), 65.2 (C-5), 67.6 (C-3′), 127.4, 128.8, 132.9, 134.0 (phenyl-C), 154.3 (C-2), 175.3 (C=O); MS (70 eV, EI): *m*/*z* (%): 391 (95) [M^+], 264 (77), 230 (80), 144 (70) [oxazolidinone$^+$+2H], 121 (100); elemental analysis calcd (%) for $C_{21}H_{29}NO_4S$ (391.53): C 64.42, H 7.47; found: C 64.65, H 7.76.

Cyclohexanol 3e: 7-Oxo-2-enimide **2b** (107 mg, 0.31 mmol) was dissolved in THF (5 mL), and thiophenol (33 μL, 0.33 mmol), butyllithium (2.5M in hexane, 131 μL, 0.33 mmol), and Me_3Al (2M in hexane, 164 μL, 0.33 mmol) were added as described above. Flash chromatography over silica gel (diethyl ether/pentane 1:1) gave **3e** (92 mg, 65%) as a white solid. M.p. 172 °C; $[\alpha]_D^{20} = -48.7$ ($c = 1.0$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 3420$ (OH), 2943

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(CH_3), 1775, 1699 (imide), 1217, 1196, 1112 cm^{-1} (C–O); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.06$ (s, 9H; *t*Bu), 1.65 (td, $J = 13.0$, 2.0 Hz, 1H; 4′-H), 1.77 (q, $J = 13.0$ Hz, 1H; 6′-H), 2.08 (dtd, $J = 13.0$, 4.0, 1.5 Hz, 1H; 4′-H), 2.30 (dtd, $J = 13.0$, 4.0, 1.5 Hz, 1H; 6′-H), 3.16 (tt, $J = 13.0$, 4.0 Hz, 1H; 5′-H), 3.76 (td, $J = 12.0$, 4.0 Hz, 1H; 1′-H), 4.25–4.36 (m, 1H; 3′-H), 4.30 (dd, $J = 9.0$, 7.5 Hz, 1H; 5-H), 4.36 (dd, $J = 9.0$, 1.5 Hz, 1H; 5-H), 4.40 (dd, $J = 12.0$, 2.0 Hz, 1H; 2′-H), 4.57 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H), 7.10–7.48 (m, 10H; phenyl-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 25.9$ (*t*Bu), 36.3 (*t*Bu), 37.0 (C-5′), 38.6, 41.5 (C-4′, C-6′), 45.6 (C-1′), 48.6 (C-2′), 61.7 (C-4), 65.3 (C-5), 67.5 (C-3′), 126.4, 127.0, 127.6, 128.5, 129.0, 133.1, 133.8, 145.0 (phenyl-C), 154.4 (C-2), 175.4 (C=O); MS (70 eV, EI): *m*/*z* (%): 453 (76) [M^+], 326 (43), 292 (47), 183 (100), 144 (63) [oxazolidinone$^+$+2H]; elemental analysis calcd (%) for $C_{26}H_{31}NO_4S$ (453.59): C 68.85, H 6.89; found: C 69.10, H 7.06.

Cyclohexanol 3f: 7-Oxo-2-enimide **2c** (40 mg, 0.10 mmol) was dissolved in THF (3 mL), and thiophenol (11 μL, 0.11 mmol), butyllithium (2.5 M in hexane, 44 μL, 0.11 mmol), and Me_3Al (2 M in hexane, 55 μL, 0.11 mmol) were added as described above. Flash chromatography over silica gel (diethyl ether/pentane 1:1) gave **3f** (31 mg, 61%) as a white solid. M.p. 111 °C; $[\alpha]_D^{20} = -28.0$ ($c = 0.5$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 3472$ (OH), 2965 (CH_3), 1780, 1704 (imide), 1222, 1186, 1113, 1071, 1027 cm^{-1} (C–O); ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.24$, 0.25 (2s, 6H; $SiMe_2$), 1.03 (s, 9H; *t*Bu), 1.30 (td, $J = 13.5$, 2.0 Hz, 1H; 4′-H), 1.38 (td, $J = 13.5$, 12.0 Hz, 1H; 2′-H), 1.50 (tt, $J = 13.5$, 3.0 Hz, 1H; 3′-H), 1.84, 2.12 (2m, 2H; 4′-H, 2′-H), 3.59 (td, $J = 12.0$, 4.0 Hz, 1H; 1′-H), 4.12 (m, 1H; 5′-H), 4.25 (dd, $J = 12.0$, 2.0 Hz, 1H; 6′-H), 4.29 (dd, $J = 9.0$, 7.5 Hz, 1H; 5-H), 4.35 (dd, $J = 9.0$, 1.5 Hz, 1H; 5-H), 4.55 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H), 7.24–7.47 (m, 10H, phenyl-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = -5.3$, -5.1 ($SiMe_2$), 17.9 (C-3′), 25.8 (*t*Bu), 31.95, 35.0 (C-4′, C-6′), 36.2 (*t*Bu), 45.8 (C-1′), 49.3 (C-6′), 61.6 (C-4), 65.2 (C-5), 67.1 (C-5′), 127.3, 127.8, 128.8, 129.0, 132.5, 133.9, 134.1, 137.1 (phenyl-C), 154.3 (C-2), 175.1 (C=O); MS (70 eV, EI): *m*/*z* (%): 511 (87) [M^+], 278 (89), 135 (100); HRMS: *m*/*z*: calcd for $C_{28}H_{37}NO_4SSi$: 511.2212, found: 511.2212.

Cyclohexanol 3g: 7-Oxo-2-enimide **2d** (75 , 0.25 mmol) was dissolved in THF (4 mL), and thiophenol (27 μL, 0.27 mmol), butyllithium (2.5 M in hexane, 107 μL, 0.27 mmol), and Me_3Al (2 M in hexane, 134 μL, 0.27 mmol) were added as described above. Flash chromatography over silica gel (diethyl ether/pentane 1:1) gave **3g** (61 mg, 59%) as a white solid. M.p. 66 °C; $[\alpha]_D^{20} = +59.3$ ($c = 0.3$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 3478$ (OH), 2965 (CH_3), 1779, 1704 (imide), 1220, 1102, 1058 cm^{-1} (C–O); ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.91$ (d, $J = 6.5$ Hz, 3H; CH_3), 0.95 (s, 9H; *t*Bu), 1.08 (d, $J = 6.5$ Hz, 3H; CH_3), 1.20–1.30 (m, 2H; 4′-H, 6′-H), 1.70–1.81 (m, 1H; 5′-H), 1.84 (dt, $J = 14.0$, 3.5 Hz, 1H; 4′-H), 2.84 (brs, 1H; OH), 3.40 (dd, $J = 12.5$, 11.0 Hz, 1H; 1′-H), 4.09 (brs, 1H; 3′-H), 4.26 (dd, $J = 9.0$, 7.5 Hz, 1H; 5-H), 4.32 (dd, $J = 9.0$, 1.5 Hz, 1H; 5-H), 4.48 (dd, $J = 12.5$, 2.0 Hz, 1H; 2′-H), 4.52 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H), 7.18–7.48 (m, 5H; phenyl-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 17.0$ (CH_3), 20.1 (CH_3), 25.7 (*t*Bu), 31.9 (C-5′), 36.0 (*t*Bu), 40.0, 45.6 (C-4′, C-6′), 50.8 (C-1′), 51.7 (C-2′), 61.5 (C-4), 65.1 (C-5), 67.2 (C-3′), 126.7, 128.7, 131.6, 135.8 (phenyl-C), 154.3 (C-2), 174.6 (C=O); MS (70 eV, EI): *m*/*z* (%): 405 (90) [M^+], 278 (29), 244 (20), 144 (45) [oxazolidinone$^+$+2H], 135 (100); elemental analysis calcd (%) for $C_{22}H_{31}NO_4S$ (405.55): C 65.15, H 7.70; found: C 65.23, H 7.82.

Cyclohexanol 4a: 7-Keto-2-enimide **2e** (56 mg, 0.19 mmol) was dissolved in THF (3 mL), and a solution of MeCu-LiI freshly prepared from CuI (181 mg, 0.95 mmol), MeLi (1.6 M in diethyl ether, 0.59 mL, 0.95 mmol), and Me_2AlCl (1 M in hexane, 0.95 mL, 0.95 mmol) was added as described above. Flash chromatography over silica gel (diethyl ether/pentane 1:1) gave **4a** (32 mg, 54%) as a colorless oil. $[\alpha]_D^{20} = +49.2$ ($c = 1.0$ in $CHCl_3$); IR (film): $\tilde{\nu} = 3498$ (OH), 2960 (CH_3), 1782, 1673 (imide), 1272, 1183, 1104 cm^{-1} (C–O); ^1H NMR (200 MHz, $CDCl_3$): $\delta = 0.68$–1.10, 1.67–1.80 (2m, 7H; CH_3, 4′-H_2, 6′-H_2), 0.88 (d, $J = 6.5$ Hz, 3H; CH_3), 0.98 (s, 9H; *t*Bu), 1.07 (s, 3H; 1′-CH_3), 1.86–2.29 (m, 2H; 3′-H, 5′-H), 3.70 (d, $J = 11.5$ Hz, 1H; 2′-H), 3.76 (s, 1H; OH), 4.20 (dd, $J = 9.5$, 7.5 Hz, 1H; 5-H), 4.34 (dd, $J = 9.5$, 1.5 Hz, 1H; 5-H), 4.52 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 19.9$ (CH_3), 21.85 (CH_3), 25.9 (*t*Bu), 26.8 (CH_3), 29.2 (C-3′), 32.0 (C-5′), 35.8 (*t*Bu), 42.9 (C-4′), 46.6 (C-6′), 53.7 (C-2′), 61.9 (C-4), 65.35 (C-5), 70.75 (C-1′), 154.6 (C-2), 178.2 (C=O); MS (70 eV, EI): *m*/*z* (%): 311 (17) [M^+], 296 (38) [$M^+ - CH_3$], 212 (67), 153 (69) [M^+ – oxazolidinone – O], 144 (100) [oxazolidinone$^+$+2H]; HRMS: *m*/*z*: calcd for $C_{17}H_{29}NO_4$: 311.2096; found: 311.2096.

Cyclohexanol 4b: CuBr/dimethylsulfide complex (146 mg, 0.72 mmol) was suspended in dry THF (3 mL) and cooled to −40 °C at which temperature ethylmagnesium bromide (3 M in diethyl ether, 0.24 mL, 0.72 mmol) was added. The solution was stirred for 1 h at −40 °C, cooled to −78 °C, and then treated with 7-keto-2-enimide **2e** (42 mg, 0.14 mmol) dissolved in THF (1 mL). The reaction mixture was slowly warmed to RT over 3–4 h and eventually stopped through the addition of saturated NH_4Cl solution. The layers were separated, and the aqueous phase was extracted twice with diethyl ether. The combined organic extracts were dried over $MgSO_4$, filtered, and evaporated. The crude product was purified by flash chromatography over silica gel (diethyl ether/pentane 1:1) to give **4b** (33 mg, 71%) as a white solid. M.p. 88 °C; $[\alpha]_D^{20} = +39.8$ ($c = 1.0$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 3499$ (OH), 2967 (CH_3), 1777, 1674 (imide), 1229, 1185, 1105 cm^{-1} (C–O); ^1H NMR (200 MHz, $CDCl_3$): $\delta = 0.68$ (q, $J = 12.5$ Hz, 1H; 4′-H), 0.90 (d, $J = 7.0$ Hz, 3H; 5′-CH_3), 0.98 (s, 9H; *t*Bu), 1.06 (s, 3H; 1′-CH_3), 0.73–2.14 (m, 10H; 3′-H, 4′-H, 5′-H, 6′-H_2, CH_2H_3), 3.65 (s, 1H; OH), 3.79 (d, $J = 11.5$ Hz, 1H; 2′-H), 4.19 (dd, $J = 9.0$, 7.5 Hz, 1H; 5-H), 4.33 (dd, $J = 9.0$, 1.5 Hz, 1H; 5-H), 4.53 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 10.8$ (CH_3), 22.0 (CH_3), 25.9 (*t*Bu), 26.7 (CH_3), 26.7 (C-1″), 29.15 (C-3′), 35.8 (*t*Bu), 38.05 (C-5′), 38.4, 46.8 (C-4′, C-6′), 52.65 (C-2′), 61.9 (C-4), 65.3 (C-5), 70.8 (C-1′), 154.5 (C-2), 178.1 (C=O); MS (70 eV, EI): *m*/*z* (%): 325 (25) [M^+], 310 (28) [$M^+ - Me$], 296 (25) [$M^+ - Et$], 226 (71), 185 (63), 167 (77), 144 (100) [oxazolidinone$^+$+2H]; elemental analysis calcd (%) for $C_{18}H_{31}NO_4$ (325.44): C 66.43, H 9.60; found: C 66.48, H 9.30.

Cyclohexanol 4c: 7-Keto-2-enimide **2e** (100 mg, 0.34 mmol) was dissolved in THF (5 mL), and CuI (323 mg, 1.70 mmol), butyllithium (2.5 M in hexane, 0.68 mL, 1.70 mmol), and Me_2AlCl (1 M in hexane, 1.70 mL, 1.70 mmol) were added as described above. Flash chromatography over silica gel (diethyl ether/pentane 1:1) gave **4c** (99 mg, 83%) as a white solid. M.p. 74 °C; $[\alpha]_D^{20} = +24.8$ ($c = 0.5$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 3502$ (OH), 2961 (CH_3), 1780, 1674 (imide), 1183, 1105 cm^{-1} (C–O); ^1H NMR (200 MHz, $CDCl_3$): $\delta = 0.68$ (q, $J = 12.0$ Hz, 1H; 4′-H), 0.81–0.97 (m, 3H; CH_3), 0.89 (d, $J = 6.5$ Hz, 3H; CH_3), 0.99 (s, 9H; *t*Bu), 1.06 (s, 3H; 1′-CH_3), 1.15–2.19 (m, 11H; 3′-H, 4′-H, 5′-H, 6′-H_2, butyl side chain), 3.69 (d, $J = 2.0$ Hz, 1H; OH), 3.78 (d, $J = 11.0$ Hz, 1H; 2′-H), 4.19 (dd, $J = 9.5$, 7.5 Hz, 1H; 5-H), 4.33 (dd, $J = 9.5$, 1.5 Hz, 1H; 5-H), 4.53 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 14.0$ (CH_3), 22.0 (CH_3), 22.9, 25.9 (*t*Bu), 26.7 (CH_3), 28.6, 29.2 (C-3′), 33.85, 35.8 (*t*Bu), 36.8 (C-5′), 39.2, 46.8 (C-4′, C-6′), 52.9 (C-2′), 61.9 (C-4), 65.3 (C-5), 70.8 (C-1′), 154.5 (C-2), 178.2 (C=O); MS (70 eV, EI): *m*/*z* (%): 353 (27) [M^+], 338 (30) [$M^+ - Me$], 296 (53) [$M^+ - Bu$], 254 (100), 211 (29) [M^+ – oxazolidinone], 195 (79) [M^+ – oxazolidinone – O], 186 (58), 185 (67), 144 (98) [oxazolidinone$^+$+2H]; elemental analysis calcd (%) for $C_{20}H_{35}NO_4$ (353.50): C 67.95, H 9.98; found: C 68.29, H 9.79.

Cyclohexanol 4d: 7-Keto-2-enimide **2e** (35 mg, 0.12 mmol) was dissolved in THF (3 mL), and CuI (113 mg, 0.59 mmol), hexyllithium (2.5 M in hexane, 0.24 mL, 0.59 mmol), and Me_2AlCl (1 M in hexane, 0.59 mL, 0.59 mmol) were added as described above. Flash chromatography over silica gel (diethyl ether/pentane 1:2) gave **4d** (28 mg, 62%) as a colorless oil. $[\alpha]_D^{20} = +28.5$ ($c = 0.4$ in $CHCl_3$); IR (film): $\tilde{\nu} = 3500$ (OH), 2927 (CH_3), 1783, 1673 (imide), 1266, 1182, 1104 cm^{-1} (C–O); ^1H NMR (200 MHz, $CDCl_3$): $\delta = 0.68$ (q, $J = 11.5$ Hz, 1H; 4′-H), 0.70–2.20 (m, 24H; 1′-CH_3, 5′-CH_3, 3′-H, 4′-H, 5′-H, 6′-H_2, hexyl side chain), 0.99 (s, 9H; *t*Bu), 3.69 (d, $J = 2.0$ Hz, 1H; OH), 3.79 (d, $J = 11.5$ Hz, 1H; 2′-H), 4.19 (dd, $J = 9.0$, 7.5 Hz, 1H; 5-H), 4.33 (dd, $J = 9.0$, 1.5 Hz, 1H; 5-H), 4.53 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.1$ (CH_3), 22.0 (CH_3), 25.95 (*t*Bu), 26.7 (C-1′-Me), 29.2 (C-3′), 22.6, 26.35, 29.5, 31.8, 34.1 (hexyl side chain), 35.8 (*t*Bu), 36.8 (C-5′), 39.2, 46.9 (C-4′, C-6′), 52.9 (C-2′), 61.9 (C-4), 65.3 (C-5), 70.8 (C-1′), 154.5 (C-2), 178.2 (C=O); MS (70 eV, EI): *m*/*z* (%): 381 (8) [M^+], 366 (14) [$M^+ - Me$], 296 (48) [$M^+ - Hexyl$], 282 (58), 223 (53), 185 (49), 144 (100) [oxazolidinone$^+$+2H]; HRMS: *m*/*z*: calcd for $C_{22}H_{39}NO_4$: 381.2879; found: 381.2879.

Cyclohexanol 4e: 7-Keto-2-enimide **2e** (41 mg, 0.14 mmol) was dissolved in THF (3 mL), and CuBr/dimethylsulfide complex (143 mg, 0.69 mmol) and allylmagnesium chloride (2 M in hexane, 0.35 mL, 0.70 mmol) were added as described above. Flash chromatography over silica gel (diethyl ether/pentane 1:2) gave **4e** (38 mg, 81%) as a colorless oil. $[\alpha]_D^{20} = +33.0$ ($c = 0.5$ in $CHCl_3$); IR (film): $\tilde{\nu} = 3501$ (OH), 2963 (CH_3), 1783, 1672 (imide), 1263, 1183, 1104 cm^{-1} (C–O); ^1H NMR (200 MHz, $CDCl_3$): $\delta = 0.68$ (q, $J = 12.0$ Hz, 1H; 4′-H_3), 0.88 (d, $J = 6.5$ Hz, 3H; 5′-CH_3), 0.99 (s, 9H; *t*Bu), 1.08 (s, 3H; 1′-CH_3), 1.20–2.30 (m, 7H; 3′-H, 4′-H, 5′-H, 6′-H_2, 1″-H_2), 3.65 (d, $J = 2.0$ Hz, 1H; OH), 3.80 (d, $J = 10.5$ Hz, 1H; 2′-H), 4.20

(dd, $J = 9.5$, 7.5 Hz, 1H; 5-H), 4.34 (dd, $J = 9.5$, 1.5 Hz, 1H; 5-H), 4.52 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H), 4.95 – 5.09 (m, 2H; CH=CH_2), 5.67 – 5.90 (m, 1H; CH=CH_2); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 21.9$ (CH_3), 26.0 (*t*Bu), 26.6, 29.1, 36.6 (C-3′, C-5′, C-1′-Me), 35.8 (*t*Bu), 38.55, 39.05, 49.8 (C-4′, C-1″, C-6′), 52.45 (C-2′), 62.0 (C-4), 65.4 (C-5), 70.8 (C-1′), 116.8 (CH=CH_2), 136.1 (CH=CH_2), 154.5 (C-2), 177.9 (C=O); MS (70 eV, EI): *m*/*z* (%): 337 (3) [M^+], 322 (15) [$M^+ -$ Me], 296 (100) [$M^+ -$ allyl], 144 (72) [oxazolidinone$^+$+2H]; HRMS: *m*/*z*: calcd for $C_{19}H_{31}NO_4$: 337.2253; found: 337.2253.

Cyclohexanol 4f: 7-Keto-2-enimide **2e** (63 mg, 0.21 mmol) was dissolved in THF (4 mL), and CuBr/dimethylsulfide complex (66 mg, 0.32 mmol) and phenylmagnesium chloride (2 M in hexane, 0.32 mL, 0.64 mmol) were added as described above. Flash chromatography over silica gel (diethyl ether/pentane 1:1) gave **4f** (42 mg, 53%) as a white solid. M.p. 130 °C; $[\alpha]_D^{20} = +24.0$ ($c = 0.5$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 3541$ (OH), 2963 (CH_3), 1772, 1701 (imide), 1268, 1225, 1186, 1102 cm^{-1} (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.38$ (s, 9H; *t*Bu), 0.89 (d, $J = 7.5$ Hz, 3H; 5′-CH_3), 0.80 – 1.25, 1.76 – 1.90 (m, 4H; 4′-H_2, 6′-H_2), 1.14 (s, 3H; 1′-CH_3), 2.02 – 2.21 (m, 1H; 5′-H), 3.30 (td, $J = 11.5$, 3.5 Hz, 1H; 3′-H), 3.54 (d, $J = 2.0$ Hz, 1H; OH), 4.06 (dd, $J = 9.0$, 7.5 Hz, 1H; 5-H), 4.15 (dd, $J = 9.0$, 1.5 Hz, 1H; 5-H), 4.31 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H), 4.55 (d, $J = 11.5$ Hz, 1H; 2′-H), 7.08 – 7.35 (m, 5H; phenyl-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 21.7$ (CH_3), 25.0 (*t*Bu), 27.4 (C-1′-Me), 29.15 (C-3′), 35.1 (*t*Bu), 43.9 (C-4′), 44.4 (C-5′), 46.4 (C-6′), 51.6 (C-2′), 61.2 (C-4), 64.9 (C-5), 70.9 (C-1′), 126.7, 128.0, 128.6, 143.5 (phenyl-C), 154.3 (C-2), 176.7 (C=O); MS (70 eV, EI): *m*/*z* (%): 373 (45) [M^+], 274 (72), 212 (50), 144 (65) [oxazolidinone$^+$+2H], 131 (100); elemental analysis calcd (%) for $C_{22}H_{31}NO_4$ (373.49): C 70.75, H 8.37; found: C 70.52, H 8.47.

Cyclohexanol 4g: 7-Keto-2-enimide **2f** (103 mg, 0.29 mmol) was dissolved in THF (5 mL), and CuI (274 mg, 1.44 mmol), butyllithium (2.5 M in hexane, 0.58 mL, 1.44 mmol), and Me_2AlCl (1 M in hexane, 1.44 mL, 1.44 mmol) were added as described above. Flash chromatography over silica gel (diethyl ether/pentane 1:2) gave **4g** (61 mg, 51%) as a white solid. M.p. 124 °C; $[\alpha]_D^{20} = +20.6$ ($c = 0.5$ in $CHCl_3$), IR (KBr): $\tilde{\nu} = 3492$ (OH), 2963 (CH_3), 1769, 1670 (imide), 1219, 1105 cm^{-1} (C–O); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.85$ (t, $J = 7.0$ Hz, 3H; CH_3), 0.88 – 0.95 (m, 1H; 6′-H), 1.00 (s, 9H; *t*Bu), 1.12 (s, 3H; 1′-CH_3), 1.15 – 1.55 (m, 7H; 4′-H, butyl side chain), 1.94 (ddd, $J = 13.5$, 3.5, 1.5 Hz, 1H; 6′-H), 2.08 (dtd, $J = 13.0$, 3.5, 1.5 Hz, 1H; 4′-H), 2.24 (m, 1H; 3′-H), 3.16 (tt, $J = 13.0$, 3.5 Hz, 1H; 5′-H), 3.85 (d, $J = 2.5$ Hz, 1H; OH), 3.96 (d, $J = 11.5$ Hz, 1H; 2′-H), 4.22 (dd, $J = 9.5$, 7.5 Hz, 1H; 5-H), 4.35 (dd, $J = 9.5$, 1.5 Hz, 1H; 5-H), 4.56 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H), 7.15 – 7.34 (m, 5H; phenyl-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 14.0$ (CH_3), 22.9, 28.6, 33.8 (butyl side chain), 25.9 (*t*Bu), 29.2 (C-1′-Me), 35.8 (*t*Bu), 37.0 (C-3′), 38.1 (C-5′), 38.2, 45.7 (C-4′, C-6′), 52.8 (C-2′), 61.9 (C-4), 65.35 (C-5), 70.8 (C-1′), 126.1, 127.0, 128.4, 146.3 (phenyl-C), 154.5 (C-2), 178.0 (C=O); MS (70 eV, EI): *m*/*z* (%): 415 (3) [M^+], 397 (52), 254 (34), 226 (100), 169 (61); elemental analysis calcd (%) for $C_{25}H_{37}NO_4$ (415.57): C 72.26, H 8.97; found: C 72.22, H 8.71.

Cyclohexanol 4h: 7-Keto-2-enimide **2e** (100 mg, 0.34 mmol) was dissolved in THF (5 mL), and thiophenol (36 μL, 0.36 mmol), butyllithium (2.5 M in hexane, 142 μL, 0.36 mmol), and Me_3Al (2 M in hexane, 178 μL, 0.36 mmol) were added as described above. Purification by flash chromatography over silica gel (diethyl ether/pentane 1:1) gave **4h** (108 mg, 76%) as a white solid. M.p. 47 °C; $[\alpha]_D^{20} = +23.0$ ($c = 0.4$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 3486$, 2960 (CH_3), 1782, 1673 (imide), 1263, 1228, 1104 cm^{-1} (C–O); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.84$ (d, $J = 6.5$ Hz, 3H; 5′-CH_3), 1.00 (dd, $J = 13.5$, 12.0 Hz, 1H; 4′-H), 1.04 (s, 9H; *t*Bu), 1.14 (s, 3H; 3′-CH_3), 1.20 (q, $J = 12.0$ Hz, 1H; 6′-H), 1.72 (dd, $J = 13.5$, 3.5 Hz, 1H; 4′-H), 1.96 (m, 1H; 5′-H), 2.07 (dt, $J = 12.0$, 4.0 Hz, 1H; 6′-H), 3.58 (td, $J = 12.0$, 4.0 Hz, 1H; 1′-H), 4.22 (d, $J = 12.0$ Hz, 1H; 2′-H), 4.24 (dd, $J = 9.0$, 7.5 Hz, 1H; 5-H), 4.36 (dd, $J = 9.0$, 1.0 Hz, 1H; 5-H), 4.58 (dd, $J = 7.5$, 1.0 Hz, 1H; 4-H), 7.23 – 7.32 (m, 5H; phenyl-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 21.4$ (CH_3), 25.9 (*t*Bu), 27.1 (CH_3), 29.1 (C-5′), 36.3 (*t*Bu), 42.4, 46.0 (C-4′, C-6′), 47.35 (C-1′), 51.8 (C-2′), 62.0 (C-4), 65.35 (C-5), 71.7 (C-3′), 127.3, 128.9, 132.6, 134.3 (phenyl-C), 154.4 (C=O, urethane), 176.4 (C=O, amide); MS (70 eV, EI): *m*/*z* (%): 405 (100) [M^+], 296 (77) [$M^+ -$ SPh], 278 (98) [$M^+ -$ OH – H], 144 (44) [oxazolidinone$^+$+2H], 135 (50); elemental analysis calcd (%) for $C_{22}H_{31}NO_4S$ (405.55): C 65.40, H 7.88; found: C 65.15, H 7.70.

Cyclohexanol 4i: 7-Keto-2-enimide **2f** (127 mg, 0.36 mmol) was dissolved in THF (5 mL), and thiophenol (40 μL, 0.39 mmol), butyllithium (2.5 M in hexane, 156 μL, 0.36 mmol), and Me_3Al (2 M in hexane, 196 μL, 0.36 mmol) were added as described above. Purification by flash chromatography over silica gel (diethyl ether/pentane 1:1) gave **4i** (100 mg, 60%) as a white solid. M.p. 198 °C; $[\alpha]_D^{20} = -49.8$ ($c = 1.0$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 3466$ (OH), 2966 (CH_3), 1775, 1689 (imide), 1258, 1215, 1192, 1104 cm^{-1} (C–O); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.05$ (s, 9H; *t*Bu), 1.20 (s, 3H; 3′-CH_3), 1.53 (td, $J = 12.5$, 2.5 Hz, 1H; 4′-H), 1.76 (q, $J = 12.5$ Hz, 1H; 6′-H), 1.93 (ddd, $J = 12.5$, 3.5, 1.0 Hz, 1H; 4′-H), 2.27 (m, 1H; 6′-H), 3.13 (tt, $J = 12.5$, 3.5 Hz, 1H; 5′-H), 3.71 (td, $J = 12.5$, 2.5 Hz, 1H; 1′-H), 3.97 (d, $J = 2.5$ Hz, 1H; OH), 4.25 (dd, $J = 9.0$, 7.5 Hz, 1H; 5-H), 4.37 (d, $J = 12.5$ Hz, 1H; 2′-H), 4.38 (dd, $J = 9.0$, 1.0 Hz, 1H; 5-H), 4.62 (dd, $J = 7.5$, 1.0 Hz, 1H; 4-H), 7.13 – 7.45 (m, 10H; phenyl-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 25.9$ (*t*Bu), 29.1 (C-3′-Me), 36.3 (*t*Bu), 38.3 (C-5′), 41.1, 45.2 (C-4′, C-6′), 47.8 (C-1′), 51.6 (C-2′), 62.0 (C-4), 65.4 (C-5), 71.7 (C-3′), 126.3, 127.0, 127.5, 128.5, 128.9, 132.8, 134.0, 145.0 (phenyl-C), 154.4 (C-2), 176.3 (C=O); MS (70 eV, EI): *m*/*z* (%): 467 (88) [M^+], 358 (53) [$M^+ -$ SPh], 340 (82), 197 (93), 157 (100), 144 (86) [oxazolidinone$^+$+2H]; HRMS: *m*/*z*: calcd for $C_{27}H_{33}NO_4S$: 467.2130; found: 467.2130.

Cyclohexanol 4k: Trimethylsilyl azide (84 μL, 0.63 mmol) was dissolved in THF (2 mL), and methanol (25 μL, 0.63 mmol) was added at 0 °C. After 1 h, Me_3Al (2 M in hexane, 0.32 mL, 0.64 mmol) was added. After stirring for 1 h, 7-keto-2-enimide **2e** (59 mg, 0.21 mmol) dissolved in THF (1 mL) was added. The solution was stirred at 0 °C and then allowed to warm to RT over 5 h. The reaction was quenched by the addition of saturated NH_4Cl solution, the layers were separated, and the aqueous phase was extracted twice with diethyl ether. The combined organic extracts were dried over $MgSO_4$, filtered, and evaporated. The crude product was purified by flash chromatography over silica gel (diethyl ether/pentane 1:1) to give **4k** (38 mg, 60%) as a white solid. M.p. 164 °C; $[\alpha]_D^{20} = -9.4$ ($c = 0.5$ in $CHCl_3$); IR (film): $\tilde{\nu} = 3523$ (OH), 2969 (CH_3), 2106 (azide), 1776, 1687 (imide), 1216, 1189, 1109, 1052 cm^{-1} (C–O); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.96$ (d, $J = 6.5$ Hz, 3H; 5′-CH_3), 0.97 (s, 9H; *t*Bu), 1.01 (dd, $J = 13.5$, 11.5 Hz, 1H; 6′-H), 1.11 (s, 3H; 1′-CH_3), 1.23 (q, $J = 11.5$ Hz, 1H; 4′-H), 1.72 (ddd, $J = 13.5$, 4.0, 1.5 Hz, 1H; 6′-H), 2.03 – 2.13 (m, 1H; 5′-H), 2.13 (dtd, $J = 11.5$, 4.0, 1.5 Hz, 1H; 4′-H), 3.65 (br s, 1H; OH), 3.87 (td, $J = 11.5$, 4.0 Hz, 1H; 3′-H), 4.12 (d, $J = 11.5$ Hz, 1H; 2′-H), 4.19 (dd, $J = 9.0$, 7.5 Hz, 1H; 5-H), 4.32 (dd, $J = 9.0$, 1.5 Hz, 1H; 5-H), 4.55 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 21.4$ (CH_3), 25.6 (*t*Bu), 26.1 (CH_3), 32.8 (C-5′), 36.05 (*t*Bu), 38.4, 45.9 (C-4′, C-6′), 52.0 (C-2′), 60.1 (C-3′), 61.3 (C-4), 65.2 (C-5), 71.5 (C-1′), 154.1 (C-2), 176.1 (C=O); MS (200 eV, DCI/NH_3): *m*/*z* (%): 695 (15) [2M^++NH_3], 373 (100) [M^++2NH_3], 356 (76) [M^++NH_3]; elemental analysis calcd (%) for $C_{16}H_{26}N_4O_4$ (338.40): C 56.79, H 7.74; found: C 57.12, H 7.75.

Cyclohexanol 4l: 7-Keto-2-enimide **2e** (51 mg, 0.17 mmol) was dissolved in CH_2Cl_2 (3 mL) and cooled to 0 °C. Piperidine (51 μL, 0.52 mmol) and then Me_2AlCl (1 M in hexane, 0.52 mL, 0.52 mmol) were added. Stirring was continued for 1 h at 0 °C, and the reaction was then stopped by the addition of saturated $NaHCO_3$ solution. The layers were separated, the aqueous phase was extracted twice with diethyl ether, and the combined organic extracts were dried over $MgSO_4$. After filtration and evaporation of the solvents, the crude product was purified by flash chromatography over silica gel (diethyl ether/pentane 1:1) to give **4l** (26 mg, 40%) as a white solid. M.p. 145 °C; $[\alpha]_D^{20} = +20.6$ ($c = 0.5$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 3538$ (OH), 2943 (CH_3), 1777, 1708 (imide), 1276, 1217, 1182, 1100, 1059 cm^{-1} (C–O); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.80 - 2.09$ (m, 11H; 4′-H_2, 5′-H, 6′-H_2, piperidine ring protons), 0.92 (d, $J = 7.5$ Hz, 3H; 5′-CH_3), 1.03 (s, 9H; *t*Bu), 1.08 (s, 3H; 1′-CH_3), 2.28 – 2.42, 2.74 – 2.88 (2m, 4H; NCH), 3.16 (td, $J = 11.5$, 3.5 Hz, 1H; 3′-H), 3.88 (d, $J = 2.0$ Hz, 1H; OH), 4.18 (dd, $J = 9.5$, 7.5 Hz, 1H; 5-H), 4.24 (d, $J = 11.5$ Hz, 1H; 2′-H), 4.31 (dd, $J = 9.5$, 1.5 Hz, 1H; 5-H), 4.55 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 21.9$ (CH_3), 25.6 (*t*Bu), 24.9, 26.3 (piperidine ring), 26.4 (C-1′-Me), 29.3 (C-5′), 31.4 (C-4′), 36.1 (*t*Bu), 46.75 (C-6′), 50.3 (NCH_2), 50.75 (C-2′), 61.5 (C-4), 64.15 (C-3′), 65.1 (C-5), 71.5 (C-1′), 154.6 (C-2), 177.5 (C=O); MS (70 eV, EI): *m*/*z* (%): 380 (54) [M^+], 138 (100); HRMS: *m*/*z*: calcd for $C_{21}H_{36}N_2O_4$: 380.2675; found: 380.2675.

Cyclohexylamine 5a: 7-Oxo-2-enimide **2a** (56 mg, 0.20 mmol) was dissolved in CH_2Cl_2 (3 mL) and cooled to 0 °C. Morpholine (52 μL, 0.60 mmol) and then Me_2AlCl (1 M in hexane, 0.40 mL, 0.40 mmol) were added. After 1 h, the reaction was stopped by the addition of saturated $NaHCO_3$ solution. The layers were separated, the aqueous phase was extracted twice with diethyl ether, and the combined organic extracts were dried over $MgSO_4$. After filtration and evaporation of solvents, the crude

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product was purified by column chromatography over silica gel (diethyl ether/pentane 1:2) to give **5a** (60 mg, 69%) as a white solid. M.p. 178 °C; $[\alpha]_D^{20} = +40.0$ ($c = 0.8$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 2956$ (CH), 2852 (N-CH_2), 1769, 1703 (imide), 1213, 1187, 1118, 1070, 1034 cm^{-1} (C–O); ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.85$, 0.89 (2q, $J = 11.5$ Hz, 2H; 4′-H, 6′-H), 0.98 (d, $J = 6.5$ Hz, 3H; 5′-Me), 0.99 (s, 9H; *t*Bu), 1.34–1.45 (m, 1H; 5′-H), 1.77 (m, 2H; 4′-H, 6′-H), 2.31, 2.39 (2ddd, $J = 11.0$, 6.0, 3.0 Hz, 4H; NCH), 2.64–2.70 (m, 2H; NCH), 2.74 (td, $J = 11.5$, 3.5 Hz, 1H; 3′-H), 2.82–2.90 (m, 2H; NCH), 2.86 (td, $J = 11.5$, 3.5 Hz, 1H; 1′-H), 3.42–3.65 (m, 8H; OCH), 4.19 (dd, $J = 9.0$, 7.5 Hz, 1H; 5-H), 4.25 (t, $J = 11.5$ Hz, 1H; 2′-H), 4.28 (dd, $J = 9.0$, 1.5 Hz, 1H; 5-H), 4.52 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 22.3$ (C-5′-Me), 25.7 (*t*Bu), 29.8 (C-5′), 31.5, 32.6 (C-4′, C-6′), 36.0 (*t*Bu), 46.7 (C-2′), 49.15, 49.9 (NCH_2), 61.6 (C-4), 65.15 (C-5), 66.2, 67.0 (C-1′, C-3′), 67.4, 68.1 (OCH_2), 155.3 (C-2), 176.1 (C=O); MS (70 eV, EI): *m/z* (%): 438 (13) [M^+], 351 (25) [$M^+ - C_4H_8NO$], 180 (46), 165, 140 (100); HRMS: *m/z*: calcd for $C_{23}H_{39}N_3O_5$: 437.2889; found: 437.2889.

Cyclohexylamine 5b: 7-Oxo-2-enimide **2a** (58 mg, 0.21 mmol) was dissolved in CH_2Cl_2 (3 mL), and diethylamine (53 μL, 0.62 mmol) and Me_2AlCl (1M in hexane, 0.41 mL, 0.41 mmol) were added as described above. Column chromatography over silica gel (diethyl ether/pentane 1:2) gave the cyclohexylamine **5b** (39 mg, 46%) as a white solid. M.p. 128 °C; $[\alpha]_D^{20} = +65.8$ ($c = 0.5$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 2870$ (CH), 1776, 1704 (imide), 1264, 1184, 1130, 1096 cm^{-1} (C–O); ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.80–1.11$ (m, 2H; 4′-H, 6′-H), 0.88 (t, $J = 7.0$ Hz, 6H; 2N-CH_2-CH_3), 0.94 (t, $J = 7.0$ Hz, 6H; 2N-CH_2-CH_3), 0.97 (s, 9H; *t*Bu), 1.36 (m, 1H; 5′-H), 1.65–1.76 (m, 2H; 4′-H, 6′-H), 2.23, 2.30 (2dq, $J = 13.0$, 6.5 Hz, 4H; NCH), 2.50, 2.70 (2dq, $J = 13.0$, 7.0 Hz, 4H; NCH), 2.88, 3.02 (2ddd, $J = 12.0$, 11.0, 3.5 Hz, 2H; 1′-H, 3′-H), 4.11 (dd, $J = 9.0$, 7.5 Hz, 1H; 5-H), 4.23 (dd, $J = 9.0$, 1.5 Hz, 1H; 5-H), 4.25 (t, $J = 11.0$ Hz, 1H; 2′-H), 4.44 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 14.1$, 14.5 (2NCH_2CH_3), 22.45 (C-5′-Me), 25.8 (*t*Bu), 30.2 (C-5′), 32.05, 32.8 (C-4′, C-6′), 35.6 (*t*Bu), 43.5, 43.6 (2NCH_2), 47.6 (C-2′), 61.1 (C-4), 61.6, 62.6 (C-1′, C-3′), 62.05 (C-5), 155.1 (C-2), 175.2 (C=O); MS (70 eV, EI): *m/z* (%): 409 (6) [M^+], 337 (35) [$M^+ - NEt_2$], 307 (16), 166 (20) [$M^+ - (NBn_2)_2 - CH_3$], 151 (26), 126 (100); elemental analysis calcd (%) for $C_{23}H_{43}N_3O_3$ (409.61): C 67.44, H 10.58; found: C 67.49, H 10.50.

Cyclohexylamine 5c: 7-Oxo-2-enimide **2a** (64 mg, 0.23 mmol) was dissolved in CH_2Cl_2 (3 mL), and dibenzylamine (131 μL, 0.68 mmol) and Me_2AlCl (1M in hexane, 0.45 mL, 0.45 mmol) were added as described above. Column chromatography over silica gel (diethyl ether/pentane 1:2) gave the cyclohexylamine **5c** (105 mg, 70%) as a white solid. M.p. 148 °C; $[\alpha]_D^{20} = +14.7$ ($c = 1.0$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 3027$ (phenyl-H), 2956 (CH), 1776, 1702 (imide), 1187, 1068 cm^{-1} (C–O); ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.87$ (d, $J = 6.5$ Hz, 3H; 5′-Me), 0.87–1.01 (m, 2H; 4′-H, 6′-H), 1.04 (s, 9H; *t*Bu), 1.15–1.31 (m, 1H; 5′-H), 1.48–1.54, 1.76–1.82 (2m, 2H; 4′-H, 6′-H), 3.07, 3.26 (2ddd, $J = 12.0$, 10.5, 3.5 Hz, 2H; 1′-H, 3′-H), 3.46, 3.47, 3.83, 3.94 (4d, $J = 14.0$ Hz, 8H; N-Bn-H), 4.15 (dd, $J = 9.0$, 7.5 Hz, 1H; 5-H), 4.21 (dd, $J = 9.0$, 1.5 Hz, 1H; 5-H), 4.44 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H), 4.54 (t, $J = 10.5$ Hz, 1H; 2′-H), 7.14–7.28 (m, 20H; phenyl-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 22.4$ (C-5′-Me), 26.0 (*t*Bu), 29.4 (C-5′), 32.9, 33.5 (C-4′, C-6′), 35.7 (*t*Bu), 47.1 (C-2′), 53.8, 54.1 (benzyl-C), 62.0, 62.5 (C-1′, C-3′), 62.65 (C-4), 65.1 (C-5), 126.6, 126.7, 127.9, 128.0, 128.1, 129.2, 139.1, 139.5 (phenyl-C), 155.1 (C-2), 175.1 (C=O); MS (70 eV, EI): *m/z* (%): 657 (2) [M^+], 567 (95) [$M^+ - Bn$], 462 (48) [$M^+ - NBn_2$], 250 (61) [$M^+ - (NBn_2)_2 - CH_3$], 91 (100); HRMS: *m/z*: calcd for $C_{43}H_{51}N_3O_5$: 657.3930; found: 657.3930.

Cyclohexylamine 5d: 7-Oxo-2-enimide **2a** (38 mg, 0.135 mmol) was dissolved in CH_2Cl_2 (3 mL), and dibutylamine (68 μL, 0.41 mmol) and Me_2AlCl (1M in hexane, 0.27 mL 0.27 mmol) were added as described above. Column chromatography over silica gel (diethyl ether/pentane 1:2) gave the cyclohexylamine **5d** (46 mg, 65%) as a white solid. M.p. 108 °C; $[\alpha]_D^{20} = +56.0$ ($c = 0.5$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 2870$ (CH), 1780, 1704 (imide), 1262, 1211, 1184, 1095 cm^{-1} (C–O); ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.83$, 0.86 (2t, $J = 7.0$ Hz, 6H; CH_3), 0.97 (s, 9H; *t*Bu), 1.02–1.48 (m, 19H; 4′-H, 5′-H, 6′-H, butyl side chain), 1.71 (m, 2H; 4′-H, 6′-H), 2.19, 2.33. 2.57 (3m, 8H; NCH), 2.77, 2.95 (2ddd, $J = 12.0$, 11.0, 3.5 Hz, 2H; 1′-H, 3′-H), 4.09 (dd, $J = 9.0$, 7.0 Hz, 1H; 5-H), 4.21 (dd, $J = 9.0$, 1.0 Hz, 1H; 5-H), 4.23 (t, $J = 11.0$ Hz, 1H; 2′-H), 4.38 (dd, $J = 7.0$, 1.0 Hz, 1H; 4-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 14.2$, 14.2 (NCH_2CH_3), 20.6, 20.85 (*N*-butyl side chain), 22.45 (C-5′-Me), 25.7 (*t*Bu), 30.1 (C-5′), 31.5 (*N*-butyl side chain), 31.9, 32.4 (C-4′, C-6′), 35.6 (*t*Bu), 47.4 (C-2′), 50.3, 50.6 (NCH_2), 61.8 (C-4), 62.3, 63.3 (C-1′, C-3′), 65.0 (C-5), 155.1 (C-2), 176.0 (C=O); MS (70 eV, EI): *m/z* (%): 521 (2) [M^+], 393 (97) [$M^+ - NBu_2$], 222 (36), 182 (100); elemental analysis calcd (%) for $C_{31}H_{59}N_3O_3$ (521.46): C 71.40, H 11.40; found: C 71.64, H 11.50.

Cyclohexylamine 5e: 7-Oxo-2-enimide **2b** (116 mg, 0.34 mmol) was dissolved in CH_2Cl_2 (5 mL), and piperidine (100 μL, 1.01 mmol) and Me_2AlCl (1M in hexane, 0.68 mL 0.68 mmol) were added as described above. Column chromatography over silica gel (diethyl ether/pentane 1:2) gave the cyclohexylamine **5e** (95 mg, 57%) as a white solid. M.p. 171 °C; $[\alpha]_D^{20} = +40.4$ ($c = 0.5$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 2933$ (CH), 1778, 1703 (imide), 1254, 1187, 1105, 1061, 1035 cm^{-1} (C–O); ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.02$ (s, 9H; *t*Bu), 1.25–1.55 (m, 14H; 4′-H, 6′-H, 6CH_2 (piperidine)), 1.91–2.01 (m, 2H; 4′-H, 6′-H), 2.31, 2.34 (2m, 4H; NCH), 2.51 (tt, $J = 12.5$, 3.0 Hz, 1H; 5′-H), 2.66, 2.85 (2m, 4H; NCH), 2.88, 2.99 (2td, $J = 11.5$, 3.5 Hz, 2H; 1′-H, 3′-H), 4.18 (dd, $J = 9.0$, 7.5 Hz, 1H; 5-H), 4.28 (dd, $J = 9.0$, 1.0 Hz, 1H; 5-H), 4.42 (t, $J = 11.5$ Hz, 1H; 2′-H), 4.54 (dd, $J = 7.5$, 1.0 Hz, 1H; 4-H), 7.18–7.33 (m, 5H; phenyl-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 24.8$, 25.0 (C-4″ (piperidine)), 25.8 (*t*Bu), 26.5 (C-3″ (piperidine)), 27.3 (C-5″ (piperidine)), 30.9, 32.0 (C-4′, C-6′), 35.9 (*t*Bu), 41.5 (C-5′), 47.1 (C-2′), 50.2, 50.9 (piperidine-NCH), 61.6 (C-4), 65.1 (C-5), 67.1, 67.8 (C-1′, C-3′), 126.2, 126.8, 128.5, 146.4 (phenyl-C), 155.1 (C-2), 176.3 (C=O); MS (70 eV, EI): *m/z* (%): 495 (24) [M^+], 411 (43) [M^+ – piperidine], 240 (38), 200 (100); elemental analysis calcd (%) for $C_{30}H_{45}N_3O_3$ (495.70): C 72.69, H 9.15; found: C 72.91, H 9.19.

Cyclohexylamine 5f: 7-Oxo-2-enimide **2c** (43 mg, 0.11 mmol) was dissolved in CH_2Cl_2 (3 mL), and piperidine (53 μL, 0.54 mmol) and Me_2AlCl (1M in hexane, 0.32 mL, 0.32 mmol) were added as described above. Column chromatography over silica gel (diethyl ether/pentane 1:2) gave the cyclohexylamine **5f** (35 mg, 59%) as a white solid. M.p. 78 °C; $[\alpha]_D^{20} = +32.0$ ($c = 0.5$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 2932$ (CH), 1778, 1702 (imide), 1262, 1230, 1187, 1104, 1060 cm^{-1} (C–O); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.23$ (s, 6H; $SiMe_2$), 0.67 (tt, $J = 13.0$, 2.5 Hz, 1H; 1′-H), 0.97 (s, 9H; *t*Bu), 0.88–1.51 (m, 14H; 2′-H, piperidine ring protons), 1.65–1.81 (m, 2H; 4′-H, 6′-H), 2.52–2.82 (m, 8H; N-CH), 2.64, 2.76 (2td, $J = 11.5$, 3.5 Hz, 2H; 3′-H, 5′-H), 4.13 (dd, $J = 9.0$, 7.5 Hz, 1H; 5-H), 4.22 (dd, $J = 9.0$, 1.5 Hz, 1H; 5-H), 4.24 (t, $J = 11.5$ Hz, 1H; 4′-H), 4.58 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H), 7.31–7.52 (m, 5H; phenyl-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.8$, -4.8 ($SiMe_2$), 21.5 (C-1′), 23.2, 24.3, 24.8, 25.0 (piperidine ring), 25.75 (*t*Bu), 26.5, 27.3 (C-2′, C-6′), 35.8 (*t*Bu), 47.6 (C-4′), 50.1, 50.8 (piperidine-NCH), 61.5 (C-4), 65.0 (C-5), 68.8, 69.6 (C-3′, C-5′), 127.8, 128.9, 133.8, 137.9 (phenyl-C), 155.1 (C-2), 176.4 (C=O); MS (70 eV, EI): *m/z* (%): 553 (40) [M^+], 469 (40) [M^+ – piperidine], 333 (59), 281 (49), 258 (100), 138 (77), 111 (49); HRMS: *m/z* calcd for $C_{32}H_{51}N_3O_3Si$: 553.3699; found: 553.3699.

Cyclohexylamine 5g: 7-Oxo-2-enimide **2c** (45 mg, 0.11 mmol) was dissolved in CH_2Cl_2 (3 mL), and morpholine (59 μL, 0.67 mmol) and Me_2AlCl (1M in hexane, 0.45 mL, 0.45 mmol) were added as described above. Column chromatography over silica gel (diethyl ether/pentane 1:2) gave the cyclohexylamine **5g** (33 mg, 53%) as a white solid. M.p. 88 °C; $[\alpha]_D^{20} = +32.0$ ($c = 0.5$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 2959$ (CH), 1775, 1701 (imide), 1270, 1216, 1186, 1117, 1069 cm^{-1} (C–O); ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.26$ (s, 6H; $SiMe_2$), 0.67 (tt, $J = 12.5$, 2.5 Hz, 1H; 1′-H), 0.88–1.02 (m, 2H; 2′-H, 6′-H), 0.97 (s, 9H; *t*Bu), 1.71–1.85 (m, 2H; 2′-H, 6′-H), 2.24–2.40 (m, 4H; N-CH), 2.60–2.67 (m, 2H; N-CH), 2.79–2.86 (m, 2H; N-CH), 2.68, 2.80 (td, $J = 11.5$, 3.5 Hz, 2H; 3′-H, 5′-H), 3.39–3.64 (m, 8H; OCH), 4.17 (dd, $J = 9.0$, 7.5 Hz, 1H; 5-H), 4.23 (t, $J = 11.5$ Hz, 1H; 4′-H), 4.27 (dd, $J = 9.0$, 1.5 Hz, 1H; 5-H), 4.51 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H), 7.35–7.42 (m, 5H; phenyl-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = -4.75$ ($SiMe_2$), 21.7 (C-1′), 23.6, 24.7 (C-2′, C-6′), 26.0 (*t*Bu), 36.2 (*t*Bu), 47.4 (C-4′), 49.3, 50.0 (N-CH), 61.8 (C-4), 65.4 (C-5), 67.6, 68.25 (OCH), 68.4, 69.2 (C-3′, C-5′), 128.1, 129.4, 134.0, 137.6 (phenyl-C), 155.5 (C-2), 176.1 (C=O); MS (70 eV, EI): *m/z* (%): 557 (74) [M^+], 471 (31) [M^+ – morpholine], 335 (73), 300 (80), 283 (83), 260 (100), 140 (73); HRMS: *m/z*: calcd for $C_{30}H_{47}N_3O_5Si$: 557.3285; found: 557.3285.

Cyclohexylamine 5h: 7-Oxo-2-enimide **2a** (79 mg, 0.28 mmol) was dissolved in CH_2Cl_2 (4 mL), and piperidine (28 μL, 0.28 mmol) and a small amount of $MgSO_4$ were added. After stirring for 1 h, the $MgSO_4$ was filtered off, and the solvent was evaporated in vacuo. In a second flask, thiophenol (35 μL, 0.34 mmol) was dissolved in THF (10 mL), and butyllithium (2.5M in hexane, 0.27 mL, 0.67 mmol) and Me_3Al (2M in hexane, 0.17 mL, 0.34 mmol) were added. After stirring for 1 h at 0 °C, the

solution was cooled to $-50\,^{\circ}C$, and the enamine dissolved in THF (1 mL) was added by syringe. After another 10 min, Me_2AlCl (1M in hexane, 0.34 mL, 0.34 mmol) was added and the reaction mixture was stirred for 8 h (at which time the reaction temperature had reached RT). Saturated NaCl solution was added, the layers were separated, and the aqueous phase was extracted twice with ether. The combined organic extracts were dried over $MgSO_4$, filtered, and evaporated. Chromatographic purification over silica gel (diethyl ether/pentane 1:1) gave cyclohexylamine **5h** (64 mg, 50%) as a colorless oil. $[\alpha]_D^{20} = +35.3$ ($c = 0.3$ in $CHCl_3$); IR (KBr): $\tilde{\nu} = 2930$ (CH), 1780, 1696 (imide), 1260, 1223, 1186, 1119, 1096 cm^{-1} (C–O); ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.89$ (d, $J = 6.5$ Hz, 3H; 5′-CH_3), 0.94 (q, $J = 12.5$ Hz, 1H; 4′-H), 1.02 (s, 9H; *t*Bu), 1.08 (q, $J = 13.0$ Hz, 1H; 6′-H), 1.20–1.70 (m, 7H; 5′-H, piperidine-CH_2), 1.74 (ddt, $J = 12.5$, 3.5, 1.5 Hz, 1H, 4′-H), 1.97 (dtd, $J = 13.0$, 3.5, 1.5 Hz, 1H; 6′-H), 2.25, 2.63 (2m, 4H; NCH), 2.75 (ddd, $J = 12.5$, 11.5, 3.5 Hz, 1H; 3′-H), 3.31 (ddd, $J = 13.0$, 11.5, 3.5 Hz, 1H; 1′-H), 4.22 (dd, $J = 9.0$, 7.5 Hz, 1H; 5-H), 4.24 (t, $J = 11.5$ Hz, 1H; 2′-H), 4.31 (dd, $J = 9.0$, 1.5 Hz, 1H; 5-H), 4.54 (dd, $J = 7.5$, 1.5 Hz, 1H; 4-H), 7.19–7.56 (m, 5H; phenyl-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 21.95$ (C-5′-Me), 24.7, 27.2 (piperidine-CH_2), 25.8 (*t*Bu), 31.2 (C-5′), 32.1 (C-4′), 35.9 (*t*Bu), 42.0 (C-6′), 48.5, 49.4 (C-1′, C-2′), 51.05 (piperidine-NCH), 62.0 (C-4), 65.2 (C-5), 68.8 (C-3′), 127.5, 128.7, 133.1, 134.3 (phenyl-C), 154.9 (C-2), 175.8 (C=O); MS (70 eV, EI): *m*/*z* (%): 458 (<1) [M^+], 457 (<1) [$M^+ - H$], 443 (<1) [$M^+ - Me$], 349 (100) [$M^+ - SPh$]; elemental analysis calcd (%) for $C_{26}H_{38}N_2O_3S$ (458.66): C 68.09, H 8.35; found: C 67.91, H 8.28.

Cyclohexanol thioester 6: Benzyl mercaptan (23 μL, 0.20 mmol) was dissolved in THF (0.5 mL), and butyllithium (2.5M in hexane, 64 μL, 0.16 mmol) was added at 0 °C. After 10 min, cyclohexanol **3d** (25 mg, 0.064 mmol) dissolved in THF (0.5 mL) was added at 0 °C, and the reaction mixture was stirred for 15 h at RT. 2M NaOH solution was added, the layers were separated, and the aqueous phase was extracted with ether. The combined organic extracts were dried over $MgSO_4$, filtered, and evaporated. Column chromatography over silica gel (diethyl ether/pentane 1:1) gave thioester **6** (17 mg, 71%) as a colorless oil. IR (film): $\tilde{\nu} = 3460$ (OH), 2960 (CH_3), 1682 (C=O), 1125, 1042 cm^{-1} (C–O); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 0.88$ (d, $J = 6.5$ Hz, 3H; 5-CH_3), 1.02–1.30 (m, 2H), 1.80–2.40 (m, 4H), 2.87 (dd, $J = 11.5$, 2.0 Hz, 1H; 2-H), 3.68 (td, $J = 11.5$, 3.5 Hz, 1H; 1-H), 3.90 (br s, 1H; 3-H), 4.07 (d, $J = 14.0$ Hz, 1H; S-CH_2-Ph), 4.12 (d, $J = 14.0$ Hz, 1H; S-CH_2-Ph), 7.13–7.45 (m, 10H; phenyl-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 21.5$ (CH_3), 26.0 (C-5), 33.1 (C-2), 39.25, 42.1 (C-4, C-6), 45.3, 51.97 (C-1, SCH_2), 68.0 (C-3), 127.1, 127.4, 128.0, 128.8, 129.2, 132.9, 134.0, 135.2 (phenyl-C), 202.1 (C=O); MS (200 eV, DCI/NH_3): *m*/*z* (%): 390 (100) [$M^+ + NH_4^+$]; elemental analysis calcd (%) for $C_{21}H_{24}O_2S_2$ (372.42): C 67.73, H 6.50; found: C 67.95, H 6.48.

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