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On the scope of diastereoselective epoxidation of various chiral auxiliaries derived enones: the conformational analysis of camphor derived *N*- and *O*-enones

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Dedicated to Professor A. B. Smith (University of Pennsylvania) on the occasion of his 60th birthday

Abstract—Various camphor derived *N*- and *O*-enones were treated with selected oxidants to provide the corresponding epoxides in a wide range of diastereoselectivity. For camphorsultam derived activated alkenes, high to excellent stereoselectivities were obtained when the *s-trans* enones were treated with methyl(trifluoromethyl)dioxirane. On the other hand, for *exo*-10,10-diphenyl-2,10-camphanediol (**3**) and *exo*-10,10-diphenyl-10-methoxy-2-camphanol (**4**) derived alkenes, the use of *s-cis* enones gave the desired epoxide with excellent diastereoselectivity under the same reaction conditions. The stereoselectivity was highly dependent on the geometry of the auxiliaries derived enones and the stereochemical induction is discussed.

1. Introduction

The development of efficient methods for the synthesis of nonracemic chiral epoxides is of considerable interest, since they are important building blocks in organic synthesis.[1] The asymmetric epoxidation of allylic alcohols,[2] the metal-catalyzed epoxidation of unfunctionalized olefins,[3] and the nucleophilic epoxidation of α,β-enones[4] have been well documented. In spite of the fact that much progress have been achieved, an efficient system for the diastereoselective epoxidation of a compound bearing a chiral auxiliary is still in demand particularly for electron-deficient olefins. Oppolzer camphorsultam (**1**) is among the most promising chiral auxiliaries presently available for asymmetric reactions and, we were surprised to find a near absence of studies of the asymmetric epoxidation of camphorsultam derived *N*-enones.[5] Three novel camphor-derived auxiliaries [camphorpyrazolidinone (**2**), *exo*-10,10-diphenyl-2,10-camphanediol (**3**) and *exo*-10,10-diphenyl-10-methoxy-2-camphanol (**4**)] were developed in this laboratory and have proved to be synthetically useful for asymmetric syntheses leading to a high degree of stereoselectivity (Fig. 1).[6] We recently reported on the diastereoselective epoxidation of camphorpyrazolidinone derived *N*-enones using a urea hydrogen peroxide complex (UHP) in the presence of trifluoroacetic anhydride (TFAA).[7] A wide range of selectivities were obtained for various chiral alkene substituents. In addition, both epoxide diastereomers were produced in high optical purity when *N*-methacryloyl camphorpyrazolidinone and *N*-tigloyl camphorpyrazolidinone were treated with UHP/TFAA and methyl(trifluoromethyl)dioxirane, respectively.[8] The synthesis of both enantiomerically enriched stereoisomers without resorting to the use of an enantiomeric chiral resource is attractive in asymmetric syntheses.[9,8,6b] We wish to report here on the scope of the epoxidation with respect to substituent tolerance on chiral auxiliaries. In general, for electron deficient alkenes high material yields were obtained when methyl(trifluoromethyl)dioxirane was used. Stereoselectivity is highly dependent on the geometry of the auxiliaries derived enones. Stereochemical bias will be discussed.

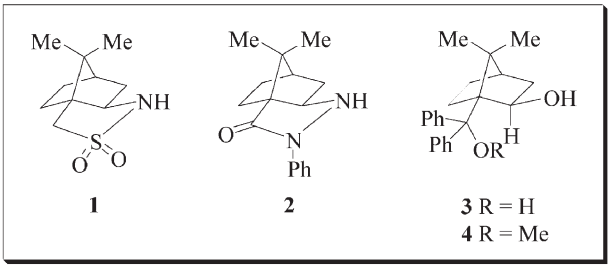

Figure 1.

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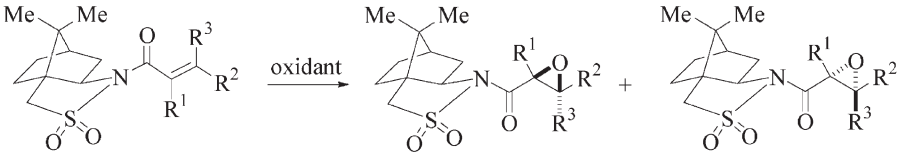
2. Results and discussion

Various chiral enones **5**–**7** can be readily prepared from the corresponding auxiliaries (**1**, **3**, and **4**) using standard acylation conditions. Three commonly used oxidants were investigated. Treatment of camphorsultam derived acrylate (**5a**, R^1=R^2=R^3=H) with in situ generated dioxirane gave the desired epoxide in low stereoselectivity (Table 1, entry 1). The use of β-substituent substrates provide the desired products with low to moderate selectivities (entries 2–4). The use of monoethyl fumaroyl camphorsultam failed to give the desired product (entry 5). This is due to the relatively poor electron density of the olefin. The selectivity was significantly improved when α-substituent substrates were used. Thus, excellent diastereoselectivity was obtained when *N*-methacryloylsultam (**5f**) was used (entry 6). The diastereoselectivity was determined to be greater than 90% de based on an ^{1}H NMR analysis of the relevant peaks. The opposite sense of diastereoselectivity was observed when the epoxidation was carried out with UHP/TFAA (entry 7). This is analogous to our previous studies in which camphorpyrazolidinone was used as a chiral auxiliary.[8] The absolute stereochemistry of the newly generated stereogenic center of both diastereomers was determined by single crystal X-ray analysis. The use of *N*-tigloylsultam (**5g**) also provide the desired epoxide in excellent stereoselectivity (entry 9). A similar phenomena was observed when the α-methy β-ethyl substituted substrate (**5h**) was treated with these two different oxidants (entries 11 and 12). Surprisingly, the use of the β,β-dimethyl substituted alkene provide the desired product in excellent stereoselectivity with the *R* configuration predominating (entry 13). The stereoselectivity dropped significantly when the reaction was carried out with the UHP/TFAA system (entry 14). In most cases, both of the diastereomeric epoxides were crystalline and could be easily recrystallized for a single crystal X-ray analysis.

An appropriate disposition of the α,β-enone functionality is extremely critical in determining the transition state structure in epoxidation reactions that affect stereodifferentiation. The conformational preference of amide linked enones is different from those of ester linked unsaturated alkenes. The reaction conditions (reagents, H-bonding, solvent polarity and etc), of course, also contribute to determining the product stereoselectivity. We then further examined the epoxidation of the *exo*-10,10-diphenyl-2,10-camphanediol (**3**) and *exo*-10,10-diphenyl-10-methoxy-2-camphanol (**4**) derived *O*-enones. Treatment of auxiliary **3** derived acrylate with methyl(trifluoromethyl)dioxirane provided the desired product in low material yield (Table 2, entry 1). The use of crotonoyl *O*-enone **6b** under the same reaction conditions afforded the desired epoxide in 82% material yield in good stereoselectivity (entry 2). The absolute stereochemistry of the newly generated stereogenic center was determined to be the (*R*, *S*) configuration based on a single crystal X-ray analysis. Similar results were obtained with β-substituted substrates (entries 3 and 4). Excellent stereoselectivity was obtained when the β,β-disubstituted substrate (**6e**) was used (entry 5). The use of UHP/TFAA as an oxidant failed to give the desired epoxide (entry 6). In contrast to the camphorsultam and camphorpyrazolidinone derived α-substituted substrates which afford the desired products in high to excellent stereoselectivity (Table 1, entries 6, 9 and 11) similar substituent substrates derived from auxiliary **3**

Table 1. Asymmetric epoxidation of chiral camphorsultam derived *N*-enones **5a**–**i** under different epoxidation conditions[a]

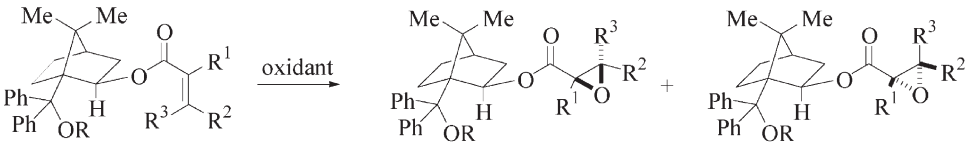


5a-i **8a-i** **9a-i**

Entry	R^1, R^2, R^3	Oxidant[b]	*t*/h	Yield (%)[c]	**8**:**9**[d]
1	**5a** R^1=R^2=R^3=H	A	10	60	31:69
2	**5b** R^1=H, R^2=Me, R^3=H	A	10	86	40:60
3	**5c** R^1=H, R^2=Pr, R^3=H	A	9	88	40[e]:60
4	**5d** R^1=H, R^2=Ph, R^3=H	A	8	91	19:81[e]
5	**5e** R^1=H, R^2=COOEt, R^3=H	A	3	0	—
6	**5f** R^1=Me, R^2=R^3=H	A	3	90	>95[e]:05
7	**5f** R^1=Me R^2=R^3=H	B	6	42	31:69[e]
8	**5f** R^1=Me R^2=R^3=H	C	4 d	88	67:33
9	**5g** R^1=R^2=Me R^3=H	A	2	95	>95[e]:05
10	**5g** R^1=R^2=Me, R^3=H	B	2	90	12:88[e]
11	**5h** R^1=Me, R^2=Et, R^3=H	A	2	99	>95[e]:05
12	**5h** R^1=Me, R^2=Et, R^3=H	B	1	99	17:83[e]
13	**5i** R^1=H, R^2=R^3=Me	A	2	97	<05:95[e]
14	**5i** R^1=H, R^2=R^3=Me	B	$\frac{1}{4}$	96	31[e]:69

[a] Unless specifically noted, all reactions were carried out with substrate **5** (0.17 mmol) at 0 °C.
[b] Method A: in situ generated dioxirane [1,1,1-trifluoroacetone (33.0 equiv.), Oxone (4.0 equiv.), Na_2EDTA (aq.), $NaHCO_3$] was used in aq. CH_3CN.; method B: UHP/TFAA (20.0/5.0 equiv.) in CH_2Cl_2; method C: *m*CPBA (6.0 equiv.) in CH_2Cl_2.
[c] Isolated yield.
[d] Determined by ^{1}H NMR analysis of relevant peaks.
[e] Absolute stereochemistry was determined by single crystal X-ray analysis.

Table 2. Asymmetric epoxidation of chiral camphor derived *O*-enones **6** and **7** under different epoxidation conditions[a]



6a-h R = H
7a-b R = Me

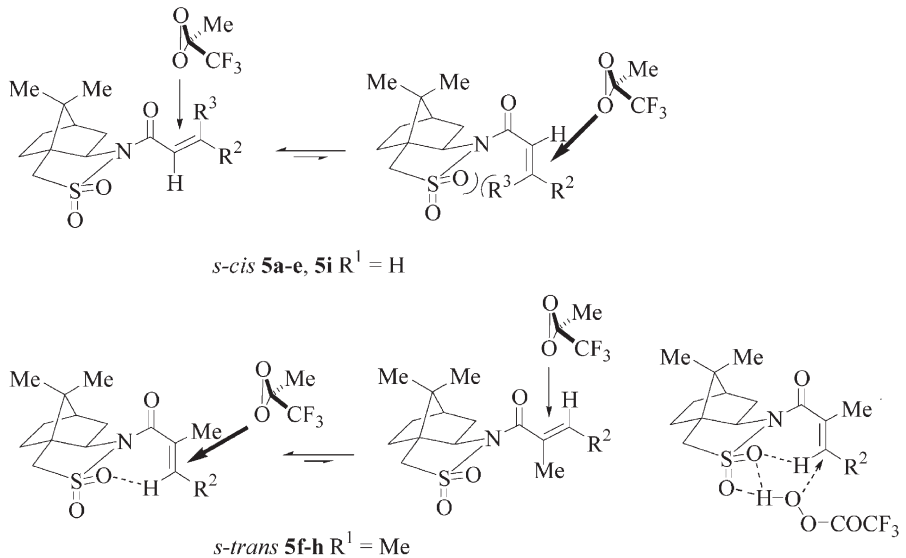
10a-h **11a-h**

Entry	R^1, R^2, R^3	Oxidant[b]	*t*/*h*	Yield (%)[c]	**10**:**11**[d]
1	**6a** R^1=R^2 =R^3=H	A	6	34	nd[e]
2	**6b** R^1=H, R^2=Me, R^3=H	A	4	82	88[f]:12
3	**6c** R^1=H, R^2=Pr, R^3=H	A	4	66	85[f]:15
4	**6d** R^1=H, R^2=Ph, R^3=H	A	2	94	93:07[f]
5	**6e** R^1=H, R^2=R^3=Me	A	2	96	>95[f]:05
6	**6e** R^1=H, R^2=R^3=Me	B	2	0	—
7	**6e** R^1=H, R^2=R^3=Me	C	3 d	85	77:23
8	**6f** R^1=Me R^2=R^3=H	A	2	95	61:39
9	**6g** R^1=R^2=Me, R^3=H	A	4	96	57:43
10	**6h** R^1=Me R^2=Et, R^3=H	A	6	80	64:36
11	**7a** R^1=H, R^2=R^3=Me	A	3	74	96:04
12	**7b** R^1=H, R^2=Ph, R^3=H	A	3	68	69:31

[a] Unless specifically noted, all reactions were carried out with substrate **6** or **7** (0.12 mmol) at 0 °C.
[b] Method A: in situ generated dioxirane [1,1,1-trifluoroacetone (47.0 equiv.), oxone (2.0 equiv.), Na_2EDTA (aq.), $NaHCO_3$] is used in aq. CH_3CN.; method B: UHP/TFAA (20.0/6.0 equiv.) in CH_2Cl_2; method C: *m*CPBA (6.0 equiv.) in CH_2Cl_2.
[c] Isolated yield.
[d] Determined by ^{1}H NMR analysis of relevant peaks.
[e] Not determined.
[f] Absolute stereochemistry was determined by single crystal X-ray analysis.

afforded the desired product in only moderate stereoselectivity (entries 8–10). The auxiliary **4** derived β,β-disubstituted enone (**7a**) provide the desired epoxide in 92% de (entry 11).

The geometry of camphorsultam conjugated enones have been studied by both Oppolzer[10] and Curren.[11] For α-unsubstituted *N*-enones, the planar *s-cis* arrangement predominates (*s-cis* **5a–e** and **5i**) while the nonplanar *s-trans*-like conformation is energetically favoured for α-substituted and α,β-disubstituted auxiliaries in the solid state conformation (*s-trans* **5f–h**; Fig. 2). The carbonyl group is oriented away from the sulfonyl moiety to minimize the unfavored dipole repulsions. It is interesting to note that, similar to camphorpyrazolidinone derived *N*-enones,[7a,8] *s-trans N*-enones **5f–h** give the epoxides in high to excellent diastereoselectivity (Table 1, entries 6, 9 and 11). The structural similarity of the α,β-enone moiety may account for the observed stereoinduction. For *s-cis* **5a–e** and **5i** an attack of methyl(trifluoromethyl)dioxirane from the top Cα *re* face gives the desired major epoxides. It is believed that this avoids electronic repulsion between the dioxirane and the α-sulfonyl oxygen atom. The low to moderate selectivity obtained with *s-cis N*-enones **5** may be due to the relative rapid equilibrium between the *s-cis N*-enones with their *s-trans* counter conformers. The fact



s-cis **5a-e**, **5i** R^1 = H

s-trans **5f-h** R^1 = Me

Figure 2. Proposed mechanism for the asymmetric epoxidation of various camphorsultam derived *N*-enones **5**.

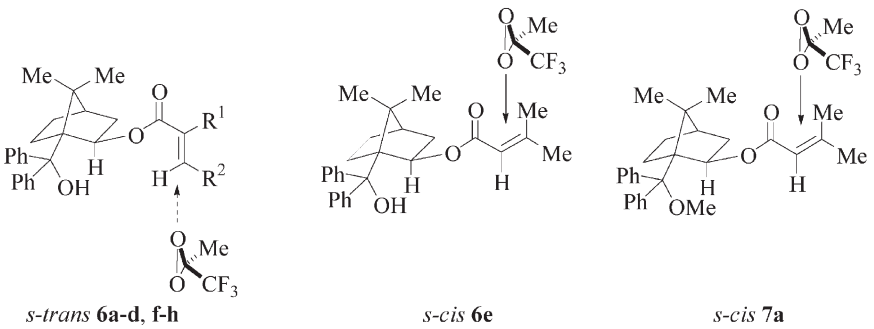


Figure 3. Proposed mechanism for the asymmetric epoxidation of the *exo*-10,10-diphenyl-2,10-camphanediol (**3**) and *exo*-10,10-diphenyl-10-methoxy-2-camphanol (**4**) derived *O*-enones **6** and **7**.

that the β,β-dimethyl substituent **5i** afforded the desired epoxide in excellent diastereoselectivity can be explained by steric interactions between the sulfonyl group with one of the β-methyl groups (Table 1, entry 13 and Fig. 2). The *s-cis* conformation in **5i** is energetically favored for the dioxirane to attack from the Cα *re* face. On the other hand, the dioxirane attacks the *s-trans* enone from the top Cα *si* face. In general, high to excellent stereoselectivity was achieved (Table 1, entries 6, 9 and 11). The intramolecular stabilization of the *s-trans* conformation between the sulfonyl group and Cβ hydrogen may contribute to the high stereoselectivity. Further, the opposite sense of diastereoselectivity was observed when *s-trans* substrates were epoxidized with UHP/TFAA. This may be due to H-bonding between the UHP/TFAA oxidant and the sulfonyl group that directs the transfer of oxygen atom from the Cα *re* face.

In contrast to the *N*-enone functionality, *exo*-10,10-diphenyl-2,10-camphanediol (**3**) and *exo*-10,10-diphenyl-10-methoxy-2-camphanol (**4**) derived *O*-enones moiety favor the *s-trans* disposition (Fig. 3). The X-ray diffraction analyses of **6b**–**c**,**f**–**g** confirmed the conformation in the solid state. On the other hand, for the β,β-dimethyl substituted **6e**, the *s-cis* conformation is energetically favored as indicated by single crystal X-ray analysis. The in situ generated methyl(trifluoromethyl)dioxirane approaches the double bond from the less hindered bottom Cα *re* face for the *s-trans* enones **6a**–**d**,**f**–**h** and from the top Cα *re* face for **6e**. The high stereoselectivity obtained for the β,β-dimethyl substituted **6e** may be due to a significant conformational change, analogous to the camphorsultam derived β,β-dimethyl substituted **5i**. A similar explanation can be applied to the β,β-dimethyl substrate **7a** derived from *exo*-10,10-diphenyl-10-methoxy-2-camphanol.

3. Conclusion

In summary, the epoxidation of various camphor derived *N*- and *O*-enones have been studied, to achieve a wide range of stereoselectivity (up to 90% de). High to excellent selectivity was obtained for α-substituted and α,β-disubstituted substrates derived from camphorsultam when methyl(trifluoromethyl)dioxirane was used. The opposite diastereoselectivity was observed when these substrates were treated with UHP/TFAA. On the other hand, a high stereoselectivity was obtained in the case of β,β-dimethyl substituted *O*-enones derived from *exo*-10,10-diphenyl-2,10-camphanediol (**3**) and *exo*-10,10-diphenyl-10-methoxy-2-camphanol (**4**) when methyl(trifluoromethyl)-dioxirane was used.

4. Experimental

4.1. General methods

All reactions were carried out in flame or oven-dried glassware under a positive pressure of nitrogen. Air- and moisture-sensitive compounds were introduced by the use of a cannula through a rubber septum. Most reagents were commercially available and were of synthetic grade. Tetrahydrofuran was distilled from sodium/benzophenone ketyl. Dichloromethane and toluene were dried over CaH_2 and distilled before use. Analytical thin layer chromatography was performed using silica gel 60F glass plates and flash column chromatography was performed using silica gel 60 (230–400 mesh). HRMS values were measured either by chemical ionization (MS-CI) or electronic impact (MS-EI). Elemental analyses were performed by Taipei Instrumentation Center, College of Science (National Taiwan University). ^1H and ^{13}C NMR spectra were recorded routinely in $CDCl_3$ on a 200 or 400 MHz instrument.

Crystallographic data for the structures in this paper have been deposited at the Cambridge Crystallographic Data Center and allocated the deposit numbers CCDC 239702–239714.[12]

4.2. General procedure for the epoxidation of various camphor derived *N*- and *O*-enones

Method A. To a solution of the *N*-tigloylsultam **5g** (50 mg, 0.17 mmol) in CH_3CN (1.5 mL), aq. Na_2EDTA (1.0 mL, 4×10^{-4} M), was added 1,1,1-trifluoroacetone (0.5 mL, 5.59 mmol) at 0 °C. This was followed by the addition of Oxone (210 mg, 0.34 mmol) and $NaHCO_3$ (85 mg, 1.01 mmol) in one portion. The reaction was monitored by TLC (hexanes/EtOAc=4/1) and additional portions of Oxone/$NaHCO_3$ (1/3) were added at 1 h intervals until the reaction was complete (a total of 4 equiv. of Oxone was used). The resulting solution was extracted with EtOAc (30 mL) and the layers separated. The organic layer was washed with brine (10 mL), dried ($MgSO_4$) and concentrated. The crude product was purified by silica gel

chromatography using hexanes/EtOAc as the eluent (4/1) to give a total of 50.0 mg (95%) of epoxides (>90% de by ^{1}H NMR analysis of crude mixtures) as a white solid.

Method B. To a solution of the *N*-tigloylsultam **5g** (50 mg, 0.17 mmol) in CH_2Cl_2 (2 mL) was added urea-hydrogen peroxide complex (316 mg, 3.36 mmol) at 0 °C. TFAA (0.12 mL, 0.84 mmol) was added to this mixture over 2 h and the reaction was then quenched with aq. $NaHCO_3$ (10 mL). The resulting solution was extracted with CH_2Cl_2 (50 mL) and the layers separated. The organic layer was washed with brine (10 mL), dried ($MgSO_4$) and concentrated. The crude product was purified by silica gel chromatography using hexanes/EtOAc as the eluent (4/1) to give a total of 47.4 mg (90%) of epoxides (76% de by ^{1}H NMR analysis of crude mixtures) as a white solid.

4.2.1. Compound 8g. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.89 (dd, 1H, J=7.5, 5.4 Hz), 3.49 (q, 1H, J=5.4 Hz), 3.47 (d, 1H, J=13.9 Hz), 3.45 (d, 1H, J=13.8 Hz), 2.14–2.03 (m, 2H), 1.96–1.86 (m, 3H), 1.56 (s, 3H), 1.45–1.40 (m, 1H), 1.35 (d, 3H, J=5.4 Hz), 1.40–1.31 (m, 1H), 1.10 (s, 3H), 0.97 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 65.3, 60.7, 59.0, 53.1, 48.8, 47.8, 44.5, 38.2, 32.8, 26.3, 20.7, 19.8, 14.3, 12.8; HRMS *m/z* 313.1388 (calcd for $C_{15}H_{23}NO_4S$: 313.1348) Anal. Calcd for $C_{15}H_{23}NO_4S$: C, 57.48; H, 7.40; N, 4.47; S, 10.23. Found: C, 57.50; H, 7.24; N, 4.35; S, 10.08. Crystal data for **8g** at 25 °C: $C_{15}H_{23}NO_4S$, M 313.41, monoclinic, $P2_1$, a=8.6983 (21) Å, b=7.8284 (21) Å, c=11.860 (3) Å, V=786.1 (4) Å^3, Z=2, λ=0.70930 Å, D_c=1.324 Mg/m^3, μ=0.22 mm^{-1}, 1566 reflections, 190 parameters, R=0.048, R_w=0.052 for all data.

4.2.2. Compound 9g. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.91 (dd, 1H, J=7.6, 4.9 Hz), 3.45 (d, 1H, J=13.7 Hz), 3.41 (d, 1H, J=13.7 Hz), 3.33 (q, 1H, J=5.4 Hz), 2.08 (dd, 1H, J=13.8, 7.8 Hz), 2.03–1.98 (m, 1H), 1.93–1.89 (m, 3H), 1.57 (s, 3H), 1.46–1.32 (m, 2H), 1.39 (d, 3H, J=5.3 Hz), 1.16 (s, 3H), 0.97 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.8, 65.0, 60.7, 58.2, 53.1, 48.7, 47.8, 44.6, 38.0, 32.7, 26.4, 20.7, 19.8, 14.8, 12.9; HRMS *m/z* 313.1337 (calcd for $C_{15}H_{23}NO_4S$: 313.1348). Crystal data for **9g** at 25 °C: $C_{15}H_{23}NO_4S$, M 313.416, triclinic, $P1$, a=8.1182 (3) Å, b=9.1785 (3) Å, c=11.3661 (4) Å, V=791.17 (5) Å^3, Z=2, λ=0.71073 Å, D_c=1.316 Mg/m^3, μ=0.22 mm^{-1}, 3248 reflections, 380 parameters, R=0.040, R_w=0.095 for all data.

4.2.3. Compounds 8a and 9a. Inseperable diastereomeric mixture: HRMS *m/z* 285.1025 (calcd for $C_{13}H_{19}NO_4S$: 285.1035).

4.2.4. Compounds 8b and 9b. Inseperable diastereomeric mixture: HRMS *m/z* 299.1193 (calcd for $C_{14}H_{21}NO_4S$: 299.1191).

4.2.5. Compound 8c. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.93 (dd, 1H, J=7.3, 5.4 Hz), 3.86 (d, 1H, J=1.8 Hz), 3.53 (d, 1H, J=13.8 Hz), 3.51 (d, 1H, J=13.9 Hz), 3.18 (ddd, 1H, J=6.5, 4.3, 1.9 Hz), 2.16–2.06 (m, 2H), 1.98–1.88 (m 3H), 1.71–1.56 (m. 2H), 1.55–1.30 (m, 4H), 1.14 (s, 3H), 0.98 (s, 3H), 0.96 (t, 3H, J=7.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.1, 65.2, 59.2, 53.1, 52.8, 49.1, 47.7, 44.6, 38.0, 33.2, 32.7, 26.3, 20.7, 19.8, 18.8, 13.6; HRMS *m/z* 327.1498 (calcd for $C_{16}H_{25}NO_4S$: 327.1504). Crystal data for **8c** at 25 °C: $C_{16}H_{25}NO_4S$, M 327.443, orthorhombic, $P2_12_12_1$, a=7.8466 (6) Å, b=12.9765 (10) Å, c=16.603 (2) Å, V=1690.5 (3) Å^3, Z=4, λ=0.71073 Å, D_c=1.287 Mg/m^3, μ=0.21 mm^{-1}, 1215 reflections, 200 parameters, R=0.055, R_w=0.095 for all data.

4.2.6. Compound 9c. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.89 (dd, 1H, J=7.7, 5.0 Hz), 3.81 (d, 1H, J=1.9 Hz), 3.52 (d, 1H, J=13.8 Hz), 3.46 (d, 1H, J=13.8 Hz), 3.12 (ddd, 1H, J=6.2, 4.6, 1.9 Hz), 2.18–2.12 (m, 1H), 2.09 (dd, 1H, J=13.9, 7.8 Hz), 1.94–1.87 (m, 3H), 1.75–1.69 (m, 1H), 1.62–1.48 (m, 3H), 1.45–1.32 (m, 2H), 1.19 (s, 3H), 0.98 (s, 3H), 0.96 (t, 3H, J=7.3 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.5, 65.0, 59.8, 53.3, 52.8, 49.2, 47.8, 44.6, 38.0, 33.4, 32.7, 26.3, 20.7, 19.8, 18.6, 13.7; HRMS *m/z* 327.1500 (calcd for $C_{16}H_{25}NO_4S$: 327.1504).

4.2.7. Compound 9d. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38–7.32 (m, 5H), 4.09 (d, 1H, J=1.8 Hz), 4.07 (d, 1H, J=1.8 Hz), 3.95 (dd, 1H, J=7.8, 5.0 Hz), 3.49 (d, 1H, J=13.8 Hz), 3.44 (d, 1H, J=13.8 Hz), 2.22–2.16 (m, 1H), 2.12 (dd, 1H, J=13.9, 7.8 Hz), 1.97–1.86 (m, 3H), 1.46–1.33 (m, 2H), 1.19 (s, 3H), 0.98 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.4, 134.7, 128.8, 128.5, 126.0, 65.1, 59.3, 56.6, 52.9, 49.3, 47.9, 44.7, 38.1, 32.8, 26.4, 20.8, 19.8; HRMS *m/z* 361.1342 (calcd for $C_{19}H_{23}NO_4S$: 361.1348) Anal. Calcd for $C_{19}H_{23}NO_4S$: C, 63.13; H, 6.41; N, 3.88; S, 8.87. Found: C, 63.14; H, 6.37; N, 3.76; S, 8.72. Crystal data for **9d** at 25 °C: $C_{19}H_{23}NO_4S$, M 361.45, monoclinic, $P2_1$, a=7.793 (10) Å, b=13.251 (6) Å, c=18.037 (4) Å, V=1827 (3) Å^3, Z=4, λ=0.70930 Å, D_c=1.314 Mg/m^3, μ=0.20 mm^{-1}, 3472 reflections, 451 parameters, R=0.049, R_w=0.055 for all data.

4.2.8. Compound 8f. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.90 (dd, 1H, J=6.9, 6.9 Hz), 3.49 (d, 1H, J=13.7 Hz), 3.46 (d, 1H, J=13.7 Hz), 3.31 (d, 1H, J=4.2 Hz), 2.88 (d, 1H, J=4.2 Hz), 2.11–2.03 (m, 2H), 1.97–1.87 (m, 3H), 1.64 (s, 3H), 1.46–1.31 (m, 2H), 1.11 (s, 3H), 0.97 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0, 65.4, 57.2, 53.6, 53.1, 48.8, 47.8, 44.6, 38.2, 32.9, 26.3, 20.7, 19.8, 18.8; HRMS *m/z* 299.1200 (calcd for $C_{14}H_{21}NO_4S$: 299.1191). Crystal data for **8f** at 25 °C: $C_{14}H_{21}NO_4S$, M 299.389, monoclinic, $P2_1$, a=16.3325 (5) Å, b=11.3516 (3) Å, c=16.9962 (6) Å, V=3094.2 (2) Å^3, Z=8, λ=0.71073 Å, D_c=1.285 Mg/m^3, μ=0.22 mm^{-1}, 3869 reflections, 716 parameters, R=0.063, R_w=0.104 for all data.

4.2.9. Compound 9f. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.93 (dd, 1H, J=7.6, 4.8 Hz), 3.48 (d, 1H, J=13.6 Hz), 3.43 (d, 1H, J=13.6 Hz), 3.14 (d, 1H, J=5.2 Hz), 2.90 (d, 1H, J=5.2 Hz), 2.08 (dd, 1H, J=13.8, 7.8 Hz), 2.04–1.86 (m, 4H), 1.66 (s, 3H), 1.46–1.33 (m, 2H), 1.16 (s, 3H), 0.98 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.8, 65.2, 57.3, 53.2, 53.1, 48.7, 47.8, 44.6, 38.1, 32.8, 26.4, 20.7, 19.8, 19.2; HRMS *m/z* 299.1192 (calcd for $C_{14}H_{21}NO_4S$: 299.1191). Crystal data for **9f** at 25 °C: $C_{14}H_{21}NO_4S$, M 299.389, orthorhombic, $P2_12_12_1$, a=12.2654 (2) Å, b=15.2353 (2) Å, c=24.3218 (4) Å, V=4544.94 (12) Å^3, Z=12, λ=0.71073 Å, D_c=1.313 Mg/m^3, μ=0.23 mm^{-1}, 3256 reflections, 542 parameters, R=0.051, R_w=0.081 for all data.

4.2.10. Compound 8h. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.89 (dd, 1H, J=7.6, 2.4 Hz), 3.47 (d, 1H, J=14.0 Hz), 3.45 (d, 1H, J=14.0 Hz), 3.34 (dd, 1H, J=7.6, 4.8 Hz), 2.14–2.03 (m, 2H), 1.96–1.86 (m, 3H), 1.79–1.68 (m, 1H), 1.56 (s, 3H), 1.54–1.46 (m, 1H), 1.45–1.25 (m, 2H), 1.12 (s, 3H), 1.08 (t, 3H, J=7.6 Hz), 0.97 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 65.4, 63.9, 61.3, 53.1, 48.8, 47.7, 44.5, 38.2, 32.9, 26.3, 21.0, 20.8, 19.8, 14.5, 10.3; HRMS m/z 327.1484 (calcd for $C_{16}H_{25}NO_4S$: 327.1504) Anal. Calcd for $C_{16}H_{25}NO_4S$: C, 58.69; H, 7.70; N, 4.28; S, 9.79. Found: C, 58.92; H, 7.48; N, 4.30; S, 9.88. Crystal data for **8h** at 25 °C: $C_{16}H_{25}NO_4S$, M 327.43, orthorhombic, $P2_12_12_1$, a=6.918 (4) Å, b=11.0011 (21) Å, c=22.216 (4) Å, V=1690.8 (11) Å^3, Z=4, λ=0.70930 Å, D_c=1.286 Mg/m^3, μ=0.21 mm^{-1}, 1733 reflections, 200 parameters, R=0.045, R_w=0.044 for all data.

4.2.11. Compound 9h. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.92 (dd, 1H, J=7.7, 4.9 Hz), 3.46 (d, 1H, J=13.7 Hz), 3.42 (d, 1H, J=13.7 Hz), 3.15 (dd, 1H, J=6.9, 5.3 Hz), 2.07 (dd, 1H, J=13.8, 7.8 Hz), 2.03–1.96 (m, 1H), 1.94–1.85 (m, 3H), 1.74–1.67 (m, 1H), 1.62–1.53 (m, 1H), 1.58 (s, 3H), 1.46–1.32 (m, 2H), 1.16 (s, 3H), 1.09 (t, 3H, J=7.6 Hz), 0.98 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.7, 65.0, 63.3, 61.1, 53.0, 48.6, 47.7, 44.5, 38.0, 32.7, 26.3, 21.0, 20.6, 19.7, 14.9, 10.1; HRMS m/z 327.1497 (calcd for $C_{16}H_{25}NO_4S$: 327.1504). Crystal data for **9h** at 25 °C: $C_{16}H_{25}NO_4S$, M 327.443, monoclinic, $P2_1$, a=12.7086 (4) Å, b=7.0864 (2) Å, c=19.3559 (7) Å, V=1716.41 (10) Å^3, Z=4, λ=0.71073 Å, D_c=1.267 Mg/m^3, μ=0.20 mm^{-1}, 2242 reflections, 398 parameters, R=0.042, R_w=0.086 for all data.

4.2.12. Compound 8i. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.92 (dd, 1H, J=7.5, 5.4 Hz), 3.89 (s, 1H), 3.50 (d, 1H, J=13.9 Hz), 3.49 (d, 1H, J=13.9 Hz), 2.21–2.10 (m, 2H), 1.97–1.87 (m, 3H), 1.46–1.32 (m, 2H), 1.45 (s, 3H), 1.28 (s, 3H), 1.12 (s, 3H), 0.98 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.9, 65.0, 61.0, 60.6, 52.7, 49.4, 47.8, 44.5, 38.2, 32.7, 26.3, 23.5, 20.6, 19.8, 18.5; HRMS m/z 313.1345 (calcd for $C_{15}H_{23}NO_4S$: 313.1348). Crystal data for **8i** at 25 °C: $C_{15}H_{23}NO_4S$, M 313.41, orthorhombic, $P2_12_12_1$, a=7.897 (4) Å, b=13.0751 (25) Å, c=15.743 (3) Å, V=1625.6 (8) Å^3, Z=4, λ=0.70930 Å, D_c=1.281 Mg/m^3, μ=0.21 mm^{-1}, 1658 reflections, 191 parameters, R=0.068, R_w=0.102 for all data.

4.2.13. Compound 9i. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.09 (dd, 1H, J=7.6, 5.1 Hz), 3.84 (s, 1H), 3.50 (d, 1H, J=13.8 Hz), 3.45 (d, 1H, J=13.8 Hz), 2.21–2.14 (m, 1H), 2.11 (dd, 1H, J=13.9, 7.8 Hz), 1.97–1.86 (m, 3H), 1.46 (s, 3H), 1.44–1.32 (m, 2H), 1.30 (s, 3H), 1.19 (s, 3H), 0.98 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.7, 64.8, 62.2, 60.2, 52.8, 49.2, 47.8, 44.5, 38.0, 32.7, 26.4, 23.8, 20.6, 19.8, 18.1; HRMS m/z 313.1347 (calcd for $C_{15}H_{23}NO_4S$: 313.1348). Crystal data for **9i** at 25 °C: $C_{15}H_{23}NO_4S$, M 313.416, orthorhombic, $P2_12_12_1$, a=10.9353 (2) Å, b=13.8847 (3) Å, c=20.9791 (4) Å, V=3185.33 (11) Å^3, Z=8, λ=0.71073 Å, D_c=1.307 Mg/m^3, μ=0.22 mm^{-1}, 3034 reflections, 380 parameters, R=0.047, R_w=0.089 for all data.

4.2.14. Compound 10a. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.79 (dd, 2H, J=7.4, 1.1 Hz), 7.62 (dd, 2H, J=7.4, 1.2 Hz), 7.28 (t, 2H, J=7.4 Hz), 7.22 (t, 2H, J=7.2 Hz), 7.18–7.10 (m, 2H), 5.29 (dd, 1H, J=8.0, 3.6 Hz), 3.79 (br, 1H), 3.06 (dd, 1H, J=4.3, 2.3 Hz), 2.83 (dd, 1H, J=6.1, 4.4 Hz), 2.63 (dd, 1H, J=6.1, 2.2 Hz) 2.30 (td, 1H, J=12.5, 4.2 Hz), 1.99–1.91 (m, 1H), 1.89 (dd, 1H, J=13.7, 8.2 Hz), 1.77–1.72 (m, 1H), 1.67–1.63 (m, 1H), 1.51–1.49 (m, 1H), 1.47 (s, 3H), 1.17–1.11 (m, 1H), 0.64 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.5, 148.7, 143.2, 128.4, 127.9, 126.8, 126.5, 126.1, 82.1, 81.1, 59.3, 51.4, 47.7, 47.0, 46.2, 38.0, 31.0, 26.9, 24.4, 22.5; HRMS m/z 392.1953 (calcd for $C_{25}H_{28}O_4$: 392.1988).

4.2.15. Compound 11a. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.71 (dd, 2H, J=7.5, 1.1 Hz), 7.51 (dd, 2H, J=7.3, 1.2 Hz), 7.28–7.19 (m, 4H), 7.16–7.10 (m, 2H), 5.29 (dd, 1H, J=8.0, 3.7 Hz), 3.78 (br, 1H), 3.20 (q, 1H, J=2.3 Hz), 2.64 (dd, 1H, J=5.9, 4.6 Hz), 2.32–2.25 (m, 1H), 2.08 (dd, 1H, J=6.0, 2.3 Hz), 2.04 (dd, 1H, J=13.0, 8.0 Hz), 1.99–1.93 (m, 1H), 1.90–1.84 (m, 1H), 1.69–1.63 (m, 1H), 1.49 (s, 3H), 1.21–1.10 (m, 2H), 0.60 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.1, 149.8, 143.8, 128.5, 128.0, 126.7, 126.6, 126.3, 126.1, 83.1, 81.3, 58.7, 51.5, 47.6, 47.3, 45.4, 38.6, 31.0, 26.9, 24.6, 22.6.

4.2.16. Compound 10b. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.78 (dd, 2H, J=7.4, 1.0 Hz), 7.62 (dd, 2H, J=7.4, 1.2 Hz), 7.28 (t, 2H, J=7.4 Hz), 7.21 (t, 2H, J=7.2 Hz), 7.17–7.10 (m, 2H), 5.27 (dd, 1H, J=11.6, 3.6 Hz), 3.86 (br, 1H), 2.90 (qd, 1H, J=5.1, 1.8 Hz), 2.81 (d, 1H, J=1.8 Hz), 2.30 (td, 1H, J=12.4, 4.1 Hz), 1.99–1.92 (m, 1H), 1.88 (dd, 1H, J=13.7, 8.3 Hz), 1.77–1.72 (m, 1H), 1.66–1.62 (m, 1H), 1.51–1.48 (m, 1H), 1.47 (s, 3H), 1.33 (d, 3H, J=5.1 Hz), 1.17–1.11 (m, 1H), 0.63 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.5, 148.8, 143.2, 128.4, 127.9, 126.7, 126.5, 126.1, 81.8, 81.1, 59.2, 54.6, 53.6, 51.3, 47.6, 38.0, 30.9, 26.9, 24.5, 22.4, 17.0; HRMS m/z 406.2144 (calcd for $C_{26}H_{30}O_4$: 406.2144). Crystal data for **10b** at 25 °C: $C_{26}H_{30}O_4$, M 406.522, monoclinic, $C2$, a=16.2748 (6) Å, b=6.9261 (3) Å, c=20.7081 (9) Å, V=2206.3 (2) Å^3, Z=4, λ=0.71073 Å, D_c=1.224 Mg/m^3, μ=0.08 mm^{-1}, 1426 reflections, 272 parameters, R=0.059, R_w=0.151 for all data.

4.2.17. Compound 11b. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.70 (dd, 2H, J=7.5, 1.1 Hz), 7.51 (dd, 2H, J=7.4, 1.2 Hz), 7.27–7.19 (m, 4H), 7.15–7.12 (m, 2H), 5.27 (dd, 1H, J=13.2, 4.8 Hz), 3.83 (br, 1H), 2.93 (d, 1H, J=4.8 Hz), 2.31–2.24 (m, 2H), 2.02 (dd, 1H, J=13.7, 8.0 Hz), 1.98–1.92 (m, 1H), 1.88–1.83 (m, 1H), 1.67–1.62 (m, 1H), 1.48 (s, 3H), 1.20 (d, 3H, J=5.1 Hz), 1.22–1.14 (m, 2H), 0.59 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.1, 149.8, 143.8, 128.5, 127.9, 126.7, 126.5, 126.4, 126.1, 82.9, 81.3, 58.7, 53.8, 53.6, 51.5, 47.6, 38.6, 31.0, 26.9, 24.6, 22.6, 17.0.

4.2.18. Compound 10c. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.78 (dd, 2H, J=7.4, 1.1 Hz), 7.62 (dd, 2H, J=7.4, 1.2 Hz), 7.28 (t, 2H, J=7.4 Hz), 7.21 (t, 2H, J=7.2 Hz), 7.17–7.10 (m, 2H), 5.28 (dd, 1H, J=8.3, 3.6 Hz), 3.89 (br, 1H), 2.84–2.81 (m, 2H), 2.30 (td, 1H, J=12.5, 4.2 Hz), 1.98–1.95 (m, 1H), 1.89 (dd, 1H, J=13.6, 8.2 Hz), 1.77–1.72 (m, 1H), 1.65–1.57 (m, 1H), 1.56–1.51 (m, 2H), 1.48 (s, 3H), 1.50–1.41 (m, 3H), 1.17–1.13 (m, 1H), 0.95 (t, 3H, J=7.1 Hz), 0.63 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.6, 148.7, 143.3,

128.4, 127.9, 126.7, 126.5, 126.2, 126.1, 81.8, 81.1, 59.2, 58.3, 52.6, 51.3, 47.7, 38.0, 33.3, 30.9, 26.9, 24.5, 22.5, 18.9, 13.7; HRMS *m/z* 434.2441 (calcd for $C_{28}H_{34}O_4$: 434.2457). Crystal data for **10c** at 25 °C: $C_{28}H_{34}O_4$, *M* 434.57, monoclinic, *P212121*, *a*=9.2875 (20) Å, *b*=10.012 (3) Å, *c*=26.376 (6) Å, *V*=2452.6 (10) Å^3, *Z*=4, λ=0.70930 Å, D_c=1.177 Mg/m^3, μ=0.08 mm^{-1}, 2463 reflections, 290 parameters, *R*=0.048, R_w=0.045 for all data.

4.2.19. Compound 10d. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.79 (dd, 2H, *J*=7.4, 1.2 Hz), 7.62 (dd, 2H, *J*=7.4, 1.2 Hz), 7.38–7.33 (m, 2H), 7.29–7.16 (m, 7H), 7.13–7.10 (m, 2H), 5.34 (dd, 1H, *J*=8.1, 3.6 Hz), 3.81 (br, 1H), 3.74 (d, 1H, *J*=1.6 Hz), 3.15 (d, 1H, *J*=1.7 Hz), 2.32 (td, 1H, *J*=12.4, 4.2 Hz), 2.01–1.90 (m, 2H), 1.86–1.80 (m, 1H), 1.70–1.63 (m, 1H), 1.52 (s, 3H), 1.55–1.53 (m, 1H), 1.19–1.13 (m, 1H), 0.64 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.4, 148.8, 143.2, 134.4, 129.0, 128.6, 128.4, 128.0, 126.8, 126.5, 126.1, 125.8, 82.2, 81.1, 59.3, 57.9, 56.2, 51.4, 47.7, 38.1, 31.0, 26.9, 24.5, 22.5; HRMS *m/z* 468.2283 (calcd for $C_{31}H_{32}O_4$: 468.2301).

4.2.20. Compound 11d. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.77 (dd, 2H, *J*=7.4, 1.2 Hz), 7.62 (dd, 2H, *J*=7.3, 1.1 Hz), 7.35–7.30 (m, 5H), 7.27–7.19 (m, 3H), 7.14–7.06 (m, 3H), 5.36 (dd, 1H, *J*=8.0, 3.8 Hz), 3.89 (br 1H), 3.24 (d, 1H, *J*=1.8 Hz), 3.07 (d, 1H, *J*=1.7 Hz), 2.30 (td, 1H, *J*=12.6, 4.3 Hz), 2.08 (dd, 1H, *J*=13.8, 8.0 Hz), 2.02–1.88 (m, 2H), 1.71–1.64 (m, 1H), 1.51 (s, 3H), 1.51–1.50 (m, 1H), 1.23–1.66 (m, 1H), 0.61 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.0, 150.2, 143.9, 134.7, 128.9, 128.6, 128.5, 128.2, 126.7, 126.6, 126.6, 126.1, 125.5, 83.2, 81.4, 58.7, 56.8, 56.6, 51.5, 47.6, 38.7, 31.0, 27.0, 24.6, 22.6; HRMS *m/z* 468.2295 (calcd for $C_{31}H_{32}O_4$: 468.2301). Crystal data for **11d** at 25 °C: $C_{31}H_{32}O_4$, *M* 468.593, monoclinic, $P2_12_12_1$, *a*=7.34060 (10) Å, *b*=16.1417 (3) Å, *c*=21.6388 (4) Å, *V*=2563.98 (8) Å^3, *Z*=4, λ=0.71073 Å, D_c=1.214 Mg/m^3, μ=0.079 mm^{-1}, 4517 reflections, 316 parameters, *R*=0.0587, R_w=0.1431 for all data.

4.2.21. Compound 10e. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.78 (d, 2H, *J*=7.8 Hz), 7.60 (d, 2H, *J*=7.7 Hz), 7.26 (t, 2H, *J*=7.5 Hz), 7.21 (t, 2H, *J*=7.4 Hz), 7.15–7.09 (m, 2H), 5.24 (dd, 1H, *J*=8.2, 3.6 Hz), 3.89 (br 1H), 2.89 (s, 1H), 2.31 (td, 1H, *J*=12.5, 4.2 Hz), 2.02–1.93 (m, 2H), 1.82–1.76 (m, 1H), 1.68–1.61 (m, 1H), 1.50 (s, 3H), 1.49–1.48 (m, 1H), 1.29 (s, 3H), 1.18–1.11 (m, 1H), 1.07 (s, 3H), 0.62 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.3, 149.2, 143.3, 128.4, 127.9, 126.7, 126.4, 126.1, 126.0, 82.6, 81.1, 60.6, 59.0, 58.9, 51.3, 47.6, 38.4, 31.0, 26.9, 24.5, 24.2, 22.4, 17.9; HRMS *m/z* 420.2266 (calcd for $C_{27}H_{32}O_4$: 420.2301). Crystal data for **10e** at 25 °C: $C_{27}H_{32}O_4$, *M* 420.54, monoclinic, *C2*, *a*=16.6348 (23) Å, *b*=7.0448 (17) Å, *c*=21.913 (10) Å, *V*=2309.7 Å^3, *Z*=4, λ=0.70930 Å, D_c=1.209 Mg/m^3, μ=0.08 mm^{-1}, 2263 reflections, 280 parameters, *R*=0.042, R_w=0.041 for all data.

4.2.22. Compound 10f. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.80 (d, 2H, *J*=7.7 Hz), 7.62 (d, 2H, *J*=7.6 Hz), 7.29 (t, 2H, *J*=7.5 Hz), 7.21 (t, 2H, *J*=7.4 Hz), 7.16–7.09 (m, 2H), 5.25 (dd, 1H, *J*=8.1, 3.3 Hz), 4.01 (br 1H), 2.85 (d, 1H, *J*=5.7 Hz), 2.69 (d, 1H, *J*=5.7 Hz), 2.29 (td, 1H, *J*=12.5, 4.2 Hz), 1.99–1.92 (m, 1H), 1.83 (dd, 1H, *J*=13.5, 8.2 Hz), 1.73–1.60 (m, 2H), 1.49–1.47 (m, 1H), 1.45 (s, 3H), 1.25 (s, 3H), 1.16–1.10 (m, 1H), 0.63 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.1, 148.7, 143.4, 128.5, 127.9, 126.7, 126.4, 126.3, 126.0, 81.5, 81.0, 59.3, 53.3, 52.7, 51.3, 47.6, 37.9, 30.9, 27.0, 24.4, 22.5, 16.7; HRMS *m/z* 406.2126 (calcd for $C_{26}H_{30}O_4$: 406.2144).

4.2.23. Compound 11f. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.69 (dd, 2H, *J*=7.4, 1.0 Hz), 7.49 (dd, 2H, *J*=7.4, 0.9 Hz), 7.26–7.18 (m, 4H), 7.14–7.09 (m, 2H), 5.26 (dd, 1H, *J*=8.0, 3.6 Hz), 3.91 (br 1H), 2.42 (d, 1H, *J*=5.5 Hz), 2.26 (td, 1H, *J*=12.5, 4.2 Hz), 2.07 (d, 1H, *J*=5.3 Hz), 2.04 (dd, 1H, *J*=10.2, 8.0 Hz), 1.99–1.92 (m, 1H), 1.87–1.81 (m, 1H), 1.69–1.61 (m, 1H), 1.53–1.47 (m, 1H), 1.49 (s, 3H), 1.43 (s, 3H), 1.20–1.14 (m, 1H), 0.58 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.9, 149.9, 144.0, 128.6, 127.9, 126.6, 126.5, 126.0, 83.0, 81.3, 58.5, 53.6, 51.9, 51.4, 47.6, 38.8, 30.9, 27.0, 24.5, 22.6, 17.4; HRMS *m/z* 406.2127 (calcd for $C_{26}H_{30}O_4$: 406.2144).

4.2.24. Compound 10g. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.79 (dd, 2H, *J*=7.4, 1.2 Hz), 7.62 (dd, 2H, *J*=7.3, 1.3 Hz), 7.28 (t, 2H, *J*=7.4 Hz), 7.21 (t, 2H, *J*=7.3 Hz), 7.17–7.09 (m, 2H), 5.24 (dd, 1H, *J*=8.1, 3.4 Hz), 4.11 (br, 1H), 3.04 (q, 1H, *J*=5.4 Hz), 2.28 (td, 1H, *J*=12.5, 4.2 Hz), 1.99–1.92 (m, 1H), 1.85 (dd, 1H, *J*=13.5, 8.2 Hz), 1.73–1.60 (m, 2H), 1.49–1.48 (m, 1H), 1.46 (s, 3H), 1.29 (d, 3H, *J*=5.4 Hz), 1.17 (s, 3H), 1.15–1.10 (m, 1H), 0.62 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0, 148.8, 143.4, 128.4, 127.9, 126.7, 126.3, 126.3, 126.0, 81.4, 80.9, 59.2, 57.9, 57.0, 51.3, 47.6, 37.8, 30.9, 26.9, 24.5, 22.5, 13.3, 12.6; HRMS *m/z* 420.2292 (calcd for $C_{27}H_{32}O_4$: 420.2301).

4.2.25. Compound 11g. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.69 (dd, 2H, *J*=7.4, 1.1 Hz), 7.48 (d, 2H, *J*=7.4 Hz), 7.25–7.18 (m, 4H), 7.14–7.09 (m, 2H), 5.23 (dd, 1H, *J*=8.0, 3.7 Hz), 4.01 (br 1H), 2.28 (td, 1H, *J*=12.4, 4.0 Hz), 2.10 (q, 1H, *J*=5.4 Hz), 2.04 (dd, 1H, *J*=13.8, 8.1 Hz), 1.99–1.92 (m, 1H), 1.87–1.82 (m, 1H,), 1.68–1.60 (m, 1H), 1.51–1.46 (m, 1H), 1.48 (s, 3H), 1.35 (s, 3H), 1.21–1.14 (m, 1H), 1.10 (d, 3H, *J*=5.4 Hz), 0.57 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.9, 150.1, 144.1, 128.6, 127.8, 126.6, 126.4, 126.0, 82.8, 81.3, 58.5, 57.3, 56.8, 51.5, 47.6, 38.8, 30.8, 27.0, 24.6, 22.6, 13.1, 13.0; HRMS *m/z* 420.2286 (calcd for $C_{27}H_{32}O_4$: 420.2301).

4.2.26. Compound 10h. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.79 (d, 2H, *J*=7.8 Hz), 7.62 (d, 2H, *J*=7.6 Hz), 7.28 (t, 2H, *J*=7.6 Hz), 7.21 (t, 2H, *J*=7.4 Hz), 7.17–7.09 (m, 2H), 5.25 (dd, 1H, *J*=8.4, 3.6 Hz), 4.12 (br 1H), 2.86 (t, 1H, *J*=6.2 Hz), 2.28 (td, 1H, *J*=12.5, 4.1 Hz), 1.99–1.93 (m, 2H), 1.84 (dd, 1H, *J*=13.5, 8.2 Hz), 1.73–1.67 (m, 1H), 1.66–1.57 (m, 1H), 1.52–1.45 (m, 2H), 1.47 (s, 3H), 1.17 (s, 3H), 1.16–1.107 (m, 1H), 1.02 (t, 3H, *J*=7.5 Hz), 0.63 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.1, 148.8, 143.4, 128.4, 127.9, 126.7, 126.3, 126.3, 126.0, 81.4, 81.0, 63.2, 59.2, 57.1, 51.3, 47.6, 37.9, 30.9, 26.9, 24.5, 22.5, 21.3, 12.7, 10.2; HRMS *m/z* 434.2443 (calcd for $C_{28}H_{34}O_4$: 434.2457).

4.2.27. Compound 11h. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.70 (dd, 2H, *J*=7.4, 1.2 Hz), 7.48 (dd, 2H, *J*=7.4 Hz), 7.25–7.18 (m, 4H), 7.15–7.11 (m, 2H), 5.24 (dd, 1H, *J*=8.0,

3.6 Hz), 4.04 (br 1H), 2.27 (td, 1H, J=12.4, 4.3 Hz), 2.04 (dd, 1H, J=13.7, 8.0 Hz), 1.99–1.93 (m, 2H), 1.86–1.82 (m, 1H), 1.67–1.55 (m, 1H), 1.48 (s, 3H), 1.47–1.45 (m, 1H), 1.44–1.29 (m, 2H), 1.36 (s, 3H), 1.21–1.15 (m, 1H), 0.88 (t, 3H, J=7.5 Hz), 0.56 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.0, 150.2, 144.2, 128.6, 128.0, 126.7, 126.6, 126.4, 126.0, 82.8, 81.4, 62.0, 58.5, 57.4, 51.5, 47.6, 38.8, 30.8, 27.0, 24.6, 22.7, 21.1, 13.1, 10.0; HRMS m/z 434.2448 (calcd for $C_{28}H_{34}O_4$: 434.2457).

4.2.28. Compound 11b. (R=Me): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.84 (d, 2H, J=7.6 Hz), 7.60 (d, 2H, J=7.6 Hz), 7.38–7.26 (m, 9H), 7.25–7.18 (m, 2H), 5.00 (dd, 1H, J=8.0, 3.6 Hz), 3.58 (d, 1H, J=1.6 Hz), 3.08 (d, 1H, J=1.8 Hz), 2.87 (td, 1H, J=13.1, 4.2 Hz), 2.78 (s, 3H), 1.91 (dd, 1H, J=13.4, 8.0 Hz), 1.69–1.59 (m, 2H), 1.46 (t, 1H, J=4.4 Hz), 1.23–1.17 (m, 1H), 1.08 (s, 3H), 1.05–0.97 (m, 1H), 0.61 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.1, 140.5, 138.8, 135.2, 131.6, 129.8, 128.8, 128.6, 127.5, 127.2, 126.9, 126.8, 125.8, 87.5, 82.5, 61.3, 57.0, 56.8, 52.5, 49.8, 49.2, 39.4, 31.7, 25.6, 23.4, 22.4; HRMS m/z 482.2447 (calcd for $C_{32}H_{34}O_4$: 482.2457).

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