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Synthesis of chiral allenes from ynamides through a highly stereoselective Saucy–Marbet rearrangement

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Abstract—A highly stereoselective Saucy–Marbet rearrangement using chiral ynamides and propargyl alcohols is described here. This rearrangement can be catalyzed by *para*-nitrobenzenesulfonic acid and leads to high diastereoselectivities for a range of different chiral propargyl alcohols and ynamides in a stereochemically intriguing matched, mismatched or indifferent manner. The stereoselective Saucy–Marbet rearrangement of ynamides provides an excellent entry to highly substituted chiral homo allenyl alcohols.

1. Introduction

The chemistry of electron deficient ynamines (Type I–V) and ynamides (Types VI–VIII) has blossomed in the past 10 years (Fig. 1).[1–11] Our own earlier efforts had focused on the use of chiral ynamides in the stereoselective Claisen rearrangement.[12,13] Specifically, we were able to establish a Brønsted acid catalyzed stereoselective Ficini–Eschenmoser–Claisen rearrangement (**1**→**2a**+**2b** in Fig. 2),[14,15] and communicated the stereospecificity in the Saucy–Marbet rearrangement[16,17] (**3**→**5a**–**d**) using chiral propargyl alcohols.[18] This latter rearrangement can provide an even greater synthetic implication because it leads to preparations of chiral allenes. Despite this potential and that Saucy and Marbet[16a] first reported this rearrangement in 1958, to our surprise, there have been very few studies concerning the stereoselectivity issues of the Saucy–Marbet

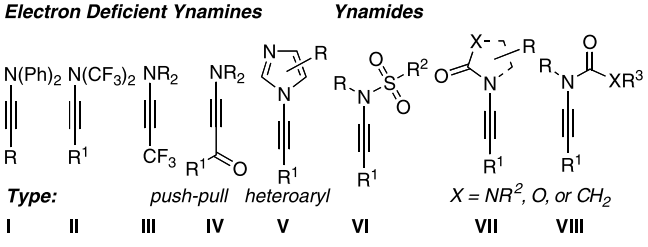

Figure 1.

Keywords: Ynamides; Saucy–Marbet rearrangement; Chiral allenes; Sibi and Evans' auxiliaries; Axial chirality.
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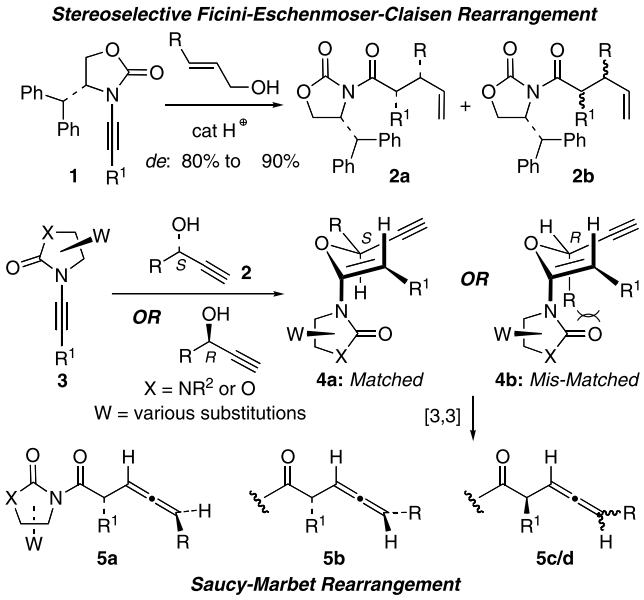


Figure 2.

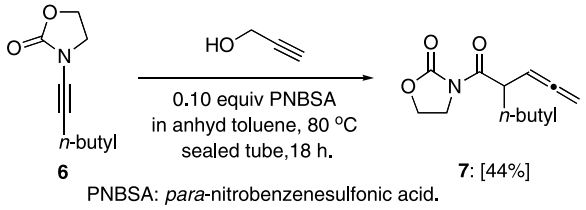
rearrangement.[19,20] We report here, our studies on stereoselective Saucy–Marbet rearrangements.

2. Results and discussions

2.1. The feasibility question

Although Ficini had reported the use of ynamines in related rearrangements,[21] it was not apparent as to how ynamides would behave in this case. Thus, reaction of achiral ynamide

6 with 2-propyn-1-ol was first examined. In the presence of 0.10 equiv of *para*-nitrobenzenesulfonic acid (PNBSA) at 80 °C in toluene, the rearrangement took place and afforded allene **7** in 44% yield (Scheme 1).

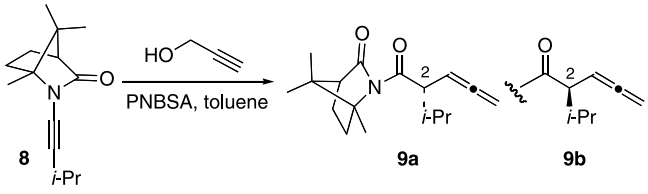


Scheme 1.

2.2. Stereoselectivity issues

Having established the feasibility of this arrangement, Boeckman's chiral lactam[22]-substituted ynamide **8** was chosen to explore conditions that could lead to high stereoselectivity at C2, because **8** represents one of the more reactive chiral ynamides and its rearrangement could proceed at lower temperatures than 80 °C.[15] As summarized in Table 1, attempts to run the reaction of **8** with 2-propyn-1-ol at temperatures below 45 °C failed to give the desired allene **9** (entries 1–4). When the reaction was carried out at 60 °C, **9** was isolated in 60% yield. However, the diastereomeric ratio was only 1.2:1, and the same ratio was observed at rt when a trace of amount product was found in ^{1}H NMR (entry 5 vs 2).

Table 1.



Entry	Temperature (°C)	PNBSA (equiv)	Yield (%)[a]	Ratio **a**:**b**[b]
1	0	0.10	NR[c]	ND[d]
2	rt	0.10	Trace	1:1
3	rt	0.20	NR[e]	ND
4	45	0.10	NR	ND
5	60	0.10	60	1.2:1
6	60	0.15	80	1:1
7	60	0.05	40	1:1
8	80	0.10	65	1:1

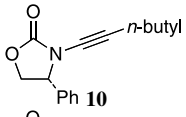
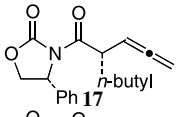
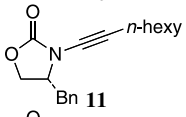
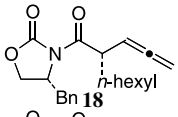
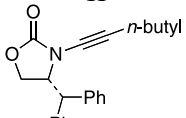
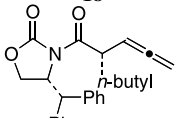
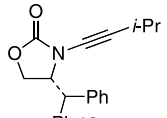
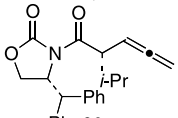
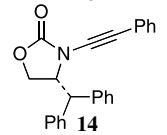
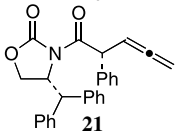
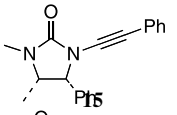
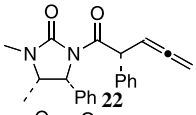
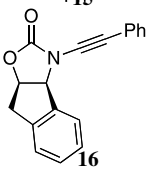
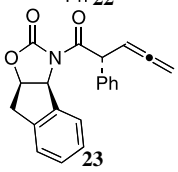
[a] Isolated yields.
[b] Ratios determined using ^{1}H NMR. Stereochemistry unassigned.
[c] NR: no reaction.
[d] ND: not determined.
[e] Hydrolysis of ynamide occurred.

Varying the amount of PNSBA did not affect the selectivity (entries 6 and 7) and the yield dropped when 0.05 equiv of PNSBA was used (entry 7). Reaction at 80 °C yielded results comparable to those at 60 °C (entry 5 vs 8).

2.3. The effect of chiral auxiliaries

Speculating that the chiral auxiliary of ynamides might play a role in the stereochemical outcome, we examined various chiral ynamides. As summarized in Table 2, ynamides **10–11** (entries 1 and 2) substituted with Evans' auxiliary,[23] and ynamides **12–14** (entries 3–5) substituted with Sibi's auxiliary[24] gave improved diastereoselectivity with **12** providing the best ratio (entry 3). However, selectivities here appeared to have reached the maximum as ynamides **13** and **14** with an *i*-Pr and Ph substituents, respectively, provided relatively lower selectivities as well as yields than **12** (entries 4 and 5 vs 3).

Table 2

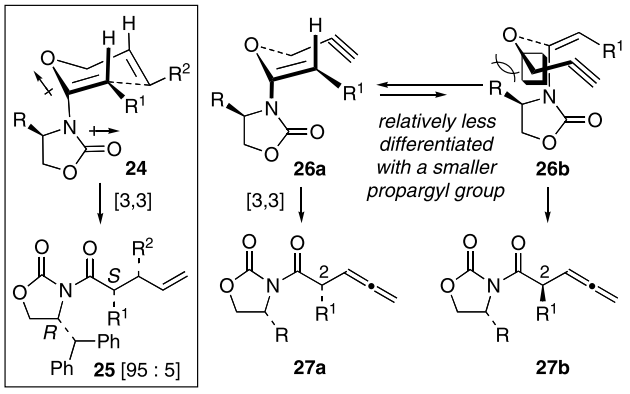
Entry	Ynamides[a]	Rearrangement products	Yield (%)[b]	Ratio[c]
1	 **10**	 **17**	60	67:33[d]
2	 **11**	 **18**	78	70:30
3	 **12**	 **19**	70	85:15
4	 **13**	 **20**	40	60:40
5	 **14**	 **21**	40	80:20
6	 **15**	 **22**	37[e]	78:22
7	 **16**	 **23**	70	63:37

[a] Reactions were carried out in toluene in the presence of 0.10 equiv of PNBSA and heated at 80–85 °C in a sealed tube for 12–18 h.
[b] Isolated yields.
[c] Ratios were determined by using ^{1}H NMR.
[d] Stereochemistry of the major isomer was assigned based on Claisen rearrangements using allyl alcohols. See Ref. 15.
[e] Extensive hydrolysis occurred.

Other auxiliaries were also screened, but none provided better ratios (entries 6–7). Ynamide **15** substituted with Close's auxiliary[25] provided a comparable ratio to that of **12**, although in lower yield in addition to hydrolysis of the ynamides (entry 6), whereas ynamide **16** substituted with chiral 1-amino-2-indanol derived auxiliary also led to a low diastereoselectivity (entry 7).

2.4. A proposed mechanistic model

Perplexed by the lack of diastereoselectivity, we examined the mechanistic model that was proposed in our previous Ficini–Claisen rearrangements using allyl alcohols.[15] As shown in Scheme 2, the rearrangement likely goes through a chair transition state shown in the *O*-allyl ketene aminal **24** (inside the left box). The ketene aminal **24** would assume a conformation similar to the Evans' model for asymmetric aldol reactions using chiral oxazolidinones,[23] minimizing the dipole interaction between the urethane C=O and vinyl C–O bond (worth ~2.6 Kcal mol^{-1}).[23] This would provide two sterically differentiated π-faces of the ketene aminal with the allylic substituent preferring the back face leading favorably to the major stereoisomer **25** after the (3,3)-sigmatropic rearrangement.

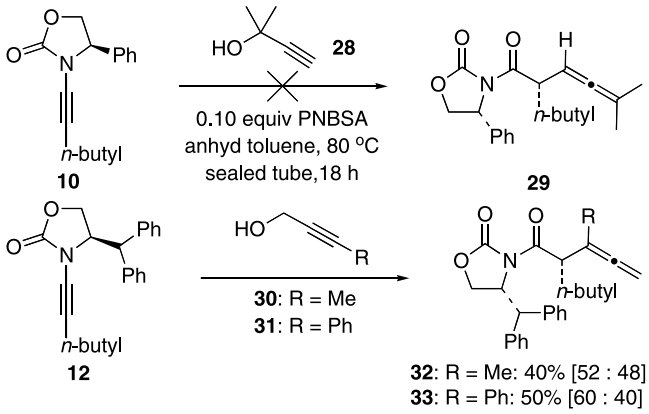


Scheme 2.

Based on this model, *O*-propargyl ketene aminals **26a** and **26b** would be responsible for the observed stereochemical outcome at C2 in which the more favored intermediate **26a** could lead to the moderately favored major isomer **27a**.[26] Larger *R* substituents such as a diphenyl methyl group in the Sibi's auxiliary should provide more differentiation to the two π-faces of the ketene aminal, thereby leading to enhanced diastereoselectivity.

However, the level of selectivity is much lower overall compared to those obtained using allyl alcohols.[15] This is likely due to the fact that the propargyl substituent is smaller than an allyl group, and thus, the π-facial differentiation of the ketene aminal is reduced with the steric interaction between the propargyl and R substituents shown in **26b** being less severe than an allyl group.

With this assessment in hand, we explored more bulky propargyl alcohols. We reacted 1,1-dimethyl-2-propyn-1-ol **28** with ynamide **10**, but it failed to produce the desired rearrangement product **29** with hydrolysis of **10** being the dominant event (Scheme 3). Because propargyl alcohol **28** is likely too bulky, thereby shutting down the formation of the ketene aminal, we turned to propargyl alcohols **30** and **31** with substituents at the terminal alkyne carbon. Reactions of **12** with propargyl alcohols **30** and **31** led to allenes **32** and **33** in 40 and 50% yields, respectively, but unfortunately with lower diastereoselectivities.

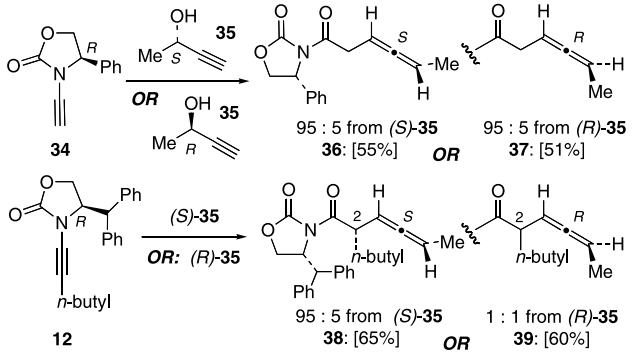


Scheme 3.

Therefore, these results were not informative. To further assess this mechanistic model, there remains one other possibility that would then involve chiral propargyl alcohols that are more bulky but with only one substituent at the propargyl carbon. However, by using chiral propargyl alcohols, we anticipated that we would run into potential match and mismatch situations (see Fig. 2), which could lead to a completely different endeavor, but one that would remain challenging stereochemically. However, this endeavor could also provide an excellent opportunity for constructing chiral allenes.

2.5. Chiral propargyl alcohols: match and mismatch

We quickly established the feasibility of Saucy–Marbet rearrangement using chiral ynamides (Scheme 4). Reactions of ynamide **34** with (*S*)-**35** and (*R*)-**35** using PNBSA at 100 °C gave allenes **36** and **37** in 55 and 51% yield, respectively, as single diastereomers, suggesting excellent chirality transfer from chiral alcohols to the allenic axial center.[16d,19a] Because **34** is unsubstituted at the terminal alkyne carbon, match and mismatch was not an issue.



Scheme 4. Conditions: 0.10–0.20 equiv PNBSA: *para*-nitrobenzenesulfonic acid. **34** or **12** in anhyd. toluene [0.025 M], 1.0–2.0 equiv alcohol, sealed tube.

However, while reactions of **12** led to **38** as a single diastereomer using (*S*)-**35**, allene **39** was isolated with 1:1 isomeric ratio when using (*R*)-**35**. Stereochemical assignment (see below) of **39** suggests that it is 1:1 at C2, thereby implying that potential mismatched intermediates were

involved. Stereochemistry of **38** was assigned by correlation with allene **40**[27] whose X-ray structure is shown in Figure 3.

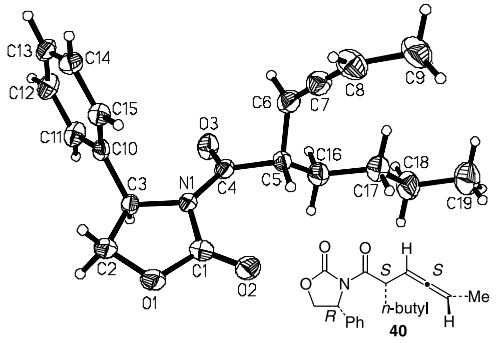
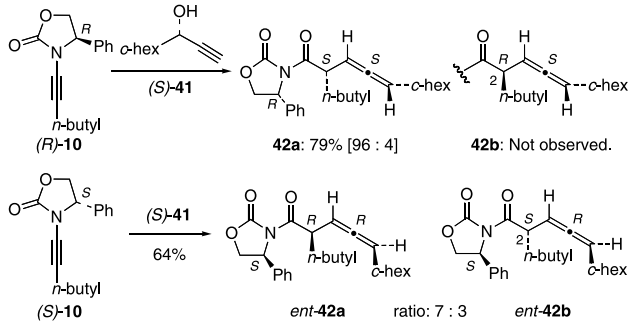


Figure 3.

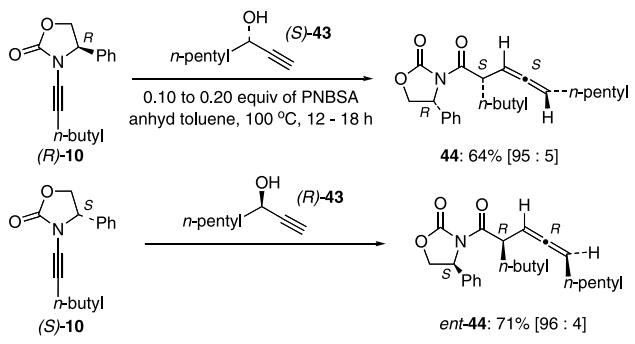
This case of match/mismatch is further confirmed via another set of experiments employing the same chiral propargyl alcohol (*S*)-**41** but changing the chirality of the ynamide. As shown in Scheme 5, reaction of (*R*)-**10** with (*S*)-**41** led to **42a** as a single diastereomer and no **42b** was observed by NMR, while the mismatched reaction of (*S*)-**10** with (*S*)-**41** gave both *ent*-**42a** and *ent*-**42b** in 64% yield but as a 7:3 mixture, again with respect to the C2 stereochemistry. It was intriguing that the ratio was not 1:1 (see below for more discussion).



Scheme 5.

2.6. Synthesis of chiral allenes

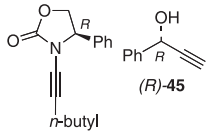
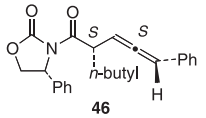
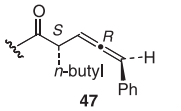
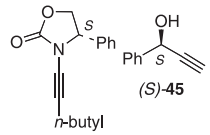
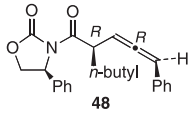
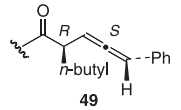
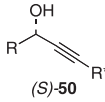
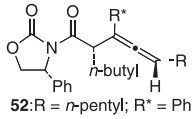
These results allowed us to construct a range of chiral allenes. For example, an appropriate matching of ynamides **10** with (*S*)-**43** and (*R*)-**43** led to **44** and *ent*-**44**, respectively, in high selectivities (Scheme 6).



Scheme 6.

In addition, we found that these rearrangements do not all experience either matching or mismatching. As shown in Table 3, reactions of both (*R*)-**10** and (*S*)-**10** with (*R*)-**45** and (*S*)-**45** gave rearranged products **46–49**, respectively, with high diastereoselectivities, although the matched cases (entries 1 and 3) are still higher overall than cases that would be presumed to be mismatched (entries 2 and 4). This finding provides the synthesis of all four possible diastereomeric homo allenyl amides.

Table 3

Entry	Ynamides and alkynols[a]	Rearrangement products	Yield[b]	Ratio[c]
1		 **46**	80	96 : 4
2	(*R*)-**10** (*S*)-**45**	 **47**	78	90 : 10
3		 **48**	77	96 : 4
4	(*S*)-**10** (*R*)-**45**	 **49**	75	89 : 11
5	(*R*)-**10**  (*S*)-**50**	 **52**:R = *n*-pentyl; R* = Ph	77	96 : 4
6	(*R*)-**10**	(*S*)-**51** **53**:R = *c*-hex; R* = *n*-butyl	71	96 : 4

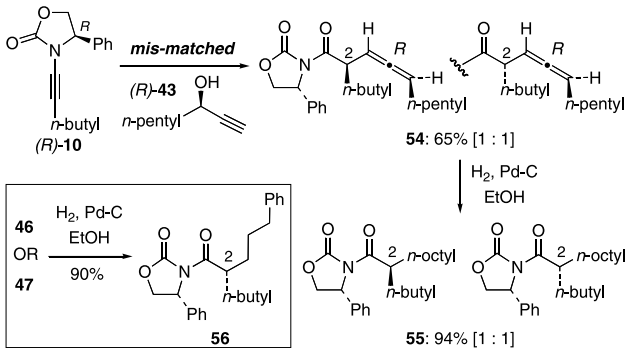
[a] Reactions were carried out in anhyd toluene in the presence of 0.10 to 0.20 equiv of PNBSA and heated at 100°C in a sealed tube for 12-18h.
[b] All are Isolated yields.
[c] Ratios were determined by using ^{1}H and/or ^{13}C NMR.

Finally, tri-substituted chiral homo allenyl amides **52** and **53** could also be obtained in high selectivities using (*S*)-**50** and (*S*)-**51**,[28] respectively (entries 5 and 6).

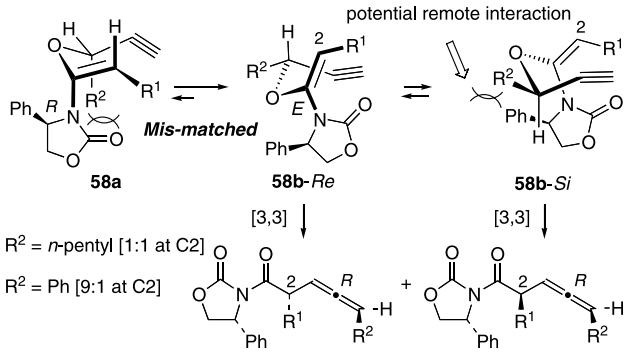
2.7. High axial stereoselectivity in the mismatch cases

To unambiguously establish all stereochemical issues, we further confirmed that (1) in the mismatched cases, stereoselectivity was very high for the allenic axial chirality, and (2) mismatching led to an isomeric mixture at the C2 stereocenter.

Toward this goal, the isomeric mixture **54** obtained with a 1:1 ratio from reaction of (*R*)-**10** with (*R*)-**43** was hydrogenated to give **55**, which remained as a 1:1 mixture (Scheme 7). This finding implies that the diastereoselectivity suffered only at C2 in mismatched cases, whereas the allene stereochemistry was transferred in high degrees of integrity from the chiral propargyl alcohol. On the other hand, hydrogenation of both **46** and **47** led to the same amide **56**, implying that stereoselectivity at C2 was the same when it was indifferent to match or mismatch.



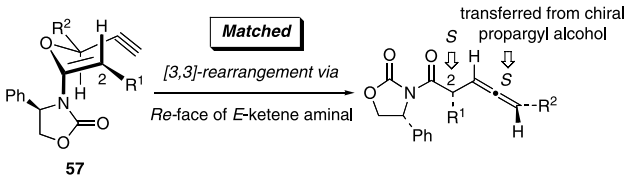
Scheme 7.



Scheme 9.

2.8. Mechanistic issues

Mechanistically, for the matched cases, that is, reactions of ynamide (*R*)-**10** (R^1=*n*-butyl) with chiral propargyl alcohols (*S*)-**41** (R^2=*c*-hex), (*S*)-**43** (R^2=*n*-pentyl), or (*R*)-**45** (R^2=Ph), (3,3)-sigmatropic rearrangement would likely proceed through the *E*-ketene aminal intermediate **57** in which the C2 stereochemistry is dictated by the preference of the rearrangement occurring at the *Re*-face of **57** (Scheme 8).[15] The allene stereochemistry is transferred directly from the chiral propargyl alcohol, and that should be true for both matched and mismatched cases.



Scheme 8.

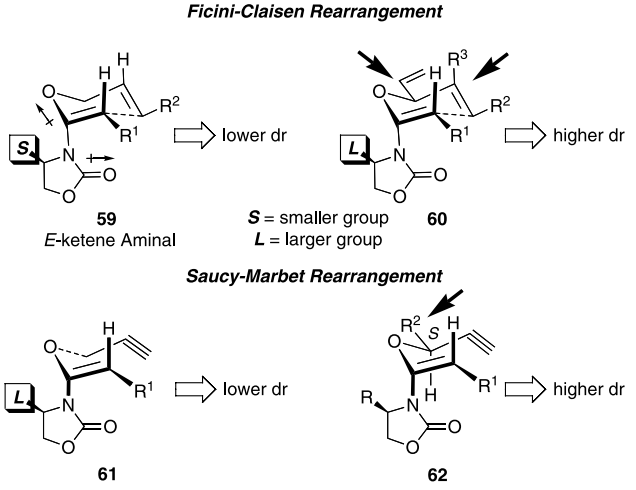
For mismatched and indifferent (for propargyl alcohols (*R*)-**45** or (*S*)-**45** with R^2=Ph in Table 3) cases, to address the C2 stereochemistry, we propose that the rearrangement could go through the same type of *E*-ketene aminal that is now mismatched as shown in **58a** owing to pseudo 1,3-diaxial interactions between the R^2 and the auxiliary groups (Scheme 9). Thus, it may be proposed that ketene aminal **58b** is the active conformation for the rearrangement with the R_2 group being equatorial. Because of this conformational preference, in the mismatched or indifferent cases, the (3,3)-sigmatropic rearrangement could occur at either or both *Re*- and *Si*-faces of **58b**, thereby providing some explanation for the observed stereochemical outcome at C2.[29]

When it is completely mismatched, that is, R^2=*n*-pentyl in the reaction of (*R*)-**43** with ynamide (*R*)-**10** to produce allene **54** (shown in Scheme 7 above), rearrangement could be proposed to proceed through both the *Re*- and *Si*-face of **58b**, and PM3 calculations using Spartan Model™ only showed a small energetic difference of ~0.6 Kcal mol^{-1}.[30] The ensuing (3,3)-rearrangement at both *Re*- and *Si*-faces of **58b** would then lead to a 1:1 isomeric ratio at C2 as observed for allene **54**[15] (Scheme 7).

On the other hand, for indifferent cases, when R^2=Ph as in (*R*)-**45** or (*S*)-**45**, the ensuing rearrangement may prefer to go through the *Re*-face of **58b** because PM3 calculations provide $\Delta E = 1.0$ Kcal mol^{-1} in favor of **58b**-*Re*.[30] This preference could be proposed as a result of the unfavorable remote interaction between the R^2 group, when it is more bulky (i.e., Ph vs *n*-pentyl in **43** or Me in **35**), with the auxiliary shown in **58b**-*Si*. This preference could then result in a 9:1 isomeric ratio at C2 in as shown in Table 3 for **46/48** versus **47/49**.

Although we remain uncertain if this remote interaction is the actual reason for the energetic preference for **58b**-*Re* over **58b**-*Si*, this phenomenon is at least consistent with the result shown in both Schemes 5 and 7. Firstly in Scheme 7, an expected 1:1 ratio was observed for allene **54** from the completely mismatched reaction of (*R*)-**10** with chiral propargyl alcohol (*R*)-**43** (R^2=*n*-pentyl). In contrast, as shown in Scheme 5, when the chiral propargyl alcohol (*S*)-**41**, where R^2=*c*-hex, was reacted with (*S*)-**10** also in a potential mismatch, instead of the expected 1:1 ratio, the corresponding allene **42** was obtained with an improved ratio of 7:3.[30] This can be attributed to the fact that the R^2 group (*c*-hex) in chiral propargyl alcohol (*S*)-**41** is larger than that (*n*-pentyl) in (*R*)-**43**

Finally, the mechanistic picture becomes even more clear and consistent when we examine the entire scope of Claisen rearrangements using ynamides. As shown in Scheme 10, the very same elements that dictate the level of



Scheme 10.

diastereoselectivity in the Ficini–Claisen rearrangement[14,15] also control the stereochemical outcome in these current Saucy–Marbet rearrangements. That is both rearrangements likely proceeds through the same chair-like transition-state shown in all four intermediates **59**–**62**, which are also all *E*-ketene aminals[15] with an orientation that are again consistent with the Evans' dipole argument.[23]

With this unified model in place, the critical element that can lead to high diastereomeric selectivity becomes the π-facial differentiation in these *E*-ketene aminals. The greater the differentiation would imply a greater selectivity. To achieve a greater π-facial differentiation, relevant factors could be deduced to the size of the chiral auxiliary (see the box in **59** and **60**) as well as the size of the allylic strand both at the allylic carbon (with a vinyl group, specifically shown in **60**[15]), and at the vinyl fragment (see black arrows in **60**) for the Ficini–Claisen rearrangement. We observed exactly these phenomena in our previous work,[15] and likewise for the Saucy–Marbet rearrangement, the relevant factors are also the size of the chiral auxiliary (see the box in **61**), and even more significantly, the size of the propargylic carbon (see the black arrow in **62**). In pursuing of this latter factor, we observed various interesting matched and mismatched scenarios that led to a greater mechanistic understanding of these pericyclic rearrangements.

Finally, one of the reviewers made an excellent suggestion. That is what would the outcome be from the reaction of an achiral ynamide with both antipodes of chiral propargyl alcohols. This suggested experiment should further provide interesting mechanistic insights. However, unfortunately, these reactions, specifically using ynamide **6** and chiral propargyl alcohols (*R*)-**45** and (*S*)-**45**, gave poor yields. Thus, we were unable to meaningfully determine their respective diastereomeric ratios.

3. Conclusion

We have described here a highly stereoselective Saucy–Marbet rearrangement using chiral ynamides and propargyl alcohols. This rearrangement provides an approach for synthesis of highly substituted chiral allenes.

4. Experimental

All reactions were performed in flame-dried glassware under nitrogen atmosphere. Solvents were distilled prior to use. Reagents were used as purchased (Aldrich, Acros), except where noted. Chromatographic separationd were performed using Bodman 60 Å SiO_2. ^1H and ^{13}C NMR spectra were obtained on Varian VI-300, VXR-300, and VI-500 spectrometers using $CDCl_3$ (except where noted) with TMS or residual solvent as standard. Melting points were determined using a Laboratory Devices MEL-TEMP and are uncorrected/calibrated. Infrared spectra were obtained using NaCl plates on a Midac M2000 FTIR. TLC analysis was performed using Aldrich 254 nm polyester-backed plates (60 Å, 250 μm) and visualized using UV and vanillin or $KMnO_4$ stains. Low-resolution mass spectra were obtained using an Agilent 1100 series LS/MSD and are APCI. High-resolution mass spectral analyses were performed at University of Minnesota Department of Chemistry Mass Spectrometry Laboratory. X-ray analyses were performed at University of Minnesota Department of Chemistry X-ray facility. All spectral data obtained for new compounds are reported here.

4.1. General procedure for propargyl alcohol addition/Saucy–Marbet rearrangement

Ynamide (0.2 mmol), anhyd *p*-nitrobenzenesulfonic acid (0.2 equiv), propargyl alcohol (1–2 equiv), and anhyd toluene (4 mL) were combined in a flame-dried 25 mL sealed tube under nitrogen atmosphere. The tube was sealed and the reaction mixture was heated at 100 °C for 24–48 h. The reaction was followed with TLC and/or LCMS analysis. Once completed by TLC analysis, the reaction was cooled to room temperature, filtered through Celite™, and concentrated in vacuo. The residue was purified by flash silica gel column chromatography (gradient: 0–25% EtOAc in hexanes) to provide the rearranged products in yields indicated in the text.

4.1.1. Allene 7. R_f=0.19 (25% EtOAc in hexanes); clear oil; ^1H NMR (500 MHz, $CDCl_3$) δ 0.87–0.97 (m, 3H), 1.29–1.38 (m, 4H), 1.56–1.62 (m, 1H), 1.78–1.84 (m, 1H), 4.03 (t, 2H, J=8.0 Hz), 4.33 (tq, 1H, J=1.5, 8.0 Hz), 4.39–4.43 (m, 1H), 4.41 (t, 1H, J=8.0 Hz), 4.79 (dd, 2H, J=2.0, 6.5 Hz), 5.31 (q, 1H, J=6.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 22.4, 29.2, 31.6, 42.7, 61.8, 88.9, 153.0, 174.0, 208.4 (missing 2 signals due to overlap); IR (thin film) cm^{-1} 2957 (m), 2930 (m), 2862 (w), 1957 (w), 1780 (s), 1698 (s); mass spectrum (APCI): *m/e* (% relative intensity) 224 (13) $(M+H)^+$, 198 (50), 196 (66), 137 (59), 109 (40), 88 (100); HRMS-ESI *m/e* calcd for $C_{12}H_{17}NO_3Na$ 246.1101, found 246.1110.

4.1.2. Allene 9. R_f=0.52 (25% EtOAc in hexanes); clear oil; ^1H NMR (500 MHz, $CDCl_3$) major isomer: δ 0.86–1.02 (m, 9H), 1.45 (s, 3H), 1.58–1.64 (m, 3H), 1.81–1.86 (m, 2H), 1.95–2.06 (m, 2H), 2.07 (m, 1H), 2.35 (t, 1H, J=5.0 Hz), 4.08 (tt, 1H, J=1.5, 7.5 Hz), 4.67–4.75 (m, 2H), 5.16 (dt, 1H, J=7.0, 9.0 Hz); minor isomer: δ 0.86–1.02 (m, 9H), 1.45 (s, 3H), 1.58–1.64 (m, 3H), 1.81–1.86 (m, 2H), 1.95–2.06 (m, 2H), 2.07 (m, 1H), 2.35 (t, 1H, J=5.0 Hz), 4.14 (tt, 1H, J=1.5, 7.5 Hz), 4.67–4.75 (m, 2H), 5.28 (dt, 1H, J=7.0, 9.0 Hz); IR (thin film) cm^{-1} 2960 (m), 1955 (w), 1743 (s), 1692 (s); mass spectrum (APCI): *m/e* (% relative intensity) 276 (100) $(M+H)^+$, 252 (8), 220 (6), 154 (13); HRMS-ESI *m/e* calcd for $C_{17}H_{25}NO_2Na$ 298.1778, found 298.1777.

4.1.3. Allene 17. R_f=0.38 (25% EtOAc in hexanes); clear oil; ^1H NMR (500 MHz, $CDCl_3$) major isomer: δ 0.89 (t, 3H, J=7.5 Hz), 1.14–1.36 (m, 4H), 1.47–1.58 (m, 1H), 1.70–1.82 (m, 1H), 4.26–4.33 (m, 2H), 4.59 (dd, 1H, J=1.5, 6.5 Hz), 4.67–4.72 (m, 1H), 4.78 (dd, 1H, J=1.5, 12.0 Hz), 5.24 (q, 1H, J=9.0 Hz), 5.45 (dd, 1H, J=4.0, 9.0 Hz), 7.27–7.39 (m, 5H); minor isomer: δ 0.82 (t, 3H, J=7.5 Hz), 1.14–1.36 (m, 4H), 1.47–1.58 (m, 1H), 1.70–1.82 (m, 1H), 4.26–4.33 (m, 2H), 4.57 (dd, 1H, J=1.5, 6.5 Hz), 4.67–4.72 (m, 2H), 5.27 (q, 1H, J=9.0 Hz), 5.44 (dd, 1H, J=4.0,

9.0 Hz), 7.27–7.39 (m, 5H); IR (thin film) cm^{-1} 2957 (m), 2931 (m), 2861 (w), 1956 (w), 1781 (s), 1705 (s); mass spectrum (APCI): *m/e* (% relative intensity) 300 (48) $(M+H)^+$, 272 (21), 164 (100), 137 (41), 120 (47), 109 (26); HRMS-ESI *m/e* calcd for $C_{18}H_{21}NO_3Na$ 322.1414, found 322.1419.

4.1.4. Allene 18. $R_f=0.42$ (25% EtOAc in hexanes); clear oil; ^1H NMR (500 MHz, $CDCl_3$) major isomer: δ 0.88 (t, 3H, $J=7.0$ Hz), 1.28–1.39 (m, 8H), 1.58–1.64 (m, 1H), 1.81–1.85 (m, 1H), 2.72–2.80 (m, 1H), 3.29 (dd, 1H, $J=3.0$, 8.5 Hz), 4.15–4.23 (m, 2H), 4.27–4.37 (m, 1H), 4.66–4.72 (m, 1H), 4.79 (dd, 1H, $J=2.0$, 6.5 Hz), 4.82–4.86 (m, 1H), 5.38 (dt, 1H, $J=6.5$, 8.0 Hz), 7.21–7.35 (m, 5H); minor isomer: δ 0.89 (t, 3H, $J=7.0$ Hz), 1.28–1.39 (m, 8H), 1.58–1.64 (m, 1H), 1.81–1.85 (m, 1H), 2.72–2.80 (m, 1H), 3.30 (dd, 1H, $J=3.0$, 8.5 Hz), 4.15–4.23 (m, 2H), 4.27–4.37 (m, 1H), 4.66–4.72 (m, 2H), 4.82–4.86 (m, 1H), 5.32 (dt, 1H, $J=6.5$, 8.0 Hz), 7.21–7.35 (m, 5H); IR (thin film) cm^{-1} 2954 (m), 2926 (m), 2856 (w), 1956 (w), 1781 (s), 1698 (s); mass spectrum (APCI): *m/e* (% relative intensity) 342 (100) $(M+H)^+$, 314 (41), 178 (73), 165 (54), 117 (46); HRMS-ESI *m/e* calcd for $C_2^1H_{27}NO_3Na$ 364.1883, found 364.1889.

4.1.5. Allene 19. $R_f=0.47$ (25% EtOAc in hexanes); clear oil; ^1H NMR (500 MHz, $CDCl_3$) major isomer: δ 0.88 (t, 3H, $J=7.5$ Hz), 1.24–1.34 (m, 4H), 1.54–1.59 (m, 1H), 1.74–1.77 (m, 1H), 4.22–4.24 (m, 1H), 4.37–4.49 (m, 2H), 4.73 (d, 1H, $J=5.5$ Hz), 4.81–4.83 (m, 2H), 5.16 (dt, 1H, $J=7.0$, 8.0 Hz), 5.34 (ddd, 1H, $J=3.5$, 5.5, 8.0 Hz), 7.11–7.20 (m, 4H), 7.24–7.34 (m, 6H); minor isomer: δ 0.88 (t, 3H, $J=7.5$ Hz), 1.24–1.34 (m, 4H), 1.54–1.59 (m, 1H), 1.74–1.77 (m, 1H), 4.22–4.24 (m, 1H), 4.37–4.49 (m, 2H), 4.70 (d, 1H, $J=5.5$ Hz), 4.81–4.83 (m, 2H), 5.24 (dt, 1H, $J=7.0$, 8.0 Hz), 5.34 (ddd, 1H, $J=3.5$, 5.5, 8.0 Hz), 7.11–7.20 (m, 4H), 7.24–7.34 (m, 6H); IR (thin film) cm^{-1} 2955 (m), 2929 (m), 2859 (w), 1955 (w), 1782 (s), 1698 (s); mass spectrum (APCI): *m/e* (% relative intensity) 390 (96) $(M+H)^+$, 364 (52), 266 (43), 254 (100), 193 (41), 137 (54); HRMS-ESI *m/e* calcd for $C_{25}H_{27}NO_3Na$ 412.1883, found 412.1893.

4.1.6. Allene 20. $R_f=0.46$ (25% EtOAc in hexanes); clear oil; ^1H NMR (500 MHz, $CDCl_3$) major isomer: δ 0.85 (d, 3H, $J=7.0$ Hz), 0.95 (d, 3H, $J=7.0$ Hz), 1.97 (septet, 1H, $J=7.0$ Hz), 4.18 (t, 1H, $J=9.0$ Hz), 4.34–4.38 (m, 1H), 4.39–4.46 (m, 1H), 4.72 (d, 1H, $J=7.0$ Hz), 4.74 (d, 1H, $J=5.0$ Hz), 4.79 (d, 1H, $J=6.0$ Hz), 5.12 (dt, 1H, $J=7.0$, 9.0 Hz), 5.33–5.37 (m, 1H), 7.10–7.34 (m, 10H); minor isomer: δ 0.79 (d, 3H, $J=7.0$ Hz), 0.93 (d, 3H, $J=7.0$ Hz), 2.06 (septet, 1H, $J=7.0$ Hz), 4.06 (t, 1H, $J=9.0$ Hz), 4.34–4.38 (m, 1H), 4.39–4.46 (m, 1H), 4.68 (d, 1H, $J=7.0$ Hz), 4.71 (d, 1H, $J=5.0$ Hz), 4.86 (d, 1H, $J=6.0$ Hz), 5.24 (dt, 1H, $J=7.0$, 9.0 Hz), 5.33–5.37 (m, 1H), 7.10–7.34 (m, 10H); IR (thin film) cm^{-1} 2965 (m), 2872 (w), 1958 (w), 1782 (s), 1696 (s); mass spectrum (APCI): *m/e* (% relative intensity) 375 (33) $(M)^+$, 350 (100), 332 (27), 254 (46), 123 (13); HRMS-ESI *m/e* calcd for $C_{24}H_{25}NO_3Na$ 398.1727, found 398.1714.

4.1.7. Allene 21. $R_f=0.37$ (25% EtOAc in hexane); orange oil; ^1H NMR (300 MHz, $CDCl_3$) δ 3.92 (d, 1H, $J=9.9$ Hz), 4.03 (dd, 1H, $J=8.1$, 9.0 Hz), 4.30 (dd, 1H, $J=8.2$, 9.0 Hz), 4.34–4.46 (m, 2H), 4.65 (d, 1H, $J=5.7$ Hz), 4.98 (dt, 1H, $J=8.4$, 9.9 Hz), 5.28–5.36 (m, 1H), 6.88–7.44 (m, 15H); IR (thin film) cm^{-1} 3060 (w), 3028 (w), 1954 (w), 1770 (s), 1368 (m), 1185 (m); mass spectrum (APCI): *m/e* (% relative intensity) 410 (100) $(M+H)^+$, 254 (15); HRMS-ESI *m/e* calcd for $C_{27}H_{23}NO_3Na$ 432.1570, found 432.1582.

4.1.8. Allene 22. $R_f=0.23$ (25% EtOAc in hexane); white solid, mp 76–77 °C; ^1H NMR (500 MHz, $CDCl_3$) major isomer: δ 0.78 (d, $J=7.0$ Hz, 3H), 2.81 (s, 3H), 3.83 (dq, $J=7.0$, 8.5 Hz, 1H), 4.60–4.80 (m, 2H), 5.24 (d, $J=8.5$ Hz, 1H), 5.56 (ddd, $J=6.5$, 6.5, 8.5 Hz, 1H), 6.03 (ddd, $J=1.5$, 1.5, 8.5 Hz, 1H), 7.10–7.45 (m, 10H); minor isomer: 0.74 (d, $J=7.0$ Hz, 3H), 2.80 (s, 3H), 3.89 (dq, $J=7.0$, 8.5 Hz, 1H), 4.65–4.80 (m, 2H), 5.37 (d, $J=8.5$ Hz, 1H), 5.63 (ddd, $J=6.5$, 6.5, 8.5 Hz, 1H), 5.94 (ddd, $J=1.5$, 1.5, 8.5 Hz, 1H), 6.80–6.90 (m, 2H), 7.10–7.45 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) major isomer only δ 14.9, 28.2, 48.6, 53.5, 59.8, 76.8, 90.7, 127.0, 127.1, 128.1, 128.3, 128.5, 128.8, 136.5, 138.8, 155.2, 171.2, 208.3 (missing 4 signals due to overlap); IR (thin film) cm^{-1} 3030w, 2925w, 1956w, 1729s, 1681m, 1372m; mass spectrum (LCMS-APCI): *m/e* (% relative intensity) 347 (100) $(M+H)^+$, 191 (25); HRMS-ESI *m/e* calcd for $C_{22}H_{22}N_2O_2Na$ 369.1573, found 369.1583.

4.1.9. Allene 23. $R_f=0.40$ (25% EtOAc in hexane); yellow oil; ^1H NMR (300 MHz, $CDCl_3$) major isomer: δ 3.34 (d, 1H, $J=2.4$ Hz), 3.37 (d, 1H, $J=2.7$ Hz), 4.67 (ddd, 1H, $J=1.6$, 6.0, 11.1 Hz), 4.76 (ddd, 1H, $J=1.4$, 6.2, 13.8 Hz), 4.83 (d, 1H, $J=5.1$ Hz), 5.26–5.33 (ddd, 1H, $J=2.0$, 5.1, 7.2 Hz), 5.63–5.76 (m, 1H), 6.01 (d, 1H, $J=7.2$ Hz), 7.16–7.54 (m, 9H); minor isomer: δ 3.34 (d, 1H, $J=2.4$ Hz), 3.37 (d, 1H, $J=2.7$ Hz), 4.67 (ddd, 1H, $J=1.6$, 6.0, 11.1 Hz), 4.76 (ddd, 1H, $J=1.4$, 6.2, 13.8 Hz), 4.81 (d, 1H, $J=4.5$ Hz), 5.16–5.22 (ddd, 1H, $J=3.1$, 4.1, 6.9 Hz), 5.63–5.76 (m, 1H), 5.90 (d, 1H, $J=6.9$ Hz), 7.16–7.54 (m, 9H); IR (thin film) cm^{-1} 3064 (w), 3031 (w), 1956 (m), 1778 (s), 1696 (s), 1365 (s), 1191 (s), 856 (m); mass spectrum (APCI): *m/e* (% relative intensity) 331 (100) $(M)^+$, 306 (34), 289 (25), 176 (86), 157 (40); HRMS-ESI HRMS-ESI *m/e* calcd for $C_{21}H_{17}NO_3Na$ 354.1101, found 354.1116.

4.1.10. Allene 32. $R_f=0.44$ (25% EtOAc in hexanes); clear oil; ^1H NMR (500 MHz, $CDCl_3$) major isomer: δ 0.88 (t, 3H, $J=6.5$ Hz), 1.21–1.33 (m, 4H), 1.64 (t, 3H, $J=3.0$ Hz), 1.60–1.68 (m, 1H), 1.70–1.78 (m, 1H), 4.29 (t, 1H, $J=6.5$ Hz), 4.40 (d, 2H, $J=6.0$ Hz), 4.72 (m, 3H), 5.34 (q, 1H, $J=5.0$ Hz), 7.11–7.15 (m, 4H), 7.24–7.34 (m, 6H); IR (thin film) cm^{-1} 3062 (m), 3027 (m), 2926 (w), 1715 (s), 1604 (m); mass spectrum (APCI): *m/e* (% relative intensity) 404 (43) $(M+H)^+$, 378 (20), 254 (23), 151 (100), 123 (21); HRMS-ESI *m/e* calcd for $C_{26}H_{29}NO_3Na$ 426.2040, found 426.2036.

4.1.11. Allene 33. $R_f=0.42$ (25% EtOAc in hexanes); clear oil; ^1H NMR (500 MHz, $CDCl_3$) major isomer δ 0.88 (t, 3H, $J=7.5$ Hz), 1.30–1.43 (m, 4H), 1.76–1.87 (m, 2H), 4.44 (d, 2H, $J=6.0$ Hz), 4.69 (d, 1H, $J=4.0$ Hz), 5.08 (tt, 1H, $J=1.5$, 7.5 Hz), 5.24 (dd, 2H, $J=1.5$, 7.5 Hz), 5.27–5.30 (m, 1H), 6.88 (d, 2H, $J=7.5$ Hz), 7.02 (d, 2H, $J=7.5$ Hz), 7.16–7.51 (m, 11H); IR (thin film) cm^{-1} 2954 (m), 2923 (m), 2857 (w), 1776 (s), 1701 (s); mass spectrum (APCI): *m/e* (% relative intensity) 466 (16) $(M+H)^+$, 440 (11), 254 (6), 213

(100), 185 (7); HRMS-ESI *m/e* calcd for $C_{31}H_{32}NO_3$ 466.2377, found 466.2378.

4.2. Employing chiral propargyl alcohols

4.2.1. Allene 36. R_f=0.38 (25% EtOAc in hexanes); clear oil; $[\alpha]_D^{23}$ −68.2 (*c* 0.51, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 1.62 (dd, 3H, *J*=3.0, 7.0 Hz), 3.66 (ddq, 2H, *J*=2.5, 7.0, 18.0 Hz), 4.31 (dd, 1H, *J*=3.5, 9.0 Hz), 4.71 (t, 1H, *J*=9.0 Hz), 5.09–5.16 (m, 1H), 5.21 (dddd, 1H, *J*=2.5, 3.0, 7.0, 7.0 Hz), 5.44 (dd, 1H, *J*=3.5, 9.0 Hz), 7.27–7.47 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 36.1, 57.5, 70.0, 82.5, 86.7, 125.9, 128.6, 129.0, 138.7, 153.2, 170.4, 205.9; IR (thin film) cm^{-1} 2970 (m), 2961 (m), 2925 (m), 2870 (w), 1776 (s), 1705 (s); mass spectrum (APCI): *m/e* (% relative intensity) 258 (23) $(M+H)^+$, 164 (28), 146 (26), 120 (100), 95 (92), 87 (21); HRMS-EI *m/e* calcd for $C_{15}H_{15}NO_3$ 257.1052, found 257.1045.

4.2.2. Allene 37. R_f=0.38 (25% EtOAc in hexanes); clear oil; $[\alpha]_D^{23}$ −51.6 (*c* 0.60, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 1.62 (dd, 3H, *J*=3.0, 7.0 Hz), 3.66 (ddq, 2H, *J*=2.5, 7.0, 18.0 Hz), 4.31 (dd, 1H, *J*=3.5, 9.0 Hz), 4.71 (t, 1H, *J*=9.0 Hz), 5.09–5.16 (m, 1H), 5.21 (dddd, 1H, *J*=2.5, 3.0, 7.0, 7.0 Hz), 5.44 (dd, 1H, *J*=3.5, 9.0 Hz), 7.27–7.47 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 36.1, 57.5, 70.0, 82.5, 86.7, 125.9, 128.6, 129.0, 138.7, 153.2, 170.4, 205.9; IR (thin film) cm^{-1} 2970 (m), 2961 (m), 2925 (m), 2870 (w), 1776 (s), 1705 (s); mass spectrum (APCI): *m/e* (% relative intensity) 258 (23) $(M+H)^+$, 164 (28), 146 (26), 120 (100), 95 (92), 87 (21); HRMS-EI *m/e* calcd for $C_{15}H_{15}NO_3$ 257.1052, found 257.1050.

4.2.3. Allene 38. R_f=0.42 (25% EtOAc in hexanes); mp 92–94 °C; $[\alpha]_D^{23}$ −122.0 (*c* 0.91, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 0.86–0.89 (m, 3H), 1.25–1.32 (m, 4H), 1.49–1.56 (m, 1H), 1.70 (dd, 3H, *J*=3.0, 7.0 Hz), 1.71–1.77 (m, 1H), 4.23 (dq, 1H, *J*=1.0, 7.5 Hz), 4.41 (dd, 1H, *J*=3.0, 9.0 Hz), 4.44 (t, 1H, *J*=9.0 Hz), 4.72 (d, 1H, *J*=5.5 Hz), 5.05 (ddt, 1H, *J*=3.5, 7.5, 11.5 Hz), 5.22 (ddq, 1H, *J*=2.0, 7.5, 7.5 Hz), 5.34 (ddd, 1H, *J*=3.5, 5.5, 8.5 Hz), 7.10–7.15 (m, 4H), 7.25–7.33 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 14.2, 29.1, 31.0, 43.3, 50.4, 56.2, 64.5, 87.3, 89.0, 126.9, 127.7, 128.2, 128.6, 128.7, 129.4, 137.8, 139.4, 152.8, 174.1, 205.4 (missing 1 signal due to overlap of the terminal allene carbons); IR (thin film) cm^{-1} 2956 (m), 2922 (m), 2854 (w), 1781 (s), 1691 (s); mass spectrum (APCI): *m/e* (% relative intensity) 404 (75) $(M+H)^+$, 378 (21), 360 (20), 254 (33), 193 (18), 151 (100); HRMS-EI *m/e* calcd for $C_{26}H_{29}NO_3$ 403.2147, found 403.2137.

4.2.4. Allene 39. R_f=0.42 (25% EtOAc in hexanes); clear oil; ^1H NMR (500 MHz, $CDCl_3$) major isomer: δ 0.86–0.89 (m, 3H), 1.24–1.32 (m, 4H), 1.51–1.59 (m, 1H), 1.70 (dd, 3H, *J*=3.0, 7.0 Hz), 1.71–1.78 (m, 1H), 4.15 (dq, 1H, *J*=1.0, 7.5 Hz), 4.36–4.46 (m, 2H), 4.74 (d, 1H, *J*=5.0 Hz), 5.08–5.14 (m, 1H), 5.20 (ddq, 1H, *J*=2.0, 7.5, 7.5 Hz), 5.30–5.34 (m, 1H), 7.10–7.15 (m, 4H), 7.25–7.33 (m, 6H); minor isomer: δ 0.86–0.89 (m, 3H), 1.24–1.32 (m, 4H), 1.51–1.59 (m, 1H), 1.63 (dd, 3H, *J*=3.0, 7.0 Hz), 1.71–1.78 (m, 1H), 4.10 (dq, 1H, *J*=1.0, 7.5 Hz), 4.36–4.46 (m, 2H), 4.69 (d, 1H, *J*=5.0 Hz), 5.08–5.14 (m, 1H), 5.20 (ddq, 1H, *J*=2.0, 7.5, 7.5 Hz), 5.30–5.34 (m, 1H), 7.10–7.15 (m, 4H), 7.25–7.33 (m, 6H); IR (thin film) cm^{-1} 2956 (m), 2922 (m), 2854 (w), 1781 (s), 1691 (s); mass spectrum (APCI): *m/e* (% relative intensity) 404 (75) $(M+H)^+$, 378 (21), 360 (20), 254 (33), 193 (18), 151 (100); HRMS-EI *m/e* calcd for $C_{26}H_{29}NO_3$ 403.2147, found 403.2140.

4.2.5. Allene 40. R_f=0.41 (25% EtOAc in hexanes); mp 74–75 °C; $[\alpha]_D^{23}$ −16.7 (*c* 1.26, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 0.89 (m, 3H), 1.25–1.27 (m, 4H), 1.51 (dd, 3H, *J*=3.5, 7.0 Hz), 1.53–1.57 (m, 1H), 1.73–1.80 (m, 1H), 4.26 (dd, 1H, *J*=4.5, 9.0 Hz), 4.26–4.30 (m, 1H), 4.69 (t, 1H, *J*=9.0 Hz), 5.11–5.17 (m, 2H), 5.45 (dd, 1H, *J*=4.5, 9.0 Hz), 7.29–7.39 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 22.4, 29.2, 30.9, 43.2, 57.7, 69.7, 87.7, 88.6, 125.8, 128.5, 129 .0, 138.8, 153.1, 173.4, 205.3 (missing 1 signal due to overlap of the terminal allene carbons); IR (thin film) cm^{-1} 2960 (m), 2927 (m), 2859 (w), 1780 (s), 1704 (s); mass spectrum (APCI): *m/e* (% relative intensity) 314 (33) $(M+H)^+$, 270 (15), 164 (20), 151 (100), 123 (36), 120 (46); HRMS-EI *m/e* calcd for $C_{19}H_{23}NO_3$ 313.1677, found 313.1676.

4.2.6. Allene 42a. R_f=0.43 (25% EtOAc in hexanes); mp 95–97 °C; $[\alpha]_D^{23}$ −8.7 (*c* 0.60, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 0.86–1.02 (m, 5H), 1.06–1.20 (m, 2H), 1.24–1.36 (m, 4H), 1.49–1.63 (m, 6H), 1.70–1.88 (m, 3H), 4.25 (dd, 1H, *J*=4.0, 9.0 Hz), 4.27 (dq, 1H, *J*=2.0, 6.5 Hz), 4.69 (t, 1H, *J*=9.0 Hz), 5.20 (dt, 1H, *J*=4.0, 6.0 Hz), 5.23 (dt, 1H, *J*=4.0, 6.0 Hz), 5.45 (dd, 1H, *J*=4.0, 9.0 Hz), 7.26–7.40 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 22.6, 26.0, 26.1, 29.4, 30.5, 32.8, 32.9, 37.0, 37.2, 43.2, 57.7, 69.8, 90.0, 99.5, 125.9, 128.6, 129.1, 138.9, 153.4, 173.5, 203.7; IR (thin film) cm^{-1} 2924 (m), 2859 (w), 1785 (s), 1707 (s), 1457 (m), 1379 (m); mass spectrum (APCI): *m/e* (% relative intensity) 382 (66) $(M+H)^+$, 219 (100), 191 (6), 164 (8), 120 (9); HRMS-EI *m/e* calcd for $C_{24}H_{31}NO_3$ 381.2304, found 381.2300.

4.2.7. Allene *ent*-42a/*ent*-42b. R_f=0.43 (25% EtOAc in hexanes); clear oil; ^1H NMR (500 MHz, $CDCl_3$) major isomer **a**: δ 0.86–1.02 (m, 5H), 1.06–1.20 (m, 2H), 1.24–1.36 (m, 4H), 1.49–1.63 (m, 6H), 1.70–1.88 (m, 3H), 4.28 (dd, 1H, *J*=4.0, 9.0 Hz), 4.34 (dq, 1H, *J*=2.0, 6.5 Hz), 4.67 (t, 1H, *J*=9.0 Hz), 5.20 (dt, 1H, *J*=2.0, 6.0 Hz), 5.26–5.31 (m, 1H), 5.43 (dd, 1H, *J*=4.0, 9.0 Hz), 7.26–7.40 (m, 5H); minor isomer **b**: δ 0.86–1.02 (m, 5H), 1.06–1.20 (m, 2H), 1.24–1.36 (m, 4H), 1.49–1.63 (m, 6H), 1.70–1.88 (m, 3H), 4.26 (dd, 1H, *J*=4.0, 9.0 Hz), 4.34 (dq, 1H, *J*=2.0, 6.5 Hz), 4.67 (t, 1H, *J*=9.0 Hz), 4.96 (dt, 1H, *J*=2.0, 6.5 Hz), 5.23–5.26 (m, 1H), 5.45 (dd, 1H, *J*=4.0, 9.0 Hz), 7.26–7.40 (m, 5H); IR (thin film) cm^{-1} 2924 (m), 2859 (w), 1785 (s), 1707 (s), 1457 (m), 1379 (m); mass spectrum (APCI): *m/e* (% relative intensity) 382 (66) $(M+H)^+$, 219 (100), 191 (6), 164 (8), 120 (9); HRMS-EI *m/e* calcd for $C_{24}H_{31}NO_3$ 381.2304, found 381.2310.

4.2.8. Allene 44. R_f=0.39 (25% EtOAc in hexanes); mp 50–51 °C; $[\alpha]_D^{23}$ −18.4 (*c* 0.38, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ 0.87 (t, 3H, *J*=7.0 Hz), 0.90 (t, 3H, *J*=7.0 Hz), 1.22–1.25 (m, 4H), 1.26–1.36 (m, 6H), 1.52–1.56 (m, 1H), 1.74–1.79 (m, 1H), 1.84–1.89 (m, 2H), 4.25 (dd, 1H, *J*=4.0, 9.0 Hz), 4.29 (dq, 1H, *J*=2.5, 8.0 Hz), 4.69

(t, 1H, J=9.0 Hz), 5.14–5.19 (m, 2H), 5.45 (dd, 1H, J=4.0, 9.0 Hz), 7.14–7.39 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 13.9, 22.3, 22.4, 28.4, 28.6, 29.2, 30.8, 31.1, 43.3, 57.6, 69.6, 89.1, 93.1, 125.7, 128.4, 128.9, 138.7, 153.1, 173.4, 204.5; IR (thin film) cm^{-1} 2965 (m), 2930 (m), 2925 (m), 2860 (w), 1777 (s), 1702 (s); mass spectrum (APCI): *m/e* (% relative intensity) 370 (40) $(M+H)^+$, 326 (7), 207 (100), 164 (6), 120 (12); HRMS-EI *m/e* calcd for $C_{23}H_{31}NO_3$ 369.2304, found 369.2296.

4.2.9. Allene *ent*-44. R_f=0.39 (25% EtOAc in hexanes); mp 52–53 °C; $[\alpha]_D^{23}$ +13.0 (*c* 0.40, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.87 (t, 3H, J=7.0 Hz), 0.90 (t, 3H, J=7.0 Hz), 1.22–1.25 (m, 4H), 1.26–1.36 (m, 6H), 1.52–1.56 (m, 1H), 1.74–1.79 (m, 1H), 1.84–1.89 (m, 2H), 4.25 (dd, 1H, J=4.0, 9.0 Hz), 4.29 (dq, 1H, J=2.5, 8.0 Hz), 4.69 (t, 1H, J=9.0 Hz), 5.14–5.19 (m, 2H), 5.45 (dd, 1H, J=4.0, 9.0 Hz), 7.14–7.39 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 13.9, 22.3, 22.4, 28.4, 28.6, 29.2, 30.8, 31.1, 43.3, 57.6, 69.6, 89.1, 93.1, 125.7, 128.4, 128.9, 138.7, 153.1, 173.4, 204.5; IR (thin film) cm^{-1} 2965 (m), 2930 (m), 2925 (m), 2860 (w), 1777 (s), 1702 (s); mass spectrum (APCI): *m/e* (% relative intensity) 370 (40) $(M+H)^+$, 326 (7), 207 (100), 164 (6), 120 (12); HRMS-EI *m/e* calcd for $C_{23}H_{31}NO_3$ 369.2304, found 369.2299.

4.2.10. Allene 46. R_f=0.25 (25% EtOAc in hexanes); mp 84–86 °C; $[\alpha]_D^{23}$ +98.7 (*c* 0.46, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, 3H, J=7.0 Hz), 1.29–1.40 (m, 4H), 1.61–1.64 (m, 1H), 1.83–1.85 (m, 1H), 4.25 (dd, 1H, J=4.0, 9.0 Hz), 4.45 (dq, 1H, J=2.0, 7.0 Hz), 4.70 (t, 1H, J=9.0 Hz), 5.45 (dd, 1H, J=4.0, 9.0 Hz), 5.70 (t, 1H, J=7.0 Hz), 6.19 (dd, 1H, J=2.0, 7.0 Hz), 7.13–7.32 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.6, 29.6, 30.8, 43.5, 57.9, 69.9, 93.7, 97.0, 126.0, 126.7, 126.9, 128.6, 128.7, 129.1, 134.0, 140.2, 153.4, 173.2, 205.6; IR (thin film) cm^{-1} 2964 (m), 2933 (m), 2865 (w), 1781 (s), 1707 (m); mass spectrum (APCI): *m/e* (% relative intensity) 376 (20) $(M+H)^+$, 332 (8), 213 (100), 185 (16), 120 (7); HRMS-EI *m/e* calcd for $C_{24}H_{25}NO_3$ 375.1834, found 375.1838.

4.2.11. Allene 47. R_f=0.25 (25% EtOAc in hexanes); mp 95–97 °C; $[\alpha]_D^{23}$ −150.8 (*c* 0.39, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, 3H, J=7.0 Hz), 1.26–1.40 (m, 4H), 1.58–1.65 (m, 1H), 1.83–1.89 (m, 1H), 4.29 (dd, 1H, J=4.0, 9.0 Hz), 4.42 (dq, 1H, J=2.0, 7.0 Hz), 4.70 (t, 1H, J=9.0 Hz), 5.47 (dd, 1H, J=4.0, 8.5 Hz), 5.73 (t, 1H, J=7.0 Hz), 6.00 (dd, 1H, J=2.0, 7.0 Hz), 7.15–7.56 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 22.6, 29.5, 31.3, 43.5, 57.7, 69.8, 93.6, 96.8, 126.0, 126.6, 126.8, 128.6, 128.7, 129.2, 133.8, 138.8, 153.3, 172.8, 205.5; IR (thin film) cm^{-1} 2964 (m), 2933 (m), 1781 (s), 1707 (m), 1385 (m); mass spectrum (APCI): *m/e* (% relative intensity) 376 (20) $(M+H)^+$, 332 (8), 213 (100), 185 (16), 120 (7); HRMS-EI *m/e* calcd for $C_{24}H_{25}NO_3$ 375.1834, found 375.1830.

4.2.12. Allene 48. R_f=0.25 (25% EtOAc in hexanes); mp 86–87 °C; $[\alpha]_D^{23}$ −99.1 (*c* 0.54, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, 3H, J=7.0 Hz), 1.29–1.40 (m, 4H), 1.61–1.64 (m, 1H), 1.83–1.85 (m, 1H), 4.25 (dd, 1H, J=4.0, 9.0 Hz), 4.45 (dq, 1H, J=2.0, 7.0 Hz), 4.70 (t, 1H, J=9.0 Hz), 5.45 (dd, 1H, J=4.0, 9.0 Hz), 5.70 (t, 1H, J=7.0 Hz), 6.19 (dd, 1H, J=2.0, 7.0 Hz), 7.13–7.32 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 22.6, 29.6, 30.8, 43.5, 57.9, 69.9, 93.7, 97.0, 126.0, 126.7, 126.9, 128.6, 128.7, 129.1, 134.0, 140.2, 153.4, 173.2, 205.6; IR (thin film) cm^{-1} 2964 (m), 2933 (m), 2865 (w), 1781 (s), 1385 (m); mass spectrum (APCI): *m/e* (% relative intensity) 376 (20) $(M+H)^+$, 332 (8), 213 (100), 185 (16), 120 (7); HRMS-EI *m/e* calcd for $C_{24}H_{25}NO_3$ 375.1834, found 375.1833.

4.2.13. Allene 49. R_f=0.25 (25% EtOAc in hexanes); mp 81–83 °C; $[\alpha]_D^{23}$ +126.5 (*c* 0.80, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, 3H, J=7.0 Hz), 1.26–1.40 (m, 4H), 1.58–1.65 (m, 1H), 1.83–1.89 (m, 1H), 4.29 (dd, 1H, J=4.0, 9.0 Hz), 4.42 (dq, 1H, J=2.0, 7.0 Hz), 4.70 (t, 1H, J=9.0 Hz), 5.47 (dd, 1H, J=4.0, 8.5 Hz), 5.73 (t, 1H, J=7.0 Hz), 6.00 (dd, 1H, J=2.0, 7.0 Hz), 7.15–7.56 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 22.6, 29.5, 31.3, 43.5, 57.7, 69.8, 93.6, 96.8, 126.0, 126.6, 126.8, 128.6, 128.7, 129.2, 133.8, 138.8, 153.3, 172.8, 205.5; IR (thin film) cm^{-1} 2964 (m), 2933 (m), 2865 (w), 1781 (s); mass spectrum (APCI): *m/e* (% relative intensity) 376 (20) $(M+H)^+$, 332 (8), 213 (100), 185 (16), 120 (7); HRMS-EI *m/e* calcd for $C_{24}H_{25}NO_3$ 375.1834, found 375.1827.

4.2.14. Allene 52. R_f=0.50 (25% EtOAc in hexanes); clear oil; $[\alpha]_D^{23}$ −94.0 (*c* 0.90, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.86 (t, 3H, J=7.0 Hz), 0.92 (t, 3H, J=7.0 Hz), 1.24–1.28 (m, 2H), 1.32–1.42 (m, 6H), 1.52–1.55 (m, 2H), 1.71–1.92 (m, 4H), 4.18 (dd, 1H, J=4.5, 9.0 Hz), 4.65 (t, 1H, J=9.0 Hz), 5.05 (dt, 1H, J=2.0, 7.0 Hz), 5.44 (dd, 1H, J=4.5, 9.0 Hz), 5.53 (dt, 1H, J=2.0, 7.0 Hz), 7.18–7.45 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 22.3, 22.6, 28.4, 29.0, 29.8, 31.3, 31.6, 43.5, 57.8, 65.5, 69.5, 90.1, 96.5, 125.7, 126.3, 128.1, 128.2, 128.8, 131.5, 136.5, 138.4, 153.4, 173.3, 204.5; IR (thin film) cm^{-1} 2960 (m), 2932 (m), 2862 (w), 1784 (s), 1702 (s); mass spectrum (APCI): *m/e* (% relative intensity) 446 (8) $(M+H)^+$, 284 (22), 283 (100); HRMS-EI *m/e* calcd for $C_{29}H_{35}NO_3$ 445.2617, found 445.2615.

4.2.15. Allene 53. R_f=0.48 (25% EtOAc in hexanes); clear oil; $[\alpha]_D^{23}$ −47.5 (*c* 0.40, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.82 (t, 3H, J=7.0 Hz), 0.92 (t, 3H, J=7.0 Hz), 0.94–0.97 (m, 2H), 1.07–1.32 (m, 12H), 1.55–1.80 (m, 9H), 4.24 (dd, 1H, J=4.5, 8.5 Hz), 4.41 (t, 1H, J=7.0 Hz), 4.67 (t, 1H, J=8.5 Hz), 5.16–5.18 (m, 1H), 5.46 (dd, 1H, J=4.5, 8.5 Hz), 7.28–7.36 (m, 5H);^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 18.2, 22.2, 22.5, 25.8, 26.0, 27.9, 29.5, 29.6, 30.2, 30.7, 33.0, 37.5, 44.2, 46.2, 57.7, 67.3, 100.1, 103.1, 125.9, 128.4, 128.8, 138.8, 153.3, 173.6, 200.9; IR (thin film) cm^{-1} 2958 (m), 2940 (m), 2856 (w), 1784 (s), 1701 (s); mass spectrum (APCI): *m/e* (% relative intensity) 438 (73) $(M+H)^+$, 394 (7), 340 (10), 275 (100), 177 (17); HRMS-EI *m/e* calcd for $C_{28}H_{39}NO_3$ 437.2930, found 437.2920.

4.2.16. Allene 54. R_f=0.39 (25% EtOAc in hexanes); clear oil; ^{1}H NMR (500 MHz, $CDCl_3$) major isomer: δ 0.81–0.91 (m, 6H), 1.21–1.57 (m, 11H), 1.70–2.01 (m, 3H), 4.26 (dd, 1H, J=4.2, 9.0 Hz), 4.31–4.36 (m, 1H), 4.68 (t, 1H, J=9.0 Hz), 5.19–5.25 (m, 2H), 5.45 (t, 1H, J=9.0 Hz), 7.27–7.40 (m, 5H); minor isomer: δ 0.81–0.91 (m, 6H), 1.21–1.57

(m, 11H), 1.70–2.01 (m, 3H), 4.28 (dd, 1H, J=4.2, 9.0 Hz), 4.31–4.36 (m, 1H), 4.70 (t, 1H, J=9.0 Hz), 4.98 (dq, 1H, J=1.8, 6.6 Hz), 5.20–5.25 (m, 1H), 5.44 (t, 1H, J=9.0 Hz), 7.27–7.40 (m, 5H); IR (thin film) cm^{-1} 2965 (m), 2930 (m), 2925 (m), 2860 (w), 1777 (s), 1702 (s); mass spectrum (APCI): *m/e* (% relative intensity) 370 (46) $(M+H)^+$, 326 (9), 207 (100), 120 (26), 87 (12); HRMS-EI *m/e* calcd for $C_{23}H_{31}NO_3$ 369.2304, found 369.2300.

4.2.17. Hydrogenated product 55. R_f=0.39 (25% EtOAc in hexanes); clear oil; ^1H NMR (500 MHz, $CDCl_3$) major isomer: δ 0.77 (t, 3H, J=6.9 Hz), 0.85–0.91 (m, 3H), 0.88 (t, 3H, J=6.9 Hz), 0.98–1.08 (m, 4H), 1.14–1.29 (m, 8H), 1.36–1.46 (m, 3H), 1.51–1.67 (m, 2H), 3.77–3.86 (m, 1H), 4.26 (dd, 1H, J=3.9, 9.0 Hz), 4.68 (t, 1H, J=9.0 Hz), 5.46 (dd, 1H, J=3.9, 9.0 Hz), 7.27–7.40 (m, 5H); minor isomer: δ 0.77 (t, 3H, J=6.9 Hz), 0.85–0.91 (m, 3H), 0.88 (t, 3H, J=6.9 Hz), 0.98–1.08 (m, 4H), 1.14–1.29 (m, 8H), 1.36–1.46 (m, 3H), 1.51–1.67 (m, 2H), 3.77–3.86 (m, 1H), 4.27 (dd, 1H, J=3.9, 9.0 Hz), 4.68 (t, 1H, J=9.0 Hz), 5.46 (dd, 1H, J=3.9, 9.0 Hz), 7.27–7.40 (m, 5H); IR (thin film) cm^{-1} 2955 (m), 2942 (m), 2862 (w), 1782 (s), 1703 (s); mass spectrum (APCI): *m/e* (% relative intensity) 374 (100) $(M+H)^+$, 282 (22), 211 (22), 183 (75), 164 (82), 120 (23); HRMS-EI *m/e* calcd for $C_{23}H_{35}NO_3$ 373.2617, found 373.2612.

4.2.18. Hydrogenated product 56. R_f=0.25 (25% EtOAc in hexanes); clear oil; $[\alpha]_D^{23}$ −32.9 (*c* 0.42, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, 3H, J=6.9 Hz), 1.24–1.28 (m, 4H), 1.33–1.52 (m, 4H), 1.54–1.70 (m, 2H), 2.48 (t, 2H, J=7.5 Hz), 3.89 (dddd, 1H, J=5.1, 7.8, 10.5, 13.2 Hz), 4.27 (dd, 1H, J=6.9, 9.0 Hz), 4.69 (t, 1H, J=9.0 Hz), 5.46 (dd, 1H, J=6.9, 9.0 Hz), 7.03–7.05 (m, 2H), 7.18–7.37 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 22.8, 28.5, 29.5, 31.5, 32.4, 35.8, 42.5, 57.8, 69.6, 125.6, 126.0, 128.2, 128.3, 128.7, 129.1, 139.2, 142.1, 153.4, 176.4; IR (thin film) cm^{-1} 2955 (m), 2942 (m), 2862 (w), 1782 (s), 1703 (s); mass spectrum (APCI): *m/e* (% relative intensity) 380 (100) $(M+H)^+$, 217 (22), 189 (73), 164 (49), 87 (41); HRMS-EI *m/e* calcd for $C_{24}H_{29}NO_3$ 379.2147, found 379.2155.

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30. These calculations were carried out with some constraints. Specifically, the terminal alkyne carbon and C2 in **58b**-*Re* and **58b**-*Si* were placed within proximity (2.31 Å) of bond formation in transition states. PM3 calculations showed an energetic difference of 1.3 Kcal mol^{-1} in favor of **58b**-*Re* when R^2=*c*-hex.