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Copper-Catalyzed Oxaziridine-Mediated Oxidation of C−H Bonds

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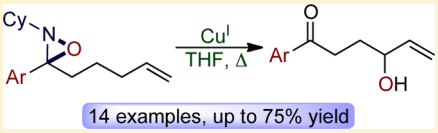
Supporting Information

ABSTRACT: The highly regio- and chemoselective oxidation of activated C−H bonds has been observed via copper-catalyzed reactions of oxaziridines. The oxidation proceeded with a variety of substrates, primarily comprising allylic and benzylic examples, as well as one example of an otherwise unactivated tertiary C−H bond. The mechanism of the reaction is proposed to involve single-electron transfer to the oxaziridines to generate a copper-bound radical anion, followed by hydrogen atom abstraction and collapse to products, with regeneration of the catalyst by a final single-electron transfer event. The involvement of allylic radical intermediates was supported by a radical-trapping experiment with TEMPO.



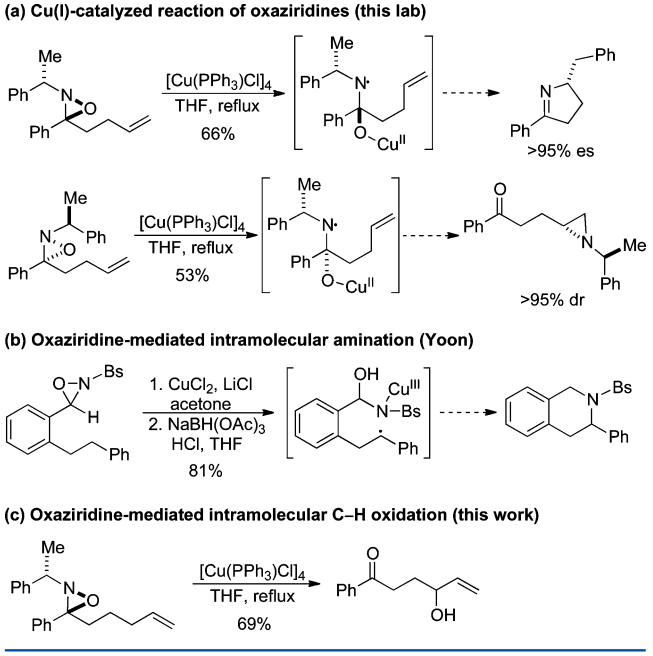
INTRODUCTION

The past decade has seen numerous advances in the development of new and versatile reagents and catalysts to mimic nature's ability to selectively oxidize C−H bonds, which has long intrigued synthetic chemists.[1,2] C−H oxidation reactions, in particular allylic C−H oxidations, have received substantial attention due to their considerable potential for synthetic applications.[3] The copper-catalyzed allylic oxidation using organic peroxide is well-known and often referred to as the Kharasch−Sosnovsky reaction.[4] Herein, we report a copper-catalyzed C−H bond oxidation via the regio- and chemoselective intramolecular transfer of oxygen from oxaziridines.

Oxaziridines, by virtue of their weak N−O bond and strained three-membered heterocyclic ring, possess unusual reactivity that has been previously exploited in heteroatom-transfer reactions.[5] Moreover, oxyfunctionalization of unactivated C−H bonds has been reported with oxaziridines bearing strong electron-withdrawing groups.[6] Recently, copper and other transition metal-catalyzed aminohydroxylation reactions of olefins using *N*-sulfonyloxaziridines have been developed by Yoon and co-workers.[7]

We previously reported the copper-catalyzed reactions of chiral oxaziridines to afford enantiomerically pure pyrrolines and aziridines (Scheme 1a).[8] The stereochemistry of the starting oxaziridines was found to have a remarkable influence on the course of the reaction. Thus, either pyrrolines or aziridines were obtained through two different highly selective reaction pathways (Scheme 1a). In each case, we proposed opening of the oxaziridine ring via single-electron transfer (SET) to afford a nitrogen-center radical/oxygen anion pair, as previously proposed by Emmons, Minisci, Black, and other pioneers of oxaziridine chemistry for reactions promoted by low-valent metals like Fe(II) or Cu(I).[9a−f] This reactive intermediate then underwent addition to the attached olefin; the product observed depended on the relative stereochemistry between the α center of the *N*-phenylethyl group and the oxaziridine C-3 atom. Recently, Yoon and co-workers reported a different radical-mediated reaction of oxaziridines, in which a benzylic C−H hydrogen atom was ultimately transferred to a Cu(II)-coordinated oxaziridine (Scheme 1b).[7e]

Scheme 1. Copper-Catalyzed Transformations of Oxaziridines



While exploring the scope of the reactions shown in Scheme 1a, we extended the linker between the oxaziridine and alkene from two to three carbons (cf. Schemes 1a and c). Under identical conditions as before, the latter reactions afforded an allylic alcohol instead of a tetrahydropyridine or aziridine, either of which might have been expected in analogy with Scheme 1a. These results were interesting, in part because they represent the chemoselective oxidation of an sp^3 C−H bond, but also

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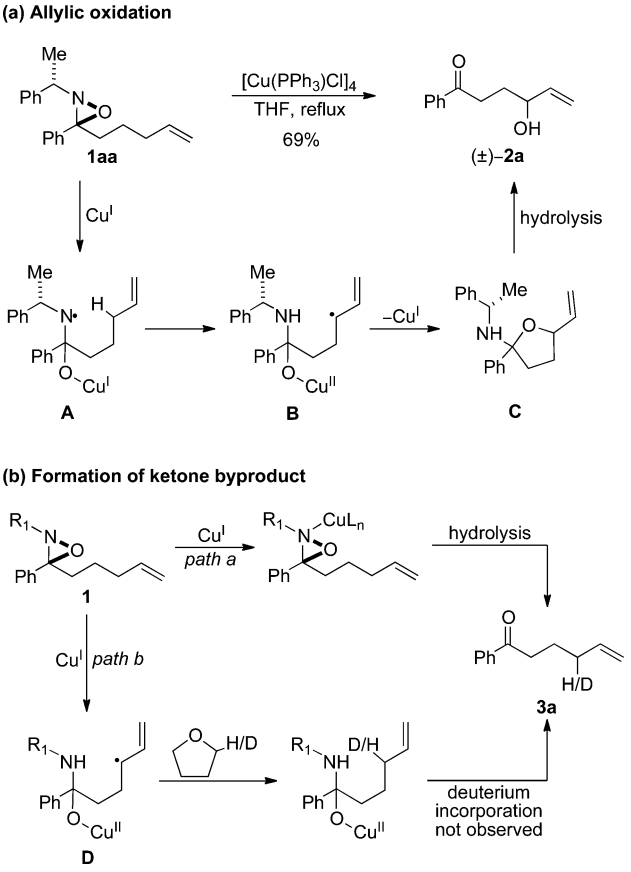
because they diverge from previously reported oxaziridine reactivity. For example, C−H oxidation by oxaziridines typically requires electron-withdrawing substituents.[6] Moreover, alkene epoxidation has been observed with oxaziridines,[6a,c,9f] but we observed no epoxide formation in these reactions.

For these reasons and because of general contemporary interest in mild means of carrying out C−H oxidation chemistry, we chose to further investigate this reaction. In this report, we describe its study through a collection of studies of substrate scope, catalyst optimization, and preliminary mechanistic studies.

RESULTS AND DISCUSSION

Initial Observations and Mechanistic Framework. We believe that reaction of oxaziridine **1aa** proceeds through a radical mechanism as outlined in Scheme 2a. In the first step,

Scheme 2. Proposed Mechanism

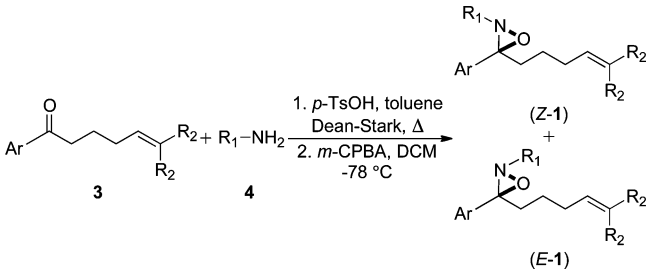


SET from the metal catalyst to the oxaziridine gives a radical/anion pair **A** as previously proposed.[8a,9f,k] 1,5-Hydrogen atom transfer to the nitrogen-centered radical via abstraction from the allylic C−H bond[2j,10] then generates the carbon-centered allylic radical **B**. Presumably, the longer tether length, which permits a six-membered transition structure culminating in an allylic hydrogen atom, makes this hydrogen transfer step more facile compared to addition to the olefin as observed previously.[8a] Conversion of **B** to intermediate **C** can be viewed in several ways. First, an oxygen-centered radical would be generated via homolysis, coupled with regeneration of the Cu(I) catalyst; the 2-aminotetrahydrofuran intermediate might then form by radical recombination. Alternatively, the radical species might attack the bound copper atom to afford an allyl Cu(III) oxide, which would undergo reductive elimination (related Cu(III) species have been proposed in ring-opening reactions of diaziridinones;[9g−j] we thank a reviewer of the first submission of this paper for this suggestion). Finally, SET between the allylic radical and the oxygen radical could afford an allylic cation/oxygen-centered anion pair that would suffer cyclization to afford the hemiaminal. In either case, hydrolysis of **C** then leads to the observed allylic alcohol product **2a**.

The major side product of the reaction is unoxidized ketone **3a** from which the oxaziridine was initially derived (Scheme 2b). This could in principle arise from Lewis acid-catalyzed hydrolysis of the oxaziridines (path a)[9a,11] or by a mechanism involving the intermolecular quenching of the allylic radical **D** by solvent (path b).[9b,12] We note that ketones and other byproducts have also been observed in other single-electron transfer reactions of oxaziridines with ferrous ions.[9a,b] When one example of an oxaziridine **1ab** (see structure below) was subjected to the above conditions in THF-d_8, no incorporation of deuterium was observed in the ketone isolated from that experiment, which is consistent with path a being operative for this side reaction.

Exploration of Reaction Conditions. Oxaziridines were prepared as described in previous reports.[8a,13] In general, imines were formed by combining ketone **3** and the respective amine in refluxing toluene using a Dean−Stark apparatus. The imine solution was then cooled to −78 °C and treated with *meta*-chloroperbenzoic acid (olefin epoxidation is known not to compete with oxaziridination under these circumstances[8a,13b,14] and that was the case here as well; Scheme 3). Where possible,

Scheme 3. Preparation of Oxaziridines



a pure oxaziridine isomer was isolated from the stereoisomeric mixture of oxaziridines. The stereochemical assignments for oxaziridine diastereomers were made on the basis of established spectroscopic trends.[8a,15]

Experiments using the single diastereomer of oxaziridine **1aa** shown gave racemic allylic alcohol **2a** (ca. 5% ee by chiral GC analysis). Consequently, we focused our initial efforts on exploring the racemic reaction of oxaziridines derived from simple primary amines and aryl-4-alkenyl ketones (Table 1). Although a variety of oxaziridines derived from branched amines were effective in executing the transformation to allylic alcohols, no such product was obtained from an oxaziridine bearing an *N*-benzyl group (Table 1, entry 4). It is possible that the relatively more accessible nitrogen atom in this system is better able to directly coordinate with the copper catalyst, resulting in hydrolysis being more competitive with SET, but the reasons for the failure of this substrate to undergo the catalytic process of interest were not further explored. Among the various nitrogen substituents tried, oxaziridines derived from cyclohexylamine gave the best results and were chosen for the optimization of reaction conditions and exploration of

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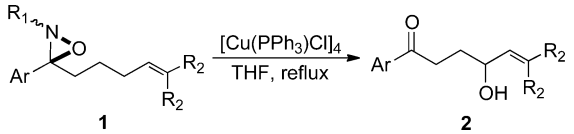
Table 1. Screening of Amine Substituent



1 2

entry	substrate **1**	Ar	R_1	R_2	*Z*/*E* ratio of oxaziridine	product **2**	yield[a] (%)
1	**1aa**	Ph	(*S*)-PhCH(CH_3)	H	>95:5	**2a**	69
2	**1ab**	Ph	*c*-C_6H_{11}	H	>95:5	**2a**	74
3	**1ac**	Ph	Ph_2CH	H	77:23[b]	**2a**	22 (26)[c]
4	**1ad**	Ph	$PhCH_2$	H	>95:5	**2a**	0[d]
5	**1ba**	3,4-di-OMePh	(*S*)-PhCH(CH_3)	H	>95:5	**2b**	48
6	**1bb**	3,4-di-OMePh	*c*-C_6H_{11}	H	>95:5	**2b**	37
7	**1ca**	Ph	(*S*)-PhCH(CH_3)	CH_3	90:10	**2c**	74
8	**1cb**	Ph	*c*-C_6H_{11}	CH_3	63:37	**2c**	64
9	**1cc**	Ph	Ph_2CH	CH_3	70:30	**2c**	65

[a]In all cases, 10−20% of unoxidized ketones **3** were also obtained. [b]Oxaziridine was contaminated with ca. 12% of dibenzhydrylamine. [c]Yield in parentheses based on the recovery of the oxaziridine substrate. [d]Ketone **3a** was the only observed product (recovered in 96% yield).

substrate scope. Such oxaziridines gave results comparable to those from α-methylbenzylamine (cf. entries 1 and 2, 5 and 6, and 7 and 8). Moreover, cyclohexylamine is inexpensive and achiral (thus lowering the number of oxaziridine stereoisomers) and conveniently has a relatively high boiling point compared to other simple aliphatic amines.

The initial results for the transformation of the oxaziridines to allylic alcohols with $[Cu(PPh_3)Cl]_4$ (Scheme 1c) were encouraging, so we examined other copper and iron salts, known to promote single-electron transfer reactions with an equal mixture of *Z*- and *E*-oxaziridine diastereomers of **1ab** (Table 2).[8a,c,9a,b,12a] In general, all of the reactions examined afforded varying quantities of oxidized product **2a** with unoxidized ketone **3a**, except for the control reaction (entry 1) where no product was observed in the absence of copper source. In some cases, minor side products were also observed but not characterized.[8c,9b] We examined the effect of both solvent and a range of copper salts, with a range of results (entries 2−15). Use of either Cu(II) (entry 13) or Cu(I) (entry 14) sources resulted in similar yield for the reaction. In contrast, iron salts were wholly ineffective (entries 10−12).

We also investigated various additives in attempts to improve the conversion to desired product (entries 16−27). Interestingly, allylic alcohol **2a** was obtained in significantly higher yield when the reaction was catalyzed by a CuCl-BINAP complex (entries 17−19). Moreover, the ratio of the **2a** to **3a** was considerably increased using these conditions (cf. entry 2 with entry 18). No improvement in yield was observed with other phosphine ligands (entries 23−27). No enantioselectivity was observed with (*S*)-BINAP, and the yield obtained was comparable to that obtained using *rac*-BINAP.[16] On the basis of these results, we chose to adopt CuCl and *rac*-BINAP as our standard reaction conditions, along with the originally identified $[Cu(PPh_3)Cl]_4$, both in 5 mol % (note that for the tetrameric $[Cu(PPh_3)Cl]_4$, this corresponds to 20 mol % of Cu(I)). Reaction yields were only slightly affected when the reaction was carried out with 10 vs 1 mol % of CuCl/*rac*-BINAP (cf. entries 20 and 21). Solvent had a substantial effect on reaction yields, either with or without additives, with THF and MeCN being best among those examined (entries 18 and 19). In contrast, nonpolar hydrophobic solvents were essentially useless in this context.

We were able to separate the two oxaziridine diastereomers for the 3,4-dimethoxyphenyl substrate **1bb**. Subjecting each separately to identical reaction conditions afforded **2b** in comparable yields (Scheme 4). Pragmatically, this means that one need not worry about obtaining diastereomerically pure samples for carrying out the oxidation process (in stark contrast to our observations for the chemistry in Scheme 1a). It is also consistent with a mechanism in which N−O bond cleavage is the first step (affording, here, enantiomeric intermediates).

The involvement of radicals in the copper-catalyzed allylic oxidations by peroxy esters, also accounting for the regeneration of the active copper(I) species, has been supported by kinetic and ESR studies.[4b,17] Recently, Yoon and co-workers have proposed and provided good evidence for a radical mechanism for the oxaziridine-mediated oxyamination reaction and oxidative functionalization of alkenes with Davis-type oxaziridines.[7d,g] However, although strong evidence for the generation of the radical species was obtained, they were unable to trap the radical intermediate leading to the amino-hydroxylation product using standard trapping reagents such as TEMPO.[7d] In order to support the mechanistic hypothesis proposed in this paper for the present C−H oxidation, we too decided to attempt a radical-trapping experiment with TEMPO.[9c,18]

To this end, the reaction was carried out under the standard conditions with a stoichiometric amount of TEMPO added (Scheme 5). The product profile of this experiment included three products that incorporated TEMPO in addition to allylic alcohol **2a**, which was obtained in 23% yield. Thus, the internally substituted product **5a** was obtained in 19% yield, and terminal radical-trapped products were obtained as a mixture of *trans* and *cis* isomers (**5b**:**5c** = 62:38) in a combined 18% yield. The formation of these TEMPO adducts provides strong evidence for the intermediacy of the allylic radical en route to the allylic alcohol.

The absence of enantioselectivity of the reaction may be explained in the context of the proposed mechanism. Even if the hydrogen abstraction step were stereoselective, the conformational flexibility of the allylic side chain could combine with lack of facial selectivity in the ensuing radical- or SET-mediated recombination step. The failure of a chiral additive to overcome these obstacles could be due to (1) too much distance between the ligand and the forming C−O bond, (2)

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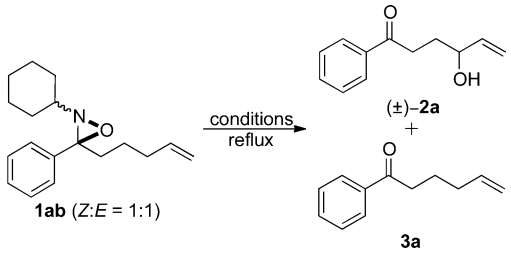
Table 2. Optimization of Reaction Conditions for the Transformation of Oxaziridines to Allylic Alcohols[a]



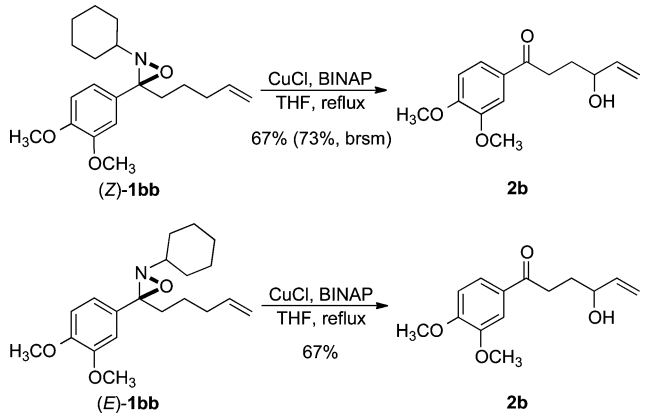
entry	catalyst (5 mol %)	ligand (5 mol %)	solvent	yield (%)[b] 2a	3a
1	none		THF	–	trace[f]
2	$[Cu(PPh_3)Cl]_4$		THF	46	23
3	$[Cu(PPh_3)Cl]_4$		Toluene	14	47
4	$[Cu(PPh_3)Cl]_4$		*i*-PrOH	30	25
5	$[Cu(PPh_3)Cl]_4$		Benzene	6	72
6	$[Cu(PPh_3)Cl]_4$		CH_2Cl_2	41	36
7	$Cu(OTf)_2$		THF	53	26
8	$Cu(acac)_2$[c]		THF	16	9
9	$CuBr{\cdot}SMe_2$		THF	16	67
10	$Fe(acac)_2$[d,f]		THF	–	–
11	$Fe(acac)_3$[f]		THF	–	–
12	$FeBr_2$[e,f]		THF	4	14
13	$CuCl_2$		THF	50	22
14	CuCl		THF	50	17
15	CuCl and LiCl		THF	31	31
16	CuCl	2,2′-Bipyridyl	THF	51	14
17	CuCl	(*S*)-BINAP	THF	61[g]	9
18	CuCl	*rac*-BINAP	THF	63	9
19	CuCl	*rac*-BINAP	MeCN	63	8
20	CuCl[h]	*rac*-BINAP[h]	THF	58	8
21	CuCl[i]	*rac*-BINAP[i]	THF	54	3
22	CuCl	*rac*-BINAP	MeOH	–[j]	76
23	CuCl	dppp[k]	THF	43	9
24	CuCl[f]	Xantphos	THF	–	11
25	CuCl	Dcppe[l]	THF	53	6
26	CuCl	(*S*)-Xylyl-P-Phos	THF	50	5
27	CuCl	Bdppmb[m]	THF	56	17

[a]Reactions were performed using 1 equiv of oxaziridine, 5 mol % of catalyst, and 5 mol % of ligand in different solvents under refluxing conditions for 1 h under Ar unless otherwise noted. [b]Isolated yields. [c]Reaction was run for 1.5 h. [d]Reaction was run for 4 h. [e]Reaction was run for 2.5 h. [f]Oxaziridine was completely recovered except for entries 12 and 24. [g]Chiral GC showed that **2a** was obtained in ca. 5% ee. [h]10 mol % of CuCl and *rac*-BINAP were used. [i]1 mol % of CuCl and *rac*-BINAP were used. [j]No product was observed in this case. [k]1,3-Bis(diphenylphosphino)propane. [l]Bis(dicyclohexylphosphino-phenyl)-ether. [m]1,2-Bis(diphenylphosphinomethyl)benzene.

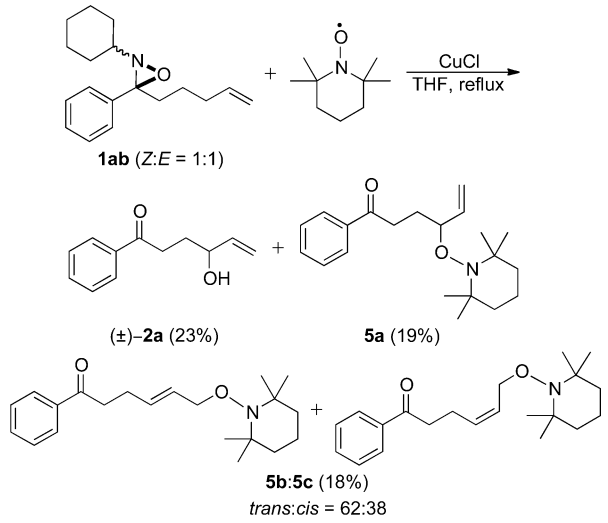
the complete disassociation of the ligand prior to this stage of the reaction, or (3) simply not enough chiral differentiation afforded by the ligands tried.

Reaction Scope. The scope of this transformation was then investigated (Table 3). Substrates were tested with two catalyst systems, $[Cu(PPh_3)Cl]_4$ and a mixture of CuCl and *rac*-BINAP. For the simple phenyl-substituted compound, both catalysts gave similar yields (entry 1). Substrates containing electron-rich (Table 3, entry 2 and Scheme 4) and electron-poor (entry 3) aromatic ring, as well as a furanyl group at C-3 (entry 4), all led to oxidation product. As observed for (*Z*)- and (*E*)-**1bb** (Scheme 4), oxaziridine diastereomers of the naphthyl substrate

Scheme 4. Examination of Oxaziridine Diastereomers



Scheme 5. Radical-Trapping Experiment with TEMPO



afforded the product in comparable yield (entries 5 and 6). The reaction proceeded in good yields with substituted alkenes as well (entries 7 and 8). Consistent with the proposed mechanism, oxidation of the methylene group closest to the oxaziridine was exclusively observed. The use of CuCl-BINAP complex resulted in better yields in most but not all cases (e.g., the sterically demanding case in entries 5 and 6). Oxaziridines bearing ortho substitution on the C-3 phenyl group or substitution alpha to the oxaziridine ring could not be synthesized using our standard protocol, presumably because of an increase in the steric environment around the carbonyl group.

In addition to the olefin-containing substrates, it proved possible to oxidize benzylic and propargylic C–H bonds in modest to good yields (Scheme 6). The potential versatility of this transformation was further shown through the oxidation of the unactivated tertiary C–H bond to afford the tertiary alcohol **11a**, albeit in low yield (Scheme 6). In this case, a cyclized product **11b** was also obtained, which could result from radical cyclization between the tertiary radical and the phenyl group[8b,c] or from electrophilic aromatic substitution with a tertiary carbocation formed from the ionization of tertiary alcohol.[19]

Two additional cases help delineate the limits of this oxidation reaction. When we examined the behavior of an oxaziridine substrate bearing a four-carbon tether (Scheme 7), we observed three different products in low yields in addition

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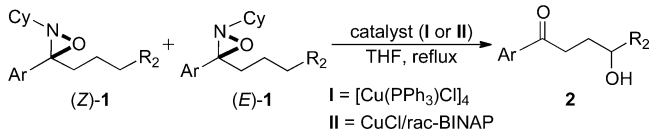
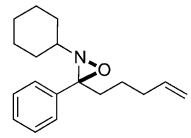
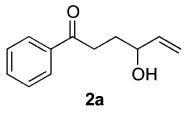
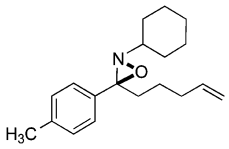
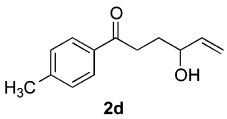
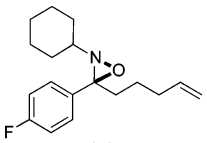
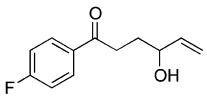
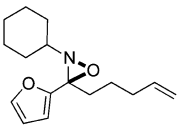
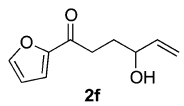
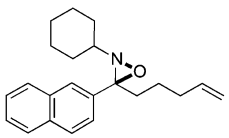
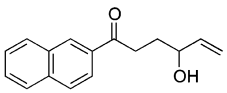
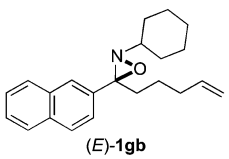
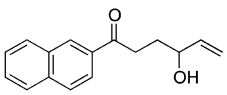
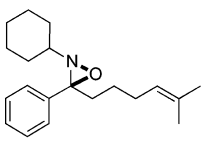
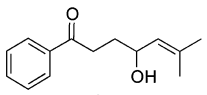
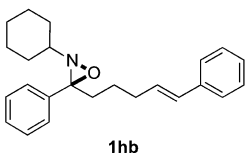
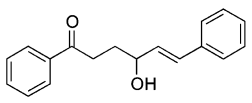
Table 3. Substrate Scope for Intramolecular C−H Oxidation[a]



entry	oxaziridine	*Z*:*E* ratio	product	catalyst: yield[b] (%)
1	 **1ab**	>95:5 >95:5	 **2a**	**I**[c]: 74 **II**[d]: 74
2	 **1db**	- 48:52	 **2d**	**I**: ND **II**[d]: 57
3	 **1eb**	88:12 58:42	 **2e**	**I**[d]: 50 **II**[d]: 66
4	 **1fb**	>95:5 -	 **2f**	**I**[d]: 51 **II**: ND
5	 (*Z*)-**1gb**	90:10 90:10	 **2g**	**I**[c]: 57[e] **II**[d]: 46 (57)[f]
6	 (*E*)-**1gb**	16:84 16:84	 **2g**	**I**[c]: 41[g] **II**[d]: 53 (73)[f]
7	 **1cb**	63:37 >95:5	 **2c**	**I**[d]: 64 **II**[d]: 75
8	 **1hb**	60:40 60:40	 **2h**	**I**[d]: 72 **II**[d]: 69

[a]Reactions were conducted using 1 equiv of oxaziridine, 5 mol % of catalyst, and 5 mol % of ligand in THF under refluxing conditions for 1 h under argon atmosphere unless otherwise noted. ND = not determined. [b]In all cases, unoxidized ketone was obtained as a side product. [c]Reaction was run for 3 h. [d]Reaction was run for 1 h. [e]4.5 mol % of $[Cu(PPh_3)Cl]_4$ was used. [f]Yields in parentheses represent the yields based on the recovery of the starting oxaziridines. [g]4.2 mol % of $[Cu(PPh_3)Cl]_4$ was used.

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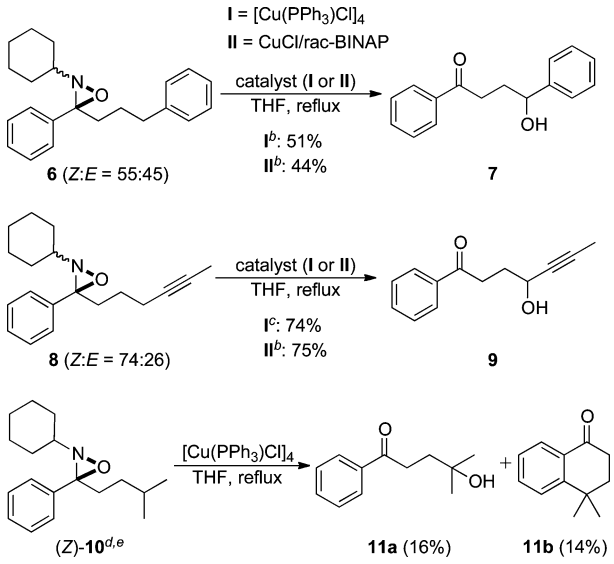
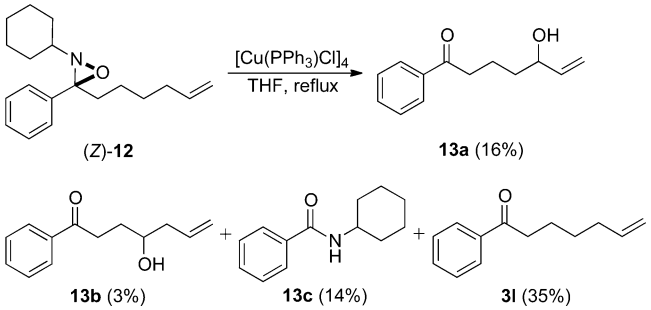
Scheme 6. Survey of Nonalkenyl Oxaziridines[a]



[a]For details, see the Experimental Section. [b]Reaction was run for 3 h. [c]Reaction was run for 1 h. [d]Reaction was run for 2 h. [e]Oxaziridine was accompanied with 22% of the starting ketone.

Scheme 7. Reaction of Oxaziridine with a Four-Carbon Tether[a,b]

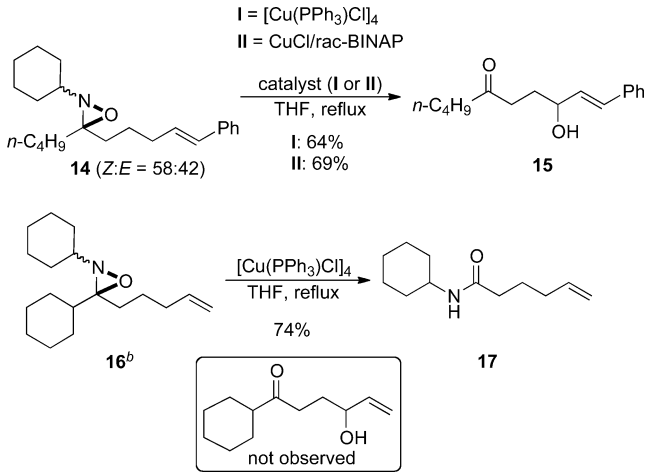


[a]For details, see the Experimental Section. [b]Reaction with the mixture of oxaziridine diastereomers and CuCl-BINAP complex was less effective than the $[Cu(PPh_3)Cl]_4$.

to the usual reversion to ketone. Allylic alcohol **13a** arising from 1,6-hydrogen transfer was obtained in very low yield, whereas homoallylic alcohol **13b** from 1,5-hydrogen transfer was formed in a trace amount. Amide **13c** was also obtained in low yield resulting from β-scission. These results are consistent with the need for both a stable radical intermediate for oxidation as well as a favorable geometry for hydrogen atom abstraction.

In our previous work, we found that the cyclization reactions shown in Scheme 1a were derailed when the oxaziridine's C-3 aryl group was replaced with an alkyl substituent capable of forming a stable carbon-centered radical. In those instances, the main reaction pathway was β-scission of the C−C bond adjacent to the proposed *N*-centered radical.[8b,c] In the present case, we found divergent behavior for primary vs secondary alkyl groups at the analogous position. Accordingly, the substrate bearing an *n*-butyl subsituent at C-3 afforded the allylic alcohol **15** in good yield, but the cleaved amide product **17** was observed upon reaction of the cyclohexyl substituent (Scheme 8).

Scheme 8. Dependence of Product on 3-Alkyl Substituent[a]



[a]For details, see the Experimental Section. [b]79:21 mixture of oxaziridine isomers, unassigned.

CONCLUSIONS

In summary, we have developed an efficient and regioselective copper-catalyzed transformation of oxaziridines to allylic alcohols via intramolecular C−H bond oxidation. The reaction works well with a variety of substrates, but activated C−H bonds are preferred. Support for a radical mechanism has been demonstrated through radical-trapping experiment with TEMPO. Future work will focus on further development of the scope of this oxidation reaction, including additional substrate types (hopefully to include intermolecular variations) and the exploration of asymmetric transformations.

EXPERIMENTAL SECTION

General Information. All reactions were performed under an inert atmosphere (argon or nitrogen) in flame-dried glassware. The stainless steel needles used for handling anhydrous solvents and reagents were oven-dried and flushed with dry argon prior to use. Plastic syringes were flushed with dry argon before use. All chemicals were used as received from the commercial source without further purification. Methylene chloride and tetrahydrofuran were dried by passage through neutral alumina columns using a commercial solvent purification system prior to use. Thin-layer chromatography (TLC) was performed using commercial glass-backed silica plates (250 μm) with an organic binder. Preparative thin layer chromatography was carried out using silica gel TLC plates (1000 μm). Visualization was accomplished using UV light, Seebach's stain, or aqueous $KMnO_4$. Flash chromatography was carried out using standard grade silica gel (40−63 μm particle size, 230 × 400 mesh) with compressed nitrogen as a source of positive pressure. Preparative reverse-phase HPLC purification was performed using UV detection (photodiode array detector). The method utilized a Prep C18 OBD column (30 × 150 mm, 5 μm) and gradient system eluting from 70:30 (**B**:**A**) to 99:1 (**B**:**A**) (solvent system **A**: 99:1, water:CH_3CN containing 0.1% trifluoroacetic acid and solvent system **B**: 99:1, CH_3CN:water containing 0.1% trifluoroacetic acid) at a constant flow rate of 50 mL/min and a run time of 13 min. The fractions were collected using an automated fraction collector. Infrared (IR) spectra were acquired as thin films or solids. All NMR samples were recorded in deuterated chloroform. Chemical shifts are reported in parts per million (ppm) and are referenced to the center line of the solvent (δ 7.26 ppm for ^{1}H NMR and 77.23 ppm for ^{13}C NMR). Coupling constants are given in Hertz (Hz). High resolution mass spectra (HRMS) were taken using a time-of-flight (TOF) mass analyzer and an electrospray ion source (ESI). Melting points were determined in open capillary tubes using a

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capillary melting point apparatus and are uncorrected. Chiral gas chromatography was carried out on a GC system with triple-axis HED-EM detector (5975C VL MSD) and helium as the carrier gas; a B-DM chiral capillary column (30.0 m × 250 μm × 0.12 μm nominal) was employed. The temperature was programmed from 45 to 190 °C with a run time of 24.50 min.

General Procedure A for the Synthesis of Oxaziridine Substrates. To a solution of starting ketone (1.0 equiv) in toluene was added amine (1.5 equiv), *p*-toluenesulfonic acid (PTSA) (0.050 equiv), and activated 4 or 5 Å molecular sieves, and the reaction mixture was allowed to reflux using a Dean−Stark apparatus for 60 h (24 h for compound **1aa**, **1aa′**, and **1aa″** and 72 h for compound **1ba** and **1ba′**) under nitrogen atmosphere (most of the toluene was distilled off into Dean−Stark trap before cooling). The crude solution of imine was then cooled to −78 °C, diluted with CH_2Cl_2, and treated slowly with a solution of purified *m*-CPBA[20] (>95%, 1.2 equiv) in CH_2Cl_2 under nitrogen atmosphere. The reaction was stirred for 30 min at −78 °C, quenched with saturated $Na_2S_2O_3$, and allowed to warm to room temperature. The resulting mixture was filtered under suction and washed with CH_2Cl_2. The filtrate was diluted with water, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 once, and the combined organic extracts were washed with saturated aqueous $NaHCO_3$ twice and brine once, dried over Na_2SO_4, and concentrated under reduced pressure. Purification by chromatography on SiO_2 or preparative TLC afforded the product. See the Supporting Information for the assignment of oxaziridine diastereomers and their structures.

General Procedure B for Intramolecular C−H Oxidation Using $[Cu(PPh_3)Cl]_4$.[21] A flame-dried two-necked round-bottom flask equipped with a reflux condenser was charged with $[Cu(PPh_3)Cl]_4$ and THF under an argon atmosphere. The solution was degassed with argon at room temperature for 5 min and was then allowed to reflux for 30 min. A solution of oxaziridine in THF was added slowly by a syringe to the refluxing solution of the catalyst, and refluxing was continued for an additional 1−3 h. The solvent was removed under reduced pressure, and the crude mixture was purified by chromatography on SiO_2 to afford the product. All successful oxidation products were accompanied by unoxidized ketones **3** (eluted out at 100% CH_2Cl_2 during chromatographic purification), from which oxaziridine was initially derived.

General Procedure C for Intramolecular C−H Oxidation Using CuCl and *rac*-BINAP. A flame-dried two-necked round-bottom flask equipped with a reflux condenser was charged with CuCl, *rac*-BINAP, and THF under an argon atmosphere. The solution was degassed with argon at room temperature for 5 min and was then allowed to reflux for 30 min. A solution of oxaziridine in THF was added slowly by a syringe to the refluxing solution of the catalyst, and refluxing was continued for an additional 1 h. The solvent was removed under reduced pressure, and the crude mixture was purified by chromatography on SiO_2 to afford the product. All successful oxidation products were accompanied by unoxidized ketones **3** (eluted out at 100% CH_2Cl_2 during chromatographic purification), from which oxaziridine was initially derived.

General Procedure D for Grignard Reaction Followed by PCC Oxidation. *Grignard Reaction.* A flame-dried two-necked round-bottom flask equipped with a dropping funnel was charged with magnesium turnings (1.2 equiv) and 1−2 small crystals of iodine in THF under argon atmosphere. A solution of 5-bromo-1-pentene (1.2 equiv) in THF was added dropwise to the stirring suspension of magnesium so as to maintain the gentle refluxing of THF (I_2 color disappears). After the addition, the reaction mixture was gently refluxed for 1 h, after which it was cooled to 0 °C. A solution of aldehyde (1.0 equiv) in THF was added slowly to the cooled suspension at 0 °C over 10 min. The reaction mixture was then stirred at room temperature for 1−2 h. The reaction mixture was quenched with a saturated aqueous solution of NH_4Cl and extracted with ether twice. The combined organic extracts were washed with water and brine once, dried over Na_2SO_4, and concentrated under reduced pressure to afford the crude alcohol, which was used for the next oxidation step without purification.

PCC Oxidation. To a stirring solution of crude alcohol in CH_2Cl_2 was added pyridinium chlorochromate (PCC) (1.5−2.0 equiv), and the reaction was maintained at room temperature under nitrogen atmosphere for 1.5−2 h (12 h for compound **3f**). The reaction mixture was filtered through Celite, rinsing with several portions of CH_2Cl_2 or ether, and the filtrate was concentrated under reduced pressure. Purification by chromatography on SiO_2 afforded the ketone product.

1-Phenylhex-5-en-1-one 3a.[22] A solution of acetophenone (20.0 g, 166 mmol, 1.0 equiv), *N*,*N*-dimethylhydrazine (25.0 g, 416 mmol, 2.5 equiv) and PTSA (1.58 g, 8.32 mmol, 0.050 equiv) in benzene (110 mL) was refluxed for 23 h under nitrogen atmosphere with removal of water by a Dean−Stark apparatus. The reaction mixture was concentrated under reduced pressure, and the residue was purified by vacuum distillation to afford the corresponding hydrazone as a yellow oil in 96% yield (26.0 g, 160 mmol). To a cooled 1.0 M lithium diisopropylamide (LDA) solution (47.5 mL, 47.5 mmol, 1.1 equiv) in THF at 0 °C under nitrogen atmosphere was added the solution of hydrazone (7.00 g, 43.2 mmol, 1.0 equiv) in THF (30 mL) slowly over 15 min, and the reaction mixture was allowed to stir at 0 °C for 5 h. The reaction mixture was then cooled to −78 °C, and a solution of 4-bromo-1-butene (7.00 g, 51.8 mmol, 1.2 equiv) in THF (15 mL) was added slowly over 10 min. The reaction was warmed to room temperature and stirred for 16 h. The reaction mixture was concentrated under reduced pressure, and the residue was diluted with ether (30 mL) and then treated with an ice-cold solution of dilute sulfuric acid (30 mL) for 30 min to hydrolyze the hydrazone. The resulting solution was diluted with water and extracted with ether (2 × 35 mL), and the combined organic extracts were washed with water (2 × 25 mL) and brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification by chromatography on SiO_2 (1% ether in hexanes) afforded the ketone **3a** as a colorless oil in 79% yield (6.00 g, 34.5 mmol).

(2*R*,3*S*,1′*S*)-3-(Pent-4″-en-1″-yl)-3-phenyl-2-(1′-phenylethyl)-1,2-oxaziridine (unlike, *cis*; 1aa), (2*S*,3*R*,1′*S*)-3-(Pent-4″-en-1″-yl)-3-phenyl-2-(1′-phenylethyl)-1,2-oxaziridine (like, *cis*; 1aa′), and (2*R*,3*R*,1′*S*)-3-(Pent-4″-en-1″-yl)-3-phenyl-2-(1′-phenylethyl)-1,2-oxaziridine (unlike, *trans*; 1aa″). Following the general procedure **A**, starting ketone **3a** (1.00 g, 5.74 mmol, 1.0 equiv), (*S*)-α-methylbenzylamine **4a** (0.95 mL, 7.46 mmol, 1.3 equiv), PTSA (54.4 mg, 0.287 mmol, 0.050 equiv), and activated 4 Å molecular sieves (10.0 g) in toluene (50 mL) were refluxed for 24 h. The crude solution of imine was cooled to room temperature, diluted with CH_2Cl_2 (25 mL), and transferred to a flask containing a suspension of purified *m*-CPBA (1.18 g, 6.88 mmol, 1.2 equiv) in CH_2Cl_2 (15 mL) at −78 °C under nitrogen atmosphere. The reaction was stirred for 30 min at −78 °C, quenched with saturated $Na_2S_2O_3$, and allowed to warm to room temperature. The resulting mixture was filtered and washed with CH_2Cl_2. The filtrate was diluted with water, and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (15 mL), and the combined organic extracts were washed with saturated aqueous $NaHCO_3$ (2 × 15 mL) and brine (15 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification by chromatography on SiO_2 (0.5% ether in hexanes) afforded a mixture of oxaziridines (3 diastereomers; **1aa**, **1aa′**, and **1aa″**) and starting ketone **3a** as a colorless oil (1.27 g, 76% corrected yield by ^1H NMR; **1aa**:**1aa′**:**1aa″** = ca. 91:5:4). Subsequent purification by chromatography on SiO_2 (0.5% EtOAc in hexanes) afforded a mixture of the major diastereomer **1aa** and **3a** followed by a mixture of oxaziridines (3 diastereomers) and **3a**. A pure sample of **1aa** for characterization was obtained from a fraction collected during this purification. First diastereomer (major) **1aa**: R_f = 0.72 (5% EtOAc/hexanes, run twice); IR (neat) 2976, 2928, 1640, 1448 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.19−1.31 (m, 2H), 1.40−1.51 (m, 1H), 1.48 (d, *J* = 6.4 Hz, 3H), 1.74 (m, 1H), 1.91−2.05 (m, 2H), 2.21 (m, 1H), 2.99 (q, *J* = 6.4 Hz, 1H), 4.86−4.94 (m, 2H), 5.68 (m, 1H), 6.86−6.91 (m, 2H), 7.12 (br s, 2H), 7.19−7.23 (m, 3H), 7.26−7.30 (m, 2H), 7.33−7.37 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.1, 23.2, 33.7, 37.9, 62.8, 88.4, 115.0, 127.6, 127.6, 127.9, 128.2, 128.4, 128.8, 135.0, 138.4, 140.8; HRMS (ESI) *m*/*z* calcd for $C_{20}H_{24}NO$ $[M + H]^+$ 294.1858, found 294.1840. Second diastereomer **1aa′**: R_f = 0.60 (5%

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EtOAc/hexanes, run twice); ^{1}H NMR (400 MHz, $CDCl_3$; diagnostic peaks only) δ 1.14 (d, J = 6.6 Hz, 3H). Third diastereomer **1aa**″: R_f = 0.60 (5% EtOAc/hexanes, run twice); ^{1}H NMR (400 MHz, $CDCl_3$; diagnostic peaks only) δ 1.62 (d, J = 6.3 Hz, 3H).

4-Hydroxy-1-phenylhex-5-en-1-one 2a. Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (49.1 mg, 0.0341 mmol, 0.050 equiv) in THF (13 mL) was reacted with a solution of oxaziridine **1aa** (200 mg, 0.682 mmol, 1.0 equiv; containing ca. 14% of starting ketone **3a**) in THF (2 mL). The reaction mixture was refluxed for 3 h. Purification by chromatography on SiO_2 (0.5% CH_3OH in CH_2Cl_2) afforded 90 mg (0.473 mmol, 69% yield; 5% ee by chiral GC, retention times for the two enantiomers were 13.882 and 13.986 min, respectively) of the allylic alcohol **2a** as a yellow oil: R_f = 0.32 (25% EtOAc/hexanes); IR (neat) 3420, 1678 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.90−1.98 (m, 1H), 2.01−2.09 (m, 1H), 2.12 (d, J = 3.4 Hz, 1H), 3.13 (t, J = 7.0 Hz, 2H), 4.24 (br s, 1H), 5.13 (td, J = 10.4, 1.3 Hz, 1H), 5.27 (td, J = 17.2, 1.4 Hz, 1H), 5.86−5.94 (m, 1H), 7.43−7.47 (m, 2H), 7.53−7.57 (m, 1H), 7.96−7.98 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.0, 34.5, 72.4, 115.1, 128.2, 128.7, 133.3, 137.0, 140.8, 200.7; HRMS (ESI) m/z calcd for $C_{12}H_{15}O_2$ $[M + H]^+$ 191.1072, found 191.1091. Ketone **3a** was not recovered.

(2*R*,3*S*)-2-Cyclohexyl-3-(pent-4′-en-1′-yl)-3-phenyl-1,2-oxaziridine (*Z*)-1ab and (2*S*,3*S*)-2-Cyclohexyl-3-(pent-4′-en-1′-yl)-3-phenyl-1,2-oxaziridine (*E*)-1ab. Following the general procedure **A**, ketone **3a** (5.50 g, 31.6 mmol, 1.0 equiv), cyclohexylamine **4b** (5.42 mL, 47.4 mmol, 1.5 equiv), PTSA (300 mg, 1.58 mmol, 0.050 equiv), and activated 5 Å molecular sieves (35.0 g) in toluene (150 mL) were refluxed for 60 h, followed by oxidation with *m*-CPBA (6.54 g, 37.9 mmol, 1.2 equiv) in CH_2Cl_2 (150 mL). Purification by chromatography on SiO_2 (0.5−1.0% EtOAc in hexanes) afforded the mixture of major diastereomer (*Z*)-**1ab** and **3a** followed by the mixture of major and minor (*E*)-**1ab** diastereomers as a colorless oil (7.8 g, 91% yield by ^{1}H NMR; (*Z*)-**1ab**:(*E*)-**1ab** = ca. 59:41). Subsequent purification of the mixture of (*Z*)-**1ab** and **3a** by chromatography on SiO_2 (0.5% EtOAc in hexanes) afforded (*Z*)-**1ab**. Major diastereomer (*Z*)-**1ab**: R_f = 0.62 (5% EtOAc/hexanes, run twice); IR (neat) 2931, 1448 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.72−0.83 (m, 1H), 0.97−1.18 (m, 2H), 1.19−1.35 (m, 3H), 1.40−1.51 (m, 3H), 1.52−1.60 (m, 1H), 1.67−1.76 (m, 3H), 1.83−1.88 (m, 1H), 1.93−2.07 (m, 2H), 2.36 (m, 1H), 4.87−4.96 (m, 2H), 5.70 (m, 1H), 7.35−7.42 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.2, 24.1, 24.2, 25.8, 28.6, 31.8, 33.7, 38.1, 61.0, 87.7, 115.0, 127.8, 128.2, 128.7, 135.3, 138.5; HRMS (ESI) m/z calcd for $C_{18}H_{26}NO$ $[M + H]^+$ 272.2014, found 272.1992. Minor diastereomer (*E*)-**1ab**: R_f = 0.52 (5% EtOAc/hexanes, run twice); IR (neat) 2932, 1449 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17−1.38 (m, 3H), 1.40−1.59 (m, 4H), 1.65−1.73 (m, 2H), 1.81−1.84 (m, 2H), 1.97−2.14 (m, 4H), 2.29 (m, 1H), 2.58 (m, 1H), 4.93−5.01 (m, 2H), 5.72 (m, 1H), 7.27−7.38 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.4, 24.6, 24.7, 25.9, 29.1, 29.3, 32.1, 33.8, 61.3, 85.8, 115.4, 126.1, 128.2, 128.3, 128.5, 138.0, 139.9; HRMS (ESI) m/z calcd for $C_{18}H_{26}NO$ $[M + H]^+$ 272.2014, found 272.1988.

Conversion of (*Z*)-1ab into 2a. Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (40.0 mg, 0.0276 mmol, 0.050 equiv) in THF (10 mL) was reacted with a solution of oxaziridine (*Z*)-**1ab** (150 mg, 0.553 mmol, 1.0 equiv) in THF (5 mL). The reaction mixture was refluxed for 3 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 99.2:0.5:0.3) afforded 78 mg (0.410 mmol, 74% yield) of the allylic alcohol **2a** as a yellow oil and 18 mg (0.103 mmol, 19% yield) of **3a**.

Following the general procedure **C**, CuCl (2.73 mg, 0.0276 mmol, 0.050 equiv) and *rac*-BINAP (17.1 mg, 0.0276 mmol, 0.050 equiv) in THF (12 mL) were reacted with a solution of oxaziridine (*Z*)-**1ab** (150 mg, 0.553 mmol, 1.0 equiv) in THF (3 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 98.7:1.0:0.3) afforded 78 mg (0.410 mmol, 74% yield) of **2a** as a yellow oil and 6.0 mg (0.0344 mmol, 6% yield) of **3a**.

Conversion of (*Z*)-1ab into 2a in THF-d_8 (Scheme 2b). Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (40.0 mg, 0.0276 mmol, 0.050 equiv) in THF-d_8 (10 mL) was reacted with a solution of oxaziridine (*Z*)-**1ab** (150 mg, 0.553 mmol, 1.0 equiv) in THF-d_8 (5 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 99.2:0.5:0.3) afforded 70 mg (0.368 mmol, 67% yield) of the allylic alcohol **2a** as a yellow oil and 25 mg (0.143 mmol, 26% yield) of **3a**. No deuterium incorporation was observed in **3a** by NMR and HRMS.

(2*R*,3*S*)-2-Benzhydryl-3-(pent-4′-en-1′-yl)-3-phenyl-1,2-oxaziridine (*Z*)-1ac and (2*S*,3*S*)-2-Benzhydryl-3-(pent-4′-en-1′-yl)-3-phenyl-1,2-oxaziridine (*E*)-1ac. Following the general procedure **A**, ketone **3a** (0.500 g, 2.87 mmol, 1.0 equiv), benzhydrylamine **4c** (0.742a mL, 4.31 mmol, 1.5 equiv), PTSA (27.3 mg, 0.143 mmol, 0.050 equiv), and 5 Å molecular sieves (3.50 g) in toluene (35 mL) were refluxed for 60 h, followed by oxidation with *m*-CPBA (0.594 g, 3.44 mmol, 1.2 equiv) in CH_2Cl_2 (20 mL). Purification by chromatography on SiO_2 (0.5% EtOAc in hexanes) afforded the mixture of major (*Z*)-**1ac** and minor (*E*)-**1ac** diastereomers along with dibenzhydrylamine impurity[23] as a pale yellow oil (0.898 g, 88% corrected yield by ^{1}H NMR; (*Z*)-**1ac**:(*E*)-**1ac** = ca. 76:24). Subsequent purification of a small amount of the mixture by preparative TLC on SiO_2 (2% EtOAc in hexanes, multiple runs) afforded analytical samples of (*Z*)-**1ac** and (*E*)-**1ac** for characterization. Major diastereomer (*Z*)-**1ac**: R_f = 0.67 (5% EtOAc/hexanes, run twice); IR (neat) 2926, 1448 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24−1.36 (m, 1H), 1.46−1.57 (m, 1H), 1.88 (m, 1H), 1.94−2.09 (m, 2H), 2.32 (m, 1H), 4.06 (s, 1H), 4.88−4.96 (m, 2H), 5.70 (m, 1H), 6.94−6.97 (m, 2H), 7.18−7.23 (m, 5H), 7.27−7.31 (m, 4H), 7.36−7.40 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.1, 33.7, 37.7, 70.5, 88.6, 115.0, 127.3, 127.6, 127.9, 128.1, 128.3, 128.4, 128.5, 129.0, 134.7, 138.5, 139.5, 142.3; HRMS (ESI) m/z calcd for $C_{25}H_{26}NO$ $[M + H]^+$ 356.2014, found 356.2044. Minor diastereomer (*E*)-**1ac**: R_f = 0.50 (5% EtOAc/hexanes, run twice); IR (neat) 2930, 1450 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.14−1.24 (m, 1H), 1.32−1.43 (m, 1H), 1.95−2.07 (m, 2H), 2.09−2.25 (m, 2H), 4.91−4.97 (m, 3H), 5.66 (m, 1H), 7.21−7.26 (m, 1H), 7.28−7.34 (m, 8H), 7.35−7.39 (m, 2H), 7.43−7.45 (m, 2H), 7.48−7.51 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 29.7, 33.7, 70.7, 86.7, 115.4, 126.3, 127.5, 127.82, 127.88, 128.0, 128.4, 128.6, 129.0, 138.0, 139.4, 140.1, 142.1; HRMS (ESI) m/z calcd for $C_{25}H_{26}NO$ $[M + H]^+$ 356.2014, found 356.2014. Dibenzhydrylamine: ^{1}H NMR (400 MHz, $CDCl_3$; diagnostic peaks only) δ 4.77 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$; diagnostic peaks only) δ 63.7.

Conversion of 1ac into 2a. Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (30.4 mg, 0.0211 mmol, 0.045 equiv) in THF (12 mL) was reacted with a solution containing oxaziridine diastereomers **1ac** (165 mg, 0.464 mmol, 1.0 equiv; *Z*:*E* = ca. 77:23, contaminated with 12% of dibenzhydrylamine) in THF (3 mL). The reaction mixture was refluxed for 1.5 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 98.7:1.0:0.3) afforded the mixture of product and impurities, which was further purified by chromatography on SiO_2 (2.5% acetone in CH_2Cl_2) to afford 19 mg (0.10 mmol, 22% yield; 26% brsm) of **2a** as a yellow oil and 39 mg (0.224 mmol, 48% yield; 57% brsm) of **3a**.

(2*R*,3*S*)-2-Benzyl-3-(pent-4′-en-1′-yl)-3-phenyl-1,2-oxaziridine (*Z*)-1ad and (2*S*,3*S*)-2-Benzyl-3-(pent-4′-en-1′-yl)-3-phenyl-1,2-oxaziridine (*E*)-1ad. Following the general procedure **A**, ketone **3a** (0.600 g, 3.44 mmol, 1.0 equiv), benzylamine **4d** (0.564 mL, 5.17 mmol, 1.5 equiv), PTSA (32.8 mg, 0.172 mmol, 0.050 equiv), and activated 4 Å molecular sieves (5.0 g) in toluene (40 mL) were refluxed for 60 h, followed by oxidation with *m*-CPBA (0.713 g, 4.13 mmol, 1.2 equiv) in CH_2Cl_2 (20 mL). Purification by chromatography on SiO_2 (0.5−0.7% EtOAc in hexanes) afforded the mixture of major diastereomer (*Z*)-**1ad** and **3a** followed by the mixture of major and minor (*E*)-**1ad** diastereomers as a colorless oil (0.866 g, 90% corrected yield by ^{1}H NMR; (*Z*)-**1ad**:(*E*)-**1ad** = ca. 87:13). Subsequent purification of the mixture of (*Z*)-**1ad** and (*E*)-**1ad** by chromatography on SiO_2 (0.6% EtOAc in hexanes) afforded partial separation of pure (*Z*)-**1ad** and a small quantity of (*E*)-**1ad** containing ca. 15% of (*Z*)-**1ad**. Major diastereomer (*Z*)-**1ad**: R_f = 0.55 (5% EtOAc/hexanes, run twice); IR (neat) 2927, 1448 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27−1.38 (m, 1H), 1.46−1.57 (m, 1H), 1.82 (m, 1H), 1.95−2.09 (m, 2H), 2.36 (m, 1H), 3.43 (1/2 AB, J = 14.1 Hz, 1H), 3.52 (1/2 AB, J =

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14.1 Hz, 1H), 4.89–4.97 (m, 2H), 5.71 (m, 1H), 7.20–7.22 (m, 2H), 7.25–7.28 (m, 2H), 7.29–7.32 (m, 1H), 7.42 (s, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.1, 33.7, 37.7, 59.3, 87.9, 115.0, 127.6, 127.8, 128.4, 128.5, 128.8, 129.0, 135.2, 136.7, 138.4; HRMS (ESI) m/z calcd for $C_{19}H_{22}NO$ $[M + H]^+$ 280.1701, found 280.1739. Minor diastereomer (*E*)-**1ad**: R_f = 0.45 (5% EtOAc/hexanes, run twice); IR (neat) 2926, 1452 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43–1.58 (m, 2H), 2.06–2.16 (m, 2H), 2.19–2.36 (m, 2H), 4.16 (s, 2H), 4.96–5.03 (m, 2H), 5.74 (m, 1H), 7.27–7.34 (m, 4H), 7.35–7.39 (m, 3H), 7.40–7.44 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.7, 29.2, 33.8, 58.2, 85.6, 115.6, 126.5, 127.8, 128.5, 128.6, 128.7, 128.8, 136.6, 137.9, 139.1; HRMS (ESI) m/z calcd for $C_{19}H_{22}NO$ $[M + H]^+$ 280.1701, found 280.1722.

1-(3,4-Dimethoxyphenyl)hex-5-en-1-one 3b. A solution of 3,4-dimethoxyacetophenone (15.0 g, 83.2 mmol, 1.0 equiv), *N*,*N*-dimethylhydrazine (15.0 g, 249 mmol, 3.0 equiv) and PTSA (0.791 g, 4.16 mmol, 0.050 equiv) in benzene (80 mL) was refluxed for 23 h under nitrogen atmosphere with removal of water by a Dean–Stark apparatus. The reaction mixture was concentrated under reduced pressure, and the residue was purified by vacuum distillation to afford the corresponding hydrazone as a pale yellow solid in 81% yield (15.0 g, 67.5 mmol). To a cooled 1.0 M LDA solution (9.90 mL, 9.90 mmol, 1.1 equiv) in THF at 0 °C under nitrogen atmosphere was added the solution of hydrazone (2.00 g, 9.00 mmol, 1.0 equiv) in THF (15 mL) slowly over 15 min, and it was allowed to stir at 0 °C for 5 h. The reaction mixture was then cooled to −78 °C, and a solution of 4-bromo-1-butene (1.45 g, 10.8 mmol, 1.2 equiv) in THF (5 mL) was added slowly over 10 min. The reaction was warmed to room temperature and stirred for 18 h. The reaction mixture was concentrated under reduced pressure, and the residue was diluted with ether (15 mL) and then treated with an ice-cold solution of dilute sulfuric acid (15 mL) for 30 min to hydrolyze the hydrazone. The resulting solution was diluted with water and extracted with ether (2 × 15 mL), and the combined organic extracts were washed with water (2 × 15 mL) and brine (15 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification by chromatography on SiO_2 (10% EtOAc in hexanes) afforded the ketone **3b** as a white solid (mp 52–54 °C) in 71% yield (1.50 g, 6.41 mmol): R_f = 0.41 (15% EtOAc/hexanes, run twice); IR (neat) 1672 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.82 (m, 2H), 2.11–2.16 (m, 2H), 2.92 (t, J = 7.3 Hz, 2H), 3.92 (s, 3H), 3.93 (s, 3H), 4.96–5.06 (m, 2H), 5.81 (m, 1H), 6.86 (d, J = 8.3 Hz, 1H), 7.51 (d, J = 2.0 Hz, 1H), 7.56 (dd, J = 8.3, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.8, 33.4, 37.4, 56.1, 56.2, 110.1, 110.3, 115.4, 122.8, 130.4, 138.2, 149.1, 153.3, 199.0; HRMS (ESI) m/z calcd for $C_{14}H_{18}O_3$ $[M]^+$ 234.1256, found 234.1236.

(2*R*,3*S*,1′*S*)-3-(3,4-Dimethoxyphenyl)-3-(pent-4″-en-1″-yl)-2-(1′-phenylethyl)-1,2-oxaziridi-ne (unlike, *cis*; 1ba) and (2*S*,3*R*,1′*S*)-3-(3,4-Dimethoxyphenyl)-3-(pent-4″-en-1″-yl)-2-(1′-phenylethyl)-1,2-oxaziridine (like, *cis*; 1ba′). Following the general procedure **A**, ketone **3b** (1.00 g, 4.27 mmol, 1.0 equiv), (*S*)-α-methylbenzylamine **4a** (0.815 mL, 6.41 mmol, 1.5 equiv), PTSA (40.6 mg, 0.213 mmol, 0.050 equiv), and activated 4 Å molecular sieves (7.0 g) in toluene (50 mL) were refluxed for 72 h, followed by oxidation with *m*-CPBA (0.883 g, 5.12 mmol, 1.2 equiv) in CH_2Cl_2 (25 mL). Purification by chromatography on SiO_2 (4–6% EtOAc in hexanes) afforded the major **1ba** and the minor **1ba′** diastereomers as a colorless oil (0.94 g, 62% yield; **1ba**:**1ba′** = ca. 83:17). A pure sample of **1ba′** for characterization was obtained during this purification. Major diastereomer **1ba**: R_f = 0.50 (10% EtOAc/hexanes, run twice); IR (neat) 1605, 1452, 1257 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19–1.31 (m, 1H), 1.40–1.51 (m, 1H), 1.47 (d, J = 6.5 Hz, 3H), 1.70 (m, 1H), 1.90–2.05 (m, 2H), 2.17 (m, 1H), 3.01 (q, J = 6.4 Hz, 1H), 3.62 (br s, 3H), 3.88 (s, 3H), 4.85–4.93(m, 2H), 5.68 (m, 1H), 6.39 (br s, 1H), 6.78 (d, J = 6.5 Hz, 2H), 6.92–6.96 (m, 2H), 7.18–7.24 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.1, 23.2, 33.6, 37.9, 55.7, 56.0, 62.7, 88.2, 110.2, 110.8, 114.9, 120.6, 127.4, 127.51, 127.56, 128.3, 138.4, 141.2, 148.1, 149.2; HRMS (ESI) m/z calcd for $C_{22}H_{28}NO_3$ $[M + H]^+$ 354.2069, found 354.2074. Minor diastereomer **1ba′**: R_f = 0.41 (10% EtOAc/hexanes, run twice); IR (neat) 1604, 1453, 1259 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.15 (d, J = 6.6 Hz, 3H), 1.24–1.35 (m, 1H), 1.43–1.54 (m, 1H), 1.81 (m, 1H), 1.95–2.09 (m, 2H), 2.44 (m, 1H), 3.09 (q, J = 6.6 Hz, 1H), 3.92 (s, 3H), 3.94 (s, 3H), 4.89–4.97(m, 2H), 5.71 (m, 1H), 6.93 (d, J = 8.2 Hz, 1H), 6.99 (d, J = 1.9 Hz, 1H), 7.07 (dd, J = 8.2, 2.0 Hz, 1H), 7.22–7.27 (m, 1H), 7.30–7.36 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.2, 23.3, 33.7, 37.8, 56.1, 56.3, 61.4, 88.5, 110.9, 111.2, 115.0, 120.6, 127.1, 127.2, 127.4, 128.6, 138.5, 143.2, 148.7, 149.5; HRMS (ESI) m/z calcd for $C_{22}H_{28}NO_3$ $[M + H]^+$ 354.2069, found 354.2076.

1-(3,4-Dimethoxyphenyl)-4-hydroxyhex-5-en-1-one 2b. Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (51.1 mg, 0.0354 mmol, 0.050 equiv) in THF (12 mL) was reacted with a solution of oxaziridine **1ba** (250 mg, 0.708 mmol, 1.0 equiv) in THF (8 mL). The reaction mixture was refluxed for 3 h. Purification by chromatography on SiO_2 (3% acetone in CH_2Cl_2) afforded 85 mg (0.340 mmol, 48% yield) of the allylic alcohol **2b** as a pink oil: R_f = 0.23 (3% acetone in CH_2Cl_2); IR (neat) 3435, 1668 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.87–1.96 (m, 1H), 1.99–2.07 (m, 1H), 2.23 (d, J = 4.3 Hz, 1H), 3.08 (t, J = 7.0 Hz, 2H), 3.92 (s, 3H), 3.93 (s, 3H), 4.23 (m, 1H), 5.12 (td, J = 10.4, 1.4 Hz, 1H), 5.26 (td, J = 17.2, 1.4 Hz, 1H), 5.89 (m, 1H), 6.87 (d, J = 8.4 Hz, 1H), 7.52 (d, J = 2.0 Hz, 1H), 7.60 (dd, J = 8.4, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.3, 34.0, 56.1, 56.2, 72.4, 110.1, 110.3, 115.0, 123.0, 130.2, 140.9, 149.1, 153.4, 199.3; HRMS (ESI) m/z calcd for $C_{14}H_{19}O_4$ $[M + H]^+$ 251.1283, found 251.1286. Ketone **3b** was also obtained in 27% yield (45 mg, 0.192 mmol).

(2*R*,3*S*)-2-Cyclohexyl-3-(3,4-dimethoxyphenyl)-3-(pent-4′-en-1′-yl)-1,2-oxaziridine (*Z*)-1bb and (2*S*,3*S*)-2-Cyclohexyl-3-(3,4-dimethoxyphenyl)-3-(pent-4′-en-1′-yl)-1,2-oxaziridine (*E*)-1bb. Following the general procedure **A**, ketone **3b** (0.900 g, 3.84 mmol, 1.0 equiv), cyclohexylamine **4b** (0.659 mL, 5.76 mmol, 1.5 equiv), PTSA (36.5 mg, 0.192 mmol, 0.050 equiv), and activated 5 Å molecular sieves (6.50 g) in toluene (40 mL) were refluxed for 60 h, followed by oxidation with *m*-CPBA (0.796 g, 4.61 mmol, 1.2 equiv) in CH_2Cl_2 (25 mL). Purification by chromatography on SiO_2 (4–6% EtOAc in hexanes) afforded the major diastereomer (*Z*)-**1bb** (0.610 g, 48% yield) as a colorless oil followed by the mixture of **3b** and minor diastereomer (*E*)-**1bb** (0.246 g, 19% corrected yield by ^{1}H NMR; (*Z*)-**1bb**:(*E*)-**1bb** = ca. 71:29). Subsequent purification of the mixture of **3b** and (*E*)-**1bb** by chromatography on SiO_2 (14% EtOAc in hexanes) afforded partial separation of (*E*)-**1bb** as a colorless oil. Major diastereomer (*Z*)-**1bb**: R_f = 0.33 (10% EtOAc/hexanes, run twice); IR (neat) 2930, 1450, 1257 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.75–0.86 (m, 1H), 0.95–1.15 (m, 2H), 1.16–1.32 (m, 3H), 1.39–1.48 (m, 3H), 1.52–1.56 (m, 1H), 1.63–1.70 (m, 2H), 1.72–1.79 (m, 1H), 1.81–1.84 (m, 1H), 1.90–2.04 (m, 2H), 2.31 (m, 1H), 3.86 (s, 3H), 3.87 (s, 3H), 4.85–4.93 (m, 2H), 5.67 (m, 1H), 6.84 (d, J = 8.3 Hz, 1H), 6.86 (d, J = 1.9 Hz, 1H), 6.93 (dd, J = 8.2, 1.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.2, 24.11, 24.15, 25.8, 28.7, 31.7, 33.7, 38.1, 55.9, 56.1, 60.7, 87.5, 110.7, 110.9, 114.9, 120.3, 127.6, 138.4, 148.5, 149.1; HRMS (ESI) m/z calcd for $C_{20}H_{30}NO_3$ $[M + H]^+$ 332.2226, found 332.2223. Minor diastereomer (*E*)-**1bb**: R_f = 0.13 (10% EtOAc/hexanes, run twice); IR (neat) 2932, 1452, 1265 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16–1.36 (m, 3H), 1.41–1.55 (m, 4H), 1.65–1.70 (m, 2H), 1.80–1.84 (m, 2H), 1.95–2.02 (m, 2H), 2.04–2.16 (m, 2H), 2.28 (m, 1H), 2.56 (m, 1H), 3.85 (s, 3H), 3.87 (s, 3H), 4.94–5.01 (m, 2H), 5.73 (m, 1H), 6.82 (d, J = 8.2 Hz, 1H), 6.88 (d, J = 1.9 Hz, 1H), 6.93 (dd, J = 8.2, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.4, 24.6, 24.8, 25.8, 28.9, 29.2, 32.1, 33.8, 56.0, 56.1, 61.4, 85.4, 109.3, 111.1, 115.4, 118.7, 132.5, 138.0, 149.13, 149.15; HRMS (ESI) m/z calcd for $C_{20}H_{30}NO_3$ $[M + H]^+$ 332.2226, found 332.2224.

Conversion of (*Z*)-1bb into 2b. Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (21.8 mg, 0.0151 mmol, 0.050 equiv) in THF (7 mL) was reacted with a solution of oxaziridine (*Z*)-**1bb** (100 mg, 0.302 mmol, 1.0 equiv) in THF (3 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 98.6:1.0:0.4) afforded 28 mg (0.112 mmol, 37% yield) of the allylic alcohol **2b** as a pink oil: R_f = 0.12 (35% EtOAc/hexanes). Ketone **3b** was also obtained in 57% yield (40 mg, 0.171 mmol).

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Following the general procedure **C**, CuCl (2.24 mg, 0.0226 mmol, 0.050 equiv) and *rac*-BINAP (14.0 mg, 0.0226 mmol, 0.050 equiv) in THF (12 mL) were reacted with a solution of oxaziridine (*Z*)-**1bb** (150 mg, 0.453 mmol, 1.0 equiv) in THF (3 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 98.6:1.0:0.4) afforded 76 mg (0.304 mmol, 67% yield; 73% brsm) of **2b** as a yellow oil and 18 mg (0.0769 mmol, 17% corrected yield) of **3b**.

Conversion of (*E*)-1bb into 2b. Following the general procedure **C**, CuCl (1.72 mg, 0.0173 mmol, 0.050 equiv) and *rac*-BINAP (10.8 mg, 0.0173 mmol, 0.050 equiv) in THF (9 mL) were reacted with a solution of oxaziridine (*E*)-**1bb** (115 mg, 0.347 mmol, 1.0 equiv) in THF (3 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 98.6:1.0:0.4) afforded 58 mg (0.232 mmol, 67% yield) of **2b** as a yellow oil and 12 mg (0.0512 mmol, 15% yield) of **3b**.

6-Methyl-1-phenylhept-5-en-1-one 3c. To a cooled 1.0 M LDA solution (10.1 mL, 10.1 mmol, 1.1 equiv) in THF at 0 °C under nitrogen atmosphere was added the solution of acetophenone *N*,*N*-dimethylhydrazone (1.50 g, 9.25 mmol, 1.0 equiv) in THF (15 mL) slowly over 15 min, and the mixture was allowed to stir at 0 °C for 5 h. The reaction mixture was then cooled to −78 °C, and a solution of 5-bromo-2-methyl-2-pentene (1.47 mL, 11.1 mmol, 1.2 equiv) in THF (5 mL) was added slowly over 10 min. The reaction was warmed to room temperature and stirred for 18 h. The reaction mixture was concentrated under reduced pressure, and the residue was diluted with ether (15 mL) and then treated with an ice-cold solution of dilute sulfuric acid (15 mL) for 30 min to hydrolyze the hydrazone. The resulting solution was diluted with water and extracted with ether (2 × 15 mL), and the combined organic extracts were washed with water (2 × 15 mL) and brine (15 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification by chromatography on SiO_2 (0.2−0.5% EtOAc in hexanes) afforded the ketone **3c** as a colorless oil in 89% yield (1.66 g, 8.24 mmol): R_f = 0.43 (5% EtOAc/hexanes, run twice); IR (neat) 1685 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.59 (s, 3H), 1.69 (d, J = 1.0 Hz, 3H), 1.78 (m, 2H), 2.08 (q, J = 7.2 Hz, 2H), 2.95 (t, J = 7.3 Hz, 2H), 5.13 (m, 1H), 7.43−7.47 (m, 2H), 7.52−7.56 (m, 1H), 7.93−7.96 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.9, 24.6, 25.9, 27.6, 38.1, 124.0, 128.2, 128.7, 132.6, 133.0, 137.3, 200.7; HRMS (EI) m/z calcd for $C_{14}H_{18}O$ $[M]^+$ 202.1358, found 202.1344.

(2*R*,3*S*,1′*S*)-3-(5-Methylhex-4″-en-1″-yl)-3-phenyl-2-(1′-phenylethyl)-1,2-oxaziridine (unlike, *cis*; 1ca), (2*S*,3*R*,1′*S*)-3-(5-Methylhex-4″-en-1″-yl)-3-phenyl-2-(1′-phenylethyl)-1,2-oxaziridine (like, *cis*; 1ca′), and (2*R*,3*R*,1′*S*)-3-(5-Methylhex-4″-en-1″-yl)-3-phenyl-2-(1′-phenylethyl)-1,2-oxaziridine (unlike, *trans*; 1ca″). Following the general procedure **A**, 6-methyl-1-phenylhept-5-en-1-one **3c** (1.00 g, 4.95 mmol, 1.0 equiv), (*S*)-α-methylbenzylamine **4a** (0.945 mL, 7.42 mmol, 1.5 equiv), PTSA (47.0 mg, 0.247 mmol, 0.050 equiv) and activated 4 Å molecular sieves (7.0 g) in toluene (50 mL) were refluxed for 60 h, followed by oxidation with *m*-CPBA (1.02 g, 5.94 mmol, 1.2 equiv) in CH_2Cl_2 (25 mL). Purification by chromatography on SiO_2 (0.5−1% EtOAc in hexanes) afforded the mixture of oxaziridine diastereomers (**1ca**, **1ca′**, and **1ca″**) and starting ketone **3c** as a colorless oil. Subsequent purification by chromatography on SiO_2 (0.2% EtOAc in hexanes) afforded the partial separation of the mixture of the two diastereomers (**1ca** and **1ca′**) followed by the mixture of three diastereomers (**1ca**, **1ca′**, and **1ca″**) containing trace quantity of **3c** (1.11 g, 70% corrected yield by ^1H NMR; **1ca**:**1ca′**:**1ca″** = ca. 50:14:36). A pure sample of the major diastereomer **1ca** for characterization was obtained during this purification: R_f = 0.71 (5% EtOAc/hexanes, run twice); IR (neat) 1448, 764, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.12−1.23 (m, 1H), 1.33−1.44 (m, 1H), 1.48 (d, J = 6.4 Hz, 3H), 1.51 (s, 3H), 1.62 (d, J = 0.9 Hz, 3H), 1.72 (m, 1H), 1.83−1.98 (m, 2H), 2.21 (m, 1H), 2.99 (q, J = 6.4 Hz, 1H), 4.97−5.01(m, 1H), 6.87−6.91 (m, 2H), 7.12−7.23 (m, 5H), 7.26−7.30 (m, 2H), 7.32−7.37 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.8, 23.1, 24.1, 25.8, 28.0, 38.1, 62.8, 88.6, 124.2, 127.6, 127.8, 128.2, 128.3, 128.8, 131.9, 135.0, 140.8; HRMS (ESI) m/z calcd for $C_{22}H_{28}NO$ $[M + H]^+$ 322.2171, found 322.2126. Second diastereomer **1ca′**: R_f = 0.60 (5% EtOAc/hexanes, run twice); ^1H NMR (400 MHz, C_6D_6; diagnostic peaks only) δ 3.19 (q, J = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6; diagnostic peaks only) δ 61.7, 87.8. Third diastereomer **1ca″**: R_f = 0.55 (5% EtOAc/hexanes, run twice); ^1H NMR (400 MHz, C_6D_6; diagnostic peaks only) δ 3.82 (q, J = 6.3 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6; diagnostic peaks only) δ 62.9, 85.8.

4-Hydroxy-6-methyl-1-phenylhept-5-en-1-one 2c. Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (44.5 mg, 0.0342 mmol, 0.044 equiv) in THF (12 mL) was reacted with a solution containing oxaziridine diastereomers **1ca** and **1ca′** (220 mg, 0.685 mmol, 1.0 equiv; **1ca**:**1ca′** = 90:10) in THF (8 mL). The reaction mixture was refluxed for 3 h. Purification by chromatography on SiO_2 (1.5 to 2% acetone in CH_2Cl_2) afforded 110 mg (0.504 mmol, 74% yield) of the allylic alcohol **2c** as a yellow oil: R_f = 0.26 (20% EtOAc/hexanes); IR (neat) 3410, 1679 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.67 (d, J = 0.8 Hz, 3H), 1.71 (d, J = 0.6 Hz, 3H), 1.74−1.76 (m, 1H), 1.87−2.01 (m, 2H), 3.08 (t, J = 7.3 Hz, 2H), 4.45 (m, 1H), 5.21 (td, J = 8.6, 1.3 Hz, 1H), 7.43−7.46 (m, 2H), 7.53−7.56 (m, 1H), 7.95−7.97 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.4, 25.9, 32.0, 34.8, 68.2, 127.9, 128.2, 128.7, 133.1, 135.7, 137.2, 200.6; HRMS (ESI) m/z calcd for $C_{14}H_{18}O_2Na$ $[M + Na]^+$ 241.1204, found 241.1189. Ketone **3c** was also obtained in 7% yield (10 mg, 0.0495 mmol).

(2*R*,3*S*)-2-Cyclohexyl-3-(5-methylhex-4′-en-1′-yl)-3-phenyl-1,2-oxaziridine (*Z*)-1cb and (2*S*,3*S*)-2-Cyclohexyl-3-(5-methylhex-4′-en-1′-yl)-3-phenyl-1,2-oxaziridine (*E*)-1cb. Following the general procedure **A**, 6-methyl-1-phenylhept-5-en-1-one **3c** (0.700 g, 3.46 mmol, 1.0 equiv), cyclohexylamine **4b** (0.594 mL, 5.19 mmol, 1.5 equiv), PTSA (32.9 mg, 0.173 mmol, 0.050 equiv) and activated 5 Å molecular sieves (5.0 g) in toluene (35 mL) were refluxed for 60 h, followed by oxidation with *m*-CPBA (0.717 g, 4.15 mmol, 1.2 equiv) in CH_2Cl_2 (25 mL). Purification by chromatography on SiO_2 (0.5−0.6% EtOAc in hexanes) afforded the partial separation of the major diastereomer (*Z*)-**1cb** as a colorless oil followed by the mixture of major and minor (*E*)-**1cb** diastereomers (0.76 g, 73% yield; (*Z*)-**1cb**:(*E*)-**1cb** = ca. 56:44). Major diastereomer (*Z*)-**1cb**: R_f = 0.58 (5% EtOAc/hexanes, run twice); IR (neat) 2929, 1447 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.72−0.83 (m, 1H), 0.97−1.16 (m, 2H), 1.17−1.28 (m, 2H), 1.31−1.42 (m, 2H), 1.43−1.49 (m, 2H), 1.52 (s, 3H), 1.52−1.58 (m, 1H), 1.62 (d, J = 0.8 Hz, 3H), 1.66−1.76 (m, 3H), 1.84−1.95 (m, 3H), 2.35 (m, 1H), 5.00 (m, 1H), 7.34−7.42 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.8, 24.1, 24.1, 24.2, 25.8, 28.0, 28.6, 31.8, 38.3, 60.9, 87.8, 124.3, 127.8, 128.1, 128.7, 131.9, 135.3; HRMS (ESI) m/z calcd for $C_{20}H_{30}NO$ $[M + H]^+$ 300.2327, found 300.2318. An analytical sample of the minor diastereomer (*E*)-**1cb** containing about 12% of (*Z*)-**1cb** was obtained for characterization during the purification: R_f = 0.51 (5% EtOAc/hexanes, run twice); IR (neat) 2930, 1448 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.20−1.35 (m, 3H), 1.36−1.49 (m, 3H), 1.52−1.59 (m, 1H), 1.56 (s, 3H), 1.66 (d, J = 0.8 Hz, 3H), 1.70−1.74 (m, 2H), 1.82−1.85 (m, 2H), 1.94−2.05 (m, 4H), 2.26 (m, 1H), 2.59 (m, 1H), 5.03 (m, 1H), 7.28−7.37 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.9, 24.4, 24.7, 25.7, 25.9, 25.9, 28.2, 29.3, 29.4, 32.1, 61.2, 85.9, 123.9, 126.2, 128.2, 128.4, 132.4, 140.0; HRMS (ESI) m/z calcd for $C_{20}H_{30}NO$ $[M + H]^+$ 300.2327, found 300.2296.

Conversion of 1cb into 2c. Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (36.2 mg, 0.0250 mmol, 0.050 equiv) in THF (12 mL) was reacted with a solution containing oxaziridine diastereomers **1cb** (150 mg, 0.501 mmol, 1.0 equiv; *Z*:*E* = ca. 63:37) in THF (3 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 98.7:1.0:0.3) afforded 70 mg (0.321 mmol, 64% corrected yield by ^1H NMR; contaminated with ∼10% of unidentified impurities) of the allylic alcohol **2c** as a pink oil and 19 mg (0.0940 mmol, 19% yield) of **3c**.

Following the general procedure **C**, CuCl (2.48 mg, 0.0250 mmol, 0.050 equiv) and *rac*-BINAP (15.6 mg, 0.0250 mmol, 0.050 equiv) in THF (12 mL) were reacted with a solution of oxaziridine (*Z*)-**1cb** (150 mg, 0.501 mmol, 1.0 equiv) in THF (3 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 98.7:1.0:0.3) afforded 82 mg (0.376 mmol,

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75% yield) of **2c** as a yellow oil and 6.0 mg (0.0297 mmol, 6% yield) of **3c**.

(2*R*,3*S*)-2-Benzhydryl-3-(5-methylhex-4′-en-1′-yl)-3-phenyl-1,2-oxaziridine (*Z*)-1cc and (2*S*,3*S*)-2-Benzhydryl-3-(5-methylhex-4′-en-1′-yl)-3-phenyl-1,2-oxaziridine (*E*)-1cc. Following the general procedure **A**, 6-methyl-1-phenylhept-5-en-1-one **3c** (0.500 g, 2.47 mmol, 1.0 equiv), benzhydrylamine **4c** (0.639 mL, 3.71 mmol, 1.5 equiv), PTSA (23.5 mg, 0.123 mmol, 0.050 equiv) and activated 4 Å molecular sieves (3.0 g) in toluene (25 mL) were refluxed for 60 h, followed by oxidation with *m*-CPBA (0.510 g, 2.96 mmol, 1.2 equiv) in CH_2Cl_2 (12 mL). Purification by chromatography on SiO_2 (0.5−0.7% EtOAc in hexanes) afforded the mixture of major (*Z*)-**1cc** and minor (*E*)-**1cc** diastereomers containing ca. 6.5% of dibenzhydrylamine impurity and 4% of starting ketone **3c** as a colorless oil (0.826 g, 87% corrected yield by ^{1}H NMR; (*Z*)-**1cc**:(*E*)-**1cc** = ca. 72:28). An analytical sample of the major diastereomer (*Z*)-**1cc** accompanied with 9% of dibenzhydrylamine was obtained for characterization during this purification: R_f = 0.60 (5% EtOAc/hexanes, run twice); IR (neat) 1448, 733, 701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20−1.31 (m, 1H), 1.41−1.52 (m, 1H), 1.55 (s, 3H), 1.66 (s, 3H), 1.86−2.02 (m, 3H), 2.35 (m, 1H), 4.09 (s, 1H), 5.04 (t, J = 6.9 Hz, 1H), 6.98−7.00 (m, 2H), 7.22−7.26 (m, 4H), 7.29−7.35 (m, 5H), 7.38 (d, J = 8.5 Hz, 2H), 7.42 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.8, 24.1, 25.8, 28.1, 37.9, 70.5, 88.7, 124.3, 127.3, 127.6, 127.7, 127.8, 127.9, 128.1, 128.3, 128.4, 128.5, 128.6, 128.9, 131.9, 134.8, 139.6, 142.4; HRMS (ESI) m/z calcd for $C_{27}H_{30}NO$ [M + H]$^+$ 384.2327, found 384.2337. Minor diastereomer (*E*)-**1cc**: R_f = 0.45 (5% EtOAc/hexanes, run twice); ^{1}H NMR (400 MHz, $CDCl_3$; diagnostic peaks only) δ 4.91 (s, 1H).

Conversion of 1cc into 2c. Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (37.7 mg, 0.0260 mmol, 0.037 equiv) in THF (12 mL) was reacted with a solution containing oxaziridine diastereomers **1cc** (269 mg, 0.702 mmol, 1.0 equiv; *Z*:*E* = ca. 70:30, containing ca. 6.4% of dibenzhydrylamine and 4% of **3c**) in THF (8 mL). The reaction mixture was refluxed for 3 h. Purification by chromatography on SiO_2 (1.5% acetone in CH_2Cl_2) afforded 100 mg (0.458 mmol, 65% yield) of the allylic alcohol **2c** as a brown oil and 18 mg (0.0891 mmol, 13% yield) of **3c**.

1-(*p*-Tolyl)hex-5-en-1-one 3d. Following the general procedure **D**, a solution of 5-bromo-1-pentene (1.77 mL, 14.9 mmol, 1.2 equiv) in THF (10 mL) was added dropwise to a stirring suspension of magnesium turnings (0.364 g, 14.9 mmol, 1.2 equiv) and one small crystal of iodine in THF (10 mL). After refluxing gently for 20 min, the reaction mixture was cooled to 0 °C and treated with a solution of *p*-tolualdehyde (1.50 g, 12.4 mmol, 1.0 equiv) in THF (5 mL). The reaction mixture was then stirred at room temperature for 1 h. The aqueous work up afforded the crude alcohol (2.50 g) as a colorless oil, which was used for the next oxidation step without purification. To a stirring solution of crude alcohol in CH_2Cl_2 (50 mL) was added Celite (5.0 g) followed by pyridinium chlorochromate (5.38 g, 24.9 mmol, 2 equiv), and the reaction was maintained at room temperature for 1.5 h. The reaction mixture was filtered through Celite, rinsing with several portions of CH_2Cl_2, and the filtrate was concentrated under reduced pressure. Purification by chromatography on SiO_2 (0.8% EtOAc in hexanes) afforded 2.12 g (11.2 mmol, 90% yield over 2 steps) of the corresponding ketone **3d** as a colorless oil: R_f = 0.52 (10% EtOAc/hexanes); IR (neat) 1681, 1180 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.78−1.85 (m, 2H), 2.13 (q, J = 7.1 Hz, 2H), 2.37 (s, 3H), 2.91 (t, J = 7.3 Hz, 2H), 4.95−5.05 (m, 2H), 5.80 (m, 1H), 7.21 (d, J = 7.9 Hz, 2H), 7.83 (d, J = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 23.4, 33.2, 37.6, 115.2, 128.1, 129.2, 134.6, 138.1, 143.6, 199.8; HRMS (ESI) m/z calcd for $C_{13}H_{17}O$ [M + H]$^+$ 189.1279, found 189.1284.

(2*R*,3*S*)-2-Cyclohexyl-3-(pent-4′-en-1′-yl)-3-(*p*-tolyl)-1,2-oxaziridine (*Z*)-1db and (2*S*,3*S*)-2-Cyclohexyl-3-(Pent-4′-en-1′-yl)-3-(*p*-tolyl)-1,2-oxaziridine (*E*)-1db. Following the general procedure **A**, 1-(*p*-tolyl)hex-5-en-1-one **3d** (0.500 g, 2.65 mmol, 1.0 equiv), cyclohexylamine **4b** (0.456 mL, 3.98 mmol, 1.5 equiv), PTSA (25.2 mg, 0.132 mmol, 0.050 equiv) and activated 5 Å molecular sieves (3.50 g) in toluene (35 mL) were refluxed for 60 h, followed by oxidation with *m*-CPBA (0.550 g, 3.19 mmol, 1.2 equiv) in CH_2Cl_2 (20 mL). Purification by chromatography on SiO_2 (0.5% EtOAc in hexanes) afforded the mixture of oxaziridine diastereomers (*Z*)-**1db** and (*E*)-**1db** and starting ketone **3d** as a colorless oil (0.480 g, 1.70 mmol, 64% corrected yield by ^{1}H NMR; (*Z*)-**1db**:(*E*)-**1db** = ca. 55:45). Subsequent purification of the mixture of (*Z*)-**1db**, (*E*)-**1db**, and **3d** afforded the partial separation of the mixture of (*Z*)-**1db** and (*E*)-**1db** as a colorless oil. A small amount of the mixture of (*Z*)-**1db** and (*E*)-**1db** was further purified by preparative TLC on SiO_2 (2% EtOAc in hexanes, 7 runs) to afford the analytical samples of the major (*Z*)-**1db** and the minor (*E*)-**1db** diastereomers for characterization. Major diastereomer (*Z*)-**1db**: R_f = 0.65 (5% EtOAc/hexanes, run thrice); IR (neat) 2930, 1450 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.74−0.86 (m, 1H), 0.97−1.18 (m, 2H), 1.19−1.34 (m, 3H), 1.39−1.58 (m, 4H), 1.66−1.78 (m, 3H), 1.83−1.87 (m, 1H), 1.92−2.06 (m, 2H), 2.30−2.39 (m, 4H), 4.86−4.94 (m, 2H), 5.69 (m, 1H), 7.16 (d, J = 7.8 Hz, 2H), 7.28 (d, J = 8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 23.3, 24.0, 24.1, 25.8, 28.5, 31.7, 33.7, 38.1, 60.7, 87.6, 114.8, 127.7, 128.8, 132.1, 138.4; HRMS (ESI) m/z calcd for $C_{19}H_{28}NO$ [M + H]$^+$ 286.2171, found 286.2137. Minor diastereomer (*E*)-**1db**: R_f = 0.51 (5% EtOAc/hexanes, run thrice); IR (neat) 2930, 1450 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21−1.38 (m, 3H), 1.42−1.60 (m, 4H), 1.64−1.73 (m, 2H), 1.81−1.85 (m, 2H), 1.96−2.13 (m, 4H), 2.25−2.33 (m, 4H), 2.58 (m, 1H), 4.94−5.02 (m, 2H), 5.74 (m, 1H), 7.15 (d, J = 7.9 Hz, 2H), 7.26 (d, J = 8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 24.3, 24.6, 24.7, 25.8, 29.0, 29.2, 32.1, 33.8, 61.2, 85.6, 115.3, 126.0, 129.1, 136.9, 138.03, 138.07; HRMS (ESI) m/z calcd for $C_{19}H_{28}NO$ [M + H]$^+$ 286.2171, found 286.2162.

4-Hydroxy-1-(*p*-tolyl)hex-5-en-1-one 2d. Following the general procedure **C**, CuCl (2.60 mg, 0.0263 mmol, 0.050 equiv) and *rac*-BINAP (16.3 mg, 0.0263 mmol, 0.050 equiv) in THF (12 mL) were reacted with a solution containing oxaziridine diastereomers **1db** (150 mg, 0.526 mmol, 1.0 equiv; *Z*:*E* = ca. 48:52) in THF (3 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 98.8:1.0:0.2) afforded 61 mg (0.299 mmol, 57% yield) of the allylic alcohol **2d** as a yellow oil: R_f = 0.32 (25% EtOAc/hexanes); IR (neat) 3411, 1674 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.88−1.97 (m, 1H), 1.99−2.07 (m, 1H), 2.23 (br s, 1H), 2.39 (s, 3H), 3.09 (t, J = 7.0 Hz, 2H), 4.22−4.24 (m, 1H), 5.12 (td, J = 10.4, 1.3 Hz, 1H), 5.26 (td, J = 17.2, 1.4 Hz, 1H), 5.89 (m, 1H), 7.24 (d, J = 7.9 Hz, 2H), 7.86 (d, J = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.8, 31.1, 34.4, 72.4, 115.0, 128.4, 129.4, 134.5, 140.9, 144.0, 200.4; HRMS (ESI) m/z calcd for $C_{13}H_{17}O_2$ [M + H]$^+$ 205.1229, found 205.1200. Ketone **3d** was also obtained in 27% yield (27 mg, 0.143 mmol).

1-(4-Fluorophenyl)hex-5-en-1-one 3e.[24] Following the general procedure **D**, a solution of 5-bromo-1-pentene (1.14 mL, 9.66 mmol, 1.2 equiv) in THF (8 mL) was added dropwise to a stirring suspension of magnesium turnings (235 mg, 9.66 mmol, 1.2 equiv) and one small crystal of iodine in THF (7 mL) under argon atmosphere. After refluxing gently for 1 h, the reaction mixture was cooled to 0 °C and treated with a solution of 4-fluorobenzaldehyde (1.0 g, 8.05 mmol, 1.0 equiv) in THF (5 mL). The reaction mixture was then stirred at room temperature for 2 h. The aqueous work up afforded the crude alcohol (1.75 g) as a yellow oil, which was used for the next oxidation step without purification. To a stirring solution of crude alcohol in CH_2Cl_2 (50 mL) was added pyridinium chlorochromate (3.47 g, 16.1 mmol, 2 equiv), and the reaction was maintained at room temperature for 2 h. The reaction mixture was filtered through Celite, rinsing with several portions of CH_2Cl_2, and the filtrate was concentrated under reduced pressure. Purification by chromatography on SiO_2 (1% EtOAc in hexanes) afforded 1.25 g (6.51 mmol, 81% yield over 2 steps) of the corresponding ketone **3e** as a colorless oil: R_f = 0.71 (15% EtOAc/hexanes); IR (neat) 1684, 1229 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.78 (m, 2H), 2.06−2.12 (m, 2H), 2.88 (t, J = 7.3 Hz, 2H), 4.91−5.01 (m, 2H), 5.75 (m, 1H), 7.01−7.07 (m, 2H), 7.89−7.94 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.2, 33.1, 37.5, 115.3, 115.6 (d, J = 86.9 Hz, 2C), 130.64 (d, J = 36.7 Hz, 2C), 133.53 (d, J = 11.8 Hz, 1C), 138.0, 165.6 (d, J = 1010.8 Hz, 1C), 196.4; HRMS (EI) m/z calcd for $C_{12}H_{14}OF$ [M + H]$^+$ 193.1029, found 193.1021.

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(2*R*,3*S*)-2-Cyclohexyl-3-(4-fluorophenyl)-3-(pent-4′-en-1′-yl)-1,2-oxaziridine (*Z*)-1eb and (2*S*,3*S*)-2-Cyclohexyl-3-(4-fluorophenyl)-3-(pent-4′-en-1′-yl)-1,2-oxaziridine (*E*)-1eb. Following the general procedure **A**, 1-(4-fluorophenyl)hex-5-en-1-one **3e** (0.500 g, 2.60 mmol, 1.0 equiv), cyclohexylamine **4b** (0.446 mL, 3.90 mmol, 1.5 equiv), PTSA (24.7 mg, 0.130 mmol, 0.050 equiv) and activated 5 Å molecular sieves (3.50 g) in toluene (30 mL) were refluxed for 60 h, followed by oxidation with *m*-CPBA (0.539 g, 3.12 mmol, 1.2 equiv) in CH_2Cl_2 (20 mL). Purification by chromatography on SiO_2 (0.5−0.7% EtOAc in hexanes) afforded the mixture of oxaziridine diastereomers (*Z*)-**1eb** and (*E*)-**1eb** and starting ketone **3e**, followed by the mixture of (*Z*)-**1eb** and (*E*)-**1eb** as a yellow oil (0.617 g, 2.13 mmol, 82% yield by ^{1}H NMR; (*Z*)-**1eb**:(*E*)-**1eb** = ca. 2:1). An analytical sample of the major diastereomer (*Z*)-**1eb** accompanied with 12% of the minor diastereomer (*E*)-**1eb** was obtained for characterization during this purification. Major diastereomer (*Z*)-**1eb**: R_f = 0.67 (5% EtOAc/hexanes, run thrice); IR (neat) 2931, 1510 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.74−0.85 (m, 1H), 0.98−1.18 (m, 2H), 1.18−1.29 (m, 3H), 1.40−1.52 (m, 3H), 1.53−1.59 (m, 1H), 1.65−1.75 (m, 3H), 1.83−1.87 (m, 1H), 1.93−2.07 (m, 2H), 2.33 (m, 1H), 4.88−4.95 (m, 2H), 5.69 (m, 1H), 7.04−7.10 (m, 2H), 7.36−7.41 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.2, 24.11, 24.18, 25.8, 28.6, 31.7, 33.7, 38.0, 60.9, 87.2, 115.0, 115.3 (d, J = 85.8 Hz, 2C), 129.65 (d, J = 32.3 Hz, 2C), 131.2 (d, J = 13.0 Hz, 1C), 138.3, 162.9 (d, J = 985.8 Hz, 1C); HRMS (ESI) m/z calcd for $C_{18}H_{25}FNO$ $[M + H]^+$ 290.1920, found 290.1887. Minor diastereomer (*E*)-**1eb**: R_f = 0.62 (5% EtOAc/hexanes, run thrice); ^{1}H NMR (400 MHz, $CDCl_3$; diagnostic peaks only) δ 2.26 (m, 1H), 2.56 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$; diagnostic peaks only) δ 29.3, 61.3, 85.2.

1-(4-Fluorophenyl)-4-hydroxyhex-5-en-1-one 2e. Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (50.0 mg, 0.0346 mmol, 0.050 equiv) in THF (12 mL) was reacted with a solution containing oxaziridine diastereomers **1eb** (200 mg, 0.692 mmol, 1.0 equiv; *Z*:*E* = ca. 88:12) in THF (8 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 98.7:1.0:0.3) afforded 72 mg (0.346 mmol, 50% yield) of the allylic alcohol **2e** as a colorless oil: R_f = 0.34 (25% EtOAc/hexanes); IR (neat) 3411, 1681, 1596 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.88−1.97 (m, 1H), 2.00−2.08 (m, 1H), 2.05 (d, J = 4.4 Hz, 1H), 3.09 (t, J = 7.0 Hz, 2H), 4.21−4.26 (m, 1H), 5.13 (td, J = 10.4, 1.3 Hz, 1H), 5.26 (td, J = 17.2, 1.4 Hz, 1H), 5.90 (m, 1H), 7.09−7.14 (m, 2H), 7.97−8.02 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.9, 34.4, 72.3, 115.1, 115.8 (d, J = 87.0 Hz, 2C), 130.9 (d, J = 36.8 Hz, 2C), 133.51 (d, J = 11.8 Hz, 1C), 140.8, 165.9 (d, J = 1012.8 Hz, 1C), 199.0; HRMS (ESI) m/z calcd for $C_{12}H_{14}FO_2$ $[M + H]^+$ 209.0978, found 209.0991. Ketone **3e** was also obtained in 19% yield (25 mg, 0.130 mmol).

Following the general procedure **C**, CuCl (2.56 mg, 0.0259 mmol, 0.050 equiv) and *rac*-BINAP (16.1 mg, 0.0259 mmol, 0.050 equiv) in THF (9 mL) were reacted with a solution containing oxaziridine diastereomers **1eb** (150 mg, 0.519 mmol, 1.0 equiv; *Z*:*E* = ca. 58:42) in THF (3 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 98.7:1.0:0.3) afforded 71 mg (0.341 mmol, 66% yield) of **2e** as a yellow oil and 17 mg (0.0885 mmol, 17% yield) of **3e**.

1-(Furan-2-yl)hex-5-en-1-one 3f.[25] Following the general procedure **D**, a solution of 5-bromo-1-pentene (4.43 mL, 37.4 mmol, 1.2 equiv) in THF (25 mL) was added dropwise to a stirring suspension of magnesium turnings (0.910 g, 37.4 mmol, 1.2 equiv) and one small crystal of iodine in THF (25 mL). After refluxing gently for 1 h, the reaction mixture was cooled to 0 °C and treated with a solution of 2-furaldehyde (3.00 g, 31.2 mmol, 1.0 equiv) in THF (10 mL). The reaction mixture was then stirred at room temperature for 1 h. The aqueous work up afforded the crude alcohol (5.24 g) as a brown oil, which was used for the next oxidation step without purification. To a stirring solution of crude alcohol in CH_2Cl_2 (125 mL), was added Celite (12.0 g) followed by pyridinium chlorochromate (13.4 g, 62.4 mmol, 2 equiv), and the reaction was maintained at room temperature for 12 h. The reaction mixture was filtered through Celite, rinsing with several portions of CH_2Cl_2, and the filtrate was concentrated under reduced pressure. Purification by chromatography on SiO_2 (3% EtOAc in hexanes) afforded 1.20 g (7.31 mmol, 23% yield over 2 steps) of the corresponding ketone **3f** as a yellow oil: R_f = 0.47 (15% EtOAc/hexanes).

(2*R*,3*S*)-2-Cyclohexyl-3-(furan-2-yl)-3-(pent-4′-en-1′-yl)-1,2-oxaziridine (*Z*)-1fb. Following the general procedure **A**, 1-(furan-2-yl)hex-5-en-1-one **3f** (0.500 g, 3.04 mmol, 1.0 equiv), cyclohexylamine **4b** (0.523 mL, 4.57 mmol, 1.5 equiv), PTSA (28.9 mg, 0.152 mmol, 0.050 equiv) and activated 5 Å molecular sieves (3.50 g) in toluene (30 mL) were refluxed for 60 h, followed by oxidation with *m*-CPBA (0.631 g, 3.65 mmol, 1.2 equiv) in CH_2Cl_2 (20 mL). Purification by chromatography on SiO_2 (0.7 to 0.8% EtOAc in hexanes) afforded the oxaziridine (*Z*)-**1fb** as a yellow oil (0.100 g, 0.383 mmol, 12% yield; sample contains some minor impurities). Oxaziridine diastereomer (*Z*)-**1fb**: R_f = 0.55 (10% EtOAc/hexanes); IR (neat) 2931, 1451 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88−0.99 (m, 1H), 1.12−1.18 (m, 2H), 1.19−1.25 (m, 2H), 1.33−1.41 (m, 1H), 1.45−1.57 (m, 3H), 1.58−1.64 (m, 1H), 1.72−1.80 (m, 2H), 1.87−1.91 (m, 1H), 2.01−2.10 (m, 3H), 2.32 (m, 1H), 4.90−4.99 (m, 2H), 5.74 (m, 1H), 6.38−6.40 (m, 2H), 7.45 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.2, 24.1, 24.4, 25.8, 28.6, 31.8, 33.7, 36.0, 61.4, 82.3, 110.3, 111.5, 115.0, 138.4, 143.5, 149.1; HRMS (ESI) m/z calcd for $C_{16}H_{24}NO_2$ $[M + H]^+$ 262.1807, found 262.1796.

1-(Furan-2-yl)-4-hydroxyhex-5-en-1-one 2f. Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (41.5 mg, 0.0287 mmol, 0.050 equiv) in THF (10 mL) was reacted with oxaziridine (*Z*)-**1fb** (150 mg, 0.574 mmol, 1.0 equiv) in THF (5 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 98.6:1.0:0.4) afforded 53 mg (0.294 mmol, 51% yield) of the allylic alcohol **2f** as a pale yellow oil: R_f = 0.11 (25% EtOAc/hexanes); IR (neat) 3420, 1666, 1467 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.86−1.95 (m, 1H), 1.97−2.05 (m, 1H), 2.09 (br s, 1H), 2.97 (t, J = 7.1 Hz, 2H), 4.22 (m, 1H), 5.12 (td, J = 10.4, 1.3 Hz, 1H), 5.26 (td, J = 17.2, 1.4 Hz, 1H), 5.88 (m, 1H), 6.51−6.53 (m, 1H), 7.20 (dd, J = 3.5, 0.6 Hz, 1H), 7.57 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.8, 34.3, 72.3, 112.4, 115.2, 117.4, 140.7, 146.6, 152.8, 189.7; HRMS (ESI) m/z calcd for $C_{10}H_{13}O_3$ $[M + H]^+$ 181.0864, found 181.0867. Ketone **3f** was also obtained in 15% yield (14 mg, 0.0853 mmol).

1-(Naphthalen-2-yl)hex-5-en-1-one 3g. A solution of 2-acetonaphthone (5.00 g, 29.3 mmol, 1.0 equiv), *N*,*N*-dimethylhydrazine (5.29 g, 88.1 mmol, 3.0 equiv) and PTSA (279 mg, 1.46 mmol, 0.050 equiv) in benzene (35 mL) was refluxed for 18 h under nitrogen atmosphere with removal of water by a Dean−Stark apparatus. The reaction mixture was concentrated under reduced pressure, and the residue was cooled to 0 °C. The yellow solid obtained was triturated with hexanes and filtered, washed with hexanes and dried under vacuum to afford the corresponding hydrazone as a creamish-yellow solid (mp 47−50 °C) in 99% yield (6.15 g, 29.0 mmol). To a cooled 1.0 M LDA solution (23.3 mL, 23.3 mmol, 1.1 equiv) in THF at 0 °C under nitrogen atmosphere was added the solution of hydrazone (4.50 g, 21.2 mmol, 1.0 equiv) in THF (35 mL) slowly over 25 min and was allowed to stir at 0 °C for 5 h. The reaction mixture was then cooled to −78 °C, and a solution of 4-bromo-1-butene (3.43 g, 25.4 mmol, 1.2 equiv) in THF (10 mL) was added slowly over 20 min. The reaction was warmed to room temperature and stirred for 36 h. The reaction mixture was concentrated under reduced pressure, and the residue was diluted with ether (20 mL) and then treated with an ice-cold solution of dilute sulfuric acid (20 mL) for 30 min to hydrolyze the hydrazone. The resulting solution was diluted with water and extracted with ether (2 × 20 mL), and the combined organic extracts were washed with water (2 × 20 mL) and brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification by chromatography on SiO_2 (4% EtOAc in hexanes) afforded the ketone **3g** as a cream-colored solid (mp 36−37 °C) in 65% yield (3.10 g, 13.8 mmol; 95% brsm): R_f = 0.74 (10% EtOAc/hexanes, run twice); IR (neat) 1678, 1624 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.91(quin, J = 7.3 Hz, 2H), 2.20 (q, J = 7.0 Hz, 2H), 3.08 (t, J = 7.3 Hz, 2H), 5.03 (d, J = 10.1 Hz, 1H), 5.09 (d, J = 17.1 Hz, 1H), 5.86 (m, 1H), 7.51−7.59 (m, 2H), 7.83−7.87 (m, 2H), 7.94 (d, J = 7.9 Hz, 1H), 8.02 (d, J = 8.6 Hz, 1H), 8.44 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.5, 33.3, 37.8,

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115.4, 124.0, 126.8, 127.8, 128.42, 128.47, 129.62, 129.65, 132.6, 134.4, 135.6, 138.1, 200.1; HRMS (ESI) m/z calcd for $C_{16}H_{17}O$ $[M + H]^+$ 225.1279, found 225.1263.

(2*R*,3*S*)-2-Cyclohexyl-3-(naphthalen-2-yl)-3-(pent-4′-en-1′-yl)-1,2-oxaziridine (*Z*)-1gb and (2*S*,3*S*)-2-Cyclohexyl-3-(naphthalen-2-yl)-3-(pent-4′-en-1′-yl)-1,2-oxaziridine (*E*)-1gb. Following the general procedure **A**, 1-(naphthalen-2-yl)hex-5-en-1-one **3g** (0.500 g, 2.23 mmol, 1.0 equiv), cyclohexylamine **4b** (0.382 mL, 3.34 mmol, 1.5 equiv), PTSA (21.2 mg, 0.115 mmol, 0.050 equiv) and activated 5 Å molecular sieves (3.50 g) in toluene (25 mL) were refluxed for 60 h, followed by oxidation with *m*-CPBA (0.461 g, 2.67 mmol, 1.2 equiv) in CH_2Cl_2 (20 mL). Purification by chromatography on SiO_2 (0.6% EtOAc in hexanes) afforded the mixture of oxaziridine diastereomers (*Z*)-**1gb** and (*E*)-**1gb** and starting ketone **3g** as a colorless oil. Subsequent purification by chromatography on SiO_2 (0.5−1% EtOAc in hexanes) afforded the mixture of the (*Z*)-**1gb** and (*E*)-**1gb**, which were separated into 2 fractions containing enrichment from each diastereomer (0.641 g, 1.99 mmol, 89% yield; (*Z*)-**1gb**:(*E*)-**1gb** = ca. 1:1). A pure sample of the first (*Z*)-**1gb** and the second diastereomer (*E*)-**1gb** for characterization was obtained during this purification. First diastereomer (*Z*)-**1gb**: R_f = 0.51 (5% EtOAc/hexanes, run thrice); IR (neat) 1449 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.66−0.77 (m, 1H), 0.94−1.17 (m, 2H), 1.21−1.33 (m, 2H), 1.35−1.39 (m, 1H), 1.41−1.57 (m, 4H), 1.67−1.71 (m, 1H), 1.76−1.84 (m, 2H), 1.88−1.92 (m, 1H), 1.95−2.08 (m, 2H), 2.48 (m, 1H), 4.87−4.95 (m, 2H), 5.69 (m, 1H), 7.50−7.56 (m, 3H), 7.85−7.90 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.3, 24.0, 24.1, 25.8, 28.7, 31.8, 33.8, 38.1, 60.9, 88.0, 115.0, 124.9, 126.72, 126.78, 127.6, 127.9, 128.1, 128.5, 132.80, 132.85, 133.4, 138.4; HRMS (ESI) m/z calcd for $C_{22}H_{28}NO$ $[M + H]^+$ 322.2171, found 322.2155. Second diastereomer (*E*)-**1gb**: R_f = 0.51 (5% EtOAc/hexanes, run thrice); IR (neat) 1450 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.21−1.45 (m, 3H), 1.46−1.65 (m, 4H), 1.69−1.72 (m, 1H), 1.79−1.89 (m, 3H), 2.04−2.19 (m, 4H), 2.44 (m, 1H), 2.67 (m, 1H), 4.95−5.03 (m, 2H), 5.73 (m, 1H), 7.46−7.51 (m, 3H), 7.82−7.87 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.3, 24.6, 24.8, 25.9, 29.0, 29.3, 32.1, 33.8, 61.3, 85.9, 115.4, 123.8, 125.4, 126.3, 127.8, 128.37, 128.39, 133.2, 133.3, 137.3, 137.9; HRMS (ESI) m/z calcd for $C_{22}H_{28}NO$ $[M + H]^+$ 322.2171, found 322.2143.

4-Hydroxy-1-(naphthalen-2-yl)hex-5-en-1-one 2g. Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (33.7 mg, 0.0233 mmol, 0.045 equiv) in THF (10 mL) was reacted with a solution containing oxaziridine diastereomers **1gb** (164 mg, 0.510 mmol, 1.0 equiv; *Z*:*E* = ca. 90:10) in THF (5 mL). The reaction mixture was refluxed for 3 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 99.4:0.5:0.1) afforded 70 mg (0.291 mmol, 57% yield) of the allylic alcohol **2g** as a creamish-orange solid (mp 59−61 °C): R_f = 0.15 (20% EtOAc/hexanes); IR (neat) 3410, 1673 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.96−2.05 (m, 1H), 2.07−2.15 (m, 1H), 2.21 (br s, 1H), 3.26 (t, J = 7.0 Hz, 2H), 4.29 (br s, 1H), 5.15 (d, J = 10.4 Hz, 1H), 5.30 (d, J = 17.2 Hz, 1H), 5.94 (m, 1H), 7.52−7.61 (m, 2H), 7.85−7.88 (m, 2H), 7.95 (d, J = 7.9 Hz, 1H), 8.03 (dd, J = 8.6, 1.5 Hz, 1H), 8.49 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.1, 34.5, 72.4, 115.1, 124.0, 126.9, 127.9, 128.64, 128.66, 129.7, 129.9, 132.7, 134.4, 135.8, 140.9, 200.6; HRMS (ESI) m/z calcd for $C_{16}H_{17}O_2$ $[M + H]^+$ 241.1229, found 241.1224. Ketone **3g** was also obtained in 19% yield (22 mg, 0.982 mmol).

Following the general procedure **C**, CuCl (1.46 mg, 0.0147 mmol, 0.050 equiv) and *rac*-BINAP (9.20 mg, 0.0147 mmol, 0.050 equiv) in THF (8 mL) were reacted with a solution containing oxaziridine diastereomers **1gb** (95.0 mg, 0.29 mmol, 1.0 equiv; *Z*:*E* = ca. 90:10) in THF (2 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 98.7:1.0:0.3) afforded 33 mg (0.137 mmol, 46% yield; 57% brsm) of **2g** as a yellow oil and 7.0 mg (0.0312 mmol, 11% yield) of **3g**.

Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (33.7 mg, 0.0233 mmol, 0.042 equiv) in THF (10 mL) was reacted with a solution containing oxaziridine diastereomers **1gb** (178 mg, 0.553 mmol, 1.0 equiv; *Z*:*E* = ca. 16:84, accompanied with 2.5% of **3g**) in THF (5 mL). The reaction mixture was refluxed for 3 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 99.2:0.5:0.3) afforded 55 mg (0.229 mmol, 41% yield) of **2g** as an orange oil and 25 mg (0.111 mmol, 20% corrected yield) of **3g**.

Following the general procedure **C**, CuCl (1.30 mg, 0.0132 mmol, 0.050 equiv) and *rac*-BINAP (8.22 mg, 0.0132 mmol, 0.050 equiv) in THF (8 mL) were reacted with a solution containing oxaziridine diastereomers **1gb** (85.0 mg, 0.264 mmol, 1.0 equiv; *Z*:*E* = ca. 16:84, accompanied with 2.5% of **3g**) in THF (2 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 98.7:1.0:0.3) afforded 34 mg (0.141 mmol, 53% yield; 73% brsm) of **2g** as a yellow oil and ∼4.0 mg (∼6% corrected yield) of **3g**.

(*E*)-1,6-Diphenylhex-5-en-1-one 3h. To a solution of Grubbs II catalyst[26] (0.195 g, 0.229 mmol, 0.04 equiv) in CH_2Cl_2 (20 mL) at room temperature under argon atmosphere was added a solution containing the mixture of 1-phenylhex-5-en-1-one **3a** (1.00 g, 5.74 mmol, 1.0 equiv) and styrene (1.97 mL, 17.2 mmol, 3.0 equiv) in CH_2Cl_2 (5 mL), and the reaction mixture was stirred at 40 °C for 4 h. The reaction mixture was concentrated under reduced pressure. Initial purification of crude residue by chromatography on SiO_2 (0.5−0.6% EtOAc in hexanes) afforded the mixture of desired product **3h** and (*E*)-1,5-diphenylpent-4-en-1-one byproduct[27] as a white solid (0.770 g, 3.08 mmol, 54% corrected yield for **3h** by ^1H NMR). Subsequent purification by chromatography on SiO_2 (0.5% EtOAc in hexanes) followed by recrystallization from hexanes afforded partial separation of the desired product **3h** as white crystals (mp 52−54 °C): R_f = 0.38 (5% EtOAc/hexanes); IR (neat) 1682, 1196 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.98 (m, 2H), 2.35 (q, J = 6.9 Hz, 2H), 3.03 (t, J = 7.2 Hz, 2H), 6.23−6.30 (m, 1H), 6.46 (d, J = 15.8 Hz, 1H), 7.24 (t, J = 7.1 Hz, 1H), 7.33 (t, J = 7.5 Hz, 2H), 7.39 (d, J = 7.3 Hz, 2H), 7.47 (t, J = 7.5 Hz, 2H), 7.57 (t, J = 7.3 Hz, 1H), 8.00 (d, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.7, 32.4, 37.7, 126.0, 127.0, 128.0, 128.54, 128.59, 129.9, 130.7, 132.9, 137.0, 137.6, 200.0; HRMS (ESI) m/z calcd for $C_{18}H_{19}O$ $[M + H]^+$ 251.1436, found 251.1424.

(2*R*,3*S*,*E*)-2-Cyclohexyl-3-phenyl-3-(5′-phenylpent-4′-en-1′-yl)-1,2-oxaziridine (*Z*)-1hb and (2*S*,3*S*,*E*)-2-Cyclohexyl-3-phenyl-3-(5′-phenylpent-4′-en-1′-yl)-1,2-oxaziridine (*E*)-1hb. Following the general procedure **A**, (*E*)-1,6-diphenylhex-5-en-1-one **3h** (0.400 g, 1.60 mmol, 1.0 equiv), cyclohexylamine **4b** (0.274 mL, 2.40 mmol, 1.5 equiv), PTSA (15.2 mg, 0.0800 mmol, 0.050 equiv) and activated 5 Å molecular sieves (3.0 g) in toluene (30 mL) were refluxed for 60 h, followed by oxidation with *m*-CPBA (0.331 g, 1.92 mmol, 1.2 equiv) in CH_2Cl_2 (15 mL). Purification by chromatography on SiO_2 (0.5−0.6% EtOAc in hexanes) afforded the mixture of major (*Z*)-**1hb** and minor (*E*)-**1hb** diastereomers as a colorless oil (0.500 g, 1.44 mmol, 90% yield; (*Z*)-**1hb**:(*E*)-**1hb** = ca. 60:40 by ^1H NMR). Subsequent purification of a small amount of the mixture of (*Z*)-**1hb** and (*E*)-**1hb** by preparative TLC on SiO_2 (2% EtOAc in hexanes, 13 runs) afforded the analytical sample of (*Z*)-**1hb** for characterization. Major diastereomer (*Z*)-**1hb**: R_f = 0.46 (5% EtOAc/hexanes, run twice); IR (neat) 2930, 2855, 1447 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.73−0.84 (m, 1H), 0.98−1.19 (m, 2H), 1.19−1.29 (m, 1H), 1.31−1.39 (m, 2H), 1.43−1.59 (m, 4H), 1.68−1.83 (m, 3H), 1.85−1.89 (m, 1H), 2.12−2.22 (m, 2H), 2.42 (m, 1H), 6.07−6.14 (m, 1H), 6.30 (d, J = 15.8 Hz, 1H), 7.15−7.19 (m, 1H), 7.24−7.30 (m, 4H), 7.37−7.43 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.7, 24.1, 24.2, 25.8, 28.6, 31.8, 33.0, 38.1, 61.0, 87.7, 126.1, 127.0, 127.8, 128.2, 128.6, 128.8, 130.42, 130.44, 135.2, 137.8; HRMS (ESI) m/z calcd for $C_{24}H_{30}NO$ $[M + H]^+$ 348.2327, found 348.2357. Minor diastereomer (*E*)-**1hb**: R_f = 0.40 (5% EtOAc/hexanes, run twice); ^1H NMR (400 MHz, $CDCl_3$; diagnostic peaks only) δ 2.36 (m, 1H), 2.61 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$; diagnostic peaks only) δ 29.1, 61.2, 85.8, 137.7, 139.9.

(*E*)-4-Hydroxy-1,6-diphenylhex-5-en-1-one 2h. Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (31.2 mg, 0.0216 mmol, 0.050 equiv) in THF (10 mL) was reacted with a solution containing oxaziridine diastereomers **1hb** (150 mg, 0.432 mmol, 1.0 equiv; *Z*:*E* = 60:40) in THF (5 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (1.0% acetone in CH_2Cl_2) afforded 83 mg (0.312 mmol, 72% yield) of the allylic alcohol **2h** as a

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cream-colored solid (mp 59−61 °C): R_f = 0.32 (25% EtOAc/hexanes); IR (neat) 3400, 1677 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.01−2.18 (m, 2H), 2.58 (d, J = 4.1 Hz, 1H), 3.16 (t, J = 7.0 Hz, 2H), 4.42 (m, 1H), 6.25 (dd, J = 15.9, 6.3 Hz, 1H), 6.61 (d, J = 15.8 Hz, 1H), 7.21−7.26 (m, 1H), 7.29−7.32 (m, 2H), 7.36−7.38 (m, 2H), 7.42−7.46 (m, 2H), 7.53−7.57 (m, 1H), 7.96−7.98 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.4, 34.5, 72.1, 126.6, 127.8, 128.2, 128.7, 130.5, 132.1, 133.2, 136.7, 136.9, 200.7; HRMS (ESI) m/z calcd for $C_{18}H_{19}O_2$ $[M + H]^+$ 267.1385, found 267.1392. Ketone **3h** was also obtained in 19% yield (21 mg, 0.0840 mmol).

Following the general procedure **C**, CuCl (2.13 mg, 0.0216 mmol, 0.050 equiv) and *rac*-BINAP (13.4 mg, 0.0216 mmol, 0.050 equiv) in THF (12 mL) were reacted with a solution containing oxaziridine diastereomers **1hb** (150 mg, 0.432 mmol, 1.0 equiv; *Z*:*E* = 60:40) in THF (3 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (1.0% acetone in CH_2Cl_2) afforded 79 mg (0.296 mmol, 69% yield) of **2h** as a yellow solid. Ketone **3h** was also obtained along with a mixture of unidentified impurities.

1,4-Diphenylbutan-1-one 3i. To a cooled 1.0 M LDA solution (15.6 mL, 15.6 mmol, 1.1 equiv) in THF at 0 °C under nitrogen atmosphere was added a solution of acetophenone *N*,*N*-dimethylhydrazone (2.30 g, 14.1 mmol, 1.0 equiv) in THF (15 mL) slowly over 15 min, and the mixture was allowed to stir at 0 °C for 5 h. The reaction mixture was then cooled to −78 °C, and a solution of (2-bromoethyl)benzene (2.49 mL, 18.4 mmol, 1.3 equiv) in THF (5 mL) was added slowly over 10 min. The reaction was warmed to room temperature and stirred for 16 h. The reaction mixture was concentrated under reduced pressure, and the residue was diluted with ether (15 mL) and then treated with an ice-cold solution of dilute sulfuric acid (15 mL) for 30 min to hydrolyze the hydrazone. The resulting solution was diluted with water and extracted with ether (2 × 15 mL), and the combined organic extracts were washed with water (2 × 15 mL) and brine (15 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification by chromatography on SiO_2 (0.25% EtOAc in hexanes) afforded the ketone **3i** in 71% yield (2.26 g, 10.0 mmol) as an off-white crystal (mp 54−56 °C): R_f = 0.60 (5% EtOAc/hexanes, run twice); IR (neat) 1682 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.07−2.14 (m, 2H), 2.74 (t, J = 7.5 Hz, 2H), 2.99 (t, J = 7.3 Hz, 2H), 7.19−7.24 (m, 3H), 7.29−7.33 (m, 2H), 7.43−7.48 (m, 2H), 7.53−7.58 (m, 1H), 7.93−7.96 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.8, 35.3, 37.8, 126.1, 128.1, 128.5, 128.6, 128.7, 133.1, 137.1, 141.8, 200.2; HRMS (ESI) m/z calcd for $C_{16}H_{16}O$ $[M]^+$ 224.1201, found 224.1195.

(2*R*,3*S*)-2-Cyclohexyl-3-phenyl-3-(3′-phenylpropyl)-1,2-oxaziridine (*Z*)-6 and (2*S*,3*S*)-2-Cyclohexyl-3-phenyl-3-(3′-phenylpropyl)-1,2-oxaziridine (*E*)-6. Following the general procedure **A**, 1,4-diphenylbutan-1-one **3i** (0.500 g, 2.23 mmol, 1.0 equiv), cyclohexylamine **4b** (0.382 mL, 3.34 mmol, 1.5 equiv), PTSA (21.2 mg, 0.111 mmol, 0.050 equiv) and activated 5 Å molecular sieves (3.50 g) in toluene (30 mL) were refluxed for 60 h, followed by oxidation with *m*-CPBA (0.462 g, 2.67 mmol, 1.2 equiv) in CH_2Cl_2 (20 mL). Purification by chromatography on SiO_2 (0.6% EtOAc in hexanes) afforded the mixture of oxaziridine diastereomers (*Z*)-**6** and (*E*)-**6** as a colorless oil (0.610 g, 1.90 mmol, 85% yield; (*Z*)-**6**:(*E*)-**6** = ca. 55:45). For mixture of (*Z*)-**6** and (*E*)-**6**: IR (neat) 2930, 1448 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.75−0.86 (m, 1H), 1.00−1.21 (m, 2H), 1.21−1.36 (m, 5H), 1.46−1.62 (m, 6H), 1.65−1.78 (m, 7H), 1.79−1.90 (m, 4H), 1.97−2.00 (m, 1H), 2.04−2.11 (m, 1H), 2.31 (m, 1H), 2.39 (m, 1H), 2.50−2.57 (m, 2H), 2.59−2.65 (m, 2H), 2.66−2.74 (m, 1H), 7.08−7.12 (m, 4H), 7.14−7.20 (m, 2H), 7.21−7.26 (m, 4H), 7.27−7.33 (m, 2H), 7.33−7.42 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.13, 24.19, 24.3, 24.6, 25.7, 25.93, 25.95, 27.1, 28.7, 29.2, 29.4, 31.8, 32.1, 35.93, 35.98, 38.2, 60.9, 61.2, 85.7, 87.7, 125.9, 126.1, 126.2, 127.8, 128.2, 128.3, 128.4, 128.52, 128.55, 128.58, 128.7, 135.4, 140.0, 141.7, 142.2; HRMS (ESI) m/z calcd for $C_{22}H_{28}NO$ $[M + H]^+$ 322.2171, found 322.2173. Major diastereomer (*Z*)-**6**: R_f = 0.43 (5% EtOAc/hexanes, run twice); ^1H NMR (400 MHz, $CDCl_3$; diagnostic peaks in the mixture) δ 2.39 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$; diagnostic peaks in the mixture) δ 38.2, 60.9, 87.7. Minor diastereomer (*E*)-**6**: R_f = 0.40 (5% EtOAc/hexanes, run twice); ^1H NMR (400 MHz, $CDCl_3$; diagnostic peaks in the mixture) δ 2.31 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$; diagnostic peaks in the mixture) δ 29.4, 61.2, 85.7.

4-Hydroxy-1,4-diphenylbutan-1-one 7.[28] Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (33.7 mg, 0.0233 mmol, 0.050 equiv) in THF (10 mL) was reacted with a solution containing oxaziridine diastereomers **6** (150 mg, 0.467 mmol, 1.0 equiv; *Z*:*E* = ca. 55:45) in THF (5 mL). The reaction mixture was refluxed for 3 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 99.3:0.5:0.2) afforded 57 mg (0.237 mmol, 51% yield) of the benzylic alcohol **7** as a white solid (mp 94−96 °C): R_f = 0.15 (15% EtOAc/hexanes); IR (neat) 3420, 1677 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.14−2.27 (m, 2H), 2.49 (d, J = 3.6 Hz, 1H), 3.10 (t, J = 6.9 Hz, 2H), 4.83 (m, 1H), 7.26−7.29 (m, 1H), 7.32−7.39 (m, 4H), 7.42−7.46 (m, 2H), 7.53−7.56 (m, 1H), 7.92−7.95 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.3, 34.9, 73.8, 125.9, 127.7, 128.3, 128.71, 128.76, 133.2, 137.1, 144.6, 200.6; HRMS (ESI) m/z calcd for $C_{16}H_{17}O_2$ $[M + H]^+$ 241.1229, found 241.1220. Ketone **3i** was also obtained in 21% yield (22 mg, 0.0982 mmol).

Following the general procedure **C**, CuCl (1.54 mg, 0.0155 mmol, 0.050 equiv) and *rac*-BINAP (9.69 mg, 0.0155 mmol, 0.050 equiv) in THF (9 mL) were reacted with a solution containing oxaziridine diastereomers **6** (100 mg, 0.311 mmol, 1.0 equiv; *Z*:*E* = ca. 55:45) in THF (3 mL). The reaction mixture was refluxed for 3 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 98.8:1.0:0.2) afforded 33 mg (0.137 mmol, 44% yield) of **7** as a creamish-yellow solid and 11 mg (0.0491 mmol, 16% yield) of **3i**.

(2*R*,3*S*)-2-Cyclohexyl-3-(hex-4′-yn-1′-yl)-3-phenyl-1,2-oxaziridine (*Z*)-8 and (2*S*,3*S*)-2-Cyclohexyl-3-(hex-4′-yn-1′-yl)-3-phenyl-1,2-oxaziridine (*E*)-8. Following the general procedure **A**, 1-phenylhept-5-yn-1-one **3j**[29] (0.500 g, 2.68 mmol, 1.0 equiv), cyclohexylamine **4b** (0.461 mL, 4.03 mmol, 1.5 equiv), PTSA (25.5 mg, 0.134 mmol, 0.050 equiv) and activated 5 Å molecular sieves (3.50 g) in toluene (30 mL) were refluxed for 60 h, followed by oxidation with *m*-CPBA (0.556 g, 3.22 mmol, 1.2 equiv) in CH_2Cl_2 (20 mL). Purification by chromatography on SiO_2 (0.6−0.8% EtOAc in hexanes) afforded the mixture of oxaziridine diastereomers (*Z*)-**8** and (*E*)-**8** as a colorless oil (0.640 g, 2.27 mmol, 85% yield; (*Z*)-**8**:(*E*)-**8** = ca. 54:46 by ^1H NMR). An analytical sample of the major diastereomer (*Z*)-**8** accompanied with 8% of the minor diastereomer (*E*)-**8** was obtained for characterization during this purification. Major diastereomer (*Z*)-**8**: R_f = 0.59 (5% EtOAc/hexanes, run thrice); IR (neat) 2931, 1447 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.72−0.83 (m, 1H), 0.96−1.17 (m, 2H), 1.18−1.27 (m, 1H), 1.29−1.40 (m, 2H), 1.42−1.49 (m, 2H), 1.50−1.58 (m, 2H), 1.66−1.75 (m, 2H), 1.71 (t, J = 2.5 Hz, 3H), 1.80−1.88 (m, 2H), 2.07 (m, 2H), 2.41 (m, 1H), 7.34−7.41 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.6, 18.9, 23.5, 24.0, 24.1, 25.8, 28.6, 31.7, 37.7, 60.9, 75.9, 78.7, 87.4, 127.8, 128.2, 128.7, 135.2; HRMS (ESI) m/z calcd for $C_{19}H_{26}NO$ $[M + H]^+$ 284.2014, found 284.2032. Minor diastereomer (*E*)-**8**: R_f = 0.47 (5% EtOAc/hexanes, run thrice); ^1H NMR (400 MHz, $CDCl_3$; diagnostic peaks only) δ 2.61 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$; diagnostic peaks only) δ 29.3, 61.2, 76.3, 78.3, 85.4.

4-Hydroxy-1-phenylhept-5-yn-1-one 9. Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (51.0 mg, 0.0353 mmol, 0.050 equiv) in THF (12 mL) was reacted with a solution containing oxaziridine diastereomers **8** (200 mg, 0.706 mmol, 1.0 equiv; *Z*:*E* = ca. 74:26) in THF (8 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 98.7:1.0:0.3) afforded 106 mg (0.524 mmol, 74% yield) of the propargylic alcohol **9** as white crystals (mp 78−80 °C): R_f = 0.26 (25% EtOAc/hexanes); IR (neat) 3405, 2232, 1678 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.82 (d, J = 2.1 Hz, 3H), 2.06−2.19 (m, 2H), 2.46 (d, J = 5.2 Hz, 1H), 3.14−3.28 (m, 2H), 4.48−4.54 (m, 1H), 7.43−7.47 (m, 2H), 7.53−7.58 (m, 1H), 7.97−8.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.7, 32.1, 34.4, 62.0, 80.0, 81.7, 128.3, 128.7, 133.3, 137.0, 200.3; HRMS (ESI) m/z calcd for $C_{13}H_{15}O_2$ $[M + H]^+$ 203.1072, found 203.1051. Ketone **3j** was also obtained in 25% yield (33 mg, 0.177 mmol).

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Following the general procedure **C**, CuCl (2.36 mg, 0.0238 mmol, 0.050 equiv) and *rac*-BINAP (14.8 mg, 0.0238 mmol, 0.050 equiv) in THF (9 mL) were reacted with a solution containing oxaziridine diastereomers **8** (0.135 g, 0.477 mmol, 1.0 equiv; *Z*:*E* = ca. 74:26) in THF (3 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 98.7:1.0:0.3) afforded 72 mg (0.356 mmol, 75% yield) of **9** as a pale yellow crystals and 7.0 mg (0.0376 mmol, 8% yield) of **3j**.

4-Methyl-1-phenylpentan-1-one 3k.[30] To a cooled 1.0 M LDA solution (6.45 mL, 6.45 mmol, 1.1 equiv) in THF at 0 °C under nitrogen atmosphere was added a solution of acetophenone *N*,*N*-dimethylhydrazone (0.950 g, 5.86 mmol, 1.0 equiv) in THF (10 mL) slowly over 15 min, and the mixture was allowed to stir at 0 °C for 5 h. The reaction mixture was then cooled to −78 °C, and a solution of 1-bromo-2-methylpropane (0.764 mL, 7.03 mmol, 1.2 equiv) in THF (5 mL) was added slowly over 10 min. The reaction was warmed to room temperature and stirred for 16 h. The reaction mixture was concentrated under reduced pressure, and the residue was diluted with ether (15 mL) and then treated with an ice-cold solution of dilute sulfuric acid (10 mL) for 30 min to hydrolyze the hydrazone. The resulting solution was diluted with water and extracted with ether (2 × 15 mL), and the combined organic extracts were washed with water (2 × 15 mL) and brine (15 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification by chromatography on SiO_2 (0.5% EtOAc in hexanes) afforded the ketone **3k** as a colorless oil in 71% yield (0.730 g, 4.14 mmol): R_f = 0.74 (5% EtOAc/hexanes, run twice).

(2*R*,3*S*)-2-Cyclohexyl-3-isopentyl-3-phenyl-1,2-oxaziridine (*Z*)-10 and (2*S*,3*S*)-2-Cyclohexyl-3-isopentyl-3-phenyl-1,2-oxaziridine (*E*)-10. Following the general procedure **A**, 4-methyl-1-phenylpentan-1-one **3k** (0.500 g, 2.84 mmol, 1.0 equiv), cyclohexylamine **4b** (0.487 mL, 4.26 mmol, 1.5 equiv), PTSA (27.0 mg, 0.142 mmol, 0.050 equiv) and activated 5 Å molecular sieves (3.50 g) in toluene (30 mL) were refluxed for 60 h, followed by oxidation with *m*-CPBA (0.588 g, 3.40 mmol, 1.2 equiv) in CH_2Cl_2 (20 mL) for 45 min. The reaction was warmed to room temperature before quenching with saturated $Na_2S_2O_3$. Purification by chromatography on SiO_2 (0.5% EtOAc in hexanes) afforded the partial separation of the major diastereomer (*Z*)-**10** containing 22% of starting ketone **3k**, followed by the mixture of major and the minor (*E*)-**10** diastereomers containing 10% of **3k** as a colorless oil (0.41 g, 53% corrected yield by ^{1}H NMR; (*Z*)-**10**:(*E*)-**10** = ca. 87:13). Major diastereomer (*Z*)-**10** containing 22% of **3k** was used for the subsequent reaction. Major diastereomer ((*Z*)-**10**, containing 22% of **3k**): R_f = 0.75 (5% EtOAc/hexanes, run twice); IR (neat) 2930, 1448 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.71−0.79 (m, 1H), 0.79 (d, J = 6.6 Hz, 6H), 0.96−1.01 (m, 1H), 1.01−1.17 (m, 2H), 1.20−1.29 (m, 2H), 1.30−1.35 (m, 1H), 1.42−1.51 (m, 3H), 1.52−1.57 (m, 2H), 1.66−1.75 (m, 3H), 1.84−1.88 (m, 1H), 2.35 (m, 1H), 7.33−7.42 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.4, 22.6, 24.11, 24.16, 25.8, 28.1, 28.6, 31.7, 32.7, 36.6, 60.9, 88.0, 127.8, 128.1, 128.6, 135.3; HRMS (ESI) m/z calcd for $C_{18}H_{28}NO$ [M + H]$^+$ 274.2171, found 274.2163. Minor diastereomer (*E*)-**10**: R_f = 0.75 (5% EtOAc/hexanes, run twice); ^{1}H NMR (400 MHz, $CDCl_3$; diagnostic peaks only) δ 2.26 (m, 1H), 2.59 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$; diagnostic peaks only) δ 61.2, 86.0.

4-Hydroxy-4-methyl-1-phenylpentan-1-one 11a[31] **and 4,4-Dimethyl-3,4-dihydronaphthalen-1(2H)-one 11b.**[19] Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (23.7 mg, 0.0164 mmol, 0.050 equiv) in THF (7 mL) was reacted with oxaziridine (*Z*)-**10** (90.0 mg, 0.329 mmol, 1.0 equiv; containing ca. 22% of ketone **3k**) in THF (3 mL). The reaction mixture was refluxed for 2 h. Purification by chromatography on SiO_2 (CH_2Cl_2, 100% to CH_2Cl_2:acetone:MeOH, 98.7:1.0:0.3) afforded ∼19 mg (0.107 mmol, 33% corrected yield) of **3k**, 8 mg (0.0459 mmol, 14% yield) of compound **11b** as a pale yellow oil, R_f = 0.71 (25% EtOAc/hexanes), and 12 mg of tertiary alcohol **11a** containing unidentified impurities. Alcohol **11a** containing impurities was further purified by chromatography on SiO_2 (CH_2Cl_2:triethylamine, 99.9:0.1% to CH_2Cl_2:acetone:triethylamine, 97.4:2.5:0.1) to afford 10 mg (0.0520 mmol, 16% yield) of **11a** as a pale yellow oil, R_f = 0.18 (25% EtOAc/hexanes).

1-Phenylhept-6-en-1-one 3l.[22] To a cooled 1.0 M LDA solution (13.5 mL, 13.5 mmol, 1.1 equiv) in THF at 0 °C under nitrogen atmosphere was added the solution of acetophenone *N*,*N*-dimethylhydrazone (2.00 g, 12.3 mmol, 1.0 equiv) in THF (15 mL) slowly over 15 min, and the mixture was allowed to stir at 0 °C for 5 h. The reaction mixture was then cooled to −78 °C, and a solution of 5-bromo-1-pentene (1.75 mL, 14.8 mmol, 1.2 equiv) in THF (5 mL) was added slowly over 10 min. The reaction was warmed to room temperature and stirred for 18 h. The reaction mixture was concentrated under reduced pressure, and the residue was diluted with ether (20 mL) and then treated with an ice-cold solution of dilute sulfuric acid (15 mL) for 30 min to hydrolyze the hydrazone. The resulting solution was diluted with water and extracted with ether (2 × 20 mL), and the combined organic extracts were washed with water (2 × 20 mL) and brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Purification by chromatography on SiO_2 (0.7−0.8% EtOAc in hexanes) afforded the ketone **3l** as a colorless oil in 92% yield (2.13 g, 11.3 mmol): R_f = 0.52 (5% EtOAc/hexanes, run twice).

(2*R*,3*S*)-2-Cyclohexyl-3-(hex-5′-en-1′-yl)-3-phenyl-1,2-oxaziridine (*Z*)-12 and (2*S*,3*S*)-2-Cyclohexyl-3-(hex-5′-en-1′-yl)-3-phenyl-1,2-oxaziridine (*E*)-12. Following the general procedure **A**, 1-phenylhept-6-en-1-one **3l** (0.500 g, 2.65 mmol, 1.0 equiv), cyclohexylamine **4b** (0.456 mL, 3.98 mmol, 1.5 equiv), PTSA (25.2 mg, 0.132 mmol, 0.050 equiv) and activated 5 Å molecular sieves (3.50 g) in toluene (30 mL) were refluxed for 60 h, followed by oxidation with *m*-CPBA (0.550 g, 3.19 mmol, 1.2 equiv) in CH_2Cl_2 (20 mL). Purification by chromatography on SiO_2 (0.6−0.7% EtOAc in hexanes) afforded the mixture of oxaziridine diastereomers (*Z*)-**12** and (*E*)-**12** with the partial separation of major diastereomer (*Z*)-**12** as a colorless oil (0.720 g, 2.54 mmol, 96% yield; (*Z*)-**12**:(*E*)-**12** = ca. 57:43 by ^{1}H NMR). Major diastereomer (*Z*)-**12**: R_f = 0.52 (5% EtOAc/hexanes, run twice); IR (neat) 1640, 1448 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.72−0.83 (m, 1H), 0.97−1.16 (m, 2H), 1.16−1.28 (m, 2H), 1.29−1.40 (m, 4H), 1.42−1.51 (m, 2H), 1.52−1.58 (m, 1H), 1.67−1.76 (m, 3H), 1.84−1.88 (m, 1H), 1.93−1.98 (m, 2H), 2.33−2.40 (m, 1H), 4.85−4.95 (m, 2H), 5.71 (m, 1H), 7.34−7.42 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.5, 24.1, 24.2, 25.8, 28.6, 29.0, 31.8, 33.7, 38.5, 60.9, 87.8, 114.5, 127.8, 128.2, 128.7, 135.3, 138.9; HRMS (ESI) m/z calcd for $C_{19}H_{28}NO$ [M + H]$^+$ 286.2170, found 286.2163. Minor diastereomer (*E*)-**12**: R_f = 0.45 (5% EtOAc/hexanes, run twice); ^{1}H NMR (400 MHz, $CDCl_3$; diagnostic peaks only) δ 2.59 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$; diagnostic peaks only) δ 29.6, 61.3, 85.8.

5-Hydroxy-1-phenylhept-6-en-1-one 13a, 4-Hydroxy-1-phenylhept-6-en-1-one 13b,[32] **and *N*-Cyclohexylbenzamide 13c.**[33] Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (38.0 mg, 0.0263 mmol, 0.050 equiv) in THF (10 mL) was reacted with oxaziridine (*Z*)-**12** (150 mg, 0.526 mmol, 1.0 equiv) in THF (5 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (CH_2Cl_2, 100% to CH_2Cl_2:acetone:MeOH, 98.6:1.0:0.4) afforded 35 mg (0.186 mmol, 35% yield) of **3l**, 15 mg (0.0738 mmol, 14% yield) of amide **13c** as a white solid, R_f = 0.46 (25% EtOAc/hexanes), and 21 mg (0.102 mmol, 16% yield for **13a** and 3% yield for **13b**, by ^{1}H NMR) of the mixture of allylic alcohol **13a** and homoallylic alcohol **13b** as a pale yellow oil. Further purification of the mixture of **13a** and **13b** by preparative TLC on SiO_2 (7% EtOAc in hexanes, 2 runs) afforded the analytical sample of **13a** and **13b** as a colorless oil for characterization. Allylic alcohol **13a**: R_f = 0.26 (25% EtOAc/hexanes); IR (neat) 3403, 1679 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.60−1.65 (m, 2H), 1.74 (br s, 1H), 1.80−1.90 (m, 2H), 3.02 (t, J = 7.4 Hz, 2H), 4.15 (q, J = 6.3 Hz, 1H), 5.12 (td, J = 10.4, 1.3 Hz, 1H), 5.25 (td, J = 17.2, 1.4 Hz, 1H), 5.88 (m, 1H), 7.44−7.47 (m, 2H), 7.54−7.57 (m, 1H), 7.95−7.97 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.1, 36.6, 38.4, 73.0, 115.0, 128.2, 128.8, 133.2, 137.1, 141.1, 200.4; HRMS (ESI) m/z calcd for $C_{13}H_{17}O_2$ [M + H]$^+$ 205.1229, found 205.1237. Homoallylic alcohol **13b** (sample obtained contains some minor impurities): R_f = 0.36 (25% EtOAc/hexanes); IR (neat) 3439, 1683

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cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.80−1.87 (m, 1H), 1.95 (br s, 1H), 1.98−2.04 (m, 1H), 2.20−2.26 (m, 1H), 2.32−2.38 (m, 1H), 3.11−3.22 (m, 2H), 3.74 (m, 1H), 5.14−5.18 (m, 2H), 5.80−5.88 (m, 1H), 7.44−7.48 (m, 2H), 7.54−7.58 (m, 1H), 7.97−7.99 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.9, 35.1, 42.5, 70.3, 118.6, 128.3, 128.8, 133.3, 134.7, 137.0, 200.8; HRMS (ESI) m/z calcd for $C_{13}H_{17}O_2$ $[M + H]^+$ 205.1229, found 205.1227.

Dec-9-en-5-one 3m.[34] Following the general procedure **D**, a solution of 5-bromo-1-pentene (2.47 mL, 20.8 mmol, 1.2 equiv) in THF (10 mL) was added dropwise to a stirring suspension of magnesium turnings (0.508 g, 20.8 mmol, 1.2 equiv) and two small crystals of iodine in THF (10 mL). After refluxing gently for 20 min, the reaction mixture was cooled to 0 °C and treated with a solution of valeraldehyde (1.50 g, 17.4 mmol, 1.0 equiv) in THF (5 mL). The reaction mixture was then stirred at room temperature for 1 h. The aqueous work up afforded the crude alcohol (3.05 g) as a colorless oil, which was used as such for the next oxidation step without purification. To a stirring solution of crude alcohol in CH_2Cl_2 (50 mL), was added Celite (6.0 g) followed by pyridinium chlorochromate (5.63 g, 26.1 mmol, 1.5 equiv), and the reaction was maintained at room temperature for 2 h. The reaction mixture was filtered through Celite, rinsing with several portions of ether, and the filtrate was concentrated under reduced pressure. Purification by chromatography on SiO_2 (0.5−1% EtOAc in hexanes) afforded 2.44 g (15.8 mmol, 91% yield over 2 steps) of the corresponding ketone **3m** as a yellow oil: R_f = 0.57 (10% EtOAc/hexanes).

(*E*)-10-Phenyldec-9-en-5-one 3n. To a solution of Grubbs II catalyst (0.264 g, 0.311 mmol, 0.04 equiv) in CH_2Cl_2 (28 mL) at room temperature under argon atmosphere was added a solution containing the mixture of dec-9-en-5-one **3m** (1.20 g, 7.79 mmol, 1.0 equiv) and styrene (2.67 mL, 23.3 mmol, 3.0 equiv) in CH_2Cl_2 (7 mL), and the reaction mixture was stirred at 40 °C for 4.5 h. The reaction mixture was concentrated under reduced pressure. Initial purification of crude residue by chromatography on SiO_2 (0.4% EtOAc in hexanes) afforded the mixture of desired product **3n** and byproduct (*E*)-1-phenylnon-1-en-5-one as a colorless oil (0.728 g, 3.16 mmol, 41% corrected yield for **3n** by ^1H NMR). Subsequent purification of the mixture of **3n** and (*E*)-1-phenylnon-1-en-5-one dissolved in DMSO was carried out using the preparative HPLC. The product was purified in multiple batches. All the fractions containing the product were evaporated to dryness, and the residue was diluted with ether (100 mL), and the organic layer was washed with water (35 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Pale yellow oil obtained was passed through a short bed of SiO_2 using 100% CH_2Cl_2 to afford 480 mg of **3n** as a colorless oil: R_f = 0.30 (5% EtOAc/hexanes); IR (neat) 2931, 1710 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, J = 7.3 Hz, 3H), 1.26−1.35 (m, 2H), 1.52−1.59 (m, 2H), 1.77 (m, 2H), 2.22 (dq, J = 7.5, 1.2 Hz, 2H), 2.38 (t, J = 7.4 Hz, 2H), 2.44 (t, J = 7.3 Hz, 2H), 6.14−6.21 (m, 1H), 6.39 (d, J = 15.8 Hz, 1H), 7.18−7.22 (m, 1H), 7.27−7.31 (m, 2H), 7.33−7.36 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.4, 23.3, 26.0, 32.4, 41.9, 42.6, 126.0, 127.0, 128.5, 129.9, 130.6, 137.6, 211.0; HRMS (ESI) m/z calcd for $C_{16}H_{23}O$ $[M + H]^+$ 231.1749, found 231.1750.

(2*S*,3*R*,*E*)-3-Butyl-2-cyclohexyl-3-(5′-phenylpent-4′-en-1′-yl)-1,2-oxaziridine (*Z*)-14 and (2*R*,3*R*,*E*)-3-Butyl-2-cyclohexyl-3-(5′-phenylpent-4′-en-1′-yl)-1,2-oxaziridine (*E*)-14. Following the general procedure **A**, (*E*)-10-phenyldec-9-en-5-one **3n** (0.450 g, 1.95 mmol, 1.0 equiv), cyclohexylamine **4b** (0.335 mL, 2.93 mmol, 1.5 equiv), PTSA (18.6 mg, 0.0978 mmol, 0.050 equiv) and activated 5 Å molecular sieves (3.50 g) in toluene (35 mL) were refluxed for 60 h, followed by oxidation with *m*-CPBA (0.405 g, 2.34 mmol, 1.2 equiv) in CH_2Cl_2 (20 mL). Purification by chromatography on SiO_2 (0.4−0.6% EtOAc in hexanes) afforded the mixture of oxaziridine diastereomers (*Z*)-**14** and (*E*)-**14** as a pale yellow oil (0.449 g, 1.37 mmol, 70% yield; (*Z*)-**14**:(*E*)-**14** = ca. 56:44 by ^1H NMR). For mixture of (*Z*)-**14** and (*E*)-**14**: R_f = 0.51 (5% EtOAc/hexanes, run thrice); IR (neat) 2929, 2856, 1449 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.89−0.96 (m, 7H), 1.21−1.28 (m, 6H), 1.31−1.37 (m, 6H), 1.39−1.45 (m, 3H), 1.46−1.57 (m, 8H), 1.63−1.66 (m, 3H), 1.68−1.74 (m, 3H), 1.74−1.82 (m, 4H), 1.83−1.87 (m, 2H), 1.89−1.95 (m, 4H), 2.20−2.32 (m, 4H), 2.33−2.41 (m, 2H), 6.19 (m, 1H), 6.23 (m, 1H), 6.39 (d, J = 16.2 Hz, 1H), 6.43 (d, J = 16.0 Hz, 1H), 7.17−7.23 (m, 2H), 7.27−7.31 (m, 4H), 7.32−7.36 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.13, 14.19, 23.0, 23.2, 24.35, 24.37, 24.4, 24.5, 24.6, 25.2, 25.9, 26.8, 27.5, 27.6, 27.9, 29.2, 29.3, 32.14, 32.16, 33.2, 36.3, 36.6, 60.44, 60.48, 85.90, 85.97, 126.1, 127.0, 127.1, 128.62, 128.67, 129.9, 130.42, 130.45, 130.8, 137.7, 137.8; HRMS (ESI) m/z calcd for $C_{22}H_{34}NO$ $[M + H]^+$ 328.2640, found 328.2635.

(*E*)-8-Hydroxy-10-phenyldec-9-en-5-one 15. Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (26.5 mg, 0.0183 mmol, 0.050 equiv) in THF (9 mL) was reacted with a solution containing oxaziridine diastereomers **14** (120 mg, 0.366 mmol, 1.0 equiv; *Z*:*E* = 58:42) in THF (3 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 twice (1.0% acetone in CH_2Cl_2) afforded the allylic alcohol **15** as a pale yellow oil containing 10% of two unidentified byproducts (58.0 mg, 0.235 mmol, 64% corrected yield by ^1H NMR): R_f = 0.30 (25% EtOAc/hexanes); IR (neat) 3405, 1705 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.3 Hz, 3H), 1.24−1.33 (m, 2H), 1.50−1.57 (m, 2H), 1.83−1.97 (m, 2H), 2.38−2.43 (m, 3H), 2.57 (t, J = 6.9 Hz, 2H), 4.31 (m, 1H), 6.18 (dd, J = 15.9, 6.3 Hz, 1H), 6.57 (d, J = 15.9 Hz, 1H), 7.21−7.25 (m, 1H), 7.28−7.32 (m, 2H), 7.35−7.37 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.4, 26.1, 30.9, 38.6, 42.8, 72.1, 126.6, 127.8, 128.7, 130.4, 132.0, 136.7, 212.0; HRMS (ESI) m/z calcd for $C_{16}H_{23}O_2$ $[M + H]^+$ 247.1698, found 247.1699. Ketone **3n** was observed in a trace amount by NMR in a mixture of unidentified impurities.

Following the general procedure **C**, CuCl (1.81 mg, 0.0183 mmol, 0.050 equiv) and *rac*-BINAP (11.3 mg, 0.0183 mmol, 0.050 equiv) in THF (9 mL) were reacted with a solution containing oxaziridine diastereomers **14** (120 mg, 0.366 mmol, 1.0 equiv; *Z*:*E* = 58:42) in THF (3 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (1.0% acetone in CH_2Cl_2) afforded **15** as a yellow oil containing 11% of two unidentified byproducts (62.0 mg, 0.252 mmol, 69% corrected yield by ^1H NMR). Ketone **3n** was observed in a trace amount by NMR in a mixture of unidentified impurities.

1-Cyclohexylhex-5-en-1-one 3o.[35] Following the general procedure **D**, a solution of 5-bromo-1-pentene (1.90 mL, 16.0 mmol, 1.2 equiv) in THF (10 mL) was added dropwise to a stirring suspension of magnesium turnings (0.390 g, 16.0 mmol, 1.2 equiv) and two small crystals of iodine in THF (10 mL). After refluxing gently for 20 min, the reaction mixture was cooled to 0 °C and treated with a solution of cyclohexane carboxaldehyde (1.50 g, 13.3 mmol, 1.0 equiv) in THF (5 mL). The reaction mixture was then stirred at room temperature for 1 h. The aqueous work up afforded the crude alcohol (2.31 g) as a colorless oil, which was used for the next oxidation step without purification. To a stirring solution of crude alcohol in CH_2Cl_2 (70 mL) was added Celite (6.0 g) followed by pyridinium chlorochromate (5.76 g, 26.7 mmol, 2.0 equiv), and the reaction was maintained at room temperature for 75 min. The reaction mixture was filtered through Celite, rinsing with several portions of CH_2Cl_2, and the filtrate was concentrated under reduced pressure. Purification by chromatography on SiO_2 (1% EtOAc in hexanes) afforded 1.68 g (9.33 mmol, 70% yield over 2 steps) of the corresponding ketone **3o** as a colorless oil: R_f = 0.62 (10% EtOAc/hexanes).

(2*R*,3*S*)-2,3-Dicyclohexyl-3-(pent-4′-en-1′-yl)-1,2-oxaziridine (*Z*)-16 and (2*S*,3*S*)-2,3-Dicyclohexyl-3-(pent-4′-en-1′-yl)-1,2-oxaziridine (*E*)-16. Following the general procedure **A**, 1-cyclohexylhex-5-en-1-one **3o** (0.500 g, 2.77 mmol, 1.0 equiv), cyclohexylamine **4b** (0.476 mL, 4.16 mmol, 1.5 equiv), PTSA (26.3 mg, 0.138 mmol, 0.050 equiv) and activated 5 Å molecular sieves (3.50 g) in toluene (30 mL) were refluxed for 60 h, followed by oxidation with *m*-CPBA (0.573 g, 3.32 mmol, 1.2 equiv) in CH_2Cl_2 (20 mL) for 45 min. Purification by chromatography on SiO_2 (0.5% EtOAc in hexanes) afforded the mixture of oxaziridine diastereomers (*Z*)-**16** and (*E*)-**16** and ketone **3o** as a colorless oil. The ketone **3o** was removed from the mixture by vacuum distillation at 65−67 °C, and the mixture of two diastereomers (*Z*)-**16** and (*E*)-**16** along with some decomposition products were left in the flask as an orange-colored residue. This residue was further purified by chromatography on SiO_2 (2% ether in hexanes) to afford

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the mixture of (*Z*)-**16** and (*E*)-**16** as a colorless oil (0.340 g, 1.22 mmol, 44% yield; ratio of two oxaziridine diastereomers = ca. 79:21 by ^{1}H NMR, unassigned). For major diastereomer in the mixture: R_f = 0.68 (5% EtOAc/hexanes, run twice); IR (neat) 2927, 2853, 1450, cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.00−1.32 (m, 8H), 1.39−1.50 (m, 3H), 1.51−1.64 (m, 6H), 1.69−1.82 (m, 7H), 1.85−1.90 (m, 1H), 2.05−2.10 (m, 2H), 2.17−2.24 (m, 1H), 4.95−5.05 (m, 2H), 5.73−5.83 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.3, 24.5, 25.2, 25.94, 25.99, 26.3, 26.4, 26.8, 28.1, 29.2, 32.0, 34.1, 44.7, 60.3, 87.4, 115.2, 138.2; HRMS (ESI) *m*/*z* calcd for $C_{18}H_{32}NO$ $[M + H]^+$ 278.2484, found 278.2475.

***N*-Cyclohexylhex-5-enamide 17.** Following the general procedure **B**, $[Cu(PPh_3)Cl]_4$ (13.0 mg, 0.00902 mmol, 0.050 equiv) in THF (5 mL) was reacted with a solution containing oxaziridine diastereomers (*Z*)-**16** and (*E*)-**16** (50.0 mg, 0.180 mmol, 1.0 equiv; two diastereomers = ca. 79:21, unassigned) in THF (2 mL). The reaction mixture was refluxed for 1 h. Purification by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 98.7:1.0:0.3) afforded 26 mg (0.133 mmol, 74% yield) of the amide **17** as a white solid (mp 57−59 °C) instead of the allylic alcohol (see Scheme 8): R_f = 0.27 (25% EtOAc/hexanes, $KMnO_4$); IR (neat) 3284, 1638, 1546 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04−1.19 (m, 3H), 1.30−1.41 (m, 2H), 1.58−1.64 (m, 1H), 1.66−1.76 (m, 4H), 1.88−1.92 (m, 2H), 2.05−2.14 (m, 4H), 3.76 (m, 1H), 4.95−5.04 (m, 2H), 5.28 (br s, 1H), 5.77 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.06, 25.08, 25.7, 33.3, 33.4, 36.3, 48.2, 115.4, 138.2, 171.9; HRMS (ESI) *m*/*z* calcd for $C_{12}H_{22}NO$ $[M + H]^+$ 196.1701, found 196.1702. Ketone **3o** was not recovered.

Radical-Trapping Experiment with TEMPO (Scheme 5): 4-Hydroxy-1-phenylhex-5-en-1-one (2a), 1-Phenyl-4-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)hex-5-en-1-one (5a), (*E*)-1-Phenyl-6-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)hex-4-en-1-one (*trans*, 5b), and (*Z*)-1-Phenyl-6-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)hex-4-en-1-one (*cis*, 5c). A flame-dried two-necked round-bottom flask equipped with a reflux condenser was charged with CuCl (1.82 mg, 0.0184 mmol, 0.050 equiv) and THF (8 mL) under an argon atmosphere. The solution was degassed with argon and allowed to reflux for 30 min. A solution of TEMPO in THF (1 mL), followed by a solution of oxaziridine diastereomers **1ab** (100 mg, 0.369 mmol, 1.0 equiv; *Z*:*E* = 1:1) in THF (3 mL) was added slowly by syringe to the resulting solution, and refluxing was continued for 1 h. The solvent was removed under reduced pressure, and the crude mixture was purified by chromatography on SiO_2 (CH_2Cl_2:acetone:MeOH, 98.9:1.0:0.1 to 98.7:1.0:0.3) to afford 9.0 mg (0.0517 mmol, 14% yield) of **3a**, 45 mg of the mixture containing three radical-trapped products (**5a**, **5b**, and **5c**), and 16 mg (0.0842 mmol, 23% yield) of the allylic alcohol **2a** as an orange oil. Further purification of the mixture of **5a**, **5b**, and **5c** by chromatography on SiO_2 (0.6−1.2% EtOAc in hexanes) afforded the internal radical-trapped product **5a** as a colorless oil (23.6 mg, 0.0717 mmol, 19% yield) and the mixture of terminal radical-trapped products (*trans*, **5b** and *cis*, **5c**) as a colorless oil (21.4 mg, 0.0650 mmol, 18% yield, **5b**:**5c** = ca. 62:38). Internal radical-trapped product **5a**: R_f = 0.36 (5% EtOAc/hexanes); IR (neat) 1686, 1360 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07−1.18 (m, 12H), 1.27−1.30 (m, 1H), 1.43−150 (m, 5H), 1.91−2.00 (m, 1H), 2.09−2.18 (m, 1H), 3.01 (t, *J* = 7.6 Hz, 2H), 4.24 (m, 1H), 5.08−5.13 (m, 2H), 5.85 (m, 1H), 7.43−7.47 (m, 2H), 7.53−7.57 (m, 1H), 7.94−7.97 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.4, 20.60, 20.67, 28.8, 34.4, 34.6, 35.2, 40.4, 59.4, 60.3, 84.8, 116.4, 128.2, 128.7, 133.0, 137.2, 140.6, 200.3; HRMS (ESI) *m*/*z* calcd for $C_{21}H_{32}NO_2$ $[M + H]^+$ 330.2433, found 330.2443. Terminal radical-trapped products (*trans*, **5b** and *cis*, **5c**): R_f = 0.30 (5% EtOAc/hexanes); IR (neat) 1686, 1358, 1202 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08−1.17 (m, 24H), 1.29−1.32 (m, 2H, *trans*), 1.42−1.45 (m, 8H), 1.50−1.59 (m, 2H, *cis*), 2.46−2.53 (m, 4H), 3.02−3.10 (m, 4H), 4.22 (dd, *J* = 6.0, 1.1 Hz, 2H, *trans*), 4.36 (d, *J* = 5.2 Hz, 2H, *cis*), 5.55−5.66 (m, 3H), 5.72−5.80 (m, 1H), 7.43−7.47 (m, 4H), 7.53−7.57 (m, 2H), 7.93−7.97 (m, 4H); ^{13}C NMR for *trans* (100 MHz, $CDCl_3$) δ 17.3, 20.4, 27.1, 33.22, 38.2, 39.8, 59.8, 78.2, 126.9, 128.2, 128.7, 132.0, 133.2, 137.1, 199.7; ^{13}C NMR for *cis* (100 MHz, $CDCl_3$) δ 17.3, 20.3, 22.8, 33.29, 38.7, 39.85, 59.84, 73.4, 126.7, 128.2, 128.7, 131.1, 133.2, 137.0, 199.5; HRMS (ESI) for *trans* *m*/*z* calcd for $C_{21}H_{32}NO_2$ $[M + H]^+$ 330.2433, found 330.2439; HRMS (ESI) for *cis* *m*/*z* calcd for $C_{21}H_{32}NO_2$ $[M + H]^+$ 330.2433, found 330.2445. For assignment of *trans* and *cis* configuration using NOE, see the Supporting Information.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

NMR data used to assign oxaziridine stereoisomers and relevant references. Copies of ^{1}H and ^{13}C NMR spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org/.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For selected reviews, see: (a) Godula, K.; Sames, D. *Science* **2006**, *312*, 67−72. (b) Newhouse, T.; Baran, P. S. *Angew. Chem., Int. Ed.* **2011**, *50*, 3362−3374. (c) Costas, M. *Coord. Chem. Rev.* **2011**, *255*, 2912−2932. (d) Lu, H.; Zhang, X. P. *Chem. Soc. Rev.* **2011**, *40*, 1899−1909. (e) Zhou, M.; Crabtree, R. H. *Chem. Soc. Rev.* **2011**, *40*, 1875−1884. (f) White, M. C. *Science* **2012**, *335*, 807−809.

(2) (a) Mello, R.; Fiorentino, M.; Fusco, C.; Curci, R. *J. Am. Chem. Soc.* **1989**, *111*, 6749−6757. (b) Bovicelli, P.; Lupattelli, P.; Mincione, E.; Prencipe, T.; Curci, R. *J. Org. Chem.* **1992**, *57*, 5052−5054. (c) Barton, D. H. R.; Doller, D. *Acc. Chem. Res.* **1992**, *25*, 504−512. (d) Reiser, O. *Angew. Chem., Int. Ed.* **1994**, *33*, 69−72. (e) Yang, J.; Gabriele, B.; Belvedere, S.; Huang, Y.; Breslow, R. *J. Org. Chem.* **2002**, *67*, 5057−5067. (f) Lee, S.; Fuchs, P. L. *J. Am. Chem. Soc.* **2002**, *124*, 13978−13979. (g) Velusamy, S.; Punniyamurthy, T. *Tetrahedron Lett.* **2003**, *44*, 8955−8957. (h) Lee, S.; Fuchs, P. L. *Org. Lett.* **2004**, *6*, 1437−1440. (i) Chen, M. S.; White, M. C. *Science* **2007**, *318*, 783−787. (j) Chen, K.; Richter, J. M.; Baran, P. S. *J. Am. Chem. Soc.* **2008**, *130*, 7247−7249. (k) Chen, K.; Eschenmoser, A.; Baran, P. S. *Angew. Chem., Int. Ed.* **2009**, *48*, 9705−9708. (l) Gómez, L.; Garcia-Bosch, I.; Company, A.; Benet-Buchholz, J.; Polo, A.; Sala, X.; Ribas, X.; Costas, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 5720−5723. (m) McNeill, E.; Du Bois, J. *J. Am. Chem. Soc.* **2010**, *132*, 10202−10204. (n) Vermeulen, N. A.; Delcamp, J. H.; White, M. C. *J. Am. Chem. Soc.* **2010**, *132*, 11323−11328. (o) Chen, M. S.; White, M. C. *Science* **2010**, *327*, 566−571. (p) Bigi, M. A.; Reed, S. A.; White, M. C. *Nat. Chem.* **2011**, *3*, 216−222. (q) Wu, J.-C.; Song, R.-J.; Wang, Z.-Q.; Huang, X.-C.; Xie, Y.-X.; Li, J.-H. *Angew. Chem., Int. Ed.* **2012**, *51*, 3453−3457. For selected examples of total syntheses utilizing C−H oxidation strategy, see: (r) Chen, K.; Baran, P. S. *Nature* **2009**, *459*, 824−828. (s) Stang, E. M.; Christina White, M. *Nat. Chem.* **2009**, *1*, 547−551. (t) Stang, E. M.; White, M. C. *Angew. Chem., Int. Ed.* **2011**, *50*, 2094−2097.

(3) (a) Yang, D.; Wong, M.-K.; Wang, X.-C.; Tang, Y.-C. *J. Am. Chem. Soc.* **1998**, *120*, 6611−6612. (b) Wong, M.-K.; Chung, N.-W.; He, L.; Yang, D. *J. Am. Chem. Soc.* **2002**, *125*, 158−162. (c) Wong, M.-K.; Chung, N.-W.; He, L.; Wang, X.-C.; Yan, Z.; Tang, Y.-C.; Yang, D. *J. Org. Chem.* **2003**, *68*, 6321−6328. (d) Chen, M. S.; Prabagaran, N.; Labenz, N. A.; White, M. C. *J. Am. Chem. Soc.* **2005**, *127*, 6970−6971. (e) Shing, T. K. M.; Yeung; Su, P. L. *Org. Lett.* **2006**, *8*, 3149−3151. (f) Delcamp, J. H.; White, M. C. *J. Am. Chem. Soc.* **2006**, *128*, 15076−15077. (g) Covell, D. J.; White, M. C. *Angew. Chem., Int. Ed.* **2008**, *47*, 6448−6451. (h) Gartner, M.; Mader, S.; Seehafer, K.; Helmchen, G. n.

J. Am. Chem. Soc. **2011**, *133*, 2072−2075. (i) Gormisky, P. E.; White, M. C. *J. Am. Chem. Soc.* **2011**, *133*, 12584−12589. (j) Huang, D.; Wang, H.; Xue, F.; Shi, Y. *J. Org. Chem.* **2011**, *76*, 7269−7274.
(4) (a) Eames, J.; Watkinson, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 3567−3571. (b) Andrus, M. B.; Lashley, J. C. *Tetrahedron* **2002**, *58*, 845−866. (c) Hoang, V. D. M.; Reddy, P. A. N.; Kim, T.-J. *Organometallics* **2008**, *27*, 1026−1027.
(5) (a) Davis, F. A.; Sheppard, A. C. *Tetrahedron* **1989**, *45*, 5703−5742. (b) Aubé, J. *Chem. Soc. Rev.* **1997**, *26*, 269−277.
(6) (a) Petrov, V. A.; Resnati, G. *Chem. Rev.* **1996**, *96*, 1809−1824. (b) Arnone, A.; Foletto, S.; Metrangolo, P.; Pregnolato, M.; Resnati, G. *Org. Lett.* **1999**, *1*, 281−284. (c) Brodsky, B. H.; Du Bois, J. *J. Am. Chem. Soc.* **2005**, *127*, 15391−15393. (d) Litvinas, N. D.; Brodsky, B. H.; Du Bois, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 4513−4516.
(7) (a) Michaelis, D. J.; Shaffer, C. J.; Yoon, T. P. *J. Am. Chem. Soc.* **2007**, *129*, 1866−1867. (b) Partridge, K. M.; Anzovino, M. E.; Yoon, T. P. *J. Am. Chem. Soc.* **2008**, *130*, 2920−2921. (c) Michaelis, D. J.; Ischay, M. A.; Yoon, T. P. *J. Am. Chem. Soc.* **2008**, *130*, 6610−6615. (d) Benkovics, T.; Du, J.; Guzei, I. A.; Yoon, T. P. *J. Org. Chem.* **2009**, *74*, 5545−5552. (e) Allen, C. P.; Benkovics, T.; Turek, A. K.; Yoon, T. P. *J. Am. Chem. Soc.* **2009**, *131*, 12560−12561. (f) Williamson, K. S.; Yoon, T. P. *J. Am. Chem. Soc.* **2010**, *132*, 4570−4571. (g) Benkovics, T.; Guzei, I. A.; Yoon, T. P. *Angew. Chem., Int. Ed.* **2010**, *49*, 9153−9157.
(8) (a) Aubé, J.; Peng, X.; Wang, Y.; Takusagawa, F. *J. Am. Chem. Soc.* **1992**, *114*, 5466−5467. (b) Aubé, J.; Gülgeze, B.; Peng, X. *Bioorg. Med. Chem. Lett.* **1994**, *4*, 2461−2464. (c) Usuki, Y.; Peng, X.; Gülgeze, B.; Aubé, J. *ARKIVOC* **2006**, 189−199.
(9) Lead references for metal-promoted ring opening reactions of oxaziridines: (a) Emmons, W. D. *J. Am. Chem. Soc.* **1957**, *79*, 5739−5754. (b) Black, D. S. C.; Watson, K. G. *Aust. J. Chem.* **1973**, *26*, 2515−2520. (c) Bravo, A.; Fontana, F.; Fronza, G.; Mele, A.; Minisci, F. *J. Chem. Soc., Chem. Commun.* **1995**, 1573−1574. (d) Minisci, F.; Zhao, L.; Fontana, F.; Bravo, A. *Tetrahedron Lett.* **1995**, *36*, 1697−1700. (e) Minisci, F.; Zhao, L.; Fontana, F.; Bravo, A. *Tetrahedron Lett.* **1995**, *36*, 1895−1898. (f) Black, D. S.; Edwards, G. L.; Laaman, S. M. *Tetrahedron Lett.* **1998**, *39*, 5853−5856. For related ring openings of diaziridinones, see: (g) Yuan, W.; Du, H.; Zhao, B.; Shi, Y. *Org. Lett.* **2007**, *9*, 2589−2591. (h) Du, H.; Zhao, B.; Yuan, W.; Shi, Y. *Org. Lett.* **2008**, *10*, 4231−4234. (i) Zhao, B.; Peng, X.; Cui, S.; Shi, Y. *J. Am. Chem. Soc.* **2010**, *132*, 11009−11011. (j) Caornwall, R. G.; Zhao, B.; Shi, Y. *Org. Lett.* **2011**, *13*, 434−437. For a recent review, see: (k) Jahn, U. *Topics in Current Chemistry*; Springer-Verlag: Berlin, 2012; Vol. *320*, pp 323−451.
(10) For a review of 1,5-hydrogen atom transfer reactions, see: Čeković, Ž. *J. Serb. Chem. Soc.* **2005**, *70*, 287−318.
(11) (a) Butler, A. R.; Challis, B. C. *J. Chem. Soc. B* **1971**, 778−782. (b) Dinizo, S. E.; Watt, D. S. *J. Am. Chem. Soc.* **1975**, *97*, 6900−6901. (c) Butler, A. R.; Challis, B. C.; Lobo, A. M. *J. Chem. Soc., Perkin Trans. 2* **1979**, 1035−1038.
(12) (a) Ningsanont, N.; Black, D. S. C.; Chanphen, R.; Thebtaranonth, Y. *J. Med. Chem.* **2003**, *46*, 2397−2403. (b) Clerici, A.; Cannella, R.; Pastori, N.; Panzeri, W.; Porta, O. *Tetrahedron* **2006**, *62*, 5986−5994.
(13) (a) Aubé, J.; Hammond, M.; Gherardini, E.; Takusagawa, F. *J. Org. Chem.* **1991**, *56*, 499−508. (b) Wang, Y.; Chackalamannil, S.; Aubé, J. *J. Org. Chem.* **2000**, *65*, 5120−5126.
(14) Aubé, J.; Ghosh, S.; Tanol, M. *J. Am. Chem. Soc.* **1994**, *116*, 9009−9018.
(15) Aubé, J.; Wang, Y.; Hammond, M.; Tanol, M.; Takusagawa, F.; Vander Velde, D. *J. Am. Chem. Soc.* **1990**, *112*, 4879−4891.
(16) No enantioselectivity was observed when reactions of oxaziridine diastereomer **1ab** with (*S*)-BINAP and oxaziridine diastereomer **1aa** (Table 1, entry 1) with (*S*)-BINAP were carried out (4−5% ee, chiral GC; data not provided).
(17) Beckwith, A. L. J.; Zavitsas, A. A. *J. Am. Chem. Soc.* **1986**, *108*, 8230−8234.
(18) We used the following papers as guides for our TEMPO trapping experiments: (a) Barton, D. H. R.; Le Gloahec, V. N.; Smith, J. *Tetrahedron Lett.* **1998**, *39*, 7483−7486. (b) Heinrich, M. R.; Wetzel, A.; Kirschstein, M. *Org. Lett.* **2007**, *9*, 3833−3835. For examples of TEMPO trapping of an unrelated carbon-centered radical generated by Cu(II) catalysis, see: (c) Fuller, P. H.; Kim, J.-W.; Chemler, S. R. *J. Am. Chem. Soc.* **2008**, *130*, 17638−17639. (d) Sequeira, F. C.; Bovino, M. T.; Chipre, A. J.; Chemler, S. R. *Synthesis* **2012**, *44*, 1481−1484.
(19) Yoneda, N.; Takahashi, Y.; Suzuki, A. *Chem. Lett.* **1978**, *7*, 231−232.
(20) K. Aggarwal, V.; Gultekin, Z.; S. Grainger, R.; Adams, H.; L. Spargo, P. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2771−2782.
(21) Churchill, M. R.; Bezman, S. A.; Osborn, J. A.; Wormald, J. *Inorg. Chem.* **1972**, *11*, 1818−1825.
(22) Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1995**, *60*, 872−882.
(23) Shintani, R.; Hayashi, S.-y.; Murakami, M.; Takeda, M.; Hayashi, T. *Org. Lett.* **2009**, *11*, 3754−3756.
(24) Zhu, J.-L.; Su, Y.-L.; Chan, Y.-H.; Chen, I.-C.; Liao, C.-C. *Heterocycles* **2009**, *78*, 369−387.
(25) Singh, V.; Singh, V. *Synth. Commun.* **2010**, *40*, 1280−1291.
(26) Chatterjee, A. K.; Toste, F. D.; Choi, T.-L.; Grubbs, R. H. *Adv. Synth. Catal.* **2002**, *344*, 634−637.
(27) Schmidt, B. *Eur. J. Org. Chem.* **2004**, *2004*, 1865−1880.
(28) (a) Desai, D.; Chang, L.; Amin, S. *Cancer Lett.* **1996**, *108*, 263−270. (b) Bach, J.; Berenguer, R.; Garcia, J.; López, M.; Manzanal, J.; Vilarrasa, J. *Tetrahedron* **1998**, *54*, 14947−14962. (c) Fujioka, H.; Komatsu, H.; Miyoshi, A.; Murai, K.; Kita, Y. *Tetrahedron Lett.* **2011**, *52*, 973−975.
(29) Kamijo, S.; Dudley, G. B. *J. Am. Chem. Soc.* **2006**, *128*, 6499−6507.
(30) Cho, C. S. *J. Mol. Catal. A: Chem.* **2005**, *240*, 55−60.
(31) Adam, W.; Grabowski, S.; Wilson, R. M. *Chem. Ber.* **1989**, *122*, 561−564.
(32) Yu, C.-M.; Kim, J.-M.; Shin, M.-S.; Cho, D. *Tetrahedron Lett.* **2003**, *44*, 5487−5490.
(33) Jo, Y.; Ju, J.; Choe, J.; Song, K. H.; Lee, S. *J. Org. Chem.* **2009**, *74*, 6358−6361.
(34) Fujita, T.; Watanabe, S.; Suga, K.; Inaba, T.; Takagawa, T. *J. Appl. Chem. Biotechnol.* **1978**, *28*, 882−888.
(35) Yanagisawa, A.; Habaue, S.; Yasue, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 6130−6141.