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Stereoselective Synthesis of 1,3-Amino Alcohols by the Pd-Catalyzed Cyclization of Trichloroacetimidates

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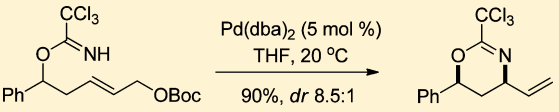
Supporting Information

ABSTRACT: The synthesis of 4-vinyl-5,6-dihydro-1,3-oxazines, precursors of 1,3-amino alcohols, using the palladium-catalyzed cyclization of trichloroacetimidates is reported. The reaction favors the formation of the 4,6-*cis*-isomers with up to >20:1 diastereoselectivity. Chemoselective hydrolysis of the resulting 5,6-dihydro-1,3-oxazines was also investigated.



INTRODUCTION

1,3-Amino alcohols are an important class of organic compounds that not only are widely represented in natural products and pharmaceuticals but also are useful synthons for organic syntheses.[1,2] The asymmetric construction of β-amino ketones or aldehydes,[3] β-hydroxy imines,[4] or 2,3-dihydroisoxazoles[5] followed by stereoselective reduction is an important pathway for the synthesis of 1,3-amino alcohols (Scheme 1a). Transition-metal-catalyzed aliphatic C−H amination with nitrenes[6] and allylic C−H amination reactions are straightforward and atom-economical methods to access this structural motif (Scheme 1b).[7] Treatment of 2-pentene-1,5-diol with tosyl isocyanate followed by palladium-catalyzed cyclization affords protected *trans*-1,3-amino alcohol derivatives selectively (Scheme 1c).[8] Following the ongoing studies of relay sequences combining hemiacetalization and intramolecular allylic amination/oxygenation using rhenium[9] or palladium catalysis,[10] Menche and co-workers developed a new method for the preparation of 1,3-amino alcohol derivatives from tosylated aldimines in the presence of a palladium catalyst. The reaction affords four diastereomeric 1,3-oxazines, generally favoring the 4,6-*cis* isomers with low to moderate selectivity (Scheme 1c).[11]

Creating new chiral centers through substrate control remains an important strategy in asymmetric synthesis. We are interested in the development of methods for the synthesis of 1,3-amino alcohol derivatives from stereodefined homoallylic alcohols using the Tsuji−Trost reaction.[12] These methods should satisfy the following requirements: (a) the reactions should use inexpensive, stable, and readily available materials; (b) the products should be readily cleaved to afford free 1,3-amino alcohols; and (c) both the hydroxyl and amino functional groups should be easily and selectively modifiable without excessive manipulations of protecting groups. We reasoned that trichloroacetimidates,[13] which have been extensively studied by the Overman group for the preparation of allylic amines,[14] might be a good candidate for our purposes. We also anticipated that the steric bulk of the trichloroacetimidate group would constrain the conformation of the transition state and enable good stereoselectivity.

RESULTS AND DISCUSSION

Our initial trials started with trichloroacetimidate **1a**, which was easily prepared in two steps from 1-phenylbut-3-en-1-ol.[15] To our delight, in the presence of 5 mol % $Pd(OAc)_2$, **1a** was converted to 5,6-dihydro-1,3-oxazine **2a** in 62% yield with 7.0:1 diastereoselectivity favoring the *cis* product after 3 days at room temperature (Table 1, entry 1). The two isomers could be separated by chromatography on silica gel, and the stereochemistry was assigned by both NMR (J values and NOESY correlations) and X-ray analysis of *cis*-**2a** (see the Supporting Information).[16] With $PdCl_2$ as the catalyst, the reaction provided a similar isolated yield, but the diastereoselectivity dropped dramatically (entry 2). It was found that the reaction was much cleaner with $Pd(dba)_2$ as the catalyst, furnishing **2a** in 86% isolated yield (*dr* 5.7:1) with Et_2O as the solvent (entry 3). Further screening revealed that THF was the optimal solvent, in which the reaction delivered the desired product in 91% yield with 7.3:1 diastereoselectivity (entries 4 and 5). The cyclization reaction gave a slightly increased stereoselectivity at 20 °C (entry 6). When substituted dibenzylideneacetones with different electronic properties (e.g., **L1** and **L2**) were used as the ligands, no significant changes in either the yield or the stereoselectivity were observed (entries 7 and 8). The combination of $Pd(dba)_2$ and a phosphite ligand [i.e., $P(OPh)_3$] reduced the rate of the reaction, and only 17% conversion was observed after 3 days at 25 °C (entry 9).[17] The reaction did not proceed at all when $Pd(PPh_3)_4$ or iridium(I) was used as the catalyst (entries 10 and 11).[18]

It should be noted that the geometry of the C=C double bond had little influence on either the yield or stereoselectivity. Treatment of (*Z*)-**1a** with $Pd(dba)_2$ under identical conditions gave **2a** in 88% overall yield favoring the *cis* product with a similar *dr* value (Scheme 2), indicating that the selectivity is not

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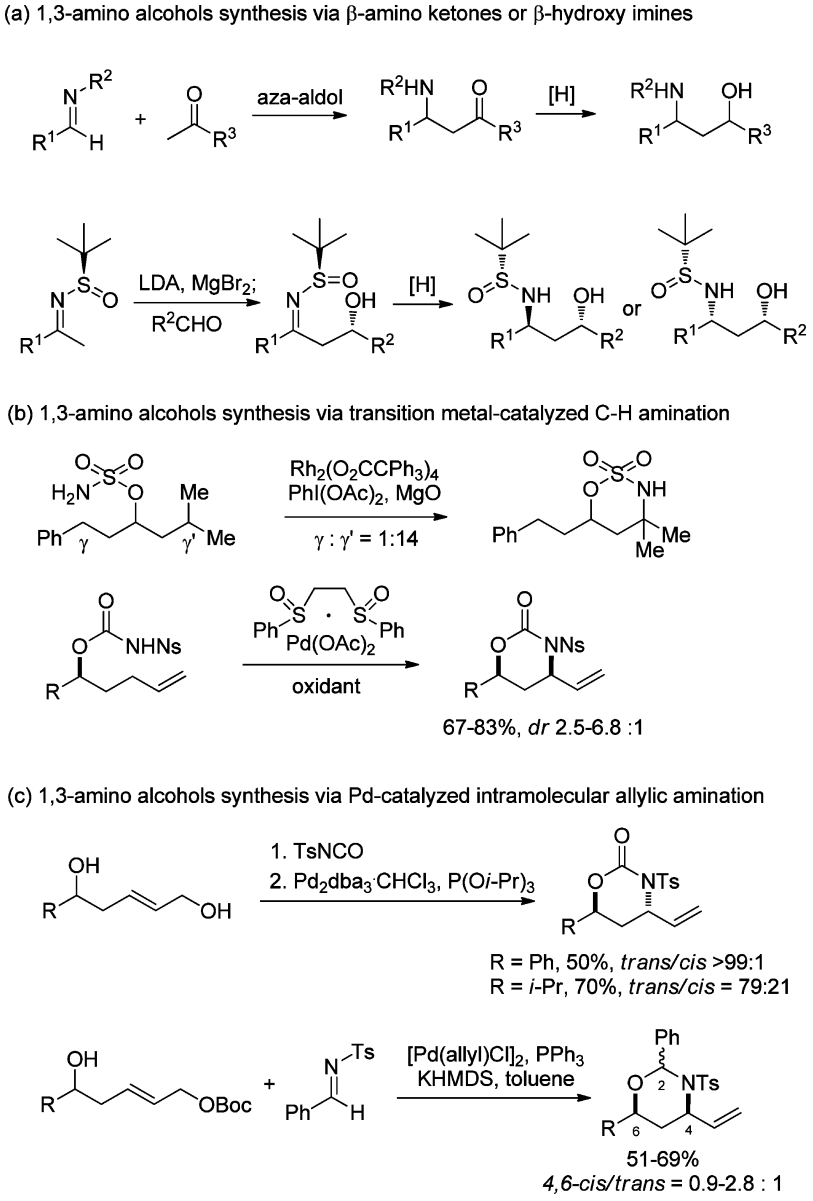
Scheme 1. Syntheses of 1,3-Amino Alcohols



dependent on the double-bond geometry in the substrate. Furthermore, independently subjecting both *cis*- and *trans*-**2a** to the standard reaction conditions showed that there is no equilibration between the two diastereomers in the presence of Pd(0) species.

We subsequently investigated the effect of the leaving group in this reaction. It was found that both the yield and the diastereoselectivity are significantly influenced by the properties of the leaving group (Table 2). With trichloroacetimidate as the leaving group, the reaction gave a moderate yield and a diastereoselectivity of 2.0:1 (entry 1). No satisfactory diastereoselectivities were observed when a carboxy ester (OAc, OPiv) or chloride was used as the leaving group (entries 2–4). Furthermore, in the case of methyl carbonate only very low conversion was observed under the same reaction conditions (entry 5).

The generality of the reaction was explored under the optimized conditions, and the results are listed in Table 3. Examination of a series of trichloroacetimidates derived from 4-substituted benzylic alcohols revealed that good to excellent yields could be achieved (**2b–f**), although the *p*-NO_2-substituted substrate gave a relatively lower diastereoselectivity (**2e**). Substrates with a 3-substituted phenyl ring or 2-naphthyl group could also be smoothly converted to 5,6-dihydro-1,3-oxazines in good yields and stereoselectivities (**2g–k**). Notably, the selectivity of this reaction is significantly impacted by the steric bulk adjacent to the trichloroacetimidate functionality. The reaction of 2-substituted phenyl or 1-naphthalene derivatives furnished the products in excellent yields and diastereoselectivities of up to >20:1 (**2l–n**). When the R group was an aliphatic group, the same steric effect was observed: the reaction with a hydrocinnamaldehyde-derived substrate afforded 5,6-dihydro-1,3-oxazines **2o** with 2.3:1 diastereoselectivity, while the α-branched substrate furnished product **2p** with >90% diastereomeric purity. A compound derived from (*R*)-glyceraldehyde-1,2-acetonide[19] was also a suitable substrate, affording cyclization product **2q** in 80% yield with moderate diastereoselectivity.

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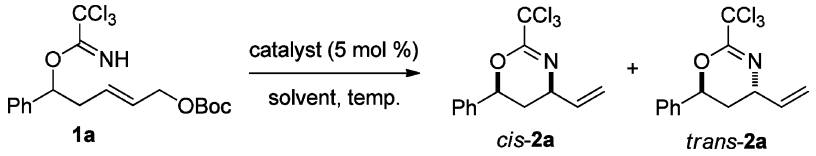
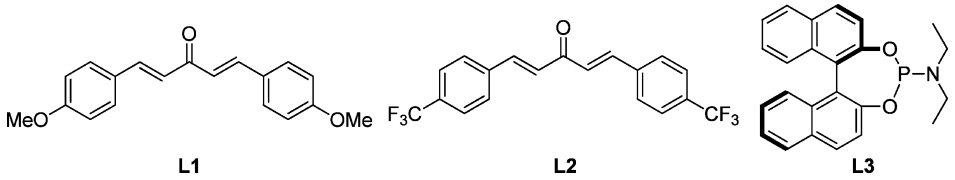
Table 1. Optimization of the Reaction Conditions[a]

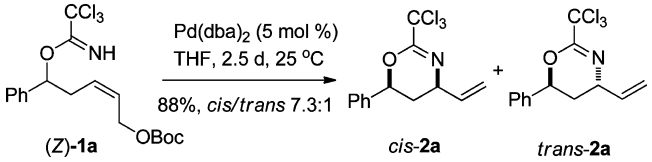


entry	catalyst	solvent	T (°C)	t (days)	% yield[b] (*cis*:*trans*) of **2a**
1	$Pd(OAc)_2$	DCM	25	3	62 (7.0:1)
2	$PdCl_2$	DCM	25	3.5	65 (3.3:1)
3	$Pd(dba)_2$	Et_2O	25	3	86 (5.7:1)
4	$Pd(dba)_2$	PhMe	25	3	87 (5.0:1)
5	$Pd(dba)_2$	THF	25	2.5	91 (7.3:1)
6	$Pd(dba)_2$	THF	20	2.5	90 (8.5:1)
7	Pd(**L1**)$_2$	THF	25	3.5	90 (7.5:1)
8	Pd(**L2**)$_2$	THF	25	3.5	86 (7.2:1)
9	$Pd(dba)_2/P(OPh)_3$	THF	25	3	17 (conv.)[d]
10	$Pd(PPh_3)_4$	THF	25	3	NR
11	$[Ir(COD)Cl]_2$/**L3**[c]	THF	70	1	NR

[a]The reactions were conducted on a 0.20 mmol scale of **1a**. [b]Isolated yields. [c]2.5 mol % $[Ir(COD)Cl]_2$ and 10 mol % **L3** were used. [d]10 mol % $P(OPh)_3$ was used; conv. = conversion.



Scheme 2. Reaction of (Z)-1a



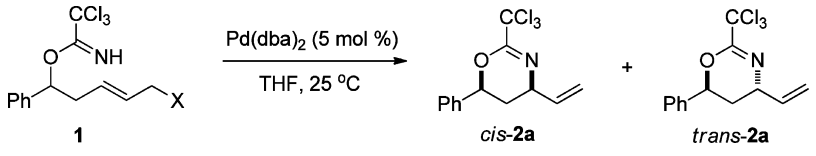
The enantioenriched trichloroacetimidate (*S*)-**1a**, which was prepared in two steps from (*S*)-1-phenylbut-3-en-1-ol,[15] was subjected to our standard conditions and formed (4*R*,6*S*)-**2a** with 8.6:1 diastereoselectivity without the loss of enantiopurity (Scheme 3).

5,6-Dihydro-1,3-oxazines could be hydrolyzed under mild conditions, which is typically a difficult operation for related benzenesulfonamide analogues. Furthermore, 1,3-amino alcohols in different protection states could be obtained selectively by controlling the reaction conditions (Scheme 4). The hydrolysis of *cis*-**2a** with 1 M aqueous HCl in THF resulted in the formation of 1-hydroxy-3-trichloroacetic amide derivative **4** in 65% yield with no epimization of the benzylic alcohol. Treatment of **4** with Na_2CO_3 under reflux in DMF resulted in the formation of 1,3-oxazinan-2-one **5** in 83% yield.[20] Compound *cis*-**2a** could also be converted to free 1,3-amino alcohol **6** by hydrolysis with 1 M HCl in methanol followed by treatment with a 1 M aqueous NaOH solution.

CONCLUSION

A palladium(0)-catalyzed cyclization reaction of homoallylic trichloroacetimidates to form 5,6-dihydro-1,3-oxazines has been reported. The stereoselectivity is sensitive to the steric bulk adjacent to the trichloroacetimidate group, and diastereoselectivites of up to >20:1 favoring the *cis* isomers were obtained. The resulting products are synthetic equivalents of variably protected 1,3-amino alcohols, which are valuable synthons for organic synthesis.

Table 2. Effect of the Leaving Group[a]



entry	X	t (days)	% yield[b] (*cis*/*trans*) of **2a**
1	$OC(=NH)CCl_3$ (**1A**)	1	52 (2.0:1)
2	OAc (**1B**)	3	60 (3.5:1)
3	OPiv (**1C**)	3	75 (1.3:1)
4	Cl (**1D**)	1.5	46 (3.0:1)
5	OCO_2Me (**1E**)	3	trace

[a]The reactions were conducted on a 0.20 mmol scale of **1**. [b]Isolated yields.

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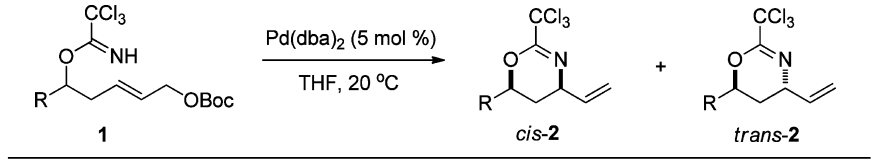
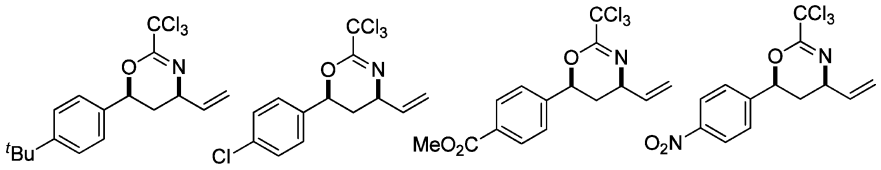
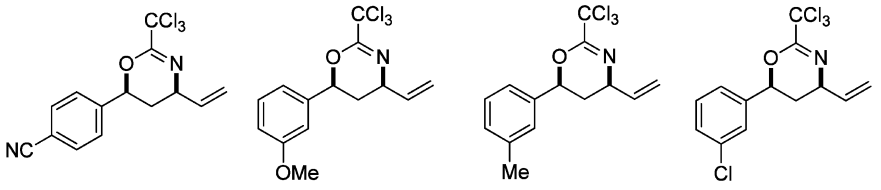
Table 3. Substrate Scope[a]

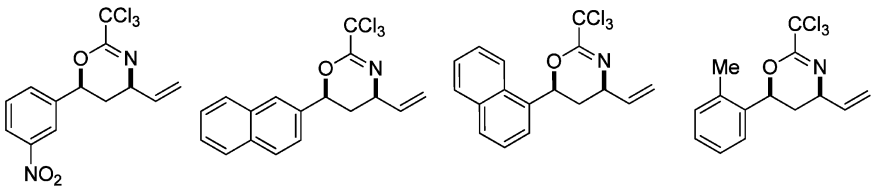




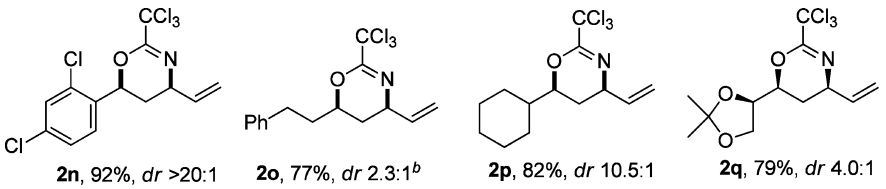
2b, 83%, *dr* 8.4:1 **2c**, 88%, *dr* 7.0:1 **2d**, 91%, *dr* 7.1:1[b] **2e**, 95%, *dr* 3.6:1[b]



2f, 84%, *dr* 4.0:1[b] **2g**, 87%, *dr* 7.2:1 **2h**, 90%, *dr* 7.4:1 **2i**, 87%, *dr* 6.7:1



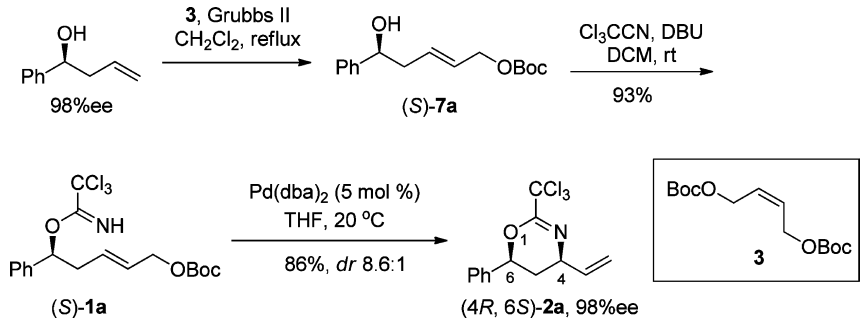
2j, 89%, *dr* 6.0:1[b] **2k**, 87%, *dr* 6.7:1[b] **2l**, 86%, *dr* 16.9:1 **2m**, 93%, *dr* >20:1



2n, 92%, *dr* >20:1 **2o**, 77%, *dr* 2.3:1[b] **2p**, 82%, *dr* 10.5:1 **2q**, 79%, *dr* 4.0:1

[a]The reactions were conducted on a 0.17−0.24 mmol scale of **1** (see the Supporting Information for details). [b]7.5 mol % $Pd(dba)_2$ was used.

Scheme 3. Synthesis of (4*R*,6*S*)-2a



EXPERIMENTAL SECTION

General Information. Reactions were performed under an inert atmosphere of dry nitrogen in flame-dried glassware, unless stated otherwise. Anhydrous solvents were distilled using standard techniques. THF and Et_2O were distilled over sodium under an atmosphere of nitrogen. PhMe, DMF, DCM, and Et_3N were distilled over calcium hydride under an atmosphere of nitrogen. All other solvents and reagents were used as obtained from commercial sources without further purification. Melting points were uncorrected. NMR spectra were recorded in $CDCl_3$ or MeOH-d_4 (^1H at 400 MHz and ^{13}C at 100 MHz) using TMS as the internal standard. Column chromatography was performed on silica gel (40−63 μm). Room-temperature reactions were performed at 25 ± 1 °C.

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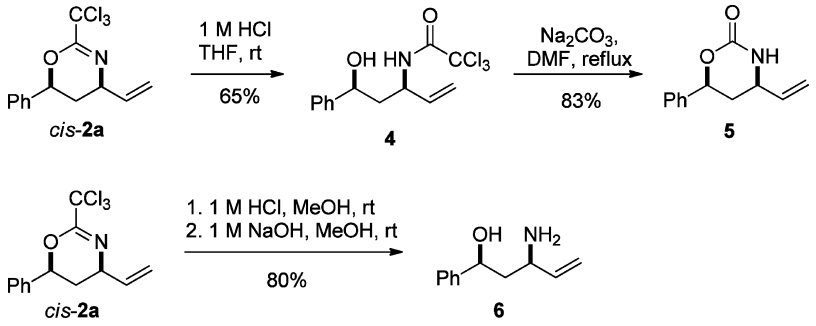
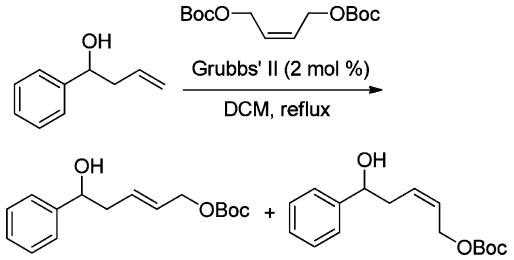
Scheme 4. Deprotection Studies



Representative Procedure for Olefin Metathesis (Typical Procedure A).

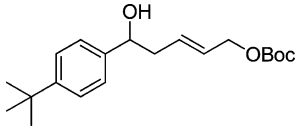


Under nitrogen, to a solution of 1-phenylbut-3-en-1-ol (2.10 g, 14.2 mmol, 1.0 equiv) and (*Z*)-but-2-ene-1,4-diyl di-*tert*-butyl dicarbonate (8.00 g, 27.7 mmol, 2.0 equiv) in 30 mL of anhydrous CH_2Cl_2 was added Grubbs second-generation catalyst (0.24 g, 0.28 mmol, 0.02 equiv), and the resulting mixture was refluxed overnight. After removal of the solvent by evaporation, the residue was purified by flash chromatography on silica gel (petroleum ether (PE)/ethyl acetate (EA), 10:1−5:1) to afford (*E*)-**7a** (2.07 g, 52%) as a viscous brown oil and (*Z*)-**7a** (0.20 g, 5.1%) as a viscous brown oil.

*(E)-tert-Butyl (5-Hydroxy-5-phenylpent-2-en-1-yl) Carbonate [(E)-**7a**].* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.25 (m, 5H), 5.84−5.68 (m, 2H), 4.73 (t, *J* = 6.8 Hz, 1H), 4.51 (dd, *J* = 0.8, 6.0 Hz, 2H), 2.51 (td, *J* = 0.8, 6.8 Hz, 1H), 1.48 (s, 9H). The NMR data were identical to those reported previously in the literature.[15]

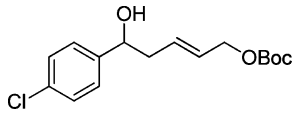
*(Z)-tert-Butyl (5-Hydroxy-5-phenylpent-2-en-1-yl) Carbonate [(Z)-**7a**].* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.22 (m, 5H), 5.76−5.61 (m, 2H), 4.74 (dd, *J* = 5.2, 7.2 Hz, 1H), 4.66−4.58 (m, 1H), 4.55−4.47 (m, 1H), 2.69−2.58 (m, 1H), 2.58−2.43 (m, 2H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 143.8, 130.6, 128.4, 127.5, 126.2, 125.7, 82.3, 73.4, 62.6, 37.4, 27.7; HRMS (Orbitrap ESI) calcd for $C_{16}H_{22}O_4Na$ $[M + Na]^+$ 301.1410, found 301.1409.

*(E)-tert-Butyl (5-(4-tert-Butylphenyl)-5-hydroxypent-2-en-1-yl) Carbonate (**7b**).*



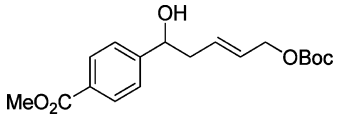
The compound (R_f = 0.15, PE/EA 10:1) (1.45 g, 72%, *E*/*Z* ∼12:1) was prepared following Typical Procedure A on a 6.0 mmol scale as a brown oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 5.78−5.69 (m, 1H), 5.68−5.58 (m, 1H), 4.62 (t, *J* = 6.4 Hz, 1H), 4.44 (dd, *J* = 0.8, 6.0 Hz, 2H), 2.43 (t, *J* = 6.8 Hz, 2H), 1.95 (br s, 1H), 1.40 (s, 9H), 1.24 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 150.5, 140.7, 132.2, 127.0, 125.5, 125.3, 82.0, 73.2, 67.2, 42.0, 34.5, 31.3, 27.7; HRMS (Orbitrap ESI) calcd for $C_{20}H_{30}O_4Na$ $[M + Na]^+$ 357.2036, found 357.2040.

*(E)-tert-Butyl (5-(4-Chlorophenyl)-5-hydroxypent-2-en-1-yl) Carbonate (**7c**).*



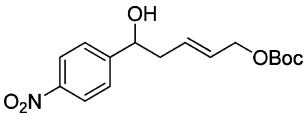
The compound (R_f = 0.15, PE/EA 10:1) (1.25 g, 66%, *E*/*Z* ∼11:1) was prepared following Typical Procedure A on a 6.0 mmol scale as a brown oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 5.82−5.62 (m, 2H), 4.71 (t, *J* = 6.4 Hz, 1H), 4.51 (d, *J* = 6.4 Hz, 2H), 2.48 (t, *J* = 6.8 Hz, 2H), 2.25 (br s, 1H), 1.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 142.2, 133.2, 131.3, 128.5, 127.6, 127.1, 82.1, 72.6, 67.1, 42.1, 27.7; HRMS (Orbitrap ESI) calcd for $C_{16}H_{21}O_4ClNa$ $[M + Na]^+$ 335.1021, found 335.1022.

*(E)-Methyl 4-(5-((tert-Butoxycarbonyl)oxy)-1-hydroxypent-3-en-1-yl)benzoate (**7d**).*



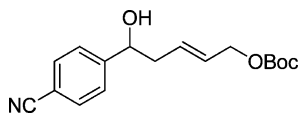
The compound (R_f = 0.2, PE/EA 5:1) (0.56 g, 58%) was prepared following Typical Procedure A on a 2.8 mmol scale as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 5.79−5.62 (m, 2H), 4.76 (dd, *J* = 5.6, 7.2 Hz, 1H), 4.47 (d, *J* = 5.6 Hz, 2H), 3.88 (s, 3H), 2.50−2.43 (m, 2H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 153.2, 148.9, 131.1, 129.7, 129.2, 127.7, 125.6, 82.1, 72.8, 67.0, 52,0, 42.1, 27.7; HRMS (Orbitrap ESI) calcd for $C_{18}H_{24}O_6Na$ $[M + Na]^+$ 359.1465, found 359.1468.

*(E)-tert-Butyl (5-Hydroxy-5-(4-nitrophenyl)pent-2-en-1-yl) Carbonate (**7e**).*



The compound (R_f = 0.2, PE/EA 5:1) (1.32 g, 68%, *E*/*Z* ∼15:1) was prepared following Typical Procedure A on a 6.0 mmol scale as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.8 Hz, 2H), 7.50 (d, *J* = 8.4 Hz, 2H), 5.81−5.62 (m, 2H), 4.85 (dd, *J* = 4.8, 8.0 Hz, 1H), 4.49 (d, *J* = 6.0 Hz, 2H), 2.58−2.39 (m, 3H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 151.0, 147.2, 130.3, 128.4, 126.5, 123.6, 82.3, 72.3, 66.9, 42.2, 27.7. The NMR data were identical to those reported previously in the literature.[21]

*(E)-tert-Butyl (5-(4-Cyanophenyl)-5-hydroxypent-2-en-1-yl) Carbonate (**7f**).*



The compound (R_f = 0.2, PE/EA 4:1) (1.03 g, 63%, *E*/*Z* >20:1) was prepared following Typical Procedure A on a 5.4 mmol scale as a pale-yellow solid: mp 104−105 °C (PE/EA); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 5.80−5.60 (m, 2H), 4.77 (dd, *J* = 4.8, 7.6 Hz, 1H), 4.47 (d, *J* = 6.0 Hz, 2H), 2.51−2.40 (m, 3H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.2, 149.1, 132.1, 130.5, 128.1, 126.4, 118.7, 111.0, 82.2, 72.4, 66.9, 42.1, 27.6; HRMS (Orbitrap ESI) calcd for $C_{17}H_{21}O_4NNa$ $[M + Na]^+$ 326.1363, found 326.1369.

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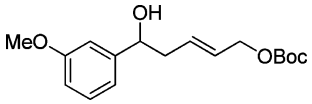
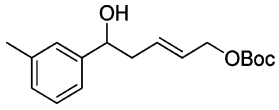
*(E)-tert-Butyl (5-Hydroxy-5-(3-methoxyphenyl)pent-2-en-1-yl) Carbonate (**7g**).*



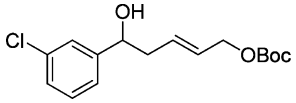
The compound (R_f = 0.5, PE/EA 3:1) (1.10 g, 59%, *E*/*Z* >20:1) was prepared following Typical Procedure A on a 6.0 mmol scale as a brown oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (t, *J* = 8.0 Hz, 1H), 6.91−6.86 (m, 2H), 6.79 (ddd, *J* = 1.2, 2.8, 8.4 Hz, 1H), 5.83−5.63 (m, 2H), 4.68 (t, *J* = 6.4 Hz, 1H), 4.48 (dd, *J* = 1.2, 6.4 Hz, 2H), 3.79 (s, 3H), 2.48 (dt, *J* = 0.8, 6.8 Hz, 2H), 2.21 (br s, 1H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 153.3, 145.5, 131.9, 129.4, 127.1, 118.0, 113.0, 111.2, 82.0, 73.2, 67.2, 55.1, 42.0, 27.7; HRMS (Orbitrap ESI) calcd for $C_{17}H_{24}O_5Na$ $[M + Na]^+$ 331.1516, found 331.1517.

*(E)-tert-Butyl (5-Hydroxy-5-(m-tolyl)pent-2-en-1-yl) Carbonate (**7h**).*



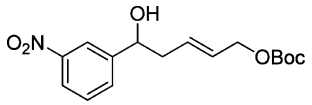
The compound (R_f = 0.2, PE/EA 10:1) (1.03 g, 58%, *E*/*Z* >20:1) was prepared following Typical Procedure A on a 6.0 mmol scale as a brown oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (t, *J* = 7.6 Hz, 1H), 7.17−7.06 (m, 3H), 5.85−5.63 (m, 2H), 4.68 (t, *J* = 6.4 Hz, 1H), 4.50 (dd, *J* = 0.8, 6.0 Hz, 2H), 2.49 (dt, *J* = 0.8, 6.4 Hz, 2H), 2.35 (s, 3H), 2.09 (br s, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 143.7, 138.0, 132.0, 128.30, 128.29, 127.1, 126.4, 122.8, 82.0, 73.4, 67.2, 42.1, 27.7, 21.4; HRMS (Orbitrap ESI) calcd for $C_{17}H_{24}O_4Na$ $[M + Na]^+$ 315.1567, found 315.1568.

*(E)-tert-Butyl (5-(3-Chlorophenyl)-5-hydroxypent-2-en-1-yl) Carbonate (**7i**).*



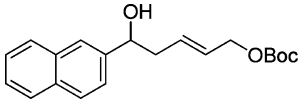
The compound (R_f = 0.2, PE/EA 10:1) (1.16 g, 62%, *E*/*Z* >20:1) was prepared following Typical Procedure A on a 6.0 mmol scale as a brown oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41−7.32 (m, 1H), 7.32−7.16 (m, 3H), 5.83−5.61 (m, 2H), 4.69 (dd, *J* = 5.6, 7.2 Hz, 1H), 4.50 (d, *J* = 6.0 Hz, 2H), 2.54−2.41 (m, 2H), 2.35 (br s, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 145.8, 134.3, 131.2, 129.6, 127.63, 127.59, 125.9, 123.9, 82.1, 72.6, 67.0, 42.1, 27.7; HRMS (Orbitrap ESI) calcd for $C_{16}H_{21}O_4ClNa$ $[M + Na]^+$ 335.1021, found 335.1027.

*(E)-tert-Butyl (5-Hydroxy-5-(3-nitrophenyl)pent-2-en-1-yl) Carbonate (**7j**).*



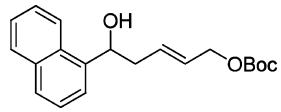
The compound (R_f = 0.2, PE/EA 5:1) (1.18 g, 60%, *E*/*Z* >20:1) was prepared following Typical Procedure A on a 6.0 mmol scale as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (t, *J* = 2.0 Hz, 1H), 8.08 (ddd, *J* = 1.2, 2.4, 8.4 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 1H), 5.81−5.63 (m, 2H), 4.83 (t, *J* = 6.0 Hz, 1H), 4.48 (d, *J* = 6.4 Hz, 2H), 2.72 (br s, 1H), 2.56−2.41 (m, 2H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.2, 148.2, 145.9, 131.9, 130.5, 129.3, 128.2, 122.4, 120.7, 82.2, 72.1, 66.9, 42.2, 27.6; HRMS (Orbitrap ESI) calcd for $C_{16}H_{21}O_6NNa$ $[M + Na]^+$ 346.1261, found 346.1262.

*(E)-tert-Butyl (5-Hydroxy-5-(naphthalen-2-yl)pent-2-en-1-yl) Carbonate (**7k**).*



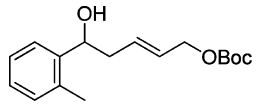
The compound (R_f = 0.2, PE/EA 10:1) (1.21 g, 62%) was prepared following Typical Procedure A on a 6.0 mmol scale as a pale-brown oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84−7.79 (m, 4H), 7.50−7.46 (m, 3H), 5.86−5.70 (m, 2H), 4.90 (t, *J* = 6.4 Hz, 1H), 4.51 (d, *J* = 6.0 Hz, 2H), 2.60 (t, *J* = 6.8 Hz, 2H), 2.02 (br s, 1H), 1.48 (s, 9H). The NMR data were identical to those reported previously in the literature.[15]

*(E)-tert-Butyl (5-Hydroxy-5-(naphthalen-1-yl)pent-2-en-1-yl) Carbonate (**7l**).*



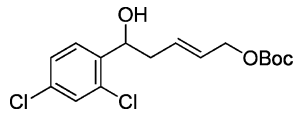
The compound (R_f = 0.2, PE/EA 10:1) (0.98 g, 69%) was prepared following Typical Procedure A on a 4.3 mmol scale as a pale-brown oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 7.2 Hz, 1H), 7.56−7.45 (m, 3H), 5.98−5.90 (m, 1H), 5.82−5.72 (m, 1H), 5.54 (dd, *J* = 3.6, 8.4 Hz, 1H), 4.54 (dd, *J* = 0.8, 6.4 Hz, 2H), 2.82−2.70 (m, 1H), 2.67−2.56 (m, 1H), 1.61 (br s, 1H), 1.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 139.3, 133.8, 132.3, 130.2, 129.0, 128.1, 127.3, 126.1, 125.6, 125.4, 122.9, 122.8, 82.2, 70.2, 67.3, 41.3, 27.8; HRMS (Orbitrap ESI) calcd for $C_{20}H_{24}O_4Na$ $[M + Na]^+$ 351.1567, found 351.1571.

*(E)-tert-Butyl (5-Hydroxy-5-(o-tolyl)pent-2-en-1-yl) Carbonate (**7m**).*



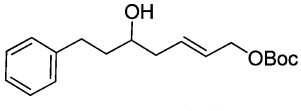
The compound (R_f = 0.4, PE/EA 10:1) (1.23 g, 70%, *E*/*Z* ~10:1) was prepared following Typical Procedure A on a 6.0 mmol scale as a brown oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.6 Hz, 1H), 7.25−7.09 (m, 3H), 5.89−5.81 (m, 1H), 5.79−5.66 (m, 1H), 4.96 (dd, *J* = 4.8, 8.0 Hz, 1H), 4.52 (d, *J* = 6.4 Hz, 2H), 2.51−2.40 (m, 2H), 2.32 (s, 3H), 1.98 (br s, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 141.8, 134.3, 132.2, 130.3, 127.3, 127.1, 126.3, 125.1, 82.1, 69.7, 67.2, 41.0, 27.7, 19.0; HRMS (Orbitrap ESI) calcd for $C_{17}H_{24}O_4Na$ $[M + Na]^+$ 315.1567, found 315.1568.

*(E)-tert-Butyl (5-(2,4-Dichlorophenyl)-5-hydroxypent-2-en-1-yl) Carbonate (**7n**).*



The compound (R_f = 0.3, PE/EA 5:1) (1.17 g, 73%) was prepared following Typical Procedure A on a 6.0 mmol scale as a pale-yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.4 Hz, 1H), 7.33 (d, *J* = 2.0 Hz, 1H), 7.26 (dd, *J* = 2.4, 8.4 Hz, 1H), 5.86−5.79 (m, 1H), 5.74−5.67 (m, 1H), 5.09 (dd, *J* = 4.0, 8.4 Hz, 1H), 4.51 (d, *J* = 6.4 Hz, 2H), 2.63−2.51 (m, 1H), 2.38−2.27 (m, 1H), 2.15 (br s, 1H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 139.7, 133.5, 132.1, 131.1, 129.0, 128.1, 127.9, 127.3, 82.2, 69.3, 67.1, 40.3, 27.7; HRMS (Orbitrap ESI) calcd for $C_{16}H_{20}O_4Cl_2Na$ $[M + Na]^+$ 369.0631, found 369.0631.

*(E)-tert-Butyl (5-Hydroxy-7-phenylhept-2-en-1-yl) Carbonate (**7o**).*



The compound (R_f = 0.3, PE/EA 5:1) (1.17 g, 64%) was prepared following Typical Procedure A on a 6.0 mmol scale as a brown oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.18 (m, 5H), 5.88−5.77 (m, 1H), 5.75−5.66 (m, 1H), 4.54 (d, *J* = 6.0 Hz, 2H), 3.75−3.66 (m, 1H), 2.87−2.64 (m, 2H), 2.38−2.17 (m, 2H), 1.86 (br s, 1H), 1.84−1.75 (m, 2H), 1.51 (s, 9H). The NMR data were identical to those reported previously in the literature.[15]

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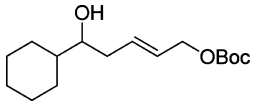
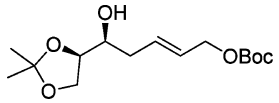
*(E)-tert-Butyl (5-Cyclohexyl-5-hydroxypent-2-en-1-yl) Carbonate (**7p**).*



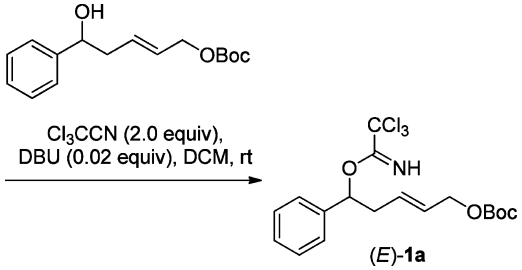
The compound (R_f = 0.2, PE/EA 10:1) (1.21 g, 71%) was prepared following Typical Procedure A on a 6.0 mmol scale as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.90−5.76 (m, 1H), 5.72−5.63 (m, 1H), 4.52 (d, J = 6.4 Hz, 2H), 3.42−3.36 (m, 1H), 2.35−2.26 (m, 1H), 2.19−2.08 (m, 1H), 1.85−1.62 (m, 5H), 1.47 (s, 9H), 1.39−0.97 (m, 6H). The NMR data were identical to those reported previously in the literature.[15]

*(E)-tert-Butyl ((S)-5-((R)-2,2-Dimethyl-1,3-dioxolan-4-yl)-5-hydroxypent-2-en-1-yl) Carbonate (**7q**).*



The compound (R_f = 0.15, PE/EA 5:1) (0.27 g, 63%) was prepared following Typical Procedure A on a 1.4 mmol scale as a pale-yellow oil: $[\alpha]_D^{25}$ = +5.4 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88−5.78 (m, 1H), 5.76−5.67 (m, 1H), 4.53 (d, J = 6.4 Hz, 2H), 4.04−3.96 (m, 2H), 3.91 (t, J = 9.6 Hz, 1H), 3.81−3.73 (m, 1H), 2.38−2.28 (m, 1H), 2.25−2.15 (m, 1H), 1.97 (d, J = 3.2 Hz, 1H), 1.48 (s, 9H), 1.42 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (100 MHz, $CHCl_3$) δ 153.3, 131.3, 127.4, 109.1, 82.2, 78.0, 70.5, 67.1, 65.2, 36.0, 27.8, 26.5, 25.2; HRMS (Orbitrap ESI) calcd for $C_{15}H_{26}O_6Na$ [M + Na]$^+$ 325.1622, found 325.1618.

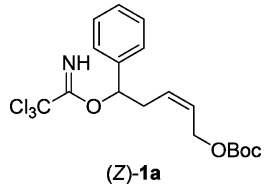
Representative Procedure for the Synthesis of Trichloroacetimidates (Typical Procedure B).



(*E*)-**1a**

To a solution of (*E*)-*tert*-butyl (5-hydroxy-5-phenylpent-2-en-1-yl) carbonate [(*E*)-**7a**] (834 mg, 3.0 mmol, 1.0 equiv) and Cl_3CCN (0.6 mL, 6.0 mmol, 2.0 equiv) in dichloromethane (15 mL) was added DBU (90 μL, 0.6 mmol, 0.02 equiv), and the mixture was stirred at room temperature overnight. After removal of the solvent in vacuo, the residue was purified by flash chromatography on silica gel (1% Et_3N in PE/EA 40:1) to afford (*E*)-**1a** (995 mg, 86%) as a pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.44−7.28 (m, 5H), 5.86 (dd, J = 5.2, 8.0 Hz, 1H), 5.83−5.74 (m, 1H), 5.74−5.65 (m, 1H), 4.48 (d, J = 5.6 Hz, 2H), 2.87−2.72 (m, 1H), 2.72−2.57 (m, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 153.3, 139.4, 130.3, 128.4, 128.1, 127.5, 126.1, 91.6, 82.0, 79.7, 67.1, 39.6, 27.7; HRMS (Orbitrap ESI) calcd for $C_{18}H_{22}O_4NCl_3Na$ [M + Na]$^+$ 444.0507, found 444.0499.

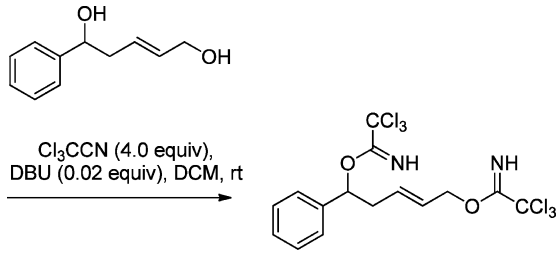
*(Z)-5-((tert-Butoxycarbonyl)oxy)-1-phenylpent-3-en-1-yl 2,2,2-Trichloroacetimidate [(Z)-**1a**].*



(*Z*)-**1a**

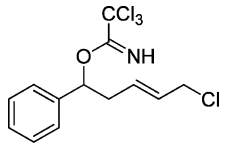
The compound (R_f = 0.5, PE/EA 20:1) (0.18 g, 79%) was obtained following Typical Procedure B on a 0.54 mmol scale as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.45−7.27 (m, 5H), 5.87 (dd, J = 5.6, 7.6 Hz, 1H), 5.76−5.63 (m, 2H), 4.56−4.49 (m, 2H), 2.91−2.80 (m, 1H), 2.78−2.67 (m, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 153.3, 139.2, 128.8, 128.4, 128.0, 126.6, 126.0, 91.5, 82.0, 79.7, 62.4, 34.8, 27.7; HRMS (Orbitrap ESI) calcd for $C_{18}H_{22}O_4NCl_3Na$ [M + Na]$^+$ 444.0507, found 444.0500.

*(E)-5-Phenylpent-2-ene-1,5-diyl Bis(2,2,2-trichloroacetimidate) (**1A**).*



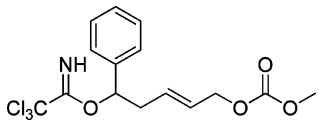
To a solution of (*E*)-5-phenylpent-2-ene-1,5-diol[8a] (0.49 g, 2.75 mmol, 1.0 equiv) and Cl_3CCN (1.1 mL, 11 mmol, 4.0 equiv) in dichloromethane (10 mL) was added DBU (0.1 mL, 0.67 mmol, 0.2 equiv), and the mixture was stirred at room temperature overnight. After removal of the solvent in vacuo, the residue was purified by flash chromatography on silica gel (1% Et_3N in PE/EA 20:1) to afford **1A** (1.01 g, 78%) as a white solid. Mp 65−66 °C (PE/EA); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.30 (s, 1H), 7.46−7.28 (m, 5H), 5.92 (dd, J = 5.2, 8.0 Hz, 1H), 5.91−5.76 (m, 2H), 4.75 (d, J = 5.6 Hz, 2H), 2.90−2.78 (m, 1H), 2.76−2.61 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 161.3, 139.3, 130.1, 128.4, 128.0, 126.8, 126.1, 91.5, 91.3, 79.6, 69.2, 39.5; HRMS (Orbitrap ESI) calcd for $C_{15}H_{14}O_2N_2Cl_6Na$ [M + Na]$^+$ 486.9079, found 486.9071.

*(E)-5-Chloro-1-phenylpent-3-en-1-yl 2,2,2-Trichloroacetimidate (**1D**).*



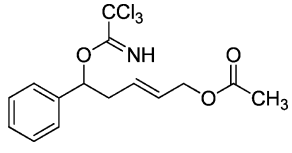
The compound (R_f = 0.5, PE/EA 20:1) (0.36 g, 73%) was obtained following Typical Procedure B on a 1.4 mmol scale as a pale-yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.48−7.29 (m, 5H), 5.89 (dd, J = 5.2, 8.0 Hz, 1H), 5.84−5.66 (m, 2H), 4.00 (d, J = 6.0 Hz, 2H), 2.85−2.75 (m, 1H), 2.72−2.61 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 139.3, 129.8, 129.5, 128.4, 128.1, 126.1, 91.6, 79.6, 44.8, 39.3; HRMS (Orbitrap ESI) calcd for $C_{13}H_{13}ONCl_4Na$ [M + Na]$^+$ 361.9644, found 361.9641.

*(E)-5-((Methoxycarbonyl)oxy)-1-phenylpent-3-en-1-yl 2,2,2-Trichloroacetimidate (**1E**).*



The compound (R_f = 0.5, PE/EA 20:1) (0.67 g, 58%) was obtained following Typical Procedure B on a 3.0 mmol scale as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.44−7.27 (m, 5H), 5.89 (dd, J = 5.2, 8.0 Hz, 1H), 5.86−5.76 (m, 1H), 5.75−5.64 (m, 1H), 4.56 (d, J = 6.4 Hz, 2H), 3.77 (s, 3H), 2.85−2.73 (m, 1H), 2.72−2.59 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 155.5, 139.3, 130.7, 128.4, 128.0, 127.1, 126.0, 91.5, 79.5, 67.9, 54.6, 39.4; HRMS (Orbitrap ESI) calcd for $C_{15}H_{16}O_4NCl_3Na$ [M + Na]$^+$ 402.0037, found 402.0031.

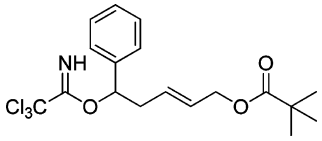
*(E)-5-Phenyl-5-(2,2,2-trichloro-1-iminoethoxy)pent-2-en-1-yl Acetate (**1B**).*



dx.doi.org/10.1021/jo402681z | J. Org. Chem. 2014, 79, 1289−1302

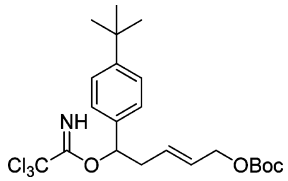
The compound (R_f = 0.5, PE/EA 20:1) (0.42 g, 79%) was obtained following Typical Procedure B on a 1.4 mmol scale as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.47−7.28 (m, 5H), 5.88 (dd, J = 5.2, 8.0 Hz, 1H), 5.83−5.72 (m, 1H), 5.72−5.63 (m, 1H), 4.49 (d, J = 6.0 Hz, 2H), 2.84−2.72 (m, 1H), 2.71−2.58 (m, 1H), 2.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 161.3, 139.4, 129.9, 128.4, 128.0, 127.7, 126.1, 91.5, 79.6, 64.6, 39.5, 20.9; HRMS (Orbitrap ESI) calcd for $C_{15}H_{16}O_3NCl_3Na$ $[M + Na]^+$ 386.0088, found 386.0084.

*(E)-5-Phenyl-5-(2,2,2-trichloro-1-iminoethoxy)pent-2-en-1-yl Pivalate (**1C**).*



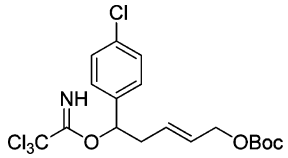
The compound (R_f = 0.6, PE/EA 20:1) (0.63 g, 77%) was obtained following Typical Procedure B on a 2.0 mmol scale as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.45−7.27 (m, 5H), 5.88 (dd, J = 5.2, 8.0 Hz, 1H), 5.80−5.60 (m, 2H), 4.48 (d, J = 5.2 Hz, 2H), 2.84−2.73 (m, 1H), 2.70−2.59 (m, 1H), 1.19 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.1, 161.4, 139.4, 128.9, 128.4, 127.99, 127.96, 126.1, 91.6, 79.7, 64.4, 39.5, 38.7, 27.1; HRMS (Orbitrap ESI) calcd for $C_{18}H_{22}O_3NCl_3Na$ $[M + Na]^+$ 428.0558, found 428.0557.

*(E)-5-((tert-Butoxycarbonyl)oxy)-1-(4-tert-butylphenyl)pent-3-en-1-yl 2,2,2-Trichloroacetimidate (**1b**).*



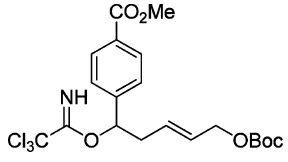
The compound (R_f = 0.5, PE/EA 20:1) (1.28 g, 75%) was obtained following Typical Procedure B on a 3.5 mmol scale as a pale-yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.37 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 5.87 (dd, J = 4.8, 8.0 Hz, 1H), 5.85−5.75 (m, 1H), 5.74−5.66 (m, 1H), 4.49 (d, J = 6.0 Hz, 2H), 2.82−2.72 (m, 1H), 2.68−2.59 (m, 1H), 1.48 (s, 9H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 153.2, 150.8, 136.3, 130.5, 127.2, 125.7, 125.3, 91.6, 81.9, 79.6, 67.1, 39.6, 34.5, 31.3, 27.7; HRMS (Orbitrap ESI) calcd for $C_{22}H_{30}O_4NCl_3Na$ $[M + Na]^+$ 500.1133, found 500.1130.

*(E)-5-((tert-Butoxycarbonyl)oxy)-1-(4-chlorophenyl)pent-3-en-1-yl 2,2,2-Trichloroacetimidate (**1c**).*



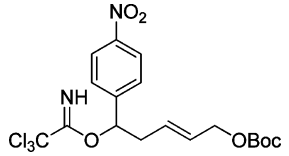
The compound (R_f = 0.5, PE/EA 20:1) (1.23 g, 84%) was obtained following Typical Procedure B on a 4.1 mmol scale as a pale-yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.37−7.28 (m, 4H), 5.82 (dd, J = 5.6, 8.0 Hz, 1H), 5.79−5.63 (m, 2H), 4.47 (d, J = 5.6 Hz, 2H), 2.81−2.70 (m, 1H), 2.65−2.54 (m, 1H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 153.2, 137.8, 133.8, 129.7, 128.6, 127.8, 127.6, 91.4, 82.0, 78.9, 66.9, 39.2, 27.7; HRMS (Orbitrap ESI) calcd for $C_{18}H_{21}O_4NCl_4Na$ $[M + Na]^+$ 478.0117, found 478.0117.

*(E)-Methyl 4-(5-((tert-Butoxycarbonyl)oxy)-1-(2,2,2-trichloro-1-iminoethoxy)pent-3-en-1-yl)benzoate (**1d**).*



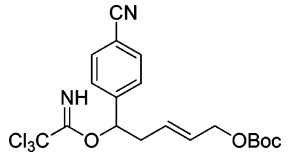
The compound (R_f = 0.4, PE/EA 10:1) (0.51 g, 63%) was obtained following Typical Procedure B on a 1.6 mmol scale as a pale-yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.03 (d, J = 8.8 Hz, 2H), 7.44 (d, J = 8.0 Hz, 2H), 5.89 (dd, J = 5.2, 8.0 Hz, 1H), 5.82−5.63 (m, 2H), 4.47 (dd, J = 0.8, 6.0 Hz, 2H), 3.90 (s, 3H), 2.82−2.71 (m, 1H), 2.70−2.60 (m, 1H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 161.3, 153.2, 144.4, 129.9, 129.8, 129.6, 128.0, 126.0, 91.3, 82.1, 79.1, 66.9, 52.1, 39.3, 27.7; HRMS (Orbitrap ESI) calcd for $C_{20}H_{24}O_6NCl_3Na$ $[M + Na]^+$ 502.0561, found 502.0561.

*(E)-5-((tert-Butoxycarbonyl)oxy)-1-(4-nitrophenyl)pent-3-en-1-yl 2,2,2-Trichloroacetimidate (**1e**).*



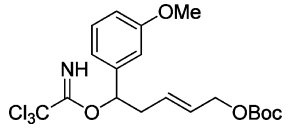
The compound (R_f = 0.5, PE/EA 5:1) (1.23 g, 85%) was obtained following Typical Procedure B on a 3.0 mmol scale as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 8.21 (d, J = 8.8 Hz, 2H), 7.54 (d, J = 8.8 Hz, 2H), 5.93 (dd, J = 5.6, 7.6 Hz, 1H), 5.80−5.63 (m, 2H), 4.47 (d, J = 5.6 Hz, 2H), 2.82−2.73 (m, 1H), 2.71−2.62 (m, 1H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 153.2, 147.6, 146.6, 128.8, 128.5, 127.0, 123.8, 91.1, 82.1, 78.5, 66.7, 39.1, 27.7; HRMS (Orbitrap ESI) calcd for $C_{18}H_{21}O_6N_2Cl_3Na$ $[M + Na]^+$ 489.0357, found 489.0356.

*(E)-5-((tert-Butoxycarbonyl)oxy)-1-(4-cyanophenyl)pent-3-en-1-yl 2,2,2-Trichloroacetimidate (**1f**).*



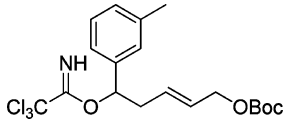
The compound (R_f = 0.5, PE/EA 5:1) (0.98 g, 92%) was obtained following Typical Procedure B on a 2.3 mmol scale as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 7.66 (d, J = 8.0 Hz, 2H), 7.49 (d, J = 8.0 Hz, 2H), 5.88 (dd, J = 5.2, 7.6 Hz, 1H), 5.80−5.61 (m, 2H), 4.48 (d, J = 5.6 Hz, 2H), 2.82−2.70 (m, 1H), 2.69−2.59 (m, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.0, 153.1, 144.5, 132.2, 128.8, 128.3, 126.7, 118.4, 111.8, 91.0, 82.0, 78.6, 66.6, 39.0, 27.6; HRMS (Orbitrap ESI) calcd for $C_{19}H_{21}O_4N_2Cl_3Na$ $[M + Na]^+$ 469.0459, found 469.0455.

*(E)-5-((tert-Butoxycarbonyl)oxy)-1-(3-methoxyphenyl)pent-3-en-1-yl 2,2,2-Trichloroacetimidate (**1g**).*



The compound (R_f = 0.5, PE/EA 20:1) (1.0 g, 85%) was obtained following Typical Procedure B on a 2.6 mmol scale as a pale-yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.26 (t, J = 8.0 Hz, 1H), 6.97−6.93 (m, 2H), 6.83 (ddd, J = 0.8, 2.8, 8.4 Hz, 1H), 5.83 (dd, J = 5.2, 8.0 Hz, 1H), 5.82−5.64 (m, 2H), 4.48 (d, J = 6.4 Hz, 2H), 3.79 (s, 3H), 2.81−2.70 (m, 1H), 2.68−2.58 (m, 1H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 159.6, 153.2, 141.1, 130.3, 129.5, 127.4, 118.3, 113.5, 111.4, 91.6, 82.0, 79.5, 67.0, 55.1, 39.6, 27.7; HRMS (Orbitrap ESI) calcd for $C_{19}H_{24}O_5NCl_3Na$ $[M + Na]^+$ 474.0612, found 474.0611.

*(E)-5-((tert-Butoxycarbonyl)oxy)-1-(m-tolyl)pent-3-en-1-yl 2,2,2-Trichloroacetimidate (**1h**).*



The compound (R_f = 0.6, PE/EA 20:1) (1.36 g, 89%) was obtained following Typical Procedure B on a 3.5 mmol scale as a pale-yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.26−7.15 (m, 3H), 7.13−7.08 (m, 1H), 5.83−5.67 (m, 3H), 4.49 (dd, J = 0.8, 6.0 Hz, 2H),

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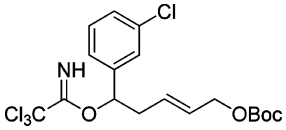
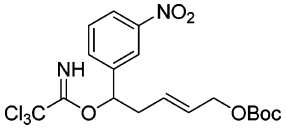
2.82−2.71 (m, 1H), 2.68−2.56 (m, 1H), 2.36 (s, 3H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 153.3, 139.4, 138.1, 130.5, 128.8, 128.3, 127.4, 126.7, 123.0, 91.6, 82.0, 79.8, 67.1, 39.7, 27.7, 21.5; HRMS (Orbitrap ESI) calcd for $C_{19}H_{24}O_4NCl_3Na$ [M + Na]$^+$ 458.0663, found 458.0662.

*(E)-5-((tert-Butoxycarbonyl)oxy)-1-(3-chlorophenyl)pent-3-en-1-yl 2,2,2-Trichloroacetimidate (**1i**).*



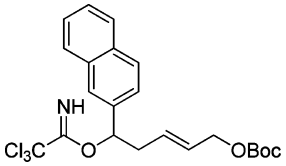
The compound (R_f = 0.5, PE/EA 20:1) (1.23 g, 84%) was obtained following Typical Procedure B on a 3.1 mmol scale as a pale-yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.43−7.37 (m, 1H), 7.35−7.21 (m, 3H), 5.84 (dd, J = 5.2, 8.0 Hz, 1H), 5.82−5.66 (m, 2H), 4.50 (dd, J = 0.8, 6.0 Hz, 2H), 2.83−2.70 (m, 1H), 2.68−2.57 (m, 1H), 1.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 153.2, 141.5, 134.4, 129.73, 129.66, 128.2, 127.9, 126.3, 124.3, 91.3, 82.0, 78.8, 66.9, 39.4, 27.7; HRMS (Orbitrap ESI) calcd for $C_{18}H_{21}O_4NCl_4Na$ [M + Na]$^+$ 478.0117, found 478.0117.

*(E)-5-((tert-Butoxycarbonyl)oxy)-1-(3-nitrophenyl)pent-3-en-1-yl 2,2,2-Trichloroacetimidate (**1j**).*



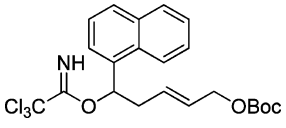
The compound (R_f = 0.2, PE/EA 5:1) (0.84 g, 79%) was obtained following Typical Procedure B on a 2.2 mmol scale as a pale-yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 8.27 (dd, J = 2.0, 2.0 Hz, 1H), 8.17 (ddd, J = 0.8, 2.0, 8.0 Hz, 1H), 7.71 (dt, J = 0.8, 7.6 Hz, 1H), 7.54 (t, J = 8.0 Hz, 1H), 5.94 (dd, J = 5.2, 8.0 Hz, 1H), 5.83−5.64 (m, 2H), 4.48 (dd, J = 0.8, 6.0 Hz, 2H), 2.87−2.76 (m, 1H), 2.73−2.62 (m, 1H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 153.2, 148.3, 141.6, 132.2, 129.5, 129.0, 128.5, 123.1, 121.2, 91.1, 82.1, 78.4, 66.8, 39.2, 27.7; HRMS (Orbitrap ESI) calcd for $C_{18}H_{21}O_6N_2Cl_3Na$ [M + Na]$^+$ 489.0357, found 489.0356.

*(E)-5-((tert-Butoxycarbonyl)oxy)-1-(naphthalen-2-yl)pent-3-en-1-yl 2,2,2-Trichloroacetimidate (**1k**).*



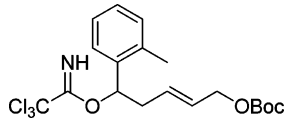
The compound (R_f = 0.5, PE/EA 20:1) (1.15 g, 80%) was obtained following Typical Procedure B on a 3.0 mmol scale as a pale-yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.90−7.78 (m, 4H), 7.56−7.45 (m, 3H), 6.04 (dd, J = 5.2, 8.0 Hz, 1H), 5.89−5.79 (m, 1H), 5.78−5.69 (m, 1H), 4.49 (d, J = 6.0 Hz, 2H), 2.95−2.85 (m, 1H), 2.78−2.70 (m, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 153.2, 136.7, 133.1, 133.0, 130.3, 128.3, 128.1, 127.7, 127.6, 126.2, 126.1, 125.4, 123.9, 91.6, 82.0, 79.9, 67.0, 39.5, 27.7; HRMS (Orbitrap ESI) calcd for $C_{22}H_{24}O_4NCl_3Na$ [M + Na]$^+$ 494.0663, found 494.0662.

*(E)-5-((tert-Butoxycarbonyl)oxy)-1-(naphthalen-1-yl)pent-3-en-1-yl 2,2,2-Trichloroacetimidate (**1l**).*



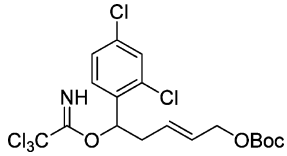
The compound (R_f = 0.5, PE/EA 20:1) (1.27 g, 90%) was obtained following Typical Procedure B on a 3.0 mmol scale as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 8.14 (d, J = 8.4 Hz, 1H), 7.89 (dd, J = 1.6, 8.0 Hz, 1H), 7.82 (d, J = 8.4 Hz, 1H), 7.69 (d, J = 7.2 Hz, 1H), 7.61−7.44 (m, 3H), 6.68 (dd, J = 4.8, 8.4 Hz, 1H), 5.99−5.86 (m, 1H), 5.82−5.71 (m, 1H), 4.52 (d, J = 6.4 Hz, 2H), 3.00−2.78 (m, 2H), 1.51 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3, 153.2, 135.3, 133.7, 130.6, 130.0, 128.9, 128.5, 127.3, 126.3, 125.6, 125.2, 123.4, 122.9, 91.6, 81.9, 77.1, 67.0, 38.9, 27.7; HRMS (Orbitrap ESI) calcd for $C_{22}H_{24}O_4NCl_3Na$ [M + Na]$^+$ 494.0663, found 494.0663.

*(E)-5-((tert-Butoxycarbonyl)oxy)-1-(o-tolyl)pent-3-en-1-yl 2,2,2-Trichloroacetimidate (**1m**).*



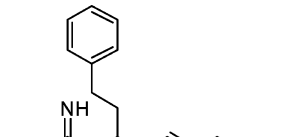
The compound (R_f = 0.5, PE/EA 50:1) (1.11 g, 89%) was obtained following Typical Procedure B on a 2.8 mmol scale as a pale-yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.48−7.42 (m, 1H), 7.25−7.11 (m, 3H), 6.03 (dd, J = 4.8, 8.8 Hz, 1H), 5.89−5.77 (m, 1H), 5.76−5.67 (m, 1H), 4.50 (dd, J = 0.8, 6.0 Hz, 2H), 2.81−2.70 (m, 1H), 2.62−2.53 (m, 1H), 2.42 (s, 3H), 1.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 153.2, 137.9, 134.9, 130.5, 130.2, 127.8, 127.3, 126.2, 125.3, 91.6, 82.0, 76.7, 67.1, 38.7, 27.7, 19.1; HRMS (Orbitrap ESI) calcd for $C_{19}H_{24}O_4NCl_3Na$ [M + Na]$^+$ 458.0663, found 458.0660.

*(E)-5-((tert-Butoxycarbonyl)oxy)-1-(2,4-dichlorophenyl)pent-3-en-1-yl 2,2,2-Trichloroacetimidate (**1n**).*



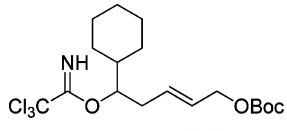
The compound (R_f = 0.5, PE/EA 20:1) (1.39 g, 92%) was obtained following Typical Procedure B on a 3.0 mmol scale as a pale-yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.42 (d, J = 8.4 Hz, 1H), 7.38 (dd, J = 0.8, 2.0 Hz, 1H), 7.28−7.22 (m, 1H), 6.18 (dd, J = 5.2, 7.6 Hz, 1H), 5.88−5.77 (m, 1H), 5.74−5.64 (m, 1H), 4.48 (d, J = 6.0 Hz, 2H), 2.73−2.59 (m, 2H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9, 153.2, 136.0, 134.1, 132.6, 129.4, 129.3, 128.0, 127.6, 127.5, 91.2, 82.0, 76.0, 66.9, 37.8, 27.7; HRMS (Orbitrap ESI) calcd for $C_{18}H_{20}O_4NCl_5Na$ [M + Na]$^+$ 511.9727, found 511.9729.

*(E)-7-((tert-Butoxycarbonyl)oxy)-1-phenylhept-5-en-3-yl 2,2,2-Trichloroacetimidate (**1o**).*



The compound (R_f = 0.5, PE/EA 10:1) (1.84 g, 68%) was obtained following Typical Procedure B on a 3.2 mmol scale as a pale-yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.23−7.05 (m, 5H), 5.77−5.65 (m, 1H), 5.64−5.54 (m, 1H), 5.02−4.93 (m, 1H), 4.41 (d, J = 6.0 Hz, 2H), 2.77−2.65 (m, 1H), 2.63−2.52 (m, 1H), 2.50−2.31 (m, 2H), 2.03−1.79 (m, 2H), 1.39 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0, 153.2, 141.3, 130.2, 128.4, 128.3, 127.3, 125.9, 91.8, 81.9, 77.5, 67.0, 35.9, 35.0, 31.4, 27.7; HRMS (Orbitrap ESI) calcd for $C_{20}H_{26}O_4NCl_3Na$ [M + Na]$^+$ 472.0820, found 472.0819.

*(E)-5-((tert-Butoxycarbonyl)oxy)-1-cyclohexylpent-3-en-1-yl 2,2,2-Trichloroacetimidate (**1p**).*

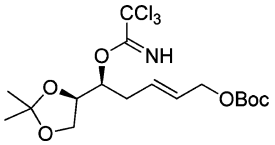


The compound (R_f = 0.5, PE/EA 20:1) (0.25 g, 15%) was obtained following Typical Procedure B on a 3.8 mmol scale as a pale-yellow oil along with recovered starting material (0.90 g, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 5.88−5.75 (m, 1H), 5.71−5.61 (m, 1H), 4.89 (dd, J = 6.4, 11.2 Hz, 1H), 4.48 (dd, J = 1.2, 6.4 Hz, 2H),

dx.doi.org/10.1021/jo402681z | J. Org. Chem. 2014, 79, 1289−1302

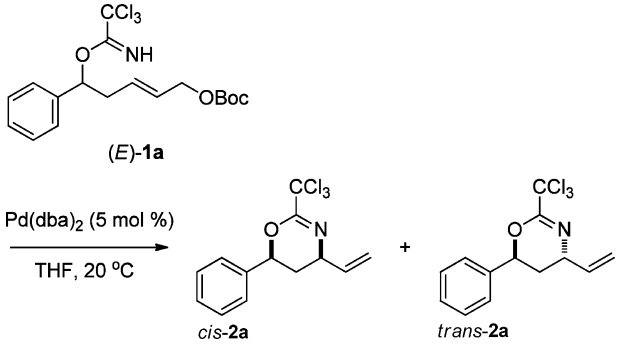
2.55−2.38 (m, 2H), 1.85 (d, J = 12.8 Hz, 1H), 1.78−1.60 (m, 5H), 1.47 (s, 9H), 1.30−1.00 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 153.3, 131.0, 126.8, 92.1, 82.00, 81.98, 67.3, 40.4, 33.3, 28.8, 28.0, 27.8, 26.3, 26.0, 25.9; HRMS (Orbitrap ESI) calcd for $C_{18}H_{28}O_4NCl_3Na$ $[M + Na]^+$ 450.0976, found 450.0976.

*(S,E)-5-((tert-Butoxycarbonyl)oxy)-1-((R)-2,2-dimethyl-1,3-dioxolan-4-yl)pent-3-en-1-yl 2,2,2-Trichloroacetimidate (**1q**).*



The compound (R_f = 0.3, PE/EA 10:1) (0.27 g, 73%) was obtained following Typical Procedure B on a 0.8 mmol scale as a colorless oil along with recovered starting material (30 mg, 12%): $[\alpha]_D^{25}$ = +16.8 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 5.87−5.76 (m, 1H), 5.76−5.66 (m, 1H), 5.15−5.07 (m, 1H), 4.49 (d, J = 6.0 Hz, 2H), 4.23 (dd, J = 6.0, 12.8 Hz, 1H), 4.06 (dd, J = 6.4, 8.8 Hz, 1H), 3.88 (dd, J = 5.6, 8.4 Hz, 1H), 2.71−2.60 (m, 1H), 2.56−2.46 (m, 1H), 1.47 (s, 9H), 1.42 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 153.3, 129.7, 127.7, 109.7, 91.4, 82.0, 77.5, 75.6, 67.1, 66.4, 33.1, 27.8, 26.6, 25.3; HRMS (Orbitrap ESI) calcd for $C_{17}H_{26}O_6NCl_3Na$ $[M + Na]^+$ 468.0718, found 468.0709.

Representative Procedure for Pd-Catalyzed Trichloroacetimidate Cyclization (Typical Procedure C).

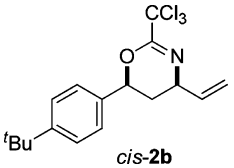


Under nitrogen, $Pd(dba)_2$ (5.75 mg, 0.01 mmol, 0.05 equiv) was added to a solution of trichloroacetimidate (*E*)-**1a** (0.20 mmol, 1.0 equiv) in anhydrous THF (2 mL), and the mixture was stirred at 20 °C for 2.5 days. The mixture was filtered through a Celite pad, and the filtrate was concentrated. The residue was purified by flash chromatography on a short silica gel column (1% Et_3N in PE/EA 40:1) to afford a mixture of diastereomers *cis*-**2a** and *trans*-**2a** (combined yield 54.8 mg, 90%; *dr* 8.5:1) as colorless oil. This mixture of diastereomers was separated by flash chromatography on silica gel (1% Et_3N in PE/toluene 1:2) to afford the pure diastereomers *cis*-**2a** and *trans*-**2a**.

*(±)-(4R,6S)-6-Phenyl-2-trichloromethyl-4-vinyl-5,6-dihydro-4H-1,3-oxazine (cis-**2a**).* White solid, mp 98−99 °C (PE/EA); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.33 (m, 5H), 5.99 (ddd, J = 5.2, 10.4, 17.2 Hz, 1H), 5.45−5.34 (m, 2H), 5.21 (ddd, J = 1.6, 1.6, 10.4 Hz, 1H), 4.39−4.29 (m, 1H), 2.35 (ddd, J = 2.8, 4.8, 14.0 Hz, 1H), 1.68 (ddd, J = 11.6, 11.6, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 139.0, 138.1, 128.8, 128.6, 125.6, 115.5, 92.4, 79.0, 55.6, 35.8; HRMS (Orbitrap ESI) calcd for $C_{13}H_{13}ONCl_3$ $[M + H]^+$ 304.0057, found 304.0059.

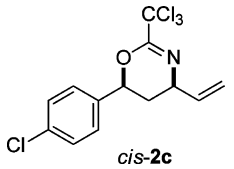
*(±)-(4S,6S)-6-Phenyl-2-trichloromethyl-4-vinyl-5,6-dihydro-4H-1,3-oxazine (trans-**2a**).* Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47−7.30 (m, 5H), 6.01 (ddd, J = 4.8, 10.4, 17.2 Hz, 1H), 5.34 (ddd, J = 1.2, 1.2, 10.4 Hz, 1H), 5.30 (dd, J = 6.4, 7.2 Hz, 1H), 5.19 (ddd, J = 1.2, 2.0, 17.2 Hz, 1H), 4.45−4.32 (m, 1H), 2.10−1.96 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 139.2, 137.7, 128.8, 128.4, 125.5, 117.2, 92.4, 75.3, 52.9, 33.2; HRMS (Orbitrap ESI) calcd for $C_{13}H_{13}ONCl_3$ $[M + H]^+$ 304.0057, found 304.0057.

*(±)-(4R,6S)-6-(4-tert-Butylphenyl)-2-trichloromethyl-4-vinyl-5,6-dihydro-4H-1,3-oxazine (cis-**2b**).*



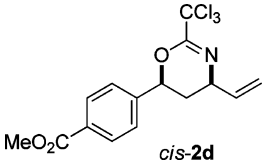
The mixture of diastereomers (R_f = 0.5, PE/EA 30:1) (60.5 mg, 83%, *dr* 8.4:1) was obtained following Typical Procedure C on a 0.20 mmol scale as a colorless oil. Data for the major diastereomer *cis*-**2b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 6.00 (ddd, J = 5.2, 10.4, 17.2 Hz, 1H), 5.41 (ddd, J = 1.2, 1.2, 16.8 Hz, 1H), 5.35 (dd, J = 2.8, 11.6 Hz, 1H), 5.21 (ddd, J = 1.2, 1.2, 10.4 Hz, 1H), 4.37−4.29 (m, 1H), 2.35 (ddd, J = 2.8, 4.8, 14.4 Hz, 1H), 1.70 (ddd, J = 11.6, 11.6, 14.0 Hz, 1H), 1.34 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) (selected peaks) δ 153.9, 151.7, 138.1, 135.9, 125.7, 125.5, 115.4, 92.5, 79.0, 55.6, 35.7, 34.6, 31.3; HRMS (TOF EI) calcd for $C_{17}H_{20}ONCl_3$ $[M]^+$ 359.0610, found 359.0610.

*(±)-(4R,6S)-6-(4-Chlorophenyl)-2-trichloromethyl-4-vinyl-5,6dihydro-4H-1,3-oxazine (cis-**2c**).*



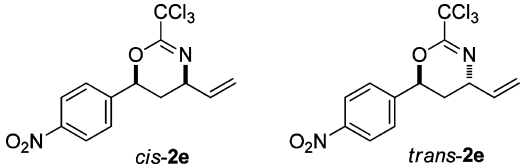
The mixture of diastereomers (R_f = 0.4, PE/EA 20:1) (72.0 mg, 88%, *dr* 7.0:1) was obtained following Typical Procedure C on a 0.24 mmol scale as a pale-yellow oil. Data for the major diastereomer *cis*-**2c**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 5.98 (ddd, J = 5.2, 10.4, 17.2 Hz, 1H), 5.41 (ddd, J = 1.6, 1.6, 17.2 Hz, 1H), 5.34 (dd, J = 2.8, 12.0 Hz, 1H), 5.22 (ddd, J = 1.6, 1.6, 10.4 Hz, 1H), 4.37−4.27 (m, 1H), 2.34 (ddd, J = 2.8, 4.4, 14.0 Hz, 1H), 1.64 (ddd, J = 11.6, 11.6, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (selected peaks) δ 153.5, 137.8, 137.4, 134.5, 129.0, 127.0, 115.7, 92.3, 78.2, 55.4, 35.6; HRMS (TOF EI) calcd for $C_{13}H_{11}ONCl_4$ $[M]^+$ 336.9595, found 336.9590.

*(±)-Methyl 4-((4R,6S)-2-Trichloromethyl-4-vinyl-5,6-dihydro-4H-1,3-oxazin-6-yl)benzoate (cis-**2d**).*



The mixture of diastereomers (R_f = 0.3, PE/EA 10:1) (71.7 mg, 91%, *dr* 7.1:1) was obtained following Typical Procedure C on a 0.21 mmol scale as a colorless oil. Data for the major diastereomer *cis*-**2d**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 8.4 Hz, 2H), 5.97 (ddd, J = 5.2, 10.4, 16.8 Hz, 1H), 5.45−5.36 (m, 2H), 5.21 (ddd, J = 1.6, 1.6, 10.4 Hz, 1H), 4.38−4.30 (m, 1H), 3.92 (s, 3H), 2.37 (ddd, J = 2.8, 4.4, 14.0 Hz, 1H), 1.64 (ddd, J = 11.6, 11.6, 14.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (selected peaks) δ 166.5, 153.3, 143.8, 137.7, 130.3, 130.1, 125.4, 115.7, 92.2, 78.3, 55.4, 52.2, 35.5; HRMS (Orbitrap ESI) calcd for $C_{15}H_{15}O_3NCl_3$ $[M + H]^+$ 362.0112, found 362.0112.

*(±)-(4R,6S)-6-(4-Nitrophenyl)-2-trichloromethyl-4-vinyl-5,6-dihydro-4H-1,3-oxazine (cis-**2e**) and (±)-(4S,6S)-6-(4-Nitrophenyl)-2-trichloromethyl-4-vinyl-5,6-dihydro-4H-1,3-oxazine (trans-**2e**).*



The mixture of diastereomers ($R_f \approx$ 0.3, PE/EA 10:1) (67.1 mg, 95%, *dr* 3.6:1) was obtained following Typical Procedure C on a 0.20 mmol

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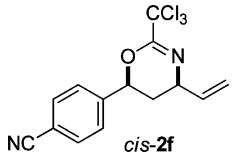
scale as a colorless oil and then separated by flash chromatography on silica gel (1% Et_3N in PE/ethyl ether 3:1) to afford the pure diastereomers *cis*-**2e** and *trans*-**2e**.

Data for *cis*-**2e**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 8.8 Hz, 2H), 7.58 (dd, J = 0.8, 8.8 Hz, 2H), 5.98 (ddd, J = 5.2, 10.4, 17.2 Hz, 1H), 5.49 (dd, J = 2.8, 12.0 Hz, 1H), 5.42 (ddd, J = 1.2, 1.2, 17.2 Hz, 1H), 5.24 (ddd, J = 1.2, 1.2, 10.4 Hz, 1H), 4.41−4.33 (m, 1H), 2.41 (ddd, J = 3.2, 4.8, 14.0 Hz, 1H), 1.64 (ddd, J = 11.6, 11.6, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.0, 148.0, 145.9, 137.4, 126.4, 124.1, 116.0, 92.1, 77.6, 55.3, 35.4; HRMS (TOF EI) calcd for $C_{13}H_{11}O_3N_2Cl_3$ $[M]^+$ 347.9835, found 347.9829.

Data for *trans*-**2e**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, J = 8.8 Hz, 2H), 7.55 (dd, J = 0.4, 8.8 Hz, 2H), 6.02 (ddd, J = 4.8, 10.4, 17.2 Hz, 1H), 5.42−5.35 (m, 2H), 5.20 (ddd, J = 1.2, 1.6, 17.2 Hz, 1H), 4.48−4.38 (m, 1H), 2.12 (ddd, J = 3.6, 3.6, 14.0 Hz, 1H), 2.03 (ddd, J = 5.2, 10.0, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 147.9, 146.1, 137.1, 126.3, 124.1, 117.9, 92.1, 74.1, 52.8, 33.1; HRMS (TOF EI) calcd for $C_{13}H_{11}O_3N_2Cl_3$ $[M]^+$ 347.9835, found 347.9836.

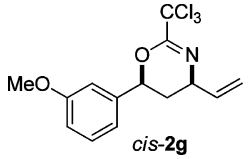
*(±)-4-((4R,6S)-2-Trichloromethyl-4-vinyl-5,6-dihydro-4H-1,3-oxazin-6-yl)benzonitrile (cis-**2f**).*



cis-**2f**

The mixture of diastereomers (R_f = 0.5, PE/EA 10:1) (56.3 mg, 84%, *dr* 4.0:1) was obtained following Typical Procedure C on a 0.20 mmol scale as a colorless oil. Data for the major diastereomer *cis*-**2f**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.4 Hz, 2H), 7.52 (d, J = 8.4 Hz, 2H), 5.97 (ddd, J = 5.2, 10.4, 17.2 Hz, 1H), 5.43 (dd, J = 2.8, 12.0 Hz, 1H), 5.41 (ddd, J = 1.6, 1.6, 17.2 Hz, 1H), 5.23 (ddd, J = 1.6, 1.6, 10.4 Hz, 1H), 4.39−4.29 (m, 1H), 2.38 (ddd, J = 2.8, 4.4, 14.0 Hz, 1H), 1.61 (ddd, J = 11.6, 11.6, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (selected peaks) δ 153.0, 144.0, 137.5, 132.7, 126.2, 118.3, 115.9, 112.5, 92.1, 77.8, 55.3, 35.4; HRMS (TOF EI) calcd for $C_{14}H_{11}ON_2Cl_3$ $[M]^+$ 327.9937, found 327.9947.

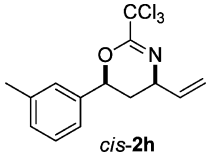
*(±)-(4R,6S)-6-(3-Methoxyphenyl)-2-trichloromethyl-4-vinyl-5,6-dihydro-4H-1,3-oxazine (cis-**2g**).*



cis-**2g**

The mixture of diastereomers (R_f = 0.5, PE/EA 20:1) (60.5 mg, 87%, *dr* 7.2:1) was obtained following Typical Procedure C on a 0.20 mmol scale as a pale-yellow oil. Data for the major diastereomer *cis*-**2g**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (t, J = 8.4 Hz, 1H), 6.99−6.86 (m, 3H), 5.99 (ddd, J = 5.2, 10.4, 17.2 Hz, 1H), 5.41 (ddd, J = 1.6, 1.6, 17.2 Hz, 1H), 5.35 (dd, J = 2.8, 11.6 Hz, 1H), 5.21 (ddd, J = 1.6, 1.6, 10.4 Hz, 1H), 4.37−4.28 (m, 1H), 3.82 (s, 3H), 2.35 (ddd, J = 2.8, 4.4, 14.0 Hz, 1H), 1.67 (ddd, J = 11.6, 11.6, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (selected peaks) δ 159.9, 153.7, 140.6, 138.0, 129.8, 117.8, 115.5, 113.9, 111.3, 92.4, 78.8, 55.5, 55.2, 35.7; HRMS (Orbitrap ESI) calcd for $C_{14}H_{15}O_2NCl_3$ $[M + H]^+$ 334.0163, found 334.0163.

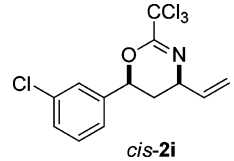
*(±)-(4R,6S)-6-(m-Tolyl)-2-trichloromethyl-4-vinyl-5,6-dihydro-4H-1,3-oxazine (cis-**2h**).*



cis-**2h**

The mixture of diastereomers (R_f = 0.5, PE/EA 20:1) (61.8 mg, 90%, *dr* 7.4:1) was obtained following Typical Procedure C on a 0.21 mmol scale as a pale-yellow oil. Data for the major diastereomer *cis*-**2h**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (t, J = 8.0 Hz, 1H), 7.23−7.14 (m, 3H), 5.99 (ddd, J = 5.2, 10.4, 16.8 Hz, 1H), 5.41 (ddd, J = 1.6, 2.8, 17.2 Hz, 1H), 5.33 (dd, J = 2.8, 12.0 Hz, 1H), 5.21 (dd, J = 0.8, 10.4 Hz, 1H), 4.38−4.28 (m, 1H), 2.39 (s, 3H), 2.34 (ddd, J = 2.8, 4.4, 14.0 Hz, 1H), 1.69 (ddd, J = 11.6, 11.6, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (selected peaks) δ 153.8, 138.9, 138.5, 138.1, 129.3, 128.7, 126.3, 122.7, 115.4, 92.4, 79.1, 55.6, 35.7, 21.5; HRMS (Orbitrap ESI) calcd for $C_{14}H_{15}ONCl_3$ $[M + H]^+$ 318.0214, found 318.0214.

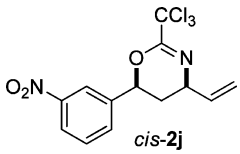
*(±)-(4R,6S)-6-(3-Chlorophenyl)-2-trichloromethyl-4-vinyl-5,6-dihydro-4H-1,3-oxazine (cis-**2i**).*



cis-**2i**

The mixture of diastereomers (R_f = 0.5, PE/EA 20:1) (60.8 mg, 87%, *dr* 6.7:1) was obtained following Typical Procedure C on a 0.20 mmol scale as a colorless oil. Data for the major diastereomer *cis*-**2i**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.31 (m, 3H), 7.30−7.26 (m, 1H), 5.98 (ddd, J = 5.2, 10.4, 17.2 Hz, 1H), 5.41 (ddd, J = 1.6, 1.6, 17.2 Hz, 1H), 5.34 (dd, J = 2.8, 11.6 Hz, 1H), 5.22 (ddd, J = 1.6, 1.6, 10.4 Hz, 1H), 4.37−4.28 (m, 1H), 2.35 (ddd, J = 2.8, 4.4, 14.0 Hz, 1H), 1.65 (ddd, J = 11.6, 11.6, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (selected peaks) δ 153.4, 140.9, 137.8, 134.7, 130.1, 128.8, 125.8, 123.7, 115.7, 92.2, 78.1, 55.4, 35.6; HRMS (Orbitrap ESI) calcd for $C_{13}H_{12}ONCl_4$ $[M + H]^+$ 337.9668, found 337.9669.

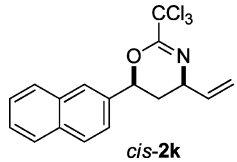
*(±)-(4R,6S)-6-(3-Nitrophenyl)-2-trichloromethyl-4-vinyl-5,6-dihydro-4H-1,3-oxazine (cis-**2j**).*



cis-**2j**

The mixture of diastereomers (R_f = 0.4, PE/EA 5:1) (68.0 mg, 89%, *dr* 6.0:1) was obtained following Typical Procedure C on a 0.21 mmol scale as a colorless oil. Data for the major diastereomer *cis*-**2j**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31−8.19 (m, 2H), 7.76 (d, J = 7.6 Hz, 1H), 7.62 (t, J = 8.0 Hz, 1H), 5.99 (ddd, J = 5.2, 10.4, 17.2 Hz, 1H), 5.49 (dd, J = 2.8, 11.6 Hz, 1H), 5.43 (ddd, J = 1.6, 1.6, 17.2 Hz, 1H), 5.24 (ddd, J = 1.6, 1.6, 10.4 Hz, 1H), 4.42−4.32 (m, 1H), 2.43 (ddd, J = 2.8, 4.4, 14.0 Hz, 1H), 1.68 (ddd, J = 11.6, 11.6, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (selected peaks) δ 153.0, 148.5, 141.1, 137.4, 131.5, 130.0, 123.6, 120.8, 116.0, 92.1, 77.6, 55.3, 35.5; HRMS (Orbitrap ESI) calcd for $C_{13}H_{12}O_3N_2Cl_3$ $[M + H]^+$ 348.9908, found 348.9907.

*(±)-(4R,6S)-6-(Naphthalen-2-yl)-2-trichloromethyl-4-vinyl-5,6-dihydro-4H-1,3-oxazine (cis-**2k**).*

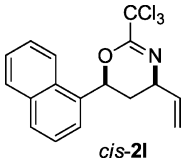


cis-**2k**

The mixture of diastereomers (R_f = 0.5, PE/EA 20:1) (59.1 mg, 87%, *dr* 6.7:1) was obtained following Typical Procedure C on a 0.19 mmol scale as a pale-yellow oil. Data for the major diastereomer *cis*-**2k**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94−7.84 (m, 4H), 7.55−7.47 (m, 3H), 6.02 (ddd, J = 5.2, 10.4, 16.8 Hz, 1H), 5.54 (dd, J = 2.4, 11.6 Hz, 1H), 5.43 (ddd, J = 1.6, 1.6, 17.2 Hz, 1H), 5.23 (ddd, J = 1.2, 1.2, 10.4 Hz, 1H), 4.44−4.34 (m, 1H), 2.44 (ddd, J = 2.8, 4.4, 14.0 Hz, 1H), 1.79 (ddd, J = 11.6, 11.6, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (selected peaks) δ 153.8, 138.1, 136.2, 133.3, 133.1, 128.8, 128.1, 127.8, 126.53, 126.49, 125.0, 123.2, 115.6, 92.5, 79.2, 55.6, 35.6; HRMS (Orbitrap ESI) calcd for $C_{17}H_{15}ONCl_3$ $[M + H]^+$ 354.0214, found 354.0220.

dx.doi.org/10.1021/jo402681z | J. Org. Chem. 2014, 79, 1289−1302

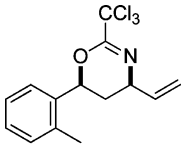
*(±)-(4R,6S)-6-(Naphthalen-1-yl)-2-trichloromethyl-4-vinyl-5,6-dihydro-4H-1,3-oxazine (cis-**2l**).*



cis-**2l**

The mixture of diastereomers (R_f = 0.5, PE/EA 20:1) (57.4 mg, 86%, *dr* 16.9:1) was obtained following Typical Procedure C on a 0.20 mmol scale as a pale-yellow oil. Data for the major diastereomer *cis*-**2l**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03−7.84 (m, 3H), 7.69 (dd, *J* = 0.8, 7.2 Hz, 1H), 7.61−7.49 (m, 3H), 6.12 (dd, *J* = 2.4, 11.6 Hz, 1H), 6.02 (ddd, *J* = 5.2, 10.4, 16.8 Hz, 1H), 5.44 (ddd, *J* = 1.2, 1.2, 17.2 Hz, 1H), 5.23 (ddd, *J* = 1.2, 1.2, 10.4 Hz, 1H), 4.54−4.42 (m, 1H), 2.59 (ddd, *J* = 2.8, 4.8, 14.4 Hz, 1H), 1.85 (ddd, *J* = 11.2, 11.2, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (selected peaks) δ 153.9, 138.0, 134.2, 133.7, 129.8, 129.2, 129.1, 126.6, 125.9, 125.5, 123.3, 122.3, 115.6, 92.5, 76.4, 55.9, 34.7; HRMS (TOF EI) calcd for $C_{17}H_{14}ONCl_3$ $[M]^+$ 353.0141, found 353.0153.

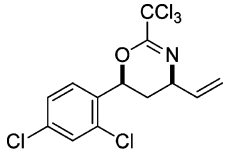
*(±)-(4R,6S)-6-(o-Tolyl)-2-trichloromethyl-4-vinyl-5,6-dihydro-4H-1,3-oxazine (cis-**2m**).*



cis-**2m**

The mixture of diastereomers (R_f = 0.4, PE/EA 20:1) (59.4 mg, 93%, *dr* >20:1) was obtained following Typical Procedure C on a 0.20 mmol scale as a colorless oil. Data for the major diastereomer *cis*-**2m**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.31 (m, 1H), 7.24−7.17 (m, 2H), 7.16−7.09 (m, 1H), 5.93 (ddd, *J* = 5.2, 10.4, 17.2 Hz, 1H), 5.48 (dd, *J* = 2.4, 11.6 Hz, 1H), 5.34 (ddd, *J* = 1.2, 1.2, 16.8 Hz, 1H), 5.14 (ddd, *J* = 1.2, 1.2, 10.4 Hz, 1H), 4.33−4.22 (m, 1H), 2.32 (s, 3H), 2.25 (ddd, *J* = 2.8, 4.8, 14.4 Hz, 1H), 1.61 (ddd, *J* = 11.2, 11.2, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) (selected peaks) δ 154.0, 138.1, 136.8, 134.7, 130.7, 128.5, 126.6, 125.4, 115.5, 92.4, 76.3, 55.8, 34.0, 19.0; HRMS (Orbitrap ESI) calcd for $C_{14}H_{15}ONCl_3$ $[M + H]^+$ 318.0214, found 318.0216.

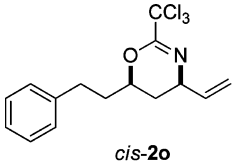
*(±)-(4R,6S)-6-(2,4-Dichlorophenyl)-2-trichloromethyl-4-vinyl-5,6-dihydro-4H-1,3-oxazine (cis-**2n**).*



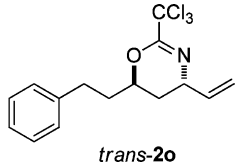
cis-**2n**

The mixture of diastereomers (R_f = 0.5, PE/EA 40:1) (70.6 mg, 92%, *dr* >20:1) was obtained following Typical Procedure C on a 0.20 mmol scale as a colorless oil. Data for the major diastereomer *cis*-**2n**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.4 Hz, 1H), 7.42 (d, *J* = 2.0 Hz, 1H), 7.34 (dd, *J* = 2.0, 8.4 Hz, 1H), 5.98 (ddd, *J* = 4.8, 10.4, 16.8 Hz, 1H), 5.68 (dd, *J* = 2.8, 11.6 Hz, 1H), 5.42 (ddd, *J* = 1.6, 1.6, 17.2 Hz, 1H), 5.22 (ddd, *J* = 1.2, 1.2, 10.4 Hz, 1H), 4.41−4.30 (m, 1H), 2.51 (ddd, *J* = 2.8, 4.8, 14.0 Hz, 1H), 1.44 (ddd, *J* = 11.2, 11.2, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.1, 137.6, 135.4, 134.8, 131.9, 129.4, 128.0, 127.7, 115.8, 92.2, 75.5, 55.3, 33.7; HRMS (Orbitrap ESI) calcd for $C_{13}H_{11}ONCl_3{}^{37}Cl_2$ $[M + H]^+$ 375.9219, found 375.9215.

*(±)-(4R,6R)-6-Phenethyl-2-trichloromethyl-4-vinyl-5,6-dihydro-4H-1,3-oxazine (cis-**2o**) and (±)-(4S,6R)-6-Phenethyl-2-trichloromethyl-4-vinyl-5,6-dihydro-4H-1,3-oxazine (trans-**2o**).*



cis-**2o**



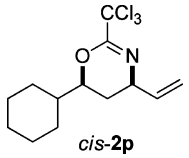
trans-**2o**

The mixture of diastereomers ($R_f \approx$ 0.4, PE/EA 20:1) (55.1 mg, 77%, *dr* 2.3:1) was obtained following Typical Procedure C on a 0.21 mmol scale as a colorless oil.

Data for *cis*-**2o**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.27 (m, 2H), 7.25−7.18 (m, 3H), 5.94 (ddd, *J* = 5.6, 10.4, 17.2 Hz, 1H), 5.35 (ddd, *J* = 1.6, 1.6, 17.2 Hz, 1H), 5.18 (ddd, *J* = 1.2, 1.2, 10.4 Hz, 1H), 4.32−4.22 (m, 1H), 4.16−4.06 (m, 1H), 2.93−2.76 (m, 2H), 2.14−2.03 (m, 2H), 2.02−1.87 (m, 1H), 1.45 (ddd, *J* = 14.0, 11.6, 11.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 140.8, 138.4, 128.6, 128.5, 126.2, 115.2, 92.5, 76.3, 55.3, 36.7, 33.1, 30.6; HRMS (Orbitrap ESI) calcd for $C_{15}H_{17}ONCl_3$ $[M + H]^+$ 332.0370, found 332.0368.

Data for *trans*-**2o**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33−7.27 (m, 2H), 7.25−7.16 (m, 3H), 5.89 (ddd, *J* = 4.8, 10.4, 17.2 Hz, 1H), 5.23 (ddd, *J* = 1.2, 1.2, 10.4 Hz, 1H), 5.10 (ddd, *J* = 1.2, 1.2, 17.2 Hz, 1H), 4.40−4.32 (m, 1H), 4.31−4.20 (m, 1H), 2.93−2.83 (m, 1H), 2.83−2.73 (m, 1H), 2.13−2.01 (m, 1H), 1.96−1.85 (m, 1H), 1.85−1.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 140.9, 138.0, 128.52, 128.47, 126.2, 116.7, 92.6, 73.2, 52.9, 36.4, 30.9, 30.6; HRMS (Orbitrap ESI) calcd for $C_{15}H_{17}ONCl_3$ $[M + H]^+$ 332.0370, found 332.0374.

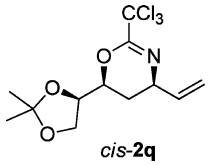
*(±)-(4R,6S)-6-Cyclohexyl-2-trichloromethyl-4-vinyl-5,6-dihydro-4H-1,3-oxazine (cis-**2p**).*



cis-**2p**

The mixture of diastereomers (R_f = 0.4, PE/EA 20:1) (46.1 mg, 82%, *dr* 10.5:1) was obtained following Typical Procedure C on a 0.18 mmol scale as a colorless oil. Data for the major diastereomer *cis*-**2p**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95 (ddd, *J* = 5.6, 10.4, 17.2 Hz, 1H), 5.36 (ddd, *J* = 1.6, 1.6, 17.2 Hz, 1H), 5.17 (ddd, *J* = 1.6, 1.6, 10.4 Hz, 1H), 4.17−4.05 (m, 2H), 2.07 (ddd, *J* = 2.8, 4.8, 13.6 Hz, 1H), 1.94 (d, *J* = 12.4 Hz, 1H), 1.81−1.59 (m, 5H), 1.42 (ddd, *J* = 11.6, 11.6, 14.0 Hz, 1H), 1.35−1.04 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.2, 138.7, 115.1, 92.6, 81.9, 55.5, 42.0, 30.1, 28.0, 27.8, 26.3, 25.9, 25.8; HRMS (Orbitrap ESI) calcd for $C_{13}H_{19}ONCl_3$ $[M + H]^+$ 310.0527, found 310.0528.

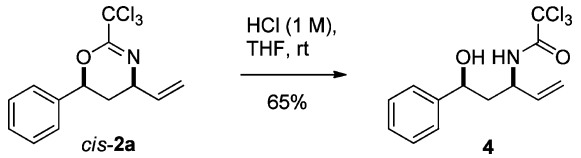
*(4R,6S)-6-((R)-2,2-Dimethyl-1,3-dioxolan-4-yl)-2-trichloromethyl-4-vinyl-5,6-dihydro-4H-1,3-oxazine (cis-**2q**).*



cis-**2q**

The mixture of diastereomers (R_f = 0.2, PE/EA 20:1) (44.2 mg, 79%, *dr* 4.0:1) was obtained following Typical Procedure C on a 0.17 mmol scale as a colorless oil. Data for the major diastereomer *cis*-**2q**: $[\alpha]_D^{25}$ = +13.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.97 (ddd, *J* = 5.2, 10.4, 17.2 Hz, 1H), 5.38 (ddd, *J* = 1.2, 1.2, 17.2 Hz, 1H), 5.20 (ddd, *J* = 1.2, 1.2, 10.4 Hz, 1H), 4.30−4.22 (m, 1H), 4.21−4.01 (m, 4H), 2.35 (ddd, *J* = 2.8, 4.8, 14.0 Hz, 1H), 1.45 (s, 3H), 1.43−1.38 (m, 1H), 1.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) (selected peaks) δ 152.8, 138.1, 115.4, 110.1, 92.1, 77.4, 76.8, 66.2, 54.7, 29.9, 26.7, 25.2; HRMS (Orbitrap ESI) calcd for $C_{12}H_{16}O_3NCl_3Na$ $[M + Na]^+$ 350.0088, found 350.0084.

Compound 4.



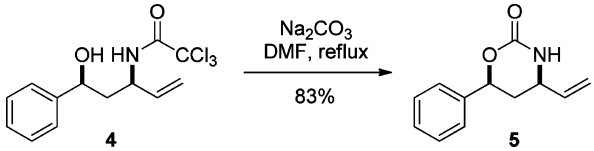
cis-**2a** **4**

To a solution of *cis*-**2a** (152 mg, 0.1 mmol) in THF (5 mL) was added 1 M HCl (5 mL), and the mixture was stirred at room temperature until complete consumption of *cis*-**2a** as monitored by TLC analysis (~1 h). The resulting mixture was extracted with EtOAc, and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography on silica

dx.doi.org/10.1021/jo402681z | J. Org. Chem. 2014, 79, 1289−1302

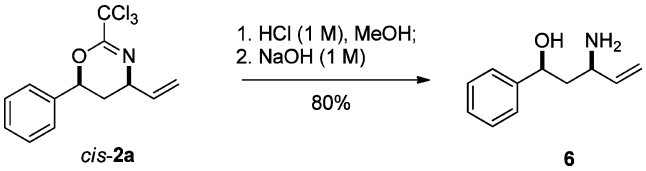
gel (PE/EA 5:1) to afford **4** (103 mg, 65%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.28 (m, 5H), 7.23 (br s, 1H), 5.83 (ddd, J = 5.6, 10.4, 17.2 Hz, 1H), 5.28 (ddd, J = 0.8, 1.2, 17.2 Hz, 1H), 5.22 (ddd, J = 1.2, 1.6, 10.4 Hz, 1H), 4.85 (dd, J = 4.4, 8.4 Hz, 1H), 4.60−4.49 (m, 1H), 2.14 (ddd, J = 8.4, 8.4, 14.4 Hz, 1H), 2.04 (ddd, J = 4.4, 5.6, 14.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 143.8, 136.2, 128.8, 128.1, 125.7, 116.3, 92.7, 72.5, 52.7, 42.8; HRMS (Orbitrap ESI) calcd for $C_{13}H_{14}O_2NCl_3Na$ $[M + Na]^+$ 343.9982, found 343.9984.

Compound 5.



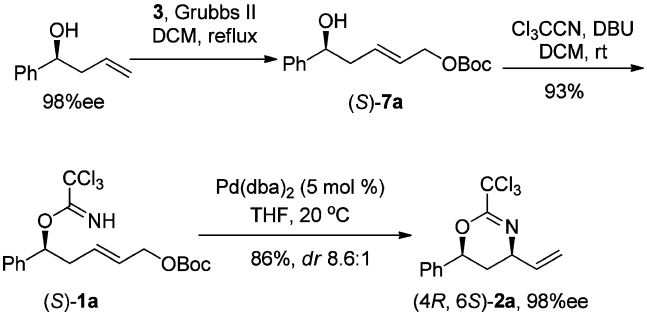
A mixture of Na_2CO_3 (21 mg, 0.2 mmol, 2.0 equiv) and **4** (32.2 mg, 0.1 mmol) in DMF (1 mL) was heated at reflux for 3 h and then cooled to room temperature. The mixture was diluted with ethyl acetate (30 mL) and washed with water three times. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography on silica gel (PE/EA 1:1) to afford **5** (16.5 mg, 83%) as a white solid. Mp 141−142 °C (PE/EA); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.30 (m, 5H), 5.77 (ddd, J = 7.2, 10.0, 17.2 Hz, 1H), 5.66 (s, 1H), 5.38−5.27 (m, 2H), 5.23 (d, J = 10.4 Hz, 1H), 4.18 (ddd, J = 4.8, 7.2, 11.6 Hz, 1H), 2.29−2.21 (m, 1H), 1.86 (ddd, J = 11.6, 11.6, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 138.6, 136.9, 128.6, 128.5, 125.8, 117.7, 78.2, 54.0, 36.2; HRMS (TOF EI) calcd for $C_{12}H_{13}NO_2$ $[M]^+$ 203.0946, found 203.0942.

Compound 6.



To a solution of *cis*-**2a** (30.4 mg, 0.1 mmol) in methanol (1 mL) was added 1 M HCl (1 mL), and the mixture was stirred until complete consumption of the starting material as monitored by TLC analysis (~1 h). After the mixture was cooled to 0 °C using an ice bath, 1 M NaOH (2 mL) was added, and the resulting mixture was stirred at room temperature overnight. The mixture was extracted with DCM three times, and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography on a short silica gel column (DCM/MeOH 10:1) to afford free amino alcohol **6** (14.1 mg, 80%) as a colorless oil. ^{1}H NMR (400 MHz, MeOH-d_4) δ 7.40−7.28 (m, 4H), 7.28−7.19 (m, 1H), 5.85 (ddd, J = 7.2, 10.4, 17.2 Hz, 1H), 5.21 (ddd, J = 1.2, 1.2, 17.2 Hz, 1H), 5.11 (ddd, J = 0.8, 1.2, 10.4 Hz, 1H), 4.73 (dd, J = 3.6, 9.6 Hz, 1H), 3.60−3.51 (m, 1H), 1.84 (ddd, J = 6.8, 9.6, 14.0 Hz, 1H), 1.72 (ddd, J = 4.0, 6.8, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, MeOH-d_4) δ 146.6, 142.6, 129.4, 128.3, 126.8, 115.3, 73.6, 53.9, 46.8; HRMS (Orbitrap ESI) calcd for $C_{11}H_{16}ON$ $[M + H]^+$ 178.1226, found 178.1226.

Synthesis of Enantiopure (4*R*,6*S*)-2a from (*S*)-1-Phenylbut-3-en-1-ol.



Under nitrogen, Grubbs second-generation catalyst (19 mg, 0.03 mmol, 0.02 equiv) was added to a solution of (*S*)-1-phenylbut-3-en-1-ol (218 mg, 1.47 mmol, 1.0 equiv) and (*Z*)-but-2-ene-1,4-diyl di-*tert*-butyl dicarbonate (**3**) (850 mg, 2.95 mmol, 2.0 equiv) in 10 mL of anhydrous CH_2Cl_2, and the resulting mixture was refluxed overnight. After the mixture was cooled, the solvent was removed by evaporation, and the residue was purified by flash chromatography on silica gel (PE/EA 10:1−5:1) to afford (*S*,*E*)-*tert*-butyl (5-hydroxy-5-phenylpent-2-en-1-yl) carbonate [(*S*)-**7a**] (225 mg, 55%) as a viscous brown oil $\{[\alpha]_D^{25} = -36.3$ (c 1.0, $CHCl_3)\}$.

To a solution of alcohol (*S*)-**7a** (250 mg, 0.90 mmol) and Cl_3CCN (0.18 mL, 1.8 mmol) in dichloromethane (5 mL) was added DBU (27 mg, 0.18 mmol), and the mixture was stirred at room temperature overnight. After removal of solvent in vacuo, the residue was purified by flash chromatography on silica gel (1% Et_3N in PE/EA 20:1) to afford (*S*,*E*)-5-((*tert*-butoxycarbonyl)oxy)-1-phenylpent-3-en-1-yl 2,2,2-trichloroacetimidate [(*S*)-**1a**] (355 mg, 93%) as a yellow oil $\{[\alpha]_D^{25} = -27.2$ (c 1.0, $CHCl_3)\}$.

Under nitrogen, $Pd(dba)_2$ (23 mg, 0.04 mmol, 0.05 equiv) was added to a solution of trichloroacetimidate (*S*)-**1a** (324 mg, 0.8 mmol) in anhydrous THF (8 mL), and the mixture was stirred at 20 °C for 2.5 days. The mixture was filtered through Celite, and the filtrate was concentrated. The residue was purified by flash chromatography on a short silica gel column (1% Et_3N in PE/EA 40:1) to afford a mixture of diastereomers (combined yield 201 mg, 86%; *dr* 8.5:1) as a colorless oil.

This mixture of diastereomers was separated by flash chromatography on silica gel (1% Et_3N in PE/toluene 1:2) to afford the pure enantiomer (4*R*,6*S*)-6-phenyl-2-trichloromethyl-4-vinyl-5,6-dihydro-4*H*-1,3-oxazine [(4*R*,6*S*)-**2a**, *cis*-**2a**] as a white solid with 98% ee as determined by HPLC [Daicel Chiralcel OD-H column, *i*-PrOH/hexane 1:99, flow rate 0.7 mL/min, t_R = 11.9 min for the (4*R*,6*S*) isomer (major) and 12.4 min for the (4*S*,6*R*) isomer (minor)]. Mp 74−75 °C (PE/EA); $[\alpha]_D^{25} = -69.2$ (c 1.0, $CHCl_3$).

■ ASSOCIATED CONTENT

Supporting Information

CIF file for *cis*-**2a**, NOESY spectra for *cis*- and *trans*-**2a**, and ^{1}H and ^{13}C NMR spectra for all 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 natural products containing 1,3-amino alcohol moieties, see: (a) Pinder, A. R. *Nat. Prod. Rep.* **1992**, *9*, 491. (b) Plunkett, A. O. *Nat. Prod. Rep.* **1994**, *11*, 581. (c) Bates, R. W.; Sa-Ei, K. *Tetrahedron* **2002**, *58*, 5957. (d) Hamada, M.; Takeuchi, T.; Kondo, S.; Ikeda, Y.; Naganawa, H.; Maeda, K.; Okami, Y.; Umezawa, H. *J. Antibiot.* **1970**, *23*, 170. (e) Kondo, S.; Shibahara, S.; Takahashi, S.; Maeda, K.; Umezawa, H.; Ohno, M. *J. Am. Chem. Soc.* **1971**, *93*, 6305. For HPA-12, a ceramide-trafficking inhibitor containing a 1,3-amino alcohol moiety, see: (f) Yasuda, S.; Kitagawa, H.; Ueno, M.; Ishitani, H.; Fukasawa, M.; Nishijima, M.; Kobayashi, S.; Hanada, K. *J. Biol. Chem.* **2001**, *276*, 43994.

(2) Lait, S. M.; Rankic, D. A.; Keay, B. A. *Chem. Rev.* **2007**, *107*, 767.

(3) (a) List, B. *J. Am. Chem. Soc.* **2000**, *122*, 9336. (b) Wenzel, A. G.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 12964. (c) Josephsohn, N. S.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004**, *126*, 3734. (d) Matsunaga, S.; Yoshid, T.; Morimoto, H.; Kumagai, N.; Shibasaki, M. *J. Am. Chem. Soc.* **2004**, *126*, 8777. (e) Westermann, B.; Neuhaus, C. *Angew. Chem., Int. Ed.* **2005**, *44*, 4077. (f) Enders, D.; Grondal, C.; Vrettou, M.; Raabe, G. *Angew. Chem., Int. Ed.* **2005**, *44*, 4079. (g) Chen, Y. K.; Yoshida, M.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2006**, *128*, 9328. (h) Fustero, S.; Jimenéz, D.; Moscardó, J.; Catalán, S.; del Pozo, C. *Org. Lett.* **2007**, *9*, 5283. (i) Millet, R.; Träff, A. M.; Petrus, M. L.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **2010**, *132*, 15182. (j) Ueno, M.; Huang, Y.; Yamano, A.; Kobayashi, S. *Org. Lett.* **2013**, *15*, 2869.

(4) (a) Kochi, T.; Tang, T. P.; Ellman, J. A. *J. Am. Chem. Soc.* **2002**, *124*, 6518. (b) Kochi, T.; Tang, T. P.; Ellman, J. A. *J. Am. Chem. Soc.* **2003**, *125*, 11276.

(5) Aschwanden, P.; Kværnø, L.; Geisser, R. W.; Kleinbeck, F.; Carreira, E. M. *Org. Lett.* **2005**, *7*, 5741.

(6) (a) Roizen, J. L.; Harvey, M. E.; Du Bois, J. *Acc. Chem. Res.* **2012**, *45*, 911. (b) Espino, C. G.; When, P. M.; Chow, J.; Du Bois, J. *J. Am. Chem. Soc.* **2001**, *123*, 6935. (c) Zalatan, D. N.; Du Bois, J. *J. Am. Chem. Soc.* **2008**, *130*, 9220. (d) Williams Fiori, K.; Espino, C. G.; Brodsky, B. H.; Du Bois, J. *Tetrahedron* **2009**, *65*, 3042. (e) Milczek, E.; Boudet, N.; Blakey, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 6825. (f) Liang, J.; Yuan, S.; Huang, J.; Yu, W.; Che, C. *Angew. Chem., Int. Ed.* **2002**, *41*, 3465. (g) Liu, Y.; Guan, X.; Wong, E. L.; Liu, P.; Huang, J.; Che, C. *J. Am. Chem. Soc.* **2013**, *135*, 7194.

(7) (a) Rice, G. T.; White, M. C. *J. Am. Chem. Soc.* **2009**, *131*, 11707. (b) Paradine, S. M.; White, M. C. *J. Am. Chem. Soc.* **2012**, *134*, 2036. (c) Qi, X.; Rice, G. T.; Lall, M. S.; Plummer, M. S.; White, M. C. *Tetrahedron* **2010**, *66*, 4816. (d) Nahra, F.; Liron, F.; Prestat, G.; Mealli, C.; Messaoudi, A.; Poli, G. *Chem.—Eur. J.* **2009**, *15*, 11078.

(8) For related studies, see: (a) Broustal, G.; Ariza, X.; Campagne, J.-M.; Garcia, J.; Georges, Y.; Marinetti, A.; Robiette, R. *Eur. J. Org. Chem.* **2007**, 4293. (b) Tamaru, Y.; Bando, T.; Kawamura, Y.; Okamura, K.; Yoshida, Z. *J. Chem. Soc., Chem. Commun.* **1992**, 1498. (c) Overman, L. E.; Remarchuk, T. P. *J. Am. Chem. Soc.* **2002**, *124*, 12. (d) Trost, B. M.; Sudhakar, A. R. *J. Am. Chem. Soc.* **1987**, *109*, 3792. (e) Trost, B. M.; Van Vranken, D. L.; Bingel, C. *J. Am. Chem. Soc.* **1992**, *114*, 9327.

(9) Hermann, A. T.; Saito, T.; Stivala, C. E.; Tom, J.; Zakarian, A. *J. Am. Chem. Soc.* **2010**, *132*, 5962.

(10) (a) Wang, L.; Menche, D. *Angew. Chem., Int. Ed.* **2012**, *51*, 9425. (b) Morgen, M.; Bretzke, S.; Li, P.; Menche, D. *Org. Lett.* **2010**, *12*, 4494.

(11) Tang, B.; Wang, L.; Menche, D. *Synlett* **2013**, *24*, 625.

(12) (a) Lee, K. Y.; Kim, Y. H.; Park, M. S.; Oh, C. Y.; Ham, W. H. *J. Org. Chem.* **1999**, *64*, 9450. (b) Butler, D. C.; Inman, G. A.; Alper, H. *J. Org. Chem.* **2000**, *65*, 5887. (c) Amador, M.; Ariza, X.; Garcia, J.; Sevilla, S. *Org. Lett.* **2002**, *4*, 4511. (d) Welter, C.; Dahnz, A.; Brunner, B.; Streiff, S.; Dübon, P.; Helmchen, G. *Org. Lett.* **2005**, *7*, 1239. (e) Trost, B. M.; Machacek, M. R.; Faulk, B. D. *J. Am. Chem. Soc.* **2006**, *128*, 6745.

(13) For cyclization reactions using trichloroacetimidates, see: (a) Bongini, A.; Cardillo, G.; Orena, M.; Sandri, S.; Tomasini, C. *J. Org. Chem.* **1986**, *51*, 4905. (b) Kang, J.-E.; Kim, H.-B.; Lee, J.-W.; Shin, S. *Org. Lett.* **2006**, *8*, 3537. (c) Matsushima, Y.; Kino, J. *Tetrahedron* **2008**, *64*, 3943. (d) Maleckis, A.; Klimovica, K.; Jirgensons, A. *J. Org. Chem.* **2010**, *75*, 7897. (e) Klimovica, K.; Grigorjeva, L.; Maleckis, A.; Popelis, J.; Jirgensons, A. *Synlett* **2011**, 2849. (f) Grigorjeva, L.; Jirgensons, A. *Eur. J. Org. Chem.* **2011**, 2421. (g) Wong, V. H.; Hor, T. S.; Hii, K. K. *Chem. Commun.* **2013**, *49*, 9272. (h) Brindle, C. S.; Yeung, C. S.; Jacobsen, E. N. *Chem. Sci.* **2013**, *4*, 2100.

(14) (a) Overman, L. E. *J. Am. Chem. Soc.* **1974**, *96*, 597. (b) Overman, L. E. *J. Am. Chem. Soc.* **1976**, *98*, 2901. (c) Overman, L. E.; Carpenter, N. E. *Org. React.* **2005**, *66*, 1.

(15) Wang, L.; Li, P.; Menche, D. *Angew. Chem., Int. Ed.* **2010**, *49*, 9270.

(16) CCDC 962965 contains the supplementary crystallographic data for complex *cis*-**2a**. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre.

(17) Our results suggest that additional ligands such as phosphite, phoshine, phosphoramide, and diene are detrimental to the reaction.

(18) The addition of phosphine or diene ligands greatly decreased the reaction rate or even inhibited the reaction. The rhodium catalyst $[Rh(COD)Cl]_2/P(OPh)_3$ failed to catalyze this transformation.

(19) Hough, L. *J. Chem. Soc.* **1935**, 3066.

(20) Nishikawa, T.; Urabe, D.; Tomita, M.; Tsujimoto, T.; Iwabuchi, T.; Isobe, M. *Org. Lett.* **2006**, *8*, 3263.

(21) Wang, L.; Menche, D. *J. Org. Chem.* **2012**, *77*, 10811.