JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

The Synthesis of Multifunctionalized 1,3-Oxazin-4-ones from Donor−Acceptor Cyclopropanes

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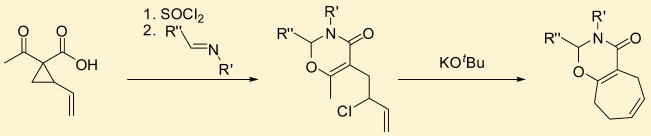
Supporting Information

ABSTRACT: A series of electronically diverse imines were found to readily react with various donor−acceptor cyclopropyl acid chlorides, with complete regioselectivity, to form 1,3-oxazin-4-ones in moderate yields (25−48% over two steps). Select oxazinones underwent a base induced rearrangement to afford the corresponding cycloheptene-fused oxazinones in good yields (up to 70%).



INTRODUCTION

The development of synthetic methods to gain access to novel substrates, or that improve access to known scaffolds, remains a key objective for many chemists. Recent structural analysis of all U.S. FDA approved pharmaceuticals showed that 59% of small-molecule drugs contain a nitrogen heterocycle.[1] Within the nitrogen-containing heterocycles, the most prevalent (21%) are six-membered saturated *N*-heterocycles with an additional heteroatom.[2]

Clearly synthetic methods which allow rapid access to such structures are of significant value. One such substructure is oxazinone, whose importance in medicine is well-documented,[3] and includes the clinically used drug ketazolam (Figure 1).[4]

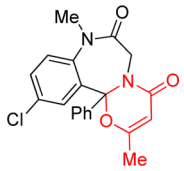


Figure 1. Clinically used ketazolam contains a 1,3-oxazin-4-one.

Despite this, access to the oxazinone scaffold has been hampered by the limited availability of synthetic methods. To date the most widely used approach involves the cycloaddition of imines to acyl ketenes, which are often generated *in situ*.[5] Recent literature describes a method to generate such acyl ketenes under mild reaction conditions[6] and has subsequently proved useful for the synthesis of oxazinones,[7] but the inherent electronic requirements of cycloaddition chemistry remain. Other methods to access 1,3-oxazin-4-ones include palladium-mediated carbonylations of α-diazo-β-dicarbonyl compounds[8] and condensation reactions between hydroxyl amides and various carbonyl-containing compounds.[9] These procedures often involve a large number of steps to construct precursors and have limited substrate scope. Therefore, there is a need for additional methods which complement existing strategies.

As part of our program looking at providing improved access to the medicinally relevant oxazinones, we recently described a procedure whereby the *in situ* generated *N*-acyl cyclopropyl iminium **3** readily undergoes nucleophilic ring opening by chloride to generate the corresponding oxazinone **4** in moderate to good yields (Scheme 1).[10]

This work looks to extend this methodology from acceptor cyclopropanes to donor−acceptor cyclopropane systems like that shown in Scheme 2, to provide access to new chemical space and building blocks. However, the question of regioselectivity would need to be addressed before embarking on such endeavors. That is, would the nucleophilic attack of chloride on the proposed *N*-acyl iminium cyclopropane intermediate **5** be regioselective (Scheme 2)?

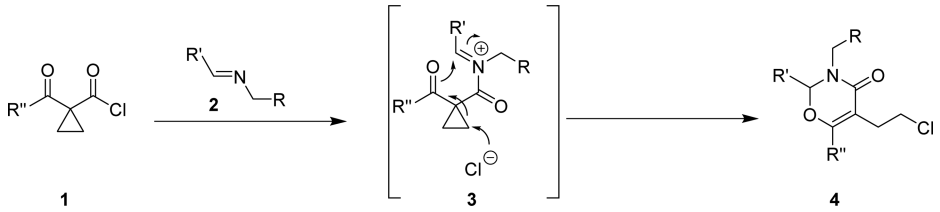
RESULTS AND DISCUSSION

In order to answer the question of regioselectivity, the donor−acceptor cyclopropane starting material **9** was prepared by hydrolysis of the corresponding ethyl ester.[11] Treatment of the carboxylic acid **9** with 1 equiv of thionyl chloride in dichloromethane provided the corresponding acid chloride which was not isolated but further diluted with dichloromethane before ethyl *N*-(diphenylmethylene) glycinate (**10**) was added (Scheme 3). After 2 h of stirring at room temperature, analysis of the TLC indicated complete consumption of the starting material. Furthermore, analysis of the proton NMR spectrum of the crude reaction mixture indicated the presence of only one isomer.[12] Following column chromatography, the oxazinone **11** was isolated in 32% yield over two steps. The structure of **11** was confirmed by X-ray crystallography as the isomer attributable to chloride attack at the vinyl-substituted carbon of the cyclopropane (Scheme 3). This result is consistent with the existing literature on nucleophilic additions to donor−acceptor cyclopropanes proceeding via an S_N1 like reaction mechanism.[13] Despite

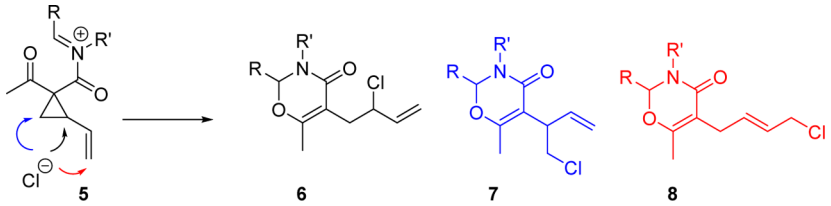
Received: January 17, 2016
Published: February 11, 2016

DOI: 10.1021/acs.joc.6b00112
J. Org. Chem. 2016, 81, 2099−2105

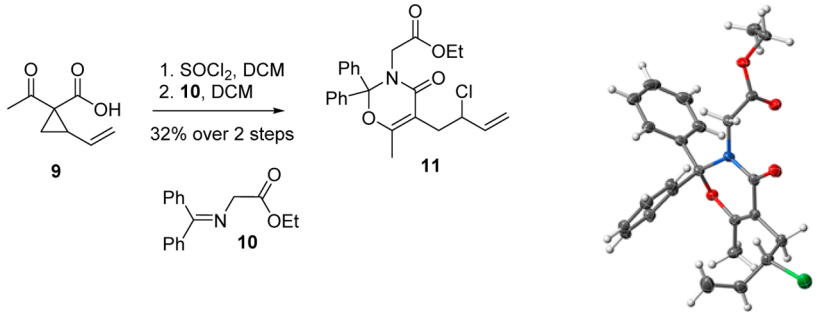
Scheme 1. Previously Reported Synthesis of 1,3-Oxazin-4-ones from 1,1-Disubstituted Acylcyclopropyl Acid Chloride



Scheme 2. Possible Reaction Outcomes from the Nucleophilic Attack of Chloride on the Vinylcyclopropyl Iminium Intermediate 5



Scheme 3. Synthesis of Oxazinone 11 and X-ray Single Crystal Structure (50% Ellipsoids)

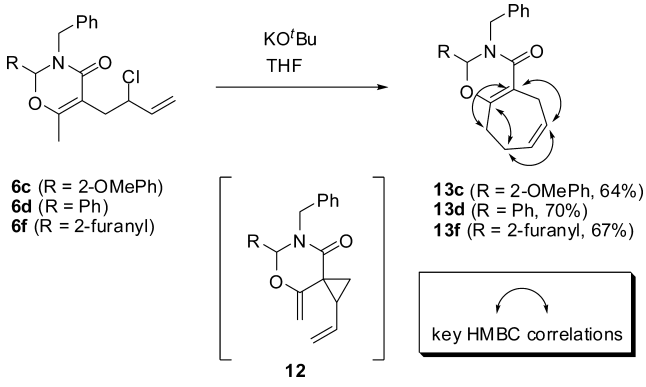


near-complete mass recovery, and relatively clean ^{1}H NMR spectra of the crude reaction mixtures,[12] significant loss in mass was observed upon chromatographic purification.

To further probe the reaction scope, a small series of electronically diverse imines **2a–g** were prepared (Table 1).[14] Under the reaction conditions outlined above, all imines were found to readily react with the vinyl cyclopropyl acid chloride, forming ~1:1 diastereomeric mixtures of the corresponding oxazinones **6a–g** as evident by analysis of the crude reaction mixture by proton NMR. Purification of the oxazinones via silica gel column chromatography in one case (**6e**) provided an enhanced diastereomeric ratio (2:1), presumably as a result of different stabilities of the diastereomers to the silica gel (Table 1, entry 5). Despite the modest yields for the transformation, the electronic nature of the imine does not appear to significantly impact the yield of the corresponding oxazinones (**6a–g**) obtained from electron-rich, *para*- and *ortho*-substituted aryl imines **2a**, **b**, and **c**, neutral **2d**, and an electron-poor aryl imine **2e**, as well as the heteroaromatic imine **2f** and the alkyl imine **2g**.

Access to functionalized vinyl cyclopropanes via cross metathesis[15] with various olefins was hampered by low yields and difficulty in isolating useful quantities. Furthermore, attempts to engage the oxazinones in cross metathesis were also met with disappointment. Surprisingly, treatment of the oxazinone **6d** with a base to induce elimination of the chloride did not provide the corresponding triene but rather the cycloheptadiene **13d** (Scheme 4). Evidence for the proposed structure was provided by analysis of the proton NMR

Scheme 4. Synthesis of Cycloheptene Fused Oxazinone 13c, d, and f

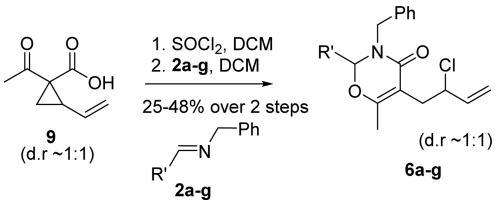


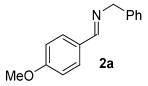
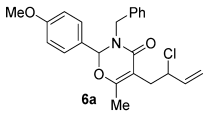
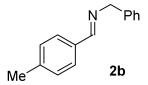
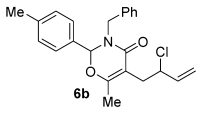
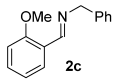
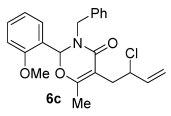
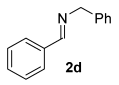
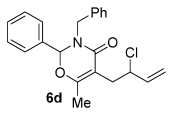
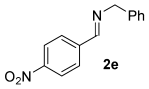
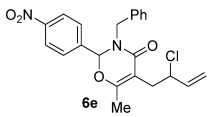
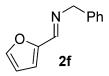
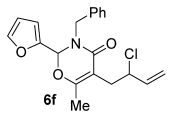
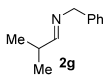
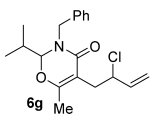
spectrum which indicated the loss of the 3H singlet resonance at 1.93 ppm, attributed to the methyl group in the starting material, and the emergence of three methylene resonances between 2.0 and 2.5 ppm. Further downfield two 1H olefinic proton resonances were found to couple to each other and two different methylene resonances (gCOSY). Analysis of the mass spectrum indicated a sodiated molecular ion (*m*/*z* 354.1462 Da) with an isotopic pattern consistent with the absence of a chlorine atom. Finally, analysis of the long-range ^{1}H–^{13}C correlations (Scheme 5) confirmed the connectivity, and thereby the structure, to be the oxazinone **13d**.

The formation of the cycloheptadiene ring system was postulated to arise via the *in situ* generation of the divinyl

DOI: 10.1021/acs.joc.6b00112
J. Org. Chem. 2016, 81, 2099–2105

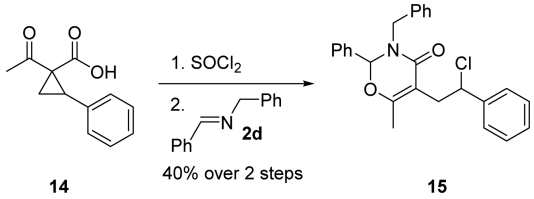
Table 1. Benzyl Benzylidenes (2a–g) Add to *in Situ* Generated Donor–Acceptor Cyclopropyl Acid Chlorides To Provide Oxazinones 6a–g



Entry	Imine	Product[a]	Yield[b]
1			45%
2			31%
3			25%
4			48%
5			32%[c]
6			27%
7			37%

[a]Reaction conditions: cyclopropyl carboxylic acid **9** (1.0 equiv), thionyl chloride (1.1 equiv) 90 min, 40 °C, then $NaHCO_3$ (2.0 equiv), DCM and imine (2 equiv), rt, 2 h. [b]Isolated yield over two steps. [c]d.r. of the crude reaction mixture was 1:1; after silica gel chromatographic purification the d.r was 2:1 which is presumed to be a result of one diastereomer possessing lower stability toward silica gel.

Scheme 5. Synthesis of Oxazinones 15



cyclopropane **12** (Scheme 4), which could then readily undergo a Cope-type rearrangement to afford **13** in good yields.[16] Presumably due to the significant ring strain of the putative cyclopropyl intermediate, no direct evidence for its formation was present in the proton NMR spectrum of the crude material. Since the imine portion of the oxazinone is expected to exert little effect on the efficiency of the Cope rearrangement, this looks promising as a general method to gain access to cycloheptene-fused 1,3-oxazin-4-ones.

In order to isolate the proposed cyclopropyl intermediate, it was postulated that the significantly higher energy required for an aromatic Cope rearrangement to occur could allow for the isolation of such an intermediate. To this end, the phenyl cyclopropane **14**, which was accessed via hydrolysis of the known ethyl ester,[17] was subjected to the standard oxazinone forming reaction conditions with imine **2d** to afford compound **15** in 40% yield over two steps (Scheme 5).

Pleasingly, treatment of the oxazinone **15** with base provided the cyclopropane **16** in a 60% yield as a 2:3 mixture of diastereomers. Analysis of the 2D NOESY spectrum indicated the relative orientation of the phenyl group for both diastereomers was toward the *exo*-alkene, with no evidence for the formation of the alternate isomers. The origin of this high selectivity is not fully understood and cannot be readily explained by steric arguments, as there is little difference between conformation **A** and **B** (Scheme 6). However, greater stabilization energy from π-stacking between the alkene and phenyl group could be envisaged in conformation **A** in the transition state where the chloride is displaced and the formation of partial charges would be expected to occur (Scheme 6).

Attempts to engage compound **16** in an aromatic Cope rearrangement were unsuccessful despite prolonged reaction at high temperatures (3 days @ 150 °C), and only starting material was recovered. Extending the reaction time or temperatures beyond these conditions resulted in extensive decomposition. Although not pursued in this study, electron-rich aromatic systems have been shown to more readily undergo such rearrangements.[18] Nevertheless, such an intermediate supports the proposed mechanism.

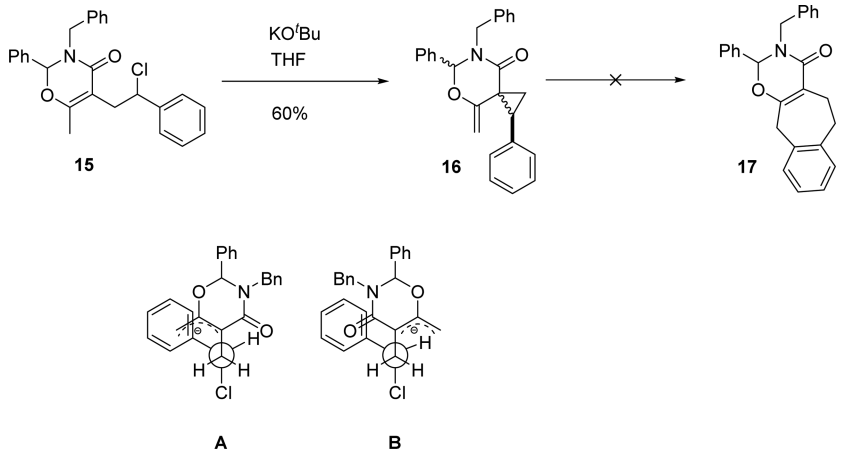
In order to further examine the mechanism, triaryl 1,3-oxazin-4-one **19** was prepared by reaction of the benzoyl vinyl cyclopropane **18**[19] with the imine **2a**, smoothly providing **19** with no other isomers observed. However, coelution with the side product 4-methoxybenzaldehyde made purification by column chromatography difficult.[12] Since compound **19** is unable to form the postulated cyclopropane intermediate, treatment with a base did not provide the cycloheptene analogue but rather underwent an elimination to cleanly provided the triene **20** in an overall yield of 38% from **18** (Scheme 7).

■ CONCLUSIONS

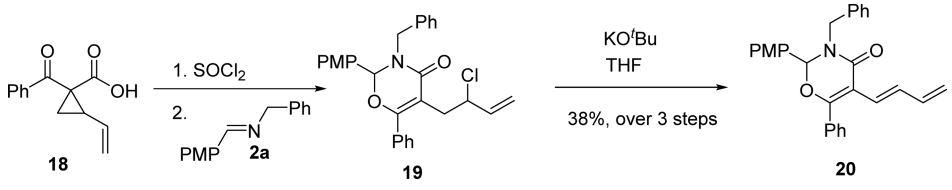
We have reported a reliable, albeit low yielding, method to access a series of structurally diverse oxazinones from donor–acceptor cyclopropanes. The low yield for the oxazinone formation step is offset by a rapid and convergent synthesis which provides highly decorated oxazinones from simple, readily available starting materials. Furthermore, the oxazinone adducts derived from vinylcyclopropyl acetoacetic acid were found to undergo a Cope rearrangement to provide cyclo-heptene-fused oxazinones. While an aromatic Cope rearrange-ment could not be invoked, the postulated cyclopropane

DOI: 10.1021/acs.joc.6b00112
J. Org. Chem. 2016, 81, 2099–2105

Scheme 6. Synthesis of Cyclopropyl Oxazinone 16



Scheme 7. Synthesis of Triene 20



PMP = *p*-methoxyphenyl

intermediate in the cycloheptene ring formation could be isolated and characterized.

EXPERIMENTAL SECTION

Thin layer chromatography (tlc) was performed on aluminum-backed UV_{254} silica gel 60 (0.20 mm) plates. Compounds were visualized with either *p*-anisaldehyde or 20% w/w phosphomolybdic acid in ethanol. Column chromatography was performed using silica gel 60. Infrared spectra were recorded on an ATR FT-IR spectrometer. High resolution mass-spectra (HRMS) were recorded on a TOF-Q mass spectrometer using an electrospray ionization (ESI) source in either the positive or negative modes. ^{1}H NMR spectra were recorded at either 400 or 500 MHz from samples in $CDCl_3$ at 25 °C in 5 mm NMR tubes. Chemical shifts are reported relative to the residual chloroform singlet at δ 7.26 ppm. Resonances were assigned as follows: chemical shift (multiplicity, number of protons, coupling constant(s), assigned proton(s)). Multiplicity abbreviations are reported by the conventions: s (singlet), d (doublet), dd (doublet of doublets), ddd (doublet of doublet of doublets), t (triplet), td (triplet of doublets), q (quartet), qd (quartet of doublets), m (multiplet). Proton decoupled ^{13}C NMR spectra were recorded at either 100 or 125 MHz under the same conditions as the ^{1}H NMR spectra. Chemical shifts have been reported relative to the $CDCl_3$ triplet at δ 77.16 ppm. Dichloromethane (CH_2Cl_2) and tetrahydrofuran (THF) were dried using a solvent purification system. All other solvents and reagents were used as received.

X-ray Crystallography. The crystal was attached with Paratone N oil to a CryoLoop supported in a copper mounting pin and then quenched in a cold nitrogen stream. Data were collected at 100 K using Cu Kα radiation (microsource, mirror monochromated). The data processing was undertaken within the CrysAlisPro software;[20] combined Gaussian and multiscan scaling absorption corrections were applied to the data.[20] The structures were solved by direct methods with SHELXS-97, and extended and refined with SHELXL-97.[21] The 2-chlorobut-3-enyl group is disordered over two sites (70:30) related by a pseudo-mirror plane; the major orientation has an *S*-configuration at the carbon center bearing the chloro group while the minor orientation has an *R*-configuration. The refinement of this disordered region used distance and displacement parameter restraints to ensure the two chains have similar and sensible geometries. The non-hydrogen atoms were modeled with anisotropic displacement parameters and a riding atom model with group displacement parameters used for the hydrogen atoms. CCDC 1447825 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures.

Crystal data for **11**: $C_{25}H_{26}ClNO_4$, M = 439.92, colorless block, 0.24 × 0.19 × 0.15 mm^3, monoclinic, a = 11.5568(2) Å, b = 16.7624(2) Å, c = 12.9551(2) Å, β = 116.227(2) °, V = 2251.29(6) Å^3, space group $P2_1/n$ (#14), Z = 4, μ(Cu Kα) = 1.758 mm^{-1}, $2\theta_{max}$ = 149.43°, 17233 reflections measured, 4425 independent reflections (R_{int} = 0.0232). The final $R(F^2)$ = 0.0466 ($I > 2\sigma(I)$); 0.0489 (all data). The final $wR(F^2)$ = 0.1031 ($I > 2\sigma(I)$); 0.1046 (all data). GoF = 1.044.

General Procedure for Oxazinone Synthesis. To a solution of the appropriate carboxylic acid (1.0 mol equiv) in anhydrous DCM was added thionyl chloride (1.1 mol equiv) at room temperature. After stirring at 40 °C for 90 min, the solution was cooled to room temperature and solid $NaHCO_3$ (2.0 mol equiv) was added. After a further 10 min, a solution of the appropriate imine (1.1 mol equiv) in anhydrous DCM was added and the reaction mixture was stirred at room temperature for a further 4 h. The reaction mixture was then diluted with EtOAc, washed with saturated aqueous $NaHCO_3$ and brine, then dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified with flash column chromatography (25%−40% EtOAc/petroleum ether) to afford the title compound.

*3-Benzyl-5-(2-chlorobut-3-en-1-yl)-2-(4-methoxyphenyl)-6-methyl-2H-1,3-oxazin-4(3H)-one [**6a**].* Following the general procedure, thionyl chloride (100 μL, 164 mg, 1.40 mmol) was added to a solution of the vinyl cyclopropane carboxylic acid **9** (200 mg, 1.30 mmol) in DCM (3.0 mL). $NaHCO_3$ (218 mg, 2.60 mmol) was added followed by a solution of the imine **2a** (319 mg, 1.40 mmol) in DCM (2 mL) to afford the title compound, after chromatography, as a 1:1 mixture of diastereomers (yellow oil, 235 mg, 45%).

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.31−6.82 (m, 18H), 5.98 (s, 1H), 5.96 (s, 1H), 5.90 (ddd, 1H, J = 16.9, 9.0, 8.1 Hz), 5.83 (ddd, 1H, J = 16.8, 9.4, 8.1 Hz), 5.31 (d, 1H, J = 15.4 Hz), 5.26 (dt, 1H, J =

DOI: 10.1021/acs.joc.6b00112
J. Org. Chem. 2016, 81, 2099−2105

16.9, 1.1 Hz), 5.20 (d, 1H, J = 15.4 Hz), 5.20−5.12 (m, 2H), 5.05 (d, 1H, J = 10.2, 0.9 Hz), 4.67−4.60 (m, 2H), 3.90−3.83 (m, 2H), 3.81 (s, 6H), 2.96 (dd, 1H J = 14.3, 5.7 Hz), 2.86 (dd, 1H, J = 14.3, 6.4 Hz), 2.78 (dd, 1H, J = 14.2, 7.9 Hz), 2.66 (dd, 1H, J = 14.3, 8.3 Hz), 1.95 (s, 3H), 1.92 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$), δ (ppm): 164.0, 163.6, 162.3, 161.9, 160.54, 160.51, 138.3, 138.2, 137.0, 136.9, 128.9, 128.8, 128.51, 128.46, 128.2, 127.7, 127.62, 127.61, 127.5, 127.4, 127.3, 116.76, 116.75, 114.4, 114.3, 113.83, 113.80, 106.7, 106.5, 87.0, 86.8, 77.2, 62.43, 62.41, 55.4, 46.57, 46.55, 34.9, 34.8, 17.90, 17.86.

FTIR (ATR/cm^{-1}): 2932, 1654, 1410, 1250, 1173, 1029, 699, 528.

HRMS-ESI calculated for $C_{23}H_{24}ClNO_3Na^+$ [M + Na]$^+$: 420.1342; found: 420.1319.

*3-Benzyl-5-(2-chlorobut-3-en-1-yl)-6-methyl-2-(4-tolyl)-2H-1,3-oxazin-4(3H)-one [**6b**].* Following the general procedure, thionyl chloride (160 μL, 255 mg, 2.14 mmol) was added to a solution of the vinyl cyclopropane carboxylic acid **9** (300 mg, 1.95 mmol) in DCM (5.0 mL). $NaHCO_3$ (252 mg, 2.14 mmol) was added, followed by a solution of the imine **2b** (448 mg, 2.14 mmol) in DCM (3.0 mL) to afford the title compound, after chromatography, as a 1:1 mixture of diastereomers (yellow oil, 230 mg, 31%).

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.31−7.10 (m, 18H), 6.01 (s, 1H), 6.00 (s, 1H), 5.91 (ddd, 1H, J = 16.9, 10.1, 8.1 Hz), 5.81 (ddd, 1H, J = 17.0, 10.2, 8.1 Hz), 5.36 (d, 1H, J = 15.4 Hz), 5.27 (d, 1H, J = 15.4 Hz), 5.25 (dt, 1H, J = 17.0, 1.1 Hz), 5.15−5.11 (m, 2H), 5.01 (dt, 1H, J = 10.2, 1.0 Hz), 4.67−4.59 (m, 2H), 3.87 (d, 1H, J = 15.4 Hz), 3.79 (d, 1H, J = 15.4 Hz), 2.99 (dd, 1H, J = 14.3, 5.9 Hz), 2.82 (d, 2H, J = 7.1 Hz), 2.66 (dd, 1H, J = 14.3, 8.2 Hz), 2.36 (s, 6H), 1.94 (s, 3H), 1.92 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$), δ (ppm): 166.5, 166.2, 164.8, 164.5, 142.23, 142.18, 140.9, 140.8, 139.63, 139.59, 135.43, 135.41, 131.9, 131.8, 131.21, 131.18, 130.4, 130.3, 130.1, 130.0, 129.97, 119.43, 119.39, 109.4, 109.3, 89.6, 89.5, 65.1, 65.0, 49.40, 49.36, 37.6, 37.5 23.92, 23.90, 20.60, 20.59.

FTIR (ATR/cm^{-1}): 2921, 1655, 1354, 1179, 927, 731, 699.

HRMS-ESI calculated for $C_{23}H_{24}ClNO_2Na^+$ [M + Na]$^+$: 404.1393; found: 404.1367.

*3-Benzyl-5-(2-chlorobut-3-en-1-yl)-6-methyl-2-(2-methoxyphenyl)-2H-1,3-oxazin-4(3H)-one [**6c**].* Following the general procedure, thionyl chloride (220 μL, 365 mg, 3.07 mmol) was added to a solution of the vinyl cyclopropane carboxylic acid **9** (431 mg, 2.79 mmol) in DCM (9.0 mL). $NaHCO_3$ (258 mg, 3.07 mmol) was added followed by a solution of the imine **6c** (806 mg, 3.58 mmol) in DCM (6.0 mL) to afford the title compound, after chromatography, as a 1:1 mixture of diastereomers (yellow oil, 278 mg, 0.70 mmol, 25%).

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.38−6.84 (m, 18H), 6.45 (s, 2H), 5.97 (ddd, 1H, J = 16.9, 10.2, 8.1 Hz), 5.94 (ddd, 1H, J = 16.9, 10.1, 8.1 Hz), 5.33 (dt, 1H, J = 16.9, 1.1 Hz), 5.31 (dt, 1H, J = 16.9, 1.1 Hz), 5.18 (dt, 1H, J = 10.2, 1.0 Hz), 5.13 (dt, 1H, J = 10.2, 1.0 Hz), 5.05 (d, 1H, J = 15.4 Hz), 4.86 (d, 1H, J = 15.5 Hz), 4.78−4.68 (m, 2H), 4.00 (d, 1H, J = 15.5 Hz), 3.86 (d, 1H, J = 15.4 Hz), 3.69 (s, 3H), 3.66 (s, 3H), 2.98 (t, 1H, J = 5.9 Hz), 2.95 (t, 1H, J = 5.4 Hz), 2.77 (t, 1H, J = 8.3 Hz), 2.74 (t, 1H, J = 8.4 Hz), 1.97 (s, 3H), 1.94 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$), δ (ppm): 167.2, 166.8, 165.7, 165.24, 160.18, 160.1, 141.1, 141.0, 140.2, 140.0, 134.8, 133.7, 133.6, 131.4, 130.9, 130.84, 130.81, 130.2, 130.1, 129.7, 129.6, 125.4, 125.2, 123.0, 122.9, 119.5, 119.4, 113.5, 113.4, 109.0, 108.6, 85.2, 84.9, 65.3, 65.2, 58.1, 58.0, 48.7, 48.6, 37.6, 20.5, 20.4.

FTIR (ATR/cm^{-1}): 2929, 1652, 1602, 1451, 1247, 929, 754, 699.

HRMS-ESI calculated for $C_{23}H_{24}ClNO_3Na^+$ [M + Na]$^+$: 420.1342; found: 420.1310.

*3-Benzyl-5-(2-chlorobut-3-en-1-yl)-6-methyl-2-phenyl-2H-1,3-oxazin-4(3H)-one [**6d**].* Following the general, procedure thionyl chloride (26 μL, 43 mg, 0.358 mmol) was added to a solution of the vinyl cyclopropane carboxylic acid **9** (50 mg, 0.325 mmol) in DCM (1.0 mL). $NaHCO_3$ (55 mg, 0.650 mmol) was added followed by a solution of the imine **2d** (90 mg, 0.358 mmol) in DCM (3.0 mL) to afford the title compound, after chromatography, as a 1:1 mixture of diastereomers (yellow oil, 58 mg, 0.157 mmol, 48%).

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.40−7.22 (m, 16H), 7.16−7.09 (m, 4H), 6.03 (s, 1H), 6.02 (s, 1H), 5.89 (ddd, 1H, J = 16.9, 10.2, 8.1 Hz), 5.78 (ddd, 1H, J = 17.0, 10.2, 8.2 Hz), 5.38 (d, 1H, J = 15.4 Hz), 5.28 (d, 1H, J = 15.4 Hz), 5.22 (dt, 1H, J = 16.9, 1.1 Hz), 5.13−5.07 (m, 2H), 4.98 (dt, 1H, J = 10.1, 1.0 Hz), 4.63−4.54 (m, 2H), 3.89 (d, 1H, J = 15.4 Hz), 3.81 (d, 1H, J = 15.4 Hz), 2.99 (dd, 1H, J = 14.3, 5.8 Hz), 2.86−2.77 (m, 2H), 2.62 (dd, 1H, J = 14.2, 8.4 Hz), 1.94 (s, 3H), 1.93 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$), δ (ppm): 162.2, 161.8, 138.2, 138.0, 136.9, 135.82, 135.78, 129.6, 129.5, 128.6, 128.54, 128.52, 128.50, 127.8, 127.7, 127.5, 127.4, 127.32, 127.27, 116.8, 106.92, 106.86, 86.9, 86.7, 62.4, 62.3, 46.9, 46.8, 34.9, 34.7, 17.94, 17.92.

FTIR (ATR/cm^{-1}): 3188, 1653, 1385, 1290, 1237, 819, 731, 697.

HRMS-ESI calculated for $C_{22}H_{22}ClNO_2Na^+$ [M + Na]$^+$: 390.1231; found: 390.1210.

*3-Benzyl-5-(2-chlorobut-3-en-1-yl)-6-methyl-2-(4-nitrophenyl)-2H-1,3-oxazin-4(3H)-one [**6e**].* Following the general procedure, thionyl chloride (67 μL, 110 mg, 0.92 mmol) was added to a solution of the vinyl cyclopropane carboxylic acid **9** (129 mg, 0.84 mmol) in DCM (1.5 mL). $NaHCO_3$ (124 mg, 1.68 mmol) was added followed by a solution of the imine **2e** (221 mg, 0.92 mmol) in DCM (2.0 mL) to afford the title compound, after chromatography, as a 2:1 mixture of diastereomers (yellow oil, 112 mg, 32%).

Major. ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 8.18 (d, 2H, J = 8.3 Hz), 7.47 (d, 2H, J = 8.3 Hz), 7.27−7.33 (m, 4H), 6.11 (s, 1H), 5.86 (ddd, 1H, J = 17.0, 10.1 Hz, 7.9), 5.40 (d, 1H, J = 15.3 Hz), 5.22 (dt, 1H, J = 17.0, 1.0 Hz), 5.12 (dt, 1H, J = 10.0, 1.0 Hz), 4.48 (m, 1H), 3.96 (d, 1H, J = 15.4 Hz), 3.03 (dd, 1H, J = 14.3, 4.9 Hz), 2.48 (dd, 1H, J = 14.3, 9.1 Hz), 1.92 (s, 3H).

Minor. ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 8.16 (d, 2H, J = 8.3 Hz, aromatic), 7.44 (d, 2H, J = 8.3 Hz, aromatic), 7.35−7.18 (m, 4H), 7.12 (m, 1H), 6.11 (s, 1H), 5.77 (ddd, 1H, J = 17.0, 10.0, 8.0 Hz), 5.27 (d, 1H, J = 15.3 Hz), 5.13 (dt, 1H, J = 17.0, 1.0 Hz), 5.00 (dt, 1H, J = 10.0, 0.9 Hz), 4.61 (m, 1H), 4.01 (d, 1H, J = 15.4 Hz), 2.79 (ABX, 2H, J = 7.9, 6.1 Hz), 1.96 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 162.6, 161.6, 148.5, 143.5, 138.03, 137.95, 136.1, 128.84, 128.79, 128.3, 128.1, 127.91, 127.85, 127.82, 127.7, 123.7, 123.6, 116.9, 116.8, 107.7, 85.6, 85.3, 62.24, 62.18, 47.5, 47.3, 34.6, 34.5, 18.0, 17.9.

FTIR (ATR/cm^{-1}): 3176, 1653, 1521, 1344, 1234, 854, 733, 697.

HRMS-ESI calculated for $C_{22}H_{21}ClN_2O_4Na^+$ [M + Na]$^+$: 435.1082; found: 435.1061.

*3-Benzyl-5-(2-chlorobut-3-en-1-yl)-2-(furan-2-yl)-6-methyl-2H-1,3-oxazin-4(3H)-one [**6f**].* Following the general procedure, thionyl chloride (104 μL, 1.43 mmol) was added dropwise to a solution of the vinyl cyclopropane carboxylic acid **9** (200 mg, 1.3 mmol, 1.0 equiv) in DCM (2.6 mL). $NaHCO_3$ (192 mg, 2.60 mmol) was added followed by a solution of the imine **2f** (265 mg, 1.43 mmol) in DCM (2.0 mL) to afford the title compound, after chromatography, as a 1:1 mixture of diastereomers (colorless oil, 125 mg, 27%).

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.42−7.20 (m, 12H), 6.36−6.26 (m, 4H), 6.03 (s, 2H), 5.97−5.78 (m, 2H), 5.36 (d, 1H, J = 15.3 Hz), 5.29 (d, 1H, J = 15.5 Hz), 5.27 (dt, 1H, J = 16.9, 0.9 Hz), 5.19 (dt, 1H, J = 16.9, 1.0 Hz), 5.13 (dt, 1H, J = 10.2, 0.9 Hz), 5.06 (dt, 1H, J = 10.1, 1.0 Hz), 4.69−4.62 (m, 1H), 4.59−4.52 (m, 1H), 3.92 (d, 1H, J = 15.3 Hz), 3.87 (d, 1H, J = 15.4 Hz), 3.05 (dd, 1H, J = 14.3, 5.3 Hz), 2.89 (dd, 1H, J = 14.2, 7.5 Hz), 2.74 (dd, 1H, J = 14.2, 6.6 Hz), 2.55 (dd, 1H, J = 14.3, 8.8 Hz), 1.97 (s, 3H), 1.95 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 165.6, 165.4, 164.1, 163.7, 151.5, 151.4, 146.30, 146.26, 140.9, 140.7, 139.18, 139.16, 131.34, 131.31, 130.6, 130.5, 130.32, 130.26, 119.5, 119.4, 113.3, 113.2, 113.1, 113.0, 109.4, 109.2, 83.3, 83.2, 65.1, 64.9, 49.3, 37.44, 37.41, 20.5, 20.4.

FTIR (ATR/cm^{-1}): 2924, 1718, 1659, 748, 699.

HRMS-ESI calculated for $C_{20}H_{20}ClNO_3Na^+$ [M + Na]$^+$: 380.1029; found: 380.1027.

*3-Benzyl-5-(2-chlorobut-3-en-1-yl)-2-isopropyl-6-methyl-2H-1,3-oxazin-4(3H)-one [**6g**].* Following the general procedure, thionyl chloride (52 μL, 85 mg, 0.714 mmol) was added to a solution of vinyl cyclopropane carboxylic acid **9** (100 mg, 0.649 mmol) in DCM (1.5 mL). $NaHCO_3$ (104 mg, 1.30 mmol) was added followed by a

DOI: 10.1021/acs.joc.6b00112
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solution of the imine **2g** (115 mg, 0.714 mmol) in DCM (0.1 mL) to afford the title compound, after chromatography, as a 1:1 mixture of diastereomers (orange oil, 80 mg, 37%).

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.35−7.20 (m, 10H), 6.01−5.81 (m, 2H), 5.48 (d, 1H, J = 15.6 Hz), 5.46 (d, 1H, J = 15.7 Hz), 5.32 (dt, 1H, J = 17.0, 0.9 Hz), 5.29 (dt, 1H, J = 17.0, 0.9 Hz), 5.16 (dt, 1H, J = 10.2, 0.9 Hz), 5.14 (dt, 1H, J = 10.1, 0.9 Hz), 4.76−4.68 (m, 3H, H-17), 4.63 (ddd, 1H, J = 9.4, 8.2, 4.9 Hz), 3.89 (d, 1H, J = 15.7 Hz), 3.85 (d, 1H, J = 15.4 Hz), 3.08 (dd, 1H, J = 14.3, 4.9 Hz), 2.96 (dd, 1H, J = 14.2, 7.2 Hz), 2.71 (dd, 1H, J = 14.2, 6.5 Hz), 2.66−2.57 (m, 1H), 2.54−2.44 (m, 2H), 2.00 (s, 3H), 1.99 (s, 3H), 0.97 (dd, 6H, J = 6.6, 1.9 Hz), 0.94 (dd, 6H, J = 6.6, 1.9 Hz).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 162.8, 162.2, 161.6, 161.3, 138.5, 138.4, 137.11, 137.07, 128.80, 128.7, 127.5, 127.41, 127.40, 127.3, 116.9, 116.8, 116.7, 106.4, 106.0, 91.7, 91.4, 76.8, 63.0, 62.5, 48.6, 48.1, 40.0, 34.7, 34.5, 31.7, 30.7, 30.4, 18.43, 18.40, 18.36, 18.0, 17.7, 17.6.

FTIR (ATR/cm^{-1}): 3274, 1652, 1354, 1192, 1142, 805, 698.

HRMS-ESI calculated for $C_{19}H_{24}ClNO_2Na^+$ [M + Na]$^+$: 356.1393; found: 356.1375.

*Ethyl 2-(5-(2-Chlorobut-3-en-1-yl)-6-methyl-4-oxo-2,2-diphenyl-2H-1,3-oxazin-3(4H)-yl)acetate [**11**].* Following the general procedure, thionyl chloride (150 μL, 245 mg, 2.06 mmol) was added to a solution of the vinyl cyclopropane carboxylic acid **9** (288 mg, 1.87 mmol) in DCM (3.0 mL). $NaHCO_3$ (277 mg, 2.06 mmol) was added followed by a solution of ethyl *N*-(diphenylmethylene)glycinate (551 mg, 2.06 mmol) in DCM (3.0 mL) to afford the title compound as a yellow solid (224 mg, 32%), mp 250 °C (decomp.).

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.40−7.26 (m, 10H), 5.56 (ddd, 1H, J = 16.9, 10.2, 8.0 Hz), 4.86 (d, 1H, J = 16.9 Hz), 4.84 (d, 1H, J = 10.1 Hz), 4.25 (q, 1H, J = 7.4 Hz), 4.04−3.90 (m, 4H), 2.76 (dd, 1H, J = 14.2, 6.8 Hz), 2.68 (dd, 1H, J = 14.2, 7.4 Hz), 1.97 (s, 3H), 1.13 (t, 3H, J = 7.1 Hz).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 168.6, 163.8, 161.8, 140.2, 140.1, 137.6, 129.41, 129.36, 128.23, 128.21, 128.20, 128.1, 116.5, 107.4, 96.6, 61.9, 61.0, 46.2, 34.8, 18.3, 14.0.

FTIR (ATR/cm^{-1}): 2980, 1747, 1660, 1640, 1449, 1199, 770, 702.

HRMS-ESI calculated for $C_{25}H_{26}ClNO_4Na^+$ [M + Na]$^+$: 462.1419; found: 462.1418.

*3-Benzyl-2-(2-methoxyphenyl)-2,3,8,9-tetrahydrocyclohepta[e][1,3]oxazin-4(5H)-one [**13c**].* A solution of the oxazinone **6c** (56 mg, 0.14 mmol) in anhydrous THF (3.0 mL) was cooled to −78 °C before KO^{t}Bu (22 mg, 0.20 mmol) was added in one portion. The reaction was maintained at this temperature for 2 h before being allowed to warm to rt over 10 min. After this time the reaction was diluted with EtOAc and quenched with saturated $NH_4Cl_{(aq)}$. The organic phase was washed with H_2O and brine then dried over $MgSO_4$, filtered, and concentrated. The crude residue was purified with flash column chromatography (gradient elution 10−30% EtOAc/petroleum ether) to afford the title compound as a yellow oil (33 mg, 64%).

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.38−7.29 (m, 3H), 7.22−7.14 (m, 4H), 7.01−6.98 (m, 2H,), 6.91 (m, 1H), 6.84(m, 1H), 6.44 (s, 1H), 5.82 (dt, 1H, J = 11.4, 5.5 Hz), 5.71 (dt, 1H, J = 10.7, 5.5 Hz), 4.85 (d, 1H, J = 15.5 Hz), 4.00 (d, 1H, J = 15.5 Hz), 3.65 (s, 1H), 3.23 (d, 2H, J = 5.5 Hz), 2.44 (dt, 2H, J = 7.9, 4.3 Hz), 2.26−2.18 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 167.7, 167.4, 160.0, 140.5, 133.6, 132.1, 131.4, 131.1, 130.8, 130.2, 129.5, 125.4, 122.9, 113.4, 111.8, 85.5, 58.0, 48.7, 33.0, 32.4, 26.6, 24.9.

FTIR (ATR/cm^{-1}): 3286, 2923, 1659, 1602, 1464, 1248, 732.

HRMS-ESI calculated for $C_{23}H_{23}NO_3Na^+$ [M + Na]$^+$: 384.1576; found: 384.1556.

*3-Benzyl-2-phenyl-2,3,8,9-tetrahydrocyclohepta[e][1,3]oxazin-4(5H)-one [**13d**].* A solution of oxazinone **6d** (49 mg, 0.133 mmol) in anhydrous THF (0.5 mL) was cooled to −78 °C, and KO^{t}Bu (32 mg, 0.266 mmol) was added in one portion. The reaction was maintained at this temperature for 2 h before being allowed to warm to rt over 10 min. After this time the reaction was diluted with EtOAc and quenched with saturated $NH_4Cl_{(aq)}$. The organic phase was washed with H_2O and brine, then dried over $MgSO_4$, filtered, and concentrated. The crude residue was purified with flash column chromatography (gradient elution 10−30% EtOAc/petroleum ether) to afford the title compound as a yellow oil (31 mg, 70%).

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.42−7.08 (m, 9H), 6.02 (s, 1H), 5.76 (dtt, 1H, J = 11.1, 5.7, 1.5 Hz), 5.65 (dtt, 1H, J = 11.0, 5.3, 1.48 Hz), 5.25 (d, 1H, J = 15.4 Hz), 3.88 (d, 1H, J = 15.4 Hz), 3.26−3.11 (m, 2H), 2.48 (ddd, 1H, J = 15.4, 9.1, 3.5 Hz), 2.34 (ddd, 1H, J = 15.4, 8.4, 3.5 Hz), 2.23 (m, 1H), 2.11 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 164.2, 163.7, 137.2, 135.7, 129.5, 129.3, 128.5, 128.4, 128.3, 127.5, 127.3, 127.3, 109.5, 87.3, 46.8, 30.4, 23.7, 22.1.

FTIR (ATR/cm^{-1}): 3062, 1645, 1412, 1310, 1269, 1202, 728, 695.

HRMS-ESI calculated for $C_{22}H_{21}NO_2Na^+$ [M + Na]$^+$: 354.1470; found: 354.1462.

*3-Benzyl-2-(furan-2-yl)-2,3,8,9-tetrahydrocyclohepta[e][1,3]-oxazin-4(5H)-one [**13f**].* A solution of oxazinone **6f** (82 mg, 0.23 mmol) in anhydrous THF (0.27 mL) was cooled to −78 °C, and KO^{t}Bu (51 mg, 0.46 mmol) was added in one portion. The reaction was maintained at this temperature for 2 h before being allowed to warm to rt over 10 min. After this time the reaction was diluted with EtOAc and quenched with saturated $NH_4Cl_{(aq)}$. The organic phase was washed with H_2O and brine, then dried over $MgSO_4$, filtered, and concentrated. The crude residue was purified with flash column chromatography to afford the title compound as a colorless oil (49 mg, 67%).

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.42−7.22 (m, 6H), 6.35−6.31 (m, 1H), 6.28 (dd, 1H, J = 3.3, 0.9 Hz), 6.02 (s, 1H), 5.78−5.71 (m, 1H), 5.66 (dt, 1H, J = 10.9, 5.0 Hz), 5.29 (d, 1H, J = 15.5 Hz), 3.91 (d, 1H, J = 15.3 Hz), 3.21 (d, 1H, J = 18.1 Hz), 3.13 (dd, 1H, J = 18.1, 6.1 Hz), 2.50 (m, 1H), 2.34 (m, 1H), 2.26 (m, 1H), 2.09 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$), δ (ppm): 166.0, 165.5, 151.6, 146.2, 139.4, 132.0, 130.7, 130.6, 130.2, 113.1, 113.0, 112.0, 83.6, 49.4, 33.0, 26.5, 24.6.

FTIR (ATR/cm^{-1}): 2927, 1655, 1495, 727, 699.

HRMS-ESI calculated for $C_{20}H_{19}NO_3Na^+$ [M + Na]$^+$: 344.1257; found: 344.1255.

*3-Benzyl-5-(2-chloro-2-phenylethyl)-6-methyl-2-phenyl-2H-1,3-oxazin-4(3H)-one [**15**].* Following the general procedure, thionyl chloride (32 μL, 53 mg, 0.431 mmol) was added to a solution of the vinyl cyclopropane carboxylic acid **14** (80 mg, 0.392 mmol) in DCM (1.0 mL). $NaHCO_3$ (63 mg, 0.784 mmol) was added followed by a solution of the imine **2d** (97 mg, 0.431 mmol) in DCM (1.0 mL) to afford the title compound, after chromatography, as a 1:1 mixture of diastereomers (colorless oil, 68 mg, 40%).

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 7.44−7.06 (m, 30H), 6.00 (s, 1H), 5.95 (s, 1H), 5.39 (d, 1H, J = 15.4 Hz), 5.31 (d, 1H, J = 15.5 Hz), 5.22 (dd, 1H, J = 8.4, 5.8 Hz), 5.10 (t, 1H, J = 7.3 Hz), 3.88 (d, 1H, J = 15.5 Hz), 3.82 (d, 1H, J = 15.4 Hz), 2.04 (m, 2H), 2.94 (m, 2H), 1.75 (s, 3H), 1.67 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$), δ (ppm): 166.4, 166.2, 165.1, 164.7, 144.2, 144.0 139.52, 139.50, 138.42, 138.40, 132.23, 132.18, 131.4, 131.24, 131.22, 131.21, 131.1, 131.0, 130.7, 130.6, 130.4, 130.3, 130.1, 130.04, 129.98, 129.9, 129.8, 129.7, 129.2, 109.62, 109.57, 89.5, 89.4, 65.4, 65.3, 49.5, 49.4, 39.8, 39.7, 20.2, 20.1.

FTIR (ATR/cm^{-1}): 3031, 1652, 1432, 1413, 908, 729, 697.

HRMS-ESI calculated for $C_{26}H_{24}ClNO_2Na^+$ [M + Na]$^+$: 440.1393; found: 440.1373.

*7-Benzyl-4-methylene-1,6-diphenyl-5-oxa-7-azaspiro[2.5]octan-8-one [**16**].* A solution of oxazinone **15** (60 mg, 0.134 mmol) in anhydrous THF (1.0 mL) was cooled to −78 °C, and KO^{t}Bu (28 mg, 0.201 mmol) was added in one portion. The reaction was maintained at this temperature for 2 h and was allowed to warm to rt over 30 min. The reaction was diluted with EtOAc and quenched with sat. $NH_4Cl_{(aq)}$. The organic phase was washed with H_2O and brine, then dried over $MgSO_4$, filtered, and concentrated. The crude residue was purified with flash column chromatography to afford the title compound as a 3:2 mixture of diastereomers (yellow oil, 34 mg, 60%).

Major. ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.48−7.40 (m, 4H, overlap), 7.39−7.25 (m, 24H, overlap), 6.03 (s, 1H), 5.27 (d, 1H, J = 15.4 Hz), 4.04 (d, 1H, J = 2.0 Hz), 3.81 (d, 1H, J = 15.4 Hz), 3.68 (d,

DOI: 10.1021/acs.joc.6b00112
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1H, J = 2.0 Hz), 3.20 (t, 1H, J = 8.4 Hz), 1.63 (dd, 2H, J = 7.6, 5.2 Hz).

Minor. ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.48−7.40 (m, 4H, overlap), 7.39−7.25 (m, 24H, overlap), 6.50 (d, J = 6.7 Hz, 2H), 5.94 (s, 1H), 5.64 (d, 1H, J = 15.3 Hz), 4.25 (d, 1H, J = 2.1 Hz), 3.91 (d, 1H, J = 15.3 Hz), 3.52 (d, 1H, J = 2.1 Hz), 2.86 (t, 1H, J = 8.6 Hz), 2.48 (dd, 1H, J = 9.4, 5.0 Hz), 1.54 (dd, 2H, J = 7.9, 5.0 Hz).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 169.6, 169.3, 152.8, 150.9, 138.1, 136.7, 136.2, 135.2, 135.1, 134.5, 129.6, 129.49, 129.48, 129.3, 129.1, 128.8, 128.6, 128.5, 128.1, 127.9, 127.72, 127.69, 127.66, 127.6, 127.5, 127.1, 126.9, 126.8, 93.5, 91.0, 86.4, 85.9, 48.4, 47.0, 38.3, 37.8, 33.0, 32.0, 19.3, 16.8.

FTIR (ATR/cm^{-1}): 3064, 2932, 2853, 1655, 1606, 1453, 1302.

HRMS-ESI calculated for $[C_{26}H_{24}NO_2]^+$ $[M]^+$: 382.1807; found 382.1781.

3-Benzyl-5-(2-chlorobut-3-en-1-yl)-2-(4-methoxyphenyl)-6-phenyl-2H-1,3-oxazin-4(3H)-one [19]. Following the general procedure thionyl chloride (52 μL, 85 mg, 0.715 mmol) was added to a solution of the vinyl cyclopropane carboxylic acid **18** (140 mg, 0.650 mmol) in DCM (2.0 mL). $NaHCO_3$ (110 mg, 1.30 mmol) was added followed by a solution of the imine **2a** (161 mg, 0.716 mmol) in DCM (3.0 mL) to afford, after chromatography, the title compound as a 1:1 mixture of diastereomers with traces of 4-methoxybenzaldhyde. This was sufficiently pure to be used in the next reaction.

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.42−6.85 (m, 28H), 6.18 (s, 1H), 6.15 (s, 1H), 5.74 (ddd, 1H, J = 16.9, 10.1, 8.2 Hz), 5.61 (ddd, 1H, J = 16.9, 10.1, 8.1 Hz), 5.41 (d, 1H, J = 15.4 Hz), 5.23 (d, 1H, J = 15.5 Hz), 5.20 (d, 1H, J = 16.9 Hz), 5.11 (d, 1H, J = 17.3 Hz), 5.07 (d, 1H, J = 10.6 Hz), 4.94 (d, 1H, J = 10.1 Hz), 4.76−4.61 (m, 2H), 3.95 (d, 1H, J = 15.5 Hz), 3.87 (d, 1H, J = 15.4 Hz), 3.83 (s, 6H), 3.12−2.92 (m, 3H), 2.84 (dd, 1H, J = 14.2, 8.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 164.6, 164.0, 161.4, 160.7, 160.6, 160.5, 138.4, 138.1, 136.9, 136.8, 132.8, 132.6, 132.0, 130.3, 130.1, 129.33, 129.29, 129.13, 129.09, 128.6, 128.5, 128.34, 128.30, 127.8, 127.6, 127.5, 127.3, 127.2, 126.9, 116.9, 116.7, 114.3, 113.9, 113.8, 107.7, 107.5, 87.8, 87.1, 61.5, 55.6, 55.36, 55.35, 46.8, 46.6, 34.9.

FTIR (ATR/cm^{-1}): 2936, 1649, 1612, 1407, 1251, 1173, 769, 699.

HRMS-ESI calculated for $C_{28}H_{26}ClNO_3Na^+$ $[M + Na]^+$: 482.1499; found: 482.1471.

(E)-3-Benzyl-5-(buta-1,3-dien-1-yl)-2-(4-methoxyphenyl)-6-phenyl-2H-1,3-oxazin-4(3H)-one [20]. A solution of oxazinone **19** (143 mg, 0.310 mmol) in anhydrous THF (2 mL) was cooled to −78 °C, and KO^{t}Bu (52 mg, 0.466 mmol) was added in one portion. The reaction was maintained at this temperature for 2 h before being warm to rt and stirred for another 2 h. The reaction was diluted with EtOAc and quenched with sat. $NH_4Cl_{(aq)}$. The organic phase was washed with H_2O and brine, then dried over $MgSO_4$, filtered, and concentrated. The crude residue was purified by flash column chromatography to afford the title compound as a yellow oil (115 mg, 38%, over 3 steps from **18**).

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.47−7.17 (m, 13H), 6.92−6.87 (m, 2H), 6.32 (m, 3H), 5.35 (d, 1H, J = 15.4 Hz), 5.23 (dd, 1H, J = 16.7, 1.9 Hz), 5.03 (dd, 1H, J = 10.2, 1.6 Hz), 3.97 (d, 1H, J = 15.4 Hz), 3.82 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 163.4, 160.6, 159.8, 138.6, 136.8, 132.5, 132.2, 130.6, 130.2, 128.9, 128.6, 128.2, 127.8, 127.4, 127.0, 125.1, 116.5, 114.0, 109.7, 87.3, 55.3, 46.6.

FTIR (ATR/cm^{-1}): 3063, 1657, 1510, 752, 695.

HRMS-ESI calculated for $C_{28}H_{25}NO_3Na^+$ $[M + Na]^+$: 446.1732; found: 446.1706.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00112.

X-ray crystal structure data (CIF)

Copies of ^{1}H NMR, ^{13}C NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors gratefully acknowledge funding from the University of Otago Research Grant scheme.

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DOI: 10.1021/acs.joc.6b00112
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