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Pd(II)-Catalyzed Cycloisomerization/Dipolar Cycloaddition Cascade of *N*-Arylnitrone Alkynes with Olefins

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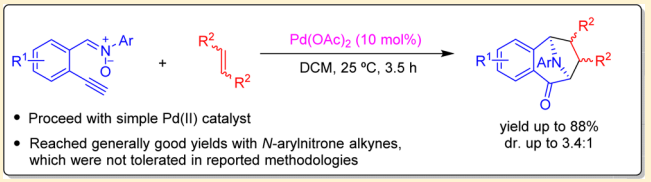
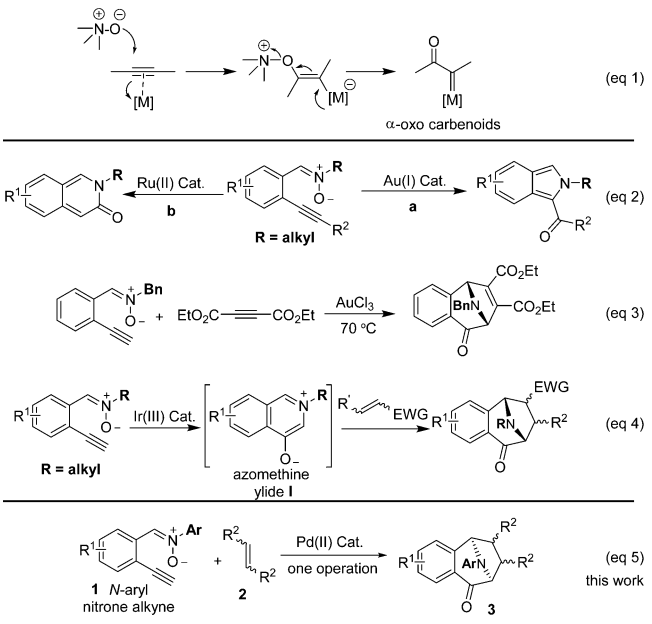
Supporting Information

ABSTRACT: A cycloisomerization/dipolar cycloaddition tandem reaction of nitrone alkynes and electron-deficient olefins was described by employing a simple palladium catalyst. *N*-Arylnitrone alkynes, which were not well tolerated in previously reported methodologies, were successfully incorporated in the tandem reaction with generally good yields and moderate diastereoselectivities.



Transition-metal-catalyzed cascade reactions, for their high efficiency and step-economy in constructing complex molecules, have attracted increasing interest, providing a huge number of versatile and important synthetic methodologies.[1] Nucleophilic attack on alkyne-triggered tandem reactions represents a promising strategy in this discipline.[2] In the cases where nucleophiles are amine *N*-oxides,[3] sulfoxides,[4] nitrones,[5] and nitro groups,[6] the cleavage of N−O σ bonds is usually involved in the formation of highly active α-oxo metal carbenoid intermediates, which could undergo versatile transformations (eq 1).[7] Significant interest has been placed on such internal redox processes as a valuable alternative approach to synthetic useful metal carbenoid species.



Comparatively speaking, employing nitrones as the nucleophile holds unique advantages such as easy accessibility of the substrates, mild reaction conditions for the redox process, and the fact that the *in situ* generated imine could be further incorporated into the reaction in a cascade manner.[8] In the presence of different transition-metal catalysts, nitrone alkynes could undergo versatile transformations. Shin and co-workers reported that under the catalysis of cationic Au(I), isoindole derivatives could be obtained efficiently (eq 2a).[5g] Pati and Liu afforded α-pyridone derivatives through a ruthenium-catalyzed cycloisomerization of nitrone alkynes (eq 2b).[5h] Shin and co-workers reported an $AuCl_3$-catalyzed tandem reaction of nitrone alkyne and diethyl acetylenedicarboxylate, obtaining the tricyclic product with fair yield (eq 3).[5i] Li's group[5e] found that the azomethine ylide[9] intermediates **I**, formed by the iridium-catalyzed cycloisomerization of nitrone alkynes, could be isolated or directly used for a one-pot [3 + 2] cycloaddition reaction (eq 4).[10] Interestingly, in all of these examples, *N*-alkylnitrones were employed exclusively for the intramolecular cycloisomerization reaction. Herein, we describe a palladium-catalyzed cycloisomerization/dipolar cycloaddition cascade of *N*-arylnitrone alkynes with electron-deficient olefins (eq 5).

As a starting point, we examined the reaction of *N*-arylnitrone alkyne **1a** and dimethyl fumarate **2a**, as the dipolarophile, in the presence of 10 mol % of $AuCl_3$, which displayed high efficiency for the cascade reaction of *N*-alkylnitrone alkyne and diethyl but-2-ynedioate (eq 3).[5i] However, in our case, the reaction resulted in a complex mixture with only a trace amount of the desired product **3** observed (Table 1, entry 1). Other transition-metal complexes, $Ph_3PAuNTf$, $Cu(OTf)_2$, and $Rh_2(OAc)_4$, also failed to provide a significant amount of the cycloaddition product (entries 2−4). $[IrCp^*Cl_2]_2$, which was the optimal catalyst for the reaction of *N*-alkylnitrone alkynes in Li's work,[5e] gave only 33% of **3** (entry 5). Surprisingly, $PdCl_2$ proved to be a better catalyst for the reaction, providing the desired product with 41% yield and 1.7:1 diastereoselectivity (entry 6). Screening of palladium(II) complexes showed that $Pd(OAc)_2$ was the best catalyst, furnishing the product with 45% yield and

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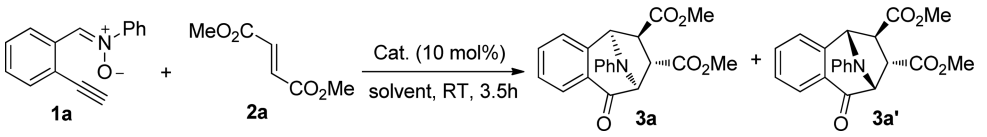
Table 1. Evaluation of Catalysts and Optimization of Reaction Conditions[a]



entry	cat.	solvent	yield (%)	dr. (3/3′)
1	$AuCl_3$	CH_2Cl_2	trace	
2	$Ph_3PAuNTf_2$	CH_2Cl_2	trace	
3	$Cu(OTf)_2$	CH_2Cl_2	trace	
4	$Rh_2(OAc)_4$	CH_2Cl_2	trace	
5	$[IrCp^*Cl_2)]_2$	CH_2Cl_2	33	3.1:1
6	$PdCl_2$	CH_2Cl_2	41	1.7:1
7	$Pd(CO_2CF_3)_2$	CH_2Cl_2	40	3.0:1
8	$Pd(OAc)_2$	CH_2Cl_2	45	3.3:1
9[b]	$Pd(OAc)_2$	CH_2Cl_2	63	3.3:1
10[b]	$Pd(OAc)_2$	$CHCl_3$	27	2.4:1
11[b]	$Pd(OAc)_2$	DCE	40	3.3:1
12[b]	$Pd(OAc)_2$	MeCN	21	2.7:1
13[b]	$Pd(OAc)_2$	toluene	29	3.0:1
14[b]	$Pd(OAc)_2$	THF	52	2.7:1
15[b]	$Pd(OAc)_2$	$MeNO_2$	59	2.3:1
16[b,c]	$Pd(OAc)_2$	CH_2Cl_2	66	3.0:1
17[b,d]	$Pd(OAc)_2$	CH_2Cl_2	78	3.3:1

[a]Unless indicated otherwise, the mixture of **1** (0.05 mmol), **2** (0.05 mmol), and $Pd(OAc)_2$ (10 mol %) in CH_2Cl_2 (0.8 mL) was stirred at 25 °C for 3.5 h. [b]A mixture of **1** (0.05 mmol) and **2** (0.05 mol) in CH_2Cl_2 (0.3 mL) was added via a syringe pump over 0.5 h to $Pd(OAc)_2$ (10 mol %) in 0.5 mL of CH_2Cl_2; the resulting mixture was then stirred at 25 °C for a further 3 h. [c]0.1 mmol of **2** was employed. [d]0.1 mmol of **1** was used.

3.3:1 diastereoselectivity (entries 7 and 8). To further improve the yield, we added the substrates and catalyst in different sequences. When dimethyl fumarate was added after the nitrone alkyne **1a** was stirred with $Pd(OAc)_2$, the reaction gave only a trace amount of the cycloaddition product. On the other hand, when the substrates (**1** and **2**) were added via a syringe pump into a DCM solution of the palladium catalyst, we obtained **3a** with 63% yield without decline of the diastereoselectivity (entry 9). Screening of the solvents showed that other solvents, such as THF and $MeNO_2$, also provided acceptable yields (entries 10−15). Tuning the ratio of substrates exhibited a significantly beneficial effect for the reaction and improved the yield to 78% (entries 16 and 17).

We next investigated the substrate scope of this *N*-aryl nitrone alkyne cycloisomerization/dipolar cycloaddition reaction (Table 2). Nitrone alkynes with different *N*-aryl groups were first examined. *p*-, *m*-, and *o*-methyl-substituted *N*-aryl groups were well tolerated, providing the cyclic products with good yields and moderate diastereoselectivities (**3b−d**). Substrates with an electron-deficient *N*-aryl group also underwent the tandem reaction smoothly, affording the corresponding products with satisfying yields and diastereoselectivities (**3e−h**). Nitrone alkynes with various substituents on the aryl core were subsequently investigated. Generally, substrates with different electron demands underwent the tandem reaction cleanly. For example, methyl-, methoxy-, and fluoro-substituted substrates all successfully afforded the tricyclic product with good yields (**3i−m**). However, when more electron-rich nitrone alkyne **3n** was employed, only 38% yield was obtained. The structure of **3n** was further confirmed by single-crystal XRD analysis (see the Supporting Information for details). Diethyl fumarate and *N*-methylmaleimide also proved to be good dipolarophiles, providing the dipolar cycloaddition products with good yields and moderate diastereoselectivities (**3o−p**).

In order to investigate the applicability of this methodology, a larger scale (1.0 mmol) experiment was conducted. The desired products were obtained with 62% yield and 3.1:1 diastereoselectivity (Figure 1).

A deuterium-labeling experiment was carried out to probe the mechanism of the Pd(II)-catalyzed cascade reaction of *N*-arylnitrone alkynes and electron-deficient olefins. **1a-D**, which was 81% deuterated at the alkynyl position, and dimethyl fumarate under the standard reaction conditions led to deuterated product **3a-D**, supporting a mechanism as shown in Figure 2. The proposed reaction pathway is consistent with the mechanism brought up by Shin[5i] and Li.[5e] First, the Pd(II) catalyst activates the C−C triple bond as a π-Lewis acid, leading to a 6-*exo*-*dig* cyclization to form intermediate **B**. After an internal N−O bond redox, palladium carbene species **C** is formed,[11] which then undergoes an intramolecular nucleophilic addition by the imine group, generating intermediate **D**. Enolization of **D** leads to the key intermediate **I-a**, which participates a [3 + 2] dipolar cycloaddition with electro-deficient olefins to form the final product **3a**. As supported by the results of the deuterium-labeling experiment, in the entire process there is no cleavage of the alkynyl C−H bond.

In summary, a cycloisomerization/dipolar cycloaddition tandem reaction of nitrone alkynes and electron-deficient olefins was revealed by employing a simple palladium(II) catalyst. In previous studies, such *N*−*O* bond redox processes were mainly catalyzed by gold, ruthenium, and iridium complexes. More importantly, *N*-arylnitrone alkynes, which were generally not tolerated in the reported methodologies, were successfully incorporated in the tandem reaction with generally good yields.

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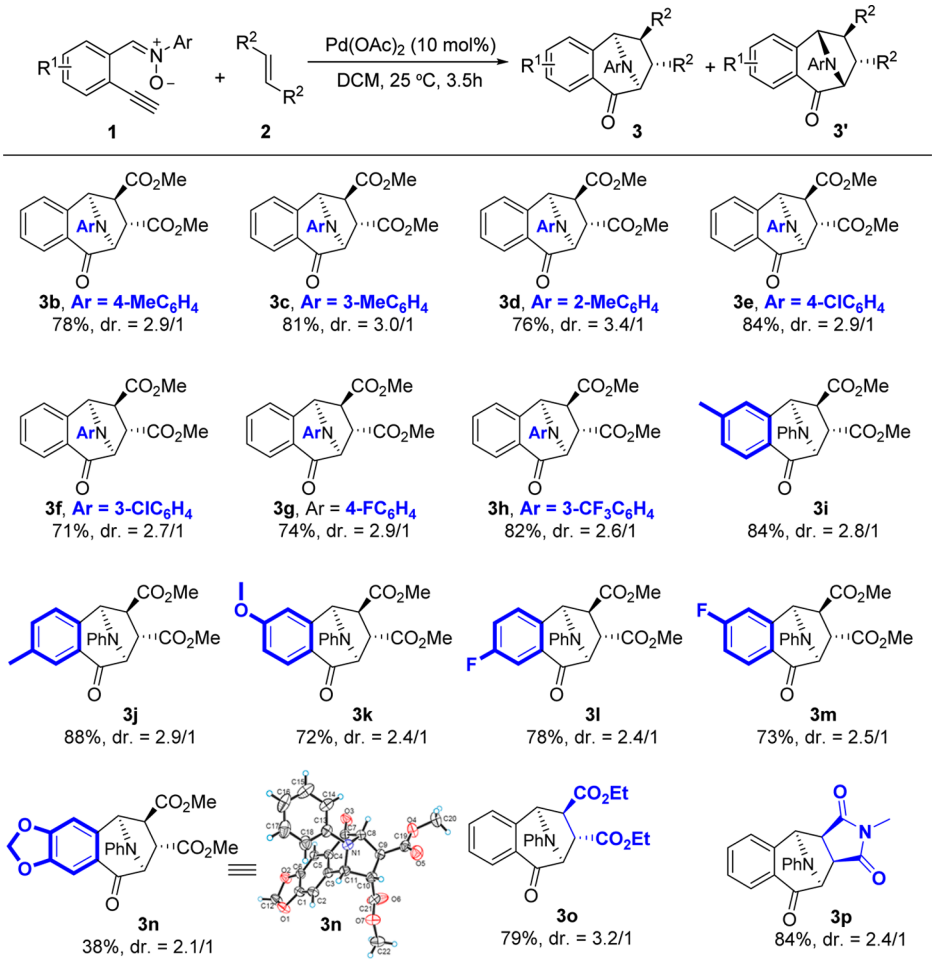
Table 2. Scope of Substrates[a–c]



[a]A mixture of **1** (0.10 mmol) and **2** (0.05 mol) in CH_2Cl_2 (0.3 mL) was added via a syringe pump over 0.5 h to $Pd(OAc)_2$ (10 mol %) in 0.5 mL of CH_2Cl_2; the resulting mixture was then stirred at 25 °C for a further 3 h. [b]Combined yield of both diastereomers. [c]The dr was determined by ^1H NMR.

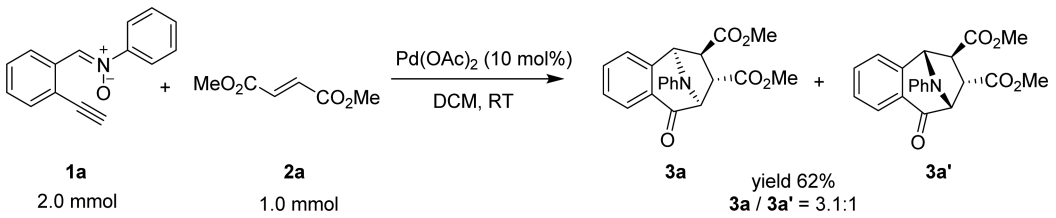


Figure 1. 1.0 mmol scale reaction of **1a** and **2a**.

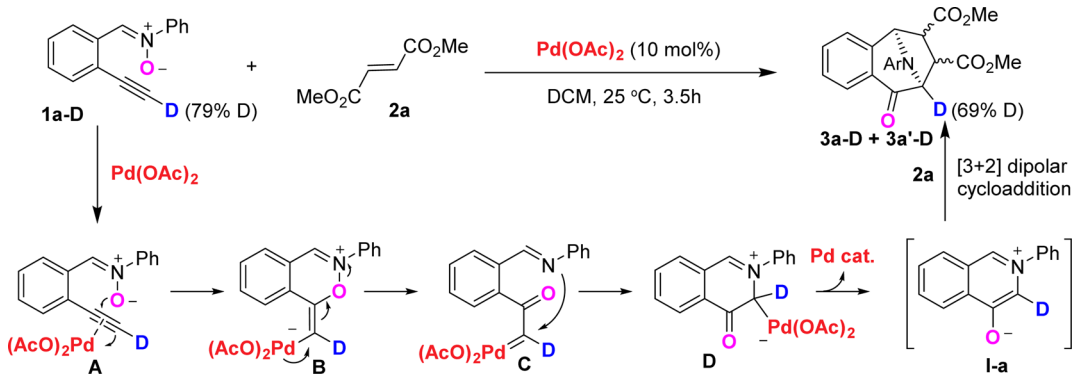


Figure 2. Proposed mechanism for the reaction.

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EXPERIMENTAL SECTION

General Methods. NMR spectra were recorded on a 400 MHz spectrometer. HRMS spectra were recorded on a TOF-Q mass spectrometer. All starting materials, reagents, and solvents were purchased from commercial suppliers and used as supplied unless otherwise stated. Toluene and THF were dried over Na and distilled prior to use. CH_2Cl_2 was dried over CaH_2 and distilled prior to use.

For the synthesis procedure and characterization of alkyne nitrone substrates, see the Supporting Information.

General Reaction Procedures. In a screw-capped vial, $Pd(OAc)_2$ (10 mol %) was flushed with argon and suspended in CH_2Cl_2 (0.3 mL). A mixture of substituted (2-ethynylbenzylidene)aniline oxide (0.1 mmol) and dienophile (0.05 mmol) was dissolved in CH_2Cl_2 (0.5 mL) before being added to the reaction by syringe pump over 30 min. The resulting mixture was allowed to stir at 25 °C for another 3 h. After that, the solvent was removed under reduced pressure, and the crude product was purified through flash column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1).

General Procedures for the Synthesis of (2-Ethynylbenzylidene)aniline Oxide Derivatives. A mixture of 2-bromobenzaldehyde derivative (10 mmol, 1.0 equiv), $Pd(PPh_3)_2Cl_2$ (140 mg, 0.2 mmol), and CuI (19 mg, 0.1 mmol) was suspended in Et_3N (10 mL). (Trimethylsilyl)acetylene (1.68 mL, 12 mmol, 1.2 equiv) was added into the reaction slowly, and then the mixture was stirred for 10 h at 60 °C. Afterward, the mixture was filtered, and the solvent was removed under reduced pressure. The crude product was purified through flash column chromatography (petroleum ether/ethyl acetate = 50:1) to obtain substituted 2-[(trimethylsilyl)ethynyl]benzaldehyde derivative.

To a mixture of substituted 2-[(trimethylsilyl)ethynyl]benzaldehyde derivative (5.0 mmol, 1.0 equiv), nitrobenzene (0.56 mL, 5.5 mmol, 1.1 equiv), and ammonium chloride (344 mg, 6.5 mmol, 1.3 equiv) in EtOH (10 mL) and H_2O (5 mL) was added Zn powder (650 mg, 10 mmol, 2 equiv) slowly over 30 min at 0 °C.[12] The mixture was then warmed to room temperature and stirred overnight. The reaction mixture was filtered through Celite, extracted by CH_2Cl_2, and dried over Na_2SO_4, and then the solvent as removed under reduced pressure. Pure 2-(trimethylsilyl)ethynyl)benzylidene aniline oxide was obtained after flash column chromatography (petroleum ether/ethyl acetate = 10:1).

A mixture of 2-(trimethylsilyl)ethynyl)benzylidene aniline oxide (3 mmol, 1 equiv) and K_2CO_3 (1.23 g, 9 mmol, 3 equiv) was suspended in MeOH (10 mL). After being stirred for 30 min, the crude mixture was filtered. Then, the solvent was removed under reduced pressure before the product was purified through flash column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to achieve the (2-ethynylbenzylidene)aniline oxide derivative **1**.

Characterization of (2-Ethynylbenzylidene)aniline Oxide Derivatives 1. *(Z)-N-(2-Ethynylbenzylidene)aniline Oxide (**1a**).* 352 mg. Yield: 64%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.53 (dd, J = 8.1, 0.5 Hz, 1H), 8.58 (s, 1H), 7.83−7.77 (m, 2H), 7.60 (dd, J = 7.6, 1.2 Hz, 1H), 7.54−7.45 (m, 4H), 7.38−7.43 (m, 1H), 3.46 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 149.5, 133.1, 132.3, 132.1, 130.2, 130.1, 129.5, 129.2, 127.7, 121.9, 121.9, 83.8, 81.1. IR: 2102, 1603, 1504, 1316, 1060, 756, 692. HR-ESI: calcd for $C_{15}H_{11}NO$ [M + H] 222.0919, found 222.0925.

*(Z)-N-(2-Ethynylbenzylidene)-4-methylaniline Oxide (**1b**).* 510 mg. Yield: 68%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.55−9.47 (m, 1H), 8.56 (s, 1H), 7.73−7.65 (m, 2H), 7.59 (dd, J = 7.7, 1.0 Hz, 1H), 7.46−7.53 (m, 1H), 7.36−7.42 (m, 1H), 7.28 (d, J = 8.1 Hz, 2H), 3.45 (s, 1H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 147.2, 140.4, 133.0, 132.2, 131.8, 130.1, 129.7, 129.4, 127.7, 121.8, 121.6, 83.7, 81.1, 21.2. IR: 2096, 1543, 1502, 1458, 1419, 1200, 1075, 812, 761. HR-ESI: calcd for $C_{16}H_{13}NO$ [M + H] 236.1075, found 236.1074.

*(Z)-N-(2-Ethynylbenzylidene)-3-methylaniline Oxide (**1c**).* 515 mg. Yield: 66%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.52 (dd, J = 8.1, 0.5 Hz, 1H), 8.55 (s, 1H), 7.64−7.48 (m, 4H), 7.43−7.33 (m, 2H), 7.28 (d, J = 7.6 Hz, 1H), 3.45 (s, 1H), 2.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 149.5, 139.5, 133.0, 132.2, 132.1, 130.8, 130.1, 129.4, 128.9, 127.7, 122.6, 121.8, 118.8, 83.7, 81.1, 21.4. IR: 2098, 1682, 1487, 1458, 1399, 1166, 1079, 787, 761. HR-ESI: calcd for $C_{16}H_{13}NO$ [M + H] 236.1075, found 236.1068.

*(Z)-N-(2-Ethynylbenzylidene)-2-methylaniline Oxide (**1d**).* 452 mg. Yield: 61%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.52 (d, J = 8.0 Hz, 1H), 8.18 (s, 1H), 7.58 (dd, J = 7.6, 1.0 Hz, 1H), 7.46−7.53 (m, 1H), 7.44−7.37 (m, 2H), 7.36−7.24 (m, 3H), 3.37 (s, 1H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 149.1, 135.3, 133.1, 131.8, 131.6, 131.6, 130.2, 129.4, 129.4, 127.6, 126.8, 123.5, 121.6, 83.8, 80.9, 17.2. IR: 2097, 1548, 1488, 1460, 1406, 1195, 1124, 1072, 765. HR-ESI: calcd for $C_{16}H_{13}NO$ [M + H] 236.1075, found 236.1069.

*(Z)-4-Chloro-N-(2-ethynylbenzylidene)aniline Oxide (**1e**).* 361 mg. Yield: 72%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.53−9.45 (m, 1H), 8.55 (s, 1H), 7.87−7.69 (m, 2H), 7.61 (dd, J = 7.6, 1.2 Hz, 1H), 7.54−7.44 (m, 3H), 7.42 (ddd, J = 7.6, 5.9, 1.3 Hz, 1H), 3.48 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 147.8, 136.0, 133.1, 132.3, 131.8, 130.5, 129.5, 129.4, 127.7, 123.1, 122.0, 84.0, 81.0. IR: 2098, 1483, 1419, 1201, 1092, 1074, 760. HR-ESI: calcd for $C_{15}H_{10}ClNO$ [M + H] 256.0529, found 256.0518.

*(Z)-3-Chloro-N-(2-ethynylbenzylidene)aniline Oxide (**1f**).* 546 mg. Yield: 64%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.49 (d, J = 8.1 Hz, 1H), 8.55 (s, 1H), 7.81−7.88 (m, 1H), 7.71−7.66 (m, 1H), 7.61 (dd, J = 7.6, 1.1 Hz, 1H), 7.55−7.49 (m, 1H), 7.48−7.39 (m, 3H), 3.48 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 150.2, 135.1, 133.1, 132.6, 131.7, 130.6, 130.3, 130.2, 129.5, 127.8, 122.6, 122.1, 119.9, 84.0, 81.0. IR: 2099, 1587, 1469, 1434, 1107, 760, 682. HR-ESI: calcd for $C_{15}H_{10}ClNO$ [M + H] 256.0529, found 256.0530.

*(Z)-N-(2-Ethynylbenzylidene)-4-fluoroaniline Oxide (**1g**).* 298 mg. Yield: 59%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.49 (d, J = 8.1 Hz, 1H), 8.53 (s, 1H), 7.86−7.77 (m, 2H), 7.60 (dd, J = 7.6, 1.0 Hz, 1H), 7.47−7.55 (m, 1H), 7.38−7.44 (m, 1H), 7.22−7.14 (m, 2H), 3.46 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.2 (d, J = 250.8 Hz), 145.6 (d, J = 2.8 Hz), 133.1, 132.1, 131.9, 130.3, 129.5, 127.7, 123.8 (d, J = 8.9 Hz), 121.9, 116.1 (d, J = 23.2 Hz), 83.8, 81.0. IR: 2097, 1500, 1235, 1200, 1074, 760. HR-ESI: calcd for $C_{15}H_{10}FNO$ [M + H] 240.0825, found 240.0818.

*(Z)-N-(2-Ethynylbenzylidene)-3-(trifluoromethyl)aniline Oxide (**1h**).* 375 mg. Yield: 64%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.50 (d, J = 8.0 Hz, 1H), 8.61 (s, 1H), 8.13 (s, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 7.7 Hz, 1H), 7.69−7.60 (m, 2H), 7.49−7.57 (m, 1H), 7.48−7.40 (m, 1H), 3.49 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 149.6, 133.2, 132.8, 132.0 (q, J = 33.4 Hz), 131.6, 130.7, 130.0, 129.5, 127.8, 126.8 (q, J = 7.2 Hz), 125.0, 123.3 (q, J = 272.8 Hz), 122.2, 119.4 (q, J = 4.0 Hz), 84.1, 80.9. IR: 2100, 1328, 1173, 1130, 1075, 761. HR-ESI: calcd for $C_{16}H_{10}F_3NO$ [M + H] 290.0793, found 290.0783.

*(Z)-N-(2-Ethynyl-5-methylbenzylidene)aniline Oxide (**1i**).* 396 mg. Yield: 75%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.38 (s, 1H), 8.56 (s, 1H), 7.83−7.77 (m, 2H), 7.55−7.45 (m, 4H), 7.23 (dd, J = 7.8, 0.9 Hz, 1H), 3.40 (s, 1H), 2.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 149.5, 139.8, 132.9, 132.5, 131.8, 131.2, 130.0, 129.2, 128.2, 121.8, 119.1, 83.0, 81.3. IR: 2096, 1485, 1460, 1407, 1204, 1071, 817, 757, 686. HR-ESI: calcd for $C_{16}H_{13}NO$ [M + H] 236.1075, found 236.1065.

*(Z)-N-(2-Ethynyl-4-methylbenzylidene)aniline Oxide (**1j**).* 653 mg. Yield: 73%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.43 (d, J = 8.3 Hz, 1H), 8.55 (s, 1H), 7.76−7.83 (m, 2H), 7.56−7.45 (m, 3H), 7.41−7.44 (m, 1H), 7.32 (d, J = 8.7 Hz, 1H), 3.42 (s, 1H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 149.4, 140.9, 133.7, 132.3, 130.3, 130.1, 129.9, 129.5, 129.2, 129.2, 127.8, 121.9, 121.8, 83.3, 81.2, 21.5. IR: 2097, 1597, 1486, 1460, 1190, 1074, 763. HR-ESI: calcd for $C_{16}H_{13}NO$ [M + H] 236.1075, found 236.1072.

*(Z)-N-(2-Ethynyl-5-methoxybenzylidene)aniline Oxide (**1k**).* 755 mg. Yield: 69%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.23 (d, J = 2.7 Hz, 1H), 8.59 (s, 1H), 7.83−7.77 (m, 2H), 7.55−7.46 (m, 4H), 6.97 (dd, J = 8.6, 2.8 Hz, 1H), 3.92 (s, 3H), 3.38 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 160.1, 149.4, 134.1, 133.4, 132.6, 130.1, 129.3, 121.8, 118.0, 114.4, 111.3, 82.4, 81.2, 55.6. IR: 2093, 1594, 1477, 1298, 1245, 1206, 1101, 1027. HR-ESI: calcd for $C_{16}H_{13}NO_2$ [M + H] 252.1024, found 252.1022.

*(Z)-N-(2-Ethynyl-4-fluorobenzylidene)aniline Oxide (**1l**).* 428 mg. Yield: 65%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.61 (dd, J = 9.1, 6.1 Hz, 1H), 8.52 (s, 1H), 7.81−7.76 (m, 2H), 7.53−7.47 (m, 3H),

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7.29 (dd, J = 8.8, 2.7 Hz, 1H), 7.17−7.24 (m, 1H), 3.51 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 162.6 (d, J = 253.9 Hz), 149.3, 131.2, 130.1 (d, J = 8.5 Hz), 130.1, 129.3, 128.7 (d, J = 3.5 Hz), 124.2 (d, J = 9.6 Hz), 121.8, 120.0 (d, J = 24.1 Hz), 116.8 (d, J = 21.1 Hz), 84.8, 79.9 (d, J = 3.2 Hz). IR: 2095, 1545, 1455, 1400, 1255, 1073, 860, 763, 689. HR-ESI: calcd for $C_{15}H_{10}FNO$ [M + H] 240.0825, found 240.0821.

*(Z)-N-(2-Ethynyl-5-fluorobenzylidene)aniline Oxide (**1m**).* 339 mg. Yield: 58%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.33 (dd, J = 11.0, 2.6 Hz, 1H), 8.58 (s, 1H), 7.76−7.82 (m, 2H), 7.57 (dd, J = 8.5, 5.7 Hz, 1H), 7.46−7.52 (m, 3H), 7.06−7.15 (m, 1H), 3.44 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 163.5 (d, J = 249.5 Hz), 150.2, 135.6 (d, J = 8.6 Hz), 135.0 (d, J = 10.3 Hz), 132.4, 131.3, 130.2, 122.7, 118.7 (d, J = 3.5 Hz), 118.3 (d, J = 23.1 Hz), 115.6 (d, J = 27.2 Hz), 84.4 (d, J = 1.5 Hz), 81.2. IR: 2100, 1595, 1570, 1485, 1466, 1273, 1202, 761, 166. HR-ESI: calcd for $C_{15}H_{10}FNO$ [M + H] 240.0825, found 240.0819.

*(Z)-N-((6-Ethynylbenzo[d][1,3]dioxol-5-yl)methylene)aniline Oxide (**1n**).* 201 mg. Yield: 51%. Yellow oil ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.15 (s, 1H), 8.52 (s, 1H), 7.89−7.68 (m, 2H), 7.56−7.41 (m, 3H), 7.03 (s, 1H), 6.07 (s, 2H), 3.41 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 149.3, 149.0, 148.4, 132.3, 129.9, 129.2, 127.9, 121.7, 117.1, 112.7, 107.9, 102.1, 82.9, 81.1. IR: 2097, 1484, 1346, 1287, 1040, 762. HR-ESI: calcd for $C_{16}H_{11}NO_3$ [M + H] 266.0817, found 266.0814.

Characterization of the Cycloaddition Products 3. *Compound **3a**.* Yield: 78% (14.1 mg). dr = 3.3/1. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92−7.86 (m, 1H), 7.47 (td, J = 7.5, 1.4 Hz, 1H), 7.29 (td, J = 7.6, 1.2 Hz, 1H), 7.26−7.23 (m, 1H), 7.14−7.08 (m, 2H), 6.80−6.71 (m, 3H), 5.43 (d, J = 6.6 Hz, 1H), 5.01 (t, J = 1.0 Hz, 1H), 4.23 (dd, J = 6.6, 6.3 Hz, 1H), 3.79 (s, 3H), 3.61 (dd, J = 6.3, 0.9 Hz, 1H), 3.54 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 194.3, 172.0, 170.0, 145.1, 140.3, 134.2, 129.9, 129.4, 128.9, 127.5, 127.5, 120.4, 116.5, 68.9, 62.8, 53.1, 52.3, 51.9, 45.7. IR: 1735, 1697, 1599, 1498, 1436, 1232, 755. HR-ESI: calcd for $C_{21}H_{19}NO_5$ [M + H] 366.1342, found 366.1332. Light yellow oil.

*Compound **3a**′.* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88−7.83 (m, 1H), 7.54 (td, J = 7.5, 1.3 Hz, 1H), 7.46−7.41 (m, 1H), 7.29 (td, J = 7.6, 1.2 Hz, 1H), 7.15−7.07 (m, 2H), 6.80−6.71 (m, 3H), 5.51 (s, 1H), 4.97 (d, J = 7.9 Hz, 1H), 4.26 (dd, J = 7.9, 5.4 Hz, 1H), 3.82 (s, 3H), 3.69 (s, 3H), 3.63 (d, J = 5.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 193.9, 172.1, 170.4, 145.0, 143.7, 134.9, 130.2, 129.4, 128.4, 127.2, 126.0, 120.3, 116.6, 68.8, 63.3, 53.0, 52.7, 52.3, 47.6. Light yellow oil.

*Compound **3b**.* Yield: 78% (14.7 mg). dr = 2.9/1. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (d, J = 7.7 Hz, 1H), 7.48 (t, J = 7.3 Hz, 1H), 7.30 (t, J = 7.5 Hz, 1H), 7.24 (d, J = 7.5 Hz, 1H), 6.91 (d, J = 8.2 Hz, 2H), 6.67 (d, J = 8.4 Hz, 2H), 5.39 (d, J = 6.6 Hz, 1H), 4.96 (s, 1H), 4.23 (dd, J = 6.6, 6.3 Hz, 1H), 3.81 (s, 3H), 3.60 (d, J = 6.3 Hz, 1H), 3.55 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 194.6, 172.0, 170.1, 142.6, 140.3, 134.2, 129.9, 129.9, 129.6, 128.8, 127.4, 116.5, 69.0, 62.9, 53.1, 52.3, 51.8, 45.7, 20.4. IR: 1737, 1694, 1515, 1176, 1014. HR-ESI: calcd for $C_{22}H_{21}NO_5$ [M + H] 380.1498, found 380.1493. Light yellow oil.

*Compound **3b**′.* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, J = 7.7 Hz, 1H), 7.54 (td, J = 7.5, 1.2 Hz, 1H), 7.42 (d, J = 7.4 Hz, 1H), 7.33−7.27 (m, 1H), 6.91 (d, J = 8.3 Hz, 2H), 6.66 (d, J = 8.5 Hz, 2H), 5.47 (s, 1H), 4.93 (d, J = 7.9 Hz, 1H), 4.26 (dd, J = 7.9, 5.4 Hz, 1H), 3.82 (s, 3H), 3.69 (s, 3H), 3.61 (d, J = 5.4 Hz, 1H), 2.14 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 194.2, 172.1, 170.5, 143.7, 142.6, 134.9, 130.2, 129.9, 129.6, 128.3, 127.1, 126.0, 116.6, 69.0, 63.4, 53.0, 52.7, 52.3, 47.6, 20.4. Light yellow oil.

*Compound **3c**.* Yield: 81% (15.4 mg). dr = 3.0/1. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, J = 7.6 Hz, 1H), 7.48 (t, J = 7.3 Hz, 1H), 7.31 (t, J = 7.5 Hz, 1H), 7.27−7.23 (m, 1H), 6.99 (t, J = 7.8 Hz, 1H), 6.63−6.53 (m, 3H), 5.43 (d, J = 6.6 Hz, 1H), 4.99 (s, 1H), 4.22 (dd, J = 6.6, 6.2 Hz, 1H), 3.81 (s, 3H), 3.60 (d, J = 6.2 Hz, 1H), 3.55 (s, 3H), 2.20 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 194.4, 172.0, 170.0, 145.0, 140.3, 139.2, 134.2, 129.8, 129.2, 128.8, 127.5, 127.4, 121.3, 117.2, 113.6, 68.7, 62.7, 53.1, 52.3, 51.7, 45.7, 21.6. IR: 1739, 1697, 1603, 1494, 1227, 1180, 775. HR-ESI: calcd for $C_{22}H_{21}NO_5$ [M + H] 380.1498, found 380.1497. Light yellow oil.

*Compound **3c**′.* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, J = 7.6 Hz, 1H), 7.54 (t, J = 7.3 Hz, 1H), 7.46−7.40 (m, 1H), 7.30 (t, J = 7.5 Hz, 1H), 6.99 (t, J = 7.8 Hz, 1H), 6.63−6.53 (m, 3H), 5.50 (s, 1H), 4.96 (d, J = 7.9 Hz, 1H), 4.25 (dd, J = 7.8, 5.4 Hz, 1H), 3.82 (s, 3H), 3.69 (s, 3H), 3.61 (d, J = 5.3 Hz, 1H), 2.19 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 194.0, 172.1, 170.5, 144.9, 143.8, 139.2, 134.9, 130.2, 129.2, 128.4, 127.2, 126.0, 121.2, 117.3, 113.6, 68.7, 63.2, 53.0, 52.7, 52.2, 47.6, 21.6. Light yellow oil.

*Compound **3d**.* Yield: 76% (14.4 mg). dr = 3.4/1. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, J = 7.6 Hz, 1H), 7.44 (t, J = 7.3 Hz, 1H), 7.31 (t, J = 7.6 Hz, 1H), 7.11 (d, J = 7.5 Hz, 1H), 7.04 (d, J = 6.8 Hz, 1H), 6.89−6.78 (m, 2H), 6.50 (d, J = 7.5 Hz, 1H), 5.07 (d, J = 6.5 Hz, 1H), 4.67 (s, 1H), 4.16 (dd, J = 6.5, 6.2 Hz, 1H), 3.72 (s, 3H), 3.48 (d, J = 6.2 Hz, 1H), 3.45 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 194.0, 171.3, 169.1, 142.4, 139.8, 133.3, 130.8, 129.7, 128.7, 127.8, 126.2, 125.5, 125.4, 122.3, 118.0, 69.4, 63.3, 52.0, 51.2, 50.8, 45.1, 18.2. IR: 1738, 1694, 1600, 1493, 1246, 1223, 1176, 759. HR-ESI: calcd for $C_{22}H_{21}NO_5$ [M + H] 380.1498, found 380.1489. Light yellow oil.

*Compound **3d**′.* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, J = 7.7 Hz, 1H), 7.56 (t, J = 7.5 Hz, 1H), 7.41−7.30 (m, 2H), 7.09 (d, J = 6.9 Hz, 1H), 6.93−6.83 (m, 2H), 6.60−6.54 (m, 1H), 5.30 (s, 1H), 4.67 (d, J = 7.7 Hz, 1H), 4.26 (dd, J = 7.7, 5.4 Hz, 1H), 3.80 (s, 3H), 3.69 (s, 3H), 3.59 (d, J = 5.3 Hz, 1H), 2.30 (d, J = 8.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 195.2, 172.3, 170.6, 143.9, 143.1, 135.1, 131.8, 130.6, 130.1, 128.4, 126.7, 126.4, 125.2, 123.3, 119.1, 70.4, 64.5, 53.0, 52.9, 52.7, 47.6, 19.2. Light yellow oil.

*Compound **3e**.* Yield: 84% (16.8 mg). dr = 2.9/1. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, J = 7.6 Hz, 1H), 7.50 (t, J = 7.4 Hz, 1H), 7.34 (t, J = 7.5 Hz, 1H), 7.29−7.21 (m, 1 H), 7.07 (d, J = 8.7 Hz, 2H), 6.69 (d, J = 8.7 Hz, 2H), 5.37 (d, J = 6.5 Hz, 1H), 4.95 (s, 1H), 4.22 (dd, J = 6.5, 6.2 Hz, 1H), 3.82 (s, 3H), 3.61 (d, J = 6.2 Hz, 1H), 3.55 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 194.0, 171.9, 169.8, 143.7, 139.9, 134.3, 129.7, 129.3, 129.1, 127.6, 127.5, 125.3, 117.8, 69.0, 62.9, 53.2, 52.4, 51.7, 45.6. IR: 1740, 1697, 1598, 1496, 1287, 1232, 821, 756. HR-ESI: calcd for $C_{21}H_{18}ClNO_5$ [M + H] 400.0951, found 400.0949. Light yellow oil.

*Compound **3e**′.* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88−7.84 (m, 1H), 7.55 (td, J = 7.5, 1.3 Hz, 1H), 7.41 (d, J = 7.6 Hz, 1H), 7.32 (td, J = 7.6, 1.1 Hz, 1H), 7.09−7.03 (m, 2H), 6.71−6.66 (m, 2H), 5.45 (s, 1H), 4.90 (d, J = 7.9 Hz, 1H), 4.24 (dd, J = 7.9, 5.4 Hz, 1H), 3.83 (s, 3H), 3.69 (s, 3H), 3.63 (d, J = 5.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 193.5, 172.0, 170.2, 143.7, 143.3, 135.0, 130.1, 129.3, 128.6, 127.3, 126.0, 125.3, 117.8, 69.0, 63.5, 53.1, 52.8, 52.2, 47.6. Light yellow oil.

*Compound **3f**.* Yield: 71% (14.2 mg). dr = 2.7/1. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, J = 7.6 Hz, 1H), 7.51 (t, J = 7.2 Hz, 1H), 7.35 (t, J = 7.5 Hz, 1H), 7.30−7.25 (m, 1H), 7.04 (t, J = 8.1 Hz, 1H), 6.79−6.75 (m, 1H), 6.72 (d, J = 7.9 Hz, 1H), 6.64 (dd, J = 8.3, 1.6 Hz, 1H), 5.39 (d, J = 6.6 Hz, 1H), 4.97 (s, 1H), 4.21 (dd, J = 6.6, 6.2 Hz, 1H), 3.82 (s, 3H), 3.61 (d, J = 6.2 Hz, 1H), 3.56 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 193.7, 171.8, 169.7, 146.2, 139.9, 135.2, 134.3, 130.4, 129.6, 129.1, 127.7, 127.4, 120.4, 116.6, 114.5, 68.8, 62.7, 53.2, 52.4, 51.7, 45.5. IR: 1738, 1698, 1594, 1483, 1435, 1287, 1234, 993, 758. HR-ESI: calcd for $C_{21}H_{18}ClNO_5$ [M + H] 400.0951, found 400.0948. Light yellow oil.

*Compound **3f**′.* ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, J = 7.6 Hz, 1H), 7.57 (dt, J = 7.5, 3.8 Hz, 1H), 7.44 (d, J = 7.4 Hz, 1H), 7.34 (t, J = 7.6 Hz, 1H), 7.03 (t, J = 8.1 Hz, 1H), 6.77−6.74 (m, 1H), 6.72 (d, J = 7.9 Hz, 1H), 6.63 (dd, J = 8.3, 2.0 Hz, 1H), 5.46 (s, 1H), 4.93 (d, J = 7.9 Hz, 1H), 4.24 (dd, J = 7.9, 5.4 Hz, 1H), 3.83 (s, 3H), 3.70 (s, 3H), 3.62 (d, J = 5.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 193.3, 171.9, 170.2, 146.2, 143.3, 135.1, 135.1, 130.4, 130.0, 128.6, 127.4, 126.0, 120.4, 116.6, 114.6, 68.7, 63.2, 53.1, 52.8, 52.2, 47.6. Light yellow oil.

*Compound **3g**.* Yield: 74% (14.2 mg). dr = 2.9/1. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, J = 7.6 Hz, 1H), 7.50 (t, J = 7.2 Hz, 1H), 7.34 (t, J = 7.5 Hz, 1H), 7.26−7.22 (m, 1H), 6.86−6.78 (m, 2H), 6.74−6.67 (m, 2H), 5.35 (d, J = 6.6 Hz, 1H), 4.93 (s, 1H), 4.23 (dd, J = 6.6, 6.3 Hz, 1H), 3.82 (s, 3H), 3.61 (d, J = 6.3 Hz, 1H), 3.55 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 194.3, 172.0, 169.9, 157.0 (d, J = 239.7 Hz), 141.4 (d, J = 2.3 Hz), 139.9, 134.3, 129.8, 129.0, 127.5, 127.5, 117.7 (d, J = 7.7 Hz), 116.0 (d, J = 22.4 Hz), 69.3, 63.2, 53.1, 52.3, 51.8, 45.7. IR: 1740, 1697, 1509, 1436, 1230, 826, 756. HR-ESI: calcd for $C_{21}H_{18}FNO_5$ [M + H] 384.1247, found 384.1239. Light yellow oil.

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J. Org. Chem. XXXX, XXX, XXX−XXX

Compound ***3g′***. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, J = 7.7 Hz, 1H), 7.56 (t, J = 7.5 Hz, 1H), 7.42 (d, J = 7.5 Hz, 1H), 7.32 (t, J = 7.6 Hz, 1H), 6.86−6.78 (m, 2H), 6.75−6.67 (m, 2H), 5.43 (s, 1H), 4.88 (d, J = 7.9 Hz, 1H), 4.25 (dd, J = 7.8, 5.4 Hz, 1H), 3.83 (s, 3H), 3.69 (s, 3H), 3.63 (d, J = 5.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 193.9, 172.1, 170.4, 157.0 (d, J = 239.6 Hz), 143.3 (d, J = 2.3 Hz), 141.3, 135.0, 130.1, 128.5, 127.2, 126.1, 117.8 (d, J = 7.7 Hz), 116.0 (d, J = 22.5 Hz), 69.3, 63.7, 53.1, 52.8, 52.3, 47.7. Light yellow oil.

Compound ***3h***. Yield: 82% (17.8 mg). dr = 2.6/1. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, J = 7.6 Hz, 1H), 7.52 (t, J = 7.3 Hz, 1H), 7.35 (t, J = 7.5 Hz, 1H), 7.29 (d, J = 7.6 Hz, 1H), 7.25−7.19 (m, 1H), 7.04−6.95 (m, 2H), 6.92 (d, J = 8.2 Hz, 1H), 5.45 (d, J = 6.6 Hz, 1H), 5.03 (s, 1H), 4.23 (dd, J = 6.6, 6.2 Hz, 1H), 3.83 (s, 3H), 3.64 (d, J = 6.2 Hz, 1H), 3.57 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 193.5, 171.8, 169.6, 145.5, 139.8, 134.4, 131,7 (q, J = 32.1 Hz), 130.0, 129.6, 129.2, 127.8,127.4, 123.9 (q, J = 272.5 Hz), 119.3, 116.9 (q, J = 3.8 Hz), 112.9 (m), 68.9, 62.8, 53.2, 52.4, 51.8, 45.6. IR: 1723, 1455, 1378, 1167, 1124, 1070, 759, 697. HR-ESI: calcd for $C_{22}H_{18}F_3NO_5$ [M + H] 434.1215, found 434.1217. Light yellow oil.

Compound ***3h′***. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89−7.85 (m, 1H), 7.57 (td, J = 7.5, 1.3 Hz, 1H), 7.46 (d, J = 7.4 Hz, 1H), 7.33 (td, J = 7.6, 1.1 Hz, 1H), 7.22 (t, J = 7.9 Hz, 1H), 7.02−6.97 (m, 2H), 6.94−6.89 (m, 1H), 5.51 (s, 1H), 5.00 (d, J = 7.9 Hz, 1H), 4.26 (dd, J = 7.9, 5.4 Hz, 1H), 3.84 (s, 3H), 3.70 (s, 3H), 3.65 (d, J = 5.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 193.1, 171.9, 170.1, 145.4, 143.3, 135.1, 132.7 (q, J = 32.0 Hz), 130.0, 129.9, 128.7, 127.5, 126.0, 123.8 (q, J = 272.5 Hz), 119.4, 116.9 (q, J = 3.6 Hz), 113.0 (m), 68.9, 63.2, 53.1, 52.8, 52.2, 47.6. Light yellow oil.

Compound ***3i***. Yield: 84% (16.0 mg). dr = 2.8/1. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, J = 7.9 Hz, 1H), 7.16−7.08 (m, 3H), 7.06−7.01 (m, 1H), 6.81−6.69 (m, 3H), 5.38 (d, J = 6.6 Hz, 1H), 4.97 (s, 1H), 4.22 (dd, J = 6.6, 6.2 Hz, 1H), 3.80 (s, 3H), 3.60 (d, J = 6.2 Hz, 1H), 3.55 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 194.2, 172.1, 170.0, 145.4, 145.1, 140.3, 129.7, 129.4, 128.0, 127.6, 127.4, 120.3, 116.5, 68.8, 62.8, 53.1, 52.2, 51.8, 45.8, 21.9. IR: 1739, 1694, 1606, 1497, 1233, 757. HR-ESI: calcd for $C_{22}H_{21}NO_5$ [M + H] 380.1498, found 380.1496. Light yellow oil.

Compound ***3i′***. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, J = 7.9 Hz, 1H), 7.23−7.21 (m, 1H), 7.14−7.06 (m, 3H), 6.79−6.71 (m, 3H), 5.45 (s, 1H), 4.93 (d, J = 7.9 Hz, 1H), 4.24 (dd, J = 7.9, 5.4 Hz, 1H), 3.82 (s, 3H), 3.69 (s, 3H), 3.61 (d, J = 5.4 Hz, 1H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 193.7, 172.2, 170.5, 146.1, 145.1, 143.8, 129.3, 129.3, 127.8, 127.3, 126.5, 120.3, 116.6, 68.8, 63.4, 53.0, 52.7, 52.3, 47.7, 22.0. Light yellow oil.

Compound ***3j***. Yield: 88% (16.7 mg). dr = 2.9/1. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (s, 1H), 7.31−7.22 (m, 1H), 7.16−7.08 (m, 3H), 6.79−6.71 (m, 3H), 5.40 (d, J = 6.6 Hz, 1H), 4.99 (s, 1H), 4.20 (dd, J = 6.6, 6.4 Hz, 1H), 3.81 (s, 3H), 3.60 (d, J = 6.4 Hz, 1H), 3.57 (s, 3H), 2.28 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 194.7, 172.1, 170.1, 145.1, 138.8, 137.3, 135.0, 129.6, 129.4, 127.9, 127.3, 120.3, 116.5, 68.8, 62.5, 53.1, 52.3, 51.7, 45.7, 21.2. IR: 1739, 1697, 1598, 1499, 1233, 1175, 755. HR-ESI: calcd for $C_{22}H_{21}NO_5$ [M + H] 380.1498, found 380.1488. Light yellow oil.

Compound ***3j′***. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (s, 1H), 7.36−7.30 (m, 2H), 7.15−7.06 (m, 2H), 6.80−6.70 (m, 3H), 5.48 (s, 1H), 4.95 (d, J = 7.9 Hz, 1H), 4.25 (dd, J = 7.8, 5.4 Hz, 1H), 3.81 (s, 3H), 3.70 (s, 3H), 3.60 (d, J = 5.2 Hz, 1H), 2.28 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 194.3, 172.2, 170.6, 145.1, 140.9, 138.3, 135.7, 129.9, 129.3, 127.5, 126.0, 120.2, 116.6, 68.8, 63.0, 53.0, 52.7, 52.3, 47.6, 21.1. Light yellow oil.

Compound ***3k***. Yield: 72% (14.2 mg). dr = 2.4/1. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, J = 8.6 Hz, 1H), 7.16−7.09 (m, 2H), 6.81−6.74 (m, 4H), 6.74−6.70 (m, 1H), 5.37 (d, J = 6.6 Hz, 1H), 4.94 (s, 1H), 4.22 (t, J = 6.5 Hz, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.57−3.62 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 193.3, 172.1, 167.0, 164.3, 145.1, 142.6, 130.1, 129.4, 123.0, 120.3, 116.5, 113.9, 113.0, 68.7, 63.0, 55.6, 53.1, 52.3, 51.8, 45.9. IR: 1737, 1683, 1599, 1496, 1264. HR-ESI: calcd for $C_{22}H_{21}NO_6$ [M + H] 396.1447, found 396.1439. Light yellow oil.

Compound ***3k′***. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, J = 8.6 Hz, 1H), 7.15−7.08 (m, 2H), 6.88 (d, J = 2.2 Hz, 1H), 6.81−6.71 (m, 4H), 5.45 (s, 1H), 4.91 (d, J = 7.8 Hz, 1H), 4.22 (dd, J = 7.7, 5.5 Hz, 1H), 3.86 (s, 3H), 3.82 (s, 3H), 3.70 (s, 3H), 3.63 (d, J = 5.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 192.6, 172.2, 170.5, 164.8, 146.1, 145.1, 129.8, 129.3, 123.3, 120.3, 116.6, 114.0, 111.0, 68.7, 63.5, 55.6, 53.0, 52.7, 52.2, 47.9. Light yellow oil.

Compound ***3l***. Yield: 74% (14.2 mg). dr = 2.4/1. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (dd, J = 8.4, 2.6 Hz, 1H), 7.29−7.23 (m, 1H), 7.20−7.16 (m, 1H), 7.15−7.09 (m, 2H), 6.81−6.71 (m, 3H), 5.44 (d, J = 6.6 Hz, 1H), 5.01 (s, 1H), 4.22 (dd, J = 6.6, 6.2 Hz, 1H), 3.80 (s, 3H), 3.59 (d, J = 6.2 Hz, 1H), 3.56 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 193.4, 171.8, 169.9, 162.5 (d, J = 249.9 Hz), 144.8, 136.2 (d, J = 3.4 Hz), 131.9 (d, J = 6.6 Hz), 129.5, 128.1, 121.3 (d, J = 22.3 Hz), 120.6, 116.5, 114.0 (d, J = 22.5 Hz), 68.4, 62.2, 53.2, 52.4, 51.7, 45.5. IR: 1740, 1704, 1599, 1499, 1267, 1231, 754. HR-ESI: calcd for $C_{21}H_{18}FNO_5$ [M + H] 384.1247, found 384.1242. Light yellow oil.

Compound ***3l′***. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (dd, J = 8.4, 2.6 Hz, 1H), 7.43 (dd, J = 8.3, 4.8 Hz, 1H), 7.23 (td, J = 8.4, 2.7 Hz, 1H), 7.15−7.08 (m, 2H), 6.79−6.70 (m, 3H), 5.52 (s, 1H), 4.96 (d, J = 7.9 Hz, 1H), 4.26 (dd, J = 7.9, 5.3 Hz, 1H), 3.82 (s, 3H), 3.70 (s, 3H), 3.60 (d, J = 5.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 193.1, 171.9, 170.4, 162.2 (d, J = 249.1 Hz), 144.7, 139.6 (d, J = 3.3 Hz), 132.2 (d, J = 6.6 Hz), 129.5, 128.1 (d, J = 7.4 Hz), 121.9 (d, J = 22.4 Hz), 120.6, 116.5, 113.7 (d, J = 22.5 Hz), 68.3, 62.7, 53.1, 52.8, 52.3, 47.5. Light yellow oil.

Compound ***3m*** *and* ***3m′***. Yield: 73% (14.0 mg). dr = 2.5/1. Compound **3m**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (dd, J = 8.4, 5.7 Hz, 1H), 7.18−7.07 (m, 2H), 7.04−6.91 (m, 2H), 6.87−6.68 (m, 3H),5.41 (d, J = 6.7 Hz, 1H), 4.99 (s, 1H), 4.25 (dd, J = 6.7, 6.4 Hz, 1H), 3.81 (s, 3H), 3.61 (d, J = 6.4 Hz, 1H), 3.60 (s, 3H). *Compound* ***3m′***: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (dd, J = 8.6, 5.6 Hz, 1H), 7.60−7.54 (m, 1H), 7.54−7.49 (m, 1H), 7.18−7.07 (m, 1H), 7.01−7.01 (m, 1H), 6.87−6.68 (m, 3H), 5.49 (s, 1H), 4.95 (d, J = 7.9 Hz, 1H), 4.25 (m, 1H), 3.82 (s, 3H), 3.70 (s, 3H), 3.65−3.55 (m, 1H). Mixture of **3m** and **3m′**. ^{13}C NMR (101 MHz, $CDCl_3$): δ 192.9, 192.4, 171.8, 171.8, 170.4, 169.8, 166.5 (d, J = 258.6 Hz), 166.0 (d, J = 258.3 Hz), 146.8 (d, J = 8.1 Hz), 144.8, 144.7, 143.5 (d, J = 8.1 Hz), 130.7 (d, J = 9.8 Hz), 130.4 (d. J = 9.9 Hz), 129.5, 129.5, 126.8 (d, J = 2.8 Hz), 126.4 (d, J = 3.0 Hz), 120.6, 120.6, 116.6, 116.5, 116.3 (d, J = 22.0 Hz), 115.9 (d, J = 22.0 Hz), 114.6 (d, J = 22.3 Hz), 113.2 (d, J = 22.2 Hz), 68.7, 68.6, 63.1, 62.6, 53.1, 53.1, 52.8, 52.4, 52.1, 51.7, 47.7, 45.7. IR: 1739, 1698, 1606, 1497, 1436, 1260, 758. HR-ESI: calcd for $C_{21}H_{18}FNO_5$ [M + H] 384.1247, found 384.1238. Light yellow oil.

Compound ***3n***. Yield: 38% (7.8 mg). dr = 2.1/1. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (s, 1H), 7.17−7.10 (m, 2H), 6.80−6.73 (m, 3H), 6.68 (s, 1H), 6.02−5.94 (m, 2H), 5.34 (d, J = 6.5 Hz, 1H), 4.93 (s, 1H), 4.19 (dd, J = 6.5, 6.2 Hz, 1H), 3.80 (s, 3H), 3.63 (s, 3H), 3.57 (d, J = 6.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 192.9, 172.0, 170.0, 152.8, 148.2, 145.0, 137.1, 129.4, 124.7, 120.4, 116.6, 107.3, 106.8, 102.0, 68.5, 62.9, 53.1, 52.4, 51.7, 45.8. IR: 1738, 1682, 1600, 1498, 1479, 1300, 1261, 1035. HR-ESI: calcd for $C_{22}H_{19}NO_7$ [M + H] 410.1239, found 410.1230. Light yellow oil.

Compound ***3n′***. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27−7.24 (m, 1H), 7.13 (t, J = 7.8 Hz, 2H), 6.85 (s, 1H), 6.81−6.71 (m, 3H), 5.97 (d, J = 6.4 Hz, 2H), 5.42 (s, 1H), 4.90 (d, J = 7.8 Hz, 1H), 4.21 (dd, J = 7.7, 5.4 Hz, 1H), 3.81 (s, 3H), 3.70 (s, 3H), 3.59 (d, J = 5.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 192.1, 172.1, 170.5, 153.3, 147.9, 145.0, 140.8, 129.4, 125.0, 120.4, 116.7, 106.4, 106.0, 102.0, 68.5, 63.5, 53.0, 52.7, 52.2, 47.6. Light yellow oil.

Compound ***3o***. Yield: 79% (15.6 mg). dr = 3.2/1. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, J = 7.6 Hz, 1H), 7.47 (dd, J = 7.5, 6.6 Hz, 1H), 7.36−7.27 (m, 2H), 7.12 (t, J = 7.9 Hz, 2H), 6.82−6.69 (m, 3H), 5.43 (d, J = 6.6 Hz, 1H), 5.00 (s, 1H), 4.32−4.17 (m, 3H), 4.08−3.87 (m, 2H), 3.59 (d, J = 6.2 Hz, 1H), 1.32 (t, J = 7.1 Hz, 3H), 1.16 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 194.5, 171.6, 169.5, 145.1, 140.3, 134.0, 129.9, 129.4, 128.8, 127.7, 127.5, 120.3, 116.5, 69.0, 62.8, 62.1, 61.4, 51.8, 45.8, 14.2, 14.1. IR: 1733, 1694, 1599, 1498, 1183, 1029. HR-ESI: calcd for $C_{23}H_{23}NO_5$ [M + H] 394.1655, found 394.1647. Light yellow oil.

Compound ***3o′***. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87−7.82 (m, 1H), 7.53 (td, J = 7.5, 1.4 Hz, 1H), 7.45−7.40 (m, 1H), 7.28 (td, J = 7.6,

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J. Org. Chem. XXXX, XXX, XXX−XXX

1.2 Hz, 1H), 7.14−7.07 (m, 2H), 6.80−6.76 (m, 2H), 6.76−6.70 (m, 1H), 5.50 (s, 1H), 4.97 (d, J = 7.9 Hz, 1H), 4.31−4.21 (m, 2H), 4.17−4.08 (m, 2H), 3.60 (d, J = 5.3 Hz, 1H), 1.33 (t, J = 7.1 Hz, 3H), 1.24 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 193.8, 171.7, 167.0, 145.1, 143.9, 134.8, 130.4, 129.3, 128.3, 127.1, 126.0, 120.2, 116.5, 68.9, 63.3, 62.0, 61.8, 52.4, 47.6, 14.3, 14.1. Light yellow oil.

Compound ***3p***. Yield: 84% (13.9 mg). dr = 2.4/1. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, J = 7.7 Hz, 1H), 7.51 (td, J = 7.5, 1.3 Hz, 1H), 7.37 (d, J = 7.4 Hz, 1H), 7.28 (td, J = 7.6, 1.0 Hz, 1H), 7.18−7.11 (m, 2H), 6.82−6.75 (m, 3H), 5.48 (d, J = 6.9 Hz, 1H), 5.06 (dd, J = 8.5, 0.7 Hz, 1H), 4.20−4.07 (m, 2H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 192.0, 174.1, 174.0, 144.7, 139.1, 134.7, 130.5, 129.6, 129.0, 128.3, 127.1, 120.9, 116.4, 67.1, 61.5, 50.3, 46.4, 24.4. IR: 1713, 1599, 1498, 1433, 1381, 1282, 1212, 994, 755. HR-ESI: calcd for $C_{20}H_{16}N_2O_3$ [M + H] 333.1239, found 333.1231. Light yellow oil.

Compound ***3p′***. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95−7.90 (m, 1H), 7.58 (td, J = 7.5, 1.4 Hz, 1H), 7.51−7.47 (m, 1H), 7.34 (td, J = 7.6, 1.2 Hz, 1H), 7.14−7.07 (m, 2H), 6.79−6.73 (m, 3H), 5.43 (s, 1H), 4.94 (s, 1H), 3.43 (d, J = 7.5 Hz, 1H), 3.36 (d, J = 7.5 Hz, 1H), 3.05 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 193.2, 176.2, 175.6, 144.5, 142.4, 135.3, 129.5, 129.3, 128.9, 127.7, 126.4, 120.9, 116.9, 68.7, 63.0, 52.4, 46.0, 25.8. Light yellow oil.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

NMR spectra and X-ray data for compound **3n** (CIF). The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00717. Crystallographic data for compound **3n** (CCDC-1401612) can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Nicolaou, K. C.; Chen, J. S. *Chem. Soc. Rev.* **2009**, *38*, 2993. (b) Nicolaou, K. C.; Edmonds, D. J.; Bulger, P. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 7134. (c) Nicolaou, K. C.; Montagnon, T.; Snyder, S. A. *Chem. Commun.* **2003**, 551. (d) Parsons, P. J.; Penkett, C. S.; Shell, A. J. *Chem. Rev.* **1996**, *96*, 195. (e) Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, *96*, 223.

(2) (a) Abu Sohel, S. M.; Liu, R. S. *Chem. Soc. Rev.* **2009**, *38*, 2269. (b) Patil, N. T.; Yamamoto, Y. In *Handbook of Cyclization Reactions*; Ma, S., Ed.; Wiley-VCH: Weinheim, 2009. (c) Galván, A.; Calleja, J.; Fañanás, F. J.; Rodríguez, F. *Chem. - Eur. J.* **2015**, *21*, 3409. (d) Li, N.; Chen, D.-F.; Wang, P.-S.; Han, Z.-Y.; Gong, L.-Z. *Synthesis* **2014**, *46*, 1355. (e) Liu, Y.; Zhen, W.; Dai, W.; Wang, F.; Li, X. *Org. Lett.* **2013**, *15*, 874. (f) Han, Z.-Y.; Chen, D.-F.; Wang, Y.-Y.; Guo, R.; Wang, P.-S.; Wang, C.; Gong, L.-Z. *J. Am. Chem. Soc.* **2012**, *134*, 6532. (g) Han, Z.-Y.; Guo, R.; Wang, P.-S.; Chen, D.-F.; Xiao, H.; Gong, L.-Z. *Tetrahedron Lett.* **2011**, *52*, 5963.

(3) (a) Ghorpade, S.; Su, M. D.; Liu, R. S. *Angew. Chem., Int. Ed.* **2013**, *52*, 4229. (b) Li, L.; Shu, C.; Zhou, B.; Yu, Y.-F.; Xiao, X.-Y.; Ye, L.-W. *Chem. Sci.* **2014**, *5*, 4057. (c) Luo, Y.; Ji, K.; Li, Y.; Zhang, L. *J. Am. Chem. Soc.* **2012**, *134*, 17412. (d) Ji, K.; Zhao, Y.; Zhang, L. *Angew. Chem., Int. Ed.* **2013**, *52*, 6508. (e) Ji, K.; Zhang, L. *Org. Chem. Front.* **2014**, *1*, 34. (f) Ye, L.; Cui, L.; Zhang, G.; Zhang, L. *J. Am. Chem. Soc.* **2010**, *132*, 3258. (g) Chen, D. F.; Han, Z. Y.; He, Y. P.; Yu, J.; Gong, L. Z. *Angew. Chem., Int. Ed.* **2012**, *51*, 12307. (h) Cui, L.; Peng, Y.; Zhang, L. *J. Am. Chem. Soc.* **2009**, *131*, 8394. (i) Ye, L.; He, W.; Zhang, L. *J. Am. Chem. Soc.* **2010**, *132*, 8550. (j) Ji, K.; Zheng, Z.; Wang, Z.; Zhang, L. *Angew. Chem., Int. Ed.* **2015**, *54*, 1245.

(4) (a) Lu, B.; Li, Y.; Wang, Y.; Aue, D. H.; Luo, Y.; Zhang, L. *J. Am. Chem. Soc.* **2013**, *135*, 8512. (b) Shapiro, N. D.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 4160. (c) Li, G.; Zhang, L. *Angew. Chem., Int. Ed.* **2007**, *46*, 5156.

(5) (a) Li, G.-H.; Zhou, W.; Li, X.-X.; Bi, Q.-W.; Wang, Z.; Zhao, Z.-G.; Hu, W.-X.; Chen, Z. *Chem. Commun.* **2013**, *49*, 4770. (b) Wang, L.; Xie, X.; Liu, Y. *Org. Lett.* **2012**, *14*, 5848. (c) Qian, Y.; Xu, X.; Wang, X.; Zavalij, P. J.; Hu, W.; Doyle, M. P. *Angew. Chem., Int. Ed.* **2012**, *51*, 5900. (d) Bhunia, S.; Chang, C.-J.; Liu, R.-S. *Org. Lett.* **2012**, *14*, 5522. (e) Song, G.; Chen, D.; Su, Y.; Han, K.; Pan, C.-L.; Jia, A.; Li, X. *Angew. Chem., Int. Ed.* **2011**, *50*, 7791. (f) Chen, D.; Song, G.; Jia, A.; Li, X. *J. Org. Chem.* **2011**, *76*, 8488. (g) Yeom, H.-S.; Lee, Y.; Lee, J.-E.; Shin, S. *Org. Biomol. Chem.* **2009**, *7*, 4744. (h) Pati, K.; Liu, R.-S. *Chem. Commun.* **2009**, 5233. (i) Yeom, H. S.; Lee, J. E.; Shin, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 7040. (j) Jeong, J.; Yeom, H.-S.; Kwon, O.; Shin, S. *Chem. - Asian J.* **2011**, *6*, 1977.

(6) (a) Cikotiene, I. *Eur. J. Org. Chem.* **2012**, *2012*, 2766. (b) Patel, P.; Ramana, C. V. *Org. Biomol. Chem.* **2011**, *9*, 7327. (c) Söderberg, B. C. G.; Gorugantula, S. P.; Howerton, C. R.; Petersen, J. L.; Dantale, S. W. *Tetrahedron* **2009**, *65*, 7357. (d) Asao, N.; Sato, K.; Yamamoto, Y. *Tetrahedron Lett.* **2003**, *44*, 5675. (e) Rosen, G. M.; Tsai, P.; Barth, E. D.; Dorey, G.; Casara, P.; Spedding, M.; Halpern, H. J. *J. Org. Chem.* **2000**, *65*, 4460. (f) Ramana, C. V.; Patel, P.; Vanka, K.; Miao, B.; Degterev, A. *Eur. J. Org. Chem.* **2010**, *2010*, 5955.

(7) (a) Nakamura, I.; Terada, M. *Heterocycles* **2014**, *89*, 845. (b) Wang, Y.; Zhang, L. *Synthesis* **2015**, *47*, 289. (c) Zhang, L. *Acc. Chem. Res.* **2014**, *47*, 877. (d) Yeom, H.-S.; Shin, S. *Acc. Chem. Res.* **2014**, *47*, 966. (e) Xiao, J.; Li, X. *Angew. Chem., Int. Ed.* **2011**, *50*, 7226.

(8) (a) Hamer, J.; Macaluso, A. *Chem. Rev.* **1964**, *64*, 473. (b) Tufariello, J. J. *Acc. Chem. Res.* **1979**, *12*, 396. (c) Freeman, J. P. *Chem. Rev.* **1983**, *83*, 241.

(9) (a) Gothelf, K. V.; Jørgensen, K. A. *Chem. Rev.* **1998**, *98*, 863. (b) Coldham, I.; Hufton, R. *Chem. Rev.* **2005**, *105*, 2765. (c) Harwood, L. M.; Vickers, R. J. In *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products*; John Wiley & Sons, Inc.: New York, 2003; p 169. (d) Adrio, J.; Carretero, J. C. *Chem. Commun.* **2011**, *47*, 6784.

(10) Actually, this type of azomethine ylides, namely the 4-oxidoisoquinolinium betaines, were previously synthesized and studied as dipolar agents by Katritzky and others. (a) Dennis, N.; Katritzky, A. R.; Takeuchi, Y. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2054. (b) Dennis, N.; Ibrahim, B.; Katritzky, A. R.; Takeuchi, Y. *J. Chem. Soc., Chem. Commun.* **1973**, 292a. (c) Undheim, K.; Hansen, P. E. *Chem. Scripta* **1973**, *3*, 113. (d) Dennis, N.; Katritzky, A. R.; Parton, S. K. *Chem. Pharm. Bull.* **1975**, *23*, 2899. (e) Katritzky, A. R.; Dennis, N. *Chem. Rev.* **1989**, *89*, 827.

(11) (a) Xia, Y.; Qu, S.; Xiao, Q.; Wang, Z.-X.; Qu, P.; Chen, L.; Liu, Z.; Tian, L.; Huang, Z.; Zhang, Y.; Wang, J. *J. Am. Chem. Soc.* **2013**, *135*, 13502. (b) Devine, S. K. J.; Van Vranken, D. L. *Org. Lett.* **2008**, *10*, 1909. (c) Fillion, E.; Taylor, N. J. *J. Am. Chem. Soc.* **2003**, *125*, 12700. (d) Carreño, M. C.; Cuerva, J. M.; Ribagorda, M.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **1999**, *38*, 1449. (e) Trost, B. M.; Hashmi, A. S. K. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1085. (f) Trost, B. M.; Tanoury, G. J. *J. Am. Chem. Soc.* **1988**, *110*, 1636.

(12) Lo, M. M.-C.; Fu, G. C. *J. Am. Chem. Soc.* **2002**, *124*, 4572.

DOI: 10.1021/acs.joc.5b00717
J. Org. Chem. XXXX, XXX, XXX−XXX