JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

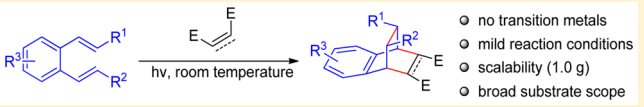
Photoinduced Intermolecular [4+2] Cycloaddition Reaction for Construction of Benzobicyclo[2.2.2]octane Skeletons

Qiang Liu, Junlei Wang, Dazhi Li, Chao Yang,* and Wujiong Xia*

School of Chemistry and Chemical Engineering, State Key Lab of Urban Water Resource and Environment, Harbin Institute of Technology, Harbin 150080, China

Supporting Information

ABSTRACT: A novel and efficient method for the synthesis of highly substituted benzobicyclo[2.2.2]octane skeletons has been explored. Under UV-light irradiation, o-divinylbenzenes underwent a pericyclic reaction to form the cyclic o-quinodimethane intermediates which were subsequently reacted with olefins through [4+2] addition to construct the benzobicyclo[2.2.2]octane skeletons in mild conditions. Gram scale reactions demonstrated the synthetic potential application of this protocol.



INTRODUCTION

Photoinduced organic reactions have played significant roles in green chemistry and total synthesis, especially the construction of complex polycyclic compounds or highly functionalized molecules, such as some bridged-ring compounds and natural products, which would be difficult to access with the standard chemistry reactions in the ground state.[1] Besides, photochemical reaction often does not need activation reagents, such as acids, bases, metals, or enzymes, so it is an economically and environmentally friendly way for many natural and unnatural products synthesis.[2]

Benzobicyclo[2.2.2]octane derivatives compounds (Figure 1) are known to possess varieties of biological activities.[3] For example, benzobicyclo[2.2.2]octenals (Figure 1A) were used as calcium channel blockers in the treatment or prevention of angina pectoris, arrhythmias, and high blood pressure.[3] Additionally, due to its inherent stereochemistry, this skeleton is also a powerful building block for other types of skeletons via cleavage of a carbon−carbon bond.[4] Therefore, significant efforts have been made to access to benzobicyclo[2.2.2]octane skeletons. For instance, Chittimalla's group reported a two-step protocol to construct such a skeleton (Scheme 1a).[5] Additionally, nickel-catalyzed intramolecular alkene insertion into cyclobutanones sequences have been established by Murakami et al. (Scheme 1b).[6] Recently, Cramer and co-workers used a Rh-catalyzed [4+2] cycloaddition to provide these bridge-ring compounds (Scheme 1c).[7] In addition, Lewis acid catalyzed intramolecular [3+3] reaction sequences have been developed by Wang's group (Scheme 1d).[4] Despite the above significant achievements, development of an efficient, transition-metal-free, and step-economical approach is still highly desirable. As part of our continuing interest in the photochemical methodologies,[8] we herein disclose a simple way to synthesize benzobicyclo[2.2.2]octane derivatives through photoinduced [4+2] reactions from substituted o-divinylbenzenes with olefins (Scheme 1e).

RESULTS AND DISCUSSION

Initially, our investigation was started from irradiation the mixture of substituted o-divinylbenzene **1a** (Table 1) and *N*-methylmaleimide **2a** in acetonitrile with 350 nm light at room temperature. To our delight, the first attempt afforded the desired product **3aa** in 74% yield (Table 1, entry 1). Encouraged by this result, different types of light were tested (Table 1, entries 2−5). Pyrex works as a filter for a shorter wavelength of UV (∼ < 280 nm), and it revealed that the best wavelength is among 300−350 nm and the shorter wavelength (∼ < 280 nm) is not suitable for this reaction (Table 1, entries 1−4). So we choose 500W medium-pressure mercury lamp with Pyrex filter as the best light source. The reaction did not take place using blue LEDs (Table 1, entry 5). On the basis of the optimal light source, a set of solvents were then examined, which suggested MeCN was the ideal choice (Table 1, entries 6−12). Acetonitrile with water as solvent also proceeded smoothly with a decreased yield (Table 1, entry 13). However, solvents, such as benzene and THF, were proven to be ineffective for this transformation (Table 1, entries 9, 12). The best yield was obtained as 84% when the reaction was carried out under a N_2 atmosphere (Table 1, entry 14). This reaction is not air and moisture sensitive (Table 1, entries 13, 14), and it is most likely because this reaction mechanism (Scheme 3) might not be a free radical process. Although oxygen does not have strong impact over the reaction (Table 1, entries 4, 14), we still chose N_2 atmosphere because oxygen can react with the carbon−carbon double bond more or less.[9]

Having the optimized reaction conditions in hand, we subsequently investigated the scope of this reaction, and the representative results were listed in Table 2. We first examined the reaction of **1a** with different olefins **2**, which smoothly afforded the target products in good to excellent yields (Table 2, **3aa**−**3ae**). However, the general utility of the reaction

Received: October 20, 2016
Published: January 5, 2017

DOI: 10.1021/acs.joc.6b02547
J. Org. Chem. 2017, 82, 1389−1402

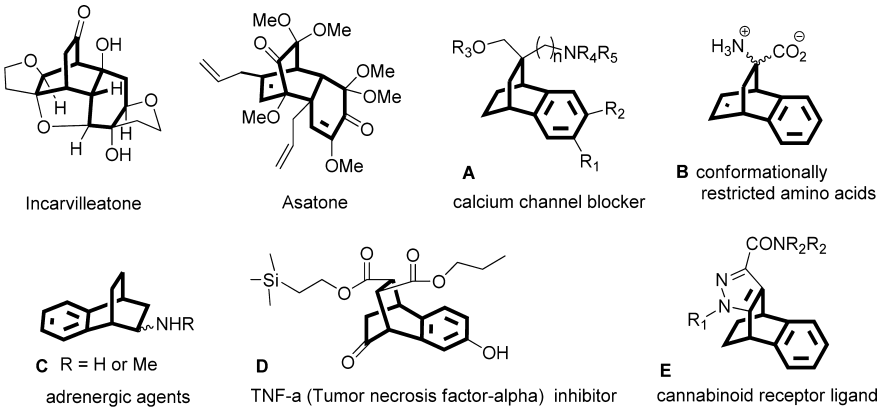
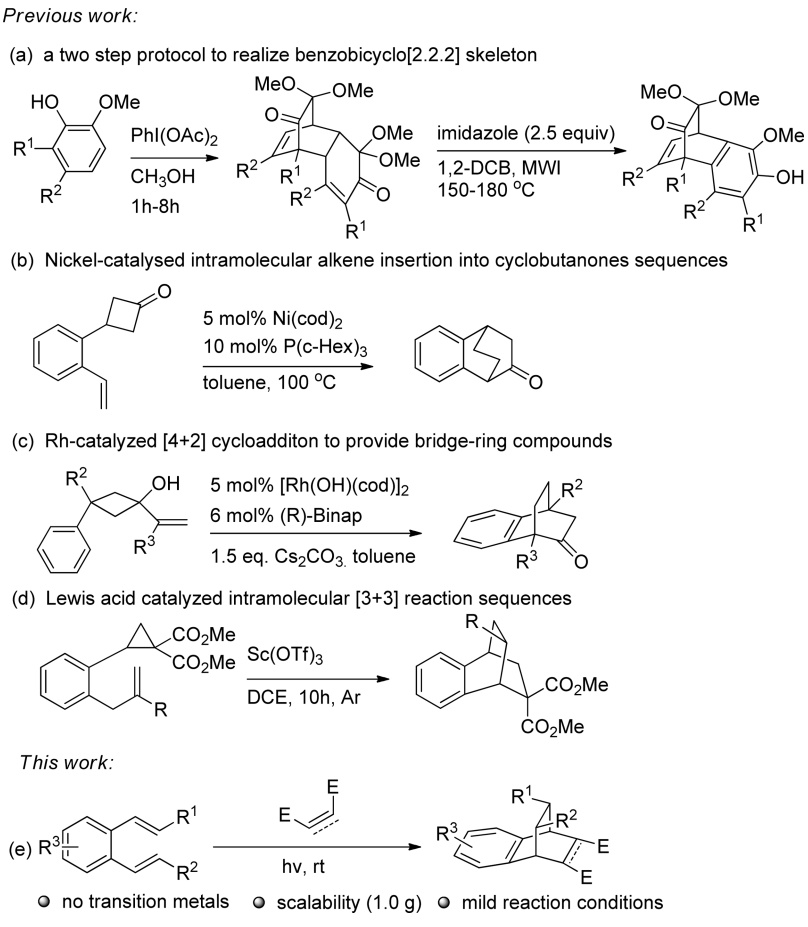


Figure 1. Products with bicyclo[2.2.2]octane skeletons and benzobicyclo[2.2.2]octane skeletons.

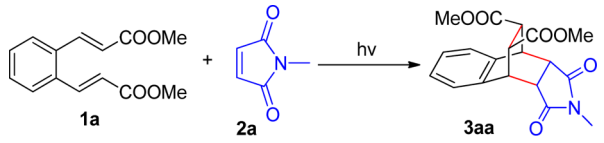
Scheme 1. Approaches for the Synthesis of Benzobicyclo[2.2.2]octane Skeletons



sequence was exemplified using maleic anhydride to give products **3af** in 45% yield. This point might be because maleic anhydride can form cyclobutane tetracarboxylic dianhydride[10] through photodimerization or it is not a better dienophile compared with maleimides. When **1a** was changed into **1b**, the reaction still worked well and the desired products (**3ba**−**3bg**) were also afforded in good yields. Both electron-donating substituents (MeO, Me) and electron-withdrawing substituents (F, Cl) on the phenyl ring were suitable for this reaction, leading to the corresponding products in moderate to good yields (**3ca**−**3ga**). Furthermore, when R^1 group and R^2 group were *n*-Bu or *i*-Pr groups, these reactions worked smoothly to get the products (**3ka**, **3la**) in good yield. However, when R^1 group and R^2 group are different, the product **3ha** and its stereo isomer (ratio 1:1) were formed (the possible process was depicted in Scheme 3, **I** and **II**). Both the stereo isomers (**3maa**, **3mab**) were obtained when R^1 and R^2 were the large steric hindrance group, e.g., *t*-Bu, which resulted from the isomerization of C−C double bond of the starting material due to steric effects and the prolonged irradiation time (to see **II** and **III** in Scheme 3). Similarly, the configuration of the reaction products (**3na**-**3sa**) are mainly the configuration of compound **3mab** when R^1, R^2 groups are the large steric hindrance groups. It is worth noting that electron-withdrawing substituents on the phenyl ring (**3ga**, **3ua**) were better than electron-donating substituent ones (**3fa**, **3ta**) for this reaction.

DOI: 10.1021/acs.joc.6b02547
J. Org. Chem. 2017, 82, 1389−1402

Table 1. Optimization of the Reaction Conditions[a]



entry	solvent	light source	yield(%)[b]
1	MeCN	350 nm	74
2	MeCN	300 nm	60
3	MeCN	mercury lamp[c]	76
4	MeCN	mercury lamp with Pyrex	80
5	MeCN	blue LEDs	0
6	toluene	mercury lamp with Pyrex	45
7	MeOH	mercury lamp with Pyrex	53
8	DCM	mercury lamp with Pyrex	62
9	benzene	mercury lamp with Pyrex	trace
10	DMF	mercury lamp with Pyrex	56
11	DMSO	mercury lamp with Pyrex	50
12	THF	mercury lamp with Pyrex	trace
13	MeCN[d]	mercury lamp with Pyrex	65
14	MeCN[e]	mercury lamp with Pyrex	84

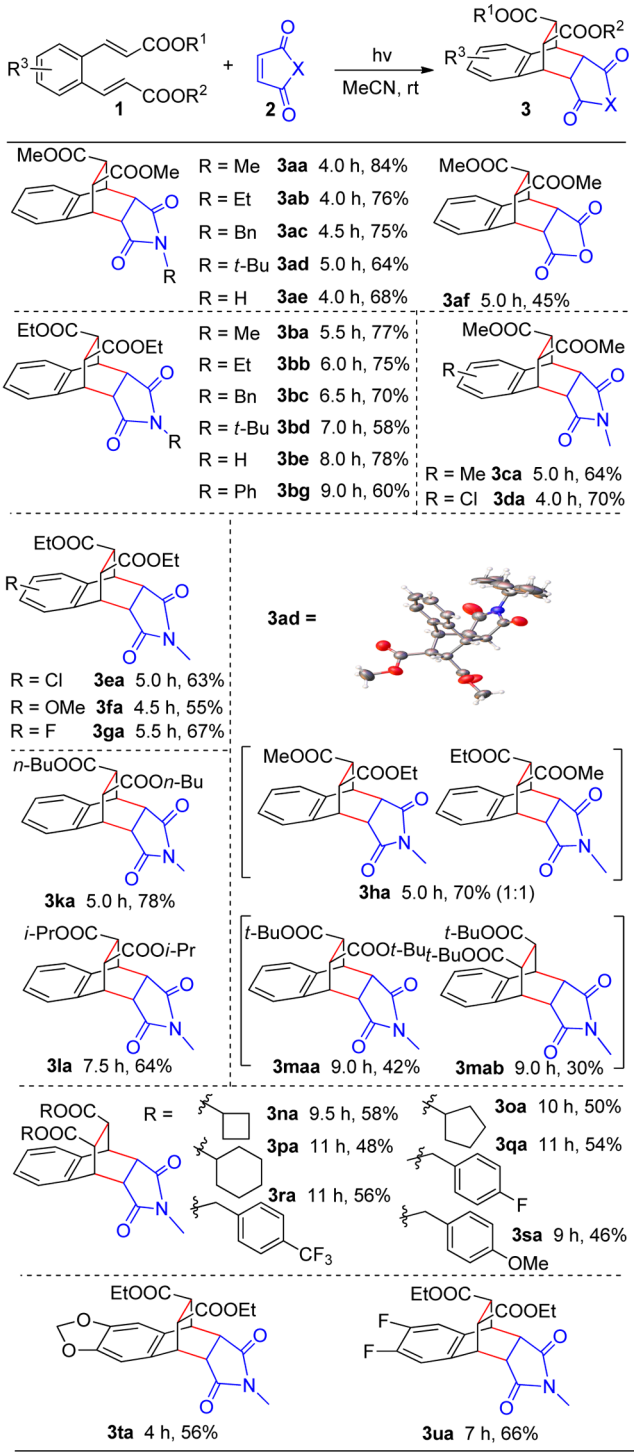
[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), solvent (anhydrous, 10 mL), rt, under air atmosphere. [b]Isolated yield. [c]500 W medium pressure mercury lamp. [d]Wet solvent. [e]N_2 atmosphere.

The structure of these products was assigned on the basis of 1D and 2D NMR, NOE, and mass spectrometry analysis. As a bonus, one of the products **3ad** (Table 2) was suitable for X-ray single-crystal structure analysis, allowing unambiguous determination of its structure and relative configuration.[11]

We envisioned that if the ester group of substrates was changed to aldehyde group, these photocycloaddition reactions would still work. So we decided to examine the substrates with aldehyde group **4** (Table 3). We found that less reaction time was needed, and this might be because these substrates containing aldehyde group are more easily excited to form excited state molecular. The yields were obtained from good to excellent (Table 3). Similar to **3ha**, the products (Table 3, **5aa**−**5ah**) are the mixture of isomers with a ratio of 1:1, likely due to the proposed reaction mechanism (Scheme 3, **I** and **II**). Moreover, we examine the substrate with two aldehyde groups **4c** for this photocycloaddition reactions, and we get the products in good yield without isomers (**5ca**, **5cb**). Whereafter, to broaden the generality of this photocycloaddition reaction we turned our attention to investigate substrates containing acetyl group, benzoyl group, and cyano group (Table 4). The reaction still underwent smoothly with good yields (**7aa**−**7ae**) and a decreased yield (**7ba**−**7bh**) probably due to the benzoyl group which is a large steric hindrance group and might cause other side reactions, e.g., Norrish type I/II reactions.[12] Then, we chose 3,3′-(1,2-phenylene)diacrylonitrile **6d** as a substrate containing cyano group to examine this reaction and the result was satisfactory (Table 4, **7da**). Other substrates containing both carbonyl group and ester group (**6c**, **6f**) or propanoyl group (**6e**) also were tested, giving the corresponding products (**7ca**, **7fa**, **7ea**) in good yield.

To study the proposed mechanism, some brief survey of literature are listed in Scheme 2. Although the study by Laarhoven[13] on the photochemistry of stilbene-like compound [Scheme 2, eq (1)] shows that transformation involves a free-radical process to get such benzobicyclo[2.1.1]hexene photoproduct, the study by Marija Šindler-Kulyk[14] on the photochemistry of stilbene-like compound with a novel substituted group [Scheme 2, eq (2)] did not detect such the benzobicclo[2.1.1]hexene photoproduct. This means that the substituted groups on the stilbene-like compound have a significant impact on the photochemistry reaction of these stilbene-like compounds. This point also can be seen from the study of Irena Škorić[15] [Scheme 2, eq (3)]. More importantly,

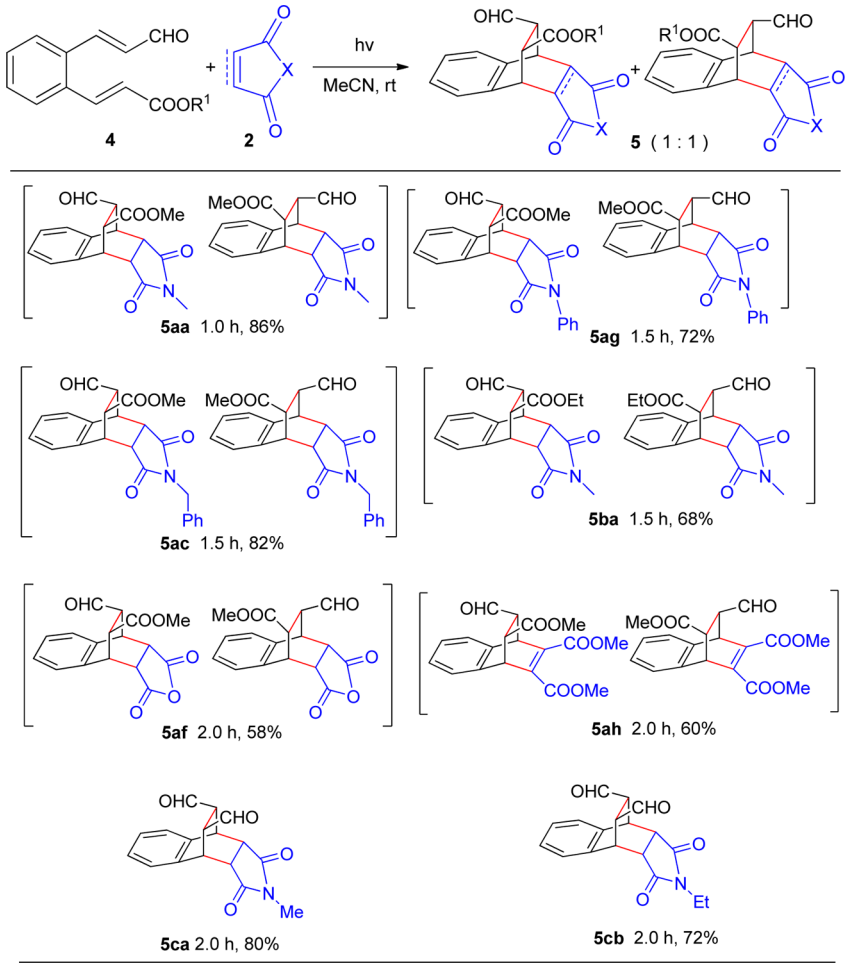
Table 2. Scope of the Reaction



[a]Reaction conditions: **1** (0.2 mmol), **2** (0.3 mmol), solvent (anhydrous, 10 mL), rt, under N_2 atmosphere, irradiated by a 500 W medium pressure mercury lamp with Pyrex filter, isolated yields are shown.

DOI: 10.1021/acs.joc.6b02547
J. Org. Chem. 2017, 82, 1389−1402

Table 3. Scope of the Substrates with Aldehyde Group[a]



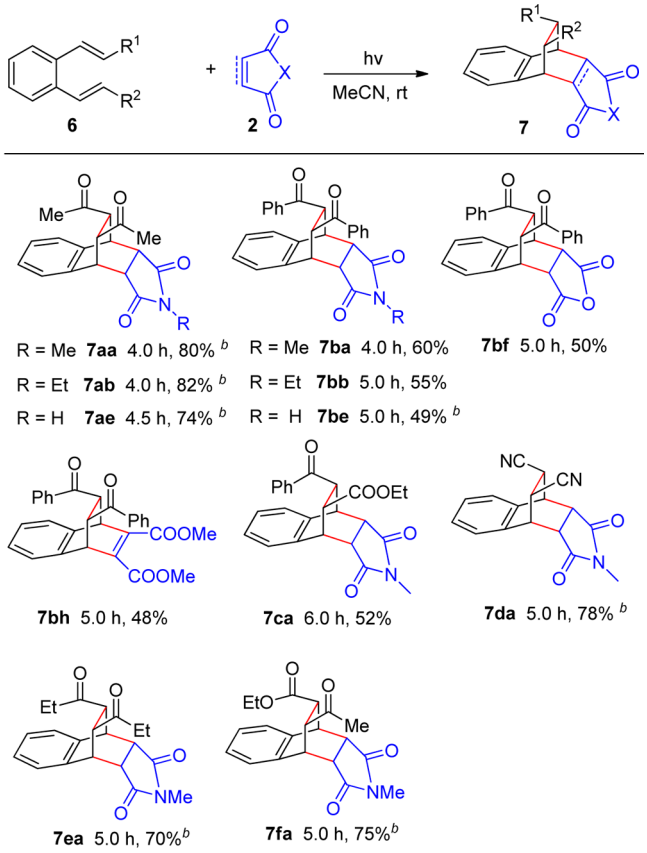
[a]Reaction conditions: **4** (0.2 mmol), **2** (0.3 mmol), solvent (anhydrous, 10 mL), rt, under N_2 atmosphere, irradiated by a 500 W medium pressure mercury lamp with Pyrex filter, isolated yields are shown.

the study of Irena Škorić is key evidence for this photoinduced intermolecular [4+2] cycloaddition. His research has shown that the reaction mechanism of eq (3) involves a six-membered ring closure followed by a sigmatropic 1,5-H shift to give photoproduct and the cyclic o-quinodimethane (o-QDM) is the key intermediate of the photoreaction [Scheme 2, eq (3)].

To investigate this reaction mechanism and collect more information about this reaction mechanism, several control experiments were carried out. In the first experiment this photoinduced [4+2] reaction succeeded to give the desired product **3aa** in 55% yield in the presence of the radical scavengers (2,2,6,6-tetramethylpiperidin-1-yl)oxidanyl (TEMPO) [Scheme 2, eq (5)], which indicated that this photoinduced reaction is not a radical pathway. Another control experiment was conducted by adding 3 equiv of butylated hydroxytoluene (BHT) in the reaction. The reaction was not prevented by BHT, and the product was obtained smoothly [Scheme 2, eq (6)]. This reaction also could not be suppressed by 1,1-diphenylethylene. These experiments indicated this photoinduced reaction is not a radical pathway. We use **1b** without **2** as starting material and we found that the compounds **8a** and **8b** were obtained in the total yield 51% under the standard conditions [Scheme 2, eq (8)], which were the products of intramolecular photoinduced [4+2] reaction, but the reaction time became longer because there was no dienophile **2** to trap the reactive intermediate cyclic-o-quinodimethane. This result is different from the Ploder's work.[16] Besides, we did not find the intramolecular reaction products [Scheme 2, eq (7)], and more importantly, out of all the experiments in Table 2 we also did not find the intramolecular reaction products, and the time of this photoinduced intermolecular [4+2] reaction is less than the time of intramolecular reaction. This result revealed that the reaction rate of intermolecular reaction of **1b** with **2a** (k_1) is larger than the reaction rate of intramolecular reaction of **1b** (k_2) [Scheme 2, eq (7), (8)] because there is dienophile (e.g., **2**) which would trap the reactive intermediate cyclic o-quinodimethane when the cyclic o-quinodimethane was once generated from the substrate **1** under UV light in the system. In addition, it is noteworthy that all the products are endotype compounds and this result is coincided with Freccero group's work [Scheme 2, eq (4)].[17] These results revealed that this photoinduced reaction may proceed a key intermediate cyclic o-quinodimethane (cyclic-o-QDM), a highly reactive species,[18] which likely is formed via a conrotatory six-membered ring closure of substrates under UV light according to Woodword–Hoffmann rules.[19] Another two control experiments were conducted by addition of cyclohexa-1,3-diene and *trans*-stilbene as a triplet quencher in the solution of **1a** and **2a** in acetonitrile, which did not depress the reaction. In addition, the oxygen,

DOI: 10.1021/acs.joc.6b02547
J. Org. Chem. 2017, 82, 1389–1402

Table 4. Scope of Substrates Containing Acetyl Group, Benzoyl Group, and Cyano Group[a]



[a]Reaction conditions: **6** (0.2 mmol), **2** (0.3 mmol), solvent (anhydrous, 10 mL), rt, under N_2 atmosphere, irradiated by a 500 W medium pressure mercury lamp with Pyrex filter, isolated yields are shown. [b]Reaction conditions: **6** (1.0 mmol), **2** (1.5 mmol), solvent (anhydrous, 50 mL), rt, under N_2 atmosphere, irradiated by a 500 W medium pressure mercury lamp with Pyrex filter, isolated yields are shown.

dissolved in the acetonitrile under air-saturated conditions (Table 1, entries 1–4), had no obvious effect on the reaction. These experiments suggest that the reaction involves a singlet state.[20]

On the basis of the above experimental results and some literatures (Scheme 2), a most plausible mechanism pathway was proposed and depicted in Scheme 3. Under UV light irradiation, the substrate **1** underwent a pericyclic reaction which is a conrotatory six-membered ring closure according to Woodword–Hoffmann rules[19] to form cyclic-o-QDM intermediate which was then trapped by an olefin through the Diels–Alder reaction. According to Woodword–Hoffmann rules,[19] the starting material, trans,trans-substrate **1**, should form the trans-o-QDM intermediate under irradiation (Scheme 3), which could be trapped by olefins from the up or down side to form the final products **I** and **II** with or without isomers. In addition, carbon–carbon double bond could undergo photochemical cis/trans-isomerization reactions under UV light, thus trans,trans-substrate **1** could be transformed to cis,trans-1 during the reaction if prolonged reaction time was involved. Then the cis-o-QDM intermediate was formed from cis,trans-1 which was trapped by olefins from down face to form the single product **III** (Scheme 3) due to the steric effects.

During our investigation, several gram-scale reactions were carried out under standard reaction conditions and the desired products were obtained in good yield (Scheme 4). The results might suggest its potential application in natural products synthesis as well as screening of compound libraries for further chemical biology study.

CONCLUSION

In summary, we have established a facile one-pot procedure for the synthesis of substituted benzobicyclo[2.2.2]octane skeletons via photoinduced [4+2] reactions of substituted o-divinylbenzenes with olefins under mild condition. The method is an efficient, transition-metal-free, and step-economical approach for the rapid construction of these bridged-ring compounds. In addition, the gram scale reactions demonstrated the synthetically potential applications.

EXPERIMENTAL SECTION

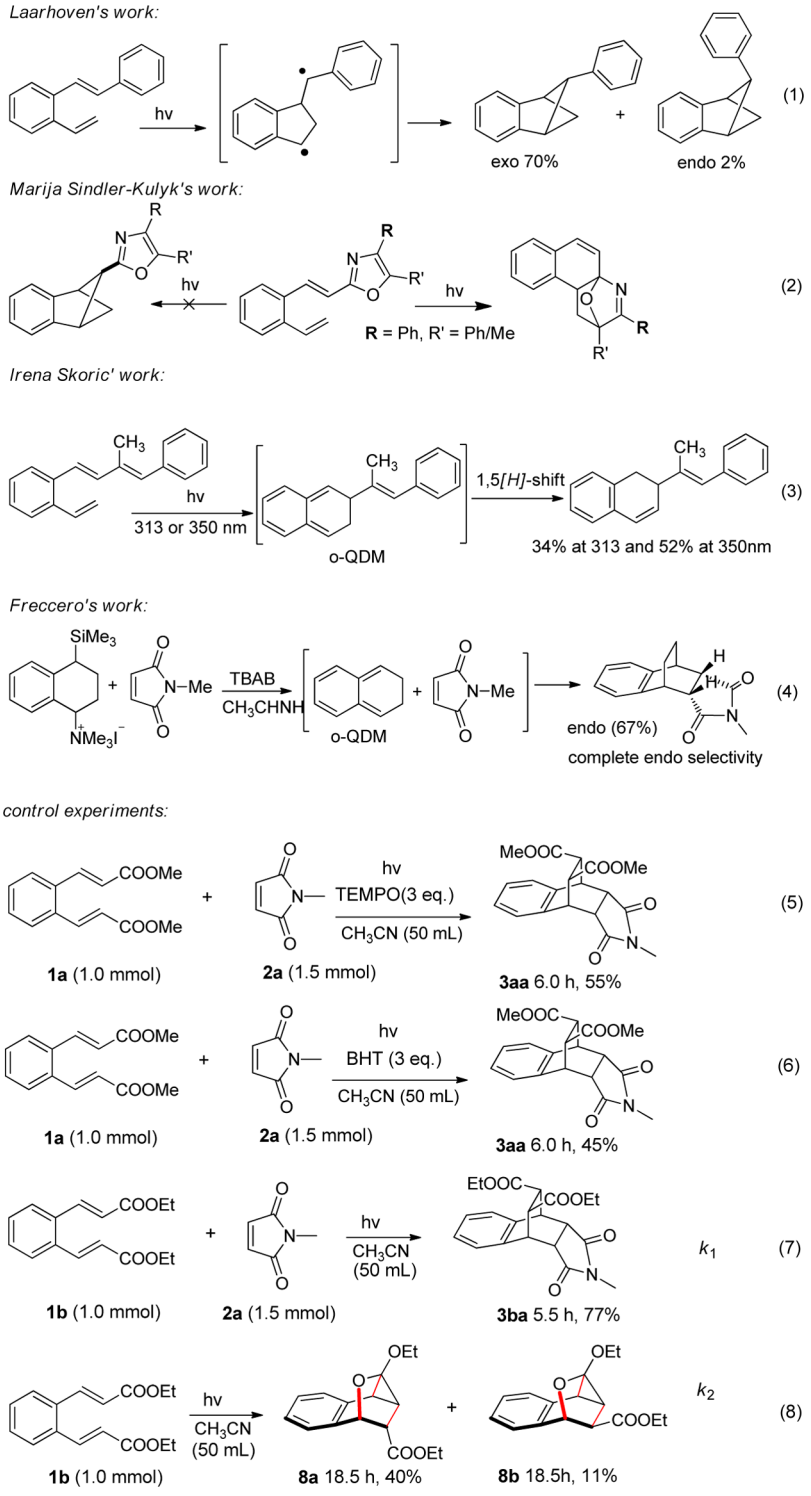
General Information. All reactions were carried out with dry solvents using anhydrous conditions unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reactions were monitored by GC-MS or thin layer chromatography (TLC) carried out on 0.20–0.25 mm silica gel plates using UV light as the visualizing agent and phosphomolybdic acid as developing agents. Silica gel was used for flash column chromatography. High-resolution mass spectra (HRMS) were recorded on a Q-TOF (ESI) mass spectrometer. Low-resolutionmass spectra were obtained from GC-MS system.

General Procedure for Syntheses of Starting Materials. *General Procedure for Syntheses of Compounds 1a–1g, 1k–1s.* Corresponding alcohol (5.0 mmol) was dissolved in dry CH_2Cl_2 (25 mL) and pyridine (7.5 mmol) was added. Reaction mixture was cooled to 0 °C and 2-bromoacetyl bromide (5.5 mmol) was added dropwise. Reaction mixture was stirred for 45 min at 0 °C and then was quenched by addition of water (25 mL). The resulting layers were separated and the aqueous layer was extracted with EtOAc (25 × 3 mL). The combined organic layers were washed sequentially with saturated aqueous $CuSO_4$ (25 mL), water (25 mL), brine (25 mL), dried over Na_2SO_4, and concentrated in vacuo evaporated to give the appropriate bromoalkyl acetates compound as a colorless oil that was used in the next step without further purification.[21] A solution of the appropriate bromoalkyl acetates compound (5 mmol) in toluene (25 mL) was added dropwise over 10 min to a solution of triphenylphosphine (5 mmol) in toluene (25 mL). The reaction mixture was stirred at room temperature for 18 h, and the resulting phosphonium salt was filtered and oven-dried. The phosphonium salt was obtained in quantitative yield, and was used without further purification.[22] NaOH (0.12 g, 30 mmol) dissolved in water (5 mL) was added to a suspension of the phosphonium salt (20.0 mmol) in H_2O (60 mL) and CH_2Cl_2 (60 mL). The mixture was stirred vigorously at room temperature for 1 h and then transferred to a separating funnel. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (20 × 3 mL). The combined organic layers were dried (Na_2SO_4) and concentrated to give the corresponding stabilized phosphonium ylides, which were used without further purification.[22] To a solution of corresponding o-phthalaldehyde (1 mmol) in THF (15 mL) was added the corresponding ester-stabilized phosphonium ylide (2.4 mmol). The mixture was stirred at room temperature for 12 h, and concentrated in vacuo. Purification of the residue by column chromatography (EtOAc:hexane, 1:4) afforded the compound **1**.[22]

General Procedure for Syntheses of Compound 4. To a solution of the compound **1** (3 mmol) in dry THF (20 mL) at −78 °C was added DIBAL-H (6.2 mL of a 1.0 M solution in toluene, 6.2 mmol) slowly. After stirring for 1 h, the reaction mixture was allowed to return to 0 °C. Four hours later, the reaction was quenched with methanol (3 mL). Then 20 mL aqueous solution of 0.5 M HCl was added. One hour later, the layers were separated and the aqueous layer was

DOI: 10.1021/acs.joc.6b02547
J. Org. Chem. 2017, 82, 1389–1402

Scheme 2. Previous Work and Control Experiments

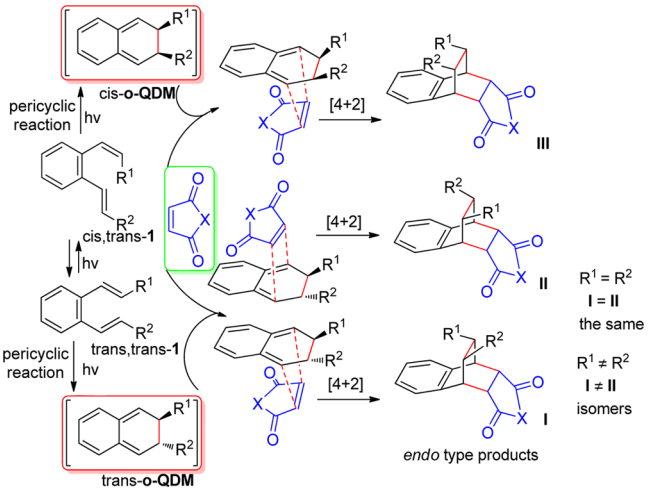


extracted with EtOAc (20 × 3 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated. Purification of the crude product by chromatography on silica gel (EtOAc/hexane, 1/3) gave the appropriate alcohol as a clear oil.[23] To a solution of oxalyl chloride (2.4 mmol) in dry CH_2Cl_2 (10 mL) cooled at −78 °C was added dropwise a solution of dimethyl sulfoxide (DMSO 2.3 mmol) in CH_2Cl_2 (10 mL). After 5 min, a solution of the appropriate alcohol (2 mmol) in CH_2Cl_2 (10 mL) was added. The reaction mixture was then stirred for 15 min at −78 °C and triethylamine (10 mmol) was added in one portion. After 10 min at −78 °C, the mixture was allowed to warm to room temperature and diluted with CH_2Cl_2 (40 mL). The organic layer was successively washed with a saturated aqueous solution of NH_4Cl (20 mL) and brine (20 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography on silica gel (petroleum ether/EtOAc: 9/1) afforded the aldehyde **4** as solid.

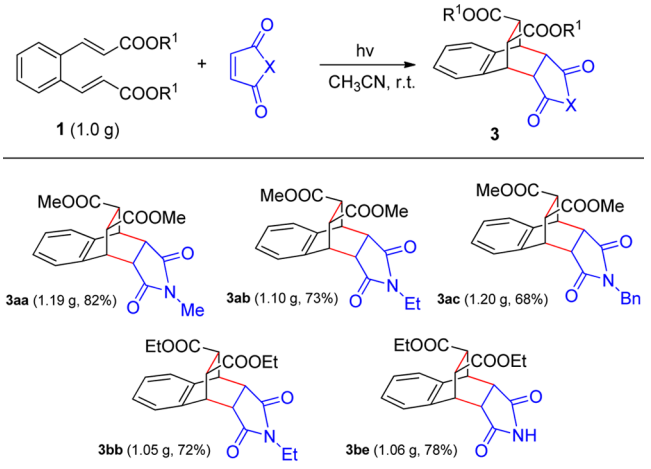
Syntheses of Substrate 4c. To a solution of the compound **1b** (10 mmol) in dry THF (200 mL) at −78 °C was added DIBAL-H (62 mL of a 1.0 M solution in toluene, 62 mmol) slowly. After stirring for 1 h, the reaction mixture was allowed to return to 0 °C. The reaction was quenched with methanol (30 mL) 24 h later. Then 200 mL aqueous

DOI: 10.1021/acs.joc.6b02547
J. Org. Chem. 2017, 82, 1389−1402

Scheme 3. Possible Reaction Pathway



Scheme 4. Reactions of 1 at Gram Scale



solution of 0.5 M HCl was added. One hour later, the layers were separated and the aqueous layer was extracted with EtOAc (200 × 3 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated. Purification of the crude product by chromatography on silica gel (EtOAc/hexane, 2:1) gave the diol as white solid. The diol (0.5 g) in dichloromethane (250 mL) was stirred with activated manganese dioxide (5 g) at ambient temperature for 24 h. The mixture was filtered through Celite, and the solid was washed well with dichoromethane. Evaporation of the solvent and purification by flash chromatography on silica gel (petroleum ether/EtOAc: 10/1) gave the dialdehyde **4c**.[24]

General Procedure for Syntheses of Compound ***6***. To a solution of o-phthalaldehyde (5.0 mmol) in THF (60 mL) was added 1-(triphenylphosphoranylidene)propan-2-one (12.5 mmol). The mixture was stirred at room temperature for 16 h and concentrated in vacuo. Purification of the residue by column chromatography (petroleum ether/EtOAc: 9/1) afforded the compound **6a**.[22] To a solution of o-phthalaldehyde (5.0 mmol) in THF (60 mL) was added 1-phenyl-2-(triphenylphosphoranylidene)ethanone (12.5 mmol). The mixture was stirred at room temperature for 16 h and concentrated in vacuo. Purification of the residue by column chromatography (petroleum ether/EtOAc: 9/1) afforded the compound **6b**.[22]

Syntheses of Substrates 1h and 6c. To a solution of o-phthalaldehyde (2.0 mmol) in THF (15 mL) at room temperature was added a solution of ethyl 2-(triphenylphosphoranylidene)acetate (2.0 mmol) in THF (10 mL) dropwise over 30 min, and the mixture was stirred at 60 °C for 18 h. Purification of the residue by column chromatography afforded the compound (*E*)-ethyl 3-(2-formylphenyl)acrylate. Then, to a solution of (*E*)-ethyl 3-(2-formylphenyl)acrylate (1.0 mmol) in THF (5 mL) at room temperature was added a solution of methyl 2-(triphenylphosphoranylidene)acetate (1.0 mmol) in THF (10 mL) dropwise over 30 min, and the mixture was stirred at 60 °C for 18 h. Purification of the residue by column chromatography (10% EtOAc/hexane -30% EtOAc/hexane) gave compound **1h** as an white solid (45%). To a solution of (*E*)-ethyl 3-(2-formylphenyl)acrylate (1.0 mmol) in THF (5 mL) at room temperature was added a solution of 1-phenyl-2-(triphenylphosphoranylidene)ethanone (1.0 mmol) in THF (10 mL) dropwise over 30 min, and the mixture was stirred at 60 °C for 18 h. Purification of the residue by column chromatography (10% EtOAc/hexane → 30% EtOAc/hexane) gave compound **6c** as yellow oil.

Syntheses of Substrate ***6d***. A solution of the 2-bromoacetonitrile (25 mmol) in toluene (100 mL) was added dropwise over 10 min to a solution of triphenylphosphine (25 mmol) in toluene (50 mL). The reaction mixture was stirred at room temperature for 18 h, and the resulting phosphonium salt was filtered and oven-dried. The phosphonium salt was obtained in quantitative yield, and was used without further purification. NaOH (0.12 g, 30 mmol) dissolved in water (5 mL) was added to a suspension of the phosphonium salt (20.0 mmol) in H_2O (60 mL) and CH_2Cl_2 (60 mL). The mixture was stirred vigorously at room temperature for 1 h and then transferred to a separating funnel. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (20 × 3 mL). The combined organic layers were dried (Na_2SO_4) and concentrated to give the corresponding stabilized phosphonium ylides, which were used without further purification.[25] To a solution of corresponding o-phthalaldehyde (1 mmol) in THF (15 mL) was added the corresponding ester-stabilized phosphonium ylide (2.4 mmol). The mixture was stirred at room temperature for 12 h, and concentrated in vacuo. Purification of the residue by column chromatography (EtOAc:hexane, 1:4) afforded the compound **6d**.

Syntheses of Substrate ***1t*** *and* ***1u***. Using Heck reactions, to a suspension of $Pd(OAc)_2$ (90 mg, 0.4 mmol), *n*-Bu_4NCl (1.14g, 5 mmol), K_2CO_3 (3.45g, 25 mmol), and LiCl (212 mg, 5 mmol) in DMF (25 mL) was added 1,2-dibromo-4,5-difluorobenzene or 5,6-dibromobenzo[*d*][1,3]dioxole (5 mmol) and ethyl acrylate (25 mmol). The mixture was stirred at 100 °C for 18 h, cooled to room temperature, diluted with Et_2O (25 mL), and washed with water (50 mL). The aqueous layer was extracted with Et_2O (50 mL × 2), and the combined organic layers were washed with brine (100 mL), dried ($MgSO_4$), and concentrated. Purification of the residue by column chromatography gave the compound **1t** and **1u**.[22]

*(E)-3-[2-{(E)-2-Methoxycarbonylvinyl}phenyl]acrylic Acid Methyl Ester (**1a**).*[22] White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 15.8 Hz, 2H), 7.57 (dd, *J* = 5.7, 3.5 Hz, 2H), 7.40 (dd, *J* = 5.8, 3.4 Hz, 2H), 6.36 (d, *J* = 15.8 Hz, 2H), 3.83 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.8, 141.5, 134.2, 130.1, 127.6, 121.4, 51.8. LRMS (EI): 246[M+], 231, 215, 199, 186, 171, 155, 143, 128, 115, 102, 92, 77. HRMS (ESI): calcd for $C_{14}H_{15}O_4$, $[M+H]^+$, 247.0970; found, 247.0976.

*(E)-3-[2-{(E)-2-Ethoxycarbonylvinyl}phenyl]acrylic Acid Ethyl Ester (**1b**).*[22] White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 15.8 Hz, 2H), 7.65−7.52 (m, 2H), 7.46−7.35 (m, 2H), 6.35 (d, *J* = 15.8 Hz, 2H), 4.29 (q, *J* = 7.1 Hz, 4H), 1.35 (t, *J* = 7.1 Hz, 6H).[13]C NMR (100 MHz, $CDCl_3$) δ 166.4, 141.3, 134.3, 130.00, 127.6, 122.00, 60.7, 14.3. HRMS (ESI): calcd for $C_{16}H_{19}O_4$, $[M+H]^+$, 275.1283; found, 275.1281.

*(2E,2′E)-Dimethyl 3,3′-(4-methyl-1,2-phenylene)diacrylate (**1c**).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 15.8, 1H), 7.97 (d, *J* = 15.8, 1H), 7.58 (dd, *J* = 8.7, 5.7 Hz, 1H), 7.26 (dd, *J* = 9.5, 2.6 Hz, 1H), 7.12 (td, *J* = 8.3, 2.6 Hz, 1H), 6.34 (d, 15.8 Hz, 1H), 6.32 (d, 15.8 Hz, 1H) 3.85 (s, 3H), 3.84 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.0, 166.9, 141.6, 141.3, 140.4, 134.2, 131.4, 131.1, 128.2, 127.5, 121.2, 120.4, 52.9, 52.8, 21.4. LRMS (EI): 260[M+], 245, 229, 213, 200, 185, 169, 155, 142, 129, 115, 99, 77. HRMS (ESI): calcd for $C_{15}H_{17}O_4$, $[M+H]^+$, 261.1127; found, 261.1128.

DOI: 10.1021/acs.joc.6b02547
J. Org. Chem. 2017, 82, 1389−1402

*(2E,2′E)-Dimethyl 3,3′-(4-chloro-1,2-phenylene)diacrylate (**1d**).*[26] White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, J = 15.8, 1H), 7.98 (d, J = 15.8, 1H), 7.58 (dd, J = 8.7, 5.7 Hz, 1H), 7.26 (dd, J = 9.5, 2.6 Hz, 1H), 7.12 (td, J = 8.3, 2.6 Hz, 1H), 6.34 (d, J = 15.8 Hz, 1H), 6.32 (d, J = 15.8 Hz, 1H), 3.85 (s, 3H), 3.84 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.6, 166.5, 140.2, 140.1, 136.2, 135.8, 132.6, 130.1, 128.9, 127.5, 122.6, 121.8, 52.1, 52.. LRMS (EI): 280[M+], 249, 228, 189, 162, 142, 126, 109, 81, 59. HRMS (ESI): calcd for $C_{14}H_{14}ClO_4$, $[M+H]^+$, 281.0581; found, 281.0582.

*(2E,2′E)-Diethyl-3,3′-(4-chloro-1,2-phenylene)diacrylate (**1e**).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, J = 15.8, 1.8 Hz, 2H), 7.52 (dd, J = 13.5, 5.2 Hz, 2H), 7.41−7.25 (m, 1H), 6.34 (dd, J = 15.8, 8.2 Hz, 2H), 4.29 (qd, J = 7.1, 1.9 Hz, 4H), 1.35 (td, J = 7.1, 1.0 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.2, 166.0, 140.0, 139.9, 136.0, 135.8, 132.6, 130.0, 128.9, 127.5, 123.1, 122.3, 60.9, 60.8, 14.3. LRMS (EI): 308[M+], 295, 281, 263, 251, 234, 219, 207, 189, 177, 163, 149, 127, 115, 101, 89. HRMS (ESI): calcd for $C_{16}H_{18}ClO_4$, $[M+H]^+$, 309.0894; found, 309.0895.

*(2E,2′E)-Diethyl-3,3′-(4-methoxy-1,2-phenylene)diacrylate (**1f**).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 15.8 Hz, 1H), 8.00 (d, J = 15.8 Hz, 1H), 7.57 (d, J = 8.7 Hz, 1H), 7.06 (d, J = 2.6 Hz, 1H), 6.96 (dd, J = 8.7, 2.6 Hz, 1H), 6.35 (d, J = 15.8 Hz, 1H), 6.29 (d, J = 15.7 Hz, 1H), 4.30 (p, J = 7.2 Hz, 4H), 3.86 (s, 3H), 1.35 (td, J = 7.1, 5.1 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.8, 166.4, 160.9, 141.3, 140.7, 136.0, 129.1, 126.9, 122.2, 119.4, 116.5, 111.9, 60.8, 60.6, 55.5, 14.4, 14.3. HRMS (ESI): calcd for $C_{17}H_{21}O_5$, $[M+H]^+$, 305.1389; found, 305.1387.

*(2E,2′E)-Diethyl-3,3′-(4-fluoro-1,2-phenylene)diacrylate (**1g**).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (dd, J = 15.8, 5.4 Hz, 2H), 7.57 (dd, J = 8.7, 5.7 Hz, 1H), 7.37−7.22 (m, 1H), 7.10 (td, J = 8.3, 2.6 Hz, 1H), 6.32 (dd, J = 17.9, 15.8 Hz, 2H), 4.29 (qd, J = 7.1, 3.3 Hz, 4H), 1.35 (td, J = 7.1, 1.9 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.3, 166.1, 163.4 (d, J = 251.3 Hz), 140.0 (d, J = 5.8 Hz), 136.4 (d, J = 7.8 Hz), 130.5 (d, J = 3.1 Hz), 129.7 (d, J = 8.7 Hz), 123.0, 121.7, 117.3 (d, J = 22.0 Hz), 114.0 (d, J = 22.5 Hz), 60.9, 60.8, 14.3, 14.3. HRMS (ESI): calcd for $C_{16}H_{18}FO_4$, $[M+H]^+$, 293.1189; found, 293.1194..

*(E)-Ethyl-3-(2-((E)-3-methoxy-3-oxoprop-1-en-1-yl)phenyl)-acrylate (**1h**).*[27] White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, J = 15.8, 3.8 Hz, 2H), 7.57 (dd, J = 5.8, 3.4 Hz, 2H), 7.49−7.34 (m, 2H), 6.35 (dd, J = 15.8, 2.0 Hz, 2H), 4.29 (q, J = 7.1 Hz, 2H), 3.83 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.9, 166.4, 141.5, 141.3, 134.4, 134.2, 130.1, 130.0, 127.6, 127.6, 122.0, 121.5, 60.8, 51.9, 14.3. HRMS (ESI): calcd for $C_{15}H_{17}O_4$, $[M+H]^+$, 261.1127; found, 261.1128.

*(E)-Butyl 3-(2-((E)-3-oxo-3-butoxyprop-1-en-1-yl)phenyl)acrylate (**1k**).*[28] Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 15.8 Hz, 2H), 7.57 (dd, J = 5.8, 3.4 Hz, 2H), 7.39 (dd, J = 5.8, 3.4 Hz, 2H), 6.35 (d, J = 15.8 Hz, 2H), 4.23 (t, J = 6.7 Hz, 4H), 1.75−1.66 (m, 4H), 1.51−1.38 (m, 4H), 0.97 (t, J = 7.4 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.5, 141.3, 134.3, 130.0, 127.7, 121.9, 64.6, 30.7, 19.2, 13.8. LRMS (EI): 330[M+], 315, 301, 274, 257, 242, 228, 214, 200, 172, 155, 101, 83, 57. HRMS (ESI): calcd for $C_{20}H_{27}O_4$, $[M+H]^+$, 331.1909; found, 331.1907.

*(E)-Isopropyl-3-(2-((E)-3-isopropoxy-3-oxoprop-1-en-1-yl)-phenyl)acrylate (**1l**).* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 15.8 Hz, 2H), 7.56 (dd, J = 5.7, 3.5 Hz, 2H), 7.38 (dd, J = 5.8, 3.3 Hz, 2H), 6.33 (d, J = 15.8 Hz, 2H), 5.24−5.03 (m, 2H), 1.33 (d, J = 6.3 Hz, 12H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.0, 141.0, 134.3, 129.9, 127.6, 122.5, 68.1, 22.0. LRMS (EI): 302[M+], 281, 260, 243, 231, 214, 200, 184, 172, 157, 144, 129, 115, 102, 89. HRMS (ESI): calcd for $C_{18}H_{23}O_4$, $[M+H]^+$, 303.1596; found, 303.1592.

*(E)-3-[2-{(E)-2-tert-Butoxycarbonylvinyl}-phenyl]acrylic Acid tert-Butyl Ester (**1m**).*[29] White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 15.8 Hz, 2H), 7.55 (dd, J = 5.7, 3.5 Hz, 2H), 7.36 (dd, J = 5.8, 3.3 Hz, 2H), 6.27 (d, J = 15.8 Hz, 2H), 1.54 (s, 18H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.8, 140.4, 134.4, 129.7, 127.6, 123.6, 80.8, 28.2. LRMS (EI): 330[M+], 274, 257, 239, 218, 200, 172, 155, 129, 115, 92, 77. HRMS (ESI): calcd for $C_{20}H_{27}O_4$, $[M+H]^+$, 331.1909; found, 331.1918.

*(E)-Cyclobutyl-3-(2-((E)-3-oxo-3-cyclobutoxyprop-1-en-1-yl)-phenyl)acrylate (**1n**).* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 15.8 Hz, 2H), 7.57 (dd, J = 5.6, 3.5 Hz, 2H), 7.39 (dd, J = 5.8, 3.4 Hz, 2H), 6.33 (d, J = 15.8 Hz, 2H), 5.13 (p, J = 7.5 Hz, 2H), 2.49−2.37 (m, 4H), 2.24−2.07 (m, 4H), 1.84 (q, J = 10.3 Hz, 2H), 1.68 (qd, J = 10.4, 5.2 Hz, 2H).[13]C NMR (150 MHz, $CDCl_3$) δ 165.8, 141.3, 134.3, 130.0, 127.6, 121.9, 69.1, 30.4, 13.6. LRMS (EI): 326[M+], 227, 157, 128, 55. HRMS (ESI): calcd for $C_{20}H_{23}O_4$, $[M+H]^+$, 327.1596; found, 327.1594.

*(E)-Cyclopentyl-3-(2-((E)-3-(cyclopentyloxy)-3-oxoprop-1-en-1-yl)phenyl)acrylate (**1o**).* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 15.8 Hz, 2H), 7.58 (dd, J = 5.7, 3.5 Hz, 2H), 7.48−7.34 (m, 2H), 6.34 (d, J = 15.8 Hz, 2H), 5.33 (td, J = 5.9, 3.0 Hz, 2H), 1.97 (m, 4H), 1.88−1.72 (m, 8H), 1.72−1.58 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.2, 141.0, 134.3, 129.9, 127.7, 122.4, 77.4, 32.8, 23.8. LRMS (EI): 354[M+], 201, 173, 129, 69. HRMS (ESI): calcd for $C_{22}H_{27}O_4$, $[M+H]^+$, 355.1909; found, 355.1906.

*(E)-Cyclohexyl-3-(2-((E)-3-(cyclohexyloxy)-3-oxoprop-1-en-1-yl)-phenyl)acrylate (**1p**).* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 15.8 Hz, 2H), 7.57 (m, 2H), 7.38 (m, 2H), 6.34 (d, J = 15.8 Hz, 2H), 5.01−4.78 (m, 2H), 2.00−1.87 (m, 2H), 1.82−1.74 (m, 4H), 1.61−1.37 (m, 10H), 1.35−1.25 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.9, 141.0, 134.3, 129.9, 127.6, 122.4, 73.0, 31.7, 25.4, 23.8. LRMS (EI): 382[M+], 367, 354, 327, 315, 300, 282, 267, 255, 237, 218, 200, 184, 172, 157, 128, 115. HRMS (ESI): calcd for $C_{24}H_{31}O_4$, $[M+H]^+$, 383.2222; found, 383.2221.

*(E)-4-Fluorobenzyl-3-(2-((E)-3-(4-fluorobenzyloxy)-3-oxoprop-1-en-1-yl)phenyl)acrylate(**1q**).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, J = 15.8 Hz, 2H), 7.58 (dt, J = 7.1, 3.6 Hz, 2H), 7.42 (dt, J = 5.5, 4.4 Hz, 6H), 7.09 (t, J = 8.6 Hz, 4H), 6.40 (d, J = 15.8 Hz, 2H), 5.25 (s, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.1, 162.7 (d, J = 246.8 Hz), 141.9, 134.2, 131.8 (d, J = 3.2 Hz), 130.4 (d, J = 7.9 Hz), 130.2, 127.7, 121.4, 115.6 (d, J = 21.8 Hz), 65.8. LRMS (EI): 434[M+], 201, 157, 109, 83.HRMS (ESI): calcd for $C_{26}H_{21}O_4F_2$, $[M+H]^+$, 435.1408; found, 435.1413.

*(E)-4-(Trifluoromethyl)benzyl-3-(2-((E)-3-(4-(trifluoromethyl)-benzyloxy)-3-oxoprop-1-en-1-yl)phenyl)acrylate (**1r**).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 15.8 Hz, 2H), 7.64 (d, J = 8.2 Hz, 4H), 7.59 (dd, J = 5.7, 3.5 Hz, 2H), 7.53 (d, J = 8.1 Hz, 4H), 7.42 (dd, J = 5.8, 3.3 Hz, 2H), 6.41 (d, J = 15.8 Hz, 2H), 5.32 (s, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.0, 142.3, 139.9, 134.1, 130.4 (q, J = 32.2 Hz), 130.4, 128.2, 127.8, 125.6 (q, J = 3.8 Hz), 124.0 (q, J = 272.2 Hz), 121.1, 65.6. LRMS (EI): 534[M+], 335, 198, 159, 109. HRMS (ESI): calcd for $C_{28}H_{21}O_4F_6$, $[M+H]^+$, 535.1344; found, 535.1349.

*(E)-4-Methoxybenzyl-3-(2-((E)-3-((4-methoxybenzyl)oxy)-3-oxo-prop-1-en-1-yl)phenyl)acrylate (**1s**).* Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 15.8 Hz, 2H), 7.53 (dd, J = 5.7, 3.5 Hz, 2H), 7.36 (m, 6H), 7.01−6.82 (m, 4H), 6.36 (d, J = 15.8 Hz, 2H), 5.20 (s, 4H), 3.81 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.2, 159.7, 141.7, 134.2, 130.2, 130.1, 128.0, 127.6, 121.7, 114.0, 66.3, 55.3. HRMS (ESI): calcd for $C_{28}H_{27}O_6$, $[M+H]^+$, 459.1802; found, 459.1809.

*(2E,2′E)-Diethyl-3,3′-(benzo[d][1,3]dioxole-5,6-diyl)diacrylate (**1t**).* Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 15.7 Hz, 2H), 7.03 (s, 2H), 6.24 (d, J = 15.7 Hz, 2H), 6.04 (s, 2H), 4.27 (q, J = 7.1 Hz, 4H), 1.34 (t, J = 7.1 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.6, 149.7, 140.4, 129.4, 120.1, 106.4, 102.0, 60.7, 14.3. HRMS (ESI): calcd for $C_{17}H_{19}O_6$, $[M+H]^+$, 319.1176; found, 319.1175.

*(2E,2′E)-Diethyl-3,3′-(4,5-difluoro-1,2-phenylene)diacrylate (**1u**).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 15.8 Hz, 2H), 7.38 (t, J = 9.4 Hz, 2H), 6.29 (d, J = 15.8 Hz, 2H), 4.29 (q, J = 7.1 Hz, 4H), 1.35 (t, J = 7.1 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.9, 151.13 (dd, J = 255.7, 15.0 Hz), 138.9, 131.4 (d, J = 4.8 Hz), 122.8, 116.23 (dd, J = 13.3, 5.6 Hz), 60.9, 14.3. HRMS (ESI): calcd for $C_{16}H_{17}O_4F_2$, $[M+H]^+$, 311.1089; found, 311.1095.

*(E)-Methyl-3-(2-((E)-3-oxoprop-1-enyl)phenyl)acrylate (**4a**).*[30] Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (d, J = 7.6 Hz, 1H), 8.09 (d, J = 15.8 Hz, 1H), 7.90 (d, J = 15.8 Hz, 1H), 7.72−7.58 (m, 2H), 7.55−7.43 (m, 2H), 6.69 (dd, J = 15.8, 7.7 Hz, 1H), 6.41 (d, J =

DOI: 10.1021/acs.joc.6b02547
J. Org. Chem. 2017, 82, 1389−1402

15.8 Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.5, 166.8, 148.8, 141.0, 134.5, 133.5, 131.4, 131.0, 130.3, 127.9, 127.7, 122.1, 52.0. LRMS (EI): 216[M+], 201, 184, 157, 143, 128, 115, 102, 89. HRMS (ESI): calcd for $C_{13}H_{13}O_3$, $[M+H]^+$, 217.0865; found, 217.0866.

*(E)-Ethyl-3-(2-((E)-3-oxoprop-1-enyl)phenyl)acrylate (**4b**).*[31] Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (d, J = 7.7 Hz, 1H), 8.06 (d, J = 15.8 Hz, 1H), 7.88 (d, J = 15.8 Hz, 1H), 7.69−7.57 (m, 2H), 7.55−7.38 (m, 2H), 6.67 (dd, J = 15.8, 7.7 Hz, 1H), 6.39 (d, J = 15.8 Hz, 1H), 4.30 (q, J = 7.1 Hz, 2H), 1.36 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.4, 166.3, 148.8, 140.7, 134.7, 133.5, 131.4, 131.0, 130.2, 127.9, 127.6, 122.6, 60.9, 14.3.

*1,2-Bis(2-formylethenyl)benzene (**4c**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (d, J = 7.5 Hz, 2H), 7.88 (d, J = 15.8 Hz, 2H), 7.66 (dt, J = 7.2, 3.6 Hz, 2H), 7.59−7.34 (m, 2H), 6.69 (dd, J = 15.8, 7.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.0, 148.1, 133.8, 132.1, 131.1, 128.1. HRMS (ESI): calcd for $C_{12}H_{11}O_2$, $[M+H]^+$, 187.0754; found, 187.0752.

*(3E,3′E)-4,4′-(1,2-Phenylene)bis(but-3-en-2-one) (**6a**).*[22] White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 16.0 Hz, 2H), 7.60 (dd, J = 5.7, 3.5 Hz, 2H), 7.43 (dd, J = 5.8, 3.3 Hz, 2H), 6.64 (d, J = 16.0 Hz, 2H), 2.41 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.9, 139.8, 134.6, 130.4, 130.3, 127.8, 28.1.

*(2E,2′E)-3,3′-(1,2-Phenylene)bis(1-phenylprop-2-en-1-one) (**6b**).*[22] Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 15.6 Hz, 2H), 8.03 (d, J = 7.6 Hz, 4H), 7.72 (dd, J = 5.5, 3.5 Hz, 2H), 7.59 (t, J = 7.3 Hz, 2H), 7.55−7.46 (m, 4H), 7.43 (d, J = 15.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.1, 141.8, 137.9, 135.4, 133.0, 130.2, 128.7, 128.6, 128.2, 126.1.

*(E)-Ethyl-3-(2-((E)-3-oxo-3-phenylprop-1-en-1-yl)phenyl)acrylate (**6c**).* Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19−7.97 (m, 4H), 7.74−7.67 (m, 1H), 7.60 (t, J = 4.6 Hz, 2H), 7.51 (t, J = 7.5 Hz, 2H), 7.47−7.40 (m, 3H), 6.37 (d, J = 15.8 Hz, 1H), 4.29 (q, J = 7.1 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.0, 166.4, 141.5, 141.5, 138.0, 134.9, 133.0, 130.2, 129.9, 128.8, 128.7, 128.6, 128.0, 127.8, 125.9, 122.1, 60.7, 14.3. HRMS (ESI): calcd for $C_{20}H_{19}O_3$, $[M+H]^+$, 307.1334; found, 307.1332.

*3,3′-(1,2-Phenylene)diacrylonitrile (**6d**).* White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99−7.39 (m, 6H), 6.14−5.50 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 147.0, 146.7, 132.9, 131.3, 131.2, 130.8, 129.0, 127.2, 126.8, 117.3, 100.9, 100.4. HRMS (ESI): calcd for $C_{12}H_9N_2$, $[M+H]^+$, 181.0766; found, 181.0768.

*(1E,1′E)-1,1′-(1,2-Phenylene)bis(pent-1-en-3-one) (**6e**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 16.0 Hz, 2H), 7.59 (dd, J = 5.7, 3.5 Hz, 2H), 7.41 (dd, J = 5.8, 3.3 Hz, 2H), 6.65 (d, J = 16.0 Hz, 2H), 2.72 (q, J = 7.3 Hz, 4H), 1.19 (t, J = 7.3 Hz, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 200.4, 138.7, 134.7, 130.1, 129.4, 127.7, 34.5, 8.1. HRMS (ESI): calcd for $C_{16}H_{19}O_2$, $[M+H]^+$, 243.1380; found, 243.1387.

*(E)-Ethyl-3-(2-((E)-3-oxobut-1-en-1-yl)phenyl)acrylate (**6f**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 15.8 Hz, 1H), 7.87 (d, J = 16.1 Hz, 1H), 7.70−7.52 (m, 2H), 7.52−7.33 (m, 2H), 6.62 (d, J = 16.1 Hz, 1H), 6.36 (dd, J = 15.8, 0.8 Hz, 1H), 4.29 (qd, J = 7.1, 0.7 Hz, 2H), 2.41 (d, J = 0.8 Hz, 3H), 1.35 (td, J = 7.1, 0.7 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.7, 161.1, 135.9, 134.6, 129.2, 128.9, 125.1, 124.9, 124.8, 122.4, 122.3, 116.8, 55.4, 22.5, 9.0. HRMS (ESI): calcd for $C_{15}H_{17}O_3$, $[M+H]^+$, 2245.1172; found, 245.1177.

General Procedures for Preparation of Products 3, 5, and 7. **3**: In a silica tube, **1** (0.2 mmol) and **2** (0.3 mmol) were added to anhydrous MeCN (10 mL), and were charged with N_2 three times. The mixture was allowed to expose to 500W medium pressure mercury lamp with Pyrex filter for 4−15 h (monitored by TLC). After the substrate **1** was consumed, the solvent was removed under vacuo, and the residue was purified by column chromatography (10% EtOAc/hexane-50% EtOAc/hexane) to give the product.

5: In a silica tube, **4** (0.2 mmol) and **2** (0.3 mmol) were added to anhydrous MeCN (10 mL), and were charged with N_2 three times. The mixture was allowed to expose to 500W medium pressure mercury lamp with Pyrex filter for 2−4 h (monitored by TLC). After the substrate **4** was consumed, the solvent was removed under vacuo, and the residue was purified by column chromatography (10% EtOAc/hexane-50% EtOAc/hexane) to give the product.

7: In a silica tube, **6** (0.2 mmol) and **2** (0.3 mmol) were added to anhydrous MeCN (10 mL), and were charged with N_2 three times. The mixture was allowed to expose to 500W medium pressure mercury lamp with Pyrex filter for 4 h (monitored by TLC). After the substrate **6** was consumed, the solvent was removed under vacuo, and the residue was purified by column chromatography (10% EtOAc/hexane-50% EtOAc/hexane) to give the product.

Gram Scale Reactions. In a silica tube, **1a**/**1b** (1.0 g) and **2** (1.5 equiv) were added to anhydrous MeCN (100 mL) and charged with N_2 three times. The mixture was allowed to expose to 500W medium pressure mercury lamp with Pyrex filter for 12−16 h (monitored by TLC). After the substrate **1a**/**1b** was consumed, the solvent was removed under vacuo, and the residue was purified by column chromatography (10% EtOAc/hexane-50% EtOAc/hexane) to give the product.

*Compound **3aa**.* Colorless oil. 60 mg. Yield 84%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26−7.14 (m, 3H), 7.14−6.99 (m, 1H), 4.06 (t, J = 2.7 Hz, 1H), 3.93 (t, J = 3.0 Hz, 1H), 3.82 (s, 3H), 3.59 (s, 3H), 3.47 (dd, J = 5.5, 2.2 Hz, 1H), 3.23 (dd, J = 8.5, 3.2 Hz, 1H), 3.19 (dd, J = 5.5, 2.9 Hz, 1H), 3.11 (dd, J = 8.5, 3.2 Hz, 1H), 2.47 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.4, 176.9, 173.3, 172.2, 136.3, 134.6, 128.2, 128.2, 126.1, 125.2, 52.8, 52.4, 44.6, 44.4, 43.9, 40.7, 38.8, 38.5, 24.3. LRMS (EI): 357[M+], 325, 286, 187, 153, 128. HRMS (ESI): calcd for $C_{19}H_{20}O_6N$, $[M+H]^+$, 358.1285; found, 358.1294.

*Compound **3ab**.* White solid. 56 mg. Yield 76%. mp 110−111 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26−7.00 (m, 4H), 4.07 (s, 1H), 3.94 (t, J = 2.8 Hz, 1H), 3.83 (s, 3H), 3.60 (s, 3H), 3.48 (dd, J = 5.4, 1.9 Hz, 1H), 3.22−3.16 (m, 2H), 3.09 (dt, J = 9.8, 5.0 Hz, 3H), 0.35 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.2, 176.8, 173.3, 172.3, 136.5, 134.8, 128.1, 128.1, 126.2, 125.3, 52.8, 52.4, 44.6, 44.4, 43.6, 40.4, 38.9, 38.6, 33.1, 11.9. LRMS (EI): 371[M+], 329, 186, 128. HRMS (ESI): calcd for $C_{20}H_{22}O_6N$, $[M+H]^+$, 372.1442; found, 372.1451.

*Compound **3ac**.* White solid. 65 mg. Yield 75%. mp 189−190 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25−7.01 (m, 7H), 6.57 (d, J = 7.1 Hz, 2H), 4.27 (s, 2H), 4.09 (t, J = 2.7 Hz, 1H), 3.96 (t, J = 3.0 Hz, 1H), 3.83 (s, 3H), 3.60 (s, 3H), 3.49 (dd, J = 5.4, 2.2 Hz, 1H), 3.26 (dd, J = 8.6, 3.2 Hz, 1H), 3.18 (dd, J = 5.4, 2.9 Hz, 1H), 3.15 (dd, J = 8.7, 3.2 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.0, 176.6, 173.3, 172.2, 136.3, 134.8, 134.5, 128.4, 128.3, 128.3, 127.4, 127.2, 126.2, 125.2, 52.9, 52.5, 44.8, 44.7, 43.8, 42.0, 40.6, 38.7, 38.5. LRMS (EI): 433[M+], 401, 369, 186, 155, 128, 91. HRMS (ESI): calcd for $C_{25}H_{24}O_6N$, $[M+H]^+$, 434.1598; found, 434.1612.

*Compound **3ad**.* White solid. 51 mg. Yield 64%. mp 138−139 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25−7.07 (m, 4H), 4.01 (t, 1H), 3.89 (t, J = 3.1 Hz, 1H), 3.82 (s, 3H), 3.60 (s, 3H), 3.46 (dd, J = 5.5, 2.3 Hz, 1H), 3.18 (dd, J = 5.5, 2.9 Hz, 1H), 3.06 (dd, J = 8.8, 3.3 Hz, 1H), 2.94 (dd, J = 8.8, 3.3 Hz, 1H), 1.08 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 178.5, 178.1, 173.3, 172.4, 136.8, 135.1, 128.0, 127.9, 126.3, 125.3, 58.1, 52.8, 52.4, 44.6, 44.4, 43.3, 40.2, 39.2, 38.9, 27.7. HRMS (ESI): calcd for $C_{22}H_{25}O_6NNa$, $[M+Na]^+$, 422.1574; found, 422.1581.

*Compound **3ae**.* White solid. 47 mg. Yield 68%. mp 169−170 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.29−7.02 (m, 4H), 4.06 (t, J = 2.7 Hz, 1H), 3.93 (t, J = 3.0 Hz, 1H), 3.83 (s, 3H), 3.62 (s, 3H), 3.45 (dd, J = 5.4, 2.2 Hz, 1H), 3.27 (dd, J = 8.7, 3.2 Hz, 1H), 3.20 (dd, J = 5.4, 2.9 Hz, 1H), 3.16 (dd, J = 8.7, 3.2 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.4, 176.8, 173.3, 172.2, 136.4, 134.6, 128.4, 126.3, 125.4, 52.9, 52.5, 45.1, 44.5, 44.4, 41.9, 38.6, 38.3. LRMS (EI): 343[M+], 311, 252, 18, 155, 128. HRMS (ESI): calcd for $C_{18}H_{17}O_6NNa$, $[M+Na]^+$, 366.0948; found, 366.0959.

*Compound **3af**.* Colorless oil. 31 mg. Yield 45%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.06 (m, 4H), 4.11 (t, J = 2.7 Hz, 1H), 3.97 (t, J = 3.0 Hz, 1H), 3.82 (s, 3H), 3.61 (s, 3H), 3.55−3.49 (m, 1H), 3.47−3.39 (m, 2H), 3.21 (dd, J = 5.4, 2.9 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.0, 171.7, 171.4, 170.9, 135.9, 134.0, 129.0, 126.5, 125.5, 53.0, 52.7, 44.6, 44.2, 44.1, 41.6, 38.5, 38.3. HRMS (ESI): calcd for $C_{18}H_{16}O_7Na$, $[M+Na]^+$, 367.0788; found, 367.0794.

DOI: 10.1021/acs.joc.6b02547
J. Org. Chem. 2017, 82, 1389−1402

Compound ***3ba***. White solid. 56 mg. Yield 77%. mp 163−164 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28−7.15 (m, 3H), 7.14−7.03 (m, 1H), 4.34−4.17 (m, 2H), 4.12−3.98 (m, 3H), 3.94 (t, J = 3.1 Hz, 1H), 3.46 (dd, J = 5.4, 2.4 Hz, 1H), 3.24 (dd, J = 8.5, 3.2 Hz, 1H), 3.20 (dd, J = 5.4, 2.9 Hz, 1H), 3.12 (dd, J = 8.5, 3.3 Hz, 1H), 2.48 (d, J = 4.1 Hz, 3H), 1.36 (t, J = 7.1 Hz, 3H), 1.19 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.5, 177.1, 172.9, 171.8, 136.5, 134.6, 128.2, 128.1, 126.1, 125.2, 61.8, 61.3, 44.6, 44.4, 43.9, 40.7, 38.8, 38.7, 24.3, 14.3, 14.2. HRMS (ESI): calcd for $C_{21}H_{24}O_6N$, $[M+H]^+$, 386.1598; found, 386.1604.

Compound ***3bb***. Colorless oil. 60 mg. Yield 75%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17−7.10 (m, 3H), 7.06 (d, J = 6.0 Hz, 1H), 4.27−4.16 (m, 2H), 4.05−3.93 (m, 3H), 3.88 (s, 1H), 3.46−3.37 (m, 1H), 3.15 (dd, J = 7.8, 3.2 Hz, 2H), 3.04 (dd, J = 12.9, 7.6 Hz, 3H), 1.30 (t, J = 7.1 Hz, 3H), 1.13 (t, J = 7.1 Hz, 3H), 0.29 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.2, 176.8, 172.8, 171.8, 136.6, 134.8, 128.0, 127.9, 126.1, 125.3, 61.7, 61.2, 44.5, 44.3, 43.6, 40.4, 38.8, 38.8, 33.0, 14.2, 14.1, 11.9. HRMS (ESI): calcd for $C_{22}H_{26}O_6N$, $[M+H]^+$, 400.1755; found, 400.1763.

Compound ***3bc***. White solid. 60 mg. Yield 70%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23−6.88 (m, 7H), 6.56 (d, J = 7.3 Hz, 2H), 4.30−4.19 (m, 4H), 4.09−3.97 (m, 3H), 3.94 (t, J = 3.0 Hz, 1H), 3.45 (dd, J = 5.3, 2.2 Hz, 1H), 3.25 (dd, J = 8.6, 3.1 Hz, 1H), 3.16 (dd, J = 5.3, 3.0 Hz, 1H), 3.13 (dd, J = 8.7, 3.2 Hz, 1H), 1.35 (t, J = 7.2 Hz, 3H), 1.17 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.1, 176.7, 172.9, 171.8, 136.4, 134.8, 134.6, 128.4, 128.3, 128.2, 127.4, 127.2, 126.1, 125.2, 61.8, 61.3, 44.8, 44.6, 43.8, 42.0, 40.7, 38.7, 38.6, 14.3, 14.2. LRMS (EI): 461[M+], 373, 186, 155, 128. HRMS (ESI): calcd for $C_{27}H_{28}O_6N$, $[M+H]^+$, 462.1911; found, 462.1909.

Compound ***3bd***. White solid. 50 mg. Yield 58%. ^{1}H NMR (400 MHz, $CDCl_3$) 7.26−6.82 (m, 4H), 4.26 (q, J = 7.1 Hz, 2H), 4.13−3.94 (m, 3H), 3.89 (t, J = 3.1 Hz, 1H), 3.44 (dd, J = 5.3, 2.3 Hz, 1H), 3.18 (dd, J = 5.3, 2.9 Hz, 1H), 3.07 (dd, J = 8.8, 3.3 Hz, 1H), 2.94 (dd, J = 8.8, 3.4 Hz, 1H), 1.35 (t, J = 7.1 Hz, 3H), 1.18 (t, J = 7.1 Hz, 3H), 1.08 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 178.6, 178.2, 172.9, 172.0, 136.9, 135.1, 127.9, 127.8, 126.2, 125.4, 61.7, 61.2, 58.0, 44.6, 44.3, 43.3, 40.2, 39.2, 39.1, 27.7, 14.3, 14.2. HRMS (ESI): calcd for $C_{24}H_{29}O_6NNa$, $[M+H]^+$, 450.1887; found, 450.1894.

Compound ***3be***. White solid. 58 mg. Yield 78%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.27−7.13 (m, 3H), 7.13−6.99 (m, 1H), 4.24 (dtt, J = 10.8, 7.2, 3.6 Hz, 2H), 4.11−3.94 (m, 3H), 3.88 (t, J = 3.0 Hz, 1H), 3.39 (dd, J = 5.3, 2.3 Hz, 1H), 3.22 (dd, J = 8.6, 3.2 Hz, 1H), 3.15 (dd, J = 5.3, 2.9 Hz, 1H), 3.10 (dd, J = 8.6, 3.3 Hz, 1H), 1.33 (t, J = 7.1 Hz, 3H), 1.17 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0, 177.5, 172.9, 171.7, 136.5, 134.6, 128.2, 128.1, 126.2, 125.3, 61.8, 61.3, 45.0, 44.5, 44.4, 41.8, 38.5, 38.5, 14.2, 14.1. HRMS (ESI): calcd for $C_{20}H_{22}O_6N$, $[M+H]^+$, 372.1442; found, 372.1448.

Compound ***3bg***. Colorless oil. 54 mg. Yield 60%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36−7.23 (m, 6H), 7.19 (d, J = 6.5 Hz, 1H), 6.46 (dd, J = 6.7, 2.9 Hz, 2H), 4.37−4.24 (m, 2H), 4.18 (t, J = 2.7 Hz, 1H), 4.13−4.04 (m, 2H), 4.04−4.01 (m, 1H), 3.52 (dd, J = 5.3, 2.3 Hz, 1H), 3.42 (dd, J = 8.5, 3.3 Hz, 1H), 3.31 (dd, J = 8.5, 3.3 Hz, 1H), 3.27 (dd, J = 5.3, 2.9 Hz, 1H), 1.38 (t, J = 7.1 Hz, 3H), 1.21 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.7, 176.3, 172.9, 171.8, 136.7, 134.9, 131.3, 129.1, 128.8, 128.3, 128.2, 126.4, 126.4, 125.5, 61.9, 61.4, 44.5, 44.4, 44.0, 40.9, 39.1, 39.1, 14.3, 14.2. HRMS (ESI): calcd for $C_{26}H_{26}O_6N$, $[M+H]^+$, 448.1755; found, 448.1760.

Compound ***3ca***. Colorless oil. 47 mg. Yield 64%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.14−6.70 (m, 3H), 4.02 (dt, J = 9.9, 2.6 Hz, 1H), 3.89 (dt, J = 10.0, 2.9 Hz, 1H), 3.82 (s, 3H), 3.60 (d, J = 7.2 Hz, 3H), 3.45 (d, J = 5.4 Hz, 1H), 3.22 (dd, J = 8.5, 3.2 Hz, 1H), 3.19−3.14 (m, 1H), 3.10 (dt, J = 8.3, 3.0 Hz, 1H), 2.50 (d, J = 3.1 Hz, 3H), 2.27 (d, J = 6.8 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.5, 177.0, 173.3, 172.3, 137.9, 134.4, 133.3, 128.8, 125.8, 124.9, 52.8, 52.4, 44.7, 44.5, 44.0, 40.7, 38.5, 38.2, 24.3, 21.3. HRMS (ESI): calcd for $C_{20}H_{21}O_6NNa$, $[M+Na]^+$, 394.1261; found, 394.1267.

Compound ***3da***. Colorless oil. 55 mg. Yield 70%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25−7.01 (m, 3H), 4.15−4.01 (m, 1H), 3.98−3.89 (m, 1H), 3.83 (s, 3H), 3.62 (d, J = 9.9 Hz, 3H), 3.55−3.40 (m, 1H), 3.23 (dd, J = 8.5, 2.9 Hz, 1H), 3.16 (dd, J = 5.2, 2.7 Hz, 1H), 3.11 (dd, J = 8.5, 3.0 Hz, 1H), 2.54 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.1, 176.6, 172.9, 172.0, 136.5, 134.9, 133.9, 128.4, 126.5, 126.4, 53.0, 52.6, 44.5, 44.3, 43.6, 40.4, 38.5, 38.1, 24.5. HRMS (ESI): calcd for $C_{19}H_{19}O_6NCl$, $[M+H]^+$, 392.0895; found, 392.0893.

Compound ***3ea***. Colorless oil. 53 mg. Yield 63%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.24−7.03 (m, 3H), 4.41−4.19 (m, 2H), 4.17−3.97 (m, 3H), 3.93 (dt, J = 13.4, 3.0 Hz, 1H), 3.45 (dt, J = 5.3, 2.7 Hz, 1H), 3.24 (dd, J = 8.5, 2.5 Hz, 1H), 3.18−3.14 (m, 1H), 3.12 (dd, J = 8.4, 2.8 Hz, 1H), 2.55 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H), 1.20 (dd, J = 15.8, 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.1, 176.7, 172.5, 171.5, 136.5, 135.0, 133.9, 128.4, 127.4, 126.5, 62.0, 61.5, 44.5, 44.3, 43.6, 40.5, 38.6, 38.2, 24.5, 14.3, 14.2. HRMS (ESI): calcd for $C_{21}H_{23}O_6NCl$, $[M+H]^+$, 420.1208; found, 420.1202.

Compound ***3fa***. Colorless oil. 46 mg. Yield 55%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (d, 8.2 Hz, 1H), 6.76−6.63 (m, 2H), 4.30−4.20 (m, 2H), 4.09−3.97 (m, 3H), 3.88 (t, J = 2.8 Hz, 1H), 3.77−3.71 (m, 3H), 3.47−3.37 (m, 1H), 3.31−3.14 (m, 2H), 3.12−3.05 (m, 1H), 2.52 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H), 1.19 (td, J = 7.1, 3.3 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.6, 177.0, 173.0, 171.7, 159.3, 135.9, 128.4, 126.2, 113.3, 112.0, 61.7, 61.3, 55.2, 45.0, 44.4, 43.8, 41.0, 39.0, 38.1, 24.4, 14.25, 14.22. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (d, 8.2 Hz, 1H), 6.76−6.63 (m, 2H), 4.30−4.20 (m, 2H), 4.09−3.97 (m, 3H), 3.88 (t, J = 2.8 Hz, 1H), 3.77−3.71 (m, 3H), 3.47−3.37 (m, 1H), 3.31−3.14 (m, 2H), 3.12−3.05 (m, 1H), 2.52 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H), 1.19 (td, J = 7.1, 3.3 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.4, 177.2, 172.9, 171.9, 159.4, 137.7, 127.0, 126.4, 113.5, 110.9, 61.8, 61.3, 55.2, 44.8, 44.5, 44.1, 40.7, 39.1, 38.1, 24.4, 14.25, 14.20. HRMS (ESI): calcd for $C_{22}H_{26}O_7N$, $[M+H]^+$, 416.1704; found, 416.1714.

Compound ***3ga***. Colorless oil. 54 mg. Yield 67%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22−7.03 (m, 1H), 6.96−6.79 (m, 2H), 4.37−4.18 (m, 2H), 4.11−4.01 (m, 3H), 3.94 (dd, J = 7.6, 3.2 Hz, 1H), 3.45 (td, J = 5.7, 2.4 Hz, 1H), 3.24 (ddd, J = 8.5, 3.0, 1.9 Hz, 1H), 3.17 (ddd, J = 8.1, 5.4, 2.9 Hz, 1H), 3.11 (ddd, J = 8.4, 4.9, 3.4 Hz, 1H), 2.53 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H), 1.23−1.16 (m, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.2, 176.7, 172.6, 171.6, 162.2 (d, J = 247.2 Hz), 136.8 (d, J = 7.8 Hz), 132.2, 126.8 (d, J = 8.6 Hz), 115.0 (d, J = 9.0 Hz), 113.6 (d, J = 22.3 Hz), 61.9, 61.4, 44.7, 44.2, 43.6, 40.7, 38.1, 24.4, 14.2. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22−7.03 (m, 1H), 6.96−6.79 (m, 2H), 4.37−4.18 (m, 2H), 4.11−4.01 (m, 3H), 3.94 (dd, J = 7.6, 3.2 Hz, 1H), 3.45 (td, J = 5.7, 2.4 Hz, 1H), 3.24 (ddd, J = 8.5, 3.0, 1.9 Hz, 1H), 3.17 (ddd, J = 8.1, 5.4, 2.9 Hz, 1H), 3.11 (ddd, J = 8.4, 4.9, 3.4 Hz, 1H), 2.53 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H), 1.23−1.16 (m, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.1, 176.9, 172.7, 171.6, 162.3 (d, J = 246.8 Hz), 138.5 (d, J = 8.3 Hz), 130.4, 127.7 (d, J = 8.6 Hz), 114.9 (d, J = 9.2 Hz), 112.8 (d, J = 22.8 Hz), 61.9, 61.5, 44.4, 44.3, 43.8, 40.7, 38.8, 24.4, 14.2. HRMS (ESI): calcd for $C_{21}H_{23}O_6NF$, $[M+H]^+$, 404.1504; found, 404.1511.

Compound ***3ha***. White solid. 52 mg. Yield 70%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26−6.96 (m, 4H), 4.27 (qd, J = 7.1, 2.2 Hz, 1H), 4.13−3.98 (m, 2H), 3.93 (dd, J = 6.0, 3.0 Hz, 1H), 3.82 (s, 3H), 3.46 (ddd, J = 15.7, 5.4, 2.3 Hz, 1H), 3.29−3.15 (m, 2H), 3.14−3.05 (m, 1H), 2.48 (s, 3H), 1.19 (t, J = 7.1 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 177.5, 177.0, 172.8, 171.7, 136.4, 134.5, 128.2, 128.2, 126.1, 125.2, 61.4, 52.4, 44.7, 44.4, 43.9, 40.7, 38.7, 38.6, 24.3, 14.2. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26−6.96 (m, 4H), 4.27 (qd, J = 7.1, 2.2 Hz, 1H), 4.13−3.97 (m, 2H), 3.93 (dd, J = 6.0, 3.0 Hz, 1H), 3.60 (s, 3H), 3.46 (ddd, J = 15.7, 5.4, 2.3 Hz, 1H), 3.28−3.15 (m, 2H), 3.15−3.03 (m, 1H), 2.48 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.4, 177.0, 173.4, 172.3, 136.4, 134.7, 128.2, 128.1, 126.1, 125.2, 61.9, 52.8, 44.5, 44.4, 43.9, 40.7, 38.8, 38.7, 24.3, 14.3. HRMS (ESI): calcd for $C_{20}H_{22}O_6N$, $[M+H]^+$, 372.1442; found, 372.1450.

Compound ***3ka***. White solid. 69 mg. Yield 78%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25−7.15 (m, 3H), 7.14−6.94 (m, 1H), 4.29−4.16 (m, 2H), 4.10−4.05 (m, 1H), 4.02−3.94 (m, 2H), 3.92 (t, J = 3.0 Hz, 1H), 3.46 (dd, J = 5.4, 2.3 Hz, 1H), 3.24 (dd, J = 8.5, 3.2 Hz, 1H), 3.19 (dd, J = 5.4, 2.9 Hz, 1H), 3.12 (dd, J = 8.5, 3.3 Hz, 1H), 2.48 (s, 3H), 1.71 (dt, J = 14.6, 6.8 Hz, 2H), 1.53 (tt, J = 10.3, 5.2 Hz, 2H), 1.43 (dt, J = 14.6, 7.5 Hz, 2H), 1.33 (dt, J = 15.1, 7.5 Hz, 2H), 0.98 (t, J = 7.4 Hz, 3H), 0.90 (t, J = 7.3 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ

DOI: 10.1021/acs.joc.6b02547
J. Org. Chem. 2017, 82, 1389−1402

177.4, 177.1, 173.0, 171.9, 136.5, 134.6, 128.2, 128.1, 126.1, 125.2, 65.7, 65.2, 44.7, 44.6, 44.0, 40.8, 38.8, 38.7, 30.6, 30.6, 24.3, 19.2, 19.1, 13.8, 13.7. HRMS (ESI): calcd for $C_{25}H_{31}O_6NNa$, $[M+Na]^+$, 464.2044; found, 464.2049.

Compound ***3maa***. Colorless oil. 37 mg. Yield 42%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21−7.14 (m, 3H), 7.09 (dd, J = 5.6, 2.0 Hz, 1H), 3.99 (t, J = 2.8 Hz, 1H), 3.88 (t, J = 3.1 Hz, 1H), 3.33 (dd, J = 5.1, 2.4 Hz, 1H), 3.21 (dd, J = 8.5, 3.2 Hz, 1H), 3.10−3.04 (m, 2H), 2.48 (s, 3H), 1.54 (s, 9H), 1.33 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.6, 177.4, 172.3, 171.1, 136.7, 134.8, 128.1, 127.8, 126.0, 125.2, 81.9, 81.4, 45.1, 44.9, 43.9, 40.8, 39.2, 38.9, 28.1, 28.0, 24.3. HRMS (ESI): calcd for $C_{25}H_{31}O_6NNa$, $[M+Na]^+$, 464.2044; found, 464.2053.

Compound ***3mab***. White solid. 26 mg. Yield 30%. mp 141−143 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (dt, J = 7.3, 3.7 Hz, 2H), 7.17−7.11 (m, 2H), 3.89 (s, 2H), 3.14 (s, 2H), 3.11 (s, 2H), 2.48 (s, 3H), 1.33 (s, 18H) ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.1, 169.8, 134.8, 127.8, 126.3, 81.0, 45.8, 44.3, 38.9, 28.0, 24.3. HRMS (ESI): calcd for $C_{25}H_{31}O_6NNa$, $[M+Na]^+$, 464.2044; found, 464.2052.

Compound ***3la***. Colorless oil. 53 mg. Yield 64%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23−7.15 (m, 3H), 7.13−7.07 (m, 1H), 5.22−4.99 (m, 1H), 4.87 (hept, J = 6.2 Hz, 1H), 4.06 (t, J = 2.8 Hz, 1H), 3.93 (t, J = 3.1 Hz, 1H), 3.43 (dd, J = 5.3, 2.4 Hz, 1H), 3.24 (dd, J = 8.5, 3.2 Hz, 1H), 3.18 (dd, J = 5.3, 3.0 Hz, 1H), 3.10 (dd, J = 8.5, 3.3 Hz, 1H), 2.50 (s, 3H), 1.36 (d, J = 6.2 Hz, 3H), 1.33 (d, J = 6.3 Hz, 3H), 1.19 (d, J = 6.3 Hz, 3H), 1.14 (d, J = 6.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.5, 177.2, 172.5, 171.3, 136.6, 134.6, 128.2, 128.0, 126.1, 125.2, 69.4, 68.8, 44.6, 44.5, 43.9, 40.8, 38.9, 38.8, 24.3, 21.9, 21.8, 21.7. HRMS (ESI): calcd for $C_{23}H_{28}O_6N$, $[M+H]^+$, 414.1911; found, 414.1907.

Compound ***3na***. Colorless oil. 51 mg. Yield 58%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23−7.07 (m, 4H), 4.74 (p, J = 7.3 Hz, 2H), 4.05−3.80 (m, 2H), 3.24 (s, 2H), 3.13 (s, 2H), 2.50 (s, 3H), 2.26−2.10 (m, 4H), 1.97−1.80 (m, 4H), 1.76−1.65 (m, 2H), 1.59−1.41 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.9, 170.0, 134.7, 127.9, 126.4, 69.1, 45.0, 44.1, 38.6, 30.1, 29.9, 24.3, 13.5. HRMS (ESI): calcd for $C_{25}H_{27}O_6NNa$, $[M+Na]^+$, 460.1731; found, 460.1735.

Compound ***3oa***. Colorless oil. 46 mg. Yield 50%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.16−7.11 (m, 2H), 7.11−6.92 (m, 2H), 5.11−4.77 (m, 2H), 3.83 (s, 2H), 3.16 (s, 2H), 3.06 (s, 2H), 2.42 (s, 3H), 1.78−1.29 (m, 16H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 175.9, 169.4, 133.7, 126.9, 125.2, 76.8, 44.3, 43.2, 37.6, 31.6, 31.2, 23.3, 22.7, 22.6. HRMS (ESI): calcd for $C_{27}H_{31}O_6NNa$, $[M+Na]^+$, 488.2044; found, 488.2045.

Compound ***3pa***. Colorless oil. 49 mg. Yield 48%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23−7.13 (m, 4H), 4.63−4.47 (m, 2H), 3.93 (s, 2H), 3.25 (s, 2H), 3.14 (s, 2H), 2.50 (s, 3H), 1.67 (dd, J = 12.3, 7.4 Hz, 8H), 1.49 (d, J = 9.8 Hz, 2H), 1.27 (dd, J = 9.0, 3.3 Hz, 10H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.0, 170.2, 134.7, 127.9, 126.3, 73.3, 45.3, 44.2, 38.8, 31.5, 31.4, 25.3, 24.3, 23.7, 23.7. HRMS (ESI): calcd for $C_{29}H_{35}O_6NNa$, $[M+Na]^+$, 516.2357; found, 516.2359.

Compound ***3qa***. Colorless oil. 59 mg. Yield 54%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (ddd, J = 14.0, 7.0, 4.3 Hz, 6H), 7.00 (dt, J = 14.5, 6.0 Hz, 6H), 4.87 (d, J = 12.1 Hz, 2H), 4.69 (d, J = 12.1 Hz, 2H), 3.91 (s, 2H), 3.32 (s, 2H), 3.12 (s, 2H), 2.47 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.6, 170.6, 162.7 (d, J = 247.3 Hz), 134.4, 131.1 (d, J = 2.9 Hz), 130.6 (d, J = 8.1 Hz), 128.9, 126.3, 115.4 (d, J = 21.7 Hz), 66.0, 45.1, 44.4, 38.6, 24.4. HRMS (ESI): calcd for $C_{31}H_{26}O_6NF_2$, $[M+H]^+$, 546.1723; found, 546.1736.

Compound ***3ra***. Colorless oil. 72 mg. Yield 56%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 8.1 Hz, 4H), 7.23 (d, J = 8.1 Hz, 4H), 7.16 (dd, J = 5.4, 3.2 Hz, 2H), 7.01 (dd, J = 5.4, 3.3 Hz, 2H), 4.93 (d, J = 12.7 Hz, 2H), 4.77 (d, J = 12.7 Hz, 2H), 3.94 (s, 2H), 3.38 (s, 2H), 3.15 (s, 2H), 2.48 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.5, 170.5, 139.1, 134.3, 130.6 (q, J = 32.4 Hz), 128.5, 128.2, 126.3, 125.4 (q, J = 3.6 Hz), 123.9 (q, J = 272.0 Hz), 65.8, 45.1, 44.0, 38.6, 24.4. HRMS (ESI): calcd for $C_{33}H_{26}O_6NF_6$, $[M+H]^+$, 646.1659; found, 646.1669.

Compound ***3sa***. Colorless oil. 50 mg. Yield 46%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.21−7.12 (m, 2H), 7.08 (d, J = 8.0 Hz, 4H), 7.06−6.96 (m, 2H), 6.83 (d, J = 8.1 Hz, 4H), 4.86 (d, J = 11.9 Hz, 2H), 4.66 (d, J = 11.9 Hz, 2H), 3.90 (s, 2H), 3.80 (s, 6H), 3.28 (s, 2H), 3.09 (s, 2H), 2.47 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 176.7, 170.7, 159.7, 134.4, 130.4, 128.0, 127.5, 126.3, 113.8, 66.5, 55.3, 45.1, 44.0, 38.5, 24.3. HRMS (ESI): calcd for $C_{33}H_{32}O_8N$, $[M+H]^+$, 570.2122; found, 570.2127.

Compound ***3ta***. Colorless oil. 48 mg. Yield 56%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.70 (s, 1H), 6.61 (s, 1H), 5.90 (dd, J = 2.5, 1.4 Hz, 2H), 4.31−4.21 (m, 2H), 4.12−4.01 (m, 2H), 4.00 (t, J = 2.8 Hz, 1H), 3.86 (t, J = 3.1 Hz, 1H), 3.40 (dd, J = 5.3, 2.4 Hz, 1H), 3.19 (dd, J = 8.4, 3.2 Hz, 1H), 3.15 (dd, J = 5.3, 3.0 Hz, 1H), 3.06 (dd, J = 8.4, 3.2 Hz, 1H), 2.59 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H), 1.22 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 177.4, 177.0, 172.8, 171.8, 147.2, 147.1, 129.8, 127.8, 107.2, 106.5, 100.9, 61.8, 61.3, 44.7, 44.6, 43.9, 40.7, 38.87, 38.84, 24.5, 14.27, 14.24. HRMS (ESI): calcd for $C_{22}H_{24}O_8N$, $[M+H]^+$, 430.1496; found, 430.1492.

Compound ***3ua***. Colorless oil. 56 mg. Yield 66%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.06 (dd, J = 9.2, 7.6 Hz, 1H), 6.98 (dd, J = 9.1, 7.7 Hz, 1H), 4.34−4.20 (m, 2H), 4.13−4.00 (m, 3H), 3.92 (t, J = 3.0 Hz, 1H), 3.45 (dd, J = 5.3, 2.3 Hz, 1H), 3.24 (dd, J = 8.5, 3.2 Hz, 1H), 3.14 (dd, J = 5.3, 3.0 Hz, 1H), 3.11 (dd, J = 8.5, 3.3 Hz, 1H), 2.58 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H), 1.21 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, CDCl3) δ 176.9, 176.5, 172.3, 171.4, 150.02 (dd, J = 253.5, 17.0 Hz), 149.90 (dd, J = 254.2, 17.7 Hz), 132.94 (dd, J = 5.8, 3.9 Hz), 131.25 (dd, J = 6.0, 4.1 Hz), 115.65 (d, J = 17.9 Hz), 114.89 (d, J = 17.8 Hz), 62.0, 61.6, 44.4, 44.2, 43.5, 40.4, 38.2, 24.6, 14.23, 14.19. HRMS (ESI): calcd for $C_{21}H_{22}O_6NF_2$, $[M+H]^+$, 422.1410; found, 422.1401.

Compound ***5aa***. White solid. 56 mg. Yield 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.96 (s, 1H), 7.34−7.04 (m, 4H), 4.12 (dd, J = 7.0, 2.9 Hz, 1H), 4.09 (t, J = 2.9 Hz, 1H), 3.61 (s, 3H), 3.51 (dd, J = 5.6, 2.2 Hz, 1H), 3.28 (dd, J = 5.6, 2.7 Hz, 1H), 3.20 (dd, J = 8.2, 3.2 Hz, 1H), 2.93 (dd, J = 8.5, 3.2 Hz, 1H), 2.49 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 199.7, 177.1, 176.7, 172.1, 136.1, 133.9, 128.5, 128.3, 125.8, 125.0, 52.6, 52.4, 44.1, 41.4, 40.5, 38.6, 36.1, 24.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.51 (s, 1H), 7.46−6.84 (m, 4H), 4.12 (dd, J = 7.0, 2.9 Hz, 1H), 3.99 (t, J = 3.0 Hz, 1H), 3.83 (s, 3H), 3.51 (dd, J = 5.6, 2.2 Hz, 1H), 3.31 (dd, J = 8.5, 3.2 Hz, 1H), 3.22 (dd, J = 4.9, 3.1 Hz, 1H), 3.12 (dd, J = 8.5, 3.2 Hz, 1H), 2.50 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 198.7, 177.2, 176.8, 173.0, 136.5, 135.2, 128.3, 128.3, 126.4, 125.3, 52.9, 51.7, 43.8, 41.6, 40.6, 38.6, 36.8, 24.4. HRMS (ESI): calcd for $C_{18}H_{18}O_5N$, $[M+H]^+$, 328.1179; found, 328.1192.

Compound ***5ag***. Colorless oil. 56 mg. Yield 72%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.51 (s, 1H), 7.82−6.90 (m, 7H), 6.69−6.22 (m, 2H), 4.25−4.16 (m, 1H), 4.06 (t, J = 3.0 Hz, 1H), 3.82 (s, 3H), 3.46 (dd, J = 3.6, 1.8 Hz, 1H), 3.37 (dd, J = 8.6, 3.2 Hz, 1H), 3.28 (dd, J = 5.4, 2.9 Hz, 1H), 3.24 (dd, J = 8.6, 3.3 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 198.8, 176.5, 176.1, 173.0, 136.8, 134.2, 131.2, 129.1, 128.6, 128.5, 128.5, 126.4, 126.1, 125.3, 53.0, 51.6, 44.2, 41.5, 40.7, 39.0, 37.1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.94 (s, 1H), 7.48−7.04 (m, 7H), 6.48−6.42 (m, 2H), 4.29−4.16 (m, 1H), 4.15 (t, J = 2.9 Hz, 1H), 3.61 (s, 3H), 3.55 (dd, J = 5.7, 2.2 Hz, 1H), 3.45 (dd, J = 7.6, 2.6 Hz, 1H), 3.31 (dd, J = 5.7, 2.6 Hz, 1H), 3.08 (dd, J = 8.6, 3.3 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.8, 176.4, 176.0, 172.2, 136.4, 135.5, 131.2, 129.1, 128.9, 128.6, 128.4, 126.6, 126.4, 125.6, 52.6, 52.3, 43.9, 41.5, 40.5, 39.0, 36.4. LRMS (EI): 389[M+], 339, 279, 186, 128. HRMS (ESI): calcd for $C_{23}H_{20}O_5N$, $[M+H]^+$, 390.1336; found, 390.1343.

Compound ***5ac***. Colorless oil. 66 mg. Yield 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.46 (s, 1H), 7.15−6.95 (m, 7H), 6.55 (dd, J = 7.1, 1.7 Hz, 2H), 4.25 (s, 2H), 4.10 (dt, J = 6.2, 2.7 Hz, 1H), 3.97 (t, J = 3.0 Hz, 1H), 3.80 (s, 3H), 3.39 (dd, J = 5.3, 2.2 Hz, 1H), 3.29 (dd, J = 8.7, 3.1 Hz, 1H), 3.17 (dd, J = 5.3, 2.9 Hz, 1H), 2.92 (dd, J = 8.7, 3.2 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 198.8, 176.9, 176.5, 173.0, 136.5, 134.7, 133.8, 128.6, 128.4, 128.4, 127.4, 127.3, 125.8, 125.3, 52.9, 51.9, 44.0, 42.0, 41.8, 40.4, 38.5, 36.7. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.91 (s, 1H), 7.18−6.94 (m, 7H), 6.55 (dd, J = 7.1, 1.7 Hz, 2H), 4.24 (s, 2H), 4.10 (dt, J = 6.2, 2.7 Hz, 1H), 4.07 (t, J = 2.9 Hz, 1H), 3.58 (s, 3H), 3.48 (dd, J = 5.6, 2.2 Hz, 1H), 3.21 (dd, J = 6.0, 2.5 Hz, 1H), 3.20 (dd, J = 5.1, 3.4 Hz, 1H), 2.92 (dd, J = 8.7, 3.2 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.8, 176.8, 176.4, 172.1, 136.1, 135.2, 134.7, 128.6, 128.4, 128.4, 127.4, 127.3, 126.4, 125.0, 52.6, 52.5, 43.7, 42.0, 41.3, 40.8, 38.5, 36.0. LRMS (EI): 403[M+], 389, 361, 175,

DOI: 10.1021/acs.joc.6b02547
J. Org. Chem. 2017, 82, 1389−1402

155, 128. HRMS (ESI): calcd for $C_{24}H_{22}O_5N$, $[M+H]^+$, 404.1492; found, 404.1502.

Compound ***5ba***. Colorless oil. 46 mg. Yield 68%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.95 (s, 1H), 7.26−7.06 (m, 4H), 4.27 (q, J = 7.1 Hz, 1H), 4.15−3.91 (m, 3H), 3.48 (dd, J = 5.5, 2.2 Hz, 1H), 3.35−3.25 (m, 1H), 3.23−3.17 (m, 1H), 2.94 (dd, J = 8.5, 3.2 Hz, 1H), 2.48 (s, 3H), 1.20 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.9, 177.2, 176.8, 171.6, 136.2, 135.2, 128.5, 128.2, 126.3, 125.0, 61.5, 52.3, 43.8, 40.7, 40.6, 38.8, 36.0, 24.4, 14.2. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.50 (s, 1H), 7.25−7.00 (m, 4H), 4.27 (q, J = 7.1 Hz, 1H), 4.14−3.95 (m, 3H), 3.43 (dd, J = 5.3, 2.2 Hz, 1H), 3.32−3.27 (m, 1H), 3.23−3.17 (m, 1H), 3.12 (dd, J = 8.5, 3.2 Hz, 1H), 2.49 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 198.9, 177.3, 176.9, 172.6, 136.5, 134.0, 128.5, 128.3, 125.9, 125.3, 62.0, 51.6, 44.1, 41.7, 41.4, 38.7, 36.8, 24.4, 14.2. HRMS (ESI): calcd for $C_{19}H_{20}O_5N$, $[M+H]^+$, 342.1336; found, 342.1329.

Compound ***5af***. Colorless oil. 36 mg. Yield 58%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.94 (s, 1H), 7.42−7.06 (m, 4H), 4.16 (dd, J = 6.2, 3.4 Hz, 1H), 4.09 (t, J = 3.0 Hz, 1H), 3.62 (s, 3H), 3.59 (dd, J = 9.5, 3.2 Hz, 1H), 3.44 (dd, J = 5.7, 2.3 Hz, 1H), 3.41 (dd, J = 9.5, 3.4 Hz, 1H), 3.29 (dd, J = 5.7, 2.6 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.8, 171.5, 170.9, 170.5, 135.6, 134.6, 129.1, 129.1, 126.2, 125.3, 52.8, 51.8, 44.5, 41.3, 40.4, 38.4, 35.9. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.49 (s, 1H), 7.42−7.06 (m, 4H), 4.16 (dd, J = 6.2, 3.4 Hz, 1H), 4.02 (t, J = 3.0 Hz, 1H), 3.83 (s, 3H), 3.54 (dd, J = 9.4, 3.2 Hz, 1H), 3.36 (dd, J = 5.4, 2.2 Hz, 1H), 3.26 (dd, J = 9.4, 3.3 Hz, 1H), 3.22 (dd, J = 5.4, 2.9 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.2, 172.7, 171.0, 170.7, 135.9, 133.3, 129.3, 129.1, 126.7, 125.6, 53.1, 51.2, 44.8, 42.2, 41.1, 38.3, 36.5. LRMS (EI): 314[M+], 244, 186, 155, 133, 113. HRMS (ESI): calcd for $C_{17}H_{15}O_6$, $[M+H]^+$, 315.0863; found, 315.0885.

Compound ***5ah***. Colorless oil. 43 mg. Yield 60%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.50 (s, 1H), 7.39−6.90 (m, 4H), 4.80 (ddd, J = 13.7, 12.5, 2.5 Hz, 2H), 3.81 (s, 3H), 3.80 (s, 3H), 3.74 (s, 3H), 3.38 (dd, J = 5.0, 2.6 Hz, 1H), 3.22 (dd, J = 5.0, 2.5 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 198.1, 172.2, 165.6, 165.1, 143.4, 141.6, 140.1, 137.6, 127.2, 127.0, 124.6, 124.0, 54.6, 52.6, 52.6, 52.5, 45.1, 44.4, 42.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.78 (s, 1H), 7.56−6.70 (m, 4H), 4.80 (ddd, J = 13.7, 12.5, 2.5 Hz, 2H), 3.80 (s, 3H), 3.78 (s, 3H), 3.60 (s, 3H), 3.44 (dd, J = 5.0, 2.7 Hz, 1H), 3.26 (dd, J = 5.1, 2.4 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 198.5, 171.5, 165.3, 165.3, 143.4, 141.1, 139.9, 138.7, 127.0, 126.9, 125.1, 123.7, 55.7, 52.6, 52.6, 52.5, 44.8, 44.2, 42.7. LRMS (EI): 358[M+], 186, 155, 128. HRMS (ESI): calcd for $C_{19}H_{19}O_7$, $[M+H]^+$, 359.1125; found, 359.1133.

Compound ***5ca***. White solid. 48 mg. Yield 80%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.95 (s, 1H), 9.53 (s, 1H), 7.26−7.19 (m, 3H), 7.14 (d, J = 6.9 Hz, 1H), 4.17 (s, 1H), 4.12 (s, 1H), 3.47 (dd, J = 5.2, 1.9 Hz, 1H), 3.30 (dd, J = 5.2, 2.6 Hz, 1H), 3.20 (dd, J = 8.5, 3.1 Hz, 1H), 2.99 (dd, J = 8.5, 3.1 Hz, 1H), 2.50 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.6, 198.6, 176.8, 176.5, 136.2, 134.4, 128.6, 128.4, 125.9, 125.1, 49.5, 47.8, 43.9, 41.2, 36.9, 36.0, 24.4. HRMS (ESI): calcd for $C_{17}H_{16}O_4N$, $[M+H]^+$, 298.1074; found, 298.1084.

Compound ***5cb***. Colorless oil. 45 mg. Yield 72%.

^{1}H NMR (600 MHz, $CDCl_3$) δ 9.94 (s, 1H), 9.53 (s, 1H), 7.28−7.17 (m, 3H), 7.15 (d, J = 7.0 Hz, 1H), 4.17 (s, 1H), 4.13 (s, 1H), 3.48 (dd, J = 5.2, 1.6 Hz, 1H), 3.30 (dd, J = 5.2, 2.5 Hz, 1H), 3.17 (dd, J = 8.4, 3.1 Hz, 1H), 3.10 (q, J = 7.2 Hz, 2H), 2.96 (dd, J = 8.4, 3.2 Hz, 1H), 0.35 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.7, 198.8, 176.7, 176.4, 136.4, 134.6, 128.4, 128.3, 126.0, 125.2, 49.4, 47.8, 43.7, 41.0, 37.0, 36.2, 33.2, 11.9. HRMS (ESI): calcd for $C_{18}H_{18}O_4N$, $[M+H]^+$, 312.1230; found, 312.1235.

Compound ***7aa***. White solid. 260 mg. Yield 80%. mp 204−205 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26−7.13 (m, 3H), 7.12−6.88 (m, 1H), 4.09−3.97 (m, 1H), 3.90 (t, J = 2.9 Hz, 1H), 3.49 (dd, J = 5.3, 2.1 Hz, 1H), 3.43 (dd, J = 5.3, 2.7 Hz, 1H), 3.26 (dd, J = 8.5, 3.2 Hz, 1H), 2.97 (dd, J = 8.5, 3.3 Hz, 1H), 2.48 (s, 3H), 2.40 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.6, 205.2, 177.4, 177.0, 136.5, 134.3, 128.4, 128.2, 125.8, 125.2, 50.9, 50.3, 44.3, 40.6, 38.8, 38.6, 29.3, 28.1, 24.3. HRMS (ESI): calcd for $C_{19}H_{20}O_4N$, $[M+H]^+$, 326.1392; found, 326.1396.

Compound ***7ab***. White solid. 278 mg. Yield 82%. mp 188−189 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.13 (m, 3H), 7.09 (d, J = 6.7 Hz, 1H), 4.19−3.99 (m, 1H), 3.90 (t, J = 2.9 Hz, 1H), 3.49 (dd, J = 5.3, 2.1 Hz, 1H), 3.43 (dd, J = 5.3, 2.7 Hz, 1H), 3.22 (dd, J = 8.4, 3.3 Hz, 1H), 3.10 (q, J = 7.2 Hz, 2H), 2.93 (dd, J = 8.4, 3.3 Hz, 1H), 2.40 (s, 3H), 2.22 (s, 3H), 0.35 (t, J = 7.2 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$) δ 207.6, 205.3, 177.2, 176.8, 136.7, 134.4, 128.2, 128.1, 125.9, 125.3, 50.8, 50.4, 44.0, 40.4, 38.9, 38.5, 33.2, 29.3, 28.1, 11.9. HRMS (ESI): calcd for $C_{20}H_{22}O_4N$, $[M+H]^+$, 340.1549; found, 340.1548.

Compound ***7ae***. White solid. 230 mg. Yield 74%. mp 201−202 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.28−7.16 (m, 3H), 7.15−6.92 (m, 1H), 4.17−3.95 (m, 1H), 3.87 (t, J = 2.9 Hz, 1H), 3.45 (dd, J = 5.3, 2.1 Hz, 1H), 3.41 (dd, J = 5.3, 2.6 Hz, 1H), 3.28 (dd, J = 8.7, 3.2 Hz, 1H), 3.01 (dd, J = 8.7, 3.3 Hz, 1H), 2.38 (s, 3H), 2.20 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 207.7, 205.2, 177.3, 176.9, 136.5, 134.2, 128.5, 128.4, 125.9, 125.4, 50.8, 50.2, 45.4, 41.8, 38.6, 38.1, 29.4, 28.1. HRMS (ESI): calcd for $C_{18}H_{18}O_4N$, $[M+H]^+$, 312.1230; found, 312.1228.

Compound ***7ba***. White solid. 54 mg. Yield 60%. mp 98−100 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 7.3 Hz, 2H), 7.90 (d, J = 7.3 Hz, 2H), 7.67−7.48 (m, 6H), 7.28−7.25 (m, 2H), 7.18 (td, J = 6.9, 2.4 Hz, 1H), 6.88 (d, J = 7.3 Hz, 1H), 4.66 (dd, J = 5.2, 1.9 Hz, 1H), 4.55 (dd, J = 5.2, 2.5 Hz, 1H), 4.06−3.97 (m, 1H), 3.91 (t, J = 2.8 Hz, 1H), 3.54 (dd, J = 8.4, 3.2 Hz, 1H), 3.18 (dd, J = 8.4, 3.3 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.9, 198.5, 177.7, 177.2, 136.4, 135.9, 135.6, 134.2, 134.1, 133.4, 129.1, 129.0, 128.8, 128.4, 128.3, 128.2, 126.2, 125.0, 46.0, 45.1, 44.3, 40.6, 40.3, 39.6, 24.3. HRMS (ESI): calcd for $C_{29}H_{23}O_4NNa$, $[M+Na]^+$, 472.1519; found, 472.1526.

Compound ***7bb***. White solid. 51 mg. Yield 55%. mp 167−168 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 7.3 Hz, 2H), 7.95−7.84 (m, 2H), 7.65 (t, J = 7.4 Hz, 1H), 7.60 (t, J = 7.4 Hz, 1H), 7.51 (dt, J = 15.4, 7.6 Hz, 4H), 7.25 (d, J = 4.2 Hz, 2H), 7.21−7.11 (m, 1H), 6.88 (d, J = 7.3 Hz, 1H), 4.65 (dd, J = 5.2, 2.0 Hz, 1H), 4.53 (dd, J = 5.2, 2.5 Hz, 1H), 4.00−3.94 (m, 1H), 3.89 (t, J = 2.9 Hz, 1H), 3.49 (dd, J = 8.3, 3.2 Hz, 1H), 3.13 (dd, J = 8.3, 3.3 Hz, 1H), 3.07 (q, J = 7.1 Hz, 2H), 0.31 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.9, 198.6, 177.5, 177.0, 136.5, 135.9, 135.6, 134.4, 134.1, 133.4, 129.1, 129.0, 128.8, 128.4, 128.2, 128.1, 126.4, 125.1, 45.9, 45.1, 44.0, 40.4, 40.3, 39.8, 33.1, 11.9. HRMS (ESI): calcd for $C_{30}H_{25}O_4NNa$, $[M+Na]^+$, 486.1676; found, 486.1677

Compound ***7be***. Colorless oil. 213 mg. Yield 49%.δ 8.06 (d, J = 7.4 Hz, 2H), 7.94 (s, 1H), 7.88 (d, J = 7.3 Hz, 2H), 7.65 (t, J = 7.4 Hz, 1H), 7.60 (t, J = 7.4 Hz, 1H), 7.56−7.43 (m, 4H), 7.32−7.24 (m, 2H), 7.19 (td, J = 7.1, 2.0 Hz, 1H), 6.87 (d, J = 7.3 Hz, 1H), 4.61 (dd, J = 5.1, 1.9 Hz, 1H), 4.51 (dd, J = 5.2, 2.5 Hz, 1H), 4.00−3.90 (m, 1H), 3.86 (t, J = 2.9 Hz, 1H), 3.53 (dd, J = 8.6, 3.2 Hz, 1H), 3.18 (dd, J = 8.6, 3.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.9, 198.5, 177.8, 177.2, 136.4, 135.8, 135.5, 134.2, 134.1, 133.4, 129.1, 129.0, 128.8, 128.4, 128.4, 128.2, 126.4, 125.1, 45.9, 45.4, 45.0, 41.7, 40.1, 39.4. HRMS (ESI): calcd for $C_{28}H_{22}O_4N$, $[M+H]^+$, 436.1549; found, 436.1548.

Compound ***7bf***. White solid. 44 mg. Yield 50%. mp 211−212 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 7.4 Hz, 2H), 7.87 (d, J = 7.3 Hz, 2H), 7.60 (m, 5H), 7.42−7.18 (m, 4H), 6.97 (d, J = 7.3 Hz, 1H), 4.57 (qd, J = 5.2, 2.2 Hz, 2H), 4.17−3.99 (m, 1H), 3.94 (t, J = 2.8 Hz, 1H), 3.84 (dd, J = 9.3, 3.3 Hz, 1H), 3.53 (dd, J = 9.4, 3.4 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.8, 197.8, 171.6, 171.1, 135.8, 135.6, 135.3, 134.4, 133.7, 133.6, 129.3, 129.1, 128.9, 128.8, 128.4, 126.6, 125.3, 45.8, 44.9, 44.5, 41.5, 40.0, 39.4. HRMS (ESI): calcd for $C_{28}H_{21}O_5$, $[M+H]^+$, 437.1384; found, 437.1393.

Compound ***7bh***. White solid. 46 mg. Yield 48%. mp 126−127 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 7.3 Hz, 2H), 7.92 (d, J = 7.3 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.58−7.48 (m, 3H), 7.44 (t, J = 7.4 Hz, 3H), 7.26 (t, J = 8.0 Hz, 1H), 7.14 (t, J = 7.4 Hz, 1H), 6.96 (d, J = 7.3 Hz, 1H), 4.73 (d, J = 1.7 Hz, 1H), 4.69 (d, J = 1.9 Hz, 1H), 4.44 (dd, J = 5.4, 2.0 Hz, 1H), 4.39 (dd, J = 5.3, 2.1 Hz, 1H), 3.87 (s, 3H), 3.80 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.4, 196.8, 166.3, 165.3, 142.1, 142.0, 140.6, 137.3, 136.1, 135.8, 133.6, 133.5,

DOI: 10.1021/acs.joc.6b02547
J. Org. Chem. 2017, 82, 1389−1402

129.0, 128.8, 128.7, 128.6, 127.2, 126.6, 125.0, 123.5, 52.6, 52.4, 50.1, 49.3, 47.0, 45.7. HRMS (ESI): calcd for $C_{30}H_{25}O_6$, $[M+H]^+$, 481.1646; found, 481.1656.

Compound ***7ca***. White solid. 43 mg. Yield 52%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98−7.79 (m, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.53 (t, J = 7.6 Hz, 2H), 7.24 (d, J = 3.5 Hz, 2H), 7.19−7.03 (m, 1H), 6.82 (d, J = 7.3 Hz, 1H), 4.40 (dd, J = 5.3, 2.1 Hz, 1H), 4.34−4.16 (m, 2H), 4.06 (t, J = 3.1 Hz, 1H), 3.95−3.77 (m, 1H), 3.53 (dd, J = 5.3, 2.9 Hz, 1H), 3.44 (dd, J = 8.5, 3.2 Hz, 1H), 3.26 (dd, J = 8.5, 3.3 Hz, 1H), 2.50 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.8, 177.5, 177.0, 173.3, 136.2, 135.8, 133.7, 133.4, 129.0, 128.4, 128.4, 128.1, 126.0, 125.2, 61.8, 47.1, 44.4, 43.0, 41.1, 40.0, 38.9, 24.4, 14.3. HRMS (ESI): calcd for $C_{25}H_{24}O_5N$, $[M+H]^+$, 418.1649; found, 418.1659.

Compound ***7da***. White solid. 227 mg. Yield 78%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.65−7.11 (m, 4H), 4.02 (s, 1H), 3.88 (s, 1H), 3.82 (s, 1H), 3.55 (s, 1H), 3.46 (s, 1H), 3.40 (s, 1H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 176.9, 176.6, 135.5, 134.0, 129.1, 129.1, 126.9, 126.3, 119.9, 119.7, 42.6, 40.2, 38.5, 38.0, 31.7, 31.1, 24.5. HRMS (ESI): calcd for $C_{17}H_{14}O_2N_3$, $[M+H]^+$, 292.1086; found, 292.1088.

Compound ***7ea***. White solid. 247 mg. Yield 70%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.29−7.13 (m, 3H), 7.07 (d, J = 7.0 Hz, 1H), 4.14−3.95 (m, 1H), 3.84 (t, J = 2.8 Hz, 1H), 3.47 (dd, J = 5.4, 1.8 Hz, 1H), 3.42 (dd, J = 5.4, 2.6 Hz, 1H), 3.26 (dd, J = 8.4, 3.2 Hz, 1H), 2.99 (dd, J = 8.4, 3.2 Hz, 1H), 2.94−2.75 (m, 1H), 2.62 (ddd, J = 13.8, 12.4, 5.1 Hz, 1H), 2.58−2.50 (m, 2H), 2.47 (s, 3H), 1.13 (t, J = 7.2 Hz, 3H), 0.98 (t, J = 7.3 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 210.6, 208.2, 177.5, 177.1, 136.6, 134.4, 128.2, 128.1, 125.7, 125.0, 50.3, 49.4, 44.4, 40.6, 38.7, 38.6, 35.3, 33.8, 24.2, 7.8, 7.7. HRMS (ESI): calcd for $C_{21}H_{24}O_4N$, $[M+H]^+$, 354.1700; found, 354.1706.

Compound ***7fa***. White solid. 266 mg. Yield 75%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.14 (m, 3H), 7.12−6.97 (m, 1H), 4.25 (qd, J = 7.1, 2.2 Hz, 2H), 4.03−4.00 (m, 1H), 3.96 (t, J = 3.1 Hz, 1H), 3.45 (dd, J = 5.4, 2.2 Hz, 1H), 3.33−3.24 (m, 2H), 3.14 (dd, J = 8.5, 3.3 Hz, 1H), 2.49 (s, 3H), 2.22 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 204.7, 177.3, 177.1, 173.0, 136.4, 133.9, 128.4, 128.2, 125.7, 125.3, 61.8, 52.4, 44.4, 42.5, 41.0, 38.7, 38.6, 28.0, 24.3, 14.2. HRMS (ESI): calcd for $C_{20}H_{22}O_5N$, $[M+H]^+$, 356.1492; found, 356.1494.

Compound ***8a***. White solid. 109 mg. Yield 40%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 6.9 Hz, 1H), 7.27−7.22 (m, 1H), 7.14 (td, J = 7.3, 1.4 Hz, 1H), 7.09 (d, J = 7.1 Hz, 1H), 5.26 (d, J = 6.1 Hz, 1H), 3.96−3.68 (m, 4H), 3.53 (dd, J = 6.1, 2.9 Hz, 1H), 2.78 (d, J = 8.4 Hz, 1H), 2.54−2.19 (m, 1H), 1.26 (t, J = 7.1 Hz, 3H), 0.89 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6, 133.1, 131.6, 128.4, 126.1, 125.1, 123.9, 94.5, 75.7, 65.7, 60.4, 43.8, 25.0, 19.5, 15.3, 13.8. HRMS (ESI): calcd for $C_{16}H_{19}O_4$, $[M+H]^+$, 275.1283; found, 275.1276.

Compound ***8b***. Colorless oil. Twenty-seven mg. Yield 11%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.24 (m, 2H), 7.23−7.11 (m, 2H), 5.27 (s, 1H), 4.26 (q, J = 7.1 Hz, 2H), 4.06−3.59 (m, 2H), 2.76 (d, J = 8.5 Hz, 1H), 2.40 (d, J = 8.5 Hz, 1H), 2.29 (s, 1H), 1.33 (t, J = 7.1 Hz, 3H), 1.28 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 134.7, 132.0, 128.3, 126.4, 125.4, 122.4, 94.0, 77.5, 65.8, 61.2, 45.2, 26.2, 19.1, 15.4, 14.2. HRMS (ESI): calcd for $C_{16}H_{19}O_4$, $[M+H]^+$, 275.1283; found, 275.1275.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02547.

^{1}H and ^{13}C NMR spectra, NOE spectra, and 2D spectra of starting materials and products (PDF)

X-ray crystal structure data for **3ad** (CIF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: xyyang@hit.edu.cn

*E-mail: xiawj@hit.edu.cn

ORCID

Qiang Liu: 0000-0001-8342-712X

Wujiong Xia: 0000-0001-9396-9520

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful for the financial supports from China NSFC (Nos. 2137205, 21472030, and 21672047), SKLUWRE (No. 2015DX01), and the Fundamental Research Funds for the Central Universities (Grant No. HIT.BRETIV.201310).

■ REFERENCES

(1) (a) Hoffmann, N. *Chem. Rev.* **2008**, *108*, 1052. (b) Bach, T.; Hehn, J. P. *Angew. Chem., Int. Ed.* **2011**, *50*, 1000. (c) Karkas, M. D.; Porco, J. A.; Stephenson, C. R. J. *Chem. Rev.* **2016**, *116*, 9683.

(2) (a) Hoffmann, N. *Photochem. Photobiol. Sci.* **2012**, *11*, 1613. (b) Ravelli, D.; Fagnoni, M.; Albini, A. *Chem. Soc. Rev.* **2013**, *42*, 97. (c) Oelgemöller, M. *Chem. Rev.* **2016**, *116*, 9664.

(3) (a) Hilpert, K.; Hubler, F.; Renneberg, D. PCT Int. Appl. WO2010/046855A1, 2010. (b) Muthuppalantappan, M.; Sukeerthi, K.; Balasubramanian, G.; Gullapalli, S.; Joshi, N. K.; Narayanan, S.; Karnic, P. V. PCT Int. Appl. WO2008/053341A2, 2008. (c) Jackson, R. W.; Gelinas, R.; Baughman, T. A.; Cox, T.; Howbert, J. J.; Kucera, K. A.; Latham, J. A.; Ramsdell, F.; Singh, D.; Darwish, I. S. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1093. (d) Liu, L.; Ishida, N.; Murakami, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 2485.

(4) Ma, W.; Fang, J.; Ren, J.; Wang, Z. *Org. Lett.* **2015**, *17*, 4180.

(5) Chittimalla, S. K.; Bandi, C.; Putturu, S. *RSC Adv.* **2015**, *5*, 8050.

(6) Murakami, M.; Ashida, S. *Chem. Commun.* **2006**, *42*, 4599.

(7) Souillart, L.; Cramer, N. *Chem. Sci.* **2014**, *5*, 837.

(8) (a) Liu, Q.; Meng, J.; Liu, Y.; Yang, C.; Xia, W.-J. *J. Org. Chem.* **2014**, *79*, 8143. (b) Zheng, L.; Huang, H.; Yang, C.; Xia, W. *Org. Lett.* **2015**, *17*, 1034. (c) Chen, M.; Yang, C.; Wang, Y.; Xia, W.; Li, D. *Org. Lett.* **2016**, *18*, 2280.

(9) Ghogare, A. A.; Greer, A. *Chem. Rev.* **2016**, *116*, 9994.

(10) Horie, T.; Sumino, M.; Tanaka, T.; Matsushita, Y.; Ichimura, T.; Yoshida, J. *Org. Process Res. Dev.* **2010**, *14*, 405.

(11) CCDC 1486727 contains the supplementary crystallographic date for **3ad**. This date can be acquired free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(12) (a) Norrish, R. G. W.; Bamford, C. H. *Nature* **1936**, *138*, 1016. (b) Norrish, R. G. W.; Bamford, C. H. *Nature* **1937**, *140*, 195.

(13) (a) Sindler-Kulyk, M.; Laarhoven, W. H. *J. Am. Chem. Soc.* **1976**, *98*, 1052. (b) Sindler-Kulyk, M.; Laarhoven, W. H. *J. Am. Chem. Soc.* **1978**, *100*, 3819.

(14) Šagud, I.; Antol, I.; Marinić, Ž.; Šindler-Kulyk, M. *J. Org. Chem.* **2015**, *80*, 9535.

(15) Škorić, I.; Kikaš, I.; Kovács, M.; Fodor, L.; Marinić, Ž.; Molčanov, K.; Kojić-Prodić, B.; Horváth, O. *J. Org. Chem.* **2011**, *76*, 8641.

(16) Tavares, D. F.; Ploder, W. H. *Tetrahedron Lett.* **1970**, *11*, 1567.

(17) Di Valentin, C.; Freccero, M.; Sarzi-Amade, M.; Zanaletti, R. *Tetrahedron* **2000**, *56*, 2547.

(18) (a) Segura, J. L.; Martin, N. *Chem. Rev.* **1999**, *99*, 3199. (b) Ito, Y.; Nakatsuka, M.; Saegusa, T. *J. Am. Chem. Soc.* **1982**, *104*, 7609.

(19) (a) Woodward, R. B.; Hoffmann, R. *J. Am. Chem. Soc.* **1965**, *87*, 395. (b) Hoffmann, R.; Woodward, R. B. *J. Am. Chem. Soc.* **1965**, *87*, 2046. (c) Hoffmann, R.; Woodward, R. B. *Acc. Chem. Res.* **1968**, *1*, 17. (d) Woodward, R. B.; Hoffmann, R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 781.

DOI: 10.1021/acs.joc.6b02547
J. Org. Chem. 2017, 82, 1389−1402

(20) Kessar, S. V.; Mankotia, A. K. S.; Scaiano, J. C.; Barra, M.; Gebicki, J.; Huben, K. *J. Am. Chem. Soc.* **1996**, *118*, 4361.
(21) Tranmer, G. K.; Tam, W. *J. Org. Chem.* **2001**, *66*, 5113.
(22) Oswald, C. L.; Peterson, J. A.; Lam, H. W. *Org. Lett.* **2009**, *11*, 4504.
(23) Chao, B.; Dittmer, D. C. *Tetrahedron Lett.* **2000**, *41*, 6001.
(24) Darby, N.; Cresp, T. M.; Sondheimer, F. *J. Org. Chem.* **1977**, *42*, 1960.
(25) Xu, S.; Zhu, S.; Shang, J.; Zhang, J.; Tang, Y.; Dou, J. *J. Org. Chem.* **2014**, *79*, 3696.
(26) Schmidt, B.; Elizarov, N. *Chem. Commun.* **2012**, *48*, 4350.
(27) Danodia, A. K.; Saunthwal, R. K.; Patel, M.; Tiwari, R. K.; Verma, A. K. *Org. Biomol. Chem.* **2016**, *14*, 6487.
(28) Ceccon, A.; Crociani, L.; Santi, S.; Venzo, A.; Biffis, A.; Boccaletti, G. *Tetrahedron Lett.* **2002**, *43*, 8475.
(29) Prasada Raju, V. V. N. K. V; Ravindra, V.; Mathad, V. T.; Dubey, P. K.; Reddy, P. P. *Org. Process Res. Dev.* **2009**, *13*, 710.
(30) Yanai, H.; Egawa, S.; Taguchi, T. *Tetrahedron Lett.* **2013**, *54*, 2160.
(31) Landa, A.; Puente, Á.; Santos, J. I.; Vera, S.; Oiarbide, M.; Palomo, C. *Chem. - Eur. J.* **2009**, *15*, 11954.

DOI: 10.1021/acs.joc.6b02547
J. Org. Chem. 2017, 82, 1389−1402