JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

Copper-Catalyzed Oxidative Coupling of Formamides with Salicylaldehydes: Synthesis of Carbamates in the Presence of a Sensitive Aldehyde Group

Balaji D. Barve,[†,‡] Yang-Chang Wu,[†,§] Mohamed El-Shazly,[†,⊥] Da-Wei Chuang,[†] Yuan-Bin Cheng,[†] Jeh-Jeng Wang,*[,‡] and Fang-Rong Chang*[,†,∥]

[†]Graduate Institute of Natural Products, College of Pharmacy, Kaohsiung Medical University, Kaohsiung 807, Taiwan

[‡]Department of Medicinal and Applied Chemistry, College of Life Sciences, Kaohsiung Medical University, Kaohsiung 807, Taiwan

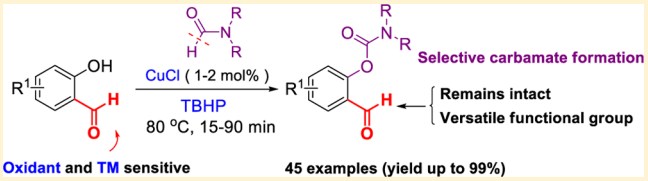
[§]School of Pharmacy, College of Pharmacy, China Medical University, Taichung 404, Taiwan

[⊥]Department of Pharmacognosy and Natural Products Chemistry, Faculty of Pharmacy, Ain-Shams University, Organization of African Unity Street, 11566 Abassia, Cairo, Egypt

[∥]Cancer Center, Kaohsiung Medical University Hospital, Kaohsiung, 807, Taiwan

Supporting Information

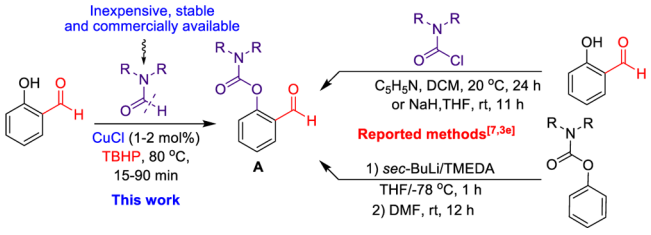
ABSTRACT: A diverse library of novel carbamates was synthesized utilizing copper-catalyzed oxidative C−O coupling of formamides and salicylaldehydes. Sensitive aldehyde groups remained intact in the presence of an oxidant and a transition-metal salt. Salicylaldehydes bearing electron-donating, electron-withdrawing, and halogen groups as well as 1-hydroxy-2-naphthaldehydes provided the desired carbamates in good to excellent yields.



Organic carbamates represent important building blocks in natural products, agrochemicals, and pharmaceutical drugs.[1,2] They play a significant role in organic chemistry as starting materials, intermediates, and protecting and directed metalating groups (DMGs).[3] Carbamates are generally prepared by employing chloroformates, isocyanates, and phosgene.[4,1a] The combination of carbon dioxide, water, and metal catalysts was introduced as a substitute for the toxic phosgene.[5,1a] Recently, Kumar et al. as well as our group have reported the synthesis of carbamates in high yields utilizing a wide diversity of substrates including enol and *o*-keto phenol derivatives under oxidative conditions.[6] The *o*-keto group of a phenolic substrate derivative is known to be comparatively more stable under oxidative conditions in comparison to the *o*-formyl group, which is sensitive to oxidants and transition metals. Thus, the synthesis of *o*-formyl carbamates under oxidative conditions while selectively preserving the aldehyde group remains a challenging task. The preparation of this class of compounds (2-formyl phenolic carbamates) has been scarcely described in the literature (Scheme 1).[7,3e]

The major disadvantages of the reported methods are the use of pyridine, air and moisture-sensitive reagents such as *N*,*N*-dialkylcarbamoyl chlorides, sodium hydride, and *sec*-BuLi. Longer reaction times, the need for temperature control, tedious workup procedures, and limited substrate scope (only two substrates were reported) are also additional limitations for the previous reports. Therefore, an expedient, safe, and environmentally benign methodology for the synthesis of phenol carbamates with an *o*-aldehyde group is required.

Scheme 1. Strategies for the Synthesis of *o*-Aldehyde-Containing Phenol Carbamates



Recent advances in C−H activation suggested its potential in providing an efficient route for the synthesis of carbamates.[8,6] Functional-group-directed C−H bond functionalization and cross-dehydrogenative couplings (CDC) under oxidative conditions have emerged as attractive techniques for the formation of carbon−carbon and carbon−heteroatom bonds.[9,8d]

For the synthesis of the carbamate, a reliable, stable, and commercially available aminocarbonyl source is required. *N*,*N*-Dimethylformamide (DMF) represents a suitable aminocarbonyl source, which is widely used in organic synthesis.[10] It is also utilized for the preparation of ureas, α-ketoamides, and 2-vinylquinolines as well as for the cyanation of arene C−H

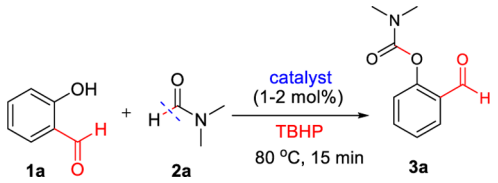
Received: January 2, 2014
Published: March 3, 2014

dx.doi.org/10.1021/jo402798k | J. Org. Chem. 2014, 79, 3206−3214

bonds, for the amidation of acids and alcohols, and as a source of aminyl radicals.[11]

Initially the reaction of salicylaldehyde (**1a**), 6.0 equiv of *tert*-butyl hydroperoxide (TBHP), and DMF (**2a**) was conducted under metal-free conditions or by using inexpensive catalysts (1−2 mol %). However, the desired product was not detected and the reaction did not proceed (Table 1, entries 1−6). The success of using copper catalysts in the preparation of phenol carbamates has encouraged us to investigate these catalyst systems in our current study.[6]

Table 1. Catalyst Optimization[a]



entry	catalyst	yield (%)[b]
1		NR[c]
2	Fe_2O_3	ND[d]
3	Bu_4NI	ND
4	NaI	ND
6	I_2	ND
7	$Cu(OAc)_2$	80
8	$Cu(OAc)_2{\cdot}H_2O$	55[e]
9	$CuSO_4$	50[e]
10	CuBr	65
11	$CuBr_2$	40
12	Cu_2O	70
13	CuI	50
14	$Cu(NO_3){\cdot}3H_2O$	60
15	CuCl	96
16	$CuCl_2$	45
17	$CuCl_2{\cdot}2H_2O$	75
18	$Cu(OTf)_2$	55
19	CuSO4·5H_2O	40

[a]Reaction conditions: **1a** (1.0 equiv), DMF (2 mL), catalyst (1.0−2.0 mol %), TBHP (70 wt % in water, 6.0 equiv), 80 °C, 15 min. [b]Isolated yields. [c]No reaction. [d]Not detected. [e]A trace amount of salicylic acid was formed.

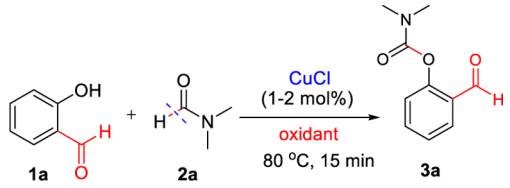
Initially, we assumed that the aldehyde group in **1a** was susceptible to oxidation in the presence of TBHP (6.0 equiv) and transition metals (copper salts) to form the corresponding acid.[12]

Surprisingly, phenol carbamate was formed (**3a**, 80%) without affecting the aldehyde group (Table 1, entry 7). Aiming to optimize the reaction conditions, we tested different copper catalysts and oxidants. As shown in Table 1, both Cu(I) and Cu(II) salts were effective in catalyzing the reaction. However, the results indicated that changing the counterion significantly affects the product yield.[11a] Trace amounts of salicylic acid were formed in the presence of $Cu(OAc)_2{\cdot}H_2O$ and $CuSO_4$ (Table 1, entries 8 and 9).[12b]

Recent reports revealed that aromatic aldehydes in the presence of TBHP form the corresponding acyl radicals, which undergo subsequent reactions.[10a,11g,h] In our current protocol, we did not observe such transformations. Further screening of the copper catalysts indicated that Cu(I)Cl (1−2 mol %) is the best optimized catalyst, providing **3a** in 96% yield (Table 1, entry 15). It is worth mentioning that certain copper salts resulted in low product yields, which may be attributed to the lower solubility of these salts in the reaction medium.[13] The solubility information of selected copper catalysts is summarized in Table S1 (see the Supporting Information).

To select the optimum oxidant for this protocol, various organic and inorganic oxidants were evaluated. The use of H_2O_2 (Table 2, entry 6) produced salicylic acid,[12c] but in the

Table 2. Oxidant Optimization[a]



entry	oxidant	yield (%)[b]
1		NR[c]
2	DDQ	NR
3	PIFA	ND[d]
4	$NaIO_4$	NR
5	CAN	*e*
6	H_2O_2	*f*
7	benzoquinone	NR
8	benzoyl peroxide	NR
9	$K_3Fe(CN)_6$	NR
10	oxone	*g*
11	MnO_2	NR
12	*tert*-butyl perbenzoate	NR
13	di-*tert*-butyl peroxide	ND
14	TBHP	96
15	*m*-CPBA	ND
16	sodium chlorite	ND
17	I_2	ND
18	UHP	NR

[a]Reaction conditions: **1a** (1.0 equiv), DMF (2.0 mL), CuCl (1.0−2.0 mol %), oxidant (6.0 equiv), 80 °C, 15 min. [b]Isolated yields. [c]No reaction. [d]Not detected. [e]5-Nitrosalicylaldehyde was formed. [f]Salicylic acid was formed. [g]Catechol was formed.

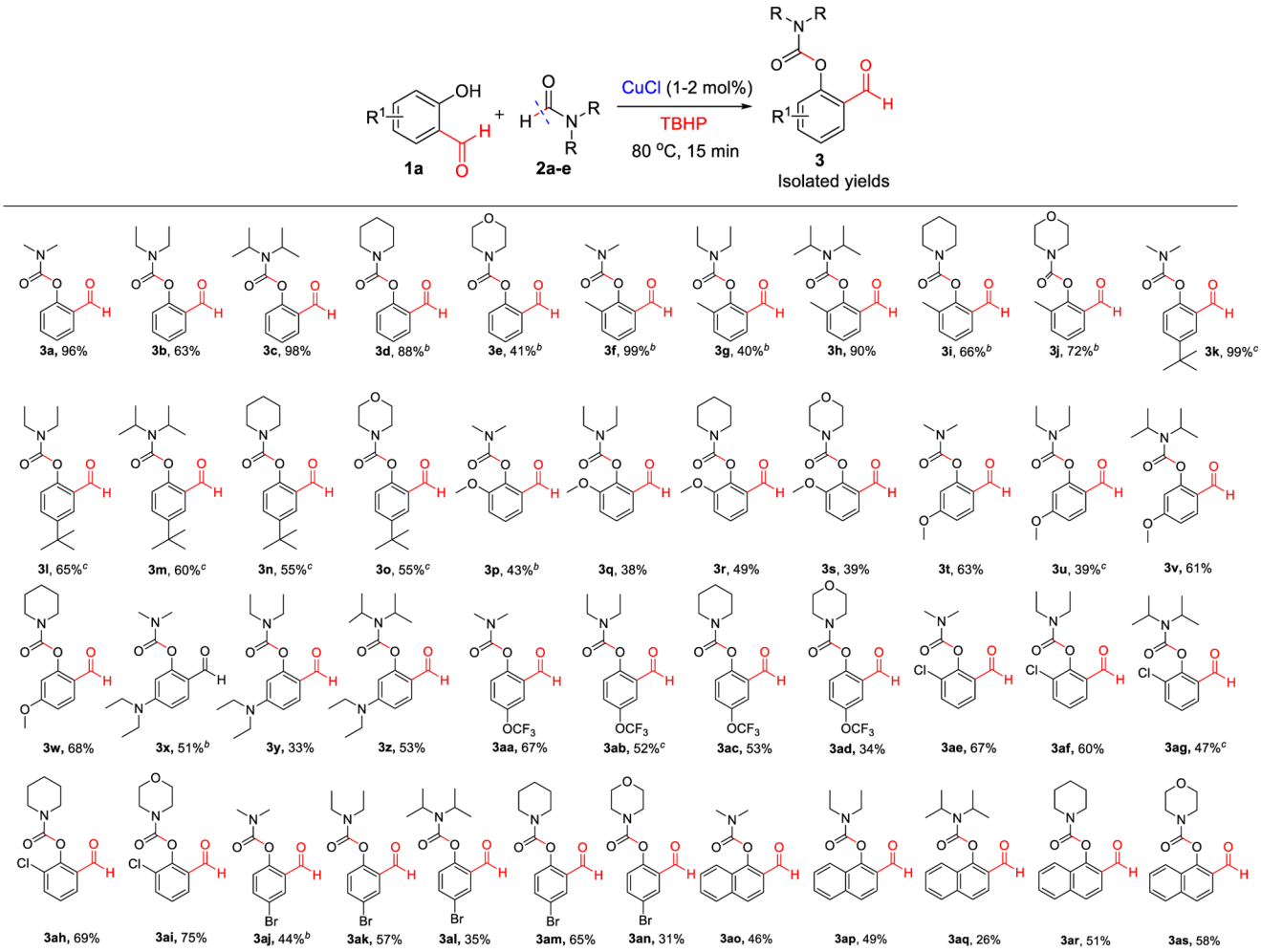
presence of oxone (Table 2, entry 10) catechol was detected.[14] Screening experiments (Table 2) revealed that TBHP is the most efficient oxidant, providing the corresponding carbamate in the highest possible yield (Table 2 entry 14). Different solvents such as acetonitrile,[12b−d] methanol,[14a] water,[12a,e] and 1,1,2-trichloroethane[11g] were examined in a 1:1 ratio with DMF, providing the desired carbamate but in lower yields (<60%) (Supporting Information, Table S2). The effect of temperature on the reaction progress was also evaluated, where the lower temperatures (<70−80 °C) resulted in lower yields (Supporting Information, Table S3).

On the basis of our screening experiments we found that using CuCl (1−2 mol %), TBHP (6.0 equiv), and DMF (**2a**) at 80 °C resulted in the formation of the target carbamate (**3a**, 96%) from salicylaldehyde (**1a**) in 15 min. With the optimized conditions in hand, we further investigated the scope of the reaction using different combinations of substituted salicylaldehydes and several formamides (Table 3).

The reaction of salicylaldehyde or its derivatives bearing electron-donating groups offered the corresponding carbamates in good to excellent yields (Table 3, **3a**−**o**). Salicylaldehyde derivatives substituted with methoxy groups on different positions of the aromatic moiety led to the formation of the

dx.doi.org/10.1021/jo402798k | J. Org. Chem. 2014, 79, 3206−3214

Table 3. Synthesis of Carbamates from Salicylaldehydes and Naphthaldehyde[a]



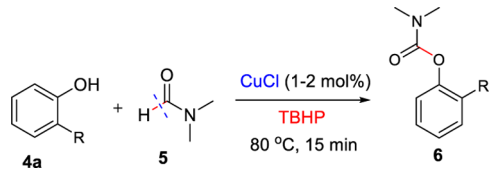
[a]Reaction conditions: **1** (1.0 equiv), formamide (47 equiv), CuCl (1.0−2.0 mol %), TBHP (70 wt % in water, 6.0 equiv), 80 °C, 15 min. [b]Reaction time 90 min. [c]5.0 mol % of CuCl used.

desired carbamates in moderate to good yields (Table 3, **3p−w**).

Dimethylamino-substituted salicylaldehyde reacted with three different formamides, providing the target products in moderate yields (Table 3, **3x−z**). Salicylaldehydes with electron-withdrawing groups such as $-OCF_3$ were also converted to carbamates in moderate to good yields (Table 3, **3aa−ad**). Halogen-substituted salicylaldehydes provided moderate to good yields of the target carbamates (Table 3, **3ae−an**). We also applied this methodology to the synthesis of naphthyl carbamates using 1-hydroxy-2-naphthaldehyde and different formamides (Table 3, **3ao−as**). Importantly, we did not observe oxidation side products in any of the transformations. However, we observed a chromatographically inseparable polar mixture with lower yield substrates. Interestingly in all of the conversions, the sensitive and versatile aldehyde group, which remained intact in the presence of oxidant and transition-metal catalyst,[15] can be transformed into other functional groups.[16]

We have also investigated the ortho effect on substrate reactivity by replacing the *o*-formyl group with different substituents (Table 4). Interestingly under our developed protocol, the *o*-nitrophenol derivative provided the corresponding carbamate, however in low yield (Table 4, **6a**). The

Table 4. Ortho Group Effect Investigation[a]



entry	R	yield (%)[b]
1	$-NO_2$	21 (**6a**)
2	−COOH	NR[c]
3	$-CH_3$	NR
4	−Cl	NR
5	$-NH_2$	ND[d]

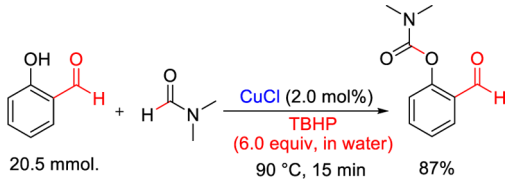
[a]Reaction conditions: **4** (1.0 equiv), DMF (2.0 mL), CuCl (1.0−2.0 mol %), TBHP (70 wt % in water, 6.0 equiv), 80 °C, 15 min. [b]Isolated yields. [c]No reaction. [d]Not detected. A complex mixture was formed.

practicality of the method has been demonstrated by performing the reaction on a multigram scale. The target carbamate was formed in excellent yield (Scheme 2).

On the basis of our findings and previous literature results, the reaction between compounds with dicarbonyl functionalities and transition metals was proposed to proceed through the formation of a coordination complex.[17,6] The complex

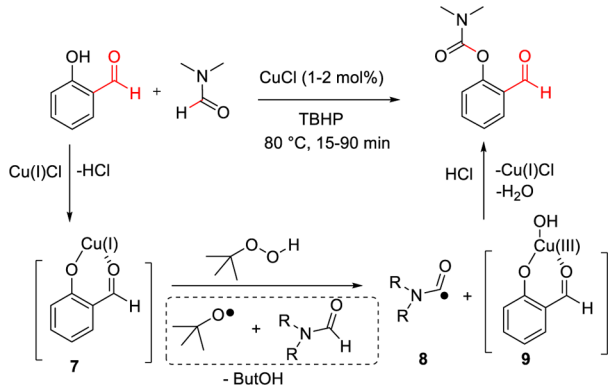
dx.doi.org/10.1021/jo402798k | J. Org. Chem. 2014, 79, 3206−3214

Scheme 2. Synthesis of Carbamate on a Multigram Scale



which is formed between an enol tautomer of the dicarbonyl moiety and the transition metal can be further transformed into different products, including carbamates.[6] The structural similarity between salicylaldehyde and the enol tautomer of the dicarbonyl moiety suggested a similar attitude toward transition metals, forming the coordination complex **7** (Scheme 3).[17] This hypothesis was also supported by the failure to form

Scheme 3. Plausible Mechanism



the target product using phenol as the starting material, which implies the crucial role of the adjacent formyl group for the formation of carbamate.[6] Aiming to reveal the underlying mechanism, we found that adding a radical scavenger such as TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl), BHT (2,6-di-*tert*-butyl-4-methylphenol), or 1,4-cyclohexadiene resulted in no product formation, which suggested a radical pathway. Recent reports suggested that, in the presence of copper catalyst, TBHP is decomposed to *tert*-butoxy radical, which can abstract a hydrogen from the formamide, generating the corresponding radical **8** (Scheme 3).[10a,11c,d,f,g,i] It is assumed that radical **8** can react with the proposed complex **9**, forming the desired carbamates (Scheme 3).

In summary, a novel, green, and phosgene-free approach was developed for the direct synthesis of carbamates, utilizing the copper-catalyzed oxidative C−O coupling of salicylaldehydes and formamides. Low catalyst loading and the use of inexpensive, stable, and commercially available starting materials as well as the high product yields and the excellent functional group tolerance are among the major advantages of this methodology. The developed protocol is base, additive, and ligand free, proceeds under mild conditions, and can be used for the selective protection of a hydroxyl group in the presence of an oxidant-sensitive aldehyde group.

EXPERIMENTAL SECTION

General Information. All chemicals used in this work were purchased from commercial sources. Flash chromatography was performed on silica gel 60 (230−400 mesh). Analytical thin-layer chromatography (TLC) was performed on Kieselgel 60, F254 (0.20 nm), and visualization was accomplished with UV light (254 and 354 nm). ^{1}H and ^{13}C NMR spectra were recorded with 200 MHz FT-NMR instruments with Me_4Si or solvent resonance as the internal standard (^{1}H NMR, Me_4Si at δ 0 ppm, $CDCl_3$ at δ 7.26 ppm; ^{13}C NMR, Me_4Si at δ 0 ppm, $CDCl_3$ at δ 77.0 ppm). ^{1}H NMR spectroscopic data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and integration. Melting points (mp) were determined using a melting point apparatus and are reported uncorrected. IR spectra were measured on a spectrophotometer. The UV−vis absorption spectra were recorded on a UV/vis spectrophotometer in methanol. High resolution mass measurements (HRMS) were performed on an FT-ESIMS spectrometer.

General Procedure for the Synthesis of Carbamates: Preparation of 3a as a Representative Example. In a flask charged with a stir bar, **1a** (50.0 mg, 0.41 mmol, 1.0 equiv), copper salt (1.0−2.0 mol %, CuCl), TBHP as the oxidant (0.24 mL, 2.4 mmol, 6.0 equiv. 70 wt % in water), and DMF as the formamide (1.5 mL, 19.3 mmol, 47.0 equiv) were mixed at room temperature. The reaction temperature was increased to 80 °C, and the reaction mixture was stirred for 15−90 min. After it was cooled to room temperature, the reaction mixture was extracted with ethyl acetate and dried over anhydrous Na_2SO_4. Removal of the solvent under vacuum yielded the crude product, which was purified by flash chromatography (ethyl acetate/hexane, 2/8) to afford the corresponding carbamate.

Analytical Data for Carbamates. *Dimethylcarbamic Acid 2-Formylphenyl Ester (**3a**).* Yield: 76 mg, 96%. Colorless liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.21 (s, 1H), 7.89 (d, J = 7.4 Hz, 1H), 7.62 (t, J = 7.4 Hz, 1H), 7.23−7.39 (m, 2H), 3.18 (s, 3H), 3.05 (s, 3H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 188.6, 154, 152.8, 135.0, 129.6, 128.3, 125.6, 123.4, 36.6, 36.4 ppm. FT IR (KBr pellet, cm^{-1}): 2930, 2755, 1728, 1695, 1604, 1456, 1383, 1274, 1157, 1006, 841, 758, 633, 524. UV (MeOH): λ_{max} (log ε) 209 (4.31), 244 (4.37), 290 (4.75) nm. MS (ESI): m/z 194 [M + H]$^+$. HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{10}H_{11}NO_3Na$ 216.0637, found 216.0635.

*Diethylcarbamic Acid 2-Formylphenyl Ester (**3b**)..*[3e,7b] Yield: 31 mg, 63%. Colorless liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.21 (s, 1H), 7.89 (d, J = 7.6 Hz, 1H), 7.61 (t, J = 7.6 Hz, 1H), 7.22−7.37 (m, 2H), 3.36−3.56 (m, 4H), 1.19−1.33 (m, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 188.6, 153.5, 153.1, 135.0, 129.5, 128.6, 125.6, 123.5, 42.4, 42.0, 14.2, 13.2 ppm. FT IR (KBr pellet, cm^{-1}): 2978, 2875, 1723, 1700, 1605, 1457, 1422, 1271, 1210, 1153, 1096, 961, 739, 702, UV (MeOH): λ_{max} (log ε) 210 (4.37), 244 (4.43), 287 (4.50) nm. MS (ESI): m/z 222 [M + H]$^+$. HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{12}H_{15}NO_3Na$ 244.0950, found 244.0949.

*Diisopropylcarbamic Acid 2-Formylphenyl Ester (**3c**).* Yield: 43 mg, 98%. Colorless gum. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.19 (s, 1H), 7.90 (d, J = 7.6 Hz, 1H), 7.60 (t, J = 7.6 Hz, 1H), 7.17−7.36 (m, 2H), 4.01−4.11 (m, 2H), 1.18−1.54 (m, 12H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 187.6, 152.1, 151.9, 134.0, 128.3, 127.8, 124.5, 122.5, 45.8, 45.6, 21.6, 20.4, 20.1, 19.4 ppm. FT IR (KBr pellet, cm^{-1}): 2971, 2929, 1720, 1695, 1605, 1431, 1371, 1317, 1212, 1152, 1042, 984, 896, 753. UV (MeOH): λ_{max} (log ε) 209 (4.42), 244 (4.48), 289 (4.56) nm. MS (ESI): m/z 250 [M + H]$^+$. HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{14}H_{19}NO_3Na$ 272.1263, found 272.1261.

*Piperidine-1-carboxylic Acid 2-Formylphenyl Ester (**3d**).* Yield: 46 mg, 88%. Colorless liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.20 (s, 1H), 7.88 (d, J = 7.8 Hz, 1H), 7.61 (t, J = 7.4 Hz, 1H), 7.21−7.38 (m, 2H), 3.67 (br m, 2H), 3.54 (br m, 2H), 1.69 (br, 6 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 188.7, 153.1, 152.9, 135.1, 129.7, 128.6, 125.6, 123.6, 45.7, 45.4, 25.9, 25.5, 24.2 ppm. FT IR (KBr pellet, cm^{-1}): 2937, 2856, 1723, 1695, 1604, 1426, 1233, 1209, 1141, 1020, 955, 874, 757. UV (MeOH): λ_{max} (log ε) 211 (4.39), 245 (4.46), 291 (4.53) nm. MS (ESI): m/z 234 [M + H]$^+$. HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{13}H_{15}NO_3Na$ 256.0950, found 256.0949.

*Morpholine-4-carboxylic Acid 2-Formylphenyl Ester (**3e**).* Yield: 39 mg, 41%. Colorless amorphous solid. Mp: 78−80 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.14 (s, 1H), 7.88 (d, J = 7.7 Hz, 1H), 7.61 (t, J = 7.7 Hz, 1H), 7.22−7.41 (m, 2H), 3.78 (br m, 6H), 3.62 (br m, 2H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 188.7, 153.0, 152.2, 135.1, 130.9, 128.5, 126.0, 123.6, 66.5 (2C), 45.1, 44.4 ppm. FT IR (KBr pellet,

dx.doi.org/10.1021/jo402798k | J. Org. Chem. 2014, 79, 3206−3214

cm^{-1}): 2924, 2857, 1726, 1700, 1605, 1455, 1425, 1274, 1242, 1210, 1117, 1060, 857, 737, 575. UV (MeOH): λ_{max} (log ε) 210 (4.39), 245 (4.46), 290 (4.53) nm. MS (ESI): m/z 236 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{12}H_{13}NO_4Na$ 258.0742, found 258.0741.

*Dimethylcarbamic Acid 2-Formyl-6-methylphenyl Ester (**3f**).* Yield: 83 mg, 99%. Colorless liquid. ^1H NMR (200 MHz, $CDCl_3$): δ 10.11 (s, 1H), 7.71 (d, J = 7.7 Hz, 1H), 7.48 (d, J = 7.7 Hz, 1H), 7.26 (t, J = 7.7 Hz, 1H), 3.20 (s, 3H), 3.05 (s, 3H), 3.26 (s, 3H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 189.2, 153.9, 151.2, 136.8, 132.4, 129.0, 127.6, 125.7, 36.9, 36.6, 15.7 ppm. FT IR (KBr pellet, cm^{-1}): 2921, 2851, 1727, 1704, 1603, 1689, 1469, 1383, 1162, 1008, 849.7, 736, 651. UV (MeOH): λ_{max} (log ε) 210 (4.34), 248 (4.41), 294 (4.48) nm. MS (ESI): m/z 208 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{11}H_{13}NO_3Na$ 230.0793, found 230.0794.

*Diethylcarbamic Acid 2-Formyl-6-methylphenyl Ester (**3g**).* Yield: 16 mg, 40%. Colorless liquid. ^1H NMR (200 MHz, $CDCl_3$): δ 10.12 (s, 1H), 7.72 (d, J = 7.5 Hz, 1H), 7.48 (d, J = 7.5 Hz, 1H), 7.26 (t, J = 7.5 Hz, 1H), 3.36−3.60 (m, 4H), 2.26 (s, 3H), 1.20−1.37 (m, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 189.2, 153.3, 151.5, 136.8, 132.4, 129.2, 127.8, 125.7, 42.5, 42.1, 15.8, 14.3, 13.3 ppm. FT IR (KBr pellet, cm^{-1}): 2919, 1722, 1700, 1604, 1689, 1464, 1420, 1275, 1205, 1154, 1088, 959, 785, 647. UV (MeOH): λ_{max} (log ε) 206 (4.38), 246 (4.46), 288 (4.53) nm. MS (ESI): m/z 236 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{13}H_{17}NO_3Na$ 258.1106, found 258.1105.

*Diisopropylcarbamic Acid 2-Formyl-6-methylphenyl ester (**3h**):* Yield: 43 mg, 90%. Yellow liquid. ^1H NMR (200 MHz, $CDCl_3$): δ 10.13 (s, 1H), 7.73 (d, J = 7.6 Hz, 1H), 7.47 (d, J = 7.6 Hz, 1H), 7.24 (t, J = 7.6 Hz, 1H), 3.93−4.24 (m, 2H), 2.26 (s, 3H), 1.18−1.37 (m, 12H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 189.1, 152.5, 151.7, 136.8, 132.5, 130.3, 127.3, 125.6, 46.9 (2C), 22.6, 21.5, 20.4, 16.0, 14.0 ppm. FT IR (KBr pellet, cm^{-1}): 2924, 2852, 1717, 1681, 1605, 1589, 1465, 1428, 1378, 1315, 1186, 1150, 1042, 984, 894, 737. UV (MeOH): λ_{max} (log ε) 211 (4.44), 249 (4.52), 294 (4.59) nm. MS (ESI): m/z 264 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{15}H_{21}NO_3Na$ 286.1419, found 286.1417.

*Piperidine-1-carboxylic Acid 2-Formyl-6-methylphenyl Ester (**3i**).* Yield: 30 mg, 66%. Colorless liquid. ^1H NMR (200 MHz, $CDCl_3$): δ 10.13 (s, 1H), 7.71 (d, J = 7.6 Hz, 1H), 7.48 (d, J = 7.6 Hz, 1H), 7.31 (t, J = 7.6 Hz, 1H), 3.70 (br m, 2 H), 3.54 (br m, 2 H), 2.26 (s, 3H), 1.69 (br, 6 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 189.1, 152.7, 151.5, 136.7, 132.4, 129.2, 127.8, 125.7, 45.6 (2C), 26.4, 25.9, 24.3, 15.7 ppm. FT IR (KBr pellet, cm^{-1}): 2925, 2855, 1722, 1684, 1603, 1589, 1425, 1393, 1256, 1232, 1184, 1142, 1021, 851, 739, 704. UV (MeOH): λ_{max} (log ε) 209 (4.41), 249 (4.49), 295 (4.56) nm. MS (ESI): m/z 248 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{14}H_{17}NO_3Na$ 270.1106, found 270.1105.

*Morpholine-4-carboxylic Acid 2-Formyl-6-methylphenyl Ester (**3j**).* Yield: 33 mg, 72%. Colorless liquid. ^1H NMR (200 MHz, $CDCl_3$): δ 10.07 (s, 1H), 7.71 (d, J = 7.7 Hz, 1H), 7.50 (d, J = 7.7 Hz, 1H), 7.30 (t, J = 7.7 Hz, 1H), 3.81 (br m, 6H), 3.64 (br m, 2 H), 2.27 (s, 3H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 189.3, 152.8, 150.4, 142.8, 136.9, 132.4, 129.3, 126.0, 66.6 (2C), 45.2, 44.4, 15.7 ppm. FT IR (KBr pellet, cm^{-1}): 2921, 2851, 1725, 1703, 1603, 1588, 1456, 1424, 1393, 1240, 1202, 1181, 1117, 1057, 923, 857, 784. UV (MeOH): λ_{max} (log ε) 210 (4.42), 249 (4.49), 294 (4.56) nm. MS (ESI): m/z 250 $[M + H]^+$ HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{13}H_{15}NO_4Na$ 272.0899, found 272.0898.

*Dimethylcarbamic Acid 2-Formyl-4-tert-butylphenyl Ester (**3k**).* Yield: 69 mg, 99%. Yellow liquid. ^1H NMR (200 MHz, $CDCl_3$): δ 10.20 (s, 1H), 7.88 (s, 1H), 7.64 (d, J = 8.8 Hz, 1H), 7.30 (t, J = 8.8 Hz, 1H), 3.16 (s, 3H), 3.04 (s, 3H), 1.34 (s, 9H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 189.0, 154.3, 150.9, 148.7, 132.4, 127.7, 126.2, 123.1, 36.8, 36.5, 34.5, 31.1 (3C) ppm. FT IR (KBr pellet, cm^{-1}): 2965, 2869, 1729, 1692, 1603, 1583, 1488, 1385, 1261, 1162, 1007, 866, 118, 752. UV (MeOH): λ_{max} (log ε) 216 (4.43), 249 (4.49), 297 (4.57) nm. MS (ESI): m/z 250 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{14}H_{19}NO_3Na$ 272.1263, found 272.1264.

*Diethylcarbamic Acid 2-Formyl-4-tert-butylphenyl Ester (**3l**).* Yield: 50 mg, 65%. Yellow liquid. ^1H NMR (200 MHz, $CDCl_3$): δ 10.20 (s, 1H), 7.89 (s, 1H), 7.63 (d, J = 8.6 Hz, 1H), 7.16 (t, J = 8.6 Hz, 1H), 3.39−3.52 (m, 4H) 1.19−1.37 (m, 15H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 190.0, 153.7, 151.0, 148.7, 132.4, 127.8, 126.0, 123.0, 42.4, 42.0, 34.5, 31.1 (3C), 14.2, 13.2 ppm. FT IR (KBr pellet, cm^{-1}): 2967, 2918, 1721, 1692, 1604, 1473, 1423, 1265, 1214, 1155, 1123, 1040, 961, 739, 704. UV (MeOH): λ_{max} (log ε) 210 (4.46), 249 (4.53), 301 (4.62) nm. MS (ESI): m/z 278 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{16}H_{23}NO_3Na$ 300.1576, found 300.1578.

*Diisopropylcarbamic Acid 2-Formyl-4-tert-butylphenyl Ester (**3m**).* Yield: 25 mg, 60%. Yellow liquid. ^1H NMR (200 MHz, $CDCl_3$): δ 10.20 (s, 1H), 7.91 (s, 1H), 7.65 (d, J = 8.6 Hz, 1H), 7.13 (t, J = 8.6 Hz, 1H), 4.01 (br m, 2 H), 1.24−1.36 (m, 21H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 189.0, 153.1, 151.0, 148.7, 132.5, 128.0, 125.8, 123.1, 47.5, 46.8, 34.6, 31.2 (3C), 22.7, 21.4, 20.4, 20.2 ppm. FT IR (KBr pellet, cm^{-1}): 2968, 2872, 1717, 1694, 1604, 1494, 1464, 1432, 1368, 1317, 1205, 1122, 1042, 985, 894, 754. UV (MeOH): λ_{max} (log ε) 214 (4.21), 249 (4.58), 298 (4.66) nm. MS (ESI): m/z 306 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{18}H_{27}NO_3Na$ 328.1889, found 328.1886.

*Piperidine-1-carboxylic Acid 2-Formyl-4-tert-butylphenyl Ester (**3n**).* Yield: 37 mg, 55%. Colorless liquid. ^1H NMR (200 MHz, $CDCl_3$): δ 10.19 (s, 1H), 7.89 (s, 1H), 7.64 (d, J = 8.6 Hz, 1H), 7.13 (t, J = 8.6 Hz, 1H), 3.67 (br m, 2 H), 3.54 (br m, 2H), 1.68 (br, 6H), 1.33 (s, 9H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 189.1, 153.2, 151.0, 148.7, 132.5, 127.8, 126.1, 123.1, 45.7, 45.4, 34.6, 31.2 (3C), 25.9, 25.5, 24.2 ppm. FT IR (KBr pellet, cm^{-1}): 2937, 2858, 1725, 1692, 1604, 1426, 1233, 1214, 1141, 1019, 904, 855, 748. UV (MeOH): λ_{max} (log ε) 214 (4.50), 248 (4.55), 296 (4.63) nm. MS (ESI): m/z 290 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{17}H_{23}NO_3Na$ 312.1576, found 312.1577.

*Morpholine-4-carboxylic Acid 2-Formyl-4-tert-butylphenyl Ester (**3o**).* Yield: 45 mg, 55%. Yellow amorphous solid. Mp: 78−80 °C. ^1H NMR (200 MHz, $CDCl_3$): δ 10.13 (s, 1H), 7.87 (s, 1H), 7.65 (d, J = 8.6 Hz, 1H), 7.15 (t, J = 8.6 Hz, 1H), 3.77 (br m, 6H), 3.61 (br m, 2H), 1.30−1.36 (m, 9H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 189.1, 153.2, 150.1, 149.1, 132.4, 127.7, 127.4, 123.1, 66.5 (2C), 45.1, 44.3, 34.6, 31.1 (3C) ppm. FT IR (KBr pellet, cm^{-1}): 2963, 2863, 1727, 1691, 1604, 1424, 1365, 1241, 1213, 1120, 1057, 929, 864, 748. UV (MeOH): λ_{max} (log ε) 214 (4.49), 249 (4.56), 297 (4.64) nm. MS (ESI): m/z 292 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{16}H_{21}NO_4Na$ 314.1368, found 314.1369.

*Dimethylcarbamic Acid 2-Formyl-6-methoxyphenyl Ester (**3p**).* Yield: 32 mg, 43%. Brown amorphous solid. Mp: 70−72 °C. ^1H NMR (200 MHz, $CDCl_3$): δ 10.20 (s, 1H), 7.47 (d, J = 7.6 Hz, 1H), 7.18−7.33 (m, 2H), 3.88 (s, 3H), 3.19 (s, 3H), 3.05 (s, 3H), ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 189.0, 154.0, 152.3, 143.0, 129.9, 126.1, 120.3, 117.8, 56.4, 37.0, 36.7 ppm. FT IR (KBr pellet, cm^{-1}): 2926, 2853, 1728, 1701, 1587, 1483, 1384, 1274, 1159, 1066, 916, 847, 784. UV (MeOH): λ_{max} (log ε) 219 (4.39), 252 (4.45), 313 (4.54) nm. MS (ESI): m/z 224 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{11}H_{13}NO_4Na$ 246.0742, found 246.0741.

*Diethylcarbamic Acid 2-Formyl-6-methoxyphenyl Ester (**3q**).* Yield: 16 mg, 38%. Yellow gum. ^1H NMR (200 MHz, $CDCl_3$): δ 10.20 (s, 1H), 7.47 (d, J = 7.4, 1H), 7.20−7.28 (m, 2H), 3.87 (s, 3H), 3.39−3.54 (m, 4H), 1.19−1.31 (m, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 188.9, 153.4, 152.3, 143.3, 130.0, 126.0, 119.9, 117.7, 56.3, 42.5, 42.3, 14.1, 13.3 ppm. FT IR (KBr pellet, cm^{-1}): 2924, 2853, 1726, 1702, 1587, 1460, 1423, 1319, 1273, 1202, 1152, 1070, 956, 916, 783. UV (MeOH): λ_{max} (log ε) 217 (4.44), 253 (4.50), 315 (4.60) nm. MS (ESI): m/z 252 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{13}H_{17}NO_4Na$ 274.1055, found 274.1054.

*Piperidine-1-carboxylic Acid 2-Formyl-6-methoxyphenyl Ester (**3r**).* Yield: 21 mg, 49%. Colorless liquid. ^1H NMR (200 MHz, $CDCl_3$): δ 10.21 (s, 1H), 7.47 (d, J = 7.8 Hz, 1H), 7.20−7.28 (m, 2H), 3.88 (s, 3H), 3.69 (br m, 2H), 3.53 (br m, 2H), 1.68 (br 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 189.0, 152.8, 152.3, 143.3, 129.9, 126.1, 120.1, 117.7, 56.3, 46.0, 45.5, 25.8, 24.7, 24.3 ppm. FT IR (KBr pellet, cm^{-1}): 2935, 2856, 1725, 1701, 1587, 1486, 1428, 1393, 1274, 1202, 1141, 1020, 915, 849, 783. UV (MeOH): λ_{max} (log ε) 219 (4.46), 253 (4.52), 314 (4.61) nm. MS (ESI): m/z 264 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{14}H_{17}NO_4Na$ 286.1055, found 286.1053.

dx.doi.org/10.1021/jo402798k | J. Org. Chem. 2014, 79, 3206−3214

*Morpholine-4-carboxylic Acid 2-Formyl-6-methoxyphenyl Ester (**3s**).* Yield: 34 mg, 39%. Colorless liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.18 (s, 1H), 7.47 (d, J = 8.4 Hz, 1H), 7.17−7.36 (m, 2H), 3.89 (s, 3H), 3.79 (br m, 6H), 3.61 (br m, 2H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 188.8, 152.8, 152.2, 142.3, 129.8, 126.4, 120.9, 117.7, 66.6 (2C), 56.3, 45.4, 44.5 ppm. FT IR (KBr pellet, cm^{-1}): 2921, 2852, 1729, 1700, 1586, 1485, 1426, 1393, 1274, 1204, 1179, 1117, 1056, 856, 767, 737. UV (MeOH): λ_{max} (log ε) 214 (4.45), 252 (4.52), 313 (4.62) nm. MS (ESI): m/z 266 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{13}H_{15}NO_5Na$ 288.0848, found 288.0847.

*Dimethylcarbamic Acid 2-Formyl-5-methoxyphenyl Ester (**3t**).* Yield: 46 mg, 63%. Colorless liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.04 (s, 1H), 7.81 (d, J = 8.8 Hz, 1H), 7.74−7.87 (m, 2H), 3.86 (s, 3H), 3.16 (s, 3H), 3.04 (s, 3H), ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 187.4, 165.1, 154.8, 154.0, 131.6, 122.1, 112.1, 108.5, 55.7, 36.8, 36.5 ppm. FT IR (KBr pellet, cm^{-1}): 3056, 2850, 1729, 1687, 1610, 1500, 1385, 1252, 1160, 1109, 1028, 945, 817, 737. UV (MeOH): λ_{max} (log ε) 207 (4.36), 223 (4.40), 274 (4.49) nm. MS (ESI): m/z 224 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{11}H_{13}NO_4Na$ 246.0742, found 246.0740.

*Diethylcarbamic Acid 2-Formyl-5-methoxyphenyl Ester (**3u**).* Yield: 16 mg, 39%. Colorless liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.1 (s, 1H), 7.47 (d, J = 8.8 Hz, 1H), 6.85 (d, J = 8.8 Hz, 1H), 6.75 (s, 1H) 3.87 (s, 3H), 3.39−3.52 (m, 4H), 1.19−1.33 (m, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 188.4, 165.2, 155.0, 153.4, 131.4, 122.3, 112.1, 108.5, 55.8, 42.4, 42.1, 14.1, 13.3 ppm. FT IR (KBr pellet, cm^{-1}): 2973, 2853, 1724, 1690, 1609, 1416, 1271, 1251, 1155, 1110, 1029, 972, 816, 786. UV (MeOH): λ_{max} (log ε) 210 (4.42), 223 (4.45), 273 (4.54) nm. MS (ESI): m/z 252 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{13}H_{17}NO_4Na$ 274.1055, found 274.1054.

*Diisopropylcarbamic Acid 2-Formyl-5-methoxyphenyl Ester (**3v**).* Yield: 28 mg, 61%. Colorless crystalline solid. Mp: 78−80 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.04 (s, 1H), 7.85 (d, J = 8.8 Hz, 1H), 6.85 (d, J = 8.8 Hz, 1H), 6.69 (s, 1H), 4.00 (br m, 2H), 3.89 (s, 3H) 1.26−1.34 (m, 12H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 187.2, 165.2, 154.9, 152.7, 131.2, 122.5, 111.9, 108.6, 55.7, 46.8 (2C), 23.4, 21.2, 20.5, 20.1 ppm. FT IR (KBr pellet, cm^{-1}): 2970, 2852, 1720, 1690, 1610, 1462, 1427, 1371, 1312, 1251, 1154, 1091, 1042, 995, 819, 752. UV (MeOH): λ_{max} (log ε) 209 (4.47), 222 (4.49), 273 (4.58) nm. MS (ESI): m/z 280 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{15}H_{21}NO_4Na$ 302.1368, found 302.1366.

*Piperidine-1-carboxylic Acid 2-Formyl-5-methoxyphenyl Ester (**3w**).* Yield: 29 mg, 68%. Brown liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.03 (s, 1H), 7.82 (d, J = 8.8 Hz, 1H), 7.73−7.87 (m, 2H), 3.87 (s, 3H), 3.66 (br m, 2H), 3.54 (br m, 2H), 1.68 (br 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 187.5, 165.2, 156.0, 152.8, 131.5, 122.2, 112.2, 108.6, 55.9, 45.8, 45.4, 25.9, 25.6, 24.2 ppm. FT IR (KBr pellet, cm^{-1}): 2926, 2855, 1724, 1688, 1609, 1419, 1249, 1231, 1158, 1141, 1109, 1022, 900, 819, 749. UV (MeOH): λ_{max} (log ε) 213 (4.45), 222 (4.47), 274 (4.55) nm. MS (ESI): m/z 264 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{14}H_{17}NO_4Na$ 286.1055, found 286.1053.

*Dimethylcarbamic Acid 2-Formyl-5-(diethylamino)phenyl Ester (**3x**).* Yield: 35 mg, 51%. Yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 9.84 (s, 1H), 7.68 (d, J = 8.8 Hz, 1H), 6.51 (d, J = 8.8 Hz, 1H), 6.69 (s, 1H), 3.36−3.46 (m, 4H), 3.15 (s, 3H), 3.04 (s, 3H), 1.68−1.26 (m, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 186.5, 155.1, 154.4, 153.1, 132.3, 116.9, 108.2, 104.7, 44.7 (2C), 36.8, 36.6, 12.5 (2C) ppm. FT IR (KBr pellet, cm^{-1}): 3055, 2929, 1726, 1671, 1604, 1547, 1526, 1451, 1406, 1383, 1357, 1266, 1196, 1164, 1101, 1013, 820, 737, 702. UV (MeOH): λ_{max} (log ε) 209 (4.44), 249 (4.52), 333 (4.64), 341 (4.65) nm. MS (ESI): m/z 264 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{14}H_{20}N_2O_3Na$ 287.1372, found 287.1371.

*Diethylcarbamic Acid 2-Formyl-5-(diethylamino)phenyl Ester (**3y**).* Yield: 12 mg, 33%. Yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 9.87 (s, 1H), 7.70 (d, J = 8.8 Hz, 1H), 6.52 (d, J = 8.8 Hz, 1H), 6.3 (s, 1H), 3.36−3.51 (m, 8H), 1.18−1.28 (m, 12H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 186.5, 155.4, 153.1, 131.9, 117.0, 112.5, 108.2, 104.5, 44.7 (2C), 42.3, 42.0, 14.2, 13.3, 12.5(2C) ppm. FT IR (KBr pellet, cm^{-1}): 2922, 2851, 1722, 1678, 1604, 1525, 1471, 1417, 1357, 1270, 1197, 1154, 1102, 972, 815, 700. UV (MeOH): λ_{max} (log ε) 209 (4.49), 249 (4.57), 333 (4.69), 342 (4.70) nm. MS (ESI): m/z 293 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{16}H_{24}N_2O_3Na$ 315.1685, found 315.1682.

*Diisopropylcarbamic Acid 2-Formyl-5-(diethylamino)phenyl Ester (**3z**).* Yield: 22 mg, 53%. Yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 9.85 (s, 1H), 7.72 (d, J = 9.0 Hz, 1H), 6.52 (d, J = 9.0 Hz, 1H), 6.27 (s, 1H), 4.04−4.16 (br m, 2H), 3.36−3.47 (m, 4H), 1.17−1.35 (m, 18H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 186.4, 155.4, 153.6, 149.8, 131.6, 117.3, 108.3, 104.5, 46.7 (2C), 44.6 (2C), 22.4, 21.5, 20.5, 20.1, 12.5 (2C) ppm. FT IR (KBr pellet, cm^{-1}): 2971, 2930, 1719, 1676, 1605, 1524, 1426, 1405, 1357, 1313, 1290, 1197, 1120, 1098, 1043, 995, 807, 752, 597 UV (MeOH): λ_{max} (log ε) 208 (4.52), 250 (4.60), 333 (4.73), 341 (4.74) nm. MS (ESI): m/z 321 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{18}H_{28}N_2O_3Na$ 343.1998, found 343.1997.

*Dimethylcarbamic Acid 2-Formyl-4-(trifluoromethoxy)phenyl Ester (**3aa**).* Yield: 45 mg, 67%. White crystalline solid. Mp: 54−56 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.2 (s, 1H), 7.88 (d, J = 2.4 Hz, 1H), 7.43 (d, J = 2.4 Hz, 1H), 7.34 (s, 1H), 3.17 (s, 3H), 3.05 (s, 3H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 187.1, 153.8, 151.3, 146.5, 129.4, 127.5, 125.8, 125.3, 121.2, 37.0, 36.6 ppm. FT IR (KBr pellet, cm^{-1}): 2925, 2856, 1733, 1699, 1613, 1487, 1388, 1257, 1222, 1160, 1005, 863, 749, 635. UV (MeOH): λ_{max} (log ε) 211 (4.47), 240 (4.52), 293 (4.60) nm. MS (ESI): m/z 278 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{11}H_{10}F_3NO_4Na$ 300.0460, found 300.0459.

*Diethylcarbamic Acid 2-Formyl-4-(trifluoromethoxy)phenyl Ester (**3ab**).* Yield: 18 mg, 52%. Yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.18 (s, 1H), 7.73 (d, J = 2.2, 1H), 7.45 (d, J = 2.2 Hz, 1H), 7.34 (s, 1H), 3.36−3.56 (m, 4H), 1.19−1.33 (m, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 187.0, 153.1, 151.4, 146.4, 129.5, 127.5, 125.3, 121.1, 117.8, 42.7, 42.2, 14.3, 13.2 ppm. FT IR (KBr pellet, cm^{-1}): 2924, 2854, 1730, 1700, 1613, 1423, 1258, 1221, 1187, 1147, 1098, 957, 880, 634. UV (MeOH): λ_{max} (log ε) 209 (4.50), 241 (4.57), 291 (4.65) nm. MS (ESI): m/z 306 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{13}H_{14}F_3NO_4Na$ 328.0773, found 328.0770.

*Piperidine-1-carboxylic Acid 2-Formyl-4-(trifluoromethoxy)-phenyl Ester (**3ac**).* Yield: 20 mg, 53%. Yellow crystalline solid. Mp: 84−86 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.2 (s, 1H), 7.73 (d, J = 2.3 Hz, 1H), 7.43 (d, J = 2.3 Hz, 1H), 7.32 (s, 1H), 3.67 (br m, 2 H), 3.54 (br m, 2H), 1.68 (br 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 187.1, 152.5, 151.4, 146.4, 129.4, 127.5, 125.4, 122.9, 121.1, 45.8, 45.5, 25.9, 25.5, 24.1 ppm. FT IR (KBr pellet, cm^{-1}): 2926, 1717, 1686, 1610, 1451, 1371, 1291, 1209, 1163, 1142, 1021, 979, 859, 743. UV (MeOH): λ_{max} (log ε) 210 (4.52), 239 (4.58), 287 (4.66) nm. MS (ESI): m/z 318 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{14}H_{14}F_3NO_4Na$ 340.0773, found 340.0775.

*Morpholine-4-carboxylic Acid 2-Formyl-4-(trifluoromethoxy)-phenyl Ester (**3ad**).* Yield: 13 mg, 34%. Colorless liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.12 (s, 1H), 7.72 (d, J = 2.0 Hz, 1H), 7.45 (d, J = 2.0 Hz, 1H), 7.33 (s, 1H), 3.78 (br m, 6H), 3.62 (br m, 2H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 187.1, 152.6, 150.6, 146.7, 129.4, 127.6, 125.4, 122.2, 119.5, 66.5 (2C), 45.2, 44.5 ppm. FT IR (KBr pellet, cm^{-1}): 2923, 2856, 1728, 1701, 1611, 1491, 1424, 1255, 1226, 1184, 1118, 1054, 861, 745, 619. UV (MeOH): λ_{max} (log ε) 210 (4.53), 241 (4.59), 293 (4.67) nm. MS (ESI): m/z 320 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{13}H_{12}F_3NO_5Na$ 342.0565, found 342.0567.

*Dimethylcarbamic Acid 2-Formyl-6-Chlorophenyl Ester (**3ae**).* Yield: 45 mg, 67%. Yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.13 (s, 1H), 7.79 (d, J = 7.7 Hz, 1H), 7.68 (d, J = 7.7 Hz, 1H), 7.41 (t, J = 7.7 Hz, 1H), 3.22 (s, 3H), 3.06 (s, 3H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 187.9, 155.1, 153.1, 149.4, 135.4, 128.0, 126.6, 126.3, 37.0, 36.7 ppm. FT IR (KBr pellet, cm^{-1}): 2926, 2851, 1729, 1699, 1594, 1464, 1456, 1387, 1282, 1222, 1162, 1141, 1073, 902, 767, 737, 677. UV (MeOH): λ_{max} (log ε) 210 (4.38), 255 (4.46), 283 (4.51) nm. MS (ESI): m/z 228 $[M + H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{10}H_{10}ClNO_3Na$ 250.0247, found 250.0246

*Diethylcarbamic Acid 2-Formyl-6-chlorophenyl Ester (**3af**).* Yield: 24 mg, 60%. Yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.14 (s, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.29 (t, J = 8.0

dx.doi.org/10.1021/jo402798k | J. Org. Chem. 2014, 79, 3206−3214

Hz, 1H), 3.40−3.58 (m, 4H), 1.20−1.38 (m, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 187.7, 152.5, 149.6, 135.5, 131.0, 129.2, 127.8, 126.5, 42.7, 42.4, 14.1, 13.2 ppm. FT IR (KBr pellet, cm^{-1}): 2925, 2854, 1732, 1698, 1593, 1455, 1421, 1393, 1273, 1215, 1150, 1074, 955, 785, 738 UV (MeOH): λ_{max} (log ε) 215 (4.44), 246 (4.50), 293 (4.57) nm. MS (ESI): *m*/*z* 256 $[M + H]^+$. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{12}H_{14}ClNO_3Na$ 278.0560, found 278.0561.

*Diisopropylcarbamic Acid 2-Formyl-6-chlorophenyl Ester (**3ag**).* Yield: 21 mg, 47%. Yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.14 (s, 1H), 7.81 (d, *J* = 7.5 Hz, 1H), 7.67 (d, *J* = 7.5 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 3.97−4.24 (m, 2H), 1.31−1.42 (m, 12H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 187.9, 151.7, 149.7, 135.5, 131.0, 129.2, 127.5, 126.4, 47.2 (2C), 21.4 (2C), 20.1 (2C) ppm. FT IR (KBr pellet, cm^{-1}): 2971, 2930, 1727, 1698, 1593, 1429, 1371, 1313, 1226, 1136, 1041, 974, 893, 784, 749. UV (MeOH): λ_{max} (log ε) 213 (4.48), 247 (4.54), 296 (4.62) nm. MS (ESI): *m*/*z* 284 $[M + H]^+$. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{18}ClNO_3Na$ 306.0873, found 306.0875.

*Piperidine-1-carboxylic Acid 2-Formyl-6-chlorophenyl Ester (**3ah**).* Yield: 29 mg, 69%. Colorless liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.14 (s, 1H), 7.80 (d, *J* = 7.2 Hz, 1H), 7.67 (d, *J* = 7.2 Hz, 1H), 7.31 (t, *J* = 7.2 Hz, 1H), 3.73 (br m, 2 H), 3.54 (br m, 2H), 1.70 (br 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 187.9, 151.9, 149.6, 135.4, 130.9, 129.0, 127.8, 126.5, 46.0, 45.7, 25.9, 25.5, 24.2 ppm. FT IR (KBr pellet, cm^{-1}): 2926, 2856, 1730, 1697, 1593, 125, 1393, 1216, 1139, 1019, 955, 849, 785, 744. UV (MeOH): λ_{max} (log ε) 212 (4.45), 246 (4.52), 296 (4.60) nm. MS (ESI): *m*/*z* 268 $[M + H]^+$. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{13}H_{14}ClNO_3Na$ 290.0560, found 290.0561.

*Morpholine-4-carboxylic Acid 2-Formyl-6-chlorophenyl Ester (**3ai**).* Yield: 45 mg, 75%. White crystalline solid. Mp: 73−75 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.1 (s, 1H), 7.80 (d, *J* = 7.7 Hz, 1H), 7.69 (d, *J* = 7.7 Hz, 1H), 7.33 (t, *J* = 7.7 Hz, 1H), 3.80 (br m, 6H), 3.61 (br m, 2H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 187.8, 151.9, 148.8, 135.4, 130.7, 129.0, 128.7, 126.8, 66.5 (2C), 45.3, 44.6 ppm. FT IR (KBr pellet, cm^{-1}): 2923, 2855, 1732, 1697, 1593, 1424, 1394, 1248, 1214, 1117, 1049, 984, 856, 787, 744. UV (MeOH): λ_{max} (log ε) 213 (4.46), 246 (4.52), 296 (4.60) nm. MS (ESI): *m*/*z* 270 $[M + H]^+$. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{12}H_{12}ClNO_4Na$ 292.0353, found 292.0352.

*Dimethylcarbamic Acid 2-Formyl-4-bromophenyl Ester (**3aj**).* Yield: 30 mg, 44%. Colorless crystalline solid. Mp: 64−66 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.14 (s, 1H), 7.99 (s, 1H), 7.70 (d, *J* = 8.6 Hz, 1H), 7.16 (d, *J* = 8.6 Hz, 1H), 3.16 (s, 3H), 3.04 (s, 3H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 187.2, 153.7, 152.0, 137.7, 132.1, 129.7, 125.5, 119.0, 37.0, 36.6 ppm. FT IR (KBr pellet, cm^{-1}): 2923, 2852, 1732, 1691, 1593, 1471, 1383, 1211, 1157, 1004, 862, 809, 748. UV (MeOH): λ_{max} (log ε) 218 (4.47), 246 (4.52), 304 (4.61) nm. MS (ESI): *m*/*z* 272 $[M + 2]^+$. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{10}H_{10}BrNO_3Na$ 293.9742, found 293.9741.

*Diethylcarbamic Acid 2-Formyl-4-bromophenyl Ester (**3ak**).* Yield: 21 mg, 57%. Yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.13 (s, 1H), 7.99 (s, 1H), 7.71 (d, *J* = 8.7 Hz, 1H), 7.16 (d, *J* = 8.7 Hz, 1H), 3.35−3.52 (m, 4H), 1.20−1.32 (m, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 187.1, 153.1, 152.1, 137.7, 131.9, 129.8, 125.4, 118.8, 42.6, 42.1, 14.3, 13.2 ppm. FT IR (KBr pellet, cm^{-1}): 2975, 2918, 1725, 1691, 1594, 1470, 1422, 1390, 1255, 1207, 1151, 1112, 959, 883, 738. UV (MeOH): λ_{max} (log ε) 214 (4.51), 248 (4.57), 295 (4.65) nm. MS (ESI): *m*/*z* 300 $[M + H]^+$, 302 $[M + 2]^+$. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{12}H_{14}BrNO_3Na$ 322.0055, found 322.0053.

*Diisopropylcarbamic Acid 2-Formyl-4-bromophenyl Ester (**3al**).* Yield: 14 mg, 35%. Yellow amorphous solid. Mp: 61−63 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.11 (s, 1H), 8.01 (s, 1H), 7.70 (d, *J* = 8.6 Hz, 1H), 7.11 (d, *J* = 8.6 Hz, 1H), 4.00−4.09 (m, 2H), 1.31−1.44 (m, 12H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 187.2, 152.5, 152.1, 137.7, 131.8, 130.1, 125.5, 118.9, 47.1 (2C), 21.4 (2C), 20.4 (2C) ppm. FT IR (KBr pellet, cm^{-1}): 2970, 2930, 1721, 1695, 1593, 1472, 1430, 1372, 1315, 1255, 1202, 1111, 1041, 980, 884, 751. UV (MeOH): λ_{max} (log ε) 219 (4.56), 247 (4.61), 305 (4.70) nm. MS (ESI): *m*/*z* 350 $[M + Na]^+$. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{18}BrNO_3Na$ 350.0368, found 350.0371.

*Piperidine-1-carboxylic Acid 2-Formyl-4-bromophenyl Ester (**3am**).* Yield: 50 mg, 65%. White amorphous solid. Mp: 64−66 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.12 (s, 1H), 7.99 (s, 1H), 7.70 (d, *J* = 8.7 Hz, 1H), 7.15 (d, *J* = 8.7 Hz, 1H), 3.52−3.70 (br m, 4H), 1.67 (br 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 187.2, 152.5, 152.2, 137.7, 132.0, 129.8, 125.5, 118.9, 45.8, 45.5, 25.9, 25.4, 24.1 ppm. FT IR (KBr pellet, cm^{-1}): 2938, 2858, 1725, 1692, 1593, 1427, 1391, 1206, 1179, 1140, 1111, 1018, 883, 855, 708, 660. UV (MeOH): λ_{max} (log ε) 216 (4.53), 248 (4.59), 305 (4.68) nm. MS (ESI): *m*/*z* 312 $[M + H]^+$. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{13}H_{14}BrNO_3Na$ 334.0055, found 334.0057.

*Morpholine-4-carboxylic Acid 2-Formyl-4-bromophenyl Ester (**3an**).* Yield: 24 mg, 31%. White amorphous solid. Mp: 130−132 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.1 (s, 1H), 7.99 (s, 1H), 7.73 (d, *J* = 8.6 Hz, 1H), 7.15 (d, *J* = 8.6 Hz, 1H), 3.77 (br m, 6H), 3.59 (br m, 2H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 187.2, 152.6, 151.3, 137.8, 133.2, 129.7, 125.5, 119.3, 66.5 (2C), 45.1, 44.4 ppm. FT IR (KBr pellet, cm^{-1}): 2973, 2867, 1731, 1684, 1454, 1401, 1241, 1208, 1182, 1120, 1054, 988, 887, 806, 746. UV (MeOH): λ_{max} (log ε) 219 (4.54), 255 (4.60), 333 (4.72) nm. MS (ESI): *m*/*z* 314 $[M + H]^+$. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{12}H_{12}BrNO_4Na$ 335.9847, found 335.9849.

*Dimethylcarbamic Acid 2-Formylnaphthyl Ester (**3ao**).* Yield: 30 mg, 46%. Yellow amorphous solid. Mp: 125−127 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.35 (s, 1H), 8.05 (d, *J* = 7.8 Hz, 1H), 7.76−7.94 (m, 3H), 7.57−7.64 (m, 2H), 3.34 (s, 3H), 3.12 (s, 3H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 188.7, 154.3, 151.6, 137.4, 129.3, 128.2, 127.7, 127.2, 126.2, 125.0, 123.2, 122.7, 37.1, 36.8 ppm. FT IR (KBr pellet, cm^{-1}): 2925, 2854, 1731, 1681, 1627, 1465, 1364, 1232, 1146, 1080, 996, 817, 772, 747. UV (MeOH): λ_{max} (log ε) 224 (4.43), 246 (4.48), 286 (4.54), 347 (4.62) nm. MS (ESI): *m*/*z* 244 $[M + H]^+$. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{13}NO_3Na$ 266.0793, found 266.0792.

*Diethylcarbamic Acid 2-Formylnaphthyl Ester (**3ap**).* Yield: 19 mg, 49%. Yellow amorphous solid. Mp: 65−67 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.35 (s, 1H), 7.99 (d, *J* = 7.4 Hz, 1H), 7.76−7.94 (m, 3H), 7.58−7.65 (m, 2H), 3.45−3.71 (m, 4H), 1.26−1.30 (m, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 188.6, 153.7, 151.8, 137.5, 129.2, 128.2, 127.8, 127.3, 126.1, 125.2, 123.1, 122.7, 42.7, 42.3, 14.5, 13.3 ppm. FT IR (KBr pellet, cm^{-1}): 2925, 2854, 1724, 1679, 1628, 1461, 1377, 1264, 1145, 1078, 954, 816, 767, 747. UV (MeOH): λ_{max} (log ε) 225 (4.49), 245 (4.52), 286 (4.59), 347 (4.68) nm. MS (ESI): *m*/*z* 272 $[M + H]^+$. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{16}H_{17}NO_3Na$ 294.1106, found 294.1107.

*Diisopropylcarbamic Acid 2-Formylnaphthyl Ester (**3aq**).* Yield: 11 mg, 26%. Yellow amorphous solid. Mp: 108−110 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.35 (s, 1H), 7.75−8.02 (m, 4H), 7.55−7.68 (m, 2H), 3.97−4.38 (m, 2H), 1.34−1.60 (m, 12H) ppm. 188.7, 153.0, 151.9, 137.6, 129.2, 128.2, 127.9, 127.2, 126.0, 125.3, 122.9, 122.8, 47.2, 47.1, 21.7 (2C), 20.4 (2C) ppm. FT IR (KBr pellet, cm^{-1}): 2924, 2852, 1723, 1682, 1628, 1464, 1434, 1373, 1306, 1231, 1146, 1082, 1040, 970, 893, 816, 765. UV (MeOH): λ_{max} (log ε) 224 (4.53), 250 (4.57), 286 (4.63), 338 (4.70) nm. MS (ESI): *m*/*z* 300 $[M + H]^+$. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{18}H_{21}NO_3Na$ 322.1419, found 322.1421.

*Piperidine-1-carboxylic Acid 2-Formylnaphthyl Ester (**3ar**).* Yield: 21 mg, 51%. Yellow amorphous solid. Mp: 86−88 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.35 (s, 1H), 7.97 (d, *J* = 7.2 Hz, 1H), 7.81−7.91 (m, 3H), 7.59−7.65 (m, 2H), 3.59−3.88 (br m, 4H), 1.76 (br 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 188.7, 153.1, 151.8, 137.5, 129.3, 128.2, 127.7, 127.2, 126.1, 125.1, 123.1, 122.7, 46.0, 45.6, 26.2, 25.6, 22.6 ppm. FT IR (KBr pellet, cm^{-1}): 2927, 2856, 1726, 1682, 1628, 1429, 1378, 1256, 1226, 1139, 1083, 1018, 956, 817, 769, 747. UV (MeOH): λ_{max} (log ε) 224 (4.50), 250 (4.55), 286 (4.61), 347 (4.69) nm. MS (ESI): *m*/*z* 284 $[M + H]^+$. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{17}H_{17}NO_3Na$ 306.1106, found 306.1108.

*Morpholine-4-carboxylic Acid 2-Formylnaphthyl Ester (**3as**).* Yield: 40 mg, 58%. Yellow amorphous solid. Mp: 124−126 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.31 (s, 1H), 8.03 (d, *J* = 7.0 Hz, 1H), 7.78−7.93 (m, 3H), 7.59−7.65 (m, 2H), 3.90 (br m, 6H), 3.64 (br m,

dx.doi.org/10.1021/jo402798k | J. Org. Chem. 2014, 79, 3206−3214

2H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 188.6, 153.1, 150.8, 137.4, 137.4, 129.4, 128.2, 127.5, 126.3, 124.8, 123.8, 122.6, 66.6 (2C), 45.3, 44.5, ppm. FT IR (KBr pellet, cm^{-1}): 2924, 2855, 1728, 1680, 1627, 1429, 1377, 1277, 1227, 1173, 1117, 1086, 1043, 983, 818, 769, 748. UV (MeOH): λ_{max} (log ε) 224 (4.50), 249 (4.55), 386 (4.61), 347 (4.70) nm. MS (ESI): m/z 286 $[M+H]^+$. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{16}H_{15}NO_4Na$ 308.0899, found 308.0897.

*Dimethylcarbamic Acid 2-Nitrophenyl Ester (**6a**).*[18] This compound is known. Yield: 16 mg, 21%. Yellow liquid. ^{1}H NMR (200 MHz, $CDCl_3$): 8.10 (d, J = 8.0 Hz, 1H), 7.62 (t, J = 8.0 Hz, 1H), 7.28−7.39 (m, 2H), 3.15 (s, 3H), 3.04 (s, 3H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ 153.4, 145.1, 143.3, 134.4, 125.8, 125.6 (2C), 36.9, 36.6 ppm. MS (ESI): m/z 211 $[M + H]^+$.

■ ASSOCIATED CONTENT

Supporting Information

Tables giving solubility data and optimization of reaction conditions and figures giving ^{1}H and ^{13}C NMR spectra of all of the compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail for J.-J.W.: jjwang@kmu.edu.tw

*E-mail for F.-R.C.: aaronfrc@kmu.edu.tw

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support from the National Science Council of Taiwan (NSC 99-2628-B-037-003-MY3) and the Department of Health Executive Yuan, Taiwan (DOH101-TD-C-111-004) is acknowledged. The authors thank the Center for Research Resources and Development (CRRD), Kaohsiung Medical University, for technical support and services in LC-MS and NMR analysis.

■ REFERENCES

(1) (a) Chaturvedi, D. *Tetrahedron* **2012**, *68*, 15. (b) Kuhr, R. J.; Dorough, H. W. *Carbamate Insecticides: Chemistry, Biochemistry and Toxicology*; CRC Press: Cleveland, OH, 1976.

(2) (a) Hen, N.; Bialer, M.; Yagen, B. *J. Med. Chem.* **2012**, *55*, 2835. (b) Niphakis, M. J.; Johnson, D. S.; Ballard, T. E.; Stiff, C.; Cravatt, B. F. *ACS Chem. Neurosci.* **2012**, *3*, 418. (c) Chang, J. W.; Nomura, D. K.; Cravatt, B. F. *Chem. Biol.* **2011**, *18*, 476. (d) Fuchs, M.; Koszelewski, D.; Tauber, K.; Kroutila, W.; Fabere, K. *Chem. Commun.* **2010**, *46*, 5500. (e) Wienstock, M.; Bejar, C.; Wang, R. H. *J. Neural Transm. Suppl.* **2000**, *60*, 157.

(3) (a) Li, J.; Kornhaab, C.; Ackermann, L. *Chem. Commun.* **2012**, *48*, 11343. (b) Quasdorf, K. W.; Finch, A. A.; Liu, P.; Silberstein, A. L.; Komaromi, A.; Blackburn, T.; Ramgren, S. D.; Houk, K. N.; Snieckus, V.; Garg, N. K. *J. Am. Chem. Soc.* **2011**, *133*, 6352. (c) Riggs, J. C.; Singh, K. J.; Yun, M.; Collum, D. B. *J. Am. Chem. Soc.* **2008**, *130*, 13709. (d) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 4th ed.; Wiley: New York. 2007; p 419. (e) Snieckus, V. *Chem. Rev.* **1990**, *90*, 879.

(4) (a) Kreye, O.; Wald, S.; Meier, M. A. R. *Adv. Synth. Catal.* **2013**, *355*, 81. (b) Yoshimura, A.; Luedtke, M. W.; Zhdankin, V. V. *J. Org. Chem.* **2012**, *77*, 2087. (c) Lebel, H.; Leogane, O. *Org. Lett.* **2006**, *8*, 5717. (d) Pasguato, L.; Modena, G.; Cotarca, L.; Delgu, P.; Mantovami, S. J. *J. Org. Chem.* **2000**, *65*, 8224. (e) Majer, P.; Randad, R. S. *J. Org. Chem.* **1994**, *59*, 1937.

(5) (a) Takeda, Y.; Okumura, S.; Tone, S.; Sasaki, I.; Minakata, S. *Org. Lett.* **2012**, *14*, 4874. (b) Padiya, K. J.; Gavade, S.; Kardile, B.; Tiwari, M.; Bajare, S.; Mane, M.; Gaware, V.; Varghese, S.; Harel, D.; Kurhade, S. *Org. Lett.* **2012**, *14*, 2814. (c) Yang, X.; Zhang, Y.; Ma, D. *Adv. Synth. Catal.* **2012**, *354*, 2443. (d) Shang, J.; Liu, S.; Ma, X.; Lua, L.; Deng, Y. *Green Chem.* **2012**, *14*, 2899. (e) Ca, N. D.; Gabriele, B.; Ruffolo, G.; Veltri, L.; Zanetta, T.; Costa, M. *Adv. Synth. Catal.* **2011**, *353*, 133. (f) Shi, F.; Deng, Y. *Chem. Commun.* **2001**, 443.

(6) (a) During our submission the Phan group investigated the use of heterogeneous catalysts for the synthesis of carbamates from phenol: Phan, N. T. S.; Nguyen, T. T.; Vu, P. H. L. *ChemCatChem* **2013**, *5*, 3068−3077. (b) Kumar, G. S.; Maheswari, C. U.; Kumar, R. A.; Kantam, M. L.; Reddy, K. R. *Angew. Chem., Int. Ed.* **2011**, *50*, 11748. (c) Barve, B. D.; Wu, Y. C.; El-Shazly, M.; Chuang, D. W.; Chung, Y. M.; Tsai, Y. H.; Wu, S. F.; Korinek, M.; Du, Y. C.; Hsieh, C. T.; Wang, J. J.; Chang, F. R. *Eur. J. Org. Chem.* **2012**, 6760.

(7) (a) Ebetino, F. H.; Mazur, A. W.; Dobson, R. L. M. (Warner Chilcott Co.) US 20110098251, 2011. (b) Pradhan, T. K.; Mukherjee, C.; Kamila, S.; De, A. *Tetrahedron* **2004**, *60*, 5215.

(8) (a) Li, B.; Dixneuf, P. H. *Chem. Soc. Rev.* **2013**, *42*, 5744. (b) Shang, X.; Liu, Z. Q. *Chem. Soc. Rev.* **2013**, *42*, 3253. (c) Arockiam, P.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879. (d) Song, G.; Wang, F.; Li, X. *Chem. Soc. Rev.* **2012**, *41*, 3651. (e) Kuhl, N.; Hopkinson, M. N.; Delord, J. W.; Glorius, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 10236. (f) Sun, C. L.; Li, B. J.; Shi, Z. J. *Chem. Rev.* **2011**, *111*, 1293. (g) Dyker, G. *Handbook of C−H Transformations. Applications in Organic Synthesis*; Wiley-VCH: Weinheim, Germany, 2005.

(9) (a) Li, B. J.; Shi, Z. J. *Chem. Soc. Rev.* **2012**, *41*, 5588. (b) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215. (c) Li, C. J. *Acc. Chem. Res.* **2009**, *42*, 335 and references therein.

(10) (a) Ding, S.; Jiao, N. *Angew. Chem., Int. Ed.* **2012**, *51*, 9226 and references therein. (b) Muzart, J. *Tetrahedron* **2009**, *65*, 8313.

(11) (a) Kumar, P. S.; Kumar, G. S.; Kumar, R. A.; Reddy, N. V.; Reddy, K. R. *Eur. J. Org. Chem.* **2013**, 1218. (b) Li, Y.; Guo, F.; Zha, Z.; Wang, Z. *Chem. Asian J.* **2013**, *8*, 534. (c) Honglai, J.; Lin, A.; Zhu, C.; Cheng, Y. *Chem. Commun.* **2013**, *49*, 819. (d) Li, D.; Wang, M.; Liu, J.; Zhao, Q.; Wang, L. *Chem. Commun.* **2013**, *49*, 3640. (e) Kim, J.; Choi, J.; Shin, K.; Chang, S. *J. Am. Chem. Soc.* **2012**, *134*, 2528. (f) Mai, W. P.; Wang, H. H.; Li, Z. C.; Yuan, J. W.; Xiao, Y. M.; Yang, L. R.; Mao, P.; Qu, L. B. *Chem. Commun.* **2012**, *48*, 10117. (g) Liu, Z.; Zhang, J.; Chen, S.; Shi, E.; Xu, Y.; Wan, X. *Angew. Chem., Int. Ed.* **2012**, *51*, 3231. (h) Xu, K.; Hu, Y.; Zhang, S.; Zha, Z.; Wang, Z. *Chem. Eur. J.* **2012**, *18*, 9793. (i) We did not observe the formation of hydrazine by the self-coupling reaction of aminyl radicals, which may be formed by the decarbonylation of aminocarbonyl radical.

(12) (a) Sodhi, R. K.; Paul, S.; Clark, J. H. *Green Chem.* **2012**, *14*, 1649. (b) Das, R.; Chakraborty, D. *Appl. Organomet. Chem.* **2011**, *25*, 437. (c) Chakraborty, D.; Gowda, R. R.; Malik, P. *Tetrahedron Lett.* **2009**, *50*, 6553. (d) Mannam, S.; Sekar, G. *Tetrahedron Lett.* **2008**, *49*, 1083. (e) Shapiro, N.; Vigalok, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 2849. (f) Grill, J. M.; Ogle, J. W.; Miller, S. A. *J. Org. Chem.* **2006**, *71*, 9291. (g) Abaee, M. S.; Sharifi, R.; Mojtahedi, M. M. *Org. Lett.* **2005**, *26*, 5893. (h) Heaney, H.; Newbold, A. J. *Tetrahedron Lett.* **2001**, *42*, 6607.

(13) (a) Lide, D. R. Physical Constants of Organic Compounds. In *CRC Handbook of Chemistry and Physics*; CRC Press: Boca Raton, FL, 2005; Internet Version, pp 4−55 (http://www.hbcpnetbase.com). (b) Richardson, H. W. *Handbook of Copper Compounds and Applications*; CRC Press: New York, 1997. (c) Becker, B. *J. Chem. Eng. Data* **1970**, *15*, 31.

(14) (a) Travis, B. R.; Sivakumar, M.; Hollist, G. O.; Borhan, B. *Org. Lett.* **2003**, *5*, 1031. (b) Webb, K. S.; Ruszkay, S. J. *Tetrahedron* **1998**, *54*, 401.

(15) During the preparation of this paper the Patel group reported *O*-aroylation of phenols with intact formyl groups. Please see: Rout, S. K.; Guin, S.; Banerjee, A.; Khatun, N.; Gogoi, A.; Patel, B. K. *Org. Lett.* **2013**, *15*, 4106.

(16) (a) Patil, N. T.; Konala, A.; Sravanti, S.; Singh, A.; Ummannib, R.; Sridhar, B. *Chem. Commun.* **2013**, *49*, 10109. (b) Hashimoto, T.; Takiguchi, Y.; Keiji, M. *J. Am. Chem. Soc.* **2013**, *135*, 11473. (c) Saxin, M. F.; Seifert, T.; Landergren, M. R.; Suuronen, T.; Kakkonen, M. L.; Jarho, E. M.; Luthman, K. *J. Med. Chem.* **2012**, *55*, 7104. (d) Patil, N.

T.; Raut, V. S.; Shinde, V. S.; Gayatri, G.; Sastry, G. N. *Chem. Eur. J.* **2012**, *18*, 5530.
(17) (a) Terentev, A. O.; Borisov, D. A.; Yaremenko, I. A.; Chernyshev, V. V.; Nikishin, G. I. *J. Org. Chem.* **2010**, *75*, 5065. (b) Yoo, W. J.; Li, C. J. *J. Org. Chem.* **2006**, *71*, 6266. (c) He, C.; Zhang, G.; Ke, J.; Zhang, H.; Miller, J. T.; Kropf, A. J.; Lei, A. *J. Am. Chem. Soc.* **2013**, *135*, 488.
(18) Valega, T. M. *J. Org. Chem.* **1965**, *31*, 1150.