JOC The Journal of Organic Chemistry

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Palladium-Catalyzed Intermolecular Cyclocarbonylation of 2-Iodoanilines with the Michael Acceptor, Diethyl Ethoxycarbonylbutendienoate

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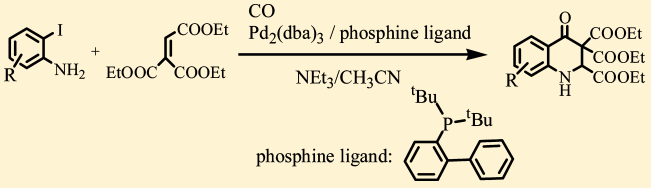
Supporting Information

ABSTRACT: Palladium-catalyzed intermolecular cyclocarbonylation of 2-iodoanilines with diethyl ethoxycarbonylbutendienoate produces 2,3,3-triethoxycarbonyl-2,3-dihydro-4(1*H*)-quinolinone derivatives in moderate to good yields. This protocol involves Michael addition and subsequent carbonylation.



2,3-Dihydro-4(1*H*)-quinolinones are known to exhibit pharmacological activities such as analgesic[1] and antimalarial[2] activity. Various methods have been developed for their preparation. Well-established approaches to construct the 2,3-dihydro-4(1*H*)-quinolinone structure include intramolecular cyclization such as Friedel−Crafts acylation of *N*-phenylpropanoic acids or its esters,[3] rearrangement of *N*-phenyl-*β*-lactams using Bronsted or Lewis acids,[4] Michael addition of 2-alkenoylanilines under basic conditions,[5] and acid-catalyzed cyclization of 2-(3′-hydroxypropynyl)anilines.[6] These methods are applied to relatively less highly functionalized 2,3-dihydro-4(1*H*)-quinolinones. Another attractive method consists in the use of a transition metal complex as a catalyst. A few examples of the intermolecular synthesis of 2,3-dihydro-4(1*H*)-quinolinones using a palladium complex as the catalyst have also been reported in the literature.[7]

A metal mediated approach, in particular intermolecular cyclization, has often found synthetic merit because multiple bond forming steps can be involved in one operation overall, resulting in the construction of highly functionalized heterocycles.[8] One of us recently developed the palladium-catalyzed intermolecular cyclocarbonylation reaction affording valuable heterocyclic compounds. For example, diethyl (2-iodoaryl)-malonates can react with methyl vinyl ketones or imidoyl chlorides under carbon monoxide affording 2-acyl-3,4-dihydronaphthalenones[9] or isoquinoline-1(2*H*)-ones,[10] respectively, in which initial intermolecular reaction of two starting substrates and subsequent cyclocarbonylation proceed in an orderly manner, resulting in practical applications.[11] These results prompted us to apply our research to the intermolecular cyclocarbonylation of 2-iodoanilines with a Michael acceptor using a palladium catalyst. Herein, we report that diethyl ethoxycarbonylbutendienoate is a reasonable Michael acceptor for 2-iodoanilines and carbon monoxide affording 4(1*H*)-quinolinones in moderate to good yields.

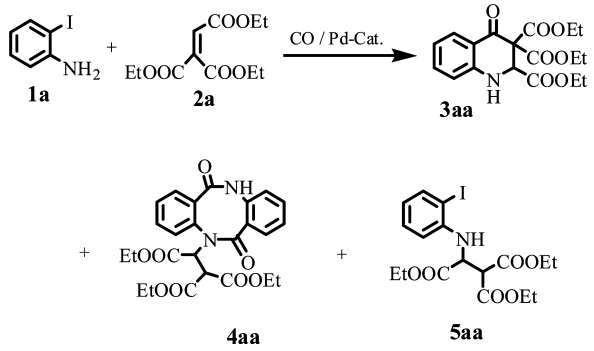
We initially tried several reactions of 2-iodoaniline (**1a**) with diethyl benzylidenemalonate as a Michael acceptor. The expected reaction, however, did not take place, and diethyl benzylidenemalonate was recovered unchanged. Then, we turned our attention to diethyl ethoxycarbonylbutendienoate (**2a**).[12] When **1a** (1.0 mmol) was treated with **2a** (1.2 mmol) in the presence of $PdCl_2(PPh_3)_2$ (0.05 mmol) and NEt_3 (2.0 mmol) in acetonitrile at 100 °C under carbon monoxide (500 psi), the cyclocarbonylation product, 2,3,3-triethoxycarbonyl-2,3-dihydro-4(1*H*)-quinolinone (**3aa**), was produced in 15% yield, together with **4aa** (13%) and **5aa** (38%) (Table 1, entry 1). Using $PdCl_2$(dppf) as the catalyst increased the yield of **3aa** to 40% (Table 1, entry 2). A comparable yield of **3aa** was obtained using $Pd_2(dba)_3/4PCy_3HBF_4$ at 100 °C, and decreasing the temperature to 80 °C as well as increasing the amount of NEt_3 to 10 mmol dramatically increased the yield of **3aa** to 68% (Table 1, entries 3−5). Further decreasing the temperature to 60 °C reduced the yield of **3aa** to 41%. When the reaction was performed in CH_2Cl_2 and THF, the Michael addition product, **5aa**, was exclusively formed in more than 80% yield, with no carbonylation taking place. A polar solvent can stabilize the malonate anion, so that the equilibrium shifts to the malonate, resulting in smooth carbonylation after the Michael addition. The inorganic base, K_2CO_3, was not as effective as NEt_3 (Table 1, entry 6). The effect of phosphines was also examined, and it was found that 2-(di-*tert*-butylphosphino)biphenyl showed comparable results to PCy_3 (Table 1, entry 13). It appears that the electron donating phosphines, i.e., trialkylphosphines and dialkylarylphosphines, generally tend to give better yields of **3aa**. It is interesting to note that Xantphos behaved differently; **4aa** was produced much more selectively than using any other ligands (Table 1, entry 11).

A number of 2-iodoanilines (**1b−j**) were then reacted with **2a** using the catalytic system of $Pd_2(dba)_3$/2-(di-*tert*-butylphosphino)biphenyl in acetonitrile at 80 °C under 500

Received: January 23, 2012
Published: April 6, 2012

dx.doi.org/10.1021/jo300173g | *J. Org. Chem.* 2012, 77, 4420−4424

Table 1. Screening for the Intermolecular Cyclocarbonylation of 1a and 2a[a]

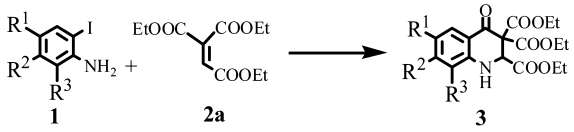


entry	catalyst	temp (°C)	yield (%)[b] 3aa/4aa/5aa
1[c]	$PdCl_2(PPh_3)_2$	100	15/13/38
2[c]	$PdCl_2$(dppf)	100	40/0/0
3[c]	$Pd_2(dba)_3$/4PCy_3HBF_4	100	43/8/13
4	$Pd_2(dba)_3$/4PCy_3HBF_4	100	49/5/6
5	$Pd_2(dba)_3$/4PCy_3HBF_4	80	68/8/6
6[d]	$Pd_2(dba)_3$/4PCy_3HBF_4	80	46/0/trace
7	$Pd_2(dba)_3$/4$P^tBu_3HBF_4$	80	57/12/6
8	$Pd_2(dba)_3$/2D^{t}BPF[e]	80	59/12/trace
9	$Pd_2(dba)_3$/2Xant^{t}B[f]	80	29/10/31
10	$Pd_2(dba)_3$/2dppp	80	0/0/89
11	$Pd_2(dba)_3$/2Xanthphos[g]	80	0/54/16
12	$Pd_2(dba)_3$/4ArPCy_2[h]	80	48/6/23
13	$Pd_2(dba)_3$/4ArP$^tBu_2$[i]	80	71/8/trace

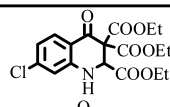
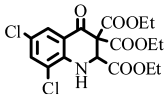
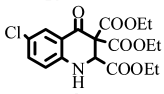
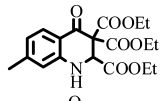
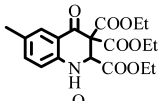
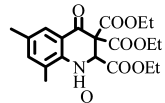
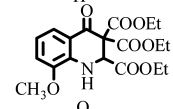
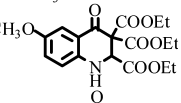
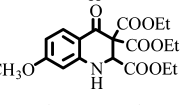
[a]Reaction conditions: **1a** (1.0 mmol), **2a** (1.2 mmol), Pd catalyst; 5 mol % of Pd atom based on **1a**, NEt_3 (10 mmol). [b]Isolated yield. [c]NEt_3 (2.0 mmol). [d]K_2CO_3 (2.0 mmol) was used instead of NEt_3. [e]1,1-Bis-(di-*tert*-butylphosphino)ferrocene. [f]9,9-Dimethyl-4,5-bis(di-*tert*-butylphosphino)xanthene. [g]9,9-Dimethyl-4,5-bis-(diphenylphosphino)xanthene. [h]2-(Dicyclohexylphosphino)biphenyl. [i]2-(Di-*tert*-butylphosphino)biphenyl.

psi of carbon monoxide (Table 2). Although there are several exceptions, the corresponding 4(1*H*)-quinolinones were isolated in moderate to good yields. The reaction seems to be sensitive to the electronic nature of the substituents at the *para*-position of the iodide group, and reactions of **1b**, **1e**, and **1j** gave the products in lower yields (Table 2, entries 1, 4, 9). These substituents obviously influence the rate of the carbonylation step as well as the Michael addition step. Thus, the successful results may rely on a favorable balance of the rate between the Michael addition step and the carbonylation step because both steps can take place independently. It is conceivable that strong electron-withdrawing or -donating groups such as chloro and methoxy largely affect both steps, resulting in a serious loss of the desired balance between the two steps. On the contrary, such a strong electron effect would not be expected for the methyl group, and the product yields are 65−81% (Table 2, entries 4−6). When the tetrasubstituted olefin, diethyl 2-ethoxycarbonyl-3-methylbutendienoate (**2b**), was used, none of the expected product was formed, with **2b** being recovered unchanged. A separate experiment conducted by heating a mixture of **1a** and **2b** in acetonitrile at 80 °C for 20 h resulted in the complete recovery of both substrates, indicating that the initial Michael addition can not take place for **2b**, possibly because of steric reasons.

Table 2. Palladium-Catalyzed Intermolecular Carbonylation of 2-Iodoanilines 1 and Diethyl Ethoxycarbonyl Butendienoate 2a[a]



1b: R^1=R^3=H, R^2=Cl
1c: R^1=R^3=Cl, R^2=H
1d: R^1=Cl, R^2=R^3=H
1e: R^1=R^3=H, R^2=CH_3
1f: R^1=CH_3, R^2=R^3=H
1g: R^1=R^3=CH_3, R^2=H
1h: R^1=R^2=H, R^3=OCH_3
1i: R^1=OCH_3, R^2=R^3=H
1j: R^1=R^3=H, R^2=OCH_3

entry	product		yield (%)[b]
1		**3ba**	39
2		**3ca**	87
3		**3da**	61
4		**3ea**	65
5		**3fa**	80
6		**3ga**	81
7		**3ha**	84
8		**3ia**	90
9		**3ja**	26

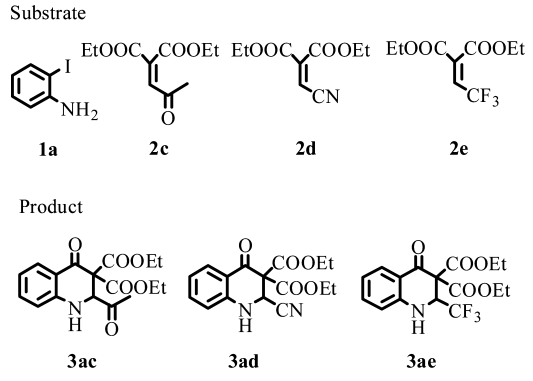
[a]Reaction conditions: **1** (1.0 mmol), **2a** (1.2 mmol), $Pd_2(dba)_3$ (0.025 mmol), 2-(di-*tert*-butylphosphino)biphenyl (0.1 mmol), NEt_3 (10.0 mmol), acetonitrile (2.0 mL), CO 500 psi, 80 °C, 20 h. [b]Isolated yield after column chromatography.

Other types of Michael acceptors were then examined under the optimized conditions for the reaction with **2a** (Table 3). Use of **2c** gave the expected product **3ac** in unsatisfactory yield (Table 3, entry 1). Assuming that the reaction conditions were not suitable for **2c**, a brief screening of reaction conditions (phosphines and bases) was performed to try to improve the yield of **3ac**. Although the **1a** and **2** used were completely consumed, the expected 4(1*H*)-quinolinones were obtained in low yields (Table 3, entries 2−8). No other indentifiable product was observed by TLC.

A possible reaction mechanism for the formation of **3aa** is shown in Scheme 1. Michael addition between 2-iodoaniline (**1a**) and diethyl ethoxycarbonylbutendienoate (**2a**) can give the initial Michael adduct **5aa**.[12] The phosphine ligated Pd(0)

dx.doi.org/10.1021/jo300173g | J. Org. Chem. 2012, 77, 4420−4424

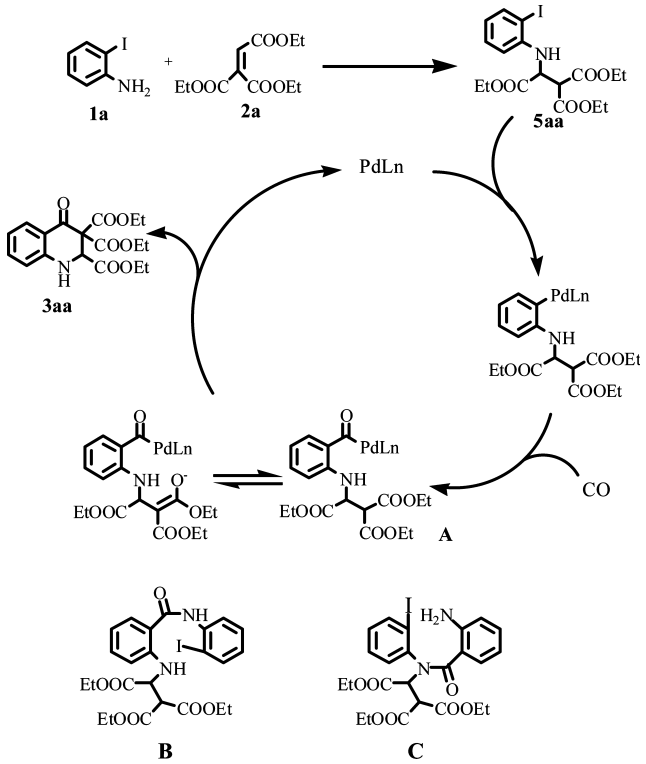
Table 3. Results of 1a with a Variety of Michael Acceptors 2[a]



entry	substrate	ligand	product (%)[b]
1	**2c**	ArP^tBu_2[c]	**3ac** (35)
2[d]	**2c**	ArP^tBu_2	**3ac** (0)
3	**2c**	PCy_3HBF_4	**3ac** (trace)
4	**2c**	$P^tBu_3HBF_4$	**3ac** (21)
5	**2c**	dppf	**3ac** (0)
6	**2c**	ArP^tB_2	**3ac** (0)
7	**2d**	ArP^tB_2	**3ad** (14)
8	**2e**	ArP^tBu_2	**3ae** (23)

[a]Reaction conditions are the same as Table 2. [b]Isolated yield after column chromatography. [c]2-(Di-*tert*-butyl-phosphino)biphenyl. [d]K_2CO_3 (2.0 mmol) was used instead of NEt_3.

Scheme 1. Possible Reaction Mechanism



species, then undergoes oxidative addition to the C−I bond of **5aa**, followed by insertion of carbon monoxide to produce an aroylpalladium intermediate **A**.[13] Nucleophilic attack of the internal malonate anion on the aroylpalladium intermediate **A** completes the catalytic cycle affording 4(1*H*)-quinolinones (**3aa**) and regenerates the Pd(0) species.[14] Formation of **4aa** can be explained by intermolecular double carbonylation of **1a** with **5aa** formed in situ. First intermolecular carbonylation takes place between **1a** and **5aa** affording an acyclic amide **B** and/or **C**, which can then undergo a second intramolecular carbonylation to give the final product **4aa**.

In summary, we have developed a novel and effective protocol for the one-step synthesis of highly functionalized 4(1*H*)-quinolinones. The reaction involves three new bond-forming steps, one C−N bond and two C−C bonds including carbonylation. This effective single-step methodology also demonstrates that well-defined substrate design can control multiple independent bond forming steps, affording interesting hetrocyclic compounds.

EXPERIMENTAL SECTION

2-Iodoanilines **1a**, **1b**, **1c**, **1d**, and **1g** are commercially available, and **1f**,[15] **1h**,[16] **1i**,[16] and **1j**[17] were prepared according to literature methods. The Michael acceptor **2e** was prepared according to the literature.[18]

Preparation of 3-Methy-6-iodoaniline (1e). To an aqueous solution (20 mL) of $NaNO_2$ (60 mmol, 4.14 g) was added dropwise a mixture of 4-methyl-2-nitroaniline (50 mmol, 7.61 g), concentrated HCl (40 mL), and H_2O (50 mL) at 0 °C. After further stirring at 0 °C for 1 h, a solution of KI (150 mmol) in H_2O (40 mL) was added and then stirred at rt for 3 h. The product was extracted with Et_2O, and the organic layer was dried over Na_2SO_4 and concentrated in vacuo to give crude 2-iodo-5-methylnitrobenzene (13.61 g), which was used in the next step without purification.

A mixture of the above crude compound (13.61 g) and Fe (250 mmol, 14.0 g) in AcOH/H_2O (50/50 mL/mL) was gently refluxed for 3 h. The reaction mixture was filtered through a pad of Celite. To the filtrate was added AcOEt and H_2O, and the product was extracted 3 times with AcOEt. The combined organic layer was washed twice with H_2O, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel chromatography with *n*-hexane/Et_2O (90/10) as the eluant to obtain the title compound (8.66 g, 75%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.21 (s, 3 H), 3.99 (brs, 1 H), 6.29−6.31 (m, 1 H), 6.56−6.58 (m, 1 H), 7.47 (d, 1 H, J = 8.0 Hz).

Preparation of 2a−2d. *Diethyl Ethoxycarbonylbutendienoate (**2a**).* To a solution of (ethoxycarbonylmethylene)-triphenylphosphorane (20 mmol, 6.96 g) in toluene (30 mL) was added diethyl ketomalonate (20 mmol, 3.48 g) at 0 °C. After addition, the mixture was stirred at rt for 3 h. After the solvent was evaporated in vacuo, the residue was purified by silica gel chromatography with *n*-hexane/Et_2O (90/10) as the eluant to obtain the title coumpound (3.68 g, 76%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27−1.33 (m, 9 H), 4.21 (q, 2 H, J = 6.8 Hz), 4.23 (q, 2 H, J = 6.8 Hz), 4.33 (q, 2 H, J = 6.8 Hz), 6.83 (s, 1 H); ^{13}C NMR δ 13.9, 14.0, 61.7, 62.0, 62.5, 130.0, 138.9, 162.3, 163.5, 164.2.

*Diethyl 2-Ethoxycarbonyl-3-methylbutendienoate (**2b**).* The title compound was prepared using (1-ethoxycarbonylethylene)-triphenylphosphorane (20 mmol, 7.25 g) and diethyl ketomalonate (20 mmol, 3.48 g) in a similar manner with **2a** (4.13 g, 81%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23−1.28 (m, 9 H), 2.15 (s, 3 H), 4.20−4.25 (m, 6 H), 5.25 (s, 1 H); ^{13}C NMR δ 13.9, 14.0, 17.1, 53.5, 129.6, 144.1, 163.9, 164.1, 167.53; HRMS (EI) Calcd for $C_{12}H_{18}O_6$ 258.1103, found 258.1123.

*Ethyl 4-Ethoxycarbonyl-2-oxopentenoate (**2c**).* The title compound was prepared using (2-oxopropylene)triphenylphosphorane (25 mmol, 7.96 g) and diethyl ketomalonate (25 mmol, 4.36 g) in a similar manner with **2a** (3.98 g, 75%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27−1.31 (m, 6 H), 2.30 (s, 3 H), 4.24 (q, 2 H, J = 7.2 Hz), 4.31 (q, 2 H, J = 7.2 Hz); ^{13}C NMR δ 13.8, 14.0, 30.7, 62.0, 62.5, 135.4, 135.8, 162.7, 164.6, 196.2; HRMS (EI) Calcd for $C_{10}H_{14}O_5$ 214.0841, found 214.0869.

*Ethyl 3-Cyano-2-ethoxycarbonylpropenoate (**2d**).* The title compound was prepared using (cyanomethylene)-triphenylphosphorane (20 mmol, 7.25 g) and diethyl ketomalonate

dx.doi.org/10.1021/jo300173g | J. Org. Chem. 2012, 77, 4420−4424

(20 mmol, 3.48 g) in a similar manner with **2a** (4.13 g, 81%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (t, 3 H, J = 7.2 Hz), 1.34 (t, 3 H, J = 7.2 Hz), 4.28 (q, 2 H, J = 7.2 Hz), 4.38 (q, 2 H, J = 7.2 Hz). 6.52 (s, 1H); ^{13}C NMR δ 13.9, 63.0, 63.1, 112.0, 113.4, 144.0, 161.2, 161.4.

General Procedure for Intermolecular Cyclocarbonylation of 1 and 2. The 2-iodoanilines **1** (1.0 mmol), Michael acceptor **2** (1.2 mmol, 293 mg), $Pd_2(dba)_3$ (0.025 mmol, 22.9 mg), 2-(di-*tert*-butylphosphino)biphenyl (0.1 mmol, 30 mg), NEt_3 (10 mmol, 1.01 g), and acetonitrile (2 mL) were placed into a glass linear, equipped with a magnetic stirring bar. The glass linear was then inserted into a 45 mL autoclave. The autoclave was flushed five times with carbon monoxide and pressurized to 500 psi. The autoclave was heated at 80 °C with stirring. After the reaction, the autoclave was cooled to rt prior to the release of carbon monoxide. The solvent was evaporated under reduced pressure, and the product was purified by silica gel column chromatography with *n*-hexane and diethyl ether (90/10−80/20) as the eluant.

*Products 3. 2,3,3-Triethoxycarbonyl-2,3-dihydro-4(1H)-quinolinone (**3aa**).* Solid (255 mg, 71%): mp 106−107 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.14 (t, 3 H, J = 7.1 Hz), 1.28 (t, 3 H, J = 7.2 Hz), 1.30 (t, 3 H, J = 7.2 Hz), 4.13−4.34 (m, 6 H), 4.85 (s, 1 H), 5.26 (s, 1 H), 6.70−6.78 (m, 2 H), 7.31−7.36 (m, 1 H), 7.83−7.85 (m, 2 H); ^{13}C NMR δ 13.7, 13.8, 14.0, 58.5, 62.4, 62.5, 62.7, 68.4, 115.7, 117.0, 118.9, 128.5, 136.1, 148.2, 164.5, 166.2, 168.7, 184.8; HRMS (EI) Calcd for $C_{15}H_{16}N_1O_5$ 290.1029 (M^+ − COOEt), found290.0995.

*5-(1,2,2-Triethoxycarbonylethyl)dibenzo[b,f][1,5]diazocine-6,12-(5H,11H)dione (**4aa**).* Solid (27 mg, 8%): mp 120−121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.13 (t, 3 H, J = 7.1 Hz), 1.22 (t, 3 H, J = 7.1 Hz), 1.26 (t, 3 H, J = 7.2 Hz), 4.13−4.27 (m, 7 H), 4.98−5.00 (m, 1 H), 6.77−6.79 (m, 1 H), 6.87 (d, 1 H, J = 8.4 Hz), 7.36−7.41 (m, 1 H), 7.45−7.48 (m, 1 H), 7.79−7.82 (m, 2 H), 8.16−8.20 (m, 2 H), 10.04 (d, 1 H, J = 8.7 Hz); ^{13}C NMR δ 13.9, 14.1, 22.7, 31.6, 54.1, 55.4, 62.0, 111.0, 111.5, 116.6, 126.8, 127.8, 128.4, 130.2, 134.1, 136.6, 146.4, 148.5, 157.4, 159.3, 166.9, 167.4, 170.3; HRMS (EI) Calcd for $C_{25}H_{26}N_2O_8$ 482.1689, found 482.1680.

*Diethyl 2-Ethoxycarbonyl-3-(2-iodophenylamino)butandienoate (**5aa**).* Liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19−1.24 (m, 6 H), 1.29 (t, 3 H, J=7.2 Hz), 4.06 (d, 1 H, J=5.2 Hz), 4.16−4.26 (m, 6 H), 4.77 (brs, 1 H), 5.27 (brs, 1 H), 6.46−6.50 (m, 1 H), 6.67 (m, 1 H), 7.17−7.24 (m, 1 H), 7.64−7.67 (m, 1 H); ^{13}C NMR δ 13.9, 14.0, 14.1 54.0, 56.7, 62.0, 86.4, 111.7, 120.2, 129.4, 130.1, 139.4, 145.9, 166.9, 167.4, 170.4; HRMS (EI) Calcd for $C_{17}H_{22}I_1N_1O_6$ 463.0492, found 463.0489.

*7-Chloro-2,3,3-triethoxycarbonyl-2,3-dihydro-4(1H)-quinolinone (**3ba**).* Solid (154 mg, 39%): mp 143−145 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (t, 3 H, J = 7.2 Hz), 1.31 (t, 3 H, J = 7.2 Hz), 1.32 (t, 3H, J = 7.2 Hz), 4.21−4.33 (m, 6 H), 4.83 (s, 1 H), 5.38 (s, 1 H), 6.71−6.75 (m, 2 H), 7.75−7.78 (m, 1H); ^{13}C NMR δ 13.8, 14.0, 58.3, 62.6, 62.7, 62.8, 68.2, 115.2, 115.5, 119.6, 130.0, 142.5, 148.6, 164.3, 165.9, 168.4, 183.9; HRMS (EI) Calcd for $C_{15}H_{15}N_1O_5$ 324.0639 (M^+ − COOEt), found 324.0643.

*6,8-Dichloro-2,3,3-triethoxycarbonyl-2,3-dihydro-4(1H)-quinolinone (**3ca**).* Solid (375 mg, 87%): mp 83−85 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16 (t, 3 H, J = 7.1 Hz), 1.26−1.54 (m, 6 H), 4.14−4.34 (m, 6 H), 4.85 (s, 1 H), 5.82 (s, 1 H), 7.75 (d, 1 H, J = 2.3 Hz), 7.44 (d, 1 H, J = 2.3 Hz); ^{13}C NMR δ 13.8, 13.8, 13.9, 58.1, 62.7, 63.0, 67.7, 118.3, 120.8, 123.4, 126.5, 135.0, 143.0, 164.0, 165.5, 167.9, 183.3; HRMS (EI) Calcd for $C_{18}H_{19}Cl_2N_1O_7$ 431.0539, found 431.0551.

*6-Chloro-2,3,3-triethoxycarbonyl-2,3-dihydro-4(1H)-quinolinone (**3da**).* Solid (243 mg, 61%): mp 95−98 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.15 (t, 3 H, J = 7.1 Hz), 1.30 (t, 3 H, J = 7.3 Hz), 1.32 (t, 3 H, J = 7.3 Hz), 4.13−4.35 (m, 6 H), 4.82 (s, 1 H), 5.31 (s, 1 H), 6.68−6.70 (m, 1 H), 7.27−7.30 (m, 2 H), 7.80−7.81 (m, 1 H); ^{13}C NMR δ 13.8, 13.8, 13.9, 58.4, 62.6, 62.7, 62.8, 68.1, 117.4, 117.6, 124.2, 127.5, 136.0, 146.7, 164.3, 165.9, 168.4, 183.8; HRMS (EI) Calcd for $C_{18}H_{20}Cl_1N_1O_7$ 397.0928, found 397.0902.

*2,3,3-Triethoxycarbonyl-2,3-dihydro-7-methyl-4(1H)-quinolinone (**3ea**).* Solid (243 mg, 65%): mp 125−127 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.13 (t, 3 H, J = 7.1 Hz), 1.28 (t, 3 H, J = 7.3 Hz), 1.32 (t, 3 H, J = 7.3 Hz), 2.27 (s, 3 H), 4.12−4.36 (m, 6 H), 4.82 (s, 1 H), 5.19 (s, 1 H), 6.51−6.52 (m, 1 H), 6.58−6.60 (m, 1 H), 7.24−7.74 (m, 1 H); ^{13}C NMR δ 13.8, 13.8, 14.0, 58.6, 62.4, 62.5, 62.6, 68.5, 114.9, 115.5, 120.6, 128.5, 147.6, 148.4, 164.7, 166.3, 168.9, 184.3; HRMS (EI) Calcd for $C_{16}H_{18}NO_5$ 304.1185 (M^+ − COOEt), found 304.1188.

*2,3,3-Triethoxycarbonyl-2,3-dihydro-6-methyl-4(1H)-quinolinone (**3fa**).* Solid (299 mg, 80%): mp 96−98 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.13 (t, 3 H, J = 7.1 Hz), 1.23 (t, 3 H, J = 7.1 Hz), 1.27 (t, 3 H, J = 7.1 Hz), 2.22 (s, 3 H), 4.07−4.34 (m, 6 H), 4.81 (s, 1 H), 5.27 (s, 1 H), 6.63−6.65 (m, 1 H), 7.14−7.17 (m, 1 H), 7.62−7.63 (m, 1 H); ^{13}C NMR δ 13.8, 13.8, 14.0, 14.2, 20.32, 58.85, 62.4, 62.4, 62.6, 68.7, 115.8, 116.9, 127.8, 128.2, 137.5, 146.5, 164.7, 166.3, 168.8, 184.9; HRMS (EI) Calcd for $C_{19}H_{23}N_1O_7$ 377.1475, found 377.1501.

*2,3,3-Triethoxycarbonyl-2,3-dihydro-6,8-dimethyl-4(1H)-quinolinone (**3ga**).* Solid (315 mg, 81%): mp 104−108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.14 (t, 3 H, J = 7.1 Hz), 1.29 (t, 3 H, J = 7.2 Hz), 1.31 (t, 3 H, J = 7.2 Hz), 2.16 (s, 3 H), 2.20 (s, 3 H), 4.10−4.33 (m, 6 H), 4.83 (s, 1 H), 5.05 (s, 1 H), 7.07 (s, 1 H), 7.55 (s, 1 H); ^{13}C NMR δ 13.8, 14.0, 16.5, 20.3, 58.6, 62.3, 62.5, 62.6, 68.3, 116.60, 123.0, 125.7, 127.5, 138.2, 144.9, 164.7, 166.4, 169.1, 185.1; HRMS (EI) Calcd for $C_{20}H_{25}N_1O_7$ 391.1631, found 391.1643.

*2,3,3-Triethoxycarbonyl-2,3-dihydro-8-methoxy-4(1H)-quinolinone (**3ha**).* Solid (302 mg, 84%): mp88−90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (t, 3 H, J = 7.1 Hz), 1.22 (t, 3 H, J = 7.1 Hz), 1.27 (s, 3 H, J = 7.1 Hz), 3.83 (s, 3 H), 4.27−4.32 (m, 6 H), 4.82 (s, 1 H), 5.70 (s, 1 H), 6.65−6.69 (m, 1 H), 6.83−6.85 (m, 1 H), 7.41−7.44 (m, 1 H); ^{13}C NMR δ 13.8, 13.9, 14.0, 55.7, 58.7, 62.4, 62.6, 68.3, 114.3, 116.8, 117.6, 119.3, 139.8, 146.8, 164.6, 166.3, 168.6, 184.8; HRMS (EI) $C_{19}H_{23}NO_8$ 393.1424, found 393.1401.

*2,3,3-Triethoxycarbonyl-2,3-dihydro-6-methoxy-4(1H)-quinolinone (**3ia**).* Solid (352 mg, 90%): mp 116−117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.14 (t, 3 H, J = 7.1 Hz), 1.28 (t, 3 H, J = 7.1 Hz), 1.32 (t, 3 H, J = 7.1 Hz), 3.75 (s, 3 H), 4.11−4.25 (m, 6 H), 4.81 (s, 1 H), 5.06 (brs, 1 H), 6.67−6.70 (m, 1 H), 7.00−7.03 (m, 1 H), 7.24−7.28 (m, 1 H); ^{13}C NMR δ 13.9, 14.0, 55.7, 59.2, 62.4, 62.7, 68.5, 108.16, 116.9, 117.5, 126.7, 143.6, 152.68, 164.7, 166.3, 168.7, 184.7; HRMS (EI) Calcd for $C_{19}H_{23}NO_8$ 393.1424, found 393.1437.

*2,3,3-Triethoxycarbonyl-2,3-dihydro-7-methoxy-4(1H)-quinolinone (**3ja**).* Solid (99 mg, 26%): mp 105−108 °C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (t, 3 H, J = 7.1 Hz), 1.22 (t, 3 H, J = 7.1 Hz), 1.30 (t, 3 H, J = 7.1 Hz), 3.77 (s, 3 H), 4.06−4.31 (m, 6 H), 4.82 (s, 1 H), 5.31 (s, 1 H), 6.11 (d, 1 H, J = 2.4 Hz), 6.31−6.35 (m, 1 H), 7.75−7.77 (m, 1 H); ^{13}C NMR δ 13.8, 14.0, 14.1, 55.5, 58.6, 62.3, 62.4, 62.58, 68.3, 97.7, 108.24, 111.2, 130.7, 150.4, 164.8, 166.2, 166.4, 168.9, 183.2; HRMS (EI) Calcd for $C_{19}H_{23}NO_8$ 393.1424, found 393.1422.

*2-Acetyl-3,3-diethoxycarbonyl-2,3-dihydro-4(1H)-quinolinone (**3ac**).* Liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.11 (t, 3 H, J = 7.1 Hz), 1.36 (t, 3 H, J = 7.1 Hz), 2.30 (s, 3 H), 4.12−4.16 (m, 2 H), 4.40 (t, 2 H, J = 7.1 Hz), 4,74 (s, 1 H), 5.60 (brs, 1 H), 6.69−6.76 (m, 2 H), 7.30−7.33 (m, 1 H), 7.80−7.82 (m, 1 H); ^{13}C NMR δ 13.6, 14.0, 27.3, 62.9, 63.1, 64.9, 69.0, 115.7, 118.6, 128.4, 136.3, 148.2, 165.2, 167.1, 184.9, 201.0; HRMS (EI) Calcd for $C_{17}H_{19}NO_6$ 333.1212, found 333.1201.

*2-Cyano-3,3-diethoxycarbonyl-2,3-dihydro-4(1H)-quinolinone (**3ad**).* Liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (t, 3 H, J = 7.1 Hz), 1.36 (t, 3 H, J = 7.1 Hz), 4.23 (t, 2 H, J = 7.1 Hz), 4.34 (t, 2 H, J = 7.1 Hz), 6.85−6.87 (m, 1 H), 7.18−7.20 (m, 1 H), 7.34−7.38 (m, 1 H), 7.80−7.82 (m, 1 H), 11.05 (brs, 1 H); ^{13}C NMR δ 14.5, 60.3, 60.6, 89.0, 95.4, 116.3, 126.1, 129.7, 140.0, 140.8, 151.2; HRMS (EI) Calcd for $C_{13}H_{11}N_2O_3$ 243.0770 (M^+ − COOEt), found 243.0755.

*2-Trifluoromethyl-3,3-diethoxycarbonyl-2,3-dihydro-4(1H)-quinolinone (**3ae**).* Liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19−1.25 (m, 6 H), 4.23−4.28 (m, 4 H), 4.81−4.87 (m, 2 H), 6.71−6.73 (m, 1 H), 6.82−6.86 (m, 1 H), 7.34−7.38 (m, 1 H), 7.85−7.87 (m, 1H); ^{13}C NMR δ 13.7, 13.7, 59.9 (q, J = 31.5 Hz), 62.8, 63.2, 65.8, 115.9, 118.0, 120.0, 124.1 (d, J = 283.9 Hz), 128.2, 136.2, 147.5, 164.0, 164.6, 183.0; HRMS (EI) Calcd for $C_{16}H_{16}F_3N_1O_5$ 359.0981, found 359.0978.

dx.doi.org/10.1021/jo300173g | *J. Org. Chem.* 2012, 77, 4420−4424

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra of compounds **1e**, **2a**−**2e**, and **3**−**5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful to the Natural Sciences and Engineering Research Council of Canada (NSERC) for financial support of this research.

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