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Synthesis of highly substituted pyrroles via oxidative free radical reactions of β-aminocinnamates

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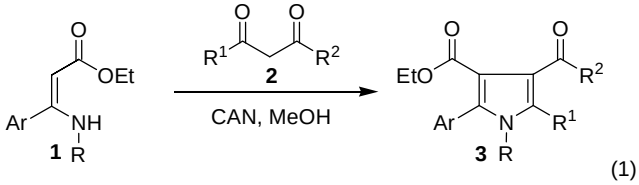
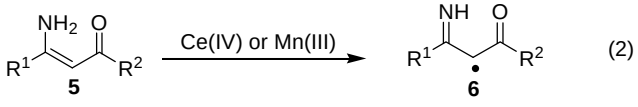
Abstract—Oxidative free radical reactions of β-aminocinnamates are described. Imine radicals produced by tetra-*n*-butylammonium cerium(IV) nitrate (TBACN) oxidation of enamines undergo efficient addition to the C–C double bond of β-aminocinnamates. This TBACN mediated free radical reaction between β-aminocinnamates and enamines provides a novel method for the synthesis of highly substituted pyrroles. The direct TBACN oxidation of β-aminocinnamates gave the dimerization products effectively.

1. Introduction

Free radical reactions have become increasingly important in organic synthesis in the last two decades.[1] The oxidative addition of an electrophilic carbon-centered radical to alkenes mediated by metal salts has received considerable attention in the organic synthesis for the construction of carbon–carbon bonds. Among these, manganese(III) acetate and cerium(IV) ammonium nitrate (CAN) have been used most efficiently.[1d–f,2,3] Pyrrole derivatives represent a class of compounds of great important in heterocyclic chemistry primarily due to the fact that pyrroles are important substructures of pharmaceutical agents and also of numerous natural products.[4] Accordingly, substantial attention has been paid to develop efficient methods for the synthesis of pyrroles.[5] Earlier, we have reported that oxidative free radical reactions between β-anilinocinnamate **1** and 1,3-dicarbonyl compound **2** produced the desired pyrrole products **3** (29–54%) and dimerization product **4** (0–18%) (Eq. 1).[6] Imine radical **6** can be generated from the oxidation of enamine **5** by metal salts (Eq. 2) and it undergoes efficient addition to the C–C double bond.[7] We describe here a much more effective method for the synthesis of highly substituted pyrroles via the oxidative free radical reaction between β-aminocinnamates and enamines.





2. Results and discussion

The oxidative free radical reaction between β-anilinocinnamate **1** and enamine **5** was first examined (Eq. 3). When β-anilinocinnamate **1a** was treated with enamine **5a** and CAN in MeOH at room temperature, pyrrole **3a** was obtained in 54% yield and no dimerization product **4a** could be found (Table 1, entry 1). A plausible mechanism for this reaction is shown in Scheme 1. Initiation occurs with CAN oxidation of enamine **5a** to produce imine radical **6a**.

Keywords: Tetra-*n*-butylammonium cerium(IV) nitrate; Oxidative; Free radical; β-Aminocinnamates.
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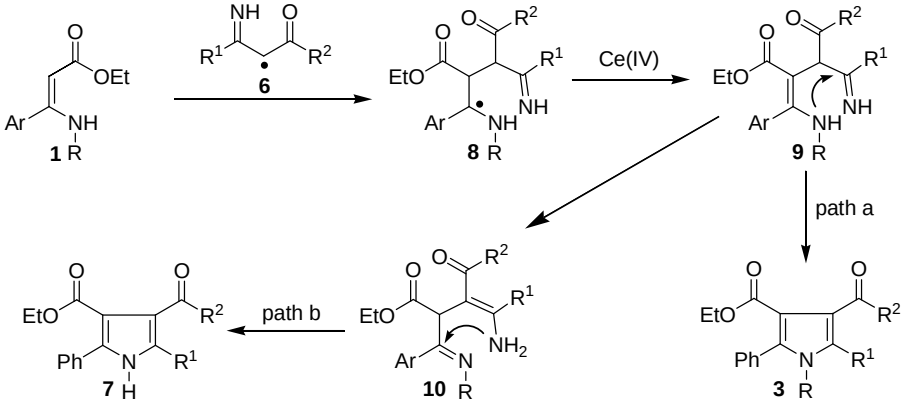
Table 1. Free radical reactions of β-aminocinnamates

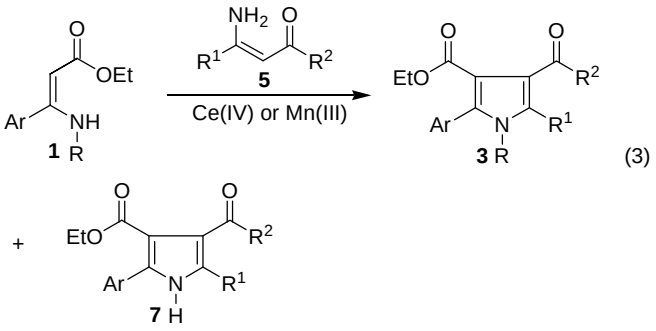
Entry	β-Aminocinnamate	Enamine	Oxidant	Solvent	Product (yield (%))
1	**1a**: R=*p*-ClPh, Ar=Ph	**5a**: R^1=Me, R^2=OEt	CAN	MeOH	**3a** (54)
2	**1a**: R=*p*-ClPh, Ar=Ph	**5a**: R^1=Me, R^2=OEt	$Me(OAc)_3$	HOAc	**3a** (62)
3	**1a**: R=*p*-ClPh, Ar=Ph	**5a**: R^1=Me, R^2=OEt	TBACN	MeOH	**3a** (92)
4	**1a**: R=*p*-ClPh, Ar=Ph	**5a**: R^1=Me, R^2=OEt	TBACN	MeCN	**3a** (88)
5	**1a**: R=*p*-ClPh, Ar=Ph	**5a**: R^1=Me, R^2=OEt	TBACN	$CHCl_3$	**3a** (92)
6	**1a**: R=*p*-ClPh, Ar=Ph	**5b**: R^1=Et, R^2=OMe	TBACN	MeOH	**3b** (61) **7b** (30)
7	**1a**: R=*p*-ClPh, Ar=Ph	**5b**: R^1=Et, R^2=OMe	TBACN	$CHCl_3$	**3b** (81)
8	**1a**: R=*p*-ClPh, Ar=Ph	**5c**: R^1=^{i}Pr, R^2=OEt	TBACN	MeOH	**3c** (17) **7c** (55)
9	**1a**: R=*p*-ClPh, Ar=Ph	**5c**: R^1=^{i}Pr, R^2=OEt	TBACN	$CHCl_3$	**3c** (45) **7c** (30)
10	**1a**: R=*p*-ClPh, Ar=Ph	**5d**: R^1=Pr, R^2=OEt	TBACN	$CHCl_3$	**3d** (75)
11	**1a**: R=*p*-ClPh, Ar=Ph	**5e**: R^1=Me, R^2=Me	TBACN	$CHCl_3$	**3e** (79)
12	**1a**: R=*p*-ClPh, Ar=Ph	**5f**: R^1=Et, R^2=Et	TBACN	$CHCl_3$	**3f** (61)
13	**1b**: R=*p*-BrPh, Ar=Ph	**5a**: R^1=Me, R^2=OEt	TBACN	$CHCl_3$	**3g** (94)
14	**1c**: R=*p*-EtO_2CPh, Ar=Ph	**5a**: R^1=Me, R^2=OEt	TBACN	$CHCl_3$	**3h** (91)
15	**1d**: R=Ph, Ar=Ph	**5a**: R^1=Me, R^2=OEt	TBACN	$CHCl_3$	**3i** (96)
16	**1e**: R=CH_2CN, Ar=Ph	**5a**: R^1=Me, R^2=OEt	TBACN	$CHCl_3$	**3j** (76)
17	**11a**: Ar=Ph	**5a**: R^1=Me, R^2=OEt	CAN	MeOH	**7a** (59)
18	**11a**: Ar=Ph	**5a**: R^1=Me, R^2=OEt	TBACN	MeOH	**7a** (87)
19	**11a**: Ar=Ph	**5a**: R^1=Me, R^2=OEt	TBACN	MeCN	**7a** (92)
20	**11a**: Ar=Ph	**5a**: R^1=Me, R^2=OEt	TBACN	$CHCl_3$	**7a** (89)
21	**11a**: Ar=Ph	**5b**: R^1=Et, R^2=OMe	TBACN	MeOH	**7b** (89)
22	**11a**: Ar=Ph	**5c**: R^1=^{i}Pr, R^2=OEt	TBACN	MeOH	**7c** (84)
23	**11a**: Ar=Ph	**5e**: R^1=Me, R^2=Me	TBACN	MeOH	**7d** (69) **12a** (14)
24	**11a**: Ar=Ph	**5f**: R^1=Et, R^2=Et	TBACN	MeOH	**7e** (72)

This radical intermediate **6a** undergoes intermolecular addition followed by oxidation to give **9a**, which undergoes nucleophilic addition of anilino group followed by elimination of ammonia to produce pyrrole **3a** (path a). There is no trace of another expected pyrrole product **7a** can be detected, which is presumably derived from the nucleophilic addition of amino group of **10a** (path b). With $Mn(OAc)_3$ in HOAc, pyrrole **3a** was obtained in 62% yield (entry 2). It has been reported that tetra-*n*-butylammonium cerium(IV) nitrate (TBACN) oxidized 1,3-dicarbonyl compounds more slowly than CAN.[8] We expected that pyrrole **3a** could be generated in a better result by using TBACN. Indeed, with TBACN, the reaction between β-anilinocinnamate **1a** and enamine **5a** in MeOH afforded pyrrole **3a** in an impressive 92% yield (entry 3).[9] With other enamines **5b** and **5c**, in addition to the formation of products **3b** and **3c**, pyrroles **7b** and **7c** were also obtained (entries 6 and 8). The ratios of **3/7** decrease as the size of substituents (R^1) on enamine **5** increases. This is presumably due to the steric effect exerted by R^1 group—the addition rate of anilino group (path a) was retarded by the larger R^1 and competitive nucleophilic addition of amino group (path b) occurred. In attempt to investigate the range of solvents compatible with this reaction, this reaction was performed in various solvents. With enamine **5a**, the change of solvent to CH_3CN or $CHCl_3$ gave only pyrrole **3a** in a similar yield (entries 4 and 5). With enamine **5b**, we are surprised to found that pyrrole **3b** was obtained in a much better yield (81%) from **1a** and no pyrrole **7b** could be isolated by using $CHCl_3$ as solvent (entry 7). Since TBACN/$CHCl_3$ is the most effective reaction condition for the formation of pyrrole **3**, so the scope of this reaction was explored with a variety of β-anilinocinnamate **1** and enamine **5** using the TBACN/$CHCl_3$ conditions. As shown in Table 1, this method proved to be of general applicability on β-anilinocinnamate **1** and enamine **5**. In most cases, β-anilinocinnamate **1** was smoothly converted to the corresponding pyrrole **3** selectively in excellent to good



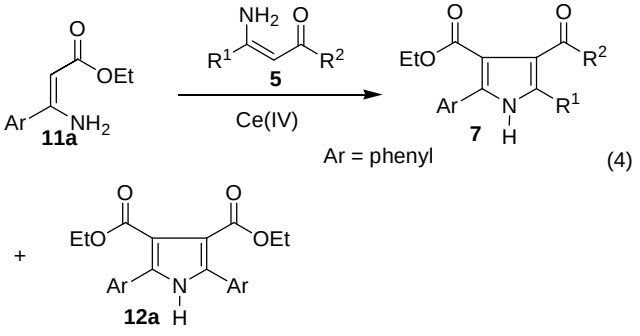
Scheme 1.

yield (entries 9–15). In addition, when β-alkylaminocinnamate **1e** was reacted with enamine **5a** under similar conditions, pyrrole **3j** was obtained in 76% yield (entry 16).



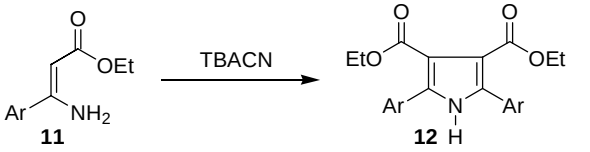
(3)

The oxidative free radical reaction of β-aminocinnamate **11a** was next studied (Eq. 4). Reaction of β-aminocinnamate **11a** with enamine **5a** and CAN in MeOH afforded pyrrole **7a** in 59% yield (entry 17) and the reaction yield was increased to 87% by replacing CAN with TBACN (entry 18). We also examined the effect of various solvents on the yield of pyrrole **7a**. Use MeCN or $CHCl_3$ as solvent, pyrrole **7a** was formed in a similar result (entries 19 and 20). Based on these results, we also examined this TBACN mediated reaction of β-aminocinnamate **11a** with various enamines **5** in MeOH and the results were also summarized in Table 1 (entries 21–24). Again, the reaction worked well and pyrrole **7** was formed in good yield. For an unknown reason, with enamine **5e**, in addition to the desired pyrrole **7e**, the dimerization product **12a** was also isolated (entry 23).



(4)

The preparation of highly substituted C_2-symmetric pyrroles by the oxidative dimerization of enamino esters has been reported.[6,10] On the basis of the generation of dimerization product **12a** in the reaction between β-aminocinnamate **11a** and enamine **5e**, we expected that the direct TBACN oxidation of β-aminocinnamate **11** would produce dimerization product **12** effectively (Eq. 5). Indeed, the formation of dimerization product **12a** (82%) was achieved by the oxidation of β-aminocinnamate **11a** with TBACN in methanol. Analogous results were obtained with other β-aminocinnamates **11** and were summarized in Table 2 (entries 1–5). The *N*-alkyl substituted β-aminocinnamate **1e** also underwent the direct TBACN oxidation reaction, producing pyrrole **4c** in a much better yield than that performed with CAN (entry 6).[6] The TBACN mediated oxidative dimerization of β-anilinocinnamates **1** was also studied. As shown in Table 2, while β-aminocinnamate **11a**–**11e** was converted to the corresponding dimerization product **12** in good yields (entries 1–5), the dimerization of β-anilinocinnamate **1** was less productive (entries 7 and 8).



(5)

Table 2. Oxidative dimerization of β-aminocinnamates

Entry	β-Aminocinnamate	Product (yield (%))
1	**11a**: Ar=Ph	**12a** (82)
2	**11b**: Ar=*p*-Tolyl	**12b** (80)
3	**11c**: Ar=*p*-BrPh	**12c** (88)
4	**11d**: Ar=*p*-ClPh	**12d** (87)
5	**11e**: R=*p*-NO_2Ph	**12e** (96)
6	**1e**: R=CH_2CN, Ar=Ph	**4c** (75)
7	**1a**: R=*p*-ClPh, Ar=Ph	**4a** (41)
8	**1c**: R=*p*-EtO_2CPh, Ar=Ph	**4b** (46)

In conclusion, imine radical **6** generated from the TBACN oxidation of enamine **5** undergoes efficient addition to the C–C double bond of β-aminocinnamates. This free radical reaction provides a novel method for the synthesis of highly substituted pyrroles from readily available β-aminocinnamates and enamines. The dimerization product **12** can also be synthesized effectively by the direct TBACN oxidation of β-aminocinnamate **11**.

3. Experimental

3.1. General considerations

Melting points are uncorrected. Infrared spectra were taken with a Hitachi 260-30 spectrometer. The NMR spectra were recorded on a Brucker AVANCE 300, AMX-400 or AVANCE 500 spectrometer. Chemical shifts are reported in ppm relative to TMS as internal reference. Elemental analyses were performed with Heraeus CHN-Rapid Analyzer. Analytical thin-layer chromatography was performed with precoated silica gel 60 F-254 plates (0.25 mm thick) from EM Laboratories and visualized by UV light. The reaction mixture was purified by column chromatography over EM Laboratories silica gel (70–230 mesh). The starting β-aminocinnamates **1**[10b,11a] and **11**[11b] were synthesized according to literature procedures. TBACN was prepared with CAN and tetra-*n*-butylammonium hydrogen sulfate.[12] Spectra data of pyrroles **3a**–**j** and dimerization products **4a**–**c** have been reported.[6]

3.2. Typical experimental procedure for the free radical reaction between β-aminocinnamates and enamines

A solution of 132 mg (0.69 mmol) of ethyl 3-aminocinnamate (**11a**), 446 mg (3.46 mmol) of ethyl 3-aminocrotonate (**5a**) and 1.39 g (1.39 mmol) of TBACN in 10 mL of MeOH was stirred at room temperature for 30 min and another 1.39 g (1.39 mmol) of TBACN was added. After

stirred for another 30 min, the reaction mixture was diluted with EtOAc (100 mL), washed with aq satd $NaHSO_3$ (50 mL) and H_2O (3×50 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was chromatographed over 15 g of silica gel (EtOAc/hexane, 1:4) followed by recrystallization (EtOAc–hexane) to give 182 mg (87%) of pyrrole **7a**.

3.2.1. 3,4-Diethoxycarbonyl-2-methyl-5-phenylpyrrole (7a). White crystals; mp 100–101 °C; IR ($CHCl_3$) 3455, 3305, 2990, 1700, 1445, 1285, 1095 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.26 (t, J=7.1 Hz, 3H, CH_3), 1.33 (t, J=7.2 Hz, 3H, CH_3), 2.51 (s, 3H, CH_3), 4.27 (q, J=7.1 Hz, 2H, OCH_2), 4.28 (q, J=7.2 Hz, 2H, OCH_2), 7.27–7.42 (m, 3H, ArH), 7.42–7.50 (m, 2H, ArH), 8.37 (br s, 1H, NH); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 12.7 (q), 14.0 (q), 14.2 (q), 59.9 (t), 61.0 (t), 112.1 (s), 114.5 (s), 126.9 (2d), 127.8 (d), 128.5 (2d), 130.6 (s), 130.9 (s), 135.4 (s), 164.7 (s), 167.1 (s). Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65. Found: C, 67.76; H, 6.35; N, 4.64.

3.2.2. 4-Ethoxycarbonyl-2-ethyl-3-methoxycarbonyl-5-phenylpyrrole (7b). White crystals; mp 88–89 °C; IR ($CHCl_3$) 3455, 3310, 2985, 1690, 1450, 1285, 1100 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.26 (t, J=7.1 Hz, 6H, $2CH_3$), 2.93 (q, J=7.6 Hz, 2H, CH_2), 3.80 (s, 3H, OCH_3), 4.26 (q, J=7.1 Hz, 2H, OCH_2), 7.28–7.39 (m, 3H, ArH), 7.43–7.49 (m, 2H, ArH), 8.50 (br s, 1H, NH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 13.6 (q), 14.0 (q), 20.2 (t), 51.1 (q), 61.0 (t), 111.3 (s), 114.6 (s), 127.1 (2d), 127.9 (d), 128.6 (2d), 130.8 (s), 130.9 (s), 140.9 (s), 165.0 (s), 166.8 (s). Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65. Found: C, 67.72; H, 6.38; N, 4.63.

3.2.3. 3,4-Diethoxycarbonyl-2-isopropyl-5-phenylpyrrole (7c). White crystals; mp 118–119 °C; IR ($CHCl_3$) 3460, 3315, 2980, 1700, 1445, 1280, 1230 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.25 (t, J=7.2 Hz, 3H, CH_3), 1.29 (d, J=7.0 Hz, 6H, $2CH_3$), 1.31 (t, J=7.1 Hz, 3H, CH_3), 3.70 (septet, J=7.0 Hz, 1H, CH), 4.24 (q, J=7.2 Hz, 2H, OCH_2), 4.25 (q, J=7.1 Hz, 2H, OCH_2), 7.28–7.39 (m, 3H, ArH), 7.43–7.49 (m, 2H, ArH), 8.52 (br s, 1H, NH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.0 (q), 14.2 (q), 21.9 (2q), 25.8 (d), 60.0 (t), 60.9 (t), 111.1 (s), 114.5 (s), 127.3 (2d), 128.0 (d), 128.6 (2d), 130.7 (s), 131.1 (s), 144.3 (s), 164.5 (s), 166.6 (s). Anal. Calcd for $C_{19}H_{23}NO_4$: C, 69.28; H, 7.04; N, 4.25. Found: C, 69.23; H, 7.10; N, 4.25.

3.2.4. 3-Acetyl-4-ethoxycarbonyl-2-methyl-5-phenylpyrrole (7d). White crystals; mp 92–93 °C; IR ($CHCl_3$) 3450, 3280, 3000, 1705, 1655, 1420, 1120 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.21 (t, J=7.1 Hz, 3H, CH_3), 2.42 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 4.22 (q, J=7.1 Hz, 2H, OCH_2), 7.31–7.40 (m, 3H, ArH), 7.46 (d, J=7.4 Hz, 2H, ArH), 8.60 (br s, 1H, NH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 13.2 (q), 13.9 (q), 30.3 (q), 60.9 (t), 113.3 (s), 122.8 (s), 127.9 (2d), 128.2 (d), 128.4 (2d), 131.0 (s), 132.8 (s), 133.7 (s), 166.4 (s), 196.5 (s). Anal. Calcd for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.71; H, 6.36; N, 5.17.

3.2.5. 3-Ethoxycarbonyl-5-ethyl-2-phenyl-4-propionylpyrrole (7e). White crystals; mp 113–114 °C; IR ($CHCl_3$) 3450, 3300, 2985, 1700, 1450, 1270 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.16 (t, J=7.3 Hz, 3H, CH_3), 1.18 (t, J=7.1 Hz, 3H, CH_3), 1.26 (t, J=7.6 Hz, 3H, CH_3), 2.77 (q, J=7.3 Hz, 2H, CH_2), 2.82 (q, J=7.6 Hz, 2H, CH_2), 4.21 (q, J=7.1 Hz, 2H, OCH_2), 7.33–7.43 (m, 3H, ArH), 7.46–7.52 (m, 2H, ArH), 8.32 (br s, 1H, NH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 8.6 (q), 13.9 (2q), 20.2 (t), 35.9 (t), 60.7 (t), 112.4 (s), 122.2 (s), 128.26 (3d), 128.30 (2d), 131.3 (s), 133.6 (s), 138.1 (s), 166.0 (s), 201.0 (s). Anal. Calcd for $C_{18}H_{21}NO_3$: C, 72.22; H, 7.07; N, 4.68. Found: C, 72.32; H, 7.13; N, 4.64.

3.3. Typical procedure for the oxidative dimerization reaction of β-aminocinnamates

A solution of 138 mg (0.72 mmol) of ethyl 3-aminocinnamate (**11a**), and 722 mg (0.72 mmol) of TBACN in 10 mL of MeOH was stirred at room temperature for 30 min. After the work-up as described for the preparation of pyrrole **7a**, the residue was chromatographed over 15 g of silica gel (EtOAc/hexane, 1:6) followed by recrystallization (EtOAc–hexane) to give dimerization product **12a** (107 mg, 82%).

3.3.1. 3,4-Diethoxycarbonyl-2,5-diphenylpyrrole (12a). White crystals; mp 149–150 °C; IR ($CHCl_3$) 3450, 2990, 1715, 1490, 1225, 1125 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.25 (t, J=7.1 Hz, 6H, $2CH_3$), 4.24 (q, J=7.1 Hz, 4H, $2OCH_2$), 7.39–7.44 (m, 6H, ArH), 7.51–7.59 (m, 4H, ArH), 8.59 (br s, 1H, NH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.0 (2q), 60.7 (2t), 114.5 (2s), 128.1 (4d), 128.5 (6d), 130.9 (2s), 134.2 (2s), 165.2 (2s). Anal. Calcd for $C_{22}H_{21}NO_4$: C, 72.71; H, 5.82; N, 3.85. Found: C, 72.63; H, 5.83; N, 3.83.

3.3.2. 3,4-Diethoxycarbonyl-2,5-di-(*p*-tolyl)pyrrole (12b). White crystals; mp 137–138 °C; IR (KBr) 3265, 2980, 1725, 1680, 1220 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.25 (t, J=7.1 Hz, 6H, $2CH_3$), 2.37 (s, 6H, $2CH_3$), 4.23 (q, J=7.1 Hz, 4H, $2OCH_2$), 7.20 (d, J=8.1 Hz, 4H, ArH), 7.44 (d, J=8.1 Hz, 4H, ArH), 8.54 (br s, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 14.0 (2q), 21.3 (2q), 60.6 (2t), 114.0 (2s), 128.0 (4d), 129.1 (4d), 134.2 (2s), 138.4 (2s), 165.3 (2s). Anal. Calcd for $C_{24}H_{25}NO_4$: C, 73.64; H, 6.44; N, 3.57. Found: C, 73.61; H, 6.41; N, 3.55.

3.3.3. 2,5-Di-(*p*-bromophenyl)-3,4-diethoxycarbonylpyrrole (12c). White crystals; mp 211–212 °C; IR (KBr) 3290, 2980, 1700, 1485, 1285 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.26 (t, J=7.1 Hz, 6H, $2CH_3$), 4.25 (q, J=7.1 Hz, 4H, $2OCH_2$), 7.40–7.46 (m, 4H, ArH), 7.52–7.57 (m, 4H, ArH), 8.55 (br s, 1H, NH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.0 (2q), 60.9 (2t), 115.0 (2s), 123.0 (2s), 129.5 (2s), 129.7 (4d), 131.8 (4d), 133.3 (2s), 164.9 (2s). Anal. Calcd for $C_{22}H_{19}Br_2NO_4$: C, 50.70; H, 3.68; N, 2.69. Found: C, 50.83; H, 3.66; N, 2.68.

3.3.4. 2,5-Di-(*p*-chlorophenyl)-3,4-diethoxycarbonylpyrrole (12d). White crystals; mp 222–223 °C; IR (KBr) 3295, 2980, 1700, 1485, 1450 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.27 (t, J=7.1 Hz, 6H, $2CH_3$), 4.26 (q, J=7.1 Hz, 4H, $2OCH_2$), 7.40 (d, J=8.5 Hz, 4H, ArH), 7.51 (d, J=8.5 Hz, 4H, ArH), 8.48 (br s, 1H, NH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.1 (2q), 60.9 (2t), 115.0 (2s), 128.9 (4d), 129.1 (2s), 129.5 (4d), 133.3 (2s), 134.8 (2s),

164.8 (2s). Anal. Calcd for $C_{22}H_{19}Cl_2NO_4$: C, 61.12; H, 4.43; N, 3.24. Found: C, 61.13; H, 4.42; N, 3.23.

3.3.5. 3,4-Diethoxycarbonyl-2,5-di-(*p*-nitrophenyl)-pyrrole (12e). Yellow crystals; mp 217–218 °C; IR (KBr) 3230, 1740, 1680, 1345, 1225 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.29 (t, $J=7.1$ Hz, 6H, $2CH_3$), 4.30 (q, $J=7.1$ Hz, 4H, $2OCH_2$), 7.76 (d, $J=8.8$ Hz, 4H, ArH), 8.29 (d, $J=8.8$ Hz, 4H, ArH), 9.01 (br s, 1H, NH); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.0 (2q), 61.4 (2t), 117.1 (2s), 123.9 (4d), 128.8 (4d), 132.7 (2s), 136.5 (2s), 147.6 (2s), 164.3 (2s). Anal. Calcd for $C_{22}H_{19}N_3O_8$: C, 58.28; H, 4.22; N, 9.27. Found: C, 58.37; H, 4.23; N, 9.30.

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