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An efficient one-pot synthesis of tetra-substituted pyrroles

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Dedicated to Prof. A. Rustaiyan on the occasion of his 85th birthday

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ABSTRACT

The three-component reaction of primary amines, dialkyl acetylenedicarboxylates and β-nitrostyrene derivatives in the presence of Iron(III) chloride afforded 1,2,3,4-tetra-substituted pyrroles in high yields. These reactions could precede via domino Michael addition/cyclization process.

1. Introduction

Pyrroles and their derivatives are one of the most important class of heterocyclic compounds.[1] They have extensive biological activities and pharmacological properties.[2] Many pyrrole derivatives exhibit interesting biological properties, such as anti-bacterial,[3] anti-inflammatory,[4] anti-oxidant,[5] anti-tumor, anti-fungal,[6] and immune suppressant activities.[7] Highly functionalized pyrroles are subunits of considerable importance in heme, chlorophyll, bile pigments, vitamin B_{12},[8] and marine source-derived pyrrole alkaloids. Some characteristic examples of these compounds with their biological activities are shown in Fig. 1.[9,10] Atrovastatin (Lipitor) is a drug for lowering the cholesterol.[11]

There have been considerable studies on the effects of substituents and the design of the pyrrole skeleton, which contain active substituents. The development of new and efficient methods for their synthesis remains an area of current interest. Many synthetic methods have been employed for the synthesis of pyrroles including Knorr,[12] Paal–Knorr,[13] Hantzsch synthesis,[14] 1,3-dipolar cycloaddition reactions,[15] reductive coupling,[16] and aza-Wittig reactions.[17] Recently, Das et al. reported three-component reaction of amines, DMAD, and phenacyl bromide catalyzed by Iron(III) chloride to synthesis of 1,2,3,5-tetra-substituted pyrroles.[18] Meanwhile, there are various pyrrole synthesis in the litratures.[19–24]

However a number of methods have some drawbacks, such as harsh reaction conditions, tedious experimental procedures, long reaction time, and low yields.[25] Although a number of methods are available as cited above, the search for newer, more efficient methods for the synthesis of pyrroles is currently being pursued. β-Nitrostyrene and its derivatives are useful synthetic intermediates and starting materials for the synthesis of a variety of useful building blocks.[26] According to their high potential for the synthesis, and in continuation of our research toward novel multicomponent reactions for the synthesis of heterocyclic skeletons,[27] we wish to report herein, the efficient one-pot three-component reaction of primary amines, dialkyl acetylenedicarboxylates, and β-nitrostyrene derivatives in the presence of $FeCl_3$, which leads to 1,2,3,4-tetra-substituted pyrroles in high yields (Scheme 1).

2. Results and discussions

We began our investigation with β-nitrostyrene **3a**, which was synthesized according to the reported method.[28] The reaction of **3a** with benzylamine and dimethyl acetylenedicarboxylate was selected as the model reaction. Heating of the mixture in toluene in the presence of 40 (mol %) CuI for 72 h did not provide our goal and the mixture of *E* and *Z* of enaminones was obtained. After this

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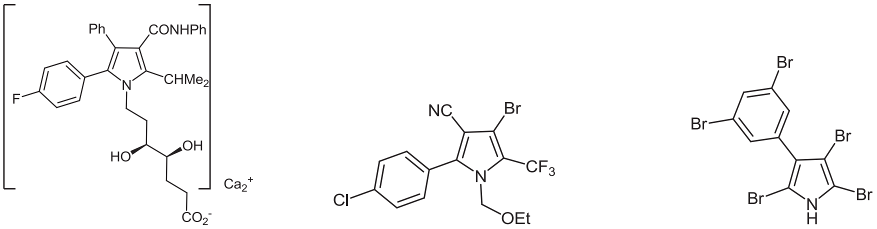
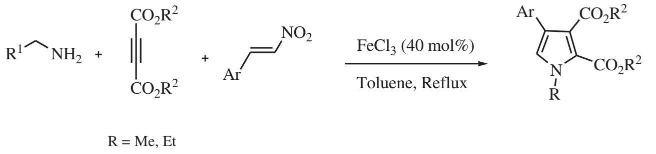


Atorvastatin (Lipitor) Chlorfenapyr (insecticide) Pentaboromopseudilin (antibacterial)

Fig. 1. Molecular structure of some biologically active compounds contained pyrrole skeleton.



1 a-e **2 a, b** **3 a-g** **4 a-p** (75-95%)

Scheme 1.

failure, we tried various Lewis acids; such as ZrO_2, $ZrCl_4$, and the desired product did not achieved. Recently, Iron(III) chloride was used as an efficient catalyst for the synthesis of carbon–heteroatom and heteroatom–heteroatom linkages with high valuable advantages.[29] We only got satisfactory results $ZnCl_2$ and $FeCl_3$. The best result was obtained with $FeCl_3$. According to this result, $FeCl_3$ was selected as the best catalyst for the synthesis of tetra-substituted pyrroles. Then the catalytic amount of this catalyst was examined in the model reaction. The reaction was checked without $FeCl_3$ as catalyst, and we did not get any product. In the presence of 10, 20, 30, and 40% of $FeCl_3$, the yield of tetra-substituted pyrrole **4a** obtained was 40, 48, 70, and 85%, respectively. This shows the important role of $FeCl_3$ in this reaction. The optimum reaction condition used of 40% $FeCl_3$ and boiling toluene as reaction medium.

In an attempt to investigate the range of solvents compatible with this reaction, β-nitrostyrene **3a** and enaminone from reaction of benzylamine and dimethyl acetylendicarboxylate were chosen for a model system, and this reaction was performed in various solvents. A change in the solvent to dichloromethane, ethanol, acetonitrile, and toluene gave pyrrole **4a** in 16–85% yield. In ethanol and acetonitrile, the reaction had low yield. The best yield for reaction model was obtained in toluene.

After finding suitable conditions, the three-component reaction of β-nitrostyrenes, dialkyl acetylenes, and also primary amines for the synthesis of tetra-substituted pyrroles were studied. The results summarized in Table 1.

Table 1
Synthesis of tetra-substituted pyrroles using β-nitrostyrene

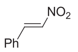
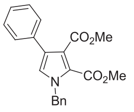
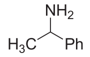
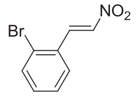
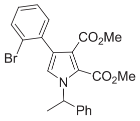
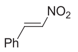
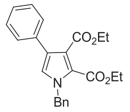
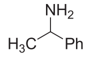
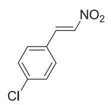
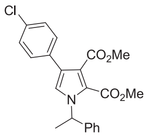
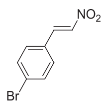
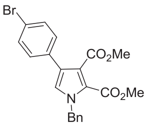
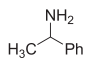
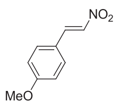
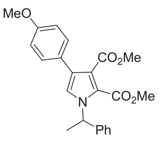
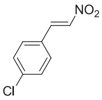
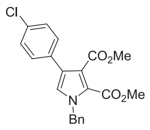
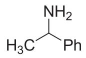
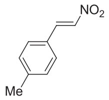
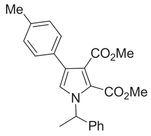
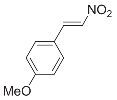
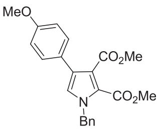
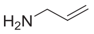
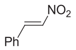
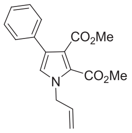
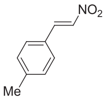
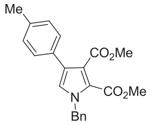
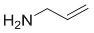
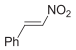
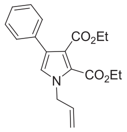
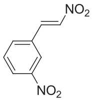
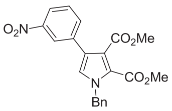
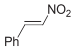
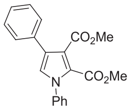
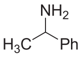
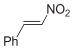
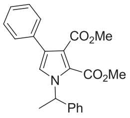
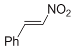
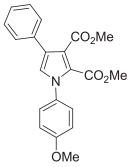
Amine	β-Nitrostyrene	Product	Amine	β-Nitrostyrene	Product
Bn–NH_2 **1a**	 **3a**	 **4a**(83%[a])	 **1b**	 **3c**	 **4i**(87%)
Bn–NH_2 **1a**	 **3a**	 **4b**(87%)	 **1b**	 **3d**	 **4j**(93%)
Bn–NH_2 **1a**	 **3b**	 **4c**(83%)	 **1b**	 **3e**	 **4k**(80%)

Table 1 (*continued*)

Amine	β-Nitrostyrene	Product	Amine	β-Nitrostyrene	Product
Bn−NH$_2$ **1a**	 **3d**	 **4d(94%)**	 **1b**	 **3f**	 **4l(80%)**
Bn−NH$_2$ **1a**	 **3e**	 **4e(87%)**	 **1c**	 **3a**	 **4m(85%)**
Bn−NH$_2$ **1a**	 **3f**	 **4f(95%)**	 **1c**	 **3a**	 **4n(87%)**
Bn−NH$_2$ **1a**	 **3g**	 **4g(82%)**	Ph−NH$_2$ **1d**	 **3a**	 **4o(75%)**
 **1b**	 **3a**	 **4h(82%)**	*P*-MeOC$_6$H$_4$−NH$_2$ **1e**	 **3a**	 **4p(78%)**

[a] Isolated yields.

Reaction condition: β-nitrostyrene (1.0 mmol), amine (1.4 mmol), dialkyl acetylenedicarboxylate (1.4 mmol), FeCl$_3$ (40%), and PhMe (reflux).

The structures of the products **4a**–**p** were deduced from their HR-mass spectrometry and NMR spectroscopic data. The scope and limitations of this three-component reaction were explored by using primary amines and also different β-nitrostyrene derivatives. Meanwhile, the structure of the products was confirmed according to the X-ray crystallographic data. Fig. 2 shows the ORTEP structure of the compound **4g**.

The possible mechanism of this conversion was shown in Scheme 2. This conversion involves the initial reaction of primary amines with dimethyl acetylenedicarboxylate to form the desired enaminone, then β-nitrostyrene could be activated by FeCl$_3$ and undergo the nucleophilic addition. The subsequent cyclization of intermediate B followed by the elimination of the nitro group leads to C. On the basis of the established chemistry of Iron(III) chemistry,[30] it is reasonable to assume that Iron(III) chloride has an essential role in the addition of enaminone to β-nitrostyrene via coordination with oxygen lone pairs. Meanwhile, the presence of Iron(III) chloride could facilitate the remove of nitro group and also formation of pyrrole moiety. Meanwhile, Fe(III) has an essential role for the oxidation process to obtain the final product **3**. Because of kinetic facility, formation of five-membered ring is observed (Scheme 2).

In conclusion, an efficient approach for the one-pot synthesis of tetra-substituted polyfunctional pyrroles catalyzed by FeCl$_3$ has been developed. Easy work-up, synthesis of polyfunctional compounds, which are ready for further reactions, and an easily available and less expensive catalyst, good to high yields are advantages of the present method.

3. Experimental section

Commercially available materials were used without further purification. Melting points were determined on an Electrothermal 9100 apparatus and were uncorrected. IR spectra were obtained on

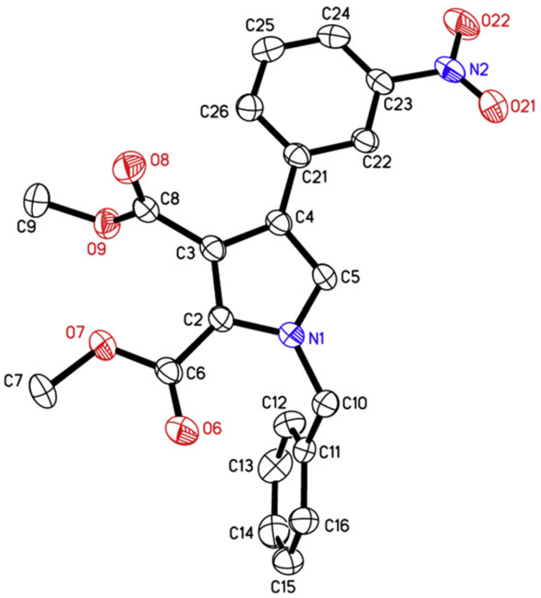
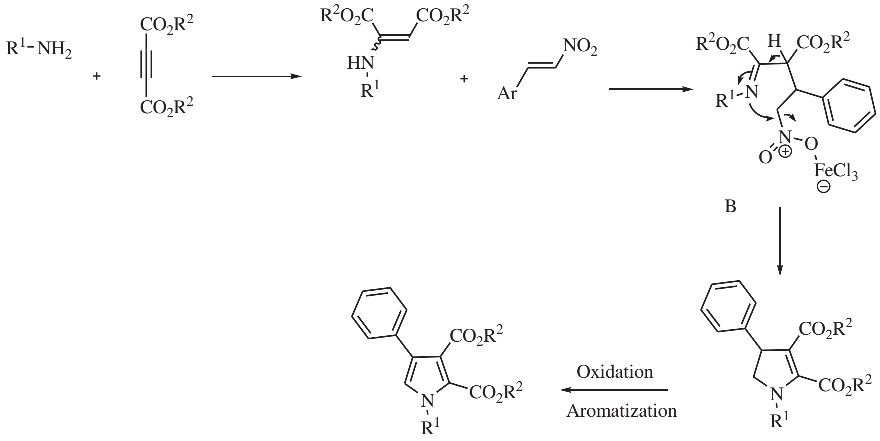


Fig. 2. ORTEP Structure of compound **4g**.



Scheme 2. Possible mechanism for the synthesis of tetra-substituted pyrroles **4a**.

an ABB FT-IR FTLA 2000 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were run on Bruker DRX-500 AVANCE spectrometers at 500 MHz for ^{1}H NMR, and 125 MHz for ^{13}C NMR. CDCl$_3$ was used as solvents. High resolution mass spectra were recorded on HR-MS was recorded on Mass-ESI-POS (Apex Qe-FT- ICR instrument) spectrometer.

3.1. General procedure for the synthesis of dimethyl 1-alkyl-4-aryl-1*H*-pyrrole-2,3-dicarboxylate (4a–k)

In a round bottom flask equipped with a magnetic stirrer, dialkyl acetylenedicarboxylate (1.4 mmol) and primary amine (1.4 mmol) in toluene (10 ml) were charged and the mixture was stirred vigorously at room temperature. Then, β-nitrostyrene derivatives (1 mmol) and FeCl$_3$ (40 mol %) were added to the mixture and the mixture was heated under reflux conditions. The reaction was completed after 5 h. The mixture was filtered and the solvent was removed under reduced pressure. Further purification was done using preparative TLC (eluent: hexane/EtOAc 3:1). In some cases, further purification was done using recrystallization with mixture of petroleum ether/dichloromethane.

*3.1.1. Dimethyl 1-benzyl-4-phenyl-1H-pyrrole-2,3-dicarboxylate (**4a**).* Yellow oil (290 mg, 83%); R_f (25% EtOAC/hexane) 0.51; ν_{max} (neat): 1715 cm^{-1}; δ_H (500 MHz, CDCl$_3$): 3.81 (3H, *s*, $-CO_2CH_3$), 3.85 (3H, *s*, $-CO_2CH_3$), 5.53 (2H, *s*, $-CH_2$N), 6.97 (1H, *s*, $=CH$pyrrole), 7.20 (2H, d, *J* 7.2 Hz, H–Ar), 7.30 (2H, t, *J* 7.5 Hz, H–Ar), 7.36 (4H, t, *J* 7.0 Hz, H–Ar), 7.43 (2H, d, *J* 8.5 Hz, H–Ar); δ_C (125 MHz, CDCl$_3$): 51.8, 52.3, 52.4, 121.2, 122.3, 124.0, 125.7, 127.0, 127.2, 127.4, 127.9, 128.06, 128.8, 133.3, 137.1, 160.6, 167.2; HR-Mass (ESI) calcd for $C_{21}H_{20}NO_4$ [M+1]$^+$ 350.1387, found 350.1387.

*3.1.2. Diethyl 1-benzyl-4-phenyl-1H-pyrrole-2,3-dicarboxylate (**4b**).* Yellow oil (328 mg, 87%); R_f (25% EtOAC/hexane) 0.52; ν_{max} (neat): 1605, 1701, 1725, 2984 cm^{-1}; δ_H (500 MHz, CDCl$_3$): 1.30 (6H, t, *J* 7.1 Hz, $2CH_3$), 4.27 (2H, q, *J* 7.1 Hz, $-CH_2$), 4.32 (2H, q, *J* 7.1 Hz, $-CH_2$), 5.53 (2H, *s*, $-CH_2$N), 6.95 (1H, *s*, $=CH$pyrrole), 7.20 (2H, d, *J* 7.5 Hz, H–Ar), 7.25–7.36 (6H, m, H–Ar), 7.42 (2H, d, *J* 7.5 Hz, H–Ar); δ_C (125 MHz, CDCl$_3$): 14.1, 52.4, 60.7, 61.3, 121.2, 122.6, 123.9, 125.5, 126.9, 127.3, 127.5, 127.8, 128.5, 128.8, 133.5, 137.1, 160.3, 166.8; HR-Mass (ESI) calcd for $C_{23}H_{24}NO_4$ [M+1]$^+$ 378.1702, found 378.1701.

*3.1.3. Dimethyl 1-benzyl-4-(4-bromophenyl)-1H-pyrrole-2,3-dicarboxylate (**4c**).* Yellow solid (378 mg, 83%); mp: 90–94 °C; R_f (25% EtOAC/hexane) 0.45; ν_{max} (neat): 1714 cm^{-1}; δ_H (500 MHz, CDCl$_3$): 3.80 (3H, *s*, $-OCH_3$), 3.82 (3H, *s*, $-OCH_3$), 5.52 (2H, *s*, $-CH_2$N), 6.91 (1H, *s*, $=CH$pyrrole), 7.19 (2H, d, *J* 7.5 Hz, H–Ar), 7.25 (2H, d, *J* 7.0 Hz, H–Ar), 7.29–7.36 (3H, m, H–Ar), 7.46 (2H, d, *J* 7.0 Hz, H–Ar); δ_C (125 MHz, CDCl$_3$): 51.8, 52.3, 52.5, 103.0, 121.6, 121.9, 123.0, 125.4, 127.3, 128.0, 128.8, 129.1, 131.6, 132.3, 136.7, 160.6, 166.8; HR-Mass (ESI) calcd for $C_{21}H_{19}{}^{79}BrNO_4$ [M+1]$^+$ 428.0495, found 428.0494; calcd for $C_{21}H_{19}{}^{81}BrNO_4$ [M+1]$^+$ 430.0475, found 430.0474.

*3.1.4. Dimethyl 1-benzyl-4-(4-chlorophenyl)-1H-pyrrole-2,3-dicarboxylate (**4d**).* Yellow solid (386 mg, 94%); mp: 85–90 °C; R_f (25% EtOAC/hexane) 0.47; ν_{max} (KBr): 1703 cm^{-1}; δ_H (500 MHz, CDCl$_3$): 3.80 (3H, *s*, $-CO_2CH_3$), 3.83 (3H, *s*, $-CO_2CH_3$), 5.52 (2H, *s*, $-CH_2$N), 6.92 (1H, *s*, $=CH$pyrrole), 7.19 (2H, d, *J* 7.5 Hz, H–Ar), 7.26–7.36 (7H, m, H–Ar); δ_C (125 MHz, CDCl$_3$): 51.8, 52.3, 52.5, 121.6, 122.0, 123.0, 125.4, 127.3, 128.0, 128.7, 128.8, 128.9, 131.8, 132.9, 136.7, 160.6, 166.9; HR-Mass (ESI) calcd for $C_{21}H_{19}\,{}^{35}ClNO_4$ [M+1]$^+$ 384.0998, found 384.0998; calcd for $C_{21}H_{19}{}^{37}ClNO_4$ [M+1]$^+$ 386.0968, found 386.0968.

*3.1.5. Dimethyl 1-benzyl-4-(4-methoxyphenyl)-1H-pyrrole-2,3-dicarboxylate (**4e**).* Yellow oil (355 mg, 87%); R_f (25% EtOAC/

hexane) 0.43; ν_{max} (neat): 1735 cm^{-1}; δ_H (500 MHz, $CDCl_3$): 3.80 (6H, *s*, $-CO_2CH_3$), 3.83 (3H, *s*, $-OCH_3$), 5.51 (2H, *s*, $-CH_2N$), 6.89 (1H, *s*, $=CH$pyrrole), 7.18 (2H, d, *J* 7.1 Hz, H–Ar), 7.26–7.34 (5H, m, H–Ar); δ_C (125 MHz, $CDCl_3$): 51.7, 53.0, 55.2, 114.1, 122.1, 123.8, 125.3, 125.8, 127.2, 127.8, 128.2, 128.6, 128.8, 129.0, 137.1, 158.8, 160.7, 167.3; HR-Mass (ESI) calcd for $C_{22}H_{22}NO_5$ $[M+1]^+$ 380.1494, found 380.1494.

*3.1.6. Dimethyl 1-benzyl-4-p-tolyl-1H-pyrrole-2,3-dicarboxylate (**4f**).* Yellow oil (345 mg, 95%); R_f (25% EtOAC/hexane) 0.54; ν_{max} (neat): 1714 cm^{-1}; δ_H (500 MHz, $CDCl_3$): 2.37 (3H, *s*, $-CH_3$), 3.81 (3H, *s*, $-CO_2CH_3$), 3.85 (3H, *s*, $-CO_2CH_3$), 5.52 (2H, *s*, $-CH_2N$), 6.95 (1H, *s*, $=CH$pyrrole), 7.18 (2H, d, *J* 8.5 Hz, H–Ar), 7.20 (2H, d, *J* 8.5 Hz, H–Ar), 7.29–7.36 (5H, m, H–Ar); δ_C (125 MHz, $CDCl_3$): 21.1, 51.7, 52.3, 52.4, 121.1, 122.3, 124.0, 125.6, 127.2, 127.3, 127.8, 128.8, 129.3, 130.4, 136.6, 137.1, 160.7, 167.3; HR-Mass (ESI) calcd for $C_{22}H_{22}NO_4$ $[M+1]^+$ 364.1545, found 364.1544.

*3.1.7. Dimethyl 1-benzyl-4-(3-nitrophenyl)-1H-pyrrole-2,3-dicarboxylate (**4g**).* Yellow solid (323 mg, 82%); mp: 100–109 °C; R_f (25% EtOAC/hexane) 0.44; ν_{max} (KBr): 1727 cm^{-1}; δ_H (500 MHz, $CDCl_3$): 3.82 (3H, *s*, $-OCH_3$), 3.86 (3H, *s*, $-OCH_3$), 5.54 (2H, *s*, $-CH_2N$), 7.02 (1H, *s*, $=CH$pyrrole), 7.20 (2H, d, *J* 7.0 Hz, H–Ar), 7.30–7.40 (3H, m, H–Ar), 7.50 (1H, t, *J* 8.0 Hz, H–Ar), 7.70 (1H, dd, *J* 8.0, 1.0 Hz, H–Ar), 8.10 (1H, dt, *J* 7.0, 1.5 Hz, H–Ar); δ_C (125 MHz, $CDCl_3$): 52.0, 52.4, 52.6, 121.6, 121.9, 122.3, 122.4, 122.5, 125.6, 127.3, 128.1, 128.9, 129.4, 133.4, 135.1, 136.4, 148.5, 160.6, 166.4; HR-Mass (ESI) calcd for $C_{21}H_{19}N_2O_6$ $[M+1]^+$ 395.1237, found 395.1237. Yellow crystal (plate), dimensions $0.36\times0.20\times0.06$ mm^3, crystal system triclinic, space group $P\bar{1}$, $Z=2$, $a=9.0976$ (2) Å, $b=9.2228$ (2) Å, $c=11.7610$ (1) Å, $\alpha=90.524$ (1)°, $\beta=110.998$ (1)°, $\gamma=94.304$ (1)°, $V=917.99(3)$ Å^3, $\rho=1.427$ g/cm^3, $T=200(2)$ K, $\theta_{max}=27.49°$, radiation Mo Kα, $\lambda=0.71073$ Å, 0.3° ω-scans with CCD area detector, covering a whole sphere in reciprocal space, 9415 reflections measured, 4191 unique (R(int)=0.0758), 2818 observed ($I>2\sigma(I)$), intensities were corrected for Lorentz and polarization effects, an empirical absorption correction was applied using SADABS[1] based on the Laue symmetry of the reciprocal space, $\mu=0.11$ mm^{-1}, $T_{min}=0.96$, $T_{max}=0.99$, structure solved by direct methods and refined against F^2 with a Full-matrix least-squares algorithm using the SHELXTL (Version 2008/4) software package,[2] 264 parameters refined, hydrogen atoms were treated using appropriate riding models, goodness of fit 1.00 for observed reflections, final residual values $R1(F)=0.053$, $wR(F^2)=0.128$ for observed reflections, residual electron density −0.28 to 0.27 e Å^{-3}. CCDC 808923 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

*3.1.8. Dimethyl 4-phenyl-1-(1-phenylethyl)-1H-pyrrole-2,3-dicarboxylate (**4h**).* Yellow oil (309 mg, 82%); R_f (25% EtOAC/hexane) 0.58; ν_{max} (neat): 1711 cm^{-1}; δ_H (500 MHz, $CDCl_3$): 1.85 (3H, d, *J* 7.0 Hz, $-CH_3$), 3.80 (3H, *s*, $-CO_2CH_3$), 3.83 (3H, *s*, $-CO_2CH_3$), 6.50 (1H, q, *J* 7.0 Hz, $-CH$), 7.05 (1H, *s*, $=CH$pyrrole), 7.21–7.30 (4H, m, H–Ar), 7.34 (4H, t, *J* 7.5 Hz, H–Ar), 7.4 (2H, d, *J* 7.5 Hz, H–Ar); δ_C (125 MHz, $CDCl_3$): 22.0, 52.2, 53.1, 56.0, 122.3, 126.4, 126.5, 126.9, 127.0, 127.4, 127.7, 128.5, 128.7, 128.8, 133.5, 141.6, 160.8, 167.3; HR-Mass (ESI) calcd for $C_{22}H_{22}NO_4$ $[M+1]^+$ 364.1544, found 364.1544.

*3.1.9. Dimethyl 4-(2-bromophenyl)-1-(1-phenylethyl)-1H-pyrrole-2,3-dicarboxylate (**4i**).* Yellow oil (396 mg, 87%); R_f (25% EtOAC/hexane) 0.48; ν_{max} (neat): 1715 cm^{-1}; δ_H (500 MHz, $CDCl_3$): 1.84 (3H, d, *J* 7.0 Hz, $-CH_3$), 3.68 (3H, *s*, $-OCH_3$), 3.87 (3H, *s*, $-OCH_3$), 6.31 (1H, q, *J* 7.0 Hz, $-CHN$), 7.02 (1H, *s*, $=CH$pyrrole), 7.15 (1H, t, *J* 8.5 Hz, H–Ar), 7.22 (2H, d, *J* 7.5 Hz, H–Ar), 7.25–7.37 (5H, m, H–Ar), 7.61 (2H, d, *J* 7.5 Hz, H–Ar); δ_C (125 MHz, $CDCl_3$): 22.0, 51.8, 51.9, 56.2, 121.6, 123.3, 123.4, 124.1, 126.3, 127.1, 127.7, 127.8, 128.6, 128.7, 131.7, 132.7, 134.8, 141.7, 161.4, 165.6; HR-Mass (ESI) calcd for $C_{22}H_{21}{}^{79}BrNO_4$ $[M+1]^+$ 442.0653, found 442.0652; HR-Mass (ESI) calcd for $C_{22}H_{21}{}^{81}BrNO_4$ $[M+1]^+$ 442.0632, found 442.0631.

*3.1.10. Dimethyl 4-(4-chlorophenyl)-1-(1-phenylethyl)-1H-pyrrole-2,3-dicarboxylate (**4j**).* Yellow oil (424 mg, 93%); R_f (25% EtOAC/hexane) 0.46; ν_{max} (neat): 1719 cm^{-1}; δ_H (500 MHz, $CDCl_3$): 1.83 (3H, d, *J* 7.0 Hz, $-CH_3$), 3.80 (3H, *s*, $-OCH_3$), 3.81 (3H, *s*, $-OCH_3$), 6.45 (1H, q, *J* 7.0 Hz, $-CHN$), 7.0 (1H, *s*, $=CH$pyrrole), 7.30 (4H, d, *J* 5.0 Hz, H–Ar), 7.20–7.40 (5H, m, H–Ar); δ_C (125 MHz, $CDCl_3$): 21.9, 39.5, 53.0, 53.4, 121.6, 122.2, 122.9, 126.4, 127.6, 127.7, 127.8, 128.7, 128.8, 128.9, 132.1, 132.8, 141.4, 160.8, 166.9; HR-Mass (ESI) calcd for $C_{22}H_{21}{}^{35}ClNO_4$ $[M+1]^+$ 398.1155, found 398.1154; calcd for $C_{22}H_{21}{}^{37}ClNO_4$ $[M+1]^+$ 400.1127, found 400.1126.

*3.1.11. Dimethyl 4-(4-methoxyphenyl)-1-(1-phenylethyl)-1H-pyrrole-2,3-dicarboxylate (**4k**).* Yellow oil (326 mg, 80%); R_f (25% EtOAC/hexane) 0.41; ν_{max} (neat): 1707 cm^{-1}; δ_H (500 MHz, $CDCl_3$): 1.84 (3H, d, *J* 7.0 Hz, $-CH_3$), 3.80 (6H, *s*, $-CO_2CH_3$), 3.82 (3H, *s*, $-CO_2CH_3$), 6.47 (1H, q, *J* 7.0 Hz, $-CHN$), 6.90 (2H, d, *J* 6.0 Hz, H–Ar), 6.97 (1H, *s*, $=CH$pyrrole), 7.24 (2H, d, *J* 7.5 Hz, H–Ar), 7.26–7.35 (5H, m, H–Ar); δ_C (125 MHz, $CDCl_3$): 21.9, 51.7, 52.2, 55.2, 55.9, 114.0, 121.4, 121.8, 121.9, 123.8, 126.0, 126.4, 127.7, 128.6, 128.7, 141.6, 158.7, 160.9, 167.3; HR-Mass (ESI) calcd for $C_{23}H_{24}NO_5$ $[M+1]^+$ 394.1645, found 394.1646.

*3.1.12. Dimethyl 1-(1-phenylethyl)-4-p-tolyl-1H-pyrrole-2,3-dicarboxylate (**4l**).* Yellow oil (313 mg, 80%); R_f (25% EtOAC/hexane) 0.52; ν_{max} (neat): 1709 cm^{-1}; δ_H (500 MHz, $CDCl_3$): 1.85 (3H, d, *J* 7.0 Hz, $-CH_3$), 2.36 (3H, *s*, $-CH_3$), 3.77 (3H, *s*, $-CO_2CH_3$), 3.84 (3H, *s*, $-CO_2CH_3$), 6.50 (1H, q, *J* 7.0 Hz, $-CH$), 7.02 (1H, *s*, $=CH$pyrrole), 7.17 (2H, d, *J* 7.5 Hz, H–Ar), 7.22 (2H, d, *J* 7.5 Hz, H–Ar), 7.30 (3H, t, *J* 7.5 Hz, H–Ar), 7.34 (2H, dd, *J* 7.5 Hz, H–Ar); δ_C (125 MHz, $CDCl_3$): 21.1, 21.9, 39.5, 53.1, 53.5, 55.9, 122.1, 122.2, 124.1, 126.5, 127.3, 127.7, 128.7, 129.3, 130.6, 136.6, 141.7, 160.9, 167.3; HR-Mass (ESI) calcd for $C_{23}H_{24}NO_4$ $[M+1]^+$ 378.1702, found 378.1701.

*3.1.13. 2-Ethyl 3-methyl1-allyl-4-phenyl-1H-pyrrole-2,3-dicarboxylate (**4m**).* Yellow oil (254 mg, 85%); R_f (25% EtOAC/hexane) 0.55; ν_{max} (neat): 1606 cm^{-1}, 1730, 2946, 3083; δ_H (500 MHz, $CDCl_3$): 3.82 (3H, *s*, $-CO_2CH_3$), 3.83 (3H, *s*, $-CO_2CH_3$), 4.92 (2H, d, *J* 5.5 Hz, $-CH_2N$), 5.11 (1H, d, *J* 17.1 Hz, $=CH$), 5.20 (1H, d, *J* 10.25 Hz, $=CH_2$), 6.0 (m, 1H, $=CH_2$), 6.93 (1H, *s*, $=CH$pyrrole), 7.25 (1H, t, *J* 7.3 Hz, H–Ar), 7.33 (2H, t, *J* 7.5 Hz, H–Ar), 7.38 (2H, d, *J* 7.8 Hz, H–Ar); δ_C (125 MHz, $CDCl_3$): 51.4, 51.8, 52.4, 117.7, 120.8, 122.1, 123.9, 125.3, 126.9, 127.3, 128.6, 133.3, 133.7, 160.6, 167.3; HR-Mass (ESI) calcd for $C_{19}H_{22}NO_4$ $[M+1]^+$ 300.1230, found 300.1230.

*3.1.14. Diethyl 1-allyl-4-phenyl-1H-pyrrole-2,3-dicarboxylate (**4n**).* Yellow oil (284 mg, 87%); R_f (25% EtOAC/hexane) 0.51; ν_{max} (neat): 1602 cm^{-1}, 1713, 2976, 3079; δ_H (500 MHz, $CDCl_3$): 1.27 (3H, t, *J* 7.0 Hz, $-CH_3$), 1.33 (3H, t, *J* 7.0 Hz, $-CH_3$), 4.28 (4H, q, *J* 7.0 Hz, 2-CH_2), 4.92 (2H, d, *J* 5.5 Hz, $-CH_2N$), 5.12 (1H, dd, *J* 18.1 Hz, $=CH^a$), 5.20 (1H, d, *J* 10.5 Hz, $=CH^b$), 5.99 (1H, m,), 6.92 (1H, *s*, $=CH$pyrrole), 7.25 (1H, t, *J* 8.5 Hz, H–Ar), 7.34 (2H, t, *J* 7.5 Hz, H–Ar), 7.40 (2H, d, *J* 7.5 Hz, H–Ar); δ_C (125 MHz, $CDCl_3$): 14.0, 14.1, 51.3, 60.7, 61.2, 117.7, 120.8, 122.4, 123.7, 125.1, 126.8, 127.4, 128.5, 133.5, 133.8, 160.2, 166.8; HR-Mass (ESI) calcd for $C_{19}H_{22}NO_4$ $[M+1]^+$ 328.1545, found 328.1545.

*3.1.15. 2-Ethyl 3-methyl 1,4-diphenyl-1H-pyrrole-2,3-dicarboxylate (**4o**).* Yellow oil (251 mg, 75%); R_f (25% EtOAC/hexane) 0.48; ν_{max} (neat): 1605, 1701, 1725, 2984 cm^{-1}; δ_H (500 MHz, $CDCl_3$): 3.71 (3H, s, $-CO_2CH_3$), 3.84 (3H, *s*, $-CO_2CH_3$), 7.0 (1H, *s*, $=CH$pyrrole), 7.25–7.45 (m, 10H, H–Ar); δ_C (125 MHz, $CDCl_3$): 51.9, 52.3, 120.8, 121.8, 125.9, 126.1, 127.1, 127.7, 128.5, 128.6, 128.9, 129.1, 133.1, 139.5, 160.4, 166.6; HR-Mass (ESI) calcd for $C_{20}H_{17}NO_4$ $[M+1]^+$ 336.1231, found 336.1231.

*3.1.16. 2-Ethyl 3-methyl 1-(4-methoxyphenyl)-4-phenyl-1H-pyrrole-2,3-dicarboxylate (**4p**).* Yellow oil (285 mg, 78%); R_f (25% EtOAC/hexane) 0.41; ν_{max} (neat): 1456, 1717, 2925, 2951 cm^{-1}; δ_H (500 MHz, $CDCl_3$): 3.72 (3H, *s*, CO_2CH_3), 3.83 (3H, *s*, $-CO_2CH_3$), 3.82 (3H, *s*, $-CO_2CH_3$), 3.83 (3H, *s*, $-CO_2CH_3$), 6.95 (2H, d, *J* 8.5 Hz, H–Ar), 6.97 (1H, *s*, =*CH*pyrrole), 7.27 (2H, d, *J* 8.8 Hz, H–Ar), 7.29 (1H, t, *J* 7.5 Hz, H–Ar), 7.37 (2H, t, *J* 7.5 Hz, H–Ar), 7.44 (2H, d, *J* 8.5 Hz, H–Ar); δ_C (125 MHz, $CDCl_3$): 51.9, 52.3, 55.5, 114.0, 120.8, 124.6, 126.2, 127.0, 127.3, 127.4, 127.7, 128.5, 132.4, 133.3, 159.6, 160.4, 166.7; HR-Mass (ESI) calcd for $C_{21}H_{20}NO_5$ $[M+1]^+$ 366.1338, found 366.1338.

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Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2011.05.076.

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