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A synergistic effect of microwave irradiation and nano-TiO_2@[DABCO($CH_2CH_2CO_2H$)]$^+$[Br]$^-$ for the expeditious synthesis of fully functionalised pyrroles incorporating benzo-thio unit†

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A quick access and sustainable strategy for the one-pot, solvent-free and chromatography free synthesis of the diversified N-aryl fully functionalised pyrroles incorporating benzo-thio unit is demonstrated here. Here synergistic effect of microwave irradiation and nano-TiO_2@[DABCO($CH_2CH_2CO_2H$)]$^+$[Br]$^-$ has been utilised. The foremost objective of this work is to emphasize the environmentally benevolent and facile nature of the combined microwave-assisted quasi-heterogeneous catalytic methods.

Keywords: Microwave irradiation, nano-TiO_2@IL, pyrroles, synergistic effect, sustainable strategy.

Introduction

Over the years, significant effort has been committed to improve the laboratory protocols for convenient and rapid transformations considering environmental benignity in the field of organic, combinatorial and medicinal chemistry[1]. Principles of green chemistry promoted by Anastas, suggested that microwave chemistry has a strong relevance with green chemistry[2]. Microwave-assisted reactions carried out at an optimized reaction temperature have been revealed as more cleaner and leading to less by-products compared to the conventionally heated processes carried out at the reflux temperature of the solvent[3]. This lenient and green methodology is highly effective for the minimization of energy consumption and considerable reduction in reaction time compared to conventional synthesis. The conventional heating necessary 3–9 times further energy than the microwave assisted organic synthesis (MAOS)[4].

Over the past few decades room temperature ionic liquids (ILs) are considered as very effective environment-friendly reaction media as well as catalyst due to their high boiling point and low vapour pressure nature[5]. Among various quaternary alkylammonium ILs, 1,4-diazobicyclo[2.2.2]-octane (DABCO) derived ionic liquids have been shown to be very effective catalysts for many important reactions[6]. In the recent time homogeneous ILs are not used alone as a catalyst, homogeneous ILs are loaded over heterogeneous metal or non-metal oxide nanoparticles to produce more effective quasi-heterogeneous catalyst[7]. This admired catalytic concept is known as Supported catalysts withan ionic liquid layer (SCILL) where ILs are immobilised as a thin layer over solid support[8]. Now, choice of TiO_2-NP as an inner core is advantageous in microwave assisted reaction as having high dielectric constant of almost 50, shows high absorption power of MW irradiation[9]. Highly ionic nature of DABCO based IL is also microwave-irradiation friendly.

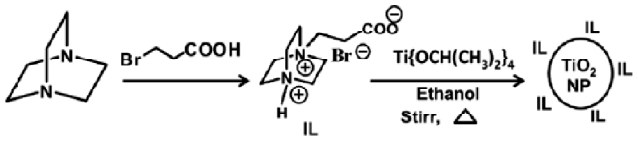
Pyrrole moiety is one of the most valuable heterocyclic compound that have been found to be useful in many fields[10]. Pyrrole based compounds are not only found in many natural products[11] and pharmaceuticals[12] but are also extensively used in material science[13] and supramolecular chemistry[14]. As a result of the significant importance of the pyrrole based heterocyclic compound, interest in the synthesis of new pyrrole compounds and improvement in the synthesis methodologies are cultivating for several years and that is continuing in recent time also.

Results and discussion

Considering biological importance of pyrrole moieties,

†Invited Lecture.

benzo-thio unit incorporating functionalised pyrroles have been tried to synthesis in more facile and environmentally benign way. Preliminary DABCO based mono-substituted amphoteric IL {[DABCO(CH_2CH_2COOH)]$^+$[Br]$^-$} was synthesised by reacting DABCO with one equivalent of 3-bromo propionic acid as precursor. In the next step, ionic liquid covered TiO_2 nanoparticles were synthesised by treating titanium tetraisopropoxide in hot ethanol with stabilising effect of IL. IL played role of "organic stencil" or structure-directing negotiator that controlled the development and function of TiO_2-NP. The schematic representation has been shown below (Scheme 1) and the details procedure has been described in Experimental section.



Scheme 1. Preparation of nano-TiO_2@[DABCO(CH_2CH_2COOH)]$^+$[Br]$^-$.

At first, formation of nano-TiO_2@[DABCO(CH_2CH_2-COOH)]$^+$[Br]$^-$ was confirmed and characterized by FT-IR spectrum (Fig. 1) with a distinguishing absorption peak at 3432 cm^{-1} and 1718 cm^{-1} which are accredited to a stretching vibration of the hydroxyl group and carboxylic carbonyl group of functionalized DABCO based IL respectively. The peaks in the region of 500 to 800 cm^{-1}, 1630 cm^{-1}and 2985 cm^{-1} credited to TiO_2-NP. According to the following FT-IR spectrum, formation of carboxylic acid group functionalised ionic liquid covered TiO_2-NP was established.

The morphology of the combined catalytic system (nano-TiO_2@[DABCO(CH_2CH_2COOH)]$^+$[Br]$^-$) was revealed by the following SEM image (Fig. 2). This image indicates that all the synthesised catalyst particles are of uniform sizes and the size of those catalysts were in the scale of 70 to 90 nm.

Few of the representative HRTEM images of the synthesised catalyst were shown in the following Fig. 3. These images were taken in different magnification to get the clear idea about surface modification. From these HRTEM images it was revealed that size of the catalyst was equivalent to data obtained from SEM image.

In order to synthesize the desired compounds in most facile way, it is really significant to control the reactions by choosing most suitable reaction conditions. For this reason, to optimize the reaction condition (Table 1) a series of synthesis works were carried out with a representative reaction of 4-chloro benzene thiol (1 mmol), phenyl glyoxal (1 mmol), para toluidine (1 mmol) and dimethyl acetylenedicarboxylate (1 mmol) with alteration of reaction parameters, such as solvent, catalyst, reaction temperature etc.

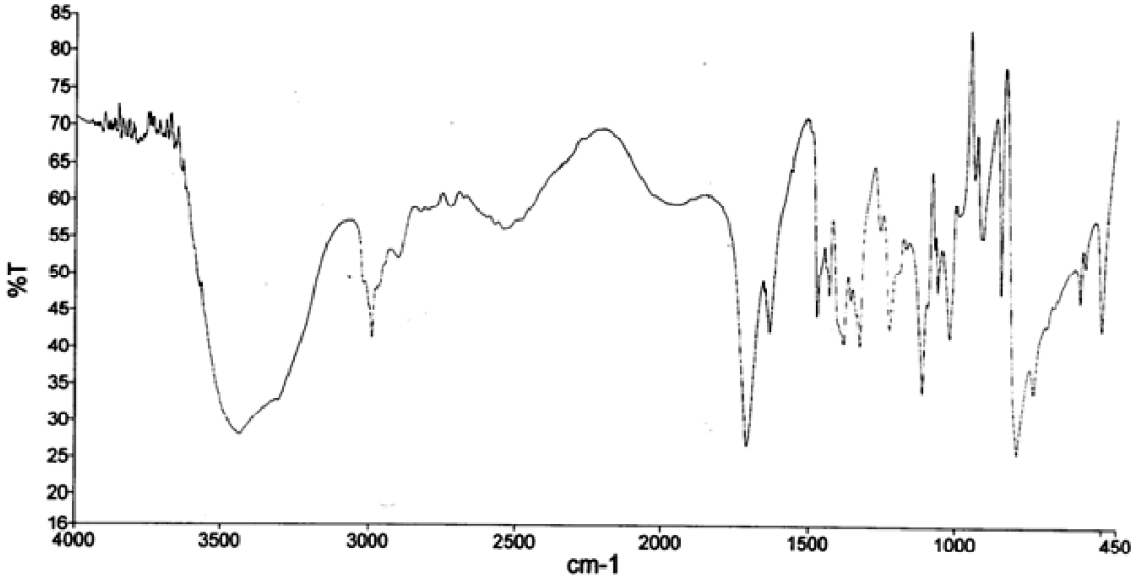


Fig. 1. FT-IR spectrum of the nano-TiO_2@[DABCO(CH_2CH_2COOH)]$^+$[Br]$^-$.

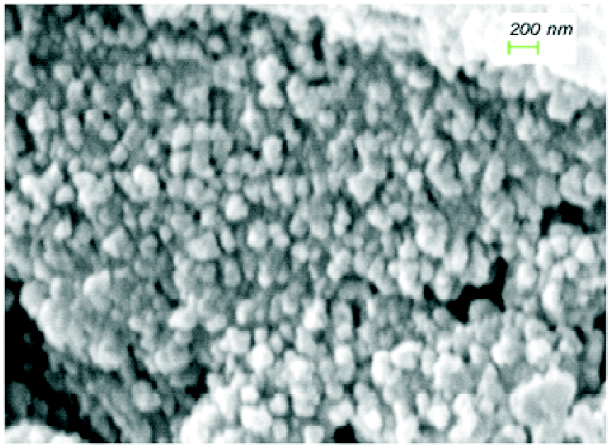


Fig. 2. SEM image of nano-TiO_2@[DABCO(CH_2CH_2COOH)]$^+$[Br]$^-$.

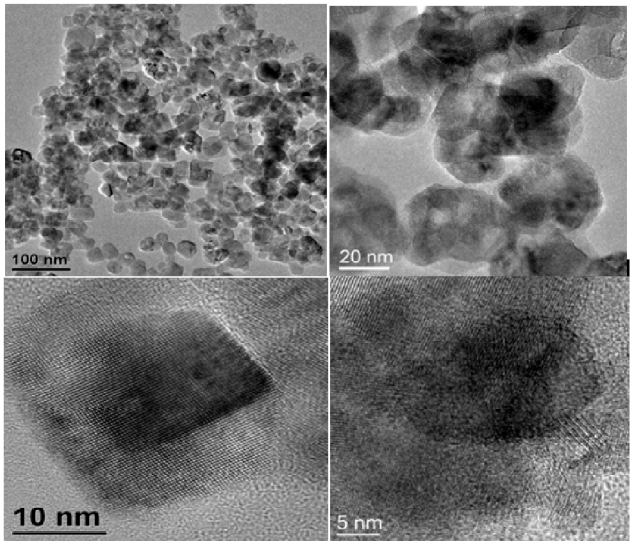
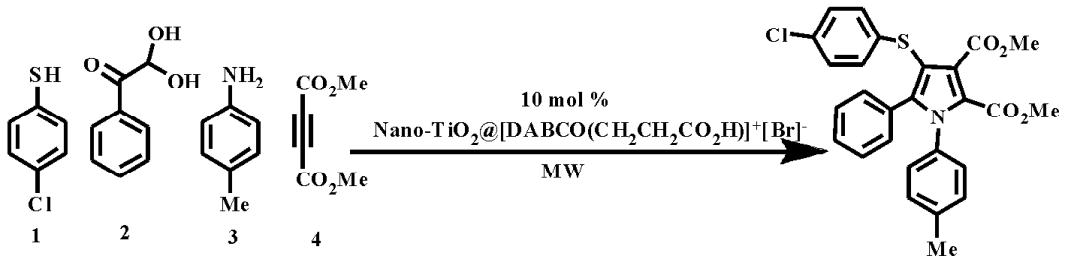


Fig. 3. HRTEM image of nano-TiO_2@[DABCO(CH_2CH_2COOH)]$^+$[Br]$^-$.

Although reactions were conducted both in conventional as well as microwave-irradiated condition our main concern was related to microwave assisted reaction. At first, the reaction was carried out in usual way, in ethanol medium without catalyst (Table 1, entry 1) followed by in neat condition (Table 1, entry 2) resulting poor yield. Reaction was also carried out

Table 1. Effect of different reaction parameters[a]



Entry	Method	Solvent	Catalyst	Time	Temp. (°C)	Yield[b] (%)
1	Conventional	Ethanol	No	5 h	78	42
2	Conventional	Neat	No	1 h	80	30
3	Microwave	Neat	No	15 min	60	40
4	Microwave	Neat	AcOH	10 min	60	52
5	Microwave	Neat	Et_3N	10 min	60	55
6	Microwave	Neat	DABCO	10 min	60	50
7	Microwave	Neat	Nano-TiO_2	10 min	60	58
8	Microwave	Neat	[DABCO-CH_2CH_2COOH]$^+$[Br]$^-$	10 min	60	70
9	Microwave	Neat	Nano-TiO_2@[DABCO(CH_2CH_2COOH)]$^+$[Br]$^-$	10 min	60	96
10	Microwave	Neat	Nano-TiO_2@[DABCO(-CH_2CH_2COOH)]$^+$[Br]$^-$	10 min	80	89
11	Microwave	Neat	Nano-TiO_2@[DABCO(CH_2CH_2COOH)]$^+$[Br]$^-$	10 min	30	81
12	Microwave	Neat	Nano-TiO_2@[DABCO(CH_2CH_2COOH)]$^+$[Br]$^-$	5 min	60	88

[a]Reaction conditions: all reactions were carried out using 4-chloro thiophenol (1 mmol), phenyl glyoxal (1 mmol), para toluidine (1 mmol) and dimethyl acetylenedicarboxylate (1 mmol) under different reaction conditions. [b]Isolated yields.

under microwave irradiation in solvent-free and catalyst free manner (Table 1, entry 3). To improve the reaction yield, various catalysts were used like acidic AcOH (Table 1, entry 4), nano-TiO_2 (Table 1, entry 7) basic Et_3N (Table 1, entry 4), DABCO (Table 1, entry 6) resulting slight improvement in the yield. Then catalyst was varied with our synthesised catalyst (nano-TiO_2@[DABCO(CH_2CH_2COOH)]$^+$[Br]$^-$) under microwave-assisted solvent-free condition at 60°C and got most satisfactory result (Table 1, entry 9). Without altering catalyst, time and temperature of the reaction system was changed (Table 1, entry 10, 11, 12) but didn't get satisfactory yield. Finally it was observed that nano-TiO_2@[DABCO(CH_2CH_2COOH)]$^+$-[Br]$^-$ catalysed microwave-assisted solvent-free condition at 60°C was the optimum reaction condition.

Catalyst loading: Subsequently, to determine the finest amount of catalyst required for the successful reaction, the reaction was conducted in the presence of miscellaneous amounts of catalyst, nano-TiO_2@[DABCO(CH_2CH_2-COOH)]$^+$[Br]$^-$ (Fig. 4). In this catalyst loading graph, it has been revealed that with increasing amount of catalyst usage enhancement in the yield of the product occurs. It was up to 12 mol% of catalyst usage, more than which resulted no further improvement in product yield. In order to spend the least amount of catalyst, catalyst usage was restricted up to 12 mol%.

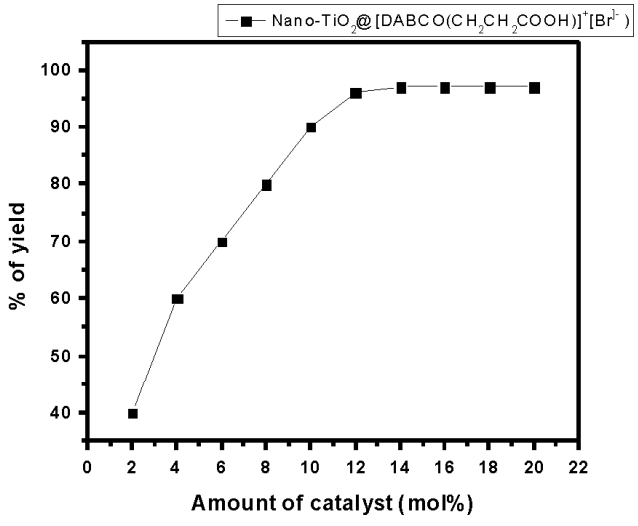


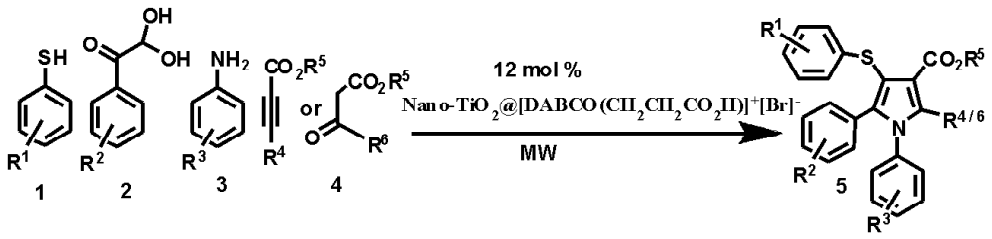
Fig. 4. Yields at different catalyst loadings in the four component reaction of phenyl glyoxal, para toluidine, ethyl acetoacetate and dimedone.

Substrate scope: With the optimized conditions in hand desired compounds are formed in two different ways with one reactant replacement (Table 2). In one way, various substituted or unsubstituted aromatic thiols, phenyl glyoxals (1 mmol), aromatic amines (1 mmol) and dialkyl acetylenedicarboxylates readily formed the desired compounds whereas in another way various substituted or unsubstituted aromatic thiols, phenyl glyoxals (1 mmol), aromatic amines (1 mmol) and β-keto ester readily formed the desired compounds. It was interesting to note that all the 4 components were varied with large extent of variety with very good to excellent yields.

Reaction mechanism: Considering the above experimental conclusions and the literature survey[15] a rational reaction mechanism was proposed of the cascade reactions which are displayed in Scheme 2. Reaction begins with nucleophilic attack of aromatic amine towards β-keto ester for the formation of enamine compound C. On the other hand, aromatic thiol reacted with phenyl glyoxal for the formation of intermediate E followed by the reaction between intermediate C and intermediate F to form intermediate G. Next, this intermediate undergoes cyclisation and after the elimination of water, aromatization occurred and formed final product J. Here all the reaction steps were successfully catalysed by nano-TiO_2@[DABCO(CH_2CH_2COOH)]$^+$[Br]$^-$. Acidic surface of nano sized titania enhances the electrophilicity of carbonyl centre and carboxylic proton simultaneously acted as very good proton donor. Since here DABCO is monosubstituted, one of the two N centers is free along with lone pair of electron and other N centre is substituted with propionic acid. All along this mono substituted DABCO based ionic liquid shows amphoteric behaviour. Thus, owing to synergetic catalytic effect of the nano-TiO_2@[DABCO(CH_2CH_2COOH)]$^+$[Br]$^-$, the reactivity is increased largely from very beginning to end.

Using dialkylacetylenedicarboxylate, a different series of fully functionalised pyrrole derivatives were synthesized effectively. A rational reaction mechanism is displayed in Scheme 3, similar to Scheme 2. Primarily, the reaction begins with nucleophilic addition of aromatic amine towards the triple bond of dialkylacetylenedicarboxylate to form enamine A. In another case nucleophilic addition reaction in be-

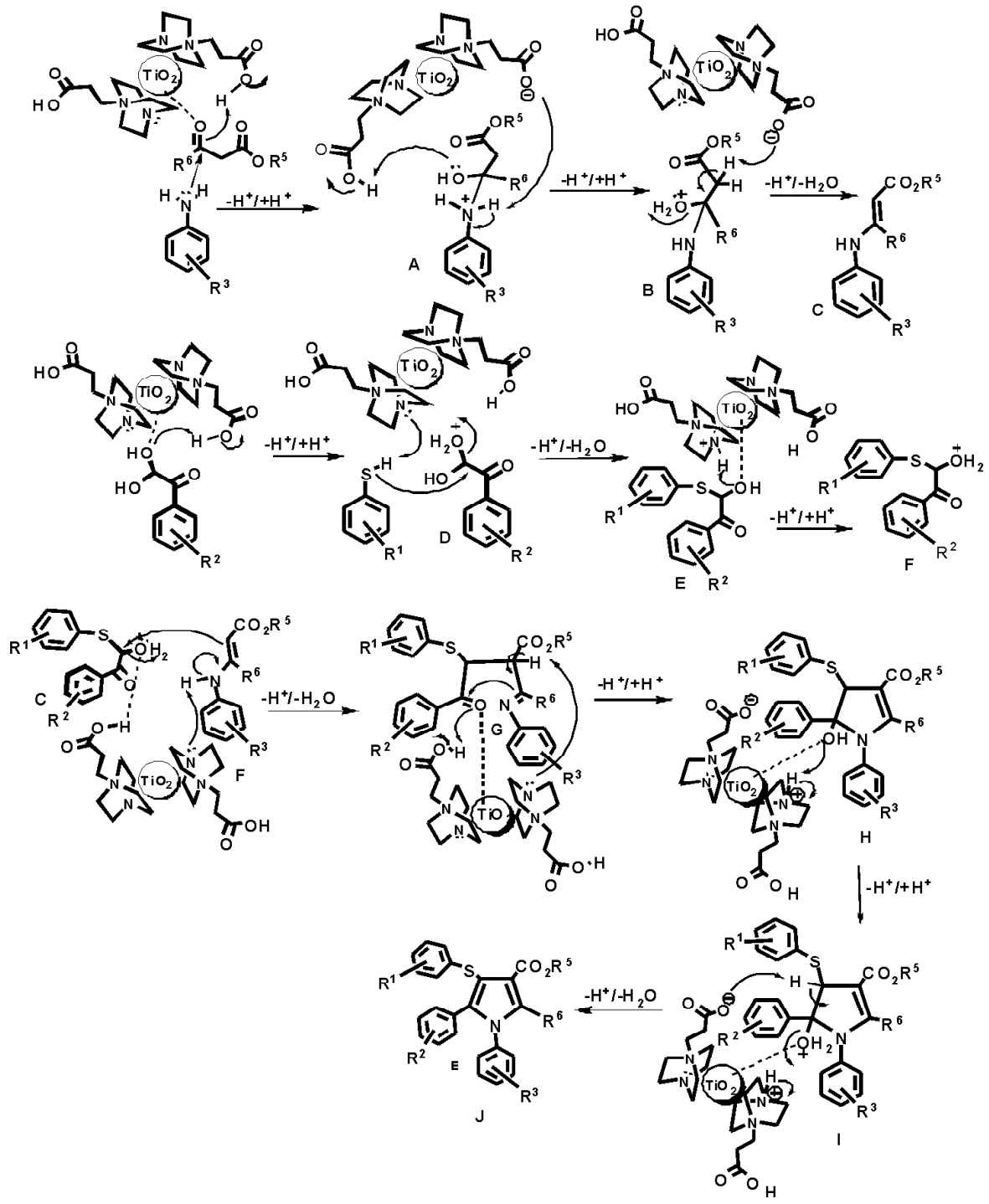
Table 2. Structure of fully functionalised pyrrole compounds[a]



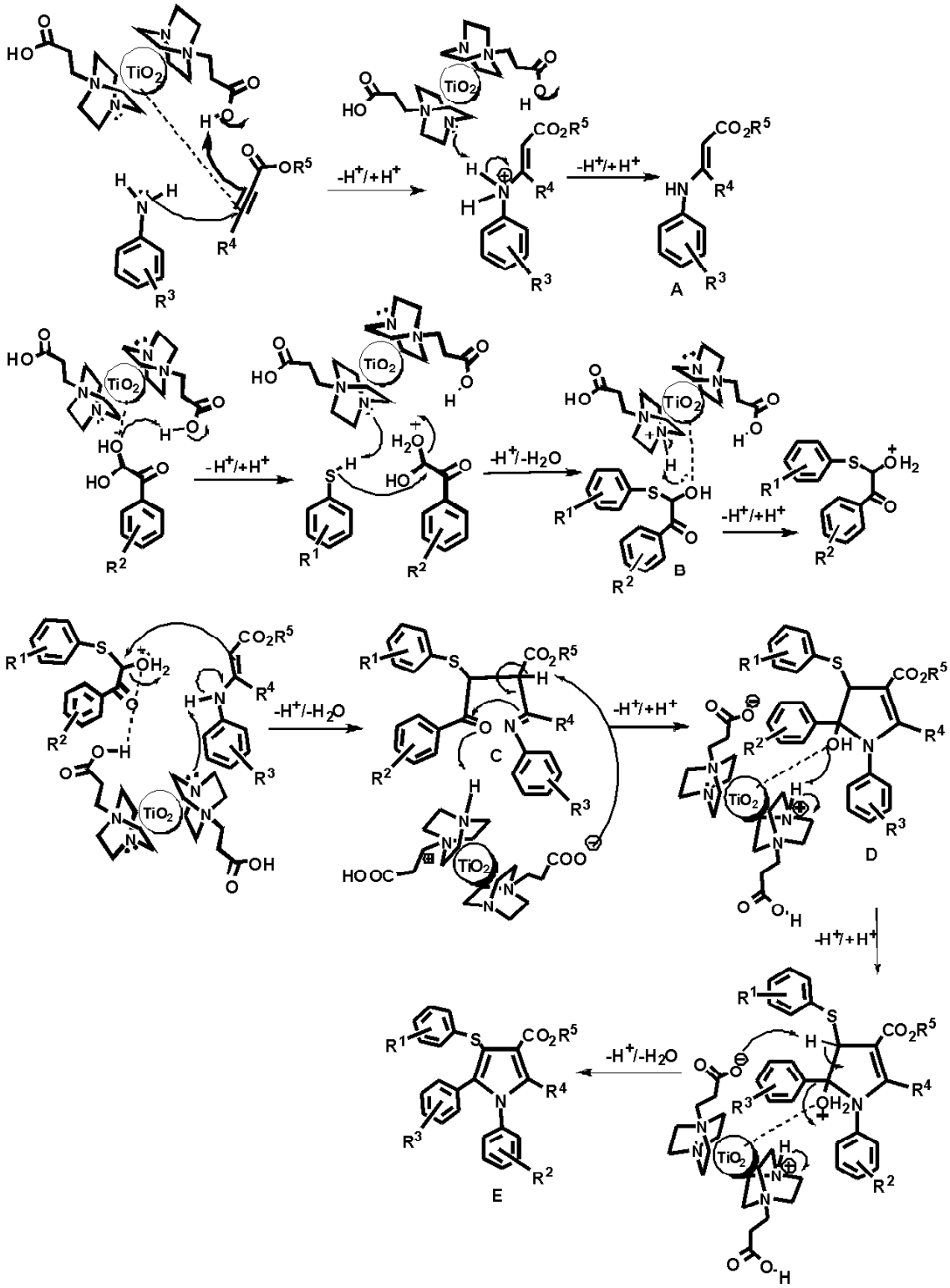
Entry	R^1	R^2	R^3	$R^{4/6}$	R^5	Yield[b]
1	4-Cl	H	4-Me	CO_2Me	Me	91
2	4-Cl	H	4-OMe	CO_2Et	Et	93
3	H	H	3,4-di Me	CO_2Me	Me	85
4	4-Me	4-Me	3-Me	CO_2Me	Me	85
5	H	H	4-OMe	CO_2Me	Me	87
6	4-Me	H	4-Br	CO_2Et	Et	84
7	4-Me	4-Me	4-Cl	CO_2Et	Et	85
8	4-Me	4-OMe	4-Cl	CO_2Et	Et	84
9	4-Me	H	4-OMe	CO_2Et	Et	86
10	4-Me	H	4-Cl	CO_2Et	Et	89
11	4-Cl	4-Cl	4-OMe	CO_2Et	Et	90
12	H	H	H	Me	Me	88
13	4-Cl	4-Cl	4-Me	4-Me	Me	88
14	4-Me	4-Cl	2-Me	Me	Me	87
15	H	4-NO_2	4-Me	Me	Me	95
16	4-Me	4-Me	4-Cl	Me	Me	88
17	4-Me	H	4-Br	Me	Et	84
18	4-Cl	H	4-Br	Me	Me	89
19	4-Cl	H	4-OMe	Me	Et	92
20	4-Me	H	4-OMe	Me	allyl	89
21	4-OMe	4-Cl	4-OMe	Me	allyl	94
22	4-Me	3-Br	4-Cl	Me	Me	90
23	butyl	H	2-Br	Me	Me	84
24	4-Me	4-Me	4-CO_2H	Me	Me	78
25	4-Cl	4-OMe	4-Br	Me	Me	89
26	4-OMe	H	3,4-di CH_3	Me	Me	92
27	4-Cl	4-OMe	H	Me	Me	86

[a]Reaction conditions: all reactions were carried out using various substituted or unsubstituted aromatic thiols, phenyl glyoxals (1 mmol), aromatic amines (1 mmol) and dialkyl acetylenedicarboxylatesor β-keto esters (1 mmol) under microwave-assisted 12 mol% nano-TiO_2@[DABCO(CH_2CH_2COOH)]$^+$[Br]$^-$ catalysed conditions. [b]Isolated yields.

tween aromatic thiol and phenyl glyoxal leads to formation of intermediate E followed by these two intermediates (C and E) went through condensation and synthesised intermediate G. Subsequently this intermediate G undergo cyclisation and aromatisation to form the final product J. Nano-TiO_2@[DABCO(CH_2CH_2COOH)]$^+$[Br]$^-$ extremely influenced the reaction mechanism from very beginning to last step as shown in Scheme 3. Here TiO_2-NP and carboxylic group shows acidic character whereas unsubstituted tertiary nitrogen centre shows basic character. Thus as a consequence



Scheme 2. A rational reaction mechanism for the formation of nano-TiO_2@[DABCO(CH_2CH_2COOH)]$^+$[Br]$^-$ catalyzed fully functionalised pyrrole from β-keto ester, aromatic thiol, phenyl glyoxal and aromatic amine.



Scheme 3. A rational mechanistic pathway to explain the nano-TiO_2@[DABCO-CH_2CH_2COOH]$^+$[Br]$^-$ catalyzed formation of penta substituted pyrrole from dialkyl acetylenedicarboxylate, aromatic thiol, phenyl glyoxal and aromatic amine.

of synergetic catalytic effect of TiO_2-NP and $[DABCO(CH_2CH_2COOH)]^+[Br]^-$ reactivity largely enhanced.

Recycling Experiment

For examining recyclability of nano-TiO_2@$[DABCO(CH_2CH_2COOH)]^+[Br]^-$ catalyst, for the formation of dimethyl 4-(4-chlorophenylthio)-5-phenyl-1-*p*-tolyl-1*H*-pyrrole-2,3-dicarboxylate (Table 2, entry 1) from the analogous starting materials under optimised conditions was considered as a model reaction. After completion of the reaction, the crude mixture was diluted with ethyl acetate (10 mL) and the catalyst was easily recovered by filtration using a sintered glass funnel. It was washed with ethyl acetate (5/10 mL) few more times to eliminate adhered organic compound and dried under vacuum. Next, to verify the activity of the catalyst, this recycling experiment was carried out using the recovered catalyst for the succeeding reactions. In a test of six cycles, it was observed that the catalyst could be reused with high catalytic activity (Fig. 5). After the recycling test, TEM analysis was also done. The result (Fig. 5) showed that there is no considerable alteration in morphology. These experiments have shown that nano-TiO_2@$[DABCO(CH_2CH_2COOH)]^+[Br]^-$ had sufficient stability and could reproduce the product several times with almost similar efficiency.

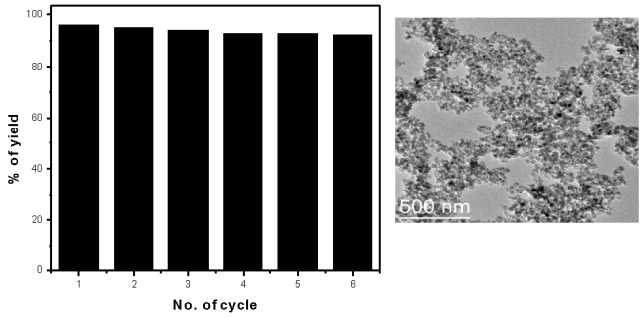


Fig. 5. Recyclability test of the catalyst nano-TiO_2@$[DABCO(CH_2CH_2COOH)]^+[Br]^-$.

Conclusions

This present protocol describes not only the expeditious but also solvent and chromatography-free synthesis of fully functionalised pyrrole moieties incorporating benzo-thio unit. Synergistic effects of microwave irradiation and nano-TiO_2@$[DABCO(CH_2CH_2CO_2H)]^+[Br]^-$ catalyst have been highlighted here. This recyclable combined catalytic system shows unprecedented catalytic performance multiple times with no loss of catalytic activity. Owing to simplicity of the procedure allied with environmentally benign features, it is hoped that this eco-compatible strategy will be embraced by the synthetic organic chemists at large.

Experimental section

General information of materials and instruments:

All the chemicals were availed from commercially accessible sources such as Aldrich, USA or Spectrochem, India or Rankem and used as received. Every reaction were performed in a closed reaction vessel under microwave irradiation using CEM Discover microwave reactor equipped with surface sensor for temperature measurement and controlled the reactions with setting time, temperature and power. The progress of the reactions was monitored by TLC checking. ^1H and ^{13}C NMR spectra were recorded on 300 MHz Bruker instrument using $CDCl_3$ or DMSO-d_6 as a solvent with tetramethylsilane (TMS) as internal reference. Chemical shifts are expressed in delta (δ) units in ppm and the data are represented as follows: for multiplicities s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet and coupling constants in Hz and integration. Infrared spectra were recorded on a Perkin-Elmer Spectrophotometer RX/FT-IR system in KBr pellets with absorptions in cm^{-1} and CHN analysis was performed using Perkin-Elmer 2400 Series II CHN analyzer. Melting points were determined on an electrical melting point apparatus with an open capillary and were uncorrected. HRMS were acquired using a Waters XEVO-G2S Q-TOF mass spertrometer with an ESI resource. Morphology and size of nano-TiO_2@$[DABCO(CH_2CH_2CO_2H)]^+[Br]^-$ system was determined by acquiring SEM images using a Zeiss EVO18 (Special Edition). To monitor the actual size of TiO_2-NPs covered with IL, TEM images were taken using a Jeol JEM 2010F transmission electron microscope operated at an accelerating voltage of 200 kV.

General procedure for the synthesis of DABCO based ionic liquid:

1,4-Diazobicyclo[2.2.2]octane (DABCO) (1 mmol) and 3-bromo propionic acid (1 mmol) were taken into a 10 ml round bottomed flask in anhydrous ethanol medium and then the mixture was refluxed for 2 h in an argon atmosphere. After completion of the reaction solvent was removed by rotor evaporator under reduced pressure. The synthesised ionic liquid was characterized by standard analytical techniques such as ^1H NMR, ^{13}C NMR.

General procedure for the synthesis of DABCO based ionic liquid embedded TiO_2 nanoparticles:

0.5 mmol titanium tetraisopropoxide was added to 10 ml ethanol and stirred in a covered flask for 10 min in 40 to 50°C (solution A). 1.5 mmol IL was dissolved into a mixture of 0.25 ml distilled water and 10 ml ethanol in a separate covered flask and stirred for 5 min (solution B). Then this titanium tetraisopropoxide solution (solution A) was added to sol B and vigorously stirred for another 1 hour in 100°C and then cooled to room temperature. Finally the ethanol was removed under vacuum and the resulting ionic liquid covered TiO_2-NP was obtained in powder form. The products were characterized by standard analytical techniques such as PXRD, SEM, TEM, TGA and DLS.

General procedure for the synthesis of pyrrole compounds:

In a closed reaction vial an equimolar mixture (1 mmol) of substiuted and unsubstituted aryl thiol, aryl glyoxal, aromatic amine and dialkyl acetylenedicarboxylate or β-keto ester along with 10 mol% of nano-TiO_2@[DABCO-CH_2CH_2COOH]$^+$[Br]$^-$ was subjected to microwave irradiation at 60°C (100 W) for 10 min. After completion of this reaction, the reaction vial was cooled to room temperature. Then crude product mixture was diluted with 5 mL ethyl acetate. Thus a white solid product was slowly precipitate out after scratching few times the crude product with spatula and collected through simple filtration technique. Finally, a pure white product was obtained directly by recrystallization from ethyl acetate without using any chromatography methodology in good to excellent yields. All the synthesized compounds were characterized by ^{1}H, ^{13}NMR, IR, melting point measurements, CHN and HRMS analysis and the structure of the product was confirmed by single-crystal X-ray diffraction.

Characterization data of the product

Dimethyl 4-(4-chlorophenylthio)-5-phenyl-1-p-tolyl-1H-pyrrole-2,3-dicarboxylate (Table 1, entry 1): White solid (91%); m.p. 120°C (EtOAc); R_f [12% EtOAc/petroleum ether (60–80°C)]: 0.53; 6% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.18–7.03 (m, 13H, ArH), 3.80 (s, 3H, -OCH_3), 3.71 (s, 3H, -OCH_3), 2.30 (s, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 165.1, 159.9, 142.7, 138.1, 137.0, 134.1, 130.8, 130.2, 129.0, 128.9, 128.3, 128.1, 128.0, 127.2, 126.0, 124.1, 109.0, 51.9, 52.0, 20.8 ppm; Anal. Calcd. for $C_{27}H_{22}ClNO_4S$: C, 65.91; H, 4.51; N, 2.85. Found: C, 65.64; H, 4.59; N, 2.99.

Diethyl 4-(4-chlorophenylthio)-1-(4-methoxyphenyl)-5-phenyl-1H-pyrrole-2,3-dicarboxylate(Table 1, entry 2): White solid (93%); m.p. 126°C (EtOAc); R_f [12% EtOAc/petroleum ether (60–80°C)]: 0.40; 8% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.27–7.02 (m, 11H, ArH), 6.79–6.76 (m, 2H, ArH), 4.25 (q, *J* 7.2 Hz, 2H, -OCH_2), 4.14 (q, *J* 7.2 Hz, 2H, -OCH_2), 3.74 (s, 3H, -OCH_3), 1.22–1.13 (m, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 164.4, 159.3, 143.5, 137.0, 130.8, 130.4, 130.1, 129.0, 129.0, 128.2, 128.0, 127.8, 127.4, 126.2, 124.1, 113.1, 108.2, 61.0, 59.7, 55.0, 13.6, 13.5 ppm; HRMS (ESI-TOF) *m/z*: [M+H]$^+$ Calcd. for [$C_{29}H_{27}ClNO_5S$]: 536.1293, Found: 536.1296; IR (KBr, υ_{max} cm^{-1}): 3436, 2926, 1715, 1508, 125, 1200, 1028, 820 cm^{-1}; Anal. Calcd. for $C_{29}H_{26}ClNO_5S$: C, 64.98; H, 4.89; N, 2.61. Found: C, 64.70; H, 4.92; N, 2.77.

Dimethyl 1-(3,4-dimethylphenyl)-5-phenyl-4-(phenylthio)-1H-pyrrole-2,3-dicarboxylate (Table 1, entry 3): White solid (85%); m.p. 112°C (EtOAc); R_f [12% EtOAc/petroleum ether (60–80°C)]: 0.54; 6% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (300 MHz, $CDCl_3$) : δ_H 7.22–7.01 (m, 10H, ArH), 6.90–6.85 (m, 2H, ArH), 3.77 (s, 3H, -OCH_3), 3.71 (s, 3H, -OCH_3), 2.20 (s, 3H, -CH_3), 2.14 (s, 3H, -CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 165.0, 160.0, 143.5, 138.2, 136.8, 136.5, 135.0, 130.6, 129.2, 129.0, 128.5, 128.1, 128.0, 127.2, 126.9, 126.0,125.0 125.0, 124.0, 109.1, 52.0, 51.6, 19.2, 19.1 ppm; Anal. Calcd. for $C_{28}H_{25}NO_4S$: C, 71.32; H, 5.34; N, 2.97. Found: C, 71.20; H, 5.39; N, 3.10.

Dimethyl 1-m-tolyl-5-p-tolyl-4-(p-tolylthio)-1H-pyrrole-2,3-dicarboxylate (Table 1, entry 4): White solid (85%); m.p. 112°C (EtOAc); R_f [12% EtOAc/petroleum ether (60–80°C)]: 0.52; 8% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.19–7.01 (m, 6H, ArH), 6.97–6.92 (m, 6H, ArH), 3.80 (s, 3H, -OCH_3), 3.69 (s, 3H, -OCH_3), 2.28 (s, 3H, -CH_3), 2.24 (s, 3H, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 165.5, 160.2, 144.0, 138.5, 138.3, 137.8, 135.2, 135.0, 130.7, 129.6, 129.5, 129.3, 128.8, 128.5, 128.2, 126.9, 126.3, 125.4, 123.9, 110.1, 52.3, 52.0, 21.3, 21.2, 21.0 ppm; HRMS (ESI-TOF) *m/z*: [M+Na]$^+$ Calcd. for [$C_{29}H_{27}ClNO_4SNa$]: 508.1553, Found: 508.1557; Anal. Calcd. for $C_{29}H_{27}NO_4S$: C, 71.70; H, 5.60; N, 2.88. Found: C, 71.58; H, 5.67; N, 3.04.

Dimethyl 1-(4-methoxyphenyl)-5-phenyl-4-(phenylthio)-1H-pyrrole-2,3-dicarboxylate (Table 1, entry 5): White solid

(87%); m.p. 112°C (EtOAc); R_f [15% EtOAc/petroleum ether (60–80°C)]: 0.52; 8% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.28–7.04 (m, 12H, ArH), 6.81–6.78 (m, 2H, ArH), 3.80 (s, 3H, -CH_3), 3.78 (s, 3H, -CH_3), 3.78 (s, 3H, -CH_3), 3.72 (s, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 165.3, 160.1 159.3, 144.0, 134.8, 130.7, 130.7, 130.4, 129.2, 129.1, 128.7, 128.6, 128.4, 127.7, 127.6, 127.3, 127.2, 127.1, 126.7, 125.3, 124.2, 113.6, 113.5, 109.6, 55.3, 52.2, 52.0 ppm; Anal. Calcd. for $C_{27}H_{23}NO_5S$: C, 68.48; H, 4.90; N, 2.96. Found: C, 68.72; H, 4.83; N, 2.82.

Dimethyl diethyl 1-(4-bromophenyl)-5-phenyl-4-(p-tolylthio)-1H-pyrrole-2,3-dicarboxylate (Table 1, entry 6): White solid (84%); m.p. 112°C (EtOAc); R_f [12% EtOAc/petroleum ether (60–80°C)]: 0.50; 6% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.42–7.38 (m, 2H, ArH), 7.26–7.14 (m, 4H, ArH), 7.07–7.01 (m, 7H, ArH), 4.29 (q, *J* 7.2 Hz, 2H, -OCH_2), 4.17 (q, *J* 7.2 Hz, 2H, -OCH_2), 2.22 (s, 3H, -CH_3), 1.25–1.15 (m, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 164.5, 159.3, 143.4, 137.0, 135.4, 134.4, 131.6, 130.7, 129.7, 129.4, 128.9, 128.6, 128.3, 127.6, 122.1, 110.7, 61.4, 61.0, 20.7, 13.9, 13.5 ppm; Anal. Calcd. for $C_{29}H_{26}BrNO_4S$: C, 61.70; H, 4.64; N, 2.48. Found: C, 61.92; H, 4.59; N, 2.33.

Diethyl 1-(4-chlorophenyl)-5-p-tolyl-4-(p-tolylthio)-1H-pyrrole-2,3-dicarboxylate (Table 1, entry 7): White solid (85%); m.p. 118°C (EtOAc); R_f [12% EtOAc/petroleum ether (60–80°C)]: 0.52; 8% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.29–7.26 (m, 2H, ArH), 7.13–6.98 (m, 8H, ArH), 6.90–6.89 (m, 2H, ArH), 4.26 (q, *J* 7.2 Hz, 2H, -OCH_2), 4.17 (q, *J* 7.2 Hz, 2H, -OCH_2), 2.28 (s, 3H, -CH_3), 2.82 (s, 3H, -CH_3), 1.23–1.16 (m, 6H, -CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 135.0, 159.2, 144.0, 138.7, 136.3, 135.1, 134.7, 134.2, 130.7, 129.8, 129.5, 128.6, 128.5, 127.7, 126.0, 123.0, 110.5, 61.3, 61.0, 21.2, 21.0, 14.0, 13.8 ppm; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd. for $[C_{30}H_{29}ClNO_4S]$: 534.1500, Found: 534.1507; Anal. Calcd. for $C_{30}H_{28}ClNO_4S$: C, 67.47; H, 5.28; N, 2.62. Found: C, 67.39; H, 5.24; N, 2.59.

Diethyl 1-(4-chlorophenyl)-5-(4-methoxyphenyl)-4-(p-tolylthio)-1H-pyrrole-2,3-dicarboxylate (Table 1, entry 8): White solid (84%); m.p. 114°C (EtOAc); R_f [12% EtOAc/petroleum ether (60–80°C)]: 0.49; 8% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.26 (d, *J* 8.4 Hz, 2H, ArH), 7.08–6.88 (m, 6H, ArH), 6.92 (d, *J* 8.8 Hz, 2H, ArH), 6.72 (d, *J* 8.8 Hz, 2H, ArH), 4.27 (q, *J* 7.2 Hz, 2H, -OCH_2), 4.14 (q, *J* 7.2 Hz, 2H, -OCH_2), 3.70 (s, 3H, -OCH_3), 2.25 (s, 3H, -CH_3), 1.20 (t, *J* 7.2 Hz, 3H, -CH_3), 1.16 (t, *J* 7.2 Hz, 3H, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 165.0, 159.4, 143.7, 136.4, 135.2, 134.3, 134.1, 132.0, 131.8, 129.3, 129.5, 128.8, 127.8, 122.9, 121.0, 112.0, 113.2, 110.0, 61.3, 60.5, 55.0, 21.0, 14.0, 13.8 ppm; Anal. Calcd. for $C_{30}H_{28}ClNO_5S$: C, 65.51; H, 5.13; N, 2.55. Found: C, 65.78; H, 5.03; N, 2.71.

Diethyl 1-(4-methoxyphenyl)-5-phenyl-4-(p-tolylthio)-1H-pyrrole-2,3-dicarboxylate (Table 1, entry 9): White solid (86%); m.p. 92°C (EtOAc); R_f [12% EtOAc/petroleum ether (60–80°C)]: 0.44; 8% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.18–7.10 (m, 2H, ArH), 7.04–6.95 (m, 8H, ArH), 6.76–6.72 (m, 2H, ArH), 4.22 (q, *J* 7.2 Hz, 2H, -OCH_2), 4.10 (q, *J* 7.2 Hz, 2H, -OCH_2), 3.71 (s, 3H, -OCH_3), 2.23 (s, 3H, -CH_3), 1.18 (t, *J* 7.2 Hz, 2H, -OCH_2), 1.15 (t, *J* 7.2 Hz, 3H, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 165.0, 159.5, 159.1, 139.7, 135.0, 134.6, 130.6, 130.4, 129.3, 129.1, 128.2, 127.5, 127.6, 127.2, 123.7, 113.4, 109.8, 61.1, 60.8, 55.1, 20.8, 13.9, 13.8 ppm; Anal. Calcd. for $C_{30}H_{29}NO_5S$: C, 69.88; H, 5.67; N, 2.72. Found: C, 69.66; H, 5.74; N, 2.89.

Diethyl 1-(4-chlorophenyl)-5-phenyl-4-(p-tolylthio)-1H-pyrrole-2,3-dicarboxylate (Table 1, entry 10): White solid (89%); m.p. 115°C (EtOAC); R_f [12% EtOAc/petroleum ether (60–80°C)]: 0.50; 6% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.25–7.03 (m, 13H, ArH), 4.27 (q, *J* 7.2 Hz, 2H, -OCH_2), 4.15 (q, *J* 7.05 Hz, 2H, -OCH_2), 2.26 (s, 3H, -CH_3), 1.24–1.15 (m, 6H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 164.5, 159.0, 143.3, 136.4, 135.1, 134.2, 130.4, 129.2, 128.7, 128.4, 128.2, 128.0, 127.5, 122.9, 110.4, 61.1, 60.6, 20.6, 13.5, 13.6 ppm, HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd. for $[C_{29}H_{27}ClNO_4S]$: 520.1344, Found: 520.1349; IR (KBr, υ_{max} cm^{-1}): 3420, 2925, 1720, 1535, 1490, 1260, 1225, 1190, 1090 cm^{-1}; Anal. Calcd. for $C_{29}H_{26}ClNO_4S$: C, 66.98; H, 5.04; N, 2.69. Found: C, 66.79; H, 5.05; N, 2.82.

Diethyl 5-(4-chlorophenyl)-4-(4-chlorophenylthio)-1-(4-methoxyphenyl)-1H-pyrrole-2,3-dicarboxylate (Table 1, entry 11): White solid (90 %); m.p. 110°C (EtOAc); R_f [15% EtOAc/petroleum ether (60–80°C)]: 0.40; 8% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.23–7.18 (m, 4H, ArH), 7.12–7.08 (m, 4H, ArH), 7.00–6.96 (m, 2H, ArH), 6.85–6.82 (m, 2H, ArH), 4.32 (q, *J* 7.2 Hz,

2H, -OCH_2), 4.20 (q, *J* 7.2 Hz, 2H, -OCH_2), 3.81 (s, 3H, -OCH_3), 1.27–1.20 (m, 6H, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 165.0, 159.6, 160.0, 142.5, 137.2, 134.7, 131.7, 131.0, 130.0, 129.3, 128.8, 128.5, 128.2, 128.0, 127.2, 127.1, 125.2, 113.3, 109.1, 61.2, 55.4, 14.0, 13.9 ppm; HRMS (ESI-TOF) *m/z*: $[M+H]^+$ Calcd. for $[C_{29}H_{26}Cl_2NO_5S]$: 570.0903, Found: 570.0900; Anal. Calcd. for $C_{29}H_{25}Cl_2NO_5S$: C, 61.06; H, 4.42; N, 2.46. Found: C, 61.36; H, 4.32; N, 2.34.

Methyl 2-methyl-1,5-diphenyl-4-(phenylthio)-1H-pyrrole-3-carboxylate (Table 1, entry 12): White solid (88%); m.p. 142°C (EtOAc); R_f [8% EtOAc/petroleum ether (60–80°C)]: 0.54; 2% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.28–7.09 (m, 15H, ArH), 3.60 (s, 3H, -OCH_3), 2.39 (s, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 164.8, 139.5, 139.0, 137.8, 137.0, 130.0, 129.9, 128.4, 128.0, 127.7, 126.8, 125.3, 123.8, 114.0, 108.0, 50.1, 12.8 ppm; Anal. Calcd. for $C_{25}H_{21}NO_2S$: C, 75.16; H, 5.30; N, 3.51. Found: C, 75.39; H, 5.21; N, 3.28.

Methyl 5-(4-chlorophenyl)-4-(4-chlorophenylthio)-2-methyl-1-p-tolyl-1H-pyrrole-3-carboxylate (Table 1, entry 13): White solid (88%); m.p. 112°C (EtOAc); R_f [8% EtOAc/petroleum ether (60–80°C)]: 0.46; 3% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (400 MHz,$CDCl_3$): δ_H 7.14–7.04 (m, 8H, ArH), 6.95–6.94 (m, 4H, ArH), 3.67 (s, 3H, -OCH_3), 2.38 (s, 3H, -CH_3), 2.30 (s, 3H, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 164.8, 138.7, 138.6, 138.5, 138.3, 134.4, 133.4, 131.8, 130.0, 129.7, 129.0, 129.0, 128.7, 128.4, 128.0, 127.0, 127.0, 114.2, 108.2, 50.7, 20.8, 13.0 ppm; Anal. Calcd. for $C_{26}H_{21}Cl_2NO_2S$: C, 64.73; H, 4.39; N, 2.90. Found: C, 64.96; H, 4.34; N, 2.78.

Methyl 5-(4-chlorophenyl)-2-methyl-1-o-tolyl-4-(p-tolylthio)-1H-pyrrole-3-carboxylate (Table 1, entry 14): White solid (87%); m.p. 122°C (EtOAc); R_f [8% EtOAc/petroleum ether (60–80°C)]: 0.52; 3% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (400 MHz,$CDCl_3$): δ_H 7.27–7.14 (m, 4H, ArH), 7.06–7.02 (m, 4H, ArH), 7.00–6.96 (m, 4H, ArH), 3.66 (s, 3H, -CH_3), 2.27 (s, 3H, -CH_3), 2.25 (s, 3H, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 165.2, 138.3, 138.0, 136.6, 136.4, 136.0, 134.1, 133.7, 131.6, 131.1, 129.3, 129.2, 129.1, 129.0, 127.8, 126.6, 125.8, 114.5, 109.2, 50.8, 21.0, 17.2, 12.6 ppm; Anal. Calcd. for $C_{27}H_{24}ClNO_2S$: C, 70.19; H, 5.24; N, 3.03. Found: C, 70.42; H, 5.15; N, 2.98.

Methyl 2-methyl-5-(4-nitrophenyl)-4-(phenylthio)-1-p-tolyl-1H-pyrrole-3-carboxylate (Table 1, entry 15): White solid (95%); m.p. 208°C (EtOAc); R_f [8% EtOAc/petroleum ether (60–80°C)]: 0.48; 8% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.94 (d, *J* 8.8 Hz, 2H, ArH), 7.24–6.92 (m, 11H ArH), 3.66 (s, 3H -OCH_3), 2.40 (s, 3H, -CH_3), 2.34 (s, 3H, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 165.0, 146.3, 139.5, 139.2, 139.0, 137.2, 136.8, 134.2, 131.5, 131.2, 130.0, 128.5, 128.3, 128.0, 126.0, 125.6, 124.9, 122.7, 115.4, 110.6, 51.0, 21.0, 13.0 ppm; Anal. Calcd. for $C_{26}H_{22}N_2O_4S$: C, 68.10; H, 4.84; N, 6.11. Found: C, 67.90; H, 4.80; N, 6.20.

Methyl 1-(4-chlorophenyl)-2-methyl-5-p-tolyl-4-(p-tolylthio)-1H-pyrrole-3-carboxylate (Table 1, entry 16): White solid (88%); m.p. 120°C (EtOAc); R_f [8% EtOAc/petroleum ether (60–80°C)]: 0.54; 2% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.30 (d, *J* 8.5 Hz, 2H, ArH), 7.04–6.99 (m, 6H, ArH), 6.95–6.90 (m, 4H, ArH), 3.65 (s, 3H, -OCH_3), 2.38 (s, 3H, -CH_3), 2.27 (s, 3H, -CH_3), 2.24 (s, 3H, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 165.2, 139.6, 137.9, 137.6, 136.8, 136.3, 134.3, 134.1, 130.7, 130.6, 129.8, 129.3, 129.3, 128.6, 127.4, 126.3, 115.0, 109.4, 96.2, 50.9, 21.3, 21.0, 13.2 ppm; Anal. Calcd. for $C_{27}H_{24}ClNO_2S$: C, 70.19; H, 5.24; N, 3.03. Found: C, 70.38; H, 5.21; N, 2.95.

Ethyl 1-(4-bromophenyl)-2-methyl-5-phenyl-4-(p-tolylthio)-1H-pyrrole-3-carboxylate (Table 1, entry 17): White solid (84%); m.p. 140°C (EtOAc); R_f [8% EtOAc/petroleum ether (60–80°C)]: 0.51; 3% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.49–746 (m, 2H, ArH), 7.19–6.99 (m, 11H, ArH), 4.19 (q, *J* 7.2 Hz, 2H, -OCH_2), 2.45 (s, 3H, -CH_3), 1.11 (t, *J* 7.05 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 164.7, 139.4, 137.9, 136.8, 136.6, 133.8, 132.2, 130.7, 130.2, 129.9, 129.1, 127.6, 125.8, 122.2, 115.2, 109.1, 59.7, 20.8, 13.9, 13.0 ppm; HRMS (ESI-TOF) *m/z*: [M+H]+ Calcd. for $[C_{27}H_{25}BrNO_2S]$: 506.0784. Found 506.0789; IR (KBr, υ_{max} cm^{-1}): 3433, 2981, 1695, 1544, 1488, 1400, 1251, 1226, 1134, 1087, 840; Anal. Calcd. for $C_{27}H_{24}BrNO_2S$: C, 64.03; H, 4.78; N, 2.77. Found: C, 64.25; H, 4.76; N, 2.63.

Methyl 1-(4-bromophenyl)-4-(4-chlorophenylthio)-2-methyl-5-phenyl-1H-pyrrole-3-carboxylate (Table 1, entry 18): White solid (89%); m.p. 122°C (EtOAc); R_f [8% EtOAc/petroleum ether (60–80°C)]: 0.48; 3% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (300 MHz,$CDCl_3$): δ_H 7.46 (d, *J* 8.4 Hz, 2H, ArH), 7.26–7.14 (m, 5H, ArH), 7.07–6.96 (m,

6H, ArH), 3.69 (s, 3H, -CH_3), 2.41 (s, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 165.1, 139.9, 139.1, 138.3, 136.6, 132.5, 130.8, 130.3, 130.2, 130.1, 128.7, 128.1, 128.0, 122.6, 115.0, 108.8, 51.1, 13.3 ppm; Anal. Calcd. for $C_{25}H_{19}BrClNO_2S$: C, 58.55; H, 3.73; N, 2.73. Found: C, 58.72; H, 3.68; N, 2.60.

Ethyl 4-(4-chlorophenylthio)-1-(4-methoxyphenyl)-2-methyl-5-phenyl-1H-pyrrole-3-carboxylate (Table 1, entry 19): White solid (92%); m.p. 128°C (EtOAc); R_f [10% EtOAc/petroleum ether (60–80°C)]: 0.49; 5% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.19–7.01 (m, 11H, ArH), 6.86–6.83 (m, 2H, ArH), 4.18(q, *J* 7.2 Hz, 2H, -OCH_2), 3.79 (s, 3H, -OCH_3), 2.43 (s, 3H, -CH_3), 1.10 (t, *J* 7.2 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 164.8, 159.2, 140.1, 139.6, 138.8, 130.7, 130.5, 130.1, 129.7, 129.3, 128.4, 127.6, 127.6, 126.8, 114.5, 114.2, 107.2, 59.6, 55.3, 13.9, 13.0 ppm; Anal. Calcd. for $C_{27}H_{24}ClNO_3S$: C, 67.84; H, 5.06; N, 2.93. Found: C, 67.70; H, 5.04; N, 3.02.

Allyl 4-(4-chlorophenylthio)-1-(4-methoxyphenyl)-2-methyl-5-phenyl-1H-pyrrole-3-carboxylate (Table 1, entry 20): White solid (89%); m.p. 126°C (EtOAc); R_f [8% EtOAc/petroleum ether (60–80°C)]: 0.49; 4% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.27–7.02 (m, 11H, ArH), 6.86–6.83 (m, 2H, ArH), 5.83–5.74 (m, 1H, -CH), 5.32–5.26 (m, 1H, -OCH_2), 4.66–4.64 (m, 2H, -CH_2), 3.79 (s, 3H, -OCH_3), 2.44 (s, 3H, -CH_3), 2.29 (s, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 164.6, 159.1, 139.9, 138.7, 137.0, 133.8, 132.6, 130.8, 130.7, 130.2, 129.4, 129.1, 127.5, 126.0, 117.3, 114.2, 114.1, 108.6, 64.4, 55.3, 20.8, 13.1 ppm; IR (KBr, υ cm^{-1}): 3423, 2925, 1706, 1546, 1514, 1400, 1251, 1220, 1070, 1488, 1400; Anal. Calcd. for $C_{28}H_{24}ClNO_3S$: C, 68.63; H, 4.94; N, 2.86. Found: C, 68.40; H, 4.91; N, 2.98.

Allyl 5-(4-chlorophenyl)-1-(4-methoxyphenyl)-4-(4-methoxyphenylthio)-2-methyl-1H-pyrrole-3-carboxylate (Table 1, entry 21): White solid (94%); m.p. 136°C (EtOAc); R_f [10% EtOAc/petroleum ether (60–80°C)]: 0.41; 5% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (400 MHz,$CDCl_3$): δ_H 7.11–7.06 (m, 4H, ArH), 7.02–6.98 (m, 4H, ArH), 6.83 (d, *J* 8.8 Hz, 2H, ArH), 6.74 (d, *J* 8.8 Hz, 2H, ArH), 5.88–5.79 (m, 1H, -CH), 5.33–5.28 (m, 1H, -CH_2), 5.15–5.12 (m, 1H, -CH_2), 4.66 (d, *J* 5.6 Hz, 2H, -CH_2), 3.76 (s, 3H, -OCH_3), 3.72 (s, 3H, -OCH_3), 2.38 (s, 3H, -OCH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C ppm 164.5, 159.3, 157.5, 138.9, 138.2, 133.5, 132.7, 132.2, 130.7, 130.0, 129.4, 129.4, 128.4, 128.0, 127.9, 117, 114.4, 114.3, 110.4, 64.6, 55.4, 55.3, 13.2; Anal. Calcd. for $C_{29}H_{26}ClNO_4S$: C, 66.98; H, 5.04; N, 2.69. Found: C, 66.78; H, 4.99; N, 2.75.

Methyl 5-(3-bromophenyl)-1-(4-chlorophenyl)-2-methyl-4-(p-tolylthio)-1H-pyrrole-3-carboxylate (Table 1, entry 22): White solid (90%); m.p. 115°C (EtOAc); R_f [8% EtOAc/petroleum ether (60–80°C)]: 0.46; 8% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (400 MHz,$CDCl_3$): δ_H 7.35–7.26 (9m, 3H, ArH), 7.19 (bs, 1H, ArH), 7.07–6.99 (m, 7H, ArH), 6.95–6.93 (m, 1H, ArH), 3.69 (s, 3H, -OCH_3), 2.38 (s, 3H, -CH_3), 2.27 (s, 3H, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 165.1, 138.4, 137.4, 135.9, 135.7, 134.6, 134.5, 133.6, 132.3, 130.7, 129.6, 129.5, 129.5, 129.3, 129.3, 129.2, 126.7, 121.6, 115.0, 110.8, 51.0, 20.9, 13.1 ppm; Anal. Calcd. for $C_{26}H_{21}BrClNO_2S$: C, 59.27; H, 4.02; N, 2.66. Found: C, 59.11; H, 4.08; N, 2.76.

Methyl 4-(butylthio)-2-methyl-1,5-diphenyl-1H-pyrrole-3-carboxylate (Table 1, entry 23): White solid (84%); m.p. 106°C (EtOAc); R_f [8% EtOAc/petroleum ether (60–80°C)]: 0.60; 2% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.29–7.26 (m, 2H, ArH), 7.16–7.01 (m, 7H, ArH), 3.90 (s, 3H, -CH_3), 2.64 (t, *J* 7.2 Hz, 3H, -CH_3), 2.32 (s, 3H, -CH_3), 0.72 (t, *J* 7.2 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 165.5, 138.2, 137.3, 137.1, 131.0, 128.6, 128.1, 128.0, 127.1, 127.0, 114.2, 112.0, 50.6, 36.1, 30.7, 21.3, 13.2, 12.8 ppm; Anal. Calcd. for $C_{23}H_{25}NO_2S$: C, 72.79; H, 6.64; N, 3.69. Found: C, 72.89; H, 6.60, N; 3.52.

4-(3-(Methoxycarbonyl)-2-methyl-5-p-tolyl-4-(p-tolylthio)-1H-pyrrol-1-yl)benzoic acid (Table 1, entry 24): White solid (78%); m.p. 138°C (EtOAc); R_f [40% EtOAc/petroleum ether (60–80°C)]: 0.45; 15% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.91 (d, *J* 8 Hz, 2H, ArH), 7.38 (d, *J* 8 Hz, 2H, ArH), 7.02–6.92 (m, 8H, ArH), 3.53 (s, 3H, -OCH_3), 2.28 (s, 3H, -CH_3), 2.17 (s, 3H, -CH_3), 2.13 (s, 3H, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 166.7, 164.4, 141.0, 139.8, 137.8, 137.2, 136.6, 134.0, 131.0, 130.6, 130.3, 129.4, 129.1, 128.6, 127.4, 125.6, 114.2, 108.0, 51.0, 21.0, 20.6, 13.0 ppm; Anal. Calcd. for $C_{28}H_{25}NO_4S$: C, 71.32; H, 5.34; N, 2.97. Found: C, 71.10; H, 5.38; N, 3.07.

Methyl 1-(4-bromophenyl)-4-(4-chlorophenylthio)-5-(4-methoxyphenyl)-2-methyl-1H-pyrrole-3-carboxylate (Table 1, entry 25): White solid (89%); m.p. 122°C (EtOAc); R_f [8% EtOAc/petroleum ether (60–80°C)]: 0.42; 4% EtOAc/petro-

leum ether (60–80°C) as eluent; ^{1}H NMR (400 MHz,$CDCl_3$): δ_H 7.44 (d, *J* 8.4 Hz, 2H, ArH), 7.12 (d, *J* 8.4 Hz, 2H, ArH), 7.03 (d, *J* 8.4 Hz, 2H, ArH), 3.65 (s, 6H, -OCH_3), 2.36 (s, 3H, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 165.0, 159.1, 139.5, 139.1, 138.0, 136.5, 132.2, 131.8, 129.9, 129.8, 128.2, 127.0, 122.2, 122.1, 114.5, 113.2, 108.1, 55.0, 50.7, 13.1 ppm; Anal. Calcd. for $C_{26}H_{21}BrClNO_3S$: C, 57.52; H, 3.90; N, 2.58. Found: C, 57.26; H, 3.95; N, 2.70.

Methyl 1-(3,4-dimethylphenyl)-4-(4-methoxyphenylthio)-2-methyl-5-phenyl-1H-pyrrole-3-carboxylate (Table 1, entry 26): White solid (92%); m.p. 130°C (EtOAc); R_f [10% EtOAc/petroleum ether (60–80°C)]: 0.51; 4% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 7.15–7.03 (m, 8H, ArH), 6.87–6.74 (m, 4H, ArH), 3.72 (s, 3H, -OCH_3), 3.71 (s, 3H, -OCH_3), 2.38 (s, 3H, -CH_3), 2.17 (s, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 165.1, 157.1, 139.1, 138.0, 137.0, 136.4, 135.0, 130.8, 130.6, 129.5, 129.0, 128.2, 127.1, 125.4, 113.8, 109.6, 54.9, 50.5, 19.3, 19.2, 12.8 ppm; Anal. Calcd. for $C_{28}H_{27}NO_3S$: C, 73.49; H, 5.95; N, 3.06. Found: C, 73.72; H, 5.91; N, 2.87.

Methyl 4-(4-chlorophenylthio)-5-(4-methoxyphenyl)-2-methyl-1-phenyl-1H-pyrrole-3-carboxylate (Table 1, entry 27): White solid (86%); m.p. 100°C (EtOAc); R_f [10% EtOAc/petroleum ether (60–80°C)]: 0.44; 6% EtOAc/petroleum ether (60–80°C) as eluent; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.30 (bs, 3H, ArH), 7.14–7.04 (m, 6H, ArH), 6.91 (d, *J* 8.5 Hz, 2H, ArH), 6.63 (d, *J* 8.85 Hz, 2H, ArH), 3.66 (s, 3H, -OCH_3), 3.66 (s, 3H, -OCH_3), 2.37 (s, 3H, -CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 164.8, 158.8, 139.6, 139.1, 138.0, 137.4, 129.7, 128.1, 122.5, 114.1, 107.4, 54.8, 50.6, 13.0 ppm; Anal. Calcd. for $C_{26}H_{22}ClNO_3S$: C, 67.30; H, 4.78; N, 3.02. Found: C, 67.54; H, 4.76; N, 2.89.

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