

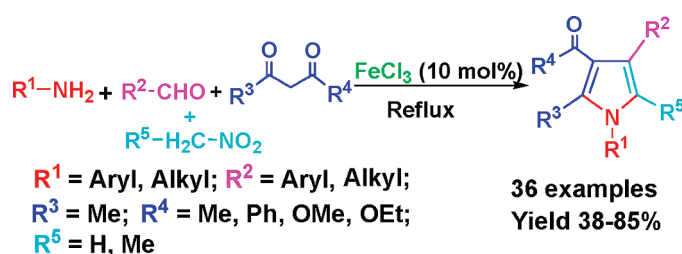
Iron(III)-Catalyzed Four-Component Coupling Reaction of 1,3-Dicarbonyl Compounds, Amines, Aldehydes, and Nitroalkanes: A Simple and Direct Synthesis of Functionalized Pyrroles

Sukhendu Maiti, Srijit Biswas, and Umasish Jana*

Department of Chemistry, Jadavpur University, Kolkata 700032, West Bengal, India

jumasish2004@yahoo.co.in

Received December 16, 2009



A simple, convenient, and multicomponent coupling strategy for the synthesis of highly functionalized pyrroles catalyzed by iron(III) salts has been developed. This strategy demonstrated four-component coupling reactions of 1,3-dicarbonyl compounds, amines, aromatic aldehydes, and nitroalkanes without an inert atmosphere. This methodology provides an alternative approach for easy access of highly substituted pyrroles in moderate to very good yields using four simple and readily available building blocks via one-pot tandem reaction. Notably, this method is very cheap, straightforward, and environmentally friendly compared to the existing methods.

Introduction

The pyrrole ring represents an important class of structural unit frequently found in many natural products¹ and biologically and pharmaceutically active compounds.² It has been widely used as antitumor,^{3a} anti-inflammatory,^{3b,c} antibacterial,^{3c,d} antioxidant,^{3e} and antifungal agents.^{3f} Furthermore, they are also extensively used in material science.⁴ Consequently, many new synthetic methods have been developed for the construction of pyrroles and their

derivatives.⁵ Among the various methods for the synthesis of pyrroles, the most frequently used methods are Hantzsch,⁶ Knorr,⁷ and Paal–Knorr⁸ reactions. Although these methods are very useful for the synthesis of pyrrole derivatives, these classical reactions have significant drawbacks such as availability of the starting materials, multisteps synthetic operations, functional group compatibility, regioselectivity,

(1) (a) Sundburg, R. J. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon Press: Oxford, 1996; Vol. 2, pp 119–206. (b) Boger, D. L.; Boyce, C. W.; Labriola, M. A.; Sehon, C. A.; Jin, Q. *J. Am. Chem. Soc.* **1999**, *121*, 54–62. (c) Bullington, J. L.; Wolff, R. R.; Jackson, P. F. *J. Org. Chem.* **2002**, *67*, 9439–9442. (d) Fürstner, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 3582. (e) Hoffmann, H.; Lindel, T. *Synthesis* **2003**, 1753–1783. (f) Agarwal, S.; Cämmerer, S.; Filali, S.; Fröhner, W.; Knöll, Krahl, M. P.; Reddy, K. R.; Knölker, H. *J. Curr. Org. Chem.* **2005**, *9*, 1601–1615. (g) Banwell, M. G.; Goodwin, T. E.; Ng, S.; Smith, J. A.; Wong, D. J. *Eur. J. Org. Chem.* **2006**, 3043. (h) Fan, H.; Peng, J.; Hamann, M. T.; Hu, J.-F. *Chem. Rev.* **2008**, *108*, 264.

(2) (a) Muchowski, J. M. *Adv. Med. Chem.* **1992**, *1*, 109. (b) Gribble, G. W. In *Comprehensive Heterocyclic Chemistry II*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon Press: Oxford, 1996; Vol. 2, pp 207. (c) Biava, M.; Fioravanti, R.; Porretta, G. C.; Deidda, D.; Maullo, C.; Pompei, P. *Bioorg. Med. Chem. Lett.* **1999**, *9*, 2983–2988. (d) Cozzi, P.; Mongelli, N. *Curr. Pharm. Des.* **1998**, *4*, 181. (e) Thompson, R. B. *FASEB J.* **2001**, *15*, 1671.

(3) (a) Denny, W. A.; Rewcastle, G. W.; Baguley, B. C. *J. Med. Chem.* **1990**, *33*, 814. (b) Toja, E.; Selva, D.; Schiatti, P. *J. Med. Chem.* **1984**, *27*, 610. (c) Demopoulos, V. J.; Rekkas, E. *J. Pharm. Sci.* **1995**, *84*, 79. (d) Bürli, R. W.; McMinn, D.; Kaizerman, J. A.; Hu, W.; Ge, Y.; Pack, Q.; Jiang, V.; Gross, M.; Garcia, M.; Tanaka, R.; Moser, H. E. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1253. (e) Lehuède, J.; Fauconneau, B.; Barrier, L.; Qurakow, M.; Piriou, A.; Vierfond, J. M. *Eur. J. Med. Chem.* **1999**, *34*, 991. (f) Del Poeta, M.; Schell, W. A.; Dykstra, C. C.; Jones, S.; Tidwell, R. R.; Czarny, A.; Bajic, M.; Bajic, M.; Kumar, A.; Boykin, D.; Perfect, J. R. *Antimicrob. Agents Chemother.* **1998**, *42*, 2495.

(4) For a review, see: (a) Higgins, S. *J. Chem. Soc. Rev.* **1997**, *26*, 247. (b) Groenendaal, L.; Meijer, E.-W.; Vekemans, J. A. J. M. In *Electronic Materials: The Oligomer Approach*; Müllen, K., Wegner, G., Eds.; Wiley-VCH: Weinheim, 1997. (c) Domingo, V. M.; Aleman, C.; Brillias, E.; Julia, L. *J. Org. Chem.* **2001**, *66*, 4058–4061. (d) Novak, P.; Müller, K.; Santhanam, S. V.; Hass, O. *Chem. Rev.* **1997**, *97*, 207–282. (e) Ramanavicius, A.; Ramanaviciene, A.; Malinauskas, A. *Electrochem. Acta* **2006**, *51*, 6025–6037. (f) Langley, P. J.; Davis, F. J.; Mitchell, G. R. *J. Chem. Soc., Perkin Trans. 2* **1997**, 2229–2240. (g) Li, X.; Run-Feng, C.; Huang, M. R.; Zhu, M.-Z.; Chen, K. *J. Polym. Sci., Part A: Polym. Chem.* **2004**, *42*, 2073–2092. (h) Kiskan, B.; Akar, A.; Kizilcan, N.; Ustamehmetoglu, B. *J. Appl. Polym. Sci.* **2005**, *96*, 1830–1834.

and harsh reaction conditions, which limit their scope. To overcome these limitations, various new efficient strategies such as multicomponent coupling^{9,5b,10y,z} and transition metal^{5b,9a,g,10} catalyzed reactions have recently been developed. Among them multicomponent coupling reactions (MCRs) offer significant advantages over classical stepwise methods, because they offer rapid and convergent construction of complex molecules without the need of isolation and purifications of any intermediates, resulting in substantial minimization of waste, labor, time, and cost.¹¹ Thus, such reactions are economically and environmentally more attractive and have become an important tool in modern organic synthesis. In this context, four-component coupling reactions for the synthesis of pyrroles have received much attention.^{9a,e,h,12} However, the use of expensive and toxic chemicals, nonavailability of the substrates, and cumbersome procedures for the product isolation limit their practical applications. Therefore, ongoing studies for the synthesis of pyrroles in terms of efficiency, minimal environmental effect, operational simplicity, economic viability, and high selectivity in the presence of less expensive catalyst are still highly desirable.

Over the past few years iron salts have been shown to be effective, alternative, and promising transition-metal catalysts and have received much attention due to their low price, sustainability, ready availability, nontoxicity, and environmentally friendly properties.¹³ Very recently, iron has also received much attention in the synthesis of heterocyclic compounds.¹⁴ However, to the best of our knowledge there are no methods

available for the iron-catalyzed synthesis of pyrroles. As part of our ongoing research program at developing various iron-salts-mediated efficient new organic transformations,¹⁵ we wish to report here a novel FeCl₃-catalyzed four-component coupling of commercially available 1,3-dicarbonyl compounds, aldehydes, amines, and nitroalkanes for the synthesis of highly functionalized pyrroles in one pot. This methodology represents a simple route to access of tetra- and pentasubstituted pyrroles in moderate to good yields under mild conditions.

Results and Discussion

According to the Grob and Cameisch reaction, it is well-known that pyrroles can be obtained from Michael reaction of β -enamino ketones or esters and nitroalkenes followed by cyclization.¹⁶ However, only little has been explored in this

(5) (a) Wang, J.-Y.; Wang, X.-P.; Yu, Z.-S.; Yu, W. *Adv. Synth. Catal.* **2009**, *351*, 2063–2066 and references therein. (b) Merkul, E.; Boersch, C.; Frank, W.; Müller, T. *J. Org. Lett.* **2009**, *11*, 2269–2272 and references therein. (c) Brichacek, M.; Njardarson, J. *T. Org. Biomol. Chem.* **2009**, *7*, 1761. (d) Zhu, Q.; Jiang, H.; Li, J.; Liu, S.; Xia, C.; Zhang, M. *J. Comb. Chem.* **2009**, *11*, 685. (e) Fu, X.; Chen, J.; Li, G.; Liu, Y. *Angew. Chem., Int. Ed.* **2009**, *48*, 5500. (f) Trofimov, B. A.; Schmidt, E. Y.; Mikhalieva, A. I.; -Gonzalo, C. P.; Pomposo, J. A.; Salsamendi, M.; Protzuk, N. I.; Zorina, N. V.; Afonin, A. V.; Vashchenko, A. V.; Levanova, E. P.; Levkovskaya, G. *Chem.—Eur. J.* **2009**, *15*, 6435. (g) Fujiwara, M.; Kawatsura, M.; Hayase, S.; Nanjo, M.; Itoh, T. *Adv. Synth. Catal.* **2009**, *351*, 123. (h) Lu, Y.; Arndtsen, B. A. *Angew. Chem., Int. Ed.* **2008**, *47*, 5430.

(6) (a) Hantzsch, A. *Ber. Dtsch. Chem. Ges.* **1890**, *23*, 1474–1483. (b) Kaupp, G.; Schmeyers, J.; Kuse, A.; Atfeh, A. *Angew. Chem., Int. Ed.* **1999**, *38*, 2896–2899. (c) Matyichuk, V. S.; Martyak, R. L.; Obushak, N. D.; Ostapiuk, Y. V.; Pidlynyi, N. I. *Chem. Heterocycl. Compd.* **2004**, *40*, 1218.

(7) (a) Knorr, L. *Ber. Dtsch. Chem. Ges.* **1884**, *17*, 1635–1642. (b) Kleinspehn, G. G. *J. Am. Chem. Soc.* **1955**, *77*, 1546. (c) Alberola, A.; Ortega, A. G.; Sadaba, M. L.; Sanudo, C. *Tetrahedron* **1999**, *55*, 6555. (d) Elghamry, I. *Synth. Commun.* **2002**, *32*, 897. (e) Manley, J. M.; Kalman, M. J.; Conway, B. G.; Ball, C. C.; Havens, J. L.; Vaidyanathan, R. *J. Org. Chem.* **2003**, *68*, 6447. (f) Shiner, C. M.; Lash, T. D. *Tetrahedron* **2005**, *61*, 11628.

(8) (a) Pall, C. *Ber. Dtsch. Chem. Ges.* **1885**, *18*, 367. (b) Jones, R. A.; Been, G. P. *The Chemistry of Pyrroles*; Academic Press: New York, 1977; Chapter 3. (c) Chiu, P. K.; Lui, K. H.; Maini, P. N.; Sammes, M. P. *J. Chem. Soc., Chem. Commun.* **1987**, 109. (d) Chiu, P. K.; Sannes, M. P. *Tetrahedron* **1990**, *46*, 3439. (e) Banik, B. K.; Samajdar, S.; Banik, I. *J. Org. Chem.* **2004**, *69*, 213–216. (f) Chen, J.; Wu, H.; Zheng, Z.; Jin, C.; Zhang, X.; Su, W. *Tetrahedron Lett.* **2006**, *47*, 5383. (g) Minetto, G.; Raveglia, L. F.; Sega, A.; Taddei, M. *Eur. J. Org. Chem.* **2005**, *24*, 5277.

(9) For a recent review, see: (a) Balme, G. *Angew. Chem., Int. Ed.* **2004**, *43*, 6238–6241 and references therein. (b) Nishibayashi, Y.; Yoshikawa, M.; Inada, Y.; Milton, M. D.; Hidai, M.; Uemura, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 2681–2684. (c) Dhawan, R.; Arndtsen, B. A. *J. Am. Chem. Soc.* **2004**, *126*, 468–469. (d) Tejedor, D.; González-Cruz, D.; García-Tellado, F.; Marrero-Tellado, J. J.; Rodríguez, M. L. *J. Am. Chem. Soc.* **2004**, *126*, 8390–8391. (e) Yamamoto, Y.; Hayashi, H.; Saigoku, T.; Nishiyama, H. *J. Am. Chem. Soc.* **2005**, *127*, 10804–10805. (f) Larionov, O. V.; Meijere, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 5664. (g) Chen, X.; Hou, L.; Li, X. *Synlett* **2009**, 828–832. (h) St. C., D. J.; Martin, N.; Arndtsen, B. A. *Org. Lett.* **2007**, *9*, 449–452. (i) Shimizu, M.; Takahashi, A.; Kawai, S. *Org. Lett.* **2006**, *8*, 3585–3587. (j) Bergner, I.; Opatz, T. *J. Org. Chem.* **2007**, *72*, 7083–7090. (k) Shiraiishi, H.; Nishitani, T.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **1998**, *63*, 6234–6238. (l) Ranu, B. C.; Hajra, A.; Jana, U. *Synlett* **2000**, 75. (m) Cadierno, V.; Gimeno, J.; Nebra, N. *Chem.—Eur. J.* **2007**, *13*, 9973–9981. (n) Khalili, B.; Jajarmi, P.; Eftekhari-Sis, B.; Hashemi, M. M. *J. Org. Chem.* **2008**, *73*, 2090–2095.

(10) For most recent strategies based on the metal-catalyzed synthesis of pyrroles, see: (a) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127. (b) Gilchrist, T. L. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2849. (c) Hartwig, J. F. *Synlett* **2006**, 1283. (d) Kel'in, A. V.; Sromek, A. W.; Gevorgyan, V. *J. Am. Chem. Soc.* **2001**, *123*, 2074. (e) Gorin, D. J.; Davis, N. R.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 11260. (f) Cyr, D. J. S.; Arndtsen, B. A. *J. Am. Chem. Soc.* **2007**, *129*, 12366. (g) Hiroya, K.; Matsumoto, S.; Ashikawa, M.; Ogiwara, K.; Sakamoto, T. *Org. Lett.* **2006**, *8*, 5349. (h) Istrate, F. M.; Gagosz, F. *Org. Lett.* **2007**, *9*, 3181. (i) Braun, R. U.; Zeitler, K.; Muller, T. J. *J. Org. Lett.* **2001**, *3*, 3297–3300. (j) Kamijo, S.; Kanazawa, C.; Yamamoto, Y. *J. Am. Chem. Soc.* **2005**, *127*, 9260. (k) Takaya, H.; Kojima, S.; Murahashi, S.-I. *Org. Lett.* **2001**, *3*, 421. (l) Siriwardana, A. I.; Kathiriarachi, K. K. A. D. S.; Nakamura, I.; Gridnev, I. D.; Yamamoto, Y. *J. Am. Chem. Soc.* **2004**, *126*, 13898. (m) Paulus, O.; Alcaraz, G.; Vautier, M. *Eur. J. Org. Chem.* **2002**, 2565. (n) Wurz, R. P.; Charette, A. B. *Org. Lett.* **2005**, *7*, 2313. (o) Ramanathan, B.; Keith, A. J.; Armstrong, D.; Odum, A. L. *Org. Lett.* **2004**, *6*, 2957. (p) Martin, R.; Rivero, M. R.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2006**, *45*, 7079. (q) Lu, L.; Chen, G.; Ma, S. *Org. Lett.* **2006**, *8*, 835. (r) Binder, J. T.; Kirsch, S. F. *Org. Lett.* **2006**, *8*, 2151. (s) Merlic, C. A.; Baur, A.; Aldrich, C. C. *J. Am. Chem. Soc.* **2000**, *122*, 7398–7399. (t) Wang, Y.; Zhu, S. *Org. Lett.* **2003**, *5*, 745–748. (u) Shu, X.-Z.; Liu, X.-Y.; Xiao, H.-Q.; Ji, K.-G.; Guo, L.-N.; Liang, Y.-M. *Adv. Synth. Catal.* **2008**, *350*, 243–248. (v) Bian, Y.-J.; Liu, X.-Y.; Ji, K.-G.; Shu, X.-Z.; Guo, L.-N.; Liang, Y.-M. *Tetrahedron* **2009**, *65*, 1424–1429. (w) Aponick, A.; Li, C.-Y.; Malinge, J.; Marques, E. F. *Org. Lett.* **2009**, *11*, 4624–4627. (x) Dou, G.; Shi, C.; Shi, D. *J. Comb. Chem.* **2008**, *10*, 810–813. (y) Galliford, C. V.; Scheidt, K. A. *J. Org. Chem.* **2007**, *72*, 1811–1813. (z) Lu, Y.; Fu, X.; Chen, H.; Du, X.; Jia, X.; Liu, Y. *Adv. Synth. Catal.* **2009**, *351*, 129.

(11) For recent reviews, see: (a) Touré, B. B.; Hall, D. G. *Chem. Rev.* **2009**, *109*, 4439–4486. (b) Balme, G.; Bossharth, E.; Monteiro, N. *Eur. J. Org. Chem.* **2003**, 4101–4111. (c) Hulme, C.; Gore, V. *Curr. Med. Chem.* **2003**, *10*, 51–80. (d) Orru, R. V. A.; de Greef, M. *Synthesis* **2003**, 1471–1499. (e) Zhu, J. *Eur. J. Org. Chem.* **2003**, 1133–1144. (f) Bienaymé, H.; Hulme, C.; Oddon, G.; Schmitt, P. *Chem.—Eur. J.* **2000**, *6*, 3321–3329. (g) Dömling, A.; Ugi, I. *Angew. Chem., Int. Ed.* **2000**, *112*, 3168–3210. (h) Tietze, L. F.; Modi, A. *Med. Res. Rev.* **2000**, *20*, 304–322. (i) Weber, L.; Ilgen, K.; Almstetter, M. *Synlett* **1999**, 366–374. (j) Dax, S. L.; McNally, J. J.; Youngman, M. A. *Curr. Med. Chem.* **1999**, *6*, 255–270.

(12) (a) Azizian, J.; Karimi, A. R.; Arefrad, H.; Mohammadi, A. A.; Mohamadzadeh, M. R. *Mol. Diversity* **2003**, *6*, 223–226. (b) Alizadeh, A.; Rezvani, A.; Bijanzadeh, H. R. *Synthesis* **2008**, 725–728.

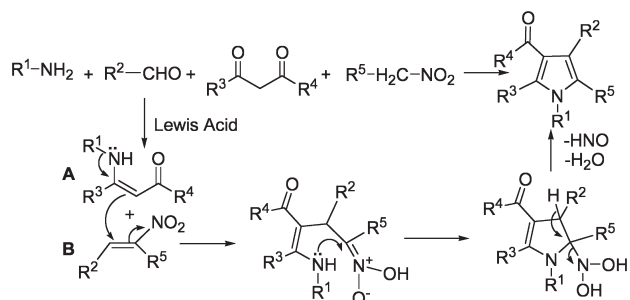
(13) For general reviews, see: (a) Correa, A.; Mancheno, O. G.; Bolm, C. *Chem. Soc. Rev.* **2008**, *37*, 1108–1117. (b) Sherry, B. D.; Fürstner, A. *Acc. Chem. Res.* **2008**, *41*, 1500–1511. (c) Bolm, C.; Legros, J.; Le Pailh, J.; Zani, L. *Chem. Rev.* **2004**, *104*, 6217–6254. (d) Fürstner, A.; Martin, R. *Chem. Lett.* **2005**, *34*, 624–629. (e) Diaz, D. D.; Miranda, P. O.; Padrón, J. I.; Martín, V. S. *Curr. Org. Chem.* **2006**, *10*, 457–476.

(14) FeCl₃-catalyzed synthesis of heterocycles. Synthesis of quinolines: (a) Cao, K.; Zhang, F.-M.; Tu, Y.-Q.; Zhuo, X.-T.; Fan, C.-A. *Chem.—Eur. J.* **2009**, *15*, 6332–6334. Synthesis of furan: (b) Ji, W.-H.; Pan, Y.-M.; Zhao, S.-Y.; Zhan, Z.-P. *Synlett* **2008**, 3046–3052. Synthesis of benzofuran: (c) Liang, Z.; Hou, W.; Du, Y.; Zhang, Y.; Pan, Y.; Mao, D.; Zhao, K. *Org. Lett.* **2009**, *11*, 4978–4981. Synthesis of 2-prolines: (d) Fan, J.; Gao, L.; Wang, Z. *Chem. Commun.* **2009**, 5021–5023. Synthesis of benzoxazoles: (e) Bonnamour, J.; Bolm, C. *Org. Lett.* **2008**, *10*, 2665–2667. Synthesis of xanthenes: (f) Li, H.; Yang, J.; Liu, Y.; Li, Y. *J. Org. Chem.* **2009**, *74*, 6797.

(15) For the FeCl₃-catalyzed activation of alcohols, see: (a) Biswas, S.; Maiti, S.; Jana, U. *Eur. J. Org. Chem.* **2009**, 2354–2359. (b) Jana, U.; Biswas, S.; Maiti, S. *Eur. J. Org. Chem.* **2008**, 5798–5804. (c) Jana, U.; Maiti, S.; Biswas, S. *Tetrahedron Lett.* **2008**, *49*, 858–862. (d) Jana, U.; Maiti, S.; Biswas, S. *Tetrahedron Lett.* **2007**, *48*, 7160–7163. (e) Jana, U.; Biswas, S.; Maiti, S. *Tetrahedron Lett.* **2007**, *48*, 4065–4069.

(16) Grob, C. A.; Camenisch, K. *Helv. Chim. Acta* **1953**, *36*, 49–58.

SCHEME 1. Strategy for the Lewis Acid Mediated One-Pot Four-Component Coupling

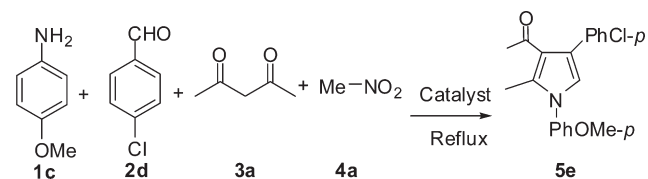


field and reported only for aliphatic nitroalkenes.¹⁷ Moreover, in this method it is a prerequisite to prepare nitroalkenes from aldehyde and nitroalkanes, and β -enaminocarbonyl derivatives from β -dicarbonyl and amines beforehand. Consequently, there are opportunities for further improvement of this reaction. In our present study, we hypothesized that if we could generate simultaneously in one pot both β -keto-enamines (A) of 1,3-dicarbonyl compounds and nitrostyrene (B) from readily available starting materials in the presence of a suitable catalyst, and if these two component undergo Michael reaction, this could represent a possible tandem synthesis of functionalized pyrroles (Scheme 1).

To achieve this goal, at first the reaction conditions were explored using four commercially available substrates such as aromatic amine **1c**, aldehyde **2d**, acetylacetone **3a**, and nitromethane **4a** in the presence of various catalysts (Table 1). Keeping in mind the advantages of iron, our initial investigation focused on the development of iron-salts-catalyzed four-component coupling reactions. In a preliminary experiment, first we tested this reaction using the above said amine, aldehyde, and acetylacetone in nitromethane in the presence of various iron salts such as FeCl₃, FeCl₃·6H₂O, FeBr₃, Fe(OTf)₃ and Fe(acac)₃. After great deal of screening on different parameters, we found that aromatic amine **1c** (1.5 mmol), aldehyde **2d** (1 mol) and acetylacetone **3a** (1 mmol) in nitromethane (1 mL) produced pyrrole **5e** in 56% yield after refluxing 7 h in the presence of anhydrous FeCl₃ (10 mol %) (Table 1, entry 7).

Next, we examined this reaction in the presence of various other catalysts such as InCl₃, Yb(OTf)₃, PTSA (*p*-toluenesulfonic acid), HCl, and CF₃SO₃H in similar reaction conditions. However, it was evident that anhydrous FeCl₃ (10 mol %) was the most effective catalyst for this transformation. Although the reaction proceeded very slowly without any catalyst, the desired product was obtained in only a small amount after heating for more than 24 h (Table 1, entry 1). Therefore, FeCl₃ dramatically accelerated this reaction and gave good yield of the product **5a**. The reaction was also studied in various solvents such as tetrahydrofuran, dichloromethane, dichloroethane, and toluene; however, the yield of the desired product was decreased. So, in this reaction nitroalkane was used both as a solvent and as one of the reactants as well.

The experimental procedure for this reaction was very simple and straightforward. A mixture of 1,3-dicarbonyl compound (1 mmol), aromatic amine (1.5 mmol), aromatic aldehyde (1 mmol), and nitro alkane (1 mL) was heated to

TABLE 1. Four-Component Coupling Reactions under Various Catalytic Conditions^a

entry	catalyst (mol %)	reaction time (h)	yield (%) ^b
1	none	24	10
2	FeCl ₃ (5)	7	40
3	FeCl ₃ (10)	7	48
4	FeCl ₃ ·6H ₂ O (10)	7	44
5	FeBr ₃ (10)	12	40
6	Fe(acac) ₃ (10)	16	19
7	FeCl ₃ (10)	7	56 ^c
8	Fe(OTf) ₃ (10)	16	38
9	InCl ₃ (10)	15	15
10	Yb(OTf) ₃ (10)	10	29
11	PTSA (10)	14	25
12	CF ₃ SO ₃ H (10)	9	27
13	FeCl ₃ (10) + CF ₃ SO ₃ H (10)	16	25
14	HCl (30)	12	trace

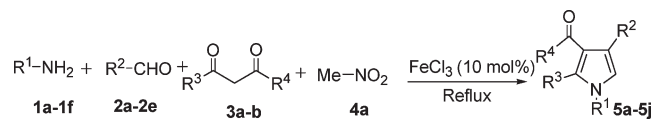
^aAll reactions were carried out using aldehyde (1 mmol), amine (1 mmol), and active methylene compounds (1 mmol) with nitromethane (1 mL) under reflux. ^bYield obtained after column chromatography. ^cAmine (1.5 mmol) was used.

reflux in the presence of anhydrous FeCl₃ (10 mol %) for a set period of time (monitored by TLC) without an inert atmosphere. Then after removal of excess nitroalkane the product was directly purified using column chromatography.

Following the general reaction conditions, we next examined the scope of this reaction with various aromatic amines, and the results are summarized in Table 2. In general the reaction was proceeded smoothly for various substituted and unsubstituted aromatic amines to produce the desired substituted pyrroles in moderate yields (47–56%). The yields were almost the same regardless of the substituent. Electron-rich aromatic amines such as *p*-toluidine (Table 2, entry 3) and *p*-methoxy aniline (Table 2, entries 4–6 and 10) were reacted, and corresponding products were afforded in moderate yields.

The weakly electron-deficient halogen-containing (-Cl, -F, and -Br) anilines were also subjected to the reaction conditions, and the desired pyrroles were obtained in moderate yields (Table 2, entries 7–9). However, in the case of strongly electron-withdrawing group such as -NO₂, the yield of the product was not satisfactory and the reaction was not studied further. This observation could be explained from the low nucleophilicity of the aromatic amine, which inhibited the formation of corresponding β -keto enamine. Moreover, to expand the scope of this reaction with respect to aldehyde substrates, various aromatic aldehydes were surveyed for this reaction. In general, the electronic properties of the substituents of aromatic aldehydes did not affect the reactivity. Both electron-donating and weakly electron-withdrawing functionalities such as methoxy, methyl, and chloro- and bromo-groups reacted smoothly to afford the desired pyrroles. Notably, when the unsymmetrical 1,3-diketone **3b** was used as the substrate, the pyrrole **5j** was chemoselectively formed in 50% yield, that is, only the more activated acetyl group participated in the condensation process. The structures all of the

(17) (a) Trautwein, A. W.; Jung, G. *Tetrahedron Lett.* **1998**, *39*, 8263. (b) Meier, H. *Liebigs Ann. Chem.* **1981**, 1534. (c) Sanchez, A. G.; Mancera, M.; Rosado, F. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1199.

TABLE 2. FeCl₃-Catalyzed Four-Component Coupling Synthesis of Functionalized Pyrrole with Aromatic Amines^a

entry	R ¹	R ²	R ³ , R ⁴	reaction time (h)	products	yield (%) ^b
1	Ph, 1a	Ph, 2a	CH ₃ , CH ₃ , 3a	14	5a	54
2	1a	<i>o</i> -BrC ₆ H ₄ , 2b	3a	14	5b	48
3	<i>p</i> -MeC ₆ H ₄ , 1b	<i>p</i> -OMeC ₆ H ₄ , 2c	3a	16	5c	47
4	<i>p</i> -OMeC ₆ H ₄ , 1c	2a	3a	14	5d	53
5	1c	<i>p</i> -ClC ₆ H ₄ , 2d	3a	8	5e	56
6	1c	2c	3a	8	5f	52
7	<i>p</i> -FC ₆ H ₄ , 1d	2c	3a	13	5g	50
8	<i>p</i> -ClC ₆ H ₄ , 1e	<i>p</i> -MeC ₆ H ₄ , 2e	3a	13	5h	51
9	<i>p</i> -BrC ₆ H ₄ , 1f	2c	3a	14	5i	49
10	1c	2d	CH ₃ , Ph, 3b	14	5j	50

^aAll reactions were carried out using aldehyde (1 mmol), amine (1.5 mmol), and 1,3-dicarbonyl compounds (1 mmol) with nitromethane (1 mL) under reflux. ^bYield obtained after column chromatography.

substituted pyrroles were unambiguously characterized by ¹H and ¹³CNMR and IR and HRMS.

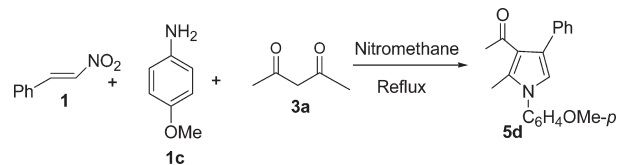
Encouraged by these investigations, subsequently, we investigated this tandem reaction with an array of amines, aromatic aldehydes, activemethylene compounds, and nitroalkanes, and the results are presented in Table 3. The reaction appeared to be quite general with respect to the amines, 1,3-dicarbonyl compounds, and aldehydes. Aliphatic amines such as *n*-hexyl amine **1g** and cyclohexylamine **1h** also reacted with acetylacetone **3a** and gave 54%, 59%, and 56% yield of **6a**, **6b**, and **6c**, respectively (Table 3, entries 1–3). Interestingly, the benzyl amine **1i** (Table 3, entries 4–13, 21, 22) and *p*-methoxybenzylamine **1j** (Table 3, entries 14–20) efficiently reacted under these conditions and generated corresponding products **6d**–**6x** in high yields. This four-component coupling reaction can also be successfully applied with heteroaromatic aldehydes such as 2-formylthiophene **2f** and 2-formylfuran **2g** (Table 3, entries 5, 6, and 20), which worked at lower temperature (80 °C) and afforded hybrid heterocyclic compounds **6e**, **6t**, and **6f** in 55%, 56%, and 46%, respectively. Notably, aldehydes bearing a strong electron-withdrawing group such as -NO₂ also underwent smooth reaction and gave high yields of the products **6g**, **6i** and **6o**, 85%, 60% and 78%, respectively (Table 3, entries 7, 9, and 15). Likewise, 2-naphthylaldehyde **2m** also reacted efficiently to produce the expected pyrrole **6s** in 65% yield (Table 3, entry 19). Furthermore, aldehyde bearing a nitrile group such as **2k** (table 3, entry 10) was also compatible and underwent smooth conversion in the present reaction conditions with β -keto esters **3c** to yield the desired compound **6j** in 61%. However, nitroethane **4b** was found to be the less reactive in this reaction and gave slightly lower yields of the desired products (Table 3, entries 21–24) compared to nitromethane; probably steric hindrance hampered this reaction. Finally, we tested the efficiency of this reaction with aliphatic aldehyde such as isobutyraldehyde (Table 3, entry 25) and *n*-butyraldehyde (Table 3, entry 26) with benzyl amine, and both of the substrates converted smoothly to the desired product. Thus, variations in all four components were accommodated very comfortably in this four-component coupling reaction, generating moderate to high yields of the functionalized pyrroles.

Although the exact role of the catalyst is not known yet, we hypothesized the *in situ* generation of β -enamino carbonyl

compounds and nitrostyrene intermediates in this reaction, which then undergo Michael reaction followed by cyclization leading to the final pyrrole products. FeCl₃ or other Lewis acids accelerated this reaction by increasing the electrophilic character of 1,3-dicarbonyl compounds and consequently accelerated the formation of β -enamino carbonyl compounds.¹⁸ The generation of nitrostyrene as an intermediate in these reaction conditions, Lewis acid catalyzed activation of Michael reaction, and subsequent ring annulations leading to the final pyrrole product were finally confirmed by a set of reactions.¹⁹ Presumably, FeCl₃ activated more strongly compared to the other Lewis or Brønsted acids and thus gave the better results. It is noteworthy to mention that formation of imine is much faster compared to the other reactions; however, we understood that during the progress of the reaction the imine was hydrolyzed back to aldehyde and amine under the reaction conditions as imine formation is a reversible process, and hence the desired product was obtained through the formation of β -enamino carbonyl compounds and nitrostyrene.²⁰

(18) During our study with activemethylene compounds we often observed the formation of β -enamino carbonyl compounds from the corresponding activemethylene compounds and anilines derivatives in the presence of catalytic amount of FeCl₃. FeCl₃-catalyzed formation of β -enamino carbonyl compounds has also reported by others; see: Hebbache, H.; Hank, Z.; Boutamine, S.; Meklati, M.; Bruneau, C.; Renaud, J.-L. *C. R. Chimie* **2008**, *11*, 612–619.

(19) Nitrostyrene **1** was prepared separately from benzaldehyde and nitromethane, and when the following three-component coupling reaction was performed without any catalyst, only 10% yield of the desired product was obtained after refluxing for 24 h. However, in the presence of FeCl₃ (10 mol%), 60% of the desired product obtained after 7 h of refluxing.



(20) To prove this, an imine was separately prepared from *p*-methoxyaniline and benzaldehyde, and when a three-component coupling reaction was conducted with this imine, acetylacetone, and nitromethane under anhydrous (argon atmosphere) conditions in the presence of FeCl₃, no desired product was obtained. However, when the reaction was carried out in the presence of water (2 equiv), the reaction worked and gave the desired product in comparable yield.

TABLE 3. FeCl₃-Catalyzed Four-Component Coupling Synthesis of Functionalized Pyrroles with Various Substrates^a

Entry	R ¹	R ²	R ³ , R ⁴	R ⁵	Reaction times (h)	Products	Yield (%) ^b
1	C ₆ H ₁₃ 1g	<i>p</i> -OMeC ₆ H ₄ 2c	Me, Me 3a	H 4a	8	6a	54 ^c
2	1g	<i>p</i> -Cl-C ₆ H ₄ 2d	3a	4a	8	6b	59 ^c
3	 1h	<i>p</i> -Cl-C ₆ H ₄ 2d	3a	4a	8	6c	56 ^c
4	C ₆ H ₅ CH ₂ 1i	2d	3a	4a	6	6d	80
5	1i	 2f	3a	4a	7	6e	55 ^d
6	1i	 2g	3a	4a	7	6f	46 ^d
7	1i	 2h	3a	4a	5	6g	85 ^d
8	1i	<i>m</i> -Br-C ₆ H ₄ 2i	Me, Ph 3b	4a	7	6h	76
9	1i	<i>p</i> -NO ₂ -C ₆ H ₄ 2j	3a	4a	7	6i	60
10	1i	<i>p</i> -CN-C ₆ H ₄ 2k	Me, OMe 3c	4a	7	6j	61
11	1i	2d	3c	4a	7	6k	80
12	1i	<i>p</i> -F-C ₆ H ₄ 2l	Me, OEt 3d	4a	7	6l	80
13	1i	2d	Ph, OEt 3e	4a	16	6m	58
14	<i>p</i> -OMeC ₆ H ₅ CH ₂ 1j	2i	3a	4a	8	6n	75
15	1j	2h	3a	4a	7	6o	78 ^d
16	1j	2l	3c	4a	8	6p	63
17	1j	2i	3c	4a	8	6q	70
18	1j	2d	3d	4a	8	6r	76
19	1j	2-Naphthyl 2m	3d	4a	8	6s	65
20	1j	2f	3a	4a	8	6t	56 ^d
21	1i	2d	3a	CH ₃ 4b	10	6u	47
22	1i	2l	3a	4b	10	6v	38
23	1j	2d	3a	4b	10	6w	44
24	1j	2e	3a	4b	10	6x	45
25	1i	CH ₃ CH(CH ₃)- 2n	3a	4a	9	6y	72 ^e
26	1i	CH ₃ (CH ₂) ₂ - 2o	3a	4a	9	6z	45 ^e

^aAll reactions were carried out using aldehyde (1 mmol), amine (1.5 mmol), and 1,3-dicarbonyl compounds (1 mmol) with nitromethane (1 mL) under reflux. ^bYield obtained after column chromatography. ^cAldehyde (1.3 mmol), amine (1 mmol), and 1,3-dicarbonyl compounds (1 mmol) were used in nitromethane (1 mL). ^dThe reactions were carried out at 80 °C. ^eThe reactions were carried out at 70 °C.

In general the reactions are quite simple and high-yielding and can be performed without an inert atmosphere, and only a catalytic amount of FeCl₃ (10 mol %) is sufficient to push the reaction forward. This reaction worked smoothly with a wide range of substrates with respect to all of the components. The conditions of this reaction were mild and a wide range of functional groups such as -OMe, -Cl, -Br, -F, -Me, -NO₂, -CN, esters, ketones, and heteroaromatic motifs such as thiophene and furan were compatible in the present reaction conditions. Moreover, it is noteworthy to mention that the Grob and Cameisch reaction is only known for aliphatic amines so far;^{16,17} however, in the present iron-salt-catalyzed four-component coupling reactions both aliphatic and aromatic amines could be used.

Conclusions

In summary, we have successfully developed a novel, operationally simple, economical, and environmentally friendly one-pot four-component coupling reaction to synthesis functionalized pyrroles by employing 1,3-dicarbonyl compounds, aromatic aldehyde, amines, and nitro alkanes. To the best of our knowledge this is first report of Grob and Cameisch's pyrrole synthesis catalyzed by a Lewis acid *via* one-pot four component-coupling reactions. Moreover, it has several advantages: (1) an inexpensive and environmentally friendly FeCl₃ (10 mol %) has been used as a catalyst, (2) all components are readily available and inexpensive, (3) it allows the direct introduction of carbonyl functionalities onto the pyrrole skeleton, (4) a wide variety of functional groups can survive, (5) it is highly selective and allows the isolation of the desired pyrroles in moderate to high yields (38–85%), and (6) the reactions were applicable to a combination of substrates such as aromatic and aliphatic amines, aromatic and aliphatic aldehydes, β -diketones and β -ketoesters and with nitroalkanes. Therefore, considering the above advantages and experimental simplicity, this one-pot catalytic transformation clearly represents an appealing methodology for the synthesis of highly functionalized pyrroles both in academia and pharmaceutical industries. Further study in this area is going on in our laboratory to improve the yield, mechanism, and possible applications of this reaction.

Experimental Section

General Methods. ¹H NMR spectra were recorded on a 300 MHz and a 500 MHz spectrometer as solutions in CDCl₃. Chemical shifts are expressed in parts per million (ppm, δ) and are referenced to CHCl₃ (δ = 7.26 ppm) as an internal standard. All coupling constants are absolute values and are expressed in hertz. The description of the signals include s = singlet, brs = broad singlet, d = doublet, dd = double doublet, t = triplet, q = quartet, m = multiplet, and dq = doublet of quartet. ¹³C NMR spectra were recorded on a 75 MHz and a 125 MHz spectrometer as solutions in CDCl₃ with complete proton decoupling. Chemical shifts are expressed in parts per million (ppm, δ) and are referenced to CHCl₃ (δ = 77.0 ppm) as an internal standard. The routine monitoring of reactions was performed with silica gel coated glass slides, which were analyzed with iodine. Solvents, reagents, and chemicals were purchased. Nitromethane was dried with CaH₂ prior to use. All reactions involving moisture-sensitive reactants were executed with oven-dried glassware.

General Procedure for FeCl₃-Catalyzed One-Pot Synthesis of Pyrroles. Representative Experimental Procedure for the Synth-

esis of 1-[4-(4-Chlorophenyl)-1-(4-methoxyphenyl)-2-methyl-1H-pyrrol-3-yl]-ethanone (Table 2, Entry 5). To a stirred solution of *p*-anisidine **1c** (185 mg, 1.5 mmol), *p*-chlorobenzaldehyde **2d** (140 mg, 1 mmol), and acetylacetone **3a** (100 mg, 1 mmol) in nitromethane (1 mL) was added anhydrous FeCl₃ (16 mg, 0.1 mmol). The mixture was heated to reflux slowly for 7 h and cooled down to room temperature. The excess solvent was removed under vacuum, and the residue was directly purified by silica gel column chromatography to afford the product **5e** as white solid (189 mg, 0.56 mmol, 56%), mp 117–119 °C. IR (neat) 3007, 2933, 1651, 1514, 1249 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 2.09 (s, 3H), 2.36 (s, 3H), 3.86 (s, 3H), 6.61 (s, 1H), 6.98 (d, *J* = 8.7 Hz, 2H), 7.23 (d, *J* = 8.7 Hz, 2H), 7.26–7.36 (m, 4H) ppm. ¹³C NMR (CDCl₃, 75 MHz) δ 12.8, 31.0, 55.5, 114.5, 121.0, 122.1, 124.7, 127.4, 128.4, 130.5, 131.4, 132.7, 134.6, 135.9, 159.3, 197.1 ppm. HRMS: *m/z* calcd for C₂₀H₁₈CINNaO₂ 362.0924; found 362.0922.

1-(2-Methyl-1,4-diphenyl-3-pyrrolyl)-ethanone (Table 2, Entry 1). Acetylacetone **3a** (100 mg, 1 mmol), benzaldehyde **2a** (106 mg, 1 mmol), aniline **1a** (140 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl₃ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the white solid **5a** (149 mg, 0.54 mmol, 54%), mp 105–107 °C. IR (neat) 3057, 3028, 1651, 1504, 1404, 1222 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 2.09 (s, 3H), 2.42 (s, 3H), 6.68 (s, 1H), 7.31–7.43 (m, 7H), 7.45–7.50 (m, 3H) ppm. ¹³C NMR (CDCl₃, 75 MHz) δ 12.8, 31.0, 120.6, 122.5, 126.2, 126.3, 126.8, 128.1, 128.2, 129.3, 129.8, 135.3, 136.0, 138.7, 197.6 ppm. HRMS: *m/z* calcd for C₁₉H₁₈NO (M + 1) 276.1388; found 276.1389.

1-[4-(2-Bromophenyl)-2-methyl-1-phenyl-1H-pyrrol-3-yl]-ethanone (Table 2, Entry 2). Acetylacetone **3a** (100 mg, 1 mmol), *o*-bromobenzaldehyde **2a** (185 mg, 1 mmol), aniline **1a** (140 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl₃ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as brown sticky liquid **5b** (170 mg, 0.48 mmol, 48%). IR (neat) 3057, 3010, 1651, 1500, 1406, 1222 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 1.98 (s, 3H), 2.45 (s, 3H), 6.64 (s, 1H), 7.17–7.23 (m, 1H), 7.31–7.52 (m, 7H), 7.66 (d, *J* = 8.0 Hz, 2H) ppm. ¹³C NMR (CDCl₃, 75 MHz) δ 13.1, 30.2, 121.1, 122.3, 124.6, 125.2, 126.3, 127.1, 128.1, 128.8, 129.3, 132.0, 132.7, 135.5, 137.5, 138.6, 196.4 ppm. HRMS: *m/z* calcd for C₁₉H₁₆BrNNaO 376.0313; found 376.0316.

1-[4-(4-Methoxyphenyl)-2-methyl-1-*p*-tolyl-1H-pyrrol-3-yl]-ethanone (Table 2, Entry 3). Acetylacetone **3a** (100 mg, 1 mmol), *p*-anisaldehyde **2c** (130 mg, 1 mmol), *p*-toluidine **1b** (161 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl₃ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as brown sticky liquid **5c** (150 mg, 0.47 mmol, 47%). IR (neat) 3001, 2926, 1651, 1504, 1402, 1246 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 2.11 (s, 3H), 2.42 (s, 3H), 2.44 (s, 3H), 3.86 (s, 3H), 6.63 (s, 1H), 6.94 (d, *J* = 6.7 Hz, 2H), 7.21–7.32 (m, 6H) ppm. ¹³C NMR (CDCl₃, 75 MHz) δ 13.0, 21.1, 30.9, 55.3, 113.7, 120.6, 122.3, 125.9, 126.0, 128.4, 129.9, 130.4, 135.6, 136.2, 138.1, 158.7, 197.8 ppm. HRMS: *m/z* calcd for C₂₁H₂₁NNaO₂ 342.1470; found 342.1473.

1-[1-(4-Methoxyphenyl)-2-methyl-4-phenyl-1H-pyrrol-3-yl]-ethanone (Table 2, Entry 4). Acetylacetone **3a** (100 mg, 1 mmol), benzaldehyde **2a** (106 mg, 1 mmol), *p*-anisidine **1c** (185 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl₃ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as yellow solid **5d** (162 mg, 0.53 mmol, 53%), mp 90–91 °C. IR (neat) 3009, 2933, 1647, 1514, 1250 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 2.07 (s, 3H), 2.38 (s, 3H), 3.86 (s, 3H), 6.63 (s, 1H), 7.0 (d, *J* = 8.9 Hz, 2H), 7.25 (d, *J* = 8.9 Hz, 2H), 7.29–7.35 (m, 1H), 7.37–7.39 (m, 4H) ppm. ¹³C NMR (CDCl₃, 75 MHz) δ 12.7, 31.0, 55.5, 114.4, 120.8, 122.2, 126.0, 126.7, 127.4, 128.2, 129.3, 131.6, 135.6, 136.1, 159.2, 197.6 ppm. HRMS: *m/z* calcd for C₂₀H₂₀NO₂ (M + 1) 306.1494; found 306.1487.

1-[1,4-Bis(4-methoxyphenyl)-2-methyl-1H-pyrrol-3-yl]-ethanone (Table 2, Entry 6). Acetylacetone **3a** (100 mg, 1 mmol), *p*-anisaldehyde **2c** (130 mg, 1 mmol), *p*-anisidine **1c** (185 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl₃ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as brown solid **5f** (174 mg, 0.52 mmol, 52%), mp 133–135 °C. IR (neat) 3005, 2964, 1645, 1504, 1249 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 2.09 (s, 3H), 2.38 (s, 3H), 3.83 (s, 3H), 3.86 (s, 3H), 6.59 (s, 1H), 6.91–6.99 (m, 4H), 7.22–7.30 (m, 4H) ppm. ¹³C NMR (CDCl₃, 75 MHz) δ 12.8, 30.9, 55.2, 55.5, 113.7, 114.4, 120.6, 122.2, 125.6, 127.4, 128.4, 130.4, 131.6, 135.5, 158.6, 159.2, 197.5 ppm. HRMS: *m/z* calcd for C₂₁H₂₁NNaO₃ 358.1419; found 358.1419.

1-[1-(4-Fluorophenyl)-4-(4-methoxyphenyl)-2-methyl-1H-pyrrol-3-yl]-ethanone (Table 2, Entry 7). Acetylacetone **3a** (100 mg, 1 mmol), *p*-anisaldehyde **2c** (130 mg, 1 mmol), *p*-fluoroaniline **1d** (167 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl₃ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as brown solid **5g** (162 mg, 0.50 mmol, 50%), mp 78–80 °C. IR (neat) 3003, 1651, 1508, 1246, 1215 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 2.08 (s, 3H), 2.39 (s, 3H), 3.85 (s, 3H), 6.61 (s, 1H), 6.94 (d, *J* = 8.5 Hz, 2H), 7.19 (t, *J* = 8.6 Hz, 2H), 7.28–7.34 (m, 4H) ppm. ¹³C NMR (CDCl₃, 75 MHz) δ 12.7, 31.0, 55.2, 113.7, 116.1, 116.4, 120.4, 122.6, 125.9, 127.9, 128.0, 128.1, 130.3, 134.8, 135.2, 158.7, 160.4, 163.6, 197.6 ppm. HRMS: *m/z* calcd for C₂₀H₁₈FNNaO₂ 346.1219; found 346.1217.

1-[1-(4-Chlorophenyl)-4-(4-methylphenyl)-2-methyl-1H-pyrrol-3-yl]-ethanone (Table 2, Entry 8). Acetylacetone **3a** (100 mg, 1 mmol), *p*-tolualdehyde **2e** (120 mg, 1 mmol), *p*-chloroaniline **1e** (191 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl₃ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as off white solid **5h** (165 mg, 0.51 mmol, 51%), mp 127–129 °C. IR (neat) 3020, 1651, 1494, 1415, 1222 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 2.08 (s, 3H), 2.39 (s, 6H), 6.62 (s, 1H), 7.18–7.29 (m, 6H), 7.44–7.48 (m, 2H) ppm. ¹³C NMR (CDCl₃, 75 MHz) δ 12.8, 21.1, 31.0, 120.2, 122.8, 126.5, 127.4, 129.0, 129.1, 129.5, 132.7, 134.0, 136.6, 137.3, 197.6 ppm. HRMS: *m/z* calcd for C₂₀H₁₈ClNNaO 346.0975; found 346.0973.

1-[1-(4-Bromophenyl)-4-(4-methoxyphenyl)-2-methyl-1H-pyrrol-3-yl]-ethanone (Table 2, Entry 9). Acetylacetone **3a** (100 mg, 1 mmol), *p*-anisaldehyde **2c** (130 mg, 1 mmol), *p*-bromoaniline **1f** (258 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl₃ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as red solid **5i** (188 mg, 0.49 mmol, 49%), mp 119–121 °C. IR (neat) 3007, 1649, 1492, 1406, 1246 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 2.07 (s, 3H), 2.39 (s, 3H), 3.84 (s, 3H), 6.60 (s, 1H), 6.93 (d, *J* = 8.5 Hz, 2H), 7.20–7.29 (m, 4H), 7.61 (d, *J* = 8.5 Hz, 2H) ppm. ¹³C NMR (CDCl₃, 75 MHz) δ 12.8, 31.0, 55.2, 113.7, 114.9, 120.1, 121.9, 122.9, 126.2, 127.7, 128.0, 130.3, 131.1, 132.5, 135.0, 137.7, 158.8, 197.6 ppm. HRMS: *m/z* calcd for C₂₀H₁₉BrNO₂ (M + 1) 384.0599; found 384.0592.

[5-(4-Chlorophenyl)-3-(4-methoxyphenyl)-2-methylcyclopenta-1,4-dienyl]phenyl-methanone (Table 2, Entry 10). Benzoylacetophenone **3b** (162 mg, 1 mmol), *p*-chlorobenzaldehyde **2d** (140 mg, 1 mmol), *p*-anisidine **1c** (185 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl₃ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as orange red sticky liquid **5j** (200 mg, 0.50 mmol, 50%). IR (neat) 3005, 1635, 1514, 1249 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 2.24 (s, 3H), 3.88 (s, 3H), 6.80 (s, 1H), 7.00–7.06 (m, 5H), 7.20–7.36 (m, 6H), 7.73 (d, *J* = 8.1 Hz, 2H) ppm. ¹³C NMR (CDCl₃, 75 MHz) δ 12.4, 55.6, 114.5, 120.3, 120.4, 125.1, 127.4, 127.9, 128.0, 128.3, 128.6, 128.8, 129.2, 129.5, 129.8, 131.5, 131.7, 132.0, 133.5, 135.7, 139.4, 159.3, 194.0 ppm. HRMS: *m/z* calcd for C₂₅H₂₁ClNO₂ (M + 1) 402.1261; found 402.1252.

1-[1-Hexyl-4-(4-methoxyphenyl)-2-methyl-1H-pyrrol-3-yl]-ethanone (Table 3, Entry 1). Acetylacetone **3a** (100 mg, 1 mmol),

p-anisaldehyde **2c** (169 mg, 1.3 mmol), *n*-hexylamine **1g** (101 mg, 1 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl₃ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as sticky dark reddish liquid **6a** (169 mg, 0.54 mmol, 54%). IR (neat) 2929, 2858, 1647, 1510, 1244 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 0.87–0.91 (m, 3H), 1.31–1.32 (m, 6H), 1.69–1.73 (m, 2H), 2.01 (s, 3H), 2.48 (s, 3H), 3.78–3.81 (m, 2H), 3.83 (s, 3H), 6.44 (s, 1H), 6.90 (d, *J* = 8.5 Hz, 2H), 7.22 (d, *J* = 8.5 Hz, 2H) ppm. ¹³C NMR (CDCl₃, 75 MHz) δ 11.5, 14.0, 22.5, 26.4, 30.7, 30.9, 31.4, 46.5, 55.3, 113.6, 114.7, 116.1, 119.3, 121.6, 125.2, 128.9, 130.4, 134.7, 158.6, 197.4 ppm. HRMS: *m/z* calcd for C₂₀H₂₈NO₂ (M + 1) 314.2120; found 314.2118.

1-[4-(4-Chlorophenyl)-1-hexyl-2-methyl-1H-pyrrol-3-yl]-ethanone (Table 3, Entry 2). Acetylacetone **3a** (100 mg, 1 mmol), *p*-chlorobenzaldehyde **2d** (182 mg, 1.3 mmol), *n*-hexylamine **1g** (101 mg, 1 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl₃ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as sticky dark reddish liquid **6b** (187 mg, 0.59 mmol, 59%). IR (neat) 2929, 1649, 1510, 1417, 1182 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 0.86–0.91 (m, 3H), 1.31–1.32 (m, 6H), 1.70–1.75 (m, 2H), 2.01 (s, 3H), 2.46 (s, 3H), 3.81 (t, *J* = 7.3 Hz, 2H), 6.47 (s, 1H), 7.23 (d, *J* = 6.6 Hz, 2H), 7.31 (d, *J* = 6.6 Hz, 2H) ppm. ¹³C NMR (CDCl₃, 75 MHz) δ 11.6, 14.1, 22.6, 26.5, 30.9, 31.1, 31.5, 46.8, 119.7, 121.6, 124.4, 128.5, 128.7, 130.7, 132.6, 135.1, 135.2, 197.2 ppm. HRMS: *m/z* calcd for C₁₉H₂₄ClNNaO 340.1444; found 340.1445.

1-[4-(4-Chlorophenyl)-1-cyclohexyl-2-methyl-1H-pyrrol-3-yl]-ethanone (Table 3, Entry 3). Acetylacetone **3a** (100 mg, 1 mmol), *p*-chlorobenzaldehyde **2d** (182 mg, 1.3 mmol), cyclohexylamine **1h** (99 mg, 1 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl₃ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as sticky off white solid **6c** (155 mg, 0.56 mmol, 56%), mp 98–100 °C. IR (neat) 2933, 2856, 1649, 1508, 1413 cm⁻¹. ¹H NMR (CDCl₃, 500 MHz) δ 1.21–1.26 (m, 2H), 1.39–1.47 (m, 2H), 1.56–1.64 (m, 2H), 1.76 (d, *J* = 13 Hz, 2H), 1.91 (d, *J* = 13 Hz, 2H), 2.02 (s, 3H), 2.49 (s, 3H), 3.89 (t, *J* = 3.5 Hz, 1H), 6.57 (s, 1H), 7.23 (d, *J* = 8.5 Hz, 2H), 7.31 (d, *J* = 8.5 Hz, 2H) ppm. ¹³C NMR (CDCl₃, 125 MHz) δ 11.4, 25.5, 25.9, 31.2, 34.1, 55.3, 116.0, 121.4, 124.5, 128.5, 130.6, 132.6, 134.6, 135.4, 197.5 ppm. HRMS: *m/z* calcd for C₁₉H₂₃ClNO (M + 1) 316.1468, found 316.1464.

1-[1-Benzyl-4-(4-chlorophenyl)-2-methyl-1H-pyrrol-3-yl]-ethanone (Table 3, Entry 4). Acetylacetone **3a** (100 mg, 1 mmol), *p*-chlorobenzaldehyde **2d** (140 mg, 1 mmol), benzylamine **1i** (161 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl₃ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as orange yellow sticky liquid **6d** (258 mg, 0.80 mmol, 80%). IR (neat) 3030, 1651, 1508, 1417, 1180 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 2.05 (s, 3H), 2.40 (s, 3H), 5.06 (s, 2H), 6.54 (s, 1H), 7.09 (d, *J* = 7.7 Hz, 2H), 7.24–7.35 (m, 7H) ppm. ¹³C NMR (CDCl₃, 75 MHz) δ 11.5, 31.1, 50.3, 120.2, 122.0, 124.6, 126.6, 127.9, 128.3, 128.9, 130.5, 132.6, 134.7, 135.3, 136.4, 197.1 ppm. HRMS: *m/z* calcd for C₂₀H₁₉ClNO (M + 1) 324.1155; found 324.1151.

1-[1-Benzyl-2-methyl-4-(thiophen-2-yl)-1H-pyrrol-3-yl]-ethanone (Table 3, Entry 5). To a stirred solution of acetylacetone **3a** (100 mg, 1 mmol), 2-thiophenylaldehyde **2f** (112 mg, 1 mmol), and benzylamine **1i** (161 mg, 1.5 mmol) in nitromethane **4a** (1 mL) was added anhydrous FeCl₃ (16 mg, 0.1 mmol). The mixture was heated at 80 °C for a set period of time and cooled to room temperature. The excess solvent was removed under vacuum, and the residue was directly purified by silica gel column chromatography to afford the product as gray solid **6e** (162 mg, 0.55 mmol, 55%), mp 136–138 °C. IR (neat) 3086, 2928, 1647, 1413, 1352 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 2.15 (s, 3H), 2.44 (s, 3H), 5.05 (s, 2H), 6.64 (s, 1H), 6.96 (d, *J* = 3.4 Hz, 1H), 7.02–7.05 (m, 1H), 7.08–7.10 (m, 2H), 7.26 (d, *J* = 4.7 Hz, 1H), 7.30–7.38 (m, 3H) ppm. ¹³C NMR (CDCl₃,

75 MHz) δ 11.6, 30.5, 50.3, 117.2, 121.5, 122.5, 124.8, 126.6, 126.9, 127.1, 127.9, 128.1, 128.9, 129.3, 135.5, 136.2, 137.1, 197.0 ppm. HRMS: m/z calcd for $C_{18}H_{17}NNaOS$ 318.0929, found 318.0929.

1-[1-Benzyl-4-(furan-2-yl)-2-methyl-1H-pyrrol-3-yl]-ethanone (Table 3, Entry 6). Acetylacetone **3a** (100 mg, 1 mmol), 2-furfuraldehyde **2g** (96 mg, 1 mmol), benzylamine **1i** (161 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous $FeCl_3$ (16 mg, 0.1 mmol) were treated as described for **6e** to obtain the product as off-white solid **6f** (128 mg, 0.46 mmol, 46%), mp 109–111 °C. IR (neat) 3030, 1651, 1556, 1413, 1180 cm^{-1} . 1H NMR ($CDCl_3$, 300 MHz) δ 2.20 (s, 3H), 2.46 (s, 3H), 5.07 (s, 2H), 6.39 (d, $J = 3.0$ Hz, 1H), 6.44–6.46 (m, 1H), 6.74 (s, 1H), 7.09 (d, $J = 6.7$ Hz, 2H), 7.31–7.39 (m, 3H), 7.47 (bs, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.9, 30.0, 50.6, 107.9, 111.2, 114.9, 121.5, 126.8, 128.1, 128.3, 129.1, 135.8, 136.4, 141.7, 149.2, 196.7 ppm. HRMS: m/z calcd for $C_{18}H_{18}NO_2$ ($M + 1$) 280.1338; found 280.1332.

1-[1-Benzyl-2-methyl-4-(3'-nitrophenyl-2-yl)-1H-pyrrol-3-yl]-ethanone (Table 3, Entry 7). Acetylacetone **3a** (100 mg, 1 mmol), *m*-nitrobiphenylaldehyde **2h** (227 mg, 1 mmol), benzylamine **1i** (161 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous $FeCl_3$ (16 mg, 0.1 mmol) were treated as described for **6e** to obtain the product as orange yellow sticky liquid **6g** (349 mg, 0.85 mmol, 85%). IR (neat) 3012, 2926, 1645, 1529, 1350 cm^{-1} . 1H NMR ($CDCl_3$, 300 MHz) δ 1.92 (s, 3H), 2.33 (s, 3H), 4.98 (s, 2H), 6.32 (s, 1H), 6.88–6.90 (m, 2H), 7.26–7.31 (m, 4H), 7.42–7.44 (m, 6H), 7.57–7.59 (m, 1H), 8.09–8.10 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.6, 30.3, 50.1, 121.3, 121.5, 122.4, 123.4, 124.4, 126.2, 127.8, 128.2, 128.7, 128.9, 129.7, 131.8, 134.9, 135.4, 135.4, 136.3, 139.0, 143.2, 147.7, 195.7 ppm. HRMS: m/z calcd for $C_{26}H_{23}N_2O_3$ ($M + 1$) 411.1709; found 411.1705.

[1-Benzyl-4-(3-bromophenyl)-2-methyl-1H-pyrrol-3-yl](phenyl)methanone (Table 3, Entry 8). Benzoylacetophenone **3b** (162 mg, 1 mmol), *m*-bromobenzaldehyde **2i** (185 mg, 1 mmol), benzylamine **1i** (161 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous $FeCl_3$ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as orange yellow sticky liquid **6h** (326 mg, 0.76 mmol, 76%). IR (neat) 3028, 1631, 1595, 1427, 1209 cm^{-1} . 1H NMR ($CDCl_3$, 500 MHz) δ 2.35 (s, 3H), 5.13 (s, 2H), 6.74 (s, 1H), 6.90 (t, $J = 8.0$ Hz, 1H), 7.0 (d, $J = 8.0$ Hz, 1H), 7.12 (d, $J = 8.0$ Hz, 1H), 7.15 (d, $J = 7.5$ Hz, 2H), 7.21 (t, $J = 7.5$ Hz, 2H), 7.29 (t, $J = 1.5$ Hz, 1H), 7.33 (q, $J = 7.5$ Hz, 2H), 7.39 (t, $J = 7.5$ Hz, 2H), 7.67 (d, $J = 7.5$ Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$, 125 MHz) δ 11.4, 50.7, 119.8, 120.2, 121.9, 124.8, 126.8, 127.1, 127.8, 128.0, 128.5, 129.1, 129.3, 129.7, 131.2, 131.8, 135.6, 136.6, 137.3, 139.7, 193.9 ppm. HRMS: m/z calcd for $C_{25}H_{21}BrNO$ ($M + 1$) 430.0807; found 430.0802.

1-[1-Benzyl-2-methyl-4-(4-nitrophenyl)-1H-pyrrol-3-yl]-ethanone (Table 3, Entry 9). Acetylacetone **3a** (100 mg, 1 mmol), *p*-nitrobenzaldehyde **2j** (151 mg, 1 mmol), benzylamine **1i** (161 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous $FeCl_3$ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as deep red sticky liquid **6i** (200 mg, 0.60 mmol, 60%). IR (neat) 3030, 1647, 1597, 1516, 1348 cm^{-1} . 1H NMR ($CDCl_3$, 300 MHz) δ 2.13 (s, 3H), 2.44 (s, 3H), 5.10 (s, 2H), 6.66 (s, 1H), 7.10 (d, $J = 6.9$ Hz, 2H), 7.27–7.40 (m, 3H), 7.47 (d, $J = 8.5$ Hz, 2H), 8.21 (d, $J = 8.5$ Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.8, 31.4, 50.8, 121.4, 122.3, 123.7, 123.8, 124.3, 126.8, 127.1, 128.3, 129.2, 129.6, 136.1, 136.2, 143.4, 146.6, 196.9 ppm. HRMS: m/z calcd for $C_{20}H_{19}N_2O_3$ ($M + 1$) 335.1396; found 335.1393.

Methyl 1-Benzyl-4-(4-cyanophenyl)-2-methyl-1H-pyrrole-3-carboxylate (Table 3, Entry 10). Methylacetoacetate **3c** (116 mg, 1 mmol), *p*-cyanobenzaldehyde **2k** (131 mg, 1 mmol), benzylamine **1i** (161 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous $FeCl_3$ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as orange yellow sticky

liquid **6j** (201 mg, 0.61 mmol, 61%). IR (neat) 3020, 2947, 2224, 1699, 1606, 1286 cm^{-1} . 1H NMR ($CDCl_3$, 300 MHz) δ 2.50 (s, 3H), 3.71 (s, 3H), 5.10 (s, 2H), 6.67 (s, 1H), 7.09 (d, $J = 6.6$ Hz, 2H), 7.34–7.38 (m, 3H), 7.48 (d, $J = 6.6$ Hz, 2H), 7.61 (d, $J = 6.7$ Hz, 2H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.6, 50.6, 50.7, 109.4, 110.6, 119.4, 121.2, 124.6, 126.5, 128.0, 129.0, 129.6, 131.4, 136.2, 137.4, 140.7, 165.7 ppm. HRMS: m/z calcd for $C_{21}H_{19}N_2O_2$ ($M + 1$) 331.1447; found 331.1445.

Methyl 1-Benzyl-4-(4-chlorophenyl)-2-methyl-1H-pyrrole-3-carboxylate (Table 3, Entry 11). Methylacetoacetate **3c** (116 mg, 1 mmol), *p*-chlorobenzaldehyde **2d** (131 mg, 1 mmol), benzylamine **1i** (161 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous $FeCl_3$ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as off-white solid **6k** (271 mg, 0.80 mmol, 80%), mp 79–80 °C. IR (neat) 3012, 1685, 1523, 1280, 1195 cm^{-1} . 1H NMR ($CDCl_3$, 300 MHz) δ 2.49 (s, 3H), 3.70 (s, 3H), 5.08 (s, 2H), 6.59 (s, 1H), 7.09 (d, $J = 6.5$ Hz, 2H), 7.28–7.37 (m, 7H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.6, 50.5, 50.5, 110.7, 120.6, 125.0, 126.5, 127.7, 127.9, 128.9, 130.4, 132.0, 134.3, 136.6, 136.8, 166.0 ppm. HRMS: m/z calcd for $C_{20}H_{19}ClNO_2$ ($M + 1$) 340.1104; found 340.1096.

Ethyl 1-Benzyl-4-(4-fluorophenyl)-2-methyl-1H-pyrrole-3-carboxylate (Table 3, Entry 12). Ethylacetoacetate **3d** (130 mg, 1 mmol), *p*-fluorobenzaldehyde **2l** (124 mg, 1 mmol), benzylamine **1i** (161 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous $FeCl_3$ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as orange yellow sticky liquid **6l** (270 mg, 0.80 mmol, 80%). IR (neat) 3032, 2980, 1693, 1529, 1282 cm^{-1} . 1H NMR ($CDCl_3$, 300 MHz) δ 1.15 (t, $J = 7.1$ Hz, 3H), 2.48 (s, 3H), 4.16 (q, $J = 7.1$ Hz, 2H), 5.07 (s, 2H), 6.56 (s, 1H), 6.97–7.09 (m, 4H), 7.29–7.38 (m, 5H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.5, 14.0, 50.5, 59.3, 111.0, 114.0, 114.3, 120.3, 125.2, 126.5, 127.8, 128.9, 130.7, 130.8, 131.8, 131.8, 136.5, 136.6, 160.0, 163.3, 165.7 ppm. HRMS: m/z calcd for $C_{21}H_{21}FNO_2$ ($M + 1$) 338.1556; found 338.1551.

Ethyl 1-Benzyl-4-(4-chlorophenyl)-2-phenyl-1H-pyrrole-3-carboxylate (Table 3, Entry 13). Ethylbenzoylacetate **3e** (192 mg, 1 mmol), *p*-chlorobenzaldehyde **2l** (140 mg, 1 mmol), benzylamine **1i** (161 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous $FeCl_3$ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as black sticky liquid **6m** (241 mg, 0.58 mmol, 58%). IR (neat) 3030, 2980, 1699, 1487, 1286 cm^{-1} . 1H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, $J = 7.1$ Hz, 3H), 3.97 (q, $J = 7.1$ Hz, 2H), 4.92 (s, 2H), 6.71 (s, 1H), 6.99–7.01 (m, 2H), 7.26–7.40 (m, 12H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.8, 50.9, 59.6, 120.9, 127.1, 127.8, 127.9, 128.0, 128.1, 128.5, 128.6, 128.8, 128.9, 129.2, 130.6, 130.8, 130.8, 132.0, 132.3, 133.9, 137.2, 139.7, 165.1 ppm. HRMS: m/z calcd for $C_{26}H_{23}ClNO_2$ ($M + 1$) 416.1417; found 416.1412.

1-[4-(3-Bromophenyl)-1-(4-methoxybenzyl)-2-methyl-1H-pyrrol-3-yl]-ethanone (Table 3, Entry 14). Acetylacetone **3a** (100 mg, 1 mmol), *m*-bromobenzaldehyde **2i** (185 mg, 1 mmol), *p*-methoxybenzylamine **1j** (206 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous $FeCl_3$ (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as orange yellow sticky liquid **6n** (299 mg, 0.75 mmol, 75%). IR (neat) 3007, 1647, 1512, 1419, 1249 cm^{-1} . 1H NMR ($CDCl_3$, 300 MHz) δ 2.08 (s, 3H), 2.46 (s, 3H), 3.82 (s, 3H), 5.00 (s, 2H), 6.53 (s, 1H), 6.90 (d, $J = 8.7$ Hz, 2H), 7.06 (d, $J = 8.7$ Hz, 2H), 7.22–7.28 (m, 2H), 7.42–7.50 (m, 1H), 7.51 (bs, 1H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.6, 31.0, 49.9, 55.3, 114.3, 120.2, 121.8, 122.2, 124.2, 128.0, 128.2, 129.5, 129.6, 131.9, 135.4, 138.4, 159.3, 197.1 ppm. HRMS: m/z calcd for $C_{21}H_{20}BrNNaO_2$ 420.0575; found 420.0577.

1-[1-(4-Methoxybenzyl)-2-methyl-4-(3'-nitrophenyl-2-yl)-1H-pyrrol-3-yl]-ethanone (Table 3, Entry 15). Acetylacetone **3a** (100 mg, 1 mmol), *m*-nitrobiphenylaldehyde **2h** (227 mg, 1 mmol), *p*-methoxybenzylamine **1j** (205 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous $FeCl_3$ (16 mg, 0.1 mmol)

were treated as described for **6d** to obtain the product as dark red sticky liquid **6o** (343 mg, 0.78 mmol, 78%). IR (neat) 3005, 1647, 1527, 1514, 1350, 1247 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 2.08 (s, 3H), 2.49 (s, 3H), 3.90 (s, 3H), 5.00 (s, 2H), 6.39 (s, 1H), 6.89–7.01 (m, 4H), 7.48–7.60 (m, 4H), 7.67 (d, $J = 7.7$ Hz, 2H), 8.17–8.19 (m, 2H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz) δ 11.8, 30.4, 49.8, 55.4, 114.3, 121.2, 121.6, 122.4, 123.4, 124.6, 127.8, 127.9, 128.3, 128.8, 129.8, 131.9, 135.0, 135.4, 135.5, 139.0, 143.3, 147.8, 159.3, 195.9 ppm. HRMS: m/z calcd for $\text{C}_{27}\text{H}_{24}\text{N}_2\text{NaO}_4$ 463.1634; found 463.1631.

Methyl 4-(4-Fluorophenyl)-1-(4-methoxybenzyl)-2-methyl-1H-pyrrole-3-carboxylate (Table 3, Entry 16). Methylacetoacetate **3c** (116 mg, 1 mmol), *p*-flourobzaldehyde **2l** (124 mg, 1 mmol), *p*-methoxybenzylamine **1j** (206 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl_3 (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as off-white solid **6p** (289.8 mg, 0.70 mmol, 70%), mp 70–72 °C. IR (neat) 3012, 2947, 1695, 1514, 1284 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 2.29 (s, 3H), 3.48 (s, 3H), 3.60 (s, 3H), 4.79 (s, 2H), 6.33 (s, 1H), 6.68 (d, $J = 6.7$ Hz, 2H), 6.78–6.84 (m, 4H), 7.10–7.13 (m, 2H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz) δ 11.6, 50.0, 50.5, 55.3, 110.6, 114.2, 114.3, 114.5, 120.2, 125.1, 128.0, 128.5, 130.5, 130.6, 131.8, 131.8, 136.5, 159.2, 160.0, 163.3, 166.1 ppm. HRMS: m/z calcd for $\text{C}_{21}\text{H}_{21}\text{FNO}_3$ ($M + 1$) 354.1503; found 354.1503.

Methyl 4-(3-Bromophenyl)-1-(4-methoxybenzyl)-2-methyl-1H-pyrrole-3-carboxylate (Table 3, Entry 17). Methylacetoacetate **3c** (116 mg, 1 mmol), *m*-bromobenzaldehyde **2i** (185 mg, 1 mmol), *p*-methoxybenzylamine **1j** (206 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl_3 (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as orange yellow sticky liquid **6q** (290 mg, 0.70 mmol, 70%). IR (neat) 2947, 1699, 1514, 1438, 1249 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 2.48 (s, 3H), 3.68 (s, 3H), 3.80 (s, 3H), 4.99 (s, 2H), 6.56 (s, 1H), 6.87 (d, $J = 8.6$ Hz, 2H), 7.02 (d, $J = 8.6$ Hz, 2H), 7.17 (t, $J = 7.8$ Hz, 1H), 7.26–7.31 (m, 1H), 7.35–7.37 (m, 1H), 7.51 (bs, 1H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz) δ 11.5, 50.1, 50.6, 55.3, 110.6, 114.4, 120.6, 121.6, 124.6, 127.9, 128.1, 128.4, 129.0, 131.9, 136.8, 138.0, 159.3, 166.0 ppm. HRMS: m/z calcd for $\text{C}_{21}\text{H}_{20}\text{BrNNaO}_3$ 436.0524; found 436.0508.

Ethyl 4-(4-Chlorophenyl)-1-(4-methoxybenzyl)-2-methyl-1H-pyrrole-3-carboxylate (Table 3, Entry 18). Ethylacetoacetate **3d** (130 mg, 1 mmol), *p*-chlorobenzaldehyde **2d** (140 mg, 1 mmol), *p*-methoxybenzylamine **1j** (206 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl_3 (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as orange yellow liquid **6r** (291 mg, 0.76 mmol 76%). IR (neat) 2980, 2837, 1693, 1514, 1249 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 1.09 (t, $J = 7.1$ Hz, 3H), 2.42 (s, 3H), 3.73 (s, 3H), 4.09 (q, $J = 7.1$ Hz, 2H), 4.92 (s, 2H), 6.47 (s, 1H), 6.80 (d, $J = 8.6$ Hz, 2H), 6.96 (d, $J = 8.5$ Hz, 2H) 7.18–7.25 (m, 4H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz) δ 11.5, 14.1, 50.0, 55.3, 59.4, 110.8, 114.3, 120.2, 124.9, 127.5, 128.0, 128.5, 130.5, 131.9, 134.4, 136.5, 159.2, 165.6 ppm. HRMS: m/z calcd for $\text{C}_{22}\text{H}_{23}\text{ClNO}_3$ ($M + 1$) 384.1366; found 384.1365.

Ethyl 1-(4-Methoxybenzyl)-2-methyl-4-(naphthalen-2-yl)-1H-pyrrole-3-carboxylate (Table 3, Entry 19). Ethylacetoacetate **3d** (130 mg, 1 mmol), 2-Naphthylaldehyde **2m** (156 mg, 1 mmol), *p*-methoxybenzylamine **1j** (206 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl_3 (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as yellow orange liquid **6s** (259 mg, 0.65 mmol, 65%). IR (neat) 3012, 2837, 1691, 1514, 1247 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 1.09 (t, $J = 7.1$ Hz, 3H), 2.53 (s, 3H), 3.81 (s, 3H), 4.16 (q, $J = 7.1$ Hz, 2H), 5.03 (s, 2H), 6.67 (s, 1H), 6.89 (d, $J = 8.6$ Hz, 2H), 7.06 (d, $J = 8.5$ Hz, 2H), 7.44 (t, $J = 3.8$ Hz, 2H), 7.55 (d, $J = 8.5$ Hz, 1H), 7.77–7.84 (m, 4H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz) δ 11.5, 14.1, 50.0, 55.3, 59.3, 111.1, 114.3, 120.5, 125.1, 125.6, 126.0, 126.5, 126.8, 127.5, 127.7, 128.0, 128.6, 128.7, 132.1, 133.2,

133.6, 136.6, 159.2, 165.9 ppm. HRMS: m/z calcd for $\text{C}_{26}\text{H}_{25}\text{NNaO}_3$ 422.1732; found 422.1731.

1-[1-(4-Methoxybenzyl)-2-methyl-4-(thiophen-2-yl)-1H-pyrrol-3-yl]-ethanone (Table 3, Entry 20). Acetylacetone **3a** (100 mg, 1 mmol), 2-thiophenylaldehyde **2f** (112 mg, 1 mmol), *p*-methoxybenzylamine **1j** (206 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl_3 (16 mg, 0.1 mmol) were treated as described for **6e** to obtain the product as off white solid **6t** (182 mg, 0.56 mmol, 56%), mp 80–82 °C. IR (neat) 3009, 1649, 1514, 1413, 1249 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 2.14 (s, 3H), 2.45 (s, 3H), 3.78 (s, 3H), 4.97 (s, 2H), 6.60 (s, 1H), 6.87 (d, $J = 6.6$ Hz, 2H), 6.94–6.95 (m, 1H), 7.01–7.06 (m, 3H), 7.25 (dd, $J = 1.0$ Hz, 5.2 Hz, 1H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz) δ 11.9, 30.5, 50.0, 55.4, 114.5, 117.3, 121.6, 122.5, 125.0, 127.1, 127.3, 128.3, 128.4, 135.8, 137.3, 159.4, 197.4 ppm. HRMS: m/z calcd for $\text{C}_{19}\text{H}_{20}\text{NO}_2\text{S}$ ($M + 1$) 326.1215; found 326.1207.

1-[1-Benzyl-4-(4-chlorophenyl)-2,5-dimethyl-1H-pyrrol-3-yl]-ethanone (Table 3, Entry 21). Acetylacetone **3a** (100 mg, 1 mmol), *p*-chlorobenzaldehyde **2d** (140 mg, 1 mmol), benzylamine **1i** (161 mg, 1.5 mmol), nitroethane **4b** (1 mL), and anhydrous FeCl_3 (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as orange yellow sticky liquid **6u** (158 mg, 0.47 mmol 47%). IR (neat) 3005, 2920, 1645, 1514, 1408 cm^{-1} . ^1H NMR (CDCl_3 , 500 MHz) δ 1.95 (s, 3H), 2.01 (s, 3H), 2.46 (s, 3H), 5.13 (s, 2H), 6.99 (d, $J = 7.5$ Hz, 2H), 7.23 (d, $J = 7.5$ Hz, 2H), 7.29–7.33 (m, 1H), 7.35–7.38 (m, 4H) ppm. ^{13}C NMR (CDCl_3 , 125 MHz) δ 10.3, 11.8, 31.1, 47.0, 121.2, 121.6, 125.6, 125.7, 126.3, 126.4, 127.6, 128.2, 128.4, 128.7, 129.0, 131.9, 132.6, 134.5, 135.7, 136.7, 196.8 ppm. HRMS: m/z calcd for $\text{C}_{21}\text{H}_{21}\text{ClNO}$ ($M + 1$) 338.1312; found 338.1305.

1-[1-Benzyl-4-(4-fluorophenyl)-2,5-dimethyl-1H-pyrrol-3-yl]-ethanone (Table 3, Entry 22). Acetylacetone **3a** (100 mg, 1 mmol), *p*-flourobzaldehyde **2l** (124 mg, 1 mmol), benzylamine **1i** (161 mg, 1.5 mmol), nitroethane **4b** (1 mL), and anhydrous FeCl_3 (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as yellow solid **6v** (122 mg, 0.38 mmol, 38%), mp 102–104 °C. IR (neat) 3032, 1649, 1514, 1408, 1220 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 1.95 (s, 3H), 1.98 (s, 3H), 2.47 (s, 3H), 5.11 (s, 2H), 6.96 (d, $J = 6.8$ Hz, 2H), 7.08 (t, $J = 8.8$ Hz, 2H), 7.21–7.34 (m, 5H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz) δ 10.4, 12.0, 31.1, 47.1, 115.1, 115.4, 125.8, 126.5, 127.7, 128.4, 129.1, 132.2, 132.3, 133.1, 136.8, 160.4, 163.6, 197.2 ppm. HRMS: m/z calcd for $\text{C}_{21}\text{H}_{20}\text{FNNaO}$ 344.1427; found 344.1427.

1-[4-(4-Chlorophenyl)-1-(4-methoxybenzyl)-2,5-dimethyl-1H-pyrrol-3-yl]-ethanone (Table 3, entry 23). Acetylacetone **3a** (100 mg, 1 mmol), *p*-tolualdehyde **2e** (120 mg, 1 mmol), *p*-methoxybenzylamine **1j** (206 mg, 1.5 mmol), nitroethane **4b** (1 mL), and anhydrous FeCl_3 (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as yellow solid **6w** (162 mg, 0.44 mmol, 44%), mp 117–119 °C. IR (neat) 3005, 1645, 1514, 1408, 1249 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 1.72 (s, 3H), 1.79 (s, 3H), 2.27 (s, 3H), 3.59 (s, 3H), 4.84 (s, 2H), 6.67–6.68 (m, 4H), 7.00 (d, $J = 8.4$ Hz, 2H), 7.16 (d, $J = 8.4$ Hz, 2H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz) δ 10.2, 11.7, 31.1, 46.4, 55.2, 114.3, 121.0, 121.4, 126.2, 126.8, 127.8, 128.3, 128.5, 131.8, 132.5, 134.5, 135.6, 158.9, 196.8 ppm. HRMS: m/z calcd for $\text{C}_{22}\text{H}_{22}\text{ClNNaO}_2$ 390.1237; found 390.1232.

1-[1-(4-Methoxybenzyl)-2,5-dimethyl-4-*p*-tolyl-1H-pyrrol-3-yl]-ethanone (Table 3, Entry 24). Acetylacetone **3a** (100 mg, 1 mmol), *p*-chlorobenzaldehyde **2d** (140 mg, 1 mmol), *p*-methoxybenzylamine **1j** (206 mg, 1.5 mmol), nitroethane **4b** (1 mL), and anhydrous FeCl_3 (16 mg, 0.1 mmol) were treated as described for **5e** to obtain the product as orange yellow sticky liquid **6x** (156 mg, 0.45 mmol, 45%). IR (neat) 2920, 1645, 1514, 1408, 1249 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 1.92 (s, 3H), 2.00 (s, 3H), 2.39 (s, 3H), 2.48 (s, 3H), 3.79 (s, 3H), 5.04 (s, 2H),

6.85–6.92 (m, 4H), 7.14–7.21 (m, 4H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz) δ 10.3, 11.8, 21.1, 30.9, 46.4, 55.2, 114.3, 121.5, 122.3, 126.0, 126.9, 127.9, 128.7, 128.8, 130.4, 133.9, 134.3, 136.1, 158.9, 197.5 ppm. HRMS: m/z calcd for $\text{C}_{23}\text{H}_{26}\text{NO}_2$ ($M + 1$) 348.1964; found 348.1955.

1-(1-Benzyl-4-isopropyl-2-methyl-1H-pyrrol-3-yl)-ethanone (Table 3, Entry 25). Acetylacetone **3a** (100 mg, 1 mmol), isobuteraldehyde **2n** (72 mg, 1 mmol), benzylamine **1i** (161 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl_3 (16 mg, 0.1 mmol) were treated as described for **6e**, the reaction was done at 70 °C to obtain the product as dark red liquid **6y** (200 mg, 0.72 mmol, 72%). IR (neat) 2960, 1641, 1496, 1417 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 1.21 (d, $J = 3.7$ Hz, 6H), 2.37 (s, 3H), 2.47 (s, 3H), 3.34 (q, $J = 6.7$ Hz, 1H), 5.01 (s, 2H), 6.40 (s, 1H), 7.00 (d, $J = 6.8$ Hz, 2H), 7.31–7.33 (m, 3H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz) δ 12.4, 24.1, 25.7, 31.1, 50.4, 117.7, 121.6, 126.2, 127.6, 128.8, 132.4, 135.0, 137.1, 195.8 ppm. HRMS: m/z calcd for $\text{C}_{17}\text{H}_{21}\text{NNaO}$ 278.1521; found 278.1524.

1-(1-Benzyl-2-methyl-4-propyl-1H-pyrrol-3-yl)-ethanone (Table 3, Entry 26). Acetylacetone **3a** (100 mg, 1 mmol), buteraldehyde **2o** (72 mg, 1 mmol), benzylamine **1i** (161 mg, 1.5 mmol), nitromethane **4a** (1 mL), and anhydrous FeCl_3 (16 mg,

0.1 mmol) were treated as described for **6e**, with the reaction performed at 70 °C to obtain the product as dark red liquid **6z** (115 mg, 0.45 mmol, 45%). IR (neat) 2956, 1643, 1496, 1417 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 0.99 (t, $J = 7.3$ Hz, 3H), 1.58–1.65 (m, 2H), 2.40 (s, 3H), 2.45 (s, 3H), 2.66 (t, $J = 7.6$ Hz, 2H), 5.00 (s, 2H), 6.37 (s, 1H), 7.00 (d, $J = 7.2$ Hz, 2H), 7.27–7.35 (m, 3H) ppm. ^{13}C NMR (CDCl_3 , 75 MHz) δ 12.3, 14.1, 23.4, 29.7, 30.9, 50.1, 119.5, 121.7, 124.7, 126.3, 127.6, 128.8, 135.6, 137.0, 195.7 ppm. HRMS: m/z calcd for $\text{C}_{17}\text{H}_{21}\text{NNaO}$ 278.1521; found 278.1526.

Acknowledgment. We gratefully acknowledge the financial and infrastructural support from the UGC-CAS programme of the Department of Chemistry, Jadavpur University. S.M. and S.B. also are thankful to the University Grants Commission (UGC), Jadavpur University and New Delhi, India, respectively, for their fellowships.

Supporting Information Available: Copies of NMR spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.