EFFICIENT SYNTHESIS OF SPIRO[DIINDENOPYRIDINE-INDOLINE]TRIONES CATALYZED BY PEG-OSO$_3$H-H$_2$O AND [NMP]H$_2$PO$_4$

Jayant Sindhu, Harjinder Singh, and J. M. Khurana
Department of Chemistry, University of Delhi, Delhi, India

GRAPHICAL ABSTRACT

Abstract One-pot, three-component synthesis of spiro[diindenopyridine-indoline]triones has been reported via the reaction of 1,3-indandione, aromatic amines, and isatins with (PEG-OSO$_3$H) as an efficient, polymeric acid surfactant–based catalyst in water and also in presence of acidic ionic liquid [NMP]H$_2$PO$_4$, which acts both as a medium and catalyst under conventional heating and ultrasonic irradiation. The reactions were complete in short reaction times with excellent yield of products. Surfactant-based PEG-OSO$_3$H could be recycled and reused several times without any significant loss of activity. The compounds exhibit fluorescence in methanol with large Stokes shift.

Keywords Biodegradable; multicomponent reactions (MCRs); [NMP]H$_2$PO$_4$; PEG-6000; polymeric; spiro compounds; water

Received January 22, 2014.
Address correspondence to J. M. Khurana, Department of Chemistry, University of Delhi, Delhi 110007, India. E-mail: jmkhurana@chemistry.du.ac.in
Color versions of one or more of the figures in the article can be found online at www.tandfonline.com/lsyc.
INTRODUCTION

The development of synthetic methods that are environmentally benign and yield complex structures from simple and inexpensive starting materials is the main challenge faced by modern organic chemists.[1] Multicomponent reactions (MCRs) have emerged as a powerful synthetic tool to achieve synthetic efficiency, as they have unique advantages such as atom economy and operational simplicity, and have played a significant role in modern synthetic chemistry. The use of ecofriendly, economically viable, recyclable catalysts and reaction media such as water and ionic liquids make the synthetic approach green and efficient. Reactions have been reported in ionic liquids (ILs)[2] and also in task-specific acidic ionic liquids that act as reaction medium and/or catalyst.[3] Development of immobilized catalysts that allow simple workup procedures, easy separation of products, and recyclability of the catalysts is an important process.[4]

Sulfuric acid–modified PEG-6000 (PEG-OSO3H) is an example of polyethylene glycol-supported catalyst that is functionalized by sulfonic acid groups. It is biodegradable, recyclable, nonvolatile, and noncorrosive organic acid that has been used for the synthesis of heterocyclic compounds.[5] It also acts as a surfactant due to the presence of long chains functionalized by sulfonic acid groups and improves the solubility of the reactants in water by acting as a phase-transfer catalyst. Indenone-fused heterocycles represent an important class of medicinally important compounds. Indenopyridines show biological activities such as cytotoxic,[6] phosphodiesterase inhibitory,[7] adenosine A2a receptor antagonist,[8] anti-inflammatory/antiallergic,[9] coronary dilating,[10] and calcium modulation[11] activities. These compounds have also been investigated for the treatment of hyperlipoproteinemia and arteriosclerosis,[12] as well as neurodegenerative diseases.[13] Our group has been involved in the development of efficient, green, economical, and new methodologies for the synthesis of biologically important heterocycles.[14] The synthesis of indenone-fused pyridines has been reported with p-TSA in acetonitrile under reflux.[15] Therefore, we decided to investigate the synthesis of indenone-fused heterocycles under a variety of green methodologies.

RESULTS AND DISCUSSION

We report herein the synthesis of indenone-fused heterocycles by three-component condensation of 1,3-indandione (1), 4-methoxyaniline (2), and isatin (3) in the presence of PEG-OSO3H as a noncorrosive organic acid catalyst and also in the presence of Brønsted acidic ionic liquid [NMP]H2PO4 under conventional heating and ultrasonic irradiation. The optimization of the reaction conditions for the three-component condensation was carried out by attempting reactions of 1,3-indandione (1) (2.0 mmol), 4-methoxyaniline (2) (1.0 mmol), and isatin (3) (1.0 mmol). This reaction was initially attempted in the presence of AcOH (30 mol%) and H2SO4 (30 mol%) in water under reflux for 60 min. The reactions were incomplete as monitored by thin-layer chromatography (TLC; ethyl acetate–petroleum ether, 30:70, v/v) but afforded the desired 5-(4-methoxyphenyl)-5H-spiro[diindeno[1,2-b:2', 1'-e]pyridine-11,3'-indoline]-2',10,12-trione (4a) in 60% and 74% yield respectively after separation (Table 1, entries 1 and 2) [Eq. (1)].
The reaction was then attempted using PEG-OSO$_3$H (30 mol%) acid as catalyst in water under reflux. The reaction was much faster and complete in 10 min. After a simple workup, it yielded the desired product $4a$ in excellent yield of 95% (Table 1, entry 3). The reaction was repeated at 80°C and was also complete in 10 min, giving 97% yield of the product $4a$ (Table 1, entry 4). However, the reaction was carried out at 60°C under otherwise identical conditions, required longer reaction time, and resulted in poorer yield (Table 1, entry 5). Also, the reaction attempted using lower loading of catalyst (20 mol%) at 80°C required longer time and resulted in slightly poorer yield of the product (Table 1, entry 6). When the reaction was attempted under solvent-free conditions using 30 mol% of PEG-OSO$_3$H, the separation of product was not easy and the reaction gave lower yield of the product $4a$ (Table 1, entry 7). The same reaction when then attempted using ultrasonic irradiation at 40°C and resulted in 95% of $4a$ (Table 1, entry 8).

It can be inferred from Table 1 that the three-component reaction yielded the product $4a$ in a rapid reaction with good yield when attempted using 30 mol% of PEG-OSO$_3$H as a catalyst in water under conventional heating at 80°C (Table 1, entry 4) and also under ultrasonic irradiation at 40°C (Table 1, entry 8). One clear advantage of the PEG-OSO$_3$H−water combination was that it afforded products that could be obtained by simple filtration. Encouraged by these results, we investigated the scope of this reaction of 1,3-indandione (1), 4-methoxyaniline (2), and isatin (3) under conventional heating at 80°C (method A1) (Table 2, Scheme 1) and also under ultrasonic irradiation at 40°C (method A2). All the products ($4a$−$4n$) were obtained in good yield and in short reaction time by both methods as shown in Table 2.

![Chemical structure of the reaction](image)

**Table 1.** Reaction of 1,3-indandione (1), 4-methoxyaniline (2), and isatin (3) under different conditions

| Entry | Solvent | Catalyst (mol %) | Temp. (°C) | Time (min) | Yield (%) ($4a$) |
|-------|---------|-----------------|------------|------------|-----------------|
| 1     | H$_2$O  | AcOH (30)       | 100        | 60         | 60$^b$         |
| 2     | H$_2$O  | H$_2$SO$_4$ (30)| 100        | 60         | 74$^b$         |
| 3     | H$_2$O  | PEG-OSO$_3$H (30)| 100       | 10         | 95             |
| 4     | H$_2$O  | PEG-OSO$_3$H (30)| 80         | 10         | 97             |
| 5     | H$_2$O  | PEG-OSO$_3$H (30)| 60         | 15         | 88             |
| 6     | H$_2$O  | PEG-OSO$_3$H (20)| 80         | 10         | 90             |
| 7     | —       | PEG-OSO$_3$H (30)| 100        | 10         | 90             |
| 8     | H$_2$O  | PEG-OSO$_3$H (30)| 40         | 5          | 95$^c$         |

$^a$Reaction carried out using 2.0 mmol of 1, 1.0 mmol of 2, and 1.0 mmol of 3.
$^b$Incomplete reaction.
$^c$Reaction performed under ultrasonic irradiation.
The scope of this reaction was further explored by using Brønsted acidic ionic liquid \([\text{NMP}]\text{H}_2\text{PO}_4\), which could be prepared in a single step without the application of organic solvents.\(^{16}\) Therefore, a model reaction of 1,3-indandione (1) (2.0 mmol), 4-methoxyaniline (2) (1.0 mmol), and isatin (3) (1.0 mmol) was investigated with \([\text{NMP}]\text{H}_2\text{PO}_4\) 30 mol% at 60°C. The reaction was complete in 15 min and afforded 5-(4-methoxyphenyl)-5H-spiro[diindeno[1,2-b:2',1'-e]pyridine-11,3'-indoline]-2',10,12-trione (4a) in 92% yield after a simple workup. The same reaction was then carried out at 80°C and 100°C in the presence of ionic liquid \([\text{NMP}]\text{H}_2\text{PO}_4\) (30 mol%). The reactions were complete in 10 min and yielded 95% and 94% of 4a respectively. The reaction was then explored by reducing the catalyst loading (20%). The reaction was complete after 15 min yielding 90% of 4a. When this reaction was attempted in the presence of \([\text{NMP}]\text{H}_2\text{PO}_4\) (30 mol%) under ultrasonic irradiation at 40°C, it yielded the product 4a in 94% yield in 5 min.

Table 2. Synthesis of indenone-fused pyridines by condensation of inden-1,3-dione, aromatic amines, and isatins catalyzed by PEG-OSO\(_3\)H\(^{\text{a}}\)

| Product | Ar          | R | Method A\(^{1b}\) | Yield (%) | Time (min) | Yield (%) | Method A\(^{2c}\) | Yield (%) | Time (min) |
|---------|-------------|---|------------------|-----------|------------|-----------|------------------|-----------|------------|
| 4a      | 4-(OMe)C\(_6\)H\(_4\) | H | 10               | 97        | 5          | 95        | 10               | 92        | 5          |
| 4b      | 4-MeC\(_6\)H\(_4\)    | H | 10               | 95        | 5          | 93        | 10               | 92        | 5          |
| 4c      | 4- (NO\(_2\))C\(_6\)H\(_4\) | H | 10               | 92        | 5          | 90        | 10               | 92        | 5          |
| 4d      | 4-BrC\(_6\)H\(_5\)     | H | 10               | 90        | 5          | 92        | 10               | 92        | 5          |
| 4e      | C\(_6\)H\(_5\)         | H | 10               | 94        | 5          | 92        | 10               | 94        | 5          |
| 4f      | 4-(OMe)C\(_6\)H\(_4\)  | NO\(_2\) | 10              | 92        | 5          | 90        | 10               | 92        | 5          |
| 4g      | 4-(NO\(_2\))C\(_6\)H\(_4\) | NO\(_2\) | 10              | 90        | 5          | 92        | 10               | 90        | 5          |
| 4h      | 4-MeC\(_6\)H\(_4\)     | NO\(_2\) | 10              | 88        | 5          | 90        | 10               | 88        | 5          |
| 4i      | 4-BrC\(_6\)H\(_5\)     | NO\(_2\) | 10              | 90        | 5          | 92        | 10               | 90        | 5          |
| 4j      | C\(_6\)H\(_5\)         | NO\(_2\) | 10              | 90        | 5          | 92        | 10               | 90        | 5          |
| 4k      | 4-MeC\(_6\)H\(_4\)     | Br  | 10              | 88        | 5          | 90        | 10               | 88        | 5          |
| 4l      | C\(_6\)H\(_5\)         | Br  | 10              | 90        | 5          | 90        | 10               | 90        | 5          |
| 4m      | 4-(NO\(_2\))C\(_6\)H\(_4\) | Br  | 10              | 92        | 5          | 94        | 10               | 94        | 5          |
| 4n      | 4-(OMe)C\(_6\)H\(_4\)  | Br  | 10              | 90        | 5          | 92        | 10               | 92        | 5          |

\(^{a}\)Reaction carried out using 2.0 mmol of 1, 1.0 mmol of 2, and 1.0 mmol of 3 in the presence of PEG-OSO\(_3\)H (30 mol%).

\(^{b}\)Reaction performed under conventional heating at 80°C.

\(^{c}\)Reaction performed under ultrasonic irradiation at 40°C.

The scope of this reaction was further explored by using Brønsted acidic ionic liquid \([\text{NMP}]\text{H}_2\text{PO}_4\), which could be prepared in a single step without the application of organic solvents.\(^{16}\) Therefore, a model reaction of 1,3-indandione (1) (2.0 mmol), 4-methoxyaniline (2) (1.0 mmol), and isatin (3) (1.0 mmol) was investigated with \([\text{NMP}]\text{H}_2\text{PO}_4\) 30 mol% at 60°C. The reaction was complete in 15 min and afforded 5-(4-methoxyphenyl)-5H-spiro[diindeno[1,2-b:2',1'-e]pyridine-11,3'-indoline]-2',10,12-trione (4a) in 92% yield after a simple workup. The same reaction was then carried out at 80°C and 100°C in the presence of ionic liquid \([\text{NMP}]\text{H}_2\text{PO}_4\) (30 mol%). The reactions were complete in 10 min and yielded 95% and 94% of 4a respectively. The reaction was then explored by reducing the catalyst loading (20%). The reaction was complete after 15 min yielding 90% of 4a. When this reaction was attempted in the presence of \([\text{NMP}]\text{H}_2\text{PO}_4\) (30 mol%) under ultrasonic irradiation at 40°C, it yielded the product 4a in 94% yield in 5 min.

Scheme 1. Synthesis of indenone-fused pyridine using one-pot, four-component condensation of inden-1, 3-dione, aromatic amines, and isatins under conventional heating and ultrasonic irradiation.
The condensation of the three components in the presence of [NMP]H$_2$PO$_4$ (30 mol%) under conventional heating at 80°C and also under ultrasonic irradiation at 40°C proved to be optimum conditions. These optimized reaction conditions were extended for a range of aromatic amines (2) and different isatins (3) (Scheme 1). All the products were obtained in good yields and in short reaction times by both of these methods (methods B1 and B2) as shown in Table 3.

The possibility of recycling of the catalyst (PEG-OSO$_3$H) was also examined using the reaction of 1,3-indandione (1), 4-methoxyaniline (2), and isatin (3) under optimized conditions. Upon completion of reaction, the product was filtered with a suction pump and washed with water. To recover the catalyst, H$_2$O was removed under reduced pressure and the resulting liquid was washed with diethyl ether and dried to recover PEG-OSO$_3$H. The recovered catalyst could be reused four times, after which there was a significant decrease in the activity of the catalyst (Fig. 1).

All the synthesized compounds 4a–4n were characterized by $^1$H NMR, $^{13}$C NMR, and melting point. A plausible mechanism for the synthesis of 4 using PEG-OSO$_3$H and [NMP]H$_2$PO$_4$ as catalyst is depicted in Scheme 2.

All the compounds formed are deep red in color. We examined their fluorescent behavior also. We observed that all compounds showed strong fluorescence in methanol when excited at wavelength 268 nm as shown in Fig. 2. The photophysical properties of all molecules are summarized in Table 4. Moreover, the ultraviolet (UV)–visible spectra of these derivatives contain intense absorption maxima in the range of 264–274 nm. These compounds exhibit emission bands in the range of 282–596 nm with Stokes shift in the range of 115–142 nm.

**Table 3.** Synthesis of indenone-fused pyridines by condensation of inden-1,3-dione, amine, and isatin catalyzed by [NMP]H$_2$PO$_4$$^a$

| Product | Ar                 | R     | Method B1$^b$ | Method B2$^c$ |
|---------|--------------------|-------|--------------|--------------|
|         |                    |       | Time (min)   | Yield (%)    | Time (min)   | Yield (%)    |
| 4a      | 4-(OMe)C$_6$H$_4$  | H     | 10           | 95           | 5            | 94           |
| 4b      | 4-MeC$_6$H$_4$     | H     | 10           | 92           | 5            | 91           |
| 4c      | 4-(NO$_2$)C$_6$H$_4$ | H   | 10           | 90           | 10           | 92           |
| 4d      | 4-BrC$_6$H$_5$     | H     | 10           | 94           | 5            | 92           |
| 4e      | C$_6$H$_5$         | H     | 15           | 92           | 10           | 90           |
| 4f      | 4-(OMe)C$_6$H$_4$  | NO$_2$| 10           | 90           | 5            | 92           |
| 4g      | 4-(NO$_2$)C$_6$H$_4$ | NO$_2$| 15           | 92           | 10           | 90           |
| 4h      | 4-MeC$_6$H$_4$     | NO$_2$| 10           | 90           | 5            | 88           |
| 4i      | 4-BrC$_6$H$_5$     | NO$_2$| 10           | 90           | 5            | 92           |
| 4j      | C$_6$H$_5$         | NO$_2$| 10           | 92           | 5            | 90           |
| 4k      | 4-MeC$_6$H$_4$     | Br    | 10           | 90           | 5            | 92           |
| 4l      | C$_6$H$_5$         | Br    | 15           | 92           | 10           | 90           |
| 4m      | 4-(NO$_2$)C$_6$H$_4$ | Br | 15           | 88           | 5            | 90           |
| 4n      | 4-(OMe)C$_6$H$_4$  | Br    | 10           | 92           | 5            | 94           |

$^a$Reaction carried out using 2.0 mmol of 1, 1.0 mmol of 2, and 1.0 mmol of 3 in the presence of [NMP]H$_2$PO$_4$ (30 mol%).

$^b$Reaction performed under conventional heating at 80°C.

$^c$Reaction performed under ultrasonic irradiation at 40°C.
Figure 1. Recyclability of PEG-OSO$_3$H for synthesis of compound 4a under conventional heating.

Scheme 2. Proposed mechanism for the synthesis of spirodiindenopyridine-indolines 4.

Figure 2. Fluorescence spectra of indenone-fused pyridine hybrids (4a-4n).
CONCLUSION

We have reported an efficient and green methodology for the synthesis of indenone-fused pyridine heterocycles using PEG-OSO$_3$H as a mild, biodegradable, recyclable, nonvolatile, and noncorrosive organic acid in water and also acidic ionic liquid [NMP]H$_2$PO$_4$, which acts as medium and catalyst under conventional heating and ultrasonic irradiation. All the compounds exhibit strong fluorescence in methanol with large Stokes shift.

EXPERIMENTAL

Structures of all of the compounds were identified by their spectral data. Silica-gel 60 F$_{254}$ (precoated aluminium plates) from Merck were used to monitor reaction progress. Melting points were determined on Buchi melting-point 545 apparatus and are uncorrected. The $^1$H and $^{13}$C NMR spectra were recorded on Jeol JNM ECX-400P at 400 and 100 MHz respectively. The chemical shift values are recorded on $\delta$ scale and the coupling constants ($J$) are in hertz. Ultrasonic bath (54 KHz, 300 W, 3 L capacity) from Throughclean Ultrasonic Pvt. Ltd. (India) was used for reactions under ultrasonic irradiation. UV-vis spectra were recorded on an Analyticjena Specord UV-Visible spectrophotometer, while fluorescence spectra were recorded on a Carry eclipse spectrophotometer. PEG(6000)-OSO$_3$H and [NMP]H$_2$PO$_4$ were prepared by the reported procedures.$^{[16]}$

| Product | $\lambda_{abs}$ (nm) | $\epsilon \times 10^5$ (Lmol$^{-1}$ cm$^{-1}$) | $\lambda_{em}$ (nm) | Stokes shift ($\Delta\nu$) nm |
|---------|---------------------|------------------------------------------|------------------|--------------------------|
| 4a      | 268                 | 1.04                                     | 407              | 139                      |
| 4b      | 272                 | 1.22                                     | 387              | 115                      |
| 4c      | 264                 | 1.03                                     | 387              | 123                      |
| 4d      | 270                 | 1.93                                     | 407              | 137                      |
| 4e      | 277                 | 1.66                                     | 402              | 125                      |
| 4f      | 270                 | 2.88                                     | 403              | 133                      |
| 4g      | 271                 | 2.89                                     | 402              | 131                      |
| 4h      | 270                 | 1.93                                     | 403              | 133                      |
| 4i      | 273                 | 2.77                                     | 409              | 136                      |
| 4j      | 272                 | 2.85                                     | 407              | 135                      |
| 4k      | 266                 | 1.95                                     | 408              | 142                      |
| 4l      | 268                 | 1.82                                     | 405              | 137                      |
| 4m      | 274                 | 2.48                                     | 406              | 132                      |
| 4n      | 271                 | 2.32                                     | 404              | 133                      |

**Table 4. Photophysical data of all compounds (4a–4n) in methanol**

**General Procedure for Synthesis of 5-(4-Methoxyphenyl)-5H-spiro [diindenol[1,2-b:2',1'-elpyridine-11,3'-indoline]-2',10,12-trione (4a)**

A mixture of indan-1,3-dione (2.0 mmol), isatin (1.0 mmol), 4-methoxyaniline (1.0 mmol), and PEG-OSO$_3$H (30 mol%, 1.8 g) as catalyst in water (10 mL) or [NMP]H$_2$PO$_4$ (30 mol%) was placed in a 50-mL, round-bottomed flask. The mixture was heated in an oil bath maintained at 80°C or in an ultrasonic bath at 40°C for
5–15 min respectively. After completion of reaction as monitored by thin-layer chromatography (TLC) using ethyl acetate–petroleum ether (30:70, v/v) as eluent, the reaction mixture was allowed to cool to room temperature. The precipitate formed was collected by filtration at pump, washed with water followed by cold ethanol, and dried to yield pure 5-(4-methoxyphenyl)-5H-spiro[diindeno[1,2-b:2′,1′-e]pyridine-11,3′-indoline]-2′,10,12-trione (4a) as red solid in good yields. 

Mp > 300 °C (ethanol); 1H NMR (400 MHz, DMSO, d6) δH: 10.62 (1H, s, NH), 8.04–8.01 (1H, m, Ar-H), 7.83–7.80 (1H, m, Ar-H), 7.30–7.23 (6H, m, Ar-H), 7.19–7.14 (3H, m, Ar-H), 6.89–6.84 (2H, m, Ar-H), 5.61 (2H, d, 3JHH = 7.2 Hz, ArH), 3.95 (3H, s, OCH3); 13C NMR (100 MHz, DMSO, d6) δC: 189.7, 177.7, 161.0, 156.3, 142.1, 136.2, 134.4, 132.5, 132.4, 131.1, 130.9, 130.3, 128.6, 124.5, 121.6, 121.5, 115.3, 115.2, 113.4, 111.4, 109.1, 55.8.

FUNDING

J. S. and H. S. thank the University Grants Commission, New Delhi, India, for the Junior and Senior Research Fellowships.

SUPPLEMENTARY MATERIAL

Supplemental data for this article can be accessed on the publisher’s website.

REFERENCES

1. Coquerel, Y.; Boddaert, T.; Presset, M.; Mailhol, D.; Rodriguez, J. In Ideas in Chemistry and Molecular Sciences: Advances in Synthetic Chemistry; B. Pignataro (Ed.); Weinheim, Germany: Wiley-VCH, 2010; pp. 187–202.
2. Hallett, J. P.; Welton, T. Chem. Rev. 2011, 111, 3508–3576.
3. (a) Davis Jr., J. H. Chem. Lett. 2004, 33, 1072–1077; (b) Khurana, J. M.; Lumb, A.; Chaudhary, A.; Nand, B. Synth. Commun. 2013, 43, 2147–2154.
4. (a) Siddiqui, Z. N.; Khan, T. Tetrahedron Lett. 2013, 54, 3759–3764; (b) Shekouhy, M. Catal. Sci. Technol. 2012, 2, 1010–1020; (c) Paul, S.; Das, A. R. Tetrahedron Lett. 2013, 54, 1149–1154.
5. (a) Debnath, K.; Pathak, S.; Pramanik, A. Tetrahedron Lett. 2013, 54, 4110–4115; (b) Wang, X. C.; Zhang, L. J.; Zhang, Z.; Quan, Z. J. Chin. Chem. Lett. 2012, 23, 423–426 (c) Hasaninejad, A.; Kazerooni, M. R.; Zare, A. Catal. Today 2012, 196, 148–155; (d) Quan, Z. J.; Da, Y. X.; Zhang, Z.; Wang, X. C. Catal. Commun. 2009, 10, 1146–1148.
6. M. R.; Javidnia, K.; Hemmateenejad, B.; Azarpira, A.; Amirghofran, Z. Bioorg. Med. Chem. 2004, 12, 2529–2536.
7. Heintzelman, G. R.; Averill, K. M.; Dodd, J. H. PCT Int. Appl. WO Patent 2002085894 A1 20021031, 2002.
8. Heintzelman, G. R.; Averill, K. M.; Dodd, J. H.; Demarest, K. T.; Tang, Y.; Jackson, P. F. Pat. Appl. Publ. U.S. Patent 2004082578 A1 20040429, 2004.
9. Cooper, K.; Fray, M. J.; Cross, P. E.; Richardson, K. Eur. Pat. Appl. EP 299727 A1 Patent 19890118, 1989.
10. Vigante, B.; Ozols, J.; Sileniece, G.; Kimenis, A.; Duburs, G. U.S.S.R. SU Patent 794006 19810107, 1989.
11. Safak, C.; Simsek, R.; Altas, Y.; Boyd, S.; Erol, K. Boll. Chim. Farm. 1997, 136, 665–669.
12. Brandes, A.; Loegers, M.; Schmidt, G.; Angerbauer, R.; Schmeck, C.; Bremm, K. D.; Bischoff, H.; Schmidt, D.; Schuhmacher, J. *Ger. Offen.* DE Patent 19627430 A1 19980115, 1998.

13. Heintzelman, G. R.; Averill, K. M.; Dodd, J. H.; Demarest, K. T.; Tang, Y.; Jackson, P. F. *PCT Int. Appl.* WO Patent 2003088963 A1 20031030, 2003.

14. (a) Sindhu, J.; Singh, H.; Khurana, J. M.; Sharma, C.; Aneja, K. R. *Aust. J. Chem.* 2013, 66, 710–717; (b) Singh, H.; Sindhu, J.; Khurana, J. M.; Sharma, C.; Aneja, K. R. *Aust. J. Chem.* 2013, 66, 1088–1096; (c) Singh, H.; Sindhu, J.; Khurana, J. M. *J. Iran. Chem. Soc.* 2013, 10, 883–888; (d) Singh, H.; Sindhu, J.; Khurana, J. M. *RSC Adv.* 2013, 3, 22360–22366; (e) Khurana, J. M.; Chaudhary, A.; Lumb, A.; Nand, B. *Green Chem.* 2012, 14, 2321–2327; (f) Singh, H.; Sindhu, J.; Khurana, J. M.; Sharma, C.; Aneja, K. R. *RSC Adv.* 2014, 4, 5915–5926; (g) Singh, H.; Sindhu, J.; Khurana, J. M. *Sens. Actuators B: Chem.* 2014, 192, 536–542.

15. Ghahremanzadeh, R.; Shakibaei, G. I.; Ahadi, S.; Bazgir, A. *J. Comb. Chem.* 2010, 12, 191–194.

16. (a) Debnath, K.; Pathak, S.; Pramanik, A. *Tetrahedron Lett.* 2013, 54, 4110–4115; (b) Guo, H.; Li, X.; Wang, J. L.; Jin, X. H.; Lin, X. F. *Tetrahedron* 2010, 66, 8300–8303.