
**Journal of Sulfur Chemistry**
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713926081

# Polyethylene glycol as an efficient and reusable solvent medium for the synthesis of thiohydantoins using $K_2CO_3$ as catalyst

Mazaahir Kidwai[a]; Anwar Jahan[a]; Divya Bhatnagar[a]
[a] Green Chemistry Research Laboratory, Department of Chemistry, University of Delhi, Delhi, India

Online publication date: 26 May 2010

**To cite this Article** Kidwai, Mazaahir , Jahan, Anwar and Bhatnagar, Divya(2010) 'Polyethylene glycol as an efficient and reusable solvent medium for the synthesis of thiohydantoins using $K_2CO_3$ as catalyst', Journal of Sulfur Chemistry, 31: 3, 161 — 167
**To link to this Article: DOI:** 10.1080/17415991003777409
**URL:** http://dx.doi.org/10.1080/17415991003777409

*Journal of Sulfur Chemistry*
Vol. 31, No. 3, June 2010, 161–167

Taylor & Francis
Taylor & Francis Group

# Polyethylene glycol as an efficient and reusable solvent medium for the synthesis of thiohydantoins using $K_2CO_3$ as catalyst

Mazaahir Kidwai*, Anwar Jahan and Divya Bhatnagar

*Green Chemistry Research Laboratory, Department of Chemistry, University of Delhi, Delhi-110007, India*

(*Received 6 February 2010; final version received 14 March 2010*)

Polyethylene glycol was found to be an inexpensive, non-toxic, recyclable and an effective medium for the synthesis of thiohydantoin derivatives in the presence of $K_2CO_3$ as the catalyst. The procedure is operationally simple and environmentally benign.

**Keywords:** green synthesis; $K_2CO_3$; PEG; thiohydantoins; recyclability



## 1. Introduction

The synthesis and exploitation of small organic molecules that have improved pharmacological properties over peptides have become a major focal point for pharmaceutical compounds in search of leads utilizing automated high-throughput biological screening. Recently, heterocyclic compounds bearing one or more nitrogen and sulfur atoms have received much attention in organic synthesis (*1*). In this context, the substituted thiohydantoin-based scaffolds have found attention in medicinal and agricultural chemistry because they display a fascinating array of biological properties (*2*), for example, 5,5-diphenyl-2-thiohydantoin (DPTH) (**I**) has been studied in respect of inhibition against thyroxin-stimulated response in mitochondria (*3*). The other reported derivatives of thiohydantoin, such as 5-arylidene-2-thiohydantoin (**II**), have been reported to have an antimicrobial activity (*4*), and 5-(-2-phenyl-3-indolal)-2-thiohydantoin (PIT) (**III**) has been evaluated as an anticancer agent (*5*), whereas glucopyranosylidene spiro-thiohydantoin (**IV**) has been reported as an efficient inhibitor of muscles and liver glycogen phosphorylases (Figure 1) (*6, 7*).

The classical method for the synthesis of thiohydantoin is the reaction of isothiocyanate with N-substituted $\alpha$-amino acids or their esters (*8, 9*). Numerous versions for the synthesis of thiohydantoin derivatives have been developed in the past including solid-phase synthesis (*10*), microwave-assisted synthesis (*11*), multi-component reaction (*12*) and fluorous synthesis (*13*). These methods suffer mainly from the drawbacks such as lack of versatility, use of expensive and corrosive reagents and solvents, long reaction times and tedious workup procedures.

*Corresponding author. Email: kidwai.chemistry@gmail.com

ISSN 1741-5993 print/ISSN 1741-6000 online

DOI: 10.1080/17415991003777409
http://www.informaworld.com

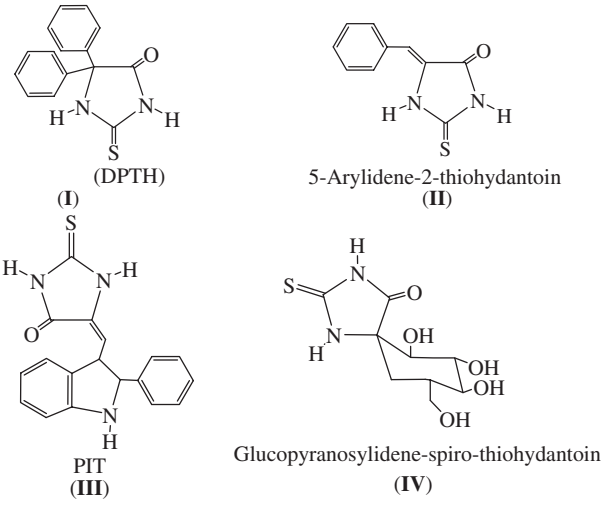



Figure 1. Reported examples of biologically active thiohydantoins.



The environment calls on the entire research enterprise to define long-term strategies for clean chemistry and to reduce the amount of pollutants produced for the reduction of ecologically unsafe chemicals. There is a need to develop an environmentally-friendly method for the synthesis of thiohydantoins. Indeed, polyethylene glycol (PEG) is recognized as an attractive recyclable green solvent medium for various organic reactions.

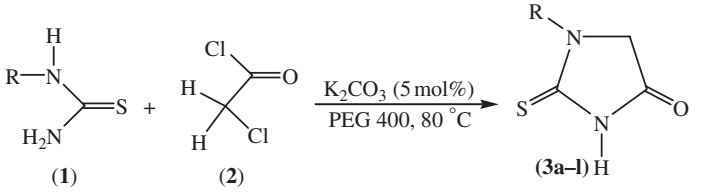
Our interest in PEG as a green reaction medium was provoked by several factors, such as thermal stability, commercial availability, non-volatility, immiscibility with a number of organic solvents and recyclability (*14*). Further, PEG is inexpensive, completely non-halogenated, easily degradable and possesses low toxicity (*15*). PEG could be used as a complexing solvent with unique properties of cationic coordination ability. On the basis of the complexing properties of PEG with $K_2CO_3$, we chose $K_2CO_3$ as the catalyst in the synthesis of thiohydantoin. Potassium carbonate has been used to provide mild basic conditions for many organic reactions (*16*). The various reported reactions of $K_2CO_3$ not only show its essentiality for a particular reaction but also depict its other characteristics, such as solubility in water, mild character, ecofriendly, non-toxic reaction, low cost and easy availability (*17, 18*). Thus, $K_2CO_3$ provides mild basic conditions for the synthesis of thiohydantoins by easy separation with water.

The versatility of $K_2CO_3$ as a catalyst and the environmentally benign nature of PEG encouraged us to couple them together and study their utility for the scope of this reaction and its utility as a new synthetic approach (*19*). We also describe herein a facile and cost-effective method for the synthesis of thiohydantoin derivatives using PEG as a solvent system and the abundantly available $K_2CO_3$ as an inexpensive catalyst. It is also noteworthy to mention that our environmentally benign reaction does not generate any toxic waste products.

## 2. Results and discussion

Initially, to verify the efficient catalytic behavior of $K_2CO_3$, a controlled reaction was performed for the synthesis of thiohydantoin derivatives by the condensation reaction of monosubstituted thiourea (1 mmol) and chloroacetylchloride (1 mmol) in PEG (3 ml) under oil bath conditions. In the absence of $K_2CO_3$, the reaction did not occur even after 8 h at 80 °C. However, under the same

condition by employing 5 mol% of $K_2CO_3$, an excellent yield (98%) of the product was obtained within 2 h of reaction time (Scheme 1).




Scheme 1. $K_2CO_3$-catalyzed synthesis of thiohydantoins.

The factors in the synthesis of thiohydantoin derivatives are often complicated (*20–22*), so a screening for optimal conditions is necessary. We chose monosubstituted thiourea and chloroacetylchloride to examine several common solvents and base catalyst at 80 °C under 5 mol% loading of the catalyst (Table 1).

The nature of reaction media has an important role in the synthesis of thiohydantoins in the presence of $K_2CO_3$ (5 mol%). The yields of thiohydantoin derivatives were excellent in polar solvents such as PEG, $CH_3OH$ and DMF, whereas the yields were much lower in less-polar solvents such as toluene, THF and dixoane (Entries 10–12). We also used various PEGs with molecular weights 200, 400, 600 and 800, but the best result was obtained with PEG 400. As the molecular weight of PEGs increases, viscosity increase was observed, which led to a highly viscous reaction mixture and provided a comparatively low yield of the product. The base catalyst also affected the yields significantly with PEG. $K_2CO_3$ gave comparable yields that were better than $Na_2CO_3$, NaOH, KOH, $K_3PO_4$ and NaOAc. Thus, we decided to use solvent PEG 400 with $K_2CO_3$ as a base catalyst for subsequent investigations (Table 1).

Encouraged by these remarkable results, we screened a variety of monosubstituted thiourea including electron-withdrawing and electron-donating groups. The monosubstituted thiourea having electron-donating groups gave thiohydantoins in good yields. However, in the case of electron-withdrawing groups, relatively low yields were obtained. In addition, we found that a



Table 1. Effect of solvent and catalyst on the synthesis of thiohydantoin derivatives.[a]

| Entry | Solvent | Catalyst | Time (h) | Yield (%)[b] |
|---|---|---|---|---|
| 1 | PEG 400 | Catalyst free | 8 | – |
| 2 | PEG 400 | $K_2CO_3$ | 2 | 98 |
| 3 | PEG 600 | $K_2CO_3$ | 2 | 95 |
| 4 | PEG 800 | $K_2CO_3$ | 2 | 90 |
| 5 | PEG 400 | $K_3PO_4$ | 3 | 70 |
| 6 | PEG 400 | NaOAc | 4 | 56 |
| 7 | PEG 400 | NaOH | 5 | 63 |
| 8 | PEG 200 | $K_2CO_3$ | 4 | 92 |
| 9 | PEG 400 | KOH | 4 | 90 |
| 10 | Methanol | $K_3PO_4$ | 4 | 60 |
| 11 | Methanol | $K_2CO_3$ | 3 | 85 |
| 12 | DMF | $K_2CO_3$ | 3 | 88 |
| 13 | Toluene | $K_2CO_3$ | 5 | 50 |
| 14 | THF | $K_2CO_3$ | 5 | 55 |
| 15 | Dioxane | $K_2CO_3$ | 4 | 48 |

Notes: [a]Reaction conditions: monosubstituted thiourea (1 mmol), chloroacetylchloride (1 mmol); solvent, PEG 400; catalyst, $K_2CO_3$; temperature, 80 °C. [b]Isolated yields.

Table 2. Synthesis of library of thiohydantoin derivatives using $K_2CO_3$ as a catalyst.[a]

| Entry | R | Product | Time (h) | Yield (%)[b] |
|---|---|---|---|---|
| 1 | Ph | **3a** | 2 | 98 |
| 2 | 4-$CH_3C_6H_5$ | **3b** | 2 | 95 |
| 3 | 4-$C_2H_5C_6H_5$ | **3c** | 2 | 94 |
| 4 | 4-$BrC_6H_5$ | **3d** | 2 | 90 |
| 5 | 4-$ClC_6H_5$ | **3e** | 2 | 88 |
| 6 | 4-$OCH_3C_6H_5$ | **3f** | 2 | 92 |
| 7 | 4-$OHC_6H_5$ | **3g** | 2 | 91 |
| 8 | 4-$NO_2C_6H_5$ | **3h** | 2 | 78 |
| 9 | 2-$CH_3C_6H_5$ | **3i** | 2 | 96 |
| 10 | 2-$OCH_3C_6H_5$ | **3j** | 2 | 91 |
| 11 | 1-Naphthyl | **3k** | 2 | 93 |
| 12 | 2-Naphthyl | **3l** | 2 | 92 |

Notes: [a]Reaction conditions: monosubstituted thiourea (1 mmol), chloroacetylchloride (1 mmol); solvent PEG 400; catalyst $K_2CO_3$; temperature 80 °C. [b]Isolated yields.



strong electron-withdrawing functionality such as $-NO_2$ on the monosubstituted thiourea dramatically decreased the reactivity, cyclization became difficult and low amount of yield was observed (Table 2).

Catalyst concentration plays a major role in the optimization of the product yield. By increasing the molar concentration of potassium carbonate from 5 to 15 mol%, it was observed that increased loading of the catalyst from 5 to 15 mol% gave almost the same yield of the product. But when we used 2–4 mol% of the catalyst, less amount of yield was obtained. It appears that the concentration of 5 mol% of potassium carbonate ($K_2CO_3$) is the suitable choice for an optimum yield of thiohydantoins (Table 3).

To test the solubility and reusability of PEG as a solvent, after the reaction, the reaction mixture was extracted with solvent ether, since PEG is immiscible with solvent ether. To the recovered crude PEG (≈3 ml), distilled ethanol (10 ml) was added and passed through a very short pad of silica gel and activated charcoal. The colorless organic layer was evaporated under reduced pressure. PEG was further dried under high vacuum overnight and used for the next run. The recovered PEG was used with a little loss of reactivity for three cycles (Table 4).

PEGs can be regarded as open-chain crown ethers as they are able to form complexes with alkaline and alkaline-earth cations in protic and aprotic solvents (*23*). We postulated that in the PEG/$K_2CO_3$ system, the $CO_3^{2-}$ anion could be brought into solution through the coordination of the cationic center of $K_2CO_3$ with the oxygen atom of PEG (*24*). Thus, the reaction of the $CO_3^{2-}$ anion with monosubstituted thiourea was elevated by enhancing the nucleophilicity of nitrogen for addition to chloroacetylchloride.

Table 3. Optimization of the concentration of potassium carbonate for the synthesis of thiohydantoins.[a]

| Entry | Catalysts | Concentration (mol%) | Time (h) | Yield (%)[b] |
|---|---|---|---|---|
| 1 | $K_2CO_3$ | 2 | 6 | 65 |
| 2 | $K_2CO_3$ | 4 | 5 | 85 |
| 3 | $K_2CO_3$ | 5 | 2 | 98 |
| 4 | $K_2CO_3$ | 10 | 2 | 95 |
| 5 | $K_2CO_3$ | 15 | 2 | 92 |

Notes: [a]Reaction conditions: thiourea (1 mmol), chloroacetylchloride (1 mmol); solvent, PEG 400; catalyst, $K_2CO_3$; temperature, 80 °C. [b]Isolated yields.

Table 4. Recyclability of PEG 400.[a]

| No. of cycles[a] | Fresh | Run 1 | Run 2 | Run 3 |
|---|---|---|---|---|
| Yield (%)[b] | 98 | 98 | 97 | 95 |
| Time (h) | 2 | 2 | 2 | 2 |

Notes: [a]Reaction conditions: thiourea (1 mmol), chloroacetylchloride (1 mmol); solvent, PEG 400; catalyst, $K_2CO_3$; temperature, 80 °C. [b]Isolated yields.

Ultimately, this methodology offers competitive advantages, and recyclability of the solvent PEG (PEG 400), which could be used without further purification. It also required less loading of the catalyst and has broad substrate applicability with ease and improved yields.

## 3. Conclusions

In conclusion, we have successfully developed a simple, efficient and environmentally benign reaction medium for the synthesis of thiohydantoin derivatives using $K_2CO_3$ as a catalyst. Here, PEG acts as a clean solvent medium by significantly enhancing the intramolecular cyclization. Our protocol is a practical approach which uses PEG as a readily commercially available, low cost, reusable and non-ionic liquid solvent. Further studies to develop new clean methodology on the synthetic application of PEG and potassium carbonate for biologically active compounds are in progress and will be reported in due course.



## 4. Experimental

### 4.1. *General*

The materials were purchased from Sigma-Aldrich and Merck and were used without any purification. All reactions and the purity of thiohydantoin derivatives were monitored by thin layer chromatography (TLC) using aluminum plates coated with silica gel (Merck) using hexane–ethylacetate (80:20) as an eluent. The isolated products were further purified by column chromatography using silica gel (100–200 mesh) purchased from Sisco Research Laboratories Pvt. Ltd, Mumbai, India. $^1$H NMR spectra were recorded on a Bruker Avance Spectrospin 300 (300 MHz). All NMR samples were run in $CDCl_3$ and chemical shifts are expressed as $\delta$ relative to internal TMS. Infrared (IR) spectra were obtained on a Perkin Elmer FT-IR spectrometer spectrum-2000 using potassium bromide pellets or liquid films between two sodium chloride pellets. ESI-MS mass spectra were recorded on a Waters LCT Micromass. The temperature of the reaction mixture was measured through a non-contact IR thermometer (AZ, Mini Gun Type, Model 8868).

### 4.2. *General procedure for the preparation of thiohydantoin derivatives*

A mixture of monosubstituted thiourea (1 mmol) and chloroacetylchloride (1 mmol), $K_2CO_3$ (5 mol%) and PEG 400 (3 ml) were added to a 50 ml round-bottom flask and stirred at 80 °C for the desired time (Table 1) during which the complete consumption of the starting material was judged by means of TLC. After completion of the reaction, the reaction mixture was allowed to return to room temperature and diluted with diethyl ether (10 ml) (PEG being insoluble in ether). The combined ether layer was washed with water, brine and dried over anhydrous sodium sulfate

($Na_2SO_4$) and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography with hexane–ethylacetate (80:20) as an eluent to provide the desired product. The structure of all the products was unambiguously established on the basis of their spectral analysis (IR, $^1$H NMR, $^{13}$C NMR and GC-MS mass spectral data).

### 4.3. *Spectroscopic data for synthesized thiohydantoins*

1-(Phenyl)-2-thiohydantoin (**3a**): White solid. MP: 175–177 °C (25*a*). $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 3.82$ (s, 2H), 7.22–7.34 (m, 5H), 10.02 (s, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 64.70, 126.61, 127.64, 130.28, 140.35, 173.20, 180.91$. IR (KBr) $\nu_{max}$ ($cm^{-1}$): 3271 (NH), 1675 (C=O), 1571 (N–C=S), 1183 (C=S). $m/z$ (ESI-MS, HRMS): 192.29.

1-(4-Methylphenyl)-2-thiohydantoin (**3b**): Light brown solid. MP: 180–182 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 2.37$ (s, 2H), 4.12 (s, 2H), 7.28 (d, $J = 6.8$ Hz, 2H), 7.37 (d, $J = 6.8$ Hz, 2H), 8.10 (s, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 21.21, 55.36, 128.54, 133.50, 135.56, 138.72, 169.35, 182.13$. IR (KBr) $\nu_{max}$ ($cm^{-1}$): 3261, 1714, 1521, 1174. $m/z$ (ESI-MS, HRMS): 207.68.

1-(4-Ethylphenyl)-2-thiohydantoin (**3c**): Light brown solid. MP: 195–197 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 1.97$ (s, 2H), 2.39 (s, 2H), 4.40 (s, 2H), 7.26 (d, $J = 8.10$ Hz, 2H), 7.40 (d, $J = 8.10$ Hz, 2H), 9.11 (s, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 14.9, 29.6, 54.88, 125.61, 129.96, 135.94, 138.01, 169.78, 182.64$. IR (KBr) $\nu_{max}$ ($cm^{-1}$): 3205, 1732, 1533, 1163. $m/z$ (ESI-MS, HRMS): 220.52.

1-(4-Bromophenyl)-2-thiohydantoin (**3d**): Dark brown solid. MP: 142–144 °C. (300 MHz, $CDCl_3$): $\delta = 7.18$ (d, $J = 8.40$ Hz, 2H), 7.35 (d, $J = 8.70$ Hz, 2H), 9.37 (s, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 50.83, 124.72, 132.60, 140.05, 141.39, 173.24, 180.90$. IR (KBr) $\nu_{max}$ ($cm^{-1}$): 3238, 1702, 1542, 1101. $m/z$ (ESI-MS, HRMS): 272.62.

1-(4-Chlorophenyl)-2-thiohydantoin (**3e**): White solid. MP: 151–153 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 4.21$ (s, 2H), 7.04 (d, $J = 7.51$ Hz, 2H), 7.44 (d, $J = 7.78$ Hz, 2H), 9.27 (s, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 53.17, 127.58, 130.97, 134.24, 138.03, 176.85, 181.17$ IR (KBr) $\nu_{max}$ ($cm^{-1}$): 3262, 1721, 1530, 1148. $m/z$ (ESI-MS, HRMS): 226.32.

1-(4-Methoxyphenyl)-2-thiohydantoin (**3f**): White solid. MP: 190–192 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 3.81$ (s, 2H), 4.10 (s, 2H), 7.12 (d, $J = 8.24$ Hz, 2H), 7.26 (d, $J = 8.16$ Hz, 2H), 9.16 (s, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 48.44, 55.42, 114.39, 127.13, 132.66, 158.72, 166.12, 174.15$. IR (KBr) $\nu_{max}$ ($cm^{-1}$): 3274, 1708, 1520, 1164. $m/z$ (ESI-MS, HRMS): 223.05.

1-(4-Hydroxyphenyl)-2-thiohydantoin (**3g**): Dark brown solid. MP: 156–158 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 4.06$ (s, 2H), 5.25 (s, 1H), 6.93 (d, $J = 8.11$ Hz, 2H), 7.10 (d, $J = 8.70$ Hz, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 58.34, 117.0, 128.50, 132.21, 155.12, 174.10, 183.31$. IR (KBr) $\nu_{max}$ ($cm^{-1}$): 3126, 1739, 1514, 1158. $m/z$ (ESI-MS, HRMS): 209.87.

1-(4-Nitrophenyl)-2-thiohydantoin (**3h**): Yellow solid. MP: 120–122 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 4.28$ (s, 2H), 6.97 (d, $J = 7.86$ Hz, 2H), 7.05 (d, $J = 7.14$ Hz, 2H), 8.93 (s, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 64.63, 125.64, 135.41, 140.93, 146.0, 173.33, 183.82$. IR (KBr) $\nu_{max}$ ($cm^{-1}$): 3268, 1753, 1507, 1172. $m/z$ (ESI-MS, HRMS): 237.57.

1-(2-Methylphenyl)-2-thiohydantoin (**3i**): Light brown solid. MP: 149–150 °C (25*b*). $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 2.42$ (s, 3H), 4.60 (s, 2H), 6.92–7.18 (m, 4H), 9.13 (s, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 21.92, 58.31, 122.51, 127.16, 129.07, 130.71, 137.45, 138.81, 170.19, 181.69$. IR (KBr) $\nu_{max}$ ($cm^{-1}$): 3238, 1783, 1527, 1132. $m/z$ (ESI-MS, HRMS): 207.23.

1-(2-Methoxyphenyl)-2-thiohydantoin (**3j**): White solid. MP: 163–165 °C. $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 3.86$ (s, 3H), 4.61 (s, 2H), 6.88–7.10 (m, 4H), 8.98 (s, 1H). $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 55.54, 55.60, 114.63, 121.34, 122.71, 127.23, 128.46, 159.15, 169.28, 182.61$. IR (KBr) $\nu_{max}$ ($cm^{-1}$): 3242, 1710, 1516, 1168. $m/z$ (ESI-MS, HRMS): 222.11.

1-(1-Naphthyl)-2-thiohydantoin (**3k**): White solid. MP: 176–178 °C (25*c*). $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 2.39$ (s, 3H), 4.59 (s, 2H), 7.42–7.78 (m, 7H), 9.16 (s, 1H). $^{13}$C NMR (75 MHz,

$CDCl_3$): $\delta = 55.48$, 120.71, 123.13, 125.0, 126.89, 127.93, 127.51, 133.17, 139.80, 174.67, 182.85. IR (KBr) $\nu_{max}$ ($cm^{-1}$): 3202, 1740, 1588, 1170. $m/z$ (ESI-MS, HRMS): 243.71.

1-(2-Naphthyl)-2-thiohydantoin (**3l**): White solid. MP: 200–202 °C. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta = 2.30$ (s, 3H), 4.01 (s, 2H), 7.39–7.65 (m, 7H), 9.16 (s, 1H). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta = 55.36, 106.0, 118.31, 121.15, 124.37, 124.93, 126.91, 127.62, 129.0, 133.09, 138.13$, 172.55, 183.15. IR (KBr) $\nu_{max}$ ($cm^{-1}$): 3187, 1772, 1541, 1157. $m/z$ (ESI-MS, HRMS): 244.03.

## Acknowledgements

Anwar Jahan and Divya Bhatnagar would like to thank the University Grants Commission (UGC), New Delhi, India, for granting a Junior Research Fellowship.

## References

(1) (a) Kidwai, M.; Bhatnagar, D.; Mothsra, P.; Singh, A.K.; Dey, S.; *J. Sulfur Chem.* **2009,** *30,* 29–36; (b) Kidwai, M.; Bansal, V.; Thakur, R. *J. Sulfur Chem.* **2006,** *27,* 57–63; (c) Kidwai, M.; Mothsra, P. *J. Sulfur Chem.* **2007,** *28,* 149–153.
(2) Teng, X.; Degterev, A.; Jagtap, P.; Xing, X.; Choi, S.; Denu, R.; Yuan, J.; Cuny, G.D. *Bioorg. Med. Chem. Lett.* **2005,** *15,* 5039–5044.
(3) Knoefel, P.K.; Lehmann, G. *J. Pharmacol. Exp. Ther.* **1942,** *76,* 194–201.
(4) Kiec-Kononowicz, K.; Szymanska, E. *Il Farmaco* **2002,** *57,* 909–916.
(5) Suzen, S.; Buyukbingol, E. *Il Farmaco* **2000,** *55,* 246–248.
(6) Kuang, R.; Epp, J.B.; Ruan, S.; Chong, L.S.; Venkataraman, R.; Tu, J.; He, S.; Truong, T.M.; Groutas, W.C. *Bioorg. Med. Chem.* **2008,** *8,* 1005–1016.
(7) He, S.; Kuang, R.; Venkataraman, R.; Tu, J.; Truong, T.M.; Chan, H.T.; Groutas, W.C. *Bioorg. Med. Chem.* **2000,** *8,* 1713–1717.
(8) Elokdah, H.; Sulkowsk, T.S.; Abou-Gharbia, M.; Butera, J.A; Chai, S.Y.; McFarlane, G.R.; Mckean, M.L.; Babiak, J.L.; Adelman, S.J.; Quinet, E.M. *J. Med. Chem.* **2004,** *47,* 681–695.
(9) Dutcher, J.D.; Johnson, J.R.; Bruce, W.F. *J. Am. Chem. Soc*. **1945,** *61,* 1736–1745.
(10) Park, K.H.; Kurth, M.J. *J. Org. Chem.* **1999,** *64,* 9297–9300.
(11) Ohberg, L.; Westman, J. *Synlett* **2001,** *12,* 1893–1896.
(12) (a) Bhambi, D.; Salvi, V.K.; Jat, J.L.; Ojha, S.; Talesara, G.L. *J. Sulfur Chem.* **2007,** *2,* 155–163; (b) Porwal, S.; Kumar, R.; Maulik, P.R.; Chauhan, P.M.S. *Tetrahedron Lett.* **2006,** *47,* 5863–5866.
(13) Zhang, W.; Lu, Y. *Org. Lett*. **2003,** *5,* 2555–2558.
(14) Jorapur, Y.R.; Rajagopal, G.; Saikia, P.J.; Pal, R.R. *Tetrahedron Lett.* **2008,** *49,* 1495–1497.
(15) (a) Heldebrant, D.J.; Jessop, P.G. *J. Am. Chem. Soc.* **2003,** *125,* 5600–5601; (b) Chandrasekar, S.; Narsihmulu, Ch.; Shameem, S.S.; Reddy, N.R. *Chem. Commun.* **2003,** 1716–1717.
(16) (a) Yanagida, S.; Takahashi, K.; Okahara, M. *Bull. Chem. Soc. Jpn* **1978,** *51,* 1294–1299; (b) Yanagida, S.; Takahashi, K.; Okahara, M. *Bull. Chem. Soc. Jpn* **1978,** *51,* 3111–3120.
(17) Kazemi, F.; Massah, A.R.; Javaherian, M. *Tetrahedron* **2007,** *63,* 5083–5087.
(18) Toma, G.; Fujita, K.-I.; Yamaguchi, R. *Eur. J. Org. Chem.* **2009,** 4586–4588.
(19) Kidwai, M.; Bhatnagar, D.; Mishra, N.K.; Bansal, V. *Catal. Commun.* **2008,** *9,* 2547–2549.
(20) Gregg, B.T.; Golden, K.C.; Quinn, J.F.; Tymoshenko, D.O.; Earley, W.G.; Maynard, D.A.; Razzavo, D.A.; Rennells, W.M.; Butcher, J. *J. Comb. Chem.* **2007,** *9,* 1036–1040.
(21) Aly, Y.L. *J. Sulfur Chem.* **2007,** *28,* 371–382.
(22) Paul, S.; Gupta, M.; Gupta, R.; Loupy, A. *Synthesis* **2002,** 75–78.
(23) Yanagida, S.; Takahashi, K.; Okahama, M. *Bull. Chem. Soc. Jpn* **1978,** *51,* 1294–1299.
(24) Wang, X.; Quan, Z.; Zhang. Z. *Tetrahedron* **2007,** *63,* 8227–8233.
(25) (a) Elmore, B.T.; Toseland, P.A. *J. Am. Chem. Soc.* **1956,** *78,* 188–191; (b) Johnson, T.B.; Pfau, G.M.; Hodge, W.W. *J. Am. Chem. Soc.* **1912,** *34,* 1041–1048; (c) Sabata, B.K.; Tripathy, P.B.; Rout, M.K. *Proc. Inst. Chem. (India)* **1960,** *32,* 147–150.