Tetrahedron Letters 53 (2012) 1637–1640

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Poly(4-vinylpyridinium) hydrogensulfate catalyzed synthesis of 12-aryl-12*H*-indeno[1,2-*b*]naphtho[3,2-*e*]pyran-5,11,13-triones

Nader Ghaffari Khaligh *

Department of Chemistry, College of Science, University of Guilan, Rasht 41335-19141, Iran

ARTICLE INFO

Article history:
Received 28 September 2011
Revised 9 January 2012
Accepted 20 January 2012
Available online 28 January 2012

Keywords:
Solid acid
Indeno[1,2-*b*]naphtho[3,2-*e*]pyran-6,11,13-triones
2-Hydroxynaphthalene-1,4-dione
2*H*-Indene-1,3-dione
Solvent-free conditions
One-pot condensation

ABSTRACT

A simple and facile synthesis of 12-aryl-12*H*-indeno[1,2-*b*]naphtho[3,2-*e*]pyran-5,11,13-trione derivatives was accomplished via the one-pot condensation of 2-hydroxynaphthalene-1,4-dione, aldehydes, and 2*H*-indene-1,3-dione at 100 °C under solvent-free conditions in the presence of the solid acid catalyst, poly(4-vinylpyridinium) hydrogensulfate. This method has the advantages of high yields, clean reactions, simple methodology, and short reaction times. The catalyst could be recycled and reused four times without significant loss of activity. The structures of the novel compounds were confirmed by IR, ^{1}H NMR, and elemental analysis.

Multicomponent reactions have attracted considerable attention as they are performed without the need to isolate any intermediates. This reduces time and saves both energy and raw materials.[1] They have merits over two-component reactions including the simplicity of a one-pot procedure, possible structural variations, and the easy synthesis of complex molecules.

The synthesis of xanthenes, especially benzoxanthenes, is important in organic synthesis due to their wide range of biological and therapeutic properties such as antibacterial,[2] antiviral,[3] and anti-inflammatory.[4] They are also useful in photodynamic therapy[5] and as antagonists of the paralyzing action of zoxazolamine.[6] Furthermore, due to their interesting spectroscopic properties, they are used as dyes,[7] in laser technologies,[8] and in fluorescent materials for the visualization of biomolecules.[9] Natural compounds possessing the naphthopyran moiety have been shown to exhibit antimicrobial,[10] antitumor,[11] antifungal,[12] cytotoxic,[13] antioxidant, and 5-lipoxygenase inhibitory activities.[14] A variety of naphthopyran derivatives have been isolated and identified as natural phytochemicals.[15] Indenopyrans are 'privileged medicinal scaffolds' which are used for the development of pharmaceutical agents with various applications.[16] Compounds with this motif show a wide spectrum of pharmacological activities including antiulcer,[17] antiallergenic,[18] and antidepressant.[19]

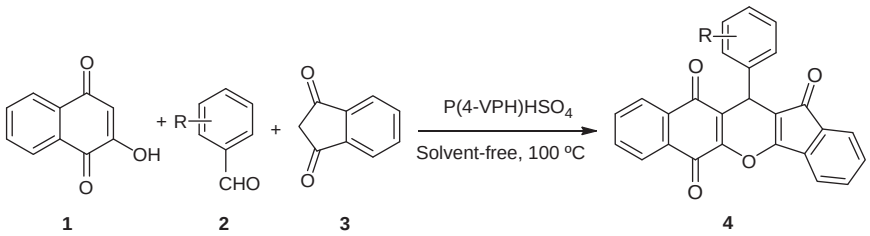
In recent years, the use of solid acidic catalysts has offered important advantages in organic synthesis, for example, operational simplicity, environmental compatibility, they are nontoxic, low cost, and the ease of isolation. As economic and ecologically benign catalysts, their applications have attracted much attention in chemistry and industry.[20–25] There were more than 100 industrial processes using over 103 solid acids as catalysts as of the end of the last century.[26] Solid acid catalysts offer unique properties that can influence the catalytic activity. However, they also have some disadvantages. Some supported catalysts undergo leaching which leads to a loss of activity.[27] Although zeolites demonstrate high activity, their reactions typically give a variety of undesired by-products due to the high temperatures employed. Ion exchange resins are limited in application because they are thermally unstable above 120 °C in the acid form.[28]

As part of continuing efforts in our laboratory toward the development of new catalysts and methods in organic synthesis,[29–31] we report a simple and efficient method for the preparation of 12-aryl-12*H*-indeno[1,2-*b*]naphtho[2,3-*e*]pyran-6,11,13-trione derivatives under solvent-free conditions in the presence of poly(4-vinylpyridinium) hydrogensulfate [P(4-VPH)HSO_4] as an efficient and versatile catalyst (Scheme 1). To the best of our knowledge, this is the first report on the synthesis of 12-aryl-12*H*-indeno[1,2-*b*]naphtho[2,3-*e*]pyran-6,11,13-triones, which may show pharmaceutical activities.

To optimize the temperature, the reaction of 2-hydroxynaphthalene-1,4-dione (**1**) (1 mmol), benzaldehyde **2** (1 mmol), and 2*H*-indene-1,3-dione (**3**) (1.1 mmol) as a model reaction was studied under solvent-free conditions using P(4-VPH)HSO_4

* Tel.: +98 2166431738; fax: +98 66934046.
E-mail addresses: ngkhaligh@guilan.ac.ir, ngkhaligh@gmail.com

0040-4039/$ - see front matter © 2012 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2012.01.092



Scheme 1. Synthesis of 12-aryl-12*H*-indeno[1,2-*b*]naphtho[2,3-*e*]pyran-5,11,13-triones.

Table 1
Temperature optimization for the synthesis of 12-aryl-12*H*-indeno[1,2-*b*]naphtho[3,2-*e*]pyran-5,11,13-triones[a]

Entry	Temp (°C)	Yield[b] (%)
1	70	54
2	90	79
3	100	88
4	120	87
5	130	84

[a] Reaction conditions: 2-hydroxynaphthalene-1,4-dione (**1**) (1 mmol), benzaldehyde **2** (1 mmol), 2*H*-indene-1,3-dione (**3**) (1.1 mmol), P(4-VPH)HSO_4 (20 mg), 90 min.
[b] Isolated yield after chromatographic purification.

Table 2
Optimization of the amount of P(4-VPH)HSO_4 for the synthesis of 12-aryl-12*H*-indeno[1,2-*b*]naphtho[3,2-*e*]pyran-5,11,13-triones[a]

Entry	Catalyst (mg)	Yield[b] (%)
1	0	0
2	10	58
3	20	88
4	30	90
5	40	89

[a] Reaction conditions: 2-hydroxynaphthalene-1,4-dione (**1**) (1 mmol), benzaldehyde **2** (1 mmol), 2*H*-indene-1,3-dione (**3**) (1.1 mmol), 100 °C, 90 min.
[b] Isolated yield after chromatographic purification.

Table 3
Synthesis of 12-aryl-12*H*-indeno[1,2-*b*]naphtho[3,2-*e*]pyran-5,11,13-triones in the presence of P(4-VPH)HSO_4[a]

Entry	R	Product	Yield[b] (%)
1	C_6H_5–	**4a**	88 (88, 86, 85, 82)[c]
2	4-Cl-C_6H_4–	**4b**	92
3	4-Br-C_6H_4–	**4c**	91
4	4-F-C_6H_4–	**4d**	93
5	4-Me-C_6H_4–	**4e**	90
6	4-MeO-C_6H_4–	**4f**	84
7	4-NO_2-C_6H_4–	**4g**	89
8	3-NO_2-C_6H_4–	**4h**	86
9	2-Cl-C_6H_4–	**4i**	90
10	3,4-Cl_2-C_6H_3–	**4j**	92
11	C_4H_9–	**4k**	–
12	C_5H_{11}–	**4l**	–

[a] Reaction conditions: 2-hydroxynaphthalene-1,4-dione (**1**) (1 mmol), aldehyde **2** (1 mmol), 2*H*-indene-1,3-dione (**3**) (1.1 mmol), P(4-VPH)HSO_4 (20 mg), 100 °C, 90 min.
[b] Isolated yield after chromatographic purification.
[c] Recycled solid acid used.

(20 mg) at different temperatures. The results are summarized in Table 1 and show that the reaction at 100 °C gave the highest yield.

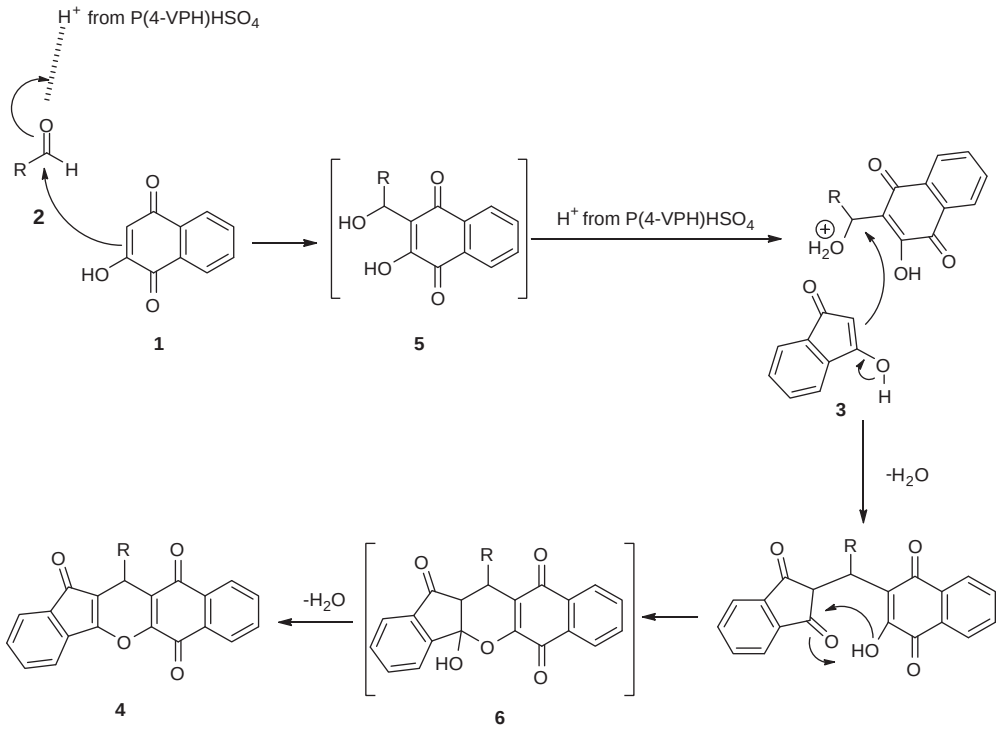
To optimize the catalyst loading, the model reaction was investigated with 10, 20, 30, 40, and 50 mg of P(4-VPH)HSO_4 at 100 °C under solvent-free conditions. The results are summarized in Table 2. A 20 mg loading of P(4-VPH)HSO_4 was found to be sufficient to promote the reaction and increased amounts of the catalyst did not lead to any significant changes in the reaction yield.

Using the optimized reaction conditions, a range of 2-aryl-12*H*-indeno[1,2-*b*]naphtho[3,2-*e*]pyran-5,11,13-triones were synthesized via the one-pot condensation of 2-hydroxynaphthalene-1,4-dione, various aldehydes, and 2*H*-indene-1,3-dione under solvent-free conditions. The reactions proceeded at 100 °C within 90 min in excellent yields using 20 mg of the solid acid catalyst P(4-VPH)HSO_4 (Table 3). Good yields were obtained using aromatic aldehydes with electron-donating or electron-withdrawing substituents. When this reaction was carried out with aliphatic aldehydes (entries 11 and 12), TLC and GC–MS analysis of the reaction mixture showed a combination of starting materials and numerous products; the yield of the expected product was very poor (<25%). It should be mentioned that when the reactions were carried out in the absence of catalyst over a long period of time (6 h) at 100 °C under solvent-free conditions, the yields of the products were low (<30%).

The structures of the products were established from their spectral properties (IR, ^{1}H NMR, mass, and elemental analysis). All the products exhibited a singlet in their ^{1}H NMR spectra at δ = 6.02–6.60 for H-12. A few of the products were partially soluble in DMSO-d_6 and a diagnostic resonance in these cases was seen in their ^{13}C NMR spectra at δ = 40.3–45.4 due to C-12). The resonances of the three non-equivalent carbonyl groups in the ^{13}C NMR spectra of the products appeared at δ = 182.3–182.6, 177.1–177.4, and 176.9–177.3. The catalyst was isolated by filtration and could be recycled up to four times without any significant loss of activity (Table 3, entry 1).

A possible mechanism for this reaction is shown in Scheme 2. A proton from P(4-VPH)HSO_4 is donated to the oxygen atom of the aldehyde. Next, the carbonyl carbon is attacked by the nucleophilic 2-hydroxynaphthalene-1,4-dione (**1**) to form intermediate **5**. Subsequent Michael addition of 2*H*-indene-1,3-dione (**3**) followed by cyclization provides cyclic hemiketal **6** which on dehydration afforded the product **4**.

In conclusion, a novel and highly efficient method for the synthesis of 12-aryl-12*H*-indeno[1,2-*b*]naphtho[3,2-*e*]pyran-5,11,13-triones derivatives has been developed. This is the first report of the synthesis of these compounds via a multicomponent condensation of 2-hydroxynaphthalene-1,4-dione, various aldehydes, and 2*H*-indene-1,3-dione in the presence of P(4-VPH)HSO_4 as a solid acid catalyst under solvent-free conditions. The current method has the advantages of a simple experimental procedure, solvent-free reaction conditions, utilization of an inexpensive and readily available catalyst, high to excellent yields of products, and reusability of the catalyst.



Scheme 2. A plausible mechanism.

Preparation of P(4-VPH)HSO_4 solid acid

H_2SO_4 (1.5 ml, 16.5 mmol, 96% standard solution) was added to a suspension of powdered poly(4-vinylpyridine) (5.0 g) in dry EtOH (25 mL). The mixture was stirred at room temperature for 8 h then EtOH was removed under reduced pressure to give the P(4-VPH)HSO_4 catalyst. Excess sulfuric acid was removed from the catalyst by washing with deionized water until the sulfate anions were absent from the eluent (checked by reaction with $BaCl_2$). The resulting solid was dried under vacuum at 65 °C for 48 h to afford P(4-VPH)HSO_4 (6.16 g) as a pale-yellow powder.[29]

Typical procedure for the preparation of 12-aryl-12*H*-indeno[1,2-*b*]naphtho[3,2-*e*]pyran-5,11,13-triones 4

To a mixture of 2-hydroxynaphthalene-1,4-dione (**1**) (1 mmol), aldehyde **2** (1 mmol), and 2*H*-indene-1,3-dione (**3**) (1.1 mmol), P(4-VPH)HSO_4 (20 mg) was added. The mixture was stirred (using a high power ball-mill mixer) at 100 °C for 90 min (Table 3). After completion of the reaction (TLC), CH_2Cl_2 (20 mL) was added, and P(4-VPH)HSO_4 was removed by filtration. The solid acid catalyst was dried at 50 °C under vacuum and then reused. The solvent was evaporated and the crude product was purified by silica gel column chromatography. Due to the very low solubility of the products we are unable to report the ^{13}C NMR data for these products.

Representative spectral data

12-Phenyl-12*H*-indeno[1,2-*b*]naphtho[3,2-*e*]pyran-5,11,13-trione (4a)

Yellow powder, mp 311–314 °C; IR (KBr) ν = 3032, 1667, 1635, 1660 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ = 5.49 (s, 1H, CH), 7.16–7.54 (m, 6H, ArH), 7.64–7.92 (m, 4H, ArH), 7.99 (d, J = 8.4 Hz, 1H, ArH), 8.12 (d, J = 7.6 Hz, 1H, ArH), 8.17 (d, J = 7.6 Hz, 1H, ArH) ppm; MS (*m/z*, %) 390 (M, 57), 313 (100). Anal. Calcd for $C_{26}H_{14}O_4$: C, 79.99; H, 3.61. Found: C, 79.64; H, 3.66.

12-(4-Nitrophenyl)-12*H*-indeno[1,2-*b*]naphtho[3,2-*e*]pyran-5,11,13-trione(4g)

Yellow powder, mp >330 °C; IR (KBr) ν = 3076, 1664, 1636, 1590 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ = 6.06 (s, 1H, CH), 7.46–7.68 (m, 6H, ArH), 7.79–7.96 (m, 4H, ArH), 8.06 (d, J = 8.8 Hz, 1H, ArH), 8.12 (d, J = 7.6 Hz, 1H, ArH) ppm; MS (*m/z*,%): 435 (35), 313 (75). Anal. Calcd for $C_{26}H_{13}NO_6$: C, 71.72; H, 3.01. Found: C, 71.68; H, 2.96.

Acknowledgment

The author is thankful to the Guilan University Research Council for partial support of this work.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2012.01.092.

References and notes

1. Devi, I.; Bhuyan, P. *Tetrahedron Lett.* **2004**, *45*, 8625–8627.
2. Hideo, T. Jpn. Tokkyo Koho JP 56005480, 1981; *Chem. Abstr.* **1981**, *95*, 80922b.
3. Lambert, R. W.; Martin, J. A.; Merrett, J. H.; Parkes, K. E. B.; Thomas, G. J. PCT Int. Appl. WO 9706178, 1997; *Chem. Abstr.* **1997**, *126*, 212377y.
4. Poupelin, J. P.; Saint-Rut, G.; Foussard-Blanpin, O.; Narcisse, G.; Uchida-Ernouf, G.; Lacroix, R. *Eur. J. Med. Chem.* **1978**, *13*, 67–71.
5. (a) Ion, R. M. *Prog. Catal.* **1997**, *2*, 55–76; (b) Ion, R. M.; Frackowiak, D.; Planner, A.; Wiktorowicz, K. *Acta Biochim. Pol.* **1998**, *45*, 833–845.
6. (a) Saint-Ruf, G.; De, A.; Hieu, H. T. *Bull. Chim. Ther.* **1972**, *7*, 83–86; (b) Saint-Ruf, G.; Hieu, H. T.; Poupelin, J. P. *Naturwissenschaften* **1975**, *62*, 584–585.

7. (a) Menchen, S. M.; Benson, S. C.; Lam, J. Y. L.; Zhen, W.; Sun, D.; Rosenblum, B. B.; Khan, S. H.; Taing, M. U.S. Patent, US6583168, 2003; *Chem. Abstr.* **2003**, *139*, 54287f.; (b) Banerjee, A.; Mukherjee, A. K. *Stain Technol.* **1981**, *56*, 83–85; (c) Reynolds, G. A.; Tuccio, S. A.; Peterson, O. G.; Specht, D. P. Ger. Offen. DE2109040, 1971; *Chem. Abstr.* **1971**, *71*, 81334c.
8. (a) Sirkeeioglu, O.; Talinli, N.; Akar, A. *J. Chem. Res.* **1995**, 502–506; (b) Ahmad, M.; King, T. A.; Ko, D. K.; Cha, B. H.; Lee, J. *J. Phys. D: Appl. Phys.* **2002**, *35*, 1473–1476.
9. Knight, C. G.; Stephens, T. *Biochem. J.* **1989**, *258*, 683–689.
10. Baker, R. A.; Tatum, J. H.; Nemec, S. *Mycopathology* **1990**, *111*, 9–15.
11. Nicolaou, K. C.; Skokotas, G.; Furaya, S.; Suemune, H.; Nicolaou, D. C. *Angew. Chem., Int. Ed.* **1990**, *29*, 1064–1067.
12. Kodama, O.; Ichikawa, H.; Akatsuka, T.; Santisopasri, V.; Kato, A.; Hayashi, Y. *J. Nat. Prod.* **1993**, *56*, 292–294.
13. Hussein, A. A.; Barberena, I.; Capson, T. L.; Kursar, T. A.; Coley, P. D.; Solis, P. N.; Gupta, M. P. *J. Nat. Prod.* **2004**, *67*, 451–453.
14. Bucar, F.; Resch, M.; Bauer, R.; Burits, M.; Knauder, E.; Schubert-Zsilavecz, M. *Pharmazie* **1998**, *53*, 875–878.
15. (a) El-Hady, S.; Bukuru, J.; Kesteleyn, B.; Van Puyvelde, L.; Van, T. N.; De Kimpe, N. *J. Nat. Prod.* **2002**, *65*, 1377–1379; (b) Brimble, M. A.; Duncalf, L. J.; Nairn, M. R. *Nat. Prod. Rep.* **1999**, *16*, 267–281; (c) Li, Y. Q.; Li, M. G.; Li, W.; Zhao, J. Y.; Ding, Z. G.; Cui, X. L.; Wen, M. L. *J. Antibiot.* **2007**, *60*, 757–761.
16. (a) Karnik, A. V.; Kulkarni, A. M.; Malviya, N. J.; Mourya, B. R.; Jadhav, B. L. *Eur. J. Med. Chem.* **2008**, *43*, 2615–2617; (b) Jin, T.-S.; Zhang, J.-S.; Liu, L.-B.; Wang, A.-Q.; Li, T.-S. *Synth. Commun.* **2006**, *36*, 2009–2015; (c) Suryavanshi, J. P.; Pai, N. R. *Indian J. Chem., Sect. B* **2006**, *45*, 1227–1230; (d) Kulkarni, A. M.; Malviya, N. J.; Karnik, A. V. *Indian J. Chem., Sect. B* **2004**, *43*, 839–842; (e) Costi, M. P.; Tondi, D.; Pecorari, P.; Rinaldi, M.; Celentano, G.; Ghelli, S.; Antolini, L.; Barlocco, D. *J. Heterocycl. Chem.* **1999**, *36*, 1043–1048.
17. Pelz, K.; Dobson, T. A. US Patent 3,904,617, 1975; *Chem. Abstr.* **2008**, *84*, 164794.
18. Goerlitzer, K.; Dehne, A.; Engler, E. *Arch. Pharm.* **1983**, *316*, 264–270.
19. Jirkovsky, I.; Humber, L. G.; Noureldin, R. *Eur. J. Med. Chem.* **1976**, *11*, 571–576.
20. Tanabe, K.; Hölderich, W. F. *Appl. Catal. A* **1999**, *181*, 399–434.
21. Cole-Hamilton, D. J. *Science* **2003**, *299*, 1702–1706.
22. Chakrabarti, A.; Sharma, M. M. *React. Polym.* **1993**, *20*, 1–45.
23. Riego, J. M.; Sedin, Z.; Zaldivar, J. M.; Marziano, N.-C.; Tortato, C. *Tetrahedron Lett.* **1996**, *37*, 513–516.
24. Turro, N. J. *Tetrahedron* **1987**, *43*, 1589–1616.
25. Zolfigol, M. A.; Chehardoli, G.; Dehghanian, M.; Niknam, K.; Shirini, F.; Khoramabadi-Zad, A. *J. Chin. Chem. Soc.* **2008**, *55*, 885–889.
26. Chehardoli, G.; Zolfigol, M. A.; Faal-Rastegar, T.; Mallakpour, S. *J. Chem. Sci.* **2009**, *121*, 441–447.
27. Weber, U. S.; Steffen, B.; Siegers, C. P. *Res. Commun. Mol. Pathol. Pharmacol.* **1998**, *99*, 193–206.
28. Patil, A. D.; Freyer, A. J.; Drake, S. E.; Haltiwanger, R. C.; Bean, M. F.; Taylor, P. B.; Caranfa, M. J.; Breen, A. L.; Bartus, H. R.; Johnson, R. K.; Hertzberg, R. P.; Westley, J. W. *J. Med. Chem.* **1993**, *36*, 4131–4138.
29. Khaligh, N. G.; Shirini, F. *J. Mol. Catal. A: Chem.* **2011**, *348*, 20–29.
30. Khaligh, N. G. *J. Mol. Catal. A: Chem.* **2011**, *349*, 63–70.
31. Khaligh, N. G. *Ultrason. Sonochem.* doi:10.1016/j.ultsonch.2011.12.004.