

Silica supported ammonium dihydrogen phosphate ($\text{NH}_4\text{H}_2\text{PO}_4/\text{SiO}_2$): A mild, reusable and highly efficient heterogeneous catalyst for the synthesis of 14-aryl-14-*H*-dibenzo[*a,j*]xanthenes

Shahnaz Rostamizadeh ^{a,*}, Ali Mohammad Amani ^a,
Gholam Hossein Mahdavinia ^{b,*}, Nasrin Shadjou ^a

^a Department of Chemistry, K.N. Toosi University of Technology, and P.O. Box 15875-4416 Tehran, Iran

^b Department of Chemistry, Islamic Azad University-Marvdasht Branch, Marvdasht, Iran

Received 24 October 2008

Abstract

Silica supported ammonium dihydrogen phosphate ($\text{NH}_4\text{H}_2\text{PO}_4/\text{SiO}_2$) is found to be a recyclable heterogeneous catalyst for a rapid and efficient synthesis of various aryl-14-*H*-dibenzo[*a,j*]xanthenes with excellent yields under solvent-free conditions. The present methodology offers several advantages such as excellent yields, simple procedure, short reaction times and milder conditions.

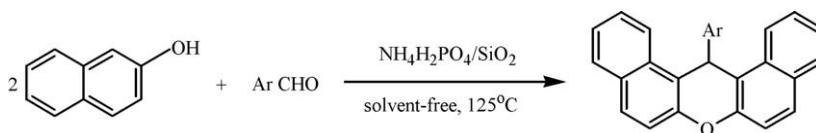
© 2009 Shahnaz Rostamizadeh. Published by Elsevier B.V. on behalf of Chinese Chemical Society. All rights reserved.

Keywords: Xanthenes; Heterogeneous catalyst; Silica supported ammonium dihydrogen phosphate

Xanthenes and benzoxanthenes are biologically important drug intermediates. They are cited as active oxygen heterocycles possessing antibacterial [1], anti-inflammatory [2], and antiviral properties [3]. These compounds are also utilized as antagonists for paralyzing action of zoxazolamine [4] and in photodynamic therapy [5]. The other useful applications of these heterocycles are as dyes [6], fluorescent materials for visualization of biomolecules [7] and in laser technologies [8]. Several polycyclic compounds containing xanthene skeleton are isolated from natural sources [9]. Xanthenes and benzoxanthenes are prepared by different methods including the reaction of aryloxymagnesium halides with triethylorthoformate [10a], cyclodehydration [10b], trapping of benzynes by phenols [10c], intramolecular phenyl carbonyl coupling reactions of benzaldehydes and acetophenones [10d], cyclization of polycyclic aryltriflate esters [10e], and cyclocondensation between 2-hydroxy aromatic aldehydes and 2-tetralone [10f]. Furthermore, 14-*H*-dibenzo [*a,j*]xanthenes and its analogues are prepared by reaction of 2-naphthol with 2-naphthol-1-methanol [11a], formamide [11b], CO [11c], and aldehydes [12]. Many of these methods, however, suffer from longer reaction times, unsatisfactory yields, harsh reaction conditions and excessive use of reagents and catalysts. It is therefore important to find more convenient methods for the preparation of these compounds.

* Corresponding authors.

E-mail addresses: shrostamizadeh@yahoo.com (S. Rostamizadeh), hmahdavinia@gmail.com (G.H. Mahdavinia).



Scheme 1.

Solid supported reagents are unique acid catalysts that have become popular over the last two decades. The activity and selectivity of these reagents are dispersed on the surface of a support and because of this, the effective surface area of the reagent is increased significantly, and hence they are expected to perform more effectively than the individual reagents [13]. Low toxicity, moisture resistance, air tolerance and low prices are other common features that the solid supported reagents are used attractive alternatives to conventional Lewis acids or metal triflates.

The leading contenders for environmentally acceptable processes are supported reagents. Use of silica-supported reagents in one-pot multi-component construction of heterocycles has received considerable importance in organic synthesis [13].

In order to expand the application of solid acids in the synthesis of heterocyclic compound, we wish to report a general, efficient and eco-friendly method for the synthesis of aryl-14-*H*-dibenzo[*a,j*]xanthenes.

No report is available in the literature describing the uses of $\text{NH}_4\text{H}_2\text{PO}_4/\text{SiO}_2$ in organic transformations but this catalyst prepared by our research group [14] and approved that this catalyst has several advantages such as low toxicity, low cost, ease of handling and high catalytic activity is a potential green catalyst. In continuation of our work to develop new and eco-friendly synthetic methodologies [15], herein we report a novel, green, facile and efficient one-pot method for the synthesis of aryl-14-*H*-dibenzo[*a,j*]xanthene derivatives catalyzed by $\text{NH}_4\text{H}_2\text{PO}_4/\text{SiO}_2$ under solvent-free condition (Scheme 1).

The experimental procedure for this reaction is remarkably simple and requires no toxic organic solvents or inert atmospheres. The reactions were carried out at 125 °C for 10–25 min by taking a 1:2 mol ratio mixture of aldehyde and β -naphthol respectively in the presence of 100 mg of $\text{NH}_4\text{H}_2\text{PO}_4/\text{SiO}_2$ under solvent-free condition.

In an initial study, for examination of the amount of catalyst in this condensation reaction, 4-bromobenzaldehyde was first reacted with β -naphthol under solvent-free condition at 125 °C in the presence of 0, 10, 20, 50, 100 and 200 mg of $\text{NH}_4\text{H}_2\text{PO}_4/\text{SiO}_2$ separately. The best results were obtained using 100 mg of catalyst (yield = 98%). Using lower amounts of catalyst resulted in lower yields, while higher amounts of catalyst did not affect the reaction time and yields and in the absence of catalyst, the yield of the product was found to be very low (Table 1).

The generality of this process was demonstrated by the wide range of substituted aryl aldehydes to synthesize the corresponding products in high to excellent yields (Table 2). The high yield transformations were carried out without any significant amounts of undesirable side products. Unlike some previously reported methods, the present method does not require toxic or toxic organic solvents to produce the aryl-14-*H*-dibenzo[*a,j*]xanthene derivatives. All the products were characterized by NMR, IR and melting point and also by comparison with the reported in literature data. A wide range of aromatic aldehydes was employed and all benzoxanthenes were obtained in high to excellent yields (Table 2) and was observed a general method that tolerates both electron-withdrawing and electron-donating constituents. The reaction conditions are mild enough not damage to moieties such as methoxy which often undergoes cleavage in strongly acidic reaction media.

Concerning the reaction mechanism, we proposed that a carbocation is initially formed; aryl-methanebisnaphthols are then formed in the second step, which then undergo dehydration to give the final product (Scheme 2).

Table 1
Comparison of the amount of catalyst and yields for the synthesis.

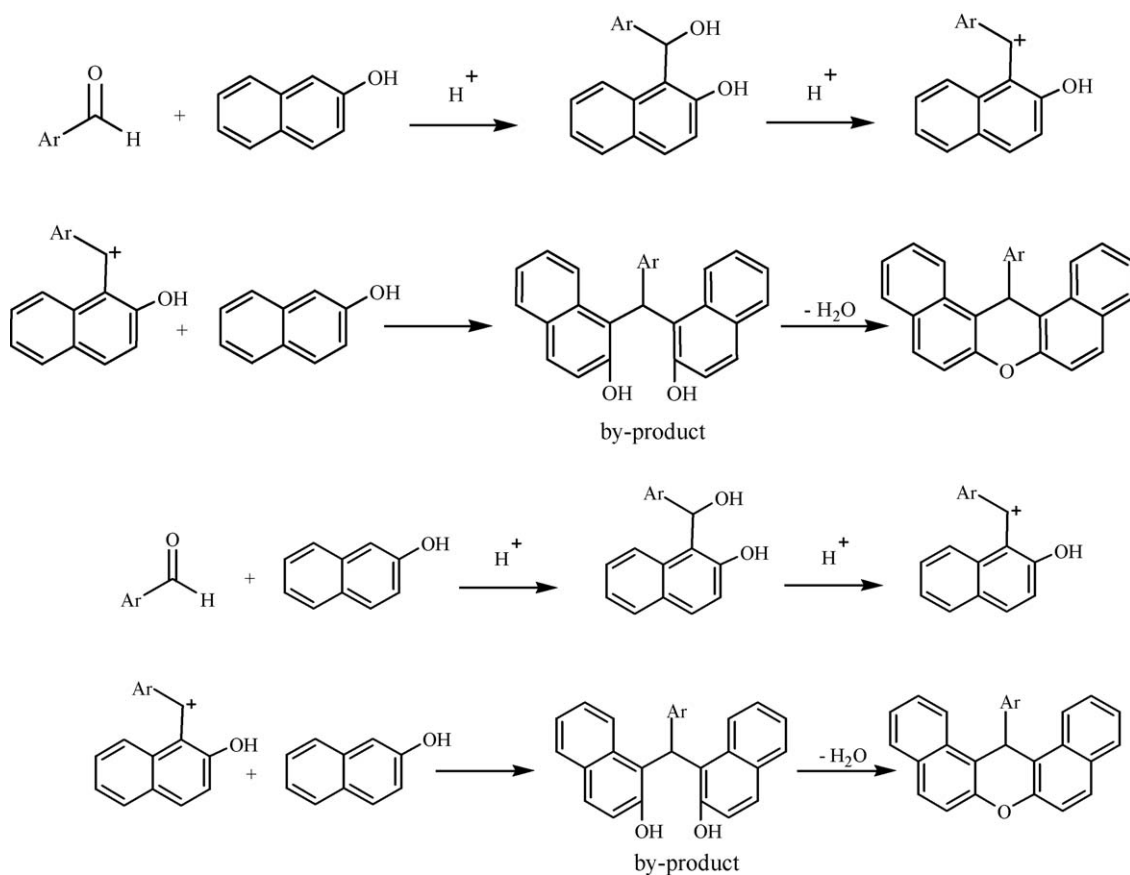
Entry	mg. of $\text{NH}_4\text{H}_2\text{PO}_4/\text{SiO}_2$	Yield (%)	Time (min)
1	0	nil	60
2	10	10	45
3	20	25	30
4	50	60	10
5	100	98	10
6	200	98	10

Table 2
 NH₄H₂PO₄/SiO₂ catalyzed synthesis of aryl-14-*H*-dibenzo [*a,j*]xanthenes.

Entry	Ar	Product	Time (min)	Yield (%)	Mp (°C)	Lit. Mp (°C)
1	C ₆ H ₅	3a	25	82	184–185	185 [12b]
2	4-BrC ₆ H ₅	3b	10	98	297–298	297 [12b]
3	3-BrC ₆ H ₅	3c	20	98	194–195	190–192[12d]
4	4-MeOC ₆ H ₅	3d	10	92	203–205	204 [12b]
5	2-MeOC ₆ H ₅	3e	20	86	258–259	260 [12b]
6	4-MeC ₆ H ₅	3f	15	90	227–229	229 [12b]
7	4-ClC ₆ H ₅	3g	20	84	289–290	289 [12b]
8	2-ClC ₆ H ₅	3h	15	73	214–216	215 [12b]
9	2,4-Cl ₂ C ₆ H ₄	3i	20	95	254–255	253–255 [12f]
10	4-NO ₂ C ₆ H ₅	3j	20	75	311–312	310 [12b]
11	3-NO ₂ C ₆ H ₅	3k	10	85	210–211	211 [12b]
12	4-FC ₆ H ₅	3l	10	85	239–240	239 [12b]
13	4-OHC ₆ H ₅	3m	15	80	135–136	140 [12e]
14	C ₆ H ₅ CH ₂	3n	20	88	178–180	178–180 [12i]

1. Experimental

Preparation of NH₄H₂PO₄/SiO₂: The catalyst was prepared by mixing silica gel (1.5 g, Merck grade 60, 230–400 mesh) with a solution of NH₄H₂PO₄ (0.6 g, 5 mmol) in distilled water (10 mL). The resulting mixture was stirred for 30 min to absorb NH₄H₂PO₄ on surface of silica gel. After removal of water in a rotary evaporator, the solid powder



Scheme 2.

Table 3

The recycling of $\text{NH}_4\text{H}_2\text{PO}_4/\text{SiO}_2$ in synthesis of 14-(4-bromophenyl)-14-*H*-dibenzo[*a,j*]xanthene.

Entry	Time (min)	Yield (%)
1	10	98
2	10	92
3	10	85
4	15	90
5	25	85

was dried at 120 °C for 2 h to 3 h under reduced pressure. The drying temperature was maintained below the decomposition temperatures of the salts.

*Synthesis of aryl-14-*H*-dibenzo[*a,j*]xanthenes. General procedure:* A mixture of aldehyde (1 mmol), 2-naphthol (2 mmol) and $\text{NH}_4\text{H}_2\text{PO}_4/\text{SiO}_2$ (100 mg) were mixed and stirred for 2 min at room temperature and then temperature was raised to 125 °C and maintained for the appropriate time (Table 2). After completion of the reaction (monitored by TLC, 2:1 petroleum ether:ethyl acetate), the reaction mixture was diluted with $\text{CHCl}_3\text{--CH}_3\text{OH}$ and the catalyst was filtrated off. The solvent was evaporated under vacuo and the resulting solid products were recrystallized from ethanol.

1.1. Selected spectral data:

Compound 3j. IR (KBr): 3068, 1589, 1511, 1456, 1340, 1237, 1106 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3 , δ ppm): 6.06(s, 1H) 7.36–8.02 (m, 14H), 8.28 (d, 2H, $J = 8.47$ Hz).

Compound 3n. IR (KBr): 3061, 3019, 1617, 1587, 1511, 1488, 1451, 1397, 1241 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3 , δ ppm): 3.27 (d, 2H, $J = 4.7$ Hz), 5.80 (t, 1H, $J = 4.7$ Hz), 6.12 (d, 2H, $J = 9.0$ Hz), 6.84–7.20 (m, 5H), 7.45–7.91 (m, 8H), 8.25 (d, 2H, $J = 9.0$ Hz).

Reusability of catalyst: Next, we investigated the reusability and recycling of $\text{NH}_4\text{H}_2\text{PO}_4/\text{SiO}_2$. At first, a mixture of *p*-bromobenzaldehyde (1 mmol), 2-naphthol (2 mmol) and $\text{NH}_4\text{H}_2\text{PO}_4/\text{SiO}_2$ (100 mg) were mixed and stirred for 2 min at room temperature and then temperature was raised to 125 °C and maintained for the appropriate time (Table 3). Then the reaction mixture was diluted with $\text{CHCl}_3\text{--CH}_3\text{OH}$ (10 mL). The catalyst was filtrated off and recovered $\text{NH}_4\text{H}_2\text{PO}_4/\text{SiO}_2$ was reused in subsequent reactions without significant decrease in activity even after five runs (Table 3).

In conclusion, we described herein ammonium dihydrogen phosphate adsorbed on silica gel ($\text{NH}_4\text{H}_2\text{PO}_4/\text{SiO}_2$) catalyzed highly efficient, one-pot, green protocol for the synthesis of aryl-14-*H*-dibenzo[*a,j*]xanthenes by the condensation of an aldehyde and β -naphthol under solvent-free conditions in excellent yields. The present methodology offers several advantages such as simple procedure, low cost, easy work-up, short reaction time and milder conditions.

References

- [1] T. Hideo, Jpn. Tokyo Koho JP 56005480, 1981 (Chem. Abstr. 95 (1981) 80922b).
- [2] J.P. Poupelin, G. Saint-Ruf, O. Foussard-Blanpin, G. Narcisse, G. Uchida-Ernouf, R. Lacroix, Eur. J. Med. Chem. 13 (1978) 67.
- [3] R.W. Lambert, J.A. Martin, J.H. Merrett, K.E.B. Parkes, G.J. Thomas, PCT Int. Appl. WO (1997) 9706178 (Chem. Abstr. 126 (1997) 212377y).
- [4] G. Saint-Ruf, A. De, H.T. Hieu, Bull. Chim. Ther 7 (1972) 83;
G. Saint-Ruf, H.T. Hieu, J.P. Poupelin, Naturwissenschaften 62 (1975) 584.
- [5] R.M. Ion, D. Frackowiak, A. Planner, K. Wiktorowicz, Acta Biochim. Pol. 45 (1998) 833.
- [6] A. Banerjee, A.K. Mukherjee, Stain. Technol 56 (1981) 83;
S.M. Menchen, S.C. Benson, J.Y.L. Lam, W. Zhen, D. Sun, B.B. Rosenblum, S.H. Khan, M. Taing, U.S. Patent, US 6583168 (2003) (Chem. Abstr. 139 (2003) 54287f).
- [7] C.G. Knight, T. Stephens, Biochem. J. 258 (1989) 683.
- [8] O. Sirkecioglu, N. Talinli, A. Akar, J. Chem. Res. (S) (1995) 502.
- [9] (a) B. Ravindranath, T.R. Seshadri, Phytochemistry 12 (1973) 2781;
(b) J. Kinjo, H. Uemura, T. Nohara, M. Yamashita, N. Marubayashi, K. Yoshihira, Tetrahedron Lett. 36 (1995) 5599.

- [10] (a) G. Casiraghi, G. Casnati, M. Cornia, *Tetrahedron Lett.* 14 (1973) 679;
(b) A. Bekaert, J. Andrieux, M. Plat, *Tetrahedron Lett.* 33 (1992) 2805;
(c) D.W. Knight, P.B. Little, *J. Chem. Soc. Perkin Trans. I* 14 (2001) 1771;
(d) C.W. Kuo, J.-M. Fang, *Synth. Commun.* 31 (2001) 877;
(e) J.-Q. Wang, R.G. Harvey, *Tetrahedron* 58 (2002) 5927;
(f) A. Jha, J. Beal, *Tetrahedron Lett.* 45 (2004) 8999.
- [11] (a) R.N. Sen, N.N. Sarkar, *J. Am. Chem. Soc.* 47 (1925) 1079;
(b) P. Papini, R. Cimmarusti, *Gazz. Chim. Ital.* 77 (1947) 142;
(c) K. Ota, T. Kito, *Bull. Chem. Soc. Jpn.* 49 (1976) 1167.
- [12] (a) J.A. Van Allan, D.D. Giannini, T.H. Whitesides, *J. Org. Chem.* 47 (1982) 820;
(b) A.R. Khosropour, M.M. Khodaei, H. Moghannian, *Synlett* (2005) 955;
(c) A. Saini, S. Kumar, J.S. Sandhu, *Synlett* (2006) 1928;
(d) B. Das, B. Ravikanth, R. Ramu, K. Laxminarayana, B. Vittal Rao, *J. Mol. Catal. A: Chem.* 255 (2006) 74;
(e) A. Khoramabadi-zad, S.A. Akbari, A. Shiri, H. Veisi, *J. Chem. Res. (S)* 5 (2005) 277;
(f) L. Nagarapu, S. Kantevvari, V.C. Mahankhali, S. Apuri, *Catal. Commun.* 8 (2007) 1173;
(g) S. Ko, C. -Fa Yao, *Tetrahedron Lett.* 47 (2006) 8827;
(h) B. Rajitha, B.S. Kumar, Y.T. Reddy, P.N. Reddy, N. Sreenivasulu, *Tetrahedron Lett.* 46 (2005) 8691;
(i) M.A. Bigdeli, M.M. Heravi, G.H. Mahdavinia, *J. Mol. Catal. A: Chem.* 275 (2007) 25;
(j) M.A. Bigdeli, M.M. Heravi, G.H. Mahdavinia, *Catal. Commun.* 8 (2007) 1595;
(k) M.A. Pasha, V.P. Jayashankara, *Bioorg. Med. Chem. Lett.* 17 (2007) 621.
- [13] A. Corma, H. Garcia, *Adv. Synth. Catal.* 348 (2006) 1391.
- [14] G.H. Mahdavinia, Sh. Rostamizadeh, A.M. Amani, Z. Emdadi, *Ultrason. Sonochem.* 16 (2008) 7.
- [15] (a) M.A. Bigdeli, S. Jafari, G.H. Mahdavinia, H. Hazarkhani, *Catal. Commun.* 8 (2007) 1641;
(b) M.A. Bigdeli, G.H. Mahdavinia, S. Jafari, H. Hazarkhani, *Catal. Commun.* 8 (2007) 2228;
(c) M.A. Bigdeli, F. Nemati, G.H. Mahdavinia, *Tetrahedron Lett.* 48 (2007) 6801;
(d) G.H. Mahdavinia, M.A. Bigdeli, M.M. Heravi, *Chin. Chem. Lett.* 19 (2008) 1171.