Dyes and Pigments 85 (2010) 133–138

Contents lists available at ScienceDirect

Dyes and Pigments

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

Short communication

The one-pot synthesis of 14-aryl or alkyl-14*H*-dibenzo[*a*,*j*]xanthenes catalyzed by P_2O_5/Al_2O_3 under microwave irradiation

Amin Zarei [a,b,*], Abdol R. Hajipour [c,d], Leila Khazdooz [e]

[a] *Department of Science, Islamic Azad University, Fasa Branch, PO Box No. 364, Fasa 7461713591, Fars, Iran*
[b] *Fasa Higher Education Complex, Fasa, 7461781189, Fars, Iran*
[c] *Department of Pharmacology, University of Wisconsin, Medical School, 1300 University Avenue, Madison, WI 53706-1532, USA*
[d] *Pharmaceutical Research Laboratory, College of Chemistry, Isfahan University of Technology, Isfahan 84156, Iran*
[e] *Department of Science, Islamic Azad University, Khorasgan Branch, Isfahan 81595-158, Iran*

ARTICLE INFO

Article history:
Received 28 April 2009
Received in revised form
18 October 2009
Accepted 21 October 2009
Available online 28 October 2009

Keywords:
Dibenzoxanthene
P_2O_5/Al_2O_3
Catalyst
2-Naphthol
Aldehyde
Microwave irradiation

ABSTRACT

A convenient and efficient procedure for the synthesis of 14-aryl or alkyl-14*H*-dibenzo[*a*,*j*]xanthenes by condensation of 2-naphthol and aldehydes in the presence of P_2O_5/Al_2O_3 is described. Both aromatic and aliphatic aldehydes react easily to afford the corresponding 14-aryl or alkyl-14*H*-dibenzo[*a*,*j*]xanthenes under microwave irradiation. This reaction was studied under different conditions; several solvents were examined for this conversion. In the terms of reaction time and yield, it was found that optimum results were obtained when reaction was carried out under microwave irradiation.

1. Introduction

Xanthenes, especially benzoxanthens, are important intermediates in organic synthesis due to their wide range of biological and therapeutic properties such as antibacterial [1], antiviral [2], anti-inflammatory activities [3] and sensitizers in photodynamic therapy for destroying the tumor cells [4]. Moreover, these heterocyclic compounds can be used as dyes [5], antagonists for the paralyzing action of zoxazolamine [6], pH-sensitive fluorescent materials for visualization of biomolecules [7] and in laser technology [8]. The reported methods for the synthesis of 14-aryl or alkyl-14*H*-dibenzo[*a*,*j*] xanthenes involve the mixing of 2-naphthol with aldehydes in the presence of an acidic catalyst such as *p*TSA [9], LiBr [10], Amberlyst-15 [11], silica sulfuric acid [12,13], molecular iodine [14,15], sulfamic acid [16], heteropoly acid [17,18], $Yb(OTf)_3$ [19], alum [20], $BF_3.SiO_2$ [21], Montmorillonite K-10 [22] and Ionic liquids [23–25].

The use of catalysts and reagents on solid supports has been developed because such reagents not only simplify purification processes but also help to prevent release of reaction residues into the environment [26]. Although there are many reports using phosphorus pentoxide as a reagent in organic reactions [27–29], P_2O_5 is difficult to handle due to its moisture sensitivity at room temperature. P_2O_5 on solid supports is easy to prepare and to handle and can be removed from the reaction mixture by simple filtration [30–35]. In continuation of our investigations on the applications of P_2O_5 on solid supports in organic synthesis [30–35], herein we report an efficient and convenient procedure for the synthesis of 14-aryl or alkyl-14*H*-dibenzo[*a*,*j*]xanthenes using catalytic amount of P_2O_5/Al_2O_3 under microwave irradiation (Fig. 1).

2. Experimental

2.1. General

All reagents were purchased from Merck and Aldrich and used without further purification. P_2O_5/Al_2O_3 was prepared according

---

* Corresponding author. Department of Science, Islamic Azad University, Fasa Branch, PO Box No. 364, Fasa 7461713591, Fars, Iran. Tel.: +98 917 1302528; fax: +98 311 2289113.
E-mail address: aj_zarei@yahoo.com (A. Zarei).

0143-7208/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.dyepig.2009.10.015

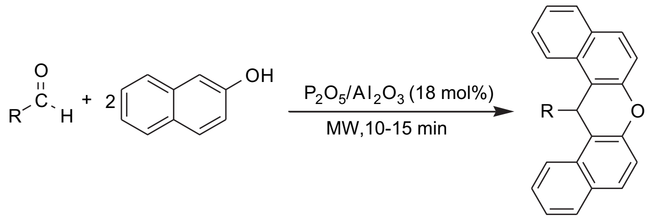


Fig. 1. . An efficient and convenient procedure for the synthesis of 14-aryl or alkyl-14*H*-dibenzo[*a*,*j*]xanthenes using catalytic amount of P_2O_5/Al_2O_3 under microwave irradiation.

to the previous work [33,35]. The reactions were irradiated by using microwave laboratory system (microsynth), model; Milestone. Melting points were measured with a Gallenkamp Apparatus and were uncorrected. IR spectra were obtained using a JASCO FT-IR-680 PLUS spectrometer. The ^1H NMR spectra were recorded on a Bruker 500 MHz spectrometer at 500 MHz with chemical shift (δ) values reported in ppm relative to an internal standard (TMS).

2.2. General procedure for the synthesis of aryl or alkyl-14H-dibenzo[a,j]xanthenes

A mixture of 2-naphthol (2 mmol), aldehyde (1 mmol), and P_2O_5/Al_2O_3 (0.05 g, 18 mol%) was taken in a sealed teflon vessel and irradiated (900 W) for 10–15 min. The progress of the reaction was monitored by TLC. After completion of the reaction, the product was extracted with chloroform and the crude product was recrystallized from ethanol to afford the pure 14-aryl or alkyl-14*H*-dibenzo[*a*,*j*] xanthene derivatives.

2.3. The spectral data of new products

Table 2, *entry 17*: ^1H NMR (400 MHz, $CDCl_3$) $\delta = 8.39$ (d, $J = 8.40$ Hz, 2 H), 7.20 (m, 4 H), 7.58 (m, 2 H), 7.48 (d, $J = 8.80$ Hz, 2 H), 7.42 (m, 4 H), 6.68 (d, $J = 8.40$ Hz, 2 H), 6.46 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) $\delta = 157.85$, 148.68, 137.36, 131.41, 131.07, 129.14, 128.79, 128.71, 126.74, 124.20, 122.68, 117.99, 117.53, 113.84, 37.09. IR (KBr): 3060, 1591, 1509, 1457, 1430, 1399, 1249, 1177, 1029, 961, 830, 808, 742 cm^{-1}. Anal. Calcd for $C_{26}H_{17}NO$: C, 86.90; H, 4.73; N, 3.90. Found: C, 86.81; H, 4.84; N, 3.82.

Table 2, entry 18: ^1H NMR (400 MHz, $CDCl_3$) $\delta = 8.68$ (d, $J = 8.40$ Hz, 2 H), 8.54 (d, $J = 4.80$ Hz, 1 H), 7.83 (d, $J = 8.80$ Hz, 4 H), 7.58 (t, $J = 7.60$ Hz, 2 H), 7.48 (d, $J = 8.80$ Hz, 2 H), 7.41 (t, $J = 7.60$ Hz, 2 H), 7.34 (m, 1 H), 7.14 (d, $J = 8.00$ Hz, 1 H), 6.91 (m, 1 H), 6.76 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) $\delta = 164.70$, 148.20, 147.74, 137.10, 131.92, 130.90, 129.18, 128.39, 126.92, 124.38, 123.99, 123.84, 121.23, 117.90, 116.00, 41.93. IR (KBr): 3044, 1620, 1588, 1513, 1458, 1429, 1407, 1255, 1244, 1147, 967, 831, 805, 773, 754 cm^{-1}. Anal. Calcd for $C_{26}H_{17}NO$: C, 86.90; H, 4.73; N, 3.90. Found: C, 86.82; H, 4.82; N, 3.84.

3. Results and discussion

Initially, to optimize the reaction conditions, we studied the reaction between 2-naphthol (2 mmol) and 4-chlorobenzaldehyde (1 mmol) as a simple model using catalytic amount of P_2O_5/Al_2O_3 (0.05 g, 18 mol%) under different conditions (Table 1). We found that the best result was obtained when the reaction was carried out under microwave irradiation (Table 1, entry 9). In the absence of P_2O_5/Al_2O_3, the reaction was carried out in low yield under the same conditions (Table 1, entry 10).

Table 1
The reaction between 2-naphthol and 4-chlorobenzaldehyde using catalytic amount of P_2O_5/Al_2O_3 under different conditions.[a]

Entry	Solvent	Conditions	Time	Yield (%)
1[b]	THF	Reflux	5 h	0
2[b]	CH_3CN	Reflux	5 h	Trace
3[b]	CH_2Cl_2	Reflux	5 h	Trace
4[b]	$ClCH_2CH_2Cl$	Reflux	5 h	20
5	Neat	60 °C	3 h	30
6	Neat	80 °C	3 h	46
7	Neat	100 °C	3 h	65
8	Neat	125 °C	1.5 h	90
9[c]	MW, neat	900 W	10 min	92
10[c,d]	MW, neat	900 W	10 min	15

[a] The yields refer to the isolated pure products.
[b] The reaction was carried out in 5 mL of solvent.
[c] The reaction was irradiated by using microwave laboratory system (microsynth), model; Milestone.
[d] The reaction was carried out in the absence of P_2O_5/Al_2O_3.

After optimization of the reaction conditions, we studied the generality of these conditions to other substrates. Using this method, different kinds of aromatic and aliphatic aldehydes were reacted with 2-naphtol to produce the corresponding 14-aryl or alkyl-14*H*-dibenzo[*a*,*j*]xanthenes under microwave irradiation (Table 2). Several aromatic aldehydes with different functional groups were subjected to the condensation reaction and the desire products were synthesized in good to high yields and short reaction time. The use of 18 mol% of P_2O_5/Al_2O_3 was sufficient to progress the reaction and an increase of the amount of catalyst did not improve the yield.

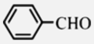
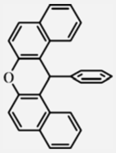
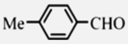
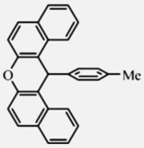
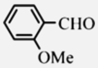
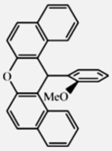
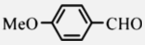
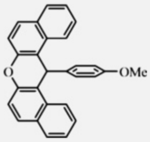
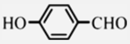
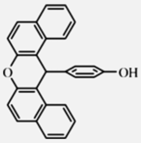
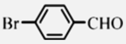
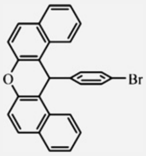
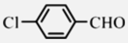
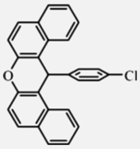
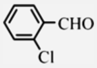
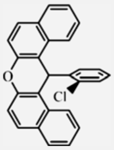
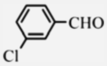
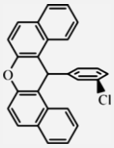
The substituted functional groups on the aromatic ring of the aldehyde affected on the yield and reaction time. In comparison with electron with-drawing groups on the aryl aldehydes, we found that the presence of electron donating groups on the aryl aldehydes decreased both the reaction rate and yield of product (Table 2, entries 3–5). We also studied the reaction between terephthaldialdehyde (1 mmol) and excess amount of 2-naphtol (4 mmol), we expected that both of the formyl groups on the aromatic ring of terephthaldialdehyde would react with 2-naphtol. However, we observed that one of the formyl groups was condensed with 2-naphtol and another group was intact because of steric effects between *o*-hydrogens of benzene ring and the xanthene ring [22] (Fig. 2).

To evaluate the role of Al_2O_3, we studied the reaction of benzaldehyde, 4-nitrobenzaldehyde, 4-methoxybenzaldehyde and butyraldehyde in the absence of Al_2O_3 using P_2O_5 alone. It was found that the yields by using P_2O_5/Al_2O_3, were greater (average, 12%) than those with P_2O_5 alone under the same conditions. In our previous work, we described the structure of P_2O_5/Al_2O_3 [35]. It was found that P_2O_5 reacted with Al_2O_3 and bonded on the surface of alumina. This structure has Brønsted and Lewis acidic sites dispersed on the surface of alumina. Furthermore, Al_2O_3 as a support may also minimize cross-contamination between the product and H_3PO_4 generated during the course of the reaction [26,35]. We think that these reasons can lead to significant improvements in its reactivity.

4. Conclusion

P_2O_5/Al_2O_3 is an inexpensive, easily available, non-corrosive and environmentally benign compound. A convenient and efficient procedure for the preparation of 14-aryl or alkyl-14*H*-dibenzo[*a*,*j*] xanthenes in good yields and short reaction times was reported in this work. The notable advantages of this methodology are operational simplicity, generality, availability of reactants, short reaction times and easy work-up.

Table 2
Synthesis of 14-aryl or alkyl-14*H*-dibenzo[*a,j*]xanthenes using catalytic amount of P_2O_5/Al_2O_3 under microwave irradiation.

Entry	Aldehyde	Product	Time (min)	Yield (%)[a]	Mp (°C)	
					Found	Reported
1			12	85	183–185	183–184 [21]
2			12	83	226–228	227–228 [21]
3			15	77	258–259	258–259 [21]
4			15	80	202–204	203–205 [21]
5			15	75	141–143	140 [13]
6			10	90	298–300	297–298 [21]
7			10	92	289–291	289–290 [21]
8			12	90	213–215	214–216 [21]
9			10	95	209–210	209–211 [21]

(*continued on next page*)

Table 2 (*continued*)

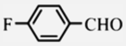
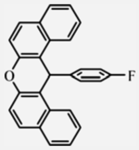
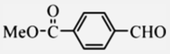
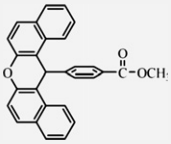
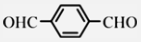
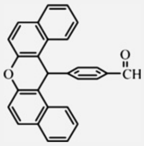
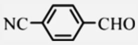
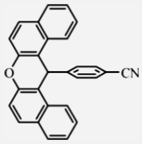
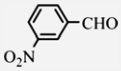
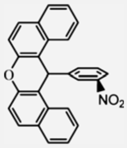
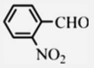
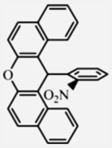
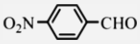
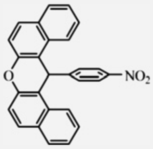
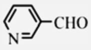
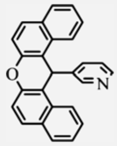
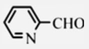
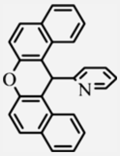
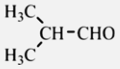
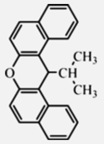
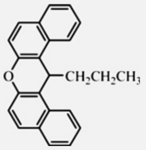
Entry	Aldehyde	Product	Time (min)	Yield (%)[a]	Mp (°C)	
					Found	Reported
10			10	90	238–240	238–240 [20]
11			12	87	250–252	249–250 [24]
12[b]			12	87	310–312	308–312 [22]
13			10	89	293–295	291–292 [19]
14			10	93	210–211	210–211 [21]
15			10	91	213–215	214–215 [21]
16			10	95	310–312	311–312 [21]
17			15	65	200–202	–
18			15	60	236–237	–

Table 2 (*continued*)

Entry	Aldehyde	Product	Time (min)	Yield (%)[a]	Mp (°C)	
					Found	Reported
19	 $(CH_3)_2CH{-}CHO$		10	80	154–156	155–157 [21]
20	$CH_3CH_2CH_2CHO$		10	83	152–154	152–154 [21]

[a] The yields refer to the isolated pure products which were characterized from their spectral data and were compared with authentic samples.

[b] The molar ratio of terephthaldialdehyde/2-naphtol is 1/4.

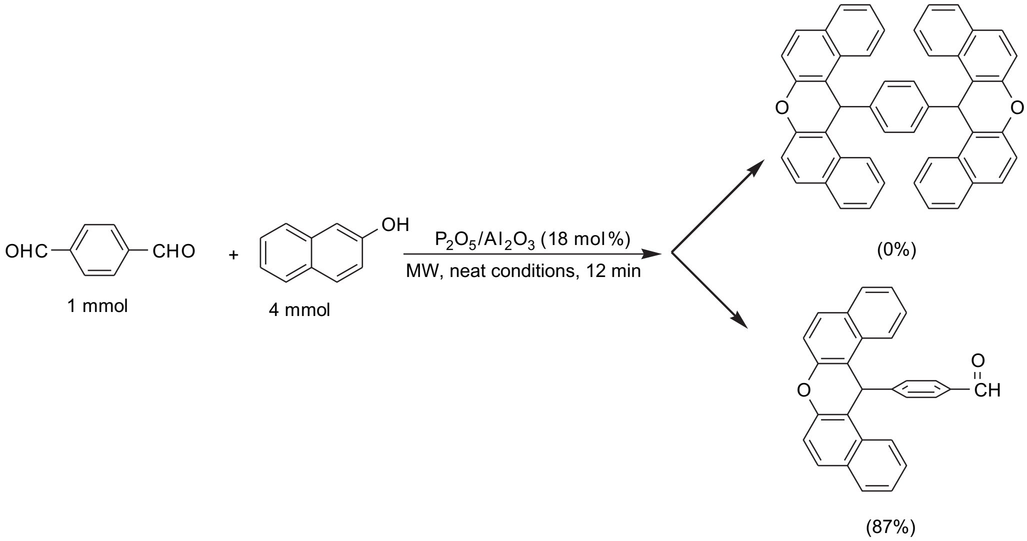


Fig. 2. . Reaction between terephthaldialdehyde and excess amount of 2-naphtol.

Acknowledgements

We gratefully acknowledge the funding support received for this project from the Islamic Azad University of Fasa and the Isfahan University of Technology (IUT).

References

[1] El-Brashy AM, Metwally ME, El-Sepai FA. Spectrophotometric determination of some fluoroquinolone antibacterials by binary complex formation with xanthene dyes. Il Farmaco 2004;59:809–17.
[2] Jamison JM, Krabill K, Hatwalkar A. Potentiation of the antiviral activity of poly r(A–U) by xanthene dyes. Cell Biology International Reports 1990;14:1075–84.
[3] Chibale K, Visser M, Schalkwyk DV, Smith PJ, Saravanamuthu A, Fairlamb AH. Exploring the potential of xanthene derivatives as trypanothione reductase inhibitors and chloroquine potentiating agents. Tetrahedron 2003;59:2289–96.
[4] Ion RM, Frackowiak D, Wiktorowicz K. The incorporation of various porphyrins into blood cells measured via flow cytometry, absorption and emission spectroscopy. Acta Biochimica Polonica 1998;45:833–45.
[5] Bhowmik BB, Ganguly P. Photophysics of xanthene dyes in surfactant solution. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 2005;61:1997–2003.
[6] Saint-Ruf G, Hieu HT, Poupelin JP. The effect of dibenzoxanthenes on the paralyzing action of zoxazolamine. Naturwissenschaften 1975;62:584–5.
[7] Knight CG, Stephens T. Xanthene-dye-labelled phosphatidylethanolamines as probes of interfacial pH. Biochemical Journal 1989;258:683–9.
[8] Ahmad M, King TA, Cha BH, Lee J. Performance and photostability of xanthene and pyrromethene laser dyes in sol–gel phases. Journal of Physics D: Applied Physics 2002;35:1473–6.
[9] Khosropour AR, Khodaei MM, Moghannian H. A facile, simple and convenient method for the synthesis of 14-alkyl or aryl-14-*H*-dibenzo [*a*, *j*]xanthenes catalyzed by pTSA in solution and solvent-free conditions. Synlett 2005:955–8.
[10] Saini A, Kumar S, Sandhu JS. A new LiBr-catalyzed, facile and efficient method for the synthesis of 14-alkyl or aryl-14*H*-dibenzo [*a*, *j*]xanthenes and tetrahydrobenzo[*b*]pyrans under solvent-free conventional and microwave heating. Synlett 2006:1928–32.
[11] Ko S, Yao CF. Heterogeneous catalyst: amberlyst-15 catalyzes the synthesis of 14-substituted-14*H*-dibenzo[*a*, *j*]xanthenes under solvent-free conditions. Tetrahedron Letters 2006;47:8827–9.
[12] Seyyedhamzeh M, Mirzaei P, Bazgir A. Solvent-free synthesis of aryl-14*H*-dibenzo[*a*, *j*]xanthenes and 1,8-dioxo-octahydro-xanthenes using silica sulfuric acid as catalyst. Dyes and Pigments 2008;76:836–9.
[13] Shaterian HR, Ghashang M, Hassankhani A. One-pot synthesis of aryl 14*H*-dibenzo[*a*, *j*]xanthene leuco-dye derivatives. Dyes and Pigments 2008;76:564–8.
[14] Pasha MA, Jayashankara VP. Molecular iodine catalyzed synthesis of aryl-14*H*-dibenzo[*a*, *j*]xanthenes under solvent-free condition. Bioorganic and Medicinal Chemistry Letters 2007;17:621–3.

[15] Das B, Ravikanth B, Ramu R, Laxminarayana K, Rao BV. Iodine catalyzed simple and efficient synthesis of 14-aryl or alkyl-14-*H*-dibenzo[*a*, *j*]xanthenes. Journal of Molecular Catalysis A: Chemical 2006;55:74–7.

[16] Rajitha B, Kumar BS, Reddy YT, Reddy PN, Sreenivasulu N. Sulfamic acid: a novel and efficient catalyst for the synthesis of aryl-14*H*-dibenzo[*a*, *j*] xanthenes under conventional heating and microwave irradiation. Tetrahedron Letters 2005;46:8691–3.

[17] Amini MM, Seyyedhamzeh M, Bazigir A. Heteropolyacid: an efficient and ecofriendly catalyst for the synthesis of 14-aryl-14*H*-dibenzo[*a*, *j*]xanthene. Applied Catalysis A: General 2007;23:242–5.

[18] Heravi MM, Bakhtiari K, Daroogheha Z, Bamoharram FF. Facile heteropolyacid-promoted synthesis of 14-substituted-14-*H*-dibenzo[*a*, *j*]xanthene derivatives under solvent-free conditions. Journal of Molecular Catalysis A: Chemical 2007;273:99–101.

[19] Su W, Yang D, Jin C, Zhang B. Yb(OTf)$_3$ catalyzed condensation reaction of β-naphthol and aldehyde in ionic liquids: a areen synthesis of aryl-14*H*-dibenzo [*a*, *j*]xanthenes. Tetrahedron Letters 2008;49:3391–4.

[20] Dabiri M, Baghbanzadeh M, Shakourinikcheh M, Arzroomchilar E. Eco-friendly and efficient one-pot synthesis of alkyl- or aryl-14*H*-dibenzo[*a*, *j*]xanthenes in water. Bioorganic and Medicinal Chemistry Letters 2008;18:436–8.

[21] Mirjalili BBF, Bamoniri AH, Akbari A. BF$_3$·SiO$_2$: an efficient alternative for the synthesis of 14-aryl or alkyl-14*H*-dibenzo[*a*, *j*]xanthenes. Tetrahedron Letters 2008;49:6454–6.

[22] Sharifi A, Abaee S, Tavakkoli A, Mirzaei M, Zolfagharei A. Facile montmorillonite K-10-supported synthesis of xanthene derivatives under microwave and thermal conditions. Synthetic Communications 2008;38:2958–66.

[23] Kantevari S, Chary MV, Das APR, Vuppalapati SVN, Lingaiah N. Catalysis by an ionic liquid: highly efficient solvent-free synthesis of aryl-14*H*-dibenzo[*a*, *j*] xanthenes by molten tetrabutylammonium bromide under conventional and microwave heating. Catalysis Communications 2008;9:1575–8.

[24] Pratibha K, Yathindranath V, Chauhan SMS. Facile and efficient synthesis of 14-alkyl- or aryl-14-*H*-dibenzo[*a*, *j*]xanthenes using sulfonyl-functionalized ionic liquids. Synthetic Communications 2008;38:637–48.

[25] Gong K, Fang D, Wang HL, Zhou XL, Liu ZL. The one-pot synthesis of 14-alkyl-or aryl-14*H*-dibenzo[*a*, *j*]xanthenes catalyzed by task-specific ionic liquid. Dyes and Pigments 2009;80:30–3.

[26] Clark JH. Catalysis of organic reactions by supported inorganic reagents. New York: VCH; 1994.

[27] Eaton PE, Carlson GR, Lee JT. Phosphorus pentoxide-methanesulfonic acid: convenient alternative to polyphosphoric acid. Journal of Organic Chemistry 1973;38:4071–3.

[28] Deevi B, Manickam B, Gone JR. The first intramolecular Friedel–Crafts reaction of Baylis–Hillman adduct: synthesis of functionalized indene and indane derivatives. Synthesis 2001:919–23.

[29] Kato Y, Okada S, Tomimoto K, Mase T. A facile bromination of hydroxyheteroarenes. Tetrahedron Letters 2001;42:4849–51.

[30] Hajipour AR, Zarei A, Khazdooz L, Pourmousavi SA, Mirjalili BBF. Direct sulfonylation of aromatic rings with aryl or alkyl sulfonic acid using supported P$_2$O$_5$/Al$_2$O$_3$. Phosphorus Sulfur Silicon 2005;180:2029–34.

[31] Hajipour AR, Koshki B, Ruoho AE. Nitric acid in the presence of supported P$_2$O$_5$ on silica gel: an efficient and novel reagent for oxidation of sulfides to the corresponding sulfoxides. Tetrahedron Letters 2005;46: 5503–6.

[32] Hajipour AR, Zarei A, Khazdooz L, Zahmatkesh S, Ruoho AE. A mild and chemoselective catalyst for thioacetalization under solvent-free conditions. Phosphorus Sulfur Silicon 2006;181:387–95.

[33] Hajipour AR, Zarei A, Ruoho AE. P$_2$O$_5$/Al$_2$O$_3$ as an efficient heterogeneous catalyst for chemoselective synthesis of 1,1-diacetates under solvent-free conditions. Tetrahedron Letters 2007;48:2881–4.

[34] Zarei A, Hajipour AR, Khazdooz L. Friedel–Crafts acylation of aromatic compounds with carboxylic acids in the presence of P$_2$O$_5$/SiO$_2$ under heterogeneous conditions. Tetrahedron Letters 2008;49:6715–9.

[35] Zarei A, Hajipour AR, Khazdooz L, Mirjalili BBF, Zahmatkesh S. Fast, efficient and chemoselective method for thioacetalization and transthioacetalization using catalytic amount of P$_2$O$_5$/Al$_2$O$_3$ under microwave irradiation. Journal of Molecular Catalysis A: Chemical 2009;301:39–46.