Dyes and Pigments 86 (2010) 93–96

Contents lists available at ScienceDirect

Dyes and Pigments

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

Short communication

Silica chloride catalyzed synthesis of 14-aryl-14*H*-dibenzo[*a*,*i*]xanthene-8,13-diones

Liqiang Wu [a,*], Jiangli Zhang [b], Lizhen Fang [a], Chunguang Yang [a], Fulin Yan [a]

[a] *School of Pharmacy, Xinxiang Medical University, Xinxiang, Henan 453003, China*
[b] *The Department Psychology of the Second Affiliated, Xinxiang Medical University, Xinxiang, Henan 453000, China*

ARTICLE INFO

Article history:
Received 18 October 2009
Received in revised form
6 December 2009
Accepted 7 December 2009
Available online 4 January 2010

Keywords:
Dibenzo[*a*,*i*]xanthenes
β-Naphthol
2-Hydroxy-1,4-naphthoquinone
Silica chloride
One-pot condensation
Solvent-free

ABSTRACT

A simple and facile synthesis of 14-aryl-14*H*-dibenzo[*a*,*i*]xanthene-8,13-dione derivatives was accomplished by the one-pot condensation of β-naphthol, aldehydes, and 2-hydroxy-1,4-naphthoquinone under solvent-free conditions in the presence of the heterogeneous catalyst, silica chloride. This method has the advantages of high yield, clean reaction, simple methodology and short reaction time. The catalyst could be recycled and reused three times without significant loss of activity. The structures of the novel compounds were confirmed by IR, ^{1}H NMR, ^{13}C NMR, and elemental analysis.

1. Introduction

Xanthenes and benzoxanthenes are important biologically active heterocycles. They possess antibacterial [1], antiflammatory [2] and antiviral activities [3] and can also be used in photodynamic therapy [4] as well as antagonists for paralyzing the action of zoxozolamine [5]. Furthermore, these heterocycles display useful spectroscopic properties and are used as dyes [6], in laser technologies [7] and as fluorescent materials for the visualization of biomolecules [8]. A number of xanthene dyes are extracted naturally from soil and plants, such as *Indigofera longeracemosa* [9]. Thus, the development of new and simple synthetic methods for the efficient preparation of new xanthenes is therefore an interesting challenge.

Homogeneous acidic catalysts such as H_2SO_4, HCl, and BF_3 are commonly used for organic synthesis. However, the above-mentioned catalysts have several disadvantages because they are corrosive, toxic or volatile, and generate large amounts of waste. Silica chloride (SiO_2–Cl), which was easily prepared from silica gel and thionyl chloride, is a good solid acid catalyst [10–13] in terms of convenience, cheapness, easy production, and insolubility in all organic solvents. In this paper, we report a simple and efficient synthesis of 14-aryl-14*H*-dibenzo[*a*,*i*]xanthene-8,13-dione derivatives using this catalyst. To the best of our knowledge, there is only one previous account describing this quinoidal system [14], and this paper is the first report in the synthesis of some 14-aryl-14*H*-dibenzo[*a*,*i*]xanthene-8,13-dione derivatives (see Fig. 1).

2. Experimental

NMR spectra were determined on Bruker AV-400 instrument at room temperature using TMS as internal standard, coupling constants (*J*) were measured in Hz; IR spectra were determined on FTS-40 infrared spectrometer; Elemental analysis were performed by a Vario-III elemental analyzer; Melting points were determined on an XT-4 binocular microscope and were uncorrected; Commercially available reagents were used throughout without further purification unless otherwise stated.

2.1. *Preparation of SiO_2–Cl*

To an oven-dried (120 °C, vacuum) sample of silica gel (10 g) in a round bottomed flask (250 mL) equipped with a condenser and a drying tube, was added thionyl chloride (40 mL) and the mixture was refluxed for 48 h. The unreacted thionyl chloride was distilled off. The resulting white-grayish powder was flask-dried and stored in a tightly capped bottle.

---

* Corresponding author. Tel./fax: +86 3733029879.
E-mail address: wliq870@163.com (L. Wu).

0143-7208/$ – see front matter Crown Copyright © 2009 Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.dyepig.2009.12.008

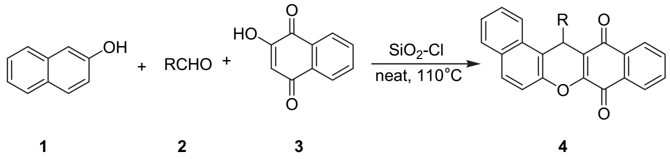

Fig. 1. Synthesis of 14-aryl-14*H*-dibenzo[*a*,*i*]xanthene-8,13-diones.

2.2. Typical procedure: preparation of 14-aryl-14H-dibenzo[a,i] xanthene-8,13-dione derivatives

To a mixture of β-naphthol (1 mmol), aldehyde (1 mmol), and 2-hydroxy-1,4-naphthoquinone (1 mmol), SiO_2–Cl (200 mg) was added. The mixture was stirred at 110 °C for 0.5–1 h. After completion of the reaction (TLC), $CHCl_3$ (20 mL) was added, and the solid catalyst was removed by filtration. The solvent was evaporated and the crude product was purified by silica gel column chromatography using $CHCl_3$ as eluent.

2.2.1. 14-Phenyl-14H-dibenzo[a,i]xanthene-8,13-dione (**4a**)

Yellow powder, m.p. 319–320 °C; IR (KBr) ν: 3082, 1663, 1635, 1590, 1575, 1370, 1286, 1237, 1213 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz) δ: 8.17 (d, 1H, J = 7.6 Hz), 8.12 (d, 1H, J = 7.6 Hz), 7.99 (d, 1H, J = 8.4 Hz), 7.91–7.77 (m, 3H), 7.61–7.41 (m, 6H), 7.20 (t, 2H, J = 15.2 Hz), 7.12–7.09 (m, 1H), 5.95 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ: 178.33, 178.29, 157.19, 147.30, 143.12, 135.11, 131.89, 131.22, 131.01, 130.89, 130.03, 129.51, 129.39, 128.58, 128.55, 127.45, 126.84, 125.53, 124.53, 123.78, 116.88, 116.77, 116.57, 35.16; Anal. calcd for $C_{27}H_{16}O_3$: C 83.49, H 4.15; found: C 83.25, H 4.12.

2.2.2. 14-(4-Chlorophenyl)-14H-dibenzo[a,i]xanthene-8, 13-dione (**4b**)

Yellow powder, m.p. 305–306 °C; IR (KBr) ν: 3046, 1667, 1637, 1591, 1577, 1488, 1367, 1286, 1235, 1213 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz) δ: 8.16 (d, 1H, J = 7.6 Hz), 8.13 (d, 1H, J = 7.6 Hz), 7.92–7.77 (m, 4H), 7.62–7.44 (m, 4H), 7.34 (d, 2H, J = 8.4 Hz), 7.15 (d, 2H, J = 8.4 Hz), 5.90 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ: 178.24, 178.18, 157.30, 147.23, 141.59, 135.17, 132.65, 131.90, 131.39, 130.81, 130.68, 130.00, 129.96, 129.79, 129.47, 128.70, 128.65, 127.58, 125.67, 124.60, 123.57, 116.79, 116.26, 116.00, 34.62; Anal. calcd for $C_{27}H_{15}ClO_3$: C 76.69, H 3.58; found: C 76.48, H 3.62.

2.2.3. 14-(4-Methoxylphenyl)-14H-dibenzo[a,i]xanthene-8, 13-dione (**4c**)

Yellow powder, m.p. 279–280 °C; IR (KBr) ν: 2919, 1664, 1635, 1591, 1575, 1367, 1286, 1249, 1235, 1212 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz) δ: 8.16 (d, 1H, J = 8.0 Hz), 8.12 (d, 1H, J = 7.6 Hz), 7.98 (d, 1H, J = 8.4 Hz), 7.89–7.76 (m, 4H), 7.60–7.43 (m, 5H), 7.31 (d, 2H, J = 8.4 Hz), 5.90 (s, 1H), 3.69 (s, 3H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ: 178.41, 178.37, 158.26, 157.02, 147.23, 135.47, 135.10, 131.88, 131.17, 131.00, 130.95, 130.00, 129.58, 129.41, 129.38, 128.53, 127.41, 125.50, 124.50, 123.81, 117.06, 116.78, 113.90, 55.13, 34.28; Anal. calcd for $C_{28}H_{18}O_4$: C 80.37, H 4.34; found: C 80.50, H 4.27.

2.2.4. 14-(4-Methylphenyl)-14H-dibenzo[a,i]xanthene-8, 13-dione (**4d**)

Yellow powder, m.p. 255–256 °C; IR (KBr) ν: 2920, 1665, 1637, 1591, 1577, 1364, 1286, 1237, 1213 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz) δ: 8.16 (d, 1H, J = 8.0 Hz), 8.11 (d, 1H, J = 7.6 Hz), 7.99 (d, 1H, J = 8.0 Hz), 7.89–7.76 (m, 3H), 7.60–7.42 (m, 4H), 7.29 (d, 2H, J = 8.0 Hz), 7.00 (d, 2H, J = 7.6 Hz), 5.90 (s, 1H), 2.21 (s, 3H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ: 178.34, 178.20, 157.08, 147.24, 140.27, 136.48, 135.08, 131.87, 131.16, 131.01, 130.92, 129.99, 129.41, 129.34, 129.24, 128.52, 128.42, 127.43, 125.50, 124.49, 123.78, 117.02, 116.78, 116.70, 34.70, 20.95; Anal. calcd for $C_{28}H_{18}O_3$: C 83.57, H 4.51; found: C 83.49, H 4.63.

2.2.5. 14-(4-Nitrophenyl)-14H-dibenzo[a,i]xanthene-8, 13-dione (**4e**)

Yellow powder, m.p. 332–333 °C; IR (KBr) ν: 3076, 1664, 1636, 1590, 1576, 1519, 1349, 1285, 1236, 1213 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz) δ: 8.20 (d, 1H, J = 7.6 Hz), 8.15 (d, 1H, J = 7.6 Hz), 8.06 (d, 2H, J = 8.8 Hz), 7.97–7.81 (m, 4H), 7.66–7.49 (m, 6H), 6.06 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ: 178.15, 177.98, 157.84, 150.06, 147.29, 146.68, 135.30, 131.99, 131.73, 130.65, 130.40, 130.32, 130.06, 129.63, 129.57, 128.83, 127.87, 125.91, 124.77, 123.88, 123.26, 116.83, 115.35, 115.03, 35.25; Anal. calcd for $C_{27}H_{15}NO_5$: C 74.82, H 3.49, N 3.23; found: C74.91, H 3.38, N 3.29.

2.2.6. 14-(3-Nitrophenyl)-14H-dibenzo[a,i]xanthene-8, 13-dione (**4f**)

Yellow powder, m.p. 304–305 °C; IR (KBr) ν: 3072, 1652, 1635, 1588, 1576, 1528, 1345, 1289, 1239, 1216 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz) δ: 8.22 (d, 1H, J = 8.0 Hz), 8.15 (d, 1H, J = 8.0 Hz), 8.12 (s, 1H), 8.00–7.82 (m, 6H), 7.66–7.61 (m, 2H), 7.52–7.41 (m, 3H), 6.06 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ: 178.14, 178.02, 157.73, 148.56, 147.33, 145.09, 135.31, 135.08, 132.03, 131.68, 130.60, 130.42, 130.35, 130.09, 129.59, 129.38, 128.87, 127.82, 125.85, 124.88, 123.32, 123.26, 122.14, 116.97, 115.27, 115.19, 35.20; Anal. calcd for $C_{27}H_{15}NO_5$: C 74.82, H 3.49, N 3.23; found: C 74.76, H 3.56, N 3.25.

2.2.7. 14-(2,4-Dichlorophenyl)-14H-dibenzo[a,i]xanthene-8, 13-dione (**4g**)

Yellow powder, m.p. 301–302 °C; IR (KBr) ν: 3056, 1662, 1637, 1591, 1577, 1466, 1362, 1288, 1238, 1213 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz) δ: 8.20 (d, 1H, J = 8.4 Hz), 8.16–8.11 (m, 2H), 7.89–7.80 (m, 3H), 7.65–7.45 (m, 4H), 7.31–7.27 (m, 2H), 7.07–7.05 (m, 1H), 6.14 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ: 178.10, 178.05, 157.55, 147.11, 139.20, 135.19, 134.02, 133.09, 132.61, 131.79, 131.52, 131.13, 130.60, 130.13, 130.01, 129.84, 129.47, 128.70, 127.69, 127.49, 125.69, 124.72, 123.71, 116.82, 33.24; Anal. calcd for $C_{27}H_{14}Cl_2O_3$: C 70.91, H 3.09; found: C 70.82, H 3.11.

2.2.8. 14-(3,4-Dichlorophenyl)-14H-dibenzo[a,i]xanthene-8, 13-dione (**4h**)

Yellow powder, m.p. 260–261 °C; IR (KBr) ν: 3050, 1682, 1594, 1564, 1488, 1384, 1286, 1216 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz) δ: 8.19 (d, 1H, J = 7.6 Hz), 8.16 (d, 1H, J = 7.6 Hz), 7.95–7.82 (m, 4H), 7.65–7.43 (m, 5H), 7.31–7.30 (m, 2H), 5.92 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ: 178.18, 178.02, 157.55, 147.28, 143.19, 135.24, 132.65, 131.96, 131.57, 131.05, 130.70, 130.54, 130.42, 130.10, 129.56, 128.75, 128.15, 127.77, 125.82, 124.73, 123.42, 116.83, 115.58, 115.44, 34.55; Anal. calcd for $C_{27}H_{14}Cl_2O_3$: C 70.91, H 3.09; found: C 70.95, H 3.02.

2.2.9. 14-(2-Chlorophenyl)-14H-dibenzo[a,i]xanthene-8, 13-dione (**4i**)

Yellow powder, m.p. 281–282 °C; IR (KBr) ν: 3068, 1666, 1638, 1591, 1577, 1361, 1289, 1237, 1213 cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz) δ: 8.25–8.22 (m, 2H), 8.14 (d, 1H, J = 7.2 Hz), 7.89–7.83 (m, 3H), 7.65–7.29 (m, 6H), 7.08–7.04 (m, 2H), 6.22 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ: 178.20, 178.13, 157.43, 147.12, 135.15, 133.32, 131.76, 131.36, 131.30, 130.81, 130.19, 130.13, 129.76, 129.40, 128.57, 128.23, 127.56, 127.11, 125.57, 124.67, 123.99, 116.82, 116.70, 115.61, 33.53; Anal. calcd for $C_{27}H_{15}ClO_3$: C 76.69, H 3.58; found: C 76.79, H 3.41.

3. Results and discussion

Initially, to optimize the amount of catalyst and the reaction temperature, the reaction of β-naphthol (**1**, 1 mmol), benzaldehyde

Table 1
Synthesis of 14-phenyl-14*H*-dibenzo[*a*,*i*]xanthene-8,13-dione under various conditions.[a]

Entry	SiO_2–Cl (mg/mmol)	Temp. (°C)	Time (min)	Yield (%)[b]
1	0	110	300	0
2	50	110	120	59
3	100	110	120	65
4	150	110	60	73
5	150	120	45	82
6	200	90	60	68
7	200	100	60	78
8	200	110	45	88
9	200	120	45	86
10	200	130	45	87
11	250	100	45	80
12	250	110	45	87
13	300	110	30	85

[a] Reaction conditions: β-naphthol (1 mmol); benzaldehyde (1 mmol); 2-hydroxy-1,4-naphthoquinone (1 mmol); neat.
[b] Isolated yield.

(**2a**, 1 mmol), and 2-hydroxy-1,4-naphthoquinone (**3**, 1 mmol) was studied under solvent-free conditions in the presence of SiO_2–Cl at different temperatures. The results are summarized in Table 1, and show that the reaction using 200 mg/mmol SiO_2–Cl at 110 °C proceeded in highest yield.

Based on the optimized reaction conditions, a range of 14-aryl-14*H*-dibenzo[*a*,*i*]xanthene-8,13-dione derivatives (**4**) was synthesized by the one-pot condensation of β-naphthol, aldehydes, and 2-hydroxy-1,4-naphthoquinone under solvent-free conditions. The reaction proceeded at 110 °C within 1 h in excellent yields after the addition of the catalyst SiO_2–Cl (200 mg/mmol) (see Table 2).

The structures of the products were established from their spectral properties (IR, ^1H NMR, ^{13}C NMR and elemental analysis). All of the products **4** exhibited a singlet in their ^1H spectra at $\delta = 5.90–6.06$ ppm for H-14 and also a distinguishing peak at $\delta = 33.2–35.3$ ppm for C-14 in their ^{13}C NMR spectra. The resonances of two non-equivalent carbonyl groups in their ^{13}C NMR spectrum of **4** appeared at $\delta = 178.10–178.41$ and 177.98–178.39 ppm. In these experiments the catalyst was isolated by filtration and could be recycled up to three times without significant loss of activity (entry 1). When this reaction was carried out with an aliphatic aldehyde such as butanal or pentanal (entry 10–11), TLC and ^1H NMR spectra of the reaction mixture showed a combination of starting materials and numerous products, the yield of the expected product was very poor.

The mode of action of the catalyst is illustrated in Fig. 2. The Si–Cl bond is labile and can give rise to Lewis acid centers on silica (see Fig. 2). The Cl is easily displaced selectively by the oxygen atom of an aldehyde by a nucleophilic substitution reaction generating a cationic center on the carbonyl carbon which is easily attacked by the nucleophilic 2-naphthol to form an *ortho*-quinone methide intermediate. Subsequent Michael addition to the *ortho*-quinone methide with nucleophile and followed by addition of the phenolic hydroxyl moiety to the carbonyl of ketone provides cyclic hemiketal which on dehydration afforded **4**. In 2-naphthol the electron density at the benzylic C-1 position (which is in conjugation with the aromatic ring) is higher than that at the C-3 position. Thus the regioselective formation of the *ortho*-quinone methide from this compound involving the C-1 and C-2 positions is favoured. In simple phenolic compounds and 1-naphthol (which are weaker nucleophiles compared to 2-naphthol) the electron density at the *ortho* position of the hydroxyl group is not sufficient for the reaction of these compounds with the aldehydes leading to the formation of the corresponding *ortho*-quinone methides.

Table 2
Preparation of 14-aryl-14*H*-dibenzo[*a*,*i*]xanthene-8,13-diones catalyzed by SiO_2–Cl.[a]

Entry	R	Time/min	Product	Yield/%[b]
1	C_6H_5	45	**4a**	88 (81,74,69)[c]
2	4-Cl-C_6H_4	45	**4b**	90
3	4-MeO-C_6H_4	30	**4c**	86
4	4-Me-C_6H_4	30	**4d**	89
5	4-NO_2-C_6H_4	30	**4e**	92
6	3-NO_2-C_6H_4	40	**4f**	90
7	2,4-Cl_2-C_6H_3	60	**4g**	85
8	3,4-Cl_2-C_6H_3	45	**4h**	86
9	2-Cl-C_6H_4	60	**4i**	88
10	Butyl	60	**4j**	0
11	Pentyl	60	**4k**	0

[a] Reaction conditions: β-naphthol (1 mmol); aldehyde (1 mmol); 2-hydroxy-1,4-naphthoquinone (1 mmol); SiO_2–Cl (200 mg); 110 °C; neat.
[b] Isolated yield.
[c] Yields after three times of catalyst recovery.

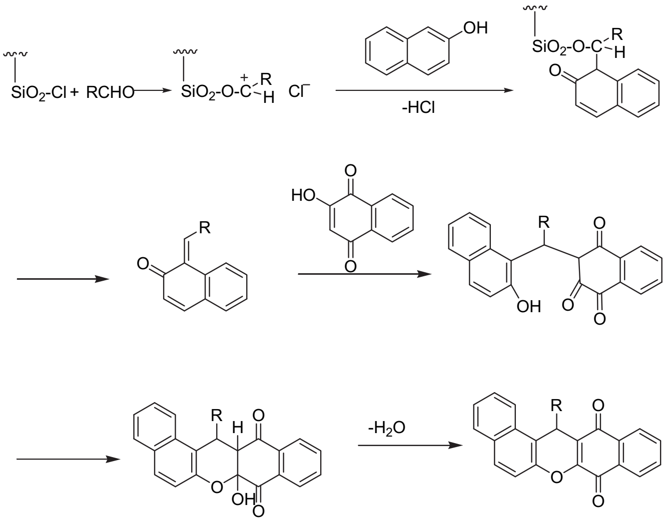

Fig. 2. Mechanism of the reaction.

4. Conclusions

In conclusion, a novel and highly efficient method for the synthesis of 14-aryl-14*H*-dibenzo[*a*,*i*]xanthene-8,13-dione derivatives from β-naphthol, aldehydes, and 2-hydroxy-1,4-naphthoquinone has been developed. The method is associated with the benefits derived from multicomponent reactions and the application of a heterogeneous catalyst. We feel that this economically viable procedure will find practical utility for the one-pot synthesis of other xanthene diones.

Acknowledgement

We are pleased to acknowledge the financial support from Xinxiang Medical University.

References

[1] Hideu T, Jpn Tokkyo Koho JP, 56005480; 1981. Chemical Abstracts 1981;95:80922b.
[2] Lamberk RW, Martin JA, Merrett JH, Parkes KEB, Thomas GJ. PCT Int. Appl. WO9706178; 1997. Chemical Abstracts 1997;126:P212377y.
[3] Poupelin JP, Saint-Rut G, Fussard-Blanpin O, Narcisse G, Uchida-Ernouf G, Lakroix R. Synthesis and anti-inflammatory properties of bis (2-hydroxy-1-naphthyl)methane, II. Polysubstituted and polycyclic derivatives. European Journal of Medicinal Chemistry 1978;13:67–71.

[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(3):833–45.

[5] Saint-Ruf G, Hieu HT, Poupelin JP. The effect of dibenzoxanthenes on the paralyzing action of zoxazolamine. Naturwissenschaften 1975;62(12):584–5.

[6] Bhowmik BB, Ganguly P. Photophysics of xanthene dyes in surfactant solution. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 2005; 61(9):1997–2003.

[7] 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(13):1473–6.

[8] Knight CG, Stephens T. Xanthene-dye-labelled phosphatidylethanolamines as probes of interfacial pH. Biochemical Journal 1989;258:683–9.

[9] Licudine PJA, Kawate MK, Li QX. Method for the analysis of phloxine B, uranine, and related xanthene dyes in soil using supercritical fluid extraction and high-performance liquid chromatography. Journal of Agricultural and Food Chemistry 1997;45:766–73.

[10] Kamitori Y, Hojo M, Masuda R, Kimura T, Yoshida T. Selective protection of carbonyl compounds. Silica gel treated with thionyl chloride as an effective catalyst for thioacetalization. Journal of Organic Chemistry 1986;51: 1427–31.

[11] Firouzabadi H, Iranpoor N, Hazarkhani H. Silica chloride (SiO_2–Cl) promotes highly efficient transformation of acylals to dithianes, dithiolanesm, and oxathiolanes. Phosphorus, Sulfur, and Silicon and the Related Elements 2001;176:165–71.

[12] Karade H, Sathe M, Kaushik MP. An efficient method for the synthesis of 2-aminothiazoles using silica chloride as a heterogeneous catalyst. Catalysis Communications 2007;8:741–6.

[13] Salehi P, Zolfigol MA, Shirini F, Baghbanzadeh M. Silica sulfuric acid and silica chloride as efficient reagents for organic reactions. Current Organic Chemistry 2006;10:2171–89.

[14] Chauhan MS, Dean FM, Matkin D, Robinson ML. Spirans. Part VIII. 1,2-naphthoquinone 1-methide and its spiro-dimer in chroman syntheses. Journal of the Chemical Society, Perkin Transactions 1973;1:120–5.