Journal of Fluorine Chemistry 130 (2009) 989–992

Contents lists available at ScienceDirect

Journal of Fluorine Chemistry

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

Short communication

$Sc[N(SO_2C_8F_{17})_2]_3$ catalyzed condensation of β-naphthol and aldehydes in fluorous solvent: One-pot synthesis of 14-substituted-14*H*-dibenzo[*a*,*j*]xanthenes

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ARTICLE INFO

Article history:
Received 20 April 2009
Received in revised form 19 June 2009
Accepted 22 June 2009
Available online 27 June 2009

Keywords:
Xanthene
Fluorous solvent
Bis(perfluorooctanesulfonyl)imide
Scandium complex

ABSTRACT

A facile synthesis of 14-substituted-14*H*-dibenzo[*a*,*j*]xanthenes was proposed by one-pot condensation of β-naphthol with aryl or alkyl aldehydes by using Scandium bis(perfluorooctanesulfonyl)imide complex as catalyst and perfluorodecalin as sole solvent.

1. Introduction

Xanthenes, especially benzoxanthenes, have drawn much attention in the field of medicinal chemistry. These oxygen-containing heterocycles have been reported to exert various biological and therapeutic properties in antibacterial [1], antiviral [2], and anti-inflammatory activities [3], as well as in photodynamic therapy (PDT) [4]. Furthermore, they are used as dyes [5], or as fluorescent materials for the visualization of biomolecular assemblies [6]. Their application is also found in laser technologies [7].

The synthesis of benzoxanthenes has been achieved by various methods [8]. Among them, condensation of β-naphthol with aldehydes has been explored using different catalysts such as sulfamic acid [9], *p*-TSA [10], selectfluor™ [11], I_2 [12], silica sulfuric acid [13] and $Yb(OTf)_3$ [14]. However, these catalyst systems suffer from some limitation such as long reaction time, high catalyst loadings, use of toxic solvent or special apparatus. The search for milder and more environmentally benign conditions is, therefore, highly demanding for the synthesis of these compounds.

Metal (e.g. Sn, Sc and Yb) complexes with bis(perfluorooctanesulfonyl)imide ligands are active and recyclable catalysts in the fluorous immobilized phase for Baeyer–Villiger oxidation [15], Diels–Alder reaction [16], esterification [17] and Friedel–Crafts acylation [18], far superior to the corresponding metal trifluoromethanesulfonates. Moreover, they are water-repellent due to highly "fluorous" nature brought about by the perfluoroalkyl chains surrounding the central metal. It is also noted that perfluorocarbon solvents have some unique properties which make them attractive alternatives for conventional organic solvents [19]. In this work we report a mild and effective method for the preparation of aryl or alkyl-14*H*-dibenzo[*a*,*j*]xanthenes using $Sc[N(SO_2C_8F_{17})_2]_3$ complex as catalyst in fluorous biphase system. It was found that under mild conditions the catalyst can function efficiently at low catalytic loadings (1 mol%) and can be easily recovered and reused.

2. Results and discussion

As a model reaction we chose condensation of benzaldehyde and β-naphthol catalyzed by $Sc[N(SO_2C_8F_{17})_2]_3$ complex in different solvent systems. As shown in Table 1, the highest yield (93%) was achieved when the reaction was conducted in perfluorodecalin ($C_{10}F_{18}$, *cis*- and *trans*-mixture) as a sole solvent at 110 °C for 5 h (Table 1, entry 8). In order to make the reaction more accessable, we explored different co-solvent systems taking a common general organic solvent. Unfortunately, the use of co-solvent system resulted in lower product yield under the similar conditions (Table 1, entries 1–7). Among the co-solvents studied, toluene was proved to be efficient (Table 1, entry 3) in terms of its relatively higher yield. Although the reasons why the use of co-solvent such as toluene decreases the product yield are not clear, we assumed that difference in solubility of the catalyst and the substrate in perfluorodecalin or in toluene would have an influence

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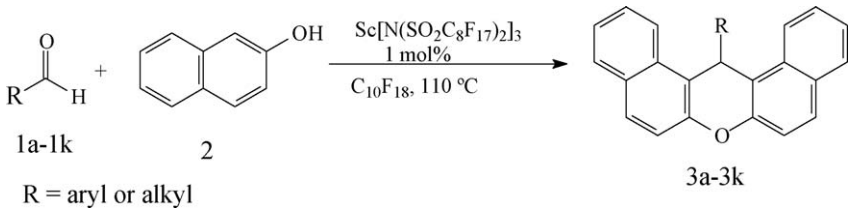
doi:10.1016/j.jfluchem.2009.06.013



Scheme 1. Synthesis of 14-substituted-14*H*-dibenzo[*a,j*]xanthenes.

Table 1
Effect of co-solvents on the condensation[a].

Entry	Co-solvent	Time (h)	Yield (%)[b]
1	$ClCH_2CH_2Cl$	6	75
2	MeCN	6	23
3	PhMe	6	81
4	EtOH	6	67
5	MeOH	6	52
6	Dioxane	6	64
7	THF	6	20
8	–	5	93

[a] Reaction conditions: benzaldehyde (1 mmol), β-naphthol (2 mmol), $Sc[N(SO_2C_8F_{17})_2]_3$ (0.01 mmol), perfluorodecalin (1.5 mL), co-solvent (2 mL), 110 °C or refluxing.
[b] Isolated yields.

on their effective miscibility. Based on these results, we employed only perfluorodecalin as sole solvent in the further experiments.

We then investigated the catalytic activity of different rare earth bis(perfluorooctanesulfonyl)imide complexes in the model reaction. The results are summarized in Table 2. It was found that several metal bis(perfluorooctanesulfonyl)imide complexes gave promising results. Especially, $Sc[N(SO_2C_8F_{17})_2]_3$ was found to be the most effective catalyst (Table 2, entry 4) based on the product yield. The catalyst system is proved again to be important since the reaction hardly proceeded without catalyst and fluorous solvent (yield less than 5%).

Next, we examined the condersation of β-naphthol with various aldehydes in the presence of $Sc[N(SO_2C_8F_{17})_2]_3$ in perfluorodecalin at 110 °C (Scheme 1). As listed in Table 3, in all cases the corresponding benzoxanthenes were obtained in good yields (70–96%) after 2–7 h. It was found that the nature of the substituent on the aromatic ring had a magnificent effect on the reaction rate. Generally, aromatic aldehydes with electron withdrawing group showed increased reaction rate (Table 3, entries 1–5). Interestingly, 4-hydroxybenzaldehyde also gave the desired product within a short reaction time in excellent yield (Table 3, entry 6). On the other hand, reactions with aliphatic aldehydes provided somewhat lower yields than those with aromatic aldehydes (Table 3, entries 10 and 11).

Table 2
Effect of various catalysts on the condensation[a].

Entry	Catalyst	Yield (%)[b]
1	$Sn[N(SO_2C_8F_{17})_2]_4$	75
2	$Hf[N(SO_2C_8F_{17})_2]_4$	82
3	$Yb[N(SO_2C_8F_{17})_2]_3$	90
4	$Sc[N(SO_2C_8F_{17})_2]_3$	93, 90, 92, 93, 92[c]
5	$Y[N(SO_2C_8F_{17})_2]_3$	72
6	$Sm[N(SO_2C_8F_{17})_2]_3$	53
7	$Eu[N(SO_2C_8F_{17})_2]_3$	80
8	$Td[N(SO_2C_8F_{17})_2]_3$	32
9	$Dy[N(SO_2C_8F_{17})_2]_3$	57

[a] Reaction conditions: benzaldehyde (1 mmol), β-naphthol (2 mmol), catalyst (0.01 mmol), perfluorodecalin (1.5 mL), 110 °C, 5 h.
[b] Isolated yields.
[c] Catalyst was reused for five times.

Table 3
Synthesis of 14-substitued-14*H*-dibenzo[*a,j*]xanthenes[a].

Entry	RCHO (1)	Time (h)	Product	Yield (%)[b]
1	2-ClC_6H_4 (1a)	2.5	3a	91
2	4-ClC_6H_4 (1b)	2	3b	96
3	2,4-$Cl_2C_6H_3$ (1c)	2	3c	95
4	3-$NO_2C_6H_4$ (1d)	3	3d	90
5	4-$NO_2C_6H_4$ (1e)	2	3e	95
6	4-HOC_6H_4 (1f)	2	3f	94
7	C_6H_5 (1g)	5	3g	93
8	4-$MeOC_6H_4$ (1h)	6	3h	85
9	4-MeC_6H_4 (1i)	5.5	3i	91
10	CH_3CH_2 (1j)	7	3j	75
11	$CH_3CH_2CH_2$ (1k)	7	3k	70

[a] Reaction conditions: aldehyde (1 mmol), β-naphthol (2 mmol), $Sc[N(SO_2C_8F_{17})_2]_3$ (0.01 mmol), 110 °C.
[b] Isolated yields.

The possibility of multi-use of $Sc[N(SO_2C_8F_{17})_2]_3$ catalyst for the synthesis of phenylderivative was also investigated. After separation of the product, fluorous phase containing the catalyst was reused for the next cycle. As shown in Table 2, even after $Sc[N(SO_2C_8F_{17})_2]_3$ catalyst was recycled five times, almost same isolated yield of the final product was realized.

3. Conclusion

In conclusion, a simple and efficient method for the synthesis of 14-substituted-14*H*-dibenzo[*a,j*]xanthenes has been developed via condensation of β-naphthol with aldehydes catalyzed by $Sc[N(SO_2C_8F_{17})_2]_3$ complex in perfluorodecalin as a sole solvent. The attractive features of this protocol are its generality, easy work-up, and catalyst reusability.

4. Experimental

4.1. General

Melting points were obtained with Shimadzu DSC-50 thermal analyzer. Inductively coupled plasma (ICP) spectra were measured on Ultima2C apparatus. Elemental analyses were performed on a Yanagimoto MT3CHN recorder. IR spectra were recorded on a Bomem MB 154S infrared analyzer. ^1H NMR and ^{19}F NMR spectra were recorded with Bruker Advance RX500. The perfluorodecalin and rare earth salts were purchased from Aldrich Co. Commercially available reagents were used without further purification.

4.2. Preparation of $(C_8F_{17}SO_2)_2NH$ and $Sc[N(SO_2C_8F_{17})_2]_3$

4.2.1. Preparation of $(C_8F_{17}SO_2)_2NH$

$(C_8F_{17}SO_2)_2NH$ was prepared according to the literature [20,21]. Ammonia was added into perfluorooctanesulfonyl fluoride (36.7 g, 73 mmol) at −20 °C. After the stirring was held at −20 °C for about 1 h, it was then continued at room temperature for another 1 h. The solid product was acidified with 2 M HCl followed by addition of Et_2O. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure, dried in vacuum to give

$C_8F_{17}SO_2NH_2$ (87% yield). Then the mixture of perfluorooctanesulfonyl fluoride (36.0 g, 72 mmol), perfluorooctanesulfonamide (34.4 g, 69 mmol) and Et_3N (60 mL) was heated at reflux for 23 h. The lower brown fluorous layer was washed with 10% HCl and dried in vacuum to afford $(C_8F_{17}SO_2)_2N\ HNEt_3$. Free $(C_8F_{17}SO_2)_2NH$ was obtained through acidic ion exchange resin column in 50% yield. Anal. Calcd. for $(C_8F_{17}SO_2)_2NH$: C, 19.58; N, 1.43; H, 0.10. Found: C, 19.61; N, 1.45; H, 0.16. ^{19}F NMR: δ −126.2, −121.8, −114.0, −81.2.

4.2.2. Preparation of $Sc[N(SO_2C_8F_{17})_2]_3$

Scandium bis(perfluorooctanesulfonyl)imide complex, $Sc[N(SO_2C_8F_{17})_2]_3$ was prepared according to the reported procedure [22]. The mixture of Scandium oxide and 3 equiv. of bis(perfluorooctanesulfonyl)imide reacted in water under reflux for 1 h. The resulting mixture was filtered through a membrane filter. The Scandium bis(perfluorooctanesulfonyl)imide complex was obtained in 98% yield. ICP: Calcd. For $Sc[N(SO_2C_8F_{17})_2]_3$: Sc, 1.51. Found: Sc, 1.47. Anal. Calcd. for $Sc[N(SO_2C_8F_{17})_2]_3$: C, 19.31. Found: C, 19.23. ^{19}F NMR: δ −126.1, −121.2, −114.2, −81.4.

4.3. Typical procedure for the preparation of aryl(alkyl)-14H-dibenzo[a,j]xanthenes

A mixture of aldehyde (1 mmol), β-naphthol (2 mmol) and $Sc[N(SO_2C_8F_{17})_2]_3$ (1 mol%) was heated at 110 °C in perfluorodecalin for appropriate time indicated in Table 3. The reaction was monitored by TLC. After completion of the reaction, the mixture was cooled to room temperature and methylene dichloride (10 mL) was added, and the mixture was stirred for another 5 min. The fluorous layer on the bottom was separated for the next cycle. The upper methylene dichloride layer was washed with brine, dried over anhydrous Na_2SO_4 and evaporated in vacuum. The residue was recrystallized from ethanol to afford pure products. Products were characterized by comparison of their physical and spectral data with those of authentic samples.

4.3.1. 14-(2-Chlorophenyl)-14H-dibenzo[a,j]xanthene (3a)

White solid; mp 216–218 °C (215 °C, Ref. [11]). IR (KBr) υ 3058, 2998, 1592, 1515, 1459, 1240, 961, 809, 745 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ: 6.80 (s, 1H), 6.87–7.13 (m, 2H), 7.42–7.67 (m, 8H), 7.79–7.86 (m, 4H), 8.73 (d, J = 8.5 Hz, 2H).

4.3.2. 14-(4-Chlorophenyl)-14H-dibenzo[a,j]xanthene (3b)

Yellow solid; mp 290–292 °C (289 °C, Ref. [11]). IR (KBr) υ 3066, 2922, 1622, 1590, 1514, 1456, 1397, 1245, 1237, 1209, 1140, 1065, 959, 812, 775, 746 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ: 6.46 (s, 1H), 6.97 (d, J = 7.2 Hz, 2H), 7.37 (t, J = 7.5 Hz, 2H), 7.42–7.76 (m, 10 H), 8.39 (d, J = 8.7 Hz, 2H).

4.3.3. 14-(2,4-Dichlorophenyl)-14H-dibenzo[a,j]xanthene (3c)

Yellow solid; mp 226–227 °C (227 °C, Ref. [14]). IR (KBr) υ 3057, 2920, 1619, 1592, 1558, 1514, 1458, 1404, 1240, 1208, 1141, 1101, 1041, 960, 863, 836, 808, 742, 699, 607 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ: 6.45 (s,1H), 6.96 (d, J = 7.5 Hz, 2H), 7.29 (d, J = 7.5 Hz, 2H), 7.38 (s, 1H), 7.48–7.65 (m, 4H), 7.79–7.84 (m, 4H), 8.37 (d, J = 8.5 Hz, 2H).

4.3.4. 14-(3-Nitrophenyl)-14H-dibenzo[a,j]xanthene (3d)

Pale yellow solid; mp 210–211 °C (211 °C, Ref. [11]). IR (KBr) υ 3038, 1610, 1582, 1515, 1246, 810, 800 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ: 6.50 (s,1H), 7.01–7.45 (m, 8H), 7.75–7.80 (m, 4H), 8.37–8.53 (m, 4H).

4.3.5. 14-(4-Nitrophenyl)-14H-dibenzo[a,j]xanthene (3e)

Yellow solid; mp 312–313 °C (310 °C, Ref. [11]). IR (KBr) υ 2925, 1590, 1516, 1335, 1236, 828 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ: 6.59 (s, 1H), 7.03 (t, J = 7.8 Hz, 2H), 7.40–7.56 (m, 6H), 7.66–7.72 (m, 4H), 8.30–8.46 (m, 4H).

4.3.6. 14-(4-Hydroxyphenyl)-14H-dibenzo[a,j]xanthene (3f)

Pink solid; mp 138–140 °C (140 °C, Ref. [12]). IR (KBr) υ 3404, 1592, 1511, 1401, 1250, 1242, 816 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ: 4.98 (s, 1H), 6.42 (s, 1H), 6.58 (d, J = 8.4 Hz, 2H), 7.38 (t, J = 10.8 Hz, 2H), 7.43 (d, J = 7.5 Hz, 2H), 7.48 (d, J = 8.9, 2H), 7.58 (t, J = 7.4 Hz, 2H), 7.79 (d, J = 5.1 Hz, 2H), 7.83 (d, J = 8.1 Hz, 2H), 8.39 (d, J = 8.4 Hz, 2H).

4.3.7. 14-Phenyl-14H-dibenzo[a,j]xanthene (3g)

Colorless solid; mp 185–187 °C (185 °C, Ref. [11]). IR (KBr) υ 3070,1585, 1445, 1250, 1080, 965 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ: 6.45 (s, 1H), 6.96 (t, J = 7.2 Hz, 1H), 7.12 (t, J = 7.2 Hz, 2H), 7.37–7.58 (m, 8H), 7.74–7.81 (m, 4H), 8.34 (d, 2H).

4.3.8. 14-(4-Methoxyohenyl)-14H-dibenzo[a,j]xanthene (3h)

White solid; mp 203–206 °C (204 °C, Ref. [11]). IR (KBr) υ 3038, 2910, 1615,1580, 1245, 820, 804 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ: 3.72 (s, 3H), 6.48 (s, 1H), 6.75 (d, J = 7.5 Hz, 2H), 7.39 (t, J = 7.2 Hz, 2H), 7.53–7.89 (m, 10H), 8.41 (d, J = 8.5 Hz, 2H).

4.3.9. 14-(4-Tolyl)-14H-dibenzo[a,j]xanthene (3i)

White solid; mp 228–229 °C (229 °C, Ref. [11]). IR (KBr) υ 3067, 3021, 2897, 1620, 1591, 1510 1458, 1432, 1399, 1246, 961, 810, 740, 608, 517, 488 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ: 2.12 (s, 3H), 6.45 (s, 1H), 6.93 (d, J = 7.5 Hz, 2H), 7.22–7.38 (m, 8H), 7.43–7.81 (m, 4H), 8.45 (d, J = 7.2 Hz, 2H).

4.3.10. 14-Ethyl-14H-dibenzo[a,j]xanthene (3j)

White solid; mp 150–152 °C (152 °C, Ref. [11]). IR (KBr) υ 3065, 2931, 1621, 1590, 1514, 1456, 1433, 1399, 1240, 1076, 960, 869, 809, 750, 705, 584, 503, 567 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ: 0.76 (t, J = 7.4 Hz, 3H), 2.14 (m, 2H), 5.57 (t, J = 4.3 Hz, 1H), 6.65 (d, J = 7.5 Hz, 2H), 7.22–7.92 (m, 4H), 7.36–7.68 (m, 4H), 8.26 (d, J = 8.4 Hz, 2H).

4.3.11. 14-Propyl-14H-dibenzo[a,j]xanthene (3k)

White solid; mp 151–153 °C (151–153 °C, Ref. [14b]). IR (KBr) υ 3061, 2953, 1591, 1434, 1399, 1243, 814, 747 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz) δ: 0.62 (t, J = 7.3 Hz, 3H), 1.01–1.08 (m, 2H), 2.03 (m, 2H), 5.58 (t, J = 4.61 Hz, 1H), 7.39 (d, J = 9.2 Hz, 2H), 7.45–7.50 (m, 2H), 7.61–7.65 (m, 2H), 7.79 (d, J = 8.8 Hz, 2H), 7.89 (d, J = 8.4 Hz, 2H), 8.26 (d, J = 8.8 Hz, 2H).

References

[1] H. Takeshiba, JP 56005480, 1981 (Chem. Abstr. 95: 80922).
[2] R.W. Lambert, J.A. Martin, J.H. Merrett, K.E.B. Parkes, G.J. Thomas, WO 9706178, 1997 (Chem. Abstr. 126: 212377).
[3] J.P. Poupelin, G. Saint-Ruf, O. Foussard-Blanpin, G. Narcisse, G. Uchida- Ernouf, R. Lacroix, Eur. J. Med. Chem. 13 (1978) 67–71.
[4] R.M. Ion, D. Frackowiak, A. Planner, K. Wiktorowicz, Acta Biochim. 45 (1998) 833–845.
[5] S.M. Menchen, S.C. Benson, J.Y.L. Lam, W. Zhen, D. Sun, B.B. Rosenblum, S.H. Khan, M. Taing, US 6583168, 2003 (Chem. Abstr. 139: 54287).
[6] C.G. Knight, T. Stephens, Biochem. J. 258 (1989) 683–687.
[7] O. Sirkecioglu, N. Talinli, A. Akar, J. Chem. Res. (S) 12 (1995) 502.
[8] (a) P. Papini, R. Cimmarusti, Gazz. Chim. Ital. 77 (1947) 142–145; (b) R.N. Sen, N. Sarkar, J. Am. Chem. Soc. 47 (1925) 1079–1091; (c) K.Z. Ahmad, S.A. Akbari, S. Azam, V. Hojat, J. Chem. Res. (S) 5 (2005) 277–279.
[9] B. Rajitha, B.S. Kumar, Y.T. Reddy, P.N. Reddy, N. Sreenivasulu, Tetrahedron Lett. 46 (2005) 8691–8693.
[10] M.M. Khodaei, A.R. Khoropour, H. Moghanian, Synlett 6 (2005) 955–958.
[11] P.S. Kumar, B. Sunil Kumar, B. Rajitha, P. Narsimha Reddy, N. Sreenivasulu, Y. Thirupathi Reddy, Arkivoc xii (2006) 46–50.
[12] M.A. Pasha, V.P. Jayashankara, Bioorg. Med. Chem. Lett. 17 (2007) 621–624.
[13] H.R. Shaterian, M. Ghashang, A. Hassankhani, Dyes Pigments 76 (2008) 564–568.
[14] (a) W.K. Su, D. Yang, J. Can, B. Zhang, Tetrahedron Lett. 49 (2008) 3391–3394; (b) L.M. Wang, Y.Y. Sui, L. Zhang, Chin. J. Chem. 26 (2008) 1105–1108.

[15] X.H. Hao, O. Yamazaki, A. Yoshida, J. Nishikido, Tetrahedron Lett. 44 (2003) 4977–4980.
[16] K. Mikami, Y. Mikami, Y. Matumoto, J. Nishikido, F. Yamamoto, H. Nakajima, Tetrahedron Lett. 42 (2001) 289–292.
[17] X.H. Hao, A. Yoshida, J. Nishikido, Tetrahedron Lett. 45 (2004) 781–785.
[18] X.H. Hao, A. Yoshida, J. Nishikido, Tetrahedron Lett. 46 (2005) 2697–2700.
[19] E.D. Wolf, G.V. Koten, B. Deelman, J. Chem. Soc. Rev. 28 (1999) 37–41.
[20] X.H. Hao, A. Yoshida, J. Nishikido, J. Fluorine Chem. 127 (2006) 193–199.
[21] Z. Benfodda, L. Delon, F. Guillen, H. Blancou, J. Fluorine Chem. 128 (2007) 1353–1358.
[22] K. Mikami, O. Kotera, Y. Motoyama, M. Tanaka, Inorg. Chem. Commun. 1 (1998) 10–11.