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A simple and efficient one-pot bis-bromine-1,4-diazabicyclo[2.2.2]octane (Br_2-DABCO) catalyzed synthesis of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes under solvent-free conditions

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Abstract

Bis-bromine-1,4-diazabicyclo[2.2.2]octane (Br_2-DABCO) is an efficient, readily available, and reusable catalyst for the synthesis of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes **3** by condensation of β-naphthol **2** and aldehydes **1**. This reaction under solvent-free conditions is very simple, affording good to excellent yields of products.

Keywords: 14-aryl-14*H*-dibenzo[*a,j*]xanthenes; bis-bromine-1,4-diazabicyclo[2.2.2]octane; one-pot synthesis; solvent-free.

Introduction

Xanthenes and benzoxanthenes are biologically important drug intermediates. They are cited in the literature as oxygen heterocycles possessing antibacterial (El-Brashy et al., 2004), anti-inflammatory (Chibale et al., 2003), and antiviral properties (Jamison et al., 1990). The synthesis of xanthene derivatives is currently of much interest, and various methods have been reported (Wang and Harvey, 2002; Khoramabadi-zad et al., 2005; Khosropour et al., 2005; Rajitha et al., 2005; Ko and Yao, 2006; Mohamed and Vaderapura, 2007; Mozhdeh et al., 2008). However, the existing methods suffer from long 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.

Results and discussion

In continuation of our research on various transformations by halogenating agents (Azarifar and Ghasemnejad-Bosra, 2006; Azarifar et al., 2006; Ghasemnejad-Bosra et al., 2008a,b; Habibzadeh et al., 2011), herein is reported the use of bis-bromine-1,4-diazabicyclo[2.2.2]octane (Br_2-DABCO) (Heravi et al., 2005) as a robust and efficient catalyst in the one-pot synthesis of the 14-aryl-14*H*-dibenzo[*a,j*]xanthenes derivatives **3a–o** by reaction of β-naphthol with different aromatic aldehydes in excellent yields (88–97%) under solvent-free conditions (Scheme 1, Table 1). As shown in Table 1, the reactions occur within 48–73 min under solvent-free conditions. The experimental results indicate that the most effective conversions occur when a molar ratio 1:0.17 of substrate/Br_2-DABCO is used. Longer reaction times are required when lower amounts of Br_2-DABCO are employed. It is important to note that no 14-aryl-14*H*-dibenzo[*a,j*]xanthenes derivatives were afforded when the reactions were performed in the absence of Br_2-DABCO.

The proposed mechanism for these reactions is shown in Scheme 2. As can be seen, the reaction likely proceeds *via* initial formation of an intermediate product **4**. The oxonium species **5** is then formed by reaction with β-naphthol, which then undergoes dehydration to afford the desired product **3**.

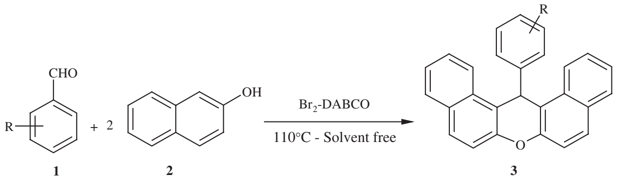
The advantages of the method described in this paper in comparison with other previously reported methods are as follows: the yields of products are higher than the previously reported yields. In addition, the catalyst Br_2-DABCO is inexpensive, without any moisture sensitivity, and no special efforts are required for the reaction.

Conclusion

We described herein bis-bromine-1,4-diazabicyclo[2.2.2]octane (Br_2-DABCO) catalyzed highly efficient, one-pot, protocol for the synthesis of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes by the condensation of an aldehyde and 2-naphthol under solvent-free conditions in excellent yields. The main advantages of the presented protocol are mild, clean and environmentally benign reaction conditions, low costs of the reagents, and high yields of the products.

Experimental section

The employed chemicals were obtained from either Merck or Fluka. The infrared spectroscopy (IR) spectra were recorded using a



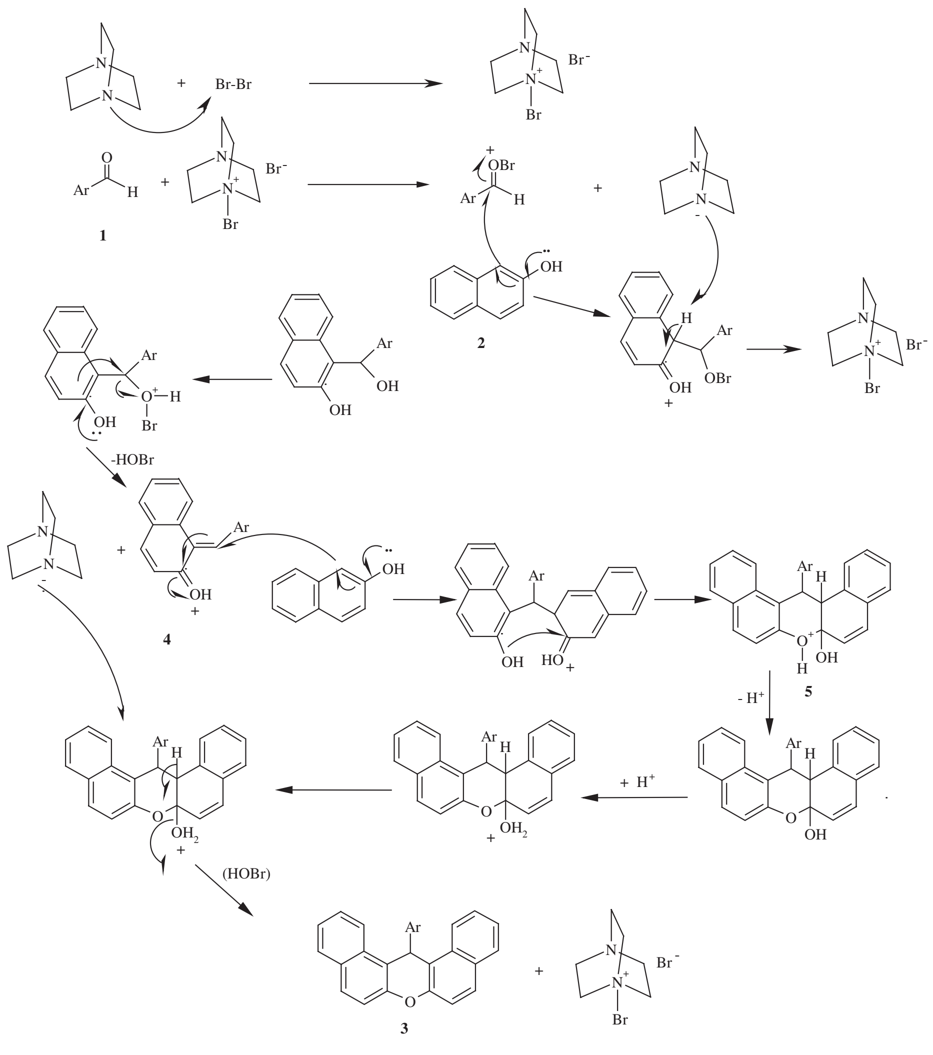
Scheme 1 Synthesis of xanthenes with Br_2-DABCO under solvent-free conditions.

Table 1 Br_2-DABCO catalyzed synthesis of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes.

Entry	Product	R	Time (min)	Yields (%)[a]	M.p. (°C)[b]
1	**3a**	H	50	96	181 (183)
2	**3b**	4-Cl	61	94	288 (287)
3	**3c**	2-Cl	67	92	214 (215)
4	**3d**	4-Br	53	91	298 (296)
5	**3e**	2-Br	60	93	191 (190)
6	**3f**	4-NO_2	66	89	309 (312)
7	**3g**	2-NO_2	71	88	292 (293)
8	**3h**	3-NO_2	61	90	214 (213)
9	**3i**	4-Me	49	95	227 (228)
10	**3j**	3-Me	50	96	206 (205)
11	**3k**	4-OMe	48	96	199 (197)
12	**3l**	2-OMe	52	97	95 (93)
13	**3m**	3-F	73	92	258 (259)
14	**3n**	2-F	50	94	210 (209)
15	**3o**	4-F	62	93	238 (239)

[a] Yields of isolated products.

[b] All products are known, characterized by IR, NMR and melting points, and compared with authentic samples. The literature melting points are given in parentheses (Wang and Harvey, 2002; Khosropour et al., 2005).



Scheme 2 Possible mechanism for the synthesis of xanthenes.

Shimadzu 435-U-04 spectrophotometer (KBr pellets) and the nuclear magnetic resonance (NMR) spectra were obtained in $CDCl_3$ using a 90 MHz JEOL FT NMR spectrometer. All melting points were determined on a Büchi 530 melting point apparatus and are uncorrected.

General procedure for the synthesis of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes

To a mixture of aldehyde **1** (1 mmol) and β-naphthol **2** (2 mmol), bis-bromine-1,4-diazabicyclo[2.2.2]octane (Br_2-DABCO) (0.17 mmol, 0.2 mg) was added and the mixture was placed in an oil bath and heated at 110°C for the period of time shown in Table 1. Completion of the reaction was indicated by thin layer chromatography (TLC). After the reaction was completed, EtOH was added and the mixture was heated until the solid crude product was dissolved. Then, the heterogeneous catalyst wasremoved from the mixture by simple filtration and the EtOH solution was concentrated. A 15% mixture of ethanol and water was added to the crude product, the precipitate was filtered and then crystallized twice from the 15% aqueous ethanol. The products were characterized on the basis of their physical and spectral analysis (Table 1) and by direct comparison with literature data.

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