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# Eco-friendly and efficient one-pot synthesis of alkyl- or aryl-14*H*-dibenzo[*a*,*j*]xanthenes in water

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**Abstract**—Alkyl- or aryl-14*H*-dibenzo[*a*,*j*]xanthene derivatives are synthesized efficiently by the reaction of β-naphthol and aliphatic and aromatic aldehydes in the presence of $KAl(SO_4)_2{\cdot}12H_2O$ (alum) under aqueous condition at 100 °C. Different types of aromatic and aliphatic aldehydes are used in the reaction and in all cases the products synthesized successfully. Several solvents were examined for this reaction; however, in terms of reaction yield and time, water was found to be the optimum solvent.


Alkyl- or aryl-14*H*-dibenzo[*a*,*j*]xanthene functionality is a key structural element of many biologically active compounds such as antibacterials,[1] antivirals,[2] anti-inflammatory agents[3] and in photodynamic therapy.[4] Xanthene-based compounds have also been investigated for agricultural bactericide activity and some other benzoxanthenes find application in industries such as dyes in laser technology[5] and fluorescent materials for visualization of biomolecules.[6] Xanthene dyes are extracted naturally from soil and plants such as Indigofera longeracemosa.[7] Thus, the synthesis of benzoxanthene derivatives currently is of great interest. Various methods have been reported for the synthesis of benzoxanthenes, including the reaction of β-naphthol with formamide,[8] 2-naphthol-1-methanol[9] and carbon monoxide.[10] However, these methods have many disadvantages such as low yields, the need for a prolonged reaction time, the use of toxic organic solvents, excess reagents and harsh reaction conditions. Because of these drawbacks, the reaction has been improved by mixing β-naphthol with aldehydes in the presence of a catalyst, such as amberlyst,[11] sulfamic acid,[12] $I_2$,[13] $AcOH–H_2SO_4$.[14] These methods also suffer from some disadvantages such as a long reaction time, the use of toxic solvent,[15] special apparatus and the use of toxic catalysts.[13] Thus, the development of a new procedure for the synthesis of dibenzoxanthene derivatives would be highly desirable.

The organic reactions in aqueous media have attracted much attention in synthetic organic chemistry, not only because water is one of the most abundant, cheapest and environmentally friendly solvents but also because water exhibits unique reactivity and selectivity, which is different from those in conventional organic solvents.[16]

Recently Sharpless and co-workers[17] reported the observation that some organic molecules can react on the surface of water and often a very strong enhancement of reaction rates was noticed in this case, particularly when at least one compound involved in these reactions bears a polar group, enabling some degree of solubility (carboxylic ether, amine, etc.,. . .) in water.

As a continuation of our research devoted to the development of green organic chemistry by performing organic transformations under solvent-free conditions,[18] or by using water as the reaction medium[19] herein we report an efficient and green procedure for the synthesis of alkyl- or aryl-14*H*-dibenzo[*a*,*j*]xanthenes in water. The results of the present work show the desired product in excellent yield (Scheme 1).

To study the reaction in water, we tested the reaction of β-naphthol and 4-chlorobenzaldehyde as a simple model substrate in different solvents in the presence

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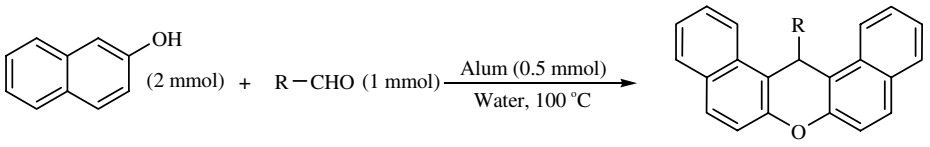


**Scheme 1.**

of $KAl(SO_4)_2{\cdot}12H_2O$ (alum) as an inexpensive and available catalyst. The results are shown in Table 1. It was found that water was a solvent of choice for the reaction and the desired product obtained in high yield in water. Entry 9 shows the effect of water in the condensation of 4-chlorobenzaldehyde and β-naphthol.

After optimizing the conditions, we next examined the generality of this condition to other substrates using β-naphthol and several aromatic and aliphatic aldehydes. The results are summarized in Table 2. Aromatic aldehydes carrying different functional groups were subjected to the reaction and in all cases the desired product synthesized in high yields and short period of time. Another advantage of this method is its efficiency for the high yield synthesis of alkyl- or aryl-14*H*-dibenzo[*a*,*j*]xanthenes from aliphatic aldehydes (Table 2, entries 11,12). Work-up procedure is so simple and includes filtration of mixture to separate the product.[20] The role of water as the reaction medium and its mechanism is not clear. Despite the low solubility of β-naphthol and aldehydes in water, the reaction is accelerated in water and proceeds efficiently in the presence of alum. This one-pot reaction with regard to the sharpless observations[17] might take place at the interface of organic substrates with water in a heterogeneous system. It is worthy to note that vigorous stirring is required for the success of this reaction.

**Table 1.** Solvent effects on the reaction of 4-chlorobenzaldehyde and β-naphthol in the presence of 50 mol% of alum

| Entry | Solvent | Yield (%)[b] | Time (h) |
|---|---|---|---|
| 1 | EtOH | 35 | 24 |
| 2 | MeOH | 40 | 24 |
| 3 | $CH_2Cl_2$ | Trace | 24 |
| 4 | $CHCl_3$ | Trace | 24 |
| 5 | $CH_3CN$ | 20 | 24 |
| 6 | $PhCH_3$ | Trace | 24 |
| 7 | $ClCH_2CH_2Cl$ | 20 | 24 |
| 8 | $H_2O$ | 90 | 4 |
| 9 | —[a] | 60 | 12 |

[a] The reaction was run under solvent-free condition at 100 °C.
[b] Isolated yield.

**Table 2.** Synthesis of alkyl- or aryl-14*H*-dibenzo[*a*,*j*]xanthenes by the reaction of β-naphthol, and aromatic aldehydes in the presence of alum in water

| Entry | R | Time (h) | Yield (%)[a] | Mp[b] |
|---|---|---|---|---|
| 1 | $C_6H_5$ | 3 | 90 | 185–186[14] |
| 2 | 4-$ClC_6H_4$ | 4 | 90 | 289–290[14] |
| 3 | 4-$BrC_6H_4$ | 3 | 89 | 296–298[14] |
| 4 | 4-$FC_6H_4$ | 4 | 91 | 238–240[15] |
| 5 | 4-$O_2NC_6H_4$ | 4 | 90 | 308–310[14] |
| 6 | 4-$H_3CC_6CH_4$ | 3 | 88 | 227–229[14] |
| 7 | 4-$CH_3OC_6H_4$ | 3 | 91 | 203–205[14] |
| 8 | 2-$CH_3OC_6H_4$ | 4 | 90 | 260–261[15] |
| 9 | 2-$O_2NC_6H_4$ | 4 | 88 | 214–215[13b] |
| 10 | 3-$O_2NC_6H_4$ | 3.5 | 90 | 210–212[15] |
| 11 | $CH_3CH_2$ | 4 | 80 | 151–153[15] |
| 12 | $(CH_3)_2CHCH_2$ | 4 | 82 | 112–113[15] |

[a] Isolated yield.
[b] The products were characterized by comparison of their spectroscopic and physical data with those reported in the literature.

**Table 3.** Effect of acidic catalyst on the reaction of 4-chlorobenzhydrazide and β-naphthol in water

| Entry | Catalyst | Time (h) | Yield (%) |
|---|---|---|---|
| 1 | *p*-TsOH | 6 | 60 |
| 2 | $NaHSO_4$ | 12 | 30 |
| 3 | $NaHSO_3$ | 12 | 20 |
| 4 | $H_2SO_4$ | 12 | 25 |
| 5 | Montmorillonite K-10 | 12 | 40 |
| 6 | Silica sulfuric acid | 6 | 75 |
| 7 | $I_2$ | 12 | Trace |
| 8 | $NH_4Cl$ | 12 | 30 |
| 9 | $(NH_4)_2HPO_4$ | 12 | Trace |
| 10 | Alum | 4 | 90 |

To emphasize the effect of catalyst the model reaction between 4-chlorobenzhydrazide and β-naphthol was described and different acidic catalysts were subjected to the reaction. All the reactions were run in the same conditions and similar amounts of catalysts (50 mol%) were used. As can be seen in Table 3 satisfactory results were obtained only with alum (entry 10).

In summary, we have reported a new and effective methodology for the eco-compatible preparation of alkyl- or aryl-14*H*-dibenzo[*a*,*j*]xanthene derivatives. The easy purification of the products by simple filtration and crystallization, short reaction times and the use of water as the solvent suggest good prospects for the applicability of this process. To the best of our knowledge this is the first report on synthesis of alkyl- or aryl-14*H*-dibenzo[*a*,*j*]xanthene derivatives in water.

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20. General procedure for the synthesis of alkyl- or aryl-14*H*-dibenzo[*a*,*j*]xanthenes: A mixture of β-naphthol (2 mmol), aldehyde (1 mmol) and alum (0.5 mmol) in water (3 mL) was heated at 100 °C with stirring for appropriate time (see Table 2). After completion of the reaction confirmed by TLC (eluent: *n*-hexane/ethylacetate 2:1), mixture was cooled to room temperature and the precipitated product was filtered and recrystallized from ethanol.