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Molecular iodine catalyzed synthesis of aryl-14*H*-dibenzo[*a*, *j*]xanthenes under solvent-free condition

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Abstract—Molecular iodine efficiently catalyzes the reaction of β-naphthol and araldehydes on a preheated hot plate at 90–95 °C to give biologically active aryl-14*H*-dibenzo[*a*, *j*]xanthenes under solvent-free condition. The yields are excellent and the reactions go to completion within 15–20 min.

Aryl-14*H*-dibenzo[*a*, *j*]xanthene functionality is a key structural element of many biologically active compounds such as antibacterials,[1] antivirals[2] and 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] Chemical synthesis of xanthenes has been documented by a variety of methods such as reactions including palladium catalyzed cyclisation of polycyclic aryltriflate esters,[8] intermolecular trapping of benzenes by phenols,[9] reaction of aryloxymagnesium halides with triethylorthoformate[10] and using conc. HCl/CH_3COOH or H_3PO_4 from β-naphthol and araldehydes or acetals.[11a,1b] Some of the methods involve tedious experimental procedures such as heating the contents at 125 °C for 6–12 h,[12a] give a mixture of products[12b] and the yields of some of the products are low.[13]

Further, Rajitha et al.[12a] and Ahmad et al.[13] carried out the synthesis of aryl-14*H*-dibenzo[*a*, *j*]xanthenes from araldehydes and β-naphthol in presence of sulfamic acid and *p*-toluenesulfonic acid, respectively, under microwave irradiation, where the chemistry community fails to carryout reactions on a large-scale.

Khosropour et al.[14] reported the synthesis of alkyl-14*H* or aryl-14*H*-dibenzo[*a*,*j*]xanthenes from aldehydes, β-naphthol and *p*-toluenesulfonic acid in 1,2-dichloroethane as solvent and under solvent-free condition. The yields of some of the products were not satisfactory; the reactions require extended time as long as 2.5–24 h. Therefore, practical methods of obtaining aryl-14*H*-dibenzo[*a*,*j*]xanthenes are of great interest in the lead optimization process of drug discovery. To avoid the limitations, we started search for new catalysts, with high catalytic activity, easy availability and short reaction time involving simple work-up procedure, and molecular iodine attracted our attention because molecular iodine is known to catalyze a number of organic transformations.[15a] Recently, we have reported the synthesis of *N*,*N*′-disubstituted ureas/thioureas catalyzed by molecular iodine[15b] and α-iodoacetates from alkenes/ammonium acetate/I_2.[15c]

Results and discussion: In continuation with the search for simple non-hazardous methods for the transformations in organic synthesis using iodine, herein we report a highly versatile and efficient synthesis of aryl-14*H*-dibenzo[*a*, *j*]xanthenes **3** (Scheme 1) from araldehydes **1**, β-naphthol **2** and catalytic amounts of iodine. In a typical reaction, a mixture of **1** and **2** (1:2) equivalents, respectively, and iodine (cat.) was taken in a 50 mL flat-bottomed flask and heated for 15–20 min on a hot plate at 90–95 °C under solvent-free condition to get **3** in excellent yield, the results are summarized in Table 1. These conditions were applied to a series of substituted araldehydes with β-naphthol.[16]

Keywords: β-Naphthol; Araldehydes; Aryl-14*H*-dibenzo[*a*,*j*]xanthenes; Solvent-free condition.

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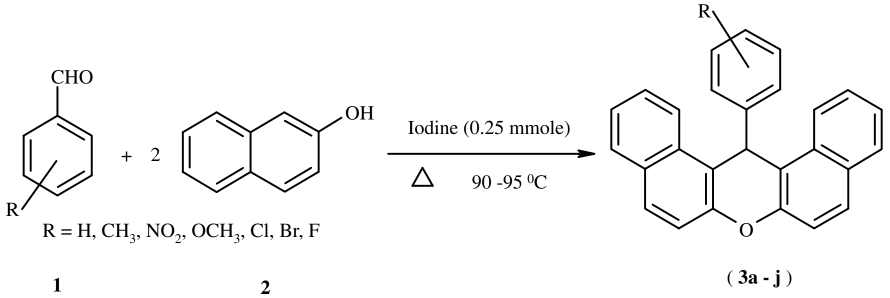

Scheme 1.

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

Entry	R (**1**)	Time (min)	Product[a] (**3**)	Yield[b] (%)	Melting points (°C)	
					Found	Reported
1	H	20	**a**	90	182–3	183
2	4-OCH_3	15	**b**	92	205–7	205
3	4-NO_2	20	**c**	95	310	312
4	2-NO_2	20	**d**	94	214	213
5	4-CH_3	20	**e**	93	230	228
6	3-CH_3	20	**f**	93	198	197–8
7	4-Br	15	**g**	94	296	296
8	4-Cl	15	**h**	93	290	287
9	2-Cl	15	**i**	90	215–16	215
10	4-F	15	**j**	94	236	238

[c] Melting points of compounds are consistent with reported values (Refs. 12a,b,13,14).

[a] All the products are known, characterized by IR, NMR spectral analysis and compared with the authentic samples.

[b] Isolated yields.

To demonstrate the protocol, we selected *p*-anisaldehyde as the model substrate and treated with β-naphthol in the presence of catalytic iodine at 90–95 °C for 15 min to get 14-(4′-methoxyphenyl)-14*H*-dibenzo[*a*, *j*]xanthene in 92% yield (Table 1, entry 2). The interesting feature of the present method of synthesis of aryl-14*H*-dibenzo[*a*, *j*]-xanthenes is that, the substituents OCH_3, Cl, Br, F and NO_2 are unaffected under the reaction condition.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.bmcl.2006.11.009.

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16. Typical procedure for the synthesis of aryl-14H-dibenzo[*a*,*j*]xanthenes: *p*-anisaldehyde (1.36 g, 10 mmol), β-naphthol (2.88 g, 20 mmol) and iodine (0.063 g, 0.25 mmol) were ground well and transferred to a 50 mL flat-bottomed flask and heated on a hot plate at 90–95 °C for 15 min. After complete conversion (monitored on TLC), the system was cooled to room temperature, the mixture was washed with 10% $Na_2S_2O_3$ solution and the separated precipitate was purified by recrystallization from aqueous ethanol to afford 14-(4′-methoxyphenyl)-14*H*-dibenzo[*a*,*j*]xanthene **3b** [(3.68 g, 92%); mp: 205–07 °C; IR (KBr) : 3042, 2924, 1620, 1591,1253, 841, 800 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 3.64$ (s, 3H), 6.56 (s, 1H), 6.75 (d, $J = 9.3$ Hz, 2H), 7.38–7.95 (m, 14H), 8.40 (d, $J = 9.5$ Hz, 2H); ^{13}C NMR (200 MHz, $CDCl_3$): $\delta = 37.7$, 54.0, 114.5, 118.2, 118.6, 124.0, 124.8, 127.3, 130.1, 131.5, 1334.0, 137.9, 149.3, 158.5; Anal. Calcd for $C_{28}H_{20}O_2$: C, 86.57; H, 5.20; Found: C, 86.60; H, 5.19; MS: $m/z = 403$ (M^+)].