

Synthesis of 14-Substituted-14*H*-dibenzo[*a,j*]xanthenes under Solvent-Free Conditions Presence of Etidronic Acid

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A simple and efficient synthesis of 14-substituted-14*H*-dibenzo[*a,j*]xanthenes has been accomplished by the one-pot condensation of β -naphthol and aldehyde under solvent-free conditions in the presence of etidronic acid.

Key Words: Dibenzo[*a,j*]xanthene, β -Naphthol, Etidronic acid, Solvent-free.

INTRODUCTION

Due to the potent biological and therapeutic properties exhibited by various 14-substituted-14*H*-dibenzo[*a,j*]xanthenes¹, there is a continuous interest for novel synthetic methods in this area. The most common methods for the synthesis of 14-substituted-14*H*-dibenzo[*a,j*]xanthenes are the reaction of β -naphthol with aldehydes or acetals in the presence of a catalyst, such as *p*-TSA², sulfamic acid³, AcOH-H₂SO₄⁴, cyanuric chloride⁵, I₂⁶, HClO₄-SiO₂⁷, Yb(OTf)₃⁸, BF₃-SiO₂⁹, LiBr¹⁰, Al(HSO₄)₃¹¹, Dowex-50W¹², NaHSO₄-SiO₂¹³, ceric sulfate¹⁴, ionic liquid¹⁵, K₅CoW₁₂O₄₀·3H₂O¹⁶, NH₄H₂PO₄/SiO₂¹⁷. However, most of these procedures have significant drawbacks such as long reaction times, low yields, harsh reaction conditions, difficult work-up and use of environmentally toxic or expensive reagents or media. Thus, there is still need of a simple and general for the one-pot synthesis of 14-substituted-14*H*-dibenzo[*a,j*] xanthenes.

Etidronic acid (Fig. 1) is a phosphonic acid with mild acidity, is non-volatile and non-corrosive and is soluble in common organic solvents. It is a white crystalline solid with outstanding physical and chemical properties and is a commercially available cheap chemical¹⁸. Its applications as a reaction catalyst in organic syntheses have not yet been fully explored. In this paper, a simple, efficient and environmentally benign synthesis of 14-substituted-14*H*-dibenzo[*a,j*]xanthenes under solvent-free conditions in the presence of etidronic acid is reported (**Scheme-I**).

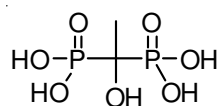
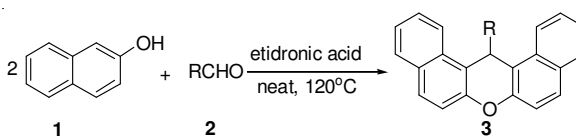


Fig. 1. Etidronic acid



Scheme-I

EXPERIMENTAL

NMR spectra were determined on Bruker AV-300 spectrometer at room temperature using TMS as internal standard, coupling constants (J) were measured in Hz; elemental analysis were performed by a Vario-III elemental analyzer; melting points were determined on a XT-4 binocular microscope and were uncorrected; commercially available reagents were used throughout without further purification unless otherwise stated.

General procedure for the preparation of 3: A mixture of the aldehyde (1 mmol), β -naphthol (2 mmol) and etidronic acid (0.2 mmol) was stirred at 120 °C for the appropriate time according to Table-1. Completion of the reaction was indicated by TLC. The reaction was cooled to room temperature, water was added and the mixture stirred for 5 min. The solid obtained was removed by filtration and recrystallized from ethyl alcohol (**Scheme-I**). All products were characterized by comparison of their physical data and ^1H and ^{13}C NMR data with those of authentic samples.

TABLE-1
PREPARATION OF 14-SUBSTITUTED-14*H*-DIBENZO[*a,j*]XANTHENES
CATALYZED BY ETIDRONIC ACID*

Entry	R	Time (h)	Yield (%)**	m.p. (ref.) (°C)
a	Ph	3.0	92	181-182 (183-185) ¹⁴
b	4-(CH ₃)C ₆ H ₄	3.5	88	225-226 (224-227) ¹⁴
c	4-(MeO)C ₆ H ₄	3.5	89	204-205 (202-204) ¹⁴
d	2-(MeO)C ₆ H ₄	3.5	86	256-257 (258-259) ⁵
e	4-(Cl)C ₆ H ₄	3.0	96	285-286 (286-289) ¹⁴
f	2-(Cl)C ₆ H ₄	3.0	92	213-214 (212-214) ¹⁴
g	4-(Br)C ₆ H ₄	3.0	94	295-296 (297-298) ^{15a}
h	4-(NO ₂)C ₆ H ₄	3.0	93	303-304 (306-308) ¹⁴
i	3-(NO ₂)C ₆ H ₄	3.0	94	208-209 (210-211) ¹⁴
j	2-(NO ₂)C ₆ H ₄	3.0	89	288-289 (290-291) ¹⁴
k	2,4-(Cl) ₂ C ₆ H ₃	4.0	87	250-251 (252-254) ¹⁴
l	3,5-(MeO) ₂ C ₆ H ₃	4.0	85	186-187 (188-189) ¹⁴
m	4-(I)C ₆ H ₄	4.0	90	306-308
n	Naphth-1-yl	4.0	83	200-201 (202-204) ¹⁴
o	Pyrid-4-yl	4.0	85	227-228 (229-230) ^{15a}
p	Et	4.0	82	146-147(148-151) ¹⁴
q	i-Pr	4.0	80	156-157 (155-157) ⁵

*All of the isolated products are known compounds and their spectra and physical data have been reported in the literatures 5, 14, 15a. **Isolated yield.

The spectral data of some new 14-substituted-14*H*-dibenzo[*a,j*]xanthenes are given below:

14-(4-Iodophenyl)-14*H*-dibenzo[*a,j*]xanthene (3m): White solid, m.p. 306-308 °C. IR (KBr, ν_{max} , cm⁻¹): 3432, 3022, 2918, 1635, 1590, 1243, 833, 802. ^1H NMR (CDCl₃, 300 MHz): δ 6.60 (s, 1H, ArCH), 7.32-7.80 (s, 14H, ArH), 8.22 (d, $J = 8.2$ Hz, 2H, ArH). ^{13}C NMR (CDCl₃, 75 MHz): δ 39.8, 116.5, 118.9, 123.2,

125.1, 126.7, 129.6, 129.8, 130.8, 131.6, 131.9, 133.4, 144.0, 150.1. Anal. calcd for C₂₇H₁₇OI: C 66.96, H 3.54; found C 67.12, H 3.34.

RESULTS AND DISCUSSION

To choose optimum conditions, first, the effect of temperature on the rate of the reaction was studied for the preparation of 14-phenyl-14*H*-dibenzo[*a,j*]xanthene from the condensation reaction of β -naphthol (2 mmol) with benzaldehyde (1 mmol) under solvent-free conditions in the presence of 20 mol % etidronic acid (Table-2). At 120 °C, the reaction proceeded smoothly and giving short reaction time and high yield.

TABLE-2
TEMPERATURE OPTIMIZATION FOR THE SYNTHESIS OF
14-PHENYL-14*H*-DIBENZO[*a,j*]XANTHENE

Entry	Temperature (°C)	Time (h)	Yield (%)
1	90	6	67
2	100	6	78
3	110	4	88
4	120	4	91
5	130	4	90
6	140	4	91

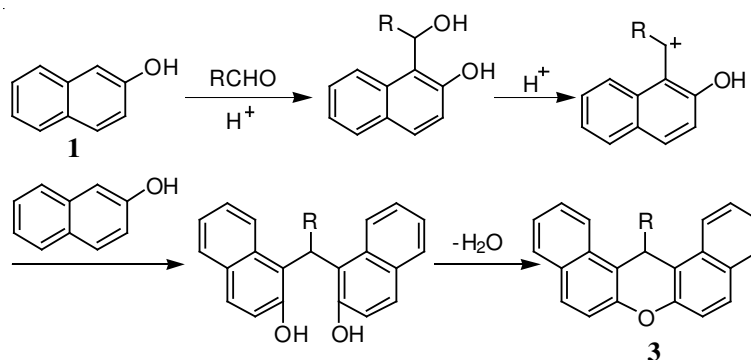
Next, the study set out to determine optimal amount of etidronic acid, the reaction was carried out by varying amount of the catalyst (Table-3). Maximum yield was obtained with 20 mol % etidronic acid. Further increase in amount of the catalyst in the mentioned reaction did not has any significant effect on the product yield.

TABLE-3
AMOUNTS OF CATALYST OPTIMIZATION FOR THE SYNTHESIS OF
14-PHENYL-14*H*- DIBENZO[*a,j*]XANTHENE

Entry	Etidronic acid/mol (%)	Time (h)	Yield (%)
1	0	10	0
2	5	8	56
3	10	6	78
4	15	4	84
5	20	4	91
6	25	4	91
7	30	4	90

Based on the optimized reaction conditions, a variety of aldehyde reacted smoothly with β -naphthol in the presence of 20 mol % of etidronic acid at 120 °C under solvent-free conditions to furnish the corresponding 14-substituted-14*H*-dibenzo[*a,j*]xanthenes in high yields. The reactions were rapid and in most cases 14-substituted-14*H*-dibenzo[*a,j*] xanthenes formation was complete in 5 h with excellent yields.

Concerning the reaction mechanism, we proposed that a carbocation is initially formed, aryl- or alkyl- methanebisnaphthols are then formed in the second step, which then undergo dehydration to give the final product **3** (Scheme-II).



Scheme-II

Conclusion

In conclusion, we have developed a convenient and efficient method for the synthesis of 14-aryl or alkyl-14H-dibenzo[a,j]xanthenes by single-pot condensation of β-naphthol with aromatic or aliphatic aldehydes in the presence of etidronic acid. The simple experimental procedure, solvent-free reaction conditions, utilization of an inexpensive and readily available catalyst, short period of conversion and excellent yields are the advantages of the present method.

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