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Polymer-Supported (Diacetoxyiodo)benzene Mediated Synthesis of Coumaran-3-ones and *cis*-3-Hydroxyflavanone dimethylacetals

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The polymer-supported (diacetoxyiodo)benzene mediated synthesis of coumaran-3-ones and *cis*-3-hydroxy-flavanone dimethylacetals has been described from 2-hydroxyphenyl alkylketones and 2′-hydroxychalcones respectively. These are clean oxidation reactions with moderate to high yield.

Key Words: Polymer, Coumaran-3-ones, *cis*-3-Hydroxy-flavanone dimethylacetals.

INTRODUCTION

(Diacetoxyiodo)benzene has attracted wide interest in view of its utility for a variety of reactions[1]. The easy handling, high selectivity and mild reaction conditions employed utilizing this reagent are of much advantage[2]. The only problem associated with this reagent is the difficult removal of iodobenzene generated during the reaction conditions. In order to overcome this difficulty polymer-supported (diacetoxyiodo)benzene proved to be excellent reagent because of ease of processing as work-up and purification of the product are reduced to simple separation and the polymer may be recovered, regenerated and recycled[3]. Further, the polymer-supported hypervalent iodine reagents has been studied for clean organic synthesis with potential application in combinatorial chemistry[4] as well as in the preparation of isoflavones from 2'-hydroxychalcones[5]. Keeping in view of these significances and our interest in polymer-supported hypervalent iodine reagents[6], we report herein polymer-supported (diacetoxyiodo)benzene mediated synthesis of the coumaran-3-ones and *cis*-3-hydroxyflavanone dimethylacetals from 2-hydroxyphenyl alkylketones and 2'-hydroxychalcones, respectively.

EXPERIMENTAL

The melting points were determined in open capillaries and are uncorrected. FTIR spectra were recorded in KBr on Shimadzu FTIR 8201 spectrophotometer and ^{1}H NMR spectra on Bruker ACF at 300 MHz using $CDCl_3$. Elemental analysis were determined on Elementar Vario EL III.

The polystyrene, 2 % cross linked with divinylbenzene (mw = 2,50,000) was purchased from Aldrich polymer-supported (diacetoxyiodo)benzene (PSDIB) was prepared according to literature procedure[7-9].

Coumaran-3-ones (3): 2-Hydroxyphenyl alkylketone (**1**) (1 mmol) in methanol (10 mL) was added dropwise to a cooled methanolic solution of potassium hydroxide (1.7 g, 3 mmol) over a period of 15 min. PSDIB (1.3 mmol, approximate loading capacity 2.81 mmol/g)) was then added and the reaction mixture was stirred overnight. After the completion of reaction (monitored by TLC), the mixture was filtered to remove the resin (iodopolystyrene) and washed with methanol (5 mL). The filtrate was concentrated under reduced pressure until about half of the methanol was removed, then 10 mL of water was added and the mixture extracted with four portions of dichloromethane. The combined dichloromethane extracts were washed with two 5 mL portions of water and dried with magnesium sulphate. The solvent was evaporated in vacuum and the crude residue was purified by column chromatography.

2a: Oil, yield 38 %; IR (neat): 1743 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 2.33 (s, 3H, CH_3), 3.49 (s, 6H, OCH_3), 6.91 (d, 1H, J = 8.28 Hz, C_7-H), 7.37-7.45 (m, 2H, C_4-H & C_6-H). Anal. Calcd. for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81. Found: C, 63.20; H, 5.77.

2b: Oil (Lit.[10] oil), yield 35 %; IR (neat): 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 3.55 (s, 6H, OCH_3), 7.07-7.13 (m, 2H, C_5-H & C_7-H), 7.62-7.69 (m, 2H, C_4-H & C_6-H).

2c: Oil (Lit.[10] oil), yield 40 %; IR (neat): 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.24 (s, 3H, CH_3), 3.02 (s, 3H, OCH_3), 6.78-6.92 (m, 1H, C_5-H), 6.90 (d, 1H, J = 8.97 Hz, C_7-H), 7.36-7.47 (m, 1H, C_6-H), 7.68 (dd, 1H, J = 8.03 & 1.3 Hz, C_4-H)

***cis*-3-Hydroxyflavanone dimethylacetals (7):** A solution of 2'-hydroxychalcone (**6**) (1 mmol) and potassium hydroxide (3 mmol) in methanol (30 mL) was stirred over a period of 15-20 min at 5-10 °C. The resulting yellow-brown solution was stirred for 6-8 h at room temperature after the addition of PSDIB (1.3 mmol). The reaction mixture was filtered to remove the resin and washed with methanol (5 mL). Excess of the methanol was removed *in vacuo* and the residue was treated with 50 mL of water (50 mL). A yellow solid separated from the solution that was filtered and recrystallized from ethanol.

7a: m.p. 154-156 °C, yield 60 %; IR: 3510 cm^{-1}; ^1H NMR ($CDCl_3$) δ: 1.80 (d, 1H, J = 3.0 Hz, OH), 2.39 (s, 3H, CH_3), 3.24 (s, 3H, $C_{4\beta}$-OCH_3), 3.44 (s, 3H, $C_{4\alpha}$-OCH_3), 4.00 (d, 1H, J = 2.4 Hz, C_3-H), 5.41 (brs, 1H, C_2-H), 6.97 (d, 1H, J = 8.4 Hz, C_8-H), 7.26 (m, 3H, C_7-H, $C_{3'}$-H & $C_{5'}$-H), 7.45 (d, 2H, J =7.8 Hz, $C_{2'}$-H & $C_{6'}$-H), 7.61 (d, 1H, J = 2.4 Hz, C_5-H). Anal. Calcd. for $C_{18}H_{19}O_4Cl$: C, 64.57; H, 5.72. Found: C, 63.68; H, 5.71.

7b: m.p. 144-145 °C (Lit.^{11} 146-147 °C), yield 64 %; IR: 3496 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 1.73 (d, 1H, *J* = 3.9 Hz, O-H), 3.17 (s, 3H, $C_{4\beta}$-OCH_3), 3.36 (s, 3H, $C_{4\alpha}$-OCH_3), 3.98 (d, 1H, *J* = 3.9 Hz, C_3-H), 5.31 (brs, 1H, C_2-H), 6.88 (d, 1H, *J* = 5.7 Hz, C_8-H), 7.19 (dd, 1H, *J* = 2.7 Hz & 5.7 Hz, C_7-H), 7.33 (d, 2H, *J* = 8.4 Hz, $C_{2'}$-H & $C_{6'}$-H), 7.42 (d, 2H, *J* = 8.4 Hz, $C_{3'}$-H & $C_{5'}$-H), 7.53 (d, 1H, *J* = 2.7 Hz, C_5-H).

7c: m.p. 137 °C (Lit.^{11} 137-138 °C), yield 68 %; IR: 3500, 2905, 1645, 1604, 1481, 1454, 1353, 1276, 1238, 1111, 1062, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 1.76 (d, 1H, *J* = 4.0 Hz, OH), 3.23 (s, 3H, $C_{4\beta}$-OCH_3), 3.42 (s, 3H, $C_{4\alpha}$-OCH_3), 4.08 (d, 1H, *J* = 1.2 Hz, C_3-H), 5.42 (brs, 1H, C_2-H), 6.87 (d, 1H, *J* = 9 Hz, C_8-H), 7.23-7.45 (m, 4H, C_7-H, $C_{3'}$-H, $C_{4'}$-H & $C_{5'}$-H), 7.54 (m, 2H, $C_{2'}$-H & $C_{6'}$-H), 7.59 (d, 1H, *J* = 2.7 Hz, C_5-H).

7d: m.p. 140-141 °C, yield 82 %; IR: 3492, 2916, 2833, 1618, 1581, 1517, 1496, 1456, 1292, 1238, 1114, 1058, 1043 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 1.79 (d, 1H, *J* = 4.5 Hz, O-H), 2.34 (s, 3H, C_6-CH_3), 2.38 (s, 3H, $C_{4'}$-CH_3), 3.25 (s, 3H, $C_{4\beta}$-OCH_3), 3.45 (s, 3H, $C_{4\alpha}$-OCH_3), 4.06 (d, 1H, *J* = 3.9 Hz, C_3-H), 5.38 (brs, 1H, C_2-H), 6.92 (d, 1H, *J* = 8.4 Hz, C_8-H), 7.11 (dd, 1H, *J* = 1.5 Hz & 8.4 Hz, C_7-H), 7.24 (d, 2H, *J* = 7.8 Hz, $C_{3'}$-H & $C_{5'}$-H), 7.42 (d, 1H, *J* = 0.9 Hz, C_5-H), 7.46 (d, 2H, *J* = 7.8 Hz, $C_{2'}$-H & $C_{6'}$-H). Anal. Calcd. for $C_{19}H_{22}O_4$: C, 72.59; H, 7.05. Found: C, 71.59 ; H, 7.22.

7e: m.p. 147-148 °C (Lit.^{11} 149-150 °C), yield 65 %; IR: 3467 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 1.84 (d, 1H, *J* = 3.8 Hz, O-H), 233 (s, 3H, C_6-CH_3), 3.24 (s, 3H, $C_{4\beta}$-OCH_3), 3.49 (s, 3H, $C_{4\alpha}$-OCH_3), 4.04 (d, 1H, *J* = 3.8 Hz, C_3-H), 5.36 (bs,1H, C_2-H), 6.97 (d, 1H, *J* = 8.7 Hz, C_8-H), 7.13 (dd, 1H, *J* = 1.5 Hz & 8.4 Hz, C_7-H), 7.36 (d, 1H, *J* = 1.5 Hz, C_5-H), 7.40 (d, 2H, *J* = 8.4 Hz, $C_{2'}$-H & $C_{6'}$-H), 7.52 (d, 2H, *J* = 8.4 Hz, $C_{3'}$-H & $C_{5'}$-H).

7f: m.p. 139-140 °C (Lit.^{11} 139-141 °C), yield 72 %; IR: 3481, 2900, 1610, 1583, 1483, 1458, 1307, 1238, 1110, 1062, 1039 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 1.79 (d, 1H, *J* = 4.2 Hz, OH), 2.39 (s, 3H, $C_{4'}$-CH_3), 3.24 (s, 3H, $C_{4\beta}$-OCH_3), 3.45 (s, 3H, $C_{4\alpha}$-OCH_3), 4.09 (d, 1H, *J* = 3.9 Hz, C_3-H), 5.41 (brs, 1H, C_2-H), 7.00 (m, 2H, C_6-H & C_8-H), 7.25 (d, 2H, *J* = 7.8 Hz, $C_{3'}$-H & $C_{5'}$-H), 7.30 (m, 1H, C_7-H), 7.47 (d, 2H, *J* = 7.8 Hz, $C_{2'}$-H & $C_{6'}$-H), 7.63 (d, 1H, *J* = 7.5 Hz, C_5-H).

7g: m.p. 153-154 °C (Lit.^{11} 155-156 °C), yield 75 %; IR: 3467, 3041, 2966, 2947, 2887, 1608, 1585, 1483, 1456, 1317, 1236, 1130, 1105, 1058, 1035 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 1.82 (d, 1H, *J* = 3.9 Hz, OH), 3.23 (s, 3H, $C_{4\beta}$-OCH_3), 3.44 (s, 3H, $C_{4\alpha}$-OCH_3), 4.07 (d, 1H, *J* = 3.0 Hz, C_3-H), 5.40 (brs, 1H, C_2-H), 7.02 (m, 2H, C_6-H & C_8-H), 7.3 (m, 1H, C_7-H), 7.41 (d, 2H, *J* = 8.4 Hz, $C_{2'}$-H & $C_{6'}$-H), 7.53 (d, 2H, *J* = 8.4 Hz, $C_{3'}$-H & $C_{5'}$-H), 7.62 (dd, 1H, *J* = 8.1 & 1.5 Hz, C_5-H).

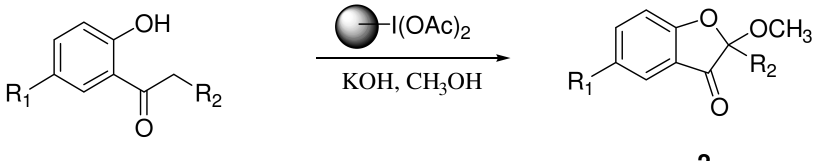
7h: m.p. 125-126 °C (Lit.^{11} 126-127 °C), yield 57 %; IR 3504, 2898, 1612, 1581, 1454, 323, 1232, 1107, 1053, 1029 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ:

1.83 (d, 1H, J = 4.2 Hz, OH), 3.25 (s, 3H, $C_{4\beta}$-OCH_3), 3.45 (s, 3H, $C_{4\alpha}$-OCH_3), 4.12 (d, 1H, J = 2.82 Hz, C_3-H), 5.44 (brs, 1H, C_2-H), 6.97-7.04 (m, 2H, C_6-H & C_8-H), 7.27-7.47 (m, 4H, C_7-H, $C_{3'}$-H, $C_{4'}$-H & $C_{5'}$-H), 7.59 (d, 2H, J = 7.2 Hz, $C_{2'}$-H & $C_{6'}$-H), 7.65 (dd, 1H, J = 7.8 Hz & 1.5 Hz, C_5-H).

Regeneration and reuse of PSDIB from recovered iodopolystyrene: Hydrogen peroxide (30 %, 40 mL) was added drop wise to acetic anhydride (150 mL) at 40 ºC and stirred for another 6 h. To this solution, 8.0 g of 2 % cross-linked polyiodostyrene, which was recovered by simply filtration after the reaction, was added and the solution was stirred at 40 °C for 1 d to give polymer-supported (diacetoxyiodo)benzene. IR (cm^{-1}): 1654, 1500, 1410, 1360, 1280, 1000, 817, 760, 700. It was reused in further reaction and was found to have similar reactivity.

RESULTS AND DISCUSSION

The reaction of 2-hydroxyphenyl aklylketones (**1**) with PSDIB yielded coumaran-3-ones (**2**) in moderate to high yield (**Scheme-I**). After completion of reaction, the product was filtered and purified by column chromatography in some cases. The structure assignment of coumaran-3-ones was based on physical characteristics and spectroscopic (IR and NMR) data. The presence of bands at 1743 cm^{-1} in IR spectrum were due to C=O *str.* in **2a** and there was no band due to OH group. In ^1H NMR spectrum of **2a**, the methyl group resonated at δ 2.33 and the methoxy group at δ 3.49 The complete assignment of other protons was found to be in agreement with the structure (**2a**) and are presented in experimental.



1

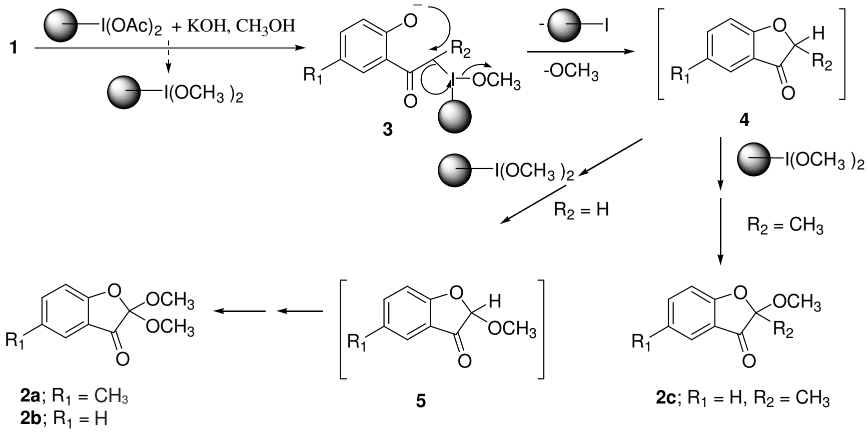
1a; R_1 = CH_3, R_2 = H
1b; R_1 = R_2 = H
1c; R_1 = H, R_2 = CH_3

2

2a; R_1 = CH_3, R_2 = OCH_3
2b; R_1 = H, R_2 = OCH_3
2c; R_1 = H, R_2 = CH_3

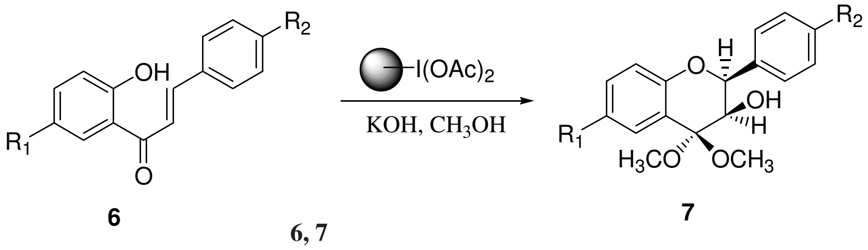
Scheme-I

The probable mechanism consists in firstly attack of enolate of **1** on $PSI(OMe)_2$ (generated *in situ*) resulting in the formation of intermediate (**3**) that underwent cyclization with the elimination of iodopolystyrene generating intermediate coumaran-3-ones (**4**). The coumaran-3-ones (**4**) are not isolable and they went further oxidation to produce **2a** and **2b** *via* the intermediacy of **5**. However, **2c** was produced directly from **4**.



Scheme-II

The reaction of 2'-hydroxychalcones (**6**) with PSDIB in methanol and potassium hydroxide furnished the corresponding *cis*-3-hydroxyflavanone dimethylacetals (**7**) in moderate to good yield (**Scheme-III**). The products were filtered and purified by crystallization. The structure assignment of *cis*-3-hydroxyflavanone dimethylacetals (**7**) was based on physical and spectroscopic (IR and NMR) data. The presence of band at 3510 cm^{-1} in the IR spectrum was due to hydroxyl group in **7a** and there was no band due to carbonyl group. In ^{1}H NMR spectrum of **7a**, the hydroxyl and methyl protons resonated at δ 1.80 and 2.39, respectively, whereas two methoxy group protons appeared at δ 3.24 and 3.44. The doublet at δ 4.00 and broad

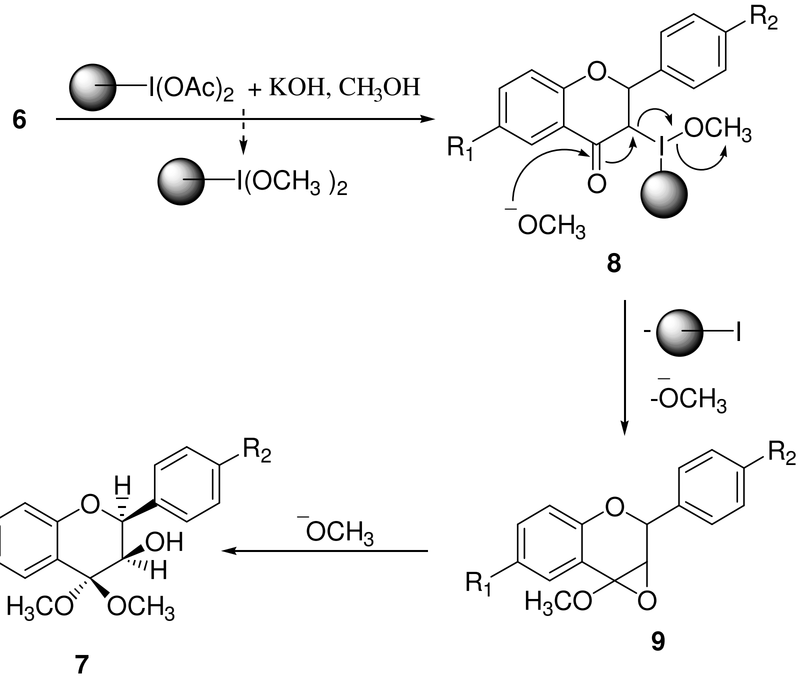


6, 7
a; $R_1 = Cl$, $R_2 = CH_3$
b; $R_1 = R_2 = Cl$
c; $R_1 = Cl$, $R_2 = H$
d; $R_1 = R_2 = CH_3$
e; $R_1 = CH_3$, $R_2 = Cl$
f; $R_1 = H$, $R_2 = CH_3$
g; $R_1 = H$, $R_2 = Cl$
h; $R_1 = R_2 = H$

Scheme-III

singlet δ 5.41 assigned to C_3-H and C_2-H, respectively were helpful in assigning the cis geometry of the product[12]. The complete assignment of other protons was found to be in agreement with the structure (**7a**) and are presented in experimental. The similar trend of cis geometry was also observed in all the compounds (**7**) (vide experimental).

The probable mechanism involves initial formation of cyclic intermediate (**8**) from **6** and PSDIB that underwent reductive elimination of iodopolystyrene resulting in the formation of epoxide intermediate (**9**). The methoxide ion opens up the epoxide ring of **9** thus producing the desired product (**7**) (**Scheme-IV**).



Scheme-IV

The use of polymer-supported (diacetoxyiodo)benzene (PSDIB) is advantageous over the use of simple DIB where removal of iodobenzene after completion of reaction is little problematic. PSDIB utilized in these reactions can be regenerated back by treatment of recovered iodopolystyrene with peracetic acid.

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