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Molecular Iodine Mediated Regioselective Synthesis of Pyranocoumarins and Bis-Fused Benzo-2*H*-pyran Derivatives

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Abstract: A simple and straightforward approach for the regioselective synthesis of pyranocoumarin and bis-fused benzo-2*H*-pyran derivatives using mild, easy to handle, and cheaper molecular iodine mediated heterocyclization is described.

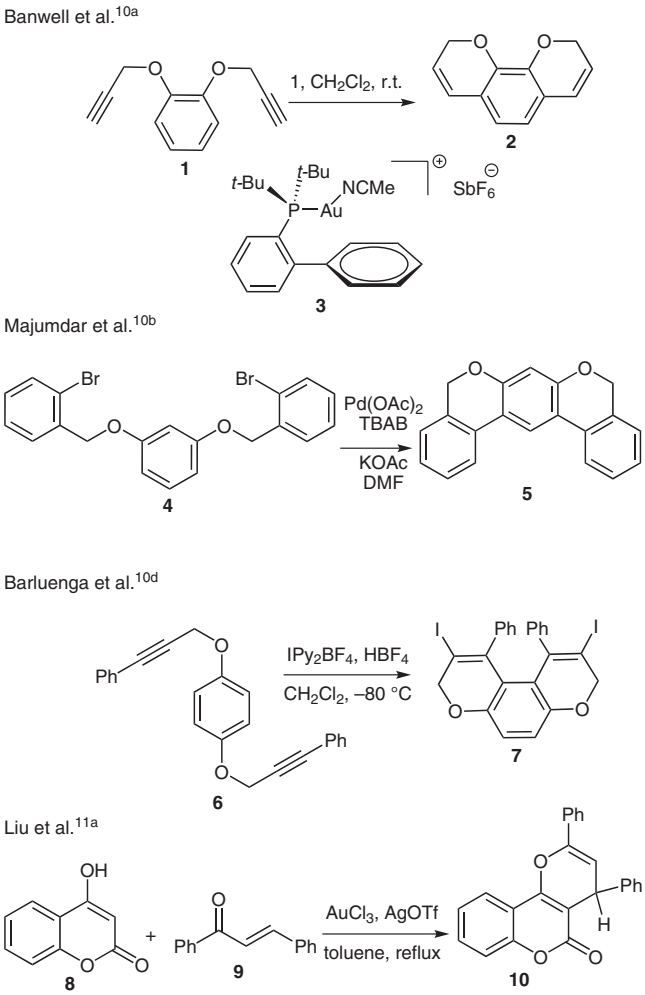
Key words: molecular iodine, 6-*endo*-dig, electrophilic cylization, bis-fused benzo-2*H*-pyrans, pyranocoumarins

2*H*-Benzopyrans or 2*H*-chromenes represent the structural units of a variety of biologically important compounds.[2] Chroman derivatives are known to possess various useful biological activities, such as antioxidant,[3] anticonvulsion,[4] anti-estrogen,[5] and neuroprotection.[6] On the other hand, pyranocoumarin and pyranopyran derivatives are also important class of heterocycles. Their structural motif is found widely in natural products and in many synthetic molecules.[7] They exhibit biological activities including antifungal, anticancer, insecticidal, anti-inflammatory, anti-HIV, and antibacterial activities (Figure 1).[8]

Because of their biological and pharmaceutical importance much attention has been paid to the isolation and synthesis of 2*H*-pyrans fused with both benzene and coumarin rings.[9] It is surprising that only few examples of bis-fused benzopyran derivatives are known. Different research groups have utilized either metal-catalyzed intramolecular cyclization strategies using $AuCl_3$, $Pd(OAc)_2$ as catalysts or iodocyclization reaction using IPy_2BF_4-HBF_4 catalytic system.[10] On the other hand, pyranocoumarins and pyranopyran derivatives have been synthesized by using gold(III)-catalyzed tandem conjugate addition/annulation reaction, ytterbium triflate-catalyzed reactions, and multicomponent reactions (Scheme 1).[11]

Therefore, it is apparent that synthesis of pyranocoumarins, pyranopyrans, and benzo-2*H*-pyran derivatives are very important. Thus, search for an alternative protocol that is easy to handle and also uses a cheaper reagent is always welcome. In this respect, molecular iodine-mediated heterocyclization can be a useful alternative for the synthesis of benzo-2*H*-pyran derivatives. This is because iodocyclization offers an easy access to the complex molecules that are not always accessible by the usual organometallic reagents.[12,13] A few attempts were made to synthesize 2*H*-benzopyran derivatives[14] utilizing molecular iodine-mediated heterocyclization, but the synthesis of bis-fused 2*H*-benzopyrans is rare. Moreover, the growing importance of pyranocoumarin derivatives also demands an easy route for their effective syntheses. Therefore, all these findings inspired us to undertake a detailed study on the molecular iodine-mediated intramolecular heterocyclization to access pyranocoumarin and bis-fused 2*H*-benzopyran derivatives. Herein we report our results.

The required precursors **13a–c** for this study were synthesized in 72–77% yields from the substrates **12** by the reaction with various *p*-substituted iodobenzenes. The



Scheme 1 Literature reports on 2*H*-pyrans fused with both benzene and coumarin rings

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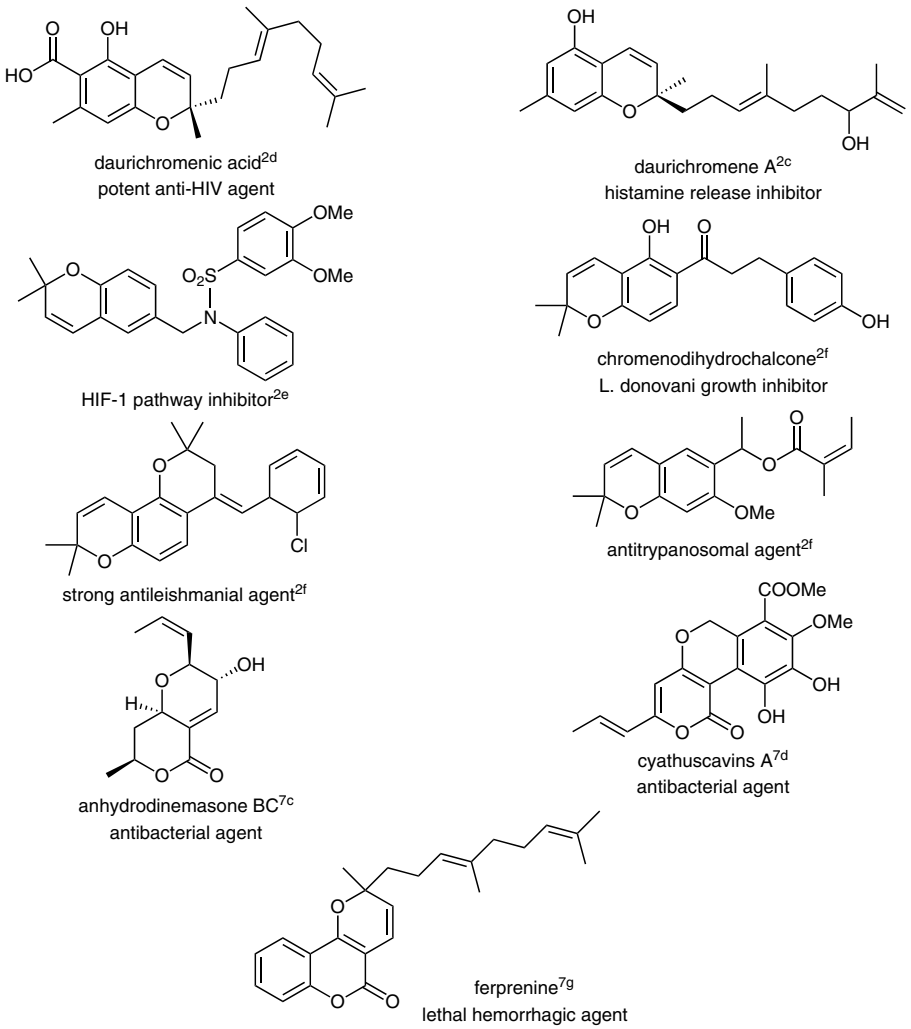
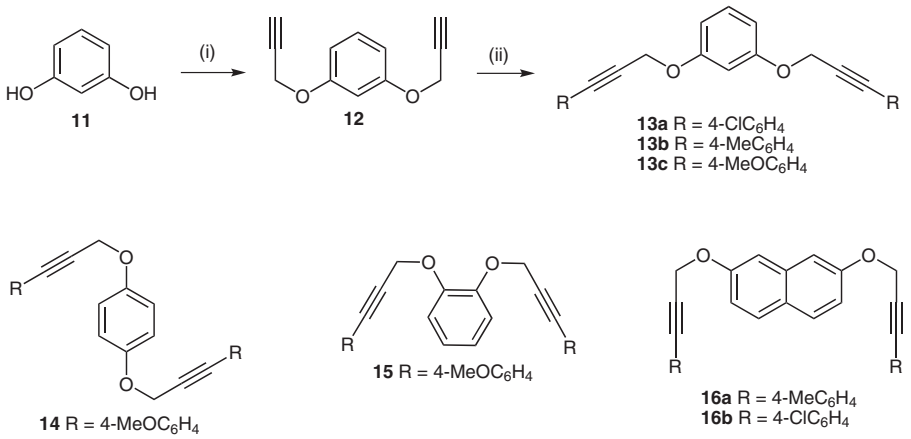


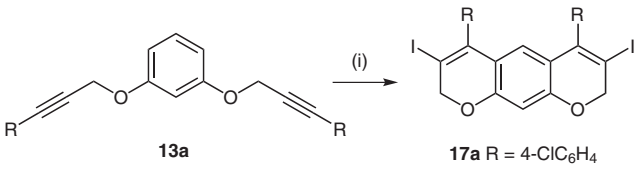
Figure 1 Some biologically active 2*H*-benzopyran, pyranopyran, and pyranocoumarin derivatives

reactions were carried out in the presence of $Pd(PPh_3)_2Cl_2$ as catalyst and copper(I) iodide as co-catalyst in anhydrous triethylamine–DMF (1:4) as mixed solvent at room temperature for three hours. The O-propargylated compound **12** was in turn prepared by refluxing resorcinol **11** with propargyl bromide in acetone in the presence of anhydrous K_2CO_3. Other precursors **14**, **15**, and **16a**,**b** were prepared accordingly starting from hydroquinone, catechol, and 2,7-dihydroxynaphthol, respectively (Scheme 2).



Scheme 2 Preparation of propargyl ethers. *Reagents and conditions*: (i) propargyl bromide, acetone, K_2CO_3, NaI, reflux; (ii) *p*-substituted iodobenzene, $Pd(PPh_3)_2Cl_2$, CuI, DMF–Et_3N, r.t.

The iodocyclization reaction was performed with the compound **13a**, molecular iodine (2 equiv), and $NaHCO_3$ (2 equiv) at room temperature in anhydrous acetonitrile for six hours to give the bis-fused benzo-2*H*-pyran derivative **17a** in 65% yield. The reaction occurred by a 6-*endo*-dig mode of cyclization. The 5-*exo*-dig cyclized product was not obtained (Scheme 3).



Scheme 3 Preparation of **17a**. *Reagents and conditions*: (i) I_2, $NaHCO_3$, MeCN, r.t.

The product **17a** was characterized by its spectral analysis. The structure was confirmed from the analysis of its single crystal X-ray diffraction[15] data (Figure 2). It is interesting to note that the reaction is regioselective and gave only the linearly cyclized product **17a**.

Optimization experiments were carried out with a view to improve the yield of the products. By varying the amounts of both the iodine and base it was found that 3 equivalents of iodine and 3 equivalents of $NaHCO_3$ were optimum and the yield of **17a** was unexpectedly increased to 90%. Further increase of the amount of $NaHCO_3$ (4 equiv) and iodine (4 equiv) did not give any better result. $NaHCO_3$ was found to be more effective compared to other bases like K_2CO_3, Na_2CO_3, etc. for the completion of the reaction. Dichloromethane or methanol gave lower yields of the product. On the basis of our observations, the optimized conditions for the above reaction is I_2 (3 equiv), $NaHCO_3$ (3 equiv), MeCN, r.t., six hours, and the results are summarized in Table 1.

Table 1 Optimization of I_2-Mediated Reactions

Entry	Electrophile (equiv)	Base (equiv)	Solvent	Product	Yield (%)[a]
1	I_2 (2)	$NaHCO_3$ (2)	MeCN	**17a**	65
2[b]	**I_2 (3)**	**$NaHCO_3$ (3)**	**MeCN**	**17a**	**90**
3	I_2 (4)	$NaHCO_3$ (4)	MeCN	**17a**	90
4	I_2 (3)	K_2CO_3 (3)	MeCN	**17a**	35
5	I_2 (3)	$NaHCO_3$ (3)	CH_2Cl_2	**17a**	25
6	I_2 (3)	Na_2CO_3 (3)	MeCN	**17a**	50
7	I_2 (3)	$NaHCO_3$ (3)	MeOH	**17a**	45

[a] Isolated yields.
[b] Optimized reaction conditions.

With the optimized reaction conditions in hand, the other substrates **13b**,**c**, **14**, **15**, and **16a**,**b** were treated similarly to afford the bis-fused 2*H*-benzopyran and naphthopyran derivatives **17b**,**c**, **18**, **19**, and **20a**,**b** in 68–85% and 62, 80% yield, respectively (Table 2).

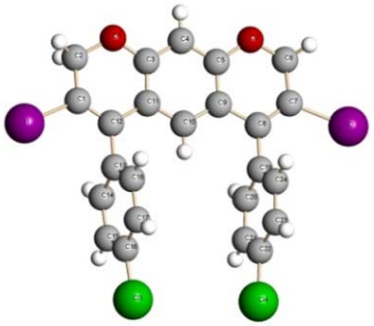
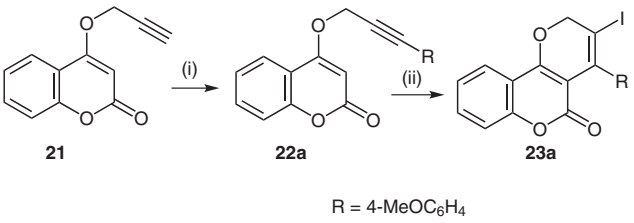


Figure 2 ORTEP diagram of the compound **17a**

After achieving the synthesis of the bis-fused iodocyclized products, the reaction was extended to the readily available starting material, 4-hydroxycoumarin to accomplish the synthesis of pyranocoumarin derivatives.

For this purpose, a number of starting materials **22a**–**d** were prepared in moderate to good yields by the Sonogashira coupling reaction of **21** with iodobenzene derivatives. The reactions were performed in the presence of $Pd(PPh_3)_2Cl_2$ as catalyst and copper(I) iodide as co-catalyst in a mixture of anhydrous triethylamine and DMF (1:4) as mixed solvent at room temperature for five hours. The substrate **22a** was treated under the optimized reaction conditions (Table 1) to give the pyranocoumarin derivative **23a** in 65% yield (Scheme 4).

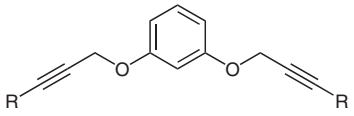
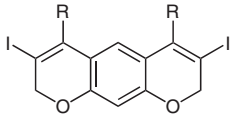
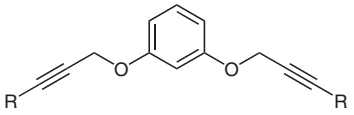
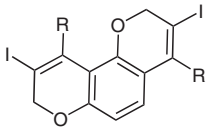
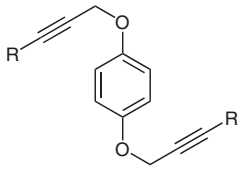
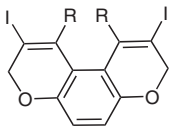
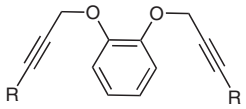
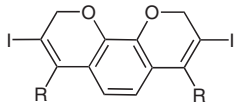
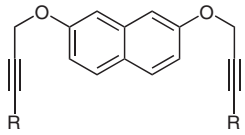
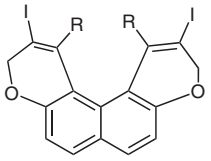
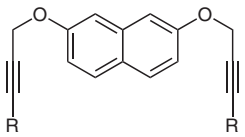
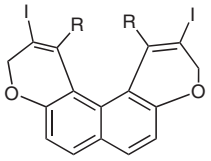


Scheme 4 Preparation of pyranocoumarin derivative **23a**. *Reaction conditions*: (i) *p*-substituted iodobenzene, $Pd(PPh_3)_2Cl_2$, CuI, DMF–Et_3N, reflux; (ii) I_2, $NaHCO_3$, MeCN, r.t., 6 h.

Detailed experiments were carried out by changing solvents and bases. It was found that the optimized reaction conditions stated in Table 1 is also suitable for the above reaction (Scheme 4). The other substrates **22b**–**d** were also subjected to react under the optimized conditions to afford the cyclized products **23b**–**d** in 55–72% yields (Table 3).

Here it should be noted that iodobenzenes containing Me, Cl, and NO_2 substituents do not undergo iodocyclization reaction. In these cases, only iodine-addition products

Table 2 Synthesis of Bis-Fused Benzo-2*H*-pyran Derivatives

Starting material	R	Product[a]	Yield (%)
 **13b**	4-MeC_6H_4	 **17b**	85
 **13c**	4-$MeOC_6H_4$	 **17c**	80
 **14**	4-$MeOC_6H_4$	 **18**	70
 **15**	4-$MeOC_6H_4$	 **19**	68
 **16a**	4-MeC_6H_4	 **20a**	80
 **16b**	4-ClC_6H_4	 **20b**	62

[a] Reaction conditions: I_2 (3 equiv), $NaHCO_3$ (3 equiv), MeCN, r.t.

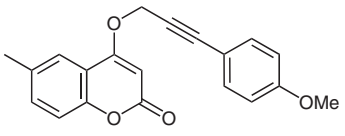
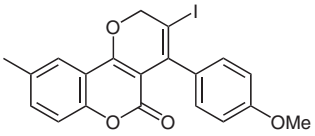
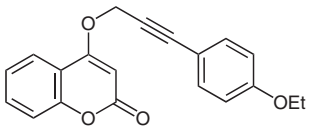
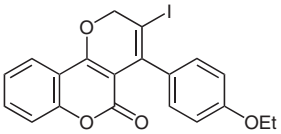
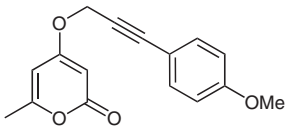
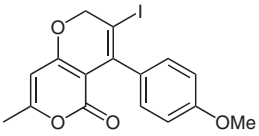
were obtained as the only isolable products. In contrast, the iodobenzenes containing *p*-methoxy and *p*-ethoxy groups, that is, strong electron-donating groups, reacted efficiently to give the desired cyclized products.

From the above discussion it is clear that the reaction conditions described above are simple and convenient compared to other available methods. They avoid the use of complex and relatively costlier reagents like palladium, ytterbium, gold, etc. and the reactions are carried out at ambient temperature.

In conclusion, the protocol reported here provides an operationally simple method for effective iodocyclization reaction. These reactions are cost effective and proceed under very mild conditions to give a number of important heterocyclic motifs including pyranocoumarins and bis-fused 2*H*-benzopyrans expeditiously from readily accessible starting materials. Moreover, during the reaction the iodine atom is incorporated in the cyclized products that offers scope for further modification.

Melting points were determined in an open capillary and are uncorrected. IR spectra were recorded on a Perkin-Elmer L 120-000A spectrometer on KBr disks. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-400 spectrometer in $CDCl_3$ with TMS as internal standard. CHN analyses were recorded on a 2400 series II CHN analyzer (Perkin-Elmer). DMF was sequentially dried (3 ×) over freshly activated 4 Å molecular sieves and Et_3N was dried by keeping overnight over anhydrous CaH_2 and then distilled after 2 h at reflux. Silica gel (60–120 mesh and 230–400 mesh, Spectrochem, India) were used for chromatographic separation. Silica gel G and silica gel GF-254 (Spectrochem, India) were used for TLC analyses.

Table 3 Synthesis of Pyranocoumarin and Pyranopyran Derivatives

Starting material	Product[a]	Yield (%)
 **22b**	 **23b**	68
 **22c**	 **23c**	72
 **22d**	 **23d**	55

[a] Reaction conditions: I_2 (3 equiv), $NaHCO_3$ (3 equiv), MeCN, r.t.

Petroleum ether (PE) refers to the fraction boiling between 60–80 °C.

Propargyl Ethers 13a–c, 14, 15, and 16a,b; Compound 13a; Typical Procedure

A mixture of compound **12** (300 mg, 1.6 mmol), *p*-chloroiodobenzene (920 mg, 3.9 mmol), anhydrous Et_3N (2 mL), $Pd(PPh_3)_2Cl_2$ (34 mg, 3 mol%), and CuI (9 mg, 3 mol%) was stirred in anhydrous DMF (8 mL) at r.t. for 3 h. Then, the reaction mixture was diluted to 30 mL with CH_2Cl_2. The organic phase was washed successively with H_2O (3 × 15 mL) and brine (15 mL), and dried (Na_2SO_4). The solvent was removed under reduced pressure and the crude product was purified by silica gel (60–120 mesh) column chromatography using EtOAc–PE (1:19) as an eluent to give the solid compound **13a**; yield: 505 mg (77%); colorless solid; mp 118–119 °C.

IR (KBr): 1608, 2237, 2845 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.88 (s, 4 H, OCH_2), 6.66–6.70 (m, 3 H, ArH), 7.22–7.28 (m, 5 H, ArH), 7.35 (d, *J* = 8.4 Hz, 4 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 56.7, 84.7, 86.1, 102.5, 107.9, 120.7, 128.7, 130.0, 133.1, 134.8, 159.0.

MS (ESI): *m*/*z* = 428.92 $[M + Na]^+$, 430.90 $[M + Na + 2]^+$, 432.90 $[M + Na + 4]^+$.

Anal. Calcd for $C_{24}H_{16}Cl_2O_2$: C, 70.77; H, 3.96. Found: C, 70.72; H, 3.88.

13b

Yield: 445 mg (75%); colorless solid; mp 112–114 °C.

IR (KBr): 1614, 2230, 2860 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.33 (s, 6 H, CH_3), 4.89 (s, 4 H, OCH_2), 6.67 (dd, *J* = 8.4, 2.4 Hz, 2 H, ArH), 6.72 (d, *J* = 2.0 Hz, 1 H, ArH), 7.09 (d, *J* = 8.0 Hz, 4 H, ArH), 7.22 (t, *J* = 8.4 Hz, 1 H, ArH), 7.33 (d, *J* = 8.0 Hz, 4 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5, 56.9, 83.1, 87.4, 102.5, 107.9, 119.2, 129.0, 129.9, 131.8, 138.8, 159.1.

HRMS (ESI): *m*/*z* calcd for $C_{26}H_{22}O_2$: 389.1517 $[M + Na]^+$; found: 389.1518 $[M + Na]^+$.

13c

Yield: 460 mg (72%); colorless solid; mp 100–101 °C.

IR (KBr): 1604, 2227, 2840 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.79 (s, 6 H, OCH_3), 4.88 (s, 4 H, OCH_2), 6.66 (dd, *J* = 8.4 Hz, 2.0 Hz, 2 H, ArH), 6.72 (d, *J* = 2.0 Hz, 1 H, ArH), 6.80 (d, *J* = 8.8 Hz, 4 H, ArH), 7.23 (t, *J* = 8.4 Hz, 1 H, ArH), 7.37 (d, *J* = 8.8 Hz, 4 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.3, 56.9, 82.4, 87.2, 102.5, 107.8, 113.9, 114.3, 129.9, 133.4, 159.1, 159.9.

Anal. Calcd for $C_{26}H_{22}O_4$: C, 78.37; H, 5.57. Found: C, 78.49; H, 5.39.

14

Yield: 405 mg (63%); colorless solid; mp 130–131 °C.

IR (KBr): 1602, 2230, 2855 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.80 (s, 6 H, OCH_3), 4.85 (s, 4 H, OCH_2), 6.81 (d, *J* = 8.8 Hz, 4 H, ArH), 6.99 (s, 4 H, ArH), 7.37 (d, *J* = 8.8 Hz, 4 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.3, 57.5, 57.6, 82.8, 87.1, 113.9, 114.4, 116.0, 116.1, 116.4, 133.3, 152.0, 152.6, 159.8.

Anal. Calcd for $C_{26}H_{22}O_4$: C, 78.37; H, 5.57. Found: C, 78.51; H, 5.42.

15

Yield: 450 mg (70%); colorless solid; mp 92–93 °C.

IR (KBr): 1604, 2224, 2836 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.79 (s, 6 H, OCH_3), 4.98 (s, 4 H, OCH_2), 6.80 (d, *J* = 8.8 Hz, 4 H, ArH), 6.97 (dd, *J* = 6.0, 4.0 Hz, 2 H, ArH), 7.14 (dd, *J* = 6.0, 3.6 Hz, 2 H, ArH), 7.34 (d, *J* = 8.8 Hz, 4 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.3, 57.8, 82.7, 87.4, 113.9, 114.0, 114.5, 115.0, 121.9, 133.3, 147.9, 159.8.

Anal. Calcd for $C_{26}H_{22}O_4$: C, 78.37; H, 5.57. Found: C, 78.29; H, 5.68.

16a
Yield: 290 mg (55%); yellow solid; mp 132–134 °C.

IR (KBr): 1625, 2233, 2921 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.33 (s, 6 H, CH_3), 5.01 (s, 4 H, OCH_2), 7.07–7.11 (m, 6 H, ArH), 7.25 (s, 2 H, ArH), 7.32 (d, *J* = 7.6 Hz, 4 H, ArH), 7.69 (d, *J* = 8.8 Hz, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5, 56.8, 83.1, 87.5, 107.1, 116.6, 119.2, 124.9, 129.1, 129.2, 131.7, 135.6, 138.8, 156.4.

Anal. Calcd for $C_{30}H_{24}O_2$: C, 86.51; H, 5.81. Found: C, 86.79; H, 5.88.

16b
Yield: 320 mg (55%); yellow solid; mp 71–72 °C.

IR (KBr): 1629, 2228, 2923 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$):δ = 5.01 (s, 4 H, OCH_2), 7.10 (dd, *J* = 8.8, 2.4 Hz, 2 H, ArH), 7.22–7.24 (m, 6 H, ArH), 7.35 (d, *J* = 8.4 Hz, 4 H, ArH), 7.70 (d, *J* = 8.8 Hz, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 56.6, 84.8, 86.2, 107.0, 116.6, 120.7, 125.0, 128.7, 129.4, 133.0, 134.8, 135.5, 156.3.

Anal. Calcd for $C_{28}H_{18}Cl_2O_2$: C, 73.53; H, 3.97. Found: C, 73.37; H, 3.88.

Bis-Fused Benzo-2*H*-pyran Derivatives 17a–c, 18, 19, and 20a,b; Compound 17a; Typical Procedure
A mixture of compound **13a** (100 mg, 0.24 mmol), molecular iodine (183 mg, 0.72 mmol), and anhydrous $NaHCO_3$ (60 mg, 0.72 mmol) was stirred in anhydrous MeCN (10 mL) at r.t. for 6 h. Then, CH_2Cl_2 (50 mL) was added to the reaction mixture. The organic phase was washed successively with 10% aq $Na_2S_2O_3$ (15 mL), H_2O (15 mL), and brine (15 mL), and dried (Na_2CO_3). The solvent was removed under reduced pressure and the crude product was purified by silica gel (230–400 mesh) column chromatography using PE–EtOAc (9.7:0.3) as eluent to give the solid product **17a**; yield: 145 mg (90%); colorless solid; mp 176–177 °C.

IR (KBr): 1612, 2831 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.00 (s, 4 H, OCH_2), 5.70 (s, 1 H, ArH), 6.36 (s, 1 H, ArH), 6.90 (d, *J* = 8.4 Hz, 4 H, ArH), 7.25 (d, *J* = 8.4 Hz, 4 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 75.4, 92.1, 113.8, 118.9, 125.4, 130.6, 131.8, 140.9, 141.4, 159.3.

MS (ESI): *m*/*z* = 658.62 $[M + H]^+$, 660.71 $[M + H + 2]^+$.

HRMS (ESI): *m*/*z* calcd for $C_{24}H_{14}Cl_2I_2O_2$: 658.8538 $[M + H]^+$; found: 658.8500 $[M + H]^+$.

17b
Yield: 145 mg (85%); colorless solid; mp 192–193 °C.

IR (KBr): 1609, 2838 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.32 (s, 6 H, CH_3), 5.00 (s, 4 H, OCH_2), 5.80 (s, 1 H, ArH), 6.34 (s, 1 H, ArH), 6.84 (d, *J* = 8.0 Hz, 4 H, ArH), 7.03 (d, *J* = 8.0 Hz, 4 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 75.1, 86.4, 103.3, 118.0, 125.2, 128.7, 128.9, 136.2, 137.4, 141.2, 154.6.

MS (ESI): *m*/*z* = 640.73 $[M + Na]^+$.

Anal. Calcd for $C_{26}H_{20}I_2O_2$: C, 50.51; H, 3.26. Found: C, 50.68; H, 3.18.

17c
Yield: 130 mg (80%); colorless solid; mp 168–170 °C.

IR (KBr): 1602, 2847 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.85 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 4.35 (s, 2 H, OCH_2), 4.93 (s, 2 H, OCH_2), 6.38 (d, *J* = 8.4 Hz, 1 H, ArH), 6.52 (d, *J* = 8.4 Hz, 1 H, ArH), 6.91–6.95 (m, 4 H, ArH), 7.05 (d, *J* = 8.0 Hz, 2 H, ArH), 7.12 (d, *J* = 8.0 Hz, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.2, 74.1, 75.6, 87.9, 90.0, 109.1, 113.0, 113.8, 114.1, 120.2, 127.6, 129.6, 130.6, 132.1, 135.2, 139.3, 141.2, 149.2, 155.8, 158.7, 159.3.

Anal. Calcd for $C_{26}H_{20}I_2O_4$: C, 48.02; H, 3.10. Found: C, 48.17; H, 2.96.

18
Yield: 115 mg (70%); colorless solid; mp 188–189 °C.

IR (KBr): 1602, 2837 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.85 (s, 6 H, OCH_3), 4.69 (d, *J* = 12.8 Hz, 2 H, OCH_aH_b), 4.94 (d, *J* = 12.8 Hz, 2 H, OCH_aH_b), 6.57 (d, *J* = 8.8 Hz, 4 H, ArH), 6.64 (d, *J* = 8.8 Hz, 4 H, ArH), 6.97 (s, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.3, 75.1, 92.6, 113.5, 114.0, 125.0, 130.5, 131.7, 141.2, 147.6, 159.4.

MS (ESI): *m*/*z* = 650.73 $[M + H]^+$.

Anal. Calcd for $C_{26}H_{20}I_2O_4$: C, 48.02; H, 3.10. Found: C, 48.21; H, 3.01.

19
Yield: 110 mg (68%); yellow solid; mp 158–159 °C.

IR (KBr): 1608, 2831 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.83 (s, 6 H, OCH_3), 5.12 (s, 4 H, OCH_2), 6.09 (s, 2 H, ArH), 6.91 (d, *J* = 8.4 Hz, 4 H, ArH), 7.07 (d, *J* = 8.4 Hz, 4 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.2, 75.4, 92.1, 113.8, 118.9, 125.4, 130.6, 131.8, 140.9, 141.4, 159.3.

MS (ESI): *m*/*z* = 672.71 $[M + Na]^+$.

Anal. Calcd for $C_{26}H_{20}I_2O_4$: C, 48.02; H, 3.10. Found: C, 48.16; H, 3.13.

20a
Yield: 130 mg (80%); yellow solid; mp 162–163 °C.

IR (KBr): 1615, 2932 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.31 (s, 6 H, CH_3), 3.57 (d, *J* = 12.4 Hz, 2 H, OCH_aH_b), 4.65 (d, *J* = 12.4 Hz, 2 H, OCH_aH_b), 6.93 (d, *J* = 8.8 Hz, 2 H, ArH), 7.64 (d, *J* = 8.4 Hz, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 76.9, 79.5, 113.9, 120.8, 125.8, 127.4, 130.0, 131.2, 136.8, 137.1, 142.4, 156.7.

MS (ESI): *m*/*z* = 669.07 $[M + H]^+$, 691.07 $[M + Na]^+$.

Anal. Calcd for $C_{30}H_{22}I_2O_2$: C, 53.92; H, 3.32. Found: C, 54.01; H, 3.41.

20b
Yield: 95 mg (62%); yellow solid; mp 194–195 °C.

IR (KBr): 1603, 2962 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.57 (d, *J* = 12.4 Hz, 2 H, OCH_aH_b), 4.67 (d, *J* = 12.8 Hz, 2 H, OCH_aH_b), 6.89 (d, *J* = 8.8 Hz, 2 H, ArH), 7.60 (d, *J* = 8.8 Hz, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.7, 76.9, 80.6, 114.3, 120.1, 125.8, 127.0, 129.4, 131.8, 133.4, 138.0, 141.3, 157.0.

HRMS (ESI): *m*/*z* calcd for $C_{28}H_{16}Cl_2I_2O_2$: 708.8695 $[M + H]^+$, 710.8695 $[M + H + 2]^+$; found: 708.8687 $[M + H]^+$, 710.8807 $[M + H + 2]^+$.

Propargyl Ethers 22a–d; Compound 22a; Typical Procedure
A mixture of compound **21** (300 mg, 1.50 mmol), *p*-methoxyiodobenzene (1.80 mmol), anhydrous Et_3N (2 mL), $Pd(PPh_3)_2Cl_2$ (3 mol%), and CuI (3 mol%) was stirred in anhydrous DMF (8 mL) at r.t. for 5 h. Then, the reaction mixture was diluted to 70 mL with

CH_2Cl_2. The organic phase was washed successively with H_2O (3 × 25 mL) and brine (25 mL), and dried (Na_2SO_4). The solvent was removed under reduced pressure and the crude product was purified by silica gel (60–120 mesh) column chromatography using EtOAc–PE (1:19) as eluent to give compound **22a**; yield: 350 mg (76%); yellow solid; mp 120–122 °C.

IR (KBr): 1728, 2232, 2931 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.82 (s, 3 H, OCH_3), 5.09 (s, 2 H, OCH_2), 5.93 (s, 1 H, ArH), 6.84 (d, *J* = 8.4 Hz, 2 H, ArH), 7.29–7.34 (m, 2 H, ArH), 7.40 (d, *J* = 8.4 Hz, 2 H, ArH), 7.56 (t, *J* = 8.4 Hz, 2 H, ArH), 7.87 (d, *J* = 7.6 Hz, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.3, 58.0, 79.6, 89.5, 91.6, 114.1, 115.6, 116.8, 123.2, 123.9, 132.5, 133.6, 153.4, 160.3, 162.7, 164.8.

MS (ESI): *m*/*z* = 321.12 $[M + H]^+$.

Anal. Calcd for $C_{19}H_{14}O_4$: C, 74.50; H, 4.61. Found: C, 74.38; H, 4.73.

22b
Yield: 365 mg (72%); brown solid; mp 108–109 °C.

IR (KBr): 1733, 2224, 2931 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.41 (s, 3 H, CH_3), 3.82 (s, 3 H, OCH_3), 5.07 (s, 2 H, OCH_2), 5.89 (s, 1 H, ArH), 6.84 (d, *J* = 7.8 Hz, 2 H, ArH), 7.21 (d, *J* = 8.4 Hz, 1 H, ArH), 7.35 (d, *J* = 8.4 Hz, 1 H, ArH), 7.40 (d, *J* = 8.4 Hz, 1 H, ArH), 7.66 (s, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.9, 55.3, 57.9, 79.7, 89.4, 91.5, 113.4, 114.0, 115.2, 116.5, 122.8, 133.5, 133.6, 133.7, 151.5, 160.3, 163.0, 164.6.

Anal. Calcd for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03. Found: C, 75.23; H, 4.85.

22c
Yield: 275 mg (58%); brown solid; mp 126–127 °C.

IR (KBr): 1725, 2221, 2945 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.40 (t, *J* = 6.8 Hz, 3 H, CH_3), 4.01 (q, *J* = 6.8 Hz, 2 H, OCH_2), 5.09 (s, 2 H, OCH_2), 5.93 (s, 1 H, =CH), 6.83 (d, *J* = 7.6 Hz, 2 H, ArH), 7.29–7.34 (m, 1 H, ArH), 7.39 (d, *J* = 7.6 Hz, 3 H, ArH), 7.56 (t, *J* = 8.0 Hz, 1 H, ArH), 7.87 (d, *J* = 8.0 Hz, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.7, 58.0, 63.6, 79.5, 89.5, 91.7, 113.2, 114.5, 116.8, 123.2, 124.0, 132.5, 133.6, 153.4, 159.7, 162.7, 164.8.

Anal. Calcd for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03. Found: C, 74.73; H, 4.88.

22d
Yield: 295 mg (73%); brown solid; mp 110–111 °C.

IR (KBr): 1734, 2229, 2931 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.21 (s, 3 H, CH_3), 3.82 (s, 3 H, OCH_3), 4.87 (s, 2 H, OCH_2), 5.62 (s, 1 H, ArH), 5.83 (s, 1 H, ArH), 6.83 (d, *J* = 8.4 Hz, 2 H, ArH), 7.38 (d, *J* = 8.4 Hz, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.1, 20.6, 29.2, 89.4, 95.1, 95.7, 99.8, 114.1, 160.1, 160.9, 163.8, 166.0, 170.0.

Anal. Calcd for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 71.03; H, 5.32.

Pyranocoumarin and Pyranopyran Derivatives 23a–d; Compound 23a; Typical Procedure
A mixture of compound **22a** (100 mg, 0.24 mmol), molecular iodine (183 mg, 0.72 mmol), anhydrous $NaHCO_3$ (60 mg, 0.72 mmol) was stirred in anhydrous MeCN (10 mL) at r.t. for 6 h and then CH_2Cl_2 (50 mL) was added to the reaction mixture. The organic phase was washed successively with 10% aq $Na_2S_2O_3$ (15 mL), H_2O (15 mL) and brine (15 mL), and dried (Na_2CO_3). The solvent was removed under reduced pressure and the crude product was purified by silica gel (230–400 mesh) column chromatography using PE–EtOAc (9.7:0.3) as eluent to give the solid product **23a**; yield: 90 mg (65%); yellow solid; mp 142–143 °C.

IR (KBr): 1732, 2931 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3 H, OCH_3), 5.29 (s, 2 H, OCH_2), 6.91 (d, *J* = 8.8 Hz, 2 H, ArH), 7.11 (d, *J* = 8.4 Hz, 2 H, ArH), 7.26–7.31 (m, 2 H, ArH), 7.56 (t, *J* = 7.6 Hz, 1 H, ArH), 7.82 (d, *J* = 7.6 Hz, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.1, 76.6, 84.8, 101.4, 113.4, 114.5, 116.7, 123.1, 124.1, 129.6, 132.2, 132.9, 139.0, 153.4, 157.7, 159.2, 161.4.

MS (ESI): *m*/*z* = 432.87 $[M + H]^+$.

Anal. Calcd for $C_{19}H_{13}IO_4$: C, 52.80; H, 3.03. Found: C, 52.97; H, 3.23.

23b
Yield: 95 mg (68%); yellow solid; mp 136–138 °C.

IR (KBr): 1727, 2924 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.43 (s, 3 H, CH_3), 3.84 (s, 3 H, OCH_3), 5.27 (s, 2 H, OCH_2), 6.91 (d, *J* = 8.8 Hz, 2 H, ArH), 7.10 (d, *J* = 8.4 Hz, 2 H, ArH), 7.16 (d, *J* = 8.4 Hz, 1 H, ArH), 7.35 (d, *J* = 8.4 Hz, 1 H, ArH), 7.62 (s, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.9, 55.1, 76.5, 84.6, 104.3, 113.4, 114.2, 116.5, 122.7, 129.6, 132.3, 133.8, 134.0, 139.1, 151.6, 157.9, 159.1, 161.5.

MS (ESI): *m*/*z* = 672.71 $[M + Na]^+$.

Anal. Calcd for $C_{20}H_{15}IO_4$: C, 53.83; H, 3.39. Found: C, 53.78; H, 3.13.

23c
Yield: 100 mg (72%); yellow solid; mp 146–148 °C.

IR (KBr): 1730, 2922 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.43 (t, *J* = 7.2 Hz, 3 H, CH_3), 4.04 (q, *J* = 7.2 Hz, 2 H, OCH_2), 5.28 (s, 2 H, OCH_2), 6.90 (d, *J* = 8.4 Hz, 2 H, ArH), 7.09 (d, *J* = 8.8 Hz, 2 H, ArH), 7.27–7.31 (m, 2 H, ArH), 7.54 (dt, *J* = 8.8, 1.2 Hz, 1 H, ArH), 7.82 (d, *J* = 8.8 Hz, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.9, 63.3, 76.6, 84.8, 104.4, 113.9, 114.5, 116.7, 123.1, 124.1, 129.6, 132.0, 132.9, 139.0, 153.4, 157.7, 158.6, 161.4.

MS (ESI): *m*/*z* = 432.87 $[M + H]^+$.

Anal. Calcd for $C_{20}H_{15}IO_4$: C, 53.83; H, 3.39. Found: C, 54.01; H, 3.26.

23d
Yield: 80 mg (55%); yellow solid; mp 135–137 °C.

IR (KBr): 1729, 2925 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.20 (s, 3 H, CH_3), 3.83 (s, 3 H, OCH_3), 5.01 (s, 2 H, OCH_2), 5.87 (s, 1 H, ArH), 6.89 (d, *J* = 8.4 Hz, 2 H, ArH), 7.07 (d, *J* = 8.4 Hz, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.4, 55.1, 76.2, 82.8, 99.3, 101.6, 113.3, 129.6, 132.1, 138.5, 159.1, 164.1, 166.4.

MS (ESI): *m*/*z* = 396.88 $[M + H]^+$.

Anal. Calcd for $C_{16}H_{13}IO_4$: C, 48.51; H, 3.31. Found: C, 48.47; H, 3.13.

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(15) CCDC-809664 contains the supplementary crystallographic data of the compound **17a**. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44(1223)336033; E-mail: deposit@ccdc.cam.ac.uk.

