

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 cyclization, bis-fused benzo-2*H*-pyrans, pyranocoumarins

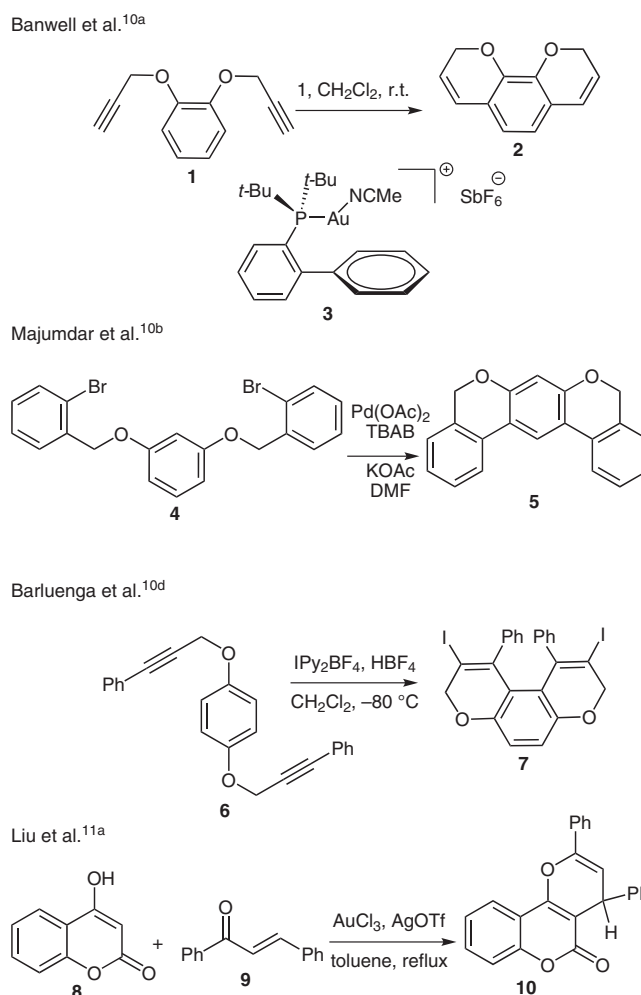
2*H*-Benzopyrans or 2*H*-chromenes represent the structural units of a variety of biologically important compounds.² Chroman derivatives are known to possess various useful biological activities, such as antioxidant,³ anticonvulsion,⁴ anti-estrogen,⁵ and neuroprotection.⁶ On the other hand, pyranocoumarin 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 AuCl₃, Pd(OAc)₂ as catalysts or iodocyclization reaction using IPy₂BF₄·HBF₄ 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 derivatives¹⁴ 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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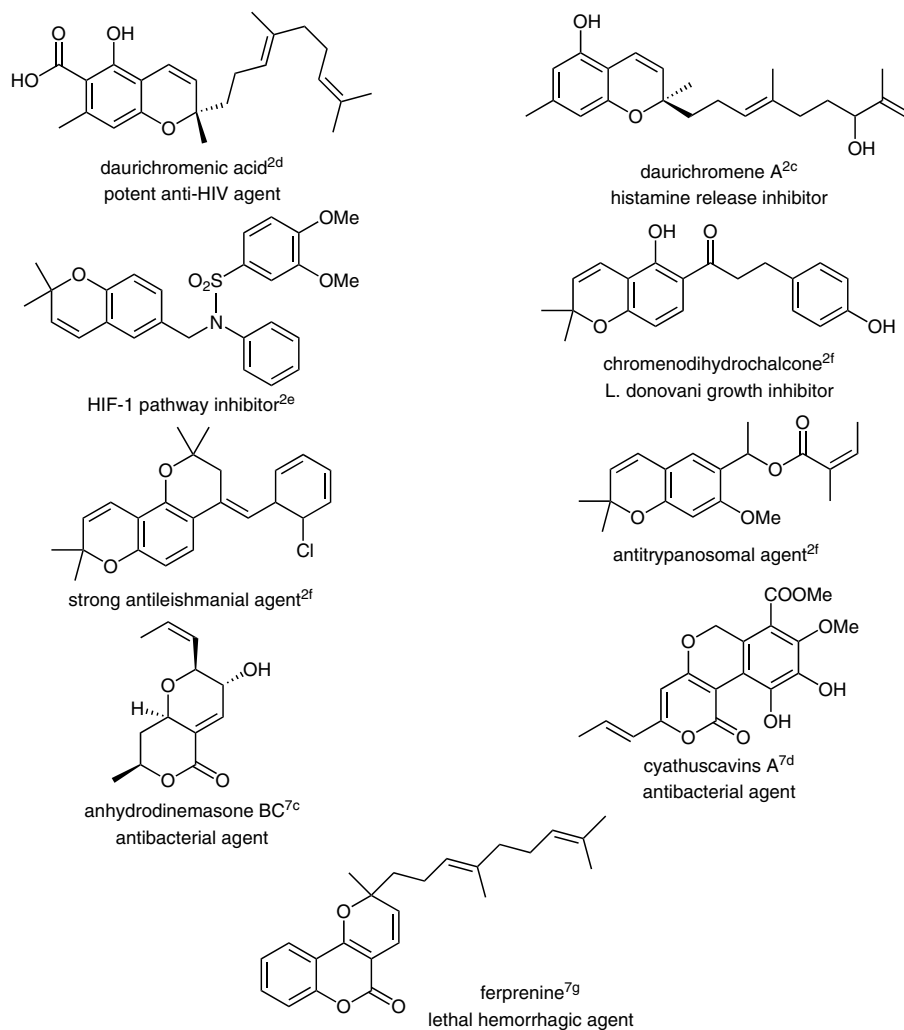
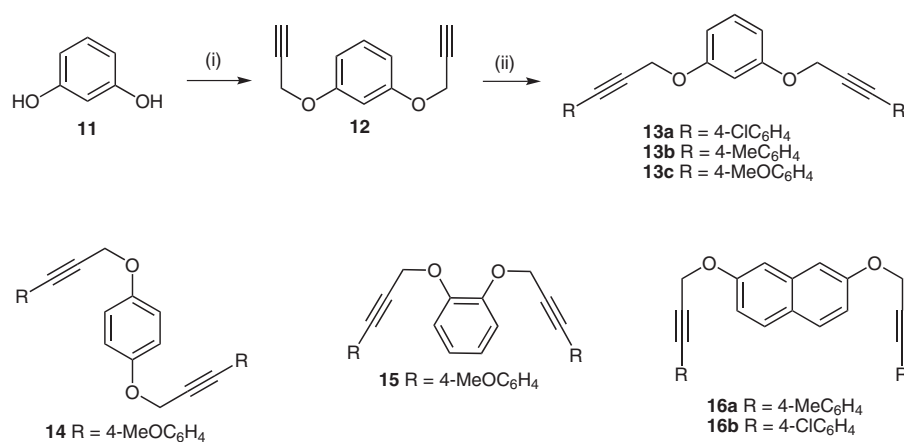


Figure 1 Some biologically active 2*H*-benzopyran, pyranopyran, and pyranocoumarin derivatives

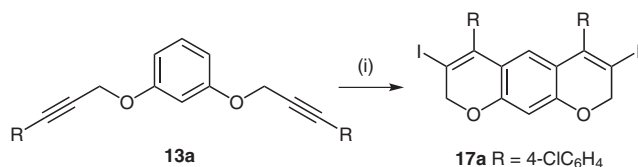
reactions were carried out in the presence of $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ as catalyst and copper(I) iodide as co-catalyst in anhydrous triethylamine–DMF (1:4) as mixed solvent at room temperature for three hours. The O-propargylated compound **12** was in turn prepared by refluxing resorcinol **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, $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$, CuI, DMF–Et₃N, r.t.

The iodocyclization reaction was performed with the compound **13a**, molecular iodine (2 equiv), and NaHCO₃ (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) I₂, NaHCO₃, 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 diffraction¹⁵ 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 NaHCO₃ were optimum and the yield of **17a** was unexpectedly increased to 90%. Further increase of the amount of NaHCO₃ (4 equiv) and iodine (4 equiv) did not give any better result. NaHCO₃ was found to be more effective compared to other bases like K₂CO₃, Na₂CO₃, 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 I₂ (3 equiv), NaHCO₃ (3 equiv), MeCN, r.t., six hours, and the results are summarized in Table 1.

Table 1 Optimization of I₂-Mediated Reactions

Entry	Electrophile (equiv)	Base (equiv)	Solvent	Product	Yield (%) ^a
1	I ₂ (2)	NaHCO ₃ (2)	MeCN	17a	65
2^b	I₂ (3)	NaHCO₃ (3)	MeCN	17a	90
3	I ₂ (4)	NaHCO ₃ (4)	MeCN	17a	90
4	I ₂ (3)	K ₂ CO ₃ (3)	MeCN	17a	35
5	I ₂ (3)	NaHCO ₃ (3)	CH ₂ Cl ₂	17a	25
6	I ₂ (3)	Na ₂ CO 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).

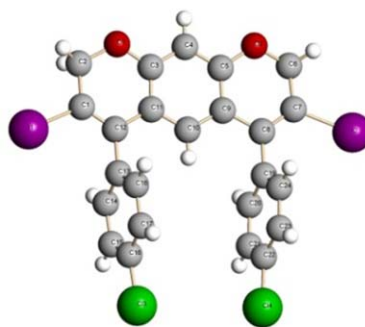
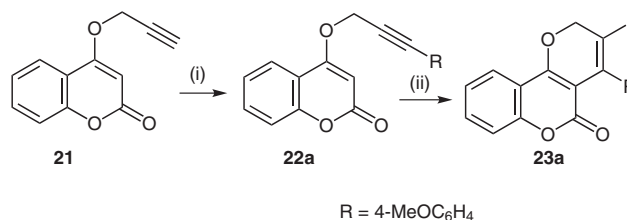


Figure 2 ORTEP diagram of the compound **17a**

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(PPh₃)₂Cl₂ 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).

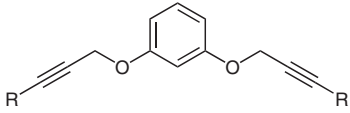
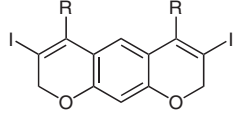
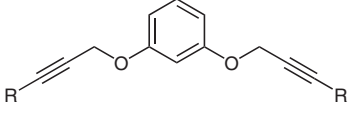
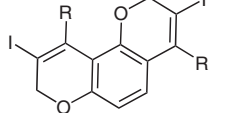
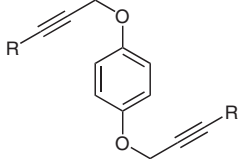
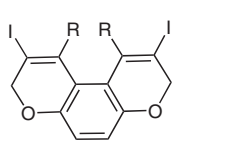
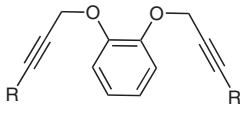
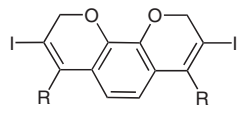
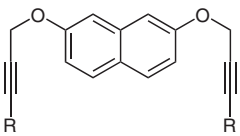
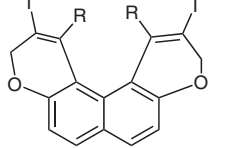
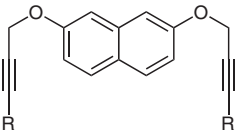
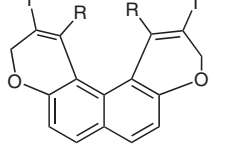


Scheme 4 Preparation of pyranocoumarin derivative **23a**. Reaction conditions: (i) *p*-substituted iodobenzene, Pd(PPh₃)₂Cl₂, CuI, DMF–Et₃N, reflux; (ii) I₂, NaHCO₃, MeCN, r.t., 6 h.

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 NO₂ 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 ₆ H ₄	 17b	85
 13c	4-MeOC ₆ H ₄	 17c	80
 14	4-MeOC ₆ H ₄	 18	70
 15	4-MeOC ₆ H ₄	 19	68
 16a	4-MeC ₆ H ₄	 20a	80
 16b	4-ClC ₆ H ₄	 20b	62

^a Reaction conditions: I₂ (3 equiv), NaHCO₃ (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.

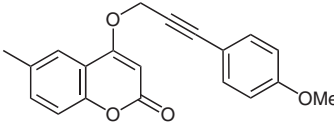
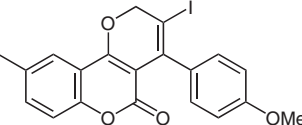
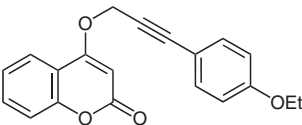
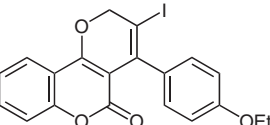
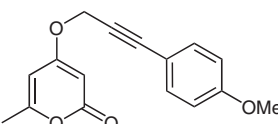
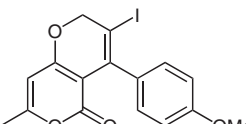
From the above discussion it is clear that the reaction conditions described above are simple and convenient compared to other available methods. They avoid the use of complex and relatively costlier reagents like palladium, ytterbium, gold, etc. and the reactions are carried out at ambient temperature.

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 ¹³C NMR spectra were recorded on a Bruker DPX-400 spectrometer in CDCl₃ 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 Et₃N was dried by keeping overnight over anhydrous CaH₂ 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: I₂ (3 equiv), NaHCO₃ (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*-chloriodobenzene (920 mg, 3.9 mmol), anhydrous Et₃N (2 mL), Pd(PPh₃)₂Cl₂ (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 CH₂Cl₂. The organic phase was washed successively with H₂O (3 × 15 mL) and brine (15 mL), and dried (Na₂SO₄). 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, CDCl₃): δ = 4.88 (s, 4 H, OCH₂), 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).

¹³C NMR (100 MHz, CDCl₃): 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 C₂₄H₁₆Cl₂O₂: 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, CDCl₃): δ = 2.33 (s, 6 H, CH₃), 4.89 (s, 4 H, OCH₂), 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).

¹³C NMR (100 MHz, CDCl₃): 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 C₂₆H₂₂O₂: 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, CDCl₃): δ = 3.79 (s, 6 H, OCH₃), 4.88 (s, 4 H, OCH₂), 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).

¹³C NMR (100 MHz, CDCl₃): 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 C₂₆H₂₂O₄: 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, CDCl₃): δ = 3.80 (s, 6 H, OCH₃), 4.85 (s, 4 H, OCH₂), 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).

¹³C NMR (100 MHz, CDCl₃): 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 C₂₆H₂₂O₄: 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, CDCl₃): δ = 3.79 (s, 6 H, OCH₃), 4.98 (s, 4 H, OCH₂), 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).

¹³C NMR (100 MHz, CDCl₃): 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 C₂₆H₂₂O₄: 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, CDCl₃): δ = 2.33 (s, 6 H, CH₃), 5.01 (s, 4 H, OCH₂), 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).¹³C NMR (100 MHz, CDCl₃): 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 C₃₀H₂₄O₂: 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, CDCl₃): δ = 5.01 (s, 4 H, OCH₂), 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).¹³C NMR (100 MHz, CDCl₃): 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 C₂₈H₁₈Cl₂O₂: C, 73.53; H, 3.97. Found: C, 73.37; H, 3.88.**Bis-Fused Benzo-2H-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 NaHCO₃ (60 mg, 0.72 mmol) was stirred in anhydrous MeCN (10 mL) at r.t. for 6 h. Then, CH₂Cl₂ (50 mL) was added to the reaction mixture. The organic phase was washed successively with 10% aq Na₂S₂O₃ (15 mL), H₂O (15 mL), and brine (15 mL), and dried (Na₂CO₃). 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, CDCl₃): δ = 5.00 (s, 4 H, OCH₂), 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).¹³C NMR (100 MHz, CDCl₃): 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 C₂₄H₁₄Cl₂I₂O₂: 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, CDCl₃): δ = 2.32 (s, 6 H, CH₃), 5.00 (s, 4 H, OCH₂), 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).¹³C NMR (100 MHz, CDCl₃): 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 C₂₆H₂₀I₂O₂: 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, CDCl₃): δ = 3.85 (s, 3 H, OCH₃), 3.87 (s, 3 H, OCH₃), 4.35 (s, 2 H, OCH₂), 4.93 (s, 2 H, OCH₂), 6.38 (d, *J* = 8.4Hz, 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).¹³C NMR (100 MHz, CDCl₃): 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 C₂₆H₂₀I₂O₄: 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, CDCl₃): δ = 3.85 (s, 6 H, OCH₃), 4.69 (d, *J* = 12.8 Hz, 2 H, OCH₂H_b), 4.94 (d, *J* = 12.8 Hz, 2 H, OCH₂H_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).¹³C NMR (100 MHz, CDCl₃): 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 C₂₆H₂₀I₂O₄: 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, CDCl₃): δ = 3.83 (s, 6 H, OCH₃), 5.12 (s, 4 H, OCH₂), 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).¹³C NMR (100 MHz, CDCl₃): 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 C₂₆H₂₀I₂O₄: 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, CDCl₃): δ = 2.31 (s, 6 H, CH₃), 3.57 (d, *J* = 12.4 Hz, 2 H, OCH₂H_b), 4.65 (d, *J* = 12.4 Hz, 2 H, OCH₂H_b), 6.93 (d, *J* = 8.8 Hz, 2 H, ArH), 7.64 (d, *J* = 8.4 Hz, 2 H, ArH).¹³C NMR (100 MHz, CDCl₃): 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 C₃₀H₂₂I₂O₂: 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, CDCl₃): δ = 3.57 (d, *J* = 12.4 Hz, 2 H, OCH₂H_b), 4.67 (d, *J* = 12.8 Hz, 2 H, OCH₂H_b), 6.89 (d, *J* = 8.8 Hz, 2 H, ArH), 7.60 (d, *J* = 8.8 Hz, 2 H, ArH).¹³C NMR (100 MHz, CDCl₃): 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 C₂₈H₁₆Cl₂I₂O₂: 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 Et₃N (2 mL), Pd(PPh₃)₂Cl₂ (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 $[\text{M} + \text{H}]^+$.

Anal. Calcd for $\text{C}_{19}\text{H}_{14}\text{O}_4$: 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 $\text{C}_{20}\text{H}_{16}\text{O}_4$: 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 $\text{C}_{20}\text{H}_{16}\text{O}_4$: 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 $\text{C}_{16}\text{H}_{14}\text{O}_4$: 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 $\text{Na}_2\text{S}_2\text{O}_3$ (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 $[\text{M} + \text{H}]^+$.

Anal. Calcd for $\text{C}_{19}\text{H}_{13}\text{IO}_4$: 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 $[\text{M} + \text{Na}]^+$.

Anal. Calcd for $\text{C}_{20}\text{H}_{15}\text{IO}_4$: 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 $[\text{M} + \text{H}]^+$.

Anal. Calcd for $\text{C}_{20}\text{H}_{15}\text{IO}_4$: 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 $[\text{M} + \text{H}]^+$.

Anal. Calcd for $\text{C}_{16}\text{H}_{13}\text{IO}_4$: 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/contents/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].