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Synthesis of Enantiopure 2-*C*-Glycosyl-3-nitrochromenes

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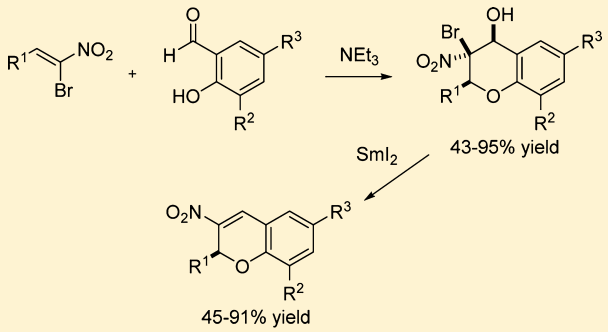
Supporting Information

ABSTRACT: A novel methodology has been developed to obtain enantiopure 2-*C*-glycosyl-3-nitrochromenes. First, (*Z*)-1-bromo-1-nitroalkenes were prepared from the corresponding sugar aldehydes through a sodium iodide-catalyzed Henry reaction with bromonitromethane followed by elimination of the resulting 1-bromo-1-nitroalkan-2-ols. In the next step, reaction of the sugar-derived (*Z*)-1-bromo-1-nitroalkenes with *o*-hydroxybenzaldehydes afforded enantiopure (2*S*,3*S*,4*S*)-3-bromo-3,4-dihydro-4-hydroxy-3-nitro-2*H*-1-benzopyrans, which, upon SmI_2-promoted *β*-elimination, yielded chiral enantiopure 2-*C*-glycosyl-3-nitrochromenes.



A wide variety of secondary metabolites isolated from plants are glycosidic in nature. Over the last 2 decades, a great deal of effort has been devoted to the study of the largest group of glycosides (i.e, *O*-glycosides).[1] Less effort has been focused on *C*-glycosyl compounds because their synthesis is more complex. *C*-Glycosides are a class of glycosides in which carbohydrates are directly attached to the aglycone through a C−C bond rather than the usual hemiacetal C−O linkage.[2] The main feature of *C*-glycosides is their resistance toward hydrolysis: the C−C bond linking the sugar residue to the aglycone is stable even upon acid treatment, and it is only cleaved under harsh conditions.[3] Because of their enhanced stability toward enzymatic and chemical hydrolysis when compared to the *O*-glycosides, *C*-glycosides are of great value in medicinal chemistry. *C*-Glycosides are relatively rare in the literature, probably because of the difficulties encountered in their preparation. Several aromatic ring systems are known to be *C*-glycosylated,[4] and on account of their biological relevance, we became interested in the preparation of chiral enantiopure *C*-glycosylated chromene derivatives.

Chromenes and their derivatives belong to an important family of heterocycles that are widespread in plants[5] and possess a wide range of biological properties.[6] Of particular relevance are the 3-nitro-2*H*-chromenes because of their potential uses as pesticides, endothelin-A (ETA)-selective receptor antagonists, inhibitors of the proliferation of cancer cells, highly potent antihypertensive drugs, and important intermediates in the synthesis of medicinally active 2*H*-benzopyrans.[7] 3-Nitro-2*H*-chromenes can be readily prepared from 2-hydroxybenzaldehydes and 2-nitroethylene,[8] but these procedures are somewhat limited in terms of yield and substrate scope. Moreover, the basic conditions required are not suitable for the preparation of enantiopure chromene derivatives because of problems with isomerization.[9]

We describe here a methodology for the preparation of 2-*C*-glycosyl-3-nitro-2*H*-chromenes that features a reaction between sugar-derived *gem*-bromonitroalkenes and *o*-hydroxybenzaldehydes followed by a samarium-promoted *β*-elimination reaction. The starting sugar-derived bromonitroalkenes were obtained by a novel tandem Henry reaction with bromonitromethane/dehydration. Our proposed synthetic procedure is based on the use of sugar-derived *gem*-bromonitroalkenes as starting materials. Accordingly, a short, reliable, and high-yielding synthetic procedure for these derivatives was needed. The general synthetic method for the preparation of *gem*-bromonitroalkenes is based on the bromination−debromination of nitroalkenes.[10] However, because the starting nitroalkene is prepared from the sugar aldehyde and nitromethane by a Henry reaction followed by elimination, it is clear that the preparation of the sugar-derived *gem*-bromonitroalkenes involves a complex multistep sequence.

A direct procedure involving the nitroaldol condensation of aldehydes with bromonitromethane in the presence of tri-*n*-butylarsine was described some years ago.[11] However, the method appears to work with aromatic aldehydes only. However, a fully heterogeneous synthetic approach for the preparation of *gem*-bromonitroalkenes was described recently.[12] Nevertheless, the procedure has proven to be problematic in our hands for the preparation of some carbohydrate-based

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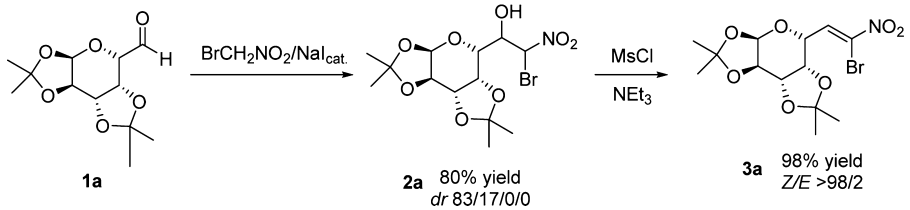
Scheme 1. Synthesis of Sugar-Based *gem*-Bromonitroalkenes 3 through a NaI-Catalyzed Bromonitromethane Addition/Dehydration Protocol



derivatives, probably because of the incompatibility between the acidic conditions used for the dehydration step and the protective groups of the common carbohydrate building blocks.

We previously reported the use of bromonitromethane and sugar aldimines for the synthesis of sugar-derived bromonitroamines.[13] On the basis of these results, we performed a new synthesis of sugar-derived *gem*-bromonitroalkenes through a sodium iodide-catalyzed reaction of bromonitromethane and sugar aldehydes[14] followed by dehydration of the resulting 2-bromo-2-nitroalkanols.

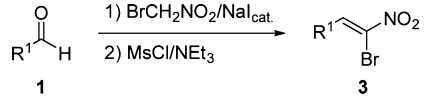
The initial reactions were performed on the sugar aldehyde derived from galactose **1a**. Treatment of a solution of bromonitromethane (1.0 equiv) and the galactose-derived aldehyde **1a** (1.0 equiv) in THF with a catalytic amount NaI (0.15 equiv) at room temperature afforded the corresponding *gem*-bromonitrosugar **2a** in an 83:17:0:0 diastereomeric ratio. Crude reaction product **2a** was reasonably pure after aqueous workup and was used in the following elimination step without the need for purification by column chromatography. We assessed several reagents (such as Ac_2O/DMAP,[15] DCC,[16] and $MsCl/NEt_3$[17]) for the dehydration reaction on **2a**. The best results in terms of yield and cleanliness of the crude product were obtained upon treating a solution of bromonitroalkanol **2a** (1.0 mmol) in CH_2Cl_2 (1.0 mL) and NEt_3 (4.0 equiv) at 0 °C with MsCl (3.0 equiv) and stirring the resulting mixture at room temperature for 1 h. Under these conditions, (*Z*)-1-bromo-1-nitroalkene **3a** was obtained as a single stereoisomer in 98% yield (Scheme 1). The (*Z*) configuration could be inferred from the low field observed for the resonance of the ethylenic protons (7.67 ppm) and is in agreement with previous results on the synthesis of sugar-derived *gem*-bromonitroalkenes.[10d,e]

These reaction conditions were used to explore the scope of this new stereoselective synthesis of *gem*-bromonitroalkenes **3** (Table 1).

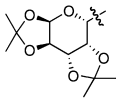
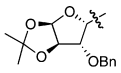
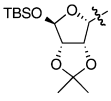
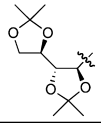
Analysis of the results compiled in Table 1 (entries 1−4) indicates the following: (a) the synthesis of *gem*-bromonitroalkenes **3** took place efficiently (87−92% yield) and with total stereoselectivity (*Z*/*E* > 98:2), (b) this process tolerates a broad scope of sugar-based aldehydes **1a−d** bearing different hydroxyl protecting groups, and (c) all reactions occurred without epimerization of any stereogenic atom on the sugar moiety.

Once we had achieved easy access to sugar-derived *gem*-bromonitroalkenes, we pursued a tandem Michael/Henry reaction between these molecules and *o*-hydroxybenzaldehydes and *gem*-bromonitroalkenes to afford the corresponding 2*H*-benzopyrans.[18] To identify the optimal conditions, we first investigated the reaction of (*Z*)-(2-bromo-2-nitrovinyl)benzene **3f** with salicylaldehyde **4a**. Thus, the reaction of alkene **3f** (1 equiv) with an excess of salicylaldehyde **4a** (5.0 equiv) and catalytic NEt_3 (0.5 equiv) in THF afforded 3-bromo-3,4-

Table 1. Synthesis of Sugar-Based *gem*-Bromonitroalkenes 3



1 3

Entry	1	R^1	3	*Z*/*E*	Yield (%)[a]
1	**1a**		**3a**	>98/2	92
2	**1b**		**3b**	>98/2	91
3	**1c**		**3c**	>98/2	87
4	**1d**		**3d**	>98/2	92

[a]The isolated yield of pure compounds **3** after column chromatography is based on sugar aldehydes **1a−d**.

dihydro-4-hydroxy-3-nitro-2*H*-1-benzopyran **5a** in good yield and with excellent diastereoselectivity; of the four possible diastereomers, only the one with the relative (2*S**,3*S**,4*S**) configuration was obtained (Table 2, entry 1). The scope of the process was investigated with a series of substituted *o*-hydroxybenzaldehydes **4b−d**, and these afforded 3-bromo-3,4-dihydro-4-hydroxy-3-nitro-2*H*-1-benzopyrans **5b−d** in good yields and with >99% de (Table 2, entries 2−4). Reaction of (*Z*)-4-(2-bromo-2-nitrovinyl)-1,2-dimethoxybenzene **3g** and salicylaldehyde **4a** also yielded the corresponding 2*H*-1-benzopyran **5e**, albeit in a lower yield (Table 2, entry 5). Taking into account these satisfactory results, the methodology was extended to the reaction of sugar-derived bromonitroalkenes and *o*-hydroxybenzaldehydes with enantiopure (2*S*,3*S*,4*S*)-3-bromo-3,4-dihydro-4-hydroxy-3-nitro-2*H*-1-benzopyrans **5f−i** obtained in good yields in all cases (Table 2, entries 6−9).

The structures of 2*H*-benzopyrans **5** were established on the basis of ^1H and ^{13}C NMR spectroscopic analysis and confirmed by X-ray crystallography by examining **5i** as a representative of this class of compounds. (Figure S1−S3 in the Supporting Information).[19]

The formation of enantiopure sugar (2*S*,3*S*,4*S*)-2*H*-1-benzopyrans as single isomers can be explained on the basis of a Felkin−Ahn/Michael addition of the alkoxide derived from the *o*-hydroxybenzaldehyde to the nitroalkene. This step is followed by an intramolecular Henry addition of the bromonitronate to the aldehyde group to give the more

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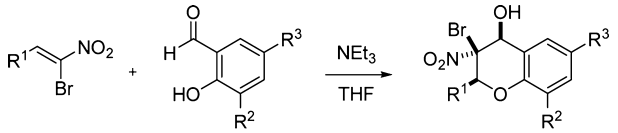
Table 2. Reactions of (*Z*)-*gem*-Bromonitroalkenes 3 and *o*-Hydroxybenzaldehydes 4



3 4 5

Entry	3	R^1	4	R^2	R^3	5	yield[b]
1			**4a**	H	H	**5a**	88
2	**3f**[a]		**4b**	H	NO_2	**5b**	72
3			**4c**	H	Cl	**5c**	75
4			**4d**	OMe	H	**5d**	63
5	**3g**[a]		**4a**	H	H	**5e**	43
6	**3a**		**4a**	H	H	**5f**	95
7			**4b**	H	NO_2	**5g**	91
8	**3b**		**4d**	MeO	H	**5h**	74
9	**3e**		**4a**	H	H	**5i**	87

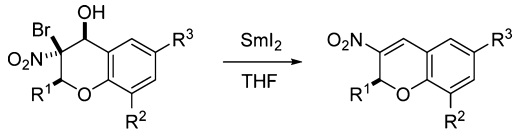
[a]Aromatic *gem*-bromonitroalkenes **3f** and **3g** were synthesized according to a literature procedure.[10] [b]The isolated yield after column chromatography is based on bromonitroalkanes **3**.

thermodynamically favored product (Figure S4 in Supporting Information).

We subsequently envisioned the synthesis of 3-nitrochromenes by SmI_2-mediated *β*-elimination on the intermediate benzopyrans **5**. SmI_2 has been widely employed to promote *β*-elimination reactions with high or total stereoselectivity.[20] We previously described the synthesis of nitroalkenes from 1-bromo-1-nitroalkan-2-ols under mild conditions by means of a samarium-promoted elimination,[21] but this procedure has not been applied to either sugar derivatives or cyclic systems. The synthetic possibility of preparing 3-nitrochromenes by means of a SmI_2-promoted *β*-elimination reaction was investigated by attempting the elimination of racemic benzopyrans **5a–e** to the corresponding 3-nitrochromenes. Accordingly, treatment of a solution of the corresponding benzopyran **5** (1.0 equiv) in THF with a 0.1 M solution of SmI_2 in THF (2.5 equiv) at room temperature for 2 h gave rise to 3-nitrochromenes **6a–d** in yields of 88–91% (Table 3, entries 1–4). Crude reaction products were obtained with high purity after an aqueous workup.

The satisfactory results obtained in the synthesis of racemic 3-nitrochromenes **6a–d** prompted us to assess the utility of this methodology for the synthesis of optically active sugar-derived 3-nitrochromenes. These studies were carried out on benzopyrans **5f–i**, which reacted with SmI_2 in THF (2.5 equiv, 0.1 M) to provide the corresponding enantiopure 3-nitrochromenes **6e–g** (Table 3, entries 5–7). Compounds **6e** and **6g** were isolated in high yield and with high purity (Table 3, entries 5 and 7), whereas compound **6f**, arising from nitro-substituted benzopyran **5g**, was isolated in moderate yield (Table 3, entry 6).

Table 3. SmI_2-Mediated *β*-Elimination Reaction of Benzopyrans 5 to Afford 3-Nitro-2*H*-chromenes 6



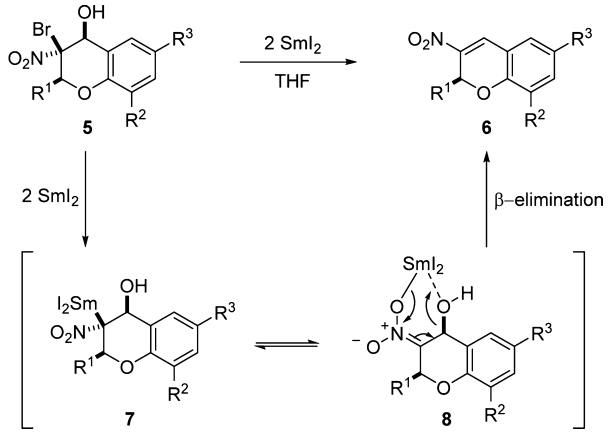
5 6

Entry	R^1	R^2	R^3	6	yield[a]
1		H	H	**6a**	91
2		H	Cl	**6b**	90
3		OMe	H	**6c**	91
4		H	H	**6d**	88
5		H	H	**6e**	82
6		H	NO_2	**6f**	45
7		H	H	**6g**	85

[a]Isolated yield after column chromatography.

We hypothesize that the generation of 3-nitrochromenes **6** proceeds through a *β*-elimination process controlled by chelation (Scheme 2).[22] Thus, metalation and removal of the

Scheme 2. Mechanistic Proposal



bromine atom by samarium diiodide would generate nitronate intermediate **7**. Chelation of the oxophilic Sm^{III} center with the oxygen atom of the alcohol group[23] would produce six-membered ring **8** in which the ability of the hydroxyl group to function as a leaving group would be increased. Consequently, a *β*-elimination process from **8** would afford 3-nitrochromenes **6**.

In conclusion, we have developed a procedure for the synthesis of carbohydrate-based (*Z*)-1-bromo-1-nitroalkenes **3** in good yields and with excellent selectivity. Compounds **3** were reacted with *o*-hydroxybenzaldehydes to yield selectively (2*S*,3*S*,4*S*)-3-bromo-3,4-dihydro-4-hydroxy-3-nitro-2*H*-1-benzopyrans **5**. A SmI_2-promoted *β*-elimination reaction of the corresponding 3-bromo-3,4-dihydro-4-hydroxy-3-nitro-2*H*-1-benzopyrans **5** allowed novel access to enantiopure 2-*C*-

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glycosyl-3-nitrochromenes **6**. To the best of our knowledge, this strategy constitutes the first approach to this type of 3-nitrochromene and also involves a series of novel processes that are of broad interest to synthetic organic chemists.

EXPERIMENTAL SECTION

General Procedure for the Preparation of (*Z*)-*gem*-Bromonitroalkenes 3. NaI (0.12 mmol, 0.15 equiv) was added to a stirred solution of bromonitromethane (0.8 mmol, 1 equiv) and the corresponding aldehyde **1** (0.8 mmol, 1 equiv) in THF (10 mL). The reaction mixture was stirred at room temperature for 5 h. After this period, the mixture was quenched with aqueous HCl (10 mL, 0.1 M) before the organic material was extracted with diethyl ether. The combined extracts were washed with an aqueous saturated solution of $Na_2S_2O_3$ and dried over Na_2SO_4, and the solvent was removed under reduced pressure, affording crude 1-bromo-1-nitroalkan-2-ols. MsCl (0.05 mL, 0.6 mmol) was added dropwise to a stirred solution of the 1-bromo-1-nitroalkan-2-ol (0.2 mmol) and Et_3N (0.12 mL, 0.8 mmol) in THF (1 mL). After stirring the reaction mixture at room temperature for 1 h, it was filtered (Celite), and the filtrate was evaporated in vacuo. The residue was dissolved in CH_2Cl_2 and washed with aqueous saturated solution of $NaHCO_3$, water, and brine. The organic material was then dried over Na_2SO_4, and the solvent was removed under reduced pressure. The residue was purified by column chromatography in mixtures of ethyl acetate/hexane, affording products **3a–d**.

*(Z)-7-Bromo-6,7-dideoxy-1,2:3,4-di-O-isopropyliden-7-nitro-β-D-galacto-hept-6-enopyranose (**3a**).* White solid, mp 148–150 °C (Et_2O/Hex), $[\alpha]_D^{20}$ −8.3° (*c* 1.2, $CHCl_3$), yield 92% (0.28 g). ^1H NMR (300 MHz, $CDCl_3$): δ 7.67 (d, *J* = 7.7 Hz, 1H), 5.55 (d, *J* = 5.0 Hz, 1H, H-1), 4.71–4.66 (m, 2H), 4.41–4.35 (m, 2H) 1.60 (s, 3H), 1.49 (s, 3H), 1.36 (s, 3H), 1.34 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.0, 130.6, 110.1, 109.2, 96.1, 71.4, 70.6, 69.9, 68.3, 26.0, 25.8, 24.8, 24.2. MS (ESI$^+$-TOF, *m*/*z*, %): 402 ([M + Na]$^+$, 92), 380 ([M + H]$^+$, 29). HRMS (ESI$^+$-TOF) calcd for $C_{13}H_{18}BrNaNO_7$ [M + Na]$^+$, 402.01674; found, 402.01589. R_f 0.35 (hexane/EtOAc 6:1).

*(Z)-3-O-Benzyl-6-bromo-5,6-dideoxy-1,2-O-isopropyliden-6-nitro-α-D-xylo-hex-5-enofuranose (**3b**).* White solid, mp 75–77 °C (Et_2O/Hex), $[\alpha]_D^{20}$ −10.7° (*c* 1.1, $CHCl_3$), yield 91% (0.29 g). ^1H NMR (300 MHz, $CDCl_3$): δ 7.75 (d, *J* = 6.9 Hz, 1H), 7.33–7.21 (m, 5H), 6.05 (d, *J* = 3.4 Hz, 1H), 4.88 (dd, *J* = 3.4, 6.9 Hz, 1H), 4.68–4.65 (m, 2H), 4.42 (d, *J* = 12.1 Hz, 1H), 4.20 (d, *J* = 3.4 Hz, 1H), 1.52 (s, 3H), 1.35 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 137.0, 130.0, 128.4, 128.2, 127.8, 112.2, 105.4, 82.3, 82.1, 79.2, 72.2, 26.7, 26.0. MS (ESI$^+$-TOF, *m*/*z*, %): 424 (100), 422 ([M + Na]$^+$, 96). HRMS (ESI$^+$-TOF) calcd for $C_{16}H_{18}BrNO_6$ [M + Na]$^+$, 422.02166; found, 422.02097. R_f 0.28 (hexane/EtOAc 7:1).

*(Z)-6-Bromo-1-O-tert-butyldimethylsilyl-5,6-dideoxy-2,3-O-isopropyliden-6-nitro-α-D-xylo-hex-5-enofuranose (**3c**).* Colorless oil, $[\alpha]_D^{20}$ −1.9° (*c* 0.7, $CHCl_3$), yield 87% (0.29 g). ^1H NMR (300 MHz, $CDCl_3$): δ 7.69 (d, *J* = 7.3 Hz, 1H), 5.40 (s, 1H), 4.97–4.94 (m, 1H), 4.82–4.79 (m, 2H), 4.60 (d, *J* = 5.6 Hz, 1H), 1.46 (s, 3H), 1.29 (s, 3H), 0.89 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 136.3, 131.0, 113.2, 102.0, 86.8, 80.7, 78.6, 26.0, 25.6, 24.7, 17.7, −4.5, −5.4. MS (ESI$^+$-TOF, *m*/*z*, %): 424 ([M + H]$^+$, 100). HRMS (ESI$^+$-TOF) calcd for $C_{15}H_{27}BrNO_6Si$ [M + H]$^+$, 424.07876; found, 424.07855. R_f = 0.26 (hexane/EtOAc 2:19).

*(Z)-1-Bromo-1-nitro-1,2-dideoxy-3,4:5,6-di-O-isopropylidene-L-xylo-hex-1-enitol (**3d**).* $[\alpha]_D^{20}$ −1.1° (*c* 1.2, $CHCl_3$), yield 92% (0.26 g). ^1H NMR (300 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.7 Hz, 1H); 4.69 (dd, *J* = 7.1, 8.7 Hz, 1H), 4.17–4.10 (m, 2H), 3.99–3.86 (m, 2H), 1.45 (s, 6H), 1.33 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 136.1, 133.2, 111.7, 110.6, 109.9, 81.0, 77.8, 76.1, 67.3, 27.0, 26.8, 26.7, 25.0. MS (ESI$^+$-TOF, *m*/*z*, %): 352 ([M + H]$^+$, 100). HRMS (ESI$^+$-TOF) calcd for $C_{12}H_{19}BrNO_6$ [M + H]$^+$, 352.03879; found, 352.03903. R_f = 0.31 (hexane/EtOAc 8:1).

General Procedure for the Preparation of 3-Bromo-3,4-dihydro-4-hydroxy-3-nitro-2*H*-1-benzopyrans 5. *Method A, for Salicylaldehyde **4a**.* Et_3N (0.04 mL) was added to a stirred solution of the corresponding *gem*-bromonitroalkene **3** (0.5 mmol) and salicylaldehyde **4a** (0.7 mL) in THF (1 mL). After stirring the reaction mixture at room temperature for 16 h, the solvents were removed under reduced pressure (0.7 Torr, 45 °C). The residue was purified by flash column chromatography in mixtures of ethyl acetate/hexane or dichloromethane/hexane affording products **5a**, **5e**, **5f**, and **5i**.

*3-Bromo-3,4-dihydro-4-hydroxy-3-nitro-2-phenyl-2H-1-benzopyran (**5a**).* Yellow oil, yield 88% (0.15 g). ^1H NMR (300 MHz, $CDCl_3$): δ 7.58–7.54 (m, 1H), 7.49–7.31 (m, 6H), 7.15–7.10 (m, 1H), 7.01 (dd, *J* = 1.0, 8.2 Hz, 1H), 5.88 (d, *J* = 12.1 Hz, 1H), 5.63 (s, 1H), 2.58 (d, *J* = 12.1 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.3, 132.0, 130.8, 130.5, 128.8, 128.2, 127.2, 123.1, 123.0, 117.1, 109.0, 80.7, 74.5. MS (ESI$^+$-TOF, *m*/*z*, %): 350 ([M + H]$^+$, 70). HRMS (ESI$^+$-TOF) calcd for $C_{15}H_{13}BrNO_4$ [M + H]$^+$, 350.0022; found, 350.0045. R_f = 0.61 (CH_2Cl_2).

*3-Bromo-3,4-dihydro-4-hydroxy-3-nitro-2-(3,4-dimethoxyphenyl)-2H-1-benzopyran (**5e**).* Yellow oil, yield 43% (0.09 g). ^1H NMR (300 MHz, $CDCl_3$): δ 7.58–7.55 (m, 1H), 7.36–7.33 (m, 1H), 7.13–6.96 (m, 4H), 6.84 (d, *J* = 8.4 Hz, 1H), 5.87 (d, *J* = 11.2 Hz, 1H), 5.29 (s, 1H), 3.90 (s, 3H), 3.88 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.5, 148.9, 147.1, 131.9, 131.0, 130.3, 128.6, 127.8, 127.4, 124.0, 123.5, 115.9, 109.4, 80.8, 75.6. MS (ESI$^+$-TOF, *m*/*z*, %): 410 ([M + H]$^+$, 90). HRMS (ESI$^+$-TOF) calcd for $C_{17}H_{17}BrNO_6$ [M + H]$^+$, 410.0234; found, 410.0250. R_f = 0.32 (CH_2Cl_2).

*3-Bromo-3,4-dihydro-4-hydroxy-3-nitro-2-[1,2:3,4-di-O-isopropyliden-β-L-arabinopyranosid-5-yl]-2H-1-benzopyran (**5f**).* Clear oil, $[\alpha]_D^{20}$ −4.9° (*c* 1.5, $CHCl_3$), yield 95% (0.24 g). ^1H NMR (300 MHz, $CDCl_3$): δ 7.49 (d, *J* = 7.7 Hz, 1H), 7.31–7.25 (m, 1H), 7.08–7.03 (m, 1H), 6.90 (dd, *J* = 0.8, 8.3 Hz, 1H), 5.59 (d, *J* = 11.4 Hz, 1H), 5.40 (d, *J* = 5.0 Hz, 1H), 5.09 (d, *J* = 8.7 Hz, 1H), 4.70 (dd, *J* = 2.7, 7.8 Hz, 1H), 4.56 (dd, *J* = 1.9, 7.8 Hz, 1H), 4.33 (dd, *J* = 2.7, 5.0 Hz, 1H), 4.22 (dd, *J* = 1.9, 8.7 Hz, 1H), 2.96 (d, *J* = 11.4 Hz, 1H), 1.63 (s, 3H), 1.44 (s, 3H), 1.38 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.5, 145.2, 125.6, 123.8, 123.2, 117.1, 110.1, 109.5, 102.7, 95.8, 76.4, 73.1, 70.4, 70.2, 70.0, 68.1, 60.6, 25.8, 25.8, 24.7, 24.6. MS (ESI$^+$-TOF, *m*/*z*, %): 503 ([M + 2H]$^+$, 28). HRMS (ESI$^+$-TOF) calcd for $C_{20}H_{25}BrNO_9$ [M + 2H]$^+$, 503.07936; found, 503.07855. R_f = 0.41 (hexane/EtOAc 5:1).

*3-Bromo-3,4-dihydro-4-hydroxy-8-methoxy-3-nitro-2-[3-O-methyl-1,2-O-isopropyliden-β-L-threofuranosid-4-yl]-2H-1-benzopyran (**5i**).* Colorless oil, $[\alpha]_D^{20}$ −2.9° (*c* 0.9, $CHCl_3$), yield 87% (0.19 g). ^1H NMR (300 MHz, $CDCl_3$): δ 7.32–6.82 (m, 8H), 5.85 (d, *J* = 3.0 Hz, 1H), 5.64 (d, *J* = 11.5 Hz, 1H), 5.00 (d, *J* = 8.6 Hz, 1H), 4.70–4.64 (m, 3H), 4.51–4.50 (m, 1H), 4.35–4.32 (m, 1H), 3.83 (s, 3H), 2.89 (bs, 1H), 1.42 (s, 3H), 1.26 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.7, 140.2, 137.5, 128.4, 127.9, 127.8 2, 123.6, 122.5, 117.9, 112.4, 112.1, 105.7, 105.6, 82.2, 81.8, 79.2, 75.6, 73.8, 73.1, 55.9, 27.0, 26.5. MS (ESI$^+$-TOF, *m*/*z*, %): 552 ([M + H]$^+$, 100). HRMS (ESI$^+$-TOF) calcd for $C_{24}H_{27}BrNO_9$ [M + H]$^+$, 552.08700; found, 552.08637. R_f = 0.28 (hexane/EtOAc 3:1).

*Method B, for o-Hydroxybenzaldehydes **4b–d**.* The corresponding *gem*-bromonitroalkene **3** (0.5 mmol) and *o*-hydroxybenzaldehyde **4b–d** (2.75 mmol) were dissolved in THF (1 mL). Et_3N (0.04 mL) was added, and the resulting solution was stirred at room temperature for 16 h. Removal of the solvents (0.7 Torr, 45 °C) left a residue, which was taken up with a lukewarm (50 °C) solution of Girard reagent T (prepared by dissolving 0.45 g of the reagent in 4 mL of a mixture of EtOH/H_2O/AcOH 8:1:1). This mixture was stirred for 2 h, diluted with H_2O (40 mL), and extracted with CH_2Cl_2 (2 × 80 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated in vacuo to give a residue that was purified by flash column chromatography in mixtures of ethyl acetate/hexane or dichloromethane/hexane affording products **5b–d** and **5g–h**.

*3-Bromo-3,4-dihydro-4-hydroxy-3,5-dinitro-2-phenyl-2H-1-benzopyran (**5b**).* White solid, mp 161–165 °C ($CHCl_3$), yield 72% (0.14 g). ^1H NMR (300 MHz, $CDCl_3$): δ 8.54 (dd, *J* = 2.7 and 1.1 Hz, 1H), 8.27–8.23 (m, 1H), 7.49–7.42 (m, 5H), 7.15 (d, *J* = 9.0 Hz, 1H), 5.94 (d, *J* = 11.7 Hz, 1H), 5.80 (s, 1H), 2.73 (d, *J* = 11.7 Hz, 1H). ^{13}C NMR (75 MHz, acetone-d_6): δ 158.1, 143.4, 132.7, 131.0, 129.1, 128.9, 126.4, 126.2, 124.2, 118.1, 107.2, 81.5, 74.1, 56.1. MS (ESI$^+$-

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TOF, *m*/*z*, %): 395 ([M + H]$^+$, 100). HRMS (ESI$^+$-TOF) calcd for $C_{15}H_{12}BrN_2O_6$ [M + H]$^+$, 394.98809; found, 394.98809. R_f = 0.32 (CH_2Cl_2).

*3-Bromo-5-chloro-3,4-dihydro-4-hydroxy-3-nitro-2-phenyl-2H-1-benzopyran (**5c**).* White solid, mp 163−166 °C ($CHCl_3$), yield 75% (0.14 g). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56 (dd, *J* = 1.1, 2.5 Hz, 1H), 7.48−7.38 (m, 5H), 7.29 (ddd, *J* = = 0.7, 2.5, 8.8, Hz, 1H), 6.96 (d, *J* = 8.8 Hz, 1H), 5.86 (d, *J* = 12.1 Hz, 1H), 5.64 (s, 1H), 2.54 (d, *J* = 12.1 Hz, 1H). ^{13}C NMR (75 MHz, acetone-d_6): δ 151.8, 133.3, 130.8, 130.3, 129.0, 128.9, 127.6, 127.4, 126.8, 118.7, 108.2, 81.1, 74.4. MS (ESI$^+$-TOF, *m*/*z*, %): 241 (100), 405 ([M + Na]$^+$, 31). HRMS (ESI$^+$-TOF) calcd for $C_{15}H_{11}BrClNaNO_4$ [M + H]$^+$, 405.94534; found, 405.94522. R_f = 0.47 (CH_2Cl_2).

*3-Bromo-3,4-dihydro-4-hydroxy-8-methoxy-3-nitro-2-phenyl-2H-1-benzopyran (**5d**).* White solid, mp 145−148 °C ($CHCl_3$), yield 63% (0.12 g). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36−7.53 (m, 5H), 7.15−7.19 (m, 1H), 7.08 (t, *J* = 8.0 Hz, 1H), 6.94 (dd, *J* = 1.2, 8.0 Hz, 1H), 5.80 (d, *J* = 12.3 Hz, 1H), 5.66 (s, 1H), 3.88 (s, 3H), 2.45 (d, *J* = 12.3 Hz, 1H). ^{13}C NMR (75 MHz, acetone-d_6): δ 148.9, 142.5, 133.7, 130.6, 129.0, 128.9, 125.6, 126.5, 119.1, 112.8, 109.0, 80.9, 74.9, 56.2. MS (ESI$^+$-TOF, *m*/*z*, %): 380 ([M + H]$^+$, 65). HRMS (ESI$^+$-TOF) calcd for $C_{16}H_{15}BrNO_5$ [M + H]$^+$, 380.01307; found, 380.01281. R_f = 0.55 (CH_2Cl_2).

*3-Bromo-3,4-dihydro-4-hydroxy-3,5-dinitro-2-[1,2:3,4-di-O-isopropyliden-β-L-arabinopyranosid-5-yl]-2H-1-benzopyran (**5g**).* Yellow oil, yield 91% (0.25 g). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.45 (dd, *J* = 1.0, 2.7 Hz, 1H), 8.17 (dd, *J* = 2.4, 8.7 Hz, 1H), 7.04 (d, *J* = 9.1 Hz, 1H), 5.66 (d, *J* = 9.3 Hz, 1H), 5.41 (d, *J* = 4.9 Hz, 1H), 5.24 (d, *J* = 8.7 Hz, 1H), 4.73 (dd, *J* = 2.7, 7.8 Hz, 1H), 4.55 (dd, *J* = 1.9, 7.8 Hz, 1H), 4.36 (dd, *J* = 2.7, 4.9 Hz, 1H), 4.25 (dd, *J* = 1.9, 8.7 Hz, 1H), 3.87 (s, 3H), 1.63 (s, 3H), 1.45 (s, 3H), 1.39 (s, 3H), 1.34 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.5, 145.2, 125.6, 123.8, 123.2, 117.1, 110.1, 109.5, 102.7, 95.8, 76.4, 73.1, 70.4, 70.2, 70.0, 68.1, 60.6, 25.8, 25.8, 24.7, 24.6. MS (ESI$^+$-TOF, *m*/*z*, %): 547 ([M + H]$^+$, 60). HRMS (ESI$^+$-TOF) calcd for $C_{20}H_{24}BrN_2O_{11}$ [M + H]$^+$, 547.0558; found, 547.0564. R_f = 0.35 (hexane/EtOAc 3:1).

*3-Bromo-3,4-dihydro-4-hydroxy-3-nitro-2-[3-O-methyl-1,2-O-isopropyliden-β-L-threofuranosid-4-yl]-2H-1-benzopyran (**5h**).* White solid, mp 219−222 °C (Et_2O/Hex), $[\alpha]_D^{20}$ −5.0° (*c* 0.8, $CHCl_3$), yield 74% (0.20 g). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.52 (d, *J* = 7.7 Hz, 1H), 7.33−7.29 (m, 1H), 7.11−7.06 (m, 1H), 5.83 (d, *J* = 3.6 Hz, 1H), 5.62 (d, *J* = 12.1 Hz, 1H), 5.04 (d, *J* = 8.7 Hz, 1H), 4.56−4.54 (m, 1H), 4.51 (d, *J* = 3.0 Hz, 1H), 4.00 (d, *J* = 3.0 Hz, 1H), 2.42 (d, *J* = 12.1 Hz, 1H), 3.47 (s, 3H), 1.51 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.6, 130.3, 126.5, 122.5, 122.5, 116.0, 112.4, 105.6, 83.5, 80.9, 79.0, 74.9, 73.8, 58.4, 27.0, 26.4. MS (ESI$^+$-TOF, *m*/*z*, %): 468 ([M + Na]$^+$, 100). HRMS (ESI$^+$-TOF) calcd for $C_{17}H_{20}BrNaNO_8$ [M + Na]$^+$, 468.02603; found, 468.02645. R_f = 0.30 (hexane/EtOAc 2:1).

General Procedure for the Preparation of 3-Nitrochromenes 6. A solution of SmI_2 in 0.1 M in THF (1 mmol) was added to a stirred solution of the 2*H*-benzopyran **5a**−**g** or **5i** (0.4 mmol) in THF (4 mL), and the reaction mixture was stirred at room temperature for 2 h. An aqueous solution of 0.1 M HCl was then added, and the resulting mixture was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated in vacuo to give a residue that was purified by flash column chromatography in mixtures of ethyl acetate/hexane, affording products **6a**−**h**.

*3-Nitro-2-phenyl-2H-chromene (**6a**).* Yellow oil, yield 88% (0.11 g). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.04 (s, 1H), 7.38−7.24 (m, 7H), 7.00−6.95 (m, 1H), 6.86−6.83 (m, 1H), 6.57 (s 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.5, 141.1, 136.7, 134.2, 130.4, 129.4, 129.2, 128.7, 127.0, 122.5, 117.8, 117.2, 74.2. MS (ESI$^+$-TOF, *m*/*z*, %): 254 ([M + H]$^+$, 100). R_f = 0.31 (hexane/EtOAc 5:1).

*5-Chloro-3-nitro-2-phenyl-2H-chromene (**6b**).* Yellow solid, mp 115−119 °C ($CHCl_3$), yield 90% (0.13 g). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.94 (s, 1H), 7.35−7.29 (m, 4H), 7.27 (d, *J* = 2.7 Hz, 1H), 7.24−7.23 (m, 1H), 7.21 (d, *J* = 2.5 Hz, 1H), 6.78 (d, *J* = 8.7 Hz, 1H), 6.56 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.8, 141.9, 136.1, 133.7, 129.6, 129.3, 128.9, 127.9, 126.9, 119.1, 118.6, 74.3. MS (ESI$^+$-TOF, *m*/*z*, %): 288 ([M + H]$^+$, 100). HRMS (ESI$^+$-TOF) calcd for $C_{15}H_{11}ClNO_3$ [M + H]$^+$, 288.04220; found, 288.04248. R_f = 0.31 (hexane/EtOAc 5:1).

*8-Methoxy-3-nitro-2-phenyl-2H-chromene (**6c**).* Orange solid, mp 123−126 °C ($CHCl_3$), yield 91% (0.13 g). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00 (s, 1H), 7.40−7.37 (m, 2H), 7.30−7.27 (m, 3H), 6.92−6.91 (m, 3H), 6.65 (s, 1H), 3.76 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.4, 142.5, 141.2, 136.5, 129.3, 129.2, 128.6, 126.8, 122.1, 122.0, 118.6, 116.6, 74.0, 56.1. MS (ESI$^+$-TOF, *m*/*z*, %): 285 ([M + H]$^+$, 100). HRMS (ESI$^+$-TOF) calcd for $C_{16}H_{14}NO_4$ [M + H]$^+$, 284.09272; found, 284.09173. R_f = 0.32 (hexane/EtOAc 5:1).

*3-Nitro-2-(3,4-dimethoxyphenyl)-2H-chromene (**6d**).* Orange oil, yield 88% (0.14 g). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.05 (s, 1H), 7.34−7.26 (m, 2H), 7.02−6.97 (m, 1H), 6.93 (d, *J* = 2.1 Hz, 1H), 6.88−6.84 (m, 2H), 6.75 (d, *J* = 8.3 Hz, 1H), 6.52 (s, 1H), 3.82 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.4, 149.9, 149.1, 141.2, 134.2, 130.3, 129.1, 129.1, 122.4, 119.3, 118.0, 117.3, 110.8, 110.4, 74.1, 55.8, 55.8. MS (ESI$^+$-TOF, *m*/*z*, %): 314 ([M + H]$^+$, 100). HRMS (ESI$^+$-TOF) calcd for $C_{17}H_{16}NO_5$ [M + H]$^+$, 314.10181; found, 314.10230. R_f = 0.42 (hexane/EtOAc 3:1).

*3-Nitro-2-[1,2:3,4-di-O-isopropyliden-β-L-arabinopyranosid-5-yl]-2H-chromene (**6e**).* Yellow oil, $[\alpha]_D^{20}$ −0.6° (*c* 0.9, $CHCl_3$), yield 82% (0.16 g). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.84 (s, 1H), 7.38−7.27 (m, 2H), 7.06−7.00 (m, 2H), 6.05 (d, *J* = 9.2 Hz, 1H), 5.39 (d, *J* = 5.0 Hz, 1H), 4.61 (dd, *J* = 2.8,7.8 Hz, 1H), 4.36 (dd, *J* = 2.0, 7.8 Hz, 1H), 4.27 (dd, *J* = 2.8, 5.0 Hz, 1H), 4.01 (dd, *J* = 2.0, 9.2 Hz, 1H), 1.54 (s, 3H), 1.41 (s, 3H), 1.21 (s, 3H), 1.03 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.0, 141.5, 133.5, 130.1, 127.1, 122.9, 118.5, 117.0, 110.3, 108.8, 96.4, 70.6, 70.5, 70.1, 68.8, 66.5, 26.0, 25.2, 25.0, 24.9. MS (ESI$^+$-TOF, *m*/*z*, %): 406 ([M + H]$^+$, 100). HRMS (ESI$^+$-TOF) calcd for $C_{20}H_{24}NO_8$ [M + H]$^+$, 406.14915; found, 406.14964. R_f = 0.28 (hexane/EtOAc 5:1).

*3,5-Dinitro-2-[1,2:3,4-di-O-isopropyliden-β-L-arabinopyranosid-5-yl]-2H-chromene (**6f**).* Yellow oil, $[\alpha]_D^{20}$ −3.3° (*c* 0.8, $CHCl_3$), yield 45% (0.10 g). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.26−8.23 (m, 2H), 7.82 (s, 1H), 7.10 (d, *J* = 10.0 Hz, 1H), 6.17 (d, *J* = 7.8 Hz, 1H), 5.37 (d, *J* = 4.9 Hz, 1H), 4.61 (dd, *J* = 2.6, 7.8 Hz, 1H), 4.32 (dd, *J* = 1.8, 7.7 Hz, 1H), 4.28−4.26 (m, 1H), 4.01 (dd, *J* = 1.8, 7.7 Hz, 1H), 1.48 (s, 3H), 1.36 (s, 3H), 1.23 (s, 3H), 1.18 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.2, 142.7, 142.5, 128.5, 125.2, 118.7, 117.3, 110.4, 109.0, 96.3, 70.8, 70.7, 70.5, 69.9, 68.2, 29.7, 25.8, 25.7, 24.8. MS (ESI$^+$-TOF, *m*/*z*, %): 451 ([M + H]$^+$, 100). HRMS (ESI$^+$-TOF) calcd for $C_{20}H_{23}N_2O_{10}$ 451.1347 [M + H]$^+$, 451.13454; found, 451.13472. R_f = 0.28 (hexane/EtOAc 5:1).

*3-Nitro-2-[3-O-methyl-1,2-O-isopropyliden-β-L-threofuranosid-4-yl]-2H-chromene (**6g**).* Yellow oil, $[\alpha]_D^{20}$ −5.7° (*c* 1.4, $CHCl_3$), yield 85% (0.15 g). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83 (s, 1H), 7.39−7.27 (m, 2H), 7.05−7.00 (m, 1H), 6.95 (d, *J* = 8.2 Hz, 1H), 6.12 (d, *J* = 8.8 Hz, 1H), 5.83 (d, *J* = 3.7 Hz, 1H), 4.57 (d, *J* = 3.7 Hz, 1H), 4.42 (dd, *J* = 3.3, 8.8 Hz, 1H), 3.80 (d, *J* = 3.3 Hz, 1H), 3.52 (s, 3H), 1.33 (s, 3H), 1.26 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.1, 140.4, 133.7, 130.5, 128.4, 122.8, 118.1, 116.6, 118.8, 105.0, 82.9, 81.4, 78.6, 67.9, 58.2, 26.6, 25.9. MS (ESI$^+$-TOF, *m*/*z*, %): 350 ([M + H]$^+$, 100). HRMS (ESI$^+$-TOF) calcd for $C_{17}H_{20}NO_7$ [M + H]$^+$, 350.12427; found, 350.12343. R_f 0.30 (hexane/EtOAc 5:1).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra for compounds **3**, **5**, and **6**. Single-crystal structure solution and refinement details for compound **5i**. Supramolecular contacts present in the crystal structure of compound **5i**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

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■ REFERENCES

(1) (a) Courtois, E.; Percheron, F. In *The Carbohydrates*; Pigman, W., Horton, D., Eds.; Academic Press: New York, 1970; Vol. 2, pp 213−240. (b) Franz, G. In *Plant Carbohydrates*; Loewus, F. A., Tanner, W., Eds.; Springer-Verlag: New York, 1982; Vol. *13A*, p 384.

(2) Bandyukova, V. A.; Yugin, V. A. *Chem. Nat. Compd.* **1981**, *17*, 1−21.

(3) Levy, D. E.; Tang, C. *The Chemistry of C-Glycosides*; Pergamon: Tarrytown, NY, 1995; Vol. *13*.

(4) Franz, G.; Grun, M. *Planta Med.* **1983**, *47*, 131−140.

(5) Ellis, G. P. *Chromenes, Chromanones, and Chromones*; Wiley: New York, 1977; p 31.

(6) Wang, G. X.; Wang, N. X.; Shi, T.; Yu, J. L.; Tang, X. L. *Prog. Chem.* **2008**, *20*, 518−524.

(7) (a) Bowers, W. S. In *Comprehensive Insect Physiology, Biochemistry, and Pharmacology*; Kerkut, G. A., Gilbert, L. I., Eds.; Pergamon Press: Oxford, 1985; Vol. *8*, p 551. (b) Bowers, W. S.; Ohta, T.; Cleere, J. S.; Marsella, P. A. *Science* **1976**, *193*, 542−547. (c) Ishizuka, N.; Matsumura, K.; Sakai, K.; Fujimoto, M.; Mihara, S.; Yamamori, T. J. *J. Med. Chem.* **2002**, *45*, 2041−2055. (d) Bergmann, R.; Gericke, R. *J. Med. Chem.* **1990**, *33*, 492−504. (e) Burrell, G.; Cassidy, F.; Evans, J. M.; Lightowler, D.; Stemp, G. *J. Med. Chem.* **1990**, *33*, 3023−3027. (f) Gericke, R.; Harting, J.; Lues, I.; Schittenhelm, C. *J. Med. Chem.* **1991**, *34*, 3074−3085. (g) Rao, T. S.; Singth, A. K.; Trievdi, G. K. *Heterocycles* **1984**, *22*, 1377−1382. (h) Deshpande, S. R.; Mathur, H. H.; Trivedi, G. K. *Synthesis* **1983**, 835−835. (i) Xiao, G.-Q.; Liang, B.-X.; Chen, S.-H.; Ou, T.-M.; Bu, X.-Z.; Yan, M. *Arch. Pharm. Chem. Life Sci.* **2012**, *345*, 767−770.

(8) Alneirabeyeh, M.; Koussini, R.; Guillaumet, G. *Synth. Commun.* **1990**, *20*, 783−788.

(9) (a) Varma, R. S.; Kabalka, G. W. *Heterocycles* **1985**, *23*, 139−141. (b) Yan, M.-C.; Jang, Y.-J.; Yao, C.-F. *Tetrahedron Lett.* **2001**, *42*, 2717−2721.

(10) For some representative examples, see: (a) Parnham, W. E.; Bleasdale, J. L. *J. Am. Chem. Soc.* **1951**, *73*, 4664−4666. (b) Carroll, F. I.; Kepler, J. A. *Can. J. Chem.* **1966**, *44*, 2909−2912. (c) Edasery, J. P.; Cromwell, N. H. *J. Heterocycl. Chem.* **1979**, *16*, 831−831. (d) Tronchet, J. M. J.; Bonenfant, A. P.; Pallie, K. D.; Habashi, F. *Helv. Chim. Acta* **1979**, *62*, 1622−1625. (e) Tronchet, J. M. J.; Pallie, K. D.; Barbalat-Rey, F. *J. Carbohydr. Chem.* **1985**, *4*, 29−52. (f) Sarkisyan, Z. M.; Sadikov, K. D.; Smirnov, A. S.; Kuzhaeva, A. A.; Makarenko, S. V.; Anisimova, N. A.; Deiko, L. I.; Berestovitskaya, V. M. *Russ. J. Org. Chem.* **2004**, *40*, 908−909. (g) Tuan, D. T.; Tung, D. T.; Langer, P. *Synlett* **2006**, 2812−2814. (h) Ganesh, M.; Namboothiri, I. N. N. *Tetrahedron* **2007**, *63*, 11973−11983.

(11) Shen, Y.; Yang, B. *Synth. Commun.* **1993**, *23*, 1−5.

(12) Palmieri, A.; Gabrielli, S.; Ballini, R. *Synlett* **2013**, *24*, 114−116.

(13) Rodríguez-Solla, H.; Concellón, C.; Alvaredo, N.; Soengas, R. G. *Tetrahedron* **2012**, *68*, 1736−1744.

(14) Concellón, J. M.; Rodríguez-Solla, H.; Concellón, C.; García-Granda, S.; Díaz, M. R. *Org. Lett.* **2006**, *8*, 5979−5982.

(15) Dunny, E.; Evans, P. *J. Org. Chem.* **2010**, *75*, 5334−5336.

(16) Knochel, P.; Seebach, D. *Synthesis* **1982**, 1017−1018.

(17) Melton, J.; McMurry, J. E. *J. Org. Chem.* **1975**, *40*, 2138−2139.

(18) Dauzonne, D.; Demerseman, P. *Synthesis* **1990**, 66−70.

(19) $C_{17}H_{20}BrNO_8$: M_w = 446.25 g mol^{-1}, pink needle (0.18 × 0.08 × 0.02 mm^3), orthorhombic, space group $P2_12_12_1$, a = 9.8090(10) Å, b = 10.7205(9) Å, c = 17.2919(16) Å, V = 1818.4(3) Å^3, Z = 4, D_c=1.630 g cm^{-3}, μ (Mo Kα) = 2.307 mm^{-1}, 45 489 reflections were collected in the range 3.67° ≤ θ ≤ 29.12°, index ranges −13 ≤ h ≤ 13, −14 ≤ k ≤ 13, −23 ≤ l ≤ 23, of which 4876 were independent (R_{int} = 0.0399), completeness to θ = 29.12° = 99.7%, final $R1$ ([$I > 2\sigma(I)$]) = 0.0269, w$R2$ ([$I > 2\sigma(I)$]) = 0.0606, $R1$ (all data) = 0.0316, w$R2$ (all data) = 0.0624. Flack parameter = −0.008(6). CCDC 962788.

(20) Procter, D. J.; Flowers, R. A.; Skrysdtrup, T. *Organic Synthesis Using Samarium Diiodide: A Practical Guide*; Royal Society of Chemistry: Cambridge, UK, 2010.

(21) Concellón, J. M.; Bernad, P. L.; Rodríguez-Solla, H.; Concellón, C. *J. Org. Chem.* **2007**, *72*, 5421−5423.

(22) Concellón, J. M.; Rodríguez-Solla, H. *Chem. Soc. Rev.* **2004**, *33*, 599−609.

(23) Other six-membered ring transition-state models have been proposed to explain the selectivity in other reactions of SmI_2: (a) Molander, G. A.; Etter, J. B.; Zinke, P. W. *J. Am. Chem. Soc.* **1987**, *109*, 453−463. (b) Urban, D.; Skrydstrup, T.; Beau, J. M. *J. Org. Chem.* **1998**, *63*, 2507−2516. (c) Concellón, J. M.; Pérez-Andrés, J. A.; Rodríguez-Solla, H. *Angew. Chem., Int. Ed.* **2000**, *39*, 2773−2775. (d) Concellón, J. M.; Pérez-Andrés, J. A.; Rodríguez-Solla, H. *Chem.—Eur. J.* **2001**, *7*, 3062−3068 and refs 21 and 22.