JOC*Note*

Generation of *ortho*-Quinone Methides by *p*-TsOH on Silica and Their Hetero-Diels−Alder Reactions with Styrenes

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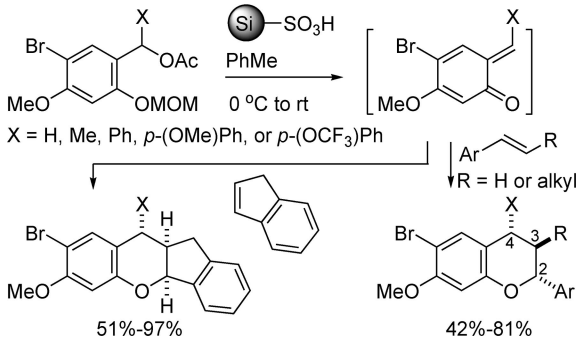

2-Arylchromans were readily prepared from the hetero-Diels−Alder reactions of styrenes with the *ortho*-quinone methides (*o*-QMs) which, in turn, were generated by treating the MOM-protected benzylacetate derivatives with *p*-TsOH immobilized on silica (PTS-Si) in toluene under mild conditions (0 °C to rt). The corresponding chromans were obtained in moderate to excellent yields (42−97%) and in moderate to excellent diastereoselectivity (up to >99:1).

The chroman, or the benzopyran, can be found as the core structure in a number of natural products such as those in the flavonoid families, which have been shown to exhibit antioxidant, antiallergic, anti-inflammatory, antimicrobial, anticancer, anxiolytic, and myorelaxant properties.[1] Eriodictyol (**1**) and hesperitin (**2**) are antioxidant 2-arylchromanone natural products (Figure 1). In addition, some synthetic 2-arylchromans (**3**−**9**) have been developed as selective estrogen receptor β (ERβ) agonists (SERBAs).[2,3] However, some of the steps in these synthetic routes were low-yielding, and the overall processes involved many chemical steps. Moreover, synthesis of compounds with substituents at the 4-position, such as sideroxylonal A (**10**), involved the hetero-Diels−Alder reaction of the *ortho*-quinone methide (*o*-QM).[4]

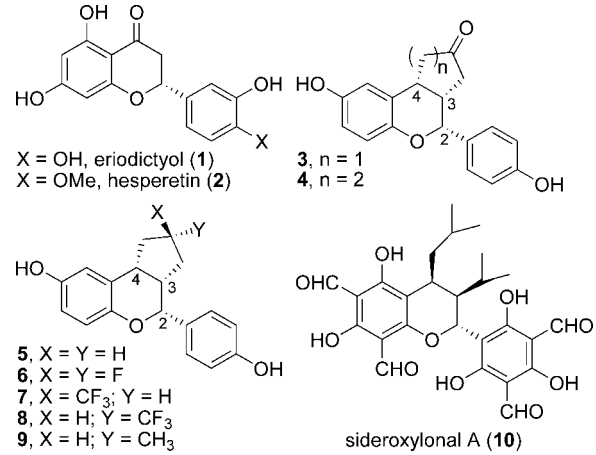

FIGURE 1. Eriodictyol (**1**), hesperetin (**2**), selective ERβ agonists (**3**−**9**), and sideroxylonal (**10**).

The hetero-Diels−Alder reactions have been employed in a number of syntheses to construct the heteroatom-containing ring systems.[5] Reactions between the *o*-QMs as the heterodienes and the properly activated olefins as the dienophiles furnish the benzopyran as well as the spiroketal frameworks.[6] Among the most commonly used procedures to generate the highly reactive *o*-QMs are thermal and base initiations.[7] These procedures

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(1) (a) Zaloni, P.; Avallone, R.; Baraldi, M. *Fitoterapia* **2000**, *71*, S117–S123. (b) Welton, A. F.; Tobias, L. D.; Fiedler-Nagy, C.; Anderson, W.; Hope, W.; Meyers, K.; Coffey, J. W. In *Plant Flavonoids in Biology and Medicine*; Cody, V., Middleton, E., Jr., Harborne, J. B., Eds.; Alan R. Liss Inc.: New York, 1986; pp 1−592. (c) Hirano, T.; Oka, K.; Akiba, M. *Res. Commun. Chem. Pathol. Pharmacol.* **1989**, *64*, 69–78. (d) Cassady, J. M.; Baird, W. H.; Chang, C.-J. *J. Nat. Prod.* **1990**, *53*, 23–41. (e) Medina, J. H.; Vioila, H.; Wolfman, C.; Marder, M.; Wasowski, C.; Calvo, D.; Paladini, A. C. *Neurochem. Res.* **1997**, *22*, 419–425.

(2) (a) Ullrich, J. W.; Miller, C. P. *Expert Opin. Ther. Pat.* **2006**, *16*, 559–572. (b) Wallace, O. B.; Richardson, T. I.; Dodge, J. A. *Curr. Top. Med. Chem.* **2003**, *3*, 1663–1680. (c) Miller, C. P. *Curr. Pharm. Des.* **2002**, *8*, 2089–2111.

(3) (a) Norman, B. H.; Dodge, J. A.; Richardson, T. I.; Borromeo, T. S.; Lugar, C. W.; Jones, S. A.; Chen, K.; Wang, Y.; Durst, G. L.; Barr, R. J.; Montrose-Rafizadeh, C.; Osborne, H. E.; Amos, R. M.; Guo, S.; Boodhoo, A.; Krishnan, V. *J. Med. Chem.* **2006**, *49*, 6155–6157. (b) Richardson, T. I.; Norman, B. H.; Lugar, C. W.; Jones, S. A.; Wang, Y.; Durbin, J. D.; Krishnan, V.; Dodge, J. A. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 3570–3574. (c) Richardson, T. I.; Dodge, J. A.; Durst, G. L.; Pfeifer, L. A.; Shah, J.; Wang, Y.; Durbin, J. D.; Krishnan, V.; Norman, B. H. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 4824–4828. (d) Norman, B. H.; Richardson, T. I.; Dodge, J. A.; Pfeifer, L. A.; Durst, G. L.; Wang, Y.; Durbin, J. D.; Krishnan, V.; Dinn, S. R.; Liu, S.; Reilly, J. E.; Ryter, K. T. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5082–5085. (e) Richardson, T. I.; Dodge, J. A.; Wang, Y.; Durbin, J. D.; Krishnan, V.; Norman, B. H. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5563–5566.

(4) Tatsuta, K.; Tamura, T.; Mase, T. *Tetrahedron Lett.* **1999**, *40*, 1925–1928.

(5) (a) Bray, C. D. *Org. Biomol. Chem.* **2008**, *6*, 2815–2819. (b) Kuboki, A.; Yamamoto, T.; Taira, M.; Arishige, T.; Konishi, R.; Hamabata, M.; Shirahama, M.; Hiramatsu, T.; Kuyama, K.; Ohira, S. *Tetrahedron Lett.* **2008**, *49*, 2558–2561.

(6) (a) Pettigrew, J. D.; Bexrud, J. A.; Freeman, R. P.; Wilson, P. D. *Heterocycles* **2004**, *62*, 445–452. (b) Adlington, R. M.; Baldwin, J. E.; Mayweg, A. V. W.; Pritchard, G. J. *Org. Lett.* **2002**, *4*, 3009–3011. (c) Zhou, G.; Zhu, J.; Xie, Z.; Li, Y. *Org. Lett.* **2008**, *10*, 721–724. (d) Marsini, M. A.; Huang, Y.; Lindsey, C. C.; Wu, K.-L.; Pettus, T. R. R. *Org. Lett.* **2008**, *10*, 1477–1480. (e) El Kaim, L.; Grimaud, L.; Oble, J. *Org. Biomol. Chem.* **2006**, *4*, 3410–3413. (f) Rosenau, T.; Netscher, T.; Ebner, G.; Kosma, P. *Synlett* **2005**, 243–246.

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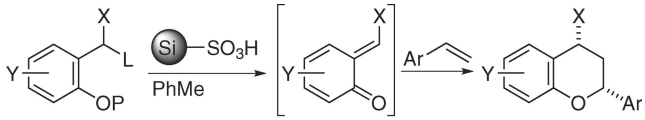
SCHEME 1. General Structure for the *o*-QM Precursor



provided the products in moderate to excellent yields with good to excellent stereoselectivity. In contrast to the thermal and base initiation procedures, only a limited number of accounts have reported the use of acid to generate the *o*-QMs, mainly due to the low compatibility of acidic conditions with the dienophiles, as well as the low stereoselectivity in the resulting products due to the greater ionic character of the reaction conditions.[8]

In recent years, our research group has investigated and reported the utility of various solid-supported reagents in total synthesis as well as in developing some synthetic methods for selective deprotection of aromatic ethers using solid-supported acids.[9] Herein, we wish to report the use of *p*-TsOH on silica (PTS-Si) to generate the *o*-QMs and their subsequent intermolecular hetero-Diels−Alder reactions with styrene derivatives, yielding the desired 2-arylchromans.

Our previous investigations in the protecting group chemistry of aromatic ethers indicated that a number of protecting groups could be cleaved under relatively mild conditions using PTS-Si in the nonpolar solvent toluene.[9b,c] Thus, an appropriate precursor to *o*-QM could assume a structure containing a phenol-protected moiety and a leaving group at the benzylic position (Scheme 1).

As shown in Scheme 2, the *o*-QM precursors were prepared to investigate the effect of substituents on the aromatic ring, protecting group, and leaving group. From the aldehydes **11**−**13**, the phenol groups were protected as their MOM ethers using standard procedures followed by $NaBH_4$ reduction of the aldehyde and the conversion of the resulting hydroxy group to the corresponding acetates **14**−**16**. Bromination of **13** gave the aldehyde **17** in 60% yield. Subsequent phenol protection as Bn, *i*-Pr, or MOM ether, $NaBH_4$ reduction, and acetylation furnished the corresponding products **18**−**20** in 62−92% yields. It should be noted that the preparation of these *o*-QM precursors, while not entirely a one-pot procedure, required only one purification by column chromatography in the final step as the crude products from phenol protection and reduction could be used in the subsequent steps without purification.

As summarized in Table 1, the nature of substituents on the aromatic ring played an important role (entries 1−4). If considering the *o*-QM precursor **14** (X = Y = H) as the reference, substituting bromine (X = H; Y = Br) for proton in **15** showed no effect on the yields of **22** and **23**. Without bromine, but with the methoxy group (X = OMe; Y = H) in **16**, the reaction gave no desired product.[10] The best yield was obtained with **18**, which contained both the methoxy group and bromine (X = OMe; Y = Br).

The effect of the protecting group was then investigated. The reaction of the *o*-QM precursor with the MOM group gave the product in 81% yield (entry 4), while those with the Bn and *i*-Pr groups gave complex mixtures (entries 5 and 6).[11] For the leaving group, the best result was obtained with the acetate.[12] Compound **21** with OMe gave **24** in 61% yield.

Various acids were explored for the cycloaddition reactions of the *o*-QM precursor **18** with styrene or styrene derivative **25**

SCHEME 2. Synthesis of the *o*-QM Precursors

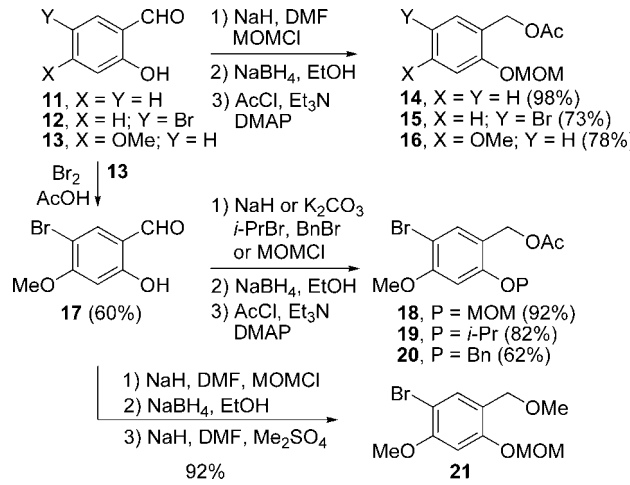
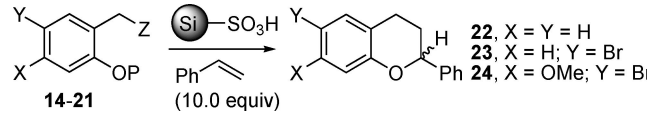


TABLE 1. The Hetero-Diels−Alder Reactions of 14−21[a]



entry	compound	X	Y	Z	P	yield (%)
1	**14**	H	H	OAc	MOM	46
2	**15**	H	Br	OAc	MOM	48
3[b]	**16**	OMe	H	OAc	MOM	0
4	**18**	OMe	Br	OAc	MOM	81
5[b,c]	**19**	OMe	Br	OAc	*i*-Pr	0
6[b,c]	**20**	OMe	Br	OAc	Bn	0
7	**21**	OMe	Br	OMe	MOM	61

[a] Unless otherwise noted, the reactions were performed in toluene at 0 °C to rt. [b] Starting materials were consumed, but complex mixtures were obtained. [c] The protecting groups were cleaved.

(7) (a) Van De Water, R. W.; Pettus, T. R. R. *Tetrahedron* **2002**, *58*, 5367–5405. (b) Sugimoto, H.; Nakamura, S.; Ohwada, T. *J. Org. Chem.* **2007**, *72*, 10088–10095. (c) Crawley, S. L.; Funk, R. L. *Org. Lett.* **2003**, *5*, 3169–3171. (d) Rodriguez, R.; Adlington, R. M.; Moses, J. E.; Cowley, A.; Baldwin, J. E. *Org. Lett.* **2004**, *6*, 3617–3619. (e) Selenski, C.; Pettus, T. R. R. *Tetrahedron* **2006**, *62*, 5298–5307. (f) Jones, R. M.; Selenski, C.; Pettus, T. R. R. *J. Org. Chem.* **2002**, *67*, 6911–6915. (g) Barrero, A. F.; Quílez del Moral, J. F.; Herrador, M. M.; Arteaga, P.; Cortés, M.; Benites, J.; Rosellón, A. *Tetrahedron* **2006**, *62*, 6012–6017. (h) Patel, A.; Netscher, T.; Rosenau, T. *Tetrahedron Lett.* **2008**, *49*, 2442–2445.

(8) (a) Lu, Z. G.; Sato, N.; Inoue, S.; Sato, K. *Chem. Lett.* **1992**, *21*, 1237–1238. (b) Chiba, K.; Hirano, T.; Kitano, Y.; Tada, M. *Chem. Commun.* **1999**, 691–692. (c) Miyazaki, H.; Honda, K.; Asami, M.; Inoue, S. *J. Org. Chem.* **1999**, *64*, 9507–9511. (d) Miyazaki, H.; Honda, Y.; Honda, K.; Inoue, S. *Tetrahedron Lett.* **2000**, *41*, 2643–2647.

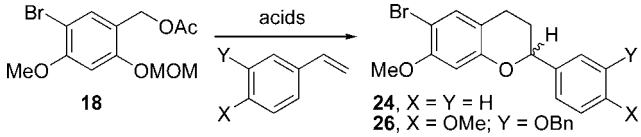
(9) (a) Ploypradith, P.; Kagan, R. K.; Ruchirawat, S. *J. Org. Chem.* **2005**, *70*, 5119–5125. (b) Petchmanee, T.; Ploypradith, P.; Ruchirawat, S. *J. Org. Chem.* **2006**, *71*, 2892–2895. (c) Ploypradith, P.; Cheryklin, P.; Niyomtham, N.; Bertoni, D. R.; Ruchirawat, S. *Org. Lett.* **2007**, *9*, 2637–2640.

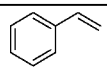
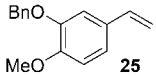
(10) The underlying reasons for the effect of aromatic substituents on the yields of the hetero-Diels−Alder reactions are currently under our investigation. The 0% yield of the corresponding product from compound **16** was presumably due to the formation of competing transient *para*-quinone methide (*p*-QM) from the protonation on the acetate group. The departure of protonated acetate could be assisted by the *p*-OMe group. Subsequent nucleophilic addition of *p*-QM with styrene gave the intermediate which could react further with additional styrene monomer(s) prior to the cleavage of the MOM group. Therefore, the reactions led to the formation of a complex mixture of inseparable product(s). For compound **18**, which gave the corresponding product in 81% yield, the presence of Br on the aromatic ring presumably resulted in the preferential formation of the *o*-QM over the *p*-QM. For the schematic proposed mechanism(s), see Supporting Information.

(11) The rate of styrene polymerization in acid might be faster than those of acid-mediated cleavage of the Bn or *i*-Pr groups in compound **19** and **20**, resulting in no cycloaddition product.

(12) Other *o*-QM precursors with the iodide or mesylate decomposed.

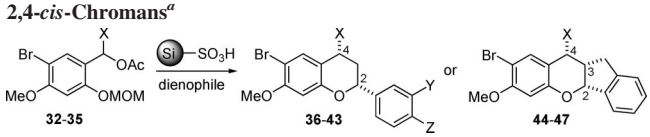
TABLE 2. Effect of Acids on the Hetero-Diels–Alder Reactions of the *o*-QM precursor 18[a]

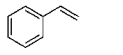
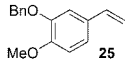


entry	dienophile	acid[b]	X	Y	yield (%)
1		PTS-Si	H	H	81
2[c]		*p*-TsOH	H	H	71
3	(10.0 equiv)	TFA	H	H	67
4		HCl	H	H	66
5		PTA	H	H	34
6		PMA	H	H	56
7		TSA	H	H	45
8		PTS-Si	OMe	OBn	73
9[c]		*p*-TsOH	OMe	OBn	58
10	MeO **25**	TFA	OMe	OBn	0
11	(1.1 equiv)	HCl	OMe	OBn	0
12		PTA	OMe	OBn	3
13		PMA	OMe	OBn	4
14		TSA	OMe	OBn	37

[a] Unless otherwise noted, the reactions were performed in toluene at 0 °C to rt (normally 4–5 h). [b] TFA = CF_3COOH; PTA = phosphotungstic acid hydrate; PMA = phosphomolybdic acid hydrate; TSA = tungstosilicic acid hydrate. [c] The reactions took 18 h.

TABLE 3. Diastereoselective Hetero-Diels–Alder Reactions of Benzyl-Substituted *o*-QM Precursors 32–35 to the 2,4-*cis*-Chromans[a]



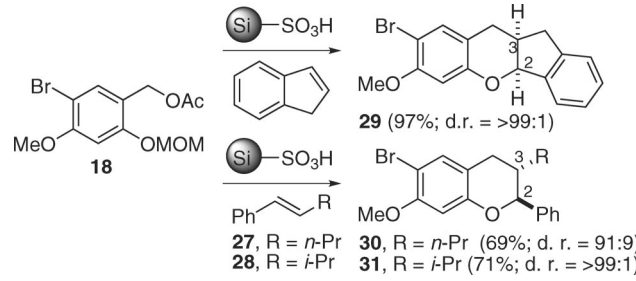
entry	dienophile	*o*-QM precursor	product	X	Y	Z	yield (%)[b]	d.r. (*cis* : *trans*)[c]
1		**32**	**36**	Me	H	H	85	76 : 24
2		**33**	**37**	Ph	H	H	66	84 : 16
3	(10.0 equiv)	**34**	**38**	Ph(OMe-*p*)	H	H	57	86 : 14
4		**35**	**39**	Ph(OCF_3-*p*)	H	H	53	93 : 7
5		**32**	**40**	Me	OBn	OMe	61	77 : 23
6		**33**	**41**	Ph	OBn	OMe	62	75 : 25
7	MeO **25**	**34**	**42**	Ph(OMe-*p*)	OBn	OMe	76	76 : 24
8	(1.1 equiv)	**35**	**43**	Ph(OCF_3-*p*)	OBn	OMe	42	> 99 : 1
9		**32**	**44**	Me	-	-	75	85 : 15
10		**33**	**45**	Ph	-	-	90	> 99 : 1
11	(10.0 equiv)	**34**	**46**	Ph(OMe-*p*)	-	-	83	78 : 22
12		**35**	**47**	Ph(OCF_3-*p*)	-	-	51	> 99 : 1

[a] Unless otherwise noted, the reactions were performed in toluene at 0 °C to rt (normally 4–5 h). [b] Isolated yields of a mixture of 2,4-*cis* and 2,4-*trans* diastereomers. [c] Diastereomeric ratio between C2 and C4 positions as determined by ^1H NMR.

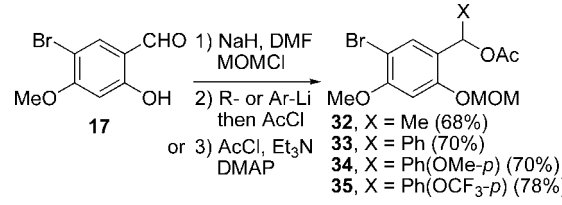
bearing two electron-donating groups (EDG) on the phenyl ring. The results are summarized in Table 2. Although both *p*-TsOH and PTS-Si gave the product **24** in comparable yields (71–81%, entries 1 and 2), the reaction using PTS-Si proceeded faster perhaps due to the greater surface area of PTS-Si. Interestingly, no desired product was obtained from (+)-camphorsulfonic acid (CSA), albeit bearing an alkyl sulfonic acid functionality, or from other Lewis acids ($BF_3 \cdot Et_2O$, $AlCl_3$, and $SnCl_4$). Comparable yields (66–67%, entries 3 and 4) of the product **24** were obtained from the reactions using TFA and HCl, while three heteropolyacids gave the product in lower yields (34–56%, entries 5–7).

In general, the reactions of *o*-QM generated from **18** with the styrene derivative **25** gave the product **26** in poorer yields than those with styrene. Interestingly, only the reactions employing PTS-Si gave both the products **24** and **26** in comparable yields (73–81%), while other acids furnished both **24** (entries 2 and 5–7) and **26** (entries 9 and 12–14) in lower yields. When TFA and HCl were used, only **24** but none of **26** was obtained.

SCHEME 3. Reactions of 18 with α,β-Disubstituted Styrenes



SCHEME 4. Synthesis of Benzyl-Substituted Compounds 32–35



Three α,β-disubstituted styrenes were employed to investigate the diastereoselectivity between the C2–C3 positions. Indene, (*E*)-1-phenylpentene (**27**),[13] and (*E*)-3-methyl-1-phenylbutene (**28**)[13] furnished the products **29–31** in 97, 69, and 71% yields, respectively (Scheme 3). Both **29** (C2–C3 *cis*) and **31** (C2–C3 *trans*) were obtained as their single C2–C3 isomers, while **30** was obtained as a 91:9 mixture of diastereomers favoring the *trans* isomer. The observed diastereoselectivity between the C2–C3 positions suggested the concerted cycloaddition for the formation of both products (**29** and **31**).

The *o*-QM precursors **32–35** were prepared (Scheme 4) to study the effects of the substituents at the benzylic position on the diastereoselectivity between C2 and C4. Simple styrene, styrene **25** bearing electron-donating groups, and indene were the dienophiles. The results are summarized in Table 3. In all cases, the styrenes gave the products favoring the *cis* isomer between C2 and C4. The monosubstituted olefins gave the products (**36–43**) favoring the C2–C4 *cis* relationship with the diastereomeric ratios ranging from 75:25 to >99:1. The electronic effect from the *para* position of the aryl substituent was evident. The substrate with an electron-donating *p*-OMe group (**34**) gave the products **38** and **42** in moderate to good yields (57–76%) but only with moderate diastereoselectivity (76:24 to 86:14). On the other hand, the *o*-QM precursor **35** with an electron-withdrawing *p*-OCF_3 group furnished the products **39** and **43** in moderate yields (42–53%) but with excellent diastereoselectivity (93:7 to >99:1). The predominant *cis* relationship between the C2–C4 positions suggested that the hetero-Diels–Alder reactions of these substrates proceeded via the *endo*-type concerted transition state.[7a]

When indene was employed, only the *cis* diastereomers between C2 and C3 were obtained from **32–35**. Moreover, the

(13) See Supporting Information for preparation and characterization.

cis relationship was also favored between C2 and C4, with moderate to excellent diastereomeric ratios of 78:22 to >99:1. Thus, the products **44**−**47** all were predominantly C2−C3−C4 *cis* isomers.

In summary, we have developed an efficient means to generate the *o*-QMs using PTS-Si. The hetero-Diels−Alder reactions of the *o*-QMs with the styrene derivatives furnished the 2-arylchroman frameworks in moderate to good yields and moderate to excellent diastereoselectivity.

Experimental Section

General Procedure for the Hetero-Diels−Alder Reactions of 2-Arylchroman Products 22−24, 26, 29−31, 36−47. To a stirred solution of benzyl acetates **14**−**16**, **18**−**21**, or **32**−**35** (1.0 equiv) in toluene (5 mL/mmol of starting material) were added styrene derivatives (10.0 equiv for commercially available styrenes, **27** and **28**, and 1.1 equiv for **25**) at room temperature. The resulting mixture was stirred at 0 °C for 10 min, and then PTS-Si (0.81 mmol/g, 1.1 equiv) was added. The reaction mixture was stirred until all benzyl acetates **14**−**16**, **18**−**21**, or **32**−**35** were consumed as indicated by TLC (typically 4−5 h). At that time, the reaction mixture was filtered to remove the silica, which was washed with excess CH_2Cl_2 (three times). The filtrate was then concentrated under reduced pressure to give a crude product mixture which was further purified by preparative TLC to furnish the desired product.

6-Bromo-7-methoxy-2-phenylchroman (24). Benzyl acetate **18** (0.025 g, 0.078 mmol) in toluene (1 mL) was treated with PTS-Si (0.106 g, 0.086 mmol) and styrene (0.092 mL, 0.78 mmol) according to the general procedure above to give the desired 2-arylchroman product **24** (0.02 g, 0.063 mmol, 81%) as a colorless oil: IR (neat) ν_{max} 2928, 1610, 1572, 1495, 1485, 1442, 1309, 1266, 1193, 1153, 1053 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.97−2.28 (m, 2H), 2.66−2.79 (m, 1H), 2.84−3.01 (m, 1H), 3.85 (s, 3H), 5.05 (dd, J = 9.4, 3.0 Hz, 1H), 6.52 (s, 1H), 7.26 (s, 1H), 7.35−7.44 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 24.1, 29.6, 56.2, 78.0, 101.1, 101.8, 115.2, 125.9, 128.0, 128.6, 133.0, 141.1, 154.8, 155.1; LRMS (EI) *m*/*z* (rel intensity) 320 (M^+ + 2, 100), 318 (M^+, 97), 239 (16), 238 (14); TOF-HRMS calcd for $C_{16}H_{16}BrO_2$ ($M + H^+$) 319.0328, found 319.0327.

6-Bromo-7-methoxy-2-phenyl-3-propylchroman (31). Benzyl acetate **18** (0.024 g, 0.076 mmol) in toluene (1 mL) was treated with PTS-Si (0.102 g, 0.083 mmol) and styrene **28** (0.11 g, 0.76 mmol) according to the general procedure above to give the desired 2-arylchroman product **31** (0.020 g, 0.054 mmol, 71%) as a colorless oil: IR (neat) ν_{max} 2958, 2926, 1611, 1575, 1496, 1444, 1402, 1310, 1283, 1201, 1157, 1063, 1049 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.76 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H), 1.44−1.52 (m, 1H), 1.93−2.00 (m, 1H), 2.53 (dd, J = 16.2, 5.3 Hz, 1H), 2.61 (dd, J = 16.3, 9.6 Hz, 1H), 3.74 (s, 3H), 3.77 (s, 3H, minor), 4.84 (d, J = 8.6 Hz, 1H), 5.34 (d, J = 3.9 Hz, 1H, minor), 6.39 (s, 1H), 6.40 (s, 1H, minor), 7.17 (s, 1H), 7.19 (s, 1H, minor), 7.23−7.34 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.4, 21.2, 23.4, 26.8, 42.7, 56.2, 81.4, 100.7, 101.7, 115.5, 126.5, 127.0, 128.2, 128.6, 133.2, 139.9, 154.7; LRMS (EI) *m*/*z* (rel intensity) 362 (M^+ + 2, 80), 360 (M^+, 83), 319 (10), 317 (11), 271 (87), 269 (100), 238 (18), 190 (40), 131 (43); TOF-HRMS calcd for $C_{19}H_{22}BrO_2$ ($M + H^+$) 361.0798, found 361.0800.

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Supporting Information Available: Experimental procedures and full spectroscopic data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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