Chromenes through Metal-Catalyzed Reactions of Styrenyl Ethers. Mechanism and Utility in Synthesis

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Received November 20, 1997

Abstract: An efficient metal-catalyzed process that converts styrenyl ethers to 2-substituted chromenes is described. This class of reactions may be carried out on either terminal or disubstituted styrenyl substrates. Depending on the level of substitution of the olefins, the Ru−carbene catalyst may initiate reaction either by interaction with the styrenyl or the carbocyclic alkene. Metal-catalyzed rearrangements, carried out under an atmosphere of ethylene, afford excellent yields of monomeric products. With disubstituted styrene ethers, the presence of ethylene is also critical to reaction efficiency. Mechanistic data that rationalize these observations are provided. Although Ru complexes $(PCy_3)_2Cl_2Ru{=}CHCH{=}CPh_2$ or $(PCy_3)_2Cl_2Ru{=}CHPh$ effectively serve as catalysts, with the more functionalized substrates, higher yields are obtained when $Mo(CHCMe_2Ph)(N(2,6\text{-}(i\text{-}Pr)_2C_6H_3))(OCMe(CF_3)_2)_2$ is used. A variety of starting materials for the metal-catalyzed chromene synthesis (disubstituted styrenes) are available in the optically pure form through the Zr-catalyzed kinetic resolution protocol, allowing several 2-substituted chromenes to be prepared in high enantiomeric purity. However, a number of functionalized substrates cannot be efficiently resolved by the latter method, indicating that more effective methods that address this deficiency are required.

Introduction and Background

We recently reported a two-step, fully catalytic process for the enantioselective synthesis of 2-substituted chromenes.[1,2] As the examples in Scheme 1 illustrate, we demonstrated that treatment of a styrenyl ether, such as **1**, with 5 mol % $(PCy_3)_2Cl_2Ru{=}CHCH{=}CPh_2$ (**2**)[3] under an atmosphere of argon (14 h) leads to the formation of **3** and **4** in 42% and 41% yield, respectively, after silica gel chromatography. When the reaction is performed under an atmosphere of ethylene, **3** is obtained in 91% isolated yield. Furthermore, as exemplified by conversion of **5** to **6**, the electronic properties of the aromatic moieties exhibit little influence on the facility of the catalytic heterocycle synthesis. Eight-membered rings are appropriate substrates as well (Scheme 1; **7** → **8**).

We conjectured that the above catalytic processes would be efficient on the basis of two principles: (1) We were mindful of studies of Crowe[4] that aromatic alkenes and aliphatic olefins are electronically suitable to undergo cross-metathesis. We envisioned that the intramolecular variant should be especially favored. (2) The general reaction appeared energetically favorable: as shown in Scheme 2, initial semiempirical calculations (PM3; geometry optimization) indicated that the 2-substituted chromenes **10**, **12**, and **14** are appreciably lower in energy than ethers **9**, **11**, and **13**. Several investigations have demonstrated that various metal-catalyzed metathesis reactions[5] are governed by thermodynamic factors;[6] this issue is particularly critical in rearrangements, where products can revert back to starting substrates.[7] Our preliminary observations indicated that the reactivity of the cycloheptenyl substrates (e.g., **1** or **5**) is consistent with the aforementioned energetics. We were, however, intrigued by the sluggish reactions of six-membered ring system **11** and the fact that <2% reaction occurs when cyclopentenyl ether **9** is used. We reasoned that a step in the catalytic cycle likely serves as a kinetic barrier to the formation of chromenes **10** and **12**.

In this article, we report our investigations in connection with the mechanism of this metal-catalyzed chromene synthesis involving terminal and disubstituted styrenyl substrates. We demonstrate that a mechanistic divergence arises as a result of subtle structural modifications. From the outset, as depicted in Chart 1, our plan has been to synthesize optically pure ether substrates through the Zr-catalyzed kinetic resolution,[8] followed by a metal-catalyzed conversion to the derived nonracemic

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(1) Harrity, J. P. A.; Visser, M. S.; Gleason, J. D.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1997**, *119*, 1488−1489.

(2) For Mn-catalyzed kinetic resolution of 2,2-disubstituted chromenes, see: Vander Velde, S. L.; Jacobsen, E. N. *J. Org. Chem.* **1995**, *60*, 5380−5381.

(3) Wu, Z.; Nguyen, S. T.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1995**, *117*, 5503−5511.

(4) (a) Crowe, W. E.; Zhang, Z. J. *J. Am. Chem. Soc.* **1993**, *115*, 10998−10999. (b) Crowe, W. E.; Goldberg, D. R. *J. Am. Chem. Soc.* **1995**, *117*, 5162−5163. (c) Crowe, W. E.; Goldberg, D. R.; Zhang, Z. J. *Tetrahedron Lett.* **1996**, *37*, 2117−2120.

(5) (a) Grubbs, R. H.; Miller, S. J.; Fu, G. C. *Acc. Chem. Res.* **1995**, *28*, 446−452. (b) Schmalz, H.-G. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1833−1836. (c) Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2036−2056.

(6) (a) Miller, S. J.; Kim, S.; Chen, Z.; Grubbs, R. H. *J. Am. Chem. Soc.* **1995**, *117*, 2108−2109. (b) Marsella, M. J.; Maynard, H. D.; Grubbs, R. H. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1101−1103 and references therein.

(7) Catalytic transformations of both terminal and disubstituted styrenyl ethers will be discussed in this article. In the former case, since the starting material and the product are isomeric, the Ru-catalyzed process constitutes a rearrangement.

(8) Visser, M. S.; Harrity, J. P. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1996**, *118*, 3779−3780. For a recent review, see: Hoveyda, A. H.; Morken, J. P. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1262−1284.

S0002-7863(97)03979-6 CCC: $15.00 © 1998 American Chemical Society
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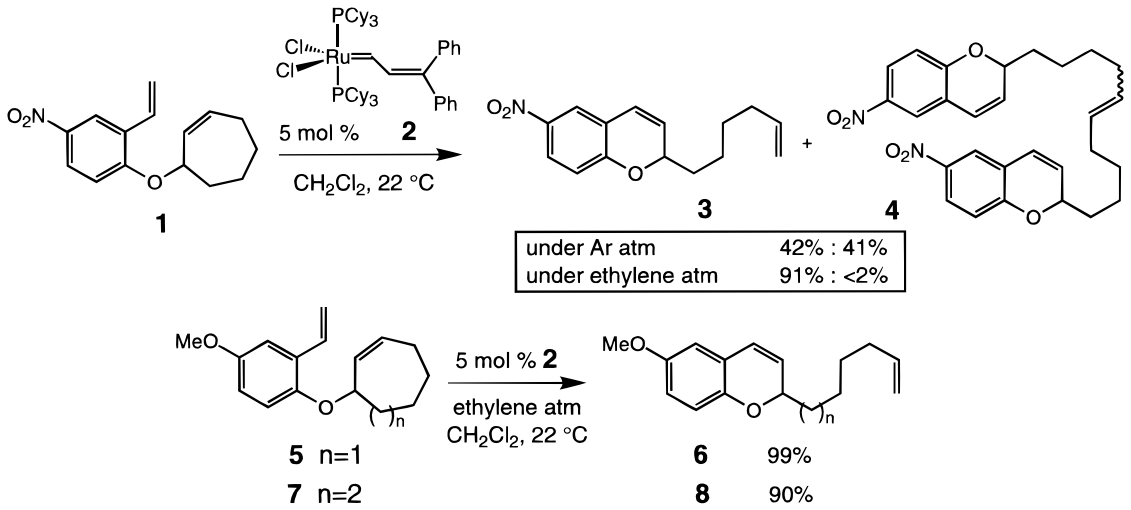
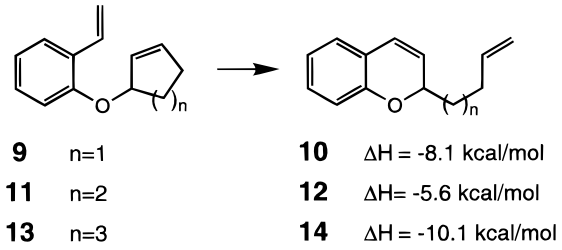
Scheme 1

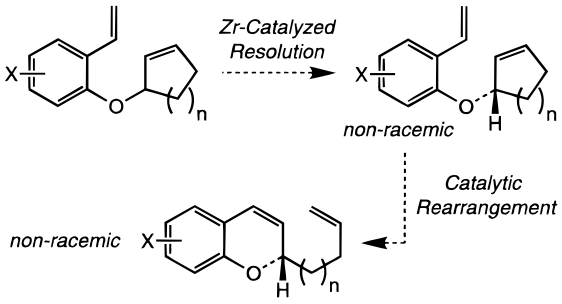


Scheme 2



chromene. We provide data indicating that with the more functionalized starting materials, catalytic resolution can be effective, but chromene synthesis requires the use of an alternative metathesis catalyst (in lieu of **2** or related Ru complexes).

Chart 1

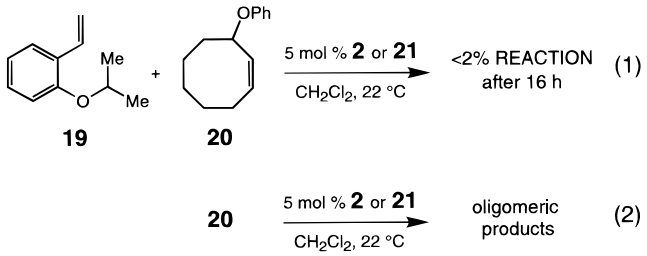


Results and Discussion

Regioselectivity in the Ru-Catalyzed Reactions of Terminal Styrenes. Initially, we surmised that with terminal styrenes such as **13**, reaction begins regioselectively with the formation of metal−carbene **15** (Scheme 3).[9] Subsequent rearrangement, via metallacyclobutane **16**, affords chromene **17**, reaction of which with a second equivalent of **13** would regenerate **15** to deliver **14**. Late in the process (under Ar atm), as the amount of **14** increases, **17** may react more frequently with the final product monomer (**14**) to afford dimer **18**.

Several factors and observations support the route proposed in Scheme 3: (1) The styrenyl alkene is expected to react preferentially (versus the disubstituted cyclic olefin) for steric reasons. (2) Involvement of a tetracyclic intermediate such as **16** provides a plausible rationale for the reluctance of six-membered ring ethers to participate in the catalytic rearrangement and for the lack of reactivity of cyclopentenyl substrates. The attendant angle strain inhibits the formation of the derived tetracyclic intermediate. (3) Reactions under ethylene atmosphere inhibit dimer formation, since **17** is intercepted with $H_2C{=}CH_2$, rather than **14**. Furthermore, we find that treatment of **18** with 5 mol % **2** under an atmposphere of ethylene leads to 50% conversion to **14** (12 h; 400 MHz ^{1}H NMR analysis). Therefore, in the presence of ethylene, even if dimer is formed, it can be readily converted to the monomeric form with reasonable efficiency.

To ascertain whether the Ru-catalyzed reaction of the terminal styrene involves initial reaction at the cyclic alkene, the following experiments were carried out. As illustrated in eq 1,



when styrenyl ether **19** and allylic phenyl ether **20** are treated with 5 mol % **2**, <2% conversion is detected by 400 MHz ^{1}H NMR analysis after 16 h. In contrast, when **20** is alone subjected to the above conditions (styrene **19** excluded), facile ring opening occurs and ^{1}H NMR analysis indicates the formation of oligomeric products.[10] Identical results are obtained with the more active $(PCy_3)_2Cl_2Ru{=}C(H)Ph$ (**21**).[11] Thus, the intermolecular variant (cross-metathesis)[12] of the title reaction (**19** + **20**) is extremely slow. These data also suggest

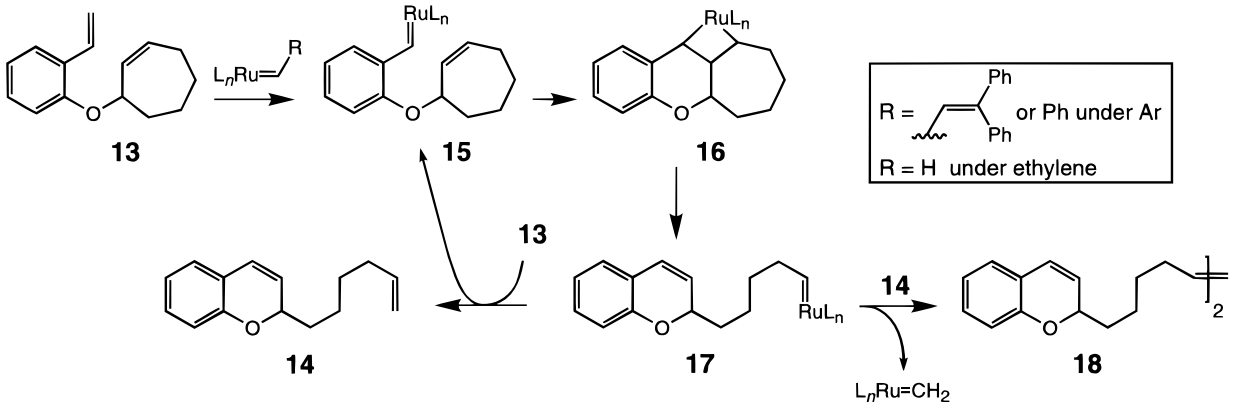
(9) For a recent report on the mechanism of the Ru-catalyzed ring-closing metathesis, see: Dias, E. L.; Nguyen, S. T.; Grubbs, R. H. *J. Am. Chem. Soc.* **1997**, *119*, 3887−3897.

(10) Hillmyer, M. A.; Laredo, W. R.; Grubbs, R. H. *Macromolecules* **1995**, *28*, 6311−6316.

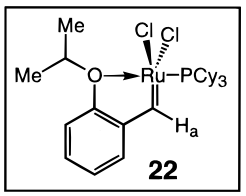
(11) Schwab, P.; Grubbs, R. H.; Ziller, J. W. *J. Am. Chem. Soc.* **1996**, *118*, 100−110.

(12) Reference 4. See also: (a) Randall, M. L.; Tallarico, J. A.; Snapper, M. L. *J. Am. Chem. Soc.* **1995**, *117*, 9610−9611. (b) Schneider, M. F.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 411−412. (c) Schuster, M.; Pernerstorfer, J.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1979−1980. (d) Tallarico, J. A.; Bonitatebus, P. J.; Snapper, M. L. *J. Am. Chem. Soc.* **1997**, *119*, 7157−7158. (e) Kinoshita, A.; Sakakibara, N.; Mori, M. *J. Am. Chem. Soc.* **1997**, *119*, 12388−12389.

Scheme 3

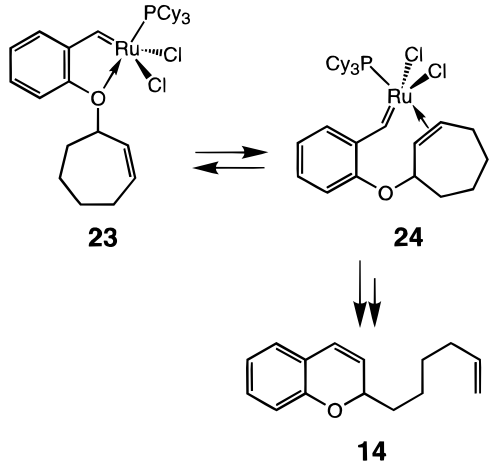


that the terminal alkene in **19** reacts more readily with the Ru alkylidene to afford metal carbene **22**. We argued that this



complex might be less reactive than **2** or **21**, sequestering the transition metal to discourage reactions with cyclooctenyl phenyl ether **20**. In the case of the intramolecular variants mentioned above, as shown in Scheme 4, chelation can occur between the metal and the cycloalkenyl π-system (**23** → **24**) to initiate rearrangement.

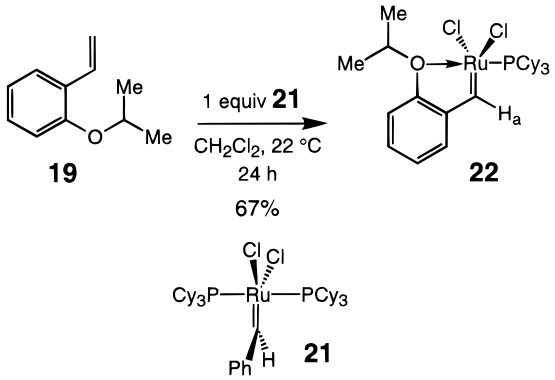
Scheme 4



To establish additional support for the intermediacy of **22**, we attempted to synthesize and isolate this Ru−carbene complex. We found that treatment of **19** with 1 equiv of **21** at 22 °C in CH_2Cl_2 for 24 h leads to the formation of **22** as a dark brown solid (mp = 200−201 °C). Inspection of the 400 MHz ^{1}H NMR spectrum of **22** indicated that there is substantial shielding of the alkylidene proton (H_a in **22**), resulting in an upfield shift of ∼2.5 ppm relative to the parent complex **21** (cf. Scheme 5). Furthermore, whereas there are no P−alkylidene couplings present in **2** or **21** (the P−Ru−C−H dihedral

(13) (a) Morken, J. P.; Didiuk, M. T.; Visser, M. S.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1994**, *116*, 3123−3124. (b) Visser, M. S.; Heron, N. M.; Didiuk, M. T.; Sagal, J. F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1996**, *118*, 4291−4298.

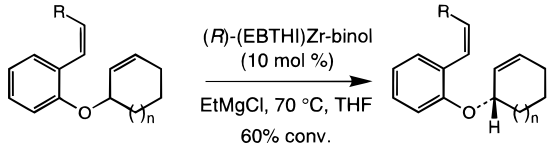
Scheme 5



angle is approximately 90°), **22** exhibits a J_{PH} = 4.4 Hz. These data suggest that in complex **22**, internal chelation between phenolic oxygen and the transition metal perhaps alters the relationship between H_a and the bound phosphine ligand, as illustrated in Scheme 5 (compare **21** and **22**).

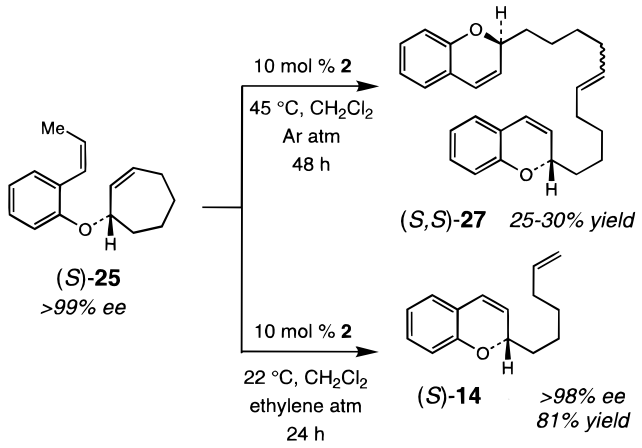
Regioselectivity in the Ru-Catalyzed Reactions of Disubstituted Styrenes. As mentioned above, we planned to obtain optically pure styrenyl ethers through the Zr-catalyzed kinetic resolution; subsequent metal-catalyzed rearrangement would afford optically pure chromenes. This strategy followed our initial unsuccessful attempts to resolve directly these 2-substituted heterocycles, an approach that was based on the effective Zr-catalyzed kinetic resolution of dihydropyrans.[13] However, as shown in Scheme 6, the recovered starting material (**13**) was obtained with <10% ee upon treatment with 10 mol % (*R*)-(EBTHI)Zr-binol and 5 equiv of EtMgCl (70 °C, THF). We conjectured that since the (EBTHI)Zr-catalyzed reaction provides efficient resolution only when asymmetric alkylation occurs at the cyclic alkene site, it must therefore be that the competitive reaction at the styrenyl terminal olefin renders the resolution process largely ineffective; analysis of the ^{1}H NMR spectra of the unpurified reaction mixture supported this contention. Catalytic resolution of disubstituted styrene **25** was thus examined. Under identical conditions as mentioned above,

Scheme 6



13	R=H	n=2	(*S*)-**13** recovered in <10% ee
25	R=Me	n=2	(*S*)-**25** recovered in >99% ee
26	R=Me	n=1	(*S*)-**26** recovered in 80% ee

Scheme 7

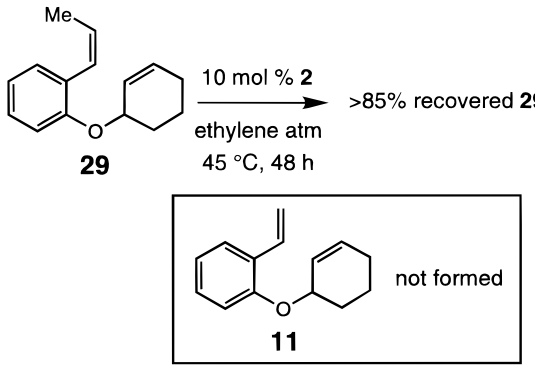


cycloheptenyl styrenyl ether (*S*)-**25** is obtained in >99% ee (chiral GLC analysis) and 98% yield (based on percent conversion). The cyclohexenyl substrate **26** is also resolved by this method, albeit less efficiently: (*S*)-**26** is obtained in 80% ee after 62% conversion.

With an effective catalytic resolution procedure in hand, we focused our attention on the Ru-catalyzed rearrangement of disubstituted styrenyl ethers (e.g., **25**). When **25** is treated with 10 mol % **2** under an atmosphere of Ar (Scheme 7), chromene formation is sluggish: 25−30% of dimer (*S,S*)-**27** is isolated after 48 h at 45 °C, together with substantial amounts of oligomeric materials. Initially, performing the reactions under an atmosphere of ethylene was not considered. At the time, we believed that the presence of the gaseous alkene *only* served to avoid dimer formation and would do little to enhance reaction efficiency. Furthermore, the use of ethylene with reactions run at higher temperatures (e.g., 45 °C vs 22 °C) would be experimentally cumbersome.

However, upon further consideration, we rationalized that with a disubstituted styrene as substrate (e.g., **25**), the desired monomer chromenes could in fact be obtained cleanly if the Ru-catalyzed reaction were to be carried out under ethylene (22 °C). This rationale, as illustrated in Scheme 8, was based on the hypothesis that initial cross-metathesis between ethylene and the styrene alkene would either lead to the formation of the corresponding terminal styrene **13** or metal carbene complex **28**, both of which would be expected to undergo facile rearrangement. Moreover, because the transformation is performed at ambient temperature under ethylene, dimer formation would be minimized. Accordingly, when (*S*)-**25**, obtained from the Zr-catalyzed kinetic resolution of **25**, was treated with 5 mol % **2** under an atmosphere of ethylene at 22 °C (CH_2Cl_2, 24 h), (*S*)-**14** was obtained in 81% isolated yield and >99% ee (Scheme 7). That is, as expected, the use of an ethylene atmosphere proved to be necessary for preferential monomer formation (10% of the derived dimer was also generated). However, these results indicate that an *ethylene atmosphere is imperative for efficient metal-catalyzed chromene formation as well* (25−30% yield of dimer **27** under argon).

The above hypothesis (i.e., initial cross-metathesis and involvement of **13** and **28** in Scheme 8) was challenged soon afterward. We discovered that when cyclohexenyl substrate **29** is treated to the same conditions as above, the unreacted starting material—even after prolonged reaction times (24 h)—still bears the disubstituted olefin (eq 3). That the six-membered styrenyl

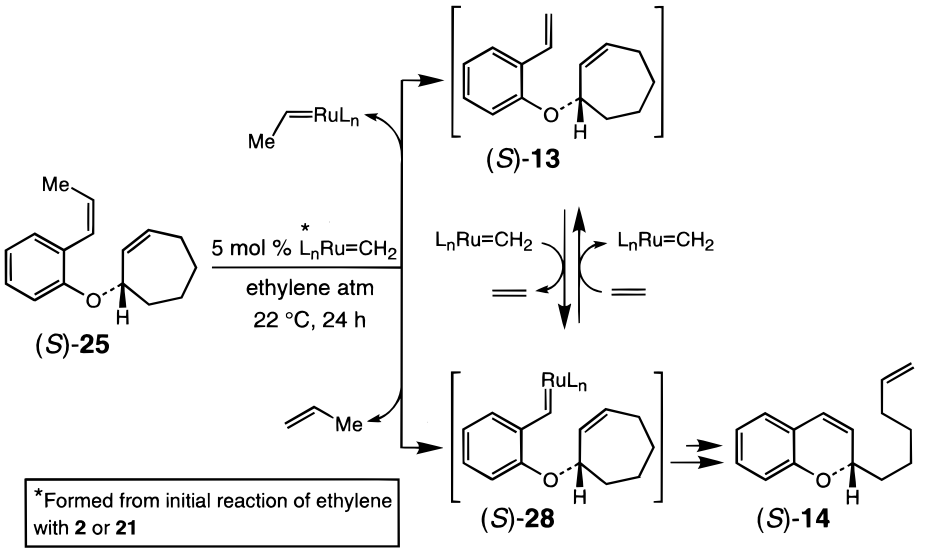


(3)

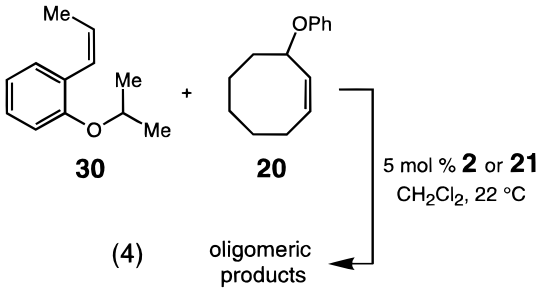
ether **29** would prove recalcitrant was expected, but the complete absence of the cross-metathesis product **11** clearly indicated that the rationale behind the successful Ru-catalyzed reaction of (*S*)-**25** may have been unfounded, despite the positive outcome (efficient formation of **14** under ethylene).

To probe the alternative mechanistic pathways, we set out to establish whether in fact, with disubstituted styrene substrates, the active Ru−carbene complex also reacts with the styrenyl olefin first. Toward this end, we found that when disubstituted styrene **30** and cyclooctenyl phenyl ether **20** are treated with 5

Scheme 8



mol % Ru complex **21** (eq 4), oligomeric products are formed



(4)

in the same manner as observed when **20** is treated with the transition metal catalyst in the *absence* of terminal styrene **19**. These experiments therefore suggested that *with the more highly substituted substrates (e.g., **25**), in contrast to the reactions of terminal styrenyl alkenes (e.g., **13** in Scheme 3), catalytic chromene formation may commence with reaction at the carbocyclic alkene site*.[14]

The aforementioned mechanistic scenario suggests two critical roles for ethylene in the catalytic reactions of disubstituted styrenes:

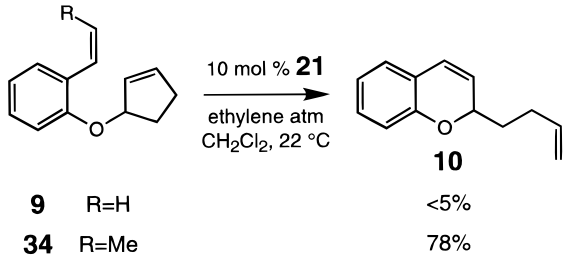
(1) Transformations of the more highly substituted styrenyl ethers are notably more facile under an atmosphere of ethylene due to the presence of the more reactive $L_nRu{=}CH_2$ (formed by the reaction of **2** or **21** with ethylene). Under an atmosphere of Ar and after the first turnover has transpired, $L_nRu{=}CHCH_3$ is likely the participating catalyst. When the reaction is performed under ethylene, $L_nRu{=}CHCH_3$ is immediately converted to $L_nRu{=}CH_2$. Reactions of monosubstituted styrenes do not require ethylene to proceed smoothly, because, as illustrated in Scheme 3, with this class of starting materials, the more reactive $L_nRu{=}CH_2$ is formed following the first catalytic cycle.

(2) Catalytic reactions of disubstituted styrenyl substrates lead to significantly lower amounts of oligomeric products because of the presence of ethylene. That is, if the initial transformation of the Ru−carbene occurs with the "undesired regiochemistry" (*e.g.*, **25** → **32** in contrast to **25** → **31**, Scheme 9), oligomerization may predominate, particularly in instances where reclosure of the carbocyclic ring is relatively sluggish (e.g., cycloheptenyl substrates).

In contrast, as illustrated in Scheme 10, in the presence of an ethylene atmosphere, the unwanted metal−carbene isomer **32** may rapidly be converted to triene **33**. The resulting triene might then react with $L_nRu{=}CH_2$ to afford metal−carbene **31** and eventually chromene **14**.

To test the validity of the above hypothesis, an authentic sample of triene **33** was prepared and treated with 5 mol % Ru complex **21** in dichloromethane at 22 °C (24 h). Thus, as depicted in Scheme 11, when the ring-forming process is carried out under an atmosphere of Ar, oligomeric products are generated. In contrast, when the reaction is performed in the presence of ethylene, **14** is readily obtained in 83% isolated yield.

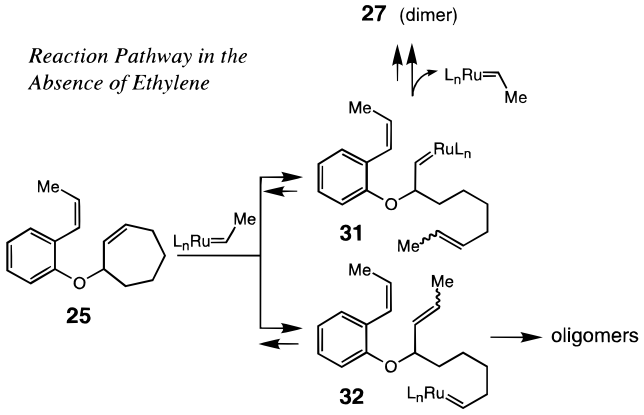
A significant implication of the mechanistic variance exhibited in reactions of disubstituted styrenyl ethers is that the related cyclopentenyl substrates should readily afford the desired chromenes by the catalytic process (in contrast to complete lack of reactivity of the derived terminal styrene **9**, eq 5). Since the



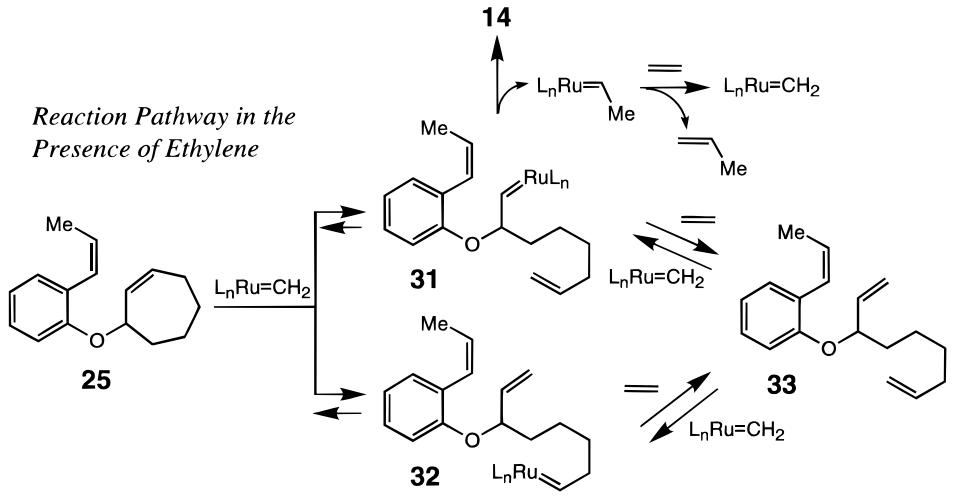
(5)

metal−carbene complex first reacts with the carbocyclic alkene, the strained tetracyclic intermediate, formed in reactions of terminal styrenes (cf. **16** in Scheme 3), can be avoided. Indeed, in contrast to **9**, which is recovered unchanged with <5%

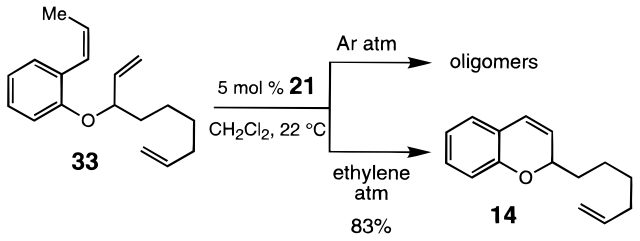
Scheme 9



Scheme 10



Scheme 11



conversion (eq 5), treatment of **34** with 10 mol % **21** (CH_2Cl_2, 22 °C, 50 h) leads to the formation of **10** in 78% yield after silica gel chromatography (eq 5).

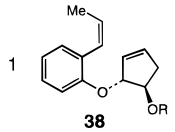
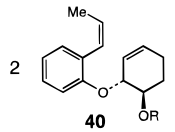
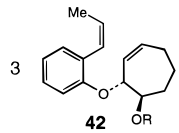
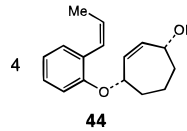
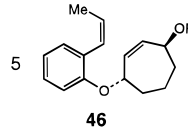
The corresponding cyclohexenyl system **35** (Scheme 12) remains relatively unreactive, however, even when the reaction is performed under an ethylene atmosphere: after 24 h (10 mol % **21**, 1 atm. ethylene, CH_2Cl_2), only 10−20% of chromene **12** is obtained. This persistent lack of reactivity is presumably because (i) the relatively strain-free six-membered ring is less prone (relative to cyclopentenyl and cycloheptenyl structures)[15] to react with $L_nRu{=}CH_2$, and (ii) in the case ring rupture does occur with the proper regiocontrol to afford **36** (vs **37**, Scheme 12), reaction with the neighboring terminal alkene (leading back to **35**) should be kinetically more favored in comparison to that with the disubstituted styrene olefin to deliver **12**. Accordingly, when triene **38** is subjected to these conditions, only 15−20% of **12** is obtained (24 h). (See below for an effective catalyst for reactions of cyclohexenyl substrates.)

Reactions of Functionalized Styrenyl Ethers. An advantage of the methods described herein is that control of relative stereochemistry on the carbocyclic substrate prior to catalytic synthesis of chromenes can lead to the formation of various functionalized heterocycles in excellent diastereochemical purity. Several examples are illustrated in Table 1.[16] Styrenyl ethers of various ring sizes can be efficiently converted to their derived chromenes in high yields. Two critical points with regard to the data depicted in Table 1 merit mention.

(1) As shown in the entries of Table 1, with the more functionalized starting substrates, chromene formation typically occurs more efficiently if Schrock's complex[17] Mo(CHCMe$_2$-Ph)(N(2,6-(*i*-Pr)$_2$C$_6$H$_3$))(OCMe(CF$_3$)$_2$)$_2$ (**48**) is used intead of Ru-based catalysts **2** or **21**. An impressive example is shown in entry 2 of Table 1; *with **48** as catalyst, even the relatively unreactive cyclohexenyl substrates such as **40a** or **40b** are converted to the derived chromenes in excellent yields.* Exceptions to this trend are found in the reactions of **42a** and **42b**. Particularly striking is the process involving **42a**, where the Ru complex **21** affords **43a** in 54% yield; in contrast, little or no product is obtained with Mo system **48** as the precatalyst. The lower activity of **48** is likely due to the higher Lewis acidic nature of the Mo center, leading to catalyst inactivation through chelation with the Lewis basic alcohol and the adjacent phenoxy oxygen.

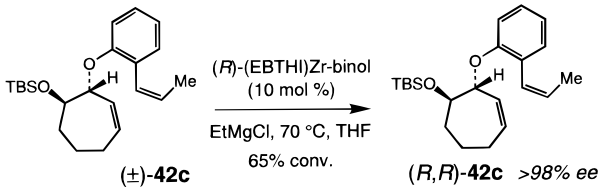
(2) The presence of an unprotected hydroxyl function, such as those shown in entries 3 and 4, result in notable diminution in yields (mass balance remains >95%). As mentioned before, the detrimental effect of the alcohol groups is likely due to association with the Lewis acidic metal centers,[18] resulting in reduction of the metathesis activity of the transition metal complexes.

Table 1. Synthesis of Functionalized Chromenes Through Ru- and Mo-Catalyzed Reactions of Styrenyl Ethers[a]

entry	substrate	product	R	yield (%) Ru cat.[b]	yield (%) Mo cat.[b]
1			**a** Bn	35	91
			b TBS	12	93
2			**a** Bn	36	79
			b TBS	32	90
3			**a** H	54	<5
			b Bn	82	75
			c TBS	88	97
4			**a** H	10	<5
			b Bn	65	98
			c TBS	55	95
5			**a** Bn	25	88
			b TBS	29	92

[a] Conditions: 9 mol % **21**, CH_2Cl_2, 22 °C, ethylene (1 atm), 36 h; 10 mol % **48**, C_6H_6, 22 °C, 24 h. [b] Isolated yields after silica gel chromatography.

Kinetic Resolution of Functionalized Styrenyl Ethers. As illustrated in Scheme 6 and discussed above, certain disubstituted styrene ethers can be efficiently resolved through the Zr-catalyzed kinetic resolution. As illustrated in eq 6, optically



(6)

pure cycloheptenyl ether **42c** is obtained by the Zr-catalyzed process (>98% ee at 65% conv by analysis of 400 MHz ^{19}F NMR of the derived (*S*)-MTPA ester). The successful catalytic resolution makes the parent alcohol and the derived benzyl ether derivatives **42a** and **42b** accessible in the optically pure form as well. However, this approach cannot be successfully applied to all the substrates shown in Table 1. For example, under identical conditions, **38b** is recovered in only 52% ee after 60% conversion. In a similar vein, **40a** is recovered in 30% ee after 55% conversion. Cycloheptenyl substrates shown in entries 4 and 5 undergo significant decomposition under the Zr-catalyzed

(14) For a related regioselectivity variance as a result of alkene substitution pattern, see: Zuercher, W. J.; Hashimoto, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **1996**, *118*, 6634−6640.

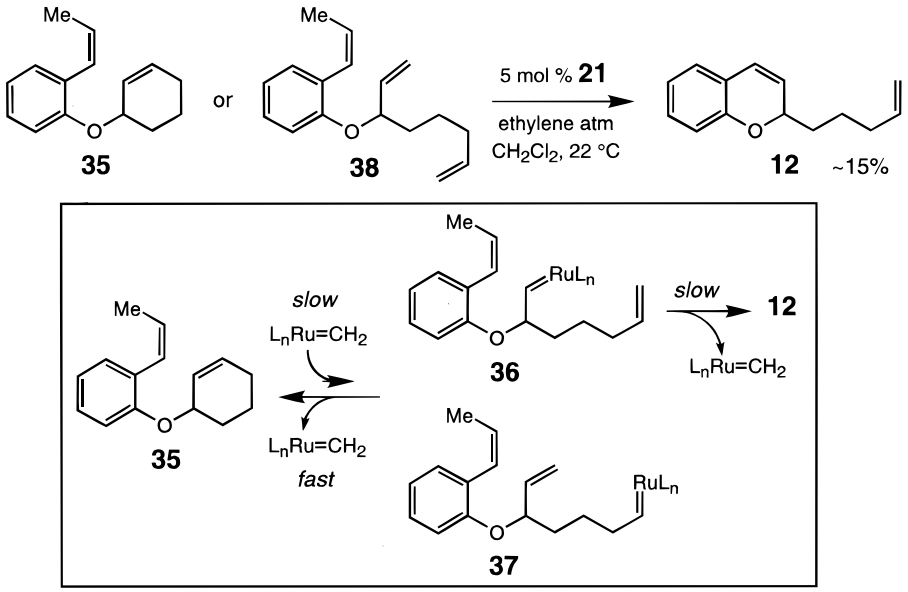
(15) For a study on the ring-opening metathesis of cyclohexene, see: Patton, P. A.; Lillya, C. P.; McCarthy, T. J. *Macromolecules* **1986**, *19*, 1266−1268.

(16) See the Supporting Information section for the synthesis of requisite starting materials.

(17) (a) Schrock, R. R.; Murdzek, J. S.; Bazan, G. C.; Robbins, J.; DiMare, M.; O'Regan, M. *J. Am. Chem. Soc.* **1990**, *112*, 3875−3886. (b) Bazan, G. C.; Schrock, R. R.; Cho, H.-N.; Gibson, V. C. *Macromolecules* **1991**, *24*, 4495−4502.

(18) For a hydroxyl-directed olefination of ketones with **48** as catalyst, see: Fujimura, O.; Fu, G. C.; Rothemund, P. W. K.; Grubbs, R. H. *J. Am. Chem. Soc.* **1995**, *117*, 2355−2356.

Scheme 12



carbomagnesation conditions. These observations clearly indicate that future work must be directed toward the development of more general methods that provide a wider range of styrenyl ethers in high optical purity. A more enticing and economical approach would be the development of a chiral metathesis catalyst that effects the chromene formation and resolves the two styrene ether enantiomers simultaneously.

Conclusions. A metal-catalyzed reaction is disclosed that converts allylic styrenyl ethers to 2-substituted chromenes in an efficient manner. Although reactions of terminal styrenes catalyzed by Ru-based catalysts **2** or **21** proceed through initial reaction with the styrenyl olefin, catalytic transformations of disubstituted substrates appear to be initiated by interaction of the metal−carbene complex with the carbocyclic π system. Use of an ethylene atmosphere significantly enhances the generality and utility of the process: (1) It leads to near exclusive formation of monomeric chromenes. (2) It allows for a more efficient conversion of disubstituted styrenes to the corresponding chromenes. (3) It permits the catalytic cycle to bypass a strained intermediate (cf. **16** in Scheme 3), thus enabling additional substrates to be readily converted to chromenes (reactions of **38** and **40a**,**b**). The use of Schrock's Mo-based catalyst **48** further enhances the power of this transition metal-catalyzed process by effecting efficient reactions of functionalized substrates (e.g., entry 2 of Table 1). An important corollary to these transformations is that, in certain cases, the starting material can be obtained optically pure through the use of Zr-catalyzed kinetic resolution (Scheme 6 and eq 6). Nonetheless, studies aimed at the development of more general technologies that afford nonracemic styrene ethers are required. These investigations and the total synthesis of medicinally important agents that examine and challenge the utility of the methods described herein are in progress.

Experimental Section

General Information. Infrared (IR) spectra were recorded on a Perkin-Elmer 781 spectophotometer, ν_{max} in cm^{-1}. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). ^1H NMR spectra were recorded on a Varian Unity 300 (300 MHz) or Varian GN-400 (400 MHz). Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and assignment. ^{13}C NMR spectra were recorded on a Varian Unity 300 (75 MHz) or Varian GN-400 (100 MHz) with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal reference ($CDCl_3$: δ 77.7 ppm). An Alltech Associates DB-1 capillary column (30 m × 0.32 mm) was used to determine conversions. Enantiomer ratios were determined by GLC with an ALPHA-DEX 120 (30 m × 0.25 mm) chiral column by Supelco. High-resolution mass spectra obtained at the Mass Spectrometry Facility of the University of Illinois (Urbana−Champaign, Illinois). Combustion analysis data could not be obtained due to the instability of 2-substituted chromene products. Since the chromene products decompose rapidly (within approximately 30 min) at 22 °C, spectral data were obtained immediately after silica gel chromatography. Samples for HRMS were stored under argon in a freezer at −20 °C until immediately prior to analysis.

All reactions were conducted in oven-dried (135 °C) and flame-dried glassware under an inert atmosphere of dry argon. Tetrahydrofuran was distilled from sodium metal/benzophenone ketyl. Dichloromethane was distilled from calcium hydride. Ethylmagnesium chloride was prepared from ethyl chloride and Mg (turnings), which were purchased from Aldrich and used without further purification. (EBTHI)Zr-binol was prepared and resolved by methods of Brintzinger and Buchwald.[19] Nonracemic (EBTHI)Zr-binol catalyst batches were stored under argon in a glovebox. $(PCy_3)_2Cl_2Ru{=}CHCH{=}CPh_2$ and $(PCy_3)_2Cl_2Ru{=}CHPh$ were prepared by the method of Grubbs.[3] $Mo(CHCMe_2Ph)(N(2,6\text{-}(i\text{-}Pr)_2C_6H_3))(OCMe(CF_3)_2)_2$ was prepared by the method of Schrock.[17]

Representative Experimental Procedure for the Ru-Catalyzed Rearrangement of (2*S*)-((1*S*)-(*tert*-Butyldimethylsiloxy)-4-pentenyl)-2*H*-3,4-dihydrobenzopyran (40b → 41b). A flame-dried 10 mL round-bottom flask was charged with **40b** (40 mg, 0.116 mmol) and CH_2Cl_2 (1.16 mL). Ruthenium complex **2** (8.6 mg, 0.01 mmol, 9 mol %) was added in three equal portions every 12 h. The reaction vessel was initially

(19) (a) Wild, F. R. W. P.; Wasiucionek, M.; Huttner, G.; Brintzinger, H. *J. Organomet. Chem.* **1985**, *288*, 63−67. (b) Grossman, R. B.; Doyle, R. A.; Buchwald, S. L. *Organometallics* **1991**, *10*, 1501−1505.

flushed with ethylene gas (vacuum−ethylene flush cycle was repeated three times); the mixture was kept under an atmosphere of ethylene (balloon). Stirring was allowed to continue at 22 °C for a total of 36 h. The reaction was quenched by the addition of 0.5 mL of undistilled ethyl vinyl ether;[20] volatiles were subsequently removed in vacuo. The resulting residue was purified through silica gel chromatography to afford chromene **41b** (13.8 mg, 36% yield). IR (NaCl, film): 3073 (w), 2955 (m), 2929 (m), 2856 (m), 1458 (w), 1257 (m), 1230 (m), 1085 (m), 835 (m), 775 (m), 751 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.07 (dt, J = 7.7, 1.6 Hz, 1H, aromatic CH), 6.92 (dd, J = 7.2, 1.6 Hz, 1H, aromatic CH), 6.81 (dt, J = 7.3, 0.8 Hz, 1H, aromatic CH), 6.72 (dd, J = 8.1, 0.8 Hz, 1H, aromatic CH), 6.43 (dd, J = 10.0, 1.9 Hz, 1H, aromatic (**H**)C═CH), 5.87−5.78 (m, 1H, **H**C═CH_2), 5.76 (dd, J = 10.0, 2.8 Hz, 1H, aromatic (H)C═C**H**), 5.04−4.99 (m, 1H, HC═C**H**H), 4.96−4.93 (m, 1H, HC═CH**H**), 4.92−4.90 (m, 1H, HC═CH−C**H**−O), 3.91 (dt, J = 8.6, 4.0 Hz, 1H, **H**C−OTBS), 2.28−2.19 (m, 1H, CH**H**CH_2), 2.13−2.04 (m, 1H, CH**H**CH_2), 1.82−1.74 (m, 1H, CH_2CH**H**), 1.61−1.51 (m, 1H, CH_2C**H**H), 0.88 (s, 9H, $C(CH_3)_3$), 0.07 (s, 6H, $SiCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.3, 139.4, 129.7, 127.2, 125.6, 122.9, 122.4, 121.6, 116.1, 115.2, 78.6, 73.8, 32.3, 30.5, 26.5, 18.8, −3.7, −3.9. HRMS Calcd for $C_{20}H_{30}O_2Si$ (M − H): 329.1937. Found: 329.1939.

Representative Experimental Procedure for the Molybdenum-Catalyzed Rearrangement of (2*S*)-((1*S*)-(*tert*-Butyldimethylsiloxy)-4-pentenyl)-2*H*-3,4-dihydrobenzopyran (40b → 41b). Styrenyl ether **40b** (52.0 mg, 0.15 mmol) was placed in a 10 mL round-bottom flask. After the addition of degassed benzene (1.51 mL), the resulting solution was charged with Mo catalyst **48** (11.6 mg, 0.015 mmol, 10 mol %). The reaction vessel was flushed with ethylene (vacuum−ethylene flush cycle was repeated three times), equipped with an ethylene-filled balloon, and stirred at 22 °C for 24 h. The reaction was quenched by the addition of 500 mL of undistilled ethyl vinyl ether, after which the volatiles were subsequently removed in vacuo. The resulting residue was purified through silica gel chromatography to afford chromene **41b** (39.2 mg, 79% yield).

2-(3-Butenyl)-2*H*-3,4-dihydrobenzopyran (10). IR (NaCl): 3062 (w), 2936 (m), 1483 (s), 1457 (m), 1231 (s), 1117 (m), 752 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.09 (dt, J = 7.6, 1.6 Hz, 1H, aromatic CH), 6.95 (dd, J = 7.6, 1.6 Hz, 1H, aromatic CH), 6.83 (dt, J = 7.6, 1.2 Hz, 1H, aromatic CH), 6.76 (d, J = 8.0 Hz, 1H, aromatic CH), 6.38 (d, J = 10.0 Hz, 1H, aryl (**H**)C═CH), 5.81 (dddd, J = 17.2, 13.6, 10.4, 6.8 Hz, 1H, alkyl **H**C═CH_2), 5.67 (dd, J = 9.6, 3.2 Hz, 1H, aryl (H)C═C**H**), 5.01 (dd, J = 16.8, 1.2 Hz, 1H, HC═C**H**H), 4.96 (dd, J = 10.4, 0.8 Hz, 1H, HC═CH**H**), 4.87−4.85 (m, 1H, HC═CHC**H**−O), 2.12−2.07 (m, 2H, CH_2−CHC**H**$_2$) 1.85−1.75 (m, 1H, O−CHC**H**H), 1.72−1.60 (m, 1H, O−CHCH**H**). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.0, 138.6, 129.8, 127.1, 126.3, 124.7, 122.6, 121.6, 116.6, 115.7, 75.1, 35.1, 29.7. HRMS Calcd for $C_{13}H_{14}O$: 186.1045. Found: 186.1041.

(2*S*)-((1*S*)-(Benzyloxy)-3-butenyl)-2*H*-3,4-dihydrobenzopyran (39a). IR (NaCl): 3075 (w), 2949 (m), 2931 (m), 2861 (m), 2886 (m), 1489 (m), 1458 (s), 1224 (m), 1088 (s), 835 (s), 776 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.29−7.16 (m, 5H, aromatic CH), 7.02 (dt, J = 7.2, 1.6 Hz, 1H, aromatic CH), 6.87 (dd, J = 7.2, 1.6 Hz, 1H, aromatic CH), 6.75 (dt, J = 7.2, 1.6 Hz, 1H, aromatic CH), 6.70 (d, J = 8.4 Hz, 1H, aromatic CH), 6.37 (d, J = 10.0, Hz, 1H, aryl (**H**)C═CH), 5.86−5.76 (m, 1H, **H**C═CH_2), 5.64 (dd, J = 6.4, 3.6 Hz, 1H, aryl (H)C═C**H**), 5.03 (d, J = 17.2 Hz, 1H, HC═C**H**H), 4.98 (d, J = 10.4 Hz, 1H, HC═CH**H**), 4.92−4.89 (m, 1H, CH═CHC**H**O), 4.60 (d, J = 10.8 Hz, 1H, aryl C**H**H−O), 4.52 (d, J = 10.8 Hz, 1H, aryl CH**H**−O), 3.62−3.58 (m, 1H, **H**C−OBn), 2.42−2.35 (m, 1H, CH_2═CHC**H**H), 2.29−2.22 (m, 1H, CH_2═CHCH**H**). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.1, 139.1, 135.5, 130.0, 129.0, 128.5, 128.3, 127.2, 125.8, 122.9, 122.4, 121.8, 117.9, 116.5, 80.5, 78.0, 73.7, 35.6. HRMS Calcd for $C_{20}H_{20}O_2$: 292.1463. Found: 292.1464.

(2*S*)-((1*S*)-(*tert*-Butyldimethylsiloxy)-3-butenyl)-2*H*-3,4-dihydrobenzopyran (39b). IR (NaCl): 3075 (w), 2949 (m), 2931 (m), 2886 (m), 2861 (m), 1489 (m), 1458 (m), 1224 (m), 1088 (s), 835 (s), 775 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.08 (dt, J = 7.2, 1.6 Hz, 1H, aromatic CH), 6.92 (dd, J = 7.2, 1.6 Hz, 1H, aromatic CH), 6.82 (dt, J = 7.2, 1.6 Hz, 1H, aromatic CH), 6.74 (d, J = 7.2 Hz, 1H, aromatic CH), 6.44 (dd, J = 9.6, 1.6 Hz, 1H, aryl (**H**)C═CH), 5.87 (dddd, J = 14.0, 14.0, 10.0, 7.7 Hz, 1H, **H**C═CH_2), 5.75 (dd, J = 10.0, 3.2 Hz, 1H, aryl (H)C═C**H**), 5.11−5.04 (m, 1H, HC═C**H**H), 4.91−4.89 (m, 1H, HC═CH**H**), 3.92 (ddd, J = 8.0, 8.0, 4.4 Hz, 1H, **H**C−OTBS), 2.50−2.44 (m, 1H, CH**H**CH_2), 2.24 (ddd, J = 14.0, 14.0, 7.6, 1H, CH_2═CHCH**H**), 0.87 (s, 9H, $C(CH_3)_3$), 0.07 (s, 3H, $SiCH_3$), 0.05 (s, 3H, $SiCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.3, 135.9, 129.7, 127.2, 125.7, 122.8, 122.3, 121.5, 117.9, 116.2, 78.5, 74.3, 38.0, 26.5, 18.8, −3.8, −3.8. HRMS Calcd for $C_{19}H_{28}O_2Si$ (M − H): 315.1781. Found: 315.1779.

(2*S*)-((1*S*)-(Benzyloxy)-4-pentenyl)-2*H*-3,4-dihydrobenzopyran (41a). ^1H NMR (400 MHz, $CDCl_3$): δ 7.36−7.29 (m, 5H, aromatic CH), 7.12 (dt, J = 7.6, 1.6 Hz, 1H, aromatic CH), 6.97 (dd, J = 7.6, 1.6 Hz, 1H, aromatic CH), 6.86 (dt, J = 7.6, 1.6 Hz, 1H, aromatic CH), 6.80 (d, J = 8.0 Hz, 1H, aromatic CH), 6.47 (dd, J = 10.0, 1.6 Hz, 1H, aryl (**H**)C═CH), 5.85−5.74 (m, 1H, **H**C═CH_2), 5.76 (dd, J = 10.0, 3.6 Hz, 1H, aryl (H)C═C**H**), 5.05−4.94 (m, 2H, HC═C**H**$_2$), 4.75 (d, J = 11.6 Hz, 1H, aryl C**H**H−O), 4.56 (d, J = 11.6 Hz, 1H, aryl CH**H**−O), 3.66 (ddd, J = 9.2, 5.6, 3.6 Hz, 1H, **H**C−OBn), 2.34−2.25 (m, 1H, CH_2═CHC**H**H), 2.18−2.08 (m, 1H, CH_2═CHCH**H**), 1.80−1.61 (m, 2H, CH_2═CHCH_2C**H**$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.0, 139.3, 139.1, 130.0, 129.0, 128.6, 127.3, 125.7, 123.0, 122.5, 121.8, 116.4, 115.5, 80.3, 77.4, 73.9, 30.5, 30.4. HRMS Calcd for $C_{21}H_{22}O_2$: 306.1620. Found: 306.1620.

(2*S*)-((1*S*)-(*tert*-Butyldimethylsiloxy)-4-pentenyl)-2*H*-3,4-dihydrobenzopyran (41b). IR (NaCl): 3073 (w), 2955 (m), 2929 (m), 2856 (m), 1458 (w), 1257 (m), 1230 (m), 1085 (m), 835 (m), 775 (m), 751 (m) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.07 (dt, J = 7.7, 1.6 Hz, 1H, aromatic CH), 6.92 (dd, J = 7.2, 1.6 Hz, 1H, aromatic CH), 6.81 (dt, J = 7.3, 0.8 Hz, 1H, aromatic CH), 6.72 (dd, J = 8.1, 0.8 Hz, 1H, aromatic CH), 6.43 (dd, J = 10.0, 1.9 Hz, 1H, aryl (**H**)C═CH), 5.87−5.78 (m, 1H, **H**C═CH_2), 5.76 (dd, J = 10.0, 2.8 Hz, 1H, aryl (H)C═C**H**), 5.04−4.99 (m, 1H, HC═C**H**H), 4.96−4.93 (m, 1H, HC═CH**H**), 4.92−4.90 (m, 1H, HC═CH−C**H**−O), 3.91 (dt, J = 8.6, 4.0 Hz, 1H, **H**C−OTBS), 2.28−2.19 (m, 1H, CH**H**CH_2), 2.13−2.04 (m, 1H, CH**H**CH_2), 1.82−1.74 (m, 1H, CH_2CH**H**), 1.61−1.51 (m, 1H, CH_2C**H**H), 0.88 (s, 9H, $C(CH_3)_3$), 0.07 (s, 6H, $SiCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.3, 139.4, 129.7, 127.2, 125.6, 122.9, 122.4, 121.6, 116.1, 115.2, 78.6, 73.8, 32.3, 30.5, 26.5, 18.8, −3.7, −3.9. HRMS Calcd for $C_{20}H_{30}O_2Si$ (M − H): 329.1937. Found: 329.1939.

(2*S*)-((1*S*)-Hydroxy-4-hexenyl)-2*H*-3,4-dihydrobenzopyran (43a). IR (NaCl, film): 3440 (br), 3075 (w), 2930 (m), 1486 (s), 1457 (s), 1230 (s), 752 (m) cm^{-1}. ^1H NMR (400

(20) (a) Reference 3. (b) Schwab, P.; France, M. B.; Ziller, J. W.; Grubbs, R. H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2039−2041.

MHz, $CDCl_3$): δ 7.12 (dt, J = 7.6, 1.6 Hz, 1H, aromatic CH), 6.97 (dd, J = 7.6, 1.2 Hz, 1H, aromatic CH), 6.87 (dt, J = 7.6, 1.6 Hz, 1H, aromatic CH), 6.82 (d, J = 7.6 Hz, 1H, aromatic CH), 6.49 (d, J = 10.4 Hz, 1H, aryl (**H**)C═CH), 5.82 (dddd, J = 16.8, 13.2, 10.4, 6.4 Hz, 1H, **H**C═CH_2), 5.78 (dd, J = 10.0, 3.6 Hz, 1H, aryl (H)C═C**H**), 5.02 (dd, J = 16.8, 1.6 Hz, 1H, HC═C**H**H), 4.97 (dd, J = 10.0, 1.6 Hz, 1H, HC═CH**H**), 4.69−4.67 (m, 1H, aryl (H)C═CH−C**H**−O), 3.80−3.75 (m, 1H, **H**C−OH), 2.40 (d, J = 3.6 Hz, 1H, C−O**H**), 2.13−2.07 (m, 2H, C**H**$_2$C(H)═CH_2), 1.70−1.46 (m, 4H, C**H**$_2$C**H**$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.4, 139.2, 130.1, 127.4, 126.2, 122.8, 122.4, 122.1, 116.5, 115.4, 79.1, 73.6, 34.3, 31.9, 25.4. HRMS Calcd for $C_{15}H_{18}O_2$: 230.1307. Found: 230.1307.

(2*S*)-((1*S*)-(Benzyloxy)-5-hexenyl)-2*H*-3,4-dihydrobenzopyran (43b). IR (NaCl): 2923 (s), 2860 (m), 1487 (m), 1457 (s), 1230 (m), 1113 (w) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39−7.29 (m, 5H, aromatic CH), 7.12 (dt, J = 7.6, 1.6 Hz, 1H, aromatic CH), 6.97 (dd, J = 7.6, 1.6 Hz, 1H, aromatic CH), 6.86 (dt, J = 7.6, 0.8 Hz, 1H, aromatic CH), 6.81 (d, J = 8.0 Hz, 1H, aromatic CH), 6.47 (d, J = 10.0 Hz, 1H, aryl (**H**)C═CH), 5.84−5.74 (m, 1H, C**H**═CH_2), 5.75 (dd, J = 10.0, 3.6 Hz, 1H, aryl (H)C═C**H**), 5.03−4.95 (m, 2H, HC═C**H**$_2$), 4.75 (d, J = 11.2 Hz, 1H, aryl C**H**H−O), 4.57 (d, J = 11.2 Hz, 1H, aryl CH**H**−O), 3.66−3.62 (m, 1H, **H**C−OBn), 2.06−2.01 (m, 2H, CH_2═CHC**H**$_2$), 1.70−1.40 (m, 4H, C**H**$_2$C**H**$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.3, 129.9, 129.1, 129.0, 128.6, 128.5, 128.3, 127.2, 125.6, 123.1, 122.5, 121.8, 116.5, 115.3, 80.8, 77.5, 34.4, 30.6, 25.6. HRMS Calcd for $C_{22}H_{24}O_2$: 320.1776. Found: 320.1776.

(2*S*)-((1*S*)-(*tert*-Butyldimethylsiloxy)-5-hexenyl)-2*H*-3,4-dihydrobenzopyran (43c). IR (NaCl): 3075 (w), 2962 (m), 2942 (s), 2855 (m), 1489 (m), 1457 (m), 1231 (m), 1205 (m), 1086 (m), 778 (s) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (dt, J = 7.6, 1.6 Hz, 1H, aromatic CH), 6.94 (dd, J = 7.2, 1.6 Hz, 1H, aromatic CH), 6.82 (dt, J = 7.6, 1.6 Hz, 1H, aromatic CH), 6.75 (d, J = 8.0 Hz, 1H, aromatic CH), 6.43 (dd, J = 10.0, 1.6 Hz, 1H, aryl (**H**)C═CH), 5.86−5.75 (m, 1H, **H**C═CH_2), 5.77 (dd, J = 10.0, 2.8 Hz, 1H, aryl (H)C═C**H**), 5.00 (dd, J = 17.2, 1.6 Hz, 1H, HC═C**H**H), 4.95 (dd, J = 10.4, 1.6 Hz, 1H, HC═CH**H**), 4.92−4.89 (m, 1H, HC═CH−C**H**−O), 3.90 (dt, J = 8.0, 4.0 Hz, 1H, **H**C−OTBS), 2.12−2.01 (m, 2H, CH═CHC**H**$_2$), 1.73−1.43 (m, 4H, CH_2═CHCH_2C**H**$_2$C**H**$_2$), 0.90 (s, 9H, C(CH_3)$_3$), 0.09 (s, 3H, $SiCH_3$), 0.08 (s, 3H, $SiCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.4, 139.4, 129.9, 127.2, 125.5, 123.0, 122.5, 121.5, 116.2, 115.1, 78.7, 74.2, 34.5, 32.5, 26.5, 26.7, 18.8, −3.7, −3.9. HRMS Calcd for $C_{21}H_{34}O_2Si$ (M − H): 345.2250. Found: 345.2241.

(2*S*)-((4*R*)-(Benzyloxy)-5-hexenyl)-2*H*-3,4-dihydrobenzopyran (45b). IR (NaCl, film): 3024 (m), 2930 (s), 2855 (m), 1489 (s), 1231 (s), 1092 (m), 752 (s) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.23 (m, 5H, aromatic CH), 7.10 (dt, J = 7.6, 1.6 Hz, 1H, aromatic CH), 6.96 (dd, J = 7.2, 1.6 Hz, 1H, aromatic CH), 6.85 (dt, J = 7.6, 1.6 Hz, 1H, aromatic CH), 6.79 (d, J = 8.0 Hz, 1H, aromatic CH), 6.39 (d, J = 10.0 Hz, 1H, aryl (**H**)C═CH), 5.25 (dd, J = 3.6, 0.8 Hz, 1H, HC═C**H**H), 5.24−5.20 (m, 1H, HC═CH**H**), 4.85−4.83 (m, 1H, HC═CH−C**H**−O), 4.61 (d, J = 11.8 Hz, 1H, aryl C**H**H−O), 4.36 (d, J = 11.8 Hz, 1H, aryl CH**H**−O), 3.78−3.73 (m, 1H, **H**C−OBn), 1.84−1.50 (m, 6H, C**H**$_2$C**H**$_2$C**H**$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.1, 139.6, 139.4, 129.7, 127.0, 128.4, 128.1, 127.1, 126.5, 124.6, 122.6, 121.6, 117.9, 116.6, 81.0, 75.7, 70.7, 36.0, 35.9, 21.5. HRMS Calcd for $C_{22}H_{24}O_2$ (M − H): 319.1698. Found: 319.1696.

(2*S*)-((4*R*)-(*tert*-Butyldimethylsiloxy)-5-hexenyl)-2*H*-3,4-dihydrobenzopyran (45c). IR (NaCl): 3081 (w), 3043 (w), 3050 (w), 2962 (s), 2936 (s), 2867 (m), 1646 (w), 1608 (w), 1495 (m), 1256 (m), 1237 (m), 1036 (m), 834 (s), 778 (s), 752 (m) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (dt, J = 7.6, 1.6 Hz, 1H, aromatic CH), 6.95 (dd, J = 7.6, 1.6 Hz, 1H, aromatic CH), 6.84 (dt, J = 7.6, 1.6 Hz, 1H, aromatic CH), 6.77 (d, J = 7.6 Hz, 1H, aromatic CH), 6.38 (d, J = 9.6 Hz, 1H, aryl (**H**)C═CH), 5.80 (ddd, J = 13.2, 10.8, 6.0 Hz, 1H, **H**C═CH_2), 5.67 (dd, J = 10.0, 3.2 Hz, 1H, aryl (H)C═C**H**), 5.15 (dd, J = 12.5, 1.2 Hz, 1H, HC═C**H**H), 5.03 (dd, J = 10.0, 1.2 Hz, 1H, HC═CH**H**), 4.86−4.82 (m, 1H, HC═CH−C**H**−O), 4.11−4.10 (m, 1H, **H**C−OTBS), 1.84−1.46 (m, 6H, C**H**$_2$C**H**$_2$C**H**$_2$), 0.90 (s, 9H, C(CH_3)$_3$), 0.04 (s, 3H, $SiCH_3$), 0.03 (s, 3H, $SiCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.2, 142.3, 129.7, 127.1, 126.5, 124.6, 122.7, 121.6, 116.6, 114.3, 75.7, 74.4, 38.5, 36.1, 26.6, 21.2, 18.9, −3.7, −4.1. HRMS Calcd for $C_{21}H_{32}O_2Si$: 344.2172. Found: 344.2172.

(2*S*)-((4*S*)-(Benzyloxy)-5-hexenyl)-2*H*-3,4-dihydrobenzopyran (47a). IR (NaCl): 3640 (w), 3027 (w), 2929 (s), 2850 (s), 1638 (w), 1601 (w), 1479 (m), 1455 (m), 1234 (m), 1087 (m), 757 (m), 696 (m) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.26 (m, 5H, aromatic CH), 7.10 (dt, J = 7.6, 1.2 Hz, 1H, aromatic CH), 6.96 (dd, J = 7.6, 1.2 Hz, 1H, aromatic CH), 6.84 (t, J = 7.6 Hz, 1H, aromatic CH), 6.77 (d, J = 7.6 Hz, 1H, aromatic CH), 6.38 (d, J = 9.6 Hz, 1H, aryl (**H**)C═CH), 5.75 (ddd, J = 15.2, 10.0, 8.0 Hz, 1H, **H**C═CH_2), 5.66 (dd, J = 9.6, 3.6 Hz, 1H, aromatic (H)C═C**H**), 5.25−5.23 (m, 1H, HC═C**H**H), 4.84−4.82 (m, 1H, HC═CH−C**H**−O), 4.60 (d, J = 12.8 Hz, 1H, aryl C**H**H−O), 4.35 (d, J = 12.8 Hz, 1H, aryl CH**H**−O), 3.77−3.72 (m, 1H, **H**C−OBn), 1.83−1.24 (m, 6H, C**H**$_2$C**H**$_2$C**H**$_2$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.2, 139.6, 139.4, 129.7, 129.0, 128.5, 128.1, 127.1, 126.5, 124.6, 122.6, 121.6, 117.9, 116.6, 81.0, 75.7, 70.7, 35.9, 35.8, 21.5. HRMS Calcd for $C_{22}H_{24}O_2$ (M − H): 319.1698. Found: 319.1696.

(2*S*)-((4*S*)-(*tert*-Butyldimethylsiloxy)-5-hexenyl)-2*H*-3,4-dihydrobenzopyran (47b). IR (NaCl): 3081 (w), 3043 (w), 2962 (s), 2924 (s), 2855 (m), 1495 (m), 1457 (m), 1231 (m), 1081 (m), 841 (s), 778 (s) cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (dt, J = 7.8, 1.6 Hz, 1H, aromatic CH), 6.95 (dd, J = 7.2, 1.6 Hz, 1H, aromatic CH), 6.84 (dt, J = 7.6, 1.2 Hz, 1H, aromatic CH), 6.77 (d, J = 8.0 Hz, 1H, aromatic CH), 6.39 (dd, J = 9.8, 0.8 Hz, 1H, aryl (**H**)C═CH), 5.84−5.76 (m, 1H, **H**C═CH_2), 5.67 (dd, J = 9.8, 3.2 Hz, 1H, aryl (H)C═C**H**), 5.17−5.12 (m, 1H, HC═C**H**H), 5.04−5.01 (m, 1H, HC═CH**H**), 4.85−4.83 (m, 1H, HC═CH−C**H**−O), 4.12−4.07 (m, 1H, **H**C−OTBS), 1.84−1.42 (m, 6H, C**H**$_2$C**H**$_2$C**H**$_2$), 0.90 (s, 9H, C(CH_3)$_3$), 0.05 (s, 3H, $SiCH_3$), 0.03 (s, 3H, $SiCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.2, 142.4, 129.7, 127.1, 126.5, 124.6, 122.7, 121.6, 116.6, 114.3, 75.7, 74.4, 38.5, 36.0, 26.6, 21.3, 18.9, −3.6, −4.1. HRMS Calcd for $C_{21}H_{32}O_2Si$: 344.2172. Found: 344.2169.

Acknowledgment. The National Institutes of Health (GM-47480) and the National Science Foundation (NSF-9632278) generously supported this research. Additional support was provided by Johnson and Johnson. A.H.H. is an Alfred P. Sloan Fellow and a Dreyfus Teacher-Scholar. D.S.L. is a Department of Education GAANN Fellow.

Supporting Information Available: ^{1}H NMR and ^{13}C NMR spectra data for select reaction products (23 pages). See any current masthead page for ordering and Web access instructions.

JA9739796