JOC The Journal of Organic Chemistry

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Mechanistic Insight into the Formal [1,3]-Migration in the Thermal Claisen Rearrangement

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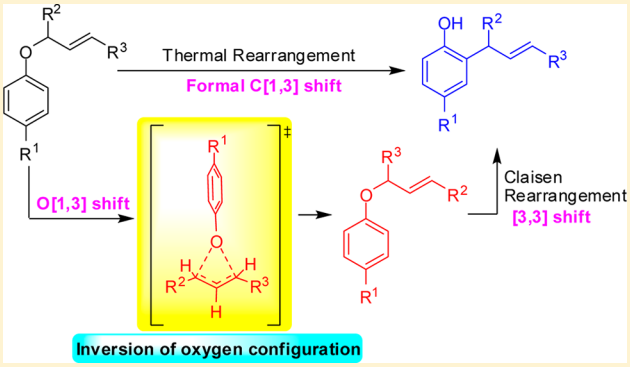
Supporting Information

ABSTRACT: The thermal formal [1,3]-sigmatropic shift of allyl aryl ethers has been studied in depth experimentally with the aid of the density functional theory (DFT) calculations of the B3LYP function. Three mechanistic possibilities, referred to as the radical, ionic, and concerted mechanisms, have previously been put forth to explain the thermal [1,3]-rearrangement process. However, the intercrossing and radical trapping experiments indicate the rearrangement is an intramolecular process. The computational studies reveal that the concerted C[1,3]-sigmatropic shift suffered from a higher energetic barrier to allow the rearrangement to proceed under the conditions used. However, a tandem O[1,3]-sigmatropic shift with a configuration inversion of the oxygen atom and [3,3]-sigmatropic shift (the Claisen rearrangement) is the most likely pathway for the formal [1,3] rearrangement. Furthermore, the rearrangement experiments with a designed optically active substrate and O[1,3]-sigmatropic shift examples verify the new cascade rearrangement. In addition, computational and experimental studies indicate that water molecule assists the proton shift during the isomerization. The combined methods provide the new insight into the mechanism of the thermal formal [1,3]-migration in the Claisen rearrangement and the novel O[1,3]-sigmatropic shift as well.



INTRODUCTION

The [1,3]-sigmatropic shift, as one of typical rearrangements in the thermal pericyclic rearrangements, is a powerful strategy for the construction of biologically active molecules in the synthetic organic chemistry.[1−5] The structure of the transition state and the configuration of the products in the [1,3]-rearrangement have been predicted by the Woodward−Hoffmann selection rule with a simple orbital symmetry of the frontier molecular orbital approach, where the thermal concerted [1,3]-migration of carbon is allowed to occur through the suprafacial transition state with an inversion of the configuration in the migrating groups (Figure 1).[6] Although the orbital symmetry rule is very versatile for the prediction of the process and the product configuration in the sigmatropic rearrangements, there is still the limitation that it is difficult to predict whether a rearrangement is really a concerted or stepwise process.

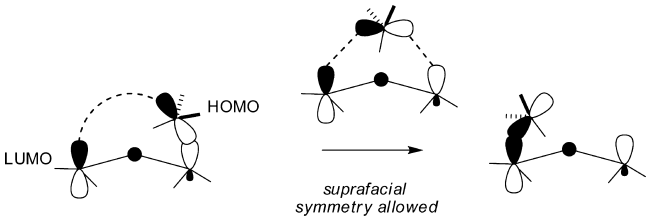
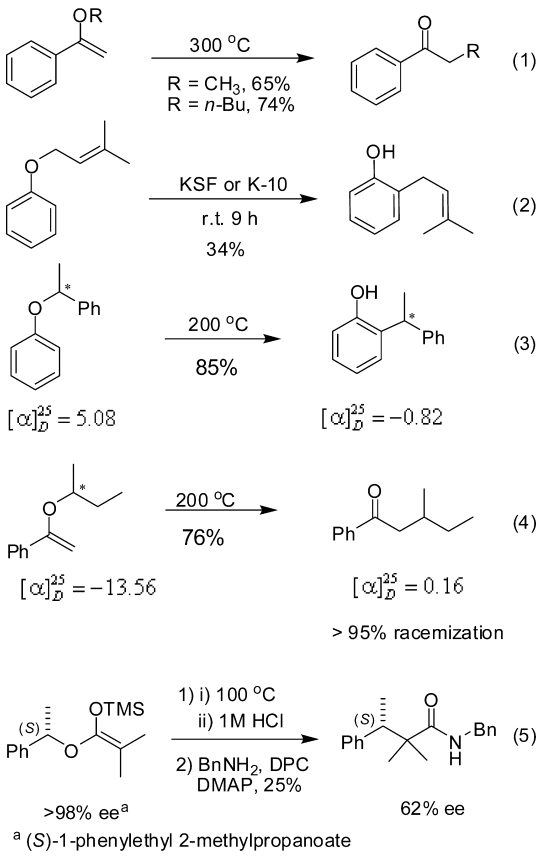


Figure 1. Concerted C[1,3]-sigmatropic shift.

The Claisen rearrangement, well-known as the [3,3]-sigmatropic shift of allyl aryl ethers,[7] furnishes a convenient access to *ortho*-allylphenols, precursors to a variety of natural products such as chromans[8] and coumarins.[9] However, since it was first mentioned by Claisen in 1896 (eq 1),[6] the formal [1,3]-migration has received less attention than [3,3]-Claisen rearrangement but has frequently been encountered in the Claisen rearrangement.[11] In 1990, Dauben reported that an allyl phenyl ether underwent a [1,3] rearrangement catalyzed by montmorillonite clays (eq 2),[11a] and then the reaction was optimized by Dintzner and co-workers to afford the product of the [1,3] rearrangement.[11b] Later, Vyvyan and co-workers reported that the triphenylphosphinegold(I) complexes catalyzed the Claisen-type rearrangement of allyl aryl ethers to produce both formal [3,3]- and [1,3]-rearrangement products through an ionic mechanism.[11c] The formal [1,3]-migration desired as an abnormal alternative to the Claisen rearrangement is still unclear in mechanism.

To date, the [1,3] oxygen to carbon rearrangement mechanism was categorized into four types: (1) the thermal rearrangement, (2) the transition metal catalyzed process, (3)

Received: October 10, 2012
Published: November 14, 2012



the nucleophilic mechanism, and (4) the Lewis acid catalyzed process.[12] The last three types have been studied very thoroughly, whereas the residual thermal one lacks generality with the radical, ionic, and concerted mechanistic possibilities. For instance, a report by Hart and Eleuterio in 1954 described the [1,3]-rearrangement of optically active α-phenethyl phenyl ether, which proceeded through partial racemization with approximately 30% retention of optical purity (eq 3).[13,14] The similar racemization process of optically active α-2-butoxystyrene was disclosed by Wiberg and Rowland in the next year, which was assumed as a radical mechanism (eq 4).[15] In 2002, Shiina and Nagasue found that (*S*)-1-trimethylsilanoxy-2-methyl-1-propenyl phenethyl ether underwent [1,3]-migration in the presence of HCl to afford (*S*)-*N*-benzyl-2,2-dimethyl-3-phenylbutanamide with ca. 60% retention of configuration at the migrating phenethyl group with assumption of the radical pair mechanism (eq 5).[16]

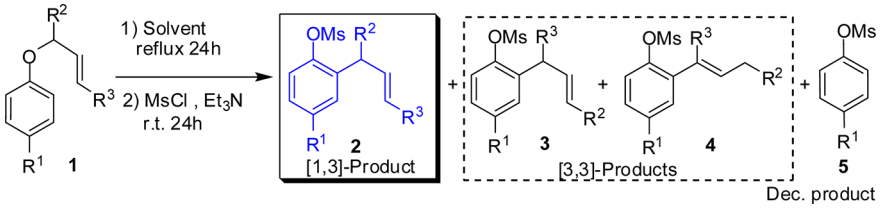
The interesting phenomena of the formal [1,3]-migration in the Claisen rearrangement have attracted some attention. However, the mechanism of the rearrangement process is still a riddle, and several questions about (a) the substrate scope and limitation, (b) the rearrangement mechanism, and (c) stereochemistry remain unanswered because of the scarce experimental evidence and computational support.

Herein, we describe a detailed experimental and computational studies on the thermal formal [1,3]-migration in the thermal Claisen rearrangement, aiming to answer the questions listed above. We believe that answering these questions is critical not only to our in-depth mechanistic understanding of these reactions, but also to studying the potential application of these reactions in total synthesis and other disciplines. We propose that the formal [1,3]-migration undergo a tandem process of the O[1,3]-sigmatropic shift with a configuration inversion of the oxygen atom and [3,3]-Claisen rearrangement on the basis of our investigation.

RESULTS AND DISCUSSION

Experimental Investigation on the Thermal Formal [1,3]-Sigmatropic Rearrangement. Since the aromatic Claisen rearrangement can undergo a [3,3]-sigmatropic rearrangement to produce *o*-allylphenols, or two tandem

Table 1. Thermal Rearrangement of Allyl Aryl Ethers 1



	allyl aryl ether **1**						isolated yield (%)		
entry	**1**	R^1	R^2	R^3	solvent	conversion (%)	**2**	**3**/**4** (*E*:*Z*)	**5**
1	**1a**	NO_2	H	Ph	DMF	51	2	7/23 (5:1)	7
2					DCB	89	10	26/4 (5:1)	25
3	**1b**	NO_2	Me	Ph	DMF	100	7	49 (4:1)/13	18
4					DCB	100	2	12 (4:1)/3	45
5	**1c**	CN	H	Ph	DMF	68	2	8/10 (6:1)	25
6					DCB	91	3	59/2 (6:1)	17
7	**1d**	CN	Me	Ph	DMF	94	3	54 (4:1)/27	4
8					DCB	100	30	24 (4:1)/4	19
9	**1e**	CN	Me	Tol	DMF	98	9	62 (4:1)/4	15
10					DCB	98	8	5 (4:1)/3	60
11	**1f**	Me	Me	Ph	DMF	89	–	37 (6:1)/–	29
12					DCB	90	–	15 (6:1)/–	42
13	**1g**	OMe	Me	Ph	DMF	98	–	41 (6:1)/–	36
14					DCB	100	–	10 (6:1)/–	57

dx.doi.org/10.1021/jo302210t | J. Org. Chem. 2012, 77, 10856−10869

[3,3]-sigmatropic shifts to yield *p*-allylphenols after isomerization, we applied allyl aryl ethers with *p*-substituents on the aromatic ring in order to prevent the occurrence of the second [3,3]-sigmatropic shift, simplifying the separation and determination of the rearrangement products. Allyl aryl ethers (**1**) with different *para*-substituents on the aromatic ring were synthesized from *p*-substituted phenols and different cinnamyl alcohols by the Mitsunobu reaction.[17] In some Mitsunobu reactions, regioisomers **1′** of the desired products **1** were also obtained via S_N2' process during the reaction.

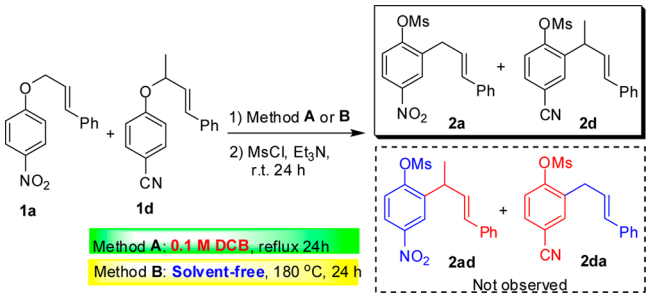
The thermal Claisen rearrangement requires generally higher temperature and relatively longer reaction time. DMF and *o*-dichlorobenzene (DCB) were chosen as solvents. Allyl aryl ether **1a** was first refluxed in DMF for 24 h. The TLC analysis indicated that R_f values of products are very close and difficult to separate by silica gel column chromatography. To separate conveniently, the phenolic hydroxyl group was protected with methanesulfonyl chloride. After the protection, the products were separated readily by column chromatography to obtain [1,3]-rearrangement product **2a** (2% yield), [3,3]-rearrangement product **3a** in 7% yield, the cascade [3,3]- and H[1,3]-rearrangement product **4a** (23% yield), and dissociation product 4-nitrophenol **5a** (7% yield) with recovery of 49% of substrate **1a** (Table 1, entry 1). When the reaction was conducted in refluxing DCB for 24 h, substrate **1a** generated **2a**, **3a**, **4a**, and **5a** in 10, 26, 4, and 25% yields, respectively, with recovery of **1a** in 10% yield (Table 1, entry 2).

To investigate the generality, substrates **1b**–**g** were subjected to the rearrangement, respectively, under the same conditions (Table 1). In particular, substrate **1d** underwent the thermal rearrangement in DCB to afford 30% yield of the [1,3]-rearrangement product **2d**, 28% yield of [3,3]-rearrangement products **3d** and **4d**, and 19% yield of dissociation product 4-cyanophenol **5b** (Table 1, entry 8). However, substrates **1f** and **1g** did not give the corresponding [1,3]-rearrangement products, only to afford [3,3]-rearrangement products and the corresponding phenols (Table 1, entries 11 and 12). The products **4** were generated from the [3,3]-products **3** through the isomerization, because the products **4** are more stable than products **3** because of the conjugative effect.

Viewing from the results of the formal [1,3]-rearrangement products, substrates with electron-withdrawing aromatic substituents produced the [1,3]-rearrangement products in 2–9% yields in DMF and in 2–30% yields in DCB. On the contrary, the ethers **1f**,**g** with electron-donating substituents can not give rise to [1,3]-rearrangement products, only producing [3,3]-Claisen rearrangement products and dissociation products phenols in 42 and 57% yields, respectively, in DCB. Therefore, the formal [1,3]-rearrangements were affected by the reaction temperature and the electronic effect of the aryl groups. The phenols were generated via a competitive radical mechanism. The results indicate that the radical mechanism exists in each of cases.

Mechanism Studies. Although it is well-known that the Claisen rearrangement is an intramolecular reaction, it is unclear that the formal [1,3]-rearrangement is an intramolecular or intermolecular process until now. To clarify in which process the formal [1,3]-rearrangement operates in the thermal aromatic Claisen rearrangement, we performed intercrossing experiments. A mixture of equimolar amounts of allyl aryl ethers **1a** and **1d** was refluxed in 0.1 M DCB for 24 h. After protection of the phenolic hydroxy groups and workup, the residue was subjected to the HPLC analysis. Only two [1,3]-rearrangement products **2a** and **2d** were detected without any intercrossing [1,3]-rearrangement products **2ad** and **2da** (see Supporting Information, Figure S1), revealing that the formal [1,3]-rearrangement is an intramolecular process (Scheme 1).

Scheme 1. Intercrossing Experiments of Allyl Aryl Ethers 1a and 1d in Solvent and Solvent-Free

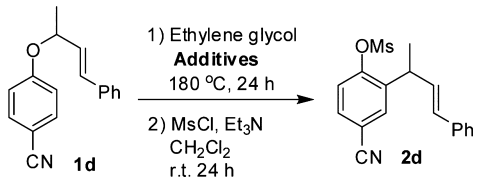


To rule out the effect of the solvent-cage in the formation of the formal [1,3]-rearrangement, a neat mixture of equimolar amounts of allyl aryl ethers **1a** and **1d** was also subjected to the intercrossing experiment. Once again, only the two [1,3]-products **2a** and **2d** were detected (see Supporting Information, Figure S2). Therefore, it can be believed that the formal [1,3]-rearrangement is not a fast intrasolvent-cage radical–radical trapping mechanism.

To further exclude the radical mechanism in the formation of the formal [1,3]-rearrangement products, the allyl aryl ether **1d** was heated in ethylene glycol as a protic solvent at 180 °C for 24 h. After the protection and workup, the residue was separated readily by column chromatography to obtain [1,3]-rearrangement product **2d** in 27% yield, similar to that in DCB. Furthermore, hydroquinone and TEMPO were employed as radical scavengers in this reaction. The results indicate that the radical trappers have no significant effect on the conversion of the [1,3]-rearrangement (Table 2), ultimately confirming that the formal [1,3]-rearrangement is not a radical mechanism.

Computational Studies. To date, there existed some arguments for the thermal formal [1,3]-oxygen-to-carbon shift;

Table 2. Radical Trapping Experiments

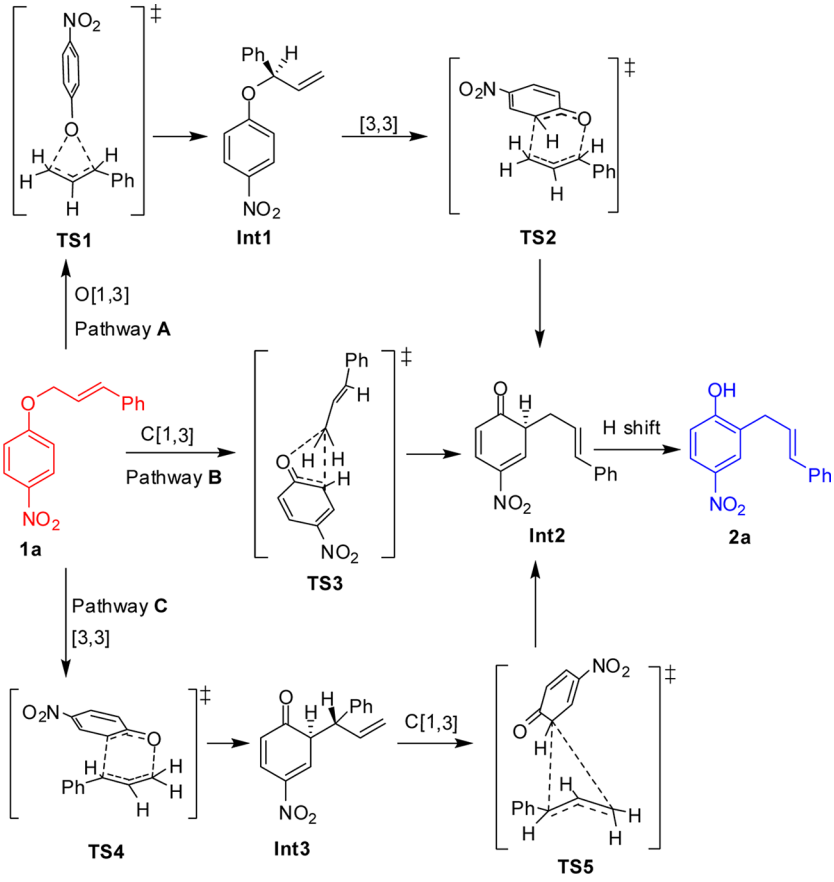


entry	additives (equiv)	isolated yield (%) **2d**
1[a]	–	27
2[b]	–	24
3[b]	hydroquinone (0.25)	20
4[b]	hydroquinone (0.5)	24
5[b]	hydroquinone (1.0)	22
6[b]	TEMPO[c] (0.5)	23
7[b]	TEMPO (1.0)	22
8[b]	TEMPO (2.0)	21

[a]1 mmol of **1d** dissolved in 10 mL of ethylene glycol. [b]0.5 mmol of **1d** dissolved in 5 mL of ethylene glycol. [c]TEMPO = 2,2,6,6-tetramethyl-1-piperidinyloxy, free radical.

dx.doi.org/10.1021/jo302210t | J. Org. Chem. 2012, 77, 10856–10869

Scheme 2. Three Proposed Mechanisms of the Thermal Formal [1,3] Rearrangement of Allyl Aryl Ether 1a



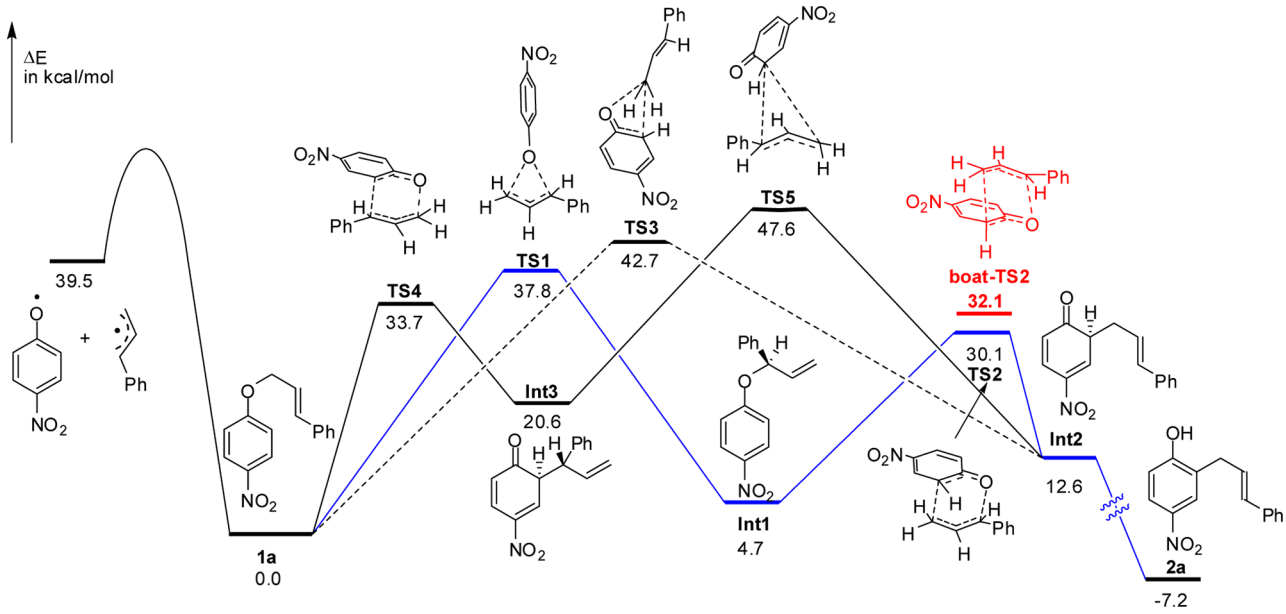


Figure 2. Potential energy surfaces of the thermal [1,3] rearrangement of allyl aryl ether **1a** at the B3LYP/6-31+G(d) level.

it was suggested that the rearrangement proceeded via a concerted C[1,3]-sigmatropic shift, ionic, or radical process. Our intercrossing experiments (in DCB and solvent-free) and radical trapping experiments can exclude the radical process, the ionic mechanism, and the fast intrasolvent-cage radical–radical trapping mechanism for the formal [1,3]-rearrangement in the thermal aromatic Claisen rearrangement. Thus, the formation of the formal [1,3]-rearrangement products should be via an intramolecular or concerted process in the thermal aromatic Claisen rearrangement. Although the radical mechanism exists in the reaction system, it produces dissociation products phenols. It is very difficult for the generated radicals to recombine in the reaction system. Furthermore, we propose three possible mechanisms for the process: (1) a tandem

dx.doi.org/10.1021/jo302210t | J. Org. Chem. 2012, 77, 10856–10869

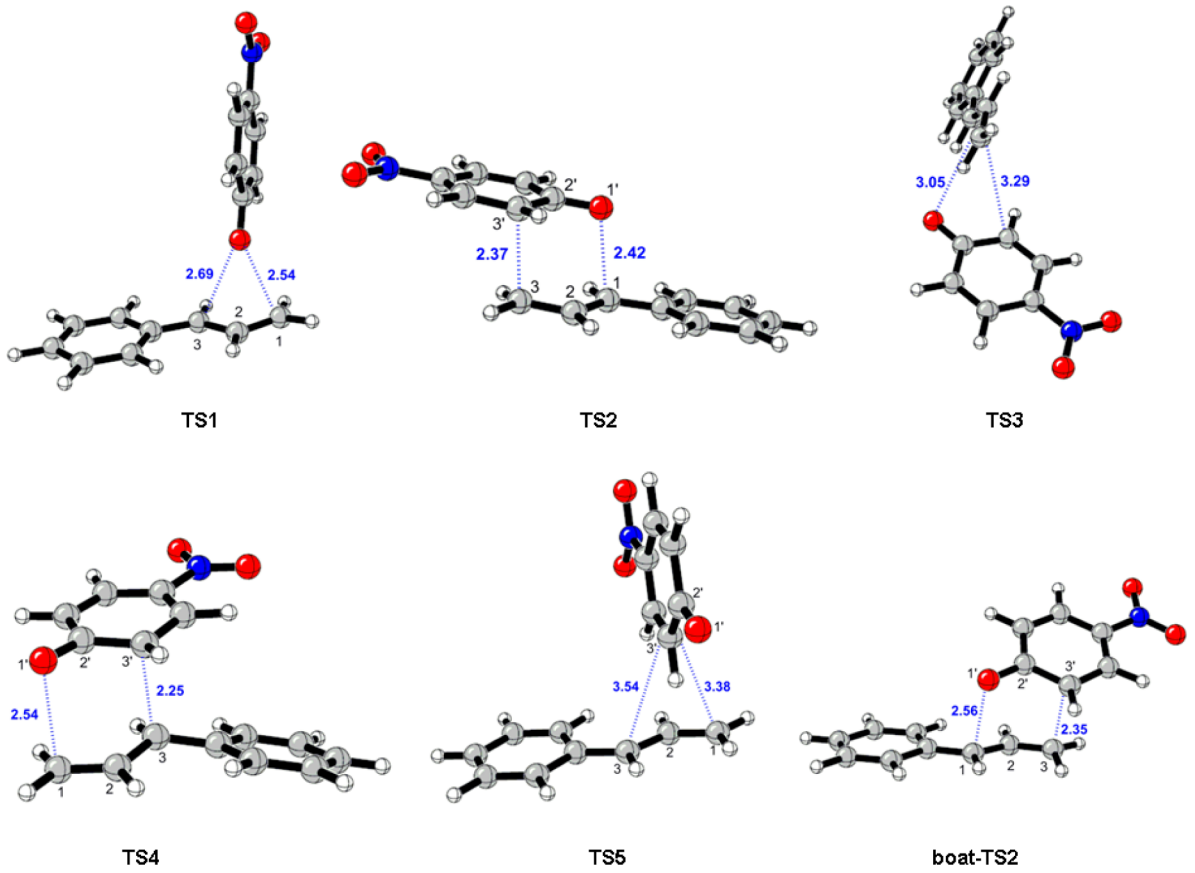


Figure 3. Structures of transition states for the rearrangement of **1a** at the B3LYP/6-31+G(d). Distances of concern are indicated by broken lines and are reported in angstroms.

O[1,3]-sigmatropic shift and [3,3]-Claisen rearrangement process (Pathway A); (2) a concerted C[1,3]-sigmatropic shift (Pathway B); and (3) a tandem [3,3]- and C[1,3]-sigmatropic shifts process (Pathway C). Both O[1,3]- and C[1,3]-sigmatropic shifts should be with a configuration inversion of the migrating groups on the basis of orbital symmetry in the Woodward–Hoffmann selection rule.

To understand the above proposed mechanisms, a representative model system with 3-phenyl-2-propenyl 4-nitrophenyl ether (**1a**) was examined with the density functional theory (DFT) calculation.[18] Substrate **1a** could undergo three possible pathways: Pathway A involves the O[1,3]-sigmatropic shift with a concomitant C–O bond cleavage and formation, leading to an intermediate **Int1**, followed by the [3,3]-sigmatropic shift with the attack of the vinyl group to the aryl ring and a concomitant C–O bond cleavage to afford an intermediate **Int2**. The concerted C[1,3]-sigmatropic shift generates the intermediate **Int2** in pathway B. In pathway C, [3,3]-Claisen rearrangement gives rise to an intermediate **Int3**, followed by a concerted C[1,3]-sigmatropic shift to yield the intermediate **Int2** as well, which undergoes a proton shift from the cyclohexadienone moiety to the oxygen atom to yield the final product **2a** (Scheme 2).

Structural optimization and single-point energy were obtained at the B3LYP/6-31+G(d) level in the gas phase.[19] The potential-energy surfaces of these proposed mechanisms were obtained and shown in Figure 2. In Pathway A, an activation energy of 37.8 kcal/mol was found for the step of substrate **1a** to **Int1**, and the activation energies for the step of **Int1** to **Int2** are 25.4 and 27.4 kcal/mol, respectively, via chair and twist boat conformational transition states; that is, the O[1,3]-shift is the rate-determining step in the Pathway A. The substrate **1a** requires an activation free energy of 42.7 kcal/mol to reach the intermediate **Int2** via the transition state **TS3** in Pathway B. In Pathway C, an activation energy of 33.7 kcal/mol has been found (from substrate **1a** to **TS4**), leading to unstable intermediate **Int3**, and the activation energy of following step from **Int3** to **TS5** is 27.0 kcal/mol, yielding the intermediate **Int2**. **Int3** is less stable than **Int1**, resulting in the low relative concentration in relative to **Int1**. Therefore, Pathway A seems the most likely approach to occur and Pathway C could not be ruled out completely on the basis of the calculations. Moreover, the calculation on the radical mechanism was also conducted. The calculated relative energy of the separated phenoxy and allylic radicals is 39.5 kcal/mol higher than the starting material **1a**. Though the transition state for the formation of the radicals was not located, its relative energy should be higher than 39.5 kcal/mol, revealing that the energy barrier of the radical mechanism is at least 1.7 kcal/mol higher than that of the O[1,3]-migration. The results reveal that the competitive radical mechanism and the tandem O[1,3]- and [3,3]-sigmatropic shifts may exist concomitantly in the reaction system.

The transition states **TS1** and **TS2** for transformation of the substrate **1a** to **Int1** and of **Int1** to **Int2**, respectively, were located. **TS1** has O–C1 and O–C3 distances of 2.54 and 2.69 Å, respectively (Figure 3). The calculation of the O[1,3]-rearrangement has not been reported to date. **TS2** corresponds to the expected transition state for Claisen rearrangements with a distance of 2.37 Å for forming the C–C bond and a distance

dx.doi.org/10.1021/jo302210t | J. Org. Chem. 2012, 77, 10856–10869

of 2.42 Å for breaking the C−O bond (Figure 3). Our results are consistent with those reported by Wiest and co-workers at the B3LYP/6-31G(d) level.[20] Furthermore, Barluenga and co-workers prepared *N*-[4,4-dideuterio-4-(2-furyl)-1-methyl-3-oxabut-1-enyl]morphol and conducted its [1,3]-rearrangement to afford 2-amino aldehyde.[21] Morphol derivatives show a secondary deuterium kinetic isotope effect as large as 1.83, which strongly suggests that there is complete C−O bond breaking in the rate-determining step of related aromatic systems of the thermal [1,3] rearrangement. The results support our rationalized mechanism that the O[1,3]-sigmatropic shift is the rate-determining step in the tandem O[1,3]-sigmatropic shift and [3,3]-Claisen rearrangement process.

DFT calculations were also performed to study the proton shift for transformation of **Int2** to product **2a** (Scheme 2). Computational results in Figure 4 indicate that the early stage

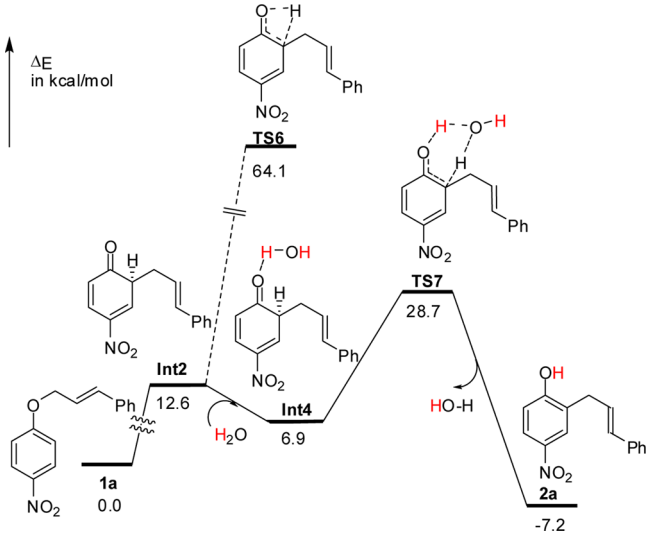
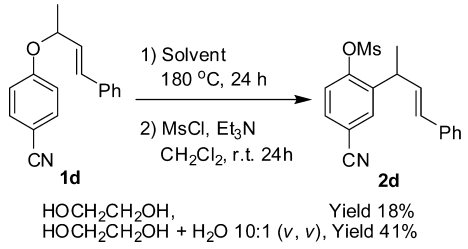


Figure 4. Potential energy surfaces of the proton shift of **Int2** at the B3LYP/6-31+G(d) level.

H[1,3]-shift via **TS6** from **Int2** is energetically disfavored because of its activation free energy as high as 51.5 kcal/mol. Gomez and co-worker studied the Claisen rearrangement of allyl phenyl ether by DFT calculated at the B3LYP/6-31G(d) level.[22] They calculated the intramolecular [1,3]-proton shift to gain 56.0 kcal/mol of energy barrier. From the calculated results, one can see that the energy barrier is very high. According to previous reports on Claisen rearrangements, water can accelerate the aliphatic Claisen rearrangements.[23] However, the effect of water on the aromatic Claisen rearrangement has been paid less attention. Until 2010, Acevedo and Armacost reported the influence of water on the aromatic Claisen rearrangement using QM/MM Monte Carlo calculations and free-energy perturbation theory.[24] Since the H[1,3]-shift in the isomerization of cyclohexadienones into phenols in the formal [1,3]-products is similar to that in the Claisen rearrangement, it is rationalized that water should be able to accelerate the formation of the formal [1,3]-products in the thermal Claisen rearrangement. Therefore, DFT calculations were performed for the main stationary points on the potential energy surface with water for the proton shift (Figure 4). Geometry optimization of the intermediate **Int2** with water leads to a stable intermediate **Int4**, with only 5.7 kcal/mol lower than the **Int2**. And **Int4** has the O1−H2 distance of 1.86 Å (Figure 5). The transition state **TS7** (from **Int4** to **2a**) shows a six-membered ring chair conformational structure with O1−H2, H2−C3′, O1−H1 and H1−O′ distances of 1.21, 1.48, 1.03, and 1.64 Å, respectively; therefore, it can be characterized as an early and dissociative transition state (Figure 5). And the activation free energy of this procedure is 21.8 kcal/mol (Figure 4), which is significantly lower than that of the intramolecular [1,3]-proton shift.

To verify the calculated results, we explored the effect of water experimentally in dry and aqueous ethylene glycol solutions. It was found that the amount of the [1,3]-product increased from 18 to 41% after water was added (Scheme 3). These findings suggested that water indeed can accelerate the formal [1,3]-rearrangement.

Scheme 3. Effect of Water on the Formal [1,3]-Product



The formal [1,3]-rearrangements were affected significantly by the electronic effect of the allyl aryl ethers bearing different electronic 4-substituted groups. The calculated transition state

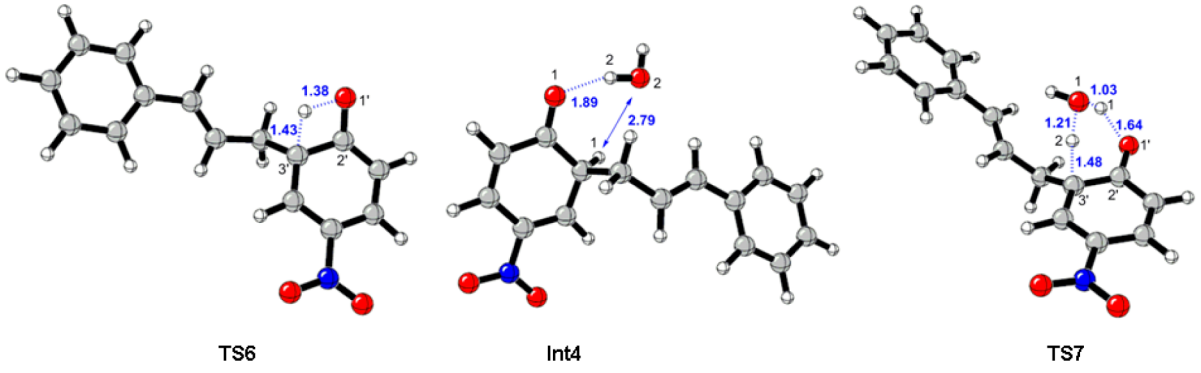


Figure 5. Geometry optimization for the proton shifts at the B3LYP/6-31+G(d) level. Distances of concern are indicated by broken lines and are reported in angstroms.

dx.doi.org/10.1021/jo302210t | J. Org. Chem. 2012, 77, 10856−10869

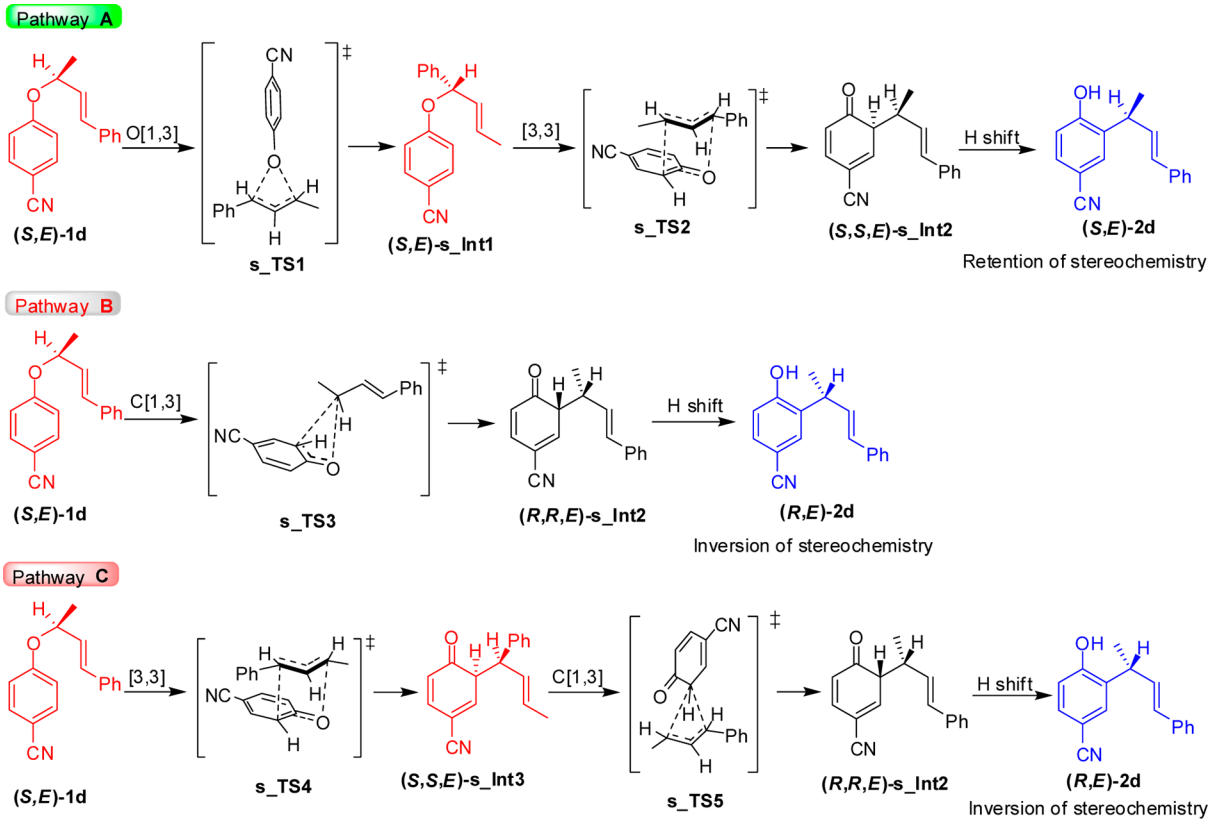
energies of the rate-determining step are listed in Table 3. It was found that the transition state energies of **TS1** are not varied regularly along with the electronic property of the substitutes. The electron rich substrates **1f,g** do not produce any [1,3]-product; it may be due to the scission of the C−O bond forming phenols via a favorably competitive radical mechanism. To verify the assumption, the relative energies of the separated radicals were calculated for the representative allyl aryl ethers bearing different electronic 4-substituted groups (Table 3). ΔE of radicals could be considered as the bond dissociation energy, ΔG of radicals decrease by 12−13 kcal/mol from ΔE, contributed to the increase of entropy. The activation energy in radical mechanism should be close to ΔE rather than ΔG because of the feature of one molecule with a little entropy effect. The results indicate that the stabilized allylic and phenoxy radicals generated from the allyl aryl ethers bearing electron-rich substituents are lower in energy than their **TS1**, perferring the radical dissociation, while the allylic and phenoxy radicals generated from the allyl aryl ethers with electron-deficient substituents are higher in energy than their **TS1**, leading to both the O[1,3]-sigmatropic shift and the radical dissociation.

Table 3. Calculated TS1 and Separated Radicals Energies of Substrates 1 with the Electronic Difference in the Formal [1,3]-Rearrangement and Radical Dissociation

entry		$\Delta E^{\ddagger}$ (TS1) (kcal/mol)	$\Delta G^{\ddagger}$ (TS1) (kcal/mol)	ΔE(radicals) (kcal/mol)	ΔG(radicals) (kcal/mol)
1	**1a**	37.8	37.8	39.5	27.0
2	**1b**	34.1	33.9	39.8	27.1
3	**1c**	38.3	38.2	37.1	24.8
4	**1d**	34.9	34.7	37.4	25.0
5	**1f**	37.5	37.0	32.4	19.1
6	**1g**	35.9	36.4	28.8	16.8

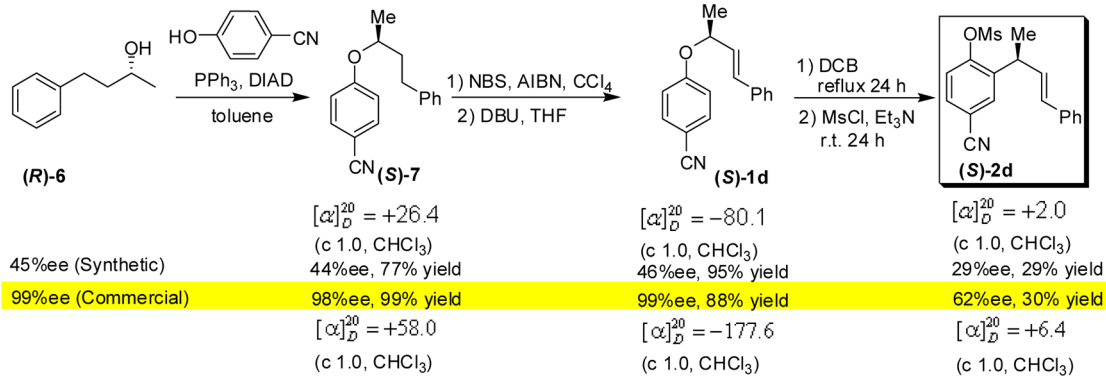
Stereochemical Studies. According to the results of calculation, the process of a tandem O[1,3]- and [3,3]-Claisen rearrangement is favorable for the formal [1,3]-rearrangement. To verify the calculation rationalized results, a thermal formal [1,3]-rearrangement experiment with an optically active allyl aryl ether was designed. Optically active allyl aryl ether (*S*)-**1d** was selected as a model substrate because the substrate **1d** gave rise to the highest yield of the [1,3]-rearrangement product. The stereochemistry of the formation of optically active **2d** from (*S*,*E*)-**1d** in the three possible pathways is presented in Scheme 4. For simplicity, we only discuss the predominant reaction processes via the stable chair transition states and the stable intermediates in all three possible pathways. In Pathway A, substrate (*S*,*E*)-**1d** undergoes the O[1,3]-sigamatropic shift to afford the intermediate (*S*,*E*)-**s_Int1**, which further furnishes the [3,3]-Claisen rearrangement via a stable chair transition state to yield (*S*,*E*)-**2d**. It is noteworthy that the tandem O[1,3]- and [3,3]-Claisen rearrangement reaction results in the product (*S*,*E*)-**2d** with the retention of configuration. However, in pathway B, substrate (*S*,*E*)-**1d** undergoes a concerted C[1,3]-sigmatropic shift with the inversion of configuration to afford the final (*R*,*E*)-**2d**. In pathway C, substrate (*S*,*E*)-**1d** yields an intermediate (*S*,*R*,*E*)-**s_Int3** via the [3,3]-rearrangement through a stable chair transition state. The intermediate (*S*,*R*,*E*)-**s_Int3** undergoes a concerted C[1,3]-sigmatropic shift with the inversion of configuration to produce the final (*R*,*E*)-**2d** with the inversion of configuration compared with

Scheme 4. Stereochemistry in Three Pathways of the Thermal Formal [1,3]-Rearrangement of (*S*)-Allyl Aryl Ether (*S*)-1d



dx.doi.org/10.1021/jo302210t | J. Org. Chem. 2012, 77, 10856−10869

Scheme 5. Synthesis and Rearrangement of Optically Active Allyl Aryl Ether (*S*)-1d

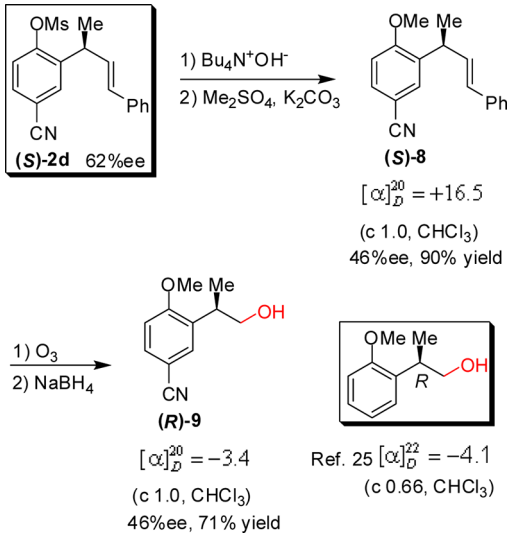


substrate (*S*,*E*)-**1d**. Thus, the experimental results with optically active substrate (*S*,*E*)-**1d** can distinguish the proposed tandem O[1,3]- and [3,3]-Claisen rearrangement process from other two.

To verify computed results experimentally, the designed optically active allyl aryl ether (*S*)-**1d** with different optical purities was synthesized from 4-hydroxybenzonitrile and different optically pure (*R*)-4-phenyl-2-butanol (*R*)-**6** via the Mitsunobu reaction, radical bromination, and elimination reaction (Scheme 5).

The optically active substrate (*S*)-**1d** was subjected to the rearrangement in refluxing DCB for 24 h to afford [1,3]-rearrangement product (*S*)-**2d**, of which the configuration was identified via the chemical relation to a known compound by comparison with their direction of optical rotation. The [1,3]-rearrangement product (*S*)-**2d** was first converted to anisole derivative (*S*)-**8** through hydrolysis with $Bu_4N^+OH^-$ and substitution with Me_2SO_4. From (*S*)-**2d** to (*S*)-**8**, the erosion of ee may be due to the fact that the base corrades the benzylic and allylic hydrogen. Anisole (*S*)-**8** was further converted to 2-arylpropanol (*R*)-**9** by ozonolysis followed by in situ reduction with sodium borohydride. The alcohol (*R*)-**9** shows the same direction of the optical rotation with (*R*)-2-(2-methoxyphenyl)-propan-1-ol,[25] assigning that they possess the same absolute configuration (Scheme 6).

Scheme 6. Identification of the Absolute Configuration of the [1,3]-Rearrangement Product



The substrate (*S*)-**1d** with 46 and 99% ee gave rise to the [1,3]-rearrangement product (*S*)-**2d** in 29 and 62% ee, respectively (see Supporting Information, Figures S5 and S6). The two results are consistent, which reveals that the allyl aryl ether (*S*)-**1d** underwent the rearrangement to give rise to the corresponding product (*S*)-**2d** with ca. 63% retention of the configuration, supporting experimentally that the tandem O[1,3]-sigmatropic and [3,3]-Claisen rearrangement mechanism is the main process for the thermal formal [1,3] rearrangement. The configuration reversed product (ca. 37%) was generated through the concomitant unfavorable twist boat-like conformation in the transition state in [3,3]-Claisen rearrangement step in the tandem process rather than the competitive direct C[1,3]-rearrangement (Pathway B) because of its higher transition state energy. Our calculated results rationalize this presumption that the erosion of optical purity of the product is mainly attributed to the small free energy difference of 1.8 kcal/mol between the chairlike and twist boat-like transition states **s_TS2** (Figure 6).

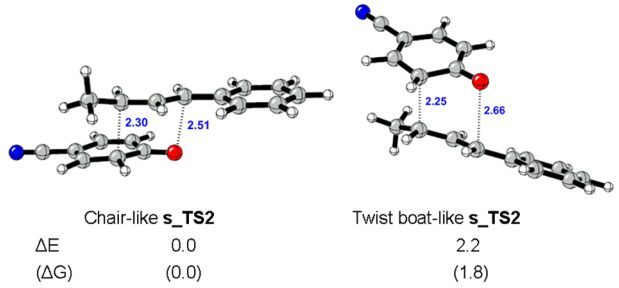


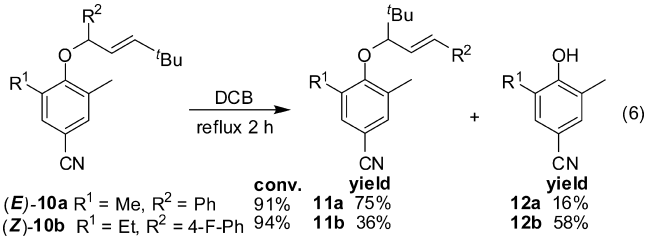
Figure 6. Calculated transition state energies for chairlike and twist boat-like **s_TS2** in Pathway A at the B3LYP/6-31+G(d) level. Distances of concern are indicated by broken lines and are reported in angstroms. Energies are given in kcal/mol.

To further exclude the solvent cage effect, the substrate (*S*)-**1d** (99% ee) was subjected to the rearrangement solvent-free at 180 °C for 24 h in a sealed test tube, to afford [1,3]-rearrangement product (*S*)-**2d** in 23% yield (65% ee), with approximately 66% retention of the configuration (see Supporting Information, Figure S7), similar to those in solution. Once again, the results support the proposed tandem O[1,3]-shift and [3,3]-Claisen rearrangement mechanism.

Oxygen [1,3]-Sigmatropic Shift. Both calculational and experimental investigations support that the formal [1,3]-sigmatropic shift is a tandem O[1,3]- and [3,3]-rearrangement process. To observe the O[1,3]-rearrangement, allyl aryl ethers

dx.doi.org/10.1021/jo302210t | J. Org. Chem. 2012, 77, 10856−10869

10a, **10b**, **11a**, and **11b** were prepared from the corresponding 2,4,6-trisubstituted phenols and α,β-unsaturated alcohols via the Mitsunobu reaction. The rearrangement was conducted in refluxing DCB for 2 h. The results indicate that compound **10a** produced **11a** in 75% yield with substrate **10a** (9%) and 4-hydroxy-3,5-dimethylbenzonitrile (16%). Similarly, compound **10b** gave rise to compound **11b** as well (eq 6). However,



compounds **11a,b** did not undergo the rearrangement because of their better stability than **10a,b**, respectively. The formation of decomposition products **12a,b** should be through a competitive radical mechanism.

Some thermal [1,3] oxygen to carbon rearrangements, such as alkyl styryl ethers and aryl benzyl ethers, may undergo the radical or C[1,3]-sigmatropic shift rearrangement under thermal reaction conditions.[10,14−16] Moreover, certain formal [1,3] oxygen to carbon rearrangements in the Claisen rearrangements may undergo the ionic mechanism under the catalysis of transition metals.[11] On the basis of our current investigation, the thermal formal [1,3]-rearrangement of allyl aryl ethers, especially the allyl groups with bulkyl γ-substituents or γ,γ-disubstituents, prefers a tandem O[1,3]-sigmatropic shift and [3,3]-Claisen rearrangement process.

■ CONCLUSION

In summary, we have proposed the mechanism for the thermal formal [1,3]-rearrangement of allyl aryl ethers after a systematic investigation on experiments and theoretical calculations. The results indicate that it is reasonable to consider the thermal formal [1,3]-rearrangement of allyl aryl ethers as a tandem O[1,3]-sigmatropic shift with a configuration inversion of the oxygen atom and [3,3]-Claisen rearrangement process. The proposed process is supported by the intercrossing experiments of different allyl aryl ethers in solvent and solvent-free, as well as radical trapping experiments, indicating that the formal [1,3]-rearrangement is an intramolecular reaction, and the rearrangement experiments of an optically active allyl aryl ether in solution and solvent-free. Although the competitive radical mechanism exists under the reaction conditions, it gives rise to phenol derivatives rather than formal [1,3]-products, and the generated radicals hardly recombine in the reaction system. This phenomenon may be because the two mechanisms are close enough to enable a mechanistic switch as a function of substituents. The current results provide not only a comprehensive understanding on the formation of the thermal formal [1,3]-rearrangement products in the Claisen rearrangement, but also a novel [1,3]-sigmatropic shift, O[1,3]-sigmatropic shift with a configuration inversion of the oxygen atom.

■ EXPERIMENTAL SECTION

General Information. Melting points were obtained on a melting point apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 300 or 400 MHz spectrometer with TMS as an internal standard in the $CDCl_3$ solution. IR spectra were taken on a FT-IR spectrometer in KBr. HRMS data were obtained with an LC/MSD TOF mass spectrometer. Optical rotations were obtained using a polarimeter using 3.5 i.d. × 100 mm cylindrical glass cell at sodium D line (589 nm), and were reported in concentration (c = g/100 mL) at 20 °C. Purification of reaction products was carried out by column chromatography using silica gel (200−300 mesh). TLC separations were performed on silica gel G plates with petroleum ether/ethyl acetate, and the plates were visualized with UV light.

General Procedure for the Synthesis of Allyl Aryl Ethers 1. To a solution of a phenol (36 mmol), alcohol (30 mmol), and PPh_3 (9.4 g, 36 mmol) in THF (30 mL) at 0 °C was added DIAD (7.3 g, 36 mmol) dropwise at below 5 °C. The reaction mixture was stirred for 2 h at room temperature and then concentrated and diluted with Et_2O/petroleum ether (v/v = 1:1, 100 mL). The precipitate was filtered, and the filtrate was concentrated. The residue was purified by column chromatography on silica gel and recrystallized from ethyl acetate/petroleum ether to afford **1a−g** and their regioisomeric compounds **1′b**, **1′d** and **1′e**.

*1-(Cinnamyloxy)-4-nitrobenzene (**1a**).*[26] 3.60 g, white solid, 47% yield: mp 143−145 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26−8.17 (m, 2H), 7.45−7.39 (m, 2H), 7.38−7.31 (m, 2H), 7.31−7.27 (m, 1H), 7.08−6.96 (m, 2H), 6.76 (d, J = 16.0 Hz, 1H), 6.39 (dt, J = 16.0, 5.9 Hz, 1H), 4.80 (dd, J = 5.9, 1.4 Hz, 2H).

*1-Nitro-4-((4-phenylbut-3-en-2-yl)oxy)benzene (**1b**).* 3.31 g, yellowish solid, 41% yield: mp 55−56 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27−8.06 (m, 2H), 7.43−7.18 (m, 5H), 7.10−6.88 (m, 2H), 6.62 (d, J = 16.1 Hz, 1H), 6.23 (dd, J = 16.1, 6.4 Hz, 1H), 5.08 (dq, J = 6.4, 6.3 Hz, 1H), 1.58 (d, J = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 141.3, 135.9, 131.7, 128.9, 128.6, 128.1, 126.5, 125.8, 115.6, 75.5, 21.6; IR (KBr) ν (cm^{-1}) 3026, 1591, 1255, 1111, 968; HRMS (ESI) calcd. for $C_{16}H_{15}NO_3$ [M + Na]$^+$ m/z 292.0944, found 292.0947.

*1-Nitro-4-((1-phenylbut-2-en-1-yl)oxy)benzene (**1′b**).* 1.78 g, yellow crystals, 22% yield: mp 52−54 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 9.2 Hz, 2H), 7.37 (m, 4H), 7.34−7.28 (m, 1H), 6.97 (d, J = 9.2 Hz, 2H), 5.82 (dq, J = 15.2, 5.6 Hz, 1H), 5.74 (dd, J = 15.2, 6.0 Hz, 1H), 5.69 (d, J = 6.0 Hz, 1H), 1.74 (d, J = 5.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 141.4, 139.4, 130.1, 129.7, 128.8, 128.1, 126.3, 125.7, 115.9, 81.5, 17.7; IR (KBr) ν (cm^{-1}) 3024, 1591, 1255, 1111, 966; HRMS (ESI) calcd. for $C_{16}H_{15}NO_3$ [M + H]$^+$ m/z 270.1125, found 270.1127.

*4-(Cinnamyloxy)benzonitrile (**1c**).* 4.08 g, colorless needle crystals, 58% yield: mp 125−126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62−7.56 (m, 2H), 7.41 (d, J = 7.3 Hz, 2H), 7.33 (t, J = 7.3 Hz, 2H), 7.30−7.24 (m, 1H), 7.03−6.97 (m, 2H), 6.73 (d, J = 16.0 Hz, 1H), 6.37 (dt, J = 16.0, 5.8 Hz, 1H), 4.74 (dd, J = 5.8, 1.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 136.0, 134.0, 133.9, 128.6, 128.2, 126.6, 123.0, 119.1, 115.5, 104.1, 68.9; IR (KBr) ν (cm^{-1}) 3289, 2223, 1257, 1110, 972; HRMS (ESI) calcd. for $C_{16}H_{13}NO$ [M + H]$^+$ m/z 236.1070, found 236.1075.

*4-((4-Phenylbut-3-en-2-yl)oxy)benzonitrile (**1d**).* 3.79 g, white solid, 51% yield: mp 59−60 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 8.8 Hz, 2H), 7.36−7.23 (m, 5H), 6.98 (d, J = 8.7 Hz, 2H), 6.60 (d, J = 16.1 Hz, 1H), 6.22 (dd, J = 15.9, 6.1 Hz, 1H), 5.02 (dq, J = 6.1, 6.3 Hz, 1H), 1.55 (d, J = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 135.9, 133.9, 131.5, 129.2, 128.6, 128.1, 126.5, 119.2, 116.4, 103.8, 75.0, 21.6; IR (KBr) ν (cm^{-1}) 3027, 2224, 1255, 1171, 969; HRMS (ESI) calcd. for $C_{17}H_{15}NO$ [M + H]$^+$ m/z 250.1226, found 250.1228.

*4-((1-Phenylbut-2-en-1-yl)oxy)benzonitrile (**1′d**).* 2.51 g, colorless oil, 34% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.9 Hz, 2H), 7.36 (m, 4H), 7.32−7.26 (m, 1H), 6.95 (d, J = 8.9 Hz, 2H), 5.79 (dq, J = 15.3, 5.6 Hz, 1H), 5.72 (dd, J = 15.3, 6.0 Hz, 1H), 5.64 (d, J = 6.0 Hz, 1H), 1.73 (d, J = 5.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.1, 139.6, 133.7, 130.2, 129.5, 128.7, 128.0, 119.1, 116.6, 103.9, 81.0, 17.7; IR (KBr) ν (cm^{-1}) 3031, 2224, 1250, 1171, 966; HRMS (ESI) calcd. for $C_{17}H_{15}NO$ [M + H]$^+$ m/z 250.1226, found 250.1227.

*4-((4-(p-Tolyl)but-3-en-2-yl)oxy)benzonitrile (**1e**).* 3.53 g, white solid, 45% yield: mp 102−104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ

7.57−7.51 (m, 2H), 7.25 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 7.00−6.95 (m, 2H), 6.57 (d, J = 16.1 Hz, 1H), 6.16 (dd, J = 16.1, 6.5 Hz, 1H), 5.01 (dq, J = 6.5, 6.5 Hz, 1H), 2.33 (s, 3H), 1.54 (d, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 138.0, 133.9, 133.2, 131.5, 129.3, 128.1, 126.4, 119.3, 116.4, 103.7, 75.2, 21.7, 21.2; IR (KBr) ν (cm^{-1}) 3020, 2224, 1255, 1172, 971; HRMS (ESI) calcd. for $C_{18}H_{17}NO$ $[M + H]^+$ m/z 264.1383, found 264.1391.

*4-((1-(p-Tolyl)but-2-en-1-yl)oxy)benzonitrile (**1′e**).* 1.31 g, colorless oil, 17% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56−7.43 (m, 2H), 7.24 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 6.98−6.92 (m, 1H), 5.78 (dq, J = 15.3, 5.2 Hz, 1H), 5.71 (dd, J = 15.3, 5.4 Hz, 1H),5.61 (d, J = 5.4 Hz, 1H), 2.33 (s, 3H), 1.72 (d, J = 5.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 137.9, 136.6, 133.8, 130.4, 129.5, 129.3, 126.3, 119.2, 116.6, 103.8, 81.0, 21.1, 17.7; IR (KBr) ν (cm^{-1}) 3020, 2224, 1250, 1171, 966; HRMS (ESI) calcd. for $C_{18}H_{17}NO$ $[M + H]^+$ m/z 264.1383, found 264.1388.

*1-Methyl-4-((4-phenylbut-3-en-2-yl)oxy)benzene (**1f**).* 3.72 g, colorless oil, 52% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.35 (m, 2H), 7.31−7.27 (m, 2H), 7.24−7.20 (m, 1H), 7.05 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 6.59 (d, J = 16.1 Hz, 1H), 6.27 (dd, J = 16.1, 6.3 Hz, 1H), 4.91 (dq, J = 6.3, 6.3 Hz, 1H), 2.26 (s, 3H), 1.50 (d, J = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 136.6, 130.9, 130.5, 130.1, 129.8, 128.5, 127.6, 126.5, 116.1, 74.7, 21.7, 20.5; IR (KBr) ν (cm^{-1}) 3026, 2977, 2927, 1612, 1583, 1508, 1449, 1235, 967; HRMS (ESI) calcd. for $C_{17}H_{18}O$ $[M + H]^+$ m/z 239.1430, found 239.1433.

*1-Methoxy-4-((4-phenylbut-3-en-2-yl)oxy)benzene (**1g**).* 4.58 g, colorless oil, 60% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.34 (m, 2H), 7.32−7.28 (m, 2H), 7.24−7.20 (m, 1H), 6.92−6.86 (m, 2H), 6.84−6.76 (m, 2H), 6.57 (d, J = 16.1 Hz, 1H), 6.27 (dd, J = 16.1, 6.3 Hz, 1H), 4.84 (ddq, J = 1.0, 6.3, 6.3, Hz, 1H), 3.75 (s, 3H), 1.50 (d, J = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 152.1, 136.6, 131.0, 130.6, 128.5, 127.7, 126.5, 117.6, 114.5, 75.7, 55.7, 21.7; IR (KBr) ν (cm^{-1}) 3025, 2977, 2832, 1597, 1578, 1505, 1449, 1227, 968; HRMS (ESI) calcd. for $C_{17}H_{18}O_2$ $[M + Na]^+$ m/z 277.1199, found 277.1195.

Typical Process for Synthesis of (*S*)-1d. A mixture of (*S*)-4-(4-phenylbutan-2-yloxy)benzonitrile ((*S*)-**7**, 44% ee, 8.6 g, 34.2 mmol), NBS (6.1 g, 34.2 mmol), and AIBN (78 mg) in dry $CC1_4$ (200 mL) was refluxed and stirred under N_2 for 2 h. Then the mixture was allowed to cool to 10 °C and filtered. The filtrate was concentrated under reduced pressure, the residue was dissolved in dry, freshly distilled THF (100 mL), and the solution was cooled to 0 °C. To the cold solution was added DBU (20 mL, 20.8 g, 0.14 mol) dropwise with occasional shaking under N_2. The mixture was kept at 0−5 °C for 48 h and then stirred at 1 °C for 2 h and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) and then dissolved in ethyl acetate (50 mL), washed successively with 2 mol/L HCl (2 × 50 mL), saturated Na_2CO_3 (2 × 50 mL), and brine (2 × 50 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to afford (*S*)-**1d**.

*(S)-4-((4-Phenylbut-3-en-2-yl)oxy)benzonitrile ((S)-**1d**).* 7.8 g, colorless crystals, 95% yield: mp 47−50 °C, $[\alpha]_D^{20}$ = −80.1 (c 1.0, $CHCl_3$), 46% ee by chiral HPLC with *i*-PrOH and *n*-hexane in a ratio of 10:90 as eluent; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56−7.53 (m, 2H), 7.37−7.29 (m, 4H), 7.27−7.23 (m, 1H), 6.99−6.97 (m, 2H), 6.60 (d, J = 16.1 Hz, 1H), 6.22 (dd, J = 16.1, 6.4 Hz, 1H), 5.03 (dq, J = 6.4, 6.4 Hz, 1H), 1.55 (d, J = 6.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4, 135.9, 133.9, 131.5, 129.2, 128.6, 128.1, 126.5, 119.2, 116.4, 103.8, 75.0, 21.6. IR (KBr) ν (cm^{-1}) 3027, 2224, 1255, 1171, 969; HRMS (ESI) calcd. for $C_{17}H_{15}NO$ $[M + H]^+$ m/z 250.1226, found 250.1228.

General Procedure for the Thermal Rearrangement of Allyl Aryl Ethers 1. A solution of allyl aryl ether **1** (1 mmol) in 10 mL of DCB (or in DMF, or in 1,2-ethanediol) was refluxed for 24 h. The reaction mixture was allowed to cool to room temperature. After dilution with CH_2Cl_2 (10 mL), Et_3N (0.6 mL, 0.44 g, 4.5 mmol) and MsCl (0.25 mL, 0.37 g, 3 mmol) were added. The resulting mixture was stirred for 24 h at room temperature, diluted with CH_2Cl_2 (50 mL), washed with brine (2 × 50 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give the pure products.

*2-Cinnamyl-4-nitrophenyl methanesulfonate (**2a**).* Yellowish oil, 33 mg, 10% yield (7 mg, 2% in DMF): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 2.8 Hz, 1H), 8.16 (dd, J = 8.9, 2.8 Hz, 1H), 7.55 (d, J = 8.9 Hz, 1H), 7.39−7.34 (m, 2H), 7.34−7.28 (m, 2H), 7.27−7.22 (m, 1H), 6.53 (d, J = 15.8 Hz, 1H), 6.29 (dt, J = 15.8, 6.8 Hz, 1H), 3.71 (d, J = 6.8 Hz, 2H), 3.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.4, 146.3, 136.6, 135.2, 133.4, 128.7, 127.8, 126.4, 126.3, 125.2, 123.3, 122.8, 38.9, 33.6; IR (KBr) ν (cm^{-1}) 3027, 1524, 1348, 1219, 1119, 967; HRMS (ESI) calcd. for $C_{16}H_{15}NO_5S$ $[M + Na]^+$ m/z 356.0563, found 356.0567.

*4-Nitro-2-(4-phenylbut-3-en-2-yl)phenyl methanesulfonate (**2b**).* Yellowish oil, 7 mg, 2% yield (24 mg, 7% in DMF): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 2.8 Hz, 1H), 8.15 (dd, J = 9.0, 2.8 Hz, 1H), 7.57 (d, J = 9.0 Hz, 1H), 7.37−7.29 (m, 4H), 7.25−7.21 (m, 1H), 6.47 (dd, J = 15.9, 1.0 Hz, 1H), 6.32 (dd, J = 15.9, 6.4 Hz, 1H), 4.12 (ddq, J = 1.0, 6.4, 7.0 Hz, 1H), 3.29 (s, 3H), 1.53 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.8, 146.5, 140.3, 136.6, 131.7, 130.5, 128.6, 127.7, 126.3, 124.4, 123.1, 122.7, 39.0, 35.8, 20.3; IR (KBr) ν (cm^{-1}) 3026, 1583, 1350, 1217, 1084, 970; HRMS (ESI) calcd. for $C_{17}H_{17}NO_5S$ $[M + H]^+$ m/z 348.0900, found 348.0907.

*2-Cinnamyl-4-cyanophenyl methanesulfonate (**2c**).* Colorless oil, 6 mg, 2% yield (9 mg, 3% in DMF): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 2.1 Hz, 1H), 7.60 (dd, J = 8.5, 2.1 Hz, 1H), 7.50 (d, J = 8.5 Hz, 1H), 7.38−7.36 (m, 2H), 7.34−7.30 (m, 2H), 7.27−7.23 (m, 1H), 6.50 (d, J = 15.8 Hz, 1H), 6.26 (dt, J = 15.8, 6.8 Hz, 1H), 3.66 (d, J = 6.8 Hz, 2H), 3.27 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.2, 136.6, 135.1, 135.0, 133.3, 131.9, 128.7, 127.8, 126.2, 125.3, 123.1, 117.8, 111.5, 38.9, 33.2. IR (KBr) ν (cm^{-1}) 3026, 2229, 1374, 1162, 1092, 967; HRMS (ESI) calcd. for $C_{17}H_{15}NO_3S$ $[M + H]^+$ m/z 314.0845, found 314.0849.

*4-Cyano-2-(4-phenylbut-3-en-2-yl)phenyl methanesulfonate (**2d**).* Colorless oil, 131 mg, 30% yield (10 mg, 3% in DMF): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 2.0 Hz, 1H), 7.57 (dd, J = 8.5, 2.0 Hz, 1H), 7.50 (d, J = 8.5 Hz, 1H), 7.37−7.29 (m, 4H), 7.25−7.21 (m, 1H), 6.45 (dd, J = 16.0, 1.0 Hz, 1H), 6.29 (dd, J = 16.0, 6.2 Hz, 1H), 4.08 (ddq, J = 1.0, 6.2, 7.0 Hz, 1H), 3.26 (s, 3H), 1.48 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.6, 140.2, 136.6, 133.1, 131.8, 131.5, 130.4, 128.6, 127.7, 126.2, 123.0, 117.9, 111.5, 38.9, 35.5, 20.2; IR (KBr) ν (cm^{-1}) 3026, 2226, 1370, 1172, 970; HRMS (ESI) calcd. for $C_{18}H_{17}NO_3S$ $[M + H]^+$ m/z 328.1002, found 328.1006.

*(S)-4-Cyano-2-(4-phenylbut-3-en-2-yl)phenyl methanesulfonate ((S)-**2d**).* 98 mg, colorless oil, 30% yield: $[\alpha]_D^{20}$ = +6.4 (c 1.0, $CHCl_3$), 62% ee (from 99% ee starting materials) by chiral HPLC with *i*-PrOH and *n*-hexane in a ratio of 30:70 as eluent; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 2.0 Hz, 1H), 7.58 (dd, J = 8.5, 2.0 Hz, 1H), 7.51 (d, J = 8.5 Hz, 1H), 7.36−7.29 (m, 4H), 7.25−7.22 (m, 1H), 6.45 (d, J = 16.0 Hz, 1H), 6.29 (dd, J = 16.0, 6.2 Hz, 1H), 4.08 (dq, J = 6.2, 7.0 Hz, 1H), 3.27 (s, 3H), 1.48 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.6, 140.2, 136.6, 133.1, 131.8, 131.5, 130.4, 128.6, 127.7, 126.2, 123.0, 117.9, 111.5, 38.9, 35.5, 20.2; IR (KBr) ν (cm^{-1}) 3026, 2226, 1370, 1172, 970; HRMS (ESI) calcd. for $C_{18}H_{17}NO_3S$ $[M + H]^+$ m/z 328.1002, found 328.1006.

*4-Cyano-2-(4-(p-tolyl)but-3-en-2-yl)phenyl methanesulfonate (**2e**).* Colorless oil, 27 mg, 8% yield (31 mg, 9% in DMF): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 2.0 Hz, 1H), 7.57 (dd, J = 8.5, 2.0 Hz, 1H), 7.50 (d, J = 8.5 Hz, 1H), 7.24 (d, J = 8.2 Hz, 2H), 7.11 (d, J = 8.2 Hz, 2H), 6.41 (d, J = 16.0 Hz, 1H), 6.23 (dd, J = 16.0, 6.3 Hz, 1H), 4.06 (dq, J = 6.3, 7.0 Hz, 1H), 3.25 (s, 3H), 2.33 (s, 3H), 1.47 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.6 140.3, 137.5, 133.8, 133.2 131.5 130.8, 130.2, 129.34, 126.1, 122.9, 117.9, 111.5, 38.9, 35.5, 21.2, 20.2; IR (KBr) ν (cm^{-1}) 3117, 2231, 1371, 1225, 1167, 971; HRMS (ESI) calcd. for $C_{19}H_{19}NO_3S$ $[M + Na]^+$ m/z 364.0977, found 364.0978.

*4-Nitro-2-(1-phenylallyl)phenyl methanesulfonate (**3a**).* Yellowish oil, 86 mg, 26% yield (23 mg, 7% in DMF): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 2.8 Hz, 1H), 8.18 (dd, J = 8.8, 2.8 Hz, 1H), 7.62

dx.doi.org/10.1021/jo302210t | J. Org. Chem. 2012, 77, 10856−10869

(d, J = 8.8 Hz, 1H), 7.38−7.31 (m, 2H), 7.29−7.23 (m, 1H), 7.19−7.14 (m, 1H), 6.26 (ddd, J = 17.1, 10.3, 6.5 Hz, 1H), 5.38 (dt, J = 10.3, 1.1 Hz, 1H), 5.15 (d, J = 6.5 Hz, 1H), 4.98 (dt, J = 17.1, 1.1 Hz, 1H), 2.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 146.0, 140.5, 137.7, 137.4, 128.9, 128.5, 127.3, 125.8, 123.6, 122.1, 118.7, 48.4, 38.4; IR (KBr) ν (cm^{-1}) 3028, 2952, 1527, 1348, 1263, 1124; HRMS (ESI) calcd. for $C_{16}H_{15}NO_5S$ $[M + H]^+$ m/z 334.0744, found 334.0750.

*4-Nitro-2-(1-phenylbut-2-en-1-yl)phenyl methanesulfonate (**3b**).* Yellowish oil, E/Z = 4:1, 42 mg, 12% yield (170 mg, 49% in DMF): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 and 8.21 (d, J = 2.8 Hz, 1H), 8.15 (dd, J = 8.9, 2.8 Hz, 1H), 7.60 (d, J = 8.9 Hz, 1H), 7.34−7.29 (m, 2H), 7.25−7.21 (m, 1H), 7.18−7.14 (m, 2H), 5.87 (ddq, J = 15.2, 7.1, 1.6 Hz) and 5.80 (dd, J = 10.5, 8.1 Hz) (1H), 5.79 (dq, J = 10.5, 5.0 Hz) and 5.45 (ddq, J = 15.2, 6.6, 1.2 Hz) (1H), 5.40 (d, J = 8.1 Hz) and 5.08 (d, J = 7.1 Hz) (1H), 2.87 and 2.84 (s, 3H), 1.77 (dt, J = 6.6, 1.2 Hz) and 1.73 (d, J = 5.0 Hz) (3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 151.4, 146.0, 145.9, 141.5, 138.6, 138.3, 130.6, 130.1, 129.6, 128.9, 128.8, 128.3, 127.8, 127.4, 127.0, 126.9, 125.7, 125.4, 123.4, 122.1, 122.0, 47.6, 42.6, 38.3, 18.0, 13.3; IR (KBr) ν (cm^{-1}) 3028, 1585, 1349, 1217, 1074, 971. HRMS (ESI) calcd. for $C_{17}H_{17}NO_5S$ $[M + Na]^+$ m/z 370.0719, found 370.0725.

*4-Cyano-2-(1-phenylallyl)phenyl methanesulfonate (**3c**).* Colorless oil, 185 mg, 59% yield (31 mg, 10% in DMF): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, J = 8.3, 2.0 Hz, 1H), 7.58 (d, J = 2.0 Hz, 1H), 7.56 (d, J = 8.3 Hz, 1H), 7.37−7.31 (m, 2H), 7.29−7.24 (m, 1H), 7.15 (d, J = 7.2 Hz, 2H), 6.21 (ddd, J = 17.2, 10.3, 6.4 Hz, 1H), 5.35 (dt, J = 10.3, 1.2 Hz, 1H), 5.13 (d, J = 6.4 Hz, 1H), 4.93 (d, J = 17.2 Hz, 1H), 2.89 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.2, 140.5, 137.8, 137.3, 134.5, 132.1, 128.8, 128.5, 127.2, 122.4, 118.5, 117.9, 111.0, 48.0, 38.4; IR (KBr) ν (cm^{-1}) 3028, 2936, 2232, 1372, 1169, 1095, 970. HRMS (ESI) calcd. for $C_{17}H_{15}NO_3S$ $[M + Na]^+$ m/z 336.0664, found 336.0670.

*4-Cyano-2-(1-phenylbut-2-en-1-yl)phenyl methanesulfonate (**3d**).* Colorless oil, E/Z = 4:1, 78 mg, 24% yield (176 mg, 54% in DMF): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65−7.53 (m, 3H), 7.33−7.29 (m, 2H), 7.25−7.22 (m, 1H), 7.16−7.12 (m, 2H), 5.81 (ddq, J = 15.3, 7.0, 1.6 Hz) and 5.74 (dd, J = 10.6, 7.8 Hz) (1H), 5.73 (ddq, J = 10.6, 5.2, 1.6 Hz) and 5.40 (ddq, J = 15.3, 6.5, 1.3 Hz) (1H), 5.37 (d, J = 7.8 Hz) and 5.05 (d, J = 7.1 Hz) (1H), 2.87 and 2.84 (s, 3H), 1.76 (dt, J = 6.5, 1.2 Hz) and 1.71 (d, J = 5.2 Hz,) (3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 150.2, 142.4, 141.5, 138.6, 138.2, 134.4, 134.1, 131.8, 130.7, 130.2, 129.4, 128.8, 128.7, 128.4, 127.9, 127.3, 127.0, 126.9, 122.4, 122.3, 118.0, 117.9, 111.0, 110.8, 47.3, 42.3, 38.3, 18.0, 13.2; IR (KBr) ν (cm^{-1}) 3027, 2232, 1358, 1168, 972, 701; HRMS (ESI) calcd. for $C_{18}H_{17}NO_3S$ $[M + Na]^+$ m/z 350.0821, found 350.0822.

*(S)-4-Cyano-2-(1-phenylbut-2-en-1-yl)phenyl methanesulfonate ((S)-**3d**).* Colorless oil, E/Z = 19:1, 81 mg, 25% yield: $[\alpha]_D^{20}$ = +25.0 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61−7.54 (m, 3H), 7.34−7.30 (m, 2H), 7.26−7.23 (m, 1H), 7.14−7.12 (m, 2H), 5.81 (dd, J = 15.2, 6.9 Hz, 1H), 5.40 (dq, J = 15.2, 6.4 Hz, 1H), 5.05 (d, J = 6.8 Hz, 1H), 2.87 and 2.84 (s, 3H), 1.76 (d, J = 6.2 Hz) and 1.71 (d, J = 6.5 Hz,) (3H).

*4-Cyano-2-(1-(p-tolyl)but-2-en-1-yl)phenyl methanesulfonate (**3e**).* Colorless oil, E/Z = 4:1, 17 mg, 5% yield (211 mg, 62% in DMF): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 and 7.59 (d, J = 2.0 Hz, 1H), 7.57 (dd, J = 8.5, 2.0 Hz, 1H), 7.53 (d, J = 8.5 Hz, 1H), 7.12 (d, J = 7.9 Hz, 2H), 7.04−7.0 (m, 2H), 5.80 (ddq, J = 15.3, 6.9, 1.4 Hz) and 5.71 (dd, J = 10.5, 7.5 Hz) (1H), 5.72 (ddq, J = 10.5, 5.3, 1.3 Hz) and 5.38 (ddq, J = 15.3, 6.5, 1.2 Hz) (1H), 5.34 (d, J = 6.9 Hz) and 5.01 (d, J = 6.9 Hz) (1H), 2.90 and 2.87 (s, 3H), 2.32 (s, 3H), 1.75 (dt, J = 6.5, 1.2 Hz) and 1.70 (d, J = 5.3 Hz) (3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.2, 150.2, 139.3, 138.9, 138.4, 136.7, 136.6, 134.4, 134.1, 131.7, 130.9, 130.4, 129.5, 129.4, 129.1, 128.3, 127.7, 127.0, 122.4, 122.3, 118.0, 118.0, 111.0, 110.8, 46.8, 41.9, 38.3, 21.0, 18.0, 13.2; IR (KBr) ν (cm^{-1}) 3117, 2231, 1370, 1223, 1167, 971, 730; HRMS (ESI) calcd. for $C_{19}H_{19}NO_3S$ $[M + H]^+$ m/z 342.1158, found 342.1159.

*4-Methyl-2-(1-phenylbut-2-en-1-yl)phenyl methanesulfonate (**3f**).* Yellowish oil, E/Z = 6:1, 47 mg, 15% yield (117 mg, 37% in DMF): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23−7.26 (m, 3H), 7.22−7.16 (m, 3H), 7.12−7.02 (m, 2H), 5.86 (ddq, J = 15.2, 7.2, 1.5 Hz) and 5.74−5.66 (m, 1H), 5.80−5.76 (m) and 5.40 (dqd, J = 15.2, 6.4, 1.3 Hz) (1H), 5.38 (d, J = 7.9 Hz) and 5.04 (d, J = 7.2 Hz) (1H), 2.84 and 2.79 (s, 3H), 2.32 and 2.31 (s, 3H), 1.73 (dt, J = 6.5, 1.3 Hz) and 1.70 (d, J = 6.6 Hz) (3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.3, 143.7, 143.0, 137.0, 136.8, 136.5, 136.0, 132.1, 131.6, 130.8, 130.6, 128.5, 128.4, 128.3, 128.03, 127.9, 126.4, 126.3, 125.9, 121.2, 121.1, 47.2, 42.0, 37.6, 37.5, 21.0, 18.0, 13.2; IR (KBr) ν (cm^{-1}) 3027, 2938, 2856, 1600, 1492, 1451, 1198, 970, 700; HRMS (ESI) calcd. for $C_{18}H_{20}O_3S$ $[M + Na]^+$ m/z 339.1025, found 339.1021.

*4-Methoxy-2-(1-phenylbut-2-en-1-yl)phenyl methanesulfonate (**3g**).* Yellowish oil, E/Z = 6:1, 33 mg, 10% yield (136 mg, 41% in DMF): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.26 (m, 3H), 7.22−7.17 (m, 3H), 6.85−6.73 (m, 2H), 5.84 (ddq, J = 15.2, 7.1, 1.5 Hz) and 5.73−5.67 (m, 1H), 5.81−5.74 (m) and 5.40 (dqd, J = 15.2, 6.5, 1.3 Hz) (1H), 5.38 (d, J = 7.9 Hz) and 5.04 (d, J = 7.0 Hz) (1H), 3.77 and 3.76 (s, 3H), 2.86 and 2.81 (s, 3H), 1.73 (dt, J = 6.5, 1.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 142.7, 140.9, 137.9, 131.9, 131.4, 128.5, 128.4, 128.1, 128.0, 126.5, 126.4, 126.2, 122.5, 122.5, 116.3, 115.8, 112.0, 111.8, 55.5, 47.4, 42.3, 37.5, 37.5, 18.0, 13.2; IR (KBr) ν (cm^{-1}) 3027, 2939, 2855, 1600, 1585, 1489, 1452, 1196, 1063, 970, 701; HRMS (ESI) calcd. for $C_{18}H_{20}O_4S$ $[M + Na]^+$ m/z 355.0975, found 355.0964.

*4-Nitro-2-(1-phenylprop-1-en-1-yl)phenyl methanesulfonate (**4a**).* Yellowish oil, E/Z = 5:1, 13 mg, 4% yield (77 mg, 23% in DMF): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 and 8.18 (dd, J = 9.0, 2.8 Hz, 1H), 8.25 and 8.18 (d, J = 2.8 Hz, 1H), 7.64 and 7.56 (d, J = 9.0 Hz, 1H), 7.39−7.24 (m, 3H), 7.22−7.17 (m, 2H), 6.44 and 6.10 (q, J = 7.1 Hz, 1H), 2.77 and 2.71 (s, 3H), 1.95 and 1.74 (d, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 145.9, 140.3, 138.2, 138.2, 136.6, 135.8, 134.0, 131.1, 129.3, 128.7, 128.4, 127.8, 127.7, 127.6, 127.1, 126.3, 124.3, 123.8, 123.3, 122.5, 38.7, 38.2, 15.9, 15.7; IR (KBr) ν (cm^{-1}) 3028, 1528, 1350, 1251, 1124, 970, 865, 733; HRMS (ESI) calcd. for $C_{16}H_{15}NO_5S$ $[M + H]^+$ m/z 334.0744, found 334.0748.

*4-Nitro-2-(1-phenylbut-1-en-1-yl)phenyl methanesulfonate (**4b**).* Yellowish oil, 10 mg, 3% yield (45 mg, 13% in DMF): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (dd, J = 9.0, 2.8 Hz, 1H), 8.18 (d, J = 2.8 Hz, 1H), 7.63 (d, J = 9.0 Hz, 1H), 7.32−7.29 (m, 3H), 7.21−7.19 (m, 2H), 2.75 (s, 3H), 2.05 (p, J = 7.5 Hz, 2H), 1.07 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 145.8, 140.2, 135.6, 134.2, 130.6, 128.7, 127.7, 126.4, 124.3, 123.2, 122.0, 38.7, 23.6, 13.8; IR (KBr) ν (cm^{-1}) 3025, 1578, 1349, 1209, 1077, 970, 857; HRMS (ESI) calcd. for $C_{17}H_{17}NO_5S$ $[M + H]^+$ m/z 348.0900, found 348.0907.

*4-Cyano-2-(1-phenylprop-1-en-1-yl)phenyl methanesulfonate (**4c**).* Colorless oil, E/Z = 6:1, 6 mg, 2% yield (25 mg, 8% in DMF): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 and 7.63 (dd, J = 8.6, 2.1 Hz, 1H), 7.65 and 7.60 (d, J = 2.1 Hz, 1H), 7.59 and 7.50 (d, J = 8.6 Hz, 1H), 7.39−7.24 (m, 3H), 7.20−7.16 (m, 2H), 6.41 and 6.05 (q, J = 7.1 Hz, 1H), 2.76 and 2.71 (s, 3H), 1.93 and 1.72 (d, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.3, 140.4, 136.4, 135.7, 135.7, 134.1, 132.9, 132.3, 130.8, 129.3, 128.6, 128.4, 128.2, 127.6, 127.6, 126.3, 123.7, 122.9, 117.7, 111.1, 38.7, 38.2, 15.9, 15.7; IR (KBr) ν (cm^{-1}) 3112, 2232, 1372, 1169, 1085, 970, 858, 701. HRMS (ESI) calcd. for $C_{17}H_{15}NO_3S$ $[M + H]^+$ m/z 314.0845, found 314.0849.

*4-Cyano-2-(1-phenylbut-1-en-1-yl)phenyl methanesulfonate (**4d**).* Colorless oil, 13 mg, 4% yield (88 mg, 27% in DMF): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71−7.69 (m, 1H), 7.59−7.57 (m, 2H), 7.32−7.26 (m, 3H), 7.19−7.17 (m, 2H), 6.29 (t, J = 7.5 Hz, 1H), 2.74 (s, 3H), 2.03 (p, J = 7.5 Hz, 2H), 1.06 (t, J = 7.5 Hz, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ 150.2, 140.3, 136.2, 135.5, 134.3, 134.0, 132.8, 128.6, 127.7, 126.3, 123.6, 117.7, 110.9, 38.7, 23.5, 13.9; IR (KBr) ν (cm^{-1}) 3024, 2232, 1363, 1169, 1093, 970, 832; HRMS (ESI) calcd. for $C_{18}H_{17}NO_3S$ $[M + Na]^+$ m/z 350.0821, found 350.0822.

*4-Cyano-2-(1-(p-tolyl)but-1-en-1-yl)phenyl methanesulfonate (**4e**).* Colorless oil, 10 mg, 3% yield (14 mg, 4% in DMF): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (dd, J = 8.6, 2.1 Hz, 1H), 7.57 (d, J = 2.1 Hz, 2H), 7.57 (d, J = 8.6 Hz, 1H), 7.10 (d, J = 8.2 Hz, 2H), 7.06 (d, J = 8.2 Hz, 2H), 6.25 (t, J = 7.5 Hz, 1H), 2.76 (s, 3H), 2.32 (s, 3H), 2.00 (p, J = 7.5 Hz, 2H), 1.05 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ 150.3, 137.6, 137.4, 136.2, 134.5, 134.5, 133.8, 132.8, 129.3, 126.2, 123.7, 117.8, 111.0, 38.8, 23.5, 21.0, 13.9; IR (KBr) ν (cm^{-1}) 3113, 2229, 1655, 1377, 1168, 971, 835; HRMS (ESI) calcd. for $C_{19}H_{19}NO_3S$ $[M + Na]^+$ m/z 364.0977, found 364.0974.

Intercrossing Experiments. *Method A.* A solution of **1a** (255 mg, 1 mmol) and **1d** (249 mg, 1 mmol) in 10 mL of DCB was refluxed for 24 h. The reaction mixture was allowed to cool to room temperature. After dilution with CH_2Cl_2 (20 mL), Et_3N (1.2 mL, 0.88 g, 9.0 mmol) and MsCl (0.5 mL, 0.74 g, 6 mmol) were added. The resulting mixture was stirred for 24 h at room temperature, diluted with CH_2Cl_2 (50 mL), washed with brine (2 × 50 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was subjected to the HPLC analysis.

Method B. A mixture of **1a** (128 mg, 0.5 mmol) and **1d** (124 mg, 0.5 mmol) in a sealed test tube was heated at 180 °C for 24 h. The reaction mixture was allowed to cool to room temperature. After dilution with CH_2Cl_2 (10 mL), Et_3N (0.6 mL, 0.44 g, 4.5 mmol) and MsCl (0.25 mL, 0.37 g, 3 mmol) were added. After workup, the residue was subjected to the HPLC analysis.

Typical Procedure for Radical Trapping Experiments. A solution of allyl aryl ether **1d** (249 mg, 1 mmol) and a radical trapper in 10 mL of ethylene glycol was heated at 180 °C for 24 h. The reaction mixture was allowed to cool to room temperature, diluted with CH_2Cl_2 (50 mL), washed with brine (2 × 50 mL), dried over anhydrous Na_2SO_4, and filtered. To the filtrate was added Et_3N (0.6 mL, 0.44 g, 4.5 mmol) and MsCl (0.25 mL, 0.37 g, 3 mmol). The resulting mixture was stirred for 24 h at room temperature, washed with brine (2 × 50 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to afford 89 mg of colorless oil in 27% yield.

Synthesis of (*R*)-4-Phenylbutan-2-ol ((*R*)-6). In a dry 250 mL Schlenk-flask, (*S*)-α,α-diphenylprolinol (1.89 g, 7.5 mmol) and phenylboronic acid (0.92 g, 7.5 mmol) were suspended in 50 mL of dry toluene. The mixture was heated to reflux in an inert atmosphere for 24 h with azeotropic removal of water, which was trapped by 10 g of 4 Å molecular sieves placed in a pressure equalizing dropping funnel between the flask and the condenser.[27] The reaction mixture was then cooled, and a solution of 4-phenylbutan-2-one (7.40 g, 50 mmol) in 40 mL of dry toluene was added. Borane in THF (60 mL of 1.0 mol/L THF solution, 60 mmol) was added dropwise over 1.5 h. The reaction mixture was stirred for 10 min at room temperature and then cooled to 0 °C in an ice bath and was quenched by the careful addition of 50 mL of methanol. After removal of volatiles in vacuo, the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to give (*R*)-**6** as a colorless liquid 7.18 g in 96% yield: $[\alpha]_D^{20}$ = −6.1 (*c* 1.0, $CHCl_3$), 45% ee; lit.[28] $[\alpha]_D^{21}$ = −14.0 (*c* 1.63, $CHCl_3$), 86% ee.

Synthesis of (*S*)-7. Prepared according to the general procedure for the synthesis of allyl aryl ethers **1** from (*R*)-4-phenylbutan-2-ol ((*R*)-**6**, 7.0 g, 46.6 mmol, 45% ee) and 4-hydroxybenzonitrile (6.7 g, 56 mmol) in toluene, and purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 8:1) to give (*S*)-**7**.

*(S)-4-(4-Phenylbutan-2-yloxy)benzonitrile ((S)-**7**).* 9.0 g, colorless liquid, 77% yield: 44% ee, $[\alpha]_D^{20}$ = +26.4 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.56−7.53 (m, 2H), 7.29−7.25 (m, 2H), 7.21−7.18 (m, 1H), 7.15−7.13 (m, 2H), 6.88−6.84 (m, 2H), 4.46−4.35 (m, 1H), 2.81−2.67 (m, 2H), 2.13−2.05 (m, 1H), 1.95−1.87 (m, 1H), 1.34 (d, J = 6.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5, 141.2, 134.0, 128.5, 128.4, 126.0, 119.3, 116.0, 103.5, 73.1, 37.8, 31.6, 19.4; IR (KBr) ν (cm^{-1}) 2976, 2933, 2224, 1604, 1572, 1506, 1454, 1257; HRMS (ESI) calcd. for $C_{17}H_{17}NO$ $[M + H]^+$ m/z 252.1383, found 252.1385. Or prepared from 4.0 g (*R*)-4-phenylbutan-2-ol (99% ee, 26.6 mmol, commercial) to afford 6.6 g in 99% yield: 98% ee, $[\alpha]_D^{20}$ = +58.0 (*c* 1.0, $CHCl_3$).

Synthesis of (*S*)-8. A solution of (*S*)-**2d** (62% ee, 0.25 g, 0.76 mmol) and tetrabutylammonium hydroxide (0.83 g, 3,16 mmol) in THF (15 mL) and water (1.5 mL) was heated at reflux for 5 h. After cooling to room temperature, the reaction mixture was acidized with 1 mol/L of HCl and extracted with 50 mL of ethyl acetate. The organic layer was washed with 50 mL of brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. To the residue was added K_2CO_3 (0.53 g, 3.84 mmol), and acetone (20 mL) and then Me_2SO_4 (0.11 mL, 0.15 g, 1.2 mmol) were added at room temperature. The reaction mixture was refluxed for 2 h. After cooling to room temperature, the mixture was filtered and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give (*S*)-**8.**

*(S)-4-Methoxy-3-(4-phenylbut-3-en-2-yl)benzonitrile ((S)-**8**).* 0.18 g, colorless oil, 90% yield: $[\alpha]_D^{20}$ = +16.5 (*c* 1.0, $CHCl_3$), 46% ee by chiral HPLC with *i*-PrOH and *n*-hexane in a ratio of 1:99 as eluent; ^1H NMR (400 MHz, $CDCl_3$) δ 7.52−7.49 (m, 2H), 7.36−7.35 (m, 2H), 7.32−7.28 (m, 2H), 7.23−7.19 (m, 1H), 6.90 (d, *J* = 8.4 Hz, 1H), 6.42 (d, *J* = 16.0 Hz, 1H), 6.33 (dd, *J* = 16.0, 6.3 Hz, 1H), 4.06 (p, *J* = 6.8 Hz, 1H), 3.90 (s, 3H), 1.40 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 137.3, 135.6, 133.1, 132.1, 131.4, 129.3, 128.5, 127.2, 126.1, 119.5, 110.8, 103.9, 55.7, 35.0, 19.6; IR (KBr) ν (cm^{-1}) 2967, 2841, 2223, 1602, 1495, 1456, 1258, 1024, 967; HRMS (ESI) calcd. for $C_{18}H_{17}NO$ $[M + H]^+$ m/z 264.1383, found 264.1390.

Synthesis of (*R*)-9. To a 100 mL, three-necked, round-bottomed flask containing a magnetic stir bar, equipped with gas dispersion tube were added (*S*)-**8** (46% ee, 155 mg, 0.59 mmol) and CH_2Cl_2 (10 mL). The solution was cooled to −78 °C under nitrogen. Ozone was bubbled through the solution until it turned blue. Nitrogen was then bubbled through the solution until colorless. While still at −78 °C, a freshly prepared solution of sodium borohydride (223 mg, 5.9 mmol, 10 equiv) in ethanol (15 mL) was added dropwise by syringe. The contents were then allowed to warm to room temperature with stirring and without removal of the cooling bath. After 24 h, the mixture was diluted with ether (20 mL), and 0.2 mol/L of HCl (35 mL) was added slowly by pipet. The biphasic mixture was then stirred for 1 h. The aqueous phase was separated and extracted with ether (2 × 20 mL). The combined organic phase was washed with brine (2× 20 mL), dried over $MgSO_4$, and filtered. The filtrate was concentrated in vacuo, and the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to afford (*R*)-**9.**

*(R)-3-(1-Hydroxypropan-2-yl)-4-methoxybenzonitrile ((R)-**9**).* 80 mg, colorless crystals, 71% yield: mp 86.5−87 °C, $[\alpha]_D^{20}$ = −3.4 (*c* 1.0, $CHCl_3$), 46% ee by chiral HPLC with *i*-PrOH and *n*-hexane in a ratio of 5:95 as eluent; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.5 Hz, 1H), 7.49 (s, 1H), 6.91 (d, *J* = 8.5 Hz, 1H), 3.89 (s, 3H), 3.81−3.60 (m, 2H), 3.42 (m, 1H), 1.63 (brs, 1H), 1.26 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 133.6, 132.2, 131.4, 119.4, 110.8, 104.0, 67.0, 55.7, 34.8, 16.3; IR (KBr) ν (cm^{-1}) 3425, 2967, 2876, 2842, 2224, 1603, 1497, 1461, 1259, 1025; HRMS (ESI) calcd. for $C_{11}H_{13}NO_2$ $[M + Na]^+$ m/z 214.0838, found 214.0834.

Synthesis of 10a and 11a. Prepared according to the general procedure of allyl aryl ethers **1** from 4,4-dimethyl-1-phenylpent-1-en-3-ol (0.49 g, 2.6 mmol) and 4-hydroxy-3,5-dimethylbenzonitrile (**12a**, 0.39 g, 2.6 mmol), and purified twice by column chromatography on silica gel to give **10a** and **11a**.

*4-((4,4-Dimethyl-1-phenylpent-1-en-3-yl)oxy)-3,5-dimethylbenzonitrile (**10a**).* 0.24 g, colorless oil, 29% yield: ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.3 Hz, 2H), 7.39 (t, *J* = 7.3 Hz, 2H), 7.36−7.33 (m, 1H), 7.29 (s, 2H), 5.59 (dd, *J* = 15.5, 7.6 Hz, 1H), 5.51 (d, *J* = 15.5 Hz, 1H), 5.22 (d, *J* = 7.6 Hz, 1H), 2.21 (s, 6H), 0.91 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5, 146.6, 140.6, 133.3, 132.5, 128.5, 128.0, 126.6, 123.4, 119.2, 107.0, 85.8, 33.0, 29.1, 17.2; IR (KBr) ν (cm^{-1}) 3031, 2958, 2867, 2223, 1217, 1140, 970; HRMS (ESI) calcd. for $C_{22}H_{25}NO$ $[M + H]^+$ m/z 320.2009, found 320.2003.

*4-((4,4-Dimethyl-1-phenylpent-2-en-1-yl)oxy)-3,5-dimethylbenzonitrile (**11a**).* 0.17 g, colorless oil, 21% yield: ^1H NMR (400 MHz, $CDCl_3$) δ 7.33−7.30 (m, 1H), 7.26 (m, 2H), 7.22 (s, 2H), 7.18 (m, 2H), 6.17 (dd, *J* = 15.8, 9.2 Hz, 1H), 6.07 (d, *J* = 15.8 Hz, 1H), 4.29 (d, *J* = 9.2 Hz, 1H), 2.28 (s, 6H), 1.15 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 135.9, 135.6, 132.9, 132.7, 128.6, 128.0, 126.4, 124.7, 119.2, 106.6, 90.4, 35.7, 26.3, 17.5; IR (KBr) ν (cm^{-1}) 2957, 2925, 2863, 2223, 1226, 1141, 968; HRMS (ESI) calcd. for $C_{22}H_{25}NO$ $[MH^+\text{-}Me_2CNC_6H_2OH]$ m/z 173.1330, found 173.1322.

dx.doi.org/10.1021/jo302210t | J. Org. Chem. 2012, 77, 10856−10869

Synthesis of 10b and 11b. Prepared according to the general procedure of allyl aryl ethers **1** from 1-(4-fluorophenyl)-4,4-dimethylpent-1-en-3-ol (**13**, 0.42 g, 2 mmol) and 4-hydroxy-3-ethyl-5-methylbenzonitrile (**12b**, 0.38 g, 2.4 mmol), and purified twice by column chromatography on silica gel to give **10b** and **11b**.

*3-Ethyl-4-((1-(4-fluorophenyl)-4,4-dimethylpent-1-en-3-yl)oxy)-5-methylbenzonitrile (**10b**).* 0.18 g, colorless oil, 26% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (m, 2H), 7.33 (s, 1H), 7.30 (s, 1H), 7.07 (m, 2H), 5.52 (d, J = 5.8 Hz, 1H), 5.52 (s, 1H), 5.18 (d, J = 5.8 Hz, 1H), 2.63 (dq, J = 15.0, 7.5 Hz, 1H), 2.53(dq, J = 15.0, 7.5 Hz, 1H), 2.20 (s, 3H), 1.16 (t, J = 7.5 Hz, 3H), 0.91 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4 (d, J = 246.5 Hz), 157.9, 146.7, 139.2, 136.5, 133.1, 132.5, 130.8, 128.2 (d, J = 8.1 Hz), 123.3, 119.3, 115.4 (d, J = 21.4 Hz), 107.3, 85.5, 32.9, 29.1, 23.37, 17.4, 14.1; IR (KBr) ν (cm^{-1}) 2960, 2929, 2868, 2225, 1212, 835; HRMS (ESI) calcd. for $C_{23}H_{26}FNO$ $[M + Na]^+$ m/z 374.1891, found 374.1887.

*3-Ethyl-4-((1-(4-fluorophenyl)-4,4-dimethylpent-2-en-1-yl)oxy)-5-methylbenzonitrile (**11b**).* 0.25 g, colorless oil, 35% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (s, 1H), 7.23 (s, 1H), 7.13 (m, 2H), 6.94 (m, 2H), 6.08 (dd, J = 15.8, 8.7 Hz, 1H), 6.01 (d, J = 15.8 Hz, 1H), 4.26 (d, J = 8.7 Hz, 1H), 2.73 (dq, J = 15.0, 7.5 Hz, 1H), 2.60 (dq, J = 15.0, 7.5 Hz, 1H), 2.29 (s, 3H), 1.20 (t, J = 7.5 Hz, 3H), 1.15 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5 (d, J = 247.9 Hz), 157.6, 139.1, 134.5, 132.8, 132.6, 132.1, 132.0, 130.9, 128.0 (d, J = 8.0 Hz), 124.5, 119.3, 115.5 (d, J = 21.7 Hz), 106.9, 90.7, 35.6, 26.3, 23.4, 17.6, 14.2; IR (KBr) ν (cm^{-1}) 2960, 2929, 2872, 2224, 1231, 967; HRMS (ESI) calcd. for $C_{23}H_{26}FNO$ $[MH^+$-MeEtCNC$_6$H$_2$OH$]$ m/z 191.1236, found 191.1228.

Typical Procedure for O[1,3]-Sigmatropic Shifts. A solution of allyl aryl ether **10a** (25 mg, 0.08 mmol) in 5 mL of DCB was refluxed for 2 h. The reaction mixture was cooled to room temperature and concentrated in vacuo. The residue was subjected to the ^{1}H NMR analysis, which found 75% yield of **11a**, 16% yield of **12a** and 9% yield of **10a**.

Typical Procedure for Synthesis of 12. To a suspension of 4-amino-3,5-dimethylbenzonitrile (**14a**, 1.43 g, 10 mmol) in ice water (20 mL) was slowly added cold 30% H_2SO_4 (32 mL) to maintain temperature below 5 °C. A solution of $NaNO_2$ (1.66 g, 24 mmol) in water (24 mL) was added dropwise, and the resulting mixture was stirred for 30 min in an ice water bath. The mixture was allowed to warm to room temperature and then kept at 80 °C for 1 h. The mixture was cooled, diluted with ethyl acetate (150 mL), washed with brine (2 × 100 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **12a**.

*4-Hydroxy-3,5-dimethylbenzonitrile (**12a**).* 0.40 g, colorless crystals, 28% yield: mp 96−98 °C, lit.[29] 105 °C.

*3-Ethyl-4-hydroxy-5-methylbenzonitrile (**12b**).* Colorless crystals, 1.27 g from 2.47 g (15.4 mmol) of **13b**, 51% yield: mp 86−89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (s, 1H), 7.30 (s, 1H), 2.64 (q, J = 7.5 Hz, 2H), 2.27 (s, 3H), 1.25 (t, J = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.7, 132.5, 131.0, 130.3, 124.2, 119.6, 103.5, 22.67, 15.68, 13.38; IR (KBr) ν (cm^{-1}) 3384, 2963, 2927, 2877, 2224; HRMS (ESI) calcd. for $C_{10}H_{11}NO$ $[M + H]^+$ m/z 162.0913, found 162.0915.

Synthesis of 13. A solution of 1-(4-fluorophenyl)-4,4-dimethylpent-1-en-3-one (1.83 g, 8.9 mmol) in methanol (6 mL) and water (6 mL) was cooled to 0 °C, and $NaBH_4$ (0.51 g, 13.4 mmol) was added in one portion. After stirring for 2 h at room temperature, the mixture was concentrated in vacuo to remove methanol. The residue was diluted with ethyl acetate (50 mL) and washed with brine (50 mL), and then the organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography (petroleum ether/ethyl acetate = 10:1) to give **13**.

*1-(4-Fluorophenyl)-4,4-dimethylpent-1-en-3-ol (**13**).* 1.81 g, colorless liquid, 98% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (m, 2H), 7.00 (m, 2H), 6.53 (d, J = 15.9 Hz, 1H), 6.20 (dd, J = 15.9, 7.2 Hz, 1H), 3.91, 3.91 (d, J = 7.2 Hz, 1H), 1.61 (s, 1H), 0.96 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3 (d, J = 246.8 Hz), 133.1, 130.6, 129.3, 127.9 (d, J = 7.9 Hz), 115.4 (d, J = 21.6 Hz), 80.9, 35.3, 25.8; IR (KBr) ν (cm^{-1}) 3399, 2956, 2929, 2869, 1230, 970; HRMS (ESI) calcd. for $C_{13}H_{17}FO$ $[M + Na]^+$ m/z 231.1156, found 231.1156.

Typical Procedure for Synthesis of 14. An oven-dried, round-bottomed flask was charged with CuCN (8.96 g, 0.1 mol), CuI (1.58 g, 8.3 mmol), 4-bromo-2,6-dimethylaniline (**15a**, 16.66 g, 83.3 mmol), and KI (2.67 g, 16.7 mmol) under nitrogen. Dry DMF (60 mL) and *N*,*N*′-dimethylethylenediamine (9.5 mL, 83.3 mmol) were added, and the reaction mixture was stirred at 100 °C for 24 h. The resulting mixture was allowed to cool to room temperature, diluted with 25% aqueous ammonia (200 mL) and extracted with ethyl acetate (200 mL). The organic layer was washed with brine (2 × 200 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to give **14a**.

*4-Amino-3,5-dimethylbenzonitrile (**14a**).*[30] 6.03 g, colorless crystals, 50% yield: mp 120−120.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.17 (s, 2H), 4.15 (s, 2H), 2.15 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.2, 131.8, 121.2, 120.5, 98.8, 17.1.

*4-Amino-3-ethyl-5-methylbenzonitrile (**14b**).* Colorless crystals, 13.1 g from 30.3 g (0.14 mol) of **15b**, 58% yield: mp 105−106 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (s, 2H), 4.09 (s, 2H), 2.50 (q, J = 7.5 Hz, 2H), 2.17 (s, 3H), 1.26 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.7, 131.6, 129.7, 126.7, 121.4, 120.6, 98.8, 23.4, 17.1, 12.1; IR (KBr) ν (cm^{-1}) 3486, 3394, 2963, 2936, 2912, 2213; HRMS (ESI) calcd. for $C_{10}H_{12}N_2$ $[M + H]^+$ m/z 161.1073, found 161.1075.

Typical Procedure for Synthesis of 15. To a solution of boric acid (2.47 g, 40 mmol) in 30% H_2O_2 (68 mL, 0.6 mol) were added 2,6-dimethylaniline (24.23 g, 0.2 mol) and water (250 mL). Then KBr (35.70 g, 0.3 mol) and 5 mol/L of H_2SO_4 (30 mL) were added. The mixture was stirred at room temperature for 3 h. The resulting mixture was extracted with *tert*-butyl methyl ether (2 × 200 mL), and the combined organic layers were washed with 5% aqueous $NaHCO_3$ (200 mL), water (200 mL), saturated aqueous Na_2SO_3 (200 mL), and brine (200 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to give **15a.**

*4-Bromo-2,6-dimethylaniline (**15a**).*[31] 32.10 g, brown liquid, 80% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.06 (s, 2H), 3.55 (s, 2H), 2.14 (s, 6H).

*4-Bromo-2-ethyl-6-methylaniline (**15b**).* Brown liquid, 33.5 g from 27.1 g (0.2 mol) of 2-ethyl-6-methylaniline, yield 78%: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.06 (s, 2H), 3.58 (s, 2H), 2.48 (q, J = 7.5 Hz, 2H), 2.14 (s, 3H), 1.24 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.1, 130.1, 129.1, 128.3, 123.7, 109.5, 23.8, 17.2, 12.5; IR (KBr) ν (cm^{-1}) 3483, 3398, 2966, 2933, 2872, 550; HRMS (ESI) calcd. for $C_9H_{12}BrN$ $[M + H]^+$ m/z 214.0226, found 214.0228.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H NMR and ^{13}C NMR spectra of the products, computational details, and HPLC analysis of intercrossing experiments, trapping experimental details, copies of HPLC diagrams for the optically active experiments. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The project was supported by National Natural Science Foundation of China (No. 21172017 and 20972013) and the specialized Research Fund for the Doctoral Program of Higher Education, Ministry of Education of China (No.

20110010110011). This paper is also supported by "Chemical Grid Project" of Beijing University of Chemical Technology.

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