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Facile Pd(II)- and Ni(II)-Catalyzed Isomerization of Terminal Alkenes into 2-Alkenes

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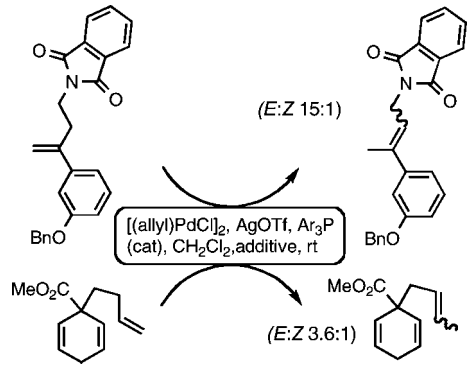

Mono- and 2,2′-disubstituted terminal alkenes can be isomerized into the more stable internal (*Z*)- and (*E*)-alkenes by treating them with catalytic amounts of $[(allyl)PdCl]_2$ or $[(allyl)NiBr]_2$, a triarylphosphine, and silver triflate at room temperature. The isomeric ratio (*E*:*Z*) depends on the alkenes, the *E*-isomer being the major one. The reaction is tolerant to a wide variety of functional groups including other reactive olefins. Unlike the more reactive Ir catalysts, monosubstituted alkenes give almost exclusively the 2-alkenes. Direct comparison to two of the best-known catalysts for this process $\{[Ir(PCy_3)_3]^+[BPh_4]^-$ and Grubbs generation II metathesis catalyst$\}$ is also described.

Introduction

Isomerization of allylic derivatives is a well-known reaction[1] that has been used in unmasking allylic protecting groups[2] and enantioselective synthesis of vinyl amines[3a] and ethers.[3b] Notable applications of the vinyl ether synthesis include the use of these intermediates for other C−C bond-forming reactions such as Claisen rearrangements.[4a,b] The isomerization reaction has also been used for the stereoselective syntheses of silyl ethers of aldehyde enols.[4c,d] Depending on the metal and the reaction conditions, varying selectivities for the isomerized (*E*)- and (*Z*)-alkenes have been observed. In general, while Ni(II) catalysts deliver the best *Z*:*E* ratios,[5] Ir catalysts are the optimal reagents for the preparation of *E*-olefins (Scheme 1).[4b–d,6] Low-yielding

SCHEME 1. Isomerization of Allyl Ethers into Vinyl Ethers

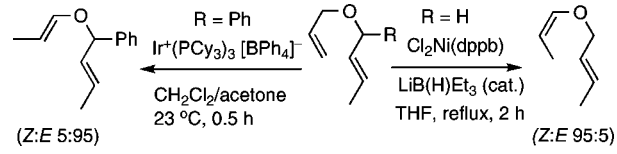

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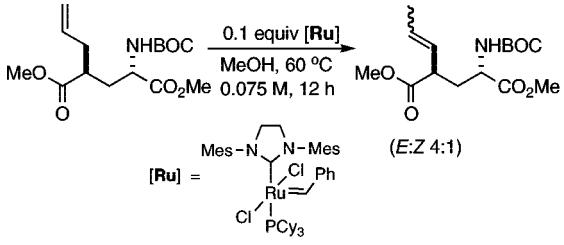
TABLE 1. Isomerization of 1-Methylenetetralin (1) and 1-(2-Phthalimidoethyl)styrene (3a)[a]

entry	catalyst (mol %), additives (mol %)	conditions	yield (%) 2	yield (%) 4 (*E*:*Z*)
1	$[(allyl)NiBr]_2$ (5), Ph_3P (10) AgOTf (5), ethylene	ethylene (1 atm), 25 °C, 2 d	0	<5
2	$[(allyl)PdCl]_2$ (5), Ph_3P (5) AgOTf (5), ethylene	ethylene (1 atm, 20 min), 25 °C, 2 d	90	79 (15:1)[b]
3	$[(allyl)PdCl]_2$ (1), Ph_3P (5) AgOTf (1), diallyl ether (1)	25 °C, 1.5 d	90	79 (8:1)[b]
4	$[(allyl)NiBr]_2$ (1), Ph_3P (2) NaBARF(1), diallyl ether (1)	25 °C, 2 d	82	
5	$[(allyl)PdCl]_2$ (5), $(o\text{-tol})_3P$ (10) AgOTf (10), CH_2Cl_2	25 °C, 2 d	>99	~10[c]
6[d]	$(Ir(COE)_2Cl]_2$, PCy_3, $NaBPh_4$, CH_2Cl_2/acetone (50:1)	25 °C, 3 h	<2	<2
7[e]	$[Cl_2RuL_3]$ Grubbs 2nd gen (10) MeOH	60 °C, 1 d	~7	~7

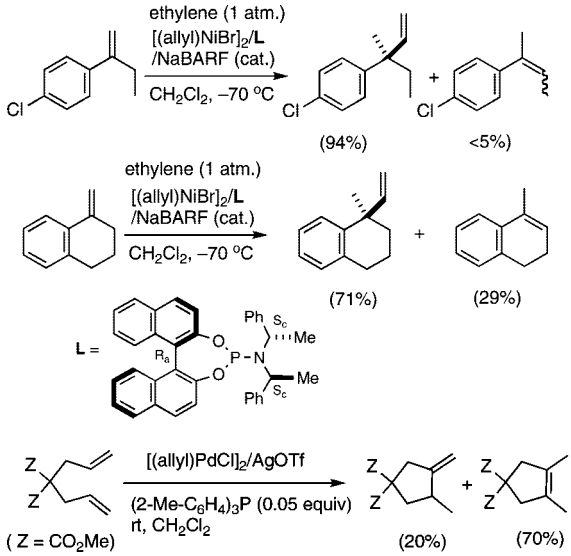
[a] See eqs 5 and 6 and Experimental Section for details. [b] 16 mol % cat., 35 °C. [c] 10 mol % cat. [d] Reference 6d, Scheme 1. [e] Reference 8a, eq 1.

isomerizations of terminal alkenes catalyzed by Pt,[7a] Rh,[7a] Pd,[7b] and Ni[7c] have been known since 1964. The role of a bulky ligand and the intermediacy of the metal hydride implied in the $[2\text{-Me-}C_6H_4\text{-}O)_3P]_3Ni/HCl$[7c] have been effectively used to design other protocols for this reaction.[7d,e] Iridium(I) catalysts originally developed by Felkin[6a] have been modified for the skeletal isomerization of functionalized terminal alkenes at room temperature.[6a–e] The most recent entry into this group of catalysts capable of effecting the skeletal isomerization of *C*-allylic appendages in highly functionalized substrates is the Grubbs generation II metathesis catalyst that has been "thermally modified" (eq 1).[8]



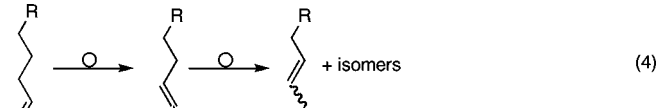
(1)

During our studies on asymmetric hydrovinylation of 2,2′-disubstituted alkenes we noticed that some substrates consistently gave varying proportions of a minor component readily identified as the allylic rearrangement product as illustrated in eqs 2a and 2b.[9] A similar rearrangement was also detected during cycloisomerization of dienes catalyzed by {$[(allyl)PdCl]_2$/AgOTf/$[(2\text{-Me-}C_6H_4)_3P]$} (eq 3).[10]

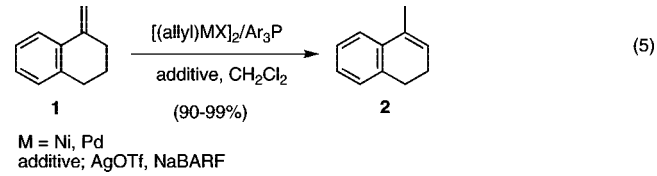


(2a)
(2b)
(3)

Since cationic metal hydrides have been implicated in these reactions, we wondered whether the hydrovinylation conditions could be modified to improve the yield of *selective isomerization* of a monosubstituted terminal alkene into a 2-alkene and of a 2,2′-disubstituted alkene into a trisubstituted alkene. We are especially interested in avoiding the complication from subsequent isomerization of the primary product, which often accompanies some of the isomerization reactions of terminal alkenes involving Ir[6b,e] and Ru.[8h] This isomerization is especially problematic when the homoallylic position of the carbon chain in the starting alkene is unsubstituted (eq 4). There are only limited reports of rearrangements of 2,2′-disubstituted alkenes to the corresponding internal trisubstituted isomer.[8h] When coupled with a Wittig, Grignard, or Keck radical allylation[8f] reaction, to produce the ethylidene derivative, this transformation could be quite useful. In acyclic systems, the configuration of the newly formed carbon−carbon double bond would also be of some interest.[11] The results of these studies are reported here.



(4)



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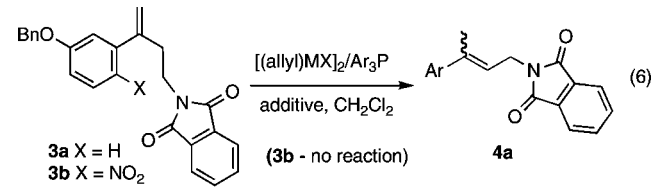


(6)

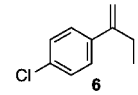
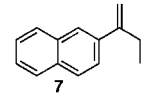
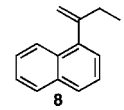
Results

Our initial studies concentrated on the little known[8h] isomerization of the 2,2′-disubstituted alkenes. Results of isomerization of the two prototypical substrates 1-methylenetetralin (**1**, eq 5) and 1-(2-phthalimidoethyl)styrene (**3**, eq 6) are shown in Table 1. When **1** was reacted under typical hydrovinylation conditions[12] using Ph_3P as a ligand,{$[(allyl)NiBr]_2$, Ph_3P, AgOTf, 25 °C, 2 d)} in an atmosphere of ethylene, no reaction ensued (entry 1, column 4). In accordance with our previous observation that Pd(II) salts show enhanced reactivity under these conditions,[12b] the use of $[(allyl)PdCl]_2$ instead of the corresponding Ni salt

leads to the expected product **2** in very good yield (entry 2, column 4).[13] Typically the reaction involving ethylene is carried out as follows: appropriate amounts of the metal salt, the phosphine, and AgOTf are mixed in CH_2Cl_2 in a drybox in a Schlenk tube, and the mixture is taken out of the box and placed in an atmosphere of ethylene for 20 min. The alkene is introduced, the ethylene atmosphere is replaced by nitrogen, and the mixture is stirred for 2 days at rt. Unlike the hydrovinylation reaction, there is no need to remove the precipitated salts (AgX) for the isomerization reactions. While the use of ethylene has a slight advantage in the recovery of products, we find that an operationally simpler procedure is to use catalytic amounts of diallyl ether (entry 3). Presumably diallyl ether, which undergoes facile cycloisomerization to 3-methylene-4-methyltetrahydrofuran, readily produces[10a,b] the requisite cationic metal hydride with minimum of contamination by other side products. Use of diallyl ether also helps the Ni-catalyzed reaction if a highly dissociated counteranion, $[(3,5\text{-}(CF_3)_2C_6H_3]_4B^-$, is used instead of OTf (entry 4, column 4).[14,12b] Thus with 1 mol % of $[(allyl)_2NiBr]_2$ and 2 mol % each of Ph_3P, $Na^+[(3,5\text{-}(CF_3)_2C_6H_3]_4B^-$ (BARF) and diallyl ether **1** gives very good yield of the isomerization product **2** (entry 4).

Isomerization of functionalized alkene **3a** (eq 6) is best carried out in the presence of ethylene or diallyl ether (entries 2 and 3, column 5), since other conditions gave virtually no reaction. The ratio of *E*:*Z* alkenes was found to depend on the additive, with ethylene giving the mixture in an *E*:*Z* ratio of 15:1 as determined by ^{1}H NMR. This reaction appears to be very sensitive to steric effects, since the *ortho*-substituted derivative **3b** gave no product.

TABLE 2. Isomerization of 2,2′-Disubstituted Alkenes[a]

entry	alkene	time (h)	product, yield (%) (*E*:*Z*)[b]
1.	 **5**	8	**9**, 94 (-)
2.	 **6**	16	**10**, 87 (19:1)
3.	 **7**	20	**11**, 97 (9:1)
4.	 **8**	12	**12**, 99 (2:1)
5.	 **9**	--	polymer

[a] $[(Allyl)PdCl]_2$ (5 mol %), (*o*-tol)$_3$P (10 mol %), AgOTf (10 mol %), CH_2Cl_2 (0.05 M). [b] Determined by ^{1}H NMR analysis.

Experimentally the use of commercially available $[(allyl)PdCl]_2$ has a clear advantage over $[(allyl)NiBr]_2$, which is a thermally sensitive solid that has to be kept at low temperature in a drybox.[15] In subsequent experiments we discovered that for simple substrates such as **1** when the Pd-catalyzed reaction is carried out in the presence of (*o*-tolyl)$_3$phosphine, there is no need to have the ethylene or diallyl ether present for a quantitative conversion to the product (entry 5, column 4).

Entries 6[6d] and 7[8a] list the use of two of the best catalysts capable of allylic isomerizations. Neither the Ir(I) nor the modified Grubbs generation II catalyst under the prescribed reaction conditions is useful for this transformation.

Further scope of the reaction is shown in Table 2, which lists other alkenes that undergo the isomerization under these conditions. The 1-indanone-derived alkene **5** gave an excellent yield of the internal alkene at room temperature (entry 1). Methylene compounds prepared via Wittig reaction of aryl alkyl ketones are excellent substrates for this reaction. 2-Arylbutenes **6**−**8** gave excellent yields of the product, an internal alkene. While the 2-naphthyl derivative **7** gave good *E*-selectivity, the 1-naphthyl analog **8** gave only a 2:1 mixture of (*E*)- and (*Z*)-alkenes. Attempted isomerization of the furyl derivative **9** led to polymerization.

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(13) See Supporting Information for ^{1}H and ^{13}C NMR spectra of key starting materials and products, and gas chromatograms of products from various reactions.

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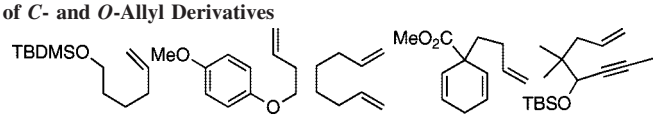
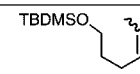
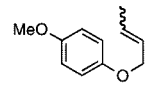
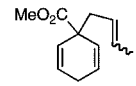
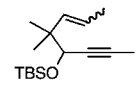
TABLE 3. Selective Isomerization of *C*- and *O*-Allyl Derivatives



13 14 15 16 17

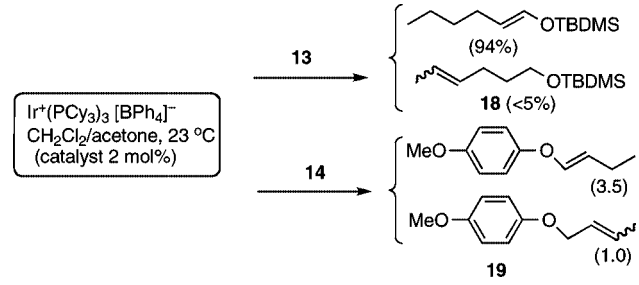
entry	substrate	catalyst (mol%), additives (mol%)	conditions	product(s)	yield (%) (*E*/*Z*)[a]
1.	**13**	[(allyl)NiBr]$_2$ (0.7), (C_6H_5)$_3$P (1.4), AgOTf (1.4), ethylene	-55 °C, 4 h	 **18**	>95 (3.5:1.0)
2.	**13**	[(allyl)PdCl]$_2$ (0.5), (*o*-Me C_6H_4)$_3$P (1.0), AgOTf (1.0), CD_2Cl_2,	rt, 24 h	**18**	80 (3.7:1.0)[b]
3.	**14**	[(allyl)PdCl]$_2$ (2.5), (*o*-Me C_6H_4)$_3$P (5.0), AgOTf (5.0), CD_2Cl_2,	rt, 24 h	 **19**	96 (5.9:1.0)[c]
4.	**15**	[(allyl)PdCl]$_2$ (2.5), (C_6H_5)$_3$P (5), AgOTf (5)	23 °C, 2 h	 **20**	90 (--)[d]
5.	**16**	[(allyl)PdCl]$_2$ (5) (*o*-Me-C_6H_4)$_3$P (10), AgOTf (10)	23 °C, 1 d	 **21**	90 (3.6:1.0)
6.	**17**	[(allyl)PdCl]$_2$ (5), (*o*-Me-C_6H_4)$_3$P (10), AgOTf (10)	23 °C, 1 d	 **22**	92 (8:1)

[a] Determined by NMR or GC. [b] 9% unidentified material and 10% starting material. [c] Rest starting material. [d] Mixture of *E*/*Z*, configuration not determined.

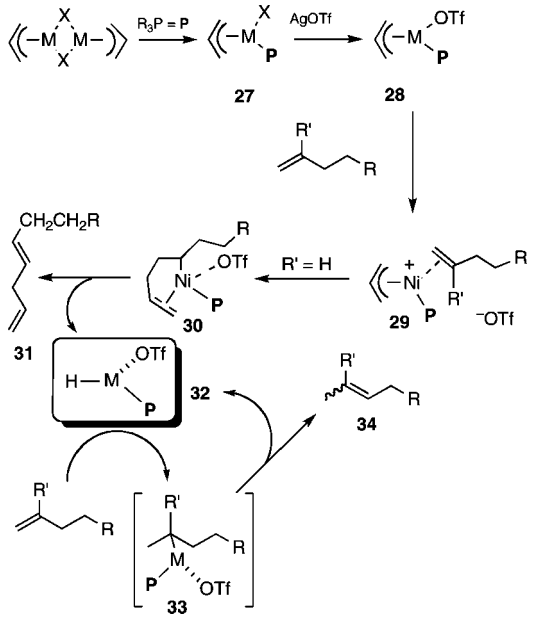
Monosubstituted terminal alkenes also undergo the isomerization with remarkable ease under the typical conditions outlined in the previous paragraph, giving exclusively the 2-alkene. Several nontrivial examples of this transformation are shown in Table 3. 6-(*tert*-Butyldimethylsiloxy)hex-1-ene **13** undergoes exceptionally clean isomerization to the corresponding (*Z*)- and (*E*)-2-hexenes (**18**) under typical hydrovinylation conditions at −55 °C (entry 1).[13] The expected internal olefin **18** is formed in >95% yield in an *E*:*Z* ratio of 3.5:1.0 as judged by ^{1}H NMR spectroscopy and gas chromatography. No trace of any other alkenes is observed under these conditions. The reaction catalyzed by Pd(II) (entry 2) gives 80% yield of (*E*)- and (*Z*)-**18** in the same ratio. This reaction is less clean compared to the Ni-catalyzed reaction, the product being contaminated with up to 10% starting material, and 9% of another isomeric alkene.[13] Isomerization of **13** using the metathesis catalyst (eq 1, 10 mol % [Ru], MeOH, 60 °C, 12 h) yields <45% of the *E*/*Z* mixture (3.8:1.0) of **18** contaminated with other isomers. The Ir(I) catalyst [(Ir(COE)Cl]$_2$, PCy_3, $NaBPh_4$, CH_2Cl_2/acetone (50:1)][4b] gave 94% yield of (*E*)-1-*tert*-butyldimethylsiloxyhexene (Scheme 2).

The proportion of starting material in the equilibrium mixture of alkenes depends on the starting alkene, as indicated by the isomerization in 1-(but-3-enyloxy)-4-methoxybenzene (**14**) to the disubstituted alkene **19**. The *E*- and *Z*-isomers are obtained in >95% yield in a ratio of 5.9:1.0 with <4% of the starting material (entry 3). The Ir(I) catalyst gives a mixture of products arising from both 1,3- and 1,6-hydrogen shifts with the latter predominating (Scheme 2).[13] The modified Grubbs catalyst gave a mixture of 14% starting material, 47% (*E*)-**19**, and 12% (*Z*)-**19** along with a mixture of isomers.[13] While 1,6-dienes readily undergo cycloisomerization followed by isomerization of the exocyclic alkylidene under Pd catalysis (eq 3),[10a] a substrate more resistant to cyclization, such as 1,7-octadiene (**15**), simply undergoes isomerization of the terminal alkenes to give a stereoisomeric mixture of 2,6-octadienes (**20**) (entry 4). Surpris-

SCHEME 2. Isomerization of a Terminal Alkene using an Ir(I) Catalyst[4b,6d]

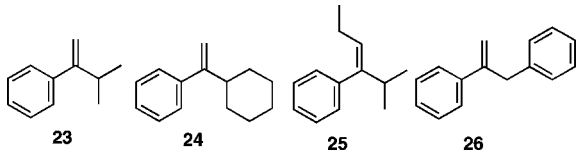


SCHEME 3. Possible Mechanism for the Alkene Isomerization



ingly, the triene **16**, prone to isomerization of the endocyclic 1,4-diene, cleanly gives 90% yield of a mixture of (*E*)- and (*Z*)-3-butenyl derivatives (**21**) arising from selective isomerization of the side chain (entry 5). Likewise, the enyne **17** undergoes just the isomerization to **22** without the expected[16] cyclization of the enyne to a bisalkylidene.

Finally, several sterically demanding substrates, **23**−**26**, failed to undergo isomerization even under more forcing conditions.



Discussion

Mechanistically the alkene isomerization is related to the olefin dimerization reaction, since both start with a common reactive intermediate in the form of an active metal hydride. Such a hydride (**32**, Scheme 3) could be generated by initial formation of the [(allyl)metal(phopshine)]$^{+}$OTf^{-} (**28**)[14] from the metal halide followed by an insertion (**29** → **30**) and β-hydride elimination. The 1,4-diene **31** is formed as a byproduct.[10b,17] Once the hydride is generated, it adds to the terminal alkene to form the organometallic **33**, which undergoes yet another β-hydride elimination to give the alkene isomers (**34**) in a thermodynamically controlled reaction. Note that almost invariably the (*E*)-alkenes predominate in the isomerization reactions. The reluctance of the 1,1-disubstituted alkene to undergo the reaction in the absence of a sterically unencumbered alkene, ethylene, is thus easily understood. A 1,1-disubstututed alkene (R′ = alkyl) could be slow to undergo the allylic insertion reaction (**29** → **30**), and ethylene is needed to generate the reactive metal hydride. The reluctance of the metal hydride to add to a 1,2-disubstituted alkene (**34**, R′ = H) might also explain why the exhaustive isomerizations seen with other catalysts (Scheme 2), most notably Ir(I), are not seen in these reactions.

Conclusions

The cationic metal hydride mediated selective skeletal isomerization of terminal alkenes provides a facile route to di- and trisubstituted alkenes. The reaction is sensitive to steric effects yet tolerant to a variety of common functional groups and, in some cases, may provide synthetically useful levels of *E*:*Z* selectivity in the formation of the trisubstituted alkenes.

Experimental Section

General Information. See Supporting Information.

Attempted Isomerization of 1-Methylene-2,3,4-trihydronaphthalene 1 under Hydrovinylation Conditions. General procedure A (Table 1, entry 1, column 4). In a flame-dried flask, [(allyl)NiBr]$_2$ or [(allyl)PdCl]$_2$, the phosphine ligand, and the silver salt were mixed in that order in CH_2Cl_2 in a drybox. After the precipitated silver salt was removed by filtration though Celite, the solution was taken out of the drybox and was connected to an ethylene line. The system was evacuated and refilled with ethylene three times. To the resulting complex was added **1** in CH_2Cl_2 dropwise at room temperature. After stirring for the prescribed time (Table 1), all volatile materials were removed, and the product was purified by column chromatography. Gas chromatography and NMR showed complete recovery of starting materials. We have since found that for most isomerization reactions described below it is not necessary to remove the precipitated silver salt.

Use of [(Allyl)PdCl]$_2$/Phosphine/AgOTf Activated by Ethylene for the Double Bond Migration. General procedure B (Table 1, entry 2, columns 4 and 5). In a flame-dried three-neck flask, [(allyl)PdCl]$_2$, PPh_3, and AgOTf were dissolved in CH_2Cl_2 in a glovebox. After the reaction vessel was taken out of the box, an ethylene line was connected to the vessel, the line was evacuated, and then ethylene was introduced. The process was repeated three times. The resulting monomeric allylic Pd complex was stirred for 20 min under 1 atm of ethylene at rt, and then the exomethylene substrate **1** or **3a** was added dropwise as a solution in CH_2Cl_2. The ethylene was exchanged with a N_2 atmosphere, and the resulting mixture was stirred at ambient temperature for the prescribed time. All volatile materials were evaporated, and then the mixture was filtered using a short pad of silica gel using EtOAc/hexane solvent. The product was analyzed by GC and NMR.

Use of [(Allyl)PdCl]$_2$/Phosphine/AgOTf Activated by Diallyl Ether for the Double Bond Migration. General procedure C (Table 1, entry 3, columns 4 and 5). To a premixed allyl-Pd complex in CH_2Cl_2 that was prepared in the same fashion as in the previous experiment (general procedure B), an equivalent amount of diallylether was added instead of ethylene, and then the mixture was stirred at rt for 20 min. The substrate dissolved in CH_2Cl_2 was added dropwise to the catalyst solution, and the resulting mixture was stirred at ambient temperature for the indicated time. The product was purified and analyzed as indicated previously.

Use of [(Allyl)PdCl]$_2$/Phosphine/AgOTf without any Additive for the Double Bond Migration. General procedure D (Table 1, entry 5, columns 4 and 5). To an (allyl)Pd(phosphine) complex in CH_2Cl_2 that was prepared in the same fashion as in the general procedure B, the substrate dissolved in CH_2Cl_2 was added dropwise, and the resulting mixture was stirred at ambient temperature for

(16) (a) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1985**, *107*, 1781. (b) Trost, B. M. *Acc. Chem. Res.* **1990**, *23*, 34.

(17) For isolation of such an insertion product in styrene dimerization, see: (a) DiRenzo, G. M. Mechanistic Studies of Catalytic Olefin Dimerization Reactions Using Electrophilic η3-allyl-Palladium(II) Complexes. Ph. D. Thesis, University of North Carolina, 1997.

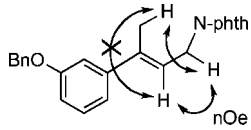
(18) (a) Kobayashi, H.; Sonoda, A.; Iwamoto, H.; Yoshimura, M. *Chem. Lett.* **1981**, *10*, 579. (b) Brookhart, M.; Grant, B.; Volpe, A. F., Jr. *Organometallics* **1992**, *11*, 3920–3922.

(19) Exon, C.; Magnus, P. *J. Am. Chem. Soc.* **1983**, *105*, 2477.

the indicated time. The product was purified and analyzed as indicated previously.

Isomerization of 1 Using [(Allyl)NiBr]$_2$/Ph$_3$P/NaBARF and Diallylether. (Table 1, entry 4, column 4). The precatalyst was prepared as follows in a glovebox. To [(allyl)NiBr]$_2$ (10.8 mg, 0.03 mmol) in CH_2Cl_2 (1 mL) were added PPh_3 (15.7 mg, 0.06 mmol) and NaBARF (53.0 mg, 0.06 mmol). The catalyst solution prepared above was removed from the drybox, and diallylether (3.7 μL, 0.03 mmol) was added as a single portion under nitrogen, and the mixture was allowed to stir for 2 min to form the active catalytic species. A solution of the substrate **1** (433 mg, 3.00 mmol) in 3 mL of CH_2Cl_2 was added dropwise over a period of 1 min, and the reaction was allowed to proceed for 2 d. The resulting product was filtered by flash column chromatography (eluted with pentane) to get the desired product **2** (0.35 g, 82%) as a colorless oil, which was then used to acquire all analytical data without further purification. ^{1}H NMR ($CDCl_3$): δ 7.23−7.17 (m, 2 H), 7.15−7.10 (m, 2 H), 5.85−5.83 (m, 1 H), 2.75 (t, J = 8.0 Hz, 2 H), 2.26−2.20 (m, 2 H), 2.04 (dd, J = 3.2 Hz, J = 1.6 Hz, 2 H). ^{13}C NMR ($CDCl_3$): δ 136.3, 135.9, 132.3, 127.3, 126.7, 126.3, 125.4, 122.8, 28.3, 23.2, 19.3.

Isomerization of 2-(3-(3-(Benzyloxy)phenyl)but-3-enyl)isoindoline-1,3-dione (3a) (Table 1, entry 2, column 5). General procedure B. In a flame-dried three-neck flask, [(allyl)PdCl]$_2$ (2.4 mg, 0.0061 mmol), PPh_3 (3.7 mg, 0.013 mmol), and AgOTf (3.4 mg, 0.013 mmol) were dissolved in distilled CH_2Cl_2 (3 mL) in a glovebox. After the reaction vessel was taken out from a box, an ethylene line was connected to the vessel, the line was evacuated, and then ethylene was introduced. This process was repeated three times. The resulting Pd complex was stirred for 20 min under 1 atm of ethylene at rt, and then the exomethylene substrate **3a** (29 mg, 0.076 mmol) in CH_2Cl_2 (1 mL) was added dropwise. Ethylene atmosphere was exchanged for a N_2 atmosphere, and the resulting mixture was stirred at 35 °C for 2 d. All volatile materials were evaporated, and then the mixture was purified by flash column chromatography to obtain 28 mg (79%) of the product **4a** (E:Z = 15:1) contaminated with 21% of starting olefin **3a**. ^{1}H NMR ($CDCl_3$): δ 7.90−7.69 (m, 4 H, phthalimidyl), 7.49−7.29 (m, 5 H, Ar), 7,19 (t, J = 6.4 Hz, 1 H, Ar), 7.05−6.85 (m, 2 H, Ar), 6.84−6.79 (m, 1 H, Ar), 5.85 (t, J = 7.0 Hz, 1 H, Ar(CH$_3$)C=C*H*CH$_2$N-phth), 5.03 (s, 2 H, OC*H*$_2$Ph), 4.50 (d, 7.5 Hz, 2 H, Ar(CH$_3$)C=CHC*H*$_2$N-phth, E), 4.22 (d, J = 6.5 Hz, 2 H, Ar(CH$_3$)C=CHC*H*$_2$N-phth, Z), 2.23 (s, 3 H, Ar(C*H*$_3$)C=CHCH$_2$NPhth, E), 2.01 (s, 3 H, Ar(C*H*$_3$)C=CHCH$_2$N-phth, Z). ^{13}C NMR ($CDCl_3$): δ 168.4, 144.5, 139.4, 137.3, 134.1, 132.5, 129.6, 128.1, 127.8, 123.4, 121.6, 119.1, 113.7, 113.1, 70.2, 36.5, 16.4. HRMS 406.1400 (M + Na$^{+\bullet}$; calcd for $C_{25}H_{21}NNaO_3$ 406.1419). The configuration of the major product was established by NOE studies.



Isomerization of 1-Methylene-1,2,3,-trihydronaphthalene (1) (Table 1, entry 2, column 4). General procedure D. Following the general procedure D using 10 mol % of preformed Pd catalyst, the isomerization of **1** (0.145 g, 1.0 mmol) was checked. After the crude product was purified by column chromatography, the product (**2**, 0.145 g, >99%) was analyzed by NMR.

Isomerization of 1-Methylene-2,3-dihydro-1*H*-indene (5) (Table 2, entry 1). General procedure D. The isomerization reaction of **5** (0.131 g, 1.0 mmol) was carried out using [(allyl)PdCl]$_2$ (5 mol %), (o-tol)$_3$P (10 mol %), and AgOTf (10 mol %) in CH_2Cl_2 with no other additive at rt for 8 h. After the solvent was evaporated, the crude product was purified by column chromatography to yield the desired product **9** (94%, isolated yield). ^{1}H NMR ($CDCl_3$): δ 7.47 (d, 1H, J = 7.2 Hz, Ar), 7.39−7.31 (m, 2H, Ar), 7.27−7.23 (m, 1H, Ar), 6.22 (s, 1H, vinyl), 3.33 (s, 2H, allylic CH$_2$), 2.19 (s, 3H, allylic CH$_3$). ^{13}C NMR ($CDCl_3$): δ 146.1, 144.3, 139.9, 128.7, 126.0, 124.4, 123.6, 118.8, 37.6, 13.0.

Isomerization of 1-(But-1-en-2-yl)-4-chlorobenzene (6) (Table 2, entry 2). General procedure D. The isomerization reaction of **6** (0.167 g, 1.0 mmol) was carried out using [(allyl)PdCl]$_2$ (5 mol %), (o-tol)$_3$P (10 mol %), and AgOTf (10 mol %) in CH_2Cl_2 with no other additive at rt for 16 h. After the solvent was evaporated, the crude product was purified by column chromatography to yield the desired product **10** (87%, E:Z = 19:1). ^{1}H NMR ($CDCl_3$): δ 7.33−7.27 (m, 4H, Ar), 5.86 (q, 1H, J = 6.50 Hz, vinyl), 2.02 (s, 3H, allylic CH$_3$), 1.80 (d, 3H, J = 6.50 Hz, allylic CH$_3$; E), 1.59 (d, 3H, J = 6.50 Hz, allylic CH$_3$; Z). ^{13}C NMR ($CDCl_3$): δ 142.4, 134.5, 132.1, 128.2, 126.8, 123.0, 15.4, 14.3.

Isomerization of 2-(But-1-en-2-yl)naphthalene (7) (Table 2, entry 3). General procedure D. The isomerization reaction of **7** (0.182 g, 1.0 mmol) was carried out using [(allyl)PdCl]$_2$ (5 mol %), (o-tol)$_3$P (10 mol %), and AgOTf (10 mol %) in CH_2Cl_2 with no other additive at rt for 16 h. After the solvent was evaporated, the crude product was purified by column chromatography to yield the desired product **11** (97%, E:Z = 9:1). ^{1}H NMR ($CDCl_3$): δ 7.83−7.81 (m, 2H, Ar), 7.79−7.76 (m, 2H, Ar), 7.58 (dd, 1H, J = 9.0, 2.0 Hz, Ar), 7.47−7.42 (m, 2H, Ar), 6.05 (q, 1H, J = 7.0 Hz, vinyl; E), 2.15 (s, 3H, allylic CH$_3$; E), 2.13 (s, 3H, allylic CH$_3$; Z), 1.87 (d, 3H, J = 7.0 Hz, allylic CH$_3$; E), 1.67 (d, 3H, J = 7.0 Hz, allylic CH$_3$; Z). ^{13}C NMR ($CDCl_3$): δ 141.2, 135.4, 133.5, 132.3, 128.0, 127.5, 127.4, 126.0, 125.3, 124.3, 123.8, 123.1, 15.5, 14.5.

Isomerization of 1-(But-1-en-2-yl)naphthalene (8) (Table 2, entry 4). General procedure D. The isomerization reaction of **8** (0.182 g, 1.0 mmol) was carried out using [(allyl)PdCl]$_2$ (5 mol %), (o-tol)$_3$P (10 mol %) and AgOTf (10 mol %) in CH_2Cl_2 at rt for 16 h. After the solvent was evaporated, the crude product was purified by column chromatography to yield the desired product **12** (99%, E:Z = 2:1). ^{1}H NMR ($CDCl_3$): δ 8.03 (dd, 1H, J = 6.0, 2.5 Hz, Ar), 7.90 (dd, 1H, J = 8.0, 3.5 Hz, Ar), 7.79 (d, 1H, J = 8.0 Hz, Ar), 7.54−7.50 (m, 3H, Ar), 7.32 (d, 1H, J = 6.5 Hz, Ar), 5.87 (q, 1H, J = 7.0 Hz, vinyl; Z), 5.66 (q, 1H, J = 6.50 Hz, 1H; E), 2.16 (s, 3H), 1.94 (d, J = 6.50 Hz, 3H), 1.42 (d, J = 6.50 Hz; Z). ^{13}C NMR ($CDCl_3$): δ (E) 144.3, 135.7, 133.8, 131.4, 128.3, 126.7, 126.0, 125.6, 125.5, 125.4, 124.9, 18.7, 14.0; (Z) 140.5, 135.8, 133.7, 130.8, 128.3, 125.8, 125.6, 125.2, 124.9, 123.3, 26.1, 14.8.

Isomerization of 1,7-Octadiene (Table 3, entry 4). General procedure D. In a nitrogen filled drybox, a dry flask was charged with [(allyl)PdCl]$_2$ (0.016 g, 0.045 mmol) in 1 mL of CH_2Cl_2. To this solution was added 2 equiv of phosphine ligand (1 equiv with respect to metal, 0.024 g, 0.09 mmol) followed by AgOTf (0.023 g, 0.09 mmol). The precipitate was filtered off using a Celite-plugged pipet. After 30 min the reaction vessel was taken out from a box. To the resulting metal catalyst was added 1,7-octadiene (0.200 g, 1.81 mmol) in CH_2Cl_2 dropwise at ambient temperature. After the resulting mixture was stirred at ambient temperature for 2 h, most of the volatile materials were evaporated, and the crude product was analyzed by NMR and GC. Total absence of the starting olefinic peaks in the ^{1}H NMR due to the starting methylene compound (δ 5.70−5.90 m; 4.90−5.05 m), and appearance of new olefinic H at δ 5.25−5.40 (4 H) and vinyl-C*H*$_3$ signals at 1.50−1.51 (6 H) indicate isomerization of the double bonds without cyclization. Since the product is volatile the conversion was estimated to be >95% by both NMR and GC. No further analysis was carried out.

Synthesis of 6-*tert*-Butyldimethylsiloxy)hex-1-ene (13). To a solution of 0.581 g (5.81 mmol) of 5-hexene-1-ol in 5 mL of DMF at 0 °C under nitrogen was added 1.19 g (17.4 mmol) of imidazole and 1.31 g (8.72 mmol) of *tert*-butyldimethylsilyl chloride. The mixture was stirred at rt for 2 days and subsequently quenched with 10 mL of water. The aqueous layer was extracted with ether (3 × 10 mL). The combined organic layers were washed with 2 N aqueous NaOH solution and then brine and dried over $MgSO_4$ before concentration in vacuo. The residue was purified by flash

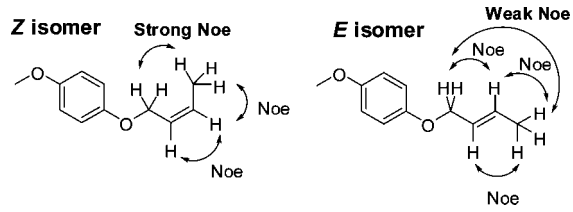
chromatography on silica gel, eluting with hexane/ethyl acetate (98:2), to afford the silyl ether (**13**) as a clear oil (1.19 g, 96%). ^{1}H NMR ($CDCl_3$): δ 5.73−5.90 (m, 1 H), 4.91−5.06 (m, 2 H), 3.62 (t, J = 6.4 Hz, 2 H), 2.03−2.12 (m, 2 H), 1.38−1.60 (m, 4 H), 0.90 (s, 9 H), 0.05 (s, 6 H).

Isomerization of 6-*tert*-Butyldimethylsiloxy)hex-1-ene. General procedure A (Table 3, entry 1). To a solution of [(allyl)NiBr]$_2$ (5.2 mg, 0.14 mmol) in 1 mL of CH_2Cl_2 under nitrogen at room temperature was added a solution of Ph_3P (7.6 mg, 0.28 mmol) in 1 mL of CH_2Cl_2. The resulting brown solution was added to a mixture of AgOTf (10.3 mg, 0.40 mmol) in 1 mL of CH_2Cl_2. After stirring for 1.5 h at rt, the mixture was filtered through a small plug of Celite, and the precipitate was rinsed with 2 mL of CH_2Cl_2. The filtrate was collected in a Schlenk flask and was taken out of the drybox. The catalyst solution was cooled to −55 °C. Under an atmosphere of ethylene, 0.428 g (2.00 mmol) of alkene **13** was added dropwise to the catalyst solution. After stirring at −55 °C for 4 h, the mixture was quenched with saturated NH_4Cl solution and extracted CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was analyzed by GC, which indicated that the alkene had completely isomerized to two new products in a ratio of 3.5:1.0. The volatile crude product (>95% estimated by GC) was purified by chromatography on silica, eluting with ethyl acetate/hexane (98:2), to afford the product(s) **18**, which was analyzed by GC and NMR. ^{1}H NMR ($CDCl_3$): δ 5.40−5.46 (m, 2 H), 3.57−3.65 (m, 2 H), 1.97−2.10 (m, 2 H), 1.54−1.67 (m, 5 H), 0.90 (s, 9 H), 0.05 (s, 6 H).

Palladium-Catalyzed Isomerization of 6-*tert*-Butyldimethylsiloxy)hex-1-ene. General procedure D (Table 3, entry 2). The isomerization reaction was carried out using [(allyl)PdCl]$_2$ (0.50 mmol), (*o*-tol)$_3$P (1 mol %), and AgOTf (1 mol %) in CD_2Cl_2. The reaction was followed by ^{1}H NMR spectroscopy, which indicated maximum conversion to the products at 24 h. The products (*E*)- and (*Z*)-**18** (80%, 3.7:1.0) were identified by comparison of gas chromatogram and spectral properties of the sample from the previous run. In addition to 10% starting material, ∼9% of an unidentified product was also detected by gas chromatography (see Supporting Information).

Synthesis of 1-(But-3-enyloxy)-4-methoxybenzene (14). To a stirred solution of 4-methoxyphenol (1 g, 8.06 mmol), 3-buten-1-ol (0.99 g, 10.48 mmol), and triphenylphosphine (2.75 g, 10.48 mmol) in anhydrous THF (20 mL) was added diisopropylazodicarboxylate (2.12 g, 10.48 mmol) slowly at 0 °C. After the reaction was stirred overnight at rt, the mixture was diluted with EtOAc (20 mL) and water (20 mL) and separated. The crude compound was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried over Na_2SO_4. The resulting product was purified by chromatography to afford 1.5 g (93%) of **14**. ^{1}H NMR ($CDCl_3$): δ 6.87−6.81 (m, 4 H, Ar), 5.94−5.86 (m, 1H, $ROCH_2CH_2CH$=CH_2), 5.18−5.09 (q, 2H, $ROCH_2CH_2CH$=CH_2), 3.97−3.95 (t, J = 7.0 Hz, 2 H, $ROCH_2CH_2CH$=CH_2), 2.53−2.49 (m, 2 H, $ROCH_2CH_2CH$=CCH_2), 3.75 (s, 3 H, $ArOCH_3$), 1.75−1.70 (d, J = 5.0 Hz, 3 H, $ROCH_2CH$=$CHCH_3$). ^{13}C NMR ($CDCl_3$): δ 154.0, 153.2, 134.8, 117.1, 115.8, 114.8, 68.1, 55.9, 33.9.

Isomerization of 1-(But-3-enyloxy)-4-methoxybenzene (14). General procedure D (Table 3, entry 3). 1-(But-3-enyloxy)-4-methoxybenzene (30 mg, 0.168 mmol) was reacted with [(allyl)PdCl]$_2$ (1.6 mg, 0.0042 mmol), (*o*-tol)$_3$P (2.6 mg, 0.0084 mmol), AgOTf (2.2 mg, 0.0084 mmol), and CH_2Cl_2 at rt for 1 d. The resulting product was purified by chromatography to afford 30 mg (>99%) of **19** as a mixture of *E*- and *Z*-isomers with the starting material. Based on ^{1}H NMR and GC, the conversion and *E*/*Z* ratio were estimated as 96% and 5.9:1.0 respectively. ^{1}H NMR ($CDCl_3$): δ 6.86−6.80 (m, 4 H, Ar), 5.84−5.80 (m, 1H, $ROCH_2CH$=$CHCH_3$, *E* and Z), 5.74−5.68 (m, 1 H, $ROCH_2CH$=$CHCH_3$, *E* and *Z*), 4.54−4.53 (d, J = 5.5 Hz, 2 H, $ROCH_2CH$=$CHCH_3$, Z), 4.53−4.39 (m, 2 H, $ROCH_2CH$=$CHCH_3$, E), 3.75 (s, 3 H, $ArOCH_3$), 1.75−1.70 (d, J = 5.0 Hz, 3 H, $ROCH_2CH$=$CHCH_3$). ^{13}C NMR δ ($CDCl_3$, *E* only): 154.2, 153.3, 130.3, 126.8, 116.0, 69.7, 56.0, 17.9, 13.5. The configuration of the major product was established by NOE studies.



Isomerization of Methyl 1-(2-Butenyl)-2,5-cyclohexadiene-1-carboxylate (16). General procedure D (Table 3, entry 5). Substrate **16** (0.1 g, 0.5 mmol) was reacted with 5 mol % [(allyl)PdCl]$_2$ (10.4 mg, 0.026 mmol), 5 mol % of (*o*-CH_3−C_6H_4)$_3$P (16 mg, 0.05 mmol), AgOTf (13 mg, 0.05 mmol), and CH_2Cl_2 at rt for 1 d. The resulting product was purified by chromatography to yield 91 mg (91%) of **21** as a mixture *E*/*Z* isomers. Based on the ^{1}H NMR, the *E*/*Z* ratio was estimated as 3.6:1.0. ^{1}H NMR ($CDCl_3$): δ 5.88−5.73 (m, 4 H, −C*H*=C*H*− in the ring), 5.41−5.22 (m, 2 H, CH_2 −C*H*=C*H*−CH_2−, *E* and *Z*), 3.69 (s, 3 H, OCH_3, *Z*), 3.67 (s, 3 H, OCH_3, *E*), 2.63 (m, 2 H, R=CH−CH_2−CH=R, *E* and *Z*), 2.43 (d, J = 5.2 Hz, 2 H, C−CH_2−CH=CHCH $_3$), 2.34 (d, J = 6.1 Hz, 2 H, C−CH_2−CH=$CHCH_3$), [δ 2.43 + δ 2.34] 2 H, 1.51−1.61 two sets of doublets (d, J = 6.7 Hz, 3 H, C=C−C H_3). ^{13}C NMR ($CDCl_3$): δ 174.7, 128.6, 127.0, 126.7, 125.4, 125.3, 51.9, 47.9, 43.4, 37.2, 26.0, 17.9; HRMS 192.1132 ($M^{+\bullet}$; calcd for $C_{12}H_{16}O_2$ 192.1150).

Isomerization of (*tert*-Butyl[[2,2-dimethyl-1-(1-propynyl)-3-pentenyl]oxy] Dimethylsilane (17). General procedure D (Table 3, entry 6). Substrate **17**[16] (0.1 g, 0.8 mmol) was reacted with 5 mol % of [(allyl)PdCl]$_2$, 10 mol % of (2-Me-C_6H_4)$_3$P, and 10 mol % AgOTf in CH_2Cl_2 at rt for 16 h. The reaction mixture was quenched with saturated ammonium chloride, and the product was extracted with ether. The dried organic layer was concentrated, and the product was purified by flash column chromatography to obtain 95 mg (95%) of **22** as a thick oil. Based on the ^{1}H NMR, the *E*/*Z* ratio was estimated as 8.0:1.0. ^{1}H NMR ($CDCl_3$): δ 5.57−5.30 (m, 2H), 4.00 (m), 3.91 (q, J = 2.3 Hz) [together 1 H, R_3Si−O−C*H*], 1.79 (d, J = 2.3 Hz, 3H, R−C≡C−CH_3), 1.66 (d, J = 5.6 Hz, 3 H, CH=C−CH_3), 1.00 (2s, separated by ∼2 Hz, 6 H, R(CH_3)$_2$), 0.10 (2s, 9H, *t*Bu in OTBS), 0.11 (s, 3H, Me in OTBS), 0.05 (s, 3H, Me in OTBS). ^{13}C NMR ($CDCl_3$): δ 137.8, 120.1, 79.8, 79.3, 70.5, 40.9, 25.5, 25.4, 22.5, 22.1, 18.0, 2.9, −4.5; HRMS 266.2057 ($M^{+\bullet}$; calcd for $C_{16}H_{30}O_4Si$ 266.2066).

Isomerization of 6-*tert*-Butyldimethylsiloxy)hex-1-ene (13) Using Grubbs Second-Generation Catalyst. [8a] Using the same procedure and catalyst (10 mol %) aforementioned, the isomerization of TBS-protected olefin **13** (11.2 mg, 0.052 mmol) was checked. The crude product was analyzed by GC. See Supporting Information for chromatograms.

Isomerization of 1-(But-3-enyloxy)-4-methoxybenzene (14) Using Grubbs Second-Generation Catalyst Shown in eq 1.[8a] The starting olefin **14** (9.3 mg, 0.052 mmol) in anhydrous MeOH (0.8 mL) was treated with Grubbs second-generation catalyst (4.4 mg, 10 mol %). The resulting solution was stirred at 60 °C for 12 h. After the solvent was evaporated in vacuo, the residue was filtered on a silica pad, eluting with ether. The crude product was directly analyzed by GC. See Supporting Information for chromatograms.

Isomerization of 1-Methylene-2,3,4-trihydronaphthalene (1) Using Grubbs Second-Generation Catalyst. Using the same procedure and catalyst (10 mol %) aforementioned, the isomerization of olefin **1** (15.0 mg, 0.104 mmol) was checked. The crude product was purified by short column chromatography and analyzed by ^{1}H NMR.

Isomerization of 2-(3-(3-(Benzyloxy)phenyl)but-3-enyl)isoindoline-1,3-dione (3a) Using Grubbs Second-Generation Catalyst. Using the same procedure and catalyst (10 mol %) aforementioned, the isomerization of olefin **3a** (10.0 mg, 0.0261 mmol) was checked.

The crude product was purified by short column chromatography and analyzed by ^{1}H NMR.

Isomerization of 6-*tert*-Butyldimethylsiloxy)hex-1-ene (13) Using Ir(COE)$_2$Cl]$_2$/PCy$_3$/NaBPh$_4$ in CH$_2$Cl$_2$/Acetone (Scheme 2).[4b,6d] Using the same procedure and catalyst (2 mol %) aforementioned, the isomerization of TBS-protected olefin **13** (25.5 mg, 0.119 mmol) was checked. After the resulting mixture was stirred at rt for 3 h, most of the volatile materials were evaporated, and the crude product was purified by column chromatography to get the isomerized silylenolether *tert*-butyl(hex-1-enyloxy)dimethylsilane (24.0 mg, 94%). The product was analyzed by ^{1}H NMR and GC. ^{1}H NMR ($CDCl_3$): δ 6.21−6.18 (dt, 1H, J = 12.0, 1.5 Hz, *n*BuCH=C*H*OTBS), 4.97−4.95 (q, 1H, 3.8 Hz, *n*BuC*H*=CHOTBS), 1.89−1.82 (m, 2H, *n*Bu), 1.30−1.26 (m, 4H, *n*Bu), 0.90−0.84 (m, 12 H, *t*BuSi and *n*Bu), 0.10 (s, 6H, $SiMe_2$).

Isomerization of 1-(But-3-enyloxy)-4-methoxybenzene (14) Using [Ir(COE)Cl]$_2$/PCy$_3$/NaBPh$_4$ in CH$_2$Cl$_2$/Acetone.[4b,6d] In a nitrogen-filled drybox, a dry flask was charged with $[Ir(COE)_2Cl]_2$ (1.1 mg, 0.0012 mmol), PCy_3 (1.9 mg, 0.0068 mmol), and $NaBPh_4$ (0.8 mg, 0.0029 mmol), and the mixture was dissolved in CH_2Cl_2/acetone (0.52 mL, 25/1). After 5 min of stirring, the starting olefin **14** (21.2 mg, 0.119 mmol) in CH_2Cl_2 (0.5 mL) was added dropwise at rt. After the resulting mixture was stirred for 3 h at rt, most of the volatile materials were evaporated, and the crude product was purified by column chromatography to yield the mixture of the desired product (**19**) and further isomerized 1-(but-1-enyloxy)-4-methoxybenzene (2-OPMP) (20.4 mg (96%), **19**:2-OPMP = 1.0:3.5 (based on ^{1}H NMR)). The product was analyzed by ^{1}H NMR and GC. ^{1}H NMR ($CDCl_3$): δ 6.92−6.88 (m, 2H, Ar), 6.84−6.79 (m, 2H, Ar), 6.36−6.33 (dt, 1H, J = 12.0, 1.5 Hz, ROC*H*=CHEt), 5.32−5.27 (m, 1H, ROCH=C*H*Et), 3.75 (s, 3H, OMe), 2.05−1.99 (m, 2H, RCH_2CH$_3$), 1.05−0.98 (t, 3H, J = 6.0 Hz, RCH$_2$CH_3).

Attempted Isomerization of 1-Methylene-2,3,4,5-trihydronaphthalene (1) Using Ir(COE)$_2$Cl]$_2$/PCy$_3$/NaBPh$_4$ in CH$_2$Cl$_2$/Acetone.[4b,6d] Using the same procedure and catalyst (2 mol %) aforementioned, the isomerization of olefin **1** (17.1 mg, 0.119 mmol) was checked. The crude product was purified by short column chromatography and analyzed by ^{1}H NMR.

Attempted Isomerization of 2-(3-(3-(Benzyloxy)phenyl)but-3-enyl)isoindoline-1,3-dione (3a) Using Ir(COE)$_2$Cl]$_2$/PCy$_3$/NaBPh$_4$ in CH$_2$Cl$_2$/Acetone.[4b,6d] Using the same procedure and catalyst (2 mol %) aforementioned, the isomerization of olefin **3a** (22.8 mg, 0.060 mmol) was checked. The crude product was purified by short column chromatography and analyzed by ^{1}H NMR.

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Supporting Information Available: Spectroscopic data (^{1}H and ^{13}C NMR) and gas chromatographic traces of starting materials, products, and crude isomerization products. This material is available free of charge via the Internet at http://pubs.acs.org.

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