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Cationic Rhodium(I)/Bisphosphane Complex-Catalyzed Isomerization of Secondary Propargylic Alcohols to α,β-Enones

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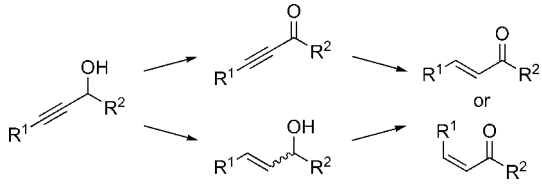
We have determined that hydrogenated cationic Rh(I)/bisphosphane complexes are highly active catalysts for the isomerization of secondary propargylic alcohols to α,β-enones. A kinetic resolution of secondary propargylic alcohols proceeded with moderate selectivity with [Rh((*R*)-BINAP)]OTf as a catalyst. Mechanistic studies revealed that the isomerization proceeds through intramolecular 1,3- and 1,2-hydrogen migration pathways. The isomerization of propargylic diol derivatives was also investigated, which revealed that 1,4-diketones, furans, and α,β-enones were obtained from 2-butyn-1,4-diol, 1-methoxy-2-butyn-4-ol, and 1-acetoxy-2-butyn-4-ol derivatives, respectively. Furthermore, chemoselectivity of the isomerization of an acetylenic diol was investigated, and preferential oxidation of a propargylic hydroxy group was observed.

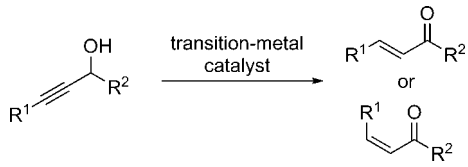
Introduction

Transition-metal-catalyzed C–H bond cleavage and formation through isomerization is a valuable transformation in organic synthesis.[1] Notably, a number of efficient isomerizations of allylic alcohols to aldehydes or ketones, which have significant synthetic utility, have been developed.[2] On the other hand, a similar isomerization of propargylic alcohols to α,β-enones and α,β-enals,[1d] which are typically prepared from propargylic alcohols by sequential oxidation and reduction (Scheme 1), has not been extensively studied despite its high atom economy (Scheme 2).[3]



Scheme 1. Transformation of propargylic alcohols into α,β-enones and α,β-enals by sequential oxidation and reduction.

In 1982, a catalytic isomerization of 2-butyne-1,4-diol to butyrolactone was developed with $RuH_2(PPh_3)_4$ as the catalyst at 145 °C for 12 h, and this reaction was proposed to proceed through an α,β-unsaturated aldehyde intermediate.[4] The first isolation of α,β-enals from the isomerization of primary propargylic alcohols was realized with



Scheme 2. Transition-metal-catalyzed isomerization of propargylic alcohols.

$RuCl_2(PPh_3)_3$/*i*Pr_3P as the catalyst at 110 °C for 30–48 h.[5] A ruthenium(II)-indenyl complex, which is an efficient catalyst for the isomerization of allylic alcohols, is also effective for the rapid isomerization of primary propargylic alcohols to α,β-enals in the presence of 20–40 mol-% $InCl_3$ at 65 °C, requiring only 1.5 h.[6] Although the isomerization of secondary propargylic alcohols also proceeds in high yield, a prolonged reaction time (24 h) is required. $Pd_2(dba)_3$-$CHCl_3$/*n*Bu_3P catalyzes the isomerization of secondary propargylic diols to 1,4-diketones in high yield at 110 °C after 15–70 h.[7] In the presence of a catalytic amount of ethylene glycol, $Pd_2(dba)_3$-$CHCl_3$/*i*Pr_3P was able to isomerize secondary propargylic mono-ols to α,β-enones in high yield at 80 °C after 40–65 h, and active palladium hydride species were supposed to be generated in situ.[8] An iridium complex [IrH_5(*i*Pr_3P)$_2$] is also an effective catalyst for the isomerization of secondary propargylic mono-ols and diols to the corresponding α,β-enones and 1,4-diketones at 110 °C after 24–40 h.[9]

Although there are many examples of cationic Rh(I)/bisphosphane complex-catalyzed isomerizations of allylic alcohols[10] including some asymmetric variants (Scheme 3),[11] the application of these complexes to the isomerization of propargylic alcohols into α,β-enones and

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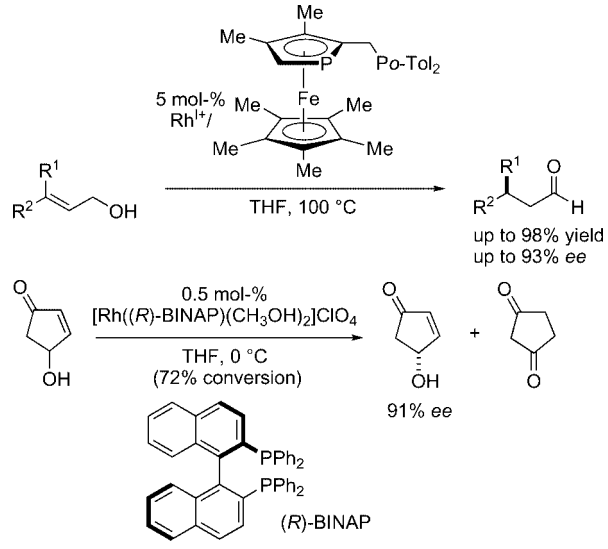
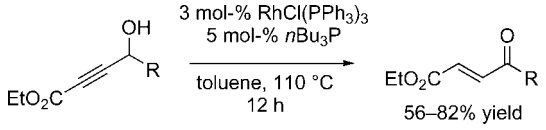
α,β-enals has not been reported. The only example of a Rh-catalyzed isomerization of this kind was that of propargylic alcohols bearing an ethoxycarbonyl group at an alkyne terminus, which isomerized in the presence of 3 mol-% $RhCl(PPh_3)_3$ and 5 mol-% nBu_3P at 110 °C after 12 h (Scheme 4).[12]



Scheme 3. Cationic Rh(I)/bisphosphane complex-catalyzed asymmetric isomerization of allylic alcohols.



Scheme 4. $RhCl(PPh_3)_3/nBu_3P$-catalyzed isomerization of propargylic alcohols.

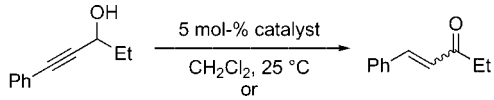
In general, the existing methods for the isomerization of secondary propargylic alcohols require long reaction times and/or high reaction temperatures, so the development of more active catalyst is highly desired. Herein, we describe a cationic Rh(I)/bisphosphane complex-catalyzed isomerization of secondary propargylic alcohols to α,β-enones.[13] We also provide a mechanistic insight into the reaction pathway, a kinetic resolution of secondary propargylic alcohols, and isomerizations of various acetylenic alcohols (propargylic diol derivatives and homopropargylic alcohols).

Results and Discussion

Rh-Catalyzed Isomerization of Propargylic Alcohols

We first examined various Rh(I) catalysts (5 mol-% based on the alcohol) for their ability to isomerize secondary propargylic alcohol **1a** (Table 1). The catalytic activities of $RhCl(PPh_3)_3$ and cationic Rh(I) complexes with monodentate phosphane ligands (PPh_3 and nBu_3P) were very low even at an elevated temperature (80 °C, Table 1, Entries 1–3). On the other hand, cationic Rh(I) complexes with bidentate phosphane ligands (dppe, dcpe, dppf, and *rac*-BINAP) were highly effective catalysts at 80 °C (Table 1, Entries 5, 7, 9, and 11), and the isomerization can proceed even at ambient temperature (25 °C) with dcpe or *rac*-BINAP as a ligand (Table 1, Entries 6 and 10). Among the ligands examined, *rac*-BINAP was the most effective ligand (Table 1, Entries 10 and 11), and the desired α,β-enone **2a** was obtained in >95% yield with complete *E* selectivity at 80 °C after only 1 h (Table 1, Entry 11). Importantly, pretreatment of the $[Rh(cod)(rac\text{-BINAP})]BF_4$ catalyst, prepared in situ by mixing $[Rh(cod)_2]BF_4$ and *rac*-BINAP, with hydrogen was essential for this isomerization (Table 1, Entry 12).

Table 1. Screening of catalysts for Rh-catalyzed isomerization of propargylic alcohol **1a**.



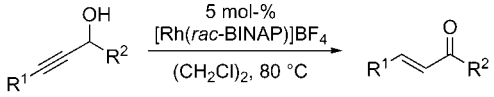
Entry	Catalyst[a]	Temp. [°C] /Time [h]	Conv. [%][b]	Yield [%][b]	*E*/*Z*
1	$RhCl(PPh_3)_3$	80/16	<1	<1	–
2	$[Rh(PPh_3)_2]BF_4$	80/16	<1	<1	–
3	$[Rh(nBu_3P)_2]BF_4$	80/16	3	2	–
4	$[Rh(dppe)]BF_4$	25/40	<1	<1	–
5	$[Rh(dppe)]BF_4$	80/16	86	43	100:0
6	$[Rh(dcpe)]BF_4$	25/40	40	32	41:59
7	$[Rh(dcpe)]BF_4$	80/16	100	82	100:0
8	$[Rh(dppf)]BF_4$	25/40	<1	<1	–
9	$[Rh(dppf)]BF_4$	80/14	100	73	100:0
10	$[Rh(rac\text{-BINAP})]BF_4$	25/40	27	27	91:9
11	$[Rh(rac\text{-BINAP})]BF_4$	80/1	100	>95	100:0
12	$[Rh(cod)(rac\text{-BINAP})]BF_4$	80/16	<1	<1	–

[a] dppe: bis(diphenylphosphanyl)ethane, dcpe: bis(dicyclohexylphosphanyl)ethane, dppf: 1,1′-bis(diphenylphosphanyl)ferrocene. [b] Determined by ^1H NMR spectroscopy.

A series of secondary and primary propargylic alcohols **1a**–**t** (R^1 = aryl, heteroaryl, or alkenyl) were subjected to the optimal reaction conditions described above (Table 2). Primary (**1a**–**d**, Table 2, Entries 1–4), secondary (**1e**, Table 2, Entry 5), and tertiary (**1f**, Table 2, Entry 6) alkyl-substituted (R^2) secondary propargylic alcohols cleanly afforded the corresponding α,β-enones **2a**–**f** in almost quantitative yield. Unfortunately, the reaction of phenyl-substituted (R^2) propargylic alcohol **1g** afforded a complex mixture of products (Table 2, Entry 7).[14] For the reaction of primary propargylic alcohol **1h**, $[Rh(cod)(rac\text{-BINAP})]BF_4$ was employed to suppress the rapid Rh-catalyzed decarbonylation of aldehyde **2h**, but **2h** was obtained in low yield (Table 2, Entry 8). The reaction of secondary propargylic alcohols **1i**,**j**, bearing coordinating substituents (R^2), were sluggish, and the corresponding α,β-enones **2i**,**j** were obtained in moderate yields (Table 2, Entries 9 and 10). The electronic and steric nature of substituents on the benzene ring did not affect the yields of α,β-enones **2k**–**p** (Table 2, Entries 11–16). The reactions of heteroaryl-substituted (R^1) secondary propargylic alcohols were also investigated. The reaction of 2-furyl-sub-

stituted secondary propargylic alcohol **1q** proceeded to give α,β-enone **2q** in moderate yield (Table 2, Entry 17), but the reaction of highly coordinating 2-pyridyl-substituted alcohol **1r** did not proceed, and **1r** was recovered (Table 2, Entry 18). In general, the [Rh(*rac*-BINAP)]BF_4-catalyzed isomerization of secondary propargylic alcohols **1** furnished α,β-enones **2** with complete *E* selectivity, although a sterically demanding substituent on the benzene ring sometimes decreased the *E*/*Z* ratio of the α,β-enones **2** (Table 2, Entries 13 and 14). Alkenyl-substituted (R^1) alcohols **1s**,**t** cleanly afforded the corresponding dienones **2s**,**t** in high yield with dppe as a ligand (Table 2, Entries 19 and 20).

Table 2. Cationic Rh(I)/*rac*-BINAP complex-catalyzed isomerization of propargylic alcohols.

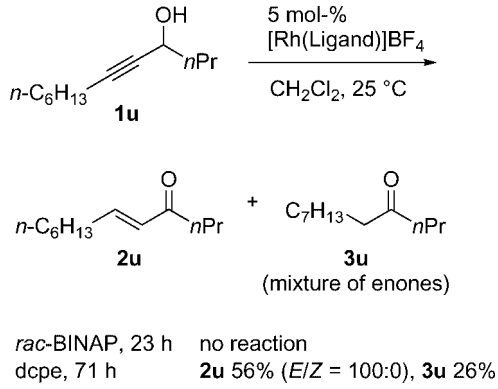


1a–t **2a–t**

Entry	Alcohol	R^1	R^2	Product	Time [h]	Yield [%][a]	*E*/*Z*
1	**1b**	Ph	Me	**2b**	1	99	100:0
2	**1a**	Ph	Et	**2a**	1	98	100:0
3	**1c**	Ph	*n*Pr	**2c**	1	97	100:0
4	**1d**	Ph	*n*Bu	**2d**	1	95	100:0
5	**1e**	Ph	*i*Pr	**2e**	1	98	100:0
6	**1f**	Ph	*t*Bu	**2f**	1	96	100:0
7	**1g**	Ph	Ph	**2g**	1	–[b]	–
8[c,d]	**1h**	Ph	H	**2h**	17	32	100:0
9[d]	**1i**	Ph	CO_2Et	**2i**	48	46	100:0
10	**1j**	Ph	CH_2OMe	**2j**	46	60	100:0
11	**1k**	4-$F_3CC_6H_4$	Et	**2k**	1	99	100:0
12	**1l**	4-$MeOC_6H_4$	Et	**2l**	1	98	100:0
13	**1m**	2-MeC_6H_4	Et	**2m**	1	94	67:33
14	**1n**	2-$F_3CC_6H_4$	Et	**2n**	1	97	57:43
15	**1o**	2-$MeOC_6H_4$	*n*Pr	**2o**	1	96	100:0
16	**1p**	1-naphthyl	Et	**2p**	4	96	100:0
17	**1q**	2-furyl	Et	**2q**	1	46	100:0
18	**1r**	2-pyridyl	Et	**2r**	18	<5	–
19[e,f]	**1s**	2-isopropenyl	*n*Pr	**2s**	3	84	100:0
20[e]	**1t**	1-cyclohexenyl	*n*Pr	**2t**	13	79	100:0

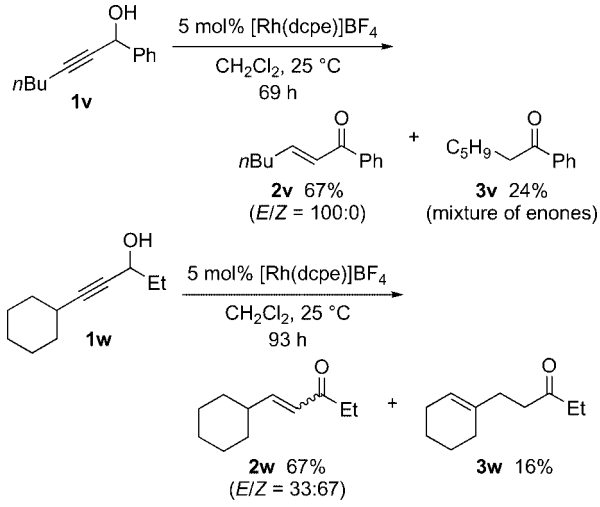
[a] Isolated yield. [b] Complex mixture of products. [c] Catalyst: [Rh(*rac*-BINAP)(cod)]BF_4. [d] Solvent: toluene, temperature: 110 °C. [e] Catalyst: [Rh(dppe)]BF_4. [f] Catalyst: 10 mol-%.

Unfortunately, the reaction of propargylic alcohol **1u** bearing a primary alkyl group at an alkyne terminus in the presence of [Rh(*rac*-BINAP)]BF_4 at 80 °C led to a complex mixture of products including the corresponding α,β-enone **2u** and the double-bond migration products **3u**. To suppress the formation of **3u**, the isomerization of **1u** was conducted at 25 °C. Although no reaction was observed with [Rh(*rac*-BINAP)]BF_4 as the catalyst, the use of [Rh(dcpe)]BF_4 suppressed the formation of **3u**, and the desired α,β-enone **2u** was obtained in 56% yield with complete *E* selectivity (Scheme 5).



Scheme 5. Cationic Rh(I)/dcpe complex-catalyzed isomerization of propargylic alcohol **1u**.

Thus, the isomerizations of secondary propargylic alcohols **1v**,**w** were also conducted in the presence of 5 mol-% of [Rh(dcpe)]BF_4 at 25 °C. The reaction of 1-phenyl-substituted propargylic alcohol **1v** furnished α,β-enone **2v** in good yield with complete *E* selectivity, and the reaction of a sterically demanding propargylic alcohol **1w**, bearing a cyclohexyl group at the alkyne terminus, furnished α,β-enone **2w** in good yield but with a decreased *E*/*Z* ratio (Scheme 6). α,β-Enones **2u**, **2v**, and **2w** could be separated from enones **3u**, **3v**, and **3w**, respectively, by silica gel chromatography.



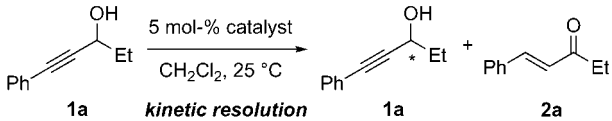
Scheme 6. Cationic Rh(I)/dcpe complex-catalyzed isomerization of propargylic alcohols **1v**,**w**.

Rh-Catalyzed Kinetic Resolution of Secondary Propargylic Alcohols

Next, a kinetic resolution of secondary propargylic alcohol **1a** was investigated with chiral Rh(I) or iridium(I) complexes with various BINAP-type ligands (Table 3, Figure 1).[15–18] Among the ligands examined (Table 3, Entries 1–4), BINAP was the most selective (Table 3, Entry 1). The use of a neutral Rh(I) complex or a cationic iridium(I) complex led to a rather complex reaction mixture, the selectivity

factors were very low (Table 3, Entries 5 and 6). The effect of counterions was also investigated (Table 3, Entries 1 and 7–9), and we found that the highest selectivity factor was obtained with the OTf counterion (Table 3, Entry 9). A similar counterion effect was observed in the enantioselective isomerization of geraniol with Rh^{I+}/BINAP.[15c]

Table 3. Screening of catalysts for the Rh-catalyzed kinetic resolution of secondary propargylic alcohol **1a**.



1a ***kinetic resolution*** **1a** **2a**

Entry	Catalyst	Time [h]	% *ee* of unreacted alcohol (% conv.[a])	*s* [selectivity factor]
1	[Rh((*R*)-BINAP)]BF_4	78	47 (46)	5.2
2	[Rh((*R*)-tol-BINAP)]BF_4	40	22 (34)	3.1
3	[Rh((*R*)-H_8-BINAP)]BF_4	40	33 (46)	3.1
4	[Rh((*S*)-Segphos)]BF_4	88	9 (14)	3.8
5[b]	[Rh((*R*)-BINAP)]Cl	38	10 (20)	2.5
6[b]	[Ir((*R*)-BINAP)]BF_4	15	8 (70)	1.2
7	[Rh((*R*)-BINAP)]SbF_6	40	41 (52)	3.3
8	[Rh((*R*)-BINAP)]ClO_4	40	– (<1)	–
9	[Rh((*R*)-BINAP)]OTf	72	76 (59)	7.3

[a] Determined by ^1H NMR spectroscopy. [b] Solvent: $(CH_2Cl)_2$, temperature: 80 °C.

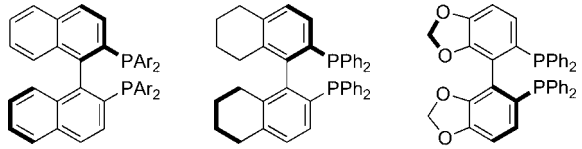
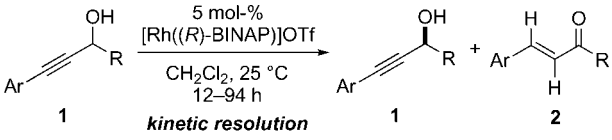


Figure 1. Structures of chiral BINAP-type ligands.

Table 4. Cationic Rh(I)/(*R*)-BINAP complex-catalyzed kinetic resolution of secondary propargylic alcohols.



1 ***kinetic resolution*** **1** **2**

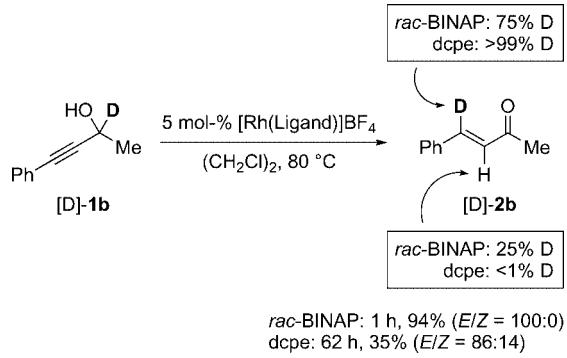
Entry	Alcohol	Ar	R	% *ee* of unreacted alcohol (% conv.[a])	*s* [selectivity factor][b]
1	**1b**	Ph	Me	42 (58)	2.8
2	**1a**	Ph	Et	76 (59)	7.3
3	**1c**	Ph	*n*Pr	54 (54)	4.4
4	**1d**	Ph	*n*Bu	82 (60)	8.2
5	**1e**	Ph	*i*Pr	58 (51)	6.1
6[c,d]	**1f**	Ph	*t*Bu	62 (58)	4.7
7	**1k**	4-$F_3CC_6H_4$	Et	78 (60)	7.2
8	**1l**	4-$MeOC_6H_4$	Et	62 (55)	5.8
9	**1m**	2-MeC_6H_4	Et	80 (55)	11.5
10[c,e]	**1n**	2-$F_3CC_6H_4$	Et	52 (51)	5.0
11	**1o**	2-$MeOC_6H_4$	*n*Pr	68 (53)	7.8
12	**1p**	1-naphthyl	Et	60 (52)	6.4

[a] Determined by ^1H NMR spectroscopy. [b] Calculated at the observed conversion. [c] Catalyst: [Rh{(*R*)-BINAP}]BF_4. [d] Solvent: $(CH_2Cl)_2$, temperature: 40 °C. [e] Solvent: $(CH_2Cl)_2$, temperature: 50 °C.

A series of secondary propargylic alcohols **1** can be resolved with 5 mol-% [Rh{(*R*)-BINAP}]OTf as a catalyst (Table 4). The length and steric demand of the alkyl groups affected the enantioselectivity of the isomerization (Table 4, Entries 1–6). Good selectivity factors were observed in Et-, *n*Bu-, and *i*Pr-substituted (R) propargylic alcohols (Table 4, Entries 2, 4, and 5). In general, both electronic and steric nature of the substituents on the benzene ring appeared to have a modest impact on the selectivity factor (Table 4, Entries 7–12), although the 2-methyl substituent on the benzene ring significantly improved the selectivity factor (Table 4, Entry 9).

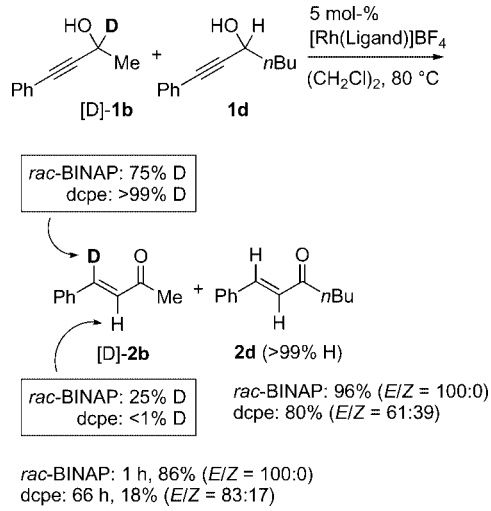
Mechanistic Consideration Regarding the Rh-Catalyzed Isomerization of Propargylic Alcohols

The reaction of a deuterated propargylic alcohol in the presence of a cationic Rh(I) complex with *rac*-BINAP or dcpe was investigated to gain mechanistic insight into this reaction (Scheme 7). The deuterium from propargylic alcohol [D]-**1b** was incorporated into both the α-position (25% D) and the β-position (75% D) of α,β-enone [D]-**2b** with the electron-deficient phosphane ligand *rac*-BINAP. On the contrary, exclusive deuterium incorporation into the β-position of α,β-enone [D]-**2b** occurred with the electron-rich phosphane ligand dcpe. Although the reaction of the deuterated propargylic alcohol in the presence of 5 mol-% [Rh(*rac*-BINAP)]BF_4 proceeded smoothly, the reaction in the presence of 5 mol-% [Rh(dcpe)]BF_4 was sluggish.



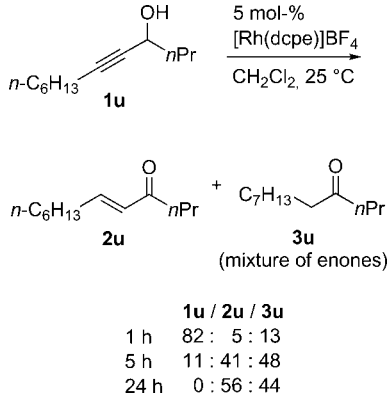
Scheme 7. Deuterium-labeling studies of propargylic alcohol [D]-**1b**.

Furthermore, we have established that the isomerization is an intramolecular process. Treatment of a 1:1 mixture of deuterated propargylic alcohol [D]-**1b** and nondeuterated propargylic alcohol **1d** with [Rh(*rac*-BINAP)]BF_4 or [Rh(dcpe)]BF_4 furnished deuterated [D]-**2b** and nondeuterated **2d**, and thus, no deuterium crossover was observed (Scheme 8).[19]



Scheme 8. Crossover experiments.

Next, a mechanism for the isomerization of a propargylic alcohol bearing an alkyl group at the alkyne terminus was investigated. The time-course of the cationic Rh(I)/dcpe complex-catalyzed isomerization of propargylic alcohol **1u** indicated that α,β-enone **2u** and a mixture of enones **3u** formed initially, and that **2u** may be generated through an isomerization of **3u** (Scheme 9).

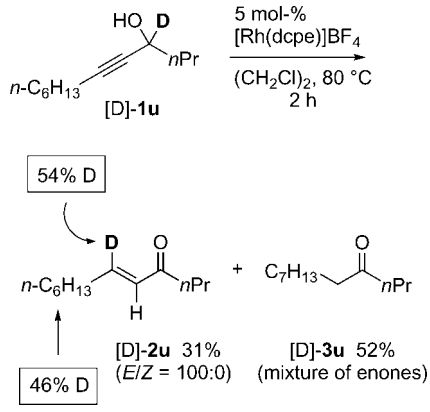


	1u / 2u / 3u
1 h	82 : 5 : 13
5 h	11 : 41 : 48
24 h	0 : 56 : 44

Scheme 9. Time-course of cationic Rh(I)/dcpe complex-catalyzed isomerization of propargylic alcohol **1u**.

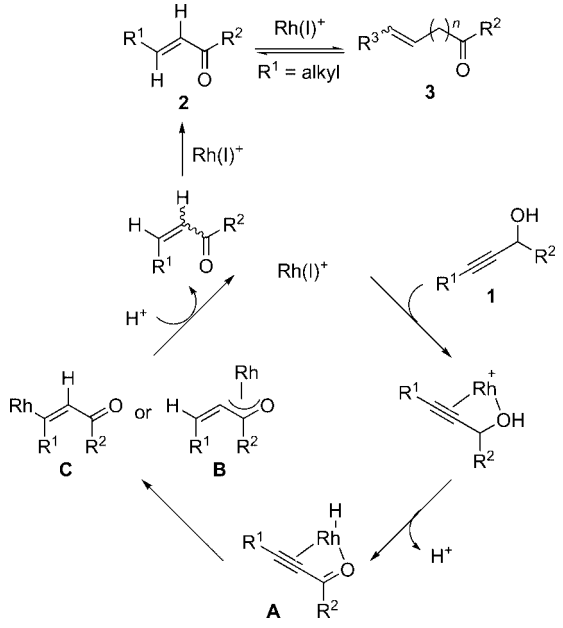
The reaction of deuterated propargylic alcohol [D]-**1u** in the presence of the cationic Rh(I)/dcpe complex was investigated to gain mechanistic insight into this reaction (Scheme 10).[20] Deuterium from the propargylic alcohol [D]-**1u** was incorporated into the β-position and the alkyl chain of α,β-enone [D]-**2u**. Although the mechanism for formation of **3u** is not clear,[21] the isomerization of [D]-**1u** to [D]-**2u** catalyzed by the cationic Rh(I)/dcpe complex obviously proceeds through a 1,3-hydrogen migration and not a 1,2-hydrogen migration.

Scheme 11 depicts a plausible mechanism for the cationic Rh(I)/bisphosphane complex-catalyzed isomerization of secondary propargylic alcohols to α,β-enones. The reaction of a Rh(I) catalyst with a propargylic alcohol **1** furnishes the Rh hydride complex **A**. The addition of Rh hydride to the alkyne furnishes the π-oxallyl Rh intermediate **B** or alk-



Scheme 10. Deuterium-labeling study of propargylic alcohol [D]-**1u**.

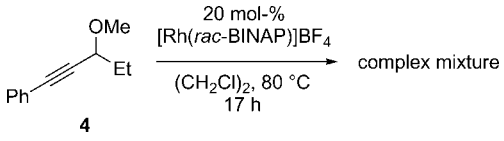
enyl Rh intermediate **C**, which is protonated to give an α,β-enone and regenerates the Rh(I) catalyst. In the case of a cationic Rh(I)/dcpe complex, π-oxallyl Rh intermediate **B** is generated exclusively, presumably due to the high nucleophilicity of an electron-rich Rh hydride. The isomerization to the thermodynamically favored (*E*)-α,β-enone **2** may be catalyzed by the cationic Rh(I) complex. α,β-Enone **2u** may be isomerized to **3u** reversibly by the Rh catalyst.



Scheme 11. Plausible mechanism for the cationic Rh(I)/bisphosphane complex-catalyzed isomerization of propargylic alcohols.

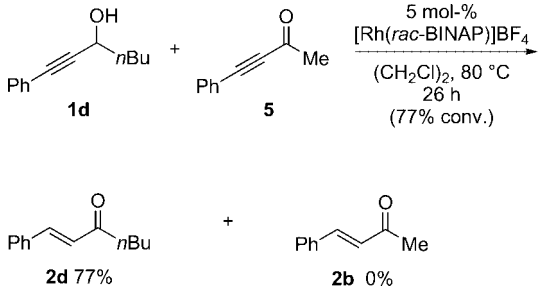
Consistent with this proposed mechanism, an attempted isomerization of propargylic ether **4** in the presence of [Rh(*rac*-BINAP)]BF_4 led to an unidentified complex mixture of products (Scheme 12).

To determine if the unbound propargylic ketone is an intermediate on the route to the desired α,β-enone, we carried out the isomerization of **1d** in the presence of propargylic ketone **5** (Scheme 13). If a portion of the desired product is formed through dissociation/reassociation of the propargylic ketone, a fraction of **5** should be converted to



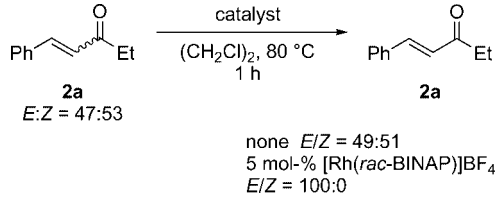
Scheme 12. Reaction of propargylic ether **4** with the cationic Rh(I)/*rac*-BINAP complex.

2b. However, no α,β-enone **2b** was formed, which indicates that the free propargylic ketone is not an intermediate in the present isomerization reaction.



Scheme 13. Isomerization of propargylic alcohol **1d** in the presence of propargylic ketone **5**.

To confirm the mechanism for the isomerization of (*Z*)-α,β-enones to (*E*)-α,β-enones, an (*E*/*Z*) mixture of α,β-enone **2a** was heated in the absence or presence of [Rh(*rac*-BINAP)]BF_4 (Scheme 14). No significant isomerization proceeded in the absence of catalyst, but complete isomerization to the *E* isomer proceeded in the presence of catalyst. Therefore, we can conclude that the isomerization of (*Z*)-α,β-enones to (*E*)-α,β-enones proceeds through coordination of the cationic Rh to the double bond, which is a similar mechanism to that proposed in the palladium(II)-catalyzed rapid isomerization of (*Z*)-α,β-enones to (*E*)-α,β-enones.[22]



Scheme 14. Isomerization of α,β-enone **2a** in the absence and presence of the cationic Rh(I)/*rac*-BINAP complex.

Consistent with this proposed mechanism, significant electronic effects were observed in the *E*/*Z* values of α,β-enones **2** obtained through the Rh-catalyzed isomerization of propargylic alcohols **1** (Figure 2). The introduction of an electron-deficient trifluoromethyl group (**2n**) onto the aromatic ring resulted in a decreased *E*/*Z* ratio. In contrast, the incorporation of an electron-donating methyl (**2m**) or methoxy (**2o**) group in the aromatic ring resulted in improved *E*/*Z* values. These observations can be explained by the electron deficiency of the benzylic carbon in the transition state of the Rh-catalyzed *E*/*Z* isomerization, which facilitates the isomerization.

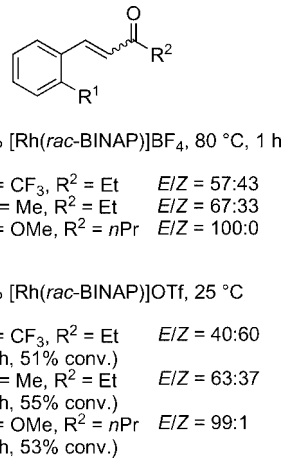
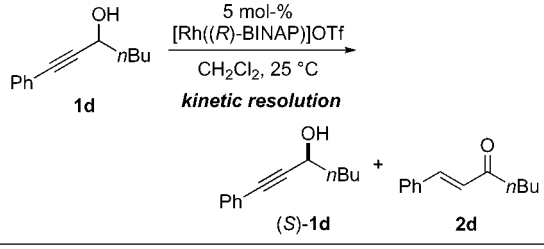


Figure 2. Electronic effect of substituents R^1 on the *E*/*Z* values of α,β-enones.

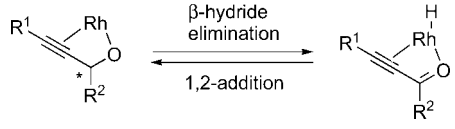
In the ruthenium(II)-catalyzed isomerization of allylic alcohols, it was reported that β-hydride elimination from the allylic alcohol and 1,2-addition of ruthenium hydride to the carbonyl group is a reversible process.[23] To examine the reversibility of the β-hydride elimination and the 1,2-addition, we studied the time-course of a Rh-catalyzed kinetic resolution of secondary propargylic alcohol **1d** (Table 5). If part of the β-hydride elimination and the 1,2-addition is reversible, calculated selectivity factors should decrease with the progress of the reaction. The study revealed that the calculated selectivity factor gradually decreased as the reaction proceeded, which indicates that race-

Table 5. Time-course of the Rh-catalyzed kinetic resolution of secondary propargylic alcohol **1d**.



Entry	Time [h]	% *ee* of unreacted alcohol [% conv.[a]]	*s* [selectivity factor][b]
1	6	38 [34]	10.0
2	14	83 [62]	7.5
3	37	99 [86]	4.9

[a] Determined by ^{1}H NMR spectroscopy. [b] Calculated at the observed conversion.



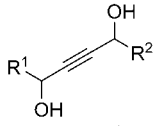
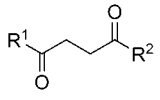
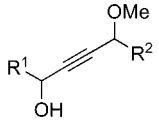
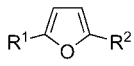
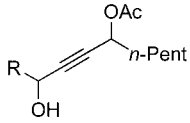
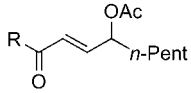
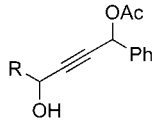
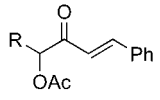
Scheme 15. β-Hydride elimination from propargylic alcohol and 1,2-addition of Rh hydride to the carbonyl group.

mization through the reversible 1,2-addition proceeds before the irreversible hydride addition to the triple bond (Scheme 15).

Rh-Catalyzed Isomerization of Propargylic Diol Derivatives and Homopropargylic Alcohol

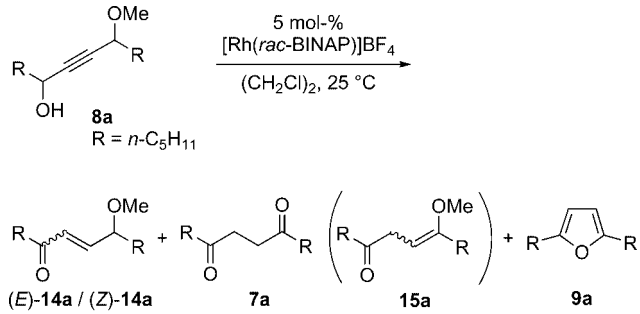
The procedure was applied to the isomerization of propargylic diol derivatives as shown in Table 6. 2-Butyne-1,4-diol derivatives **6a**–**c** were cleanly isomerized to the corresponding diones **7a**–**c** in high yield at 80 °C after a short reaction time (1 h, Table 6, Entries 1–3) compared with those previously reported for the Pd-catalyzed isomerization (110 °C, 15–70 h).[7] The isomerization of protected 2-butyne-1,4-diol derivatives **8**, **10**, and **11** was also investigated. 4-Methoxy-2-butyn-1-ol derivatives **8a**–**d** were isomerized to the corresponding furans **9a**–**d** in moderate yields (Table 6, Entries 4–7). On the other hand, 4-hydroxybut-2-ynyl acetate derivatives **10** and **11** were isomerized to two different α,β-enones **12** and **13** in moderate yields (Table 6, Entries 8–11). Although alcohols **10**, bearing an alkyl group α to the acetoxy group, furnished α,β-enones **12** (Table 6, Entries 8 and 9), alcohols **11**, bearing a phenyl group α to the acetoxy group, furnished α,β-enones **13** with a skeletal rearrangement (Table 6, Entries 10 and 11).

Table 6. Cationic Rh(I)/BINAP complex-catalyzed isomerization of 2-butyn-1,4-diol derivatives [5 mol-% [Rh(*rac*-BINAP)]BF_4 in $(CH_2Cl)_2$ at 80 °C].

Entry	Alcohol	Time [h]	Product [% yield[a]]
			
1	**6a** R^1 = *n*-C_5H_{11}, R^2 = *n*-C_5H_{11}	1	**7a** 73
2	**6b** R^1 = *n*-C_5H_{11}, R^2 = Ph	1	**7b** 79
3[b]	**6c** R^1 = Ph, R^2 = Ph	1	**7c** 89
			
4	**8a** R^1 = *n*-C_5H_{11}, R^2 = *n*-C_5H_{11}	1	**9a** 78
5	**8b** R^1 = *n*-C_5H_{11}, R^2 = Ph	1	**9b** 47
6	**8c** R^1 = Ph, R^2 = *n*-C_5H_{11}	1	**9b** 71
7	**8d** R^1 = Ph, R^2 = Ph	1	**9d** 59
			
8[c]	**10a** R = *n*-C_5H_{11}	4	**12a** 71
9	**10b** R = Ph	4	**12b** 59
			
10	**11a** R = *n*-C_5H_{11}	16	**13a** 45
11	**11b** R = Ph	16	**13b** 50

[a] Isolated yield. [b] Catalyst: 10 mol-%. [c] Ligand: dppf.

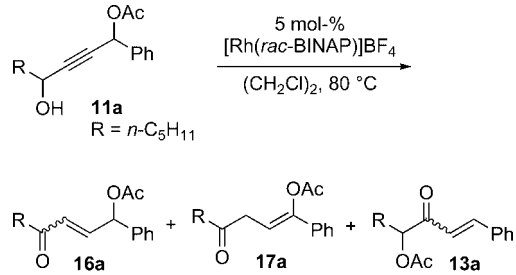
A time-course of the cationic Rh(I)/BINAP complex-catalyzed isomerization of **8a** was investigated at low temperature to gain mechanistic insight into this reaction (Scheme 16). The study revealed that (*Z*)-α,β-enone (*Z*)-**14a** was preferentially formed and might cyclize to give furan **9a**. On the other hand, the yield of 1,4-diketone **7a**, which can be generated through the isomerization of α,β-enone **14a** followed by hydrolysis, increased as the reaction progressed, so that **7a** (or the corresponding enol ether **15a**) may not be the major intermediate in the formation of furan **9a**.[24]



	8a	(*E*)-**14a**	(*Z*)-**14a**	**7a**	**9a**
1 h [%]	75	1	6	5	13
4 h [%]	27	2	13	8	43
45 h [%]	0	0	<1	12	80

Scheme 16. Time-course of the cationic Rh(I)/BINAP complex-catalyzed isomerization of **8a** (yields were determined by ^{1}H NMR with 1,4-dimethoxybenzene as an internal standard).

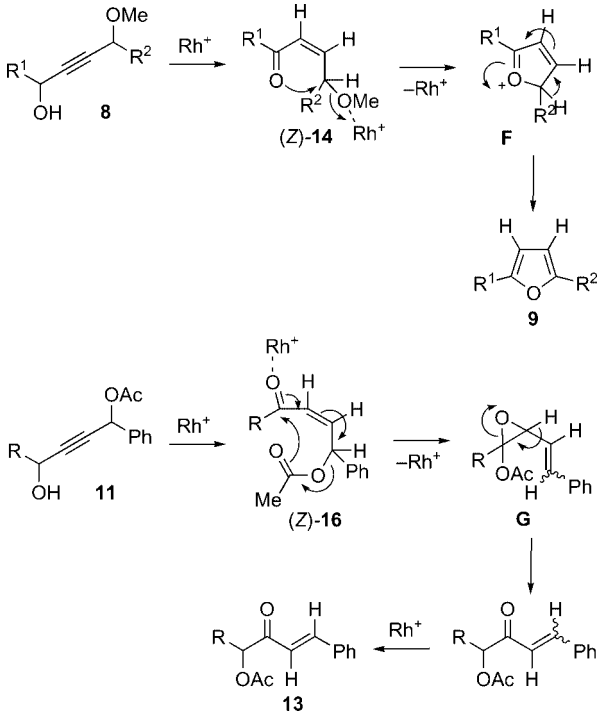
A time-course of the cationic Rh(I)/BINAP complex-catalyzed isomerization of **11a** was also investigated (Scheme 17). In this case, no α,β-enone **16a** was detected in the reaction mixture. Like the isomerization of propargylic alcohols, an *E*/*Z* mixture of α,β-enone **13a** was formed initially, and the *E* isomer was isolated after a prolonged reaction.



	11a	**16a**	**17a**	(*E*)-**13a**	(*Z*)-**13a**
1 h [%]	17	0	8	17	7
4 h [%]	0	0	9	36	1
20 h [%]	0	0	3	46	0

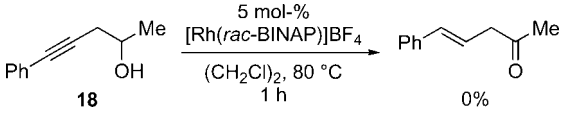
Scheme 17. Time-course of the cationic Rh(I)/BINAP complex-catalyzed isomerization of **11a** (yields were determined by ^{1}H NMR with 1,4-dimethoxybenzene as an internal standard).

Plausible mechanisms for the formation of furan **9** and α,β-enone **13** are shown in Scheme 18. Furan **9** is generated through the initial isomerization of alcohol **8** to (*Z*)-α,β-enone (*Z*)-**14**, which cyclizes and aromatizes via cation intermediate **F**.[25] α,β-Enone **13** is generated through the initial isomerization of alcohol **11** to (*Z*)-α,β-enone (*Z*)-**16**, which undergoes acetoxy-group migration and rearrangement via epoxide **G**. The phenyl group α to the acetoxy group in **11** may facilitate the acetoxy group migration because of the high stability of the conjugated product **13**.



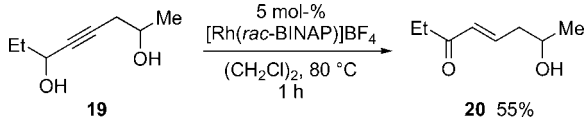
Scheme 18. Plausible mechanism for the formation of **9** and **13**.

The procedure was ultimately applied to the isomerization of a homopropargylic alcohol. However, the reaction of homopropargylic alcohol **18** in the presence of 5 mol-% [Rh(*rac*-BINAP)]BF_4 at 80 °C for 1 h did not furnish the corresponding β,γ-enone product (Scheme 19).



Scheme 19. Reaction of homopropargylic alcohol **18** with the cationic Rh(I)/*rac*-BINAP complex.

This failure of isomerization of homopropargylic alcohol **18** prompted us to investigate the chemoselective isomerization of an acetylenic alcohol. The isomerization of acetylenic diol **19** bearing both propargylic and homopropargylic hydroxy groups selectively furnished α,β-enone **20** in 55% yield, but the homopropargylic hydroxy group remained unchanged (Scheme 20).[26]



Scheme 20. Chemoselective isomerization of acetylenic diol **19** catalyzed by the cationic Rh(I)/*rac*-BINAP complex.

Conclusions

In conclusion, we have determined that the isomerization of secondary propargylic alcohols to α,β-enones proceeded in the presence of hydrogenated, cationic, Rh(I) complexes with the appropriate choice of bidentate phosphane ligands (*rac*-BINAP, dppe, or dcpe). The asymmetric variant of this reaction, a kinetic resolution of secondary propargylic alcohols, was developed with moderate selectivity with [Rh{(*R*)-BINAP}]OTf as a catalyst. Deuterium-labeling studies revealed that the isomerization proceeds through intramolecular 1,3- and 1,2-hydrogen migration pathways. The isomerization of propargylic diol derivatives was also investigated, which revealed that 1,4-diketones, furans, and α,β-enones were obtained from 2-butyn-1,4-diol, 1-methoxy-2-butyn-4-ol, and 1-acetoxy-2-butyn-4-ol derivatives, respectively. Furthermore, the chemoselectivity of the isomerization of an acetylenic diol was investigated, and the preferential oxidation of the propargylic hydroxy group was observed.

Experimental Section

General Methods: ^{1}H NMR spectra were recorded at 300 MHz (JEOL AL 300 spectrometer). ^{13}C NMR spectra were obtained with complete proton decoupling at 75 MHz (JEOL AL 300 spectrometer). HRMS data were obtained with a JEOL JMS-700 spectrometer. Infrared spectra were obtained with a JASCO A-302 spectrometer. Anhydrous CH_2Cl_2 (No. 27,099-7) and anhydrous $(CH_2Cl)_2$ (No. 28,450-5) were obtained from Aldrich and used as received. H_8-BINAP, tol-BINAP, and Segphos were obtained from Takasago International Corporation. Solvents for the synthesis of substrates were dried with molecular sieves (4 Å) prior to use. All other reagents were obtained from commercial sources and used as received. All reactions were carried out under an atmosphere of argon in oven-dried glassware with magnetic stirring, unless otherwise indicated.

Starting Materials: Propargylic alcohols **1a**,[27] **1b**,[28] **1c**,[29] **1d**,[27] **1f**,[30] **1g**,[31] **1k**,[32] **1l**, **1m**, **1n**, **1o**,[33] **1p**, **1q**, **1r**, **1s**,[34] **1t**, **1u**,[35] **1v**,[36] and **1w**[37] were synthesized through the reaction of the corresponding lithium acetylides and aldehydes. Propargylic alcohols **1e**, **1h**, and **6a** were commercially available. Propargylic ether **4**[38] was prepared according to the literature. Deuterated propargylic alcohols [D]-**1b** and [D]-**1u** were synthesized through a Jones oxidation of **1b** and **1u** followed by a reduction with $LiAlD_4$.

Alcohol 1j: *n*BuLi (1.56 M in hexane, 6.4 mL, 10.0 mmol) was added to a stirred solution of phenylacetylene (1.0 g, 10.0 mmol) in THF (30 mL) at –78 °C, and the mixture was stirred at –78 °C for 30 min. Methoxyacetyl chloride (1.9 mL, 20 mmol) was added to the resulting solution at 0 °C, and the mixture was gradually warmed to room temp. The reaction was quenched with water and extracted with Et_2O. The organic layer was washed with brine,

dried with Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc, 9:1), which furnished 1-methoxy-4-phenylbut-3-yn-2-one (1.1 g, 6.60 mmol, 66% yield) as a pale yellow oil. A mixture of 1-methoxy-4-phenylbut-3-yn-2-one (0.50 g, 2.87 mmol), $NaBH_4$ (81 mg, 2.15 mmol), and $CeCl_3·7H_2O$ (1.0 g, 2.68 mmol) in MeOH (7 mL) was stirred at room temp. for 10 min. The reaction was hydrolyzed with dilute HCl, brine was added, and the mixture was extracted with CH_2Cl_2. The organic layer was concentrated, and the residue was purified by silica gel column chromatography (hexane/EtOAc, 7:1), which furnished alcohol **1j** (0.50 g, 2.61 mmol, 91% yield) as a pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.50–7.38 (m, 2 H), 7.36–7.27 (m, 3 H), 4.82–4.70 (m, 1 H), 3.67 (dd, J = 9.9, 3.9 Hz, 1 H), 3.60 (dd, J = 9.9, 7.5 Hz, 1 H), 3.47 (s, 3 H), 2.53 (d, J = 4.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 131.7, 128.4, 128.1, 122.2, 86.5, 85.5, 76.0, 61.9, 59.2 ppm. IR (neat): $\tilde{\nu}$ = 3350, 2900, 1120, 758, 690 cm^{-1}. HRMS (EI): calcd. for $C_{11}H_{12}O_2$ [M] 176.0837; found 176.0813.

Alcohol 1l: Pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.40–7.34 (m, 2 H), 6.86–6.80 (m, 2 H), 4.54 (q, J = 6.3 Hz, 1 H), 3.80 (s, 3 H), 2.06–1.96 (m, 1 H), 1.90–1.74 (m, 2 H), 1.07 (t, J = 7.5 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 159.6, 133.1, 114.7, 113.8, 88.5, 84.8, 64.2, 55.2, 31.0, 9.5 ppm. IR (neat): $\tilde{\nu}$ = 3350, 2950, 1600, 1508, 1245, 1180, 1030, 835 cm^{-1}. HRMS (EI): calcd. for $C_{12}H_{14}O_2$ [M] 190.0994; found 190.0970.

Alcohol 1m: Pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.42–7.37 (m, 1 H), 7.25–7.09 (m, 3 H), 4.64 (q, J = 6.0 Hz, 1 H), 2.43 (s, 3 H), 2.00–1.93 (m, 1 H), 1.90–1.78 (m, 2 H), 1.09 (t, J = 7.5 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 140.0, 131.8, 129.3, 128.3, 125.4, 122.3, 93.8, 83.7, 64.3, 31.1, 20.8, 9.6 ppm. IR (neat): $\tilde{\nu}$ = 3300, 2950, 1015, 745 cm^{-1}. HRMS (EI): calcd. for $C_{12}H_{14}O$ [M] 174.1045; found 174.1011.

Alcohol 1n: Pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.65 (d, J = 7.5 Hz, 1 H), 7.58 (d, J = 7.5 Hz, 1 H), 7.49 (t, J = 7.5 Hz, 1 H), 7.41 (t, J = 7.5 Hz, 1 H), 4.58 (q, J = 6.3 Hz, 1 H), 1.92–1.78 (m, 3 H), 1.08 (t, J = 7.5 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 134.0, 131.8, 131.3, 128.1, 125.8 (q), 125.3, 121.7, 95.7, 80.8, 64.2, 30.7, 9.1 ppm. IR (neat): $\tilde{\nu}$ = 3250, 2850, 1300, 1100, 750 cm^{-1}. HRMS (EI): calcd. for $C_{12}H_{11}F_3O$ [M] 228.0762; found 228.0719.

Alcohol 1p: Orange oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.30 (d, J = 8.1 Hz, 1 H), 7.90–7.75 (m, 2 H), 7.67 (dd, J = 7.2, 1.5 Hz, 1 H), 7.62–7.45 (m, 2 H), 7.46–7.35 (m, 1 H), 4.71 (q, J = 6.3 Hz, 1 H), 2.04–1.84 (m, 3 H), 1.16 (t, J = 7.5 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 133.2, 133.1, 130.5, 128.8, 128.2, 126.8, 126.4, 126.0, 125.1, 120.3, 94.9, 82.9, 64.2, 31.1, 9.6 ppm. IR (neat): $\tilde{\nu}$ = 3220, 2850, 1370, 1000, 760 cm^{-1}. HRMS (EI): calcd. for $C_{15}H_{14}O$ [M] 210.1045; found 210.1009.

Alcohol 1q: Orange oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.76 (dd, J = 1.8, 0.9 Hz, 1 H), 6.57 (dd, J = 3.6, 0.9 Hz, 1 H), 6.38 (dd, J = 3.6, 1.8 Hz, 1 H), 4.56 (q, J = 6.3 Hz, 1 H), 1.90–1.76 (m, 3 H), 1.07 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 143.4, 136.5, 115.2, 110.7, 94.2, 75.1, 64.0, 30.5, 9.3 ppm. IR (neat): $\tilde{\nu}$ = 3250, 2850, 1620, 720 cm^{-1}. HRMS (EI): calcd. for $C_9H_{10}O_2$ [M] 150.0681; found 150.0647.

Alcohol 1r: Orange oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.60–8.55 (m, 1 H), 7.66 (dt, J = 7.8, 1.8 Hz, 1 H), 7.43 (d, J = 7.8 Hz, 1 H), 7.28–7.20 (m, 1 H), 4.70–4.50 (m, 1 H), 3.10–2.80 (m, 1 H), 2.93 (q, J = 7.2 Hz, 2 H), 1.26 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 149.6, 142.8, 136.2, 127.1, 122.8, 91.1, 83.6, 63.6, 30.6, 9.5 ppm. IR (neat): $\tilde{\nu}$ = 3150, 2810, 1560, 1410, 760 cm^{-1}. HRMS (EI): calcd. for $C_{10}H_{11}NO$ [M – OH] 144.0814; found 144.0773.

Alcohol 1t: Pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.12–6.00 (m, 1 H), 4.48 (t, J = 6.6 Hz, 1 H), 2.38–2.00 (m, 5 H), 1.85–1.42 (m, 8 H), 0.95 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 134.9, 120.1, 87.5, 86.5, 62.6, 40.0, 29.1, 25.5, 22.2, 21.4, 18.4, 13.7 ppm. IR (neat): $\tilde{\nu}$ = 3300, 2900, 1010, 920 cm^{-1}. HRMS (EI): calcd. for $C_{12}H_{18}O$ [M] 178.1358; found 178.1344.

Alcohol [D]-1b: Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.46–7.40 (m, 2 H), 7.35–7.27 (m, 3 H), 2.05–1.96 (m, 1 H), 1.55 (s, 3 H) ppm.

Alcohol [D]-1u: Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.20 (t, J = 7.2 Hz, 2 H), 1.74 (s, 1 H), 1.70–1.58 (m, 2 H), 1.56–1.20 (m, 10 H), 0.95 (t, J = 7.2 Hz, 3 H), 0.89 (t, J = 6.9 Hz, 3 H) ppm.

Alcohol 6c:[7] To a stirred mixture of $LiAlH_4$ (64.6 mg, 1.70 mmol) in THF (10 mL) at 0 °C was added a solution of **8d** (600 mg, 2.27 mmol) in Et_2O (5 mL). The resulting mixture was stirred at 0 °C for 30 min. The reaction was quenched with water (2.0 mL), and stirred at 0 °C for 10 min. The reaction mixture was extracted with Et_2O. The organic layer was washed with water and brine, dried with Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc, 5:1), which furnished alcohol **6c** (340.0 mg, 1.43 mmol, 63% yield) as a colorless solid, m.p. 121–122 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.60–7.50 (m, 4 H), 7.44–7.30 (m, 6 H), 5.57 (d, J = 6.0 Hz, 2 H), 2.30–2.21 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 140.2, 128.7, 128.5, 126.6, 86.4, 64.6 ppm.

Alcohol 6b: The title compound was prepared in 59% isolated yield from **10b** according to the procedure used for **6c**. Colorless solid; m.p. 57–58 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.70–7.50 (m, 2 H), 7.50–7.26 (m, 3 H), 5.55–5.48 (m, 1 H), 4.54–4.40 (m, 1 H), 2.40–2.35 (m, 1 H), 1.95–1.85 (m, 1 H), 1.80–1.65 (m, 2 H), 1.55–1.40 (m, 2 H), 1.40–1.20 (m, 4 H), 0.89 (t, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 140.4, 128.6, 128.4, 126.63, 126.61, 87.8, 84.5, 64.4, 62.5, 37.5, 31.4, 24.8, 22.5, 14.0 ppm. IR (neat): $\tilde{\nu}$ = 3200, 2850, 990, 680 cm^{-1}. HRMS (EI): calcd. for $C_{15}H_{20}O_2$ [M] 232.1463, found 232.1413.

Alcohol 8a: To a stirred suspension of NaH (55% in paraffin oil, 0.48 g, 20.0 mmol) in THF (30 mL) was added a THF (5 mL) solution of tetradec-7-yn-6,9-diol (2.26 g, 10.0 mmol) at room temp., and the resulting mixture was stirred at room temp. for 30 min. To the resulting solution was added iodomethane (0.6 mL, 10.0 mmol), and the mixture was stirred at room temp. overnight. The mixture was extracted with Et_2O. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc, 10:1), which furnished alcohol **8a** (1.2 g, 5.15 mmol, 55% yield) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.48–4.35 (m, 1 H), 3.97 (dt, J = 6.6, 1.5 Hz, 1 H), 3.39 (s, 3 H), 2.00–1.87 (m, 1 H), 1.80–1.57 (m, 4 H), 1.55–1.36 (m, 4 H), 1.36–1.15 (m, 8 H), 0.97–0.80 (m, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 86.98, 86.94, 83.6, 71.3, 62.5, 56.35, 56.33, 37.84, 37.81, 35.5, 31.49, 31.41, 24.9, 24.8, 22.5, 13.97, 13.94 ppm. IR (neat): $\tilde{\nu}$ = 3325, 2850, 1440, 1320, 1090 cm^{-1}. HRMS (EI): calcd. for $C_{15}H_{28}O_2$ [M – H] 239.2011; found 239.2034.

Alcohol 8d:[39] To a stirred suspension of NaH (55% in paraffin oil, 1.1 g, 44.0 mmol) in THF (40 mL) was added a THF (5 mL) solution of 1-phenylprop-2-yn-1-ol (2.6 g, 20.0 mmol) at room temp., and the resulting mixture was stirred at room temp. for 30 min. To the resulting solution was added iodomethane (5.0 mL,

80.0 mmol), and the mixture was stirred at room temp. for 30 min. The reaction was quenched with water and extracted with Et_2O. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc, 20:1), which furnished (1-methoxyprop-2-ynyl)benzene (1.6 g, 10.8 mmol, 54% yield) as a colorless oil. *n*BuLi (1.56 M in hexane, 3.6 mL, 5.59 mmol) was added to a stirred solution of (1-methoxyprop-2-ynyl)benzene (0.82 g, 5.59 mmol) in THF (15 mL) at 0 °C, and the mixture was stirred at 0 °C for 30 min. To the resulting solution was added benzaldehyde (0.56 mL, 5.59 mmol) at 0 °C, and the mixture was gradually warmed to room temp. The reaction was quenched with water and extracted with Et_2O. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc, 8:1), which furnished alcohol **8d** (1.32 g, 5.22 mmol, 93% yield) as a pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.58–7.42 (m, 4 H), 7.42–7.26 (m, 6 H), 5.54 (s, 1 H), 5.17 (s, 1 H), 3.41 (s, 3 H), 2.60–2.34 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 140.31, 140.30, 138.1, 128.6, 128.5, 128.4, 127.4, 126.6, 87.5, 84.2, 73.0, 64.61, 64.60, 55.9 ppm.

Alcohol 8b: The title compound was prepared as a pale yellow oil in 77% isolated yield from (1-methoxyprop-2-ynyl)benzene and hexanal according to the procedure used for **8d**. Pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.53–7.43 (m, 2 H), 7.43–7.30 (m, 3 H), 5.12 (s, 1 H), 4.53–4.41 (m, 1 H), 3.42 (s, 3 H), 2.00–1.80 (m, 1 H), 1.80–1.53 (m, 2 H), 1.53–1.40 (m, 2 H), 1.40–1.25 (m, 4 H), 0.94–0.83 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 138.3, 129.5, 128.44, 128.40, 127.3, 88.99, 88.98, 82.2, 72.9, 62.5, 55.77, 55.76, 37.7, 31.4, 24.8, 22.5, 13.9 ppm. IR (neat): $\tilde{\nu}$ = 3100, 2850, 1050, 690 cm^{-1}. HRMS (EI): calcd. for $C_{16}H_{22}O_2$ [M] 246.1620; found 246.1637.

Alcohol 8c: The title compound was prepared as a pale yellow oil in 17% isolated yield (2 steps) from oct-1-yn-3-ol and benzaldehyde according to the procedure used for **8d**. Pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.60–7.50 (m, 2 H), 7.44–7.30 (m, 3 H), 5.53 (d, J = 6.6 Hz, 1 H), 4.03 (t, J = 6.6 Hz, 1 H), 3.42 (s, 3 H), 2.20 (d, J = 6.6 Hz, 1 H), 1.80–1.65 (m, 2 H), 1.55–1.38 (m, 2 H), 1.38–1.20 (m, 4 H), 0.94–0.83 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 140.6, 128.6, 128.4, 126.64, 126.61, 85.8, 85.5, 71.3, 64.6, 56.5, 35.5, 31.5, 24.9, 22.5, 14.0 ppm. IR (neat): $\tilde{\nu}$ = 3300, 2850, 1070, 690 cm^{-1}. HRMS (EI): calcd. for $C_{16}H_{22}O_2$ [M] 246.1620; found 246.1663.

Alcohol 11b: 1-Phenylprop-2-yn-1-ol (1.5 g, 11.4 mmol) was added to a stirred solution of triethylamine (1.9 mL, 13.6 mmol), DMAP (69.3 mg, 0.57 mmol) and acetic anhydride (1.2 mL, 12.5 mmol) in CH_2Cl_2 (20 mL) at room temp., and the mixture was stirred at room temp. for 1 h. The reaction was quenched with water and extracted with Et_2O. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc, 20:1), which furnished 1-phenylprop-2-ynyl acetate (1.9 g, 10.6 mmol, 94% yield) as a colorless oil. *n*BuLi (1.54 M in hexane, 1.9 mL, 2.87 mmol) was added to a stirred solution of diisopropylamine (0.5 mL, 3.16 mmol) in THF (20 mL) at 0 °C, and the mixture was stirred at 0 °C for 30 min. 1-Phenylprop-2-ynyl ester (0.50 g, 2.78 mmol) was added to the resulting solution at –78 °C, and the solution was stirred at –78 °C for 15 min. To the resulting solution was added benzaldehyde (0.26 mL, 2.58 mmol) at –78 °C, and the mixture was gradually warmed to room temp. The reaction was quenched with water and extracted with Et_2O. The organic layer was washed with brine, dried with Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (hexane/EtOAc, 9:1), which furnished alcohol **11b** (0.46 g, 1.76 mmol, 61% yield) as a pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.58–7.46 (m, 4 H), 7.44–7.28 (m, 6 H), 6.58–6.52 (m, 1 H), 5.59–5.52 (m, 1 H), 2.34–2.26 (m, 1 H), 2.10 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.9, 140.0, 136.5, 128.9, 128.5, 128.4, 128.2, 127.6, 126.6, 87.0, 82.7, 65.6, 64.2, 20.9 ppm. IR (neat): $\tilde{\nu}$ = 3350, 3000, 1700, 1200, 1000 cm^{-1}. HRMS (EI): calcd. for $C_{18}H_{16}O_3$ [M] 280.1099; found 280.1103.

Alcohol 10a: The title compound was prepared as a pale yellow oil in 47% isolated yield (2 steps) from oct-1-yn-3-ol and hexanal according to the procedure used for **11b**. Pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.43–5.34 (m, 1 H), 4.45–4.35 (m, 1 H), 2.08 (s, 3 H), 1.86–1.80 (m, 1 H), 1.80–1.60 (m, 4 H), 1.50–1.37 (m, 4 H), 1.37–1.22 (m, 8 H), 0.90 (t, J = 6.9 Hz, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 170.1, 86.5, 82.3, 82.2, 64.11, 64.10, 62.3, 37.5, 34.6, 31.4, 31.2, 24.72, 24.71, 24.6, 22.5, 22.4, 21.0, 13.92, 13.91 ppm. IR (neat): $\tilde{\nu}$ = 3300, 2850, 1700, 1210, 1010 cm^{-1}. HRMS (EI): calcd. for $C_{16}H_{28}O_3$ [M – C_5H_{11}] 197.1177; found 197.1187.

Alcohol 10b: The title compound was prepared as a pale yellow oil in 51% isolated yield (2 steps) from oct-1-yn-3-ol and benzaldehyde according to the procedure used for **11b**. Pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.60–7.49 (m, 2 H), 7.48–7.26 (m, 3 H), 5.50 (d, J = 6.3 Hz, 1 H), 5.44 (tt, J = 6.6, 2.1 Hz, 1 H), 2.35–2.25 (m, 1 H), 2.09 (s, 3 H), 1.85–1.70 (m, 2 H), 1.50–1.37 (m, 2 H), 1.37–1.24 (m, 4 H), 0.89 (t, J = 6.9 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 170.1, 140.2, 128.5, 128.3, 126.6, 85.1, 85.0, 84.1, 64.36, 64.34, 64.12, 64.10, 34.5, 31.2, 24.61, 24.59, 22.4, 21.0, 14.0 ppm. IR (neat): $\tilde{\nu}$ = 3350, 2850, 1700, 1210, 1000 cm^{-1}. HRMS (EI): calcd. for $C_{17}H_{22}O_3$ [M] 274.1569; found 274.1524.

Alcohol 11a: The title compound was prepared as a pale yellow oil in 61% isolated yield (2 steps) from 1-phenylprop-2-yn-1-ol and hexanal according to the procedure used for **11b**. Pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.54–7.49 (m, 2 H), 7.49–7.30 (m, 3 H), 6.49 (s, 1 H), 4.51–4.40 (m, 1 H), 2.10 (s, 3 H), 1.87–1.80 (m, 1 H), 1.80–1.65 (m, 2 H), 1.52–1.39 (m, 2 H), 1.39–1.20 (m, 4 H), 0.89 (t, J = 6.3 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 169.8, 136.82, 136.81, 128.9, 128.6, 127.7, 88.4, 81.2, 65.57, 65.56, 62.4, 37.45, 37.43, 31.3, 24.7, 22.5, 21.1, 13.9 ppm. IR (neat): $\tilde{\nu}$ = 3300, 2850, 1700, 1210, 680 cm^{-1}. HRMS (EI): calcd. for $C_{17}H_{22}O_3$ [M] 274.1569; found 274.1534.

Alcohol 19: The title compound was prepared as a colorless oil in 31% isolated yield (2 steps) from 1-methylbut-3-ynyl acetate[40] and propionaldehyde according to the procedure used for **6c**. Colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.40–4.25 (m, 1 H), 4.05–3.88 (m, 1 H), 2.44 (ddd, J = 16.2, 6.9, 1.8 Hz, 1 H), 2.35 (ddd, J = 16.2, 6.6, 1.8 Hz, 1 H), 2.12–1.80 (m, 2 H), 1.78–1.58 (m, 2 H), 1.26 (d, J = 6.3 Hz, 3 H), 1.00 (t, J = 7.5 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 83.7, 81.6, 66.4, 66.3, 63.8, 31.0, 29.2, 22.3, 9.5 ppm. IR (neat): $\tilde{\nu}$ = 3200, 2900, 1050, 920 cm^{-1}. HRMS (FAB): calcd. for $C_8H_{14}O_2$ [M + H] 143.1072; found 143.1084.

Representative Procedure for the Isomerization of Propargylic Alcohols: (Table 2, Entry 1): A CH_2Cl_2 (0.5 mL) solution of *rac*-BINAP (15.6 mg, 0.025 mmol) was added to a CH_2Cl_2 (0.5 mL) solution of $[Rh(cod)_2]BF_4$ (10.2 mg, 0.025 mmol) at room temp., and the mixture was stirred for 5 min at room temp. H_2 was introduced to the resulting solution in a Schlenk tube. After stirring for 0.5 h at room temp., the resulting solution was concentrated to dryness and dissolved in $(CH_2Cl)_2$ (1.0 mL). To this solution was added a $(CH_2Cl)_2$ (0.5 mL) solution of 4-phenylbut-3-yn-2-ol (**1b**, 73.1 mg, 0.5 mmol), and additional $(CH_2Cl)_2$ (0.5 mL) was used to

transfer the material completely from its original flask. The solution was stirred at 80 °C for 1 h. The resulting solution was concentrated and purified by silica gel column chromatography (Et_2O), giving ketone **2b**[41] (72.5 mg, 0.495 mmol, 99% yield). Orange solid; m.p. 35–37 °C. ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.60–7.48 (m, 3 H), 7.48–7.30 (m, 3 H), 6.72 (d, J = 15.9 Hz, 1 H), 2.37 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 198.4, 143.4, 134.3, 130.5, 128.9, 128.2, 127.1, 27.5 ppm.

Ketone 2k: (Table 2, Entry 11) Yield 99% (112.5 mg). Pale brown solid; m.p. 62–64 °C. ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.65 (s, 4 H), 7.57 (d, J = 16.2 Hz, 1 H), 6.81 (d, J = 16.2 Hz, 1 H), 2.72 (q, J = 7.5 Hz, 2 H), 1.18 (t, J = 7.5 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 200.2, 140.0, 137.9, 131.8, 128.2, 127.9, 125.7 (q), 122.3, 34.4, 8.1 ppm. IR (neat): $\tilde{\nu}$ = 2950, 1660, 1320, 1160, 1120, 985, 840 cm^{-1}. HRMS (EI): calcd. for $C_{12}H_{11}F_3O$ [M] 228.0762, found 228.0736.

Ketone 2m (E/Z = 67:33): (Table 2, Entry 13) Yield 94% (81.6 mg). Orange oil. ^1H NMR ($CDCl_3$, 400 MHz) E isomer: δ = 7.86 (d, J = 15.6 Hz, 1 H), 7.60–7.54 (m, 1 H), 7.37–7.10 (m, 3 H), 6.67 (d, J = 15.6 Hz, 1 H), 2.70 (q, J = 7.2 Hz, 2 H), 2.25 (s, 3 H), 1.18 (t, J = 7.2 Hz, 3 H) ppm; Z isomer: δ = 7.37–7.10 (m, 4 H), 7.05 (d, J = 12.4 Hz, 1 H), 6.22 (d, J = 12.4 Hz, 1 H), 2.30 (s, 3 H), 2.30 (q, J = 7.2 Hz, 2 H), 0.96 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 203.8, 200.7, 139.5, 139.1, 137.7, 135.6, 135.3, 133.4, 130.7, 129.9, 129.8, 129.7, 128.8, 128.5, 126.8, 126.2, 126.1, 125.5, 36.1, 34.3, 19.9, 19.8, 8.3, 8.1 ppm. IR (neat): $\tilde{\nu}$ = 2925, 1660, 1600, 1120, 1040, 980, 745 cm^{-1}. HRMS (EI): calcd. for $C_{12}H_{14}O$ [M] 174.1045; found 174.1028.

Ketone 2n (E/Z = 57:43): (Table 2, Entry 14) Yield 97% (110.6 mg). Orange oil. ^1H NMR ($CDCl_3$, 300 MHz) E isomer: δ = 7.85–7.80 (m, 1 H), 7.80–7.65 (m, 2 H), 7.58 (t, J = 7.5 Hz, 1 H), 7.49 (t, J = 7.5 Hz, 1 H), 6.66 (d, J = 16.2 Hz, 1 H), 2.74 (q, J = 7.2 Hz, 2 H), 1.18 (t, J = 7.2 Hz, 3 H) ppm; Z isomer: δ = 7.68 (d, J = 7.5 Hz, 1 H), 7.56–7.38 (m, 2 H), 7.36 (d, J = 7.5 Hz, 1 H), 7.20–7.08 (m, 1 H), 6.33 (d, J = 12.3 Hz, 1 H), 2.33 (q, J = 7.2 Hz, 2 H), 0.97 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 202.6, 200.6, 137.7, 136.4, 135.0, 133.6, 131.4, 132.1, 130.7, 130.6, 130.2, 129.6, 128.2, 127.8, 126.5 (q), 125.80, 125.77, 125.74 (q), 122.2, 122.1, 36.6, 33.5, 8.0, 7.7 ppm. IR (neat): $\tilde{\nu}$ = 3300, 1600, 1290, 1100, 750 cm^{-1}. HRMS (EI): calcd. for $C_{12}H_{11}F_3O$ [M – Et] 199.0371; found 199.0338.

Ketone 2o: (Table 2, Entry 15) Yield 96% (97.9 mg). Orange oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.91 (d, J = 16.2 Hz, 1 H), 7.54 (dd, J = 7.8, 1.5 Hz, 1 H), 7.43–7.28 (m, 1 H), 7.00–6.85 (m, 2 H), 6.78 (d, J = 16.2 Hz, 1 H), 3.88 (s, 3 H), 2.66 (t, J = 7.2 Hz, 2 H), 1.71 (sext, J = 7.2 Hz, 2 H), 0.98 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 201.1, 158.3, 137.5, 131.5, 128.3, 126.9, 123.4, 120.7, 111.1, 55.4, 42.2, 17.8, 13.8 ppm. IR (neat): $\tilde{\nu}$ = 2850, 1580, 1440, 1230, 730 cm^{-1}. HRMS (EI): calcd. for $C_{13}H_{16}O_2$ [M] 204.1150; found 204.1125.

Ketone 2s: (Table 2, Entry 19) Yield 84% (58.1 mg). Pale yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.23 (d, J = 15.9 Hz, 1 H), 6.15 (d, J = 15.9 Hz, 1 H), 5.43–5.34 (m, 2 H), 2.58 (t, J = 7.5 Hz, 2 H), 1.92–1.86 (m, 3 H), 1.67 (sext, J = 7.5 Hz, 2 H), 0.96 (t, J = 7.5 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 201.0, 144.7, 140.9, 127.0, 124.9, 42.5, 18.5, 17.7, 13.8 ppm. IR (neat): $\tilde{\nu}$ = 2900, 1660, 1190, 980 cm^{-1}. HRMS (EI): calcd. for $C_9H_{14}O$ [M – Pr] 95.0497; found 95.0452.

Ketone 2t: (Table 2, Entry 20) Yield 79% (70.2 mg). Pale yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.16 (d, J = 15.9 Hz, 1 H), 6.38–6.15 (m, 1 H), 6.07 (d, J = 15.9 Hz, 1 H), 2.55 (t, J = 7.2 Hz, 2 H), 2.30–2.06 (m, 4 H), 1.77–1.55 (m, 6 H), 0.95 (t, J = 7.5 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 201.1, 145.9, 139.5, 135.1, 123.2, 42.3, 26.5, 24.1, 21.95, 21.91, 17.9, 13.7 ppm. IR (neat): $\tilde{\nu}$ = 2900, 1590, 1190, 980 cm^{-1}. HRMS (EI): calcd. for $C_{12}H_{18}O$ [M] 178.1358; found 178.1320.

Ketone 12a: (Table 6, Entry 8) Yield 71% (19.0 mg). Colorless oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.68 (dd, J = 16.2, 5.4 Hz, 1 H), 6.19 (dd, J = 16.2, 1.2 Hz, 1 H), 5.45–5.33 (m, 1 H), 2.55 (t, J = 7.5 Hz, 2 H), 2.10 (s, 3 H), 1.72–1.50 (m, 4 H), 1.49–1.10 (m, 10 H), 0.94–0.84 (m, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 200.3, 170.1, 142.9, 129.2, 72.7, 40.7, 33.8, 31.42, 31.37, 24.6, 23.6, 22.4, 21.0, 13.93, 13.89 ppm. IR (neat): $\tilde{\nu}$ = 2850, 1660, 1350, 1220 cm^{-1}. HRMS (EI): calcd. for $C_{16}H_{28}O_3$ [M – Ac] 225.1854; found 225.1798.

Ketone 12b: (Table 6, Entry 9) Yield 59% (76.8 mg). Pale yellow oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.98–7.90 (m, 2 H), 7.62–7.52 (m, 1 H), 7.52–7.36 (m, 2 H), 7.02 (d, J = 15.6 Hz, 1 H), 6.91 (dd, J = 15.6, 5.4 Hz, 1 H), 5.51 (q, J = 5.4 Hz, 1 H), 2.14 (s, 3 H), 1.88–1.58 (m, 2 H), 1.47–1.35 (m, 6 H), 0.89 (t, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 190.1, 170.1, 145.3, 137.4, 132.9, 128.51, 128.49, 125.3, 73.0, 33.8, 31.4, 24.6, 22.4, 21.0, 13.9 ppm. IR (neat): $\tilde{\nu}$ = 2900, 1620, 1220, 1010 cm^{-1}. HRMS (EI): calcd. for $C_{17}H_{22}O_3$ [M – Ac] 232.1463; found 232.1413.

Ketone 13a: (Table 6, Entry 10) Yield 45% (58.6 mg). Orange oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.72 (d, J = 15.9 Hz, 1 H), 7.63–7.50 (m, 2 H), 7.50–7.30 (m, 3 H), 6.86 (d, J = 15.9 Hz, 1 H), 5.29 (dd, J = 7.8, 7.2 Hz, 1 H), 2.18 (s, 3 H), 1.90–1.70 (m, 2 H), 1.51–1.36 (m, 2 H), 1.36–1.20 (m, 4 H), 0.89 (t, J = 6.9 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 196.0, 170.6, 144.4, 134.3, 130.8, 128.9, 128.5, 121.0, 78.0, 31.4, 30.8, 24.9, 22.4, 20.8, 14.0 ppm. IR (neat): $\tilde{\nu}$ = 2900, 1700, 1230, 1030, 690 cm^{-1}. HRMS (EI): calcd. for $C_{17}H_{22}O_3$ [M] 274.1569; found 274.1576.

Ketone 13b: (Table 6, Entry 11) Yield 50% (66.3 mg). Orange oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 7.70 (d, J = 15.9 Hz, 1 H), 7.65–7.10 (m, 10 H), 6.78 (d, J = 15.9 Hz, 1 H), 6.26 (s, 1 H), 2.22 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 192.5, 170.2, 144.6, 134.0, 133.3, 130.8, 129.3, 129.1, 128.8, 128.5, 128.4, 121.0, 80.2, 20.8 ppm. IR (neat): $\tilde{\nu}$ = 3050, 1680, 1200, 910, 700 cm^{-1}. HRMS (EI): calcd. for $C_{18}H_{16}O_3$ [M – C_2H_2O] 238.0993; found 238.0976.

Ketone 20: (Scheme 20) Yield 55% (31.1 mg). Orange oil. ^1H NMR ($CDCl_3$, 300 MHz): δ = 6.86 (dd, J = 15.9, 7.5 Hz, 1 H), 6.18 (dd, J = 15.9, 1.2 Hz, 1 H), 3.98 (sext, J = 6.3 Hz, 1 H), 2.59 (q, J = 7.5 Hz, 2 H), 2.42–2.32 (m, 2 H), 2.30–1.82 (m, 1 H), 2.25 (d, J = 6.3 Hz, 3 H), 1.10 (t, J = 7.5 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 201.1, 142.8, 132.2, 66.7, 42.0, 33.3, 23.3, 8.0 ppm. IR (neat): $\tilde{\nu}$ = 3300, 2900, 1620, 980 cm^{-1}. HRMS (FAB): calcd. for $C_8H_{14}O_2$ [M + H] 143.1072; found 143.1031.

Representative Procedure for the Kinetic Resolution of Secondary Propargylic Alcohols: (Table 4, Entry 4): AgOTf (6.4 mg, 0.025 mmol) and $[Rh(cod)Cl]_2$ (6.2 mg, 0.0125 mmol) were dissolved in acetone (1.0 mL), and the mixture was stirred at room temp. for 5 min. An acetone (0.5 mL) solution of (*R*)-BINAP (15.6 mg, 0.025 mmol) was added, and the mixture was stirred at room temp. for 5 min. The resulting solution was concentrated to dryness and dissolved in CH_2Cl_2 (0.5 mL). H_2 was introduced to the resulting solution in a Schlenk tube. After stirring at room temp. for 0.5 h, the resulting solution was concentrated to dryness and dissolved in CH_2Cl_2 (1.0 mL). To this solution was added a CH_2Cl_2 (0.5 mL) solution of **1d** (94.1 mg, 0.500 mmol), and additional CH_2Cl_2 (0.5 mL) was used to transfer the material completely from its original flask. The solution was stirred at 25 °C for

14 h. The conversion of the reaction was determined to be 59.8% by ^{1}H NMR with 1,4-dimethoxybenzene as an internal standard. The solution was concentrated and purified by preparative TLC (hexane/EtOAc, 4:1), which furnished **2d** (50.1 mg, 0.270 mmol, 53% yield) and (+)-**1d** [33.8 mg, 0.180 mmol, 36% yield, $[\alpha]_D^{25}$ = +1.29 (*c* = 1.69 in $CHCl_3$, 81.5% *ee*)]. Selectivity factor: 8.2. HPLC: CHIRALCEL OD-H, hexane/2-PrOH, 95:5, 1.0 mL/min, retention times: 8.3 min (minor isomer) and 27.7 min (major isomer).

Table 4, Entry 7: (–)-**1k** {$[\alpha]_D^{25}$ = –1.05 (*c* = 1.76 in $CHCl_3$, 78.0% *ee*)} was obtained for 64 h in 60.0% conversion. Selectivity factor: 7.2. HPLC: CHIRALCEL OD-H, hexane: 2-PrOH, 99:1, 1.0 mL/min, retention times: 19.7 min (minor isomer) and 22.6 min (major isomer).

Table 4, Entry 8: (–)-**1l** {$[\alpha]_D^{25}$ = –1.15 (*c* = 1.74 in $CHCl_3$, 62.3% *ee*)} was obtained for 45 h at 54.5% conversion. Selectivity factor: 5.8. HPLC: CHIRALCEL OD-H, hexane:2-PrOH, 95:5, 1.0 mL/min, retention times: 11.5 min (minor isomer) and 40.8 min (major isomer).

Table 4, Entry 9: (–)-**1m** {$[\alpha]_D^{25}$ = –3.07 (*c* = 1.79 in $CHCl_3$, 80.0% *ee*)} was obtained for 42 h at 54.9% conversion. Selectivity factor: 11.5. HPLC: CHIRALCEL OD-H, hexane/2-PrOH, 95:5, 1.0 mL/min, retention times: 8.9 min (minor isomer) and 15.8 min (major isomer).

Table 4, Entry 10: (–)-**1n** {$[\alpha]_D^{25}$ = –0.76 (*c* = 2.44 in $CHCl_3$, 51.8% *ee*)} was obtained for 12 h (50 °C) at 50.5% conversion. Selectivity factor: 5.0. HPLC: CHIRALCEL OD-H, hexane/2-PrOH, 97:3, 0.8 mL/min, retention times: 9.2 min (minor isomer) and 11.6 min (major isomer).

Table 4, Entry 11: (–)-**1o** {$[\alpha]_D^{25}$ = –0.56 (*c* = 2.26 in $CHCl_3$, 68.0% *ee*)} was obtained for 22 h at 53.4% conversion. Selectivity factor: 7.8. HPLC: CHIRALCEL OD-H, hexane/2-PrOH = 90:10, 1.0 mL/min, retention times: 11.9 min (minor isomer) and 36.7 min (major isomer).

Table 4, Entry 12: (–)-**1p** {$[\alpha]_D^{25}$ = –4.00 (*c* = 2.42 in $CHCl_3$, 60.4% *ee*)} was obtained for 94 h at 51.9% conversion. Selectivity factor: 6.4. HPLCL CHIRALPAK AD-H, hexane/2-PrOH = 97:3, 0.8 mL/min, retention times: 22.9 min (minor isomer) and 24.2 min (major isomer).

Supporting Information (see also the footnote on the first page of this article): Experimental procedures and compound characterization data for **1i**, **18**, **2a**, **2c**, **2d**, **2e**, **2f**, **2h**, **2i**, **2j**, **2l**, **2p**, **2q**, **2u**, **2v**, **2w**, [D]-**2b**, [D]-**2u**, **7a**, **7b**, **7c**, **9a**, **9b**, **9d**, and Entries 1, 2, 3, 5, and 6 of Table 4. ^{1}H and ^{13}C NMR spectra of all new compounds (**1j**, **1l**, **1m**, **1n**, **1p**, **1q**, **1r**, **1t**, **6b**, **8a**, **8b**, **8c**, **10a**, **10b**, **11a**, **11b**, **19**, **2k**, **2m**, **2n**, **2o**, **2s**, **2t**, **12a**, **12b**, **13a**, **13b**, and **20**).

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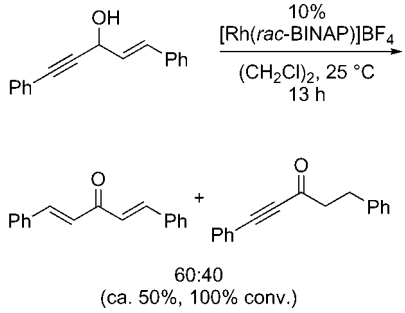

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