Lewis Acid Mediated Reactions of Zirconacyclopentenes with Aldehydes Affording Homoallyl Ketones via Oppenauer-Type Oxidation

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Three different components involving alkynes, ethylene, and aldehydes were selectively integrated in a one-pot procedure to afford homoallyl ketones in good yields, via an effective combination of zirconocene-mediated C–C bond forming reactions and Lewis acid mediated organic transformation. Mechanistic studies revealed that a formal Oppenauer oxidation of seven-membered oxazirconacycles, generated in situ from the reactions of zirconacyclopentenes and aldehydes, was promoted by Lewis acid–aldehyde adducts. As a whole, the first aldehyde was incorporated into the product and the second aldehyde was reduced to an alcohol. Multiply deuterated homoallyl ketones could be readily prepared in high yields with more than 98% deuterium incorporation by using this method.

Introduction

Among many synthetic methodologies in organic synthesis, transition metal mediated C–C bond forming reactions and Lewis acid promoted organic transformation are two of the most widely used and most powerful.[1–3] Synthetically useful methodologies can be expected from an effective combination of these two powerful protocols or an efficient cooperation of organometallic compounds with Lewis acids.[4–10] Zirconacycles, including zirconacyclopentadienes, -pentenes, and -pentanes can be easily

prepared.[2,6] These in situ formed zirconacycles are reactive organometallic intermediates and have been widely used for organic synthesis.[2] As one of our strategies to develop useful methodologies in organic synthesis, several years ago we initiated a research project on the reaction chemistry of in situ generated zirconacycles with unsaturated organic substrates in the presence of classical Lewis acids such as $AlCl_3$, BF_3, $TiCl_4$, and $SnCl_4$.[10] Aldehydes do not react with zirconacyclopentadienes **1**. However, when Lewis acids such as $AlCl_3$, $AlBr_3$, and BF_3 were added to the reaction mixture, a reaction took place immediately to afford cyclopentadiene derivatives (eq 1).[10] This reaction was the first example in which cyclopentadienes were formed in one pot from two molecules of alkynes and one molecule of aldehyde via deoxygenative cycloaddition of the aldehyde with the alkynes.
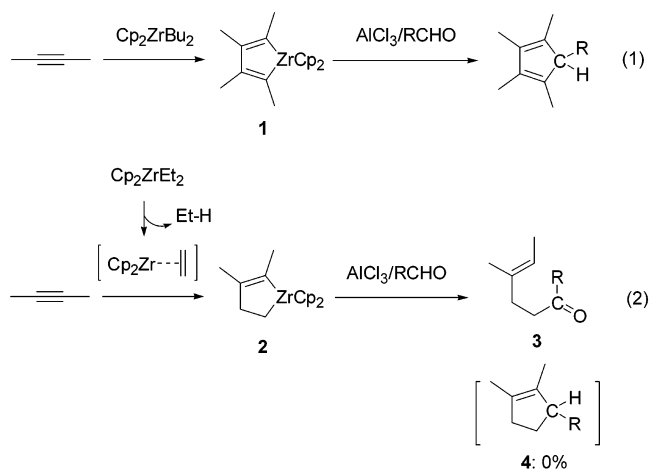
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As part of our continuous interest in Lewis acid and zirconocene mediated intermolecular carbon–carbon bond formation reactions involving carbonyl groups and other unsaturated components, we studied AlCl$_3$-mediated reactions of aldehydes with zirconacyclopentenes **2**.[11] Totally different results from those of Lewis acid mediated reaction of zirconacyclopentadienes **1** with aldehydes were obtained. Linear products, homoallyl ketones **3**, instead of the expected deoxygenative cyclization products **4**, were formed in high yields with excellent selectivities (eq 2).[11] To the best of our knowledge, this was the first example of ketone formation from three different components involving aldehydes, ethylene, and alkynes. In this full investigation, we report (1) effects of different Lewis acids on the reactions of zirconacyclopentenes with aldehydes, (2) preparation of multiply deuterated homoallyketones, and (3) mechanistic aspects.

Results and Discussion

Effects of Different Lewis Acids and Amounts of Lewis Acids and Aldehydes on Formation of Homoallyl Ketones. Addition of freshly sublimed AlCl$_3$ and aldehydes at −78 °C to the reaction mixture of zirconacyclopentenes **2** did not cause any reaction after the mixture was stirred at the same temperature for 1 h.[12] When the reaction temperature was raised to room temperature and the reaction mixture was hydrolyzed with 3 N HCl, homoallyl ketones **3** were formed (Table 1). However, yields of products **3** depended remarkably on the amounts of AlCl$_3$ and aldehydes used. Table 1 shows the effects of different Lewis acids and the amounts of Lewis acids and aldehydes on the formation of homoallyl ketones. When 1 equiv of AlCl$_3$ and 1 equiv of aldehyde were used (entry 1), no product or a trace of products was formed. Similarly, no products were obtained when 2 equiv of AlCl$_3$ and 1 equiv of aldehyde were added (entry 5). Best yields of products were obtained when 2 equiv of AlCl$_3$ and 2 equiv of aldehyde were applied (entry 4). These results show that the amount of aldehydes has a remarkable effect on the formation of homoallyl ketones and provide a useful clue to understand the reaction mechanism.

In addition to AlCl$_3$, other Lewis acids such as AlBr$_3$, AlEtCl$_2$, FeCl$_3$, and SbCl$_3$ (entries 6−9) also were found to be effective for the above reactions. However, no products were observed when Lewis acids such as BF$_3$, B(i-Pr)$_3$, ZnCl$_2$, TiCl$_4$, and SnCl$_4$ were applied (entries 10−15). In a previous report, BF$_3$ was found to be about as effective as AlCl$_3$ for the reactions of zirconacyclopentadienes with aldehydes.[10b]

TABLE 1. Effect of Different Lewis Acids and Amounts of Lewis Acids and Aldehydes on the Formation of Homoalkyl Ketones

entry	Lewis acid (n equiv)	aldehyde (m equiv)	yield of **3a** (%)[a]	yield of **3b** (%)[a]
1	AlCl$_3$ (1.0)	1.0	0	tr
2	AlCl$_3$ (1.0)	2.0	60	45
3	AlCl$_3$ (1.2)	2.0	74	68
4	AlCl$_3$ (2.0)	2.0	87 (65)	82 (53)
5	AlCl$_3$ (2.0)	1.0	0	tr
6	AlBr$_3$ (1.2)	2.0	40	62
7	AlEtCl$_2$ (1.2)	2.0	8	14
8	FeCl$_3$ (1.2)	2.0	37	57
9	SbCl$_3$ (1.2)	2.0	16	13
10	BF$_3$ (1.2)	2.0	0	0
11	BF$_3$ (2.0)	2.0	0	0
12	B(i-Pr)$_3$ (1.2)	2.0	0	0
13	ZnCl$_2$ (1.2)	2.0	0	0
14	TiCl$_4$ (1.2)	2.0	0	0
15	SnCl$_4$ (1.2)	2.0	0	0

[a] GC yields. Yields of isolated products are given in parenthese.

SCHEME 1
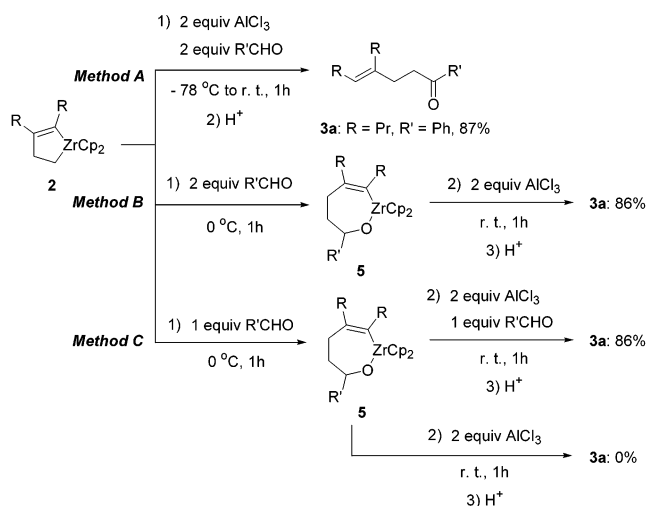
Formation of Homoallyl Ketones 3. As mentioned above, no product was observed when the reaction was carried out at − 78 °C. This indicated that formation of homoallyl ketones **3** might proceed via initial insertion of aldehydes into zirconacyclopentenes, since it has been reported that aldehydes can insert into the Zr–C bond of zirconacyclopentenes **2** at 0 °C or room temperature to form seven-membered oxazirconacycles **5** (Scheme 1).[13,14] Listed in Table 2 are homoallyl ketones obtained via two methods, Method A and Method B shown in

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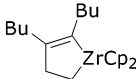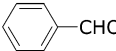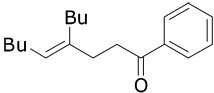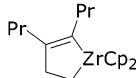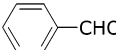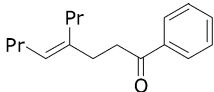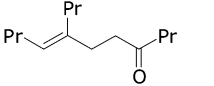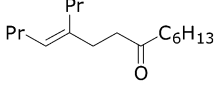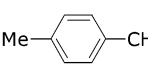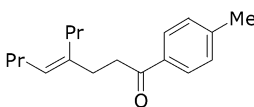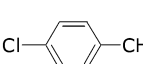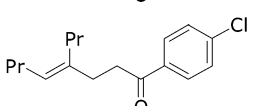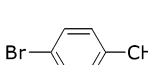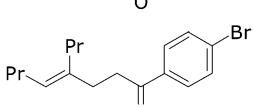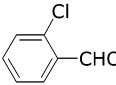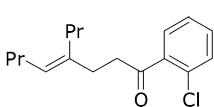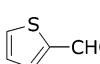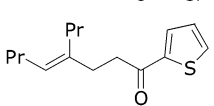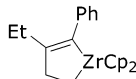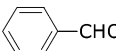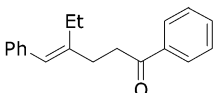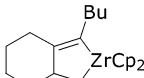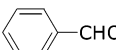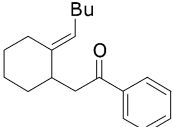
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TABLE 2. Formation of Homoalkyl ketones from Reactions of Zirconacyclopentenes with Aldehydes in the Presence of $AlCl_3$

Zirconacyclopentene 2	Aldehyde	Product 3		Yield of 3/%[a]	
				Method A	Method B
2a	PhCHO		3c	76 (55)	81
2b	PhCHO		3a	87 (65)	79
2b	PrCHO		3b	82 (53)	78
2b	$C_6H_{13}CHO$		3d	70 (59)	72
2b	Me—C6H4—CHO		3e	79 (51)	75
2b	Cl—C6H4—CHO		3f	81 (53)	75
2b	Br—C6H4—CHO		3g	78 (61)	80
2b	(2-Cl)C6H4—CHO		3h	74 (65)	75
2b	thiophene-CHO		3i	70 (48)	65
2c	PhCHO		3j	71 (51)	66
2d	PhCHO		3k	65 (48)	68

[a] GC yields. Isolated yields are given in parentheses.

Scheme 1. In Method A, 2 equiv of $AlCl_3$ and 2 equiv of R′CHO were both added at −78 °C. In Method B, 2 equiv of an aldehyde was first added to zirconacyclopentenes 2 to generate oxazirconacycles 5.[13] Two equivalents of $AlCl_3$ was then added at 0 °C and stirred at room temperature for 1h. As an alternative method, Method C provided 3a in the same yield as that obtained by Method B. Comparable yields of products were obtained by using all three methods. It is noteworthy that when oxazirconacycles 5 were treated only with $AlCl_3$ (no aldehyde was added in the second step of Method C), totally no product formation or trace amounts of products 3 were usually observed. Similarly, in the absence of $AlCl_3$, addition of 1 equiv of benzaldehyde to 5a did not cause any further reaction. In both cases, hydrolysis of the reaction mixture afforded alcohols as reported.[13a] These results further indicated that a second molecule of aldehyde and $AlCl_3$ were needed to give products 3 from oxazirconacycles 5.

(14) It has been reported (refs 12a and 13a) that when a zirconacyclopentene is treated with an aldehyde at 50 °C, a five-membered oxazirconacyclopentene is formed along with release of ethylene. However, if a zirconacyclopentene is treated with an aldehyde at room temperature or 0 °C, a seven-membered oxazirconacycle is formed via insertion.

SCHEME 2
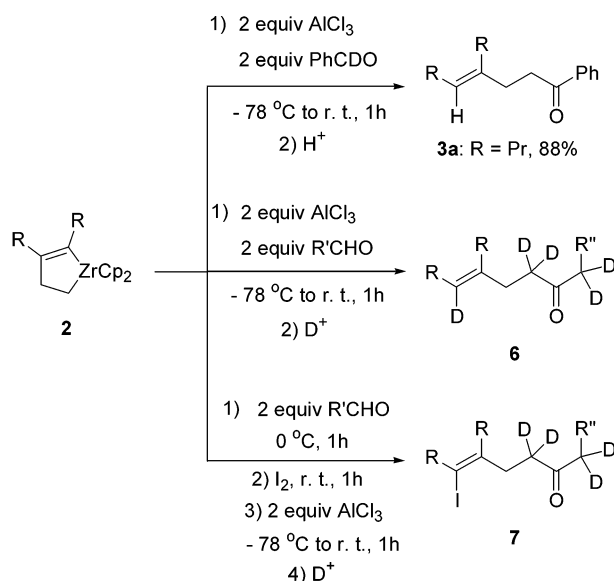
Monocyclic zirconacyclopentenes **2a**, **2b**, and **2c** bearing the same or different substituents could all react with aldehydes in the presence of AlCl$_3$ to afford their corresponding ketone products. A messy mixture was obtained when a zirconacyclopentene bearing SiMe$_3$ at its α-position was used. Bicyclic zirconacyclopentene **2d** reacted similarly to afford **3k** in 65% yield. If the substituent in **2d** was not Bu but rather Ph or SiMe$_3$, reactions with benzaldehydes resulted in messy mixtures.

Preparation of Multiply Deuterated Homoallyl Ketones. Initially, to collect more evidence for understanding the reaction mechanisms, deuteriolysis of the reaction mixtures was carried out (Scheme 2). When PhCDO instead of PhCHO was used, hydrolysis of the reaction mixture with 3 N HCl gave **3a** in 88% yield, with no detectable deuterium incorporation in the product. Significantly, multiply deuterated products **6** with more than 98% of deuterium incorporation were obtained when the reaction mixtures were deuteriolyzed with 20% DCl in D$_2$O (Table 3). Besides the alkenyl carbon, the two β-CH$_2$ moieties of the carbonyl groups were all deuterated, providing a valuable method for otherwise unavailable multiply deuterated ketones. Furthermore, if the reaction mixture of oxazirconacycles **5** was first iodinolyzed with I$_2$, followed by treatment with AlCl$_3$ and then by deuteriolysis with 20% DCl in D$_2$O, monoiodo- multiply deuterated homoallyl ketones **7** were also obtained in high yields (Table 3).

Obviously, there exists a M−C^{sp2} bond in the intermediate, which is deuterated to afford the D−C^{sp2} bond in **6** or iodinolyzed to give I−C^{sp2} bond in **7**. Formation of the two β-CD$_2$ moieties of the carbonyl groups must be explained by D−H exchange during deuteriolysis. However, messy mixtures were obtained when the isolated pure compound **3a** was treated with 20% DCl in D$_2$O both in the presence of and absence of AlCl$_3$.

Mechanistic Aspects. Results shown in Table 1 and Scheme 1 show that the amount of aldehydes played a very important role for the formation of homoallyl ketones. Best yields of products were achieved when two or more equivalents of aldehydes was used. These

TABLE 3. Deuteriolysis of AlCl$_3$-Mediated Reaction Mixtures of Zirconacyclopentenes with Aldehydes

Zirconacyclopentene 2	Aldehyde	Product 6 and 7		Yield of 6 and 7/%[a]
2a	PhCHO		**6a**	82 (58)
2b	PhCHO		**6b**	85 (64)
2b	C$_6$H$_{13}$CHO		**6c**	(55)
2a	C$_6$H$_{13}$CHO		**7a**	60 (38)
2e	C$_6$H$_{13}$CHO		**7b**	64 (45)
2e	PrCHO		**7c**	57 (42)

[a] GC yields. Isolated yields are given in parentheses. D > 98% in most cases.

TABLE 4. Isolation of Alcohols from Lewis Acid Mediated Reaction of Oxazirconacycles with Aldehydes

RCHO	Yield of 3a/%[a]	Yield of 8/%[b]
	86	PhCH$_2$OH (48)
	90	TolylCH$_2$OH (55)

[a] GC yields. [b] Isolated yields.

observations indicated that zirconacyclopentenes were not the true intermediates in these reactions. Oxazirconacycles **5** might be the most likely intermediates. However, a second molecule of aldehyde, together with Lewis acids, was needed to give products **3** from oxazirconacycles **5**. Therefore, we investigated the reaction mixtures to find out what the second equivalent of aldehyde became after the reaction mixture was quenched. As shown in Table 4, an oxazirconacycle **5** was treated with 2 equiv of AlCl$_3$ and 1 equiv of the same or a different aldehyde. Interestingly, in addition to ketone **3a**, an alcohol **8** was also isolated after hydrolysis of the reaction mixture with 3 N HCl. The oxazirconacycle **5**

SCHEME 3

12: 60% (42%)

SCHEME 4

Conclusions

We have reported a multicomponent one-pot procedure for the preparation of homoallyl ketones by combining the zirconocene-mediated C−C bond forming reaction with a Lewis acid−aldehyde adduct-promoted Oppenauer-type oxidation. A variety of homoallyl ketones and multiply deuterated homoallyl ketones were prepared in moderate to good yields.

Experimental Section

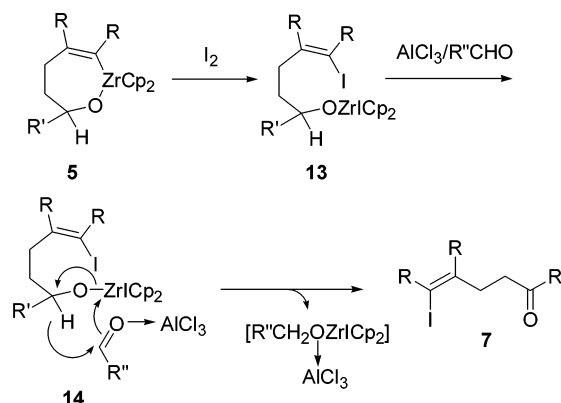**General Methods.** All reactions were conducted under a slightly positive pressure of dry, prepurified nitrogen using standard Schlenk line techniques when appropriate. Unless otherwise noted, all starting materials were commercially available and were used without further purification. Toluene was refluxed and distilled from sodium/benzophenone ketyl under a nitrogen atmosphere. EtMgBr and *n*-BuLi were obtained commercially.

^{1}H and ^{13}C NMR spectra were recorded at 300 and 75.4 MHz, respectively, in CDCl$_3$ unless stated otherwise. GC yields were determined using suitable hydrocarbons as internal standards.

Representative Procedure for Preparation of Homoallyl Ketone 3a. Method A in Scheme 1. A 50-mL Schlenk tube under dried nitrogen was charged with Cp$_2$ZrCl$_2$ (0.59 g, 2 mmol) and toluene (20 mL). To this mixture was added ethylmagnesium bromide (1.0 M THF solution, 4 mmol, 4 mL) at −78 °C. After 1 h of stirring, 4-octyne (0.29 mL, 2 mmol) was added and the reaction mixture was stirred at 0 °C for 3 h. Then to the reaction mixture was added benzaldehyde (0.4 mL, 4 mmol) and freshly sublimed AlCl$_3$ (0.54 g, 4 mmol) at −78 °C. The reaction mixture was warmed to room temperature and stirred at that temperature for 1 h. The above reaction mixture was then quenched with 3 N HCl and extracted with ether. The extract was washed with water and brine and dried over MgSO$_4$. The solvent was evaporated in vacuo to give a light yellow liquid. The liquid was subjected to silica gel column using petroleum ether and dichloromethane (1:1) as the eluent. The final product **3a** was obtained as a colorless liquid. **Method B in Scheme 1.** A 50-mL Schlenk tube under dried nitrogen was charged with Cp$_2$-ZrCl$_2$ (0.59 g, 2 mmol) and toluene (20 mL). To this mixture was added ethylmagnesium bromide (1.0 M THF solution, 4 mmol, 4 mL) at −78 °C. After 1 h of stirring, 4-octyne (0.29 mL, 2 mmol) was added and the reaction mixture was stirred at 0 °C for 3 h. After addition of benzaldehyde (0.4 mL, 4 mmol), the reaction mixture was stirred at 0 °C for 1 h. Freshly sublimed AlCl$_3$ (0.54 g, 4 mmol) was then added to the above reaction mixture at 0 °C. The reaction mixture was warmed to room temperature and stirred at the temperature for 1 h. Hydrolysis of the reaction mixture with aqueous 3 N HCl

was prepared in situ from the reaction of PhCHO (as the first aldehyde) with zirconacyclopentene **2b**. When a different aldehyde (ToylCHO) was used as the second aldehyde, the aldehyde that was incorporated into the product **3a** was exclusively the first aldehyde, and the aldehyde that was reduced to alcohols **8** was exclusively the second aldehyde.

On the basis of these observations, a formal Oppenauer oxidation is assumed to be operating in the reaction between oxazirconacycle **5** and the second molecule of aldehyde in the presence of Lewis acids. In fact, linear alkoxyzirconocenes have been reported to undergo oxidation reactions involving the Oppenauer-type oxidation,[9] ionization mechanism,[15] or hydride attack.[16] We have previously proposed transmetalation of zirconacyclopentadienes to aluminacyclopentadienes as one of the possible paths for the Lewis acid mediated reactions of zirconacyclopentadienes with aldehydes.[10b] However, in this case, transmetalation of oxazirconacycles **5** to oxaaluminacycles seems unlikely. Scheme 3 gives a proposed reaction mechanism. An adduct between AlCl$_3$ and an aldehyde is formed first.[3] Oxazirconacycles **5** then react with the AlCl$_3$−aldehyde adduct via Oppenauer-type oxidation to afford ketone **10**. Hydrolysis of the reaction mixture of **10** affords homoallyl ketones **3** and alcohols **8**. Treatment of the reaction mixture of **10** with allyl bromide and CuCl afforded allylated product **12** in 60% yield.[2] It is known that alkenyl zirconocenes can be transmetalated by CuCl to afford alkenyl copper species such as **11**.[2] Both **10** and **11** are useful organometallic intermediates that can be applied for further reactions. Formation of **7** can be similarly explained by the AlCl$_3$−aldehyde adduct-promoted Oppenauer-type oxidation of linear alkoxyzirconocenes **13**, as illustrated in Scheme 4.

(15) Jordan, R. F. *Adv. Organomet. Chem.* **1991**, *32*, 325.
(16) Negishi, E.; Takahashi, T. *Synthesis* **1988**, 1.

afforded the final product **3a**. **Method C in Scheme 1.** A 50-mL Schlenk tube under dried nitrogen was charged with Cp$_2$ZrCl$_2$ (0.59 g, 2 mmol) and toluene (20 mL). To this mixture was added ethylmagnesium bromide (1.0 M THF solution, 4 mmol, 4 mL) at −78 °C. After 1 h of stirring, 4-octyne (0.29 mL, 2 mmol) was added and the reaction mixture was stirred at 0 °C for 3 h. After addition of benzaldehyde (0.2 mL, 2 mmol), the reaction mixture was stirred at 0 °C for 1 h. Freshly sublimed AlCl$_3$ (0.54 g, 4 mmol) and benzaldehyde (0.2 mL, 2 mmol) were then added to the above reaction mixture at 0 °C. The reaction mixture was warmed to room temperature and stirred at the same temperature for 1 h. Hydrolysis of the reaction mixture with aqueous 3 N HCl afforded the final product **3a**.

Characterization data for products **3a**, **3c**, **3d**, **3e**, **3f**, **3g**, **3h**, and **3i** can be found in Supporting Information of ref 11.

Data for 3b: GC yield 82%, isolated yield 53% (3 mmol scale, 332 mg); ^{1}H NMR (CDCl$_3$, SiMe$_4$) δ 0.79−0.86 (m, 9H), 1.19−1.35 (m, 4H), 1.49−1.56 (m, 2H), 1.85−1.94 (m, 4H), 2.17 (t, J = 7.2 Hz, 2H), 2.31 (t, J = 7.2 Hz, 2H), 5.04 (t, J = 7.2 Hz, 1H); ^{13}C NMR (CDCl$_3$, SiMe$_4$) δ 13.70, 13.75, 14.02, 17.19, 21.48, 23.07, 29.73, 30.69, 32.24, 41.68, 44.69, 125.31, 137.87, 210.95; HRMS calcd for C$_{14}$H$_{26}$O 210.1984, found 210.1978.

Data for 3j: GC yield 71%, isolated yield 51% (268 mg); ^{1}H NMR (CDCl$_3$, SiMe$_4$) δ1.12 (t, J = 7.5 Hz, 3H), 2.30 (q, J = 7.5 Hz, 2H), 2.62 (t, J = 7.2 Hz, 2H), 3.19 (t, J = 7.5 Hz, 2H), 6.30 (s, 1H), 7.18−7.54 (m, 8H), 7.99 (d, J = 8.7 Hz, 2H); ^{13}C NMR (CDCl$_3$, SiMe$_4$) δ 13.10, 23.97, 30.91, 37.46, 125.01, 126.10, 128.06, 128.10, 128.55, 128.62, 133.02, 136.98, 138.15, 143.54, 199.78; HRMS calcd for C$_{19}$H$_{20}$O 264.1514, found 264.1517.

Data for 3k: GC yield 65%, isolated yield 48% (260 mg); ^{1}H NMR (CDCl$_3$, SiMe$_4$) δ 0.86 (t, J = 6.9 Hz, 3H), 1.22−1.78 (m, 10H), 1.93−2.06 (m, 3H), 2.32−2.40 (m, 1H), 2.75−2.80 (m, 1H), 2.89−2.96 (q, J = 7.8 Hz, 1H), 3.19 (dd, J = 4.0 Hz, J = 20.0 Hz, 1H), 5.00 (t, J = 7.2 Hz, 1H), 7.25−7.57 (m, 3H), 7.95 (d, J = 7.2 Hz, 2H); ^{13}C NMR (CDCl$_3$, SiMe$_4$) δ 14.00, 22.24, 24.59, 26.77, 27.63, 27.97, 32.31, 34.05, 40.63, 41.62, 120.71, 128.13, 128.53, 132.80, 137.55, 141.66, 200.28; HRMS calcd for C$_{19}$H$_{26}$O 270.1984, found 270.1987.

Representative Procedure (Method A in Scheme 1) for Preparation of Multiply Deuterated Homoallyl Ketones 6. A 50-mL Schlenk tube under dried nitrogen was charged with Cp$_2$ZrCl$_2$ (0.59 g, 2 mmol) and toluene (20 mL). To this mixture was added ethylmagnesium bromide (1.0 M THF solution, 4 mmol, 4 mL) at −78 °C. After 1 h of stirring, an alkyne (2 mmol) was added and the reaction mixture was stirred at 0 °C for 3 h. Then to the reaction mixture was added aldehyde (4 mmol) and freshly sublimed AlCl$_3$ (0.54 g, 4 mmol) at −78 °C. The reaction mixture was warmed to room temperature and stirred at the same temperature for 1 h. The above reaction mixture was then quenched with DCl (20% in D$_2$O, 2 mL) for 2 h. Normal workup procedure afforded final products **6**.

Characterization data for products **6a** and **6b** can be found in Supporting Information of ref 11.

Data for 6c: isolated yield 55% (283 mg); ^{1}H NMR (CDCl$_3$, SiMe$_4$) 0.86−0.94 (m, 6H), 0.97 (t, J = 7.2 Hz, 3H), 1.21−1.93 (m, 12H), 1.93−2.01 (m, 4H), 2.23 (s, 2H), 5.11 (t, J = 7.2 Hz, D incorporation: >80%); ^{13}C NMR (CDCl$_3$, SiMe$_4$) δ 13.84, 14.03, 14.11, 21.54, 22.50, 23.13, 23.67, 28.90, 29.79, 30.66, 31.62, 32.31, 125.37, 137.93, 211.59; HRMS calcd for C$_{17}$H$_{27}$OD$_5$ 257.2767, found 257.2763.

Representative Procedure (Method A in Scheme 1) for Preparation of Monoiodo Multiply Deuterated Homoallyl Ketones 7. A 20-mL Schlenk tube under dried nitrogen was charged with Cp$_2$ZrCl$_2$ (0.29 g, 2 mmol) and toluene (10 mL). To this mixture was added ethylmagnesium bromide (1.0 M THF solution, 2 mmol, 2 mL) at −78 °C. After 1 h of stirring, an alkyne (1 mmol) was added and the reaction mixture was stirred at 0 °C for 3 h. After addition of an aldehyde (2 mmol), the reaction mixture was stirred at 0 °C for 1 h. The reaction mixture was then treated with I$_2$ (1.2 mmol) at room temperature for 1 h, followed by addition of freshly sublimed AlCl$_3$ (0.27 g, 2 mmol) at 0 °C. The reaction mixture was warmed to room temperature and stirred at that temperature for 1 h. The above reaction mixture was then quenched with DCl (20% in D$_2$O, 1 mL) for 2 h. Normal workup procedure afforded final products **7**.

Data for 7a: GC yield 60%, isolated yield 38% (154 mg); ^{1}H NMR (CDCl$_3$, SiMe$_4$) δ 0.86−0.95 (m, 9H), 1.29−1.57 (m, 16H), 2.14 (t, J = 7.2 Hz, 2H), 2.43−2.52 (m, 4H); ^{13}C NMR (CDCl$_3$, SiMe$_4$) δ 13.92, 14.06, 21.67, 22.52, 22.66, 23.77, 28.90, 30.98, 31.63, 31.69, 32.06, 36.57, 39.63−40.48 (m, CD$_2$), 40.95, 41.82−42.68 (m, CD$_2$), 105.95, 142.70, 210.71; HRMS calcd for C$_{19}$H$_{31}$D$_4$O 283.2939, found 283.2940.

Data for 7b: GC yield 64%, isolated yield 45% (141 mg); ^{1}H NMR (CDCl$_3$, SiMe$_4$) δ 0.93 (t, J = 7.5 Hz, 3H), 0.98 (t, J = 7.5 Hz, 3H), 1.05 (t, J = 7.5 Hz, 3H), 1.62 (t, J = 6.9 Hz, 2H), 2.18 (q, J = 7.5 Hz, 2H), 2.44 (s, 2H), 2.54 (q, J = 7.5 Hz, 2H); ^{13}C NMR (CDCl$_3$, SiMe$_4$) δ 13.53, 13.75, 14.74, 17.23, 24.77, 34.95, 36.16, 39.83−40.43 (m, CD$_2$), 44.06−44.67 (m, CD$_2$), 107.17, 143.50, 210.69; HRMS calcd for C$_{12}$H$_{17}$D$_4$O 185.1844, found 185.1842.

Data for 7c: GC yield 57%, isolated yield 42% (149 mg); ^{1}H NMR (CDCl$_3$, SiMe$_4$) δ 0.88 (t, J = 6.6 Hz, 3H), 0.98−1.08 (m, 6H), 1.29−1.57 (m, 8H), 1.72 (q, J = 7.5 Hz, 2H), 2.44 (s, 2H), 2.50−2.58 (q, J = 7.5 Hz, 2H); ^{13}C NMR (CDCl$_3$, SiMe$_4$) δ 13.53, 14.05, 14.74, 22.51, 23.77, 24.77, 28.89, 31.62, 34.95, 36.16, 39.81−40.40 (m, CD$_2$), 42.21−42.71 (m, CD$_2$), 107.17, 143.52, 210.85; HRMS calcd for C$_{25}$H$_{23}$D$_4$O 227.2313, found 227.2315.

Preparation of Compound 12. A 50-mL Schlenk tube under dried nitrogen was charged with Cp$_2$ZrCl$_2$ (0.59 g, 2 mmol) and toluene (20 mL). To this mixture was added ethylmagnesium bromide (1.0 M THF solution, 4 mmol, 4 mL) at −78 °C. After 1 h of stirring, 4-octyne (0.29 mL, 2 mmol) was added and the reaction mixture was stirred at 0 °C for 3 h. Then to the reaction mixture was added benzaldehyde (0.4 mL, 4 mmol) and freshly sublimed AlCl$_3$ (0.54 g, 4 mmol) at −78 °C. The reaction mixture was warmed to room temperature and stirred at that temperature for 1 h. Copper chloride (0.2 g, 2 mmol) and allyl bromide (0.34 mL, 4 mmol) were added at 0 °C. The mixture was warmed to room temperature and stirred for 3 h. Normal workup afforded the final product **12** as a colorless liquid (239 mg) in 42% isolated yield (GC yield 60%). Characterization data for product **12** can be found in Supporting Information of ref 11.

Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra of **3a**−**3k**, **6a**−**6c**, **7a**−**7c**, and **12**. This material is available free of charge via the Internet at http://pubs.acs.org.

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