JOC The Journal of Organic Chemistry

Note

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Allylmagnesium Halides Do Not React Chemoselectively Because Reaction Rates Approach the Diffusion Limit

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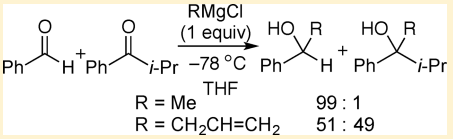
Supporting Information

ABSTRACT: Competition experiments demonstrate that additions of allylmagnesium halides to carbonyl compounds, unlike additions of other organomagnesium reagents, occur at rates approaching the diffusion rate limit. Whereas alkylmagnesium and alkyllithium reagents could differentiate between electronically or sterically different carbonyl compounds, allylmagnesium reagents reacted with most carbonyl compounds at similar rates. Even additions to esters occurred at rates competitive with additions to aldehydes. Only in the case of particularly sterically hindered substrates, such as those bearing tertiary alkyl groups, were additions slower.



Additions of carbon nucleophiles, such as organomagnesium and organolithium reagents, to carbonyl compounds are widely used transformations in synthetic chemistry. Among carbon nucleophiles, allylmetal reagents are especially synthetically useful.[1] Allylmagnesium halides are often used for such functionalizations considering that they are commercially available and highly reactive.[2−6] Their high reactivity enables them to add to hindered carbonyl compounds in cases where other allylmetal reagents may not.[5,6] Additions of allylmagnesium reagents, however, can proceed with lower diastereoselectivity compared to reactions of alkylmagnesium reagents.[7] This lack of stereoselectivity can complicate efforts to devise stereoselective syntheses of target compounds.[8]

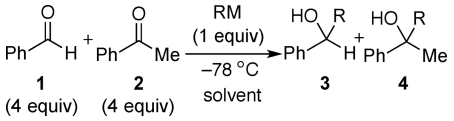
In this Note, we document that allylmagnesium reagents, unlike other organometallic[9,10] and metal hydride[11] reagents, react with most carbonyl compounds at comparable rates. The independence of rate from electronic and moderate steric effects could explain why allylmagnesium halides often do not react with chiral carbonyl compounds diastereoselectively. These studies provide evidence supporting the proposal that additions of allylmagnesium halides to carbonyl compounds occur at the diffusion rate limit.[10]

Intermolecular competition experiments were used to determine the relative rates of additions of different organomagnesium and organolithium reagents to different carbonyl compounds.[10,12] These reagents generally added selectively to an aldehyde in preference to addition to a ketone (Table 1, entries 1−5).[9,10,12] By contrast, allylmagnesium reagents did not differentiate effectively between ketones and aldehydes (Table 1, entries 6−8).[12] The rates of addition to benzaldehyde (**1**) and acetophenone (**2**) were comparable. This lack of selectivity was independent of ethereal solvent or halide counterion.[13]

The competition experiments using allylmagnesium halides required optimization to obtain precise selectivities.[14] The allylmagnesium reagent was kept at a low concentration (≤0.2 M) and added slowly to a dilute (0.1 M) solution of the two carbonyl compounds (one drop, or ∼10 μL,[15] every minute) to minimize the concentration of reagent compared to the electrophiles. A substantial excess of each electrophile (≥4 equiv) was used to ensure that their concentrations were relatively constant and to minimize complications that might be caused by impurities in the specific batches of Grignard reagent.[16] It was also important that the reaction be stirred rapidly. Stirring more slowly, using more concentrated solutions, or adding the reagent too quickly gave slightly different selectivity values (within about 10%) for allylmagnesium reagents than those shown in Table 1.[17,18] Similar effects can be observed for other fast reactions.[19,20]

The low chemoselectivity of additions of allylmagnesium halides to carbonyl compounds was general for a variety of different types of aldehydes and ketones (Scheme 1).

Table 1. Relative Reactivities of Organometallic Reagents with Benzaldehyde (1) and Acetophenone (2)



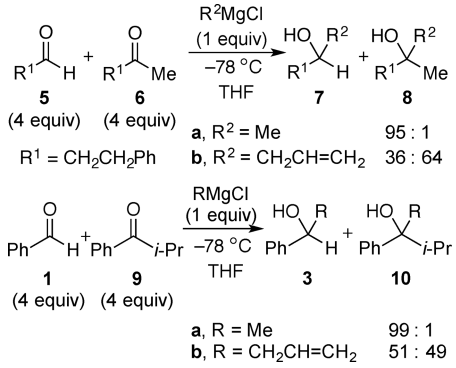
entry	RM	solvent	product	3:4[a]
1	MeMgCl	THF	**a**	221:1
2	MeLi	Et_2O	**a**	244:1
3	*n*-PrMgCl	Et_2O	**c**	143:1
4	$H_2C{=}CHMgBr$	THF	**d**	58:1
5	PhMgCl	THF	**e**	206:1
6	$H_2C{=}CHCH_2MgCl$[b]	THF	**b**	51:49[c]
7	$H_2C{=}CHCH_2MgBr$[b]	THF	**b**	42:58[c]
8	$H_2C{=}CHCH_2MgBr$[b]	Et_2O	**b**	41:59[c]

[a]Ratios determined by GC analysis of the reaction mixture. [b]The reagent was diluted to 0.2 M. [c]Product ratio was corrected for response factors.

Received: January 9, 2017
Published: January 23, 2017

DOI: 10.1021/acs.joc.7b00053
J. Org. Chem. 2017, 82, 2300−2305

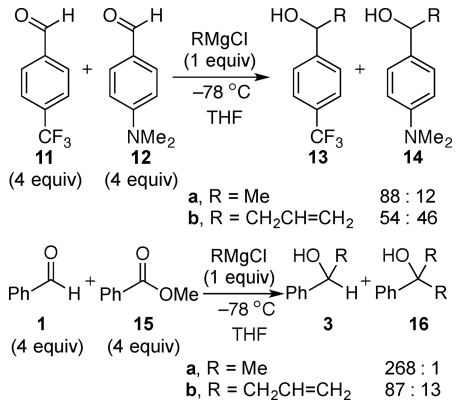
Scheme 1. Relative Rates of Additions to Aliphatic and Sterically Differentiated Carbonyl Compounds



Conjugation and branching had no effect on the lack of chemoselectivity exhibited by allylmagnesium halides. By contrast, competition experiments with MeMgCl confirmed that these nucleophiles reacted much more rapidly with aldehydes compared to ketones.[10,21] The selectivity in the case of methylmagnesium halides provides quantitative support for observations that additions of Grignard reagents to an aldehyde can usually be performed on substrates that also possess a ketone moiety.[22−25]

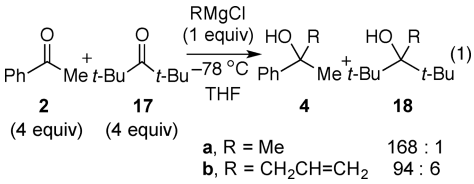
A competition experiment between electronically different carbonyl compounds also illustrates the atypical reactivity of allylmagnesium reagents (Scheme 2). Addition of MeMgCl to

Scheme 2. Relative Rates of Additions to Electronically Differentiated Carbonyl Compounds



an aromatic aldehyde with an electron-withdrawing substituent (**11**) occurred faster than addition to an aldehyde with an electron-donating substituent (**12**), but allylmagnesium halides added at similar rates. In a competition between an aldehyde and a sterically unhindered ester (**1** vs **15**), addition to the electronically stabilized ester was competitive. By comparison, MeMgCl reacted preferentially with the aldehyde, as has been observed for additions of organomagnesium reagents to substrates bearing both an aldehyde and either an ester or lactone functional group.[26−30] The fact that the rates of additions of allylmagnesium reagents are similar[31] but alkylmagnesium reagents are different is consistent with observations that reactions of substituted aryl ketones and aldehydes with allylmagnesium reagents, unlike their alkyl partners, were insensitive to electronic effects.[10,32] Allylmagnesium reagents also did not discriminate between electrophiles bearing different kinds of carbonyl groups, unlike other nucleophiles.[33,34]

Allylmagnesium halides were only able to differentiate between carbonyl compounds when one was considerably more sterically hindered than the other (eq 1). The addition of



allylmagnesium chloride to acetophenone (**2**) to form product **4b** was highly favored over addition to di-*tert*-butyl ketone (**17**). The relative rate of addition, about 20:1, was consistent when the ratios of components were varied (Table 2),

Table 2. Relative Reactivity of Acetophenone (2) vs Di-*tert*-Butyl Ketone (17) as a Function of Number of Equivalents

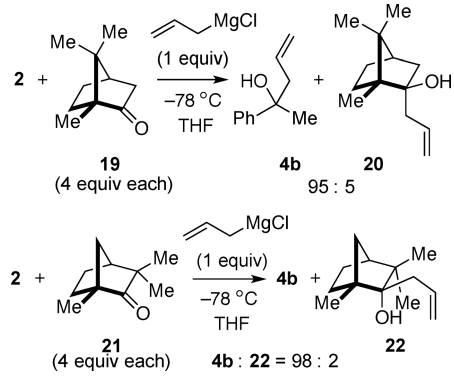
entry	equiv[a] of **2**:**17**	**4b**:**18b**	k_{rel}[b]
1	4:4	94:6	16
2	4:8	90:10	18
3	4:16	83:17	20

[a]Number of equivalents of **2** and **17** compared to allylmagnesium chloride. [b]Ratio corrected for relative number of equivalents of each ketone.

suggesting that the formation of the minor product was not an experimental artifact caused by depletion of the faster-reacting electrophile in the region of the reaction mixture where the reagent was added.[10,35] It was necessary to use the conditions developed for the competition experiments discussed in Table 1: if concentrated (2.0 M) allylmagnesium chloride were added to a mixture of ketones **2** and **17**, substantial loss of chemoselectivity was observed (79:21). The reactivity of the allylmagnesium reagent contrasts with that of MeMgCl, which added much more rapidly to the less sterically hindered ketone.[36]

The ability of a tertiary alkyl group to decrease the rate of addition to a carbonyl group[11] was observed in other systems. Addition to camphor (**19**), another hindered ketone, occurred more slowly than addition to acetophenone (**2**, Scheme 3). In this case, the reaction was diastereoselective (dr = >98:2), as it is for other organometallic reagents.[37−40] Similarly, addition to

Scheme 3. Competition Experiments between Sterically Differentiated Ketones

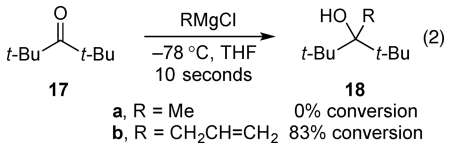


DOI: 10.1021/acs.joc.7b00053
J. Org. Chem. 2017, 82, 2300−2305

fenchone (**21**) was also relatively slow compared to addition to acetophenone (**2**), and addition to the chiral ketone was diastereoselective (dr = 93:7).[40−42] Just as observed with the mixture of ketones **2** and **17**, lower chemoselectivity (82:18) was observed when more concentrated solutions of the nucleophile were added rapidly.

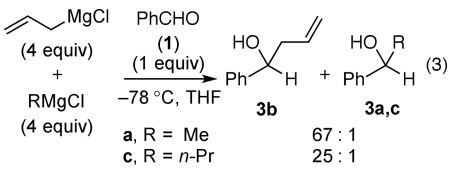
The stereoselective additions to camphor (**19**)[37−40] and fenchone (**21**, Scheme 3)[40,41] represent competition experiments of a different type. Diastereoselectivity requires that additions to the two diastereotopic faces of the ketone occur at different rates. The results from Scheme 3 reveal that even addition to the faster-reacting diastereotopic face of these ketones is slower than addition to acetophenone (**2**); addition to the diastereotopic face leading to the minor product must be even slower.

The general lack of chemoselectivity exhibited by allylmagnesium halides can be correlated to the elevated reactivity of allylmagnesium halides compared to other organomagnesium reagents.[10,35,43−45] The high reactivity of allylmagnesium chloride is illustrated by reactions with an extremely hindered ketone (**17**, eq 2). The reaction of MeMgCl and ketone **17** at



−78 °C was stopped after ten seconds by rapid addition of methanol. Under these conditions, no conversion to product was observed. By contrast, a similar experiment using allylmagnesium chloride resulted in high conversion after ten seconds.[46] The dramatic difference in conversions between methyl- and allylmagnesium reagents,[47] along with the fact that any allylation product **18b** is observed, provides evidence of the high reactivity of allylmagnesium halides with even highly hindered carbonyl compounds.[48]

The high reactivity of allylmagnesium halides compared to other Grignard reagents is also illustrated by competition experiments between organomagnesium halides.[10] Benzaldehyde (**1**) was added to a solution containing an excess of allylmagnesium chloride and an alkylmagnesium chloride (eq 3). Selectivity for the allylated product **3b** was observed. Taken

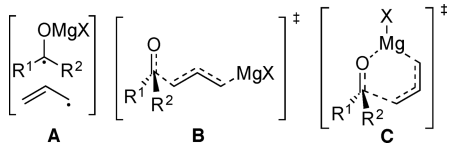


together, the results from eq 3 highlight how much more reactive allylmagnesium halides are than other Grignard reagents.

The lack of chemoselectivity exhibited for reactions involving allylmagnesium halides and the sensitivity to how the competition experiments were conducted[19,20] provide evidence that these additions occur at rates near the diffusion rate limit.[10,43,44,49] As the rates of additions approach the diffusion rate limit ($k_2 \approx 10^9$ M^{-1} s^{-1}),[50] these rates will converge on the same value.[50,51] Selectivity, which represents the ratio of rates of addition to different carbonyl compounds, would approach unity, as observed (Table 1, Scheme 1, and Scheme 2).

The diastereoselectivities observed are also consistent with the high reactivity of allylmagnesium reagents. Whereas additions to unhindered ketones could proceed at the diffusion rate limit, additions to hindered ketones could be slower, as observed for selective addition to acetophenone (**2**) in the presence of di-*tert*-butyl ketone (**17**, eq 1). In the case of the hindered ketones camphor (**19**) and fenchone (**21**), additions to both diastereotopic faces would be slower than diffusion, which could result in diastereoselectivity. With less hindered electrophiles, however, additions of allylmagnesium reagents to both faces could occur at rates approaching the diffusion limit, so the reactions would not be diastereoselective, as is often observed.[7]

The reactivity-selectivity relationships exhibited by allylmagnesium halides are difficult to reconcile with one reaction mechanism. Single-electron transfer may occur in reactions with aromatic carbonyl compounds, forming species such as **A**.[10,52,53] By contrast, single-electron pathways are unlikely to be involved in additions to aliphatic carbonyl compounds.[54] Experimental results have been used to support an open, S_E2'-like transition state (**B**),[44] although computational studies suggest that a closed six-membered ring transition state, such as **C**, is favored.[55] Regardless of the mechanism, which could depend upon the electrophile, addition must be particularly rapid to be consistent with the reactivity-selectivity relationships reported here.



In conclusion, allylmagnesium halides, unlike other organometallic reagents, do not generally exhibit chemoselectivity in reactions with carbonyl compounds. Allylmagnesium reagents do not differentiate between carbonyl compounds unless one is particularly sterically hindered. The elevated reactivity of these reagents even allows addition to an ester to be competitive with addition to an aldehyde. Additions to chiral ketones demonstrate that selectivity can be obtained when nucleophilic attack to at least one diastereotopic face occurs more slowly than addition to an unhindered carbonyl compound. The reactions of allylic Grignard reagents appear to be influenced primarily by the steric environment of the electrophile rather than electronic factors, supporting the conclusion that these reactions proceed at rates approaching the diffusion limit.

EXPERIMENTAL SECTION

^{1}H NMR spectra were obtained at room temperature using spectrometers at 400, 500, or 600 MHz, and ^{13}C NMR spectra were recorded at 100, 125, or 150 MHz, respectively. Spectroscopic data are reported as follows: chemical shifts are reported in ppm on the δ scale, referenced to residual solvent (^{1}H NMR: $CDCl_3$ δ 7.26; ^{13}C NMR: $CDCl_3$ δ 77.2),[56] multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet), coupling constants (Hz), and integration. Ratios of product to starting material for conversion studies were obtained by ^{1}H NMR, using a single scan. For the conversion experiments, products were identified by diagnostic peaks in the crude reaction mixture, drawing upon spectroscopic data of the pure compounds synthesized. Competition experiment product distributions were determined by gas chromatography (GC), using a gas chromatograph with the carrier gas (helium) set to 15 psi and equipped with a capillary column (14% cyanopropylphenyl, 86% methylpolysiloxane, 30 m × 0.321 mm × 0.25 μm). The infrared (IR) spectrum was obtained by a spectrometer using attenuated total

DOI: 10.1021/acs.joc.7b00053
J. Org. Chem. 2017, 82, 2300−2305

reflectance (ATR). The high-resolution mass spectrum (HRMS) was acquired on a time-of-flight spectrometer and was obtained using peak matching. The ionization source used was atmospheric pressure chemical ionization (APCI). Liquid chromatography was performed using forced flow (flash chromatography) of the indicated solvent system on silica gel (SiO_2, 230−400 mesh). Tetrahydrofuran and diethyl ether were dried by filtration through activated alumina. All dry reactions were run in flame-dried glassware under a stream of nitrogen. Grignard reagents were purchased from vendors. The concentrations of the Grignard reagents were assumed to be near the concentrations reported by the supplier. Over time, some reagents were titrated[57] to maintain an accurate measure of their concentration. Preparative experiments were performed with additional reagent to ensure complete conversion. Compounds **3a**, **3b**, **3c**, **3d**, **3e**, **4a** (i.e., **16a**), **4c**, **4e**, and **7a** are commercially available. Compounds **4b**,[58,59] **4d**,[60] **7b**,[59,61] **8a**,[62,63] **8b**,[59,64] **10a**,[65,66] **14a**,[67,68] **16b**,[69] **20**,[38,40] and **22**[38,40] were prepared by known methods.

Representative Procedure for Competition Experiments between Two Carbonyl Compounds with Alkyllithium, Alkylmagnesium, and Alkenylmagnesium Reagents (Alcohols 3a and 4a). To a cooled (−78 °C) solution of benzaldehyde (0.031 mL, 0.30 mmol) and acetophenone (0.035 mL, 0.30 mmol) in THF (3.0 mL) was added methylmagnesium chloride (0.025 mL, 3.0 M solution in THF, 0.075 mmol) dropwise over 1 min. After stirring for 1 h, MeOH (1 mL) was added, the reaction mixture was warmed to room temperature, and an aliquot of the reaction mixture (1 mL) was filtered through a plug of SiO_2 and analyzed by GC (oven temperature = 100 °C) to show a 221:1 mixture of products **3a**:**4a**, using the retention times of authentic samples prepared as a reference.

Representative Procedure for Optimized Competition Experiments between Two Carbonyl Compounds with Allylmagnesium Chloride in THF (Alcohols 4b and 20). To a cooled (−78 °C) and vigorously stirred solution of acetophenone (0.070 mL, 0.60 mmol) and (±)-camphor (0.091 g, 0.60 mmol) in THF (6.0 mL) was added allylmagnesium chloride (0.75 mL, 0.20 M solution in THF, 0.15 mmol) dropwise over 75 min by syringe pump. After all of the nucleophile was added, MeOH (1 mL) was added, and the reaction mixture was warmed to room temperature. An aliquot of the reaction mixture (1 mL) was filtered through a plug of SiO_2 and analyzed by GC (oven temperature = 110 °C) to show a 94:6 mixture of products **4b**:**20**, using the retention times of authentic samples prepared as a reference. Due to the presence of FID response factors, this ratio was corrected to 95:5 using a GC to ^{1}H NMR calibration curve (second-order polynomial regression, $y = 0.0017x^2 + 0.8243x + 0.0799$, $R^2 = 1.000$), where, for the less substituted product, y = the percentage by GC and x = the percentage by ^{1}H NMR spectroscopy. This curve was derived from seven mixtures of pure alcohols **4b** and **20** (ranging from 97:3 to 3:97), which were analyzed by ^{1}H NMR followed by GC.

Calibration curves were also used to correct the ratios of alcohols **3b**:**4b** (second-order polynomial regression, $y = -0.0007x^2 + 1.0798x - 2.0917$, $R^2 = 0.9982$) as well as **4b**:**18b** (second-order polynomial regression, $y = 0.0009x^2 + 0.9128x + 0.1748$, $R^2 = 0.9999$). Product ratios of other compound mixtures were not corrected due to the small deviations (0−5%) observed in these product ratios resulting from FID response factors in mixtures of **4b**:**20**, **3b**:**4b**, and **4b**:**18b**.[70]

Representative Procedure for Additions of Allylmagnesium Halides to Carbonyl Compounds (2-Methyl-3-phenylhex-5-en-3-ol (10b)). To a cooled (−78 °C) solution of isobutyrophenone (0.050 g, 0.34 mmol) in THF (1.0 mL) was added allylmagnesium chloride (0.20 mL, 2.0 M solution in THF, 0.40 mmol) dropwise over 2 min. After 15 min, MeOH (1 mL) was added, and the mixture was concentrated *in vacuo*. H_2O (7 mL) and HCl (2 mL, 1.0 M in H_2O) were added and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography (3:97 EtOAc:hexanes) afforded alcohol **10b** as a colorless oil (0.059 g, 92%). The spectroscopic data are consistent with the data reported in the literature:[71] ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40−7.36 (m, 2H), 7.35−7.30 (m, 2H), 7.25−7.21 (m, 1H), 5.48 (dddd, J = 17.0, 10.0, 9.0, 5.5, 1H), 5.16−5.11 (m, 1H), 5.09−5.05 (m, 1H), 2.82 (ddt, J = 13.8, 5.5, 1.3, 1H), 2.54 (dd, J = 13.8, 9.1, 1H), 2.02 (sept, J = 6.8, 1H), 1.94 (br d, J = 1.3, 1H), 0.95 (d, J = 6.8, 3H), 0.77 (d, J = 6.9, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.2, 134.1, 127.9, 126.4, 126.2, 119.7, 77.9, 44.1, 38.1, 17.6, 16.9; IR (ATR) 3562, 2964, 1637, 1445, 995, 701 cm^{-1}; HRMS (APCI) m/z calcd for $C_{13}H_{17}$ ((M+H) − H_2O)$^+$ 173.1325, found 173.1322.

Representative Procedure for Additions of Alkyl- and Alkenylmagnesium Halides to Carbonyl Compounds (1-(4-(Trifluoromethyl)phenyl)ethan-1-ol (13a)). To a cooled (0 °C) solution of 4-(trifluoromethyl)benzaldehyde (0.061 g, 0.35 mmol) in THF (2.0 mL) was added methylmagnesium chloride (0.24 mL, 3.0 M solution in THF, 0.72 mmol) dropwise over 2 min. After 3 h, H_2O (7 mL) and HCl (2 mL, 1.0 M in H_2O) were added, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The resulting oil was purified by flash chromatography (15:85 EtOAc:hexanes) to afford alcohol **13a** as a colorless oil (0.057 g, 85%). The spectroscopic data are consistent with the data reported in the literature:[72] ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61 (d, J = 8.2, 2H), 7.49 (d, J = 8.2, 2H), 4.97 (q, J = 6.4, 1H), 1.95 (br, 1H), 1.51 (d, J = 6.5, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 149.8, 129.8 (q, J = 32), 125.8, 125.6 (q, J = 4), 124.3 (q, J = 272), 70.0, 25.5.

1-(4-(Trifluoromethyl)phenyl)but-3-en-1-ol (13b). Following the representative procedure for additions of allylmagnesium halides to carbonyl compounds, alcohol **13b** was prepared using 4-(trifluoromethyl)benzaldehyde (0.052 g, 0.30 mmol) and allylmagnesium chloride (0.23 mL, 2.0 M solution in THF, 0.46 mmol) in THF (2.0 mL). Purification by flash chromatography (10:90 EtOAc:hexanes) afforded **13b** as a colorless oil (0.058 g, 90%). The spectroscopic data are consistent with the data reported in the literature:[59] ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61 (d, J = 8.2, 2H), 7.48 (d, J = 8.1, 2H), 5.86−5.73 (m, 1H), 5.24−5.15 (m, 2H), 4.85−4.78 (m, 1H), 2.62−2.41 (m, 2H), 2.15 (br s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 147.9, 133.8, 129.8 (q, J = 32), 126.2, 125.5 (q, J = 4), 124.3 (q, J = 272), 119.4, 72.6, 44.1.

1-(4-(Dimethylamino)phenyl)but-3-en-1-ol (14b). Following the representative procedure for additions of allylmagnesium halides to carbonyl compounds, alcohol **14b** was prepared using 4-(dimethylamino)benzaldehyde (0.050 g, 0.34 mmol) and allylmagnesium chloride (0.20 mL, 2.0 M solution in THF, 0.40 mmol) in THF (2.0 mL). Purification by flash chromatography (25:75 EtOAc:hexanes, with silica gel that had been pretreated with a solution of 1% Et_3N in hexanes) afforded **14b** as a yellow oil (0.061 g, 97%). The spectroscopic data are consistent with the data reported in the literature:[73] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27−7.21 (m, 2H), 6.76−6.71 (m, 2H), 5.82 (ddt, J = 17.2, 10.2, 7.1, 1H), 5.20−5.09 (m, 2H), 4.65 (t, J = 6.5, 1H), 2.95 (s, 6H), 2.56−2.49 (m, 2H), 1.95 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 135.2, 132.0, 127.0, 117.9, 112.6, 73.4, 43.6, 40.8.

2,2,3,4,4-Pentamethylpentan-3-ol (18a). Following the representative procedure for additions of alkyl- and alkenylmagnesium halides to carbonyl compounds, conducted instead at 20 °C, alcohol **18a** was prepared using hexamethylacetone (0.100 mL, 0.579 mmol) and methylmagnesium chloride (0.58 mL, 3.0 M in THF, 1.7 mmol) in THF (2.0 mL). Purification by flash chromatography (3:97 EtOAc:hexanes) afforded **18b** as a white solid (0.072 g, 79%). The spectroscopic data are consistent with the data reported in the literature:[74] mp 41−43 °C, lit.[74] 39−41 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.26 (s, 1H), 1.16 (s, 3H), 1.07 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 79.6, 41.2, 28.9, 21.7.

3-(tert-Butyl)-2,2-dimethylhex-5-en-3-ol (18b). Following the representative procedure for additions of allylmagnesium halides to carbonyl compounds, conducted instead at 20 °C, alcohol **18b** was prepared using hexamethylacetone (0.072 g, 0.51 mmol) and allylmagnesium bromide (0.60 mL, 1.0 M in Et_2O, 0.60 mmol) in THF (0.5 mL). Alcohol **18b** was formed cleanly as a colorless oil (0.083 g, 88% unpurified yield), and the spectroscopic data are consistent with the data reported:[74] ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95 (ddt, J = 17.6, 10.1, 7.5, 1H), 5.20−5.05 (m, 2H), 2.47 (dt, J =

DOI: 10.1021/acs.joc.7b00053
J. Org. Chem. 2017, 82, 2300−2305

7.5, 1.1, 2H), 1.57 (s, 1H), 1.07 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.4, 118.7, 79.1, 42.5, 38.1, 28.9.

Representative Procedure for 10-s Experiment (Alcohol 18b). To a cooled (−78 °C) and vigorously stirred solution of hexamethylacetone (0.070 g, 0.49 mmol) in THF (2.5 mL) was added allylmagnesium chloride (0.50 mL, 2.0 M solution in THF, 1.0 mmol) all at once. After 10 s, MeOH (1 mL) was added all at once. After 10 min at −78 °C, the reaction mixture was warmed to room temperature and concentrated *in vacuo*. H_2O (5 mL) and HCl (1 mL, 1.0 M in H_2O) were added, and the aqueous layer was extracted with CH_2Cl_2 (3 × 7 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. ^{1}H NMR spectroscopic analysis of the crude reaction mixture revealed 83% conversion to product **18b**, based on the ratio of **18b** to starting material (**17**). The spectroscopic data (^{1}H and ^{13}C NMR) match the data reported for alcohol **18b** above.

Procedure for Competition Experiments between Allyl- and Methylmagnesium Chloride for Benzaldehyde (Alcohols 3b and 3a). To a cooled (−78 °C) solution of methylmagnesium chloride (0.34 mL, 3.0 M solution in THF, 1.0 mmol) and allylmagnesium chloride (0.50 mL, 2.0 M solution in THF, 1.0 mmol) in THF (9.2 mL) was added benzaldehyde (2.5 mL, 0.10 M solution in THF, 0.25 mmol) dropwise over 10 min. After stirring for 15 min, MeOH (1 mL) was added, and the reaction mixture was warmed to room temperature. An aliquot of the reaction mixture (1 mL) was filtered through a plug of SiO_2 and analyzed by GC (oven temperature = 100 °C) to show a 67:1 mixture of products **3b**:**3a**, using the retention times of authentic samples prepared as a reference.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00053.

Selected spectra and chromatograms (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Acknowledgment is made to the Donors of the American Chemical Society Petroleum Research Fund for partial support of this research (57206-ND1). Additional support was provided by the National Institutes of Health, National Institute of General Medical Sciences (GM-61066). J.A.R. thanks the NYU Department of Chemistry for support in the form of a Margaret Strauss Kramer Fellowship. K.A.W. thanks the Global Research Initiatives, NYU and NYU Florence, for a fellowship. We thank Dr. Chin Lin (NYU) for assistance with NMR spectroscopy and mass spectrometry.

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DOI: 10.1021/acs.joc.7b00053
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