

HETEROCYCLES, Vol. 93, No. 2, 2016, pp. 833 - 844. © 2016 The Japan Institute of Heterocyclic Chemistry
Received, 18th November, 2015, Accepted, 6th January, 2016, Published online, 20th January, 2016
DOI: 10.3987/COM-15-S(T)65

MAGNESIUM-ALKOXIDE DIRECTED PHOTOADDITION OF TETRAHYDROFURANS TO γ,γ -DISUBSTITUTED ALLYLIC ALCOHOLS

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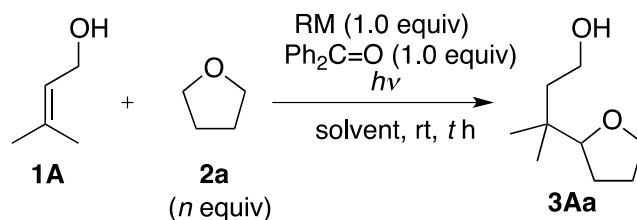
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Abstract – Magnesium-alkoxide directed photoaddition of tetrahydrofurans to γ,γ -disubstituted allylic alcohols was achieved. When the allylic alcohols were treated with Grignard reagent in THF under light, the corresponding γ -(2-tetrahydrofuryl) substituted alcohols were regioselectively obtained in up to 82% yield. The conversion of the hydroxyl group to the corresponding bromomagnesium alkoxide was crucial.

The development of the direct transformation of C–H bonds into C–C bonds is a critical challenge in synthetic organic chemistry. The functionalization of C(sp³)–H bonds is particularly advantageous for the construction of highly complex molecules.¹ Photoinduced intermolecular addition reactions onto C=C bonds are among the most attractive methods in green chemistry that have been studied.² Of these, photofunctionalization of tetrahydrofurans is one of the most investigated transformations.^{3,4}

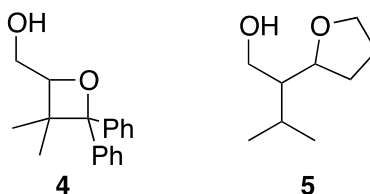
In order to control the regioselectivity in the photoreaction, hydroxy group is one of the most useful functional groups. For example, hydroxy directed Paternò-Büchi reactions of carbonyl compounds with allylic alcohols were reported to give the corresponding oxetanes regio- and diastereoselectively.⁵ However the metal directed photoreaction has scarcely been reported although various metal-promoted photoreactions were reported.² Herein, we describe the magnesium-alkoxide directed regioselective photoaddition of tetrahydrofurans to γ,γ -disubstituted allylic alcohols to realize regioselective C–C bond formation at disubstituted olefinic carbons of the allylic alcohols.

During the examination of the Paternò-Büchi reaction, we confirmed that the reaction of benzophenone with prenoI (**1A**) in benzene under light gave the cycloadduct **4^{5c}** regioselectively in 61% yield (Table 1,

Table 1. The photoaddition of tetrahydrofuran (**2a**) to prenol (**1A**)

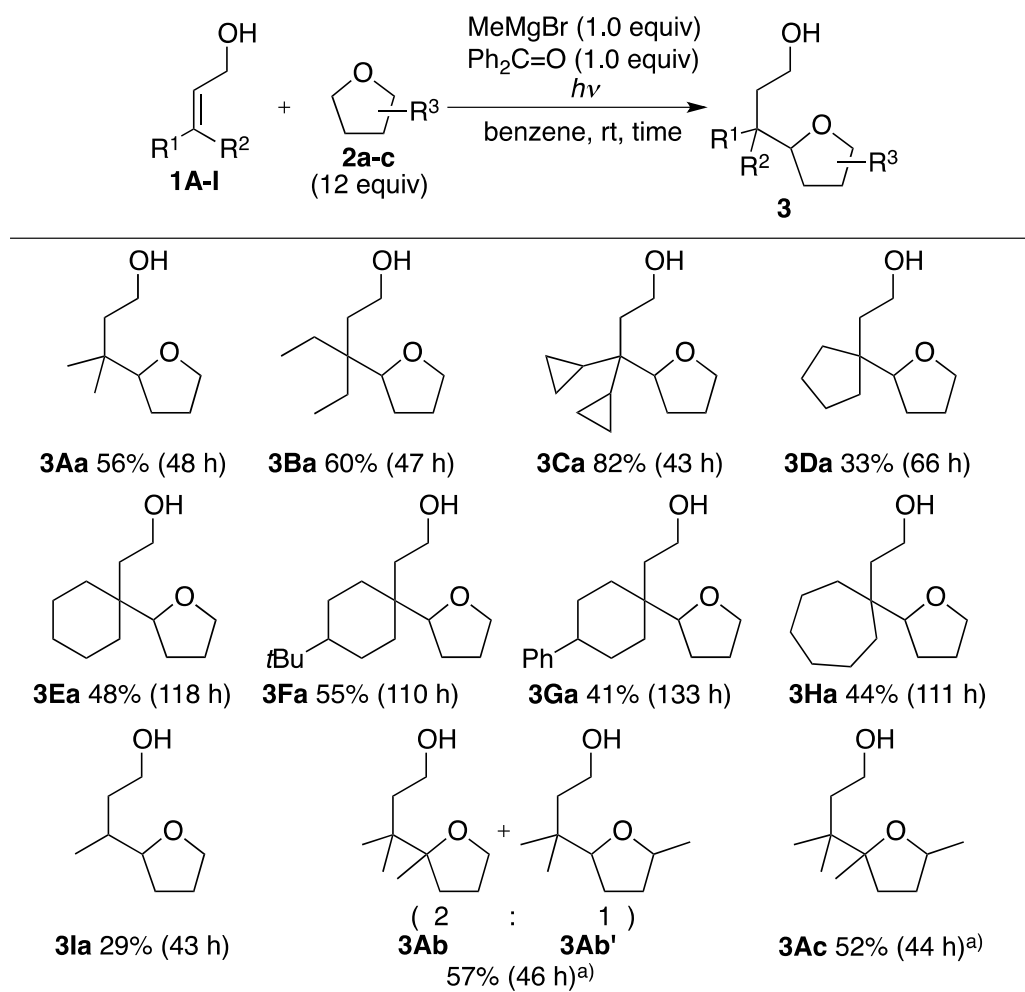
Entry	RM	<i>n</i> /equiv	solvent	<i>t</i> /h	Yield/%
1 ^{a)}	---	--	benzene	38	-- ^{b)}
2 ^{a)}	MeMgBr in THF	12 ^{c)}	benzene	48	56
3 ^{d)}			benzene	24	52
4 ^{a,e)}			benzene	44	--
5 ^{a)}			CH ₂ Cl ₂	65	53
6 ^{a)}			MeCN	62	29
7 ^{a)}			Et ₂ O	69	18
8 ^{a)}			THF	64	29
9 ^{a)}	EtMgBr in Et ₂ O	10 ^{f)}	benzene	66	39
10 ^{a)}	<i>i</i> -PrMgCl in Et ₂ O	10 ^{f)}	benzene	24	10
11 ^{a)}	MeMgI in Et ₂ O	10 ^{f)}	benzene	47	38
12 ^{a)}	Bu ₂ Mg in hepane	10 ^{f)}	benzene	24	--
13 ^{a)}	<i>n</i> -BuLi in hexane	10 ^{f)}	benzene	24	--
14 ^{a)}	Et ₂ Zn in hexane	10 ^{f)}	benzene	21	--
15 ^{a)}	Me ₃ Al in hexane	10 ^{f)}	benzene	24	13

a) The reaction was carried out using a 300 W high-pressure mercury lamp in Pyrex vessels through aqueous CuSO₄ filter. b) The Paternò-Büchi product **4** was obtained in 61% yield. c) The amount of THF calculated based on the concentration of the Grignard reagent used. d) The reaction was carried out using a 450 W high-pressure mercury lamp in Pyrex vessels through aqueous CuSO₄ filter. e) Benzophenone was not added to the reaction. f) THF was independently added to the reaction.

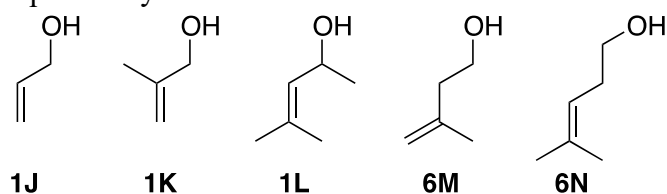


Entry 1). In contrast, the photoreaction of benzophenone with the bromomagnesium salt of prenil (**1A**), generated in situ from prenil and MeMgBr in tetrahydrofuran (THF, **2a**), was examined under light. To our surprise, the production of the desired oxetane **4** was not observed and the tetrahydrofuran addition product **3Aa** was obtained in 56% yield (Entry 2). Regioisomer **5** was not isolated. The difference in power between a 300 W and 450 W lamp had little influence on the chemical yield (Entries 2 and 3). In the absence of benzophenone, the THF adduct **3Aa** was not produced (Entry 4).⁶ The photoalkylation to prenil (**1A**) was carried out in other solvents by the use of a THF solution of MeMgBr (Entries 2, 5–8). Among the solvents examined, benzene and CH₂Cl₂ realized higher chemical yields (Entries 2 and 5). Coordinating solvents slightly retarded the reaction (Entries 6–8). Et₂O was less effective than THF (Entries 7 and 8). When THF was added independently by the use of an Et₂O solution of EtMgBr, the THF adduct **3Aa** was also obtained in 39% yield (Entry 9).⁷ The photo-induced alkylation reaction of THF (**2a**) was carried out via generation of the corresponding metal alkoxide by treatment with the appropriate metallic reagents (Entries 10–15). When **1A** was treated with *i*-PrMgCl, the addition product **3Aa** was obtained in lower yield (Entry 10). In the case of the iodomagnesium salt of **1A** generated from MeMgI, **3Aa** was produced (Entry 11); however, the use of Bu₂Mg as a metallic reagent did not afford **3Aa** (Entry 12). Generation of lithium alkoxide and zinc alkoxide using *n*-BuLi and Et₂Zn, respectively, was not effective at all (Entries 13 and 14). Treatment with Me₃Al furnished the adduct **3Aa** in 13% yield (Entry 15).

The magnesium-mediated photoaddition of tetrahydrofurans **2** to allylic alcohols **1** was performed by treatment with a THF solution of MeMgBr in benzene at rt, and the results are summarized in Table 2. The reaction of 3-ethyl-2-penten-1-ol (**1B**) gave the product **3Ba** in 60% yield. The reaction of di(cyclopropyl)-substituted allylic alcohol **1C** gave the product **3Ca** in 82% yield. In the case of allylic alcohols with cyclic 5-, 6-, and 7-membered skeletons **1D–1H**, the photoalkylation reaction proceeded to afford the products **3Da–3Ha** in 33–55% yields. Although the addition reaction to a γ -monosubstituted alcohol, crotyl alcohol (**1I**), proceeded to give the adduct **3Ia**, the corresponding THF adduct was not observed in the case of unsubstituted allyl alcohol (**1J**). Furthermore, the photoreactions of methallyl alcohol (**1K**), 1,3-dimethyl-2-butenol (**1L**), 3-methyl-3-buten-1-ol (**6M**), and 4-methyl-3-penten-1-ol (**6N**) did not produce the corresponding THF adducts. Substituted tetrahydrofurans, 2-methyltetrahydrofuran (**2b**) and 2,5-dimethyltetrahydrofuran (**2c**), could be used as substrates to give the corresponding adducts **3Ab** (+**3Ab'**) and **3Ac**.

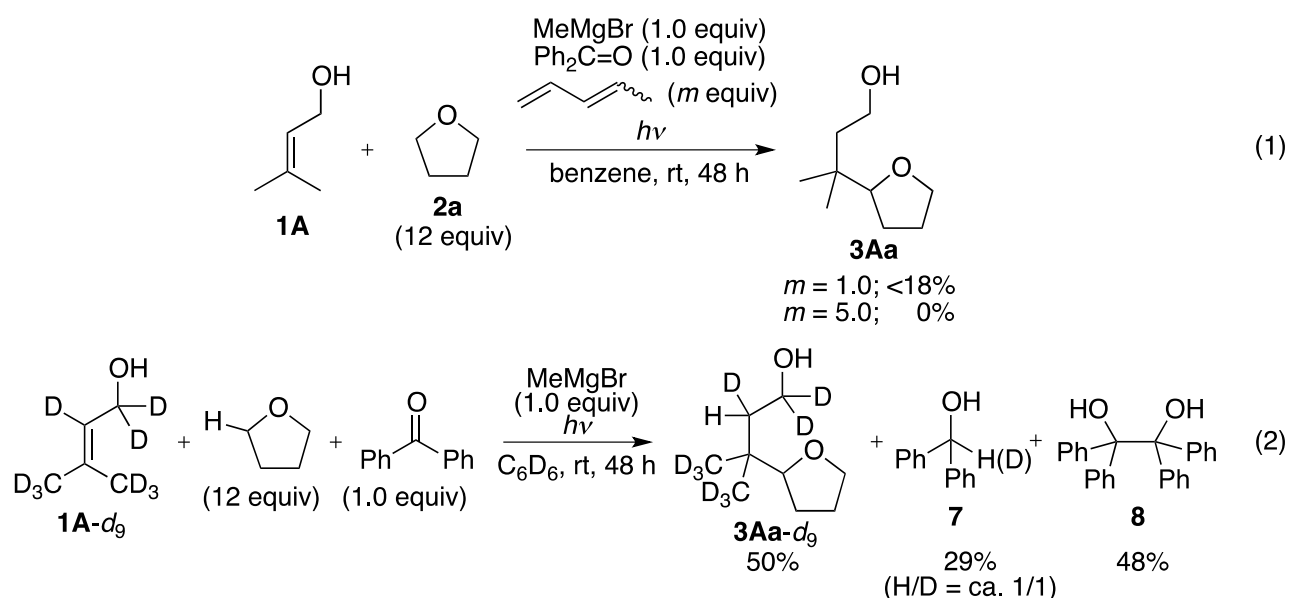
Table 2. The photoaddition of tetrahydrofurans **2** to allylic alcohols **1**

a) EtMgBr in Et₂O was used instead of MeMgBr in THF and **2b** or **2c** (10 equiv) was independently added.



In order to gain further insight of this process, the following reactions were performed. Piperylene, 1,3-pentadiene, is known as a triplet quencher.^{8,9} The photoaddition reaction in the presence of piperylene was found to be messy. When 5 equiv of piperylene was used, **3Aa** was not obtained (Eq. 1). In addition, the photoaddition using deuterated prenil (**1A-d₉**)¹⁰ was examined (Eq. 2): The corresponding deuterated adduct **3Aa-d₉** was obtained in 50% yield. The introduction of H at the β -position in **3Aa-d₉** was confirmed by ¹H NMR analysis using COSY and HMQC measurements. Furthermore, diphenylmethanol (Ph₂CHOH/Ph₂CDOH = ca. 1/1) (**7**) and a dimer **8** were also isolated in 29% and 48% yields, respectively.

From the results above, the highly reactive triplet benzophenone T₁ might be photochemically generated from benzophenone S₀ and it might abstract a hydrogen from the electron-rich etheral C(sp³)-H bond of tetrahydrofuran to generate the corresponding α -oxy radical^{2,3,4} and the subsequent addition of the generated α -oxy radical to allylic alcohol proceeds via radical pathway. Although α -hydrogen of tetrahydrofuran was confirmed to be finally transferred onto β -position of allylic alcohol, the regioselectivity of the addition of the generated α -oxy radical to the olefinic moiety in γ,γ -disubstituted allylic alcohol could not yet be well elucidated.



In conclusion, we achieved a regioselective photoaddition of tetrahydrofurans to γ,γ -disubstituted allylic alcohols to afford the γ -(2-tetrahydrofuryl) substituted alcohols. The conversion of the hydroxy group to the corresponding bromomagnesium alkoxide by the treatment with Grignard reagent was crucial toward the addition reaction itself and the regioselectivity. The present magnesium-alkoxide directed photoreaction and the revealed reactivity and regioselectivity were quite unique and unprecedented although various metal-promoted photoreactions were reported.² Further investigations to understand the mechanism of this reaction and the applications toward other organic reactions are currently underway in our laboratory.

EXPERIMENTAL

¹H NMR spectroscopy was performed in CDCl₃ using a JEOL ECS 400 NMR (400 MHz) spectrometer. Chemical shifts (δ) were determined relative to TMS ($\delta = 0$ ppm) as an internal standard. ¹³C NMR spectroscopy was performed in CDCl₃ on a JEOL ECS 400 NMR (100 MHz) spectrometer and chemical shifts (δ) were determined relative to CDCl₃ ($\delta = 77.0$ ppm) as an internal standard. IR spectra were

acquired on a JASCO FT/IR-230 spectrometer. Mass spectra were obtained using JMS-700, JMS-T100TD, and Bruker microtof II mass spectrometers. All solvents were distilled prior to use and stored over drying agents. The photoreactions were carried out using a 300W (Eikosha EHB-WIF-300) high-pressure mercury lamp or a 450 W (Ushio UM-452) high-pressure mercury lamp in Pyrex vessels through aqueous CuSO₄ filter. Merck silica gel 60 PF254 (Art. 7749), Cica silica gel 60N spherical neutral (37563-84), and JAIGL-SIL (s-043-15) were used for thin-layer chromatography (TLC), flash column chromatography, and recycle HPLC, respectively. The retention factors (*R_f*) of various compounds were determined by TLC.

Starting Materials. Allylic alcohols **1B**,¹¹ **1C**,¹² **1D**,¹¹ **1E**,¹¹ **1F**,¹³ **1G**,¹³ **1H**,¹⁴ and **1A-d₉**¹⁰ were prepared from the corresponding ketones by Horner-Wadsworth-Emmons reaction followed by the reduction according to reported procedures.

Typical Procedure for the Photoaddition of Tetrahydrofuran to Allylic Alcohol 1A. To a solution of prenol (**1A**, 43 mg, 0.5 mmol) in benzene (1 mL) was added 0.92 M methylmagnesium bromide in tetrahydrofuran (0.54 mL, 0.5 mmol) and stirred for 30 min under Ar atmosphere. After benzophenone (91 mg, 0.5 mmol) in benzene (1 mL) was added to the reaction mixture, the resulted solution was irradiated in a photoreactor for 48 h. Saturated NH₄Cl aqueous solution was added to the reaction mixture and aqueous layer was separated and extracted with AcOEt. The combined organic layers were washed with brine, dried over Na₂SO₄ and evaporated. The residue was purified by flash column chromatography (hexane/AcOEt = 3:1, v/v) to afford **3Aa** (44 mg, 56%).

3-Methyl-3-(tetrahydrofuran-2-yl)butan-1-ol (3Aa): An oil; *R_f* = 0.2 (hexane/AcOEt = 3:1); ¹H NMR (CDCl₃, 400 MHz): δ = 0.89 (s, 3H), 0.91 (s, 3H), 1.50–1.70 (m, 3H), 1.77–1.92 (m, 3H), 3.40–3.73 (m, 4H), 3.77 (dt, 1H, *J* = 8.2, 6.9 Hz), 3.84 (dt, 1H, *J* = 8.2, 6.9 Hz); ¹H NMR (CD₃OD, 400 MHz): δ = 0.795 (s, 3H), 0.800 (s, 3H), 1.38–1.51 (m, 2H), 1.52–1.62 (m, 1H), 1.68–1.80 (m, 3H), 3.44–3.51 (m, 1H), 3.54 (t, 2H, *J* = 7.3 Hz), 3.59–3.71 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ = 21.5, 25.7, 25.9, 26.3, 35.6, 44.0, 58.9, 68.1, 86.3; ¹³C NMR (CD₃OD, 100 MHz) δ = 23.3, 24.0, 27.1, 27.2, 36.7, 43.0, 59.6, 69.2, 88.0; IR (neat) 3399, 2962, 2872, 1469, 1388, 1364, 1073, 1021, 977, 929 cm⁻¹; HRMS (ESI-TOF) calcd for C₉H₁₈O₂Na [M+Na]⁺: 181.1205, found 181.1203.

3-Ethyl-3-(tetrahydrofuran-2-yl)pentan-1-ol (3Ba): Compound **3Ba** (56 mg, 60%) was obtained from **1B** (57 mg, 0.5 mmol) and 0.92 M methylmagnesium bromide in tetrahydrofuran (0.54 mL, 0.5 mmol). An oil; *R_f* = 0.2 (hexane/AcOEt = 3:1); ¹H NMR (CDCl₃, 400 MHz): δ = 0.80 (t, 3H, *J* = 7.6 Hz), 0.83 (t, 3H, *J* = 7.6 Hz), 1.18–1.29 (m, 1H), 1.36–1.58 (m, 4H), 1.63–1.91 (m, 5H), 3.59–3.73 (m, 4H), 3.89 (dt, 2H, *J* = 8.2, 6.9 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ = 7.5, 7.6, 25.3, 25.4, 26.0, 26.7, 37.1, 40.1, 58.5, 67.5, 84.7; IR (neat) 3389, 2966, 2878, 1463, 1381, 1053, 1015, 925, 871 cm⁻¹; HRMS (ESI-TOF) calcd for C₁₁H₂₂O₂Na [M+Na]⁺: 209.1518, found 199.1512.

3,3-Dicyclopropyl-3-(tetrahydrofuran-2-yl)propan-1-ol (3Ca): Compound **3Ca** (85 mg, 82%) was obtained from **1C** (69 mg, 0.5 mmol) and 0.91 M methylmagnesium bromide in tetrahydrofuran (0.55 mL, 0.5 mmol). An oil; $R_f = 0.3$ (hexane/AcOEt = 3:1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz): $\delta = 0.17\text{--}0.32$ (m, 5H), 0.33–0.43 (m, 2H), 0.46–0.55 (m, 1H), 0.55–0.64 (m, 1H), 0.75–0.82 (m, 1H), 1.08–1.15 (m, 1H), 1.24–1.31 (m, 1H), 1.80–2.02 (m, 4H), 3.70–3.91 (m, 5H), 4.23 (t, 1H, $J = 5.7$ Hz); $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz): $\delta = -1.91, -1.50, -0.09, 1.35, 12.9, 14.3, 25.5, 26.6, 35.0, 37.6, 58.4, 68.0, 86.5$; IR (neat) 3398, 3081, 2951, 2871, 1446, 1355, 1281, 1178, 1059, 928 cm^{-1} ; HRMS (ESI-TOF) calcd for $\text{C}_{13}\text{H}_{22}\text{O}_2\text{Na}$ $[\text{M}+\text{Na}]^+$: 233.1518, found 233.1517.

2-[1-(Tetrahydrofuran-2-yl)cyclopentyl]ethanol (3Da): Compound **3Da** (30 mg, 33%) was obtained from **1D** (56 mg, 0.5 mmol) and 0.92 M methylmagnesium bromide in tetrahydrofuran (0.54 mL, 0.5 mmol). An oil; $R_f = 0.2$ (hexane/AcOEt = 3:1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz): $\delta = 1.33\text{--}1.41$ (m, 1H), 1.49–1.70 (m, 9H), 1.71–1.95 (m, 4H), 3.35 (br, 1H), 3.65 (br, 1H), 3.69–3.77 (m, 3H), 3.85–3.94 (m, 1H); $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz): $\delta = 25.2, 25.3, 25.6, 26.8, 34.3, 35.6, 40.9, 47.6, 59.5, 68.0, 86.1$; IR (neat) 3393, 2950, 2868, 1451, 1184, 1068, 924, 867 cm^{-1} ; HRMS (ESI-TOF) calcd for $\text{C}_{11}\text{H}_{20}\text{O}_2\text{Na}$ $[\text{M}+\text{Na}]^+$: 207.1361, found 207.1360.

2-[1-(Tetrahydrofuran-2-yl)cyclohexyl]ethanol (3Ea): Compound **3Ea** (48 mg, 48%) was obtained from **1E** (63 mg, 0.5 mmol) and 0.92 M methylmagnesium bromide in tetrahydrofuran (0.54 mL, 0.5 mmol). An oil; $R_f = 0.2$ (hexane/AcOEt = 3:1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz): $\delta = 1.15\text{--}1.93$ (m, 3H), 1.15–1.31 (m, 4H), 1.32–1.45 (m, 4H), 1.46–1.61 (m, 5H), 3.56–3.76 (m, 3H), 3.72 (dt, 1H, $J = 8.3, 6.9$ Hz), 3.87 (dt, 1H, $J = 8.3, 6.9$ Hz), 3.98 (br, 1H); $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz): $\delta = 21.2, 21.3, 25.3, 26.2, 31.8, 32.8, 35.7, 38.0, 58.4, 67.8, 86.9$; IR (neat) 3391, 2927, 2860, 2238, 1717, 1683, 1454, 1352, 1287, 1184, 1060, 923, 734, 702, 668 cm^{-1} ; HRMS (DART) calcd for $\text{C}_{12}\text{H}_{23}\text{O}_2$ $[\text{M}+\text{H}]^+$: 199.1698, found 199.1707.

2-[4-*t*-Butyl-1-(tetrahydrofuran-2-yl)cyclohexyl]ethanol (3Fa): Compound **3Fa** (70 mg, 55%) was obtained from **1F** (91 mg, 0.5 mmol) and 0.92 M methylmagnesium bromide in tetrahydrofuran (0.54 mL, 0.5 mmol) as a single isomer. An oil; $R_f = 0.2$ (hexane/AcOEt = 3:1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz): $\delta = 0.84$ (s, 9H), 0.88–0.99 (m, 1H), 1.03–1.27 (m, 4H), 1.46–1.92 (m, 10H), 3.51 (dd, 1H, $J = 9.2, 6.4$ Hz), 3.60–3.67 (m, 3H), 3.69–3.76 (m, 1H), 3.86 (dt, 1H, $J = 9.2, 6.9$ Hz); $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz): $\delta = 21.9, 22.1, 25.4, 25.5, 27.5, 31.0, 32.4, 33.4, 34.4, 37.8, 48.2, 58.4, 67.8, 88.5$; IR (neat) 3400, 2942, 2867, 1455, 1364, 1065, 921 cm^{-1} ; HRMS (DART) calcd for $\text{C}_{16}\text{H}_{31}\text{O}_2$ $[\text{M}+\text{H}]^+$: 255.2324, found 255.2326.

2-[4-Phenyl-1-(tetrahydrofuran-2-yl)cyclohexyl]ethanol (3Ga): Compound **3Ga** (56 mg, 41%) was obtained from **1G** (101 mg, 0.5 mmol) and 0.92 M methylmagnesium bromide in tetrahydrofuran (0.54 mL, 0.5 mmol) as a single isomer. An oil; $R_f = 0.2$ (hexane/AcOEt = 3:1); $^1\text{H NMR}$ (CDCl_3 , 400 MHz): $\delta = 1.21\text{--}1.46$ (m, 2H), 1.51–1.66 (m, 3H), 1.70–2.05 (m, 9H), 2.46 (tt, 1H, $J = 12.1, 3.7$ Hz), 3.57–3.61 (dd,

1H, $J = 9.2, 6.4$ Hz), 3.61–3.82 (m, 4H), 3.89 (dt, 1H, $J = 8.2, 6.9$ Hz), 7.15–7.23 (m, 3H), 7.27–7.32 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 25.4, 25.6, 28.8, 28.9, 30.8, 33.1, 34.6, 37.7, 44.3, 58.4, 67.9, 88.2, 126.0, 126.7, 128.3, 147.1$; IR (neat) 3392, 3025, 2928, 2862, 1602, 1493, 1450, 1064, 922, 757, 700 cm^{-1} ; HRMS (ESI-TOF) calcd for $\text{C}_{18}\text{H}_{26}\text{O}_2\text{Na}$ $[\text{M}+\text{Na}]^+$: 297.1831, found 297.1836.

2-[1-(Tetrahydrofuran-2-yl)cycloheptyl]ethanol (3Ha): Compound **3Ha** (47 mg, 44%) was obtained from **1H** (70 mg, 0.5 mmol) and 0.92 M methylmagnesium bromide in tetrahydrofuran (0.54 mL, 0.5 mmol). An oil; $R_f = 0.2$ (hexane/AcOEt = 3:1); ^1H NMR (CDCl_3 , 400 MHz): $\delta = 1.28\text{--}1.96$ (m, 18H), 3.54–3.69 (m, 3H), 3.72 (dt, 1H, $J = 8.2, 6.4$ Hz), 3.87 (dt, 2H, $J = 8.2, 6.9$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 22.7, 23.1, 25.4, 25.6, 31.0, 31.1, 35.0, 36.0, 40.0, 41.2, 58.6, 67.5, 85.8$; IR (neat) 3405, 2924, 2856, 1461, 1445, 1060, 702 cm^{-1} ; HRMS (ESI-TOF) calcd for $\text{C}_{13}\text{H}_{24}\text{O}_2\text{Na}$ $[\text{M}+\text{Na}]^+$: 235.1674, found 235.1673.

3-(Tetrahydrofuran-2-yl)butan-1-ol (3Ia): Compound **3Ia** (21 mg, 29%) was obtained as a 3:1 mixture of diastereomers from **1I** (43 mg, 0.5 mmol) and 0.91 M methylmagnesium bromide in tetrahydrofuran (0.55 mL, 0.5 mmol). An oil; $R_f = 0.2$ (hexane/AcOEt = 3:1); ^1H NMR (CDCl_3 , 400 MHz): $\delta = 0.91$ (d, 2.25H, $J = 6.4$ Hz), 0.95 (s, 0.75H, $J = 6.9$ Hz), 1.42–2.04 (m, 7H), 2.27 (br, 1H), 3.49–3.55 (m, 0.75H), 3.59–3.66 (m, 1H), 3.70–3.80 (m, 2.25H), 3.82–3.90 (m, 1H); ^{13}C NMR (CDCl_3 , 100 MHz): major $\delta = 17.7, 25.6, 30.2, 37.2, 38.7, 61.5, 67.8, 84.4$; minor $\delta = 15.7, 25.8, 27.8, 34.4, 35.9, 60.7, 68.0, 83.2$; IR (neat) 3399, 2963, 2874, 1460, 1380, 1065, 967, 925 cm^{-1} ; HRMS (FAB) calcd for $\text{C}_8\text{H}_{17}\text{O}_2$ $[\text{M}+\text{H}]^+$: 145.1229, found 145.1224.

Typical Procedure for the Photoaddition of 2-Methyltetrahydrofuran to Allylic Alcohol 1A. To a solution of prenyl (**1A**, 43 mg, 0.5 mmol) in benzene (1 mL) was added 3.0 M ethylmagnesium bromide in Et_2O (0.17 mL, 0.5 mmol) and stirred for 30 min under Ar atmosphere. After benzophenone (91 mg, 0.5 mmol) in benzene (1 mL) and 2-methyltetrahydrofuran (**2b**) (430 mg, 5 mmol) were sequentially added, the resulted solution was irradiated in a photoreactor for 46 h. Saturated NH_4Cl aqueous solution was added to the reaction mixture and aqueous layer was separated and extracted with AcOEt. The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated. The residue was purified by flash column chromatography (hexane/AcOEt = 3:1, v/v) to give a 2:1 mixture of 3-methyl-3-(2-methyl-tetrahydro-furan-2-yl)-butan-1-ol (**3Ab**) and 3-methyl-3-(5-methyl-tetrahydro-furan-2-yl)-butan-1-ol (**3Ab'**) (49 mg, 57%). The mixture of **3Ab** and **3Ab'** was further separated by recycle HPLC to afford **3Ab** and **3Ab'**.

3-Methyl-3-(2-methyltetrahydrofuran-2-yl)butan-1-ol (3Ab): An oil; ^1H NMR (CDCl_3 , 400 MHz): $\delta = 0.93$ (s, 3H), 0.96 (s, 3H), 1.20 (s, 3H), 1.36 (dt, 1H, $J = 10.1, 4.6$ Hz), 1.49–1.57 (m, 1H), 1.75–2.02 (m, 4H), 3.54–3.63 (m, 1H), 3.71–3.81 (m, 2H), 3.82–3.94 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): $\delta = 21.6,$

22.1, 25.9, 26.7, 33.4, 39.5, 42.1, 59.3, 68.0, 87.6; IR (neat) 3369, 2969, 1467, 1372, 1301, 1144, 1094, 1047, 923, 849, 730 cm^{-1} ; HRMS (FAB) calcd for $\text{C}_{10}\text{H}_{21}\text{O}_2$ $[\text{M}+\text{H}]^+$: 173.1542, found 173.1540.

3-Methyl-3-(5-methyltetrahydrofuran-2-yl)butan-1-ol (3Ab'): A ca 3:1 mixture of diastereomers. ^1H NMR (CDCl_3 , 400 MHz): δ = 0.87 (s, 2.25H), 0.88 (s, 2.25H), 0.89 (s, 0.75H), 0.91 (s, 0.75H), 1.22 (d, 3H, J = 6.0 Hz), 1.35–1.90 (m, 3.5H), 1.57 (t, 1.5H, J = 6.0 Hz), 1.92–2.07 (m, 1H), 3.54–3.74 (m, 2.25H), 3.78 (dd, 0.75H, J = 10.1, 6.0 Hz), 3.88–4.12 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz): major δ = 20.5, 21.3, 26.3, 27.7, 34.1, 35.9, 45.1, 59.0, 75.9, 85.5; minor δ = 20.8, 21.5, 26.1, 26.4, 32.6, 35.4, 44.1, 58.9, 75.3, 86.4; IR (neat) 3392, 2966, 2871, 1469, 1383, 1085, 1041, 881 cm^{-1} ; HRMS (FAB) calcd for $\text{C}_{10}\text{H}_{21}\text{O}_2$ $[\text{M}+\text{H}]^+$: 173.1542, found 173.1540.

3-(2,5-Dimethyltetrahydrofuran-2-yl)-3-methylbutan-1-ol (3Ac): Compound **3Ac** (48 mg, 52%) was obtained as a ca 3:1 mixture of the diastereomers from **1A** (57 mg, 0.5 mmol) and 3.0 M ethylmagnesium bromide in Et_2O (0.17 mL, 0.5 mmol) and 2,5-dimethyltetrahydrofuran (1:1 mixture of *cis*- and *trans*-isomer; 501 mg, 5 mmol). An oil; R_f = 0.3 (hexane/AcOEt = 5:1); ^1H NMR (CDCl_3 , 400 MHz): δ = 0.89 (s, 2.25H), 0.91 (s, 0.75H), 0.97 (s, 3H), 1.22 (d, 0.75H, J = 6.4 Hz), 1.23 (s, 3H), 1.24 (d, 2.25H, J = 6.0 Hz), 1.28 (ddd, 0.25H, J = 15.2, 5.0, 3.2 Hz), 1.35–1.41 (m, 0.25H), 1.48–1.65 (m, 3H), 1.91–2.10 (m, 3H), 3.22 (br, 1H), 3.51–3.60 (m, 1H), 3.70–3.80 (m, 1H), 3.96–4.04 (m, 0.75H), 4.10–4.18 (m, 0.25H); ^{13}C NMR (CDCl_3 , 100 MHz): major δ = 21.2, 21.9, 23.9, 26.9, 33.8, 34.4, 39.8, 42.1, 59.2, 77.0, 87.6; minor δ = 20.7, 21.5, 21.9, 27.0, 33.4, 34.0, 38.9, 42.2, 59.2, 73.8, 87.7; IR (neat) 3369, 2968, 2876, 1462, 1378, 1097, 1051, 1005, 953, 879 cm^{-1} ; HRMS (FAB) calcd for $\text{C}_{11}\text{H}_{23}\text{O}_2$ $[\text{M}+\text{H}]^+$: 187.1698, found 187.1690.

Photoaddition of Tetrahydrofuran to Allylic Alcohol 1A-*d*₉: To a solution of preno-*d*₉ (**1A-*d*₉**, 48 mg, 0.5 mmol) in C_6D_6 (1 mL) was added 0.91 M methylmagnesium bromide in tetrahydrofuran (0.55 mL, 0.5 mmol) and stirred for 30 min under Ar atmosphere. After benzophenone (91 mg, 0.5 mmol) in C_6D_6 (1 mL) was added to the reaction mixture, the resulted solution was irradiated in a photoreactor for 48 h. Saturated NH_4Cl aqueous solution was added to the reaction mixture and aqueous layer was separated and extracted with AcOEt. The combined organic layers were washed with brine, dried over Na_2SO_4 and evaporated. The residue was purified by flash column chromatography (hexane/AcOEt = 3:1, v/v) to **3Aa** in 50% yield (41 mg, a ca 1:1 mixture of diastereomers), diphenylmethanol (**7**) (27 mg, 29%, as a ca 1:1 mixture of $\text{Ph}_2\text{CHOH}^{15}$ and $\text{Ph}_2\text{CDOH}^{16}$), and 1,1,2,2-tetraphenylethane-1,2-diol (**8**)¹⁷ (44 mg, 48%).

3-Methyl-3-(tetrahydrofuran-2-yl)butan-1-ol-*d*₉ (3Aa-*d*₉): An oil; R_f = 0.2 (hexane/AcOEt = 3:1); ^1H NMR (CDCl_3 , 400 MHz): δ = 1.52 (s, 0.5H), 1.58 (s, 0.5H), 1.60–1.69 (m, 1H), 1.77–1.91 (m, 3H), 3.53–3.62 (m, 2H), 3.74–3.80 (m, 1H), 3.85 (dt, 1H, J = 8.2, 6.9 Hz); ^1H NMR (CD_3OD , 400 MHz): δ = 1.38 (s, 0.5H), 1.43 (s, 0.5H), 1.50–1.62 (m, 1H), 1.68–1.80 (m, 3H), 3.40–3.53 (m, 1H), 3.55–3.72 (m, 2H), one OH proton was not observed; ^{13}C NMR (CDCl_3 , 100 MHz): δ = 20.5 (m), 25.7, 26.0 (m), 26.3, 35.1, 43.4

(t, $J = 19$ Hz), 58.8 (m), 68.2, 86.3; IR (neat) 3346, 2903, 2230, 2194, 2059, 1265, 1086, 1047, 965 cm^{-1} ; HRMS (DART) calcd for $\text{C}_9\text{H}_{10}\text{D}_9\text{O}_2$ $[\text{M}+\text{H}]^+$: 168.1950, found 168.1949.

ACKNOWLEDGEMENTS

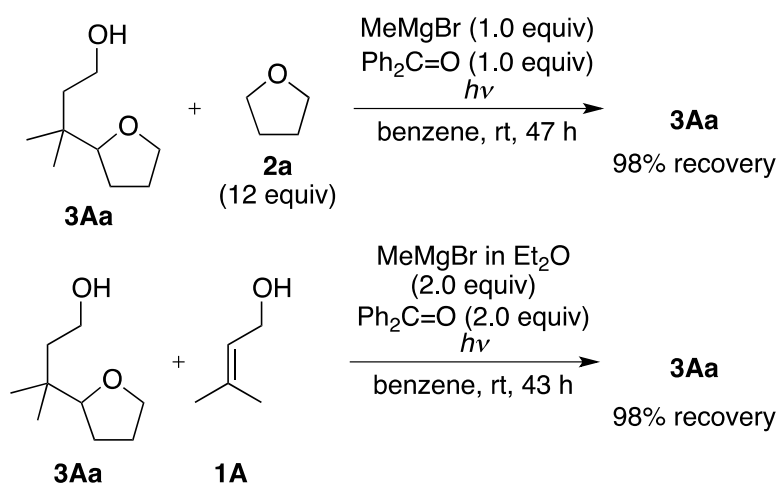
Acknowledgements may be included as a separate section. This work was financially supported in part by a Grant-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (JSPS), Kanazawa University SAKIGAKE Project, and Kanazawa University CHOZEN Project.

Dedicated with respect to Professor Lutz F. Tietze on the occasion of his 75th birthday.

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6. Among the photosensitizers examined, benzophenone gave **3Aa** in highest chemical yield: By the use of 4,4'-dichlorobenzophenone and 4,4'-difluorobenzophenone instead benzophenone, **3Aa** was obtained in 39% and 52 % yields, respectively. In the case of 4,4'-di(methoxy)benzophenone, the corresponding Paternò-Büchi product was obtained in 43% yield. When anthraquinone was used as a photosensitizer, the reaction became complicated and the desired adduct **3Aa** was not obtained. Furthermore, no reaction proceeded by the use of phenanthrene.
7. The produced THF adduct might not be subjected to further transformation under the photoreaction conditions. When the bromomagnesium salt of **3Aa** was irradiated in the presence of THF or bromomagnesium salt of prenil (**1A**), **3Aa** was recovered almost quantitatively as shown below.



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