Tetrahedron Letters 52 (2011) 426–429

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Catalytic reactions of bis-π-allylpalladium generated from allyltrifluoroborate

Hiroyuki Nakamura *, Kazuki Shimizu

Department of Chemistry, Faculty of Science, Gakushuin University, Mejiro, Toshima-ku, Tokyo 171-8588, Japan

ARTICLE INFO

Article history:
Received 19 October 2010
Revised 11 November 2010
Accepted 15 November 2010
Available online 18 November 2010

Keywords:
Bis-π-allylpalladium
Allylation
Amphiphilic
Allyltrifluoroborate

ABSTRACT

Bis-π-allylpalladium-catalyzed nucleophilic allylations to aldehydes **2** and imines **3** have been achieved by replacing allylstannanes with allyltrifluoroborate. Amphiphilic bisallylation of activated olefins **6** with allyltrifluoroborate and allyl acetate also proceeded smoothly in the presence of $Pd_2(dba)_3 \cdot CHCl_3$ and tricyclohexylphosphine catalysts.

Since the discovery of carbon–carbon bond formation in π-allylpalladium complexes[1] with carbon nucleophiles,[2–4] palladium has become one of the most useful metals in organic synthesis.[5,6] The π-allylpalladium complexes are key electrophilic intermediates in the Tsuji–Trost allylation reaction and react with various nucleophiles.

In previous studies, we found that bis-π-allylpalladium complexes[7] react with electrophiles, such as aldehydes[8] and imines,[9,10] in a nucleophilic manner (Fig. 1). The presence or absence of ligands controls the reactivity of the bis-π-allylpalladium complexes,[11] and they undergo chemoselective allylic addition to aldehydes or imines in the absence of phosphine ligands.[12] Furthermore, bis-π-allylpalladium complexes display amphiphilic reactivity with activated olefins to give the bisallylated products 1,7-octadienes in high yields.[13] This catalytic amphiphilic bisallylation can be applied to the synthesis of medium-sized carbocycles.[14] Wallner and Szabó demonstrated the detailed regio- and stereoselectivity of bis-π-allylpalladium complexes by density functional calculations.[15,16] Recently, Itami and co-workers discovered the regioselective unsymmetrical tetraallylation of C_{60} using the catalytic amphiphilic bis-π-allylpalladium reaction.[17] Not only bis-π-allylpalladium complexes but also pincer-type π-allyl-Pd–Ar complexes display nucleophilic allylation to electrophiles.[18,19]

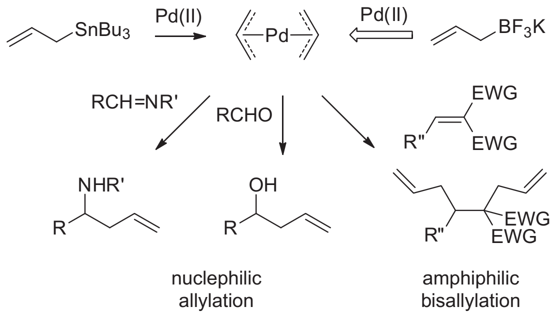


Figure 1. Catalytic reactions of bis-π-allylpalladium.

In general, in addition to bis-π-allylpalladium formation from the dimerization of butadienes,[20] bis-π-allylpalladium complexes utilized for nucleophilic allylation and amphiphilic bisallylation may be generated by the transmetalation of π-allylpalladium complexes with allylstannanes in a catalytic cycle. However, there are disadvantages to the use of organostannanes because of their toxicity as well as their byproducts. We focused on the use of allyltrifluoroborate in catalytic bis-π-allylpalladium reactions. Since the discovery of the Suzuki–Miyaura coupling reaction,[21] much attention has been paid to organoboranes. The most interesting feature of organoboranes and their byproducts is that they are less toxic compared to other organometallic reagents, in particular, organostannanes. Recently, potassium trifluoroborates, among the other organoboranes, have been utilized widely as equivalents to the corresponding organoboronic acids for Suzuki–Miyaura-type coupling reactions due to their stability, achieved without decreasing their high reactivity.[22] Malinakova and co-workers demonstrated palladium-catalyzed bisfunctionalization of allenyl esters for synthesis of unsaturated γ-lactines.[23] Furthermore, Lewis acid[24] or palladium-catalyzed[25] allylations and the allylation in a biphasic medium (CH_2Cl_2/H_2O)[26] of carbonyl compounds have been developed by using allylic boranes and/or borates. In this Letter, we describe an alternative catalytic system of bis-π-allylpalladium complexes generated from allyltrifluoroborate.

---

* Corresponding author.
E-mail address: hiroyuki.nakamura@gakushuin.ac.jp (H. Nakamura).

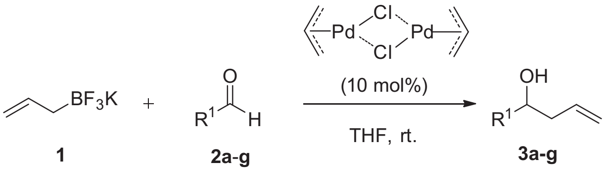
0040-4039/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2010.11.082

We first examined the reaction of allyltrifluoroborate **1**[27] and benzaldehyde **2a** in the presence of $PdCl_2(PPh_3)_2$ (10 mol %) in THF at 70 °C. The corresponding homoallylalcohol **3a** was obtained in 67% yield. Although the use of a palladium(0) catalyst, such as $Pd(PPh_3)_4$, afforded a lower yield of **3a** (43% yield), the use of π-allylpalladium chloride dimer gave the best result, and the allylation reaction proceeded in 86% yield at room temperature (Table 1, entry 1). Previously, we found that the use of platinum catalysts was more suitable for the nucleophilic allylation of aldehydes with allyltributylstannanes.[8,9] We examined this nucleophilic allylation with various aldehydes. As shown in Table 1 , 4-bromobenzaldehyde underwent nucleophilic allylation very smoothly to give the corresponding homoallylic alcohol **3b** quantitatively, without giving any allylated product at a bromo-substituted position obtained by the Suzuki–Miyaura-type coupling reaction (entry 2).[28,29] Not only aromatic aldehydes **2a–c** (entries 1–3) but also aliphatic aldehydes **2d–f** underwent the nucleophilic allylation reaction in the presence of the π-allylpalladium chloride dimer catalyst in THF at room temperature. Cyclohexycarboxaldehyde **2d** gave a lower yield of the homoallylic alcohol **3d** due to the steric hindrance of the cyclohexyl group, while the less hindered *n*-heptanal afforded the corresponding homoallylic alcohol **3d** in 94% yield (entry 4 vs 5). The nucleophilic allylation also proceeded with the conjugated aldehyde **2g** to give **3g** in 65% yield (entry 7).

We then examined the nucleophilic allylation of various imines under palladium(II)-catalyzed conditions. The results are summarized in Table 2. The aromatic imines **4a**, **4b**, and **4c** derived from 4-nitrobenzaldehyde reacted with potassium allyltrifluoroborate **1** to give the corresponding homoallylamines **5a**, **5b**, and **5c**, respectively, in high yields (Table 2, entries 1–3). The aromatic imines **4c** and **4d** derived from benzaldehyde also gave the corresponding homoallylamines **5c** and **5d** in 97% and 66% yields, respectively (entries 4 and 5). The pyridyl moiety substituted on the N-atom of imine **4d** was expected to co-ordinate with the palladium catalyst to accelerate the reaction rate. However, this pyridyl moiety was not effective in this reaction. The reactions of **4f**, derived from 4-tolaldehyde and 4-methoxyaniline, and **4g**, derived from cinnamaldehyde and 4-methoxyaniline, also proceeded smoothly to give the corresponding homoallylamines **5f** and **5g** in 85% and 84% yields, respectively (entries 6 and 7).

The aldehydes and imines underwent the palladium-catalyzed nucleophilic allylation and the corresponding homoallylic alcohols and imines were obtained in good-to-high yields. We investigated the amphiphilic bisallylation of activated olefins **6** in the presence of palladium catalysts. We first examined the optimization of palladium catalysts and ligands for the amphiphilic bisallylation. The results are shown in Table 3. The reaction of phenylidene malononitrile **6a** (1 equiv), allyltrifluoroborate **1** (1.5 equiv), and allyl acetate (1.5 equiv) in THF proceeded in the presence of $Pd(PPh_3)_4$ (10 mol %) in an Ar atmosphere at 70 °C to give the corresponding bisallylated product **7a** in 71% yield (entry 1). However, the use of allyl chloride, which was considered the most appropriate for the amphiphilic bisallylation with allyltributylstannane, was less effective (entry 2). Palladium(II) catalysts, such as $Pd(OAc)_2$ and $PdCl_2(PPh_3)_2$, were not effective in this reaction. Therefore, we examined the effect of phosphine ligands on the amphiphilic bisallylation using $Pd_2(dba)_3{\cdot}CHCl_3$ (5 mol %). Although tri-*n*-butylphosphine was more effective than triphenylphosphine (entry 1 vs 3), other trialkylphosphines, such as tri-*tert*-butylphosphine and tri-*n*-propylphosphine, afforded low yields of **7a** (entries 4 and 5). The best result was observed in the case of tricyclohexylphosphine, in which **7a** was obtained quantitatively (entry 6). Triphenylphosphite was also a suitable ligand for the reaction (entry 7); however, bidentate phosphines, such as 1,2-bis(diphenylphosphino)ethane (dppe) and bis(diphenylphosphino)ferrocene (dppf), tripentafluorophenylphosphine, and X-phos[30] were not effective in this reaction (entries 8–11).

Table 1
Allylation of various aldehydes **2**

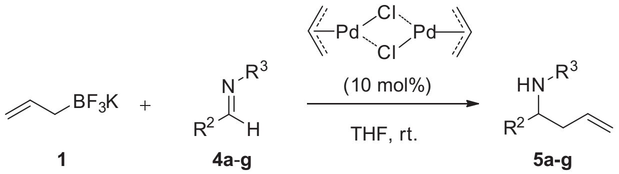


Entry	2	R^1	Time (h)	Yield[a] (%)
1	**2a**	Ph	12	86
2[b]	**2b**	$4\text{-}BrC_6H_4$	6	>99
3	**2c**	2-Naphtyl	18	67
4	**2d**	*c*-Hexyl	24	53
5	**2e**	*n*-Hexyl	24	94
6	**2f**	$PhCH_2CH_2$	11	70
7	**2g**	PhCH=CH	9	65

[a] Isolated yield based on aldehyde **2**.

[b] The reaction was carried out using $PdCl_2(PPh_3)_2$ (10 mol %).

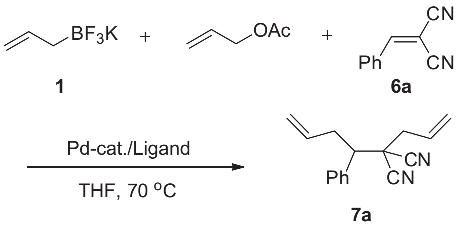
Table 2
Allylation of various imines **4**



Entry	4	R^2	R^3	Time (h)	Yield[a] (%)
1	**4a**	$4\text{-}NO_2C_6H_4$	Ph	24	93
2	**4b**	$4\text{-}NO_2C_6H_4$	$4\text{-}CO_2MeC_6H_4$	7	85
3	**4c**	$4\text{-}NO_2C_6H_4$	$4\text{-}OMeC_6H_4$	7	98
4	**4d**	Ph	Ph	24	97
5	**4e**	Ph	2-Py	24	66
6	**4f**	$4\text{-}MeC_6H_4$	$4\text{-}OMeC_6H_4$	24	85
7	**4g**	$PhCH{=}CH_2$	$4\text{-}OMeC_6H_4$	24	84

[a] Isolated yield based on imine **4**.

Table 3
Effect of various ligands on catalytic amphiphilic bisallylation



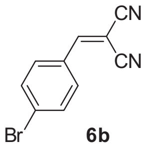
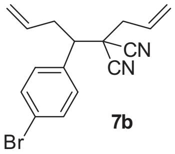
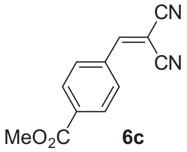
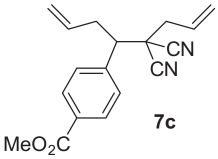
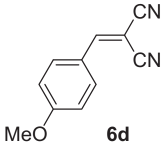
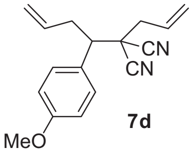
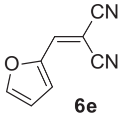
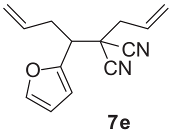
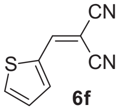
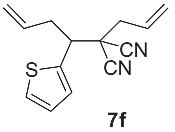
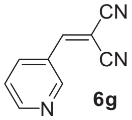
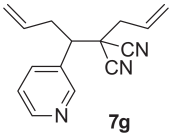
Entry	Pd-cat. (mol %)/ligand (mol %)[a]	Time (h)	Yield[b] (%)
1	$Pd(PPh_3)_4$ (10)	18	71
2[c]	$Pd(PPh_3)_4$ (10)	18	38
3	$Pd_2(dba)_3{\cdot}CHCl_3$ (5)/P(*n*-Bu)$_3$ (10)	24	85
4	$Pd_2(dba)_3{\cdot}CHCl_3$ (5)/P(*t*-Bu)$_3$ (10)	24	42
5	$Pd_2(dba)_3{\cdot}CHCl_3$ (5)/P(*n*-Pr)$_3$ (10)	24	30
6	$Pd_2(dba)_3{\cdot}CHCl_3$ (5)/PCy_3 (10)	4	>99
7	$Pd_2(dba)_3{\cdot}CHCl_3$ (5)/$P(OPh)_3$ (10)	12	80
8	$Pd_2(dba)_3{\cdot}CHCl_3$ (5)/dppe (5)	24	38
9	$Pd_2(dba)_3{\cdot}CHCl_3$ (5)/dppf (5)	24	3
10	$Pd_2(dba)_3{\cdot}CHCl_3$ (5)/$P(C_6F_5)_3$ (10)	24	4
11	$Pd_2(dba)_3{\cdot}CHCl_3$ (5)/X-Phos (10)	24	30

[a] Amount of catalyst and ligand are indicated in the parenthesis.

[b] Yield was determined by GC analysis using *n*-dodecane as an internal standard.

[c] Allyl chloride was used instead of ally acetate.

Table 4
Catalytic amphiphilic bisallylation of various activated olefins **6**[a]

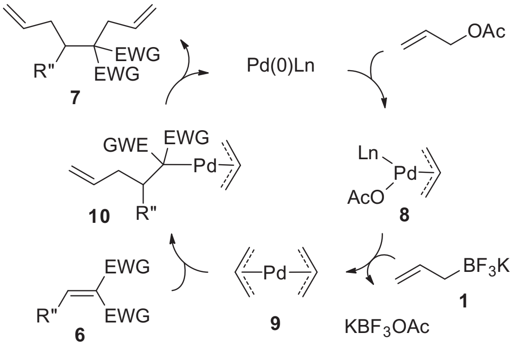
Entry	Olefin **6**	Time (h)	Product **7**	Yield[b] (%)
1	 **6b**	24	 **7b**	75
2	 **6c**	24	 **7c**	94
3	 **6d**	24	 **7d**	71
4	 **6e**	1	 **7e**	97
5	 **6f**	1	 **7f**	>99
6	 **6g**	1	 **7g**	77

[a] The reactions of olefin **6** (0.65 mmol) with potassium allyltrifluoroborate **1** (1.5 equiv) and allyl acetate (1.5 equiv) were carried out in the presence of $Pd_2(dba)_3 \cdot CHCl_3$ (5 mol %) and tricyclohexylphosphine (10 mol %) at 70 °C in THF.

[b] Isolated yield based on olefin **6**.

A suitable condition for the amphiphilic bisallylation of activated olefin **6a** was established, and then we examined the scope of the reaction by using various activated olefins. The results are summarized in Table 4. The activated olefin **6b**, which has a bromo group substituted at the *para* position of aromatic ring, underwent the amphiphilic bisallylation under standard palladium-catalyzed conditions to give the corresponding product **7b** in 75% yield (entry 1). The reactions of other aromatic olefins **6c** and **6d**, which have an electron-withdrawing group such as methoxycarbonyl and an electron-donating group such as methoxy at the *para* position gave the corresponding 1,7-octadienes **7c** and **7d** in 94% and 71% yields, respectively (entries 2 and 3). The current bisallylation also proceeded not only with benzene ring-substituted activated olefins but also with heteroaromatic group-substituted activated olefins, such as 2-furyl (**6e**), 2-thiofuryl (**6f**), and 3-pyridyl (**6g**) substituents. The reactions were complete within an hour and the desired 1,7-octadienes **7e**, **7f**, and **7g** were obtained in good to high yields (entries 4–6). The acceleration of the reaction rate may be because of the co-ordination between palladium and both CN and heteroaromatic groups. In all the above cases, monoallylated products were not obtained.

The plausible mechanism for this amphiphilic bisallylation is shown in Scheme 1. The oxidative addition of allyl acetate to palladium(0) gives π-allylpalladium acetate **8**. The transmetalation of the allyl trifluoroborate **1** to the π-allylpalladium acetate **8** would produce bis-π-allylpalladium complex **9**, which would react with activated olefins **6** to give the π-allylpalladium intermediate **10**. Finally, the reductive elimination from **10** would give the corresponding bisallylated products **7**, and palladium(0) species would be regenerated in the catalytic cycle. The π-allyl group reacts with a nucleophilic carbon center in the palladium complex **10**.



Scheme 1. Plausible mechanism for amphiphilic bisallylation.

In summary, we developed nucleophilic allylations of aldehydes and imines and amphiphilic bisallylation of activated olefins by generating bis-π-allylpalladium complexes from allyltrifluoroborate.[31] Because toxic organostannanes pollute the environment, the replacement of allylstannanes by allyltrifluoroborates achieved in our study can have many applications in organic synthesis involving a catalytic bis-π-allylpalladium reaction system.

References and notes

1. Smidt, J.; Hafner, W. *Angew. Chem.* **1959**, *71*, 284.
2. Tsuji, J.; Takahashi, H.; Morikawa, M. *Tetrahedron Lett.* **1965**, *6*, 4387–4388.
3. Trost, B. M.; Fullerton, T. J. *J. Am. Chem. Soc.* **1973**, *95*, 292–294.
4. Atkins, K. E.; Walker, W. E.; Manyik, R. M. *Tetrahedron Lett.* **1970**, *11*, 3821–3824.
5. Tsuji, J. *Palladium Reagents and Catalysis: Innovations in Organic Synthesis*; Wiley: Chichester, 1995.
6. Negishi, E.; Meijre, A. d. In *Organopalladium Chemistry for Organic Synthesis*; Wiley: New York, 2002; Vol. 2,
7. Becconsall, J.; Job, B.; O'Brien, S. *J. Chem. Soc. A* **1967**, 423–430.
8. Nakamura, H.; Asao, N.; Yamamoto, Y. *J. Chem. Soc., Chem. Commun.* **1995**, 1273–1274.
9. Nakamura, H.; Iwama, H.; Yamamoto, Y. *J. Am. Chem. Soc.* **1996**, *118*, 6641–6647.
10. Nakamura, H.; Nakamura, K.; Yamamoto, Y. *J. Am. Chem. Soc.* **1998**, *120*, 4242–4243.
11. Goliaszewski, A.; Schwartz, J. *J. Am. Chem. Soc.* **1984**, *106*, 5028–5030.
12. Nakamura, H.; Bao, M.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 3208–3210.
13. Nakamura, H.; Shim, J.-G.; Yamamoto, Y. *J. Am. Chem. Soc.* **1997**, *119*, 8113–8114.
14. Nakamura, H.; Aoyagi, K.; Shim, J.-G.; Yamamoto, Y. *J. Am. Chem. Soc.* **2001**, *123*, 372–377.

[15]. Wallner, O. A.; Szabó, K. J. *Chem. Eur. J.* **2003**, *9*, 4025–4030.

16. Szabó, K. J. *Chem. Eur. J.* **2004**, *10*, 5268–5275.
17. Nambo, M.; Wakamiya, A.; Yamaguchi, S.; Itami, K.; Szabó, K. *J. Am. Chem. Soc.* **2009**, *131*, 15112–15113.
18. Solin, N.; Kjellgren, J.; Szabó, K. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 3656–3658.
19. Solin, N.; Wallner, O. A.; Szabó, K. J. *Org. Lett.* **2005**, *7*, 689–691.
20. Benn, R.; Jolly, P. W.; Mynott, R.; Raspel, B.; Schenker, G.; Schick, K. P.; Schroth, G. *Organometallics* **1985**, *4*, 1945.
21. Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457–2483.
22. (a) Molander, G. A.; Ellis, N. *Acc. Chem. Res.* **2007**, *40*, 275; (b) Darses, S.; Genet, J.-P. *Chem. Rev.* **2008**, *108*, 288–325.
23. Hopkins, C. D.; Guan, L.; Malinakova, H. C. *J. Org. Chem.* **2005**, *70*, 6848–6862.
24. (a) Nowrouzi, F.; Thadani, A. N.; Batey, R. A. *Org. Lett.* **2009**, *11*, 2631–2634; (b) Lautens, M.; Maddess, M. L. *Org. Lett.* **2004**, *6*, 1883–1886.
25. (a) Sieber, J. D.; Liu, S.; Morken, J. P. *J. Am. Chem. Soc.* **2007**, *129*, 2214–2215; (b) Shaghafi, M. B.; Kohn, B. L.; Jarvo, E. R. *Org. Lett.* **2008**, *10*, 4743–4746.
26. Thadani, A. N.; Batey, R. A. *Org. Lett.* **2002**, *4*, 3827–3830.
27. Batey, R. A.; Thadani, A. N.; Smil, D. V. *Synthesis* **2000**, 990–998.
28. Al-Masum, M.; Alam, S. *Tetrahedron Lett.* **2009**, *50*, 5201–5204.
29. Yamamoto, Y.; Takada, S.; Miyaura, N. *Chem. Lett.* **2006**, *35*, 704–705.
30. Billingsley, K. L.; Anderson, K. W.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2006**, *45*, 3484–3488.
31. Representative procedures for the palladium(II)-catalyzed nucleophilic allylation of an aldehyde and the palladium(0)-catalyzed amphiphilic bisallylation of an activated olefin are presented here.

    1-Phenyl-3-buten-1-ol (**3**). A mixture of allyltrifluoroborate **1** (104 mg, 0.7 mmol), benzaldehyde **2a** (51 mL, 0.5 mmol), and π-allylpalladium chloride dimer (18 mg, 0.05 mmol) was dissolved in THF (3 mL) and stirred at room temperature for 12 h. The reaction mixture was heterogeneous all the while. Precipitates were removed through a Celite pad and the solvent was evaporated. The residue was purified by silica gel column chromatography with hexane/ethyl acetate (20:1) to give **3a** (63 mg, 0.43 mmol, 86% yield) as a colorless liquid: ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.25–7.36 (m, 5H), 5.76–5.85 (m, 1H), 5.13–5.19 (m, 2H), 4.72–4.76 (m, 1H), 2.46–2.57 (m, 2H), 2.02 (d, J = 2.8 Hz, 1H).

    4,4-Dicyano-5-phenyl-1,7-octadinene (**7a**). Allyl acetate (105 mL, 0.98 mmol) was added to a mixture of phenylidene malononitrile **6a** (100 mg, 0.65 mmol), allyltrifluoroborate **1** (145 mg, 0.98 mmol), $Pd_2(dba)_3 \cdot CHCl_3$ (35 mg, 0.033 mmol), and tricyclohexylphosphine (18 mg, 0.066 mmol), in THF (3 mL) in an Ar atmosphere and the mixture was stirred at 70 °C for 4 h. The reaction mixture was heterogeneous all the while. Precipitates were removed through a Celite pad and the solvent was evaporated. The residue was purified by silica gel column chromatography with hexane/ethyl acetate (50:1) to give **7a** (158 mg, 0.65 mmol, quant) as a colorless liquid: ^{1}H NMR (400 MHz; CDCl3) δ 7.26–7.42 (m, 5H), 5.83–5.93 (m, 1H), 5.43–5.54 (m, 1H), 5.40 (d, J = 9.2 Hz, 1H), 5.31 (d, J = 16.4 Hz, 1H), 5.08 (d, J = 18.8 Hz, 1H), 4.98 (d, J = 8.8 Hz, 1H), 3.08 (dd, J = 4.4 Hz, 1H), 2.84–2.96 (m, 2H), 2.47–2.52 (m, 1H), 2.35–2.41 (m, 1H).