

An Efficient Synthesis of Phospha-Morita-Baylis-Hillman Adducts via Michaelis-Arbuzov Reaction of the DABCO Salt of Morita-Baylis-Hillman Bromide

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An efficient synthesis of phospha-Morita-Baylis-Hillman adducts was carried out in good yields via the Michaelis-Arbuzov reaction of the DABCO salts of MBH bromides. Instead of a DABCO salt, a phosphonium salt could be effectively used for some substrates which showed some problems in the presence of DABCO.

Key Words : Phospha-Morita-Baylis-Hillman adducts, Michaelis-Arbuzov reaction, DABCO salt, Allylic phosphonates

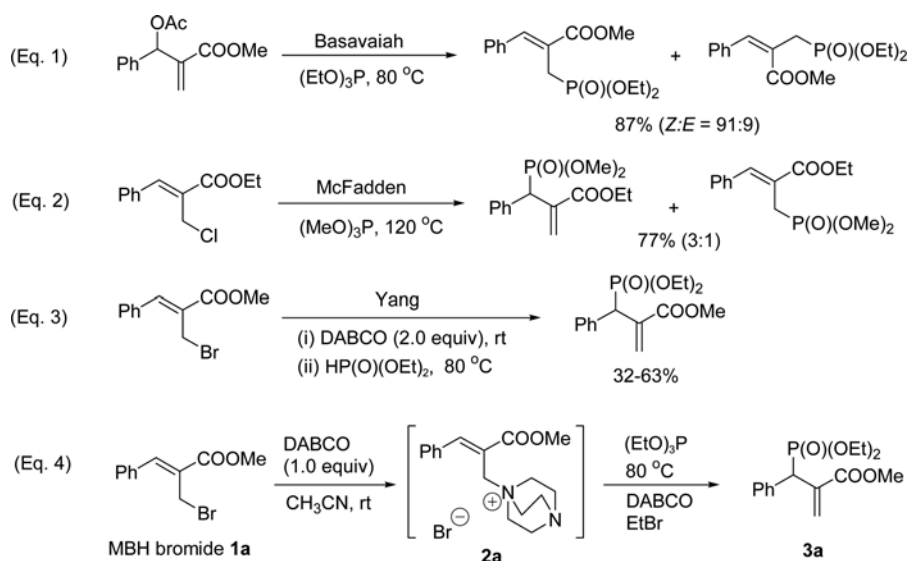
Introduction

The preparation of alkyl phosphonates was carried out most frequently using alkyl halides and trialkyl phosphites via the Michaelis-Arbuzov reaction.¹ The Morita-Baylis-Hillman (MBH) acetates or bromides could be used efficiently for the preparation of allylic phosphonates.²⁻⁴ Actually, the primary allylic phosphonate has been prepared from the acetate of MBH adducts by Basavaiah and Pandiaraju,^{2a} as shown in Eq. (1) (Scheme 1). The preparation of a secondary phosphonate was examined with MBH bromides or chlorides by McFadden and co-workers; however, a mixture of primary and secondary phosphonates was formed (Eq. 2).³ Yang and co-workers have reported the selective synthesis of secondary phosphonates via Michaelis-Becker reaction using diethyl phosphite and an excess amount of DABCO (Eq. 3).⁴ However, the reaction provided low to moderate yields (32-63%) with only two examples. The reason for the low yield must be due to insufficient generation of the anion

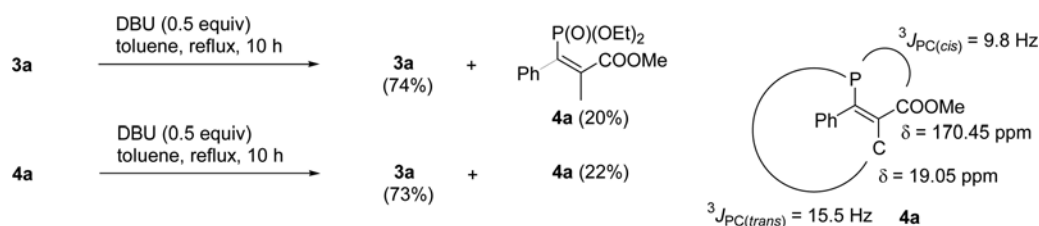
of diethyl phosphite with DABCO.^{5,6} In these contexts, we decided to examine the synthesis of secondary phosphonate **3a**, namely a phospha-Morita-Baylis-Hillman (phospha-MBH) adduct, via the Michaelis-Arbuzov reaction using trialkyl phosphite and the DABCO salt of MBH bromide (Eq. 4).⁷

Results and Discussion

The reaction of MBH bromide **1a**⁸ and DABCO (1.0 equiv) in CH₃CN readily provided a DABCO salt **2a** at room temperature within 30 min.⁹ The Michaelis-Arbuzov reaction between **2a** and triethyl phosphite (2.0 equiv) at 80 °C for 3 h afforded phospha-MBH adduct **3a** in good yield (92%) along with a trace amount of alkenylphosphonate **4a** (< 3%, *vide infra*). The tetrasubstituted alkenylphosphonate **4a** must be formed via a double-bond isomerization of **3a** by DABCO. Thus, we examined the feasibility for the isomerization of **3a** to **4a**, as shown in Scheme 2. Actually, a treatment of **3a** with DABCO or Et₃N showed very sluggish



Scheme 1



Scheme 2

Table 1. Synthesis of phospho-Morita-Baylis-Hillman adducts^a

Entry	MBH bromide	Product (%)
1		 3a (92)
2	1a	 3b (80) ^b
3	1a	 3c (84)
4		 3d (93)
5		 3e (94)
6		 3f (85)
7		 3g (78)

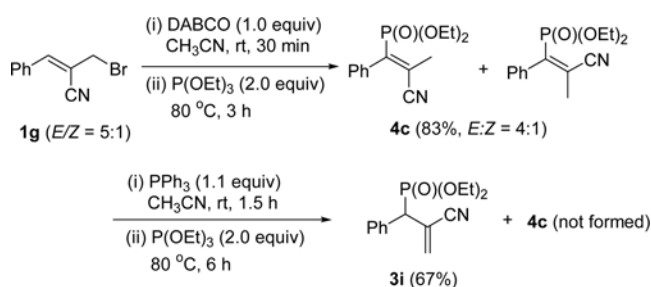
^aConditions: (i) MBH bromide (0.5 mmol), DABCO (1.0 equiv), CH₃CN, rt, 30 min. (ii) Trialkyl phosphite (2.0 equiv), 80 °C, 3 h. ^bReaction time: 8 h.

reactivity. The reaction of **3a** and DBU (0.5 equiv) in refluxing toluene showed the formation of **4a**; however, the reaction was not completed even after 10 h. The isolated yield of **4a** was 20%, and **3a** was recovered in 74%. Treatment of **4a**

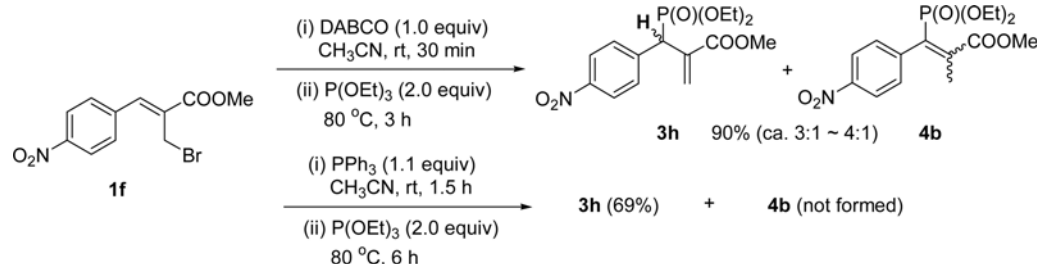
with DBU (0.5 equiv) afforded **3a** in 73% along with remaining **4a** in 22%. The results stated that these two compounds can be converted each other. Similar rearrangements between allylic and alkenylphosphonates have been reported.¹⁰ The stereochemistry of **4a** was confirmed by the three-bond coupling constant between phosphorous atom and carbon atoms, as also shown in Scheme 2.¹¹

Encouraged by the successful results, various phospho-MBH adducts **3b-g** were synthesized and the results are summarized in Table 1. Besides triethyl phosphite (entry 1), the reactions with trimethyl- and trisopropyl phosphites afforded the corresponding phosphonates **3b** and **3c** in good yields (entries 2 and 3). The reactions of other MBH bromides **1b-d** (entries 4-6) provided **3d-f** in good yields (85-94%). The bromide **1e** (entry 7), which was prepared from the corresponding MBH bromide of methyl vinyl ketone,^{8g} also afforded **3g** in good yield (78%). As noted above, the corresponding alkenylphosphonates were observed in most of the entries; however, the amount was negligible (< 5%) and the desired products **3b-g** could be separated easily.

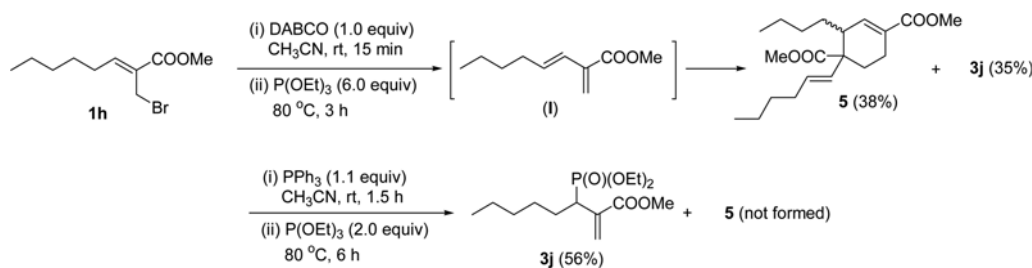
When we carried out the reaction of *p*-nitro derivative **1f**,^{8h} the desired product **3h** was formed as a major product; however, an appreciable amount of alkenylphosphonate **4b** was formed together, as shown in Scheme 3. The compound **4b** must be formed *via* the double bond isomerization of **3h**.



Scheme 4



Scheme 3



Scheme 5

The benzylic proton of **3h** would be more acidic than the corresponding protons of **3a-g**, and this could be the reason for the formation of **4b** in an increased amount. In addition, the formation of **4b** made the separation of **3h** very tedious. Thus we examined the Michaelis-Arbuzov reaction of the phosphonium salt of **1f** instead of a DABCO salt.¹² To our delight, compound **3h** could be obtained in good yield (69%) without the formation of **4b**.

The reaction of a nitrile derivative **1g**^{8b} also showed a severe isomerization problem, as shown in Scheme 4. The phosphonate **3i** was not formed at all when the DABCO salt was used in the Michaelis-Arbuzov reaction. Instead, an *E/Z* mixture of alkenylphosphonate **4c** (*E/Z* = 4:1) was obtained in 83%. Thus, we carried out the reaction with a phosphonium salt, and the secondary phosphonate **3i** was obtained in moderate yield (67%).

The use of a DABCO salt was also ineffective for the alkyl derivative **1h**.^{8b} During the synthesis of a DABCO salt of **1h**, a slow formation of a cyclohexene derivative **5** was observed. The cyclohexene derivative **5** could be formed by an E2 elimination of **1h** or its DABCO salt to form a 1,3-diene intermediate **I** and a subsequent Diels-Alder reaction,¹³ as shown in Scheme 5. In order to reduce the formation of **5**, we carried out the Michaelis-Arbuzov reaction in the presence of an excess amount (6.0 equiv) of triethyl phosphite; however, both cyclohexene **5** (38%) and phosphonate **3j** (35%) were produced together. Thus, the desired phosphonate **3j** was prepared by using a phosphonium salt in moderate yield (56%), as for the synthesis of **3h** and **3i**.

In order to compare the reactivity between DABCO salt and phosphonium salt, we examined the preparation of **3a** from **1a** via the phosphonium salt as in the Schemes 3-5. The yield of **3a** was low (68%) as compared to that of the DABCO salt (92%, entry 1 in Table 1). The Michaelis-Arbuzov reaction was also examined between triethyl phosphite and the DABCO salt of MBH acetate instead of MBH bromide. The phosphonate **3a** was obtained in only 48% yield under the same conditions (80 °C, 3 h), although the corresponding DABCO salt was formed quantitatively in aqueous THF. The formation of a DABCO salt in CH₃CN was so sluggish, thus the following Michaelis-Arbuzov reaction could not be carried out.

In summary, we disclosed an efficient synthesis of phospha-Morita-Baylis-Hillman adducts in good yields via the Michaelis-Arbuzov reaction of the DABCO salts of MBH bromides. Instead of a DABCO salt, a phosphonium salt

could be effectively used for some substrates which showed some problems in the presence of DABCO.

Experimental Section

¹H NMR (300 MHz) and ¹³C NMR (75 MHz) spectra were recorded using tetramethylsilane (TMS, δ = 0 ppm) as an internal standard. ³¹P NMR (121 MHz) spectra were recorded using 85% H₃PO₄ (δ = 0 ppm) as an external standard. The preparation of MBH bromides **1a-h** was carried out according to the literature procedure.⁸

Typical Procedure for the Synthesis of 3a. A mixture of **1a** (128 mg, 0.5 mmol) and DABCO (56 mg, 0.5 mmol) in CH₃CN (2.0 mL) was stirred at room temperature for 30 min. To the solution triethyl phosphite (166 mg, 1.0 mmol) was added, and the reaction mixture was heated to 80 °C for 3 h. After the extractive aqueous workup and column chromatographic purification process (hexanes/EtOAc/CH₂Cl₂, 2:1:1), compound **3a** was isolated as a colorless oil, 144 mg (92%). Other compounds were prepared similarly. The separation of product from the side product such as triethyl phosphate and/or triphenylphosphine oxide was somewhat tedious for some entries. Thus the following solvent system during the flash column chromatographic purification step is recommended: compounds **3a-d**, **3f** and **3g** (hexanes/EtOAc/CH₂Cl₂, 2:1:1); compounds **3e**, **3h** and **3i** (toluene/EtOAc, 4:1); compound **3j** (CHCl₃). The spectroscopic data of **3a-j**, **4a**, **4c** and **5** are as follows.

Compound 3a: 92%; colorless oil; IR (film) 1722, 1624, 1441, 1244, 1053, 1024 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 1.00 (t, *J* = 7.2 Hz, 3H), 1.20 (t, *J* = 7.2 Hz, 3H), 3.56-3.69 (m, 1H), 3.64 (s, 3H), 3.76-3.89 (m, 1H), 3.96-4.05 (m, 2H), 4.52 (d, *J*_{PH} = 24.6 Hz, 1H), 6.46 (s, 1H), 6.47 (s, 1H), 7.15-7.27 (m, 3H), 7.37-7.40 (m, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ 16.07 (*J*_{PC} = 5.7 Hz), 16.25 (*J*_{PC} = 5.7 Hz), 44.24 (*J*_{PC} = 140.8 Hz), 52.26, 62.36 (*J*_{PC} = 6.9 Hz), 62.86 (*J*_{PC} = 6.9 Hz), 127.36 (*J*_{PC} = 2.3 Hz), 128.41 (*J*_{PC} = 1.7 Hz), 128.82 (*J*_{PC} = 6.3 Hz), 129.56 (*J*_{PC} = 6.9 Hz), 134.73 (*J*_{PC} = 6.3 Hz), 136.01 (*J*_{PC} = 1.7 Hz), 166.55 (*J*_{PC} = 14.3 Hz); ³¹P NMR (CDCl₃, 121 MHz) δ 24.63; ESIMS *m/z* 313 [M⁺+H]. Anal. Calcd for C₁₅H₂₁O₅P: C, 57.69; H, 6.78. Found: C, 57.92; H, 6.61.

Compound 3b: 80%; colorless oil; IR (film) 1721, 1624, 1454, 1439, 1244, 1057, 1030 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 3.40 (d, *J* = 10.8 Hz, 3H), 3.65 (s, 3H), 3.65 (d, *J* = 11.1 Hz, 3H), 4.55 (d, *J*_{PH} = 24.6 Hz, 1H), 6.47 (d, *J* = 3.0 Hz, 1H), 6.48 (d, *J* = 3.0 Hz, 1H), 7.16-7.28 (m, 3H), 7.35-

7.40 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 43.74 ($J_{\text{PC}} = 140.8$ Hz), 52.29, 53.08 ($J_{\text{PC}} = 7.4$ Hz), 53.57 ($J_{\text{PC}} = 6.9$ Hz), 127.48 ($J_{\text{PC}} = 2.9$ Hz), 128.52 ($J_{\text{PC}} = 2.3$ Hz), 128.97 ($J_{\text{PC}} = 6.3$ Hz), 129.44 ($J_{\text{PC}} = 6.9$ Hz), 134.40 ($J_{\text{PC}} = 6.2$ Hz), 135.72 ($J_{\text{PC}} = 1.7$ Hz), 166.39 ($J_{\text{PC}} = 14.3$ Hz); ESIMS m/z 285 [M^+H]. Anal. Calcd for $\text{C}_{13}\text{H}_{17}\text{O}_5\text{P}$: C, 54.93; H, 6.03. Found: C, 54.77; H, 6.34.

Compound 3c: 84%; colorless oil; IR (film) 1722, 1624, 1454, 1385, 1242, 1021, 988 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 0.75 (d, $J = 6.3$ Hz, 3H), 1.13 (d, $J = 6.3$ Hz, 3H), 1.16 (d, $J = 6.3$ Hz, 3H), 1.22 (d, $J = 6.3$ Hz, 3H), 3.64 (s, 3H), 4.25-4.36 (m, 1H), 4.45 (d, $J_{\text{PH}} = 24.6$ Hz, 1H), 4.54-4.65 (m, 1H), 6.44 (d, $J = 3.0$ Hz, 1H), 6.50 (d, $J = 3.0$ Hz, 1H), 7.13-7.25 (m, 3H), 7.37-7.41 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 22.93 ($J_{\text{PC}} = 5.8$ Hz), 23.61 ($J_{\text{PC}} = 5.7$ Hz), 23.97 ($J_{\text{PC}} = 3.5$ Hz), 24.14 ($J_{\text{PC}} = 2.9$ Hz), 44.73 ($J_{\text{PC}} = 142.5$ Hz), 52.17, 70.68 ($J_{\text{PC}} = 7.4$ Hz), 71.37 ($J_{\text{PC}} = 6.8$ Hz), 127.20 ($J_{\text{PC}} = 2.3$ Hz), 128.25 ($J_{\text{PC}} = 1.7$ Hz), 128.48 ($J_{\text{PC}} = 6.3$ Hz), 129.73 ($J_{\text{PC}} = 6.9$ Hz), 135.13 ($J_{\text{PC}} = 5.7$ Hz), 136.43 ($J_{\text{PC}} = 1.7$ Hz), 166.64 ($J_{\text{PC}} = 14.3$ Hz); ESIMS m/z 341 [M^+H]. Anal. Calcd for $\text{C}_{17}\text{H}_{25}\text{O}_5\text{P}$: C, 59.99; H, 7.40. Found: C, 60.10; H, 7.19.

Compound 3d: 93%; colorless oil; IR (film) 1722, 1626, 1491, 1439, 1242, 1053, 1026 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 1.04 (td, $J = 7.2$ and 0.3 Hz, 3H), 1.21 (t, $J = 7.2$ Hz, 3H), 3.62-3.75 (m, 1H), 3.65 (s, 3H), 3.79-3.92 (m, 1H), 3.96-4.06 (m, 2H), 4.48 (d, $J_{\text{PH}} = 24.6$ Hz, 1H), 6.45 (d, $J = 3.0$ Hz, 1H), 6.48 (d, $J = 3.0$ Hz, 1H), 7.19-7.23 (m, 2H), 7.29-7.34 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 16.14 ($J_{\text{PC}} = 5.7$ Hz), 16.26 ($J_{\text{PC}} = 6.3$ Hz), 43.68 ($J_{\text{PC}} = 141.4$ Hz), 52.34, 62.55 ($J_{\text{PC}} = 6.9$ Hz), 62.88 ($J_{\text{PC}} = 6.8$ Hz), 128.58 ($J_{\text{PC}} = 2.3$ Hz), 129.00 ($J_{\text{PC}} = 6.3$ Hz), 130.88 ($J_{\text{PC}} = 6.8$ Hz), 133.37 ($J_{\text{PC}} = 2.9$ Hz), 133.43 ($J_{\text{PC}} = 5.7$ Hz), 135.78 ($J_{\text{PC}} = 1.7$ Hz), 166.38 ($J_{\text{PC}} = 14.3$ Hz); ESIMS m/z 347 [M^+H]. Anal. Calcd for $\text{C}_{15}\text{H}_{20}\text{ClO}_5\text{P}$: C, 51.96; H, 5.81. Found: C, 51.89; H, 6.01.

Compound 3e: 94%; colorless oil; IR (film) 1722, 1609, 1512, 1441, 1254, 1134, 1053, 1028 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 1.08 (td, $J = 7.2$ and 0.3 Hz, 3H), 1.27 (td, $J = 7.2$ and 0.3 Hz, 3H), 3.64-3.77 (m, 1H), 3.71 (s, 3H), 3.77 (s, 3H), 3.83-3.96 (m, 1H), 4.01-4.12 (m, 2H), 4.52 (d, $J_{\text{PH}} = 24.3$ Hz, 1H), 6.50-6.51 (m, 2H), 6.81-6.86 (m, 2H), 7.33-7.38 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 16.14 ($J_{\text{PC}} = 5.7$ Hz), 16.25 ($J_{\text{PC}} = 6.2$ Hz), 43.36 ($J_{\text{PC}} = 141.9$ Hz), 52.22, 55.11, 62.26 ($J_{\text{PC}} = 6.9$ Hz), 62.81 ($J_{\text{PC}} = 6.8$ Hz), 113.81 ($J_{\text{PC}} = 1.7$ Hz), 126.59 ($J_{\text{PC}} = 6.3$ Hz), 128.41 ($J_{\text{PC}} = 6.3$ Hz), 130.61 ($J_{\text{PC}} = 6.8$ Hz), 136.31 ($J_{\text{PC}} = 1.2$ Hz), 158.85 ($J_{\text{PC}} = 2.9$ Hz), 166.58 ($J_{\text{PC}} = 14.3$ Hz); ESIMS m/z 343 [M^+H]. Anal. Calcd for $\text{C}_{16}\text{H}_{23}\text{O}_6\text{P}$: C, 56.14; H, 6.77. Found: C, 56.43; H, 6.96.

Compound 3f: 85%; colorless oil; IR (film) 1722, 1624, 1439, 1240, 1134, 1053, 1026 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 0.96 (td, $J = 7.2$ and 0.6 Hz, 3H), 1.21 (t, $J = 7.2$ Hz, 3H), 3.54-3.67 (m, 1H), 3.61 (s, 3H), 3.75-3.87 (m, 1H), 3.97-4.07 (m, 2H), 4.69 (d, $J_{\text{PH}} = 24.3$ Hz, 1H), 6.51 (d, $J = 3.0$ Hz, 1H), 6.54 (d, $J = 3.0$ Hz, 1H), 7.33-7.39 (m, 2H), 7.50 (dt, $J = 8.4$ and 1.8 Hz, 1H), 7.70-7.75 (m, 3H), 7.84 (t,

$J = 2.4$ Hz, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 16.10 ($J_{\text{PC}} = 5.7$ Hz), 16.27 ($J_{\text{PC}} = 5.7$ Hz), 44.36 ($J_{\text{PC}} = 140.8$ Hz), 52.25, 62.42 ($J_{\text{PC}} = 7.5$ Hz), 62.85 ($J_{\text{PC}} = 6.9$ Hz), 125.91 ($J_{\text{PC}} = 1.1$ Hz), 126.00 ($J_{\text{PC}} = 1.1$ Hz), 127.44, 127.49 ($J_{\text{PC}} = 5.2$ Hz), 127.88 ($J_{\text{PC}} = 1.1$ Hz), 128.04 ($J_{\text{PC}} = 1.1$ Hz), 128.52 ($J_{\text{PC}} = 8.0$ Hz), 128.96 ($J_{\text{PC}} = 6.8$ Hz), 132.25 ($J_{\text{PC}} = 6.3$ Hz), 132.53 ($J_{\text{PC}} = 1.7$ Hz), 133.19 ($J_{\text{PC}} = 2.3$ Hz), 135.01 ($J_{\text{PC}} = 1.7$ Hz), 166.54 ($J_{\text{PC}} = 13.8$ Hz); ESIMS m/z 363 [M^+H]. Anal. Calcd for $\text{C}_{19}\text{H}_{23}\text{O}_5\text{P}$: C, 62.98; H, 6.40. Found: C, 62.65; H, 6.33.

Compound 3g: 78%; colorless oil; IR (film) 1682, 1624, 1495, 1366, 1246, 1055, 1026 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 0.98 (t, $J = 7.2$ Hz, 3H), 1.19 (t, $J = 7.2$ Hz, 3H), 2.27 (s, 3H), 3.57-3.71 (m, 1H), 3.76-3.89 (m, 1H), 3.93-4.03 (m, 2H), 4.74 (d, $J_{\text{PH}} = 23.7$ Hz, 1H), 6.31 (d, $J = 3.3$ Hz, 1H), 6.70 (d, $J = 3.3$ Hz, 1H), 7.12-7.25 (m, 3H), 7.37-7.41 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 16.04 ($J_{\text{PC}} = 5.7$ Hz), 16.22 ($J_{\text{PC}} = 6.3$ Hz), 25.29, 41.56 ($J_{\text{PC}} = 140.8$ Hz), 62.14 ($J_{\text{PC}} = 7.4$ Hz), 62.82 ($J_{\text{PC}} = 7.4$ Hz), 127.19 ($J_{\text{PC}} = 2.9$ Hz), 128.39 ($J_{\text{PC}} = 1.7$ Hz), 128.91 ($J_{\text{PC}} = 6.9$ Hz), 129.51 ($J_{\text{PC}} = 7.4$ Hz), 135.22 ($J_{\text{PC}} = 5.8$ Hz), 144.48 ($J_{\text{PC}} = 2.3$ Hz), 197.34 ($J_{\text{PC}} = 10.3$ Hz); ESIMS m/z 297 [M^+H]. Anal. Calcd for $\text{C}_{15}\text{H}_{21}\text{O}_4\text{P}$: C, 60.80; H, 7.14. Found: C, 60.87; H, 7.02.

Compound 3h: 69%; colorless oil; IR (film) 1722, 1597, 1524, 1441, 1348, 1244, 1051, 1024 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 1.05 (td, $J = 7.2$ and 0.3 Hz, 3H), 1.23 (td, $J = 7.2$ and 0.3 Hz, 3H), 3.66 (s, 3H), 3.68-3.81 (m, 1H), 3.82-3.95 (m, 1H), 3.99-4.09 (m, 2H), 4.61 (d, $J_{\text{PH}} = 24.3$ Hz, 1H), 6.53 (d, $J = 3.0$ Hz, 1H), 6.56 (d, $J = 3.0$ Hz, 1H), 7.53-7.59 (m, 2H), 8.09-8.13 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 16.17 ($J_{\text{PC}} = 5.8$ Hz), 16.32 ($J_{\text{PC}} = 5.8$ Hz), 44.40 ($J_{\text{PC}} = 140.8$ Hz), 52.55, 62.97 ($J_{\text{PC}} = 6.8$ Hz), 63.00 ($J_{\text{PC}} = 7.5$ Hz), 123.59 ($J_{\text{PC}} = 2.3$ Hz), 129.87 ($J_{\text{PC}} = 6.3$ Hz), 130.48 ($J_{\text{PC}} = 6.9$ Hz), 135.12 ($J_{\text{PC}} = 2.3$ Hz), 142.69 ($J_{\text{PC}} = 6.3$ Hz), 147.24 ($J_{\text{PC}} = 2.9$ Hz), 166.18 ($J_{\text{PC}} = 14.3$ Hz); ESIMS m/z 358 [M^+H]. Anal. Calcd for $\text{C}_{15}\text{H}_{20}\text{NO}_7\text{P}$: C, 50.42; H, 5.64; N, 3.92. Found: C, 50.33; H, 5.92; N, 3.76.

Compound 3i: 67%; colorless oil; IR (film) 2224, 1601, 1454, 1393, 1250, 1051, 1022, 968 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 1.05 (td, $J = 7.2$ and 0.6 Hz, 3H), 1.25 (t, $J = 7.2$ Hz, 3H), 3.65-3.79 (m, 1H), 3.84-3.97 (m, 1H), 3.90 (d, $J_{\text{PH}} = 24.3$ Hz, 1H), 4.01-4.11 (m, 2H), 6.07 (d, $J = 3.0$ Hz, 1H), 6.21 (dd, $J = 3.0$ and 1.2 Hz, 1H), 7.26-7.34 (m, 3H), 7.37-7.41 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 16.06 ($J_{\text{PC}} = 5.1$ Hz), 16.21 ($J_{\text{PC}} = 6.3$ Hz), 48.83 ($J_{\text{PC}} = 140.9$ Hz), 62.79 ($J_{\text{PC}} = 7.4$ Hz), 63.45 ($J_{\text{PC}} = 6.8$ Hz), 117.80 ($J_{\text{PC}} = 10.3$ Hz), 119.48 ($J_{\text{PC}} = 5.1$ Hz), 128.30 ($J_{\text{PC}} = 2.3$ Hz), 128.88 ($J_{\text{PC}} = 1.7$ Hz), 129.42 ($J_{\text{PC}} = 6.9$ Hz), 132.37 ($J_{\text{PC}} = 6.3$ Hz), 134.32 ($J_{\text{PC}} = 8.6$ Hz); ESIMS m/z 280 [M^+H]. Anal. Calcd for $\text{C}_{14}\text{H}_{18}\text{NO}_3\text{P}$: C, 60.21; H, 6.50; N, 5.02. Found: C, 60.46; H, 6.43; N, 4.86.

Compound 3j: 56%; colorless oil; IR (film) 1722, 1439, 1246, 1051, 1026, 959 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 0.79 (t, $J = 6.9$ Hz, 3H), 1.17-1.25 (m, 6H), 1.19 (t, $J = 7.2$ Hz, 3H), 1.22 (t, $J = 7.2$ Hz, 3H), 1.54-1.71 (m, 1H), 1.82-1.94 (m, 1H), 3.28 (ddd, $J_{\text{PH}} = 23.4$ Hz, $J = 10.8$ and 4.2 Hz,

1H), 3.72 (s, 3H), 3.93-4.07 (m, 4H), 5.83 (d, $J = 5.7$ Hz, 1H), 6.41 (d, $J = 5.7$ Hz, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 13.95, 16.30 ($J_{\text{PC}} = 5.8$ Hz), 16.35 ($J_{\text{PC}} = 6.3$ Hz), 22.32, 26.90 ($J_{\text{PC}} = 13.7$ Hz), 29.26 ($J_{\text{PC}} = 3.4$ Hz), 31.41 ($J_{\text{PC}} = 1.1$ Hz), 37.14 ($J_{\text{PC}} = 137.3$ Hz), 52.25, 62.05 ($J_{\text{PC}} = 7.4$ Hz), 62.17 ($J_{\text{PC}} = 6.8$ Hz), 127.30 ($J_{\text{PC}} = 8.6$ Hz), 136.12 ($J_{\text{PC}} = 8.0$ Hz), 167.20 ($J_{\text{PC}} = 6.3$ Hz); ESIMS m/z 307 [M^+H]. Anal. Calcd for $\text{C}_{14}\text{H}_{27}\text{O}_5\text{P}$: C, 54.89; H, 8.88. Found: C, 55.06; H, 8.69.

Compound 4a: 20%; colorless oil; IR (film) 1736, 1625, 1597, 1435, 1260, 1133, 1023, 966 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 1.16 (td, $J = 7.2$ and 0.6 Hz, 6H), 1.78 (d, $J = 3.0$ Hz, 3H), 3.81 (s, 3H), 3.87-4.06 (m, 4H), 7.10-7.14 (m, 2H), 7.22-7.34 (m, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 16.12 ($J_{\text{PC}} = 6.3$ Hz), 19.05 ($J_{\text{PC}} = 15.5$ Hz), 52.53, 62.22 ($J_{\text{PC}} = 5.7$ Hz), 127.76 ($J_{\text{PC}} = 2.3$ Hz), 128.39 ($J_{\text{PC}} = 1.1$ Hz), 128.90 ($J_{\text{PC}} = 4.6$ Hz), 130.67 ($J_{\text{PC}} = 178.1$ Hz), 135.06 ($J_{\text{PC}} = 8.0$ Hz), 146.27 ($J_{\text{PC}} = 9.8$ Hz), 170.45 ($J_{\text{PC}} = 9.8$ Hz); ^{31}P NMR (CDCl_3 , 121 MHz) δ 12.98; ESIMS m/z 313 [M^+H]. Anal. Calcd for $\text{C}_{15}\text{H}_{21}\text{O}_5\text{P}$: C, 57.69; H, 6.78. Found: C, 57.54; H, 6.91.

Compound 4c: 83%; colorless oil; IR (film) 2218, 1643, 1445, 1236, 1051, 1020 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz, *E*-form) δ 1.15 (td, $J = 7.2$ and 0.3 Hz, 6H), 2.42 (d, $J = 3.3$ Hz, 3H), 3.85-4.11 (m, 4H), 7.19-7.23 (m, 2H), 7.29-7.37 (m, 3H); ^{13}C NMR (CDCl_3 , 75 MHz, *E*-form) δ 16.03 ($J_{\text{PC}} = 6.3$ Hz), 19.64 ($J_{\text{PC}} = 5.2$ Hz), 62.73 ($J_{\text{PC}} = 5.7$ Hz), 117.76 ($J_{\text{PC}} = 30.9$ Hz), 124.82 ($J_{\text{PC}} = 20.6$ Hz), 128.37 ($J_{\text{PC}} = 4.4$ Hz), 128.42 ($J_{\text{PC}} = 1.1$ Hz), 128.95 ($J_{\text{PC}} = 1.7$ Hz), 136.07 ($J_{\text{PC}} = 6.8$ Hz), 146.76 ($J_{\text{PC}} = 176.3$ Hz); ^1H NMR (CDCl_3 , 300 MHz, *Z*-form) δ 1.90 (td, $J = 7.2$ and 0.3 Hz, 6H), 1.86 (d, $J = 2.7$ Hz, 3H), 3.85-4.11 (m, 4H), 7.08-7.12 (m, 2H), 7.29-7.37 (m, 3H); ^{13}C NMR (CDCl_3 , 75 MHz, *Z*-form) δ 20.80 ($J_{\text{PC}} = 13.7$ Hz), 63.16 ($J_{\text{PC}} = 6.3$ Hz), 121.37 ($J_{\text{PC}} = 3.5$ Hz), 128.14 ($J_{\text{PC}} = 5.1$ Hz), 128.57 ($J_{\text{PC}} = 1.7$ Hz), 128.66 ($J_{\text{PC}} = 2.3$ Hz), 133.97 ($J_{\text{PC}} = 6.9$ Hz), 147.01 ($J_{\text{PC}} = 177.4$ Hz), 2 carbon signals were overlapped; ESIMS m/z 280 [M^+H]. Anal. Calcd for $\text{C}_{14}\text{H}_{18}\text{NO}_3\text{P}$: C, 60.21; H, 6.50; N, 5.02. Found: C, 60.37; H, 6.39; N, 4.83.

Compound 5: 38%; colorless oil; IR (KBr) 1730, 1715, 1651, 1456, 1435, 1258, 1229 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 0.81 (t, $J = 7.2$ Hz, 3H), 0.83 (t, $J = 7.2$ Hz, 3H), 0.96-1.09 (m, 1H), 1.15-1.41 (m, 8H), 1.47-1.58 (m, 1H), 1.64-1.73 (m, 1H), 1.94-2.01 (m, 2H), 2.05-2.13 (m, 1H), 2.24-2.30 (m, 2H), 2.72-2.78 (m, 1H), 3.57 (s, 3H), 3.65 (s, 3H), 5.30 (d, $J = 15.6$ Hz, 1H), 5.46 (dt, $J = 15.6$ and 6.6 Hz, 1H), 6.99 (dt, $J = 5.1$ and 1.8 Hz, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 13.82, 13.92, 22.05, 22.14, 22.87, 25.37, 29.87, 31.29, 31.40, 32.44, 40.65, 50.47, 51.52, 52.05, 128.32, 130.12, 131.98, 142.65, 167.60, 175.50; ESIMS m/z 337 [M^+H]. Anal. Calcd for $\text{C}_{20}\text{H}_{32}\text{O}_4$: C, 71.39; H, 9.59. Found: C, 71.08; H, 9.51. The compound **5** was isolated as a single diastereomer presumably as a *trans* based on the reported papers;¹³ however, we did not confirm the stereochemistry decisively.

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