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Facile S_N2' Coupling Reactions of Wittig Reagents with Dimethyl Bromomethylfumarate: Synthesis of Enes, Dienes, and Related Natural Products

Ramesh M. Patel and Narshinha P. Argade*

Division of Organic Chemistry (Synthesis), National Chemical Laboratory, Pune 411 008, India

np.argade@ncl.res.in

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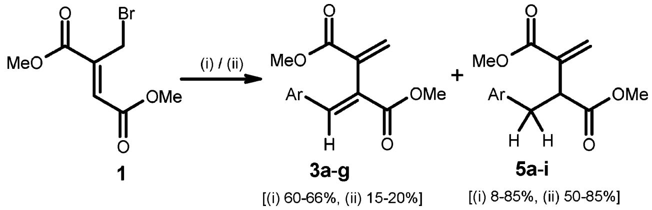

(i) Wittig reagent, -100 °C to rt, 3 h; (ii) Wittig reagent, -100 °C, 3 h, H_2O.

A new simple and efficient synthetic protocol with an ample scope has been demonstrated, by employing S_N2' coupling reactions of a variety of Wittig reagents with dimethyl bromomethylfumarate to obtain the corresponding enes, dienes, and related natural and unnatural products.

Introduction

The S_N2' coupling reaction is a very important tool to form new carbon−carbon bonds in synthetic organic chemistry,[1] and the propensity of Wittig reagents for S_N2' coupling reactions has not been studied until recently.[2] Enes and dienes are an important class of compounds, and they find applications in the preparation of dyes, UV screens, drugs, in Diels−Alder reactions, and also for the synthesis of complex natural and unnatural products.[3] Several methods are known in the literature to design enes and dienes.[4] The application of a Wittig reaction to design enes is a very standard, well-explored method in the literature.[2,5] The Wittig reagents also have been used for the preparation of cyclopropane and cycloheptane derivatives.[6] We envisaged that the S_N2' coupling reactions of Wittig reagents with substrates having appropriately placed leaving groups would be useful to provide a convenient approach to attain a variety of enes and dienes via the reductive removal of triphenylphosphine oxide and the elimination of triphenylphosphine, respectively. Now, we herein demonstrate an important new synthetic protocol to synthesize several types of enes and dienes by taking the advantage of Wittig chemistry (Schemes 1 and 2).

Results and Discussion

Dimethyl bromomethylfumarate (**1**) has been used for the synthesis of several natural and unnatural products employing S_N2' coupling reactions with a variety of carbanionic species.[1,7] In this context, we decided to study the feasibility of S_N2' coupling reactions of Wittig reagents with the substrate **1**. Initially, we performed the reaction with equimolar amounts of

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* Corresponding author. Tel.: 91-20-25902333; fax: 91-20-25902624.

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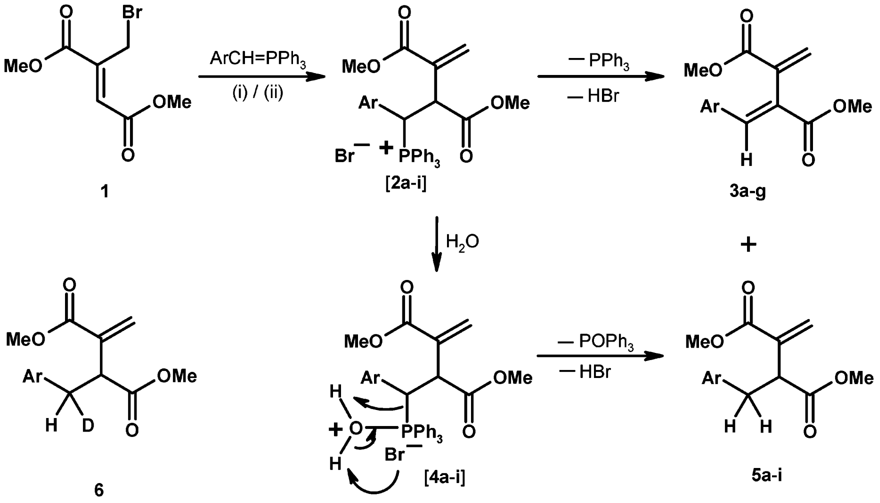
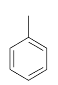
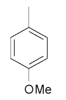
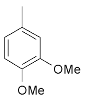
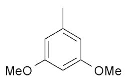
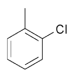
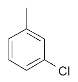
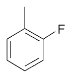
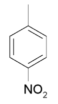
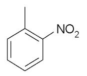
SCHEME 1. S_N2' Coupling Reactions of Wittig Reagents with 1, Synthesis of Enes and Dienes[a]



[a] (i) Wittig reagent, −100 °C to rt, 3 h [**3a**−**g**/**5a**−**i** : (60−66%)/(8−85%)]; (ii) Wittig reagent, −100 °C, 3 h, then H_2O at −100 °C [**3a**−**g**/**5a**−**i** : (15−20%)/(50−85%)].

TABLE 1. Synthesis of Variety of Enes 5 and Dienes 3 from Dimethyl Bromomethylfumarate (1)

Entry		1	2	3	4	5	6	7	8	9
-Ar										
Products **3** & **5** Condition (i)	**3a-i** (yield)[a]	**3a** (60%)	**3b** (64%)	**3c** (65%)	**3d** (64%)	**3e** (66%)	**3f** (62%)	**3g** (60%)	**3h** (00%)	**3i** (00%)
	5a-i (yield)[a]	**5a** (8%)	**5b** (11)	**5c** (10%)	**5d** (11%)	**5e** (12%)	**5f** (13%)	**5g** (10%)	**5h** (85%)	**5i** (85%)
Products **3** & **5** Condition (ii)	**3a-i** (yield)[a]	**3a** (18%)	**3b** (20%)	**3c** (15%)	**3d** (17%)	**3e** (18%)	**3f** (20%)	**3g** (18%)	**3h** (00%)	**3i** (00%)
	5a-i (yield)[a]	**5a** (50%)	**5b** (55%)	**5c** (60%)	**5d** (58%)	**5e** (60%)	**5f** (55%)	**5g** (52%)	**5h** (85%)	**5i** (85%)

[a] Obtained mixtures of enes and dienes were separated by silica gel column chromatography, and the isolated yields are in parentheses. Overall conditions: (i) Wittig reagent, −100 °C to rt; (ii) Wittig reagent, −100 °C, H_2O.

1 and the Wittig reagent benzylidenetriphenylphosphorane at 0 °C in THF, and upon quenching with water at the same temperature, we obtained the column separable mixture of ene **5a** and diene **3a** in a 2:3 ratio with 30% yield (Scheme 1). On confirmation of the feasibility of S_N2' coupling reactions of Wittig reagents with substrate **1**, we performed several experiments using different bases to generate the ylides (*n*-BuLi, NaH, $NaCH_2SOCH_3$, KOBu-*t*, and DBU) and solvents (THF, ether, 1,4-dioxane, THF-dioxane, and THF-HMPA) at different temperatures (−100, −78, −40, −20, and 0 °C and rt) to selectively obtain the enes and dienes with high yields. In the S_N2' coupling reaction of **1** with Wittig reagents, the best result was obtained when *n*-BuLi was used as a base to generate the ylide and by performing the reaction in THF at −100 °C and then quenching the reaction at room temperature after 3 h (68% yield, **3a**/**5a** = 88:12). When the same reaction of compound **1** with the Wittig reagent was quenched at −100 °C with water after 3 h, we obtained the opposite selectivity, and the ene **5a** was obtained as a major product and diene **3a** as a minor product (68% yield, **3a**/**5a** = 26:74). These experiments very clearly revealed that (i) in the formation of dienes, the Wittig reagent couples with **1** in a S_N2' fashion, which is followed by an instantaneous abstraction of the acidic methine proton by the conjugate base, the bromide anion, with anti-elimination of PPh_3 to yield the diene **3a** with exclusive E-geometry of the newly formed carbon−carbon double bond and (ii) in the same reaction on quenching with water at −100 °C, the reductive removal of $POPh_3$ takes place with the formation of ene **5a** as a major product.[8] To confirm that in the formation of enes the hydrogen atom at the benzylic position comes from water, we quenched the reaction at −100 °C with D_2O and obtained the corresponding deuterium incorporated compound **6** in 48% yield. In the

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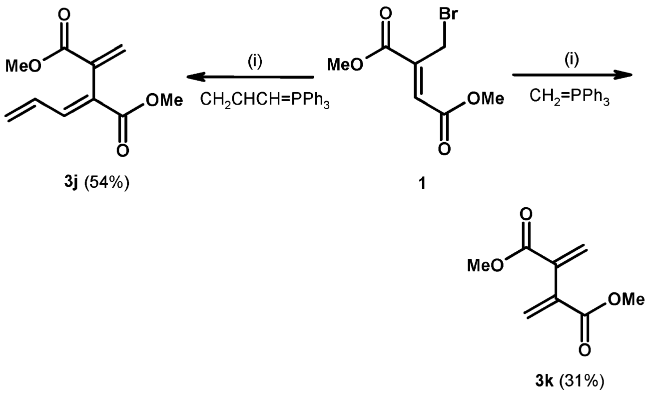
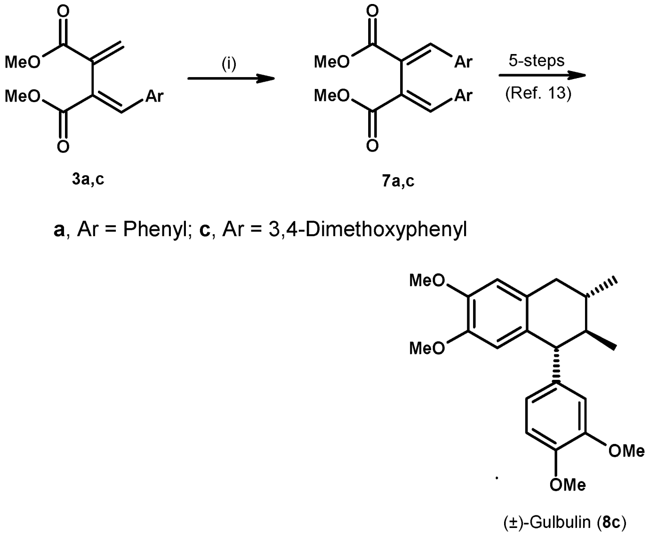
SCHEME 2. Synthesis of Symmetrical and Unsymmetrical Dienes[a]



[a] (i) Wittig reagent, −100 °C to rt, 3 h.

SCHEME 3. Heck Coupling Reactions of Dienes, Synthesis of Gulbulin[a]

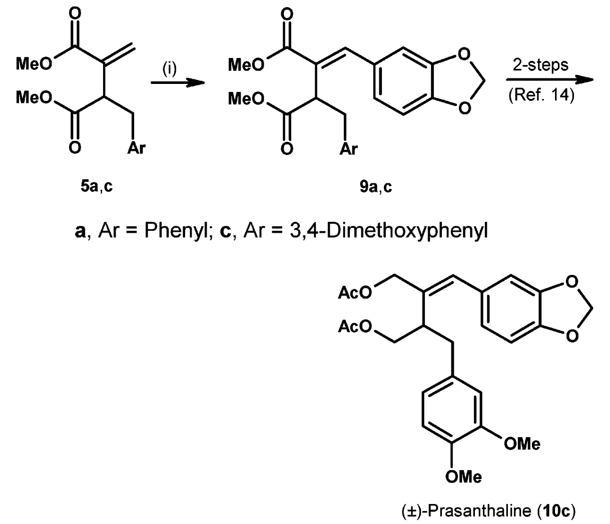


[a] (i) ArI, Pd(OAc)$_2$, Cy$_2$NH, H$_2$O, 120 °C, 24 h (*E*/*Z* = 94:6, 86%).

reactions of the Wittig reagent with **1**, we tried our best to exclusively obtain diene **3a** by using super dry THF and also by adding TEA as an external base for the elimination of PPh$_3$, but all our attempts were met with failure, and we always ended up with the isolation of ene **5a** as a minor product. We strongly believe that under the complete absence of moisture, the present reaction will provide the diene **3a** as an exclusive product. We also feel that the preparation of substrate **1** using higher alcohols and similar less activated substrates may not demand such a lower temperature for the effective S_N2' coupling reactions of the Wittig reagents.

We studied the S_N2' coupling reactions of several other Wittig reagents generated from the phosphonium salts of corresponding benzyl bromides with **1** and obtained the corresponding enes **5a**−**g** and dienes **3a**−**g**, proving the generality of the present approach (Table 1, entries 1−7). Surprisingly, the Wittig reagents generated from phosphonium salts of *ortho*- and *para*-nitrobenzyl bromides, on S_N2' condensations with **1**, exclusively furnished corresponding enes **5h**,**i** in 85% yield under both reaction conditions (Table 1, entries 8 and 9). We feel that this could be a result of higher stability of the unisolable intermediates **2h**,**i** and the nonavailability of bromide anion as a conjugate base due to the electron deficient nature of the phosphorus atom in those two cases.

SCHEME 4. Heck Coupling Reactions of Enes, Synthesis of Prasanthaline[a]



[a] (i) ArI, Pd(OAc)$_2$, Cy$_2$NH, H$_2$O, 120 °C, 24 h (*E*/*Z* = 82:18, 88%).

Then, we studied the S_N2' coupling reactions of relatively more reactive phosphoranes generated from phosphonium salts of methyl iodide and allyl bromide with **1** and exclusively obtained the corresponding diene **3j** and dimethyl ester of fulgenic acid (**3k**),[9] respectively, but in 31 and 54% yields (Scheme 2). Herein, as the ylides are relatively more reactive, the further refinements in reaction conditions for the improvement of yields of **3j** and **3k** are essential.

We decided to use both enes and dienes for the short and efficient synthesis of natural products (±)-gulbulin (from *Himantandra baccata* Bail)[10] and (±)-prasanthaline (from *Jatropha gossypifolia* Linn).[11] The dienes **3a**,**c** on Heck coupling reactions[12] with appropriate halides gave the (*E*,*E*)-dienes **7a**,**c** as a major product in 86% yield (*E*/*Z* = 94:6, by ^{1}H NMR). The five-step conversion of diene **7c** to (±)-gulbulin (**8c**) has been shown in the literature (Scheme 3).[13] Similarly, Heck coupling reactions[12] of enes **5a**,**c** with appropriate halides gave the corresponding desired diesters **9a**,**c** in 88% yield (*E*/*Z* = 82:18, by ^{1}H NMR). The reduction of two ester groups in ene **9c** followed by an in situ acylation of the formed intermediate 1,4-diol provided the natural product (±)-prasanthaline (**10c**), which has been discussed in the literature (Scheme 4).[14]

Conclusion

In summary, we have demonstrated an unprecedented S_N2' coupling reaction of Wittig reagents to selectively obtain the

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corresponding enes and dienes, which is a pivotal new application of Wittig reagents. Herein, the enes have been obtained by using the Wittig reagents rather than the corresponding Grignard reagents, while dienes have been obtained with the recovery of triphenylphosphine. We feel that the use of Wittig reagents in the place of Grignard reagents in the synthesis of enes will positively widen the scope of S_N2' coupling reactions. The use of alkyl halides and benzyl halides instead of the corresponding aldehydes to obtain these products is an added advantage. We also feel that our present protocol is general and that the Wittig reagents will undergo S_N2' coupling reactions with a variety of other activated substrates to provide the corresponding enes, dienes, related natural (Lignan family) products, and unnatural products including several useful fulgides.[15] The present approach also is useful for intramolecular cyclizations in the construction of carbocycles and heterocycles.

Experimental Section

Preparation of Different Triphenylphosphonium Salts. To a stirred solution of triphenylphosphine (2.62 g, 10.00 mmol) in benzene (10 mL) at 0 °C was added benzylbromide (1.67 mL, 14.00 mmol) in a dropwise fashion under argon atmosphere. Stirring was continued for 24 h at room temperature. The formed salt was filtered, washed with ether and petroleum ether, respectively, dried under vacuum, and stored in a desiccator over phosphorus pentoxide (4.30 g, 99%). All other triphenylphosphonium salts were prepared similarly.

(*E*)-Dimethyl 2-Benzylidene-3-methylenesuccinate (3a). To a stirred solution of benzyltriphenylphosphonium bromide (866 mg, 2.00 mmol) in THF (25 mL) at −100 °C was added *n*-BuLi (1.34 mL, 2.00 mmol) in a dropwise fashion under argon atmosphere. The reaction mixture was allowed to reach 0 °C. Then, the reaction mixture was added to a stirred solution of **1** (569 mg, 2.40 mmol) in THF (20 mL) at −100 °C under argon atmosphere in a dropwise fashion. The reaction mixture was allowed to reach room temperature, and the reaction was then quenched with water. The reaction mixture was extracted with ethyl acetate (30 mL × 4), and the combined organic layer was washed with brine and dried over Na_2SO_4. Concentration of the organic layer in vacuo followed by silica gel column chromatographic purification of the residue using a mixture of ethyl acetate/petroleum ether (1:9) as an eluent provided the major product **3a** (296 mg, 60%) and minor product **5a** (39 mg, 8%) as thick oils. ^1H NMR ($CDCl_3$, 200 MHz) δ 3.75 (s, 3H), 3.80 (s, 3H), 5.68 (d, $J = 2$ Hz, 1H), 6.49 (d, $J = 2$ Hz, 1H), 7.28−7.35 (m, 3H), 7.35−7.45 (m, 2H), 7.81 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 52.2, 52.3, 128.4, 128.5, 129.3, 130.0, 130.6, 134.3, 136.0, 141.8, 166.4, 167.2; IR ($CHCl_3$) ν_{max} 1717, 1630, 1618, 1497 cm^{-1}. Anal. Calcd for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73. Found: C, 68.13; H, 5.92.

(*E*)-Dimethyl 2-(3,4-Dimethoxybenzylidene)-3-methylenesuccinate (3c). The similarly obtained crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (1:4) as an eluent to obtain major product **3c** (65%) and minor product **5c** (10%) as thick oils. ^1H NMR ($CDCl_3$, 200 MHz) δ 3.73 (s, 3H), 3.79 (s, 3H), 3.81 (s, 3H), 3.88 (s, 3H), 5.76 (d, $J = 2$ Hz, 1H), 6.56 (d, $J = 2$ Hz, 1H), 6.82 (d, $J = 8$ Hz, 1H), 6.98−7.10 (m, 2H), 7.74 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 52.3 (2 carbons), 55.6, 55.8, 110.7, 112.5, 124.5, 125.7, 127.0, 130.5, 136.5, 141.6, 148.5, 150.2, 166.5, 167.4; IR ($CHCl_3$) ν_{max} 1717, 1636, 1601, 1514 cm^{-1}. Anal. Calcd for $C_{16}H_{18}O_6$: C, 62.74; H, 5.92. Found: C, 62.83; H, 6.04.

(*E*)-Dimethyl 2-(2-Fluorobenzylidene)-3-methylenesuccinate (3g). The similarly obtained crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (1:9) as an eluent to obtain major product **3g** (60%) and minor product **5g** (10%) as thick oils. ^1H NMR ($CDCl_3$, 200 MHz) δ 3.77 (s, 3H), 3.81 (s, 3H), 5.60 (d, $J = 2$ Hz, 1H), 6.40 (d, $J = 2$ Hz, 1H), 6.95−7.10 (m, 2H), 7.20−7.40 (m, 2H), 7.89 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 52.3, 52.4, 115.8 (d, $J = 22$ Hz), 122.5 (d, $J = 13$ Hz), 123.9 (d, $J = 3$ Hz), 130.29 (d, $J = 3$ Hz), 130.34, 130.97 (d, $J = 9$ Hz), 131.01 (d, $J = 2$ Hz), 134.3 (d, $J = 4$ Hz), 135.9, 160.5 (d, $J = 250$ Hz), 166.3, 166.7; IR ($CHCl_3$) ν_{max} 1719, 1641, 1620, 1437 cm^{-1}. Anal. Calcd for $C_{14}H_{13}FO_4$: C, 63.63; H, 4.96. Found: C, 63.44; H, 4.89. (The C−F couplings observed in the ^{13}C NMR spectrum are in parentheses.)

(*E*)-Dimethyl 2-Allylidene-3-methylenesuccinate (3j). The similarly obtained crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (1:9) as an eluent to obtain **3j** (54%) as a thick oil. ^1H NMR ($CDCl_3$, 200 MHz) δ 3.74 (s, 6H), 5.50 (dd, $J = 10$ Hz and 2 Hz, 1H), 5.65 (d, $J = 2$ Hz, 1H), 5.68 (d, $J = 16$ Hz, 1H), 6.42−6.64 (m, 1H), 6.54 (d, $J = 2$ Hz, 1H), 7.34 (d, $J = 12$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 52.0, 52.1, 126.6, 129.3, 130.3, 132.2, 135.0, 141.5, 166.2, 166.8; IR ($CHCl_3$) ν_{max} 1717, 1624, 1437 cm^{-1}. Anal. Calcd for $C_{10}H_{12}O_4$: C, 61.22; H, 6.16. Found: C, 61.09; H, 6.24.

Dimethyl 2,3-Dimethylenesuccinate (3k). The similarly obtained crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (1:9) as an eluent to obtain **3k** (31%) as a thick oil. ^1H NMR ($CDCl_3$, 200 MHz) δ 3.77 (s, 6H), 5.82 (d, $J = 2$ Hz, 2H), 6.30 (d, $J = 2$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 52.1, 127.8, 138.4, 166.1; IR ($CHCl_3$) ν_{max} 1719, 1618, 1437 cm^{-1}. Anal. Calcd for $C_8H_{10}O_4$: C, 56.47; H, 5.92. Found: C, 56.34; H, 6.06.

Dimethyl 2-Benzyl-3-methylenesuccinate (5a).[2c] To a stirred solution of benzyltriphenylphosphonium bromide (866 mg, 2.00 mmol) in THF (25 mL) at −100 °C was added *n*-BuLi (1.34 mL, 2.00 mmol) in a dropwise fashion under argon atmosphere. The reaction mixture was allowed to reach 0 °C. Then, the reaction mixture was added to a stirred solution of **1** (521 mg, 2.00 mmol) in THF (20 mL) at −100 °C under argon atmosphere in a dropwise fashion. Stirring was continued for a further 3 h at the same temperature. The reaction was then quenched with water. The reaction mixture was extracted with ethyl acetate (30 mL × 4), and the combined organic layer was washed with brine and dried over Na_2SO_4. Concentration of the organic layer in vacuo followed by silica gel column chromatographic purification of the residue using a mixture of ethyl acetate/petroleum ether (1:9) as an eluent provided major product **5a** (248 mg, 50%) and minor product **3a** (89 mg, 18%) as thick oils. ^1H NMR ($CDCl_3$, 200 MHz) δ 2.96 (dd, $J = 14$ and 8 Hz, 1H), 3.25 (dd, $J = 14$ and 8 Hz, 1H), 3.63 (s, 3H), 3.75 (s, 3H), 3.83 (t, $J = 8$ Hz, 1H), 5.67 (s, 1H), 6.31 (s, 1H), 7.10−7.35 (m, 5H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 37.4, 48.8, 52.0, 52.1, 126.4, 127.5, 128.3, 128.9, 137.6, 138.7, 166.4, 173.0; IR ($CHCl_3$) ν_{max} 1740, 1721, 1632 cm^{-1}. Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.58; H, 6.41.

3-[Deutero(phenyl)methyl]-4-methylenehexane-2,5-dione (6). Compound **6** was prepared by using the same procedure as described previously, and the reaction was quenched with D_2O. The crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (1:9) as an eluent to obtain major product **6** (48%) and minor product **3a** (21%) as thick oils. ^1H NMR ($CDCl_3$, 200 MHz) δ 2.95 (d, $J = 8$ Hz, 0.8H), 3.18−3.25 (m, 0.2H), 3.63 (s, 3H), 3.75 (s, 3H), 3.79−3.90 (m, 1H), 5.67 (s, 1H), 6.31 (s, 1H), 7.10−7.35 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 37.1 (t, $J = 10$ Hz), 48.7, 52.0, 52.1, 126.4, 127.5, 128.3, 128.9, 137.6, 138.7, 166.4, 173.0; IR ($CHCl_3$) ν_{max} 1734, 1719, 1636, 1634 cm^{-1}. (The C−D coupling observed in ^{13}C NMR spectrum are in parentheses.)

Dimethyl 2-(3,4-Dimethoxybenzyl)-3-methylenesuccinate (5c). The similarly obtained crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (1:4) as an eluent to obtain major product **5c** (60%) and minor product **3c** (15%) as thick oils. ^1H NMR ($CDCl_3$, 200 MHz) δ 2.89

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(dd, J = 14 and 6 Hz, 1H), 3.16 (dd, J = 14 and 8 Hz, 1H), 3.63 (s, 3H), 3.77 (s, 3H), 3.85 (s, 6H), 3.70−3.90 (m, 1H), 5.70 (s, 1H), 6.31 (s, 1H), 6.60−6.85 (m, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 37.3, 48.9, 52.0, 52.1, 55.8 (2 carbons), 111.2, 112.2, 121.0, 127.3, 131.3, 137.8, 147.7, 148.8, 166.3, 173.0; IR ($CHCl_3$) ν_{max} 1734, 1717, 1636 cm^{-1}. Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.33; H, 6.54. Found: C, 62.47; H, 6.70.

Dimethyl 2-(2-Fluorobenzyl)-3-methylenesuccinate (5g). The similarly obtained crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (1:9) as an eluent to obtain major product **5g** (52%) and minor product **3g** (18%) as thick oils. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.06 (dd, J = 14 and 8 Hz, 1H), 3.29 (dd, J = 14 and 8 Hz, 1H), 3.65 (s, 3H), 3.75 (s, 3H), 3.60−3.85 (m, 1H), 5.62 (s, 1H), 6.28 (s, 1H), 6.90−7.25 (m, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 30.7 (d, J = 2 Hz), 47.6 (d, J = 2 Hz), 52.07, 52.11, 115.2 (d, J = 22 Hz), 123.9 (d, J = 4 Hz), 125.6 (d, J = 16 Hz), 127.9, 128.3 (d, J = 9 Hz), 131.3 (d, J = 5 Hz), 137.4, 161.2 (d, J = 244 Hz), 166.2, 172.7; IR ($CHCl_3$) ν_{max} 1730, 1720, 1634 cm^{-1}. Anal. Calcd for $C_{14}H_{15}FO_4$: C, 63.15; H, 5.68. Found: C, 63.04; H, 5.79. (The C−F couplings observed in ^{13}C NMR spectrum are in parentheses.)

Dimethyl 2-Methylene-3-(4-nitrobenzyl)succinate (5h). The similarly obtained crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (1:9) as an eluent to obtain **5h** (85%) as a thick oil. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.07 (dd, J = 14 and 8 Hz, 1H), 3.34 (dd, J = 14 and 8 Hz, 1H), 3.64 (s, 3H), 3.77 (s, 3H), 3.70−3.90 (m, 1H), 5.66 (s, 1H), 6.32 (s, 1H), 7.34 (d, J = 8 Hz, 2H), 8.13 (d, J = 8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 37.2, 48.4, 52.2 (2 carbons), 123.5, 127.8, 129.8, 137.2, 146.6, 146.7, 166.1, 172.2; IR ($CHCl_3$) ν_{max} 1732, 1713, 1630, 1607 cm^{-1}. Anal. Calcd for $C_{14}H_{15}NO_6$: C, 57.33; H, 5.16; N, 4.78. Found: C, 57.38; H, 5.19; N, 4.69.

(2*E*,3*E*)-Dimethyl 2,3-Dibenzylidenesuccinate (7a).[16] A mixture of **3a** (246 mg, 1.00 mmol), phenyl iodide (0.074 mL, 0.66 mmol), dicyclohexyl amine (0.20 mL, 1.00 mmol), and the catalyst Pd(OAc)$_2$ (6.7 mg, 3 mol %) in water (3 mL) was heated at 120 °C for 24 h. Then, the reaction mixture was cooled and diluted with EtOAc (40 mL). The organic layer was washed with 2 N HCl (30 mL × 2) and water (30 mL × 2) and dried over Na_2SO_4. The organic layer was concentrated in vacuo followed by column chromatography purification using ethyl acetate/petroleum ether (1:9) to afford pure product **7a** (182 mg, *E*/*Z* 94:6, 86%) as a thick oil. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.70 (s, 6H), 7.15−7.30 (m, 6H), 7.30−7.45 (m, 4H), 7.88 (s, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 52.4, 126.6, 128.5, 129.4, 129.5, 134.5, 142.9, 167.3; IR ($CHCl_3$) ν_{max} 1709, 1638, 1605, 1435 cm^{-1}. Anal. Calcd for $C_{20}H_{18}O_4$: C, 74.52; H, 5.63; Found: C, 74.62; H, 5.55.

(2*E*,3*E*)-Dimethyl 2,3-Bis(3,4-dimethoxydibenzylidene)succinate (7c). The similarly obtained crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (3:7) as an eluent to obtain **7c** (*E*/*Z* 94:6, 86%) as a thick oil. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.71 (s, 6H), 3.75 (s, 6H), 3.86 (s, 6H), 6.80 (d, J = 8 Hz, 2H), 7.08−7.20 (m, 4H), 7.90 (s, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 52.1, 55.4, 55.6, 110.6, 111.6, 124.2, 124.4, 127.3, 142.0, 148.5, 150.3, 167.5; IR ($CHCl_3$) ν_{max} 1709, 1628 cm^{-1}. Anal. Calcd for $C_{24}H_{26}O_8$: C, 65.15; H, 5.92; Found: C, 65.23; H, 6.00.

(*E*)-Dimethyl 2-Benzyl-3-benzylidenesuccinate (9a).[16] The similarly obtained crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (1:9) as an eluent to obtain **9a** (*E*/*Z* 82:18, 88%) as a thick oil. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.98 (dd, J = 14 and 10 Hz, 1H), 3.42 (dd, J = 14 and 4 Hz, 1H), 3.73 (s, 3H), 3.84 (s, 3H), 4.00 (dd, J = 10 and 4 Hz, 1H), 6.81−6.92 (m, 3H), 7.06−7.16 (m, 3H), 7.18−7.31 (m, 4H), 7.76 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 35.9, 45.3, 52.0, 52.2, 126.1, 128.08, 128.12, 128.16, 128.20, 129.1, 130.4, 135.0, 138.9, 142.9, 167.0, 173.1; IR ($CHCl_3$) ν_{max} 1738, 1715, 1643, 1603 cm^{-1}. Anal. Calcd for $C_{20}H_{20}O_4$: C, 74.06; H, 6.22. Found: C, 73.89; H, 6.17.

(*E*)-Dimethyl 2-(Benzo[*d*][1,3]dioxal-5-ylmethyl)-3-(3,4-dimethoxybenzylidene)succinate (9c). The similarly obtained crude product was purified by column chromatography using a mixture of ethyl acetate/petroleum ether (1:4) as an eluent to obtain **9c** (*E*/*Z* 82:18, 88%) as a thick oil. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.91 (dd, J = 14 and 10 Hz, 1H), 3.37 (dd, J = 14 and 4 Hz, 1H), 3.66 (s, 3H), 3.73 (s, 3H), 3.81 (s, 6H), 4.05 (dd, J = 10 and 4 Hz, 1H), 5.94 (s, 2H), 6.38 (dd, J = 6 and 2 Hz, 1H), 6.46 (dd, J = 8 and 2 Hz, 1H), 6.48 (d, J = 2 Hz, 1H), 6.66 (d, J = 6 Hz, 1H), 6.67 (s, 1H), 6.73 (d, J = 8 Hz, 1H), 7.63 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 35.6, 45.4, 51.9, 52.2, 55.3, 55.8, 101.2, 108.1, 108.4, 110.8, 111.8, 121.1, 122.5, 128.8, 129.6, 131.4, 142.3, 147.3, 147.5, 147.6, 148.5, 167.0, 173.0; IR ($CHCl_3$) ν_{max} 1738, 1715, 1630, 1605 cm^{-1}. Anal. Calcd for $C_{23}H_{24}O_8$: C, 64.48; H, 5.65. Found: C, 64.53; H, 5.48.

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Supporting Information Available: The tabulated analytical and spectral data for the compounds **3b**, **3d**−**f**, **5b**, **5d**−**f**, and **5i**. ^{1}H NMR, ^{13}C NMR, and DEPT spectra of **3a**−**c**, **3e**, **3g**, **3j**,**k**, **5a**−**i**, **6**, **7a**, **7c**, **9a**, and **9c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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