

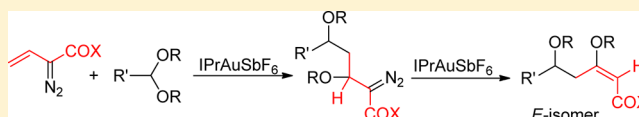
Gold-Catalyzed Reactions between Alkenyldiazo Carbonyl Species and Acetals

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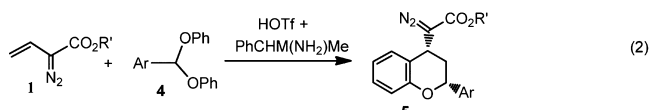
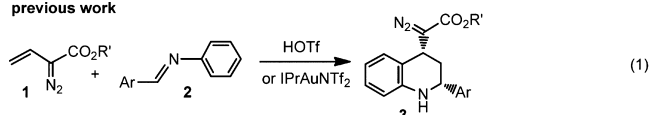
S Supporting Information

ABSTRACT: In the presence of catalyst IPrAuSbF₆ catalyst (IPr = 1,3-bis(diisopropylphenyl)imidazol-2-ylidene), alkenyldiazo carbonyl species react with organic acetals to give *E*-configured alkyl 3,5-dimethoxy-5-pent-2-enoates stereoselectively. This reaction sequence comprises an initial Prins-type reaction, followed by gold carbene formation.

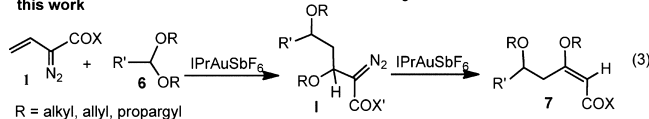


Alkenyldiazo carbonyl species are useful reagents to access complicated acyclic and cyclic molecules.¹ The major use of these reagents relies on their initial diazo decomposition with a metal catalyst to generate reactive alkenylmetal carbene intermediates, further enabling stereo- or regioselective [3 + *n*]-cycloadditions (*n* = 2–4) with suitable dipolarophiles.^{2–4} This reaction route has found widespread applications to access complicated carbo- and heterocyclic compounds.^{2–4} Alternatively, in the presence of suitable Lewis acid catalysts, these alkenyl diazo reagent work as nucleophiles to react with aldehydes and enones to give addition products to retain their diazo functionalities.⁵ We recently reported⁶ formal [4 + 2]-cycloadditions of these diazo species (**1**) with *N*-arylimines (Povarov reaction)⁷ to give isolable diazo-containing cycloadducts (**3**) using HOTf (3 mol %) or IPrAuCl/AgNTf₂ (2.5 mol %), IPr = 1,3-bis(diisopropylphenyl)imidazol-2-ylidene, as depicted in eq 1. This reaction sequence is applicable also to

previous work



this work



R = alkyl, allyl, propargyl
R' = aryl, alkenyl

diphenoxymethylbenzenes (**4**) to effect an unprecedented oxa-Povarov reaction, further affording oxacyclic products (**5**) stereoselectively (eq 2).⁶ In this work, we report a distinct and new route between alkenyldiazo carbonyl species **1** and commonly used acetal substrates **6**; this process generates 1,3-dialkoxy-4-diazo intermediate **I**, further giving *E*-configured ethyl 3,5-dimethoxy-5-pent-2-enoate **7** stereoselectively (eq 3).

Table 1 shows the reactions between vinyldiazo ester **1a** and dimethoxymethylbenzene **6a** using various acid catalysts. We

Table 1. Catalyst Screenings over Various Acid Catalysts

entry	catalyst (mol %)	time (h)	compounds (yield, %) ^b	
			1a	7a
1	IPrAuCl/AgNTf ₂ (2.5)	0.1		80
2	IPrAuCl/AgSbF ₆ (2.5)	0.1		84 (81) ^c
3	IPrAuCl/AgSbF ₆ (2.5)	1.0		77 ^d
4	LAuCl/AgSbF ₆ (2.5)	0.1		67
5	PPh ₃ AuCl/AgSbF ₆ (5)	0.3		57
6	AgSbF ₆ (2.5)	0.3		46
7	Rh ₂ (OAc) ₄ (2.5)	1.2		
8	Cu(OTf) ₂ (5)	1.5		
9	Zn(OTf) ₂ (5)	2.0		
10	HOTf (3)	2.5		
11	Sc(OTf) ₃ (5)	6.0	46	
12	In(OTf) ₃ (5)	6.0	51	
13	HOTf (2)/PhCH(NH ₂)Me(3)	6.0	76	

^a **1a** (1.0 equiv, 0.50 M), **6a** (1.0 equiv), IPr = 1,3-bis-(diisopropylphenyl)imidazol-2-ylidene, L = P(*t*-Bu)₂(*o*-biphenyl).

^b Product yields are given after purification from a silica column.

^c The value in parentheses corresponds to a prior removal of AgCl.

^d this reaction was operated at 1.0 g scale with 0.1 M.

first tested the reactions with IPrAuCl/AgX (2.5 mol %, X = NTf₂ and SbF₆) that were found to be chemoselective toward the Povarov reaction^{6,7} of vinyldiazo species **1a** (see eq 1). Herein, we obtained ethyl 3,5-dimethoxy-5-pent-2-enoate **7a** in 80–84% yields (entries 1 and 2). With IPrAuCl/AgSbF₆, the yield of compound **7a** was kept at 81% with a prior filtration of

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Reaction scheme showing the synthesis of 7b-7p from 1a and 6b-6o under the following conditions:

2.5 mol % IPrAuSbF₆
DCE, 25 °C
time

1a + 6b-6o → 7b-7p

Products 7b-7p are shown with their respective structures and yields:

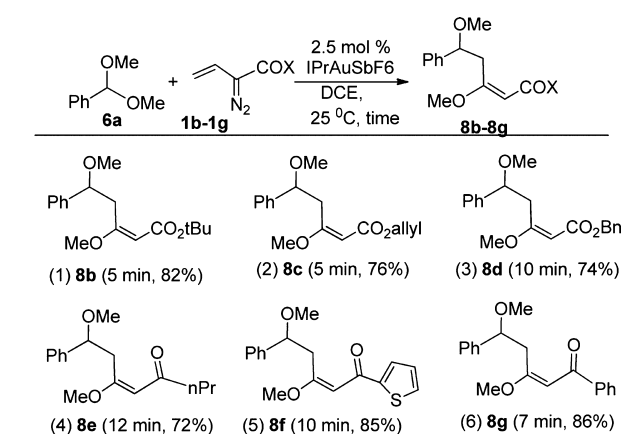
- (1) **7b** (10 min, 63%)^a
- (2) **7c** (25 min, 57%)
- (3) **7d** (8 min, 89%)
- (4) **7e** (8 min, 86%)
- (5) **7f** (8 min, 89%)
- (6) **7g** (8 min, 73%)
- (7) **7h** (5 min, 74%)
- (8) **7i** (5 min, 78%)
- (9) **7j** (10 min, 72%)
- (10) **7k** (10 min, 77%)
- (11) **7l** (10 min, 67%)
- (12) **7m** (12 min, 71%)
- (13) **7n** (10 min, 74%)
- (14) **7o** (15 min, 86%)
- (15) **7p** (12 min, 87%)

AgCl through a Celite bed. If the reaction was operated with diazo reagent **1a** (0.1 M) on a gram scale, the desired **7a** was obtained with 77% yield (entry 3). Other gold catalysts LAuCl/AgSbF₆ (L = P(*t*-Bu)₂(*o*-biphenyl)) and PPh₃AgCl/AgSbF₆ appear to be less productive, giving desired unsaturated ester **7a** in 57–67% yields (entries 4 and 5). The use of AgSbF₆ alone gave ester **7a** in 46% yield (entry 6). Other catalysts Rh₂(OAc)₄, Cu(OTf)₂, Zn(OTf)₂, and HOTf, each at 2.5–5 mol % loading (entries 7–10), gave a complicated mixture of products whereas Sc(OTf)₃, In(OTf)₃, and HOTf/PhCH(NH₂)Me led to recovery of vinyldiazo species **1a** in large proportions (46–76%, entries 11–13). The *E*-configuration of ester **7a** is inferred from the X-ray diffraction⁸ of its acid derivative **7a'**, which was obtained by LiOH-catalyzed hydrolysis in a THF/H₂O (2:1) solution.

various phenyl substituents including electron-rich 4-methyl, 4-*tert*-butyl, 4-methoxy, and 2-methoxy, affording desired unsaturated esters **7d–g** in good yields (73–89%, entries 3–6). The same reactions worked well with electron-deficient phenyl substrates **6h** and **6i** bearing 4-chloro and 4-bromo substituents, giving the expected products **7h** and **7i** in 74% and 78% yields, respectively (entries 7 and 8). We also tested the reactions on heteroaryl substrates **6j–n** including 3-furanyl, 3-thienyl, 2-benzofuranyl, 3-indolyl, and 2-benzothienyl; their corresponding products **7j–n** had 67–77% yields (entries 9–13). We tested the reactions on alkenyl acetals **6o** and **6p** to provide unsaturated esters **7o** and **7p** in 86–87% yields (entries 14 and 15).

To expand the reaction scope, we also prepared various diazovinyl carbonyl reagents **1b–g**; the results are provided in Table 3. As shown in entries 1–3, the reactions between various vinyldiazo esters **1b–d** and acetal **6a** proceeded smoothly to afford desired unsaturated esters **8b–d** (X = O^tBu), Oallyl, OBn) in 72–82% yields, respectively. The same reactions were applicable to vinyldiazo ketones **1e–g** (X = ⁿPr,

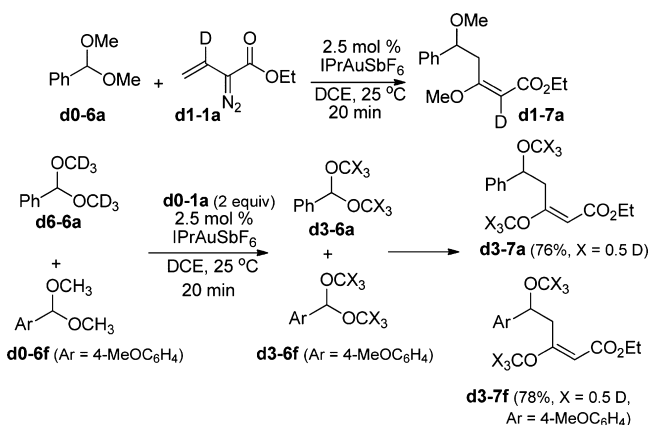
Table 3. Reaction Scope with Various Vinylidiao Substrates



2-thienyl, phenyl), giving unsaturated ketones **8e–g** in satisfactory yields (72–86%).

Shown in Scheme 1 are additional experiments undertaken to understand the reaction mechanism. We prepared deuterated

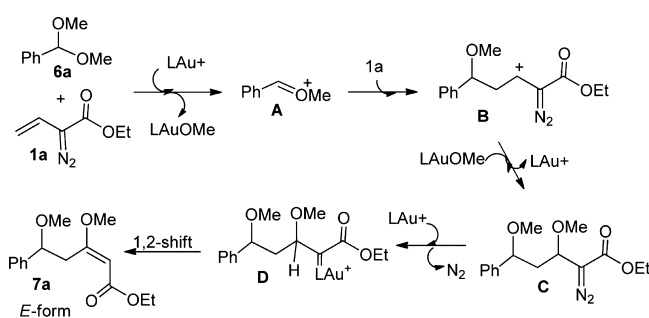
Scheme 1



sample **d1-1a** with its alkenyl C(2)-proton fully deuterated; its gold-catalyzed reaction with phenyldimethoxymethane **d0-6a** gave the desired **d1-7a** bearing a fully deuterated $\text{=CDCO}_2\text{Et}$, indicative of a 1,2-hydrogen shift. We performed the same reaction using acetals **d6-6a** and **d0-6f** in equimolar proportions, their reactions with vinylidiao ester **1a** (2 equiv) gave unsaturated esters **d3-7a** and **d3-7f** in 76% and 78% yields, respectively. The two methoxy groups of each product contained 50% deuterium content at the benzyl and alkenyl positions according to ^1H NMR analysis whereas their mass spectra revealed a 1:2:1 ratio, corresponding to the ratios of $d_0:d_3:d_6$ samples. Notably, the $d_0:d_3:d_6$ ratio remains the same even though diazo reagent **1a** was absent. This information confirms an intermolecular gold-catalyzed exchange of methoxy between two acetals to give **d3-6a** and **d3-6f** before their reactions with diazo species **1a**.

Scheme 2 shows a plausible mechanism involving the intermediacy of gold carbene species **D**. As IPrAuSbF_6 enables a rapid methoxy exchange between two acetals, as shown in Scheme 1, this observation indicates a facile formation of the oxonium intermediate **A**. We envisage that gold activates a Prins-type reaction^{9,10} between vinylidiao ester **1a** and acetal **6a** to generate 1,3-dimethoxy-4-diazo ester **C**; the success of this reaction relies on the stabilization of an adjacent

Scheme 2



carbocation by diazo functionality as in intermediate **B**. The postulated carbene intermediate **D** is supported by a 1,2-hydrogen shift^{11,12} in the deuterium labeling experiment (Scheme 1). The excellent *E*-selectivity in this 1,2-shift is indicative also of gold carbene species^{11,13} whereas the *Z*-selectivity is known for rhodium carbenes.^{12,13}

In summary, gold-catalyzed reactions between vinylidiao carbonyl species and acetals are described; the resulting *E*-configured alkyl 3,5-dimethoxy-5-pent-2-enoates are obtained in good yields. According to our experimental data, this reaction sequence comprises an initial Prins-type reaction, followed by gold-carbene generation. The success of this Prins-type reaction indicates a stabilization effect of the diazo functionality on the adjacent carbocation; this information allows new designs between alkenyldiazo species and other electrophiles.

EXPERIMENTAL SECTION

General Comments. Unless otherwise noted, all reactions to prepare the substrates were performed in oven-dried glassware under nitrogen atmosphere with freshly distilled solvents. The catalytic reactions were performed under nitrogen atmosphere. DCE, DCM, and CH_3CN were distilled from CaH_2 under nitrogen. THF were distilled from Na metal under nitrogen. All other commercial reagents were used without further purification, unless otherwise indicated. ^1H and ^{13}C NMR spectra were recorded on spectrometers 400, 500, and 600 MHz using chloroform- d_1 (CDCl_3), and dimethyl sulfoxide- d_6 (DMSO) as internal standards. Alkenyldiazo compounds (**1a–g**) were prepared according to literature references.^{4a,6,14}

General Procedure for the Gold-Catalyzed Reaction between Acetal (6a) and Vinylidiao Ester (1a). A dichloroethane (DCE, 1.0 mL) solution of IPrAuCl (7.8 mg, 0.012 mmol) and AgSbF_6 (4.3 mg, 0.012 mmol) was stirred at 25°C for 5 min, and to this solution was added a DCE (1.5 mL) solution of alkenyl diazoacetates (**1a**) (70 mg, 0.50 mmol) and acetal (**6a**) (76 mg, 0.50 mmol) over 5 min. The resulting solution was stirred at 25°C . After 10 min, the solution was filtered over a short silica bed; the solvent was evaporated under reduced pressure. The residue was purified on a flash silica gel column (hexane/ethyl acetate = 9/1) to give compound **7a** as a colorless liquid (110 mg, 84% yield).

(E)-Ethyl 3,5-dimethoxy-5-phenylpent-2-enoate (7a): colorless liquid (110 mg, 84%); ^1H NMR (600 MHz, CDCl_3) δ 7.34–7.29 (m, 4H), 7.23 (t, J = 7.0 Hz, 1H), 5.00 (s, 1H), 4.51 (dd, J = 5.3, 8.7 Hz, 1H), 4.11 (q, J = 7.0 Hz, 2H), 3.55 (s, 3H), 3.19 (s, 3H), 3.16 (dd, J = 5.2, 13.6 Hz, 1H), 3.07 (dd, J = 5.3, 13.6 Hz, 1H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 173.0, 167.3, 141.4, 128.2, 127.5, 126.6, 91.9, 81.9, 59.3, 56.9, 55.5, 40.8, 14.4; HRMS calcd for $\text{C}_{15}\text{H}_{20}\text{O}_4$ 264.1362, found 264.1362.

Deuterated (E)-ethyl 3,5-dimethoxy-5-phenylpent-2-enoate (d1-7a): colorless liquid (91 mg, 70%); ^1H NMR (600 MHz, CDCl_3) δ 7.34–7.29 (m, 4H), 7.23 (d, J = 7.1 Hz, 1H), 4.51 (dd, J = 5.4, 8.7 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 3.59 (s, 3H), 3.20–3.15 (m, 4H), 3.08 (dd, J = 5.5, 13.4 Hz, 1H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (150

MHz, CDCl₃) δ 172.9, 167.3, 141.4, 128.2, 127.5, 126.7, 91.7 (t, J = 24 Hz), 81.9, 59.3, 56.9, 55.5, 40.8, 14.4; HRMS calcd for C₁₅H₁₉DO₄ 265.1424, found 265.1428.

Deuterated (E)-ethyl 3,5-dimethoxy-5-phenylpent-2-enoate (d₃-7a): colorless liquid (101 mg, 76%); ¹H NMR (600 MHz, CDCl₃) δ 7.35–7.29 (m, 4H), 7.23 (t, J = 7.1 Hz, 1H), 5.00 (d, J = 3.4 Hz, 1H), 4.51 (dd, J = 5.2, 8.7 Hz, 1H), 4.11 (q, J = 7.2 Hz, 2H), 3.56 (s, 1.5H), 3.19 (s, 1.47 H), 3.15 (dd, J = 8.7, 13.5 Hz, 1H), 3.08 (dd, J = 5.3, 13.5 Hz, 1H), 1.25 (t, J = 7.1 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 173.0, 167.4, 141.4 (d, J = 4.8 Hz), 128.2, 127.5, 126.6, 91.9 (d, J = 6.3 Hz), 81.9 (J = 15.1 Hz), 59.3, 56.9, 55.5, 40.8, 14.4; HRMS calcd for C₁₅H₂₀O₄ 264.1362, found 264.1373, 267.1552, 270.1739.

(E)-Ethyl 3,5-dimethoxy-5-phenylpent-2-enoate (7a): white solid (56 mg, 90%); ¹H NMR (500 MHz, CDCl₃) δ 7.33 (d, J = 7.5 Hz, 2H), 7.31–7.24 (m, 3H), 4.96 (s, 1H), 4.45 (t, J = 8.5 Hz, 1H), 3.49 (s, 3H), 3.20 (dd, J = 8.0, 14.0 Hz, 1H), 3.06 (s, 3H), 2.95 (dd, J = 6.5, 14.0 Hz, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 171.4, 168.0, 141.2, 128.2, 127.5, 126.4, 92.7, 81.0, 56.1, 55.4, 39.1; HRMS calcd for C₁₅H₁₆O₄ 236.1049, found 236.1055.

(E)-Ethyl 3,5-diethoxy-5-phenylpent-2-enoate (7b): light yellow liquid (91 mg, 63%); ¹H NMR (600 MHz, CDCl₃) δ 7.32 (d, J = 7.8 Hz, 2H), 7.28 (t, J = 8.2 Hz, 2H), 7.22 (d, J = 7.2 Hz, 1H), 4.93 (s, 1H), 4.60 (dd, J = 6.4, 7.9 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 3.71 (q, J = 7.0 Hz, 1H), 3.62 (q, J = 7.0 Hz, 1H), 3.39–3.32 (m, 2H), 3.26 (dd, J = 8.0, 13.2 Hz, 1H), 3.00 (dd, J = 6.3, 13.3 Hz, 1H), 1.24 (t, J = 7.1 Hz, 3H), 1.16 (t, J = 7.0 Hz, 3H), 1.12 (t, J = 7.0 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 172.2, 167.5, 142.1, 128.0, 127.3, 126.7, 92.1, 79.5, 64.2, 63.7, 59.3, 40.9, 15.3, 14.4, 14.0; HRMS calcd for C₁₇H₂₄O₄ 292.1675, found 292.1668.

(E)-Ethyl 3,5-bis(allyloxy)-5-phenylpent-2-enoate (7c): light yellow liquid (90 mg, 57%); ¹H NMR (600 MHz, CDCl₃) δ 7.34 (d, J = 7.0 Hz, 2H), 7.30 (t, J = 7.3 Hz, 2H), 7.23 (d, J = 7.2 Hz, 1H), 5.84–5.78 (m, 2H), 5.27–5.09 (m, 4H), 4.98 (s, 1H), 4.68 (dd, J = 5.9, 8.4 Hz, 1H), 4.22–4.18 (m, 2H), 4.11 (q, J = 7.1 Hz, 2H), 3.90 (dd, J = 4.9, 13.0 Hz, 1H), 3.74 (dd, J = 5.8, 13.0 Hz, 1H), 3.34 (dd, J = 8.4, 13.5 Hz, 1H), 3.05 (dd, J = 5.9, 13.5 Hz, 1H), 1.24 (t, J = 7.1 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 171.5, 167.3, 141.5, 134.9, 131.8, 128.2, 127.5, 126.8, 118.1, 116.3, 93.0, 79.3, 69.5, 68.9, 59.4, 40.7, 14.4; HRMS calcd for C₁₉H₂₄O₄ 316.1675, found 316.1668.

(E)-Ethyl 3,5-dimethoxy-5-p-tolylpent-2-enoate (7d): colorless liquid (123 mg, 89%); ¹H NMR (600 MHz, CDCl₃) δ 7.23 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 7.8 Hz, 2H), 5.01 (s, 1H), 4.49 (dd, J = 5.2, 8.7 Hz, 1H), 4.12 (q, J = 7.1 Hz, 2H), 3.57 (s, 3H), 3.18 (s, 3H), 3.15 (dd, J = 5.2, 13.5 Hz, 1H), 3.07 (dd, J = 5.2, 13.5 Hz, 1H), 2.31 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 173.1, 167.4, 138.3, 137.1, 128.9, 126.5, 91.8, 81.7, 59.3, 56.8, 55.5, 40.8, 21.1, 14.4; HRMS calcd for C₁₆H₂₂O₄ 278.1518, found 278.1518.

(E)-Ethyl 5-(4-tert-butylphenyl)-3,5-dimethoxypent-2-enoate (7e): light yellow liquid (137 mg, 86%); ¹H NMR (600 MHz, CDCl₃) δ 7.32 (d, J = 8.4 Hz, 2H), 7.26 (d, J = 8.3 Hz, 2H), 5.01 (s, 1H), 4.48 (dd, J = 5.3, 8.7 Hz, 1H), 4.12 (q, J = 7.1 Hz, 2H), 3.57 (s, 3H), 3.19 (s, 3H), 3.14 (dd, J = 5.1, 13.5 Hz, 1H), 3.06 (dd, J = 5.1, 13.5 Hz, 1H), 1.28 (s, 9H), 1.24 (t, J = 7.1 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 173.3, 167.4, 150.4, 138.4, 126.3, 125.4, 91.8, 81.7, 59.4, 56.9, 55.5, 40.9, 33.8, 31.3, 14.4; HRMS calcd for C₁₉H₂₈O₄ 320.1988, found 320.1993.

(E)-Ethyl 3,5-dimethoxy-5-(4-methoxyphenyl)pent-2-enoate (7f): light yellow liquid (130 mg, 89%); ¹H NMR (600 MHz, CDCl₃) δ 7.25 (d, J = 8.3 Hz, 2H), 6.83 (d, J = 8.4 Hz, 2H), 4.98 (s, 1H), 4.46 (dd, J = 5.5, 8.5 Hz, 1H), 4.11 (q, J = 7.0 Hz, 2H), 3.77 (s, 3H), 3.54 (s, 3H), 3.16–3.13 (m, 4H), 3.06 (dd, J = 5.5, 13.5 Hz, 1H), 1.23 (t, J = 7.0 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 173.0, 167.3, 159.0, 133.4, 127.8, 113.5, 91.9, 81.4, 59.3, 56.6, 55.4, 55.1, 40.7, 14.3; HRMS calcd for C₁₆H₂₂O₅ 294.1467, found 294.1436.

Deuterated (E)-ethyl 3,5-dimethoxy-5-(4-methoxyphenyl)pent-2-enoate (d₃-7f): light yellow liquid (113 mg, 78%); ¹H NMR (600 MHz, CDCl₃) δ 7.26–7.24 (m, 2H), 6.84 (d, J = 8.6 Hz, 2H), 4.99 (d, J = 3.4 Hz, 1H), 4.46 (dd, J = 5.5, 8.5 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 3.77 (s, 3H), 3.55 (s, 1.5H), 3.16–3.13 (m, 2.5H), 3.06 (dd, J = 5.4, 13.5 Hz, 1H), 1.24 (t, J = 7.1 Hz, 3H); ¹³C NMR (150 MHz,

CDCl₃) δ 173.1, 167.4, 159.0, 133.4 (d, J = 5.1 Hz), 127.0, 113.5, 91.8 (d, J = 6 Hz), 81.4 (d, J = 15.3 Hz), 59.4, 56.6, 55.5, 55.2, 40.7, 14.4; HRMS calcd for C₁₆H₂₂O₅ 294.1467, found 294.1473, 297.1641, 300.1809.

(E)-Ethyl 3,5-dimethoxy-5-(2-methoxyphenyl)pent-2-enoate (7g): light yellow liquid (107 mg, 73%); ¹H NMR (600 MHz, CDCl₃) δ 7.39 (d, J = 7.5 Hz, 1H), 7.19 (t, J = 7.8 Hz, 1H), 6.93 (t, J = 7.4 Hz, 1H), 6.81 (d, J = 8.1 Hz, 1H), 4.99 (s, 1H), 4.96 (dd, J = 5.1, 8.7 Hz, 1H), 4.07 (q, J = 7.1 Hz, 2H), 3.78 (s, 3H), 3.57 (s, 3H), 3.49 (dd, J = 5.1, 14.0 Hz, 1H), 3.19 (s, 3H), 2.90 (dd, J = 5.1, 14.0 Hz, 1H), 1.21 (t, J = 7.1 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 172.7, 167.3, 157.0, 129.5, 128.2, 127.1, 120.6, 110.1, 92.1, 74.9, 59.2, 56.8, 55.3, 55.2, 38.4, 14.3; HRMS calcd for C₁₆H₂₂O₅ 294.1467, found 294.1436.

(E)-Ethyl 5-(4-chlorophenyl)-3,5-dimethoxypent-2-enoate (7h): yellow liquid (110 mg, 74%); ¹H NMR (600 MHz, CDCl₃) δ 7.27–7.26 (m, 4H), 5.00 (s, 1H), 4.48 (dd, J = 5.9, 8.1 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 3.55 (s, 3H), 3.18 (s, 3H), 3.10–3.08 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 172.6, 167.3, 139.9, 133.2, 128.4, 128.0, 92.0, 81.3, 59.4, 56.9, 55.5, 40.7, 14.2; HRMS calcd for C₁₅H₁₉ClO₄ 298.0972, found 298.0973.

(E)-Ethyl 5-(4-bromophenyl)-3,5-dimethoxypent-2-enoate (7i): yellow liquid (133 mg, 78%); ¹H NMR (600 MHz, CDCl₃) δ 7.42 (d, J = 8.8 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H), 5.00 (s, 1H), 4.47 (dd, J = 5.2, 8.7 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 3.56 (s, 3H), 3.18 (s, 3H), 3.08 (dd, J = 1.7, 7.9 Hz, 2H), 1.24 (t, J = 7.1 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 172.6, 167.3, 140.4, 131.4, 128.4, 121.4, 92.1, 81.4, 59.5, 56.9, 55.5, 40.7, 14.4; HRMS calcd for C₁₅H₁₉BrO₄ 342.0467, found 342.0461.

(E)-Ethyl 5-(furan-3-yl)-3,5-dimethoxypent-2-enoate (7j): light yellow liquid (91 mg, 72%); ¹H NMR (600 MHz, CDCl₃) δ 7.35 (d, J = 3.6 Hz, 1H), 7.34 (d, J = 3.5 Hz, 1H), 6.41 (s, 1H), 5.01 (s, 1H), 4.53 (dd, J = 6.0, 8.2 Hz, 1H), 4.12 (q, J = 7.2 Hz, 2H), 3.57 (s, 3H), 3.25 (dd, J = 5.2, 13.5 Hz, 1H), 3.22 (s, 3H), 3.11 (dd, J = 6.0, 13.5 Hz, 1H), 1.24 (t, J = 7.2 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 172.7, 167.4, 143.1, 140.1, 125.3, 108.9, 92.1, 73.7, 59.4, 56.3, 55.5, 38.9, 14.4; HRMS calcd for C₁₃H₁₈O₅ 254.1154, found 254.1145.

(E)-Ethyl 3,5-dimethoxy-5-(thiophen-3-yl)pent-2-enoate (7k): light yellow liquid (103 mg, 77%); ¹H NMR (600 MHz, CDCl₃) δ 7.24 (dd, J = 3.0, 5.1 Hz, 1H), 7.16 (d, J = 2.9 Hz, 1H), 7.08 (d, J = 5.9 Hz, 1H), 5.00 (s, 1H), 4.63 (dd, J = 5.7, 8.4 Hz, 1H), 4.11 (q, J = 7.2 Hz, 2H), 3.55 (s, 3H), 3.24–3.20 (m, 4H), 3.11 (dd, J = 5.8, 13.6 Hz, 1H), 1.24 (t, J = 7.1 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 172.8, 167.3, 142.7, 126.1, 125.6, 121.8, 91.9, 77.6, 59.4, 56.7, 55.5, 39.8, 14.4; HRMS calcd for C₁₃H₁₈O₄S 270.0926, found 270.0922.

(E)-Ethyl 5-(benzofuran-3-yl)-3,5-dimethoxypent-2-enoate (7l): light yellow liquid (101 mg, 67%); ¹H NMR (500 MHz, CDCl₃) δ 7.51 (d, J = 7.5 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.23 (t, J = 7.5 Hz, 1H), 7.18 (t, J = 7.5 Hz, 1H), 6.67 (s, 1H), 5.05 (s, 1H), 4.73 (dd, J = 6.0, 8.5 Hz, 1H), 4.12 (q, J = 7.5 Hz, 2H), 3.55–3.51 (m, 4H), 3.31 (s, 3H), 3.22 (dd, J = 6.0, 14.0 Hz, 1H), 1.24 (t, J = 7.5 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 171.8, 167.3, 156.3, 155.0, 127.9, 124.1, 122.6, 120.9, 111.4, 104.6, 92.4, 74.8, 59.5, 56.9, 55.6, 36.9, 14.3; HRMS calcd for C₁₇H₂₀O₅ 304.1311, found 304.1302.

(E)-Ethyl 3,5-dimethoxy-5-(1-tosyl-1H-indol-3-yl)pent-2-enoate (7m): yellow semisolid (231 mg, 71%); ¹H NMR (600 MHz, CDCl₃) δ 7.92 (d, J = 8.3 Hz, 1H), 7.75 (d, J = 7.8 Hz, 1H), 7.71 (d, J = 8.3 Hz, 2H), 7.50 (s, 1H), 7.27 (t, J = 7.8 Hz, 1H), 7.22–7.17 (m, 3H), 4.99 (s, 1H), 4.44 (dd, J = 5.2, 8.6 Hz, 1H), 4.09 (q, J = 7.1 Hz, 2H), 3.47 (s, 3H), 3.42 (dd, J = 8.3, 13.5 Hz, 1H), 3.30 (s, 3H), 3.17 (dd, J = 6.0, 13.5 Hz, 1H), 2.20 (s, 3H), 1.22 (t, J = 7.1 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 172.3, 167.3, 144.8, 135.4, 135.2, 129.8, 129.2, 126.7, 124.7, 123.9, 123.2, 122.6, 120.9, 113.5, 92.2, 74.9, 59.5, 56.6, 55.4, 38.4, 21.5, 14.3; HRMS calcd for C₂₄H₂₇NO₆S 457.1559, found 457.1571.

(E)-Ethyl 5-(benzo[b]thiophene-3-yl)-3,5-dimethoxypent-2-enoate (7n): light yellow liquid (118 mg, 74%); ¹H NMR (600 MHz, CDCl₃) δ 7.79 (d, J = 7.8 Hz, 1H), 7.69 (d, J = 8.2 Hz, 1H), 7.30–7.26 (m, 2H), 7.21 (s, 1H), 5.05 (s, 1H), 4.88 (dd, J = 5.6, 8.4 Hz, 1H), 4.12 (q, J = 7.1 Hz, 2H), 3.57 (s, 3H), 3.35 (dd, J = 5.2, 13.7

H₂, 1H), 3.30 (s, 3H), 3.24 (dd, *J* = 5.6, 13.6 Hz, 1H), 1.24 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 172.1, 167.3, 146.3, 139.7, 139.4, 124.0 (CH × 2), 123.3, 122.5, 121.7, 92.3, 77.9, 59.5, 56.9, 55.5, 40.7, 14.3; HRMS calcd for C₁₇H₂₀O₄S 320.1082, found 320.1091.

(2E,6E)-Ethyl 3,5-dimethoxy-7-phenylhepta-2,6-dienoate (7o): light yellow liquid (124.7 mg, 86%); ¹H NMR (600 MHz, CDCl₃) δ 7.36 (d, *J* = 7.3 Hz, 2H), 7.28 (t, *J* = 7.4 Hz, 2H), 7.21 (d, *J* = 7.3 Hz, 1H), 6.51 (d, *J* = 15.9 Hz, 1H), 6.09 (dd, *J* = 7.9, 15.9 Hz, 1H), 5.03 (s, 1H), 4.13–4.07 (m, 3H), 3.58 (s, 3H), 3.30 (s, 3H), 3.16 (dd, *J* = 7.4, 13.2 Hz, 1H), 3.01 (dd, *J* = 6.6, 13.2 Hz, 1H), 1.24 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 172.5, 167.3, 136.5, 132.1, 129.4, 128.4, 127.6, 126.4, 92.2, 80.5, 59.3, 56.4, 55.4, 38.3, 14.3; HRMS calcd for C₁₇H₂₂O₄ 290.1518, found 290.1515.

(2E,6E)-Ethyl 3,5-Dimethoxy-7-(thiophene-2-yl)hepta-2,6-dienoate (7p): light yellow liquid (128 mg, 87%); ¹H NMR (600 MHz, CDCl₃) δ 7.12 (dd, *J* = 4.1, 2.5 Hz, 1H), 6.92 (t, *J* = 1.5 Hz, 2H), 6.64 (d, *J* = 15.7 Hz, 1H), 5.92 (dd, *J* = 7.8, 15.7 Hz, 1H), 5.03 (s, 1H), 4.11 (q, *J* = 7.2 Hz, 2H), 4.03 (q, *J* = 6.7 Hz, 1H), 3.59 (s, 3H), 3.29 (s, 3H), 3.14 (dd, *J* = 7.5, 13.2 Hz, 1H), 2.96 (dd, *J* = 6.4, 13.2 Hz, 1H), 1.24 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 172.5, 167.4, 141.8, 129.1, 127.3, 125.7, 125.1, 124.3, 92.2, 80.2, 59.4, 56.5, 55.5, 38.3, 14.3; HRMS calcd for C₁₅H₂₀O₄S 296.1082, found 296.1081.

(E)-tert-Butyl 3,5-dimethoxy-5-phenylpent-2-enoate (8b): light yellow liquid (99 mg, 82%); ¹H NMR (600 MHz, CDCl₃) δ 7.31–7.28 (m, 4H), 7.24 (t, *J* = 8.4 Hz, 1H), 4.91 (s, 1H), 4.48 (dd, *J* = 5.9, 8.3 Hz, 1H), 3.52 (s, 3H), 3.19 (s, 3H), 3.15 (dd, *J* = 8.3, 13.6 Hz, 1H), 3.08 (dd, *J* = 5.8, 13.6 Hz, 1H), 1.48 (s, 9H); ¹³C NMR (150 MHz, CDCl₃) δ 171.6, 166.7, 141.3, 128.2, 127.5, 126.7, 93.8, 81.9, 79.2, 56.8, 55.3, 40.3, 28.3; HRMS calcd for C₁₇H₂₄O₄ 292.1675, found 292.1668.

(E)-Allyl 3,5-dimethoxy-5-phenylpent-2-enoate (8c): light yellow liquid (96 mg, 76%); ¹H NMR (600 MHz, CDCl₃) δ 7.32–7.28 (m, 4H), 7.23 (d, *J* = 7.4 Hz, 1H), 5.95–5.89 (m, 1H), 5.29 (dd, *J* = 1.5, 17.2 Hz, 1H), 5.20 (dd, *J* = 1.3, 10.4 Hz, 1H), 5.04 (s, 1H), 4.57–4.56 (m, 2H), 4.50 (dd, *J* = 5.2, 8.7 Hz, 1H), 3.56 (s, 3H), 3.20–3.14 (m, 4H), 3.08 (dd, *J* = 5.2, 13.6 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃) δ 173.5, 166.9, 141.3, 132.8, 128.2, 127.6, 126.6, 117.7, 91.6, 81.9, 64.3, 56.9, 55.6, 40.9; HRMS calcd for C₁₆H₂₀O₄ 276.1362, found 276.1364.

(E)-Benzyl 3,5-dimethoxy-5-phenylpent-2-enoate (8d): light yellow liquid (82 mg, 74%); ¹H NMR (600 MHz, CDCl₃) δ 7.34–7.28 (m, 10H), 5.19–5.08 (m, 2H), 5.07 (s, 1H), 4.51 (dd, *J* = 5.2, 8.7 Hz, 1H), 3.56 (s, 3H), 3.20 (s, 3H), 3.18–3.06 (m, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 173.6, 167.2, 141.3, 136.6, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 91.7, 81.9, 65.4, 56.9, 55.6, 40.9; HRMS calcd for C₂₀H₂₂O₄ 326.1518, found 326.1512.

(E)-6,8-Dimethoxy-8-phenyloct-5-en-4-one (8e): light yellow liquid (95 mg, 72%); ¹H NMR (600 MHz, CDCl₃) δ 7.34 (d, *J* = 7.3 Hz, 2H), 7.31 (t, *J* = 7.8 Hz, 2H), 7.22 (d, *J* = 7.3 Hz, 1H), 5.43 (s, 1H), 4.51 (dd, *J* = 5.1, 8.8 Hz, 1H), 3.58 (s, 3H), 3.18 (s, 3H), 3.13 (dd, *J* = 5.1, 13.3 Hz, 1H), 3.03 (dd, *J* = 8.8, 13.3 Hz, 1H), 2.37–2.34 (m, 2H), 1.62–1.57 (m, 2H), 0.90 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 199.2, 172.7, 141.5, 128.2, 127.5, 126.6, 99.5, 81.9, 56.9, 55.4, 46.7, 41.6, 18.3, 13.8; HRMS calcd for C₁₆H₂₂O₃ 262.1569, found 262.1576.

(E)-3,5-Dimethoxy-5-phenyl-1-(thiophene-2-yl)pent-2-en-1-one (8f): light yellow liquid (100 mg, 85%); ¹H NMR (500 MHz, CDCl₃) δ 7.54 (d, *J* = 5.0 Hz, 1H), 7.40 (d, *J* = 7.5 Hz, 1H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.21–7.07 (m, 4H), 6.06 (s, 1H), 4.64 (dd, *J* = 5.0, 8.5 Hz, 1H), 3.70 (s, 3H), 3.31–3.13 (m, 5H); ¹³C NMR (125 MHz, CDCl₃) δ 181.9, 174.9, 145.0, 141.4, 134.1, 132.2, 128.2, 128.1, 126.6, 124.2, 96.4, 81.8, 56.9, 55.7, 42.3; HRMS calcd for C₁₇H₁₈O₃S 302.0977, found 302.0974.

(E)-3,5-Dimethoxy-1,5-diphenylpent-2-en-1-one (8g): light yellow liquid (103 mg, 86%); ¹H NMR (400 MHz, CDCl₃) δ 7.95 (d, *J* = 8.4 Hz, 1H), 7.86 (d, *J* = 7.8 Hz, 1H), 7.54–7.40 (m, 6H), 7.34–7.30 (m, 2H), 6.18 (s, 1H), 4.67 (dd, *J* = 7.2, 13.2 Hz, 1H), 3.71 (s, 3H), 3.28–3.12 (m, 5H); ¹³C NMR (100 MHz, CDCl₃) δ 190.2, 174.9, 141.5, 128.5, 128.3, 128.2, 127.9, 127.6, 127.5, 127.0, 96.8, 81.9, 56.9, 55.7, 42.2; HRMS calcd for C₁₉H₂₀O₃ 296.1412, found 296.1410.

■ ASSOCIATED CONTENT

Supporting Information

¹H and ¹³C NMR spectra of compounds 7a–p, d₁–7a, d₃–7f, 8b–g, and crystallographic data for compound 7a'. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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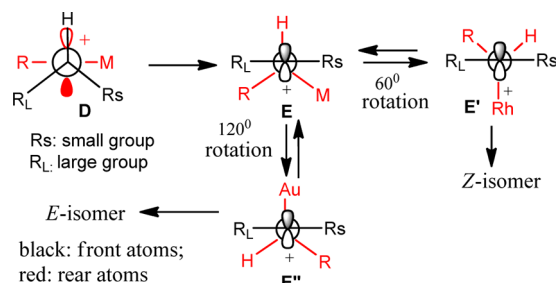
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