JOC The Journal of Organic Chemistry

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Gold-Catalyzed Reactions between Alkenyldiazo Carbonyl Species and Acetals

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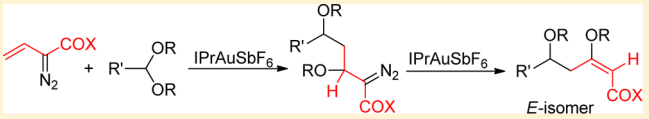
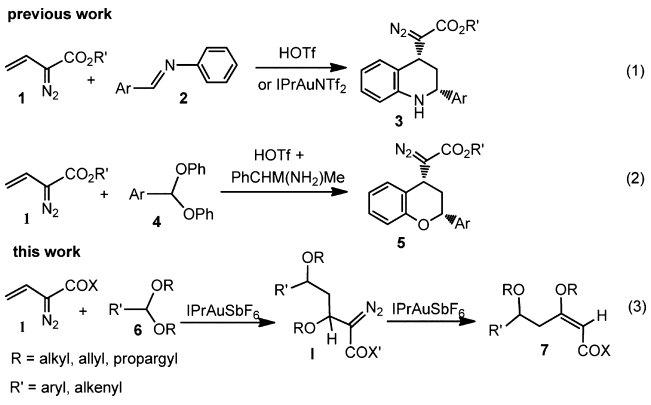
Supporting Information

ABSTRACT: In the presence of catalyst IPrAuSbF$_6$ 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.



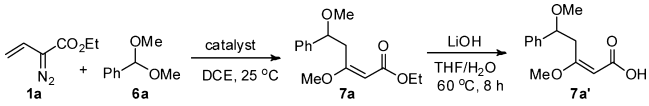
Alkenyldiazo carbonyl species are useful reagents to access complicated acyclic and cyclic molecules.[1] The major use of these reagents relies on their initial diazo decomposition with a metal catalyst to generate reactive alkenylmetal carbene intermediates, further enabling stereo- or regioselective [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 reported[6] 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/AgNTf$_2$ (2.5 mol %, IPr = 1, 3-bis(diisopropylphenyl)imidazol-2-ylidene), as depicted in eq 1. This reaction sequence is applicable also to



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



			compounds (yield, %)[b]	
entry	catalyst (mol %)	time (h)	**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	

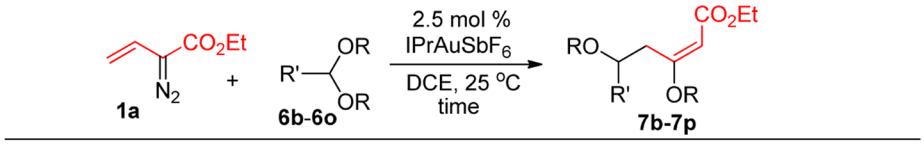
[a] **1a** (1.0 equiv, 0.50 M), **6a** (1.0 equiv), IPr = 1,3-bis-(diisopropylphenyl)imidazol-2-ylidene, L = P(*t*-Bu)2(*o*-biphenyl). [b] Product yields are given after purification from a silica column. [c] The value in parentheses corresponds to a prior removal of AgCl. [d] this reaction was operated at 1.0 g scale with 0.1 M.

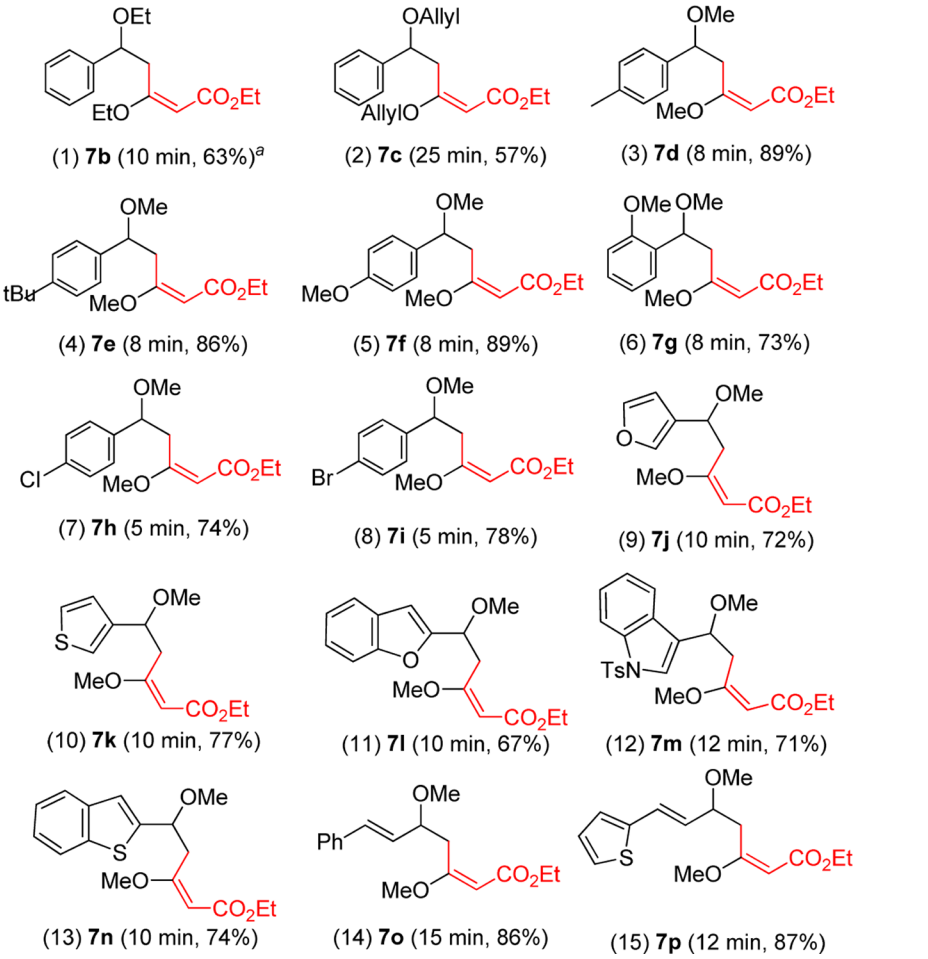
first tested the reactions with IPrAuCl/AgX (2.5 mol %, X = NTf$_2$ and SbF$_6$) that were found to be chemoselective toward the Povarov reaction[6,7] of vinyldiazo species **1a** (see eq 1). Herein, we obtained ethyl 3,5-dimethoxy-5-pent-2-enoate **7a** in 80−84% yields (entries 1 and 2). With IPrAuCl/AgSbF$_6$, the yield of compound **7a** was kept at 81% with a prior filtration of

Received: February 28, 2013
Published: May 6, 2013

   dx.doi.org/10.1021/jo400419d | *J. Org. Chem.* 2013, 78, 5711−5716

Table 2. Reaction Scope with Various Acetal Substrates





[a]Product yields are given after purification from a silica column.

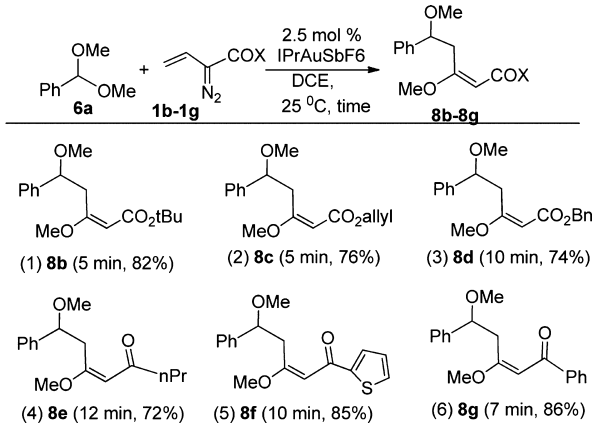
AgCl through a Celite bed. If the reaction was operated with diazo reagent **1a** (0.1 M) on a gram scale, the desired **7a** was obtained with 77% yield (entry 3). Other gold catalysts LAuCl/$AgSbF_6$ (L = P(*t*-Bu)$_2$(*o*-biphenyl)) and $PPh_3AuCl/AgSbF_6$ appear to be less productive, giving desired unsaturated ester **7a** in 57−67% yields (entries 4 and 5). The use of $AgSbF_6$ alone gave ester **7a** in 46% yield (entry 6). Other catalysts $Rh_2(OAc)_4$, $Cu(OTf)_2$, $Zn(OTf)_2$, 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-(NH_2)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 diffraction[8] of its acid derivative **7a′**, which was obtained by LiOH-catalyzed hydrolysis in a THF/H_2O (2:1) solution.

Table 2 shows the scope of this gold-catalyzed reaction with various acetals **6b−p**. The reaction is applicable to acetals **6b-6c** bearing various alkoxy groups (R = Et; allyl), giving desired unsaturated esters **7b** and **7c** in 63% and 57% yields, respectively. The scope of the reaction is expanded with its applicability to phenyldimethoxymethanes **6d−g** bearing 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^{t}Bu), Oallyl, OBn) in 72−82% yields, respectively. The same reactions were applicable to vinyldiazo ketones **1e−g** (X = ^{n}Pr,

dx.doi.org/10.1021/jo400419d | J. Org. Chem. 2013, 78, 5711−5716

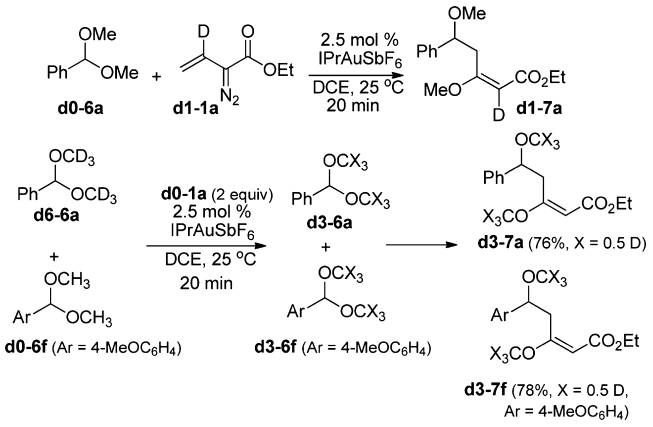
Table 3. Reaction Scope with Various Vinyldiazo Substrates



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

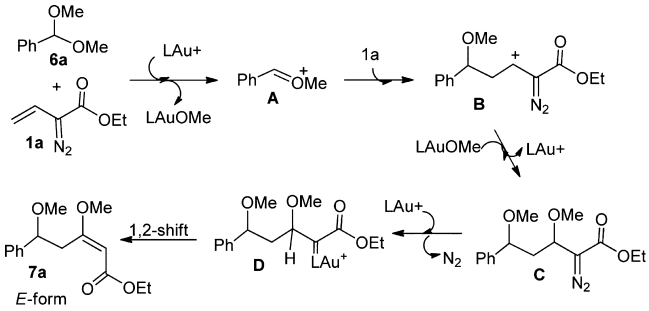
Scheme 1



sample $\mathbf{d_1}$-**1a** with its alkenyl C(2)-proton fully deuterated; its gold-catalyzed reaction with phenyldimethoxymethane $\mathbf{d_0}$-**6a** gave the desired $\mathbf{d_1}$-**7a** bearing a fully deuterated $=CDCO_2Et$, indicative of a 1,2-hydrogen shift. We performed the same reaction using acetals $\mathbf{d_6}$-**6a** and $\mathbf{d_o}$-**6f** in equimolar proportions, their reactions with vinyldiazo ester **1a** (2 equiv) gave unsaturated esters $\mathbf{d_3}$-**7a** and $\mathbf{d_3}$-**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 ^{1}H 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 $\mathbf{d_3}$-**6a** and $\mathbf{d_3}$-**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 vinyldiazo 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 daizo 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 vinyldiazo 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. ^{1}H 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 Vinyldiazo 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%); ^{1}H 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 $C_{15}H_{20}O_4$ 264.1362, found 264.1362.

Deuterated (*E*)-ethyl 3,5-dimethoxy-5-phenylpent-2-enoate ($\mathbf{d_1}$-7a): colorless liquid (91 mg,70%); ^{1}H 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

dx.doi.org/10.1021/jo400419d | J. Org. Chem. 2013, 78, 5711−5716

MHz, $CDCl_3$) 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 $C_{15}H_{19}DO_4$ 265.1424, found 265.1428.

Deuterated (*E*)-ethyl 3,5-dimethoxy-5-phenylpent-2-enoate (d_3-7a): colorless liquid (101 mg, 76%) ; ^{1}H NMR (600 MHz, $CDCl_3$) 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); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{15}H_{20}O_4$ 264.1362, found 264.1373, 267.1552, 270.1739.

(*E*)-Ethyl 3,5-dimethoxy-5-phenylpent-2-enoate (7a′): white solid (56 mg, 90%); ^{1}H NMR (500 MHz, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$) 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 $C_{13}H_{16}O_4$ 236.1049, found 236.1055.

(*E*)-Ethyl 3,5-diethoxy-5-phenylpent-2-enoate (7b): light yellow liquid (91 mg, 63%); ^{1}H NMR (600 MHz, $CDCl_3$) 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); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{17}H_{24}O_4$ 292.1675, found 292.1668.

(*E*)-Ethyl 3,5-bis(allyloxy)-5-phenylpent-2-enoate (7c): light yellow liquid (90 mg, 57%); ^{1}H NMR (600 MHz, $CDCl_3$) 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); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{19}H_{24}O_4$ 316.1675, found 316.1668.

(*E*)-Ethyl 3,5-dimethoxy-5-p-tolylpent-2-enoate (7d): colorless liquid (123 mg, 89%); ^{1}H NMR (600 MHz, $CDCl_3$) 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); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{16}H_{22}O_4$ 278.1518, found 278.1518.

(*E*)-Ethyl 5-(4-*tert*-butylphenyl)-3,5dimethoxypent-2-enoate (7e): light yellow liquid (137 mg, 86%) ; ^{1}H NMR (600 MHz, $CDCl_3$) 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); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{19}H_{28}O_4$ 320.1988, found 320.1993

(*E*)-Ethyl 3,5-dimethoxy-5-(4-methoxyphenyl)pent-2-enoate (7f): light yellow liquid (130 mg, 89%); ^{1}H NMR (600 MHz, $CDCl_3$) 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); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{16}H_{22}O_5$ 294.1467, found 294.1436.

Deuterated (*E*)-ethyl 3,5-dimethoxy-5-(4-methoxyphenyl)-pent-2-enoate (d_3-7f): light yellow liquid (113 mg, 78%); ^{1}H NMR (600 MHz, $CDCl_3$) 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); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{16}H_{22}O_5$ 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%); ^{1}H NMR (600 MHz, $CDCl_3$) 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); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{16}H_{22}O_5$ 294.1467, found 294.1436.

(*E*)-Ethyl 5-(4-chlorophenyl)-3,5-dimethoxypent-2-enoate (7h): yellow liquid (110 mg, 74%); ^{1}H NMR (600 MHz, $CDCl_3$) 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); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{15}H_{19}ClO_4$ 298.0972, found 298.0973.

(*E*)-Ethyl 5-(4-bromophenyl)-3,5-dimethoxypent-2-enoate (7i): yellow liquid (133 mg, 78%); ^{1}H NMR (600 MHz, $CDCl_3$) 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); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{15}H_{19}BrO_4$ 342.0467, found 342.0461.

(*E*)-Ethyl 5-(furan-3-yl)-3,5-dimethoxypent-2-enoate (7j): light yellow liquid (91 mg, 72%); ^{1}H NMR (600 MHz, $CDCl_3$) 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); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{13}H_{18}O_5$ 254.1154, found 254.1145.

(*E*)-Ethyl 3,5-dimethoxy-5-(thiophen-3-yl)pent-2-enoate (7k): light yellow liquid (103 mg, 77%); ^{1}H NMR (600 MHz, $CDCl_3$) 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); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{13}H_{18}O_4S$ 270.0926, found 270.0922.

(*E*)-Ethyl 5-(benzofuran-3-yl)-3,5-dimethoxypent-2-enoate (7l): light yellow liquid (101 mg, 67%); ^{1}H NMR (500 MHz, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$) 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 $C_{17}H_{20}O_5$ 304.1311, found 304.1302.

(*E*)-Ethyl 3,5-dimethoxy-5-(1-tosyl-1*H*-indol-3-yl)pent-2-enoate (7m): yellow semisolid (231 mg, 71%); ^{1}H NMR (600 MHz, $CDCl_3$) 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); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{24}H_{27}NO_6S$ 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%); ^{1}H NMR (600 MHz, $CDCl_3$) 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

dx.doi.org/10.1021/jo400419d | *J. Org. Chem.* 2013, 78, 5711−5716

Hz, 1H), 3.30 (s, 3H), 3.24 (dd, J = 5.6, 13.6 Hz, 1H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{17}H_{20}O_4S$ 320.1082, found 320.1091.

(2*E*,6*E*)-Ethyl 3,5-dimethoxy-7-phenylhepta-2,6-dienoate (7o): light yellow liquid (124.7 mg, 86%); ^{1}H NMR (600 MHz, $CDCl_3$) 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); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{17}H_{22}O_4$ 290.1518, found 290.1515.

(2*E*,6*E*)-Ethyl 3,5-Dimethoxy-7-(thiophene-2-yl)hepta-2,6-dienoate (7p): light yellow liquid (128 mg, 87%); ^{1}H NMR (600 MHz, $CDCl_3$) 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); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{15}H_{20}O_4S$ 296.1082, found 296.1081.

(*E*)-*tert*-Butyl 3,5-dimethoxy-5-phenylpent-2-enoate (8b): light yellow liquid (99 mg, 82%); ^{1}H NMR (600 MHz, $CDCl_3$) 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); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{17}H_{24}O_4$ 292.1675, found 292.1668.

(*E*)-Allyl 3,5-dimethoxy-5-phenylpent-2-enoate (8c): light yellow liquid (96 mg, 76%); ^{1}H NMR (600 MHz, $CDCl_3$) 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); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{16}H_{20}O_4$ 276.1362, found 276.1364.

(*E*)-Benzyl 3,5-dimethoxy-5-phenylpent-2-enoate (8d): light yellow liquid (82 mg, 74%); ^{1}H NMR (600 MHz, $CDCl_3$) 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); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{20}H_{22}O_4$ 326.1518, found 326.1512.

(*E*)-6,8-Dimethoxy-8-phenyloct-5-en-4-one (8e): light yellow liquid (95 mg, 72%); ^{1}H NMR (600 MHz, $CDCl_3$) 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); ^{13}C NMR (150 MHz, $CDCl_3$) 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 $C_{16}H_{22}O_3$ 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%); ^{1}H NMR (500 MHz, $CDCl_3$) 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); ^{13}C NMR (125 MHz, $CDCl_3$) 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 $C_{17}H_{18}O_3S$ 302.0977, found 302.0974.

(*E*)-3,5-Dimethoxy-1,5-diphenylpent-2-en-1-one (8g): light yellow liquid (103 mg, 86%); ^{1}H NMR (400 MHz, $CDCl_3$) 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);^{13}C NMR (100 MHz, $CDCl_3$) 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 $C_{19}H_{20}O_3$ 296.1412, found 296.1410.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra of compounds **7a**−**p**, **d$_1$-7a**, **d$_3$-7a**, **d$_3$-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.

■ ACKNOWLEDGMENTS

We thank National Science Council, Taiwan, for financial support of this work.

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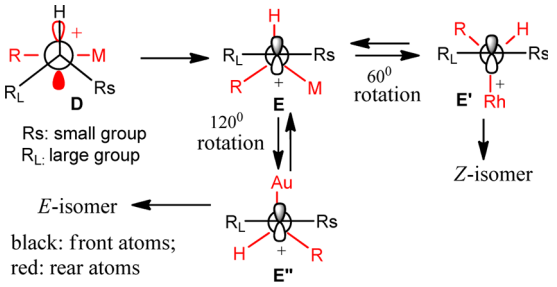

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