JOC The Journal of Organic Chemistry

Article

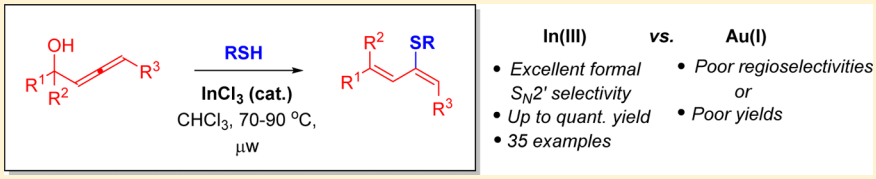
pubs.acs.org/joc

Dehydrative Thiolation of Allenols: Indium vs Gold Catalysis

S. Webster, P. C. Young, G. Barker, G. M. Rosair, and A.-L. Lee*

Institute of Chemical Sciences, Heriot-Watt University, Edinburgh EH14 4AS, United Kingdom

Supporting Information

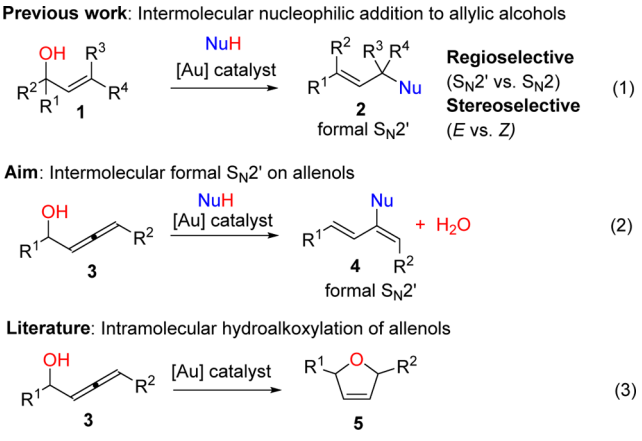


ABSTRACT: Intermolecular additions of thiols to allenols via formal S_N2' selectivity to produce functionalized dienes are described. Although this dehydrative reaction was initially developed using gold(I) catalysis, indium(III) proves to be a far superior catalyst in terms of selectivity and substrate scope.

INTRODUCTION

The use of gold catalysis in organic synthesis has expanded rapidly over recent years, mainly due to functional group compatibility, ease of handling, and the wide array of reactions that can be carried out under mild conditions.[1] Addition of heteroatoms to carbon−carbon π bonds (e.g., alkynes, allenes, and alkenes) in particular has been greatly facilitated by developments in gold catalysis, by virtue of the latter's excellent π-Lewis acidity.[2] More recently, gold-catalyzed dehydrative transformations of allylic alcohols **1** have emerged as mild and selective methods for allylations (eq 1, Scheme 1).[3,4] The benefit of such a gold-catalyzed method is that neither the allylic alcohol nor the incoming nucleophile needs to be activated (the former with a leaving group or the latter with a base, for example), producing only water as a byproduct. Therefore, unlike many traditional transition-metal-based allylating reactions,[5] additives and preactivation are usually not required.

Scheme 1. Previous Work on Allylic Alcohols (Eq 1), Our Current Aim with Allenols (Eq 2), and Literature Known Cyclizations (Eq 3)



Within this context, we have recently developed gold-catalyzed intermolecular etherification (NuH = ROH)[6] and thioetherification (NuH = RSH)[7] reactions which are highly regioselective (formal S_N2'; see eq 1, Scheme 1). Our next challenge was to extend this intermolecular dehydrative method to allenols **3**, which would produce functionalized dienes **4**—useful building blocks in organic synthesis[8] (eq 2, Scheme 1). However, this dehydrative mode[3a,9] of gold-catalyzed reaction with allenols has no literature precedent,[10,11] presumably due to the well-documented propensity for allenols to undergo cyclization instead[12] (eq 3, Scheme 1). We herein report our investigations toward this aim and present the first formal S_N2' intermolecular additions to allenols using a variety of thiols as nucleophiles. The optimal Lewis acid catalyst to emerge from our investigations turns out to be $InCl_3$, and a comparison between catalysis by Au(I) and that by In(III) for this reaction is also presented.

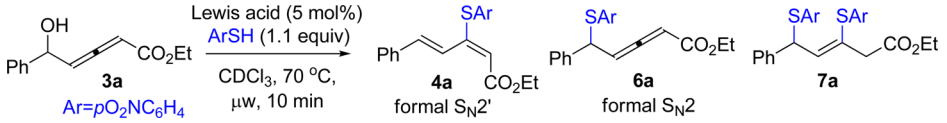
RESULTS AND DISCUSSION

We initiated this project using allenol **3a**, which is readily accessed in one step from the corresponding alkynol using a modification of Lee's procedure.[13] During our initial screens using **3a** as a model allenol, we found that *p*-nitrothiophenol successfully acts as a nucleophile, despite thiol's ability to reduce the activity of gold catalysts.[14−16] The reaction was not selective, however, and our initial results using gold(I) catalysis provided a complex mixture of several different products. Following extensive optimization (see the Supporting Information), Echavarren's catalyst **8** was found to be optimal, producing a ∼1:1 mixture of only formal S_N2':S_N2 products **4a**:**6a** in 55% combined yield after 10 min of microwave heating at 70 °C (Table 1, entry 1). Despite our best efforts including a ligand and counterion screen on the gold catalyst, the selectivity could not be improved. For example, another commonly used catalyst, PPh_3AuNTf_2, in fact produces mainly

Received: November 20, 2014
Published: December 18, 2014

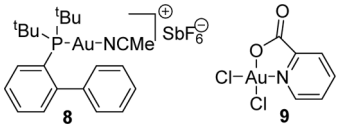
DOI: 10.1021/jo502648w
J. Org. Chem. 2015, 80, 1703−1718

Table 1. Lewis Acid Screen



entry	Lewis acid	4:6:7[a]	yield of 4a (%)	yield of 6a (%)
1	Au(I) catalyst **8**[b]	1:1:0	25[c]	30[c]
2	PPh_3AuNTf_2	1:1:5	ND[d]	ND
3[e]	$NaAuCl_4{\cdot}2H_2O$	1:0:0	5[f]	
4	Au(III) catalyst **9**[b]	no reaction		
5[c]	$InCl_3$	10:0:1	47[c]	
6	InI_3	5:0:1	31[c]	
7	$In(OTf)_3$	3:0:2	44[c]	
8[e]	$Yb(OTf)_3$	1:0:1	10[f]	
9[e]	$Sc(OTf)_3$	1:1:0	8[f]	8[f]
10[e]	$Ga(OTf)_3$	5:0:1	32[f]	
11	$FeCl_3$	complex mixture		
12	ZnI_2	1:0:2	10[c]	
13	$AgSbF_6$	1:1:0	7[c]	
14	$PtCl_2$	no reaction		

[a]Determined using ^{1}H NMR analysis of the crude reaction. [b]The structures of catalysts **8** and **9** are as follows:



[c]Isolated yields. [d]ND = not determined. [e]Incomplete conversion. [f]Yield determined using ^{1}H NMR analysis with dimethyl sulfone as the internal standard.

unwanted product **7a** (a result of conjugate addition as well as formal S_N2, Table 1, entry 2).

In an attempt to improve the selectivity of the reaction, a Lewis acid screen was carried out next (Table 1). While many other catalysts including Pt(II), Au(III), Ag(I), and Fe(III) fared worse than gold(I), to our delight, the soft Lewis acid $InCl_3$[17] showed excellent selectivity (1:0 **4a**:**6a**, entry 5). Other water-stable Lewis acids[18] were also capable catalysts (entries 6–10),[19] but $InCl_3$ produced by far the best selectivity and yield for **4a**. Thus, $InCl_3$ was chosen as the optimal catalyst for further investigation.[20] Advantages of $InCl_3$ include lower cost (cf. gold(I) catalysts), nontoxic nature, lower heterophilicity (readily tolerates S, for example), and air and water stability.[17b,e]

With these results in hand, an allenol substrate scope was carried out (Table 2). First, the substituent on the aryl ring was varied (**3a**–**3j**, entries 1–10). Allenols with electron-rich aryl substituents (including *O*- and *N*-alkyl substitutions, *ortho*, *meta*, and *para*) **3b**–**3f** reacted very efficiently to produce the desired dienes **4b**–**4f** in good to excellent yields (68–96%, entries 1–5), with the exception of the 1,3-benzodioxole derivative **4g** (47%, entry 6). Slightly electron-withdrawing aryls still give good selectivity (**4h**, 93%; **4i**, 49%; entries 8 and 9), but very electron-withdrawing substituted allenols do not react under these conditions (**4j**, entry 10). Pleasingly, replacing the aryl group with heterocycles still produces good yields of **4k**,**l** (79–84%, entries 11 and 12). Alkyl R groups on the allenol are also tolerated, with ^{t}Bu substitution (**4n**, 80%, entry 14) performing better than *n*-alkyl substitution (**4m**, 42%, entry 13). Next, chemoselectivity was probed by investigating an allenol with a pendant alkyne (**3o**, entry 15) and pendant alkene (**3p**, entry 16). Gratifyingly, **3o** reacts chemoselectively to produce ynediene **4o** (85%, entry 15) with no reaction observed at the alkyne. Triene **4p** is also successfully formed from **3p** albeit in a modest 38% yield (entry 16). Tertiary alcohol **3q** reacts well to produce **4q** in quantitative yield (entry 17). It should be noted that lowering the $InCl_3$ catalyst loading from 5 to 1 mol % and increasing the scale of the reaction from 0.105 to 0.57 mmol of **3** is not detrimental to the reaction (**4c** still formed in 96% yield, entry 2, Table 2). The crystal structure of **4a** confirms the *E*,*E* stereochemistry indicated by NOESY analysis for this series of dienes (Figure 1).

Next, allenols without an ester substituent (**3r**,**s**, R′ = H; **3t**–**3v**, R′ = ^{n}Pr) were evaluated to ascertain if the ester group is necessary for good reactivity/selectivity (entries 18–22). These substrates are generally less reactive and require higher temperature (90 °C) and longer times for good conversions. Nevertheless, when R′ = H, the desired dienes **4r** and **4s** are produced in good 72–91% yields, proving that the ester substituent is not necessary (entries 18 and 19).[21] When R′ is an alkyl group (**3t**,**u**), the reaction works equally well with electron-rich and electron-poor R substituents (**3t**,**u**, 77–88%, entries 20 and 21). Finally, **3u**, with two Ph substituents and R′ = ^{n}Pr, also reacts smoothly (**4v**, 59%, entry 22). However, unlike **4a**–**4s**, dienes with R′ = alkyl (**4t**, **4u**, and **4v**) are formed in poor *EE*:*EZ* ratio (2:1 to 1:1). This could be linked to the fact that **4t**, **4u**, and **4v** were found not to be configurationally stable, with the *EE*:*EZ* ratio changing over time.

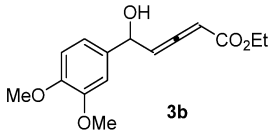
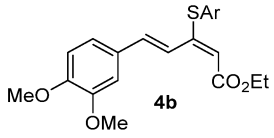
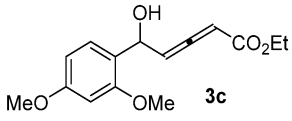
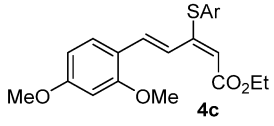
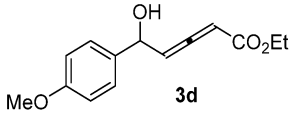
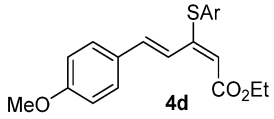
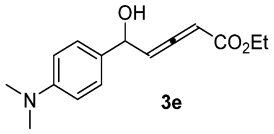
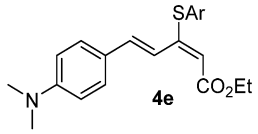
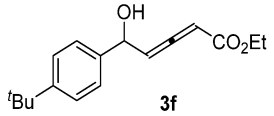
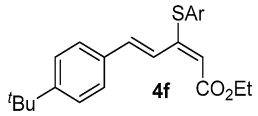
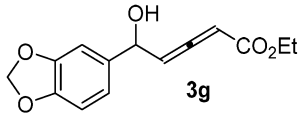
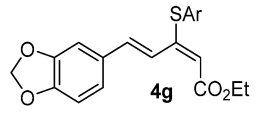
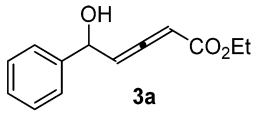
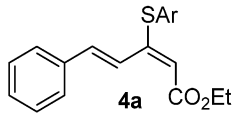
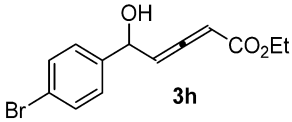
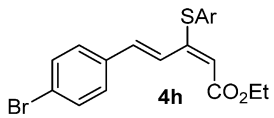
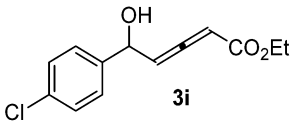
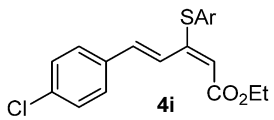
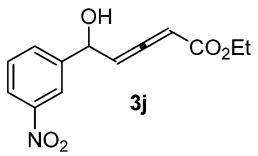
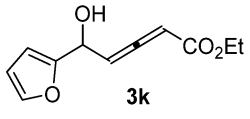
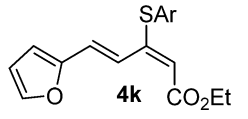
Gold(I) catalyst **8** was also evaluated alongside $InCl_3$ for several of these transformations. First, conditions were reoptimized for **3a** under gold catalysis. A temperature of 70 °C for 30 min provided the best yields, albeit with a poor selectivity of 1:1 **4a**:**6a** (38% **4a**, 34% **6a**, entry 7, Table 2).[22] Using these conditions, transformation of **3f** to **4f** also occurred but with a poor selectivity (5:2 **4f**:**6f**, entry 5). Gold catalysis fared even worse with a selection of other substrates. The use of gold(I) catalysis

DOI: 10.1021/jo502648w
J. Org. Chem. 2015, 80, 1703–1718

resulted in either a complex mixture of products (entries 1, 14, and 18) or no reaction (entries 10 and 15). Therefore, in all of the cases evaluated, regioselectivities or yields are significantly worse with Au(I) compared to $InCl_3$.

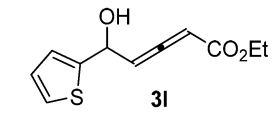
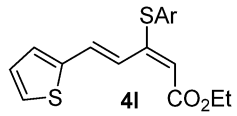
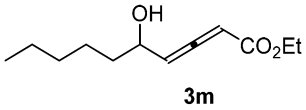
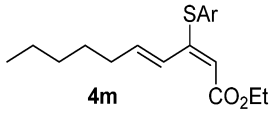
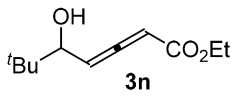
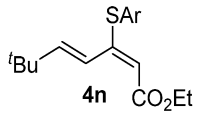
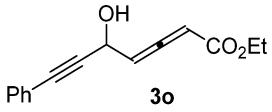
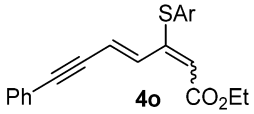
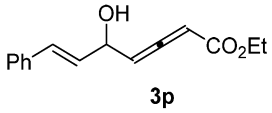
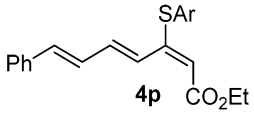
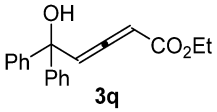
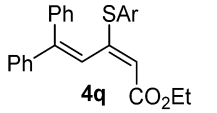
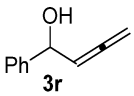
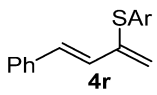
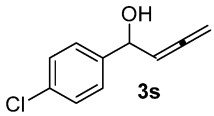
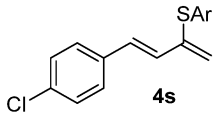
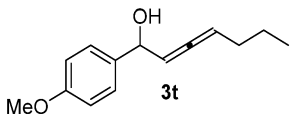
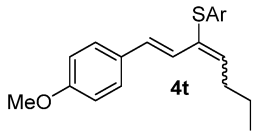
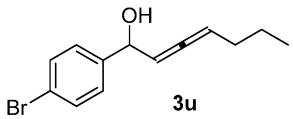
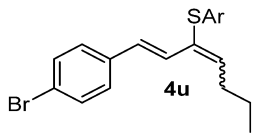
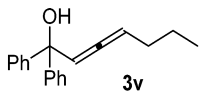
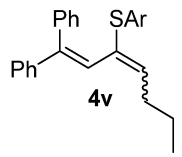
It should be noted that microwave heating[23] was adopted for ease of use and to readily heat the $InCl_3$-catalyzed reaction above the boiling point of chloroform.[24] The reaction can alternatively be carried out in a robust sealed tube under conventional heating, but we chose microwave heating as it is more practical from a safety viewpoint (for temperatures above the boiling point of solvents) and the isolated yields are also improved. For example, when the reaction in Table 2, entry 2,

Table 2. Allenol Substrate Scope

Entry	3	4	Yield (%)[a]
1	 **3b**	 **4b**	80% *(Au(I):[d] <5%[e])*
2	 **3c**	 **4c**	96%[b]
3	 **3d**	 **4d**	79%[c]
4	 **3e**	 **4e**	90%
5	 **3f**	 **4f**	68%[c] *(Au(I):[d] 5:2 **4**:**6**, 28% **4f**)*
6	 **3g**	 **4g**	47%
7	 **3a**	 **4a**	49% *(Au(I)[d] 1:1 **4**:**6**, 38% **4a** 34% **6a**)*
8	 **3h**	 **4h**	93%[c]
9	 **3i**	 **4i**	49%
10	 **3j**	No reaction	0% *(Au(I):[d] no reaction)*
11	 **3k**	 **4k**	79%[c]

DOI: 10.1021/jo502648w
J. Org. Chem. 2015, 80, 1703−1718

Table 2. continued

Entry	3	4	Yield (%)[a]
12	 **3l**	 **4l**	84[c]
13	 **3m**	 **4m**	42[h,i]
14	 **3n**	 **4n**	80[f] *(Au(I):[d] <5%[e])*
15	 **3o**	 **4o**	85[c] 4:1 *E*/*Z* *(Au(I):[d] no reaction)*
16	 **3p**	 **4p**	38[c]
17	 **3q**	 **4q**	100
18	 **3r**	 **4r**	72[h,j] *(Au(I):[d] <5%[e])*
19	 **3s**	 **4s**	91[h]
20	 **3t**	 **4t**	88[k,l]
21	 **3u**	 **4u**	77[k,l]
22	 **3v**	 **4v**	59[h,m]

[a]Isolated yields. A 0.07 mmol scale of ArSH and 0.105 mmol of **3**. [b]Same result when repeated with only 1 mol % $InCl_3$, 0.36 mmol scale of ArSH. [c]At 90 °C, 20 min. [d]Catalyst **8** (5 mol %), 70 °C, 30 min, sealed tube. [e]Complex mixture of products. [f]At 90 °C, 30 min. [g]Recovered starting material. [h]At 90 °C for 60 min. [i]Product **7** also observed in 31% yield. [j]**4r**:**6r** = 5:1. [k]At 90 °C, 18 h, sealed tube. [l]*EE*:*EZ* = 2:1. [m]*E*:*Z* = 1:1.

is repeated under conventional heating, **4c** is obtained in 76% isolated yield after 10 min as well as a longer reaction time of 30 min (vs 96% **4c** using microwave heating).

Next, we proceeded to investigate the thiol nucleophile scope using allenol **3b** as a model substrate under $InCl_3$ catalysis (Table 3). Electron-withdrawing substituents on the thiophenol perform much better than strongly electron-donating ones (entries 1−3, 65−80%, vs entry 10, 52%). The presence of acidic protons (phenol and carboxylic acid) on the thiophenol though causes a severe drop in yield (29%, 9%, entries 4 and 5) presumably because the H-bonding required in the mechanism is disrupted (vide infra). Neutral and slightly electron-donating substituents, including *ortho*-, *meta*-, and *para*-substituted thiophenols, react well (entries 6−9). Next, we evaluated the use of alkanethiols instead of thiophenols as nucleophiles (entries 11−14). Although the yields were moderate (40−52%), both primary (entries 11−13) and secondary (entry 14) alkanethiols are suitable nucleophiles. Furthermore, even the presence of furan (entry 12) and carboxylic acid (entry 13) is tolerated, although the acidic

DOI: 10.1021/jo502648w
J. Org. Chem. 2015, 80, 1703−1718

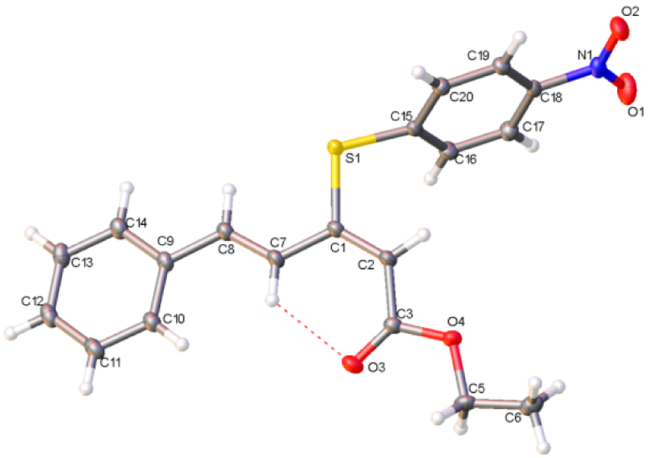


Figure 1. Crystal structure of **4a**.

proton once again causes a slightly lower yield (40%). Finally, thioacid nucleophiles were evaluated. These were competent nucleophiles but surprisingly gave the opposite selectivity to form formal S_N2 products **6bn** and **6bo** (entries 15 and 16; isomerization of **6** to **4** does not occur, vide infra).

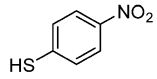
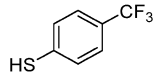
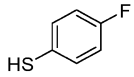
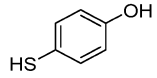
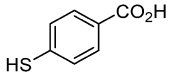
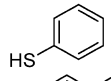
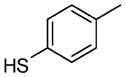
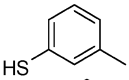
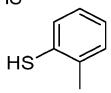
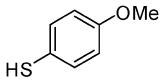
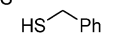
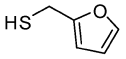
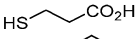
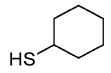
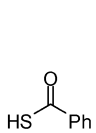
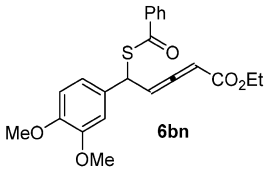
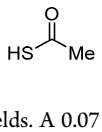
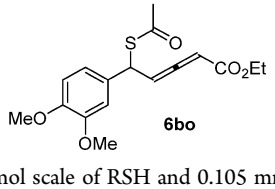
Next, several control reactions were carried out. First, the reaction with **3a** (entry 7, Table 2) was repeated in the absence of any catalyst, and no reaction was observed after 10 min at 70 °C, thereby suggesting that the desired product **4a** requires a catalyst under these conditions. Second, the reaction with **3a** was repeated with $InCl_3$ but in the absence of thiol nucleophile: this also resulted in no reaction. In contrast, under gold catalysis (**8**), **3a** is consumed to give a complex mixture of products (decomposition) in the absence of the thiol nucleophile. Finally, the formal S_N2' product **4a** (from entry 7, Table 2) was resubjected to the reaction conditions under both In(III) and Au(I) catalysis (Scheme 2). No further reaction of **4a** occurs under In(III) catalysis conditions, but further reaction of **4a** does occur under Au(I) catalysis to yield a complex mixture of products. Therefore, the superior performance of $InCl_3$ vs gold(I) catalysis in the dehydrative thiolation of allenols could in part be due to the better stability of the diene products **4** in the presence of In(III) vs Au(I).

We have recently shown that the related gold(I)-catalyzed thioetherification reaction of allylic alcohols is under equilibrium control.[7] It was therefore deemed judicious to also study the behavior of the product **6a** (formal S_N2 product in Table 1) under the reaction conditions (Scheme 3). Under gold(I) catalysis, **6a** isomerizes to **4a**, but the proportion of **4a** to **6a** remains stagnant at 1:1 even after 16 h. This ratio reflects the observed ratio of products in entry 1, Table 1, as well as entry 7, Table 2. Under $InCl_3$ catalysis, however, **6a** converts fully to **4a** over time. Full isomerization is much faster in the presence of 1 equiv of thiol (5 min vs 3 h).

The effect of temperature was also investigated for substrates which require higher temperatures (90 °C vs 70 °C, Table 2) for good selectivity. For example, under standard conditions (70 °C, 10 min), 1:1 **4d**:**6d** is produced from **3d**, and a higher temperature of 90 °C changes the selectivity to **4d** only (Scheme 4). At a lower temperature of 35 °C, the selectivity swings slightly toward **6d**: 1:1.3 **4d**:**6d** (Scheme 4).

With these results in mind, plausible mechanisms are presented in Scheme 5. $InCl_3$ has been shown to activate both soft C−C multiple bonds[25] and the *O*-center,[26] so two possible pathways are presented. In path a, the indium catalyst[27] activates the allene toward nucleophilic attack by thiol, presumably

Table 3. Thiol Nucleophile Scope

Entry	RSH	Product	Yield (%)
1		**4b**	80
2		**4ba**	74
3		**4bb**	65
4		**4bc**	29[b]
5		**4bd**	<9[c]
6		**4be**	73
7		**4bf**	72
8		**4bg**	54
9		**4bh**	75
10		**4bi**	52
11		**4bj**	52
12		**4bk**	52
13		**4bl**	40
14		**4bm**	45
15		 **6bn**	66[e]
16		 **6bo**	52[f]

[a]Isolated yields. A 0.07 mmol scale of RSH and 0.105 mmol of **3**. [b]At 90 °C, 60 min. [c]Coelutes with starting material. [d]dr = 1:2. [e]dr = 1:0.6.

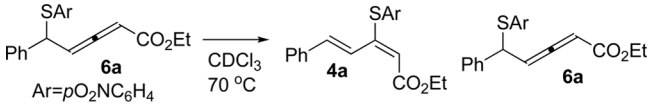
facilitated by H-bonding[28] (**I**). Elimination of the catalyst and water (**II**) then furnishes the diene product **4**. In path b, the indium catalyst activates the alcohol and direct displacement by thiol (**III**) produces the formal S_N2 product **6**,[29] which then undergoes isomerization to **4** via **IV** and **V**. At higher temperatures, either the reaction proceeds directly through path a or high temperatures facilitate the isomerization (**IV** → **V** → **4**) via path b to produce the excellent selectivity for **4**. It is possible

DOI: 10.1021/jo502648w
J. Org. Chem. 2015, 80, 1703−1718

Scheme 2. Resubjection of 4a to the Reaction Conditions (Both In and Au)

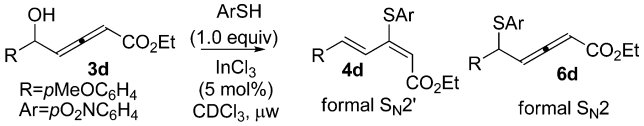
Catalyst:	**$InCl_3$ (5 mol%)**	No reaction
	+ ArSH (1 equiv.)	No reaction
	Au(I) cat. 8 (5 mol%)	Complex mixture
	+ ArSH (1 equiv.)	Complex mixture

Scheme 3. Resubjection of 6a to the Reaction Conditions (Both In and Au)



Conditions: $InCl_3$ (5 mol%), μw	5 min	1:3 **4a**:**6a**
	30 min	1:1 **4a**:**6a**
	1.5 h	5:1 **4a**:**6a**
	3 h	**4a** only
+ ArSH (1 equiv.)	5 min	**4a** only
Au(I) cat. 8 (5 mol%)	30 min	1:1 **4a**:**6a**
	1.5 h	1:1 **4a**:**6a**
	16 h	1:1 **4a**:**6a** + decomposition
+ ArSH (1 equiv.)	30 min	decomposition

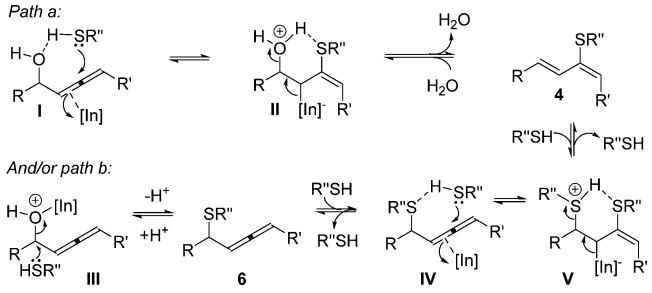
Scheme 4. Effect of Temperature on Regioselectivity



[a]Isolated yields
[b]Incomplete conversion

90 °C, 20 mins	>20:1 **4d**:**6d** (79% **4d**)[a]
70 °C, 10 mins	1:1 **4d**:**6d** (30% **4d**, 30% **6d**)[a]
35 °C, 20 mins	1:1.3 **4d**:**6d** (7% **4d**, 11% **6d**)[a,b]

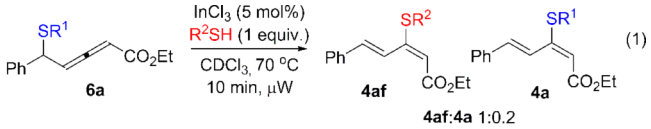
Scheme 5. Plausible Mechanism



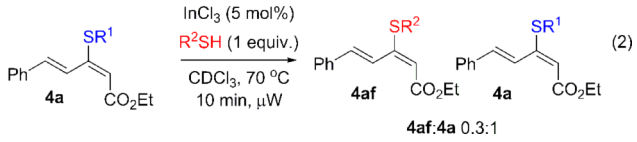
that both pathways operate, with the favored pathway being dependent on the substituents on the substrates.

In addition, crossover experiments support the possibility of path b: when **6a** (formal S_N2 product in Table 1) is resubjected to the reaction conditions but with a different thiol (R^2SH) present, isomerization to **4** occurs with incorporation of the external thiophenol (eq 1, Scheme 6). Similarly, when **4a** (formal S_N2' product in Table 1) is resubjected to the reaction conditions with thiol R^2SH present, incorporation of this external thiol is observed (eq 2), supporting the reversible nature of the process, as indicated in Scheme 6.

Scheme 6. Crossover Experiment



R^1=$pO_2NC_6H_4$; R^2=$pMeC_6H_4$



CONCLUSION

In conclusion, we have successfully developed an intermolecular formal S_N2' addition of thiols to allenols, and $InCl_3$ turned out to be far superior to Au(I) as a catalyst for this dehydrative reaction. Control reactions indicate that the latter is at least in part due to better stability of the diene products **4** in the presence of In(III) vs Au(I). The indium-catalyzed reaction has a wide substrate scope, with thiophenols and alkanethiol nucleophiles producing excellent formal S_N2' selectivity, while thioacid nucleophiles result in formal S_N2 selectivity. Mechanistic studies suggest that the regioselectivity is under equilibrium control and is determined by the thermodynamic stability of the products.

EXPERIMENTAL SECTION

Synthesis of Allenol Substrates 3. *General Procedure A (When Triethylamine is Required).* To the propargylic alcohol (1.30 mmol, 1 equiv) were added dry MeCN (1 M), CuI (5 mol %), and EDA (1.30 mmol, 1 equiv). The reaction was stirred at 25 °C overnight under argon. The reaction mixture was filtered through a plug of glass wool and washed with diethyl ether. Solvent was removed on a rotary evaporator, and the resulting crude mixture was dissolved in dry DCM (0.2 M) before Et_3N (1.2 equiv) was added. The resulting mixture was stirred at 0 °C for 1 h. Removal of solvent by rotary evaporator followed by column chromatography (hexane/ethyl acetate) yielded allenic alcohol **3** as the product.[13]

General Procedure B (When Triethylamine is Not Required). To the propargylic alcohol (1.30 mmol, 1 equiv) were added dry MeCN (1 M), CuI (5 mol %), and EDA (1.30 mmol, 1 equiv). The reaction was stirred at 25 °C overnight under argon. The reaction mixture was filtered through a plug of glass wool and washed with diethyl ether. Solvent was removed on a rotary evaporator, and the resulting crude mixture was purified by column chromatography (hexane/ethyl acetate) to give allenic alcohol **3** as the product.[13]

Note: In our hands, the one-pot procedure described by Sabbasani et al.[13] was sometimes low yielding and/or resulted in no reaction. Where this was the case, omitting triethylamine from the first step greatly improved the yields (see general procedures A and B above). In some cases, triethylamine was found to be unnecessary to form **3** (procedure B); in others, it was added in a second separate step as described above (procedure A) to isomerize any unwanted alkyne isomer to the allene **3**.

*Ethyl 5-Hydroxy-5-phenylpenta-2,3-dienoate (**3a**).*[13] General procedure A was followed using 1-phenylprop-2-yn-1-ol to yield the title product **3a** as a yellow oil and a 1:1.4 mixture of diastereomers (415 mg, 1.90 mmol, 93%): purified by column chromatography (eluent hexane/ethyl acetate, 10:1 to 3:1); R_f 0.38 (3:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3400 br (OH), 2982 (C–H), 1961 (C=C, allene), 1694 (C=O), 1493, 1450, 1421 (Ar C–C), 1156 (C–O–C), 748, 698 (*m*-C_6H_5); ^1H NMR (300 MHz, $CDCl_3$) δ 7.44–7.49 (m, 2H + 2H′), 7.28–7.41 (m, 3H + 3H′), 5.89 (m, 1H + 1H′), 5.78 (m, 1H + 1H′), 5.41 (m, 1H + 1H′), 4.20 (m, 2H + 2H′), 2.43 (br s, 1H′, minor), 2.36 (br s, 1H, major), 1.30 (m, 3H + 3H′); ^{13}C NMR (75.5

DOI: 10.1021/jo502648w
J. Org. Chem. 2015, 80, 1703–1718

MHz, $CDCl_3$), δ 211.5 (C, minor), 211.4 (C, major), 165.9 (C, minor), 165.7 (C, major), 141.8 (C, major + minor), 128.6 (CH, minor), 128.5 (CH, major), 128.2 (CH, minor), 128.0 (CH, major), 126.4 (CH, minor), 126.1 (CH, major), 100.4 (CH, minor), 100.2 (CH, major), 90.8 (CH, major + minor), 71.5 (CH, minor), 71.4 (CH, major), 61.3 (CH_2, minor), 61.1 (CH_2, major), 14.2 (CH_3, major + minor).

*Ethyl 5-(3,4-Dimethoxyphenyl)-5-hydroxypenta-2,3-dienoate (**3b**).*[13] General procedure B was followed using 1-(3,4-dimethoxyphenyl)prop-2-yn-1-ol to yield product **3b** as a yellow oil and a 1:1 mixture of diastereomers (325 mg, 0.90 mmol, 90%): purified by column chromatography (eluent hexane/ethyl acetate, 10:1 to 7:1 to 5:1 to 3:1 to 2:1); R_f 0.29 (3:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3474 br (OH), 2980 (C−H), 2836 (C−H), 1961 (C═C, allene), 1711 (C═O), 1593, 1513, 1463, 1415 (Ar C−C), 1256 (C−O−C), 1138 (C−O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.00 (m, 2H), 6.85 (d, 1H, J = 8.2 Hz), 5.88 (m, 1H), 5.78 (m, 1H), 5.36 (m, 1H), 4.20 (q, 2H, J = 7.1 Hz), 3.91 (s, 3H), 3.88 (s, 3H), 2.47 (br s, 1H), 1.28 (m, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 211.4 (C), 211.1 (C), 165.6 (C), 165.4 (C), 149.2 (C), 149.1 (C), 149.0 (C), 148.9 (C), 134.3 (C), 134.2 (C), 118.8 (CH), 118.5 (CH), 111.0 (CH), 110.9 (CH), 109.6 (CH), 109.3 (CH), 100.4 (CH), 100.2 (CH), 91.2 (CH), 90.8 (CH), 71.3 (CH), 71.2 (CH), 61.1 (CH_2), 61.0 (CH_2), 56.0 (2 × CH_3), 14.2 (2 × CH_3).

*Ethyl 5-Hydroxy-5-(2,4-dimethoxyphenyl)penta-2,3-dienoate (**3c**).* General procedure A was followed using 1-(2,4-dimethoxyphenyl)-prop-2-yn-1-ol to yield product **3c** as a yellow oil and a 1:1 mixture of diastereomers (337 mg, 1.21 mmol, 89%): purified by column chromatography (eluent hexane/ethyl acetate, 5:1 to 3:1); R_f 0.40 (3:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3400 br (OH), 3012 (C−H), 2836 (C−H), 1961 (C═C, allene), 1704 (C═O), 1588, 1505, 1464, 1416 (Ar C−C), 1260 (C−O−C), 1156 (C−O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (d, 1H, J = 9.1 Hz), 7.27 (d, 1H′, J = 9.2 Hz), 6.42−6.49 (m, 2H + 2H′), 5.99 (t, 1H, J = 6.0 Hz), 5.90 (t, 1H′, J = 6.0 Hz), 5.66−5.73 (m, 1H + 1H′), 5.52 (m, 1H + 1H′), 4.09−4.21 (m, 2H + 2H′), 3.81 (s, 3H + 3H′), 3.78 (s, 3H + 3H′), 3.31 (d, 1H, J = 6.4 Hz), 3.15 (d, 1H′, J = 6.4 Hz), 1.21−1.29 (m, 3H + 3H′); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 211.4 (C), 211.3 (C), 165.8 (C), 165.6 (C), 160.8 (C), 160.7 (C), 157.7 (C), 157.6 (C), 128.3 (CH), 128.0 (CH), 122.5 (2 × C), 104.34 (CH), 104.25 (CH), 99.8 (CH), 99.6 (CH), 98.7 (2 × CH), 90.7 (CH), 90.5 (CH), 67.7 (CH), 67.2 (CH), 60.9 (CH_2), 60.8 (CH_2), 55.43 (CH_3), 55.39 (CH_3), 14.23 (2 × CH_3), 14.21 (2 × CH_3); found (FTMS + pNSI) $[M + Na]^+$ 301.1040, $C_{15}H_{18}O_5Na$ requires 301.1046.

*Ethyl 5-Hydroxy-5-(4-methoxyphenyl)penta-2,3-dienoate (**3d**).* General procedure A was followed using 1-(4-methoxyphenyl)prop-2-yn-1-ol to yield product **3d** as a yellow oil and a 1:1 mixture of diastereomers (278 mg, 1.24 mmol, 78%): purified by column chromatography (eluent hexane/ethyl acetate, 3:1); R_f 0.33 (3:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3426 br (OH), 2982 (C−H), 1961 (C═C, allene), 1711 (C═O), 1511, 1489, 1443 (Ar C−C), 1245 (C−O−C), 1171 (C−O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (d, 2H, J = 8.8 Hz), 7.36 (d, 2H, J = 8.8 Hz), 6.87 (d, 2H, J = 8.6 Hz), 6.87 (d, 2H, J = 8.7 Hz), 5.82−5.90 (m, 1H + 1H′), 5.74 (two overlapping t, 1H + 1H′, J = 5.7, 5.9 Hz), 5.36 (m, 1H), 5.30 (m, 1H), 4.12−4.25 (m, 2H + 2H′), 3.79 (s, 3H + 3H′), 3.28 (d, 1H, J = 3.6 Hz), 3.22 (d, 1H, J = 3.8 Hz), 1.28 (m, 3H + 3H′); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 211.40 (C), 211.39 (C), 165.9 (C), 165.8 (C), 159.5 (C), 159.4 (C), 134.0 (C), 133.9 (C), 127.8 (CH), 127.5 (CH), 114.0 (CH), 113.8 (CH), 100.5 (CH), 100.3 (CH), 90.8 (CH), 90.6 (CH), 71.0 (2 × CH), 61.2 (CH_2), 61.0 (CH_2), 55.3 (2 × CH_3), 14.2 (2 × CH_3); found (FTMS + pNSI) $[M + Na]^+$ 271.0936, $C_{14}H_{16}O_4Na$ requires 271.0941.

*Ethyl 5-(4-(Dimethylamino)phenyl)-5-hydroxypenta-2,3-dienoate (**3e**).* General procedure B was followed using 1-(4-(dimethylamino)-phenyl)prop-2-yn-1-ol to yield product **3e** as a red/orange oil and a 1:1 mixture of diastereomers (147 mg, 0.56 mmol, 39%): purified by column chromatography (eluent hexane/ethyl acetate, 3:1); R_f 0.28 (3:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3400 br (OH), 2981 (C−H), 1959 (C═C, allene), 1710 (C═O), 1521, 1477, 1444, 1413 (Ar C−C), 1252 (C−O−C), 1157 (C−O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (t, 2H + 2H′, J = 8.5 Hz), 6.72 (d, 2H + 2H′, J = 8.2 Hz), 5.87 (m, 1H + 1H′), 5.70−5.84 (m, 1H + 1H′), 5.35 (m, 1H), 5.28 (m, 1H′), 4.14−4.27 (m, 2H + 2H′), 2.95 (s, 6H), 2.94 (s, 6H′), 2.35 (m, 1H + 1H′), 1.26−1.35 (m, 3H + 3H′); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 211.33 (C), 211.26 (C), 165.8 (C), 165.6 (C), 150.7 (C), 150.6 (C), 129.48 (C), 129.42 (C), 127.6 (CH), 127.2 (CH), 112.5 (CH), 112.4 (CH), 100.5 (CH), 100.3 (CH), 91.0 (CH), 90.7 (CH), 71.3 (2 × CH), 61.04 (CH_2), 60.98 (CH_2), 40.59 (CH_3), 40.57 (CH_3), 14.3 (2 × CH_3); found (FTMS + pNSI) $[M + H]^+$ 262.1441, $C_{15}H_{20}NO_3$ requires 262.1438.

*Ethyl 5-(4-tert-Butylphenyl)-5-hydroxypenta-2,3-dienoate (**3f**).* General procedure A was followed using 1-(4-(*tert*-butyl)phenyl)-prop-2-yn-1-ol to yield product **3f** as a yellow oil and a 1:1 mixture of diastereomers (236 mg, 0.86 mmol, 63%): purified by column chromatography (eluent hexane/ethyl acetate, 7:1 to 5:1); R_f 0.63 (hexane/ethyl acetate, 3:1); ν_{max}/cm^{-1} 3400 br (OH), 2962 (C−H), 1960 (C═C, allene), 1713 (C═O), 1509, 1463, 1408 (Ar C−C), 1254 (C−O−C), 1157 (C−O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (m, 4H + 4H′), 5.83−5.92 (m, 1H + 1H′), 5.77−5.80 (m, 1H), 5.74−5.77 (m, 1H′), 5.37−5.43 (m, 1H), 5.31−5.37 (m, 1H′), 4.11−4.27 (m, 2H + 2H′), 3.07 (d, 1H′, J = 4.0 Hz), 2.96 (d, 1H, J = 4.1 Hz), 1.26−1.35 (m, 12H + 12H′); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 211.42 (C), 211.40 (C), 165.9 (C), 165.6 (C), 151.1 (C), 151.0 (C), 138.8 (C), 138.7 (C), 126.2 (CH), 125.9 (CH), 125.6 (CH), 125.5 (CH), 100.4 (CH), 100.2 (CH), 90.8 (CH), 90.7 (CH), 71.3 (CH), 71.2 (CH), 61.2 (CH_2), 61.1 (CH_2), 34.60 (C), 34.58 (C), 31.3 (2 × CH_3), 14.2 (2 × CH_3); found (FTMS + pNSI) $[M + Na]^+$ 297.1458, $C_{17}H_{22}O_3Na$ requires 297.1461.

*Ethyl 5-(Benzo[d][1,3]dioxol-5-yl)-5-hydroxypenta-2,3-dienoate (**3g**).* General procedure A was followed but on a smaller scale using 1-(benzo[*d*][1,3]dioxol-5-yl)prop-2-yn-1-ol (191.3 mg, 1.09 mmol, 1 equiv), CuI (10.2 mg, 0.05 mmol, 0.05 equiv), EDA (0.14 mL, 1.31 mmol, 1.2 equiv), and MeCN (1.1 mL) to yield product **3g** as a yellow oil and a 1:0.8 mixture of diastereomers (178 mg, 0.68 mmol, 63%): purified by column chromatography (eluent hexane/ethyl acetate, 3:1); R_f 0.49 (3:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3400 br (OH), 2982 (C−H), 1961 (C═C, allene), 1709 (C═O), 1502, 1487, 1441 (Ar C−C), 1241 (C−O−C), 1158 (C−O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.96−6.98 (m, 1H′, minor), 6.94−6.96 (m, 1H, major), 6.89−6.92 (m, 1H′, minor), 6.86−6.89 (m, 1H, major), 6.77 (s, 1H, major), 6.75 (s, 1H′, minor), 5.94 (s, 2H′, minor), 5.93 (s, 2H, major), 5.79−5.86 (m, 1H + 1H′), 5.71−5.79 (m, 1H + 1H′), 9.29−9.35 (m, 1H, major), 5.23−5.29 (m, 1H′, minor), 4.12−4.24 (m, 2H + 2H′), 3.25 (d, 1H′, J = 4.2 Hz, minor), 3.19 (d, 1H, J = 4.3 Hz, major), 1.24−1.33 (m, 3H + 3H′); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 211.4 (C, major), 211.3 (C, minor), 165.9 (C, minor), 165.6 (C, major), 147.9 (C, minor), 147.8 (C, major), 147.5 (C, minor), 147.3 (C, major), 135.9 (C, major), 135.8 (C, minor), 120.0 (CH, minor), 119.6 (CH, major), 108.11 (CH, minor), 108.07 (CH, major), 107.1 (CH, minor), 106.9 (CH, major), 101.13 (CH_2, minor), 101.10 (CH_2, major), 100.4 (CH, minor), 100.2 (CH, major), 91.0 (CH, minor), 90.7 (CH, major), 71.22 (CH, minor), 71.21 (CH, major), 61.3 (CH_2, minor), 61.2 (CH_2, major), 14.2 (CH_3, major + minor); found (FTMS + pNSI) $[M + Na]^+$ 285.0735, $C_{14}H_{14}O_5Na$ requires 285.0733.

*Ethyl 5-(4-Bromophenyl)-5-hydroxypenta-2,3-dienoate (**3h**).* General procedure B was followed using 1-(4-bromophenyl)prop-2-yn-1-ol to yield product **3h** as an orange solid and a 1:1 mixture of diastereomers (212 mg, 0.71 mmol, 60%): purified by column chromatography (eluent hexane/ethyl acetate, 3:1); R_f 0.38 (3:1 hexane/ethyl acetate); mp 66−71 °C; ν_{max}/cm^{-1} 3400 br (OH), 2981 (C−H), 1962 (C═C, allene), 1694 (C═O), 1487, 1444 (Ar C−C), 1254 (C−O−C), 1159 (C−O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45−7.51 (m, 2H + 2H′), 7.32−7.34 (m, 2H′), 7.28−7.32 (m, 2H), 5.80−5.89 (m, 1H + 1H′), 5.73−5.78 (m, 1H + 1H′), 5.30−5.40 (m, 1H + 1H′), 4.11−4.25 (m, 2H + 2H′), 3.34 (d, 1H, J = 4.0 Hz), 3.17 (d, 1H′, J = 4.5 Hz), 1.17−1.41 (m, 3H + 3H′); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 211.5 (2 × C), 165.8 (C), 165.5 (C), 140.7 (C), 140.6 (C), 131.7 (CH), 131.6 (CH), 128.1 (CH), 127.9 (CH), 122.0 (C), 121.9 (C), 100.1 (CH), 99.8 (CH), 91.0 (CH), 90.9 (CH), 70.90 (CH),

DOI: 10.1021/jo502648w
J. Org. Chem. 2015, 80, 1703−1718

70.86 (CH), 61.4 (CH_2), 61.2 (CH_2), 14.2 (2 × CH_3); found (FTMS + pNSI) $[M + Na]^+$ 318.9942, $C_{13}H_{13}O_3BrNa$ requires 318.9940.

*Ethyl 5-(4-Chlorophenyl)-5-hydroxypenta-2,3-dienoate (**3i**).*[13] General procedure B was followed using 1-(4-chlorophenyl)prop-2-yn-1-ol to yield product **3i** as a brown oil and a 1:0.95 mixture of diastereomers (368 mg, 1.46 mmol, 94%); R_f 0.33 (5:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3400 br (OH), 2982 (C−H), 1962 (C═C, allene), 1712 (C═O), 1594, 1490, 1444 (Ar C−C), 1255 (C−O−C), 1159 (C−O); ^1H NMR (300 MHz, $CDCl_3$) δ 7.30−7.40 (m, 4H + 4H′), 5.79 (m, 1H + 1H′), 5.83 (m, 1H + 1H′), 5.71−5.77 (m, 1H + 1H′), 4.14−4.24 (m, 2H + 2H′), 3.50 (br s, 1H, major), 3.31 (br s, 1H′, minor), 1.25−1.31 (m, 3H + 3H′); ^{13}C NMR (75.5 MHz, $CDCl_3$), δ 211.5 (C), 211.4 (C), 165.8 (C), 165.4 (C), 140.2 (C), 140.1 (C), 133.9 (C), 133.7 (C), 128.7 (CH), 128.6 (CH), 127.8 (CH), 127.5 (CH), 100.2 (CH), 100.0 (CH), 90.9 (CH), 90.8 (CH), 70.8 (2 × CH), 61.3 (CH_2), 61.2 (CH_2), 14.2 (2 × CH_3).

*Ethyl 5-Hydroxy-5-(3-nitrophenyl)penta-2,3-dienoate (**3j**).*[13] General procedure A was followed using 1-(3-nitrophenyl)prop-2-yn-1-ol to obtain product **3j** as a yellow oil and a 1:0.7 mixture of diastereomers (11.8 mg, 0.04 mmol, 6%): purified by column chromatography (eluent hexane/ethyl acetate, 3:1); R_f 0.17 (3:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3422 br (OH), 2983 (C−H) 1963 (C═C, allene), 1713 (C═O), 1510 (NO_2), 1583, 1476, 1444 (Ar C−C), 1340 (NO_2), 1255 (C−O−C), 1178 (C−O); ^1H NMR (300 MHz, $CDCl_3$) δ 8.41 (br t, 1H, J = 1.7 Hz), 8.31 (dt, 1H, J = 12.7, 1.7 Hz), 8.11−8.20 (m, 2H), 7.85−7.91 (m, 1H), 7.75−7.83 (m, 1H), 7.52 (q, 2H, J = 7.7 Hz), 5.84−5.91 (m, 1H, minor), 5.77 (td, 1H, J = 1.9 Hz, 6.0 Hz, major), 5.54−5.61 (m, 1H, minor), 5.51 (m, 1H, major), 4.15−4.25 (m, 2H, major), 4.02−4.13 (m, 2H, minor), 3.78 (br s, 1H, minor), 3.70 (br s, 1H, major), 1.20−1.33 (m, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$), δ 211.6 (C, major + minor), 165.4 (C, minor), 165.2 (C, major), 148.4 (C, major + minor), 143.7 (C, major), 143.6 (C, minor), 132.4 (CH, minor), 132.3 (CH, major), 129.6 (CH, minor), 129.5 (CH, major), 123.1 (CH, minor), 123.0 (CH, major), 121.4 (CH, minor), 121.2 (CH, major), 99.7 (CH, minor), 99.3 (CH, major), 91.4 (CH, minor), 91.2 (CH, major), 70.8, (CH, major), 70.6 (CH, minor), 61.5 (CH_2, minor), 61.4 (CH_2, major), 14.2 (CH_3, major + minor).

*Ethyl 5-(Furan-2-yl)-5-hydroxypenta-2,3-dienoate (**3k**).*[13] General procedure B was followed using 1-(furan-2-yl)prop-2-yn-1-ol to yield product **3k** as a yellow oil and a 1:1 mixture of diastereomers (299 mg, 1.44 mmol, 71%): purified by column chromatography (eluent hexane/ethyl acetate, 3:1); R_f 0.31 (3:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3399 br (OH), 2983 (C−H), 1964 (C═C, allene), 1711 (C═O), 1502, 1445, 1414 (Ar C−C), 1255 (C−O−C), 1159 (C−O); ^1H NMR (300 MHz, $CDCl_3$) δ 7.33−7.37 (m, 1H + 1H′), 6.28−6.36 (m, 2H + 2H′), 5.88−5.99 (m, 1H + 1H′), 5.75 (dd, 1H, J = 3.5, 2.4 Hz), 5.73 (dd, 1H′, J = 3.5, 2.5 Hz), 5.38 (td, 1H, J = 5.8, 2.4 Hz), 5.33 (m, 1H′), 4.10−4.20 (m, 2H + 2H′), 3.97 (d, 1H′, J = 5.4 Hz), 3.90 (d, 1H, J = 5.7 Hz), 1.19−1.29 (m, 3H + 3H′); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 212.0 (C), 211.7 (C), 165.9 (C), 165.6 (C), 154.10 (C), 154.08 (C), 142.51 (CH), 142.49 (CH), 110.34 (CH), 110.32 (CH), 107.2 (CH), 107.1 (CH), 97.7 (CH), 97.6 (CH), 91.1 (CH), 90.9 (CH), 65.1 (CH), 64.9 (CH), 61.3 (CH_2), 61.2 (CH_2), 14.1 (2 × CH_3).

*Ethyl 5-Hydroxy-5-(thiophene-2-yl)penta-2,3-dienoate (**3l**).* General procedure A was followed using 1-(thiophene-2-yl)prop-2-yn-1-ol to yield product **3l** as a yellow oil and a 1:1.2 mixture of diastereomers (71 mg, 0.32 mmol, 16%): purified by column chromatography (eluent hexane/ethyl acetate, 4:1); R_f 0.40 (3:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3400 br (OH), 2981 (C−H), 1962 (C═C, allene), 1710 (C═O), 1517, 1445, 1414 (Ar C−C), 1254 (C−O−C), 1159 (C−O); ^1H NMR (300 MHz, $CDCl_3$) δ 7.28−7.30 (m, 1H′, minor), 7.25−7.27 (m, 1H, major), 7.07−7.11 (m, 1H + 1H′), 6.96−7.02 (m, 1H + 1H′), 5.94−6.00 (m, 1H + 1H′), 5.77−5.82 (m, 1H + 1H), 5.57−5.67 (m, 1H + 1H′), 4.41−4.25 (m, 2H + 2H′), 3.26 (d, 1H′, J = 4.9 Hz, minor), 3.15 (d, 1H, J = 5.2 Hz, major), 1.24−1.33 (m, 3H + 3H′); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 211.5 (C, minor), 211.3 (C, major), 165.7 (C, minor), 165.4 (C, major), 145.7 (C, major), 145.5 (C, minor), 126.82 (CH, major), 126.80 (CH, minor), 126.8 (CH, minor), 125.6 (CH, major), 124.9 (CH, minor), 124.8 (CH, major), 100.0 (CH, minor), 99.8 (CH, major), 91.31 (CH, major), 91.29 (CH, minor), 67.6 (CH, major), 67.4 (CH, minor), 61.3 (CH_2, minor), 61.2 (CH_2, major), 14.2 (CH_3, major + minor); found (FTMS + pNSI) $[M + Na]^+$ 247.0401, $C_{11}H_{12}O_3SNa$ requires 247.0399.

*Ethyl 5-Hydroxydeca-2,3-dienoate (**3m**).*[13] 1-Octyn-3-ol (1.00 g, 7.92 mmol, 1 equiv) was dissolved in dry MeCN (20 mL). EDA (0.87 mL, 8.32 mmol, 1.05 equiv), CuI (150.9 mg, 0.79 mmol, 10 mol %), and Et_3N (1.1 mL, 7.92 mmol, 1.0 equiv) were added sequentially, and the flask was flushed with Ar. MeCN (20 mL) was added, and the reaction mixture was allowed to stir at 25 °C for 23 h. The solvent was then removed on a rotary evaporator, and the resulting residue was quenched with a saturated solution of NH_4Cl and extracted with ethyl acetate. The organic layer was washed with brine and dried over $MgSO_4$. Following removal of solvent on a rotary evaporator, the crude mixture was purified by column chromatography (eluent hexane/ethyl acetate, 4:1) to yield **3m** as a yellow oil and a 1:1.2 mixture of diastereomers (310 mg, 1.46 mmol, 18%): R_f 0.27 (4:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3410 br (OH), 2930 (C−H), 1960 (C═C, allene), 1698 (C═O), 1251 (C−O−C), 1159 (C−O); ^1H NMR (300 MHz, $CDCl_3$) δ 5.67−5.72 (m, 2H + 2H′, major + minor), 4.24−4.34 (m, 1H + 1H′), 4.19 (q, 2H′, J = 7.1 Hz, minor), 4.18 (q, 2H, J = 7.1 Hz, major), 2.46 (br s, 1H, minor), 2.31, (br s, 1H, major), 1.55−1.71 (m, 2H + 2H′), 1.24−1.49 (m, 9H + 9H′), 0.84−0.93 (m, 3H + 3H′); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 211.2 (C, minor), 211.0 (C, major), 166.0 (C, minor), 165.8 (C, major), 100.03 (CH, minor), 99.96 (CH, major), 90.2 (CH, major), 90.0 (CH, minor), 69.44 (CH, major), 69.39 (CH, minor), 61.1 (CH_2, minor), 61.0 (CH_2, major), 37.2 (CH_2, major), 37.1 (CH_2, minor), 31.6 (CH_2, major + minor), 24.9 (CH_2, major + minor), 22.6 (CH_2, major + minor), 14.2 (CH_3, major + minor), 14.0 (CH_3, major + minor).

*Ethyl 5-Hydroxy-6,6-dimethylhepta-2,3-dienoate (**3n**).* General procedure A was followed using 4,4-dimethylpent-1-yn-3-ol to yield product **3n** as a pale yellow liquid and a 1:1.2 mixture of diastereomers (360 mg, 1.81 mmol, 72%): purified by column chromatography (eluent hexane/ethyl acetate, 10:1 to 5:1); R_f 0.67 (3:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3434 br (OH), 2955, 2906 (C−H), 1960 (C═C, allene), 1715 (C═O), 1252 (C−O−C), 1157 (C−O); ^1H NMR (300 MHz, $CDCl_3$) δ 5.61−5.75 (m, 2H + 2H′), 4.06−4.21 (m, 2H + 2H′), 3.87−4.00 (m, 1H +1H′), 2.80−2.87 (m, 1H′, minor), 2.69−2.78 (m, 1H, major), 1.19−1.28 (m, 3H + 3H′), 0.94 (s, 9H, major), 0.93 (s, 9H, minor); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 211.53 (C, major), 211.48 (C, minor), 166.3 (C, minor), 166.0 (C, major), 97.4 (CH, minor), 96.8 (CH, major), 89.7 (CH, minor), 89.2 (CH, major), 77.3 (CH, minor), 77.2 (CH, major), 61.1 (CH_2, minor), 61.0 (CH_2, major), 35.6 (C, minor), 35.5 (C, major), 25.4 (CH_3, major + minor), 14.2 (CH_3, major + minor); found (FTMS + pNSI) $[M + Na]^+$ 221.1148, $C_{11}H_{18}O_3Na$ requires 221.1148.

*Ethyl 5-Hydroxy-7-phenylhepta-2,3-dien-6-ynoate (**3o**).*[13] General procedure B was followed using 1-phenylpenta-1,4-diyn-3-ol to yield product **3o** as a yellow oil and a 1:1 mixture of diastereomers (316 mg, 1.30 mmol, 82%): purified by column chromatography (eluent hexane/ethyl acetate, 3:1); R_f 0.36 (3:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3399 br (OH), 2981 (C−H), 2232 (C≡C), 1965 (C═C, allene), 1713 (C═O), 1597, 1489, 1443 (Ar C−C), 1255 (C−O−C), 1157 (C−O); ^1H NMR (300 MHz, $CDCl_3$) δ 7.38−7.44 (m, 2H + 2H′), 7.26−7.36 (m, 3H + 3H′), 5.93−5.96 (m, 1H + 1H′), 5.81−5.87 (m, 1H + 1H′), 5.24−5.32 (m, 1H + 1H′), 4.19 (q, 2H′, J = 7.1 Hz), 4.18 (q, 2H, J = 7.1 Hz), 3.80−3.91 (m, 1H + 1H′), 1.26 (t, 3H′, J = 7.1 Hz), 1.25 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 211.9 (C), 211.8 (C), 165.6 (C), 165.5 (C), 131.8 (2 × CH), 128.7 (2 × CH), 128.3 (2 × CH), 122.2 (2 × C), 98.5 (CH), 98.4 (CH), 91.7 (CH), 91.3 (CH), 87.2 (2 × C), 86.0 (C), 85.9 (C), 61.4 (CH_2), 61.3 (CH_2), 60.3 (CH), 60.0 (CH), 14.2 (2 × CH_3).

*(E)-Ethyl 5-Hydroxy-7-phenylhepta-2,3,6-trienoate (**3p**).*[13] General procedure B was followed using (*E*)-1-phenylpent-1-en-4-yn-3-ol to yield product **3p** as a yellow oil and a 1:1 mixture of diastereomers (388 mg, 1.59 mmol, 84%): purified by column chromatography (eluent hexane/ethyl acetate, 4:1); R_f 0.40 (4:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3399 br (OH), 2981 (C−H), 1960 (C═C, allene), 1711

DOI: 10.1021/jo502648w
J. Org. Chem. 2015, 80, 1703−1718

(C═O), 1494, 1447, 1414 (Ar C−C), 1253 (C−O−C), 1156 (C−O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20−7.40 (m, 5H + 5H′), 6.68−6.72 (m, 1H′), 6.63−6.67 (m, 1H), 6.28 (d, 1H, J = 15.9 Hz), 6.26 (d, 1H′, J = 15.9 Hz), 5.79−5.87 (m, 1H + 1H′), 5.74−5.79 (m, 1H + 1H′), 4.96−5.06 (m, 1H + 1H′), 4.13−4.23 (m, 2H + 2H′), 3.60 (d, 1H′, J = 4.6 Hz), 3.47 (d, 1H, J = 5.0 Hz), 1.21−130 (m, 3H + 3H′); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 211.7 (C), 211.4 (C), 165.9 (C), 165.8 (C), 136.3 (2 × C), 131.40 (CH), 131.38 (CH), 129.37 (CH), 129.32 (CH), 128.6 (2 × CH), 128.0 (2 × CH), 126.7 (2 × CH), 99.3 (CH), 99.2 (CH), 91.0 (CH), 90.5 (CH), 70.0 (CH), 69.8 (CH), 61.3 (CH_2), 61.2 (CH_2), 14.2 (2 × CH_3).

*Ethyl 5-Hydroxy-5,5-diphenylpenta-2,3-dienoate (**3q**).* General procedure A was followed using 1,1-diphenylprop-2-yn-1-ol to yield product **3q** as a yellow oil (340 mg, 1.16 mmol, 97%): purified by column chromatography (eluent hexane/ethyl acetate, 15:1 to 10:1 to 5:1); R_f 0.34 (5:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3433 br (OH), 2981 (C−H), 1963 (C═C, allene), 1697 (C═O), 1492, 1447, 1410 (Ar C−C), 1261 (C−O−C), 1162 (C−O); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.52 (m, 2H), 7.44−7.47 (m, 2H), 7.27−7.37 (m, 6H), 6.31 (d, 1H, J = 6.1 Hz), 5.70 (d, 1H, J = 6.1 Hz), 4.14−2.24 (m, 2H), 2.86 (s, 1H), 1.31 (t, 3H, J = 7.1 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 211.0 (C), 165.4 (C), 145.0 (C), 144.9 (C), 128.24 (CH), 128.15 (CH), 127.8 (CH), 127.7 (CH), 126.8 (CH), 126.5 (CH), 104.9 (CH), 92.1 (CH), 78.4 (C), 61.1 (CH_2), 14.2 (CH_3); found (FTMS + pNSI) $[M + NH_4]^+$ 312.1597, $C_{19}H_{22}O_3N$ requires 312.1594.

*1-Phenylbuta-2,3-dien-1-ol (**3r**).*[30] A flask was charged with 1-phenylprop-2-yn-1-ol (348 mg, 2.63 mmol, 1 equiv), paraformaldehyde (157 mg, 5.22 mmol, 2 equiv), CuI (305 mg, 1.60 mmol, 0.6 equiv), diisopropylamine (0.73 mL, 5.26 mmol, 2 equiv), and dry dioxane (8.8 mL, 0.30 M). The resulting mixture was stirred at 115 °C for 18 h. The reaction mixture was then cooled and filtered through a plug of silica (eluent hexane/ethyl acetate, 4:1, 200 mL). Following removal of solvent on a rotary evaporator, the crude product was purified by column chromatography (eluent hexane/ethyl acetate, 4:1) to yield product **3r** as a yellow oil (266 mg, 1.82 mmol, 76%): R_f 0.32 (10:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3338 br (OH), 3029 (C−H) 1953 (C═C, allene); ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.27−7.43 (m, 5H), 5.45 (q, 1H, J = 6.5 Hz), 5.23−5.31 (m, 1H), 4.90−4.96 (m, 2H), 2.44 (br s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$), δ 207.1 (C), 142.7 (C), 128.5 (CH), 127.7 (CH), 126.1 (CH), 95.2 (CH), 78.2 (CH_2), 71.9 (CH).

*1-(4-Chlorophenyl)-buta-2,3-diene-1-ol (**3s**).*[31] A flask was charged with 1-(4-chlorophenyl)prop-2-yn-1-ol (191.1 mg, 1.15 mmol, 1.0 equiv), CuI (112.4 mg, 0.59 mmol, 0.5 equiv), paraformaldehyde (84.9 mg, 2.83 mmol, 2.5 equiv), and dry dioxane (1.7 mL). Diisopropylamine (0.3 mL, 2.07 mmol, 1.8 equiv) was added, and the mixture was heated to reflux for 2 h under argon. The reaction mixture was then allowed to cool to room temperature and filtered (washed with diethyl ether). Water (10 mL) was added, and the product was extracted with diethyl ether. The organic layer was then dried with $MgSO_4$ and filtered and the solvent removed using a rotary evaporator. Purification by column chromatography (eluent hexane/ethyl acetate, 5:1) yielded product **3s** as a yellow liquid (60.1 mg, 0.33 mmol, 29%): R_f 0.50 (3:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3333 (OH), 2886 (C−H), 1954 (C═C, allene), 1490, 1406, 1344 (Ar C−C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (s, 4H), 5.36−5.45 (m, 1H), 5.23−5.29 (m, 1H), 4.95−4.92 (m, 2H), 2.17 (d, 1H, J = 4.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.2 (C), 141.3 (C), 133.5 (C), 128.7 (CH), 128.6 (CH), 95.0 (CH), 78.5 (CH_2), 71.3 (CH).

*1-(4-Methoxyphenyl)hepta-2,3-dien-1-ol (**3t**).*[31] A flask was charged with 1-(4-methoxyphenyl)prop-2-yn-1-ol (190.0 mg, 1.17 mmol, 1 equiv), freshly distilled butyraldehyde (0.17 mL, 1.87 mmol, 1.6 equiv), CuI (25.5 mg, 0.10 mmol, 10 mol %), freshly distilled dibutylamine (0.28 mL, 1.64 mmol, 1.4 equiv), and dry dioxane (3.8 mL, 0.34 M). The resulting mixture was stirred at 130 °C for 18 h. The solvent was then removed on a rotary evaporator. Purification by column chromatography (eluent hexane/ethyl acetate, 10:1) yielded product **3t** as a yellow liquid and a 1:1 mixture of diastereomers (74.8 mg, 0.34 mmol, 29%): R_f 0.24 (10:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3383 (OH), 2956, 2931, 2871 (C−H), 1961 (C═C, allene), 1463, 1444 (Ar C−C), 1246 (C−O−C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, 2H, J = 8.9 Hz), 6.89 (d, 2H, J = 8.9 Hz), 5.33−5.44 (m, 2H), 5.16−5.21 (m, 1H), 3.81 (s, 3H), 2.07−2.10 (m, 1H), 1.98−2.07 (m, 2H), 1.38−1.51 (m, 2H), 0.87−0.97 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) 202.3 (C), 202.1 (C), 159.21 (C), 159.17 (C), 135.5 (C), 135.4 (C), 127.5 (CH), 127.4 (CH), 113.9 (CH), 113.8 (CH), 96.22 (CH), 96.15 (CH), 95.0 (CH), 94.7 (CH), 72.0 (CH), 71.8 (CH), 55.3 (2 × CH_3), 30.9 (CH_2), 30.8 (CH_2), 22.33 (CH_2), 22.30 (CH_2), 13.63 (CH_3), 13.61 (CH_3).

*1-(4-Bromophenyl)hepta-2,3-dien-1-ol (**3u**).* A flask was charged with 1-(4-bromophenyl)prop-2-yn-1-ol (207 mg, 0.98 mmol, 1 equiv), freshly distilled butyraldehyde (0.14 mL, 1.57 mmol, 1.6 equiv), CuI (36.2 mg, 0.10 mmol, 10 mol %), freshly distilled dibutylamine (0.23 mL, 1.37 mmol, 1.4 equiv), and dry dioxane (2.8 mL, 0.34 M). The resulting mixture was stirred at 130 °C for 18 h. The solvent was then removed on a rotary evaporator. Purification by column chromatography (eluent hexane/ethyl acetate, 10:1 to5:1) yielded product **3u** as a yellow liquid and a 1:1 mixture of diastereomers (164.4 mg, 0.62 mmol, 62%): R_f 0.24 (10:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3334 (OH), 2957, 2928, 2870 (C−H), 1961 (C═C, allene), 1485, 1455, 1398 (Ar C−C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, 2H, J = 8.6 Hz), 7.27 (d, 2H, J = 8.6 Hz), 5.34−5.39 (m, 2H), 5.16−5.21 (m, 1H), 2.16 (br t, 1H, J = 2.6 Hz), 1.97−2.05 (m, 2H), 1.42 (sext, 2H, J = 7.4 Hz), 0.88−0.97 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) 202.5 (C), 202.3 (C), 142.2 (C), 142.1 (C), 137.5 (CH), 131.5 (CH), 128.1 (CH), 127.9 (CH), 121.46 (C), 121.43 (C), 95.84 (CH), 95.76 (CH), 95.4 (CH), 95.1 (CH), 71.8 (CH), 71.6 (CH), 30.8 (CH_2), 30.7 (CH_2), 22.28 (CH_2), 22.26 (CH_2), 13.6 (2 × CH_3); found (FTMS + pAPCI) $[M + H]^+$ 267.0375, $C_{13}H_{16}BrO$ requires 267.0379.

*1,1-Diphenylhepta-2,3-dien-1-ol (**3v**).*[31] A flask was charged with 1,1-diphenylprop-2-yn-1-ol (206.5 mg, 0.99 mmol, 1 equiv), freshly distilled butyraldehyde (0.14 mL, 1.58 mmol, 1.6 equiv), CuI (39.4 mg, 20 mol %), freshly distilled dibutylamine (0.24 mL, 1.39 mmol, 1.4 equiv), and dry dioxane (3.0 mL, 0.34 M). The resulting mixture was stirred at 150 °C for 26 h. The solvent was then removed on a rotary evaporator. Purification by column chromatography (eluent hexane/ethyl acetate, 20:1 to 10:1) yielded product **3v** as a yellow liquid (50 mg, 0.19 mmol, 19%): R_f 0.38 (10:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3455 (OH), 3059, 3025, 2958, 2930, 2871 (C−H), 1962 (C═C, allene), 1491, 1447 (Ar C−C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.46 (m, 4H), 7.29−7.35 (m, 4H), 7.24−7.27 (m, 2H), 5.91 (dt, 1H, J = 6.2, 2.9 Hz), 5.41 (q, 1H, J = 6.2 Hz)), 2.66 (s, 1H), 1.96−2.04 (m, 2H), 1.38 (sext, 2H, J = 7.4 Hz), 0.87 (t, 3H, J = 7.4 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 200.9 (C), 146.42 (C), 146.40 (C), 128.01 (CH), 127.99 (CH), 127.1 (CH), 126.8 (CH), 126.7 (CH), 126.7 (CH), 100.9 (CH), 97.1 (CH), 77.2 (C), 30.9 (CH_2), 22.7 (CH_2), 13.6 (CH_3).

Preparation of 1,3-Dienes 4. *General procedure C: Using Au(I) Catalysis.* Allenol (0.070 mmol, 1 equiv) was added to a sealed tube and dissolved in $CDCl_3$ (0.35 mL). A solution of Au(I) catalyst **8** (5 mol %) and thiol (0.077 mmol, 1.1 equiv) in $CDCl_3$ (0.15 mL) was then added to the sealed tube and washed in with additional $CDCl_3$ (0.2 mL). The resulting mixture was heated at 70 °C for 30 min. The mixture was allowed to cool before it was passed through a plug of silica and washed with ether. The filtrate was then concentrated on a rotary evaporator. The products were purified by column chromatography (hexane/ethyl acetate).

General procedure D: Using $InCl_3$ Catalysis. $InCl_3$ (5 mol %) and thiol (0.07 mmol, 1 equiv) were added to a microwave tube and dissolved in $CHCl_3$ (0.35 mL). A solution of allenol (0.105 mmol, 1.5 equiv) in $CHCl_3$ (0.15 mL) was added and washed in with additional $CHCl_3$ (0.2 mL). The tube was then sealed and placed in the microwave and heated at 70 °C (external surface sensor), 300 W, for 10 min. The mixture was allowed to cool before it was passed through a plug of silica and washed with ether. The filtrate was then concentrated on a rotary evaporator. The products were purified by column chromatography (hexane/ethyl acetate).

DOI: 10.1021/jo502648w
J. Org. Chem. 2015, 80, 1703−1718

E,E stereochemistry for **4** was confirmed by X-ray structure analysis (**4a**) and NOESY where possible. The *E,E* stereochemistries for the others were assigned by analogy with the rest in the series.

*(2E,4E)-Ethyl 3-((4-Nitrophenyl)thio)-5-phenylpenta-2,4-dienoate (**4a**). Using Au(I) Catalysis.* General procedure C was followed to yield title product **4a** as a yellow solid (9.5 mg, 0.03 mmol, 38%) and product **6a** as a yellow oil (8.2 mg, 0.02 mmol, 34%): purified by column chromatography (eluent hexane/ethyl acetate, 80:1 to 70:1 to 50:1 to 25:1).

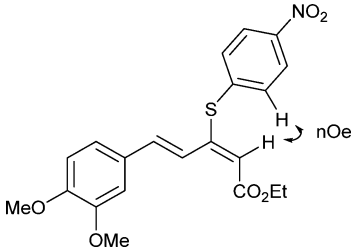
Using $InCl_3$. General procedure D was followed to yield title product **4a** as a yellow solid (12 mg, 0.03 mmol, 49%): purified by column chromatography (eluent hexane/ethyl acetate, 80:1 to 70:1 to 50:1 to 25:1); R_f 0.66 (5:1 hexane/ethyl acetate); mp 111−113 °C; ν_{max}/cm^{-1} 3097 (C−H), 2098 (C−H), 1703 (C═O), 1614 (C═C, diene conj), 1597 (C═C, diene conj), 1576, 1561 (Ar C−C), 1518 (NO_2), 1340 (NO_2), 1192 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$), δ 8.35 (dd, 1H, J = 15.9 Hz, 0.8 Hz), 8.18 (d, 2H, J = 8.9 Hz), 7.54 (d, 2H, J = 8.9 Hz), 7.47−7.52 (m, 2H), 7.28−7.41 (m, 4H), 5.95 (app s, 1H), 4.21 (q, 2H, J = 7.1 Hz), 1.30 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$), 164.8 (C), 149.9 (C), 146.8 (C), 142.7 (C), 138.9 (CH), 135.7 (C), 131.0 (CH), 129.5 (CH), 128.8 (CH), 127.8 (CH), 124.4 (CH), 123.3 (CH), 121.1 (CH), 60.6 (CH_2), 14.3 (CH_3); found (FTMS + pAPCI) $[M + H]^+$ 356.0950, $C_{19}H_{18}NO_4S$ requires 356.0951. *E,E* stereochemistry was confirmed by crystal structure analysis (Figure 1).

Crystals were grown by vapor diffusion from $CHCl_3$−hexane. Crystal data: $C_{19}H_{17}NO_4S$, M = 355.40, triclinic, a = 9.6997(7) Å, b = 9.9793(6) Å, c = 10.2055(7) Å, β = 73.565(4)°, U = 869.20(10) Å^3, T = 100 K, space group $P\bar{1}$, Z = 2, μ(Mo Kα) = 0.210 mm^{-1}, 26793 reflections measured, 7525 independent reflections (R_{int} = 0.0465). The final wR2 was 0.1146.

*Data for ethyl 5-((4-nitrophenyl)thio)-5-phenylpenta-2,3-dienoate (**6a**):* R_f 0.58 (5:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 2979 (C−H), 1980 (C═C, allene), 1698 (C═O), 1613, 1596, 1575, (Ar C−C), 1513 (NO_2), 1336 (NO_2) 1215 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$, dr = 1:1.4) δ 8.19 (d, 2H + 2H′, J = 9.1 Hz, major + minor), 8.11 (m, 1H + 1H′), 7.62 (d, 2H + 2H′, J = 9.1 Hz), 7.28−7.48 (m, 4H + 4H′), 6.04 (dd, 1H, J = 7.4, 6.1 Hz, major), 5.99 (dd, 1H′, J = 7.3, 6.1 Hz, minor), 5.71 (dd, 1H, J = 6.1, 2.2, Hz, major), 5.66 (dd, 1H, J = 6.1, 2.3 Hz, minor), 5.15 (dd, 1H, J = 7.3, 2.3 Hz, minor), 5.13 (dd, 1H, J = Hz, 7.3, 2.2 Hz, major), 4.16 (q, 2H + 2H′, J = 7.1 Hz), 1.26 (t, 3H + 3H′, J = 7.1 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 212.6 (C, minor), 212.4 (C, major), 164.8 (C, major), 164.7 (C, minor), 147.0 (C, major), 145.3 (C, major), 145.0 (C, minor), 144.1 (C, major), 137.8 (C, major), 137.7 (C, minor), 129.0 (CH, major), 128.9 (CH, minor), 128.5 (CH, major + minor), 127.9 (CH, major), 127.8 (CH, minor), 126.4 (CH, minor), 124.4 (CH, major), 123.9 (CH, major), 123.8 (CH, minor), 97.3 (CH, major), 97.1 (CH, minor), 91.6 (CH, major), 91.3 (CH, minor, SCHCH═C═CH), 61.2 (CH_2, major), 61.1 (CH_2, minor), 49.9 (CH, minor), 49.4 (CH, major), 14.2 (CH_3, major), 14.1 (CH_3, minor); found (FTMS + pAPCI) $[M + H]^+$ 356.0950, $C_{19}H_{18}NO_4S$ requires 356.0951. Note: this product decomposes within weeks.

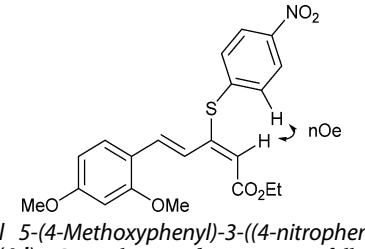
*Data for (Z)-ethyl 3,5-bis((4-nitrophenyl)thio)-5-phenylpent-3-encate (**7a**):* ν_{max}/cm^{-1} 2923 (C−H), 1731 (C═O), 1513 (NO_2), 1595, 1576, 1476, (Ar C−C), 1336 (NO_2) 1180 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$, *E*:*Z* = 1:0.3) δ 8.07 (d, 2H + 2H′, J = 8.9 Hz), 8.03 (d, 2H + 2H′, J = 8.0 Hz), 7.48 (d, 2H + 2H′, J = 9.0 Hz) 7.27−7.44 (m, 5H + 5H′), 7.20 (d, 2H + 2H′, J = 9.0 Hz), 6.56 (d, 1H, J = 10 Hz, major, C*H*═CS), 6.47 (1H′, d, J = 9.8 Hz, minor, C*H*═CS), 5.66 (1H, d, J = 9.9 Hz, major), 5.35 (d, 1H′, J = 9.8 Hz, minor), 4.10 (q, 2H + 2H′, J = 7.1 Hz), 3.26 (s, 2H + 2H′), 1.17 (m, 3H + 3H′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3 (C, major), 168.8 (C, minor), 146.4 (C, major), 146.2 (C, minor), 146.2 (C, minor), 144.1 (C, major), 143.2 (C, minor), 142.1 (CH, major + minor), 138.9 (C, minor), 137.7 (C, major), 130.4 (CH, major + minor), 129.1 (CH, major + minor), 128.4 (CH, minor), 128.3 (CH, major), 127.8 (CH, minor), 127.7 (CH, major), 126.8 (C, major + minor), 126.4 (CH, major + minor), 124.4 (CH, major + minor), 124.2 (CH, minor), 124.1 (CH, major), 123.9 (CH, major + minor), 65.8 (CH_2, minor), 61.3 (CH_2, major), 51.7 (CH, major), 50.8 (CH, minor), 43.0 (CH_2, major), 38.2 (CH_2, minor), 15.3 (CH_3, minor), 14.1 (CH_3, major); found (FTMS + pAPCI) $[M + H]^+$ 528.1251, $C_{25}H_{26}N_3O_6S_2$ requires 528.1258.

*(2E,4E)-Ethyl 5-(3,4-Dimethoxyphenyl)-3-((4-nitrophenyl)thio)-penta-2,4-dienoate (**4b**).* General procedure D was followed to obtain product **4b** as a yellow oil (23.3 mg, 0.06 mmol, 80%): purified by column chromatography (eluent hexane/ethyl acetate, 5:1); R_f 0.25 (5:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 2935 (C−H alkyl), 1699 (C═O), 1596 (C═C diene), 1578, 1557 (Ar C−C), 1510 (NO_2), 1367 (NO_2), 1177 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.25 (dd, 1H, J = 15.8, 0.8 Hz), 8.17 (d, 2H, J = 9.0 Hz), 7.52 (d, 2H, J = 9.0 Hz), 7.29 (d, 1H, J = 15.8 Hz), 7.06 (m, 2H), 6.82 (m, 1H), 5.92 (app t, 1H, J = 0.6 Hz), 4.21 (q, 2H, J = 7.1 Hz), 3.92 (s, 3H), 3.90 (s, 3H), 1.30 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$), δ 165.0 (C), 150.6 (C), 149.9 (C), 149.2 (C), 146.7 (C), 143.2 (C), 139.1 (CH), 130.7 (CH), 128.8 (C), 124.4 (CH), 122.1 (CH), 121.4 (CH), 120.4 (CH), 111.1 (CH), 109.7 (CH), 60.5 (CH_2), 55.97 (CH_3), 55.95 (CH_3), 14.2 (CH_3); found (FTMS + pAPCI) $[M + H]^+$ 416.1169, $C_{21}H_{22}NO_6S$ requires 416.1162. *E,E* stereochemistry was confirmed by NOESY (δ 5.92 and 7.52):



*(2E,4E)-Ethyl 5-(2,4-Dimethoxyphenyl)-3-((4-nitrophenyl)thio)-penta-2,4-dienoate (**4c**).* General procedure D was followed to yield product **4c** as a yellow solid (27.9 mg, 0.07 mmol, 96%): purified by column chromatography (eluent hexane/ethyl acetate, 5:1).

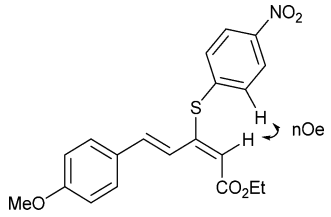
Repeated on a 0.36 mmol Scale with 1 mol % $InCl_3$. Thiol (55 mg, 0.355 mmol, 1.0 equiv) and $InCl_3$ (0.7 mg, 1 mol %) were added to a microwave tube and dissolved in $CHCl_3$ (1.6 mL). A solution of allenol **3c** (157 mg, 0.566 mmol, 1.5 equiv) in $CHCl_3$ (1 mL) was added to the microwave tube and washed in with $CHCl_3$ (1 mL). The reaction was heated at 70 °C in a microwave for 20 min to yield product **4c** as a yellow solid (142 mg, 0.34 mmol, 96% yield): R_f 0.36 (5:1 hexane/ethyl acetate); mp 126−128 °C; ν_{max}/cm^{-1} 2938 (C−H), 1698 (C═O), 1596 (C═C, diene conj), 1515 (NO_2), 1556, 1463, 1438, 1419 (Ar C−C), 1337 (NO_2), 1159 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (dd, 1H, J = 16.0, 0.8 Hz), 8.15 (d, 2H, J = 9.0 Hz), 7.67 (d, 1H, J = 16.0 Hz), 7.52 (d, 3H, J = 9.0 Hz), 6.38−6.51 (m, 2H), 5.89 (app s, 1H), 4.21 (q, 2H, J = 7.1 Hz), 3.82 (s, 3H), 3.81 (s, 3H), 1.29 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 165.1 (C), 162.3 (C), 159.2 (C), 151.1 (C), 146.7 (C), 143.5 (C), 134.2 (CH), 131.0 (CH), 129.0 (CH), 124.5 (CH), 121.2 (CH), 119.3 (CH), 117.9 (C), 105.4 (CH), 98.4 (CH), 60.3 (CH_2), 55.6 (CH_3), 55.5 (CH_3), 14.3 (CH_3); found (FTMS + pAPCI) $[M + H]^+$ 416.1161, $C_{21}H_{22}NO_6S$ requires 416.1162. *E,E* stereochemistry was confirmed by NOESY (δ 7.52 and 5.89):



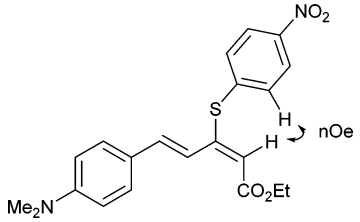
*(2E,4E)-Ethyl 5-(4-Methoxyphenyl)-3-((4-nitrophenyl)thio)penta-2,4-dienoate (**4d**).* General procedure D was followed with the following modification. The reaction was placed in a microwave at 90 °C for 20 min to yield product **4d** as a yellow solid (26.3 mg, 0.068 mmol, 79%): purified by column chromatography (eluent hexane/ethyl acetate, 10:1); R_f 0.51 (5:1 hexane/ethyl acetate); mp 80−82 °C; ν_{max}/cm^{-1} 3096 (C−H), 2979 (C−H), 1699 (C═O), 1596 (C═C, diene conj), 1509 (NO_2), 1558, 1476, 1463, 1442 (Ar C−C), 1337 (NO_2), 1184 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (dd, 1H, J = 15.8, 0.9 Hz), 8.16 (d, 2H, J = 9.0 Hz), 7.52 (d, 2H, J = 9.0 Hz),

DOI: 10.1021/jo502648w
J. Org. Chem. 2015, 80, 1703−1718

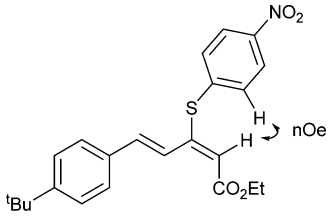
7.46 (d, 2H, J = 8.4 Hz), 7.30 (d, 1H, J = 15.8 Hz), 6.87 (d, 2H, J = 8.4 Hz), 5.92 (app t, 1H, J = 0.7 Hz), 4.21 (q, 2H, J = 7.1 Hz), 3.82 (s, 3H), 1.30 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 165.0 (C), 160.88 (C), 150.0 (C), 146.7 (C), 143.2 (C), 138.8 (CH), 130.8 (CH), 129.4 (CH), 128.5 (C), 124.4 (CH), 121.2 (CH), 120.3 (CH), 114.3 (CH), 60.5 (CH_2), 55.4 (CH_3), 14.3 (CH_3); found (FTMS + pAPCI) $[M + H]^+$ 386.1052, $C_{20}H_{20}NO_5S$ requires 386.1057. *E,E* stereochemistry confirmed by NOESY (δ 7.52 and 5.92):



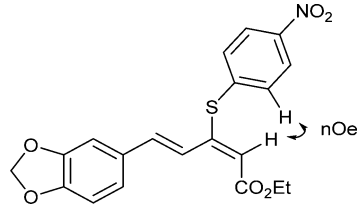
*(2E,4E)-Ethyl 5-(4-(Dimethylamino)phenyl)-3-((4-nitrophenyl)-thio)penta-2,4-dienoate (**4e**).* General procedure D was followed to yield product **4e** as a red solid (25.8 mg, 0.06 mmol, 90%): purified by column chromatography (eluent hexane/ethyl acetate, 7:1); R_f 0.44 (5:1 hexane/ethyl acetate); mp 146−149 °C; ν_{max}/cm^{-1} 2980 (C−H), 1698 (C═O), 1595 (C═C, diene conj), 1520 (NO_2), 1554, 1476, 1444 (Ar C−C), 1338 (NO_2), 1164 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (dd, 1H, J = 15.6, 0.7 Hz), 8.14 (d, 2H, J = 9.0 Hz), 7.49 (d, 2H, J = 9.0 Hz), 7.41 (d, 2H, J = 8.8 Hz), 7.29 (d, 1H, J = 15.6 Hz), 6.64 (d, 2H, J = 8.8 Hz), 5.90 (app s, 1H), 4.22 (q, 2H, J = 7.1 Hz), 3.00 (s, 6H), 1.30 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 165.3 (C), 151.4 (C), 150.1 (C), 146.4 (C), 144.2 (C), 140.1 (CH), 130.2 (CH), 129.6 (CH), 124.3 (CH), 123.6 (CH), 119.1 (C), 119.1 (CH), 118.7 (CH), 60.3 (CH_2), 40.2 (CH_3), 14.3 (CH_3); found (FTMS + pAPCI) $[M + H]^+$ 399.1374, $C_{21}H_{23}N_2O_4S$ requires 399.1373. *E,E* stereochemistry was confirmed by NOESY (δ 7.49 and 5.90):



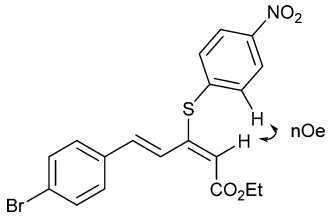
*(2E,4E)-Ethyl 5-(4-tert-Butylphenyl)-3-((4-nitrophenyl)thio)penta-2,4-dienoate (**4f**).* General procedure D was followed to yield product **4f** as a yellow solid (18.8 mg, 0.05 mmol, 68%): purified by column chromatography (eluent hexane/ethyl acetate, 25:1 to 10:1); R_f 0.70 (5:1 hexane/ethyl acetate); mp 112−114 °C; ν_{max}/cm^{-1} 2962 (C−H), 1703 (C═O), 1598 (C═C, diene conj), 1517 (NO_2), 1565, 1476, 1410 (Ar C−C), 1338 (NO_2), 1176 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (dd, 1H, J = 15.8, 0.8 Hz), 8.17 (d, 2H, J = 9.0 Hz), 7.52 (d, 2H, J = 9.0 Hz), 7.44 (d, 2H, J = 8.4 Hz), 7.36 (d, 2H, J = 8.4 Hz), 7.31 (d, 1H, J = 15.8 Hz), 5.97 (app s, 1H), 4.22 (q, 2H, J = 7.1 Hz), 1.26−1.35 (m, 12H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 164.9 (C), 153.1 (C), 149.8 (C), 146.7 (C), 143.1 (C), 139.1 (CH), 133.0 (C), 130.8 (CH), 127.7 (CH), 125.8 (CH), 124.4 (CH), 122.5 (CH), 121.0 (CH), 60.6 (CH_2), 34.8 (C), 31.2 (CH_3), 14.3 (CH_3); found (FTMS + pAPCI) $[M + H]^+$ 412.1573, $C_{23}H_{26}NO_4S$ requires 412.1577. *E,E* stereochemistry was confirmed by NOESY (δ 7.52 and 7.31):



*(2E,4E)-Ethyl 5-(Benzo[d][1,3]dioxol-5-yl)-3-((4-nitrophenyl)thio)-penta-2,4-dienoate (**4g**).* General procedure D was followed with the following modification. The reaction was placed in a microwave at 90 °C for 20 min to yield product **4g** as a yellow solid (11.6 mg, 0.03 mmol, 47%): purified by column chromatography (eluent hexane/ethyl acetate, 7:1); R_f 0.44 (5:1 hexane/ethyl acetate); mp 122−125 °C; ν_{max}/cm^{-1} 2980 (C−H), 1699 (C═O), 1596 (C═C, diene conj), 1517 (NO_2), 1559, 1502, 1487, 1446 (Ar C−C), 1338 (NO_2), 1177 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13−8.26 (m, 3H), 7.52 (d, 2H, J = 8.9 Hz), 7.24 (d, 1H, J = 15.8 Hz), 7.07 (d, 1H, J = 1.5 Hz), 6.94 (dd, 1H, J = 8.1, 1.6 Hz), 6.76 (d, 1H, J = 8.0 Hz), 5.98 (s, 2H), 5.92 (app s, 1H), 4.21 (q, 2H, J = 7.1 Hz), 1.30 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 165.0 (C), 149.8 (C), 149.1 (C), 148.4 (C), 146.8 (C), 143.1 (C), 138.8 (CH), 130.8 (CH), 130.2 (C), 124.4 (CH), 123.8 (CH), 121.6 (CH), 120.5 (CH), 108.5 (CH), 106.5 (CH), 101.5 (CH_2), 60.5 (CH_2), 14.3 (CH_3); found (FTMS + pAPCI) $[M + H]^+$ 400.0854, $C_{20}H_{18}NO_6S$ requires 400.0849. *E,E* stereochemistry was confirmed by NOESY (δ 7.52 and 5.29):



*(2E,4E)-Ethyl 5-(4-Bromophenyl)-3-((4-nitrophenyl)thio)penta-2,4-dienoate (**4h**).* General procedure D was followed with the following modification. The reaction was placed in a microwave at 90 °C for 20 min to yield product **4h** as a yellow solid (28.1 mg, 0.06 mmol, 93%): purified by column chromatography (eluent hexane/ethyl acetate, 10:1); R_f 0.71 (5:1 hexane/ethyl acetate); mp:117−120 °C; ν_{max}/cm^{-1} 3065, 2980 (C−H), 1701 (C═O), 1614 (C═C, diene conj), 1596 (C═C, diene conj), 1515 (NO_2), 1566, 1556, 1485 (Ar C−C), 1336 (NO_2), 1174 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (dd, 1H, J = 15.9, 0.8 Hz), 8.18 (d, 2H, J = 9.0 Hz), 7.53 (d, 2H, J = 9.0 Hz), 7.47 (d, 2H, J = 8.5 Hz), 7.36 (d, 2H, J = 8.5 Hz), 7.25 (d, 1H, J = 15.9 Hz), 5.94 (app s, 1H), 4.20 (q, 2H, J = 7.1 Hz), 1.30 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 164.8 (C), 149.7 (C), 147.0 (C), 142.4 (C), 137.4 (CH), 134.6 (C), 132.0 (CH), 131.3 (CH), 129.2 (CH), 124.5 (CH), 123.9 (CH), 123.6 (C), 121.3 (CH), 60.7 (CH_2), 14.3 (CH_3); found (FTMS + pAPCI) $[M + H]^+$ 434.0057, $C_{19}H_{17}NO_4SBr$ requires 434.0056. *E,E* stereochemistry was confirmed by NOESY (δ 7.53 and 5.94):

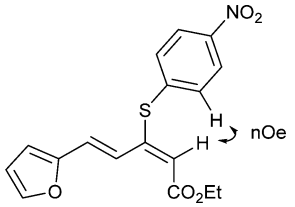


*(2E,4E)-Ethyl 5-(4-Chlorophenyl)-3-((4-nitrophenyl)thio)penta-2,4-dienoate (**4i**).* General procedure D was followed with the following modification. The reaction was placed in a microwave at 90 °C for 30 min to yield product **4i** as a yellow solid (14.3 mg, 0.04 mmol, 49%): purified by column chromatography (eluent hexane/ethyl acetate, 7:1); R_f 0.64 (5:1 hexane/ethyl acetate); mp 107−110 °C; ν_{max}/cm^{-1} 2981 (C−H), 1703 (C═O), 1616 (C═C, diene conj), 1596 (C═C, diene conj), 1517 (NO_2), 1569, 1489, 1476 (Ar C−C), 1339 (NO_2), 1187 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23 (dd, 1H, J = 15.9, 0.9 Hz), 8.11 (d, 2H, J = 9.0 Hz), 7.46 (d, 2H, J = 9.0 Hz), 7.37 (d, 2H, J = 8.4 Hz), 7.17−7.28 (m, 3H), 5.87 (app s, 1H), 4.14 (q, 2H, J = 7.1 Hz), 1.23 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 164.8 (C), 149.7 (C), 147.0 (C), 142.1 (C), 137.3 (CH), 135.3 (C), 134.2 (C), 131.2 (CH), 129.2 (CH), 129.1 (CH), 124.5 (CH), 123.8 (CH), 121.2 (CH), 60.7 (CH_2), 14.3 (CH_3); found (FTMS + pAPCI) $[M + H]^+$ 390.0561, $C_{19}H_{17}ClNO_4S$ requires 390.0561.

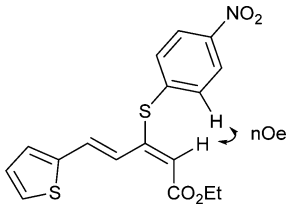
*(2E,4E)-Ethyl 5-(Furan-2-yl)-3-((4-nitrophenyl)thio)penta-2,4-dienoate (**4k**).* General procedure D was followed with the following modification. The reaction was placed in a microwave at 90 °C for 20 min to yield product **4k** as a pale yellow oil (19.0 mg, 0.06 mmol, 79%): purified by column chromatography (eluent hexane/ethyl acetate, 7:1); R_f 0.60 (5:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3097, 2981 (C−H),

DOI: 10.1021/jo502648w
J. Org. Chem. 2015, 80, 1703−1718

1702 (C═O), 1614 (C═C, diene conj), 1596 (C═C, diene conj), 1514 (NO_2), 1573, 1541, 1475 (Ar C−C), 1336 (NO_2), 1174 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (d, 1H, J = 16.1 Hz), 8.16 (d, 2H, J = 9.0 Hz), 7.49 (d, 2H, J = 9.0 Hz), 7.45 (d, 1H, J = 1.7 Hz), 7.11 (d, 1H, J = 16.1 Hz), 6.48 (d, 1H, J = 3.4 Hz), 6.42 (dd, 1H, J = 3.4, 1.7 Hz), 6.00 (s, 1H), 4.23 (q, 2H, J = 7.1 Hz), 1.30 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 164.8 (C), 152.0 (C), 148.5 (C), 146.6 (C), 144.4 (CH), 143.3 (C), 130.2 (CH), 125.9 (CH), 124.4 (CH), 122.1 (CH), 121.6 (CH), 113.3 (CH), 112.3 (CH), 60.6 (CH_2), 14.3 (CH_3); found (FTMS + pAPCI) $[M + H]^+$ 346.0747, $C_{17}H_{16}NO_5S$ requires 346.0744. *E,E* stereochemistry was confirmed by NOESY (δ 7.11 and 6.00):

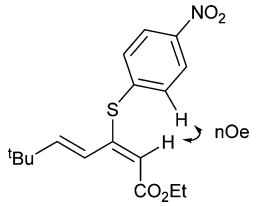


*(2E,4E)-Ethyl 3-((4-Nitrophenyl)thio)-5-(thiophene-2-yl)penta-2,4-dienoate (**4l**).* General procedure D was followed with the following modification. The reaction was placed in a microwave at 90 °C for 20 min to yield product **4l** as a yellow oil (21.6 mg, 0.06 mmol, 84%): purified by column chromatography (eluent hexane/ethyl acetate, 10:1); R_f 0.60 (5:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3099, 2980 (C−H), 1698 (C═O), 1596 (C═C, diene conj), 1513 (NO_2), 1562, 1475, 1423 (Ar C−C), 1335 (NO_2), 1174 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (d, 1H, J = 15.5 Hz), 8.16 (d, 2H, J = 9.0 Hz), 7.50 (d, 2H, J = 9.0 Hz), 7.46 (d, 1H, J = 15.5 Hz), 7.32 (dt, 1H, J = 5.0, 0.8 Hz), 7.12 (dt, 1H, J = 3.6, 0.8 Hz), 7.00 (dd, 1H, J = 5.0, 3.6 Hz), 5.97 (s, 1H), 4.22 (q, 2H, J = 7.1 Hz), 1.31 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 164.8 (C), 148.7 (C), 146.7 (C), 143.1 (C), 141.3 (C), 131.9 (CH), 130.5 (CH), 129.6 (CH), 128.1 (CH), 127.8 (CH), 124.4 (CH), 122.8 (CH), 121.6 (CH), 60.6 (CH_2), 14.3 (CH_3); found (FTMS + pAPCI) $[M + H]^+$ 362.0515, $C_{17}H_{16}NO_4S_2$ requires 362.0515. *E,E* stereochemistry was confirmed by NOESY (δ 7.50 and 5.97):

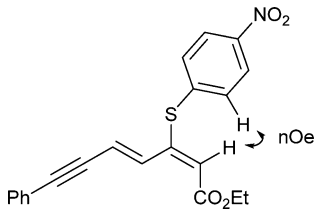


*(2E,4E)-Ethyl 3-((4-Nitrophenyl)thio)deca-2,4-dienoate (**4m**).* General procedure D was followed with the following modification. The reaction was placed in a microwave at 90 °C for 60 min to yield product **4m** as a yellow oil (6.9 mg, 0.02 mmol, 42%): purified by column chromatography (eluent hexane/ethyl acetate, 80:1 to 50:1); R_f 0.53 (5:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 2929 (C−H), 1736 (C═O), 1597 (C═C, diene), 1576 (Ar C−C), 1518 (NO_2), 1340 (NO_2), 1185 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (d, 2H, J = 8.9 Hz), 7.45−7.54 (m, 3H), 6.54 (dt, 1H, J = 14.3, 7.0 Hz), 5.79 (s, 1H), 4.17 (q, 2H, J = 7.1 Hz), 2.20 (dq, 2H, J = 7.2, 1.1 Hz), 1.15−1.44 (m, 9H), 0.85 (t, 3H, J = 7.1 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$), δ 164.7 (C), 150.4 (C), 146.9 (C), 143.4 (CH), 142.8 (C), 131.4 (CH), 124.3 (CH), 124.2 (CH), 118.9 (CH), 60.4 (CH_2), 33.0 (CH_2), 31.3 (CH_2), 28.3 (CH_2), 22.4 (CH_2), 14.3 (CH_3), 13.9 (CH_3); found (FTMS + pAPCI) $[M + H]^+$ 350.1424, $C_{18}H_{24}NO_4S$ requires 350.1421.

*(2E,4E)-Ethyl 6,6-Dimethyl-3-((4-nitrophenyl)thio)hepta-2,4-dienoate (**4n**).* General procedure D was followed with the following modification. The reaction was placed in a microwave at 70 °C for 60 min to yield product **4n** as a pale yellow oil (19.2 mg, 0.05 mmol, 80%): purified by column chromatography (eluent hexane/ethyl acetate, 10:1); R_f 0.78 (5:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 2960, 2886 (C−H), 1705 (C═O), 1628 (C═C, diene conj), 1597 (C═C, diene conj), 1518 (NO_2), 1567, 1476 (Ar C−C), 1337 (NO_2), 1175 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (d, 2H, J = 8.9 Hz), 8.42−8.52 (m, 3H), 6.52 (d, 1H, J = 15.8 Hz), 5.78 (s, 1H), 4.17 (q, 2H, J = 7.1 Hz), 1.27 (t, 3H, J = 7.1 Hz), 1.03 (s, 9H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 164.8 (C), 153.1 (CH), 151.2 (C), 146.9 (C), 142.6 (C), 131.7 (CH), 124.2 (CH), 120.3 (CH), 118.8 (CH), 60.4 (CH_2), 34.1 (C), 29.0 (CH_3), 14.3 (CH_3); found (FTMS + pAPCI) $[M + H]^+$ 336.1262, $C_{17}H_{22}NO_4S$ requires 336.1264. *E,E* stereochemistry confirmed by NOESY (δ 8.42 and 5.78):

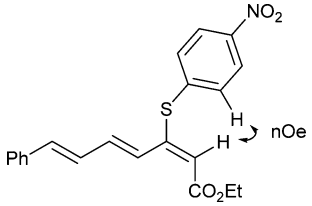


*(2E,4E)-Ethyl 3-((4-Nitrophenyl)thio)-7-phenylhepta-2,4-dien-6-ynoate (**4o**).* General procedure D was followed with the following modification. The reaction was placed in a microwave at 90 °C for 20 min to yield product **4o** as a yellow oil (22.9 mg, 0.06 mmol, 85%) with *E*:*Z* = 4:1: purified by column chromatography (eluent hexane/ethyl acetate, 10:1); R_f 0.65 (5:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3063 (C−H), 2981 (C−H), 2981 (C≡C), 1706 (C═O), 1598 (C═C, diene conj), 1517 (NO_2), 1577, 1561, 1476, 1442 (Ar C−C), 1338 (NO_2), 1186 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (d, 2H, J = 9.0 Hz, major), 8.16 (d, 2H′, J = 9.0 Hz, minor), 8.13 (dd, 1H + 1H′, J = 15.7, 0.9 Hz), 7.54 (d, 2H′, J = 9.0 Hz, minor), 7.48 (d, 2H, J = 9.0 Hz, major), 7.42−7.45 (m, 2H + 2H′), 7.31−7.36 (m, 3H + 3H′), 6.64 (dd, 1H + 1H′, J = 15.7 Hz, 0.6 Hz), 6.00 (app t, 1H, J = 0.8 Hz, major), 5.92 (app t, 1H, J = 1.0 Hz, minor), 4.23 (q, 2H, J = 7.1 Hz, major), 4.16 (q, 2H′, J = 7.1 Hz, minor), 1.30 (t, 3H, J = 7.1 Hz, major), 1.25 (t, 3H′, J = 7.1 Hz, minor); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 164.3 (C, major + minor), 149.3 (C, minor), 147.6 (C, major), 147.2 (C, minor), 146.8 (C, major), 142.5 (C, major), 141.7 (C, minor), 134.9 (CH, major), 133.1 (CH, minor), 132.4 (CH, minor), 131.9 (CH, major), 131.4 (CH, minor), 130.5 (CH, major), 129.0 (CH, major + minor), 128.5 (CH, minor), 128.4 (CH, major), 124.5 (CH, major), 124.2 (CH, minor), 123.0 (CH, major), 124.1 (C, minor), 122.6 (C, major), 121.3 (CH, minor), 119.4 (CH, major), 155.7 (CH, minor), 100.9 (C, minor), 97.8 (C, major), 88.2 (C, major), 87.0 (C, minor), 60.8 (CH_2, major), 60.7 (CH_2, minor), 14.22 (CH_3, major), 14.17 (CH_3, minor); found (FTMS + pAPCI) $[M + H]^+$ 380.0951, $C_{21}H_{18}NO_4S$ requires 380.0951. *E,E* stereochemistry for the major isomer was confirmed by NOESY (δ 7.48 and 6.00):



*(2E,4E,6E)-Ethyl 3-((4-Nitrophenyl)thio)-7-phenylhepta-2,4,6-trienoate (**4p**).* General procedure D was followed with the following modification. The reaction was placed in a microwave at 90 °C for 20 min to yield product **4p** as a yellow solid (10.2 mg, 0.03 mmol, 93%): purified by column chromatography (eluent hexane/ethyl acetate, 25:1 to 10:1); R_f 0.66 (5:1 hexane/ethyl acetate); mp 91−94 °C; ν_{max}/cm^{-1} 2981 (C−H), 1702 (C═O), 1592 (C═C, triene conj), 1515 (NO_2), 1575, 1552, 1476 (Ar C−C), 1338 (NO_2), 1176 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (d, 2H, J = 9.0 Hz), 7.89 (d, 1H, J = 14.9 Hz), 7.50 (d, 2H, J = 9.0 Hz), 7.24−7.44 (m, 5H), 7.45 (dd, 1H, J = 14.9, 10.7 Hz), 6.98 (dd, 1H, J = 16.4, 10.7 Hz), 6.73 (d, 1H, J = 16.4 Hz), 5.92 (s, 1H), 4.20 (q, 2H, J = 7.1 Hz), 1.30 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 164.8 (C), 149.3 (C), 146.8 (C), 143.1 (C), 139.6 (CH), 138.4 (CH), 136.4 (C), 130.7 (CH), 128.8 (CH), 128.7 (CH), 128.0 (CH), 127.1 (CH), 127.0 (CH), 124.4 (CH), 120.9 (CH), 60.6 (CH_2), 14.3 (CH_3); found (FTMS + pAPCI) $[M + H]^+$ 382.1108, $C_{21}H_{20}NO_4S$ requires 382.1108. *E,E,E* stereochemistry was confirmed by NOESY (δ 7.50 and 5.92):

DOI: 10.1021/jo502648w
J. Org. Chem. 2015, 80, 1703−1718



*Ethyl (E)-3-((4-Nitrophenyl)thio)-5,5-diphenylpenta-2,4-dienoate (**4q**).* General procedure D was followed to yield product **4q** as a yellow oil (29.3 mg, 0.07 mmol, 100%): purified by column chromatography (eluent hexane/ethyl acetate, 20:1 to 10:1); R_f 0.30 (10:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3056, 2980 (C−H), 1703 (C═O), 1596 (C═C, diene conj), 1516 (NO_2), 1493, 1476, 1443 (Ar C−C), 1339 (NO_2), 1183 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (d, 2H, J = 8.9 Hz), 7.27−7.41 (m, 8H), 7.20−7.23 (m, 2H), 7.19 (d, 1H, J = 1.7 Hz), 7.13−7.17 (m, 2H), 5.68 (d, 1H, J = 1.7 Hz), 4.14 (q, 2H, J = 7.1 Hz), 1.23 (t, 3H, J = 7.1 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 164.6 (C), 153.7 (C), 148.5 (C), 147.4 (C), 141.5 (C), 141.0 (C), 139.2 (C), 133.5 (CH), 130.4 (CH), 128.55 (CH), 128.51 (CH), 128.3 (CH), 128.2 (CH), 127.9 (CH), 124.1 (CH), 123.2 (CH), 118.4 (CH), 60.3 (CH_2), 14.3 (CH_3); found (FTMS + pAPCI) $[M + H]^+$ 432.1262, $C_{25}H_{22}NO_4S$ requires 432.1264.

*(E)-(4-Nitrophenyl)(4-phenylbuta-1,3-dien-2-yl)sulfane (**4r**).* General procedure D was followed with the following modification. The reaction was placed in a microwave at 90 °C for 60 min to yield product **4r** as the major product and the formal S_N2 product (**6r**) as a side product in a 5:1 ratio (14.3 mg, 0.05 mmol, 72%): purified by column chromatography (eluent hexane/ethyl acetate, 10:1); **4r** and **6r** inseparable by chromatography, with only the major **4r** being characterized; R_f 0.71 (5:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3026 (C−H), 1594 (C═C, diene conj), 1509 (NO_2), 1576, 1476, 1448 (Ar C−C), 1335 (NO_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (d, 2H, J = 9.1 Hz), 7.25−7.43 (m, 7H), 6.96 (d, 1H, J = 15.6 Hz), 6.89 (d, 1H, J = 15.6 Hz), 6.00 (s, 1H), 5.85 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 146.2 (C), 137.5 (C), 135.9 (C), 134.2 (CH), 128.7 (CH), 128.8 (CH), 127.9 (CH_2), 127.8 (C), 127.1 (CH), 126.9 (CH), 126.6 (CH), 124.0 (CH); found (FTMS + pAPCI) $[M + H]^+$ 284.0737, $C_{16}H_{14}NO_2S$ requires 284.0740.

*(E)-(4-(4-Chlorophenyl)buta-1,3-dien-2-yl)(4-nitrophenyl)sulfane (**4s**).* General procedure D was followed with the following modification. The reaction was placed in a microwave at 90 °C for 60 min to yield product **4s** (20.3 mg, 0.06 mmol, 91%): purified by column chromatography (eluent hexane/ethyl acetate, 10:1); note that the product is very unstable and decomposes at room temperature in <1 h; R_f 0.59 (5:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3096, 2921 (C−H), 1594 (C═C, diene conj), 1511 (NO_2), 1576, 1489, 1476, 1404 (Ar C−C), 1336 (NO_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, 2H, J = 9.1 Hz), 7.37 (d, 2H, J = 9.1 Hz), 7.28 (m, 4H), 6.91 (d, 1H, J = 16.0 Hz), 6.85 (d, 1H, J = 16.0 Hz), 6.01 (s, 1H), 5.86 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.9 (C), 137.4 (C), 134.5 (C), 134.2 (C), 132.5 (CH), 129.1 (C), 132.5 (CH), 128.9 (CH), 128.2 (CH_2), 128.1 (CH), 127.2 (CH), 124.0 (CH); found (FTMS + pAPCI) $[M + H]^+$ 318.0344, $C_{16}H_{13}NO_2SCl$ requires 318.0350.

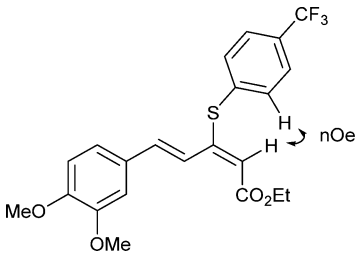
*((1E,3E)-1-(4-Methoxyphenyl)hepta-1,3-dien-3-yl)(4-nitrophenyl)-sulfane (**4t**).* In a sealed tube were placed $InCl_3$ (1.0 mg, 5 mol %) and 4-nitrothiophenol (10.9 mg, 0.07 mmol, 1.0 equiv), which were then dissolved in $CDCl_3$ (0.35 mL). A solution of allenol **3t** (22.8 mg, 0.105 mmol, 1.5 equiv) in $CDCl_3$ (0.15 mL) was added to the sealed tube and washed in with $CDCl_3$ (0.20 mL). The sealed tube was then placed in a silicon oil bath at 90 °C and allowed to stir for 16 h (the microwave does not heat continuously beyond 60 min, so for extended reaction times, conventional heating was used) to yield product **4t** as a yellow oil (21.8 mg, 0.06 mmol, 88%) with a 2:1 mixture of *EE*/*EZ* isomers: purified by column chromatography (hexane/ethyl acetate, 20:1); note that, under standard microwave conditions (90 °C, 60 min), the yield was 69%; R_f 0.51 (5:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 2958, 2930, 2870, 2835 (C−H), 1604 (C═C, diene conj), 1576 (C═C, diene conj), 1508 (NO_2), 1476, 1462, 1420 (Ar C−C), 1333 (NO_2), 1246 (C−O−C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, 2H′, J = 8.9 Hz, minor), 8.06 (d, 2H, J = 9.1 Hz, major), 7.27−7.36 (m, 4H + 4H′), 7.04 (dd, 1H, J = 15.5, 0.8 Hz), 6.89 (d, 1H, J = 15.5 Hz), 6.80−6.85 (m, 2H + 2H′), 6.50 (t, 1H′, J = 7.5 Hz), 6.36 (t, 1H, J = 7.7 Hz), 3.80 (s, 3H), 3.79 (s, 3H′), 2.40−5.51 (m, 2H + 2H′), 1.58 (sext, 2H, J = 7.4 Hz), 1.47 (sext, 2H′, J = 7.4 Hz), 1.07 (t, 3H, J = 7.4 Hz), 0.93 (t, 3H′, J = 7.4 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 159.8 (C, major), 159.5 (C, minor), 148.4 (C, major), 147.2 (C, minor), 145.5 (CH, major), 145.3 (CH, minor), 145.0 (C, major + minor), 133.2 (CH, major), 130.6 (CH, minor), 129.44 (C, major + minor), 129.37 (C, minor), 129.3 (C, major), 128.2 (CH, minor), 127.9 (CH, major), 125.9 (CH, minor), 125.8 (CH, major), 124.4 (CH, minor), 124.2 (CH, major), 119.9 (CH, major + minor), 114.2 (CH, major), 114.1 (CH, minor), 55.33 (CH_3, major), 55.31 (CH_3, minor), 32.7 (CH_2, minor), 31.6 (CH_2, major), 22.5 (CH_2, major), 22.4 (CH_2, minor), 13.89 (CH_3, major), 13.87 (CH_3, minor); found (FTMS + pAPCI) $[M + H]^+$ 356.1316, $C_{20}H_{22}NO_3S$ requires 356.1315.

*((1E,3E)-1-(4-Bromophenyl)hepta-1,3-dien-3-yl)(4-nitrophenyl)-sulfane (**4u**).* In a sealed tube were placed $InCl_3$ (1.0 mg, 5 mol %) and 4-nitrothiophenol (10.9 mg, 0.07 mmol, 1.0 equiv), which were then dissolved in $CDCl_3$ (0.35 mL). A solution of allenol **3u** (22.8 mg, 0.105 mmol, 1.5 equiv) in $CDCl_3$ (0.15 mL) was added to the sealed tube and washed in with $CDCl_3$ (0.20 mL). The sealed tube was then placed in a silicon oil bath at 90 °C and allowed to stir for 16 h (the microwave does not heat continuously beyond 60 min, so for extended reaction times, conventional heating was used) to yield product **4u** as a yellow oil (21.9 mg, 0.05 mmol, 77%) with a 2:1 mixture of *EE*/*EZ* isomers: purified by column chromatography (hexane/ethyl acetate, 50:1 to 25:1); R_f 0.62 (5:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 2958, 2928, 2873 (C−H), 1576 (C═C, diene conj), 1509 (NO_2), 1485, 1399 (Ar C−C), 1335 (NO_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, 2H′, J = 9.1 Hz, minor), 8.06 (d, 2H, J = 9.1 Hz, major), 7.42 (d, 2H, J = 8.4 Hz), 7.40 (d, 2H′, J = 8.4 Hz), 7.28 (d, 2H, J = 9.1 Hz), 7.27 (d, 2H′, J = 9.1 Hz), 7.23 (d, 2H, J = 8.4 Hz), 7.21 (d, 2H′, J = 8.4 Hz), 7.16 (dd, 1H, J = 15.5, 0.9 Hz), 6.91 (d, 1H′, J = 15.5 Hz), 6.88 (d, 1H, J = 15.5 Hz), 6.78 (d, 1H′, J = 15.5 Hz), 6.58 (t, 1H′, J = 7.5 Hz), 6.45 (t, 1H, J = 7.7 Hz), 2.41−2.51 (m, 2H + 2H′), 1.54−1.64 (m, 2H), 1.48 (sext, 2H′, J = 7.4 Hz), 1.03 (t, 3H, J = 7.3 Hz), 0.93 (t, 3H′, J = 7.4 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 147.9 (C, major), 147.5 (CH, major), 147.4 (CH, minor), 146.7 (C, minor), 145.1 (C, major + minor), 137.8 (CH, minor), 135.55 (C, minor), 135.51 (C, major) 133.4 (CH, major), 131.81 (CH, major), 131.76 (CH, minor), 129.8 (CH, minor), 129.4 (CH, major), 128.5 (C, minor), 128.3 (CH, major), 128.1 (CH, minor), 127.6 (C, major), 125.88 (CH, minor), 125.85 (CH, major), 124.1 (CH, minor), 124.0 (CH, major), 122.1 (C, major), 121.7 (C, minor), 32.8 (CH_2, minor), 31.5 (CH_2, major), 22.4 (CH_2, major), 22.3 (CH_2, minor), 13.9 (2 × CH_3); found (FTMS + pAPCI) $[M + H]^+$ 404.0308, $C_{19}H_{19}NO_2SBr$ requires 404.0314.

*(E)-(1,1-Diphenylhepta-1,3-dien-3-yl)(4-nitrophenyl)sulfane (**4v**).* General procedure D was followed with the following modification. The reaction was placed in a microwave at 90 °C for 60 min to yield product **4v** as a yellow oil with *E*:*Z* = 1:1 (14.9 mg, 0.04 mmol, 59%): purified by column chromatography (eluent hexane/ethyl acetate, 80:1 to 70:1 to 25:1); R_f 0.51 (5:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3056, 2958, 2928, 2870 (C−H), 1593 (C═C, diene conj), 1508 (NO_2), 1575, 1476, 1443 (Ar C−C), 1333 (NO_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04−8.11 (m, 2H + 2H′), 7.13−7.36 (m, 10H + 10H′), 7.03−7.11 (m, 1H + 1H′), 7.02−7.05 (m, 1H + 1H′), 7.60 (app q, 1H′, J = 1.3 Hz), 6.53 (app q, 1H, J = 1.1 Hz), 6.16 (td, 1H, J = 7.4, 1.1 Hz), 6.11 (td, 1H′, J = 7.5, 1.4 Hz), 2.24−2.18 (m, 2H), 2.20−2.14 (m, 2H′), 1.40 (sext, 2H′, J = 7.5 Hz), 1.26 (sext, 2H, J = 7.4 Hz), 0.94 (t, 3H, J = 7.4 Hz), 0.78 (t, 3H′, J = 7.5 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 147.6 (C), 146.8 (C), 146.3 (C), 145.3 (C), 145.2 (C), 143.7 (C), 142.4 (C), 142.3 (C), 139.78 (C), 139.77 (C), 130.0 (CH), 129.97 (CH), 128.4 (CH), 128.19 (2 × CH), 128.16 (CH), 128.08 (CH), 128.05 (CH), 127.92 (CH), 127.88 (CH), 127.78 (CH), 127.56 (CH), 127.52 (CH), 127.5 (CH), 127.30 (2 × C), 127.28 (CH), 127.1 (CH), 124.3 (CH), 123.77 (CH), 123.67 (CH), 122.9 (CH), 32.7 (CH_2), 32.5 (CH_2), 22.0 (CH_2), 21.97 (CH_2), 13.93 (CH_3), 13.70 (CH_3); found (FTMS + pAPCI) $[M + H]^+$ 402.1518, $C_{25}H_{24}NO_2S$ requires 402.1522.

DOI: 10.1021/jo502648w
J. Org. Chem. 2015, 80, 1703−1718

*(2E,4E)-Ethyl 5-(3,4-Dimethoxyphenyl)-3-((4-(trifluoromethyl)-phenyl)thio)penta-2,4-dienoate (**4ba**).* General procedure D was followed to yield product **4ba** as a yellow solid (23.9 mg, 0.05 mmol, 74%): purified by column chromatography (eluent hexane/ethyl acetate, 5:1); R_f 0.36 (5:1 hexane/ethyl acetate); mp 77−78 °C; ν_{max}/cm^{-1} 2936 (C−H), 1699 (C═O), 1599 (C═C, diene conj), 1580 (C═C, diene conj), 1557, 1511, 1464 (Ar C−C), 1321 (C−F), 1160 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23 (dd, 1H, J = 14.9, 0.4 Hz), 7.56−7.64 (m, 4H), 7.33 (d, 1H, J = 14.9 Hz), 7.06−7.12 (m, 2H), 6.84 (d, 1H, J = 8.2 Hz), 5.60 (app s, 1H), 4.16 (q, 2H, J = 7.1 Hz), 3.93 (s, 3H), 3.90 (s, 3H), 1.28 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 165.2 (C), 152.7 (C), 150.4 (C), 149.2 (C), 137.6 (CH), 135.0 (C), 133.1 (CH), 130.6 (C, q, J = 32.8 Hz), 129.0 (C), 127.6 (C, q, J = 272.1 Hz), 126.4 (CH, q, J = 3.7 Hz), 121.8 (CH), 121.7 (CH), 116.5 (CH), 111.1 (CH), 109.7 (CH), 60.2 (CH_2), 55.96 (CH_3), 55.93 (CH_3), 14.3 (CH_3); found (FTMS + pNSI) $[M + H]^+$ 439.1177, $C_{22}H_{22}O_4SF_3$ requires 439.1185. *E,E* stereochemistry was confirmed by NOESY (δ 7.56−7.64 and 5.60):



*(2E,4E)-Ethyl 5-(3,4-Dimethoxyphenyl)-3-((4-fluorophenyl)thio)-penta-2,4-dienoate (**4bb**).* General procedure D was followed to yield product **4bb** as a yellow solid (17.6 mg, 0.05 mmol, 65%): purified by column chromatography (eluent hexane/ethyl acetate, 5:1); R_f 0.29 (5:1 hexane/ethyl acetate); mp 113−115 °C; ν_{max}/cm^{-1} 2935 (C−H), 1697 (C═O), 1598 (C═C, diene conj), 1555, 1511 (Ar C−C), 1489 (C−F), 1177 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22 (dd, 1H, J = 16.1, 0.8 Hz), 7.50−7.55 (m, 2H), 7.34 (d, 1H, J = 16.1 Hz), 7.08−7.17 (m, 4H), 6.86 (d, 1H, J = 8.3 Hz), 5.21 (app s, 1H), 4.12 (q, 2H, J = 7.1 Hz), 3.94 (s, 3H), 3.91 (s, 3H), 1.24 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$), δ 165.3 (C), 162.0 (C, d, J 251 Hz), 155.9 (C), 150.2 (C), 149.2 (C), 137.6 (CH, d, J = 8.5 Hz), 136.1 (CH), 129.2 (C), 125.3 (C, d, J = 3.5 Hz), 121.9 (CH), 121.3 (CH), 117.3 (CH, d, J = 22.0 Hz), 112.3 (CH), 111.1 (CH), 109.7 (CH), 59.9 (CH_2), 55.95 (CH_3), 55.94 (CH_3), 14.3 (CH_3); found (FTMS + pAPCI) $[M + H]^+$ 389.1209, $C_{21}H_{22}FO_4S$ requires 389.1217.

*(2E,4E)-Ethyl 5-(3,4-Dimethoxyphenyl)-3-((4-hydroxyphenyl)-thio)penta-2,4-dienoate (**4bc**).* General procedure D was followed with the following modification. The reaction was placed in a microwave at 90 °C for 60 min to yield product **4bc** as a yellow oil (4.4 mg, 0.01 mmol, 29%): purified by column chromatography (eluent hexane/ethyl acetate, 5:1 to 3:1); note that the product is unstable and begins to decompose on the column; R_f 0.14 (3:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3412 (O−H), 2935 (C−H), 1665 (C═O), 1581 (C═C, diene conj), 1556, 1512 (Ar C−C), 1167 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$), δ 8.21 (d, 1H, J = 16.1 Hz), 7.39−7.41 (m, 3H), 7.06−7.16 (m, 2H), 6.91 (d, 2H, J = 8.6 Hz), 6.85 (d, 1H, J = 8.2 Hz), 5.17 (s, 1H), 4.12 (q, 2H, J = 7.1 Hz), 3.93 (s, 3H), 3.91 (s, 3H), 1.24 (t, 3H, J = 7.1 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 165.7 (C), 157.4 (C), 157.3 (C), 156.1 (C), 150.1 (C), 149.2 (C), 137.7 (CH), 135.6 (CH), 132.9 (CH), 129.3 (C), 121.6 (CH), 117.0 (CH), 116.1 (CH), 111.2 (CH), 109.7 (CH), 59.9 (CH_2), 55.97 (CH_3), 55.94 (CH_3), 14.4 (CH_3); found (FTMS + pNSI) $[M + H]^+$ 387.1261, $C_{21}H_{23}O_5S$ requires 387.1261.

*(2E,4E)-Ethyl 5-(3,4-Dimethoxyphenyl)-3-(phenylthio)penta-2,4-dienoate (**4be**).* General procedure D was followed to yield product **4be** as a yellow solid (19 mg, 0.05 mmol, 73%): purified by column chromatography (eluent hexane/ethyl acetate, 5:1); R_f 0.25 (5:1 hexane/ethyl acetate); mp 102−103 °C; ν_{max}/cm^{-1} 3058 (C−H_{Ar}) 2934 (C−H alkyl), 1695 (C═O), 1615 (C═C, diene conj), 1597 (C═C, diene conj), 1580, 1556, 1511 (Ar C−C), 1175 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$), δ 8.25 (dd, 1H, J = 16.0, 0.9 Hz), 7.49−7.56 (m, 2H), 7.40−7.46 (m, 3H), 7.34 (d, 1H, J = 16.0 Hz), 7.10−7.16 (m, 2H), 6.85 (d, 1H, J = 1.7 Hz), 5.31 (app s, 1H), 4.11 (q, 2H, J = 7.1 Hz), 3.93 (s, 3H), 3.91 (s, 3H), 1.23 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$), δ 165.5 (C), 155.7 (C), 150.1 (C), 149.1 (C), 136.1 (CH), 135.1 (CH), 129.8 (CH), 129.7 (C), 129.4 (CH), 129.3 (C), 122.1 (CH), 121.6 (CH), 112.8 (CH), 111.1 (CH), 109.7 (CH), 59.9 (CH_2), 55.95 (CH_3), 55.94 (CH_3), 14.3 (CH_3); found (FTMS + pNSI) $[M + H]^+$ 371.1310, $C_{21}H_{23}O_4S$ requires 371.1312.

*(2E,4E)-Ethyl 5-(3,4-Dimethoxyphenyl)-3-(p-tolylthio)penta-2,4-dienoate (**4bf**).* General procedure D was followed to yield product **4bf** as a yellow solid (20.1 mg, 0.05 mmol, 72%): purified by column chromatography (eluent hexane/ethyl acetate, 5:1); R_f 0.31 (5:1 hexane/ethyl acetate); mp 109−112 °C; ν_{max}/cm^{-1} 2934 (C−H), 1697 (C═O), 1615 (C═C, diene conj), 1597 (C═C, diene conj), 1581, 1556, 1511 (Ar C−C), 1176 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$), δ 8.23 (dd, 1H, J = 16.1, 0.7 Hz), 7.41 (m, 3H), 7.23 (m, 2H), 7.12 (m, 2H), 6.85 (d, 1H, J = 8.3 Hz), 5.25 (app s, 1H), 4.13 (q, 2H, J = 7.1 Hz), 3.93 (s, 3H), 3.91 (s, 3H), 2.40 (s, 3H), 1.24 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$), δ 165.5 (C), 156.5 (C), 150.1 (C), 149.1 (C), 139.9 (C), 135.8 (CH), 135.4 (CH), 130.6 (CH), 129.3 (C), 126.3 (C), 122.2 (CH), 121.5 (CH), 111.9 (CH), 111.1 (CH), 109.7 (CH), 59.8 (CH_2), 55.95 (CH_3), 55.94 (CH_3), 21.4 (CH_3), 14.4 (CH_3); found (FTMS + pNSI) $[M + H]^+$ 385.1470, $C_{22}H_{24}O_4S$ requires 385.1468.

*(2E,4E)-Ethyl 5-(3,4-Dimethoxyphenyl)-3-(m-tolylthio)penta-2,4-dienoate (**4bg**).* General procedure D was followed to yield product **4bg** as a yellow solid (14.7 mg, 0.04 mmol, 54%): purified by column chromatography (eluent hexane/ethyl acetate, 5:1); R_f 0.28 (5:1 hexane/ethyl acetate); mp 69−70 °C; ν_{max}/cm^{-1} 2932 (C−H), 1697 (C═O), 1615 (C═C, diene conj), 1580, 1555, 1511 (Ar C−C), 1159 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$), δ 8.23 (dd, 1H, J = 16.1, 0.8 Hz), 7.29−7.39 (m, 4H), 7.19−7.25 (m, 1H), 7.07−7.16 (m, 2H), 6.85 (d, 1H, J = 8.2 Hz), 5.31 (app s, 1H), 4.12 (q, 2H, J = 7.1 Hz), 3.94 (s, 3H), 3.91 (s, 3H), 2.38 (s, 3H), 1.24 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$), δ 165.5 (C), 156.0 (C), 150.1 (C), 149.2 (C), 139.7 (C), 136.0 (CH), 135.7 (CH), 132.2 (CH), 130.3 (CH), 129.8 (C), 129.6 (CH), 129.3 (C), 122.2 (CH), 121.6 (CH), 112.6 (CH), 111.1 (CH), 109.7 (CH), 59.9 (CH_2), 55.9 (2 × CH_3), 21.3 (CH_3), 14.4 (CH_3); found (FTMS + pNSI) $[M + H]^+$ 385.1470, $C_{22}H_{24}O_4S$ requires 385.1468.

*(2E,4E)-Ethyl 5-(3,4-Dimethoxyphenyl)-3-(o-tolylthio)penta-2,4-dienoate (**4bh**).* General procedure D was followed to yield product **4bh** as a yellow solid (20.4 mg, 0.05 mmol, 75%): purified by column chromatography (eluent hexane/ethyl acetate, 5:1); R_f 0.36 (5:1 hexane/ethyl acetate); mp 78−82 °C; ν_{max}/cm^{-1} 2934 (C−H), 1697 (C═O), 1615 (C═C, diene conj), 1597 (C═C, diene conj), 1581, 1556, 1511 (Ar C−C), 1160 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$), δ 8.26 (dd, 1H, J = 16.1, 0.8 Hz), 7.53 (d, 1H, J = 7.2 Hz), 7.34−7.41 (m, 3H), 7.25−7.29 (m, 1H), 7.10−7.17 (m, 2H), 6.86 (d, 1H, J = 8.3 Hz), 5.05 (app s, 1H), 4.11 (q, 2H, J = 7.1 Hz), 3.94 (s, 3H), 3.91 (s, 3H), 2.44 (s, 3H), 1.23 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$), δ 165.5 (C), 155.0 (C), 150.1 (C), 149.2 (C), 143.0 (C), 136.8 (CH), 135.8 (CH), 131.2 (CH), 130.3 (CH), 129.3 (C), 128.9 (C), 127.3 (CH), 122.2 (CH), 121.5 (CH), 111.1 (CH), 110.9 (CH), 109.7 (CH), 59.8 (CH_2), 56.0 (CH_3), 20.5 (CH_3), 14.4 (CH_3); found (FTMS + pNSI) $[M + H]^+$ 385.1470, $C_{22}H_{24}O_4S$ requires 385.1468.

*(2E,4E)-Ethyl 5-(3,4-Dimethoxyphenyl)-3-((4-methoxyphenyl)-thio)penta-2,4-dienoate (**4bi**).* General procedure D was followed to yield product **4bi** as a yellow solid (14.5 mg, 0.04 mmol, 52%): purified by column chromatography (eluent hexane/ethyl acetate, 5:1); R_f 0.20 (5:1 hexane/ethyl acetate); mp 127−130 °C; ν_{max}/cm^{-1} 2935 (C−H), 1695 (C═O), 1615 (C═C, diene conj), 1590, 1556, 1511 (Ar C−C), 1174 (C−O−C); ^{1}H NMR (300 MHz, $CDCl_3$), δ 8.22 (dd, 1H, J = 16.2, 0.9 Hz), 7.46 (d, 2H, J = 8.9 Hz), 7.36 (d, 1H, J = 16.2 Hz), 7.15−7.10 (m, 2H), 6.97 (d, 2H, J = 8.9 Hz), 6.85 (d, 1H, J = 9.1 Hz), 5.17 (app s, 1H), 4.11 (q, 2H, J = 7.1 Hz), 3.94 (s, 3H), 3.91 (s, 3H), 3.86 (s, 3H), 1.24 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$), δ 165.6 (C), 161.0 (C), 157.3 (C), 150.2 (C), 149.1 (C), 137.4 (CH), 135.5 (CH), 129.3 (C), 122.1 (CH), 121.4 (CH), 120.0 (C), 115.5 (CH), 111.3 (CH), 111.1 (CH), 109.8 (CH),

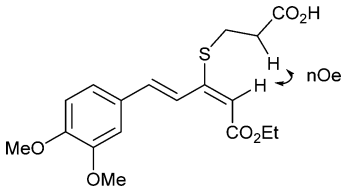
DOI: 10.1021/jo502648w
J. Org. Chem. 2015, 80, 1703−1718

59.9 (CH_2), 56.1 (2 × CH_3), 55.3 (CH_3), 14.3 (CH_3); found (FTMS + pNSI) $[M + H]^+$ 401.1417, $C_{22}H_{25}O_5S$ requires 401.1417.

*(2E,4E)-Ethyl 3-(Benzylthio)-5-((3,4-dimethoxy)phenyl)penta-2,4-dienoate (**4bj**).* General procedure D was followed to yield product **4bj** as a yellow solid (13.1 mg, 0.03 mmol, 49%): purified by column chromatography (eluent hexane/ethyl acetate, 5:1); R_f 0.29 (5:1 hexane/ethyl acetate); mp 99−102 °C; ν_{max}/cm^{-1} 2934 (C−H), 1697 (C═O), 1616 (C═C, diene conj), 1597 (C═C, diene conj), 1581, 1553, 1511 (Ar C−C), 1177 (C−O−C); ^1H NMR (300 MHz, $CDCl_3$), δ 8.19 (dd, 1H, J = 16.2, 0.9 Hz), 7.28−7.41 (m, 5H), 7.21 (d, 1H, J = 16.2 Hz), 7.05−7.10 (m, 2H), 6.83 (d, 1H, J = 8.3 Hz), 5.69 (app s, 1H), 4.19 (q, 2H, J = 7.1 Hz), 4.09 (s, 2H), 3.92 (s, 3H), 3.90 (s, 3H), 1.31 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$), δ 165.2 (C), 155.1 (C), 150.1 (C), 149.1 (C), 135.9 (C), 135.2 (CH), 129.3 (C), 129.1 (CH), 128.8 (CH), 127.7 (CH), 122.3 (CH), 121.5 (CH), 111.1 (CH), 110.4 (CH), 109.7 (CH), 59.9 (CH_2), 55.94 (CH_3), 55.91 (CH_3), 36.8 (CH_2), 14.4 (CH_3); found (FTMS + pNSI) $[M + H]^+$ 385.1469, $C_{22}H_{25}O_4S$ requires 385.1468.

*(2E,4E)-Ethyl 5-(3,4-Dimethoxyphenyl)-3-((furan-2-ylmethyl)thio)penta-2,4-dienoate (**4bk**).* General procedure D was followed to yield product **4bk** as a yellow oil (13.5 mg, 0.04 mmol, 52%): purified by column chromatography (eluent hexane/ethyl acetate, 5:1); R_f 0.27 (5:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 2935 (C−H), 1697 (C═O), 1581 (C═C, diene conj), 1555, 1511 (Ar C−C), 1177 (C−O−C); ^1H NMR (300 MHz, $CDCl_3$), δ 8.18 (1H, dd, J = 16.2, 0.7 Hz, CH═C*H*CS), 7.38 (dd, 1H, J = 1.8, 0.8 Hz), 7.21 (d, 1H, J = 16.2 Hz), 7.04−7.12 (m, 2H), 6.84 (d, 1H, J = 8.3 Hz), 6.27−6.35 (m, 2H), 5.73 (app s, 1H), 4.20 (q, 2H, J = 7.1 Hz), 4.11 (s, 2H), 3.92 (s, 3H), 3.90 (s, 3H), 1.31 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$), δ 165.2 (C), 154.0 (C), 150.1 (C), 149.1 (C), 149.0 (C), 142.6 (CH), 136.3 (CH), 129.2 (C), 122.3 (CH), 121.5 (CH), 111.3 (CH), 111.1 (CH), 110.7 (CH), 109.7 (CH), 108.6 (CH), 60.1 (CH_2), 55.94 (CH_3), 55.91 (CH_3), 29.2 (CH_2), 14.4 (CH_3); found (FTMS + pAPCI) $[M + H]^+$ 375.1285, $C_{20}H_{23}O_5S$ requires 375.1261.

*(2E,4E)-Ethyl 5-(3,4-Dimethoxyphenyl)-3-((3-ethoxy-3-oxopropyl)thio)penta-2,4-dienoate (**4bl**).* General procedure D was followed to yield product **4al** as a yellow oil (11.2 mg, 0.03 mmol, 40%): purified by column chromatography (eluent ether); R_f 0.18 (1:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 2934 br (O−H), 1700 (C═O), 1616 (C═C, diene conj), 1581 (C═C, diene conj), 1553, 1511 (Ar C−C), 1178 (C−O−C); ^1H NMR (300 MHz, $CDCl_3$), δ 8.19 (dd, 1H, J = 16.2, 0.7 Hz), 7.20 (d, 1H, J = 16.2 Hz), 7.04−7.13 (m, 2H), 6.84 (d, 1H, J = 8.3 Hz), 5.65 (app s, 1H), 4.20 (q, 2H, J = 7.1 Hz), 3.92 (s, 3H), 3.90 (s, 3H), 3.14 (t, 2H, J = 7.1 Hz), 2.79 (t, 2H, J = 7.1 Hz), 1.32 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$), δ 176.1 (C), 165.2 (C), 153.6 (C), 150.2 (C), 149.1 (C), 136.4 (CH), 129.2 (C), 122.3 (CH), 121.6 (CH), 111.1 (CH), 110.8 (CH), 109.7 (CH), 60.0 (CH_2), 55.95 (CH_3), 55.92 (CH_3), 32.7 (CH_2), 26.2 (CH_2), 14.4 (CH_3); found (FTMS + pNSI) $[M + H]^+$ 365.1057, $C_{18}H_{21}O_6S$ requires 365.1064. *E*,*E* stereochemistry was confirmed by NOESY (δ 5.65 and 3.14):



*(2E,4E)-Ethyl 3-(Cyclohexylthio)-5-(3,4-dimethoxyphenyl)penta-2,4-dienoate (**4bm**).* General procedure D was followed to yield product **4bm** as a yellow oil (12 mg, 0.03 mmol, 45%): purified by column chromatography (eluent hexane/ethyl acetate, 7:1); R_f 0.4 (5:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 2929 (C−H), 1797 (C═O), 1616 (C═C, diene conj), 1597 (C═C, diene conj), 1580, 1550, 1511 (Ar C−C), 1178 (C−O−C); ^1H NMR (300 MHz, $CDCl_3$), δ 8.19 (dd, 1H, J = 16.1, 0.8 Hz), 7.25 (d, 1H, J = 16.1 Hz), 7.05−7.13 (m, 2H), 6.84 (d, 1H, J = 8.3 Hz), 5.71 (app s, 1H), 4.19 (q, 2H, J = 7.1 Hz), 3.92 (s, 3H), 3.90 (s, 3H), 3.14−3.25 (m, 1H), 2.02−2.14 (m, 2H), 1.76−1.86 (m, 2H), 1.60−1.70 (m, 1H), 1.37−1.54 (m, 5H), 1.26−1.36 (m, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$), δ 165.5 (C), 154.0 (C), 150.0 (C), 149.1 (C), 136.1 (CH), 129.5 (C), 123.1 (CH), 121.4 (CH), 111.4 (CH), 111.1 (CH), 109.7 (CH), 59.9 (CH_2), 55.94 (CH_3), 55.91 (CH_3), 44.0 (CH), 32.7 (CH_2), 26.0 (CH_2) 25.9 (CH_2), 14.5 (CH_3); found (FTMS + pAPCI) $[M + H]^+$ 377.1774, $C_{21}H_{29}O_4S$ requires 377.1781.

*Ethyl 5-(Benzoylthio)-5-(2,4-dimethoxyphenyl)penta-2,3-dienoate (**6bn**).* General procedure D was followed to yield product **6bn** as a yellow oil and as a mixture of diastereomers in a 1:2 ratio (18 mg, 0.05 mmol, 66%): purified by column chromatography (eluent hexane/ethyl acetate, 5:1); R_f 0.19 (5:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3061 (C−H), 2979 (C−H), 1963 (C═C, allene), 1712 (C═O), 1661 (C═O), 1591, 1580, 1513, (Ar C−C), 1215 (C−O−C); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.84−7.90 (m, 2H + 2H′), 7.45−7.53 (m, 1H + 1H′), 7.33−7.41 (m, 2H + 2H′), 6.86−6.90 (m, 2H + 2H′), 6.72−6.79 (m, 1H + 1H′), 5.99−6.07 (m, 1H + 1H′), 5.68 (dd, 1H′, J = 5.1, 3.0 Hz, minor), 5.62 (dd, 1H, J = 6.0, 3.1 Hz, major), 5.43−5.49 (m, 1H + 1H′), 4.03−4.13 (m, 2H + 2H′), 3.84 (s, 3H′, minor), 3.81 (s, 3H, major), 3.78 (s, 3H + 3H′), 1.14−1.23 (m, 3H + 3H′); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 213.0 (C, major), 212.6 (C, minor), 190.3 (C, major), 190.1 (C, minor), 165.3 (C, minor), 165.2 (C, major), 149.1 (C, minor), 148.9 (C, major), 148.8 (C, major + minor), 136.5 (C, major + minor), 133.7 (CH, major + minor), 131.1 (C, minor), 130.7 (C, major), 128.7 (CH, major + minor), 127.3 (CH, major + minor), 120.5 (CH, minor), 120.4 (CH, major), 111.5 (CH, minor), 111.3 (CH, major), 111.1 (CH, minor), 110.9 (CH, major), 98.1 (CH, major + minor), 91.7 (CH, minor), 91.4 (CH, major), 61.0 (CH_2, major + minor), 56.0 (CH_3, minor), 55.9 (CH_3, minor), 55.89 (CH_3, major), 55.87 (CH_3, major), 45.8 (CH, major), 45.2 (CH, minor), 14.2 (CH_3, major + minor); found (FTMS + pNSI) $[M + H]^+$ 399.1255, $C_{22}H_{23}O_5S$ requires 399.1261.

*Ethyl 5-(Acetylthio)-5-(3,4-dimethoxyphenyl)penta-2,3-dienoate (**6bo**).* General procedure D was followed to yield product **6bo** as a yellow oil and as a mixture of diastereomers in a 1:0.6 ratio (10.5 mg, 0.03 mmol, 52%): purified by column chromatography (eluent hexane/ethyl acetate, 5:1); R_f 0.23 (5:1 hexane/ethyl acetate); ν_{max}/cm^{-1} 3061 (C−H), 2980 (C−H), 1963 (C═C, allene), 1692 (C═O), 1661 (C═O), 1590, 1513, (Ar C−C), 1215 (C−O−C); ^1H NMR (300 MHz, $CDCl_3$) δ 6.87−7.00 (m, 2H + 2H′), 6.75−6.83 (m, 1H + 1H′), 5.98 (m, 1H + 1H′), 5.75 (dd, 1H′, J = 6.1, 3.1 Hz, minor), 5.66 (dd, 1H, J = 6.1, 3.1 Hz, major), 5.27−5.34 (m, 1H + 1H′), 4.13−4.24 (m, 2H + 2H′), 3.89 (s, 3H′, minor), 3.86 (s, 6H + 3H′), 2.33 (s, 3H, major), 2.32 (s, 3H′, minor), 1.23−1.33 (m, 3H + 3H′); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 212.9 (C, major), 212.4 (C, minor), 194.1 (C, major), 193.8 (C, minor), 165.3 (C, minor), 165.2 (C, major), 149.0 (C, minor), 148.9 (C, major), 148.77 (C, minor), 148.76 (C, major), 131.2 (C, minor), 130.7 (C, major), 120.3 (CH, minor), 120.2 (CH, major), 111.3 (CH, minor), 111.2 (CH, major), 111.0 (CH, minor), 110.9 (CH, major), 98.02 (CH, major), 97.86 (CH, minor), 91.6 (CH, minor), 91.3 (CH, major), 61.0 (CH_2, major + minor), 56.0 (CH_3, minor), 55.9 (CH_3, minor), 55.88 (CH_3, major), 55.85 (CH_3, major), 45.7 (CH, major), 45.1 (CH, minor), 30.33 (CH_3, major), 30.28 (CH_3, minor), 14.2 (CH_3, major + minor); found (FTMS + pNSI) $[M + NH_4]^+$ 354.1369, $C_{17}H_{24}NO_5S$ requires 354.1370.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

General experimental information, NMR spectra, optimization studies, and X-ray data for compound **4a** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: A.Lee@hw.ac.uk. Phone: +44 (0)131-4518030.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the Engineering and Physical Sciences Research Council (EPSRC) (Grants EP/K00736X/1 for G.B. and DTA for P.C.Y.)

DOI: 10.1021/jo502648w
J. Org. Chem. 2015, 80, 1703−1718

and Heriot-Watt University (James Watt Scholarship, S.W.) for funding. We thank Dr. Dave Ellis for NMR experiments. Mass spectrometry data were acquired at the EPSRC UK National Mass Spectrometry Facility at Swansea University.

REFERENCES

(1) For selected reviews on gold catalysis, see: (a) Bandini, M. *Chem. Soc. Rev.* **2011**, *40*, 1358. (b) Bongers, N.; Krause, N. *Angew. Chem., Int. Ed.* **2008**, *47*, 2178. (c) Boorman, T. C.; Larrosa, I. *Chem. Soc. Rev.* **2011**, *40*, 1910. (d) Fürstner, A.; Davies, P. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 3410. (e) Gorin, D. J.; Sherry, B. D.; Toste, F. D. *Chem. Rev.* **2008**, *108*, 3351. (f) Gorin, D. J.; Toste, F. D. *Nature* **2007**, *446*, 395. (g) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180. (h) Hashmi, A. S. K.; Hutchings, G. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 7896. (i) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Commun.* **2007**, 333. (j) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326. (k) Li, Z. G.; Brouwer, C.; He, C. *Chem. Rev.* **2008**, *108*, 3239. (l) Marion, N.; Nolan, S. P. *Chem. Soc. Rev.* **2008**, *37*, 1776. (m) Muzart, J. *Tetrahedron* **2008**, *64*, 5815. (n) Rudolph, M.; Hashmi, A. S. K. *Chem. Soc. Rev.* **2012**, *41*, 2448. (o) Sengupta, S.; Shi, X. *ChemCatChem* **2010**, *2*, 609. (p) Shapiro, N. D.; Toste, F. D. *Synlett* **2010**, 675. (q) Shen, H. C. *Tetrahedron* **2008**, *64*, 3885. (r) Shen, H. C. *Tetrahedron* **2008**, *64*, 7847.

(2) (a) Corma, A.; Leyva-Pérez, A.; Sabater, M. J. *Chem. Rev.* **2011**, *111*, 1657. (b) Hashmi, A. S. K.; Buehrle, M. *Aldrichimica Acta* **2010**, *43*, 27.

(3) For reviews, see: (a) Biannic, B.; Aponick, A. *Eur. J. Org. Chem.* **2011**, 6605. (b) Bandini, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 994.

(4) For selected examples, see: (a) Aponick, A.; Biannic, B. *Org. Lett.* **2011**, *13*, 1330. (b) Aponick, A.; Biannic, B.; Jong, M. R. *Chem. Commun.* **2010**, *46*, 6849. (c) Aponick, A.; Li, C. Y.; Biannic, B. *Org. Lett.* **2008**, *10*, 669. (d) Bandini, M.; Monari, M.; Romaniello, A.; Tragni, M. *Chem.—Eur. J.* **2010**, *16*, 14272. (e) Biannic, B.; Ghebreghiorgis, T.; Aponick, A. *Beilstein J. Org. Chem.* **2011**, *7*, 802. (f) Cera, G.; Chiarucci, M.; Mazzanti, A.; Mancinelli, M.; Bandini, M. *Org. Lett.* **2012**, *14*, 1350. (g) Chiarucci, M.; Locritani, M.; Cera, G.; Bandini, M. *Beilstein J. Org. Chem.* **2011**, *7*, 1198. (h) Ghebreghiorgis, T.; Biannic, B.; Kirk, B. H.; Ess, D. H.; Aponick, A. *J. Am. Chem. Soc.* **2012**, *134*, 16307. (i) Kothandaraman, P.; Foo, S. J.; Chan, P. W. H. *J. Org. Chem.* **2009**, *74*, 5947. (j) Mukherjee, P.; Widenhoefer, R. A. *Org. Lett.* **2010**, *12*, 1184. (k) Mukherjee, P.; Widenhoefer, R. A. *Org. Lett.* **2011**, *13*, 1334. (l) Mukherjee, P.; Widenhoefer, R. A. *Angew. Chem., Int. Ed.* **2012**, *51*, 1405. (m) Unsworth, W. P.; Stevens, K.; Lamont, S. G.; Robertson, J. *Chem. Commun.* **2011**, *47*, 7659. (n) Mukherjee, P.; Widenhoefer, R. A. *Chem.—Eur. J.* **2013**, *19*, 3437.

(5) For selected examples, see: (a) Kanbayashi, N.; Onitsuka, K. *J. Am. Chem. Soc.* **2010**, *132*, 1206. (b) Lam, F. L.; Au-Yeung, T. T.-L.; Kwong, F. Y.; Zhou, Z.; Wong, K. Y.; Chan, A. S. C. *Angew. Chem., Int. Ed.* **2008**, *47*, 1280. (c) Liu, Z.; Du, H. *Org. Lett.* **2010**, *12*, 3054. (d) Lu, Z.; Ma, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 258. (e) Lyothier, I.; Defieber, C.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 6204. (f) Onitsuka, K.; Okuda, H.; Sasai, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 1454. (g) Roggen, M.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2011**, *50*, 5568. (h) Roggen, M.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2012**, *51*, 8652. (i) Ueno, S.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2008**, *47*, 1928.

(6) (a) Young, P. C.; Schopf, N. A.; Lee, A.-L. *Chem. Commun.* **2013**, *49*, 4262. (b) Wright, J. R.; Young, P. C.; Lucas, N. T.; Lee, A.-L.; Crowley, J. D. *Organometallics* **2013**, *32*, 7065. (c) Coutant, E.; Young, P. C.; Barker, G.; Lee, A.-L. *Beilstein J. Org. Chem.* **2013**, *9*, 1797.

(7) Herkert, L.; Green, S. L. J.; Barker, G.; Johnson, D. G.; Young, P. C.; Macgregor, S. A.; Lee, A.-L. *Chem.—Eur. J.* **2014**, *20*, 11540.

(8) (a) Bäckvall, J.-E.; Ericsson, A. *J. Org. Chem.* **1994**, *59*, 5850. (b) Heintzelman, G. R.; Meigh, I. R.; Mahajan, Y. R.; Weinreb, S. M. Diels-Alder Reactions of Imino Dienophiles. *Organic Reactions*; John Wiley & Sons, Inc.: Hoboken, NJ, 2005. (c) Proteau, P. J.; Hopkins, P. B. *J. Org. Chem.* **1985**, *50*, 141. (d) Chou, S. S. P.; Chen, K. W. *Synth. Commun.* **2004**, *34*, 4573. (e) Baeckvall, J. E.; Juntunen, S. K. *J. Am. Chem. Soc.* **1987**, *109*, 6396.

(9) Bandini, M.; Tragni, M. *Org. Biomol. Chem.* **2009**, *7*, 1501.

(10) Gold-catalyzed intermolecular hydrothiolation and hydroxythiolation of allenes, however, are known. For example, see: (a) Chan, A. O. Y.; Tsai, J. L. L.; Lo, V. K. Y.; Li, G. L.; Wong, M. K.; Che, C. M. *Chem. Commun.* **2013**, *49*, 1428. (b) Menggenbateer; Narsireddy, M.; Ferrara, G.; Nishina, N.; Jin, T.; Yamamoto, Y. *Tetrahedron Lett.* **2010**, *51*, 4627.

(11) For selected reviews on general allene chemistry, see: (a) *Modern Allene Chemistry*; Wiley-VCH: Weinheim, Germany, 2004. (b) Ma, S. *Chem. Rev.* **2005**, *105*, 2829.

(12) (a) Hashmi, A. S. K.; Schwarz, L.; Choi, J.-H.; Frost, T. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2285. (b) Hoffmann-Röder, A.; Krause, N. *Org. Lett.* **2001**, *3*, 2537. (c) Mundal, D. A.; Lutz, K. E.; Thomson, R. J. *J. Am. Chem. Soc.* **2012**, *134*, 5782. (d) Sun, T.; Deutsch, C.; Krause, N. *Org. Biomol. Chem.* **2012**, *10*, 5965.

(13) Sabbasani, V. R.; Mamidipalli, P.; Lu, H.; Xia, Y.; Lee, D. *Org. Lett.* **2013**, *15*, 1552.

(14) (a) Mudd, R. J.; Young, P. C.; Jordan-Hore, J. A.; Rosair, G. M.; Lee, A.-L. *J. Org. Chem.* **2012**, *77*, 7633. (b) Young, P. C.; Green, S. L. J.; Rosair, G. M.; Lee, A.-L. *Dalton Trans.* **2013**, *42*, 9645.

(15) For other examples using thiols as nucleophiles with gold catalysis, see refs 7 and 10. Also see: (a) Ando, K. *J. Org. Chem.* **2010**, *75*, 8516. (b) Arcadi, A.; Bianchi, G.; Di Giuseppe, S.; Marinelli, F. *Green Chem.* **2003**, *5*, 64. (c) Biswas, S.; Samec, J. S. M. *Chem. Commun.* **2012**, *48*, 6586. (d) Biswas, S.; Watile, R. A.; Samec, J. S. *Chemistry* **2014**, *20*, 2159. (e) Brouwer, C.; Rahatrian, R.; He, C. *Synlett* **2007**, 1785. (f) Corma, A.; Gonzalez-Arellano, C.; Iglesias, M.; Sanchez, F. *Appl. Catal., A* **2010**, *375*, 49. (g) Morita, N.; Krause, N. *Angew. Chem., Int. Ed.* **2006**, *45*, 1897.

(16) For examples of other low-valent sulfur compounds (thioethers) employed as nucleophiles in gold catalysis, see: (a) Davies, P. W.; Albrecht, S. J. C. *Chem. Commun.* **2008**, 238. (b) Davies, P. W.; Albrecht, S. J. C. *Synlett* **2012**, *23*, 70. (c) Nakamura, I.; Sato, T.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 4473. (d) Peng, L.; Zhang, X.; Zhang, S.; Wang, J. *J. Org. Chem.* **2007**, *72*, 1192.

(17) (a) Babu, G.; Perumal, P. T. *Aldrichimica Acta* **2000**, *33*, 16. (b) Yadav, J. S.; Antony, A.; George, J.; Subba Reddy, B. V. *Eur. J. Org. Chem.* **2010**, *2010*, 591. (c) Loh, T.-P.; Chua, G.-L. *Chem. Commun.* **2006**, 2739. (d) Podlech, J.; Maier, T. C. *Synthesis* **2003**, *2003*, 0633. (e) Singh, M. S.; Raghuvanshi, K. *Tetrahedron* **2012**, *68*, 8683.

(18) Kobayashi, S. *Eur. J. Org. Chem.* **1999**, 15.

(19) Ma, J.; Peng, L. L.; Zhang, X.; Zhang, Z.; Campbell, M.; Wang, J. B. *Chem.—Asian J.* **2010**, *5*, 2214.

(20) The allenic acetate version of **3a** gives a poorer 43% yield of **4a** under $InCl_3$ catalysis, so there is no benefit in turning the alcohol into a better leaving group (OAc).

(21) The reaction also works with R = electron-rich aryls, but the diene products were too unstable to isolate.

(22) For In(III) vs Au(I) studies in hydroarylations, see: (a) Kumar, A.; Li, Z. H.; Sharma, S. K.; Parmar, V. S.; Van der Eycken, E. V. *Chem. Commun.* **2013**, *49*, 6803. See also: (b) Alcaide, B.; Almendros, P.; Martínez del Campo, T. *Chem.—Eur. J.* **2008**, *14*, 7756.

(23) Microwave with sealed tube and external surface sensor.

(24) Kappe, C. O. *Chem. Soc. Rev.* **2008**, *37*, 1127.

(25) (a) Zhuo, L. G.; Zhang, J. J.; Yu, Z. X. *J. Org. Chem.* **2012**, *77*, 8527. (b) Zhuo, L. G.; Zhang, J. J.; Yu, Z. X. *J. Org. Chem.* **2014**, *79*, 3809.

(26) Lin, M.; Hao, L.; Liu, X.-T.; Chen, Q.-Z.; Wu, F.; Yan, P.; Xu, S.-X.; Chen, X.-L.; Wen, J.-J.; Zhan, Z.-P. *Synlett* **2011**, 665.

(27) Recent computational studies indicate $InCl_2^+$ as the active catalyst (see ref 25), although previous reports have also suggested $InCl_3$; see: Huang, G. P.; Cheng, B.; Xu, L.; Li, Y. H.; Xia, Y. Z. *Chem.—Eur. J.* **2012**, *18*, 5401.

(28) Alternatively, **6** could be formed via an allylic cation intermediate.

(29) De, S.; Day, C.; Walker, M. E. *Tetrahedron* **2007**, *63*, 10939.

(30) Kuang, J.; Xie, X.; Ma, S. *Synthesis* **2013**, *45*, 592.

(31) Kuang, J.; Luo, H.; Ma, S. *Adv. Synth. Catal.* **2012**, *354*, 933.

DOI: 10.1021/jo502648w
J. Org. Chem. 2015, 80, 1703−1718