JOC The Journal of Organic Chemistry

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The Intramolecular Allenolate Rauhut–Currier Reaction

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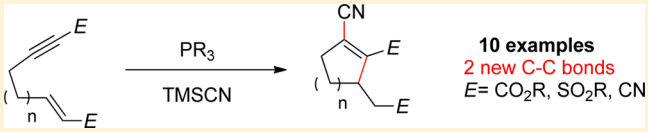
Supporting Information

ABSTRACT: An intramolecular Rauhut–Currier reaction utilizing alkynoates as the initial conjugate acceptor affords densely functionalized 5- and 6-membered rings from ynoate-enoate, ynoate-enenitrile, and alkynyl sulfone-enenitrile substrates. Trialkylphosphines catalyze the reaction, and TMSCN serves as a pronucelophile to effect turnover of the catalyst and the formation of a second C–C bond. Because of the highly electrophilic alkyne acceptor, this reaction yields products that cannot be easily accessed from the traditional Rauhut–Currier reaction.



The intramolecular phosphine catalyzed Rauhut–Currier reaction, also known as the vinylogous Morita–Baylis–Hillman reaction, has gained much attention[1,2] since independent reports by Krische[3] and Roush[4] groups in 2002. In its initial scope, the reaction leads to cyclization of two tethered electron poor alkenes using nucleophilic phosphine catalysis. Rauhut–Currier cyclization proceeds by a conjugate addition of the catalyst to one of the unsaturated carbonyl groups followed by a Michael addition of the activated carbonyl to the other unsaturated carbonyl. Noteworthy is the synthetic utility underscored by the formation of a new C–C σ bond in a densely functionalized cyclic product. Several recent developments on the intramolecular Rauhut–Currier reaction[5] have included examples of the use of nonphosphorus nucleophiles,[6−11] extensions with other electrophilic partners,[11−17] domino-type reactions,[8,18,19] and asymmetric variants.[6,8,9,11,20−23] Furthermore, intramolecular Rauhut–Currier chemistry has been utilized toward the synthesis of several natural products including waihoennsene,[24] ricciocarpin,[25] spinosyn A,[26,27] FR182877,[28] harziphilone,[29] quinine,[30] and 7-hydroxyquinine.[30]

Intramolecular Rauhut–Currier chemistry is most common using bis(enone), enone-enoate, enal-enone, and enal-enoate substrates. Notably, bis(enoate) substrates lack the necessary electrophilicity to undergo efficient cyclization. A solution to this limitation was reported using bis(thioenoate) substrates,[25] but the methodology requires highly reactive trimethylphosphine as the nucleophile and would require further synthetic manipulation of the cyclized thiono esters to afford ester products. Additionally, the intramolecular Rauhut–Currier reaction has been limited to examples where the initial conjugate acceptor is sp^2 hybridized, although Krische has demonstrated that phosphines catalyze an intramolecular [3 + 2] cycloaddition when alkynoates are tethered to electron poor alkenes.[31,32] We hypothesized that similar substrates with shorter chain lengths (i.e., **1**, Scheme 1) are likely to partake in Rauhut–Currier chemistry. Given the known propensity for the addition of nucleophiles into alkynoates, we envisioned the use of an activated alkyne for the first conjugate addition, which could afford an allenolate intermediate **I**. Cyclization can then proceed by a Michael addition to form **II** (Scheme 1). Finally, it was predicted that the phosphine catalyst could be regenerated via an addition–elimination sequence involving an anion formed from a pronucleophile (EX).[33,34] We expected that cyanide anion might not only serve to regenerate the catalyst, but also would form an additional carbon–carbon bond, thus increasing the complexity of the product.

To test this proposal, **1a** was synthesized (vide infra), and suitable reaction conditions were explored to afford cyclized product (Table 1). Treatment of **1a** with tetrabutylammonium cyanide led to immediate consumption of the reactant. However, what resulted was an unidentifiable mixture of polar products. Given the large number of possible mechanistic fates for alkyl alkynoates in the presence of nucleophiles[2] including their known propensity for polymerization, we attempted to more carefully control the concentration of cyanide using trimethylsilylcyanide as a pronucelophile. In the absence of a phosphine catalyst, no reaction took place (entry 2). Addition of triphenylphosphine did not result in cyclized product but did slowly decompose the acyclic starting material over the course of a week (entry 3). To our delight, tributylphosphine was found to rapidly catalyze the cyclization affording **2a** in 61% yield (entry 4).[35] A brief solvent screen using PBu_3 (entries 4–7) revealed that although yields were highest in acetonitrile, toluene serves as an acceptable solvent. Using dichloromethane as solvent gave low yields, and minimal product was isolated from the reaction in THF.

Following initial establishment of appropriate solvent, cyanide source, and catalyst, a series of substrates were prepared from readily available alkynols using well established chemistry. The substrates included various enoate-ynoates, ynoate-enenitriles, and one alkynyl sulfone-enenitrile substrate (Scheme 2).

Cyclization proceeds for **1a–i** under phosphine catalysis affording a new class of Rauhut–Currier products (Table 2).

Received: July 24, 2012
Published: August 6, 2012

dx.doi.org/10.1021/jo3015769 | J. Org. Chem. 2012, 77, 7768–7774

Scheme 1. Proposed Mechanism for the Intramolecular Allenolate Rauhut−Currier Reaction

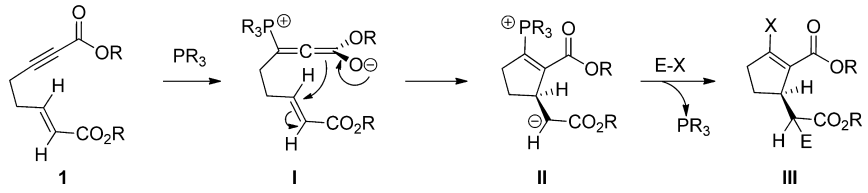
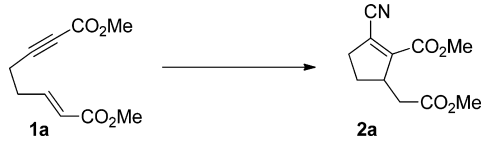


Table 1. Screening of Conditions for the Intramolecular Allenolate Rauhut−Currier Reaction

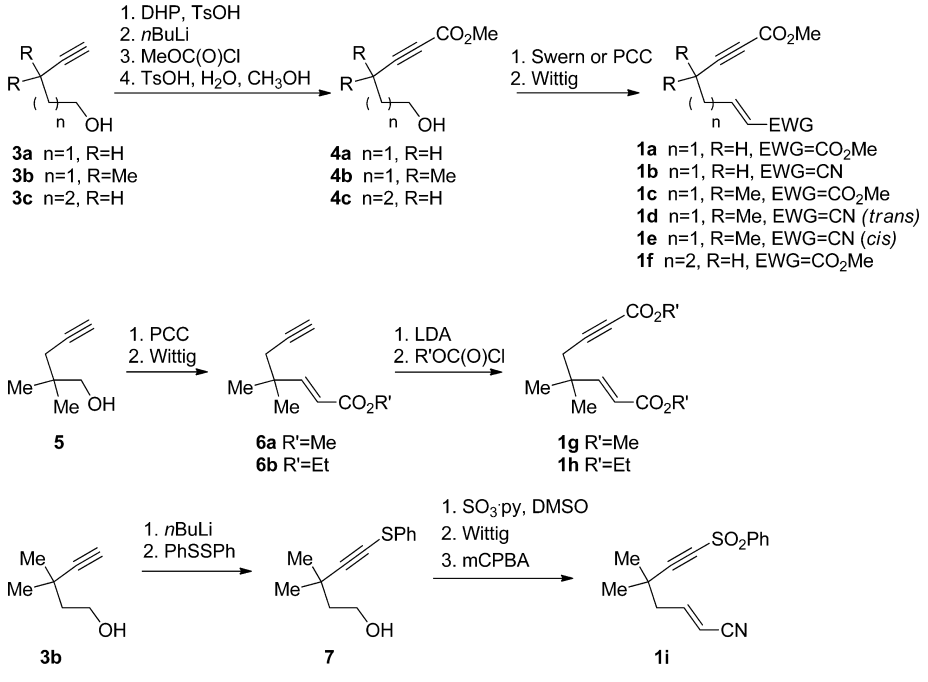


entry	solvent	cyanide source	catalyst (%)	yield (%)
1	CD_3CN	$(n\text{Bu})_4NCN$	none	0
2	CD_3CN	TMSCN	none	–
3	CH_3CN	TMSCN	PPh_3 (25)	0
4	CH_3CN	TMSCN	PBu_3 (10)	61
5	CH_2Cl_2	TMSCN	PBu_3 (15)	35
6	toluene	TMSCN	PBu_3 (15)	53
7	THF	TMSCN	PBu_3 (25)	5

Contrary to the traditional Rauhut−Currier reaction, two esters (or related electron withdrawing groups) may be used in the cyclization.[25] The more reactive ketones and aldehydes that are common to Rauhut−Currier chemistry are not necessary due to the highly reactive nature of the alkyne. Trimethylphosphine offers a slight advantage over tributylphosphine due to enhanced nucleophilicity (compare entries 2 vs 3 and 9 vs 10). However, considering the greater ease of handling and the minimal difference in product yields, tributylphosphine was used in most cases. The highest yields were obtained from the enoate-ynoate substrates with slightly lower yields for ynotate-enenitrile substrates (compare entry 1 vs 2 or 4 vs 7). Surprisingly, the geminal dimethyl groups do not promote higher yields due to the anticipated gem-dialkyl effect (entries 4−8).[36] Seemingly, substituents adjacent to the pi-bonds do not significantly hinder conjugate addition at either the alkyne or the alkene as yields are similar for substrates **1a**, **1c**, and **1g** (compare entries 1, 4, and 5). Most notably, the alkyne seems to dictate the regioselectivity of addition even when the propargylic carbon is quaternary (entries 4, 7, 8, and 11). Though Krische's work demonstrates high regiocontrol toward attack by the phosphine on the less hindered alkene in a related substrate,[3] the use of an alkyne for the initial activation overcomes this steric bias and leads to the desired products **2c**, **2d**, and **2i**. Thus, alkynes can be used to afford regiocomplementary products to traditional Rauhut−Currier products. It is also noteworthy that 6-membered rings can be formed (entries 9−10), and the nature of the alkyl group on the ester does not dramatically affect yields (entries 5 and 6).

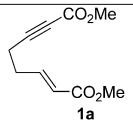
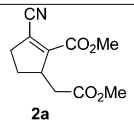
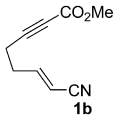
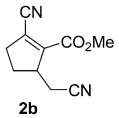
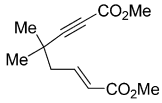
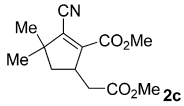
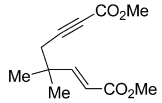
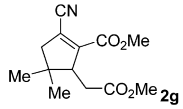
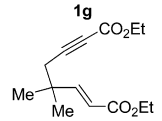
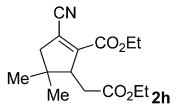
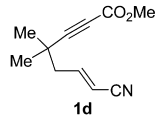
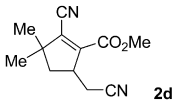
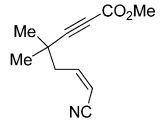
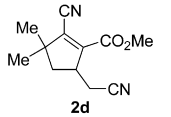
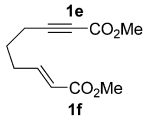
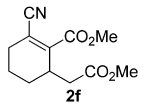
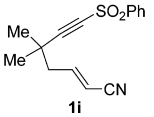
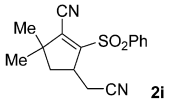
The use of additional pronucleophiles would significantly enhance the scope of this methodology providing products of varying functionality. Since there is a known propensity for alcohols to add across both alkynes[33] and alkenes[34] under phosphine catalysis, the use of methanol as a pronucleophile was briefly investigated. In the best example, substrate **1i** afforded **8** in an improved 73% yield when cyclized in acetonitrile containing 1.1 equiv of methanol (eq 1). Additionally, this reaction produced the regioisomeric cyclization product **9** in 15% yield. However, substrates lacking the gem-

Scheme 2. Synthesis of Cyclization Substrates

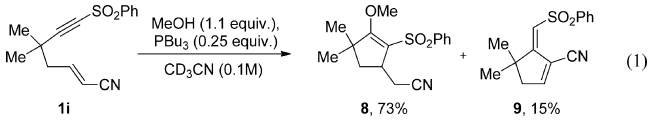


dx.doi.org/10.1021/jo3015769 | J. Org. Chem. 2012, 77, 7768−7774

Table 2. Substrate Scope for the Allenolate Variant of the Rauhut–Currier Reaction

entry	Substrate	Catalyst (%)	Product	Yield, %[a]
1	 **1a**	PBu_3 (10)	 **2a**	61
2	 **1b**	PBu_3 (15)	 **2b**	41
3		PMe_3 (15)		47
4	 **1c**	PBu_3 (50)	 **2c**	61
5	 **1g**	PBu_3 (28)[b]	 **2g**	59
6	 **1h**	PBu_3 (25)[c]	 **2h**	55
7	 **1d**	PBu_3 (15)	 **2d**	37
8	 **1e**	PBu_3 (15)	 **2d**	31
9	 **1f**	PBu_3 (15)	 **2f**	48
10		PMe_3 (15)		63
11	 **1i**	PBu_3 (15)	 **2i**	50

[a]All reactions used 0.1 M substrate in CH_3CN with 1.5 equiv of TMSCN and then were worked up with aqueous CsF unless otherwise noted. [b]0.15 M substrate. [c]0.17 M substrate and 3 equiv of TMSCN.

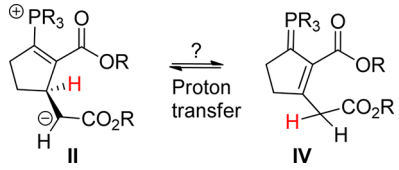


(1)

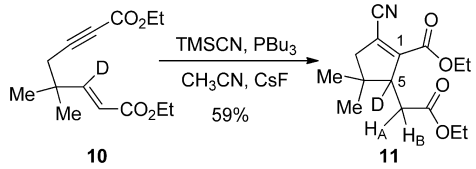
dialkyl substitution on the chain did not undergo cyclization, and alkynoate substrates with the gem-dialkyl groups gave ca. 1:1 ratios of the two regioisomeric products. Consequently, this reaction was not explored in further detail.

Gaining an understanding of the mechanism of the intramolecular allenolate Rauhut–Currier reaction is valuable because of its potential to provide insight to help guide optimization and, eventually, to develop an enantioselective reaction. As proposed previously, it is expected that the phosphine catalyst initially attacks the alkynoate **1** by 1,4-addition to form the allenolate intermediate (**I**, Scheme 1) which performs the second 1,4-addition to form the cyclic intermediate (**II**). Regeneration of the catalyst would then likely proceed through a silylation/addition–elimination mechanism affording **III** (X = CN, E = TMS), which would lead to the product **2** upon protodesilylation with CsF. In the context of developing an enantioselective reaction using a chiral catalyst, we were concerned about the potential for a proton transfer from **II** that would afford resonance stabilized phosphonium ylide **IV** (Scheme 3). If a reversible proton transfer were to occur, then competing racemization would limit enantioselectivities when using a chiral catalyst.

Scheme 3. Possible Reversible Proton Transfer



In order to test for the postulated racemization, the cyclization was performed on the deuterated substrate **10** which was prepared from **5**-d_2, the product of $LiAlD_4$ reduction of 2,2-dimethylpent-4-ynoate. Under the standard cyclization conditions, the yield of **11** was 59% (eq 2, compared to 55% **1h** → **2h**). Proton NMR analysis of **11** revealed the absence of the characteristic methine signal at C5. Furthermore, the spectrum of **11** showed a simple AB quartet (2.48 ppm) for the diastereotopic methylene protons next to the ester. In contrast, the ^{1}H NMR spectrum for **2h** has a multiplet representing both vicinal and geminal coupling for the corresponding diastereotopic methylene protons. Therefore, the ^{1}H NMR spectrum indicates that a proton transfer step does not occur under these conditions and that racemization is below detection limits.



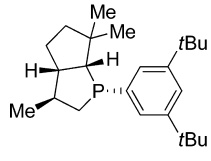
(2)

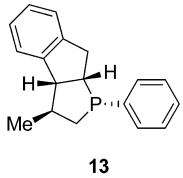
With this promising result, we were encouraged about the potential for an enantioselective reaction. However, the requirement for highly nucleophilic catalysts severely limited our choice of chiral phosphines and focused attention on the phosphabicyclooctane (PBO) catalysts because they are more nucleophilic than simple trialkyl phosphines (Table 3).[37] Substrate **1a** was thus submitted to the cyclization conditions

Table 3. Cyclizations with Chiral Phosphines

entry	substrate	catalyst (%)	product	yield (%)[a]	% ee
1	**1a**	**12** (25)	**2a**	53	28
2	**1a**	**13** (25)	**2a**	54	14
3	**1d**	**12** (25)	**2d**	43	26
4	**1i**	**12** (11)	**2i**	52	~1

[a]All reactions used 0.1 M substrate in CH_3CN with 1.5 equiv of TMSCN and then were worked up with aqueous CsF





dx.doi.org/10.1021/jo3015769 | J. Org. Chem. 2012, 77, 7768–7774

in the presence of PBO catalyst **12**, which has previously been used only in acylation reactions.[38] A respectable yield of 53% was realized for product **2a**, but the enantioselectivity was a modest 28% ee (entry 1). Catalyst **13** similarly gave good yields with low enantioselectivity (entry 2). Two additional substrates, **1d** and **1i**, were submitted to cyclization conditions using **12**; **2d** was obtained with a moderate 26% ee, whereas substrate **1i** gave nearly racemic product (entries 3 and 4). Because of the low enantioselectivity, the absolute configuration of product was not assigned and additional substrates were not investigated.[39]

In conclusion, an allenolate variation on the intramolecular Rauhut−Currier reaction using alkyne substrates is reported. The use of activated alkynes leads to the formation of reactive allenolates, which can cyclize onto tethered enoates and enenitriles. This methodology affords products of greatly increased complexity highlighted by the formation of two new C−C bonds, a highly functionalized cyclic product, and a new chirality carbon. The reaction is catalyzed by alkyl phosphines to give 5- and 6-membered rings and is applicable with several activating substituents to afford products that complement previously reported cyclizations of dienoates. Though chirality transfer is incurred from chiral PBO catalyst **12**, modest enantioselectivities necessitate the development of new catalysts to effect higher enantioselectivities.

EXPERIMENTAL SECTION

Methyl 6-Hydroxy-4,4-dimethylhex-2-ynoate (4b). To a solution of **3b**[40] (2.195 g, 19.6 mmol) in 25 mL of CH_2Cl_2 were added 3,4-dihydro-2*H*-pyran (1.95 mL, 21.5 mmol) and *p*-TsOH (12 mg, 0.06 mmol). The reaction was stirred for 1.5 h, quenched with saturated $NaHCO_3$ (15 mL), extracted with CH_2Cl_2 (3 × 30 mL), and the organic layers were combined and dried ($MgSO_4$). After removal of solvent (aspirator), the residue was purified by flash chromatography (5 × 16 cm), 20:1 hexanes/EtOAc, affording 2.53 g (66%) of THP-ether; TLC, 20:1 hexanes/EtOAc, R_f 0.18. THF was added, and the mixture was cooled to −78 °C. *n*BuLi (2.0 mL, 1.53 M, 3.01 mmol) was added dropwise. After stirring for 2 h, methyl chloroformate (0.3 mL, 3.93 mmol, freshly distilled) was added. After the mixture was stirred for 3 h at −78 °C and for 3 h at room temperature, water (10 mL) was added. The mixture was extracted with Et_2O (4 × 10 mL), dried ($MgSO_4$), and concentrated (aspirator) to a pale yellow oil, which was dissolved in MeOH (10 mL). Water (1 mL) followed by *p*-TsOH (103 mg) were added, the mixture was stirred overnight, quenched with solid $NaHCO_3$ (ca. 300 mg), and then concentrated (aspirator). Water (15 mL) was added, and the mixture was extracted with Et_2O (4 × 15 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to a crude yellow oil that was purified by flash chromatography (4 × 14 cm), 2:1 hexanes/EtOAc, affording 266 mg (60%) of a colorless oil: TLC, 2:1 hexanes/EtOAc, R_f 0.22; HRMS calcd for $C_9H_{14}O_3Na^+$ 193.0840, found m/z = 193.0835, error = 3 ppm; IR (neat, cm^{-1}) 3377, O−H; 2235, C≡C; 1714, C═O; ^1H NMR (500 MHz, $CDCl_3$) δ 3.82 (2H, dd, J = 7.1, 5.3 Hz) 3.73 (3H, s) 1.85 (1H, t, J = 5.3 Hz) 1.76 (2H, t, J = 7.1 Hz) 1.28 (6H, s); ^{13}C NMR (125.70 MHz, $CDCl_3$) δ 154.2, 95.1, 73.0, 59.9, 52.6, 44.5, 29.8, 28.6.

(*E*)-Methyl Oct-2-en-6-ynedioate (1a). To a solution of methyl 6-oxohex-2-ynoate[41] (620 mg, 4.4 mmol) in 50 mL of CH_2Cl_2 was added methyl(triphenylphosphoranylidene)acetate (1.63 mg, 4.9 mmol). The reaction was stirred for 8 h, concentrated (aspirator), and purified by flash chromatography (5 × 16 cm), 6:1 hexanes/EtOAc to afford 808 mg (93%) of colorless oil: TLC, 6:1 hexanes/EtOAc, R_f 0.20; HRMS calcd for $C_{10}H_{12}O_4Na^+$ 219.0633, found m/z = 219.0633, error = 2 ppm; IR (neat, cm^{-1}) 2238, C≡C; 1711, C═O; 1659, C═O; ^1H NMR (400 MHz, $CDCl_3$) δ 6.99−6.90 (1H, m) 5.91 (1H, dt, J = 16.1, 1.5 Hz) 3.77 (3H, s) 3.74 (3H, s) 2.52−2.48 (4H, m); ^{13}C NMR (100.57 MHz, $CDCl_3$) δ 166.5, 153.9, 145.4, 122.6, 87.3, 73.6, 52.6, 51.5, 29.9, 17.6.

Methyl 7-Cyanohept-6-en-2-ynoate (1b). Similar to **1a**; methyl 6-oxohex-2-ynoate[41] (350 mg, 2.5 mmol) and (triphenylphosphoranylidene)acetonitrile (827 mg, 2.75 mmol) afforded 318 mg (78%) of colorless oil, which was a 2:1 mixture of inseparable *E* and *Z* isomers: TLC, 3:1 hexanes/EtOAc, R_f 0.23; HRMS calcd for $C_9H_9NO_2Na^+$ 186.0531, found m/z = 186.0528, error = 2 ppm; IR (neat, cm^{-1}) 2365, 2358, C≡N; 2241, 2224 C≡C; 1709, C═O; ^1H NMR (400 MHz, $CDCl_3$) for the major isomer, (*E*)-methyl 7-cyanohept-6-en-2-ynoate δ 6.77−6.67 (1H, m) 5.46 (1H, d, J = 16.1 Hz) 3.78 (3H, s) 2.58−2.48 (4H, m); for the minor isomer, (*Z*)-methyl 7-cyanohept-6-en-2-ynoate δ 6.57 (1H, dt, J = 11.0, 8.1 Hz) 5.46 (1H, dt, J = 11.0, 1.5 Hz) 3.77 (3H, s) 2.71 (2H, ddd, J = 14.7, 7.3, 7.3 Hz) 2.58−2.48 (2H, m); ^{13}C NMR (100.57 MHz, $CDCl_3$) for the mixture of isomers δ 153.8, 151.8, 151.1, 116.8, 115.3, 102.0, 101.8, 86.3, 86.1, 74.2, 74.1, 52.7, 30.9, 29.4, 17.7, 17.3.

Methyl 4,4-Dimethyl-6-oxohex-2-ynoate. Oxalyl chloride (1.1 mL, 12.7 mmol, distilled) was added dropwise to a solution of DMSO (1.5 mL, 21.2 mmol) in CH_2Cl_2 at −78 °C. After 5 min, a solution of alcohol **4b** (722 mg, 4.24 mmol) was added over 2 min, and stirring was continued for an additional 30 min, at which point Et_3N (3.7 mL, 25.4 mmol) was added. After an additional 15 min, the mixture was warmed to rt, stirred 30 min, and then quenched with 15 mL of water. The mixture was extracted with CH_2Cl_2 (3 × 15 mL) and dried ($MgSO_4$). Removal of solvent (aspirator) and purification by flash chromatography (7 × 15 cm), 3:1 hexanes/Et_2O, afforded 658 mg (93%) of a yellow oil: TLC, 3:1 hexanes/Et_2O, R_f 0.22; HRMS calcd for $C_{10}H_{16}O_4Na^+$ 223.0946, found m/z= 223.0941, error = 2 ppm; IR (neat, cm^{-1}) 2239, C≡C; 1710, C≡N; 2849, C−H; 2741, C−H; ^1H NMR (400 MHz, $CDCl_3$) δ 9.86 (1H, t, J = 2.9 Hz) 3.77 (3H, s) 2.52 (2H, d, J = 2.9 Hz) 1.39 (6H, s); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 200.4, 153.9, 92.6, 73.8, 54.1, 52.7, 28.7, 28.4.

(*E*)-Dimethyl 5,5-Dimethyloct-2-en-6-ynedioate (1c). Similar to **1a**; Methyl 4,4-dimethyl-6-oxohex-2-ynoate (103 mg, 0.61 mmol) and methyl(triphenylphosphoranylidene)acetate (225 mg, 0.67 mmol) afforded 130 mg (95%) of colorless oil: TLC, 3:1 hexanes/EtOAc, R_f 0.22; HRMS calcd for $C_{12}H_{16}O_4Na^+$ 247.0946, found m/z = 247.0944, error = 1 ppm; IR (neat, cm^{-1}) 2237, C≡C; 1711, C═O; 1658, C═O; ^1H NMR (400 MHz, $CDCl_3$) δ 6.99 (1H, ddd, J = 15.4, 7.3, 7.3 Hz) 5.90 (1H, d, J = 16.1 Hz) 3.77 (3H, s) 3.75 (3H, s) 2.38 (2H, d, J = 7.3 Hz) 1.29 (6H, s); ^{13}C NMR (100.57 MHz, $CDCl_3$) δ 166.6, 154.3, 144.1, 124.6, 94.1, 73.5, 52.8, 51.7, 45.0, 31.4, 28.2.

Methyl 7-Cyano-4,4-dimethyl-hept-6-en-2-ynoate (1d/1e). Similar to **1a**; Methyl 4,4-dimethyl-6-oxohex-2-ynoate (137 mg, 0.81 mmol) and (triphenylphosphoranylidene)acetonitrile (270 mg, 0.89 mmol) afforded crude mixture containing a 1.6:1 ratio of *E*:*Z* isomers. The residue was purified by flash chromatography (3.5 × 16 cm), 5:1 hexanes/EtOAc, affording 95 mg of **(*E*)-1d** (50%), a colorless oil: TLC, 5:1 hexanes/EtOAc, R_f 0.22; HRMS calcd for $C_{11}H_{13}NO_2Na^+$ 214.0844, found m/z = 214.0839, error = 2 ppm; IR (neat, cm^{-1}) 2240, C≡N; 2224, C≡C; 1710, C═O; ^1H NMR (400 MHz, $CDCl_3$) δ 6.78 (1H, dt, J = 16.1, 7.6 Hz) 5.43 (1H, dt, J = 16.1, 1.5 Hz) 3.78 (3H, s) 2.38 (2H, dd, J = 7.3, 1.5 Hz) 1.29 (6H, s); ^{13}C NMR (100.57 MHz, $CDCl_3$) δ 153.9, 150.8, 116.8, 103.1, 92.7, 73.9, 52.7, 45.7, 31.3, 28.0.

55 mg (29%) of **(*Z*)-1e**, a colorless oil was isolated: TLC, 5:1 hexane/EtOAc, R_f 0.28; HRMS calcd for $C_{11}H_{13}NO_2Na^+$ 214.0844, found m/z = 214.0843, error = 0 ppm; IR (neat, cm^{-1}) 2237, C≡N; 2221, C≡C; 1711, C═O; ^1H NMR (400 MHz, $CDCl_3$) δ 6.65 (1H, dt, J = 11.0, 7.3 Hz) 5.52 (1H, dt, J = 11.0, 1.5 Hz) 3.77 (3H, s) 2.60 (2H, dd, J = 7.3, 1.5 Hz) 1.33 (6H, s); ^{13}C NMR (100.57 MHz, $CDCl_3$) δ 154.0, 150.2, 115.6, 102.5, 93.4, 73.7, 52.7, 44.0, 31.3, 28.0.

(*E*)-Dimethyl Non-2-en-7-ynedioate (1f). Similar to **1a**; Methyl 7-oxohept-2-ynoate[41] (215 mg, 1.39 mmol) and methyl-(triphenylphosphoranylidene)acetate (512 mg, 1.53 mmol) afforded 260 mg (89%), a colorless oil: TLC, 2:1 hexanes/Et_2O, R_f 0.28; HRMS calcd for $C_{11}H_{14}O_4Na^+$ 233.0789, found m/z = 233.0784, error = 2 ppm; IR (neat, cm^{-1}) 2236, C≡C; 1711, C═O; 1657, C═O; ^1H NMR (400 MHz, $CDCl_3$) δ 6.91 (1H, dt, J = 15.4, 6.6 Hz) 5.86 (1H,

dx.doi.org/10.1021/jo3015769 | J. Org. Chem. 2012, 77, 7768−7774

dt, J = 16.1, 1.5 Hz) 3.76 (3H, s) 3.72 (3H, s) 2.40−2.30 (4H, m) 1.75 (2H, pent, J = 7.3 Hz); ^{13}C NMR (100.57 MHz, $CDCl_3$) δ 166.8, 154.0, 147.3, 122.1, 88.3, 73.5, 52.6, 51.4, 30.9, 25.8, 18.0.

(*E*)-Methyl 4,4-Dimethylhept-2-en-6-ynoate (6a). To a solution of PCC (1.28 g, 6.0 mmol) in CH_2Cl_2 (5.5 mL) was added 2,2-dimethylpent-4-yn-1-ol (**5**)[42] (383 mg, 3.41 mmol) in CH_2Cl_2 (1.5 mL) via cannula. The solution was stirred for 4 h, after which the reaction was diluted with Et_2O (25 mL) and decanted from the black solid that formed. The solid was rinsed with additional Et_2O (4 × 5 mL), and the combined organic layers were filtered through Florisil (1 in). Toluene (11 mL) was added, and the Et_2O was removed (aspirator), taking care to avoid evaporation of the volatile aldehyde. Methyl(triphenylphosphoranylidene)acetate (1.25 g, 3.75 mmol) was added, and the mixture refluxed for 3 days. The reaction mixture was concentrated (aspirator) and purified by flash chromatography (2.5 × 15 cm), 10:1 hexanes/EtOAc, to afford 311 mg (55%), a colorless oil: TLC, 10:1 hexanes/EtOAc, $KMnO_4$ stain, R_f 0.34; HRMS calcd for $C_{20}H_{28}O_4Na^+$ 355.187959, found m/z = 355.187959, error = 0 ppm. IR (neat, cm^{-1}) 3298, ≡C—H; 2118, C≡C; 1727, C═O; 1655, C═C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 (1H, d, J = 16 Hz) 5.79 (1H, d, J = 16 Hz) 3.72 (3H, s) 2.22 (2H, d, J = 2.8 Hz) 2.00 (1H, t, J = 2.8 Hz) 1.14 (6H, s); ^{13}C (100.53 MHz, $CDCl_3$) δ 167.3, 156.1, 118.1, 80.8, 70.9, 51.5, 36.5, 31.4, 25.9.

(*E*)-Dimethyl 4,4-Dimethyloct-2-en-6-ynedioate (1g). To a solution of diisopropylamine (52 μL, 0.4 mmol) in THF (0.6 mL) was added *n*BuLi (1.6 M in hexanes, 0.21 mL, 0.34 mmol) dropwise at −78 °C. The temperature was increased to 0 °C and stirred for 20 min. The LDA was cannulated into a −78 °C solution of **6a** (48 mg, 0.28 mmol) in THF (1.5 mL) and stirred at −78 °C. The solution stirred for 3 h. Methyl chloroformate (30 μL, 0.39 mmol) was added via syringe, and the mixture was stirred for 3 h, with the bath slowly warming to 0 °C, and then for 2 h at room temperature. The reaction was quenched with water (5 mL) and extracted with 1:1 hexanes/Et_2O (3 × 10 mL). The organic layers were combined, dried ($MgSO_4$), concentrated (aspirator) and purified by flash chromatography (1 × 15 cm), 5:1 hexanes/Et_2O to afford 59 mg (94%), a colorless oil: TLC, 10:1 hexanes/EtOAc, R_f 0.12; HRMS calcd for $C_{12}H_{16}O_4Na^+$ 247.094080, found m/z = 247.093905, error = 1 ppm. IR (neat, cm^{-1}) 2237, C≡C; 1717, C═O; 1655, C═C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.92 (1H, d, J = 16.7 Hz) 5.80 (1H, d, J =16.7 Hz) 3.74 (3H, s) 3.73 (3H, s) 2.38 (2H, s) 1.18 (6H, s); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 167.0, 155.1, 154.0, 118.6, 85.9, 75.1, 52.6, 51.6, 36.8, 31.5, 26.1.

(*E*)-Diethyl 4,4-Dimethyloct-2-en-6-ynedioate (1h). Similar to **1g**; **6b**[42] (245 mg, 1.34 mmol) and ethyl chloroformate (178 μL, 1.87 mmol) afforded 256 mg (91%), a colorless oil: TLC, 10:1 CH_2Cl_2/benzene, R_f 0.34; HRMS calcd for $C_{14}H_{20}O_4Na^+$ 275.125380, found m/z = 275.125147, error = <1 ppm. IR (neat, cm^{-1}) 2234, C≡C; 1713, C═O; 1652, C═C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93 (1H, d, J = 15.9 Hz) 5.81 (1H, d, J = 15.9 Hz) 4.22 (2H, q, J = 7.1 Hz) 4.20 (2H, q, J = 7.1 Hz) 2.39 (2H, s) 1.31 (3H, t, J = 7.1 Hz) 1.30 (3H, t, J = 7.1 Hz) 1.20 (6H, s); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 166.7, 154.9, 153.6, 119.0, 85.5, 75.5, 61.9, 60.5, 36.8, 31.5, 26.2, 14.2, 14.0.

3,3-Dimethyl-5-phenylsulfanyl-pent-4-yn-1-ol (7). Following literature precedent,[43] a solution of phenyl disulfide (633 mg, 2.90 mmol) and MeI (186 μL, 2.98 mmol) in 4 mL of THF was stirred for 1 h. To a separate flask charged with alkyne **3b** (310 mg, 2.76 mmol) and 8 mL of THF was added *n*BuLi (3.8 mL, 1.81 M in hexanes, 6.9 mmol) at −30 °C. The lithioacetylide solution was stirred at −30 °C for 30 min, followed by the addition of the phenyl disulfide solution via cannula. Stirring was continued at −30 °C for 30 min and then an additional 3 h at room temperature. The reaction was quenched with 20 mL of dilute aqueous NH_4Cl and extracted with Et_2O (3 × 20 mL). The organic layers were combined, dried ($MgSO_4$), and concentrated (aspirator). The residue was purified by flash chromatography (3 × 16 cm), 20:1 CH_2Cl_2/Et_2O, affording 609 mg (99%) of a colorless oil: TLC, 20:1 CH_2Cl_2/ Et_2O R_f 0.26; HRMS calcd for $C_{13}H_{16}OSNa^+$ 243.0820, found m/z = 243.0814, error = 2 ppm; IR (neat, cm^{-1}) 3339, O−H; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40−7.30 (4H, m) 7.23−7.18 (1H, m) 3.89 (2H, dt, J = 6.8, 5.9 Hz) 1.81 (2H, t, J = 6.8 Hz) 1.58 (1H, t, J = 5.4 Hz) 1.35 (6H, s); ^{13}C NMR (100.57 MHz, $CDCl_3$) δ 133.4, 129.1, 126.2, 125.7, 105.8, 65.9, 60.4, 45.3, 31.2, 29.6.

(*E*)-5,5-Dimethyl-7-(phenylthio)hept-2-en-6-ynenitrile. DMSO (2.4 mL, 34.3 mmol, freshly distilled) and Et_3N (2 mL, 13.7 mmol, freshly distilled) were added to a solution of **7** (755 mg, 3.42 mmol) in 10 mL of CH_2Cl_2. The solution was cooled to 0 °C, and SO_3·pyridine (1.05 g, 6.84 mmol) was added. The cooling bath was removed, and the solution was stirred for 4 h. Solvent was removed (aspirator), and the residue was purified by flash chromatography (4 × 16 cm), 9:1 hexanes/Et_2O, to afford 625 mg (84%) of 3,3-dimethyl-5-(phenylthio)pent-4-ynal, a yellow oil: TLC, 9:1 hexanes/Et_2O R_f 0.21; 400 MHz NMR ($CDCl_3$) δ 9.93 (1H, t, J = 2.9 Hz) 7.40−7.30 (4H, m) 7.24−7.17 (1H, m) 2.51 (2H, d, J = 2.9 Hz) 1.42 (6H, s). Dichloromethane (50 mL) was added followed by (triphenylphosphoranylidene)acetonitrile (991 mg, 3.29 mmol) and 9 h of stirring. The residue was concentrated and triturated with 50 mL of Et_2O. The filtrate was concentrated and purified by flash chromatography (4 × 16 cm), 15:1 hexanes/EtOAc, affording 382 mg of (*E*)-5,5-dimethyl-7-(phenylthio)hept-2-en-6-ynenitrile (55%), a yellow oil: TLC, 15:1 hexanes/EtOAc, R_f 0.19; HRMS calcd for $C_{15}H_{15}NSNa^+$ 264.0823, found m/z = 264.0811, error = 5 ppm; IR (neat, cm^{-1}) 2223, C≡N; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42−7.32 (3H, m) 7.25−7.19 (1H, m) 6.86 (1H, ddd, J = 16.5, 7.8, 7.8 Hz) 5.42 (1H, dt, J = 16.3, 1.5 Hz) 2.39 (2H, dd, J = 7.8, 1.5 Hz) 1.33 (6H, s); ^{13}C NMR (125.70 MHz, $CDCl_3$) δ 152.1, 133.1, 129.2, 126.4, 125.9, 117.1, 103.8, 103.5, 67.3, 46.7, 32.9, 29.0.

(*E*)-5,5-Dimethyl-7-(phenylsulfonyl)hept-2-en-6-ynenitrile (1i). To a solution of (*E*)-5,5-dimethyl-7-(phenylthio)hept-2-en-6-ynenitrile (128 mg, 0.53 mmol) in 10 mL of CH_2Cl_2 at 0 °C was added *m*CPBA (488 mg, 70−75% with water). The suspension was stirred for 45 min at 0 °C. The cooling bath was removed, and the milky suspension was stirred for an additional 45 min, during which the solution became homogeneous. The reaction mixture was concentrated (aspirator), taken up in Et_2O (20 mL) and washed with 10% $Na_2S_2O_4$ (20 mL). The aqueous layer was extracted with Et_2O (2 × 20 mL); the combined organic layers were washed with saturated $NaHCO_3$ (2 × 20 mL) and brine (50 mL). The organic extract was dried ($MgSO_4$) and concentrated (aspirator) to yield 127 mg of solid **1i** (88%). Pure material was obtained by crystallization from 1:1 hexane/Et_2O: mp 85.5−86.5 °C; HRMS calcd for $C_{15}H_{15}NO_2SNa^+$ 296.0721, found m/z = 296.0708, error = 4 ppm; IR (neat, cm^{-1}) 2223, C≡N; 2192, C≡C; 1324, S═O; 1154, S═O; ^{1}H NMR (500 MHz, C_6D_6) δ 8.00−7.95 (2H, m) 6.98−6.94 (3H, m) 5.81 (1H, ddd, J = 16.1, 7.8, 7.8 Hz) 4.42 (1H, d, J = 16.1 Hz) 1.26 (2H, dd, J = 7.3, 1.0 Hz) 0.48 (6H, s); ^{13}C NMR (125.70 MHz, C_6D_6) δ 148.7, 142.8, 134.0, 129.5, 127.3, 116.7, 103.6, 99.9, 80.6, 44.5, 31.3, 26.6.

(*E*)-Ethyl 4,4-Dimethylhept-2-en-6-ynoate-(3-d_1). To a solution of $LiAlD_4$ (554 mg, 13.2 mmol) in Et_2O (30 mL) was added methyl 2,2-dimethylpent-4-ynoate[44] (1.847 mg, 13.2 mmol) in Et_2O (3 mL) via cannula at 0 °C and stirred for 1 h. The reaction was quenched with saturated Rochelle's salt solution (10 mL), stirred for 1 h, and extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$), and concentrated (aspirator) to afford 1.448 g of **5**-d_2 [2,2-dimethylpent-4-yn-1-ol-(1,1-d_2)] (95%): TLC, 2:1 hexanes/EtOAc, R_f 0.37; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.15 (1H, d, J = 2.5 Hz) 1.99 (2H, t, J = 2.5 Hz) 1.47 (1H, br s) 0.97 (6H, s). Similar to **6a**; 2,2-dimethylpent-4-yn-1-ol-(1,1-d_2) (1.425 g, 12.5 mmol) afforded 1.590 g of (*E*)-ethyl 4,4-dimethylhept-2-en-6-ynoate-(3-d_1) (69%), a colorless oil: TLC, 4:1 hexanes/EtOAc, R_f 0.44; HRMS calcd for $C_{11}H_{15}DO_2Na^+$ 204.110528, found m/z = 204.110533, error = <1 ppm. IR (neat, cm^{-1}) 3304, ≡C—H; 2119, C≡C; 1720, C═O; 1640, C═C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.80 (1H, t, J = 2.1 Hz) 4.20 (2H, q, J = 7.2 Hz) 2.24 (2H, d, J = 2.7 Hz) 2.03 (1H, t, J = 2.7 Hz) 1.30 (3H, t, J = 7.2 Hz) 1.17 (6H, s); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 166.9, 155.5 (t, $J_{C\text{-}D}$= 24.4 Hz), 118.4, 70.8, 60.3, 36.4, 31.4, 26.0, 14.2.

(*E*)-Diethyl 4,4-Dimethyloct-2-en-6-ynedioate-(3-d_1) (10). Similar to **1g**; (*E*)-ethyl 4,4-dimethylhept-2-en-6-ynoate-(3-d_1) (268 mg, 1.46 mmol) afforded 203 mg of a colorless oil (68%): TLC, 10:1

dx.doi.org/10.1021/jo3015769 | J. Org. Chem. 2012, 77, 7768−7774

CH_2Cl_2/benzene, R_f 0.34; HRMS calcd for $C_{14}H_{19}DO_4Na^+$ 276.131657, found m/z = 276.131365, error = 1.1 ppm. IR (neat, cm^{-1}) 2235, C≡C; 1716, C═O; 1640, C═C; ^1H NMR (400 MHz, $CDCl_3$) δ 5.80 (1H, t, J = 2.1 Hz) 4.22 (2H, q, J = 7.1 Hz) 4.20 (2H, q, J = 7.1 Hz) 2.39 (2H, s) 1.31 (3H, t, J = 7.1 Hz) 1.30 (3H, t, J = 7.1 Hz) 1.20 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 154.5 (t, $J_{C\text{-}D}$= 23.9 Hz), 153.6, 118.9, 85.5, 75.4, 61.9, 60.4, 36.7, 31.5, 26.1, 14.2, 14.0.

General Method for TMSCN Cyclizations. A flask containing **1** was purged with N_2. CH_3CN (0.1 M) and TMSCN (1.5 equiv) were added, followed by the trialkylphosphine (0.1−0.5 equiv). The mixture was stirred for 8−15 h or until the reaction was complete by TLC. Alternatively, some reactions were performed using deuterated solvents and monitored by NMR. When the reaction reached completion, the solution was poured onto aqueous CsF (0.1 M solution) and stirred for 2 h. The solution was extracted with CH_2Cl_2, dried ($MgSO_4$), and concentrated (aspirator) to yield an orange oil, which was purified by flash chromatography.

Methyl 2-Cyano-5-(2-methoxy-2-oxoethyl)cyclopent-1-enecarboxylate (2a). 1a (26 mg, 0.13 mmol) and PBu_3 (0.013 mmol) afforded 18 mg (61%) of **2a**: colorless oil; TLC, 1:1 hexane/Et_2O, R_f 0.26; HRMS calcd for $C_{11}H_{13}NO_4Na^+$ 246.0742, found m/z = 246.0742, error = 0 ppm; IR (neat, cm^{-1}) 2223, C≡N; 1722, C═O; ^1H NMR (500 MHz, $CDCl_3$) δ 3.86 (3H, s) 3.68 (3H, s) 3.55−3.48 (1H, m) 2.86−2.67 (2H, m) 2.81 (1H, dd, J = 15.9, 3.7 Hz) 2.44 (1H, dd, J = 15.9, 9.5 Hz) 2.33 (1H, dddd, J = 13.7, 9.3, 9.3, 6.3 Hz) 1.80 (1H, dddd, J = 13.8, 8.7, 5.3, 5.3 Hz); ^{13}C NMR (100.57 MHz, $CDCl_3$) δ 171.9, 162.3, 149.7, 122.8, 114.7, 52.4, 51.8, 42.5, 37.0, 34.7, 28.8. Chiral HPLC analysis: CHIRALPAK AS, flow rate 1 mL/min, 5% isopropanol/hexanes. Retention times 13.3 min, 15.0 min.

Methyl 2-Cyano-5-(cyanomethyl)cyclopent-1-enecarboxylate (2b). 1b (80 mg, 0.49 mmol) and PMe_3 (0.07 mmol) afforded 44 mg (47%) of **2b**: crystalline solid. Pure material was obtained by crystallization from Et_2O: mp 59.2−60.1 °C; TLC, 1:2 hexane/Et_2O, R_f 0.22; HRMS calcd for $C_{10}H_{10}N_2O_2Na^+$ 213.0640, found m/z = 213.0640, error = 0 ppm; IR (neat, cm^{-1}) 2235, C≡N; 2225, C≡N; 1721, C═O; ^1H NMR (400 MHz, $CDCl_3$) δ 3.89 (3H, s) 3.49−3.41 (1H, m) 3.05−2.94 (1H, m) 2.85−2.71 (3H, m) 2.49−2.36 (1H, m) 2.07−1.95 (1H, m); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 161.8, 146.7, 125.2, 117.5, 114.0, 52.7, 42.6, 35.1, 28.1, 21.7.

Methyl 2-Cyano-5-(2-methoxy-2-oxoethyl)-3,3-dimethylcyclopent-1-enecarboxylate (2c). 1c (49 mg, 0.22 mmol) and PBu_3 (0.11 mmol) afforded 34 mg (61%) of **2c**: colorless oil; TLC, 2:1 hexane/Et_2O, R_f 0.23; HRMS calcd for $C_{13}H_{17}NO_4Na^+$ 274.1055, found m/z = 274.1049, error = 2 ppm; IR (neat, cm^{-1}) 2223, C≡N; 1728, C═O; ^1H NMR (500 MHz, $CDCl_3$) δ 3.85 (3H, s) 3.68 (3H, s) 3.55 (1H, dddd, J = 9.3, 8.3, 6.9, 3.9 Hz) 2.92 (1H, dd, J = 16.1, 3.9 Hz) 2.43 (1H, dd, J = 16.1, 9.3 Hz) 2.23 (1H, dd, J = 13.1, 8.3 Hz) 1.60 (1H, dd, J = 13.1, 6.9 Hz) 1.29 (3H, s) 1.23 (3H, s); ^{13}C NMR (100.57 MHz, $CDCl_3$) δ 172.0, 162.6, 146.7, 132.5, 113.9, 52.4, 51.7, 47.5, 44.2, 41.1, 37.8, 27.8, 26.9.

Methyl 2-Cyano-5-(cyanomethyl)-3,3-dimethylcyclopent-1-enecarboxylate (2d). 1d (50 mg, 0.26 mmol) and PBu_3 (0.04 mmol) afforded 21 mg (37%) of **2d**: colorless oil; TLC, 1:2 hexane/Et_2O, R_f 0.29; HRMS calcd for $C_{12}H_{14}N_2O_2Na^+$ 241.0953, found m/z = 241.0957, error = 2 ppm; IR (neat, cm^{-1}) 2248, C≡N; 2224, C≡N; 1723, C═O; ^1H NMR (400 MHz, $CDCl_3$) δ 3.90 (3H, s) 3.47 (1H, dddd, J = 8.1, 8.1, 8.1, 4.4 Hz) 2.87 (1H, dd, J = 16.8, 4.4 Hz) 2.79 (1H, dd, J = 16.8, 8.1 Hz) 2.30 (1H, dd, J = 13.6, 8.1 Hz) 1.81 (1H, dd, J = 13.6, 8.1 Hz) 1.39 (3H, s) 1.27 (3H, s); ^{13}C NMR (100.57 MHz, $CDCl_3$) δ 162.1, 143.5, 135.0, 117.5, 113.3, 52.7, 47.8, 43.3, 41.1, 27.6, 27.0, 21.9. Chiral HPLC analysis: CHIRALPAK AS, flow rate 1 mL/min, 20% ethanol/hexanes. Retention times 6.4 min, 9.9 min.

Methyl 2-Cyano-6-(2-methoxy-2-oxoethyl)cyclohex-1-enecarboxylate (2f). 1f (80 mg, 0.38 mmol) and PMe_3 (0.06 mmol) afforded 57 mg (63%) of **2f**: yellow oil; TLC, 1:1 hexane/Et_2O, R_f 0.25; HRMS calcd for $C_{12}H_{15}NO_4Na^+$ 260.0898, found m/z= 260.0894, error = 2 ppm; IR (neat, cm^{-1}) 2215, C≡N; 1725, C═O; 1625, C═O; ^1H NMR (400 MHz, $CDCl_3$) δ 3.87 (3H, s) 3.69 (3H, s) 3.34−3.22 (1H, m) 2.56 (1H, dd, J = 16.1, 3.7 Hz) 2.53−2.36 (2H, m) 2.33 (1H, dd, J = 16.1, 10.3 Hz) 1.79−1.59 (4H, m); ^{13}C NMR (100.57 MHz, $CDCl_3$) δ 171.1, 165.0, 145.8, 119.5, 117.4, 52.6, 51.9, 37.5, 31.8, 29.6, 25.7, 17.3. Chiral HPLC analysis: CHIRALPAK AS, flow rate 1 mL/min, 10% ethanol/hexanes. Retention times 38.9 min, 45.2 min.

Methyl 2-Cyano-5-(2-methoxy-2-oxoethyl)-4,4-dimethylcyclopent-1-enecarboxylate (2g). 1g (39 mg, 0.17 mmol) and PBu_3 (0.048 mmol) afforded 26 mg (59%) of **2g**: colorless oil; TLC, 4:1 hexane/EtOAc, R_f 0.21; HRMS calcd for $C_{13}H_{17}NO_4Na^+$ 274.104979, found m/z = 274.104797, error = 1.0 ppm. IR (neat, cm^{-1}) 2223, C≡N; 1736, C═O; 1725, C═O; 1628, C═C; ^1H NMR (400 MHz, $CDCl_3$) δ 3.83 (3H, s) 3.66 (3H, s) 3.17 (1H, m) 2.64−2.41 (4H, m) 1.12 (3H, s) 1.00 (3H, s); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 172.3, 162.5, 149.8, 121.0, 114.8, 52.4, 51.9, 51.5, 49.1, 41.8, 33.2, 29.1, 22.9.

Ethyl 2-Cyano-5-(2-ethoxy-2-oxoethyl)-4,4-dimethylcyclopent-1-enecarboxylate (2h). 1h (601 mg, 2.38 mmol) and PBu_3 (0.72 mmol) afforded 365 mg (55%) of **2h**: colorless oil; TLC, 4:1 hexanes/EtOAc, R_f 0.31; HRMS calcd for $C_{15}H_{21}NO_4Na^+$ 302.136279, found m/z = 302.135945, error = 1.1 ppm. IR (neat, cm^{-1}) 2223, C≡C; 1735, C═O; 1720, C═O; 1625, C═C; ^1H NMR (400 MHz, $CDCl_3$) δ 4.28 (2H, m) 4.11 (2H, m) 3.17 (1H, m) 2.51 (4H, m) 1.34 (3H, t, J =7.2 Hz) 1.23 (3H, t, J =7.2 Hz) 1.12 (3H, s) 1.01 (3H, s); ^{13}C (100.52 MHz NMR) ($CDCl_3$) δ 171.9, 162.1, 150.1, 120.5, 114.9, 61.8, 60.7, 51.4, 49.1, 41.7, 33.4, 29.2, 23.0, 14.1, 13.9.

3-(Cyanomethyl)-5,5-dimethyl-2-(phenylsulfonyl)cyclopent-1-enecarbonitrile (2i). 1i (26 mg, 0.095 mmol) and PBu_3 (0.014 mmol) afforded 14 mg (50%) of **2i**: yellow oil; TLC, 1:2 hexane/Et_2O, R_f 0.14; HRMS calcd for $C_{16}H_{16}N_2O_2SNa^+$ 323.0831, found m/z = 323.0828, error = 1 ppm; IR (neat, cm^{-1}) 2251, C≡N; 2226, C≡N; 1327, SO_2 ss; 1157, SO_2 as; ^1H NMR (400 MHz, $CDCl_3$) δ 8.05−7.99 (2H, m) 7.81−7.74 (1H, m) 7.70−7.62 (2H, m) 3.52−3.44 (1H, m) 3.00 (1H, dd, J = 16.8, 4.1 Hz) 2.79 (1H, dd, J = 16.8, 8.1 Hz) 2.31 (1H, dd, J = 13.6, 8.5 Hz) 1.86 (1H, dd, J = 13.6, 7.0 Hz) 1.37 (3H, s) 1.22 (3H, s); ^{13}C NMR (100.57 MHz, $CDCl_3$) δ 152.7, 138.1, 135.2, 134.2, 130.0, 128.4, 116.9, 111.3, 48.4, 43.6, 41.8, 27.4, 26.9, 22.4.

Ethyl 2-Cyano-5-(2-ethoxy-2-oxoethyl)-4,4-dimethylcyclopent-1-enecarboxylate-(5-d_1) (11). 10 (40 mg, 0.16 mmol) and PBu_3 (0.05 mmol) afforded 26 mg (59%) of **11**: yellow oil; TLC, 4:1 hexanes/EtOAc, R_f 0.31; HRMS calcd for $C_{15}H_{20}DNO_4Na^+$ 303.14256, found m/z = 303.142215, error = 1.1 ppm. IR (neat, cm^{-1}) 2224, C≡N; 1732, C═O; 1721, C═O; 1624, C═C; ^1H NMR (400 MHz, $CDCl_3$) δ 4.28 (2H, m) 4.11 (2H, m) 2.51 (2H, dd, J = 63.0, 17.4 Hz) 2.48 (2H, dd, J = 40.0, 16.3 Hz) 1.34 (3H, t, J = 7.2 Hz) 1.23 (3H, t, J = 7.2 Hz) 1.12 (3H, s) 1.01 (3H, s); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 171.9, 162.1, 150.1, 120.6, 114.9, 61.8, 60.7, 51.0 ($J_{C\text{-}D}$= 20.8 Hz), 49.1, 41.6, 33.3, 29.2, 23.0, 14.1, 13.9.

(2-Benzenesulfonyl-3-methoxy-4,4-dimethylcyclopent-2-enyl)acetonitrile (8). Alkynyl sulfone **1i** (29 mg, 0.11 mmol) was added to an N_2-purged flask with CH_3CN (2.2 mL). Methanol (4.7 μL, 0.12 mmol) was added followed by PBu_3 (6.6 μL, 0.03 mmol), and the reaction was stirred for 3 h. Ethyl iodide (10 μL) was added to quench the catalyst. The solution was concentrated (aspirator) to afford a 4:1 ratio of products **8** and **9**. Purification by flash chromatography (2 × 16 cm), 1:1 hexane/Et_2O, afforded 24.4 mg of pure **8** (73%): amorphous solid; TLC, 1:1 hexane/Et_2O, R_f 0.29; HRMS calcd for $C_{16}H_{19}NO_3SNa^+$ 328.0984, found m/z = 328.0978, error = 2 ppm; IR (neat, cm^{-1}) 2246, C≡N; 1602, ═C—O; 1304, SO_2; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95−7.88 (2H, m) 7.65−7.58 (1H, m) 7.58−7.49 (2H, m) 3.92 (3H, s) 3.22 (1H, dddd, J = 8.1, 8.1, 5.9, 3.7 Hz) 3.00 (1H, dd, J = 16.8, 3.7 Hz) 2.70 (1H, dd, J = 16.8, 8.1 Hz) 2.10 (1H, dd, J = 13.1, 8.8 Hz) 1.68 (1H, dd, J = 13.1, 5.9 Hz) 1.28 (3H, s) 1.15 (3H, s); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 175.0, 142.2, 129.0, 127.0, 118.3, 115.1, 61.6, 45.0, 42.8, 37.3, 33.7, 26.9, 26.9, 24.0.

dx.doi.org/10.1021/jo3015769 | J. Org. Chem. 2012, 77, 7768−7774

■ ASSOCIATED CONTENT

Supporting Information

General experimental information and ^{1}H and ^{13}C spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The authors acknowledge the donors of the American Chemical Society Petroleum Research Fund (42856-GB1) for support of this research and the National Science Foundation for instrumentation support (CHE-0958425). We also thank Prof. Edwin Vedejs (University of Michigan) for helpful conversations and samples of phosphine catalysts **12** and **13**.

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