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Palladium-catalyzed decarboxylative coupling of alkynyl carboxylic acids and alkenyl tosylates for the synthesis of enynones

*Subeen Yu, Eunjeong Cho, Jimin Kim, and Sunwoo Lee**

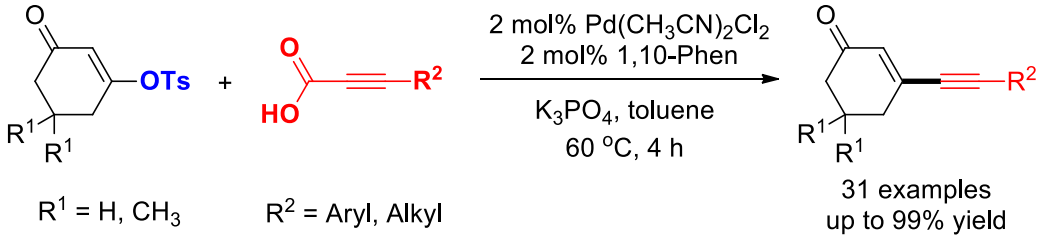
Department of Chemistry, Chonnam National University, Gwangju, 61186, Republic of Korea

Corresponding Author: S. Lee (sunwoo@chonnam.ac.kr)

Keywords: palladium, decarboxylative coupling, propiolic acid, 3-oxoalkenyl tosylate, 3-(1-alkynyl)-2-cyclohexen-1-one

Abstract

A palladium-catalyzed decarboxylative coupling reaction was developed for the synthesis of 3-(1-alkynyl)-2-cyclohexen-1-ones. A variety of alkynyl carboxylic acids were coupled with 3-oxocyclohexenyl tosylates to afford the corresponding enynones in good to excellent yields. The developed catalytic system is phosphine free and showed good tolerance towards various functionalities such as chloride, cyano, nitro, ester, ketone, aldehyde, and alcohol groups. In addition, phenylpropiolic acid exhibited higher reactivity in the reaction with alkenyl toslyate than phenyl acetylene.

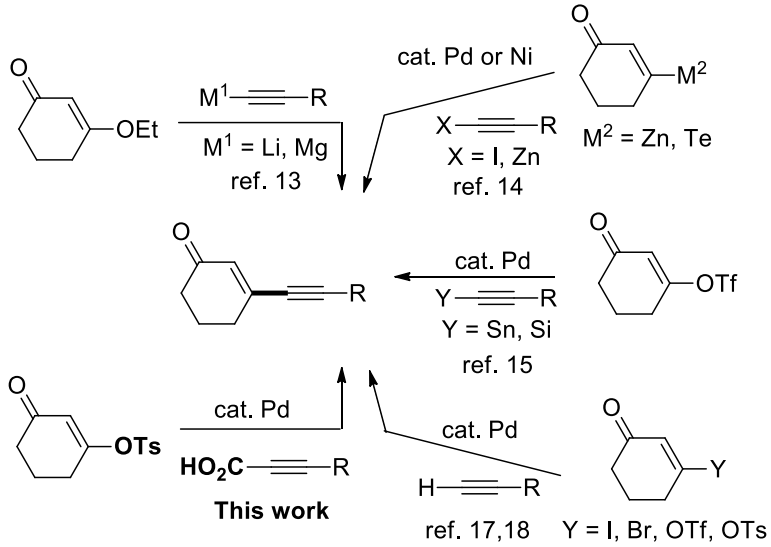


INTRODUCTION

Conjugated enynes have been applied in electro- and optical materials, pharmaceuticals,[1] and as useful synthetic building blocks because they can be transformed into various important moieties.[2] Among them, conjugated enynones have garnered attention in the synthesis of bioactive agents[3] and have been used as starting materials for the preparation of useful organic molecules such as allenes,[4] cyclooctatetraenes,[5] pyrrolizines,[6] chromenes,[7] fused rings,[8] and polycyclic compounds.[9]

Many synthetic methods have been developed. Specifically, allylic alcohol rearrangements,[10] copper-catalyzed multicomponent reactions,[11] and nucleophilic 1,2-additions[12] have been reported. The coupling reactions of 3-oxoalkenyl and alkynyl compounds are straightforward as shown in Scheme 1. Reactions with ethoxyalkenes and alkynyl lithium or magnesium have been used in early stage syntheses.[13] However, such approaches suffer from low functional group tolerance. To address this problem, palladium or nickel-catalyzed coupling reactions have been developed. Alkenyl zinc, telluride, and halides have been employed in the coupling reaction with alkynyl compounds.[14] In addition, an alkenyl triflate was reacted with alkynyl stannane or silane in the presence of a palladium catalyst.[15] One of the most efficient methods is the Sonogashira coupling of alkenyl halides and terminal alkynes.[16] Alkenyl triflates were also employed as coupling partners in the synthesis of 3-(1-alkynyl)-2-cyclohexen-1-ones.[17] Fu and co-workers reported a palladium-catalyzed coupling reaction with 3-oxocyclohex-1-enyl tosylates and terminal acetylenes.[18] They showed good yields of the coupled products; however, only one example was shown in the case of the reaction with an aryl acetylene.

Scheme 1. Synthesis of 3-(1-alkynyl)-2-cyclohexen-1-ones.



Since we first reported a decarboxylative coupling reaction with an arylpropiolic acid, continuous efforts towards the expansion of decarboxylative coupling reactions have been put forth in our lab.[19] Aryl halides are mainly used as coupling partners in the presence of palladium or copper catalysts. Recently, we reported that aryl silane and boronic acid can also be employed as coupling partners in the presence of a nickel catalyst.[20] In addition, a variety of decarboxylative coupling reactions have been reported.[21]

However, the decarboxylative coupling reaction with vinyl substrate has much less studied than those with aryl substrate. Realizing the need for a simple and efficient method for the decarboxylative coupling with alkenyl tosylate, we focused on a decarboxylative coupling reaction with 3-oxocyclohex-1-enyl tosylates. Alkenyl tosylates are readily prepared, stable, and cost efficient. Moreover, we envisioned that the facile accessibility of a variety of aryl propiolic acids would provide diverse 3-(1-alkynyl)-2-cyclohexen-1-ones.

RESULTS AND DISCUSSION

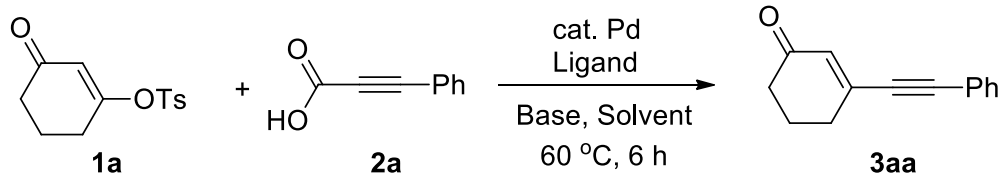
First, 3-oxocyclohex-1-enyl tosylate was prepared from 1,3-cyclohexanedione and *p*-toluenesulfonyl chloride in the presence of a base, and was allowed to react with phenylpropiolic acid under various reaction conditions. The results are summarized in Table.

Using $Pd(MeCN)_2Cl_2$ as the palladium source, various ligands were tested in the presence of K_3PO_4. The results are summarized in Table 1. Chelating phosphine ligands such as dppb, dppe, Xantphos, and Josiphos did not give satisfactory results (entries 1–4). It was found that Josiphos, which showed good activity in the decarboxylative coupling reaction with aryltosylates and arylpropiolic acids, was not a suitable ligand in this coupling reaction. X-Phos and PPh_3 afforded the desired products in 42% and 79% yields, respectively (entries 5 and 6). On the other hand, PPh_3, which was a good ligand in the coupling reaction with 3-oxocyclohex-1-enyl tosylate and terminal acetylenes, also showed reasonable activity in the decarboxylative coupling reaction. When chelating diamine-type ligands such as *t*-BuBipy, Me_4Phen, Me_2Phen, and 1,10-Phen were employed, the yields of the products improved in most cases, except with Me_2Phen (entries 7–10). The steric hindrance of Me_2Phen might reduce the yield of the product (entry 9). 1,10-Phen was chosen as a suitable ligand (entry 10). This phosphine free system is the advantage over the previous report.[16]

Among the tested palladium sources, $Pd(MeCN)_2Cl_2$ resulted in a higher yield than other palladium sources such as Pd(allyl)Cl, $Pd(OAc)_2$, $Pd(acac)_2$, $Pd(dba)_2$, and $Pd_2(dba)_3$ (entries 11–15). When carbonate bases such as Cs_2CO_3, K_2CO_3, and Na_2CO_3 were employed instead of K_3PO_4, the desired products formed in 59%, 70%, and 81% yields, respectively (entries 16–18). The reactions with organic bases such as 1,8-diazabicylco(5.4.0)undec-7-ene (DBU), *i*-Pr_2EtN, and *i*-Pr_2NH provided the desired products in 32%, 67%, and 83% yields, respectively (entries

19–21). The reactions in ether-type solvents such as 1,4-dioxane and THF afforded the desired products in higher yields than in polar solvents such as DMF, NMP, and DMSO (entries 22–26). However, they did not result in a higher yield than that obtained in toluene.

Table 1. Optimization of synthesis of 3-(1-phenylethynyl)-2-cyclohexen-1-ones.[a]

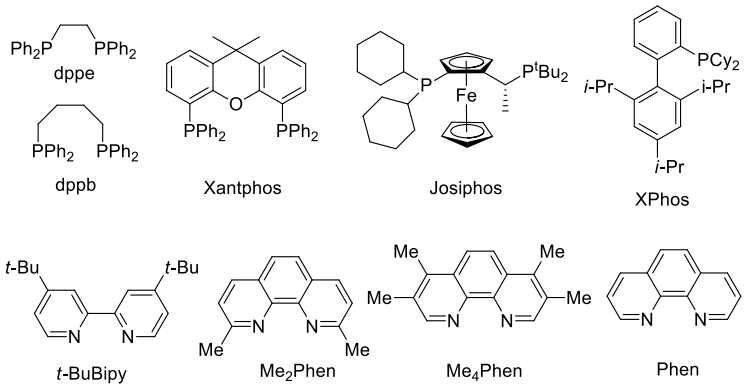


1a **2a** **3aa**

Entry	Pd	Ligand	Base	Solvent	Yield (%)[b]
1	$Pd(CH_3CN)_2Cl_2$	Dppb	K_3PO_4	Toluene	34
2	$Pd(CH_3CN)_2Cl_2$	Dppe	K_3PO_4	Toluene	30
3	$Pd(CH_3CN)_2Cl_2$	Xantphos	K_3PO_4	Toluene	10
4	$Pd(CH_3CN)_2Cl_2$	Josiphos	K_3PO_4	Toluene	40
5	$Pd(CH_3CN)_2Cl_2$	X-Phos	K_3PO_4	Toluene	42
6	$Pd(CH_3CN)_2Cl_2$	PPh_3	K_3PO_4	Toluene	79
7	$Pd(CH_3CN)_2Cl_2$	*t*-BuBipy	K_3PO_4	Toluene	95
8	$Pd(CH_3CN)_2Cl_2$	Me_4Phen	K_3PO_4	Toluene	96
9	$Pd(CH_3CN)_2Cl_2$	Me_2Phen	K_3PO_4	Toluene	41
10	$Pd(CH_3CN)_2Cl_2$	1,10-Phen	K_3PO_4	Toluene	98
11	Pd(allyl)Cl	1,10-Phen	K_3PO_4	Toluene	81
12	$Pd(OAc)_2$	1,10-Phen	K_3PO_4	Toluene	77
13	$Pd(acac)_2$	1,10-Phen	K_3PO_4	Toluene	55
14	$Pd(dba)_2$	1,10-Phen	K_3PO_4	Toluene	82
15	$Pd_2(dba)_3$	1,10-Phen	K_3PO_4	Toluene	67
16	$Pd(CH_3CN)_2Cl_2$	1,10-Phen	Cs_2CO_3	Toluene	59
17	$Pd(CH_3CN)_2Cl_2$	1,10-Phen	K_2CO_3	Toluene	70
18	$Pd(CH_3CN)_2Cl_2$	1,10-Phen	Na_2CO_3	Toluene	81
19	$Pd(CH_3CN)_2Cl_2$	1,10-Phen	DBU	Toluene	32
20	$Pd(CH_3CN)_2Cl_2$	1,10-Phen	i-Pr_2EtN	Toluene	67
21	$Pd(CH_3CN)_2Cl_2$	1,10-Phen	i-Pr_2NH	Toluene	83
22	$Pd(CH_3CN)_2Cl_2$	1,10-Phen	K_3PO_4	1,4-Dioxane	86
23	$Pd(CH_3CN)_2Cl_2$	1,10-Phen	K_3PO_4	THF	85
24	$Pd(CH_3CN)_2Cl_2$	1,10-Phen	K_3PO_4	DMF	79
25	$Pd(CH_3CN)_2Cl_2$	1,10-Phen	K_3PO_4	NMP	46
26	$Pd(CH_3CN)_2Cl_2$	1,10-Phen	K_3PO_4	DMSO	57

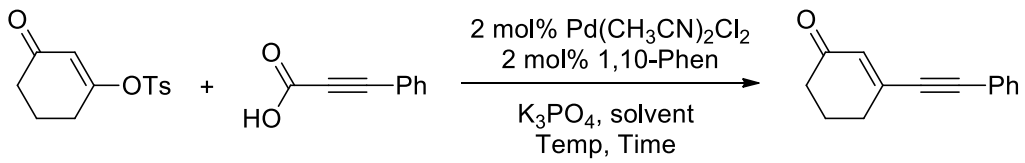
[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.2 mmol), Pd (0.004 mmol), ligand (0.004 mmol), and base (0.24 mmol) were reacted in a solvent (1.0 mL) at 60 °C for 6 h. [b]Determined by gas chromatography with an internal standard.

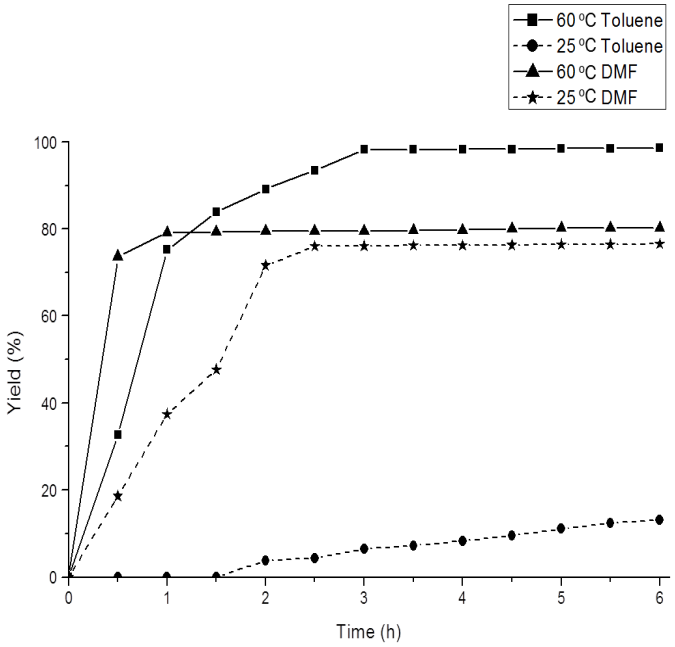
Ligand



With the optimized reaction conditions in hand (i.e., $Pd(MeCN)_2Cl_2$, 1,10-Phen, and K_3PO_4 in toluene), the coupling reaction was carried out at different temperatures in order to identify the optimal reaction time and temperature. As shown in Figure 1, when the reaction was carried out at 60 °C in toluene, the reaction was complete within 3 h and the product was obtained in 98% yield. At 60 °C in DMF, the reaction was complete within 1 h, and the product yield was 79%; however, the yield did not increase after 6 h. When the reaction was carried out at 25 °C, the reaction in toluene showed a very low yield, but the reaction in DMF afforded 75% yield of the product in 3 h. Based on these results, the optimized conditions were determined to be 60 °C in toluene for 4 h.

Figure 1. Optimization of reaction time and temperature.

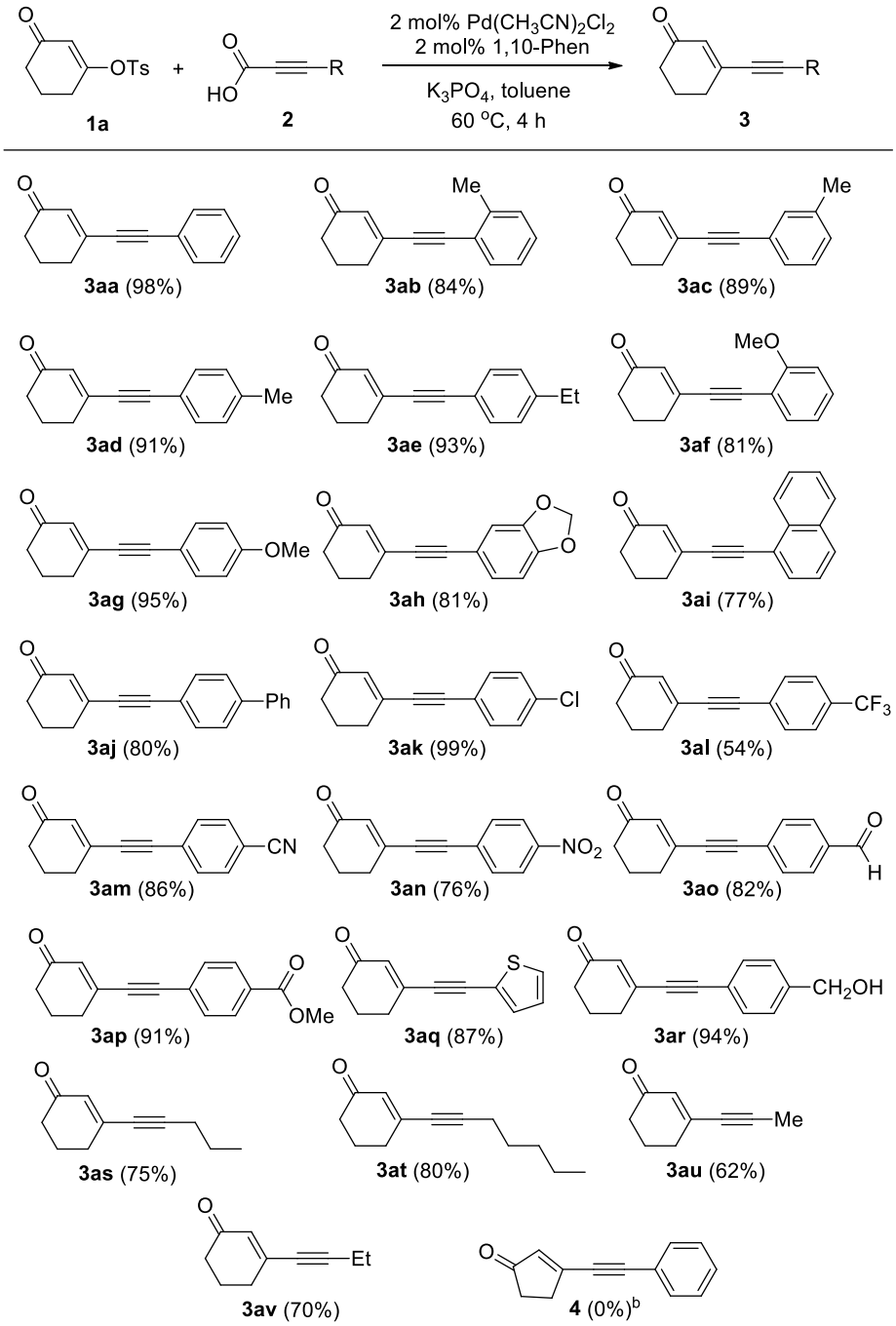




To evaluate the scope of the methodology, a variety of arylpropiolic acids were employed in the reaction with enone tosylates. The results are summarized in Scheme 2. As expected, phenylpropiolic acid afforded desired product **3aa** in 98% yield. Methyl- and ethyl-substituted phenylpropiolic acids **2b**, **2c**, **2d**, and **2e** provided the corresponding enynones **3ab**, **3ac**, **3ad**, and **3ae** in 84%, 89%, 91%, and 93% yields, respectively. The alkoxy-substituted phenylpropiolic acids resulted in good to excellent yields of **3af**, **3ag**, and **3ah**. Naphthyl- and biphenyl-substituted propiolic acids gave **3ai** and **3aj** in 77% and 80% yields, respectively. Interestingly, an arylpropiolic acid with a chloride group provided **3ak** in 99% yield without the concomitant coupling reaction at the chloride. The trifluoromethyl-substituted analogue gave a low yield of **3al**. Arylpropiolic acids bearing electron-withdrawing groups such as cyano, nitro, aldehyde, and ester moieties provided **3am**, **3an**, **3ao**, and **3ap** in good to excellent yields. 3-(Thiophen-2-yl)propiolic acid gave the corresponding product in 87% yield. The hydroxymethyl-substituted starting material gave the desired product in 94% yield. In addition, alkyl-substituted

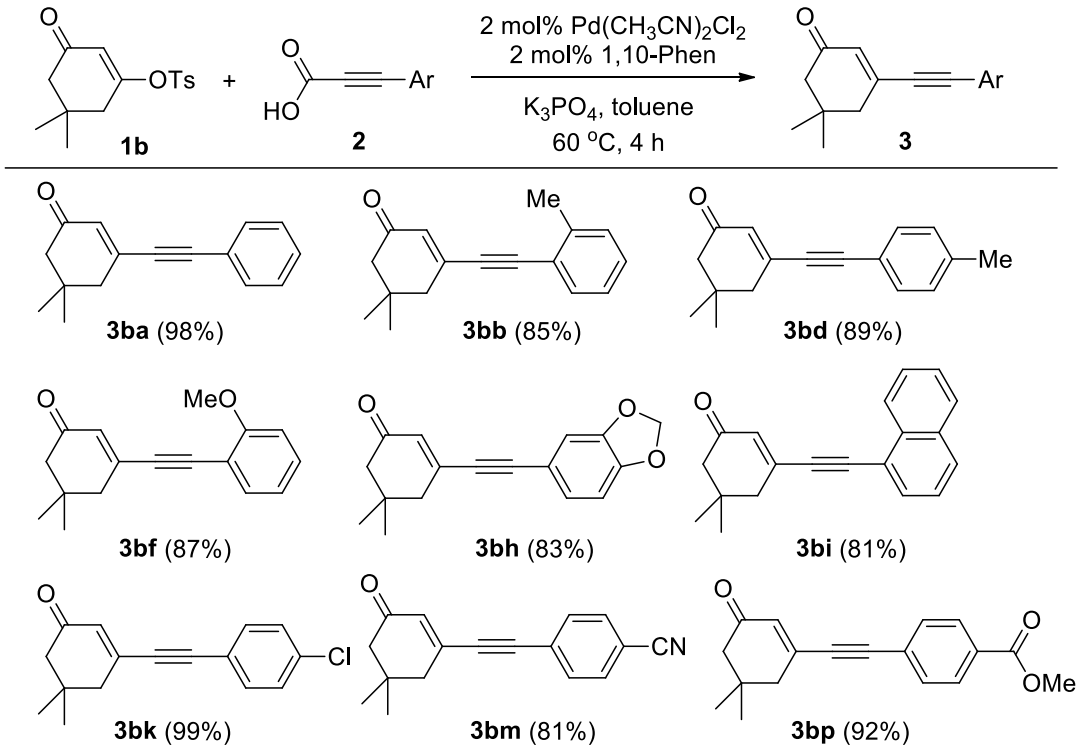
propiolic acids such as hexynoic, octynoic, butynoic and pentynoic acids provided **3as**, **3at**, **3au** and **3av** in 75%, 80%, 62% and 70% yields, respectively. However, unfortunately, the reaction with 3-oxocyclopent-1-enyl tosylate and phenylpropiolic acid did not give the desired coupled product **4**.

Scheme 2. Decarboxylative coupling of alkynyl carboxylic acids and **1a.**[a]



[a]Reaction conditions: **1a** (2.0 mmol), **2** (2.0 mmol), $Pd(MeCN)_2Cl_2$ (0.04 mmol), 1,10-Phen (0.04mmol), and K_3PO_4 (2.4 mmol) were reacted in toluene (10.0 mL) at 60 ºC for 4 h. The numbers in parentheses are yields. [b]3-Oxocyclopent-1-enyl tosylate was used instead of **1a**.

Scheme 3. Decarboxylative coupling of alkynyl carboxylic acids and **1b**. [a]



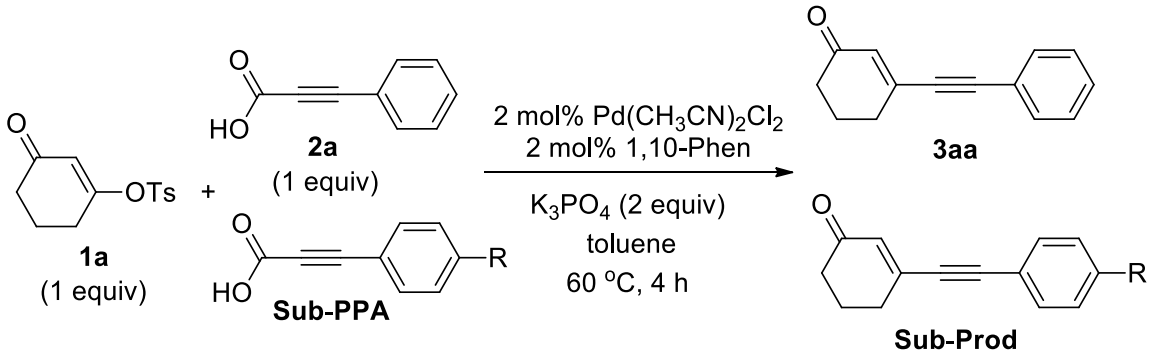
[a]Reaction conditions: **1b** (2.0 mmol), **2** (2.0 mmol), $Pd(MeCN)_2Cl_2$ (0.04 mmol), 1,10-Phen (0.04 mmol), and K_3PO_4 (2.4 mmol) were reacted in toluene (10.0 mL) at 60 ºC for 4 h. The numbers in parentheses are yield.

To expand the scope of enone tosylates, 5,5-dimethyl-3-oxocyclohex-1-enyl tosylate (**1b**) was also employed. As shown in Scheme 3, the reactions with a variety of arylpropiolic acids provided the desired coupled products in good to excellent yields. Compared to the reactions of alkenyl tosylate **1a**, the reactions with **1b** gave similar product yields in most cases. In addition, similar functional group tolerance was shown in the reaction with **1b**. However, the employment of an acyclic alkenyl tosylate was unsuccessful. When we attempted to react with phenyl propiolic acid and (*E*)-2-phenylethenoyl tosylate, the desired coupled product was not formed under this optimized condition.

To investigate the effect of substituents, phenylpropiolic acid (**2a**) was allowed to react with

substituted arylpropioic acids such as **3ad**, **3ag**, and **3ap**. The results are summarized in Table 2. In the competitive reactions, phenylpropiolic acid gave a higher yield than **2d** and **2p**, which had methyl and ester groups, respectively (entries 1 and 2). Methoxy-substituted arylpropiolic acid **2g** afforded **3ag** in a slightly higher yield than **3aa** (entry 3). From these results, we postulated that the reactivity of the arylpropiolic acid was not related to the substituent on the phenyl ring.

Table 2. Substituent effect on arylpropiolic acids.[a]



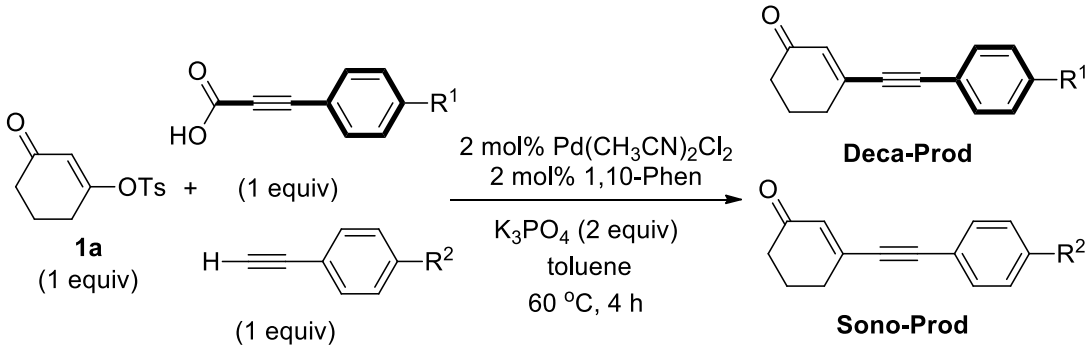
Entry	Sub-PPA	Product (Yield)[b]		Ratio
		3aa	**Sub-Prod**	**3aa/Sub-Prod**
1	**2d** (R = Me)	**3aa** (50%)	**3ad** (34%)	1/0.7
2	**2p** (R = CO_2Me)	**3aa** (41%)	**3ap** (36%)	1/0.9
3	**2g** (R = OMe)	**3aa** (41%)	**3ag** (45%)	1/1.1

[a]Reaction conditions: **1a** (0.3 mmol), **2a** (0.3 mmol), **Sub-PPA** (0.3 mmol), $Pd(MeCN)_2Cl_2$ (0.006 mmol), 1,10-Phen (0.006 mmol), and K_3PO_4 (0.6 mmol) were reacted in toluene (1.5 mL) at 60 °C for 4 h. [b]Determined by gas chromatography with an internal standard.

Competitive experiments were carried out in order to compare the relative reactivity of terminal alkynes and alkynyl carboxylic acids towards alkenyl tosylates (Table 3). When equal amounts of *para*-tolylpropiolic acid and phenylacetylene were allowed to react with alkenyl tosylate **1a**

under the optimized conditions, the decarboxylative coupling product formed at a 4.7/1 ratio over the Sonogashira coupling product (entry 1). To account for electronic effects of the substituents on the phenyl rings, phenylpropiolic acid and *para*-tolylacetylene were employed in the competitive reaction. The decaroxylative coupling product still formed at a 3.9/1 ratio over the Sonogashira coupling product. Accordingly, we determined that the decarboxylic coupling was much more reactive than the Sonogashira coupling in the reaction with alkenyl tosylate **1a**.

Table 3. Competitive decarboxylative and Sonogashira coupling reactions.[a]



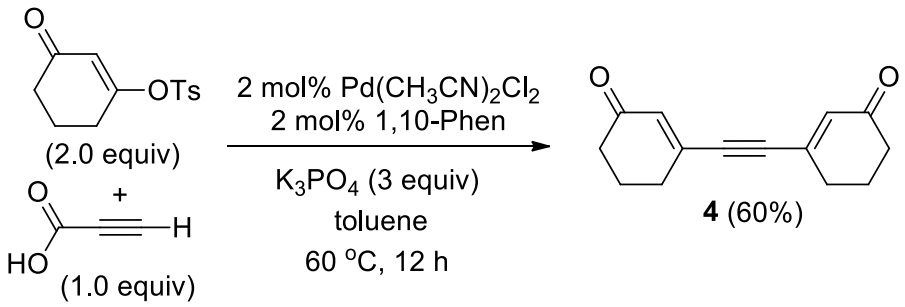
Entry	R^1	R^2	Product (Yield)[b]		Ratio
			Deca-Prod	**Sono-Prod**	**Deca-Prod/ Sono-Prod**
1	H	Me	**3aa** (71%)	**3ad** (15%)	4.7/1
2	Me	H	**3ad** (70%)	**3aa** (18%)	3.9/1

[a]Reaction conditions: **1a** (0.3 mmol), arylpropiolic acid (0.3 mmol), arylalkyne (0.3 mmol), $Pd(MeCN)_2Cl_2$ (0.006 mmol), 1,10-Phen (0.006 mmol), and K_3PO_4 (0.6 mmol) were reacted in toluene (1.5 mL) at 60 °C for 4 h. [b]Determined by gas chromatography with an internal standard.

Propiolic acid reacted with aryl halides to produce symmetrically diaryl alkynes. To evaluate the reactivity of propiolic acids towards alkenyl tosylates **1a**, propiolic acids were allowed to react

with **2** equivalents of **1a** under the optimized conditions. As shown in Scheme 4, disubstituted alkynes **4** was formed in 60% yield.

Scheme 4. Synthesis of symmetric dialkenyl alkynes.[a]



[a]Reaction conditions: **1a** (2.0 mmol), propiolic acid (1.0 mmol), $Pd(MeCN)_2Cl_2$ (0.004 mmol), 1,10-Phen (0.004 mmol), and K_3PO_4 (3.0 mmol) were reacted in toluene (4.0 mL) at 60 ºC for 12 h. The numbers in parentheses are yield.

CONCLUSION

In conclusion, we developed a decarboxylative coupling reaction between alkenyl carboxylic acids and 3-oxocyclohex-1-enyl tosylates (**1a** and **1b**) in the presence of a palladium catalyst. This catalytic system is phosphine free and works under mild conditions. The decarboxylative coupling reactions provided the desired products in good to excellent yields and showed good tolerance towards various functional groups such as chloride, cyano, nitro, aldehyde, ester, ketone, and alcohol moieties. Toluene was determined to be the best solvent, but DMF afforded a higher yield than toluene at 25 °C. Competitive experiments with phenylpropiolic acids and substituted arylpropilic acids confirmed that there were no substituent effects. Notably, phenylpropiolic acid showed a higher reactivity than phenylacetylene.

EXPERIMENTAL SECTION

General Experimental Procedure

Decarboxylative coupling reactions of alkynyl carboxylic acids and alkenyl tosylates: Alkynyl carboxylic acid (2.0 mmol), 1,10-phenanthroline (7 mg, 0.04 mmol), bis(acetonitrile)dichloropalladium(II) (10 mg, 0.04 mmol), K_3PO_4 (849 mg, 4.0 mmol), alkenyl tosylate (2.0 mmol), and toluene (6.0 mL) were added to the reaction vial. The mixture was stirred at 60 °C for 4 h. The mixture was filtered once the reaction was complete, the filtrate was washed with water/brine, and the aqueous solution was extracted with Et_2O. The organic layer was dried over magnesium sulfate. Evaporation of the solvent under reduced pressure provided the crude product, which was purified by column chromatography on silica gel.(eluent : pentane / ethyl acetate = 5 / 1)

3-(Phenylethynyl)cyclohex-2-enone (3aa)[17c]

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and 3-phenylpropiolic acid (**2a**) (292 mg, 2.0 mmol) afforded 3-(phenylethynyl)cyclohex-2-enone (**3aa**) (385 mg, 1.96 mmol, 98% yield); Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50-7.48 (m, 2H), 7.38-7.34 (m, 3H), 6.29 (t, J = 1.7 Hz, 1H), 2.55 (td, J = 6.1 Hz, 1.7 Hz, 2H), 2.46-2.43 (m, 2H), 2.10-2.05 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 198.7, 143.3, 132.4, 131.9, 129.4, 128.5, 122.0, 99.7, 88.4, 37.3, 30.5, 22.6; MS (EI) m/z = 196 (M^+).

3-(*o*-Tolylethynyl)cyclohex-2-enone. (3ab)

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and 3-(*o*-tolyl)propiolic acid (**2b**) (320 mg, 2.0 mmol) afforded 3-(*o*-tolylethynyl)cyclohex-2-enone (**3ab**) (353 mg, 1.68 mmol, 84% yield); Yellow solid; mp 42.3-44.0 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (dd, J = 7.6 Hz, 1.0

Hz, 1H), 7.28 (td, *J* = 7.5 Hz, 1.3 Hz, 1H), 7.24-7.23 (m, 1H), 7.19-7.16 (m, 1H), 6.30 (t, *J* = 1.6 Hz, 1H), 2.57 (td, *J* = 6.1 Hz, 1.6 Hz, 2H), 2.47-2.44 (m, 5H), 2.12-2.06 (m, 2H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$)) δ 198.7, 143.6, 140.7, 132.2, 132.1, 129.7, 129.6, 125.8, 121.7, 98.8, 92.3, 37.3, 30.6, 22.6, 20.6; HRMS (EI-MSES double focusing) m/z: cacld. for $C_{15}H_{14}O$ (M^+): 210.1045, found: 210.1046.

3-(*m*-Tolylethynyl)cyclohex-2-enone (3ac)

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and 3-(*m*-tolyl)propiolic acid (**2c**) (320 mg, 2.0 mmol) afforded 3-(*m*-tolylethynyl)cyclohex-2-enone (**3ac**) (374 mg, 1.78 mmol, 89% yield); Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33-7.32 (m, 1H), 7.32-7.30(m, 1H), 7.26 (t, *J* = 7.4 Hz, 1H), 7.22-7.19 (m, 1H), 6.30 (t, *J* = 1.7 Hz, 1H), 2.56 (td, *J* = 6.1Hz, 1.6Hz, 2H), 2.46 (t, *J* = 6.7 Hz, 5H), 2.11-2.06 (m, 2H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 198.8, 143.5, 138.3, 132.5, 132.3, 130.4, 129.1, 128.4, 121.8, 100.1, 88.1, 37.3, 30.6, 22.6, 21.2; HRMS (EI-MSES double focusing) m/z cacld. for $C_{15}H_{14}O$ (M^+): 210.1045, found: 210.1045.

3-(*p*-Tolylethynyl)cyclohex-2-enone (3ad)

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and 3-(*p*-tolyl)propiolic acid (**1d**) (320 mg, 2.0 mmol) afforded 3-(*p*-tolylethynyl)cyclohex-2-enone (**3ad**) (383 mg, 1.82 mmol, 91% yield); Yellow solid; mp 79.1-82.0 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.1 Hz, 2H), 7.18 (d, *J* = 8.5 Hz, 2H), 6.29 (t, *J* = 1.6 Hz, 1H), 2.56 (td, *J* = 6.1 Hz, 1.6 Hz, 2H), 2.46 (t, *J* = 6.8 Hz, 2H), 2.39 (s, 3H), 2.11-2.06 (m, 2H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 198.8, 143.6, 139.9, 132.1, 131.9, 129.3, 118.9, 100.2, 88.0, 37.4, 30.6, 22.7, 21.6; HRMS (EI-MSES double focusing) m/z cacld. for $C_{15}H_{14}O$ (M^+): 210.1045, found: 210.1048.

3-((4-Ethylphenyl)ethynyl)cyclohex-2-enone (3ae)

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and 3-(4-ethylphenyl)propiolic acid (**2e**)

(348 mg, 2.0 mmol) afforded 3-((4-ethylphenyl)ethynyl)cyclohex-2-enone (**3ae**) (417 mg, 1.86 mmol, 93% yield); Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.3 Hz, 2H), 7.21-7.19 (m, 2H), 6.29 (t, *J* = 1.7 Hz, 1H), 2.68 (q, *J* = 7.6 Hz, 2H), 2.56 (td, *J* = 6.1 Hz, 1.6Hz, 2H), 2.45 (t, *J* = 6.7 Hz, 2H), 2.11-2.06 (m, 2H), 1.25 (t, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 198.8, 146.2, 143.7, 132.1, 132.0, 128.1, 119.1, 100.2, 88.0, 37.4, 30.6, 28.9, 22.6, 15.3; HRMS (EI-MSES double focusing) m/z cacld. for $C_{16}H_{16}O$ (M^+): 224.1201, found: 224.1200.

3-((2-Methoxyphenyl)ethynyl)cyclohex-2-enone (3af)

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and 3-(2-methoxyphenyl)propiolic acid (**2f**) (352 mg, 2.0 mmol) afforded 3-((2-methoxyphenyl)ethynyl)cyclohex-2-enone (**3af**) (367 mg, 1.62 mmol, 81% yield); Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 7.5 Hz, 1.6 Hz, 1H), 7.39-7.35 (m, 1H), 6.95 (td, *J* = 7.5 Hz, 1.0 Hz, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.33 (t, *J* = 1.6 Hz, 1H), 3.91 (s, 3H), 2.59 (td, *J* = 6.1 Hz, 1.6 Hz, 2H), 2.47-2.44 (m, 2H), 2.11-2.06 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 198.8, 160.2, 143.7, 133.8, 132.2, 131.1, 120.6, 111.2, 110.8, 96.5, 92.5, 55.8, 37.4, 30.6, 22.7; HRMS (EI-MSES double focusing) m/z cacld. for $C_{15}H_{14}O_2$ (M^+): 226.0994, found: 226.0992.

3-((4-Methoxyphenyl)ethynyl)cyclohex-2-enone (3ag)[17c]

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and 3-(4-methoxyphenyl)propiolic acid (**2g**) (352 mg, 2.0 mmol) afforded 3-((4-methoxyphenyl)ethynyl)cyclohex-2-enone (**3ag**) (430 mg, 1.9 mmol, 95% yield); Yellow solid; mp 95.0-96.0 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44-7.41 (m, 2H), 6.89-6.86 (m, 2H), 6.25 (t, *J* = 1.6 Hz. 1H), 3.82 (s, 3H), 2.53 (td, *J* = 6.1 Hz, 1.6 Hz, 2H), 2.44-2.41 (m, 2H), 2.08-2.03(m, 2H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 198.6, 160.5, 143.7, 133.6, 131.5, 114.1, 113.9, 100.3, 87.6, 55.3, 37.2, 30.5, 22.6; MS (EI) m/z = 226 (M^+).

3-(Benzo[d][1,3]dioxol-5-ylethynyl)cyclohex-2-enone (3ah)

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and 3-(benzo[d][1,3]dioxol-5-yl)propiolic acid (**2h**) (380 mg, 2.0 mmol) afforded 3-(benzo[d][1,3]dioxol-5-ylethynyl)cyclohex-2-enone (**3ah**) (389 mg, 1.62 mmol, 81% yield); Yellow solid; mp 119.0-120.4 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (dd, *J* = 8.1, 1.6Hz, 1H), 6.93 (d, *J* = 1.6 Hz, 1H), 6.80 (d, *J* = 8.1 Hz, 1H), 6.26 (t, *J* = 1.6 Hz, 1H), 6.01 (s, 2H), 2.53 (td, *J* = 6.1 Hz, 1.6Hz, 2H), 2.44 (t, *J* = 6.7 Hz, 2H), 2.09-2.04 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 198.7, 149.0, 147.6, 143.5, 131.9, 127.2, 115.1, 111.7, 108.7, 101.6, 100.1, 87.3, 37.3, 30.5, 22.6; HRMS (EI-MSES double focusing) m/z cacld. for $C_{15}H_{12}O_3$ (M^+): 240.0786, found: 240.0784.

3-(Naphthalen-1-ylethynyl)cyclohex-2-enone (3ai)

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and 3-(naphthalen-1-yl)propiolic acid (**2i**) (392 mg, 2.0 mmol) afforded 3-(naphthalen-1-ylethynyl)cyclohex-2-enone (**3ai**) (379 mg, 1.54 mmol, 77% yield); Yellow solid; mp 87.0-88.1 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29-8.27 (m, 1H), 7.92-7.88 (m, 2H), 7.75 (dd, *J* = 7.2 Hz, 1.2 Hz, 1H), 7.64-7.55 (m, 2H) 7.48 (dd, *J* = 8.2 Hz, 7.2 Hz, 1H) 6.44 (t, *J* = 1.7 Hz, 1H), 2.69 (td, *J* = 6.1 Hz, 1.6 Hz, 2H), 2.50 (t, *J* = 6.7 Hz, 2H), 2.18-2.13 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 198.7, 143.4, 133.1, 133.0, 132.4, 131.3, 130.2, 128.5, 127.2, 126.7, 125.8, 125.2, 119.5, 97.9, 92.3, 37.4, 30.6, 22.7; HRMS (EI-MSES double focusing) m/z cacld. for $C_{18}H_{14}O$ (M^+): 246.0145, found: 246.1047.

3-([1,1'-Biphenyl]-4-ylethynyl)cyclohex-2-enone (3aj)

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and 3-([1,1'-biphenyl]-4-yl)propiolic acid (**2j**) (444 mg, 2.0 mmol) afforded 3-([1,1'-biphenyl]-4-ylethynyl)cyclohex-2-enone (**3aj**) (436 mg, 1.6 mmol, 80% yield); Yellow solid; mp 87.0-88.0 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63-7.60 (m, 4H), 7.59-7.57 (m, 2H), 7.49-7.45 (m, 2H), 7.39 (tt, *J* = 4.2 Hz, 1.5 Hz, 1H), 6.33 (t, *J* = 1.7 Hz, 1H), 2.59 (td, *J* = 6.1 Hz, 1.6 Hz, 2H), 2.49-2.46 (m, 2H), 2.13-2.08 (m, 2H);

$^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 198.7, 143.4, 142.2, 140.0, 132.4, 132.3, 128.9, 128.0, 127.2, 127.0, 120.8, 99.7, 89.1, 37.4, 30.5, 22.7; HRMS (EI-MSES double focusing) m/z cacld. for $C_{20}H_{16}O$ (M^+): 272.1201, found: 272.1200.

3-((4-Chlorophenyl)ethynyl)cyclohex-2-enone (3ak)

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and 3-(4-chlorophenyl)propiolic acid (**2k**) (361 mg, 2.0 mmol) afforded 3-((4-chlorophenyl)ethynyl)cyclohex-2-enone (**3ak**) (457 mg, 1.98 mmol, 99% yield); Yellow solid; mp 101.5-103.0 ^{o}C ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.8 Hz, 2H), 7.35 (d, *J* = 8.8 Hz, 2H), 6.30 (t, *J* = 1.7 Hz, 1H), 2.56 (td, *J* = 6.1 Hz, 1.7Hz, 2H), 2.46 (t, *J* = 6.7 Hz, 2H), 2.12-2.07 (m, 2H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 198.6, 142.9, 135.6, 133.1, 132.7, 128.9, 120.5, 98.3, 89.2, 37.3, 30.4, 22.6; HRMS (EI-MSES double focusing) m/z cacld. for $C_{14}H_{11}ClO$ (M^+): 230.0498, found: 230.0496.

3-((4-(Trifluoromethyl)phenyl)ethynyl)cyclohex-2-enone (3al)

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and 3-(4-(trifluoromethyl)phenyl)propiolic acid (**2l**) (428 mg, 2.0 mmol) afforded 3-((4-(trifluoromethyl)phenyl)ethynyl)cyclohex-2-enone (**3al**) (285 mg, 1.08 mmol, 54% yield); Brown oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63-7.58 (m, 4H), 6.32 (t, *J* = 1.7 Hz, 1H), 2.56 (td, *J* = 6.1 Hz, 1.7 Hz, 2H), 2.48-2.45 (m, 2H), 2.12-2.07 (m, 2H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 198.4, 142.4, 133.1, 132.1, 130.9(q, $J_{C\text{-}F}$ = 32.8 Hz), 125.7 (q, $J_{C\text{-}F}$ = 1.3 Hz), 125.4 (q, $J_{C\text{-}F}$ = 3.8 Hz), 123.6 (q, $J_{C\text{-}F}$ = 272.9 Hz), 97.4, 90.2, 37.3, 30.2, 22.5; HRMS (EI-MSES double focusing) m/z cacld. for $C_{15}H_{11}F_3O$ (M^+): 264.0762, found: 264.0765.

4-((3-Oxocyclohex-1-en-1-yl)ethynyl)benzonitrile (3am)

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and 3-(4-cyanophenyl)propiolic acid (**2m**) (342 mg, 2.0 mmol) afforded 4-((3-oxocyclohex-1-en-1-yl)ethynyl)benzonitrile (**3am**) (380

mg, 1.72 mmol, 86% yield); Yellow solid; mp 114.6-115.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.57 (d, *J* = 8.7 Hz, 2H), 6.32 (t, *J* = 1.7 Hz, 1H), 2.55 (td, *J* = 6.1Hz, 1.7 Hz, 2H), 2.47 (t, *J* = 6.7 Hz, 2H), 2.12-2.07 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) 198.4, 142.0, 133.5, 132.3, 132.1, 126.8, 118.2, 112.7, 96.9, 91.9, 37.3, 30.2, 22.6; HRMS (EI-MSES double focusing) m/z cacld. for $C_{15}H_{11}NO$ (M^+): 221.0841, found: 221.0842.

3-((4-Ntrophenyl)ethynyl)cyclohex-2-enone (3an)

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and 3-(4-nitrophenyl)propiolic acid (**2n**) (382 mg, 2.0 mmol) afforded 3-((4-nitrophenyl)ethynyl)cyclohex-2-enone (**3an**) (367 mg, 1.52 mmol, 76% yield); Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25-8.22 (m, 2H), 7.65-7.63 (m, 2H), 6.34 (t, *J* = 1.7 Hz, 1H), 2.56 (td, *J* = 6.1 Hz, 1.7 Hz, 2H), 2.49-2.46 (m, 2H), 2.13-2.08 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 198.3, 147.7, 141.9, 133.7, 132.7, 128.7, 123.7, 96.5, 92.6, 37.3, 30.2, 22.6; HRMS (EI-MSES double focusing) m/z cacld. for $C_{14}H_{11}NO_3$ (M^+): 241.0739, found: 241.0737.

4-((3-Oxocyclohex-1-en-1-yl)ethynyl)benzaldehyde (3ao)

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and 3-(4-formylphenyl)propiolic acid (**2o**) (348 mg, 2.0 mmol) afforded 4-((3-oxocyclohex-1-en-1-yl)ethynyl)benzaldehyde (**3ao**) (368 mg, 1.64 mmol, 82% yield); White solid; mp 106.0-108.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.1 (s, 1H), 7.90-7.88 (m, 2H), 7.66-7.64 (m, 2H), 6.34 (t, *J* = 1.7 Hz, 1H), 2.58 (td, *J* = 6.1 Hz, 1.7 Hz, 2H), 2.49-2.46 (m, 2H), 2.13-2.08 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 198.4, 191.2, 142.3, 136.2, 133.3, 132.4, 129.6, 128.0, 97.8, 91.6, 37.3, 30.3, 22.6; HRMS (EI-MSES double focusing) m/z cacld. for $C_{15}H_{12}O_2$ (M^+): 224.0837, found: 224.0837.

Mthyl 4-((3-oxocyclohex-1-en-1-yl)ethynyl)benzoate (3ap)

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and 3-(4-

(methoxycarbonyl)phenyl)propiolic acid (**2p**) (408 mg, 2.0 mmol) afforded methyl 4-((3-oxocyclohex-1-en-1-yl)ethynyl)benzoate (**3ap**) (463 mg, 1.82 mmol, 91% yield); Whtie solid; mp 111.2-113.1 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.7 Hz, 2H), 7.53 (d, *J* = 8.7 Hz, 2H), 6.30 (t, *J* = 1.7 Hz, 1H), 3.92 (s, 3H), 2.54 (td, *J* = 6.1 Hz, 1.7 Hz, 2H), 2.44(t, *J* = 6.7 Hz, 2H), 2.10-2.05 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 198.5, 166.3, 142.6, 133.1, 131.8, 130.5, 129.6, 126.5, 98.1, 90.5, 52.3, 37.3, 30.3, 22.6; HRMS (EI-MSES double focusing) m/z cacld. for $C_{16}H_{14}O_3$ (M^+): 254.0943, found: 254.0944.

3-(Tiophen-2-ylethynyl)cyclohex-2-enone (3aq)

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and 3-(thiophen-2-yl)propiolic acid (**2q**) (304 mg, 2.0 mmol) afforded 3-(thiophen-2-ylethynyl)cyclohex-2-enone (**3aq**) (352 mg, 1.74 mmol, 87% yield); Brown oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 5.1 Hz, 1.1 Hz, 1H), 7.33 (dd, *J* = 3.7 Hz, 1.1 Hz, 1H), 7.05 (dd, *J* = 5.1 Hz, 3.7 Hz, 1H), 6.28 (t, *J* = 1.6 Hz, 1H), 2.55 (td, *J* = 6.1 Hz, 1.6 Hz, 2H), 2.45 (t, *J* = 6.7 Hz, 2H), 2.11-2.06 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 198.5, 142.9, 133.7, 131.9, 129.4, 127.5, 121.9, 93.1, 92.4, 37.3, 30.2, 22.6; HRMS (EI-MSES double focusing) m/z cacld. for $C_{12}H_{10}OS$ (M^+): 202.0452, found: 202.0455.

3-((4-(Hydroxymethyl)phenyl)ethynyl)cyclohex-2-enone (3ar)

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and 3-(4-(hydroxymethyl)phenyl)propiolic acid (**2r**) (352 mg, 2.0 mmol) afforded 3-((4-(hydroxymethyl)phenyl)ethynyl)cyclohex-2-enone (**3ar**) (425 mg, 1.88 mmol, 94% yield); White solid; mp 103.6-105.2 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.3 Hz, 2H), 7.38 (d, *J* = 8.6 Hz, 2H), 6.30 (t, *J* = 1.65 Hz, 1H), 4.74 (s, 2H), 2.57 (td, *J* = 6.1Hz, 1.6Hz, 2H), 2.46 (t, *J* = 6.73 Hz, 2H), 2.12-2.06 (m, 2H), 1.74 (br, s, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 198.7, 143.4, 142.4, 132.4, 132.1, 126.8, 121.1, 99.6, 88.5, 64.8, 37.3, 30.5, 22.6; HRMS (EI-MSES

double focusing) m/z cacld. for $C_{15}H_{14}O_2$ (M^+): 226.0994, found: 226.0993.

3-(Pent-1-yn-1-yl)cyclohex-2-enone (3as)

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and hex-2-ynoic acid (**2s**) (224 mg, 2.0 mmol) afforded 3-(pent-1-yn-1-yl)cyclohex-2-enone (**3as**) (243 mg, 1.5 mmol, 75% yield); Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.15 (t, *J* = 1.6 Hz, 1H), 2.45-2.38 (m, 6H), 2.05-2.00 (m, 2H), 1.64-1.57 (m, 2H), 1.02 (t, *J* = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 199.0, 144.6, 131.9, 102.2, 80.6, 37.3, 30.9, 22.6, 21.8, 21.7, 13.5; HRMS (EI-MSES double focusing) m/z cacld. for $C_{11}H_{14}O$ (M^+): 162.1045, found: 162.1046.

3-(Hept-1-yn-1-yl)cyclohex-2-enone (3at)

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and oct-2-ynoic acid (**2t**) (280 mg, 2.0 mmol) afforded 3-(Hept-1-yn-1-yl)cyclohex-2-enone **(3at**) (296 mg, 1.6 mmol, 80% yield); Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) 6.13 (t, *J* = 1.6 Hz, 1H), 2.42-2.37 (m, 6H), 2.03-1.98 (m, 2H), 1.59-1.53 (m, 2H), 1.41-1.29 (m, 4H), 0.91 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 199.1, 144.7, 131.8, 102.5, 80.4, 37.3, 31.0, 30.9, 28.0, 22.6, 22.1, 19.8, 13.9; HRMS (EI-MSES double focusing) m/z cacld. for $C_{13}H_{18}O$ (M^+): 190.1358, found: 190.1358.

3-(Prop-1-yn-1-yl)cyclohex-2-enone (3au)[13b]

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and but-2-ynoic acid (**2u**) (168 mg, 2.0 mmol) afforded 3-(Prop-1-yn-1-yl)cyclohex-2-enone **(3au**) (166mg, 1.24mmol, 61% yield); Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) 6.13 (s, 1H), 2.43-2.37 (m, 4H), 2.06 (s, 3H), 2.03-1.98 (m, 2H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ199.0, 144.6, 131.9, 97.8, 79.6, 37.2, 30.7, 22.5, 4.8; MS (EI) m/z = 134 (M^+).

3-(But-1-yn-1-yl)cyclohex-2-enone (3av)

3-Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and pent-2-ynoic acid (**2v**) (196 mg, 2.0

mmol) afforded 3-(But-1-yn-1-yl)cyclohex-2-enone **(3av)** (207mg, 1.4mmol, 70% yield); Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) 6.12 (t, *J* = 1.6 Hz, 1H), 2.42-2.36 (m, 6H), 2.02-1.96 (m, 2H), 1.18 (t, *J* = 7.5 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ199.0, 144.6, 131.9, 103.5, 79.7, 37.3, 30.8, 22.6, 13.5, 13.4; HRMS (EI-MSES double focusing) m/z cacld. for $C_{10}H_{12}O$ (M^+): 148.0888, found: 148.0886

5,5-Dimethyl-3-(phenylethynyl)cyclohex-2-enone (3ba)[14b]

5,5-Dimethyl-3-oxocyclohex-1-enyl tosylate (**1b**) (589 mg, 2.0 mmol) 3-phenylpropiolic acid (**2a**) (292 mg, 2.0 mmol) afforded 5,5-dimethyl-3-(phenylethynyl)cyclohex-2-enone (**3ba**) (440 mg, 1.96 mmol, 98% yield); Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51-7.49 (m, 2H), 7.40-7.35 (m, 3H), 6.31 (t, *J* = 1.7 Hz, 1H), 2.45 (d, *J* = 1.7 Hz, 2H), 2.30 (s, 2H), 1.11 (s, 6H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 199.0, 141.2, 131.9, 131.3, 129.4, 128.5, 122.0, 99.3, 88.7, 51.1, 44.3, 33.8, 28.1; MS (EI) m/z = 224 (M^+).

5,5-Dimethyl-3-(*o*-tolylethynyl)cyclohex-2-enone (3bb)[16b]

5,5-Dimethyl-3-oxocyclohex-1-enyl tosylate (**1b**) (589 mg, 2.0 mmol3-(*o*-tolyl)propiolic acid (**2b**) (320 mg, 2.0 mmol) afforded 5,5-dimethyl-3-(*o*-tolylethynyl)cyclohex-2-enone (**3bb**) (405 mg, 1.7 mmol, 85% yield); Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 7.6 Hz, 1.3 Hz, 1H), 7.28 (td, *J* = 7.4 Hz, 1.3 Hz, 1H), 7.24-7.22 (m, 1H), 7.17 (tdd, *J* = 7.8 Hz, 1.5 Hz, 0.6 Hz, 1H), 6.30 (t, *J* = 1.7 Hz, 1H), 2.45 (s, 3H), 2.44 (d, *J* = 1.7 Hz, 2H), 2.29 (s, 2H), 1.10 (s, 6H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 198.9, 141.3, 140.7, 132.2, 130.9, 129.6, 129.5, 125.7, 121.7, 98.4, 92.6, 60.0, 44.3, 33.7, 28.1, 20.6; MS (EI) m/z = 238 (M^+).

5,5-Dimethyl-3-(*p*-tolylethynyl)cyclohex-2-enone (3bd)

5,5-Dimethyl-3-oxocyclohex-1-enyl tosylate (**1b**) (589 mg, 2.0 mmol) 3-(*p*-tolyl)propiolic acid

(**2d**) (320 mg, 2.0 mmol) afforded 5,5-dimethyl-3-(*p*-tolylethynyl)cyclohex-2-enone (**3bd**) (424 mg, 1.78 mmol, 89% yield); Yellow solid; mp 59.2-61.0 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.38 (m, 2H), 7.18-7.16 (m, 2H), 6.29 (t, *J* = 1.7 Hz, 1H), 2.43 (d, *J* = 1.7 Hz, 2H), 2.38 (s, 3H), 2.30 (s, 2H), 1.10 (s, 6H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 199.0, 141.2, 139.8, 131.9, 131.3, 129.4, 128.5, 122.0, 99.3, 88.7, 51.1, 44.3, 33.8, 28.1; HRMS (EI-MSES double focusing) m/z cacld. for $C_{17}H_{18}O$ (M^+): 238.1358, found: 238.1355.

3-((2-Methoxyphenyl)ethynyl)-5,5 dimethylcyclohex-2-enone (3bf)[16b]

5,5-Dimethyl-3-oxocyclohex-1-enyl tosylate (**1b**) (589 mg, 2.0 mmol) 3-(2-methoxyphenyl)propiolic acid (**2f**) (352 mg, 2.0 mmol) afforded 3-((2-methoxyphenyl)ethynyl)-5,5-dimethylcyclohex-2-enone (**3bf**) (443 mg, 1.74 mmol, 87% yield); Brown oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45-7.43 (m, 1H), 7.35 (ddd, *J* = 8.4 Hz, 7.5 Hz, 1.7 Hz, 1H), 6.94 (td, *J* = 7.5 Hz, 1.0 Hz, 1H), 6.90 (dd, *J* = 8.4 Hz, 0.5 Hz, 1H), 6.32 (t, *J* = 1.7 Hz, 1H), 3.90 (s, 3H), 2.46 (d, *J* = 1.7 Hz, 2H), 2.29 (s, 2H), 1.09 (s, 6H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 199.1, 160.1, 141.6, 133.8, 131.1, 131.0, 120.5, 111.1, 110.7, 96.1, 92.7, 55.8, 51.0, 44.3, 33.7, 28.1; MS (EI) m/z = 254 (M^+).

3-(Benzo[d][1,3]dioxol-5-ylethynyl)-5,5-dimethylcyclohex-2-enone (3bh)

5,5-Dimethyl-3-oxocyclohex-1-enyl tosylate (**1b**) (589 mg, 2.0 mmol) 3-(benzo[d][1,3]dioxol-5-yl)propiolic acid (**2h**) (380 mg, 2.0 mmol) afforded 3-(benzo[d][1,3]dioxol-5-ylethynyl)-5,5-dimethylcyclohex-2-enone (**3bh**) (445 mg, 1.66 mmol, 83% yield); Yellow solid; mp 101.6-103.2 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H), 6.92 (d, *J* = 1.6 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 6.26 (t, *J* = 1.7 Hz, 1H), 6.00 (s, 2H), 2.41 (d, *J* = 1.7 Hz, 2H), 2.28 (s, 2H), 1.09 (s, 6H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 198.9, 148.9, 147.6, 141.3, 130.8, 127.2, 115.1, 111.6, 108.6, 101.5, 99.7, 87.5, 51.0, 44.3, 33.7, 28.1; HRMS (EI-MSES double

focusing) m/z cacld. for $C_{17}H_{16}O_3$ (M^+): 268.1099, found: 268.1101.

5,5-Dimethyl-3-(naphthalen-1-ylethynyl)cyclohex-2-enone (3bi)

5,5-Dimethyl-3-oxocyclohex-1-enyl tosylate (**1b**) (589 mg, 2.0 mmol) 3-(naphthalen-1-yl)propiolic acid (**2i**) (392 mg, 2.0 mmol) afforded 5,5-dimethyl-3-(naphthalen-1-ylethynyl)cyclohex-2-enone (**3bi**) (444 mg, 1.62 mmol, 81% yield); Brwon solid; mp 116.4-118.2 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 8.27 (dd, J = 8.5 Hz, 0.8 Hz, 1H), 7.88 (dd, J = 9.3 Hz, 8.5 Hz, 2H), 7.74 (dd, J = 7.2 Hz, 1.2 Hz, 1H), 7.61 (ddd, J = 8.3 Hz, 6.9 Hz, 1.4 Hz, 1H), 7.55 (ddd, J = 8.1 Hz, 6.9 Hz, 1.3 Hz, 1H), 7.46 (dd, J = 8.2 Hz, 7.2 Hz, 1H), 6.43 (t, J = 1.7 Hz, 1H), 2.5 (d, J = 1.7 Hz, 2H), 2.33 (s, 2H), 1.14 (s, 6H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 198.9, 141.1, 133.1, 133.0, 131.3, 131.3, 130.1, 128.4, 127.2, 126.7, 125.7, 125.2, 119.5, 97.5, 93.5, 51.1, 44.4, 33.8, 28.2; HRMS (EI-MSES double focusing) m/z cacld. for $C_{20}H_{18}O$ (M^+): 274.1358, found: 274.1359.

3-((4-Chlorophenyl)ethynyl)-5,5-dimethylcyclohex-2-enone (3bk)[22]

5,5-Dimethyl-3-oxocyclohex-1-enyl tosylate (**1b**) (589 mg, 2.0 mmol) 3-(4-chlorophenyl)propiolic acid (**2k**) (361 mg, 2.0 mmol) afforded 3-((4-chlorophenyl)ethynyl)-5,5-dimethylcyclohex-2-enone **(3bk**) (512 mg, 1.98 mmol, 99% yield); Yellow solid; mp 97.0-98.9 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.43 (dt, J = 8.6 Hz, 2.1 Hz, 2H), 7.36 (dt, J = 8.6 Hz, 2.1 Hz, 2H), 6.31 (t, J = 1.7 Hz, 1H), 2.44 (d, J = 1.7 Hz, 2H), 2.31 (s, 2H), 1.11 (s, 6H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 198.8, 140.7, 135.6, 133.1, 131.6, 128.9, 120.4, 97.9, 89.5, 51.0, 44.2, 33.8, 28.1; MS (EI) m/z = 258 (M^+).

4-((5,5-Dimethyl-3-oxocyclohex-1-en-1-yl)ethynyl)benzonitrile (3bm)

5,5-Dimethyl-3-oxocyclohex-1-enyl tosylate (**1b**) (589 mg, 2.0 mmol) 3-(4-cyanophenyl)propiolic acid (**2m**) (342 mg, 2.0 mmol) afforded 4-((5,5-dimethyl-3-oxocyclohex-

1-en-1-yl)ethynyl)benzonitrile (**3bm**) (404 mg, 1.62 mmol, 81% yield); Yellow solid; mp 129.3-131.1 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67-7.65 (m, 2H), 7.59-7.56 (m, 2H), 6.33 (t, *J* = 1.7 Hz, 1H), 2.44 (d, *J* = 1.8 Hz, 2H), 2.31 (s, 2H), 1.11 (s, 6H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 198.6, 139.8, 132.5, 132.3, 132.1, 126.8, 118.2, 112.7, 96.5, 92.2, 51.0, 44.0, 33.8, 28.1; HRMS (EI-MSES double focusing) m/z cacld. for $C_{17}H_{15}NO$ (M^+): 249.1154, found: 249.1152.

Methyl 4-((5,5-dimethyl-3-oxocyclohex-1-en-1-yl)ethynyl)benzoate (3bp)

5,5-Dimethyl-3-oxocyclohex-1-enyl tosylate (**1b**) (589 mg, 2.0 mmol) 3-(4-(methoxycarbonyl)phenyl)propiolic acid (**2p**) (408 mg, 2.0 mmol) afforded methyl 4-((5,5-dimethyl-3-oxocyclohex-1-en-1-yl)ethynyl)benzoate (**3bp**) (519 mg, 1.84 mmol, 92% yield); Yellow solid; mp 83.0-85.0 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.27 (t, *J* = 1.7 Hz, 2H), 2.49 (td, *J* = 6.1 Hz, 1.7 Hz, 4H), 2.46-2.43 (m, 4H), 2.10-2.05 (m, 4H) 1.11 (s, 6H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 198.3, 141.7, 133.7, 97.0, 37.3, 30.0, 22.5.; MS (EI) m/z cacld. for $C_{18}H_{18}O_3$ (M^+): 282.1256, found: 282.1256

3,3'-(Ethyne-1,2-diyl)bis(cyclohex-2-enone) (4)

Oxocyclohex-1-enyl tosylate (**1a**) (533mg, 2.0 mmol) and propiolic acid (70 mg, 1.0 mmol) afforded 3,3'-(ethyne-1,2-diyl)bis(cyclohex-2-enone) (**5**) (128 mg, 0.6 mmol, 60% yield); Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ .27 (t, *J* = 1.7 Hz, 2H), 2.49 (td, *J* = 6.1 Hz, 1.7 Hz, 4H), 2.46-2.43 (m, 4H), 2.10-2.05 (m, 4H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 198.3, 141.7, 133.7, 97.0, 37.3, 30.0, 22.5.; HRMS (EI-MSES double focusing) m/z cacld. for $C_{14}H_{14}O_2$ (M^+): 214.0996, found: 214.0994.

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Supporting Information

The supporting information is available free of charge on the ACS Publications website at DOI : ^{1}H and ^{13}C NMR spectra of all products.

REFERENCES

(1) (a) Irie, T.; Izawa, M.; Kurosawa, E. *Tetrahedron* **1970**, *26*, 851–870. (b) Fenical, W. *J. Am. Chem. Soc*. **1974**, *96*, 5580 (c) Fukuzawa, A.; Kurosawa, E. *Tetrahedron Lett*. **1979**, *20*, 2797–2800. (d) Ciulei, S. C.; Tykwinski, R. R. *Org. Lett*. **2000**, *2*, 3607–3610. (e) Tykwinski, R. R.; Gholami, M.; Eisler, S.; Zhao, Y.; Melin, F.; Echegoyen, L. *Pure Appl. Chem.* **2008**, *80*, 621–637.

(2) (a) Trost, B. M. *Science* **1991**, *254*, 1471–1477. (b) Nicolaou, K. C.; Smith, A. L. *In Modern Acetylene Chemistry*; Stang, P. J.; Diederich, F.; Eds. VCH: Weinheim, Germany, 1995. (c) Hofman, S.; Gao, L.-J.; Van Dingenen, H.; Hosten, N. G. C.; Van Haver, D.; De Clercq, P. J.; Milanesio, M.; Viterbo, D. *Eur. J. Org. Chem*. **2001**, 2851. (d) Fürstner, A.; De Souza, D.; Turet, L.; Fenster, M. D. B.; Parra-Rapado, L.; Wirtz, C.; Mynott, R.; Lehmann, C. W. *Chem. Eur. J.* **2007**, *13*, 115-134 (e) Woo, S. K.; Y, Lu.; Krische, M. J. *J. Am. Chem. Soc*. **2011**, *133*, 13876–13879. (f) Kus, M.; Artok, L.; Aygün, M. *J. Org. Chem*. **2015**, *80*, 5494–5506.

(3) (a) Larsen, D. S.; O'Shea, M. D. *J. Chem. Soc*. Perkin Trans. **1995**, 1019–1028. (b) Nicolaou,

K. C.; Sun, Y.-P.; Peng, X.-S.; Polet, D.; Chen, D. Y.-K. *Angew*. *Chem*. *Int*. *Ed*. **2008**, *47*, 7310–7313. (c) Klahn, P.; Duschek, A.; Liébert, C.; Kirsch, S. F.; *Org*. *Lett*. **2012**, *14*, 1250–1253. (d) Hernandez-Martin, A.; Fernandez, S. Verstuyf, A. Verlinden, M.Ferrero, L. *Eur*. *J*. *Org*. *Chem*. **2017**, 504–513.

(4) (a) Hayashi, T.; Tokunaga, N.; Inoue, K. *Org*. *Lett*. **2004**, *6*, 305–307. (b) Gubbels, M. A.; Hulce, M.; Kum, J. M.; Urick, A. K.; Villa, E. M. *Tetrahedron* **2016**, *72*, 6052–6063

(5) Blouin, S.; Gandon, V.; Blond, G.; Suffert, J. *Angew*. *Chem*. *Int*. *Ed*. **2016**, *55*, 7208–7211

(6) Yan, Z.-Y.; Xiao, Y.; Zhang, L. *Angew*. *Chem*. *Int*. *Ed*. **2012**, *51*, 8624–8627.

(7) Chen, W.-L.; Li, J.; Zhu, Y.-H.; Hu, W.; Mo, W.-M. *ARKIVOC* **2012**, 16–25.

(8) Brummond, K. M.; Chen, D.; Davis, M. *J*. *Org*. *Chem*. **2008**, *73*, 5064–5068.

(9) (a) Shen, R.; Huang, X. *Org*. *Lett*. **2008**, *10*, 3283–3286. (b) Kolodziej, I.; Green, J. R. *Org*. *Biomol*. *Chem*. **2015**, *13*, 10852–10864.

(10) (a) Vatele, J.-M. *Tetrahedron* **2010**, *66*, 904–912. (b) Uyanik, M.; Fukatsu, R.; Ishihara, K. *Org*. *Lett*. **2009**, *11*, 3470–3473.

(11) Cheng, D.; Ling, F.; Li, Z.; Yao, W.; Ma, C. *Org*. *Lett*. **2012**, *14*, 3146–3149.

(12) Liotta, D.; Brown, D.; Hoekstra, W.; Monahan, R. III *Tetrahedron Lett*. **1987**, *28*, 1069–1072.

(13) (a) Guingant, A.; Barreto, M. M. *Tetrahedron Lett*. **1987**, *28*, 3107–3110. (b) Rathjen, H. J.; Margaretha, P.; Wolff, S.; Agosta, W. C. *J*. *Am*. *Chem*. *Soc*. **1991**, *113*, 3904–3909 (c) Tissot, M.; Poggiali, D.; Hénon, H.; Muller, D.; Guénée, L.; Mauduit, M.; Alexakis, A. *Chem*. *Eur*. *J*. **2012**, *18*, 8731–8747. (d) Rozek, T.; Janowski, W.; Hevko, J. M.; Tiekink, E. R. T.; Dua, S.; Stone, D.

J. M.; Bowie, J. H. *Australian* J. *Chem*. **1998**, *51*, 515–524.

(14) (a) Rao, C. J.; Knochel, P. *J. Org. Chem*. **1991**, *56*, 4593–4596. (b) Raminelli, C.; Gargalaka, J. Jr.; Silveira, C. C.; Comasseto, J. V. *Tetrahedron* **2007**, *63*, 8801–8809.

(15) (a) Houpis, I. N. *Tetrahedron Lett*. **1991**, *32*, 6675–6678. (b) Bertus, P.; Halbes, U.; Pale, P. *Eur. J. Org. Chem*. **2001**, 4391–4393.

(16) (a) Montalbetti, C.; Savignac, M.; Bonnefis, F.; Genêt, J. P. *Tetrahedron Lett*. **1995**, *36*, 5891–5894. (b) Khalaf, J.; Estrella-Jimenez, M. E.; Shashack, M. J.; Phatak, S. S.; Zhang, S.; Gilbertson, S. R. *ACS Comb. Sci*. **2011**, *13*, 351–356. (c) Paju, A.; Kanger, T.; Müürisepp, A.-M.; Aid, T.; Pehk, T.; Lopp, M. *Teterahedron* **2014**, *70*, 5843–5848.

(17) (a) Halbes-Letinois, U.; Pale, P. J. *Organomet. Chem*. **2003**, *687*, 420–424. (b) Pouwer, R. H.; Schill, H.; Williams, C. M.; Bernhardt, P. V. *Eur. J. Org. Chem*. **2007**, 4699–4705. (c) Jiang, C.; Zhang, Z.; Xu, H.; Sun, L.; Liu, L.; Wang, C. *Appl. Organometal. Chem*. **2010**, *24*, 208–214.

(18) Fu, X.; Zhang, S.; Yin, J.; Schumacher, D. P. *Tetrahedron Lett*. **2002**, *43*, 6673–6676.

(19) (a) Moon, J.; Jeong, M.; Nam, H.; Ju, J.; Moon, J. H.; Jung, H. M.; Lee, S. *Org. Lett*. **2008**, *10*, 945–948. (b) Park, K.; Bae, G.; Moon, J.; Choe, J.; Song, K. H.; Lee, S. *J. Org. Chem*. **2010**, *75*, 6244–6251. (c) Park, K.; You, J. -M.; Jeon, S.; Lee, S. *Eur. J. Org. Chem.* **2013**, 1973–1978.

(20) (a) Jang, J.; Raja, G. C. E.; Lee, J. -H.; Son, Y.; Kim, J.; Lee, S. *Tetrahedron Lett*. **2016**, *57*, 4581–4584. (b) Lee, J. -H.; Raja, G. C. E.; Son, Y.; Jang, J.; Kim, J.; Lee, S. *Tetrahedron Lett*. **2016**, *57*, 4824–4828. (c) Raja, G. C. E.; Irudayanathan, F. M.; Kim, H.-S.; Kim, J.; Lee, S. *J. Org. Chem*. **2016**, *81*, 5244–5249.

(21) (a) Rodríguez N.; Goossen, L. J. *Chem. Soc. Rev.* **2011**, *40*, 5030–5048. (b) Shang, R.; and

Liu, L. *Sci. China: Chem.* **2011**, *54*, 1670–1687. (c) Dzik, W. I.; Lange, P. P.; and Goossen, L. J. *Chem. Sci.* **2012**, *3*, 2671–2678. (d) Cornella, J.; and Larrosa, I. *Synthesis* **2012**, 653–676. (e) Guo, L.-N.; Wang, H.; and Duan, X.-H. *Org. Biomol. Chem.* **2016**, *14*, 7380–7491.

(22) Yang, S.-M.; Kuo, Gee-Hong; Gaul, Michael D.; and Murray, William V. *J. Org. Chem.* **2016**, *81*, 3464−3469