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Palladium-Catalyzed Carbonylative Coupling of Aryl Iodides and Benzyl Acetylenes to 3-Alkylidenefuran-2-ones under Mild Conditions and Its Density Functional Theory Modeling

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Abstract: A general and efficient method for the palladium-catalyzed carbonylative coupling of aryl iodides to benzyl acetylenes has been developed. Various furanones have been prepared in excellent yields from their corresponding benzyl acetylenes at room temperature under a CO atmosphere. For aliphatic alkynes, their corresponding alkynones were obtained in good yields. Detailed DFT calculations have also been carried out to understand the reaction pathway and the most probable reaction mechanism has been proposed.

Keywords: carbonylation · coupling reactions · density functional calculations · furanones · palladium

Introduction

Palladium-catalyzed coupling reactions are already a powerful toolbox for the formation of C–X (X = C, N, O, S) bonds,[1] for example, the Sonogashira reaction for the synthesis of alkynes,[2] the Heck reaction for alkenes,[3] and Negishi and Suzuki reactions for the syntheses of biaryl compounds.[4] Among all of the palladium-catalyzed coupling reactions that have been developed, the carbonylation reaction offers an attractive procedure for producing carbonyl-containing compounds.[5] The palladium-catalyzed carbonylative reaction, which was first reported by Heck and co-workers in 1974,[6] has made impressive progress over the past few decades. Several interesting carbonylation reactions have also been developed in our group, such as the aminocarbonylation reaction with ammonia gas, carbonylative vinylation, and carbonylative C–H activation.[7] More recently, a general and efficient method for the palladium-catalyzed carbonylative coupling of aryl bromides and triflates with benzyl acetylenes to afford 3-alkylidenefuran-2-ones was developed,[8] which afforded the isolated products in moderate to good yields. The same reaction, starting from aryl iodides, has previously been described by Alper and co-workers.[9] However, in both cases, elevated temperatures (110–120 °C) and relatively high CO pressures (10–60 bar) were required.

In addition, furanones are important compounds with various biological activities,[10] such as anti-inflammatory, cardiotonic, analgesic, anticancer, anticonvulsant, antimicrobial, and antiviral activity. Selected examples of currently marketed drugs that contain the furanone scaffold include basidalin, ascorbic acid, narthogenin, butalactin, and rofecoxib. The traditional preparation procedure for 3-alkylidenefuran-2-ones involves the cyclodehydration of γ-keto acids and subsequent aldol condensation with aromatic aldehydes; only a few alternative routes have been reported, which involved the transition-metal-catalyzed cyclization of appropriately functionalized acetylenic substrates (Figure 1).[11]

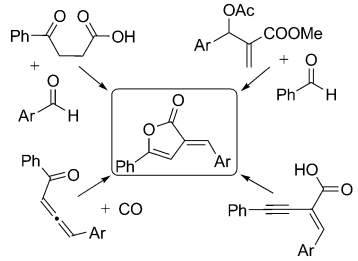

Figure 1. Various methods for the synthesis of furanones.

Owing to their importance and the scarcity of useful procedures for their synthesis, we herein report a general and efficient method for the synthesis of furanones. Starting from aryl iodides and benzyl acetylenes at room temperature and under a CO atmosphere, 3-alkylidenefuran-2-ones were isolated in excellent yields. Detailed DFT computations were also carried out to understand the reaction mechanism. On the basis of these results, a possible reaction pathway has been proposed.

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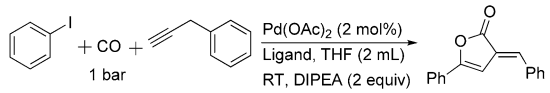
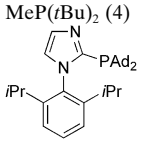
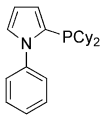
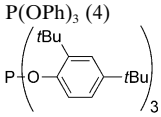
Results and Discussion

The first test reaction was carried out between 1 mmol iodobenzene and 1 mmol benzyl acetylene in the presence of 2 mol% $Pd(OAc)_2$ and 4 mol% PPh_3. To our delight, 95% of the desired furanone was formed at 50°C under 1 bar CO (Table 1, entry 1). The conversion of iodobenzene decreased

Table 1. Palladium-catalyzed carbonylative coupling between iodobenzene and benzyl acetylene: scope of the ligand.[a]



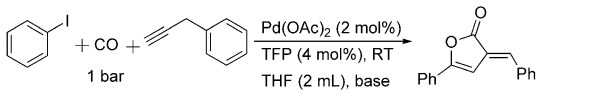
Entry	Ligand (mol%)	Conversion [%][b]	Yield [%][b]
1	PPh_3 (4)	98	95[c]
2	PPh_3 (4)	51	50
3	PCy_3 (4)	10	8
4	P(*o*-tolyl)$_3$ (4)	11	5
5	$BuPAd_2$ (4)	0	0
6	P(*t*Bu)$_3$ (4)	0	0
7	MeP(*t*Bu)$_2$ (4)	0	0
8		30	2
9		30	13
10	P(OPh)$_3$ (4)	48	32
11		30	21
12	P(OBu)$_3$ (4)	31	3
13	$OPPh_3$ (4)	34	9
14	TFP (4)	99	98
15	IMes·HCl (2)	0	0
16	IPr·HCl (2)	0	0
17	DPPF (2)	20	13
18	D*t*BPF (2)	0	0
19	Phen (2)	18	0

[a] Reaction conditions: $Pd(OAc)_2$ (2 mol%), iodobenzene (1 mmol), benzyl acetylene (1 mmol), THF (2 mL), DiPEA (2 mmol), CO (1 bar), 25°C, 20 h. [b] Conversions and yields were determined by GC, based on iodobenzene, with hexadecane as an internal standard. [c] 50°C. TFP: tri(2-furyl)phosphine, IMes·HCl: 1,3-dimesitylimidazolium chloride, IPr·HCl: 1,3-(2,6-diisopropylphenyl)imidazolium chloride, DPPF: 1,1′-bis(diphenylphosphino)ferrocene, DtBPF: 1,1′-bis(di-tert-butylphosphino)ferrocene, Phen: 1,10-phenanthroline, DiPEA: *N*,*N*-diisopropylethylamine.

to 51% when the reaction was carried out at 25°C (Table 1, entry 2). With these two results in hand, we started to test different ligands at 25°C. All of the tested electron-rich monophosphine ligands gave low or no yield of the desired product (Table 1, entries 3–9). This result hinted that electron-withdrawing ligand might favor this transformation. Indeed, phosphites gave improved yields of the product (3–32%; Table 1, entries 10–12). More electron-poor ligands, like phosphine oxide, only resulted in 9% formation of the furanone (Table 1, entry 13). Based on these data, we decided to use tri(2-furyl)phosphine (TFP) as the ligand for this cyclocarbonylation reaction (Table 1, entry 14). As expected, 98% of the desired product was formed with 99% conversion of iodobenzene, and this reaction was reproducible. Other tested ligands, including NHCs, bidentate ligands, and nitrogen ligands, did not give any product, except for DPPF, which afforded 13% of the furanone (Table 1, entries 15–19).

Next, we started to test the influence of various bases on this reaction (Table 2). The use of organic bases resulted in lower yields of the product (Table 2, entries 1–3), whereas, by comparison, inorganic bases did not afford the furanone

Table 2. Palladium-catalyzed carbonylative coupling between iodobenzene and benzyl acetylene: scope of the base.[a]



Entry	Base (mol%)	Conversion [%][b]	Yield [%][b]
1	NEt_3 (2)	100	88
2	DBU (1)	50	0
3	TMEDA (1)	48	11
4	K_2CO_3 (2)	15	5
5	Na_2CO_3 (2)	20	0
6	K_3PO_4 (2)	18	0
7	DiPEA (2)	69	68[c]

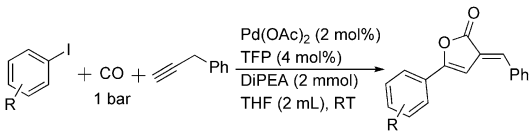
[a] Reaction conditions: $Pd(OAc)_2$ (2 mol%), TFP (4 mol%), iodobenzene (1 mmol), benzyl acetylene (1 mmol), THF (2 mL), base, CO (1 bar), 25°C, 20 h. [b] Conversions and yields were determined by GC, based on iodobenzene, with hexadecane as an internal standard. [c] $Pd(OAc)_2$ (1 mol%), TFP (2 mol%). DBU: 1,8-diazabicyclo[5.4.0]undec-7-ene, TMEDA: *N*,*N*,*N*′,*N*′-tetramethylethane-1,2-diamine.

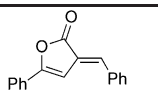
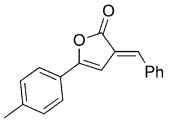
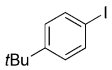
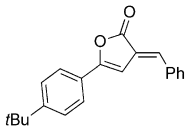
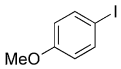
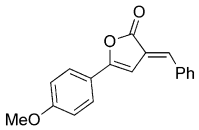
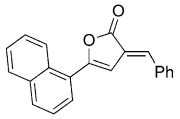
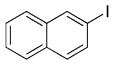
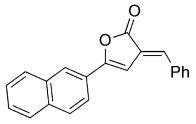
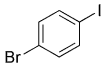
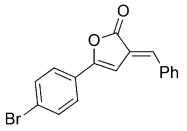
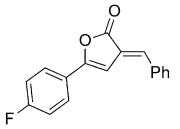
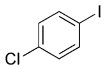
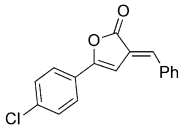
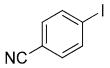
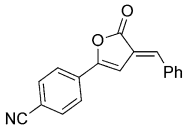
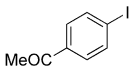
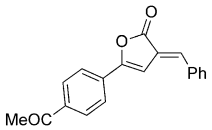
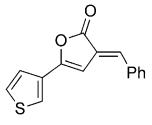
at all (Table 2, entries 4–6). A yield of 68% was obtained with 1 mol% of the palladium catalyst (Table 2, entry 7).

With the optimal reaction conditions in hand, we started to examine the scope of this method (Table 3 and Table 4). Methyl-, *tert*-butyl-, and methoxy-substituted aryl iodides gave excellent yields of their corresponding furanones (Table 3, entries 2–4). Naphthyl iodides were also successfully transformed into their desired furanones in 93–95% yield (Table 3, entries 5 and 6). Halogen-decorated iodides could be applied as substrates and resulted in excellent yields of their corresponding 3-alkylidenefuran-2-ones (Table 3, entries 7–9). In addition, the reactions between strongly electron-withdrawing aryl iodides and benzyl acetylene gave the products in 82–86% yield (Table 3, entries 10 and 11). Moreover, as an example of a heterocycle, 3-iodothiophene also gave its corresponding furanone in 89% yield (Table 3, entry 12).

Several benzyl acetylenes and some other alkynes were also tested. The furanones were synthesized in excellent yields by the palladium-catalyzed carbonylative coupling of benzyl acetylenes with iodobenzene (95–98%; Table 4, entries 2–6). The tested aliphatic alkynes gave their corre-

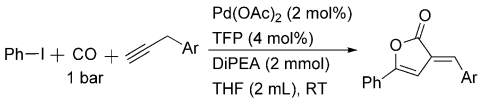
Table 3. Palladium-catalyzed carbonylative coupling of various aryl iodides.[a]

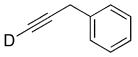
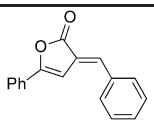
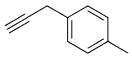
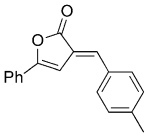
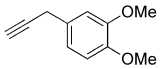
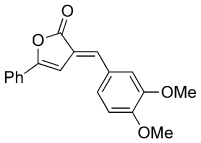
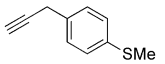
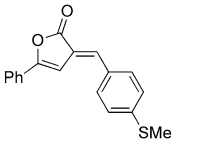
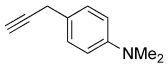
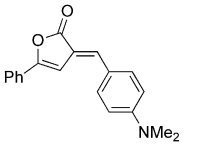
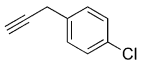
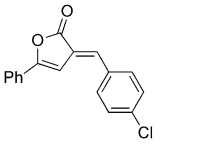
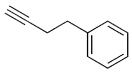
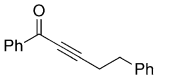


Entry	Aryl iodide	Product	Yield [%][b]
1			98
2			99
3			98
4			98
5			93
6			95
7			90
8			95
9			90
10			82
11			86
12			89

[a] Reaction conditions: $Pd(OAc)_2$ (2 mol%), TFP (4 mol%), aryl iodide (1 mmol), benzyl acetylene (1 mmol), THF (2 mL), DiPEA (2 mmol), CO (1 bar), 25 °C, 20 h. [b] Yield of isolated product.

Table 4. Palladium-catalyzed carbonylative coupling of various acetylenes.[a]



Entry	Acetylene	Product	Yield [%][b]
1			90
2			96
3			97
4			97
5			98
6			95
7			82
8			62
9			88
10			85
11			70
12			75

[a] Reaction conditions: $Pd(OAc)_2$ (2 mol%), TFP (4 mol%), iodobenzene (1 mmol), acetylene (1 mmol), THF (2 mL), DiPEA (2 mmol), CO (1 bar), 25 °C, 20 h. [b] Yield of isolated product.

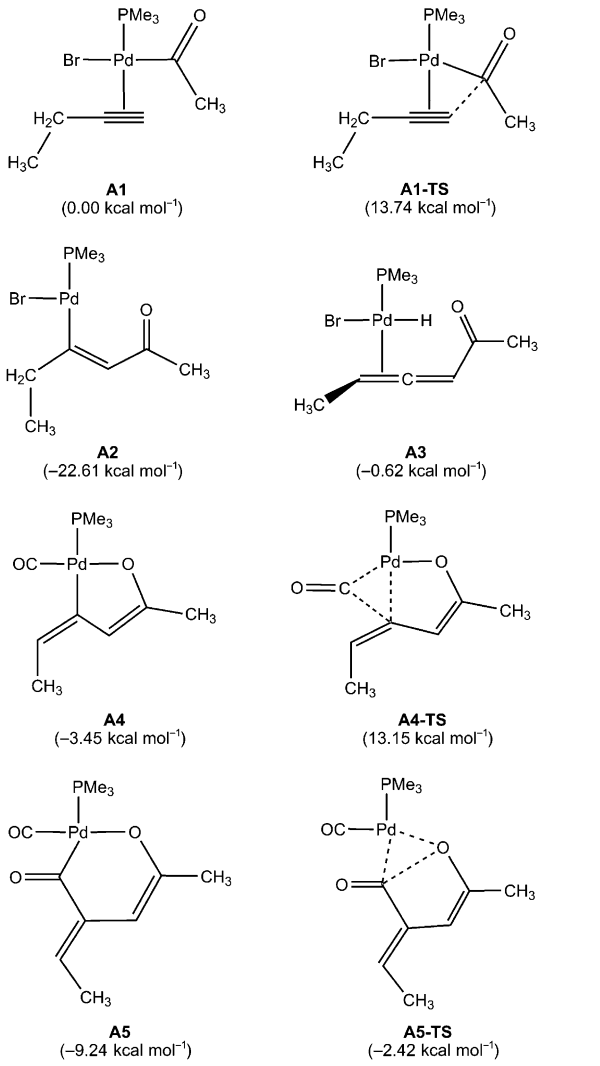
sponding alkynones in good yields and no furanones were formed (Table 4, entries 7–12). As described in our previous paper,[8] aliphatic alkynones could be transformed into their

corresponding furanones at 110 °C, but they were not isolatable. Remarkably, no deuterium labeling was found in the furanone when deuterium-labeled benzyl acetylene was used instead of normal benzyl acetylene under the same conditions (Table 4, entry 1). This result demonstrated that deprotonation of alkynes occurred in the reaction mechanism.

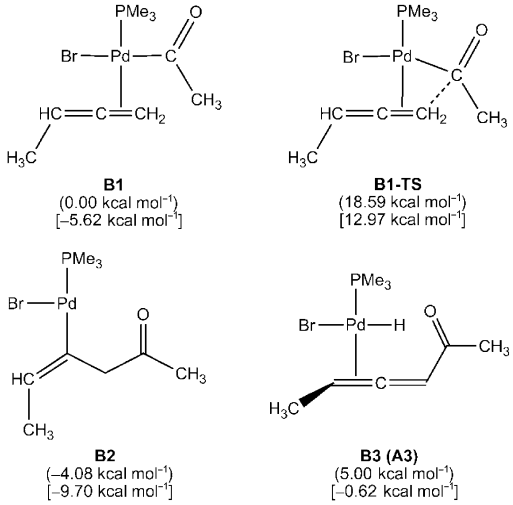
To understand the reaction mechanism in more detail, density functional theory (DTF) calculations were carried out. For further information, see the computational details section; the energies and coordinates for all of the species are provided in the Supporting Information. At first, we used $CH_3CH_2C{\equiv}CH$ as the substrate to map the potential-energy surface, that is, to estimate the more stable or most stable intermediates and the resting state. In our model calculations, we not only used 1-butyne (**A**) but also 1,2-butadiene (**B**) to consider the possible isomeric equilibrium between the alkyne and the allene. In addition, we also used 1-butynyl ($CH_3CH_2C{\equiv}C$, **C**), because aliphatic alkynes only gave their corresponding alkynones (Table 4), and, therefore, we believed that the alkynes were deprotonated prior to their reductive C–C coupling. Following the generally accepted Heck-reaction mechanism, the first step of the catalytic reaction is the oxidative addition of the X–Ph bond and the second step is CO addition/insertion for the formation of the acyl complex (LPdX(COPh)). Because these steps have been the subject of intensive theoretical studies, we did not pay attention to them in our computations; instead, we used the acyl complex as our starting point. For all of the intermediates as energy minimums, the 16-electron configurations were maintained and CO was the ligand for the necessary coordination.

First, we used 1-butyne (**A**) as the substrate. As shown in Scheme 1, the first step is the coordination of 1-butyne (**A**) to the acyl complex, [(Me_3P)PdBr(COMe)], to form intermediate **A1**, followed by the C–C coupling step via transition state **A1-TS**, with the formation of the vinyl complex (**A2**). The free-energy barrier for C–C coupling is 13.74 kcal mol^{-1} and the coupling reaction is exergonic by 22.61 kcal mol^{-1}. However, the isomerization from **A2** to **A3** costs about 20 kcal mol^{-1} of free energy. The reductive removal of HBr from **A3** and the subsequent addition of CO, thereby resulting in **A4**, is exergonic by 2.83 kcal mol^{-1}. The free-energy barrier for CO insertion via transition state **A4-TS** is 16.60 kcal mol^{-1} and the formation of intermediate **A5** is exergonic by 5.79 kcal mol^{-1}. The reductive elimination of the corresponding furanone, (*E*)-3-ethylidene-5-methylfuran-2-(3*H*)-one, needs a relative low free-energy barrier of 6.82 kcal mol^{-1}.

For 1,2-butadiene (**B**) as the substrate, as shown in Scheme 2, the first step is the coordination of 1,2-butadiene (**B**) to the acyl complex [(Me_3P)PdBr(COMe)] to form intermediate **B1**, followed by the C–C coupling via transition state **B1-TS**, with the formation of the vinyl complex (**B2**). The free-energy barrier for C–C coupling is 18.59 kcal mol^{-1} and the coupling reaction is exergonic by 4.08 kcal mol^{-1}. However, the isomerization from **B2** to **B3** costs about



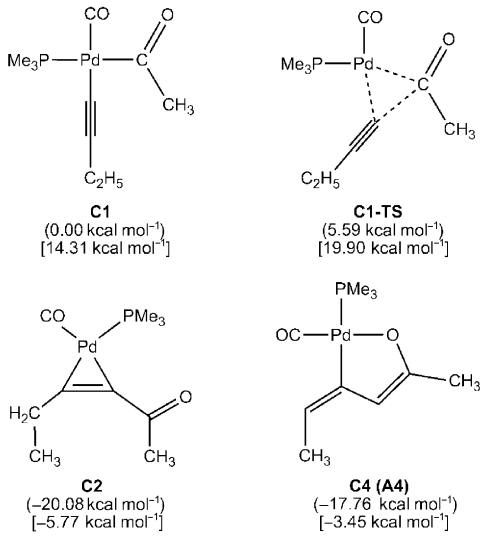
Scheme 1. Computed (BP86/TZVP) relative Gibbs free energies with 1-butyne as the substrate (relative to **A1**+2CO).



Scheme 2. Computed (BP86/TZVP) relative Gibbs free energies with 1,2-butadiene as the substrate; the relative energy to **A1**+2CO is given in square brackets.

9.08 kcal mol^{-1} of free energy. Because **B3** is equal to **A3**, the subsequent reaction steps remain the same as that shown in Scheme 1. Our computations show that **B1** is more stable than **A1** by 5.62 kcal mol^{-1} and that **A1-TS** and **B1-TS** are close in energy, within 0.77 kcal mol^{-1} of each other (13.74 versus 12.97 kcal mol^{-1}). Therefore, there is no significant difference between using the alkyne and the allene as the substrate.

As an alternative to the alkyne and the allene, we used 1-butynyl (**C**) with the elimination of HX and the coordination of CO to maintain the 16-electron configuration of complex **C1**. Three conformations of the coordination of 1-butynyl and [Pd(CO)(PMe_3)(COMe)] are possible, that is, **C1** and **C1′**, in which the 1-butynyl and acyl moieties are in the *cis* position and **C1** is more stable than **C1′** by 4.26 kcal mol^{-1}, and the third confirmation in which the 1-butynyl and acyl moieties are in the *trans* position (4.83 kcal mol^{-1} higher in free energy). Therefore, we only used conformation **C1** for the reductive C–C coupling reaction. Compared to **A1**, the formation of **C1** from CO coordination and HBr elimination costs 14.31 kcal mol^{-1} of free energy (**A1**+CO = **C1**+HBr). The subsequent reaction of HBr with an amine as the base should at least compensate for this energy cost. As shown in Scheme 3, the reductive C–C coupling step



Scheme 3. Computed (BP86/TZVP) relative Gibbs free energies with 1-butynyl as the substrate; the relative energy to the formation of **C1** (**A1**+CO = **C1**+HBr) is given in square brackets.

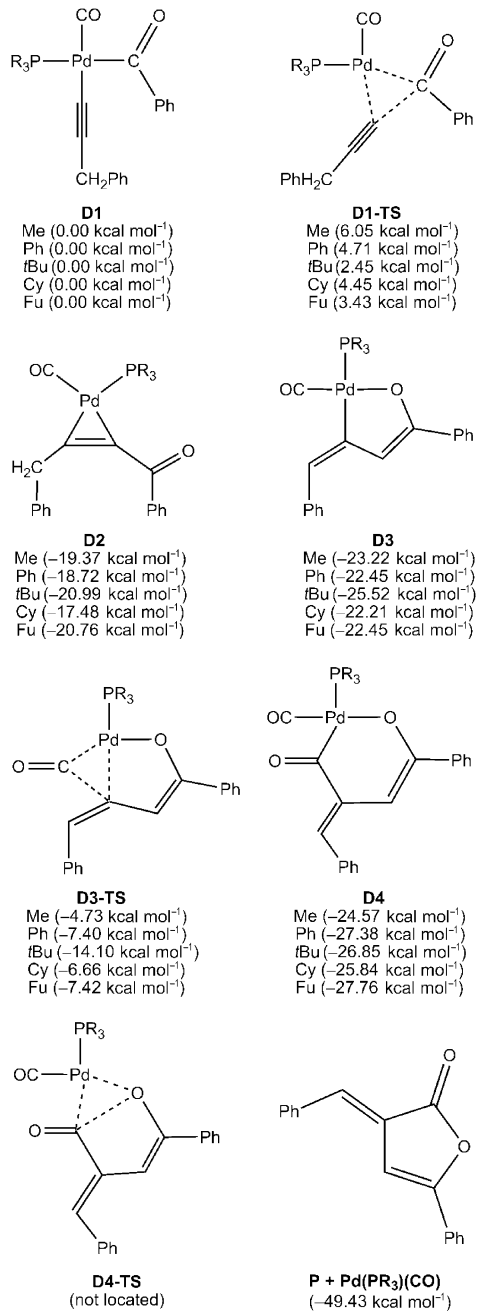
needs a free-energy barrier of 5.59 kcal mol^{-1} for **C1** via transition state **C1-TS**; this barrier is much lower than those for **A1** and **B1**. The next step is the isomerization from **C2** into **C4**, which is endergonic by 2.32 kcal mol^{-1}. Because **C4** is equal to **A4**, the subsequent reaction steps remain the same as that shown in Scheme 1.

On the basis of these three possible mechanisms, the steps from CO coordination and CO insertion are the same and their differences are in the C–C coupling reaction. Because aliphatic alkynes only gave their corresponding alkynones (Table 4, entries 7–12), thereby indicating that alkynes are deprotonated prior to their reductive C–C coupling, the proposed reaction route C, which has a much lower C–C coupling barrier (5.59 kcal mol^{-1}) than those in routes A (13.74 kcal mol^{-1}) and B (18.59 kcal mol^{-1}), should be reasonable. Therefore, we used acyl complex [Pd(CO)(PR_3)(COPh)] and 3-phenyl-1-propyne as the substrate by following the proposed reaction route in Scheme 4 (R = Me, Ph, *t*Bu, Cy, and TFP). As shown in Scheme 4, the starting complex (**D1**) is the coordination of 3-phenyl-1-propynyl (**D**) to the acyl complex [(R_3P)Pd(CO)(COPh)]. We found that there were no significant differences between the activation barriers and reaction energies with these ligands and, hence, we used PMe_3 for comparison purposes.

The reductive C–C coupling free-energy barrier via transition state **D1-TS** is rather low (6.05 kcal mol^{-1}), and the coupling reaction that results in **D2** is exergonic (−19.37 kcal mol^{-1}). This step is close to that in route C (Scheme 3). The isomerization from **D2** into **D3** is energetically more favorable (3.85 kcal mol^{-1}), in contrast to that from **C2** into **C4**, which is less favorable by 2.32 kcal mol^{-1} (Scheme 3). This difference in activity might come from the fact that the benzylic hydrogen atoms are more activated than the aliphatic hydrogen atoms, that is, benzylic alkynes gave their corresponding furanones, whereas aliphatic alkynes afforded alkynones. This energy difference can be easily explained by the conjugation that is introduced following benzylic substitution (Ph–CH_2) onto the phenyl-substituted olefin (Ph–CH=C); for example, Ph–CH=CH–CH_3 is more stable than Ph–CH_2–CH=CH_2 by 6.40 kcal mol^{-1}.

The next step is CO insertion; the free-energy barrier is 18.49 kcal mol^{-1}, which is somewhat higher than that in Scheme 1 (route A) (16.60 kcal mol^{-1}). The formation of **D4** from **D3** is slightly energetically favored (1.35 kcal mol^{-1}). The most significant difference between the reductive eliminations of **D4** and **A5** is the energy barrier. It is not possible to locate the corresponding transition state (**D4-TS**) for the reductive elimination, whilst a much lower barrier is found for **A5-TS** (5.79 kcal mol^{-1}). Overall, we can clearly see that intermediate **D3** is the resting state and that the rate-determining step is the CO insertion.

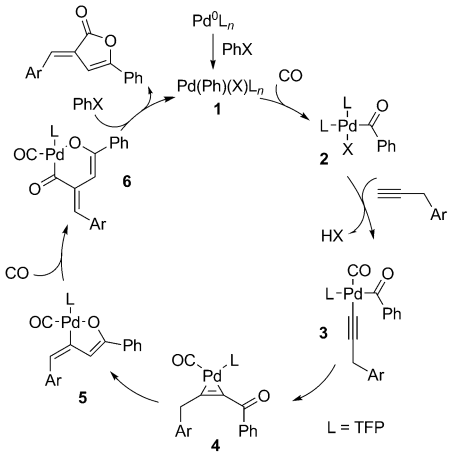
The data in Scheme 4 enable a comparison of the ligand effect, especially in the rate-determining step for CO insertion. All of the "real-size" ligands have lower activation free energies than PMe_3 (18.49 kcal mol^{-1}); the lowest activation barrier is found for P*t*Bu_3 (11.42 kcal mol^{-1}) and almost the same barriers are found for PPh_3 (15.05 kcal mol^{-1}), PCy_3 (15.55 kcal mol^{-1}), and P($Fu)_3$ (15.03 kcal mol^{-1}). These results indicate that there are no significant differences between these real-size ligands in the proposed reaction route and, therefore, they cannot explain the differences in activity observed in Table 1, that is, why the electron-rich alkylphosphines do not give any product, whilst electron-poor TFP (or PPh_3) ligands can give the product. This discrepancy between the computational and experimental data might be attributed, at least, to the stability of the phosphine li-



Scheme 4. Computed (BP86/TZVP) relative Gibbs free energies with 3-phenyl-1-propynyl as the substrate and different phosphine ligands.

gands and the formed complexes. For example, it is well-known that electron-rich phosphine ligands are air-sensitive and that the formed complexes can decompose with the formation of phosphonium salts; all of these factors are related to their catalytic activity.[17] In addition, strongly polar solvent, such as water, with high dielectric constants can lower the CO-insertion barrier to some extent; for example, 1.30 kcal mol^{-1} for **D3-PPh$_3$** (13.74 kcal mol^{-1}) and 0.58 kcal mol^{-1} for **D3-TFP** (14.45 kcal mol^{-1}, see the computational details section).

On the basis of our experimental and computational results, the following most probable reaction mechanism is proposed (Scheme 5): the reaction starts with the oxidative



Scheme 5. Proposed reaction mechanism.

addition of PhX to the Pd^0 center to form Pd(Ph)(X)(L)$_n$ (**1**), followed by CO coordination and insertion to form acyl complex **2**. Subsequent ligand exchange of X with the alkynyl moiety forms complex **3**, which undergoes reductive C–C coupling to afford complex **4**. The isomerization of complex **4** forms complex **5**. Further CO insertion forms complex **6** and subsequent reductive C–O coupling forms the product and regenerates the catalyst.

Conclusion

In conclusion, a general and efficient methodology for palladium-catalyzed carbonylative coupling of aryl iodides to benzyl acetylenes has been developed. Different furanones were prepared in excellent yields from their corresponding benzyl acetylenes at room temperature under a CO atmosphere. When aliphatic alkynes were used as substrates, the reaction gave their corresponding alkynones in good yields. DFT calculations were also carried out to understand the reaction pathway. On the basis of our experimental and computational results, a possible mechanism has been proposed.

Experimental Section

General comments: All of the reactions were carried out under an argon atmosphere. THF was distilled from sodium ketyl and stored in Aldrich Sure/Stor flasks under an argon atmosphere. Aryl iodides, benzyl acetylene, and TFP were purchased from Aldrich and used as received. The other benzyl acetylenes were synthesized according to literature procedures.[1] Column chromatography on silica gel was performed by using Merck Silica gel 60 (0.043–0.06 mm). NMR data were recorded on Bruker ARX 300 and Bruker ARX 400 spectrometers. ^{13}C and ^{1}H NMR spectra were referenced to signals of the deuterated solvents and the residual protonated solvents, respectively. GC analysis was performed on

an Agilent HP-5890 instrument with a FID detector, a HP-5 capillary column (polydimethylsiloxane with 5% phenyl groups, length: 30 m, internal diameter: 0.32 mm, film thickness: 0.25 μm), and argon as the carrier gas. GCMS was carried out on an Agilent HP-5890 instrument with an Agilent HP-5973 Mass-Selective Detector (EI), a HP-5 capillary column (polydimethylsiloxane with 5% phenyl groups, length: 30 m, internal diameter: 0.25 mm, film thickness: 0.25 μm), and helium as the carrier gas. MS (ESI) was performed on an Agilent 1969A TOF mass spectrometer.

Typical procedure: $Pd(OAc)_2$ (2 mol%) and TFP (4 mol%) were transferred into a vial (reaction volume: 4 mL) that was equipped with a septum, a small cannula, and a stirrer bar. After the vial was purged with argon, iodobenzene (1 mmol), benzyl acetylene (1 mmol), THF (2 mL), and DiPEA (2 mmol) were injected into the vial by using a syringe. Then, the vial was placed on an alloy plate that was transferred into an autoclave (300 mL, 4560 series Parr Instruments) under an argon atmosphere. After flushing the autoclave three times with CO, the pressure was adjusted to 1 bar, and the reaction was performed for 20 h at 25 °C. After this time, the pressure was carefully released. Water (6 mL) was added to the mixture and the solution was extracted 3–5 times with EtOAc (2–3 mL). The extracts were evaporated by adsorption onto silica gel and the crude product was purified by column chromatography (*n*-heptane to *n*-heptane/EtOAc, 10:1). The product was obtained as a yellow solid (248 mg, 98% yield).

Computational details: On the basis of our previous computational investigations into the competitive Heck and carbonylative Heck reaction,[7k] for geometry optimization and the frequency calculations, we decided to use the BP86 functional[12] in combination with the all-electron TZVP[13] basis set for C, H, O, P, and Br and the effective potential LANL2DZ[14] basis set for Pd. All of the optimized structures were either characterized by frequency calculations as energy minima without imaginary frequencies or as transition states with only one imaginary frequency; the imaginary model connected the initial and final states. At first, we used trimethylphosphine (PMe_3) as the ligand and small substrates (CH_3Br and $CH_3CH_2C{\equiv}CH$) to map the potential-energy surface, that is, to estimate the more-stable or the most-stable intermediates and the resting states. On the basis of these results, under the consideration of the more- or most-favorable potential-energy surface, we used the "real-sized" substrates (PhBr and $PhCH_2C{\equiv}CH$) for our calculations to estimate the difference between aliphatic and benzylic alkynes. We also used the real-size tri-*tert*-butylphosphine ($PtBu_3$), tricyclohexylphosphine (PCy_3), tri(2-furyl)phosphine (TFP, PFu_3), and triphenylphosphine (PPh_3) ligands to calculate the barriers to the rate-determining step (Scheme 4). Because the preferred reaction cycle does not directly involve PhBr or PhI (Scheme 4), we used PhI as our starting substrate. For discussion and comparison, we used the Gibbs free energies (ΔG) at 298 K (unless otherwise noted). We also carried out self-consistent reaction-field (SCRF) computations by using the polarizable continuum model (PCM[15]) with water as a polar solvent to estimate the influence of the solvent on the reaction energies. These results show that such a polar solvent does not affect the barrier for the rate-determining step (less than 1 kcal mol^{-1}). The Gaussian 03 program package was used for all calculations.[16]

(*E*)-3-Benzylidene-5-phenylfuran-2(3*H*)-one:
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75–7.81 (m, 2H), 7.62–7.67 (m, 2H), 7.42–7.52 (m, 7H), 6.95 ppm (d, J = 0.98 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.3, 156.8, 135.4, 135.0, 130.4, 130.2, 130.0, 129.0, 128.8, 127.9, 125.3, 125.2, 99.8 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 248 (60) $[M]^+$, 105 (100), 77 (25).

(*E*)-3-Benzylidene-5-*p*-tolylfuran-2(3*H*)-one:
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45–7.58 (m, 4H), 7.23–7.39 (m, 4H), 7.12 (d, J = 8.14 Hz, 2H), 6.74 (br s, 1H), 2.27 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.4, 157.0, 140.9, 135.1, 134.6, 130.0, 129.9, 129.5, 128.9, 125.4, 125.21, 125.18, 98.9, 21.5 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 262 (70) $[M]^+$, 119 (100), 91 (30), 65 (15).

(*E*)-3-Benzylidene-5-(4-*tert*-butylphenyl)furan-2(3*H*)-one:
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.48–7.62 (m, 4H), 7.26–7.40 (m, 6H), 6.79 (d, J = 0.96 Hz, 1H), 1.24 ppm (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.5, 157.1, 154.1, 135.2, 134.7, 130.1, 129.9, 129.0, 125.8, 125.4, 125.2, 125.1, 99.1, 34.9, 31.1 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 304 (100) $[M]^+$, 289 (60), 161 (60), 115 (30), 91 (10).

(*E*)-3-Benzylidene-5-(naphthalen-1-yl)furan-2(3*H*)-one:
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.30 (d, J = 8.6 Hz, 1H), 7.73–7.84 (m, 3H), 7.27–7.58 (m, 9H), 6.85 ppm (d, J = 1.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.4, 157.3, 136.0, 135.2, 133.9, 131.3, 130.4, 130.3, 130.2, 129.2, 129.0, 127.4, 127.2, 126.4, 126.1, 125.3, 125.2, 104.7 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 298 (100) $[M]^+$, 269 (30), 220 (15), 155 (80), 127 (85).

(*E*)-3-Benzylidene-5-(naphthalen-2-yl)furan-2(3*H*)-one:
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.18 (s, 1H), 7.66–7.83 (m, 4H), 7.55–7.61 (m, 2H), 7.36–7.48 (m, 6H), 6.95 ppm (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.4, 157.0, 135.5, 135.2, 134.2, 133.1, 130.4, 130.2, 129.2, 128.9, 128.8, 127.9, 127.6, 127.0, 125.7, 125.5, 125.2, 122.0, 100.5 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 298 (85) $[M]^+$, 281 (25), 207 (100), 155 (95), 127 (70), 96 (10).

(*E*)-3-Benzylidene-5-(4-methoxyphenyl)furan-2(3*H*)-one:
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50–7.66 (m, 4H), 7.26–7.42 (m, 4H), 6.84–6.92 (m, 2H), 6.72 (d, J = 0.94 Hz, 1H), 3.78 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.7, 161.6, 157.0, 135.4, 133.9, 130.0, 129.1, 127.1, 125.7, 120.7, 114.5, 98.0, 55.5 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 278 (65) $[M]^+$, 207 (40), 135 (100), 77 (10).

(*E*)-3-Benzylidene-5-(4-bromophenyl)furan-2(3*H*)-one:
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.47–7.57 (m, 6H), 7.33–7.41 (m, 4H), 6.86 ppm (d, J = 0.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.1, 155.9, 136.2, 135.1, 132.3, 130.5, 130.2, 129.2, 127.0, 126.8, 125.2, 124.9, 100.4 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 328 (80), 327 (80) $[M]^+$, 185 (100), 183 (100), 157 (20), 155 (20), 115 (10), 76 (10).

(*E*)-3-Benzylidene-5-(4-chlorophenyl)furan-2(3*H*)-one:
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.51–7.66 (m, 4H), 7.31–7.44 (m, 6H), 6.85 ppm (d, J = 0.98 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.1, 155.9, 136.5, 136.1, 135.1, 130.5, 130.2, 129.3, 129.2, 126.6, 125.2, 100.3 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 282 (50) $[M]^+$, 207 (35), 139 (100), 111 (30), 75 (10).

(*E*)-3-Benzylidene-5-(4-fluorophenyl)furan-2(3*H*)-one:
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.64–7.73 (m, 2H), 7.53–7.57 (m, 2H), 7.34–7.44 (m, 4H), 7.03–7.12 (m, 2H), 6.81 ppm (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.5 (d, J = 270.63 Hz), 156.0, 135.6, 135.1, 130.4, 130.1, 129.2, 127.5, 127.4, 125.3, 124.4 (d, J = 3.82 Hz), 116.2 (d, J = 22.49 Hz), 99.5 ppm (d, J = 2.33 Hz); GCMS (EI, 70 eV): *m*/*z* (%): 266 (65) $[M]^+$, 207 (15), 123 (100), 95 (40).

(*E*)-4-(4-Benzylidene-5-oxo-4,5-dihydrofuran-2-yl)benzonitrile:
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.77 (d, J = 8.8 Hz, 2H), 7.66 (d, J = 8.8 Hz, 2H), 7.55–7.61 (m, 2H), 7.49 (br s, 1H), 7.39–7.44 (m, 3H), 7.02 ppm (d, J = 1.0 Hz, 1H); GCMS (EI, 70 eV): *m*/*z* (%): 273 (80) $[M]^+$, 207 (10), 130 (100), 115 (15), 102 (20).

(*E*)-5-(4-Acetylphenyl)-3-benzylidenefuran-2(3*H*)-one:
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.92–8.01 (m, 3H), 7.77 (d, J = 8.7 Hz, 2H), 7.56–7.61 (d, 2H), 7.38–7.46 (m, 3H), 7.00 (d, J = 1.1 Hz, 1H), 2.56 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = δ 197.4, 169.1, 155.9, 138.0, 137.4, 135.0, 132.1, 130.8, 130.3, 129.3, 128.9, 125.5, 125.1, 102.3, 26.9 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 290 (80) $[M]^+$, 207 (70), 147 (100), 115 (10), 91 (10).

(*E*)-3-Benzylidene-5-(thiophen-3-yl)furan-2(3*H*)-one:
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.64 (dd, J^1 = 2.63 Hz, J^2 = 1.52 Hz, 1H), 7.48–7.54 (m, 2H), 7.27–7.39 (m, 6H), 6.63 ppm (d, J = 0.76 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.3, 153.3, 135.1, 135.0, 130.2, 130.1, 129.9, 129.0, 127.2, 125.1, 124.4, 99.4 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 254 (50) $[M]^+$, 111(100), 83 (10).

(*E*)-3-(3,4-Dimethoxybenzylidene)-5-phenylfuran-2(3*H*)-one:
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.56–7.66 (m, 2H), 7.26–7.37 (m, 3H), 7.21 (s, 1H), 7.15 (dd, J^1 = 8.55 Hz, J^2 = 2.06 Hz, 1H), 6.96 (d, J = 1.90 Hz, 1H), 6.82 (d, J = 8.28 Hz, 1H), 6.76 (d, J = 0.80 Hz, 1H), 3.83 (s, 3H), 3.82 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.6, 155.9, 151.0, 149.1, 135.6, 130.1, 128.7, 128.0, 127.9, 125.1, 124.3, 122.9, 112.6, 111.3, 99.7, 55.9 ppm (br s); GCMS (EI, 70 eV): *m*/*z* (%): 308 (100) $[M]^+$, 175 (50), 131 (10), 105 (90), 77 (40).

(*E*)-3-(4-Methylbenzylidene)-5-phenylfuran-2(*3H*)-one:
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.58–7.66 (m, 2H), 7.39 (d, J = 8.32 Hz, 2H), 7.23–7.35 (m, 4H), 7.13 (d, J = 8.32 Hz, 2H), 6.78 (d, J = 0.95 Hz, 1H), 2.27 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.3, 156.3, 141.0, 135.7, 132.3, 130.2, 130.1, 129.8, 128.7, 128.0, 125.1, 124.2, 99.9, 21.5 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 262 (80) $[M]^+$, 128 (10), 105 (100), 77 (40).

(*E*)-3-(4-Chlorobenzylidene)-5-phenylfuran-2(*3H*)-one:
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.66–7.75 (m, 2H), 7.47–7.53 (m, 2H), 7.30–7.41 (m, 6H), 6.82 ppm (d, J = 0.93 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.5, 136.3, 133.7, 133.6, 131.2, 130.8, 129.5, 129.0, 127.9, 125.9, 125.5, 99.5 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 282 (60) $[M]^+$, 105 (100), 77 (40).

(*E*)-3-(4-(Methylthio)benzylidene)-5-phenylfuran-2(*3H*)-one:
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.63–7.70 (m, 2H), 7.42–7.49 (m, 2H), 7.26–7.38 (m, 4H), 7.16–7.22 (m, 2H), 6.82 (d, J = 0.94 Hz, 1H), 2.44 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.5, 156.6, 142.7, 134.8, 131.5, 130.4, 130.3, 128.8, 128.1, 125.8, 125.2, 124.2, 99.9, 14.9 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 294 (100) $[M]^+$, 266 (10), 207 (20), 161 (15), 105 (100), 77 (30).

(*E*)-3-(4-(Dimethylamino)benzylidene)-5-phenylfuran-2(*3H*)-one:
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.60–7.68 (m, 2H), 7.41–7.50 (m, 2H), 7.24–7.38 (m, 4H), 6.83 (d, J = 0.78 Hz, 1H), 6.62 (d, J = 9.07 Hz, 2H), 2.97 ppm (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.7, 154.0, 151.5, 136.9, 132.4, 129.5, 128.7, 128.6, 124.7, 122.9, 119.4, 111.9, 100.4, 40.0 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 291 (65) $[M]^+$, 263 (20), 207 (10), 158 (100), 142 (10), 77 (10).

1,5-Diphenylpent-2-yn-1-one: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.83–7.99 (m, 2H), 7.41–7.51 (m, 1H), 7.12–7.38 (m, 7H), 2.87 (t, J = 7.3 Hz, 2H), 2.69 ppm (t, J = 7.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.2, 139.7, 136.8, 134.0, 129.7, 128.7, 128.6, 128.5, 126.8, 95.6, 80.3, 34.0, 21.4 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 234 (15) $[M]^+$, 233 (20), 216 (10), 105 (15), 91 (100), 77 (10), 65 (10), 51 (10).

4-Cyclopentyl-1-phenylbut-2-yn-1-one: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.02–8.11 (m, 2H), 7.47–7.57 (m, 1H), 7.35–7.44 (m, 2H), 2.44 (d, J = 6.9 Hz, 2H), 2.04–2.22 (m, 1H), 1.73–1.91 (m, 2H), 1.44–1.68 (m, 4H), 1.19–1.36 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.3, 137.0, 133.9, 129.6, 128.5, 96.5, 79.8, 38.5, 32.3, 25.2, 25.1 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 212 (5) $[M]^+$, 211 (10), 183 (40), 144 (100), 115 (40), 105 (40), 77 (40), 66 (25), 51 (15).

3-Cyclohexyl-1-phenylprop-2-yn-1-one: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.00–8.08 (m, 2H), 7.45–7.53 (m, 1H), 7.32–7.43 (m, 2H), 2.51–2.68 (m, 1H), 1.77–1.90 (m, 2H), 1.61–1.74 (m, 2H), 1.40–1.59 (m, 3H), 1.19–1.37 ppm (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.3, 137.1, 133.9, 129.5, 128.5, 100.4, 79.6, 31.7, 29.4, 25.7, 24.7 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 212 (5) $[M]^+$, 211 (10), 183 (20), 155 (10), 144 (100), 128 (10), 115 (10), 105 (70), 77 (50), 51 (10).

3-Cyclopentyl-1-phenylprop-2-yn-1-one: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.98–8.06 (m, 2H), 7.43–7.52 (m, 1H), 7.31–7.39 (m, 2H), 2.70–2.90 (m, 1H), 1.85–2.04 (m, 2H), 1.61–1.78 (m, 4H), 1.43–1.60 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.3, 137.0, 133.8, 129.5, 128.5, 101.0, 79.2, 33.4, 30.3, 25.3 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 198 (95) $[M]^+$, 183 (10), 170 (30), 157 (95), 142 (100), 141 (100), 128 (75), 121 (40), 115 (40), 105 (100), 91 (30), 77 (100), 65 (10), 51 (20).

1-Phenylhept-2-yn-1-one: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.00–8.09 (m, 2H), 7.45–7.54 (m, 1H), 7.33–7.41 (m, 2H), 2.41 (t, J = 7.1 Hz, 2H), 1.50–1.62 (m, 2H), 1.33–1.47 (m, 2H), 0.87 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.3, 136.9, 133.9, 129.5, 128.5, 96.9, 79.7, 29.9, 22.1, 18.9, 13.5 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 186 (10) $[M]^+$, 185 (20), 158 (20), 157 (40), 144 (100), 129 (30), 128 (30), 115 (70), 105 (80), 77 (70), 66 (20), 51 (20).

1-Phenyloct-2-yn-1-one: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.00–8.09 (m, 2H), 7.46–7.54 (m, 1H), 7.33–7.42 (m, 2H), 2.40 (t, J = 7.1 Hz, 2H), 1.51–1.66 (m, 2H), 1.20–1.43 (m, 4H), 0.84 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.3, 136.9, 133.9, 129.6, 128.5, 96.9, 79.7, 31.1, 27.5, 22.2, 19.2, 13.9 ppm; GCMS (EI, 70 eV): *m*/*z* (%): 200 (10) $[M]^+$, 199 (40), 185 (30), 171 (15), 157 (60), 144 (50), 128 (30), 115 (50), 105 (100), 77 (40), 66 (10), 51 (10).

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