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Palladium-catalyzed carbonylative annulation of terminal alkynes: synthesis of coumarins and 2-quinolones

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Dedicated to Professor Jean-Pierre Genêt on the occasion of his 60th birthday

Abstract

o-Iodophenols and *o*-iodoaniline derivatives react with terminal alkynes under 1 atm of CO in the presence of pyridine and catalytic amounts of $Pd(OAc)_2$ to generate coumarins and 2-quinolones, respectively, as the only products. Terminal alkynes bearing alkyl, aryl, silyl, hydroxyl, ester and cyano substituents are effective in these processes affording the desired products in moderate yields. The formation of coumarins and 2-quinolones in this process is in stark contrast with all previously described palladium-catalyzed reactions of *o*-iodophenols or *o*-iodoanilines with terminal alkynes and CO, which have afforded chromones and 4-quinolones. Moreover, under our reaction conditions terminal alkynes insert into the carbon–palladium bond instead of undergoing a Sonogashira-type coupling as confirmed by an isotope labeling experiment.

Keywords: Palladium; Terminal alkyne; Carbon monoxide; Annulation

1. Introduction

Both internal and terminal alkynes have been utilized in a variety of transition metal-catalyzed reactions for the construction of new carbon–carbon and carbon–heteroatom bonds [1,2]. However, the reactivity of terminal and internal alkynes is generally quite different. The reactions of alkynes catalyzed by transition-metal complexes can be roughly divided into three categories: (1) reactions involving attack of various nucleophiles on the triple bond coordinated to the transition metal; (2) reactions involving insertion of the triple bond into the transition metal–carbon bond; and (3) reactions proceeding through the formation of transition metal–alkynyl complexes (Scheme 1). Both terminal and internal alkynes have been utilized in processes in which a nucleophile attacks the triple bond activated by coordination to a transition-metal complex [3]. The main reaction pathway for internal alkynes, however, is insertion into the transition metal–carbon bond, while most of the reactions involving terminal alkynes proceed through the formation of alkynyl-transition metal complexes [1].

The palladium-catalyzed annulation of internal alkynes by *ortho*-substituted aryl iodides developed in our laboratories in the last 15 years [4,5] generally proceeds by insertion of an alkyne into a carbon–palladium bond. Terminal alkynes are generally ineffective in those processes. Analogous methods for the synthesis of benzofurans [6], indoles [7,8], isocoumarins [9], quinolines [10], pyridines [10] and carbolines [11] from terminal alkynes and related *ortho*-substituted aryl iodides always require the use of a copper co-catalyst and undoubtedly involve the initial formation of an *ortho*-substituted alkynylbenzene by a Sonogashira coupling [12], followed by cyclization to form the desired heterocycle. Quite often it is necessary to use reagents other than palladium complexes, such as NaOEt [7], n-Bu_4NF [8], $ZnCl_2$ [9] or CuI [10], to affect cyclization.

We have recently developed general and efficient syntheses of 3,4-disubstituted coumarins [13] and 2-

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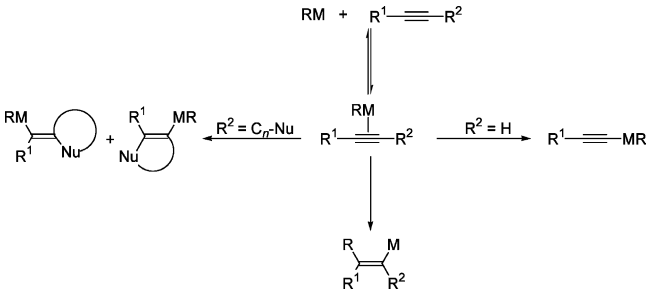
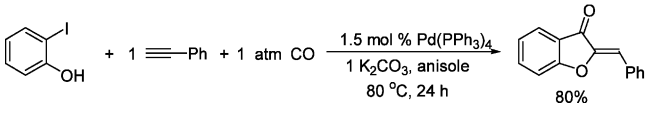


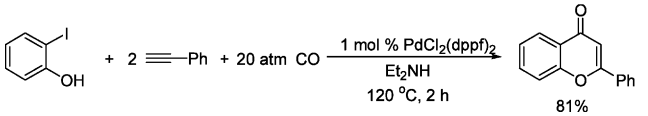
Scheme 1.

quinolones [14] by three-component processes involving an *ortho*-functionalized aryl iodide, an internal alkyne, and CO (Scheme 2). One of the interesting features of these processes is the fact that insertion of the carbon–carbon triple bond into the carbon–palladium bond occurs in preference to insertion of CO, while all previous alkyne/CO reactions have afforded products in which CO inserts first.

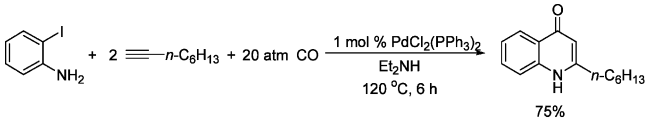
Analogous palladium-catalyzed reactions of terminal alkynes with *o*-iodophenols or *o*-iodoanilines and CO are well known. The reaction of *o*-iodophenol, a terminal alkyne and CO affords either aurones [15–17] (Eq. (1)) or chromones [17–19] (Eq. (2)) depending on the reaction conditions employed. Alternatively, chromones can be obtained as the sole products under mild conditions by using *o*-iodophenyl acetates as annulating agents [20]. The analogous reaction employing *o*-iodoanilines is also known and affords exclusively 6-membered ring 4-quinolones (Eq. (3)) [19,21].



(1)

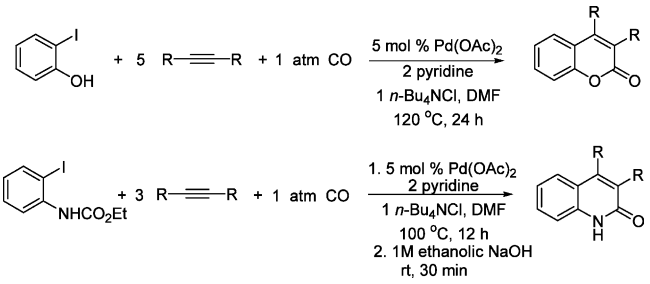


(2)



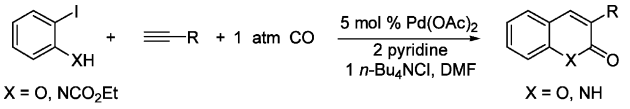
(3)

Thus, the outcome of these reactions is quite different from the carbonylative annulation of internal alkynes developed by us. These processes clearly involve initial formation of an ynone, which cyclizes to either 5- or 6-membered rings depending on the base used (Scheme 3).



Scheme 2.

The unusual alkyne/CO insertion selectivity of the carbonylative annulation of internal alkynes developed by us has prompted us to examine analogous reactions of terminal alkynes. Herein, we wish to report that, under our conditions for the palladium-catalyzed carbonylative annulation of internal alkynes, terminal alkynes undergo insertion into the carbon–palladium bond in preference to the insertion of CO, thus affording coumarins or 2-quinolones (Eq. (4)).

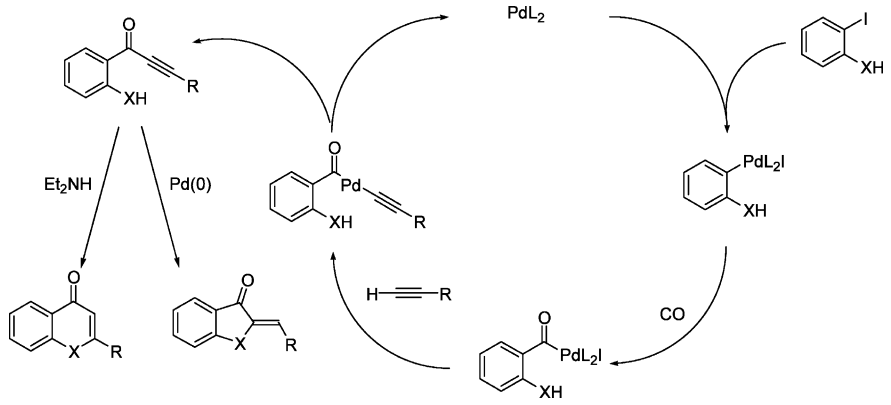


(4)

2. Results and discussion

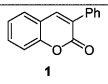
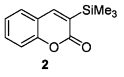
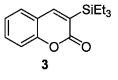
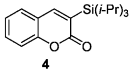
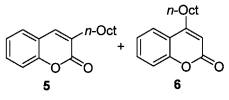
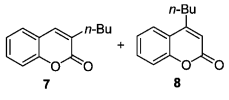
2.1. Synthesis of coumarins

The reaction of *o*-iodophenol with phenylacetylene in the presence of 1 atm of CO under our standard reaction conditions for the synthesis of coumarins from internal alkynes [13] afforded 3-phenylcoumarin (**1**) in a 23% yield (Eq. (5)). This is the product that would be expected if the terminal alkyne reacted in the same manner as an internal alkyne. None of the other annulation products we might have reasonably expected, namely 2-phenylchromone or 2-phenylbenzofuran, were detected. The reaction, however, was very messy, and a significant amount of a low polarity viscous purple oil was isolated. This oil most likely results from polymerization of phenylacetylene. Since studies of the palladium-catalyzed dimerization of terminal alkynes have shown that phenylacetylene is by far the most reactive acetylene [22], we have examined a number of different alkynes in order to identify a more suitable alkyne for our optimization studies (Eq. (6)). The results are summarized in Table 1.



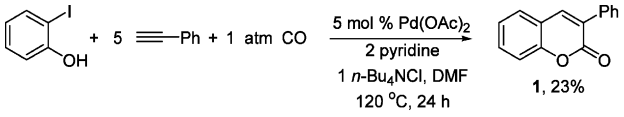
Scheme 3.

Table 1
Palladium-catalyzed carbonylative annulation of terminal alkynes by *o*-iodophenol (Eq. (6)) [a]

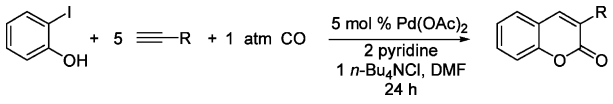
entry	R	temp. (°C)	product(s)	% yield (ratio of isomers)	% recovery of o-iodophenol
1	Ph	120	 1	23	26
2	$SiMe_3$		 2	12	15
3	$SiEt_3$		 3	24	5
4	$Si(i\text{-}Pr)_3$		 4	18	5
5	$n\text{-}C_8H_{17}$	120	 5 6	36 (62:38)	-
6		100		19 (68:32)	35-40
7		80		0	*ca* 80
8[b]		120		28 (69:31)	-
9	$n\text{-}C_4H_9$		 7 8	33 (70:30)	-

[a] Typical reaction conditions: *o*-iodophenol (0.5 mmol); the alkyne (2.5 mmol); pyridine (1.0 mmol); $n\text{-}Bu_4NCl$ (0.5 mmol); and $Pd(OAc)_2$ (5 mol%, 0.025 mmol) under 1 atm of CO in DMF (5 ml) was stirred at 120 °C for 24 h.

[b] Three equivalents of alkyne were used.



(5)



(6)

The reaction of trimethylsilylacetylene (entry 2) was significantly cleaner, and only the product and *o*-iodophenol were observed by Thin-layer chromatography (TLC) analysis. The yield of the desired product, however, was very low, and the reaction was not complete even after 24 h. The low yield might be attributed to the high volatility of this acetylene (b.p. 53 °C). Therefore, two other silyl acetylenes with higher boiling points have been examined (entries 3 and 4). In both cases a higher yield of the desired coumarin was obtained, and the starting material was almost completely consumed. The slight decrease in the yield in the reaction of triisopropylsilylacetylene relative to the yield in the reaction of triethylsilylacetylene is most likely due to the increased steric hindrance about the triple bond. The alkyl acetylene, 1-decyne, was examined next (entry 5). Surprisingly, both 3- and 4-*n*-octylcoumarins were isolated from the reaction mixture in an ca. 2:1 ratio. The combined yield of the coumarins was the highest observed so far (36%). However, it should be noted that a small amount of apparent polymeric product is present in the isolated coumarin, as evidenced by the alkyl portion of the ^{1}H-NMR spectrum. Indeed, a significant amount of polymeric product was also isolated from the reaction mixture. To minimize the amount of polymerization, the reaction was run at lower temperatures (entries 6 and 7). Unfortunately, the decrease in the reaction temperature led to incomplete reactions and significantly lower yields of the coumarins. None of the desired product was formed in the reaction run at 80 °C.

The experiments conducted with *N*-substituted *o*-anilines (see below) showed that the use of a lower amount of the alkyne improves the yield of the desired

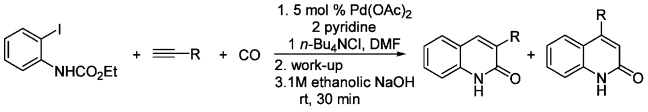
product. Higher yields were also obtained using 1-hexyne instead of 1-decyne. Therefore, two experiments were conducted to determine if the same changes would be observed in the reactions of *o*-iodophenol (Table 1, entries 8 and 9). However, no improvement in the yield was observed in either case. The use of three equivalents of 1-decyne (entry 8) led to a small decrease in the yield of the coumarins. The reaction of 1-hexyne (entry 9) was significantly cleaner than the reaction of 1-decyne, and a much lower amount of the polymeric products was formed. However, the yield of the coumarins did not increase.

Our initial experiments have established that the carbonylative annulation of terminal alkynes under our reaction conditions follows a different mechanism than under previously developed conditions and leads to the formation of different products. The formation of 4-*n*-octylcoumarin (**6**) in the reaction with 1-decyne strongly suggests that the triple bond of the terminal alkyne does insert into the carbon–palladium bond, since no mechanism involving a Sonogashira-like coupling between *o*-iodophenol and a terminal alkyne can account for the formation of such a product.

However, the results of the experiments shown in Table 1, as well as the reactivity patterns established for the carbonylative annulation of internal alkynes [13,14], indicate that the number of reaction parameters that can be varied to improve the yield of the process is very limited. Therefore, we decided to switch to *N*-substituted *o*-iodoanilines, which in many cases have proven to be more reactive than *o*-iodophenols.

2.2. Synthesis of 2-quinolones—optimization of the reaction conditions

Ethyl *N*-(2-iodophenyl)carbamate and 1-decyne were chosen as model substrates (Eq. (7)). Under the standard coumarin reaction conditions (Table 2, entry 1), the reaction afforded 3- and 4-*n*-octyl-2-quinolones (R = *n*-Oct) in a 73:27 ratio and an overall 29% yield. Although the yield is slightly lower than the yield of the corresponding reaction with *o*-iodophenol (Table 1, entry 5), the quinolones were much purer than the coumarins (as judged by their ^{1}H-NMR spectra). The significantly higher polarity of 2-quinolones allows more efficient separation from the polymeric by-products by column chromatography. As is the case with internal alkynes, treatment of the crude reaction mixture with ethanolic NaOH is required to achieve complete removal of the ethoxycarbonyl group from the quinolone products. When the reaction was run without such treatment, all four possible products with N–H and N–CO_2Et groups were observed.



(7)

Lowering the temperature to 100 °C and shortening the reaction time to 12 h did not significantly affect the yield of the desired quinolones (compare entries 1 and 2). Since a decrease in the temperature did not lead to a decrease in the reaction yield, 1-hexyne was examined as a model substrate (entry 3). Despite the fact that the boiling point of 1-hexyne is only 71–72 °C, the yield of the 2-quinolone actually increased to 44%. Moreover, both quinolone isomers were essentially pure, as judged by ^{1}H-NMR spectroscopy. Therefore, 1-hexyne was used as a model substrate for optimization from this point on. Further variation of the reaction temperature and time (entries 4 and 5) showed that this terminal alkyne behaves under our reaction conditions quite similar to internal alkynes. The annulation reaction is complete after 6 h at 100 °C (entry 4). A further decrease

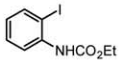
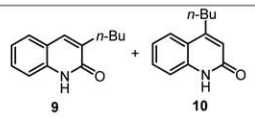
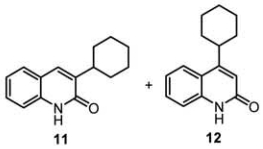
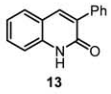
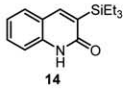
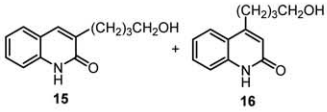
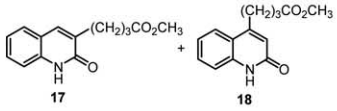
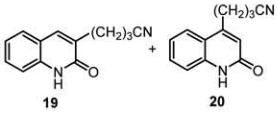
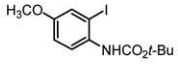
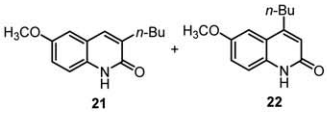
Table 2
The effect of the reaction temperature and stoichiometry on the palladium-catalyzed carbonylative annulation of terminal alkynes with ethyl *N*-(2-iodophenyl)carbamate (Eq. (7)) [a]

Entry	R	Equivalents	Temperature (°C)	Time (h)	% Yield	Ratio of isomers [b]
1	*n*-C_8H_{17}	3	120	24	29	73:27
2		3	100	12	32	76:24
3	*n*-C_4H_9	3	100	12	44	73:27
4		3	100	6	43	70:30
5		3	80	24	31	74:26
6		10	100	24	33	73:27
7		5	100	24	44	73:27
8		3	100	24	55	70:30
9		2	100	24	47	70:30

[a] Typical reaction conditions: ethyl *N*-(2-iodophenyl)carbamate (0.5 mmol), the alkyne, pyridine (1.0 mmol), *n*-Bu_4NCl (0.5 mmol), and $Pd(OAc)_2$ (5 mol%, 0.025 mmol) under 1 atm of CO in DMF (5 ml) were stirred at 100 °C for 12 h, then the crude product was treated with 1 M ethanolic NaOH (5 ml) at room temperature for 30 min.

[b] The ratio of 3-alkyl- to 4-alkyl-2-quinolones.

Table 3
Synthesis of 2(1*H*)-quinolones via palladium-catalyzed annulation of terminal alkynes (Eq. (7)) [a]

entry	*N*-substituted *o*-iodoaniline	R	product(s)	% yield (ratio of isomers)
1		*n*-Bu	 **9** **10**	55 (70:30)
2		*c*-C_6H_{11}	 **11** **12**	50 (82:18)
3		Ph	 **13**	42
4[b]		Ph	13	41
5		$SiEt_3$	 **14**	38
6		CH_2OH		0[c]
7		CO_2Et		0[c]
8		$(CH_2)_3CH_2OH$	 **15** **16**	~25 (80:20)
9		$(CH_2)_3CO_2CH_3$	 **17** **18**	47 (81:19)
10		$(CH_2)_3CN$	 **19** **20**	41 (81:19)
11		*n*-Bu	 **21** **22**	53 (69:31)

[a] Typical reaction conditions: ethyl *N*-(2-iodophenyl)carbamate (0.5 mmol), the alkyne (1.5 mmol), pyridine (1 mmol), *n*-Bu_4NCl (0.5 mmol), $Pd(OAc)_2$ (5 mol %, 0.025 mmol) under 1 atm of CO in DMF (5 ml) was stirred at 100 °C for 12 h, and then the crude product was treated with 1M ethanolic NaOH (5 ml) at rt for 30 min.

[b] The reaction was run as in footnote a, except that all reagents, but phenylacetylene, were stirred at 100 °C for 15 min, then phenylacetylene (1.5 mmol) in 0.5 ml of DMF was added in one portion.

[c] A very messy reaction. None of the desired product was detected in the crude reaction mixture by ^1H NMR spectroscopy. No separation by column chromatography has been attempted.

in the reaction temperature to 80 °C results in a very slow reaction, and a lower yield even after 24 h (entry 5).

Since oligomerization of the alkyne is presumed to be the major competing process, the amount of the alkyne in the reaction mixture was varied to establish the optimal aryl iodide to alkyne ratio (entries 6–9). Increasing the amount of 1-hexyne to 10 equivalents (entry 6) led to a significant decline in the yield of the

desired product, while the use of lesser amounts of 1-hexyne (entries 8 and 9) resulted in higher yields. The highest yield was obtained using three equivalents of 1-hexyne (entry 8). It is noteworthy, that even the use of only two equivalents of the alkyne afforded a higher yield of the quinolones than the use of five equivalents. These results are in contrast with the carbonylative annulation of internal alkynes, in which the yield of the product increased with an increase in the amount of alkyne up to a certain point and then remained constant.

We have subsequently examined the effect of a number of other reaction parameters on the yield of 2-quinolones. No significant change in the yield of 2-quinolone was observed when a different Pd(II) catalyst, $PdCl_2(PhCN)_2$, or a Pd(0) catalyst, $Pd(dba)_2$, were employed. However, the yield dropped to 26%, when 10 mol% of PPh_3 was added. It is noteworthy, that the regioselectivity of the reaction is not at all affected by the choice of the palladium catalyst, suggesting that in all cases the reaction proceeds through the same arylpalladium intermediate. Similarly, change of the base (pyridine, 2,4,6-collidine, 3-cyanopyridine, DMAP, NEt_3), removal of *n*-Bu_4NCl, or an increase in the amount of the catalyst did not raise the yield of 2-quinolone. The ratio of regioisomers varied only slightly from a low of 61:39 to a high of 80:20.

Thus, at this point, the optimized reaction conditions are actually the same as the reaction conditions used for the carbonylative annulation of internal alkynes: 0.5 mmol of ethyl *N*-(2-iodophenyl)carbamate, three equivalents of alkyne, two equivalents of pyridine, one equivalent of *n*-Bu_4NCl, 5 mol% of $Pd(OAc)_2$ in 5 ml of DMF. The reactions are run at 100 °C for 12 h, and the crude reaction products are treated with 5 ml of 1 M ethanolic NaOH at room temperature for 30 min to remove the carbamate protecting group. The carbonylative annulation of other terminal alkynes was investigated next using these reaction conditions.

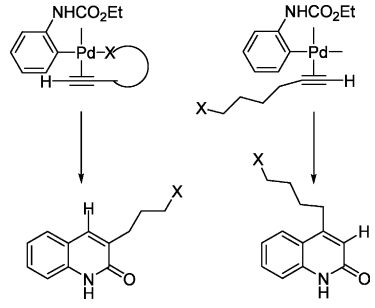
2.3. Synthesis of 2-quinolones—scope and limitations

Alkyl-substituted terminal alkynes afford the desired 2-quinolones as mixtures of regioisomers in 50–55% yields (Table 3, entries 1 and 2). The regioselectivity of the reaction improves with an increase in the size of the substituent on the triple bond. These results support our hypothesis that the terminal alkynes behave in this process just like the internal alkynes in our earlier annulation chemistry [4,5]. Namely, they undergo *insertion* into the carbon–palladium bond, and the regioselectivity of the insertion is governed by steric factors.

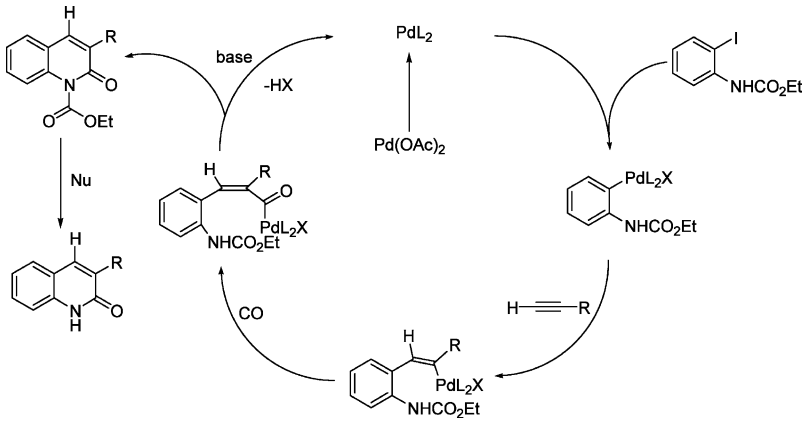
The carbonylative annulation of phenylacetylene gives rise to 3-phenyl-2-quinolone (**13**) as the sole product in a 42% yield (entry 3). Despite the fact that phenylacetylene is significantly more reactive in the palladium-catalyzed homocoupling reaction [22], the yield of **13** is only slightly lower than the yields of 2-quinolones from alkyl acetylenes. Still, a significantly greater amount of polymeric by-products is formed in the reaction with phenylacetylene. In fact, the reaction mixture turns purple at room temperature immediately upon mixing the reagents in the reaction vial. Unfortunately, an attempt to improve the yield of **13** by adding phenylacetylene to the reaction mixture at 100 °C failed (entry 4). Excellent regioselectivity is the other interesting feature of this phenylacetylene reaction. The carbonylative annulation of cyclohexylacetylene afforded a ca. 4:1 mixture of isomers (entry 2), although the size of a cyclohexyl and a phenyl group are almost the same. Therefore, it is likely that the steric bulk of the substituents on the triple bond is a major, but not the only, factor determining the regioselectivity of the process. The electronic effects of the substituents on the carbon–carbon triple bond should favor alkyne insertion when it affords a vinylpalladium complex with the palladium atom next to a substituent better able to stabilize a negative charge. Since a phenyl group is much more effective in stabilizing a negative charge than a cyclohexyl group is, this would account for the better regioselectivity observed in the reaction of phenylacetylene.

The carbonylative annulation of terminal alkynes bearing various functional groups was examined next. Triethylsilylacetylene afforded the desired product **14** in a 38% yield with excellent regioselectivity (entry 5). The carbonylative annulation of terminal alkynes bearing hydroxyl, ester and cyano groups shows that the outcome of the process strongly depends on the proximity of the group to the carbon–carbon triple bond. The carbonylative annulations of propargyl alcohol (entry 6) and ethyl propiolate (entry 7) afforded very messy reactions, producing significant amounts of polymeric products. None of the desired 2-quinolones were detected by ^{1}H-NMR spectroscopy.

The carbonylative annulation of terminal alkynes in which the same functional groups are 3–4 carbon atoms removed from the triple bond affords 2-quinolone products. Although the yield in the reaction with 5-hexyn-1-ol remains low (entry 8) perhaps due to carbonylation of the alcohol group, the yield obtained



Scheme 4.



Scheme 5.

employing methyl 5-hexynoate (entry 9) is only slightly lower than the yield of the reaction with 1-hexyne. The carbonylative annulation of 5-hexynenitrile also afforded the desired products in a 41% yield (entry 10). The surprising feature of these reactions is an evident improvement in the regioselectivity. The ratio of isomers is around 4 to 1 when functionalized acetylenes are used, compared to the 2.2 to 1 ratio obtained in most of the reactions with 1-hexyne (entry 1, see also entry 11). It is conceivable that additional coordination of the palladium atom by the functional group of the alkyne stabilizes the palladium complex from which the major isomer arises upon insertion (Scheme 4). It is surprising, however, that the nature of the functional group does not affect the regioselectivity, since a cyano group and an hydroxyl group are expected to have significantly different affinities towards palladium.

The carbonylative annulation of 1-hexyne with an iodoaniline bearing a methoxy group in the para position to the carbamate group afforded the desired product in a 53% yield as a 69:31 mixture of regioisomers (entry 11). Thus, an electron-donating group on the aromatic ring affects neither the yield nor the regioselectivity of the process.

2.4. Mechanism

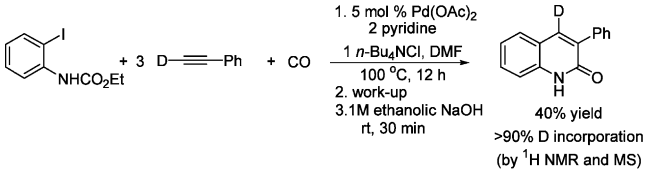
Since the carbonylative annulation of terminal alkynes closely resembles the carbonylative annulation of internal alkynes in all major features (the nature of the products, the regioselectivity, etc.), we believe that the mechanisms of these two processes must be similar. Thus, for the carbonylative annulation of terminal alkynes we propose the mechanism shown in Scheme 5. The in situ reduction of $Pd(OAc)_2$ to Pd(0) generates the active catalyst. Oxidative addition of the aryl iodide to Pd(0) leads to formation of an arylpalladium complex, which in turn reacts with the terminal alkyne to generate a vinylpalladium intermediate. Insertion of CO into the vinylpalladium bond produces an acylpalladium complex. Nucleophilic attack of the carbamate nitrogen on the carbonyl group of the acylpalladium complex leads to formation of the *N*-protected 2-quinolone with regeneration of the Pd(0) catalyst. Subsequent hydrolysis of the carbamate group affords the desired product.

Thus, our process differs from the previously reported palladium-catalyzed reaction of *o*-iodoanilines with terminal alkynes and CO in two aspects [19]. First, the terminal alkyne inserts into the carbon–palladium bond, instead of undergoing a Sonogashira-type coupling. Second, this insertion of the alkyne occurs prior to the insertion of CO, thus leading to 2- and not 4-quinolone derivatives.

The insertion of a carbon–carbon triple bond of a terminal alkyne into the carbon–palladium bond is not unprecedented [23–26], although it is certainly very rare. The Sonogashira-type coupling prevails in almost all cases, and even in those cases where insertion apparently occurs, it sometimes competes with coupling [25]. However, in our case, invoking such a coupling as the first step of the process could hardly account for the formation of 3-substituted 2-quinolones, and no reasonable mechanism for the formation of the 4-substituted isomer from the coupling product can be envisioned. Indeed, the formation of both regioisomers and the fact that the regioselectivity is apparently governed by steric factors, just as in the annulation of internal alkynes, provides the strongest support for the idea that alkyne insertion does occur.

Still, we sought more direct evidence for the insertion step. Therefore, the carbonylative annulation of deuterated phenylacetylene has been examined (Eq. (8)). To our delight, the reaction afforded 3-phenyl-4-deutero-2-quinolone with better than 90% deuterium incorporation, as determined by ^{1}H-NMR spectroscopic and MS analysis. This result proves unambiguously that insertion of the terminal alkyne does indeed occur under our reaction conditions. It also shows that relatively little exchange of the acetylenic proton occurs under our reaction conditions, even with phenylacetylene, and,

therefore, the formation of alkynylpalladium complexes is irreversible. It is also remarkable that phenylacetylene survives long enough to participate in the annulation, even though it has been reported that the dimerization of phenylacetylene proceeds in a 63% yield after just 40 min at room temperature in the presence of just 2 mol% of an appropriate palladium catalyst [22].



(8)

3. Conclusions

The reaction of *o*-iodophenol or ethyl *N*-(2-iodophenyl)carbamate with terminal alkynes and CO under our standard carbonylative annulation conditions ($Pd(OAc)_2$/pyridine) affords exclusively coumarins or 2-quinolones. This is the first example of such chemoselectivity. All previous work has reported the formation of chromones or 4-quinolones from these starting materials, respectively. Terminal alkynes with alkyl, phenyl, silyl, hydroxyl, ester, and cyano substituents react with ethyl *N*-(2-iodophenyl)carbamate to afford 2-quinolones in modest yields. Both 3- and 4-substituted 2-quinolones are obtained in the reactions with terminal alkynes bearing long alkyl chains. Such unusual behavior for terminal alkynes indicates that the key step in this process is insertion of the terminal alkyne into the carbon–palladium bond and not the Sonogashira-type coupling. This reactivity pattern is unambiguously proven by an isotope labeling experiment. The annulation of *d*-phenylacetylene affords 4-deutero-3-phenyl-2-quinolone in a 40% yield with better than 90% deuterium incorporation.

4. Experimental

4.1. General

All ^{1}H- and ^{13}C-NMR spectra were recorded at 400 and 100.5 MHz, respectively. TLC was performed using commercially prepared 60-mesh silica gel plates (Scientific Adsorbents Co.), and visualization was effected with short wavelength UV light (254 nm) or a basic $KMnO_4$ solution (3 g $KMnO_4$+20 g K_2CO_3+5 ml NaOH (5%)+300 ml of H_2O). All melting points are uncorrected. Low resolution mass spectra were recorded on a Finnigan TSQ700 triple quadrupole mass spectrometer (Finnigan MAT, San Jose, CA). High resolution mass spectra were recorded on a Kratos MS50TC double focusing magnetic sector mass spectrometer using EI at 70 eV.

4.2. Reagents

All reagents were used directly as obtained commercially unless otherwise noted. DMF, hexanes, and ethyl acetate were purchased from Fisher Scientific Co. Pyridine was purchased from Fisher Scientific Co. and purified by distillation from CaH_2. Et_3N, 2,4,6-collidine, 3-cyanopyridine and DMAP were purchased from Aldrich Chemical Co. *n*-Bu_4NCl was purchased from Lancaster Synthesis, Inc. 1-Hexyne, 1-octyne, phenylacetylene, *d*-phenylacetylene, trimethylsilylacetylene, triethylsilylacetylene, triisopropylsilylacetylene, propargyl alcohol, 5-hexyn-1-ol and ethyl propiolate were purchased from Aldrich Chemical Co. Methyl 5-hexynoate and 5-hexynenitrile were purchased from GFS Chemicals Co. Cyclohexylacetylene was purchased from Farchan Chemical Co. Ethyl *N*-(2-iodophenyl)carbamate [14] and *tert*-butyl *N*-(2-iodo-4-methoxyphenyl)carbamate [27] were prepared following literature procedures. All palladium salts were donated by Johnson Matthey Inc. and Kawaken Fine Chemicals Co. Ltd. Triphenylphosphine was donated by Kawaken Fine Chemicals Co. Ltd.

4.3. General procedure for the synthesis of coumarins

o-Iodophenol (0.5 mmol), the alkyne (2.5 mmol), pyridine (79 mg, 1.0 mmol), *n*-Bu_4NCl (139 mg, 0.5 mmol), $Pd(OAc)_2$ (5.6 mg, 5 mol%, 0.025 mmol) and DMF (5 ml) were placed in a 4 dram vial. The vial was purged with CO for 2 min and then connected to a balloon of CO. The reaction mixture was stirred at 120 °C for 24 h, then allowed to cool to room temperature (r.t.), diluted with EtOAc, washed with water, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The product was isolated by column chromatography on silica gel. The following coumarins were prepared using this procedure.

4.3.1. 3-Phenyl-2H-1-benzopyran-2-one (**1**)

The compound was identified by comparing its ^{1}H- and ^{13}C-NMR spectral properties with the literature data [28].

4.3.2. 3-Trimethylsilyl-2H-1-benzopyran-2-one (**2**)

Yellowish solid, m.p. 85–88 °C; ^{1}H-NMR ($CDCl_3$): δ 7.79 (s, 1H), 7.45–7.52 (m, 2H), 7.22–7.31 (m, 2H), 0.33 (s, 9H); ^{13}C-NMR ($CDCl_3$): δ 163.0, 154.9, 150.1, 131.6, 130.1, 127.8, 124.2, 119.5, 116.8, −1.8; MS *m*/*z* (relative intensity): 218 (27, M^+), 203 (100), 175 (52),

145 (16), 135 (17), 94 (16); HRMS Calc. for $C_{12}H_{14}O_2Si$: 218.0763, Found: 218.0770.

4.3.3. 3-Triethylsilyl-2H-1-benzopyran-2-one (3)

White solid, m.p. 80–83 °C; ^{1}H-NMR ($CDCl_3$): δ 7.77 (s, 1H), 7.45–7.52 (m, 2H), 7.22–7.31 (m, 2H), 0.96–1.01 (m, 9H), 0.84–0.90 (m, 6H); ^{13}C-NMR ($CDCl_3$): δ 163.0, 154.9, 151.4, 131.8, 127.8, 127.6, 124.2, 119.5, 116.8, 7.6, 2.7; IR (neat, cm^{-1}): 2954, 2918, 2873; MS *m/z* (relative intensity): 230 (100, $[M-C_2H_5]^+$), 203 (22), 175 (21).

4.3.4. 3-Triisopropylsilyl-2H-1-benzopyran-2-one (4)

Off-white solid, m.p. 113–118 °C; ^{1}H-NMR ($CDCl_3$): δ 7.82 (s, 1H), 7.46–7.51 (m, 2H), 7.25–7.31 (m, 2H), 1.53 (septet, $J = 7.6$ Hz, 3H), 1.13 (d, $J = 7.6$ Hz, 18H); ^{13}C-NMR ($CDCl_3$): δ 163.2, 154.9, 152.3, 131.9, 127.8, 126.1, 124.1, 119.4, 116.7, 18.9, 11.3; IR (neat, cm^{-1}): 2943, 2868, 1701; MS *m/z* (relative intensity): 259 (100, $[M-C_3H_7]^+$), 69 (29); HRMS $(M-C_3H_7)^+$ Calc. for $C_{15}H_{19}O_2Si$: 259.1154, Found: 259.1159.

4.3.5. 3-Octyl-2H-1-benzopyran-2-one (5)

White solid, m.p. 59–62 °C (lit. [29] m.p. 64 °C); ^{1}H-NMR ($CDCl_3$): δ 7.48 (s, 1H), 7.42–7.46 (m, 2H), 7.31 (d, $J = 8.0$ Hz, 1H), 7.25 (ddd, $J = 1.0$, 7.2, 8.0 Hz, 1H), 2.56 (t, $J = 7.4$ Hz, 2H), 1.60–1.66 (m, 2H), 1.20–1.40 (m, 10H), 0.87 (t, $J = 7.6$ Hz, 3H); ^{13}C-NMR ($CDCl_3$): δ 162.1, 153.3, 138.5, 130.6, 130.3, 127.3, 124.4, 119.8, 116.6, 32.0, 31.0, 29.6, 29.5, 29.4, 28.2, 22.8, 14.3. All spectral properties are identical to those reported in the literature [29].

4.3.6. 4-Octyl-2H-1-benzopyran-2-one (6)

Off-white solid, m.p. 60–63 °C; ^{1}H-NMR ($CDCl_3$): δ 7.64 (dd, $J = 1.2$, 8.0 Hz, 1H), 7.53 (ddd, $J = 1.6$, 7.0, 8.6 Hz, 1H), 7.27–7.36 (m, 2H), 6.29 (s, 1H), 2.77 (t, $J = 7.8$ Hz, 1H), 1.66–1.74 (m, 2H), 1.20–1.40 (m, 10H), 0.89 (t, $J = 6.8$ Hz, 3H); ^{13}C-NMR ($CDCl_3$): δ 161.3, 156.6, 154.0, 131.8, 124.5, 124.3, 119.6, 117.5, 114.1, 32.01, 31.97, 29.7, 29.5, 29.4, 28.3, 22.8, 14.3; MS *m/z* (relative intensity): 258 (27, M^+), 173 (19), 160 (100), 132 (37); HRMS Calc. for $C_{17}H_{22}O_2$: 258.1620, Found: 258.1623.

4.3.7. 3-Butyl-2H-1-benzopyran-2-one (7)

White solid, m.p. 60–63 °C (lit. [28] m.p. 64 °C). The spectral properties are identical to those reported in the literature [28].

4.3.8. 4-Butyl-2H-1-benzopyran-2-one (8)

Yellow oil, the spectral properties are identical to those reported in the literature [30].

4.4. General procedure for the synthesis of 2-quinolones

Ethyl *N*-(2-iodophenyl)carbamate (0.5 mmol), the alkyne (1.5 mmol), pyridine (79 mg, 1 mmol), *n*-Bu_4NCl (139 mg, 0.5 mmol), and $Pd(OAc)_2$ (5.6 mg, 5 mol%, 0.025 mmol) were placed in a 4 dram vial and dissolved in 5 ml of DMF. The vial was purged with CO for 2 min, and then connected to a balloon of CO. The reaction mixture was stirred at 100 °C for 12 h, then allowed to cool to r.t., diluted with EtOAc, washed with water, and concentrated under reduced pressure. The residue was treated with 5 ml of 1 M ethanolic NaOH at r.t. for 30 min. Then 15 ml of satd aq. NH_4Cl were added, and the resulting mixture was extracted with EtOAc. The organic extracts were combined, washed with satd aq. NH_4Cl and water, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was separated by column chromatography on silica gel. The following 2-quinolones were prepared using this procedure.

4.4.1. 3-n-Butyl-2(1H)-quinolinone (9)

White solid, m.p. 145–147 °C; ^{1}H-NMR ($CDCl_3$): δ 7.60 (s, 1H), 7.50 (d, $J = 7.6$ Hz, 1H), 7.40–7.47 (m, 2H), 7.18 (ddd, $J = 8.0$, 6.4, 2.0 Hz, 1H), 2.70 (t, $J = 7.8$ Hz, 2H), 1.66–1.74 (m, 2H), 1.41–1.51 (m, 2H), 0.99 (t, $J = 7.4$ Hz, 3H); ^{13}C-NMR ($CDCl_3$): δ 164.7, 137.7, 136.6, 134.5, 129.4, 127.1, 122.5, 120.5, 115.9, 30.8, 30.1, 22.8, 14.2; IR ($CDCl_3$, cm^{-1}): 2958, 2859, 1656, 1566; MS *m/z* (relative intensity): 201 (26, M^+), 172 (25), 159 (100), 158(51), 130 (40); HRMS Calc. for $C_{13}H_{15}NO$: 201.1154, Found: 201.1158.

4.4.2. 4-n-Butyl-2(1H)-quinolinone (10)

White solid, m.p. 140–142 °C; ^{1}H-NMR ($CDCl_3$): δ 7.73 (d, $J = 8.0$ Hz, 1H), 7.48–7.50 (m, 2H), 7.21–7.27 (m, 1H), 6.61 (s, 1H), 2.87 (t, $J = 7.6$ Hz, 2H), 1.68–1.76 (m, 2H), 1.43–1.52 (m, 2H), 0.98 (t, $J = 7.2$ Hz, 3H); ^{13}C-NMR ($CDCl_3$): δ 164.8, 153.6, 138.8, 130.5, 124.3, 122.6, 120.1, 119.6, 117.1, 32.2, 31.1, 22.8, 14.1; IR (neat, cm^{-1}): 2963, 1646, 1556; MS *m/z* (relative intensity): 201 (28, M^+), 159 (78), 130 (100); HRMS Calc. for $C_{13}H_{15}NO$: 201.1154, Found: 201.1158.

4.4.3. 3-Cyclohexyl-2(1H)-quinolinone (11)

White solid, m.p. 229–231 °C; ^{1}H-NMR ($CDCl_3$): δ 7.58 (s, 1H), 7.52 (d, $J = 7.6$ Hz, 1H), 7.45 (ddd, $J = 1.2$, 7.0, 8.2 Hz, 1H), 7.38 (d, $J = 8.0$ Hz, 1H), 7.18 (ddd, $J = 1.2$, 7.2, 8.0 Hz, 1H), 3.00–3.06 (m, 1H), 2.01–2.04 (m, 2H), 1.79–1.89 (m, 3H), 1.48–1.58 (m, 3H), 1.27–1.40 (m, 3H); ^{13}C-NMR ($CDCl_3$): δ 164.2, 139.4, 137.3, 134.5, 129.4, 127.4, 122.5, 120.6, 115.7, 37.3, 32.8, 27.0, 26.6; IR (neat, cm^{-1}): 2933, 2853, 1651, 1566; MS *m/z* (relative intensity): 227 (32, M^+), 198 (44), 183 (54), 170 (100), 154 (64), 128 (44); HRMS Calc. for $C_{15}H_{17}NO$: 227.1310, Found: 227.1316.

4.4.4. 4-Cyclohexyl-2(1H)-quinolinone (**12**)

Off-white solid, m.p. 233–235 °C; ^{1}H-NMR ($CDCl_3$): δ 7.78 (d, $J = 8.0$ Hz, 1H), 7.50 (ddd, $J = 1.2$, 7.2, 8.2 Hz, 1H), 7.40 (dd, $J = 0.8$, 8.0 Hz, 1H), 7.24 (ddd, $J =$ 1.2, 6.8, 8.0 Hz, 1H), 6.62 (s, 1H), 3.00–3.05 (m, 1H), 1.82–2.02 (m, 5H), 1.25–1.54 (m, 5H); ^{13}C-NMR ($CDCl_3$): δ 164.5, 158.2, 138.7, 130.4, 124.0, 122.6, 120.0, 117.3, 117.0, 39.4, 33.3, 27.0, 26.5; IR (neat, cm^{-1}): 2928, 2853, 1656, 1556; MS *m/z* (relative intensity): 227 (100, M^+), 198 (16), 184 (20), 172 (14), 170(14), 159 (16); HRMS Calc. for $C_{15}H_{17}NO$: 227.1310, Found: 227.1314.

4.4.5. 3-Phenyl-2(1H)-quinolinone (**13**)

White solid, m.p. 230–231 °C (lit. [31] m.p. 231–232 °C); ^{1}H-NMR (d_6-DMSO): δ 8.10 (s, 1H), 7.72–7.77 (m, 2H), 7.50 (ddd, $J = 1.2$, 7.2, 8.4 Hz, 1H), 7.32–7.45 (m, 4H), 7.19 (dd, $J = 7.2$, 7.6 Hz, 1H); ^{13}C-NMR (d_6-DMSO): δ 161.0, 138.4, 137.6, 136.3, 131.5, 130.2, 128.7, 128.1, 127.9, 127.8, 121.9, 119.5, 114.7; MS *m/z* (relative intensity): 221 (49, M^+), 220 (100), 165 (39); HRMS Calc. for $C_{15}H_{11}NO$: 221.0841, Found: 221.0846.

4.4.6. 3-Triethylsilyl-2(1H)-quinolinone (**14**)

White solid, m.p. 138–140 °C; ^{1}H-NMR ($CDCl_3$): δ 7.88 (s, 1H), 7.53 (dd, $J = 1.2$, 8.4 Hz, 1H), 7.48 (ddd, $J = 1.2$, 7.2, 8.4 Hz, 1H), 7.33 (d, $J = 8.0$ Hz, 1H), 7.17 (ddd, $J = 1.0$, 7.0, 8.0 Hz, 1H), 1.00–1.05 (m, 9H), 0.92–0.98 (m, 6H); ^{13}C-NMR ($CDCl_3$): δ 167.4, 148.8, 139.7, 131.7, 130.7, 127.8, 122.2, 120.4, 115.9, 7.8, 3.1; IR (neat, cm^{-1}): 2953, 2868, 1636, 1596, 1546; MS *m/z* (relative intensity): 259 (10, M^+), 230 (100), 174 (30), 172 (48), 144 (43); HRMS Calc. for $C_{15}H_{21}NOSi$: 259.1392, Found: 259.1397.

4.4.7. 3-(4-Hydroxybutyl)-2(1H)-quinolinone (**15**)

White solid, m.p. 148–150 °C; ^{1}H-NMR ($CDCl_3$): δ 7.64 (s, 1H), 7.52 (d, $J = 7.6$ Hz, 1H), 7.47 (ddd, $J = 1.4$, 7.0, 8.4 Hz, 1H), 7.38 (d, $J = 8.0$ Hz, 1H), 7.20 (ddd, $J =$ 1.0, 7.0, 8.0 Hz, 1H), 3.78 (t, $J = 6.2$ Hz, 2H), 2.73 (t, $J = 7.6$ Hz, 2H), 1.99 (br s, 1H), 1.77–1.84 (m, 2H), 1.67–1.74 (m, 2H); ^{13}C-NMR ($CDCl_3$): δ 164.3, 137.5, 137.1, 134.1, 129.7, 127.3, 122.8, 120.5, 115.7, 62.7, 32.2, 30.0, 25.0; IR (neat, cm^{-1}): 2923, 2848, 1656; MS *m/z* (relative intensity): 217 (33, M^+), 199 (50), 172 (100), 159 (65), 158 (71), 130 (60); HRMS Calc. for $C_{13}H_{15}NO_2$: 217.1103, Found: 217.1108.

4.4.8. 4-(4-Hydroxybutyl)-2(1H)-quinolinone (**16**)

White solid, m.p. 147–150 °C; ^{1}H-NMR ($CDCl_3$): δ 7.74 (d, $J = 8.0$ Hz, 1H), 7.51 (ddd, $J = 0.8$, 7.2, 8.0 Hz, 1H), 7.37 (d, $J = 8.0$ Hz, 1H), 7.24 (ddd, $J = 1.2$, 7.2, 8.4 Hz, 1H), 6.59 (s, 1H), 3.73 (t, $J = 6.4$ Hz, 2H), 2.91 (t, $J = 7.4$ Hz, 2H), 1.80–1.88 (m, 2H), 1.68–1.79 (m, 2H), only a small amount of **16** was isolated; therefore, no other spectral data have been obtained; MS *m/z* (relative intensity): 217 (40, M^+), 159 (42), 130 (100), 102 (44); HRMS Calc. for $C_{13}H_{15}NO_2$: 217.1103, Found: 217.1107.

4.4.9. Methyl 4-(2(1H)-oxoquinolin-3-yl)butanoate (**17**)

Colorless solid, m.p. 145–148 °C; ^{1}H-NMR ($CDCl_3$): δ 7.65 (s, 1H), 7.52 (d, $J = 8.0$ Hz, 1H), 7.47 (ddd, $J =$ 1.4, 7.0, 8.4 Hz, 1H), 7.39 (d, $J = 8.0$ Hz, 1H), 7.20 (ddd, $J = 1.0$, 7.0, 8.0 Hz, 1H), 3.69 (s, 1H), 2.74 (t, $J = 7.6$ Hz, 2H), 2.46 (t, $J = 7.4$ Hz, 2H), 2.04–2.11 (m, 2H); ^{13}C-NMR ($CDCl_3$): δ 174.2, 164.4, 137.8, 137.4, 133.2, 129.8, 127.4, 122.7, 120.4, 115.8, 51.8, 33.8, 29.9, 23.9; IR (neat, cm^{-1}): 3003, 2953, 2848, 1736, 1661, 1576; MS *m/z* (relative intensity): 245 (32, M^+), 244 (19), 172 (100), 171 (55), 159 (38), 158 (25); HRMS Calc. for $C_{14}H_{15}NO_3$: 245.1052, Found: 245.1056.

4.4.10. Methyl 4-(2(1H)-oxoquinolin-4-yl)butanoate (**18**)

Brown solid, m.p. 164–167 °C; ^{1} H-NMR ($CDCl_3$): δ 7.78 (d, $J = 8.0$ Hz, 1H), 7.52 (dd, $J = 7.2$, 8.0 Hz, 1H), 7.43 (d, $J = 8.0$ Hz, 1H), 7.26 (dd, $J = 7.2$, 8.0 Hz, 1H), 3.71 (s, 3H), 2.92 (t, $J = 7.8$ Hz, 2H), 2.48 (t, $J = 7.0$ Hz, 2H), 2.05–2.11 (m, 2H); ^{13}C-NMR ($CDCl_3$): δ 173.7, 164.3, 152.3, 138.7, 130.7, 124.4, 122.8, 120.0, 119.8, 116.9, 51.9, 33.5, 31.8, 24.2; IR (neat, cm^{-1}): 3013, 2953, 2853, 1736, 1651, 1435, 1171; MS *m/z* (relative intensity): 245 (100, M^+), 172 (81), 130 (59); HRMS Calc. for $C_{14}H_{15}NO_3$: 245.1052, Found: 245.1058.

4.4.11. 4-(2(1H)-Oxoquinolin-3-yl)butanenitrile (**19**)

Solid, m.p. 164–167 °C; ^{1}H-NMR ($CDCl_3$): δ 7.70 (s, 1H), 7.55 (d, $J = 8.0$ Hz, 1H), 7.50 (ddd, $J = 1.2$, 7.2, 8.4 Hz, 1H), 7.41 (d, $J = 8.4$ Hz, 1H), 7.23 (ddd, $J = 1.0$, 7.0, 8.0 Hz, 1H), 2.86 (t, $J = 7.2$ Hz, 2H), 2.45 (t, $J = 7.2$ Hz, 2H), 2.08–2.16 (m, 2H); ^{13}C-NMR ($CDCl_3$): δ 164.2, 138.3, 137.9, 131.6, 130.2, 127.5, 122.9, 120.2, 119.8, 115.9, 30.0, 24.4, 17.0; IR (neat, cm^{-1}): 2953, 2856, 2238, 1655; MS *m/z* (relative intensity): 212 (M^+, 28), 172 (50), 159 (100); HRMS Calc. for $C_{13}H_{12}N_2O$: 212.0950, Found: 212.0953.

4.4.12. 4-(2(1H)-Oxoquinolin-4-yl)butanenitrile (**20**)

Brown oil; ^{1} H-NMR ($CDCl_3$): δ 7.71 (d, $J = 8.0$ Hz, 1H), 7.55 (dd, $J = 7.2$, 8.0 Hz, 1H), 7.43 (d, $J = 8.4$ Hz, 1H), 7.28 (dd, $J = 7.2$, 8.0 Hz, 1H), 3.06 (t, $J = 7.6$ Hz, 2H), 2.50 (t, $J = 6.8$ Hz, 2H), 2.08–2.16 (m, 2H), only a small amount of **20** was isolated; therefore, no other spectral data have been obtained; MS *m/z* (relative intensity): 212 (M^+, 39), 159 (41), 143 (100), 130 (72), 115 (53); HRMS Calc. for $C_{13}H_{12}N_2O$: 212.0950, Found: 212.0953.

*4.4.13. 3-n-Butyl-6-methoxy-2(1H)-quinolinone(**21**)*

White solid, m.p. 165–168 °C; ^{1}H-NMR ($CDCl_3$): δ 7.56 (s, 1H), 7.32 (d, $J = 8.8$ Hz, 1H), 7.09 (dd, $J = 2.8$, 8.8 Hz, 1H), 6.95 (d, $J = 2.8$ Hz, 1H), 3.85 (s, 3H), 2.69 (t, $J = 7.6$ Hz, 2H), 1.65–1.73 (m, 2H), 1.41–1.51 (m, 2H), 0.98 (t, $J = 7.2$ Hz, 3H); ^{13}C-NMR ($CDCl_3$): δ 164.1, 155.2, 136.2, 135.0, 132.2, 121.1, 118.8, 117.1, 108.5, 55.9, 30.8, 30.2, 22.8, 14.3; IR (neat, cm^{-1}): 2933, 2834, 1651, 1621, 1501; MS *m/z* (relative intensity): 231 (38, M^+), 202 (61), 189 (86), 188 (56), 174 (100); HRMS Calc. for $C_{14}H_{17}NO_2$: 231.1259, Found: 231.1263.

*4.4.14. 4-n-Butyl-6-methoxy-2(1H)-quinolinone (**22**)*

White solid, m.p. 195–198 °C; ^{1}H-NMR ($CDCl_3$): δ 7.42 (d, $J = 8.4$ Hz, 1H), 7.13–7.16 (m, 2H), 3.87 (s, 1H), 2.83 (t, $J = 7.6$ Hz, 2H), 1.69–1.76 (m, 2H), 1.44–1.51 (m, 2H), 0.99 (t, $J = 7.4$ Hz, 3H); ^{13}C-NMR ($CDCl_3$): δ 164.2, 155.2, 152.8, 133.4, 120.8, 120.0, 119.2, 118.2, 106.6, 56.0, 32.2, 30.9, 22.8, 14.1; IR (neat, cm^{-1}): 2963, 1651; MS *m/z* (relative intensity): 231 (27, M^+), 189 (21), 41 (100); HRMS Calc. for $C_{14}H_{17}NO_2$: 231.1259, Found: 231.1262.

4.5. Isotope labeling experiment

Ethyl *N*-(2-iodophenyl)carbamate (146 mg, 0.5 mmol), *d*-phenylacetylene (98% D, 155 mg, 1.5 mmol), pyridine (79 mg, 1.0 mmol), *n*-Bu_4NCl (139 mg, 0.5 mmol), and $Pd(OAc)_2$ (5.6 mg, 5 mol%, 0.025 mmol) were placed in a 4 dram vial and dissolved in 5 ml of DMF. The vial was purged with CO for 2 min, and then connected to a balloon of CO. The reaction mixture was stirred at 100 °C for 12 h, then allowed to cool to r.t., diluted with EtOAc, washed with water, and concentrated under reduced pressure. The residue was treated with 5 ml of 1 M ethanolic NaOH at r.t. for 30 min. Then 15 ml of satd aq. NH_4Cl were added, and the resulting mixture was extracted with EtOAc. The organic extracts were combined, washed with satd aq. NH_4Cl and water, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. Column chromatography on silica gel using 1:1 hexane/ethyl acetate as an eluent afforded 46 mg (40%) of 4-deutero-3-phenyl-2(1*H*)-quinolinone: colorless solid, m.p. 239–240 °C; ^{1}H-NMR (d_6-DMSO): δ 8.10 (s, 0.11H), 7.72–7.77 (m, 2H), 7.50 (ddd, $J = 1.2$, 7.2, 8.4 Hz, 1H), 7.32–7.45 (m, 4H), 7.19 (dd, $J = 7.2$, 7.6 Hz, 1H); ^{13}C-NMR (d_6-DMSO): δ 161.0, 138.4, 136.3, 131.5, 130.2, 128.7, 128.1, 127.9, 127.8, 121.9, 119.5, 114.7 (the signal of the carbon bound to the deuterium is not observed); MS *m/z* (relative intensity): 222 (43, M^+), 221 (100), 192 (17), 191 (14), 166 (22), 165 (23); HRMS Calc. for $C_{15}H_{10}DNO$: 222.0903, Found: 222.0906.

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References

[1] J. Tsuji, Palladium Reagents and Catalysts: Innovations in Organic Synthesis, John Wiley & Sons, Ltd, Chichester, 1995.
[2] N.E. Schore, Chem. Rev. 88 (1988) 1081.
[3] S. Cacchi, J. Organomet. Chem. 576 (1999) 42.
[4] R.C. Larock, J. Organomet. Chem. 576 (1999) 111.
[5] R.C. Larock, Pure Appl. Chem. 71 (1999) 1435.
[6] A. Arcadi, F. Marinelli, S. Cacchi, Synthesis (1986) 749.
[7] T. Sakamoto, Y. Kondo, H. Yamanaka, Heterocyles 24 (1986) 31.
[8] A. Yasuhara, Y. Kanamori, M. Kaneko, A. Numata, Y. Kondo, T. Sakamoto, J. Chem. Soc., Perkin Trans. 1 (1999) 529.
[9] H.-Y. Liao, C.-H. Cheng, J. Org. Chem. 60 (1995) 3711.
[10] K.R. Roesch, R.C. Larock, J. Org. Chem. 67 (2002) 86.
[11] H. Zhang, R.C. Larock, Tetrahedron Lett. 43 (2002) 1359.
[12] K. Sonogashira, in: F. Diederich, P.J. Stang (Eds.), Metal-catalyzed Cross-coupling Reactions, Wiley-VCH, Weinheim, 1998, p. 203.
[13] D.V. Kadnikov, R.C. Larock, Org. Lett. 2 (2000) 3643.
[14] D.V. Kadnikov, R.C. Larock, manuscript in preparation.
[15] Z.-W. An, M. Catellani, G.P. Chiusoli, Gazz. Chim. Ital. 120 (1990) 383.
[16] Z.-W. An, M. Catellani, G.P. Chiusoli, J. Organomet. Chem. 371 (1989) C51.
[17] P.G. Ciattini, E. Morera, G. Ortar, S.S. Rossi, Tetrahedron 47 (1991) 9449.
[18] V.N. Kalinin, M.V. Shostakovsky, A.B. Ponomaryov, Tetrahedron Lett. 31 (1990) 4073.
[19] S. Torii, H. Okumoto, L.H. Xu, M. Sadakane, M.V. Shostakovsky, A.B. Ponomaryov, V.N. Kalinin, Tetrahedron 49 (1993) 9773.
[20] H. Miao, Z. Yang, Org. Lett. 2 (2000) 1765.
[21] S. Torii, H. Okumoto, L.H. Xu, Tetrahedron Lett. 32 (1991) 237.
[22] B.M. Trost, M.T. Sorum, C. Chan, A.E. Harms, G. Rühter, J. Am. Chem. Soc. 119 (1997) 698.
[23] E. Negishi, M. Ay, T. Sugihara, Tetrahedron 49 (1993) 5471.
[24] J.W. Bae, S.H. Lee, Y.J. Cho, Y.J. Jung, H.-J. Hwang, C.M. Yoon, Tetrahedron Lett. 41 (2000) 5899.
[25] H. Dang, M.A. Garcia-Garibay, J. Am. Chem. Soc. 123 (2001) 355.
[26] E. Rossi, A. Arcadi, G. Abbiati, O.A. Attanasi, L.D. Crescentini, Angew. Chem. Int. Ed. 41 (2002) 1400.
[27] Y. Kondo, S. Kojima, T. Sakamoto, J. Org. Chem. 62 (1997) 6507.
[28] E. Yoneda, T. Sugioka, K. Hirao, S.-W. Zhang, S. Takahashi, J. Chem. Soc., Perkin Trans. 1 (1998) 477.
[29] P. Bouvier, J. Andrieux, H. Cunha, D. Molho, Bull. Soc. Chim. Fr. (1977) 1187.
[30] A. Alberosa, B. Calvo, A.G. Ortega, R. Pedrosa, J. Chem. Soc., Perkin Trans. 1 (1992) 3075.
[31] M.O. Terpko, R.F. Heck, J. Am. Chem. Soc. 101 (1979) 5281.