Coupling and Carboxylation of Iodoaromatics and Terminal Alkynes or Alkynols Catalyzed by a Dimeric Palladium Hydroxide

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Received 13 December 1993; revised 25 May 1994

The palladium(II) complex ([Ph₂P)Pd(Ph)(μ-OH)]₂ is an effective catalyst for the coupling and carboxylation of alkynes and iodoarenes to give acetylenic ketones in 63–94% yields. Acetylenic hydroxy ketones were formed using secondary or tertiary alkynes as reactants.

A common route to α,β-acetylenic ketones involves the reaction of a metallic acetylide with an acyl chloride or another carboxylic acid derivative (Equation 1). The main organometallic compounds used for these syntheses include alkynyl silver,1 copper(I),2,3,4 sodium,5 lithium,6,7 and cadmium salts.8,9 Silylated alkynes also react with acyl chlorides in the presence of aluminium chloride.10,11 Moreover, this Lewis acid catalyses the Friedel–Crafts reaction of phenylpropynyl chloride with anisole, toluene and naphthalene (Equation 2).12 The direct coupling between acyl chlorides and 1-alkynes has been reported by Hagihara et al. (Equation 3)13 to occur in the presence of a mixture of copper(I) iodide and of dichlorobis(triphenylphosphine)palladium(II). This complex is also of value in the transfer of an alkynyl group from (1-alkynyl)tributylstannanes to acyl chlorides (Equation 4).14

RCOX + MC ≡ CR' → RCOCl ≡ CR' + MX
ArH + CICOC ≡ CPh + AlCl₃
ArCOC ≡ CPh + HX
RCOCI + HC ≡ CR L₂PdCl₂/CuI, Et₃N
RCOC ≡ CR' + [Et₃NH]⁺Cl⁻
RCOCI + Bu₃SnC ≡ CR L₂PdCl₂
RCOC ≡ CR' + Bu₃SnCl

Acetylenic ketones can also be obtained via the one-pot formation of two carbon–carbon bonds under catalytic carboxylation conditions (Equation 5). Little attention has been paid to this route as there are only two reports, to our knowledge, which describe the catalytic carboxylation of organic halides in the presence of terminal alkynes.15,16 In most cases, dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium(II) was the best catalyst from a wide range of palladium(II) phosphate or arsine complexes.

R ≡ CH + R'X + CO PdCl₂(dppf), Et₃N
RCOC ≡ CR' + [Et₃NH]⁺Cl⁻

Recently, we succeeded in isolating dimeric palladium complexes of the type [LPd(Ph)(μ-OH)]₂ which contain bridging hydroxy ligands.17 Such complexes are key intermediates in the palladium-catalyzed carboxylation of haloarenes to carboxylic acids. We now wish to report that ([Ph₂P)Pd(Ph)(μ-OH)]₂ (I) is an effective catalyst for the synthesis of acetylenic ketones from alkynes or alkynols, iodoarenes, and carbon monoxide.

Initial carboxylation experiments utilized iodobenzene and phenylacetylene as substrates. Treatment of equimolar amounts of phenylacetylene (2, R = Ph) and iodobenzene

RC ≡ CH + R'Cl + CO [Ph₂P)Pd(Ph)(μ-OH)]₂ 1
Et₃N, 17 atm. 90°C, 1–2 h
RCOC ≡ CR' + [Et₃NH]⁺Cl⁻ 4

(3, R' = Ph) with carbon monoxide, triethylamine, and a catalytic amount of 1 (100/1 ratio of 2 or 3/1) for one hour at 90°C, afforded diphenylpropynone (4, R = R' = Ph) in 91% yield and diphenylacetylene in 1% yield. The influence of different parameters was examined using the noted reactants. Increase (120°C) or decrease (60°C) in temperature results in reduced yields of 4 (i.e. 59% at 60°C, 79% at 120°C). The reaction proceeds at one atmosphere pressure, but the yield of 4 decreases to 60%, and diphenylacetylene is isolated in 16% yield.

<p>| Table 1. Carboxylation Reactions of Alkynes and Iodoarenes Catalyzed by I⁺ |</p>
<table>
<thead>
<tr>
<th>2, R=</th>
<th>3, R'=</th>
<th>Yield of 4, % ^a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ph</td>
<td>Ph</td>
<td>91</td>
</tr>
<tr>
<td>p-CH₃C₆H₄</td>
<td>p-CH₃C₆H₄</td>
<td>94</td>
</tr>
<tr>
<td>p-CIC₆H₄</td>
<td>p-BrC₆H₄</td>
<td>75</td>
</tr>
<tr>
<td>PhCH₂CH₂</td>
<td>Ph</td>
<td>74</td>
</tr>
<tr>
<td>Ph(CH₂)₃</td>
<td>Ph</td>
<td>87</td>
</tr>
<tr>
<td>(CH₂)₅Si</td>
<td>Ph</td>
<td>70</td>
</tr>
<tr>
<td>(CH₂)₅C</td>
<td>Ph</td>
<td>63</td>
</tr>
<tr>
<td>CH₂(CH₂)₃</td>
<td>Ph</td>
<td>78</td>
</tr>
<tr>
<td>CH₂(CH₂)₃</td>
<td>Ph</td>
<td>83</td>
</tr>
<tr>
<td>CH₂(CH₂)₇</td>
<td>Ph</td>
<td>88</td>
</tr>
<tr>
<td>CH₂CH(OH)</td>
<td>Ph</td>
<td>43</td>
</tr>
<tr>
<td>(CH₂)₆COH</td>
<td>Ph</td>
<td>67</td>
</tr>
<tr>
<td>C₆H₅CH₂CH₂(OH)</td>
<td>Ph</td>
<td>78</td>
</tr>
<tr>
<td>(CH₂)₅CH₂CH₂CH₂(OH)</td>
<td>Ph</td>
<td>82</td>
</tr>
<tr>
<td>(C₆H₅)₂COH</td>
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<tr>
<td>PhCH₂(OH)</td>
<td>Ph</td>
<td>55</td>
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<tr>
<td>PhC(OH)</td>
<td>Ph</td>
<td>71</td>
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</tbody>
</table>

^a Reaction conditions: 2 (1.0 mmol), 3 (1.0 mmol), 1 (0.01 mmol), Et₃N (5 mL), 17 atm, 1–2 h, 90°C.

^b Products from the reaction of alkynes with carbon monoxide and iodoarenes were identified by comparison of physical data (IR, NMR [¹H,¹³C], MS) with those of authentic materials. Analytical and spectral data were supportive of the structure of 4 derived from alkynols.
Higher pressures of carbon monoxide (e.g. 34 atm.) are also not favorable in terms of product yield. The best bases for the reaction are triethylamine and disopropylethylamine which afford 4 in nearly the same yield. Much less effective in this regard are pyridine (13% conversion to give 5% 4) and N,N,N',N'-tetramethylethylenediamine (24% yield of 4 and < 1% of diphenylacetylene). Using triethylamine as both solvent and base gave the best results, while dilution of triethylamine in toluene (72% yield of 4), N,N-dimethylformamide (85%), acetonitrile (29%), and tetrahydrofuran (34%) resulted in inferior yields. Finally, 1 is superior to Pd/C (4% yield), PdCl2 (9%), and PdCl2(PPPh3)2 (74%) as a catalyst.

The optimum conditions developed for the iodobenzene-phenylacetylene carboxylation reaction were applied to a series of alkynes and halides (Table 1). The process was useful for a variety of alkynes, including aliphatic and aromatic alkynes. The yields are very good with most alkynes, as they are when using a series of iodoarenes in reaction with phenylacetylene. The reactions are rapid, and are selective for iodoarenes in the presence of chloro or bromo functional groups. Bromobenzene is appreciably less reactive than the iodo analog, with 3 (R' = Ph) being obtained in only 7% yield from phenylacetylene. However, vinyl bromides are more reactive, since β-bromo-styrene reacted with phenylacetylene and carbon monoxide to form PhC≡CCOCH=CH2Ph in 46% yield.

It is noteworthy that 1 is also a fine catalyst for the synthesis of acetylenic hydroxy ketones from secondary and tertiary alkynols and iodoarenes. Finally, these results are related to those for the palladium(0) catalyzed coupling reaction of haloarenes and terminal alkynes.

Melting points were recorded on a Fisher-Johns apparatus and are uncorrected. Spectral determinations were made using the following instrumentation: Bomem MB-100 spectrometer (IR), Varian Gemini 280 or XL300 spectrometers (NMR), and a VG 7070E mass spectrometer.

Alk-2-yrones, 4; General Procedure:
A mixture of the alkyne or alkylnol (1.0 mmol), iodoarene (1.0 mmol), Et2N (5 mL), and 0.0093 g (0.11 mmol) of I was heated in a 45 mL autoclave at 17 atm. of CO for 1–2 h at 90°C. The autoclave was cooled to r.t., opened, and the solution was filtered. Et2O (75 mL) was added to the filtrate, and the organic solution was washed with cold 2 N HCl (25 mL), water (2 × 25 mL), dried (MgSO4), and concentrated. Purification was realized by silica gel preparative TLC, using a 9:1 mixture of hexane and ethyl acetate as developer. Products were identified as follows:

4 R = Ph, R' = CH(C6H4)C≡CH: Mp 46–47°C, lit.15 mp 46–48°C.
IR (neat): ν = 2199, 1649 cm⁻¹.
1H NMR (CDCl3): δ = 7.20–7.70 (m, 8 H), 8.20 (m, 2 H).
13C NMR (CDCl3): δ = 86.9, 93.1, 120.1, 128.6, 128.7, 129.6, 130.8, 133.1, 134.1, 136.8, 178.0
MS: m/z = 206 (M⁺).

4 R = Ph, R' = p-CH3OC6H4C≡CH: Mp 97–98°C, lit.20 mp 100°C.
IR (KBr): ν = 2197, 1629 cm⁻¹.
1H NMR (CDCl3): δ = 3.87 (s, 3 H), 6.95 (d, 2 H), 7.40 (m, 3 H), 7.65 (d, 2 H), 8.20 (d, 2 H).
13C NMR (CDCl3): δ = 55.6, 86.9, 92.3, 113.9, 120.3, 128.6, 130.2, 130.6, 131.9, 132.9, 164.5, 176.6.
MS: m/z = 236 (M⁺).

4 R = Ph, R' = p-ClC6H4C≡CH: Mp 104°C, lit.26 mp 105°C.
IR (KBr): ν = 2197, 1653 cm⁻¹.
1H NMR (CDCl3): δ = 7.20–7.50 (m, 5 H), 7.72 (m, 2 H), 8.10 (m, 2 H).
13C NMR (CDCl3): δ = 86.6, 93.6, 119.8, 128.7, 129.0, 130.8, 131.0, 133.1, 135.2, 140.7, 176.6.
MS: m/z = 242 (M⁺).

4 R = Ph, R' = p-BrC6H4C≡CH: Mp 106–107°C, lit.21 mp 110°C.
IR (KBr): ν = 2196, 1650 cm⁻¹.
1H NMR (CDCl3): δ = 7.30–8.10 (m, 9 H).
13C NMR (CDCl3): δ = 86.6, 93.7, 119.8, 128.7, 129.6, 130.9, 131.0, 132.0, 133.1, 135.6, 176.7.
MS: m/z = 286, 284 (M⁺).

4 R = Ph, R' = I-C6H4C≡CH: Mp 93–94°C, lit.12 mp 95°C.
IR (KBr): ν = 2192, 1632 cm⁻¹.
1H NMR (CDCl3): δ = 7.9–9.0 (m, 12 H).
13C NMR (CDCl3): δ = 88.6, 91.8, 120.3, 124.5, 126.0, 126.8, 128.7, 129.0, 130.68, 130.74, 132.8, 133.0, 133.9, 134.7, 135.2, 179.7.
MS: m/z = 256 (M⁺).

4 R = PhCH2CH2C≡CH, R' = Ph:
IR (neat): ν = 2233, 2201, 1644 cm⁻¹.
1H NMR (CDCl3): δ = 2.80 (t, 2 H), 3.04 (t, 2 H), 7.20–8.0 (m, 10 H).
13C NMR (CDCl3): δ = 21.3, 33.9, 80.3, 95.5, 126.7, 128.48, 128.5, 128.6, 129.6, 133.9, 136.8, 139.7, 178.1.
MS: m/z = 234 (M⁺).

4 R = Ph(CH2)3, R' = Ph: oil.
IR (neat): ν = 2233, 2200, 1643 cm⁻¹.
1H NMR (CDCl3): δ = 1.99 (q, 2 H), 2.51 (t, 2 H), 2.80 (t, 2 H), 7.10–8.11 (m, 10 H).
13C NMR (CDCl3): δ = 18.6, 29.5, 34.9, 80.1, 96.3, 126.2, 128.6, 129.6, 134.0, 136.9, 140.9, 178.1.
MS: m/z = 248 (M⁺).

4 R = Si(CH3)3, R' = Ph: oil.
IR (neat): ν = 2153, 1647 cm⁻¹.
1H NMR (CDCl3): δ = 0.30 (s, 9 H), 7.40–8.00 (s, 5 H).
13C NMR (CDCl3): δ = −0.7, 100.5, 100.8, 128.6, 129.6, 134.2, 136.4, 177.6.
MS: m/z = 202 (M⁺).

4 R = C(CH3)3, R' = Ph: oil.
IR (neat): ν = 2211, 1645 cm⁻¹.
1H NMR (CDCl3): δ = 1.35 (s, 9 H), 7.2–8.1 (m, 15 H).
13C NMR (CDCl3): δ = 28.0, 30.1, 78.1, 103.9, 128.4, 129.4, 133.8, 136.9, 178.2.
MS: m/z = 186 (M⁺).

4 R = CH2(CH3)3, R' = Ph: oil.
IR (neat): ν = 2213, 1646 cm⁻¹.
1H NMR (CDCl3): δ = 0.95 (t, 3 H), 1.40–1.70 (m, 4 H), 2.48 (t, 2 H), 7.30–8.10 (m, 5 H).
13C NMR (CDCl3): δ = 13.5, 18.9, 22.1, 29.8, 79.6, 96.9, 128.5, 129.5, 133.9, 136.9, 178.2.
MS: m/z = 186 (M⁺).
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4 \( R = \text{CH}_3(\text{CH}_2)_2 \), \( R' = \text{Ph} \): oil.
IR (neat): \( \nu = 2215, 1646 \text{ cm}^{-1} \).

H NMR (CDCl₃): \( \delta = 0.90 \) (t, 3 H), 1.20–1.80 (m, 8 H), 2.52 (t, 2 H), 7.20–7.62 (m, 3 H), 8.11 (m, 2 H).

13C NMR (CDCl₃): \( \delta = 14.0, 19.2, 22.5, 27.8, 28.6, 31.2, 79.6, 96.8, 128.4, 129.5, 133.8, 136.9, 178.1 \).

MS: \( m/z = 214 \) (M⁺).

4 \( R = \text{CH}_3(\text{CH}_2)_2 \), \( R' = \text{Ph} \): oil.
IR (neat): \( \nu = 2234, 2201, 1645 \text{ cm}^{-1} \).

H NMR (CDCl₃): \( \delta = 0.85 \) (t, 3 H), 1.20–1.80 (m, 12 H), 2.51 (t, 2 H), 7.20–8.10 (m, 5 H).

13C NMR (CDCl₃): \( \delta = 14.1, 19.2, 22.6, 27.8, 28.9, 29.0, 29.1, 31.8, 79.6, 96.8, 128.4, 129.5, 133.8, 136.9, 178.1 \).

MS: \( m/z = 242 \) (M⁺).

4 \( R = \text{CH}(\text{OH})(\text{CH}_2)_2 \), \( R' = \text{Ph} \): oil.
IR (neat): \( \nu = 3369, 2214, 1640 \text{ cm}^{-1} \).

H NMR (CDCl₃): \( \delta = 1.59 \) (d, 3 H), 3.80 (br s, 1 H), 4.82 (q, 1 H), 7.40–8.10 (m, 5 H).

13C NMR (CDCl₃): \( \delta = 23.4, 58.2, 81.5, 96.0, 128.6, 129.7, 134.4, 136.3, 178.1 \).

MS: \( m/z = 174 \) (M⁺).

4 \( R = (\text{CH}_3)_2(\text{C}(\text{OH}) \cdot \text{CH}_2)_2 \), \( R' = \text{Ph} \): oil.
IR (neat): \( \nu = 3390, 2213, 1640 \text{ cm}^{-1} \).

H NMR (CDCl₃): \( \delta = 1.65 \) (s, 6 H), 3.60 (br s, 1 H), 7.40–8.20 (m, 5 H).

13C NMR (CDCl₃): \( \delta = 30.6, 65.0, 79.6, 99.1, 128.5, 129.6, 134.2, 136.3, 178.3 \).

MS: \( m/z = 188 \) (M⁺).

4 \( R = \text{C}_2\text{H}_5\text{C}(\text{CH}_2)_2(\text{C}(\text{OH}) \cdot \text{CH}_2)_2 \), \( R' = \text{Ph} \): oil.
IR (neat): \( \nu = 3402, 2211, 1640 \text{ cm}^{-1} \).

H NMR (CDCl₃): \( \delta = 1.12 \) (t, 3 H), 1.63 (s, 3 H), 1.80 (q, 2 H), 4.25 (br s, 1 H), 7.40–8.10 (m, 5 H).

13C NMR (CDCl₃): \( \delta = 9.0, 28.5, 36.1, 68.8, 80.9, 98.1, 128.6, 129.6, 134.3, 136.4, 178.2 \).

MS: \( m/z = 202 \) (M⁺).


4 \( R = \text{CH}_3(\text{CH}_2)_2 \), \( R' = \text{Ph} \): oil.
IR (neat): \( \nu = 3421, 2211, 1640 \text{ cm}^{-1} \).

H NMR (CDCl₃): \( \delta = 1.06 \) (d, 6 H), 1.66 (s, 3 H), 1.76 (d, 2 H), 2.03 (m, 1 H), 3.60 (br s, 1 H), 7.40–8.10 (m, 5 H).

13C NMR (CDCl₃): \( \delta = 24.1, 25.1, 30.2, 51.2, 68.1, 81.3, 98.7, 128.6, 129.6, 134.2, 136.4, 178.0 \).

MS: \( m/z = 215 \) (M⁺).

Anal. calc. for C₂₃H₄₅O₂: C, 78.28; H, 7.82. Found: C, 78.62; H, 8.01.

4 \( R = \text{CH}_3(\text{C}(\text{OH}) \cdot \text{CH}_2)_2 \), \( R' = \text{Ph} \): oil.
IR (neat): \( \nu = 3427, 2210, 1640 \text{ cm}^{-1} \).

H NMR (CDCl₃): \( \delta = 1.12 \) (t, 3 H), 1.85 (q, 4 H), 3.4 (br s, 1 H), 3.43 (br s, 1 H), 7.41–8.20 (m, 5 H).

13C NMR (CDCl₃): \( \delta = 8.6, 33.9, 72.3, 82.1, 97.5, 128.6, 129.6, 134.2, 136.5, 178.0 \).

We are grateful to the Natural Sciences and Engineering Research Council of Canada, and to British Petroleum, for support of this research. We thank Dr. V. Grushin for providing a sample of 1.

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