A Gold(III)-Catalyzed Double Wacker-Type Reaction of 1,1-Diethynyl Acetate

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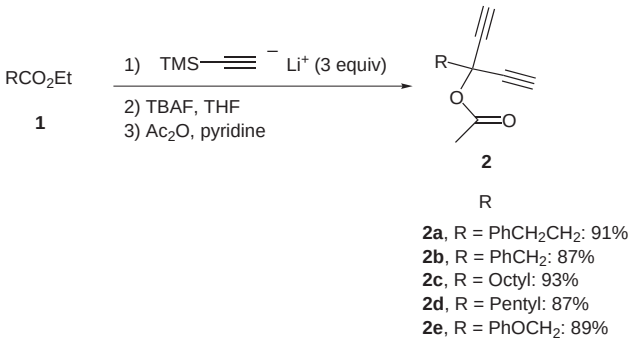
Abstract: Treatment of 1,1-diethynyl acetates in the presence of Au or Pt catalyst (5 mol%) in methanol at 60 °C for 20–48 hours gave γ-ketoesters and lactones in 40–54% and 19–39% yields, respectively. An oxygen atom is introduced to the first acetylene moiety in accordance with Markovnikov's rule, and to the second acetylene moiety with anti-Markovnikov regioselectivity.

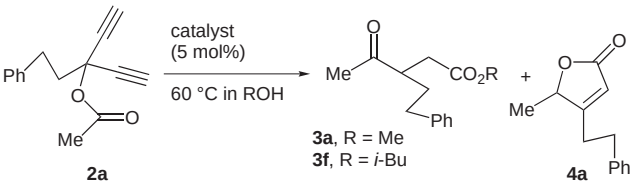
Key words: 1,1-diethynyl acetates, double Wacker-type reaction, gold, platinum, catalyst

Transition-metal-catalyzed reaction of unsaturated systems has recently proven to be a powerful method for the construction of a variety of carbo- and heterocycles.[1] Gold and platinum salts are recognized as efficient catalysts for hydration and related cyclization of alkynes.[2] A large number of reactions of propargylic esters mediated by gold and platinum catalysts have been recently reported.[3] However, the reactions of 1,1-diethynyl acetates are extremely rare.[4] Previously, we have reported the intramolecular oxycarbonylation of 4-yne-1-ols,[5a–c] 4-yne-1-ones[5d] and propargyl acetates[5e,f] catalyzed by Pd(II) complexes. Herein, we report a Au(III)-catalyzed double Wacker-type reaction of 1,1-diethynyl acetates **2**. 1,1-Diethynyl acetates **2** were prepared from the corresponding esters **1** by the following three step procedure with a single column purification.[6] Addition of lithiated acetylene moiety to **1** followed by desilylation, and subsequent acetylation afforded **2** in good yields (Equation 1).



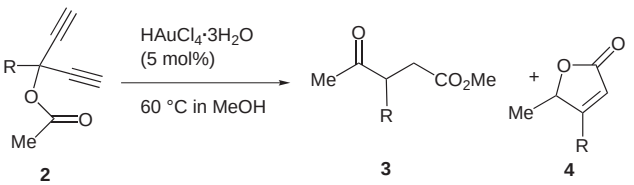
Equation 1

As the starting point in this study, we selected **2a** as a standard substrate to search for potential catalysts and suitable reaction conditions (Equation 1 and Table 1). Treatment of **2a** in the presence of Au or Pt catalyst (5 mol%) in methanol at 60 °C for 20–48 hours gave the γ-ketoester **3a** and the lactone **4a** in 40–54% and 19–39% yields, respectively (entries 1–6). Commercially available gold(I) chloride (AuCl), chloroauric acid hydrate ($HAuCl_4 \cdot 3H_2O$), platinum(IV) chloride ($PtCl_4$), platinum(II) chloride ($PtCl_2$), gold(III) chloride ($AuCl_3$) and cationic triphenylphosphinegold(I) chloride (Ph_3PAuCl)–silver hexafluoroantimonate ($AgSbF_6$)[3g] exhibited almost the same catalytic activity. Among these, $HAuCl_4 \cdot 3H_2O$ gave better total yield (entry 1). When isobutanol was used as a solvent, isobutyl ester **3f** and **4a** were obtained in similar yields (entry 7). However, a complex mixture was obtained when toluene was used as the solvent (entry 8).



Equation 2

Next, substrates **2b**–**e** were tested for the reaction using 5 mol% of $HAuCl_4 \cdot 3H_2O$ as catalyst; the corresponding results are listed in Table 2 (Equation 3).[7] The reaction of **2b** containing a benzyl group, afforded the corresponding products **3b** and **4b** in 53% and 27% yields, respectively (entry 1). In the case of **2c** and **2d** containing long alkyl chains, **3c**,**d** and **4c**,**d** were obtained in about a 1:1 ratio (entries 2 and 3). The present reaction was performed under an argon atmosphere, suggesting that the reaction does not require molecular oxygen (entry 4). When the substrate **2e**, containing a phenyloxy group, was employed in the reaction, a complex mixture was obtained.



Equation 3

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Table 1 Double Wacker-type Reaction of **2a** (Equation 2)

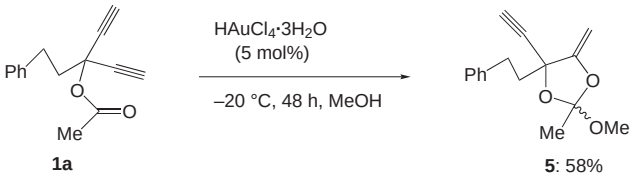
Entry	Catalyst (5 mol%)	Solvent	Time	**3a** Yield (%)	**4a** Yield (%)
1	$HAuCl_4·3H_2O$	MeOH	20 h	51	39
2	AuCl	MeOH	20 h	46	26
3	$AuCl_3$	MeOH	48 h	52	22
4	$PtCl_4$	MeOH	20 h	40	30
5	$PtCl_2$	MeOH	20 h	42	19
6	$Ph_3PAuCl–AgSbF_6$	MeOH	48 h	54	26
7	$HAuCl_4·3H_2O$	*i*-BuOH	20 h	52: **3f**	26
8	$HAuCl_4·3H_2O$	toluene	20 h	complex mixture	

Table 2 $HAuCl_4·3H_2O$-Catalyzed Double Wacker-Type Reaction of **2**

Entry	R	Time	Yield (%)	Yield (%)
1	**2b**: $PhCH_2$	22 h	**3b** (53)	**4b** (27)
2	**2c**: Octyl	22 h	**3c** (46)	**4c** (47)
3	**2d**: Pentyl	18 h	**3d** (46)	**4d** (40)
4[a]	**2a**: $Ph(CH_2)_2$	20 h	**3a** (48)	**4a** (38)

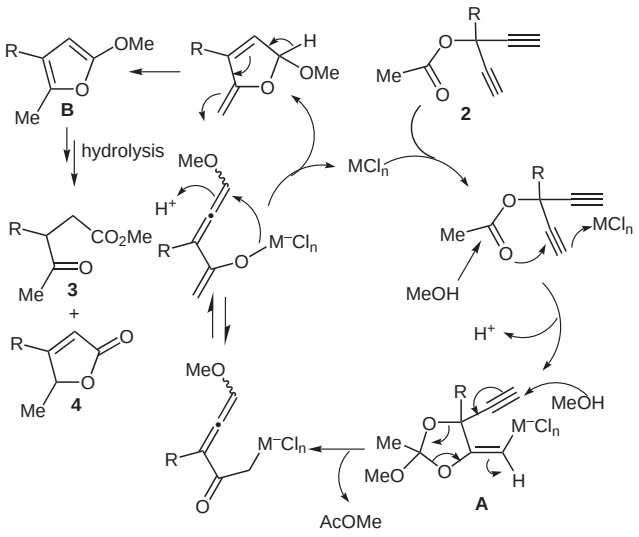
[a] The reaction was performed under an argon atmosphere.

To elucidate the mechanism of the present reaction, **1a** was treated with the same catalyst at –20 °C for 48 hours to afford the orthoester **5** in 58% yield (Equation 4). This result is in good accordance with a previous report;[3f] the double Wacker-type reaction depicted in Equations 2 and 3 should be initiated by cyclization of the acetyl group.



Equation 4

A plausible mechanism of the present reactions is proposed as shown in Scheme 1. 5-*exo*-*dig*-Cyclization of 1,1-diethynyl acetates **2** via nucleophilic attack of the first alkyne by a carbonyl oxygen in accordance with Markovnikov's rule generates the intermediate **A**. Elimination of MeOAc should induce a nucleophilic attack of the second alkyne by methanol with anti-Markovnikov regioselectivity, followed by cyclization to produce the furan intermediate **B**. Hydrolysis of the furan intermediate **B** gives the products **3** and **4**.



Scheme 1

In conclusion, we have reported the double Wacker-type reaction of 1,1-diethynyl acetates. During the reaction, the acetate has dual functions: 1) neighboring group participation of the carbonyl oxygen leads to the 'Markovnikov' hydration of the first acetylene moiety; 2) elimination of the MeOAc leaving group leads to addition of methanol to the second acetylene, which follows 'anti-Markovnikov' addition. As a result, simple ester groups can be successfully converted into γ-ketoesters and lactones.

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(6) **Preparation of Substrates 2; General Procedure**: To a solution of trimethylsilyl acetylene (3.32 g, 33.8 mmol) in THF (30 mL) under Ar was added *n*-BuLi (13.0 mL of 2.6 M in hexane, 33.8 mmol) at –78 °C and the mixture was stirred for 0.5 h at 0 °C. After the solution was cooled to –78 °C, the corresponding ester **1** (11.3 mmol) in THF (3 × 8 mL) was slowly added dropwise. The mixture was stirred at –10 °C for 12 h and quenched with H_2O (80 mL) and EtOAc (80 mL). The organic layers were separated, the aqueous layer was extracted with EtOAc (50 mL), and combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. To a solution of the crude product in THF (30 mL) was added TBAF (22.4 mL of 1 M in THF, 22.4 mmol) and the mixture was stirred for 0.5 h at r.t. The mixture was diluted with H_2O (80 mL) and EtOAc (80 mL). The organic layers were separated, the aqueous layer was extracted with EtOAc (2 × 50 mL), and combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. To a solution of the crude product in pyridine (3 mL) and Ac_2O (2 mL) was added 4-dimethylaminopyridine (50 mg) and the mixture was stirred for 3–10 h at r.t. The mixture was diluted with H_2O (50 mL) and EtOAc (50 mL). The organic layers were separated, the aqueous layer was extracted with EtOAc (50 mL), and combined organic layers were washed with aq 10% HCl, dried with $MgSO_4$ and concentrated in vacuo. The crude product was purified by column chromatography on silica gel. The fraction eluted with hexane–EtOAc (100:1–20:1) afforded **2**. **2a**: colorless needles; mp 51 °C. ^{1}H NMR ($CDCl_3$): δ = 2.09 (s, 3 H), 2.37–2.41 (m, 2 H), 2.70 (s, 2 H), 2.93–2.97 (m, 2 H), 7.19–7.32 (m, 5 H). ^{13}C NMR ($CDCl_3$): δ = 21.3, 30.4, 43.8, 66.3, 74.4, 80.0, 126.2, 128.5, 128.5, 140.6, 168.3. FAB–MS: *m*/*z* = 249 [M^+ + Na]. IR (KBr): 3253, 2935, 2120, 1748 cm^{-1}. Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.41; H, 6.41. **2b**: colorless oil. ^{1}H NMR ($CDCl_3$): δ = 2.07 (s, 3 H), 2.66 (s, 2 H), 3.37 (s, 2 H), 7.25–7.39 (m, 5 H). ^{13}C NMR ($CDCl_3$): δ = 21.4, 47.6, 66.7, 74.9, 79.8, 127.5, 127.9, 131.2, 133.7, 168.2. HRMS–EI: *m*/*z* [M^+] calcd for $C_{14}H_{12}O_2$: 212.0837; found: 212.0833. IR (KBr): 3270, 2122, 1744 cm^{-1}. **2c**: colorless oil. ^{1}H NMR ($CDCl_3$): δ = 0.89 (t, *J* = 6.8 Hz, 3 H), 1.26–1.38 (m, 10 H), 1.58–1.66 (m, 2 H), 2.04–2.08 (m, 2 H), 2.09 (s, 3 H), 2.64 (s, 2 H). ^{13}C NMR ($CDCl_3$): δ = 14.1, 21.4, 22.7, 23.9, 29.1, 29.2, 29.4, 31.8, 42.2, 66.8, 73.5, 80.3, 168.3. FAB–MS: *m*/*z* = 235 [M^+ + H]. IR (KBr): 3291, 2929, 2123, 1757 cm^{-1}. Anal. Calcd for $C_{15}H_{22}O_2$: C, 77.88; H, 9.46. Found: C, 76.12; H, 9.53. **2d**: colorless oil. ^{1}H NMR ($CDCl_3$): δ = 0.92 (t, *J* = 7.0 Hz, 3 H), 1.33–1.38 (m, 4 H), 1.59–1.67 (m, 2 H), 2.03–2.08 (m, 2 H), 2.09 (s, 3 H), 2.64 (s, 2 H). ^{13}C NMR ($CDCl_3$): δ = 13.9, 21.4, 22.4, 23.6, 31.3, 42.2, 66.8, 73.6, 80.3, 168.4. HRMS–EI: *m*/*z* [M^+] calcd for $C_{12}H_{16}O_2$: 192.1150; found: 192.1143. IR (KBr): 3292, 2958, 2123, 1756 cm^{-1}. **2e**: colorless needles; mp 47 °C. ^{1}H NMR ($CDCl_3$): δ = 2.09 (s, 3 H), 2.69 (s, 2 H), 4.36 (s, 2 H), 6.97–7.01 (m, 3 H), 7.24–7.31 (m, 2 H). ^{13}C NMR ($CDCl_3$): δ = 21.2, 65.7, 73.4, 74.9, 77.7, 115.4, 121.9, 129.5, 158.4, 168.1. HRMS–EI: *m*/*z* [M^+] calcd for $C_{14}H_{12}O_3$: 228.0787; found: 228.0786. IR (KBr): 3281, 2132, 1767 cm^{-1}.

(7) **Reaction of 2; General Procedure**: A 20-mL round-bottomed flask, containing a magnetic stirring bar, catalyst (0.015 mmol), **2** (0.3 mmol) and MeOH (5 mL) was fitted with a Dimroth condenser capped with a rubber septum. After being stirred for a certain period at 60 °C, the mixture was diluted with EtOAc (20 mL) and washed with aq 3% $NaHCO_3$ (20 mL). The organic layers were separated, the aqueous layer was extracted with EtOAc (30 mL), and combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The crude product was purified by column chromatography on silica gel. The fraction eluted with hexane–EtOAc (100:1–50:1 and 10:1) afforded **3** and **4**, respectively. **3a**: colorless oil. ^{1}H NMR ($CDCl_3$): δ = 1.69–1.78 (m, 1 H), 1.91–2.00 (m, 1 H), 2.22 (s, 3 H), 2.43 (dd, *J* = 4.4, 16.8 Hz, 1 H), 2.58–2.62 (m, 2 H), 2.80 (dd, *J* = 9.6, 16.8 Hz, 1 H), 2.99–3.07 (m, 1 H), 3.66 (s, 3 H), 7.15–7.32 (m, 5 H). ^{13}C NMR ($CDCl_3$): δ = 29.5, 32.8, 33.1, 34.9, 47.4,

51.7, 126.2, 128.2, 128.5, 140.9, 172.7, 210.5. HRMS–EI: *m*/*z* [M$^+$] calcd for $C_{14}H_{18}O_3$: 234.1256; found: 234.1252. IR (KBr): 1736, 1712 cm^{-1}. **3b**: colorless oil. ^{1}H NMR ($CDCl_3$): δ = 2.06 (s, 3 H), 2.28 (dd, *J* = 4.4, 17.0 Hz, 1 H), 2.54 (dd, *J* = 8.4, 13.6 Hz, 1 H), 2.70 (dd, *J* = 10.0, 17.0 Hz, 1 H), 2.87 (dd, *J* = 7.2, 13.6 Hz, 1 H), 3.18–3.25 (m, 1 H), 3.55 (s, 3 H), 7.07–7.24 (m, 5 H). ^{13}C NMR ($CDCl_3$): δ = 30.3, 35.0, 37.6, 49.6, 51.6, 126.7, 128.6, 128.8, 138.1, 172.6, 210.6. HRMS–EI: *m*/*z* [M$^+$] calcd for $C_{13}H_{16}O_3$: 220.1100; found: 220.1097. IR (KBr): 1738, 1205 cm^{-1}. **3c**: colorless oil. ^{1}H NMR ($CDCl_3$): δ = 0.81 (t, *J* = 6.8 Hz, 3 H), 1.14–1.38 (m, 13 H), 1.49–1.56 (m, 1 H), 2.16 (s, 3 H), 2.28 (dd, *J* = 4.4, 16.8 Hz, 1 H), 2.67 (dd, *J* = 10.0, 16.8 Hz, 1 H), 2.88–2.95 (m, 1 H), 3.58 (s, 3 H). ^{13}C NMR ($CDCl_3$): δ = 14.0, 22.6, 26.8, 29.1, 29.3, 29.5, 29.5, 31.3, 31.8, 34.9, 47.9, 51.6, 173.0, 210.9. HRMS–EI: *m*/*z* [M$^+$] calcd for $C_{14}H_{26}O_3$: 242.1882; found: 242.1893. IR (KBr): 2928, 1739, 1715 cm^{-1}. **3d**: colorless oil. ^{1}H NMR ($CDCl_3$): δ = 0.81 (t, *J* = 6.8 Hz, 3 H), 1.17–1.21 (m, 6 H), 1.25–1.38 (m, 1 H), 1.50–1.59 (m, 1 H), 2.16 (s, 3 H), 2.28 (dd, *J* = 4.4, 16.8 Hz, 1 H), 2.67 (dd, *J* = 10.0, 16.8 Hz, 1 H), 2.88–2.95 (m, 1 H), 3.58 (s, 3 H). ^{13}C NMR ($CDCl_3$): δ = 13.9, 22.3, 26.5, 29.5, 31.2, 31.7, 34.9, 47.9, 51.6, 172.9, 210.9. HRMS–EI: *m*/*z* [M$^+$] calcd for $C_{11}H_{20}O_3$: 200.1413; found: 200.1416. IR (KBr): 2932, 1739, 1714 cm^{-1}. **3f**: colorless oil. ^{1}H NMR ($CDCl_3$): δ = 0.92 (d, *J* = 6.8 Hz, 6 H), 1.69–1.78 (m, 1 H,), 1.86–2.01 (m, 2 H), 2.22 (s, 3 H), 2.44 (dd, *J* = 4.8, 16.8 Hz, 1 H), 2.55–2.66 (m, 2 H), 2.81 (dd, *J* = 9.6, 16.8 Hz, 1 H), 2.99–3.06 (m, 1 H), 3.80–3.88 (m, 2 H), 7.15–7.31 (m, 5 H). ^{13}C NMR ($CDCl_3$): δ = 19.0, 27.6, 29.5, 32.9, 33.1, 35.2, 47.5, 70.8, 126.2, 128.2, 128.5, 141.0, 172.3, 210.5. HRMS–EI: *m*/*z* [M$^+$] calcd for $C_{17}H_{24}O_3$: 276.1726; found: 276.1721. IR (KBr): 2962, 1733, 1160 cm^{-1}. **4a**: colorless oil. ^{1}H NMR ($CDCl_3$): δ = 1.41 (d, *J* = 6.8 Hz, 3 H), 2.54–2.76 (m, 2 H), 2.92 (t, *J* = 8.0 Hz, 2 H), 4.90 (dq, *J* = 1.6, 6.8 Hz, 1 H), 5.81 (q, *J* = 1.6 Hz, 1 H), 7.18–7.34 (m, 5 H). ^{13}C NMR ($CDCl_3$): δ = 18.2, 29.5, 33.1, 80.4, 115.6, 126.7, 128.1, 128.7, 139.7, 172.9, 173.1. HRMS–EI: *m*/*z* [M$^+$] calcd for $C_{13}H_{14}O_2$: 202.0994; found: 202.0996. IR (KBr): 2928, 1755, 1639 cm^{-1}. **4b**: colorless oil. ^{1}H NMR ($CDCl_3$): δ = 1.38 (d, *J* = 6.8 Hz, 3 H), 3.48 (dd, *J* = 1.6, 16.8 Hz, 1 H), 3.68 (d, *J* = 16.8 Hz, 1 H), 4.86 (br q, *J* = 6.8 Hz, 1 H), 5.59 (d, *J* = 1.6 Hz, 1 H), 7.10–7.30 (m, 5 H). ^{13}C NMR ($CDCl_3$): δ = 18.3, 34.6, 79.9, 116.7, 127.3, 128.8, 129.0, 135.5, 172.6, 172.9. HRMS–EI: *m*/*z* [M$^+$] calcd for $C_{12}H_{12}O_2$: 188.0837; found: 188.0834. IR (KBr): 2932, 1737, 1639 cm^{-1}. **4c**: colorless oil. ^{1}H NMR ($CDCl_3$): δ = 0.84 (t, *J* = 6.4 Hz, 3 H), 1.17–1.34 (m, 10 H), 1.38 (d, *J* = 6.8 Hz, 3 H), 1.48–1.58 (m, 2 H), 2.16–2.37 (m, 2 H), 4.89 (dq, *J* = 1.6, 6.8 Hz, 1 H), 5.72 (d, *J* = 1.6 Hz, 1 H). ^{13}C NMR ($CDCl_3$): δ = 14.0, 18.2, 22.5, 26.9, 27.9, 29.0, 29.1, 29.1, 31.7, 80.3, 114.8, 173.1, 174.5. HRMS–EI: *m*/*z* [M$^+$] calcd for $C_{13}H_{22}O_2$: 210.1620; found: 210.1629. IR (KBr): 2927, 1755, 1639 cm^{-1}. **4d**: colorless oil. ^{1}H NMR ($CDCl_3$): δ = 0.84 (t, *J* = 7.2 Hz, 3 H), 1.26–1.31 (m, 4 H), 1.36 (d, *J* = 6.8 Hz, 3 H), 1.49–1.57 (m, 2 H), 2.14–2.35 (m, 2 H), 4.87 (dq, *J* = 1.2, 6.8 Hz, 1 H), 5.70 (d, *J* = 1.6 Hz, 1 H). ^{13}C NMR ($CDCl_3$): δ = 13.8, 18.2, 22.2, 26.5, 27.8, 31.3, 80.3, 114.8, 173.1, 174.5. HRMS–EI: *m*/*z* [M$^+$] calcd for $C_{10}H_{16}O_2$: 168.1150; found: 168.1144. IR (KBr): 2932, 1754, 1638 cm^{-1}. **5**: colorless oil; diastereomeric mixture, ratio = 2.3:1. ^{1}H NMR ($CDCl_3$, major diastereomer): δ = 1.66 (s, 3 H), 2.05–2.25 (m, 2 H), 2.66 (s, 1 H), 2.79–2.96 (m, 2 H), 3.40 (s, 3 H), 4.18 (d, *J* = 2.8 Hz, 1 H), 4.50 (d, *J* = 2.8 Hz, 1 H), 7.18–7.32 (m, 5 H). ^{13}C NMR ($CDCl_3$, major diastereomer): δ = 24.0, 30.3, 44.4, 50.1, 73.9, 78.8, 80.8, 82.4, 123.1, 126.1, 128.4, 128.5, 141.0, 159.8. HRMS–EI: *m*/*z* [M$^+$] calcd for $C_{16}H_{18}O_3$: 258.1256; found: 258.1258. IR (KBr): 3287, 2117, 1687, 1052 cm^{-1}.