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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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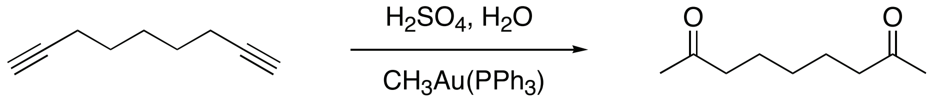
AU(I)-CATALYZED HYDRATION OF ALKYNES: 2,8-NONANEDIONE



Submitted by Eiichiro Mizushima,[1] Dong-Mei Cui,[1] Dilip Chandra Deb Nath,[1] Teruyuki Hayashi,*[1] and Masato Tanaka.[1,2]
Checked by Rick L. Danheiser and Tin Yiu Lam.
Discussion Addendum: *Org. Synth*. **2012**, *89*, 126.

1. Procedure[3]

2,8-Nonanedione. A 250-mL, three-necked, round-bottomed flask fitted with a rubber septum, a glass stopper, a reflux condenser equipped with an argon inlet, and a magnetic stirbar is evacuated and filled with argon, and then charged with 1,8-nonadiyne (6.3 mL, 5.0 g, 42 mmol, 1 equiv) (Note 1), methyl(triphenylphosphine)gold[4] (CH_3AuPPh_3) (0.042 g, 0.088 mmol, 0.2 mol%) (Note 2), sulfuric acid (prepared by diluting 2.08 g (21.2 mmol, 0.5 equiv) of concentrated H_2SO_4 with 21 mL of water) (Note 3), and methanol (120 mL) (Note 4). The mixture is heated and stirred at reflux (oil bath temperature 70–75 °C) for 2 h, at which time analysis by gas chromatography (Note 5) shows that the conversion of 1,8-nonadiyne is complete. The reaction mixture is allowed to cool to room temperature and then transferred to a 250-mL, round-bottomed flask and most of the methanol is removed by rotary evaporation (30–40 °C, 20 mmHg). The resulting viscous, colorless, and cloudy oil (about 20 mL) is diluted with water (70 mL) and diethyl ether (50 mL). The mixture is stirred for 5 min and then the aqueous layer is separated and extracted with ether (3 x 50 mL). The combined ether layers are washed with saturated $NaHCO_3$ solution (50 mL) and saturated NaCl solution (50 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated by rotary evaporation (20 °C, 20 mmHg) to give 5.80 g of a colorless solid. This material is dissolved in boiling pentane (about 30 mL) in a 50-mL Erlenmeyer flask heated on a hot plate and the solution is cooled to 0 °C. The resulting solid is collected by vacuum filtration on a Büchner funnel, washed with ice-cold pentane (10 mL), and then dried at 20 mmHg to afford 5.57 g (86%) of 2,8-nonanedione as colorless crystals (Note 6).

2. Notes

1. 1,8-Nonadiyne (98% purity) was purchased by the submitters from Acros Organics and used as received. The checkers obtained the diyne (98% purity) from Aldrich Chemical Co.

2. Methyl(triphenylphosphine)gold(I) was prepared as follows according to the procedure of ref. 4. A 100-mL, two-necked, round-bottomed flask equipped with a rubber septum, a reflux condenser fitted with an argon inlet, and a magnetic stirbar was evacuated and filled with argon. Chloro(triphenylphosphine)gold(I) (Strem Chemicals, 98+% purity) (0.5 g, 1.0 mmol, 1 equiv) and 6 mL of diethyl ether (purified by pressure filtration through activated alumina) were added and the resulting colorless suspension was cooled to 0 °C. Methylmagnesium iodide solution (3M in diethyl ether, Aldrich Chemical Co.) (1.7 mL, 5.1 mmol, 5.1 equiv) was added dropwise via syringe over 10 min. The resulting mixture was heated at reflux (oil bath temperature 50–55 °C) for 1 h and then allowed to cool to room temperature. Ice-cold 0.5% H_2SO_4 solution (24 mL, degassed by argon purging for 30 min before use) was added, resulting in the formation of a purple precipitate. Diethyl ether (3 mL, purified by pressure filtration through activated alumina) was added and the resulting mixture of two liquid phases and the precipitate was vacuum filtered through a Büchner funnel (washing with three 10-mL portions of toluene that had been purified by pressure filtration through activated alumina). The combined filtrates were transferred to a separatory funnel and the layers were separated. The organic phase was washed with 50 mL of water, dried over anhydrous Na_2SO_4, filtered, and concentrated to a volume of about 10 mL. This solution was transferred to a 50-mL Erlenmeyer flask, diluted with 30 mL of hexane (degassed by purging with argon for 30 min prior to use), and then slowly cooled to –18 °C. The resulting crystals were collected on a Büchner funnel by vacuum filtration (washing with ca. 15 mL of ice-cold hexane) and air-dried to give 0.248 g (52%) of methyl(triphenylphosphine)gold(I) as colorless crystals. The product exhibits the following physical properties: mp: 164–167 °C (lit.[4] 167–168 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.55 (d, J_{PH} = 7.8 Hz, 3 H), 7.43–7.58 (m, 15 H); ^{31}P NMR (121 MHz, $CDCl_3$) δ: 47.6; Anal. Calcd for $C_{19}H_{18}AuP$: C, 48.12; H, 3.83; Found: C, 48.11; H, 3.51.

3. Concentrated sulfuric acid was obtained by the checkers from Mallinckrodt Chemicals and was diluted with deionized water. The aqueous acid was degassed by purging with argon for 30 min prior to use.

4. Methanol was purchased by the submitters from Wako Pure Chemical Industries, Ltd. and used as received. The checkers obtained anhydrous methanol from Mallinckrodt Chemicals. The methanol was degassed by purging with argon for 30 min prior to use.

5. The submitters employed a Shimadzu GC-17A gas chromatograph equipped with a capillary column of Ultra Alloy UA1-30M-0.25F with a stationary phase of poly(dimethylsiloxane) using the following conditions: initial temperature at 50 °C, then increased at a rate of 10 °C/min, and held at 250 °C for 30 min. The checkers used a HP 6890 Series GC system equipped with a capillary column HP-5 with 5% phenyl dimethylpolysiloxane as the stationary phase under the following conditions: initial temperature 50 °C, then increased at a rate of 10 °C/min, and held at 240 °C for 30 min. Retention time of 1,8-nonadiyne: 4.37 min.

6. The product has the following characteristics: mp 47–48 °C (lit.[5] 47–48 °C); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.22–1.28 (m, 2 H), 1.54 (apparent quintet, J = 7.5 Hz, 4 H), 2.10 (s, 6 H), 2.40 (t, J = 7.5 Hz, 4 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 23.6, 28.7, 30.1, 43.5, 209.1; IR (KBr): 2936, 2866, 1716, 1702, 1464, 1408, 1378, 1360, 1230, 1163, 958 cm^{-1}; Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 68.92; H, 10.56.

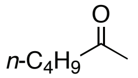
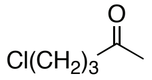
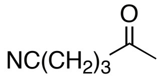
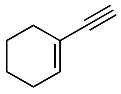
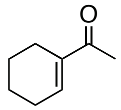
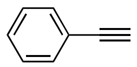
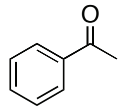
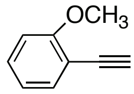
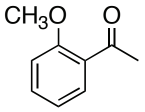
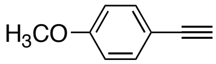
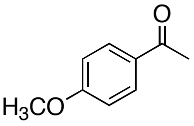
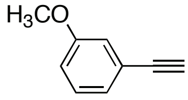
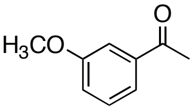
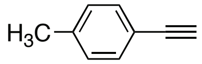
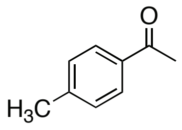
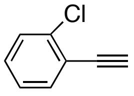
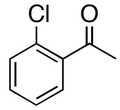
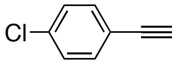
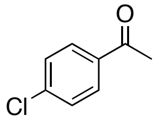
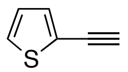
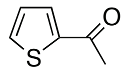
Safety and Waste Disposal Information

All hazardous materials should be handled and disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

2,8-Nonanedione is a useful synthetic intermediate for the synthesis of rootworm sex pheromones, among other applications. The methods for the synthesis of 2,8-nonanedione have been recently summarized by Keinan and coworkers[6] as follows: (1) mercury-catalyzed hydration of 1,8-nonadiyne,[7] (2) palladium-catalyzed Wacker oxidation of 1,8-nonadiene,[8] (3) reaction of 1,5-pentylene biscadmium halide with acetyl chloride,[9] (4) oxidative cleavage of 2-methylcycloheptanone,[5] and (5) reaction of bromohexanone ketal and acetoacetate.[6] Other synthetic routes include (6) alkylation of acetone dimethylhydrazone followed by hydrolysis,[10] (7) condensation of an alkoxyalkyl phenyl sulfone and a dihalopentane,[11] (8) imidazolylation of pimelonamide followed by alkylation and elimination,[12] and (9) alkylation of a phosphonium salt of pimeloyl chloride followed by hydrolysis.[13]

Table 1 Preparation of Various Methyl Ketones[a]

Alkyne	Product	$[(PPh_3)AuCH_3]$/mmol	Time	Yield[b]
n-C_4H_9—≡		0.002	2 h[c]	99%
$Cl(CH_2)_3$—≡		0.01	4 h[d]	72%
$NC(CH_2)_3$—≡		0.002	1 h	83%
		0.01	1 h	90%
		0.002[e]	1 h	98%
		0.002	1 h	95%
		0.002	1 h	93%
		0.01	1 h	77%
		0.002[e]	1 h	96%
		0.002	1 h	66%
		0.01	1 h	54%
		0.01	1h	92%

a) Catalyst $[(Ph_3P)AuCH_3]$, alkyne 1 mmol, water 0.5 mL, H_2SO_4 0.5 mmol, methanol 1-3 mL, 70 °C. b) Yields by GC c) 60 °C. d) Under CO atmosphere. e) CF_3SO_3H instead of H_2SO_4.

However, reactions (3) - (9) are multi-step procedures that give massive salt waste. Wacker oxidation (2) is principally the best reaction, while the oxidation of 1,8-nonadiene[8] itself is not selective.

On the other hand, acid-catalyzed hydration of alkynes to give carbonyl compounds is one of the most straightforward methods to form the carbon-oxygen bond and is long known.[14] However, only electron-rich alkynes react satisfactorily. The reaction of simple alkynes is sluggish and requires a co-catalyst such as mercury(II) salts[6,15] as in reaction (1). To avoid the use of toxic mercury(II) salts, the use of various transition metal complexes such as Ru(II),[16] Ru(III),[17] Rh(III),[18] Pt(II),[19] and Au(III)[20] have been examined. However, the efficiencies of these catalyst systems have remained insufficient and the highest turnover frequency is in the 100/h range. Recently, Teles and coworkers[21] have claimed in a patent application that hydration of propargyl alcohol is catalyzed by an Au(I)-acid catalyst system. However, the efficiency is still low.

We have discovered that simple alkynes can be hydrated by the CH_3AuPPh_3-acid catalyst system to give the corresponding methyl ketones in high yields.[3] The reaction is significantly affected by the reaction media and methanol is the best solvent. Turnover frequency increases in methanol to 15600/h.[22]

The reaction is applied not only to simple alkynes and diynes, but also to various alkynes as shown in Table 1. Aliphatic terminal alkynes give corresponding methyl ketones in good yields, even when electron withdrawing substituents such as chloro and cyano groups are attached. The use of CO atmosphere is required in some cases. Though C=C and C≡N groups can be potentially hydrated or hydrolyzed, both groups remain intact in the presence of this CH_3AuPPh_3-acid catalyst system. Aromatic alkynes give the corresponding acetophenones in high yields, while the use of CF_3SO_3H instead of H_2SO_4 is required in some cases. The presence of electronegative *o*- and *p*-chloro- and *m*-methoxy-substituents results in lower yields. The present catalyst CH_3AuPPh_3 is also applicable to hydroamination of alkynes.[23]

1. National Institute of Advanced Industrial Science and Technology.
2. Present affiliation: Tokyo Institute of Technology.
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Appendix
Chemical Abstracts Nomenclature (Registry Number)

Methyl(triphenylphosphine)gold (CH_3AuPPh_3); (23108-72-7)
1,8-Nonadiyne; (2396-65-8)
2,8-Nonanedione; (30502-73-9)