Efficient Transformation of Methyl Propargyl Ethers into α,β-Unsaturated Ketones

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Synopsis. Methyl propargyl ethers, obtained from carbonyl compounds by successive treatment with an acetylide and MeI, were easily converted to the corresponding α,β-unsaturated ketone by regioselective hydration of acetylenic moiety followed by elimination of methanol under the catalytic action of Au(III).

Hydration of an acetylenic moiety has been utilized for the preparation of ketones from easily accessible alkynes. Various transition metal catalysts have been employed for the hydration of unactivated alkynes.[1-14] As a propargylic alcohol **1** is a suitable precursor of α-hydroxy ketone **2** or α,β-unsaturated ketone **4** by the regiocontrolled hydration, generally applicable methodologies have been needed. We have disclosed the regioselective formation of **2** (R=Ac) from acetate **1** (R=Ac) under the catalytic action of Au(III).[15] As for selective formation of **4**, Hg(II) catalysts are applied in strongly acidic conditions, other effective catalysts are needed for the transformation in mild conditions.

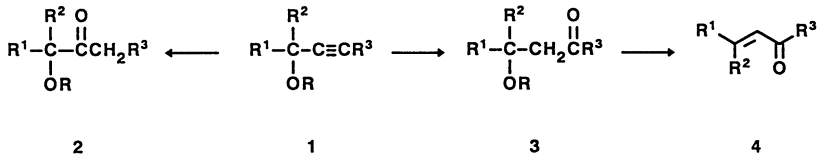
During the continuous studies on selective hydration of the derivatives of propargyl alcohols **1**, we have observed the highly regioselective hydration of methyl ethers to give **4** exclusively. This paper describes Au(III) catalyzed regioselective hydration of **1** (R=Me) under mild conditions.

Internal methyl propargyl ethers **1** (R=Me, R^1 and/or $R^2 \neq H$, $R^3 \neq H$) were treated with $NaAuCl_4$ (5 mol%) in refluxing aqueous methanol to give α,β-unsaturated ketones by regioselective hydration followed by elimination of methanol. A propargyl methyl ether **1f** (R=Me, $R^1=R^2=H$, $R^3=n\text{-}C_5H_{11}$), on the other hand, afforded β-methoxy ketone **3f** (R=Me, $R^1=R^2=H$, $R^3=n\text{-}C_5H_{11}$) in an excellent yield. Results are summarized in Table 1.

Although the hydration of internal propargyl methyl ethers afforded α,β-unsaturated ketone **4** mainly, small amount of methoxy ketone **3** was obtained as a by-product. Pure **4** was obtained by column chromatography. An attempt to obtain **4** in pure state by employing nonalcoholic solvent was unsuccessful; the reaction of 4-methoxy-2-nonyne (**1b**) in aqueous tetrahydrofuran or acetonitrile resulted in quantitative recovery of the starting material.

The stereochemistry around the double bond was exclusively *trans* in the cases of disubstituted olefins (Entry 1—3). It should be noted that alkynes bearing a methoxyl substituent on the propargylic position were regioselectively hydrated as described above, whereas no regioselectivity was observed in the hydration of simple alkynes catalyzed by Au(III) salt.[12,15] This regioselectivity might be realized both by electron withdrawing effect of the methoxyl group or by the interaction of oxygen with Au(III) at transition state; the reverse regioselectivity was observed for acetoxy alkynes where anchimeric interaction of carbonyl oxygen with Au(III) could control the regioselectivity.[10,12,13]

In contrast to the regioselective hydration giving **3** or **4** from methyl propargyl ethers (**1**, R=Me, $R^3 \neq H$), a methyl ether of α-ethynyl alcohol (**1g**, R=Me, $R^1=n$-



2 **1** **3** **4**

Scheme 1. Hydration of propargyl alcohol derivatives.

Table 1. Au(III) Catalyzed Hydration of Methyl Propargyl Ether **1** (R=Me)

Entry	Starting material	R^1	R^2	R^3	Reaction time[a]/h	Product	Yield/%[b]
1	**1a**	$n\text{-}C_5H_{11}$	H	$n\text{-}C_4H_9$	2	**4a**	79
2	**1b**	$n\text{-}C_5H_{11}$	H	CH_3	2	**4b**	75
3	**1c**	C_2H_5	H	Ph	10	**4c**	21
4	**1d**	CH_3	CH_3	$n\text{-}C_6H_{13}$	10	**4d**	70
5	**1e**	$-(CH_2)_5-$		CH_3	10	**4e**	30
6	**1f**	H	H	$n\text{-}C_5H_{11}$	5	**3f**	91
7	**1g**	$n\text{-}C_5H_{11}$	H	H	1	**2g**	91

a) Refluxed in MeOH containing 10% H_2O. b) Isolated yield after column chromatography.

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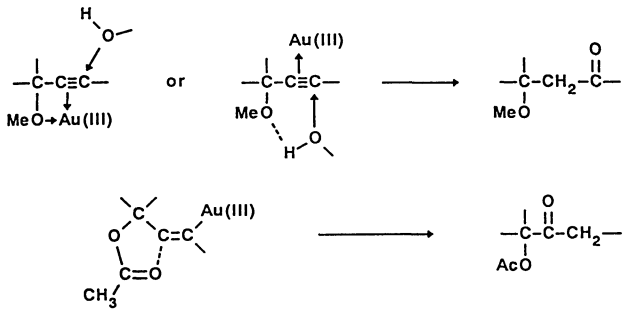

Scheme 2. Regioselective hydration.

C_5H_{11}, R^2=R^3=H) afforded α-methoxyketone **2g** (Table 1, Entry 7).

The conversion of propargyl alcohols into, α,β-unsaturated ketones has been known as Meyer–Schuster rearrangement.[16] This rearrangement, however, requires strongly acidic conditions, and aliphatic propargyl alcohols were not applicable to the reaction.

Compared with reported procedures, the Au(III) catalyzed reaction described above produces α,β-unsaturated ketones in good yields under mild and neutral conditions. Since methyl propargyl ethers are easy accessible by the etherification of propargyl alcohols,[17,18] the above described hydration would find practical uses in organic synthesis.

Experimental

IR spectra were obtained on a JASCO IR-810 spectrometer. ^{1}H NMR (200 MHz) were measured on a Varian XL-200. Elemental analyses were performed at Elemental Analysis Center of Kyoto University.

Preparation of Methyl Propargyl Ethers 1: Methyl propargyl ethers were prepared from 1-alkyne, aldehyde or ketone, and methyl iodide described in the literature.[18] Alternatively, they were synthesized by the reaction of propargyl alcohols, whose easy synthesis is known as Favorskii–Babayan synthesis,[19] with methyl iodide in the presence of solid potassium hydroxide in DMSO (dimethyl sulfoxide).[17]

Hydration of Methyl Propargyl Ethers 1 to α,β-Unsaturated Ketones 4 (General Procedure): Methyl propargyl ether (**1**, 1 mmol) was dissolved in a mixture of methanol (10 ml) and water (1 ml) and $NaAuCl_4 \cdot 2H_2O$ (20 mg, 0.05 mmol, 5 mol%) was added to this solution. The reaction mixture was heated at reflux for 2—10 h and then concentrated under reduced pressure. The residue was diluted with ether and washed with 1 : 1 mixture of brine and aqueous ammonia. The ethereal solution was dried over Na_2SO_4 and concentrated to give the crude product, which was purified by column chromatography (silica gel; hexane–ethyl acetate).

7-Methoxy-5-dodecyne (1a): ^{1}H NMR ($CDCl_3$), δ=0.89 (3H, t, *J*=7.0 Hz), 0.92 (3H, t, *J*=7.0 Hz), 1.22—1.74 (12H, m), 2.23 (2H, td, *J*=6.8, 2.0 Hz), 3.39 (3H, s), 3.91 (1H, tt, *J*=6.3, 2.0 Hz); IR (neat) 2220, 1378, 1337, 1186, 1143, 1121, 1097, 984, 925, 899, 728 cm^{-1}; Found: C, 79.35; H, 12.42%. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32%.

4-Methoxy-2-nonyne (1b): ^{1}H NMR ($CDCl_3$), δ=0.89 (3H, t, *J*=6.4 Hz), 1.23—1.52 (8H, m), 1.87 (3H, d, *J*=2.0 Hz), 3.39 (3H, s), 3.89 (1H, tq, *J*=6.9, 2.0 Hz); IR (neat) 2250, 1021, 1095, 927, 900 cm^{-1}; Found: C, 77.60; H, 11.96%. Calcd for $C_{10}H_{18}O$: C, 77.86; H, 11.76%.

3-Methoxy-1-phenyl-1-pentyne (1c): ^{1}H NMR ($CDCl_3$), δ=1.08 (3H, t, *J*=7.2 Hz), 1.84 (2H, quint, *J*=7.2 Hz), 3.49 (3H, s), 4.12 (1H, t, *J*=7.2 Hz), 7.34 (3H, m), 7.46 (2H, m); IR (neat) 3075, 3050, 2220, 1595, 1490, 1464, 1444, 1338, 1128, 1105, 1085, 755, 690 cm^{-1}; Found: C, 82.58; H, 8.17%. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10%.

2-Methoxy-2-methyl-3-decyne (1d): ^{1}H NMR ($CDCl_3$), δ=0.90 (3H, t, *J*=6.7 Hz), 1.24—1.58 (8H, m), 1.42 (6H, s), 2.19 (2H, t, *J*=6.9 Hz), 3.35 (3H, s); IR (neat) 2225, 1376, 1359, 1225, 1172, 1150, 1079 cm^{-1}; Found: C, 78.85; H, 12.27%. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16%.

1-Methoxy-1-(1-propynyl)cyclohexane (1e): ^{1}H NMR ($CDCl_3$), δ=1.18—1.93 (10H, m), 1.88 (3H, s), 3.35 (3H, s); IR (neat) 1294, 1185, 1146, 1094, 926 cm^{-1}; Found: C, 78.71; H, 10.84%. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59%.

6-Dodecen-5-one (4a): ^{1}H NMR ($CDCl_3$), δ=0.90 (3H, t, *J*=6.7 Hz), 0.93 (3H, t, *J*=7.2 Hz), 1.29—1.67 (10H, m), 2.23 (2H, tdd, *J*=7.3, 7.3, 1.6 Hz), 2.53 (2H, t, *J*=7.5 Hz), 6.10 (1H, dt, *J*=16.0, 1.6 Hz), 6.83 (1H, dt, *J*=16.0, 7.3 Hz); IR (neat) 3050, 1699, 1676, 1631, 1378, 1192, 983 cm^{-1}; Found: C, 78.86; H, 12.35%. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16%.

Pure **3a** was obtained in 6% yield: ^{1}H NMR ($CDCl_3$), δ=0.90 (3H, t, *J*=6.9 Hz), 0.92 (3H, t, *J*=7.0 Hz), 1.25—1.72 (12H, m), 2.44 (1H, dd, *J*=16.1, 5.1 Hz), 2.46 (2H, t, *J*=7.3 Hz), 2.68 (1H, dd, *J*=16.1, 7.7 Hz), 3.32 (3H, s), 3.45 (1H, m); IR (neat) 1714, 1128, 1093 cm^{-1}; Found: C, 72.69; H, 12.44%. Calcd for $C_{13}H_{26}O_2$: C, 72.84; H, 12.23%.

3-Nonen-2-one (4b): ^{1}H NMR ($CDCl_3$), δ=0.89 (3H, t, *J*=6.8 Hz), 1.24—1.55 (6H, m), 2.22 (2H, tdd, *J*=6.2, 6.2, 1.6 Hz), 2.23 (3H, s), 6.02 (1H, dt, *J*=16.0, 1.6 Hz), 6.83 (1H, dt, *J*=16.0, 7.0 Hz); IR (neat) 3050, 3000, 1698, 1675, 1624, 1360, 1254, 980 cm^{-1}; Found: C, 76.82; H, 11.80%. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50%.

1-Phenyl-2-penten-1-one (4c): ^{1}H NMR ($CDCl_3$), δ=1.16 (3H, t, *J*=7.2 Hz), 2.36 (2H, qdd, *J*=7.2, 6.2, 1.6 Hz), 6.87 (1H, dt, *J*=16.0, 1.6 Hz), 7.12 (1H, dt, *J*=16.0, 6.2 Hz), 7.50 (3H, m), 7.95 (2H, m); IR (neat) 3050, 1671, 1648, 1621, 1283, 1215, 990, 972, 691 cm^{-1}; Found: C, 82.31; H, 7.52%. Calcd for $C_{11}H_{12}O$: C, 82.46; H, 7.55%.

2-Methyl-2-decen-4-one (4d): ^{1}H NMR ($CDCl_3$), δ=0.88 (3H, t, *J*=6.7 Hz), 1.22—1.71 (8H, m), 1.89 (3H, d, *J*=2.0 Hz), 2.14 (3H, d, *J*=2.0 Hz), 2.40 (2H, t, *J*=7.4 Hz), 6.08 (1H, septi, *J*=2.0 Hz); IR (neat) 1689, 1622, 1378, 1132, 730 cm^{-1}; Found: C, 78.69; H, 12.01%. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98%.

1-Cyclohexylidene-2-propanone (4e): ^{1}H NMR ($CDCl_3$), δ=1.52—1.75 (6H, m), 2.12 (2H, m), 2.13 (3H, s), 2.81 (2H, br-t, *J*=6.0 Hz), 6.02 (1H, s); IR (neat) 3000, 1687, 1620, 1173, 960 cm^{-1}; Found: C, 77.99; H, 10.05%. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21%.

Hydration of 1-Methoxy-2-octyne (1f): **1f** was prepared from commercially available 2-octyn-1-ol by the reaction with methyl iodide according to the procedure described above.

1-Methoxy-2-octyne (1f): ^{1}H NMR ($CDCl_3$), δ=0.90 (3H, t, *J*=7.0 Hz), 1.25—1.63 (6H, m), 2.23 (2H, tt, *J*=7.2, 2.4 Hz), 3.37 (3H, s), 4.08 (2H, t, *J*=2.4 Hz); IR (neat), 2170, 1184, 1131, 1096, 1000, 905 cm^{-1}; Found: C, 77.02; H, 11.44%. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50%.

1-Methoxy-3-octanone (3f): ^{1}H NMR ($CDCl_3$), δ=0.88 (3H, t, *J*=6.8 Hz), 1.20—1.72 (6H, m), 2.44 (2H, t, *J*=7.2 Hz), 2.65 (2H, t, *J*=6.4 Hz), 3.34 (3H, s), 3.65 (2H, t, *J*=6.4 Hz); IR (neat) 1716, 1119 cm^{-1}; Found: C, 68.01; H, 11.55%. Calcd for $C_9H_{18}O_2$: C, 68.31; H, 11.47%.

3-Methoxy-1-octyne (1g): **1g** was obtained by the methylation of commercially available 1-octyne-3-ol. ^{1}H NMR ($CDCl_3$), δ=0.90 (3H, t, *J*=6.5 Hz), 1.25—1.80 (8H, m), 2.46 (1H, d, *J*=2.0 Hz), 3.40 (3H, s), 3.95 (1H, td, *J*=6.3, 2.0 Hz); IR (neat) 3300, 2100, 1120, 1096, 940, 917 cm^{-1}; Found: C, 76.80; H, 11.69%. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50%.

Hydration of Methyl Ether of α-Ethynyl Alcohol (1g): 3-Methoxy-1-octyne (**1g**, 140 mg, 1 mmol) was dissolved in a mixture of methanol (10 ml) and water (1 ml) and

$NaAuCl_4 \cdot 2H_2O$ (8 mg, 0.025 mmol, 2 mol%) was added to this solution. The reaction mixture was heated at reflux for 1 h, concentrated in vacuo and then diluted with ether. The ethereal solution was washed with 1 : 1 mixture of brine and aqueous ammonia, dried (Na_2SO_4) and concentrated. Column chromatographical purification gave 3-methoxy-2-octanone (**2g**, 143 mg, 0.91 mmol, 91% yield).

3-Methoxy-2-octanone (2g): ^1H NMR ($CDCl_3$), δ=0.89 (3H, t, J=6.2 Hz), 1.18—1.67 (8H, m), 2.15 (3H, s), 3.36 (3H, s), 3.59 (1H, t, J=7.0 Hz); IR (neat) 1717, 1354, 1123, 1100 cm^{-1}; Found: C, 68.32; 11.63%. Calcd for $C_9H_{18}O_2$: C, 68.31; H, 11.47%.

References

1) P. F. Hudrlik and A. M. Hudrlik, "The Chemistry of Carbon-Carbon Triple Bond," John Wiley and Sons, New York (1978), Part I.
2) V. Jager and H. G. Viehe, "Methoden der Organishen Chemie (Houben-Weyl)," 4th ed, ed by E. Muller, (1977), Vol. V/2a.
3) T. F. Rutledge, "Acetylenes and Allenes," Reinhold, New York (1969).
4) G. A. Olah and D. Meidar, *Synthesis,* **1978**, 671.
5) G. Chandra, D. Devaprahakara, and M. S. Muthana, *Curr. Sci.,* **40**, 400 (1971).
6) G. W. Stacy and R. A. Mikulec, *Org. Synth.,* Coll. Vol. IV, 13 (1963).
7) M. S. Newman, *J. Am. Chem. Soc.,* **75**, 4740 (1953).
8) M. A. Islam and R. A. Raphael, *J. Chem. Soc.,* **1952**, 4086.
9) A. Janout and S. L. Regen, *J. Org. Chem.,* **47**, 3331 (1982).
10) G. Stork and R. Borch, *J. Am. Chem. Soc.,* **86**, 935, 936 (1964).
11) W. D. Harman, J. C. Dobson, and H. Taube, *J. Am. Chem. Soc.,* **111**, 3061 (1989).
12) K. Imi, K. Imai, and K. Utimoto, *Tetrahedron Lett.,* **28**, 3127 (1987).
13) K. Utimoto, *Pure Appl. Chem.,* **55**, 1845 (1983).
14) W. C. Hiscox and P. W. Jennings, *Organometallics,* **9**, 1997 (1990).
15) Y. Fukuda and K. Utimoto, *J. Org. Chem.,* **56** (1991), in press.
16) K. Meyer and K. Schuster, *Ber,* **55**, 819 (1922).
17) R. A. W. Johnstone and M. E. Rose, *Tetrahedron,* **35**, 2169 (1979).
18) L. Bransma and H. D. Verkruijsse, "Synthesis of Acetylenes, Allenes and Cumulenes," Elsevier, Amsterdam (1981), p. 231.
19) A. W. Johnson, "The Chemistry of Acetylenic Compounds," London (1946), Vol. 1, p. 14.