Communication to the Editor

A Fluorinated Cobalt(III) Porphyrin Complex for Hydroalkoxylation of Alkynes

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A fluorinated cobalt(III) porphyrin complex [Co(TPFPP)-$NTf_2 \cdot 2C_2H_5OH$, where TPFPP=5,10,15,20-tetrakis(pentafluorophenyl)porphyrin, Tf=CF_3SO_2] promotes hydroalkoxylation of alkynes to give acetals in good to excellent yields. The acetals can be directly functionalized with nucleophiles in a one-pot procedure.

Key words hydroalkoxylation; acetal; alkyne; alcohol; cobalt; porphyrin

Acetals are synthetic equivalents of carbonyl compounds, reacting with various carbon and heteroatom nucleophiles, and are widely used as synthetic intermediates in medicinal chemistry and materials science.[1)] We here report that a fluorinated Co^{III} porphyrin complex, Co(TPFPP)$NTf_2 \cdot 2C_2H_5OH$ [**1a**, TPFPP=5,10,15,20-tetrakis(pentafluorophenyl)porphyrin, Tf=CF_3SO_2],[2)] catalyzes Markovnikov hydroalkoxylation of terminal alkynes to acetals[3–5)] (Fig. 1). This method compares well with the earlier procedures catalyzed by Hg,[6,7)] Pd,[8–10)] Pt,[9,11,12)] Au,[13–22)] Ir[23–26)] and Zn.[27)]

The active pentafluorophenylated Co^{III} catalyst **1a** was developed by structural modification of **1b** used previously for alkyne hydration[2)] (Fig. 1). Reaction of tetrakis(pentafluorophenyl)porphyrin (H_2TPFPP) and cobalt(II) acetate[28)] followed by aerobic oxidation in the presence of $HNTf_2$ and recrystallization from a mixture of chloroform, ethanol, and hexane afforded **1a** in 67% yield. X-Ray structural analysis of **1a** indicated that (1) the cobalt center adopts octahedral geometry, with porphyrin ligand in the equatorial positions and ethanol in the apical positions (Fig. 2); (2) the counter anion, Tf_2N^-, is spatially separated from the cobalt center [Figure S2(b)]. The bound ethanol molecules were labile in CD_3OD and free ethanol molecules were observed in the ^{1}H-NMR spectrum [Figure S1(a)].

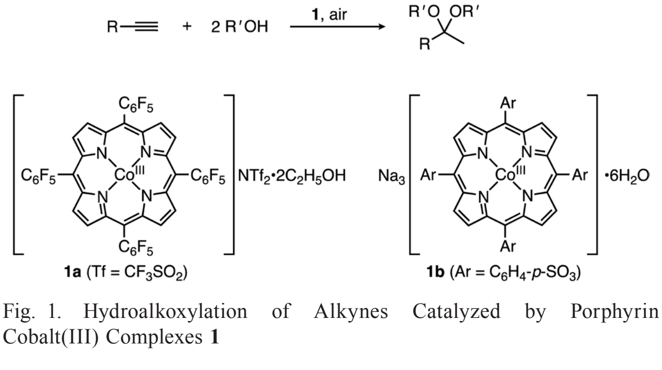

Fig. 1. Hydroalkoxylation of Alkynes Catalyzed by Porphyrin Cobalt(III) Complexes **1**

The catalyst **1a** was found to be more reactive than **1b** in the hydroalkoxylation of phenylacetylene (**2a**) with methanol (Table 1, entries 1 *vs.* 7). When a mixture of **2a** (2.0 mmol), **1a** (0.05 mol%), and $HNTf_2$ (0.18 mol%) in methanol (0.9 mL, 11 equiv) was heated at 70°C for 4 h under aerobic conditions, acetal **3a** was obtained in 97% yield (entry 1).[29)] The initial turnover frequency (TOF) was 4000 h^{-1} (t=12 min). This value is comparable to those of gold catalysts and higher than those of catalysts based on other metals (entry 2).[30)] Hydroalkoxylation of **2a** in the absence of $HNTf_2$ required higher catalyst loading (entries 3 and 4). The reaction proceeded under N_2 atmosphere, but yielded **3a** in a lower yield than that under air (entry 5 *vs.* entry 1). Double hydroalkoxylation of **2a** at 27°C (room temperature) afforded acetal **3a** in 97% yield (entry 6). Co^{III}TPPCl [TPP=5,10,15,20-tetrakis(phenyl)porphyrin] was less reactive than **1a** and **1b** (entry 8 *vs.* entries 1 and 7). The reaction hardly proceeded with analogous metal complexes such as Fe^{III}TPPCl or Mn^{III}TPPCl under otherwise identical conditions (entries 9 and 10).

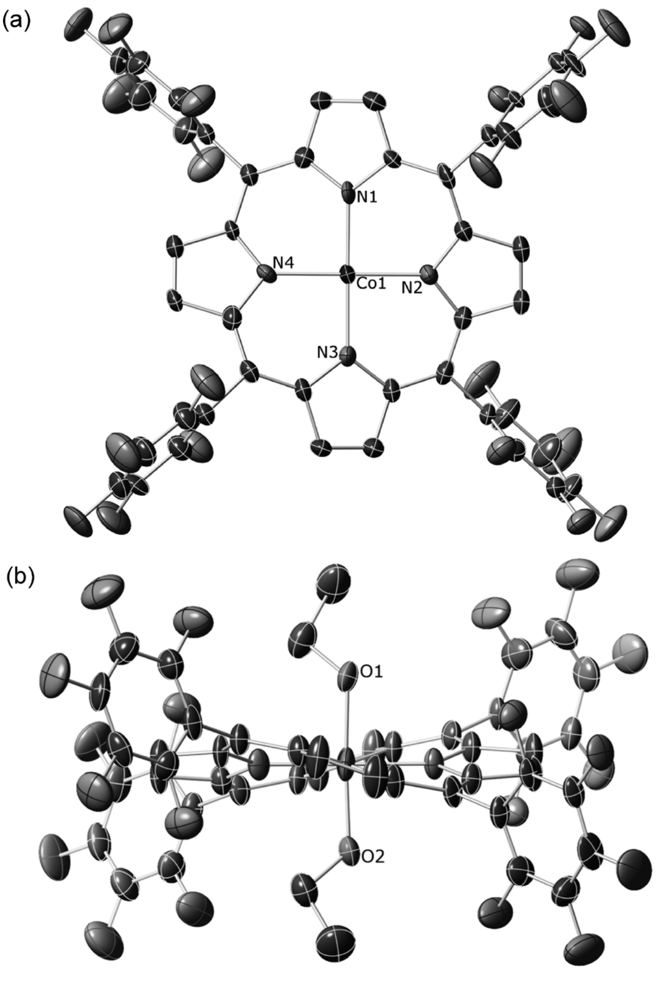

Fig. 2. ORTEP Drawing of **1a**: (a) Top View and (b) Side View

Thermal ellipsoids are drawn at 50% probability. Coordinated ethanol molecules in (a) as well as the counter anion and hydrogen atoms in (a) and (b) are omitted for clarity.

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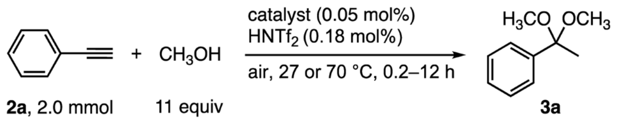
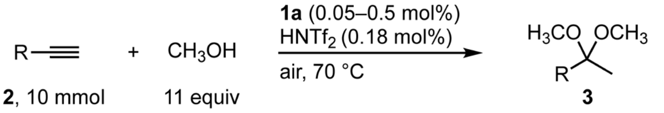
Table 1. Double Hydromethoxylation of Alkynes with Methanol[a]

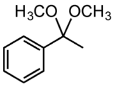
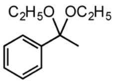
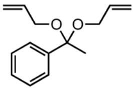
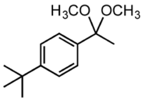
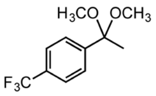
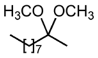
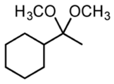
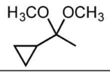


Entry	Catalyst	T (°C)	t (h)	Yield (%)[b]
1	**1a**	70	4	97
2	**1a**	70	0.2	40
3[c]	**1a**	70	4	<2
4[c]	**1a** (0.5 mol%)	70	4	>97
5[d]	**1a**	70	4	84
6	**1a** (0.5 mol%)	27	12	97
7	**1b**	70	4	78
8	Co^{III}TPPCl[e]	70	4	58
9	Fe^{III}TPPCl[e]	70	4	<2
10	Mn^{III}TPPCl[e]	70	4	<2

[a] Conditions: **2a** (2.0 mmol), catalyst (0.05 mol%), HNTf$_2$ (0.18 mol%), CH$_3$OH (0.9 mL, 11 equiv) under aerobic conditions in a closed reaction vessel. [b] Determined by ^{1}H-NMR using mesitylene as an internal standard. [c] In the absence of HNTf$_2$. [d] Under N$_2$ atmosphere. [e] TPP=tetrakis(phenyl)porphyrin.

Table 2. Double Hydromethoxylation of Alkynes Using Co (TPFPP) NTf$_2$·2C$_2$H$_5$OH Complex (**1a**)[a]



Entry	**2**	Acetal (**3**)		**1a** (mol%)	t (h)	Yield (%)[b]
1	**2a**		**3a**	0.05	12	94
2[c,d]	**2a**		**3ab**	0.13	16	67
3[c,d]	**2a**		**3ac**	0.30	16	59
4	**2b**		**3b**	0.05	12	82
5	**2c**		**3c**	0.50	12	96
6[e]	**2d**		**3d**	0.05	24	83
7	**2e**		**3e**	0.25	12	86
8[c]	**2f**		**3f**	0.25	24	76

[a] Conditions: **2** (10 mmol), **1a** (0.05 mol%), CH$_3$OH (4.5 mL, 11 equiv), HNTf$_2$ (0.18 mol%) at 70°C under aerobic conditions in a closed reaction vessel. [b] Isolated yield. [c] In the absence of HNTf$_2$, 50°C. [d] Ethanol (4.5 mL, 7.7 equiv, entry 2) or allyl alcohol (4.5 mL, 6.6 equiv, entry 3) was used instead of methanol. [e] 20 mmol scale.

Other examples of this transformation are listed in Table 2. Reaction of **2a** (10 mmol) with methanol in the presence of **1a** (0.05 mol%) and HNTf$_2$ (0.18 mol%) at 70°C for 12 h under aerobic conditions gave the corresponding acetal **3a** in 94% isolated yield after distillation (Table 2, entry 1). Double hydroalkoxylation of **2a** using ethanol and allyl alcohol gave the corresponding acetals in acceptable yields (entries 2 and 3). Reactions using 2-propanol and *tert*-butyl alcohol were slug-

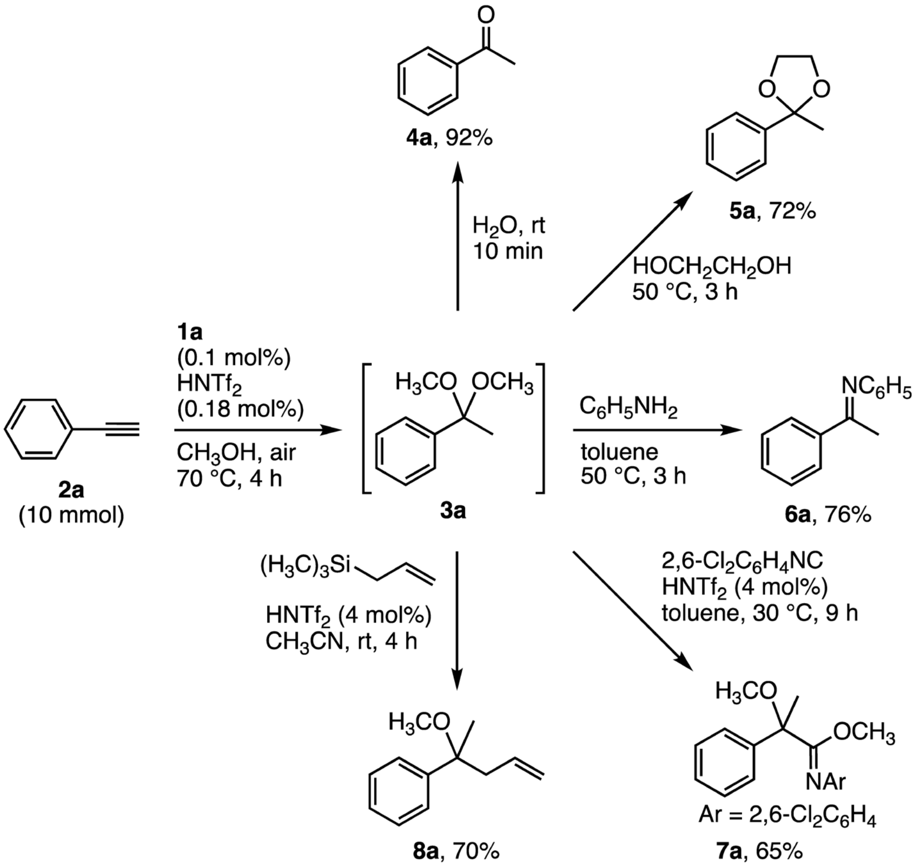


Chart 1.

gish. *t*-Butyl-substituted phenyl acetylene **2b** was as reactive as **2a** (entry 4). Although trifluoromethyl analogue **2c** was less reactive, complete conversion was obtained at 12 h with the use of 0.5 mol% of catalyst **1a** (entry 5). This method was also effective for aliphatic alkynes **2d**–**f** (entries 6–8). Double hydroalkoxylation of **2f** in the absence of $HNTf_2$ proceeded without destruction of the cyclopropyl moiety in **2f**. Unfortunately, the present method was not effective for internal alkynes (*e.g.* diphenylacetylene) or propargylic substrates (*e.g.* propargyl alcohol), as is also the case for alkyne hydration catalyzed by **1b**.[2)]

Next, because acetals are reactive electrophiles,[31–34)] one-pot conversion of *in-situ*-generated acetal **3a** with nucleophiles was examined (Chart 1). Double hydroalkoxylation of alkyne **2a** with methanol using **1a** (0.1 mol%) in the presence of $HNTf_2$ (0.18 mol%), followed by trapping of acetal **3a** with water, ethylene glycol, and aniline, gave the corresponding ketone **4a**, cyclic acetal **5a** and imine **6a**, respectively, in good yields. This stepwise protocol gave better results than the direct addition of these nucleophiles to **2a**. Insertion of arylisonitrile into the C–O linkage of **3a** gave α-methoxyimidate **7a**.[35)] Analogously, Hosomi–Sakurai reaction of acetal **3a** with allyltrimethylsilane afforded ether **8a**.[36,37)] Overall, the present method allowed direct conversion of alkyne to a variety of substituted Markovnikov-type products, using methanol and nucleophiles.

In summary, the cationic cobalt porphyrin complex **1a** was found to catalyze hydroalkoxylation of terminal alkynes to acetals under slightly acidic, aerobic conditions. The acetal intermediates can be directly functionalized with nucleophiles.

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Conflict of Interest The authors declare no conflict of interest.

Supplementary Materials The online version of this article contains supplementary materials: experimental procedures and characterization of **1a**.

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