# Novel Migrating Group in 1,2-Anionotropic Reactions: Cobalt Complexation Facilitates 1,2-Shift of Alkynyl Groups

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It is well documented that an alkyne−Co complex strongly stabilizes a cationic charge at its α-position,[1a] a phenomenon reminiscent of cyclopropylcarbinyl stabilization.[1b] The effect is attributed to the metallacyclopropyl structure of the complex isolobal to tetrahedrane,[2] where participation of the C−Co bond-(s) with the adjacent vacant orbital enables the effective charge delocalization onto the cluster (see canonical forms **A** and **A′**).[1a,2] By analogy, we focused our attention on *the behavior toward the β-positive charge*, with which a cyclopropyl group is known to undergo neighboring group participation, ultimately undergoing a 1,2-shift without ring opening as shown in **B**.[3] The corresponding behavior of the Co complex is unknown; does the alkyne−Co complex behave similarly as shown in **C**? In this communication, we report an affirmative answer to this question: a Co-complexed alkynyl group is an excellent migrator in 1,2-anionotropic reactions.[4] The finding enables the 1,2-shift of alkynyl groups (eq 1), otherwise an unfavorable process,[5,6] to be used to access various stereodefined alkyne-containing building blocks of potentially broad synthetic utility.

(1)
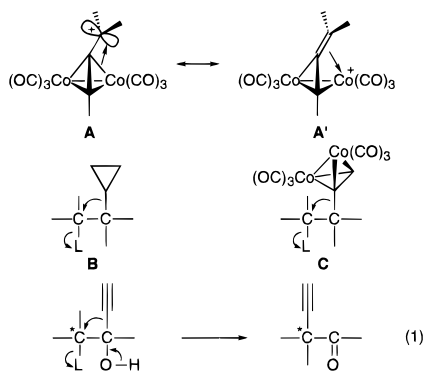
Scheme 1 shows the preliminary experiment that gave the initial promising result of our study. As reported by Wender et al.,[6a] the alkynyl chlorohydrin **1a**[7] remained unchanged when subjected to the conditions for alkoxide-induced 1,2-shift (EtMgBr/benzene, 55 °C, 2 h). In sharp contrast, the corre-

**Scheme 1**

**Table 1.** Me₃Al-Promoted 1,2-Rearrangement of Complexes **3**

| run | R | | product | $T/°C^a$ | yield/% |
|---|---|---|---|---|---|
| 1 | *n*-Bu− | (**3a**) | **4a** | 20 | 78 |
| 2 | Me₃Si− | (**3b**) | **4b** | 0 | 84 |
| 3 | MeOCH₂− | (**3c**) | **4c** | −20 | 80 |
| 4 | H₂C=CMe− | (**3d**) | **4d** | 20 | 58 |

$^a$ At this temperature, each reaction proceeds smoothly, thereby completing within ca. 2 h.

sponding Co complex **3a** underwent clean 1,2-shift to give the ketone **4a** in 61% yield.[8] Oxidative decomplexation gave unstable α-hexynyl ketone **2a** in 99% yield.[8]

When Me₃Al was used as a promoter, the reaction proceeded smoothly at lower temperature, giving the ketone **4a** in high yield (Table 1, run 1).[8,9] Notably, these Lewis acidic conditions did not induce any Nicholas-type alkylation, even though the expulsion of the hydroxyl in **3a** could generate a highly stabilized cationic species.[1a] As can be seen in other runs, the migratory aptitudes of the complexes vary depending on the alkynyl substituent. A silyl or a methoxymethyl group enhances the migratory aptitude,[10] while a propenyl group makes the complex less prone to migrate (run 4).

The migratory aptitude of these complexes proved to be far larger than we expected and, in fact, exceeds that of alkyl (see eq 4) or even aryl groups as shown in eq 2.[11] Competition with a phenyl group (see the reaction of **5a**) gave **6a** as the exclusive product.[8,12,13] Surprisingly, the migratory aptitude of

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(1) (a) For a review, see: Nicholas, K. M. *Acc. Chem. Res.* **1987**, *20*, 207. (b) Olah, G. A.; Reddy, V. P.; Prakash, G. K. *Chem. Rev.* **1992**, *92*, 69 and references cited therein.

(2) (a) Hoffman, D. M.; Hoffmann, R.; Fisel, C. R. *J. Am. Chem. Soc.* **1982**, *104*, 3858 and references cited therein. (b) Schreiber, S. L.; Sammakia, T.; Crowe, W. E. *J. Am. Chem. Soc.* **1986**, *116*, 5505. (c) Schreiber, S. L.; Klimas, M. T.; Sammakia, T. *J. Am. Chem. Soc.* **1987**, *109*, 5749.

(3) For the 1,2-shift of cyclopropyl groups, see: (a) Shono, T.; Fujita, K.; Kumai, S.; Watanabe, T.; Nishiguchi, I. *Tetrahedron Lett.* **1972**, 3249. (b) Shimazaki, M.; Hara, H.; Suzuki, K. *Tetrahedron Lett.* **1989**, *30*, 5443.

(4) For reviews on 1,2-anionotropic reactions, see: (a) Saunders, M.; Chandrasekhar, J.; Schleyer, P. v. R. In *Rearrangement in Ground and Excited States*; Mayo, P. de, Ed.; Academic Press: New York, 1980; Vol. 1, p 1. (b) Shubin, V. G. In *Topics in Current Chemistry*; Rees, C., Ed.; Springer: Berlin, 1984; Vol. 116−117, p 267. (c) Collins, C. J.; Eastham, J. F. *The Chemistry of the Carbonyl Group (The Chemistry of Functional Groups)*; Patai, S., Ed.; Wiley: New York, 1966; Chapter 15, p 761. (d) Bartók, M.; Molnár, A. *The Chemistry of Functional Groups, Supplement E*; Patai, S., Ed.; Wiley: New York, 1980; Chapter 16, p 721. For reviews on pinacol rearrangement, see: (e) Rickborn, B. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3, Chapter 3.2, p 721. (f) Suzuki, K. *J. Synth. Org. Chem., Jpn.* **1988**, *46*, 365.
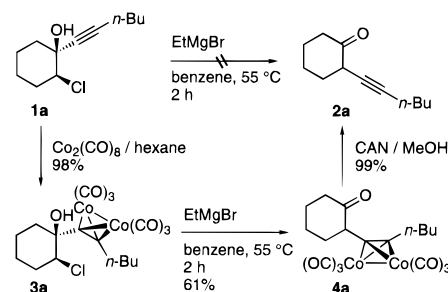
(5) The poor migratory aptitude of an alkynyl group is attributed to the deficiency of its π-electrons to participate to the neighboring cationic species in terms of electronic (the *sp* hybridization) and/or spatial (the linearity) factors. Computational studies showed that the activation energy of the ethynyl shift is larger than, for example, that of the vinyl migration by 10.5 kcal/mol. Nakamura, K.; Osamura, Y. *J. Am. Chem. Soc.* **1993**, *115*, 9112.

(6) (a) Wender, P. A.; Holt, D. A.; Sieburth, S. M. *J. Am. Chem. Soc.* **1983**, *105*, 3348. (b) Suzuki, K.; Ohkuma, T.; Miyazawa, M.; Tsuchihashi, G. *Tetrahedron Lett.* **1986**, *27*, 373. (c) Shoenen, F. J.; Porco, J. A.; Schreiber, S. L.; VanDuyne, G. D.; Clardy, J. *Tetrahedron Lett.* **1989**, *30*, 3765.

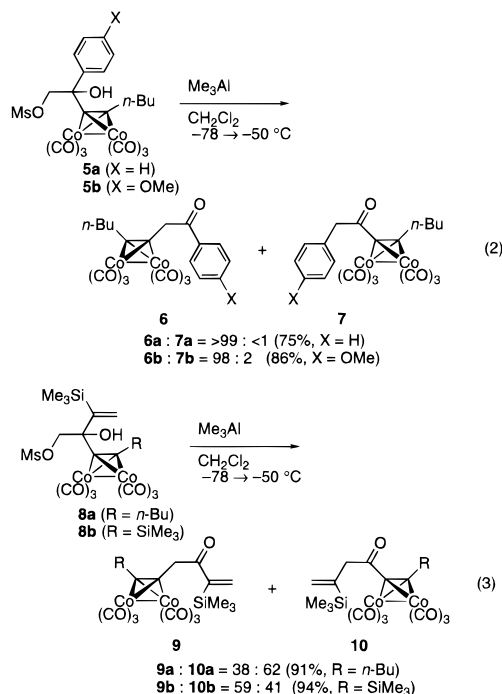(7) For preparation of the chlorohydrins, see supporting information.

(8) All new compounds were fully characterized by spectroscopic means (¹H and ¹³C NMR, IR), high-resolution MS, and/or combustion analysis (see supporting information).

(9) The parent chlorohydrin **1a** did not undergo 1,2-shift even after 2 h reflux in CH₂Cl₂.
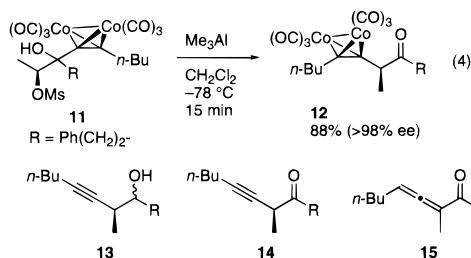
(10) Note that the reactions proceed at lower temperatures in runs 2 and 3. Origin of the substituent effect is under investigation. At present, we assume that the migratory aptitude is enhanced by a substituent that stabilizes a positive charge that would develop at the migrating cluster during the 1,2-shift by analogy with the α-cation stabilization (see **A** and **A′**).

(11) For organoaluminum-promoted 1,2-shift of aryl groups in β-mesyloxy alcohols, see: (a) Suzuki, K.; Katayama, E.; Tsuchihashi, G. *Tetrahedron Lett.* **1983**, *24*, 4997. For a classical example under solvolytic conditions, see: (b) Winstein, S.; Lindegren, C. R.; Marshall, H.; Ingraham, L. L. *J. Am. Chem. Soc.* **1953**, *75*, 147.

the Co complex exceeds that of a *p*-methoxyphenyl group[14] as shown by the predominant formation of **6b** from **5b**. The TMS-substituted vinyl group, which is one of the best migrating groups known,[15] can, however, compete with the Co complex (eq 3).



(2)

**5a** (X = H)
**5b** (X = OMe)

**6a : 7a** = >99 : <1 (75%, X = H)
**6b : 7b** = 98 : 2 (86%, X = OMe)



(3)

**8a** (R = *n*-Bu)
**8b** (R = SiMe₃)

**9a : 10a** = 38 : 62 (91%, R = *n*-Bu)
**9b : 10b** = 59 : 41 (94%, R = SiMe₃)

The stereospecificity of the 1,2-shift should also be noted. (*S*)-Lactate-derived mesylate **11** underwent 1,2-rearrangement to give ketone **12** in enantiomerically pure form (eq 4)[8] as evidenced by analysis of the derived diastereomeric alcohols **13** [(1) DIBAL/toluene, −78 °C, (2) CAN/MeOH].[16] Unfortunately, attempts to obtain the enantiopure ketone **14** were unsuccessful due to the isomerization to allenyl ketone **15**; this isomerization occurred particularly readily upon attempted purification by silica-gel chromatography.



(4)

**11**
R = Ph(CH₂)₂-

**12**
88% (>98% ee)

**13**       **14**       **15**

The process, however, offers a highly useful access to compounds with a quaternary chiral center,[17] which are devoid of such configurational instability. For example, isomeric epoxy silyl ethers **16** and **17** were converted to the corresponding Co complexes and treated with TMSOTf (5 mol %) at −78 °C,[18,19] respectively. The reaction occurred rapidly at this temperature, and workup with CAN gave quaternary aldols **18** and **19** in excellent yields.[20,21] The products showed no trace of the other isomer,[22] thereby further providing evidence for the stereospecificity of the 1,2-shift.



(5)

**16**       **18**
90%



(6)

**17**       **19**
81%

a) Co₂(CO)₈ / hexane, b) TMSOTf (5 mol%) / CH₂Cl₂, −78 °C, 1 h, c) CAN / MeOH

Equation 7 shows a further example, a reductive version of the reaction,[19] that is relevant to the total synthesis of the furaquinocin antibiotics.[23] The 1,2-shift occurred smoothly at −78 °C, and further reaction at an elevated temperature completed the reduction of the aldol formed.



(7)

**20**       **21**
77%

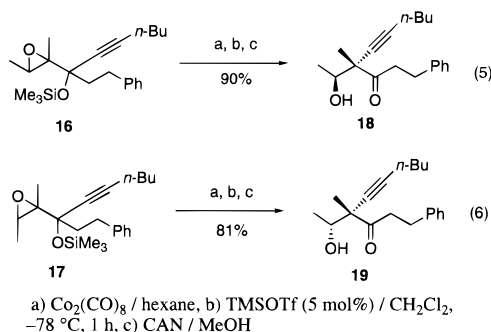a) Co₂(CO)₈ / hexane, b) BF₃•OEt₂, Et₃SiH / CH₂Cl₂, −78 → −20 °C, 1 h, c) CAN / MeOH

(12) Me₃Al serves as a Lewis acid to activate the mesylate and also as a captor of methanesulfonic acid. For these aspects in general, see: Suzuki, K.; Tomooka, K.; Tsuchihashi, G. *Tetrahedron Lett.* **1984**, *25*, 4253; Suzuki, K.; Tomooka, K.; Shimazaki, M.; Tsuchihashi, G. *Tetrahedron Lett.* **1985**, *26*, 4781. One of the referees pointed out the possible intermediacy of an epoxide. Under these conditions, however, epoxide formation is rarely observed and limited to the case where poor migrating groups like an alkyl are concerned. To test the behavior of a relevant epoxide under the reaction conditions, mesylate **5a** was treated with a base, e.g. KH, thereby giving, however, a complex mixture of products. The epoxide, obtained in 2−3% yield, was not converted to **6a** even when treated with Me₃Al. It is also a significant point to note that, stereochemically, the 1,2-shift of mesyloxy alcohols proceeds with inversion (*cf.* double inversion for the epoxide mechanism).

(13) In the reaction of the noncomplexed congener of **5a**, the 1,2-shift of the phenyl group prevailed over that of the 1-hexynyl group (selectivity: 9/1). Since the reaction only occurred at 20 °C, the carbonyls in the products were thoroughly methylated (96% combined yield).
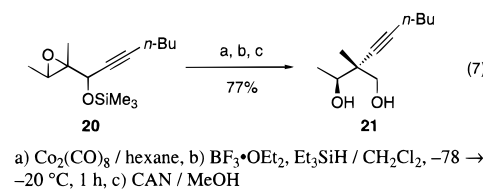
(14) The migratory aptitude of the *p*-methoxyphenyl group is reportedly 500 times higher than that of the phenyl group in pinacol rearrangement. Acheson, R. M. *Acc. Chem. Res.* **1971**, 4, 177.

(15) (a) Suzuki, K.; Katayama, E.; Tsuchihashi, G. *Tetrahedron Lett.* **1984**, *25*, 1817. (b) Suzuki, K.; Tomooka, K.; Katayama, E.; Matsumoto, T.; Tsuchihashi, G. *J. Am. Chem. Soc.* **1986**, *108*, 5221.

(16) A 1/1 diastereomeric mixture. For the ee analysis by chiral capillary GC, see supporting information.

(17) For a review, see Martin, S. F. *Tetrahedron* **1980**, *36*, 419.

(18) For stereospecific synthesis of α,α-disubstituted aldols via epoxy silyl ether (epoxy alcohol) rearrangements, see: Shimazaki, M.; Hara, H.; Suzuki, K.; Tsuchihashi, G. *Tetrahedron Lett.* **1987**, *28*, 5891. For review, see ref 6f. See also: (a) Maruoka, K.; Hasegawa, M.; Yamamoto, H.; Suzuki, K.; Shimazaki, M.; Tsuchihashi, G. *J. Am. Chem. Soc.* **1986**, *108*, 3827. (c) Suzuki, K.; Miyazawa, M.; Tsuchihashi, G. *Tetrahedron Lett.* **1987**, *28*, 3515. (d) Suzuki, K.; Miyazawa, M.; Shimazaki, M.; Tsuchihashi, G. *Tetrahedron* **1988**, *44*, 4061.

(19) Silyl ethers **16**, **17**, **20** are epimeric mixture with respect to the *tert*- or *sec*-siloxy substituted carbon. No noticeable difference in the reactivity was seen for the epimers.

(20) For the stereostructure of aldols **18** and **19**, see supporting information.

(21) Parent epoxide **16** underwent 1,2-shift (10 mol % TMSOTf/CH₂-Cl₂, 25 °C), which, however, was hardly reproducible due to the retro-aldol reaction, giving rise to varying amount of racemic ketone **14**. Such a situation was even more the case for isomer **17**, and none of **19** was obtained.

(22) Diastereomeric purity was >98% for **18** and **19**, respectively, as proven by ¹H NMR (C₆D₆). Diagnostic signals appear at δ 4.13 (dq) for **18** and at δ 3.97 (q) for **19**. It should be noted that partial isomerization (**18** → **19** and *vice versa*) occurs upon prolonged exposure to silica gel.

(23) Saito, T.; Morimoto, M.; Akiyama, C.; Matsumoto, T.; Suzuki, K. *J. Am. Chem. Soc.* **1995**, *117*, 10757.