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Divergent Behavior of Cobalt-Complexed Enyne Having a Leaving Group

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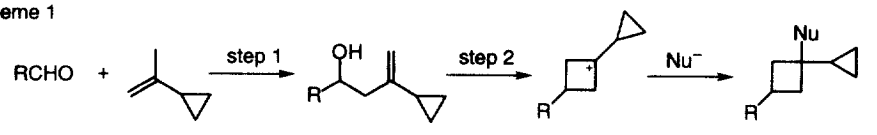
Abstract: Behavior of the compounds **2** with a Co-complexed enyne moiety was examined. When R in **2** was a *prim*-alkyl group, the cyclization to give a cyclobutane proceeded in high yield, whereas, when R was bulkier, an interesting substitution involving a 1,2-shift was observed.

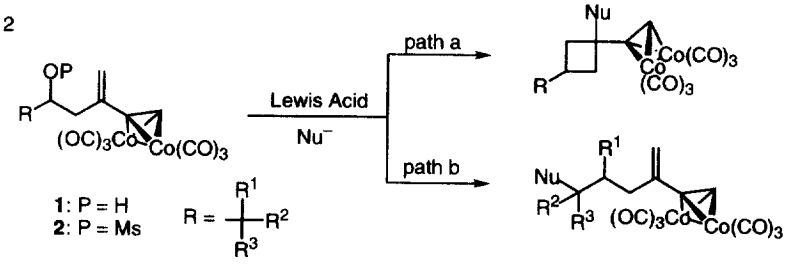
We previously reported a [3+1] synthetic route to cyclobutane derivatives via two steps, *i.e.*, (1) the carbonyl-ene reaction, (2) the cyclobutane cyclization (Scheme 1).[1] Both of these processes are facilitated by the presence of a cyclopropyl group, which strongly promotes the development of the α-cation.[2] By the analogy that a Co-complexed alkynyl group also exhibits a similar strong cation-stabilizing ability,[3, 4] we became interested in applying the same chemistry to a cobalt-complexed conjugated enynyl system.

Scheme 1



The outcome for the step 1 has been already described:[5] [2-methyl-1-buten-3-yne]dicobalt hexacarbonyl serves as a good ene donor in the Me_2AlCl-promoted carbonyl-ene reaction to give alcohol **1**. The behavior of the derived mesylate **2** under Lewis acidic conditions was then studied, which is described in this communication. The results are summarized in Scheme 2. When R in **2** was a *prim*-alkyl group, the cyclobutane cyclization proceeded in high yield (path a) in the same manner as that of the cyclopropyl case (vide supra), whereas, when R was bulkier, an interesting substitution reaction involving a 1,2-shift was observed (path b).

Scheme 2



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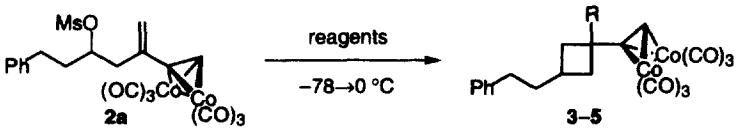
The primary case: When R was a *prim*-alkyl group, the Lewis acid-promoted cyclobutane cyclization proceeded in high yield (Table 1).[6, 7] Treatment of the mesylate **2a** with Me_3Al (toluene, –78 °C → 0 °C, 40 min) gave cyclobutane **3** as a diastereomeric mixture[8, 9] via the sequential cyclization and methylation (run 1). Similarly, the reaction of **2a** with allylsilane (run 2) or triethylsilane (run 3) in the presence of $TiCl_4$ gave the cyclobutanes **4** and **5**, respectively.[8]

Table 1

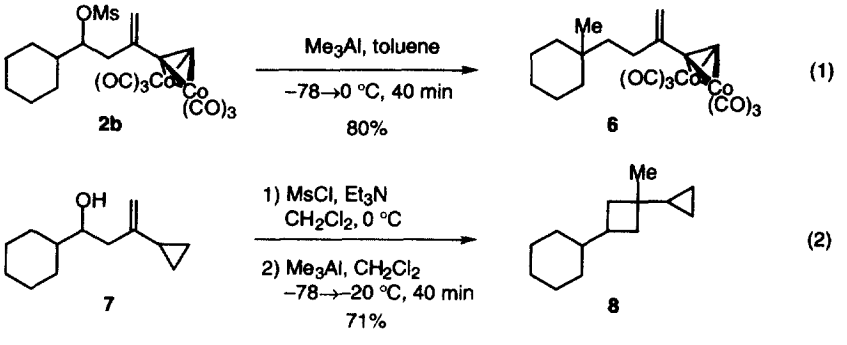


2a **3–5**

Run	Reagents	Conditions	Product	R	Yield/% (*trans/cis*)
1	Me_3Al	toluene, 40 min	**3**	Me	86 (71/29)[a]
2	 $SiMe_3$, $TiCl_4$	CH_2Cl_2, 2 h	**4**		84 (61/39)[b]
3	Et_3SiH, $TiCl_4$	CH_2Cl_2, 2 h	**5**	H	59 (60/40)[a]

a) For structure assignment, see ref. 9; b) Relative configuration unassigned; the ratio may be reversed.

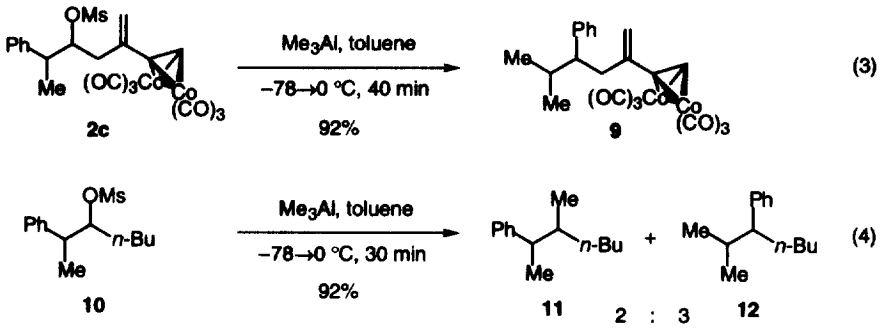
The sec- and tert-cases: When R in **2** was bulkier (R = *sec*- or *tert*-alkyl), totally different results were obtained. Treatment of **2b** with Me_3Al gave a single product (eq. 1), which, amazingly, proved to be **6**[7] *possessing a methyl group on the cyclohexane ring!*[10] This outcome could be rationalized by (1) departure of the mesylate facilitated by Me_3Al,[6] (2) 1,2-shift of a hydride on the cyclohexane ring, and (3) trapping of the *tert*-cationic center by Me_3Al.



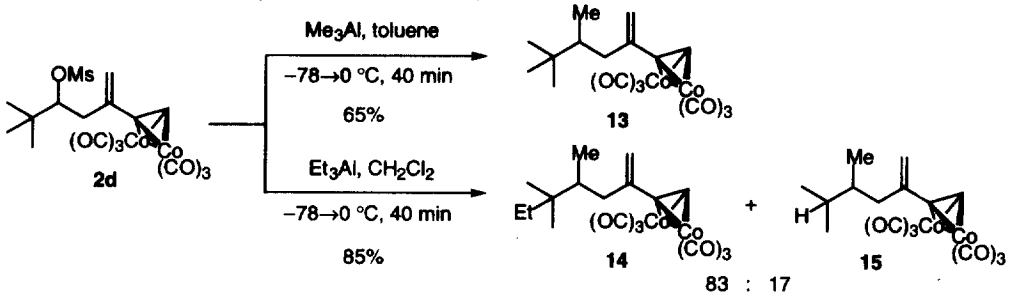
2b **6** **7** **8**

In sharp contrast, the corresponding cyclopropyl compound **7**, upon conversion to the mesylate and the treatment with Me_3Al, gave the cyclobutane **8** as shown in eq. 2 (N.B. Although our previous report has dealt with the *prim*-substrates, the cyclization turned out to be the sole event observed also for a *sec*-substrate).

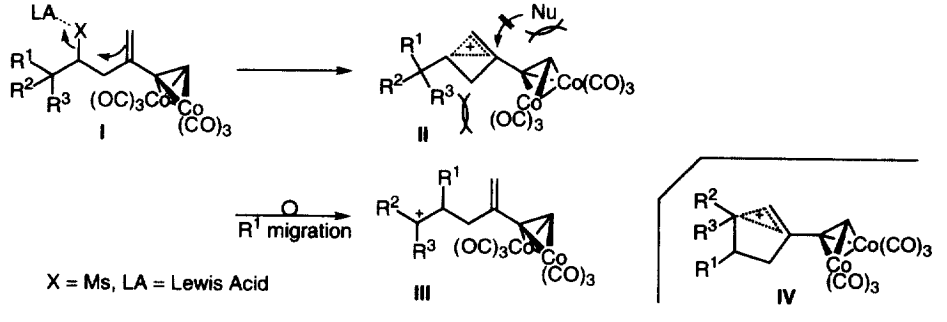
In further study on other related Co-complexes, the migration–alkylation was observed. For example, **2c** that has an even better migrating group (phenyl) was converted to the product **9** (eq. 3).[7, 11] A characteristic feature common to the processes (eqs. 1 and 3) is that the attack of an external nucleophile occurs only *after* the 1,2-shift. It was not clear at this stage whether the Co-containing moiety was essential for such a reaction course to be followed. However, it has been proven necessary, since the reaction of the substrate **10** lacking such a group only gave a mixture of **11** and **12**, arising from the methylation with/without the 1,2-shift (eq. 4).



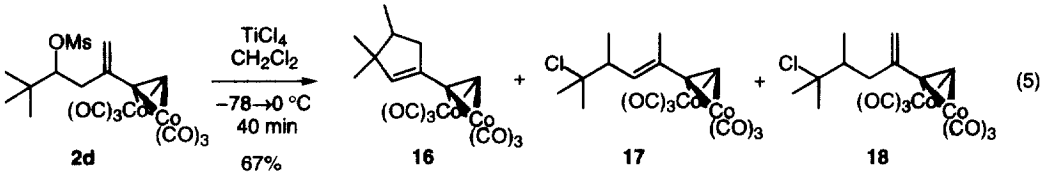
The reaction pattern was valid also for a more substituted system, even provoking an alkyl migration. The reaction of *t*-butyl substrate **2d** with Me_3Al gave the product **13**,[7] although it was not evident whether a 1,2-shift occurred or not. However, the reaction with Et_3Al clearly showed that the 1,2-shift was involved, as the product was **14**,[7] arising from a sequence of the 1,2-shift of a methyl group and the ethylation. The minor product **15**[7] with a terminal *i*-propyl group should share the mechanism with **14**, except for the final stage, *i.e.*, the β-hydride delivery from Et_3Al, rather than the ethylation.



A plausible rationale for this migratory alkylation follows. Although the departure of the mesylate is assisted by the neighboring group participation to form a delocalized cationic species as **II**, which, however, could not undergo the direct trapping by a nucleophile because of the high steric constraint around the four-membered ring posed by the two large substituents (cf. eq. 2; a smaller steric demand of a cyclopropyl in comparison with a Co-complexed alkynyl). Thus, instead, the species **II** undergoes a 1,2-shift of R^1 to generate the cationic species **III** (maybe better drawn as a delocalized form **IV**), which eventually undergoes the trapping by a nucleophile.



An interesting relevant observation was made when we employed $TiCl_4$, a Lewis acid without alkylation ability. Treatment of **2d** with $TiCl_4$ gave the *cyclopentene* **16** as the major product along with the olefins **17**[12] and **18** (eq. 5).[7] It should be noted that formation of all these products is explained by the 1,2-shift of a methyl group. The cyclization to a five-membered ring suggests the contribution of such a species as **IV**, at least partially.



Typical procedure is described for the synthesis of **6**: To a solution of **2b** (62.3 mg, 0.115 mmol) in toluene (2 mL) was slowly added a solution of Me_3Al in hexane (1.0 M, 0.18 mL, 0.18 mmol) at −78 °C. The reaction mixture was warmed to 0 °C during 40 min with stirring. The reaction was quenched by adding saturated aqueous Na_2SO_4. The products were extracted with EtOAc (×3), and the combined extracts were washed with brine and dried over anhydrous Na_2SO_4. Purification with preparative TLC (hexane) gave **6**[10] (42.3 mg, 80%) as a dark brown oil.

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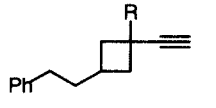
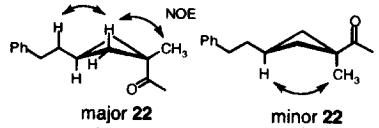
References and Notes

1. Nagasawa, T.; Suzuki, K. *Synlett* **1993**, 29.
2. Olah, G. A.; Prakash Reddy, V.; Surya Prakash, G. K. *Chem. Rev* **1992**, *92*, 69.
3. Nicholas, K. M. *Acc. Chem. Res.* **1987**, *20*, 207.
4. For the extension of this idea, see Nagasawa, T.; Taya, K.; Kitamura, M.; Suzuki, K. *J. Am. Chem. Soc.* **1996**, *118*, 8949; Taya, K.; Nagasawa, T.; Suzuki, K. *Synlett* **1997**, 304.
5. Nagasawa, T.; Kitamura, M.; Suzuki, K. *Synlett* **1995**, 1183.
6. For the activation of sulfonate esters with R_3Al, see Maruoka, K.; Miyazaki, T.; Ando, M.; Matsumura, Y.; Sakane, S.; Hattori, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1983**, *105*, 2831; Suzuki, K.; Tomooka, K.; Katayama, E.; Matsumoto, T.; Tsuchihashi, G. *J. Am. Chem. Soc.* **1986**, *108*, 5221.
7. All new compounds were fully characterized by ^1H NMR, ^{13}C NMR, IR, and HRMS and/or combustion analysis.
8. Oxidative decomplexation of **3**–**5** (CAN, MeOH, room temperature) gave the corresponding alkynes **19**–**21** in high yields.



	R	Yield/%
19	Me	92
20	$CH_2CH{=}CH_2$	94
21	H	92

9. The relative configuration of **3** was assigned by the NOE experiments, after conversion to methyl ketone **22** (**19**→**22**: HgO, aq. H_2SO_4). The stereochemistry of **5** was similarly assigned.



10. The structure of **6** was determined by the analysis of ^1H NMR, ^{13}C NMR, DEPT, H-H COSY, HMQC and HMBC.
11. The diastereomers of **2c**, separable by silica-gel preparative TLC, showed essentially the same reactivities in this reaction. Unfortunately, their relative configurations could not be assigned.
12. Formation of **17** could be rationalized by the isomerization of **18** caused by the protic acid produced by the formation of **16**. The (*E*)-geometry was assigned by the NOE experiment.