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Allenes as New Partners In Intramolecular Cobalt-Mediated [2+2+2] Cycloaddition Reactions.

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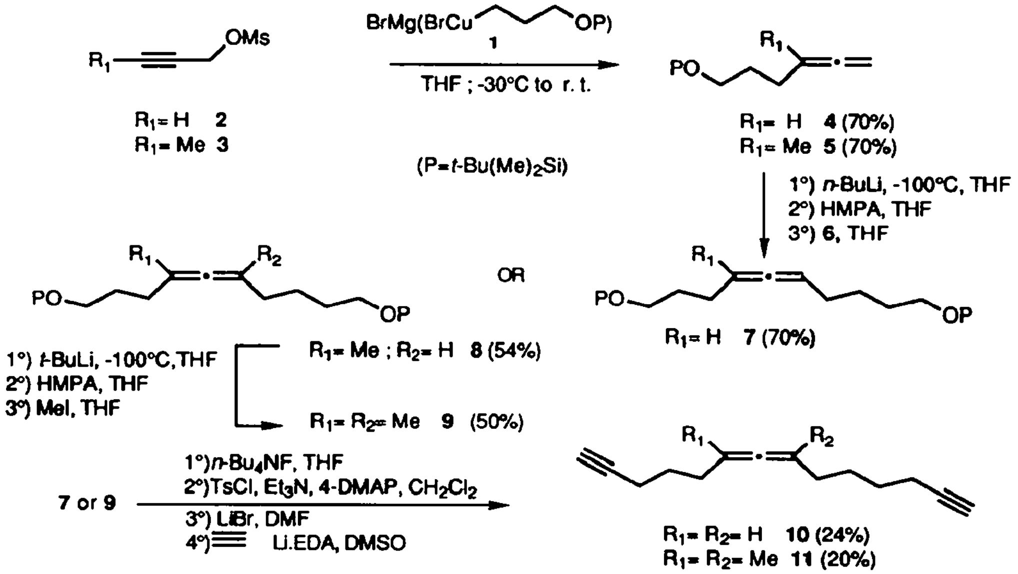
Abstract : *For the first time, allenes were involved in cobalt-mediated [2+2+2] cycloaddition reactions. The η^4–cobalt complexes were isolated. Decomplexation on silica gel led to the corresponding free ligands.*

Inter- and intramolecular cobalt-mediated [2+2+2] cycloaddition reactions of linear achiral enediynes containing di-, tri-, or tetrasubstituted double bonds have been well described by Vollhardt *et al.*.[1] Remarkable selectivity and high yields have been observed and have allowed the synthesis of a range of polycyclic natural products.[2]

In this connection, allenes might be very promising new unsaturated partners in the cobalt-catalyzed [2+2+2] cycloaddition reactions. Despite allenes are known to be good ligands in organometallic complexes,[3] only one example involving allenes in [2+2+2] cycloadditions catalyzed with nickel(II) as catalyst has been reported.[4]

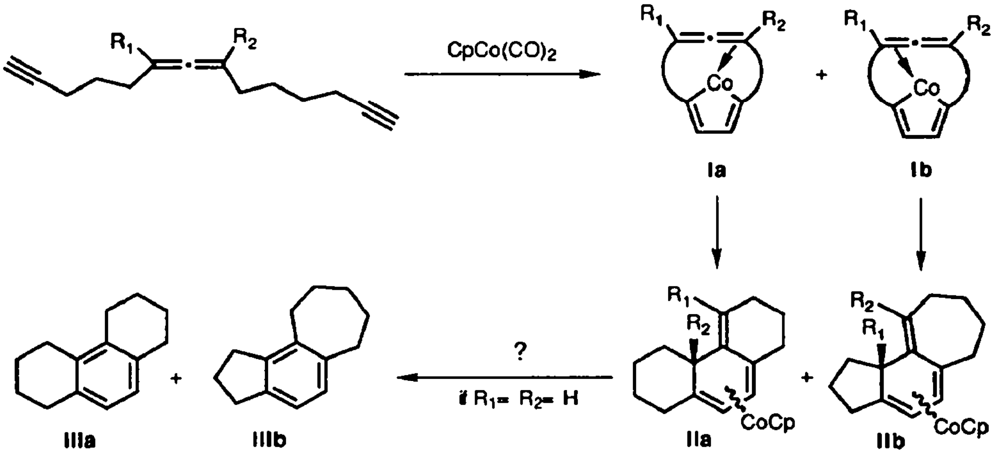
In order to explore the scope of such a cycloaddition, a rapid access to some allenediynes was envisaged. Here, we present their synthesis and the results of their cobalt-mediated cyclization. Their straightforward preparation is outlined in Scheme 1.



Scheme 1

The reaction between the organocopper reagent **1** and the propargylic mesylates **2** and **3** in THF provided the allene educts **4** and **5** in 70 % yield. These were lithiated in THF at -100°C using *n*-butyllithium. Reaction with 1-(*tert*-butyldimethylsilyl)-4-iodo-1-butanol **6** in the presence of HMPA (20 equiv) gave di- and trisubstituted allenes **7** and **8** in 70 % and 54 % yield respectively. Deprotonation of **8** at -100°C with *tert*-butyllithium, followed by alkylation with MeI in the presence of HMPA led to the tetrasubstituted allene **9** (50 %).[6] Compounds **7** and **9** were converted into the corresponding diols which were subsequently tosylated and brominated.[1c] The reaction of the dibromides with lithium acetylide-ethylenediamine complex in DMSO[7] achieved the synthesis of the allenediynes **10** and **11** in 24 % and 20 % yield from **7** and **9**.

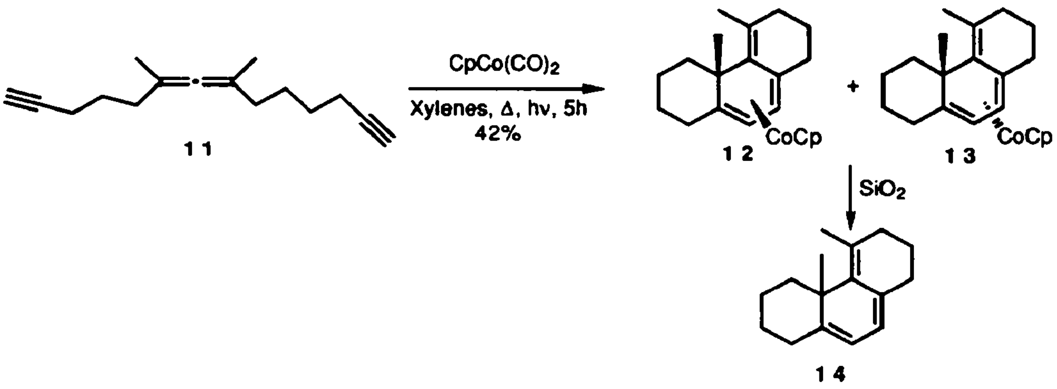
The cyclizations were carried out under standard conditions.[1] Based on the results of intramolecular cyclizations of the enediynes[1] with (η^5-cyclopentadienyl)cobalt dicarbonyl [$CpCo(CO)_2$], two cobaltacyclopentadienyl intermediates $\mathbf{I_a}$ and $\mathbf{I_b}$ could be considered (Scheme 2). When $R_1 = R_2 = H$, *a priori*, a 1,3-migration of hydrogen would have been expected to afford aromatic stable structures $\mathbf{III_a}$, $\mathbf{III_b}$ and the regeneration of the cyclopentadienyl moiety, suggesting that the process may turn out to be catalytic.



Scheme 2

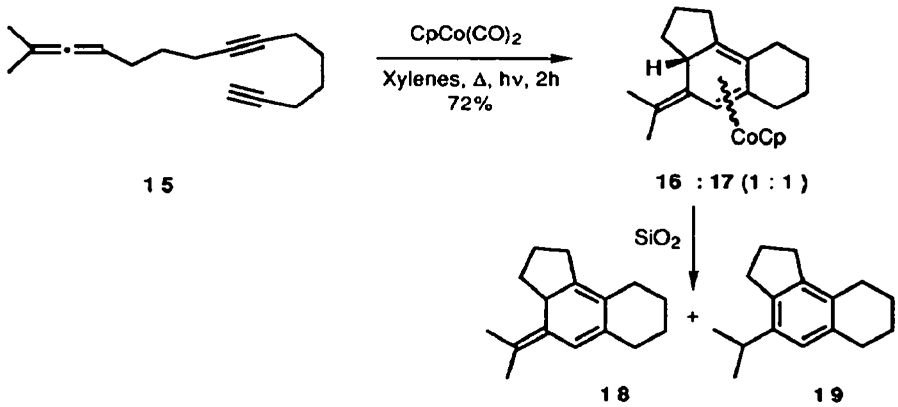
No significant evolution was noticed when a catalytic amount of $CpCo(CO)_2$ was used in boiling xylenes under irradiation. However, with one equivalent of $CpCo(CO)_2$, the allenediyne **10** ($R_1 = R_2 = H$) was consumed. Neither the cobalt complexes nor the decomplexated structures were isolated, only untractable materials were formed. We anticipated that the sensitivity of the diene to uncontrolled rerrangement was at the origin of polymerization.

Gratifyingly, exposure of **11** to a stoichiometric amount of $CpCo(CO)_2$ in boiling xylenes under irradiation for 5 hours furnished red-brown complexes in 42 % isolated yield. A 7 : 3 mixture of two diastereomers **12** and **13** was obtained.[8] The ^{1}H and ^{13}C-NMR spectra were consistent with two structures of II_a type meaning that the selectivity was in favor of the thermodynamically most stable products (Scheme 3). Particularly, their assignments were based on the characteristic chemical shifts[1b] of the dienic, cyclopentadienyl and methyl hydrogens. The major isomer **12** exhibited two doublets at 5.11 and 5.27 ppm with a coupling constant of 3.8 Hz and three singlets at 4.60, 1.72 and 1.62 ppm. Free ligand **14** was formed from the mixture of **12** and **13** on filtration through silica gel. Triene **14** turned to be very oxygen-sensitive as had already been observed in the case of the diene resulting from the intramolecular tetrasubstituted enediynes cyclization.[1c]



Scheme 3

Similarly, the trisubstituted allenediyne **15** was cyclized under the same conditions as described for compound **11** to provide a 1 : 1 mixture of two diastereomers **16** and **17** in 72 % isolated yield (Scheme 4). Decomplexation on silica gel gave an unseparable mixture of tricyclic compounds **18** and **19** ; **19** resulting from a partial aromatization.



Scheme 4

In summary, we have shown that allenes are new partners in cobalt-mediated [2+2+2] cycloaddition reactions. Allenediynes cyclizations are of great interest for synthetic purposes since free ligands may be regarded as constituting the BCD- and ABC-portions of steroids with an angular methyl group at the AB ring junction. Thus, we are currently investigating an approach to corticosteroids from suitable substituted alkoxyallenediynes. Finally, we are considering the ability of transfering axial allenic chirality into a centered one.

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(8) **Typical procedure for the cyclization of 11:** The reaction was carried out under argon in a flame-dried flask and xylenes were degassed by three freeze-pump-thaw cycles. $CpCo(CO)_2$ (1mmol ; 125 µl) was added to a solution of **11** (1 mmol ; 214 mg) in boiling xylenes (10 mL) ; the resulting solution was refluxed and irradiated (projector lamp ELW 300W, 70 % of its power) over 5h, at which point TLC indicated that the starting material had been consumed. The solvent was removed by vacuum transfer. The crude mixture was chromatographed on alumina (activity III) under argon with degassed pentane as eluent affording **12** and **13** as a 7 : 3 mixture of diastereoisomers (142 mg ; 42 %). ^{1}H and ^{13}C-NMR spectral data for the major isomer **12** : ^{1}H-NMR (400 MHZ ; C_6D_6) δ 5.11 (d, 1H, J = 3.8 Hz), 4.60 (s, 5H), 4.27 (d, 1H, J = 3.8 Hz), 2.22-2.16 (m, 2H), 2.10-1.45 (m, 8H), 1.72 (s, 3H), 1.62 (s, 3H), 1.28-1.16 (m, 2H), 1.11-1.01(m, 2H) ; ^{13}C-NMR (100 MHZ, C_6D_6) δ 141.6, 125.5, 81.2, 79.0, 76.2, 73.9, 70.7, 56.6, 37.5, 36.5, 35.3, 31.8, 28.2, 26.0, 25.1, 24.2, 21.5.

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