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# Formal [6+4] cycloaddition of a dicobalt acetylene complex with furan derivatives

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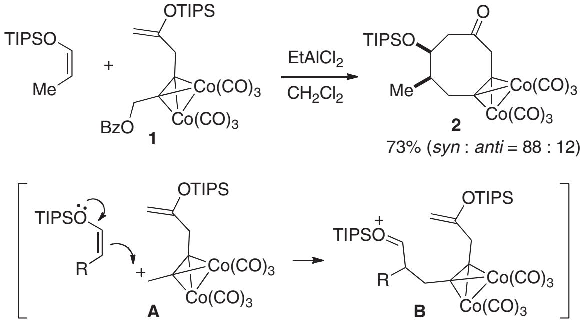
## ABSTRACT

An efficient method for constructing a 10-membered carbocycle with an oxygen bridge has been developed on the basis of a formal [6+4] cycloaddition reaction. Under the influence of $EtAlCl_2$, a dicobalt hexacarbonyl acetylene complex possessing a benzoyloxy group and an allylsilane moiety reacted with furan to give a 11-oxabicyclo[6.2.1]undec-9-ene derivative. On treatment with iodine, the cycloadduct underwent decomplexation followed by rearrangement of the oxygen bridge to afford a 11-oxabicyclo[5.3.1]undeca-1,5-diene derivative.

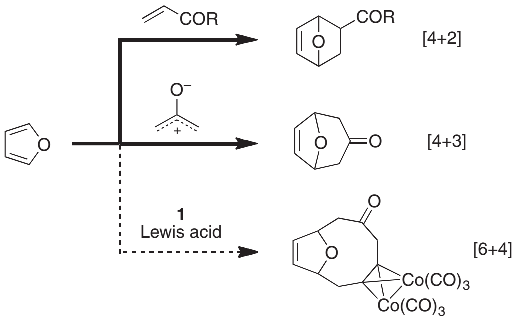
The development of a new synthetic method for medium-sized carbocyclic compounds has been one of the most challenging subjects in organic chemistry.[1] While the ring closing metathesis of various dienes has found wide use for this purpose,[2] a cycloaddition approach which produces two C–C bonds in one-stage is advantageous from the viewpoint of efficiency.[3] Recently, we have reported a novel method for constructing an eight-membered carbocycle via a formal [6+2] cycloaddition reaction using dicobalt acetylene complex **1** as a six-carbon unit (Scheme 1).[4,5]



**Scheme 1.** Formal [6+2] cycloaddition reaction of dicobalt acetylene complex **1** with an enol silyl ether.

The reaction proceeds through intermolecular addition of an enol triisopropylsilyl (TIPS) ether to the dicobalt propargyl cation **A** giving rise to the silyloxonium ion **B** which in turn undergoes an intramolecular addition reaction. In this transformation, the large bond angles of the dicobalt acetylene complex moiety[6] were effective to avoid the formation of a six-membered ring via an intramolecular cyclization reaction of the cation intermediate **A**.

On the other hand, furan derivatives are employed as a four-carbon unit in a Diels–Alder reaction[7] or a [4+3] cycloaddition reaction with a 2-oxyallyl cation species[8] (Scheme 2).



**Scheme 2.** Cycloaddition reactions of furan.

While these cycloaddition reactions of furan may proceed through the concerted mechanisms,[9] we became intrigued with the possibility of a formal [6+4] cycloaddition reaction with dicobalt acetylene complex **1** via a stepwise pathway similar to that shown in Scheme 1.

Initially, the reaction of six-carbon unit **1** with furan was examined under the influence of $EtAlCl_2$ (Scheme 3). While a rather complex mixture was formed, the desired cycloadduct **3** having a

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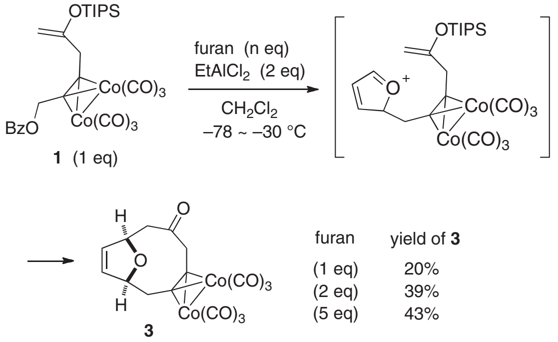
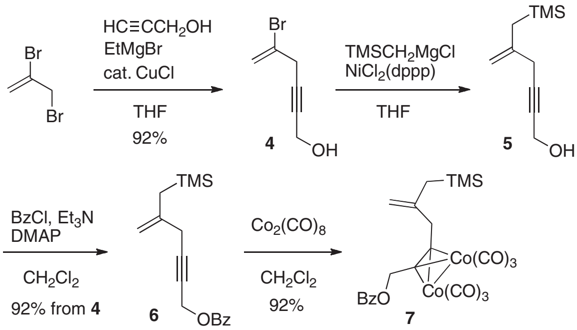


**Scheme 3.** Formal [6+4] cycloaddition reaction of dicobalt acetylene complex **1** with furan.



**Scheme 4.** Synthesis of new six-carbon unit **7**.

11-oxabicyclo[6.2.1]undec-9-ene skeleton[10] was isolated in 20% yield. The use of an excess amount of furan led to an increase in yield up to 43%, suggesting that furan is not nucleophilic enough to undergo faster addition with the dicobalt propargyl cation (**A** in Scheme 1) than another molecule of **1** possessing an enol silyl ether moiety.

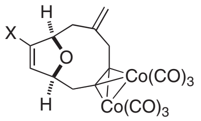
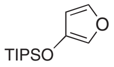
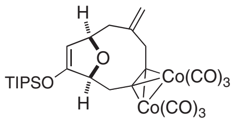
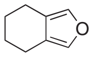
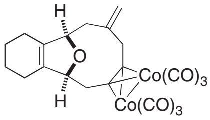
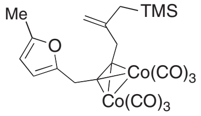
These results led us to design a new six-carbon unit with slightly reduced nucleophilicity, and allylsilane derivative **7** was prepared as shown in Scheme 4. The copper-catalyzed coupling reaction[11] between propargyl alcohol and 2,3-dibromopropene afforded vinyl bromide **4** which in turn was subjected to the Kumada coupling reaction[12] with Me$_3$SiCH$_2$MgCl. The resulting propargyl alcohol **5** was converted to the six-carbon unit **7** through benzoylation followed by treatment with Co$_2$(CO)$_8$ in high overall yield.

With the new six-carbon unit **7** in hand, the formal [6+4] cycloaddition reactions with furan and substituted furans were explored (Table 1). As expected, allylsilane **7** reacted with furan more cleanly than enol silyl ether **1**, and cycloadduct **8a** was obtained in 77% yield (entry 1). Similarly, the reactions of **7** with 3-methylfuran, 3-bromofuran, and 3-(phenylthio)furan afforded the corresponding cycloadducts **8b**, **8c**, and **8d**, respectively (entries 2–4). Since the formal [6+4] cycloaddition reaction proceeds by a stepwise mechanism, the regioselective formation of these cycloadducts stemmed from initial addition of the dicobalt propargyl cation at the less hindered C5 position of 3-substituted furan derivatives. In contrast, the reversal of regioselectivity was observed in the reaction with 3-(triisopropylsilyloxy)furan (entry 5).[13] The exceptional result can be rationalized by the strong electron donating effect of the silyloxy group to enhance the initial addition at the C2 position. While 3,4-tetramethylenefuran also underwent the formal cycloaddition reaction giving rise to tricyclic compound **10** in moderate yield (entry 6), 2-methylfuran failed to give the desired product (entry 7). Formation of 2,5-disubstituted furan **11** having an allylsilane moiety suggests that the cyclization step of the cationic intermediate suffered from steric hindrance at the C5 position.

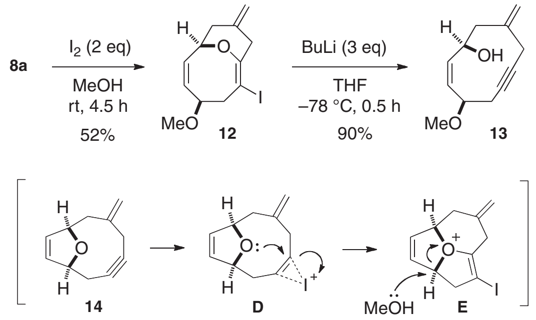
Next, we explored the transformation of the cycloadducts into the corresponding acetylenes by oxidative decomplexation.[14] While the reaction of **8a** with ceric ammonium nitrate (CAN) merely gave a complex mixture, an unexpected product **12** having a 11-oxabicyclo[5.3.1]-undeca-1,5-diene skeleton[15] was obtained by the use of iodine in methanol (Scheme 5). Treatment of the resulting iodide **12** with butyllithium induced cleavage of the oxygen bridge, and 10-membered acetylene **13** was produced in high yield.

The formation of compound **12** can be explained by assuming tricyclic oxonium ion intermediate **E**.[16] Thus, decomplexation of **8a** affords strained nine-membered acetylene **14** with a highly reactive nature toward addition reactions. Subsequently, **14** would undergo addition with iodine to form epiiodonium ion **D** that is converted to tricyclic oxonium ion **E** through participation of the

**Table 1**
Formal [6+4] cycloaddition reactions of dicobalt acetylene complex **7** with furan derivatives[a]

| Entry | Furan derivative | Product | | Yield[b] |
|---|---|---|---|---|
| 1 | Furan |  | **8a** (X = H) | 77% |
| 2 | 3-Methylfuran | | **8b** (X = Me) | 85% |
| 3 | 3-Bromofuran | | **8c** (X = Br) | 78% |
| 4 | 3-(Phenylthio)furan | | **8d** (X = PhS) | 79% |
| 5 |  |  | 9 | 83% |
| 6 |  |  | 10 | 47% |
| 7 | 2-Methylfuran |  | 11 | 45% |

[a] Typical reaction conditions: six-carbon unit **7** (0.5 mmol), furan (2.5 mmol), EtAlCl$_2$ (1.1 mmol), CH$_2$Cl$_2$ (2.5 mL), −20 °C to 0 °C.
[b] Isolated yield.



**Scheme 5.** Novel decomplexation reaction of cycloadduct **8a** mediated by iodine.

oxygen bridge. While oxonium ion **E** possesses two reactive allylic carbon atoms to be attacked by a nucleophile, regioselective introduction of methanol occurs so as to effect maximum relief of ring strain in the 1-oxabicyclo[3.3.0]octan-2,6-diene substructure.[17]

In summary, we have developed an efficient method for constructing a 10-membered carbocycle with an oxygen bridge via a formal [6+4] cycloaddition reaction. Under the influence of $EtAlCl_2$, dicobalt acetylene complex **7** possessing an allylsilane moiety reacted with a furan derivative to afford a 11-oxabicyclo[6.2.1]undec-9-ene derivative. The product can be transformed into 10-membered acetylene through a novel decomplexation reaction mediated by iodine. It is noteworthy that a 11-oxabicyclo[6.2.1]undecane skeleton is widely found as a substructure of natural products (e.g., oxygenated germacrane sesquiterpenoids and cladiellin diterpenoids).[18] We are currently exploring the synthetic studies of marine terpenoids on the basis of the formal [6+4] cycloaddition reaction.

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## Supplementary data

Supplementary data (experimental procedures and characterization data for the new compounds) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.12.063.

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