

The strategy for $\text{Co}_2(\text{CO})_8$ -catalyzed double carbonylative [2 + 2 + 1] cycloaddition or [2 + 2 + 2] cycloaddition reaction of triynes: a new synthetic method for tetracyclic compounds †

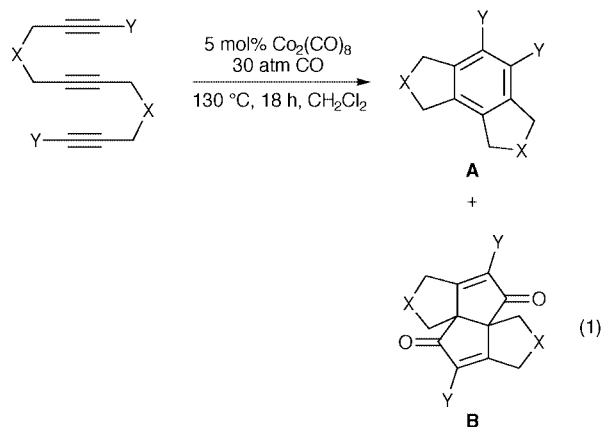
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Novel tetracyclic compounds containing cyclopentenones have been constructed by the cobalt octacarbonyl-catalyzed double [2 + 2 + 1] cycloaddition reaction of triynes under CO pressure.

The [2 + 2 + 1] cycloaddition catalyzed by transition metal complexes provides a powerful tool for the assembly of five-membered rings related to polycyclic natural products.¹ In particular, the [2 + 2 + 1] cycloaddition of alkyne, alkene, and carbon monoxide (known as the Pauson–Khand cycloaddition)² is now regarded as the method of choice for the preparation of cyclopentenones. However, the [2 + 2 + 1] cycloaddition of two alkynes and carbon monoxide has rarely been used in the construction of five-membered rings.³ Although generation and stabilization of cyclopentadienones through the employment of transition metals is quite attractive,⁴ the application of this method to organic synthesis has been hindered by the necessity for the presence of specific substituents and a demetalation step⁵ until our very recent publication.⁶ Recently, we realized that through judicious design of the triyne, the double [2 + 2 + 1] cycloaddition can be carried out selectively in place of the formation of arene **A** [eqn. (1)].



Herein we report a facile construction of novel tetracyclic compounds **B** containing cyclopentenones by the cobalt octacarbonyl-catalyzed double [2 + 2 + 1] cycloaddition reaction of triynes under CO pressure.

Treatment of **1** with $\text{Co}_2(\text{CO})_8$ (5 mol%) in CH_2Cl_2 at 130 °C for 18 h afforded **1A** in 83% yield (Table 1).⁷ The tricyclic prod-

uct **1A** is an intramolecular [2 + 2 + 2] cycloaddition product as expected from previous studies.⁸ However, reaction of **2** under the same reaction conditions gave a 4:1 mixture of **2A** and **2B** † in 90% yield. Compound **2B** is a new tetracyclic compound derived from a double [2 + 2 + 1] cycloaddition. Tetraquinanes having the same skeleton as in **B** had been synthesized previously.⁹ Encouraged by the formation of **2B**, we have screened a variety of triynes (Table 1). Subjecting the substrate **3** to the same conditions provided a 70:26 mixture of **3B** and **3C** in 96% yield. The tetracyclic compound **3C** has apparently been derived from intramolecular [2 + 2 + 1]–[2 + 2] cycloadditions. The transition metal-catalyzed [2 + 2] cycloadditions of alkenes with acetylenes are known,¹⁰ albeit not very common. Reaction of **4** gave a 58:34 mixture of **4A** and **4B** in 92% yield. Thus, changing an oxygen bridge to a carbon one appears to increase the amount of **B**. Treatment of **5** gave a 1:2 mixture of **5A** and **5B** in 91% yield. When two oxygen bridges were changed to two carbon bridges, the ratio of **A**:**B** was completely reversed. Finally, **6** and **7** gave **6B** and **7B** in 72 and 74% yield, respectively, without trace of **6A** and **7A**.

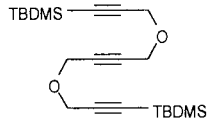
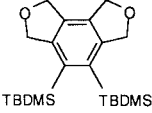
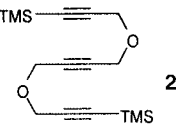
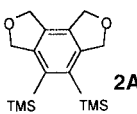
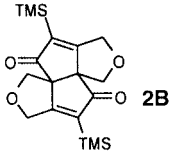
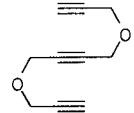
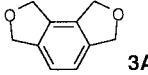
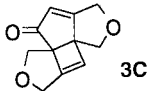
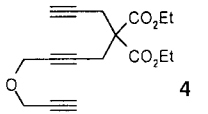
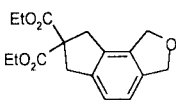
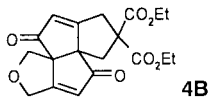
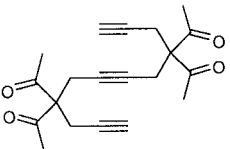
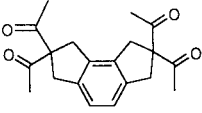
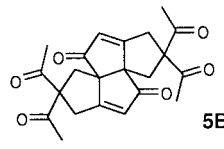
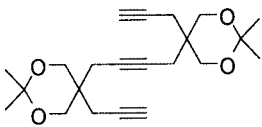
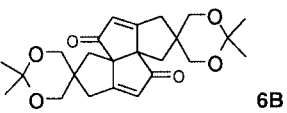
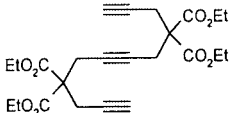
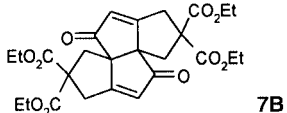
The above results suggest that the oxygen atom of the ether linkage may play a key role in the transition state for the [2 + 2 + 2] cycloaddition, the oxygen atom coordinating to the cobalt, thus positioning the triple bonds to yield [2 + 2 + 2] cycloaddition products. Therefore, for substrates with (an) oxygen bridge(s), the [2 + 2 + 2] cycloaddition is prevalent. A similar coordinating role of the oxygen atom of an ether linkage has been reported¹¹ in other cycloaddition reactions. In the case of substrates without the oxygen bridge, the double [2 + 2 + 1] cycloaddition is more favored than the [2 + 2 + 2] cycloaddition. Hence, a reaction pathway can be chosen by judicious design of the substrate. Following the generally accepted mechanism of metal-catalyzed acetylene trimerization and the Pauson–Khand reaction, a plausible mechanism is proposed in Scheme 1.^{2,12} The precise mechanism in Scheme 1, however, must await further studies.

In conclusion we have demonstrated that through the judicious design of the substrate either a double [2 + 2 + 1] cycloaddition or a [2 + 2 + 2] cycloaddition reaction can be carried out selectively providing for a viable route to yield tetracyclic or tricyclic compounds. These reactions provide rapid access to tetracyclic skeletons of 5-5-5-5 and/or tricyclic skeletons of 5-6-5 ring systems. Important features of this catalytic reaction are the experimental simplicity and a high conversion rate. Further studies on the scope of the reactions and their application to organic synthesis are underway.

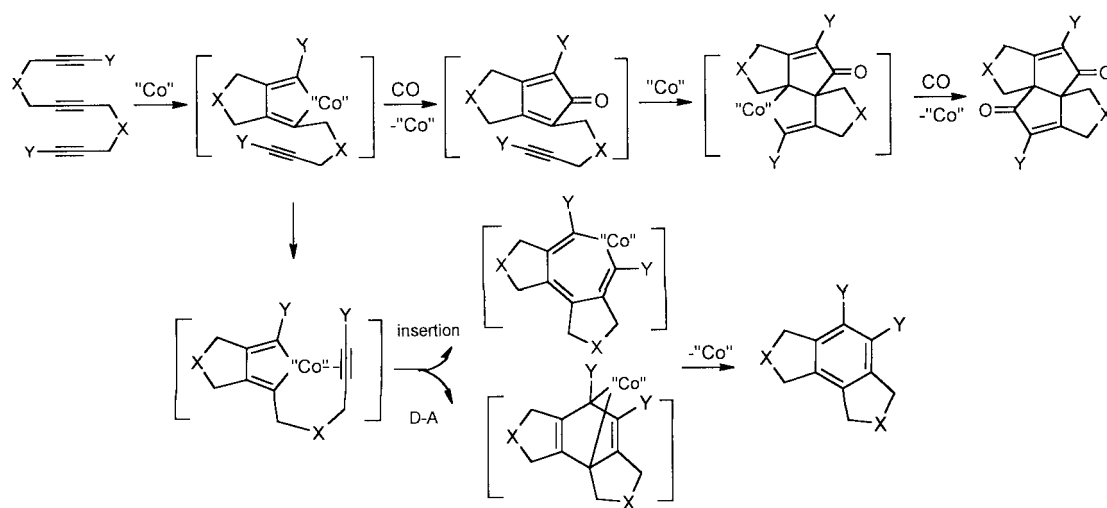
We acknowledge the Ministry of Education of Korea (1998-015-D00165) and the KOSEF through the Center for Molecular Catalysis at Seoul National University.

† Data for characterization of new compounds are available as supplementary data. For direct electronic access see <http://www.rsc.org/suppdata/p1/a9/a909605a/>.

Table 1 Cycloaddition reaction catalyzed by $\text{Co}_2(\text{CO})_8$ ^a

Entry	Substrate	Product	Yield (%) ^b
1			83
2		 	72/18(90)
3		 	70/26(96)
4		 	58/34(92)
5		 	30/61(91)
6			72
7			74

^a Reaction conditions: 130 °C, 18 h, 30 atm CO, 5 mol% $\text{Co}_2(\text{CO})_8$, CH_2Cl_2 . ^b Isolated yields.



Scheme 1

Notes and references

‡ Selected data for **2B**. ^1H NMR (C_6D_6 , 300 MHz): δ 4.85 (d, J 15.0, 2 H), 4.43 (d, J 15.0, 2 H), 3.88 (d, J 8.3, 2 H), 3.28 (d, J 8.4, 2 H), 0.04 (s, 18 H) ppm; ^{13}C NMR (C_6D_6 , 75 MHz): δ 206.2, 185.4, 131.9, 71.4, 67.9, 66.6, -1.79 ppm; HRMS calcd for $(\text{M})^+$ m/z 363.1448, found m/z 363.1441.

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- 7 Substrate **1** (0.30 g, 0.77 mmol) was put in a high pressure reactor. $\text{Co}_2(\text{CO})_8$ (0.013 g) and CH_2Cl_2 (10 mL) were transferred into the bomb under CO atmosphere. After flushing with CO for 2 min, the bomb was pressurized to 30 atm at room temperature. Then the bomb was heated at 130 °C for 18 h. The reactor was cooled to room temperature, the excess CO gas was released and the resulting solution was separated. Chromatography on the silica gel column eluting with hexane–diethyl ether (v/v, 5:1) gave **1A** in 83% yield (0.25 g, 0.64 mmol).
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