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Catalytic one-pot synthesis of [5.5.5.6]fenestrane systems via a dicobalt octacarbonyl-catalyzed tandem cycloaddition of dienediynes†

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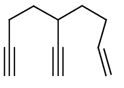
Catalytic one-pot synthesis of fenestrane derivatives from dienediynes was developed: fenestranes were synthesized in high yields by a dicobalt octacarbonyl-catalyzed tandem cycloaddition of dienediynes.

One of the challenging uses of organometallic chemistry is to find reactions and strategies that allow for the facile conversion of simple compounds into complex materials, medicines, or molecules of theoretical interest.[1] Recently we have demonstrated[2] that the dicobalt octacarbonyl-catalyzed carbonylative cycloaddition of diene or triyne with/without diene or alkyne can produce up to four new 5-membered rings in one step. This success encouraged us to analyze the retrosynthesis of fenestranes,[3] which has been studied in relation to the question of whether a tetrahedral carbon can be flattened.

Most of the previous syntheses of fenestranes are based on the Pauson-Khand reaction,[4] photocycloaddition,[5] Pd-catalyzed carbonylative cyclization,[6] aldolization[7] or cyclodehydration[8] as the key step(s). They gave only small quantities of the desired tetracycles and suffered from a low selectivity and tedious separating problems. Now we report a catalytic synthesis of fenestrane derivatives using dicobalt octacarbonyl-catalyzed tandem cycloaddition of dienediynes under CO pressure.

Keese's group reported a one-pot synthesis of [5.5.5.5]fenestranes from enediyne *via* the Pauson-Khand reaction.[4b] However, the reported yields were low.

Thus, at first we thought that enediyne (**1**) or triynes (**2**) might be appropriate precursors for the construction of a fenestrane structure through two sequential [2 + 2 + 1] cycloaddition reactions. The inner triple bond of triynes might permit the construction of a quaternary center from two sequential carbon–carbon bond formation steps. Contrary to our expectation, a fenestrane structure was not formed. Instead, in the case of enediynes, polymeric materials were obtained and, in the case of triynes, an unnatural tetracyclic structure was obtained as the sole product.[9]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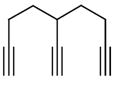
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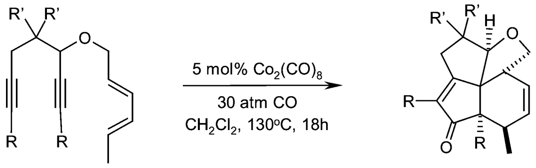
After many experimental trials, we chose dienediyne as a precursor to fenestrane.

For the cyclization, dienediyne derivatives **1a**, **1b**, and **1c** (Scheme 1) were prepared from the α-hydroxy diynes **2a**, **2b** and **2c**. Compound **2b** was prepared according to the procedures in the literature.[10] The same procedure as used for the synthesis of **2b** has been applied to the synthesis of **2a** and **2c**. The reaction of α-hydroxy diynes with sodium hydride followed by hexa-2,4-dienyl bromide led to the isolation of **1a**, **1b**, and **1c** in high yields which were fully characterized.[11]‡

Treatment of dienediyne **1a** (0.68 mmol) with dicobalt octacarbonyl (5 mol%) in dichloromethane at 130 °C under 30 atm of CO for 18 h yielded a fenestrane derivative **3a** in 84% yield [eqn. (1)].§

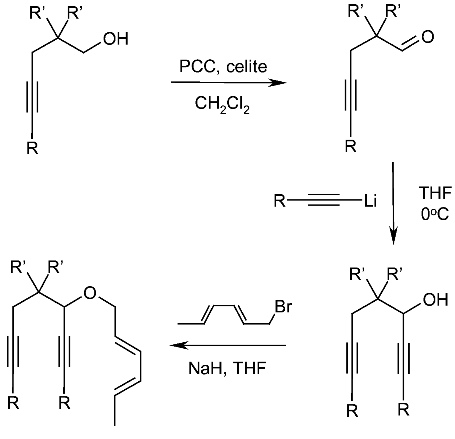


(1)

R = Ph, R' = Me **3a** 84%
R = Ph, R' = H **3b** 74%
R = R' = H **3c** 51%

The structure of **3a** was established by ^{1}H and ^{13}C NMR spectroscopic investigations (COSY, long range COSY, DEPT, HECTOR, long range HECTOR, phase sensitive NOESY, and 2D-INADEQUATE), and mass spectrometry.¶ The correlation peaks obtained from the COSY spectrum allow us to identify the consecutive connections of methyl-14 protons to methyine-9 proton, 9 to 10, 10 to 11, 11 to 12 and 12 to 13. The other connections were derived from the combinative information observed from the DEPT, 2D C–H correlation, and 2D long range C–H correlation spectra. No other products were observed. The reaction involves the formation of five carbon–carbon bonds.

Although this multibond formation reaction seems to be complex, it may be simple: the dicobalt octacarbonyl-catalyzed carbonylative [2 + 2 + 1] cycloaddition of diyne with carbon monoxide followed by a subsequent intramolecular [4 + 2] cycloaddition provides **3a**. Another feasible reaction pathway is that the diene unit reacts first with the closer triple bond and the thus formed cyclohexa-1,4-diene undergoes a Pauson-Khand reaction with the remote triple bond.[12] The central triple bond acts as a double functionality that could be used in both cyclizations. In the same way as in the synthesis of **3a**, the dicobalt octacarbonyl-catalyzed tandem cyclization of dien-



R = Ph, R' = Me **1a** **2a**
R = Ph, R' = H **1b** **2b**
R = R' = H **1c** **2c**

Scheme 1

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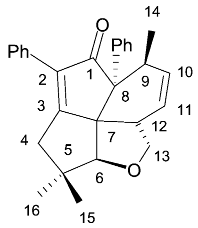
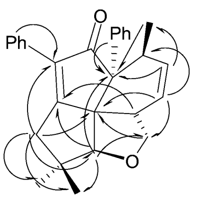
† Electronic supplementary information (ESI) available: characterization of synthesized compounds. See http://www.rsc.org/suppdata/cc/b1/b108034b/





diynes **1b** and **1c** afforded **3b** and **3c** in 74% and 51% yields, respectively.

In conclusion, we have developed a new catalytic route to fenestrane derivatives *via* dicobalt octacarbonyl-catalyzed cycloaddition of dienediynes. The following significant points are noteworthy. All the reactions described here are catalytic with high conversion rates and experimentally a simple reaction, a one-pot reaction.

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Notes and references

‡ Compound **2a** (0.20 g, 0.69 mmol) was dissolved in 15 ml of THF. The solution was cooled to 0 °C. To the solution was added NaH (40 mg, 50 wt% in oil). After the solution was stirred for 1 h, hexa-2,4-dienyl bromide (0.17 g, 1.05 mmol) was added to the solution. The resulting solution was stirred for 12 h and was quenched with diethyl ether and sat. NH_4Cl solution. The ether layer was separated, dried over anhydrous $MgSO_4$, concentrated and the residue separated on a silica gel eluting with hexane and diethyl ether (v/v, 10:1). Yield: 0.23 g (89%). **1a**: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.39 (m, 4 H), 7.28 (m, 6 H), 6.27 (dd, 15.0, 10.0 Hz, 1 H), 6.00 (dd, 15.0, 10.0 Hz, 1 H), 5.70 (m, 2 H), 4.37 (dd, 13.0, 5.4 Hz, 1 H), 4.26 (s, 1 H), 4.08 (dd, 13.0, 7.2 Hz, 1 H), 2.65 (d, 17.0 Hz, 1 H), 2.47 (d, 17.0 Hz, 1 H), 1.71 (d, 6.2 Hz, 3 H), 1.20 (s, 3 H), 1.19 (s, 3 H) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz): δ133.6, 131.7, 131.6, 130.9, 129.8, 128.2, 128.1, 127.5, 126.7, 124.1, 122.9, 87.9, 86.9, 82.6, 75.4, 69.7, 39.1, 29.4, 23.7, 22.8, 18.0 ppm; exact mass calc. 368.2140, obsd. 368.2137.

§ Compound **1a** (0.25 g, 0.68 mmol), 15 ml of CH_2Cl_2, and $Co_2(CO)_8$ (12 mg, 0.035 mmol) were put in a high pressure reactor (100 ml). After the solution was bubbled with nitrogen for 1 min, the reactor was pressurized with 30 atm of CO. The reactor was heated at 130 °C for 18 h. After the reactor was cooled to rt, excess gas was released and the reaction mixture was transferred into a one-neck flask (50 ml). Removal of the solvent followed by chromatography on a silica gel column eluting with hexane and diethyl ether (v/v, 5:1) gave **3a** in 84% yield (0.23 g, 0.58 mmol).

¶ ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.60–7.24(m, 10 H), 6.04 (m, 1 H), 5.73 (m, 1 H), 4.16 (dd, 8.7, 5.5 Hz, 1 H), 3.84 (dd, 8.7, 5.5 Hz, 1 H), 3.70 (s, 1 H), 2.90 (m, 1 H), 2.72 (m, 1 H), 2.68 (d, 15.0 Hz, 1 H), 2.43 (d, 15.0 Hz, 1 H), 1.22 (d, 7.3 Hz, 3 H), 1.04 (s, 3 H), 0.00 (s, 3 H) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz): δ 209.2, 180.7, 139.2, 137.9, 134.8, 131.3, 129.8, 128.9, 128.3, 127.7, 126.6, 89.6, 75.3, 70.3, 65.9, 48.0, 43.9, 42.7, 36.8, 25.9, 23.3, 18.9 ppm; IR νCO 1693 cm^{-1}; exact mass calc. 396.2089, obsd. 396.2088.

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11 See the Supporting Information.†

12 A referee suggested this reaction pathway. The authors thank the referee for this suggestion.