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Dicobalt Octacarbonyl Catalyzed Carbonylated Cycloaddition of Triynes to Functionalized Tetracycles

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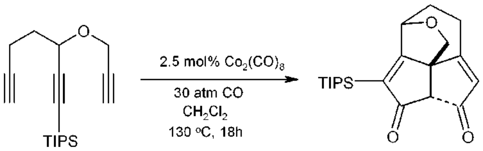
ABSTRACT



We have demonstrated that a dicobalt octacarbonyl catalyzed double [2 + 2 + 1] carbonylative cycloaddition reaction of triyne can be carried out to yield a novel 5.5.5.6 tetracyclic di-enone system.

Recently, we have demonstrated[1] that the generation and stabilization of cyclopentadienones through the use of cobalt carbonyl could be an attractive method for the construction of five-membered ring systems. Reaction sequences starting from dienyne or ene-diyne[2] have successfully provided [4.5.5.5] fenestrane (**A**) and [5.5.5.5]fenestrane (**B**), respectively (Figure 1). These studies suggested that triynes (**C**) might be appropriate precursors for the construction of tetracycles possessing a fenestrane structure[3] through two sequential [2 + 2 + 1] cycloaddition reactions. However, when a triyne was treated with dicobalt octacarbonyl in the presence of CO, a 5.5.5.6 tetracyclic structure was obtained as a sole product.

Herein we report a new cobalt carbonyl catalyzed double [2 + 2 + 1]carbonylative cycloaddition reaction of triynes yielding novel 5.5.5.6 tetracyclic compounds, which can be utilized as versatile intermediates for polyquinane synthesis.

For the cyclization, a variety of triyne derivatives (compound **1**, Scheme 1) were prepared, where X,Y = O, NR, and CH_2. Treatment of triyne **1a** with $Co_2(CO)_8$ (2.5 mol %) in CH_2Cl_2 at 130 °C for 1 day afforded the tetracyclic compound **2a** in 75% yield.[4]

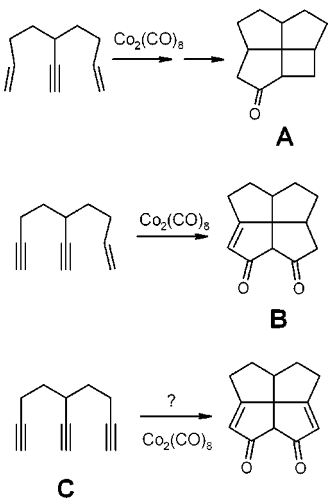


Figure 1. Some tandem cyclizations for synthesis of polyquinanes.

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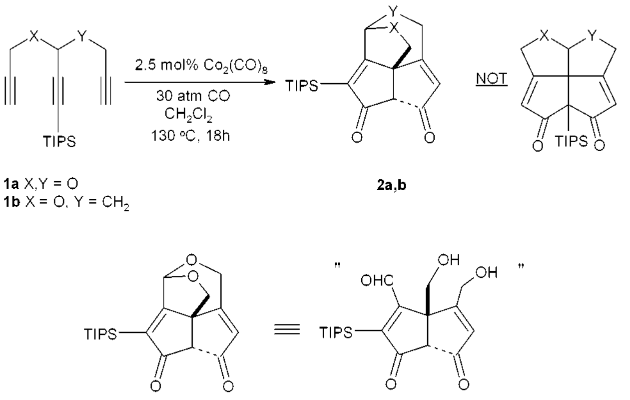
[1] (a) Hong, S. H.; Choi, D. S.; Chung, Y. K.; Lee, S. *Chem. Commun.* **1999**, 2099. (b) Son, S. U.; Paik, S.-J.; Lee, S. I.; Chung, Y. K. *J. Chem. Soc., Perkin Trans. 1* **2000**, 141. (c) Son, S. U.; Choi, D. S.; Chung, Y. K. *Org. Lett.* **2000**, *2*, 2097. (d) Son, S. U.; Chung, Y. K.; Lee, S. G. *J. Org. Chem.* **2000**, *65*, 6142.

[2] (a) Smit, W. A.; Buhanjuk, S. M.; Simonyan, S. O.; Shahkov, A. S.; Struchkov, Y. T.; Yanovsky, A. I.; Caple, R.; Gybin, A. S.; Anderson, L. G.; Whiteford, J. A. *Tetrahedron Lett.* **1991**, *32*, 2105. (b) Thommen, M.; Veretenov, A.; Guidetti-Grept, R.; Keese, R. *Helv. Chim. Acta.* **1996**, *79*, 461. (c) van der Waals, A.; Keese, R. *J. Chem. Soc., Chem. Commun.* **1992**, 570. (d) Thommen, M.; Gerber, P.; Keese, R. *Chimia* **1991**, 21−24.

10.1021/ol015635x CCC: $20.00

Scheme 1



The product **2a** could provide a ready access to a variety of substituted polyquinane structures, which belong to a rapidly growing subgroup of terpene natural products and are associated with a wide range of biological activities.[5] It is of a particular note that, in one operation, six carbon−carbon bonds have been formed simultaneously, housing four rings in a single molecule. As expected, the double bond of the cyclopentadienone from the first cyclization has been used as an alkene part of the second Pauson−Khand reaction. However, as a result of the steric effect of the TIPS group, the second reaction occurred in the intermediate between the unsubstituted double bond and the triple bond. The structural proof of the tetracyclic structure was obtained through an X-ray study of **2b** (Figure 2).[6]

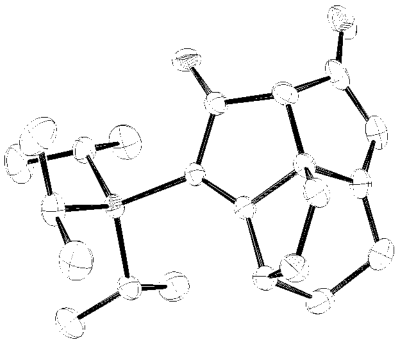
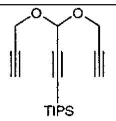
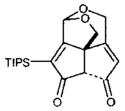
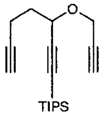
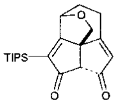
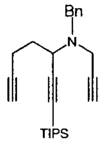
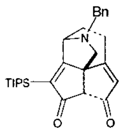
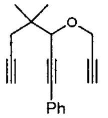
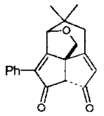
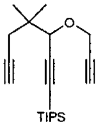
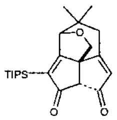


Figure 2. X-ray stucture of **2b**.

Encouraged by the formation of **2a** and **2b**, we have tested a variety of triynes (Table 1). Cycloaddition reaction of **1c**−**e** under the same reaction conditions gave tetracyclic dienone **2c,d** in reasonable to high yields. However, treatment of **1e** under the same reaction conditions gave **2e** in 10% yield. It was expected that the yield of **2e** would be close to that of **2b** since **1e** appears to be quite akin to **1b** except for the dimethyl substituents on the carbon bridge. However, the steric effect of the dimethyl group on the cycloaddition reaction would be considerably larger than expected. A subtle change in the steric environment appears to impose a substantial effect on the reaction course. Despite the poor yield, the formation of **2e** is still catalytic with a turnover number of 4. Treatment of **1f** under the same reaction conditions provided no detectable products. Instead, formation of an untractable polymeric material was observed.

Table 1. Double [2 + 2 + 1] Reaction in Triynes[a]

entry	substrate	product	yield(%)[b]
1	 **1a**	 **2a**	75
2	 **1b**	 **2b**	71
3	 **1c**	 **2c**	74
4	 **1d**	 **2d**	45
5	 **1e**	 **2e**	10

[a] Reaction conditions: 130 °C, 18 h 30 atm CO, 2.5 mol % $Co_2(CO)_8$, CH_2Cl_2. [b] Isolated yield.

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(3) Reviews on fenestrane chemistry: (a) Kuck, D. In *Advances in Theoretically Interesting Molecules*; Thummel, R. P., Ed.; JAI Press: Greenwich, CT, 1998; Vol. 4, p 81 f. (b) Thommen, M.; Keese, R. *Synlett* **1997**, 231. (c) Luef, W.; Keese, R. In *Advances in Strain in Organic Chemistry*; Halton, B., Ed.; JAI Press: Greenwich, CT, 1993; Vol. 3, p 229 f. (d) Agosta, W. C. In *The Chemistry of Alkanes and Cycloalkanes*; Patai. S., Rappoport, Z., Eds.; Wiley: New York, 1992; p 927 f. (e) Gupta, A. K.; Fu, X.; Snyder, J. P.; Cook, J. M. *Tetrahedron* **1991**, *47*, 3665. (f) Krohn, K. In *Organic Synthesis Highlights*; Mulzer, J., Altenbach, H.-J., Braun, M., Krohn, K., Reissig, H.-U., Eds.; VCH: Weinheim, 1991; p 121 f. (g) Venepalli, B. R.; Agosata, W. C. *Chem. Rev.* **1987**, *87*, 399. (h) Keese, R. In *Organic Synthesis: Modern Trends*; Chizhov, O., Ed.; Blackwell: Oxford, 1987; p 43 f. (i) Keese, R. *Nach. Chem. Technol. Lab.* **1982**, *30*, 844.

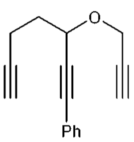
(4) **Characterization of 2a.** ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.98 (s, 1 H), 5.54 (br s, 1 H), 4.79 (d, 14.0 Hz, 1 H), 4.69 (d, 14.0 Hz, 1 H), 4.45 (d, 8.1 Hz, 1 H), 4.09 (d, 8.1 Hz, 1 H), 3.35 (s, 1 H), 1.36 (m, 3 H), 1.01 (m, 18 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ 201.9, 196.1, 184.7, 174.4, 124.5, 120.1, 94.2, 69.1, 62.9, 60.1, 58.8, 18.4, 18.3, 10.9 ppm. IR (NaCl) ν C═O 1724, 1691 cm^{-1}. Anal. Calcd for $C_{20}H_{28}O_4Si$: C, 66.63; H, 7.83. Found: C, 66.50; H, 8.10.

(5) For a review on polyquinanes, see: (1) Mehta, G.; Srikrishna, A. *Chem. Rev.* **1997**, *97*, 671−719. (2) Paquette, L. A.; Doherty, A. M. *Recent Synthetic Developments in Polyquinane Chemistry*; Springer-Verlag: New York, 1987. (3) Paquette, L. A. *Top. Curr. Chem.* **1984**, *119*, 1. (4) Ramaiah, M. *Synthesis* **1984**, 529. (5) Trost, B. M. *Chem. Soc. Rev.* **1982**, *11*, 141. (6) Paquette, L. A. *Top. Curr. Chem.* **1979**, *79*, 41.

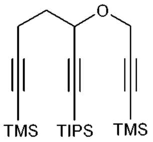
(6) Information for crystal. Crystal system, triclinic, space group, P-1, unit cell dimensions $a = 7.8074(3)$, $b = 14.7100(6)$, $c = 18.4775(8)$ Å; $\alpha = 104.428(2)°$, $\beta = 94.084(3)°$, $\gamma = 92.151(3)°$. Final R indices [$I > 2\sigma(I)$], R1 = 0.0716, wR2 = 0.1759.

It is interesting to note that, in all cases examined, the first cyclization occurred to form a bicyclic dienone containing a heteroatom in the ring system.

For compound **1g**, no reaction was observed under the same reaction conditions as a result of the steric effect of the substituents. Thus, it seems that the steric bulkiness helps the cycloaddition reaction to afford tetracyclic compounds; however, excess steric effect hinders the progress of the cycloaddition reaction.



1f



1g

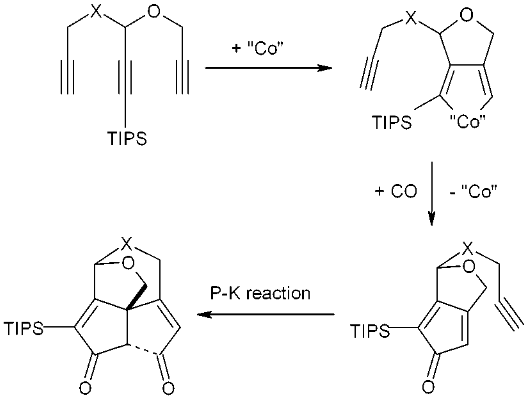
We have screened other triynes having an alkyl and benzyl group at center alkyne that are sterically less cumbersome than **1a**−**e**. Instead of cycloaddition products, untractable polymeric materials were obtained.

Thus, the steric effect of the substituent in the inner triple bond plays an important role in controlling the destiny of the reaction path. Thus, the dicobalt octacarbonyl catalyzed double [2 + 2 + 1] carbonylative cycloaddition of triyne is quite unique for triynes having a TIPS group in the inner triple bond.

A plausible reaction mechanism is provided in Scheme 2.

In conclusion, we have demonstrated that by designing triynes bearing a proper steric group, a dicobalt octacarbonyl catalyzed double [2 + 2 + 1] carbonylative cycloaddition reaction of triyne can be carried out to yield a novel 5.5.5.6 tetracyclic di-enone system. The experimental simplicity and high conversion rate of the cycloaddition reaction are noteworthy. The reaction described will doubtlessly be further developed since the assembly of four rings in one operational step makes it a worthwhile competitor to other methods.

Scheme 2



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Supporting Information Available: General experimental procedures and characterization data of compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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