CYCLOADDITION REACTIONS OF OXAQUADRICYCLANE, OXANORBORNADIENE, AND RELATED COMPOUNDS WITH CYCLOOCTYNE

Kiyoshi Matsumoto,*[1] Hiroyuki Taketsuna,[1] Yukio Ikemi,[2]
Akikazu Kakehi,[3] Takane Uchida,[4] and Shinichi Otani[2]

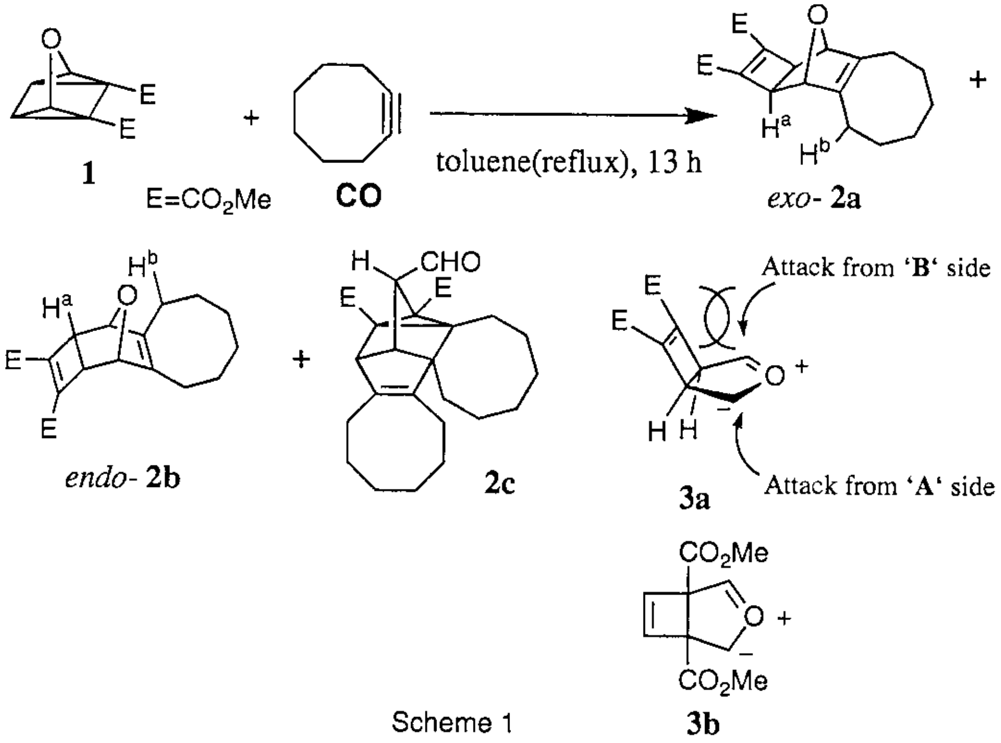
1 Graduate School of Human and Environmental Studies, Kyoto University, Kyoto 606-8501, Japan
2 Faculty of Integrated Human Studies, Kyoto University, Kyoto 606-8501, Japan
3 Faculty of Engineering, Shinshu University, Nagano 380-8533, Japan
4 Faculty of Education, Fukui University, Fukui 910-8507, Japan

Abstract-Dimethyl oxaquadricyclane-2,3-dicarboxylate (**1**) with cyclooctyne (**CO**) gave, *via* carbonyl ylide (**3a**), a mixture of the *exo* and *endo* 1:1 adducts (**2a**, **2b**) along with the novel 1:2 adduct (**2c**), whereas the carbocyclic analogs underwent [σ2s + σ2s + π2s]cycloaddition. The first examples of inverse electron demand homo-Diels-Alder reactions of oxa-, aza- and carbo-norbornadienes with **CO** were also described.

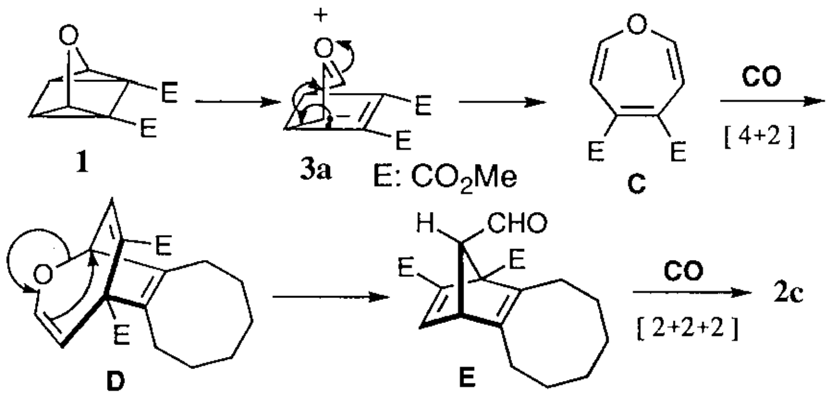
Cyclooctyne is the smallest cyclic alkyne that is stable at room temperature and has been prepared by a number of methods which either start from cyclooctene or from cyclooctanone.[1] In spite of high strain and high reactivity of cyclooctyne as well as synthetic potential of its cycloadditions, relatively few examples of cycloaddition reactions have been reported.[2] Specifically, its cycloadditions and subsequent ring enlargement have been elegantly utilized for construction of the medium and large ring compounds.[3] Since cyclooctyne is now readily available,[1c] we envisaged that its cycloadditions with oxaquadricyclane, oxanorbonadiene, and related compounds would provide a facile route to the medium and large ring compounds as well as molecular cages, belts, rods, and spacers. This is a subject of the present communication.

Reaction of dimethyl oxaquadricyclane-2,3-dicarboxylate (**1**) with cyclooctyne (**CO**) in refluxing toluene for 7 h gave a mixture of *exo*-**2a** (46 %), *endo*-**2b** (42 %), and **2c**

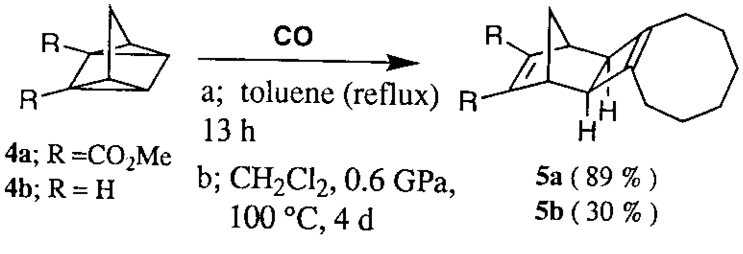
Dedicated to Prof. Dr. Bernhard Witkop on the occasion of his 80th birthday



Scheme 1



Scheme 2

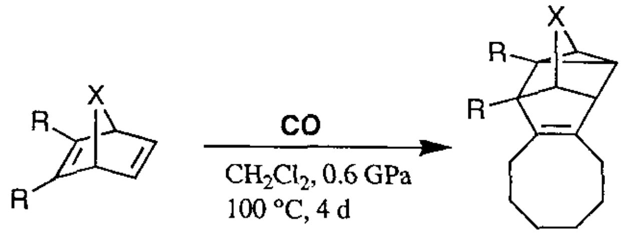


Scheme 3

(0.4 %).[4] The *exo* stereochemical assignment was made based upon the its NOESY spectra (H^a and H^b). The reaction is known to proceed *via* carbonyl ylide (**3a**)[5a] and the subsequent cycloaddition has been established to take place in *exo* fashion with dienophiles such as maleic anhydride.[5b] Indeed, the calculated heats of formation (kcal · mol^{-1}) obtained by AM1 and PM3 methods of **3a** are smaller than those of its isomer (**3b**).[6] The predominant formation of *exo*-adduct is presumably due to the favorable attack of **CO** from 'A' side as shown in Scheme 1. This is in agreement with the calculated heats of formation (kcal · mol^{-1}) obtained by AM1 method(**2a**: -120.85. **2b**: -112.72). Interestingly, the *exo*-selectivity was increased up to 98 : 2 (*exo*:*endo* ratio by NMR analysis) under high pressure of 0.6 GPa at room temperature, presumably because of the smaller activation volume leading to the *exo*-adduct (**2a**) than to the *endo*-adduct (**2b**). The formation of **2c** is very novel and can be explained by an initial isomerization of **1** to the oxepine (**C**),[5a] followed by Diels-Alder reaction with **CO**, rearrangement, and further homo-Diels-Alder reaction with second molecule of **CO**. Unfortunately, the initial Diels-Alder adduct (**D**) of **CO** with the oxepine (**C**) could not be isolated in our hand. The examples of this type of the initial Diels-Alder adducts of the related oxepines with azo compounds are known,[7] although, to our knowledge, the subsequent rearrangement of the initial Diels-Alder adduct like **D** to **E** has not been previously reported. The driving force of the rearrangement is presumably due to the strain imposed by an additional double bond, compared with the reported adduct with the azo compounds.

In contrast with **1**, dimethyl quadricyclane-2, 3-dicarboxylate (**4a**) underwent regio- and stereo-specific [$\sigma 2s + \sigma 2s + \pi 2s$] cycloaddition[8] with **CO** in refluxing toluene to give the adduct (**5a**), whereas the parent quadricyclane (**4b**) reacted with only under high pressure and at 100 °C. This is not surprising because the LUMO(**4a**)-HOMO(**CO**) and LUMO(**4b**)-HOMO(**CO**) energy gaps were estimated to be 10.665 and 12.131 (eV) based upon the semiempirical PM3 calculations.

Neither dimethyl oxanorbornadiene-2,3-dicarboxylate (**6a**) nor the related analogs (**6b-d**) reacted with **CO** at 100 °C in sealed tube. The homo-Diels-Alder reactions, [$\pi 2s + \pi 2s + \pi 2s$] processes, of norbornadiene with dimethyl acetylenedicarboxylate and tetracyanoethylene are reported to have activation volume of about -30 $cm^3 \cdot mol^{-1}$.[9] Thus, at 0.6 GPa and 100 °C, the above reactions took place to give the corresponding homo-



6a; X = O, R = CO$_2$Me
6b; X = N-CO$_2$Me, R = CO$_2$Me
6c; X = CH$_2$, R = H
6d; X =CH$_2$, R = CO$_2$Me

7a (31 %)
7b (22 %)
7c (11 %)
7d (11 %)

Scheme 4

Diels-Alder adducts (**7a-d**) in moderate yields.[10] Based upon the results of semiempirical MO calculations (PM3), the reaction is, besides the parent norbornadiene (**6d**), presumably controlled by LUMO(**6**)-HOMO(**CO**).[11] To our knowledge, this is the first example of the inverse electron demand homo-Diels-Alder reactions.

Further work is envisaged to explore a facile method leading to molecular racks, rods, cages, and spacers.

ACKNOWLEDGEMENTS

This work was supported in part by Grants-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture, Japan (Nos. 07304047 and 08221214 to KM).

REFERENCES AND NOTES

1. a) A. T. Blomquist and L. H. Liu, *J. Am. Chem. Soc.*, 1953, **75**, 2153; b) G. Wittig and H. L. Dorsch, *Liebigs Ann.*, 1968, **74**, 46; c) H. Meier and I. Menzel, *J. Chem. Soc. D*, 1971, 1059; d) P. Caubere and G. Coudert, *Bull. Soc. Chim. Fr.*, 1973, 3067; e) L. Brandsma and H. D. Verkruijesse, *Synthesis*, 1978, 290.
2. P. Konig, J. Zountsa, K. Bleckmann, and H. Meier, *Chem. Ber.*, 1983, **116**, 3580; C. Gerninghous, A. Kummel, and Seitz, *Chem. Ber.*, 1993, **126**, 733; N. Biedermann and J. Sauer, *Tetrahedron Lett.*, 1994, **35**, 7935.
3. W. Tochtermann and P. Kraft, *Synlett*, 1996, 1029.
4. **2a**: mp 114.0-115.0 ℃; ^{1}H-NMR (270 MHz; CDCl$_3$) δ 4.78 (s;2H), 3.82 (s;6H), 2.51 (s;2H), 2.17 (m; 4H), 1.65 (m; 4H), 1.55 (m; 4H); ^{13}C-NMR (67.5 MHz; CDCl$_3$) δ 163.4, 143.4, 140.9, 77.8, 52.3, 44.0, 27.8, 26.4, 24.2. **2b**: oil; ^{1}H-NMR (270 MHz; CDCl$_3$) δ 4.45 (s;2H), 3.82 (s;6H), 2.82 (s;2H), 2.52-2.25 (m;4H), 1.80-1.38 (m;4H), 1.58 (m; 4H); ^{13}C-NMR (67.5 MHz; CDCl$_3$) δ 161.4, 144.0, 140.0, 79.8, 51.9, 44.9, 26.5, 25.7, 24.5. **2c**: mp180.5-183.5 ℃; ^{1}H NMR (270 MHz; CDCl$_3$) δ 9.91 (s;1H),

4.47 (s;1H), 3.50 (s;6H), 2.92 (m;1H), 2.38-2.15 (m;8H), 2.02 (d;1H), 1.85-0.80(m; 18H); ^{13}C-NMR (67.5 MHz; CDCl$_3$) δ 185.4, 173.1, 171.6, 168.6, 147.0, 145.1, 140.6, 128.3, 54.9, 52.2, 41.8, 39.2, 37.1, 36.7, 32.0, 30.2, 28.5, 27.2, 26.9, 26.8, 26.6, 25.8, 24.4, 24.1.

5. a) H. Prinzbach, H. Bingmann, J. Markert, G. Fischer, L. Knothe, W. Eberbach, and J. Brokatzky-Geiger, *Chem. Ber.*, 1986, **119**, 589. b) H. Prinzbach, M. Argeguelles. P. Vogel, and W. Eberbach, *Angew. Chem.*, 1967, **79**, 1103.
6. The heats of formation of the carbonyl ylides (**3a**) and (**3b**) were obtained using CAChe systems (Version 3.7, CAChe Scientific, Oxford Molecular Group; AM1: M. J. S. Dewar, E. G. Zoebisch, E. F. Hearly, and J. J. P. Stewart, *J. Am. Chem. Soc.*, 1985, **107**, 3902; PM3: J. J. P. Stewart, *J. Comp. Chem.*, 1989, **10**, 209). Heat of formation of ylide (**3a**):-120.85(AM1), -92.33(PM3) kcal/mol; heat of formation of cation (**3b**): -112.72(AM1), -81.96(PM3) kcal/mol.
7. D. R. Boyd and G. A. Berchtold, *J. Org. Chem.*, 1979, **44**, 468.
8. I. Tabushi, K. Yamamura, and Z. Yoshida, *J. Am. Chem. Soc.*, 1972, **94**, 787 and reference cited.
9. G. Jenner and M. Papadopoulos, *Tetrahedron Lett.*, 1982, **23**, 4333.
10. The yields in Scheme 4 are based on the pure and isolated compounds. Representative data: **7a**: oil; ^{1}H-NMR (270 MHz; CDCl$_3$) δ 5.02 (d;1H,J=2.5 Hz), 4.20 (d;1H,J=3.0 Hz), 3.74 (s;3H), 3.66 (s;3H), 2.61 (m;1H), 1.27 (m;1H), 2.58-2.36 (m;4H), 2.23 (m;1H), 1.80-1.60 (m;4H); ^{13}C-NMR (67.5 MHz; CDCl$_3$) δ 170.3, 170.2, 138.9, 136.0, 92.8, 69.8, 66.2, 53.2, 51.9, 51.6, 41.6, 37.5, 28.0, 27.9,27.3, 25.9, 25.8. **7b**:oil; ^{1}H-NMR (270 MHz; CDCl$_3$) δ 4.62 (br;1H), 3.61 (s;3H), 3.59 (s;3H), 3.57 (s;3H), 2.58 (m;1H); ^{13}C-NMR (67.5 MHz; CDCl$_3$) δ 170.2, 155.2, 140.1, 137.3, 134.2, 129.0, 125.8, 74.7, 65.2, 53.2, 52.6, 51.6, 50.5, 42.7, 36.7, 28.1, 27.9, 27.1, 26.0, 25.8, 25.5.
11. The HOMO and LUMO energy gaps between **6a**, **6b**, **7c**, **7d** and **1** obtained by PM3 method are summarized as follows:

Table Energy gaps between **CO** and **6a-d**

Norbornadiene	HOMO-LUMO$_{CO}$ (eV)	LUMO-HOMO$_{CO}$ (eV)
6a	11.846	9.059
6b	11.879	8.882
6c	10.816	10.899
6d	11.391	9.546

Received, 11th May, 1998