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Complexation-Initiated Intramolecular Diels–Alder Reaction

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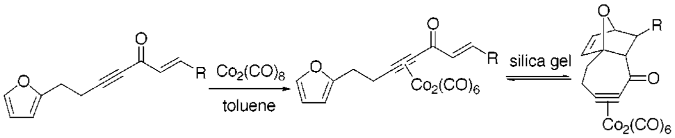
ABSTRACT



A complexation-initiated intramolecular Diels–Alder reaction was demonstrated for the first time. On adsorbing the alkyne–$Co_2(CO)_6$ complexes having a diene and a dienophile on opposite ends of the alkyne on silica gel, the Diels–Alder reaction was accelerated and the equilibrium was shifted toward the adduct formation to a greater extent compared to that in solution. Seven-membered ring formation was apparently favorable in this system.

Complexation between transition metals and organic molecules such as alkenes and alkynes has widely been utilized in organic synthesis to enable various types of useful reaction; however, the change in structure of alkynes on such complexation itself has seldom been employed for the control of synthetic reactions. It is known that alkynes change from a linear structure to a bent one with an angle of around 140° between substituents on reaction with octacarbonyldicobalt ($Co_2(CO)_8$) at room temperature to give alkyne−$Co_2(CO)_6$ complexes.[1] We expected that complexation of an alkyne having a diene and a dienophile unit on opposite ends with $Co_2(CO)_8$ would bring the diene and the dienophile in close, initiating an intramolecular Diels−Alder reaction. In this Letter we describe a successful realization of this possibility by using furan as the diene[2] and a unique effect of silica gel on the rate and the equilibrium of this Diels−Alder reaction.

When methoxycarbonyl derivative **1a** ($R = COOMe$) was treated with a 1.1 molar amount of $Co_2(CO)_8$ in toluene, smooth formation of the alkyne−$Co_2(CO)_6$ complex **2a** was observed by TLC within 15 min; however, formation of the Diels−Alder adduct **3a** was not observed even after a few hours at rt. Furthermore, heating this complex up to 100 °C gave a complex mixture of products, from which the double bond-hydrogenated compound was isolated as an identifiable complex. Since formation of this reduction product was thought to be due to the presence of cobalt hydride species generated by the decomposition of the small amount of remaining $Co_2(CO)_8$,[3] separation of the alkyne−$Co_2(CO)_6$ complex **2a** was performed by silica gel column chromatography.

When the alkyne−$Co_2(CO)_6$ complex **2a** was subjected to silica gel column chromatography under an argon atmosphere, formation of an additional alkyne−$CO_2(CO)_6$ complex was observed, and this and **2a** were separated by rapid elution.[4] The major complex was the starting alkyne−$Co_2(CO)_6$ complex **2a** obtained in about 60% yield, and the other, more polar complex, obtained in about 20% yield, was found to be the desired intramolecular Diels−Alder adduct **3a** obtained as a single diastereomer.[5] Thus, the alkyne−

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(1) (a) Sternberg, H. W.; Greenfield, H.; Friedel, R. A.; Wotiz, J.; Markby, R.; Wender, I. *J. Am. Chem. Soc.* **1954**, *76*, 1457. (b) Greenfield, H.; Sternberg, H. W.; Friedel, R. A.; Wotiz, J. H.; Markby, R.; Wender, I. *J. Am. Chem. Soc.* **1956**, *78*, 120. (c) Kemmitt, R. D. W.; Russell, D. R. In *Comprehensive Organometallic Chemistry*; Wilkinson G., Ed.; Pergamon Press: Oxford, 1982; Vol. 5, p 1.

(2) Kappe, C. O.; Murphree, S. S.; Padwa, A. *Tetrahedron* **1997**, *53*, 14179.

(3) Seyferth, D.; Williams, G. H.; Traficante, D. D. *J. Am. Chem. Soc.* **1974**, *96*, 604.

(4) It is necessary to carry out the elution rapidly because rapid equilibration occurs on silica gel. To achieve clean separation, it is better to cool the column to 0 °C.

(5) The stereochemistry of the adducts **3a** and **3b** was determined to be as shown in **3** on the basis of proton coupling constants.

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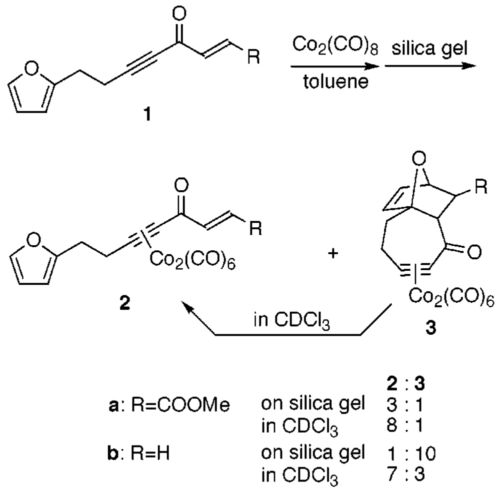
$Co_2(CO)_6$ complex **2a** was found to undergo intramolecular Diels–Alder reaction rapidly at room temperature on absorption on silica gel.[6] The Diels–Alder adduct **3a** was stable in $CDCl_3$ for 1 day at 0 °C, but at room temperature **3a** underwent retro Diels–Alder reaction without decomplexation. For example, the separated adduct **3a** gave an equilibrium mixture of **2a** and **3a** (about 8:1) in $CDCl_3$ within 1 day at room temperature (Scheme 1).

Scheme 1. Complexation Initiated Intramolecular Diels–Alder Reaction of Methoxycarbonyl Derivative **1a** and Vinyl Ketone Derivative **1b**



Such acceleration of the Diels–Alder reaction and equilibration to the adduct on adsorption of the complex on silica gel were more explicitly seen in the following reaction of the vinyl ketone derivative **1b** (R = H). When **1b** was treated with $Co_2(CO)_8$ and then subjected to silica gel column chromatography, the $Co_2(CO)_6$ complex of the starting material **2b** and that of the Diels–Alder adduct **3b**[5] were obtained in a 1:10 ratio in 91% yield. Thirty minutes of adsorption on silica gel was sufficient for equilibration as shown in Table 1. Furthermore, both the starting complex **2b** and the separated Diels–Alder adduct **3b** underwent slow equilibration in solution, with both giving a 7:3 mixture of **2b** and **3b** after 2 or 3 days in $CDCl_3$ at room temperature. (Table 2) Thus, acceleration of the Diels–Alder reaction and an equilibrium shift to the adduct were observed explicitly in this case, and the equilibrium is much more in favor of adduct formation when compared to that for the methoxycarbonyl derivative **1a**.

Table 1. Equilibrium of **2b** and **3b** on Silica Gel[a]

absorption time on silica gel	**2a**:**2b**
10 min	4:5
30 min	1:10 (91% isolated yield)
135 min	1:10

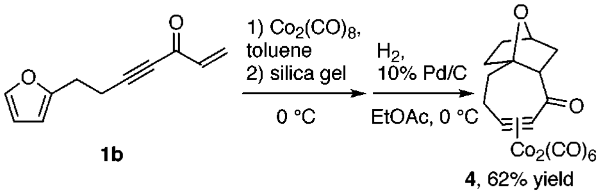
[a] After **1b** was treated with $Co_2(CO)_8$ for 1 h in toluene, the mixture was charged on silica gel. After the indicated time, the complexes were eluted rapidly and the ratio was determined by NMR measurement.

Table 2. Equilibrium of **2b** and **3b** in $CDCl_3$ at Room Temperature

	2b:**3b**	
time	from **2b**	from **3b**
0 h	1:0	0:1
6 h	9:1	1:4
22 h	4:1	1:1
47 h	3:1	7:3
72 h	7:3	7:3

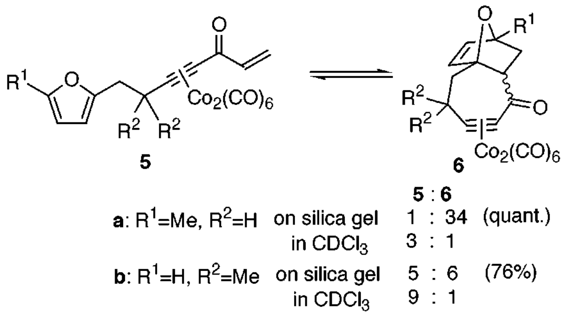
Furthermore, the hydrogenated complex **4** would be isolated as a stable complex in good yield by rapid treatment of the eluted mixture of the alkyne–$Co_2(CO)_6$ complex derived from **1b** with H_2 and Pd/C as shown in Scheme 2.

Scheme 2. Preparation of Hydrogenated Cycloadduct **4**



As shown in Scheme 3, 5-methylfuran derivative **5a** and dimethyl derivative **5b** also gave similar results. In particular, almost complete equilibrium shift to the adduct **6a** was observed in the case of the 5-methylfuran derivative **5a**. Again **6a** was obtained as a single diastereomer, but in the reaction of **5b**, **6b** was obtained as a mixture of stereoisomers in about a 3:1 ratio.[7]

Scheme 3. Complexation-Initiated Intramolecular Diels–Alder Reaction of Methylfuran Derivative **5a** and Dimethyl Derivative **5b**



A noteworthy feature of this reaction is the facile formation of a seven-membered ring by the carbon tether.[8] This is probably due to the rigid and planar structure of the alkyne−$Co_2(CO)_6$ moiety with its substituent angle of ca. 140°,[1] which makes seven-membered ring formation easier.[9] Combined with the simple preparation of the starting material possible using the coupling reaction of alkynes, and the possibility for the use of the alkyne−$Co_2(CO)_6$ complex part for further transformations,[10] this reaction should find abundant use as a method for the construction of complex polycyclic carbon frameworks containing a seven-membered ring.

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Supporting Information Available: Preparation of the Diels−Alder precursors, experimental procedure for the Diels−Alder reaction, and spectral and analytical data for these compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(6) Acceleration of the intramolecular Diels−Alder reaction of furan derivatives by absorbing the substrate on silica gel or Florisil has several precedents. See the following examples: (a) Clercq, P. J. D.; Royen, L. A. V. *Synth. Commun*. **1979**, *9*, 771. (b) Wang, W. B.; Roskamp, E. J. *Tetrahedron Lett.* **1992**, *33*, 7631. (c) Rogers, C.; Keay, B. A. *Can. J. Chem.* **1993**, *71*, 611.

(7) **6a** was obtained as a single diastereomer, whose stereochemistry was assigned to be the same as that of **3** on the basis of comparison of their ^1H NMR spectra. **6b** was obtained as a mixture of diastereomers in about a 3:1 ratio. The major isomer has the same stereochemistry as that of **3**.

(8) Seven-membered ring formation by the intramolecular Diels−Alder reaction of furan derivatives is difficult, and only a few examples are known. See for examples: (a) Parker, K. A.; Adamchuk, M. R. *Tetrahedron Lett.* **1978**, 1689. (b) Harwood, L. M.; Jackson, B.; Jones, G.; Prout, G.; Thomas, R. M.; Witt, F. J. *J. Chem. Soc., Chem. Commun.* **1990**, 608.

(9) Formation of medium-sized cyclic alkyne−$Co_2(CO)_6$ complexes has several precedents, where in almost all cases a Nicholas-type reaction was employed for the cyclization. See for example: (a) Nakamura, T.; Matsui, T.; Tanino, K.; Kuwajima, I. *J. Org. Chem.* **1997**, *62*, 3032. (b) Isobe, M.; Hosokawa, S.; Kira, K. *Chem. Lett.* **1996**, 473. (c) Tanaka, S.; Isobe, M. *Synthesis* **1995**, 859. (d) Caddick, S.; Delisser, V. M. *Tetrahedron Lett.* **1997**, *38*, 2355. (e) Jamison, T. F.; Shambayati, S.; Crowe, W. E.; Schreiber, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 4353. (f) Magnus, P.; Miknis, G. F.; Press: N. J.; Grandjean, D.; Taylor G. M.; Harling, J. *J. Am. Chem. Soc.* **1997**, *119*, 6739. (g) Green, J. R. *Chem. Commun.* **1998**, 1751. (h) Iwasawa, N.; Satoh, H. *J. Am. Chem. Soc.* **1999**, *121*, 7951.

(10) (a) Caffyn, A. J. M.; Nicholas, K. M. In *Comprehensive Organometallic Chemistry II, Vol 12: Transition Metal Alkyne Complexes: Transition Metal-stabilized Propargyl System*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon Press: Oxford, 1995; p 685. (b) Schore, N. E. In *Comprehensive Organometallic Chemistry II, Vol 12: Transition Metal Alkyne Complexes: Pauson-Khand Reaction*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon Press: Oxford, 1995; p 703.