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Ketene Is a Dienophile for [4 + 2] (Diels−Alder) Reactions across Its C=O Bond[1]

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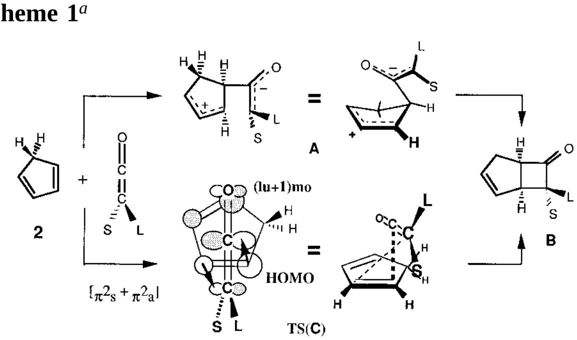
We report herein a new feature that ketenes[2] take part in 1,4-cycloaddition with 1,3-dienes, followed by subsequent (3,3) sigmatropic (Claisen) rearrangement to give 1,2-adducts.

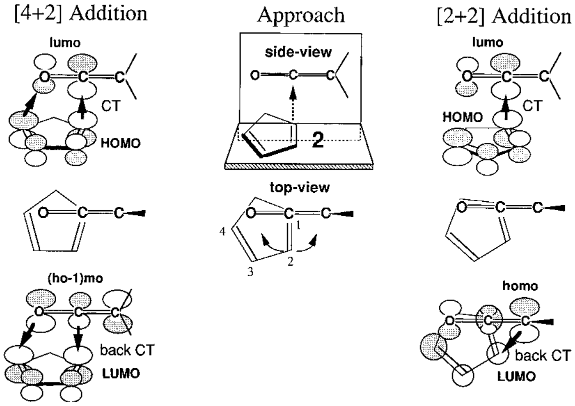
It has been well-known that allenes[3] (>C=C=C<) and heterocumulenes[4] [such as ketenimines (>C=C=N−) and keteniminium ions (>C=C=N$^+$<)] participate in Diels−Alder reactions ([4 + 2] cycloadditions) with conjugated dienes. Carbonyl groups of ketenes also react with dienes,[2,5,6] in what have been, however, regarded as exceptional examples. In many cases, ketenes (>C=C=O) do not react as dienophiles but lead to products resulting from 1,2-addition ([2 + 2] cycloaddition) to the C=C bond of 1,3-dienes.[2,4,7] For example, diphenylketene (**1a**) does not add as a dienophile to the 1,4-positions of cyclopentadiene (**2**) but yields cyclobutanone (**4a**) (Staudinger reaction) exclusively.[2,8,9] Scheme 1 illustrates traditional mechanism of the Staudinger reaction for the cycloadduct **B**. One pathway includes a zwitterionic intermediate **A** and is of two steps.[2b,7,10] The other is for a concerted $[_{\pi}2_{s} + {}_{\pi}2_{a}]$ cycloaddition via a transition state (TS) **C**. The $[_{\pi}2_{s} + {}_{\pi}2_{a}]$ path has been shown to be unlikely by experimental studies[10c−e] and various theoretical calculations.[11,12]

Scheme 1[a]



[a] The conventional scheme for the cycloaddition reaction of ketenes toward conjugated 1,3-dienes to give a [2 + 2] cycloadduct (**B**) through either a two-step mechanism via a zwitterionic intermediate (**A**) or a concerted $[_{\pi}2_{s} + {}_{\pi}2_{a}]$ pathway via a transition state **C**. TS(**C**) shows the charge-transfer model from the HOMO of **2** to the (lu + 1)mo of ketene. L and S stand for large and small substituents, respectively.

Scheme 2[a]



[a] An FMO selectivity between [2 + 2] and [4 + 2] cycloadditions between ketene and cyclopentadiene **2**. This selectivity corresponds to the counterclockwise and clockwise rotations of the pentadiene ring, respectively. HOMO and LUMO belong to **2**, and homo and lumo to the ketene. CT stands for the charge transfer.

Yet, it is a primitive question why ketenes do not undergo [4 + 2] cycloadditions in most cases. Scheme 2 illustrates frontier molecular orbital (FMO) interactions for the selectivity of [4 + 2] and [2 + 2] cycloadditions between ketene and **2**. While both additions are basically possible, the [4 + 2] one with in-phase FMO overlaps is better than the [2 + 2] one.[13,14] The latter path suffers the perpendicular overlap between the highest occupied MO (homo) of ketene and the lowest unoc-

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(1) Dedicated to Professor Emeritus Rolf Huisgen, Universität München, on the occasion of his 76th birthday and lifelong career in organic chemistry. For his biography and research history, see: Huisgen, R. The Adventure Playground of Mechanisms and Novel Reactions. In *Profiles, Pathways, and Dreams: Autobiographies of Eminent Chemists*; Seeman, J. I., Ed.; American Chemical Society: Washington, DC, 1994.

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(12) Recently, [2 + 2] paths between **1b** and **2** (not the [2 + 2] one in Scheme 2) have been reported. Salzner, U.; Bachrach, S. M. *J. Org. Chem.* **1996**, *61*, 237−242.

(13) Yamabe, S.; Minato, T.; Osamura, Y. *J. Chem. Soc., Chem. Commun.* **1993**, 450−452. While this [2 + 2] path is concerned with mutual charge transfers, the $[_{\pi}2_{s} + {}_{\pi}2_{a}]$ path in Scheme 1 is concerned with the one-sided transfer.

(14) The transition state of the [2 + 2] cycloaddition was determined precisely by Wang and Houk. Wang, X.; Houk, K. N. *J. Am. Chem. Soc.* **1990**, *112*, 1754−1756.

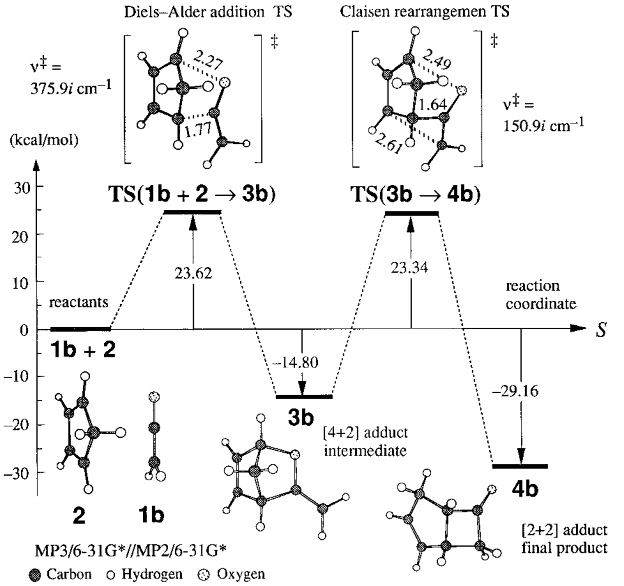
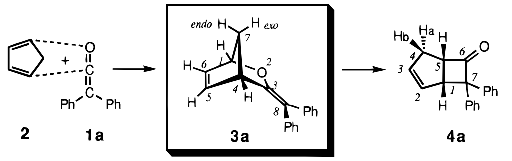


Figure 1. Energy diagram of the Diels−Alder reaction between ketene (**1b**) and cyclopentadiene (**2**) and the subsequent Claisen rearrangement to yield the [2 + 2] cycloadduct (**4b**). Optimized geometries were determined with MP2/6-31G*, and energies were obtained with single-point calculations of MP3/6-31G* on the MP2/6-31G* geometries, MP3/6-31G*// MP2/6-31G*. Distances attached to two TSs are in Å. MP2/6-31G* single-point self-consistent reaction field (SCRF) (solvent effect, dielectric constant $\epsilon = 9.08$[16] for CH$_2$Cl$_2$) stabilization energies are 1.23 kcal/mol at TS(**1b** + **2** → **3b**) and 1.07 kcal/mol at TS(**3b** → **4b**), respectively. This small SCRF effect arises from relatively small changes of MP2/6-31G* dipole moments (in D), 3.08 for TS(**1b** + **2** → **3b**), 2.08 for **3b**, 2.98 for TS(**3b** → **4b**), and 2.63 for **4b**.

cupied MO (LUMO) of **2** in the back charge transfer (CT). FMO predicts that cycloadditions should occur between the carbonyl (not C═C) bond of ketene and 1,3-diene of **2**.

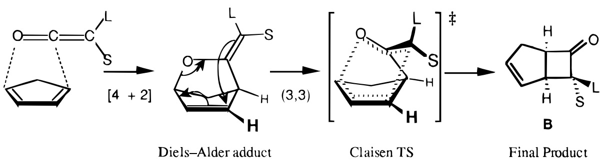
In order to test the prediction in Scheme 2, ab initio calculations[15] have been performed for all cycloadditions ([2 + 2] and [4 + 2]) between the parent ketene (**1b**) and **2**. We have sought their TSs and compared activation energies. Surprisingly, a TS of the target [2 + 2] cycloaddition competing with the [4 + 2] one (in Scheme 2) has not been found. As expected in Scheme 2, the [4 + 2] addition is calculated to be of the smallest activation energy among all the computationally obtained cycloadditions.[12] Next, interest is directed to interrelation between the [4 + 2] cycloadduct and the experimentally observed [2 + 2] one. The [4 + 2] adduct can isomerize to the [2 + 2] one via a (3,3) sigmatropic (here called Claisen) rearrangement. MP3/6-31G*// MP2/6-31G* energies are shown in Figure 1. The FMO theory and the computational results provide a new mechanism independent of those in Scheme 1.

Scheme 3[a]



[a] Experimental detection of an initially formed [4 + 2]-type cycloadduct (**3a**) from the reactions of diphenylketene (**1a**) with cyclopentadiene (**2**). The initial cycloadduct undergoes a (3,3) sigmatropic rearrangement to give the final product, cyclobutanone (**4a**). Conditions: (i) **1a** + **2** → **3a**, **1a** (1 equiv), **2** (1.1 equiv), CD$_2$Cl$_2$, −20 °C, 3 h, maximum concentration for **3a**, 43%; (ii) **1a** + **2** → **4a**, **1a** (1 equiv), **2** (3 equiv), CH$_2$Cl$_2$, 20 °C, 2 h, 98−99%.

Scheme 4[a]



[a] Stereochemistry of cycloadditions of ketenes to cyclopentadiene. L and S are large and small substituents, respectively.

The second test for Scheme 2 is a low-temperature experiment. Diphenylketene (**1a**) reacts smoothly with cyclopentadiene (**2**) *at room temperature* to give the 1,2-cycloadduct[17] (**4a**). However, careful experiment with the low-temperature NMR spectroscopies at −30 °C has detected a metastable reaction intermediate, α-methylenedihydropyran **3a** (Scheme 3). Modern NMR (^{1}H and ^{13}C) spectroscopies[18] have demonstrated that the structure of the intermediate **3a** is the 1,4-cycloadduct[19] **4a** across the C═O bond of the ketene. Intermittent ^{1}H NMR spectroscopic monitoring at low temperatures has also proved that **3a** is converted gradually to the final product, cyclobutanone **4a**, when the reaction temperature is elevated above −30 °C. Surprisingly, the maximum concentration of the [4 + 2]-cycloadduct **3a** exceeds 40% of the reaction mixture at a stage (3 h at −20 °C) of the reaction (see Table 1 in the supporting information). Thus, the reaction of **1a** with **2** is a Diels−Alder one, followed by a Claisen rearrangement.

The [4 + 2] adduct isomerizes to the [2 + 2] one due to the remarkably large difference of average bond energies between C−O (85.5 kcal/mol) and C═O (178 kcal/mol). The great stability by the carbonyl bond must be recovered starting from the α-methylenedihydropyran intermediate **3a**. Thus, the first step [4 + 2] is kinetically (FMO) controlled, and the second step (3,3) is thermodynamically controlled.

In conclusion, we have proposed a new two-step reaction mechanism (Scheme 4) composed of the [4 + 2] addition and the subsequent (3,3) sigmatropic rearrangement. Historically, by the high-temperature experiment, this combination has been overlooked. In simple ketene−diene systems, two-step processes seem to mean not an intervention of zwitterionic intermediates but an addition−isomerization combination.

Acknowledgment. We appreciate the referees' indication of important precedents of [4 + 2] cycloadditions across carbonyl groups of ketenes.

Supporting Information Available: *Z*-Matrices of optimized geometries of the six species shown in Figure 1, NMR (^{13}C and ^{1}H) spectral charts for the key intermediate **3a** (Lorentz-transformed spectrum and those resolution-enhanced with the sine-bell wind function), ^{1}H NMR monitoring result (charts and table) of the reaction (**1a** + **2** → **3a** → **4a**), and survey of precedent Diels−Alder reactions (15 pages). See any current masthead page for ordering and Internet access instructions.

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(15) GAUSSIAN 92 was used for calculations. Frisch, M. J.; Trucks, G. W.; Head-Gordon, M.; Gill, P. M. W.; Wong, M. W.; Foresman, J. B.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Raghavachari, K.; Binkley, J. S.; Gonzalez, C.; Martin, R. L.; Fox, D. J.; DeFrees, D. J.; Baker, J.; Stewart, J. J. P.; Pople, J. A. *GAUSSIAN 92*, Revision C; Gaussian, Inc.: Pittsburgh, PA, 1992.

(16) This value of the dielectric constant is taken from a recent theoretical study. Lecea, B.; Arrieta, A.; Lopez, X.; Ugalde, J. M.; Cossio, F. P. *J. Am. Chem. Soc.* **1995**, *117*, 12314−12321.

(17) **4a**: IR (CH$_2$Cl$_2$) $\nu_{\max}$ 1772 (s) cm^{-1} ; ^{1}H NMR (CD$_2$Cl$_2$, Me$_4$Si) δ 5.79 (tq, H-2), 5.57 (dq, H-3), 4.38 (ddt, H-1), 3.94 (ddd, H-5), 2.74 (ddtd, H-4a), 2.51 (ddq, H-4b), $J_{4a,4b} = -17.2$ Hz; ^{13}C NMR δ 212.47 (s, C═O), 134.32 (d, C-2), 131.44 (d, C-3), 80.15 (s, C-7), 58.91 (d, C-5), 49.76 (d, C-1), 34.91 (t, C-4).

(18) For accurate analyses, we have applied 1D NMR resolution-enhanced with the sine-bell wind function as well as various 2D ones.

(19) **3a**: FT-IR (CH$_2$Cl$_2$, −60 °C) $\nu_{\max}$ 1138 (s) cm^{-1}; ^{1}H NMR (CD$_2$Cl$_2$, −60 °C) δ 6.70 (ddd, H-5), 6.49 (dd, H-6), 5.40 (ddt, H-1), 3.73 (dq, H-4), 2.08 (dt, H-7-*endo*), 1.77 (dd, H-7-*exo*), $J_{7,7} = -8.5$ Hz; ^{13}C NMR (CD$_2$Cl$_2$, −60 °C) δ 150.23 (s, C-3), 138.06 (d, C-5), 133.34 (d, C-6), 110.71 (s, C-8), 84.81 (d, C-1), 53.20 (t, C-7), 49.22 (d, C-4).