Ring-Expansion of MCPs in the Presence of DIAD or DEAD and Lewis Acids

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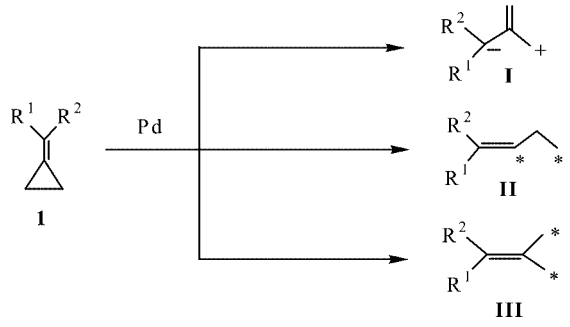
Treatment of methylenecyclopropanes (MCPs) with DIAD or DEAD in MeCN under mild conditions in the presence of Lewis acid $Zr(OTf)_4$ gave the cyclobutanone ring-expansion products in good to high yields based on the employed DIAD or DEAD. From a deuterium labeling experiment, the oxygen atom is derived from ambient water.

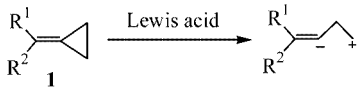
Introduction

Methylenecyclopropanes (MCPs) **1** are highly strained but readily accessible molecules that have served as useful building blocks in organic synthesis. MCPs **1** undergo a variety of ring-opening reactions because the relief of ring strain provides a potent thermodynamic driving force.[1]

Transition metal (such as Pd, Rh, Ru, and Pt) catalysis of reactions of MCPs with various reactants has attracted much attention,[2] first place being held by Pd^0- or Pd^{II}-catalyzed ring-opening reactions (Scheme 1). We recently found that Lewis acid-catalyzed [$M(OTf)_n$, M = Yb, Sc, Sn, etc.] ring-opening reactions between MCPs **1** and alcohols and other nucleophiles took place in a different, novel manner to give the corresponding ring-opened products in good yields under mild conditions (Scheme 2).[3] This interesting result encouraged us to investigate further the Lewis acid-catalyzed reactions between MCPs **1** and other reactants. In this paper we wish to report an unprecedented Lewis acid-catalyzed ring-expansion reaction of MCPs **1** in the presence of diisopropyl azodicarboxylate (DIAD) or diethyl azodicarboxylate (DEAD).[4,5]



Scheme 1



Scheme 2

Results and Discussion

During our investigations into the ring-opening reaction of MCPs 1 in the presence of various Lewis acids (50 mol %), we found that the Lewis acid-catalyzed reaction of diphenylmethylenecyclopropane **1a** in the presence of diisopropyl azodicarboxylate (DIAD) in CH_3CN as a solvent produced a ring-expansion product cyclobutanone **2a** (MCP/DIAD, 2.5:1). The roles played by the Lewis acids in this reaction were critical, no reaction occurring in their absence (Table 1, entry 1). When $Sn(OTf)_2$, $Cu(OTf)_2$, $Sc(OTf)_3$, $Zn(OTf)_2$, or $BF_3{\cdot}Et_2O$ (50 mol %) were employed as Lewis acids, **2a** was obtained in low to moderate yields based on the employed DIAD (Table 1, entries 2−3, 6−8). The Brønsted acid CF_3SO_3H (HOTf) did not catalyze the reaction (Table 1, entry 5). Use of $Zr(OTf)_4$ as a Lewis acid at room temperature for 48 h, though, resulted in **2a** being produced in 100% yield based on the employed DIAD (Table 1, entry 4). In other solvents such as acetone or THF, 2a was obtained in 82% and 69% yields, respectively, under otherwise the same conditions (Table 1, entries 9−10). Control experiment showed that: i) no reaction occurred in the absence of DIAD, and ii) **2a** was formed in relatively lower yields (78% and 68% respectively) when anhydrous CH_3CN was used as a solvent under the optimized

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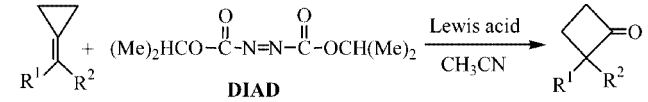
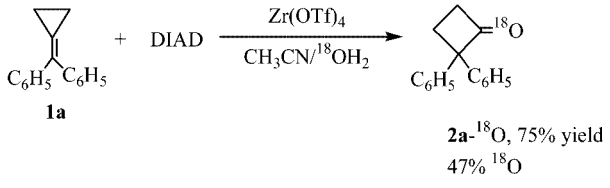
conditions or in the presence of molecular sieves (4 Å), even with prolonged reaction times. In addition, no reaction occurred when the procedure was carried out under oxygen atmosphere in the absence of catalyst. These results suggest that the oxygen atom of **2a** might be derived from water present in solvent and the ambient environment. In order to clarify the source of the oxygen in this reaction, we carried out the $Zr(OTf)_4$-catalyzed reaction of MCP **1a** in the presence of $^{18}OH_2$ and DIAD (Scheme 3).[6] As a result, we found that **2a**-^{18}O was formed in 75% yield,[7] its ^{18}O content being 47% (Scheme 3)[8] (see Supporting Information). From this result we can conclude that the oxygen atom is derived from the ambient water during the reaction.

Table 1. The effects of various Lewis acids in the reaction between MCP **1a** and DIAD; a) the reaction was carried out with MCP **1a**/DIAD = 5:2 in the presence of Lewis acid (50 mol %) at room temperature for 48 h; b) isolated yields based on employed DIAD; c) the reaction was carried out in THF; d) the reaction was carried out in acetone



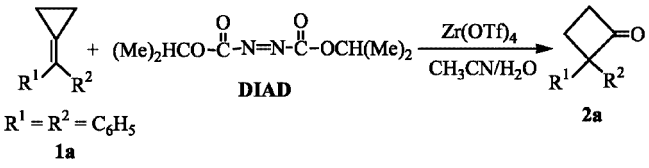
entry[a]	Lewis acid	yield/%[b]
1	–	NR
2	$Sc(OTf)_3$	41
3	$Cu(OTf)_2$	81
4	$Zr(OTf)_4$	100
5	HOTf	NR
6	$BF_3 \cdot OEt_2$	58
7	$Sn(OTf)_2$	17
8	$Zn(OTf)_2$	23
9	$Zr(OTf)_4$	69[c]
10	$Zr(OTf)_4$	82[d]



Scheme 3

In order further to clarify the effect of water on this ring-expansion of MCPs **1**, we also carried out the reaction in freshly distilled MeCN containing various concentrations of water. The results, including the result without the addition of water (Table 2, entry 1), are summarized in Table 2. As can be seen, the concentration of water has only a slight effect on this reaction (Table 2, entries 2−5), 1.0 equiv. of water being enough to give **2a** in high yield in the ring-expansion reaction.

Table 2. The effect of different concentrations of water in the reaction between MCP **1a** and DIAD in the presence of $Zr(OTf)_4$; a) all reactions were carried out with MCP **1a**/DIAD = 0.5:0.2 mmol in the presence of $Zr(OTf)_4$ (0.1 mol) under an argon atmosphere at room temperature for 36 h; b) isolated yields based on employed DIAD

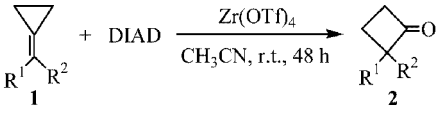


entry[a]	Water	yield/%[b]
1	–	78
2	1 eq.	96
3	2 eq.	94
4	4 eq.	84
5	8 eq.	90

Moreover, to gauge the repeatability of this interesting ring-expansion reaction, we used freshly distilled MeCN as the solvent and carried out this reaction three times under argon atmosphere with subsequent hydrolysis of the reaction mixture with water. It was found that **2a** was formed in 80~84% yields.[9] All these results suggest that this interesting ring expansion reaction is reproducible.

For other aromatic MCPs **1b-g** (both R^1 and R^2 are aromatic groups), the reactions proceeded very well to give the corresponding cyclobutanones **2b-g** in good to high yields based on the employed DIAD under the optimized conditions (Table 3, entries 1−6). For MCPs **1h-k** (R^1 is an aromatic group and R^2 is an aliphatic group), the corre-

Table 3. The ring-expansion of MCPs **1** in the presence of DIAD and $Zr(OTf)_4$; a) isolated yields based on DIAD

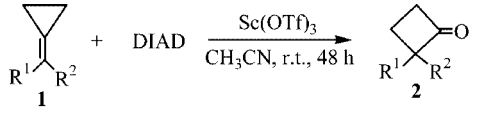


entry	R^1/R^2	substrate	yield/%[a] 2
1	*p*-$MeOC_6H_4$/*p*-$MeOC_6H_4$	**1b**	**2b**, 53
2	*p*-$MeOC_6H_4$/C_6H_5	**1c**	**2c**, 99
3	*p*-MeC_6H_4/*p*-MeC_6H_4	**1d**	**2d**, 92
4	*o*-ClC_6H_4/C_6H_5	**1e**	**2e**, 86
5	*p*-ClC_6H_4/*p*-ClC_6H_4	**1f**	**2f**, 91
6	*p*-FC_6H_4/*p*-FC_6H_4	**1g**	**2g**, 78
7	*p*-$EtOC_6H_4$/Me	**1h**	**2h**, 42
8	*m,p*-(OCH_2CH_2O)-C_6H_3/Me	**1i**	**2i**, 91
9	*p*-MeC_6H_4/Me	**1j**	**2j**, 57
10	*p*-BrC_6H_4/Me	**1k**	**2k**, 71

sponding cyclobutanones **2h-k** were also obtained in moderate to high yields under the same conditions (Table 3, entries 7−10).

On the other hand, we also found that the MCPs are rather sensitive to the Lewis acid employed in this reaction. With MCPs **1b** and **1h**, use of $Sc(OTf)_3$ (50 mol %) − which is not as effective as $Zr(OTf)_4$ in the case of MCP **1a** − as a Lewis acid gave the corresponding cyclobutanones **2b** and **2h** in higher yields than were obtained by use of $Zr(OTf)_4$ under the same conditions (Table 4, entries 1 and 4), although it was still not effective for MCPs **1d** and **1f** (Table 4, entries 2 and 3). Thus, for other MCP substrates not examined in this paper, a careful survey of the Lewis acid catalyst is likely to be required for this novel ring-expansion reaction to achieve higher yields.

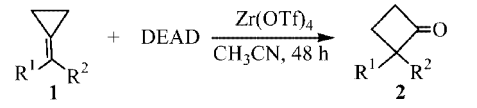
Table 4. Reactions between MCPs **1** and DIAD in the presence of $Sc(OTf)_3$; a) isolated yields based on DIAD



entry	R^1/R^2	substrate	yield/%[a]
1	*p*-$MeOC_6H_4$/*p*-$MeOC_6H_4$	**1b**	**2b**, 94
2	*p*-MeC_6H_4/*p*-MeC_6H_4	**1d**	**2d**, 48
3	*p*-ClC_6H_4/*p*-ClC_6H_4	**1f**	**2f**, 16
4	*p*-$EtOC_6H_4$/Me	**1h**	**2h**, 61

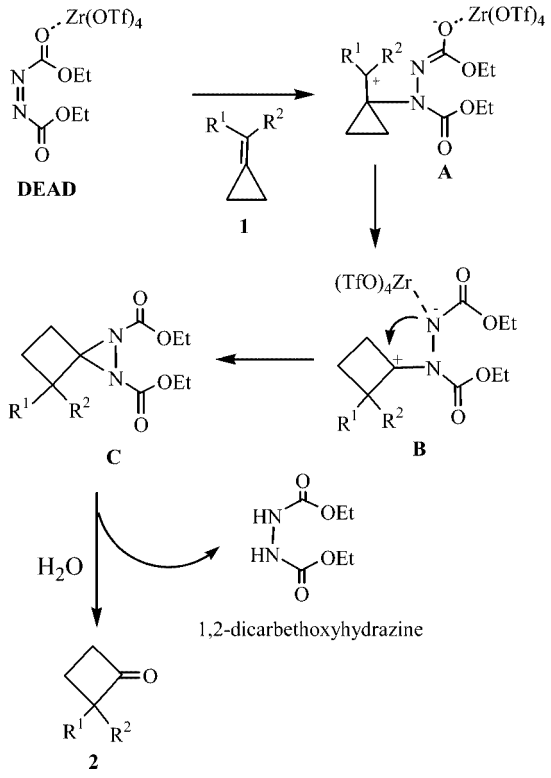
The same ring-expansion reaction can also take place with diethyl azodicarboxylate (DEAD, 40% in toluene) as a reagent; the results are shown in Table 5. However, we found that the yields of cyclobutanones **2** in the presence of Lewis acid $Zr(OTf)_4$ under the same conditions were slightly decreased (Table 5, entries 1−3). This may be because the less polar toluene solvent used for the DEAD solution disturbs this reaction to some extent.

Table 5. Reactions between MCPs **1** and DEAD in the presence of $Zr(OTf)_4$; a) isolated yields based on DEAD



entry	R^1/R^2	substrate	yield/%[a]
1	C_6H_5/C_6H_5	**1a**	**2a**, 96
2	*p*-MeC_6H_4/*p*-MeC_6H_4	**1d**	**2d**, 68
3	*p*-ClC_6H_4/*p*-ClC_6H_4	**1f**	**2f**, 52

A plausible mechanism for this ring-expansion reaction of MCPs **1** promoted by DEAD and $Zr(OTf)_4$ is shown in Scheme 4. The Lewis acid activates the DEAD towards reaction with the MCPs **1** to afford a zwitterion **A**. The rearrangement of **A** gave a ring-expansion zwitterion **B**, which is neutralized to give the intermediate **C**. Hydrolysis of **C** by ambient water produces **2** and diethyl hydrazine-1,2-dicarboxylate (see Supporting Information).[10] Quantitative GLC analysis showed that in the reaction mixture, the molar ratio of product **2a** to the formed diethyl hydrazine-1,2-dicarboxylate was 1.25 to 1 (see Supporting Information).



Scheme 4. Plausible reaction mechanism

In conclusion, we found that MCPs in the presence of DIAD or DEAD as a reagent and $Zr(OTf)_4$ as catalyst in MeCN undergo ring-expansion reactions to give cyclobutanones **2** in good to high yields. This method provides a safer and more convenient synthetic route for the synthesis of substituted cyclobutanones **2** under mild conditions than traditional procedures such as epoxidation of MCPs followed by rearrangement.[5] The Lewis acid, DIAD, and ambient moisture are crucial for this interesting ring-expansion reaction of MCPs. Efforts to elucidate the mechanistic details of this reaction and to delineate its scope and limitations are underway.

Experimental Section

General Remarks: ^1H NMR spectra were recorded on a 300 MHz spectrometer in $CDCl_3$ with tetramethylsilane as the internal standard. Infrared spectra were measured on a PERKIN-ELMER 983 spectrometer. Mass spectra were recorded with a HP-5989 instrument and HRMS was measured on a Finnigan MA^+ mass spectrometer. Satisfactory CHN microanalyses were obtained with a Carlo-Erba 1106 analyzer. Melting points are uncorrected. All reactions were monitored by TLC with Huanghai GF254 silica gel-coated plates. Flash column chromatography was carried out on 300−400 mesh silica gel.

General Procedure: The MCPs (0.50 mmol), DIAD (0.20 mmol), Lewis acid catalyst (0.10 mmol), and distilled acetonitrile (CH_3CN) (1.0 mL) were placed in a Schlenk reaction tube under ambient atmosphere. The mixture was stirred at room temperature. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (SiO2).

The Ring-Expansion of MCP 1a in the Presence of $Zr(OTf)_4$, DIAD, and $H_2{}^{18}O$: MCP **1a** (0.5 mmol), DIAD (0.2 mmol), $Zr(OTf)_4$ (0.1 mmol), freshly distilled acetonitrile (CH_3CN) (1.0 mL), and $H_2{}^{18}O$ (0.5 mmol) were placed in a Schlenk reaction tube under argon atmosphere. The mixture was stirred at room temperature under argon atmosphere. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography (SiO_2).

2,2-Diphenylcyclobutanone (2a): Colorless liquid and a known compound. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ = 2.83 (t, *J* = 8.1 Hz, 2 H, CH_2), 3.15 (t, *J* = 8.1 Hz, 2 H, CH_2), 7.17−7.39 (m, 10 H, Ar) ppm [ref.: J. K. Crandall, W. W. Conover, *J. Org. Chem.* **1978**, *43*, 3533]. ^{1}H NMR ($CDCl_3$, 60 MHz, TMS): δ = 2.76 (t, *J* = 8.5 Hz, 2 H, CH_2), 3.08 (t, *J* = 8.5 Hz, 2 H, CH_2), 7.0−7.8 (m, 10 H, Ar)] ppm. ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ = 25.50, 43.33, 76.05, 126.32, 126.85, 128.66, 142.00, 209.09 ppm. MS (%): *m*/*z* = 222 [M^+] (1.68), 180 (100).

2,2-Bis(4-methoxyphenyl)cyclobutanone (2b): White solid, M.p. 63−64 °C. IR (CH_2Cl_2): ṽ = 1778, 1509, 1409, 1266, 739 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ = 2.75 (t, *J* = 8.4 Hz, 2 H, CH_2), 3.14 (t, *J* = 8.4 Hz, 2 H, CH_2), 3.75 (s, 6 H, 2 CH_3O), 6.83 (d, *J* = 9.0 Hz, 4 H, Ar), 7.25 (d, *J* = 9.0 Hz, 4 H, Ar) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ = 25.70, 43.21, 55.12, 74.64, 113.90, 127.43, 134.35, 158.25, 209.73 ppm. MS (%): *m*/*z* = 282 [M^+] (4.74), 240 (98.20), 223 (100). $C_{18}H_{18}O_3$: calcd. C 76.57, H 6.42%; found C 76.28, H 6.28%.

2-(4-Methoxyphenyl)-2-phenylcyclobutanone (2c): Colorless liquid, IR (CH_2Cl_2): ṽ = 1779, 1608, 1510, 1266, 739 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ = 2.81 (t, *J* = 9.8 Hz, 2 H, CH_2), 3.17(t, *J* = 9.8 Hz, 2 H, CH_2), 3.77 (s, 3 H, OCH_3), 6.85 (d, *J* = 9 Hz, 2 H, Ar), 7.28−7.38 (m, 7 H, Ar) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ = 25.62, 43.30, 55.19, 75.43, 113.99, 126.32, 126.78, 127.50, 128.63, 134.14, 142.29, 158.37, 209.22 ppm. MS (%): *m*/*z* = 252 [M^+] (5.84), 210 (100). HRMS calcd. for C17H16O2: 252.1150; found: 252.1138.

2,2-Bis(4-methylphenyl)cyclobutanone (2d): Colorless liquid, IR (CH_2Cl_2): ṽ = 1781, 1510, 1266, 739 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ = 2.28 (s, 6 H, 2 CH_3), 2.78 (t, *J* = 8.7 Hz, 2 H), 3.13 (t, *J* = 8.7 Hz, 2 H), 7.10 (d, *J* = 8.7 Hz, 4 H, Ar), 7.24 (d, *J* = 8.7 Hz, 4 H, Ar) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ = 21.26, 25.87, 43.57, 75.88, 126.52, 129.63, 136.73, 139.60, 209.72 ppm. MS (%): *m*/*z* = 250 [M^+] (2.28), 208 (100). HRMS calcd. for $C_{18}H_{18}O$: 250.1358; found: 250.1330.

2-(2-Chlorophenyl)-2-phenylcyclobutanone (2e): Pale yellow liquid, IR (CH_2Cl_2): ṽ = 1780, 1597, 1265, 739 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ = 2.71−2.78 (m, 1 H), 3.15−3.31 (m, 3 H), 7.21−7.39 (m, 8 H, Ar), 7.77−7.79 (m, 1 H, Ar) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ = 24.35, 43.01, 75.15, 120.34, 126.79, 126.95, 128.13, 128.43, 128.48, 131.15, 133.28, 137.83, 139.40, 207.70 ppm. MS (%): *m*/*z* = 221 [M^+ − Cl] (36.98), 179 (100). HRMS calcd. for $C_{16}H_{13}ClO$: 221.0966; found: 221.0990 (M^+ − Cl).

2,2-Bis(4-chlorophenyl)cyclobutanone (2f): White solid, M.p. 103−105 °C. IR (CH_2Cl_2): ṽ = 1784, 1491, 1401, 1093, 825 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ = 2.80 (t, *J* = 8.4 Hz, 2 H), 3.19 (t, *J* = 8.4 Hz, 2 H), 7.28 (s, 8 H, Ar) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ = 25.55, 43.54, 74.67, 127.68, 128.97, 132.94, 139.99, 207.87 ppm. MS (%): *m*/*z* = 290 [M^+] (0.50), 248 (100). $C_{16}H_{12}Cl_2O$: calcd. C 66.00, H 4.15%; found C 66.20, H 4.07%.

2,2-Bis(4-flurophenyl)cyclobutanone (2g): Colorless liquid, IR (CH_2Cl_2): ṽ = 1782, 1597, 1266, 742 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ = 2.80 (t, *J* = 8.7 Hz, 2 H, CH_2), 3.19 (t, *J* = 8.7 Hz, 2 H, CH_2), 6.95−7.06 (m, 4 H, Ar), 7.28−7.35 (m, 4 H, Ar) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ = 25.80, 43.41, 74.66, 115.60 (d, $J_{C,F}$ = 20.6 Hz), 127.94 (d, $J_{C,F}$ = 8.8 Hz), 137.71, 161.67 (d, $J_{C,F}$ = 245.9 Hz), 208.30 ppm. MS (%): *m*/*z* = 258 [M^+] (0.51), 216 (100). HRMS calcd. for $C_{16}H_{12}F_2O$: 258.0856; found: 258.0879.

2-(4-Ethoxyphenyl)-2-methylcyclobutanone (2h): Colorless liquid, IR (CH_2Cl_2): ṽ = 1778, 1509, 1266, 739 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ = 1.40 (t, *J* = 6.9 Hz, 3 H, CH_3), 1.43 (s, 3 H, CH_3), 2.12 (dt, *J* = 10.5, 6.9 Hz, 1 H), 2.48 (dt, *J* = 10.8, 6.6 Hz, 1 H), 2.98−3.22 (m, 2 H), 4.01 (q, *J* = 6.9 Hz, 2 H, OCH_2), 6.86 (d, *J* = 9.0 Hz, 2 H, Ar), 7.26 (d, *J* = 8.4 Hz, 2 H, Ar) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ = 14.83, 25.53, 26.18, 42.56, 63.40, 67.33, 114.48, 126.65, 134.27, 157.63, 212.67 ppm. MS (%): *m*/*z* = 204 [M^+] (17.98), 162 (100). HRMS calcd. for $C_{13}H_{16}O_2$: 204.1150; found: 204.1163.

2-Benzo[1,3]dioxol-5-yl-2-methylcyclobutanone (2i): Colorless liquid, IR (CH_2Cl_2): ṽ = 2959, 2923, 2864, 1781, 1514, 1446, 1394, 1109, 1095, 1055, 817 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ = 1.50 (s, 3 H), 2.07−2.17 (m, 1 H), 2.40−2.49 (m, 1 H), 2.98−3.22 (m, 2 H), 5.93 (dd, *J* = 1.5, 2.1 Hz, 2 H, Ar), 6.75−6.82 (m, 2 H, Ar), 6.86 (d, *J* = 1.5 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ = 25.76, 26.39, 42.47, 67.63, 100.96, 106.48, 108.21, 118.51, 136.30, 146.21, 147.76, 212.11 ppm. MS (%): *m*/*z* = 204 [M^+] (18.06), 162 (100). HRMS calcd. for $C_{12}H_{12}O_3$: 204.0786; found: 204.0778.

2-Methyl-2-*p*-tolylcyclobutanone (2j): Colorless liquid, IR (CH_2Cl_2): ṽ = 2960, 2922, 1773, 1608, 1505, 1485, 1434, 1239, 1108, 1038, 936, 811 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ = 1.52 (s, 3 H), 2.09−2.18 (m, 1 H), 2.33 (s, 3 H), 2.45−2.55 (m, 1 H), 2.98−3.22 (m, 2 H), 7.15 (d, *J* = 8.4 Hz, 2 H, Ar), 7.25 (d, *J* = 8.1 Hz, 2 H, Ar) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ = 20.98, 25.50, 26.25, 42.58, 67.75, 125.50, 129.27, 136.33, 139.40, 212.51 ppm. MS (%): *m*/*z* = 174 (M^+) [4.11], 132 (100). HRMS calcd. for $C_{12}H_{14}O$: 174.1045; found: 174.1023.

2-(4-Bromophenyl)-2-methylcyclobutanone (2k): Yellow liquid, IR (CH_2Cl_2): ṽ = 2961, 2924, 2859, 1775, 1489, 1396, 1245, 1096, 1009, 823 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS): δ = 1.52 (s, 3 H), 2.12−2.21 (m, 1 H), 2.42−2.51 (m, 1 H), 2.98−3.26 (m, 2 H), 7.24 (d, *J* = 8.7 Hz, 2 H, Ar), 7.46 (d, *J* = 8.4 Hz, 2 H, Ar) ppm. ^{13}C NMR ($CDCl_3$, 75 MHz, TMS): δ = 25.32, 26.34, 42.60, 67.40, 120.58, 127.37, 131.63, 141.34, 211.51 ppm. MS (%): *m*/*z* = 238 [M^+] (100), 196 (66.00). HRMS calcd. for $C_{11}H_{11}BrO$: 237.9993; found: 237.9996.

Supporting Information Available: ^{13}C NMR charts of spectroscopic data of **2a**−**k** and GLC and GC-MS data for the formation of diethyl hydrazine-1,2-dicarboxylate and ^{18}O-labeled cyclobutanone (see also the footnote on the first page of this article).

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[6] $H_2{}^{18}O$ was purchased from Aldrich Co. The ^{18}O content in the product was determined by magnetic mass spectroscopy. We found by mass spectroscopy that the relative abundance of 222 (*m*/*e* is 0.84 (ionic flux: 23281) and that of 224 is 0.76 (ionic flux: 20775). From this result we confirmed by calculation that the ^{18}O content is 47.2%, which greatly exceeds the natural ^{18}O content in **2**.

[7] We believe that the low ^{18}O content is due to scrambling of the oxygen atom ^{16}O by ambient water ($H_2{}^{16}O$) during the reaction.

[8] The lower yield in relation to that shown in Table 1, entry 4 may be caused by the primary or secondary isotope effect. [8a] K. B. Wiberg, *Chem. Rev.* **1955**, *55*, 713. [8b] F. H. Westheimer, *Chem. Rev.* **1961**, *61*, 265. [8c] For a review of secondary isotope effects. See: E. A. Halevi, *Prog. Phys. Org. Chem.* **1963**, *1*, 109. [8d] A. J. Streitwieser, R. H. Jagow, R. C. Fahey, S. Suzuki, *J. Am. Chem. Soc.* **1958**, *80*, 2326.

[9] Actually, in order to remove the effect of the quality of the solvent (MeCN), we carried out the reactions by use of distilled MeCN under ambient atmosphere for other MCPs **1**. The results are summarized in Tables 3−5. As can be seen from these Tables, this interesting ring-expansion reaction is also reproducible for various MCPs **1**.

[10] The formation of diethyl hydrazine-1,2-dicarboxylate was confirmed by GLC and GC-MS. Quantitative analysis has also been carried out (see Supporting Information).

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