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Organoselenium-Catalyzed Oxidative Ring Expansion of Methylenecyclopropanes with Hydrogen Peroxide

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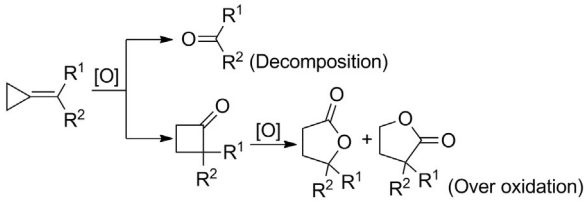
Catalyst screening and optimization of reaction conditions allowed control of the organoselenium-catalyzed oxidative ring expansion of highly active methylenecyclopropanes to give substituted cyclobutanones selectively. This protocol employs H_2O_2 as a clean oxidant and generates no waste and, therefore, provides green access to useful, but not readily available, substituted cyclobutanones under mild conditions.

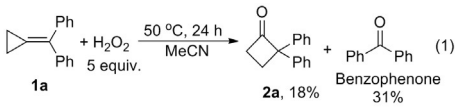
Methylenecyclopropanes (MCPs) are highly strained but readily available building blocks that have been widely employed to synthesize a variety of useful compounds.[1,2] Ring-expansion reactions of MCPs[1d,3,4] are significant, because they provide more opportunities to construct difficult-to-access four-membered-ring structures that widely exist in bioactive intermediates in drug discovery.[5] Among the reported works, the oxidative ring expansion of MCPs to useful substituted cyclobutanones has attracted much attention during the past decade.[4] In 2004, Shi et al. reported the Lewis acid mediated ring expansion of MCPs with the use of either diisopropyl azodicarboxylate or diethyl azodicarboxylate.[4a] Later, Huang et al. found that MCPs could be oxidized by Ce^{IV} to produce cyclobutanones in moderate yields through a single-electron-transfer mechanism.[4b] The reaction could be improved with the assistance of O_2.[4c] These pioneering methods provide convenient access to substituted cyclobutanones. However, they require the use of an excess amount of a chemical oxidant, which inevitably results in the generation of waste; furthermore, the substrates are limited to disubstituted MCPs. As such, there is still sufficient room for further improvement.

On the other hand, the chemistry of organoselenium compounds has been developing rapidly in recent years.[6,7] The ecofriendly aspects of this field have attracted much attention.[8–11] Besides, because of its clean procedures and transition-metal-free conditions in addition to the fact that the catalyst element can be metabolized and is safe to the environment,[12] organoselenium catalysis has been noted as a potential alternative for transition-metal-catalyzed reactions in the synthesis of medicines.[9–11] During our continuous studies on green synthetic methodologies, we performed a series of organoselenium-catalyzed transformations by using H_2O_2 as a clean oxidant.[11] On this basis, we envisioned that the oxidative ring expansion of MCPs to cyclobutanones might be achieved by an organoselenium-catalyzed method by using H_2O_2 as the oxidant. The organoselenium-catalyzed oxidation of simple alkenes by H_2O_2 has already been reported,[10j,11g,h] but its application to the ring expansion of MCPs is still unknown. Given that MCPs are highly active molecules with multiple reaction sites and that the produced cyclobutanones may also undergo further Baeyer–Villiger oxidation,[11d,f] selective oxidation by using the strong oxidant H_2O_2 faces tremendous challenges (Scheme 1). Recently, after careful catalyst screening and optimization of the reaction conditions, we achieved the organoselenium-catalyzed selective oxidative ring expansion of MCPs by using H_2O_2 as the oxidant. Herein, we wish to report our findings.



Scheme 1. Challenges for the selective oxidation of MCPs.

The oxidation of 1,1′-(cyclopropylidenemethylene)dibenzene (**1a**) with H_2O_2 was chosen as the model reaction to optimize the reaction conditions. A blank reaction without any catalyst was initially performed, but it led to a mixture of products, in which desired product **2a** was isolated in only 18% yield and benzophenone, the decomposition product of **1a**, was obtained in 31% yield [Eq. (1)].



Then, the reaction with various organoselenium catalysts was investigated. Heating **1a** and H_2O_2 in MeCN with $(PhSe)_2$ (5 mol%) as the catalyst at 40 °C afforded desired product **2a** in 55% yield (Table 1, entry 1). The yield was enhanced to 60% at 50 °C but began to decrease at elevated temperatures (Table 1, entry 2 vs. entries 3–5). A series of organoselenium

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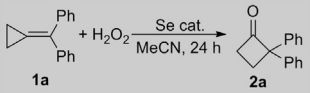
Table 1. Optimization of the reaction conditions.[a]



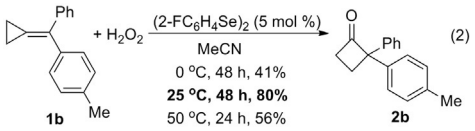
1a 2a

Entry	Se catalyst[b] [(mol%)]	*T* [°C]	H_2O_2 [equiv.][c]	Yield[d] [%]
1	$(PhSe)_2$ (5)	40	5.0	55[e]
2	$(PhSe)_2$ (5)	50	5.0	60[e]
3	$(PhSe)_2$ (5)	60	5.0	45[e]
4	$(PhSe)_2$ (5)	70	5.0	41[e]
5	$(PhSe)_2$ (5)	80	5.0	38[e]
6	$(4\text{-}MeOC_6H_4Se)_2$ (5)	50	5.0	47[e]
7	$(4\text{-}Me_2NC_6H_4Se)_2$ (5)	50	5.0	37[e]
8	$(4\text{-}FC_6H_4Se)_2$ (5)	50	5.0	63
9	$(3\text{-}FC_6H_4Se)_2$ (5)	50	5.0	65
10	$(2\text{-}FC_6H_4Se)_2$ (5)	50	5.0	71
11	$[3,5\text{-}(CF_3)_2C_6H_3Se]_2$ (5)	50	5.0	48
12	$(1\text{-}C_{10}H_7Se)_2$ (5)	50	5.0	43[e]
13	$(BnSe)_2$ (5)	50	5.0	24[e]
14	$(CySe)_2$ (5)	50	5.0	26[e]
15	R^1SeR^2 (5)[f]	50	5.0	8–23[e]
16	$(PhS)_2$ or $(PhTe)_2$ (5)	50	5.0	22–28[e]
17	SeO_2 (5)	50	5.0	17[e]
18	$(2\text{-}FC_6H_4Se)_2$ (5)	50	1.2–3.0	39–52[e]
19	$(2\text{-}FC_6H_4Se)_2$ (5)	50	6.0	60
20	$(2\text{-}FC_6H_4Se)_2$ (10)	50	5.0	59
21	$(2\text{-}FC_6H_4Se)_2$ (0.1–2)	50	5.0	24–62[e]

[a] Compound **1a** (0.3 mmol) and MeCN (1 mL) were employed. [b] Catalyst loading based on **1a**. [c] H_2O_2 molar dosage based on **1a**. [d] Yield of isolated **2a** based on **1a**. [e] Reaction was incomplete. [f] PhSePh, EtSePh, *i*PrSePh, and CySePh were employed.[13]

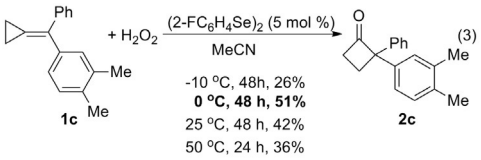
compounds were then employed as catalysts for screening. Electron-enriched diselenides gave the products in very poor yields (Table 1, entries 6 and 7), whereas electron-deficient diselenides clearly improved the reaction yield (Table 1, entries 8–10). Among the studied candidates, $(2\text{-}FC_6H_4Se)_2$ was screened to be the best catalyst, and it gave **2a** in 71% yield (Table 1, entry 10 vs. entries 8 and 9). Bearing two electron-withdrawing groups (EWGs), electron-deficient $[3,5\text{-}(CF_3)_2C_6H_3Se]_2$ led to **2a** in a very low yield and a series of unidentified byproducts were generated simultaneously (Table 1, entry 11). Bulky bis(1-naphthyl) diselenide $(1\text{-}C_{10}H_7Se)_2$ and the alkyl diselenides dibenzyl diselenide $[(BnSe)_2]$ and dicyclohexyl diselenide $[(CySe)_2]$ were not efficient catalysts for this reaction (Table 1, entries 12–14). Reactions with selenides as catalysts afforded **2a** in low yields (Table 1, entry 15). $(PhS)_2$, $(PhTe)_2$, and SeO_2 also showed poor catalytic activity for the reaction (Table 1, entries 16 and 17).[13] The reaction required an excess amount of H_2O_2, but more than 5.0 equivalents of H_2O_2 resulted in a decreased yield of **2a** as a result of overoxidation (Table 1, entry 10 vs. entries 18 and 19).[13] The catalyst loading was also examined, and fortunately, 5 mol% of the catalyst, as we initially employed, was the best dosage (Table 1, entry 10 vs. entries 20 and 21).[13]

The scope of the reaction was next investigated. Substituents on the substrate largely affected the reaction. Introduction of a methyl group as an electron-donating group (EDG) on the aryl ring resulted in improved reactivity of MCP **1b** relative to that of unsubstituted **1a**, and the reaction of **1b** under the standard conditions led to **2b** in a decreased yield of 56%, whereas a series of unidentified complexes were observed by thin-layer chromatography (TLC). Fortunately, the reaction proceeded smoothly at 25 °C to give **2b** in a good yield of 80% [Eq. (2)].



1b 2b

Bearing two EDGs, MCP **1c** was even more reactive than **1a** and **1b**. Thus, ice-bath cooling was necessary to slow down the reaction to decrease the amount of overoxidation. The reaction at 0 °C afforded **2c** in 51% yield, but at −10 °C, **2c** was obtained in only 26% yield, and a large amount of substrate **1c** was observed by TLC [Eq. (3)].

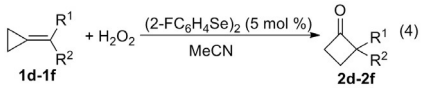


1c 2c

In contrast, bearing EWGs, electron-deficient MCPs **1d–f** were much more stable than **1a–c**, and they afforded products **2d–f** in very poor yields under the standard conditions, whereas most of the starting material remained unreacted [Eq. (3)]. However, at an elevated reaction temperature (80 °C), the substrates were oxidized smoothly to give corresponding cyclobutanones **2d–f** in moderate yields [Eq. (4)].

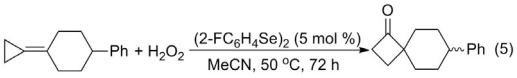
Dialkyl MCP **1g** was also a favorable substrate for the reaction, and it gave **2g** in moderate yield [Eq. (5)]. Notably, **2g** is a useful but inaccessible intermediate in drug discovery.[14]

The oxidative ring expansion of monosubstituted MCPs **1h–l** was tested. Unfortunately, similar to that already reported,[4] reaction of these monosubstituted MCPs under the standard conditions led to a series of unidentified complexes, possibly



1d-1f 2d-2f

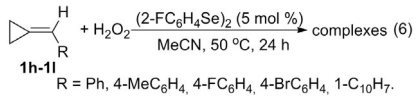
R^1, R^2 (**1**)	*T*, *t*, yield (**2**)
Ph, 2-ClC_6H_4 (**1d**)	50 °C, 72 h, 26% (**2d**)
	80 °C, 72 h, 62% (2d)
Ph, 4-ClC_6H_4 (**1e**)	50 °C, 72 h, 23% (**2e**)
	80 °C, 48 h, 60% (2e)
4-ClC_6H_4, 4-ClC_6H_4 (**1f**)	50 °C, 72 h, 11% (**2f**)
	80 °C, 72 h, 65% (2f)



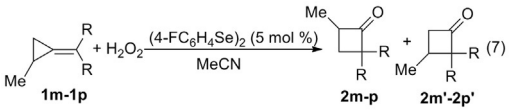
1g

2g, 52%
cis : *trans* = 64 : 36

because of the fact that the substrates were too active and decomposed under the oxidative conditions [Eq. (6)]. Efforts to optimize the reaction conditions for the selective oxidative ring expansion of monosubstituted MCP **1h** (R = Ph) failed.[13]

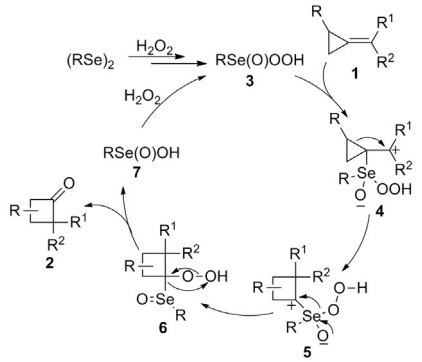


Cyclopropyl-ring-substituted MCPs **1m–p** were also employed as substrates [Eq. (7)]. A methyl group as an EDG on the cyclopropyl ring largely enhanced the electron density of the substrate and, thus, made the substrate even more reactive than the simple MCP. In the oxidation of MCPs **1m–p**, $(4\text{-}FC_6H_4Se)_2$ instead of previously employed $(2\text{-}FC_6H_4Se)_2$ was the preferred catalyst. The oxidation of MCP **1m** at 25 °C led to isomers **2m** and **2m′** in 53% yield, with a molar ratio of **2m**/**2m′** = 4:1. The oxidation of electron-rich MCP **1n** was performed at a low temperature to afford isomers **2n** and **2n′** in a 1:2 molar ratio in 38% yield. Electron-deficient MCP **1o** was more stable and an elevated reaction temperature was required. At 80 °C, **1o** was smoothly oxidized to **2o** and **2o′** in 60% yield with a 4:1 molar ratio. Interestingly, the oxidation of MCP **1p** led to **2p** as the sole product in moderate yield [Eq. (7)].



R (**1**)	*T*, *t*, yield (**2**)
Ph (**1m**)	25 °C, 24 h, 53 % (**2m : 2m'** = 4 : 1)
4-MeC_6H_4 (**1n**)	0 °C, 72 h, 38 % (**2n : 2n'** = 1 : 2)
4-FC_6H_4 (**1o**)	80 °C, 24 h, 60 % (**2o : 2o'** = 4 : 1)
4-ClC_6H_4 (**1p**)	25 °C, 72 h, 51 % (**2p**)

On the basis of our previous work as well as literature precedent, a plausible mechanism is proposed (Scheme 2). As confirmed by ^{77}Se NMR spectroscopy, the oxidation of the diselenide by H_2O_2 leads to seleninoperoxoic acid **3**.[11f] Electrophilic addition of **3** to MCP **1** leads to intermediate **4**.[3o,11b] As the cyclopropylmethylium cation bears a selenium group at the α position, ring expansion of **4** occurs to give intermediate cyclobutyl cation **5**, which affords **6** through intramolecular rearrangement.[3e,h,o,p,15] Decomposition of **6** affords final product **2** and organoseleninic acid **7**, which regenerates catalytic species **3** after oxidation by H_2O_2 (Scheme 2).[11f] Although this mechanism remains to be fully clarified and alternative processes may also exist, Scheme 2 should be the most likely mechanism on the basis of the above experimental findings and related literature.



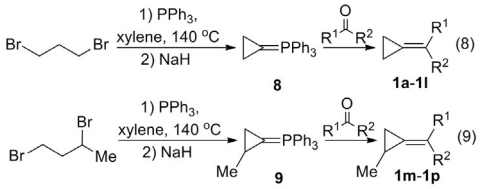
Scheme 2. Possible mechanism.

In conclusion, we developed a novel method for the synthesis of useful substituted cyclobutanones through the organoselenium-catalyzed ring-expansion reaction of methylenecyclopropanes by using H_2O_2 as a green oxidant. The oxidation level and selectivity of the reaction were controlled through modification of the reaction conditions. It seems that the reaction is very sensitive to substituents in the substrate, that is, different substrates might require quite different conditions. Further studies on the organoselenium-catalyzed ring-expansion reaction are ongoing in our laboratory.

Experimental Section

General methods

MCPs **1a–l** were prepared according to the literature through Wittig reaction of cyclopropylidene ylide **8** with ketones or aldehydes [Eq. (8)].[1l,16] MCPs **1m–p** were synthesized by a similar reaction by using commercially available 1,3-dibromobutane as the starting material to produce ylide **9** [Eq. (9)].



Organoselenium catalysts were commercially available or were prepared through known methods.[11g] Solvents were analytically pure (AR) and were directly used without any special treatment. All reactions were monitored by TLC. IR spectra were measured with a Bruker Tensor 27 infrared spectrometer. ^1H NMR and ^{13}C NMR spectra were recorded with a Bruker Avance 600/400 instrument (600/400 MHz for ^1H and 150/100 MHz for ^{13}C NMR) by using $CDCl_3$ as the solvent. Chemical shifts for ^1H NMR and ^{13}C NMR were referred to internal Me_4Si ($\delta = 0$ ppm). Mass spectra were measured with a Shimadzu GCMS-QP2010 Ultra spectrometer (EI). Elemental analysis was measured with a Vario EL cube elemental analysis instrument.

Typical procedure for the synthesis of 2

A reaction tube was charged with MCP **1** (0.3 mmol) and the organoselenium catalyst (5 mol%, 0.015 mmol). A solution of 30 w/w aq H_2O_2 (1.5 mmol) in MeCN (1 mL) was then injected by syringe. The mixture was stirred at the temperatures mentioned above. The reaction was monitored by TLC (petroleum ether/EtOAc = 15:1). Upon completion of the reaction, the solvent was evaporated under reduced pressure, and the residue was isolated by preparative TLC (petroleum ether/EtOAc = 15:1) to afford product **2**.

Characterization data

2,2-Diphenylcyclobutanone (**2a**): Yield: 47.3 mg, 71%; oil; IR (film): $\tilde{\nu}$ = 3022, 1777, 1657, 1596, 1490, 1445, 1177, 1074, 695 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$, Me_4Si): δ = 7.37 (d, J = 7.8 Hz, 4H), 7.29 (t, J = 7.8 Hz, 4H), 7.19 (t, J = 7.5 Hz, 2H), 3.13 (t, J = 8.7 Hz, 2H), 2.81 ppm (t, J = 8.7 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 208.7, 142.1, 128.7, 126.9, 126.4, 76.2, 43.4, 25.6 ppm; MS (EI, 70 eV): m/z (%): 222 (2) [M^+], 180 (100), 179 (47), 165 (72); known compound.[4c]

2-(4-Methylphenyl)-2-phenylcyclobutan-1-one (**2b**): Yield: 56.7 mg, 80%; oil; IR (film): $\tilde{\nu}$ = 2921, 1779, 1656, 1598, 1445, 812, 698 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$, Me_4Si): δ = 7.36–7.35 (m, 2H), 7.30–7.28 (m, 2H), 7.25 (d, J = 8.4 Hz, 2H), 7.20–7.18 (m, 1H), 7.11 (d, J = 7.8 Hz, 2H), 3.16–3.13 (m, 2H), 2.80 (t, J = 8.7 Hz, 2H), 2.29 ppm (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 208.9, 142.3, 139.2, 136.6, 129.4, 128.7, 126.8, 126.4, 126.3, 76.0, 43.4, 25.7, 21.0 ppm; MS (EI, 70 eV): m/z (%): 236 (2) [M^+], 194 (100), 179 (72), 178 (46); known compound.[4c]

2-(3,4-Dimethylphenyl)-2-phenylcyclobutanone (**2c**): Yield: 38.3 mg, 51%; oil; IR (film): $\tilde{\nu}$ = 2921, 1779, 1655, 1605, 1495, 1447, 699 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$, Me_4Si): δ = 7.37 (d, J = 7.8 Hz, 2H), 7.29 (t, J = 7.8 Hz, 2H), 7.20 (t, J = 7.2 Hz, 1H), 7.13 (s, 1H), 7.10–7.06 (m, 2H), 3.16–3.12 (m, 2H), 2.82–2.79 (m, 2H), 2.22 (s, 3H), 2.20 ppm (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 209.1, 142.4, 139.6, 137.0, 135.3, 129.9, 128.7, 127.6, 126.8, 126.4, 123.8, 76.0, 43.3, 25.7, 19.9, 19.3 ppm; MS (EI, 70 eV): m/z (%): 250 (1) [M^+], 207 (100), 192 (66), 177 (34); elemental analysis calcd (%) for $C_{18}H_{18}O$ (250.33): C 86.36, H 7.25; found: C 86.19, H 7.12.

2-(2-Chlorophenyl)-2-phenylcyclobutanone (**2d**): Yield: 47.7 mg, 62%; oil; IR (film): $\tilde{\nu}$ = 1779, 1652, 1471, 1445, 755, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 7.77–7.74 (m, 1H), 7.36–7.18 (m, 8H), 3.27–3.22 (m, 1H), 3.18–3.12 (m, 2H), 2.75–2.68 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 207.6, 139.4, 137.9, 133.3, 131.2, 128.5, 128.4, 128.2, 126.9, 126.8, 126.5, 75.2, 43.0, 24.4 ppm; MS (EI, 70 eV): m/z (%): 221 (1) [M^+−Cl], 179 (100); known compound.[4a]

2-(4-Chlorophenyl)-2-phenylcyclobutanone (**2e**): Yield: 46.2 mg, 60%; oil; IR (film): $\tilde{\nu}$ = 1782, 1660, 1596, 1490, 1077, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 7.78–7.14 (m, 1H), 7.50–7.44 (m, 1H), 7.35–7.21 (m, 7H), 3.24–3.09 (m, 2H), 2.87–2.73 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 208.2, 141.6, 140.5, 132.8, 128.8, 128.8, 127.7, 127.1, 126.2, 75.5, 43.4, 25.5 ppm; MS (EI, 70 eV): m/z (%): 221 (1) [M^+−Cl], 104 (100); known compound.[4b]

2,2-Bis(4-chlorophenyl)cyclobutanone (**2f**): Yield: 56.8 mg, 65%; oil; IR (film): $\tilde{\nu}$ = 1653, 1587, 1459, 850, 753 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$, Me_4Si): δ = 7.27 (s, 8H), 3.17 (t, J = 8.7 Hz, 2H), 2.78 ppm (t, J = 8.7 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 207.8, 140.1, 133.1, 129.0, 127.7, 74.9, 43.6, 25.6 ppm; MS (EI, 70 eV): m/z (%): 255 (1) [M^+−Cl], 251 (8), 249 (12), 140 (38), 138 (100); known compound.[4c]

7-Phenylspiro[3.5]nonan-1-one (**2g**): Yield: 33.4 mg, 52%. *cis*-**2g**: oil; IR (film): $\tilde{\nu}$ = 1759, 1658, 1631, 1600, 1493, 1444, 760, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 7.30–7.26 (m, 2H), 7.24–7.15 (m, 3H), 2.97 (t, J = 8.4 Hz, 2H), 2.43–2.49 (m, 1H), 2.15 (d, J = 13.6 Hz, 2H), 1.86–1.97 (m, 2H), 1.77–1.81 (m, 4H), 1.56–1.64 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 215.3, 146.8, 128.3, 126.9, 125.9, 64.1, 43.6, 40.8, 33.6, 30.9, 24.7 ppm; MS (EI, 70 eV): m/z (%): 214 (12) [M^+], 104 (100); *trans*-**2g**: oil; IR (film): 1774, 750, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 7.32–7.28 (m, 2H), 7.21–7.19 (m, 3H), 3.04 (t, J = 8.4 Hz, 2H), 2.45–2.53 (m, 1H), 1.95 (t, J = 8.4 Hz, 2H), 1.89–1.83 (m, 4H), 1.69–1.75 (m, 2H), 1.55–1.47 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 216.1, 146.6, 128.3, 126.7, 126.1, 65.5, 43.1, 41.7, 31.4, 29.5, 23.6 ppm; MS (EI, 70 eV): m/z (%): 214 (5) [M^+], 103 (100); known compound.[14]

4-Methyl-2,2-diphenylcyclobutan-1-one (**2m**) and 3-methyl-2,2-diphenylcyclobutan-1-one (**2m′**): Yield: 37.6 mg, 53%; oil; IR (**2m** and **2m′**, film): $\tilde{\nu}$ = 1774, 1658, 1598, 1492, 1446, 1083, 762, 638, 537 cm^{-1}; ^1H NMR (**2m**, 400 MHz, $CDCl_3$, Me_4Si): δ = 7.35–7.03 (m, 10H), 3.37–3.15 (m, 1H), 3.05–2.99 (m, 1H), 2.32–2.27 (m, 1H), 1.14–1.12 ppm (d, J = 7.2 Hz, 3H); ^1H NMR (**2m′**, 400 MHz, $CDCl_3$, Me_4Si): δ = 7.35–7.03 (m, 10H), 3.37–3.15 (m, 2H), 2.67–2.61 (m, 1H), 0.97–0.96 ppm (d, J = 7.2 Hz, 3H); ^{13}C NMR (**2m** and **2m′**, 100 MHz, $CDCl_3$): δ = 211.5, 209.2, 142.6, 142.2, 128.9, 128.5, 127.7, 127.0, 126.7, 126.5, 77.9, 73.9, 51.1, 50.6, 34.2, 29.8, 18.6, 13.8 ppm; MS (**2m** and **2m′**, EI, 70 eV): m/z (%): 236 (26) [M^+], 180 (100); elemental analysis calcd (%) for $C_{17}H_{16}O$ (**2m** and **2m′**, 236.31): C 86.40, H 6.82; found: C 86.56, H 6.61.

4-Methyl-2,2-bis(4-methylphenyl)cyclobutan-1-one (**2n**) and 3-methyl-2,2-bis(4-methylphenyl)cyclobutan-1-one (**2n′**): Yield: 30.1 mg, 38%; oil; IR (**2n** and **2n′**, film): $\tilde{\nu}$ = 1737, 1654, 1608, 1510, 1455, 1277, 926, 819, 749, 468 cm^{-1}; ^1H NMR (**2n**, 400 MHz, $CDCl_3$, Me_4Si): δ = 7.23–6.91 (m, 8H), 2.66–2.60 (m, 1H), 2.29 (d, J = 2.4 Hz, 1H), 2.26 (d, J = 2.4 Hz, 1H), 2.20 (s, 6H), 0.98–0.96 ppm (d, J = 6.8 Hz, 3H); ^1H NMR (**2n′**, 400 MHz, $CDCl_3$, Me_4Si): δ = 7.23–6.91 (m, 8H), 3.37–3.15 (m, 2H), 3.01–2.96 (m, 1H), 2.21 (s, 6H), 1.14 ppm (d, J = 7.2 Hz, 3H); ^{13}C NMR (**2n** and **2n′**, 100 MHz, $CDCl_3$): δ = 212.0, 209.8, 139.9, 139.4, 136.6, 136.2, 129.5, 129.2, 127.5, 126.4, 77.3, 73.3, 51.1, 50.5, 34.2, 26.9, 21.0, 21.0, 18.6, 13.9 ppm; MS (**2n** and **2n′**, EI, 70 eV): m/z (%): 264 (23) [M^+], 208 (100), 193 (90); elemental analysis calcd (%) for $C_{19}H_{20}O$ (**2n** and **2n′**, 264.36): C 86.32, H 7.63; found: C 86.18, H 7.50.

2,2-Bis(4-fluorophenyl)-4-methylcyclobutan-1-one (**2o**) and 2,2-bis(4-fluorophenyl)-3-methylcyclobutan-1-one (**2o′**):Yield: 49.0 mg, 60%; oil; IR (**2o** and **2o′**, film): $\tilde{\nu}$ = 1775, 1601, 1507, 1455, 1410, 1229, 913, 834, 768, 731, 588, 577, 540 cm^{-1}; ^1H NMR (**2o**, 400 MHz, $CDCl_3$, Me_4Si): δ = 7.75–6.87 (m, 8H), 3.42–3.32 (m, 1H), 3.02–2.96 (m, 1H), 2.28–2.23 (m, 1H), 1.16–1.14 ppm (d, J = 7.6 Hz, 3H); ^1H NMR (**2o′**, 400 MHz, $CDCl_3$, Me_4Si): δ = 7.75–6.87 (m, 8H), 3.24–3.19 (m, 2H), 2.70–2.62 (m, 1H), 0.97 ppm (d, J = 6.8 Hz, 3H); ^{13}C NMR (**2o** and **2o′**, 100 MHz, $CDCl_3$): δ = 211.1, 208.7, 162.9 (d, J_{C-F} = 17.6 Hz), 160.5 (d, J_{C-F} = 17.0 Hz), 138.2 (d, J_{C-F} = 3.2 Hz), 137.7 (d, J_{C-F} = 3.2 Hz), 129.2(d, J_{C-F} = 7.9 Hz), 128.6 (d, J_{C-F} = 7.9 Hz), 128.1–128.0(m), 115.9–115.3(m), 76.5, 72.4, 51.2, 50.7, 34.4, 29.9, 18.5, 13.8 ppm; MS (**2o** and **2o′**, EI, 70 eV): m/z (%): 272 (2) [M^+], 216 (100); elemental analysis calcd (%) for $C_{17}H_{14}F_2O$ (**2o** and **2o′**, 272.29): C 74.99 H 5.18; found: C 74.82, H 5.23.

2,2-Bis(4-chlorophenyl)-4-methylcyclobutan-1-one (**2p**): Yield: 46.7 mg, 51%; oil; IR (film): $\tilde{\nu}$ = 1776, 1652, 1490, 1399, 1285, 1089, 1012, 830, 753, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, Me_4Si): δ = 7.66–7.64 (d, J = 8.0 Hz, 4H), 7.41–7.39 (d, J = 8.0 Hz, 4H), 3.40–3.34 (m, 1H), 3.02–2.96 (m, 1H), 2.29–2.24 (m, 1H), 1.16–1.15 ppm (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.4, 140.2, 139.2, 135.5, 133.2, 131.3, 129.1, 128.8, 127.8, 72.6, 50.9, 34.1, 13.9 ppm; MS (EI, 70 eV): m/z (%): 304 (2) [M^+], 248 (100), 178 (95); elemental analysis calcd (%) for $C_{17}H_{14}Cl_2O$ (305.20): C 66.90, H 4.62; found: C 66.74, H 4.45.

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