Synthesis of transient functionalized dienes by electrocyclic ring-opening of cyclobutene derivatives

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Dedicated to Professor Keiichiro Fukumoto on his 70th birthday

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Abstract

Cyclobutenes bearing various functional groups were synthesized by derivatization of squaric acid, and their thermolytic ring-opening reactions were investigated. This sequence was found an effective approach to prepare a multi-functionalized diene, which could be used for subsequent Diels-Alder cycloaddition provided that its s-*cis* form was fixed.

Keywords: Cyclobutenes, 1,3-dienes, Diels-Alder cycloaddition, thermal ring-opening

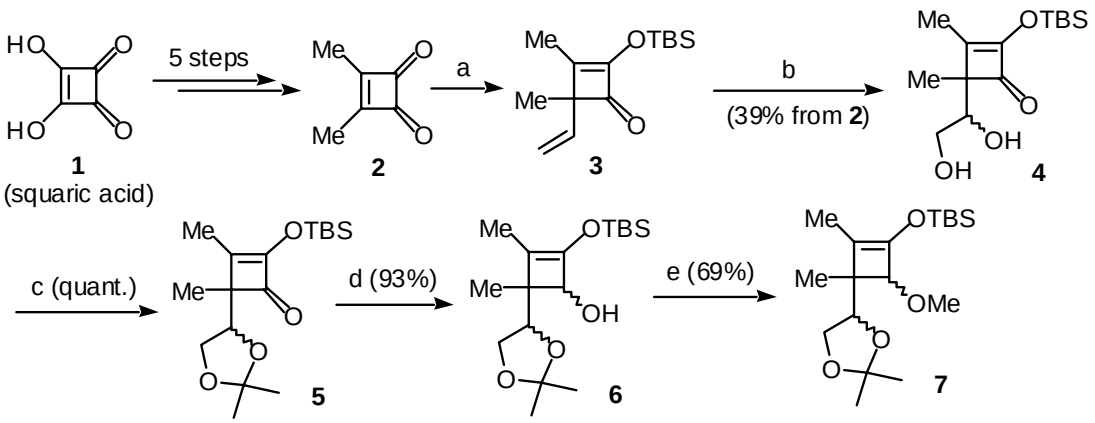
Introduction

Thermal electrocyclic ring-opening of cyclobutene derivatives, to produce 1,3-diene compounds, has been extensively studied since the 1960's, and the theoretical aspects of this fundamental reaction have been elucidated by means of the theory of conservation of orbital symmetry.[1] While numerous studies concerning the stereochemical course of this ring-opening reaction have enabled prediction of the structure of the asymmetric 1,3-diene product, researches aiming at utilizing the resulting dienes as tools for organic synthesis appear to be limited to a few examples. Particularly notable is the synthesis of differently benzoquinones and phenols, in which conjugated ketene intermediates generated by the thermolysis of ethynyl- or

vinyl-substituted cyclobutenones yielded the ring-expanded aromatic products as a result of subsequent ring closure and tautomerization.[2] This methodology has also been applied for intermolecular trapping of the vinylketene intermediate by alkynes,[3] and this process has been applied for the synthesis of natural products such as cylindrocyclophane.[4] On the other hand, the 1,3-diene compounds generated by the thermolysis of substituted cyclobutenes, except for the unstable vinylketenes mentioned above, have rarely been utilized for organic synthesis in spite of their importance as synthetic blocks for the construction of complex molecules. We report herein the syntheses of several substituted cyclobutenes by functionalization of commercially available squaric acid, their thermal ring-opening to prepare multi-functionalized dienes, and the investigation of their synthetic utility.

Results and Discussion

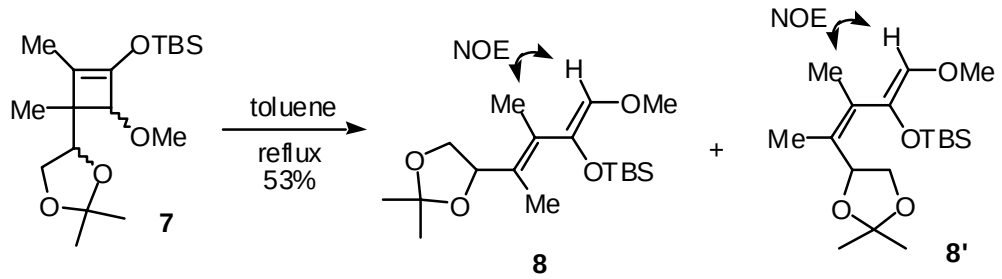
The symmetrically substituted 3,4-dimethylcyclobutene-1,2-dione (**2**), readily synthesized from squaric acid (**1**) in five steps,[5] was selected as a starting material for functionalization of the cyclobutene ring. Introduction of a vinyl group, which is a versatile functional group for further transformations *via* conjugate addition, was performed using higher-order vinylcuprate according to the reported procedure,[6] and the resulting enolate was trapped as a silyl ether. The adduct **3** was transformed with osmium tetroxide into the corresponding diol **4**, which was protected as an isopropylidene ketal. The ketone **5** was treated with sodium borohydride, and the alcohol **6** thus obtained was subjected to methylation using methyl triflate and 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) to afford the methyl ether **7** (Scheme 1). Although the cyclobutene **7** was a mixture of diastereomers and the ratio and stereo-structures could not be determined from its spectral data, introduction of the multi-functionality on the cyclobutene ring was achieved successfully in this way, providing a precursor for a functionalized diene.



Reagents: (a) (vinyl)Cu(Me)CNLi$_2$, THF, then TBSOTf; (b) OsO_4, NMO, acetone-H_2O; (c) $Me_2(OMe)_2$, PPTs, CH_2Cl_2; (d) $NaBH_4$, MeOH; (e) MeOTf, DTBMP, CH_2Cl_2.

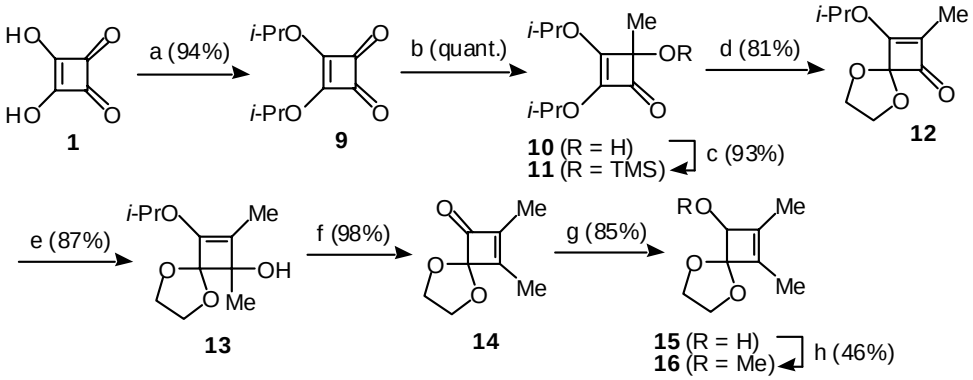
Scheme 1. Preparation of the functionalized cyclobutene **7.**

Thermal ring-opening of the cyclobutene **7** proceeded in refluxing toluene to give a *ca*. 1:1 mixture of two geometrical isomers (dienes **8** and **8'**), the structures of which were determined on the basis of the conrotatory ring-opening process[1] and NOE experiments (indicated in Scheme 2). Formation of these products indicates that preferential outward rotation of the methoxy group occurred,[7] and that the cyclobutene **7**, having the *trans* relative configuration (of the methoxy group and the dioxolane unit) was converted into the diene **8**, and the *cis*- isomer produced **8'**. These functionalized dienes, which would be difficult to synthesize in other ways, are expected to be versatile synthetic blocks.



Scheme 2. Thermolysis of the cyclobutene **7**.

In the course of our study on *o*-quinodimethane chemistry, *i.e.*, the thermolytic cleavage of benzocyclobutene derivatives and subsequent Diels-Alder cycloaddition,[8] we were interested in the extension to monocyclic cyclobutenes. Moore's group have reported that cyclobutenes possessing a dithioacetal structure readily underwent ring-opening reaction, while the resulting dienes resisted Diels-Alder reaction except for a particular case.[9] We supposed that replacement of the dithioacetal structure by the more electron-donating ethylene ketal would facilitate Diels-Alder reaction, to increase their utility as synthetic blocks. Thus, the cyclobutenes having an ethylene ketal structure were prepared by the modified procedure developed by Liebeskind *et al*.[10] Di-isopropyl squarate (**9**), easily prepared from squaric acid (**1**),[10] was treated with methyllithium to yield the alcohol **10**, which was converted into the TMS ether **11**. For the ketalization, Noyori's conditions[11] were adopted and the monoketal **12** was obtained selectively. These transformations have already been reported.[10] Subsequent addition of methyllithium followed by acid treatment afforded the cyclobutenone **14**, which was subjected to DIBAL reduction and methylation to furnish the required cyclobutene derivative **16** (Scheme 3).

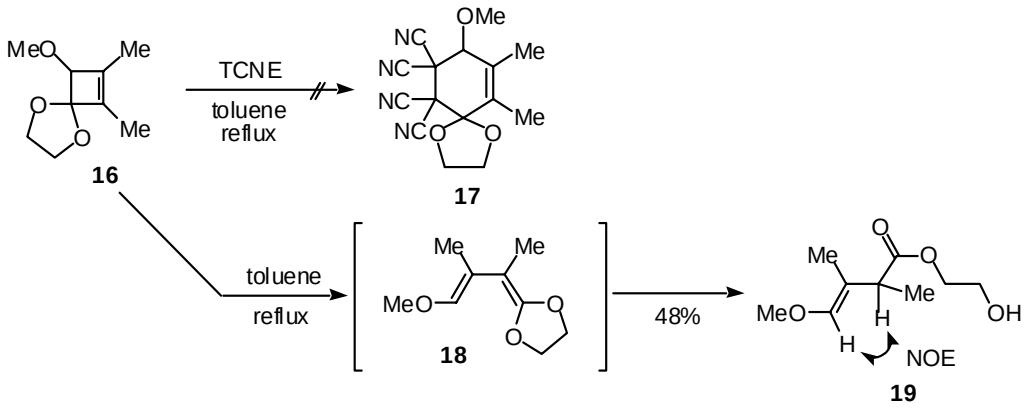


Reagents: (a) *i*-PrOH, benzene; (b) MeLi, THF; (c) TMSCl, Et_3N, Et_2O; (d) $TMSO(CH_2)_2OTMS$, TMSOTf, THF; (e) MeLi, THF; (f) HCl, THF-H_2O; (g) DIBAL, THF; (h) MeOTf, DTBMP, CH_2Cl_2.

Scheme 3. Preparation of the functionalized cyclobutene **16**.

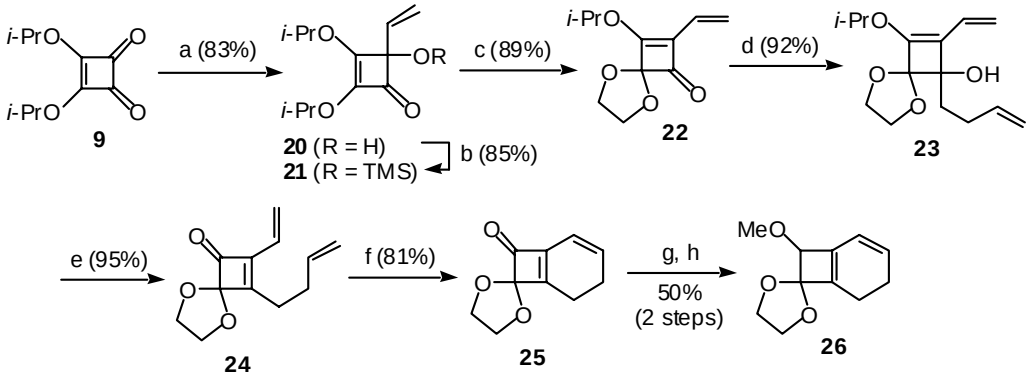
However, the thermolysis of the cyclobutene **16** in the presence of tetracyanoethylene (TCNE) as a dienophile afforded some unidentified products, and the cycloadduct **17** could not be detected. In the absence of the dienophile, the product **19**, presumably formed by hydrolysis of the diene **18** during the work-up process, was isolated in 48% yield (Scheme 4). These results suggest an insufficient reactivity of the diene **18** toward Diels-Alder reaction, probably due to its

preference for the s-*trans* form. The geometry of **19**, determined by a NOE experiment, shows again the preferential outward rotation of the methoxy group.



Scheme 4. Thermolysis of the cyclobutene **16**.

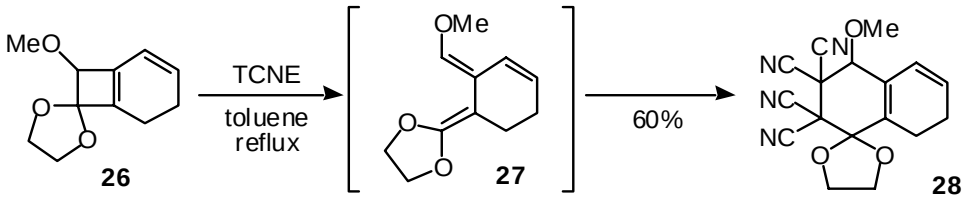
With these results in hand, we tried to synthesize a fused-cyclobutene derivative **26** and to investigate its electrocyclic reaction. According to the procedure shown in Scheme 3, the cyclobutene **24** bearing vinyl and butenyl substituents was prepared, namely, by vinylation of the squarane **9**,[12] ketalization, introduction of the butenyl group, and treatment with hydrochloric acid (Scheme 5). The cyclobutene **24** thus obtained was subjected to ring-closing metathesis using Grubbs' catalyst[12] to give the fused-cyclobutene derivative **25**, which was transformed into the methyl ether **26**.



Reagents: (a) (vinyl)MgBr, THF; (b) TMSCl, Et_3N, Et_2O; (c) $TMSO(CH_2)_2OTMS$, TMSOTf, THF; (d) (3-butenyl)MgBr, THF; (e) HCl, THF-H_2O; (f) $(Cy_3P)_2Ru(styryl)Cl_2$, CH_2Cl_2; (g) DIBAL, THF; (h) MeOTf, DTBMP, CH_2Cl_2.

Scheme 5. Preparation of the fused-cyclobutene **26**.

The result of the thermolysis of **26** is shown in Scheme 6. As expected, in the presence of TCNE thermolytic cleavage and subsequent Diels-Alder reaction proceeded to give the cycloadduct **28** in 60% yield. In this case, the inevitable fixation of the diene **27** to the *s-cis* form would serve as the factor facilitating Diels-Alder reaction.



Scheme 6. Thermolysis of the fused-cyclobutene **26**.

Conclusions

In this study, we have reported the synthesis of functionalized cyclobutenes as precursors of multi-functionalized dienes. Several derivatizations of the commercially available squaric acid and the stereospecific electrocyclic ring-opening of the derivatives could be exemplified. The attempt to illustrate the utility of the resulting dienes in Diels-Alder cycloaddition revealed that, in the case of the fused-cyclobutene derivative, such applications were warranted. The construction of polycyclic systems for the synthesis of natural products using this methodology is now in progress.

Experimental Section

General Procedures. All non-aqueous reactions were carried out under an Ar atmosphere. Reagents were purchased from commercial sources and used as received. Anhydrous solvents were obtained from commercial sources or dried by distillation over CaH_2 or P_2O_5. ^1H- and ^{13}C NMR spectra were obtained on a Varian Gemini 300 instrument (300 MHz for ^1H and 75.46 MHz for ^{13}C) or a Varian UNITY plus 500 instrument (500 MHz for ^1H and 125 MHz for ^{13}C),

using tetramethylsilane or chloroform as internal reference. Mass spectra were measured on JEOL D-200 or JEOL AX 505 mass spectrometers, by electron impact (EI, 70 eV). IR spectra were recorded on a Perkin-Elmer 1600 spectrometer. Melting points were taken with a Yanagimoto micro melting point apparatus and are uncorrected. Column chromatography was carried out by employing Cica Silica Gel 60N (spherical, neutral, 40–50 μm or 63–210 μm). RT denotes room temperature.

2-(*tert*-Butyldimethylsilyloxy)-4-(1,2-dihydroxyethyl)-3,4-dimethylcyclobut-2-en-1-one (4). A suspension of CuCN (342 mg, 3.81 mmol) in dry THF (4.5 mL) under Ar was cooled to 0°C and a solution of methyllithium in Et_2O (1.04 M, 7.6 mL, 7.90 mmol) was added dropwise to the mixture. The reaction mixture was warmed to RT and tri-*n*-butylvinyltin (1.47 g, 4.63 mmol) in dry THF (4 mL) was added. After stirring at RT for 1.75 h, the mixture was cooled to -78°C, and a solution of **2**[5] (300 mg, 2.72 mmol) in dry THF (4 mL) was added. After stirring at -78°C for 20 min, *tert*–butyldimethylsilyl trifluoromethanesulfonate (1.9 mL, 8.17 mmol) was added, and the mixture was stirred at the same temperature for 15 min. The reaction was quenched with H_2O, and extracted with AcOEt. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was subjected to column chromatography on silica gel (AcOEt / hexane, 1 / 3) to afford **3** (617 mg, containing a little amount of *n*-butylvinyltin) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300MHz) δ 5.81 (dd, *J*=17.4, 10.5 Hz, 1H), 5.19 (d, *J*=10.5 Hz, 1H), 5.11 (d, *J*=17.4 Hz, 1H), 1.94 (s, 3H), 2.38 (s, 3H), 0.91 (s, 9H), 0.21 (s, 6H); MS *m/e* 252 (M^+).

To a solution of crude **3** (617 mg) in acetone (16 mL) and H_2O (4 mL) were added NMO (50% in H_2O, 0.57 mL, 2.4 mmol) and OsO_4 (1.4 M in H_2O, 3 drops, catalytic amount) at 0°C, and the mixture was stirred for 1 h at RT. The reaction was quenched with aqueous $Na_2S_2O_3$ and the mixture was stirred for 15 min, then extracted with AcOEt. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (AcOEt / hexane, 2 / 3) to afford **4** (304 mg, 2 steps 39%) as a colorless oil (a mixture of diastereomers). ^{1}H NMR ($CDCl_3$, 300MHz) δ 3.81-3.53 (m, 3H), 2.02 (s, 3H), 1.19, 1.16 (s x 2, 3H), 0.93 (s, 9H), 0.22 (s, 6H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 193.2, 192.7, 159.7, 158.4, 145.7, 145.5, 74.9, 72.7, 64.1, 63.0, 60.6, 59.7, 25.9, 25.7, 18.2, 16.6, 15.3, 14.5, 11.2, 10.3, -3.3, -4.2; IR (neat) 3446 cm^{-1} (OH), 1761 cm^{-1} (C=O), 1645 cm^{-1} (C=C); MS *m/z* 286 (M^+); HRMS calcd for $C_{14}H_{26}O_4Si$ (M^+): 286.1600, found: 286.1591.

2-(*tert*-Butyldimethylsilyloxy)-4-(2,2-dimethyl-1,3-dioxolan-4-yl)-3,4-dimethyl-cyclobut-2-en-1-one (5). Under an Ar atmosphere, to a solution of **4** (60 mg, 0.2 mmol) in dry CH_2Cl_2 (4 mL) were added acetone dimethylacetal (0.06 mL, 0.5 mmol) and PPTs (catalytic amount) at RT, and the mixture was stirred for 40 min at RT. The reaction mixture was diluted with sat. $NaHCO_3$ and extracted with AcOEt. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (AcOEt / hexane, 1 / 2) to afford **5** (68 mg, quant.) as a colorless oil (a mixture of diastereomers). ^{1}H NMR ($CDCl_3$, 300MHz) δ4.16-3.81 (m, 3H), 2.02, 1.98 (s x 2, 3H), 1.39, 1.37, 1.31 (s x 3, 6H), 1.15, 1.12 (s x 2, 3H), 0.93 (s, 9H), 0.22 (s, 6H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 191.6, 191.5, 157.8, 157.0, 145.8, 145.7, 109.5, 109.3, 66.5, 66.0, 60.6, 59.0, 58.3, 25.8, 21.3, 18.3, 16.3, 14.6, 14.5, 10.9, 10.1, -4.2, -4.3; IR (neat) 1767 cm^{-1} (C=O), 1649 cm^{-1} (C=C); MS *m/z* 326 (M^+); HRMS calcd for $C_{17}H_{30}O_4Si$ (M^+): 326.1913, found: 326.1870.

1-(*tert*-Butyldimethylsilyloxy)-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-2,3-dimethyl-cyclobut-1-en-4-ol (6). Under an Ar atmosphere, to a solution of **5** (263 mg, 0.81 mmol) in abs. MeOH (8 mL) was added sodium borohydride (61 mg, 1.61 mmol) at 0°C, and the mixture was stirred for 4.5 h at RT. The reaction mixture was diluted with H_2O and the mixture extracted with AcOEt. The combined organic layer was dried over $MgSO_4$ and evaporated to leave a residue, which was purified by column chromatography on silica gel (AcOEt / hexane, 2 / 3) to afford **6** (245 mg, 93%) as a colorless oil (mixture of diastereomers). ^{1}H NMR ($CDCl_3$, 300MHz) δ 4.34-4.32 (m, 1H), 4.09-3.90 (m, 2H), 3.70-3.63 (m, 1H), 1.54, 1.50, 1.40, 1.32 (s x 4, 9H), 1.06, 1.03 (s x 2, 3H), 0.94 (s, 9H), 0.19 (s, 6H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 144.4, 122.2, 121.2, 109.1, 108.7, 79.7, 79.1, 75.9, 75.8, 66.6, 66.1, 46.8, 46.6, 27.0, 26.7, 25.9, 25.3, 25.2, 18.4, 15.9, 15.5, 8.7, 8.2, -4.0; IR (neat) 3450 cm^{-1} (OH), 1705 cm^{-1} (C=C); MS *m/z* 328 (M^+); HRMS calcd for $C_{17}H_{32}O_4Si$ (M^+): 328.2070, found: 328.2053.

1-(*tert*-Butyldimethylsilyloxy)-3-(2,2-dimethyl-1,3-dioxolan-4-yl)-4-methoxy-2,3-dimethyl-cyclobut-1-ene (7). To a solution of **6** (25 mg, 0.08 mmol) and 2,6-di-*tert*-butyl-4-methylpyridine (78 mg, 0.38 mmol) in dry CH_2Cl_2 (1 mL) was added methyl trifluoromethanesulfonate (0.03 mL, 0.30 mmol) at RT under an Ar atmosphere, and the mixture was stirred for 18 h. The reaction was quenched with sat. $NaHCO_3$ at 0°C and the mixture extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (AcOEt / hexane, 1 / 5) to afford **7** (18 mg, 69%) as a colorless oil (a mixture of diastereomers). ^{1}H NMR ($CDCl_3$, 300MHz) δ 4.13-

3.85 (m, 3H), 3.75-3.60 (m, 1H), 3.37, 3.32 (s x 2, 3H), 1.55, 1.49, 1.47, 1.42, 1.39, 1.34 (s x 6, 9H), 1.17, 1.09, 1.06, 1.03 (s x 4, 3H), 0.93 (s, 9H), 0.16 (s, 6H); ^{13}C NMR ($CDCl_3$, 75MHz) δ143.5, 120.0, 89.4, 82.3, 66.8, 58.8, 47.9, 27.3, 26.3, 25.9, 18.8, 18.2, 9.3, -3.6; IR (neat) 1706 cm^{-1} (C=C); MS *m/z* 342 (M^+); HRMS calcd for $C_{18}H_{34}O_4Si$ (M^+): 342.2226, found: 342.2242.

2-(tert-Butyldimethylsilyloxy)-4-(2,2-dimethyl-1,3-dioxolan-4-yl)-1-methoxy-3-methylpenta -1(Z),3-diene (8 and 8'). Under an Ar atmosphere, a solution of **7** (85 mg, 0.25 mmol) in dry toluene (10 mL) was heated at reflux for 12 h. The solvent was evaporated to leave a residue, which was purified by column chromatography on silica gel (AcOEt / hexane, 1 / 3) to afford a mixture of **8** and **8'** (45 mg, 53 %) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300MHz) δ 4.97 (m, 1H), 4.94, 4.90 (s x 2, 1H), 4.07 (m, 1H), 3.55 (m, 1H), 3.39, 3.38 (s x 2, 3H), 1.91, 1.89 (s x 2, 3H), 1.76, 1.75 (s x 2, 3H), 1.45 (s, 3H), 1.39 (s, 3H), 0.90 (s, 9H), 0.14 (s, 3H), 0.10 (s, 3H); ^{13}C NMR ($CDCl_3$, 75MHz) δ137.8, 137.4, 132.3, 132.1, 109.6, 99.0, 98.6, 74.6, 67.2, 54.8, 54.7, 26.2, 25.5, 18.1, 14.3, 4.7; IR (neat) 1719 cm^{-1} (C=C); MS *m/z* 342 (M^+), 311 (M^+-OMe), 285 (M^+-*t*-Bu); HRMS calcd for $C_{18}H_{34}O_4Si$ (M^+): 342.2226, found: 342.2213.

3-Isopropoxy-1,2-dimethyl-5,8-dioxaspiro[3.4]oct-2-en-1-ol (13). Under an Ar atmosphere, to a solution of **12**[10] (1.62 g, 8.17 mmol) in dry THF (12 mL) was added a solution of methyllithium in Et_2O (1.04 M, 9.4 mL, 9.81 mmol) at -78°C, and the mixture stirred for 30 min. The reaction was quenched with H_2O at -78°C and the aqueous mixture extracted with AcOEt. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (AcOEt / hexane, 4 / 5) to afford **13** (1.53 g, 87%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300MHz) δ 4.38 (sept., *J*=6.3 Hz, 1H), 4.12-3.95 (m, 4H), 1.67 (s, 3H), 1.30 (s, 3H), 1.27 (d, *J*=6.3 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75MHz) δ178.5, 156.7, 120.4, 70.7, 66.3, 64.3, 26.6, 25.5, 10.0, 8.0; IR (neat) 3525 cm^{-1} (OH); MS *m/z* 214 (M^+); HRMS calcd for $C_{11}H_{18}O_4$ (M^+): 214.1205, found: 214.1193.

2,3-Dimethyl-5,8-dioxaspiro[3.4]oct-2-en-1-one (14). A solution of **13** (1.52 g, 7.09 mmol) in THF (28 mL) was treated with 5% HCl (3 mL) at RT. After continuous stirring for 20 min, the reaction mixture was diluted with sat. $NaHCO_3$ at 0°C and the aqueous mixture was extracted with AcOEt. The organic layer was dried over $MgSO_4$ and evaporated. The residue was purified by column chromatography on silica gel (AcOEt / hexane, 1 / 1) to afford **14** (1.07 g, 98%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300MHz) δ 4.17-4.04 (m, 4H), 2.10 (s, 3H), 1.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 75MHz) δ196.2, 178.4, 156.6, 120.4, 66.3, 9.9, 7.9; IR (neat) 1768 cm^{-1} (C=O),

1641 cm^{-1} (C=C); MS *m/z* 154 (M^+); HRMS calcd for $C_8H_{10}O_3$ (M^+): 154.0630, found: 154.0611.

2,3-Dimethyl-5,8-dioxaspiro[3.4]oct-2-en-1-ol (15). Under an Ar atmosphere, to a solution of **14** (100 mg, 0.65 mmol) in dry Et_2O (1.3 mL) was added a solution of DIBAL in *n*-hexane (0.95 M, 0.8 mL, 0.78 mmol) at -25°C, and the mixture was stirred at the same temperature for 5 min. The reaction mixture was diluted with Et_2O and H_2O at -25°C, and the mixture stirred at RT for 20 min. The suspension was filtered through Celite and the filtrate concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (AcOEt / hexane, 4 / 5) to afford **15** (86 mg, 85%) as a colorless solid, which was used immediately for the next reaction without further purification because of its instability. ^{1}H NMR ($CDCl_3$, 300MHz) δ4.39 (d, *J*=10.7 Hz, 1H), 4.02-3.94 (m, 4H), 2.10-2.03 (m, 1H), 1.69 (s, 3H), 1.58(s, 3H).

3-Methoxy-1,2-dimethyl-5,8-dioxaspiro[3.4]oct-1-ene (16). To a solution of **15** (84 mg, 0.54 mmol) and 2,6-di-*tert*-butyl-4-methylpyridine (773 mg, 3.76 mmol) in dry CH_2Cl_2 (5.3 mL) was added methyl trifluoromethanesulfonate (0.3 mL, 2.69 mmol) at RT under an Ar atmosphere, and the mixture was stirred for 14 h. The reaction mixture was diluted with sat. $NaHCO_3$ at 0°C and extracted with AcOEt. The combined organic layer was dried over $MgSO_4$ and evaporated to leave a residue, which was purified by column chromatography on silica gel (AcOEt / hexane, 1 / 2) to afford **16** (42 mg, 46%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300MHz) δ4.06-3.90(m, 5H), 3.40 (s, 3H), 1.72 (s, 3H), 1.58 (s, 3H); ^{13}C NMR ($CDCl_3$, 75MHz) δ141.5, 139.9, 110.4, 89.3, 65.5, 65.1, 57.3, 11.3, 8.0; IR (neat) 1645 cm^{-1} (C=C); MS *m/z* 170 (M^+); HRMS calcd for $C_9H_{14}O_3$ (M^+): 170.0943, found: 170.0901.

2-Hydroxyethyl-4-methoxy-2,3-dimethylbut-3(E)-enoate (19). Under an Ar atmosphere, a solution of **16** (19 mg, 0.11 mmol) in dry toluene (1 mL) was heated at reflux for 40 min. The solvent was evaporated off, and the residue subjected to column chromatography on silica gel (AcOEt / hexane, 1 / 2) to afford **19** (10 mg, 48%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300MHz) δ 5.94 (d, *J*=0.9, 1H), 4.22-4.20 (m, 2H), 3.82-3.81 (m, 2H), 3.58 (s, 3H), 3.03 (q, *J*=6.9 Hz, 1H), 1.97 (br., 1H), 1.59 (d, J=0.9 Hz, 3H), 1.26 (d, J=6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 175.2, 144.2, 112.2, 112.5, 66.2, 61.3, 59.5, 43.2, 15.9, 10.3; IR (neat) 3451 cm^{-1} (OH), 1725 cm^{-1} (C=O); MS *m/z* 188 (M^+); HRMS calcd for $C_9H_{16}O_4$ (M^+): 188.1049, found: 188.1031.

4-Hydroxy-2,3-diisopropoxy-4-vinylcyclobut-2-en-1-one (20). According to the reported procedure,[12] under an Ar atmosphere, to a solution of **9**[10] (4.00 g, 20.2 mmol) in dry THF

(100 mL) was added a solution of vinylmagnesium bromide in THF (1.0 M, 22.2 mL, 22.2 mmol) at -78°C, and the mixture was stirred for 30 min. The reaction was quenched with H_2O at -78°C and the resulting mixture extracted with Et_2O. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (AcOEt / hexane, 1 / 4) to afford **20** (3.78 g, 83%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 300MHz) δ5.96 (dd, *J*=17.1, 10.7 Hz, 1H), 5.53 (d, *J*=17.1 Hz, 1H), 5.35 (d, *J*=10.7 Hz, 1H), 4.87 (sept., *J*=6.4 Hz, 2H), 2.69 (s, 1H), 1.29 (d, *J*=6.4 Hz, 6H), 1.25 (d, *J*=6.4 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75MHz) δ184.6, 166.4, 143.6, 137.0, 132.3, 86.6, 75.0, 73.8, 22.8, 22.7, 22.6, 22.5; IR (neat) 3415 cm^{-1} (OH); MS *m/z* 226 (M^+); HRMS calcd for $C_{12}H_{18}O_4$ (M^+): 226.1205, found: 226.1196.

2,3-Diisopropoxy-4-(trimethylsilyloxy)-4-vinylcyclobut-2-en-1-one (21).[12] Under an Ar atmosphere, to a solution of **20** (3.40 g, 15.0 mmol) and triethylamine (6.3 mL, 45.1 mmol) in dry Et_2O (60 mL) was added trimethylsilyl chloride (2.9 mL, 22.5 mmol) at RT, and the mixture was stirred at the same temperature for 17 h. The reaction mixture was diluted with H_2O at 0°C and extracted with Et_2O. The combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (AcOEt / hexane, 1 / 2) to afford **21** (3.81 g, 85%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300MHz) δ5.86 (dd, *J*=17.3, 10.4 Hz, 1H), 5.41 (d, *J*=17.3 Hz, 1H), 5.24 (d, *J*=10.4 Hz, 1H), 4.86 (m, 2H), 1.38-1.16 (m, 12H), 0.15 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ184.5, 166.9, 136.2, 132.2, 117.3, 88.2, 73.5, 66.0, 23.0, 22.9, 22.7, 22.6, -3.6; IR (neat) 1774 cm^{-1} (C=O), 1630 cm^{-1} (C=C); MS *m/z* 298 (M^+); HRMS calcd for $C_{15}H_{26}O_4Si$ (M^+): 298.1600, found: 298.1589.

3-Isopropoxy-2-vinyl-5,8-dioxaspiro[3.4]oct-2-en-1-one (22). To a solution of **21** (2.77 g, 9.3 mmol) and ethylenedioxy-*bis*-(trimethylsilane) (2.3 mL, 9.4 mmol) in dry THF (19 mL) was added trimethylsilyl trifluoromethanesulfonate (0.08 mL, 0.5 mmol) at 0°C under an Ar atmosphere, and the mixture was stirred at the same temperature for 10 min. The solvent was evaporated to leave a residue, which was purified by column chromatography on silica gel (AcOEt / hexane, 1 / 2) to afford **22** (1.74 g, 89%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300MHz) δ 6.15 (dd, *J*=17.5, 11.1 Hz, 1H), 6.03 (dd, *J*=17.5, 1.7 Hz, 1H), 5.45 (dd, *J*=11.1, 1.7 Hz, 1H), 4.77 (sept., *J*=6.4 Hz, 1H), 4.23-4.07 (m, 4H), 1.44 (d, *J*=6.4 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75MHz) δ190.7, 178.6, 131.1, 123.0, 121.9, 117.7, 78.0, 66.3, 22.8; IR (neat) 1760 cm^{-1} (C=O), 1639 cm^{-1} (C=C); MS *m/z* 210 (M^+); HRMS calcd for $C_{11}H_{14}O_4$ (M^+): 210.0892, found: 210.0885.

1-(3-Buten-1-yl)-3-isopropoxy-2-vinyl-5,8-dioxaspiro[3.4]oct-2-en-1-ol (23). Under an Ar atmosphere, to a solution of **22** (100 mg, 0.48 mmol) in dry Et_2O (2 mL) was added a solution of butenylmagnesium bromide in Et_2O (prepared from 4-bromobut-1-ene) (1.0 M, 0.95 mL, 0.95 mmol) at -78°C, and the mixture was stirred for 45 min. The reaction was quenched with H_2O at -78°C and the aqueous mixture extracted with Et_2O. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (AcOEt / hexane, 1 / 4) to afford **23** (116 mg, 92%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300MHz) δ 6.26(dd, *J*=17.9, 11.1 Hz, 1H), 5.85 (m, 1H), 5.50 (dd, *J*=17.9, 1.7 Hz, 1H), 5.16 (dd, *J*=11.1, 1.7 Hz, 1H), 5.02 (d, *J*=17.1 Hz, 1H), 4.92 (d, *J*=10.3 Hz, 1H), 4.46 (sept., *J*=6.4 Hz, 1H), 4.11-3.92 (m, 4H), 2.47 (s, 1H), 2.30-2.23 (m, 1H), 2.17-1.95 (m, 2H), 1.86-1.80 (m, 1H), 1.29 (d, *J* =6.4 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75MHz) δ145.3, 139.3, 125.5, 123.3, 117.4, 113.9, 111.9, 81.9, 73.0, 66.0, 64.6, 32.8, 29.6, 22.8, 22.6; IR (neat) 3488 cm^{-1} (OH); MS *m/z* 266 (M^+); HRMS calcd for $C_{15}H_{22}O_4$ (M^+): 266.1518, found: 266.1499.

3-(3-Buten-1-yl)-2-vinyl-5,8-dioxaspiro[3.4]oct-2-en-1-one (24). A solution of 23 (56 mg, 0.21 mmol) in THF was treated with 1 drop of 5% HCl at RT. After stirring for 1 h, the reaction mixture was diluted with sat. $NaHCO_3$ at 0°C and extracted with AcOEt. The combined organic layer was dried over MgSO4 and concentrated in vacuo. The residue was purified by column chromatography on silica gel (AcOEt / hexane, 4 / 5) to afford 24 (41 mg, 95%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300MHz) δ6.28 (dd, J=17.5, 10.6 Hz, 1H), 6.15 (dd, J=17.5, 2.1 Hz, 1H), 5.84 (m, 1H), 5.60 (dd, J=10.6, 2.1 Hz, 1H), 5.09 (d, J=17.1 Hz, 1H), 5.04 (d, J=10.2 Hz, 1H), 4.19-4.08 (m, 4H), 2.70-2.67 (m, 2H), 2.44-2.39 (m, 2H); ^{13}C NMR ($CDCl_3$, 75MHz) δ194.3, 177.0, 153.2, 136.4, 125.6, 123.0, 120.4, 115.7, 66.0, 30.3, 25.5; IR (neat) 1766 cm^{-1} C=O); MS *m/z* 206 (M^+); HRMS calc. for $C_{12}H_{14}O_3$ (M+), found; 206.0941.

Bicyclo[4.2.0]octa-1(6),2-diene-7,8-dione 7-ethylene ketal (25). Under an Ar atmosphere, to a solution of 24 (200 mg, 0.97 mmol) in dry CH2Cl2 (120 mL) was added Grubbs' catalyst (80 mg, 0.1 mmol) at RT, and the mixture was stirred for 4 h. The solvent was evaporated to leave a residue, which was purified by column chromatography on silica gel (AcOEt / hexane, 1 / 2) to afford 25 (140 mg, 81%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300MHz) δ 6.11-6.05 (m, 2H), 4.20-4.06 (m, 4H), 2.78-2.53 (m, 4H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 190.3, 179.3, 155.9, 134.3, 121.5, 115.6, 66.1, 66.0, 22.6, 19.0; IR (neat) 1765 cm^{-1} (C=O); MS m/z 178 (M+); HRMS calcd for $C_{10}H_{10}O_3$ (M+): 178.0630, found: 178.0627.

8-Methoxybicyclo[4.2.0]octa-1(6),2-dien-7-one 7-ethylene ketal (26). Under an Ar atmosphere, to a solution of **25** (20 mg, 0.11 mmol) in dry Et_2O (0.8 mL) was added a solution of DIBAL in *n*-hexane (0.95 M, 0.14 mL, 0.13 mmol) at -25°C, and the mixture was stirred at the same temperature for 10 min. The reaction mixture was dilute with Et_2O and H_2O at -25°C, and the mixture was stirred at RT for 20 min. The suspension was filtered through Celite and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (AcOEt / hexane, 1 / 1) to afford a corresponding alcohol (19 mg, 94%) as a colorless solid. ^{1}H NMR ($CDCl_3$, 300MHz) δ6.00 (dt, *J*=9.6, 1.0 Hz, 1H), 5.90 (m, 1H), 4.60 (s, 1H), 4.09-3.99 (m, 4H), 2.46-2.37 (m, 2H), 2.29-2.04 (m, 2H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 148.7, 140.2, 131.6, 118.7, 111.8, 80.2, 65.0, 64.4,22.8, 17.0; IR (neat) 3448 cm^{-1} (OH); MS *m/z* 180 (M^+); HRMS calcd for $C_{10}H_{12}O_3$ (M^+): 180.0786, found: 180.0786.

To a solution of the alcohol (19 mg, 0.11 mmol) and 2,6-di-*tert*-butyl-4-methylpyridine (260 mg, 1.27 mmol) in dry CH_2Cl_2 (1 mL) was added methyl trifluoromethanesulfonate (0.08 mL, 0.74 mmol) at RT under an Ar atmosphere, and the mixture was stirred for 18 h. The reaction was quenched with sat. $NaHCO_3$ at 0°C and the aqueous mixture extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (AcOEt / hexane, 4 / 5) to afford **26** (11 mg, 53%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300MHz) δ 6.01-5.99 (m, 1H), 5.90-5.87 (m, 1H), 4.39 (s, 1H), 4.08-3.93 (m, 4H), 3.41 (s, 3H), 2.42-2.17 (m, 4H); ^{13}C NMR ($CDCl_3$, 75MHz) δ145.8, 131.2, 123.9, 119.3, 88.3, 65.5, 65.2, 64.8, 56.6, 22.8, 17.2; IR (neat) 1715 cm^{-1} (C=C); MS *m/z* 194 (M^+); HRMS calcd for $C_{11}H_{14}O_3$ (M^+): 194.0943, found: 194.0956.

2,2,3,3-Tetracyano-1-methoxy-4-oxo-1,2,3,4,5,6-hexahydronaphthalene 4-ethylene ketal (28). Under an Ar atmosphere, a solution of **26** (8 mg, 0.04 mmol) and tetracyanoethylene (11 mg, 0.08 mmol) in dry toluene (1 mL) was heated at reflux for 40 min. The solvent was evaporated to leave a residue, which was purified by column chromatography on silica gel (AcOEt / hexane, 1 / 2) to afford **28** (8 mg, 60%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 300MHz) δ6.17-6.13 (m, 1H), 5.99-5.96 (m, 1H), 4.66-4.58 (m, 2H), 4.50-4.49 (m, 1H), 4.39-4.34 (m, 2H), 3.87 (s, 3H), 2.30-2.19 (m, 4H); ^{13}C NMR ($CDCl_3$, 75MHz) δ132.2, 130.3, 128.1, 121.2, 110.8, 109.3, 109.1, 107.9, 106.8, 78.7, 68.9, 68.3, 62.8, 43.6, 29.7, 21.9, 20.2; IR (neat) 2258 cm^{-1} (CN), 1657, 1601 cm^{-1} (conjugated C=C); MS *m/z* 322 (M^+); HRMS calcd for $C_{17}H_{14}N_4O_3$ (M^+): 322.1066, found: 322.1035.

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