Tetrahedron Vol. 49, No 29, pp. 6349-6358, 1993
Printed in Great Britain

0040-4020/93 $6.00+.00

Mild and Efficient Diels-Alder Reaction Using Cationic Dienophiles Generated *in Situ*

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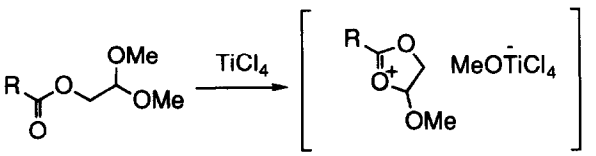
(*Received in Japan* 12 *April* 1993)

Abstract: On the action of a Lewis acid, 2,2-dimethoxyethyl acrylate is readily transformed into a reactive cationic dienophile, and it reacts with dienes under mild conditions to give Diels-Alder adducts in good yields with high stereo- and/or regioselectivity 2-Oxopropyl acrylate and 2-oxocyclopentyl acrylate are also found to be converted into alternative cationic dienophiles by a facile procedure

The Diels-Alder reaction is one of the most efficient reactions for the stereoselective construction of six-membered rings. Along with the current demands for synthetic tools to obtain enantiomerically pure substances, a number of investigations have been done on the asymmetric Diels-Alder reaction,[2] and some of them have achieved to the level where almost enantiomerically pure materials are available. However, in not a few cases, there is some restriction of the kind of dienes to be used for sufficient results (especially yield). Therefore, if a more reactive dienophile is easily prepared, it will broaden the synthetic utility of the Diels-Alder reaction toward various kinds of dienes. As one of the solutions to this problem, cationic dienophiles have been adopted by several groups. They have revealed the efficiency of the cationic dienophiles in the Diels-Alder reaction including applications to asymmetric synthesis.[3]

We have recently developed new synthetic intermediates, 2,2-dimethoxyethyl esters, for the generation of cationic species through neighboring group participation as depicted in Scheme 1, and their potential in organic reactions has been established for these years.[4] For example, we have reported that the Michael reaction proceeded smoothly between the cationic species (**1**, R = 1-alkenyl) and enamines under mild conditions to give the adducts in good yields with high *syn*-selectivity, which is quite rare in the Michael reaction between α,β-unsaturated ester derivatives and ketone enolate equivalents.[4a,c] As this reaction indicates, the cationic species are expected not only to improve the yield of a reaction under mild conditions but also to provide distinctive selectivity due to their peculiar electronic structures.

In the present paper, we report on the reaction of a cationic dienophile, derived from 2,2-dimethoxyethyl acrylate, with various dienes under mild conditions, and on the alternative method to obtain cationic dienophiles from 2-oxoalkyl acrylates by the facile procedure.[5]



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Scheme 1.

At first, we investigated the Diels-Alder reaction of 2,2-dimethoxyethyl acrylate (**2**), which could be easily prepared by the condensation reaction between acrylic acid and 2,2-dimethoxyethanol[4c] by using 2-chloro-1-methylpyridinium iodide[6] or diethyl azodicarboxylate/triphenylphosphine[7] as a dehydrating reagent.[4c] As mentioned above, 2,2-dimethoxyethyl esters were converted into cationic species on the action of a Lewis acid in dichloromethane. Then, we examined the efficiency of various Lewis acids in the Diels-Alder reaction between **2** and 1,3-cyclopentadiene. The results are summarized in Table 1. As can be seen from Table 1, titanium tetrachloride or gallium trichloride was the best for the synthesis of norbornenecarboxylate **3** at –78 °C. However, it was found that the gallium trichloride-mediated reaction proceeded only sluggishly at –78 °C when other dienes were used. In contrast, trimethylsilyl trifluoromethanesulfonate gave satisfactory results in such cases, although it suffered somewhat low yield in the reaction with 1,3-cyclopentadiene (the reason is not clear). The results of the Diels-Alder reaction of acrylate **2** with various dienes are summarized in Table 2.

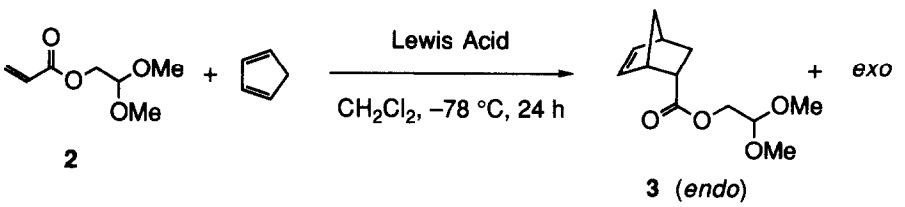

Table 1. The Diels-Alder Reaction of 2,2-Dimethoxyethyl Acrylate (**2**) with 1,3-Cyclopentadiene in the Presence of Various Lewis Acids

Lewis acid	Yield (%)	*endo* : *exo*
$TiCl_4$	85	25 : 1
Me_3SiOTf	41	34 : 1
$BF_3{\cdot}OEt_2$	21	69 : 1
$SnCl_4$	28	11 : 1
$GaCl_3$	84	45 : 1

It is noted that various dienes including acyclic ones react with acrylate **2** smoothly at –78 °C. Control experiments indicated that the similar Diels-Alder reaction of ethyl acrylate hardly proceeded under the same conditions. Thus, the intermediate cationic species plays an important role in this reaction.[8] Also, the high selectivity of this reaction is noteworthy. In each case, almost one diastereo- and/or regioisomer was obtained and, in some cases, the minor isomer was not detected at all by the GLC analysis. The present method is superior to the cationic Diels-Alder reaction starting from orthoesters[3c,d] in the points of the availability of the starting materials and of high diastereo- and regioselectivities.

Next, the reaction was carried out in the presence of a catalytic amount of a Lewis acid. Unfortunately, titanium tetrachloride and trimethylsilyl trifluoromethanesulfonate were not suitable for this purpose, although they were the most effective in stoichiometric reactions. However, trityl perchlorate, now a widespread Lewis acid catalyst for the reaction of silylated nucleophiles with electrophiles such as acetals,[9] is found to give the satisfactory result (Scheme 2). In this case, higher stereoselectivity was achieved in acetonitrile (*endo* : *exo* = 29 : 1) than in dichloromethane (*endo* : *exo* = 17 : 1).

In the course of our investigation to apply such a cationic dienophile toward the asymmetric Diels-Alder reaction, more general approach for the synthesis of 2,2-dialkoxyalkyl esters was desired. We next investigated the acetalization of 2-oxoalkyl esters in order to synthesize various acetals including chiral ones from a common precursor. We chose 2-oxopropyl acrylate (**4**) as a model compound for the synthesis of an acetal because of the simplicity of the preparation. Upon acetalization of ester **4** under appropriate reaction conditions, cationic

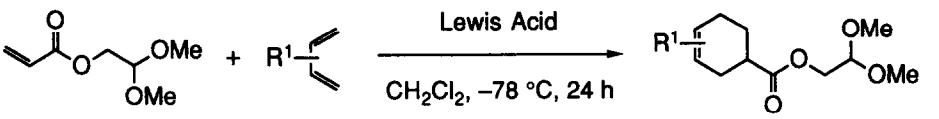

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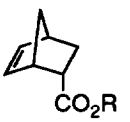
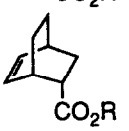
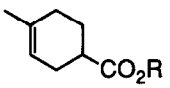
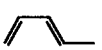
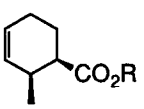
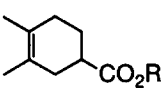
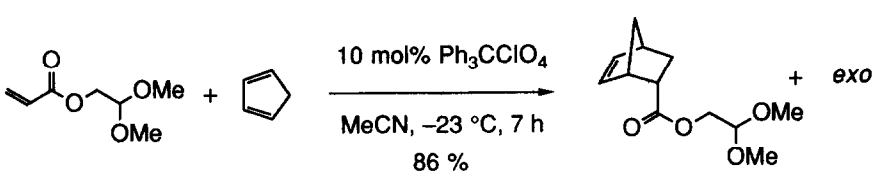
Table 2. The Diels-Alder Reaction of 2,2-Dimethoxyethyl Acrylate (**2**) with Dienes

Diene	Lewis Acid	Major product	Yield (%)	Selectivity[a]
	$TiCl_4$		85	*endo* : *exo* = 25 : 1
	Me_3SiOTf		41	*endo* : *exo* = 34 : 1
	$TiCl_4$		89	*endo* : *exo* = 100 : 0[b]
	Me_3SiOTf		83	*endo* : *exo* = 100 : 0[b]
	$TiCl_4$		66	1,4- : 1,3- = 33 : 1
	Me_3SiOTf		78	1,4- : 1,3- = 120 : 1
	$TiCl_4$		87	major : minor = 80 : 1[c]
	Me_3SiOTf		82	major : minor = 280 : 1[c]
	$TiCl_4$		89	—
	Me_3SiOTf		86	—

(R = 2,2-dimethoxyethyl)

a) Determined by GLC analysis.
b) *Exo*-isomer was not detected by GLC analysis
c) Two isomeric products were obtained The minor product was 1,3-disubstituted isomer, of which stereochemistry was not determined. *Exo*-1,2-isomer (*trans*-2,2-dimethoxyethyl 2-methyl-3-cyclohexenecarboxylate) was not detected.



2

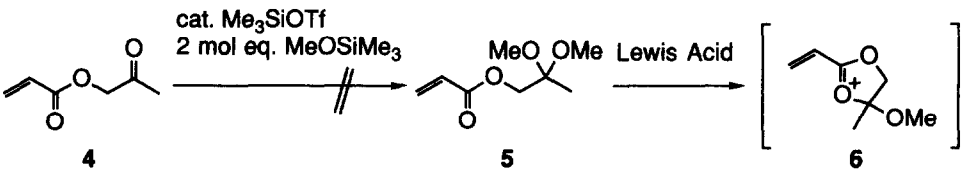
3 (*endo*)

29 : 1

Scheme 2.

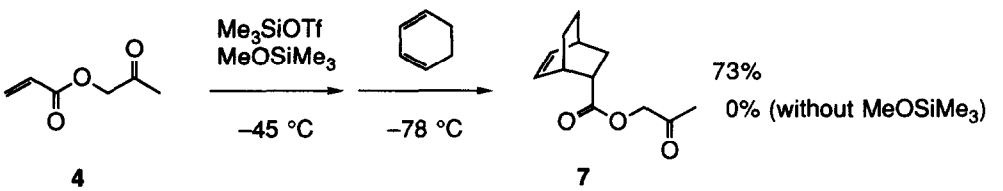
intermediate **6** would be prepared by simply adding a Lewis acid to the mixture containing acetal **5** through one-pot procedure. According this expectation, the acetalization reaction was performed by treating 2-oxopropyl acrylate (**4**) with 2.8 molar equivalent of methoxytrimethylsilane and a catalytic amount (6 mol%) of

trimethylsilyl trifluoromethanesulfonate at –78 °C, and the reaction was quenched after 5 h by pyridine.[10] However, the crude mixture contained no acetalized product **5** (Scheme 3).



Scheme 3.

In this acetalization reaction, cationic species **6** is possibly generated before acetal formation, and the result would be explained in terms of the intermediacy of this stable cationic species. Therefore, if 2-oxopropyl acrylate is treated with equimolar amounts of trimethylsilyl trifluoromethanesulfonate and methoxytrimethylsilane, the direct generation of cationic dienophile **6** was anticipated. Based on this consideration, we tried the Diels-Alder reaction of 2-oxopropyl acrylate (**4**) with 1,3-cyclohexadiene in the presence of trimethylsilyl trifluoromethanesulfonate and methoxytrimethylsilane at –78 °C. The reaction without methoxytrimethylsilane was also carried out at the same temperature for comparison. As depicted in Scheme 4, the results were of contrast. While the reaction did not proceed at all without methoxytrimethylsilane, the corresponding adduct was obtained in 73% yield in the presence of methoxytrimethylsilane even at –78 °C.[11] This result would strongly suggest that the reaction proceeds not by a simple Lewis acid-activation of **4**, but by way of cationic species **6**,[8] and methoxytrimethylsilane plays an important role for the generation of the intermediate.

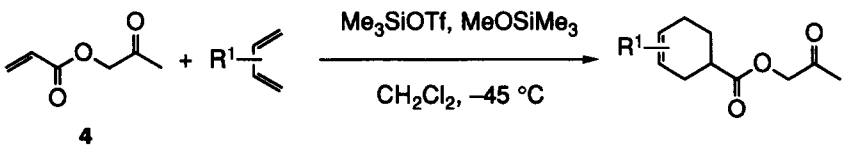


Scheme 4.

Following the above observation, we anticipated a 2-oxoalkyl ester could be a valuable dienophile and investigated to utilize this dienophile in the reaction with various dienes. Since the reaction of dienophile **4** and 1,3-cyclohexadiene was observed to be moderately slow at –78 °C, all of the reactions were carried out at –45 °C. The reactions were monitored by TLC, and quenchings were performed after the reactions reached to stationary state. The results are listed in Table 3.

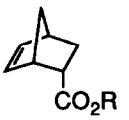
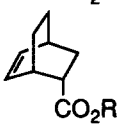
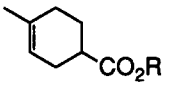
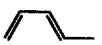
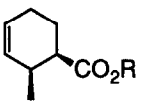
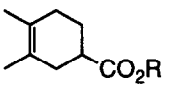
The adduct was obtained in moderate to good yield in each case. Considering the high reactivity of 1,3-cyclopentadiene in the Diels-Alder reaction, the yield (65%) was unsatisfactory; this result could be attributable to the oligomerization of 1,3-cyclopentadiene. Therefore, the reaction was carried out by slow-addition of 1,3-cyclopentadiene over a period of 2 h at –78 °C. As a result, yield was improved to 85%. Thus, the 2-oxopropyl ester was found to be a useful precursor for the generation of a reactive cationic dienophile similar to 2,2-dimethoxyethyl esters.

Since the transformation from the 2-oxopropyl ester to the cationic species is initiated by neighboring participation, it is considered that a conformationally less flexible molecule having a favorable structure for the participation should more readily be converted into the corresponding cationic intermediate. On the basis of these considerations, 2-oxocyclopentyl acrylate (**8**) was designed, and the Diels-Alder reaction was tried by using it. After **8** was treated with equimolar amounts of trimethylsilyl trifluoromethanesulfonate and methoxytrimethylsilane, 1,3-cyclopentadiene (1.5 molar equivalent) was added to the mixture over a period of 10 min at



4

Table 3. The Diels-Alder Reaction of 2-Oxopropyl Acrylate (**4**)

Diene	Reaction time (h)	Major product	Yield (%)	Selectivity[a]
	8		65	*endo* : *exo* = 31 : 1
	14		85	*endo* : *exo* = 53 : 1[b]
	10		89	*endo* : *exo* = >110 : 1
	12		66	1,4- : 1,3- = 85 : 1
	26		61	1,2- : 1,3- = 56 : 1 *endo* : *exo* = 220 : 1
	14		75	—

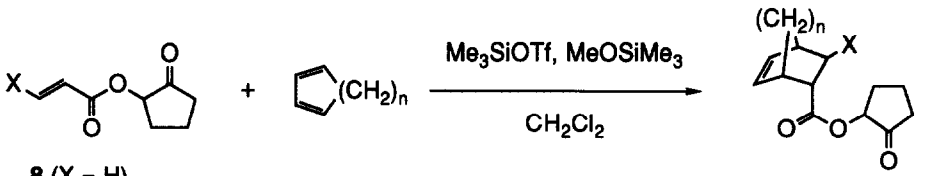
(**R** = 2-oxopropyl)

a) Determined by GLC analysis
b) 1,3-Cyclopentadiene was added over a period of 2 h at –78 °C

–78 °C. Monitoring the reaction by TLC shortly after the addition of the diene showed the complete consumption of the acrylate. Since oligomerization of 1,3-cyclopentadiene did not occur under the conditions, the product was easily purified by chromatography and was obtained in almost quantitative yield (95%) with high stereoselectivity (*endo* : *exo* = 34 : 1). This result indicates the rapid formation of a cationic intermediate and the high reactivity of the cationic dienophile under mild conditions. The results of the Diels-Alder reaction of 2-oxocyclopentyl esters **8** and **9** are listed in Table 4.

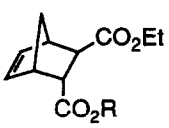
It should be noted that ethyl 2-oxocyclopentyl fumarate (**9**) also gave the corresponding adduct with good stereoselectivity (Table 4, Entry 3). This result indicates that the 2-oxocyclopentyl ester group is activated much strongly than the ethyl ester group in the same molecule. Using the 2-oxocyclopentyl ester, differentiation of two kinds of esters could be easily accomplished in the Diels-Alder reaction. Furthermore, it was found that the 2-oxocyclopentyl ester can be hydrolyzed more easily than the ethyl ester. Thus, treatment of mixed ester **10** with lithium hydroperoxide afforded half ester **11**, in which the carboxyl group is oriented to the *endo* position (Scheme 5).

In conclusion, we have developed a facile method for the generation of highly reactive cationic dienophiles from 2,2-dimethoxyethyl acrylate, 2-oxopropyl acrylate, and 2-oxocyclopentyl acrylate, all of which are



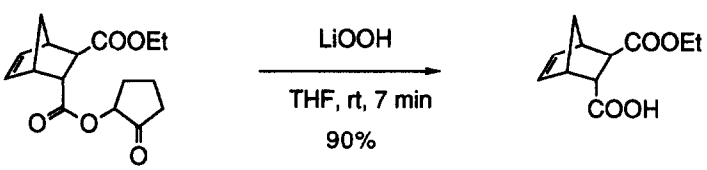
8 (X = H)
9 (X = CO_2Et)

Table 4. The Diels-Alder Reaction of 2-Oxocyclopentyl Esters **8**, **9**

Entry	X	Diene	Reaction conditions	Major product	Yield (%)	*endo* : *exo* [a]
1	H		–78 °C, 2.5 h		95	34 : 1
2	H		–45 °C, 5 h		75	480 : 1
3[b]	COOEt		–78 °C, 21 h		81	15 : 1[c]

(R = 2-oxocyclopentyl)

a) Determined by GLC analysis, otherwise stated.
b) Benzyloxytrimethylsilane was used instead of methoxytrimethylsilane
c) Determined by 400 MHz ^{1}H-NMR



10 **11**

Scheme 5.

available by simple esterification of acrylic acid or acryloyl chloride with the corresponding alcohols. Under mild conditions, the cationic dienophiles provided the adducts in good yields with high stereo- and/or regioselectivity.

EXPERIMENTAL SECTION

All melting points are uncorrected. ^{1}H-NMR spectra were recorded on a JEOL JNM-GX400 or a JEOL JNM-EX270 FT NMR instrument in chloroform-*d* with tetramethylsilane as an internal standard. The chemical-shift values were recorded as parts per million. IR spectra were recorded on a JASCO IR-810 Infrared

Spectrophotometer. GLC analyses were performed on a Shimadzu GC-14A system with a capillary column (CBP10-M25-025). Low- and high-resolution mass spectra were recorded at an ionization potential of 70 eV on a Shimadzu GCMS-QP2000 and a JEOL JMS-AX505H instrument, respectively. All reaction solvents were distilled from an appropriate dehydrating agent before use.

2,2-Dimethoxyethyl Acrylate (2). To a suspension of 2-chloro-1-methylpyridinium iodide[6] (9.20 g, 36.0 mmol) in dichloromethane (45 ml) were successively added acrylic acid (2.16 ml, 31.5 mmol), triethylamine (10.45 ml, 75 mmol), and a dichloromethane (5 ml) solution of 2,2-dimethoxyethanol[4c] (3.18 g, 30.0 mmol) at 0 °C. After the solution was stirred at room temperature for 24 h, 100 ml of water was added. The organic layer was removed, and the aqueous layer was extracted with dichloromethane (3 x 50 ml). The combined organic layers were dried (Na_2SO_4), and the solvent was removed in vacuo. The residue was chromatographed over silica gel (70 - 230 mesh, ether / hexane = 1 : 10) to give 2,2-dimethoxyethyl acrylate (3.89 g, 24.3 mmol) in 81% yield as a colorless liquid. ^{1}H-NMR (270 MHz) δ = 3.41 (6H, s), 4.20 (2H, d, J = 5.3 Hz), 4.61 (1H, t, J = 5.3 Hz), 5.87 (1H, dd, J = 10.4 and 1.5 Hz), 6.17 (1H, dd, J = 17.3 and 10.4 Hz), 6.45 (1H, dd, J = 17.3 and 1.5 Hz); IR (neat) 1730, 1640, 1415, 985, 900, 810 cm^{-1}; HRMS found: m/z 160.0742, calcd for $C_7H_{12}O_4$: M, 160.0735.

According to the method using diethyl azodicarboxylate/triphenylphosphine as a dehydrating reagent,[4c] ester **2** was obtained in 82% yield.

***endo*-2,2-Dimethoxyethyl Bicyclo[2.2.1]hept-5-enecarboxylate (3) (Typical Procedure for the Diels-Alder Reaction of 2,2-Dimethoxyethyl Acrylate (2)).** To a dichloromethane solution of titanium tetrachloride (1.07 M, 1.2 ml, 1.3 mmol) was added drop by drop a dichloromethane (3 ml) solution of 2,2-dimethoxyethyl acrylate (**2**, 169.6 mg, 1.06 mmol) and 1,3-cyclopentadiene (1.26 ml, 3.2 mmol) at –78 °C. The solution was stirred at that temperature for 24 h. After the addition of dry methanol (5 ml), the solution was allowed to warm up to room temperature and stirred for 10 min. Then, triethylamine (1 ml) and saturated aqueous $NaHCO_3$ solution (10 ml) were successively added, and the mixture was stirred for an additional 30 min at room temperature. Insoluble solid mass was filtered off through a Celite pad, and the organic materials were extracted with dichloromethane (3 x 10 ml). After the combined organic layers were dried with Na_2SO_4 and concentrated, the residue was purified by silica gel column chromatography (ether / hexane = 5 : 95 → 20 : 80) to afford 2,2-dimethoxyethyl bicyclo[2.2.1]hept-5-ene-2-carboxylate (203.3 mg, 0.90 mmol) in 85% yield (*endo* : *exo* = 25 : 1). ^{1}H-NMR (400 MHz) δ = 1.28 (1H, d, J = 7.9 Hz), 1.39 - 1.45 (2H, m), 1.88 - 1.95 (1H, m), 2.91 (1H, br. s), 2.99 (1H, dt, J = 9.5 and 4.0 Hz), 3.23 (1H, br. s), 3.39 (6H, s), 4.03 (1H, dd, J = 11.6 and 5.5 Hz), 4.10 (1H, dd, J = 11.6 and 5.2 Hz), 4.55 (1H, t, J = 5.3 Hz), 5.94 (1H, dd, J = 5.6 and 2.8 Hz), 6.20 (1H, dd, J = 5.6 and 3.1 Hz); IR (neat) 1740, 715 cm^{-1}; MS m/z (rel intensity) 226 (M^+; 0.2), 194 (2.9), 129 (55), 75 (100), 66 (92), 55 (65); HRMS found m/z 226.1197, calcd for $C_{12}H_{18}O_4$: M, 226.1205.

Stereochemistry and selectivity were determined by GLC comparison with an authentic sample prepared through the thermal Diels-Alder reaction between acrylic acid and 1,3-cyclopentadiene followed by DCC esterification with 2,2-dimethoxyethanol.

***endo*-2,2-Dimethoxyethyl Bicyclo[2.2.2]oct-5-enecarboxylate.** ^{1}H-NMR (400 MHz) δ = 1.20 - 1.34 (2H, m), 1.45 - 1.61 (2H, m), 1.65 - 1.78 (2H, m), 2.59 - 2.61 (1H, m), 2.67 (1H, ddd, J = 9.8, 5.5, and 2.1 Hz), 2.94 - 2.95 (1H, m), 3.38 (6H, s), 4.04 (1H, dd, J = 11.8 and 5.3 Hz), 4.10 (1H, dd, J = 11.8 and 5.3 Hz), 4.55 (1H, t, J = 5.3 Hz), 6.14 (1H, t, J = 7.4 Hz), 6.32 (1H, t, J = 7.4 Hz); IR (neat) 1745, 705 cm^{-1}; MS m/z (rel intensity) 240 (M^+; 0.1), 209 (2.3), 80 (18), 79 (15), 75 (100), 55 (11); HRMS found m/z 240.1358, calcd for $C_{13}H_{20}O_4$: M, 240.1361.

2,2-Dimethoxyethyl 4-Methyl-3-cyclohexenecarboxylate. ^{1}H-NMR (400 MHz) δ = 1.65 (3H, br. s), 1.60 - 1.77 (2H, m), 1.99 - 2.03 (2H, m), 2.22 - 2.25 (2H, m), 2.51 - 2.57 (1H, m), 3.40 (6H, s), 4.11 (1H, dd, J = 11.8 and 5.3 Hz), 4.14 (1H, dd, J = 11.8 and 5.3 Hz), 4.57 (1H, t, J = 5.3 Hz), 5.37 (1H, br. s); IR (neat) 1740, 1440, 800 cm^{-1}; HRMS found m/z 228.1383, calcd for $C_{12}H_{20}O_4$: M, 228.1362.

***cis*-2,2-Dimethoxyethyl 2-Methyl-3-cyclohexenecarboxylate.** ^{1}H-NMR (400 MHz) δ = 0.92 (3H, d, J = 7.0 Hz), 1.68 - 1.86 (2H, m), 1.97 - 2.12 (2H, m), 2.62 - 2.65 (1H, m), 2.72 (1H, ddd, J = 12.2,

5.5, and 3.1 Hz), 3.40 (6H, s), 4.10 (1H, dd, J = 11.6 and 5.5 Hz), 4.17 (1H, dd, J = 11.6 and 5.5 Hz), 4.59 (1H, t, J = 5.5 Hz), 5.61 - 5.68 (2H, m); IR (neat) 1740, 710 cm^{-1}; MS *m/z* (rel intensity) 197 (6.2), 196 (8.1), 95 (24), 79 (13), 75 (100), 59 (13), 58 (51), 55 (12); HRMS found *m/z* 197.1193 and 196.1116, calcd for $C_{11}H_{17}O_3$: M–MeO, 197.1178, and for $C_{11}H_{16}O_3$: M–MeOH, 196.1100.

2,2-Dimethoxyethyl 3,4-Dimethyl-3-cyclohexenecarboxylate. ^{1}H-NMR (400 MHz) δ = 1.61 (3H, s), 1.62 (3H, s), 1.65 - 2.25 (6H, m), 2.54 - 2.61 (1H, m), 3.39 (6H, s), 4.10 (1H, dd, J = 11.6 and 5.5 Hz), 4.13 (1H, dd, J = 11.6 and 5.5 Hz), 4.57 (1H, t, J = 5.5 Hz); IR (neat) 1740, 1440 cm^{-1}; HRMS found *m/z* 242.1548, calcd for $C_{13}H_{22}O_4$: M, 242.1518.

Trityl Perchlorate-Catalyzed Diels-Alder Reaction of 2,2-Dimethoxyethyl Acrylate (2). To a solution of trityl perchlorate (29.3 mg, 0.090 mmol) in acetonitrile (1 ml) was added an acetonitrile (4 ml) solution of 2,2-dimethoxyethyl acrylate (**2**, 144.3 mg, 0.90 mmol) and 1,3-cyclopentadiene (0.22 ml, 2.66 mmol) at –23 °C. The solution was stirred at that temperature for 7 h. After the addition of dry methanol (2 ml), the solution was allowed to warm up to room temperature and stirred for 10 min. Then, triethylamine (0.2 ml) and saturated aqueous $NaHCO_3$ solution (10 ml) were successively added, and the mixture was stirred for an additional 30 min at room temperature. The organic materials were extracted with dichloromethane (3 x 15 ml), and the combined organic layers were dried with Na_2SO_4. After the solvent was removed under reduced pressure, the residue was purified by silica gel column chromatography (ether / hexane = 5 : 95 → 20 : 80) to afford 2,2-dimethoxyethyl bicyclo[2.2.1]hept-5-ene-2-carboxylate (174.5 mg, 0.77 mmol) in 86% yield (*endo* : *exo* = 29 : 1).

2-Oxopropyl Acrylate (4). To a solution of hydroxyacetone (1.8 g, 25 mmol) in 50 ml of dichloromethane was added 4 ml of triethylamine, and the mixture was cooled to 0 °C. Into the stirred mixture, acryloyl chloride (2.0 g, 22 mmol) was added drop by drop, and the cooling bath was removed. The mixture was stirred overnight at room temperature. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (20 ml). The organic layer was removed, and the aqueous layer was extracted with dichloromethane (3 × 10 ml). The organic layers were combined and dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by silica gel column chromatography (hexane / EtOAc = 5 : 1), followed by distillation (60 - 61 °C at 1.5 mmHg), to give 2-oxopropyl acrylate (1.36 g, 11 mmol) in 48% yield. ^{1}H-NMR (270 MHz) δ = 2.19 (3H, s), 4.74 (2H, s), 5.94 (1H, dd, J = 10.4 and 1.5 Hz), 6.23 (1H, dd, J = 17.3 and 10.4 Hz), 6.51 (1H, dd, J = 17.3 and 1.5 Hz); IR (neat) 1750, 1730, 1640, 810 cm^{-1}; HRMS found *m/z* 128.0476, calcd for $C_6H_8O_3$: M, 128.0474.

2-Oxocyclopentyl Acrylate (8). To a solution of 2-hydroxycyclopentanone[12] (3.1 g, 31 mmol) and triethylamine (12 ml) in 70 ml of dichloromethane was added 4.4 g of acryloyl chloride (48 mmol) at 0 °C. The reaction was exothermic, and a large amount of white salt was precipitated. After the mixture was stirred overnight at room temperature, the reaction was quenched by the addition of saturated aqueous $NaHCO_3$. The organic layer was removed, and the aqueous layer was extracted with dichloromethane (3 × 10 ml). The combined organic layers were dried over Na_2SO_4, and evaporated. The residue was purified by silica gel column chromatography (hexane / EtOAc = 15 : 1), followed by Kugelrohr distillation (120 - 130 °C at 0.75 mmHg), to give 2-oxocyclopentyl acrylate (0.83 g, 5.4 mmol) in 18% yield. ^{1}H-NMR (400 MHz) δ = 1.83 - 1.99 (2H, m), 2.08 - 2.54 (4H, m), 5.16 (1H, br. t, J = 10 Hz), 5.90 (1H, dd, J = 10.1 and 1.4 Hz), 6.18 (1H, dd, J = 17.4 and 10.1 Hz), 6.48 (1H, dd, J = 17.4 and 1.4 Hz); IR (neat) 1765, 1735, 1640, 810 cm^{-1}; HRMS found *m/z* 154.0660, calcd for $C_8H_{10}O_3$: M, 154.0630.

Ethyl 2-Oxocyclopentyl Fumarate (9). To a dichloromethane (60 ml) solution of ethyl hydrogen fumarate (1.57 g, 10.9 mmol) and 4-dimethylaminopyridine (0.1 g, 0.82 mmol) was added *N,N'*-dicyclohexylcarbodiimide (4 g) at room temperature. A dichloromethane (2 ml) solution of 2-hydroxycyclopentanone (1.45 g, 14 mmol) was then added to the solution, and the mixture was stirred for 9 h at an ambient temperature. After the precipitate was removed by filtration, the filtrate was concentrated in vacuo. The residue was applied to a short column chromatography, followed by purification with distillation (180 °C at 1 mmHg) and silica gel column chromatography (hexane / EtOAc / toluene = 8 : 3 : 3) to give ethyl 2-oxocyclopentyl fumarate (0.89 g, 3.93 mmol) in 36% yield. ^{1}H-NMR (400 MHz) δ = 1.32 (3H, t, J = 7.2 Hz), 1.84 - 2.52 (6H, m), 4.26 (2H,

q, J = 7.1 Hz), 5.19 (1H, br. t, J = 10 Hz), 6.90 (2H, s); IR (neat) 1765, 1725, 1645, 980 cm^{-1}; MS m/z (rel intensity) 227 (0.5), 226 (M^+; 1.1), 181 (1.0), 128 (57), 127 (65), 100 (15), 99 (100), 83 (27), 82 (24), 71 (59), 55 (81), 54 (25), 53 (21); HRMS found m/z 226.0866, calcd for $C_{11}H_{14}O_5$: M, 226.0841.

***cis*-2-Oxopropyl 2-Methyl-3-cyclohexenecarboxylate (Typical procedure for the Diels-Alder reaction of 2-Oxopropyl Acrylate (4) and 2-Oxocyclopentyl Acrylate (8)).** To a solution of 2-oxopropyl acrylate (52.8 mg, 0.412 mmol) in 3 ml of dichloromethane was added a dichloromethane (0.6 ml) solution of trimethylsilyl trifluoromethanesulfonate (0.435 mmol) at –45 °C. After 30 min, methoxytrimethylsilane (52.3 mg, 0.502 mmol) was added, and the mixture was stirred for 2 h at that temperature. Then, a solution of *trans*-1,3-pentadiene (133.3 mg, 1.96 mmol) in dichloromethane (1 ml) was added drop by drop over a 10-min period. The reaction mixture was stirred for 26 h at –45 °C. Shortly after the cooling bath was removed, the reaction was quenched by adding water (10 ml) in one portion under vigorous stirring. The organic layer was removed, and the aqueous layer was extracted with dichloromethane (3 × 10 ml). The combined organic layers were dried over anhydrous sodium sulfate, and the solvent was evaporated under reduced pressure. Purification of the crude product by silica gel column chromatography (hexane / EtOAc = 20 : 1) and subsequent preparative TLC afforded the Diels-Alder adduct (49.6 mg, 0.25 mmol) in 61% yield. ^{1}H-NMR (400 MHz) δ = 0.98 (3H, d, J = 7.0 Hz), 1.72 - 1.91 (2H, m), 2.00 - 2.15 (2H, m), 2.18 (3H, s), 2.64 - 2.72 (1H, m), 2.81 (1H, ddd, J = 11.9, 5.5, and 3.1 Hz), 4.67 (2H, s), 5.66 (2H, br. s); IR (neat) 1730, 710 cm^{-1}; HRMS found m/z 196.1069, calcd for $C_{11}H_{16}O_3$: M, 196.1099.

***endo*-2-Oxopropyl Bicyclo[2.2.1]hept-5-enecarboxylate.** ^{1}H-NMR (400 MHz) δ = 1.31 (1H, d, J = 8.2 Hz), 1.43 - 1.47 (2H, m), 1.95 (1H, ddd, J = 11.9, 9.2, and 3.7 Hz), 2.15 (3H, s), 2.93 (1H, br. s), 3.08 (1H, dt, J = 9.2 and 4.0 Hz), 3.29 (1H, br. s), 4.57 (1H, d, J = 16.8 Hz), 4.64 (1H, d, J = 17.1 Hz), 6.02 (1H, dd, J = 5.4 and 2.7 Hz), 6.22 (1H, dd, J = 5.5 and 3.2 Hz); IR (neat) 1740, 715 cm^{-1}; HRMS found m/z 194.0941, calcd for $C_{11}H_{14}O_3$: M, 194.0943.

***endo*-2-Oxopropyl Bicyclo[2.2.2]oct-5-enecarboxylate (7).** ^{1}H-NMR (400 MHz) δ = 1.21 - 1.36 (2H, m), 1.47 - 1.82 (4H, m), 2.14 (3H, s), 2.60 - 2.65 (1H, m), 2.77 (1H, ddd, J = 9.8, 5.5, and 2.1 Hz), 3.00 - 3.04 (1H, m), 4.57 (1H, d, J = 16.8 Hz), 4.65 (1H, d, J = 17.1 Hz), 6.19 (1H, t, J = 6.7 Hz), 6.33 (1H, t, J = 7.0 Hz); IR (neat) 1740, 1730, 700 cm^{-1}; HRMS found m/z 208.1105, calcd for $C_{12}H_{16}O_3$: M, 208.1099.

2-Oxopropyl 4-Methyl-3-cyclohexenecarboxylate. ^{1}H-NMR (400 MHz) δ = 1.61 - 1.81 (2H, m), 1.66 (3H, d, J = 1.5 Hz), 1.98 - 2.10 (3H, m), 2.16 (3H, s), 2.20 - 2.32 (1H, m), 2.59 - 2.67 (1H, m), 4.66 (2H, s), 5.39 (1H, br. s); IR (neat) 1745, 1735, 800 cm^{-1}; HRMS found m/z 196.1136, calcd for $C_{11}H_{16}O_3$: M, 196.1099.

2-Oxopropyl 3,4-Dimethyl-3-cyclohexenecarboxylate. ^{1}H-NMR (400 MHz) δ = 1.62 (3H, s), 1.64 (3H, s), 1.66 - 1.75 (2H, m), 2.00 - 2.08 (2H, m), 2.16 (3H, s), 2.13 - 2.31 (2H, m), 2.66 (1H, dddd, J = 11.6, 9.8, 5.8, and 2.8 Hz), 4.66 (2H, s); IR (neat) 1750, 1730 cm^{-1}; HRMS found m/z 210.1264, calcd for $C_{12}H_{18}O_3$: M, 210.1256.

***endo*-2-Oxocyclopentyl Bicyclo[2.2.1]hept-5-enecarboxylate.** ^{1}H-NMR (400 MHz) δ = 1.28 (1H, d, J = 8.9 Hz), 1.43 - 1.47 (2H, m), 1.81 - 1.97 (3H, m), 2.10 (1H, br. s), 2.21 - 2.39 (3H, m), 2.92 (1H, br. s), 2.99 - 3.08 (1H, m), 3.23 (0.5 H, br. s), 3.25 (0.5H, br. s), 4.95 - 5.03 (1H, m), 5.92 (0.5H, dd, J = 5.5 and 2.8 Hz), 6.06 (0.5H, dd, J = 5.5 and 2.8 Hz), 6.20 (1H, br. s); IR (neat) 1765, 1740, 715 cm^{-1}; HRMS found m/z 220.1061, calcd for $C_{13}H_{16}O_3$: M, 220.1100.

***endo*-2-Oxocyclopentyl Bicyclo[2.2.2]oct-5-enecarboxylate.** ^{1}H-NMR (400 MHz) δ = 1.19 - 1.35 (2H, m), 1.45 - 1.92 (6H, m), 2.03 - 2.15 (1H, m), 2.20 - 2.44 (3H, m), 2.58 - 2.64 (1H, m), 2.69 - 2.76 (1H, m), 2.94 (0.5H, br. s), 2.99 (0.5H, br. s), 4.98 - 5.04 (1H, m), 6.13 (0.5H, t, J = 6.7 Hz), 6.22 (0.5H, t, J = 7.0 Hz), 6.33 (1H, t, J = 7.3 Hz); IR (neat) 1765, 1740, 700 cm^{-1}; HRMS found m/z 234.1247, calcd for $C_{14}H_{18}O_3$: M, 234.1256.

2-*exo*-3-*endo*-2-Ethyl 3-(2-Oxocyclopentyl) Bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (10). ^{1}H-NMR (400 MHz) δ = 1.28 (3H, t, J = 7.1 Hz), 1.45 (1H, br. d, J = 9 Hz), 1.60 - 1.64 (1H, m), 1.78 - 2.42 (6H, m), 2.68 - 2.70 (1H, m), 3.13 (1H, br. s), 3.29 - 3.31 (1H, m), 3.39 - 3.51 (1H, m), 4.16

(2H, q, J = 7.1 Hz), 4.96 (0.6H, br. t, J = 9 Hz), 5.07 (0.4H, br. t, J = 9 Hz), 6.07 - 6.09 (0.6H, m), 6.22 - 6.24 (0.4H, m), 6.30 (1H, br. s); IR (neat) 1760, 1730, 720 cm^{-1}; HRMS found m/z 292.1297, calcd for $C_{16}H_{20}O_5$: M, 292.1311.

2-*exo*-3-*endo*-2-Ethyl Hydrogen Bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (11). To a THF (5 ml) solution of mixed ester **10** (74 mg, 0.25 mmol) was added an aqueous solution (1.5 ml) of lithium hydroperoxide (0.50 mmol), prepared from lithium hydroxide and aqueous hydrogen peroxide (35%). After being stirred for 7 min at room temperature, saturated aqueous ammonium chloride solution (10 ml) was added to the mixture, and the reaction mixture was extracted with dichloromethane (3 x 10 ml). The combined organic layers were dried (Na_2SO_4), and the solvent was removed. The residue was chromatographed over silica gel (CH_2Cl_2 / MeOH = 20 : 1) to give 2-*exo*-3-*endo*-2-ethyl hydrogen bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (48 mg, 0.23 mmol) in 90% yield. Mp 58 - 60 °C; ^{1}H-NMR (400 MHz) δ = 1.28 (3H, t, J = 7.1 Hz), 1.47 (1H, dd, J = 8.9 and 1.7 Hz), 1.63 (1H, d, J = 8.9 Hz), 2.64 (1H, dd, J = 4.6 and 1.5 Hz), 3.14 (1H, br. s), 3.29 (1H, br. s), 3.44 (1H, t, J = 4.1 Hz), 4.17 (2H, q, J = 7.1 Hz), 6.14 (1H, dd, J = 5.6 and 2.9 Hz), 6.30 (1H, dd, J = 5.6 and 3.2 Hz); IR (KBr) 3310, 1720, 1685, 1640, 1185 cm^{-1}. Anal. Calcd for $C_{11}H_{14}O_4$: C, 62.85; H, 6.71. Found: C, 62.65; H, 6.68.

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