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The Synthetic Utilization of 2-Hydroxymethyl-2,5-dihydrothiophene 1,1-Dioxide in the Intramolecular Diels-Alder Reaction

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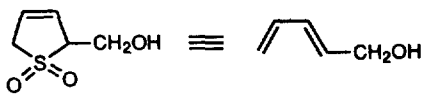
2-Hydroxymethyl-2,5-dihydrothiophene 1,1-dioxide (**1**) was prepared from thiophene-2-carboxylic acid by consecutive reactions involving the Birch reduction, esterification, reduction with lithium aluminum hydride, and oxidation with Oxone®. The esterification of alcohol **1** with various unsaturated carboxylic acids provided the precursors **8** for the intramolecular Diels-Alder reaction. The cheletropic expulsion of sulfur dioxide from the esters **8** followed by intramolecular Diels-Alder reaction furnished bicyclic γ- and δ-lactones.

Introduction

The intramolecular Diels-Alder reaction provides a six-membered ring with a fused or a bridged ring of various sizes and has become very useful in organic synthesis.[1,2] However, one of its limiting factors in the synthetic application is the development of method for the preparation of trienes. As a part of synthetic efforts toward cyclohexyl fragment of tetronasin,[2] we became interested in the intramolecular Diels-Alder reaction that could lead to bicyclic δ-lactones. In order to carry out the intramolecular Diels-Alder reaction, we had to prepare *s-trans*-penta-2,4-dien-1-ol as a diene for the Diels-Alder reaction. Although several methods for the preparation of *s-trans*-penta-2,4-dien-1-ol were reported in the literatures employing the use of Knoevenagel reaction,[4] sodium acetylide[5,6] and dihydropyran,[6] we found most of them impractical because of difficulties in distillation or storage of product due to its polymerization or decomposition. This fact inspired us to prepare a precursor of 1,3-diene and investigate its application in the intramolecular Diels-Alder reaction.

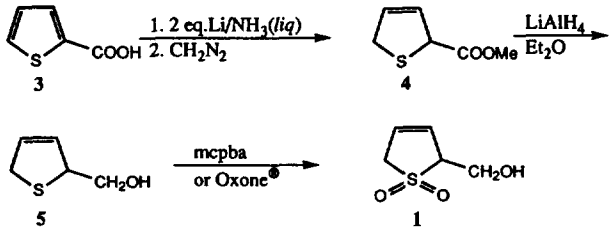
2,5-Dihydrothiophene 1,1-dioxides (3-sulfolenes) have been utilized as synthetic equivalents of 1,3-dienes because the cheletropic expulsion of sulfur dioxide from those compounds furnishes 1,3-dienes. However, so far there has been no report on the preparation of 2-hydroxymethyl-2,5-dihydrothiophene 1,1-dioxide (**1**). Herein we would like to report the preparation of **1** and its application to the intramolecular Diels-Alder reaction.



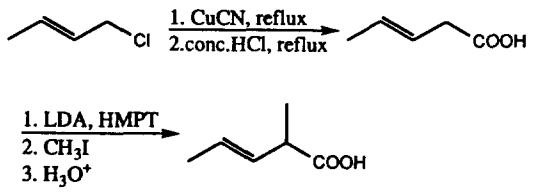
1

Results and Discussion

Lithiation of 2,5-dihydrothiophene 1,1-dioxides (3-sulfolenes) had been known to furnish 2- and 3-lithio derivatives under the kinetic and thermodynamic reaction conditions, respectively.[7] The lithiation reaction of sulfolene **2** at −110 ℃ was expected to give 2- or 3-lithiosulfolene. After quenching

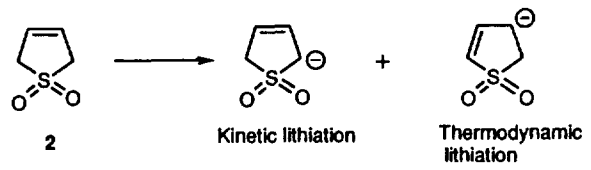


Scheme 1.



Scheme 2.

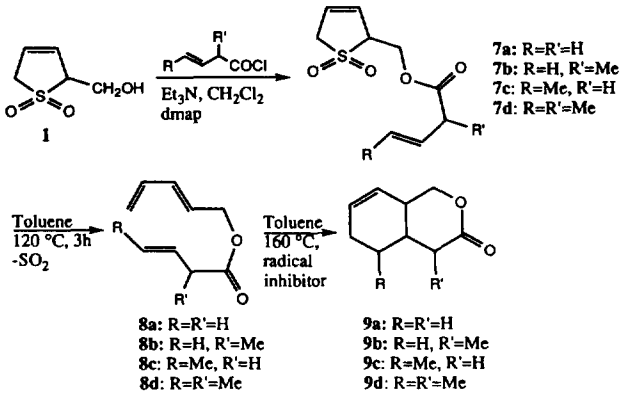
this reaction with either gaseous formaldehyde or pulverized paraformaldehyde, only starting material **2** was recovered in our hands.



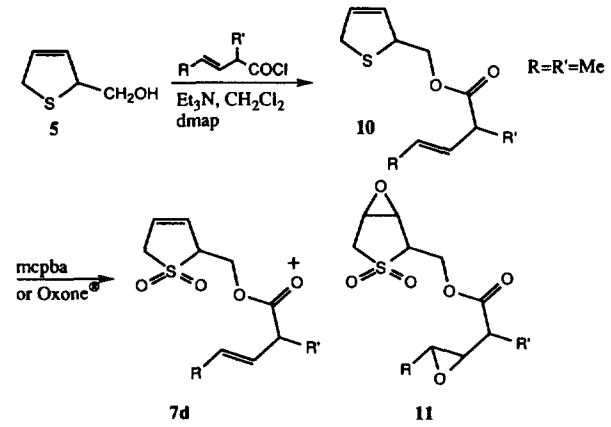
As an alternative way for the preparation of the hydroxymethyl compound, the sulfone derivative **1** from the Birch reduction of thiophene-2-carboxylic acid (**3**) seemed to be appropriate to this purpose (Scheme 1). There have been very few reports about the utilization of sulfone of 5-substituted thiophene-2-carboxylic acid for 1,3-dienes in the literatures.[8,9] First of all, we prepared methyl ester of 2,5-dihydrothiophene-2-carboxylic acid **4** using the Birch reduction of lithium salt of the acid **3** according to the method of Blenderman and Joullié.[10] Although the ^{1}H-NMR spectral data showed the complete consumption of thiophene-2-carboxylic acid in the Birch reduction, significant amount (more than 10% of the product) of the methyl ester of thiophene-2-carboxylic acid was recovered after the conversion of the reduced product to methyl ester by treating with ethereal diazomethane. The rationale for this oxidation back to the ester of the starting material seemed to be air oxidation of dihydrothiophene ring to the aromatic thiophene ring during esterification. The reduction of methyl ester **4** with lithium aluminum hydride gave 2-hydroxymethyl derivatives **5**. The oxidation with mcpba gave the desired sulfolene **1**, but Oxone® ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) was found to provide better yield and easier handling.[11]

As one of dienophiles for the intramolecular Diels-Alder reaction, 2-methyl-3-pentenoic acid (**6**) was prepared as shown in Scheme 2 according to the method of Lane *et al.*[12]

When the methylation at α-position of 3-pentenoic acid was carried out without HMPT, dimethylated product was obtained. The acid was converted to the acid chloride by treating with oxalyl chloride. The coupling of the acid chlorides with sulfolenyl alcohol **1** gave the corresponding esters **7** for the intramolecular Diels-Alder reaction.



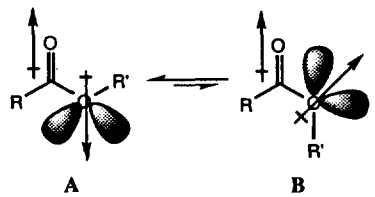
Scheme 3.



Scheme 4.

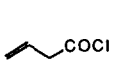
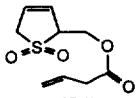
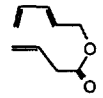
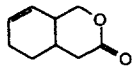
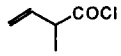
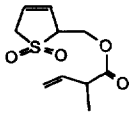
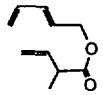
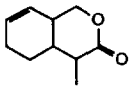
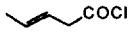
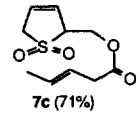
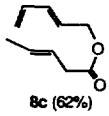
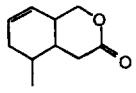
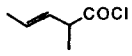
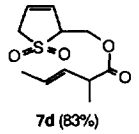
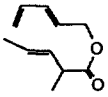
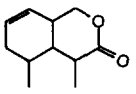
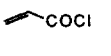
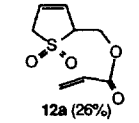
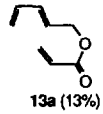
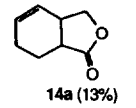
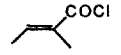
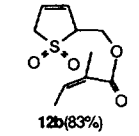
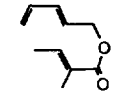
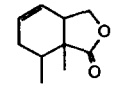
The expulsion of sulfur dioxide from **7** in a pressure tube at 120 ℃ gave the desired triene compounds **8**. Intramolecular Diels-Alder reaction to bicyclic δ-lactones **9** was carried out in the presence of radical scavenger of 3-*t*-butyl-4-hydroxy-5-methylphenyl sulfide to prevent undersirable polymerization.

In order to carry out one-pot reaction for the stepwise cyclization of sulfolenyl esters, ZnO was added to remove SO_2 and then the temperature was raised to 160 ℃. However this reaction was found futile because of the decomposition of the starting material. And also in a hope of the acceleration of cyclization, solvent was changed to polar solvent such as CH_3CN or DMSO to stabilize the more polar *s-cis* conformation *B* about ester bond as shown below.[13,14] But the result showed rather decreased yields. Also the addition of Lewis acid of dimethylaluminum chloride in dichloromethane did not give any improvement.



As a modification of reaction pathway in Scheme 3, the

Table 1. The Intramolecular Diels-Alder Reaction of Triene Esters

Entry	Dienophile	Ester (% yield)	Triene (% yield)	Unsaturated lactone (% yield)
1		 7a (65%)	 8a (70%)	 9a (40%)
2		 7b (77%)	 8b (70%)	 9b (27%)
3		 7c (71%)	 8c (62%)	 9c (52%)
4		 7d (83%)	 8d (79%)	 9d (52%)
5		 12a (26%)	 13a (13%)	 14a (13%)
6		 12b(83%)	 13b (57%)	 14b (51%)

esterification of 2-hydroxymethyl-2,5-dihydrothiophene and selective oxidation at sulfur atom were attempted (Scheme 4). But the overoxidation product **11** was obtained along with the desired product **7d**. Thus the reaction pathway in Scheme 3 was proved better reaction route.

Likewise 2-enoic acid chlorides were coupled with the compound **1** to provide the corresponding esters **12**, which were consecutively converted to triens **13** and cyclized to bicyclic γ-lactones **14**. The results of the intramolecular Diels-Alder reaction of sulfolenyl esters for bicyclic γ or δ-lactones were shown in Table 1.

Experimental

General Comments

Melting points were determined on a Thomas-Hoover Uni-Melt apparatus in capillary tubes and are uncorrected. Infrared (IR) spectra were recorded on a Shimadzu IR-435 spectrophotometer. ^{1}H-NMR spectra were obtained on Bruker AM-300 NMR, Varian 360 EM, and Varian Gemini 200 and measured in $CDCl_3$ solution, unless otherwise stated, relative to Me_4Si, as an internal standard (δ=0.00). Mass spectra were obtained on a Schimadzu GCMS-QP 1000 at 70 eV and recorded herein (relative intensity and assignment). High resolution mass spectra (HRMS) were recorded on Joel JMS-DX303 mass spectrometer. Unless otherwise indicated in a specific experiment, all of the chemicals used were reagent grade and no additional purification has been done. Triethylamine was distilled over CaH_2 and stored over KOH. CH_2Cl_2 was distilled over P_2O_5. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl immediately prior to use. Thin layer chromatography (TLC) was performed on Merck 60 F-254 glass plated without activation. Column chromatography procedures utilized silica gel (Merck, silica gel 60, 70-230 mesh).

Methyl 2,5-dihydrothiophene-2-carboxylate (4)[5]

To a stirred solution of 2-thiophenecarboxylic acid (10 g, 78 mmol) in anhydrous THF (40 mL) at 0℃ was added LiH (0.62 g, 78 mmol) in anhydrous THF (70 mL) dropwise under the nitrogen atmosphere. After stirring for 30 min, the solvent was removed *in vacuo* to get crude lithium salt almost quantitatively (10 g). The crude lithium salt was washed with cold THF and dried over P_2O_5. To a stirred solution of lithium 2-thiophenecarboxylate (5.00 g, 37.3 mmol) in anhydrous liquid ammonia (135 mL) dried over Na, was added lithium (520 mg, 74.6 mmol) in small pieces. After all the lithium was added, the resulting dark blue solution was further stirred for 40 min. The solid ammonium chloride (4.28 g) was added to quench the reaction. And then ammonia was allowed to evaporate overnight and the residue was dissolved in water (20 mL) and acidified with 6 N HCl to a pH of 1. The resulting mixture was extracted with dichloromethane (3×50 mL) and the combined extracts were washed with brine, dried over anhydrous magnesium sulfate, and filtered. The extracts were concentrated *in vacuo* to obtain the residue (4.04 g). The residue was dissolved in ether etheral diazomethane prepared from Diazald® was added in small portions with swirling. When nitrogen gas was no longer evolved, the solution was left overnight to remove the excess reagent. The ether was evaporated to give the crude methyl ester, which was separated on a silica gel column by eluting with hexane : ethyl acetate=10 : 1 to get the desired ester as a colorless liquid : 3.95 g (73%); ^{1}H-NMR (60 MHz, $CDCl_3$): δ 3.70 (s, -OCH_3, 3H), 3.80 (d, J=2 Hz, 2H), 4.62-4.95 (m, 1H), 5.69-6.18 (m, 1H); IR (ν_{max}, cm^{-1}, liquid film): 1740, 1640.

2-Hydroxymethyl-2,5-dihydrothiophene (5)

To a stirred solution of lithium aluminum hydride (1.15 g, 30.1 mmol) in anhydrous ether (50 mL) was added methyl 2,5-dihydrothiophene-2-carboxylate (3.95 g, 34.6 mmol) in ether (40 mL) dropwise. The reaction mixture was refluxed for 3 hrs. After cooling to room temperature, 1.15 mL of water, 1.15 mL of 15% aqueous NaOH solution, and 1.15 mL of water were added to the stirred reaction mixture in that order. After filtration the reaction mixture was dried over anhydrous magnesium sulfate and filtered again. The filtrate was concentrated *in vacuo* to furnish the crude product, which was purified through column chromatography (silica gel, hexane : ethyl acetate=2 : 1) to give product as a colorless liquid : 3.04 g (96%); ^{1}H-NMR (60 MHz, $CDCl_3$) δ 2.28 (brs, OH, 1H), 3.65 (d, J=4 Hz, 2H), 3.76 (d, J=2 Hz, 2H), 4.30-4.65 (m, 1H), 5.67-6.15 (m, 2H); MS (m/z, relative int.): 117 (M^++1, 8.3), 116 (M^+, 11.1), 85 (M^+-S, 100), 45 (43.1); IR (ν_{max}, cm^{-1}, liquid film): 3400, 1620.

2-Hydroxymethyl-2,5-dihydrothiophene 1,1-dioxide (1)

To a stirred solution of 2-hydroxymethyl-2,5-dihydrothiophene (3.95 g, 34 mmol) in methanol (140 mL) at 0 ℃, was added Oxone® (31.1 g, 51 mmol) in small portions. Stirring was continued for two more hours. The reaction mixture was concentrated *in vacuo* and extracted with dichloromethane using continuous extractor on an oil bath at 50 ℃. The extract was concentrated carefully *in vacuo* to give the crude product: (4.96 g, 98%); ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.72 (t, J=6.9 Hz, 1H), 3.80 (dt, J=1.5 and 2.5 Hz, 2H), 3.88 (m, 1H), 3.96 (m, 1H), 4.10 (m, 1H), 6.03 (ddd, J=2.3, 4.7, and 8.6 Hz, 1H), 6.17 (ddd, J=2.7, 4.7, and 8.6 Hz, 1H); MS (m/z, relative int.) 149 (M^++1, 10.5), 118 (M^+-CH_2OH, 100), 83 (M^+-SO_2, 23.4), 70 (27.6), 55 (34.8); HRMS, m/z 149.0244 ($C_5H_9O_3S$ (M^++1) requires 149.0272).

General Procedure for the Preparation of the Esters of 2-Hydroxymethyl-2,5-Dihydrothiophene 1,1-Dioxide

To a stirred solution of 2-hydroxymethyl-2,5-dihydrothiophene 1,1-dioxide (0.347 g, 2.34 mmol), triethylamine (0.33 mL) and catalytic amount of dmap in anhydrous CH_2Cl_2 (10 mL) at 0 ℃ was added a solution of one equivalent of enoic acid chloride in CH_2Cl_2 (3 mL) dropwise *via* hypodermic syringe. After 30 min, the temperature was allowed to rise to room temperature and stirring was continued for 30 min. Water (0.5 mL) was added to the reaction mixture and the solvent was removed *in vacuo*. The residue was partitioned between water (10 mL) and ether (10 mL). The layers were separated and the aqueous layer was extracted with ether (2×10 mL). The organic layers were combined, dried over anhydrous $MgSO_4$, filtered and evaporated on a rotary evaporator. The residue was column chromatographed on silica gel to furnish the desired esters.

1,1-Dioxo-2,5-dihydrothiophen-2-ylmethyl 3-butenoate (7a). 65%, colorless liquid; ^{1}H-NMR (200 MHz, $CDCl_3$): δ 3.15 (d, J=6.8 Hz, 2H), 3.78 (brs, 2H), 3.98 (m, 1H), 4.45-4.53 (m, 2H), 5.14-5.23 (m, 2H), 5.84-6.19 (m, 3H); MS (relative int.): 217 (M^++1, 3.9), 216 (M^+, 0.8), 152 (M^+-SO_2, 2.5), 131 (M^+-$C_4H_5O_2$, 6.5), 117 (M^+-$C_2H_7O_2$, 0.3), 85 (M^+-$C_5H_5O_2S$, 18.9), 68 (100), 67 (M^+-$C_4H_5O_4S$, 88.4), 53 (M^+, $C_5H_7O_4S$, 17.5); IR (ν_{max}, cm^{-1}, liquid film): 1740, 1640, 1320, 1250, 1140.

1,1-Dioxo-2,5-dihydrothiophen-2-ylmethyl 2-methyl-3-butenoate (7b). 77%, colorless liquid; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.28 (d, J=7.0 Hz, 3H), 3.20 (dq, J=7.0 and 7.2 Hz, 1H), 3.77 (dd, J=0.7 and 0.7 Hz, 2H), 3.98 (m, 1H), 4.44-4.63 (m, 2H), 5.15-5.21 (m, 2H), 5.86 (ddd, J=2.6, 7.0 and 9.7 Hz, 1H), 5.39-6.19 (m, 2H); MS (m/z, relative int.): 231 (M^++1, 2.9), 230 (M^+, 1.3), 166 (M^+-SO_2, 1.9), 82 (63.3), 67 (62.0), 55 (100); IR (ν_{max}, cm^{-1}, liquid film): 1740, 1640, 1320, 1260, 1120.

1,1-Dioxo-2,5-dihydrothiophen-2-ylmethyl 3-pentenoate (7c). 71%, colorless liquid; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.69 (d, J=4.6 Hz, 3H), 3.05 (m, 2H), 3.76 (brs, 2H), 3.96 (brs, 1H), 4.35-4.56 (m, 2H), 5.44-5.65 (m, 2H), 5.95-6.03 (m, 1H), 6.11-6.18 (m, 1H); MS (m/z, relative int) 231 (M^++1, 12.8), 119 (5.9), 101 (6.1), 82 (75.1), 67 (98.8), 56 (100); IR (ν_{max}, cm^{-1}, liquid film): 1760, 1660, 1340, 1280, 1160.

1,1-Dioxo-2,5-dihydrothiophen-2-ylmethyl 2-methyl-3-*trans*-pentenoate (7d). 84%, colorless liquid: ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.22 (d, J=7.1 Hz, 3H), 1.65 (d, J=4.9 Hz, 3H), 3.10 (dq, J=6.8 and 13.5 Hz, 1H), 3.73 (brs, 2H), 3.93 (brs, 1H), 4.39-4.51 (m, 2H), 5.47-5.54 (m, 2H), 5.95-5.99 (m, 1H), 6.12-6.15 (m, 1H); MS (m/z, relative int.): 245 (M^++1, 1.2), 149 (M^+-C_6H_9O, 6.5), 96 (25.1), 69 (96.8), 41 (100); IR (ν_{max}, cm^{-1}, liquid film): 1760, 1630, 1320, 1240, 1140; HRMS, m/z 245.0801 ($C_{11}H_{17}O_4S$ (M+1) requires 245.0848).

1,1-Dioxo-2,5-dihydrothiophen-2-ylmethyl 2-propenoate (12a). 26%, colorless liquid; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 3.79 (m, 2H), 4.02 (m, 1H), 4.53-4.63 (m, 2H), 5.87-6.21 (m, 4H), 6.42-6.52 (m, 1H); MS (m/z, relative int.): 203 (M^++1, 1.9), 202 (M^+, 0.5), 147 (M^+-C_3H_3O, 0.4), 138 (M^+-SO_2, 4.1), 131 (M^+-$C_3H_3O_2$, 4.1), 67 (M^+-$C_3H_3O_4S$, 42.4), 56 (100); IR (ν_{max}, cm^{-1}, liquid film): 1760, 1640, 1320, 1270, 1140.

1,1-Dioxo-2,5-dihydrothiophen-2-ylmethyl 2-methyl-2-butenoate (12b). 83%, colorless liquid; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.80 (d, J=7.5 Hz, 6H), 1.83 (d, J=7.7 Hz), 3.78 (m, 1H), 4.00 (brs, 1H), 4.51 (d, J=6.0 Hz, 2H), 5.97-6.05 (m, 1H), 6.11-6.20 (m, 1H), 6.86-6.96 (m, 1H); MS (m/z, relative int.): 230 (M^+, 1.5), 166 (M^+-SO_2, 3.0), 147 (M^+-C_5H_7O, 1.0), 131 (M^+-$C_5H_7O_2$, 3.5), 82 (100), 67 (M^+-$C_5H_7O_4S$, 22.2); IR (ν_{max}, cm^{-1}, liquid film): 1720, 1645, 1320, 1270, 1150.

General Procedure for the Cheletropic Extrusion of SO_2 from the Esters of 2-Hydroxymethyl-2,5-dihydrothiophene

Argon gas was bubbled through anhydrous toluene (1.5 mL) in a pressure tube and sulfone (*ca.* 1.0 g) and small amount of radical inhibitor (3-*t*-butyl-4-hydroxy-5-methyl phenyl sulfide) was added. Then reaction mixture was heated at 120 ℃ under the sealed argon atmosphere. After cooling to room temperature, the solvent was removed under the reduced pressure. The residue was chromatographed on a silica gel column to furnish the desired product.

2,4-Petadienyl 3-butenoate (8a). 70%, colorless liquid; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 3.12 (dd, J=1.4 and 7.0 Hz, 2H), 4.64 (d, J=6.0 Hz, 2H), 5.13-5.31 (m, 4H), 5.74-6.01 (m, 2H), 6.27-6.40 (m, 2H); MS (m/z, relative int.): 152 (M^+, 7.7), 111 (M^+-C_3H_5, 11.5), 85 (M^+-C_5H_7, 14.8), 83 (M^+-C_4H_5O, 13.1), 67 (M^+-$C_4H_5O_2$, 100), 43 (96.8); IR (ν_{max}, cm^{-1}, liquid film): 1740, 1650, 1260.

2,4-Pentadienyl 2-methyl-3-butenoate (8b). 70%, colorless liquid; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.30 (d, J=7.0 Hz, 3H), 3.11-3.25 (m, 1H), 4.64 (d, J=6.0 Hz, 2H), 5.09-5.35 (m, 4H), 5.70-6.03 (m, 2H), 6.22-6.45 (m, 2H); MS (relative int.) 167 (M^++1, 24.4), 121 (100), 91 (44.1), 84 (22.7); IR (ν_{max}, cm^{-1}, liquid film): 1740, 1640, 1260.

2,4-Pentadienyl 3-pentenoate (8c). 62%, colorless liquid; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.70 (d, J=4.9 Hz, 3H), 3.03 (m, 2H), 4.63 (d, J=5.9 Hz, 2H), 5.13 (d, J=9.7 Hz, 1H), 5.25 (d, J=15.8, 1H), 5.56-5.62 (m, 1H), 5.69-5.84 (m, 1H), 6.21-6.44 (m, 2H); MS (m/z, relative int.): 166 (M^+, 5.5), 111 (M^+-C_4H_7, 1.3), 83 (M^+-C_5H_7O, 24.4), 67 (M^+-$C_5H_7O_2$, 100); IR (ν_{max}, cm^{-1}, liquid film): 1740, 1660, 1260.

2,4-Pentadienyl 2-methyl-3-pentenoate (8d). 79%, colorless liquid; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.24 (d, J=7.1 Hz, 3H), 1.68 (d, J=4.5 Hz, 3H), 3.12 (dq, J=6.5 and 13.0 Hz, 2H), 4.61 (d, J=5.9 Hz, 2H), 5.15 (d, J=9.7 Hz, 1H), 5.24 (d, J=15.8 Hz, 1H), 5.52-5.60 (m, 2H), 5.74-5.80 (m, 1H), 6.26-6.39 (m, 2H); MS (m/z, relative int.): 180 (M^+, 2.7), 140 (1.3), 117 (M^+-C_5H_7, 0.9), 97 (M^+-C_5H_7O, 0.9), 83 (M^+-C_6H_9O,

36.1), 69 (M^+-$C_6H_7O_2$, 55.7), 41 (100); IR (ν_{max}, cm^{-1}, liquid film): 1740, 1660, 1260.

2,4-Pentadienyl 2-propenoate (13a). 13%, colorless liquid; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 4.71 (d, J=5.9 Hz, 2H), 5.15-5.30 (m, 1H), 5.32 (brs, 1H), 5.86 (dd, J=1.7 and 6.5 Hz, 2H), 6.15 (dd, J=10.2 and 17.2 Hz, 1H), 6.25-6.38 (m, 2H), 6.45 (dd, J=1.7 and 17.2 Hz, 1H); MS (relative int.): 138 (M^+, 7.5), 111 (M^+-C_2H_3, 3.9), 83 (M^+-C_3H_3O, 8.3), 71 (M^+-C_5H_7, 0.9), 67 (M^+-$C_3H_3O_2$, 24.2), 56 (100); IR (ν_{max}, cm^{-1}, liquid film): 1730, 1650, 1260.

2,4-Pentadienyl 2-methyl-2-butenoate (13b). 57%, colorless liquid; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.79 (dd, J=1.2 and 7.0 Hz, 3H), 1.84 (brs, 3H), 4.67 (d, J=6.3 Hz, 2H),5.08-5.28 (m, 2H), 5.74-5.90 (m, 1H), 6.23-6.45 (m, 2H), 6.83-6.95 (m, 1H); MS (m/z, relative int.): 166 (M^+, 10.8), 83 (M^+-C_5H_7O, 100), 67 (M^+-$C_5H_7O_2$, 52.9), 55 (M^+-$C_6H_7O_2$, 1.6); IR (ν_{max}, cm^{-1}, liquid film): 1720, 1660, 1270.

General Procedure for the Intramolecular Diels-Alder Reaction of Trienes

A solution of triene (5.0 mmol) and small amout of radical inhibitor (3-*t*-butyl-4-hydroxy-5-methyl phenyl sulfide) in anhydrous toluene, which was previously flushed with argon, was heated at 160 ℃ for 24 h in a sealed pressure tube filled with argon. After cooling to the room temperature, toluene was removed *in vacuo*. The residue was chromatographed on a silica gel column to furnish the desired product.

1,4,4a,5,6,8a-hexahydroisochromen-3-one (9a). 40%, colorless liquid; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.71 (m, 1H), 2.03-2.18 (m, 2H), 2.18 (m, 1H), 3.07-3.13 (m, 2H), 3.86-4.06 (m, 1H), 4.53-4.57 (m, 1H), 5.22 (m, 2H), 5.52-6.01 (m, 3H); MS (m/z, relative int.): 151 (M^+-1, 0.7), 132 (59.1), 117 (51.7), 83 (100), 56 (17.5); IR (ν_{max}, cm^{-1}, liquid film): 1740, 1650.

4-Methyl-1,4,4a,5,6,8a-hexahydroisochromen-3-one (9b). 27%, colorless liquid; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.27 (dd, J=1.0 and 7.0 Hz, 3H), 1.70-1.83 (m, 2H), 2.06 (m, 1H), 2.58 (m, 1H), 3.10-3.19 (m, 1H), 3.91-3.98 (m, 1H), 4.52-4.55 (m, 1H), 5.08-5.18 (m, 2H), 5.56-6.01 (m, 3H); MS (m/z, relative int.): 167 (M^++1, 24.4), 121 (100), 91 (44.1), 84 (22.7); IR (ν_{max}, cm^{-1}, liquid film): 1740, 1640.

5-Methyl-1,4,4a,5,6,8a-hexahydroisochromen-3-one (9c). 52%, colorless liquid; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.70 (d, J=4.5 H, 3H), 1.69-1.84 (m, 1H), 2.07 (m, 2H), 2.59 (m, 1H), 3.03 (brs, 2H), 3.90-3.99 (m, 1H), 4.52-4.55 (m, 1H), 5.53-5.84 (m, 4H); MS (m/z, relative int.): 166 (M+, 3.5), 117 (41.7), 91 (40.5), 56 (100); IR (ν_{max}, cm^{-1}, liquid film): 1750, 1650.

4,5-Dimethyl-1,4,4a,5,6,8a-hexahydroisochromen-3-one (9d). 52%, colorless liquid; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.30 (d, J=7.2 Hz, 3H), 1.70 (d, J=4.4 Hz, 3H), 2.00-2.20 (m, 2H), 2.57-2.69 (m, 1H), 3.12 (m, 1H), 3.82-4.09 (m, 1H), 4.53 (m, 1H), 5.54-5.82 (m, 4H); MS (m/z, relative int.): 180 (M+, 4.4), 149 (12.1), 165 (M^+-CH_3), 152 (M^+-CO, 4.9), 136 (M^+-CO_2, 5.6), 85 (42.4), 69 (78.2), 43 (100); IR (ν_{max}, cm^{-1}, liquid film): 1740, 1660.

3a,6,7,7a-Tetrahydro-3*H*-isobenzofuran-1-one (14a). 13%, colorless liquid; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 2.15-2.20 (m, 2H), 2.45-2.71 (m, 1H), 4.06-4.20 (m, 1H), 4.59-4.69 (m, 1H), 5.79-5.88 (m, 2H), 6.03-6.48 (m, 2H); MS (m/z, relative int.): 166 (M^+, 3.5), 117 (41.7), 91 (40.5), 56 (100); IR (ν_{max}, cm^{-1}, liquid film): 1720, 1660.

7,7a-Dimethyl-3a,6,7,7a-tetrahydro-3*H*-isobenzofuran-1-one (14b). 51%, colorless liquid; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.83 (s, 3H), 1.84 (d, J=4.9 Hz, 3H), 1.73-1.85 (m, 1H), 2.05 (m, 1H), 2.62 (m, 1H), 3.96-4.04 (m, 1H), 4.52-4.62 (m, 1H), 5.56-5.85 (m, 2H), 6.86 (m, 1H); MS (m/z, relative int.): 152 (7.8), 132 (100), 117 (64.5), 91 (41.5); IR (ν_{max}, cm^{-1}, liquid film): 1720, 1660.

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