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Lewis Acid-Promoted Disproportionation Reaction of Aromatic Vinyl Ethers and Acetals and Its Application to the Synthesis of Paracotoin

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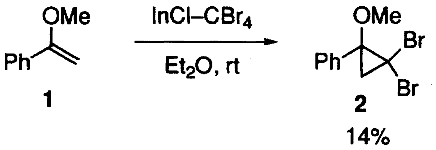
Aromatic vinyl ethers and acetals underwent a novel addition-fragmentation reaction affording olefins and esters in the presence of a Lewis acid. This reaction was applied to intramolecular cyclization reaction, giving five or six membered ring compounds in good yields. Paracotoin, an intermediate in the biosynthesis of shikimic acid, was synthesized using this cyclization reaction as the key step.

Use of acetals in synthetic organic reaction is mostly confined to two purposes: that is, as a protective group of carbonyl functionality[1] and as an equivalent of a carbonyl group in Lewis acid-catalyzed reactions.[2] In the latter cases, acetals are activated by a Lewis acid to act as electrophilic reagents. However, in the presence of an acid catalyst, acetals are known to be in equilibrium with vinyl ethers and alcohols,[3] and vinyl ethers could act as nucleophilic reagents.[4] Thus it is expected to be possible to carry out a reaction where acetals in equilibrium with vinyl ethers (or vice versa) work as a source of both a nucleophile and an electrophile. During the study on the cyclopropanation reaction of electron-rich olefins using indium(I) chloride and carbon tetrabromide, we happened to find a novel Lewis acid-promoted addition-fragmentation reaction of aromatic vinyl ethers (or acetals) where the above-mentioned binary character of acetals (and vinyl ethers) takes place during the reaction.[5] In this paper we describe the details of the above reaction and its application to the synthesis of paracotoin, an intermediate in the biosynthesis of shikimic acid.

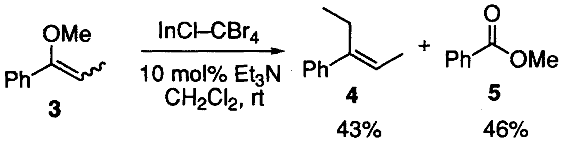
Results and Discussion

We have been exploring new reactions utilizing the reducing ability of indium(I) compounds[6] and among the trials was included the reaction of indium carbenoid species generated by the reaction of indium(I) chloride and carbon tetrabromide. For an example, when 1-methoxy-1-phenylethylene (**1**) was added to a mixture of indium(I) chloride and carbon tetrabromide in ether at r.t., 1,1-dibromo-2-methoxy-2-phenylcyclopropane (**2**), a dibromocyclopropanation product, was obtained in 14% yield, presumably via an indium carbenoid species.



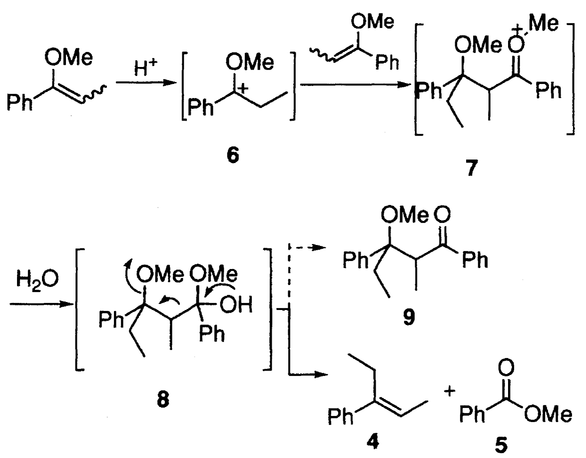
(1)

All efforts to improve the yield of this cyclopropanation reaction turned out to be fruitless; however, when the reaction of 1-methoxy-1-phenyl-1-propene (**3**) was carried out in dichloromethane, a completely different reaction took place. Analysis of the products revealed that (*E*)-3-phenyl-2-pentene (**4**) and methyl benzoate (**5**) were produced along with propiophenone, the hydrolyzed product of the vinyl ether (**3**). In particular, by carrying out the reaction in the presence of 10 mol% of Et_3N to suppress the formation of the hydrolyzed product, olefin **4** and methyl benzoate were obtained in 43 and 46% yields, respectively. Furthermore, it was found that this reaction is not a specific reaction of the indium reagent, but is a Lewis acid-promoted reaction, as the reaction proceeded smoothly in the same manner using typical Lewis acids such as $BF_3\cdot OEt_2$ and $EtAlCl_2$.

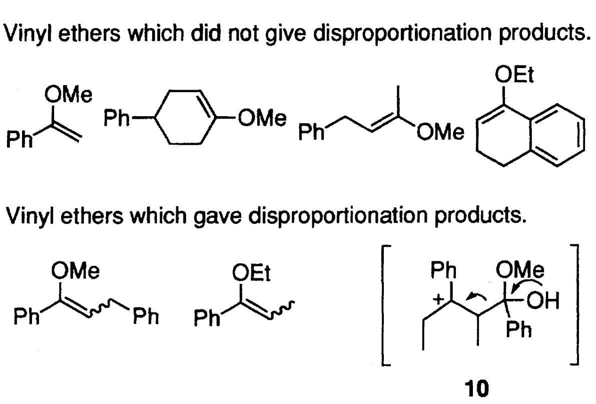


(2)

The mechanism of the reaction can be explained as follows. The reaction is initiated by the protonation of the vinyl ether, which is caused by the water present in a small amount in the reaction medium, to generate an electrophilic species **6**. A nucleophilic attack of the second vinyl ether to the protonated species **6** produces an oxonium intermediate **7**. Then another molecule of water reacts with this oxonium intermediate to give **8**, which is supposed to give, after elimination of methanol, an aldol type product **9**. However, in this reaction, a Grob-type fragmentation reaction[7] occurs at this stage to give olefin **4** and methyl benzoate **5** (Scheme 1). Various other vinyl ethers were examined as shown in Scheme 2, but most of them gave only the corresponding hydrolyzed ketones or complex mixtures of products and only aromatic trisubstituted vinyl ethers gave the fragmentation products in good yield. Thus, the driving force for this fragmentation reaction is dependent on the relief of steric congestion and/or



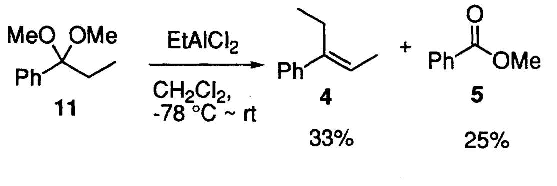
Scheme 1. Mechanism of the disproportionation reaction.



Scheme 2. Appropriate substrates for this reaction.

the stability of benzylic cation, which enables the generation of cationic intermediate **10** as an initiation of the fragmentation reaction.

As already mentioned in the beginning, there exists an equilibrium between an acetal and a vinyl ether (and an alcohol) in the presence of a Lewis acid. As acetals are much easier to prepare than the corresponding vinyl ethers, we next examined the possibility of using acetals instead of vinyl ethers in this reaction. The reaction was examined employing propiophenone dimethyl acetal **11** as a substrate: When $EtAlCl_2$ was employed as a Lewis acid, the same addition-fragmentation reaction proceeded smoothly at room temperature to give the olefin **4** and methyl benzoate in 33 and 25% yields, respectively.



(3)

Next, the application of this reaction to substrates having two aromatic acetal moieties was examined to achieve an intramolecular cyclization reaction. Aromatic diketones with various lengths of connecting methylene chains were synthesized by the Friedel–Crafts reaction of the corresponding dicarboxylic acid chlorides and benzene. Acetalization was then achieved using trimethyl orthoformate and methanol in the presence of a catalytic amount of sulfuric acid. Diacetals were subjected to the disproportionation reaction conditions ($EtAlCl_2$, CH_2Cl_2, −78 °C—r.t.), and five- and six-membered ring formation reactions were found to proceed in high yields, as shown in Table 1. A cycloheptene derivative was also obtained, albeit in moderate yield, by carrying out the reaction under high dilution conditions. However, formation of 4- and 8-membered-ring turned out to be difficult by this procedure.

Finally, this five-membered ring construction reaction was applied to the synthesis of paracotoin, an intermediate in the biosynthesis of shikimic acid.[8,9] It was expected that paracotoin could be prepared from 1-arylcyclopentene **17**, which would be obtained by the intramolecular addition-fragmentation reaction of diacetal **18** (Scheme 3).

This key intermediate **18** was straightforwardly synthesized by the procedure shown in Scheme 4. Grignard reagent prepared from 1,4-dibromobutane was reacted with piperonal to give a diol **19** in 74% yield. The diol **19** was oxidized with CrO_3 to give the corresponding diketone **20**, which was converted to its diacetal **18** using trimethyl orthoformate and methanol in the presence of a catalytic amount of *p*-toluenesulfonic acid in 81% overall yield. By treating this diacetal **18** with $EtAlCl_2$, the cyclization reaction proceeded smoothly to give cyclopentene derivative **17** in 82% yield with methyl

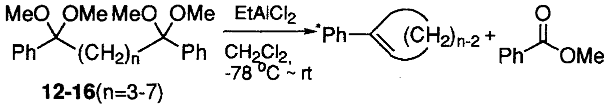
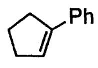
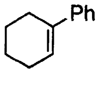
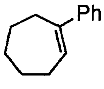
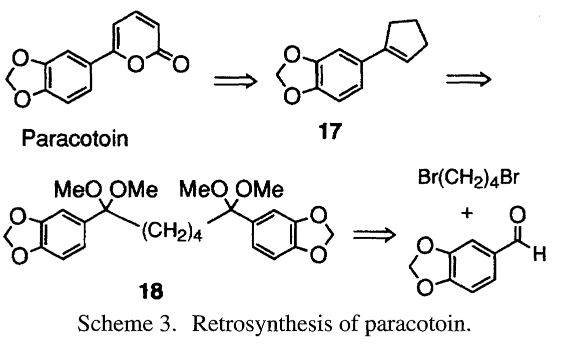
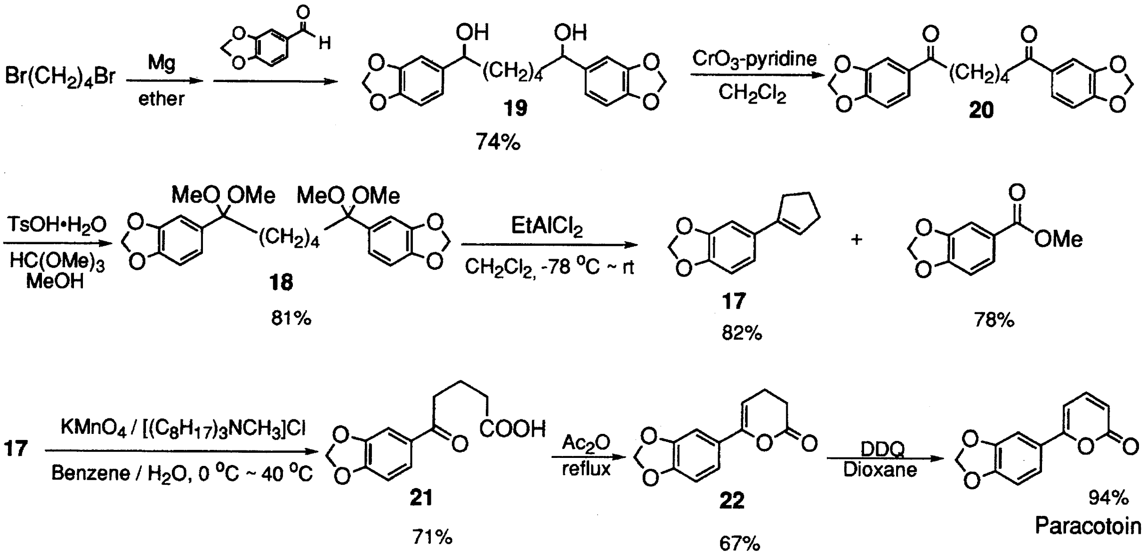


Table 1. Intramolecular Disproportionation Reactions

n	Concentrations mmol dm^{-3}	Products	Yield %
3(**12**)	50	—	0
4(**13**)	50		93
5(**14**)	50		86
6(**15**)	8		29
7(**16**)	8	—	0



Scheme 3. Retrosynthesis of paracotoin.



Scheme 4. Synthesis of paracotoin.

piperonylate in 78% yield.

Conversion of the cyclopentene moiety to a 4*H*-pyran-2(3*H*)-one derivative was efficiently carried out as follows. Firstly, the double bond of cyclopentene **17** was oxidatively cleaved with $KMnO_4$ under phase transfer conditions[10] to give a keto acid **21** in 71% yield. Then treatment of this keto acid **20** with acetic anhydride gave 71% yield of the cyclized 4*H*-pyran-2(3*H*)-one derivative **22**, which was dehydrogenated with DDQ[11] to give paracotoin in 94% yield.

Experimental

General. ^1H NMR spectra were recorded on a Bruker AM500 (500 MHz) spectrometer using $CHCl_3$ as an internal standard (δ = 7.24) or on a Hitachi R24B (60 MHz) using tetramethylsilane as an internal standard (δ = 0.00). IR spectra were recorded on a Horiba FT-300S spectrometer. High resolution mass spectra (HRMS) were recorded on a JEOL JMS-SX102A mass spectrometer operating at 70 eV. Preparative HPLC was carried out with Japan Analytical Industry Co., Ltd., LC-908 liquid chromatography using JAIGEL-1H and -2H GPC column (mobile phase: chloroform). Melting points were uncorrected. Flash column chromatography was conducted on silica gel (Merck, 230—400 mesh) and preparative thin-layer chromatography (TLC) was carried out on silica gel (Wako gel B-5F). Dichloromethane was distilled from P_2O_5 and then from CaH_2, and was dried over MS4A.

A Typical Procedure for the Intermolecular Disproportionation Reactions. To a stirred 1 M CH_2Cl_2 solution (1 M = 1 mol dm^{-3}) (1 ml) of $EtAlCl_2$ (1 mmol) was added a dichloromethane solution (5 ml) of the propiophenone dimethyl acetal **11** (171.1 mg, 0.95 mmol) at −78 °C under an argon atmosphere. The mixture was stirred for 1 h at −78 °C and then warmed up to room temperature. The reaction was quenched with pH 7 phosphate buffer solution, and the mixture was filtered through Celite. The organic materials were extracted with dichloromethane three times and the combined extracts were washed with brine and dried over Na_2SO_4. After the solvent was removed in vacuo, the crude material was purified by thin-layer chromatography (hexane : ethyl acetate = 10 : 1) to give (*E*)-3-phenyl-2-pentene **4** (96.3 mg, 33% yield) and methyl benzoate **5** (65.1 mg, 25% yield).

(*E*)-3-Phenyl-2-pentene: ^1H NMR (500 MHz, $CDCl_3$) δ = 1.00 (t, 3H, J = 7.5 Hz), 1.80 (d, 3H, J = 6.5 Hz), 2.55 (q, 2H, J = 7.5 Hz), 5.75 (q, 1H, J = 6.5 Hz), 7.20 (t, 1H, J = 7.2 Hz), 7.27—7.37 (m, 4H). This compound is known in the literature.[12]

A Typical Procedure for the Synthesis of Diphenyl Diketones (Precusors of 12—16). To a stirred benzene suspension (10 ml) of $AlCl_3$ (6.17 g, 45.50 mmol) was added a benzene solution (5 ml) of 1,6-hexanedicarboxylic acid (1.74 g, 9.99 mmol) at 0 °C under argon atmosphere. The mixture was stirred for 0.5 h at room temperature and then refluxed for 12 h. The reaction mixture was poured into chilled 5 M hydrochloric acid and organic materials were extracted with dichloromethane three times. The combined extracts were washed with 1 M aqueous NaOH solution, H_2O and saturated NaCl solution successively, and then dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the residue was recrystallized from methanol to afford 1,8-diphenyloctane-1,8-dione (1.12 g, 38% yield). Other diphenyl diketones were prepared by the same procedure.

1,5-Diphenylpentane-1,5-dione (the Precusor of 12): Mp 62 °C; IR (KBr) 1685, 737, 688 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 2.18 (quint, 2H, J = 6.9 Hz), 3.10 (t, 4H, J = 6.9 Hz), 7.41—7.46 (m, 4H), 7.51—7.57 (m, 2H), 7.94—7.98 (m, 4H). HRMS Found: m/z 252.1146. Calcd for $C_{17}H_{16}O_2$; M, 252.1150.

1,6-Diphenylhexane-1,6-dione (the Precusor of 13): Mp 105 °C; IR (KBr) 2912, 1685, 1227, 737, 688 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ = 1.54—1.96 (m, 4H), 2.83—3.16 (m, 4H), 7.11—7.54 (m, 6H), 7.76—8.03 (m, 4H). HRMS Found: m/z 266.1305. Calcd for $C_{18}H_{18}O_2$: M, 266.1307.

1,7-Diphenylheptane-1,5-dione (the Precusor of 14): Mp 65 °C; IR (KBr) 1685, 1348, 1248, 688 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ = 1.00—2.00 (m, 6H), 2.84 (t, 4H, J = 6.6 Hz), 6.92—7.56 (m, 6H), 7.56—7.95 (m, 4H). HRMS Found: m/z 280.1478. Calcd for $C_{19}H_{20}O_2$: M, 280.1463.

1,8-Diphenyloctane-1,8-dione (the Precusor of 15): Mp 90 °C; IR (KBr) 2931, 1684, 1240, 744, 688 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ = 1.21—2.03 (m, 8H), 2.97 (t, 4H, J = 7.0 Hz), 7.17—7.61 (m, 6H), 7.84—8.10 (m, 4H). HRMS Found: m/z 294.1625. Calcd for $C_{20}H_{22}O_2$: M, 294.1620.

1,9-Diphenylnonane-1,9-dione (the Precusor of 16): Mp 47 °C; IR (KBr) 2920, 1680, 1232, 741, 688 cm^{-1}; ^1H NMR (60 MHz,

$\mathrm{CDCl_3}$) $\delta = 1.07$—2.08 (m, 10H), 2.96 (t, 4H, $J = 6.4$ Hz), 7.05—7.24 (m, 6H), 7.77—8.05 (m, 4H). HRMS Found: *m/z* 308.1786. Calcd for $\mathrm{C_{21}H_{24}O_2}$: M, 308.1776.

A Typical Procedure for the Synthesis of Dimethyl Acetal of Diphenyl Diketones (12—16). To a methanol solution (15 ml) of 1,8-diphenyloctane-1,8-dione (775 mg, 2.64 mmol) and a drop of concentrated sulfuric acid was added trimethyl orthoformate (1.0 ml) at room temperature. After the mixture was stirred at r.t. overnight, the mixture was poured into 1 M aqueous KOH solution. The organic materials were extracted with dichloromethane three times and the combined extracts were dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the residue was recrystallized from methanol to afford 1,1,8,8-tetramethoxy-1,8-diphenyloctane (808 mg, 79% yield). Other dimethyl acetals of diphenyl diketones were prepared by the same procedure. Some of the substrates were not sufficiently stable and were used without further purification.

1,1,5,5-Tetramethoxy-1,5-diphenylpentane (12): Mp 60 °C; IR (KBr) 2945, 1435, 1320, 1038 cm^{-1}; ^{1}H NMR (60 MHz, $\mathrm{CDCl_3}$) $\delta = 0.50$—0.99 (m, 2H), 1.53—2.01 (m, 4H), 3.00 (s, 12H), 7.11—7.37 (m, 10H). Anal. Calcd for $\mathrm{C_{21}H_{28}O_4}$: C, 73.23; H, 8.19%. Found: C, 73.22; H, 8.17%.

1,1,6,6-Tetramethoxy-1,6-diphenylhexane (13): Mp 104 °C; IR (KBr) 1440, 1316, 1038 cm^{-1}; ^{1}H NMR (60 MHz, $\mathrm{CDCl_3}$) $\delta = 0.63$—1.00 (m, 4H), 1.53—1.92 (m, 4H), 3.05 (s, 12H), 7.09—7.35 (m, 10H). Anal. Calcd for $\mathrm{C_{22}H_{30}O_4}$: C, 73.71; H, 8.43%. Found: C, 73.41; H, 8.36%.

1,1,7,7-Tetramethoxy-1,7-diphenylheptane (14): IR (KBr) 2949, 1448, 1311, 1045 cm^{-1}; ^{1}H NMR (60 MHz, $\mathrm{CDCl_3}$) $\delta =$ 0.60—1.86 (m, 10H), 3.01 (s, 12H), 7.09—7.25 (m, 10H). HRMS Found: *m/z* 341.2102. Calcd for $\mathrm{C_{22}H_{29}O_3}$: M−OMe, 341.2117.

1,1,8,8-Tetramethoxy-1,8-diphenyloctane (15): Mp 81 °C; IR (KBr) 2945, 1448, 1313, 1063, 702 cm^{-1}; ^{1}H NMR (60 MHz, $\mathrm{CDCl_3}$) $\delta = 0.84$—1.09 (br, 8H), 1.58—1.99 (m, 4H), 3.11 (s, 12H), 7.16—7.44 (m, 10H). HRMS Found: *m/z* 355.2273. Calcd for $\mathrm{C_{23}H_{31}O_3}$: M−OMe, 355.2273.

1,1,9,9-Tetramethoxy-1,9-diphenylnonane (16): Mp 56 °C; IR (KBr) 2942, 1448, 1308, 1138, 1065, 1039 cm^{-1}; ^{1}H NMR ($\mathrm{CDCl_3}$) $\delta = 0.87$—1.15 (br, 10H), 1.40—1.99 (m, 4H), 3.09 (s, 12H), 7.10—7.40 (m, 10H). HRMS Found: *m/z* 369.2422. Calcd for $\mathrm{C_{24}H_{33}O_3}$: M−OMe, 369.2430.

A Typical Procedure for the Intramolecular Disproportionation Reactions of the Dimethyl Acetals 12—16. To a dichloromethane solution (5 ml) of $\mathrm{EtAlCl_2}$ (78.0 mg, 0.61 mmol) was added a dichloromethane solution (15 ml) of 1,1,6,6-tetramethoxy-1,6-diphenylhexane **13** (100.0 mg 0.28 mmol) at −78 °C under argon atmosphere. The mixture was stirred at −78 °C for 0.5 h and then for 0.5 h at room temperature. The reaction was quenched with pH 7 phosphate buffer solution, and the mixture was filtered through Celite. The organic materials were extracted with dichloromethane three times and the combined extracts were washed with brine and dried over $\mathrm{Na_2SO_4}$. After the solvent was removed under reduced pressure, the residue was purified by thin-layer chromatography (hexane : ethyl acetate = 10 : 1) to give 1-phenylcyclopentene (37.4 mg, 93% yield) and methyl benzoate (43.1 mg, 71% yield). Reactions of substrates **12**—**16** were carried out by the same procedure.

1-Phenylcyclopentene: ^{1}H NMR (60 MHz, $\mathrm{CCl_4}$) $\delta =$ 1.64—2.84 (m, 6H), 5.95—6.13 (m, 1H), 6.98—7.31 (m, 5H). This compound is known in the literature.[13)]

1-Phenylcyclohexene: ^{1}H NMR (60 MHz, $\mathrm{CCl_4}$) $\delta =$ 1.66—2.56 (m, 8H), 5.87—6.09 (m, 1H), 6.96—7.30 (m, 5H). This compound is commercially available.

1-Phenylcycloheptene: ^{1}H NMR (500 MHz, $\mathrm{CDCl_3}$) $\delta =$ 1.50—1.56 (m, 2H), 1.60—1.65 (m, 2H), 1.79—1.84 (m, 2H), 2.23—2.28 (m, 2H), 2.57—2.60 (m, 2H), 6.07 (t, 1H, $J = 6.7$ Hz), 7.13—7.18 (m, 1H), 7.22—7.31 (m, 4H). This compound is known in the literature.[14)]

Synthesis of Paracotoin. **Synthesis of 1,6-Bis(3,4-methylenedioxyphenyl)hexane-1,6-diol (19):** A Grignard reagent, prepared from magnesium turnings (2.92 g, 120.11 mmol) and 1,4-dibromobutane (8.64 g, 40.0 mmol) in dry diethyl ether (105 ml), was added to a diethyl ether solution (50 ml) of piperonal (9.01 g, 60.0 mmol) at 0 °C. After the mixture was stirred at room temperature overnight, the reaction was quenched with chilled saturated $\mathrm{NH_4Cl}$ solution. The organic materials were extracted with ethyl acetate, and the combined extracts were dried over $\mathrm{MgSO_4}$. After the solvent was removed under reduced pressure, the residue was purified by column chromatography (hexane : ethyl acetate = 2 : 1) to give 1,6-bis(3,4-methylenedioxyphenyl)hexane-1,6-diol **19** (7.46 g, 74% yield): IR (KBr) 3400, 2914, 1502, 1487, 1442, 1248 cm^{-1}; ^{1}H NMR (500 MHz, $\mathrm{CDCl_3}$) $\delta = 1.15$—1.23 (m, 2H), 1.28—1.37 (m, 2H), 1.50—1.60 (m, 2H), 1.64—1.72 (m, 2H), 2.50 (br, 2H), 4.43—4.48 (m, 2H), 5.86 (s, 4H), 6.67—6.71 (m, 4H), 6.77 (s, 2H). Anal. Calcd for $\mathrm{C_{20}H_{22}O_6}$: C, 67.03; H, 6.19%. Found: C, 66.81; H, 6.15%.

Synthesis of 1,6-Bis(3,4-methylenedioxyphenyl)hexane-1,6-dione (20): Chromium(VI) oxide (3.40 g, 34.0 mmol) was added to pyridine (45 ml) suspended with Celite (2.0 g) at room temperature under an argon atmosphere. Then 1,6-bis(3,4-methylenedioxyphenyl)hexane-1,6-diol **19** (1.90 g, 5.30 mmol) was added. After the mixture was stirred for 8 h at room temperature, the reaction mixture was filtered through silica-gel column chromatography (hexane : ethyl acetate = 1 : 1) to give 1,6-bis(3,4-methylenedioxyphenyl)hexane-1,6-dione **20** (1.45 g, 77% yield): IR (KBr) 1670, 1601, 1506, 1487, 1442, 1259, 1030 cm^{-1}; ^{1}H NMR (500 MHz, $\mathrm{CDCl_3}$) $\delta = 1.78$—1.81 (m, 4H), 2.93—2.95 (m, 4H), 6.04 (s, 4H), 6.65 (d, 2H, $J = 8.2$ Hz), 7.43 (d, 2H, $J = 1.7$ Hz), 7.65 (dd, 2H, $J = 1.7$, 8.2 Hz). Anal. Calcd for $\mathrm{C_{20}H_{18}O_6}$: C, 67.79; H, 5.12%. Found: C, 67.50; H, 4.99%.

Synthesis of 1,1,6,6-Tetramethoxy-1,6-bis(3,4-methylenedioxyphenyl)hexane (18): To a stirred solution of 1,6-bis(3,4-methylenedioxyphenyl)hexane-1,6-dione **20** (2.60 g, 7.34 mmol) in methanol (17 ml) were added trimethyl orthoformate (31.14 g, 293.6 mmol) and *p*-toluenesulfonic acid monohydrate (138.8 mg, 0.73 mmol) at room temperature. After the mixture was stirred for 12 h, the mixture was filtered and the solids were washed with $\mathrm{NaHCO_3}$ solution, water, and hexane. The obtained solids were dried in vacuo to give 1,1,6,6-tetramethoxy-1,6-bis(3,4-methylenedioxyphenyl)hexane **18** (2.41 g, 73% yield): IR (KBr) 2949, 1501, 1439, 1250 cm^{-1}; ^{1}H NMR (500 MHz, $\mathrm{CDCl_3}$) $\delta = 0.80$—0.87 (m, 4H), 1.67—1.73 (m, 4H), 3.06 (s, 12H), 5.91 (s, 4H), 6.71 (d, 2H, $J = 8.0$ Hz), 6.81—6.84 (m, 4H). Anal. Calcd for $\mathrm{C_{24}H_{30}O_8}$: C, 64.56; H, 6.77%. Found: C, 64.31; H, 6.57%.

1-(3,4-Methylenedioxyphenyl)cyclopentene **17** was prepared by the procedure described in A Typical Procedure for the Intramolecular Disproportionation Reactions of the Dimethyl Acetals. IR (KBr) 1504, 1491, 1225 cm^{-1}; ^{1}H NMR (500 MHz, $\mathrm{CDCl_3}$) $\delta = 1.99$ (quint, 2H, $J = 7.0$ Hz), 2.45—2.50 (m, 2H), 2.60—2.65 (m, 2H), 5.93 (s, 2H), 6.00—6.02 (m, 1H), 6.73 (d, 1H, $J = 8.0$ Hz), 6.88 (d, 1H, $J = 8.0$ Hz), 6.98 (s, 1H). HRMS Found: *m/z* 188.0847. Calcd for $\mathrm{C_{12}H_{12}O_2}$: M, 188.0837.

Synthesis of 5-(3,4-Methylenedioxyphenyl)-5-oxopentanoic Acid (21): 1-(3,4-Methylenedioxyphenyl)cyclopentene **17** (188.0

mg, 1.00 mmol) was added to a benzene and water solution (7 ml each) of methyltrioctylammonium chloride (122.0 mg, 0.30 mmol) and $KMnO_4$ (948.2 mg, 6.00 mmol) at such a rate that the temperature was maintained at 40—45 °C for 0.5 h.[10] After the mixture was further stirred for an additional 1 h, excess permanganate was destroyed by addition of sodium sulfinate solution and the mixture was filtered to remove MnO_2. The filtrate was acidified with 2 M HCl solution, extracted with ethyl acetate three times, and the combined extracts were dried with Na_2SO_4. After the solvent was removed under reduced pressure, the residue was purified by thin-layer chromatography (hexane : ethyl acetate = 1 : 1) to give 5-(3,4-methylenedioxyphenyl)-5-oxopentanoic acid **21** (168.0 mg, 71% yield): IR (KBr) 2970, 1697, 1670, 1441, 1240 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) $\delta = 1.91$ (quint, 2H, $J = 7.1$ Hz), 2.28 (t, 2H, $J = 7.1$ Hz), 2.87 (t, 2H, $J = 7.1$ Hz), 5.93 (s, 2H), 6.72 (d, 1H, $J = 8.0$ Hz), 7.31 (s, 1H), 7.45 (d, 1H, $J = 8.0$ Hz), 10.50 (br, 1H). Anal. Calcd for $C_{12}H_{12}O_5$: C, 61.02; H, 5.08%. Found: C, 60.81; H, 4.99%.

Synthesis of 3,4-Dihydro-6-(3,4-methylenedioxyphenyl)-4*H*-pyran-2(3*H*)-one (22): 5-(3,4-Methylenedioxyphenyl)-5-oxopentanoic acid **21** (85.0 mg, 0.36 mmol) was suspended in acetic anhydride (4 ml) and the suspension was gradually heated to reflux for 8 h. The reaction mixture was cooled, diluted with $NaHCO_3$ solution and extracted with diethyl ether three times. The combined extracts were dried with $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by thin-layer chromatography (hexane : ethyl acetate = 1 : 1) to give 3,4-dihydro-6-(3,4-methyleneoxyphenyl)-4*H*-pyran-2(3*H*)-one **22** (52.8 mg, 67% yield): IR (KBr) 2900, 1761, 1491, 1225 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) $\delta = 2.48$ (dt, 2H, $J = 4.7, 7.6$ Hz), 2.66 (t, 2H, $J = 7.6$ Hz), 5.64 (t, 1H, $J = 4.7$ Hz), 5.96 (s, 2H), 6.77 (d, 1H, $J = 8.2$ Hz), 7.03 (d, 1H, $J = 1.7$ Hz), 7.11 (dd, 1H, $J = 8.2, 1.7$ Hz). Anal. Calcd for $C_{12}H_{10}O_4$: C, 66.06; H, 4.59%. Found: C, 65.93; H, 4.66%.

Synthesis of Paracotoin: A dioxane suspension (5 ml) of 3,4-dihydro-6-(3,4-methylenedioxyphenyl)-4*H*-pyran-2(3*H*)-one **22** (43.6 mg, 0.20 mmol) and DDQ (95.3 mg, 0.42 mmol) was refluxed for 5 h.[11] The reaction mixture was diluted with dichloromethane and the mixture was filtered through a column of neutral alumina. After the concentration of the filtrate, the residue was purified by thin-layer chromatography (hexane : ethyl acetate = 1 : 1) to give paracotoin (40.7 mg, 94% yield): IR (KBr) 1718, 1504, 1491, 1236 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) $\delta = 6.02$ (s, 2H), 6.20 (d, 1H, $J = 9.4$ Hz), 6.49 (d, 1H, $J = 6.8$ Hz), 6.85 (d, 1H, $J = 8.3$ Hz), 7.24 (s, 1H), 7.35—7.39 (m, 2H). Anal. Calcd for $C_{12}H_8O_4$: C, 66.67; H, 3.73%. Found: C, 66.63; H, 3.85%.

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