Reductive Dimerization of 2-Substituted Cyclopropane-1,1-dicarboxylates Using Samarium(II) Diiodide[1)]

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In the presence of samarium diiodide, 2-aryl and 2-heteroaryl cyclopropane-1,1-dicarboxylic esters were readily dimerized to give 3,4-disubstituted 1,1,6,6-hexanetetracarboxylic esters as diastereomeric mixtures in moderate to good yields. The diastereomeric mixtures were separated by preparative HPLC and stereochemistries of the isolated meso and racemic compounds were determined on the basis of HPLC analysis on chiral stationary phases. Between the ^{1}H-NMR spectra of the separated diastereomers, the characteristic differences in the chemical shifts of the C2-H (C5-H) signals were observed and explained based on the MOPAC calculation.

Key words samarium diiodide; cyclopropane-1,1-dicarboxylate; reductive dimerization; ring-opening; 1,1,6,6-hexanetetracarboxylate; MOPAC calculation

Kagan and his co-workers reported in 1977 the first work on the use of samarium diiodide (SmI_2) in synthetic organic chemistry,[2)] and recently the reagent has become important as a one-electron reducing agent because of its easy handling and wide range of utility.[3)] Many synthetic applications of the reagent have been developed, and we also reported several new reactions using the reagent.[4)] The cyclopropane ring-opening is an interesting research subject,[5)] but only a few examples using SmI_2 have been reported.[4b,4c,6)] We previously reported that treatment of 2-substituted cyclopropanecarboxylic esters and cyclopropane-1,1-dicarboxylic esters (**1**) in a SmI_2–hexamethylphosphoramide (HMPA)–tetrahydrofuran (THF) system in the presence of *tert*-butyl alcohol (*tert*-BuOH) as a proton source gave 4-substituted butyric esters and/or (2-substituted ethyl)malonic esters (**2**), which were raised by the regioselective C1–C2 bond cleavage.[4b,c)] In the reactions of **1**, we found, interestingly, by-production of a small amount of 3,4-disubstituted 1,1,6,6-hexanetetracarboxylic ester (dimer) **3**, which was presumed to be derived from dimerization of a γ-carbon radical intermediate (**5**).

Though dimerizations of various substrates such as acid chlorides, ketones or aldehydes, α,β-unsaturated esters, imines, and isocyanates in the presence of SmI_2 have been reported,[4d,7)] there has been no report on ring-opening/dimerization of cyclopropane compounds using SmI_2. This paper deals with the reductive dimerization of 2-aryl and 2-heteroaryl cyclopropane-1,1-dicarboxylic esters (**1**) giving 3,4-disubstituted 1,1,6,6-hexanetetracarboxylic esters (**3**) in the SmI_2-THF system, and stereochemistry of these products.

A plausible mechanism of the present cyclopropane ring-opening of **1** is shown in Chart 2 and the ring-opening seems to include the intermediate (**5**). When HMPA as an additive

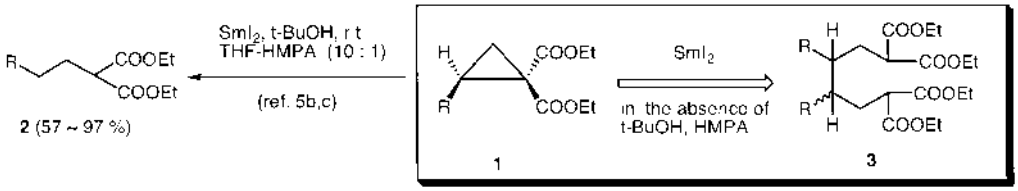

Chart 1

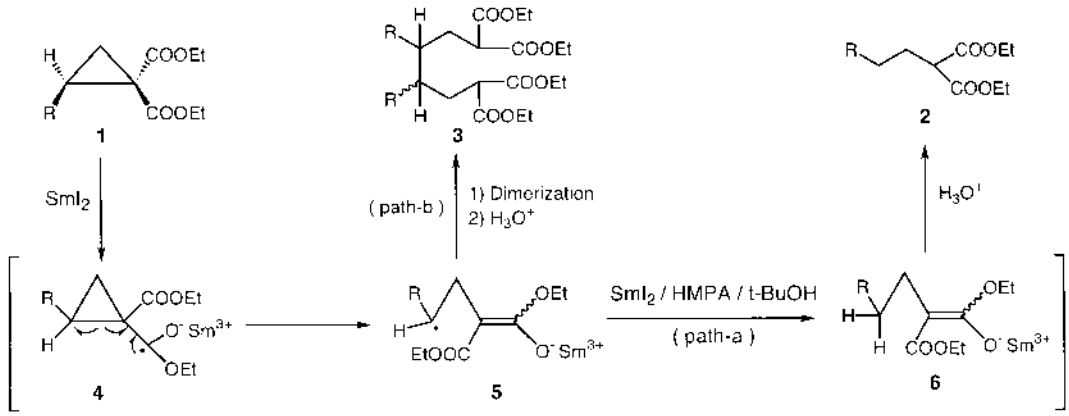

Chart 2

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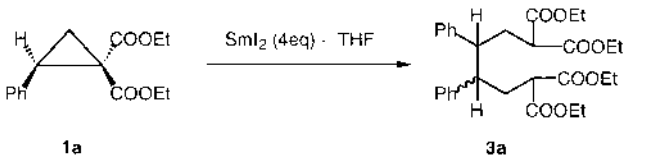
Table 1. Reductive Dimerization of **1a**

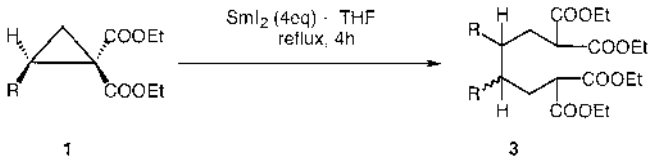


1a **3a**

Run	THF (ml)[a]	HMPA (eq)	Temp.	Isolated yield (%)[b]
1	3	2.6	r.t.	20
2	5	2.6	r.t.	30
3	8	2.6	r.t.	22
4	5	15.6	r.t.	28
5	3	none	r.t.	47
6	3	none	reflux	67

a) **1a** (0.5 mmol) was used. *b*) A diastereomeric mixture was obtained.

Table 2. Reductive Dimerization of **1**



1 **3**

Run	Starting material		Product		Diastereomeric ratio
		R		Isolated yield (%)	*meso* : *rac*
1	**1a**	Ph-	**3a**	67	5 : 4[a]
2	**1b**	4-MeC_6H_4–	**3b**	85	5 : 4[a]
3	**1c**	4-MeOC_6H_4–	**3c**	55	10 : 1[a]
4	**1d**	3,4-(OCH_2O)C_6H_3–	**3d**	64	3 : 2[a]
5	**1e**	2-Thienyl	**3e**	93	—[b]
6	**1f**	1-Naphthyl	**3f**	94	—[b]
7	**1g**	Me_2CH–	—	—[c]	—
8	**1h**	Et_2CH–	—	—[c]	—

a) The diastereoisomers were isolated by preparative HPLC and their ratio was determined on the basis of peak area. Each diastereoisomer was subjected to HPLC analysis on chiral stationary phases. *b*) A diastereomeric mixture was obtained but its ratio could not be determined. *c*) Most of the starting material was recovered.

and *tert*-BuOH as a proton source existed in the reaction system, the ring-opened products (**2**) *via* the enolate species (**6**) were predominantly obtained (path-a). We therefore assumed that dimerization of the γ-carbon radicals (**5**) (path-b) would be preferred in the absence of *tert*-BuOH.

When 2-phenylcyclopropane-1,1-dicarboxylic ester (**1a**: R=Ph) was treated with SmI_2 (4.0 eq) in THF in the presence of HMPA (2.6 eq) at room temperature, the reductive dimerization product (**3a**: R=Ph) was obtained in 20% yield as a diastereomeric mixture along with diethyl (2-phenylethyl)malonate (**2a**: R=Ph) (Run 1 in Table 1). The structure of **3a** was determined on the basis of spectral data. The FAB high-resolution MS (FAB-HRMS) revealed that the dimer product (**3a**) possessed the formula $C_{30}H_{38}O_8$, and the IR spectrum ($CHCl_3$) showed carbonyl band absorptions at 1735 and 1722 cm^{-1}. Though the ^{1}H-NMR spectrum was somewhat complex, it supported that the dimer product (**3a**) was a mixture consisting of the *meso* and the racemic compounds. Yield of the dimer (**3a**) could not be improved by altering amounts of THF and HMPA (Runs 2—4). When the reaction was carried out in the absence of HMPA at room temperature (Run 5), the dimer was obtained in 47% yield. Yield of this dimer rose to 67% when the reaction was carried out in a THF-refluxing condition (70 °C) in the absence of HMPA (Run 6).[8]

Inanaga *et al*. however reported that hexanedioic acid ester derivatives were produced (48—90%) when α,β-unsaturated esters were treated in the SmI_2–HMPA–THF system in the presence of a proton source. They also reported that almost no dimerization reaction or simple reduction of the double bond took place slowly in the absence of HMPA.[7e] Their reaction and ours were presumed to proceed *via* the carbon radical species such as β-carbon radical esters or γ-carbon radical diesters (**5**). Although the mechanism of the effect of HMPA and *tert*-BuOH in these reactions is not clear, it is interesting that Inanaga's observation is in contrast to our results.

To examine the generality of the present dimerization, various cyclopropyl esters (**1b**—**h**) were prepared in the usual manner[4c] and subjected to the same reaction conditions as those of Run 6 in Table 1 to give the corresponding dimers **3b**—**f** in variable diastereomer ratios, except for the cases of **1g** and **1h** (which were almost completely recovered); the results are summarized in Table 2.

The 2-aryl or 2-heteroaryl cyclopropane derivatives (**1b**—**f**) were successfully dimerized in moderate to high yields while the 2-alkyl derivatives (**1g**, **h**) were inactive. These results suggest that the existence of aromatic groups at 2-position in cyclopropane compounds (**1**) is indispensable for the cyclopropane ring-opening/dimerization reaction. Namely, the easy access of the 2-aryl (**1a**—**d**, **f**) and 2-heteroaryl derivatives (**1e**) to the dimerization products (**3a**—**f**) may be attributable to the stability of the corresponding intermediate benzyl radicals (**5a**—**d**, **f**) or thienylmethyl radical (**5e**).[9]

This result supports that the carbon radical (**5**) is also an important intermediate in the present dimerization as well as in the regioselective cyclopropane ring-opening from 2-substituted cyclopropane-1,1-dicarboxylic esters (**1**) to (2-substituted ethyl)malonic esters (**2**).[4b,c]

The diastereomeric mixtures of the product **3** could not be separated into the respective *meso* and racemic compounds by simple silica gel column chromatography. After several examinations, it was found that some of them (**3a**—**d**) were separable by normal-phase preparative HPLC on silica gel as filling material [Shim-pack PREP-SIL, 20 mm i.d.×25 cm (Shimadzu Co.)]. Pappas' group determined the stereochemistries of *meso* and racemic dimethyl 2,3-diphenyltartarate using HPLC analysis on chiral stationary phases.[10] The stereochemistries of the isolated *meso* (**3am**—**dm**; "**m**" means *meso* form) and racemic compounds (**3ar**—**dr**; "**r**" means racemic form) were determined according to method of the Pappas group. Namely, the *meso* compounds showed only a single peak whereas the racemic compounds showed two peaks of approximately the same magnitude under identical HPLC conditions. For example, only one peak at 16.80 min appeared for the *meso* compound (**3cm**) on the chiral stationary phases [CHIRALCEL OD, 4.6 mm i.d.×25 cm (DAICEL Chemical Industries, Ltd.)] using a mixture of hexane–2-propanol (98 : 2 in volume) as an eluent, and two peaks at 14.54 and 17.77 min appeared for the racemic compound (**3cr**) under the same conditions (Chart 3). The diastereomeric ratios of the mixtures (**3a**—**d**) were determined on the basis of their preparative HPLC peak areas. In the

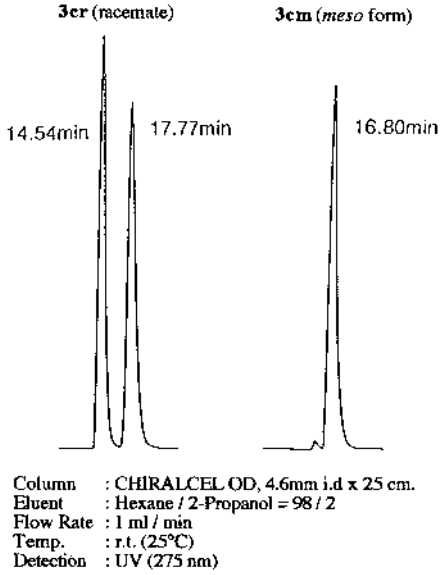
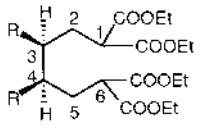
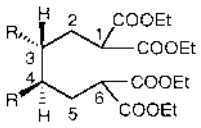


Chart 3. HPLC Pattern of **3cr** and **3cm**

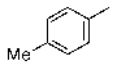
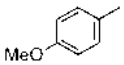
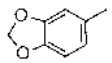
Table 3. ^{1}H-NMR Chemical Shift (δ ppm) of Compounds **3a**—**d**[a)]



3m (*meso* form)



3r (racemate)

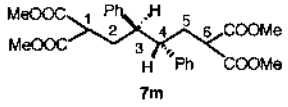
R		C1,C6-H	C2,C5-H	C3,C4-H
	**3ar** (racemate)	3.00	2.14, 2.61	2.86
	3am (*meso* form)	2.86	1.93, 1.97	2.79
	**3br** (racemate)	2.99	2.07, 2.52	2.80
	3bm (*meso* form)	2.87	1.83, 1.96	2.70
	**3cr** (racemate)	3.00	2.05, 2.51	2.78
	3cm (*meso* form)	2.88	1.83, 1.97	2.69
	**3dr** (racemate)	3.02	2.01, 2.56	2.73
	3dm (*meso* form)	2.92	1.72, 1.97	2.63

a) 270 MHz, in $CDCl_3$.

cases of **3a**, **b**, and **d**, their *meso* and racemic ratios were 5 : 4—3 : 2 (Runs 1, 2, and 4 in Table 2). It is noteworthy that the *meso* compound (**3cm**) was obtained predominantly over the racemic compound (**3cr**) (Run 3 in Table 2).

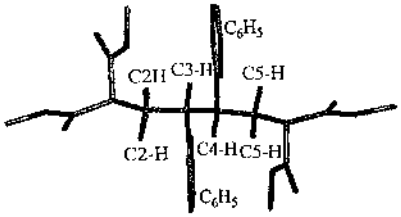
In the ^{1}H-NMR spectra of these separated diastereomers (**3am**—**dm**, **3ar**—**dr**), characteristic differences between the *meso* and the racemic compounds were observed (Table 3).

Signals of the protons on the C1–C6 group in the *meso* compounds (**3am**—**dm**) were all observed in a higher magnetic field than those in the racemic compounds (**3ar**—**dr**), and an especially significant difference was observed in the signals of C2-H and C5-H. For example, signals of C2,5-H_a and -H_b of **3am** and **3ar** were observed at 1.93 and 1.97 ppm, and at 2.14 and 2.61 ppm, respectively. To learn the reason for the difference, we performed a semiempirical molecular orbital calculation of these molecules to determine their most



7m

	Dihedral angle of C1-C2-C3--H (°)	Heat of formation (kcal/mol)
7m-I	49.9	-290.5
7m-II	178.7	-288.3
7m-III	343.5	-289.7



Stick Drawing
Only hydrogens of C2, C3, C4, and C5 positions are shown.

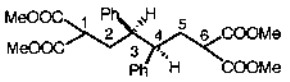
Fig. 1. MOPAC (PM3) Calculation of **7m** and the Most Stable Structure (**7m-I**)

stable structures. The model compound (**7m**) for the *meso* compounds and the model compound (**7r**) for the racemic compounds were calculated by the MOPAC PM3 method.[11)] In the *meso* compound (**7m**), three local minimum dihedral angles of C1–C2–C3–H were found at 49.9, 178.7, and 343.5 degrees, respectively, and the most stable conformer calculated was **7m-I** as shown in Fig. 1. Heat of formation for the most stable conformer (**7m-I**) was lower than those of the conformers **7m-II** and **7m-III** by differences of 2.2 and 0.8 kcal/mol, respectively.

In the racemic compound (**7r**), on the other hand, three local minimum dihedral angles of C1–C2–C3–H were also found at 48.8, 168.4, and 305.6 degrees, respectively, and the most stable conformer calculated was **7r-I** as shown in Fig. 2. Heat of formation for the most stable conformer (**7r-I**) was lower than those of the conformers **7r-II** and **7r-III** by differences of 4.1 and 2.4 kcal/mol, respectively.

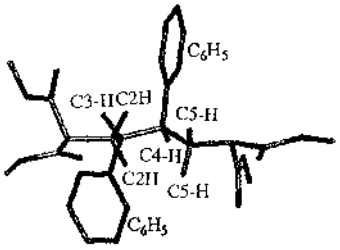
The differences between the *meso* compounds (**3am**—**dm**) and the racemic compounds (**3ar**—**dr**) in ^{1}H-NMR spectra might be explained from these calculated results. In **7m-I**, one of the C2(C5) protons locates at the magnetic shield area of the benzene ring, and the other proton locates at the magnetic deshielded area. Due to the average resulting from rotation, the signals of these protons seem to appear at relatively high magnetic field. In **7r-I**, all of the C2(C5) protons locate at the magnetic deshielded area, so the signals of these protons seem to appear at relatively low magnetic field. These results would be useful for determination of the stereochemistry of similar compounds.

In conclusion, we found that the reductive C–C dimerization at the γ-position under ring-opening of cyclopropane-1,1-dicarboxylates (**1**) bearing 2-aryl or 2-heteroaryl groups at the 2-position occurred by SmI_2 in refluxing THF to give diastereomeric mixtures of the 3,4-disubstituted 1,1,6,6-hexanetetracarboxylates (**3**), and stereochemistries of **3** could be determined on the basis of their ^{1}H-NMR spectra.



7r

	Dihedral angel of C1-C2-C3-H (°)	Heat of formation (kcal/mol)
7r-I	48.8	-291.5
7r-II	168.4	-287.4
7r-III	305.6	-289.1



Stick Drawing
Only hydrogens of C2, C3, C4, and C5 positions are shown.

Fig. 2. MOPAC (PM3) Calculation of **7r** and the Most Stable Structure (**7r-I**)

Experimental

IR spectra were taken with a Shimadzu IR-435 spectrophotometer. ^{1}H-NMR spectra were measured on a JEOL EX-270 (270 MHz) and a Varian XL-300 (300 MHz) with tetramethylsilane as an internal standard and chemical shifts are reported in ppm. Mass spectra were recorded with a JEOL JMS-SX 102A QQ spectrometer. Silica gel 60 PF_{254} (Nacalai Tesque Inc.) were used for preparative TLC (PTLC). HPLC was carried out on a Shimadzu instrument unless otherwise stated. As columns, Shim-pack PREP-SIL [20 mm i.d.×25 cm (Shimadzu Co.)] was used for preparative HPLC and CHIRALCEL OD [4.6 mm i.d.×25 cm (DAICEL Chemical Industries, Ltd.)] for HPLC analysis on chiral stationary phases.

Diethyl 2-substituted 1,1-cyclopropanedicarboxylate (**1a**—**h**) was prepared by treatment of diethyl substituted methylidenemalonates with dimethylsulfoxonium methylide according to Landor's method.[12)]

Reductive Dimerization of Diethyl 2-Phenyl-1,1-cyclopropanedicarboxylate (1a) Using SmI_2 (General Procedure) To a suspension of samarium metal (360 mg, 2.40 mmol) in THF (0.5 ml) was added dropwise a solution of 1,2-diiodoethane (562 mg, 2.00 mmol) in THF (1.5 ml) at room temperature under an N_2 atmosphere and the whole was stirred for 1 h. A solution of **1a** (131 mg, 0.50 mmol) in THF (1 ml) was added dropwise to the blue suspension of SmI_2 at room temperature and the whole was refluxed at 75 °C with stirring for an additional 4 h. After addition of 3% HCl under ice-cooling, the mixture was extracted with diethyl ether. The combined organic layer was washed successively with water, saturated $Na_2S_2O_3$ solution, water, and brine, dried over anhydrous sodium sulfate, and evaporated under reduced pressure. The residue was purified with PTLC (ethyl acetate : *n*-hexane=1 : 5) to give tetraethyl 3,4-diphenyl-1,1,6,6-hexanetetracarboxyate (**3a**, 88.0 mg, 67%) as a diastereomeric mixture. An aliquot of the mixture of **3a** was subjected to preparative HPLC separation [*n*-hexane : 2-propanol= 99.3 : 0.7; Flow, 4 ml/min; Temp., 25 °C; Detection, UV (260 nm)].

3ar (Racemate): t_R, 58.37 min. Colorless oil. IR ($CHCl_3$): 1737, 1721 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.18 (6H, t, J=7.3 Hz, –OCH$_2$C<u>H</u>$_3$), 1.24 (6H, t, J=7.1 Hz, –OCH$_2$C<u>H</u>$_3$), 2.10—2.18 (2H, m, ArCHC<u>H</u>$_2$–), 2.61 (2H, t like, J=12.4 Hz, ArCHC<u>H</u>$_2$–), 2.86 (2H, d like, J=10.2 Hz, ArC<u>H</u>CH$_2$–), 3.00 (2H, dd, J=4.0, 10.9 Hz, –C<u>H</u>(COOEt)$_2$), 3.99—4.22 (8H, m, –OC<u>H</u>$_2$CH$_3$), 6.80—6.84 (4H, m, Ar-H), 7.06—7.13 (6H, m, Ar-H). FAB-LRMS *m/z*: 527 (M+H)$^+$. FAB-HRMS *m/z* (M+H)$^+$: Calcd for $C_{30}H_{39}O_8$: 527.2645. Found: 527.2632. Analytical HPLC [*n*-hexane : 2-propanol=99 : 1; Flow, 0.5 ml/min; Temp., 25 °C; Detection, UV (260 nm); t_R, 34.41, 39.16 min].

3am (Mesoform): t_R, 54.24 min. Colorless crystals, mp 67.0—69.5 °C. IR ($CHCl_3$): 1735, 1722 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.10 (6H, t, J=7.1 Hz, –OCH$_2$C<u>H</u>$_3$), 1.19 (6H, t, J=7.1 Hz, –OCH$_2$C<u>H</u>$_3$), 1.88—1.97 (2H, m, ArCHC<u>H</u>$_2$–), 1.92—2.01 (2H, m, ArCHC<u>H</u>$_2$–), 2.79 (2H, d like, J=9.2 Hz, ArC<u>H</u>CH$_2$–), 2.86 (2H, dd, J=4.5, 10.7 Hz, –C<u>H</u>(COOEt)$_2$), 3.95 (4H, q, J=7.0 Hz, –OC<u>H</u>$_2$CH$_3$), 4.12 (4H, q, J=7.2 Hz, –OC<u>H</u>$_2$CH$_3$), 7.17—7.37 (10H, m, Ar-H). FAB-LRMS *m/z*: 527 (M+H)$^+$. FAB-HRMS *m/z* (M+H)$^+$: Calcd for $C_{30}H_{39}O_8$: 527.2645. Found: 527.2659. Analytical HPLC [*n*-hexane : 2-propanol=99 : 1; Flow, 0.5 ml/min; Temp., 25 °C; Detection, UV (260 nm), t_R, 39.35 min].

Tetraethyl 3,4-Di(4-methylphenyl)-1,1,6,6-hexanetetracarboxylate (3b) Purified by PTLC (ethyl acetate : *n*-hexane=1 : 5) to give **3b** (85%) as a diastereomeric mixture. An aliquot of the mixture of **3b** was subjected to preparative HPLC separation [*n*-hexane : 2-propanol=99.2 : 0.8; Flow, 5 ml/min; Temp., 25 °C; Detection, UV (264 nm)].

3br (Racemate): t_R, 33.93 min. Colorless oil. IR ($CHCl_3$): 1738, 1723 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.17 (6H, t, J=7.1 Hz, –OCH$_2$C<u>H</u>$_3$), 1.23 (6H, t, J=7.1 Hz, –OCH$_2$C<u>H</u>$_3$), 1.99—2.15 (2H, m, ArCHC<u>H</u>$_2$–), 2.24 (6H, s, Ar-CH$_3$), 2.52 (2H, t like, J=10.9 Hz, ArCHC<u>H</u>$_2$–), 2.81 (2H, d like, J=10.9 Hz, ArC<u>H</u>CH$_2$–), 2.99 (2H, dd, J=4.0, 10.9 Hz, –C<u>H</u>(COOEt)$_2$), 3.93—4.10 (4H, m, –OC<u>H</u>$_2$CH$_3$), 4.17 (4H, q, J=7.0 Hz, –OC<u>H</u>$_2$CH$_3$), 6.71 (4H, d, J=7.9 Hz, Ar-H), 6.93 (4H, d, J=7.9 Hz, Ar-H). FAB-LRMS *m/z*: 555 (M+H)$^+$. FAB-HRMS *m/z* (M+H)$^+$: Calcd for $C_{32}H_{43}O_8$: 555.2958. Found: 555.2945. Analytical HPLC [*n*-hexane : 2-propanol=98 : 2; Flow, 0.5 ml/min; Temp., 25 °C; Detection, UV (264 nm), t_R, 15.16, 16.29 min].

3bm (Mesoform): t_R, 29.53 min. Colorless crystals, mp 103.5—106.1 °C. IR ($CHCl_3$): 1738, 1722 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.10 (6H, t, J=7.3 Hz, –OCH$_2$C<u>H</u>$_3$), 1.20 (6H, t, J=7.1 Hz, –OCH$_2$C<u>H</u>$_3$), 1.75—1.88 (2H, m, ArCHC<u>H</u>$_2$–), 1.96 (2H, t like, J=11.1 Hz, ArCHC<u>H</u>$_2$–), 2.33 (6H, s, Ar-CH$_3$), 2.71 (2H, d like, J=9.2 Hz, ArC<u>H</u>CH$_2$–), 2.87 (2H, dd, J=4.0, 11.2 Hz, –C<u>H</u>(COOEt)$_2$), 3.96 (4H, q, J=6.7 Hz, –OC<u>H</u>$_2$CH$_3$), 4.12 (4H, q, J=6.9 Hz, –OC<u>H</u>$_2$CH$_3$), 7.05 (4H, d, J=8.1 Hz, Ar-H), 7.13 (4H, d, J=8.1 Hz, Ar-H). FAB-LRMS *m/z*: 555 (M+H)$^+$. FAB-HRMS *m/z* (M+H)$^+$: Calcd for $C_{32}H_{43}O_8$: 555.2958. Found: 555.2972. Analytical HPLC [*n*-hexane : 2-propanol=98 : 2; Flow, 0.5 ml/min; Temp., 25 °C; Detection, UV (264 nm); t_R, 14.50 min].

Tetraethyl 3,4-Di(4-methoxyphenyl)-1,1,6,6-hexanetetracarboxylate (3c) Purified by PTLC (ethyl acetate : *n*-hexane=1 : 5) to give **3c** (55%) as a diastereomeric mixture. An aliquot of the mixture of **3c** was subjected to preparative HPLC separation [*n*-hexane : 2-propanol=98 : 2; Flow, 5 ml/min; Temp., 25 °C; Detection, UV (275 nm)].

3cr (Racemate): t_R, 36.68 min. Colorless oil. IR ($CHCl_3$): 1738, 1721 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.18 (6H, t, J=7.1 Hz, –OCH$_2$C<u>H</u>$_3$), 1.24 (6H, t, J=7.1 Hz, –OCH$_2$C<u>H</u>$_3$), 1.99—2.10 (2H, m, ArCHC<u>H</u>$_2$–), 2.51 (2H, t like, J=10.7 Hz, ArCHC<u>H</u>$_2$–), 2.78 (2H, d like, J=10.2 Hz, ArC<u>H</u>CH$_2$–), 3.00 (2H, dd, J=4.0, 11.2 Hz, –C<u>H</u>(COOEt)$_2$), 3.74 (6H, s, –OC<u>H</u>$_3$), 4.01—4.22 (8H, m, –OC<u>H</u>$_2$CH$_3$), 6.67 (4H, d, J=8.9 Hz, Ar-H), 6.72 (4H, d, J=8.9 Hz, Ar-H). EI-LRMS *m/z*: 586 (M$^+$). EI-HRMS *m/z* (M$^+$): Calcd for $C_{32}H_{42}O_{10}$: 586.2780. Found: 586.2753. Analytical HPLC [*n*-hexane : 2-propanol=98 : 2; Flow, 1 ml/min; Temp., 25 °C; Detection, UV (275 nm); t_R, 14.54, 17.77 min].

3cm (Mesoform): t_R, 40.70 min. Colorless crystals, mp 111.0—113.5 °C. IR ($CHCl_3$): 1737, 1721 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.11 (6H, t, J=7.1 Hz, –OCH$_2$C<u>H</u>$_3$), 1.21 (6H, t, J=7.1 Hz, –OCH$_2$C<u>H</u>$_3$), 1.81—1.84 (2H, m, ArCHC<u>H</u>$_2$–), 1.97 (2H, t like, J=11.6 Hz, ArCHC<u>H</u>$_2$–), 2.69 (2H, d like, J = 9.6 Hz, ArC<u>H</u>CH$_2$–), 2.88 (2H, dd, J = 4.0, 11.2 Hz, –C<u>H</u>(COOEt)$_2$), 3.81 (6H, s, –OCH$_3$), 3.97 (4H, q, J=6.7 Hz, –OC<u>H</u>$_2$CH$_3$), 4.21 (4H, q, J=7.2 Hz, –OC<u>H</u>$_2$CH$_3$), 6.87 (4H, d, J=8.6 Hz, Ar-H), 7.07 (4H, d, J=8.2 Hz, Ar-H). EI-LRMS *m/z*: 586 (M$^+$). EI-HRMS *m/z* (M$^+$): Calcd for $C_{32}H_{42}O_{10}$: 586.2780. Found: 586.2802. Analytical HPLC [*n*-hexane : 2-propanol=98 : 2; Flow, 1 ml/min; Temp., 25 °C; Detection, UV (275 nm); t_R, 16.80 min)].

Tetraethyl 3,4-Di(3,4-methylenedioxyphenyl)-1,1,6,6-hexanetetracarboxylate (3d) Purified by PTLC (ethyl acetate : *n*-hexane=1 : 5) to give **3d** (64%) as a diastereomeric mixture. An aliquot of the mixture of **3d** was subjected to preparative HPLC separation with a Waters instrument [*n*-hexane : 2-propanol=98 : 2; Flow, 9 ml/min (recycle 4 times); Temp., 25 °C; Detection, UV (285 nm)].

3dr (Racemate): t_R, 20.18 min. Colorless oil. IR ($CHCl_3$): 1735, 1722 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.20 (6H, t, J=7.3 Hz, –OCH$_2$C<u>H</u>$_3$), 1.25 (6H, t, J=7.3 Hz, –OCH$_2$C<u>H</u>$_3$), 1.97—2.04 (2H, m, ArCHC<u>H</u>$_2$–), 2.56 (2H, t like, J=12.4 Hz, ArCHC<u>H</u>$_2$–), 2.73 (2H, d like, J=10.6 Hz, ArC<u>H</u>CH$_2$–), 3.02 (2H, dd, J=3.6, 11.2 Hz, –C<u>H</u>(COOEt)$_2$), 4.09 (4H, q, J=7.0 Hz, –OC<u>H</u>$_2$CH$_3$), 4.19 (4H, q, J=7.1 Hz, –OC<u>H</u>$_2$CH$_3$), 5.87 (4H, s, –OC<u>H</u>$_2$O–), 6.29—6.57 (6H, m, Ar-<u>H</u>). FAB-LRMS *m/z*: 615 (M+H)$^+$. FAB-HRMS *m/z* (M+H)$^+$: Calcd for $C_{32}H_{39}O_{12}$: 615.2441. Found: 615.2432. Analytical HPLC [*n*-hexane : 2-propanol=95 : 5; Flow, 0.5 ml/min; Temp., 25 °C; Detection, UV (285 nm); t_R, 24.38, 26.63 min].

3dm (Mesoform): t_R, 21.12 min. Colorless crystals, mp 144.5—147.5 °C.

IR ($CHCl_3$): 1738, 1722 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.14 (6H, t, J=7.1 Hz, –$OCH_2C\underline{H}_3$), 1.22 (6H, t, J=7.1 Hz, –$OCH_2C\underline{H}_3$), 1.65—1.77 (2H, m, $ArCHC\underline{H}_2$–), 1.97 (2H, t like, J=11.4 Hz, $ArCHC\underline{H}_2$–), 2.63 (2H, d like, J=9.4 Hz, $ArC\underline{H}CH_2$–), 2.92 (2H, dd, J=3.6, 11.2 Hz, –$C\underline{H}(COOEt)_2$), 4.01 (4H, q, J=7.3 Hz, –$OC\underline{H}_2CH_3$), 4.14 (4H, q, J=6.9 Hz, –$OC\underline{H}_2CH_3$), 5.96 (4H, s, –$OC\underline{H}_2O$–), 6.61—6.76 (6H, m, Ar-H). FAB-LRMS *m/z*: 615 $(M+H)^+$. FAB-HRMS *m/z* $(M+H)^+$: Calcd for $C_{32}H_{39}O_{12}$: 615.2441. Found: 615.2436. Analytical HPLC [*n*-hexane : 2-propanol=95 : 5; Flow, 0.5 ml/min; Temp., 25 °C; Detection, UV (285 nm); t_R, 24.43 min].

Tetraethyl 3,4-Di(2-thienyl)-1,1,6,6-hexanetetracarboxylate (3e) Purified by PTLC (ethyl acetate : *n*-hexane=1 : 5) to give **3e** (93%) as a diastereomeric mixture. Colorless oil. IR ($CHCl_3$): 1739, 1722 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.10—1.29 (total 12H, m, –$OCH_2C\underline{H}_3$), 2.15—2.26, 2.60—2.66, 2.75—2.82, and 3.00—3.40 (total 8H, each m, $ArCHC\underline{H}_2$–, $ArC\underline{H}CH_2$–, –$C\underline{H}(COOEt)_2$), 4.00—4.50 (total 8H, m, –$OC\underline{H}_2CH_3$), 6.61 and 6.71 (total 2H, each d, J=3.6 Hz, Ar-H), 6.84—6.97 (total 2H, m, Ar-H), 7.10—7.24 (total 2H, m, Ar-H). EI-LRMS *m/z*: 538 (M^+). EI-HRMS *m/z* (M^+): Calcd for $C_{26}H_{34}O_8S_2$: 538.1700. Found: 538.1702.

Tetraethyl 3,4-Di(1-naphthyl)-1,1,6,6-hexanetetracarboxylate (3f) Purified by PTLC (ethyl acetate : *n*-hexane=1 : 5) to give **3f** (94%) as a diastereomeric mixture. Colorless oil. IR ($CHCl_3$): 1736, 1722 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.90—1.30 (total 12H, m, –$OCH_2C\underline{H}_3$), 2.10—2.20, 2.40—2.55, 2.70—3.10 and 3.30—3.50 (total 8H, each m, $ArCHC\underline{H}_2$–, $ArC\underline{H}CH_2$–, –$C\underline{H}(COOEt)_2$), 3.80—4.30 (total 8H, m, –$OC\underline{H}_2CH_3$), 6.50—8.30 (total 14H, m, Ar-H). EI-LRMS *m/z*: 626 (M^+). EI-HRMS *m/z* (M^+): Calcd for $C_{38}H_{42}O_8$: 626.2879. Found: 626.2874.

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References and Notes

1) Yamashita M., Okuyama K., Ohhara T., Kawasaki I., Ohta S., *Synlett*, **1996**, 547—548.
2) *a*) Namy J. L., Girard P., Kagan H. B., *Nouv. J. Chim*., **1**, 5—7 (1977); *b*) Girard P., Namy J. L., Kagan H. B., *J. Am. Chem. Soc.*, **102**, 2693—2698 (1980).
3) For reviews: *a*) Kagan H. B., Namy J. L., *Tetrahedron*, **42**, 6573—6614 (1986); *b*) Inamoto T., *Yuki Gosei Kagaku Kyokai Shi*, **46**, 540—552 (1988); *c*) Inanaga J., *ibid*., **47**, 200—211 (1989); *d*) *Idem*, *ibid.*, **48**, 1024—1025 (1990); *e*) Kagan H. B., *New J. Chem*., **14**, 453—460 (1990); *f*) Soderquist J. A., *Aldrichimica Acta*, **24**, 15—23 (1991); *g*) Molander G. A., *Chem. Rev*., **92**, 29—68 (1992); *h*) *Idem*, *Org. React*., **46**, 211—367 (1994); *i*) Kamochi Y., Kudo T., *Yuki Gosei Kagaku Kyokai Shi*, **52**, 285—294 (1994); *j*) Molander G. A., Harris C. R., *Chem. Rev.*, **96**, 307—338 (1996); *k*) Skrydstrup T., *Angew. Chem*., *Int. Ed. Engl*., **36**, 345—347 (1997); *l*) Molander G. A., Harris C. R., *Tetrahedron*, **54**, 3321—3354 (1998); *m*) Kunishima M., Tani S., *Yuki Gosei Kagaku Kyokai Shi,* **57**, 127—135 (1999); *n*) Krief A., Laval A.-M., *Chem. Rev.*, **99**, 745—777 (1999).
4) *a*) Yamashita M., Kitagawa K., Ohhara T., Iida Y., Masumi A., Kawasaki I., Ohta S., *Chem. Lett*., **1993**, 653—656; *b*) Yamashita M., Okuyama K., Ohhara T., Kawasaki I., Ohta S., *Chem. Pharm. Bull*., **43**, 708—710 (1995); *c*) Yamashita M., Okuyama K., Ohhara T., Kawasaki I., Sakai K., Nakata N., Kawabe T., Kusumoto M., Ohta S., *ibid*., **43**, 2075—2081 (1995); *d*) Yamashita M., Okuyama K., Kawasaki I., Ohta S., *Tetrahedron Lett.*, **37**, 7755—7756 (1996).
5) For reviews: *a*) Tunemoto D., Kondo K., *Yuki Gosei Kagaku Kyokai Shi*, **35**, 1070—1086 (1977); *b*) Murakami M., Nishida S., *ibid*., **41**, 22—37 (1983); *c*) Saigo K., Shimada S., *ibid*., **49**, 928—936 (1991); *d*) Nonhebel D. C., *Chem. Soc. Rev*., **1993**, 347—359.
6) Other groups reported the ring opening of cyclopropyl ketones or cyclopropane-1,1-dicarboxylates. *a*) Molander G. A., McKie J. A., *J. Org. Chem*., **56**, 4112—4120 (1991); *b*) Batey R. A., Motherwell W. B., *Tetrahedron Lett*., **32**, 6211—6214 (1991); *c*) Beerli R., Brunner E. J., Borschberg H.-J., *ibid*., **33**, 6449—6452 (1992); *d*) Imamoto T., Hatajima T., Yoshizawa T., *ibid*., **35**, 7805—7808 (1994).
7) *a*) Girard P., Couffignal R., Kagan H. B., *Tetrahedron Lett*., **22**, 3959—3960 (1981); *b*) Namy J. L., Kagan H. B., *ibid*., **24**, 765—766 (1983); *c*) Enholm E. J., Forbes D. C., Holub D. P., *Synth. Commun*., **20**, 981—987 (1990); *d*) Imamoto T., Nishimura S., *Chem. Lett*., **1990**, 1141—1142; *e*) Inanaga J., Handa Y., Tabuchi T., Otsubo K., Yamaguchi M., Hanamoto T., *Tetrahedron Lett*., **32**, 6557—6558 (1991); *f*) Liu Y.-S., Bei M.-Z., Zhou Z.-H., Takaki K., Fujiwara Y., *Chem. Lett*., **1992**, 1143—1144; *g*) Shiue J.-S., Lin C.-C., Fang J.-M., *Tetrahedron Lett*., **34**, 335—338 (1993); *h*) Aurreecoechea J. M., Accedes A., *Synlett*, **1996**, 39—42; *i*) Canberra A., Le Lagadec R., Sharma P., Arias J. L., Toscano R. A., Velasco L., Gaviño R., Alvarez C., Salmón M., *J. Chem. Soc*., *Perkin Trans. 1*, **1998**, 3609—3617.
8) Excess of SmI_2 (4 eq) was used without detailed examination.
9) Golden D. M., Benson S. W., *Chem. Rev*., **69**, 125—134 (1969).
10) Pappas S. P., Pappas B. C., Okamoto Y., Sakamoto H., *J. Org. Chem*., **53**, 4404—4404 (1988).
11) *a*) Stewart J. J. P., *J. Am. Chem. Soc*., **107**, 3902—3909 (1985); *b*) *idem*., *J. Comp. Chem*., **10**, 209—220 (1989); *c*) *Idem*, *ibid.*, **10**, 221—264 (1989); *d*) PM3 calulations were performed using MOPAC ver. 6.0 (QCPE No. 445): *Idem*, *QCPE Bull*., **10**, 86 (1990) .
12) Landor S. R., Punja N., *J. Chem. Soc*., **1967**, 2495—2500.