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(3 + 3)-Cyclodimerization of Donor−Acceptor Cyclopropanes. Three Routes to Six-Membered Rings

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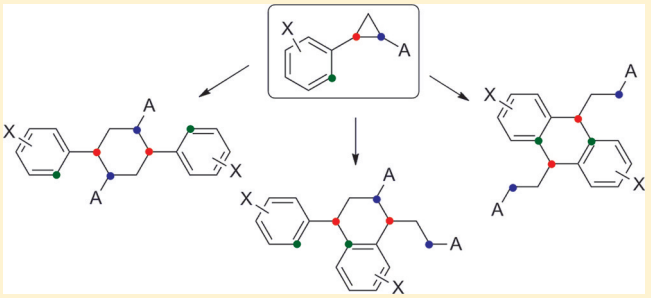
Supporting Information

ABSTRACT: The ability of donor−acceptor cyclopropanes to (3 + 3)-cyclodimerize is disclosed. It has been found that Lewis acid-induced transformations of 2-(hetero)-arylcyclopropane-1,1-dicarboxylates containing electron-abundant aromatic substituents led to the construction of six-membered cyclic systems. Depending on the substrate properties and the Lewis acid applied, three types of products can be obtained: (1) 1,4-diarylcyclohexanes, (2) 1-aryl-1,2,3,4-tetrahydronaphthalenes, and (3) 9,10-dihydroanthracenes.



INTRODUCTION

The cyclodimerizations of unsaturated compounds attract the attention of organic chemists as atom-economic reactions allowing for one-step construction of cyclic molecules with a considerable increase of structure complexity. The most investigated types of these processes are (2 + 2)-cyclodimerization of alkenes, allenes, and ketenes and (4 + 2)-cyclodimerization of dienes, affording four- and six-membered rings, respectively.[1,2] On the other hand, (3 + *n*)-cyclodimerizations are much less explored in spite of their great potential for construction of a diversity of carbo- and heterocycles.

In general, there are three types of species that can participate in (3 + *n*)-cyclodimerizations: (1) 1,3-dipoles, (2) 1,3-biradicals, and (3) three-membered rings. Thus, (3 + 2)-cyclodimerization of nitrile oxides is a preparative method of furoxans synthesis.[3,4] There are also scarce examples of other (3 + 2)-cyclodimerizations,[5−7] among which the most important is a formation of cyclopentanes from the corresponding cyclopropane derivatives.[8,9] Alternatively, (3 + 3)-cyclodimerizations have been reported for various 1,3-dipoles including nitrile oxides,[10,11] carbonyl oxides,[12−14] carbonyl imides,[15] nitrile imides,[16,17] carbonyl ylides,[18] thiocarbonyl ylides,[19−21] azomethine ylides,[22] etc.[23,24] (3 + 3)-Cyclodimerization has also been reported for 1,3-biradicals, such as trimethylenemethanes;[25] however, this reaction usually proceeds with low yields and is accompanied by formation of various side products.[26−28] Additionally, there are limited reports of (3 + 3)-cyclodimerization for three-membered heterocycles (oxiranes,[29−31] dioxiranes,[32] thiiranes,[33,34] thiirenes,[35] aziridines,[36,37] and azirines[38−40]), which can be considered as precursors of the corresponding 1,3-dipoles.

The (3 + 3)-cyclodimerization of three-membered carbocycles is an almost unexplored field except for nickel-catalyzed dimerizations of methylenecyclopropanes.[8,41] Meanwhile, there is a special class of cyclopropanes, namely donor−acceptor (D−A) cyclopropanes, which appear to be very appropriate as candidates for (3 + 3)-cyclodimerization.[42−46] They are considered to be well-proven synthetic equivalents of a three-carbon 1,3-zwitterionic synthon of **I** type (Scheme 1) possessing a dual nature and showing both 1,3-dipole-like[47−54] and dipolarophile-like[55−57] properties. However, to date there have not been any reports where these two types of reactivity of D−A cyclopropanes were combined in one reaction proceeding as (3 + 3)-cyclodimerization and leading to the cyclohexane formation (**I**+**I** path, Scheme 1).

In addition, the alternative behavior of D−A cyclopropanes as synthetic equivalents of unusual synthon **II** (Scheme 1) was recently disclosed for cyclopropanes containing electron-rich aromatic or heteroaromatic substituents.[58−62] For such cyclopropanes, the (hetero)aromatic ring takes place in reactions as nucleophilic moiety. Therefore, the rival (3 + 3)-cyclodimerization affording dihydroanthracenes (**II**+**II** path, Scheme 1) can be hypothesized in this case.

Finally, a process combining the reactivity of D−A cyclopropanes as equivalents of both synthon **I** and synthon

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Scheme 1. Three Hypothetical Paths of (3 + 3)-Cyclodimerization of Aryl-Derived D−A Cyclopropanes

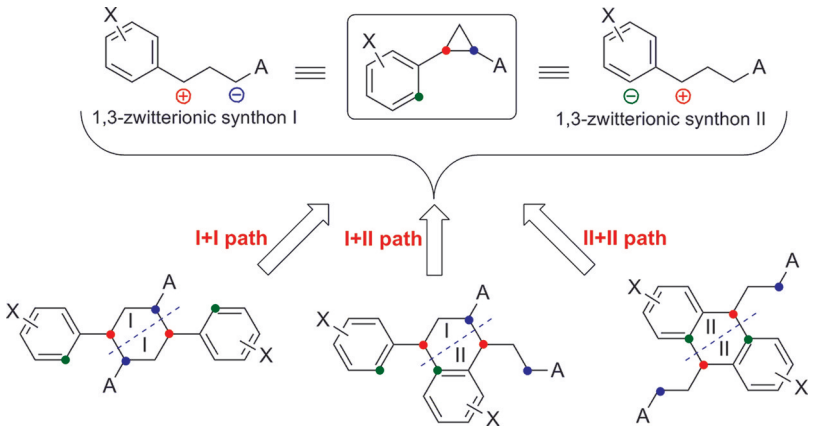
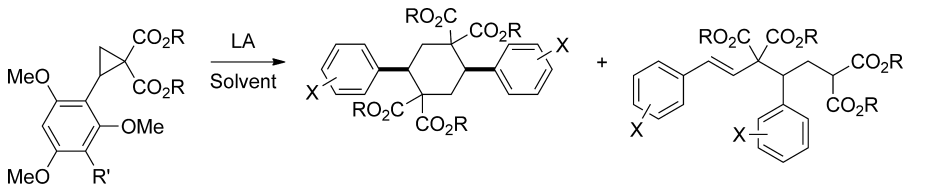


Table 1. Cyclopropane-to-Cyclohexane (3 + 3)-Cyclodimerization of 1a−c



1a: R = Et, R' = H
1b: R = Me, R' = H
1c: R = Et, R' = Br

2a: R = Et, X = 2,4,6-(MeO)$_3$
2b: R = Me, X = 2,4,6-(MeO)$_3$
2c: R = Et, X = 3-Br-2,4,6-(MeO)$_3$

3a: R = Et, X = 2,4,6-(MeO)$_3$
3b: R = Me, X = 2,4,6-(MeO)$_3$
3c: R = Et, X = 3-Br-2,4,6-(MeO)$_3$

entry	1	solvent	LA (mol %)	T (°C)	time (h)	yield of 2 (%)	yield of 3 (%)
1	1a	CH_2Cl_2	$SnCl_4$ (120)	−20[a]	22	81	
2	1a	$C_2H_5NO_2$	$SnCl_4$ (120)	−60[a]	3	82	13
3	**1a**	**CH_3NO_2**	**$SnCl_4$(120)**	**55**	**3**	**83**	**5**
4	1a	C_6H_6	$SnCl_4$ (120)	reflux	3	*b*	*b*
5	1b	CH_2Cl_2	$AlCl_3$ (100)	−25/1 h→5/22 h		5	70
6	1b	CH_2Cl_2	$TiCl_4$ (120)	−20/15 min→20/1.5 h		27[c]	17[c]
7	1b	CH_3NO_2	$TiCl_4$ (120)	−20/15 min→20/3 h			traces
8	1b	C_6H_6	$TiCl_4$ (200)	reflux	3		*b*
9	1b	CH_2Cl_2	$ZnCl_2$ (120)	20	4		86
10	1b	$C_2H_4Cl_2$	$ZnCl_2$ (200)	reflux	2	*d*	*d*
11	1b	CH_2Cl_2	$BF_3{\cdot}Et_2O$ (120)	reflux	6		85
12	1b	CH_3NO_2	$GaCl_3$ (40)	20	4	26	19
13	1c	CH_2Cl_2	$SnCl_4$ (200)	−20	20		76
14	1c	CH_3NO_2	$SnCl_4$ (220)	50	2	81	

[a]The reaction mixture was then allowed to warm to room temperature for 0.5 h. [b]Oligomeric and polymeric ring-opening products were only formed. [c]NMR yields. [d]Product of cyclopropane isomerization **4** was also formed in 10% yield.

II should result in the formation of tetrahydronaphthalenes (**I+II** path, Scheme 1). A single investigation mentioning an intermediate formation of dimers through **I+II** path is related to the synthesis of carbazoles from the indole-derived D−A cyclopropanes.[59,60]

In this study, we aimed to perform a (3 + 3)-cyclodimerization of the (hetero)aryl-substituted D−A cyclopropanes. The challenge was to find appropriate conditions for controlling of the chemoselectivity of the process. During this investigation, we have revealed each of the three dimerization pathways presented in Scheme 1 and determined the main factors influencing these dimerizations. Herein we report the results of our research opening new synthetic routes to 1,4-diarylcyclohexanes, 1-aryl-1,2,3,4-tetrahydronaphthalenes, and 9,10-dihydroanthracenes.

RESULTS AND DISCUSSION

Substrate Selection. For the present research, 2-aryl- and 2-heteroarylcyclopropane-1,1-dicarboxylates were chosen according to the following prerequisites. First, they would give cyclodimers of all three types represented in Scheme 1. Second, these substrates revealed the tendency to easy ring-opening and have previously demonstrated high reactivity in various Lewis acid-induced transformations.[42−57] In the presence of strongly activating Lewis acids, these cyclopropanes are readily converted into 1,3-zwitterions[63] in which anionic and cationic centers are efficiently stabilized by two electron-withdrawing ester groups and an electron-abundant (hetero)aromatic substituent, respectively. Finally, these compounds are readily accessible from (hetero)aromatic aldehydes through the sequence of Knoevenagel/Corey−Chaykovsky reactions.[64,65]

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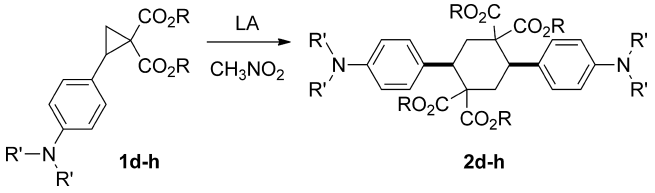
Table 2. Cyclopropane-to-Cyclohexane (3 + 3)-Cyclodimerization of 2-[4-(Dialkylamino)phenyl]cyclopropane-1,1-dicarboxylates 1d−h



entry	1,2	R	R′	R′	LA (mol %)	*T* (°C)	time (h)	yield of **2** (%)
1	**d**	Me	Me	Me	$SnCl_4$ (120)	55	3	76
2	**e**	Et	Me	Me	$SnCl_4$ (120)	55	3	86
3	**f**	Me	$-(CH_2)_5-$		$SnCl_4$ (120)	50	3	18
4	**f**	Me	$-(CH_2)_5-$		$TiCl_4$ (240)	50	3	84
5	**g**	Me	$-(CH_2)_4-$		$TiCl_4$ (240)	60	2.5	58
6	**h**	Me	$-(CH_2)_2O(CH_2)_2-$		$TiCl_4$ (210)	60	3	83

The chemoselectivity of the process is determined by the relative reactivity of two nucleophilic sites (marked blue and green in Scheme 1). Evidently, if both *ortho*-positions of an aryl substituent are occupied, D−A cyclopropanes cannot react as an equivalent of synthon **II**. Therefore, to perform a direct dimerization via the **I**+**I** path and avoid two other paths (**I**+**II** and **II**+**II**) we have chosen 2-(2,4,6-trimethoxyphenyl)-cyclopropane-1,1-diesters as model substrates.

Oppositely, a (3 + 3)-cyclodimerization of D−A cyclopropanes into dihydroanthracenes via the **II**+**II** path implies utilization of D−A cyclopropanes with aryl groups which are prone to electrophilic attack onto the *ortho*-position. Therefore, 2-(3,4,5-trimethoxyphenyl)cyclopropane-1,1-dicarboxylate was selected as a model compound for this reaction.

The formation of tetrahydronaphthalenes through **I**+**II** path is a borderline case between two foregoing dimerizations, so the prediction of substrates, which should afford these products, is not so straightforward, as in two reactions above.

Cyclopropane-to-Cyclohexane (3 + 3)-Cyclodimerization (I+I Path). According to the above arguments, we initially examined cyclopropanes **1a**,**b** as model substrates. The utilization of **1a**,**b** with strong electron-donating substituent vicinal to the diester moiety proved to be necessary but insufficient condition to furnish (3 + 3)-cyclodimerization. Thus, we have found that the weakly or moderately activating Lewis acids ($Yb(OTf)_3$, $Sn(OTf)_2$, $Sc(OTf)_3$, $Nd(OTf)_3$) failed to induce this reaction at all. To our delight, more activating Lewis acids were revealed to promote the formation of cyclohexanes **2a**,**b** (Table 1). However, the utilization of $AlCl_3$, $BF_3{\cdot}Et_2O$, or $GaCl_3$ was not efficient providing low yields of **2a**,**b**. The isomeric acyclic dimers **3a**,**b** were usually formed as major products in these reactions. Among the studied Lewis acids, the best results were obtained with $SnCl_4$; in this case cyclohexane **2a** was formed in ca. 80% yield. The presence of a bromine atom in aromatic substituent, as it is in **1c**, had no significant effect on the reaction outcome. Further variations of the reaction conditions (solvent, temperature, duration, Lewis acid loading) disclosed that this cyclodimerization was the most efficient when it proceeded in CH_3NO_2 at 50−55 °C in the presence of 120−200 mol % of $SnCl_4$. Thus, the utilization of more than stoichiometric amounts of Lewis acid was caused by its competitive binding to methoxy groups or other donors of an electron pair in an aromatic substituent.

We have found that the occupation of *ortho*-positions in aromatic ring is not a necessary condition for cyclopropane-to-cyclohexane (3 + 3)-cyclodimerization. Thus, a series of cyclopropanes **1d−h**, which have a highly electron-donating NR_2 group at the *para*-position of the aromatic ring, was found to smoothly transform into the corresponding cyclohexanes **2d−h** in moderate to good yields (Table 2). For cyclopropanes **1f−h** the utilization of $SnCl_4$ led to low yields of **2**, whereas $TiCl_4$ was employed efficiently. For all compounds except **1g**, which decomposed partially under reaction conditions, the corresponding dimers were obtained in ca. 80% yields.

The cyclopropane-to-cyclohexane (3 + 3)-cyclodimerization proceeded with excellent diastereoselectivity: according to the NMR data, the cycloadducts **2a−h** were formed as single diastereomers. In comparison to ^1H and ^{13}C NMR spectra of the parent cyclopropanes **1a−h**, the corresponding spectra of dimeric products **2a−h** were characterized by a low-field shift of resonances of alicyclic protons and carbon atoms. Additionally, ^1H NMR spectra of **2a−h** revealed the full coupling patterns for the ABX-system of the protons involving into two equivalent CH_2-CH fragments, namely ^2J of ca. 14 Hz and ^3J of ca. 3−5 and 13−14 Hz, which are also characteristic for saturated common rings.

The restricted rotation of aryl groups with bulky *ortho*-substituents in cyclohexanes **2a**,**b** led to magnetic non-equivalency for protons of the aromatic rings and methoxy groups which gave at room temperature two and three different signals, respectively (for **2a**, see Figure 1). Variable-temperature ^1H NMR study revealed that the coalescence of signals of aromatic protons was achieved at 323 K. Using the approximate Eyring equation, we estimated the energy barrier for rotation of aryl groups in this molecule to be ca. 70 kJ/mol.

Structure of **2d** was unambiguously proved by single-crystal X-ray analysis.[66,67] These data showed that **2** has a *cis*-arrangement of aromatic substituents and the central six-membered ring in the molecule adopts a twist-conformation with quasi-equatorial location of the aromatic substituents (Figure 2). The similarity in NMR spectra for all isolated compounds **2** as well as single-crystal X-ray data for **2i** (Figure 3, see below) allowed us to conclude that all cyclohexanes **2** were formed in this (3 + 3)-cyclodimerization as *cis*-isomers only.

The exclusive formation of *cis*-isomers of **2** seems to be quite unusual as *trans*-1,4-disubstituted cyclohexanes are well-known to be more preferable.[1,2] Actually, our ab initio calculations at HF/6-31G level showed that *cis*-**2b** in a twist-conformation has 6.9 kj/mol lower energy than the most stable chair conformer

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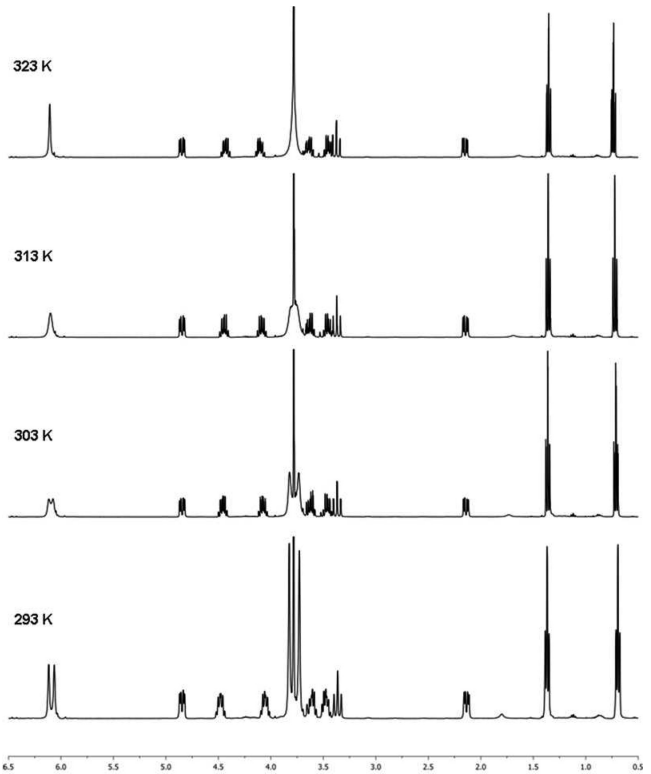


Figure 1. Temperature dependence of 600 MHz ^{1}H NMR spectrum of **2a** in $CDCl_3$.

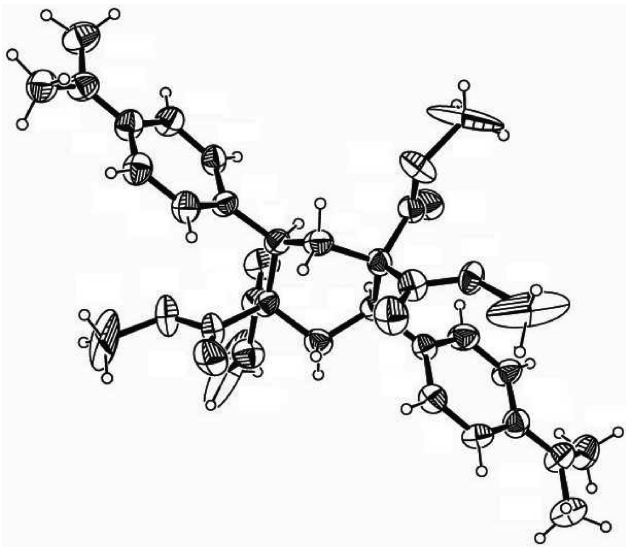


Figure 2. Single crystal X-ray structure of **2d**.

of *trans*-**2b**. This trend, namely the preference of *cis*-isomer over *trans*-isomer, is observed in the series of various tetramethyl 2,5-bis(aryl)cyclohexane-1,1,4,4-tetracarboxylates.[67] It can be related to larger steric repulsions between ester groups and aryl substituents in the chair-conformation of *trans*-**2b** vs those in the twist-conformation of *cis*-**2b**. Similarly, significant steric hindrances can occur in the chairlike transition state leading to *trans*-**2b**, while twist-like transition state minimalizes them that could be a possible reason for the exclusive formation of *cis*-**2b**.

Structures of acyclic dimers **3** were established by analysis of NMR spectra. In particular, the ^3J coupling constants for

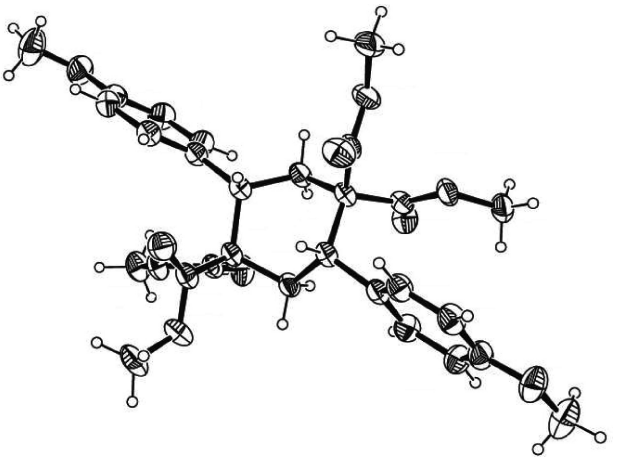
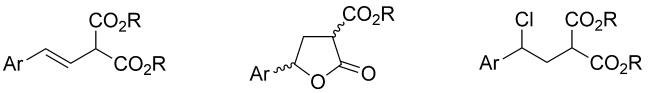


Figure 3. Single crystal X-ray structure of **2i**.

C(Ar)H═CH− fragment are ca. 17 Hz, confirming the formation of **3** as *E*-isomers exclusively.

We suggest that the cyclopropane-to-cyclohexane (3 + 3)-cyclodimerization proceeds by a mechanism which is shown in Scheme 2. The coordination of strongly activating Lewis acid to ester group(s) leads to the cyclopropane C(1)−C(2) bond heterolysis affording zwitterion **A**. Its formation is in accordance with results of a previous study of 2-arylcyclopropane-1,1-dicarboxylate reactivity in the absence of highly nucleophilic agents.[63] A valid argument toward formation of **A** is an isolation of side products **4** and **5** under milder reaction conditions. Indeed, it was previously found that γ-aryl-γ-butyrolactones **5** were formed from D−A cyclopropanes in the presence of strongly activating Lewis acids as 1:1 mixtures of two diastereomers,[68] which is consistent with the intermediate formation of zwitterion **A**. Similarly, styrylmalonates **4** are the result of D−A cyclopropane isomerization by a stepwise mechanism, where the first step is the Lewis acid-induced heterolysis of the C−C bond in the small ring.[68] Additionally, polymeric products, which we observed under nonoptimized reaction conditions, are formed via zwitterion **A** too.



4 **5** **6**

The second step is the attack of nucleophilic center of one zwitterionic species **A** onto the electrophilic center of another one affording new zwitterion **B**. The formation of **B** is supported by isolation of dimeric alkenes **3** either together with **2** or as single products under nonoptimized reaction conditions (Table 1). Therefore, malonic anion fragment in intermediate **B** has a dual reactivity. As a nucleophile, it interacts with benzylic cation to yield cyclohexane **2** (path ***b***). As a base, it captures a proton from δ-position leading to acyclic dimer **3** (path ***c***). A similar dual behavior of this moiety was previously found for the D−A cyclopropanes isomerization into styrylmalonates.[68]

Cyclopropane-to-cyclohexane (3 + 3)-cyclodimerization is a conceptually new efficient approach to the symmetrically substituted cyclohexane derivatives. Moreover, to date there have not been efficient diastereoselective approaches to *cis*-1,4-diarylcyclohexanes.[69] Therefore, cyclopropane-to-cyclohexane (3 + 3)-cyclodimerization followed by appropriate transformations

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Scheme 2. Proposed Mechanism for Cyclopropane-to-Cyclohexane (3 + 3)-Cyclodimerization

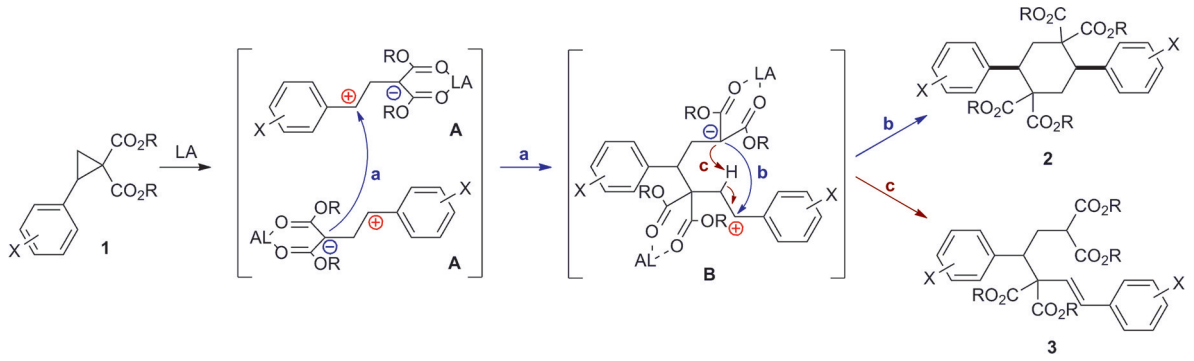
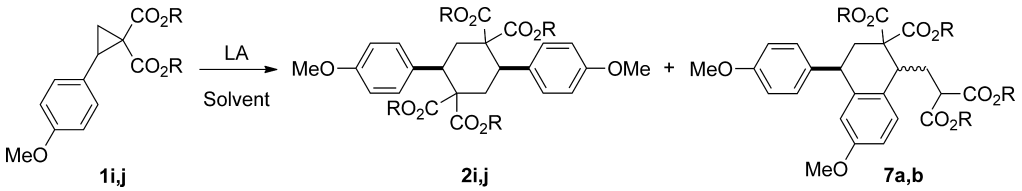


Table 3. Optimization of Reaction Conditions for (3 + 3)-Cyclodimerization of 2-(4-Methoxyphenyl)cyclopropane-1,1-dicarboxylates 1i,j



entry	R	Lewis acid (mol %)	solvent	T (°C)	time (h)	yield of **2** (%)	yield of **7** (%) (*trans*/*cis* ratio)
1	Me	$TiCl_4$ (120)	CH_3NO_2	−25	23		*a*
2	Me	$TiCl_4$ (120)	CH_3NO_2	−5 → 0	2		*b*
3	Me	$TiCl_4$ (200)	CH_3NO_2	5	2	45	*c*
4	Me	$SnCl_4$ (100)	CH_3NO_2	50	3		49 (93:7)
5	Me	$SnCl_4$ (100)	CH_2Cl_2	−20[d]	24		90 (95:5)
6	Me	$SnCl_4$ (100)	C_6H_6	20	24		81 (91:9)
7	Me	$SnCl_4$ (150)	C_6H_6	40	2		59 (90:10)[e]
8	Me	$BF_3{\cdot}OEt_2$ (100)	CH_3NO_2	50	3		*c*
9	Et	$SnCl_4$ (100)	CH_3NO_2	50	3		87 (91:9)
10	Et	$SnCl_4$ (100)	CH_3NO_2	20	30	38	49 (95:5)
11	Et	$SnCl_4$ (200)	CH_3NO_2	20	22	40	
12	Et	Me_3SiOTf (100)	CH_3NO_2	50	3		*c*
13	Et	$AlCl_3$ (240)	CH_3NO_2	−25[d]	70	62	

[a]Chloride **6** was only formed in 80% yield. [b]Lactone **5** was only formed in 70% yield. [c]Oligomeric and polymeric ring-opening products were only formed. [d]Afterward the reaction mixture was allowed to warm to room temperature for 0.5 h. [e]Compound **8** was obtained as a side product in 30% yield (see Scheme 3 and related discussion).

of **2** into other cyclohexane derivatives provide convenient access to these systems. The formed 2,5-diarylcyclohexane-1,1,4,4-tetracarboxylates of type **2** are of particular interest as direct precursors of liquid crystalline compounds[70] or anticholesteremic agents.[71]

(3 + 3)-Cyclodimerization of 2-(4-Methoxyphenyl)-cyclopropane-1,1-dicarboxylates (I+I and I+II Paths). Other substrates, which contain a phenyl group with a strongly electron-donating substituent at the *para*-position and can undergo (3 + 3)-cyclodimerization via the **I+I** path, are 4-methoxyphenylcyclopropanes **1i,j**. A short survey of Lewis acids indicated that $TiCl_4$, which was a favorable initiator for dimerization of 4-(dialkylamino)phenyl-containing D−A cyclopropanes **1f−h**, was inefficient for dimerization of 4-methoxyphenyl D−A cyclopropanes **1i,j**. Thus, the treatment of **1i** with $TiCl_4$ in CH_3NO_2 at −25 °C only afforded chloride **6**, the product of $TiCl_4$-induced cyclopropane ring-opening[61,68,72] (Table 3, entry 1). The reverse addition of **1i** to a $TiCl_4$ solution at −5 to 0 °C yielded γ-butyrolactone **5** as a single product (entry 2). Gratifyingly, the treatment of **1i** with $TiCl_4$ at 5 °C allowed us to obtain the product of the (3 + 3)-cyclodimerization **2i** in 45% yield (entry 3). Further increase in reaction temperature did not result in better yield of **2i** due to the significant formation of oligomeric and polymeric ring-opening products.

The utilization of $SnCl_4$ unexpectedly resulted in alteration of the reaction pathway from **I+I** to **I+II** (3 + 3)-cyclodimerization. Thus, the treatment of **1i** with 1 equiv of $SnCl_4$ in various solvents produced **7a** in moderate to good yields (entries 4−6). The careful optimization of reaction conditions for dimerization of **1j** showed that $SnCl_4$ (1 equiv) induced the formation of a tetraline **7b** in high yield when the reaction was performed in CH_3NO_2 under moderate heating (entry 9). However, when the same reaction was carried out at room temperature, both tetraline **7b** and cyclohexane **2j** were obtained in ca. 5:4 ratio (entry 10). The increase in a Lewis acid loading allowed for suppression of **7b** formation but did not increase yield of cyclohexane **2j** (entry 11). The utilization of $BF_3{\cdot}Et_2O$ and TMSOTf did not lead to both **2** and **7** affording polymeric products only. Oppositely, $AlCl_3$ was found to furnish (3 + 3)-cyclodimer **2j** in the reasonable yield (entry 13).

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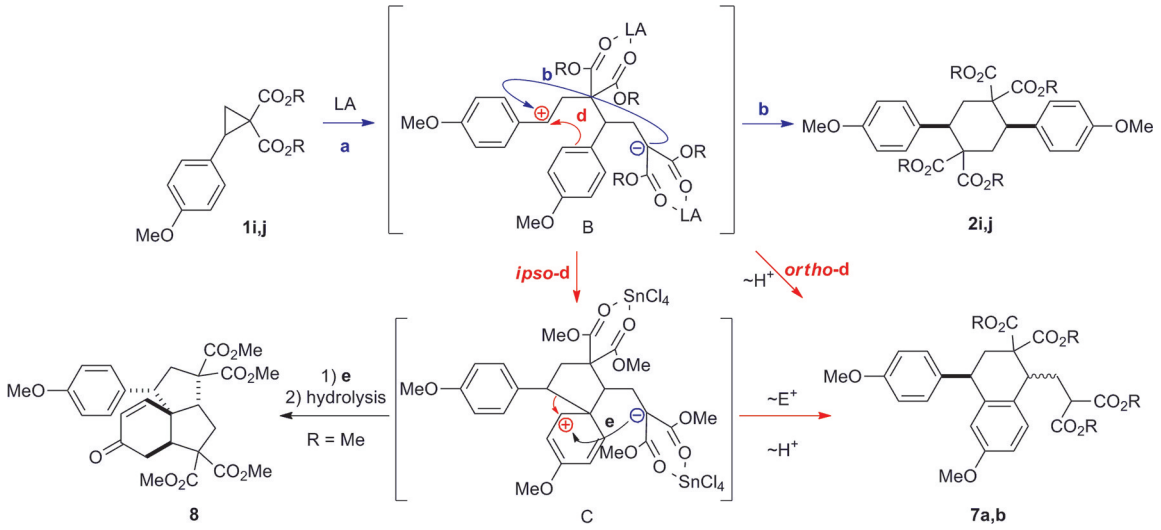
Scheme 3. Proposed Mechanism for Cyclodimerizations of 4-Methoxyphenyl-Derived D−A Cyclopropanes 1i,j



Structures of **2i,j** were assigned by comparison of their spectral data with those for **2a−h** and proved unambiguously by single crystal X-ray analysis of **2i** (Figure 3).[66,67] Structures of **7a,b** were determined as discussed below.

The mechanism that can be proposed for the (3 + 3)-cyclodimerizations of **1i,j** is shown in Scheme 3. The formation of zwitterion **B** in the case of the cyclodimerization through **I+II** path is the same as that for the cyclopropane-to-cyclohexane dimerization (**I+I** path). The coupling between benzylic cation and malonate moiety in **B** (path **b** in Scheme 3) leads to cyclohexane **2**, whereas electrophilic substitution at *ortho*-position of an aromatic fragment furnishes tetraline **7** (path ***ortho*-d**). The transformation of **B** into **7** can also proceed via initial electrophilic attack onto the activated *ipso*-position of aromatic group resulting in intermediate **C** (path ***ipso*-d**) followed by migration of electrophile to *ortho*-position. The *ipso*-intermediate of **C** type was recently proposed for dimerization of the indole-derived D−A cyclopropanes.[73] The competition between *ortho*- and *ipso*-attack is well-known and regulated by a balance of steric and electronic factors.[1,2] The high electron-donating ability of *para*-methoxy group makes more preferable the electrophilic attack to *ipso*-position. Oppositely, the higher steric repulsions for *ipso*-attack make *ortho*-attack more preferable. We confirmed the possibility of *ipso*-attack by the isolation of unusual side-product **8** (Scheme 3) containing angularly fused benzo[c]pentalene scaffold. It was formed in 30% yield when dimerization of **1i** was performed in benzene in the presence of 1.5 equiv of $SnCl_4$ (Table 3, entry 7).

Compound **8** was formed as a single diastereomer. Its structure was assigned by 1D and 2D COSY, HETCOR, HMBC, and NOESY NMR spectral data. The following criteria were used to elucidate the structure of **8**. (1) In ^1H NMR spectrum three ABX systems correspond to the protons of three isolated $CH-CH_2$ fragments, which, according to the HMBC, are connected to two different $C(CO_2Me)_2$ groups in such a way that one of the $CHCH_2$ fragments is located between two $C(CO_2Me)_2$ groups. (2) The presence of a cyclohexenone moiety is easily determined by characteristic signals at δ_C 154.9, 127.8, and 195.8 ppm assigned to three consecutive carbon atoms of CH=CHC=O conjugated system. (3) In the aromatic region, only one set of signals for the *p*-methoxyphenyl substituent is observed. The relative stereochemistry of **8** was deduced from its NOESY spectrum. The central benzo[*c*]pentalene core has the only possible relative configuration, whereas aromatic substituent at C(1) atom is arranged in a *trans*-position relative to the cyclohexenone motif (Figure 4).

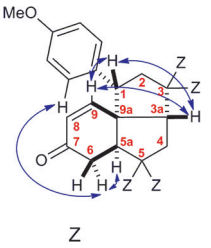


Figure 4. Representative NOE responses for **8**.

Cyclopropane-to-Tetrahydronaphthalene (3 + 3)-Cyclodimerization (I+II Path). Cyclopropanes **1k,l** and **1m,n** containing 3,4-dialkoxyphenyl and thienyl groups, respectively, were found to readily give cyclic dimers **7c−f** via **I+II** path of (3 + 3)-cyclodimerization (Table 4). The most efficient promoter for these reactions was found to be $SnCl_4$. The increase in donating ability of aryl substituent enhanced the tendency to polymerization of initial cyclopropanes **1k−n**. To inhibit the polymerization, we added Lewis acid to a cooled solution of a cyclopropane and then stirred the reaction mixture under cooling (for **1k,n**) or slowly heated it to temperature specified in Table 4 (for **1l,m**).

All structural assignments for **7a−f** were made from analysis of ^1H and ^{13}C NMR data. The presence of a benzannulated central motif in the molecules of **7a−f** was confirmed by a new signal arising for a quaternary carbon atom of the aromatic ring instead of the signal of a methine carbon. The ^1H NMR spectra revealed resonances of two independent systems which are formed by the protons of CH_2-CH fragment of a new six-membered ring and $CH-CH_2-CH$ aliphatic side chain. The products **7c,d** were formed as single regioisomers via electrophilic attack onto C(6) rather than C(2) atom of arene ring. Compounds **7a−f** were formed as mixtures of two diastereomers. The stereochemical assignments were

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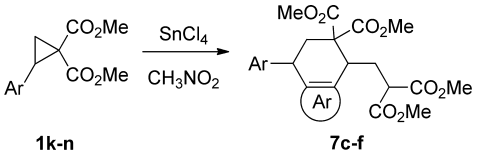
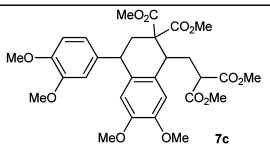
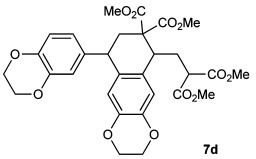
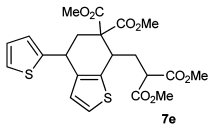
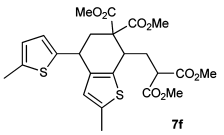
Table 4. (3 + 3)-Cyclodimerization of D−A Cyclopropanes 1k−n via I+II Path



1k-n **7c-f**

entry	1	Ar	mol % of $SnCl_4$	T (°C)	t (h)	7	yield	*trans* : *cis* ratio
1	**1k**	3,4-$(MeO)_2C_6H_3$	110	–25[a]	22[a]	 **7c**	71	55:45
2	**1l**	3,4-$(OCH_2CH_2O)C_6H_3$	150	–40 → 20 for 3 h		 **7d**	40	57:43
3	**1m**	2-Th	120	–20 → 50 for 0.5 h[b]		 **7e**	78	71:29
4	**1n**	5-Me-2-Th	125	–20[a]	6[a]	 **7f**	54	56:44

[a]Afterwards the reaction mixture was allowed to warm to room temperature for 0.5 h. [b]Reaction mixture was kept at 50 °C for additional 0.5 h.

accomplished on the basis of NOE experiments for the major isomer of **7e** (Figure 5). According to these data, the major

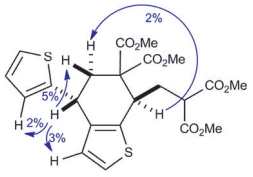


Figure 5. Representative NOE responses for the *trans*-**7e**.

isomers of **7a−f** have a *trans*-arrangement of aryl and 2,2-bis(alkoxycarbonyl)ethyl substituents.

The mechanism of (3 + 3)-cyclodimerization of **1k−n** via the **I+II** path was described above using the example of **1i** dimerization (Scheme 3). It is noteworthy that cyclopropanes **1k,l** have an additional donor alkoxy group at the C(3) position. This group facilitates electrophilic attack onto both *ortho*-positions (path ***ortho-d***). Thus, the *ipso*-attack (path ***ipso*-d**) seems to be redundant for the explanation of the obtained results in this case. Additionally, the *m*-alkoxy group introduces desymmetrization into the arene substituent leading to the possibility of formation of two regioisomers during the dimerization of these substrates. However, the cyclodimerization in this case proceeded with excellent regioselectivity exclusively producing regioisomers **7c,d** via electrophilic substitution at the 6-position of the aryl ring.

A fragment of 1-aryl-1,2,3,4-tetrahydronaphthalenes is present in many lignans including biologically active ones.[74] Two of them (etoposide and teniposide) are now being used as anticancer drugs.[75] Therefore, the (3 + 3)-cyclodimerization of D−A cyclopropanes via path **I+II** opens broad possibilities for both synthetic and medicinal chemists.

Cyclopropane-to-Dihydroanthracene (3 + 3)-Cyclodimerization (II+II Path). (3,4,5-Trimethoxyphenyl)-cyclopropane **1o** was found to be an excellent model for (3 + 3)-cyclodimerization via the **II+II** path leading to dihydroanthracene **9a** in good yield (Scheme 1, Table 5) due to the efficient activation of *ortho*-positions in an aromatic substituent. The optimization of reaction conditions demonstrated that this transformation proceeded efficiently at 50−60 °C in the presence of 2 equiv of $SnCl_4$ (entry 3). The variation of reaction temperature or Lewis acid loading resulted in diminished yield of **9a**. Thus, utilization of 1.2 equiv of $SnCl_4$ afforded the target product **9a** in 65% yield together with the corresponding tetrahydronaphthalene **7g** in 21% yield (entry 2). The catalytic version of this transformation can be performed using moderately activating $Sn(OTf)_2$ (entry 4). Moreover, dihydroanthracene **9a** was obtained in this case in higher yield and diastereoselectivity in comparison with $SnCl_4$-induced reactions. Cyclopropanes **1p,q**, containing 3,5- and 2,3-dimethoxyphenyl groups, respectively, as donor substituents, also produced dihydroanthracenes **9b,c** when activated with 1−1.5 equiv of $SnCl_4$ or catalytic amounts of $Sn(OTf)_2$. Diastereoselectivity of (3 + 3)-cyclodimerization of **1o,p** was

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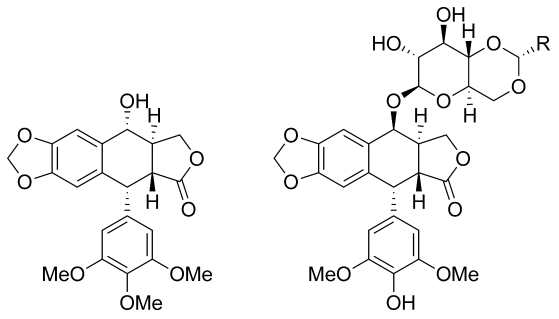
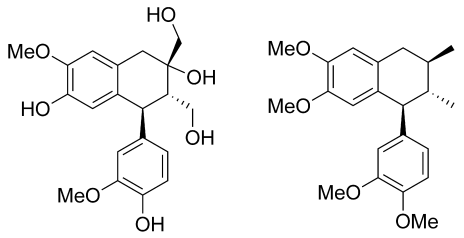




poor: anthracenes **9a,b** were formed as mixtures of two diastereomers in a slight excess of *trans*-isomer. In contrast, dimerization of D−A cyclopropane **1q**, possessing a methoxy group in the *ortho*-position, proceeded with high diastereoselectivity affording mostly *trans*-**9c**.

The mass spectral data unambiguously proved the dimeric composition of **9a−c**, while NMR data evidenced a symmetric structure of compounds synthesized. ^{1}H NMR spectra completely revealed coupling patterns for a system of the protons of two identical $CHCH_2CH$ fragments. In the ^{13}C NMR spectra, a new signal of a quaternary carbon atom was observed in the aromatic region instead of resonance of a methine carbon that confirmed additional substitution in aromatic ring. Furthermore, single-crystal X-ray data were obtained for *trans*-**9a** and *trans*-**9c** providing unambiguous proof for dihydroanthracene scaffold.[67]

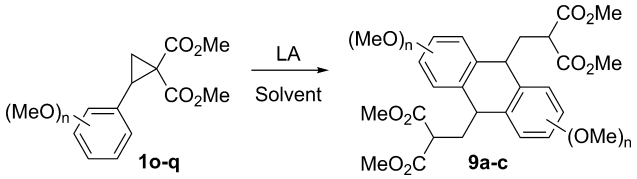
The construction of dihydroanthracene core of **9** from **1** consists in formation of two C−C bonds by two consecutive S_EAr reactions (Scheme 4). It can be achieved by Lewis acid-induced cyclopropane ring-opening with formation of zwitterion **A** followed by its attack onto the starting cyclopropane **1** containing highly nucleophilic aromatic substituent[76] (path **f**, Scheme 4). Then Lewis acid induces opening of the second cyclopropane into zwitterion **D**. The intramolecular attack of the nucleophilic aromatic ring by electrophilic center in **D** (path **g**, Scheme 4) completes the transformation.

Despite significant attention paid to various 9,10-dihydroanthracenes that is reflected to multiple publications dealing with their chemical and biological properties, compounds of type **9** have not been studied yet mainly due to the complexity of their synthesis. Therefore, this method of (3 + 3)-cyclodimerization of the D−A cyclopropanes can be useful as an efficient approach to these compounds.

Overall Mechanistic Scheme for (3 + 3)-Cyclodimerizations of the D−A Cyclopropanes. Therefore, D−A cyclopropanes with electron-abundant aromatic groups as donor substituent revealed an ability to undergo three types of (3 + 3)-cyclodimerization affording cyclohexanes **2**, tetrahydronaphthalenes **7**, or 9,10-dihydroanthracenes **9**. The putative rationale of their formation is given above. Nevertheless, some mechanistic aspects should be specified.

The first question is a sequence of C−C bonds formation in tetralines **7** via the **I+II** path. Above we postulated that the first C−C bond is formed by the coupling of malonate anion with benzyl cation of two zwitterions **A** furnishing intermediate **B** and the formation of the second C−C bond is a result of S_EAr reaction. However, the reverse sequence can be hypothesized, which involves initial S_EAr reaction followed by coupling of malonate anion with benzyl cation. For dimerization of **1i,j** the latter sequence is not appropriate as in these compounds arene ring is activated to electrophilic substitution at the *ortho*-position to methoxy group rather than to the *ortho*-position to cyclopropyl moiety, while actually, the substitution proceeds at the *ortho*-position to the cyclopropyl ring. Another argument toward reaction path presented in Scheme 3 is the formation of **8** that is in accordance with intermediate **B** generation. Moreover, S_EAr reaction should be accompanied by a proton migration from arene to malonate moiety what prevents participation of a latter nucleophilic site in further transformation. Therefore, we are inclined to the mechanism of tetraline **7** formation wherein anion−cation coupling precedes S_EAr process rather than reverse sequence.

Table 5. (3 + 3)-Cyclodimerization of D−A Cyclopropanes 1o−q via II+II Path



entry	**1**	$(MeO)_n$	Lewis acid (mol %)	solvent	*T* (°C)	time (h)	yield of **9** (%)	*trans*/*cis* ratio
1	**1o**	3,4,5-$(MeO)_3$	$SnCl_4$ (5)	CH_3NO_2	50	3		
2	**1o**	3,4,5-$(MeO)_3$	$SnCl_4$ (120)	CH_3NO_2	60	3	65[a]	54:46
3	**1o**	3,4,5-$(MeO)_3$	$SnCl_4$ (200)	CH_3NO_2	50	1	77	58:42
4	**1o**	3,4,5-$(MeO)_3$	$Sn(OTf)_2$ (10)	CH_3NO_2	50	4.5	88	63:37
5	**1p**	3,5-$(MeO)_2$	$SnCl_4$ (150)	CH_3NO_2	50	3	65	55:45
6	**1p**	3,5-$(MeO)_2$	$Sn(OTf)_2$ (10)	CH_3NO_2	60	3	80	64:36
7	**1q**	2,3-$(MeO)_2$	$SnCl_4$ (100)	CH_3NO_2	55	2	31	>95:5
8	**1q**	2,3-$(MeO)_2$	$Sn(OTf)_2$ (10)	CH_3NO_2	100	8	61	90:10

[a]Tetrahydronaphthalene **7g** (dr 72:28) was also isolated in 21% yield.

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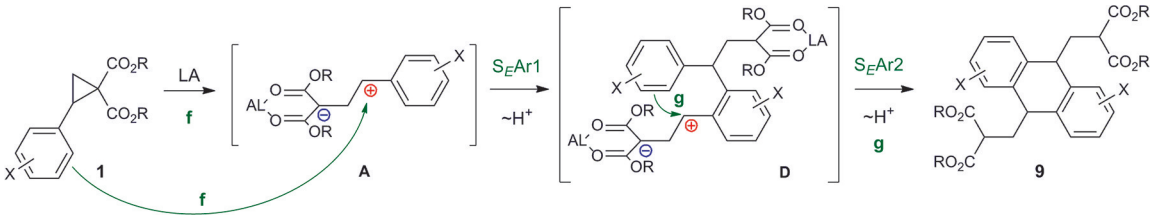
Scheme 4. Proposed Mechanism for Aryl-Substituted Cyclopropane-to-Dihydroanthracene (3 + 3)-Cyclodimerization



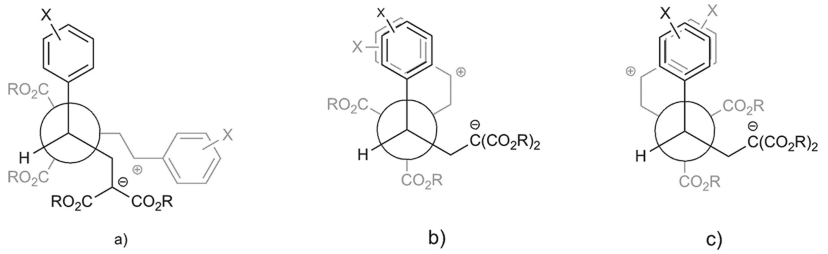
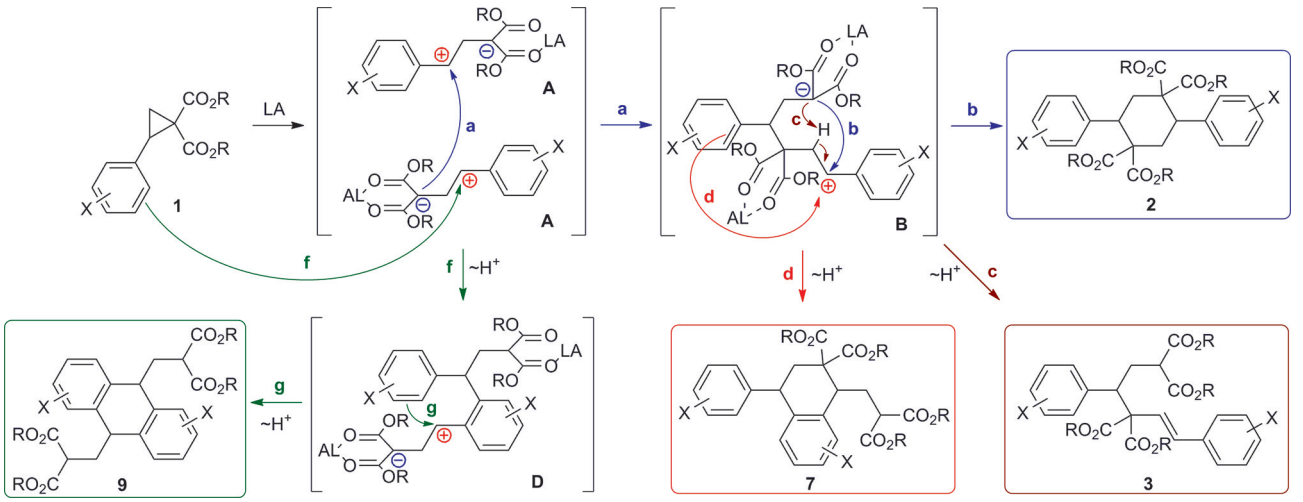


Figure 6. Conformations of intermediate **B** leading to formation of (a) *cis*-**2**, (b) *trans*-**7**, and (c) *cis*-**7**.

Scheme 5. Overall Mechanistic Scheme Including Three (3 + 3)-Cyclodimerizations of D−A Cyclopropanes 1



The second question is the competition between formation of cyclohexanes **2** and tetralines **7** from the same intermediate **B**. This dual behavior can be explained by means of analysis of the reactive conformations of intermediate **B** which are shown in Figure 6. Eclipsed twist-like conformation **a** is a direct precursor for the transition state leading to cyclohexane **2** with a *cis*-arrangement of aromatic groups. Meanwhile, the staggered conformations **b** and **c** favored for *trans*-**7** and *cis*-**7** construction, respectively, can be stabilized by interaction of the electron-depleted benzyl cation and the electron-enriched second aromatic ring resulting in a $\pi-\pi^*$ donor−acceptor complex.[62,73] In this case, chemoselectivity is provided by the close proximity of two reaction centers, namely benzyl cation and nucleophilic *ortho*-position of aryl substituent. Despite the higher nucleophilicity of the malonyl anion,[77] its attack in this case is not competitive. The same preference of nucleophilic site at the *ortho*-position of an aromatic substituent rather than malonyl anion was recently found for heteroaryl-substituted D−A cyclopropanes.[58−62]

One more possibility should be analyzed, which involves initial formation of one cycloadduct followed by its rearrangement into another product. Similar transformations were found recently in reactions of D−A cyclopropanes with enols[78,79] and aldehydes.[51] For example, cyclopropanes **1i,j** form either cyclohexanes **2i,k** or tetrahydronaphthalenes **7a,b** depending on the reaction conditions. We checked the possibility of rearrangement of one cyclodimer into another one. For this purpose, we treated a solution of cyclohexane **2i** in CH_3NO_2 with 5 equiv of $SnCl_4$ or $TiCl_4$ and heated the reaction mixture under reflux for 2−24 h. Similarly, tetrahydronaphthalene **7a** was treated with 3 equiv of $SnCl_4$ in benzene and heated at 50 °C for 5 h. No interconversion of **2i** and **7a** was observed according to the NMR spectra. Similarly, we have not found conversion of **7** into dihydroanthracene **9**. Therefore, we believe that cyclodimers **2**, **7**, and **9** are formed along three independent paths **a**−**b**, **a**−**d**, and **f**−**g**, respectively. The overall scheme of (3 + 3)-cyclodimerizations of the D−A cyclopropanes can be represented in the following way (Scheme 5).

On the whole, a balance of numerous factors, such as substrate nature, activating ability of a Lewis acid, temperature, solvent, etc., controls the outcome of the (3 + 3)-cyclodimerization. The further studies on the reaction mechanism in detail are now in progress.

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CONCLUSION

In the present research, we demonstrated for the first time the possibility of the Lewis acid-induced (3 + 3)-cyclodimerization of 2-(hetero)arylcyclopropane-1,1-dicarboxylates with formation of three different types of six-membered cyclic systems. In these processes three reaction centers of a D−A cyclopropane molecule can be involved, namely C(1) atom of small ring and *ortho*-carbon atom of an aromatic substituent as nucleophilic sites and C(2) atom of cyclopropane as an electrophilic site. As a result, the facile synthetic approach to 1,4-diarylcyclohexanes, 1-aryl-1,2,3,4-tetrahydronaphthalenes, and 9,10-dihydroanthracenes from easily available reagents using inexpensive promotor has been developed. The (3 + 3)-cyclodimerization leading to 1,4-diarylcyclohexanes proceeded with excellent diastereoselectivity furnishing *cis*-isomer excusively, while diastereoselectivity of 1-aryl-1,2,3,4-tetrahydronaphthalenes and 9,10-dihydroanthracenes construction varied from moderate to high with the predominante formation of *trans*-isomers. To provide chemoselectivity of the processes, the careful optimization of reaction conditions was undertaken which resulted in the development of procedures affording these three types of products of (3 + 3)-cyclodimerization in good yields.

EXPERIMENTAL SECTION

General Procedure for the Synthesis of Cyclopropanes 1a,b,d−q.[64,65] To a stirred suspension of NaH (0.24 g, 6 mmol) in dry DMSO (10 mL) was added trimethylsulfoxonium iodide (1.32 g, 6 mmol) in a single portion at room temperature. Vigorous evolution of hydrogen lasted ca. 10 min, after which the reaction mixture was stirred for an additional 25 min. Then a solution of alkylidenemalonate (5 mmol) in dry DMSO (2 mL) was added in a single portion. The resulted mixture was stirred under the conditions specified, poured into H_2O−ice (10 mL), and extracted with diethyl ether (5 × 5 mL). The combined organic layers were washed with water (5 × 5 mL), dried with Na_2SO_4, and concentrated in vacuo. Cyclopropanes were purified by column chromatography (SiO_2, eluent: diethyl ether).

Dimethyl 2-(4-Piperidinophenyl)cyclopropane-1,1-dicarboxylate (1f). Compound **1f** was synthesized from dimethyl 2-(4-piperidinobenzylidene)malonate (**10a**), reaction time 1 h, and isolated as an orange oil (1.06 g, 67%): R_f 0.48 (diethyl ether/hexane 1:1); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.52−1.57 (m, 2H, CH_2), 1.65−1.69 (m, 4H, CH_2), 1.70 (dd, ^2J = 5.0 Hz, ^3J = 9.5 Hz, 1H, CH_2), 2.15 (dd, ^2J = 5.0 Hz, ^3J = 7.9 Hz, 1H, CH_2), 3.08−3.12 (m, 4H, CH_2N), 3.15 (dd, ^3J = 7.9 Hz, ^3J = 9.5 Hz, 1H, CH), 3.37 (s, 3H, CH_3O), 3.76 (s, 3H, CH_3O), 6.82 (d, ^3J = 8.3 Hz, 2H, CH, Ar), 7.05 (d, ^3J = 8.3 Hz, 2H, CH, Ar); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 19.3 (CH_2), 24.2 (CH_2), 25.8 (2 × CH_2), 32.6 (CH), 37.1 (C), 50.4 (2 × CH_2N), 52.3 (CH_3O), 52.7 (CH_3O), 116.0 (2 × CH, Ar), 124.5 (C, Ar), 129.1 (2 × CH, Ar), 151.4 (C, Ar), 167.2 (CO_2Me), 170.4 (CO_2Me); IR (Nujol, cm^{-1}) 2952, 2865, 2820, 1740, 1619, 1524, 1455, 1390, 1340, 1290, 1250, 1184, 1145, 1035, 930, 840, 781, 740; GC−MS *m*/*z* 318 (27), 317 (100) $[M]^+$, 316 (57), 258 (31), 198 (88), 142 (24), 130 (30), 115 (83), 59 (34). Anal. Calcd for $C_{18}H_{23}NO_4$: C, 68.12; H, 7.30; N, 4.41. Found: C, 67.82; H, 7.14; N, 4.61.

Dimethyl 2-(2,3-Dihydrobenzo[*b*][1,4]dioxin-6-yl)-cyclopropane-1,1-dicarboxylate (1l). Compound **1l** was synthesized from dimethyl 2-[(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)-methylene]malonate (**10b**), reaction time 1 h, and isolated as a white solid (1.12 g, 77%): mp 92−93 °C; R_f 0.52 (diethyl ether/hexane ether 1:2); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.65 (dd, ^2J = 5.1 Hz, ^3J = 9.3 Hz, 1H, CH_2), 2.05 (dd, ^2J = 5.1 Hz, ^3J = 8.0 Hz, 1H, CH_2), 3.08 (dd, ^3J = 8.0 Hz, ^3J = 9.3 Hz, 1H, CH), 3.40 (s, 3H, CH_3O), 3.72 (s, 3H, CH_3O), 4.16 (s, 4H, OCH_2CH_2O), 6.61 (dd, ^3J = 8.4 Hz, ^4J = 2.0 Hz, 1H, CH, Ar), 6.62 (d, ^4J = 2.0 Hz, 1H, CH, Ar), 6.70 (d, ^3J = 8.4 Hz, 1H, CH, Ar); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 19.3 (CH_2), 32.1 (CH), 37.0 (C), 52.3 (CH_3O), 52.7 (CH_3O), 64.2 (CH_2O), 64.3 (CH_2O), 116.9 (CH, Ar), 117.3 (CH, Ar), 121.4 (CH, Ar), 127.6 (C, Ar), 142.9 (C, Ar), 143.2 (C, Ar), 167.0 (CO_2Me), 170.2 (CO_2Me); IR (Nujol, cm^{-1}) 3450, 2975, 2895, 1735, 1630, 1593, 1518, 1445, 1380, 1290, 1220, 1138, 1080, 940, 897, 828, 780, 710; GC−MS *m*/*z* 292 (52) $[M]^+$, 232 (51), 228 (82), 200 (21), 179 (59), 173 (100), 117 (30), 89 (57), 78 (29), 59 (70). Anal. Calcd for $C_{15}H_{16}O_6$: C, 61.64; H, 5.52. Found: C, 61.79; H, 5.75.

Dimethyl 2-(3,5-Dimethoxyphenyl)cyclopropane-1,1-dicarboxylate (1p). Compound **1p** was synthesized from dimethyl 2-(3,5-dimethoxybenzylidene)malonate (**10c**), reaction time 1 h, and isolated as white solid (0.98 g, 67%): mp 69−70 °C; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.68 (dd, ^2J = 5.1 Hz, ^3J = 9.2 Hz, 1H, CH_2), 2.10 (dd, ^2J = 5.1 Hz, ^3J = 8.0 Hz, 1H, CH_2), 3.13 (dd, ^3J = 8.0 Hz, ^3J = 9.2 Hz, 1H, CH), 3.41 (s, 3H, CH_3O), 3.71 (s, 6H, 2 × CH_3O), 3.74 (s, 3H, CH_3O), 6.26 (br.d, ^4J = 2.0 Hz, 1H, CH, Ar), 6.28 (d, ^4J = 2.0 Hz, 2H, 2 × CH, Ar); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 19.4 (CH_2), 32.6 (CH), 37.1 (C), 52.4 (CH_3O), 52.8 (CH_3O), 55.2 (2 × CH_3O), 99.6 (CH, Ar), 106.3 (2 × CH, Ar), 137.0 (C, Ar), 160.5 (2 × C, Ar), 167.0 (CO_2Me), 170.2 (CO_2Me); IR (Nujol, cm^{-1}) 2960, 2875, 1730, 1600, 1480, 1385, 1250, 1210, 1160, 1085, 1065, 940, 870, 840, 820, 775, 745. Anal. Calcd for $C_{15}H_{18}O_6$: C, 61.22; H, 6.16. Found: C, 61.13; H, 6.11.

Diethyl 2-(3-Bromo-2,4,6-trimethoxyphenyl)cyclopropane-1,1-dicarboxylate (1c). *N*-Bromosuccinimide (NBS, 0.10 g, 0.57 mmol) was added to a solution of diethyl 2-(2,4,6-trimethoxyphenyl)-cyclopropane-1,1-dicarboxylate (**1a**) (0.20 g, 0.57 mmol) in CH_2Cl_2 (6 mL) at −60 °C. The reaction mixture was slowly warmed to −20 °C and stirred at that temperature until **1a** was consumed (TLC monitoring). Then the reaction mixture was quenched at −20 °C with 10% aqueous K_2CO_3 (2 mL), warmed to room temperature, diluted with H_2O (10 mL), and extracted with CH_2Cl_2 (2 × 20 mL). The combined organic extracts were dried with $MgSO_4$, concentrated in vacuo, and purified by flash chromatography (eluent: hexane/ethyl acetate 3:1) to yield **1c** (223 mg, 91%) as a yellowish oil: R_f 0.42 (hexanes/ethyl acetate 2:1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.88 (t, ^3J = 7.1 Hz, 3H, CH_3), 1.24 (t, ^3J = 7.1 Hz, 3H, CH_3), 1.75 (dd, ^2J = 4.8 Hz, ^3J = 9.4 Hz, 1H, CH_2), 2.37 (dd, ^2J = 4.8 Hz, ^3J = 8.3 Hz, 1H, CH_2), 2.84 (dd, ^3J = 8.3 Hz, ^3J = 9.4 Hz, 1H, CH), 3.72 (s, 3H, CH_3O), 3.74 (s, 3H, CH_3O), 3.78−3.83 (m, 2H, CH_2O), 3.80 (s, 3H, CH_3O), 4.16−4.23 (m, 2H, CH_2O), 6.20 (s, 1H, CH, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.7 (CH_3), 14.1 (CH_3), 21.3 (CH_2), 25.2 (CH), 35.3 (C), 55.8 (CH_2O), 56.3 (CH_2O), 60.6 (CH_3O), 60.8 (CH_3O), 61.2 (CH_3O), 92.2 (CH, Ar), 97.9 (C, Ar), 110.6 (C, Ar), 156.4 (C, Ar), 158.1 (C, Ar), 159.7 (C, Ar), 167.3 (CO_2Et), 170.1 (CO_2Et); IR (Nujol, cm^{-1}) 2995, 2935, 2865, 1730, 1600, 1590, 1460, 1400, 1325, 1290, 1210, 1185, 1130, 1035, 920, 880, 810, 745. Anal. Calcd for $C_{18}H_{23}BrO_7$: C, 50.13; H, 5.38. Found: C, 50.04; H, 5.23.

General Procedure for the Lewis Acid-Induced Dimerization of Cyclopropanes 1a−q. Lewis acid ($AlCl_3$, $Sn(OTf)_2$, $ZnCl_2$) or a solution of Lewis acid ($SnCl_4$, $TiCl_4$) in dry solvent (1 mL) was added to a vigorously stirred solution of cyclopropane **1** containing molecular sieves 4 Å. The resulting mixture was kept under the conditions specified and poured into 10 mL of saturated aqueous $NaHCO_3$. After extraction with CH_2Cl_2 (3 × 10 mL), the combined organic fractions were washed with aqueous Trilon B (3 × 10 mL) and water (2 × 10 mL) and dried with Na_2SO_4. The solvent was evaporated under vacuum, and the residue was purified by column chromatography (SiO_2) to yield the desired product.

Tetraethyl *cis*-2,5-Bis(2,4,6-trimethoxyphenyl)cyclohexane-1,1,4,4-tetracarboxylate (2a). A solution of **1a** (350 mg, 1.0 mmol) in CH_3NO_2 (14 mL) was treated with $SnCl_4$ (280 mg, 0.13 mL, 1.1 mmol), and the resulting mixture was stirred at 55 °C for 3 h affording **2a** (292 mg, 83%) as a white foam: mp 153−154 °C; R_f 0.50 (dietyl ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.69 (t, ^3J = 7.1 Hz, 6H, 2 × CH_3), 1.37 (t, ^3J = 7.1 Hz, 6H, 2 × CH_3), 2.14 (dd, ^2J = 13.7 Hz, ^3J = 5.2 Hz, 2H, 2 × CH^aH), 3.36 (dd, ^2J = 13.7 Hz, ^3J = 13.6 Hz, 2H, 2 × CH^bH), 3.43−3.51 (m, 2H, OCH_2), 3.57−3.66 (m, 2H, OCH_2), 3.73 (s, 6H, 2 × OCH_3), 3.78 (s, 6H, 2 × OCH_3), 3.82 (s, 6H, 2 × OCH_3), 4.01−4.09 (m, 2H, OCH_2), 4.44−4.52 (m, 2H, OCH_2), 4.85 (dd, ^3J = 5.2 Hz, ^3J = 13.6 Hz, 2H, 2 × CH), 6.06 (br.s, 2H, 2 × CH, Ar), 6.12 (br.s, 2H, 2 × CH, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.4

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(2 × CH_3), 14.2 (2 × CH_3), 29.9 (2 × CH), 30.3 (2 × CH_2), 54.5 (2 × OCH_3), 55.3 (2 × OCH_3), 56.8 (2 × OCH_3), 58.6 (2 × C), 60.2 (2 × OCH_2), 61.5 (2 × OCH_2), 90.9 (2 × CH, Ar), 91.4 (2 × CH, Ar), 113.6 (2 × C, Ar), 159.3 (2 × C, Ar), 159.6 (2 × C, Ar), 159.9 (2 × C, Ar), 170.4 (2 × CO_2Et), 172.3 (2 × CO_2Et); IR (Nujol, cm^{-1}) 2930, 2870, 1720, 1600, 1480, 1380, 1335, 1160, 1125, 1070, 965, 880, 820, 740. Anal. Calcd for $C_{36}H_{48}O_{14}$: C, 61.35; H, 6.86. Found: C, 61.21; H, 7.01.

Tetramethyl *cis*-2,5-Bis(2,4,6-trimethoxyphenyl)-cyclohexane-1,1,4,4-tetracarboxylate (2b). A solution of **1b** (160 mg, 0.5 mmol) in CH_3NO_2 (7 mL) was treated with $GaCl_3$ (36 mg, 0.2 mmol), and the resulting mixture was stirred at 20 °C for 4 h affording **2b** (42 mg, 26%) and **3b** (31 mg, 19%). **2b**: colorless liquid; R_f 0.45 (diethyl ether); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.13 (dd, ^2J = 13.8 Hz, ^3J = 5.2 Hz, 2H, 2 × CH^aH), 3.08 (s, 6H, 2 × OCH_3), 3.35 (dd, ^2J = 13.8 Hz, ^3J = 14.0 Hz, 2H, 2 × CH^bH), 3.67 (s, 6H, 2 × OCH_3), 3.79 (s, 12H, 4 × OCH_3), 3.82 (s, 6H, 2 × OCH_3), 4.80 (dd, ^3J = 5.2 Hz, ^3J = 14.0 Hz, 2H, 2 × CH), 6.08 (br.s, 2H, 2 × CH, Ar), 6.13 (br.s, 2H, 2 × CH, Ar); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 30.3 (2 × CH), 30.5 (2 × CH_2), 51.4 (2 × OCH_3), 52.2 (2 × OCH_3), 52.8 (2 × OCH_3), 55.3 (2 × OCH_3), 55.6 (2 × OCH_3), 57.2 (2 × C), 90.4 (2 × CH, Ar), 90.8 (2 × CH, Ar), 113.5 (2 × C, Ar), 159.2 (2 × C, Ar), 159.6 (2 × C, Ar), 160.1 (2 × C, Ar), 170.7 (2 × CO_2Me), 172.8 (2 × CO_2Me). Anal. Calcd for $C_{32}H_{40}O_{14}$: C, 59.25; H, 6.22. Found: C, 59.17; H, 6.30.

Tetraethyl *cis*-2,5-Bis(3-bromo-2,4,6-trimethoxyphenyl)-cyclohexane-1,1,4,4-tetracarboxylate (2c). A solution of **1c** (200 mg, 0.464 mmol) in CH_3NO_2 (15 mL) was treated with $SnCl_4$ (270 mg, 0.12 mL, 1.02 mmol), and the resulting mixture was stirred at 50 °C for 2 h affording **2c** (162 mg, 81%) as a white solid: mp 225−226 °C dec; R_f 0.50 (diethyl ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.73 (t, ^3J = 7.1 Hz, 6H, 2 × CH_3), 1.36 (t, ^3J = 7.1 Hz, 6H, 2 × CH_3), 2.23 (dd, ^2J = 13.8 Hz, ^3J = 5.3 Hz, 2H, 2 × CH^aH), 3.33 (dd, ^2J = 13.8 Hz, ^3J = 13.5 Hz, 2H, 2 × CH^bH), 3.48−3.66 (m, 2H, OCH_2), 3.65−3.67 (m, 2H, OCH_2), 3.78 (s, 6H, 2 × OCH_3), 3.89 (s, 6H, 2 × OCH_3), 3.92 (s, 6H, 2 × OCH_3), 4.20−4.25 (m, 2H, OCH_2), 4.34−4.39 (m, 2H, OCH_2), 4.78 (dd, ^3J = 5.3 Hz, ^3J = 13.5 Hz, 2H, 2 × CH), 6.27 (s, 1H, CH, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.4 (2 × CH_3), 14.1 (2 × CH_3), 30.5 (2 × CH_2), 31.9 (2 × CH), 54.8 (2 × OCH_3), 56.5 (2 × OCH_3), 58.5 (2 × C), 60.5 (2 × OCH_3), 61.2 (2 × OCH_2), 62.0 (2 × OCH_2), 92.6 (2 × CH, Ar), 98.4 (2 × C, Ar), 119.8 (2 × C, Ar), 155.8 (2 × C, Ar), 157.0 (2 × C, Ar), 158.7 (2 × C, Ar), 170.0 (2 × CO_2Et), 171.8 (2 × CO_2Et); IR (Nujol, cm^{-1}) 2940, 2875, 1725, 1595, 1465, 1370, 1340, 1220, 1200, 1115, 1055, 975, 930, 810; MS MALDI-TOF m/z calcd for $C_{36}H_{46}Br_2O_{14}$ 860, found $[M]^+$ 860. Anal. Calcd for $C_{36}H_{46}Br_2O_{14}$: C, 50.13; H, 5.38. Found: C, 49.95; H, 5.32.

Tetramethyl *cis*-2,5-Bis[4-(dimethylamino)phenyl]-cyclohexane-1,1,4,4-tetracarboxylate (2d). A solution of **1d** (350 mg, 1.264 mmol) in CH_3NO_2 (16 mL) was treated with $SnCl_4$ (400 mg, 0.18 mL, 1.544 mmol), and the resulting mixture was stirred at 55 °C for 3 h affording **2d** (266 mg, 76%) as a yellowish solid: mp 123−124 °C; R_f 0.25 (diethyl ether/hexane 1:1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.37 (dd, ^2J = 14.3 Hz, ^3J = 2.8 Hz, 2H, 2 × CH^aH), 2.89 (s, 12H, 4 × CH_3), 3.14 (s, 6H, 2 × OCH_3), 3.16 (dd, ^2J = 14.3 Hz, ^3J = 12.5 Hz, 2H, 2 × CH^bH), 3.63 (dd, ^3J = 2.8 Hz, ^3J = 12.5 Hz, 2H, 2 × CH), 3.67 (s, 6H, 2 × OCH_3), 6.64 (d, ^3J = 8.8 Hz, 4H, 4 × CH, Ar), 7.20 (d, ^3J = 8.8 Hz, 4H, 4 × CH, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 32.9 (2 × CH_2), 39.0 (2 × CH), 40.6 (4 × CH_3), 52.0 (2 × OCH_3), 52.7 (2 × OCH_3), 60.6 (2 × C), 112.0 (4 × CH, Ar), 128.6 (2 × C, Ar), 129.2 (4 × CH, Ar), 149.5 (2 × C, Ar), 170.4 (2 × CO_2Et), 172.5 (2 × CO_2Et); IR (Nujol, cm^{-1}) 2950, 2880, 1730, 1610, 1525, 1375, 1235, 1170, 1045, 955, 892, 825, 720; MS MALDI-TOF m/z calcd for $C_{30}H_{39}N_2O_8$ 555, found $[M + H]^+$ 555. Anal. Calcd for $C_{30}H_{38}N_2O_8$: C, 64.97; H, 6.91; N, 5.05. Found: C, 64.75; H, 7.15; N, 5.09.

Tetraethyl *cis*-2,5-Bis[4-(dimethylamino)phenyl]-cyclohexane-1,1,4,4-tetracarboxylate (2e). A solution of **1e** (180 mg, 0.60 mmol) in CH_3NO_2 (8 mL) was treated with $SnCl_4$ (190 mg, 0.085 mL, 0.73 mmol), and the resulting mixture was stirred at 55 °C for 3 h affording **2e** (160 mg, 86%) as a yellowish solid: mp 131−132 °C; R_f 0.30 (diethyl ether/hexane 1:1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.78 (t, ^3J = 7.1 Hz, 6H, 2 × CH_3), 1.14 (t, ^3J = 7.1 Hz, 6H, 2 × CH_3), 2.37 (dd, ^2J = 14.4 Hz, ^3J = 2.8 Hz, 2H, 2 × CH^aH), 2.90 (s, 12H, 2 × NMe_2), 3.18 (dd, ^2J = 14.4 Hz, ^3J = 13.2 Hz, 2H, 2 × CH^bH), 3.41−3.50 (m, 2H, OCH_2), 3.64−3.72 (m, 4H, 2 × CH, OCH_2), 4.10−4.28 (m, 4H, 2 × OCH_2), 6.63 (d, ^3J = 8.4 Hz, 4H, 4 × CH, Ar), 7.20 (d, ^3J = 8.4 Hz, 4H, 4 × CH, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.4 ($^1J_{CH}$ = 125 Hz, 2 × CH_3), 13.9 ($^1J_{CH}$ = 125 Hz, 2 × CH_3), 33.0 ($^1J_{CH}$ = 133 Hz, 2 × CH_2), 39.0 ($^1J_{CH}$ = 130 Hz, 2 × CH), 40.8 ($^1J_{CH}$ = 134 Hz, 4 × CH_3), 60.5 (2 × C), 60.9 ($^1J_{CH}$ = 148 Hz, 2 × OCH_2), 61.4 ($^1J_{CH}$ = 148 Hz, 2 × OCH_2), 112.2 ($^1J_{CH}$ = 156 Hz, 4 × CH, Ar), 129.2 (2 × C, Ar), 129.3 ($^1J_{CH}$ = 154 Hz, 4 × CH, Ar), 149.6 (2 × C, Ar), 170.1 (2 × CO_2Et), 172.1 (2 × CO_2Et); IR (Nujol, cm^{-1}) 2940, 2875, 1725, 1615, 1530, 1375, 1185, 1045, 955, 825; MS MALDI-TOF m/z calcd for $C_{34}H_{46}N_2O_8$ 610, found $[M]^+$ 610. Anal. Calcd for $C_{34}H_{46}N_2O_8$: C, 66.86; H, 7.59; N, 4.59. Found: C, 66.75; H, 7.50; N, 4.41.

Tetramethyl *cis*-2,5-Bis(4-piperidinophenyl)cyclohexane-1,1,4,4-tetracarboxylate (2f). A solution of **1f** (200 mg, 0.63 mmol) in CH_3NO_2 (15 mL) was treated with $TiCl_4$ (290 mg, 0.17 mL, 1.55 mmol), and the resulting mixture was stirred at 50 °C for 3 h affording **2f** (168 mg, 84%) as a yellowish solid: mp 97−98 °C; R_f 0.70 (diethyl ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.50−1.62 (m, 4H, 2 × CH_2), 1.64−1.75 (m, 8H, 4 × CH_2), 2.42 (dd, ^2J = 14.4 Hz, ^3J = 2.7 Hz, 2H, 2 × CH^aH), 3.09−3.14 (m, 8H, 4 × CH_2), 3.14 (s, 6H, 2 × OCH_3), 3.22 (dd, ^2J = 14.4 Hz, ^3J = 13.1 Hz, 2H, 2 × CH^bH), 3.64 (dd, ^2J = 2.7 Hz, ^3J = 13.1 Hz, 2H, CH), 3.68 (s, 6H, 2 × OCH_3), 6.86 (d, ^3J = 8.6 Hz, 4H, 4 × CH, Ar), 7.22 (d, ^3J = 8.6 Hz, 4H, 4 × CH, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.2 ($^1J_{CH}$ = 124 Hz, 2 × CH_2), 25.8 ($^1J_{CH}$ = 125 Hz, 4 × CH_2), 32.8 ($^1J_{CH}$ = 133 Hz, 2 × CH_2), 39.1 ($^1J_{CH}$ = 133 Hz, 2 × CH), 50.7 ($^1J_{CH}$ = 136 Hz, 4 × NCH_2), 52.0 ($^1J_{CH}$ = 147 Hz, 2 × OCH_3), 52.8 ($^1J_{CH}$ = 147 Hz, 2 × OCH_3), 60.5 (2 × C), 115.8 (4 × CH, Ar), 129.2 (4 × CH, Ar), 131.1 (2 × C, Ar), 151.1 (2 × C, Ar), 170.4 (2 × CO_2Me), 172.5 (2 × CO_2Me); IR (Nujol, cm^{-1}) 3310, 3015, 2965, 2860, 1735, 1445, 1370, 1270, 1230, 1170, 1080, 1000, 960, 935, 892, 800, 744, 690; HRMS MALDI-TOF m/z calcd 634.3254 for $C_{36}H_{46}N_2O_8$, found $[M]^+$ 634.3250. Anal. Calcd for $C_{36}H_{46}N_2O_8$: C, 68.12; H, 7.30; N, 4.41. Found: C, 67.95; H, 7.19; N, 4.41.

Tetramethyl *cis*-2,5-Bis(4-pyrrolidinophenyl)cyclohexane-1,1,4,4-tetracarboxylate (2g). A solution of **1g** (200 mg, 0.66 mmol) in CH_3NO_2 (14 mL) was treated with $TiCl_4$ (300 mg, 0.18 mL, 1.6 mmol), and the resulting mixture was stirred at 60 °C for 2.5 h affording **2g** (116 mg, 58%) as a white solid: mp 241−242 °C dec; R_f 0.15 (diethyl ether); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.97−2.05 (m, 8H, 4 × CH_2), 2.42 (dd, ^2J = 14.4 Hz, ^3J = 2.7 Hz, 2H, 2 × CH^aH), 3.19 (s, 6H, 2 × OCH_3), 3.20 (dd, ^2J = 14.4 Hz, ^3J = 13.2 Hz, 2H, 2 × CH^bH), 3.24−3.30 (m, 8H, 4 × CH_2N), 3.64 (dd, ^3J = 2.7 Hz, ^3J = 13.2 Hz, 2H, 2 × CH), 3.70 (s, 6H, 2 × OCH_3), 6.48 (d, ^3J = 8.6 Hz, 4H, 4 × CH, Ar), 7.21 (d, ^3J = 8.6 Hz, 4H, 4 × CH, Ar); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 25.4 ($^1J_{CH}$ = 131 Hz, 4 × CH_2), 33.1 ($^1J_{CH}$ = 133 Hz, 2 × CH_2), 39.1 ($^1J_{CH}$ = 130 Hz, 2 × CH), 47.7 ($^1J_{CH}$ = 139 Hz, 4 × NCH_2), 51.9 ($^1J_{CH}$ = 147 Hz, 2 × OCH_3), 52.6 ($^1J_{CH}$ = 147 Hz, 2 × OCH_3), 60.8 (2 × C), 111.1 (4 × CH, Ar), 127.5 (2 × C, Ar), 129.3 (4 × CH, Ar), 147.0 (2 × C), 170.5 (2 × CO_2Me), 172.6 (2 × CO_2Me); IR (Nujol, cm^{-1}) 2940, 2875, 1725, 1615, 1530, 1470, 1380, 1340, 1260, 1230, 1180, 1120, 1055, 1040, 975, 940, 840, 825, 795, 740; HRMS MALDI-TOF m/z calcd for $C_{34}H_{42}N_2O_8$ 606.2941, found $[M]^+$ 606.2946. Anal. Calcd for $C_{34}H_{42}N_2O_8$: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.29; H, 6.95; N, 4.62.

Tetramethyl *cis*-2,5-Bis(4-morpholinophenyl)cyclohexane-1,1,4,4-tetracarboxylate (2h). A solution of **1h** (300 mg, 0.94 mmol) in CH_3NO_2 (14 mL) was treated with $TiCl_4$ (370 mg, 0.21 mL, 1.97 mmol), and the resulting mixture was stirred at 60 °C for 3 h affording **2h** (250 mg, 83%) as a cream-colored solid: mp 249−250 °C dec; R_f 0.80 (CH_2Cl_2/MeOH 20:1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.42 (dd, ^2J = 14.4 Hz, ^3J = 2.7 Hz, 2H, 2 × CH^aH), 3.10−3.13 (m, 8H, 4 × CH_2), 3.14 (s, 6H, 2 × OCH_3), 3.17 (dd, ^2J = 14.4 Hz, ^3J = 13.1 Hz, 2H, 2 × CH^bH), 3.67 (dd, ^3J = 2.7 Hz, ^3J = 13.1 Hz, 2H,

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2 × CH), 3.69 (s, 6H, 2 × OCH_3), 3.81−3.85 (m, 8H, 4 × CH_2), 6.81 (d, ^3J = 8.7 Hz, 4H, 4 × CH, Ar), 7.24 (d, ^3J = 8.7 Hz, 4H, 4 × CH, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 32.5 ($^1J_{CH}$ = 132 Hz, 2 × CH_2), 38.8 ($^1J_{CH}$ = 130 Hz, 2 × CH), 48.9 ($^1J_{CH}$ = 134 Hz, 4 × NCH_2), 51.4 ($^1J_{CH}$ = 147 Hz, 2 × OCH_3), 52.3 ($^1J_{CH}$ = 147 Hz, 2 × OCH_3), 60.1 (2 × C), 66.4 ($^1J_{CH}$ = 144 Hz, 4 × OCH_2), 114.5 (4 × CH), 129.0 (4 × CH), 131.7 (2 × C), 149.7 (2 × C), 169.8 (2 × CO_2Me), 171.9 (2 × CO_2Me); IR (Nujol, cm^{-1}) 2960, 2880, 1725, 1620, 1525, 1470, 1385, 1275, 1250, 1225, 1130, 1060, 1045, 940, 845, 735; HRMS MALDI-TOF *m/z* calcd for $C_{34}H_{42}N_2O_{10}$ 638.2839, found $[M]^+$ 638.2844. Anal. Calcd for $C_{34}H_{42}N_2O_{10}$: C, 63.94; H, 6.63; N, 4.39. Found: C, 63.94; H, 6.58; N, 4.58.

Tetramethyl *cis*-2,5-Bis(4-methoxyphenyl)cyclohexane-1,1,4,4-tetracarboxylate (2i). A solution of $TiCl_4$ (290 mg, 0.17 mL, 0.15 mmol) in CH_3NO_2 (1 mL) was added to a solution of **1i** (200 mg, 0.75 mmol) in CH_3NO_2 (7 mL) at −20 °C. The resulting mixture was allowed to warm to 5 °C for 1 h, kept at this temperature for 2 h, and worked up as described above to yield **2i** (90 mg, 45%) as colorless crystals: mp 174−175 °C; R_f 0.44 (diethyl ether/hexane 1:1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.41 (dd, ^2J = 14.4 Hz, ^3J = 2.8 Hz, 2H, 2 × C*H*^{a}H), 3.15 (s, 6H, 2 × OCH_3), 3.19 (dd, ^2J = 14.4 Hz, ^3J = 13.2 Hz, 2H, 2 × C*H*^{b}H), 3.68 (dd, ^3J = 2.8 Hz, ^3J = 13.2 Hz, 2H, 2 × CH), 3.71 (s, 6H, 2 × OCH_3), 3.79 (s, 6H, 2 × OCH_3), 6.82 (d, ^3J = 8.7 Hz, 4H, 4 × CH, Ar), 7.28 (d, ^3J = 8.7 Hz, 4H, 4 × CH, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 32.9 (2 × CH_2), 39.1 (2 × CH), 52.0 (2 × OCH_3), 52.9 (2 × OCH_3), 55.2 (2 × OCH_3), 60.5 (2 × C), 113.2 (4 × CH, Ar), 129.7 (4 × CH, Ar), 132.7 (2 × C, Ar), 158.4 (2 × C, Ar), 170.3 (2 × CO_2Me), 172.4 (2 × CO_2Me); IR (Nujol, cm^{-1}) 2950, 2860, 1720, 1610, 1520, 1465, 1380, 1135, 1040, 935, 850, 745; GC−MS *m/z* 528 (85) $[M]^+$, 347 (94), 265 (72), 207 (80), 145 (94), 134 (100), 121 (45); MS MALDI-TOF *m/z* calcd for $C_{28}H_{32}O_{10}$ 528, found $[M]^+$ 528. Anal. Calcd for $C_{28}H_{32}O_{10}$: C, 63.63; H, 6.10. Found: C, 63.75; H, 6.15.

Tetraethyl *cis*-2,5-Bis(4-methoxyphenyl)cyclohexane-1,1,4,4-tetracarboxylate (2j). $AlCl_3$ (150 mg, 1.1 mmol) was added in one portion to a solution of **1j** (130 mg, 0.45 mmol) in CH_3NO_2 (9 mL) at −20 °C. The resulting mixture was allowed to warm to room temperature for 1 h, kept at this temperature for 1 h, and worked up as described above to yield **2j** (80 mg, 62%) as colorless crystals: mp 105−106 °C; R_f 0.21 (diethyl ether/hexane 1:1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.78 (t, ^3J = 7.1 Hz, 6H, 2 × CH_3), 1.15 (t, ^3J = 7.1 Hz, 6H, 2 × CH_3), 2.39 (dd, ^2J = 14.4 Hz, ^3J = 2.9 Hz, 2H, 2 × C*H*^{a}H), 3.17 (dd, ^2J = 14.4 Hz, ^3J = 12.7 Hz, 2H, 2 × C*H*^{b}H), 3.43−3.48 (m, 2H, OCH_2), 3.63−3.71 (m, 2H, OCH_2), 3.77 (s, 6H, 2 × OCH_3) 3.78 (dd, ^3J = 2.9 Hz, ^3J = 12.7 Hz, 2H, 2 × CH), 4.09−4.26 (m, 4H, 2 × OCH_2), 6.79 (d, ^3J = 8.8 Hz, 4H, 4 × CH, Ar), 7.28 (d, ^3J = 8.8 Hz, 4H, 4 × CH, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.4 (2 × CH_3), 13.9 (2 × CH_3), 33.1 (2 × CH_2), 39.1 (2 × CH), 55.2 (2 × OCH_3), 60.3 (2 × C), 61.0 (2 × OCH_2), 61.6 (2 × OCH_2), 113.1 (4 × CH, Ar), 129.8 (4 × CH, Ar), 133.2 (2 × C, Ar), 158.4 (2 × C, Ar), 169.9 (2 × CO_2Et), 171.9 (2 × CO_2Et); IR (Nujol, cm^{-1}) 2955, 1720, 1615, 1520, 1460, 1380, 1130, 1115, 1055, 870, 850; MS MALDI-TOF *m/z* calcd for $C_{32}H_{40}O_{10}$ 584, found $[M]^+$ 584. Anal. Calcd for $C_{32}H_{40}O_{10}$: C, 65.74; H, 6.90. Found: C, 65.60; H, 6.93.

Tetraethyl (5*E*)-3,6-Bis(2,4,6-trimethoxyphenyl)hex-5-ene-1,1,4,4-tetracarboxylate (3a). $AlCl_3$ (70 mg, 0.53 mmol) was added in one portion to a solution of **1a** (180 mg, 0.51 mmol) in CH_2Cl_2 at −50 °C (10 mL). The resulting mixture was warmed to −25 °C and kept at this temperature for 1 h, and then it was warmed up to 5 °C, kept at this temperature for additional 22 h, and worked up as described above to yield **3a** (126 mg, 70%) as a colorless oil: R_f 0.54 (diethyl ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.12 (t, ^3J = 7.1 Hz, 3H, CH_3), 1.20 (t, ^3J = 7.1 Hz, 3H, CH_3), 1.27 (t, ^3J = 7.1 Hz, 3H, CH_3), 1.31 (t, ^3J = 7.1 Hz, 3H, CH_3), 2.55 (ddd, ^2J = 13.6 Hz, ^3J = 3.6 Hz, ^3J = 8.8 Hz, 1H, C*H*^{a}H), 2.82 (ddd, ^2J = 13.6 Hz, ^3J = 5.6 Hz, ^3J = 12.1 Hz, 1H, C*H*^{b}H), 3.07 (dd, ^3J = 5.6, ^3J = 8.8 Hz, 1H, CH), 3.52 (s, 3H, OCH_3), 3.66 (s, 6H, 2 × OCH_3), 3.70 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 3.83−3.96 (m, 2H, OCH_2), 4.05 (dq, ^2J = 10.8 Hz, ^3J = 7.1 Hz, 1H, OCH_2), 4.12−4.27 (m, 4H, OCH_2), 4.34 (dq, ^2J = 10.6 Hz, ^3J = 7.1 Hz, 1H, OCH_2), 4.43 (dd, ^3J = 3.6 Hz, ^3J = 12.1 Hz, 1H, CH), 5.96 (d, ^4J = 2.5 Hz, 1H, Ar), 6.02 (d, ^4J = 2.5 Hz, 1H, Ar), 6.04 (s, 2H, Ar), 6.45 (d, ^3J = 17.3 Hz, 1H, CH═), 6.77 (d, ^3J = 17.3 Hz, 1H, CH═); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.9 (2 × CH_3), 14.1 (2 × CH_3), 28.9 (CH_2), 39.3 (CH), 51.5 (CH), 54.9 (OCH_3), 55.1 (OCH_3), 55.2 (OCH_3), 55.4 (OCH_3), 55.5 (2 × OCH_3), 60.6 (OCH_2), 60.8 (OCH_2), 60.9 (2 × OCH_2), 64.0 (C), 90.1 (CH), 90.3 (CH), 90.5 (2 × CH), 107.2 (C), 108.1 (C), 120.0 (CH), 129.1 (CH), 159.2 (2 × C), 159.6 (C), 160.08 (C), 160.14 (C), 160.5 (C), 169.5 (CO_2Et), 170.1 (CO_2Et), 170.5 (CO_2Et), 172.9 (CO_2Et); IR (Nujol, cm^{-1}) 2960, 2860, 1730, 1600, 1470, 1380; MS MALDI-TOF *m/z* calcd for $C_{36}H_{48}O_{14}$ 704, found $[M]^+$ 704. Anal. Calcd for $C_{36}H_{48}O_{14}$: C, 61.35; H, 6.86. Found: C, 61.44; H, 6.75.

Tetramethyl (5*E*)-3,6-Bis(2,4,6-trimethoxyphenyl)hex-5-ene-1,1,4,4-tetracarboxylate (3b). Method A. $BF_3{\cdot}OEt_2$ (78 mg, 0.07 mL, 0.55 mmol) was added in one portion to a solution of **1b** (150 mg, 0.46 mmol) in CH_2Cl_2 (8 mL) at room temperature. The resulting mixture was heated under reflux for 6 h and worked up as described above to yield **3b** (128 mg, 85%).

Method B. $ZnCl_2$ (300 mg, 2.2 mmol) was added in one portion to a solution of **1b** (180 mg, 0.55 mmol) in CH_2Cl_2 (7 mL). The resulting mixture was heated under reflux for 6 h and worked up as described above to yield **3b** (154 mg, 86%): colorless foam; mp 70−71 °C; R_f 0.48 (diethyl ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.53 (ddd, ^2J = 13.6 Hz, ^3J = 3.5 Hz, ^3J = 8.4 Hz, 1H, C*H*^{a}H), 2.78 (ddd, ^2J = 13.6 Hz, ^3J = 6.2 Hz, ^3J = 12.2 Hz, 1H, C*H*^{b}H), 3.12 (dd, ^3J = 6.2 Hz, ^3J = 8.4 Hz, 1H, CH), 3.43 (s, 3H, OCH_3), 3.52 (s, 3H, OCH_3), 3.62 (s, 3H, OCH_3), 3.65 (s, 6H, 2 × OCH_3), 3.69 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 4.37 (dd, ^3J = 3.5 Hz, ^3J = 12.2 Hz, 1H, CH), 5.96 (d, ^4J = 2.3 Hz, 1H, CH, Ar), 6.01 (d, ^4J = 2.3 Hz, 1H, CH, Ar), 6.02 (s, 2H, 2 × CH, Ar), 6.38 (d, ^3J = 17.0 Hz, 1H, CH═), 6.70 (d, ^3J = 17.0 Hz, 1H, CH═); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 29.0 (CH_2), 39.4 (CH), 51.3 (CH), 51.9 (OCH_3), 52.0 (OCH_3), 52.2 (2 × OCH_3), 55.0 (OCH_3), 55.1 (OCH_3), 55.2 (OCH_3), 55.5 (OCH_3), 55.6 (2 × OCH_3), 64.3 (C), 90.2 (CH), 90.4 (CH), 90.7 (2 × CH), 106.9 (C), 108.0 (C), 120.1 (CH═), 128.8 (CH═), 159.2 (2 × C), 159.8 (C), 160.0 (C), 160.3 (C), 160.4 (C), 169.8 (CO_2Me), 170.2 (CO_2Me), 171.1 (CO_2Me), 171.4 (CO_2Me); IR (Nujol, cm^{-1}) 2940, 2870, 1730, 1605, 1470, 1380, 1335, 1240, 1205, 1160, 1130, 1070, 1030, 960, 820, 730; MS MALDI-TOF *m/z* calcd for $C_{32}H_{40}O_{14}$ 648, found $[M]^+$ 648. Anal. Calcd for $C_{32}H_{40}O_{14}$: C, 59.25; H, 6.22. Found: C, 59.30; H, 6.39.

Tetraethyl (5*E*)-3,6-Bis(3-bromo-2,4,6-trimethoxyphenyl)-hex-5-ene-1,1,4,4-tetracarboxylate (3c). A solution of $SnCl_4$ (216 mg, 0.097 mL, 0.83 mmol) in CH_2Cl_2 (1 mL) was added to a solution of **1c** (180 mg, 0.42 mmol) in CH_2Cl_2 (8 mL) at −20 °C. The resulting mixture was kept at −20 °C for 20 h, warmed to room temperature, and worked up as described above to yield **3c** (136 mg, 75%) as a colorless solid: mp 107−108 °C; R_f 0.55 (diethyl ether); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.11 (t, ^3J = 7.2 Hz, 3H, CH_3), 1.20 (t, ^3J = 7.2 Hz, 3H, CH_3), 1.23 (t, ^3J = 7.2 Hz, 3H, CH_3), 1.31 (t, ^3J = 7.2 Hz, 3H, CH_3), 2.55 (ddd, ^2J = 14.0 Hz, ^3J = 6.5 Hz, ^3J = 4.0 Hz, 1H, C*H*^{a}H), 2.73 (ddd, ^2J = 14.0 Hz, ^3J = 7.0 Hz, ^3J = 11.6 Hz, 1H, C*H*^{b}H), 3.18 (dd, ^3J = 6.5 Hz, ^3J = 7.0 Hz, 1H, CH), 3.63 (s, 3H, OCH_3), 3.64 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 3.76−3.80 (m, 2H, OCH_2), 3.85−3.93 (m, 2H, OCH_2), 3.86 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 4.11−4.17 (m, 3H, OCH_2), 4.30 (dq, ^2J = 9.0 Hz, ^3J = 7.2 Hz, 1H, OCH_2), 4.39 (dd, ^3J = 11.6 Hz, ^3J = 4.0 Hz, 1H, CH), 6.22 (s, 1H, CH, Ar), 6.23 (s, 1H, CH, Ar), 6.28 (d, ^3J = 17.1 Hz, 1H, CH═), 6.73 (d, ^3J = 17.1 Hz, 1H, CH═); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 13.5 (2 × CH_3), 13.7 (2 × CH_3), 29.1 (CH_2), 41.1 (CH), 50.7 (CH), 54.6 (OCH_3), 55.0 (OCH_3), 55.9 (2 × OCH_3), 60.1 (OCH_3), 60.4 (OCH_3), 60.5 (OCH_2), 60.6 (OCH_2), 60.8 (OCH_2), 61.0 (OCH_2), 64.2 (C), 91.7 (CH), 92.1 (CH), 97.5 (C), 98.0 (C), 113.1 (C), 114.4 (C), 120.2 (CH), 131.2 (CH), 155.6 (C), 156.0 (C), 156.3 (C), 157.6 (C), 157.8 (C), 158.9 (C), 168.9 (CO_2Et), 169.3 (CO_2Et), 169.8 (CO_2Et), 170.2 (CO_2Et); IR (Nujol, cm^{-1}) 2940, 2870, 1730, 1600, 1475, 1380, 1320, 1120, 1025, 925, 815, 730; MS MALDI-TOF *m/z* calcd for $C_{36}H_{46}Br_2O_{14}$ 860, found

$[M]^+$ 860. Anal. Calcd for $C_{36}H_{46}Br_2O_{14}$: C, 50.13; H, 5.38. Found C, 49.95; H, 5.49.

Dimethyl 6-Methoxy-1-(3-methoxy-2-(methoxycarbonyl)-3-oxopropyl)-4-(4-methoxyphenyl)-3,4-dihydronaphtalene-2,2-(1*H*)-dicarboxylate (7a). A solution of $SnCl_4$ (260 mg, 0.12 mL, 1.0 mmol) in CH_3NO_2 (1 mL) was added to a solution of **1i** (260 mg, 1.00 mmol) in C_6H_6 (13 mL) at room temperature, and the resulting mixture was stirred for 24 h affording **7a** (210 mg, 81%, dr 91:9). (**1*RS*,4*RS***)-**7a** (major isomer): white crystals; mp 72−73 °C; R_f 0.28 (diethyl ether/hexane 1:1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.02 (ddd, ^2J = 13.6 Hz, ^3J = 5.1 Hz, ^3J = 10.6 Hz, 1H, CH_2), 2.12 (ddd, ^2J = 13.6 Hz, ^3J = 3.0 Hz, ^3J = 10.3 Hz, 1H, CH_2), 2.34 (dd, ^2J = 14.4 Hz, ^3J = 11.9 Hz, 1H, CH_2), 2.75 (ddd, ^2J = 14.4 Hz, ^3J = 7.2 Hz, ^4J = 1.5 Hz, 1H, CH_2), 3.44 (ddd, ^3J = 3.0 Hz, ^3J = 10.6 Hz, ^4J = 1.5 Hz, 1H, CH), 3.60 (dd, ^3J = 5.1 Hz, ^3J = 10.3 Hz, 1H, C*H*(CO_2Me)$_2$), 3.61 (s, 3H, OCH_3), 3.64 (s, 3H, OCH_3), 3.66 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.90 (dd, ^3J = 7.2 Hz, ^3J = 11.9 Hz, 1H, CH), 6.35 (d, ^4J = 2.7 Hz, 1H, CH, Ar), 6.73 (dd, ^3J = 8.6 Hz, ^4J = 2.7 Hz, 1H, CH, Ar), 6.86 (br.d, ^3J = 8.6 Hz, 2H, 2 × CH, Ar), 7.09−7.11 (m, 3H, 3 × CH, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 33.2 (CH_2), 33.9 (CH_2), 40.1 (CH), 42.8 (CH), 49.5 (*C*H(CO_2Me)$_2$), 52.7 (OCH_3), 52.8 (3 × OCH_3), 55.2 (OCH_3), 55.3 (OCH_3), 58.6 (C), 112.3 (CH, Ar), 114.1 (2 × CH, Ar), 115.2 (CH, Ar), 129.6 (2 × CH, Ar), 129.9 (C, Ar), 130.3 (CH, Ar), 137.8 (C, Ar), 138.5 (C, Ar), 158.3 (2 × C, Ar), 169.4 (CO_2Me), 169.5 (CO_2Me), 170.3 (CO_2Me), 170.5 (CO_2Me); IR (Nujol, cm^{-1}) 2960, 2870, 1735, 1610, 1515, 1470, 1360, 1055, 845, 740; GC−MS *m*/*z* 528 (96) $[M]^+$, 362 (32), 347 (100), 265 (72), 207 (63), 145 (72), 134 (70), 121 (25); MS MALDI-TOF *m*/*z* calcd for $C_{28}H_{32}O_{10}$ 528, found $[M]^+$ 528. Anal. Calcd for $C_{28}H_{32}O_{10}$: C, 63.63; H, 6.10. Found: C, 63.81; H, 6.21.

Diethyl 1-[3-Ethoxy-2-(ethoxycarbonyl)-3-oxopropyl]-6-methoxy-4-(4-methoxyphenyl)-3,4-dihydronaphthalene-2,2(1*H*)-dicarboxylate (7b). A solution of $SnCl_4$ (260 mg, 0.12 mL, 1.0 mmol) in CH_3NO_2 (1 mL) was added to a solution of **1j** (290 mg, 1.0 mmol) in CH_3NO_2 (13 mL) at −25 °C. The resulting mixture was warmed to room temperature for 3 h and worked up as described above to yield **7b** (240 mg, 80%, dr 90:10). (**1*RS*,4*RS***)-**7b** (major isomer): colorless oil; R_f 0.31 (diethyl ether/hexane 1:1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.13 (t, ^3J = 7.1 Hz, 3H, CH_3), 1.23 (t, ^3J = 7.1 Hz, 3H, CH_3), 1.30 (t, ^3J = 7.1 Hz, 3H, CH_3), 1.36 (t, ^3J = 7.1 Hz, 3H, CH_3), 2.03 (ddd, ^2J = 13.7 Hz, ^3J = 4.7 Hz, ^3J = 10.9 Hz, 1H, CH_2), 2.17 (ddd, ^2J = 13.7 Hz, ^3J = 3.2 Hz, ^3J = 10.3 Hz, 1H, CH_2), 2.34 (dd, ^2J = 14.4 Hz, ^3J = 11.9 Hz, 1H, CH_2), 2.75 (ddd, ^2J = 14.4 Hz, ^3J = 7.2 Hz, ^4J = 1.5 Hz, 1H, CH_2), 3.50 (ddd, ^3J = 3.2 Hz, ^3J = 10.9 Hz, ^4J = 1.5 Hz, 1H, CH), 3.55 (dd, ^3J = 4.7 Hz, ^3J = 10.3 Hz, 1H, C*H*(CO_2Me)$_2$), 3.62 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 3.92 (dd, ^3J = 7.2 Hz, ^3J = 11.9 Hz, 1H, CH), 4.05−4.17 (m, 4H, OCH_2), 4.18−4.37 (m, 4H, OCH_2), 6.36 (d, ^4J = 2.7 Hz, 1H, CH, Ar), 6.73 (dd, ^3J = 8.6 Hz, ^4J = 2.7 Hz, 1H, CH, Ar), 6.86 (br.d, ^3J = 8.6 Hz, 2H, 2 × CH, Ar), 7.09−7.11 (m, 3H, 3 × CH, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.9 (CH_3), 14.0 (2 × CH_3), 14.2 (CH_3), 33.2 (CH_2), 33.7 (CH_2), 39.9 (CH), 42.8 (CH), 49.7 (*C*H(CO_2Et)$_2$), 55.0 (OCH_3), 55.3 (OCH_3), 58.6 (C), 61.4 (OCH_2), 61.5 (2 × OCH_2), 61.8 (OCH_2), 112.2 (CH, Ar), 114.1 (2 × CH, Ar), 115.0 (CH, Ar), 129.6 (2 × CH, Ar), 130.2 (C, Ar), 130.5 (CH, Ar), 138.1 (C, Ar), 138.6 (C, Ar), 158.3 (2 × C, Ar), 169.1 (CO_2Et), 169.2 (CO_2Et), 169.9 (CO_2Et), 170.1 (CO_2Et); IR (Nujol, cm^{-1}) 2990, 1740, 1610, 1510, 1470, 1380, 1050, 870, 850; HRMS MALDI-TOF *m*/*z* calcd for $C_{32}H_{40}O_{10}$ 584.2621, found $[M]^+$ 584.2618. Anal. Calcd for $C_{32}H_{40}O_{10}$: C, 65.74; H, 6.90. Found: C, 65.84; H, 7.08.

Dimethyl 4-(3,4-dimethoxyphenyl)-6,7-dimethoxy-1-(3-methoxy-2-(methoxycarbonyl)-3-oxopropyl)-3,4-dihydronaphtalene-2,2(1*H*)-dicarboxylate (7c). A solution of $SnCl_4$ (318 mg, 0.14 mL, 1.22 mmol) in CH_3NO_2 (1 mL) was added to a solution of **1k** (300 mg, 1.02 mmol) in CH_3NO_2 (14 mL) at −25 °C. The resulting mixture was kept at −25 °C for 22 h, warmed to room temperature, and worked up as described above to yield **7c** (210 mg, 71%, dr 55:45) as colorless oil: R_f 0.44 (diethyl ether/methanol 20:1); ^{1}H NMR ($CDCl_3$, 400 MHz) for mixture of diastereomers δ 1.98−2.17 (m, 2H+2H, CH_2, **A** + **B**), 2.29−2.36 (m, 1H, CH_2, **A**), 2.58−2.67 (ddd, ^2J = 14.6 Hz, ^3J = 3.2 Hz, ^4J = 1.1 Hz, 1H, CH_2, **B**), 2.77 (ddd, ^2J = 14.6 Hz, ^3J = 7.2 Hz, ^4J = 1.3 Hz, 1H, CH_2, **A**), 2.91 (dd, ^2J = 14.6 Hz, ^3J = 8.7 Hz, 1H, CH_2, **B**), 3.17 (s, 3H, OCH_3, **A**), 3.41−3.46 (m, 1H+1H, CH, **A**, **B**), 3.52 (dd, ^3J = 10.2 Hz, ^3J = 5.1 Hz, 1H, CH, **B**), 3.63 (s, 3H, OCH_3, **B**), 3.65 (s, 3H, OCH_3, **B**), 3.66 (s, 3H, OCH_3, **A**), 3.67 (s, 3H, OCH_3, **A**), 3.68 (s, 3H, OCH_3, **B**), 3.72−3.75 (m, 1H, CH, **A**), 3.77 (s, 3H, OCH_3, **B**), 3.80 (s, 3H, OCH_3, **B**), 3.81 (s, 3H, OCH_3, **A**), 3.83 (s, 3H, OCH_3, **A**), 3.84 (s, 3H, OCH_3, **B**), 3.85 (s, 3H, OCH_3, **A**), 3.86 (s, 3H, OCH_3, **B**), 3.89−3.92 (m, 1H, CH, **A**), 3.90 (s, 3H, OCH_3, **A**), 3.94 (s, 3H, OCH_3, **B**), 3.96 (s, 3H, OCH_3, **A**), 4.27 (dd, ^3J = 3.2 Hz, ^3J = 8.7 Hz, 1H, CH, **B**), 6.32 (s, 1H, CH, Ar, **B**), 6.39 (s, 1H, CH, Ar, **A**), 6.46 (dd, ^3J = 8.3 Hz, ^4J = 2.0 Hz, 1H, CH, Ar, **B**), 6.58 (d, ^4J = 2.0 Hz, 1H, CH, Ar, **B**), 6.68 (s, 1H+1H, CH, Ar, **A** + **B**), 6.74 (d, ^3J = 8.3 Hz, 1H, CH, Ar, **B**), 6.75 (d, ^3J = 8.3 Hz, 1H, CH, Ar, **A**), 6.79 (s, 1H, CH, Ar, **A**), 6.84 (d, ^3J = 8.3 Hz, 1H, CH, Ar, **A**); ^{13}C NMR ($CDCl_3$, 100 MHz) for mixture of diastereomers δ 32.1 (CH_2, **A**), 33.0 (CH_2, **A**), 33.3 (CH_2, **B**), 33.7 (CH_2, **B**), 40.5 (CH, **A**), 40.7 (2 × CH, **A**, **B**), 42.6 (CH, **B**), 49.8 (CH, **B**), 49.9 (CH, **A**), 52.1 (OCH_3), 52.57 (2 × OCH_3), 52.64 (OCH_3), 52.68 (2 × OCH_3), 52.81 (OCH_3), 52.84 (OCH_3), 55.56 (OCH_3), 55.61 (OCH_3), 55.68 (2 × OCH_3), 55.76 (2 × OCH_3), 55.81 (2 × OCH_3), 57.1 (C, **B**), 58.5 (C, **A**), 110.6 (CH, **A**), 111.1 (CH, **B**), 111.3 (CH, **B**), 111.6 (2 × CH, **A** + **B**), 112.1 (CH, **A**), 112.5 (CH, **B**), 113.0 (CH, **A**), 120.5 (CH, **B**), 121.0 (CH, **A**), 127.8 (C, **A**), 128.7 (C, **B**), 129.5 (C, **B**), 129.7 (C, **A**), 138.7 (2 × C, **A**, **B**), 147.1 (2 × C, **A**), 147.3 (C, **B**), 147.6 (2 × C, **A**, **B**), 147.8 (C, **B**), 148.5 (C, **A**), 149.1 (C, **B**), 169.16 (CO_2Me, **B**), 169.22 (CO_2Me, **A**), 169.4 (CO_2Me, **A**), 169.5 (CO_2Me, **B**), 170.2 (CO_2Me, **B**), 170.3 (CO_2Me, **B**), 170.6 (CO_2Me, **A**), 170.8 (CO_2Me, **A**); IR (Nujol, cm^{-1}) 2950, 2870, 1735, 1520, 1470, 1380, 1250, 1160, 1035, 820, 730; MS MALDI-TOF *m*/*z* calcd for $C_{30}H_{36}O_{12}Na$ 601, found $[M + Na]^+$ 601. Anal. Calcd for $C_{30}H_{36}O_{12}$: C, 61.22; H, 6.16. Found: C, 61.51; H, 6.28.

Dimethyl 9-(2″,3″-Dihydro-1″,4″-benzodioxin-6″-yl)-6-[3′-methoxy-2′-(methoxycarbonyl)-3′-oxopropyl]-2,3,8,9-tetrahydronaphtho[2,3-*b*][1,4]dioxine-7,7(6*H*)-dicarboxylate (7d). A solution of $SnCl_4$ (318 mg, 0.14 mL, 1.22 mmol) in $C_2H_5NO_2$ (1 mL) was added to a solution of **1l** (210 mg, 0.82 mmol) in $C_2H_5NO_2$ (13 mL) at −40 °C. The resulting mixture was allowed to warm to room temperature during 3 h and worked up as described above to yield **7d** (85 mg, 40%, dr 57:43) as colorless oil. R_f 0.17 (hexane/ethyl acetate 2:1); (**6*RS*,9*RS***)-**7d** (major isomer): ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.03 (ddd, ^2J = 13.7 Hz, $^3J_{1',2'}$ = 4.6 Hz, $^3J_{1',6}$ = 10.9 Hz, 1H, C(1′)H$_2$), 2.16 (ddd, ^2J = 13.7 Hz, $^3J_{1',6}$ = 3.0 Hz, $^3J_{1',2'}$ = 10.5 Hz, 1H, C(1′)H$_2$), 2.57 (ddd, ^2J = 14.8 Hz, $^3J_{8,9}$ = 5.0 Hz, $^4J_{8,6}$ = 0.9 Hz, 1H, C(8)H$_2$), 2.86 (dd, ^2J = 14.8 Hz, $^3J_{8,9}$ = 9.0 Hz, 1H, C(8)H$_2$), 3.34−3.36 (m, 1H, C(6)H), 3.36 (s, 3H, OCH_3), 3.50 (dd, $^3J_{2',1'}$ = 4.6 Hz, $^3J_{2',1'}$ = 10.5 Hz, 1H, C(2′)H), 3.65 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 4.09 (br. dd, $^3J_{9,8}$ = 5.0 Hz, $^3J_{9,8}$ = 9.0 Hz, 1H, C(9)H), 4.16−4.24 (m, 8H, CH_2O), 6.31 (d, $^4J_{10,9}$ = 0.7 Hz, 1H, C(10)H), 6.55 (dd, ^3J = 8.3 Hz, ^4J = 2.2 Hz, 1H, C(7″)H), 6.58 (d, ^4J = 2.2 Hz, 1H, C(5″)H), 6.70 (s, 1H, C(5)H), 6.76 (d, ^3J = 8.3 Hz, 1H, C(8″)H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 31.2 (CH_2), 33.8 (CH_2), 40.0 (CH), 41.2 (CH), 49.9 (CH), 52.4 (OCH_3), 52.6 (OCH_3), 52.7 (OCH_3), 52.8 (OCH_3), 57.2 (OCH_2), 60.4 (C), 64.3 (OCH_2), 64.4 (2 × OCH_2), 116.9 (CH, Ar), 117.1 (CH, Ar), 117.3 (CH, Ar), 118.1 (CH, Ar), 121.9 (CH, Ar), 130.3 (C, Ar), 130.4 (C, Ar), 139.2 (C, Ar), 141.8 (C, Ar), 142.0 (C, Ar), 142.4 (C, Ar), 143.2 (C, Ar), 169.4 (CO_2Me), 169.5 (CO_2Me), 170.8 (CO_2Me), 170.9 (CO_2Me). (**6*RS*,9*SR***)-**7d** (minor isomer): ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.99 (ddd, ^2J = 13.7 Hz, $^3J_{1',2'}$ = 4.8 Hz, $^3J_{1',6}$ = 10.5 Hz, 1H, C(1′)H$_2$), 2.08 (ddd, ^2J = 13.7 Hz, $^3J_{1',6}$ = 3.0 Hz, $^3J_{1',2'}$ = 10.5 Hz, 1H, C(1′)H$_2$), 2.28 (dd, ^2J = 14.4 Hz, $^3J_{8,9}$ = 12.1 Hz, 1H, C(8)H$_2$), 2.69 (ddd, ^2J = 14.4 Hz, $^3J_{8,9}$ = 7.1 Hz, $^4J_{8,6}$ = 1.6 Hz, 1H, C(8)H$_2$), 3.32−3.33 (m, 1H, C(6)H), 3.64 (dd, $^3J_{2',1'}$ = 4.8 Hz, $^3J_{2',1'}$ = 10.5 Hz, 1H, C(2′)H), 3.66 (s, 3H, CH_3), 3.68 (s, 3H, CH_3), 3.70−3.71 (m, 1H, C(9)H), 3.78 (s, 3H, CH_3), 3.83 (s, 3H, CH_3), 4.16−4.24 (m, 8H, CH_2O), 6.34 (d, ^4J = 0.7 Hz, 1H, C(10)H), 6.64 (dd, ^3J = 8.2 Hz, ^4J = 2.1 Hz, 1H, C(7″)H), 6.65 (d, ^4J = 2.1 Hz, 1H, C(5″)H), 6.66 (s, 1H,

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C(5)H), 6.80 (d, ^3J = 8.2 Hz, 1H, C(8″)H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 33.0 (CH_2), 33.8 (CH_2), 40.5 (CH), 42.3 (CH), 49.5 (CH), 52.63 (OCH_3), 52.67 (OCH_3), 52.72 (OCH_3), 52.85 (OCH_3), 58.6 (OCH_2), 58.9 (C), 64.3 (OCH_2), 64.4 (2 × OCH_2), 116.9 (CH, Ar), 117.2 (CH, Ar), 117.7 (CH, Ar), 118.4 (CH, Ar), 121.4 (CH, Ar), 129.9 (C, Ar), 130.8 (C, Ar), 139.2 (C, Ar), 141.8 (C, Ar), 142.2 (C, Ar), 142.5 (C, Ar), 143.5 (C, Ar), 169.3 (CO_2Me), 169.5 (CO_2Me), 170.3 (CO_2Me), 170.4 (CO_2Me); IR (Nujol, cm^{-1}) 2945, 2865, 1735, 1595, 1510, 1475, 1380, 1300, 1220, 1085, 900, 825, 755, 735; MS MALDI-TOF m/z calcd for $C_{30}H_{32}O_{12}Na$ 607, found $[M + Na]^+$ 607. Anal. Calcd for $C_{30}H_{32}O_{12}$: C, 61.64; H, 5.52. Found: C, 61.53; H, 5.75.

Dimethyl 7-(3-Methoxy-2-(methoxycarbonyl)-3-oxopropyl)-4-(thiophene-2-yl)-4,5-dihydrobenzo[*b*]thiophene-6,6(7*H*)-dicarboxylate (7e). A solution of $SnCl_4$ (260 mg, 0.12 mL, 1.00 mmol) in CH_3NO_2 (1 mL) was added to a solution of **1m** (200 mg, 0.83 mmol) in CH_3NO_2 (13 mL) at −20 °C. The resulting mixture was heated to 50 °C within 0.5 h, stirred at this temperature for 0.5 h, and worked up as described above to yield **7e** (156 mg, 78%, dr 71:29) as a colorless oil: R_f 0.46 (CH_2Cl_2). (**4*RS*,7*RS***)-**7e** (major isomer): ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.23−2.29 (m, 2H, CH_2), 2.64 (dd, ^2J = 14.3 Hz, ^3J = 5.3 Hz, 1H, CH_2), 2.86 (dd, ^2J = 14.3 Hz, ^3J = 6.9 Hz, 1H, CH_2), 3.33 (s, 3H, OCH_3), 3.57 (dd, ^3J = 6.1 Hz, ^3J = 6.6 Hz, 1H, CH), 3.73 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.81−3.83 (m, 1H, C*H*(CO_2Me)$_2$), 4.47 (dd, ^3J = 5.3 Hz, ^3J = 6.9 Hz, 1H, CH), 6.52 (br. d, ^3J = 3.5 Hz, 1H, CH, Th), 6.74 (d, ^3J = 5.2 Hz, 1H, CH, Th), 6.83 (dd, ^3J = 3.5 Hz, ^3J = 5.1 Hz, 1H, CH, Th), 7.12 (d, ^3J = 5.2 Hz, 1H, CH, Th), 7.16 (dd, ^3J = 5.1 Hz, ^4J = 1.0 Hz, 1H, CH, Th); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 32.9 (CH_2), 35.2 (C(4)H), 36.3 (C(5)H_2), 38.3 (C(7)H), 50.4 (*C*H(CO_2Me)$_2$), 52.4 (OCH_3), 52.66 (OCH_3), 52.69 (OCH_3), 52.70 (OCH_3), 58.0 (C), 122.8 (CH, Th), 124.0 (CH, Th), 125.4 (CH, Th), 126.2 (CH, Th), 127.8 (CH, Th), 134.7 (C, Th), 138.1 (C, Th), 148.2 (C, Th), 169.2 (*C*O_2Me), 169.3 (CO_2Me), 169.7 (CO_2Me), 170.1 (CO_2Me). (**4*RS*,7*SR***)-**7e** (minor isomer): ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.06 (ddd, ^2J = 13.9 Hz, ^3J = 4.6 Hz, ^3J = 10.3 Hz, 1H, CH_2), 2.13 (ddd, ^2J = 13.9 Hz, ^3J = 3.3 Hz, ^3J = 10.7 Hz, 1H, CH_2), 2.43 (dd, ^2J = 14.4 Hz, ^3J = 11.3 Hz, 1H, CH_2), 2.90 (ddd, ^2J = 14.4 Hz, ^3J = 6.6 Hz, ^4J = 1.0 Hz, 1H, CH_2), 3.68 (s, 3H, OCH_3), 3.71 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.80−3.82 (m, 1H, CH), 3.83 (s, 3H, OCH_3), 3.83−3.85 (m, 1H, CH), 4.18 (dd, ^3J = 6.6 Hz, ^3J = 11.3 Hz, 1H, CH) 6.65 (d, ^3J = 5.1 Hz, 1H, CH, Th), 6.90 (br.d, ^3J = 3.5 Hz, 1H, CH, Th), 6.95 (dd, ^3J = 3.5 Hz, ^3J = 5.2 Hz, 1H, CH, Th), 7.07 (d, ^3J = 5.2 Hz, 1H, CH, Th), 7.18 (br. d, ^3J = 5.1 Hz, 1H, CH, Th); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 33.4 (CH_2), 33.9 (C(5)H_2), 36.0 (CH), 37.0 (C(7)H), 49.9 (CH(CO_2Me)$_2$), 52.69 (OCH_3), 52.70 (OCH_3), 52.95 (OCH_3), 52.97 (OCH_3), 59.8 (C), 123.4 (CH, Th), 123.9 (CH, Th), 124.6 (CH, Th), 126.7 (CH, Th), 127.4 (CH, Th), 135.9 (C, Th), 137.0 (C, Th), 147.8 (C, Th), 169.1 (CO_2Me), 169.3 (CO_2Me), 169.7 (CO_2Me), 170.1 (CO_2Me); IR (film, cm^{-1}) 2955, 2870, 1745, 1440, 1250, 1160, 1080, 925, 850, 800, 715; HRMS MALDI-TOF m/z calcd for $C_{22}H_{24}O_8S_2$ 480.0913, found $[M]^+$ 480.0950. Anal. Calcd for $C_{22}H_{24}O_8S_2$: C, 54.99; H, 5.03. Found: C, 54.85; H, 5.15.

Dimethyl 7-(3-Methoxy-2-(methoxycarbonyl)-3-oxopropyl)-2-methyl-4-(5-methylthiophene-2-yl)-4,5-dihydrobenzo[b]-thiophene-6,6(7*H*)- dicarboxilate (7f). A solution of $SnCl_4$ (260 mg, 0.12 mL, 1.00 mmol) in CH_3NO_2 (1 mL) was added to a solution of **1n** (200 mg, 0.79 mmol) in CH_3NO_2 (9 mL) at −20 °C. The resulting mixture was kept at −20 °C for 6 h, warmed to room temperature, and worked up as described above to yield **7f** (130 mg, 54%, dr 56:44) as a yellow oil: R_f 0.25−0.35 (diethyl ether/hexane 1:1). (**4*RS*,7*RS***)-**7f** (major isomer): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.20−2.29 (m, 2H, CH_2), 2.38 (br. s, 3H, Me), 2.41 (d, ^4J = 0.9 Hz, 3H, Me), 2.56 (dd, ^2J = 14.2 Hz, ^3J = 5.6 Hz, 1H, CH_2), 2.78 (dd, ^2J = 14.2 Hz, ^3J = 6.8 Hz, 1H, CH_2), 3.40 (s, 3H, OCH_3), 3.45 (dd, ^3J = 6.1 Hz, ^3J = 6.3 Hz, 1H, CH), 3.74 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 3.80−3.86 (m, 1H, CH(CO_2Me)$_2$), 4.28 (dd, ^3J = 5.6 Hz, ^3J = 6.8 Hz, 1H, CH), 6.34 (d, ^3J = 3.3 Hz, 1H, Th), 6.39 (d, ^4J = 0.9 Hz, 1H, Th), 6.48 (dd, ^3J = 3.3, ^4J = 1.0 Hz, 1H, Th); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.3 (2 × CH_3), 32.8 (CH_2), 35.3 (C(4)H), 36.3 (C(5)H_2), 38.3 (C(7)H), 50.4 (CH(CO_2Me)$_2$), 52.3 (OCH_3), 52.7 (3 × OCH_3), 59.6 (C), 125.1 (CH, Th), 125.2 (CH, Th), 125.9 (CH, Th), 134.5 (C, Th), 135.4 (C, Th), 136.9 (C, Th), 138.3 (C, Th), 145.7 (C, Th), 169.3 (2 × CO_2Me), 170.2 (CO_2Me), 170.3 (CO_2Me); (**4*RS*,7*SR***)-**7f** (minor isomer): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.99−2.13 (m, 2H, CH_2), 2.34 (d, ^4J = 0.9 Hz, 3H, Me), 2.43 (d, ^4J = 0.9 Hz, 3H, Me), 2.41−2.46 (m, 1H, CH_2), 2.82 (dd, ^2J = 14.2 Hz, ^3J = 6.5 Hz, 1H, CH_2), 3.57 (dd, ^3J = 3.0, ^3J = 9.8 Hz, 1H, CH), 3.69 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 3.80−3.86 (m, 1H, CH(CO_2Me)$_2$), 4.00 (dd, ^3J = 6.5 Hz, ^3J = 10.9 Hz, 1H, CH), 6.31 (d, ^4J = 0.9 Hz, 1H, Th), 6.58 (dd, ^3J = 3.3 Hz, ^4J = 0.9 Hz, 1H, Th), 6.68 (d, ^3J = 3.3 Hz, 1H, Th); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.3 (CH_3), 15.4 (CH_3), 33.4 (CH_2), 33.7 (C(5)H_2), 36.3 (CH), 36.8 (C(7)H), 49.9 (CH(CO_2Me)$_2$), 52.6 (OCH_3), 52.7 (OCH_3), 52.9 (OCH_3), 53.0 (OCH_3), 58.0 (C), 124.3 (CH, Th), 124.5 (CH, Th), 125.5 (CH, Th), 134.3 (C, Th), 135.7 (C, Th), 137.7 (C, Th), 138.3 (C, Th), 145.7 (C, Th), 169.27 (*C*O_2Me), 169.32 (CO_2Me), 169.8 (2 × CO_2Me); IR (Nujol, cm^{-1}) 2965, 2930, 2869, 1740, 1660, 1460, 1380, 1255, 1087, 1054, 800; GC−MS m/z 508 (12) $[M]^+$, 376 (38), 317 (354), 281 (49), 207 (100), 191 (10). Anal. Calcd for $C_{24}H_{28}O_8S_2$: C, 56.68; H, 5.55. Found: C, 56.43; H, 5.45.

Dimethyl 5,6,7-Trimethoxy-1-[3-methoxy-2-(methoxycarbonyl)-3-oxopropyl]-4-(3,4,5-trimethoxyphenyl)-3,4-dihydronaphthalene-2,2(1*H*)-dicarboxylate (7g). A solution of $SnCl_4$ (193 mg, 0.086 mL, 0.74 mmol) in CH_3NO_2 (1 mL) was added to a solution of **1o** (200 mg, 0.62 mmol) in CH_3NO_2 (6 mL) at room temperature. The resulting mixture was heated to 60 °C, stirred at this temperature for 3 h, and worked up as described above to yield **7g** (50 mg, 21%, dr 72:28) and **9a** (130 mg, 65%, dr 54:46). (**1*RS*,4*RS***)-**7g** (major isomer): colorless oil, R_f 0.50 (diethyl ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.09−2.14 (m, 2H, CH_2), 2.19 (dd, ^2J = 14.8 Hz, ^3J = 10.4 Hz, 1H, CH_2), 2.91 (dd, ^2J = 14.8 Hz, ^3J = 8.8 Hz, 1H, CH_2), 3.21 (s, 3H, OCH_3), 3.43 (dd, ^3J = 8.6 Hz, ^3J = 9.0 Hz, 1H, CH), 3.61 (s, 3H, OCH_3), 3.63 (s, 3H, OCH_3), 3.66−3.70 (m, 1H, CH), 3.75 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 3.79 (s, 6H, 2 × OCH_3), 3.82 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 4.07 (dd, ^3J = 8.8 Hz, ^3J = 10.4 Hz, 1H, CH), 6.35 (s, 2H, 2 × CH, Ar), 6.46 (s, 1H, CH, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 33.1 (^1J = 130 Hz, CH_2), 33.2 (^1J = 132 Hz, CH_2), 39.4 (^1J = 130 Hz, CH), 41.7 (^1J = 138 Hz, CH), 49.9 (^1J = 132 Hz, CH(CO_2Me)$_2$), 52.6 (^1J = 148 Hz, CO_2CH_3), 52.7 (^1J = 148 Hz, CO_2CH_3), 52.8 (^1J = 148 Hz, CO_2CH_3), 52.9 (^1J = 148 Hz, CO_2CH_3), 55.6 (^1J = 144 Hz, OCH_3), 56.1 (^1J = 144 Hz, 2 × OCH_3), 58.6 (C), 59.6 (^1J = 144 Hz, OCH_3), 60.4 (^1J = 145 Hz, OCH_3), 60.9 (^1J = 146 Hz, OCH_3), 103.9 (^1J = 157 Hz, 2 × CH, Ar), 107.8 (^1J = 158 Hz, CH, Ar), 122.6 (C, Ar), 133.2 (C, Ar), 136.1 (C, Ar), 141.4 (C, Ar), 144.4 (C, Ar), 152.2 (C, Ar), 152.5 (C, Ar), 153.3 (2 × C, Ar), 169.2 (*C*O_2Me), 169.5 (CO_2Me), 169.9 (CO_2Me), 170.1 (CO_2Me); IR (Nujol, cm^{-1}) 2970, 2855, 1745, 1602, 1505, 1480, 1366, 1245, 1120, 1007, 875; HRMS MALDI-TOF m/z calcd for $C_{32}H_{40}O_{14}$ 648.2412, found $[M]^+$ 648.2418. Anal. Calcd for $C_{32}H_{40}O_{14}$: C 59.25; H, 6.22. Found: C, 59.23, H, 6.38.

Tetramethyl (1*RS*,3a*SR*,5a*RS*,9a*SR*)-1-(4-Methoxyphenyl)-7-oxo-3a,4,6,7-tetrahydro-1*H*-cyclopenta[*c*]indene-3,3,5,5-(2*H*,5a*H*)-tetracarboxylate (8). A solution of $SnCl_4$ (287 mg, 0.13 mL, 1.1 mmol) in C_6H_6 (1 mL) was added to a solution of **1i** (200 mg, 0.76 mmol) in C_6H_6 (10 mL) at 40 °C, and the resulting mixture was kept at this temperature for 2 h affording **7a** (120 mg, 59%, dr 90:10) and **8** (60 mg, 30%). **8**: colorless crystals; mp 159−160 °C; R_f 0.40 (diethyl ether); ^{1}H NMR (600 MHz, $CDCl_3$) 0.78 (dd, ^2J = 18.7 Hz, ^3J = 7.8 Hz, 1H, C(6)H_2), 1.34 (dd, ^2J = 12.5 Hz, ^3J = 10.6 Hz, 1H, C(4)H_2), 2.30 (br.d, ^2J = 18.7 Hz, 1H, C(6)H_2), 2.36 (ddd, ^2J = 12.8 Hz, ^3J = 4.6 Hz, ^4J = 1.0 Hz, 1H, C(2)H_2), 2.57 (dd, ^2J = 12.5 Hz, ^3J = 8.6 Hz, 1H, C(4)H_2), 2.84 (br.d, ^3J = 7.8 Hz, 1H, C(5a)H), 2.89 (dd, ^2J = 12.8 Hz, ^3J = 14.6, Hz, 1H, C(2)H_2), 2.94 (dd, ^3J = 14.6 Hz, ^3J = 4.6 Hz, 1H, C(1)H), 3.47 (s, 3H, OCH_3), 3.64−3.67 (m, 1H, C(3a)H), 3.69 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 5.86 (d, ^3J = 10.3 Hz, 1H, C(8)H), 6.84 (d, ^3J = 7.8 Hz, 2H, C(3′)H, C(5′)H), 6.95 (dd, ^3J = 10.3 Hz, ^4J = 1.7 Hz, 1H, C(9)H), 7.13 (br.d, ^3J = 7.8 Hz, 2H, C(2′)H, C(6′)H); ^{13}C

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NMR (150 MHz, $CDCl_3$) 33.9 ($C(2)H_2$), 34.0 ($C(6)H_2$), 35.5 ($C(4)H_2$), 45.7 (C(5a)H), 48.7 (C(1)H), 51.9 (CH_3), 52.1 (C(3a)H), 52.3 (CH_3), 52.4 (CH_3), 52.8 (CH_3), 53.6 (C(9a)), 54.8 (CH_3), 61.7 (C), 61.9 (C), 114.3 (C(3′)H, C(5′)H), 127.1 (C(8)H), 127.8 (C(1′)), 128.4 (C(2′)H, C(6′)H), 154.5 (C(9)H), 158.8 (C(4′)), 169.6 (CO_2Me), 170.1 (CO_2Me), 170.3 (CO_2Me), 171.9 (CO_2Me), 195.8 (C(7)). Anal. Calcd for $C_{27}H_{30}O_{10}$: C 63.03; H, 5.88. Found: C, 63.23, H, 5.94.

Tetramethyl 2,2′-[(1,2,3,5,6,7-Hexamethoxy-9,10-dihydroanthracene-9,10-diyl)di(methylene)]dimalonate (9a). A solution of $SnCl_4$ (339 mg, 0.15 mL, 1.3 mmol) in CH_3NO_2 (1 mL) was added to a solution of **1o** (210 mg, 0.65 mmol) in CH_3NO_2 (12 mL) at −20 °C. The resulting mixture was heated to 50 °C, stirred at this temperature for 1 h, and worked up as described above to yield (**9*RS*,10*SR***)-**9a** (93 mg, 44%) and (**9*RS*,10*RS***)-**9a** (67 mg, 32%): dr 58:42. (**9*RS*,10*SR***)-**9a** (major isomer): white crystals; mp 214−215 °C; R_f 0.42 (diethyl ether); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.47 (ddd, ^2J = 14.2 Hz, ^3J = 5.8 Hz, ^3J = 4.7 Hz, 2H, 2 × CH^aH), 2.63 (dd, ^3J = 5.8 Hz, ^3J = 6.8 Hz, 2H, 2 × CH), 2.86 (ddd, ^2J = 14.2 Hz, ^3J = 6.8 Hz, ^3J = 3.8 Hz, 2H, 2 × CH^bH), 3.39 (s, 6H, OCH_3), 3.45 (s, 6H, OCH_3), 3.90 (s, 12H, OCH_3), 4.01 (s, 6H, OCH_3), 4.45 (dd, ^3J = 3.8 Hz, ^3J = 4.7 Hz, 2H, 2 × CH), 6.61 (s, 2H, 2 × CH, Ar); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 36.1 (2 × CHAr), 37.9 (2 × CH_2), 47.6 (2 × $CH(CO_2Me)_2$), 52.2 (4 × OCH_3), 55.9 (4 × OCH_3), 60.7 (2 × OCH_3), 106.2 (2 × CH, Ar), 121.9 (2 × C, Ar), 131.6 (2 × C, Ar), 140.7 (2 × C, Ar), 150.9 (2 × C, Ar), 152.5 (2 × C, Ar), 169.79 (2 × CO_2Me), 169.84 (2 × CO_2Me); IR (Nujol, cm^{-1}) 2970, 2855, 1745, 1602, 1505, 1480, 1366, 1245, 1120, 1007, 875. Anal. Calcd for $C_{32}H_{40}O_{14}$: C, 59.25; H, 6.22. Found: C, 59.23; H, 6.33. (**9*RS*,10*RS***)-**9a** (minor isomer): colorless oil; R_f 0.58 (diethyl ether); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.21−2.34 (m, 4H, 2 × CH_2), 3.66 (dd, ^3J = 7.3 Hz, ^3J = 8.1 Hz, 2H, 2 × CH), 3.75 (s, 6H, 2 × OCH_3), 3.78 (s, 6H, 2 × OCH_3), 3.88 (s, 6H, 2 × OCH_3), 3.90 (s, 6H, 2 × OCH_3), 3.92 (s, 6H, 2 × OCH_3), 4.17 (dd, ^3J = 6.9 Hz, ^3J = 8.5 Hz, 2H, 2 × CH), 6.77 (s, 2H, Ar); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 37.6 (2 × CHAr), 39.3 (2 × CH_2), 50.2 (2 × $CH(CO_2Me)_2$), 52.4 (2 × OCH_3), 52.5 (2 × OCH_3), 55.6 (2 × OCH_3), 56.0 (2 × OCH_3), 60.7 (2 × OCH_3), 107.9 (2 × CH, Ar), 124.6 (2 × C, Ar), 134.8 (2 × C, Ar), 140.3 (2 × C, Ar), 150.7 (2 × C, Ar), 152.1 (2 × C, Ar), 169.6 (2 × CO_2Me), 170.1 (2 × CO_2Me). Anal. Calcd for $C_{32}H_{40}O_{14}$: C, 59.25; H, 6.22. Found: C, 59.34; H, 6.35.

Tetramethyl 2,2′-[(1,3,5,7-Tetramethoxy-9,10-dihydroanthracene-9,10-diyl)di(methylene)]dimalonate (9b). $Sn(OTf)_2$ (14 mg, 0.034 mmol) was added to a solution of **1p** (100 mg, 0.340 mmol) in CH_3NO_2 (3.4 mL) at room temperature. The resulting mixture was heated up to 60 °C, stirred at this temperature for 4 h, and worked up as described above to yield **9b** (80 mg, 80%, dr 64:36). (**9*RS*,10*SR***)-**9b** (major isomer): colorless crystals; mp 124−125 °C; R_f 0.4 (diethyl ether); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.42 (ddd, ^2J = 14.1 Hz, ^3J = 5.1 Hz, ^3J = 3.7 Hz, 2H, 2 × CH^aH), 2.67 (dd, ^3J = 5.1 Hz, ^3J = 8.0 Hz, 2H, 2 × CH), 2.98 (ddd, ^2J = 14.1 Hz, ^3J = 8.0 Hz, ^3J = 3.9 Hz, 2H, 2 × CH^bH), 3.34 (s, 6H, 2 × OCH_3), 3.46 (s, 6H, 2 × OCH_3), 3.83 (s, 6H, 2 × OCH_3), 3.87 (s, 6H, 2 × OCH_3), 4.48 (dd, ^3J = 3.7 Hz, ^3J = 3.9 Hz, 2H, 2 × CH), 6.34 (d, ^4J = 2.4 Hz, 2H, 2 × CH, Ar), 6.44 (d, ^4J = 2.4 Hz, 2H, 2 × CH, Ar); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 35.7 ($^1J_{CH}$ = 133 Hz, 2 × CHAr), 36.6 ($^1J_{CH}$ = 132 Hz, 2 × CH_2), 47.5 ($^1J_{CH}$ = 129 Hz, 2 × $CH(CO_2Me)_2$), 52.2 (4 × OCH_3), 55.3 (4 × OCH_3), 97.2 (2 × CH, Ar), 103.2 (2 × CH, Ar), 117.0 (2 × C, Ar), 138.4 (2 × C, Ar), 157.9 (2 × C, Ar), 159.2 (2 × C, Ar), 169.9 (2 × CO_2Me), 170.1 (2 × CO_2Me). Anal. Calcd for $C_{30}H_{36}O_{12}$: C, 61.22; H, 6.16. Found: C, 60.95; H, 5.97. (**9*RS*,10*RS***)-**9b** (minor isomer): colorless oil; R_f 0.66 (diethyl ether); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.24 (ddd, ^2J = 13.9 Hz, ^3J = 7.1 Hz, ^3J = 8.2 Hz, 2H, 2 × CH^aH), 2.37 (ddd, ^2J = 13.9 Hz, ^3J = 7.1 Hz, ^3J = 8.1 Hz, 2H, 2 × CH^bH), 3.66 (dd, ^3J = 7.1 Hz, ^3J = 8.1 Hz, 2H, 2 × CH), 3.72 (s, 6H, 2 × OCH_3), 3.78 (s, 12H, 4 × OCH_3), 3.85 (s, 6H, 2 × OCH_3), 4.26 (dd, ^3J = 7.1 Hz, ^3J = 8.2 Hz, 2H, 2 × CH), 6.35 (d, ^4J = 2.3 Hz, 2H, 2 × CH, Ar), 6.57 (d, ^4J = 2.3 Hz, 2H, 2 × CH, Ar); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 37.1 ($^1J_{CH}$ = 131 Hz, 2 × CHAr), 38.8 ($^1J_{CH}$ = 134 Hz, 2 × CH_2), 50.3 ($^1J_{CH}$ = 133 Hz, 2 × $CH(CO_2Me)_2$), 52.4 (2 × OCH_3), 52.5 (2 × OCH_3), 55.2 (2 × OCH_3), 55.4 (2 × OCH_3), 96.7 (2 × CH, Ar), 104.6 (2 × CH, Ar), 119.5 (2 × C, Ar), 142.2 (2 × C, Ar), 157.4 (2 × C, Ar), 159.2 (2 × C, Ar), 169.7 (2 × CO_2Me), 170.2 (2 × CO_2Me); IR (Nujol, cm^{-1}) 3000, 2955, 2840, 1735, 1610, 1585, 1489, 1456, 1437, 1346, 1327, 1262, 1200, 1145, 1107, 1055, 1025, 831; MS MALDI-TOF m/z calcd for $C_{30}H_{36}O_{12}$ 588, found $[M]^+$ 588. Anal. Calcd for $C_{30}H_{36}O_{12}$: C, 61.22; H, 6.16. Found: C, 60.99; H, 6.01.

Tetramethyl 2,2′-[(1,2,5,6-Tetramethoxy-9,10-dihydroanthracene-9,10-diyl)di(methylene)]dimalonate (9c). $Sn(OTf)_2$ (14 mg, 0.034 mmol) was added to a solution of **1q** (100 mg, 0.340 mmol) in CH_3NO_2 (3.4 mL) at room temperature. The resulting mixture was heated to 100 °C, stirred at this temperature for 4 h, and worked up as described above to yield **9c** (66 mg, 66%, dr 90:10). (**9*RS*,10*SR***)-**9c** (major isomer): colorless crystals; mp 153−154 °C; R_f 0.5 (diethyl ether); H NMR ($CDCl_3$, 400 MHz) δ 2.44 (ddd, ^2J = 14.1 Hz, ^3J = 4.7 Hz, ^3J = 6.3 Hz, 2H, 2 × CH^aH), 2.65 (dd, ^3J = 6.3 Hz, ^3J = 6.9 Hz, 2H, 2 × CH), 2.98 (ddd, ^2J = 14.1 Hz, ^3J = 6.9 Hz, ^3J = 3.9 Hz, 2H, 2 × CH^bH), 3.36 (s, 6H, 2 × OCH_3), 3.42 (s, 6H, 2 × OCH_3), 3.88 (s, 6H, 2 × OCH_3), 3.96 (s, 6H, 2 × OCH_3), 4.57 (dd, ^3J = 3.9 Hz, ^3J = 4.7 Hz, 2H, 2 × CH), 6.90 (d, ^3J = 8.7 Hz, 2H, 2 × CH, Ar), 7.06 (d, ^3J = 8.7 Hz, 2H, 2 × CH, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 35.8 (2 × CHAr), 38.1 (2 × CH_2), 47.8 (2 × $CH(CO_2Me)_2$), 52.1 (2 × OCH_3), 52.2 (2 × OCH_3), 55.9 (2 × OCH_3), 60.6 (2 × OCH_3), 112.0 (2 × CH, Ar), 123.6 (2 × CH, Ar), 129.4 (2 × C, Ar), 130.0 (2 × C, Ar), 146.2 (2 × C, Ar), 150.8 (2 × C, Ar), 169.6 (2 × CO_2Me), 169.8 (2 × CO_2Me); IR (Nujol, cm^{-1}) 2945, 2865, 1735, 1725, 1602, 1500, 1470, 1295, 1220, 1105, 1088, 1042, 1000, 830; MS MALDI-TOF m/z calcd for $C_{30}H_{36}O_{12}$ 588, found $[M]^+$ 588. Anal. Calcd for $C_{30}H_{36}O_{12}$: C, 61.22; H, 6.16. Found: C, 61.32; H, 6.18.

Arylidenemalonates were synthesized according to the reported procedures.[64,65] All compounds, except **10a−c**, were described earlier.

Dimethyl 2-(4-Piperidinobenzylidene)malonate (10a). Condensation of 4-(piperidin-1-yl)benzaldehyde (2.0 g, 10.5 mmol) with dimethyl malonate (1.40 g, 10.6 mmol) in benzene (20 mL) in the presence of piperidine (0.04 mL, 0.6 mmol) and acetic acid (0.12 mL, 2.2 mmol) yielded **10a** (2.9 g, 91%) as a yellow solid: mp 96−97 °C (from ethyl acetate/hexane 1:1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.59−1.75 (m, 6H), 3.25−3.49 (m, 4H), 3.83 (s, 3H, CH_3O), 3.89 (s, 3H, CH_3O), 6.84 (d, ^3J = 8.9 Hz, 2H, 2 × CH, Ar), 7.32 (d, ^3J = 8.9 Hz, 2H, 2 × CH, Ar), 7.67 (s, 1H, CH); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 23.3 (CH_2), 26.0 (2 × CH_2), 47.7 (2 × NCH_2), 52.4 (OCH_3), 52.5 (OCH_3), 114.3 (2 × CH, Ar), 121.3 (C), 123.2 (C), 131.5 (2 × CH, Ar), 142.8 (CH═), 152.7 (C), 165.1 (CO_2Me), 167.9 (CO_2Me); IR (Nujol, cm^{-1}) 2965, 2870, 1730, 1605, 1522, 1460, 1387, 1280, 1230, 1180, 1130, 928, 827, 770, 740; GC−MS m/z 304 (17), 303 (100) $[M]^+$, 272 (28), 212 (15), 184 (15), 156 (10), 129 (17), 115 (10), 102 (12), 59 (52). Anal. Calcd for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.58; H, 6.96; N, 4.80.

Dimethyl 2-[(2,3-Dihydrobenzo[*b*][1,4]dioxin-6-yl)-methylene]malonate (10b). Condensation of [1,4]benzodioxane-6-carbaldehyde (2.0 g, 12.2 mmol) with dimethyl malonate (1.61 g, 12.2 mmol) in benzene (20 mL) in the presence of piperidine (0.12 mL, 1.22 mmol) and acetic acid (0.35 mL, 6.1 mmol) yielded **10b** (3.2 g, 95%) as a white solid: mp 82−83 °C (from ethyl acetate/hexane 1:1); ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.73 (s, 3H, CH_3O), 3.78 (s, 3H, CH_3O), 4.08−4.10 (m, 2H, CH_2O), 4.12−4.14 (m, 2H, CH_2O), 6.77 (d, ^3J = 8.4 Hz, 1H, CH, Ar), 6.86 (dd, ^3J = 8.4 Hz, ^4J = 2.2 Hz, 1H, CH, Ar), 6.89 (d, ^4J = 2.2 Hz, 1H, CH, Ar), 7.56 (s, 1H, CH═); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 52.5 (OCH_3), 52.6 (OCH_3), 64.1 (OCH_2), 64.6 (OCH_2), 117.7 (CH, Ar), 118.5 (CH, Ar), 123.4 (C), 123.8 (CH, Ar), 126.1 (C), 142.4 (CH═), 143.6 (C), 146.1 (C), 164.7 (CO_2Me), 167.4 (CO_2Me); GC−MS m/z 278 (100) $[M]^+$, 247 (28), 218 (58), 189 (14), 179 (49), 160 (38), 76 (16), 59 (27); IR (Nujol, cm^{-1}) 2950, 2875, 1720, 1640, 1615, 1580, 1505, 1470, 1440, 1380, 1320, 1300, 1250, 1170, 1140, 1000, 980, 960, 940, 920, 895, 880, 845, 780, 730, 720. Anal. Calcd for $C_{14}H_{14}O_6$: C, 60.43; H, 5.07. Found: C, 60.55; H, 5.18.

Dimethyl 2-(3,5-Dimethoxybenzylidene)malonate (10c). Condensation of 3,5-dimethoxybenzaldehyde (0.5 g, 3.0 mmol) with

dimethyl malonate (0.4 g, 3.0 mmol) in benzene (6 mL) in the presence of piperidine (0.03 mL, 0.3 mmol) and acetic acid (0.09 mL, 1.5 mmol) yielded **10c** (0.72 g, 85%) as white solid: mp 68−69 °C. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.80 (s, 6H, 2 × CH_3O), 3.87 (s, 6H, 2 × CH_3O), 6.52 (t, ^4J = 2.2 Hz, 1H, CH, Ar), 6.60 (d, ^4J = 2.2 Hz, 2H, 2 × CH, Ar), 7.72 (s, 1H, CH═); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 52.6 (2 × OCH_3), 55.4 (2 × OCH_3), 103.2 (CH, Ar), 107.2 (2 × CH, Ar), 126.0 (C), 134.5 (C), 142.8 (CH═), 161.0 (2 × C), 164.4 (CO_2Me), 167.0 (CO_2Me); GC−MS m/z 280 (100) $[M]^+$, 249 (28), 218 (49), 190 (23), 181 (48), 162 (24), 59 (31); IR (Nujol, cm^{-1}) 2940, 2875, 1725, 1600, 1475, 1380, 1250, 1210, 1170, 1085, 1060, 975, 935, 840, 730. Anal. Calcd for $C_{14}H_{16}O_6$: C, 59.99; H, 5.75. Found: C, 60.27; H, 5.76.

■ ASSOCIATED CONTENT

Supporting Information

NMR spectra of synthesized compounds, crystal X-ray structures of *trans*-**9a** and *trans*-**9c** (CIF), and results of ab initio calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ REFERENCES

(1) Clayden, J.; Greeves, N.; Warren, S.; Wothers, P. *Organic Chemistry*; Oxford University Press: New York, 2001; 1536 pp.
(2) Smith, M. B.; March, J. *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, 6th ed.; John Wiley & Sons: New York, 2007; 2384 pp.
(3) Cerecetto, H.; Gonzalez, M. *Top. Heterocycl. Chem.* **2007**, *10*, 265−308.
(4) Sheremetev, A. B.; Makhova, N. N.; Friedrichsen, W. *Adv. Heterocycl. Chem.* **2001**, *78*, 65−188.
(5) Grigg, R.; Donegan, G.; Nimal Gunaratne, H. Q.; Kennedy, D. A.; Malone, J. F.; Sridharan, V.; Thianpatanagul, S. *Tetrahedron* **1989**, *45*, 1723−1746.
(6) Amornraksa, K.; Barr, D.; Donegan, G.; Grigg, R.; Ratananukul, P.; Sridharan, V. *Tetrahedron* **1989**, *45*, 4649−4668.
(7) Groundwater, P. W.; Morton, A. J.; Salter, R. *J. Chem. Soc., Chem. Commun.* **1993**, 1789−1790.
(8) Ohashi, M.; Taniguchi, T.; Ogoshi, S. *Organometallics* **2010**, *29*, 2386−2389, and references cited therein.
(9) Chagarovskiy, A. O.; Ivanova, O. A.; Budynina, E. M.; Trushkov, I. V.; Melnikov, M. Ya. *Tetrahedron Lett.* **2011**, *52*, 4421−4425.
(10) Morrocchi, S.; Ricca, A.; Selva, A.; Zanarotti, A. *Gazz. Chim. Ital.* **1969**, *99*, 165−175.
(11) Groundwater, P. W.; Nyerges, M.; Fejes, I.; Hibbs, D. E.; Bendell, D.; Anderson, R. J.; McKillop, A.; Sharif, T.; Zhang, W. *ARKIVOC* **2000**, *1*, 684−697.
(12) Bunnelle, W. H. *Chem. Rev.* **1991**, *91*, 335−362.
(13) Griesbaum, K.; Kim, W.-S. *J. Org. Chem.* **1992**, *57*, 5574−5577.
(14) Schank, K.; Beck, H.; Buschlinger, M.; Eder, J.; Heisel, T.; Pistorius, S.; Wagner, C. *Helv. Chim. Acta* **2000**, *83*, 801−826.
(15) Buchi, G.; Aver, D. E. *J. Am. Chem. Soc.* **1956**, *78*, 689−690.
(16) Ito, S.; Kakehi, A.; Matsuno, T.; Yoshida, J. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 2007−2011.
(17) Lisowskaya, N. A.; Maslivets, A. N.; Aliev, Z. G. *Tetrahedron* **2004**, *60*, 5319−5323.
(18) Padwa, A.; Precedo, L.; Semones, M. A. *J. Org. Chem.* **1999**, *64*, 4079−4088.
(19) Hartke, K.; Bien, N.; Massa, W.; Wocadlo, S. *Liebigs Ann. Chem.* **1996**, 1159−1166.
(20) Huisgen, R.; Kalwinsch, I.; Li, X.; Mloston, G. *Eur. J. Org. Chem.* **2000**, 1685−1694.
(21) Lesniak, S.; Mloston, G.; Urbaniak, K.; Wasiak, P.; Linden, A.; Heimgartner, H. *Tetrahedron* **2006**, *62*, 7776−7782.
(22) Freeman, F.; Govindarajoo, G. *Rev. Heteroatom Chem.* **1995**, *13*, 123−147.
(23) Huisgen, R. *Angew. Chem., Int. Ed.* **1963**, *2*, 565−598.
(24) Foehlish, B.; Herter, R.; Wolf, E.; Stezowski, J. J.; Eckle, E. *Chem. Ber.* **1982**, *115*, 355−380.
(25) Nakamura, E.; Yamago, S. *Acc. Chem. Res.* **2002**, *35*, 867−877.
(26) Billera, C. F.; Little, R. D. *J. Am. Chem. Soc.* **1994**, *116*, 5487−5488.
(27) Paul, G. C.; Gajewski, J. J. *J. Org. Chem.* **1996**, *61*, 1399−1404.
(28) Witt, O.; Mauser, H.; Friedl, T.; Wilhelm, D.; Clark, T. *J. Org. Chem.* **1998**, *63*, 959−967.
(29) Koppenhoefer, B.; Winter, W.; Bayer, E. *Liebigs Ann. Chem.* **1983**, 1986−1995.
(30) Klys, A.; Czardybon, W.; Warkentin, J.; Werstiuk, N. H. *Can. J. Chem.* **2004**, *82*, 1769−1773.
(31) Concellon, J. M.; Bernad, P. L.; del Solar, V.; Garcia-Granda, S.; Diaz, M. R. *Adv. Synth. Catal.* **2008**, *350*, 477−481.
(32) Murray, R. W.; Jeyaraman, R. *J. Org. Chem.* **1985**, *50*, 2847−2853.
(33) Kobayashi, Y.; Kumadaki, I.; Ohsawa, A.; Sekine, Y.; Ando, A. *Heterocycles* **1977**, *6*, 1587−1592.
(34) Iranpoor, N.; Firouzabadi, H.; Chitsazi, M.; Jafari, A. A. *Tetrahedron* **2002**, *58*, 7037−7042.
(35) Adam, W.; Fröhling, B.; Weinkötz, S. *J. Org. Chem.* **1998**, *63*, 9154−9155.
(36) Hansen, G. R.; Burg, T. E. *J. Heterocycl. Chem.* **1968**, *5*, 305.
(37) Ramaiah, D.; Muneer, M.; Gopidas, K. R.; Das, P. K.; Rath, N. P.; George, M. V. *J. Org. Chem.* **1996**, *61*, 4240−4246.
(38) Chandrasekhar, B. P.; Schmid, U.; Schmid, R.; Heimgartner, H.; Schmid, H. *Helv. Chim. Acta* **1975**, *58*, 1191−1200.
(39) Wade, T. N.; Kheribet, R. *J. Org. Chem.* **1980**, *45*, 5333−5335.
(40) Palacios, F.; Ochoa de Retana, A. M.; Gil, J. I.; Lopez de Munain, R. *Org. Lett.* **2002**, *4*, 2405−2408, and references cited therein.
(41) Kawasaki, T.; Saito, S.; Yamamoto, Y. *J. Org. Chem.* **2002**, *67*, 4911−4915.
(42) Reissig, H.-U.; Zimmer, R. *Chem. Rev.* **2003**, *103*, 1151−1196.
(43) Yu, M.; Pagenkopf, B. L. *Tetrahedron* **2005**, *61*, 321−347.
(44) Agrawal, D.; Yadav, V. K. *Chem. Commun.* **2008**, 6471−6488.
(45) De Simone, F.; Waser, J. *Synthesis* **2009**, 3353−3374.
(46) Carson, C. A.; Kerr, M. A. *Chem. Soc. Rev.* **2009**, *38*, 3051−3060.
(47) Moustafa, M. M. A. R.; Pagenkopf, B. L. *Org. Lett.* **2010**, *12*, 3168−3171.
(48) Hu, B.; Xing, S.; Ren, J.; Wang, Z. *Tetrahedron* **2010**, *66*, 5671−5674.
(49) Campbell, M. J.; Johnson, J. S.; Parsons, A. T.; Pohlhaus, P. D.; Sanders, S. D. *J. Org. Chem.* **2010**, *75*, 6317−6325.
(50) Karadeolian, A.; Kerr, M. A. *J. Org. Chem.* **2010**, *75*, 6830−6841.
(51) Yang, G.; Shen, Y.; Li, K.; Sun, Y.; Hua, Y. *J. Org. Chem.* **2011**, *76*, 229−233.
(52) Grover, H. K.; Lebold, T. P.; Kerr, M. A. *Org. Lett.* **2011**, *13*, 220−223.
(53) Lu, Z.; Shen, M.; Yoon, T. P. *J. Am. Chem. Soc.* **2011**, *133*, 1162−1164.
(54) Smith, A. G.; Slade, M. C.; Johnson, J. S. *Org. Lett.* **2011**, *13*, 1996−1999.
(55) Perreault, C.; Goudreau, S. R.; Zimmer, L. E.; Charette, A. B. *Org. Lett.* **2008**, *10*, 689−692.
(56) Ding, Q.; Wang, Z.; Wu, J. *Tetrahedron Lett.* **2009**, *50*, 198−200.

(57) Dias, D. A.; Kerr, M. A. *Org. Lett.* **2009**, *11*, 3694−3697.
(58) Hantawong, K.; Murphy, W. S.; Russell, N.; Boyd, D. R. *Tetrahedron Lett.* **1984**, *25*, 999−1000.
(59) Venkatesh, G.; Ila, H.; Junjappa, H.; Mathur, S.; Hush, V. *J. Org. Chem.* **2002**, *67*, 9477−9480.
(60) While the present paper was being prepared for publication, the transformation of 2-phenylcyclopropane-1,1-dicarboxylate into the corresponding tetraline was independently reported: Novikov, R. A.; Korolev, V. A.; Timofeev, V. P.; Tomilov, Y. V. *Tetrahedron Lett.* **2011**, *52*, 4996−4999.
(61) Ivanova, O. A.; Budynina, E. M.; Grishin, Yu. K.; Trushkov, I. V.; Verteletskii, P. V. *Eur. J. Org. Chem.* **2008**, 5329−5335.
(62) Ivanova, O. A.; Budynina, E. M.; Chagarovskiy, A. O.; Kaplun, A. E.; Trushkov, I. V.; Melnikov, M. Ya. *Adv. Synth. Catal.* **2011**, *353*, 1125−1134.
(63) Korotkov, V. S.; Larionov, O. V.; Hofmeister, A.; Magull, J.; de Meijere, A. *J. Org. Chem.* **2007**, *72*, 7504−7510.
(64) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353−1364.
(65) Fraser, W.; Suckling, C. J.; Wood, H. C. S. *J. Chem. Soc., Perkin Trans. 1* **1990**, 3137−3144.
(66) The X-ray CIF files for these structures have been deposited at the Cambridge Crystallographic Data Center (CCDC): deposition nos. CCDC 767227 (**9c**), 767228 (**2d**), 768587 (**9a**), and 779712 (**2i**). Copies of the data can be obtained, free of charge, from the CCDC, 12 Union Road, Cambridge, CB2 1EZ UK (e-mail: deposit@ccdc.cam.ac.uk; Internet: www.ccdc.cam.ac.uk).
(67) See the Supporting Information.
(68) Chagarovskiy, A. O.; Ivanova, O. A.; Rakhmankulov, E. R.; Budynina, E. M.; Trushkov, I. V.; Melnikov, M. Ya. *Adv. Synth. Catal.* **2010**, *352*, 3179−3184.
(69) Mueller, G. P.; Bateman, F. C. *J. Am. Chem. Soc.* **1952**, *74*, 5631−5632.
(70) Kobayashi, M. European Patent EP2266941, 2010.
(71) Minai, M.; Suzuki, Y.; Hamma, N.; Murayama, E. Ger. Offen. 2431561; *Chem. Abstr.* **1975**, *82*, 139717a.
(72) Sapeta, K.; Kerr, M. A. *Org. Lett.* **2009**, *11*, 2081−2084.
(73) Ivanova, O. A.; Budynina, E. M.; Chagarovskiy, A. O.; Rakhmankulov, E. R.; Trushkov, I. V.; Semeykin, A. V.; Shimanovskii, N. L.; Melnikov, M. Ya. *Chem. Eur. J.* **2011**, *11*, 11738−11742.
(74) Xu, H.; Lv, M.; Tian, X. *Curr. Med. Chem.* **2009**, *16*, 327−349.
(75) Gordaliza, M.; Garcia, P. A.; Miguel del Corral, J. M.; Castro, M. A.; Gomez-Zurita, M. A. *Toxicon* **2004**, *44*, 441−459, and references cited therein.
(76) We suppose that the more than stoichiometric loading of Lewis acid does not cause complete ring-opening of the small ring due to the competitive binding of Lewis acid to methoxy groups. It provides the appropriate concentration of a parent cyclopropane in the reaction mixture.
(77) The higher nucleophilicity of malonate ion in comparison with activated arenes in reactions with stabilized carbocations was shown definitively: Mayr, H.; Ofial, A. R. *J. Phys. Org. Chem.* **2008**, *21*, 584−595.
(78) Fang, J.; Ren, J.; Wang, Z. *Tetrahedron Lett.* **2008**, *49*, 6659−6662.
(79) Qu, J.-P.; Deng, C.; Zhou, J.; Sun, X.-L.; Tang, Y. *J. Org. Chem.* **2009**, *74*, 7684−7689.