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Dimerization of donor–acceptor cyclopropanes

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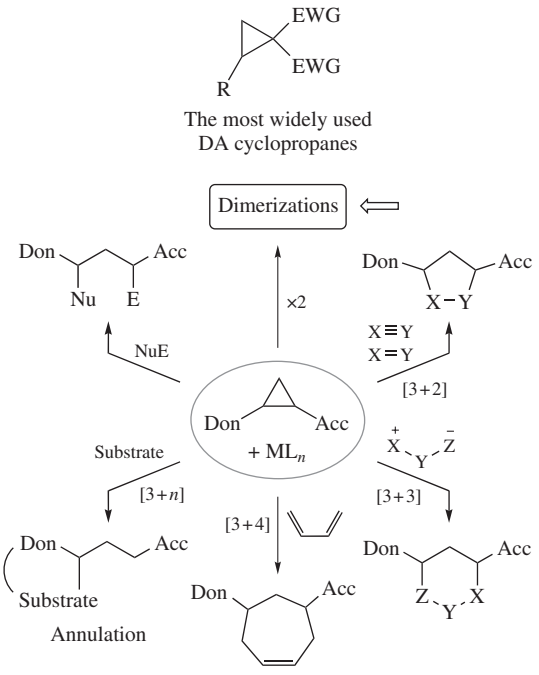
Donor–acceptor cyclopropanes are sources of 1,3-dipoles. Owing to this, they readily enter into cycloaddition and annulation with various substrates and thus play an important role in contemporary organic chemistry. In the absence of substrates, donor–acceptor cyclopropanes can undergo dimerization reactions in quite various ways which are summarized in this review.

1. Introduction

Donor–acceptor cyclopropanes (DACs) containing donor (Don) and acceptor (Acc) substituents at vicinal positions are of particular importance among diverse cyclopropane derivatives. They are characterized by capability of three-membered ring opening on treatment with Lewis acids or transition metal complexes, with generation of 1,3-dipoles that enter various cycloadditions and annulations with different counterparts (Scheme 1).[1,2]



Scheme 1

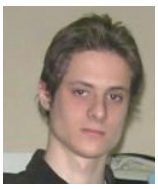
In the absence of 'counter-reactants', DACs can undergo isomerization or dimerization. This pathway of their transformation is the topic of the present review. The majority of data were obtained quite recently.

2. A general review of DAC dimerization reactions

Dimerizations are interesting and intensely studied reactions of DACs. They make it possible to construct complex systems from one rather simple substrate in one experimental stage. The regio- and diastereoselectivity of these reactions are generally very high. The mechanistic aspects of these transformations appear particularly interesting. Just a few years ago, only two examples of DAC dimerizations were known, whereas more than 20 various types of dimerization have been discovered to date, four of which are accompanied by fragmentation of intermediate species. The greatest contribution in this field was independently made by two groups of researchers, namely, by I. V. Trushkov, E. M. Budynina and O. A. Ivanova (M. V. Lomonosov Moscow State University)[3–7] and by the authors of this review (N. D. Zelinsky Institute of Organic Chemistry of the Russian Academy of Sciences).[8–15]

Due to the wide variety of DAC dimerization processes, a classification of these processes needs to be introduced in order to facilitate their examination and simplify the search for regularities. In fact, I. V. Trushkov[3,4] suggested a convenient approach based on a retrosynthetic analysis of dimers. According to this method, dimers are split into two halves matching the two original DAC molecules. These halves are represented by two formal dipoles that correspond to charge redistribution during dimerization (Scheme 2).

In the majority of known dimerization processes, DACs serve as synthetic equivalents of five different 1,2-, 1,3- and 1,4-dipoles (**I**–**V**). Moreover, some other dimerization types are known that



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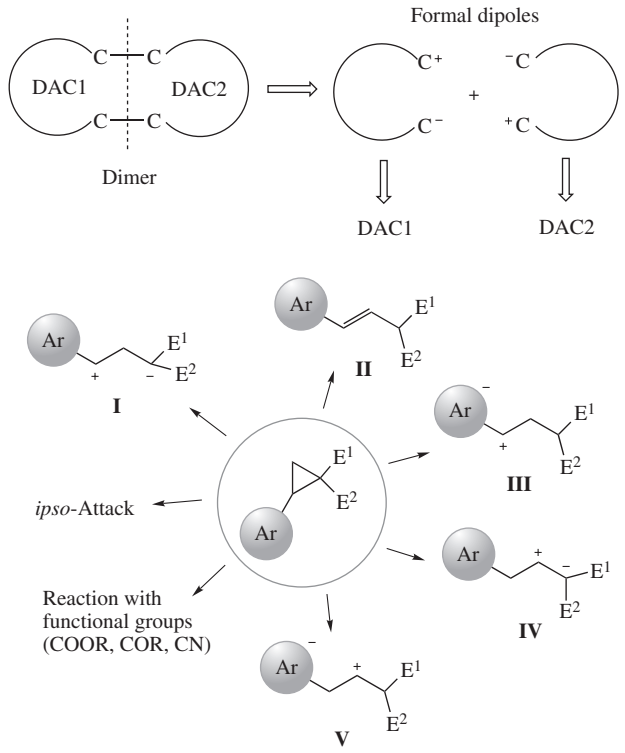
Yury V. Tomilov, Dr. Sci. (1991), Professor (2007), head of Laboratory of chemistry of diazo compounds, N. D. Zelinsky Institute of Organic Chemistry of the Russian Academy of Sciences. His scientific interests cover chemistry of carbenes, aliphatic diazo compounds and strained compounds with small rings in a molecule. He performed pioneering studies on diazocyclopropane and a new synthon, heptamethyl cycloheptatriene-1,2,3,4,5,6,7-heptacarboxylate. Lately, the main focus has been given to the transformations of donor–acceptor cyclopropanes under the effect of Lewis acids.

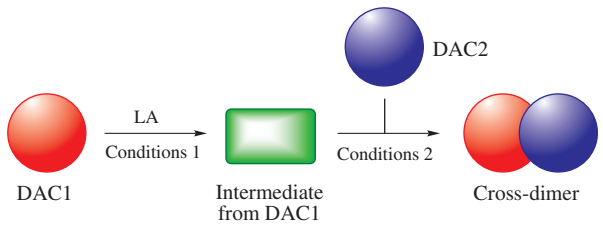


Scheme 2

do not fit into this picture, *viz.*, processes involving electron-withdrawing functional groups and dimerization accompanied by an *ipso*-attack on the aromatic substituent. So far, 9 of the 15 possible combinations have been found experimentally, namely, **I** + **I**, **I** + **II**, **I** + **III**, **I** + **V**, **II** + **III**, **II** + **IV**, **II** + **V**, **III** + **III** and **V** + **V**.

Summarizing data on DAC dimerization types, we revealed that the observed diversity of dimerization processes can be reduced to five main types (Scheme 2). The first type covers dimerization reactions that involve only atoms of the small ring but not substituents. These processes occur as [3+2]- and [3+3]-cycloaddition, or give acyclic dimers. In these reactions, DAC acts as a synthetic equivalent of 1,3-dipole **I**, and additionally as alkene **II** in [3+2]-cycloaddition. The second type of dimerization is annulation to an aromatic substituent ([3+2], [3+3] and [3+4]). In these reactions DAC mainly acts as a synthetic equivalent of 1,3-dipole **III**; *ipso*-annulation can also be attributed to this group. The third type of processes involves dimerization of species in which migration of cationic and/or anionic centers occurs to give formal even 1,2- and 1,4-dipoles **IV** and **V**. These processes also occur as [2+2]-cycloaddition, annulation ([4+2], [4+3] and [5+4]), or afford acyclic dimers. Two other types of DAC dimerization are the least studied reactions in which electron-withdrawing functional groups participate and dimerization is accompanied by fragmentation.

The above dimerization examples involve two equal DAC molecules, which imposes some limitation. It can be a good challenge to create strategies of selective cross-dimerization of two different DAC molecules.[5,10]



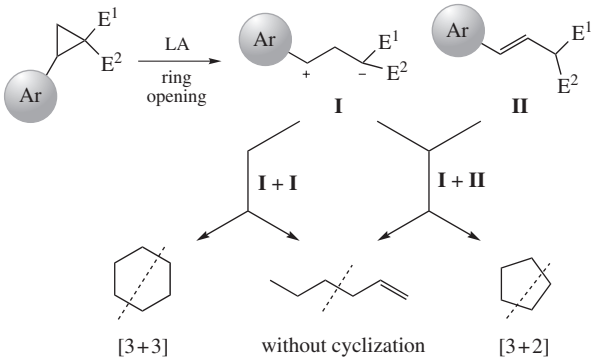
Scheme 3

A cross-dimerization strategy provides separation of the chemical reactions of two different DAC molecules in time (Scheme 3). At first, an intermediate is generated from the first DAC molecule under the action of a Lewis acid (LA) and then it is brought into reaction with the second DAC molecule.

The so broad diversity of DAC dimerization reactions undoubtedly deserves a more detailed consideration.

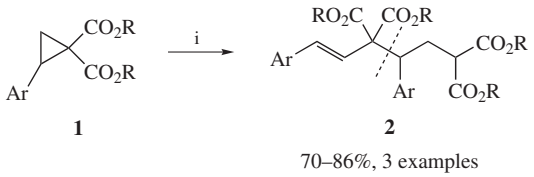
3. Formal cycloaddition and formation of linear dimers

The first and simplest type of DAC dimerization covers reactions in which the carbon frame of the dimer is formed only from atoms belonging to the three-membered ring of the original molecule. In this case, DACs, alkyl 2-arylcyclopropanedicarboxylates **1** in particular, are synthetic equivalents of 1,3-dipolar synthon **I** or isomeric alkene **II** (Scheme 4).



Scheme 4

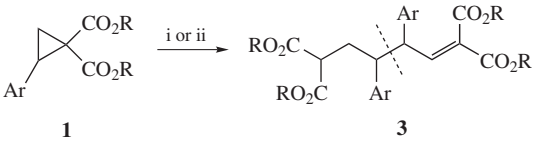
Acyclic dimers can be formed in two ways: **I** + **I** or **I** + **II** which give polysubstituted hexenes **2** and **3**, respectively (Schemes 5 and 6).[3,4] These types of dimerization were successfully performed for DACs containing polymethoxyphenyl substituents. The direction of dimerization was controlled by LA used and the reaction conditions.



70–86%, 3 examples

Ar = 2,4,6-$(MeO)_3C_6H_2$, 3-Br-2,4,6-$(MeO)_3C_6H$
R = Me, Et

Scheme 5 *Reagents and conditions*: i, $AlCl_3$, $ZnCl_2$, $BF_3{\cdot}Et_2O$ or $SnCl_4$ (100–200 mol%), –25 °C to reflux, CH_2Cl_2, 4–22 h.

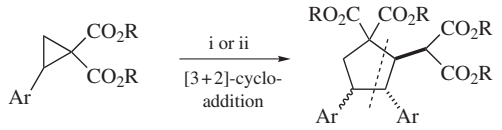


i: Ar = 2,4,6-$(MeO)_3C_6H_2$
R = Me, Et
15–25%, single diastereomer
ii: Ar = 4-$MeOC_6H_4$,
R = Me
60%, dr 61:39

Scheme 6 *Reagents and conditions*: i, $Yb(OTf)_3$ or $Sn(OTf)_2$ (5–10 mol%), reflux, CH_2Cl_2 or C_6H_6, 4–6 h; ii, MgI_2, 4 Å MS, 50–60 °C, 3 h, $EtNO_2$.

The first example of DAC cyclodimerization was found to be the formation of polysubstituted cyclopentanes **4** *via* [3+2]-cyclodimerization (**I** + **II** path) (Scheme 7).[4,8,9,16] A broad range of DACs with various aryl and heteroaryl substituents can be

involved in this reaction that occurs with high regioselectivity as well as moderate to high diastereoselectivity. Cyclopropanes with donor aryl substituents were found to efficiently undergo this reaction in the presence of moderately activating LA, such as $Yb(OTf)_3$ and $Sn(OTf)_2$ (conditions ii),[4] whereas a strong LA ($GaCl_3$) was suitable for activating the cyclodimerization of DACs substituted with less electron-abundant aryl groups (conditions i).[8,9,16]

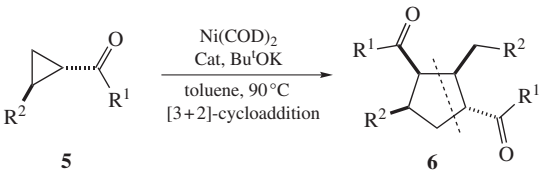


1 **4**

i: Ar = Ph, 4-FC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4, 4-MeC_6H_4, 1-naphthyl
R = Me
50–90%, dr (*trans*:*cis*) 2:1 to single diastereomer, 6 examples
ii: Ar = Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-$Me_2NC_6H_4$, 4-(pyrrolidino)C_6H_4, 4-(morpholino)C_6H_4, 2,4,6-$(MeO)_3C_6H_2$, 2-thienyl
R = Me, Et
50–80%, dr (*trans*:*cis*) 51:49 to single diastereomer, 10 examples

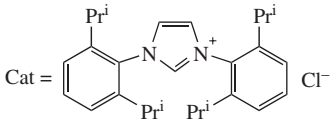
Scheme 7 *Reagents and conditions*: i, $GaCl_3$ (20 mol%), 5–20 °C, 30–60 min, CH_2Cl_2; ii, $Yb(OTf)_3$ or $Sn(OTf)_2$ (5–10 mol%), reflux, CH_2Cl_2 or PhCl, 3.5–11 h.

Alternative [3+2]-cycloaddition was carried out for cyclopropyl ketones **5** under $Ni(COD)_2$ catalysis (Scheme 8).[17] It was supposed that this dimerization proceeds *via* chemoselective cleavage of the least hindered C(1)–C(3) bond of **5**, that results in highly diastereoselective formation of cyclopentanes **6** which are regioisomeric to cyclodimers **4**.



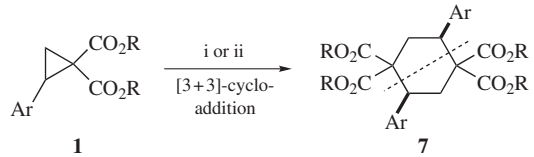
5 **6**

R^1 = Ph, 4-$MeOC_6H_4$, 4-FC_6H_4, 2-thienyl, 2-furyl
R^2 = H, Me
24–90%, dr 90:1 to 99:1, 6 examples



Scheme 8

Cyclodimerization *via* [3+3]-cycloaddition (**I** + **I** path) leads to symmetrically *cis*-substituted cyclohexanes **7** (Scheme 9).[3]



1 **7**

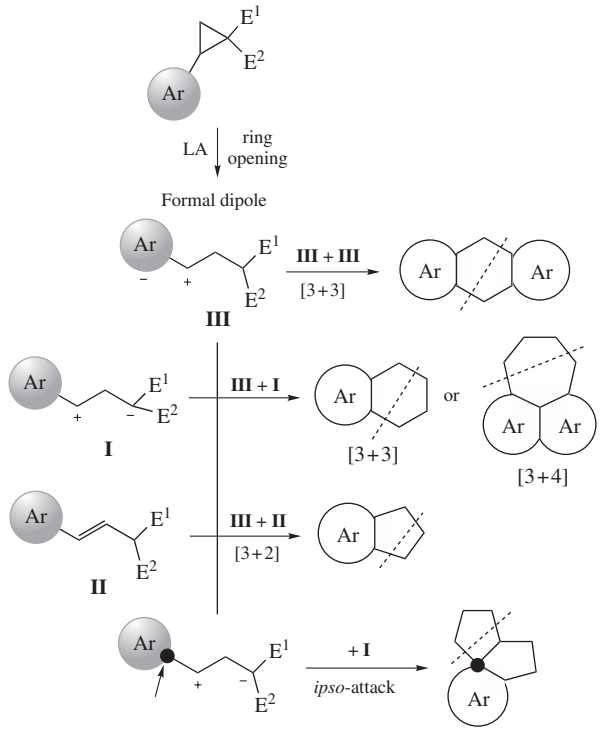
i: Ar = 2,4,6-$(MeO)_3C_6H_2$, 3-Br-2,4,6-$(MeO)_3C_6H$, 4-$MeOC_6H_4$, 4-$Me_2NC_6H_4$, 4-(pyrrolidino)C_6H_4, 4-(piperidino)C_6H_4, 4-(morpholino)C_6H_4
R = Me, Et
40–86%, single diastereomer, 10 examples
ii: Ar = 4-$MeOC_6H_4$
R = Et
62%, single diastereomer

Scheme 9 *Reagents and conditions*: i, $SnCl_4$ or $TiCl_4$ (120–240 mol%), 5–20 °C to 50–60 °C, $MeNO_2$, 2–3 to 22 h; ii, $AlCl_3$ (240 mol%), –25 °C, 70 h, $MeNO_2$.

This process, which can be considered as a double homo-version of alkene [2+2]-cyclodimerization, is typical of DACs bearing electron-abundant aryl groups, such as *o*- and *p*-methoxyphenyl, *p*-aminophenyl, *etc*.

4. Dimerization with annulation at an aromatic ring

A more complicated type of DAC dimerization includes annulation to aromatic ring *via* electrophilic aromatic substitution (Scheme 10). In this case, DACs react as synthetic equivalents of dipolar synthon **III** containing nucleophilic center at aromatic ring. In most processes, this nucleophilic center is localized at *ortho*-position (1,3-dipolar synthon), while depending on aromatic substituent DACs can react as equivalents of 1,4-dipolar synthon (Ar = 1-naphthyl) or more complicated synthons with nucleophilic center at *ipso*-position. This type of DAC reactivity was observed in their [3+2]-, [3+3]- and [3+4]-cyclodimerizations *via* **III** + **III**, **III** + **I** and **III** + **II** paths, as well as more complex processes leading to polycyclic systems.[3,5–9,18]

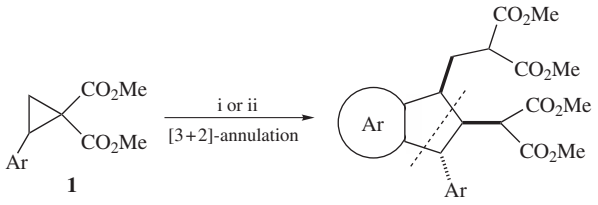


Scheme 10

Dimerization, proceeding *via* regio- and diastereoselective [3+2]-annulation (**III** + **II** path) and affording compounds **8**, was found for DACs containing electron-rich aryl and heteroaryl substituents (Scheme 11).[5,6] Depending on an aromatic group, the reaction can be triggered by moderately activating $Sn(OTf)_2$ (Ar = 3,4-dialkoxyphenyl, conditions i)[5] or strongly activating $BF_3{\cdot}Et_2O$ (Ar = 3-indolyl, conditions ii).[6] For 3-indolyl derivatives **1**, the dimerization makes it possible to construct the cyclopenta[*b*]indole skeleton (Scheme 10, *ipso*-attack).

For [3+2]-cyclodimerization *via* annulation, two-step cross-variant was developed when two different DAC molecules participate in reaction.[5] The first step is a LA-initiated isomerization of DAC to a styrylmalonate **9** followed by its reaction with the second molecule of DAC under harsher conditions (Scheme 12). [3+2]-Cross-dimerization can be extended to a wider range of DACs and, thus, has a slight priority in generality compared to homo-dimerization.

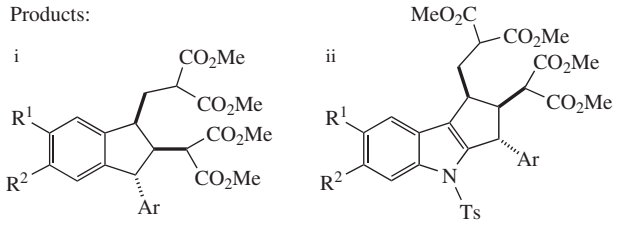
The [3+2]-dimerization with annulation to the aromatic ring can also occur with different regioselectivity (Scheme 13).[10] In such a case, though the same cyclic system is produced, the type



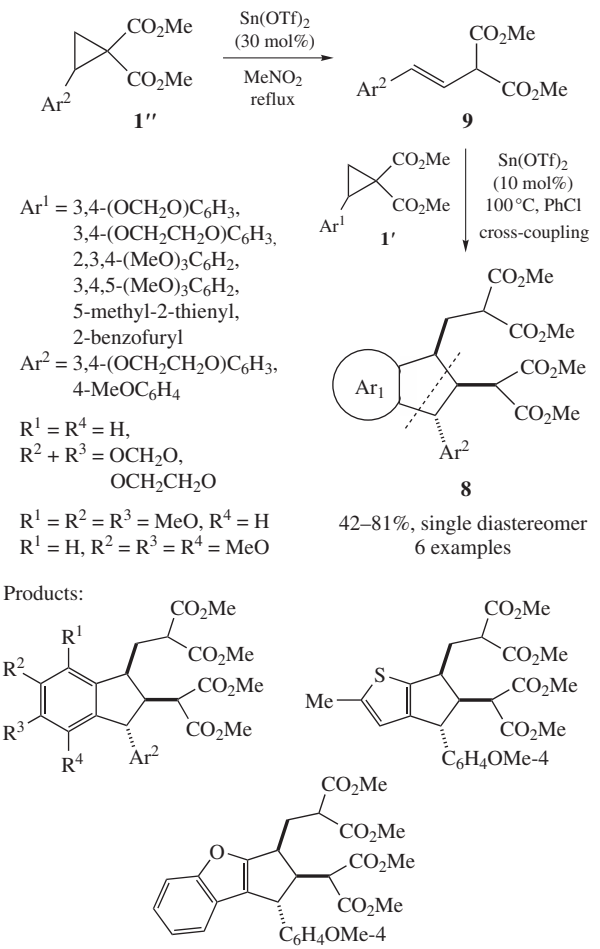
1 **8**

i: Ar = 3-R^1-4-R^2-C_6H_3
R^1, R^2 = MeO, $R^1 + R^2 = OCH_2O$, OCH_2CH_2O
67–80%, single diastereomer, 3 examples
ii: Ar = 5-R^1-6-R^2-1-tosyl-3-indolyl
R^1, R^2 = H, F, Cl, Br, CN
35–85%, single diastereomer, 6 examples

Products:



Scheme 11 *Reagents and conditions*: i, $Sn(OTf)_2$ (30 mol%), reflux, $MeNO_2$, 0.5–2 h; ii, $BF_3{\cdot}Et_2O$ (200 mol%), room temperature to reflux, 90–210 min, CH_2Cl_2.



1″ **9** **1′** **8**

Ar^1 = 3,4-$(OCH_2O)C_6H_3$, 3,4-$(OCH_2CH_2O)C_6H_3$, 2,3,4-$(MeO)_3C_6H_2$, 3,4,5-$(MeO)_3C_6H_2$, 5-methyl-2-thienyl, 2-benzofuryl
Ar^2 = 3,4-$(OCH_2CH_2O)C_6H_3$, 4-$MeOC_6H_4$

$R^1 = R^4$ = H,
$R^2 + R^3 = OCH_2O$, OCH_2CH_2O

$R^1 = R^2 = R^3$ = MeO, R^4 = H
R^1 = H, $R^2 = R^3 = R^4$ = MeO

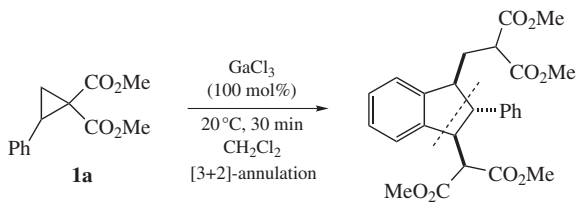
42–81%, single diastereomer
6 examples

Products:

Scheme 12

of dimer **10** formed is different. Indane **10** is obtained in this reaction as a minor dimer in low yield (the main products are cyclopentane **4** and tetralin **21**, see Schemes 7 and 23).

[3+3]-Cyclodimerization that proceeds as annulation *via* the **I + III** path is one of the more general dimerizations of DAC **1**.

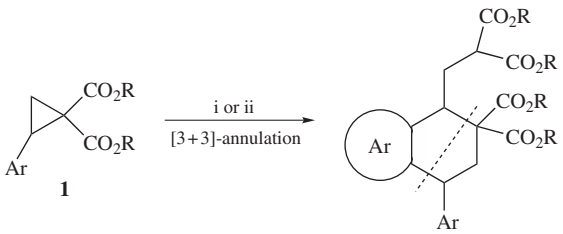


1a **10**

11%, single diastereomer

Scheme 13

The reaction gives compounds **11** which contain a six-membered carbocycle annulated to an aromatic ring (Scheme 14).[3,8,9,16,18] Depending on aryl substituents in **1**, the following methods were developed: (1) dimerization of electron-rich aryl- and heteroaryl-derived cyclopropanes **1** in the presence of strongly activating $SnCl_4$ (conditions ii);[3] (2) dimerization of **1** containing no highly nucleophilic aryl substituents under the action of the moderately activating complex $GaCl_3{\cdot}THF$ (conditions i);[8,9,16] (3) dimerization of 3-indolylcyclopropaneketones **12** also triggered by $SnCl_4$ (conditions iii).[18]



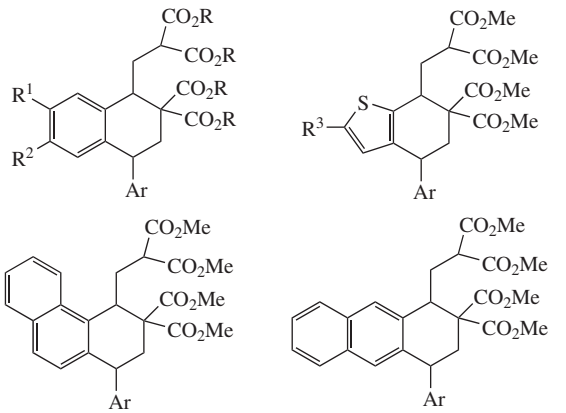
1 **11**

i: Ar = Ph, 4-FC_6H_4, 4-ClC_6H_4, 4-MeC_6H_4, 4-$MeOC_6H_4$, 1-naphthyl, 2-naphthyl
R = Me
30–90%, dr (*trans*:cis) 1:1 to 10:1, 7 examples
ii: Ar = 4-$MeOC_6H_4$, 3,4-$(MeO)_2C_6H_4$, 3,4-$(OCH_2CH_2O)C_6H_4$, 2-thienyl, 5-methyl-2-thienyl
R = Me, Et
40–90%, dr (*trans*:*cis*) 55:45 to 95:5

Products:

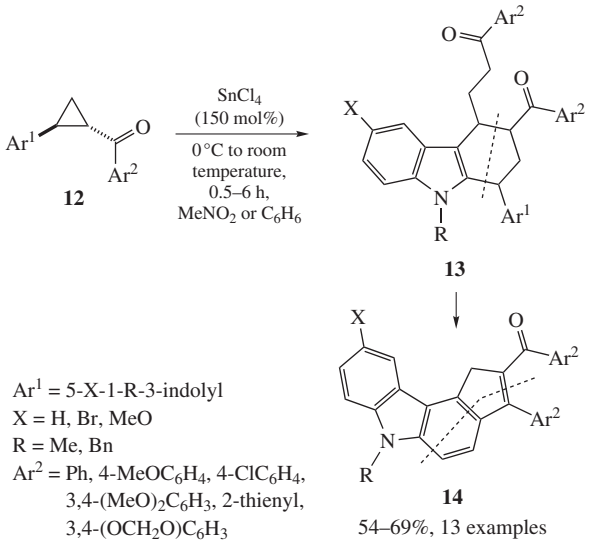
R = Me, Et
R^1 = H, OMe
R^2 = H, F, Cl, Me, OMe

$R^1 + R^2 = OCH_2CH_2O$;
R^3 = H, Me



Scheme 14 *Reagents and conditions*: i, $GaCl_3{\cdot}THF$ (100 mol%), room temperature, CH_2Cl_2, up to 24 h; ii, $SnCl_4$ (100–150 mol%), –40 °C to 50 °C, 0.5–24 h, $MeNO_2/CH_2Cl_2$.

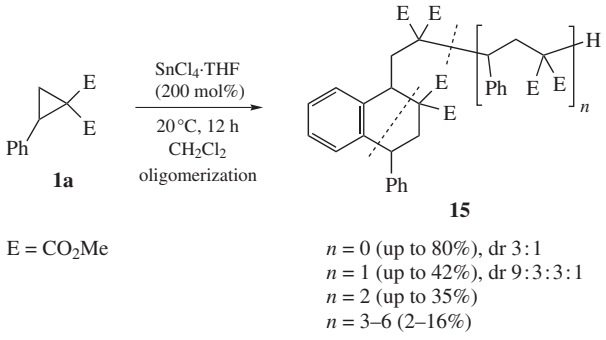
In the case of (3-indolyl)cyclopropylketones **12** the circle of substituents appears quite limited, since the initially formed tetrahydrocarbazoles **13** readily undergo fragmentation under the reaction conditions, which is accompanied by indole elimination,



Scheme 15

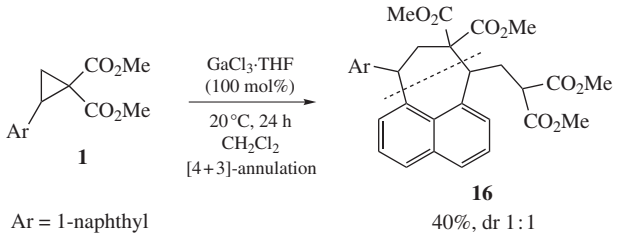
aromatization and aldol condensation to yield cyclopenta[*c*]-carbazoles **14** (Scheme 15).[18]

Activation of phenylcyclopropane diester **1a** with the $SnCl_4$·THF complex gives tetralines **15** containing an acyclic side chain which is formed *via* cyclopropane **1a** oligomerization (Scheme 16).[8] The degree of oligomerization depends on the concentration of the parent cyclopropanedicarboxylate in the reaction mixture.



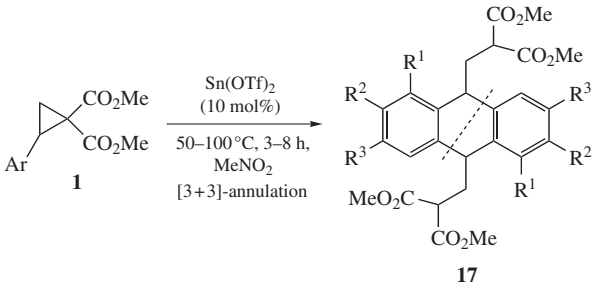
Scheme 16

Dimerization of 1-naphthyl-substituted DAC **1** occurs as [4+3]-annulation to afford the cyclohepta[*de*]naphthalene system **16** (Scheme 17).[9] The opportunity of the seven-membered ring generation in the course of this dimerization, which is analogous to [3+3]-annulation, is provided by the presence of a nucleophilic center at the α-position of the second benzene ring in the naphthalene core.



Scheme 17

The third type of dimerization, [3+3]-annulation *via* the **III** + **III** path, furnishes symmetrically substituted dihydroanthracenes **17** (Scheme 18).[3] This reaction proceeds through double aromatic electrophilic *ortho*-substitution and, thus, is typical



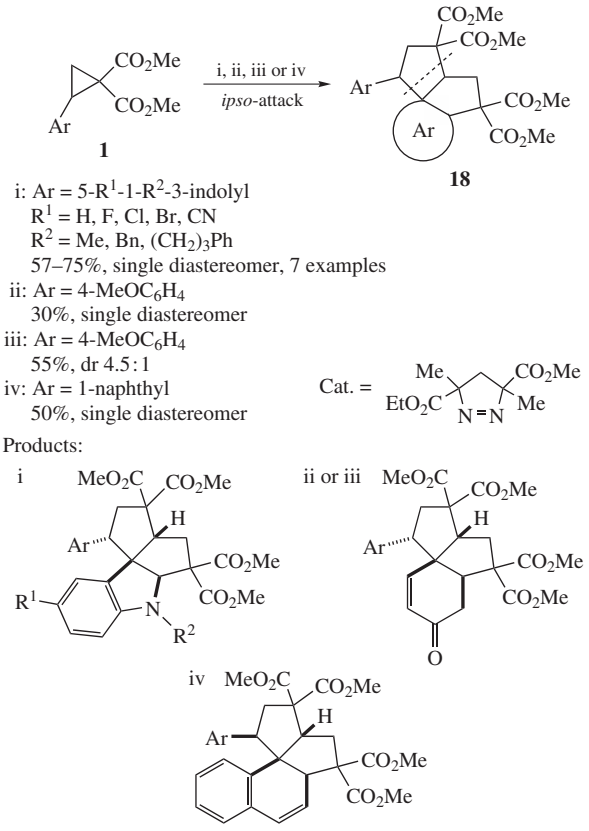
Scheme 18

of DACs containing *ortho*-unsubstituted electron-abundant aryl groups, such as polyalkoxyphenyls.

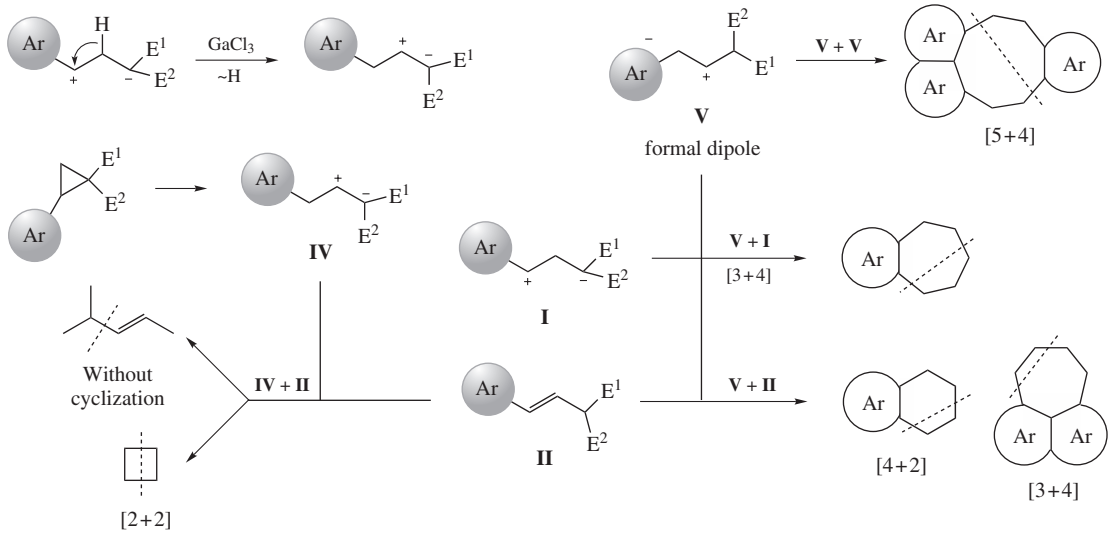
5. *ipso*-Annulation at the aromatic ring

Dimerization of 3-indolyl-,[7] *p*-methoxyphenyl,[3,9,13] and 1-naphthyl-cyclopropane diesters[9] **1** can involve electrophilic *ipso*-attack on aromatic ring that induces a cascade of transformations affording complex polycyclic systems **18** (Scheme 19). The most efficient process was found to be dimerization of 3-indolyl derivatives **1** occurring in the presence of $SnCl_4$ (conditions i) with high diastereoselectivity and yielding pentaleno[1,6-*a*,*b*]indoles **18a**.[7] For 1-naphthyl derivative **1**, the reaction proceeds with the opposite diastereoselectivity under catalysis with $GaCl_3$ together with an organocatalyst (conditions iv), that results in pentaleno[6a,1-*a*]-naphthalene **18d**.[9]

The mechanism of DAC dimerization reactions considered in this and preceding sections is very complicated but still fits



Scheme 19 *Reagents and conditions*: i, $SnCl_4$ (120 mol%), 60 °C, 2–3 h, $MeNO_2$; ii, $SnCl_4$ (150 mol%), 40 °C, 2 h, C_6H_6; iii, $GaCl_3$ (20 mol%), Cat. (20 mol%), –30 °C, 1.5 h, CH_2Cl_2; iv, $GaCl_3$ (20 mol%), Cat. (20 mol%), 30 °C, 1.5 h, CH_2Cl_2.



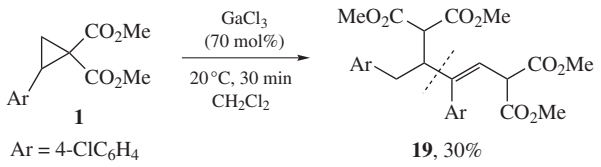
Scheme 20

well in the general concepts of organic chemistry. It is described in detail in original publications for each particular case.[3–9,16,18] All reactions are initiated by coordination of LA to acceptor groups leading to selective polarization of a C–C σ-bond between the donor and acceptor or its complete cleavage that affords 1,3-dipole **I**. Under appropriate conditions, species **I** can isomerize to styrylmalonate **II**.

6. DAC dimerization involving a 1,2-dipole

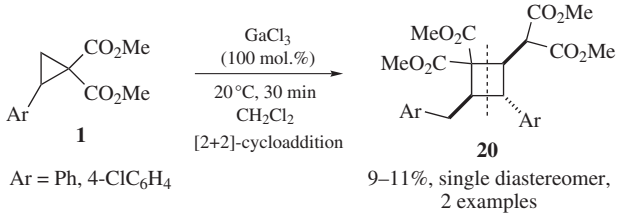
We can distinguish a set of DAC dimerizations accompanied by hydride shift, *i.e.* occurring with 'positive charge displacement' from the benzyl center of the initially generated 1,3-dipole **I**, as a separate group. Note that this pathway is only achieved if anhydrous $GaCl_3$ is used, and in this case DACs act as sources of formal even dipoles (1,2- and 1,4-) **IV** and **V**. These two dipoles undergo coupling with intermediates **I** and **II** (see section 3) to give four different types of dimers, namely, **IV** + **II**, **V** + **I**, **V** + **II** and **V** + **V**, while dimerization can yield either acyclic or cyclic dimers (Scheme 20).[10,15]

A combination of intermediates **IV** + **I** leads to aliphatic dimer **19** (Scheme 21)[16] which differs in structure from the two previously described dimers **2** and **3**.



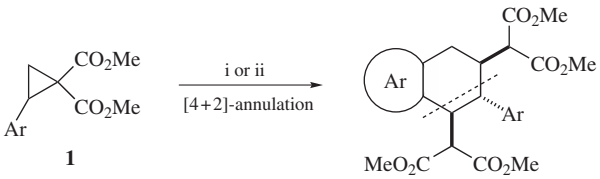
Scheme 21

The same combination of intermediates (**IV** + **I**) followed by cyclization gives [2+2]-cycloaddition products, though polysubstituted cyclobutanes **20** are only formed here as minor products (Scheme 22).[10,15,16] The main products are cyclopentane **4** and tetralin **21**, see Schemes 7 and 23.



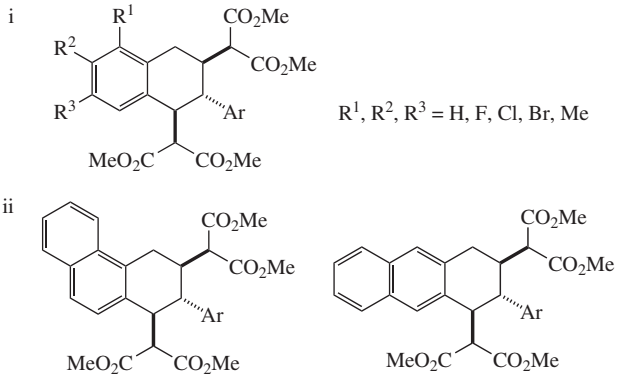
Scheme 22

More often, a 'positive charge shift' results in formal 1,4-dipoles **V**; this reaction is best studied in their coupling with styrylmalonate **II**. In this case, dimerization in the presence of $GaCl_3$ occurs with high regio- and diastereoselectivity as [4+2]-annulation with involvement of the aromatic substituent to give compound **21** (Scheme 23).[10] A limitation of this reaction is that strong electron-donating aryl substituents cannot be used under the described conditions.



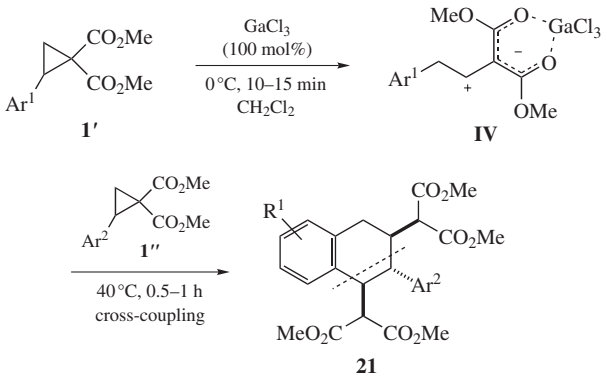
i: Ar = Ph, 4-FC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4, 4-MeC_6H_4, 3-ClC_6H_4, 3-BrC_6H_4, 2-ClC_6H_4
44–88%, single diastereomer, 8 examples
ii: Ar = 1-naphthyl, 2-naphthyl
30–79%, single diastereomer, 2 examples

Products:



Scheme 23 *Reagents and conditions*: i, $GaCl_3$ (60–75 mol%), 20–40 °C, 0.5–4 h, CH_2Cl_2; ii, $GaCl_3$ (100 mol%), 0 °C, then THF (0–100 mol%), 20 °C, 6 h, CH_2Cl_2.

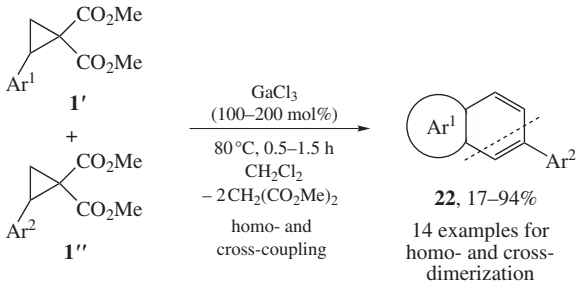
[4+2]-Cyclodimerization can be performed in the version of selective cross-coupling of two different DAC molecules.[10] In general, the same strategy is used as in the case of [3+2]-cross-annulation. At the first stage, a poorly stable 1,2-dipolar gallium complex **IV** is formed from one DAC molecule whose aryl substituent will later be involved in annulation. This complex



Scheme 24

then reacts with the second DAC molecule under more drastic conditions to provide the final tetraline **21** (Scheme 24).

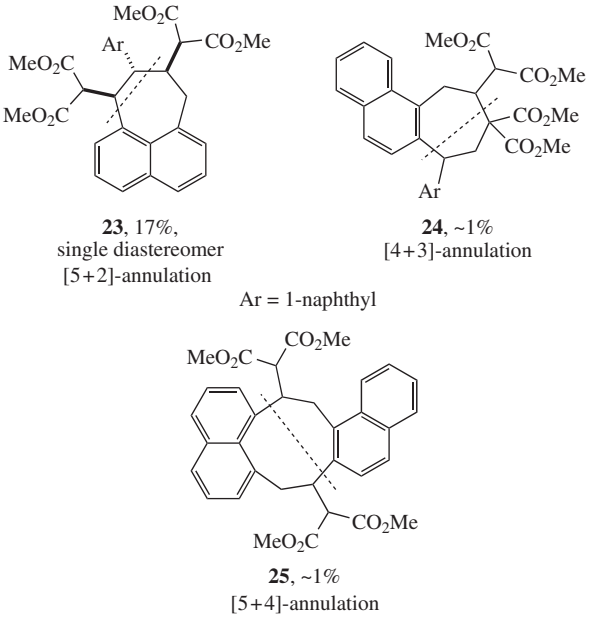
It is interesting to note that dimers **21** are not formed under more drastic conditions. Instead, the readily occurring fragmentation with elimination of two dimethyl malonate molecules produces polysubstituted naphthalenes or phenanthrenes **22** (Scheme 25).[11,12] This process can be performed both as homo-[11] and cross-dimerization.[12] In the case of cross-dimerization, both reactants are mixed at once and the selectivity of the process is controlled by the electronic properties of the aryl substituents in DAC.



Scheme 25

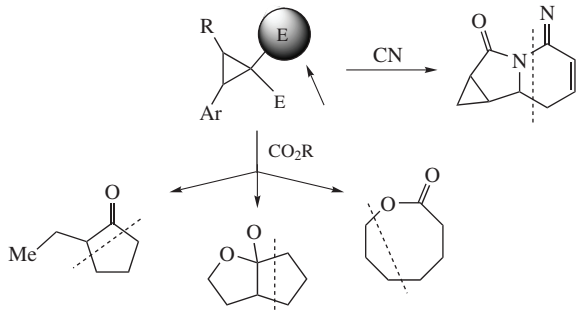
Three more types of dimers (**23**–**25**) formed in low yields as side products were found in the reaction of (1-naphthyl)cyclopropanedicarboxylate on treatment with 0.5–1.0 equiv. $GaCl_3$ at 0 °C followed by treatment of the reaction mixture with THF at 20 °C.[10]

The mechanism of DAC dimerization with 'positive charge shift' is similar to that of DAC dimerization involving 1,3-dipoles. The difference is that an additional 1,2-dipole **IV** is generated, which leads the reaction and changes the direction of dimerization. The corresponding mechanisms were considered in detail in original studies.[10,15]



7. Other types of DAC dimerization

An interesting version of DAC dimerization includes reactions involving acceptor groups, *e.g.* CO_2R and CN. In this case, oxygen- or nitrogen-containing heterocycles are formed (Scheme 26). It is rather difficult to classify them by the type of the occurring processes, especially since elimination of some molecule fragments proceeds in certain cases.



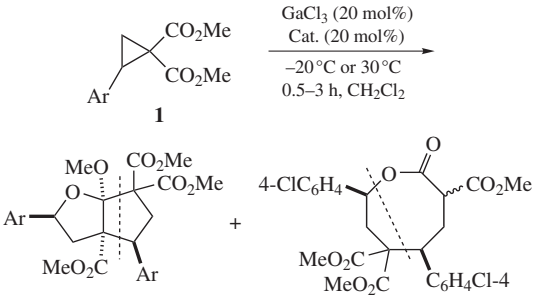
Scheme 26

In fact, under double catalysis conditions [$GaCl_3$ and tetrasubstituted 1-pyrazoline (cat.) as an organic catalyst], arylcyclopropanedicarboxylates **1** undergo diastereoselective dimerization at 30 °C to produce oxabicyclooctanes **26** (Scheme 27).[13] This process involves one of the four ester groups of DAC. The acetal moiety formed remains unchanged under the reaction conditions. However, due to the high lability of compounds **26** in acidic media, the process requires a thorough control of time and temperature, as well as special conditions of isolation of these compounds.

It is interesting to note that in case of 4-chlorophenyl substituent, this catalytic system also gives, along with oxabicyclooctane, one more type of dimer, *viz.,* eight-membered lactone **27**, as a minor product (Scheme 27).[16] This process also involves one of the ester groups.

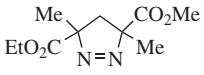
Under more drastic conditions (heating and increased amounts of $GaCl_3$ and 1-pyrazolines) no formation of oxabicyclooctanes **26** is observed. Instead, another process occurs that is accompanied by elimination of azomethine imine and formation of cyclopentanes **28** as the main reaction products (Scheme 28).[14]

The mechanism[13,14,16] of observed transformations was studied in detail by NMR spectroscopy. It includes two catalytic cycles where $GaCl_3$ and the organocatalyst (1-pyrazoline) act inde-

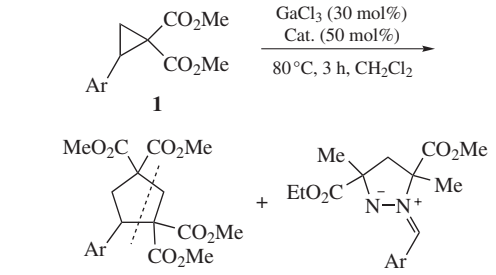


Ar = Ph, 4-FC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4, 4-MeC_6H_4, 4-$MeOC_6H_4$, 3-ClC_6H_4, 3-BrC_6H_4, 2-naphthyl

Cat. =

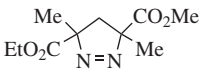


Scheme 27



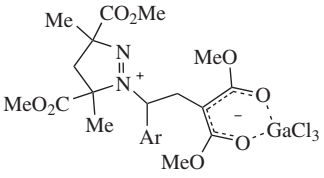
Ar = Ph, 4-FC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4, 4-MeC_6H_4, 3-ClC_6H_4, 3-BrC_6H_4, 2-ClC_6H_4, 1-naphthyl, 2-naphthyl

Cat. =



Scheme 28

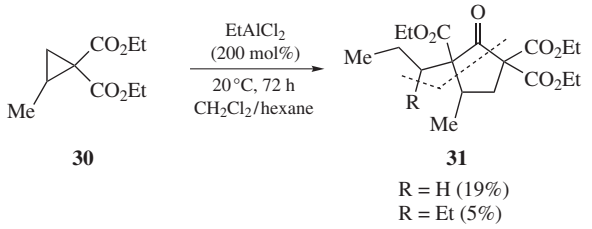
pendently and do not bind with each other. The reaction occurs *via* the key intermediate **29** that is formed from a 1,3-dipole due to addition of 1-pyrazoline.



29

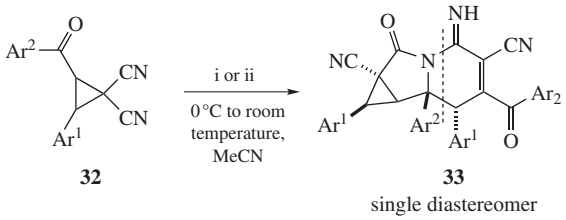
A special type of dimerization–elimination was observed in the reaction of 2-methylcyclopropanedicarboxylate **30** with $EtAlCl_2$ as LA.[19] In this case, generation of 1,3-dipole **I** and styrylmalonate **II** was followed by addition of a hydride or ethyl anion from the organoaluminium LA with the subsequent Dieckmann cyclization. Attack of the malonyl anion on one of the ester groups and abstraction of the ethoxide anion result in cyclopentanones **31** (Scheme 29), though in quite poor yields.

An interesting type of dimerization was observed for 3-aryl-2-aroylcyclopropane-1,1-dicarbonitriles **32**.[20] The reaction occurs under conditions of basic catalysis with triethylamine. Either ready cyclopropane **32** can be used or it can be generated *in situ*. Dimerization involves two cyano groups and one aroyl moiety, and a cyclopropane ring is opened only in one of the two reactants.



Scheme 29

The reaction produces fused nitrogen-containing heterocycle **33** as a single diastereomer (Scheme 30).

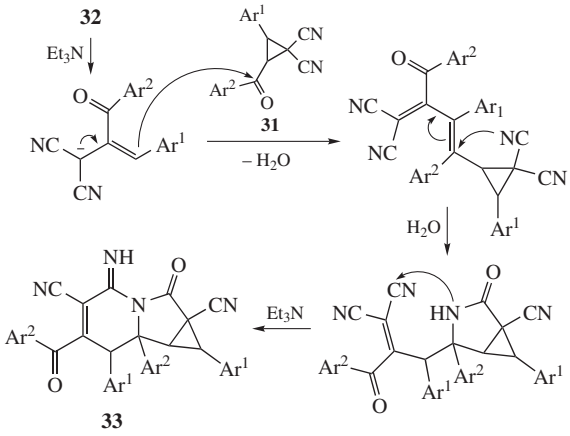


i: Ar^1 = Ph, 4-MeC_6H_4, 4-BrC_6H_4
Ar^2 = Ph, 4-ClC_6H_4
32–57%, 4 examples

ii: Ar^1 = Ph, 4-MeC_6H_4, 4-FC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4, 3-MeC_6H_4, 3-FC_6H_4, 3-ClC_6H_4
Ar^2 = Ph, 4-ClC_6H_4
43–84%, 13 examples

Scheme 30 *Reagents and conditions*: i, Et_3N (100 mol%), 0–10 °C, 12 h, MeCN; ii, Et_3N (150 mol%), room temperature, 24 h, MeCN, then 0–10 °C, 12 h. Cyclopropane **32** was synthesized *in situ* from corresponding $Ar^1CH{=}C(CN)_2$ and $Ar^2COCH_2Py^+Br^-$.

The mechanism of the observed transformations is presented in Scheme 31.



Scheme 31

8. Control of the types of dimers formed

To control the selectivity of DAC dimerization, in particular, that of 2-arylcyclopropanedicarboxylates, one should take into consideration the electronic and steric properties of the aromatic substituent, the nature of LA and the process conditions (temperature, solvent, time) (Figure 1). For example, only two dimers out of nearly twenty can be formed for some (het)aryl substituents (*e.g.* indolyl, thienyl, alkoxyphenyl), whereas numerous directions of dimerization are observed for other substituents (phenyl-, *p*-substituted phenyls, naphthyls). The Lewis acidity strongly affects the dimerization process. Some LAs, *e.g.* $Yb(OTf)_3$ and $GaCl_3$–cat., are well suitable for a certain process type characteristic of them, and the nature of dimers is the same for various aryl substituents. In case of nonspecific LAs ($SnCl_4$),

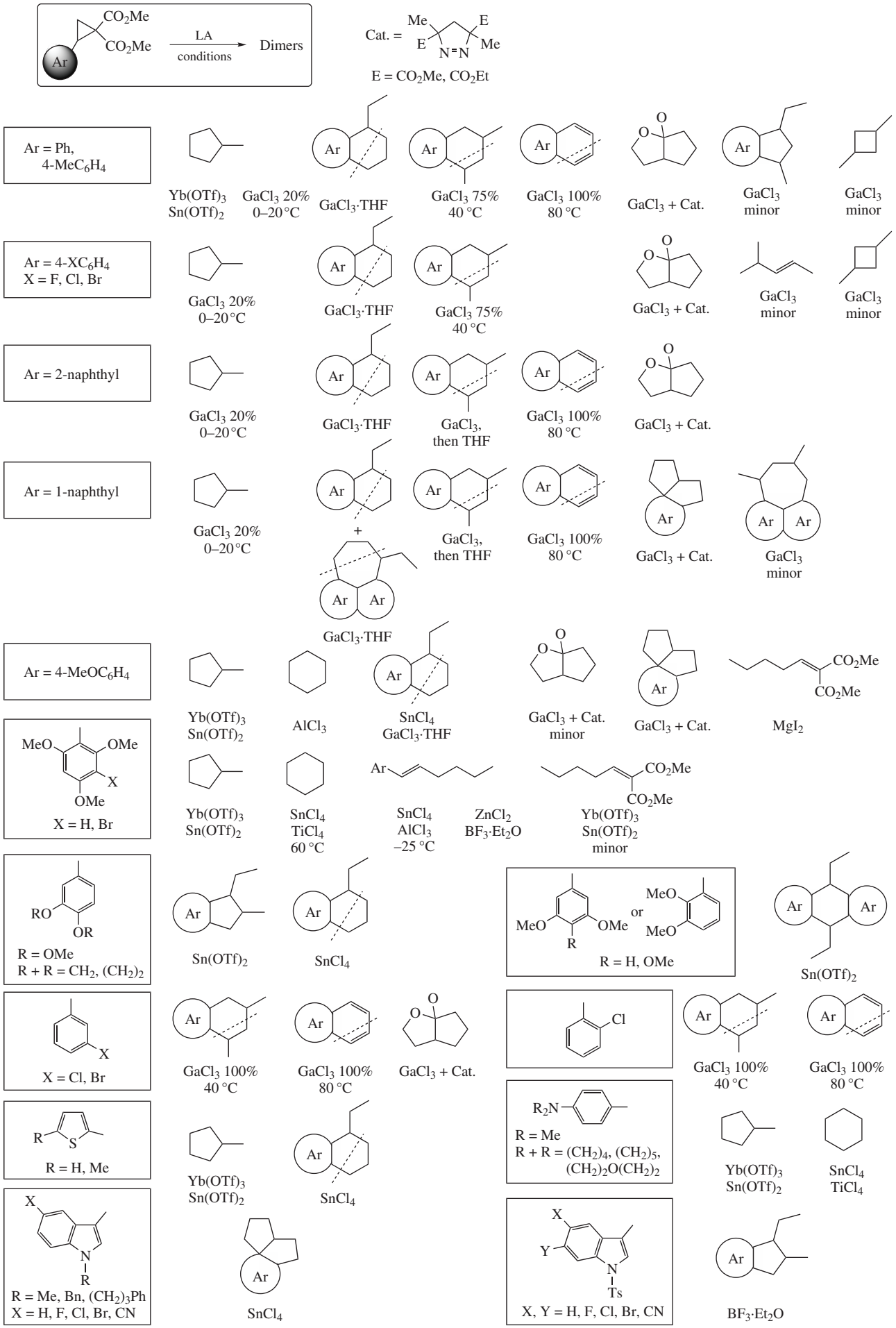


Figure 1 Classification of dimerization products of arylcyclopropanedicarboxylates depending on the nature of the aryl substituent.

formation of a number of dimers is possible. Sometimes, even an insignificant modification of conditions results in a total change of the reaction pathway ($GaCl_3$). Therefore, the process selectivity can be controlled and a certain required type of dimers can be created only by using a combination of all the three methods. Figure 1 presents the generalized optimum conditions of the processes and types of major dimers formed from 2-arylcyclopropane-1,1-dicarboxylates.

9. Conclusion

The data presented above demonstrate how diverse and interesting are the reactions of DAC dimerization that proceed under the action of LAs in the absence of trapping agents. DAC dimerization processes occur as formation of linear dimers, cycloaddition and annulation, reactions involving functional groups and cyclization into heterocycles. Their regio- and diastereoselectivity are generally very high. Based on a single cyclopropane-containing substrate, it is possible to create complex carbo- and hetero-, mono- and polycyclic systems in one experimental stage. Therefore, DAC dimerization reactions undoubtedly deserve an important place in organic synthesis.

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