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Gallium trichloride-mediated reactions of 'double' donor–acceptor cyclopropanes with alkenes and dienes

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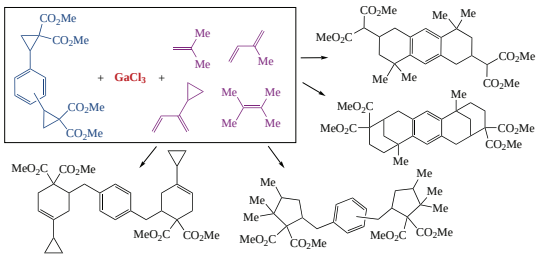
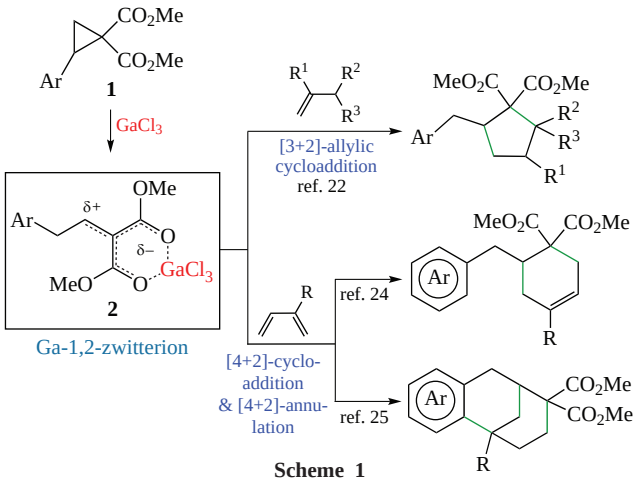
The reactions of 'double' donor–acceptor cyclopropanes containing a *p*- or *m*-phenylene moiety with alkenes or dienes in the presence of $GaCl_3$ comprise formation of gallium 1,2-zwitterionic intermediates, the structure of final products being substrate dependent. In contrast to the *para*- or *meta*-isomers, reaction of 2,2′-(1,2-phenylene)bis(cyclopropane-1,1-dicarboxylate) does not involve alkene and affords isomeric tricyclo[6.2.2.0^{2,7}]dodeca-2,4,6-triene-9,9,11,11-tetracarboxylate, a product of intramolecular rearrangement.



Keywords: 'double' donor–acceptor cyclopropanes, gallium trichloride, alkenes, dienes, cycloaddition, annulation, polycyclic carbocycles.

Donor–acceptor cyclopropanes (DACs),[1–6] and 2-arylcyclopropane-1,1-diesters **1** in particular, would undergo ring opening in the presence of Lewis acids with involvement of the resulting 1,3-zwitterionic intermediates in various chemical reactions.[7–14] Reactions occurring in the presence of equimolar amounts of Ga^{III} halides represent a special case.[15–19] In this instance, 1,3-zwitterions generated initially undergo 1,2-hydride shift to give fairly stable 1,2-zwitterionic intermediates **2** that are, in essence, complexes of alkylidenemalonates with Ga^{III} halides (Scheme 1).[17–21] The diverse reactivity of 1,2-zwitterionic gallium complexes has been widely studied in our laboratory in the past decade.[20–25] Of the processes studied, the reactions with unsaturated substrates that result in the construction of various carbocyclic structures *via* cycloaddition[22–25] and annulation[20,21,25] are of particular interest (see Scheme 1).

Apart from the classical 2-arylcyclopropane 1,1-diesters **1**, the so-called 'double' DACs in which two cyclopropane moieties are bound to one benzene ring are of certain interest. However, very few substrates of this kind are known to date. For example, Tang used tetraethyl 2,2′-(1,4-phenylene)bis(cyclopropane-1,1-dicarboxylate) as a monomer for synthesizing new polyesters by opening cyclopropane rings in the presence of $Cu(OTf)_2$/bioxazoline complex.[26] Budynina reported an example of cyclopropane ring opening in tetramethyl 2,2′-(1,3-phenylene)-bis(cyclopropane-1,1-dicarboxylate) in the presence of the azide ion to give the corresponding bis-azide derivative[27] (see Online Supplementary Materials, Scheme S2).



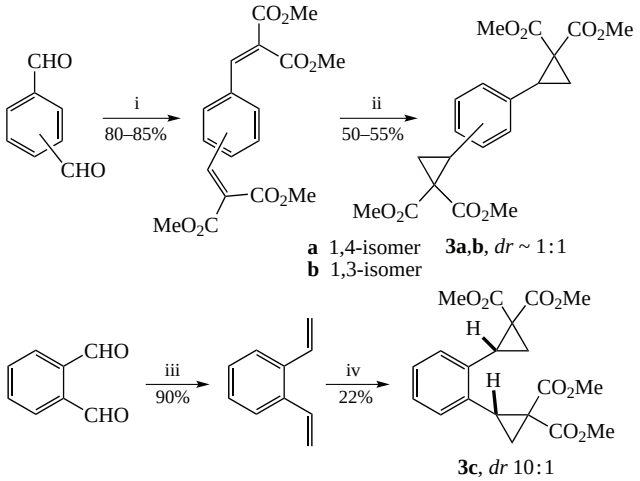
Scheme 1

It should be noted that the reactions described above formally occur *via* the formation of the corresponding 1,3-zwitterions. Data on the use of 'double' DACs in reactions with unsaturated compounds and, in particular, as precursors for the generation of 1,2-zwitterion complexes were not found to date.

Therefore, we decided to study the reactivity of 'double' DACs containing a phenylene moiety with alkenes and dienes, using them primarily as possible sources of 1,2-zwitterionic intermediates. For this end, we obtained all the three isomers of 2,2′-phenylenebis(cyclopropane-1,1-dicarboxylates) **3a–c** with *para*-, *meta*-, and *ortho*-positions of cyclopropane rings at the benzene ring.

The starting DACs **3a**,**b** were synthesized in a 'classical' way using the Knoevenagel condensation of 1,4- or 1,3-benzenedicarbaldehydes with malonic ester followed by the Corey–Chaykovsky cyclopropanation of the resulting methylidene malonates.[27–29] The *ortho*-isomer **3c** was synthesized by the Wittig reaction of phthalic dialdehyde followed by Rh-catalyzed cyclopropanation of the resulting 1,2-divinylbenzene with dimethyl diazomalonate (Scheme 2, Figure 1).†

† *Crystal data for* **3c**. $C_{20}H_{22}O_8$, M = 390.37, monoclinic, space group *Pn*, 100 K, a = 8.6811(2), b = 8.2465(2) and c = 13.7461(4) Å, α = 90°, β = 93.8170(10)°, γ = 90°, Z = 2, V = 981.88(4) Å^3, d_{calc} = 1.320 g cm^{-3}.



Scheme 2 *Reagents and conditions*: i, $CH_2(CO_2Me)_2$, piperidine, AcOH, PhH; ii, $Me_3S^+(O)I^-$, NaH, DMSO; iii, Ph_3PCH_3Br, NaH, THF; iv, $N_2=C(CO_2Me)_2$, $Rh_2(esp)_2$, CH_2Cl_2, room temperature.

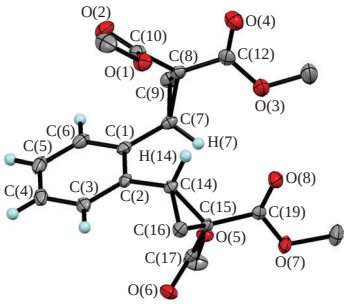
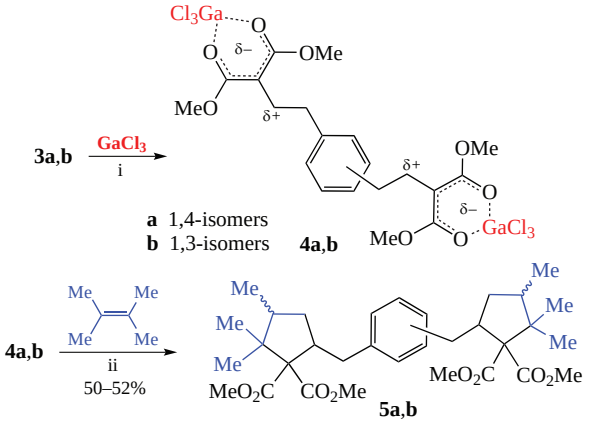


Figure 1 X-ray crystallographic data for *ortho*-isomer **3c**.

As we have shown previously,[20–25] the reaction of dimethyl 2-phenylcyclopropane-1,1-dicarboxylate **1** (Ar = Ph, see Scheme 1) with an equimolar amount of anhydrous $GaCl_3$ even at 0 °C for 10 min results in gallium 1,2-zwitterionic complex **2** (Ar = Ph) in a yield of no less than 95%. It is subsequently involved in various reactions, including those with unsaturated substrates. 1,2-Zwitterionic intermediates are also formed from *para*- or *meta*-alkyl- or halo-substituted DACs under nearly the same conditions. If there are acceptor substituents at the aromatic ring or any *ortho*-substituents, the formation time of 1,2-zwitterionic intermediates **2** increases to 1.5 h, or the process has to be performed at room temperature. We have found that in the case of 'double' DACs **3a**,**b** the most acceptable conditions for the generation of 'double' 1,2-zwitterionic complexes with $GaCl_3$ (2.3 equiv.) are to conduct the process at room temperature for 30 min, which is confirmed by their almost complete conversion to *p*- or *m*-bis[3,3-bis(methoxycarbonyl)prop-2-en-1-yl]benzenes in the presence of methanol. Further, an excess of an unsaturated substrate is added to the resulting complexes **4a**,**b**, and the reaction is carried out under conditions depending on the nature of the substrate used.

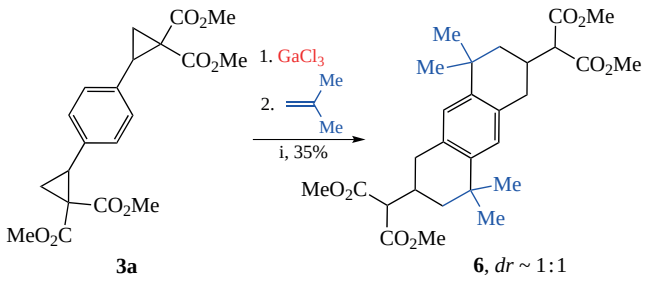
The first example of successful trapping of a 'double' 1,2-zwitterionic gallium complex **4a** was found in its reaction with tetramethylethylene. Refluxing the reaction mixture in dichloromethane for 1.5 h gave a product of independent addition of two tetramethylethylene molecules to both reaction centers of the zwitterionic intermediate **4a**. In this case, by analogy with DAC **1a**, the reaction occurs as 'inverted' [3 + 2]-cycloaddition[22] where the reactive moiety of the gallium complex acts as a two-carbon synthon and tetramethylethylene acts as a three-carbon one (Scheme 3). The target bis-adduct **5a** was isolated in ~52% yield as a mixture of diastereomers (~1.3 : 1.3 : 1 : 1). The reaction of tetramethylethylene with gallium complex **4b** occurs similarly to afford regioisomeric bis-adduct **5b** in ~50% yield.



Scheme 3 *Reagents and conditions*: i, $GaCl_3$ (2.3 equiv.), CH_2Cl_2, room temperature, 30 min; ii, $Me_2C=CMe_2$ (6 equiv.), 40 °C, 1 h.

The reaction of gallium complex **4a** with 2-methylpropene occurs in a different manner. In this case, the carbocationic center of gallium complex **4a** directly attacks the unsubstituted C atom of the double bond in the alkene, while the resulting tertiary carbocation alkylates the aromatic ring by electrophilic substitution.[20,21] Unfortunately, it is not the only process and it is complicated by trapping of the resulting tertiary carbocation by other 2-methylpropene molecules to give unidentified compounds. As a result, the yield of the target tetramethyl (octahydroanthracene-2,6-diyl)dimalonate **6** amounts to 35% (Scheme 4).

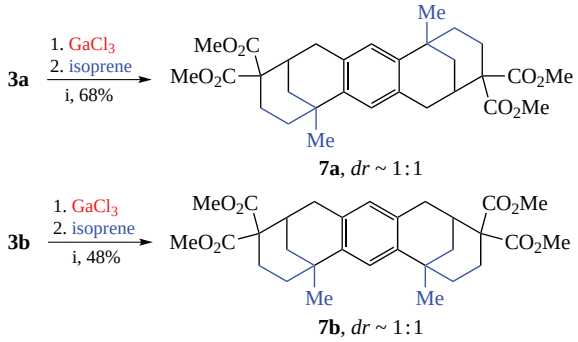
Further, we studied the reactions of gallium 1,2-zwitterionic complexes **4a**,**b** with conjugated dienes taken in 5–6-fold excess to make the reaction proceed more completely at both reactive moieties. The most successful result was obtained in the case of 'double' DAC **3a**, *i.e.*, in the reaction of 1,2-zwitterionic intermediate **4a** with isoprene. If the reaction is performed in dichloromethane under reflux conditions, it occurs as a one-pot cascade ionic [2 + 4]-cycloaddition/Friedel–Crafts type cyclization process[24,25] to give pentacyclic bis-adduct **7a** with a benzene ring in the centre in up to 68% yield (Scheme 5, Figure 2).‡ The reaction of complex **4b** occurs similarly and



Scheme 4 *Reagents and conditions*: i, $GaCl_3$ (2.3 equiv.), then $Me_2C=CH_2$, CH_2Cl_2, 0 °C, 30 min.

A colourless single crystal with dimensions of 0.22 × 0.13 × 0.1 mm was selected and the intensities of 13793 reflections were measured using a Bruker QUEST diffractometer (graphite monochromator, φ and ω scan mode), λ[MoKα] = 0.71073 Å, μ = 0.103 mm^{-1}, $2\theta_{max}$ = 61.074°. After merging of equivalents and absorption correction, 4956 independent reflections (R_{int} = 0.0299) were used for the structure solution and refinement. Final R factors: R_1 = 0.0365 [4956 reflections with $I > 2\sigma(I)$], wR_2 = 0.0934 (all reflections), GOF = 1.083.

‡ *Crystal data for* **7a**. $C_{15}H_{19}O_4$, M = 263.30, monoclinic, space group $P2_1/c$, 100 K, a = 11.0167(9), b = 5.8484(5) and c = 20.3245(16) Å, α = 90°, β = 92.414(5)°, γ = 90°, Z = 4, V = 1308.35(19) Å^3, d_{calc} = 1.337 g cm^{-3}.



Scheme 5 *Reagents and conditions*: i, $GaCl_3$, then $H_2C{=}CHC(Me){=}CH_2$, CH_2Cl_2, 40 °C, 1 h.

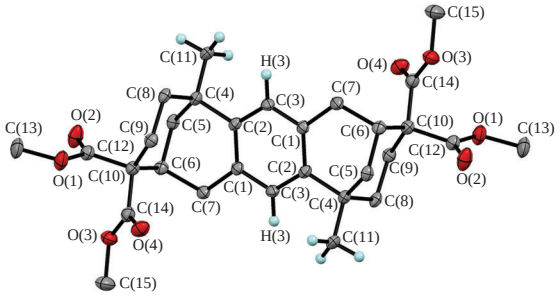
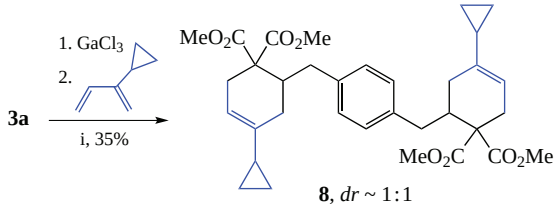


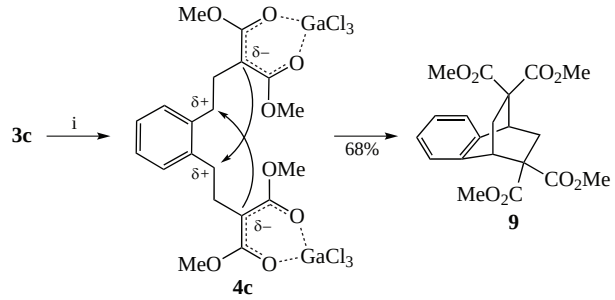
Figure 2 X-ray crystallographic data for **7a**.

results in pentacyclic bis-adduct **7b** in 48% yield. Both bis-adducts **7a**,**b** are formed as mixtures of two diastereomers in an approximately equal ratios. If the reaction of gallium complex **4a** with isoprene is performed at 18 °C, a complex mixture of products cycloaddition and annulation is obtained (see Online Supplementary Materials, Scheme S3).

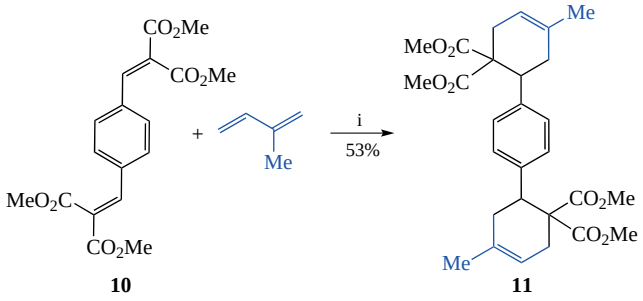
In contrast to isoprene, the reaction of 1,2-zwitterionic intermediate **4a** with 2-cyclopropylbutadiene occurs more



Scheme 6 *Reagents and conditions*: i, $GaCl_3$ (2.3 equiv.), then $H_2C{=}CHC(c\text{-}C_3H_5){=}CH_2$ (5 equiv.), CH_2Cl_2, 40 °C, 1 h.



Scheme 7 *Reagents and conditions*: i, $GaCl_3$, CH_2Cl_2, room temperature, 15 min.



Scheme 8 *Reagents and conditions*: i, $AlCl_3$, CH_2Cl_2, 40 °C, 1 h.

selectively, and even at 25 °C bis-cyclohexene adduct **8** can be obtained almost without an admixture of aromatic annulation products (Scheme 6). It is important to note that under these conditions, cyclopropane ring opening in the starting 2-cyclopropylbutadiene was not observed, unlike in the reaction of gallium complex **2** (Ar = Ph, see Scheme 1) with the same 2-cyclopropylbutadiene.[24,25]

In contrast to the *para*- and *meta*-isomers **3a**,**b**, *ortho*-isomer **3c** undergoes opening of both cyclopropane rings in the presence of $GaCl_3$ rather quickly with a 'cross' cyclization process to give an isomeric tetraester with a benzobicyclo[2.2.2]octane frame **9** (Scheme 7). Obviously, olefinic substrate is not involved in this transformation.

It is known that the formation of substituted cyclohex-3-ene-1,1-dicarboxylates also occurs in reactions of arylmethylidene-malonates with conjugated dienes. This formal [4+2]-cyclo-addition process is catalyzed by $AlCl_3$ and occurs under mild conditions.[30] In order to find out how 'double' methylidene-malonates would behave in reactions with unsaturated compounds, we studied the reaction of 1,4-phenylenebis-(methanylylidene)dimalonate **10** with isoprene in the presence of $AlCl_3$. In fact, the reaction also corresponded to the formal [4+2]-cycloaddition at both unsaturated moieties and afforded bis-cyclohexenylbenzene **11** in 53% yield (Scheme 8).

In conclusion, we developed the reactions of 'double' DACs containing *p*-, *m*-, and *o*-phenylene moiety with alkenes and dienes in the presence of $GaCl_3$. These DACs act as sources of gallium 1,2-zwitterionic intermediates with opening of both cyclopropane rings, which in the case of the *para*- or *meta*-isomers react with alkenes and dienes *via* [3+2]- and [4+2]-cycloaddition/annulation pathways to form polycyclic carbocycles. In contrast, the *ortho*-analogue reacts differently to give intramolecular [3+3]-adduct.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2023.01.009.

A colorless single crystal with dimensions of 0.13 × 0.12 × 0.1 mm was selected and the intensities of 12520 reflections were measured using a Bruker QUEST diffractometer (graphite monochromator, φ and ω scan mode), λ[MoKα] = 0.71073 Å, μ = 0.096 mm^{-1}, $2\theta_{max}$ = 52.182°. After merging of equivalents and absorption correction, 2590 independent reflections (R_{int} = 0.0744) were used for the structure solution and refinement. Final R factors: R_1 = 0.0653 [2590 reflections with $I > 2\sigma(I)$], wR_2 = 0.1831 (all reflections), GOF = 1.073.

The structures of **3c** and **7a** were solved by the direct method and refined in anisotropic approximation for non-hydrogen atoms. The hydrogen atoms of methyl, methylene and aromatic moieties were calculated according to the idealized geometry and refined with constraints applied to C–H bond lengths and equivalent displacement parameters [U_{eq}(H) = 1.2 U_{eq}(X), X is the central atom of the XH group; U_{eq}(H) = 1.5 U_{eq}(Y), Y is the central atom of the YH group]. All the structures were solved with the ShelXT[31] program and refined with the ShelXL[32] program. Molecular graphics were drawn using the OLEX2[33] program.

CCDC 2172101 and 2172102 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

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