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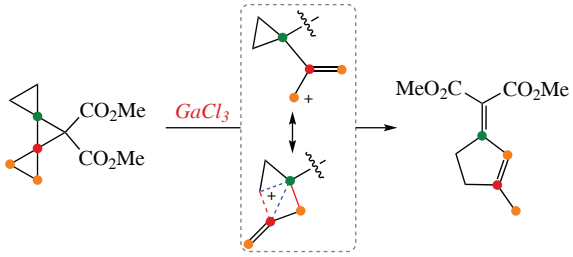
Lewis acid mediated rearrangements of dispiro[2.1.2.0]heptane-4,4-dicarboxylate: evidence for non-classical behavior of 2-cyclopropylallyl carbocation

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Dimethyl dispiro[2.1.2.0]heptane-4,4-dicarboxylate containing three spiro-linked cyclopropane rings has been proven to be a valuable building block for the Lewis acid catalyzed rearrangements to give a set of products involving the cleavage of two or three cyclopropane rings. Among various Lewis acids tested, $GaCl_3$ was able to selectively generate a non-classical 2-cyclopropylallyl carbocation that further isomerized to produce (3-methylcyclopent-2-enylidene)malonate as almost exclusive product.



Keywords: dispiro[2.1.2.0]heptane-4,4-dicarboxylate, Lewis acids, methylenespiro[2.3]hexanes, ring expansion, carbocation rearrangements, non-classical carbocations.

Donor–acceptor cyclopropanes (DACs) are widely used in modern synthetic chemistry as valuable building blocks due to their unique reactivity caused by the presence of vicinally-positioned electron-donor and electron-withdrawing substituents on the cyclopropane ring.[1–3] Most common Lewis acid mediated ring-opening transformations of DACs involve reactions of nucleophilic or electrophilic addition, (3+*n*)-cycloadditions, annulations and other transformations, where DAC is serving as a formal synthetic equivalent of 1,3-dipole.[4–10]

Donor–acceptor cyclopropanes containing one or more additional small cycles are of particular interest due to their increased ring strain energy that should facilitate ring-opening rearrangements to cause additional more complicated cascade transformations. For instance, the reactions of spiro[2.2]pentanes ('monospiro-DACs') are well documented proceeding either with the second cyclopropane ring retained,[11–17] or with the cleavage of both of them.[18,19] Rearrangements of polyspiroalkanes are also known and include only carbocationic[20–25] and radical transformations;[26] while the reactions of polycyclic DACs *via* zwitter-ionic intermediates are limited. We have recently demonstrated that DACs containing additional cycloalkane scaffolds either in linearly-arranged substituention or in a spiro-coupled fashion exhibited a wide variety of synthetic pathways. These include transformations *via* classical 1,3-zwitter-ionic intermediates proceeding with the only one three-membered ring cleavage, as well as more complex cascade rearrangements with the both rings cleaved *via* the formal generation of 1,*n*-zwitter-ionic intermediates (*n* = 2–6).[27–30]

In the current work, we have studied Lewis acid mediated rearrangements of a more complex spirocyclic scaffold consisting of three spiro-coupled cyclopropanes, namely, dimethyl dispiro[2.1.2.0]heptane-4,4-dicarboxylate **1** (Scheme 1). In fact, dispiroheptane **1** readily reacted with 1–2 equiv. of $TiCl_4$ and $SnCl_4$ with the full consumption over 1 h to afford malonate derivatives of 2-cyclopropylallyl chloride **2** and 4-methylene-spiro[2.3]hexane **3** indicating that two of the three cyclopropane rings were cleaved (Scheme 1, Table 1, entries 1, 2).

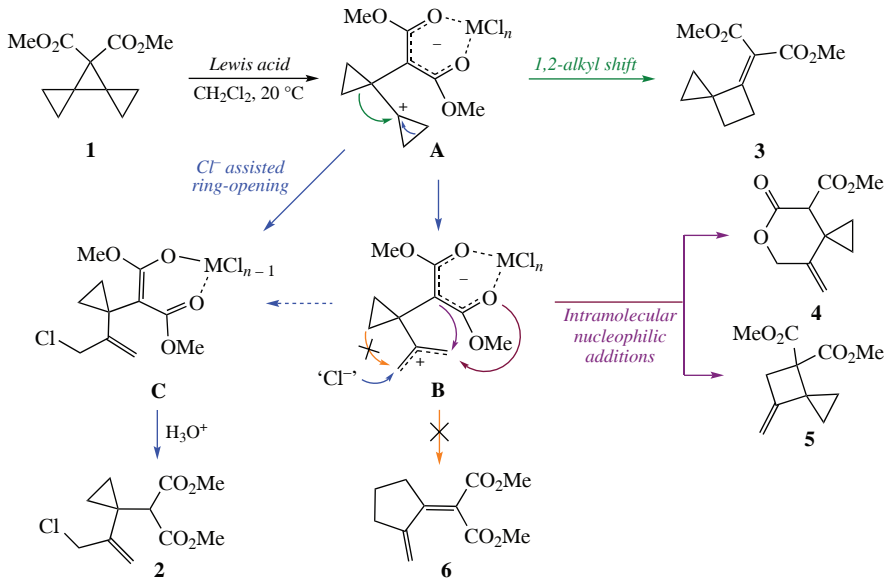
Evidently, the formation of methylenecyclobutane **3** is the result of 1,2-alkyl shift in the intermediate **A** similarly to the rearrangements of spiro[2.*n*]alkane-1,1-dicarboxylates that we recently studied.[30] In turn, allyl chloride **2** is the product of formal nucleophilic addition of Lewis acid derived Cl^- to the allyl intermediate **B** that might exist in the reaction mixture as a complex with Lewis acid (see Scheme 1, structure **C**). Replacing these Lewis acids with $EtAlCl_2$ and Et_2AlCl led to significant increase in the reaction selectivity affording allyl chloride **2** as the predominant product (see Table 1, entries 3, 4). The use of 0.1 equiv. of $Yb(NTf_2)_3$ or $HNTf_2$ (which do not contain nucleophilic anions) as the catalysts prevents the formation of allyl chloride **2** in favor of lactone **4** as the product of the *O*-cyclization of intermediate **B** (entries 6, 7). Furthermore, in the case of $Yb(NTf_2)_3$ the yield of the *C*-cyclization product,

Table 1 Product distribution in Lewis acid mediated rearrangements of **1**.[a]

Entry	Lewis acid (equiv.)	Yield (%)[b]			
		2	**3**	**4**	**5**
1	$TiCl_4$ (2)[c]	61	11	–	–
2	$SnCl_4$ (2)[c,d]	34	41	–	<5
3	$EtAlCl_2$ (1)[e]	86 (84)[f]	4	–	–
4	Et_2AlCl (1)	77 (74)[f]	–	–	–
5	$BF_3 \cdot Et_2O$ (1)	Low conversion of **1**			
6	$Yb(NTf_2)_3$ (0.1)[d]	–	12	19	17
7	$HNTf_2$ (0.1)	–	43	45	–

[a] Reaction conditions: CH_2Cl_2, 25 °C, 2 h, Ar. [b] ^1H NMR yields using 1,4-dinitrobenzene as the internal standard. [c] 1 equiv. of the Lewis acid slightly lowered the yields. [d] Additional formation of product **8** in *ca.* 10% yield was noted (see Scheme 2). [e] 2 equiv. of the Lewis acid afforded a complex product mixture. [f] Isolated yields are in parentheses.

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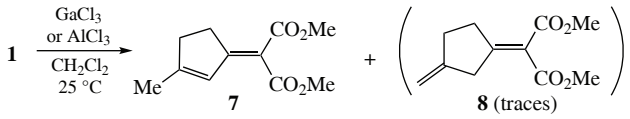


Scheme 1

6-methylenespiro[2.3]hexane-4,4-dicarboxylate **5** that is an isomer of **3**, is notable (entry 6).

Using significantly stronger Lewis acids such as $GaCl_3$ and $AlCl_3$ revealed an unusual reaction pathway. For instance, when 1 equiv. of $GaCl_3$ or $AlCl_3$ was used, products **2** and **3** were formed similarly to $TiCl_4$ and $SnCl_4$ mediated reactions (Table 2, entries 1, 3). However, when the amount of $GaCl_3$ or $AlCl_3$ was raised from 1 to 2 equiv. the reaction proceeded differently: the fractions of compounds **2** and **3** dropped significantly, and (3-methylcyclopent-2-en-1-ylidene)malonate **7** became the major product (Scheme 2, Table 2, entries 2, 4). Furthermore, in the case of $GaCl_3$, very high selectivity could be achieved. Thus, a further increase in the amount of $GaCl_3$ to 3 equiv. allows achieving a product ratio of **7** to **3** greater than 10 to 1 with only trace amounts of allyl chloride **2** (entry 5).

The methyl group position in the diene **7** has been unequivocally confirmed by ^{13}C, COSY and HMBC NMR spectra (Figure 1). It is difficult to explain the formation of such a product in terms of classical carbocations. To clarify the formation mechanism, we conducted a control experiment by adding $GaCl_3$ to DAC **1** in two portions of 1 equiv. each 1 h apart (see Table 2, entry 6). In this case, the first equivalent of $GaCl_3$ generated a mixture of allyl chloride **2** and methylenecyclobutane



Scheme 2

Table 2 Product distribution in $GaCl_3/AlCl_3$-mediated rearrangements of **1**.[a]

Entry	Lewis acid (equiv.)	Yield (%)[b]			
		2	**3**	**7**	**8**
1	$AlCl_3$ (1)	55	9	–	–
2	$AlCl_3$ (2)	20	12	33	–
3	$GaCl_3$ (1)	43	34	–	–
4	$GaCl_3$ (2)	<5	11	51	–
5	$GaCl_3$ (3)	<5	3	51 (48)[c]	
6	$GaCl_3$ (1 + 1)	7	22	32	<5

[a] Reaction conditions: CH_2Cl_2, 25 °C, 2 h, Ar. [b] ^1H NMR yields using 1,4-dinitrobenzene as the internal standard. [c] Isolated yields are in parentheses.

3 in the form of gallium complexes. Treatment with the second equivalent of $GaCl_3$ led to the nearly complete disappearance of allyl chloride **2** and the formation of an equivalent amount of diene **7**. This observation clearly indicates that the formation of diene **7** proceeds sequentially *via* an allyl intermediate (either allyl chloride **2** or allyl carbocation **B**). Note that the amount of methylenecyclobutane **3** also decreased by ~10%, which correlates with the overall decrease in yield, likely due to oligomerization.

The observed virtually exclusive formation of diene **7** when 2–3 equiv. of $GaCl_3$ are used immediately at the initial stage of the reaction, with products **2** and **3** being virtually absent, is likely due to the facilitated formation of complex **C** compared to the 1,2-alkyl shift in intermediate **A**. In turn, an excess of $GaCl_3$ causes the conversion of complex **C** into the ionic intermediate **D**, which is essentially a nonclassical carbocation (Scheme 3).

Thus, intermediate **D** has a structure that combines a malonate fragment, whose negative charge is compensated by the positive charge of the Ga^{3+} cation, and a (2-cyclopropyl)allyl carbocation fragment that is stabilized by a weakly coordinating polychlorogallate anion $Ga_xCl^-_{3x+1}$. The (2-cyclopropyl)allyl carbocation in **D** is also a β-cyclopropylcarbinyl carbocation, which is well known for its nonclassical nature from the works of Olah and Masamune.[31–33] The representation of this cation as resonance structures **D–G** reveals structure **G**, which is a precursor to the stable 1,2-zwitterionic gallium complex of the final diene **7** (see Scheme 3, structure **H**). Notably, the transition between resonance structures **D–G** occurs exclusively *via* the formation and cleavage of two-electron three-centered bonds, without any hydride shifts.[31–34] The formation of complex **H** is the driving force that determines the preferred resonance form of the nonclassical (2-cyclopropyl)allyl cation.

Additional experiments were conducted to investigate whether the intermediates **A** and **B** participate in the reaction and

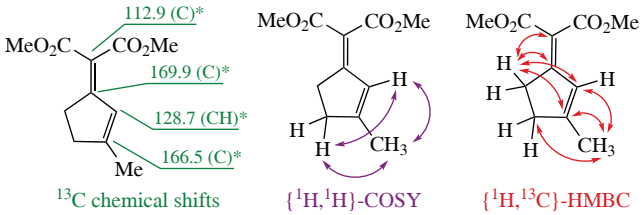
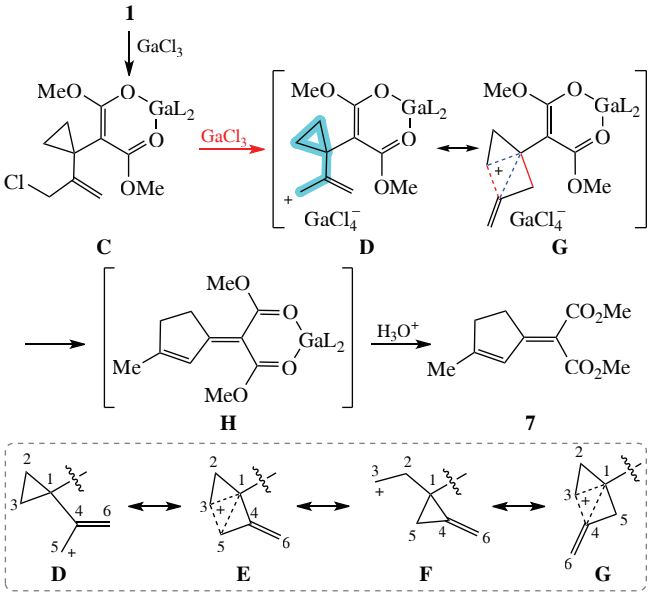
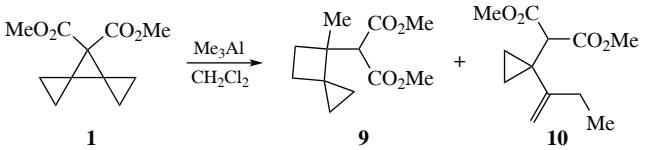


Figure 1 ^{13}C NMR data and selected $\{^1H,^1H\}$-COSY and $\{^1H,^{13}C\}$-HMBC correlations. * Multiplicities from $\{^1H, ^{13}C\}$ edited HSQC.



Scheme 3



	1	**9**	**10**
1 equiv. of Me_3Al		57%	23%
2 equiv. of Me_3Al		43%	26%

Scheme 4

can be captured by a non-halogen nucleophile. In this way, we used 1 and 2 equiv. of Me_3Al, which can serve as both a Lewis acid and a source of a formal methyl anion able to irreversibly quench the carbocation centers of the corresponding zwitterionic intermediates. Under these conditions, both expected products, **9** and **10**, were obtained, while their ratio was practically independent on the amount of Me_3Al used (Scheme 4).

In summary, we have demonstrated that the ring-opening Lewis acid mediated rearrangements of dimethyl dispiro[2.1.2.0]-heptane-4,4-dicarboxylate **1** occurs through the cleavage of two of its three cyclopropane rings *via* intermediates **A**–**H**. When 2 equiv. of $GaCl_3$ or $AlCl_3$ are used, the rearrangement proceeds further, involving the cleavage of the third cyclopropane ring, leading to 3-methylcyclopent-2-enylidene malonate **7** *via* a cascade of nonclassical carbocations.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.71267/mencom.8119.

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Contents entry

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