Lewis acid-mediated reactions of donor-acceptor cyclopropanes with diazo esters

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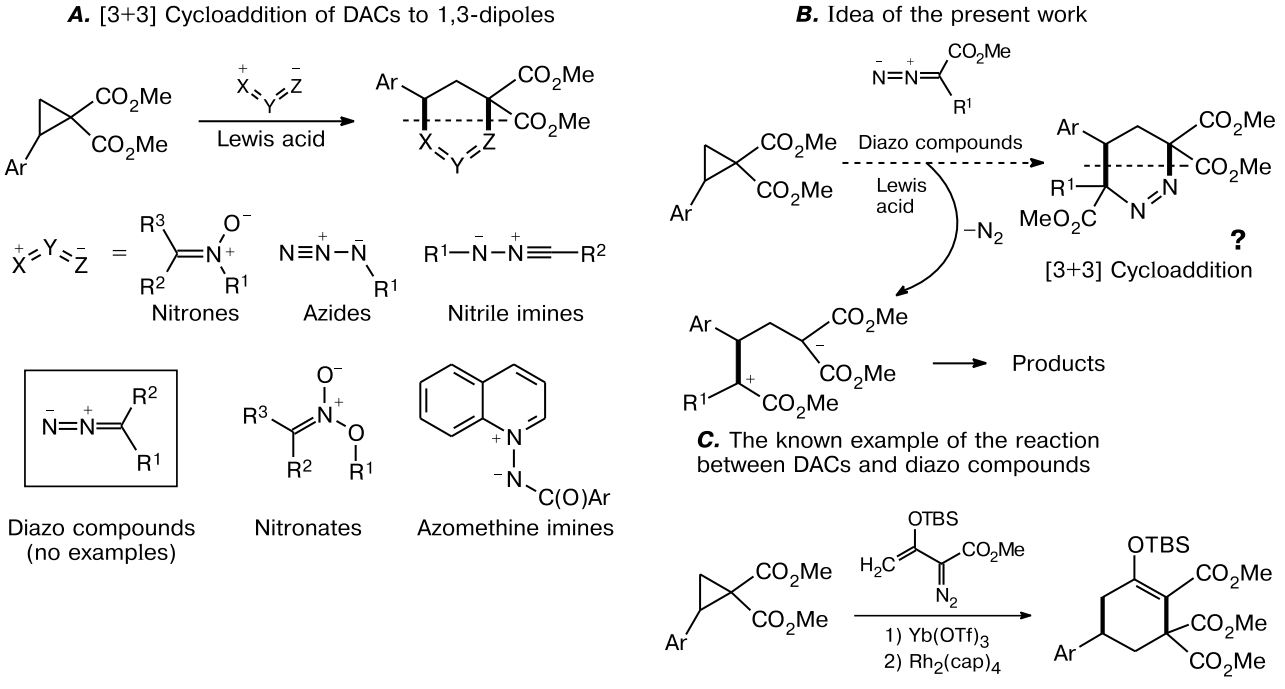
The reactions of diazo esters with 2-arylcyclopropane-1,1-dicarboxylates, the representatives of donor-acceptor cyclopropanes (DACs), mediated by $Sc(OTf)_3$, $SnCl_4$, and $GaCl_3$ proceeded with nitrogen elimination to give the C—C coupling products. No products of the formal [3+3] cycloaddition of diazo compounds to DACs were formed but the main reaction direction was addition of diazo ester to either 1,3- or 1,2-zwitterions generated upon Lewis acid-mediated cyclopropane ring opening giving rise to new 1,4- and 1,3-zwitterionic intermediates. The formed intermediates underwent further fragmentations and rearrangements to give substituted cyclopropanedi-, -tri-, and -tetracarboxylates. Mechanistic aspects of the observed reactions were discussed.

Key words: donor-acceptor cyclopropanes, diazo esters, Lewis acids, C—C bond formation.

Cyclopropanes bearing vicinal donor and acceptor substituents (donor-acceptor cyclopropanes, DACs)[1] can be readily activated by Lewis acids to give 1,3-zwitterionic intermediates resulting from three-membered ring opening.[2—8] These zwitterions readily underwent [3+2],[9—12] [3+3],[13—23] and [3+4] cycloadditions[24—26] and more complex cascade processes[27—30] and, therefore, found wide applications in modern organic synthesis. Cycloaddition reactions are the most characteristic transformations for this class of cyclopropanes and most often associated exactly with these compounds. For instance, the reactions of 1,3-zwitterions generated from

Scheme 1



Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 2, pp. 0265—0273, February, 2018.

DACs with other 1,3-dipoles manly proceed as the formal [3+3] cycloaddition to afford six-membered heterocycles (Scheme 1, ***A***). Among these reactions, the reactions of DACs with nitrones[13–15] are the most deeply studied. The reactions involving azides,[16] nitrile imines,[17] nitronates,[18,19] and azomethine imines[20] are also known. All these processes are extensively employed in synthetic organic chemistry and were used to achieve total syntheses of several natural compounds.[21–23].

However, diazo compounds have not yet been studied as 1,3-dipoles for these reactions. It is known that diazo compounds are able to play a role of 1,3-dipoles in [3+2] cycloadditions involving substrates with different multiple bonds.[31–33] The aim of the present work is the extension of these processes to the reactions involving DACs, *i.e.*, the attempts to realize the formal [3+3] cycloadditions producing tetrahydropyridazines (Scheme 1, ***B***). It should be emphasized that Doyle and co-workers[34] have described the reaction between DACs and enol diazoacetates, which proceeded as common [3+2] cycloaddition of 1,3-zwitterion to the vinyl double bond followed by ring expansion *via* rhodium-catalyzed dediazotization (Scheme 1, ***C***).

Results and Discussion

Apparently, the absence of the published examples of a formal [3+3] cycloaddition of DACs to diazo compounds is not a simple gap. This process is very difficult to realize taking into account lability of diazo compounds in the presence of the Lewis acids[35,36] used for the activation of the DAC cyclopropane rings. With the aim to study the possible directions of the reactions of DACs with diazo compounds, we tested the performance of a series of Lewis acids in a model reaction of 2-phenylcyclopropane-1,1-dicarboxylate (**1a**) with diazoacetate **2a** under different conditions (Table 1).

In the presence of mild Lewis acids, *e.g.*, $Ni(ClO_4)_2$, $In(OTf)_3$, and $Yb(OTf)_3$, the reactions do not take place. A strong Lewis acid, $Sc(OTf)_3$, facilitates the reaction and stronger Lewis acids ($SnCl_4$, $TiCl_4$, $GaCl_3$) cause a relatively fast transformation of both starting components. The reactions practically stop both at low temperatures (below –90 °C) and in the presence of different ligands (pyridine, Et_3N) used to control the Lewis acidity. Performing the reactions in the presence of $Rh_2(OAc)_4$ and $Rh_2(OAc)_4/Sc(OTf)_3$ results only in decomposition of diazoacetate **2a** to dimethyl fumarate and dimethyl maleate.

Screening of Lewis acids and the reaction conditions revealed four main directions of chemical transformations of DAC **1a** in the reaction with diazoacetate **2a** (Scheme 2). Unfortunately, neither lowering the reaction temperature, nor changing the solvents and reagent ratios allow us to perform the formal [3+3] cycloaddition of **1a** to **2a** and obtain tetrahydropyridazine. All identified products contain no nitrogen thus indicating the complete dediazotization of the starting diazo ester. Nevertheless, the coupling of DAC and diazo ester proceeds efficiently with the C—C bond formation. In nearly all cases, the main reaction products were methyl cinnamate **3a** and cyclopropane-1,1,2-tricarboxylate (**4**) (see Scheme 2, Table 1). Unluckily, the obtained products are of low synthetic value but the process itself has some theoretical interest.

An explanation of the formation of compounds **3a** and **4** is shown on Scheme 3. The reaction of 1,3-zwitterion **I** initially generated from DAC with diazo ester in the presence of Lewis acid[1–8] *via* the C—C bond formation to give unstable intermediate **II**, which readily eliminates the nitrogen molecule. Theoretically, intermediate **II** can

Scheme 2

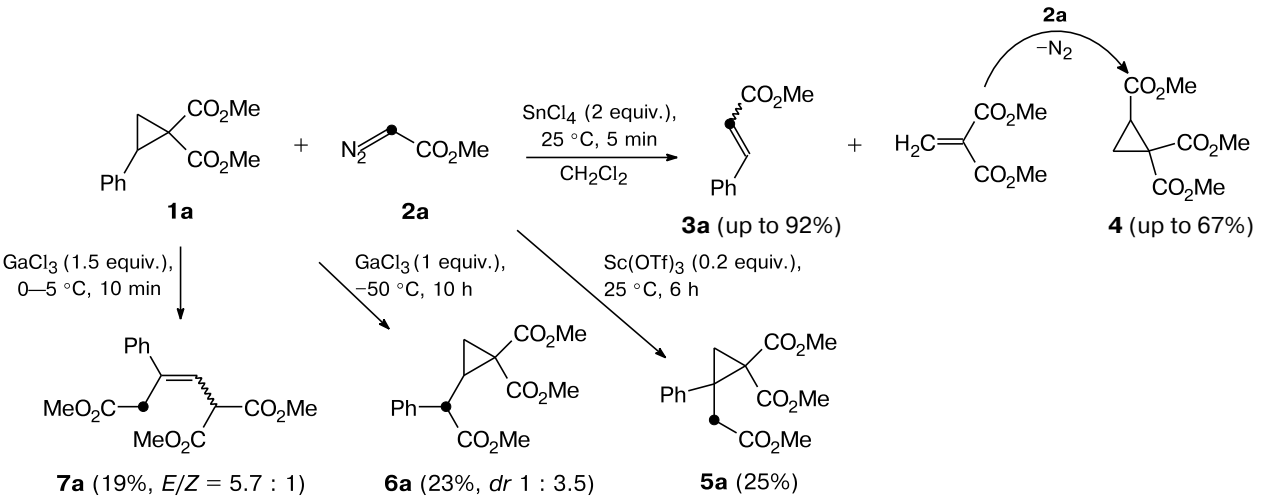


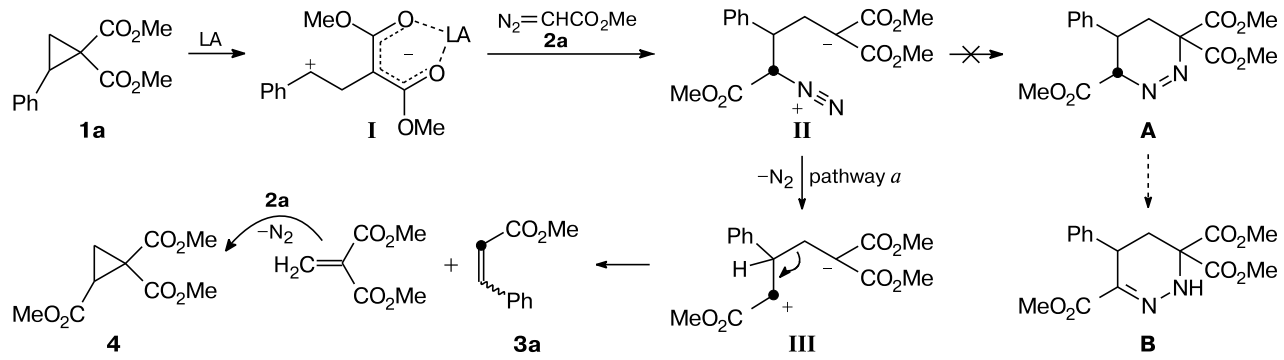
Table 1. Lewis-acid mediated reactions of dimethyl 2-phenylcyclopropane-1,1-dicarboxylate (**1a**) with diazoacetate **2a**

Ratio **1a** : **2a**	Lewis acid (mol.%)	Reaction conditions[a]		Conversion of **1a** (%)	Yields of the reaction products (%)[b]					
		T/°C	*t*/h		**3a** (*E*/*Z*)	**4**	**5a**	**6a** (*dr*)	**7a** (*E*/*Z*)	**9**
1 : 1	$SnCl_4$ (100)	−78	0.5	64	47 (1 : 1.6)	32	12	—	—	—
1 : 1.5	$SnCl_4$ (200)	25	0.1	100	92 (1 : 1.2)	48	—	—	—	—
1 : 1.1	$GaCl_3$ (20)	25	0.1	57	41 (1 : 1.7)	34	—	5 (1 : 2)	3 (5 : 1)	—
1 : 1.5	$GaCl_3$ (20)	25[c]	0.2	78	47 (1.4 : 1)	8	11	8 (1 : 2)	—	4
1 : 1.4	$GaCl_3$ (40)	25[c]	1	100	72 (1.3 : 1)	24	—	6 (1 : 2)	7 (5 : 1)	— 6
1 : 2	$GaCl_3$ (20)	25	2	100	63 (1 : 1.7)	52	4	11 (1 : 4)	16 (5 : 1)	8
1 : 2	$GaCl_3$ (100)	−50	6	86	63 (1 : 3.7)	58	—	18 (1 : 3.5)	—	—
1 : 2	$GaCl_3$ (100)	−50	10	100	71 (1 : 3.4)	67	—	23 (1 : 3.5)	—	—
1 : 2	$GaCl_3$ (150)	0–5	0.2	100	39 (1 : 1.7)	47	—	15 (1 : 1.9)	19 (5.7 : 1)	8[d]
1 : 1	$Sc(OTf)_3$ (10)	25	3	42	21 (1 : 1.2)	11	10	7 (1 : 1.2)	—	—
1 : 2	$Sc(OTf)_3$ (20)	25	6	96	47 (1 : 1.3)	34	25	14 (1 : 1.4)	3 (5 : 1)	—
1 : 2	$Yb(OTf)_3$ (10)	25	72	0	—	—	—	—	—	—

[a] In CH_2Cl_2.
[b] Total yields of the products can be greater than 100%, since compounds **3a** and **4** result from fragmentation of the activated complexes (see Scheme 3).
[c] In diethyl ether.
[d] Compound **10a** (see Scheme 6) was also isolated in 23% yield (*trans*/*cis* = 1 : 1.4).

cyclize to tetrahydropyridazine ring **A** and further to tautomer **B** but we failed to detect these intermediates in the reaction mixtures also by low temperature (−30 °C) NMR experiments. A nitrogen elimination gives 1,4-zwitterionic intermediate **III**; this intermediate is unstable due to the presence of the acceptor group destabilizing its positive charge and undergoes fast transformations. The main directions of these transformations are the fragmentation

Scheme 3

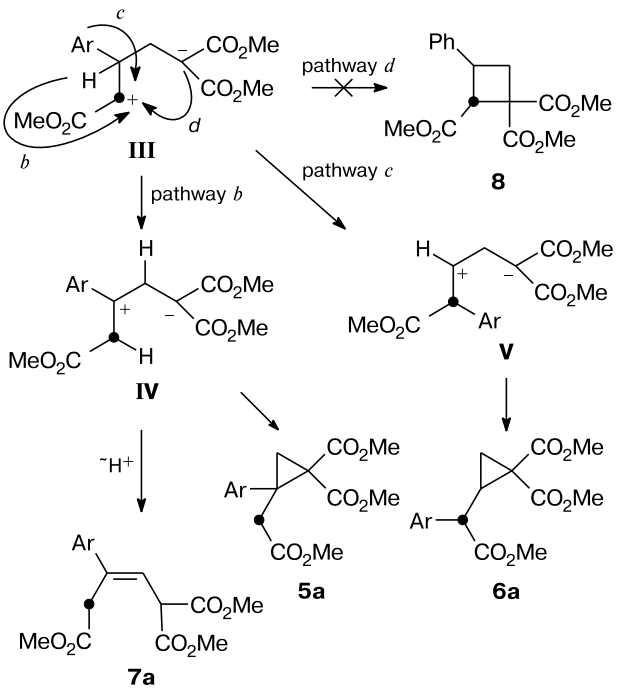


LA is Lewis acid.

of intermediate **III** with the C—C bond cleavage and formation of two alkene species, compound **3a** and dimethyl 2-methylidenemalonate (Scheme 3, pathway *a*). Next, 2-methylidenemalonate undergoes Lewis acid-mediated reaction with an excess of the starting diazo ester **2a** producing cyclopropanetricarboxylate **4**[35] and also partially polymerizes.

The other revealed directions of the process give regioisomers **5a**, **6a**, and **7a** and are more synthetically interesting (see Scheme 2) despite the lower product yields than in the reactions resulting in compounds **3a** and **4**. We succeeded to find the reaction conditions that give compounds **5a**, **6a**, and **7a** as the main products. Thus, 20% $Sc(OTf)_3$ enable a formal insertion of diazo ester into the C—H bond of the starting cyclopropane **1a** to give compound **5a**. In the reactions carried out in the presence of $GaCl_3$, the structure of the product depends on the reaction temperature. Thus, at −50 °C compound **6a**, the product of formal diazo ester insertion into the C—Ph bond is formed; while, at room temperature the reaction is also accompanied with the three-membered ring opening to produce 3-phenylbut-2-ene-1,1,4-tricarboxylate (**7a**) (see Scheme 2, Table 1). These reactions require the excess of diazoacetate since it is partially consumed by the reaction with methylidenemalonate and is partially destroyed by Lewis acid. It should be noted that the compositions of the products of the reactions of DAC **1a** with diazoacetate **2a** generally depend not only on the nature of the Lewis acid but also on the reaction temperature and the solvent used (see Table 1).

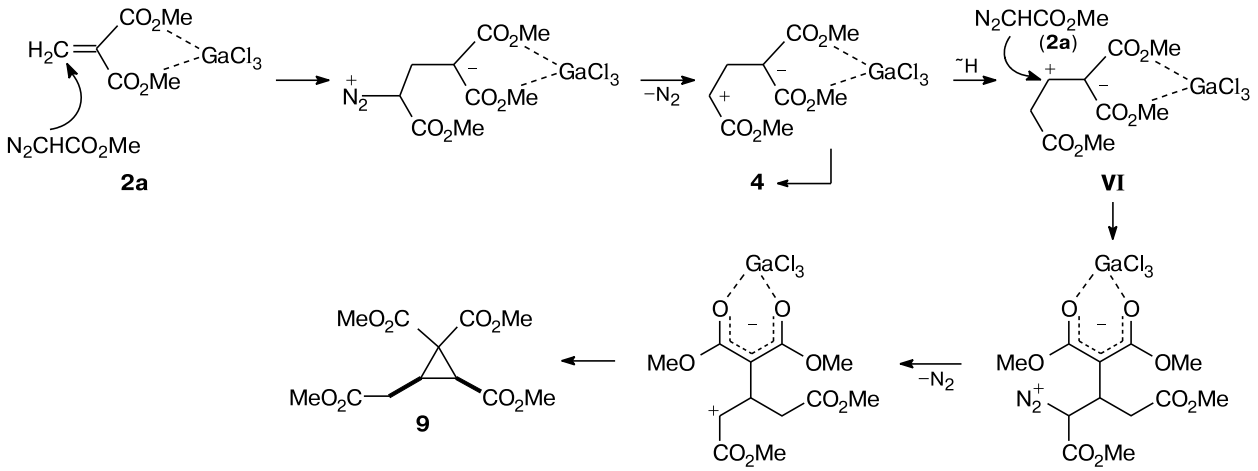
Scheme 4



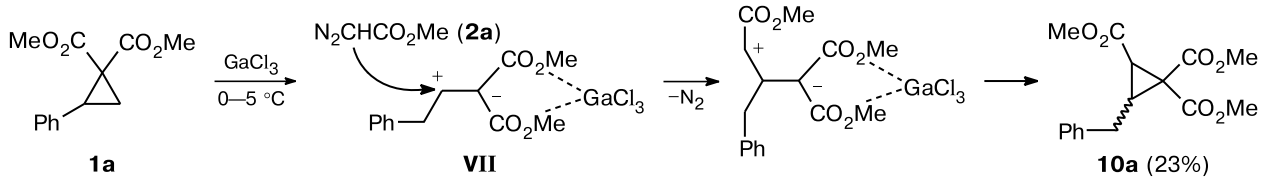
The formation of regioisomers **5a**, **6a**, and **7a** also proceeds *via* zwitterionic intermediate **III** undergoing either a hydride shift (Scheme 4, pathway *b*) or an aryl shift (pathway *c*) to give 1,3-zwitterionic intermediates **IV** and **V**. Zwitterions **IV** and **V** readily cyclize into the corresponding cyclopropanes **5a** and **6a**, respectively. These compounds are relatively stable and do not undergo further transformations. Under more drastic conditions, intermediate **IV** is partially converted into isomeric but-2-enetricarboxylates **7a**. Interestingly, neither reactions show the evidence of formation of substituted cyclobutane **8**, however this product could be formed by cyclization of zwitterion **III** (pathway *d*).

Other reaction products were isolated in some cases, for instance, compounds **9** and **10a**, along with the already described compounds. Compound **9** can arise from successive addition of diazoacetate **2a** to the methylidenemalonate intermediate and further to 1,2-zwitterion **VI** (Scheme 5).

Scheme 5



Scheme 6



A key step in the pathway leading to cyclopropane **10a** is generation of 1,2-zwitterion **VII** upon treatment of DAC **1a** with $GaCl_3$ at 0—5 °C.[37—43] The reaction of intermediate **VII** with **2a** after dediazotization results in cyclopropane derivative **10a** (Scheme 6). It should be underlined that both these reactions similarly to the formation of compounds **5a** and **6a** proceed as the ring closure of the corresponding 1,3-zwitterions to the three-membered rings.

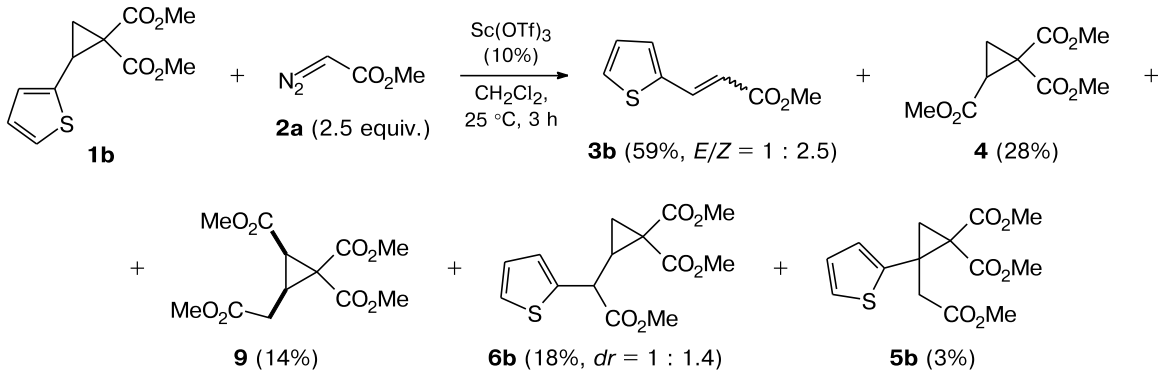
Cyclopropanetricarboxylate **9** is identified as the *cis* isomer and compound **10a** is a 1 : 1.4 mixture of *trans* and *cis* isomers.

2-(2-Thienyl)cyclopropane-1,1-dicarboxylate (**1b**) reacts with diazoacetate **2a** similarly; however, in this reaction both $SnCl_4$ and $GaCl_3$ gave no satisfactory results since they caused almost complete polymerization of the starting DAC. Scandium(III) triflate ($Sc(OTf)_3$) was proved to be the most suitable Lewis acid for this transformation providing compounds **3b**, **4**, and **6b** as the main products. Note that this reaction gives the higher yield of cyclopropane **9** than the reaction of DAC **1a** (Scheme 7).

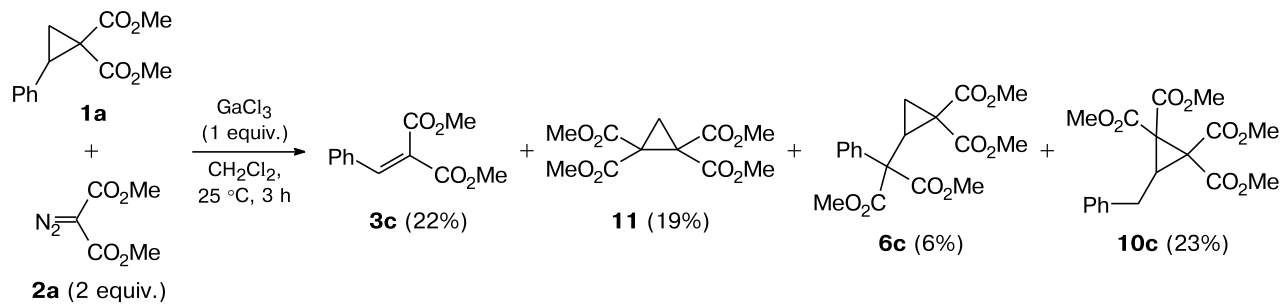
Besides diazoacetate **2a**, diazomalonate **2b** also reacts with DAC **1a** (Scheme 8); however, to enable this reaction more active Lewis acid, $GaCl_3$, should be employed instead of $Sc(OTf)_3$. The number of minor products in this reaction was lower than in the case of diazoacetate **2a**; however, the yields of the main expected products, *e.g.*, compound **3c**, were also noticeably lower. Note the relatively high yield of cyclopropane **10c**; similarly to cyclopropane **10a**, derivative **10c** is formed *via* 1,2-zwitterionic intermediate **VII**.[37—43]

To minimize the role of intermediate **I** (see Scheme 3) in the reactions with diazo esters and, conversely, to

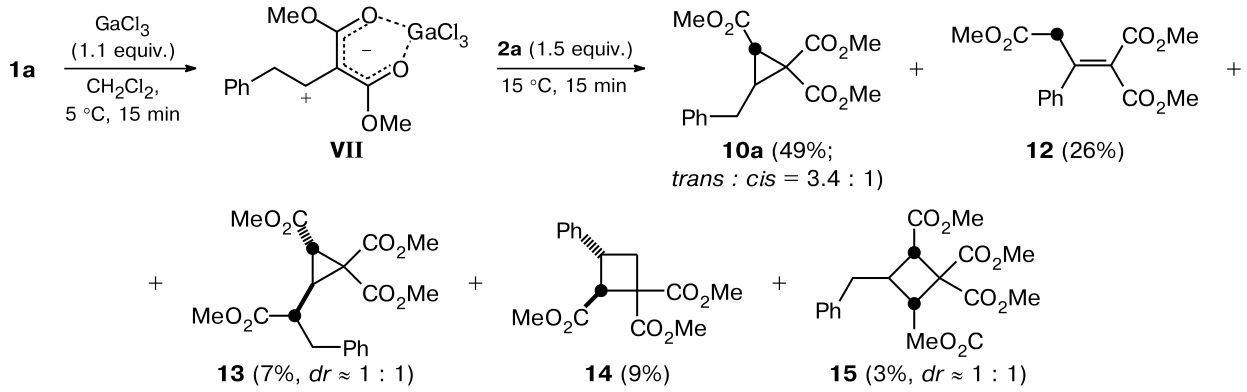
Scheme 7



Scheme 8



Scheme 9



enhance the role of 1,2-zwitterion **VII** (see Scheme 6), we preliminary generated this zwitterion from cyclopropane **1a** and $GaCl_3$ at 0—5 °C (1,2-zwitterion **VII** is stable at this temperature within several hours[44,45]) and studied its behavior in the reactions with diazoacetate **2a**. Indeed, in this case the product composition differed from that obtained by the simultaneous mixing of all reagents. Expectedly, the formation of cyclopropanetricarboxylate **10a** was the main pathway of this reaction (Scheme 9); however, unsaturated triester **12** was also obtained in relatively high yield (26%). Among the minor products **13**—**15**, it should be mentioned the formation of cyclobutanecarboxylates **14** and **15**. Compound **13** was identified as two diastereomers with the *trans* arranged cyclopropane ring substituents.

In summary, we pioneered in studying the reactions of DACs with diazo esters mediated by Lewis acids, *e.g.*, $Sc(OTf)_3$, $SnCl_4$, and $GaCl_3$, using 2-arylcyclopropane-1,1-dicarboxylates **1** as the models. Depending on the reaction conditions, all observed transformations proceed as the C—C bond forming reactions accompanied with the nitrogen molecule elimination. No products of the formal [3+3] cycloaddition of diazo compounds to DACs were detected in any of the reactions. The main directions of the reactions of DACs with diazo esters are additions of diazo esters to 1,3- and 1,2-zwitterionic intermediates generated upon the Lewis acid-mediated opening of the DAC cyclopropane ring. Subsequent elimination of the nitrogen molecule generates 1,4- and 1,3-zwitterionic intermediates, which undergo fragmentation and rearrangement to give substituted cyclopropanes bearing either two, three or four ester groups per molecule.

Experimental

^1H and ^{13}C NMR spectra were recorded with Bruker AMX-III 400 (working frequencies of 400.1 and 100.6 MHz, respectively) and Bruker AVANCE II 300 (working frequencies of 300 and 75 MHz, respectively) instruments in $CDCl_3$. The chemical shifts are given in the δ scale relative to Me_4Si (0.05%) as an internal standard. The NMR signals were attributed and isomeric compositions were established by homo- and heteronuclear 1D (DEPT-135) and 2D (COSY, TOCSY, NOESY, HSQC, edited-HSQC, and HMBC) correlation techniques. IR spectra were recorded on a IR-Fourier-transform spectrometer in $CHCl_3$ (0.5—2%). Electron impact (EI) mass spectra were run on a Finnigan MAT INCOS-50 instrument using 70 eV electrons. High resolution electrospray ionization (ESI) mass spectrometry was performed with a Bruker micro TOFII instrument.[46] Thin layer chromatography was carried out on the precoated plates Merck Silica gel 60 F_{254}. Preparative chromatography was performed with Merck silica gel 60 (0.040—0.063 mm). All manipulations with anhydrous $GaCl_3$ (Aldrich) were carried out under dry argon. The solvents (purity no less than 99.5%) were used as purchased. Dichloromethane used in the reactions with $GaCl_3$ was first dried over KOH pellets and then distilled over P_2O_5 under dry argon.

Reactions of cyclopropanes 1a,b with diazo compounds 2a,b (general procedure). To a solution of cyclopropane **1a**,**b** (0.6 mmol) and diazo compound **2a,b** (1.2—1.5 mmol) in anhydrous dichloromethane (5—7 mL), Lewis acid ($Sc(OTf)_3$, 5—20 mol.%; $SnCl_4$, 1.2 mmol; $GaCl_3$, 0.6—0.9 mmol) was added at the selected temperature (see Table 1) under argon. The reactions were carried out with stirring under the conditions specified in Schemes 2, 7, and 8 and in Table 1. Then the reaction mixture was treated with 5% HCl (7 mL) and extracted with dichloromethane (3×10 mL). The combined organic layers were dried with anhydrous $MgSO_4$ and concentrated *in vacuo*. The obtained products were isolated and purified by either column or preparative thin layer chromatography (silica gel, elution with benzene and ethyl acetate mixed in different ratios). To resolve the isomers and isolate pure products, a sequence of several chromatography steps was used if required.

Methyl 3-phenylacrylate (3a), a 1 : 1.2 mixture of *E* and *Z* isomers, was synthesized following the general procedure from cyclopropane **1a** (141 mg, 0.6 mmol), diazoacetate **2a** (120 mg, 1.2 mmol), and $SnCl_4$ (312 mg, 1.2 mmol) at 25 °C within 5 min. Total yield 89 mg (92%); colorless oils. The isomers were resolved. ^1H and ^{13}C NMR spectra are in agreement with those published earlier.[47,48]

Trimethyl cyclopropane-1,1,2-tricarboxylate (4) was synthesized following the general procedure from cyclopropane **1a** (141 mg, 0.6 mmol), diazoacetate **2a** (120 mg, 1.2 mmol), and $SnCl_4$ (312 mg, 1.2 mmol) at 25 °C within 5 min. Yield 62 mg

(48%); colorless oil. ^{1}H and ^{13}C NMR spectra are in agreement with those published earlier.[49]

Dimethyl 2-(2-methoxy-2-oxoethyl)-2-phenylcyclopropane-1,1-dicarboxylate (5a) was synthesized following the general procedure from cyclopropane **1a** (141 mg, 0.6 mmol), diazoacetate **2a** (120 mg, 1.2 mmol), and $Sc(OTf)_3$ (59 mg, 0.12 mmol) at 25 °C within 6 h. Yield 45 mg (25%); colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$), δ: 1.89 (d, 1 H, H(3), ^2J = 5.7 Hz); 2.39 (dd, 1 H, H(3), ^2J = 5.7, ^4J = 1.2 Hz); 2.80 (d, 1 H, H(1′), ^2J = 16.0 Hz); 3.14 (dd, 1 H, H(1′), ^2J = 16.0 Hz, ^4J = 1.2 Hz); 3.31 (s, 3 H, CO_2Me); 3.55 (s, 3 H, CO_2Me); 3.81 (s, 3 H, CO_2Me); 7.15—7.38 (m, 5 H, H_{Ar}). ^{13}C NMR (100.6 MHz, $CDCl_3$), δ: 24.5 (C(3)), 38.3 (C(2)), 39.4 (C(1)), 41.0 (C(1′)), 51.6, 52.3 and 52.9 (3 OMe), 127.6 (C(*p*)), 128.2 and 129.3 (2 C(*o*) and 2 C(*m*)), 138.3 (C(*ipso*)), 167.3, 169.2 and 171.2 (3 COO). MS (ESI): found *m/z* 329.0983. $C_{16}H_{18}O_6$. Calculated: 329.0996 $[M + Na]^+$.

Dimethyl 2-(2-methoxy-2-oxo-1-phenylethyl)cyclopropane-1,1-dicarboxylate (6a), two diastereomers in a 1 : 3.5 ratio, was synthesized following the general procedure from cyclopropane **1a** (141 mg, 0.6 mmol), diazoacetate **2a** (120 mg, 1.2 mmol), and $GaCl_3$ (106 mg, 0.6 mmol) at −50 °C within 10 h. Total yield 42 mg (23%); colorless oil. Diastereomers were resolved. **Major diastereomer.** ^{1}H NMR (400.1 MHz, $CDCl_3$), δ: 1.42 (dd, 1 H, H(3), ^2J = 5.1 Hz, ^3J = 9.1 Hz); 1.47 (dd, 1 H, H(3), ^2J = 5.1 Hz, ^3J = 7.8 Hz); 2.65 (ddd, 1 H, H(2), ^3J = 11.1 Hz, ^3J = 9.1 Hz, ^3J = 7.8 Hz); 3.16 (d, 1 H, H(2′), ^3J = 11.1 Hz); 3.68 (s, 3 H, CO_2Me); 3.75 (s, 3 H, CO_2Me); 3.79 (s, 3 H, CO_2Me); 7.22—7.41 (m, 5 H, H_{Ar}). ^{13}C NMR (100.6 MHz, $CDCl_3$), δ: 20.0 (C(3)), 30.4 (C(2)), 34.6 (C(1)), 51.1 (C(2′)), 52.3, 52.8 and 52.9 (3 OMe), 127.90 and 129.0 (2 C(*o*) and 2 C(*m*)), 127.92 (C(*p*)), 137.5 (C(*ipso*)), 168.5, 169.9 and 172.6 (3 COO). MS (EI), *m/z* (I_{rel} (%)): 306 (2), $[M]^+$, 288 (2), 274 (40), 242 (24), 233 (2), 214 (44), 210 (43), 199 (7), 186 (42), 185 (21), 171 (7), 155 (28), 143 (7), 128 (67), 121 (17), 115 (76), 105 (17), 91 (43), 77 (36), 59 (100). MS (ESI): found *m/z* 329.0989. $C_{16}H_{18}O_6$. Calculated: 329.0996 $[M + Na]^+$. **Minor diastereomer.** ^{1}H NMR (400.1 MHz, $CDCl_3$), δ: 1.58 (dd, 1 H, H(3), ^2J = 5.0 Hz, ^3J = 9.1 Hz); 1.75 (dd, 1 H, H(3), ^2J = 5.0 Hz, ^3J = 7.6 Hz); 2.81 (ddd, 1 H, H(2), ^3J = 11.0 Hz, ^3J = 9.1 Hz, ^3J = 7.6 Hz); 3.37 (d, 1 H, H(2′), ^3J = 11.0 Hz); 3.46 (s, 3 H, CO_2Me); 3.68 (s, 3 H, CO_2Me); 3.69 (s, 3 H, CO_2Me); 7.04—7.39 (m, 5 H, H_{Ar}). ^{13}C NMR (100.6 MHz, $CDCl_3$), δ: 21.4 (C(3)), 29.5 (C(2)), 33.4 (C(1)), 50.4 (C(2′)), 52.3 (3 OMe), 127.7 (C(*p*)), 127.9 and 128.6 (2 C(*o*) and 2 C(*m*)), 137.2 (C(*ipso*)), 168.5, 169.8 and 172.9 (3 COO). MS (ESI): found *m/z* 329.0996. $C_{16}H_{18}O_6$. Calculated: 329.0996 $[M + Na]^+$.

Trimethyl 3-phenylbut-2-ene-1,1,4-tricarboxylate (7a), a 5.7 : 1 mixture of *E* and *Z* isomers, was synthesized following the general procedure from cyclopropane **1a** (141 mg, 0.6 mmol), diazoacetate **2a** (120 mg, 1.2 mmol), and $GaCl_3$ (106 mg, 0.6 mmol) at 0—5 °C within 10 min. Total yield 34 mg (19%); colorless oil. The isomers were partially resolved; *E* isomer was isolated pure. ***E* Isomer.** ^{1}H NMR (400.1 MHz, $CDCl_3$), δ: 3.58 (s, 2 H, CH_2); 3.64 (s, 3 H, CO_2Me); 3.78 (s, 6 H, 2 CO_2Me); 4.50 (d, 1 H, H(1), ^3J = 9.8 Hz); 6.24 (d, 1 H, H(2), ^3J = 9.8 Hz); 7.24—7.37 (m, 3 H, *meta*-H and *para*-H); 7.39—7.45 (m, 2 H, *ortho*-H). ^{13}C NMR (100.6 MHz, $CDCl_3$), δ: 36.4 (CH_2(4)), 52.1 (CH(1)), 52.2 (OMe), 53.0 (2 OMe), 122.9 (CH(2)), 126.4 and 128.7 (2 CH(*o*) and 2 CH(*m*)), 128.1 (CH(*p*)), 137.6 (C(*ipso*)), 141.0 (C(3)), 168.1 (COO), 170.8 (2 COO). MS (ESI): found *m/z* 329.0992. $C_{16}H_{18}O_6$. Calculated: 329.0996 $[M + Na]^+$. ***Z* Isomer.** ^{1}H NMR (400.1 MHz, $CDCl_3$), δ: 3.44 (d, 2 H, CH_2, ^4J = 1.1 Hz); 3.60 (s, 3 H, CO_2Me); 3.72 (s, 6 H, 2 CO_2Me); 4.11 (d, 1 H, H(1), ^3J = = 10.2 Hz); 5.91 (dt, 1 H, H(2), ^3J = 10.2 Hz, ^4J = 1.1 Hz); 7.14—7.38 (m, 5 H, Ph). ^{13}C NMR (100.6 MHz, $CDCl_3$), δ: 44.4 (CH_2(4)), 51.9 (OMe), 52.2 (CH(1)), 52.8 (2 OMe), 122.6 (CH(2)), 128.0 (CH(*p*)), 128.3 and 128.6 (2 CH(*o*) and 2 CH(*m*)), 138.2 (C(*ipso*)), 139.9 (C(3)), 168.5 (COO), 171.0 (2 COO).

Reaction of dimethyl 2-(2-thienyl)cyclopropane-1,1-dicarboxylate (1b) with diazoacetate 2a was carried out following the general procedure. The reaction of cyclopropane **1b** (144 mg, 0.6 mmol), diazoacetate **2a** (150 mg, 1.5 mmol), and $Sc(OTf)_3$ (30 mg, 0.06 mmol) at 25 °C for 3 h gave compounds **3b** (59%), **4** (28%), **6b** (18%), and **9** (14%), which were isolated pure.

Methyl 3-(2-thienyl)acrylate (3b), a 1 : 2.5 mixture of *E* and *Z* isomers. Total yield 59 mg (59%). The isomers were resolved; both isomers are colorless oils. ^{1}H and ^{13}C NMR spectra are in agreement with those published earlier.[47,50]

Dimethyl 2-[2-methoxy-2-oxo-1-(2-thienyl)ethyl]cyclopropane-1,1-dicarboxylate (6b), a 1 : 1.4 mixture of two diastereomers. Total yield 33 mg (18%); colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$), δ: 1.46—1.60 (m, 3 H, 2 H_{major}(3) and H_{minor}(3)); 1.73 (dd, 1 H, H_{minor}(3), ^2J = 5.1 Hz, ^3J = 7.6 Hz); 2.63 (ddd, 1 H, H_{major}(2), ^3J = 11.0 Hz, ^3J = 9.1 Hz, ^3J = 7.6 Hz); 2.73 (ddd, 1 H, H_{minor}(2), ^3J = 11.0 Hz, ^3J = 9.1 Hz, ^3J = 7.6 Hz); 3.48 (d, 1 H, H_{major}(1′), ^3J = 11.0 Hz); 3.67 (d, 1 H, H_{minor}(1′), ^3J = 11.0 Hz); 3.70 (s, 3 H, CO_2Me_{minor}); 3.71 (s, 3 H, CO_2Me_{major}); 3.72 (s, 3 H, CO_2Me_{minor}); 3.73 (s, 3 H, CO_2Me_{major}); 3.74 (s, 3 H, CO_2Me_{major}); 3.77 (s, 3 H, CO_2Me_{major}); 6.90—7.00 (m, 3 H, H_{Ar}); 7.02 (dd, 1 H, $H_{Ar,minor}$, ^3J = 5.1 Hz, ^3J = 3.8 Hz); 7.19 (dd, 1 H, $H_{Ar,major}$, ^3J = 5.0 Hz, ^3J = 1.4 Hz); 7.23 (dd, 1 H, $H_{Ar,minor}$, ^3J = 5.1 Hz, ^3J = 3.8 Hz). ^{13}C NMR (100.6 MHz, $CDCl_3$), δ: 20.1 and 21.2 (C(3)), 30.6 and 30.7 (C(2)), 33.4 and 34.5 (C(1)), 45.5 and 46.3 (C(1′)), 52.5, 52.6, 52.7, 52.8, 52.9 (6 OMe), 125.1, 125.2, 125.7, 126.6, 126.9 and 128.1 (6 CH_{Ar}), 139.2 and 139.4 (C(2″)), 168.3, 169.2, 169.5, 169.6, 171.6 and 171.9 (6 COO). MS (ESI). Found: *m/z* 335.0555. $C_{14}H_{16}O_6S$. Calculated: 335.0560 $[M + Na]^+$.

Trimethyl (2*RS*,3*SR*)-3-(2-methoxy-2-oxoethyl)cyclopropane-1,1,2-tricarboxylate (9). Yield 24 mg (14%), colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$), δ: 2.28 (ddd, 1 H, H(3), ^3J = 9.6 Hz, ^3J = 8.5 Hz, ^3J = 6.9 Hz); 2.73 (d, 1 H, H(2), ^3J = 9.6 Hz); 2.89 (dd, 1 H, H(1′), ^2J = 17.8 Hz, ^3J = 8.5 Hz); 3.03 (dd, 1 H, H(1′), ^2J = 17.8 Hz, ^3J = 6.9 Hz); 3.70 (s, 3 H, CO_2Me); 3.71 (s, 3 H, CO_2Me); 3.75 (s, 3 H, CO_2Me); 3.76 (s, 3 H, CO_2Me). ^{13}C NMR (100.6 MHz, $CDCl_3$), δ: 27.6 (C(3)), 28.7 (C(1′)), 29.8 (C(2)), 38.5 (C(1)), 51.9, 52.3, 52.8 and 53.4 (4 OMe), 165.5, 168.8, 169.0 and 172.2 (4 COO). MS (ESI). Found: *m/z* 311.0743. $C_{12}H_{16}O_8$. Calculated: 311.0737 $[M + Na]^+$.

Reaction of cyclopropane 1a with diazomalonate 2b was carried out by the general procedure. The reaction of cyclopropane **1a** (141 mg, 0.6 mmol), diazomalonate **2b** (190 mg, 1.2 mmol), and $GaCl_3$ (106 mg, 0.6 mmol) at 25 °C for 3 h gave compounds **3c** (22%), **11** (19%), **6c** (6%), and **10c** (23%), which were isolated pure.

Dimethyl 2-benzylidenemalonate (3c). Yield 29 mg (22%), colorless oil. ^{1}H and ^{13}C NMR spectra are in agreement with those published earlier.[51]

Tetramethyl cyclopropane-1,1,2,2-tetracarboxylate (11). Yield 31 mg (19%), colorless oil. ^{1}H and ^{13}C NMR spectra are in agreement with those published earlier.[52]

Dimethyl 2-(1,3-dimethoxy-1,3-dioxo-2-phenylprop-2-yl)-cyclopropane-1,1-dicarboxylate (6c). Yield 13 mg (6%), colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$), δ: 1.64 (dd, 1 H, CH_2(3)-a, ^2J = 5.0 Hz, ^3J = 9.9 Hz); 1.91 (dd, 1 H, CH_2(3)-b, ^2J = 5.0 Hz, ^3J = 8.5 Hz); 2.75 (dd, 1 H, CH(2), ^3J = 8.5 Hz, ^3J = 9.9 Hz); 3.61, 3.72, 3.75, and 3.76 (all s, 3 H each, 4 CO_2Me); 7.28—7.42 (m, 5 H, Ph). ^{13}C NMR (100.6 MHz, $CDCl_3$), δ: 18.4 (CH_2(3)), 32.8 (CH(2)), 33.8 (C(1)), 52.5, 53.0, 53.1, and 53.2 (4 OMe), 62.6 (C(1′)), 128.02 (C(*p*)), 128.04 and 128.4 (2 C(*o*) and 2 C(*m*)), 137.4 (C(*ipso*)), 167.4, 169.6, 169.7, and 170.8 (4 COO). MS (ESI). Found: *m/z* 387.1041. $C_{18}H_{20}O_8$. Calculated: 387.1050 $[M + Na]^+$.

Tetramethyl 3-benzylcyclopropane-1,1,2,2-tetracarboxylate (10c). Yield 50 mg (23%), colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$), δ: 2.76 (t, 1 H, H(3), ^3J = 7.5 Hz); 3.21 (d, 2 H, H(1′), ^3J = 7.5 Hz); 3.74 (s, 6 H, 2 CO_2Me); 3.46 (s, 6 H, 2 CO_2Me); 6.78—7.46 (m, 5 H, H_{Ar}). ^{13}C NMR (100.6 MHz, $CDCl_3$), δ: 28.8 (C(1′)), 36.5 (C(3)), 44.0 (C(1) and C(2)), 52.9 and 53.3 (4 OMe), 126.4 (C(*p*)), 128.3 and 128.5 (2 C(*o*) and 2 C(*m*)), 139.0 (C(*ipso*)), 165.1 and 166.9 (4 COO). MS (ESI). Found: *m/z* 387.1045. $C_{18}H_{20}O_8$. Calculated: 387.1050 $[M + Na]^+$.

Reaction of cyclopropane 1a with diazoacetate 2a under conditions of preliminary generation of 1,2-zwitterion VII. To a solution of cyclopropane **1a** (141 mg, 0.6 mmol) in anhydrous dichloromethane (6 mL), solid $GaCl_3$ (106 mg, 0.6 mmol) was added at 5 °C under argon. After 15 min stirring, a solution of diazoacetate **2a** (120 mg, 1.2 mmol) in dichloromethane (2 mL) was added and the resulting mixture was stirred at 15 °C for 15 min. Then 5% HCl (7 mL) was added and the mixture was extracted with dichloromethane (3×10 mL). The combined organic layers were dried with anhydrous $MgSO_4$ and concentrated *in vacuo*. The products were isolated and purified by silica gel column chromatography (elution with benzene—ethyl acetate, 10 : 1). Compounds **10a** (49%) and **12** (26%) were isolated pure. Compounds **13—15** were not isolated and were analyzed by NMR spectroscopy as the mixtures.

Trimethyl 3-benzylcyclopropane-1,1,2-tricarboxylate (10a), a 3.4 : 1 mixture of *E* and *Z* isomers. Total yield 89 mg (49%), colorless oil. The isomers were partially resolved. *E* isomer was isolated pure. ***E* Isomer.** ^{1}H NMR (400.1 MHz, $CDCl_3$), δ: 2.68 (dt, 1 H, CH(3), ^3J = 7.6 Hz, ^3J = 7.2 Hz); 2.75 (d, 1 H, CH(2), ^3J = 7.2 Hz); 2.82 (dd, 1 H, CH_2(1′)-a, ^2J = 15.4 Hz, ^3J = = 7.6 Hz); 2.94 (dd, 1 H, CH_2(1′)-b, ^2J = 15.4 Hz, ^3J = 7.2 Hz); 3.68 (s, 6 H, 2 CO_2Me); 3.74 (s, 3 H, CO_2Me); 7.17—7.34 (m, 5 H, Ph). ^{13}C NMR (100.6 MHz, $CDCl_3$), δ: 31.9 (CH_2(1′)), 32.7 and 32.8 (CH(2) and CH(3)), 42.2 (C(1)), 52.5, 53.0 and 53.1 (3 OMe), 126.6 (C(*p*)), 128.2 and 128.7 (2 C(*o*) and 2 C(*m*)), 138.8 (C(*ipso*)), 166.7, 167.1, and 169.8 (3 COO). MS (ESI). Found: *m/z* 329.0990. $C_{16}H_{18}O_6$. Calculated: 329.0996 $[M + Na]^+$. ***Z* Isomer.** ^{1}H NMR (400.1 MHz, $CDCl_3$), δ: 2.21 (ddd, 1 H, CH(3), ^3J = 9.7 Hz, ^3J = 9.4 Hz, ^3J = 5.4 Hz); 2.67 (d, 1 H, CH(2), ^3J = 9.7 Hz); 3.12 (dd, 1 H, CH_2(1′)-a, ^2J = 15.5 Hz, ^3J = 9.4 Hz); 3.31 (dd, 1 H, CH_2(1′)-b, ^2J = 15.5 Hz, ^3J = 5.4 Hz); 3.70, 3.76, and 3.80 (all s, 3 H each, 3 CO_2Me); 7.17—7.33 (m, 5 H, Ph). ^{13}C NMR (100.6 MHz, $CDCl_3$), δ: 29.3 (CH_2(1′)), 30.4 (CH(2)), 33.7 (CH(3)), 39.5 (C(1)), 52.2, 52.7, and 53.4 (3 OMe), 126.4 (C(*p*)), 128.5, and 128.6 (2 C(*o*) and 2 C(*m*)), 140.1 (C(*ipso*)), 165.6, 168.9, and 169.5 (3 COO).

Trimethyl 2-benzylprop-1-ene-1,1,3-tricarboxylate (12). Yield 47 mg (26%), colorless oil. ^{1}H NMR (400.1 MHz, $CDCl_3$), δ: 3.43 and 3.72 (both s, 2 H each, 2 CH_2); 3.63, 3.77, and 3.84 (all s, 3 H each, 3 CO_2Me); 7.21—7.33 (m, 5 H, Ph). MS (ESI). Found: *m/z* 329.0985. $C_{16}H_{18}O_6$. Calculated: 329.0996 $[M + Na]^+$.

This work was financially supported by the Council on Grants of the President of the Russian Federation (Program for State Support of Young PhD-Scientists, Grant MK-3465.2017.3).

References

1 Yu. V. Tomilov, L. G. Menchikov, R. A. Novikov, O. A. Ivanova, I. V. Trushkov, *Russ. Chem. Rev.*, 2018, **87**, 201.
2. C. A. Carson, M. A. Kerr, *Chem. Soc. Rev.*, 2009, **38**, 3051.
3. M. Ya. Melnikov, E. M. Budynina, O. A. Ivanova, I. V. Trushkov, *Mendeleev Commun.*, 2011, **21**, 293.
4. T. F. Schneider, J. Kaschel, D. B. Werz, *Angew. Chem.*, *Int. Ed.*, 2014, **53**, 5504.
5. F. de Nanteuil, F. de Simone, R. Frei, F. Benfatti, E. Serrano, J. Waser, *Chem. Commun.*, 2014, **50**, 10912.
6. R. A. Novikov, Yu. V. Tomilov, *Mendeleev Commun.*, 2015, **25**, 1.
7. M. A. Cavitt, L. H. Phun, S. France, *Chem. Soc. Rev.*, 2014, **43**, 804.
8. V. P. Ananikov, D. B. Eremin, S. A. Yakukhnov, A. D. Dilman, V. V. Levin, M. P. Egorov, S. S. Karlov, L. M. Kustov, A. L. Tarasov, A. A. Greish, A. A. Shesterkina, A. M. Sakharov, Z. N. Nysenko, A. B. Sheremetev, A. Yu. Stakheev, I. S. Mashkovsky, A. Yu. Sukhorukov, S. L. Ioffe, A. O. Terent´ev, V. A. Vil´, Yu. V. Tomilov, R. A. Novikov, S. G. Zlotin, A. S. Kucherenko, N. E. Ustyuzhanina, V. B. Krylov, Yu. E. Tsvetkov, M. L. Gening, N. E. Nifantiev, *Mendeleev Commun.*, 2017, **27**, 425.
9. F. de Nanteuil, J. Waser, *Angew. Chem.*, *Int. Ed.*, 2011, **50**, 12075.
10. S. Chakrabarty, I. Chatterjee, B. Wibbeling, C. G. Daniliuc, A. Studer, *Angew. Chem.*, *Int. Ed.*, 2014, **53**, 5964.
11. C. A. Carson, M. A. Kerr, *J. Org. Chem.*, 2005, **70**, 8242.
12. V. S. Korotkov, O. V. Larionov, A. Hofmeister, J. Magull, A. de Meijere, *J. Org. Chem.*, 2007, **72**, 7504.
13. I. S. Young, M. A. Kerr, *Angew. Chem.*, *Int. Ed.*, 2003, **42**, 3023.
14. C. M. Braun, E. A. Congdon, K. A. Nolin, *J. Org. Chem.*, 2015, **80**, 1979.
15. Y.-B. Kang, X.-L. Sun, Y. Tang, *Angew. Chem.*, *Int. Ed.*, 2007, **46**, 3918.
16. H.-H. Zhang, Y.-C. Luo, H.-P. Wang, W. Chen, P.-F. Xu, *Org. Lett.*, 2014, **16**, 4896.
17. L. K. B. Garve, M. Petzold, P. G. Jones, D. B. Werz, *Org. Lett.*, 2016, **18**, 564.
18. E. O. Gorbacheva, A. A. Tabolin, R. A. Novikov, Yu. A. Khomutova, Yu. V. Nelyubina, Yu. V. Tomilov, S. L. Ioffe, *Org. Lett.*, 2013, **15**, 350.
19. A. A. Tabolin, E. O. Gorbachova, R. A. Novikov, Yu. A. Khoroshutina, Yu. V. Nelyubina, S. L. Ioffe, *Russ. Chem. Bull.*, 2016, **65**, 2243.
20. C. Perreault, S. R. Goudreau, L. E. Zimmer, A. B. Charette, *Org. Lett.*, 2008, **10**, 689.
21. I. S. Young, M. A. Kerr, *Org. Lett.*, 2004, **6**, 139.
22. I. S. Young, M. A. Kerr, *J. Am. Chem. Soc.*, 2007, **129**, 1465.

23. D. A. Dias, M. A. Kerr, *Org. Lett.*, 2009, **11**, 3694.
24. O. A. Ivanova, E. M. Budynina, Yu. K. Grishin, I. V. Trushkov, P. V. Verteletskii, *Angew. Chem., Int. Ed.*, 2008, **47**, 1107.
25. H. Xu, J.-L. Hu, L. Wang, S. Liao, Y. Tang, *J. Am. Chem. Soc.*, 2015, **137**, 8006.
26. C. Zhang, J. Tian, J. Ren, Z. Wang, *Chem. Eur. J.*, 2017, **23**, 1231.
27. J. Sabbatani, N. Maulide, *Angew. Chem., Int. Ed.*, 2016, **55**, 6780.
28. D. D. Borisov, R. A. Novikov, A. S. Eltysheva, Ya. V. Tkachev, Yu. V. Tomilov, *Org. Lett.*, 2017, **19**, 3731.
29. C. R. Pitts, B. Ling, J. A. Snyder, A. E. Bragg, T. Lectka, *J. Am. Chem. Soc.*, 2016, **138**, 6598.
30. D. A. Denisov, R. A. Novikov, K. V. Potapov, V. A. Korolev, E. V. Shulishov, Yu. V. Tomilov, *ChemistrySelect*, 2016, **1**, 6374.
31. M. Regitz, H. Heydt, *1,3-Dipolar Cycloaddition Chemistry*, Ed. A. Padwa, Wiley Interscience, New York, 1984, v. **1**, p. 393.
32. G. Mass, in *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry toward Heterocycles, Natural Products*, Eds A. Padwa, W. H. Pearson, Wiley and Sons, Hoboken, New York, 2003, Ch. 8, p. 539.
33. T. Kano, T. Hashimoto, K. Maruoka, *J. Am. Chem. Soc.*, 2006, **128**, 2174.
34. Q.-Q. Cheng, Y. Qian, P. Y. Zavalij, M. P. Doyle, *Org. Lett.*, 2015, **17**, 3568.
35. R. A. Novikov, D. N. Platonov, V. A. Dokichev, Yu. V. Tomilov, O. M. Nefedov, *Russ. Chem. Bull.*, 2010, **59**, 984.
36. R. A. Novikov, Yu. V. Tomilov, O. M. Nefedov, *Russ. Chem. Bull.*, 2014, **63**, 404.
37. R. A. Novikov, A. V. Tarasova, V. A. Korolev, V. P. Timofeev, Yu. V. Tomilov, *Angew. Chem., Int. Ed.*, 2014, **53**, 3187.
38. D. D. Borisov, R. A. Novikov, Yu. V. Tomilov, *Angew. Chem., Int. Ed.*, 2016, **55**, 12233.
39. R. A. Novikov, A. V. Tarasova, V. A. Korolev, E. V. Shulishov, V. P. Timofeev, Yu. V. Tomilov, *J. Org. Chem.*, 2015, **80**, 8225.
40. R. A. Novikov, A. V. Tarasova, D. A. Denisov, D. D. Borisov, V. A. Korolev, V. P. Timofeev, Yu. V. Tomilov, *J. Org. Chem.*, 2017, **82**, 2724.
41. R. A. Novikov, A. V. Tarasova, Yu. V. Tomilov, *Mendeleev Commun.*, 2015, **25**, 341.
42. D. D. Borisov, R. A. Novikov, Yu. V. Tomilov, *Tetrahedron Lett.*, 2017, **58**, 3712.
43. R. A. Novikov, A. V. Tarasova, Yu. V. Tomilov, *Synlett*, 2016, **27**, 1367.
44. R. A. Novikov, D. O. Balakirev, V. P. Timofeev, Yu. V. Tomilov, *Organometallics*, 2012, **31**, 8627.
45. R. A. Novikov, K. V. Potapov, D. N. Chistikov, A. V. Tarasova, M. S. Grigoriev, V. P. Timofeev, Yu. V. Tomilov, *Organometallics*, 2015, **34**, 4238.
46. A. M. Tsedilin, A. N. Fakhrutdinov, D. B. Eremin, S. S. Zalesskiy, A. O. Chizhov, N. G. Kolotyrkina, V. P. Ananikov, *Mendeleev Commun.*, 2015, **25**, 454.
47. Z. She, Y. Shi, Y. Huang, Y. Cheng, F. Song, J. You, *Chem. Commun.*, 2014, **50**, 13914.
48. F. Masing, H. Nusse, J. Klingauf, A. Studer, *Org. Lett.*, 2017, **19**, 2658.
49. T. Matsuki, N. X. Hu, Y. Otsubo, F. Ogura, *Bull. Chem. Soc. Jpn.*, 1989, **62**, 2105.
50. L. Shi, W. Wang, Y. Wang, Y.-Z. Huang, *J. Org. Chem.*, 1989, **54**, 2027.
51. Y. Ogiwara, K. Takahashi, T. Kitazawa, N. Sakai, *J. Org. Chem.*, 2015, **80**, 3101.
52. U. Eichenauer, R. Huisgen, A. Mitra, J. R. Moran, *Heterocycles*, 1987, **25**, 129.

Received November 2, 2017;
in revised form December 5, 2017;
accepted December 8, 2017