Stereoselective functionalization of 1-alkoxy-2-(phenylethynyl)cyclopropanes *via* lithiation and subsequent reactions with electrophilic reagents

V. D. Gvozdev,[a] K. N. Shavrin,[a] A. A. Ageshina,[b] and O. M. Nefedov[a]*

[a]N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky prosp., 119991 Moscow, Russian Federation. Fax: +7 (499) 135 532. E-mail: vgvozdev2006@yandex.ru
[b]Higher Chemical College, Russian Academy of Sciences, 9 Miusskaya pl., 125047 Moscow, Russian Federation

trans-1-Alkoxy-2-(phenylethynyl)cyclopropanes undergo lithiation at the hydrogen atom in the α-position to the triple bond on treatment with BuLi in THF at −(65—70) °C. The resulting organolithium derivatives react with acetaldehyde, acetone, dimethyl disulfide, and methyl chloroformate giving the corresponding alcohols, sulfides, and esters with the yields up to 69% with complete retention of cyclopropane ring stereoconfiguration. The obtained methyl 3-alkoxy-2,2-dimethyl-1-(phenylethynyl)cyclopropanecarboxylates and the corresponding acid readily undergo ring opening with addition of water molecule or HCl.

Key words: 1-alkoxy-2-alkylnylcyclopropanes, butyllithium, lithation, reactions with electrophiles, 3-alkoxy-2,2-dimethyl-1-(phenylethynyl)cyclopropanecarboxylates, ring opening.

At present, functional alkynylcyclopropanes are widely used in various chemical transformations.[1—12] They play an important role in biochemical processes and exhibit valuable pharmacological properties.[13—15] One of the synthetically promising and at the same time relatively poorly studied types of such alkynylcyclopropanes are 1-alkoxy-2-alkynylcyclopropanes. Previously, these compounds have been subjected to hydrogenation reactions,[16] the triple bond cross-couplings,[17] as well as were successfully used in the synthesis of unsaturated polycyclic alcohols[18] and ketones.[16]

Recently,[19] we have suggested a convenient approach to various 1-alkynyl-2-alkoxycyclopropanes *via* the reaction of easily available 1-alkynyl-1-halocyclopropanes with alcohols in the superbasic system KOH—DMSO. In continuation of these studies, it was interesting to explore a possibility of rational functionalizations of these compounds in order to develop methods for the selective synthesis of alkynylcyclopropanes having multiple functional groups. One of the possible approaches to such functionalization is lithiation of 1-alkynyl-2-alkoxycyclopropanes at the hydrogen atom at the α-position to the triple bond and subsequent reactions of the lithiated species with electrophilic reagents. Note that this process was described[18] only for 3-unsubstituted 1-alkoxy-2-(trimethylsilylethynyl)cyclopropanes and has not been systematically investigated to date.

The present work is devoted to the study of the regularities of lithiation of *gem*-dimethyl-substituted 1-alkoxy-2-(phenylethynyl)cyclopropanes and the reactions of the resulting organolithium species with various electrophiles.

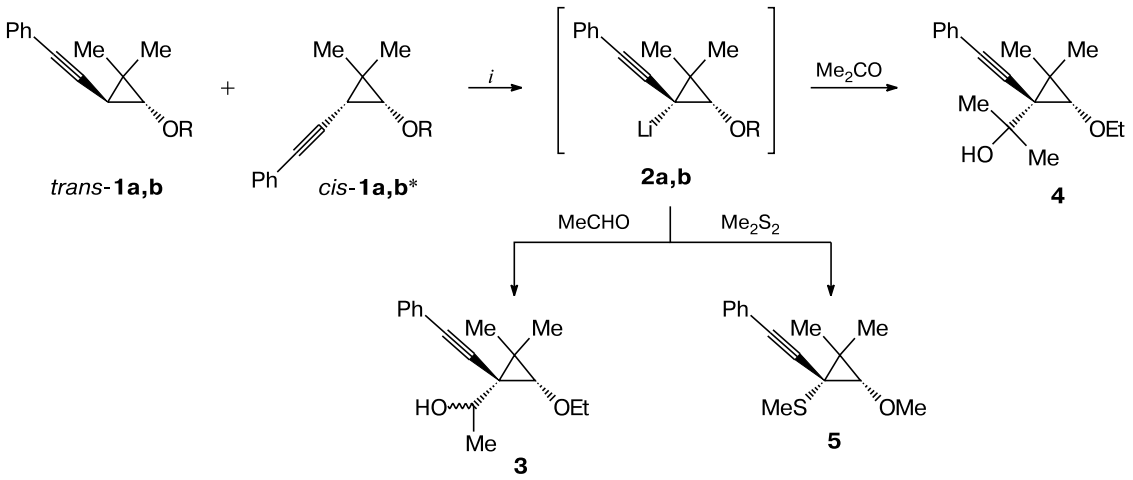
Results and Discussion

Herein, we found that addition of equimolar amount of a solution of BuLi in hexane to a solution of alkoxycyclopropane **1a** (*trans*-**1a** : *cis*-**1a** = 2.9 : 1) in THF at −(65—70) °C and keeping the reaction mixture at this temperature for 3 h with subsequent treatment with excess acetaldehyde results in alcohol **3** obtained as a 1.4 : 1 mixture of two diastereomers. Product **3** was isolated by column chromatography in 69% yield (Scheme 1). Besides, unreacted *cis*-isomer of the starting cyclopropane **1a** (26%) was recovered from the reaction mixture.

Taking into account that compounds **3** and *cis*-**1a** were obtained in the molar ratio close to the *cis* : *trans* isomer ratio of the starting cyclopropane **1a** and the complete absence of isomers of alcohol **3**, in which 1-hydroxyethyl fragment and ethoxy group are located on opposite sides of the cyclopropane ring plane, it may be concluded that lithiation of only *trans*-isomer of cyclopropane **1a** occurs under used reaction conditions and the corresponding *cis*-isomer remains unchanged. Most likely that such stereoselectivity is caused by effective coordination of the lithium atom by the oxygen atom of the alkoxy group of the *cis*-β-alkoxylithiocyclopropane **2a** being formed. This fact was confirmed by quantum chemical calculations (on B3LYP/6-31G level of theory) of the structure of model [(1*S**,3*R**)-1-ethynyl-3-methoxy-2,2-

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 5, pp. 0862—0866, May, 2017.
1066-5285/17/6605-0862

Scheme 1



* Isomers *cis*-**1a**,**b** are not reactive under the used reaction conditions.

1, 2: R = Et (**a**), Me (**b**)

Reagents and conditions: *i*. THF, BuLi (1 equiv.), –(65—70) °C.

dimethylcyclopropyl]lithium. It was shown that the distance between lithium and oxygen atoms in this compound is 1.86 Å, the C—O and C—Li bonds lie almost in the same plane, and the angle between them is only 13°.

Unfortunately, our attempt to metallate *cis*-**1a** at elevated temperature failed. Thus, reaction of the mixture of isomers of cyclopropane **1a** with equimolar amount of BuLi in THF at –(30—40) °C for 3 h was unselective and addition of acetaldehyde finalizing the reaction produced a complex mixture arising most likely from β-elimination of lithium ethoxide from lithiocyclopropane **2a** and subsequent transformations of unstable alkynylcyclopropene produced. According to the GC-analysis data, the reaction mixture contained some amount of *cis*-**1a** but due to the general low selectivity of the reaction, no quantitative determination of its conversion was performed.

Further, we discovered that functionalization of *trans*-1-alkoxy-2-alkynylcyclopropanes **1** by lithiation on treatment with BuLi and subsequent reactions with electrophilic agents is rather general. Thus, the use of anhydrous acetone as an electrophile allowed preparation of tertiary alcohol **4** in 62% yield based on the mixture of isomers of cyclopropane **1a** and in 84% based on the reacted *trans*-**1a** (see Scheme 1). Similarly, lithiation of cyclopropane **1b** (*trans*-**1b** : *cis*-**1b** = 2.1 : 1) with subsequent quenching with a slight excess of dimethyl disulfide affords sulfide derivative **5c** in 59% yield, which was separated from unreacted *cis*-**5b** by silica gel column chromatography.

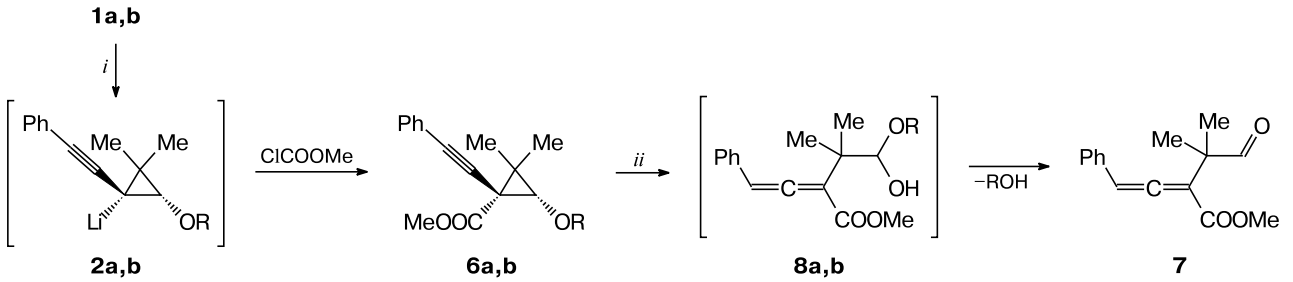
An attempt to introduce the ester substituent by treating cyclopropane **1a** with methyl chloroformate gave unexpected results. Despite the fact that according to the NMR data the reaction mixture after aqueous workup contained mainly the unreacted *cis*-**1a** and the expected cyclopropane ester **6a**, silica gel chromatography gives another product in 48% yield. Spectral characteristics of the latter correspond to allene aldehyde ester **7**. Similar results were obtained by using cyclopropane **1b** as the starting material (Scheme 2).

Most likely, the formation of compound **7** can be explained by strong polarization of the endocyclic C—C bond between an electron-withdrawing ester group and an electron-donating alkoxy group in esters **6a**,**b**. As a result, the ring opening with addition of water molecule occurs on silica gel with simultaneous acetylene-allene rearrangement and the final product **7** is formed by elimination of the alcohol molecule from hemiacetals **8a**,**b** (see Scheme 2).

At the same time, replacement of the sorbent by neutral aluminum oxide made it possible to exclude these transformations and to isolate individual esters **6a**,**b** in the yields of 55 and 51%, respectively, based on both isomers of the starting cyclopropanes **1a**,**b**.

Spatial arrangement of the substituents in compounds **3**—**5** was determined based on the data of 2D NOESY spectra. For alcohols **3** and **4**, correlations between the signals of the methylene protons of the ethoxy group and the signals of methyl protons of 1-hydroxyethyl (for **3**) and 2-hydroxyprop-2-yl (for **4**) moieties were observed. In the case of sulfide **5**, similar correlations between the signals of the protons for methoxy and methylthio groups were found. These results point to the fact that compounds **3**—**5** have *cis*-arrangement of the alkoxy group and the substituent introduced by the reaction with electrophile. Apparently, esters **6a**,**b** obtained by the reaction

Scheme 2



1, 2, 6, 8: R = Et (**a**), Me (**b**)

Reagents and conditions: *i*. THF, BuLi (1 equiv.), −(65—75) °C; *ii*. SiO_2, THF—hexane.

of organolithium compounds **2a**,**b** with methyl chloroformate have the same structure. Thus, stereoconfiguration of the cyclopropane ring is completely retained upon the studied processes.

Metallation of cyclopropane **1a** with BuLi in THF followed by the addition of an excess solid carbon dioxide failed to produce the expected cyclopropanecarboxylic acid. Instead, aqueous workup of the reaction mixture, acidification of the aqueous layer, extraction, and chromatographic separation on neutral Al_2O_3 give another product in 57% yield. According to NMR data, this product was found to be 2-(1-chloro-1-ethoxy-2-methylprop-2-yl)-4-phenylbut-3-ynoic acid (**9**) obtained as a 1.2 : 1 mixture of two diastereomers. Probably, the formation of acid **9**, similarly to esters **6**, is a result of easy cleavage of the C—C bond of the three-membered cycle of the initially formed acid **10** accompanied with addition of the HCl molecule (Scheme 3).

Therefore, both esters **6** and acid **9** bearing a vicinal electron-donor alkoxy group and an electron-acceptor carboxyl substituent exhibit pronounced properties of donor-acceptor cyclopropanes[20] readily undergoing heterolytic cleavage of the endocyclic C—C bond.

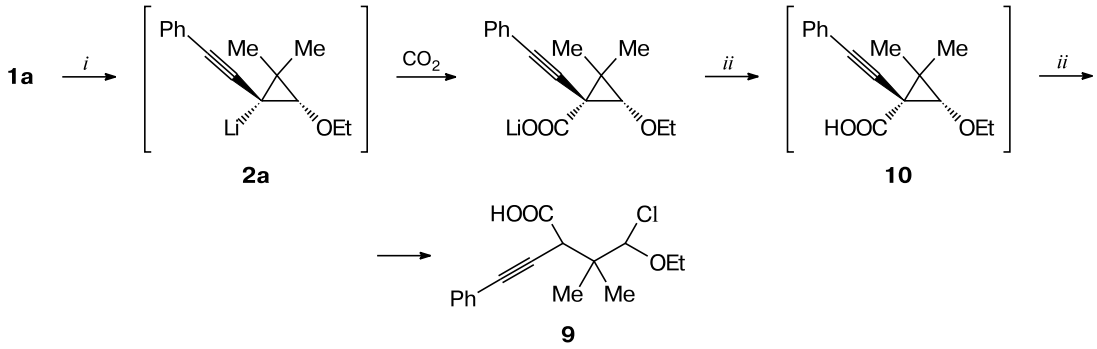
Experimental

The starting compounds and products were analyzed by GC using a Hewlett—Packard 5890 Series II chromatograph equipped with a HP-1 (30 m×0.153 mm) capillary column and a Hewlett—Packard 3396A automatic integrator. ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-200p instrument in $CDCl_3$. The chemical shifts are given in the δ scale and referenced to $SiMe_4$ (an internal standard). Two-dimensional NOESY spectra of compounds **3**—**5** were recorded on a Bruker AMX-400 instrument at working frequency of 400 MHz.

High resolution electrospray ionization mass spectrometry was performed on a Bruker micrOTOF II instrument operating in a positive ion mode (capillary voltage of 4500 V); an operating mass range (*m*/*z*) of 50—3000 Da; calibration was internal and external (Fluka Electrospray Calibrant Solution). The samples (solutions in MeCN) were introduced *via* syringe inlet at a flow rate of 3 μL min^{-1}; nebulizer gas was nitrogen (flow rate of 4 L min^{-1}), interface temperature was 180 °C.

Density functional theory calculations of the structure of model compound, [(1*S**,3*R**)-1-ethynyl-3-methoxy-2,2-dimethylcyclopropyl]lithium was performed at B3LYP level[21,22] with 6-31G basis set using Gamess calculation module integrated into CambridgeSoft Chemoffice Ultra 2014 suite.

Scheme 3



Reagents and conditions: *i*. THF, BuLi (1 equiv.), −(65—75) °C; *ii*. HCl, H_2O.

Tetrahydrofuran was dried by distillation over $LiAlH_4$ immediately prior to use. The starting alkoxycyclopropanes **1a**,**b** were synthesized from the corresponding 1-alkynyl-1-chlorocyclopropanes by the reaction with alcohols (ethanol, methanol) in DMSO in the presence of KOH following the procedure developed by us earlier.[19]

Synthesis of cyclopropane derivatives 3—7 from alkoxycyclopropanes 1a,b (general procedure). To a solution of the corresponding cyclopropane **1** (1 mmol) in anhydrous THF (3 mL), 1.6 *M* solution of BuLi in hexane (0.7 mL, 1.12 mmol) was added at −(65—70) °C under a dry argon atmosphere. The reaction mixture was stirred for 3 h at the same temperature and treated with a solution of the corresponding electrophile (1.2 mmol) (acetaldehyde, acetone, dimethyl disulfoxide, methyl chloroformate) in anhydrous THF (1 mL). When the reaction temperature reached ambient, the mixture was treated with water (10 mL) and CH_2Cl_2 (30 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried with anhydrous Na_2SO_4 and the solvent was removed. Purification of the residue by column chromatography afforded compounds **3**—**5**, **6a**,**b**, **7**, and unreacted *cis* isomers of cyclopropanes **1a**,**b**.

1-[(1*S,3*S**)-2,2-Dimethyl-1-phenylethynyl-3-ethoxycyclopropyl]ethanol (3)** was synthesized from cyclopropane **1a** and acetaldehyde. Compound **3** was isolated in 69% yield by silica gel column chromatography (elution with hexane—Et_2O, 20 : 1→5 : 1) as a mixture of two diastereomers in a ratio of 1.4 : 1. Along with the target product **3**, from the first fractions cyclopropane *cis*-**1a** (52 mg (26%) with >90% purity was isolated. MS (ESI), found: *m*/*z* 259.1697 $[M + H]^+$; calculated for $C_{17}H_{22}O_2$, $[M + H]^+$: *m*/*z* 259.1693.

Major diastereomer. ^{1}H NMR, δ: 1.21 (t, 3 H, $OCH_2C\underline{H}_3$, J = 7.0 Hz); 1.32 (s, 3 H, CH_3); 1.34 (s, 3 H, CH_3); 1.48 (d, 3 H, $C\underline{H}_3CH(OH)$, J = 6.3 Hz); 1.96 (br.s, 1 H, OH); 3.12 (s, 1 H, C<u>H</u>OEt); 3.55 (q, 2 H, $OC\underline{H}_2CH_3$, J = 7.0 Hz); 3.96 (q, 1 H, C<u>H</u>OH, J = 6.3 Hz); 7.23—7.32 (m, 3 H, Ph); 7.37—7.48 (m, 2 H, Ph). ^{13}C NMR, δ: 14.2, 15.1, 22.9, 23.7 (4 CH_3); 26.7 ($\underline{C}(CH_3)_2$); 32.8 (C≡C<u>C</u>, *cyclo*-C_3); 65.4 (CHOH); 66.7 ($O\underline{C}H_2CH_3$); 71.7 (<u>C</u>HOEt); 81.7, 88.9 (C≡C); 123.8 (C(1), Ph); 127.5 (C(4), Ph); 128.1, 131.6 (C(2), C(3), C(5), C(6), Ph).

Minor diastereomer. ^{1}H NMR, δ: 1.17 (s, 3 H, CH_3); 1.24 (t, 3 H, $OCH_2C\underline{H}_3$, J = 7.1 Hz); 1.27 (s, 3 H, CH_3); 1.40 (d, 3 H, $C\underline{H}_3CH(OH)$, J = 6.4 Hz); 2.24 (br.s, 1 H, OH); 3.20 (s, 1 H, C<u>H</u>OEt); 3.61 (dq, 1 H, $OC\underline{H}HCH_3$, ^2J = 9.4 Hz, ^3J = 7.1 Hz); 3.78 (dq, 1 H, $OC\underline{H}HCH_3$, ^2J = 9.4 Hz, ^3J = 7.1 Hz); 3.88—3.97 (m, 1 H, C<u>H</u>OH); 7.23—7.32 (m, 3 H, Ph); 7.37—7.48 (m, 2 H, Ph). ^{13}C NMR, δ: 14.4, 15.2, 21.2, 23.5 (4 CH_3); 26.8 ($\underline{C}(CH_3)_2$); 33.0 (C≡C<u>C</u>, *cyclo*-C_3); 64.6 (CHOH); 66.8 ($O\underline{C}H_2CH_3$); 70.7 (<u>C</u>HOEt); 81.7, 88.8 (C≡C); 123.7 (C(1), Ph); 127.5 (C(4), Ph); 128.1, 131.6 (C(2), C(3), C(5), C(6), Ph).

2-[(1*R,3*S**)-3-Ethoxy-2,2-dimethyl-1-(phenylethynyl)-cyclopropyl]propan-2-ol (4)** was synthesized from cyclopropane **1a** and acetone. Compound **4** was isolated by silica gel column chromatography (elution with hexane—Et_2O, 20 : 1→10 : 1) in 62% yield. ^{1}H NMR, δ: 1.26 (t, 3 H, $OCH_2C\underline{H}_3$, J = 7.0 Hz); 1.33 (s, 3 H, CH_3); 1.46 (s, 3 H, CH_3); 1.53 (s, 3 H, CH_3); 1.63 (s, 3 H, CH_3); 3.28 (s, 1 H, C<u>H</u>OEt); 3.64 (dq, 1 H, $OC\underline{H}HCH_3$, ^2J = 9.4 Hz, ^3J = 7.0 Hz); 3.67 (dq, 1 H, $OC\underline{H}HCH_3$, ^2J = 9.4 Hz, ^2J = 7.0 Hz); 3.89 (br.s, 1 H, OH); 7.23—7.40 (m, 5 H, Ph). ^{13}C NMR, δ: 14.8 (CH_3); 15.3 (CH_3); 26.2 (CH_3); 26.9 ($\underline{C}(CH_3)_2$); 28.0 (CH_3); 32.6 (C≡C<u>C</u>, *cyclo*-C_3); 32.7 (CH_3); 67.6 ($O\underline{C}H_2CH_3$); 73.1 (<u>C</u>HOEt); 74.3 ($\underline{C}(CH_3)_2OH$); 79.8, 92.6 (C≡C); 124.1 (C(1), Ph); 127.6 (C(4), Ph); 128.3, 131.4 (C(2), C(3), C(5), C(6), Ph). MS (ESI), found: *m*/*z* 273.1853 $[M + H]^+$; calculated for $C_{18}H_{24}O_2$, $[M + H]^+$: *m*/*z* 273.1849.

[(1*R,3*S**)-3-Methoxy-2,2-dimethyl-1-(phenylethynyl)-cyclopropyl] methyl sulfide (5)** was synthesized from cyclopropane **1b** and dimethyl disulfide. Compound **5** was isolated by silica gel column chromatography (elution with hexane—Et_2O, 30 : 1) in the yield of 59%. ^{1}H NMR, δ: 1.39 (s, 6 H, 2 CH_3); 2.35 (s, 3 H, SCH_3); 3.23 (s, 1 H, C<u>H</u>OCH_3); 3.52 (s, 3 H, OCH_3); 7.25—7.36 (m, 3 H, Ph); 7.40—7.52 (m, 2 H, Ph). ^{13}C NMR, δ: 14.8, 14.9 (2 CH_3, SCH_3); 23.2 (CH_3); 30.2 ($\underline{C}(CH_3)_2$); 30.8 (C≡C<u>C</u>, *cyclo*-C_3); 59.2 (OCH_3); 73.8 (<u>C</u>HOCH_3); 80.8, 89.5 (C≡C); 123.5 (C(1), Ph); 127.7 (C(4), Ph); 128.1, 131.6 (C(2), C(3), C(5), C(6), Ph). MS (ESI), found: *m*/*z* 247.1148 $[M + H]^+$; calculated for $C_{15}H_{18}OS$, $[M + H]^+$: *m*/*z* 247.1151.

Methyl (1*R,3*S**)-3-ethoxy-2,2-dimethyl-1-(phenylethynyl)cyclopropanecarboxylate (6a)** was synthesized from cyclopropane **1a** and methyl chloroformate. Compound **6a** was isolated by column chromatography on neutral Al_2O_3 (elution with hexane—Et_2O, 20 : 1→10 : 1) in the yield of 55%. ^{1}H NMR, δ: 1.25 (t, 3 H, $OCH_2C\underline{H}_3$, J = 7.0 Hz); 1.40 (s, 3 H, CH_3); 1.42 (s, 3 H, CH_3); 3.50 (s, 1 H, C<u>H</u>OEt); 3.66 (q, 2 H, $OC\underline{H}_2CH_3$, J = 7.0 Hz); 3.75 (s, 3 H, $COOCH_3$); 7.23—7.32 (m, 3 H, Ph); 7.37—7.49 (m, 2 H, Ph). ^{13}C NMR, δ: 14.3, 15.4, 23.0 (3 CH_3); 29.9 ($\underline{C}(CH_3)_2$); 33.7 (C≡C<u>C</u>, *cyclo*-C_3); 52.3 ($COO\underline{C}H_3$); 67.1 ($O\underline{C}H_2CH_3$); 77.2 (<u>C</u>HOCH_2CH_3); 81.3, 87.3 (C≡C); 123.4 (C(1), Ph); 127.8 (C(4), Ph); 128.1, 131.6 (C(2), C(3), C(5), C(6), Ph); 167.2 (<u>C</u>$OOCH_3$). MS (ESI), found: *m*/*z* 273.1487 $[M + H]^+$; calculated for $C_{17}H_{20}O_3$, $[M + H]^+$: *m*/*z* 273.1485.

Methyl (1*R,3*S**)-3-methoxy-2,2-dimethyl-1-(phenylethynyl)cyclopropanecarboxylate (6b)** was synthesized from cyclopropane **1b** and methyl chloroformate. Compound **6b** was isolated by column chromatography on neutral Al_2O_3 (elution with hexane—Et_2O, 20 : 1→10 : 1) in the yield of 51%. ^{1}H NMR, δ: 1.39 (s, 3 H, CH_3); 1.40 (s, 3 H, CH_3); 3.42 (s, 1 H, C<u>H</u>OCH_3); 3.47 (s, 3 H, OCH_3); 3.75 (s, 3 H, $COOCH_3$); 7.23—7.32 (m, 3 H, Ph); 7.37—7.49 (m, 2 H, Ph). ^{13}C NMR, δ, 14.4, 23.1 (2 CH_3); 29.8 ($\underline{C}(CH_3)_2$); 33.5 (C≡C<u>C</u>, *cyclo*-C_3); 52.1 ($COO\underline{C}H_3$); 58.8 (OCH_3); 77.5 (<u>C</u>HOCH_3); 81.4, 87.2 (C≡C); 123.3 (C(1), Ph); 127.8 (C(4), Ph); 128.1, 131.6 (C(2), C(3), C(5), C(6), Ph); 167.3 (<u>C</u>$OOCH_3$). MS (ESI), found: *m*/*z* 259.1332 $[M + H]^+$; calculated for $C_{16}H_{18}O_3$, $[M + H]^+$: *m*/*z* 259.1329.

Methyl 2-(1,1-dimethyl-2-oxoethyl)-4-phenylbuta-2,3-dienoate (7) was synthesized from cyclopropane **1a** and methyl chloroformate. Compound **7** was isolated by silica gel column chromatography (elution with hexane—Et_2O, 5 : 1) in the yield of 48%. ^{1}H NMR, δ: 1.31 (s, 6 H, 2 CH_3); 3.72 (s, 3 H, $COOCH_3$); 6.71 (s, 1 H, PhC<u>H</u>=); 7.25—7.37 (m, 5 H, Ph); 9.66 (s, 1 H, CHO). ^{13}C NMR, δ: 21.9, 22.2 (2 CH_3); 48.0 ($\underline{C}(CH_3)_2$); 52.4 ($COO\underline{C}H_3$); 100.3 (Ph<u>C</u>H=); 108.6 (=<u>C</u>$COOCH_3$); 127.2, 129.0 (C(2), C(3), C(5), C(6), Ph); 128.2 (C(4), Ph); 131.4 (C(1), Ph); 165.9 (<u>C</u>$OOCH_3$); 201.9 (CHO); 212.1 (=C=). MS (ESI), found: *m*/*z* 245.1176 $[M + H]^+$; calculated for $C_{15}H_{16}O_3$, $[M + H]^+$: *m*/*z* 245.1172.

2-(1-Chloro-1-ethoxy-2-methylprop-2-yl)-4-phenylbut-3-ynoic acid (9). To a solution of cyclopropane **1a** (200 mg, 1 mmol) in anhydrous THF (3 mL), 1.6 *M* solution of BuLi in hexane (0.7 mL, 1.12 mmol) was added at −(65—70) °C under

argon. The mixture was stirred for 3 h at the same temperature and treated with excess solid carbon dioxide. When the reaction temperature reached room temperature, water (10 mL) and Et_2O (30 mL) were added and the organic layer was separated. The aqueous layer was washed with Et_2O (10 mL) and acidified with diluted HCl. The liberated oil was extracted with CH_2Cl_2 (2×10 mL). The combined organic layers were dried with anhydrous Na_2SO_4 and concentrated. Purification of the residue by column chromatography on neutral Al_2O_3 (elution with hexane—CH_2Cl_2, 10 : 1) afforded 170 mg (57%) of compound **9** as a mixture of two diastereomers in a ratio of 1.2 : 1. Found (%): C, 65.31; H, 6.39. $C_{16}H_{19}ClO_3$. Calculated (%): C, 65.19; H, 6.50.

Major diastereomer. ^{1}H NMR, δ: 1.24 (s, 3 H, CH_3); 1.26 (s, 3 H, CH_3); 1.29 (t, 3 H, $OCH_2C\underline{H}_3$, J = 6.9 Hz); 3.55—4.01 (m, 2 H, $O\underline{C}H_2CH_3$); 3.77 (s, 1 H, C<u>H</u>COOH); 5.09 (s, 1 H, CHCl(OEt)); 7.26—7.38 (m, 3 H, Ph); 7.43—7.52 (m, 2 H, Ph); 10.85 (br.s, 1 H, COOH). ^{13}C NMR, δ: 14.8 ($OCH_2\underline{C}H_3$); 20.3 (CH_3); 23.3 (CH_3); 44.1 (<u>C</u>HCOOH); 44.7 ($\underline{C}(CH_3)_2$); 65.3 ($O\underline{C}H_2CH_3$); 80.2, 86.4 (C≡C); 108.6 (CHCl(OEt)); 122.5 (C(1), Ph); 128.2, 128.4, 131.5 (C(2), C(3), C(4), C(5), C(6), Ph); 173.0 (COOH).

Minor diastereomer. ^{1}H NMR, δ: 1.20 (s, 3 H, CH_3); 1.25 (t, 3 H, $OCH_2C\underline{H}_3$, J = 6.9 Hz); 1.27 (s, 3 H, CH_3); 3.55—4.01 (m, 2 H, $O\underline{C}H_2CH_3$); 3.54 (s, 1 H, C<u>H</u>COOH); 5.17 (s, 1 H, CHCl(OEt)); 7.26—7.38 (m, 3 H, Ph); 7.43—7.52 (m, 2 H, Ph); 10.85 (br.s, 1 H, COOH). ^{13}C NMR, δ: 14.9 ($OCH_2\underline{C}H_3$); 17.1 (CH_3); 22.1 (CH_3); 44.8 ($\underline{C}(CH_3)_2$); 46.9 (<u>C</u>HCOOH); 67.0 ($O\underline{C}H_2CH_3$); 80.3, 86.3 (C≡C); 109.6 (CHCl(OEt)); 122.5 (C(1), Ph); 128.2, 128.4, 131.5 (C(2), C(3), C(4), C(5), C(6), Ph); 170.9 (COOH).

This work was financially supported by the Council on Grants of the President of the Russian Federation (Program for State Support of the Leading Scientific Schools, Grant NSh-8012.2016.3).

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Received November 23, 2016;
in revised form February 1, 2017