Article

Ring Opening of Donor-Acceptor Cyclopropanes with Cyanide Ion and Its Surrogates

Maksim Boichenko, Ivan Andreev, Alexey O. Chagarovskiy, Irina I. Levina, Sergey S. Zhokhov, Igor V. Trushkov, and Olga A. Ivanova

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.9b03098 • Publication Date (Web): 05 Dec 2019

Ring Opening of Donor-Acceptor Cyclopropanes with Cyanide Ion and Its Surrogates

Maksim A. Boichenko,[†] Ivan A. Andreev,[‡,II] Alexey O. Chagarovskiy,[‡,II] Irina I. Levina,[§] Sergey S. Zhokhov,[†] Igor V. Trushkov,[‡,II,*] Olga A. Ivanova[†,‡,*]

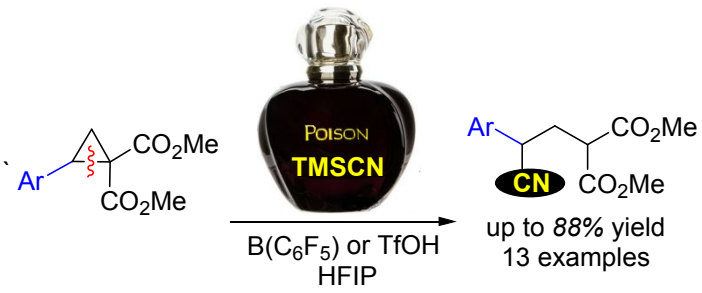
[†] Department of Chemistry, M. V. Lomonosov Moscow State University, Leninskie gory 1-3, Moscow 119991, Russian Federation; iv@kinet.chem.msu.ru

[‡] N. D. Zelinsky Institute of Organic Chemistry Russian Academy of Sciences, Leninsky pr. 47, Moscow 119991, Russian Federation; trush@ioc.ac.ru

[II] Laboratory of Chemical Synthesis, Dmitry Rogachev National Medical Research Center of Pediatric Hematology, Oncology and Immunology, Samory Mashela 1, Moscow 117997, Russian Federation

[§] N. M. Emanuel Institute of Biochemical Physics, Russian Academy of Sciences, Kosygina 4, Moscow 119334, Russian Federation

Abstract:



A straightforward method for ring opening of donor-acceptor cyclopropanes with trimethylsilyl cyanide as a surrogate of cyanide ion in the presence of $B(C_6F_5)_3$

or trifluoromethanesulfonic acid as a catalyst has been developed. The methodology provides a short route to γ-cyanoesters that can be useful synthetic intermediates for the synthesis of diverse bioactive molecules such as glutaric and δ-aminovaleric acid derivatives, 3-arylpiperidines or other substituted phenethylamines. Oppositely, the attempts to synthesize these γ-cyanoesters by direct reaction of cyclopropanes with sodium cyanide under typical S_N2 conditions led to the formation of 2-arylsuccinonitriles.

Introduction

Even though cyclopropanes with donor and acceptor substituents at the vicinal carbon atoms (DA cyclopropanes) are known more than 125 years,[1] they were predominantly considered as exotic compounds until seminal works by Wenkert[2] and Reissig[3] who laid the foundations for the explosive growth of the study of DA cyclopropanes as building blocks in the synthesis of a broad diversity of acyclic, alicyclic, and heterocyclic compounds, observed in the last two decades.[4] The presence of donor and acceptor substituents at vicinal carbon atoms provides excellent reactivity of three-membered rings as synthetic equivalents of all-carbon 1,3-dipoles in diverse (3+n)-cycloadditions[5] or 1,3-difunctionalizations.[6] Moreover, DA cyclopropanes usually demonstrate higher reactivity against nucleophiles in comparison with the corresponding electrophilic cyclopropanes without a donor substituent.[7] Ring openings of DA cyclopropanes with diverse nucleophiles including anilines,[8] phenols,[9] indoles,[10] other electron-abundant

(het)arenes,[11] as well as various anions such as CH-acid-derived enolates,[12] azide-ion,[7a,11a,13] etc. are well studied and employed in total syntheses.[4b,g,7a] Therefore, we were surprised that despite multiple investigations of electrophilic cyclopropanes reactivity towards cyanide ion (Scheme 1, a)[14] there is only one reported example of DA cyclopropanes opening with this nucleophile (Scheme 1, b).[15] We decided to bridge this gap and developed the method for the synthesis of 2-(het)aryl-2-cyanoethyl-substituted malonates (Scheme 1, c), given that they contain 2-arylacetonitrile moiety which is present in diverse bioactive compounds including approved drugs such as antiarrhythmic and antihypertensive agent verapamil[16] or opioid analgesic piritramide (Figure 1).[17] Moreover, such products could be intermediates for the synthesis of a broad diversity of valuable compounds, being, for example, latent 2-arylethylamines and 3-arylpiperidines; these structural motifs are encountered in many important bioactive products and pharmaceuticals (anxiolytic phenibut,[18] σ and D_2 receptors antagonist preclamol,[19] *etc*., see Figure 1). Herein, we report the results of our investigations.

Scheme 1. Cyclopropanes Hydrocyanation

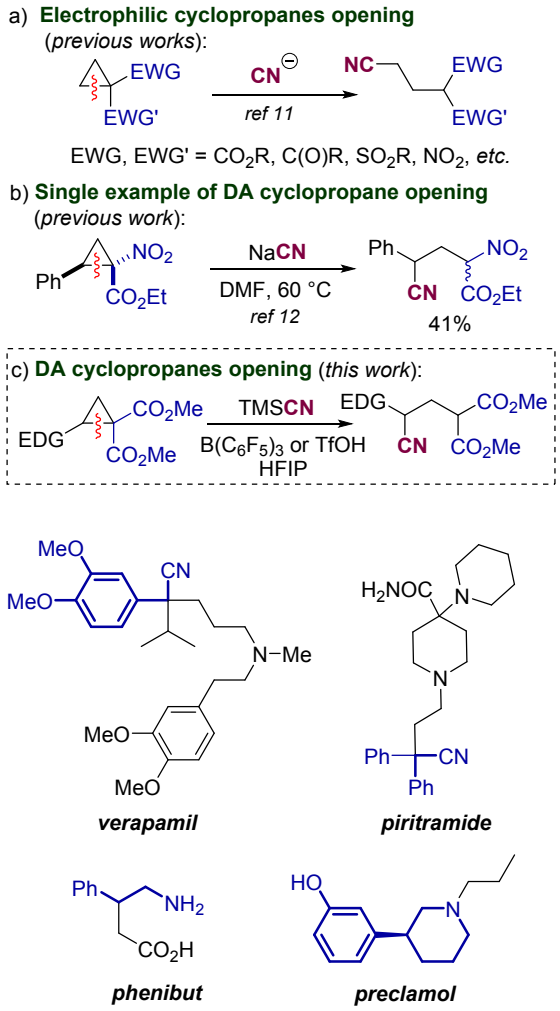


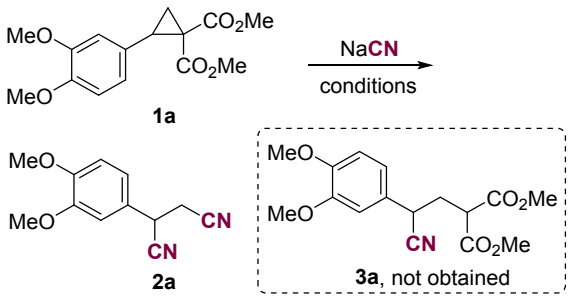
Figure 1. Selected Bioactive Arylacetonitriles and 3-Arylpiperidines

Results and Discussion

We commenced this study with the ring opening of 3,4-dimethoxyphenyl-substituted cyclopropane **1a** as a model substrate with sodium cyanide under typical S_N2 conditions. The reaction conditions optimization was performed under the variation of solvents, reaction temperature and additives. We found that heating of **1a** with NaCN in DMF or DMSO was inefficient (Table 1, entries 1–3). One of the possible reasons can be the reversibility of the studied reaction similar to that found for the reaction of **1** with azide ion;[7a] as a result, side

reactions, such as oligomers formation, dominated over the target process. In the above study,[7a] the use of triethylamine hydrochloride allowed to prevent the reverse cyclization *via* protonation of the incipient malonate anion; however, this additive was found to be inefficient for the reaction in question (Table 1, entries 5, 6). The use of nitromethane as a mild protonating agent allowed us to obtain a low-molecular-weight product, but we found that 3,4-dimethoxyphenyl-substituted succinonitrile **2a** was obtained instead of the target product **3a** (Table 1, entry 7). A further variation of reaction conditions allowed to increase the yield of **2a** up to 43% (Table 1, entry 9) but was unsuccessful in terms of **3a** preparation.

Table 1. Optimization of the Reaction Conditions[a]



entry	additive	Solvent	T, °C	t, h	Yield, %
1		DMSO	80	3	-[b]
2		DMSO	140	3	-[b]
3		DMF	100	3	-[b]
4		[BMIM]PF_6[c]	100	5	-
5	$Et_3N{\cdot}HCl$	DMF	100	3	-[b]
6	$Et_3N{\cdot}HCl$	DMSO	100	3	-[b]

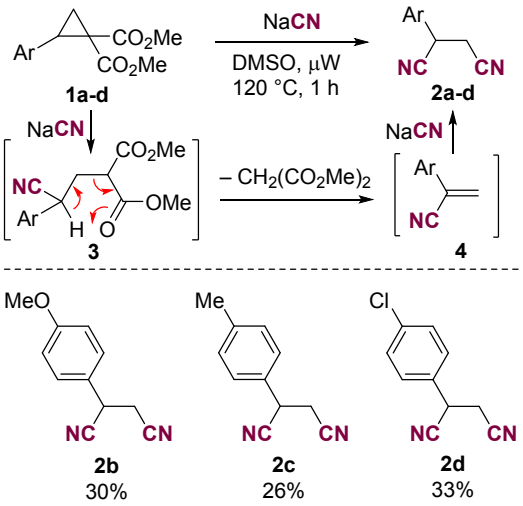
7	CH_3NO_2	DMSO	100	8	31
8	CH_3NO_2	DMSO	100	3[d]	41
9	**CH_3NO_2**	**DMSO**	**120**	**1[d]**	**43**
10	CH_3NO_2	DMSO	140	0.25	37
11	CH_3NO_2	NMP	100	3	39
12	HFIP[e]	DMSO	120	1	31

[a] Concentration of **1a** was 0.1 M. [b] Oligomers of starting cyclopropane and product of hydrolysis were detected in the reaction mixture. [c] 1-Butyl-3-methylimidazolium hexafluorophosphate. [d] Under microwave irradiation. [e] 1,1,1,3,3,3-Hexafluoroisopropanol.

Under the same conditions, cyclopropanes **1b-d** were transformed into 2-arylsuccinonitriles **2b-d**, but products were obtained in low yields in comparison with those in reported methods[20] making this approach inappropriate for further development.

The possible mechanism of products **2** formation is shown in Scheme 2. The attack of cyanide ion on DA cyclopropane affords the desired product **3**, which decomposes to dimethyl malonate and α-cyanostyrene **4**. The Michael addition of the second cyanide ion to this acceptor alkene accomplishes the formation of succinonitrile **2**.[21] The intermediacy of styrene **4** and, therefore, the disclosed chemoselectivity can result from the conjugation of the formed C=C bond with both nitrile group and aromatic moiety. The last conjugation seems to be crucial as cyclopropanes without an aromatic group afforded "normal" products of cyanide ion addition.[14]

Scheme 2. 2-Arylsuccinonitriles Obtained and Possible Mechanism of Their Formation[a]



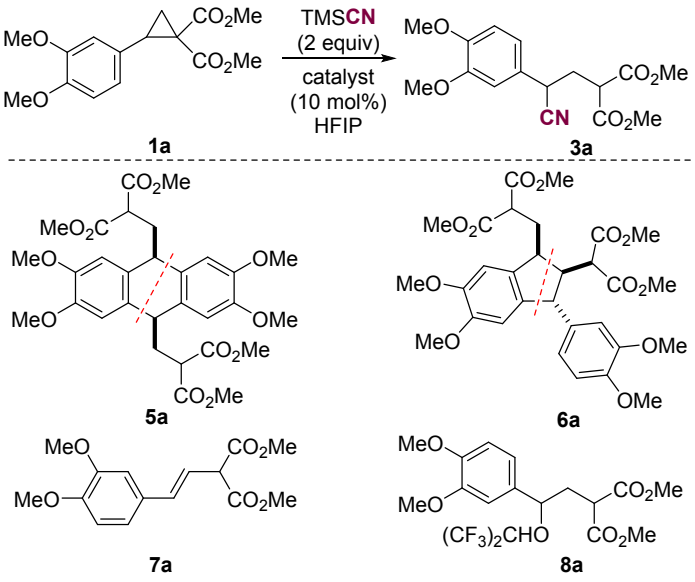
[a] For reaction conditions, see Table 1, entry 9.

Our attempts to use sodium cyanide in combination with Lewis acids as well as acetone cyanohydrin as a surrogate of cyanide ion were unsuccessful, and thus we switched our attention to trimethylsilyl cyanide. This reagent was previously used for the formal addition of hydrogen cyanide to Michael acceptors.[20b,22] Moreover, DA cyclopropane opening with $TMSN_3$ in the presence of TfOH (10 mol %) in HFIP at room temperature was recently demonstrated to be a good alternative to the direct reaction with sodium azide.[11b]

Indeed, under disclosed conditions, TMSCN afforded the desired cyanoethyl-substituted malonate **3a** in 25% yield (Table 2, entry 1). The variation of reaction temperature, catalyst loading, *etc.* did not increase the target product yield. We studied other catalysts and found that under similar conditions $B(C_6F_5)_3$ induced the formation of **3a** in comparable yield; products of cyclopropane **1a** dimerizations (**5a**,[23] **6a**[24]) and isomerization (**7a**)[24,25] were also formed (Table 2,

entry 2). Under microwave irradiation, the yield of **3a** did not change, but only one side product (dimer **5a**) was formed (entry 3). When the reaction was performed in the presence of $Sc(OTf)_3$, product **3a** was not obtained at all; the product of cyclopropane **1a** opening with HFIP (compound **8a**) was predominantly formed (Table 2, entry 4). It is the first example of DA cyclopropane ring opening with this low-nucleophilic alcohol.[26] The increase of temperature, reaction time and TMSCN loading did not increase the yield of **3a** (entries 5-9). Oppositely, the highest yield was obtained under stirring at 0 °C (entry 10). This temperature dependence comports with the decomposition of cyanomalonates **3**, yielding succinonitriles **2** under heating with NaCN at 100 °C and higher temperatures.

Table 2. Optimization of Conditions for the Reaction between DA Cyclopropane 1a and TMSCN[a]



entry	catalyst	T, °C	t, h	Yield, %[b]
1	TfOH	20	3	(25)
2	$B(C_6F_5)_3$	20	17	40[c]
3	$B(C_6F_5)_3$	20[d]	2	41[e]
4	$B(C_6F_5)_3$	20[f]	3	-[g]
5	$B(C_6F_5)_3$	58[h]	4	25[i]
6	$B(C_6F_5)_3$	60[d,h]	14	30
7	$B(C_6F_5)_3$	80[d]	7	58 (50)
8	$B(C_6F_5)_3$	80[d,h]	24	36[j]
9	**$B(C_6F_5)_3$**	**0[k]**	**1**	**60 (55)[i]**

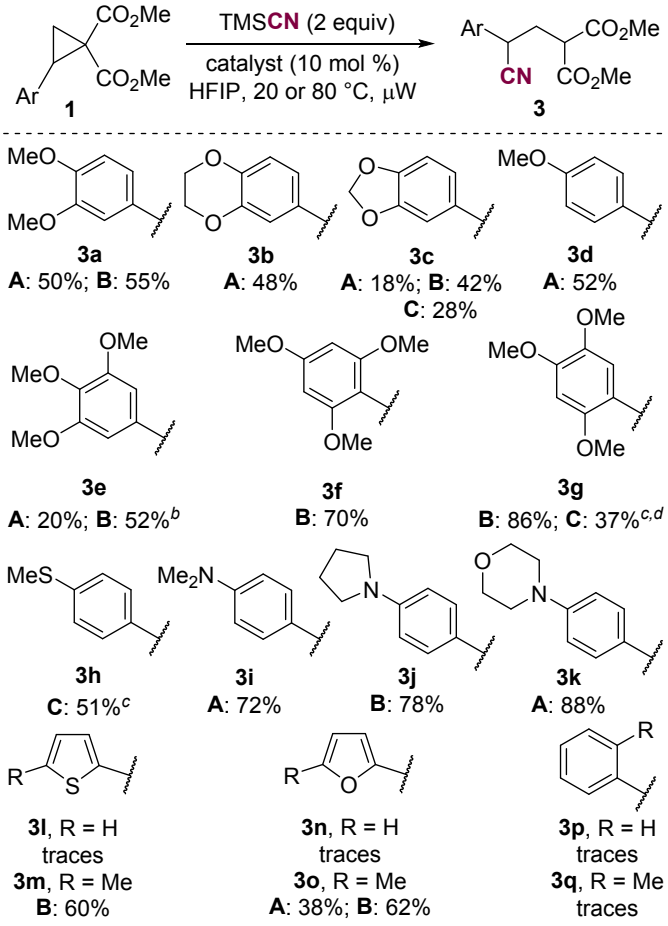
[a] Concentration of **1a** was 2 M. [b] NMR yields (hexamethyldisiloxane was used as internal standard); in parentheses – yields after chromatography. [c] **5a** (10%), **6a** (15%), **7a** (5%) were also formed. [d] Under microwave irradiation. [e] **5a** (25%) was also obtained. [f] Concentration of **1a** was 0.06 M; in the presence of $Sc(OTf)_3$ (10 mol %). [g] **7a** (15%) and **8a** (55%) were formed. [h] 3 equiv of TMSCN. [i] **5a** (15%) was also formed. [j] **5a** (17%) was also formed. [k] Concentration of **1a** was 1.3 M.

Next, we studied the scope of the disclosed reaction employing a series of DA cyclopropanes wherein a donor substituent is either a phenyl group containing diverse substituents or five-membered heterocycles. Three procedures were applied: $B(C_6F_5)_3$-induced reaction under microwave irradiation at 80 °C (method **A**), reaction in a sealed vial in the presence of the same Lewis acid at 0 °C, rt or moderate heating (method **B**), as well as TfOH-catalyzed process at room temperature (method **C**) (Scheme 3).

The obtained results demonstrated that yields of products **3** were consistently higher when method **B** was used; for compounds **3i**,**k** bearing electron-rich aromatic groups high yields were achieved even with method **A**.

Oppositely, for substrates **1** with electron-neutral aryl substituents all methods furnished the desired products **3p**,**q** in trace amounts only. Other cyclopropanes with electron-abundant (hetero)aromatic groups afforded **3** with yields varying from 37 to 86%. In reactions with moderate yields of products, dimerization and/or oligomerization of starting cyclopropanes were predominant side processes. It is worth noting that a three-membered ring opening with TMSCN proceeds exclusively *via* attack of the carbon atom of cyanide moiety on the benzylic atom of cyclopropane, providing no isomeric products.

Scheme 3. Scope of DA Cyclopropanes Ring Opening with TMSCN[a]

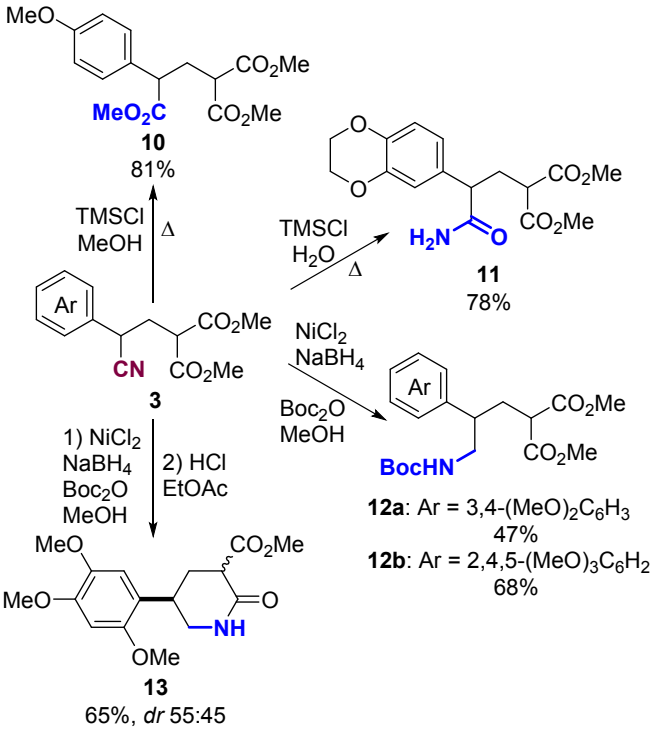


[a] Reaction conditions: 2 M solution of **1** in HFIP, TMSCN (2 equiv). **Method A**: microwave irradiation, $B(C_6F_5)_3$ (10 mol %), 80 °C, 7 h; **Method B**: closed vial, $B(C_6F_5)_3$ (10 mol %),

0 °C, rt or 50 °C; **Method C**: closed vial, TfOH (10 mol %), rt. [b] At 70 °C. [c] 20 mol % TfOH. [d] Cyclopropane **1i** dimer **9** with tetralin framework was also obtained in 33% yield; see Experimental part.

A series of further transformations of nitriles **3** was performed to demonstrate the synthetic utility of these compounds (Scheme 4). In particular, we converted nitrile moieties in **3** into the corresponding ester **10**, amide **11** and Boc-protected amines **12a**,**b**. Moreover, we synthesized arylpiperidone **13** by HCl-induced cyclization of **12a**, demonstrating that the developed method can be used as a short route to 3-arylpiperidines (preclamol,[19] OSU-6162,[27] *etc*.) which have important bioactivities.

Scheme 4. Post-modifications of Compounds 3

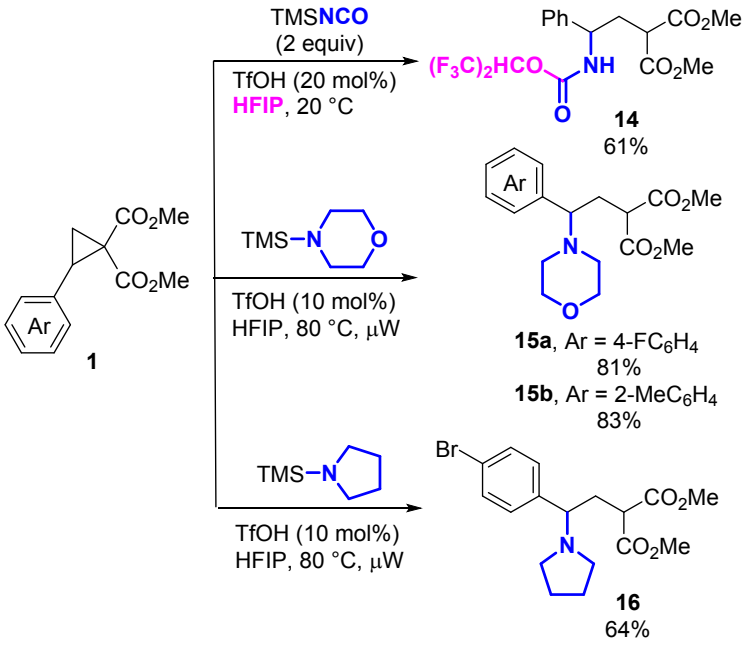


Encouraged by the obtained results, we investigated the efficiency of the TMS-Nu/catalyst/HFIP combination for the ring opening of DA cyclopropanes **1**

with other *N*-containing nucleophiles. Indeed, under catalysis with triflic acid, the reaction of phenyl-substituted cyclopropane **1r** with trimethylsilyl isocyanate produced carbamate **14** *via* a three-membered ring opening followed by the interception of the intermediate isocyanate with HFIP (Scheme 5). It is worth noting that the secondary reaction with alcohol allowed to suppress side-processes and isolate the ring opening product in reasonable yield even for cyclopropane, which was inefficient in the reaction with TMSCN.

Moreover, *N*-silylated morpholine and pyrrolidine reacted with DA cyclopropanes **1** affording the corresponding amines **15** and **16**. After a short screening of the reaction conditions, we found that the best yields were obtained under heating of HFIP solution of **1** with *N*-trimethylsilylamine (2 equiv) and TfOH (10 mol %) at 80 °C under microwave irradiation for 10 h (Scheme 5). Again, a reverse reaction was impossible for three-membered ring opening with amines that allowed moderately active substrates to react efficiently.

Scheme 5. DA Cyclopropanes Ring Opening with Various TMSNu Reagents



Conclusions

In conclusion, we have developed a method for the ring opening of DA cyclopropanes with trimethylsilyl cyanide, providing direct access to the synthetically important γ-cyanoesters, which are valuable building blocks toward a variety of bioactive molecules. On the contrary, heating of DA cyclopropanes with sodium cyanide in dipolar solvents produced 2-arylsuccinonitriles. The developed approach was successfully applied for DA cyclopropanes ring opening with trimethylsilyl isocyanate and *N*-silylated secondary amines (morpholine, pyrrolidine) providing γ-aminobutyric acid derivatives. Moreover, post-modifications of the obtained γ-cyanoesters allowed to synthesize 2-arylglutaric acid and 5-amino-4-arylvaleric acid derivatives, including 5-arylpiperidin-2-ones, scaffolds presenting in various bioactive compounds.

Experimental Section

General Information

NMR spectra were recorded on Agilent-400MR (400 MHz for ^{1}H and 100 MHz for ^{13}C), Bruker Avance 500 (500 MHz for ^{1}H and 125 MHz for ^{13}C), and Bruker Avance 600 (600 MHz for ^{1}H and 150 MHz for ^{13}C) spectrometers at room temperature if not specified other; the chemical shifts δ were measured in ppm with respect to solvent ($CDCl_3$: ^{1}H: δ = 7.26 ppm, ^{13}C: δ = 77.0 ppm; DMSO-d_6: ^{1}H: δ = 2.50 ppm, ^{13}C: δ = 39.5 ppm). ^{19}F NMR spectra were recorded at 470 MHz with fluorobenzene as an internal reference (δ = –112.96 ppm in $CDCl_3$). Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublets and br (broad). Coupling constants (*J*) are given in Hz. The structures of synthesized compounds were elucidated with the aid of 1D NMR (^{1}H, ^{13}C, ^{19}F) and 2D NMR (COSY ^{1}H-^{1}H, HSQC and HMBC ^{1}H-^{13}C, HMBC ^{1}H-^{15}N, NOESY ^{1}H-^{1}H) spectroscopies. IR spectra were recorded on Thermo Nicolet IR 200 FT-IR spectrometer. Registration of spectra was carried out at a resolution of 4 cm^{-1}, the number of scans 20. Samples were placed on the working surface of the internal reflection (ATR) element from ZnSe with the angle of incidence of 45°. High resolution mass spectra were recorded on a Bruker microTOF-Q™ spectrometer with electrospray ionization (ESI). Analytical thin-layer chromatography (TLC) was carried out using precoated aluminum sheets of silica gel 60 (F254). The visualization of the TLC plates was done by UV lamp (365 nm). Column chromatography was performed on silica gel 60 (230-400 mesh). Melting points (mp) were determined using

Electrothermal 9100 and SMP-20 capillary melting point apparatus. Column chromatography was performed on silica gel 60 (230-400 mesh). All the reactions were carried out using freshly distilled and dry solvents from solvent stills. Experiments under microwave irradiation were performed in sealed tubes using Anton Paar Monowave 200 equipment with an external surface sensor. Cyclopropanes **1** were prepared by Knoevenagel/Corey-Chaykovsky reactions sequence from the corresponding aldehydes.[28] Compounds **6a**, **7a** were described previously.[24]

Dimethyl 2-(2,4,5-trimethoxyphenyl)cyclopropane-1,1-dicarboxylate (**1i**). To a stirred suspension of NaH (60% suspension in oil, 329 mg, 8.2 mmol) in dry DMF (14 mL) trimethylsulfoxonium iodide (1.81 g, 8.2 mmol) was added in a single portion under argon atmosphere at room temperature. Vigorous evolution of hydrogen lasted *ca.* 10 min, after which the reaction mixture was stirred for additional 30 min. Dimethyl 2-(2,4,5-trimethoxybenzylidene)malonate (2.22 g, 6.9 mmol) in dry DMF (2 mL) was added in portions. The resulted mixture was stirred for 2 h, poured into ice-cooled aq. solution NH_4Cl (25 mL) and extracted with ethyl acetate (5×10 mL). The combined organic fractions were washed with water (5×10 mL), dried with Na_2SO_4 and concentrated *in vacuo*. The resulting residue was purified by recrystallization from Et_2O yielding cyclopropane **1i**. Yield 1.38 g (60%); colorless solid; mp 109–110 ºC. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.71 (dd, ^2J = 5.2 Hz, ^3J = 9.4 Hz, 1H, CH_2), 2.13 (dd, ^2J = 5.2 Hz, ^3J = 8.4

Hz, 1H, CH_2), 3.26 (dd, ^3J = 9.4 Hz, ^3J = 8.4 Hz, 1H, CH), 3.37 (s, 3H, CH_3O), 3.76 (s, 3H, CH_3O), 3.77 (s, 6H, 2×CH_3O), 3.84 (s, 3H, CH_3O), 6.45 (s, 1H, Ar), 6.50 (s, 1H, Ar). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ = 19.0 (CH_2), 28.3 (CH), 36.2 (C), 52.0 (CH_3O), 52.5 (CH_3O), 55.8 (CH_3O), 56.40 (CH_3O), 56.44 (CH_3O), 97.1 (CH, Ar), 111.9 (CH, Ar), 114.1 (C, Ar), 142.2 (C, Ar), 148.8 (C, Ar), 153.5 (C, Ar), 167.2 (CO_2Me), 170.3 (CO_2Me). IR (KBr): ν = 2926, 2950, 2841, 1721, 1515, 1471, 1440, 1431, 1401, 1318, 1294, 1276, 1211, 1123, 1030 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+Na]^+$ Calcd for $C_{16}H_{20}NaO_7$ 347.1101; Found 347.1098. Anal. Calcd for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 59.16; H, 6.05.

Dimethyl 2-[4-(methylsulfanyl)phenyl]cyclopropane-1,1-dicarboxylate (**1j**). To a stirred suspension of NaH (60% suspension in oil, 271 mg, 6.8 mmol) in dry DMF (30 mL) trimethylsulfoxonium iodide (1.49 g, 6.8 mmol) was added in a single portion under argon atmosphere at room temperature. Vigorous evolution of hydrogen lasted *ca.* 10 min, after which the reaction mixture was stirred for additional 30 min. Then dimethyl 2-[4-(methylsulfanyl)benzylidene]malonate (1.5 g, 5.6 mmol) in dry DMF (2 mL) was added in a single portion. The resulted mixture was stirred for 3 h, poured into ice-cooled aq. solution of NH_4Cl (25 mL) and extracted with ethyl acetate (5×10 mL). The combined organic fractions were washed with water (5×10 mL), dried with Na_2SO_4 and concentrated *in vacuo*. The resulting residue was purified by column chromatography on silica gel yielding cyclopropane **1j**. Yield 1.12 g (71%); colorless solid; R_f = 0.70 (petroleum ether

: ethyl acetate; 4:1); mp 58–59 ºC. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.69 (dd, ^{2}J = 5.2 Hz, ^{3}J = 9.2 Hz, 1H, CH_2), 2.12 (dd, ^{2}J = 5.2 Hz, ^{3}J = 8.1 Hz, 1H, CH_2), 2.41 (s, 3H, CH_3S), 3.15 (dd, ^{3}J = 9.2 Hz, ^{3}J = 8.1 Hz, 1H, CH), 3.36 (s, 3H, CH_3O), 3.74 (s, 3H, CH_3O), 7.06–7.12 (m, 4H, Ar). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ = 15.6 (CH_3S), 19.1 (CH_2), 32.1 (CH), 37.1 (C), 52.2 (CH_3O), 52.7 (CH_3O), 126.0 (2×CH, Ar), 128.8 (2×CH, Ar), 131.2 (C, Ar), 137.6 (C), 166.9 (CO_2Me), 170.1 (CO_2Me). IR (KBr): ν = 3022, 2944, 2951, 2921, 2846, 1729, 1599, 1497, 1436, 1332, 1284, 1217, 1131, 1092, 1017, 967 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{17}O_4S$ 281.0842; Found 281.0835. Anal. Calcd for $C_{14}H_{16}O_4S$: C, 59.98; H, 5.75. Found: C, 60.29; H, 5.78.

Synthesis of 2-arylsuccinonitriles 2a-d (*General procedure*). A dry reaction microwave tube was charged with 0.5 M solution of cyclopropane **1** (1 equiv) in DMSO under Ar atmosphere, $MeNO_2$ (5 equiv) and NaCN (4 equiv) were added. The reaction mixture was heated in a microwave reactor at 120 °C for 1 h, quenched with conc. aqueous $NaHCO_3$ and extracted with ethyl acetate (3×10 mL). The combined organic extracts were washed with $NaHCO_3$ and brine, dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on a silica gel to afford the desired product.

2-(3,4-Dimethoxyphenyl)succinonitrile (**2a**) was obtained according to the General procedure from cyclopropane **1a**[23b] (300 mg, 1.01 mmol), NaCN (200 mg, 4.08 mmol), $MeNO_2$ (310 mg, 5.09 mmol) in DMSO (2.0 mL). Yield 90 mg

(41%); beige solid; R_f = 0.58 (petroleum ether : ethyl acetate; 1:1). Spectral data are consistent with previously reported ones.[29]

2-(4-Methoxyphenyl)succinonitrile (**2b**) was obtained according to the General procedure from cyclopropane **1b**[23b] (270 mg, 1.02 mmol), NaCN (200 mg, 4.08 mmol), $MeNO_2$ (310 mg, 5.09 mmol) in DMSO (2.0 mL). Yield 58 mg (30%); pale-yellow oil; R_f = 0.80 (petroleum ether : ethyl acetate; 1:1). Spectral data are consistent with previously reported ones.[30]

2-(4-Methylphenyl)succinonitrile (**2c**) was obtained according to the General procedure from cyclopropane **1c**[31] (255 mg, 1.03 mmol), NaCN (200 mg, 4.08 mmol), $MeNO_2$ (305 mg, 5.00 mmol) in DMSO (2.0 mL). Yield 56 mg (33%); yellow oil; R_f = 0.73 (petroleum ether : ethyl acetate; 2:1). Spectral data are consistent with previously reported ones.[30]

2-(4-Chlorophenyl)succinonitrile (**2d**) was obtained according to the General procedure from cyclopropane **1d**[12c] (300 mg, 1.12 mmol), NaCN (220 mg, 4.50 mmol), $MeNO_2$ (340 mg, 5.60 mmol) in DMSO (2.3 mL). Yield 70 mg (33%); yellow oil; R_f = 0.69 (petroleum ether : ethyl acetate; 1:1). Spectral data are consistent with previously reported ones.[30]

Synthesis of dimethyl 2-cyano-2-(het)arylethylmalonates 3. ***Method A*****.** A dry reaction microwave tube was charged with 2 M solution of cyclopropane **1** in HFIP, TMSCN (2 equiv) and $B(C_6F_5)_3$ (10 mol %) were added under N_2 atmosphere. The reaction mixture was heated in a microwave reactor at 80 °C for 7 h, quenched with conc. aqueous $NaHCO_3$ and extracted with ethyl acetate (3×10

mL). The combined organic extracts were washed with $NaHCO_3$ and brine, dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on a silica gel to afford the desired product.

Method B. A dry reaction vial was charged with 2 M solution of cyclopropane **1** in HFIP, TMSCN (2 equiv) and $B(C_6F_5)_3$ (10 mol %) were added under N_2 atmosphere. The reaction mixture was stirred at the specified temperature for the specified time, quenched with conc. aqueous $NaHCO_3$ and extracted with ethyl acetate (3×10 mL). The combined organic extracts were washed with $NaHCO_3$ and brine, dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on a silica gel to afford the desired product.

Method C. A flame dried flask, equipped with a reflux condenser, was charged with cyclopropane **1** (1 equiv), TMSCN (2 equiv) and molecular sieves (4 Å) under N_2 atmosphere, then TfOH (10 mol %) in HFIP (2 M) was added. The reaction mixture was stirred at room temperature for 3 h, quenched with conc. aqueous $NaHCO_3$ and extracted with ethyl acetate (3×10 mL). The combined organic extracts were washed with brine, dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on a silica gel to afford the desired product.

Dimethyl 2-[2-cyano-2-(3,4-dimethoxyphenyl)ethyl]malonate (**3a**) was obtained according to the **Method A** from cyclopropane **1a**[23b] (200 mg, 0.68 mmol) and TMSCN (135 mg, 0.17 mL, 1.36 mmol) using $B(C_6F_5)_3$ (36 mg, 0.07 mmol) in

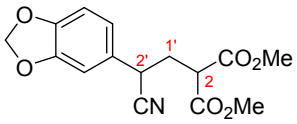
HFIP (0.35 mL). Yield 109 mg (50%); yellow oil; R_f = 0.57 (petroleum ether : ethyl acetate; 4:1).

The compound **3a** was also obtained according to the **Method B** at 0 ºC for 1 h from cyclopropane **1a** (200 mg, 0.68 mmol), TMSCN (135 mg, 0.17 mL, 1.36 mmol) using $B(C_6F_5)_3$ (36 mg, 0.07 mmol) in HFIP (0.35 mL). Yield 120 mg (55%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.44–2.54 (m, 2H, CH_2), 3.55 (dd, ^3J = 7.9 Hz, ^3J = 6.9 Hz, 1H, CH), 3.76 (s, 3H, CH_3O), 3.79 (s, 3H, CH_3O), 3.89 (s, 3H, CH_3O), 3.85 (dd, ^3J = 8.1 Hz, ^3J = 7.4 Hz, 1H, CH), 3.92 (s, 3H, CH_3O), 6.84 (d, ^4J = 2.0 Hz, 1H, Ar), 6.87 (d, ^3J = 8.3 Hz, 1H, Ar), 6.89 (dd, ^3J = 8.3 Hz, ^4J = 2.0 Hz, 1H, Ar). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ = 34.7 (CH_2), 34.9 (CH), 49.1 (CH), 53.08 (CH_3O), 53.10 (CH_3O), 56.17 (CH_3O), 56.20 (CH_3O), 110.5 (CH, Ar), 111.8 (CH, Ar), 120.0 (CH, Ar), 120.1 (CN), 126.9 (C, Ar), 149.4 (C, Ar), 149.8 (C, Ar), 168.7 (CO_2Me), 168.8 (CO_2Me). IR (KBr): ν = 3095, 2956, 2841, 2241, 1751, 1736, 1595, 1518, 1440, 1344, 1259, 1242, 1146, 1026 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{20}NO_6$ 322.1285; Found 322.1284. Anal. Calcd for $C_{16}H_{19}NO_6$: C, 59.81; H, 5.96; N, 4.36. Found: C, 60.08; H, 5.86; N, 4.32.

Dimethyl 2-[2-cyano-2-(2,3-dihydro[1,4]benzodioxin-6-yl)ethyl}malonate (**3b**) was obtained according to the **Method A** from cyclopropane **1e**[23b] (200 mg, 0.68 mmol) and TMSCN (136 mg, 0.17 mL, 1.37 mmol) using $B(C_6F_5)_3$ (40 mg, 0.078 mmol) in HFIP (0.35 mL). Yield 105 mg (48%); yellow oil; R_f = 0.73 (petroleum

ether : ethyl acetate; 2:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.33–2.45 (m, 2H, CH_2), 3.47 (^{3}J = 7.7 Hz, ^{3}J = 6.7 Hz, 1H, CH), 3.80 (d, ^{3}J = 7.7 Hz, ^{3}J = 6.7 Hz, 1H, CH), 3.70 (s, 3H, CH_3O), 3.71 (s, 3H, CH_3O), 4.20 (s, 4H, CH_2O), 6.73 (dd, ^{3}J = 8.1 Hz, ^{4}J = 2.2 Hz, 1H, CH, Ar), 6.79 (br. d, ^{4}J = 2.2 Hz, 1H, CH, Ar), 6.80 (br. d, ^{3}J = 8.1 Hz, 1H, CH, Ar). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ = 34.4 (CH), 34.5 (CH_2), 48.9 (CH), 52.98 (CH_3O), 53.00 (CH_3O), 64.37 (CH_2O), 64.38 (CH_2O), 116.4 (CH, Ar), 118.0 (CH, Ar), 120.0 (CN), 120.4 (CH), 127.4 (C, Ar), 143.8 (C, Ar), 144.1 (C, Ar), 168.6 (CO_2Me), 168.7 (CO_2Me). IR (KBr): ν = 3465, 2983, 2955, 2881, 2242, 1750, 1736, 1592, 1510, 1437, 1334, 1289, 1252, 1200, 1157, 1067, 1049, 921, 889 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+Na]^+$ Calcd for $C_{16}H_{17}NNaO_6$ 342.0948; Found 342.0953. Anal. Calcd for $C_{16}H_{17}NO_6$: C, 60.18; H, 5.37; N, 4.39. Found: C, 60.00; H, 5.03; N, 4.40.

Dimethyl 2-[2-([1,3]benzodioxol-5-yl)-2-cyanoethyl]malonate (**3c**) was obtained according to the **Method A** from cyclopropane **1f**[32] (150 mg, 0.54 mmol) and TMSCN (107 mg, 0.13 mL, 1.08 mmol) using $B(C_6F_5)_3$ (28 mg, 0.055 mmol) in HFIP (0.27 mL). Yield 30 mg (18%).



The compound **3c** was obtained according to the **Method B** at room temperature for 26 h from cyclopropane **1f** (150 mg, 0.54 mmol) and TMSCN (107 mg, 0.13 mL, 1.08 mmol) using $B(C_6F_5)_3$ (28 mg, 0.05 mmol) in HFIP (0.27 mL). Yield 69 mg (42%).

The compound **3c** was also obtained according to the **Method C** from cyclopropane **1f** (150 mg, 0.54 mmol) and TMSCN (108 mg, 0.13 mL, 1.09 mmol) using TfOH (4.8 μL, 0.05 mmol) in HFIP (0.27 mL). Yield 45 mg (28%); colorless oil; R_f = 0.52 (petroleum ether : ethyl acetate; 4:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.41–2.51 (m, 2H, C(1')H_2), 3.52 (dd, ^3J = 8.1 Hz, ^3J = 6.9 Hz, 1H, C(2)H), 3.77 (s, 3H, CH_3O), 3.79 (s, 3H, CH_3O), 3.89 (dd, ^3J = 8.5 Hz, ^3J = 7.2 Hz, 1H, C(2')H), 6.00 (s, 2H, OCH_2O), 6.80 (dd, ^3J = 8.2 Hz, ^4J = 1.2 Hz, 1H, Ar), 6.82 (br. d, ^3J = 8.2 Hz, 1H, Ar), 6.83 (br. d, ^4J = 1.2 Hz, 1H, Ar). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ = 34.8 (C(1')H_2), 34.9 (C(2')H), 49.0 (C(2)H), 53.08 (CH_3O), 53.11 (CH_3O), 101.7 (OCH_2O), 107.9 (CH, Ar), 109.0 (CH, Ar), 120.0 (CN), 121.2 (CH, Ar), 128.2 (C, Ar), 148.1 (C, Ar), 148.7 (C, Ar), 168.68 (CO_2Me), 168.75 (CO_2Me). IR (KBr): ν = 2956, 2917, 2849, 2242, 1736, 1611, 1505, 1510, 1437, 1334, 1289, 1252, 1200, 1157, 1067, 1049, 921, 889 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{15}NNaO_6$ 328.0792; Found 328.0790. Anal. Calcd for $C_{15}H_{15}NO_6$: C, 59.02; H, 4.95; N, 4.59. Found: C, 59.13; H, 4.95; N, 4.34.

Dimethyl 2-[2-cyano-2-(4-methoxyphenyl)ethyl]malonate (**3d**) was obtained according to the **Method A** from cyclopropane **1b**[23b] (200 mg, 0.83 mol) and TMSCN (165 mg, 0.21 mL, 1.67 mmol) using $B(C_6F_5)_3$ (39 mg, 0.076 mmol) in HFIP (0.38 mL). Yield 114 mg (52%); yellow oil; R_f = 0.85 (petroleum ether : ethyl acetate; 4:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.37–2.50 (m, 2H, CH_2),

3.50 (dd, ^3J = 8.1 Hz, ^3J = 6.9 Hz, 1H, CH), 3.71 (s, 3H, CH_3O), 3.74 (s, 3H, CH_3O), 3.78 (s, 3H, CH_3O), 3.89 (dd, ^3J = 8.1 Hz, ^3J = 7.4 Hz, 1H, CH), 6.87 (br. d, ^3J = 8.5 Hz, 2H, Ar), 7.23 (br. d, ^3J = 8.5 Hz, 2H, Ar). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ = 34.3 (CH), 34.6 (CH_2), 48.9 (CH), 53.0 (2×CH_3O), 55.4 (CH_3O), 114.7 (2×CH), 120.1 (CN), 126.2 (C, Ar), 128.6 (2×CH, Ar), 159.7 (C, Ar), 168.6 (*C*O_2Me), 168.7 (*C*O_2Me). IR (ZnSe): ν = 3005, 2954, 2840, 2241, 1751, 1736, 1612, 1514, 1437, 1306, 1254, 1180, 1157, 1032 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{17}NNaO_5$ 309.1445; Found 309.1445. Anal. Calcd for $C_{15}H_{17}NO_5$: C, 61.85; H, 5.88; N, 4.81. Found: C, 61.86; H, 6.01; N, 4.78.

Dimethyl 2-[2-cyano-2-(3,4,5-trimethoxyphenyl)ethyl]malonate (**3e**) was obtained according to the **Method A** from cyclopropane **1g**[23b] (200 mg, 0.62 mmol) and TMSCN (122 mg, 0.15 mL, 1.23 mmol) using $B(C_6F_5)_3$ (32 mg, 0.06 mmol) in HFIP (0.31 mL). Yield 43 mg (20%); yellow oil; R_f = 0.48 (petroleum ether : ethyl acetate; 2:1).

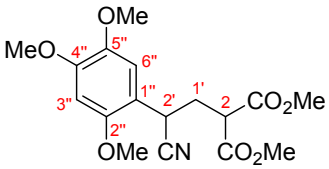
The compound **3e** was also obtained according to the **Method B** at 70 °C for 26 h from cyclopropane **1g** (200 mg, 0.62 mmol) and TMSCN (122 mg, 0.15 mL, 1.23 mmol) using $B(C_6F_5)_3$ (32 mg, 0.06 mmol) in HFIP (0.31 mL). Yield 113 mg (52%). ^1H NMR ($CDCl_3$, 400 MHz): δ = 2.45–2.49 (m, 2H, CH_2), 3.56 (t, ^3J = 7.4 Hz, 1H, CH), 3.75 (s, 3H, CH_3O), 3.78 (s, 3H, CH_3O), 3.83 (s, 3H, CH_3O), 3.87 (s, 6H, 2×CH_3O), 3.90 (t, ^3J = 7.8 Hz, 1H, CH), 6.52 (s, 2H, Ar). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ = 34.7 (CH_2), 35.5 (CH), 49.1 (CH), 53.1

(CH_3O), 56.4 (3×CH_3O), 61.0 (CH_3O), 104.5 (2×CH, Ar), 119.9 (CN), 130.0 (C, Ar), 138.1 (C, Ar), 153.9 (2×C, Ar), 168.7 (CO_2Me), 168.8 (CO_2Me). IR (KBr): ν = 3002, 2953, 2842, 2241, 1752, 1738, 1593, 1510, 1463, 1435, 1426, 1336, 1242, 1153, 1128, 1052, 1006 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{21}NNaO_7$ 374.1210; Found 374.1203. Anal. Calcd for $C_{17}H_{21}NO_7$: C, 58.11; H, 6.02; N, 3.99. Found: C, 58.10; H, 6.13; N, 3.64.

Dimethyl 2-[2-cyano-2-(2,4,6-trimethoxyphenyl)ethyl]malonate (**3f**) was obtained according to the **Method B** at room temperature for 17 h from cyclopropane **1h**[25] (200 mg, 0.62 mol) and TMSCN (122 mg, 154 μL, 1.23 mmol) using $B(C_6F_5)_3$ (32 mg, 0.06 mmol) in HFIP (0.31 mL). Yield 152 mg (70%); yellow oil; R_f = 0.52 (petroleum ether : ethyl acetate; 2:1). ^1H NMR ($CDCl_3$, 500 MHz): δ = 2.34 (ddd, ^2J = 13.8 Hz, ^3J = 9.3 Hz, ^3J = 6.8 Hz, 1H, C(1')H_2), 2.47 (ddd, ^2J = 13.8 Hz, ^3J = 8.1 Hz, ^3J = 6.5 Hz, 1H, C(1')H_2), 3.18 (dd, ^3J = 8.1 Hz, ^3J = 6.8 Hz, 1H, C(2)H), 3.54 (s, 3H, CH_3O), 3.63 (s, 3H, CH_3O), 3.69 (s, 3H, CH_3O), 3.70 (s, 6H, 2×CH_3O), 4.31 (dd, ^3J = 9.3 Hz, ^3J = 6.5 Hz, 1H, C(2')H), 6.01 (s, 2H, Ar). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ = 23.2 (C(2')H), 30.3 (C(1')H_2), 49.1 (CH), 52.6 (CH_3O), 53.0 (CH_3O), 56.3 (CH_3O), 56.6 (2×CH_3O), 90.8 (2×CH), 101.9 (C, Ar), 120.3 (CN), 158.6 (2×C, Ar), 161.7 (C, Ar), 168.8 (CO_2Me), 169.0 (CO_2Me). IR (KBr): ν = 3002, 2954, 2839, 2240, 1752, 1736, 1612, 1515, 1439, 1401, 1347, 1318, 1279, 1210, 1156, 1118, 1032 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{22}NNaO_7$ 374.1210; Found 374.1202.

Anal. Calcd for $C_{17}H_{21}NO_7$: C, 58.11; H, 6.02; N, 3.99. Found: C, 57.95; H, 6.08; N, 3.85.

Dimethyl 2-[2-cyano-2-(2,4,5-trimethoxyphenyl)ethyl]malonate (**3g**) was



obtained according to the **Method C** from cyclopropane **1i** (0.40 g, 1.2 mmol) and TMSCN (0.46 mL, 0.37 g, 2.4 mmol) using TfOH (0.02 mL, 0.23 mmol) in HFIP (0.5 mL). Yield 160 mg (37%); yellowish oil; R_f = 0.58 (petroleum ether : ethyl acetate; 1:1). Additionally, the dimeric product **9** was isolated in 33% yield (130 mg).

Compound **3g** was also obtained according to the **Method B** at room temperature for 17 h from cyclopropane **1i** (0.20 g, 0.62 mmol) and TMSCN (0.15 mL, 122 mg, 1.24 mmol) using $B(C_6F_5)_3$ (32 mg, 0.062 mmol) in HFIP (0.31 mL). Yield 187 mg (86%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.39–2.45 (m, 1H, CH_2), 2.53–2.59 (m, 1H, CH_2), 3.48 (t, ^3J = 7.4 Hz, 1H, C(2)H), 3.75 (s, 3H, CH_3O), 3.76 (s, 3H, CH_3O), 3.84 (s, 3H, CH_3O), 3.88 (s, 3H, CH_3O), 3.92 (s, 3H, CH_3O), 4.28 (t, ^3J = 7.7 Hz, 1H, C(2')H), 6.53 (s, 1H, C(3")H, Ar), 6.89 (s, 1H, C(6")H, Ar). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ = 29.2 (C(2')H), 32.7 (C(1')H_2), 49.2 (C(2)H), 52.94 (CH_3O), 53.01 (CH_3O), 56.40 (CH_3O), 56.41 (CH_3O), 56.9 (CH_3O), 97.6 (C(3")H, Ar), 112.4 (C(6")H, Ar), 113.4 (C(1"), Ar), 120.3 (CN), 143.6 (C(5"), Ar), 150.3 (C(2"), Ar), 150.9 (C(4"), Ar), 168.8 (CO_2Me), 168.9 (CO_2Me). IR (KBr): ν = 3003, 2954, 2848, 2241, 1752, 1737, 1612, 1514, 1440, 1401, 1347, 1317, 1210, 1156, 1118, 1033 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+Na]^+$

Calcd for $C_{17}H_{21}NNaO_7$ 374.1210; Found 374.1208. Anal. Calcd for $C_{17}H_{21}NO_7$: C, 58.11; H, 6.02; N, 3.99. Found: C, 58.12; H, 6.03; N, 3.91.

Dimethyl 2-{2-cyano-2-[4-(methylsulfanyl)phenyl]ethyl}malonate (**3h**) was prepared according to the **Method C** at 50 °C from cyclopropane **1j** (160 mg, 0.57 mmol) and TMSCN (131 mg, 0.16 mL, 1.32 mmol) using TfOH (10 μL, 0.115 mmol) in HFIP (0.28 mL). Yield 89 mg (51%); colorless oil; R_f = 0.64 (petroleum ether : ethyl acetate; 4:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.40–2.48 (m, 2H, CH_2), 2.46 (s, 3H, CH_3S), 3.52 (dd, ^3J = 7.8 Hz, ^3J = 7.2 Hz, 1H, CH), 3.72 (s, 3H, CH_3O), 3.75 (s, 3H, CH_3O), 3.91 (dd, ^3J = 8.2 Hz, ^3J = 7.6 Hz, 1H, CH), 7.23 (br. s, 4H, Ar). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ = 15.5 (CH_3S), 34.4 (CH), 34.6 (CH_2), 48.8 (CH), 52.9 (2×CH_3O), 119.6 (CN), 126.9 (2×CH, Ar), 127.8 (2×CH, Ar), 130.8 (C, Ar), 139.5 (C, Ar), 168.45 (CO_2Me), 168.53 (CO_2Me). IR (ZnSe): ν = 3002, 2954, 2924, 2850, 2242, 1752, 1737, 1600, 1496, 1437, 1409, 1354, 1302, 1275, 1253, 1232, 1201, 1157, 1096, 1045, 1016 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+NH_4]^+$ Calcd for $C_{15}H_{21}N_2O_4S$ 325.1217; Found 325.1213.

Dimethyl 2-{2-cyano-2-[4-(dimethylamino)phenyl]ethyl}malonate (**3i**) was obtained according to the **Method A** from cyclopropane **1k**[23b] (100 mg, 0.36 mmol) and TMSCN (0.1 mL, 0.8 mmol) using $B(C_6F_5)_3$ (18 mg, 0.035 mmol) in HFIP (0.18 mL). Yield 79 mg (72%); yellow oil; R_f = 0.44 (petroleum ether : ethyl acetate; 3:1). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.41–2.52 (m, 2H, C(1')H_2),

2.97 (s, 6H, $N(CH_3)_2$), 3.50 (dd, ^3J = 7.5 Hz, ^3J = 6.7 Hz, 1H, C(2)H), 3.76 (s, 3H, CH_3O), 3.77 (s, 3H, CH_3O), 3.86 (dd, ^3J = 8.6 Hz, ^3J = 7.3 Hz, 1H, C(2')H), 6.72 (br. d, ^3J = 8.7 Hz, 2H, Ar), 7.18 (br. d, ^3J = 8.7 Hz, 2H, Ar). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ = 34.3 (C(2')H), 34.7 ($C(1')H_2$), 49.1 (C(2)H), 40.5 ($N(CH_3)_2$), 53.0 ($2\times CH_3O$), 112.9 (C(3")H, C(5")H), 120.5 (CN), 121.5 (C(1"), Ar), 128.3 (C(2")H, C(6")H, Ar), 150.6 (C(4"), Ar), 168.8 (CO_2Me), 168.9 (CO_2Me). IR (KBr): ν = 2993, 2954, 2924, 2894, 2850, 2807, 2240, 1752, 1738, 1615, 1602, 1567, 1525, 1483, 1437, 1356, 1289, 1256, 1230, 1207, 1164, 1092, 1046 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{21}N_2O_4$ 305.1496; Found 305.1491. Anal. Calcd for $C_{16}H_{20}N_2O_4$: C, 63.14; H, 6.62; N, 9.20. Found: C, 63.04; H, 6.62; N, 9.17.

Dimethyl 2-{2-cyano-2-[4-(pyrrolidin-1-yl)phenyl]ethyl}malonate (**3j**) was obtained according to the **Method B** from cyclopropane **1l**[33] (195 mg, 0.64 mmol) and TMSCN (0.16 mL, 1.28 mmol) using $B(C_6F_5)_3$ (33 mg, 0.06 mmol) in HFIP (0.32 mL) at room temperature for 4 h. Yield 166 mg (78%); yellow oil; R_f = 0.36 (petroleum ether : ethyl acetate; 1:1). ^1H NMR ($CDCl_3$, 600 MHz): δ = 1.98–2.02 (m, 4H, $2\times CH_2$), 2.42 (ddd, ^2J = 14.0 Hz, ^3J = 7.6 Hz, ^3J = 7.0 Hz, 1H, $C(1')H_2$), 2.48 (ddd, ^2J = 14.0 Hz, ^3J = 8.6 Hz, ^3J = 7.0 Hz, 1H, $C(1')H_2$), 3.25–3.28 (m, 4H, $2\times CH_2N$), 3.51 (dd, ^3J = 7.6 Hz, ^3J = 7.0 Hz, 1H, C(2)H), 3.74 (s, 3H, CH_3O), 3.75 (s, 3H, CH_3O), 3.83 (dd, ^3J = 8.6 Hz, ^3J = 7.0 Hz, 1H, C(2')H), 6.53 (br. d, ^3J = 8.6 Hz, 2H, C(3")H, C(5")H), Ar), 7.14 (br. d, ^3J = 8.6 Hz, 2H, C(2")H,

C(6")H, Ar). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ = 25.3 (2×CH_2), 34.1 (C(2')H), 34.5 (C(1')H_2), 47.5 (2×CH_2), 48.8 (C(2)H), 52.7 (2×CH_3O), 119.2 (C(2")H, C(6")H, Ar), 120.1 (C(1"), Ar), 120.4 (CN), 128.1 (C(2")H, C(6")H, Ar), 147.27 (C(4"), Ar), 168.6 (*C*O_2Me), 168.7 (*C*O_2Me). IR (ZnSe): ν = 2956, 2925, 2853, 2242, 1749, 1733, 1683, 1600, 1516, 1436, 1393, 1305, 1287, 1260, 1228, 1161 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{23}N_2O_4$ 347.1652; Found 331.1645. Anal. Calcd for $C_{18}H_{22}N_2O_4$: C, 65.44; H, 6.71; N, 8.48. Found: C, 65.10; H, 6.69; N, 8.09.

Dimethyl 2-[2-cyano-2-(4-morpholinophenyl)ethyl]malonate (**3k**) was obtained according to the **Method A** from cyclopropane **1m**[33] (200 mg, 0.63 mmol) and TMSCN (124 mg, 0.16 mL, 1.25 mmol) using $B(C_6F_5)_3$ (32 mg, 0.063 mmol) in HFIP (0.32 mL). Yield 190 mg (88%); yellow solid; mp = 75–76 ºC; R_f = 0.53 (petroleum ether : ethyl acetate; 1:1). ^1H NMR ($CDCl_3$, 500 MHz): δ = 2.49–2.90 (m, 2H, C(1')H_2), 3.14–3.16 (m, 4H, 2×CH_2), 3.51 (dd, ^3J = 7.9 Hz, ^3J = 6.8 Hz, 1H, C(2)H), 3.73 (s, 3H, CH_3O), 3.75 (s, 3H, CH_3O), 3.83–3.84 (4H, 2×CH_2), 3.88 (dd, ^3J = 7.9 Hz, ^3J = 7.1 Hz, 1H, C(2')H), 6.89 (br. d, ^3J = 8.6 Hz, 2H, C(3")H, C(5")H, Ar), 7.21 (br. d, ^3J = 8.6 Hz, 2H, C(2")H, C(6")H, Ar). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ = 34.0 (C(1')H_2), 34.3 (C(2')H), 48.67 (2×CH_2), 48.74 (C(2)H), 52.7 (2×CH_3O), 66.6 (2×CH_2), 115.7 (2×CH, C(3")H, C(5")H, Ar), 119.9 (CN, Ar), 124.9 (C(1"), Ar), 128.1 (C(2")H, C(6")H, Ar), 151.1 (C(4"), Ar), 168.4 (*C*O_2Me), 168.5 (*C*O_2Me). IR (KBr): ν = 2956, 2923, 2896, 2855,

2241, 1751, 1736, 1612, 1518, 1450, 1437, 1345, 1306, 1265, 1237, 1158, 1122, 1050, 927 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{23}N_2O_5$ 347.1601; Found 347.1609. Anal. Calcd for $C_{18}H_{22}N_2O_5$: C, 62.42; H, 6.40; N, 8.09. Found: C, 62.56; H, 6.46; N, 7.93.

Dimethyl 2-[2-cyano-2-(5-methylthiophen-2-yl)ethyl]malonate (**3m**) was obtained according to the **Method B** at room temperature for 26 h from cyclopropane **1o**[34] (0.20 g, 0.79 mmol) and TMSCN (0.20 mL, 156 mg, 1.57 mmol) using $B(C_6F_5)_3$ (40 mg, 0.079 mmol) in HFIP (0.39 mL). Yield 135 mg (60%); yellowish oil; R_f = 0.58 (petroleum ether : ethyl acetate; 4:1). ^1H NMR ($CDCl_3$, 500 MHz): δ = 2.47 (d, ^4J = 1.0 Hz, 3H, CH_3), 2.49–2.60 (m, 2H, CH_2), 3.58 dd, ^3J = 7.9 Hz, ^3J = 7.2 Hz, 1H, CH), 3.77 (s, 3H, CH_3O), 3.78 (s, 3H, CH_3O), 4.07 (dd, ^3J = 8.3 Hz, ^3J = 7.2 Hz, 1H, CH), 6.63 (dq, ^3J = 3.5 Hz, ^4J = 1.0 Hz, 1H, Ar), 6.20 (d, ^3J = 3.5 Hz, 1H, Ar). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ = 15.4 (CH_3), 30.5 (CH), 34.5 (CH_2), 48.8 (CH), 53.07 (CH_3O), 53.10 (CH_3O), 119.1 (CN), 125.3 (CH, Ar), 126.9 (CH, Ar), 133.6 (C, Ar), 141.1 (C, Ar), 168.55 (*C*O_2Me), 168.63 (*C*O_2Me). IR (ZnSe): ν = 2955, 2922, 2851, 2244, 1751, 1738, 1437, 1351, 1308, 1267, 1237, 1159, 1043 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+Na]^+$ Calcd for $C_{13}H_{15}NNaO_4S$ 304.0614; Found 304.0609. Anal. Calcd for $C_{13}H_{15}NO_4S$: C, 55.50; H, 5.37; N, 4.98. Found: C, 55.88; H, 5.33; N, 4.63.

Dimethyl 2-[2-cyano-2-(5-methylfuran-2-yl)ethyl]malonate (**3o**) was obtained according to the **Method B** at room temperature for 2.5 h from cyclopropane **1q**[35]

(175 mg, 0.74 mol) and TMSCN (146 mg, 184 μL, 1.47 mmol) using $B(C_6F_5)_3$ (38 mg, 0.074 mmol) in HFIP (0.37 mL). Yield 121 mg (62%); colorless oil; R_f = 0.40 (petroleum ether : ethyl acetate; 2:1).

Compound **3o** was also obtained according to the **Method A** from cyclopropane **1q** (0.20 g, 0.84 mmol) and TMSCN (0.21 mL, 166 mg, 1.68 mmol) using $B(C_6F_5)_3$ (43 mg, 0.084 mmol) in HFIP (0.4 mL). Yield 84 mg (38%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.29 (s, 3H, CH_3), 2.51–2.60 (m, 2H, CH_2), 3.57 (t, ^3J = 7.4 Hz, 1H, CH), 3.76 (s, 3H, CH_3O), 3.78 (s, 3H, CH_3O), 4.07 (t, ^3J = 7.6 Hz, 1H, CH), 5.93 (dq, ^3J = 3.1 Hz, ^4J = 1.0 Hz, 1H, Ar), 6.20 (d, ^3J = 3.1 Hz, 1H, Ar). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ = 13.6 (CH_3), 29.1 (CH), 31.2 (CH_2), 48.9 (CH), 53.05 (CH_3O), 53.09 (CH_3O), 106.7 (CH, Ar), 109.5 (CH, Ar), 118.0 (CN), 144.3 (C, Ar), 153.5 (C, Ar), 168.57 (CO_2Me), 168.64 (CO_2Me). IR (KBr): ν = 3473, 3132, 3005, 2956, 2926, 2850, 2247, 1740, 1734, 1564, 1520, 1357, 1267, 1240, 1215, 1157, 1097, 1047, 1024 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+NH_4]^+$ Calcd for $C_{13}H_{19}N_2O_5$ 283.1289; Found 283.1291.

Tetramethyl (9RS,10RS)-2,2'-[(2,3,6,7-tetramethoxy-9,10-dihydroanthracene-9,10-diyl)di(methylene)]dimalonate (**5a**). A dry reaction vial was charged with cyclopropane **1a** (155 mg, 0.53 mmol), TMSCN (135 mg, 0.17 mL, 1.36 mmol) and HFIP (0.41 mL) under N_2 atmosphere. $B(C_6F_5)_3$ (27 mg, 0.053 mmol) was added and the reaction mixture was stirred at room temperature for 2 h, quenched with conc. aqueous $NaHCO_3$ and extracted with ethyl acetate (3×4 mL). The

combined organic extracts were washed with $NaHCO_3$ and brine, dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on a silica gel to afford cyanide **3a** (yield 69 mg, 41%) and dimer **5a** (yield 39 mg, 25%) as colorless oil; R_f = 0.60 (petroleum ether : ethyl acetate; 2:1). The relative configuration of stereocenters was assigned by comparison with NMR data of the related dihydroanthracene dimers of DA cyclopropanes.[23b] ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.26–2.30 (m, 4H, 2×CH_2), 3.61 (br. d, ^3J = 7.8 Hz, 2H, 2×CH), 3.72 (s, 12H, 4×CH_3O), 3.79 (br. d, ^3J = 7.8 Hz, 2H, 2×CH), 3.85 (s, 12H, 4×CH_3O), 6.70 (s, 4H, Ar). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ = 40.0 (2×CH_2), 43.0 (2×CH), 50.3 (2×CH), 52.6 (4×CH_3O), 55.8 (4×CH_3O), 111.5 (4×CH, Ar), 130.5 (4×C, Ar), 147.4 (4×C, Ar), 169.3 (4×*C*O_2Me). HRMS ESI-TOF *m/z*: $[M+Na]^+$ Calcd for $C_{30}H_{36}NaO_{12}$ 611.2104; Found 611.2103.

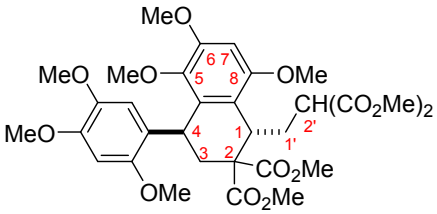
Dimethyl 2-{2-(3,4-dimethoxyphenyl)-2-[(1,1,1,3,3,3-hexafluoropropan-2-yl)oxy]ethyl}malonate (**8a**). To cyclopropane **1a** (100 mg, 0.34 mmol) TfOH (3.0 µL, 10 mol %) in HFIP (0.17 mL) was added. The reaction mixture was stirred at room temperature for 3 h under N_2 atmosphere, quenched with conc. aqueous $NaHCO_3$ and extracted with ethyl acetate (3×10 mL). The combined organic extracts were washed with brine, dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on a silica gel to afford the desired product. Yield 64 mg (41%); colorless oil; R_f = 0.51 (petroleum

ether : ethyl acetate; 4:1). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.34 (ddd, ^2J = 14.3 Hz, ^3J = 8.6 Hz, ^3J = 4.2 Hz, 1H, CH_2), 2.54 (ddd, ^2J = 14.3 Hz, ^3J = 9.6 Hz, ^3J = 6.0 Hz, 1H, CH_2), 3.67 (dd, ^3J = 8.6 Hz, ^3J = 6.0 Hz, 1H, CH), 3.75 (s, 3H, CH_3O), 3.76 (s, 3H, CH_3O), 3.89 (s, 3H, CH_3O), 3.90 (s, 3H, CH_3O), 3.96 (sep, ^3J = 6.3 Hz, 1H, CH), 4.74 (dd, ^3J = 9.6 Hz, ^3J = 4.2 Hz, 1H, CH), 6.86–6.87 (m, 3H, Ar). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ = 36.6 (CH_2), 48.4 (CH), 52.7 (CH_3O), 52.8 (CH_3O), 56.0 (CH_3O), 56.1 (CH_3O), 72.2 (sept, $^2J_{CF}$ = 32 Hz, $CH(CF_3)_2$), 82.5 (CHO), 110.0 (CH, Ar), 111.1 (CH, Ar), 121.2 (CH, Ar), 120.5 (q, $^1J_{CF}$ = 282 Hz, CF_3), 123.8 (q, $^1J_{CF}$ = 282 Hz, CF_3), 129.2 (C), 149.8 (C, Ar), 150.3 (C, Ar), 169.4 (CO_2Me), 169.6 (CO_2Me). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = –73.4, –72.4. IR (KBr): ν = 3004, 2957, 2842, 1752, 1738, 1595, 1519, 1466, 1439, 1368, 1285, 1264, 1219, 1192, 1158, 1125, 1102, 1027 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{20}F_6NaO_7$ 485.1005; Found 485.0996.

Dimethyl 2-{2-[(1,1,1,3,3,3-hexafluoropropan-2-yl)oxy]-2-phenylethyl}malonate (**8b**). To a solution of cyclopropane **1r** (200 mg, 0.41 mmol) in HFIP (0.5 mL) (4 Å) TfOH (7.5 µL, 10 mol %) in HFIP (0.9 mL) was added. The reaction mixture was stirred at room temperature for 3 h under N_2 atmosphere, quenched with conc. aqueous $NaHCO_3$ and extracted with ethyl acetate (3×10 mL). The combined organic extracts were washed with brine, dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on a silica gel to afford the product **8b**. Yield 45 mg (13%); colorless oil; R_f =

0.50 (petroleum ether : ethyl acetate; 6:1). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.37 (ddd, ^{2}J = 13.1 Hz, ^{3}J = 8.8 Hz, ^{3}J = 4.3 Hz, 1H, CH_2), 2.56 (ddd, ^{2}J = 13.1 Hz, ^{3}J = 9.6 Hz, ^{3}J = 5.9 Hz, 1H, CH_2), 3.70 (dd, ^{3}J = 8.8 Hz, ^{3}J = 5.9 Hz, 1H, CH), 3.76 (s, 3H, CH_3O), 3.77 (s, 3H, CH_3O), 3.96 (sep, ^{3}J = 5.9 Hz, 1H, CH), 4.80 (dd, ^{3}J = 9.6 Hz, ^{3}J = 4.3 Hz, 1H, CH), 7.34–7.37 (m, 2H, Ar), 7.40–7.44 (m, 3H, Ar). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ = 36.6 (CH_2), 48.4 (CH), 52.8 (CH_3O), \52.9 (CH_3O), 72.6 (sept, $^{2}J_{CF}$ = 32 Hz, $CH(CF_3)_2$), 82.8 (CHO), 128.0 (2×CH, Ar), 128.8 (2×CH, Ar), 129.8 (CH, Ar), 137.1 (C, Ar), 169.4 (CO_2Me), 169.5 (CO_2Me).[35] IR (KBr): ν = 2957, 1754, 1438, 1367, 1287, 1264, 1220, 1196, 1127, 1159, 1103 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+Na]^+$ Calcd for $C_{16}H_{17}F_6O_5$ 403.0975; Found 403.0976.

Dimethyl (1RS,4RS)-5,6,8-trimethoxy-1-[3-methoxy-2-(methoxycarbonyl)-3-oxopropyl]-4-(2,4,5-trimethoxyphenyl)-3,4-dihydronaphthalene-2,2(1H)-dicarboxylate (**9**)



was obtained as by-product in the reaction of cyclopropane **1i** with TMSCN in 33% yield. Colorless solid; mp 89–91 °C; R_f = 0.60 (petroleum ether : ethyl acetate; 1:2). ^{1}H NMR (DMSO-d_6, 500 MHz, 353 K): δ = 1.78–1.84 (m, 1H, C(1')H_2), 1.91–1.99 (m, 1H, C(3)H_2), 2.01–2.09 (m, 1H, C(1')H_2), 2.75–2.79 (m, 1H, C(3)H_2), 3.08 (s, 3H, CH_3O), 3.48 (s, 3H, CH_3O), 3.49 (dd, ^{3}J = 10.4 Hz, ^{3}J = 3.5 Hz, 1H, C(2')H), 3.54 (s, 3H, CH_3O), 3.57 (s, 3H, CH_3O), 3.73 (s, 3H, CH_3O), 3.77 (s, 6H, 2×CH_3O), 3.786 (s, 3H, CH_3O),

3.794 (s, 6H, 2×CH_3O), 3.93 (br. d, ^3J = 10.9 Hz, 1H, C(1)H), 4.39–4.49 (m, 1H, C(4)H), 6.29 (br. s, $\nu_{1/2}$ = 23 Hz, 1H, Ar), 6.64 (s, 1H, Ar), 6.72 (s, 1H, Ar). $^{13}C\{^1H\}$ NMR (DMSO-d_6, 125 MHz, 353 K): δ = 31.1 (C(3)H_2), 31.92 (C(1')H_2), 33.6 (C(4)H, C(1)H), 48.9 (C(2')H), 52.1 (CH_3O), 52.2 (2×CH_3O), 52.5 (CH_3O), 55.6 (CH_3O), 55.8 (CH_3O), 56.2 (CH_3O), 56.6 (CH_3O), 56.7 (CH_3O), 58.2 (C), 58.6 (CH_3O), 96.7 (CH, Ar), 100.0 (CH, Ar), 113.3 (CH, Ar), 119.3 (C, Ar), 128.1 (C, Ar), 131.5 (C, Ar), 140.7 (C, Ar), 143.2 (C, Ar), 148.1 (C, Ar), 151.0 (C, Ar), 151.3 (C, Ar), 152.3 (C, Ar), 168.6 ($C$$O_2$Me), 169.5 ($C$$O_2$Me), 169.6 ($C$$O_2$Me), 170.1 ($C$$O_2$Me). IR (KBr): ν = 3004, 2954, 2840, 1756, 1736, 1597, 1511, 1485, 1436, 1396, 1326, 1241, 1207, 1105, 1070, 1034 cm^{-1}. HRMS ESI-TOF *m/z*: $[M]^+$ Calcd for $C_{32}H_{40}O_{14}$ 648.2413; Found 648.2418. Anal. Calcd for $C_{32}H_{40}O_{14}$: C, 59.25; H, 6.22. Found: C, 59.22; H, 6.20.

Trimethyl 3-(4-methoxyphenyl)propane-1,1,3-tricarboxylate (**10**). TMSCl (3.78 mL, 29.7 mmol) was added dropwise to a dry flask containing nitrile **3d** (100 mg, 0.34 mmol), and MeOH (2.4 mL, 59.3 mmol) under nitrogen atmosphere at room temperature. Then the reaction mixture was heated at 57 ºC (oil bath) for 5 h. After that, the reaction mixture was cooled to room temperature, water (0.7 mL), Na_2CO_3 (1.0 g, 9.4 mmol) and CH_2Cl_2 (7 mL) were successively added to it. The mixture was dried with Na_2SO_4 and concentrated at reduced pressure to afford product **10** in 81% yield (90 mg) as colorless oil. ^1H NMR ($CDCl_3$, 600 MHz): δ = 2.37 (ddd, ^2J = 14.3 Hz, ^3J = 8.5 Hz, ^3J = 6.7 Hz, 1H, CH_2), 2.61 (^2J = 14.3 Hz,

^3J = 8.2 Hz, ^3J = 7.2 Hz, 1H, CH_2), 3.27 (dd, ^3J = 8.2 Hz, ^3J = 6.7 Hz, 1H, CH), 3.59 (dd, ^3J = 8.5 Hz, ^3J = 7.2 Hz, 1H, CH), 3.66 (s, 3H, CH_3O), 3.69 (s, 3H, CH_3O), 3.74 (s, 3H, CH_3O), 3.79 (s, 3H, CH_3O), 6.86 (d, ^3J = 8.8 Hz, 2H, Ar), 7.18 (d, ^3J = 8.8 Hz, 2H, Ar). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ = 32.0 (CH_2), 47.9\ (CH), 49.3 (CH), 52.2 (CH_3O), 52.6 (2×CH_3O), 55.2 (CH_3O), 114.3 (2×CH, Ar), 129.0 (2×CH, Ar), 129.5 (C, Ar), 159.1 (C, Ar), 169.3 (CO_2Me), 169.4 (CO_2Me), 173.6 (CO_2Me). IR (ZnSe): ν = 3000, 2954, 2925, 2848, 1760, 1732, 1610, 1512, 1436, 1327, 1303, 1249, 1156, 1032 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+NH_4]^+$ Calcd for $C_{16}H_{24}NO_7$ 342.1547; Found 342.1560.

Dimethyl [2-carbamoyl-2-(2,3-dihydro[1,4]benzodioxin-6-yl)ethyl]malonate (**11**). TMSCl (40 μL, 0.31 mmol) and water (10 μL) were successively added to nitrile **3b** (50 mg, 0.16 mmol) keeping temperature below 5 ºC, after that the reaction mixture was allowed to warm up to 25 ºC and stirred for 4 h. The mixture was neutralized with saturated $NaHCO_3$ solution (2 mL) and extracted with CH_2Cl_2 (5 × 3 mL). The combined organic fractions were washed with water (2 × 10 mL), dried with Na_2SO_4 and concentrated *in vacuo*. The resulting residue was purified by column chromatography on silica gel affording amide **11**. Yield 42 mg (78%); colorless oil; R_f = 0.20 (ethyl acetate). ^1H NMR ($CDCl_3$, 600 MHz): δ = 2.29 (ddd, ^2J = 14.7 Hz, ^3J = 8.5 Hz, ^3J = 6.9 Hz, 1H, CH_2), 2.66 (ddd, ^2J = 14.7 Hz, ^3J = 8.2 Hz, ^3J = 7.2 Hz, 1H, CH_2), 3.35 (dd, ^3J = 8.2 Hz, ^3J = 6.9 Hz, 1H, CH), 3.41 (dd, ^3J = 8.5 Hz, ^3J = 7.2 Hz, 1H, CH), 3.69 (s, 3H, CH_3O), 3.73

(s, 3H, CH_3O), 4.24 (s, 4H, 2×CH_2O), 5.42 (br. s, 1H, NH_2), 5.50 (br. s, 1H, NH_2), 6.72 (dd, ^3J = 8.1 Hz, ^4J = 2.1 Hz, 1H, Ar), 6.79 (d, ^4J = 2.1 Hz, 1H, Ar), 6.82 (d, ^3J = 8.1 Hz, 1H, Ar). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 150 MHz): δ = 31.7 (CH_2), 48.8 (CH), 49.3 (CH), 52.5 (2×CH_3O), 64.28 (2×CH_2O), 116.8 (CH, Ar), 117.8 (CH, Ar), 120.9 (CH, Ar), 131.5 (C, Ar), 143.2 (C, Ar), 143.9 (C, Ar), 169.4 (CO_2Me), 169.6 (CO_2Me), 174.7 ($CONH_2$). IR (ZnSe): ν = 3458, 3357, 3199, 2956, 2939, 1733, 1674, 1590, 1507, 1436, 1288, 1261, 1158, 1068 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+H]^+$ calcd for $C_{16}H_{20}NO_7$ 338.1234; Found 338.1226.

General procedure D for the synthesis of **12**. To a cooled to 0 °C 0.133 M solution of cyanide **3** in dry methanol, Boc_2O (2 equiv) and $NiCl_2$ (1 equiv) were successively added under stirring. Then $NaBH_4$ (10 equiv) was added in small portions under cooling the reaction mixture with cold water. When effervescence has entirely ceased, the resulting reaction mixture containing a finely divided black precipitate was allowed to warm to room temperature and stirred for 48 h, at which point aqueous solution of EDTA was added. The mixture was stirred for additional 30 min before solvent evaporation. The blue residue was dissolved in EtOAc (10 mL) and extracted with saturated $NaHCO_3$ (3×10 mL). The combined organic fractions were dried with Na_2SO_4, filtered, and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel to afford amine **12**.

Dimethyl 2-[3-(tert-butoxycarbonyl)amino-2-(3,4-dimethoxyphenyl)propyl]-malonate (**12a**) was prepared according to the General Procedure D from cyanide **3a** (0.16 g, 0.50 mmol), Boc_2O (217 mg, 100 mmol) and $NiCl_2$ (65 mg, 0.50 mmol) in methanol (3.7 mL). Yield 100 mg (47%); yellowish oil; R_f = 0.41 (petroleum ether : ethyl acetate; 2:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.35 (s, 9H, 3×CH_3), 2.04 (ddd, ^2J = 13.7 Hz, ^3J = 11.5 Hz, ^3J = 4.9 Hz, 1H, CH_2), 2.27 (ddd, ^2J = 13.7 Hz, ^3J = 9.8 Hz, ^3J = 3.8 Hz, 1H, CH_2), 2.62–2.72 (m, 1H, CH_2N), 3.11–3.19 (m, 2H, 2×CH), 3.33–3.42 (m, 1H, CH_2N), 4.44–4.48 (m, 1H, NH), 3.56 (s, 3H, CH_3O), 3.68 (s, 3H, CH_3O), 3.81 (s, 3H, CH_3O), 3.82 (s, 3H, CH_3O), 6.61 (br. s, 1H, Ar), 6.64 (d, ^3J = 8.1 Hz, 1H, Ar), 6.78 (d, ^3J = 8.1 Hz, 1H, Ar). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ= 28.2 (3×CH_3), 32.3 (CH_2), 43.3 (CH), 45.8 (CH_2), 49.3 (CH), 52.4 (2×CH_3O), 55.7 (2×CH_3O), 79.1 (C), 110.6 (CH, Ar), 111.2 (CH, Ar), 119.8 (CH, Ar), 132.8 (C, Ar), 147.9 (C, Ar), 149.0 (C, Ar), 155.6 (CONH), 169.4 (CO_2Me), 169.6 (CO_2Me). IR (ZnSe): ν = 3384, 2955, 2838, 1752, 1735, 1712, 1606, 1592, 1518, 1454, 1440, 1422, 1404, 1366, 1262, 1163, 1087, 1028 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{32}NO_8$ 426.2122; Found 426.2122. Anal. Calcd for $C_{21}H_{31}NO_8$: C, 59.28; H, 7.34; N, 3.29. Found: C, 58.89; H, 7.14; N, 3.14.

Dimethyl 2-[3-(tert-butoxycarbonyl)amino-2-(2,4,5-trimethoxyphenyl)propyl]-malonate (**12b**) was obtained according to the General Procedure D from cyanide **3g** (0.283 g, 0.81 mmol), Boc_2O (352 mg, 1.61 mmol) and $NiCl_2$ (104 mg, 0.81

mmol) in methanol (6 mL). Yield 251 mg (68%); yellowish oil; R_f = 0.33 (petroleum ether : ethyl acetate; 2:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.33 (s, 9H, 3×CH_3), 2.07 (^2J = 13.9 Hz, ^3J =11.1 Hz, ^3J = 5.1 Hz, 1H, CH_2), 2.26 (^2J = 13.9 Hz, ^3J = 9.6 Hz, ^3J = 4.1 Hz, 1H, CH_2), 3.06–3.17 (m, 2H, 2×CH), 3.17–3.25 (m, 1H, CH_2N), 3.34–3.43 (m, 1H, CH_2N), 4.43–4.48 (m, 1H, NH), 3.54 (s, 3H, CH_3O), 3.67 (s, 3H, CH_3O), 3.70 (s, 3H, CH_3O), 3.77 (s, 3H, CH_3O), 3.82 (s, 3H, CH_3O), 6.44 (br. s, 1H, Ar), 6.57 (br. s, 1H, Ar). ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz): δ = 28.2 (3×CH_3), 31.4 (CH_2), 37.0 (CH), 44.6 (CH_2), 49.6 (CH), 52.3 (CH_3O), 52.4 (CH_3O), 55.97 (CH_3O), 56.04 (CH_3O), 56.5 (CH_3O), 78.9 (C), 97.5 (CH, Ar), 112.1 (CH, Ar), 119.4 (C, Ar), 143.1 (C, Ar), 148.3 (C, Ar), 152.0 (C, Ar), 156.8 (CONH), 169.5 (CO_2Me), 169.8 (CO_2Me). IR (KBr): ν = 3391, 2954, 2837, 1752, 1734, 1713, 1611, 1512, 1456, 1439, 1399, 1366, 1316, 1270, 1249, 1207, 1171, 1081, 1035 cm^{-1}. HRMS ESI-TOF m/z: $[M+Na]^+$ Calcd for $C_{22}H_{33}NNaO_9$ 478.2048; Found 478.2042.

Methyl 2-oxo-5-(2,4,5-trimethoxyphenyl)piperidine-3-carboxylate **(13)**. To a cooled to 0 °C solution of cyanide **3g** (0.283 g, 0.81 mmol) in dry methanol (6 mL) Boc_2O (352 mg, 1.61 mmol) and $NiCl_2$ (104 mg, 0.81 mmol) were successively added under stirring. $NaBH_4$ (308 mg, 8.1 mmol) was then added in small portions under the same temperature. When effervescence has entirely ceased, the resulting mixture containing a finely divided black precipitate was allowed to warm to room temperature and stirred for 48 h, at which point EDTA

aqueous solution was added. The mixture was stirred for additional 30 min before solvent evaporation. The blue residue was dissolved in EtOAc (10 mL) and extracted with saturated $NaHCO_3$ (3×10 mL). The combined organic fractions were dried with Na_2SO_4, filtered and concentrated in vacuo. The crude Boc-protected amine **12b** was further used without additional purification. This amine (250 mg, *ca*. 0.55 mmol) was dissolved in 3 M solution of HC1 in EtOAc (304 μL) and stirred at room temperature for 1 h. Then EtOAc (2 mL) was added and mixture was refluxed for 1.5 h. The solution was concentrated *in vacuo*; the resulting residue was purified by column chromatography on silica gel yielding product **13** as a mixture of diastereomers (**A** and **B**) in a ratio of 55:45. Yield 170 mg (65%); yellowish oil; R_f = 0.31 (ethyl acetate). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 2.18–2.22 (m, 1H), 2.29–2.35 (m, 1H), 2.40–2.46 (m, 1H), 3.27–3.36 (m, 1H), 3.40–3.48 (m, 1H), 3.54–3.61 (m, 1H), 3.76, 3.77, 3.80, 3.81, 3.82, 3.88 (s, 12H, 4×CH_3O), 6.51 (br. s, 1H, Ar), 6.70 (br. s, 1H, Ar), 6.99–6.74 (m, 1H, NH). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ = 29.6 (CH_2, **B**), 30.0 (CH, **B**), 30.4 (CH_2, **A**), 31.9 (CH, **A**), 46.8 (CH_2, **B**), 47.3 (CH_2, **A**), 49.4 (CH, **A** + CH, **B**), 56.1 (3×CH_3O, **A** + 3×CH_3O, **B**), 56.7 (CH_3O, **A**), 56.8 (CH_3O, **B**), 97.3 (CH, Ar, **A**), 97.5 (CH, Ar, **B**), 110.9 (CH, Ar, **A**), 111.5 (CH, Ar, **B**), 119.8 (C, Ar, **A**), 120.2 (C, Ar, **B**), 142.8 (C, Ar, **B**), 143.0 (C, Ar, **A**), 148.6 (C, Ar, **A**), 148.7 (C, Ar, **B**), 151.3 (C, Ar, **A**), 151.6 (C, Ar, **B**), 167.9 (CONH, **A** + CONH, **B**), 171.1 (*C*O_2Me, **A**), 171.2 (*C*O_2Me, **B**). IR (ZnSe): ν = 3200, 3074, 2943, 1737, 1663, 1522, 1471,

1457, 1267, 1207, 1033 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+Na]^+$ Calcd for $C_{16}H_{21}NNaO_6$ 346.1261; Found 346.1264.

Dimethyl 2-[2-({[(1,1,1,3,3,3-hexafluoropropan-2-yl)oxy]carbonyl}amino)-2-phenylethyl]malonate (**14**). To a mixture of cyclopropane **1r**[31] (138 mg, 0.59 mmol) and TMSNCO (0.17 mL, 1.26 mmol) the solution of TfOH (0.01 mL, 0.11 mmol, 20 mol %) in HFIP (0.3 mL) was added under N_2 atmosphere. The reaction mixture was stirred at room temperature for 22 h, quenched with conc. aqueous $NaHCO_3$ and extracted with ethyl acetate (3×10 mL). The combined organic fractions were washed with brine, dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on a silica gel to afford carbamate **14**. Yield 160 mg (61%); colorless solid; mp 94–95 °C; R_f = 0.78 (petroleum ether : ethyl acetate; 2:1). ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 2.45 (ddd, ^2J = 14.2 Hz, ^3J = 6.4 Hz, ^3J = 6.1 Hz, 1H, CH_2), 2.50 (ddd, ^2J = 14.2 Hz, ^3J = 9.3 Hz, ^3J = 7.6 Hz, 1H, CH_2), 3.44 (dd, ^3J = 7.6 Hz, ^3J = 6.4 Hz, 1H, CH), 3.72 (s, 3H, CH_3O), 3.76 (s, 3H, CH_3O), 4.80 (ddd, ^3J = 9.3 Hz, ^3J = 8.3 Hz, ^3J = 6.1 Hz, 1H, C*H*NH), 5.75 (d, ^3J = 8.3 Hz, 1H, NH), 7.27–7.33 (m, 3H, Ph), 7.36–7.39 (m, 2H, Ph). ^{13}C{^{1}H} NMR ($CDCl_3$, 150 MHz): δ = 34.9 (CH_2), 49.0 (CH), 52.85 (CH_3O), 52.90 (CH_3O), 54.8 (CH), 67.7 (sept, $^2J_{CF}$ = 35 Hz, *C*H(CF_3)$_2$), 120.5 (q, $^1J_{CF}$ = 277 Hz, CF_3), 120.6 (q, $^1J_{CF}$ = 277 Hz, CF_3), 126.1 (2×CH, Ph), 128.3 (CH, Ph), 129.1 (2×CH, Ph), 139.9 (C, Ph), 151.9 (CONH), 169.2 (*C*O_2Me), 169.7 (*C*O_2Me). IR (ZnSe): ν = 3366, 3339, 2973, 1746, 1733, 1531,

1521, 1447, 1393, 1290, 1264, 1228, 1200, 1107 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+NH_4]^+$ Calcd for $C_{17}H_{21}F_6N_2O_6$ 463.1298; Found 463.1290. (Anal. Calcd for $C_{17}H_{17}F_6NO_6$: C, 45.85; H, 3.85; N, 3.15. Found: C, 46.20; H, 3.76; N, 3.15.

General procedure E for DA cyclopropanes **1** ring opening with silylated amines. A dry tube for microwave oven was charged with 2 M solution of cyclopropane **1** (1 equiv) in HFIP and 4-(trimethylsilyl)morpholine or 1-(trimethylsilyl)pyrrolidine (2 equiv) under N_2 atmosphere. TfOH (10 mol %) was added, and the reaction mixture was heated in a microwave reactor at 80 °C for 10 h, quenched with conc. aqueous $NaHCO_3$ and extracted with ethyl acetate (3×10 mL). The combined organic extracts were washed with $NaHCO_3$ and brine, dried with anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on a silica gel to afford the desired product. *Dimethyl 2-[2-(4-fluorophenyl)-2-morpholinoethyl]malonate* (**15a**) was obtained according to the General Procedure E from cyclopropane **1t**[25] (108 mg, 0.43 mmol), 4-(trimethylsilyl)morpholine (137 mg, 152 μL, 0.86 mmol) and TfOH (3.8 μL, 0.043 mmol) in HFIP (0.22 mL). Yield 118 mg (81%); yellowish oil; R_f = 0.39 (petroleum ether : ethyl acetate; 4:1). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.10–2.16 (m, 1H, C(1')H_2), 2.26–2.33 (m, 2H, $(CH_2)_2$N), 2.37–2.42 (m, 2H, $(CH_2)_2$N), 2.62–2.71 (m, 1H, C(1')H_2), 3.35–3.39 (m, 1H, C(2')H), 3.38 (dd, ^3J = 8.4 Hz, ^3J = 5.6 Hz, 1H, C(2)H), 3.59–3.64 (m, 4H, $(CH_2)_2$O), 3.66 (s, 3H, CH_3O), 3.73 (s, 3H, CH_3O), 7.00–7.05 (m, 2H, Ar), 7.13–7.17 (m, 2H, Ar). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ = 31.3 (CH_2), 48.9 (C(2)H), 49.7 (2×CH_2), 50.4 (CH_3O), 52.8 (CH_3O), 67.3 (2×CH_2), 67.5 (C(2')H), 114.6 (d, ^2J = 21 Hz, 2×CH, Ar), 129.6 (d, ^3J = 8 Hz, 2×CH, Ar), 133.6 (C, Ar), 162.4 (d, ^1J = 246.0 Hz, CF), 169.9 (2×*C*O_2Me). ^{19}F NMR ($CDCl_3$, 470 MHz): δ = –114.7. IR (KBr): ν = 2954, 2854, 2818, 1752, 1734, 1603, 1510, 1453, 1436, 1347, 1288, 1268, 1224, 1202, 1159, 1118 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{23}FNO_5$ 340.1555;

Found 340.1559. Anal. Calcd for $C_{17}H_{22}FNO_5$: C, 60.17; H, 6.53; N, 4.13. Found: C, 60.15; H, 6.54; N, 4.06.

Dimethyl 2-[2-(2-methylphenyl)-2-morpholinoethyl]malonate (**15b**) was obtained according to the General Procedure E from cyclopropane **1s**[36] (106 mg, 0.43 mmol), 4-(trimethylsilyl)morpholine (137 mg, 152 μL, 0.86 mmol) and TfOH (3.8 μL, 0.043 mmol) in HFIP (0.22 mL). Yield 119 mg (83%); colorless oil; R_f = 0.34 (petroleum ether : ethyl acetate; 4:1). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.23 (ddd, ^2J = 13.8 Hz, ^3J = 8.4 Hz, ^3J = 4.8 Hz, 1H, C(1')H_2), 2.63 (ddd, ^2J = 13.8 Hz, ^3J = 9.1 Hz, ^3J = 5.7 Hz, 1H, C(1')H_2), 2.31 (s, 3H, CH_3), 2.36–2.46 (m, 2H, $(CH_2)_2$N), 2.47–2.52 (m, 2H, $(CH_2)_2$N), 3.25 (dd, ^3J = 9.1 Hz, ^3J = 4.8 Hz, 1H, C(2)H), 3.62 (dd, ^3J = 8.4 Hz, ^3J = 5.7 Hz, 1H, C(2')H), 3.61–3.65 (m, 4H, $(CH_2)_2$O), 3.63 (s, 3H, CH_3O), 3.68 (s, 3H, CH_3O), 7.12–7.18 (m, 3H, Ar), 7.23–7.26 (m, 1H, Ar). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ = 19.7 (CH_3), 30.5 (C(1')H_2), 48.9 (C(2)H), 50.7 (2×CH_2), 52.40 (CH_3O), 52.47 (CH_3O), 62.9 (C(2')H), 67.2 (2×CH_2), 125.8 (CH, Ar), 127.1 (CH, Ar), 127.8 (CH, Ar), 130.7 (CH, Ar), 136.9 (C, Ar), 137.1 (C, Ar), 169.70 (*C*O_2Me), 169.72 (*C*O_2Me). IR (ZnSe): ν = 3020, 2954, 2854, 2811, 1753, 1735, 1452, 1436, 1344, 1329, 1269, 1237, 1199, 1152, 1119 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{26}NO_5$ 336.1805; Found 336.1805. Anal. Calcd for $C_{18}H_{25}NO_5$: C, 64.46; H, 7.51; N, 4.18. Found: C, 64.49; H, 7.53; N, 4.21.

Dimethyl 2-[2-(4-bromophenyl)-2-pyrrolidinoethyl]malonate (**16**) was obtained according to the General Procedure E from cyclopropane **1u**[32] (160 mg, 0.51 mmol), 1-(trimethylsilyl)pyrrolidine (146 mg, 178 μL, 1.02 mmol) and TfOH (4.5 μL, 0.051 mmol) in HFIP (0.26 mL) for 10 h. Yield 125 mg (64%); yellowish oil; R_f = 0.52 (petroleum ether : ethyl acetate; 1:1). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.64–1.69 (m, 4H, CH_2), 2.16 (ddd, ^2J = 13.8 Hz, ^3J = 9.4 Hz, ^3J = 4.6 Hz,

1H, CH_2), 2.28–2.35 (m, 2H, CH_2), 2.43–2.49 (m, 2H, CH_2), 2.59 (ddd, ^2J = 13.8 Hz, ^3J = 10.0 Hz, ^3J = 5.0 Hz, 1H, CH_2), 3.09 (dd, ^3J = 10.0 Hz, ^3J = 4.6 Hz, 1H, CH), 3.14 (dd, ^3J = 9.4 Hz, ^3J = 5.0 Hz, 1H, CH), 3.59 (s, 3H, CH_3O), 3.68 (s, 3H, CH_3O), 7.11 (br. d, ^3J = 8.4 Hz, 2H, Ar), 7.40 (br. d, ^3J = 8.4 Hz, 2H, Ar). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz): δ= 23.2 (2×CH_2), 34.2 (CH_2), 48.8 (CH), 51.9 (2×CH_2), 52.4 (CH_3O), 52.5 (CH_3O), 67.2 (CH), 121.2 (C, Ar), 130.0 (2×CH, Ar), 131.4 (2×CH, Ar), 139.8 (C, Ar), 169.5 (CO_2Me), 169.6 (CO_2Me). IR (ZnSe): ν = 2966, 2875, 2797, 1761, 1741, 1590, 1486, 1437, 1407, 1348, 1319, 1282, 1240, 1204, 1157, 1072, 1054, 1011 cm^{-1}. HRMS ESI-TOF *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{23}BrNO_4$ 384.0805; Found = 384.0807. Anal. Calcd for $C_{18}H_{22}BrNO_4$: C, 53.14; H, 5.77; N, 3.65. Found: C, 53.49; H, 5.73; N, 3.41..

Supporting Information

The supporting information is available free of charge on the ACS Publications website at doi:… Copies of 1D and 2D NMR spectra (pdf).

Acknowledgement

We thank the Russian Science Foundation (grant 18-13-00449) for support of this work.

References

(1) Buchner, E.; Dessauer, H. Ueber Carbonsäuren des Phenyltrimethylens. *Chem. Ber.* **1892**, *25*, 1147.

(2) Wenkert, E. Oxycyclopropanes in Organochemical Synthesis. *Acc. Chem. Res.* **1980**, *13*, 27. See also: Hudlicky, T. Contributions of Ernest Wenkert to the Use of Cyclopropanes in Synthesis – Impact, Reflections, and Recollections. *Isr. J. Chem.* **2016**, *56*, 540.

(3) (a) Reissig, H.-U.; Hirsch, E. Donor-Acceptor Substituted Cyclopropanes: Synthesis and Ring Opening to 1,4-Dicarbonyl Compounds. *Angew. Chem. Int. Ed.* **1980**, *19*, 813. (b) Reissig, H.-U. Donor-Acceptor Substituted Cyclopropanes: Versatile Building Blocks in Organic Synthesis. *Top. Curr. Chem,* **1988**, *144*, 73. (c) Reissig, H.-U.; Zimmer, R. Donor–Acceptor Substituted Cyclopropane Derivatives and Their Application in Organic Synthesis. *Chem. Rev.* **2003**, *103*, 1151.

(4) For some recent reviews, see: (a) Werz, D. B.; Biju, A. T. Uncovering the Neglected Similarities of Arynes and Donor–Acceptor Cyclopropanes. *Angew. Chem. Int. Ed.* doi:10.1002/anie.201909213. (b) Ivanova, O. A.; Trushkov, I. V. Donor–Acceptor Cyclopropanes in the Synthesis of Carbocycles. *Chem. Rec.* **2019**, *19*, 2189. (c) Tomilov, Y. V.; Menchikov, L. G.; Novikov, R. A.; Ivanova, O. A.; Trushkov, I. V. Methods for the synthesis of donor–acceptor cyclopropanes. *Russ. Chem. Rev.* **2018**, *87*, 201. (d) Budynina, E. M.; Ivanov, K. L.; Sorokin, I. D.; Melnikov, M. Ya. Ring Opening of Donor–Acceptor Cyclopropanes with *N*-Nucleophiles. *Synthesis* **2017**, *49*, 3035. (e) Pagenkopf, B. L.; Vemula, N. Cycloadditions of Donor–Acceptor Cyclopropanes and Nitriles. *Eur. J. Org. Chem.* **2017**, 2561. (f)

Grover, H. K.; Emmett, M.; Kerr, M. A. Carbocycles from donor–acceptor cyclopropanes. *Org. Biomol. Chem.* **2015**, *13*, 655. (g) Novikov, R. A.; Tomilov, Y. V. Dimerization of donor–acceptor cyclopropanes *Mendeleev Commun.* **2015**, *25*, 1. (h) De Nanteuil, F.; De Simone, F.; Frei, R.; Benfatti, F.; Serrano, E.; Waser, J. Cyclization and annulation reactions of nitrogen-substituted cyclopropanes and cyclobutanes. *Chem. Commun.* **2014**, *50*, 10912. (i) Schneider, T. F.; Kaschel, J.; Werz, D. B. A New Golden Age for Donor–Acceptor Cyclopropanes. *Angew. Chem. Int. Ed.* **2014**, *53*, 5504. (j) Cavitt, M. A.; Phun, L. H.; France, S. Intramolecular donor–acceptor cyclopropane ring-opening cyclizations. *Chem. Soc. Rev.* **2014**, *43*, 804.

(5) (a) Verma, K.; Taily, I. M.; Banerjee, P. Exploitation of donor–acceptor cyclopropanes and *N*-sulfonyl-1-azadienes towards the synthesis of spirocyclopentane benzofuran derivatives. *Org. Biomol. Chem.* **2019**, *17*, 8149. (b) Mondal, M.; Panda, M.; McKee, V.; Kerrigan, N. J. Asymmetric Synthesis of Tetrahydrofurans through Palladium(0)-Catalyzed [3+2]-Cycloaddition of Vinylcyclopropanes with Ketenes. *J. Org. Chem.* **2019**, *84*, 11983. (c) Petzold, M.; Jones, P. G.; Werz, D. B. (3+3)-Annulation of Carbonyl Ylides with Donor–Acceptor Cyclopropanes: Synergistic Dirhodium(II) and Lewis Acid Catalysis. *Angew. Chem. Int. Ed.* **2019**, *58*, 6225. (d) Tamilarasan, V. J.; Srinivasan, K. $SnCl_4$-Promoted [3+2] Annulation of γ-Butyrolactone-Fused Donor–Acceptor Cyclopropanes with Nitriles: Access to γ-Butyrolactone-Fused 1-Pyrrolines. *J. Org. Chem.* **2019**,

84, 8782. (e) Dhote, P. S.; Ramana, C. V. One-Pot Au(III)-/Lewis Acid Catalyzed Cycloisomerization of Nitroalkynes and [3+3] Cycloaddition with Donor–Acceptor Cyclopropanes. *Org. Lett.* **2019**, *21*, 6221. (f) Xie, M.-S.; Zhao, G.-F.; Qin, T.; Suo, Y.-B.; Qu, G.-R.; Guo, H.-M. Thiourea participation in [3+2] cycloaddition with donor–acceptor cyclopropanes: a domino process to 2-aminodihydrothiophenes. *Chem. Commun.* **2019**, *55*, 1580. (g) Huang, X.-B.; Li, X.-J.; Li, T.-T.; Chen, B.; Chu, W.-D.; He, L.; Liu, Q.-Z. Palladium-Catalyzed Highly Enantioselective Cycloaddition of Vinyl Cyclopropanes with Imines. *Org. Lett.* **2019**, *21*, 1713.

(6) (a) Singh, K.; Bera, T.; Jaiswal, V.; Biswas, S.; Mondal, B.; Das, D.; Saha, J. Lewis Acid Catalyzed Nucleophilic Ring Opening and 1,3-Bisfunctionalization of Donor–Acceptor Cyclopropanes with Hydroperoxides: Access to Highly Functionalized Peroxy/ (α-Heteroatom Substituted)Peroxy Compounds. *J. Org. Chem.* **2019**, *84*, 710. (b) Das, S.; Daniliuc, C. G.; Studer, A. Lewis Acid Catalyzed Stereoselective Dearomative Coupling of Indolylboron Ate Complexes with Donor–Acceptor Cyclopropanes and Alkyl Halides. *Angew. Chem. Int. Ed.* **2018**, *57*, 4053. (c) Das, S.; Daniliuc, C. G.; Studer, A. Stereospecific 1,3-Aminobromination of Donor–Acceptor Cyclopropanes. *Angew. Chem. Int. Ed.* **2017**, *56*, 11554. (d) Garve, L. K. B.; Jones, P. G.; Werz, D. B. Ring-Opening 1-Amino-3-aminomethylation of Donor–Acceptor Cyclopropanes via 1,3-Diazepanes. *Angew. Chem. Int. Ed.* **2017**, *56*, 9226. (e) Wallbaum, J.; Garve, L. K. B.;

Jones, P. G.; Werz, D. B. Ring-Opening 1,3-Halochalcogenation of Cyclopropane Dicarboxylates. *Org. Lett.* **2017**, *19*, 98.

(7) (a) Ivanov, K. L.; Villemson, E. V.; Budynina, E. M.; Ivanova, O. A.; Trushkov, I. V.; Melnikov, M. Ya. Ring Opening of Donor–Acceptor Cyclopropanes with the Azide Ion: A Tool for Construction of *N*-Heterocycles. *Chem. Eur. J.* **2015**, *21*, 4975. (b) Gopinath, P.; Chandrakala, R. N.; Chandrasekaran, S. A Mild Protocol for the Regioselective Ring Opening of Doubly Activated Cyclopropanes by Using Selenolates Generated in Situ: Synthesis of Functionalized Organoselenium Compounds. *Synthesis* **2015**, *47*, 1488. (c) Nambu, H.; Fukumoto, M.; Hirota, W.; Yakura, T. Ring-Opening Cyclization of Cyclohexane-1,3-dione-2-spirocyclopropanes with Amines: Rapid Access to 2-Substituted 4-Hydroxyindole. *Org. Lett.* **2014**, *16*, 4012.

(8) (a) Han, J.-Q.; Zhang, H.-H.; Xu, P.-F.; Luo, Y.-C. Lewis Acid and (Hypo)iodite Relay Catalysis Allows a Strategy for the Synthesis of Polysubstituted Azetidines and Tetrahydroquinolines. *Org. Lett.* **2016**, *18*, 5212. (b) Kim, A.; Kim, S.-G. Lewis-Acid-Catalysed Friedel–Crafts Alkylation of Donor–Acceptor Cyclopropanes with Electron-Rich Benzenes to Generate 1,1-Diarylalkanes. *Eur. J. Org. Chem.* **2015**, 6419. (c) Wang, P.; Song, S.; Miao, Z.; Yang, G.; Zhang, A. $InBr_3$-Mediated One-Pot Synthesis of 2-(Polyhydroxylatedalkyl)-*N*-aryl-/-alkylpyrroles from 1,2-Cyclopropa-3-pyranone and Amines. *Org. Lett.* **2013**, *15*, 3852.

(9) (a) Zhu, M.; Wang, D.-C.; Xie, M.-S.; Qu, G.-R.; Guo, H.-M. Enantioselective Friedel-Crafts Alkylation Reactions of β-Naphthols with Donor–Acceptor Aminocyclopropanes. *Chem. Eur. J.* **2018**, *24*, 15512. (b) Xia, Y.; Chang, F.; Lin, L.; Xu, Y.; Liu, X.; Feng, X. Asymmetric ring-opening of cyclopropyl ketones with β-naphthols catalyzed by a chiral *N*,*N*'-dioxide–scandium(III) complex. *Org. Chem. Front.* **2018**, *5*, 1293. (c) Ma, H.; Hu, X.-Q.; Luo, Y.-C.; Xu, P.-F. 3,4,5-Trimethylphenol and Lewis Acid Dual-Catalyzed Cascade Ring-Opening/Cyclization: Direct Synthesis of Naphthalenes. *Org. Lett.* **2017**, *19*, 6666. (d) Luo, Y.-C.; Ma, H.; Hu, X.-Q.; Xu, P.-F. $Sc(OTf)_3$-Catalyzed [4 + 2]-Annulation Reaction between Electron-Rich Phenols and Donor–Acceptor Cyclopropanes: Synthesis of Polysubstituted Dihydronaphthols. *J. Org. Chem.* **2017**, *82*, 1013.

(10) (a) Perrotta, D.; Wang, M.-M.; Waser, J. Lewis Acid Catalyzed Enantioselective Desymmetrization of Donor–Acceptor *meso*-Diaminocyclopropanes. *Angew. Chem. Int. Ed.* **2018**, *57*, 5120. (b) Irwin, L. C.; Renwick, C. R.; Kerr, M. A. Nucleophilic Opening of Donor–Acceptor Cyclopropanes with Indoles via Hydrogen Bond Activation with 1,1,1,3,3,3-Hexafluoroisopropanol. *J. Org. Chem*. **2018**, *83*, 6235. (c) Lee, J.; Ko, K. M.; Kim, S.-G. $Ni(ClO_4)_2$-Catalyzed Friedel-Crafts Reaction of Coumarin-Fused Donor–Acceptor Cyclopropanes with Indoles: Stereoselective Synthesis of *trans*-3,4-Disubstituted-3,4-dihydrocoumarins. *Eur. J. Org. Chem*. **2018**, 4166.

(11) (a) Kilic, H.; Dalkilic, O. The Reaction of Donor–Acceptor Cyclopropanes with 4,7-Dihydroindole: A New Protocol for the Synthesis of Divergent C2-Alkylated Indoles. *ChemistrySelect* **2019**, *4*, 3737. (b) Richmond, E.; Vuković, V. D.; Moran, J. Nucleophilic Ring Opening of Donor–Acceptor Cyclopropanes Catalyzed by a Brønsted Acid in Hexafluoroisopropanol. *Org. Lett.* **2018**, *20*, 574. (c) Maloney, T. P.; Murphy, K. L.; Mainsah, T. L.; Nolin, K. L. Friedel-Crafts alkylation of benzo[*b*]furan with activated cyclopropanes catalyzed by a calcium(II) complex. *Tetrahedron Lett.* **2018**, *59*, 18.

(12) (a) Saha, M.; Bhattacharyya, A.; Talukdar, R.; Ghorai, M. K. Stereospecific Syntheses of Enaminonitriles and β-Enaminoesters via Domino Ring-Opening Cyclization (DROC) of Activated Cyclopropanes with Pronucleophilic Malononitriles. *J. Org. Chem.* **2018**, *83*, 2131. (b) Budynina, E. M.; Ivanov, K. L.; Chagarovskiy, A. O.; Rybakov, V. B.; Trushkov, I. V.; Melnikov, M. Ya. From Umpolung to Alternation: Modified Reactivity of Donor–Acceptor Cyclopropanes Toward Nucleophiles in Reaction with Nitroalkanes. *Chem. Eur. J.* **2016**, *22*, 3692. (c) Ghorai, M. K.; Talukdar, R.; Tiwari, D. P. A Route to Highly Functionalized β-Enaminoesters via a Domino Ring-Opening Cyclization/Decarboxylative Tautomerization Sequence of Donor–Acceptor Cyclopropanes with Substituted Malononitriles. *Org. Lett.* **2014**, *16*, 2204.

(13) (a) Akaev, A. A.; Villemson, E. V.; Vorobyeva, N. S.; Majouga, A. G.; Budynina, E. M.; Melnikov, M. Ya. 3-(2-Azidoethyl)oxindoles: Advanced Building Blocks for One-Pot Assembly of Spiro[pyrrolidine-3,3'-oxindoles]. *J. Org. Chem.* **2017**, *82*, 5689. (b) Villemson, E. V.; Budynina, E. M.; Ivanova, O. A.; Skvortsov, D. A.; Trushkov, I. V.; Melnikov, M. Ya. Concise approach to pyrrolizino[1,2-*b*]indoles from indole-derived donor-acceptor cyclopropanes. *RSC Adv.* **2016**, *6*, 62014. (c) Emmett, M. R.; Grover, H. K.; Kerr, M. A. Tandem Ring-Opening Decarboxylation of Cyclopropane Hemimalonates with Sodium Azide: A Short Route to γ-Aminobutyric Acid Esters. *J. Org. Chem.* **2012**, *77*, 6634.

(14) For examples, see: (a) Wenderski, T. A.; Marsini, M. A.; Pettus, T. R. R. A Diastereoselective Formal Synthesis of Berkelic Acid. *Org. Lett.* **2011**, *13*, 118. (b) Takeda, H.; Watanabe, H.; Nakada, M. Asymmetric total synthesis of enantiopure (–)-methyl jasmonate via catalytic asymmetric intramolecular cyclopropanation of α-diazo-β-keto sulfone. *Tetrahedron* **2006**, *62*, 8054. (c) Budynina, E. M.; Ivanova, O. A.; Averina, E. B.; Kuznetsova, T. S.; Zefirov, N. S. Ring opening of 1,1-dinitrocyclopropane by addition of C, N, O and S nucleophiles. *Tetrahedron Lett.* **2006**, *47*, 647. (d) Singh, P.; Paul, K. A Practical Approach for Spiro- and 5-Monoalkylated Barbituric Acids. *J. Heterocyclic Chem.* **2006**, *43*, 607.

(15) O'Bannon, P. E.; Dailey, W. P. Nitrocyclopropanes from nitrodiazomethanes. Preparation and reactivity. *Tetrahedron* **1990**, *46*, 7341.

(16) Brogden, R. N.; Benfield, P. Verapamil: a review of its pharmacological properties and therapeutic use in coronary artery disease. *Drugs* **1996**, *51*, 792.

(17) Kay, B. A clinical investigation of piritramide in the treatment of postoperative pain. *Brit. J. Anaesth.* **1971**, *43*, 1167.

(18) Lapin, I. Phenibut (β-Phenyl-GABA): A Tranquilizer and Nootropic Drug. *CNS Drug Rev.* **2001**, *7*, 471.

(19) Hjorth, S.; Carlsson, A.; Clark, D.; Svensson, K.; Wikström, H.; Sanchez, D.; Lindberg, P.; Hacksell, U.; Arvidsson, L.-E.; Johansson, A.; Nilsson, J. L. G. Central dopamine receptor agonist and antagonist actions of the enantiomers of 3-PPP. *Psychopharmacol.* **1983**, *81*, 89.

(20) (a) Li, M.; Kong, D.; Zi, G.; Hou, G. Rh-Catalyzed Asymmetric Hydrogenation of 1,2-Dicyanoalkenes. *J. Org. Chem.* **2017**, *82*, 680. (b) Kiyokawa, K.; Nagata, T.; Hayakawa, J.; Minakata, S. Straightforward Synthesis of 1,2-Dicyanoalkanes from Nitroalkenes and Silyl Cyanide Mediated by Tetrabutylammonium fluoride. *Chem. Eur. J.* **2015**, *21*, 1280. (c) Citterio, A.; Cominelli, A.; Bonavoglia, F. Reductive Arylation of Maleic and Fumaric Acid Derivatives by Arenediazonium and Titanium(III) Salts. *Synthesis* **1986**, 308. (d) Crider, A. M.; Hemdi, T. F.; Hassan, M. N.; Fahn, S. Synthesis and Dopaminergic Activity of 3-(3,4-Dihydroxyphenyl)-1-*n*-propylpyrrolidine Hydrobromide. *J. Pharm. Sci.* **1984**, *73*, 1585.

(21) A related domino reaction including addition/elimination/addition sequence but with the participation of two equivalents of DA cyclopropane was recently reported: Chidley, T.; Vemula, N.; Carson, C. A.; Kerr, M. A.; Pagenkopf, B. L. Cascade Reaction of Donor–Acceptor Cyclopropanes: Mechanistic Studies on Cycloadditions with Nitrosoarenes and *cis*-Diazenes. *Org. Lett.* **2016**, *18*, 2922.

(22) (a) Guchhait, S. K.; Sisodiya, S.; Saini, M.; Shah, Y. V.; Kumar, G.; Daniel, D. P.; Hura, N.; Chaudhary, V. Synthesis of Polyfunctionalized Pyrroles via a Tandem Reaction of Michael Addition and Intramolecular Cyanide-Mediated Nitrile-to-Nitrile Condensation. *J. Org. Chem.* **2018**, *83*, 5807. (b) Guo, S.; Mi, X. Tetraarylphosphonium inner-salts (TAPIS) as both Lewis base catalyst and phase tag. *Tetrahedron Lett.* **2017**, *58*, 2881. (c) Yu, Y.; Chen, Y.; Wu, W.; Jiang, H. Facile synthesis of cyanofurans *via* Michael addition/cyclization of ene-yne-ketones with trimethylsilyl cyanide. *Chem. Commun.* **2017**, *53*, 640. (d) Hatano, M.; Yamakawa, K.; Ishihara, K. Enantioselective Conjugate Hydrocyanation of α,β-Unsaturated *N*-Acylpyrroles Catalyzed by Chiral Lithium(I) Phosphoryl Phenoxide. *ACS Catalysis* **2017**, *7*, 6686.

(23) For related (3+3)-cyclodimerizations, see: (a) Ivanova, O. A.; Budynina, E. M.; Khrustalev, V. N.; Skvortsov, D. A.; Trushkov, I. V.; Melnikov, M. Ya. A Straightforward Approach to Tetrahydroindolo[3,2-*b*]carbazoles and 1-Indolyltetrahydrocarbazoles through [3+3] Cyclodimerization of Indole-Derived Cyclopropanes. *Chem. Eur. J.* **2016**, *22*, 1223. (b) Ivanova, O. A.; Budynina, E. M.; Chagarovskiy, A. O.; Trushkov, I. V.; Melnikov, M. Ya. (3+3)-

Cyclodimerization of Donor–Acceptor Cyclopropanes. Three Routes to Six-Membered Rings. *J. Org. Chem.* **2011**, *76*, 8852.

(24) Ivanova, O. A.; Budynina, E. M.; Skvortsov, D. A.; Limoge, M.; Bakin, A. V.; Chagarovskiy, A. O.; Trushkov, I. V.; Melnikov, M. Ya. A bioinspired route to indanes and cyclopentannulated hetarenes *via* (3+2)-cyclodimerization of donor–acceptor cyclopropanes. *Chem. Commun.* **2013**, *49*, 11482.

(25) For the related isomerization, see: Chagarovskiy, A. O.; Ivanova, O. A.; Rakhmankulov, E. R.; Budynina, E. M.; Trushkov, I. V.; Melnikov, M. Ya. Lewis Acid-Catalyzed Isomerization of 2-Arylcyclopropane-1,1-dicarboxylates: A New Efficient Route to 2-Styrylmalonates. *Adv. Synth. Catal.* **2010**, *352*, 3179.

(26) In control TfOH-catalyzed reaction in the absence of TMSCN cyclopropane **1a** afforded **8a** in 41% yield while the less reactive dimethyl 2-phenylcyclopropane-1,1-dicarboxylate **1r** underwent ring opening with HFIP affording **8b** with only 13% yield.

(27) Tedroff, J.; Torstenson, R.; Hartvig, P.; Sonesson, C.; Waters, N.; Carlsson, A.; Neu, H.; Fasth, K.-J.; Långström, B. Effect of the substituted (*S*)-3-phenylpiperidine (–)-OSU6162 on PET measurements in subhuman primates: evidence for tone-dependent normalization of striatal dopaminergic activity. *Synapse* **1998**, *28*, 280.

(28) (a) Fraser, W.; Suckling, C. J.; Wood, H. C. S. Latent Inhibitors. Part 7. Inhibition of Dihydro-orotate Dehydrogenase by Spirocyclopropanobarbiturates. *J. Chem. Soc. Perkin Trans. 1* **1990**, 3137. (b) Corey, E. J.; Chaykovsky, M.

Dimethyloxosulfonium Methylide ($(CH_3)_2SOCH_2$) and Dimethylsulfonium Methylide ($(CH_3)_2SCH_2$). Formation and Application to Organic Synthesis. *J. Am. Chem. Soc.* **1965**, *87*, 1353.

(29) Crider, A. M.; Hemdi, T. F.; Hassan, M. N.; Fahn, S. Synthesis and Dopaminergic Activity of 3-(3,4-Dihydroxyphenyl)-1-*n*-propylpyrrolidine Hydrobromide. *J. Pharm. Sci.* **1984**, *73*, 1585.

(30) Kiyokawa, K.; Nagata, T.; Hayakawa, J.; Minakata, S. Straightforward Synthesis of 1,2-Dicyanoalkanes from Nitroalkenes and Silyl Cyanide Mediated by Tetrabutylammonium Fluoride. *Chem. Eur. J.* **2015**, *21*, 1280.

(31) Goldberg, A. F. G.; O'Connor, N. R.; Craig, R. A.; Stoltz, B. M. Lewis Acid Mediated (3 + 2) Cycloadditions of Donor–Acceptor Cyclopropanes with Heterocumulenes. *Org. Lett.* **2012**, *14*, 5314.

(32) Sapeta, K.; Kerr, M. A. Synthesis of Cyclohexanes via [3 + 3] Hexannulation of Cyclopropanes and 2-Chloromethyl Allylsilanes. *Org. Lett.* **2009**, *11*, 2081.

(33) Chagarovskiy, A. O.; Ivanova, O. A.; Budynina, E. M.; Trushkov, I. V.; Melnikov, M. Ya. [3+2] Cyclodimerization of 2-Arylcyclopropane-1,1-diesters. Lewis acid induced reversion of cyclopropane umpolung. *Tetrahedron Lett.* **2011**, *52*, 4421.

(34) Ivanova, O. A.; Budynina, E. M.; Chagarovskiy, A. O.; Kaplun, A. E.; Trushkov, I. V.; Melnikov, M. Ya. Lewis Acid-Catalyzed [3+4] Annulation of 2-(Heteroaryl)cyclopropane-1,1-dicarboxylates with Cyclopentadiene. *Adv. Synth. Catal.* **2011**, *353*, 1125.

(35) Signal of CF_3-groups was not observed in ^{13}C NMR spectrum.

(36) Dias, D. A.; Kerr, M. A. Domino Synthesis of Bridged Bicyclic Tetrahydro-1,2-oxazines: Access to Stereodefined 4-Aminocyclohexanols. *Org. Lett.* **2009**, *11*, 3694.