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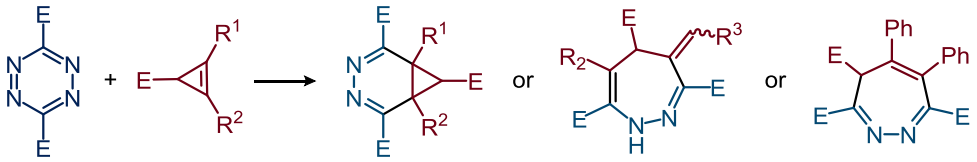

E = CO_2Me; $R_{1,2}$ = H, Alk, Ph, TMS, R_3 = H, Pr

Methyl cyclopropenecarboxylates and dimethoxycarbonyltetrazine undergo cascade cycloaddition and retro-cycloaddition reactions. Depending on substituents in cyclopropenes the reaction either leads to diazanorcaradienes or is accompanied with an electrocyclic ring-opening and a proton migration or a "walk" rearrangement.

Synthesis of Diazanorcaradienes and 1,2-Diazepines *via* the Tandem [4+2]-Cycloaddition/Retro-[4+2]-Cycloaddition Reaction between Methoxycarbonyl-cyclopropenes and Dimethoxycarbonyltetrazine

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Abstract. The reaction of di(methoxycarbonyl)tetrazine with substituted cycloprop-2-ene-1-carboxylates gives a series of 3,4-diazanorcaradienes and 1,2-diazepines. The influence of the nature of cyclopropenes and the reaction conditions on its selectivity was investigated. The addition of nucleophiles to norcaradienes was studied and a rare example of the "walk" rearrangement in this class of compounds was revealed.

Introduction

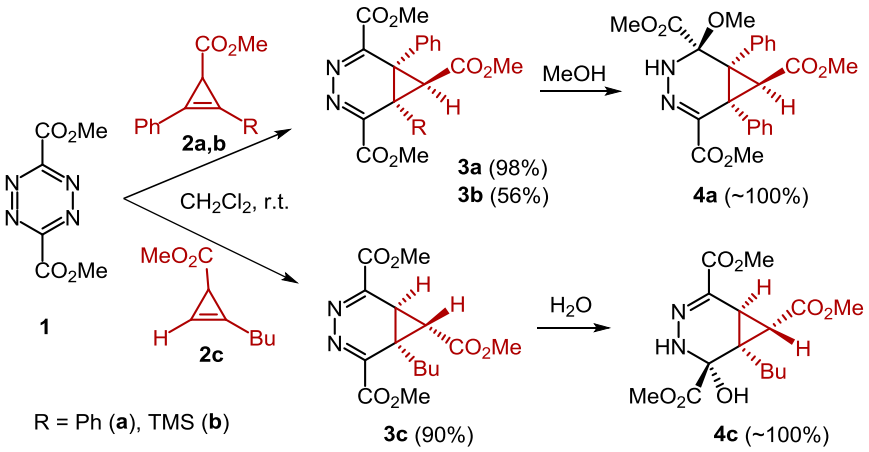
The derivatives of cycloheptatriene sometimes existing in an equilibrium with norcaradiene[1,2] as well as other seven-membered polyene systems are attractive for their high reactivity in pericyclic reactions. Therein diazepines and diazanorcaradienes have been paid essentially less attention having shown a slight difference from the carbocyclic systems. Thus, 3,4-diazepines are significantly less stable than their isomeric 1,2-diazanorcaradienes in most cases[3] and are often regarded as intermediates in the formation and interconversions of the latter.[4] So far the main method for the synthesis of diazanorcaradienes consists in the cycloaddition reaction of cyclopropenes with tetrazines which is accompanied with the retro-[4+2]-cycloaddition to give target products wherein cyclopropenecarboxylates containing alkyl and aryl substituents were used as starting material.[5–7] The diazanorcaradiene derivatives were demanded for the investigation of the rearrangements in these cyclic systems, however the final scope was restricted, no diazepines formed therein. Methods for the synthesis of condensed diazepines which do not transform into norcaradienes due to the presence of an aromatic cycles annulated are known.[8–11] Additionally, a series of diazepines have demonstrated biological activity[12–14] and

the reaction between cyclopropenes and tetrazines is of interest as a bioorthogonal copper – free analog of the "click-reaction".[4]

Results and discussion

Our previous investigations of polyunsaturated cyclic molecules abundant with electron-withdrawing groups revealed their rich reactivity towards either nucleophilic or electrophilic reagents as well as in the pericyclic reactions.[15–22] One of the key synthons therein was 1,2,3,4,5,6,7-hepta(methoxycarbonyl)cycloheptatriene (HMCH),[15,16] as well as its closely related carbocyclic analogs, relatively high acidity of HMCH being one of the key properties determining its high reactivity.[14] Electron-deficient 1,2-diazepines are analogues of HMCH in which the two C–CO_2Me moieties are substituted with nitrogen atoms which similarly stabilize the negative charge. It is noteworthy that HMCH itself was not observed to undergo isomerization into corresponding norcaradiene, although within some of its transformations such as the reaction of hepta(methoxycarbonyl)cycloheptatrienide potassium with tropylium tetrafluoroborate this process takes place even at –30°C.[20]

Apparently, the most convenient method for the synthesis of diazanorcaradienes containing three ester groups in a molecule is the reaction of dimethoxycarbonyltetrazine **1**[23] with substituted methyl cycloprop-2-ene-1-carboxylates **2**, which were in turn obtained via catalytic cyclopropenation of acetylenes with methyl diazoacetate. Thus, the reactions of tetrazine **1** with cycloprop-2-ene-1-carboxylates containing either two phenyl groups (**2a**) or a phenyl and a trimethylsilyl (**2b**) or only one butyl group (**2c**) proceed in mild conditions at room temperature to form stable 3,4-diazanorcaradienes **3a–c** (Scheme 1). The structures of products **3b** and **3c** (indirectly via the adduct **4c**) were established by single crystal X-ray diffraction analysis (XRD, Figure 1). The ester group at the C(7) atom in **3a** is *anti*-configured relative to the phenyl groups and *syn*-configured towards the dihydropyridazine ring (the geometry of **3b** was proved to be similar to that of **3a** on the basis of NOESY data), whereas in **3c** (**4c**) it is otherwise *anti*-configured towards the ring, which is more likely due to their thermodynamic stabilities rather than the kinetic differences within the first cycloaddition stage. Dissolved in methanol both **3a** and **3b** add one molecule of methanol to form adducts **4a,b**. Conversely, diazanorcaradiene **3c** turned out highly hygroscopic and the formation of hydrate **4c** was observed even at the presence of trace water. Thus, it forms in deuterochloroform and on silica gel which makes purification of **3c** hardly possible. The high hygroscopicity of similar compounds was observed previously.[5]



Scheme 1. Formation of substituted 3,4-diazanorcaradien-2,5,7-tricarboxylates **3a–c** and their reactions with methanol or water.

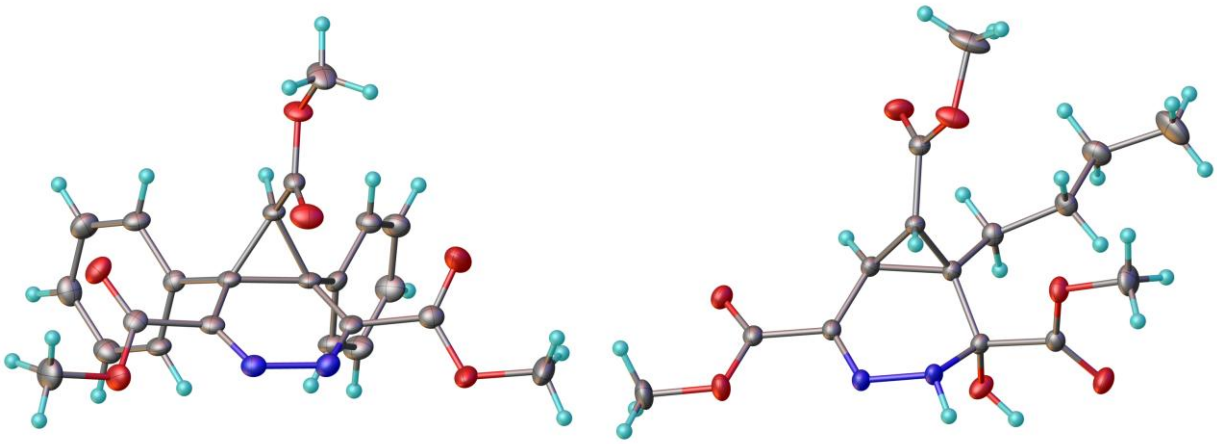
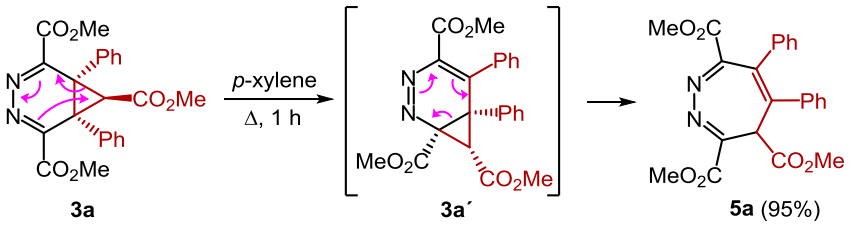


Figure 1. Single crystal X-ray structures of molecules **3a** (left) and **4c** (right). Atoms are represented as thermal ellipsoids (p=50%).

Upon heating in either toluene or xylene the compound **3a** rearranges into 1,2-diazepine **5a**. The latter can be obtained via direct reaction of tetrazine **1** with cyclopropane **2a** upon heating in xylene at reflux for 2h. According to XRD, the structure of **5a** does not correspond to the expected C(1)–C(6) bond cleavage in diazanorcaradiene **3a**. Apparently, the product **5a** is formed via subsequent walk rearrangement[2] of **3a** into **3a´** and electrocyclic ring-expansion into **5a** (Scheme 2, Figure 2), wherein the relative configuration of intermediate **3a´** was suggested according to the previous calculations of [1,5]-shifts within norcaradiene systemes.[2] Unfortunately, upon heating in xylene at reflux, diazanorcaradienes **3b** and **3c** gave unidentifiable mixtures. It is worth mentioning that to the best of our knowledge the transformation of **3a** into **5a** is the first example of a rearrangement of a norcaradiene into a diazepine.[3]



Scheme 2. Isomerization of diazanorcaradiene **3a** into 1,2-diazepine **5a** via the walk rearrangement into **3a´**.

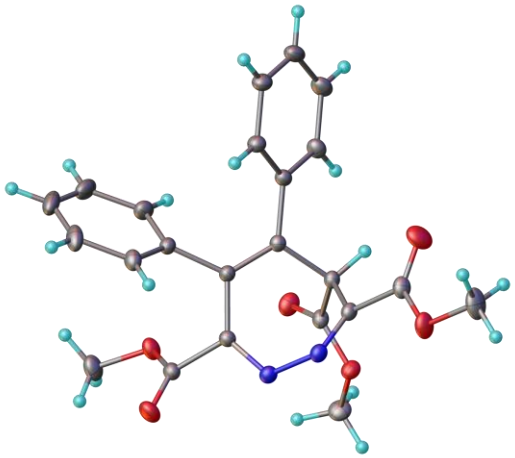
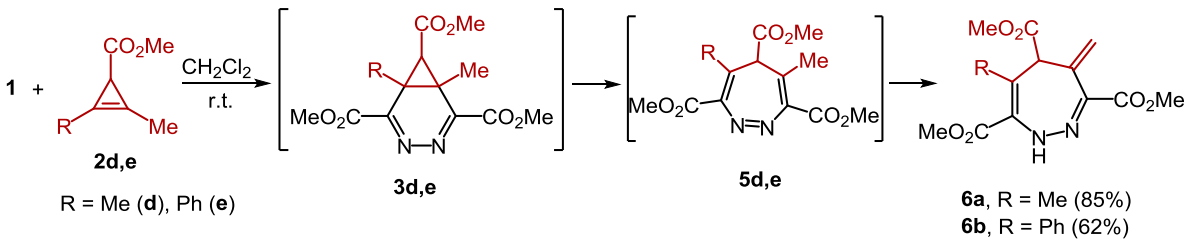


Figure 2. Single crystal X-ray structure of molecule **5a**. Atoms are represented as thermal ellipsoids (p=50%).

Formation of diazanorcaradienes **3d,e** in the reaction of tetrazine **1** with cyclopropenecarboxylates **2d,e** could not be observed even at low temperatures (–30°C). Herein 1,2-diazepines are formed and immediately isomerized into 4-methylene-4,5-dihydro-1*H*-1,2-diazepine-3,5,7-tricarboxylates **6a,b** containing exo-cyclic double bonds (Scheme 3). The structure of **6b** was established by means of XRD (Figure 3). As it was mentioned previously, diazepines in most cases are not stable, however they are regarded as stable intermediates in interconversions of diazanorcaradienes. Herein the driving force of the ring-expansion is likely the formation of exo-double-bonded products **6a,b**.



Scheme 3. Formation of substituted 4-methylene-4,5-dihydro-1*H*-1,2-diazepines **6a,b**.

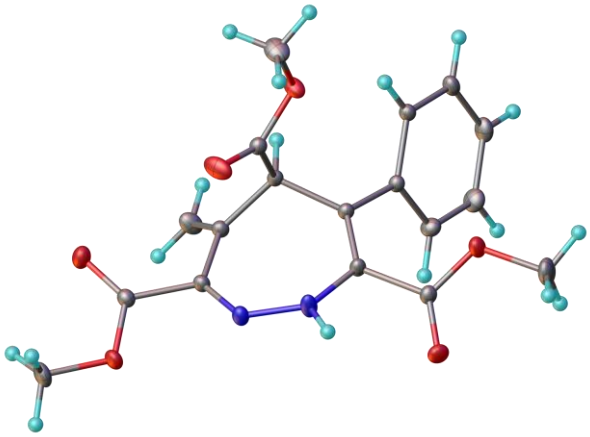
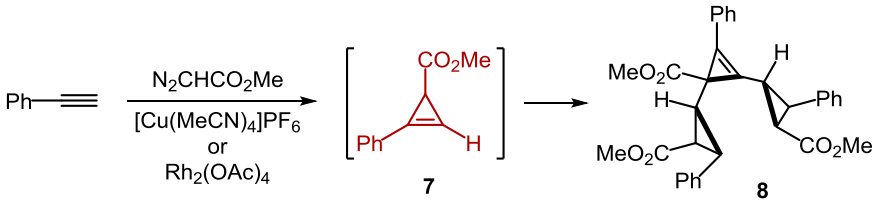


Figure 3. Single crystal X-ray structure of molecule **6b**. Atoms are represented as thermal ellipsoids (p=50%).

Analogously, formation of dihydrodiazepine fragment with an exo-alkylidene double bond is observed in the reaction of tetrazine **1** with cyclopropene **2f** (see SI). However, the reaction leads to a mixture of isomeric products whose separation was accompanied with desilylation and isomerization reaction and was unsuccessful. In this case the reaction requires heating in toluene which is apparently due to the low reactivity at the first stages. It is worth noting, that 2-(*tert*-butyl)-3-(trimethylsilyl)cycloprop-2-ene-1-carboxylate gives no reaction with **1**.

Methyl 2-phenylcycloprop-2-ene-1-carboxylate **7** could not be used in the synthesis of the corresponding diazanorcaradiene via the reaction with tetrazine **1** because it trimerizes into **8** upon formation (Scheme 4, Figure 4), the mechanism presumably including ene reaction.[24,25]



Scheme 4. Formation of trimer **8**. The relative stereochemistry is shown for one of the diastereomers formed which was established by means of XRD.

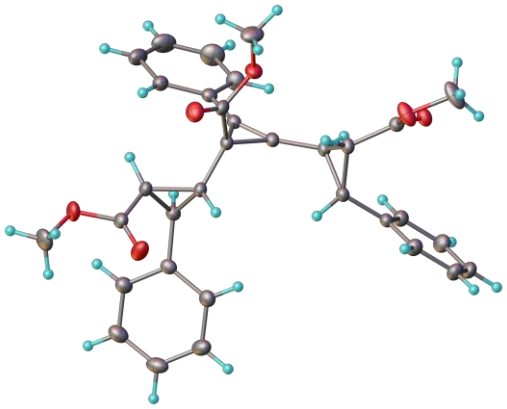
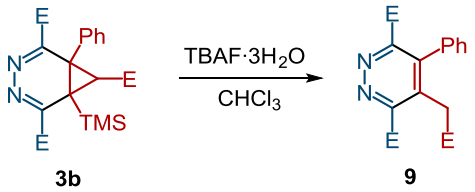


Figure 4. Single crystal X-ray structure of molecule **8**. Atoms are represented as thermal ellipsoids (p=50%).

The introduction of a trimethylsilyl substituent into cyclopropane could be an alternative pathway to diazanorcaradienes with a hydrogen atom at one of the angular positions, however the reaction of **3b** with TBAF initiates the rearrangement into pyridazine **9** (Scheme 5).



3b **9**

Scheme 5. Cleavage of TMS-substituted diazanorcaradiene **3b** into pyridazine **9**.

Conclusion

Thus, the cycloaddition reaction between substituted methyl cycloprop-2-ene-1-carboxylates and di(methoxycarbonyl)tetrazine was found to be an appropriate approach to the synthesis of diazanorcaradienes and 1,2-diazepines. Diazanorcaradienes are formed from diaryl- and aryltrimethylsilyl- and monoalkylated cyclopropenecarboxylates, while the presence of an alkyl group in trisubstituted cyclopropenes brings to formation of diazepines containing an exomethylene double bond.

Experimental Section

General: ^{1}H and ^{13}C NMR spectra were recorded on a 300 and 75.5 MHz NMR spectrometer for solutions in $CDCl_3$ containing 0.05% of Me_4Si as an internal standard. High resolution mass spectra were obtained using a BrukermicrOTOF II instrument (ESI, positive or negative ion modes, capillary voltage 4500 V). All chemical reagents and solvents were purchased from commercial sources and used without additional purification. Dimethoxycarbonyltetrazine **1**,[23] methyl 2-phenyl-3-(trimethylsilyl)cycloprop-2-ene-1-carboxylate **2b**[26], methyl 2,3-dimethylcycloprop-2-ene-1-carboxylate **2d**,[27] 2-(*tert*-butyl)-3-(trimethylsilyl)cycloprop-2-ene-1-carboxylate[28] were synthesized according to the literature procedures.

X-ray diffraction data for **2a**, **2c** and **4a** were collected on a SMART APEX II area-detector diffractometer (graphite monochromator, ω-scan technique), using $Mo_{K\alpha}$-radiation (0.71073 Å). The intensity data were integrated by the SAINT program[29] and were corrected for absorption and decay using SADABS[30]. All structures were solved by direct methods using SHELXS[31], and were refined on F^2 using SHELXL-2014/2017.[32] All non-hydrogen atoms were refined with

anisotropic displacement parameters. All hydrogen atoms were placed in ideal calculated positions and refined as riding atoms with relative isotropic displacement parameters taken as $U_{iso}(H)=1.5U_{eq}(C)$ for methyl groups and $U_{iso}(H)=1.2U_{eq}(C)$ for the rest ones. Crystal data and structure refinement parameters of compounds **3a**, **4c**, **5a**, **6b** and **8** can be retrieved free of charge from www.ccdc.cam.ac.uk/conts/retrieving.html (CCDC 1886318–1886322).

Trimethyl 1,6-diphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene-2,5,7-tricarboxylate (3a): A mixture of dimethoxycarbonyltetrazine **1** (0.20 g, 1.0 mmol), methyl 2,3-diphenylcycloprop-2-ene-1-carboxylate **2a** (0.28 g, 1.1 mmol) and CH_2Cl_2 (6 mL) stirred for 30 h, the solvent was removed in vacuo. The residue was recrystallized from methyl-*tert*-butyl ether (MTBE) to give the desired product (0.39 g, 91%). M.p. 129–132 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.17–6.96 (m, 10 H), 4.14 (s, 1 H), 3.74 (s, 3 H), 3.64 (s, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.9, 163.6, 153.7, 133.7, 129.5, 128.7, 128.6, 52.9, 52.8, 42.6, 21.3 ppm. HRMS (ESI^+): *m/z* calcd. for $C_{23}H_{21}N_2O_6^+$ $[M+H]^+$ 421.1394; found 421.1390.

Trimethyl 1-phenyl-6-(trimethylsilyl)-3,4-diazabicyclo[4.1.0]hepta-2,4-diene-2,5,7-tricarboxylate (3b): A mixture of dimethoxycarbonyltetrazine **1** (0.20 g, 1.0 mmol), methyl 2-phenyl-3-(trimethylsilyl)cycloprop-2-ene-1-carboxylate **2b** (0.27 g, 1.1 mmol) and CH_2Cl_2 (6 mL) stirred for 7 days, the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/$CHCl_3$, 1:4), recrystallization from MTBE gave the desired product (0.24 g, 56%). M.p. 122–124 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.22 (m, 5H), 3.93 (s, 3H), 3.71 (s, 3H), 3.56 (s, 3H), 3.24 (s, 1H), –0.21 (s, 9H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.8, 165.6, 163.8, 156.5, 153.2, 136.9, 130.8, 129.4, 128.8, 53.0, 52.6, 52.5, 39.7, 29.3, 19.3, –0.9 ppm. HRMS (ESI^+): *m/z* calcd. for $C_{20}H_{25}N_2O_6Si^+$ $[M+H]^+$ 417.1476; found 417.1467.

Trimethyl 1-butyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene-2,5,7-tricarboxylate (3c): A mixture of dimethoxycarbonyltetrazine **1** (0.20 g, 1.0 mmol), methyl 2-butylcycloprop-2-ene-1-carboxylate **2c** (0.17 g, 1.1 mmol) and THF (6 mL) stirred for 20 h under argon, the solvent was removed in vacuo. The residue was recrystallized from MTBE to give the desired product (0.37 g, 86%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.00 (s, 3 H), 3.97 (s, 3 H), 3.81 (s, 3 H), 3.37 (d, *J* = 5.1 Hz, 1 H), 2.38–2.17 (m, 1 H), 1.62–1.47 (m, 1 H), 1.29 (d, *J* = 5.1 Hz, 1 H), 1.26–1.11 (m, 4 H), 0.94–0.76 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.2, 163.7, 163.7, 158.8, 154.3, 53.6, 53.3, 53.1, 34.6, 30.5, 29.7, 26.8, 24.7, 22.2, 13.7 ppm. HRMS (ESI^+): *m/z* calcd. for $C_{15}H_{23}N_2O_6^+$ $[M+H]^+$ 325.1394; found 325.1395.

Trimethyl 5-methoxy-1,6-diphenyl-3,4-diazabicyclo[4.1.0]hept-2-ene-2,5,7-tricarboxylate (4a): Trimethyl 1,6-diphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene-2,5,7-tricarboxylate **3a** (0.2 g, 0.48 mmol) was dissolved in MeOH (5.5 mL), stirred for 24 h, the solvent was removed in vacuo to give the desired product (0.2 g, 94%). M.p. 136–138 °C. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ = 8.43 (br.s, 1 H), 7.39–7.21 (m, 4 H), 7.07–6.88 (m, 6 H), 3.69 (s, 1 H), 3.67 (s, 3 H), 3.55 (s, 3 H), 3.42 (s, 3 H), 3.25 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ = 166.7, 166.4, 164.3, 142.6, 137.2, 136.3, 133.1, 127.6, 126.7, 126.5, 126.2, 82.4, 51.4, 51.1, 50.8, 50.3, 36.6, 32.7 ppm. HRMS (ESI^+): *m/z* calcd. for $C_{24}H_{21}N_2O_7^+$ $[M+H]^+$ 453.1656; found 453.1649.

Trimethyl 1-butyl-5-hydroxy-3,4-diazabicyclo[4.1.0]hept-2-ene-2,5,7-tricarboxylate (4c): A mixture of dimethoxycarbonyltetrazine **1** (0.20 g, 1.0 mmol), methyl 2-butylcycloprop-2-ene-1-carboxylate **2c** (0.17 g, 1.1 mmol) and CH_3CN (6 mL) stirred for 5 h, the solvent was removed in vacuo. The residue was recrystallized from MTBE to give the desired product (0.34 g, 97%). M.p. 148–151 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.62 (c, 1 H), 4.26 (s, 1 H), 3.90 (s, 3 H), 3.86 (s, 3 H), 3.72 (s, 3 H), 2.98 (d, *J* = 5.0 Hz, 1 H), 2.87 (d, *J* = 5.0 Hz, 1 H), 2.21–2.01 (m, 1 H), 1.63–1.47 (m, 1 H), 1.29–0.97 (m, 4 H), 0.83 (т, *J* = 7.0 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.2, 170.4, 163.3, 140.3, 80.0, 53.9, 52.6, 52.2, 40.8, 28.6, 27.5, 25.5, 23.5, 22.8, 13.7 ppm. HRMS (ESI^+): *m/z* calcd. for $C_{15}H_{23}N_2O_7^+$ $[M+H]^+$ 343.1500; found 343.1499.

Trimethyl 5,6-diphenyl-4H-1,2-diazepine-3,4,7-tricarboxylate (5a): ***(a)*** A mixture of dimethoxycarbonyltetrazine **1** (0.20 g, 1.0 mmol), methyl 2,3-diphenylcycloprop-2-ene-1-carboxylate **2a** (0.28 g, 1.1 mmol) and *p*-xylene (6 mL) was heated at reflux 1 h, the solvent was removed in vacuo. The residue was recrystallized from MTBE to give the desired product (0.36 g, 84%); ***(b)*** Trimethyl 1,6-diphenyl-3,4-diazabicyclo[4.1.0]hepta-2,4-diene-2,5,7-tricarboxylate **3a** (0.2 g, 0.48 mmol) and *p*-xylene (4.0 mL) was heated at reflux for 1 h, the solvent was removed in vacuo. The residue was recrystallized from MTBE to give the desired product (0.19 g, 95%). M.p. 123–125 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.22 (m, 5 H), 3.93 (s, 3 H), 3.71 (s, 3 H), 3.56 (s, 3 H), 3.24 (s, 1 H), –0.21 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.8, 165.6, 163.8, 156.5, 153.2, 136.9, 130.8, 129.4, 128.8, 53.0, 52.6, 52.5, 39.7, 29.3, 19.3, –0.9 ppm. HRMS (ESI^+): *m/z* calcd. for $C_{23}H_{21}N_2O_6^+$ $[M+H]^+$ 421.1394; found 421.1390.

Trimethyl 6-methyl-4-methylene-4,5-dihydro-1*H*-1,2-diazepine-3,5,7-tricarboxylate (6a): A mixture of dimethoxycarbonyltetrazine **1** (0.20 g, 1.0 mmol), methyl 2,3-dimethylcycloprop-2-ene-1-carboxylate **2d** (0.13 g, 1.1 mmol) and *p*-xylene (6 mL) was heated at reflux for 1 h, the solvent was removed in vacuo. The residue was recrystallized from MTBE to give the desired product (0.25 g, 85%) as yellow crystals. M.p. 114-115 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ =

8.64 (br. s, 1 H), 5.59 (s, 1 H), 5.18 (s, 1 H), 3.93 (s, 1 H), 3.87 (s, 3 H), 3.86 (s, 3 H), 3.68 (s, 3 H), 2.34 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.0, 164.9, 163.8, 135.9, 134.6, 131.5, 127.8, 116.1, 61.6, 52.6, 52.6, 52.6, 21.5 ppm. HRMS (ESI^+): *m/z* calcd. for $C_{13}H_{17}N_2O_6^+$ $[M+H]^+$ 297.1081; found 297.1079.

Trimethyl 4-methylene-6-phenyl-4,5-dihydro-1*H*-1,2-diazepine-3,5,7-tricarboxylate (6b): A mixture of dimethoxycarbonyltetrazine **1** (0.20 g, 1.0 mmol), methyl 2-methyl-3-phenylcycloprop-2-ene-1-carboxylate **2e** (0.21 g, 1.1 mmol) and CH_2Cl_2 (5 mL) stirred for 4 days, the solvent was removed in vacuo. The residue was purified by column chromatography on on silica gel (EtOAc/$CHCl_3$, 1:4), recrystallization from MTBE to give the desired product (0.24 g, 65%) as yellow crystals. M.p. 143-145 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.80 (br.s, 1 H), 7.43–7.31 (m, 3 H), 7.26–7.20 (m, 2 H), 5.57 (s, 1 H), 4.99 (s, 1 H), 4.40 (s, 1 H), 3.89 (s, 3 H), 3.76 (s, 3 H), 3.50 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.2, 164.9, 164.3, 140.5, 137.5, 133.0, 131.5, 128.3, 128.2, 128.0, 127.9, 117.5,69.8, 61.7, 52.9, 52.7, 52.5 ppm. HRMS (ESI^+): *m/z* calcd. for $C_{18}H_{19}N_2O_6^+$ $[M+H]^+$ 359.1238; found 359.1232.

Dimethyl 4-(2-methoxy-2-oxoethyl)-5-phenylpyridazine-3,6-dicarboxylate (7): A mixture of trimethyl 1-phenyl-6-(trimethylsilyl)-3,4-diazabicyclo[4.1.0]hepta-2,4-diene-2,5,7-tricarboxylate **3b** (0.15 g, 0.36 mmol) $Bu_4NF{\times}3H_2O$ (0.114 g, 0.36 mmol) and $CHCl_3$ (5 mL) stirred for 2 days, washed with water (3×5mL), the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/CH_2Cl_2, 1:1) to give the desired product (0.12 g, 45%) as light yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.53–7.42 (m, 3 H), 7.25–7.17 (m, 2 H), 4.06 (s, 3 H), 3.87 (s, 2 H), 3.72 (s, 3 H), 3.67 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.4, 165.1, 164.8, 154.4, 152.3, 140.8, 134.2, 132.2, 129.5, 128.8, 128.3, 53.4, 53.0, 52.5, 34.7 ppm. HRMS (ESI^+): *m/z* calcd. for $C_{17}H_{17}N_2O_6^+$ $[M+H]^+$ 345.1081; found 345.1079.

Trimer of methyl 2-phenylcycloprop-2-ene-1-carboxylate (8): To a mixture of phenylacetylene (5.0 g, 49 mmol), $Cu[CH_3CN]_4PF_6$ (0.22 g, 0.59 mmol) and CH_2Cl_2 (10 mL) was added a solution of methyl diazoacetate (6.0 g, 60 mmol) in CH_2Cl_2 (10 mL) via a syringe pump in 8 h. After addition the reaction mixture was stirred for 30 min, the reaction mixture filtered through silica gel, the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/Petroleum ether, 1:4) to give the desired product (6.4 g, 75%) as colorless crystals. M.p. 146–147 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.51–7.38 (m, 6 H), 7.36–7.15 (m, 9 H), 3.73 (s, 3 H), 3.53 (s, 3 H), 3.46 (s, 3 H), 3.21 (dd, *J* = 6.4, 5.0 Hz, 1 H), 3.00 (m, 2 H), 2.60 (dd, *J* = 9.7, 5.0 Hz, 1 H), 2.31 (dd, *J* = 9.3, 7.5 Hz, 1 H), 2.03 (dd, *J* = 9.3, 5.2 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.8, 170.3, 169.2, 136.0, 134.4, 129.4, 129.2, 129.1, 128.9, 128.9, 128.3, 128.0, 127.4, 126.7, 126.0, 111.6, 108.0, 52.2, 51.9, 51.4,

33.3, 32.6, 31.1, 30.2, 28.5, 20.1 ppm. HRMS (ESI^+): *m/z* calcd. for $C_{33}H_{34}NO_6^+$ $[M+NH_4]^+$ 540.2381; found 540.2380.

Methyl 2,3-diphenylcycloprop-2-enecarboxylate (2a): To a mixture of 1,2-diphenylacetylene (3.0 g, 16.85 mmol), $Cu[CH_3CN]_4PF_6$ (63 mg, 5.9 mmol) and CH_2Cl_2 (10 mL) was added a solution of methyl diazoacetate (2.53 g, 25.3 mmol) in CH_2Cl_2 (10 mL) via a syringe pump in 8 h. After addition the reaction mixture was stirred for 30 min, the reaction mixture filtered through silica gel, the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/Petroleum ether, 1:9) to give the desired product (1.6 g, 39%) as colorless crystals. M.p. 83–84 °C. ^1H NMR (300 MHz, $CDCl_3$): δ =7.72 (d, *J* = 7.4 Hz, 4 H), 7.60–7.33 (m, *J* = 6 H), 3.73 (s, 3 H), 2.87 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.3, 130.0, 129.3, 128.9, 127.1, 107.6, 51.7, 21.5 ppm. HRMS (ESI^+): *m/z* calcd. for $C_{17}H_{14}O_2Na^+$ $[M+Na]^+$ 273.086; found 273.0884.

Methyl 2-methyl-3-phenylcycloprop-2-ene-1-carboxylate (2d): To a mixture of 1-methyl-2-phenylacetylene (1.5 g, 12.9 mmol), $Cu[CH_3CN]_4PF_6$ (70 mg, 0.18 mmol) and CH_2Cl_2 (5 mL) was added a solution of methyl diazoacetate (1.93 g, 19 mmol) in CH_2Cl_2 (10 mL) via a syringe pump in 10 h. After addition the reaction mixture was stirred for 30 min, the reaction mixture filtered through silica gel, the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc/Petroleum ether, 1:4) to give the desired product (1.72 g, 71%) as colorless oil; ^1H NMR (300 MHz, $CDCl_3$): δ= 7.60–7.23 (m, 1 H), 3.71 (d, *J* = 7.9 Hz, 1 H), 2.46 (d, *J* = 5.9 Hz, 1 H), 2.38–2.29 (m, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.2, 129.23, 128.6, 127.8, 106.3, 105.3, 51.5, 22.4, 10.7 ppm. HRMS (ESI^+): *m/z* calcd. for $C_{12}H_{12}O_2Na^+$ $[M+Na]^+$ 211.0736; found 211.0730.

Methyl 2-butylcycloprop-2-ene-1-carboxylate (2c): To a mixture of 1-hexyne (3.28 g, 40 mmol), $Rh_2(OAc)_4$ (44 mg, 0.01 mmol) and CH_2Cl_2 (10 mL) was added a solution of methyl diazoacetate (2,0 g, 20 mmol) in CH_2Cl_2 (8 mL) via a syringe pump in 10 h. After addition the reaction mixture was stirred for 30 min, the reaction mixture filtered through silica gel, the solvent was removed in vacuo. The residue was purified by column chromatography on silica gel (EtOAc–Petroleum ether, 1:4) to give the desired product (2.3 g, 75%) as colorless oil. ^1H NMR (300 MHz, $CDCl_3$): δ = 6.34 (d, J = 1.3 Hz, 1 H), 3.70 (s, 3 H), 2.51 (t, *J* = 7.0 Hz, 2 H), 2.15 (d, *J* = 1.3 Hz, 1 H), 1.57 (m, 2 H), 1.40 (m, 2 H), 0.93 (t, *J* = 7.3 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.0, 115.6, 93.89, 51.4, 28.7, 24.6, 22.2, 19.5, 13.7 ppm. HRMS (ESI^+): *m/z* calcd. for $C_9H_{15}O_2^+$ $[M+H]^+$ 155.1067; found 155.1064.

Methyl 2-butyl-3-(trimethylsilyl)cycloprop-2-enecarboxylate (2f): (a) Preparation of LiHMDS solution: To a solution of bis(trimethylsilyl)amine (4.38g, 27 mmol) in THF (10 mL)

was added a solution of *n*-butyllithium in hexane (11.8 mL, 27 mmol) dropwise under argon, maintaining the temperature at –30ºC.

(b) To a mixture of methyl 2-butylcycloprop-2-ene-1-carboxylate (3.22 g, 21 mmol), TMSCl (3.4 g, 31 mmol) and THF (50 mL) was added the solution of LiHMDS in 5 min, maintaining the temperature –80ºC. Then 10 mL of a saturated NH_4Cl solution was added at –80°C, organic phase were separated and dried over Na_2SO_4. The solvent was removed in vacuo and the residue was purified by flash column chromatography on silica gel (EtOAc/Petroleum ether, 1:25) to give the desired product (4.05 g, 85%) as colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.63 (s, 3 H), 2.59–2.43 (m, 1 H), 2.00 (s, 1 H), 1.67–1.49 (m, 2 H), 1.39 (m, 2 H), 0.92 (t, *J* = 7.3 Hz, 3 H), 0.19 (s, 9 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.5, 126.6, 103.2, 51.1, 29.1, 26.1, 22.2, 20.6, 13.7, –1.6 ppm. HRMS (ESI^+): *m/z* calcd. for $C_{12}H_{23}O_2Si^+$ $[M+H]^+$ 227.1462; found 227.1465.

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Keywords

Cycloadditions, Rearrangements, Nitrogen heterocycles, Pericyclic reaction, Ring contraction

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