Reduction of 1-Nitrospiro[2.2]pentanecarboxylates: Convenient Synthesis of Novel Polyspirocyclic Cyclopropane Amino Acids

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Abstract: A facile method for the preparation of a series of racemic spiropentane amino acids is described. An approach involving sequential catalytic cyclopropanation of polycyclic methylenecyclopropanes with nitrodiazoesters and reduction of the nitro group is described.

Key words: [1+2] cycloaddition, reductions, spiropentane α-amino acids, carbenes/diazo compounds

Most of the known amino acids containing a cyclopropyl group are an integral part of many biologically active compounds.[1] These compounds are of growing biological interest, particularly as source for plant hormone ethylene or, on the contrary, inhibitors of ethylene-forming enzyme (1-aminocyclopropanecarboxylic acid or its derivatives).[1] Cyclopropane amino acids have received extensive attention over the two last decades as conformationally restricted analogues of natural amino acids.[2]

The more strained polyspirocyclopropane amino acids are even more reactive and might show important physiological properties in their own right. Few precedents of bioactive substances incorporating the spiropentane moiety are known.[3] Recently, the synthesis of amino acids containing the spiropentyl group such as (+)-spiropentylglycine and (+)-1-aminospiropentane carboxylic acid has been reported.[4] For instance, racemic 1-aminospiro[2.2]pentane carboxylic acid was prepared by the rhodium-catalyzed cycloaddition of dimethyl diazomalonate to methylenecyclopropane followed by Curtius rearrangement with the resulting carboxylic acid.[4]

The present work is a continuation of our program to prepare the representative series of polyspirocyclopropane amino acids. We have recently reported the synthetic protocol affording spirohexane amino acids using ammonium formate in the presence of palladium on charcoal as a 'H_2' source for the reduction of spirohexane nitrocarboxylates.[5] We now wish to report our results on the synthesis of novel polycyclic amino acids containing a spiro[2.2]pentane framework by the rhodium-catalyzed [1+2] cycloaddition of ethyl nitrodiazoacetate (ENDA) to a series of methylenecyclopropanes followed by reduction of nitrocarbethoxy adducts and subsequent hydrolysis. In fact, the development of an efficient and expedient method for synthesis of spiropentane amino acids via the reduction of a nitro group is of particular interest due to the presence of a rather sensitive spiropentane moiety in substrates to be reduced. There are only two examples of the reduction of nitro cyclopropanecarboxylates.[6,7] The first example was reported by Seebach and Häner[6] using Pd/C–H_2 (1 atm) system for reduction of 1-nitrocarbethoxycyclopropane, while the second example was recently reported by Wurz and Charette[7] about reducing a diverse series of aryl nitrocyclopropyl carboxylates using Zn/HCl in *i*-PrOH.

It is also noteworthy to mention the absence of reports in the literature for the reduction of nitrocarbalkoxyspiropentanes.

Our approach to the synthesis of α-amino spiro[2.2]pentane carboxylic acids includes as initial stage the preparation of base precursors, 1-nitro-ethoxycarbonylspiropentanes (**2a–e**, Table 1) from methylenecyclopropanes **1a–e** and nitrodiazoacetate by known dirhodium(II) tetraacetate-catalyzed cyclopropanation.[5,8,9]

The reaction of methylenecyclopropanes **1a–d** with ENDA in the presence of catalytic amounts of dirhodium tetraacetate afforded ethyl nitrospiro[2.2]pentane carboxylates **2a–d** in good yields (Table 1). Only cyclic methylenecyclopropane **1e** gave a different result (Scheme 1). The expected adduct **2e** was obtained as by-product and the main product was ester of hydroxamic acid **2f** which was formed as a result of the rearrangement of nitrocarbene into acylnitrosoacetate followed by addition to olefin **1e** that was analogous to previously reported data.[8b]

The crucial stage in the synthesis of polyspirocyclic amino acids is the reduction of nitro esters **2a–e** into amino esters **3a–e**. The choice of an effective reducing agent is important because spiropentane fragment is a strained moiety and undergoes ring opening under the action of various reagents.

Previously we have found that the most suitable system for the reduction of 1-nitrospiro[2.3]hexanecarboxylates is ammonium formate in the presence of catalytic amounts of palladium on charcoal.[5] However only nitroesters **2d** and **2e** containing cyclooctane ring were reduced with this system in good yields to give the corresponding amino esters **3d**,**e**. Nitroesters **2a** and **2b** under these conditions gave complex reaction mixtures of products of small rings opening. The results of the reduction of nitroesters **2a** and

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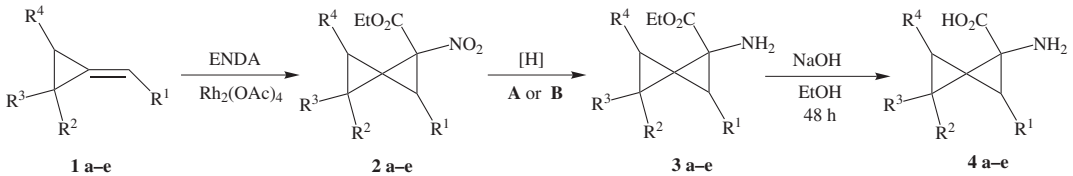
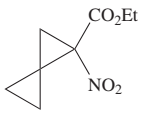
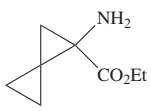
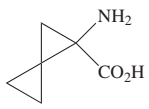
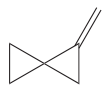
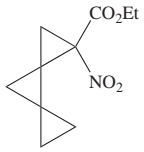
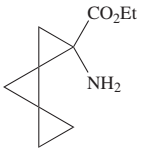
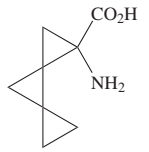
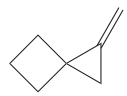
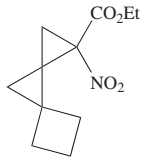
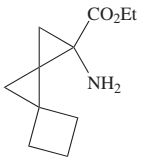
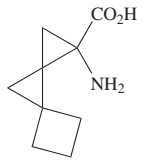
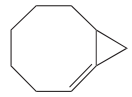
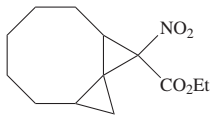
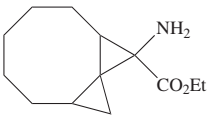
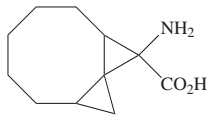
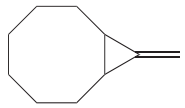
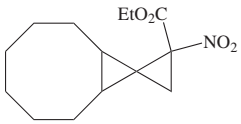
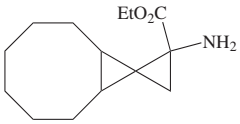
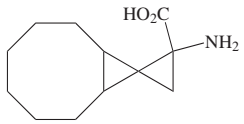
Table 1 Syntheses of Spiropentane Amino Acids[a]



1 a–e **2 a–e** **3 a–e** **4 a–e**

Entry	Methylene-cyclopropane **1**	Nitroester **2**	Yield (%)[b]	Amino ester **3**	Method	Yield (%)	Amino acid (**4**)	Yield (%)
a			85[9]		B	89		87
b			85[9] dr = 3:1		B	91 dr = 4:1		90 dr 3:1
c			85 dr = 3:1		B	76 dr = 8:1		85[c]
d			24 dr = 4:1		A	68 dr = 5:1		70[c]
e			70[c]		A	89[c]		87[c]

[a] *Reagents and conditions*: A: HCO_2NH_4, Pd/C (10%), MeOH. B: Zn–AcOH–*i*-PrOH.
[b] Yields refer to the isolated pure products after column chromatography.
[c] A single diastereomer was obtained.

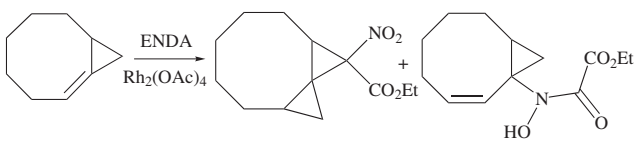
2c under different conditions are presented in the Schemes 2 and 3.

Dispirononane **2c** gives hydroxylamine **5** under the action of the reducing agent. Hydroxylamine **5** was isolated in a good yield. The increase of the reaction time provides ring opening. The introduction of the compounds **5** in the reaction mixture also gave the product of the ring opening.

Use of other catalytic systems containing Pd was not successful. Thus, the catalytic hydrogenation of nitrospiropentane **2a** in the presence of Pd/C resulted in a formation of oxime **6** accompanied by the hydrogenolysis of the C–C bond of small ring (Scheme 3).

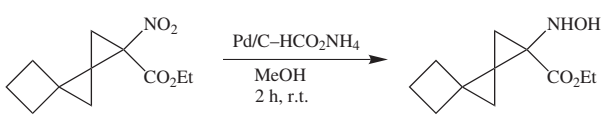
Spiropentylcarbinol **7** was the only product of the reduction of nitro ester **2a** via $NaBH_4$–Pd/C system. Clearly, the reduction of nitrocarbethoxyspiropentanes **2a–d** was problematic using catalytic systems on the base of palladium.

We turned our attention to zinc–HCl system due to its success in the reduction of phenyl substituted 1-nitrocyclopropanecarboxylates.[6] Under these conditions opening of the substituted small ring of nitroester **2a** is found to take place forming 1,1-disubstituted cyclopropane **8** (Scheme 3).



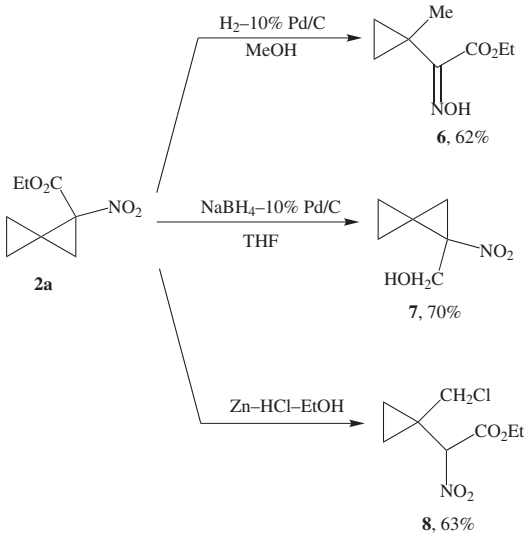
1e **2e**, 24% (dr 4:1) **2f**, 49 % (dr 1:1)

Scheme 1



2c **5**, 74% (dr 5:1)

Scheme 2



Scheme 3

We succeeded in the reduction of nitrospiropentane esters **2a–c** using system Zn–AcOH–*i*-PrOH and obtained amino esters **3a–c** in high yields (Table 1).

Finally, the amino esters **3a–e** were converted into amino acids **4a–e** by saponification of ester group according to the previously reported methods.[5,8,9] The polyspiro amino acids synthesized are shown in Table 1.

In summary, we have outlined the synthesis of unnatural racemic spiropentane α-amino acids, containing ACC-fragment via the [1+2]-cycloaddition of nitrodiazoacetic ester to methylenecyclopropanes followed by the reduction of 1-nitrocarbethoxyspiropentanes. This facile and convenient method may be extended to a variety of polyspirocyclopropane amino acids. Development of the stereoselective version of this method is underway now.

NMR spectra were recorded on Bruker DPX-400 spectrometer at r.t.; the chemical shifts (δ) were measured in ppm with respect to solvent (^{1}H: $CDCl_3$, δ = 7.24; ^{13}C: $CDCl_3$, δ = 77.13). Mass spectra were taken on Finnigan MAT 95 XL instrument at 70 eV using electron impact ionization (EI) and GC–MS coupling. Analytical TLC was carried out with Silufol silica gel plates (supported on aluminum); the detection was done by UV lamp (254 and 365 nm) and chemical staining (I_2 vapor). Melting points were determined on a Electrothermal 9100 capillary apparatus and are uncorrected. Column chromatography was performed using silica gel 60 (230–400 mesh, Merck). Petroleum ether (PE) used refers to the 40–60 °C bp fraction. All reagents except commercial products of satisfactory quality were purified with literature procedures prior to use. Microanalyses were performed on a Karlo Erba 1106 instrument. Compounds obtained as mixtures of diastereomers were not separated into the single isomers. 1-Methylenespiro[2.2]pentane (**1b**),[10] 1-methylenespiro[2.3]hexane (**1c**),[10] bicyclo[6.1.0]non-1-ene (**1d**),[11] 9-methylenebicyclo[6.1.0]nonane (**1e**),[12] 1-nitrospiro[2.2]pentane-1-carboxylic acid ethyl ester (**2a**),[9] 1-nitrodispiro[2.0.2.1]heptane-1-carboxylic acid ethyl ester (**2b**)[9] and ethyl nitrodiazoacetate[13] were synthesized by known procedures. Methylenecyclopropane (**1a**) is commercially available.

Preparation of Compounds 2a–e; General Procedure

Ethyl nitrodiazoacetate (1 mmol) was slowly added to a stirred mixture of alkene **1** (5 mmol) and $Rh_2(OAc)_4$ (0.03 mmol) at 0–5 °C. Then the reaction mixture was warmed to r.t. and stirred at r.t. for 1 h. An excess of alkene was removed under reduced pressure, the catalyst was filtered through silica gel and the product (a colorless oil) was purified by flash column chromatography (Et_2O–PE as the eluent, 0–30%).

1-Nitrodispiro[2.0.3.1]octane-1-carboxylic Acid Ethyl Ester (2c)

Yield: 0.191 g (85%); mixture of stereoisomers (3:1); colorless oil; R_f 0.60 (PE–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ (major isomer) = 1.08 (d, $^2J_{H^aH^b}$ = 5.7 Hz, 1 H, C*H*^{a}H^b), 1.22 (d, $^2J_{H^bH^a}$ = 5.7 Hz, 1 H, CH^a*H*^{b}), 1.29 (t, ^3J = 7.1 Hz, 3 H, CH_3,), 1.87–2.30 (m, 6 H, cy-Bu), 1.94 (d, $^2J_{H^aH^b}$ = 5.4 Hz, 1 H, C*H*^{a}H^b), 2.40 (d, $^2J_{H^bH^a}$ = 5.4 Hz, 1 H, CH^a*H*^{b}), 4.28 (m, ^3J = 7.1 Hz, 2 H, CH_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ (minor isomer) = 1.13 (d, $^2J_{H^aH^b}$ = 5.9 Hz, 1 H, C*H*^{a}H^b), 1.16 (d, $^2J_{H^bH^a}$ = 5.9 Hz, 1 H, CH^a*H*^{b}), 1.32 (t, ^3J = 7.1 Hz, 3 H, CH_3), 1.87 (d, $^2J_{H^aH^b}$ = 5.3 Hz, 1 H, C*H*^{a}H^b), 1.87–2.30 (m, 6 H, cy-Bu), 2.16 (d, $^2J_{H^bH^a}$ = 5.4 Hz, 1 H, CH^a*H*^{b}), 4.27 (m, ^3J = 7.1 Hz, 2 H, CH_2O).

^{13}C NMR (100 MHz, $CDCl_3$): δ (major isomer) = 13.69 ($^1J_{CH}$= 127 Hz, CH_3), 16.78 ($^1J_{CH}$ = 138 Hz, CH_2, cy-Bu), 18.09 ($^1J_{CH}$ = 163 Hz, CH_2, cy-Pr), 21.58 ($^1J_{CH}$ = 168 Hz, CH_2, cy-Pr), 25.19 ($^1J_{CH}$ = 138 Hz, CH_2, cy-Bu), 27.97 (C_{spiro}, cy-Pr, cy-Pr), 28.28 ($^1J_{CH}$ = 135 Hz, CH_2, cy-Bu), 32.57 (C_{spiro}, cy-Bu, cy-Pr), 62.13 ($^1J_{CH}$ = 149 Hz, OCH_2), 70.28 (C), 164.03 (*C*O_2Et).

^{13}C NMR (100 MHz, $CDCl_3$): δ (minor isomer) = 13.68 (CH_3), 16.51 (CH_2, cy-Bu), 17.62 (CH_2, cy-Pr), 21.57 (CH_2, cy-Pr), 27.11 (CH_2, cy-Bu), 27.63 (CH_2, cy-Bu), 28.29 (C_{spiro}, cy-Pr, cy-Pr), 33.63 (C_{spiro}, cy-Bu, cy-Pr), 62.29 (OCH_2), 70.38 (C), 164.85 (*C*O_2Et).

Anal. Calcd for $C_{11}H_{15}NO_4$: C, 58.66; H, 6.71. Found: C, 58.91; H, 6.62.

2-Nitrotricyclo[7.1.0.0^{1,3}]decane-2-carboxylic Acid Ethyl Ester (2d)

Yield: 0.061 g (24%); mixture of stereoisomers (4:1); colorless oil; R_f 0.70 (PE–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ (major isomer) = 0.90 (dd, $^2J_{H^aH^b}$ = 5.5 Hz, $^3J_{H^aH^c}$ = 5.8 Hz, 1 H, CH^{c}C*H*^{a}H^{b}C$_{spiro}$), 1.02 (dd, $^2J_{H^bH^a}$ = 5.5 Hz, $^3J_{H^bH^c}$ = 9.1 Hz, 1 H, CH^{c}CH^a*H*^{b}C$_{spiro}$), 1.31 (t, ^3J = 7.1 Hz, 3 H, CH_3), 2.30–1.35 (m, 11 H, cy-Oct), 2.89 (dd, $^3J_{HH^b}$ = 5.3 Hz, $^3J_{HH^a}$ = 7.6 Hz, 1 H, CC*H*CH^{a}H^b), 4.12–4.28 (m, 2 H, OCH_2).

^{1}H NMR (400 MHz, $CDCl_3$): δ (minor isomer) = 0.81 (dd, $^2J_{H^aH^b}$ = 5.5 Hz, $^3J_{H^aH^c}$ = 5.6 Hz, 1 H, CH^{c}C*H*^{a}H^{b}C$_{spiro}$), 1.04 (dd, $^2J_{H^bH^a}$ = 5.5 Hz, $^3J_{H^bH^c}$ = 9.5 Hz, 1 H, CH^{c}CH^a*H*^{b}C$_{spiro}$), 1.27 (t, ^3J = 7.1 Hz, 3 H, CH_3), 1.35–2.30 (m, 11 H, cy-Oct), 2.48 (dd, $^3J_{HH^a}$ = 6.3 Hz, $^3J_{HH^b}$ = 6.4 Hz, 1 H, C-C*H*CH^{a}H^b), 4.12–4.28 (m, 2 H, OCH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ (major isomer) = 10.40 ($^1J_{CH}$ = 165 Hz, CH_2, cy-Pr), 14.02 ($^1J_{CH}$ = 127 Hz, CH_3), 18.54 ($^1J_{CH}$ = 160 Hz, CH, cy-Pr), 20.25 ($^1J_{CH}$ = 130 Hz, CH_2, cy-Oct), 24.14 (CH_2, cy-Oct), 25.42 (CH_2, cy-Oct), 27.89 (CH_2, cy-Oct), 31.19 (CH_2, cy-Oct), 32.55 (C_{spiro}), 34.12 ($^1J_{CH}$ = 164 Hz, CH, cy-Pr), 62.24 ($^1J_{CH}$ = 148 Hz, OCH_2), 72.93 (C), 163.29 (*C*O_2Et).

^{13}C NMR (100 MHz, $CDCl_3$): δ (minor isomer) = 10.17 (CH_2, cy-Pr), 14.03 (CH_3), 18.54 (CH, cy-Pr), 20.12 (CH_2, cy-Oct), 24.30 (CH_2, cy-Oct), 25.93 (CH_2, cy-Oct), 27.67 (CH_2, cy-Oct), 31.20 (CH_2, cy-Oct), 32.56 (C_{spiro}), 33.09 (CH, cy-Pr), 62.61 (OCH_2), 73.84 (C), 165.57 (*C*O_2Et).

Anal. Calcd for $C_{13}H_{19}NO_4$: C, 61.64; H, 7.56. Found: C, 61.54; H, 7.58.

1-Nitrospiro(cyclopropane-2,9′-bicyclo[6.1.0]nonane)-1-carboxylic Acid Ethyl Ester (2e)

A single diastereomer of **2e** was obtained.

Yield: 0.187 g (70%); colorless oil; R_f 0.70 (PE–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95–1.14 (m, 2 H, cy-Oct), 1.25–1.65 (m, 10 H, cy-Oct), 1.29 (t, ^3J = 7.1 Hz, 3 H, CH_3), 1.70–1.85 (m, 2 H, cy-Oct), 1.94 (d, $^2J_{H^aH^b}$ = 5.5 Hz, 1 H, C*H*^{a}H^b), 2.17 (d, $^2J_{H^bH^a}$ = 5.5 Hz, 1 H, CH^a*H*^{b}), 4.10–4.30 (m, 2 H, OCH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.94 (CH_3), 19.37 (CH_2, cy-Pr), 22.20 (CH), 22.85 (CH), 24.08 (CH_2, cy-Oct), 24.22 (CH_2, cy-Oct), 26.35 (2 × CH_2, cy-Oct), 28.49 (CH_2, cy-Oct), 28.54 (CH_2, cy-Oct), 34.39 (C_{spiro}), 61.93 (OCH_2), 70.23 (C), 164.78 (*C*O_2Et).

Anal. Calcd for $C_{14}H_{21}NO_4$: C, 62.90; H, 7.92. Found: C, 62.84; H, 7.89.

***N*-Bicyclo[6.1.0]non-2-en-1-yl-*N*-hydroxyoxalamic Acid Ethyl Ester (2f)**

Yield: 0.124 g (49%); mixture of stereoisomers (1.1:1); colorless oil; R_f 0.15 (PE–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ (major isomer) = 0.50 (dd, $^2J_{H^aH^b}$ = 6.5 Hz, $^3J_{H^aH^c}$ = 7.6 Hz, 1 H, CH^{c}C*H*^{a}H^{b}C), 1.05–0.85 (m, 1 H, cy-Pr), 1.38 (t, ^3J = 7.1 Hz, 3 H, CH_3), 1.45–2.30 (m, 8 H, cy-Oct), 2.61–2.82 (m, 1 H, cy-Oct), 4.26 (m, 2 H, CH_2O), 5.64 (d, ^3J = 11.8 Hz, 1 H, CH^a=C*H*C), 8.1 (br s, 1 H, NOH).

^{1}H NMR (400 MHz, $CDCl_3$): δ (minor isomer) = 0.57 (dd, $^2J_{H^aH^b}$ = 6.1 Hz, $^3J_{H^aH^c}$ = 6.6 Hz, 1 H, CH^{c}C*H*^{a}H^{b}C), 1.05–0.85 (m, 1 H, cy-Pr), 1.32 (t, ^3J = 7.1 Hz, 3 H, CH_3), 1.45–2.30 (m, 8 H, cy-Oct), 2.61–2.82 (m, 1 H, cy-Oct), 4.37 (m, ^3J = 7.1 Hz, 2 H, CH_2O), 5.72 (d, $^3J_{HH^a}$ = 11.6 Hz, 1 H, CH^a=C*H*C), 5.81–5.96 (m, 1 H, CH_2C*H*=CH), 8.1 (br s, 1 H, NOH).

^{13}C NMR (100 MHz, $CDCl_3$): δ (major isomer) = 14.08 ($^1J_{CH}$ = 129 Hz, CH_3), 20.90 ($^1J_{CH}$ = 162 Hz, CH_2, cy-Pr), 22.77 ($^1J_{CH}$ = 125 Hz, CH_2, cy-Oct), 26.04 ($^1J_{CH}$ = 159, CH, cy-Pr), 28.26 ($^1J_{CH}$ = 125 Hz, CH_2, cy-Oct), 29.53 ($^1J_{CH}$ = 123 Hz, CH_2, cy-Oct), 29.65 ($^1J_{CH}$ = 123 Hz, CH_2, cy-Oct), 42.14 (C), 62.78 ($^1J_{CH}$ = 149 Hz, OCH_2), 121.93 ($^1J_{CH}$ = 161 Hz, CH=), 137.58 ($^1J_{CH}$ = 152 Hz, CH=), 157.14 (C=O), 161.62 (C=O).

^{13}C NMR (100 MHz, $CDCl_3$): δ (minor isomer) = 13.99 ($^1J_{CH}$ = 127 Hz, CH_3), 20.74 (CH_2, cy-Pr), 23.96 (CH_2, cy-Oct), 26.33 (CH, cy-Pr), 28.58 (CH_2, cy-Oct), 29.54 (CH_2, cy-Oct), 29.64 (CH_2, cy-Oct), 41.62 (C), 62.30 ($^1J_{CH}$ = 150 Hz, OCH_2), 122.29 ($^1J_{CH}$ = 161 Hz, CH=), 137.16 ($^1J_{CH}$ = 145 Hz, CH=), 160.97 (C=O), 163.65 (C=O).

Anal. Calcd for $C_{13}H_{19}NO_4$: C, 61.64; H, 7.56; N, 5.53. Found: C, 61.56; H, 7.86; N, 5.69.

Reduction for Preparation of Amino Esters 3a–c via Zn–AcOH System; General Procedure

To the stirred mixture of 1-nitrocyclopropanecarboxylate (1 mmol), AcOH (2.5 mL), *i*-PrOH (5 mL) and zinc dust (1.95 g, 30 mmol) were added. The resulting mixture was stirred for 6 h at r.t., treated with sat. $NaHCO_3$ solution to pH 7 and then filtered. The filtrate was extracted with CH_2Cl_2 (2 × 10 mL) and the organic extract was dried over $MgSO_4$. After removing the solvent, pure amino esters (> 90% pure according to ^{1}H and ^{13}C NMR data) were obtained.

1-Aminospiro[2.2]pentane-1-carboxylic Acid Ethyl Ester (3a)

Yield: 0.138 g (89%); yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.78–1.02 (m, 4 H, 2 × CH_2, cy-Pr), 1.24 (t, ^3J = 7.1 Hz, 3 H, CH_3), 1.31 (d, $^2J_{H^aH^b}$ = 4.9 Hz, 1 H, C*H*^{a}H^b), 1.80 (d, $^2J_{H^bH^a}$ = 4.9 Hz, 1 H, CH^a*H*^{b}), 2.30 (br s, 2 H, NH_2), 4.07–4.27 (m, 2 H, CH_2O).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 4.98 ($^1J_{CH}$ = 163 Hz, CH_2, cy-Pr), 7.17 ($^1J_{CH}$ = 162 Hz, CH_2, cy-Pr), 14.30 ($^1J_{CH}$ = 127 Hz, CH_3), 22.81 ($^1J_{CH}$ = 161 Hz, CH_2, cy-Pr), 23.77 (C_{spiro}), 40.08 (C), 60.66 ($^1J_{CH}$ = 149 Hz, OCH_2), 175.43 (*C*O_2Et).

MS (EI, 70 eV): *m*/*z* (%) = 155 (1) [M]$^+$, 140 (1) [M – CH_3]$^+$, 127 (12) [M – C_2H_4]$^+$, 126 (100) [M – C_2H_5]$^+$, 115 (9), 108 (16) [M – NH_2 – C_2H_5]$^+$, 98 (17) [M – C_2H_4 – C_2H_5] $^+$, 82 (54) [M – $CO_2C_2H_5$]$^+$, 80 (26), 71 (8), 55 (24), 42 (14).

1-Aminodispiro[2.0.2.1]heptane-1-carboxylic Acid Ethyl Ester (3b)

Yield: 0.165 g (91%); mixture of diastereomers (4:1); yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (for major isomer) = 0.51–0.78 (m, 2 H, CH_2, cy-Pr), 0.78–1.02 (m, 2 H, CH_2, cy-Pr), 0.82–0.95 (m, 2 H, $C_{spiro}CH_2C_{spiro}$, cy-Pr), 1.14 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.19 (d, $^2J_{H^aH^b}$ = 3.5 Hz, 1 H, C*H*^{a}H^b), 1.69 (d, $^2J_{H^bH^a}$ = 3.5 Hz, 1 H, CH^a*H*^{b}), 2.26 (br s, 2 H, NH_2), 3.97–4.18 (m, 2 H, CH_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ (for minor isomer) = 0.51–0.78 (m, 2 H, CH_2, cy-Pr), 0.78–1.02 (m, 2 H, CH_2, cy-Pr), 0.82–0.95 (m, 2 H, $C_{spiro}CH_2C_{spiro}$, cy-Pr), 1.13 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.25 (d, $^2J_{H^aH^b}$ = 4.0 Hz, 1 H, C*H*^{a}H^b), 1.58 (d, $^2J_{H^bH^a}$ = 4.0 Hz, 1 H, CH^a*H*^{b}), 2.26 (br s, 2 H, NH_2), 3.97–4.18 (m, 2 H, CH_2O).

^{13}C NMR (100 MHz, $CDCl_3$): δ (for major isomer) = 3.36 (CH_2, cy-Pr), 4.81 (CH_2, cy-Pr), 12.96 (CH_2, cy-Pr), 14.22 (CH_3), 15.41 (C_{spiro}), 22.89 (CH_2, cy-Pr), 28.06 (C_{spiro}), 41.48 (C), 60.63 (OCH_2), 175.21 (*C*O_2Et).

^{13}C NMR (100 MHz, $CDCl_3$): δ (for minor isomer) = 4.23 (CH_2, cy-Pr), 4.84 (CH_2, cy-Pr), 10.36 (CH_2, cy-Pr), 14.39 (CH_3), 16.17 (C_{spiro}), 22.90 (CH_2, cy-Pr), 29.13 (C_{spiro}), 40.23 (C), 60.54 (OCH_2), 175.19 (*C*O_2Et).

MS (EI, 70 eV): *m*/*z* (%) = 181 (1) [M]$^+$, 166 (2) [M – CH_3]$^+$, 154 (2) [M – C_2H_4]$^+$, 152 (10) [M – C_2H_5]$^+$, 134 (3), 124 (6) [M – C_2H_4 – C_2H_5]$^+$, 109 (7), 108 (100) [M – $CO_2C_2H_5$]$^+$, 106 (17), 93 (11), 91 (7), 81 (11), 79 (14).

1-Aminodispiro[2.0.3.1]octane-1-carboxylic Acid Ethyl Ester (3c)

Yield: 0.148 g (76%); mixture of diastereomers (8:1); yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (for major isomer) = 0.70 (d, $^2J_{H^aH^b}$ = 5.2 Hz, 1 H, C*H*^{a}H^b), 0.73 (d, $^2J_{H^bH^a}$ = 5.2 Hz, 1 H, CH^a*H*^{b}), 1.29 (t, ^3J = 7.1 Hz, 3 H, CH_3), 1.16 (d, $^2J_{H^aH^b}$ = 3.4 Hz, 1 H, C*H*^{a}H^b), 1.41 (d, $^2J_{H^bH^a}$ = 3.4 Hz, 1 H, CH^a*H*^{b}), 1.55–2.32 (m, 6 H, cy-Bu), 2.65 (br s, 2 H, NH_2), 3.91–4.17 (m, 2 H, CH_2O).

^{1}H NMR (400 MHz, $CDCl_3$): δ (for minor isomer) = 0.42 (d, $^2J_{H^aH^b}$ = 5.0 Hz, 1 H, C*H*^{a}H^b), 0.59 (d, $^2J_{H^bH^a}$ = 5.0 Hz, 1 H, CH^a*H*^{b}), 1.29 (t, ^3J = 7.1 Hz, 3 H, CH_3), 1.38 (d, $^2J_{H^aH^b}$ = 4.1 Hz, 1 H, C*H*^{a}H^b), 1.53 (d, $^2J_{H^bH^a}$ = 4.1 Hz, 1 H, CH^a*H*^{b}), 1.55–2.32 (m, 6 H, cy-Bu), 2.65 (br s, 2 H, NH_2), 3.91–4.17 (m, 2 H, CH_2O).

^{13}C NMR (100 MHz, $CDCl_3$): δ (for major isomer) = 14.22 (CH_3), 16.83 (CH_2, cy-Bu), 18.51 (CH_2, cy-Pr), 22.27 (CH_2, cy-Pr), 27.08 (CH_2, cy-Bu), 27.46 (C_{spiro}, cy-Pr, cy-Pr), 29.09 (CH_2, cy-Bu), 31.87 (C_{spiro}, cy-Bu, cy-Pr), 42.28 (C), 60.61 (OCH_2), 175.37 (*C*O_2Et).

^{13}C NMR (100 MHz, $CDCl_3$): δ (for minor isomer) = 14.06 (CH_3), 16.57 (CH_2, cy-Bu), 18.97 (CH_2, cy-Pr), 22.74 (CH_2, cy-Pr), 27.08 (CH_2, cy-Bu), 27.67 (C_{spiro}, cy-Pr, cy-Pr), 28.08 (CH_2, cy-Bu), 34.29 (C_{spiro}, cy-Bu, cy-Pr), 40.46 (C), 60.75 (OCH_2), 172.83 (*C*O_2Et).

MS (EI, 70 eV): *m*/*z* (%) = 195 (1) [M]$^+$, 180 (1) [M – CH_3]$^+$, 167 (20) [M – C_2H_4]$^+$, 166 (35) [M – C_2H_5]$^+$, 138 (94) [M – C_2H_4 – C_2H_5] $^+$, 124 (10), 122 (71) [M – $CO_2C_2H_5$] $^+$, 120 (73), 106 (22), 94 (100), 93 (32), 79(28), 77 (23), 67 (20), 42 (26), 29 (21).

Reduction for Preparation of Compounds 3d,e and 5 via HCO_2NH_4–Pd/C System; General Procedure

Ammonium formate (10 mmol) was added to a stirred mixture of 1-nitrocylopropanecarboxylate (1 mmol) and 10% Pd/C (10 mol%) in

anhyd EtOH (10 mL). The reaction mixture was stirred for 40 h at r.t. and the catalyst was removed by filtering. Then the solvent was evaporated under reduced pressure and pure amino esters were obtained.

2-Aminotricyclo[7.1.0.0^{1,3}]decane-2-carboxylic Acid Ethyl Ester (3d)

Yield: 0.152 g (68%); mixture of diastereomers (5:1); yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ (for major isomer) = 0.65 (dd, $^3J_{H^bH^c}$ = 5.0 Hz, $^2J_{H^aH^b}$ = 4.7 Hz, 1 H, CH_2, cy-Pr), 0.89 (dd, $^3J_{H^bH^c}$ = 8.5 Hz, $^2J_{H^aH^b}$ = 4.7 Hz, 1 H, CH_2, cy-Pr), 1.26 (t, ^3J = 7.1 Hz, 3 H, CH_3), 1.29–1.93 (m, 14 H, cy-Oct, NH_2), 4.05–4.22 (m, 2 H, OCH_2).

^{1}H NMR (400 MHz, $CDCl_3$): δ (for minor isomer) = 0.70 (dd, $^2J_{H^aH^b}$ = 4.2 Hz, $^3J_{H^aH^c}$ = 4.4 Hz, 1 H, CH_2, cy-Pr), 0.81–0.86 (m, 1 H, CH_2, cy-Pr), 1.27 (t, ^3J = 7.1 Hz, 3 H, CH_3), 1.29–1.93 (m, 14 H, cy-Oct, NH_2), 4.05–4.22 (m, 2 H, OCH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ (for major isomer) = 8.28 (CH_2, cy-Pr), 14.51 (CH_3), 18.06 (CH, cy-Oct, cy-Pr), 20.50 (CH_2, cy-Oct), 24.43 (CH_2, cy-Oct), 24.79 (C_{spiro}), 26.45 (CH_2, cy-Oct), 27.83 (CH_2, cy-Oct), 31.14 (CH_2, cy-Oct), 37.90 (CH, cy-Oct, cy-Pr), 42.53 (C), 60.63 (OCH_2), 174.46 (CO_2Et).

^{13}C NMR (100 MHz, $CDCl_3$): δ (for minor isomer) = 7.89 (CH_2, cy-Pr), 14.71 (CH_3), 18.75 (CH, cy-Oct, cy-Pr), 20.23 (CH_2, cy-Oct), 24.27 (CH_2, cy-Oct), 26.60 (CH_2, cy-Oct), 29.65 (CH_2, cy-Oct), 31.16 (CH_2, cy-Oct), 35.27 (CH, cy-Oct, cy-Pr), 43.72 (C), 62.49 (OCH_2).

In the ^{13}C NMR spectrum of minor isomer of **3d** the signals of C_{spiro} and CO_2Et carbon atoms are not observed.

MS (EI, 70 eV): *m*/*z* (%) = 223 (2) $[M]^+$, 195 (1), 194 (61) $[M - C_2H_5]^+$, 180 (4), 176 (8), 166 (4) $[M - C_2H_4 - C_2H_5]^+$, 152 (12), 150 (100) $[M - CO_2C_2H_5]^+$, 149 (25), 148 (55), 128 (13), 120 (12), 112 (11), 106 (34), 100 (12), 94 (30), 91 (36), 79 (33), 67 (30), 54 (34), 41 (45), 28 (35).

2-Aminotricyclo[7.1.0.0^{1,3}]decane-2-carboxylic Acid Ethyl Ester (3e)

Yield: 0.211 g (89%); yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85–2.03 (m, 16 H, cy-Oct, NH_2), 1.26 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.54 (d, $^2J_{H^aH^b}$ = 5.5 Hz, 1 H, C*H*^{a}H^b), 1.72 (d, $^2J_{H^bH^a}$ = 5.5 Hz, 1 H, CH^a*H*^{b}), 4.10–4.40 (m, 2 H, OCH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.90 (CH_3), 17.53 (CH_2, cy-Pr), 21.90 (CH, cy-Oct, cy-Pr), 23.07 (CH, cy-Oct, cy-Pr), 25.55 (CH_2, cy-Oct), 25.65 (CH_2, cy-Oct), 27.71 (CH_2, cy-Oct), 27.82 (CH_2, cy-Oct), 30.10 (2 × CH_2, cy-Oct), 32.35 (C_{spiro}), 40.50 (C), 62.99 (OCH_2), 172.17 (CO_2Et).

MS (EI, 70 eV): *m*/*z* (%) = 237 (2) $[M]^+$, 210 (1), 209 (12), 208 (100) $[M - C_2H_5]^+$, 191 (5), 190 (8), 180 (4) $[M - C_2H_4 - C_2H_5]^+$, 165 (9), 164 (53) $[M - CO_2C_2H_5]^+$, 152 (5), 134 (6), 120 (13), 106 (12), 94 (22), 79 (28), 71 (11), 67 (24), 55 (30), 41 (24).

1-Hydroxyaminodispiro[2.0.3.1]octane-1-carboxylic Acid Ethyl Ester (5)

Yield: 0.156 g (74%); mixture of diastereomers (5:1); yellow oil.

^{1}H NMR (400 MHz, CD_3OD): δ (for major isomer) = 0.84 (d, $^2J_{H^aH^b}$ = 5.2 Hz, 1 H, C*H*^{a}H^b,), 0.90 (d, $^2J_{H^bH^a}$ = 5.2 Hz, 1 H, CH^a*H*^{b}), 1.22 (t, ^3J = 7.1 Hz, 3 H, CH_3), 1.57 (d, $^2J_{H^aH^b}$ = 4.1 Hz, 1 H, C*H*^{a}H^b), 1.72 (d, $^2J_{H^bH^a}$ = 4.1 Hz, 1 H, CH^a*H*^{b}), 1.90–2.36 (m, 6 H, cy-Bu), 4.10–4.35 (m, 2 H, CH_2O).

^{1}H NMR (400 MHz, CD_3OD): δ (for minor isomer) = 0.99 (d, $^2J_{H^aH^b}$ = 5.6 Hz, 1 H, C*H*^{a}H^b), 1.02 (d, $^2J_{H^bH^a}$ = 5.6 Hz, 1 H, CH^a*H*^{b}), 1.34 (t, ^3J = 7.1 Hz, 3 H, CH_3), 1.46 (d, $^2J_{H^aH^b}$ = 4.9 Hz, 1 H, C*H*^{a}H^b), 1.88 (dd, $^2J_{H^bH^a}$ = 4.9Hz, 1 H, CH^a*H*^{b}), 1.90–2.36 (m, 6 H, cy-Bu), 4.10–4.35 (m, 2 H, CH_2O).

^{13}C NMR (100 MHz, CD_3OD): δ (for major isomer) = 13.53 (CH_3), 16.24 (CH_2, cy-Bu), 18.26 (CH_2, cy-Pr), 19.27 (CH_2, cy-Pr), 27.20 (CH_2, cy-Bu), 27.95 (C_{spiro}, cy-Pr, cy-Pr), 28.59 (CH_2, cy-Bu), 33.54 (C_{spiro}, cy-Bu, cy-Pr), 50.84 (C), 60.84 (OCH_2), 173.33 (CO_2Et).

MS (EI, 70 eV): *m*/*z* (%) = 211 (2) $[M]^+$, 194 (1) $[M - OH]^+$, 183 (8) $[M - C_2H_4]^+$, 182 (42) $[M - C_2H_5]^+$, 166 (48) $[M - C_2H_4 - OH]^+$, 148 (11), 138 (26) $[M - CO_2C_2H_5]^+$, 120 (76), 110 (29), 93 (52), 79 (34), 77 (23), 71 (48), 41 (43), 29 (100).

Hydrolysis for Preparation of Amino Esters 4a–e; General Procedure

1-Aminocyclopropanecarboxylate (1 mmol) was added to a 1 M EtOH solution of NaOH (2 mL). The resulting mixture was stirred for 48 h at r.t. and then acidified with 0.2 M HCl to pH 3. The solvent was evaporated under reduced pressure; the residue was dissolved in the distilled water (2 mL), put on a Dowex 50 ion-exchange column and eluted with a 0.9 N NH_3 solution. The solvent was evaporated and crystalline residue was recrystallized from EtOH–H_2O (1:1).

1-Aminospiro[2.2]pentane-1-carboxylic Acid (4a)

Yield: 0.111 g (87%); a white crystalline; mp 152–154 °C (Lit.[4] mp 156 °C).

^{1}H NMR (400 MHz, D_2O): δ = 1.32–1.47 (m, 4 H, 2 × CH_2, cy-Pr), 1,29 (d, $^2J_{H^aH^b}$ = 6.1 Hz, 1 H, CH^a*H*^{b}), 2.12 (d, $^2J_{H^aH^b}$ = 6.1 Hz, 1 H, C*H*^{a}H^b).

^{13}C NMR (100 MHz, D_2O): δ = 5.97 ($^1J_{CH}$ = 163 Hz, CH_2, cy-Pr), 6.80 ($^1J_{CH}$ = 169 Hz, CH_2, cy-Pr), 19.64 ($^1J_{CH}$ = 168 Hz, CH_2, cy-Pr), 22.53 (C_{spiro}), 39.08 (C), 172.81 (COOH).

1-Aminodispiro[2.0.2.1]heptane-1-carboxylic Acid (4b)

Yield: 0.138 g (90%); mixture of stereoisomers (3:1); white crystals; mp 156–158 °C.

^{1}H NMR (400 MHz, D_2O): δ (for major isomer) = 0.85–1.20 (m, 6 H, cy-Pr), 1.85 (d, $^2J_{H^aH^b}$ = 6.3 Hz, 1 H, C*H*^{a}H^b), 2,16 (d, $^2J_{H^bH^a}$ = 6.3 Hz, 1 H, CH^a*H*^{b}).

^{1}H NMR (400 MHz, D_2O): δ (for minor isomer) = 0.85–1.20 (m, 6 H, cy-Pr), 1.97 (d, $^2J_{H^aH^b}$ = 6.2 Hz, 1 H, C*H*^{a}H^b), 2.07 (d, $^2J_{H^bH^a}$ = 6.2 Hz, 1 H, CH^a*H*^{b}).

^{13}C NMR (100 MHz, D_2O): δ (for major isomer) = 4.73 (CH_2, cy-Pr), 4.99 (CH_2, cy-Pr), 12.67 (CH_2, cy-Pr), 15.21 (C_{spiro}), 18.98 (CH_2, cy-Pr), 26.64 (C_{spiro}), 39.93 (C), 172.55 (COOH).

^{13}C NMR (100 MHz, D_2O): δ (for minor isomer) = 3.68 (CH_2, cy-Pr), 4.89 (CH_2, cy-Pr), 10.70 (CH_2, cy-Pr), 15.38 (C_{spiro}), 18.73 (CH_2, cy-Pr), 26.49 (C_{spiro}), 38.77 (C), 172.56 (COOH).

Anal. Calcd for $C_8H_{11}NO_2$: C, 62.73; H, 7.24. Found: C, 62.59; H, 7.11.

1-Aminodispiro[2.0.3.1]octane-1-carboxylic Acid (4c)

Only major isomer of amino ester **3c** was put into the hydrolysis.

Yield: 0.142 g (85%); white crystals; mp 168–170 °C.

^{1}H NMR (100 MHz, D_2O): δ = 1.38 (d, $^2J_{H^aH^b}$ = 5.6 Hz, 1 H, C*H*^{a}H^b), 1.49 (d, $^2J_{H^bH^a}$ = 5.6 Hz, 1 H, CH^a*H*^{b}), 1.96 (d, $^2J_{H^aH^b}$ = 6.1 Hz, 1 H, C*H*^{a}H^b), 2.07 (d, $^2J_{H^bH^a}$ = 6.1 Hz, 1 H, CH^a*H*^{b}), 2.10–2.55 (m, 6 H, cy-Bu).

^{13}C NMR (100 MHz, D_2O): δ = 15.79 (CH_2), 17.95 (CH_2), 18.36 (CH_2), 26.84 (CH_2, cy-Bu), 27.49 (C_{spiro}), 27.91 (CH_2, cy-Bu), 28.61 (C_{spiro}), 39.63 (C), 171.97 (COOH).

Anal. Calcd for $C_9H_{13}NO_2$: C, 64.65; H, 7.84. Found: C, 64.79; H, 7.46.

2-Aminotricyclo[7.1.0.0^{1,3}]decane-2-carboxylic Acid (4d)
Yield: 0.137 g (70%); white crystals; mp 195–197 °C;

^{1}H NMR (400 MHz, D_2O–CF_3CO_2H, 40:1): δ = 0.76 (dd, $^2J_{H^aH^b}$ = 5.0 Hz, $^3J_{H^aH^c}$ = 5.2, 1 H, cy-Pr), 0.98–1.60 (m, 13 H, cy-Oct, cy-Pr).

It was not possible to register ^{13}C NMR spectrum and establish isomer ratio of amino acid **4d** owing to its poor solubility.

Anal. Calcd for $C_{12}H_{19}NO_2$: C, 67.66; H, 8.78. Found: C, 67.52; H, 8.91.

1-Aminospiro[cyclopropane-2,9′-bicyclo[6.1.0]nonane]-1-carboxylic Acid (4e)
Yield: 0.182 g (87%); white crystals; mp 189–190 °C.

^{1}H NMR (400 MHz, D_2O–CF_3CO_2H, 10:1): δ = 0.98–1.60 (m, 14 H, cy-Oct), 1.51 (d, $^2J_{H^aH^b}$ = 5.9 Hz, 1 H, C*H*^{a}H^b), 1.75 (d, $^2J_{H^bH^a}$ = 5.9 Hz, 1 H, CH^a*H*^{b}).

^{13}C NMR (100 MHz, D_2O–CF_3CO_2H, 10:1): δ = 16.62 (CH_2, cy-Pr), 21.21 (cy-Oct), 22.08 (cy-Oct), 24.08 (cy-Oct), 24.55 (cy-Oct), 26.52 (cy-Oct), 26.64 (cy-Oct), 28.83 (cy-Oct), 28.94 (cy-Oct), 31.30 (C_{spiro}), 39.61 (C), 173.58 (*C*OOH).

Anal. Calcd for $C_{12}H_{19}NO_2$: C, 68.87; H, 9.15. Found: C, 68.52; H, 8.91.

Hydroxyimino(1-methylcyclopropyl)acetic Acid Ethyl Ester (6)
A mixture of nitroester **2a** (180 mg, 1 mmol) and 10% Pd/C in anhyd MeOH(15 mL) was stirred at r.t. under H_2 (1 atm) for 24 h. The catalyst was filtered, the solvent was evaporated under reduced pressure and the colorless oil obtained was purified by column chromatography (SiO_2, PE–EtOAc, 2:1).

Yield: 0.106 g (62%); white crystals; mp 45 °C; R_f 0.10 (SiO_2, PE–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.62–0.71 (m, 2 H, CH_2, cy-Pr), 0.77–0.84 (m, 2 H, CH_2, cy-Pr), 1.29 (s, 3 H, CH_3), 1.34 (t, ^3J = 7.1 Hz, 3 H, CH_3), 4.28 (q, ^3J = 7.1 Hz, 2 H, CH_2), 9.8 (br s, 1 H, =NOH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.62 (2 × CH_2, cy-Pr), 14.26 (*C*H$_3$CH$_2$), 21.67 (*C*H$_3$C), 22.88 (C), 61.71 (OCH_2), 154.03 (C=N), 163.42 (*C*O$_2$Et).

Anal. Calcd for $C_8H_{13}NO_3$: C, 56.13; H, 7.65; N, 8.18. Found: C, 56.00; H, 7.40; N, 8.12.

(1-Nitrospiro[2.2]pent-1-yl)methanol (7)
To the mixture of nitroester **2a** (130 mg, 0.75 mmol) and 10% Pd/C (30 mg, 10 mol%) in THF (4 mL) at 0 °C $NaBH_4$ (70 mg, 1.75 mmol) was added. The resulting mixture was stirred for 2 h. Then the catalyst was filtered and the solvent was evaporated under reduced pressure.

Yield: 0.075 g (70%); yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91–0.99 (m, 1 H, CH_2, cy-Pr), 1.01–1.05 (m, 1 H, CH_2, cy-Pr), 1.17–1.32 (m, 2 H, CH_2, cy-Pr), 1.81 (d, $^2J_{H^aH^b}$ = 5.4 Hz, 1 H, C*H*^{a}H^{b}C$_{spiro}$), 2.34 (d, $^2J_{H^bH^a}$ = 5.4 Hz, 1 H, CH^a*H*^{b}C$_{spiro}$), 3.96 (d, $^2J_{H^aH^b}$ = 13.8 Hz, 1 H, C*H*^{a}H^{b}OH), 4.29 (d, $^2J_{H^bH^a}$ = 13.8 Hz, 1 H, CH^a*H*^{b}OH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 6.98 (CH_2, cy-Pr), 7.86 (CH_2, cy-Pr), 23.25 (C*C*H$_2$C$_{spiro}$), 27.76 (C_{spiro}), 63.07 (CH_2OH), 71.70 (C).

(1-Chloromethylcyclopropyl)nitroacetic Acid Ethyl Ester (8)
To the mixture of nitroester **2a** (0.185 g, 1 mmol), EtOH (5 mL), 20% aq HCl (0.44 g, 2.4 mmol) and zinc dust (1.3 g, 20 mmol) were slowly added. The reaction mixture was stirred for 2 h at r.t. After filtration, the solvent was evaporated under reduced pressure to yield crude **8** (0.198 g), which was than isolated by column chromatography (SiO_2, PE–EtOAc, 4:1).

Yield: 0.139 g (63%); slightly yellow oil; R_f 0.45 (PE–EtOAc, 4:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83–0.95 (m, 2 H, CH_2, cy-Pr), 1.03–1.09 (m, 1 H, CH_2, cy-Pr), 1.12–1.21 (m, 1 H, CH_2, cy-Pr), 1.31 (t, ^3J = 7.2 Hz, 3 H, CH_3), 3.61 (d, $^2J_{H^aH^b}$ = 12.3 Hz, 1 H, C*H*^{a}H^{b}Cl), 3.80 (d, $^2J_{H^bH^a}$ = 12.3 Hz, 1 H, CH^a*H*^{b}Cl), 4.18–4.36 (m, 2 H, CH_2O), 5.07 (s, 1 H, CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.30 ($^1J_{CH}$ = 165 Hz, CH_2, cy-Pr), 13.69 ($^1J_{CH}$ = 128 Hz, CH_3), 14.05 ($^1J_{CH}$ = 166 Hz, CH_2, cy-Pr), 23.00 (C), 49.84 ($^1J_{CH}$ = 149 Hz, CH_2Cl), 63.26 ($^1J_{CH}$ = 149 Hz, OCH_2), 90.36 ($^1J_{CH}$ = 151 Hz, CH), 163.23 (*C*O$_2$Et).

Anal. Calcd for $C_8H_{12}NO_4Cl$: C, 43.35; H, 5.46. Found: C, 43.21; H, 5.30.

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