Supporting information

**Fluoronitroalkenes in tandem [4+1]/[3+2]-cycloaddition: one-pot three-component assembly of fluorinated bicyclic nitroso acetals**

Vladimir A. Motornov,\textsuperscript{a,b} Andrey A. Tabolin,\textsuperscript{a} Roman A. Novikov,\textsuperscript{a,c} Yulia V. Nelyubina,\textsuperscript{d} Valentine G. Nenajdenko\textsuperscript{e} and Sema L. Ioffe\textsuperscript{a}

\textsuperscript{a} N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky prosp. 47, Moscow, 119991, Russia.
\textsuperscript{b} Higher Chemical College, D. I. Mendeleev University of Chemical Technology of Russia, Miusskaya sq. 9, Moscow 125047, Russia.
\textsuperscript{c} V. A. Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, Vavilov str. 32, Moscow, 119991, Russia.
\textsuperscript{d} A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, Vavilov str. 28, Moscow, 119991, Russia.
\textsuperscript{e} Department of Chemistry, M. V. Lomonosov Moscow State University, Leninskie Gory 1, Moscow 119991, Russia.
**General experimental**

All reactions were performed in oven-dried (150 °C) glassware. Most of the chemicals were acquired from commercial sources and used as received. TLC were performed on silica coated on aluminium with UV254 indicator. Visualization was generally accomplished with UV and anisaldehyde/H$_2$SO$_4$ stain. For visualisation of compound 10 UV and Ceric Ammonium Molybdate stain were used. Column chromatography was performed on silica (0.04–0.063 mm, 60 Å). NMR spectra were recorded at the following spectrometer frequencies: 300 MHz (1H NMR), 75 MHz or 100 MHz (13C NMR), 282 MHz (19F NMR). Multiplicities are assigned as s (singlet), d (doublet), t (triplet), q (quadruplet), p (pentet), m (multiplet), br (broad), app (apparent). High resolution mass spectra were acquired at TOF spectrometer using electrospray ionization (ESI). Tandem HPLC-HRMS was made on Agilent Poroshell 120 EC-C18 column (3.0 × 50 mm; 2.7 µm). The column was eluted in a gradient of concentrations of solvent A (acetonitrile) and solvent B (water) with the flow rate of 400 µl/min in the following gradient parameters: 0-15% A for 6.0 min, then 15%–85% A for 1.5 min, then 85%–100% A for 0.1 min, 100% A for 2.4 min.

Starting compounds were prepared according to literature procedures: (Z)-1-chloro-4-(2-fluoro-2-nitrovinyl)benzene 1a, (Z)-methyl 4-(2-fluoro-2-nitrovinyl)benzoate 1b, (Z)-1-fluoro-4-(2-fluoro-2-nitrovinyl)benzene 1c, (Z)-1-(2-fluoro-2-nitrovinyl)-4-methoxybenzene 1d, (Z)-1-(2-fluoro-2-nitrovinyl)-3-methoxybenzene 1e, (Z)-1-bromo-2-(2-fluoro-2-nitrovinyl)benzene 1f, methyl 4-vinylbenzoate, 4-vinylbiphenyl, 1-vinylnaphthalene, p-methoxy-β-nitrostyrene 5, p-methoxy-β-bromo-β-nitrostyrene 7b, PhICl.
Optimizations of reaction conditions

![Optimizations of reaction conditions](image)

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<th>Entry</th>
<th>Conditions</th>
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<th>Yield 2a, %</th>
<th>Yield 3a, %</th>
<th>Yield 4a, %</th>
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* a = FNMR yields; b = isolated yields in brackets; c = n. r. = no reaction (1a was recovered);

General procedure 1 for the one-pot synthesis of fluorinated 5,5-annulated nitrosoacetals 4a-4w.

The solution of α-fluoronitroalkene 1 (0.3 mmol), dimethyl bromomalonate (0.33 mmol, 1.1 equiv.) and dipolarophile (6 mmol, 20 equiv., unless otherwise mentioned) in dry DMF (6 ml) was cooled to 0°C using ice bath and finely powdered K₂CO₃ (0.45 mmol, 1.5 equiv.) was added. Mixture was stirred at 0°C for 10 min., then warmed to r. t. and stirring was continued for additional 2-6 hours. After the reaction was complete (TLC monitoring), mixture was poured into H₂O (15 ml), and product was extracted with t-BuOMe (3x20 ml). Organic layer was dried over anhydrous Na₂SO₄ and evaporated under reduced pressure. Crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc = 9:1 – 7:3) to afford fluorinated nitrosoacetals 4a-4w.
rel-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-5-cyano-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4a (major isomer) and rel-(3R,3aR,5R)-Dimethyl 3-(4-chlorophenyl)-5-cyano-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4′a (minor isomer)

Nitrosoacetals 4, 4′a was obtained from α-fluoronitroalkene 1a (91 mg, 0.45 mmol) and acrylonitrile following the general procedure 1. Column chromatography (eluent: 9:1, then 5:1, then 7:3 PE/EtOAc) afforded 4a (82 mg, 47%) and 4′a (26 mg, 15%) as colorless oils.

Major isomer (4a):
Rf = 0.37 (PE/EtOAc, 1:1)
mp = 135-136 °C (EtOH).

\(^{1}\)H NMR (300 MHz, CDCl₃): δ 2.98 (ddd, J = 20.4, 14.2, 4.8 Hz, 1H, CH₃), 3.31 (ddd, J = 23.7, 14.2, 9.4 Hz, 1H, CH₂), 3.34 (s, 3H, CO₂Me), 3.87 (s, 3H, CO₂Me), 4.85 (d, J = 6.5 Hz, Ar-CH), 5.16 (ddd, J = 9.4, 4.7, 0.6 Hz, O-CH-CN), 7.29-7.38 (m, 4H, CH₂).

\(^{13}\)C NMR (75 MHz, CDCl₃): δ 41.4 (d, \(^{2}\)J_CF = 29.0 Hz, CH₂), 53.0 (-CO₂Me), 54.4 (-CO₂Me), 55.7 (d, \(^{2}\)J_CF = 22.6 Hz, CH–Ar), 66.5 (CH-CN), 92.0 (C-O), 115.5 (CN), 118.8 (d, \(^{1}\)J_CF = 222.5 Hz, C-F), 128.7 (CH Ar), 128.8 (d, \(^{3}\)J_CF = 3.7 Hz, C Ar), 131.8 (d, \(^{4}\)J_CF = 1.4 Hz, CH Ar), 135.2 (C Ar), 164.4 (-CO₂Me), 167.0 (-CO₂Me).

\(^{19}\)F NMR (282 MHz, CDCl₃): δ -133.9 (td, J = 20.0, 4.9 Hz).

HRMS (ESI): m/z calcd. for [C₁₆H₁₄ClFNO₆ + H⁺]: 385.0597, found: 385.0593.

X-ray data was deposited in the Cambridge Crystallographic Data Centre (CCDC 1849100).
General view of the compound 4a in representation of atoms via thermal ellipsoids at 50% probability level.

Minor isomer (4'a):

R_f = 0.48 (PE/EtOAc, 1:1)

H NMR (300 MHz, CDCl_3): δ 3.12 (ddd, J = 24.0, 14.7, 9.5 Hz, 1H, CH_2a), 3.29 (ddd, J = 24.6, 14.7, 4.9 Hz, 1H, CH_2b), 3.32 (s, 3H, CO_2Me), 3.92 (s, 3H, CO_2Me), 5.00 (s, Ar–CH), 5.31 (dd, J = 9.5, 4.9 Hz, O–CH–CN), 7.31–7.37 (m, 4H, CH_Ar).

C NMR (75 MHz, CDCl_3): δ 42.0 (d, J_{CF} = 30.4 Hz, CH_2), 52.8 (-CO_2Me), 53.8 (d, J_{CF} = 21.9 Hz, CH–Ar), 54.6 (-CO_2Me), 68.6 (CH–CN), 89.0 (C–O), 116.7 (CN), 118.9 (d, J_{CF} = 225.2 Hz, C–F), 128.6 (CH_Ar), 129.5 (d, J_{CF} = 3.5 Hz, C_Ar), 132.0 (CH_Ar), 135.0 (C_Ar), 165.3 (-CO_2Me), 166.3 (-CO_2Me).

F NMR (282 MHz, CDCl_3): δ -133.2 (t, J = 24.1 Hz).

HRMS (ESI): m/z calcd. for [C_{16}H_{14}ClFN_2O_6 + Na]^+: 407.0417, found: 407.0411.

rel-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4b (major) and rel-(3R,3aR,5R)-Dimethyl 3-(4-
Nitrosoacetals 4, 4'b was obtained from α-fluoronitroalkene 1a (60.4 mg, 0.3 mmol) and styrene following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded 4b (87.2 mg, 64%, dr (4b:4'b)= 10:1) as colorless solid. Pure major isomer was obtained by recrystallization from chloroform as colorless crystals. Mother liquor was evaporated to give mixture of 4b:4'b = 2:1.
Rf = 0.61 (PE/EtOAc, 1:1)
mp = 142-146 °C (CHCl3)
Major isomer (4b):
1H NMR (300 MHz, CDCl3, COSY, NOESY): δ 2.66 (ddd, J = 24.6, 14.1, 7.7 Hz, 1H, CH2α(4)), 3.20 (ddd, J = 20.1, 14.1, 8.4 Hz, 1H, CH2b(4)), 3.36 (s, 3H, CO2Me), 3.91 (s, 3H, CO2Me), 4.95 (d, J = 3.9 Hz, 1H, CH(3)), 5.16 (app td, J = 8.2, 1.7 Hz, 1H, CH(5)), 7.33-7.45 (m, 9H, CHAr). Characteristic NOESY interactions: CH(3)-CH2b(4); CH2b(4)-CH(5).
Characteristic HOESY interactions: F-CH2a(4); CHAr-F.
13C NMR (75 MHz, CDCl3): δ 44.7 (d, 2JCF = 28.0 Hz, CH2(4)), 52.7 (-CO2Me), 54.1 (-CO2Me), 55.8 (d, 2JCF = 22.5 Hz, CH(3)), 85.2 (C(5)), 89.4 (C(2)), 119.1 (d, 1JCF = 221.7 Hz, C-F), 127.0 (CHAr), 128.4 (CHAr), 128.8 (CHAr), 129.0 (CHAr), 130.3 (d, 3JCF = 3.2 Hz, CAr), 132.1 (d, J = 1.2 Hz, CHAr), 134.7 (CAr), 137.0 (CAr), 165.9 (-CO2Me), 167.2 (-CO2Me).
19F NMR (282 MHz, CDCl3): δ -131.4 (ddd, J = 24.6, 20.1, 3.9 Hz).
15N NMR (30 MHz, CDCl3, from 1H-15N HMBC): δ 288 (d, 2JNF = 36 Hz).
X-ray data was deposited in the Cambridge Crystallographic Data Centre (CCDC 1849099).
General view of the compound 4b in representation of atoms via thermal ellipsoids at 50% probability level.

Minor isomer (4'b):

$^1$H NMR (300 MHz, CDCl$_3$, COSY, NOESY): $\delta$ 2.85 (ddd, $J = 26.6, 13.9, 9.5$ Hz, 1H, CH$_{2b}(4)$), 2.90-3.03 (m, 1H, CH$_{2a}(4)$), 3.36 (s, 3H, CO$_2$Me), 3.77 (s, 3H, CO$_2$Me), 4.93-4.94 (m, 1H, CH(3)), 5.50 (dd, $J = 9.5, 7.1$ Hz, 1H, CH(5)), 7.33-7.45 (m, 9H, CH$_{Ar}$).

Characteristic NOESY interactions: CH(5)-CH$_{2a}$ (4).

Characteristic HOESY interactions: F-CH(5); F-CH$_{2a}$ (4); CH$_{Ar}$-F.

$^{13}$C NMR (75 MHz, CDCl$_3$, HSQC, HMBC): 44.4 (d, $^2J_{CF} = 28.1$ Hz, CH$_2(4)$), 52.7 (-CO$_2$Me), 53.8 (-CO$_2$Me), 56.6 (d, $^2J_{CF} = 23.3$ Hz, CH(3)), 81.9 (C-3), 92.9 (C(5)), 120.1 (d, $^1J_{CF} = 222.6$ Hz, C-F), 126.7 (CH$_{Ar}$), 128.6 (CH$_{Ar}$), 128.7 (CH$_{Ar}$), 129.0 (CH$_{Ar}$), 129.8 (d, $^3J_{CF} = 3.6$ Hz, C$_{Ar}$), 131.9 (d, $J = 1.6$ Hz, CH$_{Ar}$), 134.7 (C$_{Ar}$), 137.2 (C$_{Ar}$), 165.9 (-CO$_2$Me), 167.6 (-CO$_2$Me).

$^{19}$F NMR (282 MHz, CDCl$_3$): $\delta$ -134.1 (ddd, $J = 27.0, 20.2, 6.6$ Hz).

HRMS (ESI, from HPLC-HRMS): m/z calcd. for [C$_{21}$H$_{19}$ClFNO$_6$ + H$^+$]: 436.0958, found: 436.0955.

$rel$-(3R,3aR,5S)-Dimethyl 3a-fluoro-3-(4-(methoxycarbonyl)phenyl)-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4c (major isomer)
Nitrosoacetals **4,4’c** was obtained from α-fluoronitroalkene **1b** (30 mg, 0.13 mmol) and styrene following the general procedure 1. Column chromatography (eluent: 2:1 PE/EtOAc) afforded **4,4’c** (31 mg, 56%, dr (**4c**:**4’c**) = 7:1, ¹H NMR) as colorless solid.  

R<sub>f</sub> = 0.59 (PE/EtOAc, 1:1)  
mp = 151-152 °C (PE/EtOAc, 10:1)  
¹H NMR (300 MHz, CDCl<sub>3</sub>): δ 2.67 (ddd, J = 24.8, 14.1, 7.6 Hz, 1H, CH<sub>2a</sub>(4)), 3.23 (ddd, J = 20.5, 14.1, 8.4 Hz, 1H, CH<sub>2b</sub>(4)), 3.29 (s, 3H, CO<sub>2</sub>Me), 3.91 (s, 3H, CO<sub>2</sub>Me), 3.94 (s, 3H, CO<sub>2</sub>Me), 5.03 (d, J = 3.9 Hz, 1H, Ar-CH<sub>H</sub>), 5.63 (td, J = 8.4, 1.7 Hz, 1H, O-CH<sub>H</sub>-Ph), 7.35-7.43 (m, 5H, CH<sub>Ar</sub>), 7.54 (d, J = 8.2 Hz, 2H, CH<sub>Ar</sub>), 8.04 (d, J = 8.2 Hz, 2H, CH<sub>Ar</sub>). Minor isomer (characteristic signal): δ 5.50 (dd, J = 9.6, 7.0 Hz, 1H, O-CH<sub>H</sub>-Ph).  
¹³C NMR (75 MHz, CDCl<sub>3</sub>): δ 44.6 (d, ²J<sub>CF</sub> = 27.9 Hz, CH<sub>2</sub>), 52.2 (CO<sub>2</sub>Me), 52.7 (CO<sub>2</sub>Me), 54.2 (CO<sub>2</sub>Me), 56.2 (d, ³J<sub>CF</sub> = 22.4 Hz, CH–Ar), 85.3 (PhCH–O), 89.3 (C–O), 119.2 (d, ¹J<sub>CF</sub> = 222.2 Hz, C–F), 127.0 (CH<sub>Ar</sub>), 128.8 (CH<sub>Ar</sub>), 129.0 (CH<sub>Ar</sub>), 129.3 (CH<sub>Ar</sub>), 130.2 (C<sub>Ar</sub>), 130.8 (CH<sub>Ar</sub>), 136.8 (d, ³J<sub>CF</sub> = 3.0 Hz, C<sub>Ar</sub>), 137.0 (C<sub>Ar</sub>), 165.8 (-CO<sub>2</sub>Me), 166.6 (-CO<sub>2</sub>Me), 167.0 (-CO<sub>2</sub>Me).  
¹⁹F NMR (282 MHz, CDCl<sub>3</sub>): δ -131.3 (t, J<sub>HF</sub> = 22.4 Hz). Minor isomer: δ -133.8 (t, J<sub>HF</sub> = 25.8 Hz).  
HRMS (ESI): m/z calcd. for [C<sub>23</sub>H<sub>22</sub>FN<sub>8</sub>O<sub>8</sub>+ Na<sup>+</sup>]: 482.1222, found: 482.1219.

**rel-(3R,3aR,5S)-Dimethyl 3a-fluoro-3-(4-fluorophenyl)-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4d** (major isomer)  

Nitrosoacetals **4,4’d** was obtained from α-fluoronitroalkene **1c** (62 mg, 0.33 mmol) and styrene following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded **4,4’d** (105 mg, 72%, dr (**4d**:**4’d**) = 10:1) as colorless solid.  

R<sub>f</sub> = 0.50 (PE/EtOAc, 1:1)  
mp = 134-135 °C (PE/EtOAc, 10:1)  
¹H NMR (300 MHz, CDCl<sub>3</sub>): δ 2.66 (ddd, J = 24.5, 14.1, 7.7 Hz, 1H, CH<sub>2a</sub>(4)), 3.20 (ddd, J = 20.0, 14.1, 8.4 Hz, 1H, CH<sub>2b</sub>(4)), 3.35 (s, 3H, CO<sub>2</sub>Me), 3.91 (s, 3H, CO<sub>2</sub>Me), 4.97 (d, J = 4.4 Hz, 1H, Ar-CH<sub>H</sub>), 5.60 (app td, J = 8.1, 1.7 Hz, 1H, O-CH<sub>H</sub>-Ph), 7.07 (t, J = 8.7 Hz, 2H, CH<sub>Ar</sub>), 7.36-7.47 (m, 7H, CH<sub>Ar</sub>). Minor isomer (characteristic signal): 5.50 (dd, J = 9.5, 7.0 Hz, 1H, O-CH<sub>H</sub>-Ph).  
¹³C NMR (75 MHz, CDCl<sub>3</sub>): δ 44.6 (d, ²J<sub>CF</sub> = 18.8 Hz, CH<sub>2</sub>), 52.6 (CO<sub>2</sub>Me), 54.0 (CO<sub>2</sub>Me), 55.6 (d, ³J<sub>CF</sub> = 10.6 Hz, CH–Ar), 85.2 (PhCH–O), 89.3 (C–O), 115.2 (d, ²J<sub>CF</sub> = 21.6 Hz, CH<sub>Ar</sub>), 119.1 (d, ¹J<sub>CF</sub> = 221.9 Hz, C–F), 127.0 (CH<sub>Ar</sub>), 127.6 (t, J<sub>CF</sub> = 3.5 Hz, C<sub>Ar</sub>), 128.8 (CH<sub>Ar</sub>), 129.0
Nitrosoacetals 4,4'e was obtained from α-fluoronitroalkene 1d (55.1 mg, 0.28 mmol) and styrene following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded 4,4'e (79 mg, 63%), dr (4e:4'e) = 10:1. 1H NMR as slightly yellow oil which solidifies upon storage in a refrigerator.

Rf = 0.51 (PE/EtOAc, 1:1)

1H NMR (300 MHz, CDCl3): δ 2.64 (ddd, J = 24.1, 14.0, 7.8 Hz, 1H, CH2a(4)), 3.19 (ddd, J = 19.0, 14.0, 8.3 Hz, 1H, CH2b(4)), 3.35 (s, 3H, CO2Me), 3.82 (s, 3H, OMe), 3.90 (s, 3H, CO2Me), 4.92 (d, J = 5.5 Hz, 1H, Ar-CH), 5.60 (td, J = 8.0, 1.5 Hz, 1H, O-CH-Ph), 6.89 (d, J = 8.8 Hz, 2H, CHAr), 7.36-7.43 (m, 7H, CHAr). Minor isomer (characteristic signal): 5.49 (dd, J = 9.5, 7.1 Hz, 1H, O-CH-Ph).

13C NMR (75 MHz, CDCl3): δ 44.8 (d, 2JCF = 28.1 Hz, CH2), 52.6 (-CO2Me), 54.0 (CO2Me), 55.2 (OMe), 55.8 (d, 3JCF = 22.6 Hz, CH–Ar), 84.9 (PhCH–O), 89.7 (C–O), 113.6 (CHAr), 119.2 (d, 1JCF = 221.2 Hz, C–F), 123.5 (d, 2JCF = 3.2 Hz, CAr), 127.0 (CHAr), 128.8 (CHAr), 128.9 (CHAr), 131.9 (d, J = 0.6 Hz, CHAr), 137.3 (CAr), 159.7 (CAr-OMe), 166.2 (CO2Me), 167.3 (CO2Me).

19F NMR (212 MHz, CDCl3): δ -132.0 (t, J = 20.9 Hz). Minor isomer: δ -134.6 (br t, J = 22.6 Hz)

HRMS (ESI): m/z calcd. for [C23H22FNO7 + H+]: 432.1453, found: 432.1449.

Nitrosoacetals 4,4'f was obtained from α-fluoronitroalkene 1e (59 mg, 0.3 mmol) and styrene following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded 4,4'f (105 mg, 78%), dr (4f:4'f) = 16:1. 19F NMR as colorless solid.

Rf = 0.58 (PE/EtOAc, 1:1)

mp (decomp.) = 168-169 ºC (PE/EtOAc, 3:1)
\[ ^1\text{H} \text{NMR (300 MHz, CDCl}_3\]: } \delta 2.66 (ddd, \textit{J} = 24.5, 13.6, 7.9 Hz, 1H, CH\textsubscript{2a}(4)), 3.21 (ddd, \textit{J} = 20.1, 13.4, 8.5 Hz, 1H, CH\textsubscript{2b}(4)), 3.33 (s, 3H, CO\textsubscript{2}Me), 3.83 (s, 3H, OMe), 3.90 (s, 3H, CO\textsubscript{2}Me), 4.93 (d, \textit{J} = 3.9 Hz, 1H, Ar-CH), 5.60 (app t, \textit{J} = 7.5 Hz, 1H, O-CH-Ph), 6.88 (d, \textit{J} = 7.7 Hz, 1H, CH\textsubscript{Ar}), 6.95-7.31 (m, 1H, CH\textsubscript{Ar}), 7.31-7.44 (m, 5H, CHPh).

\[ ^{13}\text{C} \text{NMR (75 MHz, CDCl}_3\]: } \delta 44.8 (d, \textit{J}_{\text{CF}} = 28.1 Hz, \text{CH}_2), 52.6 (-CO_2Me), 54.0 (CO_2Me), 55.3 (OMe), 56.4 (d, \textit{J}_{\text{CF}} = 22.7 Hz, \text{CH–Ar}), 85.0 (\text{PhCH–O}), 89.7 (C–O), 114.5 (CH\textsubscript{Ar}), 115.9 (CH\textsubscript{Ar}), 119.3 (d, \textit{J}_{\text{CF}} = 222.2 Hz, C–F), 123.0 (CH\textsubscript{Ar}), 127.0 (CH\textsubscript{Ar}), 128.8 (CH\textsubscript{Ar}), 128.9 (CH\textsubscript{Ar}), 130.1 (CH\textsubscript{Ar}), 131.3 (d, \textit{J}_{\text{CF}} = 3.1 Hz, C\textsubscript{Ar}), 137.3 (C\textsubscript{Ar}), 159.4 (C\textsubscript{Ar}-OMe), 166.0 (-CO\textsubscript{2}Me), 167.2 (-CO\textsubscript{2}Me).

\[ ^{19}\text{F} \text{NMR (282 MHz, CDCl}_3\]: } \delta -132.3 (t, \textit{J} = 21.5 Hz). Minor isomer: \delta -135.0 (t, \textit{J} = 23.3 Hz).

HRMS (ESI): m/z calcd. for [C\textsubscript{22}H\textsubscript{22}FNO\textsubscript{7}]+: 454.1273, found: 454.1270.

**rel-(3R,3aR,5S)-Dimethyl 3-(2-bromophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4g (major isomer)**

Nitrosoacetals 4,4’g was obtained from \(\alpha\)-fluoronitroalkene 1f (42.5 mg, 0.17 mmol) and styrene following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded 4,4’g (61 mg, 70%, dr (4g:4’g) = 11:1) as colorless oil which solidifies upon storage in a refrigerator.

R\textsubscript{f} = 0.55 (PE/EtOAc, 1:1)

\[ ^1\text{H} \text{NMR (300 MHz, CDCl}_3\]: } \delta 2.69 (ddd, \textit{J} = 25.2, 14.1, 7.5 Hz, 1H, CH\textsubscript{2a}(4)), 3.29 (s, 3H, CO\textsubscript{2}Me), 3.36 (ddd, \textit{J} = 21.3, 14.1, 8.5 Hz, 1H, CH\textsubscript{2b}(4)), 3.93 (s, 3H, CO\textsubscript{2}Me), 5.61 (app td, \textit{J} = 8.0, 1.8 Hz, 1H, O-CH-Ph), 5.84 (d, \textit{J} = 2.6 Hz, 1H, Ar-CH), 7.18 (td, 1H, \textit{J} = 7.7, 1.6 Hz, CH\textsubscript{Ar}), 7.33-7.44 (m, 6H, CH\textsubscript{Ar}), 7.63 (dd, \textit{J} = 8.0, 1.1 Hz, 1H, CH\textsubscript{Ar}), 7.72 (dd, \textit{J} = 7.9, 2.4, 1.8 Hz, 1H, CH\textsubscript{Ar}). Minor isomer (characteristic signals): \delta 3.77 (s, 3H, -CO\textsubscript{2}Me), 5.48 (dd, \textit{J} = 8.7, 8.0 Hz, 1H, O-CH-Ar).

\[ ^{13}\text{C} \text{NMR (75 MHz, CDCl}_3\]: } \delta 44.7 (d, \textit{J}_{\text{CF}} = 28.0 Hz, \text{CH}_2), 52.5 (-CO\textsubscript{2}Me), 54.0 (d, \textit{J}_{\text{CF}} = 21.7 Hz, C–Ar), 54.1 (-CO\textsubscript{2}Me), 86.2 (\text{PhCH–O}), 89.4 (C–O), 119.2 (d, \textit{J}_{\text{CF}} = 222.8 Hz, C–F), 126.2 (C\textsubscript{Ar}), 127.0 (CH\textsubscript{Ar}), 127.2 (CH\textsubscript{Ar}), 128.8 (CH\textsubscript{Ar}), 128.9 (CH\textsubscript{Ar}), 129.8 (CH\textsubscript{Ar}), 131.8 (d, \textit{J}_{\text{CF}} = 3.2 Hz, C\textsubscript{Ar}), 132.7 (d, \textit{J}_{\text{CF}} = 3.2 Hz, CH\textsubscript{Ar}), 132.8 (CH\textsubscript{Ar}), 137.3 (C\textsubscript{Ar}), 165.8 (-CO\textsubscript{2}Me), 167.8 (-CO\textsubscript{2}Me).

\[ ^{19}\text{F} \text{NMR (282 MHz, CDCl}_3\]: } \delta -131.1 (t, \textit{J} = 23.1 Hz). Minor isomer: \delta -132.3 (t, \textit{J} = 23.6 Hz).

HRMS (ESI): m/z calcd. for [C\textsubscript{22}H\textsubscript{19}BrFNO\textsubscript{6}+H\textsuperscript{+}]: 480.0453, found: 480.0444.

**rel-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(4-methoxyphenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4h (major isomer)**
Nitrosoacetals 4,4’h was obtained from α-fluoronitroalkene 1a (70.4 mg, 0.35 mmol) and 4-vinylanisole following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded 4,4’h (114 mg, 68%, dr (4h:4’h) = 19:1, 1H NMR) as slightly yellow oil, which solidifies upon storage in a refrigerator.

Rf = 0.51 (PE/EtOAc, 1:1)

1H NMR (300 MHz, CDCl3): δ 2.63 (ddd, J = 25.0, 14.2, 7.8 Hz, 1H, CH2(4)), 3.15 (ddd, J = 20.4, 14.2, 8.3 Hz, 1H, CH2(4)), 3.32 (s, 3H, CO2Me), 3.81 (s, 3H, OMe), 3.89 (s, 3H, CO2Me), 4.93 (d, J = 4.1 Hz, 1H, Ar-CH), 5.55 (td, J = 8.0, 1.5 Hz, 1H, O-CH-Ar), 6.91 (d, J = 8.7 Hz, 2H, CHAr), 7.31-7.41 (m, 6H, CHAr). Minor isomer (characteristic signal): δ 5.40 (dd, J = 9.1, 7.5 Hz, 1H, O-CH-Ar).

13C NMR (75 MHz, CDCl3): δ 44.5 (d, 2JCF = 28.0 Hz, CH2), 52.6 (CO2Me), 54.0 (CO2Me), 55.2 (OMe), 55.7 (d, 2JCF = 22.5 Hz, CH–Ar), 85.2 (ArCH–O), 89.1 (C–O), 114.1 (CHAr), 119.1 (d, 1JCF = 221.5 Hz, C–F), 128.3 (CHAr), 128.5 (CAr), 128.6 (CHAr), 130.3 (d, 2JCF = 3.3 Hz, CAr), 132.0 (CHAr), 134.5 (CAr), 160.1 (C–OMe), 165.9 (CO2Me), 166.9 (CO2Me).


rel-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(4- (methoxycarbonyl)phenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4i
(major isomer)

Nitrosoacetals 4,4’i was obtained from α-fluoronitroalkene 1a (40.3 mg, 0.20 mmol) and methyl 4-vinylbenzoate (10 equiv.) following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded 4i,4’i (59 mg, 58%, dr (4i:4’i) = 12:1, 1H NMR) as colorless solid.

Rf = 0.46 (PE/EtOAc, 1:1)

mp = 133-135°C (CHCl3)

1H NMR (300 MHz, CDCl3): δ 2.62 (ddd, J = 24.0, 14.1, 7.4 Hz, 1H, CH2a), 3.25 (ddd, J = 20.2, 14.1, 8.6 Hz, 1H, CH2b), 3.34 (s, 3H, CO2Me), 3.89 (s, 3H, CO2Me), 3.92 (s, 3H, CO2Me), 4.95 (d, J = 4.7 Hz, 1H, Ar-CH), 5.65 (app t, J = 7.9 Hz, 1H, O-CH-Ar), 7.31-7.40 (m, 4 H, CHAr), 7.47 (d, J = 8.3 Hz, 2 H, CHAr), 8.05 (d, J = 8.3 Hz, 2 H, CHAr). Minor isomer (characteristic signal): δ 5.57 (dd, J = 9.2, 7.3 Hz, 1H, O-CH-Ar).

13C NMR (75 MHz, CDCl3, DEPT, HMBC): δ 44.6 (d, 2JCF = 27.8 Hz, CH2), 52.2 (-CO2Me), 52.7 (-CO2Me), 54.2 (-CO2Me), 55.7 (d, 2JCF = 22.4 Hz, CH–Ar), 84.2 (ArCH–O), 89.6 (C–O), 119.1 (d, 1JCF = 222.3 Hz, C–F), 126.7 (CHAr), 128.5 (CHAr), 130.1 (CHAr), 130.6 (CAr), 132.0 (CAr), 132.1 (CHAr), 134.7 (CAr), 142.3 (CAr), 165.8 (-CO2Me), 166.5 (-CO2Me), 167.0 (-CO2Me).

19F NMR (282 MHz, CDCl3): δ -131.8 (app t, J = 20.7 Hz).

HRMS (ESI): m/z calcd. for [C23H21ClFNO8 + Na]+: 516.0832, found: 516.0827.
**rel-(3R,3aR,5S)-Dimethyl 5-(biphenyl-4-yl)-3-(4-chlorophenyl)-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4j** (major isomer)

Nitrosoacetals 4j was obtained from α-fluoronitroalkene 1a (40.3 mg, 0.20 mmol) and 4-vinylbiphenyl (10 equiv.) following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded 4,4′j (63 mg, 60%, dr (4j:4′j)= 14:1, 1H NMR) as colorless oil which solidifies upon storage in a refrigerator.

Rf = 0.56 (PE/EtOAc, 1:1)

1H NMR (300 MHz, CDCl3): δ 2.71 (ddd, J = 24.6, 14.1, 7.6 Hz, CH2), 3.24 (ddd, J = 20.3, 14.1, 8.4 Hz, 1H, CH2b), 3.37 (s, 3H, CO2Me), 3.93 (s, 3H, CO2Me), 4.98 (d, J = 4.3 Hz, 1H, Ar-CH), 5.65 (app td, J = 8.3, 1.3 Hz, 1H, O-CH-Ar), 7.35-7.65 (m, 13 H, CHAr). Minor isomer (characteristic signal): δ 5.55 (dd, J = 9.4, 7.0 Hz, 1H, O-CH-Ar).

13C NMR (75 MHz, CDCl3, DEPT): δ 44.7 (d, 2JC=CF = 27.7 Hz, CH2), 52.7 (-CO2Me), 54.2 (-CO2Me), 55.8 (d, tJC=CF = 22.6 Hz, CH–Ar), 85.1 (ArCH–O), 89.4 (C–O), 119.2 (d, tJC=CF = 222.4 Hz, C–F), 127.1 (CHAr), 127.5 (CHAr), 127.6 (2 × CHAr), 128.5 (CHAr), 128.8 (CHAr), 130.3 (d, J = 3.1 Hz, CHAr), 132.1 (d, J = 0.6 Hz, CHAr), 134.7 (CHAr), 135.9 (CHAr), 140.4 (CAr), 142.0 (CAr), 166.0 (CO2Me), 167.1 (-CO2Me).

19F NMR (282 MHz, CDCl3): δ -131.3 (app t, J = 21.6 Hz).

HRMS (ESI): m/z calcd. for [C28H23ClFNO6 + H]+: 512.1271, found: 512.1255.

**rel-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(3-methoxyphenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4k** (major isomer)

Nitrosoacetals 4,4′k was obtained from α-fluoronitroalkene 1a (40.3 mg, 0.20 mmol) and 3-vinylanisole (10 equiv.) following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded 4,4′k (53 mg, 55%, dr (4k:4′k)= 7:1, 1H NMR) as colorless oil which solidifies upon storage in a refrigerator.

Rf = 0.56 (PE/EtOAc, 1:1)

1H NMR (300 MHz, CDCl3): δ 2.64 (ddd, J = 24.5, 14.1, 7.6 Hz, 1H, CH2a), 3.19 (ddd, J = 20.1, 14.1, 8.4 Hz, 1H, CH2b), 3.35 (s, 3H, CO2Me), 3.81 (s, 3H, CO2Me), 3.90 (s, 3H, OMe), 4.95 (d, J = 4.5 Hz, 1H, Ar-CH), 5.58 (app td, J = 7.9, 1.1 Hz, 1H, O-CH-Ar), 6.88-6.98 (m, 3 H, CHAr), 7.27-7.41 (m, 5 H, CHAr). Minor isomer (characteristic signal): δ 5.46 (dd, J = 9.4, 7.1 Hz, 1H, O-CH-Ar).

13C NMR (75 MHz, CDCl3, DEPT): δ 44.7 (d, tJC=CF = 27.9 Hz, CH2), 52.7 (-CO2Me), 54.2 (-CO2Me), 55.3 (-OMe), 55.8 (d, tJC=CF = 22.5 Hz, CH–Ar), 85.0 (ArCH–O), 89.5 (C–O), 112.2 (CHAr), 114.7 (CHAr), 119.1 (d, tJC=CF = 222.0 Hz, C–F), 119.1 (CHAr), 128.4 (CHAr), 129.8
(CH₂), 130.3 (d, J = 3.5 Hz, C₆H), 132.1 (CH₂), 134.7 (C₆H), 138.7 (C₆H), 160.0 (C₆H-O), 165.9 (-CO₂Me), 167.1 (-CO₂Me).

¹⁹F NMR (282 MHz, CDCl₃): δ -131.7 (app t, J = 21.9 Hz). Minor isomer: δ -134.5 (app t, J = 20.2 Hz).

HRMS (ESI): m/z calcd. for [C₂₂H₂₁ClFNO₇ + Na⁺]: 488.0883, found: 488.0883.

rel-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(naphthalen-1-yl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4l (major isomer)

Nitrosoacetals 4,4'l was obtained from α-fluoronitroalkene 1a (40.3 mg, 0.20 mmol) and 1-vinylnaphthalene (10 equiv.) following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded 4,4'l (59 mg, 59%, dr (4l:4l') = 16:1, ¹⁹F NMR) as colorless oil which solidifies upon storage in a refrigerator.

Rf = 0.62 (PE/EtOAc, 1:1)

¹H NMR (300 MHz, CDCl₃): δ 2.76 (ddd, J = 24.2, 13.9, 7.9 Hz, 1H, CH₂), 3.39 (s, 3H, CO₂Me), 3.45 (ddd, J = 22.1, 13.9, 8.2 Hz, 1H, CH₂b), 3.96 (s, 3H, CO₂Me), 5.04 (d, J = 4.6 Hz, 1H, Ar-CH), 6.30 (app t, J = 7.9 Hz, 1H, O-CH-Ar), 7.36-7.61 (m, 7H, CH₂), 7.77 (d, J = 7.2 Hz, 1H, CH₂), 7.86 (d, J = 8.3 Hz, 1H, CH₂), 7.90-7.93 (m, 2H, CH₂).

¹³C NMR (75 MHz, CDCl₃, DEPT, HSQC): δ 44.1 (d, ²JC = 27.8 Hz, CH₂), 52.8 (-CO₂Me), 54.2 (-CO₂Me), 56.4 (d, ²JC = 22.8 Hz, CH-Ar), 81.8 (ArCH-O), 90.1 (C-O), 119.3 (d, ¹JC = 222.7 Hz, C-F), 122.7 (CH₂), 123.4 (CH₂), 125.6 (CH₂), 126.0 (CH₂), 126.6 (CH₂), 128.5 (CH₂), 129.1 (CH₂), 130.2 (C₆H), 130.2 (d, J = 3.5 Hz, CH₂), 132.1 (2 × CH₂), 133.0 (C₆H), 133.7 (C₆H), 134.7 (C₆H), 165.8 (-CO₂Me), 167.4 (-CO₂Me).

¹⁹F NMR (282 MHz, CDCl₃): δ -131.6 (app t, J = 20.6 Hz). Minor isomer: δ -135.1-135.4 (m).

HRMS (ESI): m/z calcd. for [C₂₃H₂₁ClFNO₇ + Na⁺]: 508.0934, found: 508.0947.

rel-(3R,3aR,5S)-Dimethyl 5-cyano-3a-fluoro-3-(4-(methoxycarbonyl)phenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4m (major isomer) and rel-(3R,3aR,5R)-Dimethyl 5-cyano-3a-fluoro-3-(4-(methoxycarbonyl)phenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4'm (minor isomer)

Nitrosoacetals 4,4'm was obtained from α-fluoronitroalkene 1b (67.5 mg, 0.2 mmol) and acrylonitrile following the general procedure 1. Column chromatography (eluent: 7:3 PE/EtOAc) afforded 4m (69.6 mg of mixture 4m:4'm = 15:1) and 24.3 mg of 4k:4'k = 1:4.5, total yield 66%, total dr 4m:4'm = 3:1, as colorless oils.

Major isomer (4m):

Rf = 0.27 (PE/EtOAc, 3:1).
mp = 126-127 °C (PE/EtOAc, 3:1)

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 2.99 (ddd, \(J = 20.1, 14.2, 4.7\) Hz, 1H, CH\(_{2a}\)), 3.28 (s, 3H, CO\(_2\)Me), 3.34 (ddd, \(J = 23.6, 14.2, 9.5\) Hz, 1H, CH\(_{2b}\)), 3.87 (s, 3H, CO\(_2\)Me), 3.94 (s, 3H, CO\(_2\)Me), 4.94 (d, \(J = 6.1\) Hz, 1H, Ar-CH), 5.18 (dd, \(J = 9.4, 4.7\) Hz, 1H, O-CH-CN), 7.45 (d, \(J = 8.2\) Hz, 2H, CH\(_{Ar}\)), 8.04 (d, \(J = 8.3\) Hz, 2H, CH\(_{Ar}\)).

Characteristic NOESY interactions: CH(3)-CH\(_{2b}(4)\).

Characteristic HOESY interactions: F-CH\(_{2a}(4)\); CH\(_{Ar}\)-F.

\(^1\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 41.5 (d, \(^2J_{CF} = 29.0\) Hz, CH\(_2\)), 52.2 (-CO\(_2\)Me), 52.9 (-CO\(_2\)Me), 54.4 (-CO\(_2\)Me), 56.1 (d, \(^2J_{CF} = 22.5\) Hz, CH–Ar), 66.6 (CH–CN), 92.0 (C–O), 115.4 (CN), 118.9 (d, \(^1J_{CF} = 226.5\) Hz, C–F), 129.6 (CH\(_{Ar}\)), 130.6 (d, \(^4J_{CF} = 1.3\) Hz, CH\(_{Ar}\)), 130.7 (C\(_{Ar}\)), 135.3 (d, \(^3J_{CF} = 3.2\) Hz, C\(_{Ar}\)), 164.3 (-CO\(_2\)Me), 166.3 (-CO\(_2\)Me), 166.9 (-CO\(_2\)Me).

\(^1\)F NMR (282 MHz, CDCl\(_3\)): \(\delta\) -133.7 (app t, \(J = 18.9\) Hz).

HRMS (ESI): m/z calcd. for [C\(_{18}\)H\(_{17}\)FN\(_2\)O\(_8\) + Na\(^+\)]: 431.0861, found: 431.0866.

Minor isomer (4'\(n\)):

R\(_f\) = 0.38 (PE/EtOAc, 3:1).

\(^1\)H NMR (300 MHz, CDCl\(_3\), COSY, NOESY): \(\delta\) 3.15 (ddd, \(J = 24.1, 14.7, 9.6\) Hz, 1H, CH\(_{2a}\)), 3.26 (s, 3H, CO\(_2\)Me), 3.33 (ddd, \(J = 24.7, 14.7, 5.0\) Hz, 1H, CH\(_{2b}\)), 3.92 (s, 3H, CO\(_2\)Me), 3.94 (s, 3H, CO\(_2\)Me), 5.10 (s, 1H, Ar-CH), 5.32 (dd, \(J = 9.5, 4.9\) Hz, 1H, O-CH-CN), 7.48 (d, \(J = 8.3\) Hz, 2H, CH\(_{Ar}\)), 8.04 (d, \(J = 8.3\) Hz, 2H, CH\(_{Ar}\)).

Characteristic NOESY interactions: CH(3)-CH\(_{2b}(4)\).

Characteristic HOESY interactions: F-CH(5); F-CH\(_{2a}(4)\); CH\(_{Ar}\)-F.

\(^1\)C NMR (75 MHz, CDCl\(_3\), HSQC, HMBC): \(\delta\) 42.0 (d, \(^2J_{CF} = 30.4\) Hz, CH\(_2(4)\)), 52.2 (-CO\(_2\)Me), 52.8 (-CO\(_2\)Me), 54.2 (d, \(^2J_{CF} = 21.9\) Hz, CH(3)–Ar), 54.6 (CO\(_2\)Me), 68.6 (CH(5)–CN), 89.0 (C(2)–O), 116.7 (CN), 119.0 (d, \(^1J_{CF} = 226\) Hz, C–F), 129.5 (CH\(_{Ar}\)), 130.6 (C\(_{Ar}\)), 130.7 (C\(_{Ar}\)), 135.9 (d, \(^1J_{CF} = 3.3\) Hz, C\(_{Ar}\)), 135.2 (C\(_{Ar}\)), 165.2 (-CO\(_2\)Me), 166.3 (-CO\(_2\)Me), 166.4 (-CO\(_2\)Me).

\(^1\)F NMR (282 MHz, CDCl\(_3\)): \(\delta\) -133.5 (t, \(J = 24.1\) Hz).

\(^1\)N NMR (from \(^1\)H-\(^1\)\(^5\)N HMBC): \(\delta\) 285 (d, \(J = 40\) Hz).

HRMS (ESI): m/z calcd. for [C\(_{18}\)H\(_{17}\)FN\(_2\)O\(_8\) + Na\(^+\)]: 431.0861, found: 431.0857.

rel-(3R,3aR,5S)-Dimethyl 5-cyano-3a-fluoro-3-(4-methoxyphenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4\(n\) (major isomer) and rel-(3R,3aR,5R)-Dimethyl 5-cyano-3a-fluoro-3-(4-methoxyphenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4'\(n\)

Nitrosoacetalts 4,4'\(n\) was obtained from \(\alpha\)-fluoronitroalkene 1\(c\) (32 mg, 0.16 mmol) and acrylonitrile following the general procedure 1. Column chromatography (eluent: 7:3 PE/EtOAc) afforded 4\(n\) (31.2 mg) and 4'\(n\) (12.2 mg) (total yield 71%) as colorless oils which solidifies upon storage in a refrigerator.

Major isomer (4\(n\)):

R\(_f\) = 0.37 (PE/EtOAc, 1:1).
$^1$H NMR (300 MHz, CDCl$_3$, COSY, NOESY): $\delta$ 2.94 (dd, $J = 20.0, 14.2, 4.9$ Hz, 1H, CH$_2$(4)), 3.29 (ddd, $J = 19.2, 14.2, 9.4$ Hz, 1H, CH$_2$(4)), 3.33 (s, 3H, CO$_2$Me), 3.81 (s, 3H, OMe), 3.85 (s, 3H, CO$_2$Me), 4.81 (d, $J = 7.7$ Hz, 1H, CH(3)), 5.15 (ddd, $J = 9.4, 4.9, 0.6$ Hz, 1H, CH(5)), 6.88 (d, $J = 8.9$ Hz, 2H, CH$_2$Ar), 7.27 (d, $J = 8.9$ Hz, 2H, CH$_2$Ar).

Characteristic NOESY interactions: CH(3)-CH$_2$(4).

Characteristic HOESY interactions: F-CH$_2$(4).

$^{13}$C NMR (75 MHz, CDCl$_3$, HSQC, HMBC): $\delta$ 41.4 (d, $^2$J$_{CF}$ = 29.0 Hz, CH$_2$(4)), 53.0 (-CO$_2$Me), 54.4 (-CO$_2$Me), 55.3 (OMe), 55.8 (d, $^2$J$_{CF}$ = 22.7 Hz, CH(3)), 66.2 (C(5)), 92.4 (C-O), 113.8 (CH$_2$Ar), 115.6 (CN), 118.8 (d, $^1$J$_{CF}$ = 226 Hz, C-F), 121.9 (d, $^3$J$_{CF}$ = 3.3 Hz, C$_{Ar}$), 131.7 (d, $^4$J$_{CF}$ = 1.6 Hz, CH$_2$Ar), 159.9 (C$_{Ar}$-OMe), 164.4 (-CO$_2$Me), 167.2 (-CO$_2$Me).

$^{19}$F NMR (282 MHz, CDCl$_3$): $\delta$ -134.5 (td, $J = 19.5, 7.8$ Hz).

HRMS (ESI): m/z calcd. for [C$_{17}$H$_{17}$FN$_2$O$_7$+ H$^+$]: 381.1093, found: 381.1083.

Minor isomer (4’n):
R$_f$ = 0.48 (PE/EtOAc, 1:1).

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 3.11 (ddd, $J = 24.0, 14.7, 9.5$ Hz, 1H, CH$_2$a), 3.30 (ddd, $J = 24.4$, 14.7, 5.0 Hz, 1H, CH$_2$b), 3.31 (s, 3H, CO$_2$Me), 3.88 (s, 3H, OMe), 3.92 (s, 3H, CO$_2$Me), 4.98 (s, 1H, Ar-CH), 5.29 (dd, $J = 9.5, 5.0$ Hz, 1H, O-CH-CN), 6.89 (d, $J = 8.8$ Hz, 2H, CH$_2$Ar), 7.30 (d, $J = 8.8$ Hz, 2H, CH$_2$Ar).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 42.2 (d, $^2$J$_{CF}$ = 30.6 Hz, CH$_2$), 52.8 (CO$_2$Me), 53.9 (-CO$_2$Me), 53.9 (d, $^2$J$_{CF}$ = 22.1 Hz, CH- Ar), 54.5 (CO$_2$Me), 55.3 (CO$_2$Me), 68.5 (CH-CN), 89.6 (C-O), 116.7 (CN), 113.8 (CH$_2$Ar), 116.8 (CN), 119.1 (d, $^1$J$_{CF}$ = 224.4 Hz, C-F), 122.9 (CH$_2$Ar), 160.0 (-C$_{Ar}$-OMe), 165.7 (-CO$_2$Me), 166.7 (-CO$_2$Me).

$^{19}$F NMR (282 MHz, CDCl$_3$): $\delta$ -133.2 (t, $J = 23.8$ Hz).

HRMS (ESI): m/z calcd. for [C$_{17}$H$_{17}$FN$_2$O$_7$+ Na$^+$]: 403.0912, found: 403.0903.

rel-(3R,3aR,5R)-Dimethyl 5-butyl-3-(4-chlorophenyl)-3a-fluorotetrahydro-2H-isozaxolo[2,3-b]isoxazole-2,2-dicarboxylate 4o (major isomer)

Nitrosoacetals 4,4’o was obtained from α-fluoronitroalkene 1a (60.4 mg, 0.3 mmol) and 1-hexene following the general procedure 1. Column chromatography (eluent: 4:1 PE/EtOAc) afforded 4,4’o (86 mg, 66%), dr 4o:4’o = 6:1) as colorless oil which solidifies upon storage in a refrigerator. Pure sample of 4o was obtained by recrystallization (-20°C) from hexane (dr 4o:4’o = 16:1, $^1$H NMR)
R$_f$ = 0.60 (PE/EtOAc, 1:1)

$^1$H NMR (300 MHz, CDCl$_3$, COSY, NOESY): $\delta$ 0.91 (t, $J = 7.0$ Hz, CH$_3$(9)), 1.27-1.49 (m, 4H, CH$_2$(7,8)), 1.63-1.74 (m, 1H, CH$_2$(6)), 1.78-1.90 (m, 1H, CH$_2$(6)), 2.28 (ddd, $J = 25.2, 13.7, 7.7$ Hz, 1H, CH$_2$(4)), 2.85 (ddd, $J = 19.2, 13.7, 7.7$ Hz, 1H, CH$_2$(4)), 3.34 (s, 3H, CO$_2$Me), 3.86 (s, 3H, CO$_2$Me), 4.61 (pd, $J = 7.7, 1.8$ Hz, 1H, CH(5)), 4.84 (d, $J = 4.3$ Hz, 1H, CH(3)), 7.31-7.38 (m, 4H, CH$_2$Ar). Minor isomer (characteristic signal): $\delta$ 4.39-4.49 (m, 1H, CH(5)).

Characteristic NOESY interactions: CH$_2$(4)-CH(3); CH$_2$(4)-CH(5); CH$_2$(4)-CH$_2$(6).

Characteristic HOESY interactions: CH$_2$(4)-F; CH(3)-F; CH$_{Ar}$-F.
$^{13}$C NMR (75 MHz, CDCl$_3$, HSQC, HMBC): δ 13.9 (CH$_3$(9)), 22.4 and 27.8 (CH$_2$(7) and CH$_2$(8)), 33.3 (CH$_2$(6)), 42.4 (d, $^2J_{CF} = 27.6$ Hz, CH$_2$(4)), 52.6 (CO$_2$Me), 54.0 (CO$_2$Me), 56.1 (d, $^2J_{CF} = 22.9$ Hz, CH(3)), 83.9 (CH(5)), 89.4 (C(2)), 118.9 (d, $^1J_{CF} = 221.1$ Hz, C–F), 128.4 (CH$_{Ar}$), 130.4 (d, $^3J_{CF} = 3.4$ Hz, C$_{Ar}$), 132.1 (d, $^4J_{CF} = 1.3$ Hz, CH$_{Ar}$), 134.6 (C$_{Ar}$), 166.0 (CO$_2$Me), 167.1 (CO$_2$Me).

$^{19}$F NMR (282 MHz, CDCl$_3$): δ -131.3 (td, $J_{HF} = 25.2$, 19.2, 4.3 Hz). Minor isomer: δ -133.1 (ddd, $J = 23.1$, 21.5, 7.5 Hz).

$^{15}$N NMR (30 MHz, CDCl$_3$, from $^1$H–$^{15}$N-HMBC): δ 288.

HRMS (ESI): m/z calcd. for [C$_{19}$H$_{23}$ClFNO$_6$+ H$^+$]: 416.1271, found: 416.1262.

rel-(3R,3aR,5R)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(2-hydroxyethyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4p (major isomer)

Nitrosoacetals 4,4′p were obtained from α-fluoronitroalkene 1a (50.4 mg, 0.25 mmol) and 3-buten-1-ol (10 equiv.) following the general procedure 1. Column chromatography (eluent: 1:2 PE/EtOAc) afforded 4,4′p (49.6 mg, 47 %, dr (4p:4′p) = 5:1, $^{19}$F NMR) as colorless solid. R$_f$ = 0.09 (PE/EtOAc, 1:1) mp = 121-122 °C (PE/EtOAc, 1:1)

$^{1}$H NMR (300 MHz, CDCl$_3$): δ 1.73 (br s, 1H, OH), 1.92-2.12 (m, 2H, HO-CH$_2$-CH$_2$-), 2.39 (ddd, $J = 24.9$, 13.8, 7.5 Hz, 1H, CH$_2$(4)), 2.92 (ddd, $J = 19.4$, 13.7, 7.8 Hz, 1H, CH$_2$(b(4)), 3.33 (s, 3H, CO$_2$Me), 3.77-3.83 (m, 2H, CH$_2$OH), 3.86 (s, 3H, CO$_2$Me), 4.78-4.85 (m, 1H, CH–O), 4.84 (d, $J = 5.1$ Hz, 1H, Ar-CH), 7.29-7.34 (m, 4H, CH$_{Ar}$).

$^{13}$C NMR (75 MHz, CDCl$_3$, DEPT): δ 36.3 (-CH$_2$-CH$_2$-OH), 42.4 (d, $^2J_{CF} = 27.6$ Hz, CH$_2$(4)), 52.7 (CO$_2$Me), 54.0 (CO$_2$Me), 56.0 (d, $^2J_{CF} = 22.6$ Hz, CH–Ar), 59.4 (-CH$_2$OH), 81.5 (C-3), 89.6 (C–O), 119.0 (d, $^1J_{CF} = 221.5$ Hz, C–F), 128.4 (CH$_{Ar}$), 130.1 (d, $^3J_{CF} = 1.4$ Hz, C$_{Ar}$), 132.0 (d, $J = 0.9$ Hz, CH$_{Ar}$), 134.7 (C$_{Ar}$), 165.8 (CO$_2$Me), 167.0 (CO$_2$Me).

$^{19}$F NMR (212 MHz, CDCl$_3$): δ -131.6 (t, $J = 21.6$ Hz). Minor isomer: δ -133.3 (t, $J = 22.9$ Hz). HRMS (ESI): m/z calcd. for [C$_{19}$H$_{19}$ClFNO$_7$+ H$^+$]: 426.0726, found: 426.0728.

rel-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-5-ethoxy-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4q (major isomer)

Nitrosoacetals 4,4′q was obtained from α-fluoronitroalkene 1a (34 mg, 0.17 mmol) and ethyl vinyl ether following the general procedure 1. Column chromatography (eluent: 7:3 PE/EtOAc) afforded mixture of isomers 4q,4′q (59 mg, 83%, dr (4q:4′q) = 5:1) as colorless oil, which solidifies upon storage in a refrigerator.

R$_f$ = 0.46 (PE/EtOAc, 1:1)
**1H NMR (300 MHz, CDCl3, COSY, NOESY):** δ 1.24 (t, J = 7.1 Hz, CH3), 2.60 (ddd, J = 19.5, 14.1, 2.6 Hz, 1H, CH2a(4)), 3.08 (td, J = 14.1, 6.6 Hz, 1H, CH2b(4)), 3.36 (s, 3H, CO2Me), 3.51 (dq, J = 9.6, 7.1 Hz, 1H, -OHCH2-Me), 3.84 (s, 3H, CO2Me), 3.87-3.95 (m, 1H, -OHCH2-Me), 4.78 (d, J = 13.1 Hz, 1H, CH(2)), 5.32 (ddd, J = 6.6, 2.6, 0.8 Hz, 1H, CH(5)), 7.30-7.33 (m, 4H, CHAr). Minor isomer (characteristic signals): δ 2.71-2.92 (m, 2H, CH2(4)), 3.39 (s, 3H, CO2Me), 3.51-3.62 (m, 1H, -OHCH2-Me), 5.07 (d, J = 10.3 Hz, 1H, CH(2)), 5.63 (ddd, J = 5.8, 2.4 Hz, 1H, CH(5)).

Characteristic NOESY interactions (major isomer): CH2b(4)-CH(3); CH2b(4)-CH(5); CH(3)-CH(5).

Characteristic HOESY interactions (major isomer): F-CHAr; F-CH2a(4).

Characteristic HOESY interactions (minor isomer): F-CHAr.

**13C NMR (75 MHz, CDCl3, HSQC, HMBC):** δ 14.9 (CH3), 42.7 (d, JCF = 26.4 Hz, CH2), 52.8 (CO2Me), 53.9 (CO2Me), 58.3 (d, JCF = 23.8 Hz, CH(2)), 64.4 (-OHCH2-Me), 94.3 (C(2)), 102.5 (d, JCF = 3.4 Hz, C(5)), 119.3 (d, JCF = 224.4 Hz, C–F), 128.5 (CHAr), 129.2 (d, JCF = 3.2 Hz, CAr), 131.9 (d, JCF = 2.7 Hz, CHAr), 134.8 (CAr), 164.4 (CO2Me), 167.9 (CO2Me). Minor isomer: δ 14.8 (CH3), 45.3 (d, JCF = 28.7 Hz, CH2(4)), 52.7 (CO2Me), 53.7 (CO2Me), 55.8 (d, JCF = 22.0 Hz, CH(2)), 64.7 (-OHCH2-Me), 90.2 (C(2)), 109.0 (d, JCF = 1.6 Hz, C(5)), 118.8 (d, JCF = 220.2 Hz, C–F), 128.4 (CHAr), 129.7 (d, JCF = 2.1 Hz, CAr), 132.3 (d, JCF = 2.1 Hz, CHAr), 134.7 (CAr), 166.3 (CO2Me), 166.9 (CO2Me).

**19F NMR (282 MHz, CDCl3):** δ -136.9 (dt, J = 19.5, 13.3 Hz). Minor isomer: -134.0 (ddd, J = 22.2, 17.2, 10.3 Hz).

**15N NMR (30 MHz, from 1H-15N HMBC):** δ 282 (d, JNF = 44 Hz). Minor isomer: δ 287 (d, JNF = 42 Hz).


**rel-(3R,3aR,5R)-Trimethyl 3-(4-chlorophenyl)-3a-fluorotetrahydro-2H-isoxazoliz-2,3-bjisoxazole-2,2,5-tricarboxylate 4r (major isomer) and rel-(3R,3aR,5S)-Trimethyl 3-(4-chlorophenyl)-3a-fluorotetrahydro-2H-isoxazoliz-2,3-bjisoxazole-2,2,5-tricarboxylate 4r (minor isomer)**

Nitrosoacetals 4r,4′r were obtained from α-fluoronitroalkene 1a (89 mg, 0.44 mmol) and methyl acrylate following the general procedure 1. Column chromatography (eluent: 7:3 PE/EtOAc) afforded 4r (125 mg, 65%, dr (4r:4′r)= 1:1.1) as colorless which solidifies upon storage in a refrigerator. Enriched major isomer (dr = 4:1) was obtained by recrystallization (-20°C) from PE/EtOAc (10:1).

Rf = 0.31; 0.27 (PE/EtOAc, 1:1)

Major isomer (4′r):

**1H NMR (300 MHz, CDCl3, COSY, NOESY):** δ 2.83 (ddd, J = 23.7, 14.5, 9.3 Hz, 1H, CH2a(4)), 3.26 (ddd, J = 25.3, 14.5, 5.2 Hz, 1H, CH2b(4)), 3.29 (s, 3H, CO2Me), 3.81 (s, 3H, CO2Me), 3.87 (s, 3H, CO2Me), 5.01 (d, J = 2.4 Hz, 1H, CH(3)), 5.04 (dd, J = 9.3, 5.2 Hz, 1H, CH(5)), 7.31-7.38 (m, 4H, CHAr).
Characteristic NOESY interactions: CH$_2$(4)-CH(5); CH$_{2b}$(4)-CH(2).

Characteristic HOESY interactions: F-CH$_{2a}$(4); F-CH$_{Ar}$; F-CH(5).

$^{13}$C NMR (75 MHz, CDCl$_3$, HSQC, HMBC): δ 38.2 (d, $^2J_{CF}$ = 28.6 Hz, CH$_2$), 52.7 (CO$_2$Me), 52.9 (CO$_2$Me), 54.0 (CO$_2$Me), 54.3 (d, $^2J_{CF}$ = 21.9 Hz, CH(2)), 79.8 (C(5)), 89.4 (C(2)), 118.6 (d, $^1J_{CF}$ = 223.9 Hz, C-F), 128.4 (CH$_{Ar}$), 130.0 (d, $^2J_{CF}$ = 3.2 Hz, C$_{Ar}$), 132.1 (d, $^4J_{CF}$ = 1.3 Hz, CH$_{Ar}$), 134.7 (C$_{Ar}$), 165.6 (CO$_2$Me), 166.2 (CO$_2$Me), 169.6 (CO$_2$Me).

$^{19}$F NMR (282 MHz, CDCl$_3$): δ -134.1 (td, $J$ = 24.6, 2.3 Hz).

$^{15}$N NMR (30 MHz, from $^1$H-$^{15}$N HMBC): δ 284 (d, $^2J_{NF}$ = 50 Hz).

Minor isomer (4r):

$^1$H NMR (300 MHz, CDCl$_3$ COSY, NOESY): δ 2.91 (ddd, $J$ = 18.2, 14.1, 9.7 Hz, 1H, CH$_{2a}$(4)), 3.11 (ddd, $J$ = 18.2, 14.1, 9.7 Hz, 1H, CH$_{2b}$(4)), 3.34 (s, 3H, CO$_2$Me), 3.84 (s, 3H, CO$_2$Me), 3.86 (s, 3H, CO$_2$Me), 4.89 (d, $J$ = 8.0 Hz, 1H, CH(3)), 4.96 (dd, $J$ = 9.7, 5.9 Hz, 1H, CH(5)), 7.25-7.36 (m, 4H, CH$_{Ar}$).

Characteristic NOESY interactions: CH$_2$(4)-CH(5); CH$_{2b}$(4)-CH(5); CH$_{2b}$(4)-CH(2).

Characteristic HOESY interactions: F-CH$_{2a}$(4); F-CH$_{Ar}$.

$^{13}$C NMR (75 MHz, CDCl$_3$, HSQC, HMBC): δ 39.1 (d, $^2J_{CF}$ = 28.4 Hz, CH$_2$(4)), 52.7 (CO$_2$Me), 53.0 (CO$_2$Me), 54.0 (CO$_2$Me), 56.0 (d, $^2J_{CF}$ = 22.7 Hz, CH(3)), 78.0 (C(5)), 91.7 (C(2)), 118.7 (d, $^1J_{CF}$ = 224.4 Hz, C-F), 128.6 (CH$_{Ar}$), 129.4 (d, $^3J_{CF}$ = 3.1 Hz, C$_{Ar}$), 132.0 (d, $^4J_{CF}$ = 1.9 Hz, CH$_{Ar}$), 134.9 (C$_{Ar}$), 165.0 (CO$_2$Me), 167.3 (CO$_2$Me), 169.0 (CO$_2$Me).

$^{19}$F NMR (282 MHz, CDCl$_3$): δ -136.0 (ddd, $J$ = 21.3, 18.2, 8.3 Hz).

$^{15}$N NMR (30 MHz, from $^1$H-$^{15}$N HMBC): δ 284 (d, $^2J_{NF}$ = 38 Hz).

HRMS (ESI): m/z calcd. for [C$_{17}$H$_{17}$ClFNO$_3$+Na$^+$]: 440.0519, found: 440.0523.

rel-(3R,3aR,5R)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-methyl-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4s (major isomer) and rel-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-methyl-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4’s (minor isomer)

Nitrosoacetals 4,s was obtained from α-fluoronicotinolene 1a (70.4 mg, 0.35 mmol) and α-methylstyrene following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded mixture of diastereomers 4s,4’s (101 mg, 62%), dr (4s:4’s)= 1.1:1 as colorless oil.

R$_f$ = 0.60 (PE/ EtOAc, 1:1)

Major isomers (4s):

$^1$H NMR (300 MHz, CDCl$_3$, COSY, NOESY): δ 1.74 (s, 3H, Me), 2.90 (dd, $J$ = 22.6, 14.1 Hz, 1H, CH$_{2a}$(4)), 3.13 (dd, $J$ = 27.1, 14.1 Hz, 1H, CH$_{2b}$(4)), 3.29 (s, 3H, CO$_2$Me), 3.42 (s, 3H, CO$_2$Me), 4.78 (d, $J$ = 4.7 Hz, 1H, Ar-CH), 7.26-7.49 (m, 9H, CH$_{Ar}$).

Characteristic NOESY interactions: Me-CH$_2$(4); CH(3)-CH$_{2b}$(4).

Characteristic HOESY interactions: F-CH$_{2a}$(4); F-Me; F-CH$_{Ar}$; F-CH(3).

$^{13}$C NMR (75 MHz, CDCl$_3$, HSQC, HMBC): δ 30.8 (Me), 48.8 (d, $^2J_{CF}$ = 25.8 Hz, CH$_2$(4)), 52.6 (CO$_2$Me), 53.6 (CO$_2$Me), 55.3 (d, $^2J_{CF}$ = 22.9 Hz, CH(3)), 90.1 (C(2)), 91.3 (CH(5)); 119.7 (d,
$^{1}J_{CF}$ = 221.7 Hz, C-F), 124.3 (CH$_{ar}$), 127.1 (CH$_{ar}$), 128.1 (CH$_{ar}$), 128.4 (CH$_{ar}$), 130.1 (d, $^{3}J_{CF}$ = 3.3 Hz, C$_{ar}$), 132.1 (d, $^{4}J_{CF}$ = 1.1 Hz, CH$_{ar}$), 134.6 (C$_{ar}$), 145.6 (C$_{ar}$), 165.8 (CO$_{2}$Me), 166.7 (CO$_{2}$Me).

$^{19}$F NMR (282 MHz, CDCl$_{3}$): δ -134.1 (ddd, $J$ = 27.1, 22.6, 4.7 Hz).

$^{15}$N NMR (30 MHz, from $^{1}$H-$^{15}$N HMBC): δ 285 (d, $^{2}J_{NF}$ = 47 Hz).

Minor isomer (4’s):

$^{1}$H NMR (300 MHz, CDCl$_{3}$, COSY, NOESY): δ 1.67 (s, 3H, Me), 2.97-3.14 (m, CH$_{2}$(4)), 3.37 (s, 3H, CO$_{2}$Me), 3.90 (s, 3H, CO$_{2}$Me), 4.92 (d, $^{2}J_{HF}$ = 8.6 Hz, 1H, Ar-CH), 7.26-7.49 (m, 9H, CH$_{ar}$).

Characteristic HOESY interactions: F-Ar; F-CH(3); F-Ph.

$^{13}$C NMR (75 MHz, CDCl$_{3}$, HSQC, HMBC): δ 29.4 (Me), 49.8 (d, $^{2}J_{CF}$ = 25.3 Hz, CH$_{2}$(4)), 52.8 (CO$_{2}$Me), 53.9 (CO$_{2}$Me), 58.2 (d, $^{2}J_{CF}$ = 24.0 Hz, CH(3)), 86.3 (CH(5)), 93.7 (C(2)), 120.7 (d, $^{1}J_{CF}$ = 223.2 Hz, C-F), 124.4 (CH$_{ar}$), 127.3 (CH$_{ar}$), 128.2 (CH$_{ar}$), 128.4 (CH$_{ar}$), 129.7 (d, $^{3}J_{CF}$ = 3.6 Hz, C$_{ar}$), 131.9 (d, $^{4}J_{CF}$ = 2.0 Hz, CH$_{ar}$), 134.6 (C$_{ar}$), 144.6 (C$_{ar}$), 164.6 (CO$_{2}$Me), 167.9 (CO$_{2}$Me).

$^{19}$F NMR (282 MHz, CDCl$_{3}$): δ -131.5 (td, $J$ = 21.2, 8.7 Hz).

$^{15}$N NMR (30 MHz, from $^{1}$H-$^{15}$N HMBC): δ 283 (d, $^{2}J_{NF}$ = 42 Hz).

HRMS (ESI): m/z calcd. for [C$_{2}$_H$_{2}$ClF$_{2}$NO$_{2}$+ H$^+$]: 450.1114, found: 450.1112.

rel-(3R,3aR,5R)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-methoxy-5-methyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4t (minor isomer)

Nitrosoacetals 4,4’t was obtained from α-fluoronitroalkene 1a (60.4 mg, 0.3 mmol) and 2-methoxypropene following the general procedure 1. Column chromatography (eluent: 2:1 PE/EtOAc) afforded mixture of diastereomers 4t,4’t (61 mg, 48%, dr (4t:4’t) = 1.5:1) as slightly yellow oil, which solidifies upon storage in a refrigerator.

Major isomer (4t):

R$_{f}$ = 0.47 (PE/EtOAc, 1:1)

$^{1}$H NMR (300 MHz, CDCl$_{3}$): δ 1.60 (Me), 2.63 (dd, $J$ = 23.5, 14.2, 1H, CH$_{2}$(4)), 2.96 (dd, $J$ = 15.3, 14.2, 1H, CH$_{2}$(4)), 3.33 (s, 3H, OMe), 3.41 (s, 3H, CO$_{2}$Me), 3.83 (s, 3H, CO$_{2}$Me), 5.05 (d, $J$ = 10.7 Hz, 1H, CH(3)), 7.27-7.39 (m, 4H, CH$_{ar}$).

Characteristic NOESY interactions: Me-CH$_{2}$(4); CH(3)-CH$_{2}$(4).

Characteristic HOESY interactions: F-CH$_{ar}$; F-CH(3); F-CH$_{2}$(4).

$^{13}$C NMR (75 MHz, CDCl$_{3}$): δ 21.2 (Me), 49.4 (d, $^{2}J_{CF}$ = 28.7 Hz, CH$_{2}$(4)), 50.0 (OMe), 52.7 (CO$_{2}$Me), 53.6 (CO$_{2}$Me), 56.5 (d, $^{2}J_{CF}$ = 22.7 Hz, CH(3)), 90.2 (C(2)), 115.5 (d, $^{3}J_{CF}$ = 1.7 Hz, C(5)), 119.9 (d, $^{1}J_{CF}$ = 219.4 Hz, C-F), 128.4 (CH$_{ar}$), 129.7 (d, $^{3}J_{CF}$ = 2.4 Hz, C$_{ar}$), 132.3 (d, $^{4}J_{CF}$ = 2.2 Hz, CH$_{ar}$), 134.7 (C$_{ar}$), 166.4 (-CO$_{2}$Me), 167.1 (-CO$_{2}$Me).

$^{19}$F NMR (282 MHz, CDCl$_{3}$): δ -130.7 (ddd, $J$ = 23.5, 15.3, 10.7 Hz).

$^{15}$N NMR (30 MHz, from $^{1}$H-$^{15}$N HMBC): δ 289 (d, $^{2}J_{NF}$ = 48 Hz).
Minor isomer (4'i):

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 1.46 (Me), 2.76 (dd, $J = 20.6, 14.2, 1H, CH$_2$(4)), 2.93 (dd, $J = 17.4, 14.2, 1H, CH$_2$(4)), 3.37 (s, 3H, CO$_2$Me), 3.38 (s, 3H, OMe), 3.84 (s, 3H, CO$_2$Me), 4.77 (d, $J = 10.1$ Hz, 1H, CH(3)), 7.27-7.39 (m, 4H, CH$_2$Ar).  

Characteristic NOESY interactions: Me-CH$_2$b(4); CH(3)-CH$_2$b(4). 

Characteristic HOESY interactions: F-CH$_2$Ar; F-CH(3); F-CH$_2$a(4). 

$^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 20.2 (Me), 48.9 (d, $^2$J$_{CF}$ = 25.8 Hz, CH$_2$(4)), 49.6 (OMe), 52.9 (CO$_2$Me), 53.8 (CO$_2$Me), 59.5 (d, $^2$J$_{CF}$ = 25.0 Hz, CH(3)), 95.3 (C(2)), 106.4 (d, $^2$J$_{HF}$ = 2.4 Hz, C(5)), 120.6 (d, $^1$J$_{CF}$ = 224.4 Hz, C-F), 128.4 (CH$_2$Ar), 129.3 (d, $^3$J$_{CF}$ = 4.0 Hz, C$_{Ar}$), 131.8 (d, $^4$J$_{CF}$ = 2.3 Hz, CH$_2$Ar), 134.7 (C$_{Ar}$), 163.9 (CO$_2$Me), 167.9 (CO$_2$Me). 

$^{19}$F NMR (282 MHz, CDCl$_3$): $\delta$ -130.2 (ddd, $J = 20.6, 17.4, 10.1$ Hz). 

$^{15}$N NMR (30 MHz, from $^1$H-$^{15}$N HMBC): $\delta$ 284 (d, $^2$J$_{NF}$ = 46 Hz). 

HRMS (ESI): m/z calcd. for [C$_{17}$H$_{19}$ClFNO$_7$ + Na$^+$]: 426.0726, found: 426.0718.

rel-(3R,3aR)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5,5-dimethyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4u 

Nitrosoacetal 4u was obtained from $\alpha$-fluoronitroalkene 1a (60.4 mg, 0.3 mmol) and isobutylene following the general procedure 1. Column chromatography (eluent: 3:1 PE/EtOAc) afforded 4u (67 mg, 55%, single diastereomer) as colorless solid. 

R$_f$ = 0.62 (PE/EtOAc, 1:1) 

mp = 98-100 °C (PE/EtOAc, 1:1) 

$^1$H NMR (300 MHz, CDCl$_3$): COSY, NOESY): $\delta$ 1.45 (s, 3H, Me$_b$), 1.47 (s, 3H, Me$_c$), 2.48 (dd, $J = 21.7, 13.8$ Hz, 1H, CH$_2$(4)), 2.68 (ddd, $J = 25.3, 13.8$ Hz, 1H, CH$_2$(4)), 3.32 (d, 3H, CO$_2$Me), 3.84 (s, 3H, CO$_2$Me), 4.83 (d, $J = 6.7$ Hz, 1H, CH(3)), 7.31 (s, 4H, CH$_2$Ar). 

Characteristic NOESY interactions: Me$_c$-CH$_2$a(4); Me$_b$-CH$_2$b(4). 

Characteristic HOESY interactions: F-CH$_2$a(4); F-CH$_2$Ar; F-CH(3); F-Me$_c$. 

$^{13}$C NMR (75 MHz, CDCl$_3$, HSQC, HMBC): $\delta$ 28.1 (2 × Me), 48.3 (d, $^2$J$_{CF}$ = 25.1 Hz, CH$_2$(4)), 52.6 (CO$_2$Me), 53.8 (CO$_2$Me), 56.8 (d, $^2$J$_{CF}$ = 23.1 Hz, CH(3)), 86.0 (C(5)), 91.6 (C(2)), 120.1 (d, $^1$J$_{CF}$ = 221.8 Hz, C-F), 128.3 (CH$_2$Ar), 130.1 (d, $J_{CF}$ = 3.7 Hz, C$_{Ar}$), 132.0 (d, $J_{CF}$ = 1.7 Hz, CH$_2$Ar), 134.5 (C$_{Ar}$), 165.3 (CO$_2$Me), 167.7 (CO$_2$Me). 

$^{19}$F NMR (282 MHz, CDCl$_3$): $\delta$ -32.8 (ddd, $J = 25.3, 21.7, 6.7$ Hz). 

$^{15}$N NMR (30 MHz, from $^1$H-$^{15}$N HMBC): $\delta$ 285 (d, $^2$J$_{NF}$ = 44 Hz). 

HRMS (ESI): m/z calcd. for [C$_{17}$H$_{19}$ClFNO$_6$ + H$^+$]: 388.0958, found: 388.0958. 

rel-(3R,3aR,5S)-diethyl 3-(4-chlorophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4v (major isomer)
Nitrosoacetals 4,4’v was obtained from α-fluoronitroalkene 1a (75 mg, 0.37 mmol) and styrene following the general procedure 1 with diethyl bromomalonate (92 mg, 0.41 mmol, 1.1 equiv.) instead of diethyl bromomalonate. Column chromatography (eluent: 9:1, then 3:1, then 7:3 PE/EtOAc) afforded 4,4’v (126 mg, 75%, dr = 7:1, 1H NMR) as slightly yellow oil.

Rf = 0.63 (PE/EtOAc, 1:1).

1H NMR (300 MHz, CDCl3): δ 0.90 (t, J = 7.1 Hz, 3 H, Me), 1.32 (t, J = 7.1 Hz, 3 H, Me), 2.64 (ddd, J = 24.9, 14.1, 7.7 Hz, 1H, CH2a(4)), 3.22 (ddd, J = 20.0, 14.1, 8.4 Hz, 1H, CH2b(4)), 3.67-3.77 (m, 1H, CH2aO), 3.81-3.92 (m, 1H, CH2bO), 4.27-4.44 (m, 2H, CH2aO), 4.96 (d, J = 3.7 Hz, 1H, Ar-CH), 5.59 (td, J = 8.0, 1.2 Hz, 1H, O-CH-Ar), 7.32-7.43 (m, 9H, CHAr). Minor isomer (characteristic signal): δ 5.49 (dd, J = 9.3, 7.2 Hz, 1H, O-CH-Ar).

13C NMR (75 MHz, CDCl3, DEPT): δ 13.5 (Me), 13.9 (Me), 44.8 (d, 1/2JCF = 28.1 Hz, CH2), 55.6 (d, 1/2JCF = 22.6 Hz, CH–Ar), 62.2 (CH2O), 63.4 (CH2O), 85.1 (ArCH–O), 89.3 (C–O), 119.3 (d, 1/2JCF = 221.5 Hz, C–F), 127.0 (CHAr), 128.4 (CHAr), 128.8 (CHAr), 128.9 (CHAr), 130.5 (d, 1/2JCF = 3.3 Hz, CAr), 132.3 (CHAr), 134.6 (CAr), 137.1 (CAr), 165.4 (CO2Et), 166.6 (CO2Et).

19F NMR (282 MHz, CDCl3): δ -131.2 (t, J = 22.3 Hz). Minor isomer: δ -134.5 (t, J = 21.4 Hz).

HRMS (ESI): m/z calcd. for [C23H23ClFNO6 + Na]+: 486.1090, found: 486.1086.

**Rel-1,1’-(3R,3aR,5S)-3-(4-chlorophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-bjisoxazole-2,2-diyldiethanone 4w** (major isomer)

Nitrosoacetals 4,4’w was obtained from α-fluoronitroalkene 1a (75 mg, 0.37 mmol) and styrene following the general procedure 1 with 3-chloro-2,4-pentandione (55 mg, 0.41 mmol, 1.1 equiv.) instead of dimethylbromomalonate. Column chromatography (eluent: 9:1, then 3:1, then 7:3 PE/EtOAc) afforded 4,4’w (36 mg, 24%, dr = 8:1, 1H NMR) as slightly yellow oil.

Rf = 0.55 (PE/EtOAc, 1:1).

1H NMR (300 MHz, CDCl3): δ 2.16 (Me), 2.27 (Me), 2.65 (ddd, J = 22.7, 14.1, 7.7 Hz, 1H, CH2a(4)), 2.94 (ddd, J = 17.0, 14.1, 8.3 Hz, 1H, CH2b(4)), 4.92 (d, J = 7.3 Hz, 1H, Ar-CH), 5.45 (td, J = 8.1, 1.1 Hz, 1H, O-CH-Ar), 7.33-7.43 (m, 9H, CHAr). Minor isomer (characteristic signal): δ 5.35 (dd, J = 9.8, 6.4 Hz, 1H, O-CH-Ar).

13C NMR (75 MHz, CDCl3, HMBC): δ 25.6 (Me), 27.8 (Me), 44.3 (d, 1/2JCF = 27.3 Hz, CH2), 54.0 (d, 1/2JCF = 21.9 Hz, CH–Ar), 84.1 (ArCH–O), 89.1 (C–O), 100.0 (C–O), 119.6 (d, 1/2JCF = 234 Hz, C–F), 126.8 (CHAr), 128.8 (CHAr), 128.9 (CHAr), 129.0 (CHAr), 129.8 (d, 1/2JCF = 3.0 Hz, CAr), 132.1 (d, 1/2JCF = 1.9 Hz, CHAr), 134.7 (CAr), 137.4 (CAr), 198.8 (C=O), 203.8 (C=O).

19F NMR (282 MHz, CDCl3): δ -133.1 (app t, J = 17.4 Hz).


**Reaction of bromo-malonate, styrene and β-nitrostyrene 5.**

Application of the general procedure 1 for p-methoxy-β-nitrostyrene 5 led to the formation of nitrocyclopropane 6 (Yield 57%, according to 1H NMR with 1,4-dinitrobenzene as standard). The spectral characteristics match previously reported data.9
1-[(Z)-2-chloro-2-nitroethenyl]-4-(methoxy)benzene 7a

Obtained by modified literature procedure. To the stirring solution of p-methoxy-β-nitrostyrene 5 (0.20 g, 1.1 mmol) and pyridine (0.18 mL, 2.2 mmol, 2 equiv.) in THF (2.2 mL) PhICl₂ (0.46 g, 1.7 mmol, 1.5 equiv.) was added. The reaction mixture was stirred overnight and poured into EtOAc (40 mL)/ H₂O (30 mL) mixture. Organic layer was washed with NaHSO₄ (0.5 M in H₂O, 20 mL), brine (20 mL), dried over Na₂SO₄ and evaporated. Crude product was purified by column chromatography on silica gel (elucent: PE, then PE/EtOAc = 9:1) to afford 7a (0.13 g, 54%) as a yellow solid. ¹H NMR matched previously reported data. Rₚ = 0.29 (PE/EtOAc, 9:1).

¹H NMR (300 MHz, CDCl₃): 3.91 (s, 3H, OMe), 7.02 (d, J = 8.9 Hz, 2H, CH₂), 7.87 (d, J = 8.9 Hz, 2H, CH₂), 8.36 (s, 1H, =CH).

¹³C NMR (75 MHz, CDCl₃): δ 55.6 (OMe), 114.7 (CH₂), 122.1 (C₅), 131.7 (=CH), 133.6 (CH₂), 162.7 (C₆=O). C–NO₂ could not be unambiguously identified due to broadening/low intensity.

3-Chloro-5,5-bis(methoxycarbonyl)-4-(4-methoxyphenyl)-4,5-dihydroisoxazole 2-oxide 8a

To the solution of p-methoxy-β-chloro-β-nitrostyrene 7a (26.5 mg, 0.12 mmol), dimethyl bromomalonate (29 mg, 0.14 mmol, 1.1 equiv.) and acrylonitrile (127 mg, 2.4 mmol, 20 equiv.) in dry DMF (2.4 ml) finely powdered K₂CO₃ (25 mg, 0.18 mmol, 1.5 equiv.) was added at 0 °C. Mixture was stirred for 20 min, warmed to r.t. and stirred for additional 1 hour (TLC monitoring). After that the reaction mixture was poured into t-BuOMe (40 mL) / H₂O (30 mL). Organic layer was washed with H₂O (20 mL), brine (20 mL), dried over Na₂SO₄ and evaporated. Crude product was purified by column chromatography on silica gel (elucent: PE/EtOAc = 5:1, then 1:1) to afford 8a (38.9 mg, 91%) as a colorless oil.

Rₚ = 0.20 (PE/EtOAc, 1:1).

¹H NMR (300 MHz, CDCl₃): δ 3.35 (s, 3H, CO₂Me), 3.82 (s, 3H, OMe), 3.92 (s, 3H, CO₂Me), 5.39 (s, 1H, Ar-CH), 6.91 (d, J = 8.7 Hz, 2H, CH₂), 7.18 (d, J = 8.7 Hz, 2H, CH₂).

¹³C NMR (75 MHz, CDCl₃, DEPT, HMBC): δ 53.1 (CO₂Me), 54.3 (CO₂Me), 54.8 (CH(4)), 55.3 (OMe), 84.8 (C(5)), 109.2 (C(3)), 114.4 (CH₂), 123.0 (C₃), 130.3 (CH₂), 160.5 (C₆=O), 163.5 (-CO₂Me), 165.9 (-CO₂Me).

HRMS (ESI): m/z calcd. for [C₁₄H₁₄⁵ClNO₇ + NH₄⁺]: 361.0797, found: 361.0798.
3-Bromo-5,5-bis(methoxycarbonyl)-4-(4-methoxyphenyl)-4,5-dihydroisoxazole 2-oxide 8b

To the solution of p-methoxy-β-bromo-β-nitrostyrene 7b (26.2 mg, 0.1 mmol), dimethyl bromomalonate (25 mg, 0.11 mmol, 1.1 equiv.) and acrylonitrile (106 mg, 2 mmol, 20 equiv.) in dry DMF (1 ml) finely powdered K₂CO₃ (21 mg, 0.15 mmol, 1.5 equiv.) was added. Mixture was stirred at r. t. for 1 hour (TLC monitoring). After that the reaction mixture was poured into H₂O, and product was extracted with t-BuOMe (3 x 30 ml). Organic layer was dried over anhydrous Na₂SO₄ and evaporated under reduced pressure. Crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOA c = 2:1) to afford 8b (31.0 mg, 76%) as a colorless oil.

Rf = 0.45 (PE/EtOAc, 1:1).

¹H NMR (300 MHz, CDCl₃): δ 3.34 (s, 3H, CO₂Me), 3.81 (s, 3H, OMe), 3.91 (s, 3H, CO₂Me), 5.39 (s, 1H, Ar-CH), 6.90 (d, J = 8.8 Hz, 2H, CHAr), 7.15 (d, J = 8.8 Hz, 2H, CHAr).

¹³C NMR (75 MHz, CDCl₃): δ 53.1 (CO₂Me), 54.2 (CO₂Me), 55.3 (Ome), 56.6 (CH(4)), 85.2 (C(5)), 97.1 (C(3)), 114.3 (CHAr), 123.5 (CAr), 130.3 (CAr), 160.4 (CAr-OMe), 164.3 (-CO₂Me), 166.0 (-CO₂Me).


Synthesis of 3-fluroisoxazolines 9a-9b.

To the solution of 3-cyano-substituted fluorinated nitrosoacetal 4 (0.05 mmol) in CH₂Cl₂ (0.5 ml) Et₃N (0.10mmol, 10 mg, 2 equiv.) was added. Mixture was stirred at r.t. for 48 hours, then evaporated on silica gel and purified by column chromatography (PE/EtOAc, 3:1) to afford isoxazolines 9 as colorless oils.

Dimethyl 4-(4-chlorophenyl)-3-fluoroisoxazole-5,5(4H)-dicarboxylate 9a

Yield 13.2 mg (64%). Rf = 0.48 (PE/EtOAc, 1:1).

¹H NMR (300 MHz, CDCl₃): δ 3.39 (s, 3H, CO₂Me), 3.93 (s, 3H, CO₂Me), 5.37 (d, JHF = 4.5 Hz, 1H, Ar-CH), 7.21 (d, J = 8.4 Hz, 2H, CHAr), 7.40 (d, J = 8.4 Hz, 2H, CHAr).

¹³C NMR (75 MHz, CDCl₃): δ 52.6 (d, JₐHF = 24.4 Hz, C(4)), 52.9 (CO₂Me), 54.2 (CO₂Me), 93.7 (d, JCF = 3.5 Hz, C(5)), 128.3 (d, JCF= 3.7 Hz, CAr), 129.4 (CHAr), 130.3 (CHAr), 135.7 (CAr), 163.9 (-CO₂Me), 166.2 (-CO₂Me), 166.8 (d, JCF = 286.5 Hz, C(3)).

¹⁹F NMR (282 MHz, CDCl₃): δ -120.5 (s).

HRMS (ESI): m/z calcd. for [C₁₃H₁₁ClFNO₅ + Na⁺]: 338.0202, found: 338.0202.
Dimethyl 3-fluoro-4-(4-(methoxycarbonyl)phenyl)isoxazole-5,5(4H)-dicarboxylate 9m

Yield 15.0 mg (68%). Rf = 0.45 (PE/EtOAc, 1:1).

1H NMR (300 MHz, CDCl3): δ 3.31 (s, 3H, CO2Me), 3.95 (s, 3H, CO2Me), 3.96 (s, 3H, CO2Me), 5.45 (d, JHF = 4.5 Hz, 1H, Ar-CH), 7.35 (d, J = 7.8 Hz, 2H, CHAr), 8.09 (d, J = 7.8 Hz, 2H, CHAr).

13C NMR (75 MHz, CDCl3): δ 52.3 (-CO2Me), 52.9 (CO2Me), 53.0 (d, JCF = 24.4 Hz, Ar-CH), 54.2 (CO2Me), 93.8 (d, JCF = 3.6 Hz, C–O), 129.0 (CHAr), 130.2 (CHAr), 131.3 (CHAr), 134.7 (d, JCF = 3.6 Hz, CHAr), 163.8 (C=O), 166.1 (C=O), 166.8 (d, JCF = 286.8 Hz, C=N).

19F NMR (282 MHz, CDCl3): δ -120.1 (s).

HRMS (ESI): m/z calcd. for [C18H14FNO7 + Na+]: 362.0647, found: 362.0648.

Dimethyl 2-hydroxy-2-(2-(hydroxyimino)-1-(4-methoxyphenyl)-4-phenylbutyl)malonate 10

To the solution of nitroso acetal 4e (57.6 mg, 0.13 mmol) in MeOH (0.53 mL) over 10% Pd/C (23 mg) was added. The mixture was hydrogenated with stirring at 30 atm of H2 for 14 hours. After that it was filtered through Celite®, Celite® was washed with MeOH (20 mL) and combined filtrate was evaporated. Column chromatography (PE/EtOAc, 3:1 then 1:1) afforded oxime 10 (24.3 mg, 44%) as colorless oil.

Rf = 0.22 (PE/EtOAc, 1:1).

1H NMR (300 MHz, CDCl3, COSY): δ 2.13-2.21 (m, 1H) and 2.66-2.89 (m, 3H) (2xCH2), 3.65 (s, 3H, CO2Me), 3.80 (s, 3H, OMe), 3.84 (s, 3H, CO2Me), 4.65 (s, 1H, Ar-CH), 5.26 (br s, 1H, OH), 6.86 (d, J = 8.7 Hz, 2H, CHAr), 7.12-7.15 (m, 2H, CHAr), 7.17-7.21 (m, 1H, CHAr), 7.24-7.30 (m, 4H, CHAr), 8.10 (br s, 1H, OH).

13C NMR (75 MHz, CDCl3, HSQC, HMBC): δ 30.2 (CH2), 31.3 (CH2), 53.18 (CH–Ar), 53.23 (-CO2Me), 53.5 (CO2Me), 55.2 (OMe), 82.5 (C–O), 113.9 (CHAr), 125.6 (CHAr), 126.1 (CHPh), 128.2 (CHAr), 128.4 (CHAr), 131.4 (CHAr), 141.2 (CHPh), 159.5 (CHAr–OMe), 160.8 (C=O), 168.2 (C=O), 170.4 (C=O).


rel-(3R,3aR,5S)-3a-Fluroo-3-(4-fluorophenyl)-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-diyl)dimethanol 13

To the stirred solution of nitrosoacetal 4d (40 mg, 0.09 mmol) in THF (0.9 mL) lithium aluminium hydride was added in small portions for 5 min. The mixture was stirred at room
temperature for 4 hours, then poured into EtOAc/aqueous KOH (5% solution). Water layer was extracted with EtOAc (4×20 ml), combined organic layer was washed with brine, dried over anhydrous Na$_2$SO$_4$ and evaporated. Column chromatography (2:3 PE/EtOAc) afforded 13 (21 mg, 54%) as colorless solid. 

R$_f$ = 0.15 (PE/EtOAc, 1:1) 

mp = 141-143 °C (CHCl$_3$) 

$^1$H NMR (300 MHz, acetone-d$_6$): $\delta$ 2.47 (ddd, J = 22.2, 12.8, 10.3 Hz, 1H, CH$_2$(4)), 3.14-3.25 (m, 2H, CH$_2$(4) and CH$_2$O), 3.48 (dd, J = 12.5, 7.7 Hz, 1H, CH$_2$O), 3.57 (br dd, J = 6.7, 5.6 Hz, 1H, OH), 3.89 (dd, J = 11.9, 4.8 Hz, 1H, CH$_2$O), 3.96 (dd, J = 12.5, 4.7 Hz, 1H, CH$_2$O), 4.21 (dd, J = 7.7, 4.7 Hz, 1H, OH), 4.45 (d, J = 21.9 Hz, 1H, Ar-CH), 5.91 (dd, J = 10.2, 5.8 Hz, 1H, O-CH-Ph), 7.14 (t, J = 8.8 Hz, 2H, CH$_2$Ar), 7.37-7.57 (m, 7H, CH$_2$Ar). 

$^1$H NMR (300 MHz, acetone-d$_6$, after H/D-exchange; 10 d storage): $\delta$ 2.47 (ddd, J = 22.2, 12.8, 10.3 Hz, 1H, CH$_2$(4)), 3.08-3.17 (m, 1H, CH$_2$(4)), 3.18 (d, J = 12.0 Hz, CH$_2$O), 3.44 (d, J = 12.5 Hz, 1H, CH$_2$O), 3.88 (d, J = 12.0 Hz, 1H, CH$_2$O), 3.93 (d, J = 12.5 Hz, 1H, CH$_2$O), 4.40 (d, J = 21.9 Hz, 1H, Ar-CH), 5.89 (dd, J = 10.2, 5.8 Hz, 1H, O-CH-Ph), 7.10 (t, J = 8.8 Hz, 2H, CH$_2$Ar), 7.37-7.57 (m, 7H, CH$_2$Ar). 

$^{13}$C NMR (75 MHz, acetone-d$_6$, DEPT, HMBC): $\delta$ 47.4 (d, $^{2}J_{CF}$ = 29.0 Hz, CH(3)-Ar), 54.1 (d, $^{2}J_{CF}$ = 20.1 Hz, CH$_2$(4)), 62.1 (CH$_2$OH), 63.1 (CH$_2$OH), 85.6 (CH–Ph), 87.6 (C(2)), 115.5 (d, $^{2}J_{CF}$ = 21.3 Hz, CH$_2$Ar), 122.1 (d, $^{1}J_{CF}$ = 218.6 Hz, C–F), 128.0 (CH$_2$Ph), 129.4 (br s, C$_{Ar}$), 129.5 (CH$_2$Ph), 129.6 (CH$_2$Ph), 134.3 (dd, $^{2}J_{CF}$ = 8.1, 3.6 Hz, CH$_2$Ar), 137.9 (C$_{Ph}$), 162.4 (d, $^{1}J_{CF}$ = 245.1 Hz, C$_{Ar}$). 

$^{19}$F NMR (282 MHz, acetone-d$_6$): $\delta$ -115.6 (br s, 1F, Ar-F), -129.0-129.3 (m, 1F, N–C–F). 

HRMS (ESI): m/z calcd. for [C$_{19}$H$_{19}$F$_2$NO$_4$+ H$^+$]: 386.1174, found: 386.1164.
References:


(s8) X.-F. Zhao, C. Zhang, *Synthesis*, 2007, **551**.


(s11) D. Dauzonne, P. Demerseman, *Synthesis*, 1990, **66**.
*rel*-[(3R,3aR,5S)]-Dimethyl 3-(4-chlorophenyl)-5-cyano-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4a (major isomer)

$^1$H NMR
$^{13}$C NMR
$^{19}$F NMR
rel-(3R,3aR,5R)-Dimethyl 3-(4-chlorophenyl)-5-cyano-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4'a (minor isomer)

$^1$H NMR
$^{13}$C NMR
$^{19}\text{F NMR}$

![Chemical Structure and NMR Spectrogram](image-url)
rel-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4b (major)

$^1$H NMR
$^{13}$C NMR
rel-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4b (major) and rel-(3R,3aR,5R)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4'b (minor)

$^1$H NMR
$^{13}$C NMR
$^{19}$F NMR
$^1$H-$^1$H COSY
${}^1$H-1H NOESY
$^{1}H^{13}C$ HSQC
$^1$H-$^{13}$C HMBC
$^1$H-$^{19}$F HOESY

[Chemical Structures]
$^1$H-$^{15}$N HMBC
rel-(3R,3aR,5S)-Dimethyl 3a-fluoro-3-(4-(methoxycarbonyl)phenyl)-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4c (major isomer)

$^1$H NMR
$^{13}$C NMR

[Chemical structure and spectrum image]

major isomer
$^{19}$F NMR

major isomer
rel-(3R,3aR,5S)-Dimethyl 3a-fluoro-3-(4-fluorophenyl)-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4d (major isomer)

$^1$H NMR
$^{13}$C NMR
$^{19}$F NMR

major isomer
rel-(3R,3aR,5S)-Dimethyl 3a-fluoro-3-(4-methoxyphenyl)-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4e (major isomer)

$^1$H NMR

![NMR spectrum](image-url)
$^{13}$C NMR

major isomer
$^{19}$F NMR

![Chemical structure and NMR spectrum]

**major isomer**
rel-(3R,3aR,5S)-Dimethyl 3a-fluoro-3-(3-methoxyphenyl)-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4f (major isomer)

$^1$H NMR
$^{13}$C NMR
rel-(3R,3aR,5S)-Dimethyl 3-(2-bromophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4g (major isomer)

$^1$H NMR
$^{13}$C NMR

[Chemical structure image]

major isomer
$^{13}$C NMR (DEPT)

major isomer
$^{19}$F NMR

![Chemical Structure and NMR Spectrum]

- Major isomer

[Chemical Structure Image]

- Br
- MeO
- CO$_2$Me
- Ph

[NMR Spectrum Image]
rel-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(4-methoxyphenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4h (major isomer)

$^1$H NMR
$^{13}$C NMR

Figure: A $^{13}$C NMR spectrum of a compound with the major isomer labeled.
$^{19}\text{F NMR}$

The figure shows a spectrometer trace with peaks at approximately -131.0 to -131.5 ppm. The structure at the top left is labeled as the major isomer.
rel-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(4-(methoxycarbonyl)phenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4i (major isomer)

$^1$H NMR
\[ ^{13}C \text{NMR (DEPT)} \]

![Chemical structure with peak assignments](image)

Major isomer

- 132.07
- 130.08
- 128.48
- 128.74
- 55.80
- 54.18
- 52.22
- 44.41

Peak assignments in ppm.
$^{19}$F NMR
rel-(3R,3aR,5S)-Dimethyl 5-(biphenyl-4-yl)-3-(4-chlorophenyl)-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4j (major isomer)

$^1$H NMR
$^{13}$C NMR
$^{13}$C NMR (expanded region 114-146 ppm)

Major isomer
$^{13}$C NMR (DEPT)
$^{19}$F NMR
rel-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(3-methoxyphenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4k (major isomer)

$^1$H NMR
$^{13}$C NMR

![Chemical Structure with NMR Spectra]

- Major isomer

Chemical shifts:
- 167.06
- 165.91
- 159.95
- 134.69
- 132.11
- 130.29
- 129.84
- 128.45
- 120.56
- 119.14
- 117.62
- 114.65
- 112.15
- 89.52
- 85.02
- 55.91
- 55.61
- 55.28
- 54.14
- 52.71
- 44.84
- 44.47
$^{19}$F NMR

major isomer
rel-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(naphthalen-1-yl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4l (major isomer)

$^1H$ NMR
$^{13}$C NMR (expanded region 115-138 ppm)
$^{13}$C NMR (DEPT)

Chemical shifts:
- 128.61
- 129.09
- 129.31
- 123.44
- 123.87
- 125.37
- 126.61

Major isomer.
$^{19}F$ NMR

major isomer
$^1$H-$^{13}$C HSQC

major isomer
rel-(3R,3aR,5S)-Dimethyl 5-cyano-3a-fluoro-3-(4-(methoxycarbonyl)phenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4m (enriched major isomer)

$^1$H NMR
$^{19}$F NMR

major isomer
rel-(3R,3aR,5R)-Dimethyl 5-cyano-3a-fluoro-3-(4-(methoxycarbonyl)phenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4’m (enriched minor isomer)

$^1$H NMR
\(^{13}\)C NMR
$\textsuperscript{19}F$ NMR

![Chemical structure with NMR spectrum]

Minor isomer
$^1$H-$^1$H COSY

![Chemical structure and H COSY spectrum of a minor isomer.](image-url)
$^1$H-$^{13}$C HSQC

Minor isomer
$^1$H-$^{13}$C HMBC
$^1$H-$^{19}$F HOESY

minor isomer
1H-15N HMBC

minor isomer
rel-(3R,3aR,5S)-Dimethyl 5-cyano-3a-fluoro-3-(4-methoxyphenyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4n (major isomer)

$^1$H NMR
$^{13}$C NMR
$^{19}$F NMR
$^1$H-$^1$H COSY

major isomer
1H-1H NOESY

major isomer
$^{1}H^{13}C$ HSQC

major isomer
$^1$H-$^{13}$C HMBC

[Chemical structure diagram]

major isomer
$^{1}H$-$^{19}F$ HOESY

major isomer
*rel-*\((3R,3\text{a}R,5R)-\text{Dimethyl}~5\text{-cyano-3-a-fluoro-3-(4-methoxyphenyl)}\uber{\text{tetrahydro-2H-isoxazolo}[2,3-b]isoxazole-2,2-dicarboxylate~4′n}^1\text{H} \text{NMR}

\[\text{Minor isomer}\]
13C NMR
$^{19}$F NMR
rel-(3R,3aR,5R)-Dimethyl 5-butyl-3-(4-chlorophenyl)-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4o (major isomer)

$^1$H NMR
$^{13}$C NMR
$^{1}H^{13}C$ HSQC
$^{1}H^{13}C$ HMBC

major isomer
$^{1}H-{ }^{19}F$ HOESY

[Chemical structure image]

major isomer
$^{1}H-^{15}N$ HMBC

[Chemical structure image]

major isomer
rel-(3R,3aR,5R)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-(2-hydroxyethyl)tetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4p (major isomer)

$^1$H NMR
$^{13}$C NMR

Major isomer
$^{19}$F NMR

[Chemical structure diagram]

major isomer
rel-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-5-ethoxy-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4q (major isomer)

$^1$H NMR

![NMR spectrum of the compound](image)
$^{19}$F NMR

![Chemical Structure](image)

**major isomer**
$^1$H-$^1$H COSY

major isomer
$^{1}\text{H}^{13}\text{C}$ HSQC
$^1$H-$^{13}$C HMBC

major isomer
$^1\text{H}^{-19}\text{F HOESY}$
$^1$H-$^{15}$N HMBC

major isomer
rel-(3R,3aR,5R)-Trimethyl 3-(4-chlorophenyl)-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2,5-tricarboxylate 4'r (major isomer) and rel-(3R,3aR,5S)-Trimethyl 3-(4-chlorophenyl)-3a-fluorotetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2,5-tricarboxylate 4r (minor isomer)

$^1$H NMR
$^{13}$C NMR

Major isomer

Minor isomer
$^{19}$F NMR

[Chemical structure images with major and minor isomers labeled]

[19F NMR spectrum with peak assignments]
$^1$H-$^1$H COSY
\[ ^1H-^1H \text{NOESY} \]

![Diagram of 
\[ ^1H-^1H \text{NOESY} \] with two isomers and their corresponding spectra.](image-url)
$^1$H-$^{13}$C HSQC

Major isomer

Minor isomer
$^{1}H^{13}C$ HMBC
$^1$H-^{19}$F HOESY
$^{1}H-^{15}N$ HMBC
rel-(3R,3aR,5R)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-methyl-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4s (major isomer) and rel-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-methyl-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4’s (minor isomer)

$^1$H NMR
$^{13}$C NMR

major isomer

minor isomer
$^{19}$F NMR

[Diagram showing two isomers with their respective chemical structures and a 19F NMR spectrum with peaks at -130.5, -131.5, -132.5, -133.5, and -134.5 ppm.]

major isomer

minor isomer
$^1$H-$^1$H COSY
$^1$H-$^1$H NOESY
\(^1\text{H}-^{13}\text{C}\) HSQC

major isomer

minor isomer
$^{1}H^{13}C$ HMBC

Major isomer

Minor isomer
$^1$H-$^{19}$F HOESY

![Major Isomer](image1)

![Minor Isomer](image2)
$^1\text{H}-^{15}\text{N}$ HMBC

[Diagram of chemical structures showing major and minor isomers]
rel-(3R,3aR,5R)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-methoxy-5-methyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4t (major isomer) and rel-(3R,3aR,5S)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5-methoxy-5-methyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4't (minor isomer)

$^1$H NMR
$^{13}$C NMR

[Chemical structures and spectra diagram]

- Major isomer
- Minor isomer
$^{19}$F NMR

major isomer

minor isomer

Graph showing $^{19}$F NMR spectra with peaks at different chemical shifts.
$^1\text{H}-^1\text{H NOESY}$
$^{1}H^{13}C$ HSQC

![HSQC Spectrum with major and minor isomers](image-url)
$^{1}H^{13}C$ HMBC
$^1$H-$^{19}$F HOESY

![HOESY Spectrum]

**Major Isomer**

![Chemical Structure]

**Minor Isomer**

![Chemical Structure]
$^1$H-$^{15}$N HMBC

[Diagram of major and minor isomers with chemical structures and spectra]
rel-(3R,3aR)-Dimethyl 3-(4-chlorophenyl)-3a-fluoro-5,5-dimethyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4u

$^1$H NMR
$^{13}$C NMR
$^{19}$F NMR
$^1$H-$^1$H COSY
\( ^1\text{H}-^1\text{H NOESY} \)
$^{1}H^{13}C$ HSQC
$^1$H-$^{13}$C HMBC
$^1$H-$^{19}$F HOESY
\(^{1}H-^{15}N\) HMBC
rel-(3R,3aR,5S)-diethyl 3-(4-chlorophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-dicarboxylate 4v (major isomer)

$^1$H NMR
$^{13}$C NMR

major isomer
$^{13}$C NMR (DEPT)

major isomer
$^{19}$F NMR
rel-1,1'-(3R,3aR,5S)-3-(4-chlorophenyl)-3a-fluoro-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-diyl)diethanone 4w (major isomer)

$^1$H NMR

![NMR spectrum image]
$^{13}$C NMR

![Chemical Structure](image)

**Major Isomer**

- 203.84 ppm
- 198.80 ppm
- 182.41 ppm
- 142.67 ppm
- 131.12 ppm
- 128.81 ppm
- 128.01 ppm
- 126.75 ppm
- 119.88 ppm
- 80.48 ppm
- 54.16 ppm
- 44.48 ppm
- 27.77 ppm
- 25.61 ppm

**Chemical Shifts**

- Cl
- F
- MeO
- C(O)Me

**Formula**

\[ \text{formula} \]
$^{19}$F NMR

[Chemical structure image]

major isomer
1-[(Z)-2-chloro-2-nitroethenyl]-4-(methyloxy)benzene 7a

$^1$H NMR
$^{13}$C NMR
$^{13}$C NMR (DEPT)
3-Chloro-5,5-bis(methoxycarbonyl)-4-(4-methoxyphenyl)-4,5-dihydroisoxazole 2-oxide 8a

$^1$H NMR
$^{13}$C NMR
$^{13}$C NMR (DEPT)
$^{13}$C NMR (DEPT-90)
$^1$H-$^{13}$C HMBC
3-Bromo-5,5-bis(methoxycarbonyl)-4-(4-methoxyphenyl)-4,5-dihydroisoxazole 2-oxide 8b

$^1$H NMR
$^{13}$C NMR
Dimethyl 4-(4-chlorophenyl)-3-fluoroisoxazole-5,5(4H)-dicarboxylate 9a

$^1$H NMR
$^{13}$C NMR

![C NMR spectrum with chemical shifts labeled]
$^{19}$F NMR
Dimethyl 3-fluoro-4-(4-(methoxycarbonyl)phenyl)isoxazole-5,5(4H)-dicarboxylate 9m

$^{1}$H NMR
$^{13}$C NMR
$^{19}$F NMR
Dimethyl 2-hydroxy-2-(2-(hydroxyimino)-1-(4-methoxyphenyl)-4-phenylbutyl)malonate 10

$^1$H NMR
13C NMR
$^1$H-$^1$H COSY
$^{1}H$-$^{13}C$ HSQC
$^1H-^{13}C$ HMBC
rel-((3R,3aR,5S)-3a-Fluoro-3-(4-fluorophenyl)-5-phenyltetrahydro-2H-isoxazolo[2,3-b]isoxazole-2,2-diyl)dimethanol 13

${}^1$H NMR
$^{13}$C NMR
\( \text{\(^{19}\)F NMR} \)
$^1$H NMR after H/D exchange
$^{13}$C NMR after H/D-exchange
$^1$H-$^{13}$C HMBC after H/D-exchange