

ELECTRONIC SUPPLEMENTARY INFORMATION (ESI)

Electronic Effects in the Ruthenium-catalyzed 1,3-Dipolar Cycloaddition Reactions of *N*-Alkyl and *N*-Benzyl Nitrones with Methacrolein

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General: Complex (*R,R*)-**11** was prepared by published procedures.¹ Reactions were carried out under a positive pressure of nitrogen unless otherwise noted. Glassware was oven dried (70 °C), and further dried by placing under vacuum. THF, diethyl ether, *n*-hexane, toluene and dichloromethane were dried by passing through activated Al₂O₃ (SolvtekH[®] purification system). The other solvents were purified by distillation under N₂ over the appropriate drying agent. The precursors used were purchased from commercial sources and used without further purification. 4Å molecular sieves were powdered in a mortar, dried by heating at 200 °C for 16 hours under vacuum and were then stored under N₂. Flash column chromatography (FCC) was carried out using silica gel (60, 230-400 mesh ASTM, Fluka). Thin-layer chromatography was performed on pre-coated aluminium plates (Merck silica 60F254), and visualized using UV light and aqueous KMnO₄ stain. ¹H and ¹³C NMR spectra were recorded on Bruker AMX 300 or 400 spectrometers. Chemical shifts are quoted relative to tetramethylsilane and referenced to residual solvent peaks as appropriate. Infrared spectra were recorded on a Perkin–Elmer Spectrum One spectrophotometer as neat liquids. Polarimetry was performed using a Perkin–Elmer 241 Polarimeter with a Na lamp (589 nm, continuous). LR-MS were acquired using a Varian CH4 or SM1 spectrometer with the ionizing voltage at 70 eV while HR-MS were measured in + TOF mode in the ESI-MS or EI modes using an Applied Biosystems/Sciex (Q-STA) spectrometer. HPLC analyses were recorded on a Agilent HP 1100 Series instrument (hexanes/2-propanol mixtures).

***N*-methyl and *N*-benzyl, α -aryl nitrones**

The nitrones below were synthesized by condensation of the appropriate substituted benzaldehyde with phenylhydroxylamine.²

***N*-methyl, α -(4-dimethylamino)-phenyl nitrone (1a)**

***N*-methyl, α -(4-methoxy)-phenyl nitrone (1b)**

***N*-methyl, α -(4-methyl)-phenyl nitrone (1c)**

***N*-methyl, α -phenyl nitrone (1d)**

***N*-methyl, α -(4-fluoro)-phenyl nitrone (1e)**

***N*-methyl, α -(4-chloro)-phenyl nitrone (1f)**

***N*-methyl, α -(4-bromo)-phenyl nitrone (1g)**

***N*-methyl, α -(4-trifluoromethyl)-phenyl nitrone (1h)**

***N*-methyl, α -(4-cyano)-phenyl nitrone (1i)**

***N*-methyl, α -(4-nitro)-phenyl nitrone (1j)**

***N*-methyl, α -(2-fluoro)-phenyl nitronone (1k)**

***N*-methyl, α -pentafluoro nitronone (1l)**

***N*-methyl, α -(η^6 -Cr(CO)₃) nitronone (1m)**

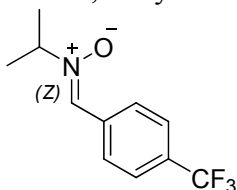
***N*-methyl, α -(2-pyridyl) nitronone (1n)**

***N*-tert-butyl, α -(4-trifluoromethyl)-phenyl nitronone (1p)**

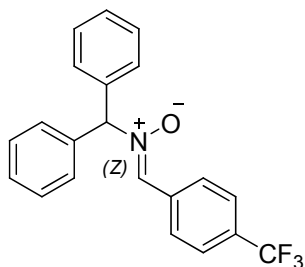
***N*-benzyl, α -(4-trifluoromethyl)-phenyl nitronone (1q)**

***N*-(4-methoxy)-benzyl, α -(4-trifluoromethyl)-phenyl nitronone (1r)**

The following nitrones were prepared according to this following general procedure: to a Schlenk tube equipped with a magnetic stirring bar, the hydroxylamine hydrochloride (10 mmol, 1 equiv.) was dissolved in ethanol (5 mL) and *para*-trifluoromethyl benzaldehyde (10 mmol, 1 equiv.) was added in one portion. Sodium hydroxide (400 mg, 10 mmol, 1 equiv.) was added dropwise, by means of a syringe, as an aqueous solution, when the hydrochloride salt of the hydroxylamine was used (6 mL). The resulting mixture was stirred for 12-24h at r. t. under N₂ atmosphere. Upon the mentioned time of stirring, water (10-20 mL) was added and the mixture was extracted with ethyl acetate (20 + 3 x 10 mL), the organic phases were combined, dried on anhydrous MgSO₄ or Na₂SO₄, filtered and volatiles were removed *in vacuo* to give the desired nitrones as semi-crystalline solids. If needed, recrystallization from dichloromethane/pentanes was further performed.



***N*-iso-propyl, α -(4-trifluoromethyl)-phenyl nitronone (1o):** obtained according to the general procedure in quantitative yield: **IR** (film): ν (cm⁻¹) = 656, 852, 1016, 1067, 1091, 1124, 1166, 1319, 1367, 1408, 1455, 1560, 1580, 1615, 2983, 2939; **¹H NMR** (400 MHz, CDCl₃): δ (ppm) = 1.52-1.54 (d, 6H, *J* = 6.6 Hz, CH₃), 4.23-4.32 (hept, 1H, *J* = 6.6 Hz, CH), 7.53 (s, 1H, CHN), 7.66-7.68 (d, 2H, *J* = 8.3 Hz, H-*Carom*), 8.35-8.37 (d, 2H, *J* = 8.3 Hz, H-*Carom*); **¹³C NMR** (125.8 MHz, CDCl₃): δ (ppm) = 20.9, 68.4, 77.2, 125.3, 125.4, 125.5, 128.4, 130.5; **MS** (TS) *m/z* = 232.3 (M+1), 190.4, 172.1, 170.3, 152.1; **HRMS** (ESI+) *m/z*: calcd. for C₁₁H₁₃F₃NO [M+H]⁺: 232.0943, found: 232.0950.



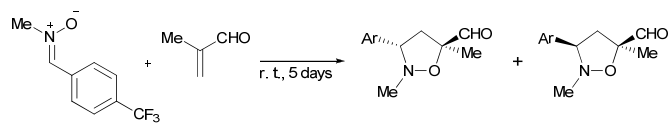
***N*-(diphenylmethyl), α -(4-trifluoromethyl)-phenyl nitronium ion (1s):** obtained according to the general procedure in 60 % yield: **IR** (film): ν (cm⁻¹) = 661, 698, 723, 852, 1014, 1067, 1125, 1167, 1317, 1325, 1410, 1456, 1497, 158, 3029; **¹H NMR** (400 MHz, CDCl₃): δ (ppm) = 6.41 (s, 1H, CH), 7.36-7.44 (m, 10H, H-Carom), 7.57 (s, 1H, CHN), 7.64-7.66 (d, 2H, J = 8.3 Hz, H-Carom), 8.35-8.37 (d, 2H, J = 8.3 Hz, H-Carom); **¹³C NMR** (125.8 MHz, CDCl₃): δ (ppm) = 77.2, 84.2, 125.3, 125.4, 128.6, 128.7, 128.8, 128.9, 133.5; **MS** (TS) m/z = 356.1 (M+1), 169.3, 168.3, 165.3, 154.1; **HRMS** (ESI+) m/z : calcd. for C₂₁H₁₆F₃NONa [M+H]⁺: 378.1076, found: 378.1068.

Non-catalyzed 1,3-DCs of *N*-“alkyl” nitrones with methacrolein

General procedure: In a 50 mL Schlenk tube equipped with a magnetic stirring bar, a solution of the nitronium ion (0.5 mmol, 1 equiv.) in CH₂Cl₂ (2 mL) is stirred at r. t. to give a clear solution. Methacrolein (1 mmol, 2 equiv.) is added dropwise, by syringe, at r. t. The reaction mixture is stirred at r. t. until TLC analysis (SiO₂, AcOEt/cyclohexane 2/3 or CH₂Cl₂) shows no unreacted nitronium ion. Addition of dry pentane (10 mL), filtration of the precipitated nitronium ion through a plug of cotton in a Pasteur pipette and *in vacuo* removal of solvents leads to an oil. Purification by a quick filtration through a SiO₂ plug (H_{dry} = 5 cm, Φ_e = 1 cm) with CH₂Cl₂ gives viscous, clear oils that solidify at -30 °C. Diastereomeric ratios are determined by ¹H NMR of the crude mixture. Clear signals for the racemic mixture can be observed in the HPLC analysis on the corresponding primary alcohols obtained by a standard NaBH₄ reduction in ethanol (CHIRACEL OD, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254 nm or CHIRALPACK AD, Grad 99+1-85+15, 0.5 mL/min, 80 min, 254).

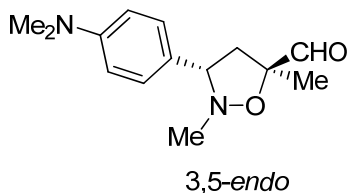
Note: Most isoxazolidines proved to be too unstable for MS analysis. MS data for the corresponding alcohols is given in the following section.

Solvent screening^a



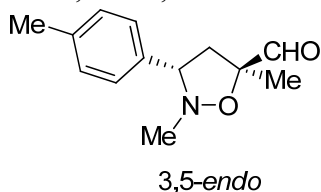
1h	3	2h-endo	2h-exo
SOLVENT	yield (%)^b	endo / exo^c	
CH ₂ Cl ₂	92	60 / 40	
THF	86	60 / 40	
toluene	79	58 / 42	
hexanes	94	61 / 39	
EtOH	77	60 / 40	
CH ₃ CN	97	60 / 40	
AcOEt	61	58 / 42	
DMSO	0	n.d.	
DMF	0	n.d.	
acetone	0	n.d.	

^a All reactions were carried out under N₂, using **1h** (0.5 mmol) and **3** (1 mmol), in 1 mL of dry solvent. ^b Isolated yield. ^c Determined by ¹H NMR analysis. ^d Nitron decomposition.



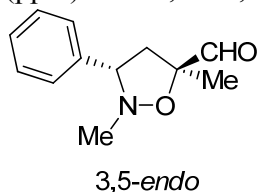
rac-5-methyl-3-(4-dimethylamino-phenyl)-2-methyl-isoxazoline-5-carbaldehyde

(rac-2a): obtained according to the general procedure in 60 % yield (*endo/exo* 17/83): **IR** (film): ν (cm^{-1}) = 728, 795, 810, 842, 895, 920, 947, 1068, 1089, 1165, 1188, 1229, 1297, 1315, 1362, 1446, 1483, 1524, 1556, 1598, 1614, 1677, 1721, 2815, 2847, 2968; **^1H NMR** (300 MHz, CDCl_3): δ (ppm) = 1.35 (A, s, 3H, Me), 2.33-2.38 (A, dd, 1H, $J = 9, 13$ Hz, H-C₄), 2.57 (A, s, 3H, NMe), 2.61-2.67 (A, bdd, 1H, $J = 9, 13$ Hz, H-C₄), 3.03 (A, s, 6H, NMe₂), 3.40-3.45 (A, t, 1H, $J = 9$ Hz, H-C₃), 6.66-6.68 (A, d, 2H, $J = 9$ Hz, H-C_m), 7.10-7.12 (A, d, 2H, $J = 9$ Hz, H-C_o), 9.75 (A, s, 1H, CHO); **^{13}C NMR** (125.8 MHz, CDCl_3): δ (ppm) = 19.15, 40.1, 40.3, 40.5, 42.4, 46.5, 71.9, 73.0, 111.0, 112.5, 128.7, 128.8, 190.3, 205.2.



rac-5-methyl-3-(4-methyl-phenyl)-2-methyl-isoxazoline-5-carbaldehyde (rac-2c):

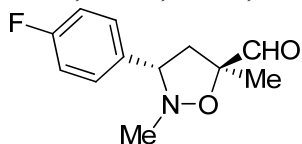
obtained according to the general procedure in 75 % yield (*endo/exo* 37/63): **IR** (film): ν (cm^{-1}) = 718, 759, 814, 848, 896, 921, 956, 1021, 1092, 1107, 1140, 1178, 1217, 1289, 1306, 1373, 1454, 1515, 2849, 2962, 2924; **^1H NMR** (300 MHz, CDCl_3): δ (ppm) = 1.33 (B, s, 3H, Me), 1.45 (A, s, 3H, Me), 2.19-2.25 (A, dd, 1H, $J = 9, 13$ Hz, H-C₄), 2.30 (B, s, 3H, *p*-Me), 2.32 (A, s, 3H, *p*-Me), 2.35-2.41 (B, dd, 1H, $J = 9, 13$ Hz, H-C₄), 2.61 (A+B, s, 3H, *N*-Me), 2.59-2.64 (B, dd, 1H, $J = 9, 13$ Hz, H-C₄), 2.85-2.93 (A, bm, 1H, H-C₄), 3.44-3.48 (B, t, 1H, $J = 9$ Hz, H-C₃), 4.00 (A, bs, 1H, H-C₃), 7.12-7.14 (B, d, 2H, $J = 9$ Hz, H-C_m), 7.19-7.21 (B, d, 2H, $J = 9$ Hz, H-C_m), 8.09-8.11 (A+B, d, 2H, $J = 9$ Hz, H-C_o), 9.65 (A, s, 1H, CHO), 9.72 (B, s, 1H, CHO); **^{13}C NMR** (125.8 MHz, CDCl_3): δ (ppm) = 19.0, 21.1, 42.5, 46.8, 73.1, 127.5, 127.8, 129.3, 129.4, 205.0.



rac-5-methyl-3-(phenyl)-2-methyl-isoxazoline-5-carbaldehyde (rac-2d):

obtained according to the general procedure in 60 % yield (*endo/exo* 40/60): **IR** (film): ν (cm^{-1}) = 699, 753, 793, 845, 894, 914, 956, 973, 1025, 1073, 1091, 1139, 1177, 1290, 1307, 1361, 1374, 1455, 1494, 1604, 1732, 2808, 2849, 2963; *endo*: **^1H NMR** (300 MHz, CDCl_3): δ (ppm) = 1.38 (s, 3H, Me), 2.40-2.46 (bdd, 1H, $J = 9, 12$ Hz, H-C₄), 2.61 (s, 3H, NMe), 2.66-2.71 (bdd, 1H, $J = 9, 12$ Hz, H-C₄), 3.51-3.55 (bt, 1H, $J = 8$ Hz, H-C₃), 7.25-7.33 (m, 5H, H-C_{Ar}), 9.76 (s, 1H, CHO); *exo*: **^1H NMR** (300 MHz, CDCl_3): δ (ppm) = 1.53 (s, 3H, Me), 2.29-2.35 (dd, 1H, $J = 9, 12$ Hz, H-C₄), 2.67 (s, 3H, NMe), 2.99-3.03 (bm, 1H,

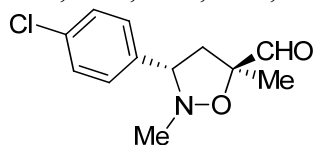
H-C₄), 3.71 (bs, 1H, H-C₃), 7.32-7.41 (m, 5H, H-C_{Ar}), 9.74 (s, 1H, CHO); ¹³C NMR of the mixture (100.6 MHz, CDCl₃): δ (ppm) = 20.4, 34.6, 48.5, 85.6, 121.8, 125.8, 125.9, 128.1, 128.3, 130.9, 141.9, 200.5.



3,5-endo

rac-5-methyl-3-(4-fluoro-phenyl)-2-methyl-isoxazoline-5-carbaldehyde (rac-2e):

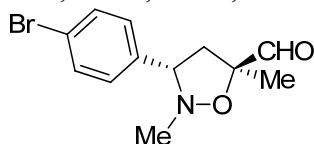
obtained according to the general procedure in 85 % yield (*endo/exo* 43/57): **IR** (film): ν (cm⁻¹) = 718, 761, 772, 837, 893, 979, 1015, 1091, 1134, 1158, 1223, 1295, 1378, 1473, 1509, 1606, 1640, 1733, 2850, 2963; **¹H NMR** (300 MHz, CDCl₃): δ (ppm) = 1.46 (s, 3H, Me), 2.17-2.23 (dd, 1H, *J* = 9, 13 Hz, H-C₄), 2.59 (s, 3H, NMe), 2.93-2.97 (bdd, 1H, *J* = 9, 13 Hz, H-C₄), 3.65 (bs, 1H, *J* = 9 Hz, H-C₃), 7.02-7.06 (m, 2H, H-C_{Ar}), 7.31-7.34 (m, 2H, H-C_{Ar}), 9.67 (s, 1H, CHO); **¹³C NMR** (100.6 MHz, CDCl₃): δ (ppm) = 19.1, 47.7, 72.8, 85.1, 128.1, 129.4, 129.7, 129.9, 161.5, 163.9, 205.0.



3,5-endo

rac-5-methyl-3-(4-chloro-phenyl)-2-methyl-isoxazoline-5-carbaldehyde (rac-2f):

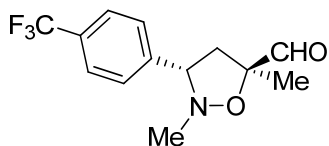
obtained according to the general procedure in 87 % yield (*endo/exo* 49/51): **IR** (film): ν (cm⁻¹) = 700, 717, 825, 850, 893, 922, 979, 1015, 1089, 1134, 1174, 1296, 1376, 1411, 1474, 1491, 1519, 1599, 1640, 1733, 2849, 2962; **¹H NMR** (300 MHz, CDCl₃): δ (ppm) = 1.43 (s, 3H, Me), 2.15-2.20 (dd, 1H, *J* = 9, 13 Hz, H-C₄), 2.59 (s, 3H, NMe), 2.94-2.98 (bdd, 1H, *J* = 9, 13 Hz, H-C₄), 3.65 (bs, 1H, *J* = 9 Hz, H-C₃), 7.27-7.33 (m, 4H, H-C_{Ar}), 9.65 (s, 1H, CHO); **¹³C NMR** (100.6 MHz, CDCl₃): δ (ppm) = 19.0, 47.6, 61.2, 85.2, 128.3, 128.5, 129.1, 129.4, 134.0, 137.0, 204.9.



3,5-endo

rac-5-methyl-3-(4-bromo-phenyl)-2-methyl-isoxazoline-5-carbaldehyde (rac-2g):

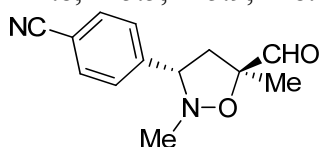
obtained according to the general procedure in 90 % yield (*endo/exo* 52/48): **IR** (film): ν (cm⁻¹) = 822, 851, 893, 979, 1011, 1071, 1091, 1134, 1296, 1376, 1409, 1474, 1488, 1519, 1734, 2847, 2960; **¹H NMR** (300 MHz, CDCl₃): δ (ppm) = 1.46 (s, 3H, Me), 2.16-2.21 (dd, 1H, *J* = 9, 13 Hz, H-C₄), 2.60 (s, 3H, NMe), 2.95-3.00 (bdd, 1H, *J* = 9, 13 Hz, H-C₄), 3.65 (bs, 1H, *J* = 9 Hz, H-C₃), 7.23-7.25 (d, 2H, *J* = 9 Hz, H-C_{Ar}), 7.47-7.49 (d, 2H, *J* = 9 Hz, H-C_{Ar}), 9.67 (s, 1H, CHO); **¹³C NMR** (100.6 MHz, CDCl₃): δ (ppm) = 15.5, 21.2, 47.6, 66.1, 85.2, 122.2, 128.3, 129.1, 129.5, 132.1, 137.5, 200.2.



3,5-endo

rac-5-methyl-3-(4-trifluoromethyl-phenyl)-2-methyl-isoxazoline-5-carbaldehyde (*rac-2h*):

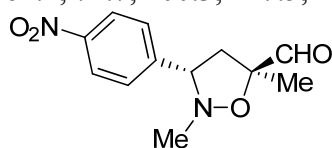
obtained according to the general procedure in 92 % yield (*endo/exo* 62/38): **IR** (film): ν (cm^{-1}) = 762, 839, 894, 979, 1019, 1068, 1123, 1165, 1324, 1378, 1421, 1474, 1520, 1620, 1735, 2853, 2963; **$^1\text{H NMR}$** (300 MHz, CDCl_3): δ (ppm) = 1.46 (s, 3H, Me), 2.18-2.23 (dd, 1H, $J = 9, 13$ Hz, H-C₄), 3.01-3.06 (bdd, 1H, $J = 9, 13$ Hz, H-C₄), 3.76 (bs, 1H, $J = 9$ Hz, H-C₃), 7.48-7.50 (d, 2H, $J = 9$ Hz, H-C_m), 7.61-7.63 (d, 2H, $J = 9$ Hz, H-C_o), 9.68 (s, 1H, CHO); **$^{13}\text{C NMR}$** (100.6 MHz, CDCl_3): δ (ppm) = 21.1, 33.5, 47.5, 85.4, 122.8, 125.5, 125.9, 128.1, 130.3, 130.6, 142.8, 201.5.



3,5-endo

rac-5-methyl-3-(4-cyano-phenyl)-2-methyl-isoxazoline-5-carbaldehyde (*rac-2i*):

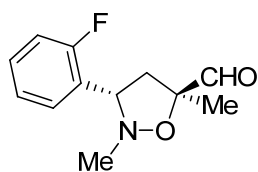
obtained according to the general procedure in 78 % yield (*endo/exo* 72/28): **IR** (film): ν (cm^{-1}) = 732, 834, 895, 919, 958, 1021, 1056, 1103, 1133, 1176, 1288, 1304, 1374, 1415, 1456, 1505, 1610, 1732, 2228, 2877, 2930, 2978; **$^1\text{H NMR}$** (300 MHz, CDCl_3): δ (ppm) = 1.36 (B, s, 3H, Me), 1.43 (A, s, 3H, Me), 2.12-2.19 (A, dd, 1H, $J = 9, 13$ Hz, H-C₄), 2.40-2.47 (B, dd, 1H, $J = 9, 13$ Hz, H-C₄), 2.61 (A+B, s, 3H, N-Me), 2.63-2.66 (B, dd, 1H, $J = 9, 13$ Hz, H-C₄), 3.01-3.08 (A, bdd, 1H, $J = 9, 13$ Hz, H-C₄), 3.54-3.59 (B, t, 1H, $J = 9$ Hz, H-C₃), 3.75-3.81 (A, bt, 1H, $J = 9$ Hz, H-C₃), 7.34-7.36 (B, d, 2H, $J = 9$ Hz, H-C_m), 7.58-7.61 (B, d, 2H, $J = 9$ Hz, H-C_m), 7.68-7.70 (A, d, 2H, $J = 9$ Hz, H-C_m), 8.29-8.32 (A, d, 2H, $J = 9$ Hz, H-C_o), 9.66 (A, s, 1H, CHO), 9.68 (B, s, 1H, CHO); **$^{13}\text{C NMR}$** (125.8 MHz, CDCl_3): δ (ppm) = 15.1, 18.2, 18.6, 20.8, 21.5, 22.9, 27.9, 42.6, 46.4, 46.9, 61.2, 72.7, 100.3, 127.5, 128.2, 128.6, 132.0, 132.5, 137.4, 204.3.



3,5-endo

rac-5-methyl-3-(4-nitro-phenyl)-2-methyl-isoxazoline-5-carbaldehyde (*rac-2j*):

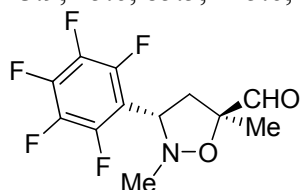
obtained according to the general procedure in 75 % yield (*endo/exo* 73/27): **IR** (film): ν (cm^{-1}) = 751, 856, 981, 1016, 1092, 1292, 1347, 1382, 1474, 1520, 1601, 1641, 1734, 2929; **$^1\text{H NMR}$** (300 MHz, CDCl_3): δ (ppm) = 1.45 (s, 3H, Me), 2.16-2.21 (dd, 1H, $J = 9, 13$ Hz, H-C₄), 2.64 (s, 3H, NMe), 3.07-3.12 (bdd, 1H, $J = 9, 13$ Hz, H-C₄), 3.86 (bs, 1H, $J = 9$ Hz, H-C₃), 7.55-7.57 (d, 2H, $J = 9$ Hz, H-Carom), 8.21-8.24 (d, 2H, $J = 9$ Hz, H-Carom), 9.68 (s, 1H, CHO); **$^{13}\text{C NMR}$** (125.8 MHz, CDCl_3): δ (ppm) = 15.1, 18.6, 31.2, 42.7, 46.4, 46.9, 59.5, 61.3, 72.4, 77.2, 100.1, 123.4, 124.0, 127.7, 128.3, 128.7, 204.2.



3,5-endo

rac-5-methyl-3-(2-fluoro-phenyl)-2-methyl-isoxazoline-5-carbaldehyde (rac-2k):

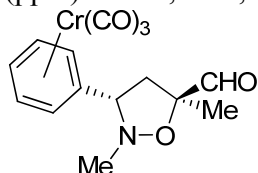
obtained according to the general procedure in 85 % yield (*endo/exo* 55/45): **IR** (film): ν (cm^{-1}) = 727, 757, 798, 816, 853, 895, 941, 978, 1034, 1091, 1135, 1179, 1231, 1277, 1376, 1455, 1473, 1489, 1519, 1587, 1617, 1733, 2876, 2963; **$^1\text{H NMR}$** (300 MHz, CDCl_3): δ (ppm) = 1.43 (s, 3H, Me), 2.18-2.23 (dd, 1H, $J = 9, 13$ Hz, H-C₄), 2.65 (s, 3H, NMe), 3.01-3.06 (bdd, 1H, $J = 9, 13$ Hz, H-C₄), 4.12 (bs, 1H, $J = 9$ Hz, H-C₃), 7.02-7.06 (m, 1H, H-Carom), 7.14-7.18 (m, 1H, H-Carom), 7.24-7.30 (m, 1H, H-Carom), 7.51-7.54 (m, 1H, H-Carom), 9.68 (s, 1H, CHO); **$^{13}\text{C NMR}$** (100.6 MHz, CDCl_3): δ (ppm) = 21.1, 43.9, 45.6, 85.5, 115.6, 115.8, 124.7, 125.8, 125.9, 128.5, 129.5, 159.7, 162.2, 201.0.



3,5-endo

rac-5-methyl-3-(pentafluoro-phenyl)-2-methyl-isoxazoline-5-carbaldehyde (rac-2l):

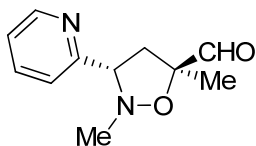
obtained according to the general procedure in 93 % yield (*endo/exo* 43/57): **IR** (film): ν (cm^{-1}) = 736, 771, 842, 973, 1009, 1095, 1134, 1149, 1292, 1372, 1476, 1504, 1523, 1655, 1736, 2970; **$^1\text{H NMR}$** (300 MHz, CDCl_3): δ (ppm) = 1.39 (s, 3H, Me), 2.37-2.43 (dd, 1H, $J = 9, 13$ Hz, H-C₄), 2.64 (s, 3H, NMe), 2.83-2.89 (dd, 1H, $J = 9, 13$ Hz, H-C₄), 3.95-3.99 (t, 1H, $J = 9$ Hz, H-C₃), 9.74 (s, 1H, CHO); **$^{13}\text{C NMR}$** (100.6 MHz, CDCl_3): δ (ppm) = 15.5, 19.6, 43.3, 62.4, 66.1, 85.0, 111.3, 136.8, 144.5, 146.9, 205.1.



3,5-endo

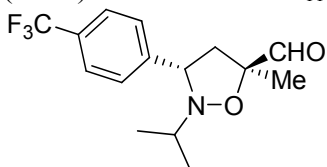
rac-5-methyl-3-(η^6 -Cr(CO)₃-phenyl)-2-methyl-isoxazoline-5-carbaldehyde (rac-2m):

obtained according to the general procedure in 95 % yield (*endo/exo* 86/14): **IR** (CH_2Cl_2): ν (cm^{-1}) = 631, 660, 816, 1092, 1291, 1474, 1520, 1615, 1732, 1874, 1962, 2873, 2951; **$^1\text{H NMR}$** (400 MHz, CDCl_3): δ (ppm) = 1.40 (s, 3H, CH₃), 2.14-2.19 (dd, 1H, $J = 6, 13$ Hz, H-C₄), 2.76 (s, 3H, N-CH₃), 3.19-3.25 (dd, 1H, $J = 8, 13$ Hz, H-C₄-endo), 3.69-3.72 (bt, 1H, $J = 7$ Hz, H-C₃), 5.34-5.42 (m, 5H, H-Carom), 9.67 (s, 1H, CHO-endo); **$^{13}\text{C NMR}$** (100.6 MHz, CDCl_3): δ (ppm) = 28.6, 45.5, 69.8, 86.0, 91.6, 92.2, 92.6, 92.7, 93.3, 93.7, 93.9, 109.7, 201.1; **HRMS** (ESI⁺) m/z : calcd. for $\text{C}_{11}\text{H}_{15}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$: 207.1128, found: 207.1132.



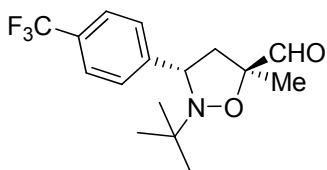
3,5-endo

rac-5-methyl-3-(2-pyridyl)-2-methyl-isoxazoline-5-carbaldehyde (rac-2n): obtained according to the general procedure in 94 % yield (*endo/exo* 95/5): **IR** (CH₂Cl₂): ν (cm⁻¹) = 621, 639, 698, 749, 761, 807, 978, 1020, 1036, 1090, 1133, 1290, 1381, 1435, 1472, 1519, 1590, 1641, 1732, 2871, 2930, 2960, 3061; **¹H NMR** (400 MHz, CDCl₃): δ (ppm) = 1.43 (s, 3H, CH₃), 2.53-2.59 (dd, 1H, *J* = 8, 12 Hz, H-C₄), 2.76 (s, 3H, N-CH₃), 2.77-2.82 (dd, 1H, *J* = 8, 12 Hz, H-C₄-endo), 3.83-3.88 (bt, 1H, *J* = 8 Hz, H-C₃), 7.24-7.27 (m, 1H, H-Carom), 7.34-7.36 (bd, 1H, H-Carom), 7.70-7.74 (m, 1H, H-Carom), 8.57-8.58 (bm, 1H, H-Carom), 9.78 (s, 1H, CHO-endo); **¹³C NMR** (100.6 MHz, CDCl₃): δ (ppm) = 19.1, 43.3, 74.5, 84.7, 86.0, 121.9, 123.0, 123.2, 137.1, 149.4, 158.8, 204.8; **HRMS** (ESI+) *m/z*: calcd. for C₁₁H₁₅N₂O₂ [M+H]⁺: 207.1128, found: 207.1132.



3,5-endo

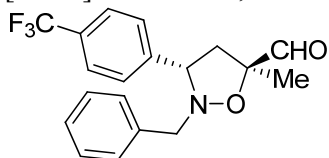
rac-5-methyl-3-(4-trifluoromethyl-phenyl)-2-iso-propyl-isoxazoline-5-carbaldehyde (rac-2o): obtained according to the general procedure in 34 % yield (*endo/exo* >95/5): **IR** (CH₂Cl₂): ν (cm⁻¹) = 734, 838, 909, 1019, 1067, 1124, 1165, 1324, 1369, 1421, 1457, 1619, 1733, 2978; **¹H NMR** (400 MHz, CDCl₃): δ (ppm) = 1.00-1.02 (d, 6H, *J* = 6 Hz, CH₃), 2.07-2.12 (ddd, 1H, *J* = 0.5, 7, 13 Hz, H-C₄), 2.80-2.89 (hept, 1H, *J* = 6 Hz, CH), 3.11-3.16 (dd, 1H, *J* = 7, 13 Hz, H-C₄), 4.22-4.25 (t, 1H, *J* = 7 Hz, H-C₃), 7.53-7.55 (d, 2H, *J* = 8 Hz, H-Carom), 7.58-7.60 (d, 2H, *J* = 8 Hz, H-Carom), 9.66 (d, 1H, *J* = 0.5 Hz, CHO); **¹³C NMR** (100.6 MHz, CDCl₃): δ (ppm) = 16.7, 19.7, 19.9, 21.6, 46.9, 125.7, 128.0, 128.1, 129.7, 130.0, 205.5; **MS** (TS) *m/z* = 302.5 (M+1), 216.3, 191.3, 190.3, 174.5, 172.5, 159.3; **HRMS** (ESI+) *m/z*: calcd. for C₁₅H₁₉F₃NO₂ [M+H]⁺: 302.1371, found: 302.1362.



3,5-endo

rac-5-methyl-3-(4-trifluoromethyl-phenyl)-2-tert-butyl-isoxazoline-5-carbaldehyde (rac-2p): obtained according to the general procedure in 38 % yield (*endo/exo* 93/7): **IR** (CH₂Cl₂): ν (cm⁻¹) = 747, 1068, 1126, 1165, 1276, 1326, 1462, 1730, 2163, 2932; **¹H NMR** (400 MHz, CDCl₃): δ (ppm) = 1.63 (s, 9H, *tert*-butyl), 2.10-2.15 (m, 1H, H-C₄), 2.98-3.03 (dd, 1H, *J* = 7, 13 Hz, H-C₄), 4.20-4.24 (m, 1H, H-C₃), 7.53-7.55 (d, 2H, *J* = 3, 6 Hz, H-Carom), 7.70-7.72 (d, 2H, *J* = 3, 6 Hz, H-Carom), 9.64 (d, 1H, *J* = 0.8 Hz, CHO); **¹³C NMR** (100.6 MHz, CDCl₃): δ (ppm) = 14.3, 23.2, 26.5, 30.6, 31.2, 68.4,

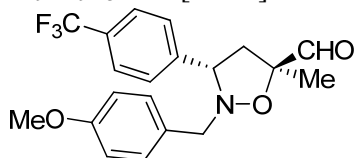
125.7, 127.6, 129.0, 131.1, 200.9; **MS** (TS) m/z = 316.5 (M+1), 279.5, 260.3, 242.3, 205.3, 190.3, 188.3, 174.5, 172.5, 167.3; **HRMS** (ESI+) m/z : calcd. for $C_{16}H_{21}F_3NO_2$ $[M+H]^+$: 316.1519, found: 316.1518.



3,5-endo

rac-5-methyl-3-(4-trifluoromethyl-phenyl)-2-benzyl-isoxazoline-5-carbaldehyde

(rac-2q): obtained according to the general procedure in 86 % yield (*endo/exo* 84/14): **IR** (CH_2Cl_2): ν (cm^{-1}) = 734, 839, 909, 1018, 1068, 1125, 1165, 1217, 1229, 1326, 1366, 1455, 1619, 1737, 2971; Diastereomers separated by FCC. *endo*: 1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.43 (s, 3H, CH_3 -endo), 2.18-2.23 (m, 1H, H-C₄-endo), 3.07-3.12 (dd, 1H, J = 8, 13 Hz, H-C₄-endo), 3.83-3.86 (bd, 1H, J = 14 Hz, CH_2), 3.92-3.95 (bd, 1H, J = 14 Hz, CH_2), 4.04-4.08 (bt, 1H, J = 7 Hz, H-C₃-endo), 7.27-7.31 (m, 5H, H-Carom), 7.52-7.54 (d, 2H, J = 8 Hz, H-Carom), 7.61-7.63 (d, 2H, J = 8 Hz, H-Carom), 9.65 (s, 1H, CHO-endo); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 15.7, 21.6, 31.2, 46.7, 63.7, 85.7, 125.6, 125.9, 127.7, 128.2, 128.5, 128.8, 130.2, 159.1, 205.3; *exo*: 1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.35 (s, 3H, CH_3 -exo), 2.44-2.49 (dd, 1H, J = 9, 13 Hz, H-C₄-exo), 2.65-2.70 (dd, 1H, J = 9, 13 Hz, H-C₄-exo), 3.74-3.77 (d, 1H, J = 14 Hz, CH_2), 3.85-3.89 (t, 1H, J = 8 Hz, H-C₃-exo), 3.91-3.95 (d, 1H, J = 14 Hz, CH_2), 7.30-7.31 (m, 5H, H-Carom), 7.43-7.43 (d, 2H, J = 8 Hz, H-Carom), 7.58-7.61 (d, 2H, J = 8 Hz, H-Carom), 9.65 (s, 1H, CHO-exo); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 19.0, 31.2, 46.5, 59.4, 70.4, 84.7, 125.9, 127.5, 128.5; 137.3, 143.3, 205.0; **MS** (TS) m/z = 350.5 (M+1), 280.5, 264.3, 230.3, 188.3, 173.3, 153.3; **HRMS** (ESI+) m/z : calcd. for $C_{19}H_{19}F_3NO_2$ $[M+H]^+$: 350.1365, found: 350.1362.

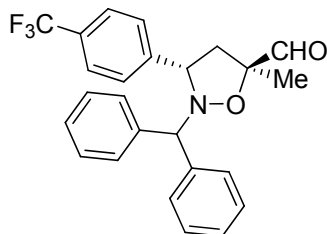


3,5-endo

rac-5-methyl-3-(4-trifluoromethyl-phenyl)-2-(4-methoxy-benzyl)-isoxazoline-5-

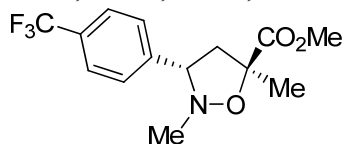
carbaldehyde (rac-2r): obtained according to the general procedure in 78 % yield (*endo/exo* 79/21): **IR** (CH_2Cl_2): ν (cm^{-1}) = 729, 834, 859, 1018, 1035, 1067, 1104, 1120, 1163, 1247, 1323, 1421, 1465, 1513, 1586, 1615, 1733, 2837, 2937; 1H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.35 (s, 3H, CH_3 -exo), 1.42 (s, 3H, CH_3 -endo), 2.17-2.22 (dd, 1H, J = 8, 17 Hz, H-C₄-endo), 2.42-2.48 (dd, 1H, J = 9, 13 Hz, H-C₄-exo), 2.63-2.68 (dd, 1H, J = 8, 17 Hz, H-C₄-exo), 3.06-3.11 (dd, 1H, J = 8, 17 Hz, H-C₄-endo), 3.69-3.73 (d, 1H, J = 14 Hz, CH_2), 3.79 (s, 3H, OMe-endo), 3.80 (s, 3H, OMe-exo), 3.82-3.90 (m, 2H, CH_2 and H-C₃-endo), 4.04-4.08 (bt, 1H, J = 7 Hz, H-C₃-exo), 6.82-6.84 (d, 2H, J = 8 Hz, H-Carom), 7.20-7.22 (d, 2H, J = 8 Hz, H-Carom), 7.51-7.53 (d, 2H, J = 8 Hz, H-Carom), 7.60-7.62 (d, 2H, J = 8 Hz, H-Carom), 9.64 (s, 1H, CHO-exo), 9.65 (s, 1H, CHO-endo); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 15.5, 19.0, 20.8, 31.2, 46.6, 58.8, 66.1, 70.1, 84.6, 85.7, 113.8, 113.9, 125.6, 125.7, 125.8, 125.9, 128.2, 128.5, 128.7, 129.3, 129.9,

130.1, 130.2, 130.4, 143.6, 159.1, 159.2, 205.1; **MS** (TS) $m/z = 380.3$ (M+1), 350.3, 332.5, 175.5; **HRMS** (ESI+) m/z : calcd. for $C_{20}H_{20}F_3NO_3$ $[M+H]^+$: 380.1451, found: 380.1468.



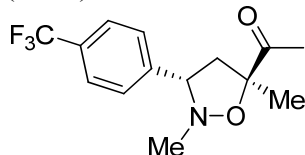
3,5-endo

rac-5-methyl-3-(4-trifluoromethyl-phenyl)-2-diphenylmethyl-isoxazoline-5-carbaldehyde (rac-2s): obtained according to the general procedure in 68 % yield (*endo/exo* 93/7): **IR** (CH_2Cl_2): ν (cm^{-1}) = 730, 904, 1019, 1068, 1124, 1165, 1326, 1455, 1735, 2969; **1H NMR** (400 MHz, $CDCl_3$): δ (ppm) = 1.32 (bs, 4H, CH and CH_3), 3.25-3.30 (bdd, 1H, $J = 9, 13$ Hz, H-C₄), 4.31-4.34 (dd, 1H, $J = 5, 9$ Hz, H-C₄), 4.75 (bs, 1H, H-C₃), 7.14-7.54 (m, 14H, H-Carom), 9.57 (bs, 1H, CHO); **^{13}C NMR** (100.6 MHz, $CDCl_3$): δ (ppm) = 17.7, 19.6, 21.2, 31.2, 46.9, 125.4, 125.7, 127.7, 128.0, 128.3, 128.6, 128.7, 129.7, 130.0, 194.2.



3,5-endo

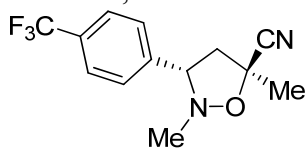
rac-5-methyl-3-(4-trifluoromethyl-phenyl)-2-methyl-isoxazoline-5-ethylcarboxylate (rac-8): obtained according to the general procedure in 64 % yield (*endo/exo* 56/44): **IR** (film): ν (cm^{-1}) = 606, 765, 839, 907, 1019, 1068, 1125, 1166, 1203, 1325, 1421, 1437, 1620, 1737, 2854, 2956; **1H NMR** (400 MHz, $CDCl_3$): δ (ppm) = 1.56 (s, 3H, Me-endo), 1.63 (s, 3H, Me-exo), 2.22-2.30 (dd, 1H, $J = 13, 17$ Hz, H-C₄-endo), 2.47-2.54 (m, 1H, $J = 12, 17$ Hz, H-C₄-exo), 2.58 (s, 3H, NMe-exo), 2.65 (s, 3H, NMe-endo), 2.95-3.02 (dd, 1H, $J = 12, 17$ Hz, H-C₄-exo), 2.22-2.30 (dd, 1H, $J = 13, 17$ Hz, H-C₄-endo), 3.57-3.63 (t, 1H, $J = 11$ Hz, H-C₃-exo), 3.78 (bm, 1H, H-C₃-endo), 3.81 (s, 3H, CO₂Me-exo), 3.83 (s, 3H, CO₂Me-endo), 7.48-7.51 (d, 2H, $J = 11$ Hz, H-Carom), 7.59-7.61 (d, 2H, $J = 11$ Hz, H-Carom); **^{13}C NMR** (125.8 MHz, $CDCl_3$): δ (ppm) = 23.6, 24.8, 43.0, 43.7, 48.6, 50.2, 52.7, 52.8, 73.1, 125.6, 125.7, 127.8, 128.3; **MS** (TS) $m/z = 304.1$ (M+1), 286.0, 272.0, 258.1, 254.1, 244.3, 226.1, 213.1, 202.4, 197.1, 186.3, 177.1, 172.3, 151.1; **HRMS** (ESI+) m/z : calcd. for $C_{14}H_{17}O_3N_1F_3$ $[M+H]^+$: 304.1155, found: 304.1150.



3,5-endo

rac-5-methyl-3-(4-trifluoromethyl-phenyl)-2-methyl-isoxazoline-5-ethanone (rac-9): obtained according to the general procedure in 60 % yield (*endo/exo* 50/50): **IR** (film): ν (cm^{-1}) = 606, 758, 836, 879, 905, 973, 1019, 1067, 1122, 1163, 1323, 1354, 1421, 1620,

1717, 2854, 2934, 2963; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) = 1.32 (s, 3H, Me-endo), 1.43 (s, 3H, Me-exo), 2.03-2.10 (dd, 1H, $J = 12, 17$ Hz, H-C₄-endo), 2.25-2.35 (dd, 1H, $J = 13, 17$ Hz, H-C₄-exo), 2.26 (s, 3H, COMe-exo), 2.32 (s, 3H, COMe-endo), 2.50 (s, 3H, NMe-exo), 2.52 (bs, 3H, NMe-endo), 2.72-2.80 (dd, 1H, $J = 13, 17$ Hz, H-C₄-exo), 3.02-3.09 (bdd, 1H, $J = 12, 17$ Hz, H-C₄-endo), 3.46-3.52 (t, 1H, $J = 11$ Hz, H-C₃-exo), 3.61 (bm, 1H, H-C₃-endo), 7.55-7.58 (d, 2H, $J = 11$ Hz, H-Carom), 7.60-7.62 (d, 2H, $J = 11$ Hz, H-Carom); $^{13}\text{C NMR}$ (125.8 MHz, CDCl_3): δ (ppm) = 21.6, 23.4, 42.7, 47.5, 73.0, 125.6, 125.7, 127.8, 128.2; **MS** (TS) $m/z = 288.1$ (M+1), 270.3, 242.1, 226.3, 204.1, 199.1, 188.4, 186.1, 172.3, 159.3; **HRMS** (ESI+) m/z : calcd. for $\text{C}_{14}\text{H}_{17}\text{F}_3\text{NO}_2$ [M+H]⁺: 288.1205, found: 288.1204.



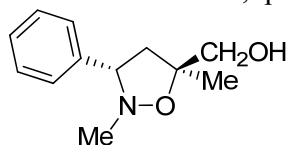
3,5-endo

rac-5-methyl-3-(4-trifluoromethyl-phenyl)-2-methyl-isoxazoline-5-nitrile (rac-10): obtained according to the general procedure in 30 % yield (*endo/exo* 33/67): **IR** (film): ν (cm^{-1}) = 611, 840, 894, 1019, 1068, 1126, 1166, 1326, 1422, 1621, 1724, 2930; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) = 1.72 (s, 3H, Me-endo), 1.73 (s, 3H, Me-exo), 2.41-2.49 (dd, 1H, $J = 13, 17$ Hz, H-C₄-endo), 2.26 (s, 3H, NMe-exo), 2.70-2.74 (m, 2H, H-C₄-exo), 2.32 (s, 3H, NMe-endo), 3.12-3.18 (dd, 1H, $J = 13, 17$ Hz, H-C₄-exo), 3.60-3.65 (t, 1H, $J = 11$ Hz, H-C₃-exo), 4.20 (bm, 1H, H-C₃-endo), 7.50-7.52 (d, 2H, $J = 11$ Hz, H-Carom), 7.59-7.61 (d, 2H, $J = 11$ Hz, H-Carom); $^{13}\text{C NMR}$ (125.8 MHz, CDCl_3): δ (ppm) = 10.9, 14.0, 23.0, 23.7, 24.2, 25.4, 28.9, 29.7, 30.3, 38.7, 42.6, 44.5, 51.2, 52.2, 68.1, 72.0, 72.2, 73.0, 73.3, 77.6, 121.2, 121.9, 125.0, 125.8, 125.9, 127.6, 128.3, 128.8, 130.5, 130.9, 141.5; **MS** (TS) $m/z = 271.1$ (M+1), 261.3, 240.1, 226.3, 222.1, 202.1, 198.1, 192.3, 188.1, 186.1, 177.1, 171.1, 167.3, 159.3, 151.1; **HRMS** (ESI+) m/z : calcd. for $\text{C}_{13}\text{H}_{14}\text{F}_3\text{N}_2\text{O}$ [M+H]⁺: 271.1052, found: 271.1060.

Reduction of the products from the Ru-catalyzed 1,3-DCs of *N*-methyl and *N*-benzyl nitrones with methacrolein

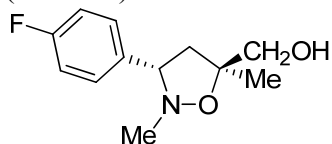
General procedure: In a 10 mL conical flask equipped with a magnetic stirring bar, the corresponding aldehyde (50 mg, 1.35 equiv.) is added to EtOH (2 mL), followed by NaBH_4 (5.3 mg, 1 equiv.). The solution is stirred for 1 to 12 hours at r. t., then the excess NaBH_4 is quenched with water, the organic phase extracted with Et_2O , dried on anhydrous MgSO_4 or Na_2SO_4 , filtered and concentrated to give a dense clear oil. Purification by column chromatography (SiO_2 , $H_{\text{dry}} = 15$ cm, $\Phi_e = 1$ cm), gradient cyclohexane/AcOEt (9/1, 30 mL; 8/2, 20 mL; 7/3, 20 mL) ($R_f = 0.45$ in 7/3 mixture) gives viscous, clear oils that solidify at -30 °C.

Note: In all cases, partial data for the *endo* diastereomer is given (in the mixture).



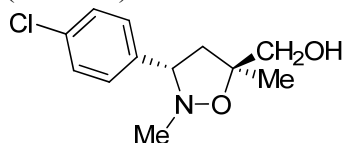
3,5-*endo*

rac-5-methyl-3-(phenyl)-2-methyl-isoxazoline-5-methanol (*rac-2d-alc*): obtained according to the general procedure in 90 % yield: **IR** (film): ν (cm⁻¹) = 714, 822, 858, 881, 929, 1011, 1069, 1131, 1215, 1298, 1367, 1408, 1456, 1488, 1592, 2869, 2962, 3426; **¹H NMR** (300 MHz, CDCl₃): δ (ppm) = 1.44 (s, 3H, Me), 2.09-2.14 (m, 1H, H-C₄), 2.50 (bs, 1H, OH), 2.54 (s, 3H, NMe), 2.75-2.78 (dd, 1H, J = 8, 16 Hz, H-C₄), 3.46-3.49 (bd, 2H, J = 11 Hz, CH₂OH + H-C₃), 3.60-3.63 (bd, 1H, J = 11 Hz, CH₂OH), 7.30-7.45 (m, 5H, H-C_{arom}); **¹³C NMR** (125.8 MHz, CDCl₃): δ (ppm) = 16.3, 23.3, 28.5, 32.2, 45.7, 48.5, 49.1, 59.5, 67.8, 68.5, 71.5, 74.3, 127.7, 127.9, 128.4, 128.5, 128.7, 130.5; **MS** (TS) m/z = 208.6 (M+1), 190.6, 184.6, 161.6; **HRMS** (ESI+) m/z : calcd. for C₁₂H₁₈NO₂ [M+H]⁺: 208.1332, found: 208.1333; **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): t_R (min) = 21.39 (49.51 %), 27.55 (50.49 %).



3,5-*endo*

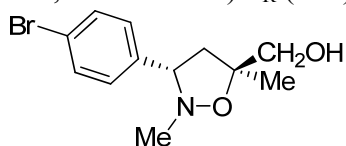
rac-5-methyl-3-(4-fluoro-phenyl)-2-methyl-isoxazoline-5-methanol (*rac-2e-alc*): obtained according to the general procedure in 92 % yield: **IR** (film): ν (cm⁻¹) = 718, 837, 859, 883, 929, 1056, 1131, 1158, 1225, 1297, 1367, 1458, 1509, 1607, 2870, 2965, 3413; **¹H NMR** (300 MHz, CDCl₃): δ (ppm) = 1.42 (s, 3H, Me), 2.02-2.07 (m, 1H, H-C₄), 2.12 (bs, 1H, OH), 2.52 (s, 3H, NMe), 2.72-2.77 (dd, 1H, J = 8, 16 Hz, H-C₄), 3.44-3.47 (bd, 2H, J = 11 Hz, CH₂OH + H-C₃), 3.59-3.61 (bd, 1H, J = 11 Hz, CH₂OH), 7.01-7.05 (m, 2H, H-C_{arom}), 7.32-7.35 (m, 2H, H-C_{arom}); **¹³C NMR** (125.8 MHz, CDCl₃): δ (ppm) = 15.3, 22.8, 29.7, 30.3, 31.2, 42.6, 47.3, 47.8, 59.5, 65.6, 65.8, 71.2, 73.6, 115.1, 115.2, 115.4, 115.5, 115.6, 115.7, 129.2, 129.3, 129.4, 129.5, 131.2, 131.3; **MS** (TS) m/z = 226.3 (M+1), 203.3, 179.3, 177.3, 161.3, 152.3; **HRMS** (ESI+) m/z : calcd. for C₁₂H₁₇FNO₂ [M+H]⁺: 226.1230, found: 226.1237; **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): t_R (min) = 19.20 (49.56 %), 28.35 (50.44 %).



3,5-*endo*

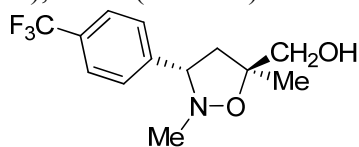
rac-5-methyl-3-(4-chloro-phenyl)-2-methyl-isoxazoline-5-methanol (*rac-2f-alc*): obtained according to the general procedure in 94 % yield: **IR** (film): ν (cm⁻¹) = 717, 804, 826, 858, 882, 929, 1015, 1055, 1090, 1131, 1216, 1298, 1368, 1411, 1458, 1492, 1599, 2869, 2964, 3409; **¹H NMR** (300 MHz, CDCl₃): δ (ppm) = 1.41 (s, 3H, Me), 2.00-2.06

(m, 1H, H-C₄), 2.18 (bs, 1H, OH), 2.52 (s, 3H, NMe), 2.73-2.78 (dd, 1H, *J* = 8, 16 Hz, H-C₄), 3.44-3.47 (bd, 2H, *J* = 11 Hz, CH₂OH + H-C₃), 3.58-3.61 (bd, 1H, *J* = 11 Hz, CH₂OH), 7.28-7.32 (m, 4H, H-Carom); ¹³C NMR (125.8 MHz, CDCl₃): δ (ppm) = 15.3, 22.8, 29.7, 31.2, 42.7, 47.3, 47.9, 59.5, 65.6, 65.8, 71.1, 73.6, 128.5, 128.8, 128.9, 129.1, 129.2, 130.9; MS (TS) *m/z* = 242.5 (M+1), 232.1, 205.1, 197.3, 175.5, 173.5, 168.3, 165.5, 156.1, 154.3; HRMS (ESI+) *m/z*: calcd. for C₁₂H₁₇ClNO₂ [M+H]⁺: 242.0940, found: 242.0942; HPLC (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): *t_R* (min) = 21.25 (48.63 %), 28.93 (51.37 %).



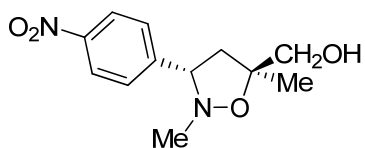
3,5-endo

rac-5-methyl-3-(4-bromo-phenyl)-2-methyl-isoxazoline-5-methanol (rac-2g-alc): obtained according to the general procedure in 60 % yield (*endo/exo* 40/60): IR (film): ν (cm⁻¹) = 714, 822, 858, 881, 929, 1011, 1069, 1131, 1215, 1298, 1367, 1408, 1456, 1488, 1592, 2869, 2962, 3426; ¹H NMR (300 MHz, CDCl₃): δ (ppm) = 1.41 (s, 3H, Me), 2.00-2.06 (m, 1H, H-C₄), 2.15 (bs, 1H, OH), 2.52 (s, 3H, NMe), 2.73-2.78 (dd, 1H, *J* = 8, 16 Hz, H-C₄), 3.43-3.46 (bd, 2H, *J* = 11 Hz, CH₂OH + H-C₃), 3.58-3.61 (bd, 1H, *J* = 11 Hz, CH₂OH), 7.24-7.26 (d, 2H, *J* = 9 Hz, H-Carom), 7.46-7.48 (d, 2H, *J* = 9 Hz, H-Carom); ¹³C NMR (125.8 MHz, CDCl₃): δ (ppm) = 22.8, 29.68, 30.30, 31.22, 42.7, 47.3, 48.0, 59.5, 65.7, 71.0, 73.7, 129.4, 129.5, 131.2, 131.4, 131.8, 131.9; MS (TS) *m/z* = 286.3 (M+1), 214.3, 212.3, 200.3, 199.3, 198.3, 183.1, 171.3, 172.5, 169.3; HRMS (ESI+) *m/z*: calcd. for C₁₂H₁₇ClNO₂ [M+H]⁺: 242.0940, found: 242.0942; HPLC (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): *t_R* (min) = 22.51 (52.21 %), 29.28 (47.79 %).



3,5-endo

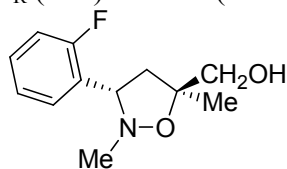
rac-5-methyl-3-(4-trifluoromethyl-phenyl)-2-methyl-isoxazoline-5-methanol (rac-2h-alc): obtained according to the general procedure in 95 % yield: IR (film): ν (cm⁻¹) = 761, 804, 837, 860, 884, 931, 994, 1019, 1067, 1121, 1163, 1323, 1369, 1421, 1458, 1620, 2872, 2964, 3432; ¹H NMR (300 MHz, CDCl₃): δ (ppm) = 1.42 (s, 3H, Me), 2.78-2.83 (dd, 1H, *J* = 8, 16 Hz, H-C₄), 3.46-3.49 (m, 1H, H-C₄), 3.56 (bs, 1H, H-C₃), 3.60-3.63 (m, 2H, CH₂OH), 7.49-7.51 (d, 2H, *J* = 8 Hz, H-Carom), 7.60-7.62 (d, 2H, *J* = 8 Hz, H-Carom); ¹³C NMR (125.8 MHz, CDCl₃): δ (ppm) = 22.7, 24.4, 29.7, 42.8, 43.1, 47.5, 48.5, 67.6, 71.0, 73.7, 125.5, 125.6, 125.7, 127.9, 128.1; MS (TS) *m/z* = 276.3 (M+1), 204.3, 202.3, 188.5, 186.5, 159.3; HRMS (ESI+) *m/z*: calcd. for C₁₃H₁₇F₃NO₂ [M+H]⁺: 276.1209, found: 276.1205; HPLC (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): *t_R* (min) = 23.65 (49.03 %), 26.54 (50.7 %).



3,5-endo

rac-5-methyl-3-(4-nitro-phenyl)-2-methyl-isoxazoline-5-methanol (rac-2j-alc):

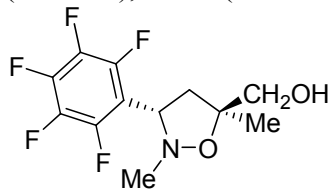
obtained according to the general procedure in 93 % yield: **IR** (film): ν (cm^{-1}) = 732, 804, 845, 884, 915, 1056, 1092, 1174, 1235, 1295, 1348, 1475, 1521, 1604, 2872, 2969, 3426; **^1H NMR** (300 MHz, CDCl_3): δ (ppm) = 1.44 (s, 3H, Me), 2.02-2.08 (m, 1H, H-C₄), 2.18 (bs, 1H, OH), 2.57 (s, 3H, NMe), 2.81-2.87 (m, 1H, H-C₄), 3.46-3.49 (bd, 2H, J = 11 Hz, CH₂OH + H-C₃), 3.61-3.64 (m, 1H, CH₂OH), 7.49-7.57 (m, 2H, H-Carom), 8.15-8.29 (m, 2H, H-Carom); **^{13}C NMR** (125.8 MHz, CDCl_3): δ (ppm) = 15.1, 22.7, 24.4, 31.2, 43.0, 43.1, 47.6, 48.5, 61.3, 67.6, 70.8, 73.4, 77.2, 100.1, 123.4, 124.0, 127.7, 128.4, 128.6; **MS** (TS) m/z = 253.1 (M+1), 235.1, 219.1, 203.1, 188.1, 179.3, 168.1, 165.1, 162.3; **HRMS** (ESI+) m/z : calcd. for $\text{C}_{12}\text{H}_{17}\text{N}_2\text{O}_4$ [M+H]⁺: 253.1182, found: 253.1189; **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): t_R (min) = 49.05 (51.01 %), 51.89 (48.99 %).



3,5-endo

rac-5-methyl-3-(2-fluoro-phenyl)-2-methyl-isoxazoline-5-methanol (rac-2k-alc):

obtained according to the general procedure in 98 % yield: **IR** (film): ν (cm^{-1}) = 756, 818, 857, 886, 931, 1054, 1130, 1231, 1277, 1367, 1455, 1492, 1587, 1617, 2872, 2965, 3403; **^1H NMR** (300 MHz, CDCl_3): δ (ppm) = 1.41 (s, 3H, Me), 2.04-2.10 (m, 1H, H-C₄), 2.18 (bs, 1H, OH), 2.59 (s, 3H, NMe), 2.78-2.83 (dd, 1H, J = 8, 16 Hz, H-C₄), 3.47-3.50 (bd, 1H, J = 11 Hz, CH₂OH), 3.60-3.63 (bd, 1H, J = 11 Hz, CH₂OH), 3.87 (bs, 1H, H-C₃), 7.02-7.06 (m, 1H, H-Carom), 7.14-7.18 (m, 1H, H-Carom), 7.23-7.27 (m, 1H, H-Carom), 7.50-7.54 (m, 1H, H-Carom); **^{13}C NMR** (125.8 MHz, CDCl_3): δ (ppm) = 22.7, 24.3, 29.7, 30.3, 31.2, 43.0, 45.8, 46.4, 47.8, 59.1, 59.5, 65.6, 70.7, 115.2, 115.3, 115.4, 115.5, 123.8, 123.9, 124.4, 124.5, 124.6, 128.2, 128.4, 129.0, 129.1, 129.2, 129.3, 129.4, 132.3; **MS** (TS) m/z = 226.3 (M+1), 222.3, 180.3, 176.3, 165.3, 161.3, 152.3; **HRMS** (ESI+) m/z : calcd. for $\text{C}_{12}\text{H}_{17}\text{FNO}_2$ [M+H]⁺: 226.1233, found: 226.1237; **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): t_R (min) = 25.05 (51.05 %), 29.71 (48.95 %).

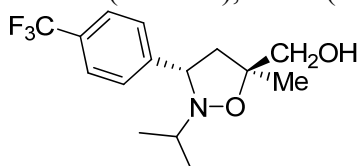


3,5-endo

rac-5-methyl-3-(pentafluoro-phenyl)-2-methyl-isoxazoline-5-methanol (rac-2l-alc):

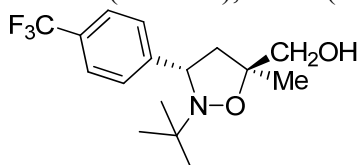
obtained according to the general procedure in 60 % yield (*endo/exo* 40/60): **IR** (film): ν

(cm^{-1}) = 736, 771, 806, 837, 894, 956, 978, 1005, 1043, 1131, 1149, 1215, 1302, 1372, 1461, 1502, 1524, 1655, 2971, 3392; $^1\text{H NMR}$ (300 MHz, CDCl_3): δ (ppm) = 1.36 (s, 3H, Me), 2.05 (bs, 1H, OH), 2.25-2.30 (m, 1H, $J = 8, 12$ Hz, H-C₄), 2.56 (s, 3H, NMe), 2.66-2.72 (dd, 1H, $J = 10, 16$ Hz, H-C₄), 3.55-3.58 (d, 2H, $J = 11$ Hz, CH_2OH), 3.77-3.80 (bd, 1H, $J = 11$ Hz, CH_2OH), 3.95-4.00 (dd, 1H, $J = 8, 10$ Hz, H-C₃); $^{13}\text{C NMR}$ (125.8 MHz, CDCl_3): δ (ppm) = 15.2, 22.7, 42.5, 43.2, 63.2, 65.8, 68.9; **MS** (TS) $m/z = 298.5$ (M+1), 226.3, 224.3, 211.3, 210.3, 208.1, 192.3, 190.3, 181.3, 179.1, 163.3; **HRMS** (ESI+) m/z : calcd. for $\text{C}_{12}\text{H}_{13}\text{F}_5\text{NO}_2$ [M+H]⁺: 298.0864, found: 298.0860; **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): t_R (min) = 18.70 (49.32 %), 19.81 (50.68 %).



3,5-endo

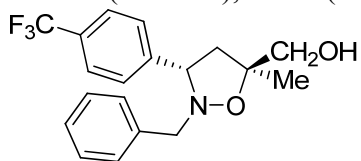
rac-5-methyl-3-(4-trifluoromethyl-phenyl)-2-iso-propyl-isoxazoline-5-methanol (rac-2o-alc): obtained according to the general procedure in 98 % yield: **IR** (film): ν (cm^{-1}) = 731, 804, 837, 905, 1019, 1067, 1124, 1164, 1324, 1368, 1420, 1455, 1619, 1739, 2928, 2971, 3415; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) = 0.98-1.00 (d, 6H, $J = 6$ Hz, CH_3), 1.97-2.02 (dd, 1H, $J = 8, 12$ Hz, H-C₄), 2.82-2.89 (m, 2H, CH and H-C₄), 3.46-3.48 (d, 1H, $J = 11$ Hz, CH_2OH), 3.62-3.65 (d, 1H, $J = 11$ Hz, CH_2OH), 4.06-4.09 (bt, 1H, $J = 7$ Hz, H-C₃), 7.53-7.55 (d, 2H, $J = 8$ Hz, H-Carom), 7.58-7.60 (d, 2H, $J = 8$ Hz, H-Carom); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3): δ (ppm) = 21.7, 28.9, 31.2, 36.4, 37.9, 50.0, 80.8, 125.6, 125.7, 128.3, 129.4; **MS** (TS) $m/z = 304.0$ (M+1), 297.1, 279.0, 194.4, 177.5, 102.6; **HRMS** (ESI+) m/z : calcd. for $\text{C}_{15}\text{H}_{21}\text{F}_3\text{NO}_2$ [M+H]⁺: 304.1512, found: 304.1518; **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): t_R (min) = 16.15 (46.28 %), 17.46 (46.64 %).



3,5-endo

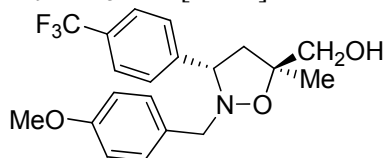
rac-5-methyl-3-(4-trifluoromethyl-phenyl)-2-tert-butyl-isoxazoline-5-methanol (rac-2p-alc): obtained according to the general procedure in 63 % yield: **IR** (film): ν (cm^{-1}) = 733, 837, 904, 1018, 1067, 1127, 1165, 1218, 1325, 1364, 1459, 1618, 1725, 2856, 2926; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) = 1.44 (s, 9H, *tert*-butyl), 1.91-1.96 (m, 1H, $J = 8, 12$ Hz, H-C₄), 2.98-3.03 (dd, 1H, $J = 8, 12$ Hz, H-C₄), 3.42-3.44 (d, 1H, $J = 11$ Hz, CH_2OH), 3.59-3.62 (d, 1H, $J = 11$ Hz, CH_2OH), 4.11-4.15 (t, 1H, $J = 8$ Hz, H-C₃), 7.53-7.55 (m, 2H, $J = 3, 6$ Hz, H-Carom), 7.71-7.73 (m, 2H, $J = 3, 6$ Hz, H-Carom); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3): δ (ppm) = 26.6, 29.9, 30.5, 34.4, 38.9, 50.0, 64.6, 125.5, 127.8, 128.9, 130.0; **MS** (TS) $m/z = 318.3$ (M+1), 317.3, 290.2, 262.2, 240.3, 227.4, 161.4; **HRMS** (ESI+) m/z : calcd. for $\text{C}_{16}\text{H}_{23}\text{F}_3\text{NO}_2$ [M+H]⁺: 318.1669, found: 318.1675; **HPLC**

(CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): t_R (min) = 14.47 (48.34 %), 27.45 (51.66 %).



3,5-endo

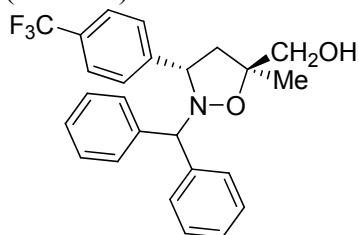
rac-5-methyl-3-(4-trifluoromethyl-phenyl)-2-benzyl-isoxazoline-5-methanol (rac-2q-alc): obtained according to the general procedure in 84 % yield: **IR** (film): ν (cm^{-1}) = 732, 905, 1068, 1127, 1166, 1325, 1619, 2926; separated diastereomers: *endo*: $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) = 1.18-1.24 (m, 1H, H-C₄-endo), 1.30 (s, 3H, CH₃-endo), 2.43-2.49 (bdd, 1H, H-C₄-endo), 3.19 (bs, 1H, H-C₃-endo), 3.60-3.67 (bm, 2H, CH₂OH), 3.85-3.92 (bm, 2H, CH₂), 7.26-7.32 (m, 5H, H-Carom), 7.57-7.63 (m, 4H, H-Carom); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3): δ (ppm) = 15.9, 22.3, 31.8, 46.9, 65.7, 87.7, 125.6, 125.8, 127.7, 128.1, 128.5, 128.8, 130.1, 159.1; **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): t_R (min) = 17.25 (45.08 %), 18.57 (45.34 %); *exo*: $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) = 1.41 (s, 3H, CH₃-exo), 2.01-2.07 (dd, 1H, $J = 9, 13$ Hz, H-C₄-exo), 2.78-2.83 (dd, 1H, $J = 9, 13$ Hz, H-C₄-exo), 3.48-3.51 (m, 1H, CH₂), 3.57-3.60 (m, 1H, CH₂), 3.81-3.85 (bt, 1H, $J = 8$ Hz, H-C₃-exo), 3.70-3.73 (d, 1H, $J = 11$ Hz, CH₂OH), 4.00-4.04 (d, 1H, $J = 11$ Hz, CH₂OH), 7.30-7.32 (m, 5H, H-Carom), 7.55-7.57 (d, 2H, $J = 8$ Hz, H-Carom), 7.60-7.62 (d, 2H, $J = 8$ Hz, H-Carom); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3): δ (ppm) = 15.8, 21.3, 31.5, 47.9, 65.2, 87.3, 125.3, 125.8, 128.1, 128.5, 128.9, 130.1, 159.1; **HPLC** (CHIRALPAK AD, Grad. 99+1—85+15, 1 mL/min, 80 min, 254+320 nm): t_R (min) = 20.01 (49.81 %), 21.33 (50.19 %); **MS** (TS) $m/z = 374.2$ (M+Na), 352.2 (M+1), 304.2, 102.6; **HRMS** (ESI+) m/z : calcd. for $\text{C}_{19}\text{H}_{21}\text{F}_3\text{NO}_2$ [M+H]⁺: 352.1525, found: 352.1518.



3,5-endo

rac-5-methyl-3-(4-trifluoromethyl-phenyl)-2-(4-methoxy-benzyl)-isoxazoline-5-methanol (rac-2r-alc): obtained according to the general procedure in 94 % yield: **IR** (film): ν (cm^{-1}) = 732, 808, 1068, 1131, 1170, 1249, 1325, 1513, 1611, 2256, 2929, 3691; $^1\text{H NMR}$ (400 MHz, CDCl_3): δ (ppm) = 1.40 (s, 3H, CH₃-endo), 1.44 (s, 3H, CH₃-exo), 2.00-2.06 (dd, 1H, $J = 10, 12$ Hz, H-C₄-endo), 2.41-2.48 (m, 2H, H-C₄-exo), 2.76-2.81 (dd, 1H, $J = 8, 17$ Hz, H-C₄-endo), 3.21 (bm, 1H, H-C₃-exo), 4.04-4.08 (bm, 1H, H-C₃-endo), 3.56-3.99 (m, 4H, CH₂ and CH₂OH), 3.80 (s, 3H, OMe), 6.83-6.85 (d, 2H, $J = 8$ Hz, H-Carom), 7.20-7.22 (d, 2H, $J = 8$ Hz, H-Carom), 7.52-7.54 (d, 2H, $J = 8$ Hz, H-Carom), 7.60-7.62 (d, 2H, $J = 8$ Hz, H-Carom); $^{13}\text{C NMR}$ (100.6 MHz, CDCl_3): δ (ppm) = 15.7, 19.5, 21.8, 33.4, 46.7, 55.4, 58.5, 66.4, 70.1, 81.1, 81.7, 113.8, 113.9, 125.7, 125.8, 125.9, 128.2, 128.4, 128.8, 128.9, 129.3, 129.9, 130.0, 130.2, 130.4, 159.1, 159.2; **MS** (TS) $m/z = 404.4$ (M+Na), 384.4, 308.2, 307.4; **HRMS** (ESI+) m/z : calcd. for $\text{C}_{20}\text{H}_{23}\text{F}_3\text{NO}_3$ [M+H]⁺: 382.1640, found: 382.1624; **HPLC** (CHIRACEL OD-H, Grad.

99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): t_R (min) = 33.76 (47.13 %), 36.74 (52.87 %).



3,5-endo

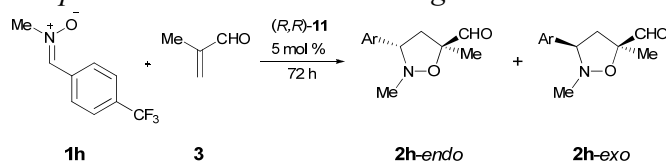
rac-5-methyl-3-(4-trifluoromethyl-phenyl)-2-diphenylmethyl-isoxazoline-5-methanol (rac-2s-alc): obtained according to the general procedure in 98 % yield: **IR** (film): ν (cm^{-1}) = 729, 1051, 1068, 1130, 1169, 1325, 1384, 1420, 1453, 1494, 1619, 2245, 2873, 2928, 2977, 3221, 3555; **^1H NMR** (400 MHz, CDCl_3): δ (ppm) = 1.44 (bs, 4H, CH and CH_3), 2.03-2.08 (bm, 1H, H- C_4), 2.29-2.37 (bm, 2H, CH_2OH), 2.74-2.76 (bm, 1H, H- C_4), 3.91 (bs, 1H, H- C_3), 7.16-7.58 (m, 14H, $J = 8$ Hz, H-*Carom*); **^{13}C NMR** (100.6 MHz, CDCl_3): δ (ppm) = 14.36, 15.5, 29.9, 30.5, 47.7, 66.1, 122.1, 125.7, 125.8, 127.1, 128.0, 128.2, 128.3, 129.8, 130.2, 130.4; **MS** (TS) m/z = 450.4 (M+Na), 450.1, 445.4, 413.4, 403.3, 402.3, 400.3, 389.2, 348.3, 304.2, 279.1, 242.3, 219.3, 167.4, 102.6; **HRMS** (ESI+) m/z : calcd. for $\text{C}_{25}\text{H}_{25}\text{F}_3\text{NO}_2$ $[\text{M}+\text{H}]^+$: 428.1819, found: 428.1831; **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): t_R (min) = 17.45 (47.7 %), 20.75 (45.00 %).

Ru-catalyzed 1,3-dipolar cycloaddition reaction between nitrones and methacrolein

General procedure: In a 50 mL Schlenk tube equipped with a magnetic stirring bar, the catalyst (36 mg, 0.025 mmol, 5 mol %) is loaded and CH₂Cl₂ (1 mL) is added. The solution is stirred at the appropriate temperature and methacrolein (62 μL, 0.75 mmol, 1.5 equiv.) is added. The mixture stirred for further 20 minutes before addition of the corresponding nitron (0.5 mmol, 1 equiv.) as a solid and in one portion. The extent of the reaction is followed by TLC analysis (SiO₂, AcOEt/cyclohexane 2/3 or CH₂Cl₂) until no traces of nitron are observed. Pentane is added to precipitate the catalyst and most of the unreacted nitron and the reaction mixture is passed through a plug of Celite 545 (P3-frit, Celite 545, H_{dry} = 1.5 cm, Φ_e = 2 cm) followed by *in vacuo* removal of volatiles. Purification by a quick filtration through a SiO₂ plug (H_{dry} = 5 cm, Φ_e = 1 cm) with CH₂Cl₂ gives viscous, clear oils that solidify at -30 °C. Diastereomeric ratios are determined by ¹H NMR of the crude mixture.

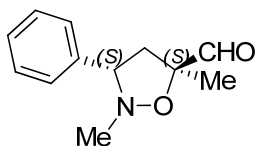
Note: In all cases, partial data for the *endo* diastereomer is given (in the mixture). Most isoxazolidines proved to be too unstable for MS analysis. MS data for the corresponding alcohols is given in the following section.

Temperature and solvent screening^a



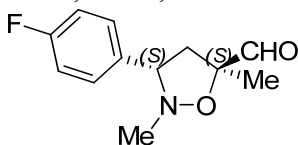
SOLVENT	T (° C)	yield (%) ^b	<i>endo</i> / <i>exo</i> ^c	<i>ee</i> (%) <i>endo</i> ^d
dry CH ₂ Cl ₂	- 10	65	> 95 / 5	91
dry CH ₂ Cl ₂	- 5	86	94 / 6	92
dry CH ₂ Cl ₂	0	86	88 / 12	91
CH ₂ Cl ₂	- 5	85	94 / 6	92
THF	- 5	89	95 / 5	89
toluene	- 5	60	84 / 16	90
AcOEt	- 5	76	95 / 5	90
CHCl ₃	- 5	60	> 95 / 5	81
<i>i</i> -PrOH	- 5	0	n.d.	n.d.
<i>i</i> -PrOH _{F6}	- 5	50	95 / 5	86
water	0	30	95 / 5	88

^a All reactions were carried out under N₂, using **(R,R)-11** (5 mol %), **1h** (0.5 mmol) and **3** (1 mmol), in 1 mL of dry solvent. ^b Isolated yield. ^c Determined by ¹H NMR analysis. ^d Determined by chiral phase HPLC.



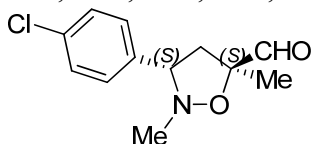
3,5-endo

(3S,5S)-5-methyl-3-(phenyl)-2-methyl-isoxazoline-5-carbaldehyde (S,S-2d):³ obtained according to the general procedure in 84 % yield (*endo/exo* 93/7): **IR** (film): ν (cm^{-1}) = 699, 753, 793, 845, 894, 914, 956, 973, 1025, 1073, 1091, 1139, 1177, 1290, 1307, 1361, 1374, 1455, 1494, 1604, 1732, 2808, 2849, 2963; *endo*: **¹H NMR** (300 MHz, CDCl_3): δ (ppm) = 1.38 (s, 3H, Me), 2.40-2.46 (bdd, 1H, $J = 9, 12$ Hz, H-C₄), 2.61 (s, 3H, NMe), 2.66-2.71 (bdd, 1H, $J = 9, 12$ Hz, H-C₄), 3.51-3.55 (bt, 1H, $J = 8$ Hz, H-C₃), 7.25-7.33 (m, 5H, H-C_{Ar}), 9.76 (s, 1H, CHO); *exo*: **¹H NMR** (300 MHz, CDCl_3): δ (ppm) = 1.53 (s, 3H, Me), 2.29-2.35 (dd, 1H, $J = 9, 12$ Hz, H-C₄), 2.67 (s, 3H, NMe), 2.99-3.03 (bm, 1H, H-C₄), 3.71 (bs, 1H, H-C₃), 7.32-7.41 (m, 5H, H-C_{Ar}), 9.74 (s, 1H, CHO); **¹³C NMR** (100.6 MHz, CDCl_3): δ (ppm) = 20.4, 34.6, 48.5, 85.6, 121.8, 125.8, 125.9, 128.1, 128.3, 130.9, 141.9, 200.5.



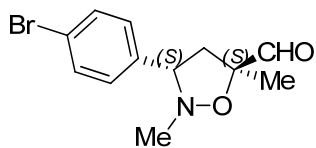
3,5-endo

(3S,5S)-5-methyl-3-(4-fluoro-phenyl)-2-methyl-isoxazoline-5-carbaldehyde (S,S-2e):³ obtained according to the general procedure in 73 % yield (*endo/exo* 94/6): **IR** (film): ν (cm^{-1}) = 718, 761, 772, 837, 893, 979, 1015, 1091, 1134, 1158, 1223, 1295, 1378, 1473, 1509, 1606, 1640, 1733, 2850, 2963; **¹H NMR** (300 MHz, CDCl_3): δ (ppm) = 1.46 (s, 3H, Me), 2.17-2.23 (dd, 1H, $J = 9, 13$ Hz, H-C₄), 2.59 (s, 3H, NMe), 2.93-2.97 (bdd, 1H, $J = 9, 13$ Hz, H-C₄), 3.65 (bs, 1H, $J = 9$ Hz, H-C₃), 7.02-7.06 (m, 2H, H-C_{arom}), 7.31-7.34 (m, 2H, H-C_{arom}), 9.67 (s, 1H, CHO); **¹³C NMR** (100.6 MHz, CDCl_3): δ (ppm) = 19.1, 47.7, 72.8, 85.1, 128.1, 129.4, 129.7, 129.9, 161.5, 163.9, 205.0.



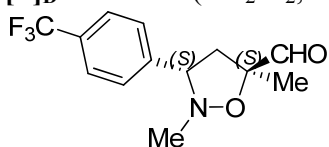
3,5-endo

(3S,5S)-5-methyl-3-(4-chloro-phenyl)-2-methyl-isoxazoline-5-carbaldehyde (S,S-2f):³ obtained according to the general procedure in 79 % yield (*endo/exo* 94/6): **IR** (film): ν (cm^{-1}) = 700, 717, 825, 850, 893, 922, 979, 1015, 1089, 1134, 1174, 1296, 1376, 1411, 1474, 1491, 1519, 1599, 1640, 1733, 2849, 2962; **¹H NMR** (300 MHz, CDCl_3): δ (ppm) = 1.43 (s, 3H, Me), 2.15-2.20 (dd, 1H, $J = 9, 13$ Hz, H-C₄), 2.59 (s, 3H, NMe), 2.94-2.98 (bdd, 1H, $J = 9, 13$ Hz, H-C₄), 3.65 (bs, 1H, $J = 9$ Hz, H-C₃), 7.27-7.33 (m, 4H, H-C_{arom}), 9.65 (s, 1H, CHO); **¹³C NMR** (100.6 MHz, CDCl_3): δ (ppm) = 19.0, 47.6, 61.2, 85.2, 128.3, 128.5, 129.1, 129.4, 134.0, 137.0, 204.9.



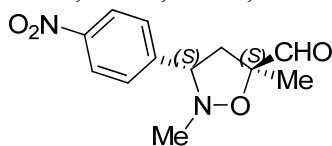
3,5-endo

(3*S*,5*S*)-5-methyl-3-(4-bromo-phenyl)-2-methyl-isoxazoline-5-carbaldehyde (S,S-2g):³ obtained according to the general procedure in 73 % yield (*endo/exo* >95/5): **IR** (film): ν (cm⁻¹) = 822, 851, 893, 979, 1011, 1071, 1091, 1134, 1296, 1376, 1409, 1474, 1488, 1519, 1734, 2847, 2960; **¹H NMR** (300 MHz, CDCl₃): δ (ppm) = 1.46 (s, 3H, Me), 2.16-2.21 (dd, 1H, *J* = 9, 13 Hz, H-C₄), 2.60 (s, 3H, NMe), 2.95-3.00 (bdd, 1H, *J* = 9, 13 Hz, H-C₄), 3.65 (bs, 1H, *J* = 9 Hz, H-C₃), 7.23-7.25 (d, 2H, *J* = 9 Hz, H-Carom), 7.47-7.49 (d, 2H, *J* = 9 Hz, H-Carom), 9.67 (s, 1H, CHO); **¹³C NMR** (100.6 MHz, CDCl₃): δ (ppm) = 15.5, 21.2, 47.6, 66.1, 85.2, 122.2, 128.3, 129.1, 129.5, 132.1, 137.5, 200.2; **[α]_D²⁰** = - 67.6 (CH₂Cl₂, *c* = 0.42 mgmL⁻¹, 98 % ee, **3*S*,5*S***).



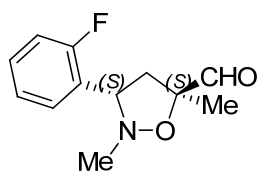
3,5-endo

(3*S*,5*S*)-5-methyl-3-(4-trifluoromethyl-phenyl)-2-methyl-isoxazoline-5-carbaldehyde (S,S-2h):³ obtained according to the general procedure in 85 % yield (*endo/exo* 94/6): **IR** (film): ν (cm⁻¹) = 762, 839, 894, 979, 1019, 1068, 1123, 1165, 1324, 1378, 1421, 1474, 1520, 1620, 1735, 2853, 2963; **¹H NMR** (300 MHz, CDCl₃): δ (ppm) = 1.46 (s, 3H, Me), 2.18-2.23 (dd, 1H, *J* = 9, 13 Hz, H-C₄), 3.01-3.06 (bdd, 1H, *J* = 9, 13 Hz, H-C₄), 3.76 (bs, 1H, *J* = 9 Hz, H-C₃), 7.48-7.50 (d, 2H, *J* = 9 Hz, H-C_m), 7.61-7.63 (d, 2H, *J* = 9 Hz, H-C_o), 9.68 (s, 1H, CHO); **¹³C NMR** (100.6 MHz, CDCl₃): δ (ppm) = 21.1, 33.5, 47.5, 85.4, 122.8, 125.5, 125.9, 128.1, 130.3, 130.6, 142.8, 201.5.



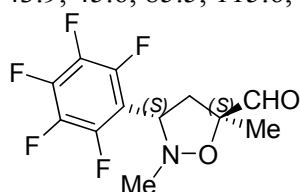
3,5-endo

(3*S*,5*S*)-5-methyl-3-(4-nitro-phenyl)-2-methyl-isoxazoline-5-carbaldehyde (S,S-2j):³ obtained according to the general procedure in 43 % yield (*endo/exo* 80/20): **IR** (film): ν (cm⁻¹) = 751, 856, 981, 1016, 1092, 1292, 1347, 1382, 1474, 1520, 1601, 1641, 1734, 2929; **¹H NMR** (300 MHz, CDCl₃): δ (ppm) = 1.45 (s, 3H, Me), 2.16-2.21 (dd, 1H, *J* = 9, 13 Hz, H-C₄), 2.64 (s, 3H, NMe), 3.07-3.12 (bdd, 1H, *J* = 9, 13 Hz, H-C₄), 3.86 (bs, 1H, *J* = 9 Hz, H-C₃), 7.55-7.57 (d, 2H, *J* = 9 Hz, H-Carom), 8.21-8.24 (d, 2H, *J* = 9 Hz, H-Carom), 9.68 (s, 1H, CHO); **¹³C NMR** (125.8 MHz, CDCl₃): δ (ppm) = 15.1, 18.6, 31.2, 42.7, 46.4, 46.9, 59.5, 61.3, 72.4, 77.2, 100.1, 123.4, 124.0, 127.7, 128.3, 128.7, 204.2.



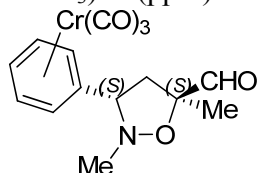
3,5-endo

(3S,5S)-5-methyl-3-(2-fluoro-phenyl)-2-methyl-isoxazoline-5-carbaldehyde (S,S-2k):³ obtained according to the general procedure in 74 % yield (*endo/exo* 95/5): **IR** (film): ν (cm⁻¹) = 727, 757, 798, 816, 853, 895, 941, 978, 1034, 1091, 1135, 1179, 1231, 1277, 1376, 1455, 1473, 1489, 1519, 1587, 1617, 1733, 2876, 2963; **¹H NMR** (300 MHz, CDCl₃): δ (ppm) = 1.43 (s, 3H, Me), 2.18-2.23 (dd, 1H, J = 9, 13 Hz, H-C₄), 2.65 (s, 3H, NMe), 3.01-3.06 (bdd, 1H, J = 9, 13 Hz, H-C₄), 4.12 (bs, 1H, J = 9 Hz, H-C₃), 7.02-7.06 (m, 1H, H-Carom), 7.14-7.18 (m, 1H, H-Carom), 7.24-7.30 (m, 1H, H-Carom), 7.51-7.54 (m, 1H, H-Carom), 9.68 (s, 1H, CHO); **¹³C NMR** (100.6 MHz, CDCl₃): δ (ppm) = 21.1, 43.9, 45.6, 85.5, 115.6, 115.8, 124.7, 125.8, 125.9, 128.5, 129.5, 159.7, 162.2, 201.0.



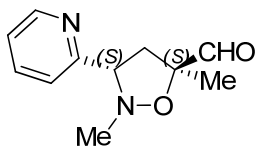
3,5-endo

(3S,5S)-5-methyl-3-(pentafluoro-phenyl)-2-methyl-isoxazoline-5-carbaldehyde (S,S-2l):³ obtained according to the general procedure in 60 % yield (*endo/exo* 91/9): **IR** (film): ν (cm⁻¹) = 736, 771, 842, 973, 1009, 1095, 1134, 1149, 1292, 1372, 1476, 1504, 1523, 1655, 1736, 2970; **¹H NMR** (300 MHz, CDCl₃): δ (ppm) = 1.39 (s, 3H, Me), 2.37-2.43 (dd, 1H, J = 9, 13 Hz, H-C₄), 2.64 (s, 3H, NMe), 2.83-2.89 (dd, 1H, J = 9, 13 Hz, H-C₄), 3.95-3.99 (t, 1H, J = 9 Hz, H-C₃), 9.74 (s, 1H, CHO); **¹³C NMR** (100.6 MHz, CDCl₃): δ (ppm) = 15.5, 19.6, 43.3, 62.4, 66.1, 85.0, 111.3, 136.8, 144.5, 146.9, 205.1.



3,5-endo

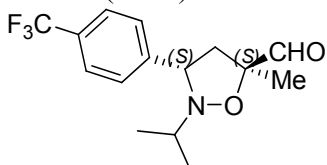
(3S,5S)-5-methyl-3-(η^6 -Cr(CO)₃-phenyl)-2-methyl-isoxazoline-5-carbaldehyde (S,S-2m): obtained according to the general procedure in 95 % yield (*endo/exo* 86/14): **IR** (CH₂Cl₂): ν (cm⁻¹) = 631, 660, 816, 1092, 1291, 1474, 1520, 1615, 1732, 1874, 1962, 2873, 2951; **¹H NMR** (400 MHz, CDCl₃): δ (ppm) = 1.40 (s, 3H, CH₃), 2.14-2.19 (dd, 1H, J = 6, 13 Hz, H-C₄), 2.76 (s, 3H, N-CH₃), 3.19-3.25 (dd, 1H, J = 8, 13 Hz, H-C₄-endo), 3.69-3.72 (bt, 1H, J = 7 Hz, H-C₃), 5.34-5.42 (m, 5H, H-Carom), 9.67 (s, 1H, CHO-endo); **¹³C NMR** (100.6 MHz, CDCl₃): δ (ppm) = 28.6, 45.5, 69.8, 86.0, 91.6, 92.2, 92.6, 92.7, 93.3, 93.7, 93.9, 109.7, 201.1.



3,5-endo

(3S,5S)-5-methyl-3-(2-pyridyl)-2-methyl-isoxazoline-5-carbaldehyde (S,S-2n):

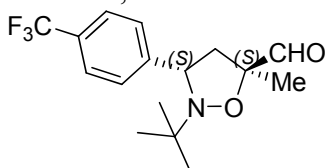
obtained according to the general procedure in 94 % yield (*endo/exo* 95/5 **IR** (CH₂Cl₂): ν (cm⁻¹) = 621, 639, 698, 749, 761, 807, 978, 1020, 1036, 1090, 1133, 1290, 1381, 1435, 1472, 1519, 1590, 1641, 1732, 2871, 2930, 2960, 3061; ¹H NMR (400 MHz, CDCl₃): δ (ppm) = 1.43 (s, 3H, CH₃), 2.53-2.59 (dd, 1H, *J* = 8, 12 Hz, H-C₄), 2.76 (s, 3H, N-CH₃), 2.77-2.82 (dd, 1H, *J* = 8, 12 Hz, H-C₄-endo), 3.83-3.88 (bt, 1H, *J* = 8 Hz, H-C₃), 7.24-7.27 (m, 1H, H-Carom), 7.34-7.36 (bd, 1H, H-Carom), 7.70-7.74 (m, 1H, H-Carom), 8.57-8.58 (bm, 1H, H-Carom), 9.78 (s, 1H, CHO-endo); ¹³C NMR (100.6 MHz, CDCl₃): δ (ppm) = 19.1, 43.3, 74.5, 84.7, 86.0, 121.9, 123.0, 123.2, 137.1, 149.4, 158.8, 204.8; **HRMS** (ESI+) *m/z*: calcd. for C₁₁H₁₅N₂O₂ [M+H]⁺: 207.1128, found: 207.1132.



3,5-endo

(3S,5S)-5-methyl-3-(4-trifluoromethyl-phenyl)-2-iso-propyl-isoxazoline-5-

carbaldehyde (S,S-2o): obtained according to the general procedure in 50 % yield (*endo/exo* 95/5): **IR** (CH₂Cl₂): ν (cm⁻¹) = 734, 838, 909, 1019, 1067, 1124, 1165, 1324, 1369, 1421, 1457, 1619, 1733, 2978; ¹H NMR (400 MHz, CDCl₃): δ (ppm) = 1.00-1.02 (d, 6H, *J* = 6 Hz, CH₃), 2.07-2.12 (ddd, 1H, *J* = 0.5, 7, 13 Hz, H-C₄), 2.80-2.89 (hept, 1H, *J* = 6 Hz, CH), 3.11-3.16 (dd, 1H, *J* = 7, 13 Hz, H-C₄), 4.22-4.25 (t, 1H, *J* = 7 Hz, H-C₃), 7.53-7.55 (d, 2H, *J* = 8 Hz, H-Carom), 7.58-7.60 (d, 2H, *J* = 8 Hz, H-Carom), 9.66 (d, 1H, *J* = 0.5 Hz, CHO); ¹³C NMR (100.6 MHz, CDCl₃): δ (ppm) = 16.7, 19.7, 19.9, 21.6, 46.9, 125.7, 128.0, 128.1, 129.7, 130.0, 205.5; **MS** (TS) *m/z* = 302.5 (M+1), 216.3, 191.3, 190.3, 174.5, 172.5, 159.3; **HRMS** (ESI+) *m/z*: calcd. for C₁₅H₁₉F₃NO₂ [M+H]⁺: 302.1371, found: 302.1362.

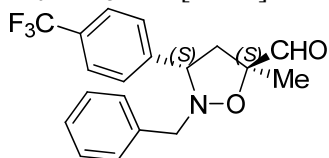


3,5-endo

(3S,5S)-5-methyl-3-(4-trifluoromethyl-phenyl)-2-tert-butyl-isoxazoline-5-

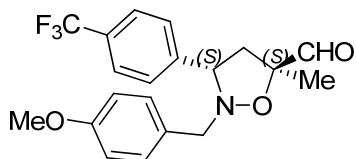
carbaldehyde (S,S-2p): obtained according to the general procedure in 19 % yield (*endo/exo* 95/5): **IR** (CH₂Cl₂): ν (cm⁻¹) = 747, 1068, 1126, 1165, 1276, 1326, 1462, 1730, 2163, 2932; ¹H NMR (400 MHz, CDCl₃): δ (ppm) = 1.63 (s, 9H, *tert*-butyl), 2.10-2.15 (m, 1H, H-C₄), 2.98-3.03 (dd, 1H, *J* = 7, 13 Hz, H-C₄), 4.20-4.24 (m, 1H, H-C₃), 7.53-7.55 (d, 2H, *J* = 3, 6 Hz, H-Carom), 7.70-7.72 (d, 2H, *J* = 3, 6 Hz, H-Carom), 9.64 (d, 1H, *J* = 0.8 Hz, CHO); ¹³C NMR (100.6 MHz, CDCl₃): δ (ppm) = 14.3, 23.2, 26.5, 30.6,

31.2, 68.4, 125.7, 127.6, 129.0, 131.1, 200.9; **MS** (TS) m/z = 316.5 (M+1), 279.5, 260.3, 242.3, 205.3, 190.3, 188.3, 174.5, 172.5, 167.3; **HRMS** (ESI+) m/z : calcd. for $C_{16}H_{21}F_3NO_2$ [M+H]⁺: 316.1519, found: 316.1518.



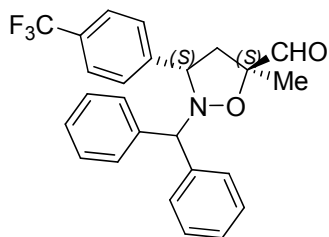
3,5-endo

(3S,5S)-5-methyl-3-(4-trifluoromethyl-phenyl)-2-benzyl-isoxazoline-5-carbaldehyde (S,S-2q): obtained according to the general procedure in 95 % yield (*endo/exo* 95/5): **IR** (CH_2Cl_2): ν (cm^{-1}) = 734, 839, 909, 1018, 1068, 1125, 1165, 1217, 1229, 1326, 1366, 1455, 1619, 1737, 2971; **¹H NMR** (400 MHz, $CDCl_3$): δ (ppm) = 1.43 (s, 3H, CH_3 -endo), 2.18-2.23 (m, 1H, H-C₄-endo), 3.07-3.12 (dd, 1H, J = 8, 13 Hz, H-C₄-endo), 3.83-3.86 (bd, 1H, J = 14 Hz, CH_2), 3.92-3.95 (bd, 1H, J = 14 Hz, CH_2), 4.04-4.08 (bt, 1H, J = 7 Hz, H-C₃-endo), 7.27-7.31 (m, 5H, H-Carom), 7.52-7.54 (d, 2H, J = 8 Hz, H-Carom), 7.61-7.63 (d, 2H, J = 8 Hz, H-Carom), 9.65 (s, 1H, CHO-endo); **¹³C NMR** (100.6 MHz, $CDCl_3$): δ (ppm) = 15.7, 21.6, 31.2, 46.7, 63.7, 85.7, 125.6, 125.9, 127.7, 128.2, 128.5, 128.8, 130.2, 159.1, 205.3; **MS** (TS) m/z = 350.5 (M+1), 280.5, 264.3, 230.3, 188.3, 173.3, 153.3; **HRMS** (ESI+) m/z : calcd. for $C_{19}H_{19}F_3NO_2$ [M+H]⁺: 350.1365, found: 350.1362.



3,5-endo

(3S,5S)-5-methyl-3-(4-trifluoromethyl-phenyl)-2-(4-methoxy-benzyl)-isoxazoline-5-carbaldehyde (S,S-2r): obtained according to the general procedure in 80 % yield (*endo/exo* 95/5): **IR** (CH_2Cl_2): ν (cm^{-1}) = 729, 834, 859, 1018, 1035, 1067, 1104, 1120, 1163, 1247, 1323, 1421, 1465, 1513, 1586, 1615, 1733, 2837, 2937; **¹H NMR** (400 MHz, $CDCl_3$): δ (ppm) = 1.35 (s, 3H, CH_3 -exo), 1.42 (s, 3H, CH_3 -endo), 2.17-2.22 (dd, 1H, J = 8, 17 Hz, H-C₄-endo), 2.42-2.48 (dd, 1H, J = 9, 13 Hz, H-C₄-exo), 2.63-2.68 (dd, 1H, J = 8, 17 Hz, H-C₄-exo), 3.06-3.11 (dd, 1H, J = 8, 17 Hz, H-C₄-endo), 3.69-3.73 (d, 1H, J = 14 Hz, CH_2), 3.79 (s, 3H, OMe-endo), 3.80 (s, 3H, OMe-exo), 3.82-3.90 (m, 2H, CH_2 and H-C₃-endo), 4.04-4.08 (bt, 1H, J = 7 Hz, H-C₃-exo), 6.82-6.84 (d, 2H, J = 8 Hz, H-Carom), 7.20-7.22 (d, 2H, J = 8 Hz, H-Carom), 7.51-7.53 (d, 2H, J = 8 Hz, H-Carom), 7.60-7.62 (d, 2H, J = 8 Hz, H-Carom), 9.64 (s, 1H, CHO-exo), 9.65 (s, 1H, CHO-endo); **¹³C NMR** (100.6 MHz, $CDCl_3$): δ (ppm) = 15.5, 19.0, 20.8, 31.2, 46.6, 58.8, 66.1, 70.1, 84.6, 85.7, 113.8, 113.9, 125.6, 125.7, 125.8, 125.9, 128.2, 128.5, 128.7, 129.3, 129.9, 130.1, 130.2, 130.4, 143.6, 159.1, 159.2, 205.1; **MS** (TS) m/z = 380.3 (M+1), 350.3, 332.5, 175.5; **HRMS** (ESI+) m/z : calcd. for $C_{20}H_{20}F_3NO_3$ [M+H]⁺: 380.1451, found: 380.1468.



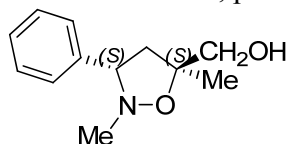
3,5-endo

(3*S*,5*S*)-5-methyl-3-(4-trifluoromethyl-phenyl)-2-diphenylmethyl-isoxazoline-5-carbaldehyde (*S,S*-2s): obtained according to the general procedure in 94 % yield (*endo/exo* 95/5): **IR** (CH₂Cl₂): ν (cm⁻¹) = 730, 904, 1019, 1068, 1124, 1165, 1326, 1455, 1735, 2969; **¹H NMR** (400 MHz, CDCl₃): δ (ppm) = 1.32 (bs, 4H, CH and CH₃), 3.25-3.30 (bdd, 1H, *J* = 9, 13 Hz, H-C₄), 4.31-4.34 (dd, 1H, *J* = 5, 9 Hz, H-C₄), 4.75 (bs, 1H, H-C₃), 7.14-7.54 (m, 14H, H-C_{arom}), 9.57 (bs, 1H, CHO); **¹³C NMR** (100.6 MHz, CDCl₃): δ (ppm) = 17.7, 19.6, 21.2, 31.2, 46.9, 125.4, 125.7, 127.7, 128.0, 128.3, 128.6, 128.7, 129.7, 130.0, 194.2.

Reduction of the products from the Ru-catalyzed 1,3-DCs of *N*-methyl and *N*-benzyl nitrones with methacrolein

General procedure: In a 10 mL conical flask equipped with a magnetic stirring bar, the corresponding aldehyde (50 mg, 1.35 equiv.) is added to EtOH (2 mL), followed by NaBH₄ (5.3 mg, 1 equiv.). The solution is stirred for 1 to 12 hours at r. t., then the excess NaBH₄ is quenched with water, the organic phase extracted with Et₂O, dried on anhydrous MgSO₄ or Na₂SO₄, filtered and concentrated to give a dense clear oil. Purification by column chromatography (SiO₂, H_{dry} = 15 cm, Φ_e = 1 cm), gradient cyclohexane/AcOEt (9/1, 30 mL; 8/2, 20 mL; 7/3, 20 mL) (*R_f* = 0.45 in 7/3 mixture) gives viscous, clear oils that solidify at -30 °C.

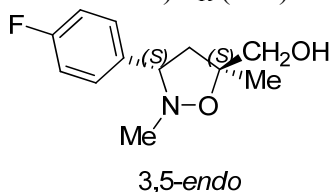
Note: In all cases, partial data for the *endo* diastereomer is given (in the mixture).



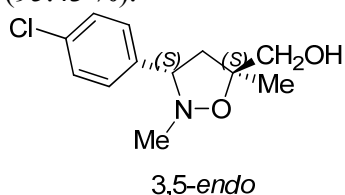
3,5-endo

(3*S*,5*S*)-5-methyl-3-(phenyl)-2-methyl-isoxazoline-5-methanol (*S,S*-2d-alc):³ obtained according to the general procedure in 90 % yield: **IR** (film): ν (cm⁻¹) = 763, 814, 825, 894, 930, 1005, 1016, 1086, 1142, 11683, 1323, 1379, 1481, 1453, 1621, 2875, 2974, 3458; **¹H NMR** (300 MHz, CDCl₃): δ (ppm) = 1.44 (s, 3H, Me), 2.09-2.14 (m, 1H, H-C₄), 2.50 (bs, 1H, OH), 2.54 (s, 3H, NMe), 2.75-2.78 (dd, 1H, *J* = 8, 16 Hz, H-C₄), 3.46-3.49 (bd, 2H, *J* = 11 Hz, CH₂OH + H-C₃), 3.60-3.63 (bd, 1H, *J* = 11 Hz, CH₂OH), 7.30-7.45 (m, 5H, H-C_{arom}); **¹³C NMR** (125.8 MHz, CDCl₃): δ (ppm) = 16.3, 23.3, 28.5, 32.2, 45.7, 48.5, 49.1, 59.5, 67.8, 68.5, 71.5, 74.3, 127.7, 127.9, 128.4, 128.5, 128.7, 130.5; **MS** (TS) *m/z* = 208.6 (M+1), 190.6, 184.6, 161.6; **HRMS** (ESI+) *m/z*: calcd. for C₁₂H₁₈NO₂ [M+H]⁺: 208.1332, found: 208.1333; **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): *t_R* (min) = 21.32 (96.47 %), 27.45

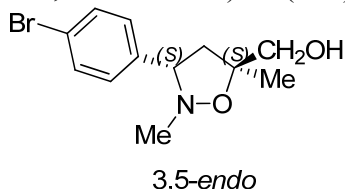
(3.53 %); **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+210 nm): t_R (min) = 21.32 (96.46 %), 27.45 (3.53 %).



(3*S*,5*S*)-5-methyl-3-(4-fluoro-phenyl)-2-methyl-isoxazoline-5-methanol (S,S-2e-alc):³ obtained according to the general procedure in 96 % yield: **IR** (film): ν (cm⁻¹) = 718, 837, 859, 883, 929, 1056, 1131, 1158, 1225, 1297, 1367, 1458, 1509, 1607, 2870, 2965, 3413; **¹H NMR** (300 MHz, CDCl₃): δ (ppm) = 1.42 (s, 3H, Me), 2.02-2.07 (m, 1H, H-C₄), 2.12 (bs, 1H, OH), 2.52 (s, 3H, NMe), 2.72-2.77 (dd, 1H, J = 8, 16 Hz, H-C₄), 3.44-3.47 (bd, 2H, J = 11 Hz, CH₂OH + H-C₃), 3.59-3.61 (bd, 1H, J = 11 Hz, CH₂OH), 7.01-7.05 (m, 2H, H-Carom), 7.32-7.35 (m, 2H, H-Carom); **¹³C NMR** (125.8 MHz, CDCl₃): δ (ppm) = 15.3, 22.8, 29.7, 30.3, 31.2, 42.6, 47.3, 47.8, 59.5, 65.6, 65.8, 71.2, 73.6, 115.1, 115.2, 115.4, 115.5, 115.6, 115.7, 129.2, 129.3, 129.4, 129.5, 131.2, 131.3; **MS** (TS) m/z = 226.3 (M+1), 203.3, 179.3, 177.3, 161.3, 152.3; **HRMS** (ESI+) m/z : calcd. for C₁₂H₁₇FNO₂ [M+H]⁺: 226.1230, found: 226.1237; **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): t_R (min) = 19.42 (4.56 %), 28.58 (95.43 %).

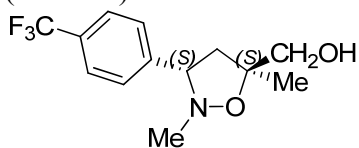


(3*S*,5*S*)-5-methyl-3-(4-chloro-phenyl)-2-methyl-isoxazoline-5-methanol (S,S-2f-alc):³ obtained according to the general procedure in 90 % yield: **IR** (film): ν (cm⁻¹) = 717, 804, 826, 858, 882, 929, 1015, 1055, 1090, 1131, 1216, 1298, 1368, 1411, 1458, 1492, 1599, 2869, 2964, 3409; **¹H NMR** (300 MHz, CDCl₃): δ (ppm) = 1.41 (s, 3H, Me), 2.00-2.06 (m, 1H, H-C₄), 2.18 (bs, 1H, OH), 2.52 (s, 3H, NMe), 2.73-2.78 (dd, 1H, J = 8, 16 Hz, H-C₄), 3.44-3.47 (bd, 2H, J = 11 Hz, CH₂OH + H-C₃), 3.58-3.61 (bd, 1H, J = 11 Hz, CH₂OH), 7.28-7.32 (m, 4H, H-Carom); **¹³C NMR** (125.8 MHz, CDCl₃): δ (ppm) = 15.3, 22.8, 29.7, 31.2, 42.7, 47.3, 47.9, 59.5, 65.6, 65.8, 71.1, 73.6, 128.5, 128.8, 128.9, 129.1, 129.2, 130.9; **MS** (TS) m/z = 242.5 (M+1), 232.1, 205.1, 197.3, 175.5, 173.5, 168.3, 165.5, 156.1, 154.3; **HRMS** (ESI+) m/z : calcd. for C₁₂H₁₇ClNO₂ [M+H]⁺: 242.0940, found: 242.0942; **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): t_R (min) = 21.28 (5.24 %), 28.97 (91.48 %).



(3*S*,5*S*)-5-methyl-3-(4-bromo-phenyl)-2-methyl-isoxazoline-5-methanol (S,S-2g-alc):³ obtained according to the general procedure in 93 % yield: **IR** (film): ν (cm⁻¹) = 714, 822, 858, 881, 929, 1011, 1069, 1131, 1215, 1298, 1367, 1408, 1456, 1488, 1592, 2869, 2962,

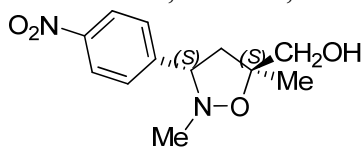
3426; $^1\text{H NMR}$ (300 MHz, CDCl_3): δ (ppm) = 1.41 (s, 3H, Me), 2.00-2.06 (m, 1H, H-C₄), 2.15 (bs, 1H, OH), 2.52 (s, 3H, NMe), 2.73-2.78 (dd, 1H, $J = 8, 16$ Hz, H-C₄), 3.43-3.46 (bd, 2H, $J = 11$ Hz, $\text{CH}_2\text{OH} + \text{H-C}_3$), 3.58-3.61 (bd, 1H, $J = 11$ Hz, CH_2OH), 7.24-7.26 (d, 2H, $J = 9$ Hz, H-Carom), 7.46-7.48 (d, 2H, $J = 9$ Hz, H-Carom); $^{13}\text{C NMR}$ (125.8 MHz, CDCl_3): δ (ppm) = 22.8, 29.68, 30.30, 31.22, 42.7, 47.3, 48.0, 59.5, 65.7, 71.0, 73.7, 129.4, 129.5, 131.2, 131.4, 131.8, 131.9; **MS** (TS) $m/z = 286.3$ (M+1), 214.3, 212.3, 200.3, 199.3, 198.3, 183.1, 171.3, 172.5, 169.3; **HRMS** (ESI+) m/z : calcd. for $\text{C}_{12}\text{H}_{17}\text{ClNO}_2$ $[\text{M}+\text{H}]^+$: 242.0940, found: 242.0942; **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): t_{R} (min) = 22.71 (1.12 %), 29.35 (96.14 %).



3,5-endo

(3S,5S)-5-methyl-3-(4-trifluoromethyl-phenyl)-2-methyl-isoxazoline-5-methanol

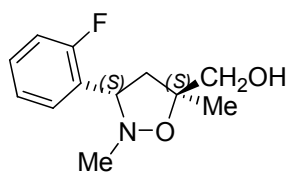
(S,S-2h-alc):³ obtained according to the general procedure in 90 % yield: **IR** (film): ν (cm^{-1}) = 761, 804, 837, 860, 884, 931, 994, 1019, 1067, 1121, 1163, 1323, 1369, 1421, 1458, 1620, 2872, 2964, 3432; $^1\text{H NMR}$ (300 MHz, CDCl_3): δ (ppm) = 1.42 (s, 3H, Me), 2.78-2.83 (dd, 1H, $J = 8, 16$ Hz, H-C₄), 3.46-3.49 (m, 1H, H-C₄), 3.56 (bs, 1H, H-C₃), 3.60-3.63 (m, 2H, CH_2OH), 7.49-7.51 (d, 2H, $J = 8$ Hz, H-Carom), 7.60-7.62 (d, 2H, $J = 8$ Hz, H-Carom); $^{13}\text{C NMR}$ (125.8 MHz, CDCl_3): δ (ppm) = 22.7, 24.4, 29.7, 42.8, 43.1, 47.5, 48.5, 67.6, 71.0, 73.7, 125.5, 125.6, 125.7, 127.9, 128.1; **MS** (TS) $m/z = 276.3$ (M+1), 204.3, 202.3, 188.5, 186.5, 159.3; **HRMS** (ESI+) m/z : calcd. for $\text{C}_{13}\text{H}_{17}\text{F}_3\text{NO}_2$ $[\text{M}+\text{H}]^+$: 276.1209, found: 276.12051 **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): t_{R} (min) = 23.74 (95.57 %), 26.61 (4.43 %).



3,5-endo

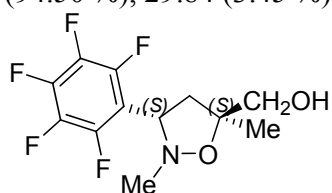
(3S,5S)-5-methyl-3-(4-nitro-phenyl)-2-methyl-isoxazoline-5-methanol **(S,S-2j-alc)**:³

obtained according to the general procedure in 99 % yield: **IR** (film): ν (cm^{-1}) = 732, 804, 845, 884, 915, 1056, 1092, 1174, 1235, 1295, 1348, 1475, 1521, 1604, 2872, 2969, 3426; $^1\text{H NMR}$ (300 MHz, CDCl_3): δ (ppm) = 1.44 (s, 3H, Me), 2.02-2.08 (m, 1H, H-C₄), 2.18 (bs, 1H, OH), 2.57 (s, 3H, NMe), 2.81-2.87 (m, 1H, H-C₄), 3.46-3.49 (bd, 2H, $J = 11$ Hz, $\text{CH}_2\text{OH} + \text{H-C}_3$), 3.61-3.64 (m, 1H, CH_2OH), 7.49-7.57 (m, 2H, H-Carom), 8.15-8.29 (m, 2H, H-Carom); $^{13}\text{C NMR}$ (125.8 MHz, CDCl_3): δ (ppm) = 15.1, 22.7, 24.4, 31.2, 43.0, 43.1, 47.6, 48.5, 61.3, 67.6, 70.8, 73.4, 77.2, 100.1, 123.4, 124.0, 127.7, 128.4, 128.6; **MS** (TS) $m/z = 253.1$ (M+1), 235.1, 219.1, 203.1, 188.1, 179.3, 168.1, 165.1, 162.3; **HRMS** (ESI+) m/z : calcd. for $\text{C}_{12}\text{H}_{17}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]^+$: 253.1182, found: 253.1189; **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): t_{R} (min) = 48.66 (67.49 %), 51.32 (2.86 %).



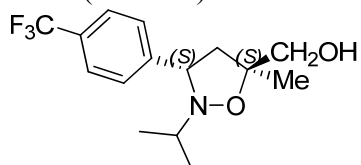
3,5-endo

(3S,5S)-5-methyl-3-(2-fluoro-phenyl)-2-methyl-isoxazoline-5-methanol (S,S-2k-alc):³ obtained according to the general procedure in 92 % yield: **IR** (film): ν (cm⁻¹) = 756, 818, 857, 886, 931, 1054, 1130, 1231, 1277, 1367, 1455, 1492, 1587, 1617, 2872, 2965, 3403; **¹H NMR** (300 MHz, CDCl₃): δ (ppm) = 1.41 (s, 3H, Me), 2.04-2.10 (m, 1H, H-C₄), 2.18 (bs, 1H, OH), 2.59 (s, 3H, NMe), 2.78-2.83 (dd, 1H, *J* = 8, 16 Hz, H-C₄), 3.47-3.50 (bd, 1H, *J* = 11 Hz, CH₂OH), 3.60-3.63 (bd, 1H, *J* = 11 Hz, CH₂OH), 3.87 (bs, 1H, H-C₃), 7.02-7.06 (m, 1H, H-Carom), 7.14-7.18 (m, 1H, H-Carom), 7.23-7.27 (m, 1H, H-Carom), 7.50-7.54 (m, 1H, H-Carom); **¹³C NMR** (125.8 MHz, CDCl₃): δ (ppm) = 22.7, 24.3, 29.7, 30.3, 31.2, 43.0, 45.8, 46.4, 47.8, 59.1, 59.5, 65.6, 70.7, 115.2, 115.3, 115.4, 115.5, 123.8, 123.9, 124.4, 124.5, 124.6, 128.2, 128.4, 129.0, 129.1, 129.2, 129.3, 129.4, 132.3; **MS** (TS) *m/z* = 226.3 (M+1), 222.3, 180.3, 176.3, 165.3, 161.3, 152.3; **HRMS** (ESI+) *m/z*: calcd. for C₁₂H₁₇FNO₂ [M+H]⁺: 226.1233, found: 226.1237; **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): *t_R* (min) = 25.13 (94.50 %), 29.84 (3.45 %).



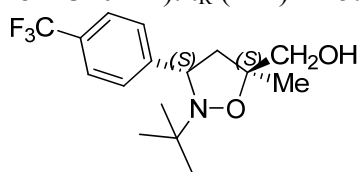
3,5-endo

(3S,5S)-5-methyl-3-(pentafluoro-phenyl)-2-methyl-isoxazoline-5-methanol (S,S-2l-alc):³ obtained according to the general procedure in 94 % yield: **IR** (film): ν (cm⁻¹) = 736, 771, 806, 837, 894, 956, 978, 1005, 1043, 1131, 1149, 1215, 1302, 1372, 1461, 1502, 1524, 1655, 2971, 3392; **¹H NMR** (300 MHz, CDCl₃): δ (ppm) = 1.36 (s, 3H, Me), 2.05 (bs, 1H, OH), 2.25-2.30 (m, 1H, *J* = 8, 12 Hz, H-C₄), 2.56 (s, 3H, NMe), 2.66-2.72 (dd, 1H, *J* = 10, 16 Hz, H-C₄), 3.55-3.58 (d, 2H, *J* = 11 Hz, CH₂OH), 3.77-3.80 (bd, 1H, *J* = 11 Hz, CH₂OH), 3.95-4.00 (dd, 1H, *J* = 8, 10 Hz, H-C₃); **¹³C NMR** (125.8 MHz, CDCl₃): δ (ppm) = 15.2, 22.7, 42.5, 43.2, 63.2, 65.8, 68.9; **MS** (TS) *m/z* = 298.5 (M+1), 226.3, 224.3, 211.3, 210.3, 208.1, 192.3, 190.3, 181.3, 179.1, 163.3; **HRMS** (ESI+) *m/z*: calcd. for C₁₂H₁₃F₅NO₂ [M+H]⁺: 298.0864, found: 298.0860; **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): *t_R* (min) = 18.53 (5.44 %), 19.63 (44.68 %).



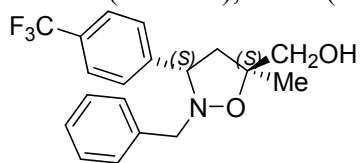
3,5-endo

(3*S*,5*S*)-5-methyl-3-(4-trifluoromethyl-phenyl)-2-iso-propyl-isoxazoline-5-methanol (S,S-2o-alc): obtained according to the general procedure in 99 % yield: **IR** (film): ν (cm⁻¹) = 731, 804, 837, 905, 1019, 1067, 1124, 1164, 1324, 1368, 1420, 1455, 1619, 1739, 2928, 2971, 3415; **¹H NMR** (400 MHz, CDCl₃): δ (ppm) = 0.98-1.00 (d, 6H, *J* = 6 Hz, CH₃), 1.97-2.02 (dd, 1H, *J* = 8, 12 Hz, H-C₄), 2.82-2.89 (m, 2H, CH and H-C₄), 3.46-3.48 (d, 1H, *J* = 11 Hz, CH₂OH), 3.62-3.65 (d, 1H, *J* = 11 Hz, CH₂OH), 4.06-4.09 (bt, 1H, *J* = 7 Hz, H-C₃), 7.53-7.55 (d, 2H, *J* = 8 Hz, H-Carom), 7.58-7.60 (d, 2H, *J* = 8 Hz, H-Carom); **¹³C NMR** (100.6 MHz, CDCl₃): δ (ppm) = 21.7, 28.9, 31.2, 36.4, 37.9, 50.0, 80.8, 125.6, 125.7, 128.3, 129.4; **MS** (TS) *m/z* = 304.0 (M+1), 297.1, 279.0, 194.4, 177.5, 102.6; **HRMS** (ESI+) *m/z*: calcd. for C₁₅H₂₁F₃NO₂ [M+H]⁺: 304.1512, found: 304.1518; **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): *t_R* (min) = 15.89 (89.30 %), 17.16 (10.70 %).



3,5-endo

(3*S*,5*S*)-5-methyl-3-(4-trifluoromethyl-phenyl)-2-tert-butyl-isoxazoline-5-methanol (S,S-2p-alc): obtained according to the general procedure in 92 % yield: **IR** (film): ν (cm⁻¹) = 733, 837, 904, 1018, 1067, 1127, 1165, 1218, 1325, 1364, 1459, 1618, 1725, 2856, 2926; **¹H NMR** (400 MHz, CDCl₃): δ (ppm) = 1.44 (s, 9H, *tert*-butyl), 1.91-1.96 (m, 1H, *J* = 8, 12 Hz, H-C₄), 2.98-3.03 (dd, 1H, *J* = 8, 12 Hz, H-C₄), 3.42-3.44 (d, 1H, *J* = 11 Hz, CH₂OH), 3.59-3.62 (d, 1H, *J* = 11 Hz, CH₂OH), 4.11-4.15 (t, 1H, *J* = 8 Hz, H-C₃), 7.53-7.55 (m, 2H, *J* = 3, 6 Hz, H-Carom), 7.71-7.73 (m, 2H, *J* = 3, 6 Hz, H-Carom); **¹³C NMR** (100.6 MHz, CDCl₃): δ (ppm) = 26.6, 29.9, 30.5, 34.4, 38.9, 50.0, 64.6, 125.5, 127.8, 128.9, 130.0; **MS** (TS) *m/z* = 318.3 (M+1), 317.3, 290.2, 262.2, 240.3, 227.4, 161.4; **HRMS** (ESI+) *m/z*: calcd. for C₁₆H₂₃F₃NO₂ [M+H]⁺: 318.1669, found: 318.1675; **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): *t_R* (min) = 13.69 (79.59 %), 15.08 (20.41 %).

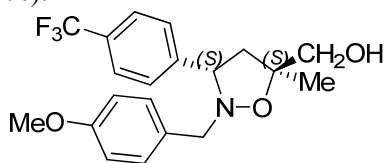


3,5-endo

(3*S*,5*S*)-5-methyl-3-(4-trifluoromethyl-phenyl)-2-benzyl-isoxazoline-5-methanol (S,S-2q-alc):

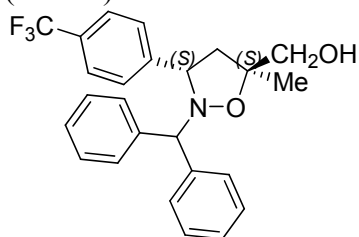
obtained according to the general procedure in 93 % yield: **IR** (film): ν (cm⁻¹) = 732, 905, 1068, 1127, 1166, 1325, 1619, 2926; **¹H NMR** (400 MHz, CDCl₃): δ (ppm) = 1.18-1.24 (m, 1H, H-C₄-endo), 1.30 (s, 3H, CH₃-endo), 2.43-2.49 (bdd, 1H, H-C₄-endo), 3.19 (bs, 1H, H-C₃-endo), 3.60-3.67 (bm, 2H, CH₂OH), 3.85-3.92 (bm, 2H, CH₂), 7.26-7.32 (m, 5H, H-Carom), 7.57-7.63 (m, 4H, H-Carom); **¹³C NMR** (100.6 MHz, CDCl₃): δ (ppm) = 15.9, 22.3, 31.8, 46.9, 65.7, 87.7, 125.6, 125.8, 127.7, 128.1, 128.5, 128.8, 130.1, 159.1; **MS** (TS) *m/z* = 374.2 (M+Na), 352.2 (M+1), 304.2, 102.6; **HRMS** (ESI+) *m/z*: calcd. for C₁₉H₂₁F₃NO₂ [M+H]⁺: 352.1525, found: 352.1518; **HPLC** (CHIRALPAK AD, Grad.

99+1—85+15, 1 mL/min, 80 min, 254+320 nm): t_R (min) = 19.72 (87.08 %), 21.21 (5.99 %).



3,5-endo

(3*S*,5*S*)-5-methyl-3-(4-trifluoromethyl-phenyl)-2-(4-methoxy-benzyl)-isoxazoline-5-methanol (*S,S*-2*r*-alc): obtained according to the general procedure in 99 % yield: **IR** (film): ν (cm^{-1}) = 732, 808, 1068, 1131, 1170, 1249, 1325, 1513, 1611, 2256, 2929, 3691; **$^1\text{H NMR}$** (400 MHz, CDCl_3): δ (ppm) = 1.40 (s, 3H, CH_3 -endo), 1.44 (s, 3H, CH_3 -exo), 2.00-2.06 (dd, 1H, $J = 10, 12$ Hz, H-C₄-endo), 2.41-2.48 (m, 2H, H-C₄-exo), 2.76-2.81 (dd, 1H, $J = 8, 17$ Hz, H-C₄-endo), 3.21 (bm, 1H, H-C₃-exo), 4.04-4.08 (bm, 1H, H-C₃-endo), 3.56-3.99 (m, 4H, CH_2 and CH_2OH), 3.80 (s, 3H, OMe), 6.83-6.85 (d, 2H, $J = 8$ Hz, H-Carom), 7.20-7.22 (d, 2H, $J = 8$ Hz, H-Carom), 7.52-7.54 (d, 2H, $J = 8$ Hz, H-Carom), 7.60-7.62 (d, 2H, $J = 8$ Hz, H-Carom); **$^{13}\text{C NMR}$** (100.6 MHz, CDCl_3): δ (ppm) = 15.7, 19.5, 21.8, 33.4, 46.7, 55.4, 58.5, 66.4, 70.1, 81.1, 81.7, 113.8, 113.9, 125.7, 125.8, 125.9, 128.2, 128.4, 128.8, 128.9, 129.3, 129.9, 130.0, 130.2, 130.4, 159.1, 159.2; **MS** (TS) $m/z = 404.4$ (M+Na), 384.4, 308.2, 307.4; **HRMS** (ESI+) m/z : calcd. for $\text{C}_{20}\text{H}_{23}\text{F}_3\text{NO}_3$ [M+H]⁺: 382.1640, found: 382.1624; **HPLC** (CHIRACEL OD-H, Grad. 99+1—90+10, 0.75 mL/min, 100 min, 254+340 nm): t_R (min) = 33.60 (94.74 %), 36.61 (5.26 %).



3,5-endo

(3*S*,5*S*)-5-methyl-3-(4-trifluoromethyl-phenyl)-2-diphenylmethyl-isoxazoline-5-methanol (*S,S*-2*s*-alc): obtained according to the general procedure in 99 % yield: **IR** (film): ν (cm^{-1}) = 729, 1051, 1068, 1130, 1169, 1325, 1384, 1420, 1453, 1494, 1619, 2245, 2873, 2928, 2977, 3221, 3555; **$^1\text{H NMR}$** (400 MHz, CDCl_3): δ (ppm) = 1.44 (bs, 4H, CH and CH_3), 2.03-2.08 (bm, 1H, H-C₄), 2.29-2.37 (bm, 2H, CH_2OH), 2.74-2.76 (bm, 1H, H-C₄), 3.91 (bs, 1H, H-C₃), 7.16-7.58 (m, 14H, $J = 8$ Hz, H-Carom); **$^{13}\text{C NMR}$** (100.6 MHz, CDCl_3): δ (ppm) = 14.36, 15.5, 29.9, 30.5, 47.7, 66.1, 122.1, 125.7, 125.8, 127.1, 128.0, 128.2, 128.3, 129.8, 130.2, 130.4; **MS** (TS) $m/z = 450.4$ (M+Na), 450.1, 445.4, 413.4, 403.3, 402.3, 400.3, 389.2, 348.3, 304.2, 279.1, 242.3, 219.3, 167.4, 102.6; **HRMS** (ESI+) m/z : calcd. for $\text{C}_{25}\text{H}_{25}\text{F}_3\text{NO}_2$ [M+H]⁺: 428.1819, found: 428.1831; **HPLC** (CHIRALPAK AD, Grad. 99+1—85+15, 1 mL/min, 80 min, 254+320 nm): t_R (min) = 11.42 (81.03 %), 12.47 (15.08 %).

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