Electronic supplementary information (ESI)

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Doping effect of fluorinated aromatic hydrocarbon solvents on the performance of common olefin metathesis catalysts: application in preparation of biologically active compounds

Cezary Samojłowicz,[a] Michał Bieniek,[a] Andrzej Zarecki,[a] Renat Kadyrov,[b] Karol Grela[a]

[a] Institute of Organic Chemistry, Polish Academy of Sciences, Kasprzaka 44/52, 01-224 Warsaw, Poland; Fax: +48-22-343-21-09; E-mail: klgrela@gmail.com; Web: http: //www.karolgrela.eu/

[b] Evonik Degussa GmbH, Rodenbacher Chaussee 4, 63457 Hanau-Wolfgang, Germany, Telefax +49 6181 59-78710; E-mail: renat.kadyrov@degussa.com

1. General

1.1. Equipment and chemicals used

All reactions were carried out under Ar in pre-dried glassware using Schlenk techniques. The solvents: 1,2-dichloroethane (Aldrich), octafluorotoluene (FluoroChem), hexafluorobenzene (FluoroChem) and toluene (Fluka) were dried by destilation over CaH2 under argon and stored under argon.

Flash column were performed using silica gel 60 (230–400 mesh). NMR spectra were recorded in $CDCl_3$ or C_6D_6; chemical shifts (δ) are given in ppm relative to TMS, coupling constants (J) are in Hz. IR spectra: wavenumbers are in cm^{-1}. MS (EI) spectra were recorded on AMD 604 Intectra GmbH spectrometer. MS (ESI) spectra were recorded on Mariner Perseptive Biosystems, Inc. IR spectra were recorded on a Perkin-Elmer Spectrum One FTIR spectrometer with diamond ATR accessory. Optical rotations $[\alpha]_D$ were measured at RT in a 10 cm cell in the stated solvent (concentration c given as g/100 mL),

using Polarimeter P-2000 JASCO. Melting point was recorded by EZ-Melt Automated Melting Point Apparatus.

Micro-analyses were provided by Institute of Organic Chemistry, PAS, Warsaw.

Catalysts **1b**, **1c**, **2b** were purchased from Aldrich or Strem and used as received. CatMetium^{TM} (**3b**) was obtained from Evonik Degussa GmbH.

2. Comparative solvent screening (Scheme 1 and 3)

2.1 General information

All stock solutions were prepared using drybox techniques. Reactions were carried out at 70 ºC using Ventage unit (a device that enables the simultaneous performance of up to 96 reactions at a fixed temperature). All aliquots for GC analysis were taken automatically at the specified time intervals using the same device. Gas chromatography (GC) was conducted using an HP 6890 equipped with an HP-5 capillary column.

2.2 General procedure for comparative solvent screening (Scheme 1 and 3)

In a glovebox, 4 mL vials with screw-cap septum tops were charged with the required substrates and catalysts. The vials were then placed in the Vantage array and heated at 70 ºC for at least 5 h. Aliquots were taken at the specified time intervals.

2.3 Stock solution preparation for comparative solvent screening (Scheme 1 and 3)

A single stock solution containing enough catalyst (**1b**, **1c**, **2b**, **2c** and **3b**) was prepared for at least a few series of metathesis reactions. Inside a glovebox, a volumetric flask was charged with catalyst (0.03 mmol) and the requisite solvent was added to prepare a stock solution (10 mL, [*c*] = 0.003 M). In this way, solutions of all of the complexes (**1b**, **1c**, **2b**, **2c** and **3b**) in all needful solvents (toluene, 1,2-dichloroethane, hexafluorobenzene and octafluorotoluene) were prepared. Such prepared stock solutions should be used within a few hours because prolonged storage, even in glovebox, can lead to partial decomposition of the catalysts.

Substrates for RCM (s1)[1] and CM (s4)[2]: A single stock solution containing enough substrate for metathesis reactions with all five catalysts was prepared. Inside a glovebox, a volumetric flask was charged with the appropriate diene (**s1**) or alkene (**s4**) (0.6 mmol), along with dodecane (for alkenes **s1**) or tetradecane (for alkenes **s4**) (0.3 mmol), as an internal standard. The requisite solvent was then added to prepare a stock solution (10 mL, [*c*] = 0.06 M). In this way, solutions of the alkenes (**s1** or **s4**) in all needful solvents (toluene, 1,2-dichloroethane, hexafluorobenzene and octafluorotoluene) were prepared. All of these solutions could be stored in sealed vials under argon for extended periods of time.

Cross-metathesis partner for CM: In a glovebox, a volumetric flask was charged with *cis*-1,4-diacetoxy-2-butene (1.2 mmol) and then an appropriate solvent was added to prepare a stock solution (10 mL, [*c*] = 0.12 M). In this way, solutions olefins in all needful solvents (toluene, 1,2-dichloroethane, hexafluorobenzene and octafluorotoluene) were prepared. All of these solutions could be stored in sealed vials under Ar for extended periods of time.

2.4 Comparative RCM of s1 (Scheme 1)

In a glovebox, 4 mL vials were charged with alkene (**s1**) stock solution ([*c*] = 0.06 M, 1 mL, 0.06 mmol) and the required solvent (1.6 mL). The appropriate catalyst stock solution ([*c*] = 0.003 M, 0.4 mL, 1.2 μmol) was then added to each vial by means of an adjustable-volume pipette. As a result, solutions in 1,2- dichloroethane, toluene, hexafluorobenzene, and octafluorotoluene were obtained with the following parameters: concentration of **s1**: [*c*] = 0.02 M, catalyst loading **1b**, **1c**, **2b**, **2c** and **3b** respectively): 2 mol%, solution volume: 3 mL.

2.5. Comparative CM of s4 with *cis*-1,4-diacetoxy-2-butene (Scheme 3)

In a glovebox, 4 mL vials were charged with alkene (**s4**) stock solution ([*c*] = 0.06 M, 1 mL, 0.06 mmol) and cross-metathesis partner (*cis*-1,4-diacetoxy-2-butene) stock

[1] Michrowska, A.; Bujok, R.; Harutyunyan, S.; Sashuk, V.; Dolgonos, G.; Grela, K., *J. Am. Chem. Soc.* 2004, **126**, 9318;

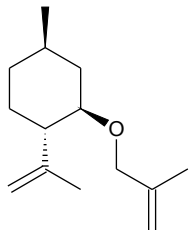
[2] Bieniek, M.; Michrowska, A.; Usanov, D. L.; Grela, K., *Chem. Eur. J.* 2008, **14**, 806;

solution ([*c*] = 0.12 M, 1 mL, 0.12 mmol). The appropriate catalyst stock solution ([*c*] = 0.003 M, 1 mL, 3 μmol) was then added to each vial by means of an adjustable-volume pipette. As a result, solutions in 1,2-dichloroethane, toluene, hexafluorobenzene, and octafluorotoluene were obtained with the following parameters: concentration of **s4**: [*c*] = 0.02 M, catalyst loading (**1b**, **2b**, and **3b** respectively): 5 mol%, solution volume: 3 mL.

3. Preparative experiments

3.1 Synthesis of substrates for metathesis reactions

(1*R*,2*S*,5*R*)-2-Isopropenyl-5-methyl-1-(2-methyl-allyloxy)-cyclohexane (s2)



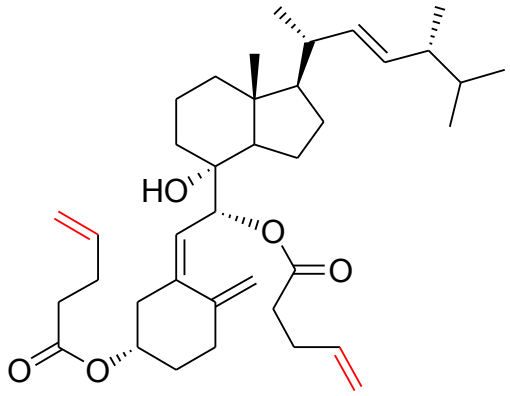
Under argon atmosphere, the reaction flask was charged with dry DMF (10 ml) and sodium hydride (60 % suspension in oil, 552 mg, 13.8 mmol, 1.58 eq), and then immersed in a cold water bath. (−)-Isopulegol (1.351 g, 8.76 mmol) was added dropwise and the resulting mixture was stirred for 30 min. Then, methallyl chloride (3 mL, 30.7 mmol, 3.5 eq) was slowly added followed by sodium iodide (12 mg, 0.08 mmol). After stirring overnight, satd. NH_4Cl solution (10 mL) was carefully added, with external cooling, to the flask followed by hexane (20 mL). The hexane phase was washed with brine (10 mL), dried with Na_2SO_4, concentrated *in vacuo* and purified on silica gel to afford methallyl ether **s2** (colourless liquid), 634 mg (34.7 % yield) together with some mixed fractions.

^{1}H NMR ($CDCl_3$, 500 MHz): 4.95 – 4.93 (m, 1H), 4.82 – 4.80 (m, 1H), 4.78 – 4.75 (m, 2H), 3.97 (d, *J* = 12.2, 1H), 3.76 (d, *J* = 12.2, 1H), 3.20 (dt, *J* = 10.6, 4.1, 1H), 2.12 – 2.07 (m, 1H), 2.07 – 2.00 (m, 1H), 1.72 (s 3H), 1.71 (s, 3H), 1.67 – 1.59 (m, 2H), 1.46 – 1.37 (m, 1H), 1.36 – 1.29 (m, 1H), 0.93 (d, *J* = 6.6, 3H, overlapping with m, 2H).

^{13}C NMR ($CDCl_3$, 125 MHz): 19.6 (CH_3), 20.1 (CH_3), 22.3 (CH_3), 31.1 (CH_2), 31.6 (CH), 34.5 (CH_2), 40.4 (CH_2), 51.8 (CH), 72.7 (CH_2), 79.5 (CH), 110.8 (CH_2), 111.5 (CH_2), 143.1 (C), 148.0 (C).

HRMS (EI): calcd. for $C_{14}H_{24}O$: 208.1827; found 208.1832

(5*Z*,22*E*-(7*R*)-3β,7-*di*-(pent-4-enoyloxy)-9,10-seco-ergosta-5,10(19),22-triene-8α-ol (s3)



To a suspension of 7,8-dihydroxy-7,8-dihydrovitamin D_2 (425 mg; 0.99 mmol)[3] in dichloromethane (5 mL) were added pent-4-enoic acid (385 mg, 3.85 mmol, 3.9 eq), N,N-diisopropylcarbodiimide (496 mg, 3.93 mmol, 3.98 eq), and DMAP (12 mg, 0.1 mmol). The reaction mixture was stirred overnight at room temperature. The whole mixture was applied on a top of the column and flash chromatographed. The diester (**s3**) fraction (colourless oil) weighed 512 mg (87.2 % yield).

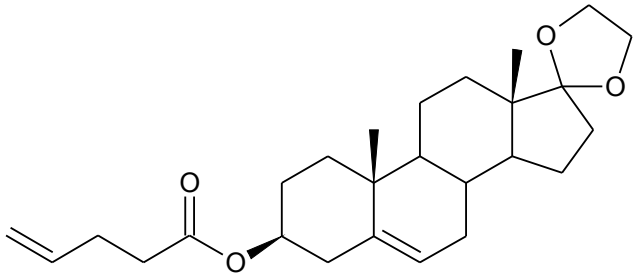
^{1}H NMR ($CDCl_3$, 500 MHz): 6.10 (d, J = 9.5, 1H), 5.86 – 5.76 (m, 2H), 5.44 (s, 1H), 5.37 (d, J = 9.4, 1H), 5.22 – 5.09 (m, 2H), 5.08 – 5.05 (m, 2H), 5.40 – 4.98 (m, 2H), 4.90 – 4.84 (m, 1H), 2.57 – 2.50 (m, 2H), 2.46 – 2.34 (m, 6H), 2.27 – 2.21 (m, 1H), 2.15 – 1.92 (m, 2H), 1.91 – 1.80 (m, 2H), 1.73 – 1.28 (m, 6H), 1.20 – 1.08 (m, 3H), 0.97 (d, J = 6.6, 3H), 0.90 (d, J = 9.8, 3H), 0.83 (d, J = 6.8, 3H), 0.81 (d, J = 6.8, 3H), 0.75 (s, 3H).

^{13}C NMR ($CDCl_3$, 125 MHz): 13.0 (CH_3), 17.6 (CH_3), 19.6 (CH_3), 19.9 (CH_3), 20.5 (CH_2), 20.7 (CH_3), 21.6 (CH_2), 27.6 (CH_2), 28.6 (CH_2), 28.9 (CH_2), 32.5 (CH_2), 33.1 (CH), 33.2 (CH_2) , 33.8 (CH_2), 34.0 (CH_2), 37.1 (CH_2), 40.0 (CH), 40.1 (CH_2), 42.8 (CH), 42.9 (CH_2), 43.8(C), 57.0 (CH), 59.5 (CH), 72.1 (CH), 75.0 (CH), 75.2 (CH), 111.9 (CH_2), 115.5 (CH_2), 115.6 (CH_2), 122.1 (CH), 132.2 (CH), 135.3 (CH), 136.5 (CH), 136.6 (CH), 140.8 (C), 144.9 (C), 171.2 (C), 172.2 (C).

HRMS (EI): calcd. for $C_{38}H_{58}O_5$: 594.4284; found 594.4305.

[3] H. T. Toh, W. H. Okamura, *J. Org. Chem.*, 1983, **48**, 1414;

3β-Pent-4-enoyloxy-17,17-ethylenedioxy-5-androstene (s5)



A solution of 17-(ethylenedioxy)-3β-hydroxy-5-androstene[4] (807 mg, 2.43 mmol), pent-4-enoic acid (373 mg, 3.73 mmol, 1.53 eq), N,N-diisopropylcarbodiimide (709 mg, 5.62 mmol, 2.31 eq) and DMAP (30 mg, 0.25 mmol, 0.10 eq) in dichloromethane (15 ml) was stirred overnight at room temperature. The reaction mixture was then concentrated, transferred on a top of the column and flash chromatographed to furnish the product as a colourless oil (655 mg, 64.0 % yield).

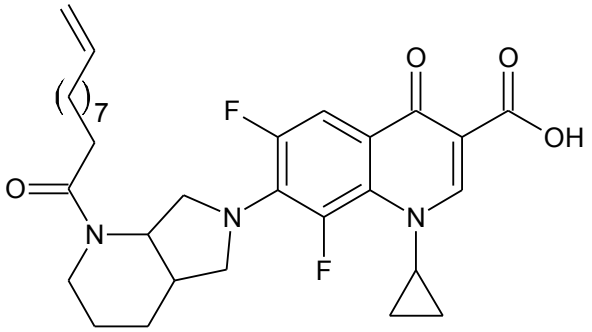
^{1}H NMR ($CDCl_3$, 500 MHz): 5.87 – 5.77 (m, 1H), 5.39 – 5.36 (m, 1H), 5.08 – 4.98 (m, 2H), 4.66 – 4.59 (m, 1H), 3.96 – 3.83 (m, 4H), 2.38 – 2.29 (m, 6H), 2.04 – 1.96 (m, 2H), 1.89 – 1.76 (m, 3H), 1.72 – 1.64 (m, 1H), 1.63 – 1.54 (m, 4H), 1.52 – 1.38 (m, 4H), 1.30 – 1.18 (m, 1H), 1.11 (dt, J = 13.1, 3.3, 1H), 1.03 – 0.97 (m, 1H) overlapping 1.03 (s, 3H), 0.86 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 172.4 (C), 139.6 (C), 136.8 (CH), 122.4 (CH), 119.5 (C), 115.4 (CH_2), 73.8 (CH), 65.2 (CH_2), 64.5 (CH_2), 50.6 (CH_3), 49.9 (CH_3), 45.7 (C), 38.1 (CH_2), 37.0 (CH_2), 36.6 (C), 34.2 (CH_2), 33.9 (CH_2), 32.1 (CH), 31.2 (CH_2) , 30.5 (CH_2), 28.9 (CH_2), 27.8 (CH_2), 22.8 (CH_2), 20.4 (CH_2), 19.3 (CH), 14.2 (CH);

HRMS (ESI+): calcd. for $C_{26}H_{38}O_4Na$: 437.2662; found 437.2665.

[4]Y. Shen, D. C. Burgoyne, *J. Org. Chem.*, 2002, **67**, 3908;

1-Cyclopropyl-6,8-difluoro-4-oxo-7-(1-undec-10-enoyl-octahydro-pyrrolo[3,4-b]pyridin-6-yl)-1.4-dihydro-quinoline-3-carboxylic acid (s6)



To a suspension of the aminoacid[5] (1.438 g, 3.69 mmol) in chloroform 3 ml) and pyridine (402 mg, 5.58 mmol, 1.51 eq) a solution of 10-undecenoyl chloride (775 mg, 3.82 mmol, 1.04 eq) in chloroform (2 mL) and the reaction mixture was stirred overnight at room temperature. The solvent was removed *in vacuo*, the solid residue was suspended in water (15 mL), filtered off with suction and washed with water (10 mL). The crude product was dissolved in hot acetone (15 mL) and left for crystallization. Finally, the mixture was cooled down to about 0 °C, the crystals were collected on the filter, washed with cold acetone and air dried. Yield 1.468 g (71 %).

^{1}H NMR ($CDCl_3$, 400 MHz): 14.84 (brs, 1H), 8.72 (s, 1H), 7.80 (dd, J = 13.8, 1.7, 1H), 5.88 – 5.74 (m, 1H), 5.26 – 5.20 (m, 1H), 5.04 – 4.88 (m, 3H), 4.68 – 4.52 (m, 1H), 4.24 – 3.50 (m, 6H), 3.44 (d, J = 10.5, 2H), 3.14 (t, J = 12.1, 1H), 2.69 (t, J = 13.5, 0.3, 1H), 2.55 – 2.17 (m, 3H), 2.10 – 1.98 (m, 2H), 1.92 – 1.77 (m, 2H), 1.72 – 1.50 (m, 5H), 1.42 – 1.25 (m, 12H), 1,25 – 1.05 (m, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz): 8.8 (d, $J_{C,F}$ = 7.8, CH_2), 9.5 (d, $J_{C,F}$ = 7.8, CH_2), 23.8 (CH_2), 24.6 (CH_2), 24.9 (CH_2), 25.2 (CH_2), 28.9 (CH_2), 29.0 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 33.7 (CH_2), 34.1 (CH_2), 35.3 (CH), 40.0 (d, $J_{C,F}$ = 13.7, CH), 41.1 (CH_2), 48.5 (CH_2), 48.8 (CH), 56.7 (CH_2), 107.4 (C), 108.0 (d, $J_{C,F}$ = 24.5, CH), 114.1 (CH_2), 116.7 (C), 129.1 (C), 132.7 (C), 139.1 (CH), 142.1 (d, $J_{C,F}$ = 238.7, C) ,149.2 (CH), 151.3 (dd, $J_{C,F}$ = 248.5, 7.7 ,C), 166.7 (C), 173.4 (C), 176.1 (C);

^{19}F NMR ($CDCl_3$, 376 MHz): −132.9 (d, J = 123, 1F), −121.0 (s 1F).

HRMS (ESI+): calcd. for $C_{31}H_{39}N_2O_4F_2Na$: 578.2801; found 578.2800.

[5] a) G. Cianchetta, R. Mannhold, G. Cruciani, M. Baroni, V. Cecchetti, *J. Med. Chem.* 2004, **47**, 3193; b) U. Petersen, et al., EP 350,733, 1990;

3.2 General procedure for preparative CM reactions

To a solution of **s5** (132.7 mg, 0.32 mmol) (or **s6**) and (perfluorohexyl)ethylene (1.1 g, 3.2 mmol) (or 3,3-dimethyl-1-butene) in hexafluorobenzene (6.5 mL) (or mixture of octafluorotoluene:1,2-dichloroethane 2:1) was added Ru-catalyst **2b** as a solid (0.016 mmol, 5 mol%). The resulting solution was stirred at 60 °C for 20 h. The solvent was removed under reduced pressure. The crude product was purified by flash chromatography (*c*-hexane-EtOAc).

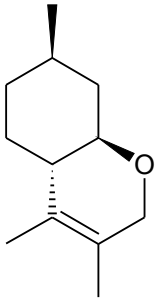
3.3. General procedure for preparative RCM reactions

To a solution os **s2** or **s3** (94 mg, 0.45 mmol) in octafluorotoluene or in hexafluorobenzene (23 mL) was added Ru-catalyst as a solid (0.023 mmol, 5 mol%). The resulting mixture was stirred at 70 ºC for 6 or 20 h. The solvent was removed under reduced pressure. The crude product was purified by flash chromatography (*c*-hexane-EtOAc).

2.4. Characterisation data of products

(7*R*,9*R*,10*S*)-3,4,7-trimethylbicyclo[4,4,0]oxadec-3-ene (p2)

The crude product was purified by preparative flash chromatography (*c*-hexane/EtOAc = 20:1), R_f = 0.4. Colourless oil (98%).



IR (film) ν 2948, 2919, 2858, 2805, 2734, 2704, 1719, 1676, 1648, 1454, 1386, 1377, 1352, 1309, 1271, 1255, 1227, 1195, 1178, 1166, 1116, 1072, 1046, 1001, 970, 953, 924, 906, 854, 838, 816, 766, 747, 676, 557, 541, 502, 489, 457, 429, 416 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.14 – 4.07 (m, 1H), 3.98 – 3.92 (m, 1H), 3.10 (ddd, *J* =

3.7, 9.3, 11.4 Hz, 1H), 2.04 – 1.98 (m, 1H), 1.93 – 1.87 (m, 1H), 1.85 – 1.65 (m, 4H), 1.60 – 1.50 (m, 3H), 1.12 – 1.02 (m, 1H), 1.00 – 0.85 (m, 1H), 0.96 (s, 3H), 0.94 (s, 3H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 127.1 (C), 124.9 (C), 78.8 (CH), 70.3 (CH_2), 43.7 (CH), 40.9 (CH_2), 35.0 (CH_2), 31.6 (CH), 27.4 (CH_2), 22.2 (CH_3), 14.2 (CH_3), 14.1 (CH_3);

MS (EI) *m*/*z* (rel intensity): 180 ($M^{+\bullet}$, 100), 165 (91), 95 (72), 85 (43);

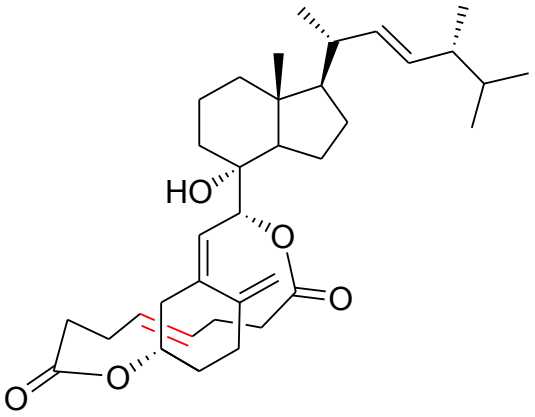
HRMS (EI) calcd for $C_{12}H_{20}O$ 180.1514, found 180.1509;

EA Anal. calcd for $C_{12}H_{20}O$: C 79.94, H 11.18; found C 79.23, H 11.46.

$[\alpha]_D^{21} = -6.6$ (*c* 3.0, benzene)

(1*S*,6*E*,12*R*,13*Z*)-12-((1*S*,4*S*,7a*R*)-1-((2*R*,5*R*,*E*)-5,6-dimethylhept-3-en-2-yl)-4-hydroxy-7a-methyloctahydro-1*H*-inden-4-yl)-15-methylene-2,11-dioxabicyclo[12.3.1]octadeca-6,13-diene-3,10-dione (p3)

The crude product was purified by flash chromatography (*c*-hexane-EtOAc = 20:1) $R_f = 0.4$. Colourless oil (71 %);



IR (film) ν 3598, 3491, 3180, 3085, 2955, 2869, 2252, 1730, 1661, 1640, 1603, 1444, 1381, 1371, 1348, 1331, 1305, 1258, 1216, 1175, 1151, 1117, 1100, 1069, 1047, 1018, 1006, 971, 962, 926, 894, 877, 858, 735, 704, 647, 611, 577, 510, 475, 435 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.92 (d, *J* = 9.6, 1H), 5.57 – 5.45 (m, 3H), 5.20 (dd, *J* = 7.6, 15.3, 1H), 5.12 (dd, *J* = 8.3, 15.3, 1H), 5.04 (m, 2H), 4.76 (s, 2H), 3.48 (q, *J* = 7.0 Hz, 1H), 2.62 (m, 1H), 2.55 – 2.19 (m, 10H), 2.08 (m, 1H), 2.00 – 1.88 (s, 3H), 1.85 (sextet, *J* = 6.5, 1H), 1.78 – 1.68 (m, 2H), 1.65 – 1.55 (m, 3H), 1.50 – 1.34 (m, 3H), 1.26 – 1.12 (m, 2H), 0.99 (d, *J* = 6.6, 3H), 0.90 (d, *J* = 6.8, 3H), 0.82 (dd, *J* = 6.9, 8.5, 6H), 0.74 (s, 3H);

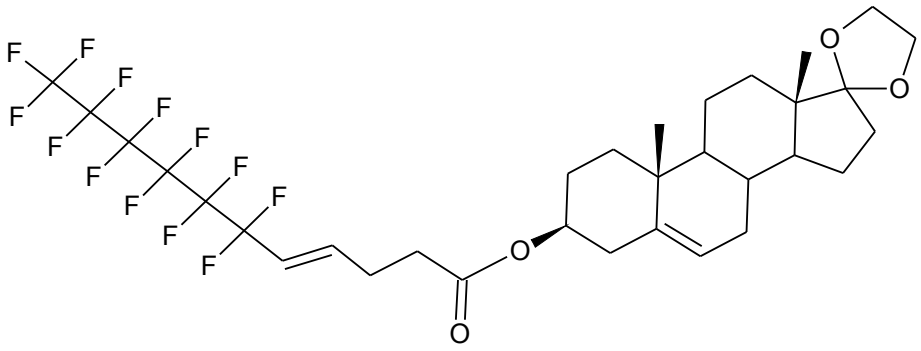
^{13}C NMR (125 MHz, $CDCl_3$) δ 173.1 (C), 172.2 (C), 147.8 (C), 142.5 (C), 135.3 (CH), 132.2 (CH), 130.2 (CH), 129.1 (CH), 120.8 (CH), 109.7 (CH_2), 75.0 (C), 74.1 (CH), 71.6 (CH), 59.6 (CH), 56.8 (CH), 43.4 (C), 42.8 (CH), 41.8 (CH_2), 40.1 (CH), 40.0 (CH_2), 36.0 (CH_2), 35.2 (CH_2), 34.2 (CH_2), 33.0 (CH), 32.1 (CH_2), 31.9 (CH_2), 27.6 (CH_2), 27.1 (CH_2), 25.9 (CH_2), 21.7 (CH_2), 20.8 (CH_3), 20.4 (CH_2), 19.9 (CH_3), 19.6 (CH_3), 17.6 (CH_3), 13.1 (CH_3);

HRMS (ESI^+): calcd for $C_{36}H_{54}O_5Na$ $[M+Na]^+$: 589.38635; found *m*/*z* 589.38523;

$[\alpha]_D^{24} = -5.1$ (*c* 4.5, CH_2Cl_2)

3β-(1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoroundec-7*E*-en-11-oxo)oxy-17,17-ethylenedioxy-5-androstene (p5):

The crude product was purified by flash chromatography (*c*-hexane-EtOAc = 20:1) R_f = 0.1. White crystals were obtained (90 %), m.p. = 69 - 71 °C;



IR (film) ν 3452, 2947, 1738, 1675, 1469, 1455, 1440, 1364, 1307, 1239, 1200, 1171, 1145, 1120, 1079, 1060, 1045, 990, 976, 905, 881, 849, 812, 801, 732, 716, 708, 694, 653, 603, 568, 531, 486 cm^{-1};

^{1}H NMR (400 MHz, CDCl3) δ 6.41 (dtt, *J* = 15.9, 6.7, 2.9, 1H), 5.7 (m, 1H), 5.38 (m, 1H), 4.65 (m, 1H), 3.90 (m, 4H), 2.55 (m, 2H), 2.45 (td, *J* = 6.8, 1.8, 2H), 2.32 (d, *J* = 7.7, 2H), 2.31 (d, *J* = 7.7, 1H), 2.00 (m, 2H), 1.85 (m, 3H), 1.68 (m, 1H), 1.60 (m, 3H), 1.45 (m, 4H), 1.26 (ddd, *J* = 23.4, 11.81, 6.3, 1H), 1.14 (td, *J* = 14.0, 4.6, 1H) , 1.03 (s, 3H), 1.00 (m, 1H) ,0.87 (s, 3H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3 (C), 141.0 (t, $J_{C,F}$ = 9.1, CH), 139.4 (C), 122.5 (CH), 119.4 (C), 117.9 (t, $J_{C,F}$ = 23.3, CH), 74.3 (CH), 65.2 (CH_2), 64.5 (CH_2), 50.5 (CH_3), 49.9 (CH_3), 45.7 (C), 38.0 (CH_2), 36.9 (CH_2), 36.6 (C), 34.2 (CH_2), 32.8 (CH_2),

32.1 (CH), 31.2 (CH_2) , 30.5 (CH_2), 27.7 (CH_2), 27.2 (CH_2), 22.7 (CH_2), 20.4 (CH_2), 19.2 (CH), 14.2 (CH);

^{19}F NMR (376.4 MHz, $CDCl_3$) δ −81.3 (m,CF_3), −112.0 (m, CF_2), 121.2 (m, CF_2), 123.4 (m, CF_2), 124.0 (m, CF_2), 126.7 (m, CF_2);

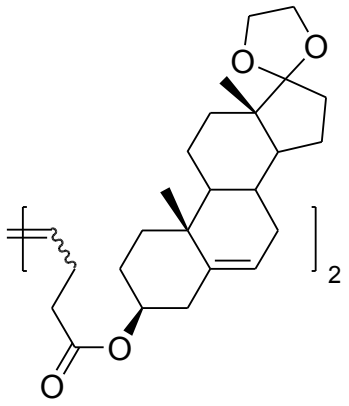
HRMS (ESI^+): calcd for $[M+Na]^+$: 755.2377; found *m*/*z* 755.2369;

EA anal. calcd for $C_{32}H_{37}F_{13}O_4$: C 52.46, H 5.09, F 33.71; found: C 52.49, H 5.08, F 33.74.

$[\alpha]_D^{20} = -39.5$ (*c* 7.3, benzene)

4*Z*-Octen-1,8-dioxo-di[17-(ethylenedioxy)-3β-oxy-5-androstene] (p5')

The crude product was purified by flash chromatography (*c*-hexane-EtOAc = 5:1) $R_f = 0.1$. White crystals were obtained (23 %);



IR (film) ν 3442, 2946, 2907, 2252, 1735, 1669, 1467, 1454, 1439, 1374, 1362, 1339, 1306, 1256, 1218, 1171, 1139, 1090, 1059, 1025, 991, 913, 883, 843, 811, 800, 733, 647, 601, 581, 527 cm^{-1};

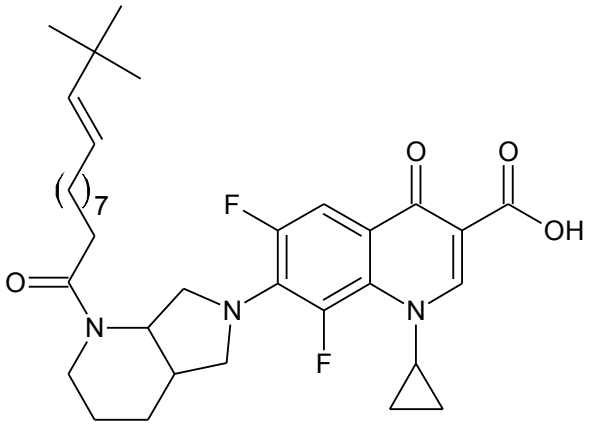
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.47 (m, 2H), 5.37 (m, 2H), 4.65 – 4.55 (m, 2H), 3.95 – 3.78 (m, 8H), 2.40 – 2.25 (m, 12H), 2.05 – 1.95 (m, 4H), 1.90 – 1.76 (m, 6H), 1.72 – 1.64 (m, 2H), 1.62 – 1.54 (m, 8H), 1.52 – 1.38 (m, 8H), 1,25 (ddd, *J* = 23.7, 11.8, 6.2, 2H), 1.18 – 1.10 (td, *J* = 14.1, 4.0, 2H), 1.02 (s, 6H), 1.06 – 0.94 (m, 2H), 0.86 (s, 6H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 172.4 (C), 139.6 (C), 129.4 (CH), 122.4 (CH), 119.4 (C), 73.8 (CH), 65.2 (CH_2), 64.5 (CH_2), 50.5 (CH_3), 49.9 (CH_3), 45.7 (C), 38.1 (CH_2), 37.0 (CH_2), 36.6 (C), 34.5 (CH_2), 34.2 (CH_2), 32.1 (CH), 31.2 (CH_2) , 30.5 (CH_2), 27.9 (CH_2), 27.8 (CH_2), 22.8 (CH_2), 20.4 (CH_2), 19.3 (CH), 14.2 (CH);

HRMS (ESI^+): calcd for $C_{50}H_{72}O_8Na$ $[M+Na]^+$: 823.51194; found *m*/*z* 823.50993;

1-Cyclopropyl-6,8-difluoro-4-oxo-7-(2,2-dimethyl-3*E*-tridec-10-enoyl-octahydro-pyrrolo-[3,4-b]pyridin-6-yl)-1.4-dihydro-quinoline-3-carboxylic acid (p6):

The crude product was purified by flash chromatography (*c*-hexane-acetone = 3:2); R_f = 0.3. White crystals were obtained (81 %);



IR (film) ν 3454, 3280, 3072, 3017, 2955, 2925, 2853, 2738, 2679, 2056, 1952, 1855, 1733, 1642, 1630, 1606, 1542, 1518, 1493, 1475, 1458, 1427, 1417, 1377, 1365, 1324, 1307, 1263, 1243, 1228, 1190, 1171, 1160, 1131, 1115, 1057, 1035, 1020, 1004, 970, 920, 892, 885, 869, 847, 832, 817, 801, 773, 759, 726, 706, 685, 656, 617, 580, 549, 528, 512, 482, 457, 413 cm^{-1};

^{1}H NMR ($CDCl_3$, 400 MHz): 14.84 (brs, 1H), 8.72 (s, 1H), 7.80 (d, J = 6.0, 1H), 5.50 – 5.40 (m, 1H), 5.35 – 5.20 (m, 1H), 5.04 – 4.88 (m, 1H), 4.68 – 4.52 (m, 1H), 4.24 – 3.50 (m, 3H), 3.44 (d, J = 10.5, 2H), 3.14 (t, J = 12.1, 1H), 2.69 (t, J = 13.5, 0.3, 1H), 2.55 – 2.17 (m, 3H), 2.10 – 1.98 (m, 2H), 1.92 – 1.77 (m, 2H), 1.72 – 1.50 (m, 4H), 1.42 – 1.25 (m, 10H), 1.25 – 1.05 (m, 3H), 0.99 (s, 9H).

^{13}C NMR ($CDCl_3$, 100 MHz): 8.8 (d, $J_{C,F}$ = 7.8, CH_2), 9.5 (d, $J_{C,F}$ = 7.8, CH_2), 23.8 (CH_2), 24.6 (CH_2), 24.9 (CH_2), 25.2 (CH_2), 28.9 (CH_2), 29.0 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 30.1 (CH_3), 32.3 (C), 33.7 (CH_2), 34.1 (CH_2), 35.3 (CH), 40.0 (d, $J_{C,F}$ = 13.7, CH), 41.1 (CH_2), 48.5 (CH_2), 48.8 (CH), 56.7 (CH_2), 107.4 (C), 108.0 (d, $J_{C,F}$ = 24.5, CH), 114.1 (CH_2), 116.7 (C), 129.1 (C), 132.7 (C), 139.1 (CH), 142.1 (d, $J_{C,F}$ = 238.7, C) ,149.2 (CH), 151.3 (dd, $J_{C,F}$ = 248.5, 7.7 ,C), 166.7 (C), 173.4 (C), 176.1 (C);

^{19}F NMR ($CDCl_3$, 376 MHz): −132.6 (d, J = 123, 1F), −121.0 (s 1F).

HRMS (ESI^+): calcd for $C_{35}H_{47}N_3O_4F_2Na$ $[M+Na]^+$: 634.34268; found m/z 634.34169;