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Synthesis, Microwave-Assisted Polymerization, and Polymer Properties of Fluorinated 2-Phenyl-2-oxazolines: A Systematic Study

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Abstract: We present a detailed systematic study of the synthesis and ability of fluorinated 2-phenyl-2-oxazolines to undergo polymerization. The synthesis of these compounds is based on a two-step procedure that gives the desired 2-oxazolines in moderate-to-good yields. All the compounds were fully characterized by IR and NMR (^{1}H, ^{13}C, and ^{19}F) spectroscopy, mass spectrometry, and elemental analysis. The 2-oxazolines were subsequently used as monomers for living cationic ring-opening polymerization (CROP) with microwave irradiation as the heat source ($T=140\,^{\circ}C$), nitromethane as the solvent, and methyl tosylate as the initiator. The linear first-order kinetic plots of the polymerizations accompanied by a linear increase of the molecular weight with conversion and low polydispersity index (PDI) values (generally below 1.30) indicate a living polymerization mechanism. The resulting polymerization rates reflect a strong sensitivity to the quantity of fluorine substituents in general and the presence or absence of *ortho*-fluoro substituents of the phenyl ring in particular. All the polymers were isolated and characterized by size-exclusion chromatography and MALDI-TOF mass spectrometry. Finally, a detailed investigation of selected polymer properties was performed by using differential scanning calorimetry, thermogravimetric analysis, and contact-angle measurements, thus resulting in structure–property relationships. Whereas the thermal properties of the polymers are mostly influenced by the presence of *ortho*-fluoro substituents, the surface properties are mainly determined by the presence of *para*- and/or *meta*-fluoro substituents.

Keywords: fluorine · oxazolines · polymerization · surface energy · thermal properties

Introduction

The synthesis of well-defined linear amphiphilic block copolymers receives significant scientific interest because such copolymers can assemble into micellar aggregates, whereby the exact form of the micelles is defined by the structure of the copolymer and the solvent. If the copolymer consists of three[1] or four blocks of very different characters—for example, a hydrophilic block and two incompatible hydrophobic blocks—the formation of multicompartment micelles is possible.[1–3] To achieve incompatibility of the hydrophobic blocks a (aromatic) hydrocarbon block can be combined with a fluorinated block.[1,3] In addition, a large difference in polarity and thermal properties of the hydrophobic blocks can induce segregation.[4] So far, these kind of structures are mainly based on vinylic monomers, which were polymerized through anionic or controlled radical mechanisms, such as atom-transfer radical polymerization (ATRP)[5,6] or reversible addition–fragmentation chain transfer (RAFT).[7]

The versatility of 2-oxazolines as monomers in polymerization reactions[8–12] makes them ideal candidates to transfer

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this concept of multicompartment micelles to polymers based on living cationic ring-opening polymerizations (CROPs). (Co)polymers based on 2-oxazolines are of wide interest in chemical, biochemical, and biomedical research[13–21] and, because their synthetic accessibility could be optimized by using single-mode microwave reactors,[22–24] the gate to a broader applicability of 2-oxazoline monomers was opened. The pressurized microwave conditions lead to a significant decrease in the polymerization time to only a few minutes,[22] and additionally enables the polymerization of 2-phenyl-2-oxazolines substituted with electron-withdrawing fluoro substituents, as we recently demonstrated.[25,26] Furthermore, di-,[27] tri-,[28] and tetrablock[29] oxazoline copolymers can be synthesized in a controlled manner under microwave irradiation, thus leading to well-defined multiblock copolymers in a reasonable time span.

The general polymerization mechanism of 2-oxazolines (Scheme 1) starts with a nucleophilic attack of the lone pair of the ring nitrogen atom of a monomer onto an electrophilic initiator species, such as methyl tosylate or benzyl bromide.[30,31] The thus-formed intermediate oxazolinium species is attacked by a second monomer, thus causing a ring rearrangement that leads to the cleavage of the C–O bond. In general, chain-transfer or termination reactions are absent under appropriate reaction conditions, and hence the polymerization proceeds in a living manner until all the monomer is consumed or a terminating agent, such as water, is added. This process leads to the formation of well-defined polymers that reveal narrow molecular-weight distributions with polydispersity index (PDI) values below 1.20.

The obtained polymers feature a polyalkylenimine backbone, and their properties are mainly defined by their amidic side arms, the former 2-substituent of the monomer. This feature allows direct fine-tuning of the properties of oxazoline-based (co)polymers with various 2-substituents (R).[12,32]

Recently, the scope of monomers was successfully expanded to fluorinated 2-phenyl-2-oxazolines **1a–c**, and **2a**,**b**, thus revealing a strong relationship between the presence and amount of *ortho*-fluoro substituents at the phenyl unit with the polymerization kinetics.[25] To delve into the effect of fluorine substituents, we performed a systematic study by synthesizing and polymerizing all the possible fluorinated 2-phenyl-2-oxazolines (Scheme 2). Herein, we discuss the polymerization kinetics of the fluorinated 2-phenyl-2-oxazolines. The second part of this contribution focuses on the thermal and surface properties of the polymers, which were investigated by means of differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), and contact-angle measurements, respectively. The determined polymer properties are discussed in relation to the fluorine substitution pattern. This insight into the thermal and surface properties of the fluorinated poly(2-phenyl-2-oxazoline)s will be important for the design of triblock copolymers that will form multicompartment micelles in future work.

Experimental Section

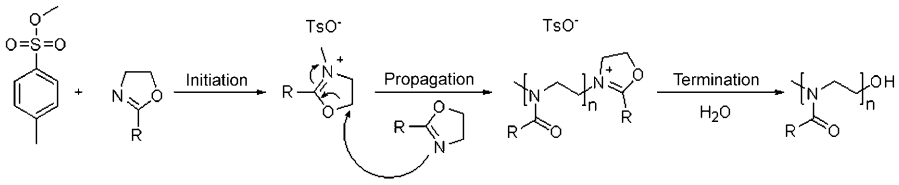
Materials and instrumentation: Analytical-grade solvents were purchased from Biosolve Ltd. All chemicals were purchased from Aldrich (Germany), except the fluorinated compounds which were purchased from Fluorochem (UK). Methyl tosylate and the 2-oxazolines were distilled prior to use (the latter over barium oxide) and stored under argon. Nitromethane, dried over molecular sieves (3 Å), was obtained from Fluka.

The polymerizations were performed in capped reaction vials (0.5–2 mL) in the single-mode microwave reactor Emrys Liberator (Biotage), equipped with a noninvasive IR sensor (accuracy: 2% for the measurement of the reaction temperatures).

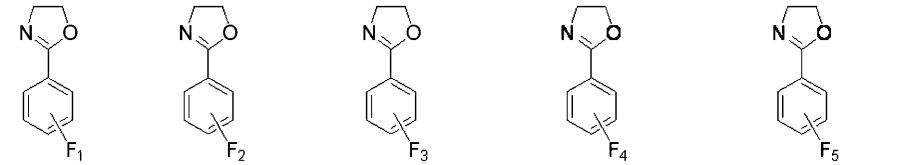
GC measurements were performed utilizing an Interscience Trace GC with a Trace Column RTX-5 connected to a PAL autosampler. For the injection of the polymerization mixtures, a special Interscience liner with additional glass wool was used.

Size-exclusion chromatography (SEC) was measured on a Shimadzu SEC equipped with a system controller SCL-10 Avp, LC-10 AD pump, RID-10 A refractive-index detector, UV/Vis detector DPD-10 A, PSS ETA-2010 differential viscometer, degasser DGU-14 A, CTO-10 A column oven, and two PSS GRAM 10µ, 8×300 mm, 1000/30 Å columns with *N*,*N*-dimethylacetamide (DMA)/LiCl as the eluent (piezo spectroscopic calibration).

GC–MS measurements were performed on a Shimadzu GC-17 A machine (column: DB-SMS (equivalent to phenylpolysiloxane/dimethylpoly-



Scheme 1. Methyl tosylate (TsO)-initiated cationic ring-opening polymerization of 2-substituted 2-oxazolines (TsO^- represents the tosylate anion).



1a: *o*-FOx
1b: *m*-FOx
1c: *p*-FOx

2a: 3,5-DFOx
2b: 2,6-DFOx
2c: 3,4-DFOx
2d: 2,3-DFOx
2e: 2,5-DFOx
2f: 2,4-DFOx

3a: 2,4,6-TFOx
3b: 2,4,5-TFOx
3c: 2,3,6-TFOx
3d: 2,3,5-TFOx
3e: 2,3,4-TFOx
3f: 3,4,5-TFOx

4a: 2,3,4,5-TFOx
4b: 2,3,4,6-TFOx
4c: 2,3,5,6-TFOx

5: 2,3,4,5,6-PFOx

Scheme 2. The synthesized monomers. Fox = monofluorophenyl-2-oxazoline (**1a–c**), DFOx = difluorophenyl-2-oxazoline (**2a–f**), TFOx = trifluorophenyl-2-oxazoline (**3a–f**), TFOx = tetrafluorophenyl-2-oxazoline (**4a–c**), PFOx = pentafluorophenyl-2-oxazoline (**5**).

siloxane, 5:95), length = 30 m, inner diameter = 0.25 mm, film thickness = 0.1 μm) connected to an AOC-20i autoinjector and a GC–MS QP5050 A mass spectrometer. Ionization was managed by electron impact (EI; 70 eV).

Thermogravimetic analyses were performed on a TG 209 F1 Iris by Netzsch in a nitrogen atmosphere in the range from ambient temperature to 800 °C with a heating rate of 10 K min^{-1}. The samples (each 5 mg) were dried in a vacuum oven at 40 °C for 24 h prior to use.

DSC was performed on a DSC 204 F1 Phoenix by Netzsch in a nitrogen atmosphere with a heating rate of 10 K min^{-1} and a cooling rate of 20 K min^{-1}. Three heating–cooling cycles were performed and the third heating run was used for the determination of the glass transition temperature T_g.

Contact-angle measurements were performed on polymer films prepared by spin-coating of solutions of the polymers in $CHCl_3$ (20 mg mL^{-1}) on precleaned microscopy glass slides at 1000 rpm for 90 s using a WS-400/500 series spincoater from Laurell Technologies Corporation. An automated OCA 30 optical contact-angle measuring instrument from Dataphysics was used to determine the contact angles of both diiodomethane and ethylene glycol as apolar and polar test liquids, respectively, by using the equation-of-state theory to calculate the surface energy (SE).[33]

Elemental analyses were carried out on a EuroVector EuroEA3000 elemental analyzer for CHNS.

All the MALDI experiments were performed on a Voyager-DE PRO Biospectrometry Workstation (Applied Biosystems, Foster City, CA) time-of-flight mass spectrometer in the linear mode. All the spectra were obtained in the positive-ion mode. Ionization was performed with a 337-nm pulsed nitrogen laser. Samples were prepared with a multiple-layer spotting technique with 2-(3-(4-*tert*-butylphenyl)-2-methyl-2-propenylidene)-malononitrile (DCTB) as the matrix and NaI as the salt, similar to previous reports.[34] All the data were processed using the Data Explorer software package (Applied Biosystems). All the spectra are averaged over 500 laser shots that covered the complete sample area.

The ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on a Varian AM-400 spectrometer in $CDCl_3$ or CD_3NO_2, and the chemical shifts are given relative to the residual solvent signal.

Monomer synthesis

***N*-(2-Chloroethyl)-2-(fluorophenyl)acid amides**: Fluorobenzoic acid chloride **6** (0.08 mol) and 2-ethylammonium chloride (0.08 mol) were suspended in dry dichloromethane (150 mL) in an argon atmosphere, and the reaction mixture was cooled to 0 °C. Triethylamine (0.19 mol) was added dropwise within 1 h, and the reaction mixture was stirred for an additional 2 h. Water (50 mL) was added and the aqueous phase was extracted with dichloromethane (2 × 50 mL). The combined organic phases were washed with water and brine and subsequently dried over $MgSO_4$. Removing the solvent under vacuum gave **7** as a beige crude product. As a result of the high purity (> 95 %) of the crude products, they were converted into the desired oxazolines **2b**–**5** without further purification. Purification for the characterizations of **7** was managed by column chromatography (SiO_2, eluent: cyclohexane/ethyl acetate (3:1) + 2 % triethylamine) to yield the amides **7** as colorless solids.

***N*-(2-Chloroethyl)-2-(3,4-difluorophenyl)acid amide**: Yield: 93 %; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.74 (t, 2H, ^3J(H,H) = 5 Hz, NCH_2), 3.81 (m, 2H, OCH_2), 6.47 (bs, 1H, NH), 7.23 (m, 1H, 5-H), 7.53 (m, 6-H), 7.66 ppm (m, 1H, 2-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.79/43.82 (2 × s, NCH_2/OCH_2), 116.85/117.51 (2 × d, ^2J(C,F) = 17 Hz, C-2/C-5), 123.38 (m, C-6), 131.01 (s, *i*-C_{Ar}), 151.42 (dd, ^1J(C,F) = 235 Hz, ^2J(C,F′) = 13 Hz, C-3/4), 153.86 (dd, ^1J(C,F) = 238 Hz, ^2J(C,F′) = 13 Hz, C-3/4), 165.47 ppm (s, N*C*=O); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −132.20 (m, 1F, F-3)/−135.98 ppm (m, 1F, F-4); IR: $\tilde{\nu}$ = 3277/3108 (NH), 3082 (CH), 2978/2920/2884 (CH_2), 1604/1509 (C=C), 16385/1559 (C=O), 1281/1207/1186 (CF), 831 (CH), 774/685 cm^{-1} (CCl); MS: *m/z* (%): 219 (11) [M^+], 183 (9) [M^+−Cl], 170 (15) [M^+−CH_2Cl], 141 (100) [M^+−C_2H_5ClN], 113 (45) [M^+−C_3H_5ClNO]; elemental analysis (%) calcd for $C_9H_8NOClF_2$: C 49.22, H 3.67, N 6.38; found: C 49.20, H 3.40, N 6.20.

***N*-(2-Chloroethyl)-2-(2,4-difluorophenyl)acid amide**: Yield: 72 %; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.73 (m, 2H, NCH_2), 3.82 (m, 2H, OCH_2), 6.88 (m, 1H, 5-H), 6.99 (m, 1H, 3-H), 7.06 (bs, 1H, NH), 8.12 ppm (m, 1H, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.70/43.61 (2 × s, NCH_2/OCH_2), 104.31 (t, ^2J(C-3,F-2/4) = 26 Hz, C-3), 112.38 (m, C-5), 116.99 (t, ^2J(*i*-C_{Ar},F-2) = 12 Hz, *i*-C_{Ar}), 133.80 (m, C-6), 160.94 (dd, ^1J(C-2,F-2) = 250 Hz, ^3J(C-2,F-4) = 12 Hz, C-2), 162.54 (s, NC=O), 164.91 ppm (d, ^1J(C-4,F-4) = 243 Hz, C-4); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −103.55/−109.05 ppm (2 × s, 2F, ^4J(F,F) = 11 Hz) (F-2/F-4); IR: $\tilde{\nu}$ = 3380/3098 (NH), 3081 (CH), 2975/2950 (CH_2), 1648/1490 (C=C), 1616/1525 (C=O), 1266/1253/1187 (CF), 862 (CH), 772/745 cm^{-1} (CCl); MS: *m/z* (%): 219 (9) [M^+], 184 (5) [M^+−Cl], 170 (26) [M^+−CH_2Cl], 141 (100) [M^+−C_2H_5ClN], 113 (25) [M^+−C_3H_5ClNO]; elemental analysis (%) calcd for $C_9H_8NOClF_2$: C 49.22, H 3.67, N 6.38; found: C 49.22, H 3.80, N 6.24.

***N*-(2-Chloroethyl)-2-(2,5-difluorophenyl)acid amide**: Yield: 84 %; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.72 (m, 2H, NCH_2), 3.81 (m, 2H, OCH_2), 7.13 (m, 3H, NH, 3-H,4-H), 7.76 ppm (m, 1H, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.76/43.45 (2 × s, NCH_2/OCH_2), 117.50 (m, C-4), 118.08 (d, ^3J(C-3,F) = 26 Hz, C-3), 120.14 (m, C-6), 121.98 (m, *i*-C_{Ar}), 156.41 (dd, ^1J(C-2,F-2) = 226 Hz, ^4J(C-2,F-5) = 3 Hz, C-2), 158.85 (d, ^1J(C-5,F-5) = 229 Hz, C-5), 162.20 ppm (s, NC=O); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −116.95/−119.30 ppm (2 × m, 2 × 1F) (F-2/F-5); IR: $\tilde{\nu}$ = 3377/3121 (NH), 3089 (CH), 2968/2862 (CH_2), 1647/1520 (C=O), 1595/1481 (C=C), 1276/1258/1175 (CF), 887/833 (CH), 762/753/691 cm^{-1} (CCl); MS: *m/z* (%): 219 (11) [M^+], 184 (5) [M^+−Cl], 170 (30) [M^+−CH_2Cl], 141 (100) [M^+−C_2H_5ClN], 113 (27) [M^+−C_3H_5ClNO]; elemental analysis (%) calcd for $C_9H_8NOClF_2$: C 49.22, H 3.67, N 6.38; found: C 49.12, H 3.38, N 6.23.

***N*-(2-Chloroethyl)-2-(2,3-difluorophenyl)acid amide**: Yield: 87 %; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.74 (t, 2H, ^3J(1-H,2-H) = 6 Hz, NCH_2), 3.83 (m, 2H, OCH_2), 7.03 (bs, 1H, NH), 7.20 (m, 1H, 4-H), 7.31 (m, 1H, 5-H), 7.81 ppm (t, 1H, ^4J(H,H) = 6.6 Hz, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.79/43.49 (2 × s, NCH_2/OCH_2), 120.50 (d, ^3J(C-6,F-2) = 17.5 Hz, C-6), 122.85 (d, ^2J(*i*-C_{Ar},F-2) = 8.5 Hz, *i*-C_{Ar}), 124.59 (m, C-4), 126.35 (d, ^2J(C-5,F-3) = 3 Hz, C-5), 149.06 (dd, ^1J(C-3,F-3) = 250 Hz, ^2J(C-3,F-2) = 14.5 Hz, C-3), 150.52 (dd, ^1J(C-2,F-2) = 250 Hz, ^2J(C-2,F-3) = 14.5 Hz, C-2), 162.49 ppm (s, NC=O); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −137.64/−139.68 ppm (2 × m, 2 × 1F) (F-2/F-3); IR: $\tilde{\nu}$ = 3302/3268 (NH), 3084 (CH), 2968/2940 (CH_2), 1651/1639/1548 (C=O), 1589 (C=C), 1474 (CH), 1267 (CF), 806 (CH), 757/659 (CCl), 724 cm^{-1} (CH_2); MS: *m/z* (%): 219 (10) [M^+], 184 (7) [M^+−Cl], 170 (27) [M^+−CH_2Cl], 141 (100) [M^+−C_2H_5ClN], 113 (27) [M^+−C_3H_5ClNO]; elemental analysis (%) calcd for $C_9H_8NOClF_2$: C 49.22, H 3.67, N 6.38; found: C 49.50, H 3.39, N 6.34.

***N*-(2-Chloroethyl)-2-(2,4,6-trifluorophenyl)acid amide**: Yield: 89 %; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.72 (m, 2H, NCH_2), 3.78 (m, 2H, OCH_2), 6.47 (bs, 1H, NH), 6.72 ppm (m, 2H, 3-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.67/43.47 (2 × s, NCH_2/OCH_2), 101.06 (t, ^2J(C-3,F-2/4) = 28 Hz, C-3), 110.42 (t, ^2J(*i*-C_{Ar},F-2) = 20 Hz, *i*-C_{Ar}), 159.74 (s, NC=O), 160.59 (dm, ^1J(C-2,F-2) = 264 Hz, C-2), 163.56 ppm (dt, ^1J(C-4,F-4) = 255 Hz, ^3J(C-4,F-2) = 15 Hz, C-4); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −103.31 (quin, 1F, ^4J(F-4,F-2) = 9 Hz, F-4), −108.50 ppm (t, 2F, ^4J(F-2,F-4) = 9 Hz, F-2); IR: $\tilde{\nu}$ = 3268/3072 (NH), 3096 (CH), 2975/2928/2868 (CH_2), 1640/1543 (C=O), 1614/1435 (C=C), 1301/1176/1126 (CF), 846 (CH), 740/667 cm^{-1} (CCl); MS: *m/z* (%): 237 (7) [M^+], 202 (7) [M^+−Cl], 188 (16) [M^+−CH_2Cl], 159 (100) [M^+−C_2H_5ClN], 131 (15) [M^+−C_3H_5ClNO]; elemental analysis (%) calcd for $C_9H_7NOClF_3$: C 45.49, H 2.97, N 5.89; found: C 45.73, H 2.74, N 5.78.

***N*-(2-Chloroethyl)-2-(2,3,6-trifluorophenyl)acid amide**: Yield: 87 %; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.71 (t, 2H, ^2J(H,H) = 6 Hz, NCH_2), 3.78 (m, 2H, OCH_2), 6.64 (bs, 1H, NH), 6.89 (tt, 1H, ^3J(5-H,F-6) = 10 Hz, ^4J-(5-H,F-3) = 3 Hz, 5-H), 7.20 ppm (m, 1H, 4-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.72/43.43 (2 × s, NCH_2/OCH_2), 111.67 (m, C-4), 115.22 (m, *i*-C_{Ar}), 118.85 (m, C-5), 147.06 (dm, ^1J(C,F) = 251 Hz)/147.91 (dm, ^1J-(C,F) = 263 Hz)/155.01 (dm, ^1J(C,F) = 250 Hz) (C-2/C-3/C-6), 159.50 ppm (s, NC=O); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −117.37 (m, 1F, F-3), −135.20/−140.75 ppm (2 × m, 2 × 1F) (F-2/F-6); IR: $\tilde{\nu}$ = 3302/3245 (NH), 3087 (CH), 2973/2928/2864 (CH_2), 1639/1558 (C=O), 1607/1489 (C=C), 1242/1203 (CF), 815 (CH), 703/657 cm^{-1} (CCl); MS: *m/z* (%): 237 (9) [M^+], 202 (8) [M^+−Cl], 188 (20) [M^+−CH_2Cl], 159 (100) [M^+

$-C_2H_5ClN$], 131 (22) [$M^+-C_3H_5ClNO$]; elemental analysis (%) calcd for $C_9H_7NOClF_3$: C 45.49, H 2.97, N 5.89; found: C 45.55, H 2.81, N 5.61.

***N*-(2-Chloroethyl)-2-(2,4,5-trifluorophenyl)acid amide**: Yield: 83%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=3.73$ (m, 2H, NCH_2), 3.82 (m, 2H, OCH_2), 7.02 (m, 1H, 3-H), 7.09 (bs, 1H, NH), 7.95 ppm (m, 1H, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=42.15/43.78$ (2×s, NCH_2/OCH_2), 106.56 (2d, ^2J(C-3,F-2/4)=21 Hz, C-3), 117.62 (m, i-C_{Ar}), 120.23 (d, ^2J(C-6,F-5)=21 Hz, C-6), 147.59 (dm, ^1J(C-5,F-5)=247 Hz, C-5), 152.57 (dm, ^1J(C-4,F-4)=246 Hz, C-4), 156.21 (dm, ^1J(C-2,F-2)=247 Hz, C-2), 161.79 ppm (s, NC=O); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-114.45$ (s, 1F, F-5), −126.59 (s, 1F, F-4), −140.28 ppm (s, 1F, F-2); IR: $\tilde{\nu}=3355/3056$ (NH), 3093 (CH), 2978/2943 (CH_2), 1638/1555 (C=O), 1606/1511 (C=C), 1329/1199/1147 (CF), 906 (CH), 729/662 cm^{-1} (CCl); MS: m/z (%): 237 (9) [M^+], 202 (5) [M^+-Cl], 188 (27) [M^+-CH_2Cl], 159 (100) [$M^+-C_2H_5ClN$], 131 (28) [$M^+-C_3H_5ClNO$]; elemental analysis (%) calcd for $C_9H_7NOClF_3$: C 45.49, H 2.97, N 5.89; found: C 45.74, H 2.91, N 5.68.

***N*-(2-Chloroethyl)-2-(2,3,5-trifluorophenyl)acid amide**: Yield: 85%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=3.73$ (t, 2H, ^3J(H,H)=6 Hz, NCH_2), 3.83 (m, 2H, OCH_2), 7.02 (m, 1H, 6-H), 7.08 ppm (m, 2H, NH/4-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=41.78/43.41$ (2×s, NCH_2/OCH_2), 112.85 (m, C-6), 118.30 (d, ^3J(i-C_{Ar},F-2)=10 Hz, i-C_{Ar}), 125.73 (m, C-4), 139.86 (dm, ^1J(C,F)=253 Hz)/150.07 (dd, ^1J(C,F)=259 Hz, ^3J(C,F)=8 Hz)/153.30 (dd, ^1J(C,F)=253 Hz, ^3J(C,F)=7 Hz, C-2/C-3/C-5), 161.73 ppm (s, NC=O); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-112.92$ (s, 1F, F-5), −132.20 (m, 1F, F-3), −144.16 ppm (s, 1F, F-2); IR: $\tilde{\nu}=3327$ (NH), 3066 (CH), 2978/2944 (CH_2), 1645/1548 (C=O), 1603/1486 (C=C), 1213/1122 (CF), 864 (CH), 756/655 cm^{-1} (CCl); MS: m/z (%): 237 (10) [M^+], 202 (6) [M^+-Cl], 188 (27) [M^+-CH_2Cl], 159 (100) [$M^+-C_2H_5ClN$], 131 (30) [$M^+-C_3H_5ClNO$]; elemental analysis (%) calcd for $C_9H_7NOClF_3$: C 45.49, H 2.97, N 5.89; found: C 45.62, H 2.68, N 5.62.

***N*-(2-Chloroethyl)-2-(2,3,4-trifluorophenyl)acid amide**: Yield: 83%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=3.73$ (t, 2H, ^3J(H,H)=6 Hz, NCH_2), 3.82 (m, 2H, OCH_2), 6.97 (bs, 1H, NH), 7.08 (m, 1H, 5-H), 7.83 ppm (m, 1H, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=41.82/43.49$ (2×s, NCH_2/OCH_2), 112.91 (dd, ^2J(C-5,F-4)=18 Hz, ^3J(C-5,F-3)=3 Hz, C-4), 118.16 (m, i-C_{Ar}), 125.82 (m, C-6), 139.55 (dt, ^1J(C-3,F-3)=253 Hz, ^2J(C-3,F-2/4)=17 Hz, C-3), 150.00 (dm, ^1J(C-4,F-4)=252 Hz, C-4), 152.95 (dm, ^1J(C-2,F-2)=257 Hz, C-2), 161.70 ppm (s, NC=O); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-127.64$ (m, 1F, F-3), −134.90 (m, 1F, F-4), −159.25 ppm (m, 1F, F-2); IR: $\tilde{\nu}=3292$ (NH), 3078 (CH), 2971/2935/2876 (CH_2), 1645/1548 (C=O), 1608/1508 (C=C), 1281/1095 (CF), 831 (CH), 688/662 cm^{-1} (CCl); MS: m/z (%): 237 (8) [M^+], 202 (7) [M^+-Cl], 188 (22) [M^+-CH_2Cl], 159 (100) [$M^+-C_2H_5ClN$], 131 (24) [$M^+-C_3H_5ClNO$]; elemental analysis (%) calcd for $C_9H_7NOClF_3$: C 45.49, H 2.97, N 5.89; found: C 45.76, H 2.66, N 5.56.

***N*-(2-Chloroethyl)-2-(3,4,5-trifluorophenyl)acid amide**: Yield: 51%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=3.73$ (t, 2H, ^3J(H,H)=5 Hz, NCH_2), 3.78 (m, 2H, OCH_2), 6.63 (bs, 1H, NH), 7.46 ppm (t, 1H, ^3J(2-H,F-3)=7 Hz, 2-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=42.14/43.91$ (2×s, NCH_2/OCH_2), 112.05 (m, C-2), 129.70 (d, ^3J(i-C_{Ar},F-3)=5 Hz, i-C_{Ar}), 141.83 (dt, ^1J(C-4,F-4)=259 Hz, ^2J(C-4,F-3)=14 Hz, C-4), 151.03 (dm, ^1J(C-3,F-3)=253 Hz, C-3), 164.33 ppm (s, NC=O); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-132.04$ (m, 2F, F-3), −154.54 ppm (m, 1F, F-4); IR: $\tilde{\nu}=3303$ (NH), 3075/2978 (CH), 2928/2843 (CH_2), 1642/1557 (C=O), 1618/1514 (C=C), 1434 (CH), 1232 (CF), 878 (CH), 674/661 cm^{-1} (CCl); MS: m/z (%): 237 (10) [M^+], 202 (5) [M^+-Cl], 188 (16) [M^+-CH_2Cl], 159 (100) [$M^+-C_2H_5ClN$], 131 (37) [$M^+-C_3H_5ClNO$]; elemental analysis (%) calcd for $C_9H_7NOClF_3$: C 45.49, H 2.97, N 5.89; found: C 45.36, H 3.30, N 5.67.

***N*-(2-Chloroethyl)-2-(2,3,4,5-tetrafluorophenyl)acid amide**: Yield: 39%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=3.72$ (t, 2H, ^3J(H,H)=5 Hz, NCH_2), 3.80 (m, 2H, OCH_2), 7.02 (bs, 1H, NH), 7.72 ppm (m, 1H, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=42.09/43.45$ (2×s, NCH_2/OCH_2), 113.00 (d, ^2J(C-6,F-5)=21 Hz, C-6), 117.17 (s, i-C_{Ar}), 140.76 (dm, ^1J(C,F)=256 Hz)/142.82 (dm, ^1J(C,F)=261 Hz) (C-3/C-4), 146.31 (ddm, ^1J(C,F)=248 Hz, ^2J(C,F)=11 Hz)/147.39 (ddm, ^1J(C,F)=250 Hz, ^2J(C,F)=10 Hz) (C-2/C-5), 160.74 ppm (s, NC=O); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-136.65$ (m, 1F, F-4), −139.37 (m, 1F, F-5), −148.73 (m, 1F, F-3), −153.83 ppm (t, 1F, ^3J(F-2,F-3)=20 Hz, F-2); IR: $\tilde{\nu}=3345/3056$ (NH), 3063 (CH), 2978/2940 (CH_2), 1654/1555 (C=O), 1626/1513/1477 (C=C), 1356/1252/1041/1009 (CF), 907 (CH), 707/663 cm^{-1} (CCl); MS: m/z (%): 255 (9) [M^+], 220 (6) [M^+-Cl], 206 (34) [M^+-CH_2Cl], 177 (100) [$M^+-C_2H_5ClN$], 149 (28) [$M^+-C_3H_5ClNO$]; elemental analysis (%) calcd for $C_9H_6NOClF_4$: C 42.29, H 2.37, N 5.48; found: C 42.50, H 2.53, N 5.15.

***N*-(2-Chloroethyl)-2-(2,3,5,6-tetrafluorophenyl)acid amide**: Yield: 84%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=3.73$ (t, 2H, ^3J(H,H)=6 Hz, NCH_2), 3.81 (m, 2H, OCH_2), 6.56 (bs, 1H, NH), 7.16 ppm (tt, 1H, ^3J(4-H,F-3)=9.5 Hz, ^4J(4-H,F-3)=7.3 Hz, 4-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=41.51/43.01$ (2×s, NCH_2/OCH_2), 107.51 (t, ^2J(C-4,F-3)=22 Hz, C-4), 116.10 (t, ^2J(i-C_{Ar},F-2)=18 Hz, i-C_{Ar}), 143.38 (dm, ^1J(C,F)=238 Hz)/146.11 (dm, ^1J(C,F)=246 Hz) (C-2/C-3), 158.12 ppm (s, NC=O); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-137.01$ (m, 2F)/−141.18 ppm (m, 2F) (F-2/F-3); IR: $\tilde{\nu}=3289/3246$ (NH), 3080 (CH), 2973/2936/2865 (CH_2), 1643 (C=O), 1618/1558/1498 (C=C), 1182 (CF), 861 (CH), 709/655 cm^{-1} (CCl); MS: m/z (%): 255 (10) [M^+], 220 (8) [M^+-Cl], 206 (30) [M^+-CH_2Cl], 177 (100) [$M^+-C_2H_5ClN$], 149 (31) $M^+-C_3H_5ClNO$]; elemental analysis (%) calcd for $C_9H_6NOClF_4$: C 42.29, H 2.37, N 5.48; found: C 42.49, H 2.59, N 5.30.

***N*-(2-Chloroethyl)-2-(2,3,4,6-tetrafluorophenyl)acid amide**: Yield: 89%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=3.72$ (t, 2H, ^3J(H,H)=6 Hz, NCH_2), 3.80 (m, 2H, OCH_2), 6.51 (bs, 1H, NH), 6.85 ppm (m, 1H, 5-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=41.77/43.25$ (2×s, NCH_2/OCH_2), 101.64 (m, C-5), 111.24 (s, i-C_{Ar}), 137.27 (dm, ^1J(C-6,F-6)=252 Hz, C-6), 149.08 (dm, ^1J(C,F)=252 Hz)/151.86 (dm, ^1J(C,F)=256 Hz)/154.17 (dm, ^1J(C,F)=261 Hz) (C-2/C-3/C-4), 158.74 ppm (s, NC=O); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-115.17$ (t, 1F, J(F,F)=9 Hz)/−127.70 (m, 1F)/−132.65 (dd, 1F, J(F,F)=21 Hz, J(F,F)=8 Hz)/−163.22 ppm (m, 1F) (F-2/F-3/F-4/F-6); IR: $\tilde{\nu}=3292$ (NH), 3087/3024 (CH), 2977/2944/2857 (CH_2), 1644/1555 (C=O), 1505 (C=C), 1462 (CH), 1245/1161 (CF), 850 (CH), 663 cm^{-1} (CCl); MS: m/z (%): 255 (8) [M^+], 220 (7) [M^+-Cl], 206 (23) [M^+-CH_2Cl], 177 (100) [$M^+-C_2H_5ClN$], 149 (20) [$M^+-C_3H_5ClNO$]; elemental analysis (%) calcd for $C_9H_6NOClF_4$: C 42.29, H 2.37, N 5.48; found: C 42.13, H 2.64, N 5.22.

***N*-(2-Chloroethyl)-2-(pentafluorophenyl)acid amide**: Yield: 88%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=3.74$ (m, 2H, NCH_2), 3.83 (m, 2H, OCH_2), 6.35 ppm (bs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=42.03/43.24$ (2×s, NCH_2/OCH_2), 111.16 (t, ^2J(i-C_{Ar},F-2)=18 Hz, i-C_{Ar}), 137.66 (dm, ^1J(C,F)=256 Hz)/142.43 (dm, ^1J(C,F)=258 Hz)/144.19 (dm, ^1J(C,F)=253 Hz) (C-2/C-3/C-4), 157.88 ppm (s, NC=O); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-140.10$ (m, 2F, F-2), −149.99 (m, 1F, F-4), −159.74 ppm (m, 2F, F-3); IR: $\tilde{\nu}=3284/3076$ (NH), 3063 (CH), 2967 (CH_2), 1654/1553 (C=O), 1519/1486 (C=C), 1332/1254/986 (CF), 663 cm^{-1} (CCl); MS: m/z (%): 273 (9) [M^+], 238 (8) [M^+-Cl], 224 (28) [M^+-CH_2Cl], 195 (100) [$M^+-C_2H_5ClN$], 167 (24) [$M^+-C_3H_5ClNO$]; elemental analysis (%) calcd for $C_9H_5NOClF_5$: C 39.51, H 1.84, N 5.12; found: C 39.57, H 1.87, N 5.27.

Synthesis of the fluorinated 2-phenyl-2-oxazolines

Method A (2c, 2e, 2f): Acid amide **7** (65 mmol) was dissolved in THF (35 mL) at ambient temperature, and this solution was added dropwise within 30 min to an aqueous potassium hydroxide solution (25%). After stirring for an additional 24 h, the organic phase was separated, diethyl ether (150 mL) was added, and the organic phase was washed with water (4×) and brine (2×). After drying over $MgSO_4$ and removing the solvent under vacuum, a beige crude product was obtained. Further purification was carried out by column chromatography (SiO_2, eluent: cyclohexane/ethylacetate (3:1)+2% NEt_3) to yield the desired oxazolines as colorless solids.

Method B (2b, 5): Acid amide **7** (15 mmol) was dissolved in dry THF (60 mL) and heated to 35°C in an argon atmosphere. At this temperature, potassium *tert*-butoxide (23 mmol) was added portionwise within 5 min. The reaction was stopped after 1 h by adding the mixture to water (50 mL). The aqueous phase was extracted with dichloromethane (2×50 mL) and the combined organic phases were washed with water and brine. After drying over $MgSO_4$ and removing the solvent under vacuum, a yellowish crude product was obtained. Purification was managed by sublimation (45°C, 8×10^{-3} Torr) to yield the desired oxazolines as colorless waxy solids.

Method C (2d, 3a–f, 4a–c): Acid amide **7** (20 mmol) and [18]crown-6 (1 mmol) were dissolved in dry THF (60 mL) in an argon atmosphere. Potassium hydroxide (60 mmol) was added portionwise at room temperature. The reaction was stopped after 1 h by adding the mixture to water (100 mL). The aqueous phase was extracted with diethyl ether (2× 50 mL), and the combined organic phases were washed with water (4×) and brine (2×). After drying over $MgSO_4$ and removing the solvent under vacuum, a slightly yellow crude product was obtained. Further purification was performed by column chromatography (SiO_2, eluent: cyclohexane/ethylacetate (3:1)+2% NEt_3) for **2d**, **3b**, and **3d–f**; sublimation (50 °C, 1×10^{-2} Torr) for **3a** and **4a–c**; and distillation (58 °C, 1.2×10^{-2} Torr) for **3c**.

2-(3,4-Difluorophenyl)-2-oxazoline (2c): Yield: 80%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=4.05$ (t, 2H, ^3J(H,H)=9.5 Hz, NCH_2), 4.43 (t, 2H, ^3J(H,H)=9.5 Hz, OCH_2), 7.18 (m, 1H, 5-H), 7.70 (m, 1H, 6-H), 7.76 ppm (m, 1H,2-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=54.80$ (s, NCH_2), 67.75 (s, OCH_2), 117.05 (2×m, C-2, C-5), 124.50 (m, C-6), 124.71 (s, *i*-C_{Ar}), 149.83 (dd, ^1J(C,F)=248 Hz, ^2J(C,F′)=13 Hz, C-2/3), 152.16 (dd, ^1J(C,F)=254 Hz, ^2J(C,F′)=13 Hz, C-2/3), 162.61 ppm (s, N=CO); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-133.10$ (m, 1F)/−137.07 ppm (m, 1F) (F-3/F-4); IR: $\tilde{\nu}$=3066/3050 (CH), 2985/2945/2916/2889 (CH_2), 1652 (C=N), 1605/1515 (C=C), 1436 (CH), 1366/1185 (CF), 1280/1063 (CO), 831 (CH), 721 cm^{-1} (CH_2); MS: *m/z* (%): 183 (56) [M^+], 153 (100) [M^+-CH_2O], 141 (14) [$M^+-C_2H_4N$], 126 (12) [$M^+-C_2H_3NO$], 113 (35) [$M^+-C_3H_4NO$]; elemental analysis (%) calcd for $C_9H_7NOF_2$: C 59.02, H 3.85, N 7.65; found: C 58.92, H 3.56, N 7.44.

2-(2,3-Difluorophenyl)-2-oxazoline (2d): Yield: 80%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=4.11$ (t, 2H, ^3J(H,H)=9.5 Hz, NCH_2), 4.43 (t, 2H, ^3J(H,H)=9.5 Hz, OCH_2), 7.11 (m, 1H, 4-H), 7.27 (m, 1H, 5-H) 7.63 ppm (dt, 1H, ^3J(6-H,5-H)=8 Hz, ^4J(6-H,F-2)=1.5 Hz, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=55.00$ (s, NCH_2), 67.11 (s, OCH_2), 117.89 (d, ^2J(*i*-C_{Ar},F-2)=7.5 Hz, *i*-C_{Ar}), 119.57 (d, ^3J(C-6,F-2)=17.5 Hz, C-6), 123.82 (m, C-4), 125.37 (d, ^2J(C-5,F-3)=4 Hz, C-5), 149.06 (dd, ^1J(C-3,F-3)=250 Hz, ^2J(C-3,F-2)=14.5 Hz, C-3), 150.52 (dd, ^1J(C-2,F-2)=250 Hz, ^2J(C-2,F-3)=14.5 Hz, C-2), 162.49 ppm (s, N=CO); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-135.40/-137.10$ ppm (2×m, 2×1F) (F-2/F-3); IR: $\tilde{\nu}$=3030 (CH), 2986/2956/2913/2885 (CH_2), 1643 (C=N), 1586/1492 (C=C), 1479 (CH), 1278/1079 (CO), 1226/1137 (CF), 800 (CH), 730 cm^{-1} (CH_2); MS: *m/z* (%): 183 (45) [M^+], 153 (100) [M^+-CH_2O], 141 (9) [$M^+-C_2H_4N$], 126 (13) [$M^+-C_2H_3NO$], 113 (19) [$M^+-C_3H_4NO$]; elemental analysis (%) calcd for $C_9H_7NOF_2$: C 59.02, H 3.85, N 7.65; found: C 59.17, H 3.78, N 7.48.

2-(2,5-Difluorophenyl)-2-oxazoline (2e): Yield: 54%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=4.11$ (t, 2H, ^3J(H,H)=9.5 Hz, NCH_2), 4.42 (t, 2H, ^3J(H,H)=9.5 Hz, OCH_2), 6.92 (m, 2H, 3-H/4-H), 7.56 ppm (m, 1H, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=55.35$ (s, NCH_2), 67.30 (s, OCH_2), 117.13 (m, *i*-C_{Ar}), 117.25, (m, C-3), 117.95 (m, C-6), 119.40 (m, C-4), 157.25 (dd, ^1J(C-5,F-5)=255 Hz, ^4J(C-5,F-2)=2 Hz, C-5), 158.07 (dd, ^1J(C-2,F-2)=243 Hz, ^4J(C-2,F-5)=2 Hz, C-5), 160.30 ppm (m, N=CO); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-115.50/-118.46$ ppm (2×m, F-2/F-5); IR: $\tilde{\nu}$=3125/3088/3043 (CH), 2985/2943/2912/2888 (CH_2), 1649 (C=N), 1596/1502/1493 (C=C), 1437 (CH), 1266/1043 (CO), 1222/1176 (CF), 888/827 (CH), 737 cm^{-1} (CH_2); MS: *m/z* (%): 183 (41) [M^+], 153 (100) [M^+-CH_2O], 141 (9) [$M^+-C_2H_4N$], 126 (11) [$M^+-C_2H_3NO$], 113 (18) [$M^+-C_3H_4NO$]; elemental analysis (%) calcd for $C_9H_7NOF_2$: C 59.02, H 3.85, N 7.65; found: C 58.87, H 4.00, N 7.58.

2-(2,4-Difluorophenyl)-2-oxazoline (2f): Yield: 75%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=4.08$ (t, 2H, ^3J(1-H,2-H)=9.5 Hz, NCH_2), 4.39 (t, 2H, ^3J(2-H,1-H)=9.5 Hz, OCH_2), 6.89 (m, 2H, 3-H,5-H) 7.87 ppm (m, 1H, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=55.16$ (s, NCH_2), 67.14 (s, OCH_2), 105.00 (t, ^2J(C-3,F-2/4)=26 Hz, C-3), 111.47 (m, C-5), 112.55 (m, *i*-C_{Ar}), 132.38 (dd, ^3J(C-6,F)=10 Hz, ^3J(C-6,F′)=4 Hz, C-6), 160.50 (d, ^2J(C,F-2)=6 Hz, N=CO), 161.84 (dd, ^1J(C-2,F-2)=262 Hz, ^3J(C-2,F-4)=13 Hz, C-2), 164.63 ppm (dd, ^1J(C-4,F-4)=255 Hz, ^3J(C-4,F-2)=12 Hz, C-4); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-104.70$ ppm (m, 2F, F-2/F-4); IR: $\tilde{\nu}$=3062 (CH), 2985/2958/2913/2886 (CH_2), 1642 (C=N), 1611/1592/1505 (C=C), 1428 (CH), 1201/1110 (CF), 1264/1048 (CO), 865/857 (CH), 733 cm^{-1} (CH_2); MS: *m/z* (%): 183 (50) [M^+], 153 (100) [M^+-CH_2O], 141 (15) [$M^+-C_2H_4N$], 126 (14) [$M^+-C_2H_3NO$], 113 (13) [$M^+-C_3H_4NO$]; elemental analysis (%) calcd for $C_9H_7NOF_2$: C 59.02, H 3.85, N 7.65; found: C 58.97, H 3.78, N 7.56.

2-(2,4,6-Trifluorophenyl)-2-oxazoline (3a): Yield: 79%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=4.11$ (t, 2H, ^3J(H,H)=9.5 Hz, NCH_2), 4.45 (t, 2H, ^3J(H,H)=9.5 Hz, OCH_2), 6.74 ppm (t, 2H, ^3J(3-H,F)=8.5 Hz, 3-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=55.10$ (s, NCH_2), 67.57 (s, OCH_2), 94.75 (s, *i*-C_{Ar}), 100.97 (td, ^2J(C-3,F-2/4)=26 Hz, ^4J(C-3,F-6)=4 Hz, C-3), 161.63 (dd, ^1J(C-2,F-2)=258 Hz, ^3J(C-2,F-4)=16 Hz, C-2), 161.79 (dd, ^1J(C-4,F-4)=266 Hz, ^2J(C-4,F-2)=8 Hz, C-4), 165.27 ppm (s, N=CO); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-103.26$ (q, 1F, ^4J(F-4,F-2)=8 Hz, F-4), −105.23 ppm (m, 2F, ^4J(F-2,F-4)=8 Hz, F-2); IR: $\tilde{\nu}$=3040 (CH), 2988/2959/2918/2888 (CH_2), 1637 (C=N), 1616/1598 (C=C), 1439 (CH), 1256/1043 (CO), 1179/1130 (CF), 870/847 cm^{-1} (CH); MS: *m/z* (%): 201 (52) [M^+], 171 (100) [M^+-CH_2O], 159 (15) [$M^+-C_2H_4N$], 131 (11) [$M^+-C_3H_4NO$]; elemental analysis (%) calcd for $C_9H_6NOF_3$: C 53.74, H 3.01, N 6.96; found: C 53.96, H 2.84, N 6.78.

2-(2,4,5-Trifluorophenyl)-2-oxazoline (3b): Yield: 77%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=4.10$ (t, 2H, ^3J(H,H)=10 Hz, NCH_2), 4.41 (t, 2H, ^3J(H,H)=10 Hz, OCH_2), 7.01 (m, 1H, 3-H), 7.72 ppm (m, 1H, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=55.44$ (s, NCH_2), 67.52 (s, OCH_2), 106.95 (2d, ^2J(C-3,F-2/4)=21 Hz, C-3), 112.64 (m, *i*-C_{Ar}), 119.00 (d, ^2J(C-6,F-5)=19 Hz, C-6), 146.62 (dm, ^1J(C-5,F-5)=261 Hz, C-5), 152.03 (dm, ^1J(C-4,F-4)=257 Hz, C-4), 156.91 (dm, ^1J(C-2,F-2)=247 Hz, C-2), 159.78 ppm (d, ^3J(C,F-2)=7 Hz, N=CO); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-110.16$ (m, 1F, F-5), −127.93 (m, 1F, F-4), −141.84 ppm (m, 1F, F-2); IR: $\tilde{\nu}$=3038/3016 (CH), 2986/2890 (CH_2), 1642 (C=N), 1626/1515 (C=C), 1438 (CH), 1364/1141 (CF), 1238/1034 (CO), 899/806 (CH), 727 cm^{-1} (CH_2); MS: *m/z* (%): 201 (35) [M^+], 171 (100) [M^+-CH_2O], 159 (20) [$M^+-C_2H_4N$], 131 (20) [$M^+-C_3H_4NO$]; elemental analysis (%) calcd for $C_9H_6NOF_3$: C 53.74, H 3.01, N 6.96; found: C 54.15, H 2.96, N 6.86.

2-(2,3,6-Trifluorophenyl)-2-oxazoline (3c): Yield: 71%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=4.10$ (t, 2H, ^3J(H,H)=9.5 Hz, NCH_2), 4.45 (t, 2H, ^3J(H,H)=9.5 Hz, OCH_2), 6.89 (m, 1H, 4-H), 7.22 ppm (m, 1H, 5-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=55.13$ (s, NCH_2), 67.65 (s, OCH_2), 108.85 (dd, ^2J(*i*-C_{Ar},F-2)=^2J(*i*-C_{Ar},F-6)=14 Hz, *i*-C_{Ar}), 111.44 (dm, ^2J(C-5,F-6)=24 Hz, C-5), 119.01 (m, C-4), 147.18 (dm, ^1J(C-3,F-3)=246 Hz, C-3), 149.08 (dm, ^1J(C-2,F-2)=259 Hz, C-2), 156.22 (dm, ^1J(C-9,F-9)=266 Hz, C-9), 156.41 (t, ^3J(C-3,F-5)=^3J(C-3,F-9)=4 Hz, C-3), 161.79 (dd, ^1J(C-7,F-7)=266 Hz, ^2J(C-7,F-5)=8 Hz, C-7), 165.27 ppm (s, N=CO); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-114.14$ (m, 1F, F-3), −132.04 (m, 1F, F-2), −141.37 ppm (s, 1F, F-6); IR: $\tilde{\nu}$=3080 (CH), 2984/2911/2886 (CH_2), 1664/1635 (C=N), 1602/1492 (C=C), 1265/1017 (CO), 1176/1111 (CF), 848/814 cm^{-1} (CH); MS: *m/z* (%): 201 (49) [M^+], 171 (100) [M^+-CH_2O], 159 (12) [$M^+-C_2H_4N$], 131 (18) [$M^+-C_3H_4NO$]; elemental analysis (%) calcd for $C_9H_6NOF_3$: C 53.74, H 3.01, N 6.96; found: C 53.66, H 3.07, N 7.06.

2-(2,3,5-Trifluorophenyl)-2-oxazoline (3d): Yield: 77%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=4.13$ (t, 2H, ^3J(H,H)=9.6 Hz, NCH_2), 4.45 (t, 2H, ^3J(H,H)=9.6 Hz, OCH_2), 7.05 (m, 1H, 4-H), 7.38 ppm (m, 1H, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=55.31$ (s, NCH_2), 67.53 (s, OCH_2), 108.11 (2d, ^2J(C-4,F-3/5)=21 Hz, C-4), 112.00 (dd, ^2J(C-6,F-5)=26 Hz, ^3J(C-6,F-2)=4 Hz, C-6), 118.42 (m, *i*-C_{Ar}), 146.43 (dm, ^1J(C,F)=261 Hz)/151.02 (dm, ^1J(C,F)=240 Hz)/156.91 (dm, ^1J(C,F)=247 Hz) (C-2/C-3/C-5), 159.72 ppm (m, N=CO); ^{19}F NMR (376 MHz, $CDCl_3$): $\delta=-114.69$ (m, 1F, F-5), −131.79 (m, 1F, F-3), −140.00 ppm (m, 1F, F-2); IR: $\tilde{\nu}$=3094/3035 (CH), 2917/2889 (CH_2), 1638 (C=N), 1603/1496 (C=C), 1458 (CH), 1248/1020 (CO), 1174/1109 (CF), 873/827 cm^{-1} (CH); MS: *m/z* (%): 201 (62) [M^+], 171 (100) [M^+-CH_2O], 159 (13) [$M^+-C_2H_4N$], 131 (29) [$M^+-C_3H_4NO$]; elemental analysis (%) calcd for $C_9H_6NOF_3$: C 53.74, H 3.01, N 6.96; found: C 53.82, H 2.86, N 6.72.

2-(2,3,4-Trifluorophenyl)-2-oxazoline (3e): Yield: 77%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=4.11$ (t, 2H, ^3J(H,H)=10 Hz, NCH_2), 4.43 (t, 2H, ^3J(H,H)=10 Hz, OCH_2), 7.01 (m, 1H, 5-H), 7.64 ppm (m, 1H, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=55.18$ (s, NCH_2), 67.36 (s, OCH_2), 112.05 (m, C-5), 113.93 (m, *i*-C_{Ar}), 124.80 (m, C-6), 140.61 (dt, ^1J(C-3,F-3)=252 Hz, ^2J(C-3,F-2/4)=15 Hz, C-3), 150.84 (dd, ^1J(C-4,F-4)=266 Hz, ^2J(C-4,F-3)=11 Hz, C-4), 152.93 (dd, ^1J(C-2,F-2)=256 Hz, ^2J(C-2,F-3)=

4 Hz, C-2), 159.88 ppm (s, N=CO); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −128.91/−130.24 (2×m, 2×1F, F-3/F-4), −159.15 ppm (m, 1F, F-2); IR: $\tilde{\nu}$ = 3054/3008/2989 (CH), 2940/2919/2880 (CH_2), 1650 (C=N), 1611/1509/1493 (C=C), 1262/1032 (CO), 1132/1107 (CF), 838 cm^{-1} (CH); MS: *m/z* (%): 201 (66) [M^+], 171 (100) [M^+-CH_2O], 159 (19) [$M^+-C_2H_4N$], 131 (25) [$M^+-C_3H_4NO$]; elemental analysis (%) calcd for $C_9H_6NOF_3$: C 53.74, H 3.01, N 6.96; found: C 53.90, H 2.67, N 6.66.

2-(3,4,5-Trifluorophenyl)-2-oxazoline (3f): Yield: 68%; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.06 (t, 2H, ^3J(H,H) = 9.5 Hz, NCH_2), 4.45 (t, 2H, ^3J(H,H) = 9.5 Hz, OCH_2), 7.58 ppm (t, 1H, ^3J(2-H,F-3) = 8.0 Hz, 5-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.06 (s, NCH_2), 68.21 (s, OCH_2), 112.66 (m, C-2), 123.81 (m, *i*-C_{Ar}), 141.79 (dt, ^1J(C-3,F-4) = 258 Hz, ^2J(C-3,F-5) = 15 Hz, C-3), 150.86 (dm, ^1J(C-4,F-4) = 247 Hz, C-4), 162.03 ppm (d, ^4J(C,F-3) = 3 Hz, N=CO); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −133.36 (dd, 2F, ^3J(F-3,F-4) = 12 Hz, ^3J(F-3,F-3′) = 7.5 Hz, F-3), −155.62 ppm (m, 1F, F-4); IR: $\tilde{\nu}$ = 3039/2987 (CH), 2966/2943/2919/2888 (CH_2), 1651 (C=N), 1609/1527 (C=C), 1432 (CH), 1239/1042 (CO), 1203 (CF), 899/881 (CH), 713 cm^{-1} (CH_2); MS: *m/z* (%): 201 (80) [M^+], 171 (100) [M^+-CH_2O], 159 (19) [$M^+-C_2H_4N$], 131 (43) [$M^+-C_3H_4NO$]; elemental analysis (%) calcd for $C_9H_6NOF_3$: C 53.74, H 3.01, N 6.96; found: C 53.87, H 2.65, N 6.67.

2-(2,3,4,5-Tetrafluorophenyl)-2-oxazoline (4a): Yield: 61%; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.12 (t, 2H, ^3J(H,H) = 10 Hz, NCH_2), 4.44 (t, 2H, ^3J(H,H) = 10 Hz, OCH_2), 7.56 ppm (m, 1H, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.24 (s, NCH_2), 67.59 (s, OCH_2), 111.51 (m, *i*-C_{Ar}), 111.94 (m, C-6), 141.29 (dm, ^1J(C,F) = 253 Hz)/142.24 (dm, ^1J(C,F) = 259 Hz)/146.45 (dm, ^1J(C,F) = 246 Hz)/146.98 (dm, ^1J(C,F) = 258 Hz) (C-2/C-3/C-4/C-5), 159.08 ppm (s, N=CO); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −134.88 (m, 1F, F-4), −138.40 (m, 1F, F-5), −150.20 (m, 1F, F-3), −154.00 ppm (t, 1F, ^3J(F-2,F-3) = 20 Hz, F-2); IR: $\tilde{\nu}$3039 (CH), 2991/2960/2943/2920/2891 (CH_2), 1643 (C=N), 1623/1524 (C=C), 1479 (CH), 1266/1082 (CO), 1191/1150 (CF), 804 cm^{-1} (CH); MS: *m/z* (%): 219 (43) [M^+], 189 (100) [M^+-CH_2O], 177 (12) [$M^+-C_2H_4N$], 149 (18) [$M^+-C_3H_4NO$]; elemental analysis (%) calcd for $C_9H_5NOF_4$: C 49.33, H 2.30, N 6.39; found: C 49.40, H 2.10, N 6.27.

2-(2,3,4,6-Tetrafluorophenyl)-2-oxazoline (4b): Yield: 65%; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.11 (t, 2H, ^3J(H,H) = 10 Hz, NCH_2), 4.45 (t, 2H, ^3J(H,H) = 10 Hz, OCH_2), 6.83 ppm (m, 1H, 5-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.07 (s, NCH_2), 67.64 (s, OCH_2), 101.46 (m, C-5), 104.87 (m, *i*-C_{Ar}), 137.31 (dt, ^1J(C-6,F-6) = 255 Hz, ^3J(C-6,F-2) = 15 Hz, C-6), 150.36 (dm, ^1J(C,F) = 260 Hz)/152.05 (dm, ^1J(C,F) = 261 Hz)/155.65 (dm, ^1J(C,F) = 255 Hz) (C-2/C-3/C-4), 155.85 ppm (s, N=CO); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −111.72 (m, 1F)/−127.63 (m, 1F)/−129.36 (m, 1F)/−163.93 ppm (m, 1F) (F-2/F-3/F-4/F-6); IR: $\tilde{\nu}$ = 3046/3010 (CH), 2923/2896 (CH_2), 1651/1638 (C=N), 1613/1514 (C=C), 1474 (CH), 1270/1058 (CO), 1206/1164 (CF), 842 cm^{-1} (CH); MS: *m/z* (%): 219 (35) [M^+], 189 (100) [M^+-CH_2O], 177 (10) [$M^+-C_2H_4N$], 149 (11) [$M^+-C_3H_4NO$]; elemental analysis (%) calcd for $C_9H_5NOF_4$: C 49.33, H 2.30, N 6.39; found: C 49.05, H 2.02, N 6.06.

2-(2,3,5,6-Tetrafluorophenyl)-2-oxazoline (4c): Yield: 73%; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.14 (t, 2H, ^3J(H,H) = 10 Hz, NCH_2), 4.48 (t, 2H, ^3J(H,H) = 10 Hz, OCH_2), 7.18 ppm (quin, 1H, $^3J/^4J$(H,F) = 8 Hz, 4-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.18 (s, NCH_2), 67.84 (s, OCH_2), 108.02 (dt, ^2J(C-4,F-3) = 14 Hz, ^3J(C-4,F-2) = 10 Hz, C-4), 110.01 (s, *i*-C_{Ar}), 144.89 (dm, ^1J(C,F) = 264 Hz)/145.95 (dm, ^1J(C,F) = 252 Hz) (C-2/C-3), 155.66 ppm (s, N=CO); ^{19}F NMR (376 MHz, $CDCl_3$): δ = − 137.96 (s, 2F)/−137.99 ppm (s, 2F) (F-2/F-3); IR: $\tilde{\nu}$ = 3028 (CH), 2921/2888 (CH_2), 1635 (C=N), 1610 (C=C), 1492 (CH), 1273/1001 (CO), 1185/1174 (CF), 885 cm^{-1} (CH); MS: *m/z* (%): 219 (31) [M^+], 189 (100) [M^+-CH_2O], 177 (7) [$M^+-C_2H_4N$], 149 (16) [$M^+-C_3H_4NO$]; elemental analysis (%) calcd for $C_9H_5NOF_4$: C 49.33, H 2.30, N 6.39; found: C 49.29, H 2.40, N 6.27.

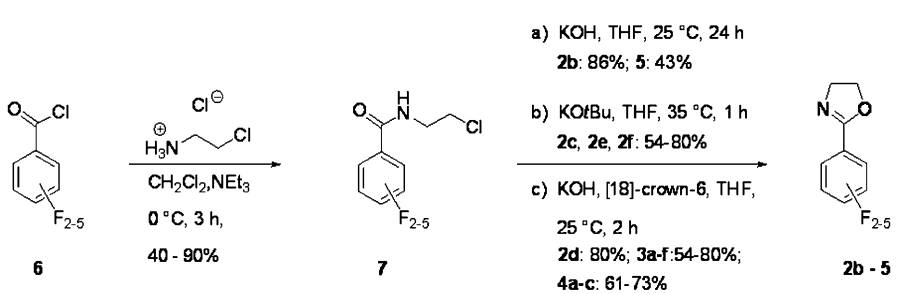
2-(2,3,4,5,6-Pentafluorophenyl)-2-oxazoline (5): Yield: 43%; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.14 (t, 2H, ^3J(H,H) = 9.5 Hz, NCH_2), 4.48 ppm (t, 2H, ^3J(H,H) = 9.5 Hz, OCH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 53.36 (s, NCH_2), 68.05 (s, OCH_2), 104.93 (td, ^2J(*i*-C_{Ar},F-2) = 15 Hz, ^3J(*i*-C_{Ar},F-3) = 5 Hz, *i*-C_{Ar}), 137.85 (dm, ^1J(C,F) = 250 Hz)/142.72 (dm, ^1J(C,F) = 259 Hz)/145.68 (dm, ^1J(C,F) = 259 Hz) (C-2/C-3/C-4), 155.32 ppm (s, N=CO); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −136.89 (m, 2F, F-2), −149.88 (m, 1F, F-4), −160.91 ppm (m, 2F, F-3); IR: $\tilde{\nu}$ = 2989/2964/2948/2921/2895 (CH_2), 1680 (C=N), 1655/1524 (C=C), 1488 (CH), 1359/980/954 (CF), 1207/1076 cm^{-1} (CO); MS: *m/z* (%): 237 (31) [M^+], 207 (100) [M^+-CH_2O], 195 (9) [$M^+-C_2H_4N$], 181 (8) [$M^+-C_2H_4NO$], 167 (12) [$M^+-C_3H_4NO$]; elemental analysis (%) calcd for $C_9H_4NOF_5$: C 45.59, H 1.70, N 5.91; found: C 45.18, H 1.51, N 5.56.

Microwave-assisted polymerization of 2-oxazolines: The microwave vials were heated to 105 °C, allowed to cool to room temperature, and filled with argon prior to use. For each polymerization, stock solutions (c(Ox) = 1.4 M) were prepared with a monomer/initiator (MeOTs) ratio of [Ox]/[MeOTs] = 60:1 and divided over the different reaction vials (depending on the amount of solution, the volume varied between 750 and 900 μL). After microwave irradiation for predefined times, the polymerization mixtures were quenched by the automated addition of water (50 μL; on the Emrys Liberator). The polymerization mixtures were diluted once with $CHCl_3$ to homogenize the solution, and the resulting mixtures were analyzed by GC and SEC to investigate the polymerization kinetics.

Results and Discussion

Synthesis: The synthesis of the monofluorinated oxazolines **1a–c** and the difluorinated oxazoline **2a** was performed by reaction of the corresponding fluorobenzonitriles with 2-ethanolamine in the presence of $Zn(OAc)_2$ as a Lewis acid catalyst to yield the desired oxazolines, as recently reported.[25,26] To avoid undesired side reactions, such as nucleophilic substitution reactions of the *para*- or *ortho*-fluoro substituents of the benzonitriles, all other di-, tri-, tetra-, and pentafluoro-substituted 2-phenyl-2-oxazolines **2b–f**, **3a–f**, **4a–c**, and **5** were synthesized according to the two-step procedure outlined in Scheme 3.

Starting from acid chlorides **6** one can obtain amides **7** through a modified one-step reaction with the hydrochloride salt of chloroethylamine in moderate-to-good yields (**2f**, **3f**, **4a**: 40–72%; **2b–e**, **3a–e**, **4b**,**c**, **5**: 80–90%).[25,35] Finally, the desired oxazolines can be obtained by the elimination of hydrogen chloride by using different kind of bases, such as KOH or potassium *tert*-butoxide, respectively. The difluoro-substituted 2-phenyl-2-oxazolines could be synthesized by performing the reaction over 24 h with KOH as the base in



Scheme 3. Two-step synthesis of 2-fluorophenyl-2-oxazolines **2b–5**.

THF at room temperature (**2c**,**e**,**f**: 54–80% yield). Potassium *tert*-butoxide was required as the base for the synthesis of **5**, produced in a yield of 43%, and led to a higher yield of 86% being obtained for **2b**, instead of the yield of 66% that was obtained under the previously described conditions. However, the reaction conditions for the other fluorophenyl oxazolines turned out to be optimal with KOH as the base, [18]crown-6 as a phase-transfer catalyst, and THF as the solvent at room temperature to give the oxazolines **2d**, **3a**–**f**, and **4a**–**c** after a reaction of 2 h in moderate-to-good yields (54–80%). These mild reaction conditions were accompanied by minor side-product formation and hence easier purification. These optimized conditions represent a general route for the successful synthesis of such kind of oxazolines.

Polymerization: All the new monomers and the nonfluorinated analogue 2-phenyl-2-oxazoline (PhOx) were polymerized through cationic ring-opening polymerization in nitromethane at 140°C with methyl tosylate as the initiator and microwave irradiation as the heat source. Stock solutions were prepared that contained solvent, monomer, and initiator with a ratio of [monomer]/[initiator] = 60:1. The initial monomer concentration $[M]_0$ was in all cases $[M]_0 = 1.4$ M. Between five and seven vials were prepared, and the polymerizations were performed for different reaction times. The reactions were quenched after the desired time by the addition of water, and the monomer conversion, represented as $\ln(M_0/M_t)$, was monitored by GC, whereas the molecular weights and PDI values were investigated by SEC.

In all cases, the first-order kinetic plots of monomer consumption with respect to the reaction time revealed a linear relationship (Figures 1–3, left), thus demonstrating a constant amount of propagating species. All the monomers could be polymerized to full conversion in less than 3 h at 140°C under microwave irradiation, except for 2-(3,4,5-trifluorophenyl)-2-oxazoline (3,4,5-TFOx; **3f**), which only

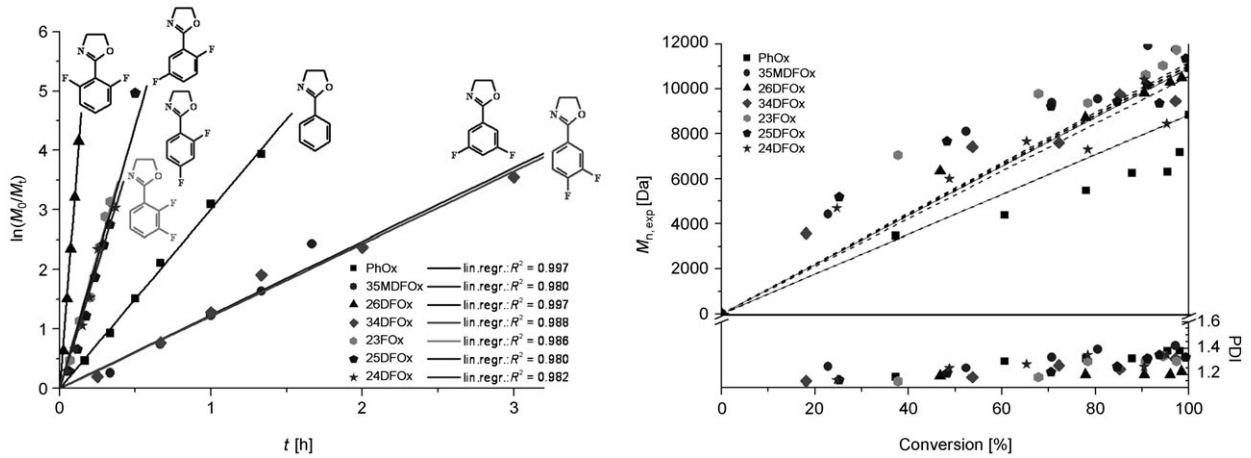


Figure 1. Polymerization of the 2-difluorophenyl-2-oxazolines **2a**–**f** and PhOx as a reference. Left: first-order kinetics; right: number-average molecular weight M_n against conversion. lin. regr. = linear regression.

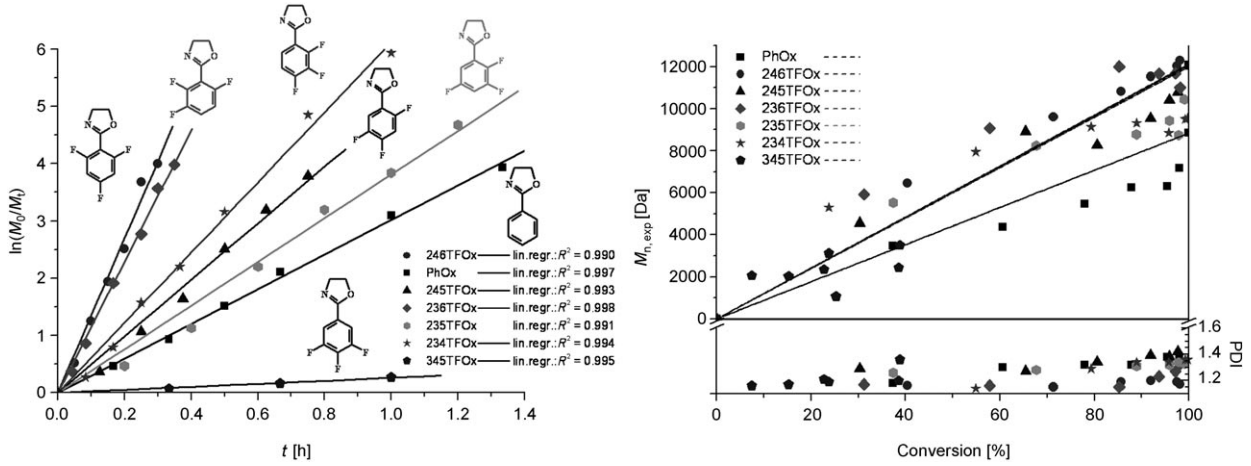


Figure 2. Polymerization of the 2-trifluorophenyl-2-oxazolines **3a**–**f** and PhOx as a reference. Left: first-order kinetics; right: number-average molecular weight M_n against conversion.

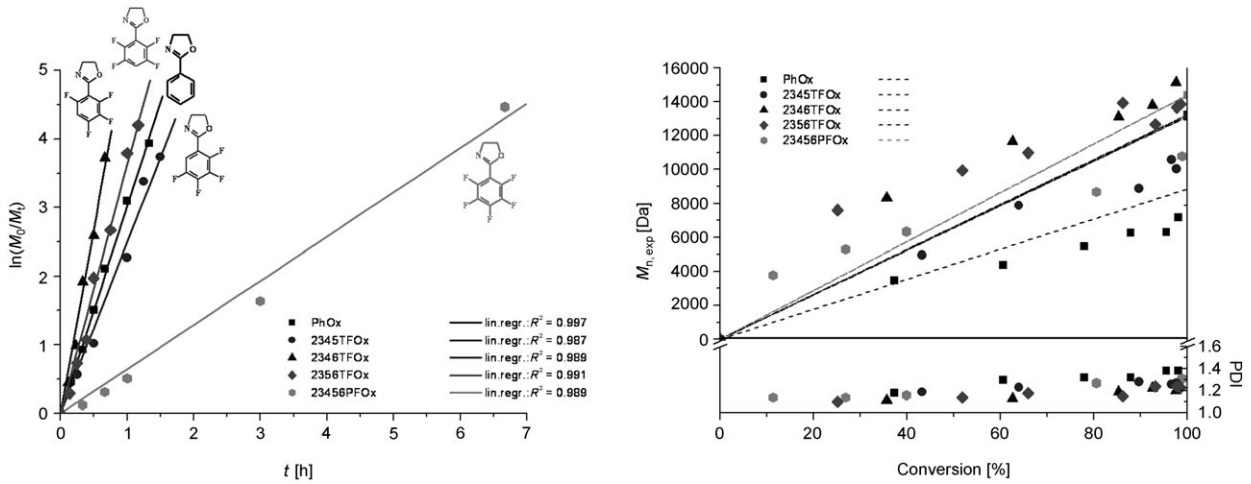


Figure 3. Polymerization of the 2-tetrafluorophenyl-2-oxazolines **4a–c** and 2-pentafluorophenyl-2-oxazoline **5** and PhOx as a reference. Left: first-order kinetics; right: number-average molecular weight M_n against conversion.

reached 15% conversion within 1 h, and 2-(2,3,4,5,6-pentafluorophenyl)-2-oxazoline (2,3,4,5,6-PFOx; **5**), which reached full conversion within 7 h. Surprisingly, most of the fluorinated aromatic monomers revealed faster polymerizations than the unsubstituted PhOx, even though the electron-withdrawing effect of the fluorine atoms was expected to lead to a decreased reaction speed and hence longer reaction times. The effect of the fluorine substitution pattern on the polymerization rate will be discussed later.

Subsequent SEC analysis resulted in constantly increasing molecular weights with conversion during all the polymerizations (Figures 1–3, right). The M_n values correlated in a reasonably linear way to the monomer conversion, thus demonstrating a living polymerization behavior. Discrepancies with the theoretical M_n value might be related to the occurrence of some chain-transfer reactions and to the utilized polystyrene standards. However, the PDI values of all the oxazoline polymers are below 1.30 at $<90\%$ conversion, thus indicating that the polymerizations take place in a living manner. The higher PDI values for conversions greater than 90% are presumably caused by the high viscosity of the polymerization mixture and therefore the hindered diffusion of the last monomer units to the reaction centers. Nonetheless, the polymerizations of **2b**, **3a**,**c**, and **4b**,**c** revealed low PDI= values of 1.2 at $<99\%$ conversion. Furthermore, all the polymers could be characterized by MALDI-TOF mass-spectrometric analysis. The spectrum of poly(**3a**) features a monomodal mass distribution and equidistant peaks with a difference of $\Delta = 201$ Da according to the mass of one monomer unit (Figure 4). The spectra of the other polymers were similar with equidistant peaks of $\Delta =$ 165 (**1a–c**), 183 (**2a–f**), 201 (**3a–f**), 219 (**4a–c**), and 237 Da (**5**), respectively (see Figures S1–S19 in the Supporting Information).

From the slopes of the first-order kinetic plots (Figures 1–3, left), the corresponding polymerization rates were determined (Table 1). 2-Aryl-2-oxazolines feature lower polymer-

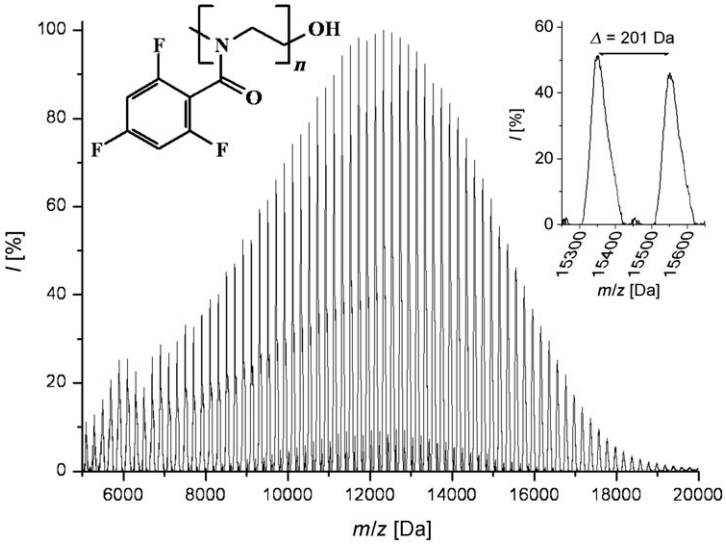


Figure 4. MALDI-TOF mass spectrum of polymer poly(**3a**).

ization rates than the corresponding 2-alkyl-2-oxazolines as a result of the +M effect of the phenyl substituent onto the oxazoline ring. The positive charge of the oxazolinium ring of the growing species is partially compensated by resonance with the aromatic system, thus lowering its electrophilicity and hence causing a slower chain growth. For example, PhOx polymerizes three times more slowly than 2-alkyl-2-oxazolines such as 2-ethyl-2-oxazoline.[22] As a consequence, it is expected that the polymerization of 2-phenyl-2-oxazolines substituted with electron-withdrawing groups such as fluorine exhibit even slower polymerization rates. Surprisingly, only the polymerization rates for **2a**,**c**, **3f**, and **5** are significantly lower than for PhOx, thus representing the monomers with a predominantly negative impact on the +M effect.

Table 1. Polymerization rates k_P [$\times 10^{-3}$ L mol^{-1} s^{-1}] of PhOx and the fluorinated 2-aromatic-2-oxazoline monomer library in nitromethane at 140 °C.

Oxazolines with no *ortho*-fluoro substituents			Mono-*ortho*-fluoro oxazolines			Di-*ortho*-fluoro oxazolines		
Monomer		k_P	Monomer		k_P	Monomer		k_P
PhOx		35.8	*o*-Fox	**1a**	173.1	2,6-DFOx	**2b**	382.4
m-Fox	**1b**	29.3	2,3-DFOx	**2d**	102.4	2,4,6-TFOx	**3a**	103.5
p-Fox	**1c**	26.7	2,5-DFOx	**2e**	103.9	2,3,6-TFOx	**3c**	134.1
3,5-DFOx	**2a**	14.8	2,4-DFOx	**2f**	96.4	2,3,4,6-TFOx	**4b**	64.2
3,4-DFOx	**2c**	14.2	2,4,5-TFOx	**3b**	57.1	2,3,5,6-TFOx	**4c**	41.7
3,4,5-TFOx	**3f**	5.5	2,3,5-TFOx	**3d**	46.5	2,3,4,5,6-PFOx	**5**	7.3
			2,3,4-TFOx	**3e**	68.9			
			2,3,4,5-TFOx	**4a**	29.4			

However, the polymerization rates for all other monomers containing one or two *ortho*-fluoro substituents are higher or similar to PhOx. As recently discussed in detail, *ortho*-fluoro substituents have two positive effects on the rate of the polymerization of such oxazolines.[25] First, the coplanarity of the oxazoline and the phenyl rings is repealed, thus resulting in a higher nucleophilicity of the monomer; second, the *ortho*-fluoro substituent stabilizes the cationic reaction center—the tetra-coordinated nitrogen atom—during the polymerization by donation of electron density through space. Both effects overcompensate for the negative electron-withdrawing effect of the fluorine substituent(s) and contribute to a significant acceleration of the polymerization. This behavior is especially noticeable from the polymerization rates of the *ortho*-difluoro oxazoline **2b**, oxazolines **1a** and **2d**,**e**,**f** containing one *ortho*-fluoro substituent, and even the trifluoro oxazolines **3a**,**c** containing two *ortho*-fluoro substituents. Whereas 2-(2,6-difluorophenyl)-2-oxazoline (*o*-DFOx; **2b**) polymerizes ten times faster than PhOx and even three times faster than 2-*n*-alkyl-2-oxazolines,[25,36] the other monomers polymerize three to five times faster than the unsubstituted PhOx analogue. The trifluoro oxazolines with one *ortho*-fluoro substituent **3b**,**d**,**e** and even the tetrafluoro oxazolines **4a**–**c** polymerize slightly faster or at a comparable rate to PhOx. Here, the positive effects of the *ortho*-fluoro substituents balance the negative electron-withdrawing effect of the *meta*- and/or *para*-fluoro substituents. As mentioned previously, only the monomers without any *ortho*-fluoro substituents have significantly slower polymerization rates. PhOx polymerizes approximately two times faster than the difluoro monomers **2a**,**c** and five times faster than the pentafluoro monomer **5**. In this case, the electron-withdrawing effect of the *meta*- and/or *para*-fluoro substituents overcompensates for the positive effect of the *ortho*-difluoro substitution. This destabilizing effect is even more pronounced for the trifluoro oxazoline lacking any *ortho* substituents 3,4,5-TFOx (**3f**), which only be polymerized at $<25\%$ of monomer conversion (degree of polymerization (DP) ≈ 15) within 16 hours. It is noteworthy that *o*-DFOx (**2b**) is the fastest 2-oxazoline monomer in the living cationic ring-opening polymerization to date.

Polymer properties: All synthesized polymers (DP ≈ 60) were characterized by thermogravimetric analysis (TGA), differential scanning calorimetry (DSC), and contact-angle measurements to investigate selected thermal and surface properties, respectively. Before the analysis, the end samples of the polymerization kinetic experiments were precipitated in cold diethyl ether, isolated by filtration, and dried for 24 h at 40 °C and 1 mbar prior to use.

The thermal stability of the library of oxazoline polymers was determined by TGA in a temperature range of 25–800 °C. All the heating curves are depicted in the Supporting Information (Figure S24–S27), and the results are summarized in Figure 5 and Table S1 in the Supporting Information.

All the polymers are stable up to at least 292 °C (i.e., **2b**) but the range of temperatures over 5% degradation is

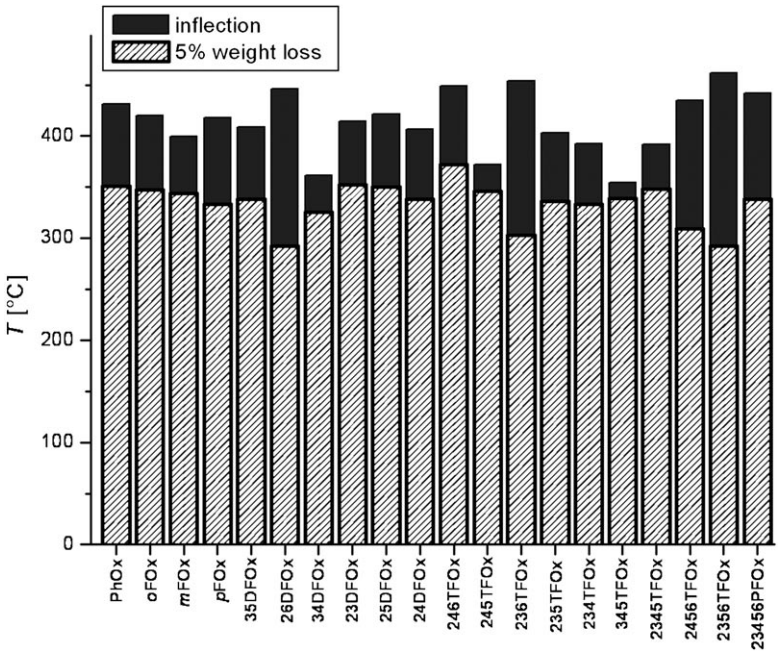


Figure 5. Thermostability of the polymers of the fluorophenyl oxazolines **2a**–**f**, **3a**–**f**, **4a**–**c**, **5**, and PhOx determined by TGA.

broad up to 372 °C for the most stable polyoxazoline 2,4,6-TFOx (**3a**). All the fluorinated oxazoline polymers degrade in one step, and the temperatures of the inflection point range from 361 to 449 °C, comparable to the properties of polymers based on 2-alkyl-2-oxazolines.[27] A more detailed look into the inflection temperatures reveals a significant influence of the substitution pattern. All the polymers with two *ortho*-fluoro substituents (**2a**, **3a**,**c**, **4b**,**c**, and **5**) reveal significantly higher inflection temperatures relative to the analogue polymers with or without any *ortho*-fluoro substituents. Furthermore, the latter are even less thermally stable than PhOx, as indicated by lower inflection temperatures.

The DSC measurements (see Figures S20–S23 in the Supporting Information for the corresponding graphs) led to the conclusion that all the polymers exhibit one glass transition temperature T_g, but no melting point could be observed in any case. The glass transition temperature characterizes the chain mobility of a polymer, which means that a high T_g value represents a low chain mobility.[37] It is known that polymers based on aromatic 2-oxazolines, such as PhOx, feature glass-transition temperatures of $T_g = 103$[32] or 105 °C,[12] which are significantly higher than the T_g values of 2-methyl- or 2-ethyl-2-oxazolines (between 60 and 80 °C)[12,38] because of the influence of the rigid aromatic phenyl ring. The T_g values of the present fluorinated polymer library are comparable to PhOx or higher (see Figure 6 and Table S1 in the Supporting Information). The polymers with two *ortho*-fluoro substituents on the phenyl ring (**2a**, **3a**,**c**, **4b**,**c**, and **5**) revealed significantly higher T_g values than the other copolymers. These observed T_g values of above 120 °C in such cases reflect the limited rotational freedom of the phenyl rings carrying two *ortho*-fluoro substituents, thus culminating for the sterically most demanding oxazolines **3a** and **5** in maximal T_g values of 133 and 135 °C, respectively, which is approaching the highest reported T_g value of 139 °C for poly(2-oxazoline)s bearing very bulky adamantyl side groups. The high T_g values of the polymers with *ortho*-fluoro substituents is most likely because of the presence of attractive C–F···C=O interactions, which decrease the chain mobility and thus increase the T_g value.[39,40] These attractive interactions are also evidenced by the fact that the T_g value for polystyrene ($T_g = 100$ °C), which has no heteroatoms to form such attractive interactions, only slightly increases when fluoro substituents are introduced, that is, poly(pentafluorophenyl)styrene and poly(4-fluoro)styrene have T_g values of 106 and 108 °C, respectively.[41] The extremely low T_g value for 3,4,5-TFOx (**3f**) of around 60 °C can be explained by the short length of the polymer chain, which is only DP ≈ 15 as discussed before.

To characterize the surface properties of the present oxazoline polymer library, the oxazolines were spin-coated onto glass slides and the contact angles were measured for two different test liquids, namely, diiodomethane and ethylene glycol. Next, the polymer films were annealed by leaving them overnight in an oven at 140 °C, which is higher than the corresponding T_g value. The surface energies (see Figure 7 and Table S1 in the Supporting Information) were calculated from the resulting contact angles. Unfortunately, not all polymers formed perfect homogenous clear films on the glass slide by spin-coating. The polymers based on the trifluoro oxazolines **3e** and **3f** and the tetrafluoro monomers **4a–c** formed films that featured slightly opaque parts. Hence, the surface properties were determined from the clear parts.

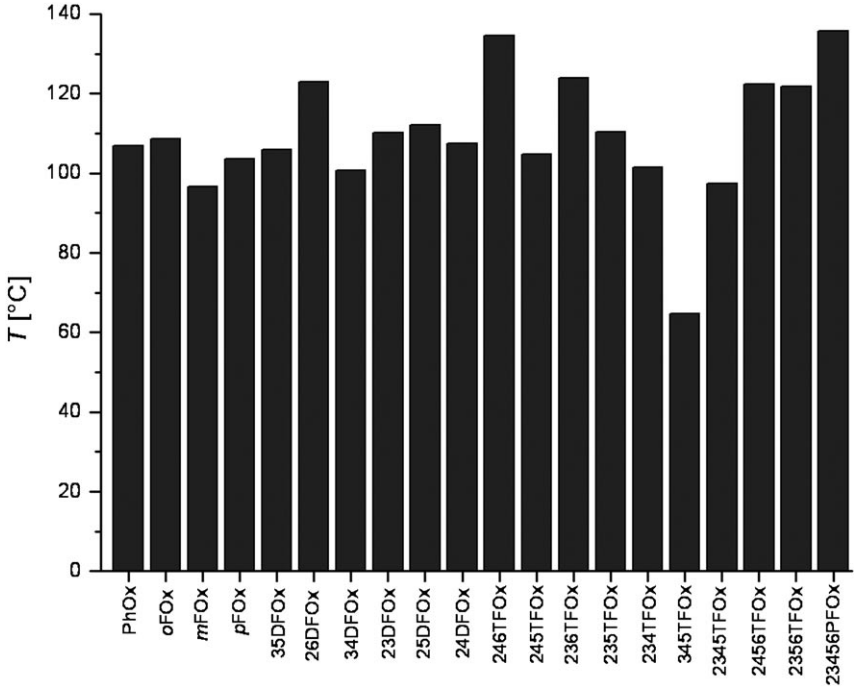


Figure 6. Glass-transition temperatures T_g of the polymers based on the fluorophenyl oxazolines **2a–f**, **3a–f**, **4a–c**, **5**, and PhOx determined by DSC.

All the obtained surface energies are lower than the surface energy of the unfluorinated PhOx (42.6 mN m^{-1}); overall, the presence of fluorine substituents on the phenyl ring led to lower surface energies as expected for fluorine-based polymers. However, the surface energy does not continuously decrease with increasing fluorine substitution, although the tetrafluoro oxazoline polymer of **4b** and the pentafluoro oxazoline polymer of **5** represent the polymers with the lowest surface energies of 25.7 mN m^{-1} after annealing.

In general, annealing led to significantly lower surface energies relative to the untreated

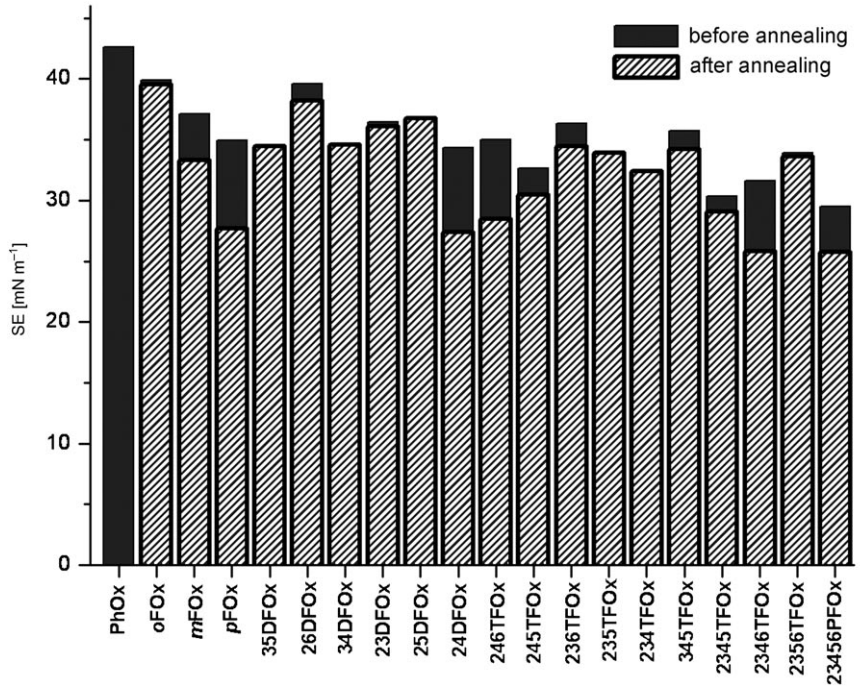


Figure 7. Surface energies (SEs) of the polymers of the fluorophenyl oxazolines **2a–f**, **3a–f**, **4a–c**, **5**, and PhOx before and after annealing (16 h, 140 °C).

polymer films. As a result of the heat-induced flexibility of the polymer side chain, the optimal arrangement of the fluoro-substituted phenyl rings of the polymers is enabled during the annealing step. Therefore, the outer fluorine substituents can orient directly toward the air surface, thus resulting in lower surface energy values. This behavior becomes obvious by a detailed look at the substitution pattern of the polymers with the lowest surface energies beside **4b** and **5**, which are in fact **1c** ($1\times p$), **2c** ($1\times p$, $1\times m$), **3a** ($1\times p$, $2\times o$), **3b** ($1\times p$, $1\times m$, $1\times o$), and **4a** ($1\times p$, $2\times m$, $1\times o$) with surface energies between 27–29 mN m^{-1}. All these polymers carry a *para*-fluoro substituent that causes an efficient decrease of the corresponding surface energy. The importance of especially the *para*-fluoro substituent in lowering the surface energy is further confirmed by a detailed look onto the surface energies of the polymers based on the tetrafluoro oxazolines, in which **4c**, without a *para*-fluoro substituent, displays a significantly higher surface energy than **4a**,**b**. This trend is further supported by the the fact that the highest surface energy (40 mN m^{-1}; not considering PhOx) was obtained for the fluorinated polymer **2b**, which is substituted with two *ortho*-fluoro substituents that cannot be readily oriented towards the surface. The surface energy values of the remaining oxazolines span the range between the pentafluoro-substituted oxazoline and PhOx. The relatively high surface energy for 3,4,5-TFOx **3f** (34 mN m^{-1}) with two *meta*- and one *para*-fluorine substituents is not understood at the moment, but might be related to the short polymer chain length.

In conclusion, the presence of a *para*-fluoro substituent is sufficient for a reasonable reduction of the surface energy, although the minimal surface energy is obtained for the pentafluoro oxazoline **5**.

Conclusions and Outlook

The synthesis and polymerization of all possible fluorinated 2-phenyl-2-oxazolines was successfully performed and selected polymer properties were analyzed in detail. All the monomers could be polymerized through a living cationic ring-opening polymerization with microwave irradiation as the heat source. The fluoro-substituted 2-phenyl-2-oxazolines containing one or two *ortho*-fluoro substituents polymerize faster than the parent unsubstituted 2-phenyl-2-oxazoline for two reasons: First, the interaction of the cationic reaction center of N^+ with the *ortho*-fluoro substituent overcompensates for the negative electron-withdrawing effect; second, the nucleophilic character of the monomers are increased because of the nonplanarity of the oxazoline ring and the phenyl substituent. The lack of *ortho*-fluoro substituents significantly decreases the polymerization rates for the difluoro monomers **2a**,**c** and the trifluoro monomer **3f**.

The different substitution patterns were found to have a remarkable influence on the polymer properties as well. The thermal stability and the glass-transition temperatures were found to increase in the presence of *ortho*-fluoro substituents, which is attributed to attractive C–F···C=O interactions that decrease the chain mobility, thus increasing the glass-transition temperatures. Furthermore, these interactions seem to stabilize the amidic side chains, thus resulting in higher decomposition temperatures. In contrast to the thermal properties, the surface energy of the fluorinated aromatic poly(2-oxazoline)s was found to be mostly dependent on the presence of *para*-fluoro substituents; that is, the surface energy decreases when *para* substituents are present, which can be understood by the easier orientation of such *para* substituents toward the surface without exposing the polar polymer backbone to the surface.

Within this oxazoline library, especially the polymers of **3a**, **4b**, and **5**, which feature both a high T_g value and a low surface energy, there might be useful candidates for the formation of multicompartment micelles once integrated into an amphiphilic triblock copolymeric structure. Therefore, future investigations will focus on the synthesis of well-de-

fined triblock copolymers based on 2-ethyl-2-oxazoline as a hydrophilic monomer, 2-phenyl-2-oxazoline as a hydrophobic monomer, and pentafluoro 2-phenyl-2-oxazoline **5** as a fluorophilic monomer and the study of its aggregation behavior in aqueous solution.

Acknowledgements

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