Lithium Diisopropylamide-Mediated Ortholithiations:
Lithium Chloride Catalysis

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**Supporting Information**

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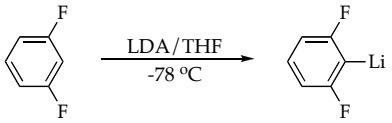
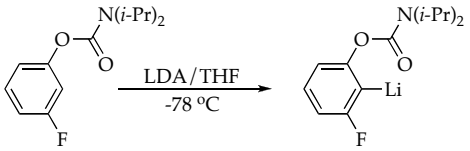
**IR Rate Studies**

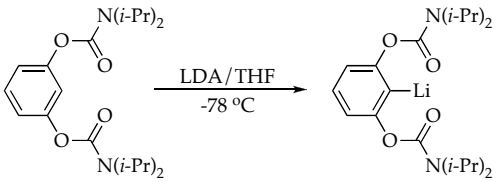


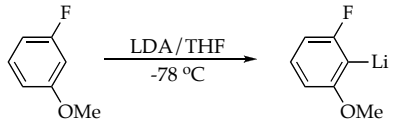




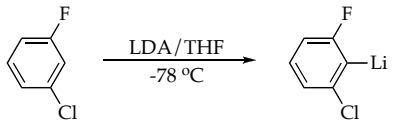





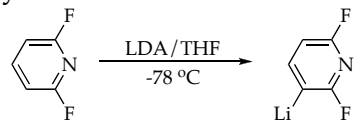





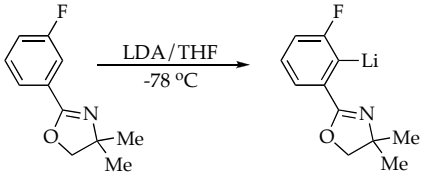


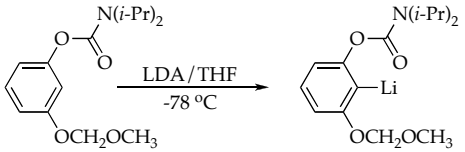


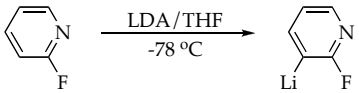


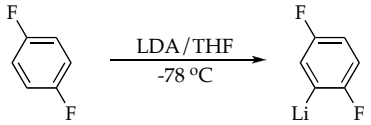





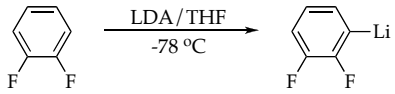





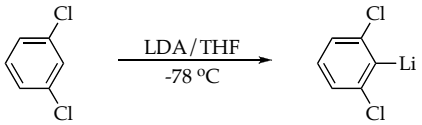





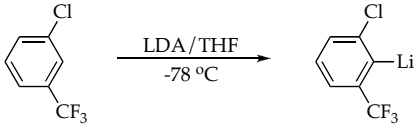


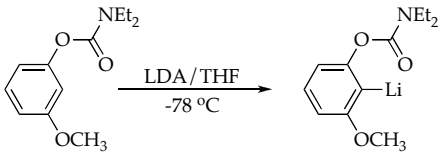


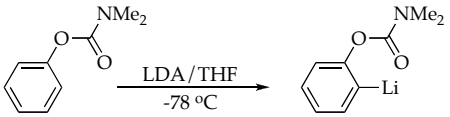






**Note:**

1) All reported LiCl mol percentages are with respect to [LDA].
2) Rates corresponding to the plots from **XV** to **XVIII** were determined at temperatures other than -78 ºC.
3) Be aware of frequent changes in the scale on x-axis.

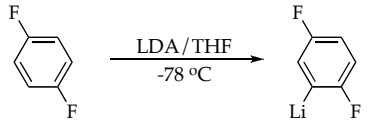
## Experimental

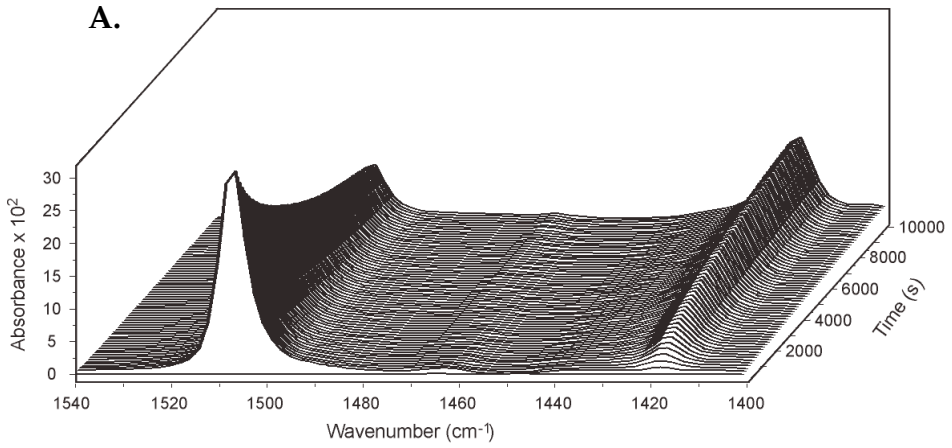
**I.** Measurement of chloride concentration:

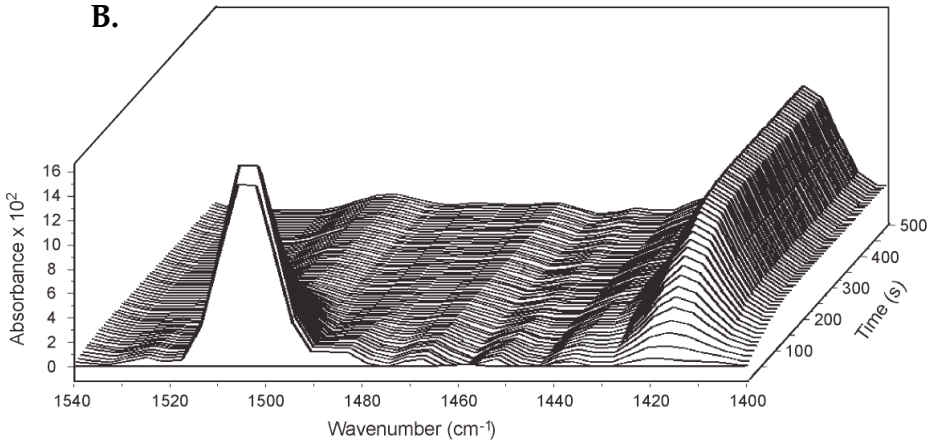
**Potentiometry:** The chloride concentration was determined potentiometrically by measuring the potential against a saturated potassium chloride solution. After calibrating with known concentrations of chloride, the concentration was calculated with the Nernst equation ($E=E°-(RT/zF)log_{10}Q$, where $Q=[Cl^-]$; $RT/zF$ is determined via calibration and is ideally 59.1 mV). The potential was measured with a potentiostat of low impedence. Both reference and indicating electrodes are made of silver plated with silver chloride (Ag/AgCl). Samples were prepared by quenching 25 mg of LDA or 100 µl of 1.6 M *n*-BuLi with high-purity water (from Abruña group), evacuating to dryness and redissolving in water. Because the electrodes require a near neutral pH, the quenched base solutions needed to be neutralized with $HNO_3$. The LiCl standards were accordingly enriched with $NaNO_3$ to ensure comparable activity. Both $HNO_3$ and $NaNO_3$ contained <0.5 ppm and <0.0003% $Cl^-$, respectively. The lower detection limit for $Cl^-$ is approximately 0.5 ppm.

**Ion Chromatography:** Ion chromatography was performed on a Dionex ICS-2000 system (Sunnyvale, CA) with a Dionex Ionpac AG18 guard column and a Dionex Ionpac AS18 separation column. Samples and standards were run in the isocratic mode (1.0 ml/min) using 38 mM KOH as eluent. Elution time of chloride varied from 3.94 to 4.23 min. The suppression was achieved by a Dionex ASRS ULTRA II 4 mm self-regenerating suppressor. The column temperature was 30 °C and the working electric current was 100 mA. The eluent flow rate is 1.0 ml/min. The injection volume is 25 µl. Samples were prepared by quenching 25 mg of LDA or 100 µl of 1.6 M *n*-BuLi with high-purity water (from Abruña group), evacuating to dryness and redissolving in water. Aqueous samples of pH 12-13 were injected in duplicate into the chromatograph. The lower detection limit is approximately 10 ppb.

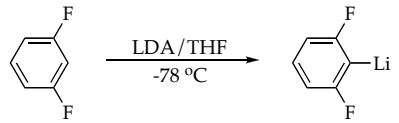
## IR Rate Studies

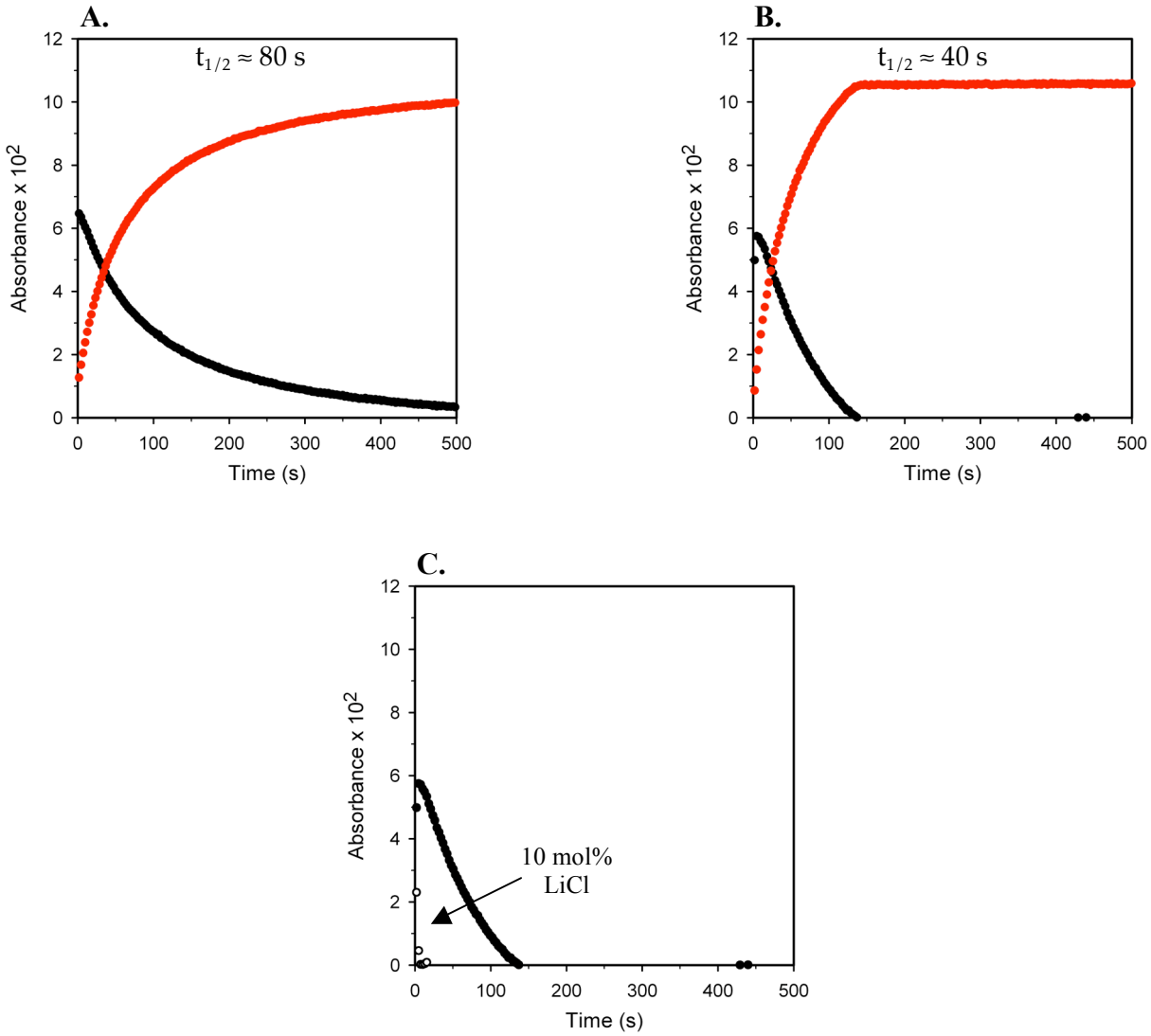


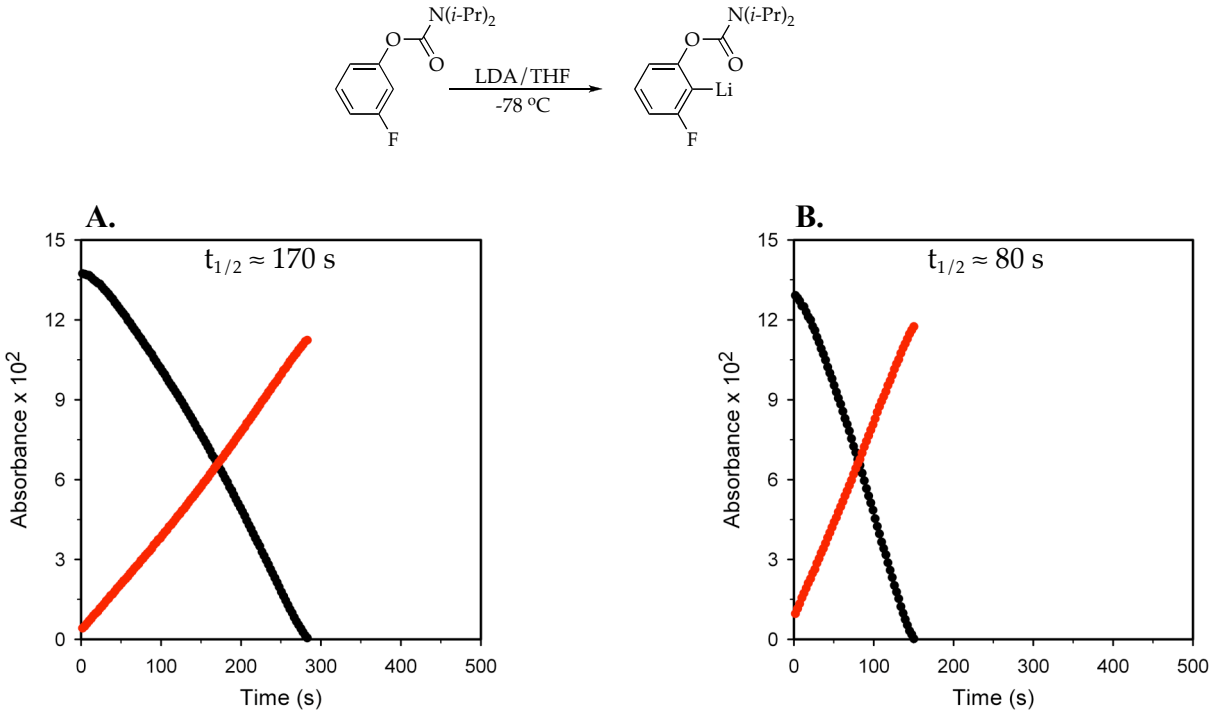




**I**. Representative in situ IR spectroscopic analysis of the ortholithiation of 1,4-difluorobenzene (0.1 M) with LDA (0.12 M) in neat THF at -78 ºC: (A) no added LiCl; (B) 0.5 mol % LiCl. The IR absorbance at 1507 $cm^{-1}$ corresponds to 1,4-difluorobenzene, whereas the absorbance at 1418 $cm^{-1}$ corresponds to its lithiated form.

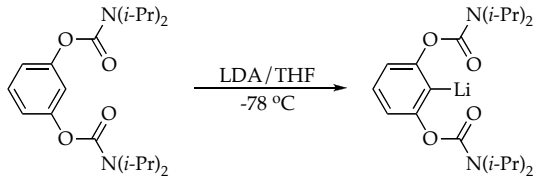


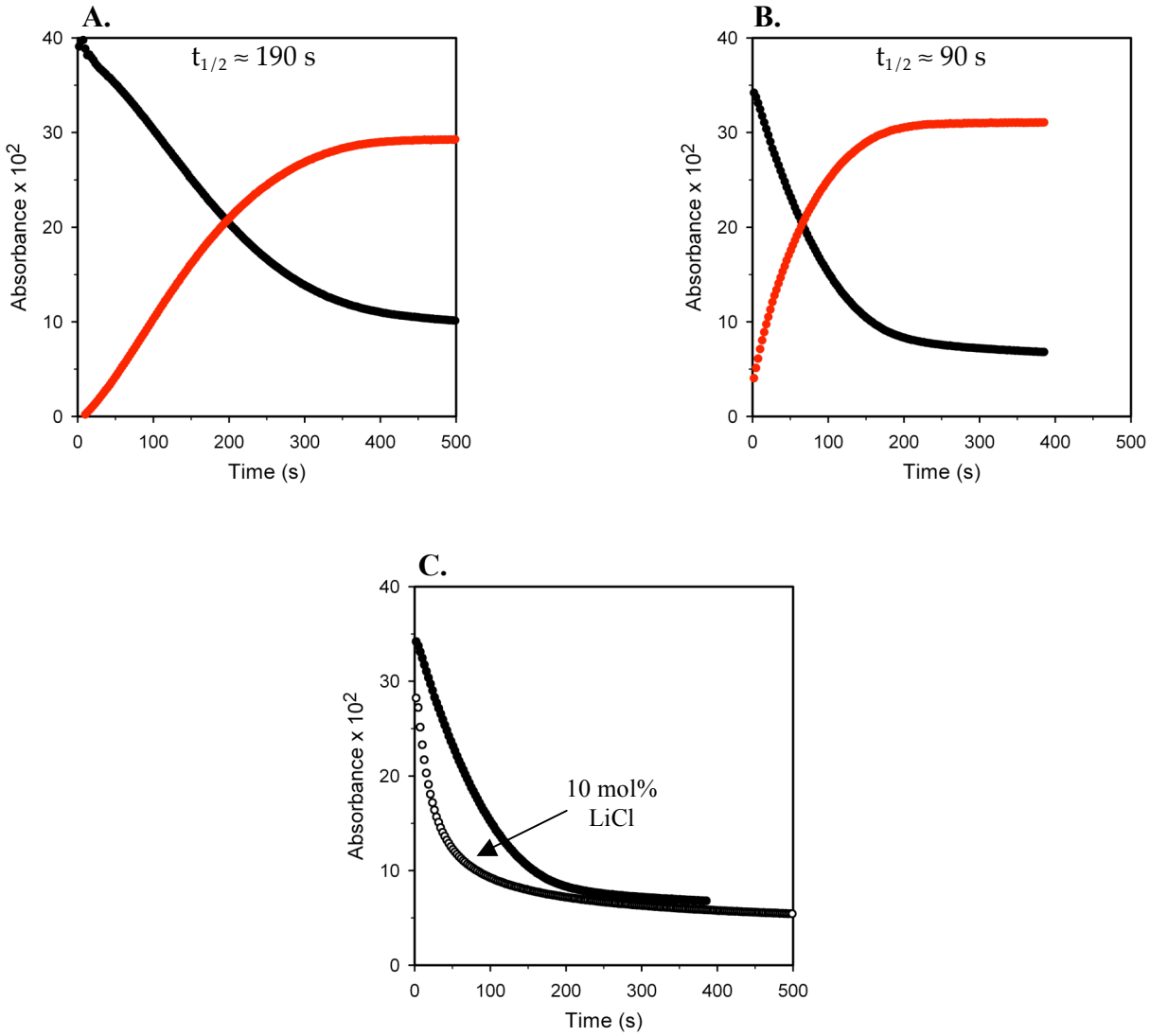




**II.** Plot of IR absorbances (black – 1606 $cm^{-1}$, red – 1406 $cm^{-1}$) versus time for the ortholithiation of 1,3-difluorobenzene (0.10 M) with LDA (0.12 M) in neat THF at -78 °C: (A) no added LiCl; (B) 0.5 mol% LiCl; (C) 0.5 and 10 mol% LiCl.

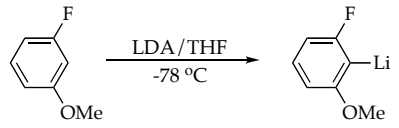


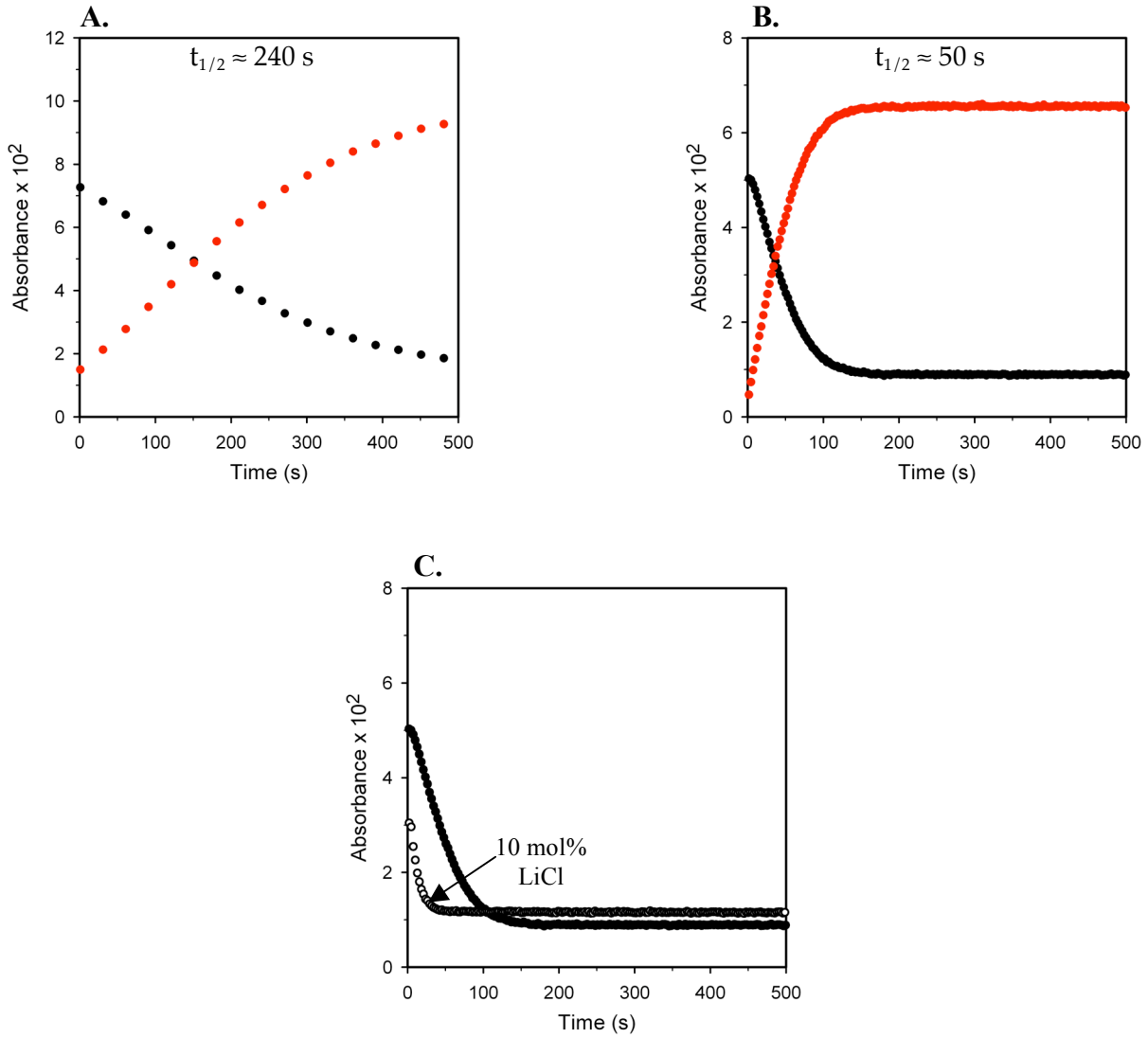

**III.** Plot of IR absorbances (black – 1715 $cm^{-1}$, red – 1657 $cm^{-1}$) versus time for the ortholithiation of 3-fluorophenyl-*N,N*-diisopropylcarbamate (0.10 M) with LDA (0.12 M) in neat THF at -78 °C: (A) no added LiCl; (B) 0.5 mol% LiCl.



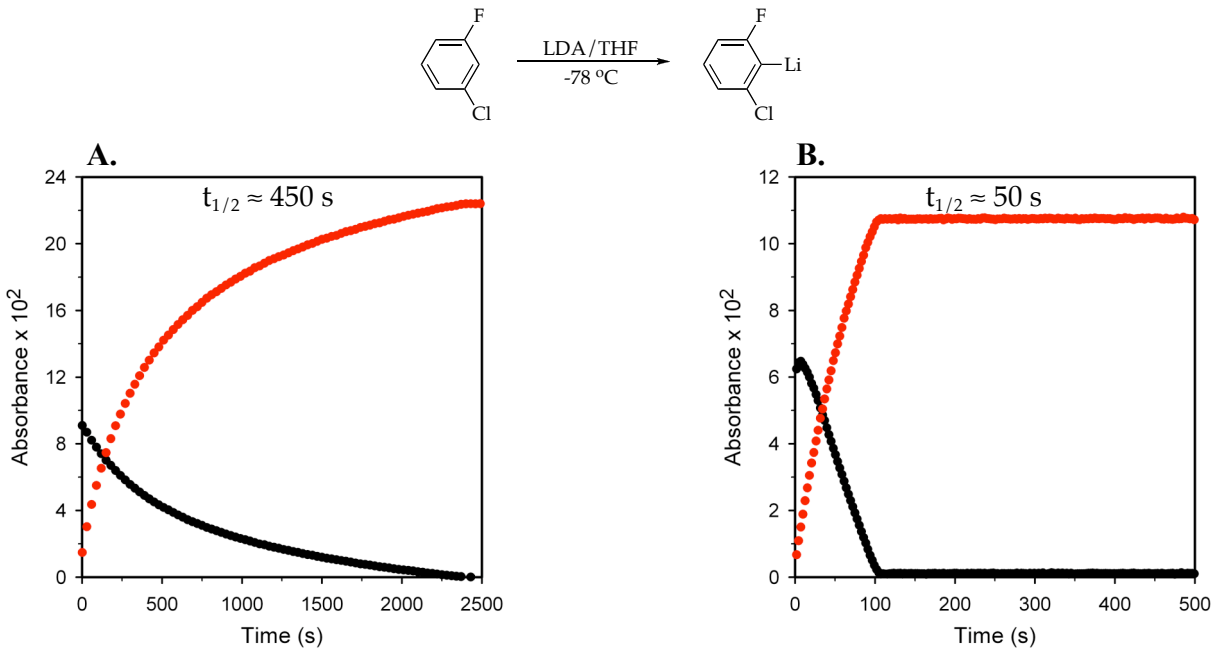




**IV.** Plot of IR absorbances (black – 1721 $cm^{-1}$, red – 1661 $cm^{-1}$) versus time for the ortholithiation of 1,3-bis(*N*,*N*-diisopropylcarbamoyl)benzene (0.10 M) with LDA (0.12 M) in neat THF at -78 °C: (A) no added LiCl; (B) 0.5 mol% LiCl; (C) 0.5 and 10 mol% LiCl.

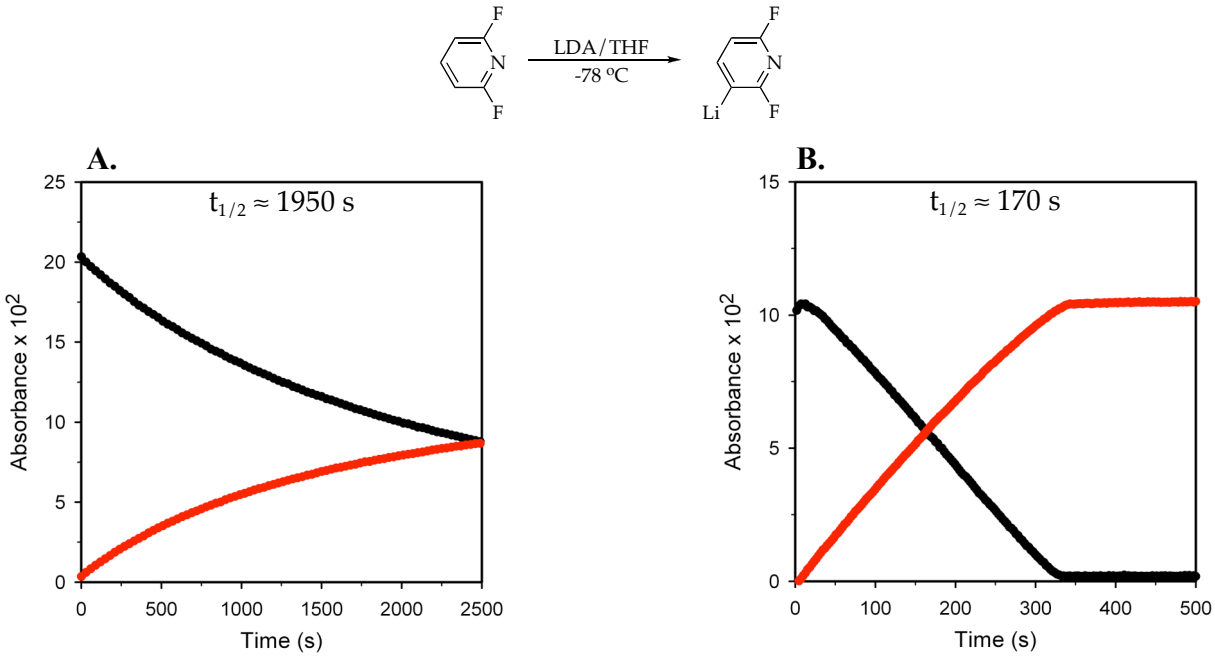


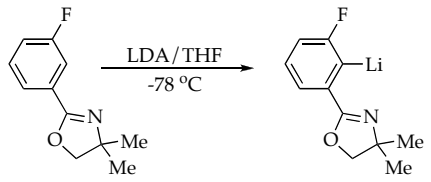

**V.** Plot of IR absorbances (black – 1617 $cm^{-1}$, red – 1412 $cm^{-1}$) versus time for the ortholithiation of 3-fluoroanisole (0.10 M) with LDA (0.12 M) in neat THF at -78 °C: (A) no added LiCl; (B) 0.5 mol% LiCl (C) 0.5 and 10 mol% LiCl.

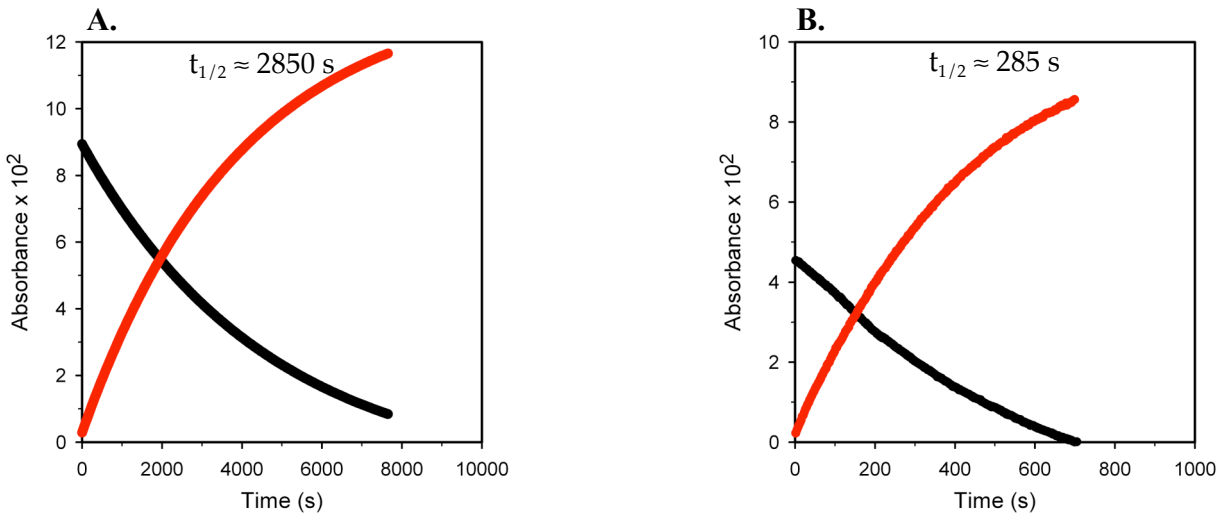



**VI.** Plot of IR absorbances (black – 1595 $cm^{-1}$, red – 1397 $cm^{-1}$) versus time for the ortholithiation of 1-chloro-3-fluorobenzene (0.10 M) with LDA (0.12 M) in neat THF at -78 °C: (A) no added LiCl; (B) 0.5 mol% LiCl.

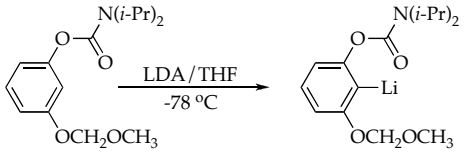


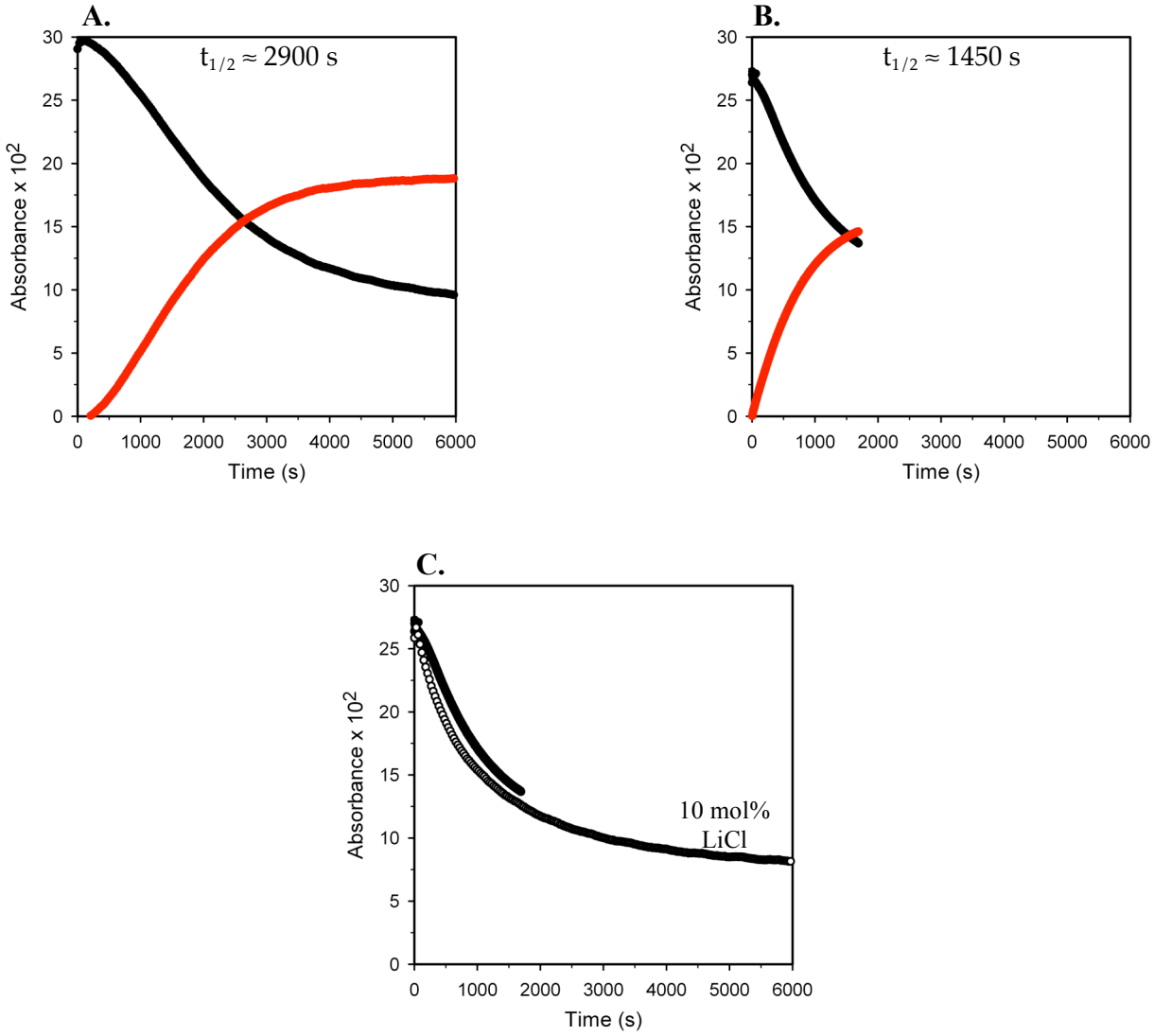

**VII.** Plot of IR absorbances (black – 1610 $cm^{-1}$, red – 1514 $cm^{-1}$) versus time for the ortholithiation of 2,6-difluoropyridine (0.10 M) with LDA (0.12 M) in neat THF at -78 °C: (A) no added LiCl; (B) 0.5 mol% LiCl.



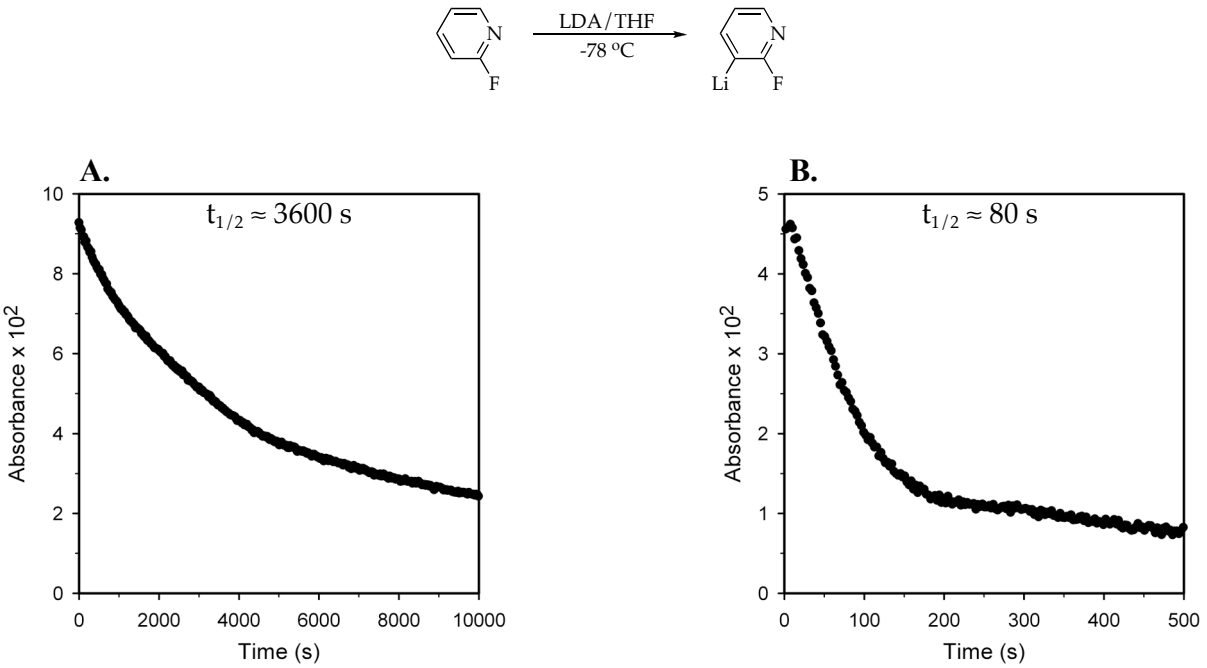




**VIII.** Plot of IR absorbances (black – 1653 $cm^{-1}$, red – 1622 $cm^{-1}$) versus time for the ortholithiation of 2-(3-fluorophenyl)-4,4-dimethyl-4,5-dihydro-1,3-oxazole (0.10 M) with LDA (0.12 M) in neat THF at -78 °C: (A) no added LiCl; (B) 0.5 mol% LiCl.

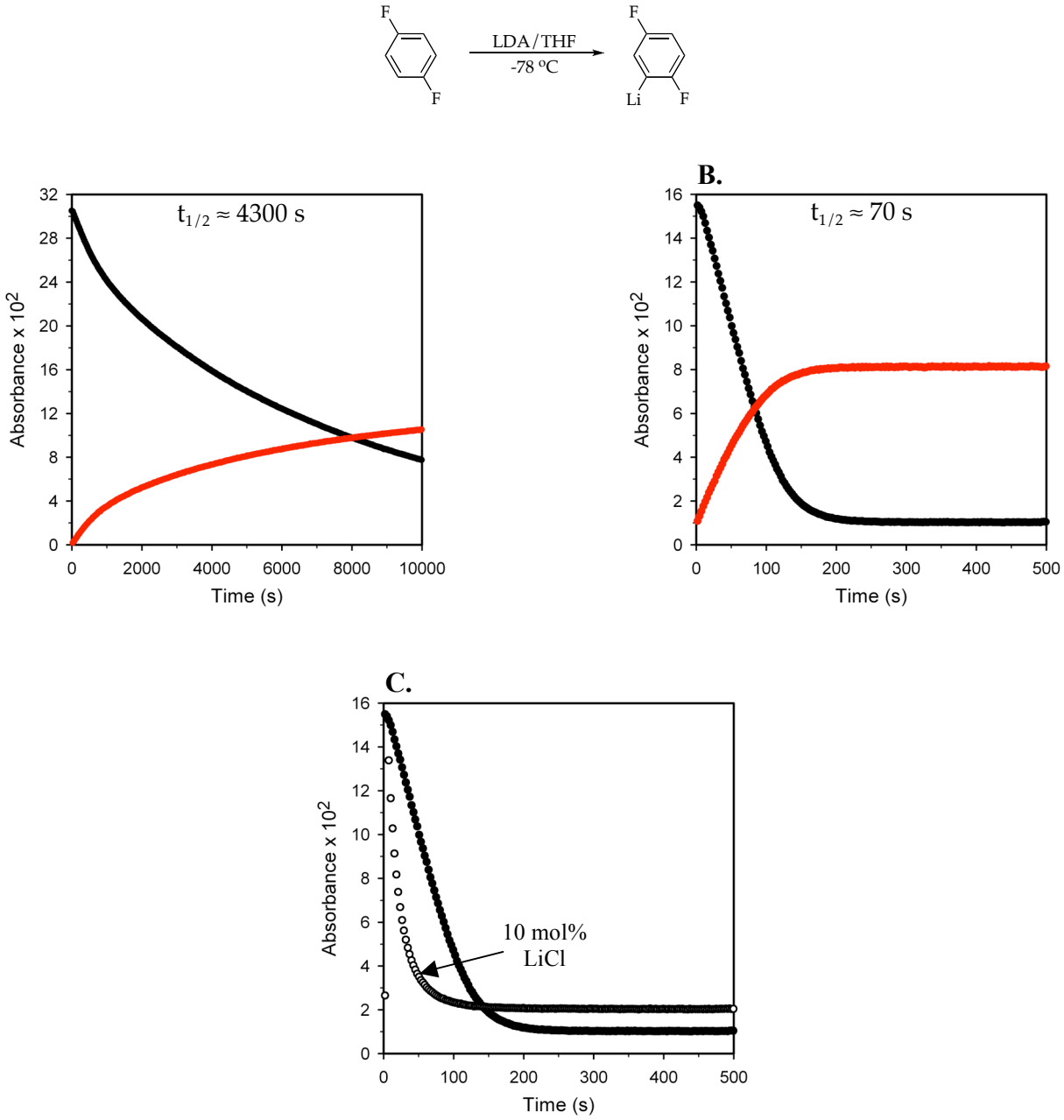


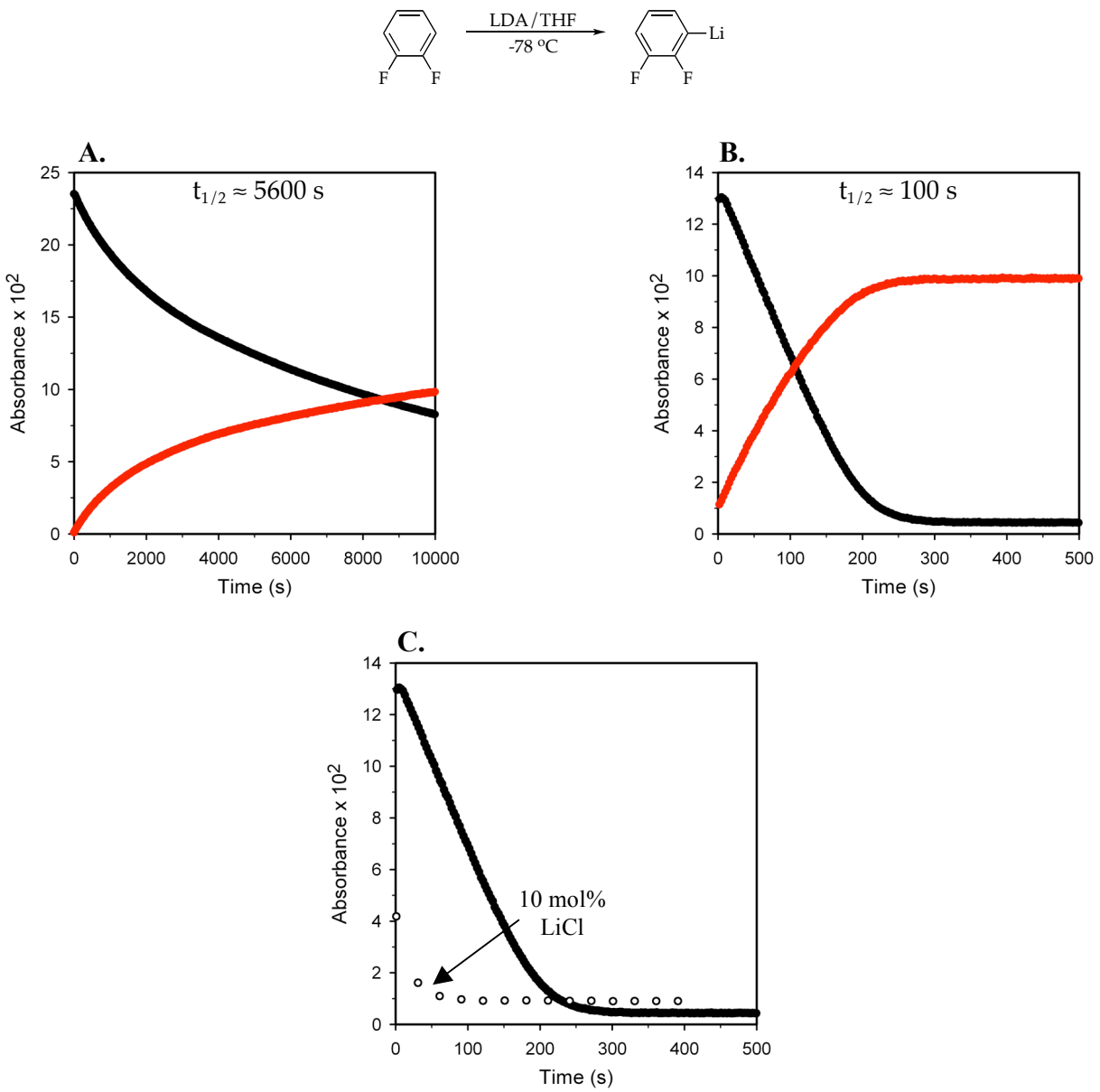

**IX.** Plot of IR absorbances (black – 1719 $cm^{-1}$, red – 1659 $cm^{-1}$) versus time for the ortholithiation of 3-methoxymethoxyphenyl-*N*,*N*-diisopropylcarbamate (0.10 M) with LDA (0.12 M) in neat THF at -78 °C: (A) no added LiCl; (B) 0.5 mol% LiCl; (C) 0.5 and 10 mol% LiCl.



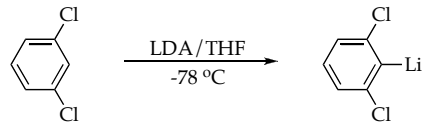

**X.** Plot of IR absorbances (black – 1597 $cm^{-1}$) versus time for the ortholithiation of 2-fluoropyridine (0.10 M) with LDA (0.12 M) in neat THF at -78 °C: (A) no added LiCl; (B) 0.5 mol% LiCl.

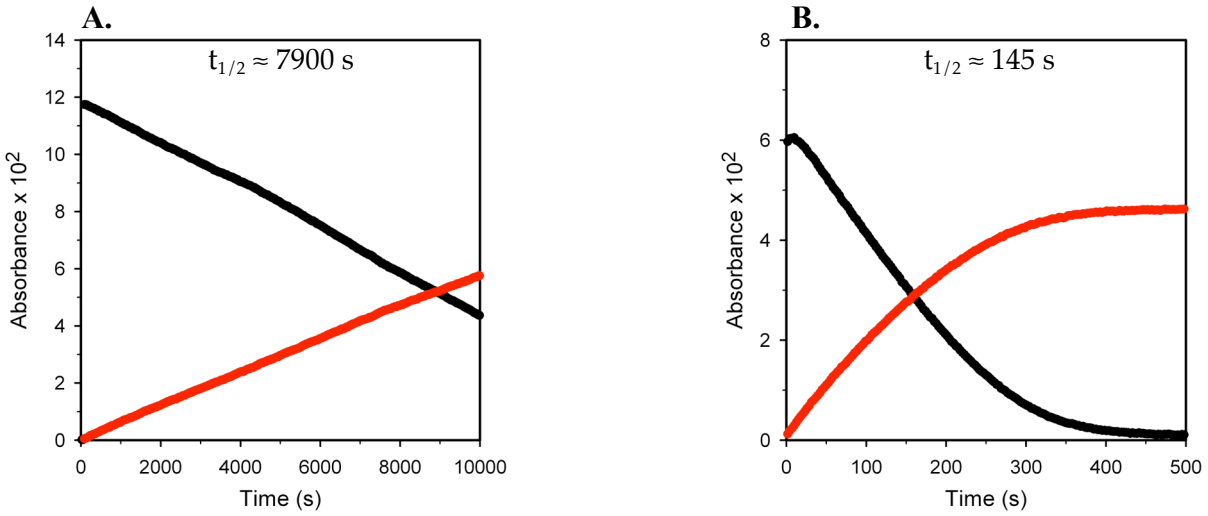



**XI.** Plot of IR absorbances (black – 1507 $cm^{-1}$, red – 1418 $cm^{-1}$) versus time for the ortholithiation of 1,4-difluorobenzene (0.10 M) with LDA (0.12 M) in neat THF at -78 °C: (A) no added LiCl; (B) 0.5 mol% LiCl; (C) 0.5 and 10 mol% LiCl.

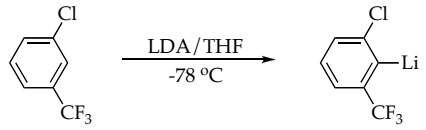


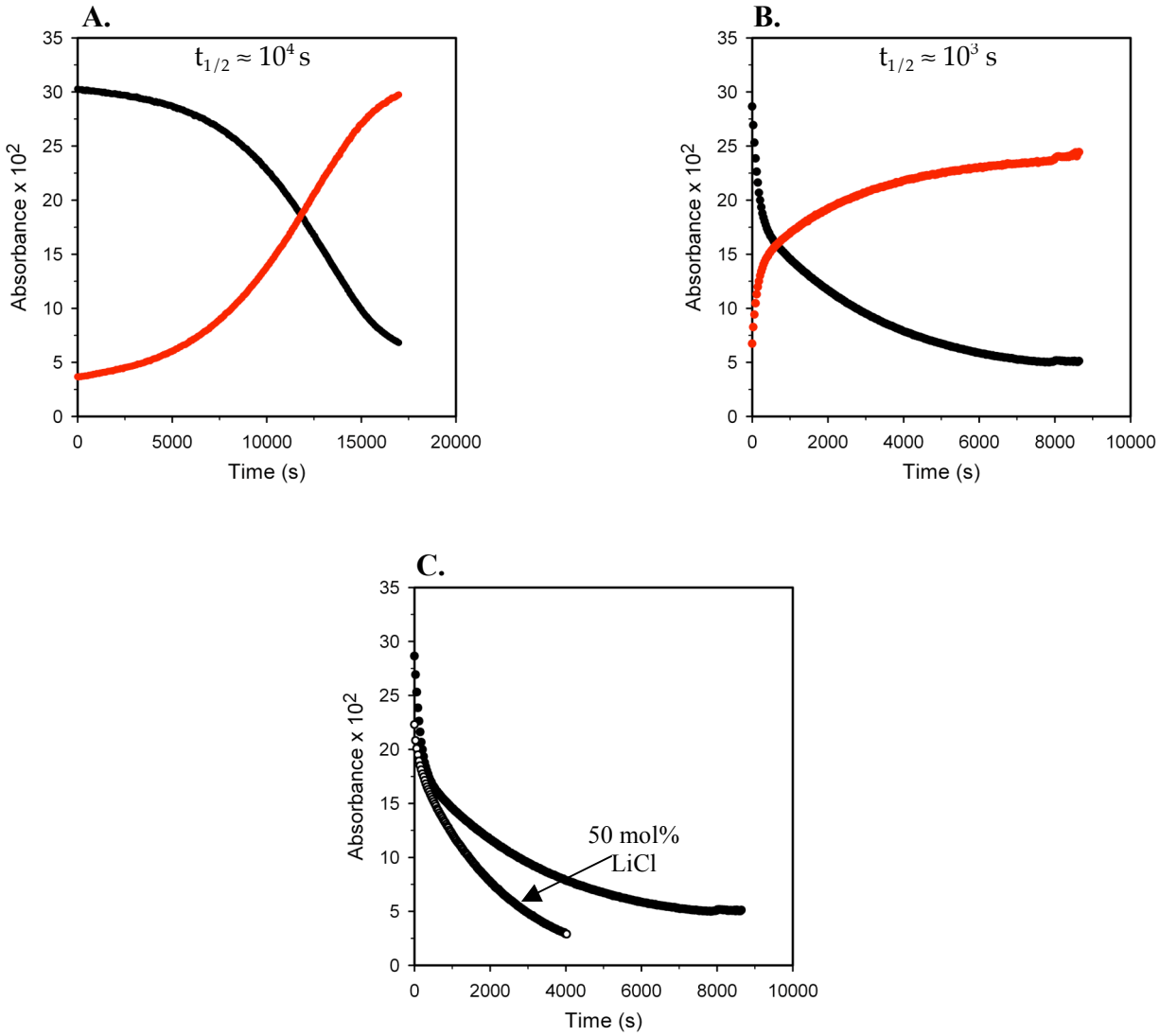

**XII.** Plot of IR absorbances (black – 1509 $cm^{-1}$, red – 1391 $cm^{-1}$) versus time for the ortholithiation of 1,2-difluorobenzene (0.10 M) with LDA (0.12 M) in neat THF at -78 °C: (A) no added LiCl; (B) 0.5 mol% LiCl; (C) 0.5 and 10 mol% LiCl.



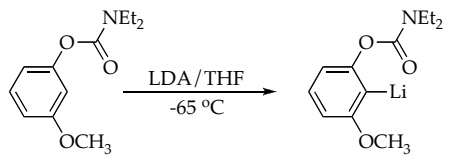



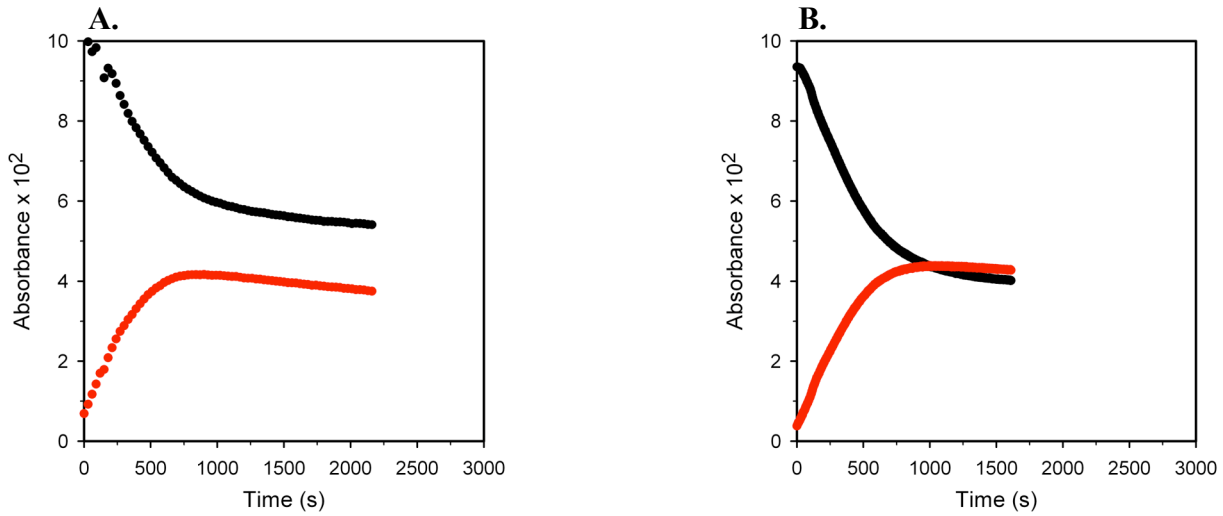

**XIII.** Plot of IR absorbances (black – 1576 $cm^{-1}$, red – 1534 $cm^{-1}$) versus time for the ortholithiation of 1,3-dichlorobenzene (0.10 M) with LDA (0.12 M) in neat THF at -78 °C: (A) no added LiCl; (B) 0.5 mol% LiCl.



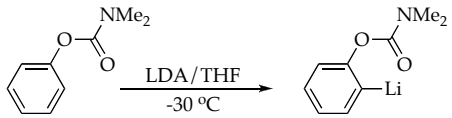



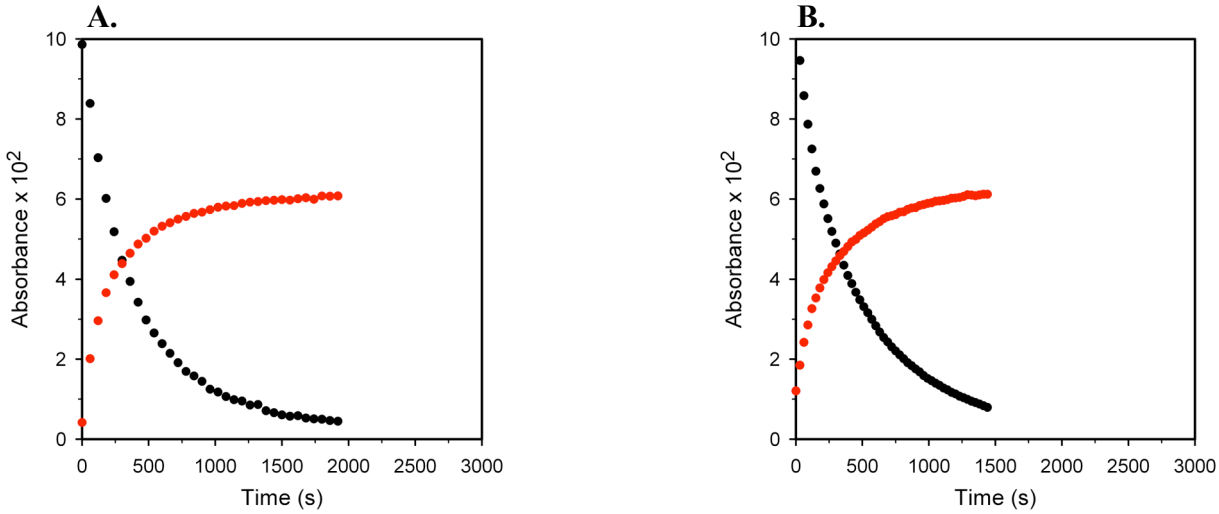

**XIV.** Plot of IR absorbances (black – 1326 $cm^{-1}$, red – 1306 $cm^{-1}$) versus time for the ortholithiation of 3-chlorobenzotrifluoride (0.10 M) with LDA (0.12 M) in neat THF at -78 °C: (A) no added LiCl; (B) 0.5 mol% LiCl; (C) 0.5 and 50 mol% LiCl.



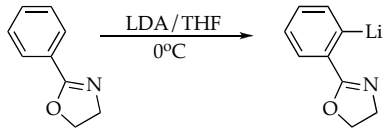



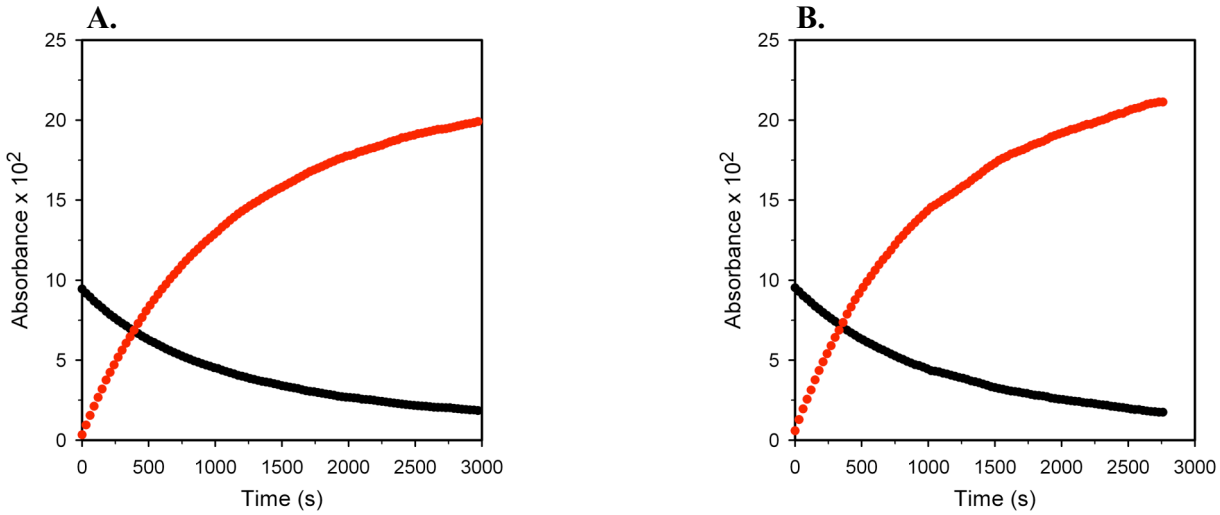

**XV.** Plot of IR absorbances (black – 1725 $cm^{-1}$, red – 1675 $cm^{-1}$) versus time for the ortholithiation of 3-methoxyphenyl-*N,N*-diethylcarbamate (0.10 M) with LDA (0.12 M) in neat THF at -65 °C: (A) no added LiCl; (B) 0.5 mol% LiCl.



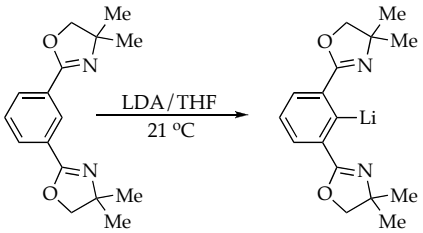



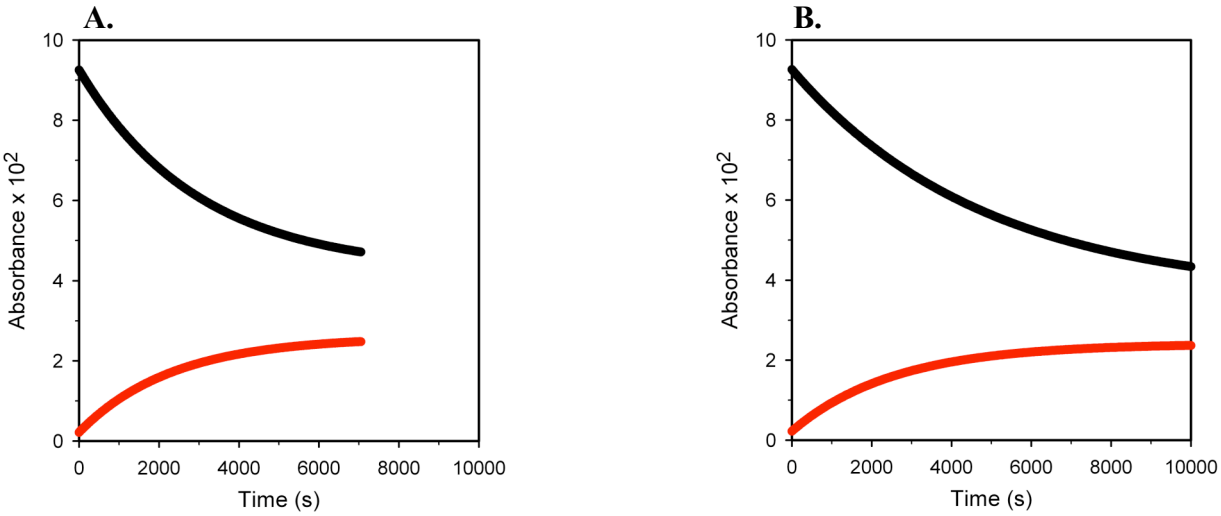

**XVI.** Plot of IR absorbances (black – 1725 $cm^{-1}$, red – 1675 $cm^{-1}$) versus time for the ortholithiation of phenyl-*N,N*-dimethylcarbamate (0.10 M) with LDA (0.12 M) in neat THF at -30 °C: (A) no added LiCl; (B) 0.5 mol% LiCl.



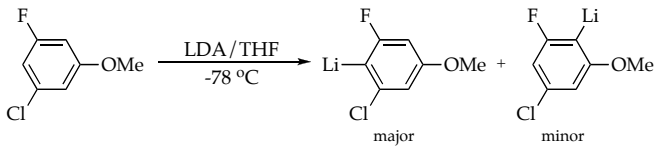



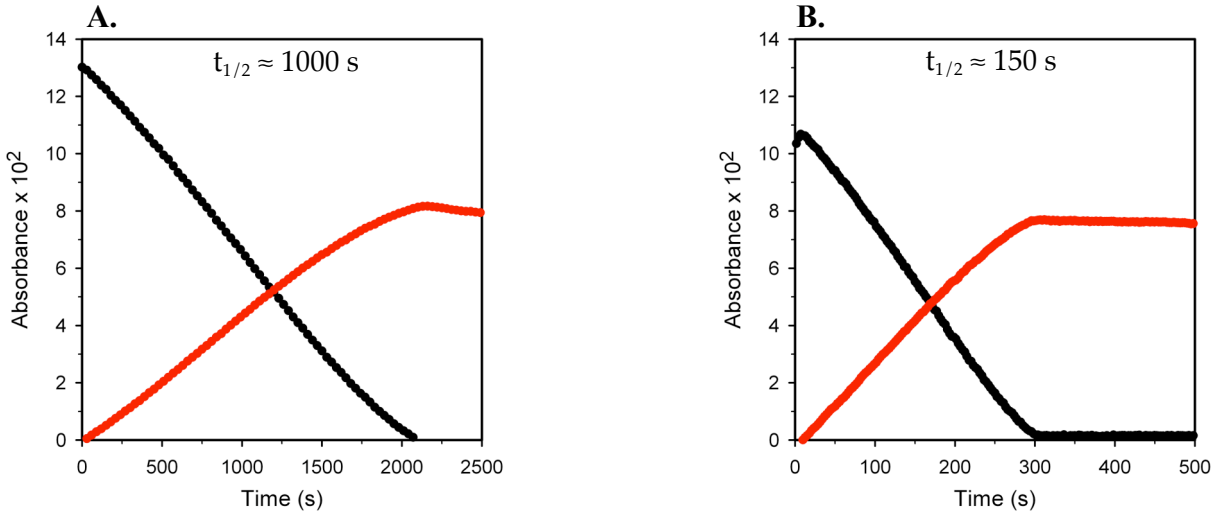

**XVII.** Plot of IR absorbances (black – 1652 $cm^{-1}$, red – 1526 $cm^{-1}$) versus time for the ortholithiation of 2-phenyl-2-oxazoline (0.10 M) with LDA (0.12 M) in neat THF at 0 °C: (A) no added LiCl; (B) 0.5 mol% LiCl.



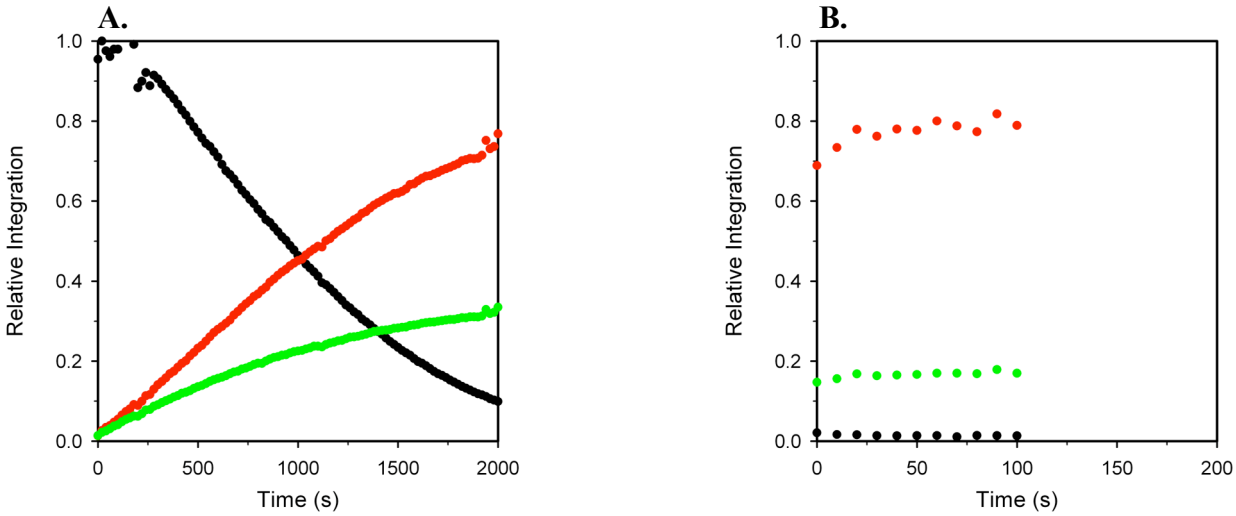




**XVIII.** Plot of IR absorbances (black – 1654 $cm^{-1}$, red – 1520 $cm^{-1}$) versus time for the ortholithiation of 1,3-bis(4′,4′-dimethyl-2′-oxazolinyl)benzene (0.10 M) with LDA (0.12 M) in neat THF at 21 °C: (A) no added LiCl; (B) 0.5 mol% LiCl.

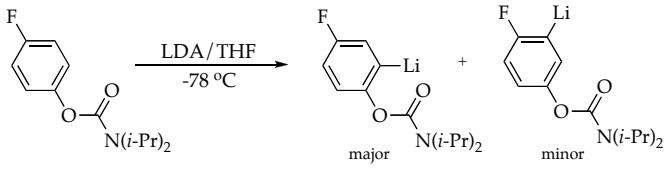


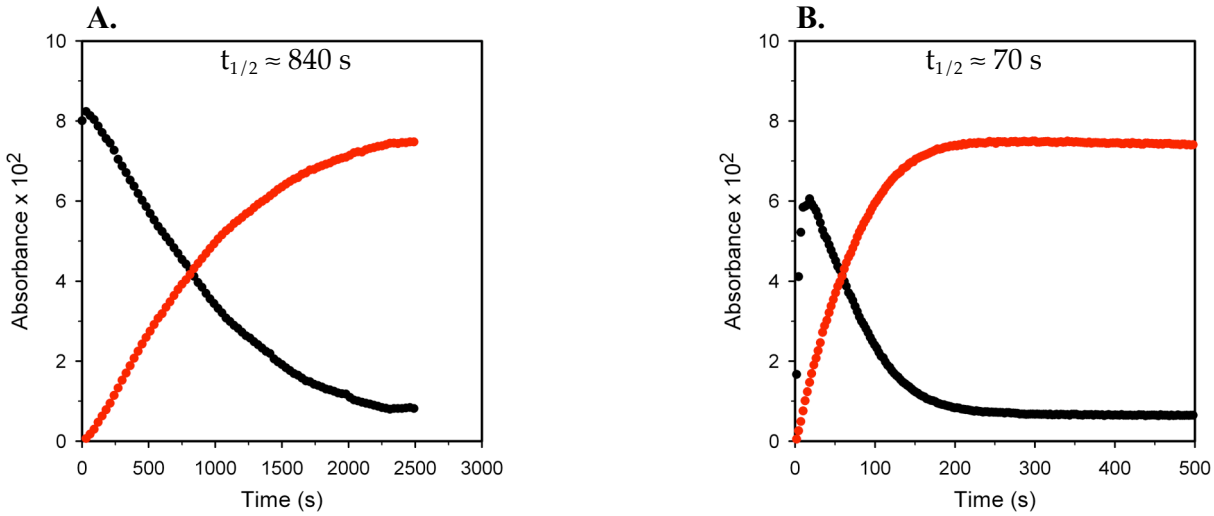




**XIX.** Plot of IR absorbances (black – 1611 $cm^{-1}$, red – 1553 $cm^{-1}$) versus time for the ortholithiation of 3-chloro-5-fluoroanisole (0.10 M) with LDA (0.12 M) in neat THF at -78 ºC: (A) no added LiCl; (B) 0.5 mol% LiCl.

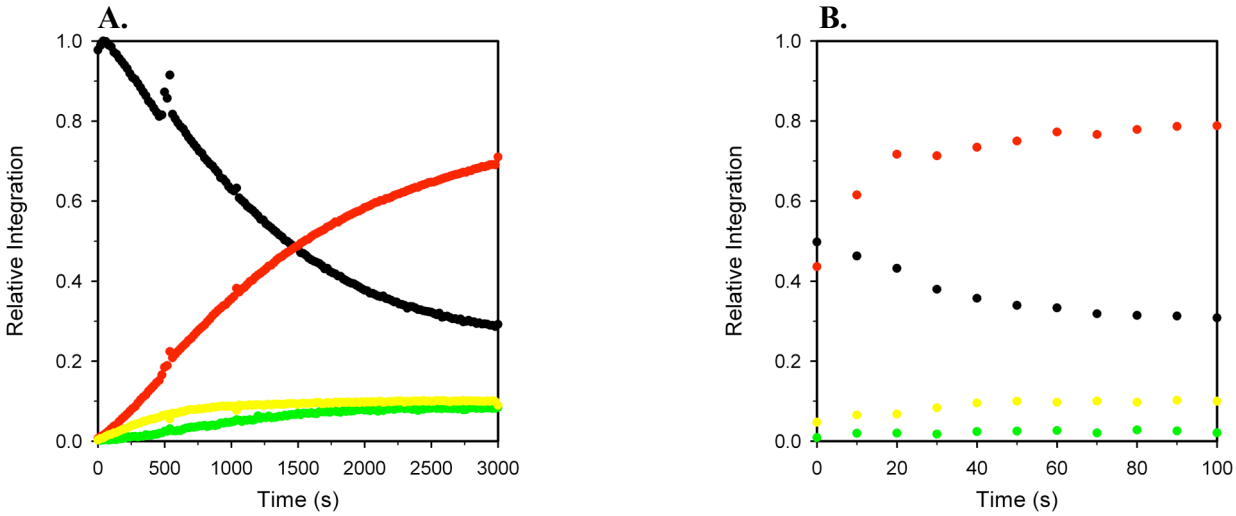



**XX.** Plot of $^{19}F$ NMR peak integrations (black: $\delta$ -110.1, red: δ -77.8, green: δ -76.6) versus time for the ortholithiation of 3-chloro-5-fluoroanisole (0.05 M) with LDA (0.20 M) in neat THF at -78 ºC: (A) no added LiCl; (B) 10 mol% LiCl.

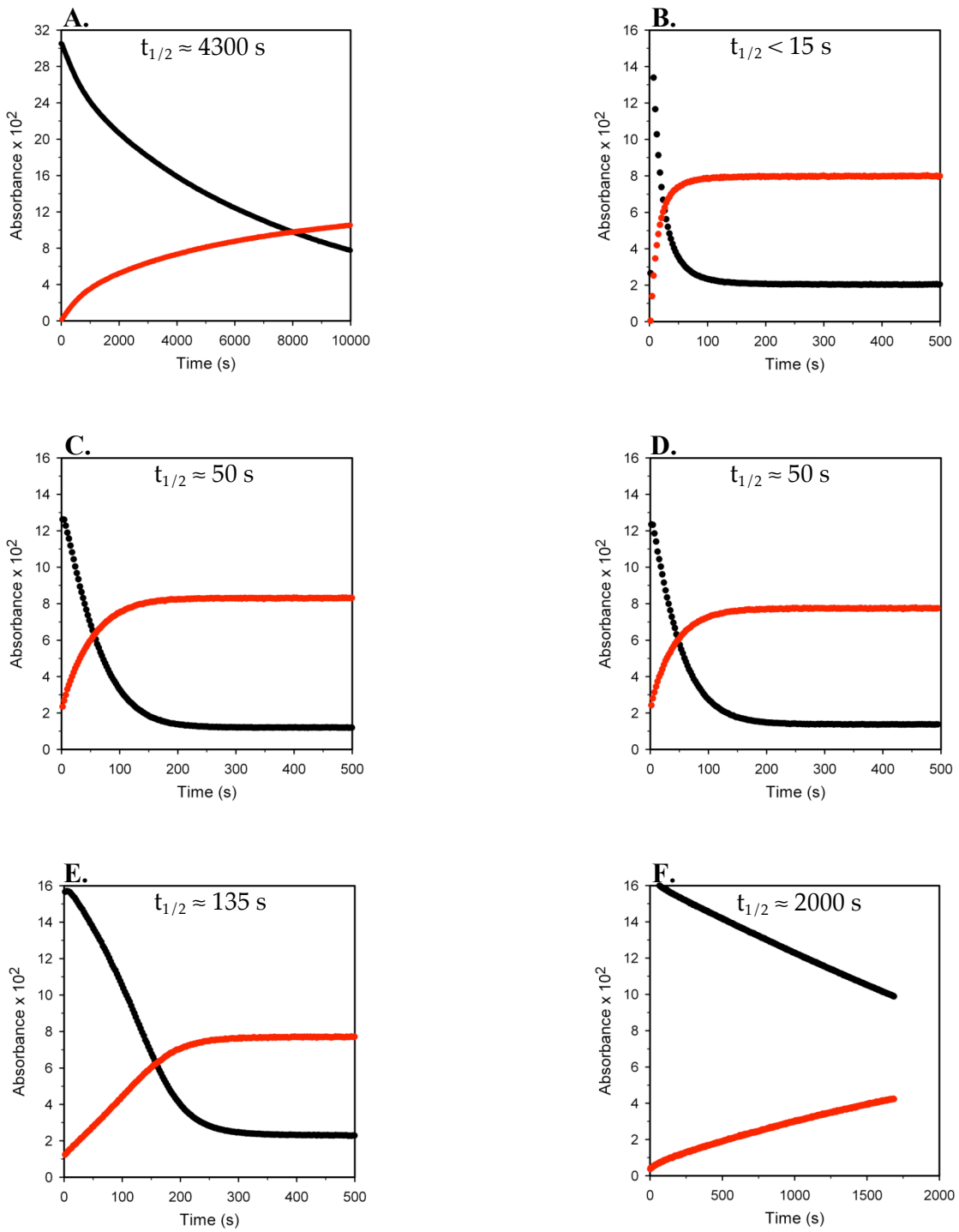


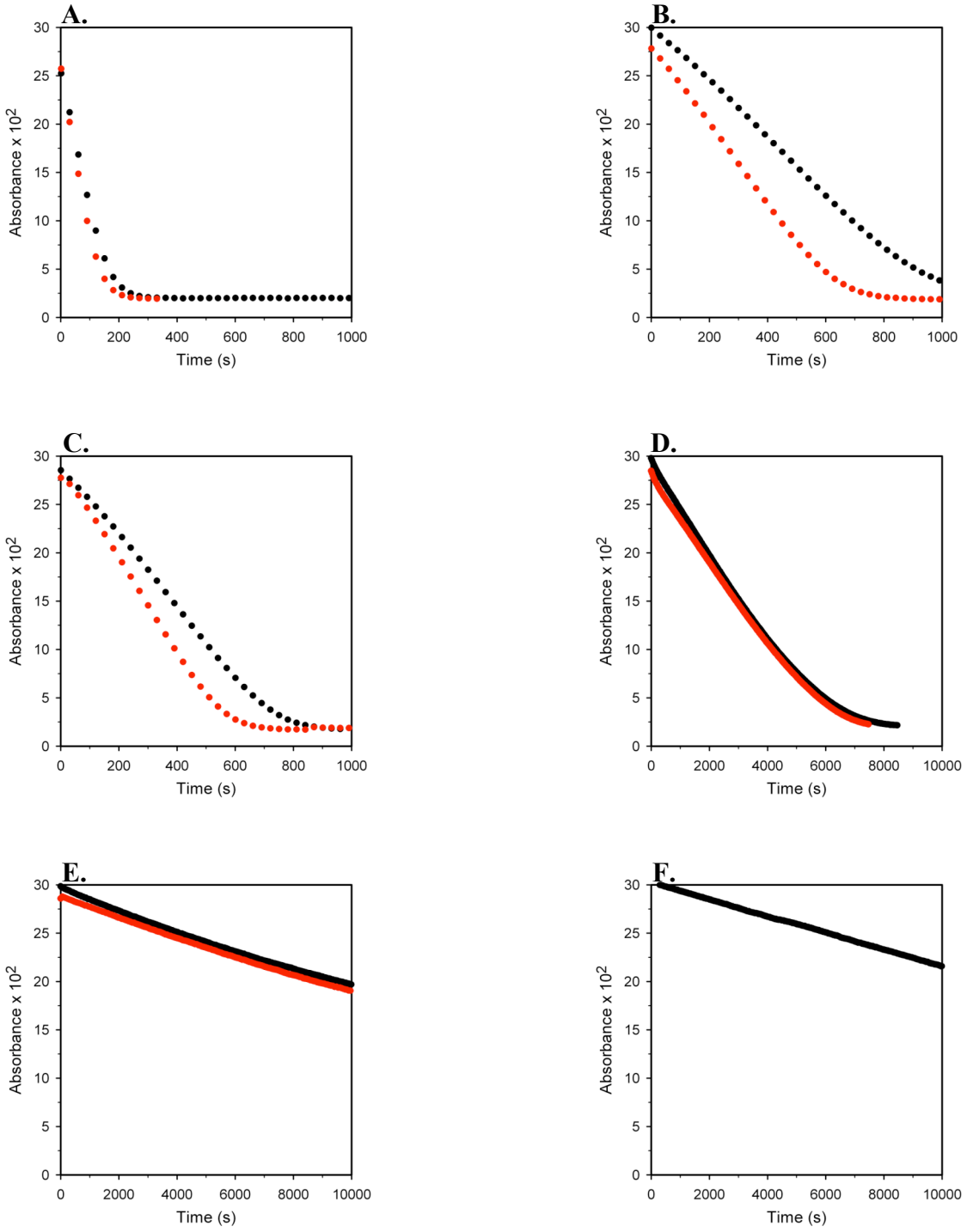

**XXI.** Plot of IR absorbances (black – 1717 $cm^{-1}$, red – 1657 $cm^{-1}$) versus time for the ortholithiation of 4-fluorophenyl-*N,N*-diisopropylcarbamate (0.025 M) with LDA (0.12 M) in neat THF at -78 °C: (A) no added LiCl; (B) 0.5 mol% LiCl.




**XXII.** Plot of $^{19}F$ NMR peak integrations (black: $\delta$ -118.8, red: δ -123.7, green: δ 85.5, yellow: δ -124.1) versus time for the ortholithiation of 4-fluorophenyl-*N,N*-diisopropylcarbamate (0.05 M) with LDA (0.20 M) in neat THF at -78 °C: (A) no added LiCl; (B) 10 mol% LiCl.




**XXIII.** Plot of IR absorbances (black – 1507 $cm^{-1}$, red – 1418 $cm^{-1}$) versus time for the ortholithiation of 1,4-difluorobenzene (0.10 M) with LDA (0.12 M) in neat THF at -78 °C: (A) no additive; (B) 10 mol% LiCl; (C) 10 mol% LiBr; (D) 10 mol% PhCCLi; (E) 10 mol% PhCOOLi; (F) 10 mol% PhOLi.




**XXIV.** Plot of IR absorbances (black/red – duplicated rates) versus time for the ortholithiation of 1,4-difluorobenzene (0.10 M) with LDA (0.12 M) in 10.0 M THF/hexane at -78 °C using: (A) Acros *n*-BuLi – batch1; (B) Acros *n*-BuLi – batch2; (C) Aldrich *n*-BuLi – batch1; (D) Aldrich *n*-BuLi – batch2; (E) Acros LDA; (F) Aldrich LDA