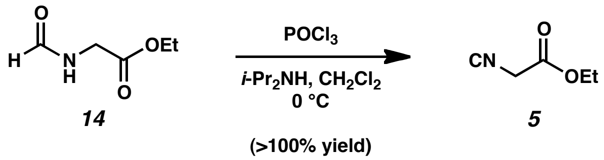
1.1 Experimental Section

1.1.1 Materials and Methods

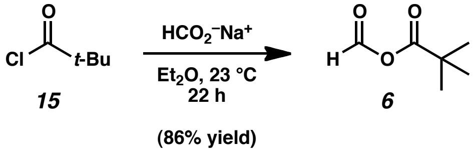
Unless stated otherwise, reactions were conducted in flame-dried glassware under an atmosphere of nitrogen using anhydrous solvents (either freshly distilled or passed through activated alumina columns). All commercially obtained reagents were used as received. Reaction temperatures were controlled using an IKAmag temperature modulator. Thin-layer chromatography (TLC) was conducted with E. Merck silica gel 60 F254 pre-coated plates (0.25 mm) and visualized using a combination of UV, anisaldehyde, ceric ammonium molybdate, and potassium permanganate staining. ICN silica gel (particle size 0.032–0.063 mm) or SiliCycle Silia*Flash* P60 Academic silica gel (particle size 0.040–0.063 mm; pore diameter 60 Å) was used for flash column chromatography. ^{1}H NMR spectra were recorded on a Varian Mercury 300 (at 300 MHz), or a Varian Inova 500 (at 500 MHz) and are reported relative to Me_4Si (δ 0.0). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz), and integration. ^{13}C NMR spectra were recorded on a Varian Mercury 300 (at 75 MHz), or a Varian Inova 500 (at 125 MHz) and are reported relative to Me_4Si (δ 0.0). Data for ^{13}C NMR spectra are reported in terms of chemical shift (δ ppm) and coupling constant (^{19}F, Hz). ^{19}F NMR spectra were recorded on a Varian Mercury 300 (at 282 MHz) and are reported relative to external F_3CCO_2H standard (δ –76.53). Data for

^{19}F NMR spectra are reported in terms of chemical shift (δ ppm). IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer or a Perkin Elmer Spectrum BXII spectrometer and are reported in frequency of absorption (cm^{-1}). Optical rotations were measured with a Jasco P-1010 polarimeter. High-resolution mass spectra were obtained from the California Institute of Technology Mass Spectral Facility. X-Ray crystallographic data were obtained from the California Institute of Technology Beckman Institute X-Ray Crystallography Laboratory.

1.1.2 Preparative Procedures



Ethyl Isocyanoacetate (5). To a solution of *N*-formylglycine ethyl ester (**14**, 52.9 mL, 403.4 mmol) in CH_2Cl_2 (330 mL) at 0 °C was added *i*-Pr_2NH (142 mL, 1.013 mol). $POCl_3$ (41.0 mL, 447.9 mmol) was added dropwise over 1 h (1 drop/s addition rate). The reaction was stirred for 3 h at 0 °C, then quenched by slow addition of Na_2CO_3 (90.0 g in 400 mL H_2O), keeping the internal temperature below 15 °C. After the addition was complete, the reaction was stirred for 2 h at 23 °C. CH_2Cl_2 (500 mL) and H_2O (400 mL) were added, and the phases were partitioned. The aqueous layer was further extracted with CH_2Cl_2 (2 x 250 mL). The organic layers were combined, washed with H_2O (200 mL), dried over $MgSO_4$, filtered, and evaporated in vacuo to furnish ethyl isocyanoacetate (**5**, 46.2 g, 45.6 g theoretical, >100% yield) as an orange oil. This crude material was used without any further purification. R_f 0.61 (1:1 hexanes:EtOAc); ^1H NMR (300 MHz, $CDCl_3$) δ 4.27 (q, J = 7.1 Hz, 2H), 4.20 (s, 2H), 1.31 (t, J = 7.2 Hz, 3H). This compound is also commercially available from Aldrich (226319).



Mixed Anhydride 6.[1] To a suspension of finely powdered oven-dried sodium formate (63.78 g, 937.9 mmol) in Et_2O (590 mL) was added pivaloyl chloride (**15**, 57.7 mL, 468.7 mmol) over 2 min. The suspension was vigorously stirred at 23 °C for 22 h. The solid was removed by filtration, and the filtrate was evaporated in vacuo at 0 °C, affording mixed anhydride **6** (52.3 g, 86% yield) as a volatile, colorless oil. This material was immediately used in the next step without further purification. Characterization data for this compound have been previously reported.[1]

*NOTE: The rate of this heterogeneous reaction seems to be dependent on the particle size of sodium formate as well as the stirring rate. It is highly advised to monitor the reaction by ^{1}H NMR until the pivaloyl chloride (**15**) is consumed.*

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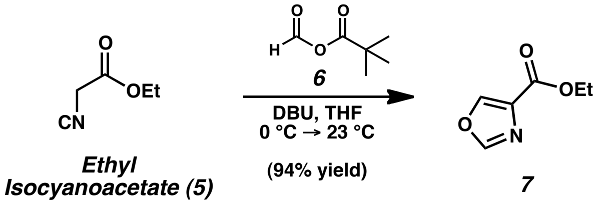
(1) (a) Behforouz, M.; Haddad, J.; Cai, W.; Arnold, M. B.; Farahnaz, M.; Sousa, A. C.; Horn, M. A. *J. Org. Chem.* **1996**, *61*, 6552–6555. (b) Fife, W. K.; Zhang, Z.-d. *J. Org. Chem.* **1986**, *51*, 3744–3746. (c) Hutchinson, C. R.; Harmon, A. D. *J. Org. Chem.* **1975**, *40*, 3474–3480.



Oxazole Ester 7.[2] To a stirring solution of ethyl isocyanoacetate (**5**, 5.74 g, 5.54 mL, 50.7 mmol) in THF (60 mL) at 0 °C was added DBU (15.2 mL, 101.6 mmol), followed by a solution of mixed anhydride **6** (13.2 g, 101.4 mmol) in THF (40 mL) added over 5 min. The mixture was stirred at 0 °C for 30 min, and then at 23 °C for 15 h. The reaction mixture was concentrated, and the crude product was filtered over a plug of silica gel (1:1 hexanes:EtOAc eluent). The solvent was evaporated under reduced pressure, and the residue was purified by flash chromatography (3:2 hexanes:EtOAc eluent) to afford oxazole ester **7** (6.44 g, 90% yield) as a yellow oil, which solidified upon refrigeration.

Alternate Procedure. To a solution of ethyl isocyanoacetate (**5**, 22.4 g, 197.6 mmol) in THF (221 mL) at 0 °C was added DBU (60.0 mL, 401.2 mmol), followed by additional THF (30 mL). To this solution was added freshly prepared mixed anhydride **6** (51.7 g, 397.5 mmol) in THF (120 mL) via cannula over 25 min at 0 °C, followed by additional THF (40 mL). The reaction was stirred for 4 h, and the temperature was allowed to increase gradually from 0 °C → 23 °C. EtOAc (255 mL) and H_2O (130 mL) were added, and the phases were partitioned. The aqueous layer was further extracted with EtOAc (3 x 250 mL). The organic layers were combined and washed with 0.5 M

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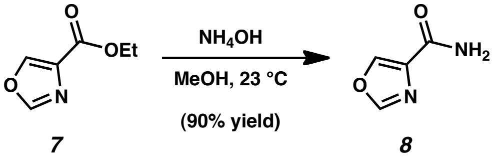
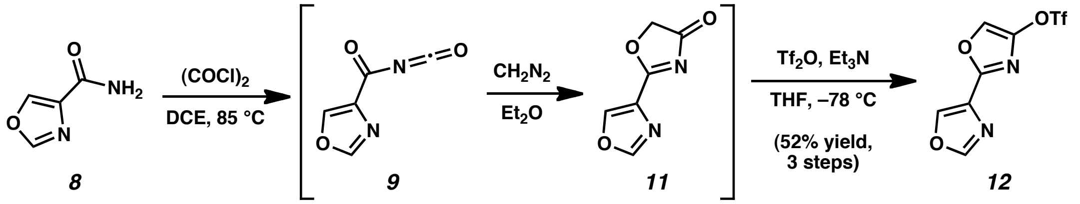
(2) Shafer, C. M.; Molinski, T. F. *Heterocycles* **2000**, *53*, 1167–1170.

HCl (2 x 100 mL), saturated aq. Na_2CO_3 (100 mL), H_2O (100 mL), and brine (100 mL). The combined organic layers were dried over $MgSO_4$, filtered, and evaporated to yield a dark, orange oil. The crude product was purified by passage over a plug of silica gel (1:1 hexanes:EtOAc eluent) to provide oxazole ester **7** (14.80 g, 53% yield) as a yellow oil. R_f 0.43 (1:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.25 (d, J = 0.8 Hz, 1H), 7.91 (d, J = 0.8 Hz, 1H), 4.38 (q, J = 7.2 Hz, 2H), 1.37 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.2, 151.6, 144.2, 133.6, 61.5, 14.5; IR (film) 3131, 2983, 1740, 1312, 1148, 1102 cm^{-1}; HRMS-EI (*m/z*): $[M]^+$ calc'd for $C_6H_7NO_3$, 141.0426; found, 141.0423.



Oxazole Amide 8. To a solution of oxazole ester **7** (1.41 g, 10.0 mmol) in MeOH (25 mL) was added concentrated ammonium hydroxide (28.0–30.0% in H_2O, 25 mL) in one portion at 23 °C. After stirring at 23 °C for 3 h, the solvent was evaporated in vacuo. The crude product was adsorbed onto silica gel using MeOH as solvent, and purified by flash chromatography (10:1 $CHCl_3$:MeOH eluent) to furnish amide **8** (1.02 g, 90% yield) as a white solid.

Alternate Procedure. To a solution of oxazole ester **7** (28.92 g, 204.9 mmol) in MeOH (134 mL) was added concentrated ammonium hydroxide (28–30%, 127 mL) in one portion at 23 °C. The reaction was stirred for 11 h at 23 °C, and then the solvent was evaporated in vacuo. Following further coevaporation under reduced pressure with acetonitrile (3 x 150 mL), the crude product was dissolved in boiling EtOAc (750 mL). Solid impurities were removed by decantation, and the solution was allowed to cool to 23 °C. Hexanes (1 L) was added, and the solution was cooled to 12 °C and allowed to crystallize. The product was collected by vacuum filtration and dried further under high vac to yield oxazole amide **8** (14.30 g, 62% yield) as a pale yellow solid. The filtrate was concentrated, and the crystallization procedure was repeated to afford a second batch of **8** (3.59 g), which was combined with the first batch to provide oxazole amide **8** (17.89 g, 78% combined yield) as a pale yellow solid. R_f 0.35 (10:1 $CHCl_3$:MeOH); mp 156–158 °C; ^1H NMR (300 MHz, DMSO-d_6) δ 8.56 (d, J = 1.1 Hz, 1H), 8.48 (d, J = 1.1 Hz, 1H), 7.66 (br s, 1H), 7.51 (br s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 161.8, 152.2, 142.0, 135.8; IR (KBr) 3379, 3154, 3111, 1664 (br), 1413, 1111 cm^{-1}; HRMS-EI (*m/z*): $[M]^+$ calc'd for $C_4H_4N_2O_2$, 112.0273; found, 112.0271.



Bis-oxazole Triflate 12. To oxazole amide **8** (224.0 mg, 2.0 mmol) and 1,2-dichloroethane (20 mL) in a Schlenk flask at 23 °C was added $(COCl)_2$ (0.720 mL, 8.25 mmol) in a rapid dropwise fashion. The flask was sealed, and the mixture was heated at 85 °C for 2 h. The reaction was allowed to cool to 23 °C, and the solvent was carefully evaporated in vacuo under an inert atmosphere to afford **9** as a pale yellow solid, which was immediately used in the subsequent reaction without further purification.

To crude acylisocyanate **9** dissolved in Et_2O (20 mL) was added a sodium-dried ethanol-free solution of freshly prepared CH_2N_2 in Et_2O[3] (20 mL) in a rapid dropwise fashion. When bubbling ceased, and the solution turned pale yellow, the solvent was carefully concentrated in vacuo under an inert atmosphere to afford crude oxazolone **11** as a yellow solid, which was directly used in the following step.

To oxazolone **11** in THF (30 mL) at –78 °C was added Et_3N (0.700 mL, 5.02 mmol), followed by dropwise addition of Tf_2O (0.512 mL, 3.04 mmol). The reaction was stirred at –78 °C for 1 h, and allowed to thaw at 23 °C for 30 min. Et_2O (30 mL) was then

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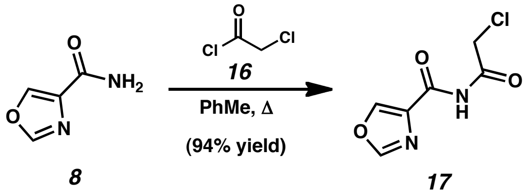
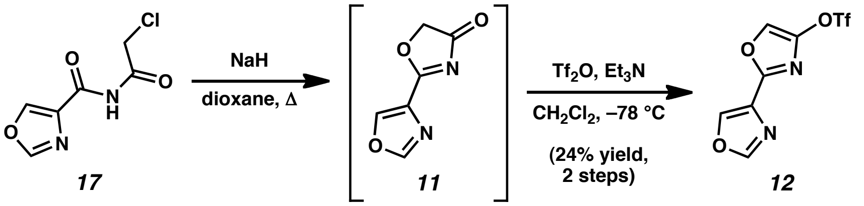
(3) de Boer, T. J.; Backer, H. J. *Org. Synth.* **1956**, *36*, 16–19.

added, and the precipitates were removed by vacuum filtration. The filtrate was concentrated in vacuo, and the residue was purified by flash chromatography (2:1 hexanes:EtOAc eluent) to afford bis-oxazole triflate **12** (298.0 mg, 52% yield, 3 steps) as a yellow oil, which solidified upon refrigeration. R_f 0.64 (1:1 hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30 (d, J = 0.8 Hz, 1H), 8.00 (d, J = 0.8 Hz, 1H), 7.75 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.1, 152.3, 145.8, 140.0, 129.7, 126.9, 118.8 (q, J_{CF} = 320 Hz); ^{19}F NMR (282 MHz, $CDCl_3$) δ –73.2; IR (film) 3133, 1585, 1429, 1215, 1131 cm^{-1}; HRMS-EI (*m/z*): $[M]^+$ calc'd for $C_7H_3N_2O_5F_3S$, 283.9715; found, 283.9707.

Alternate procedure for the preparation of ***12*****:**

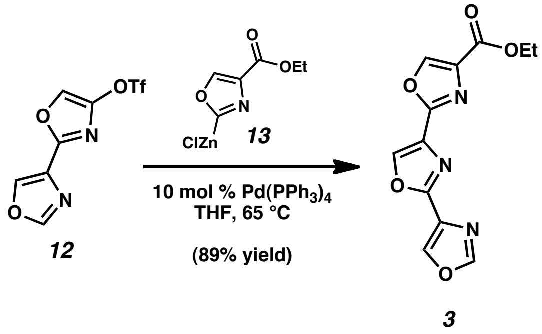


Oxazole Chloro Imide 17. To a suspension of oxazole amide **8** (3.20 g, 28.6 mmol) in toluene (30 mL) was added chloroacetyl chloride (**16**, 3.0 mL, 37.7 mmol) over 30 sec at 23 °C. The flask was fitted with reflux condenser and a drying tube containing Drierite®, and the reaction mixture was heated at 115 °C for 4.5 h under gentle reflux. The reaction was allowed to cool to 23 °C, and hexanes (150 mL) was added. After cooling to 0 °C, the product was collected by vacuum filtration, washed with hexanes (3 x 30 mL), and further dried under high vac to furnish oxazole imide **17** (5.04 g, 94% yield) as a light brown powder. R_f 0.33 (1:1 hexanes:EtOAc); mp 126–128 °C; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 11.06 (br s, 1H), 8.97 (d, J = 1.1 Hz, 1H), 8.62 (d, J = 1.1 Hz, 1H), 4.73 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 167.5, 158.9, 152.8, 144.9, 133.9, 45.5; IR (KBr) 3307, 3139, 1734, 1700, 1578, 1471, 1287, 1188, 1095, 1050 cm^{-1}; HRMS-EI (*m/z*): [M]$^+$ calc'd for $C_6H_5N_2O_3Cl$, 187.9989; found, 187.9992.

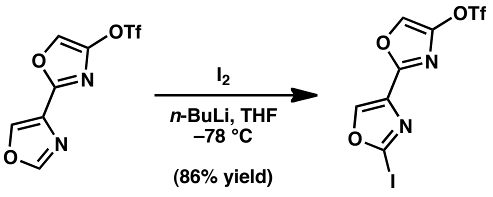


Bis-oxazole Triflate 12. To a whipped suspension of NaH (60% dispersion in mineral oil, 1.81 g, 45.3 mmol) in dioxane (725 mL) at 23 °C was added oxazole imide **17** (8.00 g, 42.4 mmol) portionwise over 1 min. The mixture was stirred at 23 °C for 15 min and then was heated at 110 °C for 40 min. After cooling to 23 °C over 1 h, the reaction mixture was filtered over a pad of Celite® (Et_2O eluent). The filtrate was coevaporated under reduced pressure with heptane (3 x 500 mL) and benzene (300 mL), and was further dried under high vac to provide oxazolone **11** as an orange solid. This material was immediately carried to the subsequent step without further purification. Although oxazolone **11** is typically used in crude form, it has been observed by ^{1}H NMR. ^{1}H NMR (300 MHz, DMSO-d_6) δ (9.31, J = 0.9 Hz, 1H), 8.75 (d, J = 0.9 Hz, 1H), 4.91 (s, 2H).

To oxazolone **11** dissolved in CH_2Cl_2 (230 mL) at –78 °C was added Et_3N (12.0 mL, 86.1 mmol) over 1 min, followed by dropwise addition of freshly prepared Tf_2O (8.6 mL, 51.1 mmol) over 2 min. The reaction was held at –78 °C for 45 min, and was then immediately warmed to 0 °C for 15 min. H_2O (100 mL) was added, and the phases were partitioned. The aqueous phase was further extracted with CH_2Cl_2 (2 x 300 mL), and the combined organics were dried over $MgSO_4$ and concentrated under reduced pressure to afford a dark colored syrup. The residue was purified by flash chromatography (7:3 hexanes:CH_2Cl_2 → 1:1 hexanes:CH_2Cl_2 eluent), and the product-containing fractions were collected and concentrated in vacuo. The crude product was further purified by flash chromatography (4:1 hexanes:EtOAc eluent) to afford bis-oxazole triflate **12** (2.927 g, 24% yield, 2 steps) as an off-white solid.



Tris-oxazole Ester 3. To oxazole ester **7** (155.2 mg, 1.10 mmol) in THF (9.5 mL) at –78 °C was added LiHMDS (1.0 M in THF, 1.23 mL, 1.23 mmol) in a dropwise fashion. The reaction was stirred at –78 °C for 30 min, and then $ZnCl_2$ (0.5 M in THF, 6.70 mL, 3.35 mmol) was added over 3 min. The solution was kept at –78 °C for an additional 5 min and was then held at 0 °C for 2.5 h to deliver Negishi reagent **13**. In a separate flask was prepared a solution of bis-oxazole triflate **12** (267.8 mg, 0.94 mmol), $Pd(PPh_3)_4$ (109.5 mg, 0.09 mmol), and THF (9.5 mL). This freshly prepared solution was then transferred into the flask containing Negishi reagent **13** via cannula, and the resulting mixture was heated at 65 °C for 1.5 h. After cooling to 23 °C, the reaction mixture was diluted with CH_2Cl_2 (30 mL) and filtered over a plug of silica gel (1:1 hexanes:EtOAc → EtOAc eluent). The product containing-fractions were concentrated under reduced pressure, adsorbed onto silica gel using a 1:1 mixture of $THF:CH_2Cl_2$ as solvent, and purified further by flash chromatography (3:1 hexanes:EtOAc → EtOAc eluent). The product-containing fractions were concentrated in vacuo and redissolved in a minimum of hot CH_2Cl_2:THF (1:1, 4 mL). Hexanes (12 mL) was added, and the suspension was stirred for 2 h. The solvent was carefully removed, and the solid was triturated with hexanes (2 x 10 mL). The solid was dried under high vac to provide tris-oxazole ester **3** (230.4 mg, 89% yield) as a fluffy, white solid.[4] R_f 0.31 (3:1 EtOAc:hexanes); ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.10 (s, 1H), 9.05 (d, J = 1.1 Hz, 1H), 8.99 (s, 1H), 8.68 (d, J = 0.8 Hz, 1H), 4.32 (q, J = 7.2 Hz, 2H), 1.31 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 160.4, 155.6, 154.9, 153.6, 145.6, 141.1, 141.0, 133.5, 130.0, 128.5, 60.8, 14.1; IR (film) 3136, 1721, 1277, 1164 cm^{-1}; HRMS-FAB (*m/z*): $[M + H]^+$ calc'd for $C_{12}H_{10}N_3O_5$, 276.0620; found, 276.0629.



3 *14*

Bis-oxazole Iodo Triflate 14. To bis-oxazole triflate **12** (41.3 mg, 0.15 mmol) in THF (3.0 mL) at –78 °C was added *n*-BuLi (2.5 M in hexanes, 65 μL, 0.16 mmol) in a

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[4] The synthesis of **3** has also been reported by: E. F. Flegeau, M. E. Popkin, and M. F. Greaney, *Org. Lett.*, 2008, **10**, 2717–2720; characterization data is provided in $CDCl_3$.

dropwise fashion. After stirring at –78 °C for 30 min, a separate solution of I_2 (43.9 mg, 0.17 mmol) in THF (1.0 mL) cooled to –78 °C was added via cannula. Additional THF (0.5 mL) was used to rinse the cannula, which was added to the reaction mixture. The reaction was stirred at –78 °C for 1.5 h, allowed to thaw to 23 °C, and concentrated in vacuo. The residue was purified directly by flash chromatography (3:1 hexanes:EtOAc eluent) to provide bis-oxazole iodo triflate **14** (51.5 mg, 86% yield) as a yellow solid. Suitable crystals for X-ray diffraction were obtained by vapor diffusion of heptane into an EtOAc solution of **14** at 23 °C. R_f 0.30 (4:1 hexanes:EtOAc); mp 96–98 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (s, 1H), 7.74 (s, 1H), 7.75 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.0, 145.8, 145.1, 132.9, 127.1, 118.8 (q, J_{CF} = 320 Hz), 103.4; ^{19}F NMR (282 MHz, $CDCl_3$) δ –73.2; IR (film) 3451 (br), 1585, 1430, 1221 cm^{-1}; HRMS-EI (*m/z*): $[M]^+$ calc'd for $C_7H_2F_3IN_2O_5S$, 409.8681; found, 409.8693.

1.2 NMR and IR Spectra

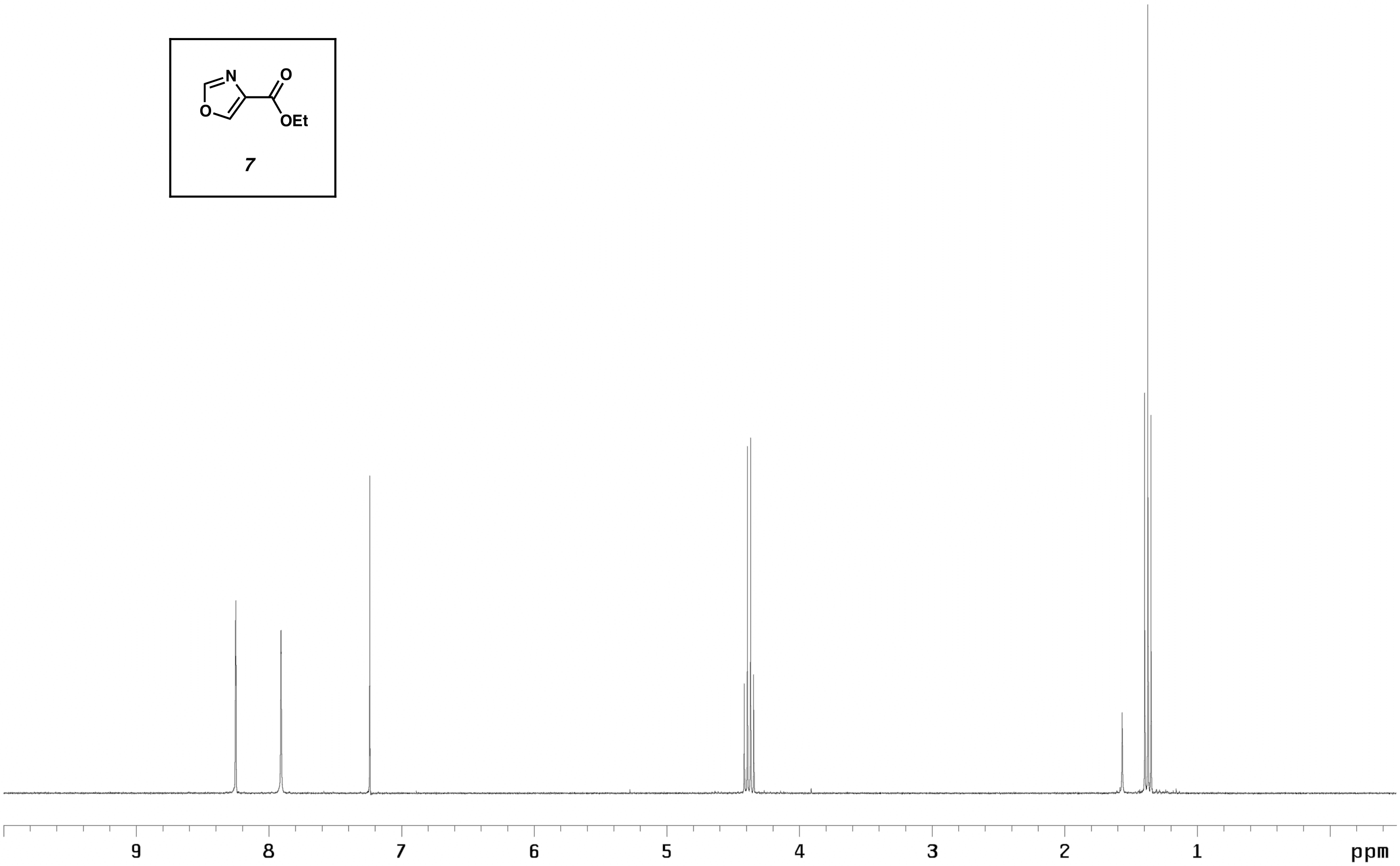

Figure A4.1 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **7**

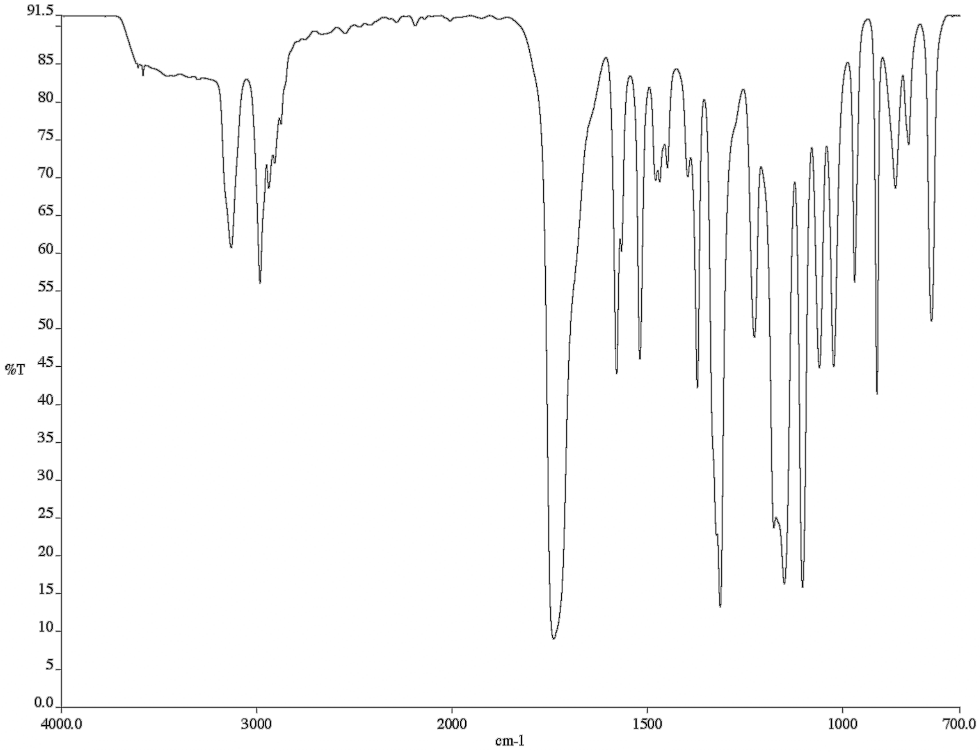

Figure A4.2 Infrared spectrum (thin film/NaCl) of compound **7**

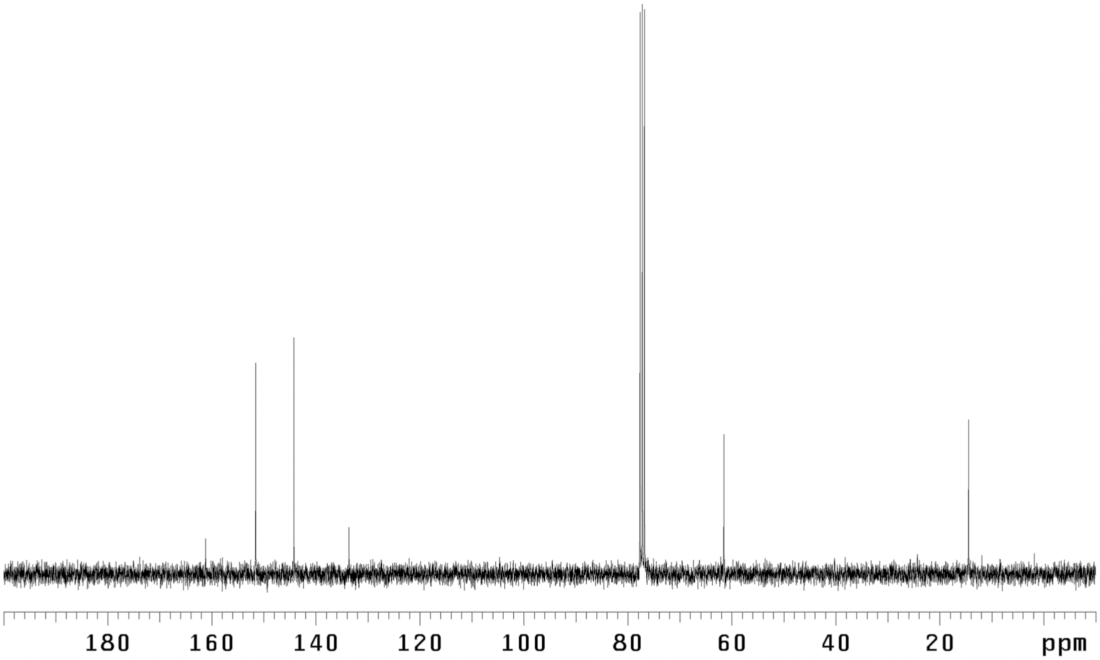

Figure A4.3 ^{13}C NMR (75 MHz, CDCl$_3$) of compound **7**

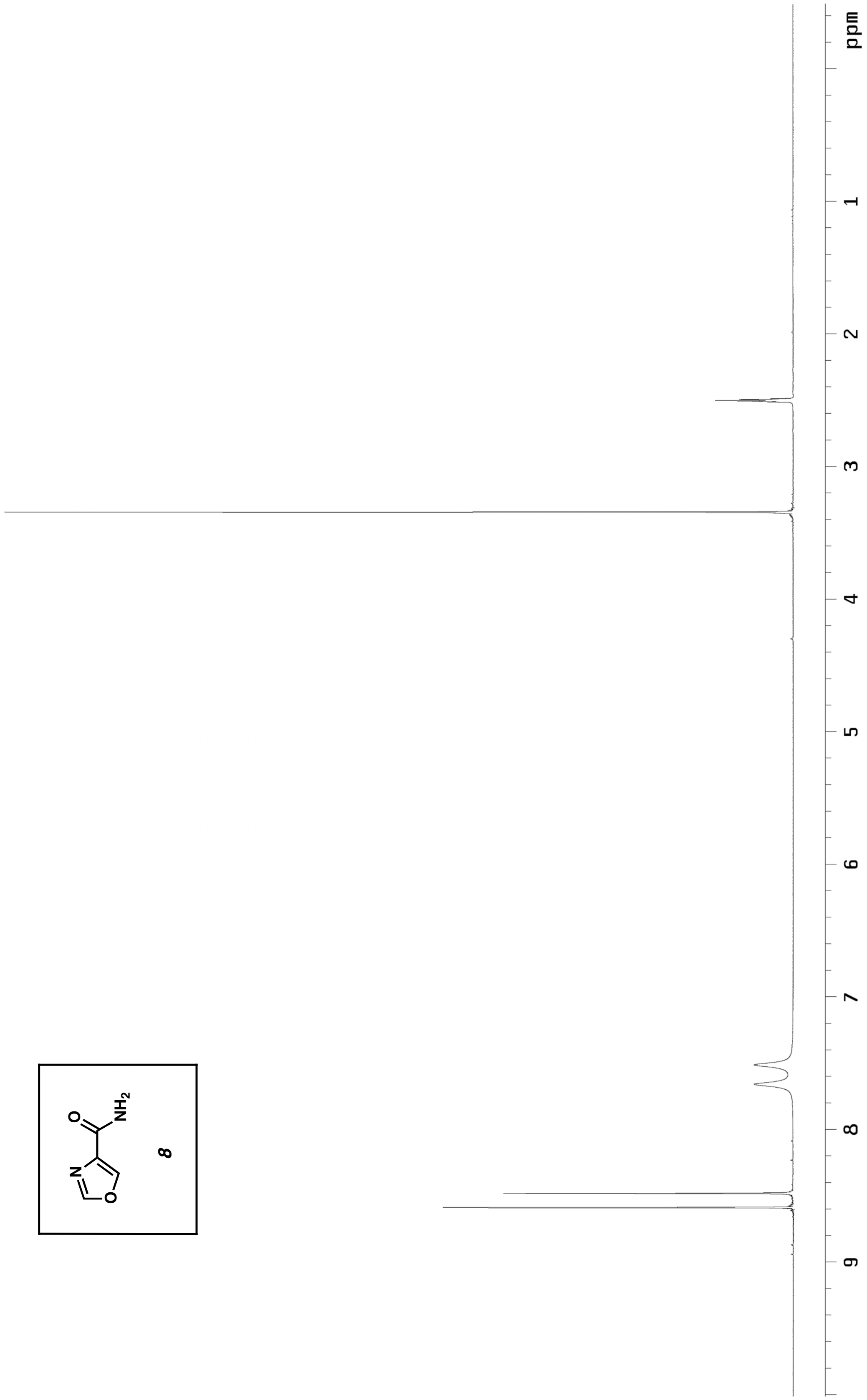

Figure A4.4 ^{1}H NMR (300 MHz, DMSO-d_6) of compound **8**

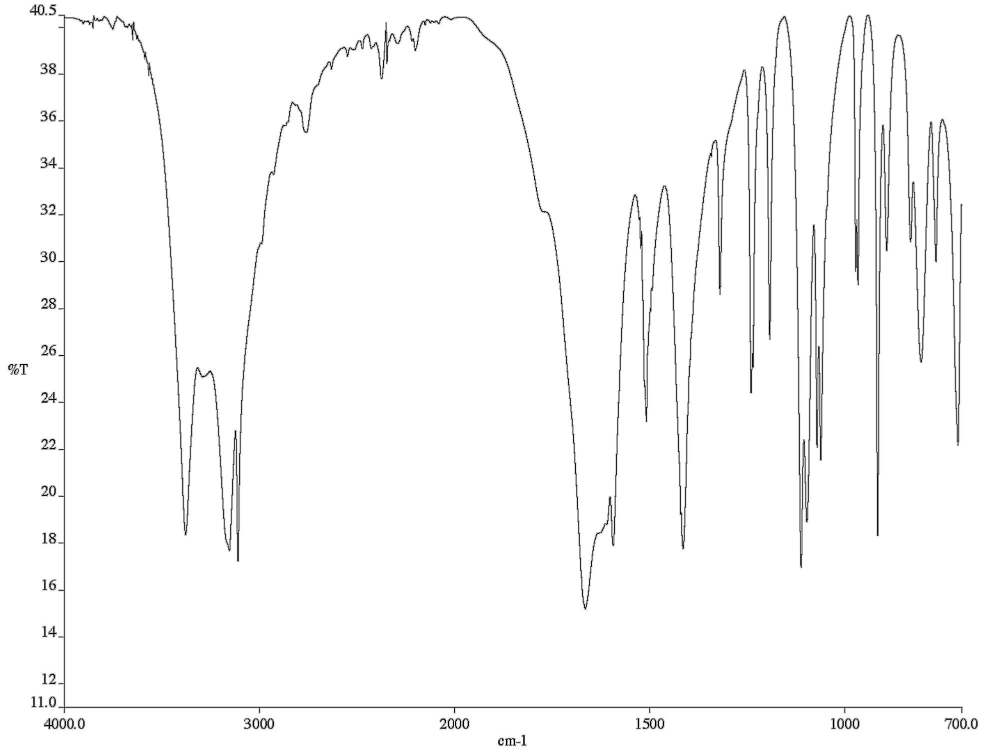

Figure A4.5 Infrared spectrum (KBr pellet) of compound **8**

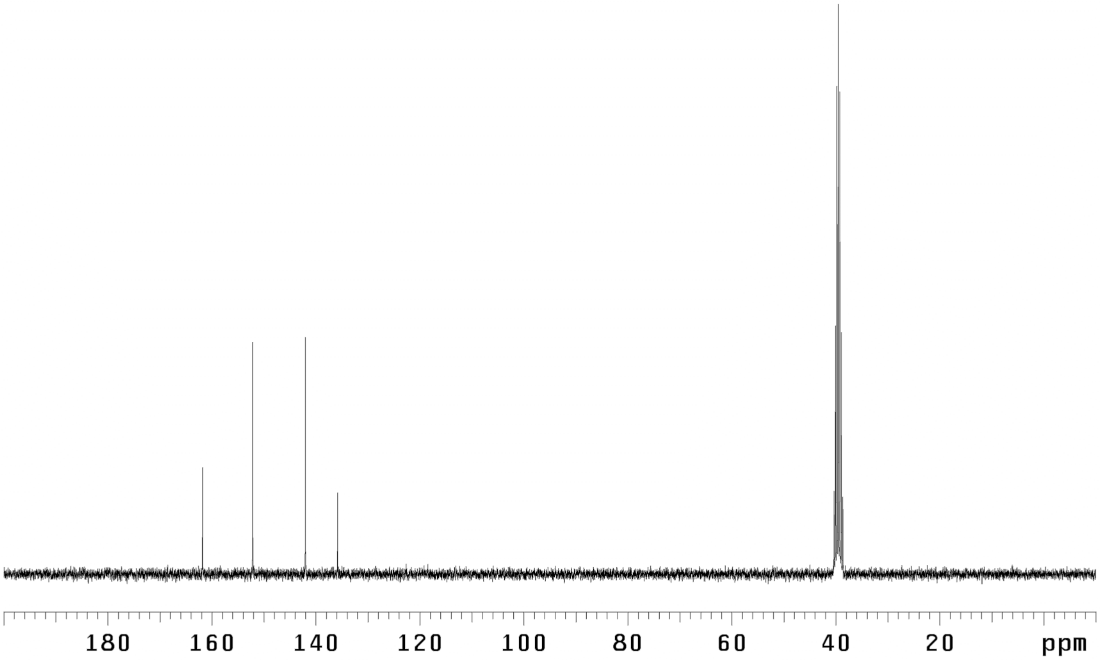

Figure A4.6 ^{13}C NMR (75 MHz, DMSO-d_6) of compound **8**

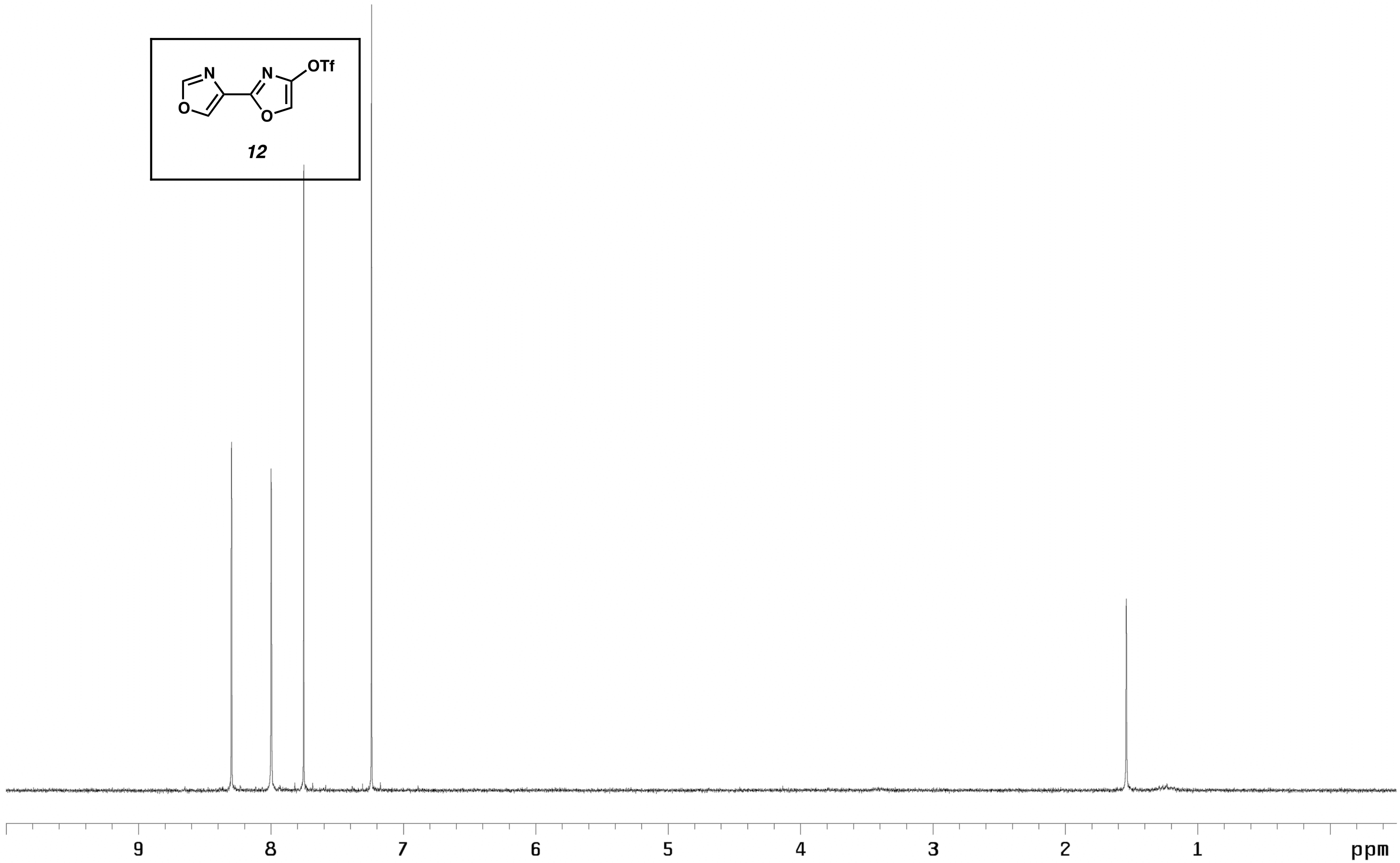

Figure A4.7 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **12**

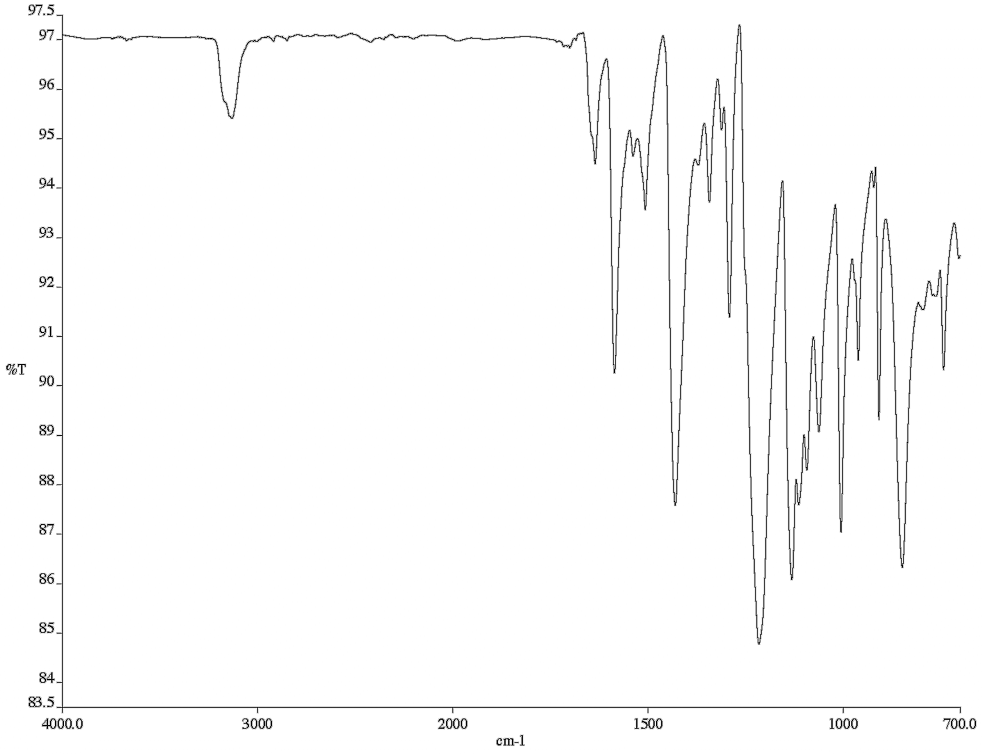

Figure A4.8 Infrared spectrum (thin film/NaCl) of compound **12**

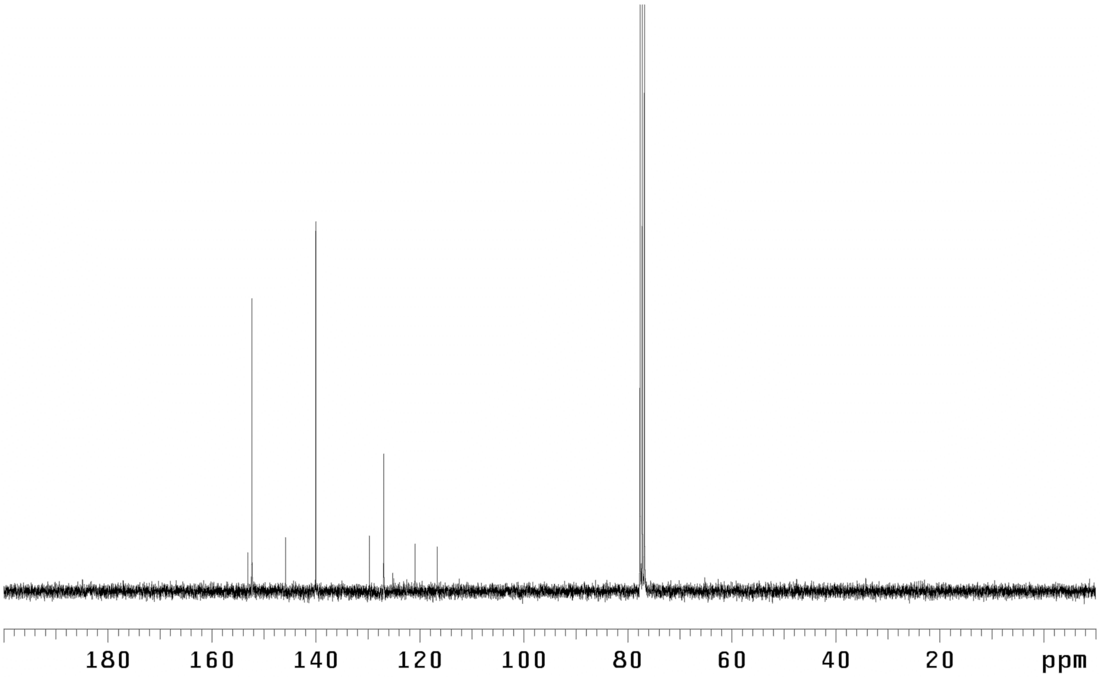

Figure A4.9 ^{13}C NMR (75 MHz, $CDCl_3$) of compound **12**

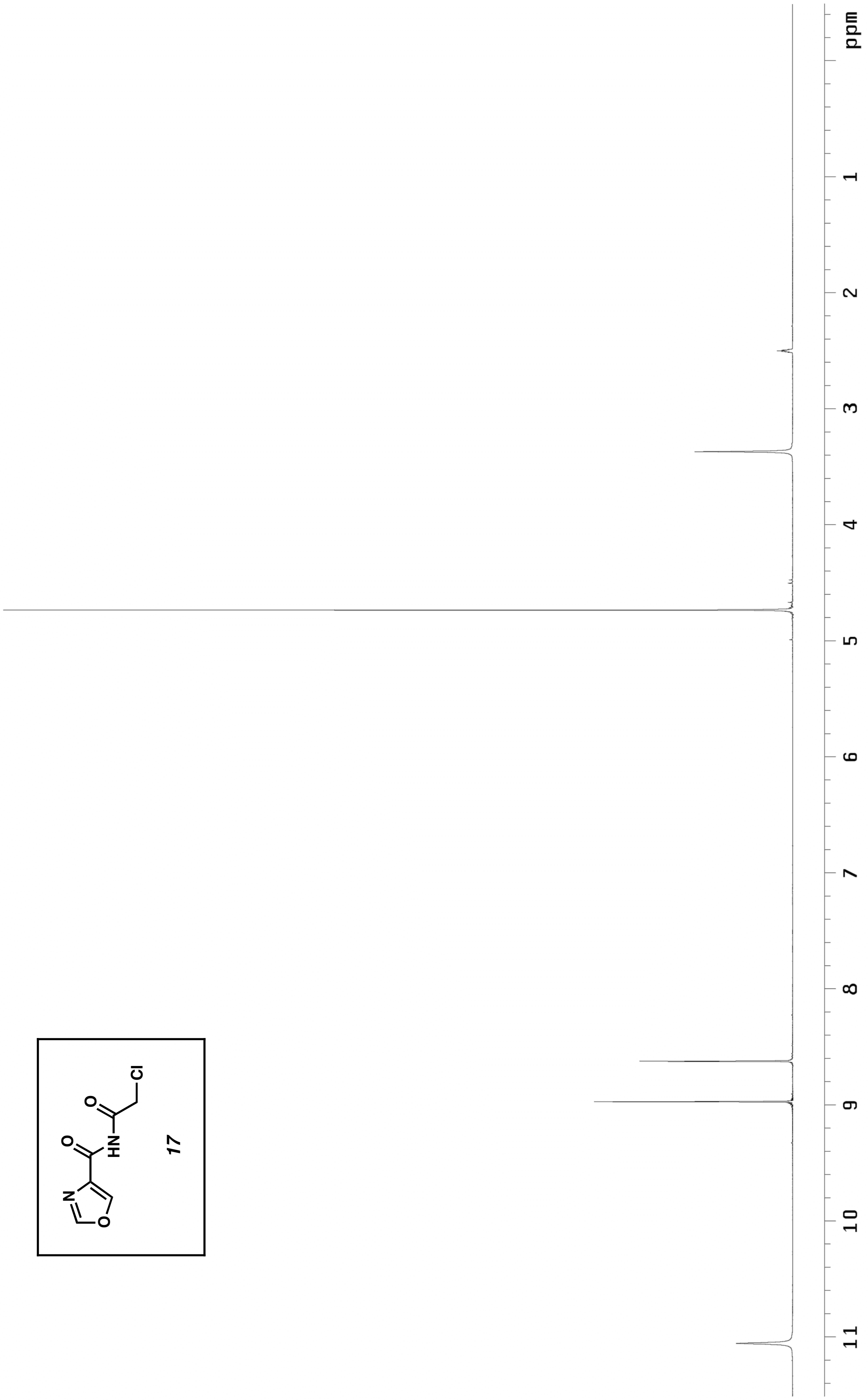

Figure A4.10 ^{1}H NMR (300 MHz, DMSO-d_6) of compound **17**

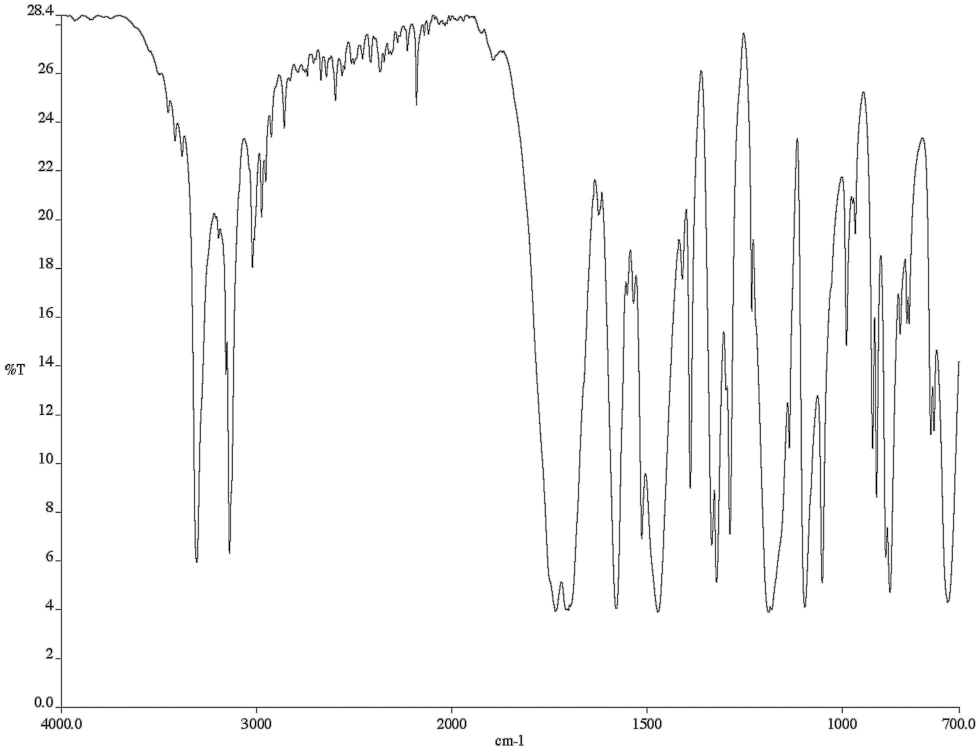

Figure A4.11 Infrared spectrum (KBr pellet) of compound **17**

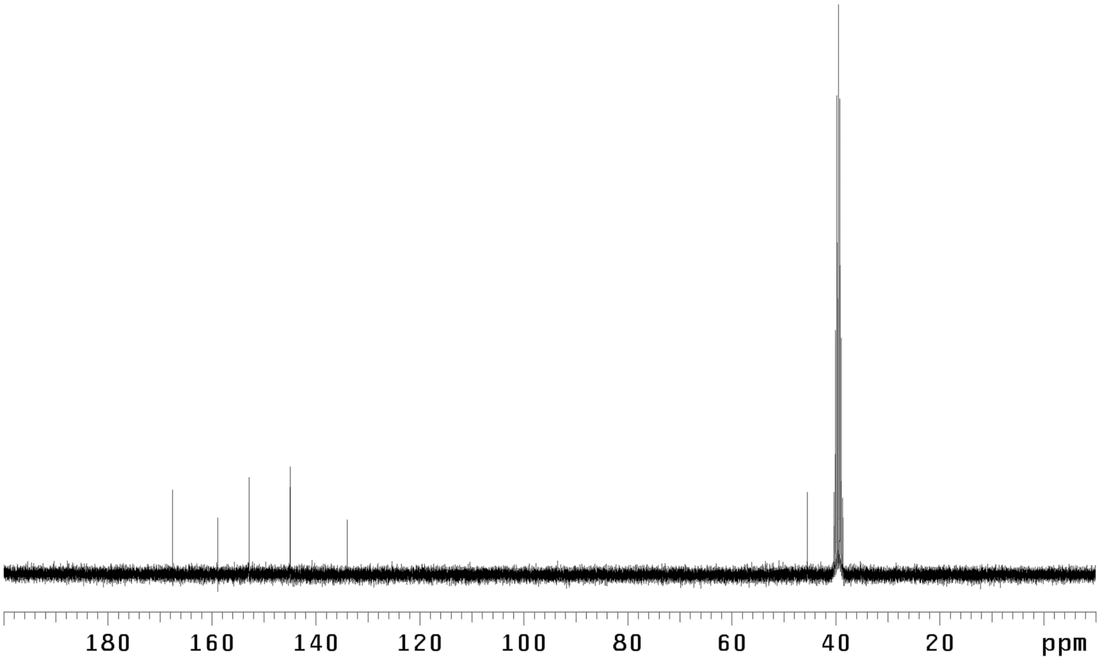

Figure A4.12 ^{13}C NMR (75 MHz, DMSO-d_6) of compound **17**

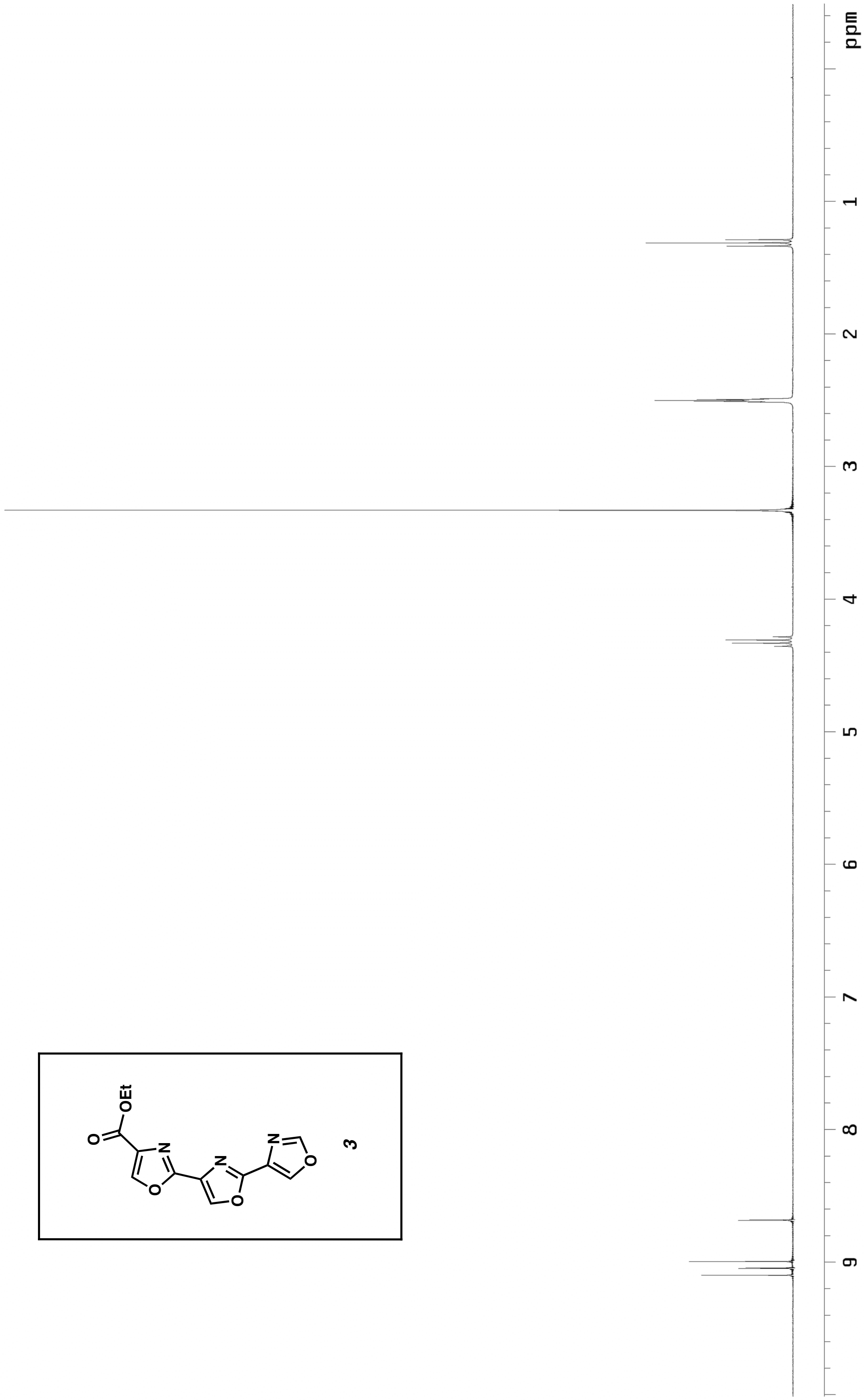

Figure A4.13 ^{1}H NMR (300 MHz, DMSO-d_6) of compound **3**

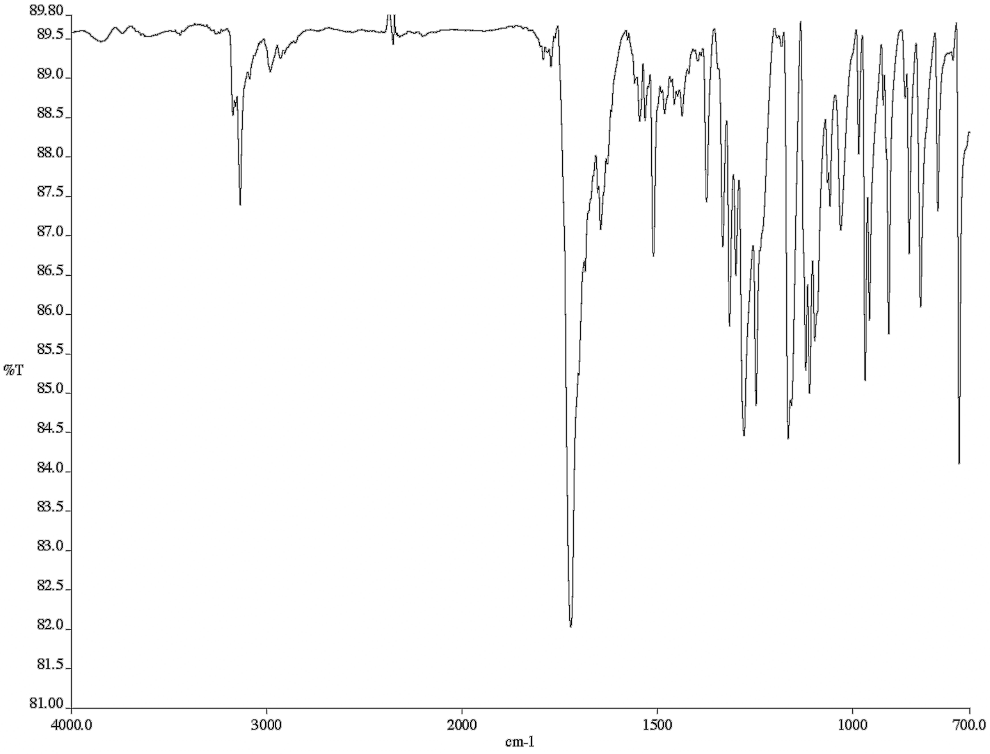

Figure A4.14 Infrared spectrum (thin film/NaCl) of compound **3**

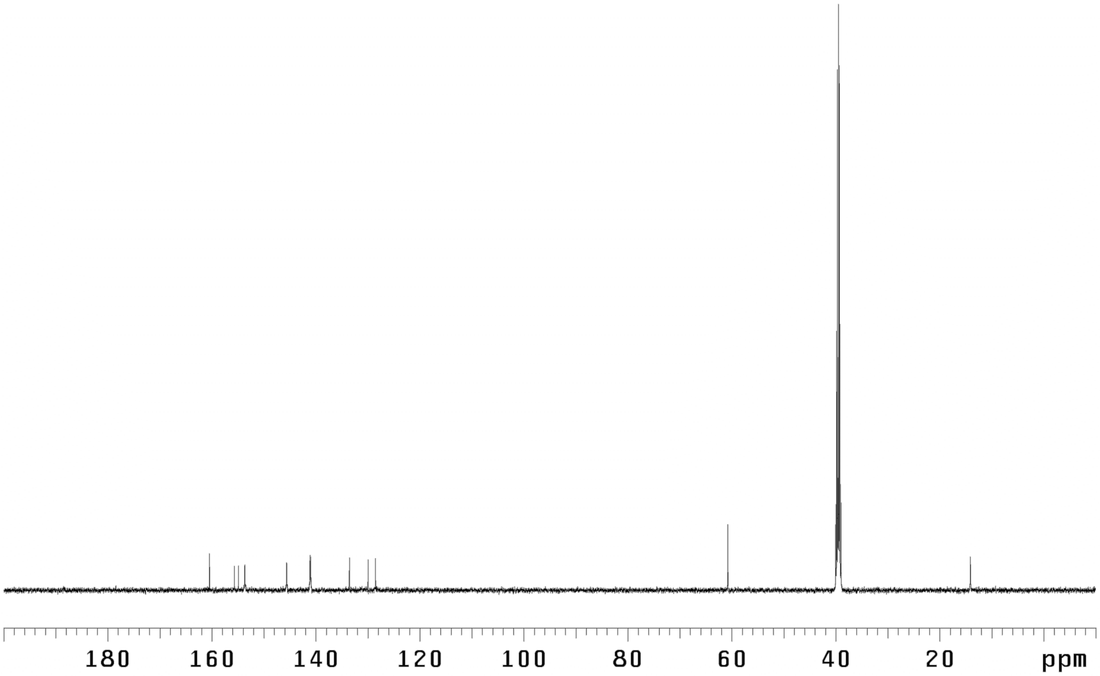

Figure A4.15 ^{13}C NMR (125 MHz, DMSO-d_6) of compound **3**

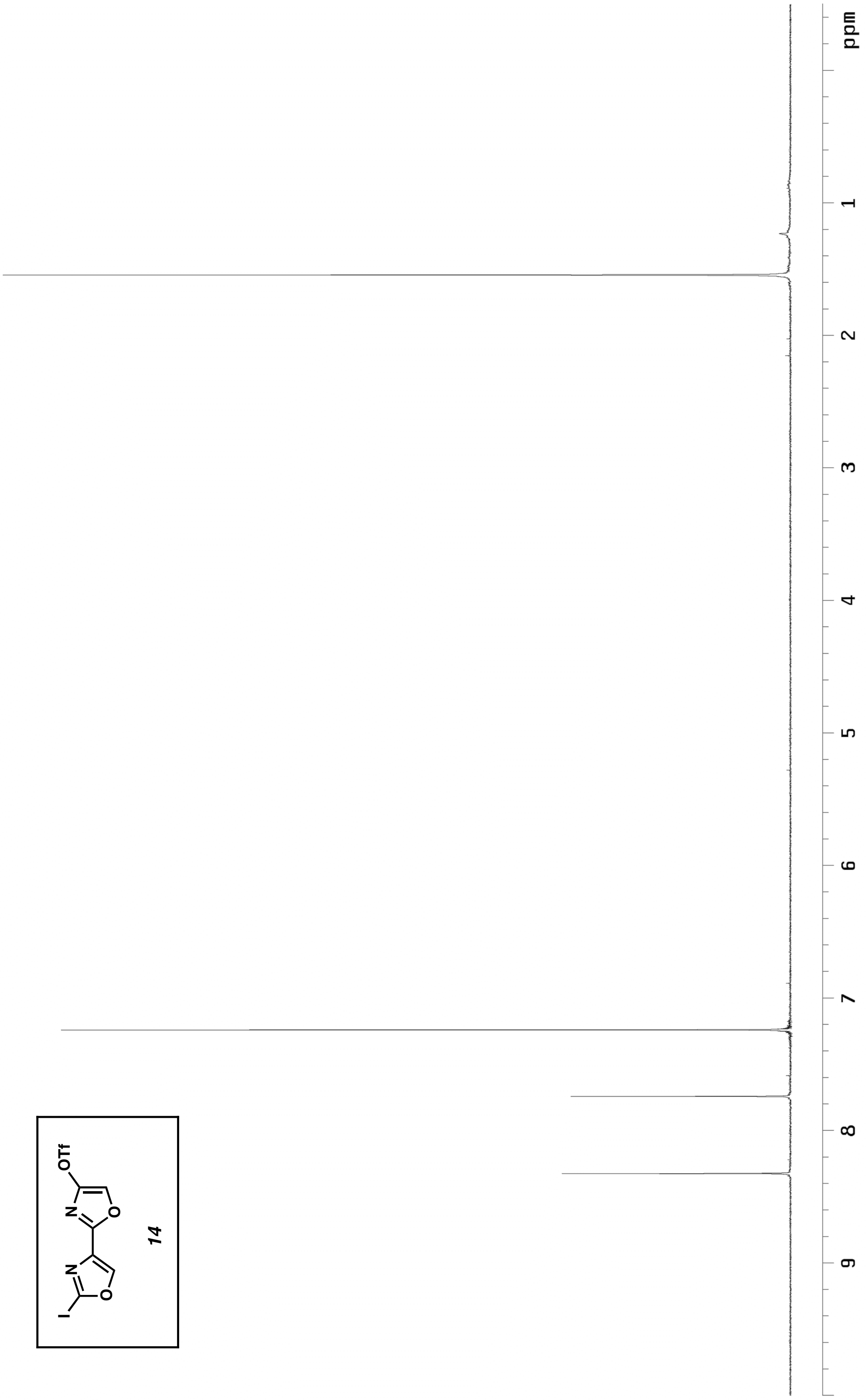

Figure A4.16 ^{1}H NMR (300 MHz, $CDCl_3$) of compound **14**

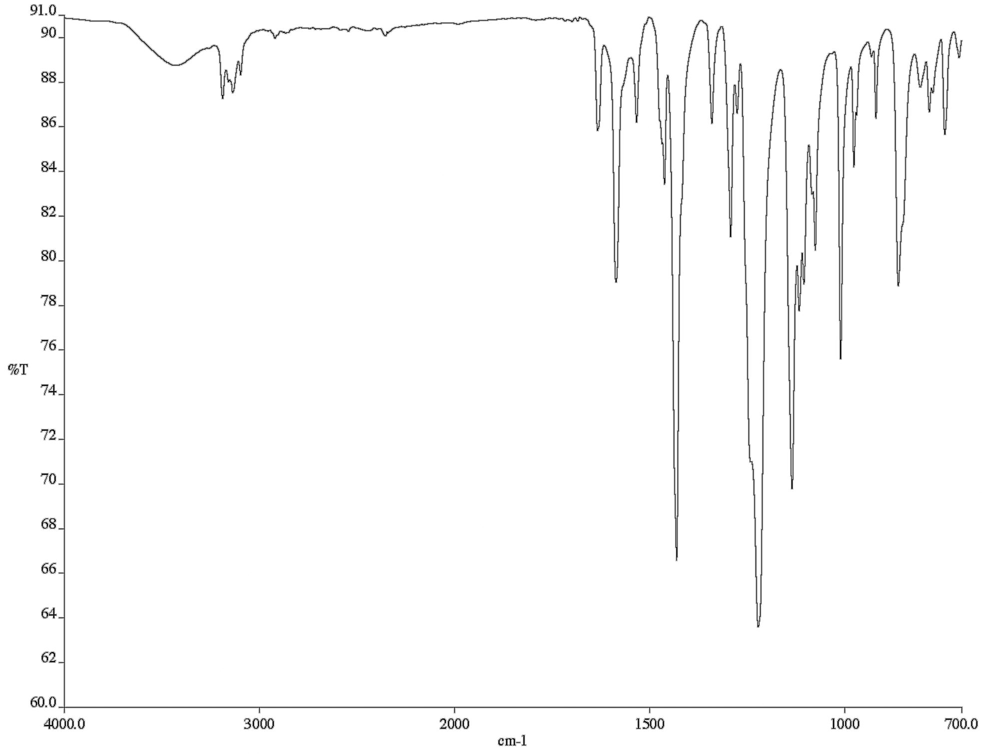

Figure A4.17 Infrared spectrum (thin film/NaCl) of compound **14**

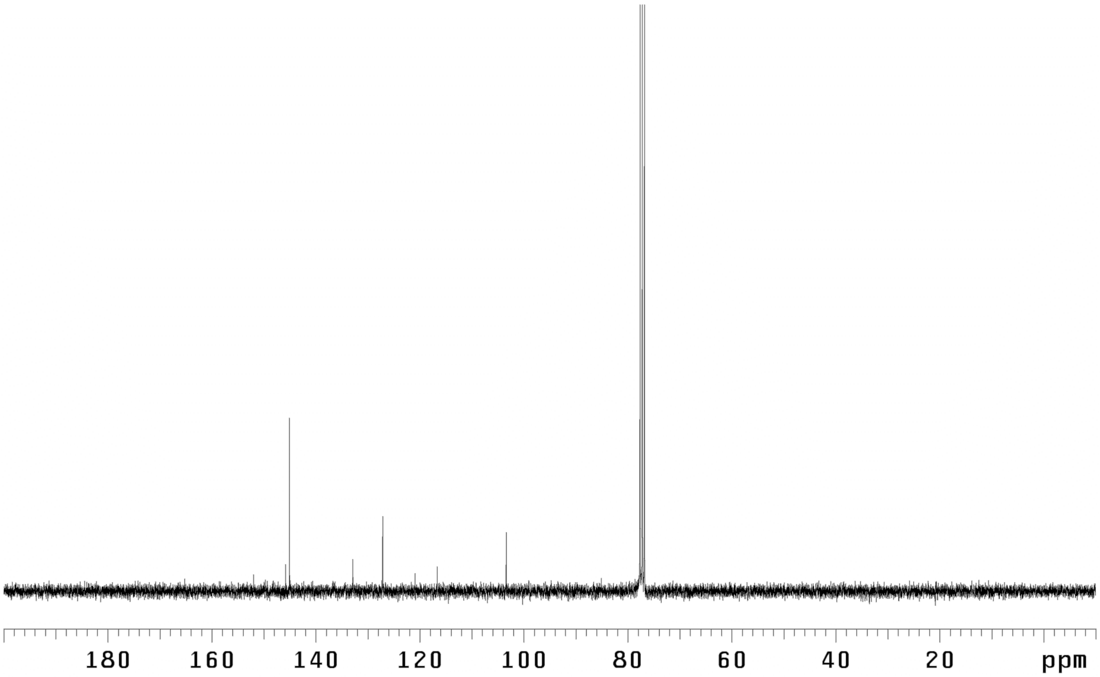

Figure A4.18 ^{13}C NMR (75 MHz, CDCl$_3$) of compound **14**

1.3 X-Ray Crystallography Reports

A5.1 Crystal Structure Analysis of 14

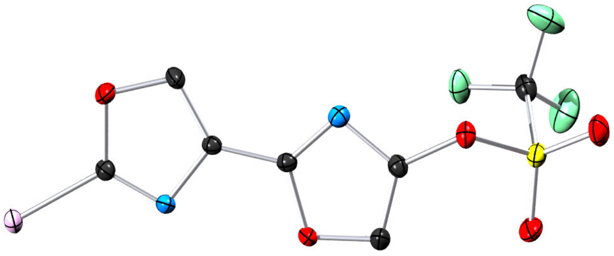

Figure A5.1.1 Iodobis-oxazole triflate **14** is shown with 50% probability ellipsoids (Note: Only Molecule A is depicted). Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition number 282586.

Table A5.1.1 Crystal data and structure refinement for **14** (CCDC 282586)

Empirical formula	$C_7H_2F_3IN_2O_5S$	
Formula weight	410.07	
Crystallization Solvent	Diethylether	
Crystal Habit	Plate	
Crystal size	0.48 x 0.22 x 0.19 mm^3	
Crystal color	Colorless	

Data Collection

Type of diffractometer	Bruker SMART 1000	
Wavelength	0.71073 Å MoKα	
Data Collection Temperature	100(2) K	
θ range for 9170 reflections used in lattice determination	2.74 to 33.18°	
Unit cell dimensions	a = 5.3805(5) Å	α= 92.205(2)°
	b = 14.4770(13) Å	β= 92.046(2)°
	c = 14.8833(13) Å	γ = 90.356(2)°
Volume	1157.68(18) Å^3	
Z	4	
Crystal system	Triclinic	
Space group	P-1	
Density (calculated)	2.353 Mg/m^3	
F(000)	776	
Data collection program	Bruker SMART v5.630	
θ range for data collection	1.93 to 33.66°	
Completeness to θ = 33.66°	82.2 %	
Index ranges	$-8 \le h \le 7, -19 \le k \le 20, -22 \le l \le 22$	
Data collection scan type	ω scans at 5 ϕ settings	
Data reduction program	Bruker SAINT v6.45A	
Reflections collected	19450	
Independent reflections	7576 [R_{int}= 0.0597]	
Absorption coefficient	3.006 mm^{-1}	
Absorption correction	Gaussian	
Max. and min. transmission	0.91449 and 0.56264	

5.1.1 (cont.)

Structure solution and Refinement

Structure solution program	SHELXS-97 (Sheldrick, 1990)
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Difference Fourier map
Structure refinement program	SHELXL-97 (Sheldrick, 1997)
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	7576 / 0 / 359
Treatment of hydrogen atoms	Unrestrained
Goodness-of-fit on F^2	1.034
Final R indices [$I>2\sigma(I)$, 5482 reflections]	R1 = 0.0311, *w*R2 = 0.0538
R indices (all data)	R1 = 0.0539, *w*R2 = 0.0583
Type of weighting scheme used	Sigma
Weighting scheme used	$w=1/\sigma^2(Fo^2)$
Max shift/error	0.002
Average shift/error	0.000
Largest diff. peak and hole	0.827 and -0.793 e.Å^{-3}

Special Refinement Details

This molecule crystallizes with two unique conformations in the asymmetric unit, differing from each other by the torsion angles around the C(6*)-O(3*) and the O(3*)-S1* bonds, as illustrated in Figures A5.1.1 thru A5.1.4 and listed in Table A5.1.6. The difference in the environment of these two molecules is illustrated in Figure A5.1.5 and A5.1.6. A short intermolecular contact between the I1 and N(1B), distance = 3.05Å, is **NOT** present between I2 and N(1A).

Another interesting feature observed in this structure are the CH-N and CH-O hydrogen bonds listed in Table A5.1.7. Although these are not the "classical" hydrogen bonds they are not without precedent[5,6] and the values observed herein are consistent with those observed elsewhere[1].

Refinement of F^2 against ALL reflections: The weighted R-factor (*w*R) and goodness of fit (S) are based on F^2, conventional R-factors (R) are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors(gt), etc., and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R-factors based on ALL data will be even larger.

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full

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([5]) Rahman, A. N. M. M.; Bishop, R.; Craig, D. C.; Scudder, M. L. *Eur. J. Org. Chem.* **2001**, 863–873.

([6]) Jiang, L.; Lai, L. *J. Biol. Chem.* **2002**, 37732–37740.

covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles, and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

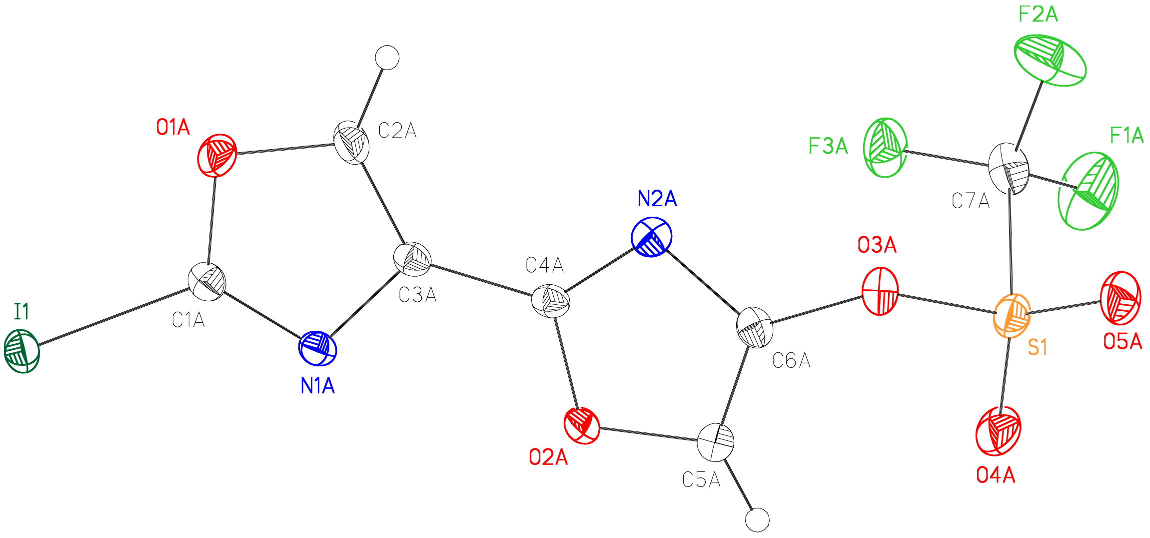

Figure A5.1.2 *Molecule A*

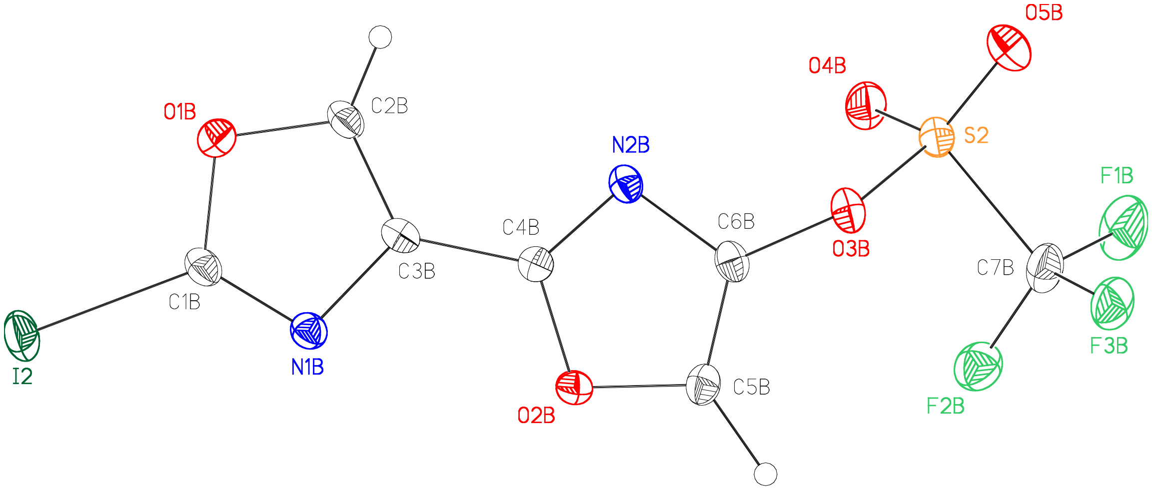

Figure A5.1.3 *Molecule B*

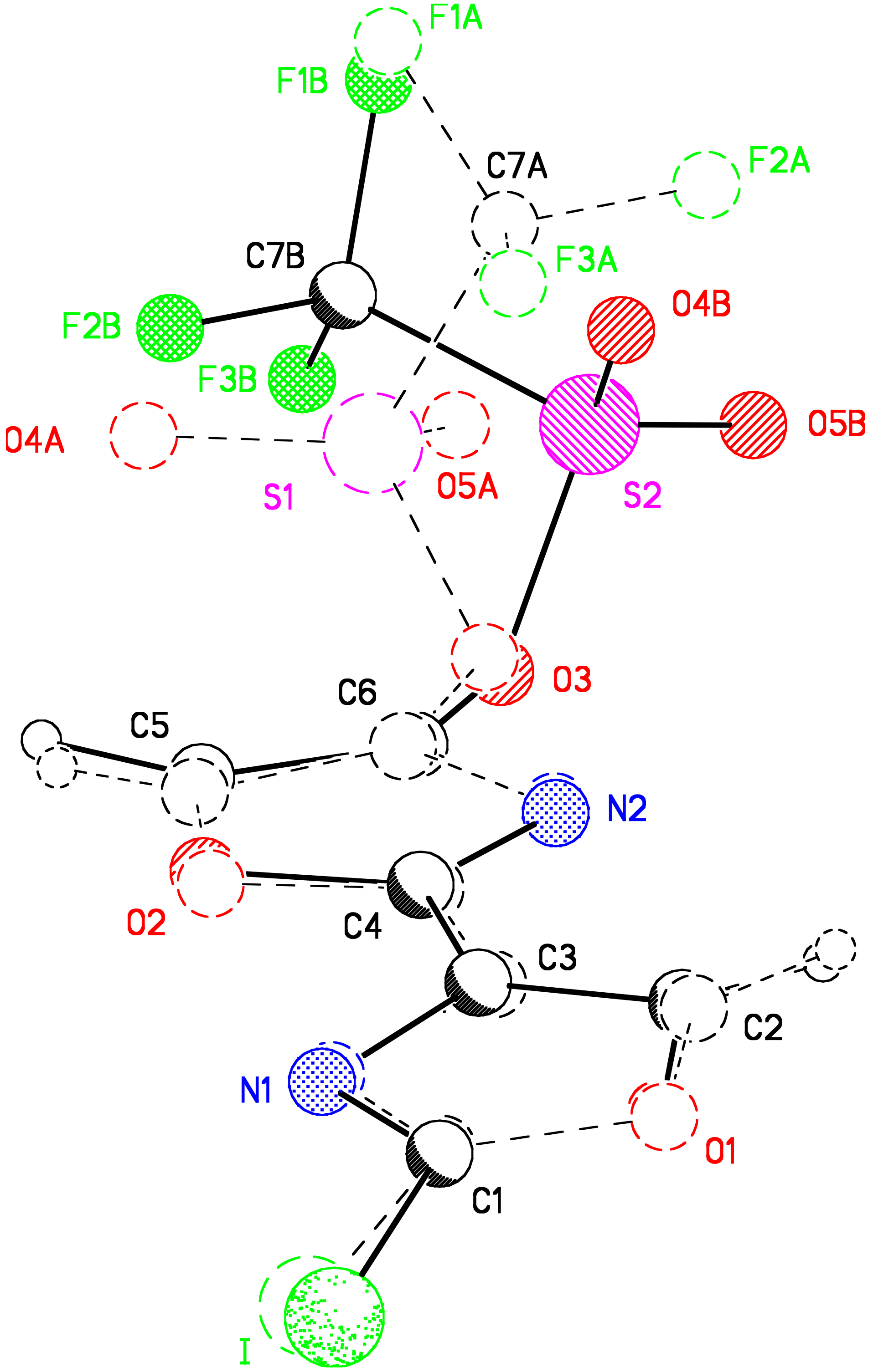

Figure A5.1.4 *Overlap of molecule A and B emphasizing the torsion angle around the*

C(6)-O(3) bond

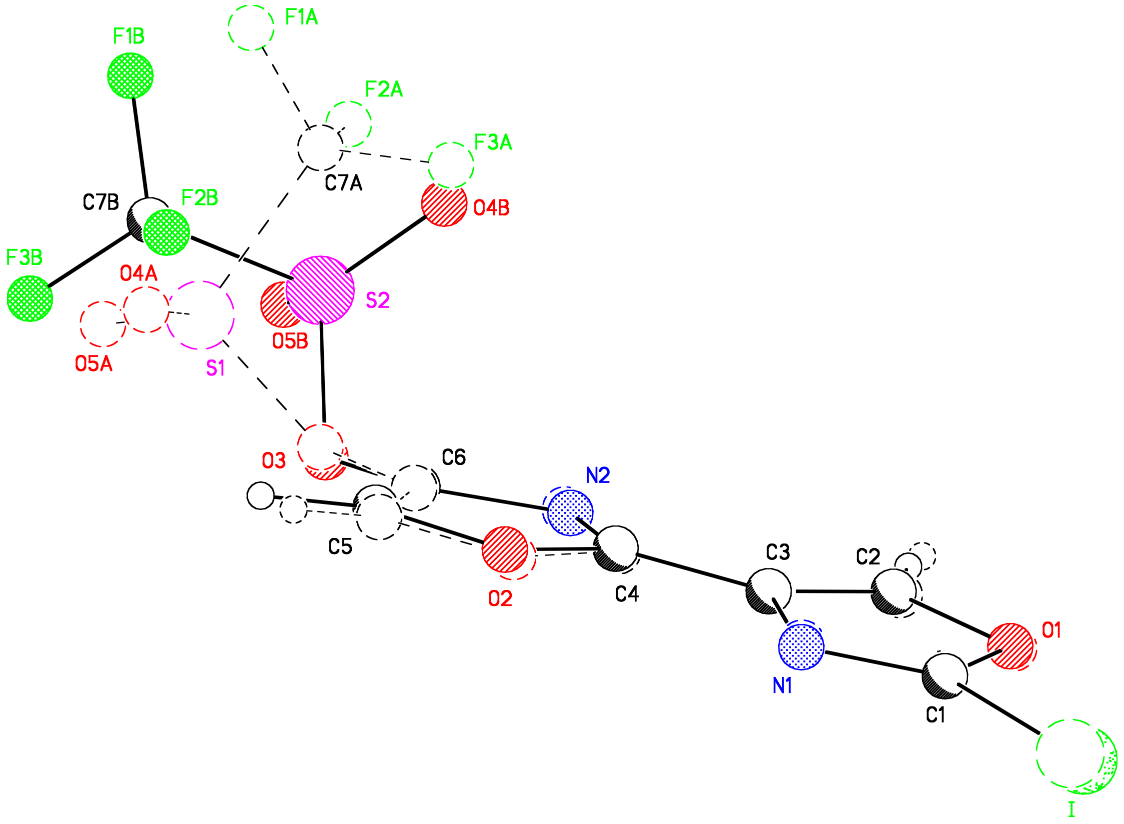

Figure A5.1.5 *Overlap of molecule A and B emphasizing the torsion angle around the O(3)-S bond*

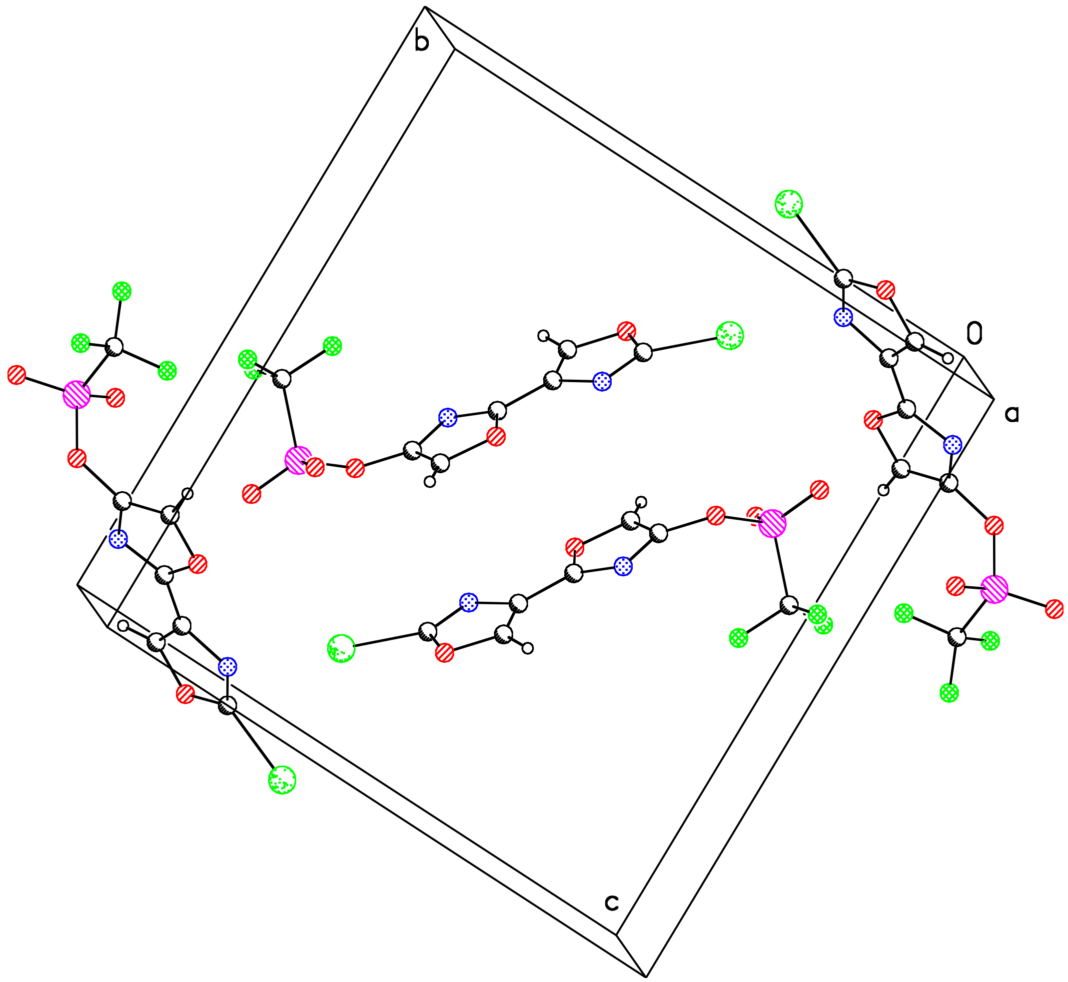

Figure A5.1.6 *Packing in the unit cell with the I(1)-N(1B) interaction emphasized*

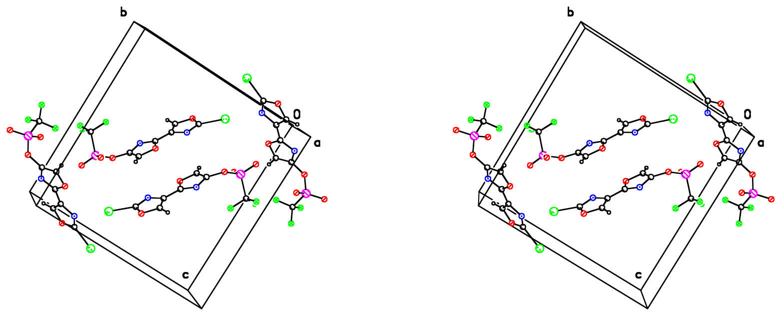

Figure A5.1.7 *Stereo view of the packing in the unit cell with the I(1)-N(1B) interaction emphasized*

Table A5.1.2 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for **14** (CCDC 282586). U(eq) is defined as the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
I(1)	2611(1)	3487(1)	1553(1)	17(1)
S(1)	2125(1)	8201(1)	6603(1)	18(1)
F(1A)	2445(4)	9715(1)	5750(1)	44(1)
F(2A)	-1292(4)	9274(1)	5935(1)	39(1)
F(3A)	903(3)	8577(1)	4943(1)	29(1)
O(1A)	-1301(3)	4609(1)	2445(1)	21(1)
O(2A)	3752(3)	5878(1)	4665(1)	19(1)
O(3A)	701(3)	7278(1)	6286(1)	17(1)
O(4A)	4719(4)	8117(2)	6483(1)	28(1)
O(5A)	1112(4)	8483(1)	7431(1)	25(1)
N(1A)	2396(4)	4804(2)	3161(1)	15(1)
N(2A)	-68(4)	6392(2)	4929(1)	16(1)
C(1A)	1153(5)	4399(2)	2502(2)	15(1)
C(2A)	-1614(5)	5227(2)	3160(2)	20(1)
C(3A)	609(5)	5342(2)	3598(2)	13(1)
C(4A)	1312(5)	5888(2)	4403(2)	13(1)
C(5A)	3925(5)	6421(2)	5442(2)	20(1)
C(6A)	1616(5)	6724(2)	5578(2)	15(1)
C(7A)	954(5)	8991(2)	5757(2)	22(1)
I(2)	2895(1)	5915(1)	10688(1)	27(1)
S(2)	3024(1)	11753(1)	7553(1)	19(1)
F(1B)	3756(3)	12036(2)	5882(1)	39(1)
F(2B)	6039(3)	10962(1)	6438(1)	27(1)
F(3B)	6889(3)	12400(1)	6769(1)	29(1)
O(1B)	596(3)	7723(1)	10466(1)	19(1)
O(2B)	6105(3)	9010(1)	8594(1)	16(1)
O(3B)	4951(3)	11381(1)	8288(1)	18(1)
O(4B)	1164(4)	11076(2)	7332(1)	26(1)
O(5B)	2497(4)	12676(2)	7808(2)	32(1)
N(1B)	4077(4)	7636(2)	9688(1)	15(1)
N(2B)	3301(4)	10062(2)	9005(1)	14(1)
C(1B)	2595(5)	7220(2)	10211(2)	17(1)
C(2B)	865(5)	8548(2)	10051(2)	17(1)
C(3B)	2946(5)	8489(2)	9579(2)	14(1)
C(4B)	4040(5)	9214(2)	9059(2)	13(1)
C(5B)	6713(5)	9817(2)	8192(2)	17(1)
C(6B)	5014(5)	10439(2)	8451(2)	15(1)
C(7B)	5080(5)	11791(2)	6599(2)	23(1)

Table A5.1.3 Bond lengths [Å] and angles [°] for **14** (CCDC 282586)

I(1)-C(1A)	2.074(3)
S(1)-O(5A)	1.4128(19)
S(1)-O(4A)	1.419(2)
S(1)-O(3A)	1.5838(19)
S(1)-C(7A)	1.833(3)
F(1A)-C(7A)	1.317(3)
F(2A)-C(7A)	1.311(3)
F(3A)-C(7A)	1.329(3)
O(1A)-C(1A)	1.357(3)
O(1A)-C(2A)	1.378(3)
O(2A)-C(4A)	1.356(3)
O(2A)-C(5A)	1.373(3)
O(3A)-C(6A)	1.404(3)
N(1A)-C(1A)	1.287(3)
N(1A)-C(3A)	1.404(3)
N(2A)-C(4A)	1.304(3)
N(2A)-C(6A)	1.372(3)
C(2A)-C(3A)	1.348(4)
C(2A)-H(2A)	0.96(3)
C(3A)-C(4A)	1.447(3)
C(5A)-C(6A)	1.340(4)
C(5A)-H(5A)	0.92(3)
I(2)-C(1B)	2.049(3)
S(2)-O(5B)	1.408(2)
S(2)-O(4B)	1.418(2)
S(2)-O(3B)	1.591(2)
S(2)-C(7B)	1.833(3)
F(1B)-C(7B)	1.323(3)
F(2B)-C(7B)	1.325(4)
F(3B)-C(7B)	1.321(3)
O(1B)-C(1B)	1.361(3)
O(1B)-C(2B)	1.374(3)
O(2B)-C(4B)	1.357(3)
O(2B)-C(5B)	1.376(3)
O(3B)-C(6B)	1.394(3)
N(1B)-C(1B)	1.295(3)
N(1B)-C(3B)	1.392(3)
N(2B)-C(4B)	1.298(3)
N(2B)-C(6B)	1.381(3)
C(2B)-C(3B)	1.345(4)
C(2B)-H(2B)	0.95(3)
C(3B)-C(4B)	1.461(4)
C(5B)-C(6B)	1.344(4)
C(5B)-H(5B)	1.14(3)
O(5A)-S(1)-O(4A)	122.97(13)
O(5A)-S(1)-O(3A)	106.06(12)
O(4A)-S(1)-O(3A)	110.99(12)
O(5A)-S(1)-C(7A)	107.22(13)

O(4A)-S(1)-C(7A)	106.61(13)
O(3A)-S(1)-C(7A)	100.73(12)
C(1A)-O(1A)-C(2A)	104.0(2)
C(4A)-O(2A)-C(5A)	105.2(2)
C(6A)-O(3A)-S(1)	119.74(17)
C(1A)-N(1A)-C(3A)	103.7(2)
C(4A)-N(2A)-C(6A)	102.6(2)
N(1A)-C(1A)-O(1A)	115.2(2)
N(1A)-C(1A)-I(1)	125.35(19)
O(1A)-C(1A)-I(1)	119.42(17)
C(3A)-C(2A)-O(1A)	107.7(2)
C(3A)-C(2A)-H(2A)	131.2(19)
O(1A)-C(2A)-H(2A)	120.6(19)
C(2A)-C(3A)-N(1A)	109.4(2)
C(2A)-C(3A)-C(4A)	130.7(2)
N(1A)-C(3A)-C(4A)	119.9(2)
N(2A)-C(4A)-O(2A)	114.1(2)
N(2A)-C(4A)-C(3A)	129.4(2)
O(2A)-C(4A)-C(3A)	116.4(2)
C(6A)-C(5A)-O(2A)	105.6(2)
C(6A)-C(5A)-H(5A)	135(2)
O(2A)-C(5A)-H(5A)	119(2)
C(5A)-C(6A)-N(2A)	112.5(2)
C(5A)-C(6A)-O(3A)	130.0(2)
N(2A)-C(6A)-O(3A)	117.5(2)
F(2A)-C(7A)-F(1A)	108.7(3)
F(2A)-C(7A)-F(3A)	108.9(2)
F(1A)-C(7A)-F(3A)	108.4(2)
F(2A)-C(7A)-S(1)	111.1(2)
F(1A)-C(7A)-S(1)	109.2(2)
F(3A)-C(7A)-S(1)	110.4(2)
O(5B)-S(2)-O(4B)	123.51(14)
O(5B)-S(2)-O(3B)	107.15(13)
O(4B)-S(2)-O(3B)	110.21(11)
O(5B)-S(2)-C(7B)	106.84(14)
O(4B)-S(2)-C(7B)	107.37(13)
O(3B)-S(2)-C(7B)	98.96(12)
C(1B)-O(1B)-C(2B)	104.3(2)
C(4B)-O(2B)-C(5B)	104.9(2)
C(6B)-O(3B)-S(2)	119.66(16)
C(1B)-N(1B)-C(3B)	103.1(2)
C(4B)-N(2B)-C(6B)	102.8(2)
N(1B)-C(1B)-O(1B)	114.9(2)
N(1B)-C(1B)-I(2)	128.2(2)
O(1B)-C(1B)-I(2)	116.89(18)
C(3B)-C(2B)-O(1B)	107.2(2)
C(3B)-C(2B)-H(2B)	131.5(18)
O(1B)-C(2B)-H(2B)	121.3(18)
C(2B)-C(3B)-N(1B)	110.5(2)
C(2B)-C(3B)-C(4B)	126.9(2)
N(1B)-C(3B)-C(4B)	122.5(2)

N(2B)-C(4B)-O(2B)	114.6(2)
N(2B)-C(4B)-C(3B)	127.2(2)
O(2B)-C(4B)-C(3B)	118.2(2)
C(6B)-C(5B)-O(2B)	105.9(2)
C(6B)-C(5B)-H(5B)	131.3(14)
O(2B)-C(5B)-H(5B)	122.7(14)
C(5B)-C(6B)-N(2B)	111.8(2)
C(5B)-C(6B)-O(3B)	128.0(2)
N(2B)-C(6B)-O(3B)	120.0(2)
F(3B)-C(7B)-F(2B)	109.7(2)
F(3B)-C(7B)-F(1B)	109.1(2)
F(2B)-C(7B)-F(1B)	109.2(2)
F(3B)-C(7B)-S(2)	110.4(2)
F(2B)-C(7B)-S(2)	109.83(19)
F(1B)-C(7B)-S(2)	108.5(2)

Table A5.1.4 Anisotropic displacement parameters ($Å^2 \times 10^4$) for **14** (CCDC 282586). The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$.

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
I(1)	213(1)	135(1)	163(1)	-16(1)	4(1)	9(1)
S(1)	183(3)	205(4)	153(3)	-35(3)	0(2)	-9(3)
F(1A)	608(14)	276(11)	434(11)	62(9)	-48(10)	-215(10)
F(2A)	367(11)	449(13)	360(10)	124(9)	119(8)	207(9)
F(3A)	441(11)	258(10)	157(8)	-11(7)	8(7)	21(8)
O(1A)	131(10)	257(11)	224(10)	-80(8)	-11(8)	-7(8)
O(2A)	136(9)	185(11)	236(10)	-76(8)	-20(8)	45(8)
O(3A)	206(10)	161(10)	152(9)	-19(7)	26(7)	-28(8)
O(4A)	150(10)	334(13)	327(11)	-115(10)	-19(8)	-27(9)
O(5A)	324(12)	273(12)	146(9)	-47(8)	16(8)	33(9)
N(1A)	124(11)	134(12)	187(11)	-6(9)	-6(8)	15(8)
N(2A)	144(11)	171(12)	151(10)	12(9)	13(8)	-11(9)
C(1A)	140(13)	128(14)	174(12)	9(10)	20(10)	-9(10)
C(2A)	145(14)	194(16)	259(14)	-88(12)	25(11)	18(11)
C(3A)	118(12)	121(13)	160(12)	17(10)	12(9)	3(9)
C(4A)	124(13)	112(13)	164(12)	28(10)	-1(10)	2(9)
C(5A)	195(15)	192(16)	195(13)	-46(11)	-42(11)	41(11)
C(6A)	157(13)	135(14)	164(12)	-2(10)	29(10)	-5(10)
C(7A)	239(15)	191(16)	226(14)	-28(12)	57(11)	-15(12)
I(2)	383(1)	149(1)	293(1)	70(1)	73(1)	31(1)
S(2)	176(3)	178(4)	232(3)	67(3)	23(3)	11(3)
F(1B)	316(11)	599(14)	258(9)	217(9)	-64(8)	-25(9)
F(2B)	304(10)	273(10)	239(8)	-8(7)	55(7)	-9(8)
F(3B)	225(9)	261(10)	377(10)	80(8)	25(8)	-79(7)
O(1B)	205(10)	185(11)	195(9)	21(8)	56(8)	14(8)
O(2B)	177(10)	152(10)	161(9)	11(7)	36(7)	36(7)
O(3B)	237(10)	140(10)	158(9)	28(7)	-17(7)	-3(8)
O(4B)	143(10)	293(12)	344(11)	134(10)	-20(8)	-26(8)
O(5B)	366(13)	186(12)	423(13)	75(10)	110(10)	88(9)
N(1B)	172(12)	139(12)	150(10)	0(9)	7(9)	14(9)
N(2B)	179(12)	122(12)	129(10)	5(8)	-3(8)	5(9)
C(1B)	210(14)	129(14)	160(12)	-2(10)	1(10)	30(10)
C(2B)	222(15)	126(14)	155(12)	4(10)	2(10)	47(11)
C(3B)	145(13)	130(14)	129(11)	-25(10)	-29(9)	18(10)
C(4B)	142(13)	144(14)	106(11)	-9(9)	-12(9)	1(10)
C(5B)	187(14)	150(14)	175(12)	18(10)	18(10)	-29(10)
C(6B)	196(14)	115(14)	145(11)	0(10)	-21(10)	-10(10)
C(7B)	189(15)	260(17)	235(14)	86(12)	-16(11)	-58(12)

Table A5.1.5 Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3) for **14** (CCDC 282586)

	x	y	z	U_{iso}
H(2A)	-3150(60)	5540(20)	3230(20)	29(9)
H(5A)	5460(60)	6530(20)	5710(20)	31(9)
H(2B)	-260(50)	9040(20)	10145(19)	16(7)
H(5B)	8370(50)	9877(18)	7738(17)	12(7)

Table A5.1.6 Torsion angles [°] for **14** (CCDC 282586)

N(2A)-C(6A)-O(3A)-S(1)	-135.1(2)
N(2B)-C(6B)-O(3B)-S(2)	-81.0(3)
C(6A)-O(3A)-S(1)-C(7A)	81.2(2)
C(6B)-O(3B)-S(2)-C(7B)	-96.8(2)

Table A5.1.7 CH···N hydrogen bonds for **14** (CCDC 282586) [Å and °]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(2A)-H(2A)...N(1A)#1	0.96(3)	2.61(3)	3.277(4)	127(2)
C(5A)-H(5A)...N(2A)#2	0.92(3)	2.72(3)	3.348(4)	127(2)
C(2B)-H(2B)...N(2B)#3	0.95(3)	2.45(3)	3.334(4)	155(2)
C(5B)-H(5B)...O(5A)#2	1.14(3)	2.54(3)	3.269(3)	120.1(17)
C(5B)-H(5B)...O(4B)#2	1.14(3)	2.40(3)	3.323(3)	136.6(18)

Symmetry transformations used to generate equivalent atoms:
#1 x-1,y,z
#2 x+1,y,z
#3 -x,-y+2,-z+2