Supplementary information

Hybrids of acylated homoserine lactone and nitric oxide donors as inhibitors of quorum sensing and virulence factors in *Pseudomonas aeruginosa*

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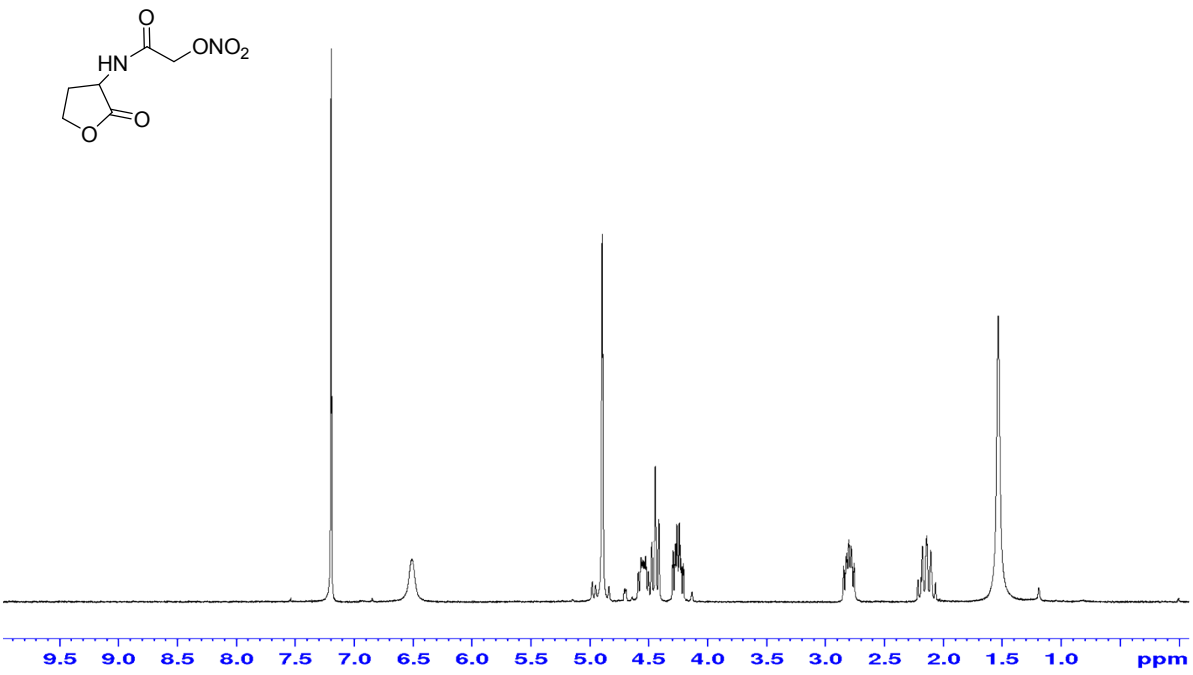
Supporting Information

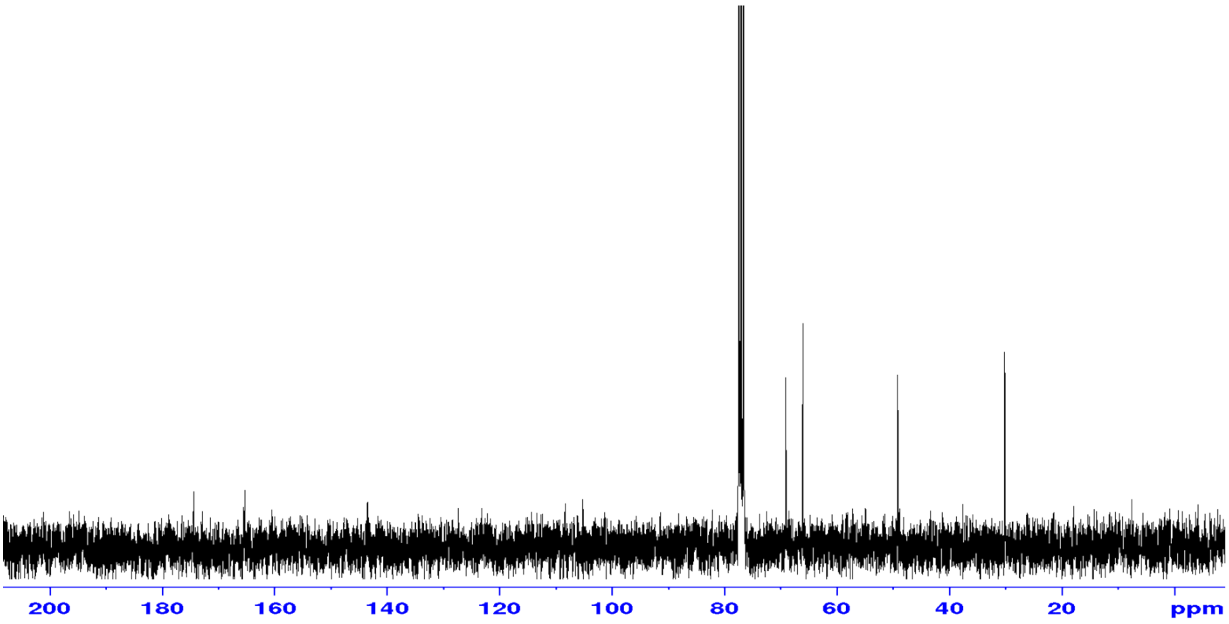
1) ^{1}H and ^{13}C NMR spectra of synthesised compounds tested for activity
2) X-ray crystal structure information for **7a** and **22a**

1) ^{1}H and ^{13}C NMR spectra of synthesised compounds

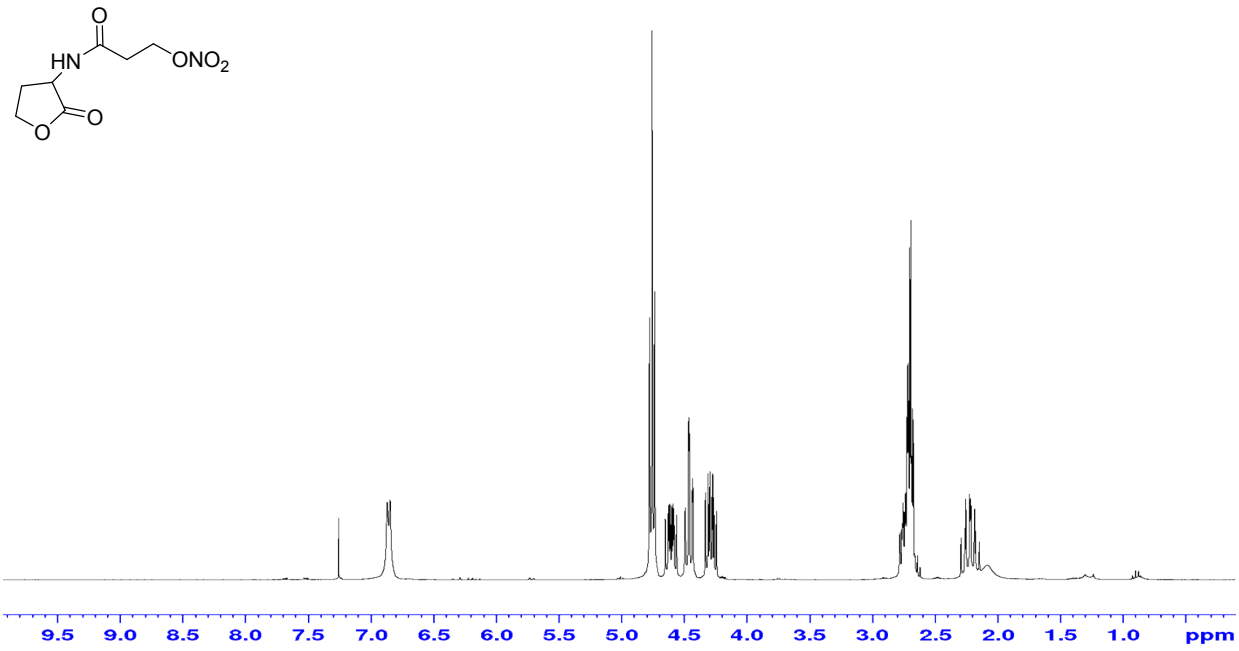
^{1}H NMR spectrum of Compound **7a** in $CDCl_3$



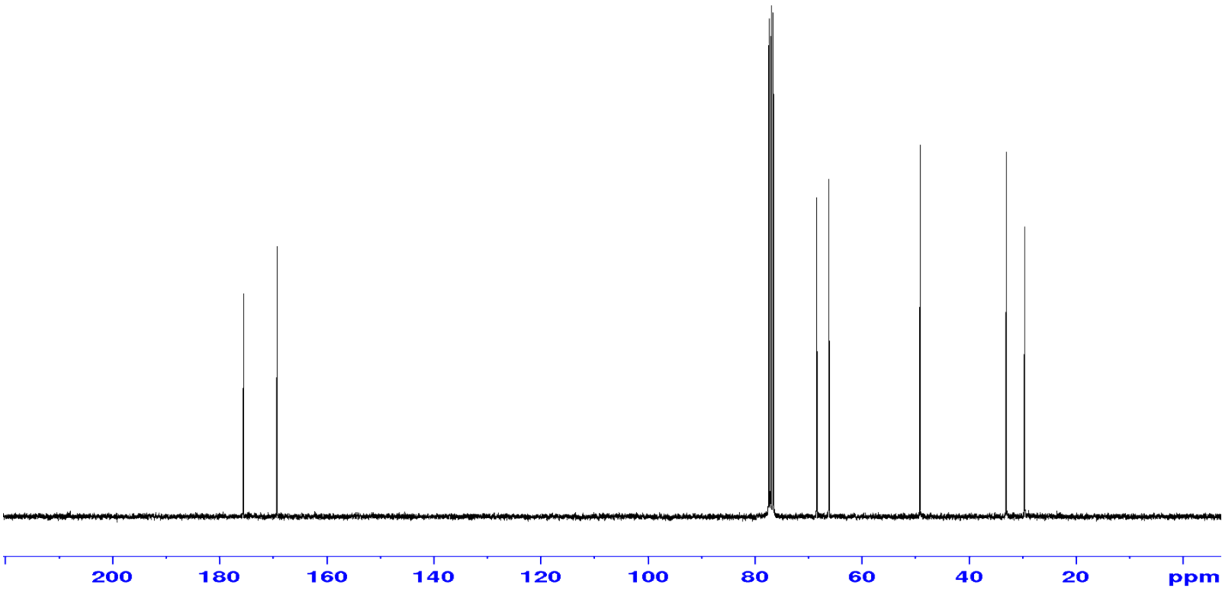
^{13}C NMR spectrum of Compound **7a** in $CDCl_3$



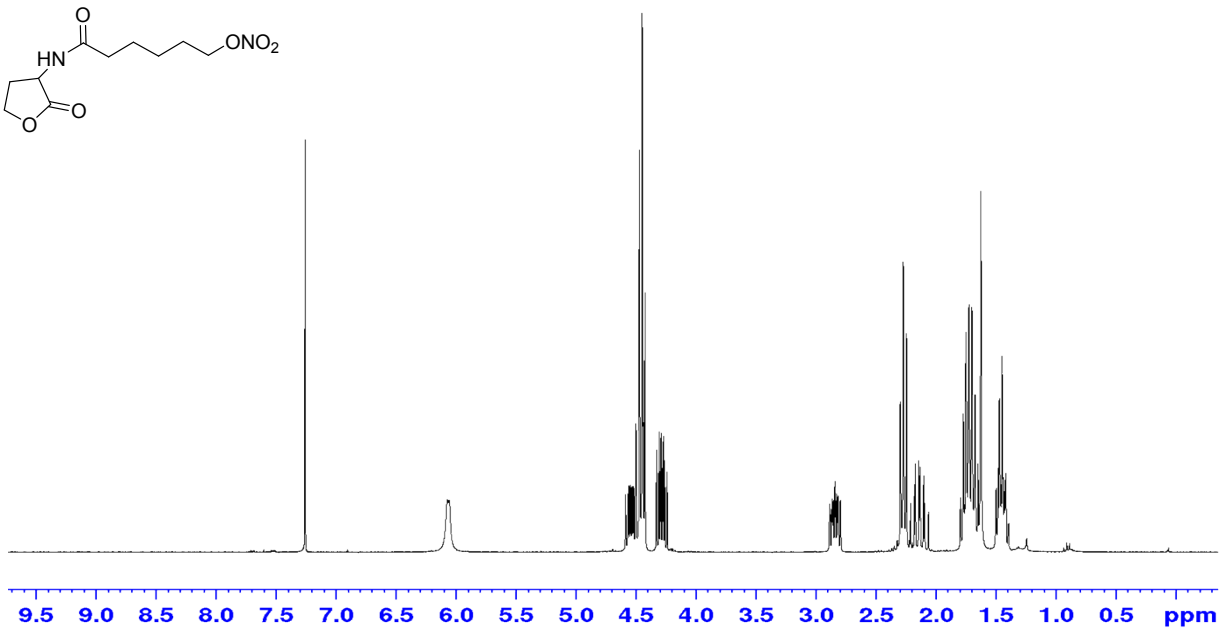
^{1}H NMR spectrum of Compound **7b** in $CDCl_3$



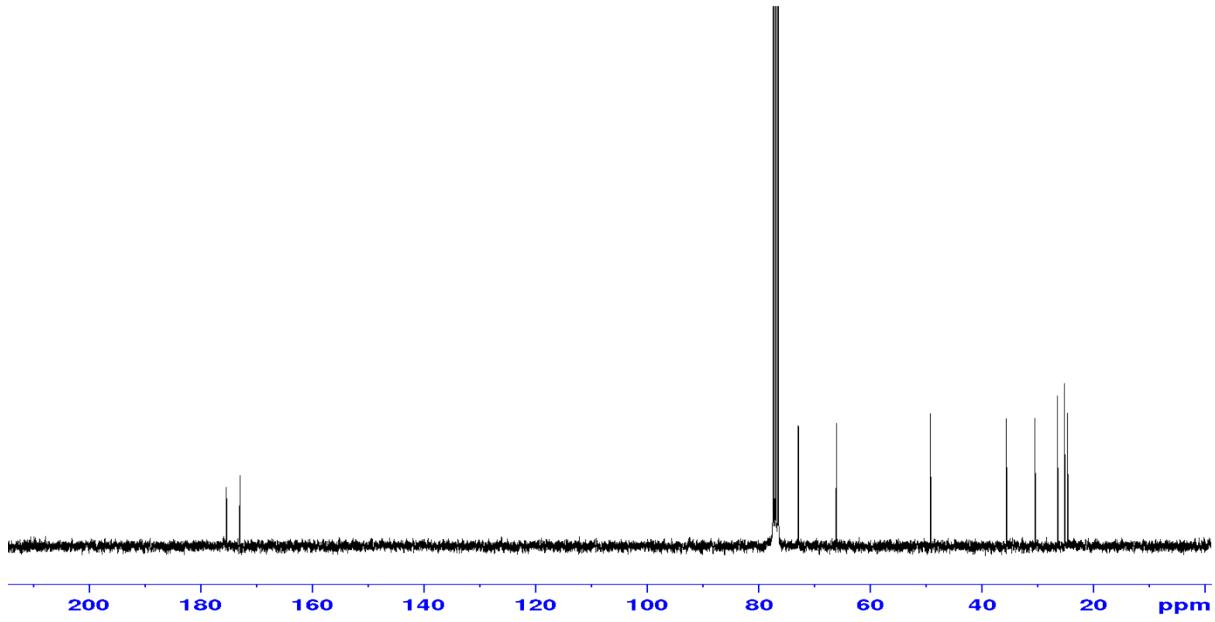
^{13}C NMR spectrum of Compound **7b** in $CDCl_3$



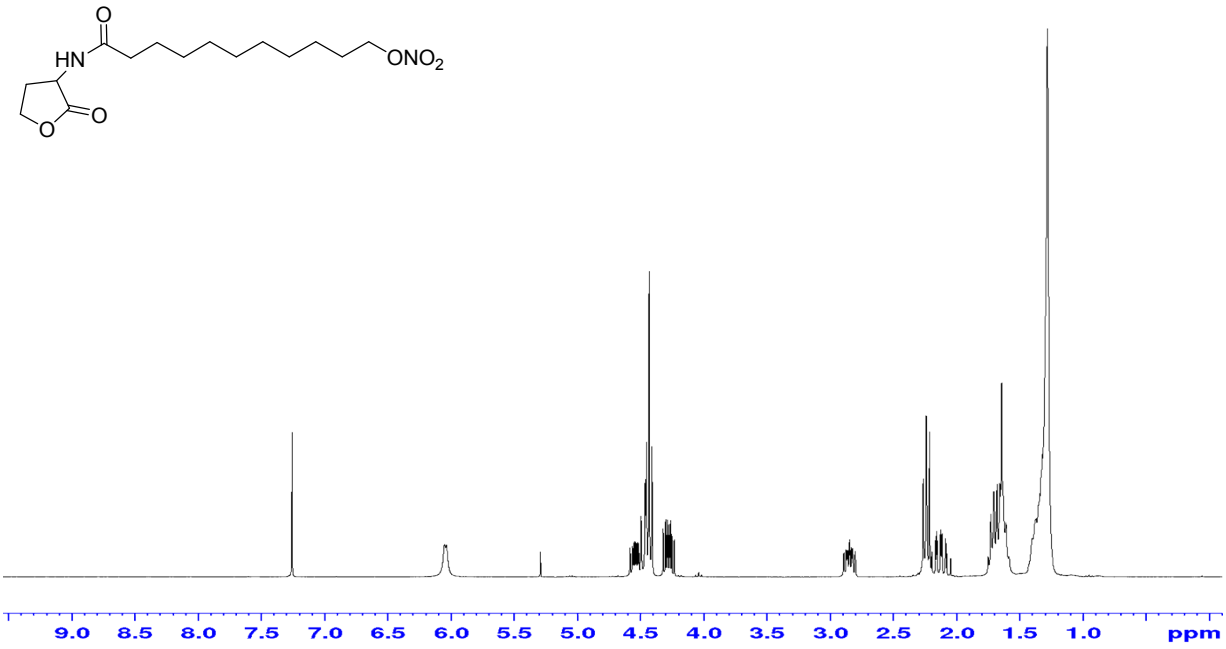
^{1}H NMR spectrum of Compound **7c** in $CDCl_3$



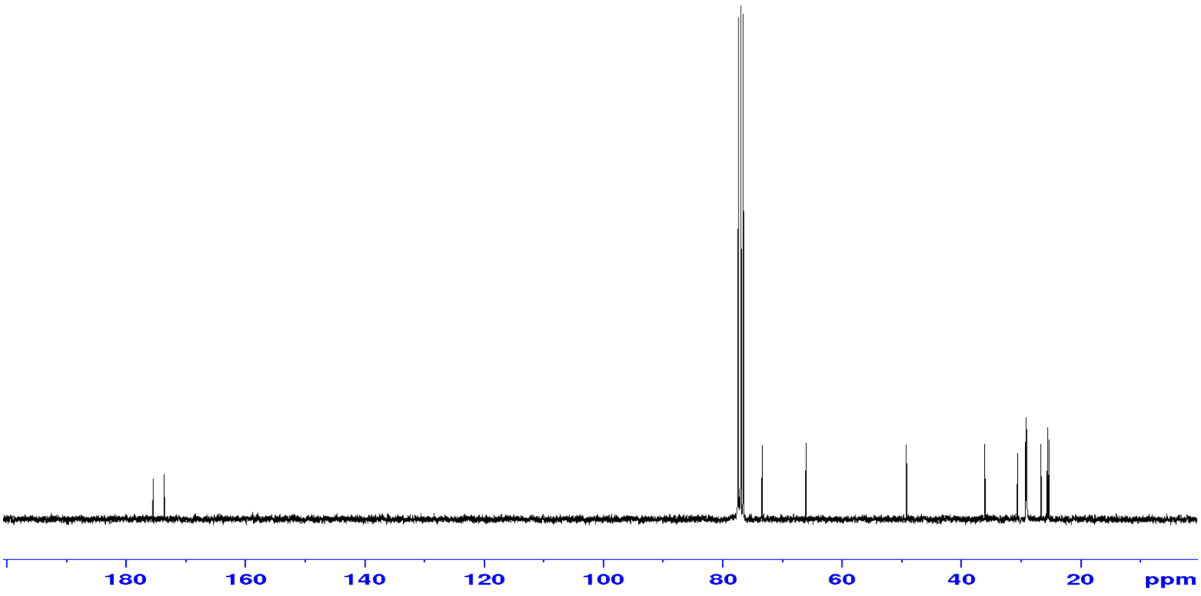
^{13}C NMR spectrum of Compound **7c** in $CDCl_3$



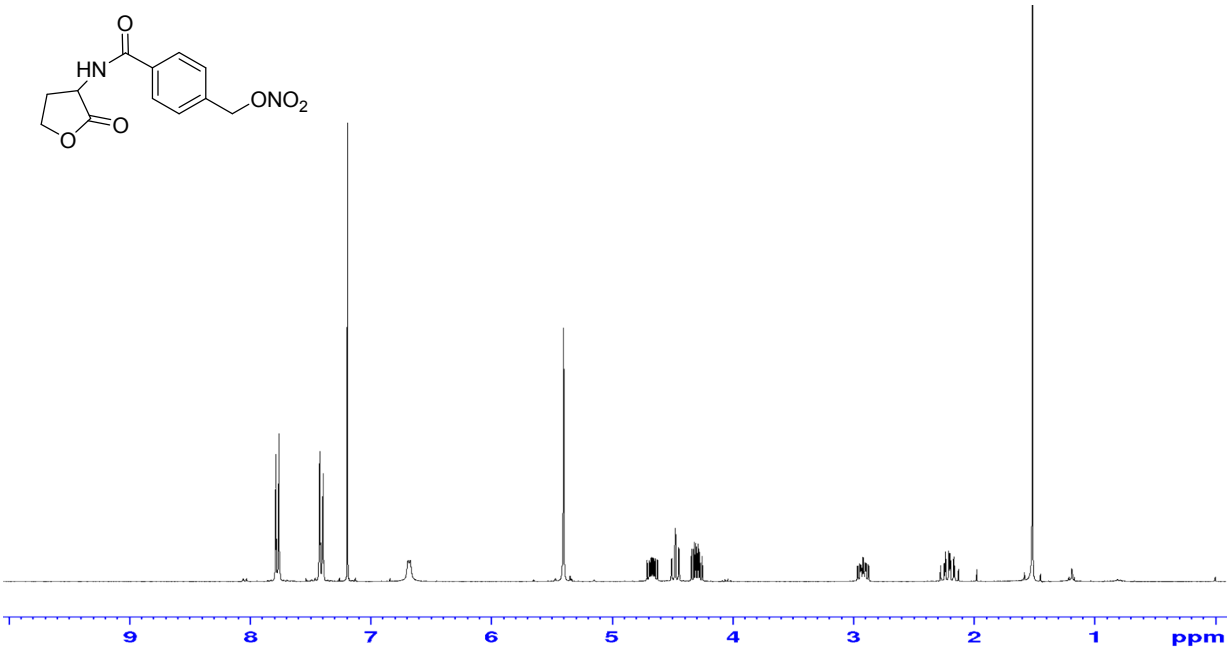
^{1}H NMR spectrum of Compound **7d** in $CDCl_3$



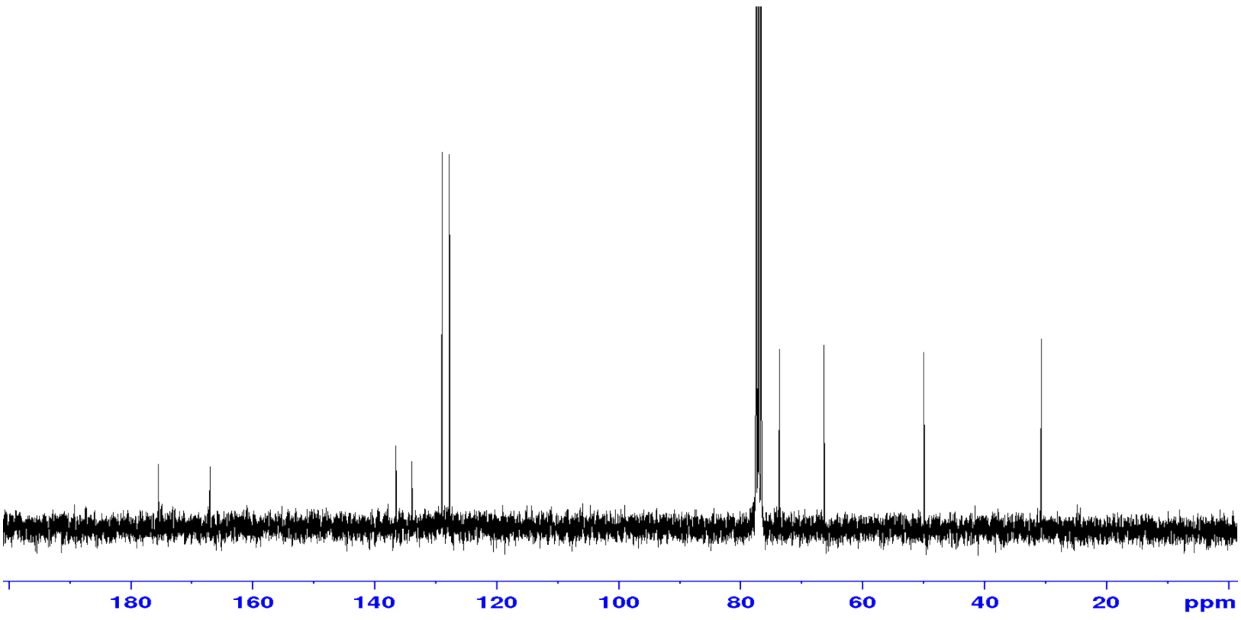
^{13}C NMR spectrum of Compound **7d** in $CDCl_3$



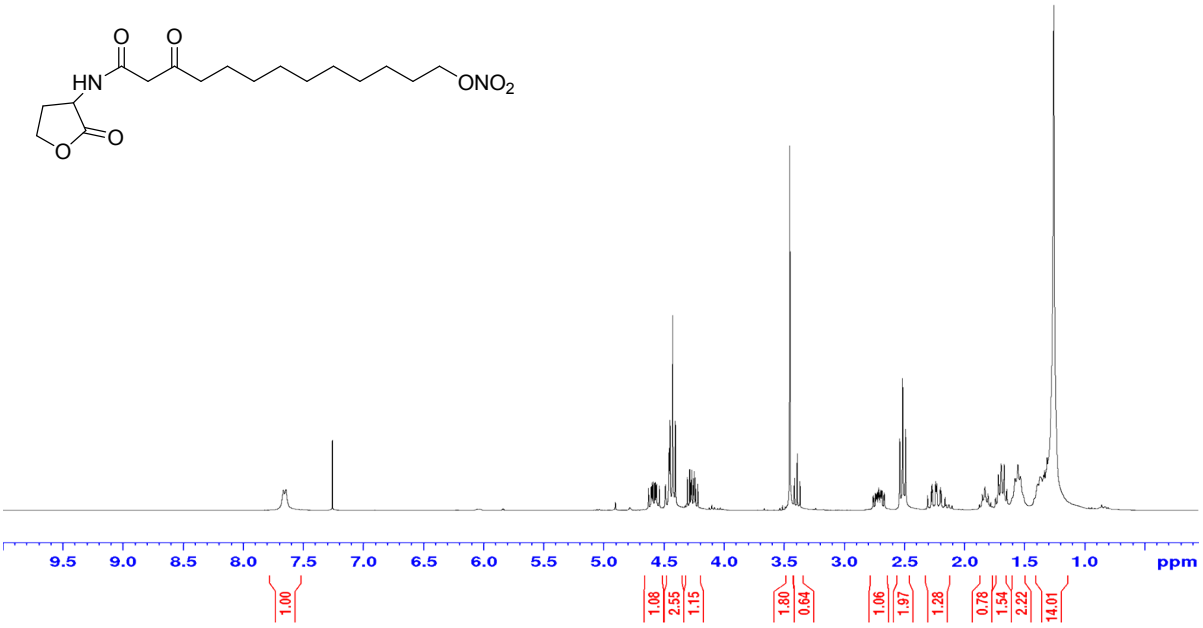
^{1}H NMR spectrum of Compound **7e** in $CDCl_3$



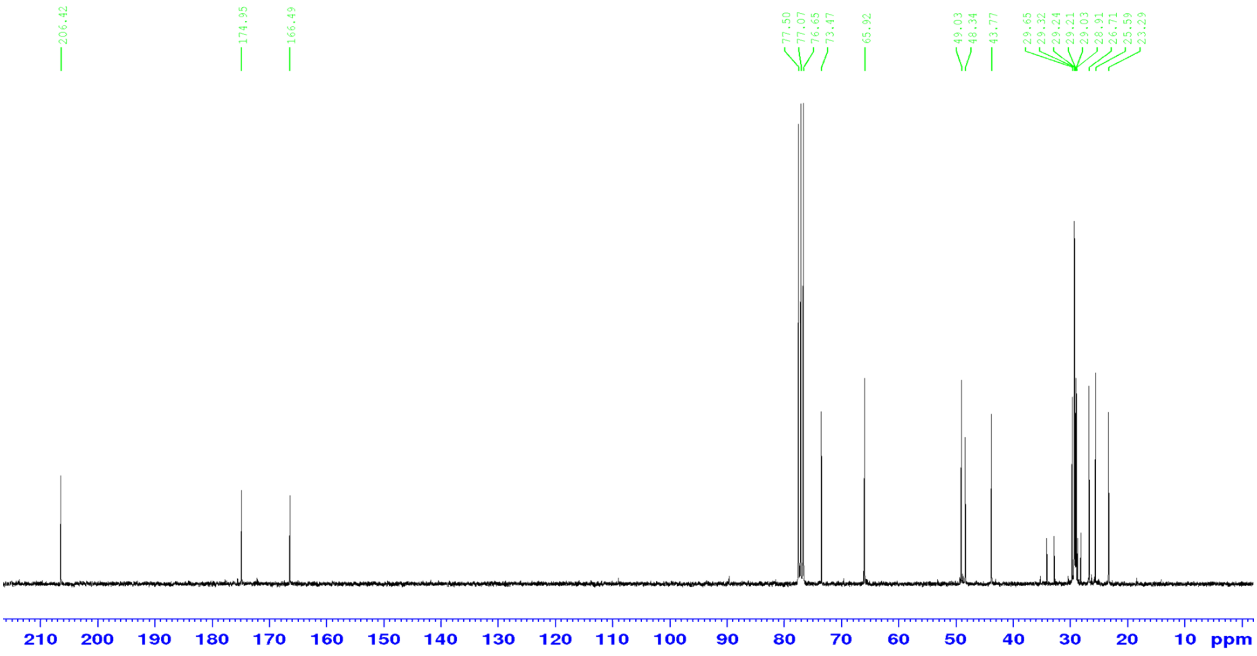
^{13}C NMR spectrum of Compound **7e** in $CDCl_3$



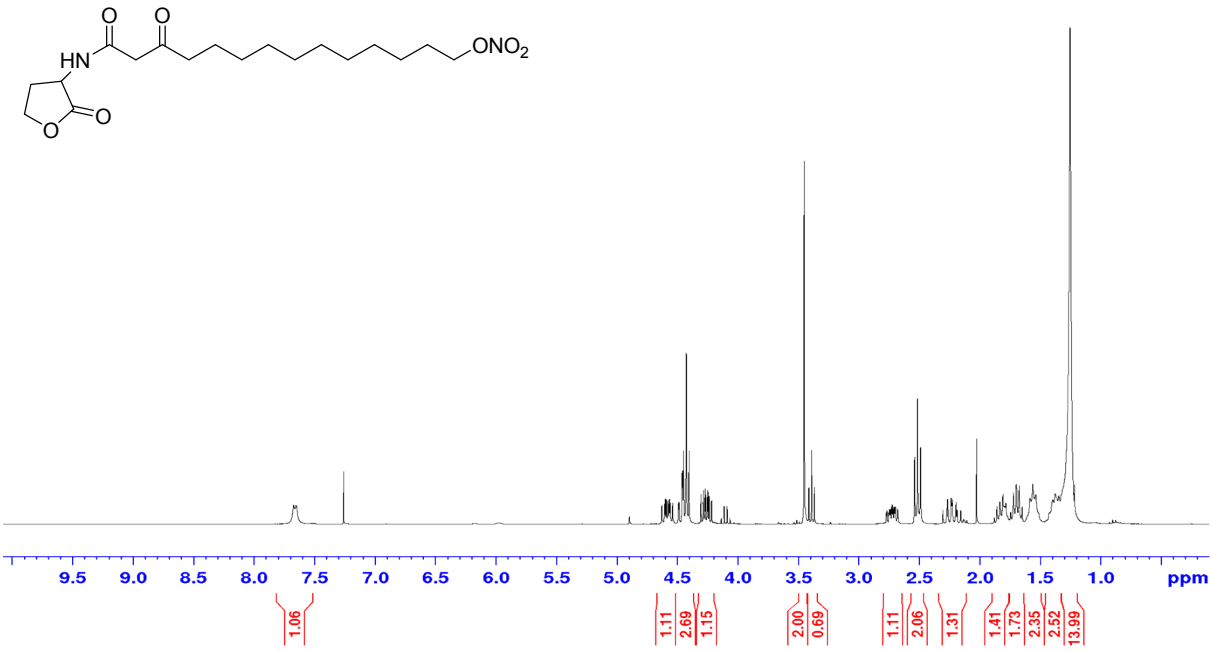
^{1}H NMR spectrum of Compound **10a** in $CDCl_3$



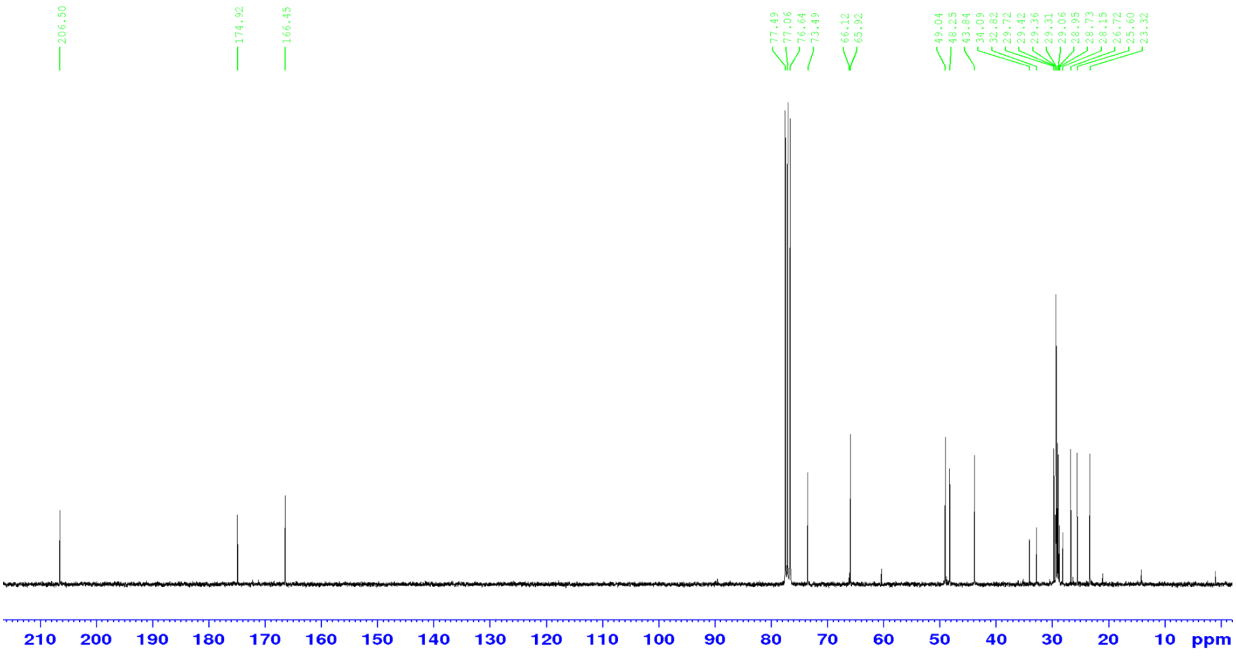
^{13}C NMR spectrum of Compound **10a** in $CDCl_3$



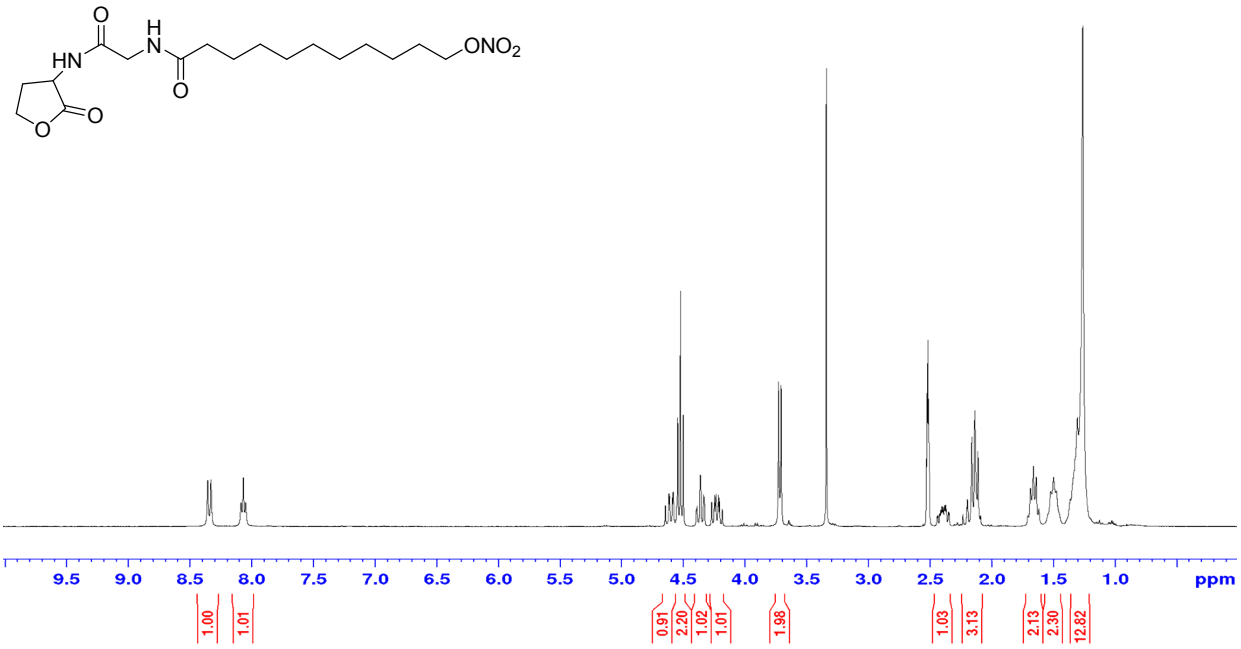
^{1}H NMR spectrum of Compound **10b** in $CDCl_3$



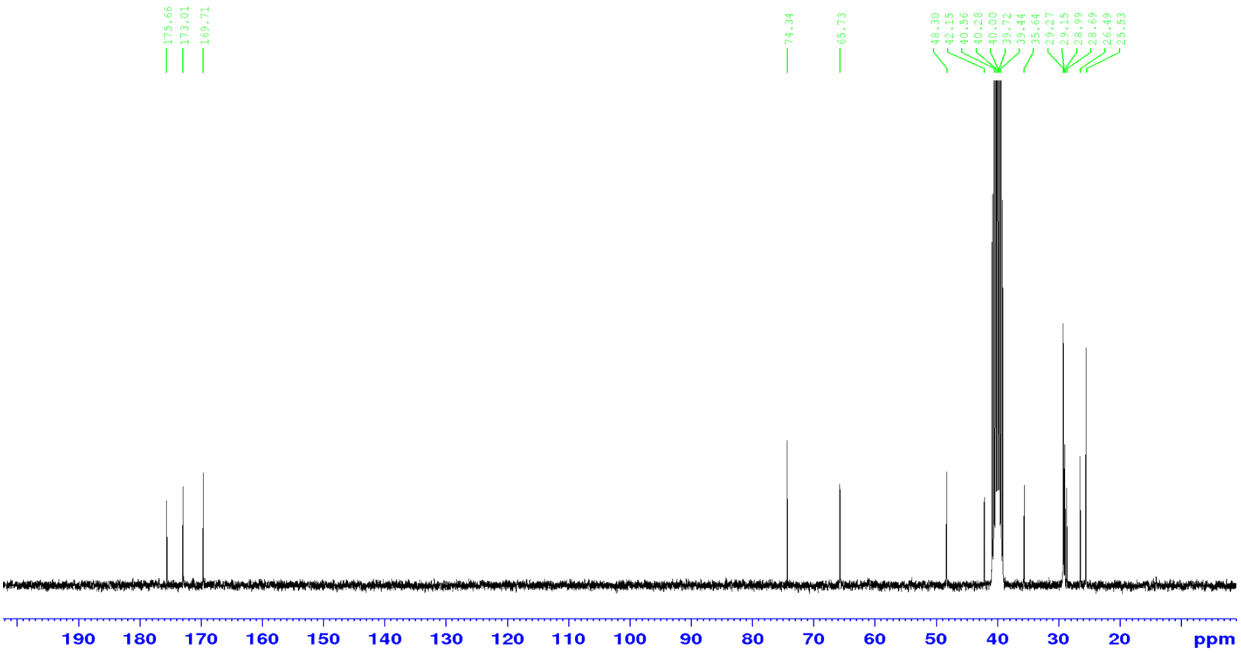
^{13}C NMR spectrum of Compound **10b** in $CDCl_3$



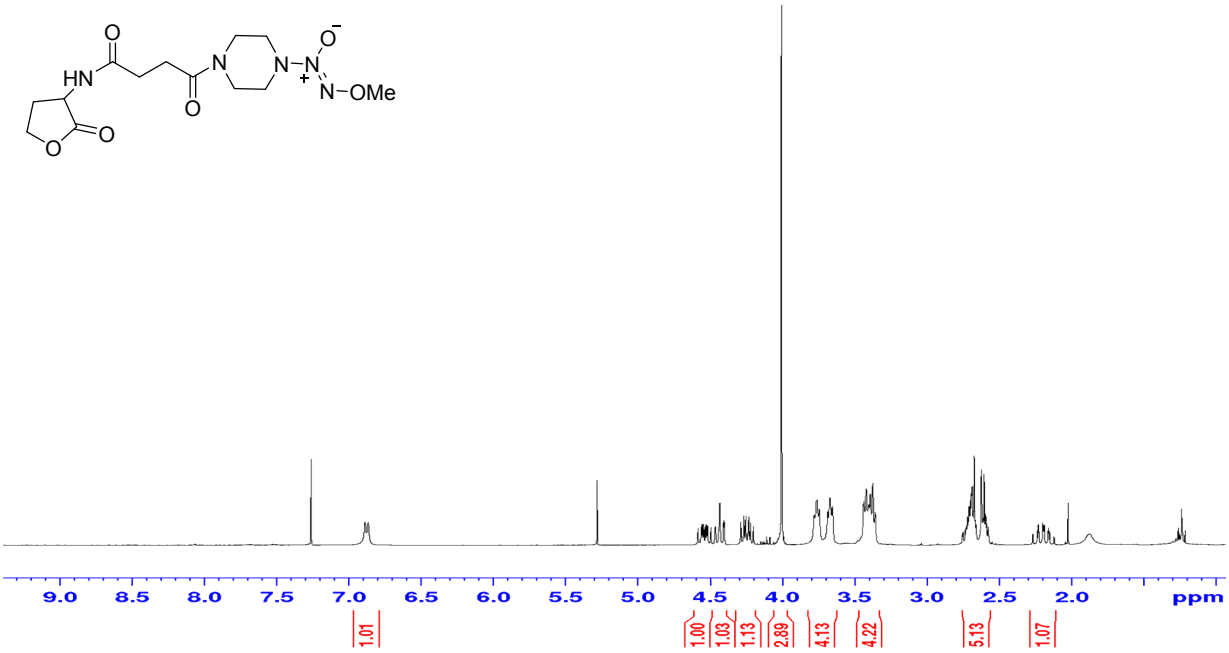
[1]H NMR spectrum of Compound **13** in DMSO-*d6*



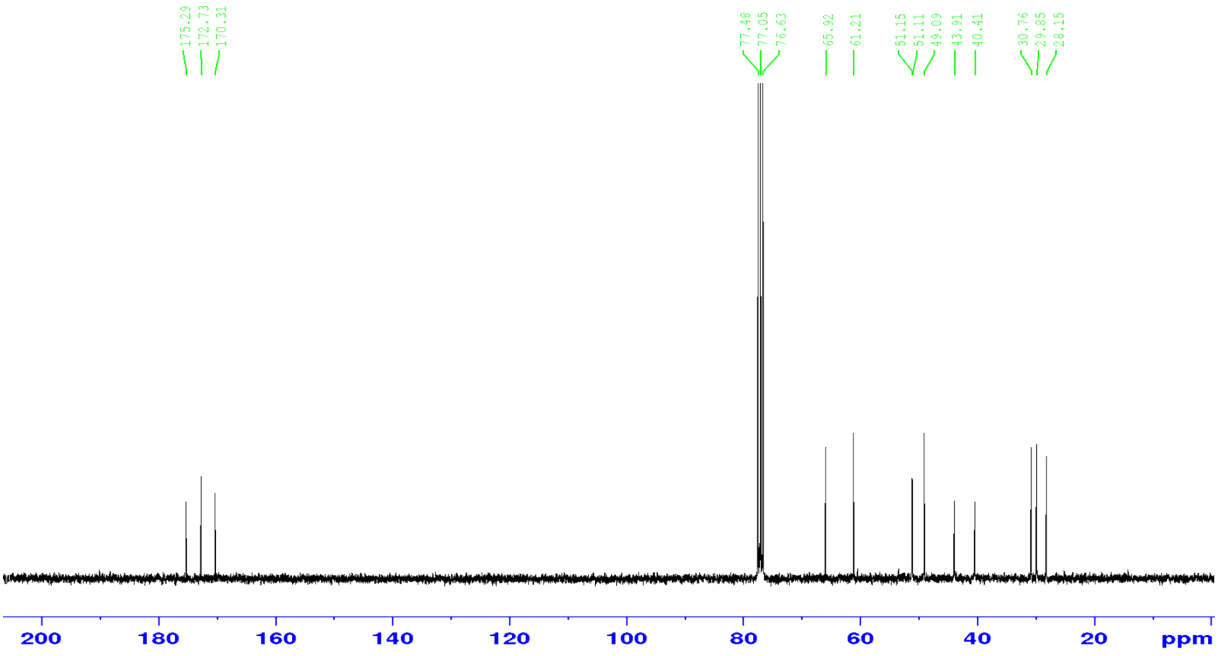
[13]C NMR spectrum of Compound **13** in DMSO-*d6*



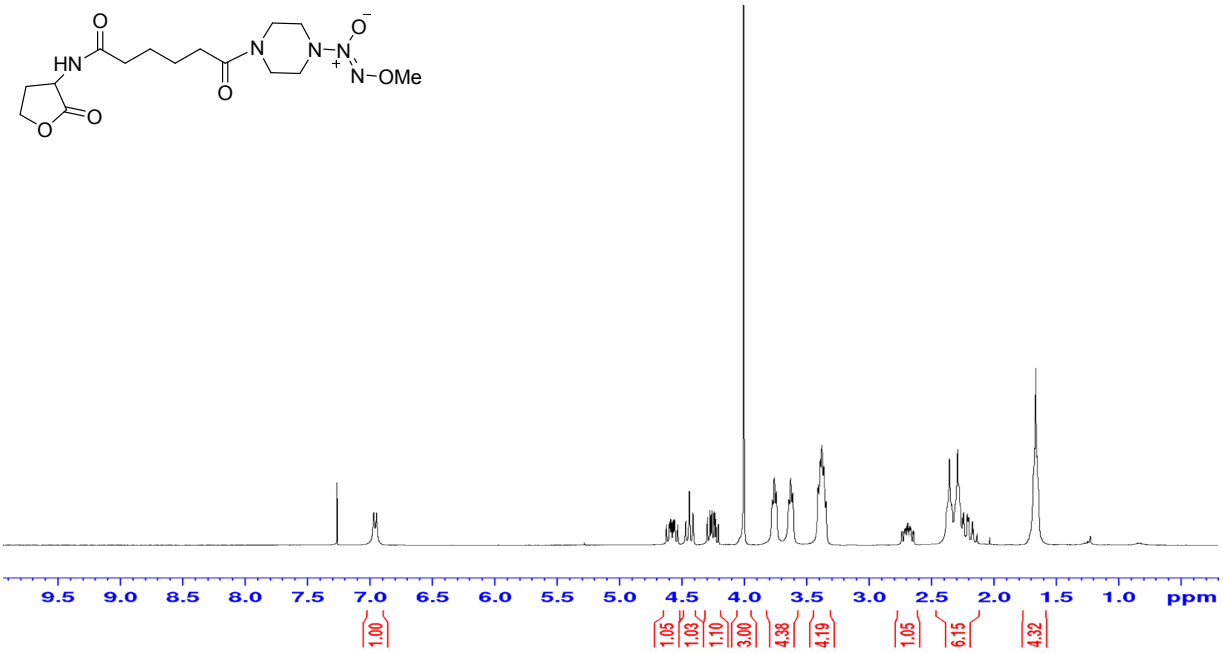
^{1}H NMR spectrum of Compound **21a** in $CDCl_3$



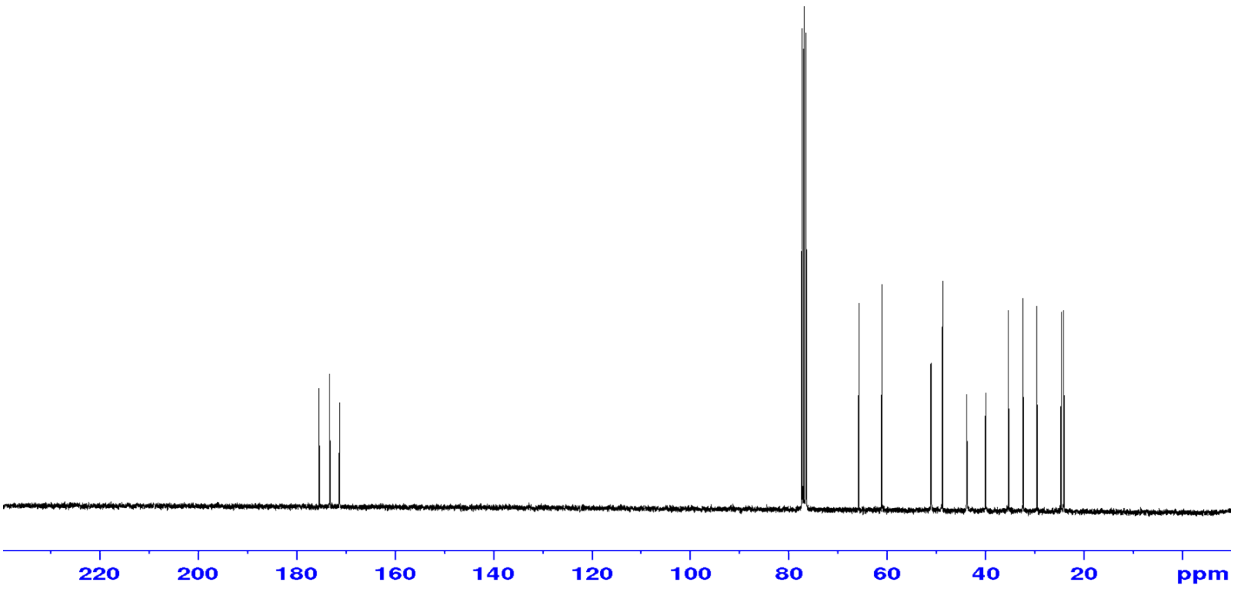
^{13}C NMR spectrum of Compound **21a** in $CDCl_3$



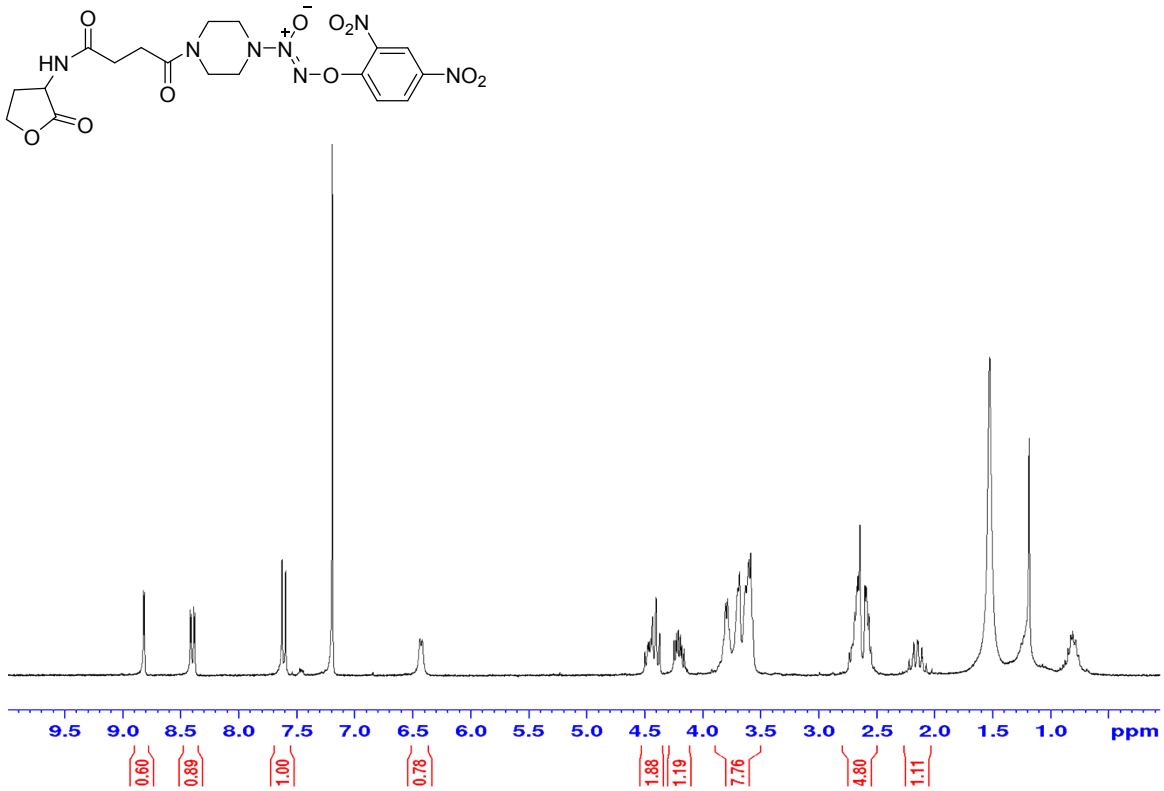
^{1}H NMR spectrum of Compound **21b** in $CDCl_3$



^{13}C NMR spectrum of Compound **21b** in $CDCl_3$



^{1}H NMR spectrum of Compound **22a** in $CDCl_3$



2) X-ray crystal structure information

Structure determination

Reflexion data were measured with an Enraf-Nonius CAD-4 diffractometer in θ/2θ scan mode using nickel filtered copper radiation (γ 1.5418Å). Reflexions with I>3σ(I) were considered observed. The structures were determined by direct phasing and Fourier methods. Hydrogen atoms were included in calculated position s and were assigned thermal parameters equal to those of the atom to which they were bonded. Positional and anisitropic thermal parameters for the noNHydrogen atoms were refined using full matrix least squares. Reflexion weights used were 1/σ2(Fo), with σ(Fo) being derived from σ(Io) = [σ2(Io) + (0.04Io)2]1/2. The weighted residual is defined as Rw = (ΣwΔ2/ΣwFo2)1/2. Atomic scattering factors and anomalous dispersion parameters were from International Tables for X-ray crystallography1. Structure solutions were performed by SIR922 and refinements used RAELS3. ORTEP-II4 running on a Macintosh was used for the structural diagrams.

Compound: 2-Oxo-2-(2-oxotetrahydrofuran-3-ylamino)ethyl nitrate (7a)

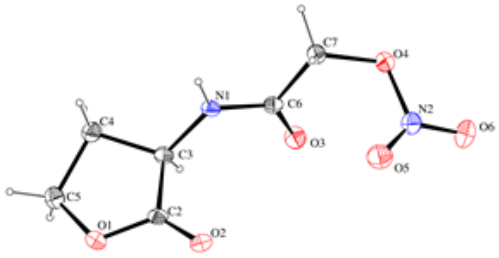


Figure 1: ORTEP diagram for **7a**

CCDC number: 1408469

Table 1. Experimental details

	inp21byn
Crystal data	
Chemical formula	$C_6H_8N_2O_6$
M_r	204.14
Crystal system, space group	Monoclinic, $P2_1/n$
Temperature (K)	152
a, *b*, *c* (Å)	10.0324 (6), 5.2469 (2), 16.1420 (9)
b (°)	101.826 (3)
V (Å^3)	831.66 (8)
Z	4
Radiation type	Mo *K*a
m (mm^{-1})	0.15
Crystal size (mm)	0.47 × 0.27 × 0.08
Data collection	
Diffractometer	Bruker kappa APEXII CCD Diffractometer
Absorption correction	Multi-scan *SADABS* (Bruker, 2001)
T_{min}, T_{max}	0.934, 0.988
No. of measured, independent and observed [$I > 2s(I)$] reflections	6746, 1812, 1552
R_{int}	0.032
Refinement	
$R[F^2 > 2s(F^2)]$, $wR(F^2)$, S	0.032, 0.089, 1.04
No. of reflections	1812

No. of parameters	127
No. of restraints	0
H-atom treatment	H-atom parameters constrained
$D\rho_{max}$, $D\rho_{min}$ (e Å^{-3})	0.27, -0.24

Computer programs: *APEX2* (Bruker, 2007), *SHELXS-97* (Sheldrick, 2008), *SHELXL-97* (Sheldrick, 2008), *SHELXTL-Plus* (Sheldrick, 2008).

Table 2. Selected geometric parameters (Å, º)

O1—C2	1.3362 (15)	C2—C3	1.5171 (17)
O1—C5	1.4634 (17)	C3—C4	1.5223 (17)
O2—C2	1.2065 (16)	C3—H3	1.0000
O3—C6	1.2210 (15)	C4—C5	1.5226 (19)
O4—N2	1.4037 (15)	C4—H4B	0.9900
O4—C7	1.4400 (15)	C4—H4A	0.9900
O5—N2	1.2017 (16)	C5—H5B	0.9900
O6—N2	1.2005 (15)	C5—H5A	0.9900
N1—C6	1.3363 (16)	C6—C7	1.5244 (17)
N1—C3	1.4388 (15)	C7—H7B	0.9900
N1—H1	0.8800	C7—H7A	0.9900
C2—O1—C5	109.89 (10)	C5—C4—H4B	111.5
N2—O4—C7	112.50 (9)	C3—C4—H4A	111.5
C6—N1—C3	121.31 (10)	C5—C4—H4A	111.5
C6—N1—H1	119.3	H4B—C4—H4A	109.3
C3—N1—H1	119.3	O1—C5—C4	105.00 (10)
O6—N2—O5	129.31 (13)	O1—C5—H5B	110.7
O6—N2—O4	112.44 (11)	C4—C5—H5B	110.7
O5—N2—O4	118.25 (11)	O1—C5—H5A	110.7
O2—C2—O1	122.41 (12)	C4—C5—H5A	110.7
O2—C2—C3	127.51 (11)	H5B—C5—H5A	108.8
O1—C2—C3	110.08 (10)	O3—C6—N1	124.92 (11)
N1—C3—C2	112.01 (10)	O3—C6—C7	121.16 (11)
N1—C3—C4	116.74 (10)	N1—C6—C7	113.91 (10)
C2—C3—C4	102.41 (10)	O4—C7—C6	109.72 (10)
N1—C3—H3	108.4	O4—C7—H7B	109.7

C2—C3—H3	108.4	C6—C7—H7B	109.7
C4—C3—H3	108.4	O4—C7—H7A	109.7
C3—C4—C5	101.36 (10)	C6—C7—H7A	109.7
C3—C4—H4B	111.5	H7B—C7—H7A	108.2
C7—O4—N2—O6	170.32 (11)	N1—C3—C4—C5	-153.99 (11)
C7—O4—N2—O5	-10.48 (16)	C2—C3—C4—C5	-31.27 (12)
C5—O1—C2—O2	179.63 (11)	C2—O1—C5—C4	-19.87 (14)
C5—O1—C2—C3	-1.07 (13)	C3—C4—C5—O1	31.65 (13)
C6—N1—C3—C2	98.81 (13)	C3—N1—C6—O3	2.77 (19)
C6—N1—C3—C4	-143.60 (12)	C3—N1—C6—C7	-177.92 (10)
O2—C2—C3—N1	-33.54 (17)	N2—O4—C7—C6	-65.25 (13)
O1—C2—C3—N1	147.21 (10)	O3—C6—C7—O4	-11.01 (16)
O2—C2—C3—C4	-159.40 (12)	N1—C6—C7—O4	169.65 (10)
O1—C2—C3—C4	21.34 (13)		

Compound: *O*²-(2,4-Dinitrophenyl)-1-(4-(4-oxo-4-(2-oxotetrahydrofuran-3-ylamino)butanoyl)piperazin-1-yl)diazen-1-ium-1,2-diolate (22a).

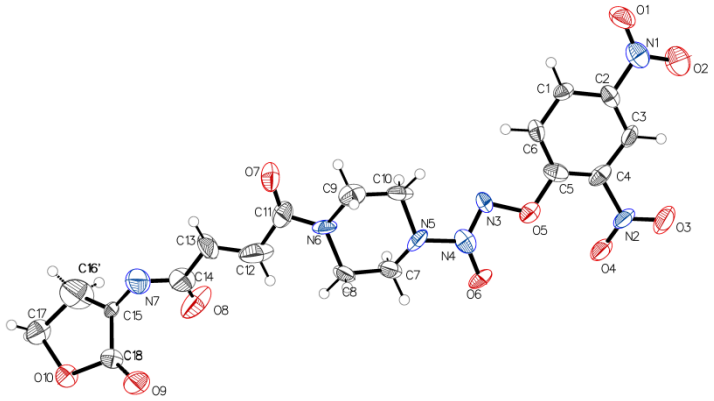


Figure 2: ORTEP diagram for **22a.**

CCDC number 1408468

Table 3. Experimental details

	sam12_p21byc
Crystal data	

Chemical formula	$C_{18}H_{17}N_7O_{10}\cdot CHCl_3$
M_r	610.75
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	156
a, b, c (Å)	12.6131 (5), 26.049 (1), 8.1912 (4)
β (°)	108.884 (2)
V (Å^3)	2546.43 (19)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.43
Crystal size (mm)	0.30 × 0.10 × 0.05
Data collection	
Diffractometer	CCD area detector diffractometer
Absorption correction	Multi-scan *SADABS2007*/4 (Bruker,2007/4) was used for absorption correction. wR2(int) was 0.0516 before and 0.0439 after correction. The Ratio of minimum to maximum transmission is 0.8938. The λ/2 correction factor is 0.0015.
T_{min}, T_{max}	0.667, 0.746
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	17884, 4460, 3699

R_{int}	0.038
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.595
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.270, 0.675, 3.51
No. of reflections	4460
No. of parameters	380
No. of restraints	12
H-atom treatment	H-atom parameters constrained
$\Delta\rangle_{max}$, $\Delta\rangle_{min}$ (e Å^{-3})	1.44, -1.25

Computer programs: *SAINT* v7.46A (Bruker, 2008), *SHELXL* (Sheldrick, 2008), Olex2 (Dolomanov *et al.*, 2009).

Table 4: Geometric parameters *(Å, º)*

C1—C2	1.431 (19)	C15—C19'	1.50 (3)
C1—H1	0.9500	C15'—C16'	1.58 (4)
C1CL—H1CL	1.0000	C16'—C17'	1.46 (5)
C2—N1	1.464 (19)	C16'—H2XA	0.9900
C3—C2	1.34 (2)	C16'—H2XB	0.9900
C3—C4	1.44 (2)	C17—C16	1.60 (5)
C3—H3	0.9500	C17—H3XA	0.9900
C4—C5	1.33 (2)	C17—H3XB	0.9900
C4—N2	1.506 (17)	C17'—H1AA	0.9900
C5—O5	1.414 (17)	C17'—H1AB	0.9900
C6—C1	1.404 (19)	C19—C15'	1.56 (3)
C6—C5	1.40 (2)	C19—O9	1.211 (17)
C6—H6	0.9500	C19—O10'	1.35 (3)
C7—C8	1.50 (2)	Cl1—C1CL	1.725 (18)
C7—H7A	0.9900	Cl2—C1CL	1.741 (19)
C7—H7B	0.9900	Cl3—C1CL	1.78 (2)
C8—H9A	0.9900	N1—O1	1.252 (18)
C8—H9B	0.9900	N1—O2	1.242 (19)
C8—N6	1.496 (19)	N2—O3	1.183 (17)
C9—C10	1.53 (2)	N2—O4	1.205 (16)
C9—H2	0.9900	N3—N4	1.276 (17)
C9—H4	0.9900	N4—N5	1.466 (17)
C9—N6	1.431 (18)	N4—O6	1.225 (16)
C10—H10A	0.9900	N5—C7	1.44 (2)

C10—H10B	0.9900	N5—C10	1.479 (18)
C11—C12	1.47 (3)	N6—C11	1.37 (2)
C11—O7	1.17 (2)	N7—C15	1.57 (4)
C12—H12	0.9500	N7—C15'	1.39 (3)
C13—C12	1.44 (3)	O5—N3	1.409 (16)
C13—H13	0.9500	O6—H6A	0.8400
C14—C13	1.46 (2)	O9—C19'	1.211 (17)
C14—N7	1.36 (3)	O10—C17	1.64 (5)
C14—O8	1.21 (2)	O10—C19'	1.55 (2)
C15—C16	1.27 (3)	O10'—C17'	1.59 (4)
Cl1—C1CL—Cl2	116.5 (12)	N6—C9—H2	109.6
Cl1—C1CL—Cl3	108.5 (11)	N6—C9—H4	109.6
Cl1—C1CL—H1CL	108.1	N6—C9—C10	110.4 (12)
Cl2—C1CL—Cl3	107.2 (11)	H2—C9—H4	108.1
Cl2—C1CL—H1CL	108.1	C10—C9—H2	109.6
Cl3—C1CL—H1CL	108.1	C10—C9—H4	109.6
N3—O5—C5	109.8 (10)	N5—C10—C9	107.6 (11)
N4—O6—H6A	109.5	N5—C10—H10A	110.2
C19'—O10—C17	108.5 (19)	N5—C10—H10B	110.2
O1—N1—C2	121.1 (13)	C9—C10—H10A	110.2
O2—N1—O1	123.9 (14)	C9—C10—H10B	110.2
O2—N1—C2	114.7 (14)	H10A—C10—H10B	108.5
O3—N2—O4	122.5 (12)	O7—C11—N6	118.7 (17)
O3—N2—C4	119.6 (13)	O7—C11—C12	128.0 (18)
O4—N2—C4	117.8 (12)	N6—C11—C12	112.8 (16)
N4—N3—O5	103.0 (11)	C11—C12—H12	122.5
O6—N4—N3	130.6 (13)	C13—C12—C11	115.0 (16)
O6—N4—N5	115.6 (12)	C13—C12—H12	122.5
N3—N4—N5	113.8 (12)	C12—C13—H13	122.2
N4—N5—C10	111.5 (12)	C12—C13—C14	115.5 (17)
C7—N5—N4	111.7 (11)	C14—C13—H13	122.2
C7—N5—C10	112.6 (12)	O8—C14—N7	120.7 (16)
C9—N6—C8	114.7 (13)	O8—C14—C13	127 (2)
C11—N6—C8	124.9 (13)	N7—C14—C13	112.3 (16)
C11—N6—C9	120.3 (13)	N7—C15'—C19	114 (2)
C14—N7—C15'	136 (2)	N7—C15'—C16'	113 (2)
C14—N7—C15	108 (2)	C19—C15'—C16'	100 (2)
C2—C1—H1	120.9	O9—C19—C15'	125.7 (18)
C6—C1—H1	120.9	O9—C19—O10'	116.8 (15)
C6—C1—C2	118.2 (12)	O10'—C19—C15'	117.4 (19)
C1—C2—N1	117.6 (13)	O9—C19'—O10	122.8 (13)
C3—C2—N1	118.9 (13)	O9—C19'—C15	136.4 (15)
C3—C2—C1	123.6 (12)	C15—C19'—O10	100.8 (15)
C2—C3—H3	122.0	C19—O10'—C17'	97 (2)
C2—C3—C4	115.9 (12)	C19'—C15—N7	108.0 (19)
C4—C3—H3	122.0	C16—C15—N7	122 (3)
C3—C4—N2	112.5 (12)	C16—C15—C19'	120 (2)
C5—C4—N2	124.8 (13)	O10'—C17'—H1AA	109.8
C5—C4—C3	122.6 (12)	O10'—C17'—H1AB	109.8
C4—C5—O5	118.5 (13)	H1AA—C17'—H1AB	108.3

C4—C5—C6	121.1 (12)	C16'—C17'—O10'	109 (3)
C6—C5—O5	120.2 (13)	C16'—C17'—H1AA	109.8
C1—C6—H6	120.8	C16'—C17'—H1AB	109.9
C5—C6—C1	118.3 (12)	C15'—C16'—H2XA	111.8
C5—C6—H6	120.8	C15'—C16'—H2XB	111.9
N5—C7—H7A	110.1	C17'—C16'—C15'	100 (2)
N5—C7—H7B	110.1	C17'—C16'—H2XA	111.8
N5—C7—C8	108.1 (14)	C17'—C16'—H2XB	111.9
H7A—C7—H7B	108.4	H2XA—C16'—H2XB	109.6
C8—C7—H7A	110.1	O10—C17—H3XA	112.0
C8—C7—H7B	110.1	O10—C17—H3XB	112.0
N6—C8—C7	107.4 (11)	H3XA—C17—H3XB	109.6
N6—C8—H9A	110.2	C16—C17—O10	99 (3)
N6—C8—H9B	110.2	C16—C17—H3XA	112.0
C7—C8—H9A	110.2	C16—C17—H3XB	112.0
C7—C8—H9B	110.2	C15—C16—C17	111 (2)
H9A—C8—H9B	108.5		
O5—N3—N4—O6	−4.0 (19)	C4—C3—C2—C1	3.5 (19)
O5—N3—N4—N5	175.4 (10)	C4—C5—O5—N3	−179.5 (11)
O6—N4—N5—C7	−41.6 (16)	C5—O5—N3—N4	−179.7 (10)
O6—N4—N5—C10	−168.6 (12)	C5—C4—N2—O3	−164.6 (15)
O7—C11—C12—C13	−13 (3)	C5—C4—N2—O4	19 (2)
O8—C14—N7—C15'	10 (4)	C5—C6—C1—C2	−2.4 (17)
O8—C14—N7—C15	−7 (2)	C6—C1—C2—N1	179.1 (11)
O8—C14—C13—C12	−26 (3)	C6—C1—C2—C3	−1.9 (18)
O9—C19—C15'—N7	46 (3)	C6—C5—O5—N3	4.9 (17)
O9—C19—C15'—C16'	167.7 (17)	C7—N5—C10—C9	60.4 (15)
O9—C19—O10'—C17'	169 (3)	C7—C8—N6—C9	−57.2 (19)
O10—C17—C16—C15	−7 (4)	C7—C8—N6—C11	127.2 (17)
N2—C4—C5—O5	3.7 (19)	C8—N6—C11—O7	177.4 (15)
N2—C4—C5—C6	179.3 (11)	C8—N6—C11—C12	5 (2)
N3—N4—N5—C7	138.9 (13)	C9—N6—C11—O7	2 (2)
N3—N4—N5—C10	11.9 (16)	C9—N6—C11—C12	−170.6 (16)
N4—N5—C7—C8	168.7 (13)	C10—N5—C7—C8	−64.9 (17)
N4—N5—C10—C9	−173.1 (10)	C10—C9—N6—C8	54.7 (16)
N5—C7—C8—N6	59.1 (19)	C10—C9—N6—C11	−129.5 (15)
N6—C9—C10—N5	−53.0 (15)	C13—C14—N7—C15'	−174 (3)
N6—C11—C12—C13	158.4 (19)	C13—C14—N7—C15	168.2 (18)
N7—C14—C13—C12	159 (2)	C14—N7—C15'—C19	33 (4)
N7—C15'—C16'—C17'	151 (3)	C14—N7—C15'—C16'	−80 (3)
N7—C15—C19'—O9	−28 (4)	C14—N7—C15—C19'	90 (2)
N7—C15—C19'—O10	151 (2)	C14—N7—C15—C16	−125 (3)
N7—C15—C16—C17	−139 (3)	C14—C13—C12—C11	167 (2)
C1—C2—N1—O1	6.9 (18)	C15'—C19—O10'—C17'	−15 (4)
C1—C2—N1—O2	−178.5 (13)	C15'—C16'—C17'—O10'	−42 (5)
C1—C6—C5—O5	−179.6 (11)	C19—C15'—C16'—C17'	29 (3)
C1—C6—C5—C4	4.9 (19)	C19—O10'—C17'—C16'	36 (5)
C2—C3—C4—N2	176.8 (11)	C19'—O10—C17—C16	10 (3)
C2—C3—C4—C5	−1.0 (19)	C19'—C15—C16—C17	1 (5)
C3—C2—N1—O1	−172.3 (13)	O10'—C19—C15'—N7	−129 (3)

C3—C2—N1—O2	2.4 (19)	O10'—C19—C15'—C16'	−8 (3)
C3—C4—N2—O3	17.7 (18)	C17—O10—C19'—O9	170 (2)
C3—C4—N2—O4	−158.4 (12)	C17—O10—C19'—C15	−10 (3)
C3—C4—C5—O5	−178.8 (12)	C16—C15—C19'—O9	−173 (3)
C3—C4—C5—C6	−3 (2)	C16—C15—C19'—O10	6 (4)
C4—C3—C2—N1	−177.4 (11)		