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Visible-Light-Mediated Generation of Nitrile Oxides for the Photoredox Synthesis of Isoxazolines and Isoxazoles

Thomas D. Svejstrup,[a] Wojciech Zawodny,[a]
James J. Douglas,[b] Damon Bidgelli,[a] Nadeem S. Sheikh,[c] and Daniele Leonori[a]*

[a] *School of Chemistry, University of Manchester, Oxford Road, M13 9PL, Manchester, UK*
b AstraZeneca, Silk Road Business Park, Macclesfield SK10 2NA, United Kingdom
[c] *Department of Chemistry, Faculty of Science, King Faisal University, Al-Ahsa 31982, Saudi Arabia*
daniele.leonori@manchester.ac.uk

Table of Contents

1 General Experimental Details

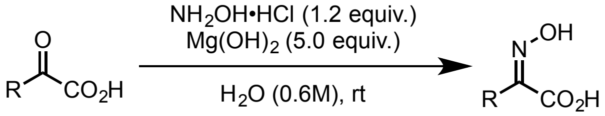
All required fine chemicals were used directly without purification unless stated otherwise. All air and moisture sensitive reactions were carried out under nitrogen atmosphere using standard Schlenk manifold technique. THF was distilled from sodium/benzophenone, CH_2Cl_2 and was distilled from CaH_2, CH_3CN was distilled from activated 4Å molecular sieves, Et_3N was distilled over KOH. *O*-(2,4-dinitrophenyl)hydroxylamine was purchased by Fluorochem and used without further purification. ^1H and ^{13}C Nuclear Magnetic Resonance (NMR) spectra were acquired at various field strengths as indicated and were referenced to $CHCl_3$ (7.27 and 77.0 ppm for ^1H and ^{13}C respectively). ^1H NMR coupling constants are reported in Hertz and refer to apparent multiplicities and not true coupling constants. Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, qi = quintet, sx = sextet, sp = septet, m = multiplet, dd = doublet of doublets, etc.), proton assignment (determined by 2D NMR experiments: COSY, HSQC and HMBC) where possible. High-resolution mass spectra were obtained using a JEOL JMS-700 spectrometer or a Fissions VG Trio 2000 quadrupole mass spectrometer. Spectra were obtained using electron impact ionization (EI) and chemical ionization (CI) techniques, or positive electrospray (ES). Infra-red spectra were recorded using a JASCO FT/IR 410 spectrometer or using an ATI Mattson Genesis Seris FTIR spectrometer as evaporated films or liquid films. Analytical TLC: aluminum backed plates pre-coated (0.25 mm) with Merck Silica Gel 60 F254. Compounds were visualized by exposure to UV-light or by dipping the plates in permanganate ($KMnO_4$) stain followed by heating. Flash column chromatography was performed using Merck Silica Gel 60 (40–63 μm). All mixed solvent eluents are reported as v/v solutions. UV/Vis spectra were obtained using an Agilent 6453 spectrometer and 1 mm High Precision Cell made of quartz from Hellma Analytics.

The LEDs were bought from LEDLightZone.

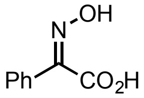
All the reactions were conducted in CEM 10 mL glass microwave tubes.

2 Starting Material Synthesis

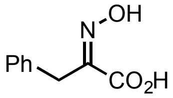
General procedure for the synthesis of hydroxyimino acids – GP1



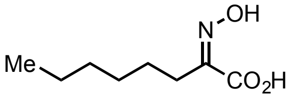
1a–c



1a



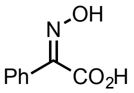
1b



1c

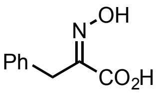
A round bottomed flask equipped with a stirring bar was charged with the oxoacid (1.0 equiv.), $Mg(OH)_2$ (5.0 equiv.) and H_2NOH•HCl (1.2 equiv.). Water (0.7 M) was added and the mixture was stirred overnight. The mixture was cooled to 0 °C and Et_2O was added. Concentrated HCl was added dropwise until the pH of the solution was ~1. The layers were separated and the aqueous phase was extracted with Et_2O (x 2). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and evaporated to give the product that was used without further purification.

(Z)-2-(Hydroxyimino)-2-phenylacetic Acid (1a)



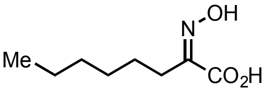
Following **GP1**, phenylglyoxylic acid (1.0 g, 6.66 mmol) gave **1a** (1.03 g, 94%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6, OH missing) δ 7.57–7.34 (5H, m); ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.4, 151.2, 130.9, 129.9, 129.1, 129.0, 127.7, 125.5. This compound has been reported in the literature, but no spectroscopic data were given.[1]

(Z)-2-(Hydroxyimino)-3-phenylpropanoic Acid (1b)



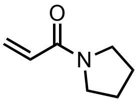
Following **GP2**, phenylpyruvic acid (0.5 g, 3.05 mmol) gave **1b** (0.52 g, 95%) as a white solid. ^{1}H NMR (500 MHz, DMSO-d_6, OH missing) δ 7.31–7.17 (5H, m), 3.81 (2H, s), 3.32 (1H, br s); ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.2, 150.2, 136.8, 128.6, 128.4, 126.2, 29.9. Data in accordance with literature.[2]

(Z)-2-(Hydroxyimino)octanoic Acid (1c)



Following **GP2**, 2-oxooctanoic acid (0.5 g, 3.16 mmol) gave **1c** (0.49 g, 89%) as a white solid. R$_f$ 0.56 [CH_2Cl_2–MeOH (95:5)]; FT-IR ν_{max} (film)/cm^{-1} 3222, 2096, 2955, 2929, 2857, 1695, 1467, 1022; HRMS *m/z* (APCI): Found MH$^+$ 174.1120 $C_8H_{16}NO_3$ requires 174.1125 ^{1}H NMR (400 MHz, DMSO) δ 2.45–2.39 (2H, m), 1.46–1.35 (2H, m), 1.30– 1.16 (3H, m), 0.85 (3H, t, *J* = 6.7 Hz); ^{13}C NMR (101 MHz, DMSO) δ 165.4, 152.0, 30.9, 28.7, 25.4, 24.1, 22.0, 13.9.

1-(Pyrrolidin-1-yl)prop-2-en-1-one (SI-1)

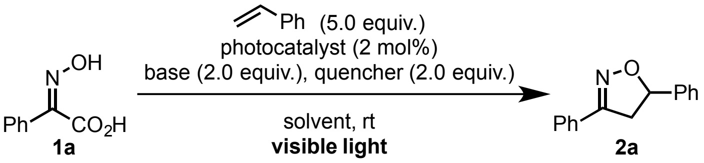


A solution of pyrrolidine (0.45 mL, 5.52 mmol) and Et_3N (1.54 mL, 11.05 mmol) in CH_2Cl_2 (25 mL) was cooled to 0 °C and treated with acryloyl chloride (0.45 mL, 5.52 mmol). The resulting mixture was stirred at 0 °C for 3 h. The reaction was quenched by the addition of water (15 mL). The aqueous phase was separated and extracted with Et_2O (3 × 20 mL). The combined organic layers were washed with HCl (1 M, 15 mL) and brine (15 mL), dried (Na_2SO_4) and evaporated. Purification y column chromatography on silica gel, eluting with petrol–EtOAc (9:1), gave **SI-1** (469 mg, 68%) as an oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.44 (1H, dd, *J* = 16.8, 10.1 Hz), 6.35 (1H, dd, *J* = 16.8, 2.3 Hz), 5.64 (1H, dd. *J* = 10.1, 2.3 Hz), 3.59–3.41 (4H, m), 1.99–1.81 (4H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.6, 128.9, 127.4, 46.7, 46.0, 26.3. Data in accordance with literature.[3]

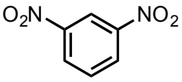
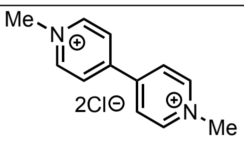
3 [3 + 2] Dipolar Cycloaddition Reactions

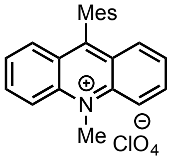
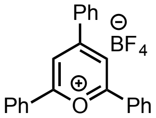
3.1 Reaction Optimization with 1a and styrene

General procedure for the reaction optimization – GP2



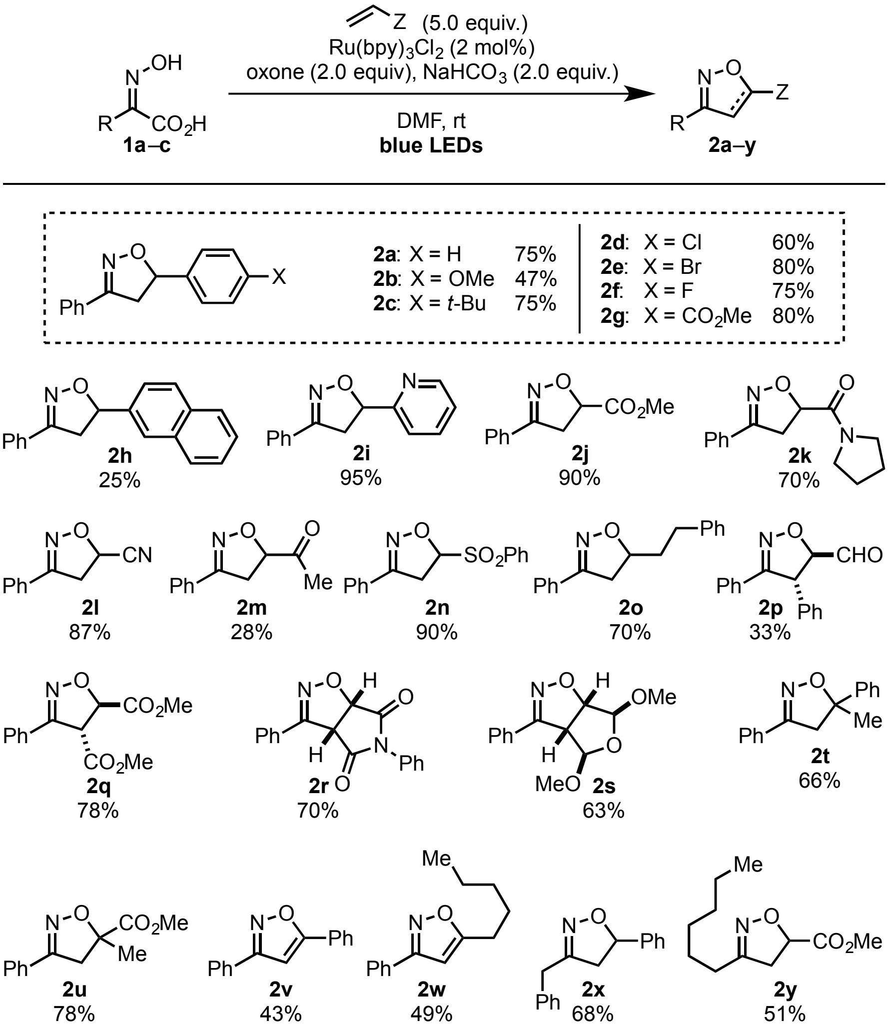
A dry tube equipped with a stirring bar was charged with **1a** (1.0 equiv.), the base (if solid) (2.0 equiv.), the photocatalyst (2 mol%) and the quencher (if solid) (2.0 equiv.). The tube was sealed and styrene (5.0 equiv.) and the solvent (0.3 M) were added. The mixture was stirred for 1 min and then the light was turned ON. The mixture was stirred under irradiation at room temperature overnight. The light was turned OFF and the internal standars 1,3-dintritrobeneze (33%) was added. The mixture was diluted with H_2O and EtOAc. The aqueous layer was extracted with EtOAc (x 2). The combined organic layers were dried ($MgSO_4$), filtered and evaporated. The reaction yields were obtained by ^1H NMR spectroscopy analysis.

Entry	Photocatalyst	Base	Quencher	Solvent	Light	Yield (%)
1	EY	$NaHCO_3$	Air	DMF	30W CFL	6
2	EY	$NaHCO_3$	$BrCCl_3$	DMF	green LEDs	12
3	EY	$NaHCO_3$		DMF	green LEDs	traces
4	EY	$NaHCO_3$		DMF	green LEDs	traces
5	EY	$NaHCO_3$	oxone	DMF	green LEDs	38
6	$Ru(bpy)_3Cl_2$	$NaHCO_3$	oxone	DMF	30W CFL	41
7	**$Ru(bpy)_3Cl_2$**	**$NaHCO_3$**	**oxone**	**DMF**	**blue LEDs**	**75**
8	–	$NaHCO_3$	oxone	DMF	blue LEDs	traces
9	$Ru(bpy)_3Cl_2$	–	oxone	DMF	blue LEDs	traces
10	$Ru(bpy)_3Cl_2$	$NaHCO_3$	–	DMF	blue LEDs	traces
11	$Ru(bpy)_3Cl_2$	$NaHCO_3$	oxone	DMF	–	traces
12	$Ru(bpy)_3Cl_2$	$NaHCO_3$	oxone	MeCN	blue LEDs	11
13	$Ru(bpy)_3Cl_2$	$NaHCO_3$	oxone	DMSO	blue LEDs	traces
14	$Ru(bpy)_3Cl_2$	Cs_2CO_3	oxone	DMF	blue LEDs	31
15	$Ru(bpy)_3Cl_2$	$(i\text{-}Pr)_2NEt$	oxone	DMF	blue LEDs	18
16	$Ir(ppy)_3$	$NaHCO_3$	oxone	DMF	blue LEDs	16

17		$NaHCO_3$	oxone	DMF	30W CFL	3
18		$NaHCO_3$	oxone	DMF	30W CFL	63

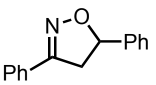
3.2 Substrate Scope

General procedure for the [3 + 2] dipolar cycloaddtion – GP3



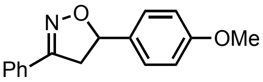
A dry tube equipped with a stirring bar was charged with the hydroxyliminoacid (1.0 equiv.), $Ru(bpy)_3Cl_2$ (2 mol%), $NaHCO_3$ (2.0 equiv.) and oxone (2.0 equiv.). DMF (0.3 M) and the dipolarophile (5.0 equiv.) were then added to the mixture and the tube was sealed. The blue LEDs were switched on and the mixture was stirred under blue LEDs irradiation for 18 hrs. The mixture was diluted with H_2O and EtOAc, the layers were separated and the aqueous phase was extracted with EtOAc (x 2). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and evaporated. Purification by column chromatography on silica gel gave the desired products.

3,5-Diphenyl-4,5-dihydroisoxazole (2a)



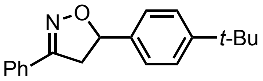
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2a** (75%) as an oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.72–7.31 (10H, m), 5.75 (1H, dd, *J* = 8.4, 10.8 Hz), 3.79 (1H, dd, *J* = 10.8, 17.3 Hz), 3.35 (1H, dd, *J* = 8.4, 17.3 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.9, 140.8, 130.0, 129.3, 128.7, 128.1, 126.6, 125.8, 82.5, 43.2; GC-MS *m/z* (ESI): 223 (M^+), 77. Data in accordance with the literature.[4]

5-(4-Methoxyphenyl)-3-phenyl-4,5-dihydroisoxazole (2b)



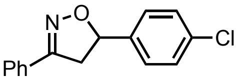
Following **GP3** but using eosin Y as the photoredox catalyst, **1a** (50 mg, 0.30 mmol) gave **2b** (47%) as an oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72–7.70 (2H, m), 7.42–7.40 (3H, m), 7.32 (2H, d, *J* = 8.4 Hz), 6.90 (2H, d, *J* = 8.4 Hz), 5.69 (1H, dd, *J* = 10.8, 8.4 Hz), 3.80 (3H, s), 3.73 (1H, dd, *J* = 16.5, 10.8 Hz), 3.32 (1H, dd, *J* = 16.5, 8.4 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.5, 156.1, 132.7, 130.0, 128.6, 127.3, 126.6, 122.0, 114.0, 82.4, 55.2, 42.8; GC-MS *m/z* (ESI): 253 (M^+), 222, 77. Data in accordance with literature.[5]

5-(4-(*tert*-Butyl)phenyl)-3-phenyl-4,5-dihydroisoxazole (2c)



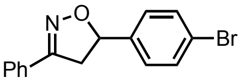
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2c** (75%) as an oil. R_f 0.47 [petrol–EtOAc (80:20)]; FT-IR ν_{max} (film)/cm^{-1}2963, 2903, 2868, 1510, 1463, 1447, 1279, 1109, 1019; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (2H, dd, *J* = 6.6, 3.0 Hz), 7.42 (5H, dd, *J* = 6.4, 2.4 Hz), 7.35 (2H, t, *J* = 7.1 Hz), 5.76–5.70 (1H, m), 3.76 (1H, dd, *J* = 16.6, 10.9 Hz), 3.37 (1H, dd, *J* = 16.6, 8.4 Hz), 1.33 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.3, 151.4, 137.9, 130.2, 129.7, 128.9, 126.9, 125.8, 125.8, 82.6, 43.1, 34.7, 31.4; GC-MS *m/z* (ESI): 279 (M^+), 264, 222, 77; HRMS *m/z* (APCI): Found MH^+ 280.1690 $C_{19}H_{22}NO_3$ requires 280.1696.

5-(4-Chlorophenyl)-3-phenyl-4,5-dihydroisoxazole (2d)



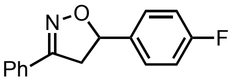
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2d** (60%) as a white solid.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71–7.66 (2H, m), 7.45–7.39 (3H, m), 7.37–7.31 (4H, m), 5.72 (1H, dd, *J* = 11.0, 8.0 Hz), 3.79 (1H, dd, *J* = 16.8, 11.0 Hz), 3.30 (1H, dd, *J* = 16.8, 8.0 Hz); GC-MS *m/z* (ESI): 257 (M^+), 222, 77. Data in accordance with literature.[6]

5-(4-Bromophenyl)-3-phenyl-4,5-dihydroisoxazole (2e)



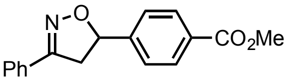
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2e** (94%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79–7.62 (2H, m), 7.60–7.50 (2H, m), 7.47–7.38 (3H, m), 7.29 (2H, dd, *J* = 8.8, 2.0 Hz), 5.72 (1H, dd, *J* = 11.0, 8.0 Hz), 3.81 (1H, dd, *J* = 16.6, 11.0 Hz), 3.31 (1H, dd, *J* = 16.6, 8.0 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.1, 140.0, 131.9, 130.3, 129.2, 128.8, 127.6, 126.8, 122.2, 81.8, 43.2; GC-MS *m/z* (ESI): 301 & 303 (M^+), 222, 77. Data in accordance with the literature.[7]

5-(4-Fluorophenyl)-3-phenyl-4,5-dihydroisoxazole (2f)



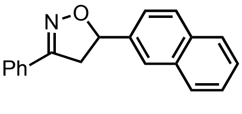
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2f** (75%) as a white solid.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (2H, dd, *J* = 8.0, 4.0 Hz), 7.36–7.43 (5H, m), 7.04–7.09 (2H, m), 5.73 (1H, dd, *J* = 11.0, 8.2 Hz), 3.78 (1H, dd, *J* = 16.7, 11.0 Hz), 3.31 (1H, dd, *J* = 16.7, 8.2 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5 (d, *J* = 245 Hz), 156.5, 136.7, 136.7, 130.2, 128.8, 127.7, 127.6, 126.7, 115.6 (d, *J* = 21.2 Hz), 81.9, 43.2; GC-MS *m/z* (ESI): 241 (M^+), 222, 77. Data in accordance with literature.[8]

Methyl 4-(3-Phenyl-4,5-dihydroisoxazol-5-yl)benzoate (2g)



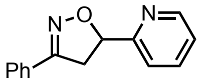
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2g** (80%) as white solid. R_f 0.47 [CH_2Cl_2]; FT-IR ν_{max} (film)/cm^{-1} 2959, 2925, 2385, 2307, 1719, 1440, 1411, 1282, 1260, 1114, 1020; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (2H, d, *J* = 8.4 Hz), 7.68 (2H, dt, *J* = 8.3, 3.5 Hz), 7.49–7.38 (5H, m), 5.78 (1H, dd, *J* = 11.1, 8.0 Hz), 3.91 (3H, s), 3.82 (1H, dd, *J* = 16.7, 11.1 Hz), 3.31 (1H, dd, *J* = 16.7, 8.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.8, 156.2, 146.2, 130.5, 130.2, 130.1, 129.3, 128.9, 126.9, 125.9, 82.0, 52.3, 43.4; GC-MS *m/z* (ESI): 281 (M^+), 266, 222, 77; HRMS *m/z* (APCI): Found MH^+ 282.1123 $C_{17}H_{16}NO_3$ requires 282.1125.

5-(Naphthalen-2-yl)-3-phenyl-4,5-dihydroisoxazole (2h)



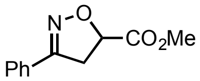
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2h** (25%) as white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.86–7.81 (4H, m), 7.71–7.68 (2H, m), 7.48–7.39 (6H, m), 5.89 (1H, dd, *J* = 10.8, 8.1 Hz), 3.82 (1H, dd, *J* = 16.8, 10.8 Hz), 3.40 (1H, dd, *J* = 16.8, 8.1 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.3, 138.3, 133.4, 130.4, 129.7, 129.1, 129.0, 128.2, 127.9, 127.0, 126.6, 126.5, 125.2, 123.7, 83.0, 43.6; GC-MS *m/z* (ESI): 273 (M^+), 146, 127, 77. Data in accordance with literature.[9]

3-Phenyl-5-(pyridin-2-yl)-4,5-dihydroisoxazole (2i)



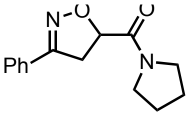
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2i** (90%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60–8.55 (1H, m), 7.75–7.65 (3H, m), 7.60–7.55 (1H, m), 7.40–7.35 (3H, m), 7.30–7.20 (1H, m), 5.88 (1H, dd, *J* = 11.1, 6.8 Hz), 3.86 (1H, dd, *J* = 16.8, 11.1 Hz), 3.69 (1H, dd, *J* = 16.8, 6.8 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.6, 156.3, 149.1, 136.8, 129.9, 129.0, 128.5 (2C), 126.6 (2C), 122.7, 120.4, 82.2, 41.2; GC-MS *m/z* (ESI): 257 (M^+), 146, 77. Data in accordance with literature.[10]

Methyl 3-Phenyl-4,5-dihydroisoxazole-5-carboxylate (2j)



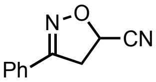
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2j** (94%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70–7.66 (2H, m), 7.43–7.26 (3H, m), 5.20 (1H, dd, *J* = 7.8, 11.1 Hz), 3.82 (3H, s), 3.66 (2H, dd, *J* = 7.8, 11.1 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 155.9, 130.4, 128.7, 128.3, 126.8, 77.9, 52.9, 38.9; GC-MS *m/z* (ESI): 205 (M^+), 146, 77. Data in accordance with the literature.[4]

(3-phenyl-4,5-dihydroisoxazol-5-yl)(pyrrolidin-1-yl)methanone (2k)



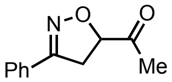
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2k** (70%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (2H, dd, *J* = 7.6, 2.2 Hz), 7.47–7.43 (3H, m), 5.40 (1H, dd, *J* = 11.3, 7.3 Hz), 3.74 (1H, dd, *J* = 17.1, 7.3 Hz); 3.62–3.51 (3H, m), 3.30–3.34 (2H, m); 1.96–1.86 (2H, m), 1.82–1.77 (2H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.1, 158.3, 131.5, 130.3, 129.9 (x 2), 127.9 (x 2), 79.7, 47.8, 47.5, 38.4, 27.0, 25.0; GC-MS *m/z* (ESI): 244 (M^+), 146, 77. Data in accordance with literature.[11]

3-Phenyl-4,5-dihydroisoxazole-5-carbonitrile (2l)



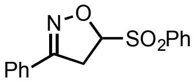
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2l** (94%) as an oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65–7.63 (2H, m), 7.48–7.41 (3H, m), 5.35 (1H, dd, *J* = 6.3, 10.8 Hz), 3.76 (1 H, dd, *J* = 10.8, 16.7 Hz), 3.70 (1H, dd, *J* = 6.1, 16.7 Hz); GC-MS *m/z* (ESI): 172 (M^+), 146, 77. Data in accordance with the literature.[12]

1-(3-Phenyl-4,5-dihydroisoxazol-5-yl)ethan-1-one (2m)



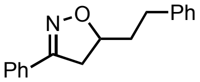
Following **GP3** but using eosin Y as the photoredox catalyst, **1a** (50 mg, 0.30 mmol) gave **2m** (28%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71–7.59 (2H, m), 7.50–7.36 (3H, m), 5.01 (1H, dd, J = 11.7, 6.5 Hz), 3.65 (1H, dd, J = 17.0, 6.5 Hz), 3.47 (1H, dd, J = 17.0, 11.7 Hz), 2.38 (3H, s); GC-MS m/z (ESI): 189 (M^+), 174, 146, 77. Data in accordance with the literature.[13]

3-Phenyl-5-(phenylsulfonyl)-4,5-dihydroisoxazole (2n)



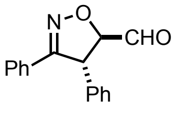
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2n** (75%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97–8.07 (2H, m), 7.80–7.66 (2H, m), 7.63–7.57 (4H, m), 7.45–7.39 (3H, m), 5.56 (1H, dd, J = 10.1, 1.2 Hz), 4.56 (1H, dd, J = 17.8, 1.2 Hz), 4.09 (1H, dd, J = 17.8, 1.2 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.9, 135.2, 129.7, 129.5, 129.2, 127.5, 127.0, 124.4, 93.9, 37.0, 21.5; GC-MS m/z (ESI): 287 (M^+), 146, 77. Data in accordance with literature.[14]

5-Phenethyl-3-phenyl-4,5-dihydroisoxazole (2o)



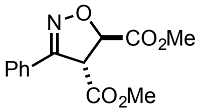
Following **GP3**, **1a** gave **2o** (70%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (2H, m), 7.35–7.33 (3H, m), 7.26 (2H, m), 7.19–7.15 (3H, m), 4.67 (1H, m), 3.29 (1H, dd, J = 16.5, 10.4), 2.90 (1H, dd, J = 16.5, 8.1), 2.78 (1H, ddd, J = 13.9, 9.7, 5.7), 2.74 (1H, dd, J = 13.9, 9.4, 6.8), 2.05 (2H, m), 1.89 (2H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.4, 141.1, 129.9, 129.8, 128.6, 128.4, 128.4, 126.5, 126.2 , 80.2, 39.9, 37.0, 31.8; GC-MS m/z (ESI): 251 (M^+), 174, 146, 77. Data in accordance with literature.[15]

3,4-Diphenyl-4,5-dihydroisoxazole-5-carbaldehyde (2p)



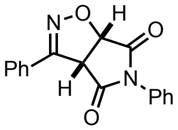
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2p** (33%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (1H, d, J = 0.7 Hz), 7.70–7.19 (10H, m), 4.97 (1H, d, J = 3.5), 4.85 (1H, dd, J = 3.5, 0.7 Hz); GC-MS m/z (ESI): 251 (M^+), 222, 77. Data in accordance with literature.[3]

Dimethyl 3-Phenyl-4,5-dihydroisoxazole-4,5-dicarboxylate (2q)



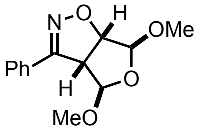
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2q** (78%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78–7.74 (2H, m), 7.44–7.26 (3H, m), 5.46 (1H, d, $J = 4.9$ Hz), 4.62 (1H, d, $J = 4.9$ Hz), 4.29 (2H, qd, $J = 7.3$, 1.6 Hz), 4.18 (2H, q, $J = 7.3$ Hz), 1.33 (3H, t, $J = 7.3$ Hz), 1.18 (3H, t, $J = 7.3$ Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.6, 167.6, 153.8, 130.5, 128.5,127.4, 127.3, 82.1, 62.4, 56.7, 14.1, 13.9; GC-MS *m/z* (ESI): 263 (M^+), 204, 77. Data in accordance with the literature.[4]

3,5-Diphenyl-3a,6a-dihydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)-dione (2r)



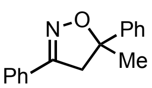
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2r** (70%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03–8.00 (2H, m), 7.46–7.40 (6H, m), 7.26–7.24 (2H, m), 5.65 (1H, d, J = 9.5 Hz), 4.96 (1H, d, J = 9.5 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 169.6, 152.6, 131.1, 130.7, 129.2, 129.1, 128.7, 128.0, 126.6, 126.0, 80.4, 54.9; GC-MS *m/z* (ESI): 292 (M^+), 77. Data in accordance with literature.[4]

4,6-Dimethoxy-3-phenyl-3a,4,6,6a-tetrahydrofuro[3,4-*d*]isoxazole (2s)



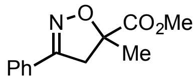
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2s** (70%) as an oil. R_f 0.43[CH_2Cl_2]; FT-IR ν_{max} (film)/cm^{-1} 2964, 2583, 2383, 2354, 2307, 1668, 1646, 1518, 1260, 1105, 1036; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73–7.67 (2H, m), 7.47–7.42 (3H, m), 5.30 (1H, s), 5.23 (1H, d, $J = 9.0$ Hz), 5.17 (1H, s), 4.32 (1H, d, $J = 9.0$ Hz), 3.49 (6H, d, $J = 8.8$ Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.3, 130.6, 129.2, 128.4, 127.0, 111.4, 109.5, 89.7, 59.9, 56.1, 55.9; HRMS *m/z* (APCI): Found MH^+ 250.1072 $C_{13}H_{16}NO_4$ requires 250.1074.

5-Methyl-3,5-diphenyl-4,5-dihydroisoxazole (2t)



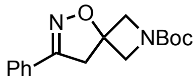
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2t** (66%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72–7.68 (2H, m), 7.56–7.53 (2H, m), 7.42–7.38 (5H, m), 7.33–7.30 (1H, m), 3.53 (2H, q, $J = 15.0$ Hz), 1.85 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.1, 145.4, 129.86, 129.8, 128.6, 128.41, 127.3, 126.5, 124.6, 88.3, 48.6, 28.1; GC-MS *m/z* (ESI): 189 (M^+), 174, 146, 77; GC-MS *m/z* (ESI): 237 (M^+), 222, 77. Data in accordance with literature.[7]

Methyl 5-Methyl-3-phenyl-4,5-dihydroisoxazole-5-carboxylate (2u)



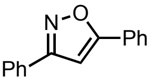
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2u** (78%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68–7.64 (2H, m), 7.42–7.38 (3H, m), 3.89 (1H, d, *J* = 16.9 Hz), 3.81 (3H, s), 3.23 (1H, d, *J* = 16.9 Hz), 1.72 (3H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7, 156.4, 130.4, 129.2, 128.9, 126.9, 86.3, 53.0, 23.7; GC-MS *m/z* (ESI): 219 (M^+), 204, 77. Data in accordance with the literature.[16]

***tert*-Butyl 7-Phenyl-5-oxa-2,6-diazaspiro[3.4]oct-6-ene-2-carboxylate (2v)**



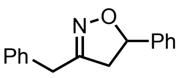
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2v** (65%) as an oil. R_f 0.34 [CH_2Cl_2]; FT-IR ν_{max} (film)/cm^{-1} 2978, 2877, 1698, 1477, 1447, 1401, 1366, 1254, 1156, 1079; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67–7.61 (2H, m), 7.42 (3H, br s), 4.33 (2H, d, *J* = 9.6 Hz, 1H), 4.08 (2H, d, *J* = 9.5 Hz, 1H), 3.59 (2H, s), 1.46 (9H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.8, 156.3, 130.7, 129.0, 126.8, 80.4, 80.3, 63.1, 44.9, 28.5; GC-MS *m/z* (ESI): 288 (M^+), 211, 77; HRMS *m/z* (APCI): Found MH^+ 289.1541 $C_{16}H_{21}N_2O_3$ requires 289.1547.

3,5-Diphenylisoxazole (2w)



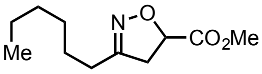
Following **GP3**, **1a** (50 mg, 0.30 mmol) gave **2w** (94%) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90–7.83 (4H, m); 7.52–7.45 (6H, m); 6.83 (1H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 163.1, 130.3, 130.1, 129.2, 129.1, 129.0, 127.6, 126.9, 125.9, 97.6; GC-MS *m/z* (ESI): 221 (M^+), 144, 77. Data in accordance with literature.[17]

5-Benzyl-3-phenyl-4,5-dihydroisoxazole (2y)



Following **GP3**, **1b** (100 mg, 0.56 mmol) gave **2y** (68%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69–7.65 (2H, m), 7.43–7.39 (3H, m), 7.38–7.33 (2H, m), 7.31–7.26 (3H, m), 5.05–4.99 (1H, m), 3.34 (1H, dd, J = 15.0, 10.0 Hz), 3.20 (2H, dd, J = 15.0, 5.0 Hz),3.08 (1H, dd, J = 15.0, 5.0 Hz), 2.92 (2H, dd, J = 15.0, 10.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.4, 136.9, 130.0, 129.7, 129.4, 128.8, 127.1, 126.7, 81.8, 41.0, 39.4; GC-MS *m/z* (ESI): 237 (M^+), 160, 146, 91, 77. Data in accordance with literature.[7]

Methyl 3-Hexyl-4,5-dihydroisoxazole-5-carboxylate (2z)

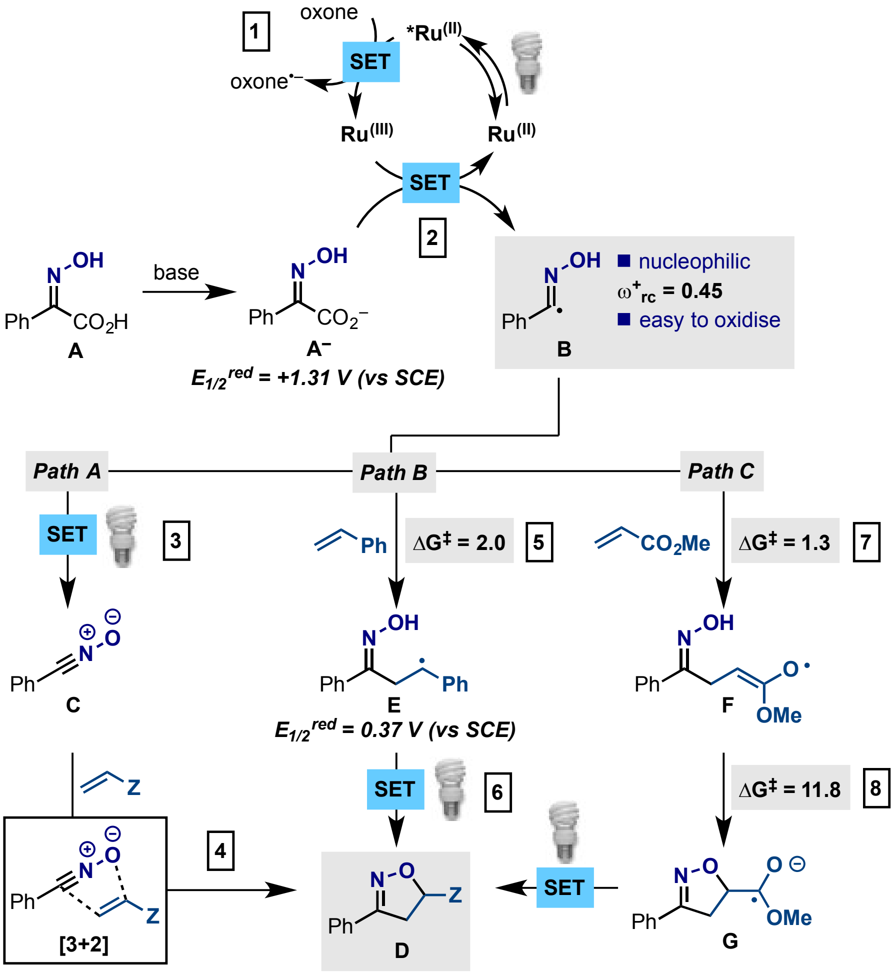


Following **GP3**, **1c** (100 mg, 0.578 mmol) gave **2z** (51%) as a colourless oil; R_f 0.39 [petrol–EtOAc (80:20)]; FT-IR ν_{max} (film)/cm^{-1} 2955, 2857, 1743, 1437, 1288, 1214, 1026; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.98 (1H, t, *J* = 8.9 Hz), 3.79 (3H, s), 3.21 (2H, d, *J* = 8.7 Hz), 2.36 (2H, t, *J* = 7.7 Hz), 1.56 (2H, p, *J* = 7.3 Hz), 1.37–1.20 (6H, m), 0.88 (3H, t, *J* = 6.7 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2, 158.7, 77.0, 52.9, 41.1, 31.5, 29.0, 27.4, 26.4, 22.6, 14.1; GC-MS *m/z* (ESI): 213 (M^+), 198, 154; HRMS *m/z* (APCI): Found MH^+ 214.1434 $C_{11}H_{20}NO_3$ requires 214.1438.

4 Mechanistic Studies

4.1 Proposed Mechanism

There are three possible mechanisms that can explain the formation of **D** from **A**. Both of them start with the photoredox generation of **B**. We propose Path A as the mechanism for the reaction based on the following evidences:



The photoredox cycle is overall supported by all the control experiments present in Section 3.1: entries 8–11 and the Light ON/OFF reaction (Section 4.4).

STEP 1. Oxone is a known oxidant and its potential fell in the range for SET oxidation from *Ru(II). This step is further supported by the evidence that oxone is the only reagent able to quench *Ru(II) (see Stern-Volmer plot, Section 4.3).

STEP 2. We have measured the oxidation potential of **1a**$^-$**Cs**$^+$ to be +1.31 vs SCE. This electrochemical potential is accessible by Ru(III) [$E_{1/2}^{red}$ Ru(III)/Ru(II) = 1.29 V vs

SCE]. The fact that **1a** and **1a**$^{-}$**Na**$^{+}$ do not quench *Ru(II) exclude the possibility of a direct oxidative decarboxylation from *Ru(II) (see Stern-Volmer plot, Section 4.3).

STEP 3. Acyl radicals can easily be oxidised by known oxidants like oxone or by photoredox catalysis. It is difficult here to distinguish between them, but a SET oxidation is feasible.

STEP 4. The cycloaddition with styrene and methylacrylate is a know reaction of nitrile oxides.

Radical **B** is expected to be very nucleophilic. We have performed DFT studies and determined its electrophilicity index. According to our studies, radical **B** is even more nucleophilic than an acyl radical (see Section 5.2).

STEP 5/7. Acyl radicals are known to react with olefin so the radical addition of **B** to styrene and methylacrylate is feasible. We have performed DFT studies and indeed the barriers for radical addition are very small (see Section 5.3).

STEP 6. The oxidation of benzylic radicals is feasible owing to their low oxidation potential. In order to distinguish between Path A and B we have determined the rate of reaction of a series of differentially *para*-substituted styrenes and constructed an Hammett Plot. The Hammett plot had a V-shape that does not support Path B.

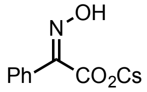
STEP 8. The oxidation of radical **F** is unlikely but a direct cyclization to give the ketyl-radical **G** is feasible. We have calculated the barrier for this process to be 11.8 kcal/mol (see Section

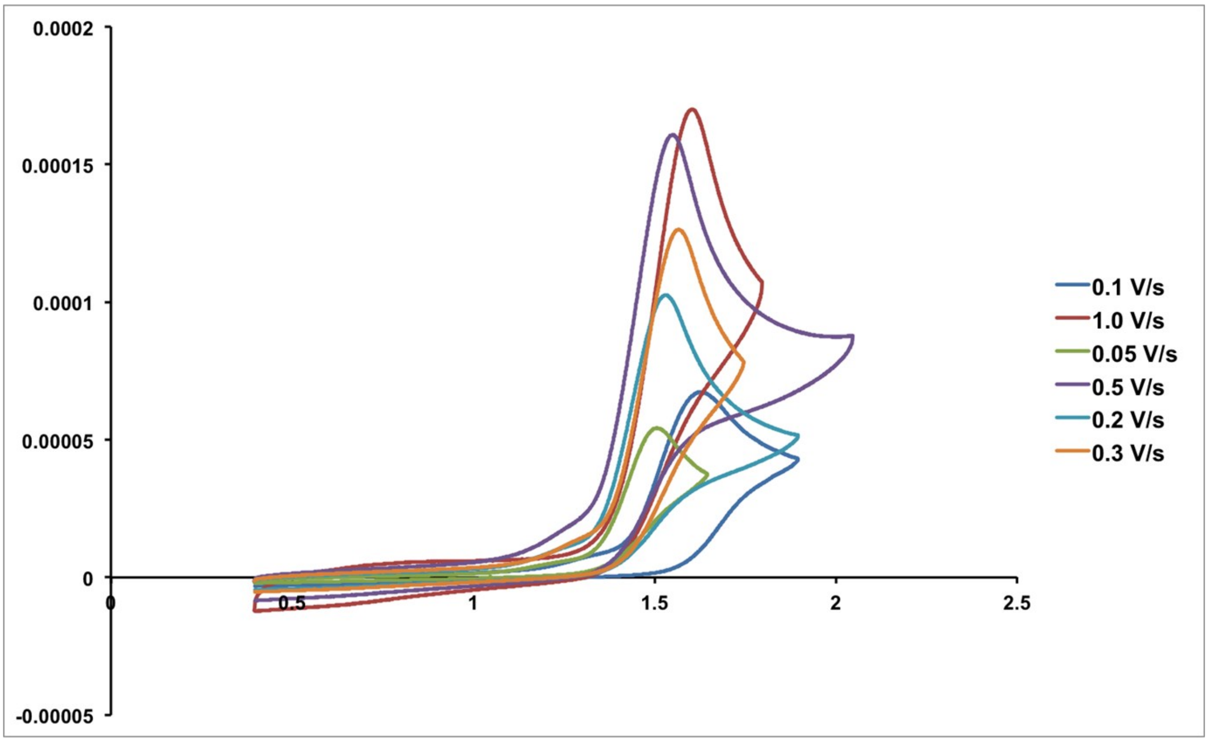
4.2 Electrochemical studies

4.2.1 General Experimental Details

Cyclic voltammetry was conducted on an Autolab PGSTAT100 (Metrohm) using a 3-electrode cell configuration. A glassy carbon working electrode was employed alongside a platinum flag counter electrode and a silver pseudo-reference electrode. Ferrocene solution was added as an internal standard to determine the precise potential scale.[18] These values were converted to a saturated calomel electrode (SCE) scale. 5 mM oxime solutions were freshly prepared in acetonitrile along with 0.1 M supporting electrolyte (tetrabutylammonium tetrafluoroborate). Nitrogen was passed through the sample between measurements to avoid the deleterious influence of oxygen reduction, either directly or through indirect reaction with the oxime-derived species. Samples were examined at 8 different scan rates 0.05 V s^{-1} – 2.00 V s^{-1}. The fragmented species reacted too rapidly to produce an oxidation peak on reversal of the potential sweep direction for all except oxime **c** in Scheme 3. Without the presence of an oxidation peak, or other kinetic information about the species formed, the formal reduction potential can only be estimated to within ~50 mV. As a result, we have used the $E_p$max (potential corresponding to the maximum reductive current in the voltammogram from the fastest scan-rate, 1 V s^{-1}).[19]

4.2.2 Electrochemical Potential and Cyclic Voltammogram

1a^{-}Cs^{+}[1]	$E_{1/2}^{red}$ (vs SCE)
	1.51 V



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[1] The Cs salt of **1a** was used owing to the low solubility of the Na and K salts of **1a** in DMF and MeCN.

4.3 Emission Quenching Experiments – Stern-Volmer Plots

Emission intensities were recorded using a Steady State emission spectra were recorded on an Edinburgh Instrument FP920 Phosphorescence Lifetime Spectrometer equipped with a 5 watt microsecond pulsed xenon flash lamp and a 450 watt steady state xenon lamp and a red sensitive photomultiplier in peltier (air cooled) housing, (Hamamatsu R928P). spectrophotometer. All the of $Ru(bpy)_3Cl_2$ solutions were excited at 470 nm and the emission intensity was collected at 620 nm.[20]

Experimental procedures:

Oxone *as the quencher*

A screw-top quartz cuvette was charged with a 0.05 mM solution of $Ru(bpy)_3Cl_2$ in H_2O (2.0 mL) and the initial emission was collected then the appropriate amount of **oxone** as a 1.0 M solution in H_2O was added. The sample was shaken for 1 min and then the emission of the sample was collected.

1a *as the quencher*

A screw-top quartz cuvette was charged with a 0.05 mM solution of $Ru(bpy)_3Cl_2$ in DMF (2.0 mL) and the initial emission was collected then the appropriate amount of **1a** as a 1.0 M solution in DMF was added. The sample was shaken for 1 min and then the emission of the sample was collected.

$1a^-Na^+$ *as the quencher*

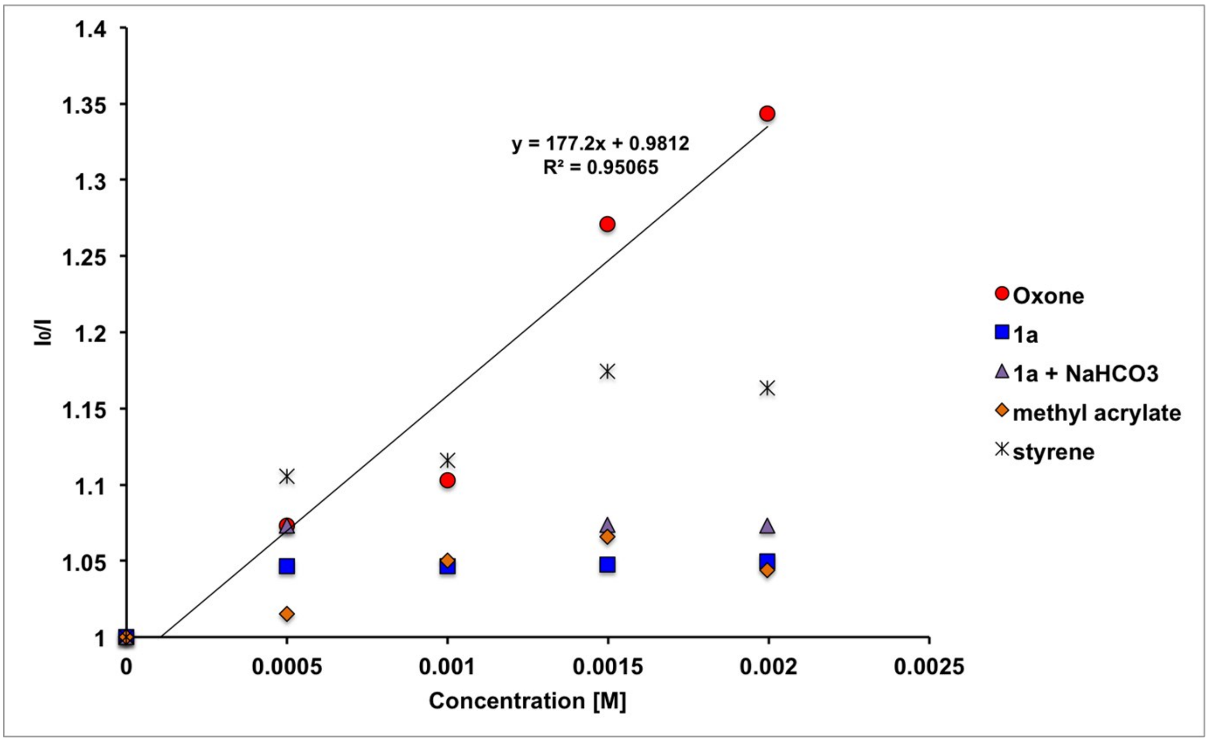
A screw-top quartz cuvette was charged with a 0.05 mM solution of $Ru(bpy)_3Cl_2$ in DMF–H_2O (2.0 mL, 1:1) and the initial emission was collected then the appropriate amount of **$1a^-Na^+$** as a 1.0 M solution in DMF–H_2O (1:1) was added. The sample was shaken for 1 min and then the emission of the sample was collected.

Styrene *as the quencher*

A screw-top quartz cuvette was charged with a 0.05 mM solution of $Ru(bpy)_3Cl_2$ in DMF (2.0 mL) and the initial emission was collected then the appropriate amount of **styrene** as a 1.0 M solution in DMF was added. The sample was shaken for 1 min and then the emission of the sample was collected.

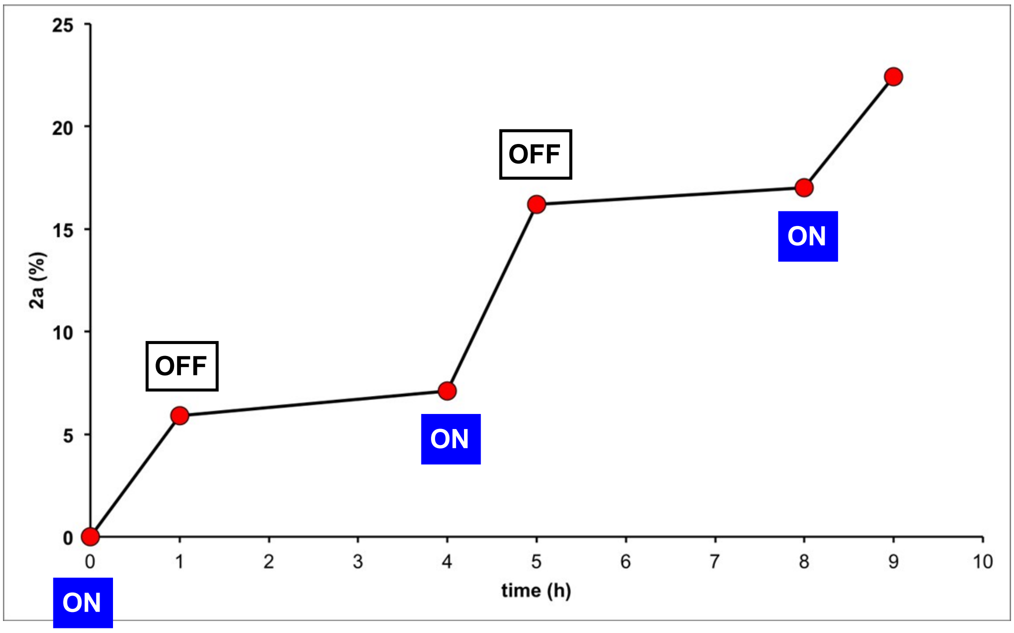
Methyl acrylate *as the quencher*

A screw-top quartz cuvette was charged with a 0.05 mM solution of $Ru(bpy)_3Cl_2$ in DMF (2.0 mL) and the initial emission was collected then the appropriate amount of **methyl acrylate** as a 1.0 M solution in DMF was added. The sample was shaken for 1 min and then the emission of the sample was collected.


1.4
1.35
1.3
1.25
1.2
1.15
1.1
1.05
1
Io/I
0
0.0005
0.001
0.0015
0.002
0.0025
Concentration [M]
y = 177.2x + 0.9812
R² = 0.95065
Oxone
1a
1a + NaHCO3
methyl acrylate
styrene

4.4 Light ON-OFF Experiments

A dry tube equipped with a stirring bar was charged with the **1a** (50 mg, 0.30 mmol, 1.0 equiv.), $Ru(bpy)_3Cl_2$ (4.5 mg, 6.3 µmol, 2 mol%), $NaHCO_3$ (50 mg, 0.61 mmol, 2.0 equiv.) and oxone (186 mg, 0.61 mmol, 2.0 equiv.). DMF (1.0 mL), styrene (0.17 mL, 1.51 mmol, 5.0 equiv.) and undecane as the internal standard (13 µL, 0.06 mmol, 20 mol%) (see Section 8.1 for the calibration curve) were then added to the mixture and the tube was sealed. A reaction aliquot (50 µL) was taken, diluted with EtOAc, filtered through a short pad of silica and analysed by gas chromatography. The blue LEDs were switched ON and the mixture was stirred under blue LEDs irradiation for 1 h at witch time a reaction aliquot (50 µL) was taken, diluted with EtOAc, filtered through a short pad of silica and analysed by gas chromatography. The LEDs were switch OFF and the mixture was stirred in the dark for 3 h at which time a reaction aliquot (50 µL) was taken, diluted with EtOAc, filtered through a short pad of silica and analysed by gas chromatography. The blue LEDs were switched ON and the mixture was stirred under blue LEDs irradiation for 1 h at witch time a reaction aliquot (50 µL) was taken, diluted with EtOAc, filtered through a short pad of silica and analysed by gas chromatography. The LEDs were switch OFF and the mixture was stirred in the dark for 3 h at which time a reaction aliquot (50 µL) was taken, diluted with EtOAc, filtered through a short pad of silica and analysed by gas chromatography. The blue LEDs were switched ON and the mixture was stirred under blue LEDs irradiation for 1 h at witch time a reaction aliquot (50 µL) was taken, diluted with EtOAc, filtered through a short pad of silica and analysed by gas chromatography.

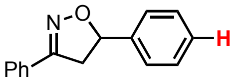


4.5 Kinetic Studies

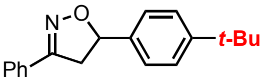
The initial rate kinetic studies were performed following the reactions by gas chromatography analysis using undecane as internal standard.

4.5.1 Calibration Curves

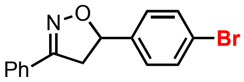
In order to obtain initial rate kinetics, we run calibration curves for all the following reaction products and undecane as the internal standard.



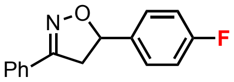
2a



2c

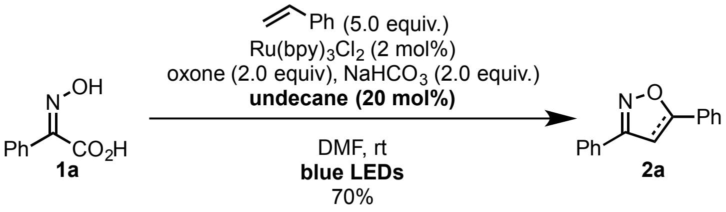


2f

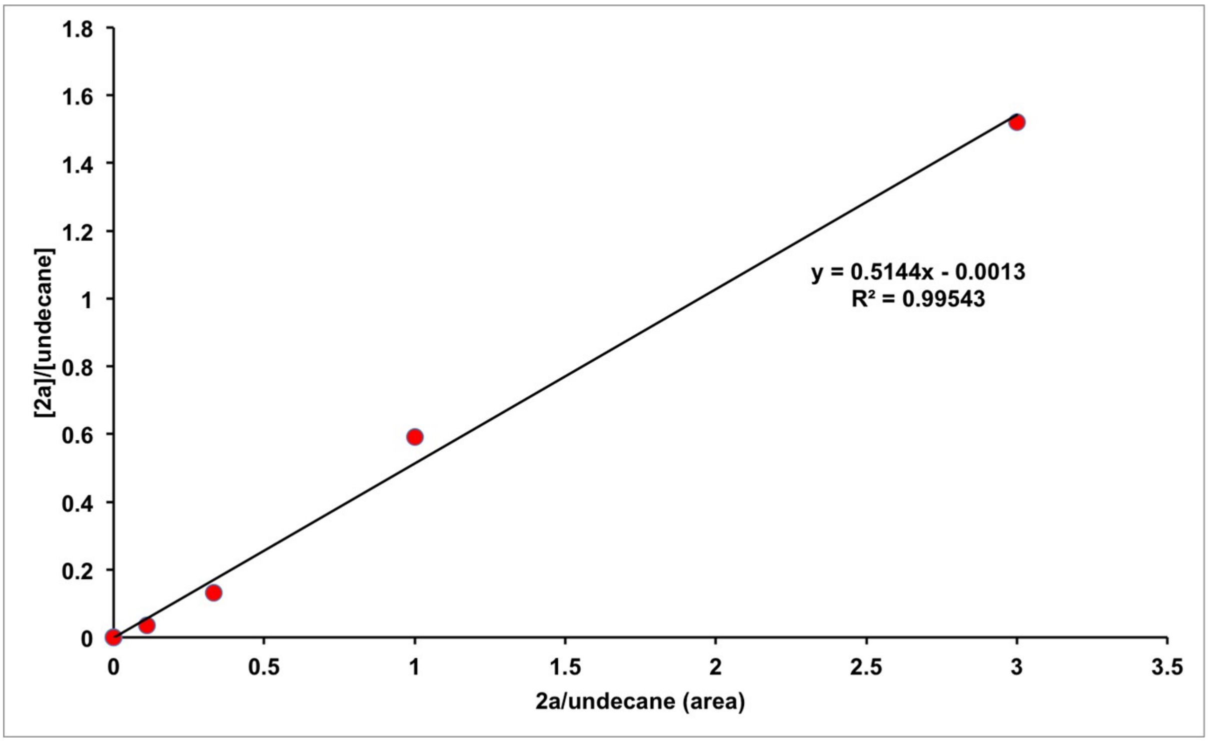


2g

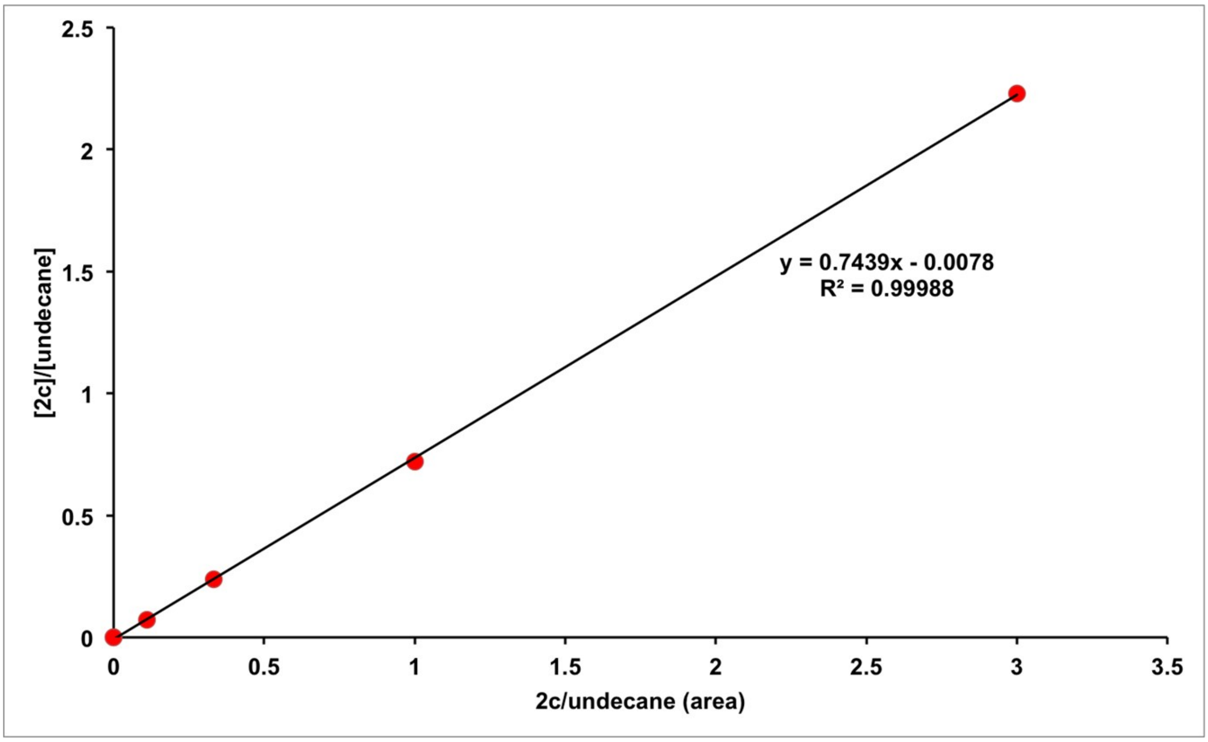
The viability of undecane as internal standard was determined by running the following reaction:



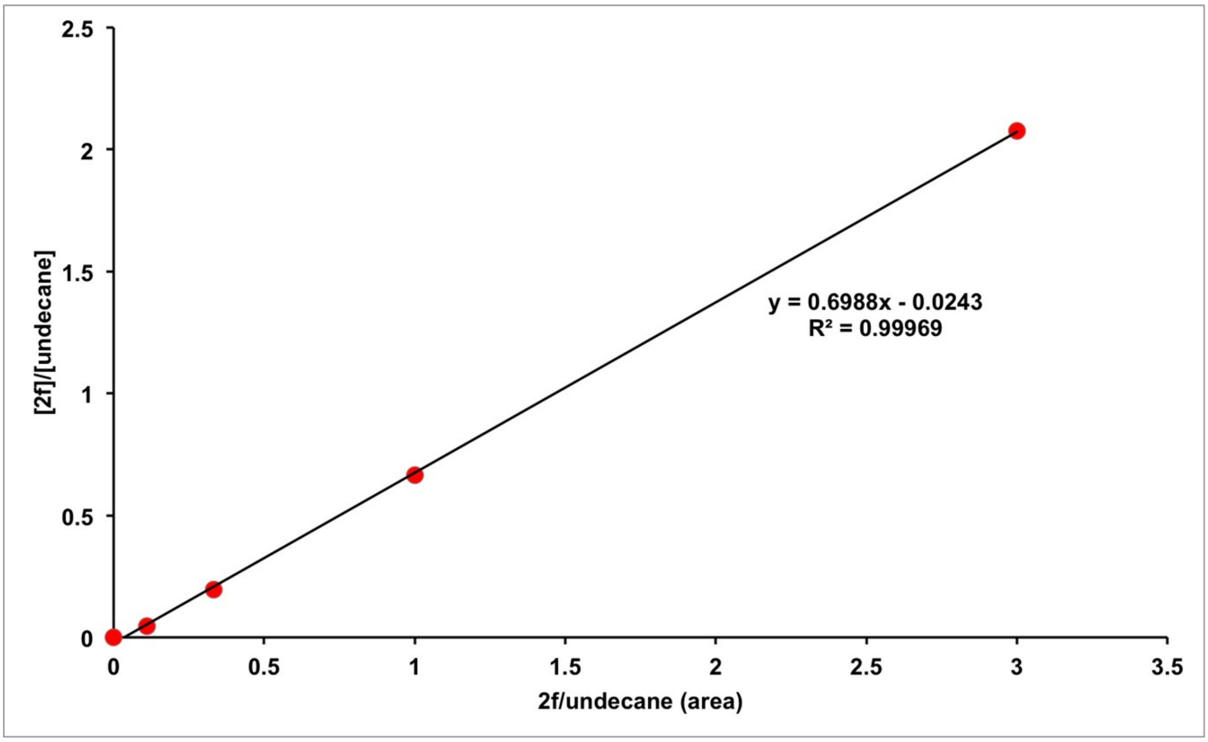
- Calibration curve for **2a** and undecane



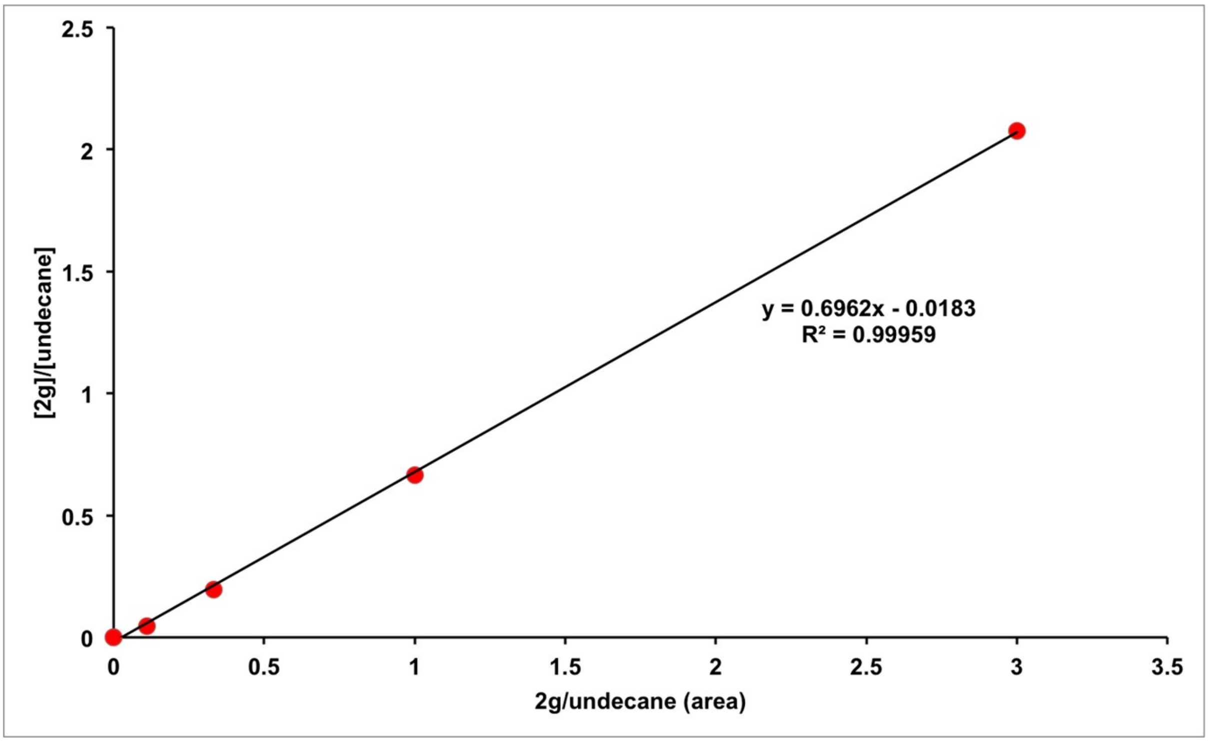
- Calibration curve for **2c** and undecane



- Calibration curve for **2f** and undecane

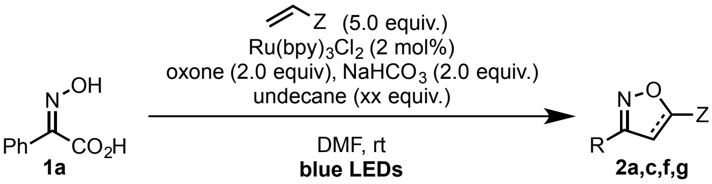


• Calibration curve for **2g** and undecane



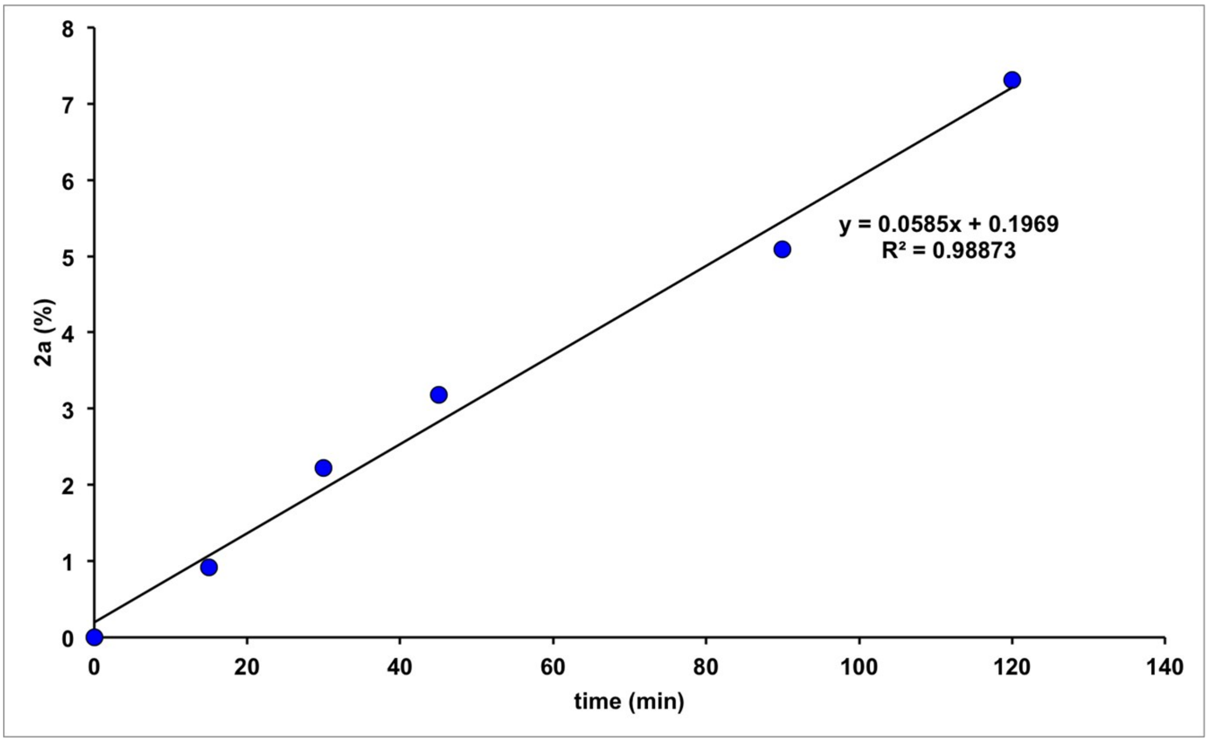
4.5.2 Kinetic Studies – Initial rates

General procedure for the kinetic studies – GP4

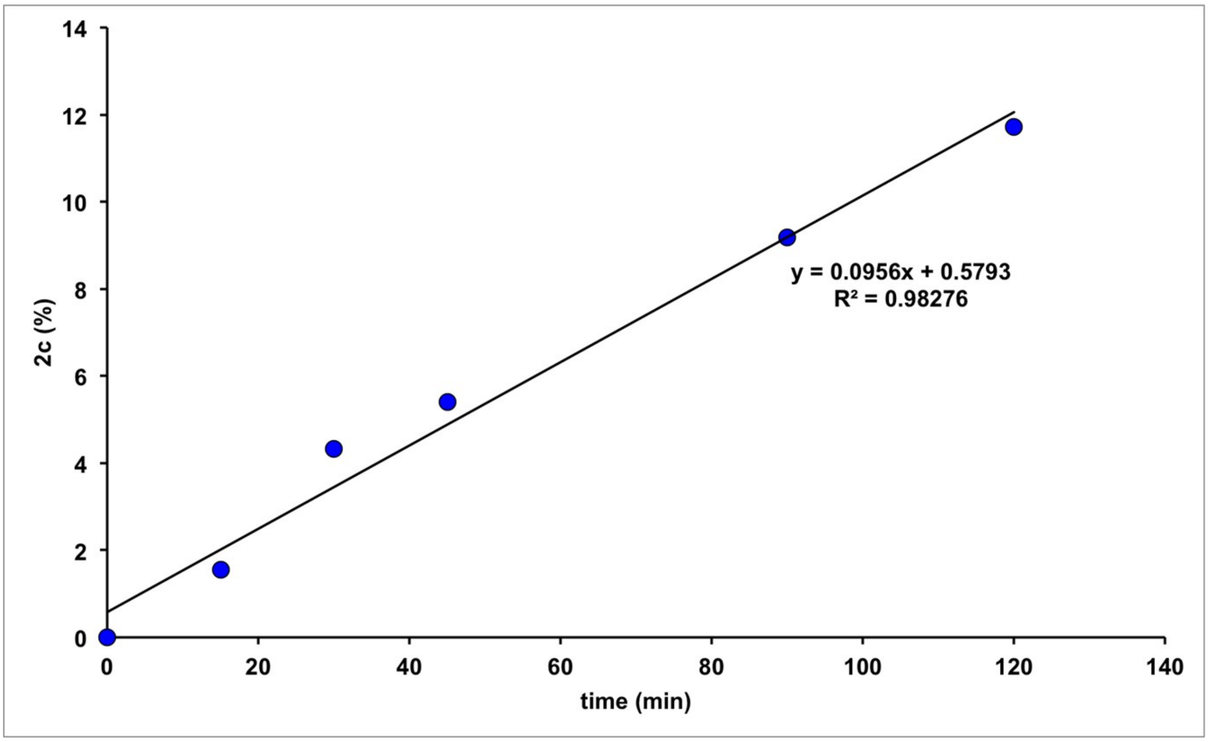


A dry tube equipped with a stirring bar was charged with the **1a** (50 mg, 0.30 mmol, 1.0 equiv.), $Ru(bpy)_3Cl_2$ (4.5 mg, 6.3 μmol, 2 mol%), $NaHCO_3$ (50 mg, 0.61 mmol, 2.0 equiv.) and oxone (186 mg, 0.61 mmol, 2.0 equiv.). DMF (1.0 mL), the appropriate styrene (1.51 mmol, 5.0 equiv.) and undecane as the internal standard (13 μL, 0.06 mmol, 20 mol%) were then added to the mixture and the tube was sealed. The mixture was stirred for 1 min and a reaction aliquot (50 μL) was taken, diluted with EtOAc, filtered through a short pad of silica and analysed by gas chromatography. The blue LEDs were turned on and the reaction was stirred under LEDs irradiation. Aliquots (50 μL) were taken at regular intervals and, following dilution with EtOAc and filtration through a short pad of silica, were analysed by gas chromatography.

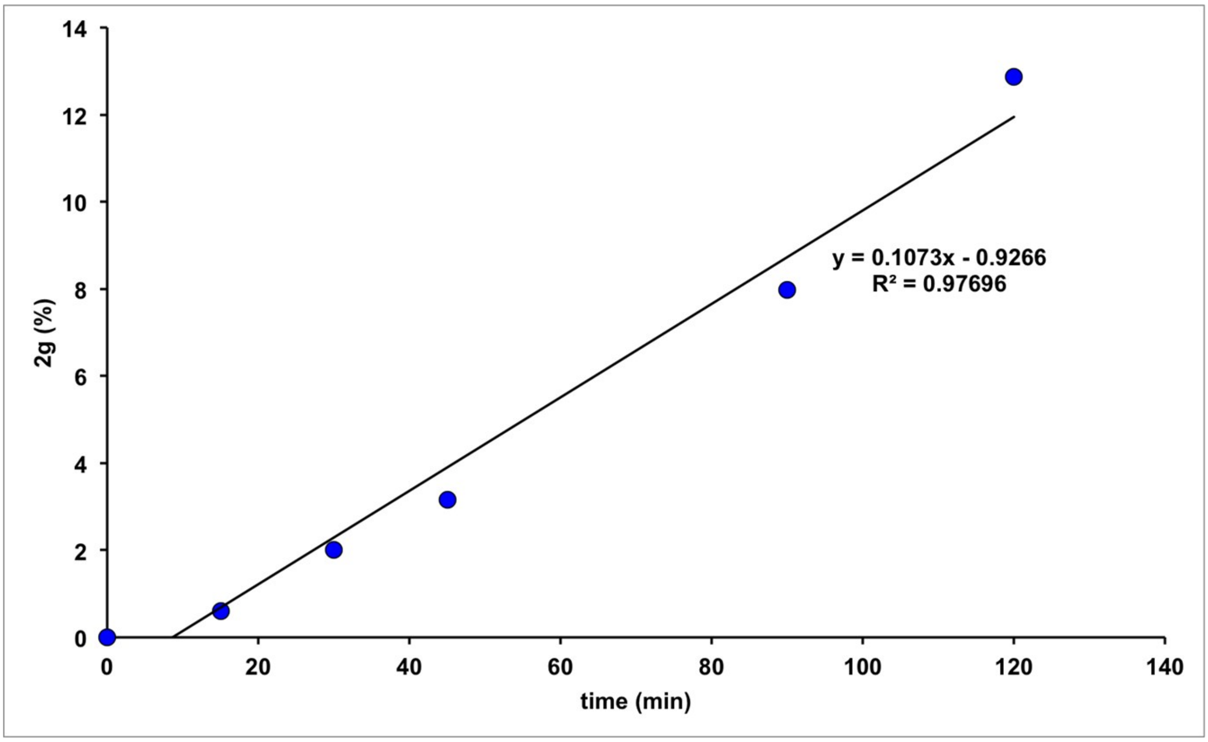
- **2a**: k_{obs} 0.0585



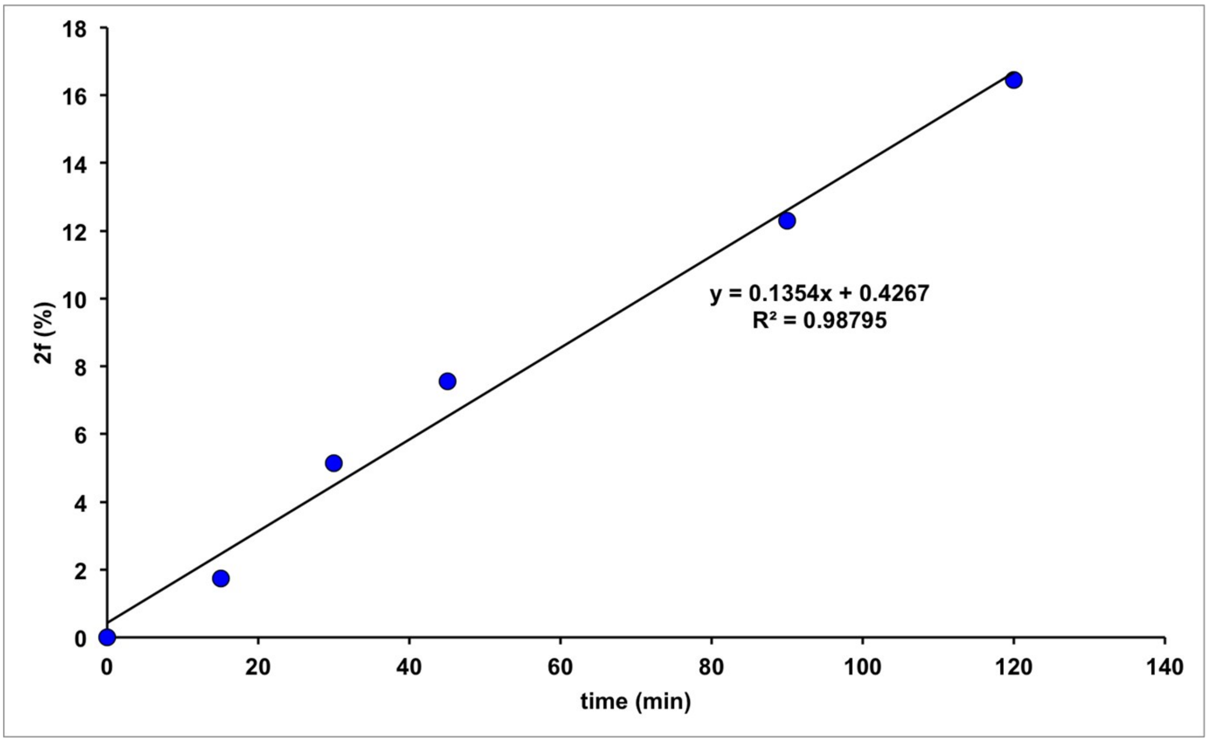
- **2c**: k_{obs} 0.0956



- **2f**: k_{obs} 0.1073

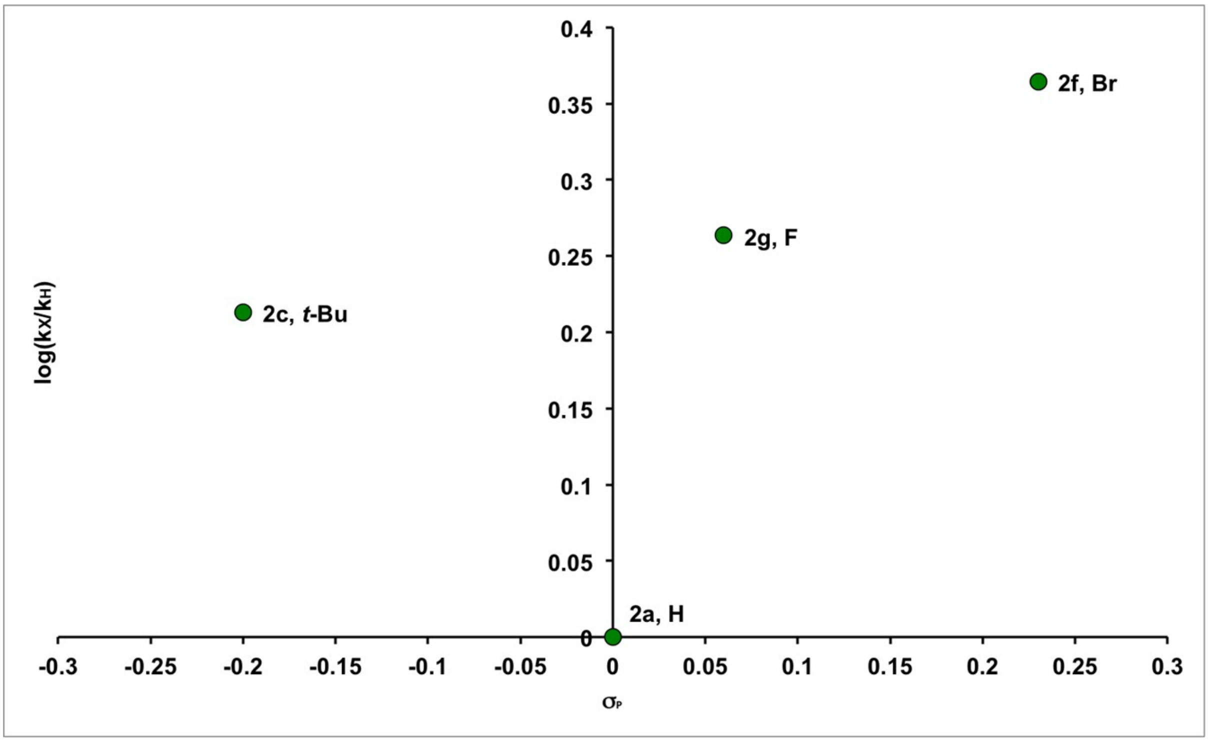


- **2g**: k$_{obs}$ 0.1354



4.6 Hammett Plot

Substrate	k_{obs}	$\log(k_X/k_H)$	σ_{para}
2a (**H**)	0.0585	0	0
2c (***t*-Bu**)	0.0956	0.213302026	-0.2
2f (**Br**)	0.1073	0.263443856	0.06
2g (**F**)	0.1354	0.364462798	0.23



5 DFT Studies

5.1 Computational Methods

Density functional theory (DFT)[21] calculations were performed using the Gaussian 09W programme[22] and the results were produced with GaussView 5.0. For calculation of global and local electrophilicity index,[23] B3LYP functional[24-27] was used and the geometries of studied radicals were optimized at the UB3LYP/6-31+G(d,p) level of theory, followed by frequency calculations at the same level. The computed Hirshfeld charges[28] on the carbon radicals, the transition structures for 3+2 cycloadditions,[29] radical addition, intramolecular hydrogen-atom abstraction and enolization mediated cyclization related calculations were also performed at the same level of theory. The frequency calculations were run to confirm each stationary point to be either a minimum or a transition structure. Representative transition states were also linked to their corresponding minima through the intrinsic reaction coordinate (IRC)[30-32] calculations, which confirm the connection of transition structures with the reactants and products. For substrates having more than one conformations, low energy conformation of the transition state could possibly be different from the low energy ground state.[332] In such a situation, the conformations with the lowest energy have been chosen.

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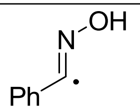
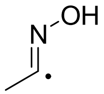
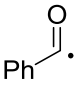
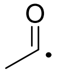
[2] Due to unsuccessful IRC calculations for some cases, the transition state structures were linked to their corresponding minima *via* perturbing their structures in the direction along the vibrational coordinate linked with the imaginary frequency, followed by optimization.

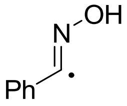
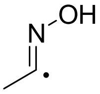
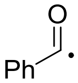
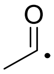
5.2 Acyl Radical Electrophilicity

DFT Method: UB3LYP/6-31+G(d,p) [values are in eV]

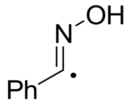
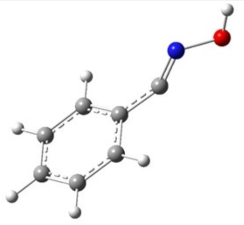
5.2.1 Molecular Descriptors

No.	**Radical**	**Ionization Potential (I)**	**Electron Affinity (A)**	**Electronegativity (χ)**	**Electronic Chemical Potential (μ)**	**Chemical Hardness (η)**	**Global Electrophilicity (ω)**	**Electrophilicity Index ($\omega^{\square}_{rc}$)**	**Hirshfeld Charges on C-radical**
1		7.345	1.225	4.285	-4.285	6.120	1.500	0.447	0.051633
2		8.691	0.608	4.650	-4.650	8.083	1.337	0.671	0.039257
3		8.031	0.100	4.066	-4.066	7.931	1.042	0.484	0.093664
4		8.700	0.012	4.356	-4.356	8.688	1.092	0.478	0.107188

2.2 **Computed Energies** [values are in Hartree]

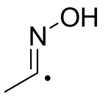
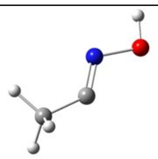
No.	Radical	Total Electronic Energy	Sum of Electronic and Zero-point Energies	Gibbs Free Energy
1		-400.2344094	-400.122157	-400.156046
2		-208.4823484	-208.423028	-208.450678
3		-344.9447367	-344.847281	-344.878587
4		-153.1945098	-153.151376	-153.177049

5.2.2 Optimized Structures and Cartesian Coordinates

No.	Radical	Optimized Structure
1		

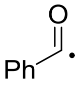
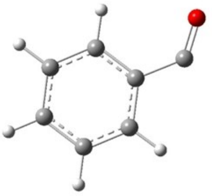
Cartesian Coordinates

C	-2.09414600	1.21222100	0.01157700
C	-0.70504100	1.22154000	-0.05305500
C	0.01437300	-0.00032100	-0.06980800
C	-0.70549000	-1.22179000	-0.05304600
C	-2.09462100	-1.21189000	0.01156800
C	-2.79651100	0.00028700	0.04332900
H	-2.63476800	2.15380600	0.03677800
H	-0.15968100	2.15913900	-0.08325900
H	-0.16057000	-2.15965200	-0.08320200
H	-2.63560100	-2.15326800	0.03676600
H	-3.88120300	0.00048400	0.08947200
C	1.42643400	-0.00019100	-0.18385300
N	2.46640900	-0.00010700	0.48210600
O	3.69761000	0.00011800	-0.25807300
H	4.35609400	0.00016100	0.45301500

No.	Radical	Optimized Structure
2		

Cartesian Coordinates

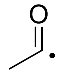
C	-0.45164800	-0.32036300	0.00030100
N	0.55055700	0.40929800	0.00021900
O	1.82473400	-0.22698900	-0.00008700
H	2.43040400	0.52894900	-0.00076200
C	-1.89406100	0.01249500	-0.00014300
H	-2.04814100	1.09979700	0.00088400
H	-2.37917200	-0.41447300	-0.88371500
H	-2.38060300	-0.41623900	0.88180700

No.	Radical	Optimized Structure
3		

Cartesian Coordinates

C	2.01853400	0.51600100	0.00059700
O	2.93174300	-0.25397400	-0.00009200
C	0.56564900	0.23267700	-0.00032200
C	-0.33778600	1.30499500	-0.00020800

C	0.09201600	-1.09304800	-0.00016600
C	-1.71109200	1.05727100	-0.00001400
H	0.04725300	2.32023700	-0.00012900
C	-1.27965600	-1.33382400	0.00003000
H	0.80497700	-1.91168900	-0.00030200
C	-2.17973200	-0.25994600	0.00017500
H	-2.41330600	1.88531900	-0.00003300
H	-1.65170500	-2.35423500	0.00019300
H	-3.24876000	-0.45259000	0.00044400

4		

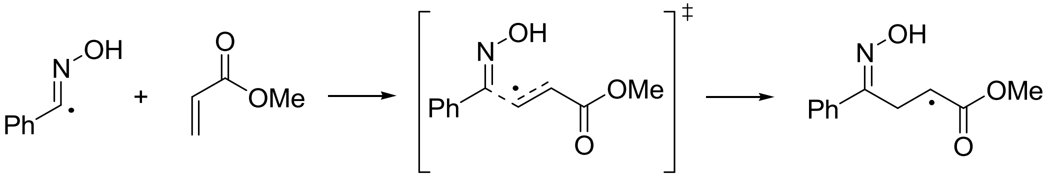
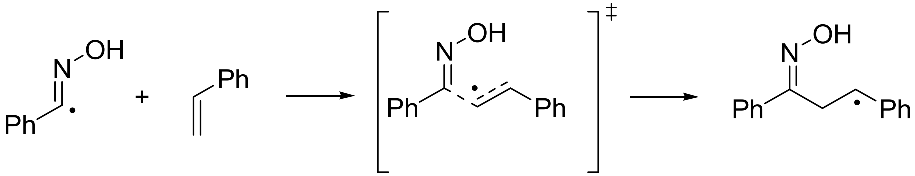
Cartesian Coordinates

C	1.17035200	-0.09884500	0.00019800
H	1.68803300	0.28662900	-0.88353300
H	1.69211300	0.29231500	0.87870700
H	1.18295600	-1.19531100	0.00302100
C	-0.24421400	0.43423800	0.00006100
O	-1.26499200	-0.17449900	0.00003100

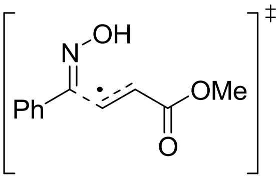
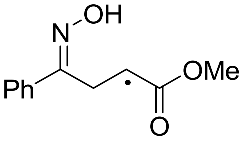
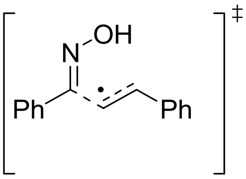
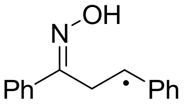
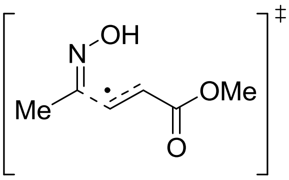
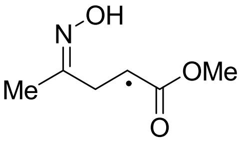
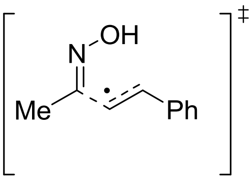
5.3 Radical Addition

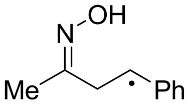
DFT Method: UB3LYP/6-31+G(d,p) [values are in Kcal mol^{-1}]

5.3.1 Activation and Reaction Energies

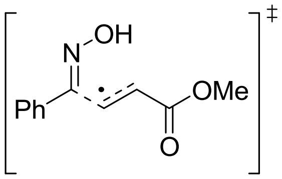
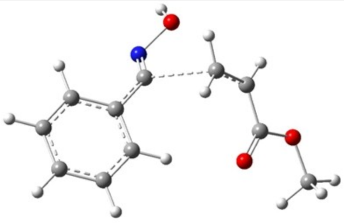
Entry	***Radical Addition***	**Activation Energy ($\Delta G^{\neq}$)**	**Energy of Reaction (ΔG)**
1		1.3	-30.6
2		2.0	-32.7

5.3.2 Computed Energies [values are in Hartree]

No.	Species	Total Electronic Energy	Sum of Electronic and Zero-point Energies	Gibbs Free Energy
1		-706.7237726	-706.514448	-706.559723
2		-706.7746003	-706.561437	-706.605378
3		-709.9051086	-709.658119	-709.705148
4		-709.9604557	-709.709588	-709.754986
5		-514.9731338	-514.817550	-514.859054
6		-515.0270974	-514.867561	-514.907243
7		-518.1551404	-517.961497	-518.003264

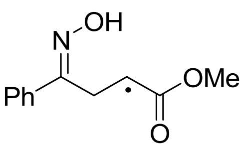
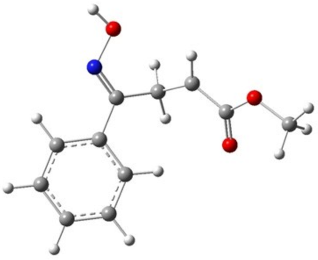
8		-518.213544	-518.016056	-518.056322

5.3.3 Optimized Structures and Cartesian Coordinates

No.	Radical	Optimized Structure
1		

Cartesian Coordinates

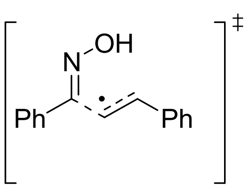
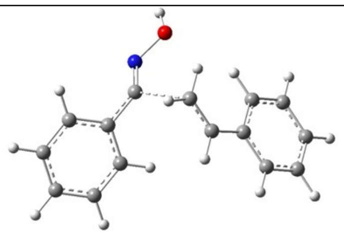
C	-2.34370000	-2.17110100	-0.04709400
C	-1.39482800	-1.14960500	-0.04711300
C	-1.81375600	0.19641700	-0.07979100
C	-3.19466200	0.49372200	-0.07698400
C	-4.13151800	-0.53694100	-0.06996700
C	-3.71019800	-1.87147000	-0.05765800
H	-2.01332400	-3.20548000	-0.03177900
H	-0.33521200	-1.38568200	-0.02016500
H	-3.51333700	1.53093400	-0.08852700
H	-5.19151800	-0.29974500	-0.07520900
H	-4.44334200	-2.67276800	-0.04972500
C	-0.84901200	1.27389100	-0.06888000
N	-0.79041100	2.31474200	-0.75518700
O	0.19146700	3.26901700	-0.37071000
H	0.09460000	3.94909700	-1.05323800
C	0.97635900	0.98509000	1.48063700
C	2.11750300	0.86453800	0.75346800
H	2.69127600	1.73449100	0.45412800
H	0.68714900	1.94718200	1.88650300
H	0.47147100	0.10206900	1.85669600
C	2.59283000	-0.44690300	0.28816200
O	2.00532900	-1.51208800	0.41878300
O	3.79584600	-0.34361500	-0.33022600
C	4.35643000	-1.57258200	-0.82318500
H	5.31078800	-1.29700300	-1.27140000
H	4.50465300	-2.28105300	-0.00430600
H	3.69585300	-2.02208100	-1.56901200

No.	Radical	Optimized Structure
2		

Cartesian Coordinates

C	3.87618400	-0.76145800	-0.44527000
C	3.00085300	0.31157600	-0.30007800
C	1.66028100	0.09782100	0.07631300
C	1.22573700	-1.21909800	0.30711100
C	2.10853300	-2.29223700	0.15683300
C	3.43413600	-2.07017300	-0.21813600
H	4.90815500	-0.57706800	-0.73015400

H	3.34485800	1.32555100	-0.47038800
H	0.19866200	-1.42105700	0.59331700
H	1.75279700	-3.30276100	0.33538800
H	4.11940600	-2.90569000	-0.32832500
C	0.72686700	1.24521000	0.21937700
N	1.06472700	2.34604200	-0.35644700
O	0.11415700	3.36744400	-0.15438600
H	0.51510500	4.12039700	-0.60926100
C	-0.56677300	1.10708900	1.02333100
C	-1.75692700	0.90662900	0.14695500
H	-2.05516400	1.68835900	-0.54276200
H	-0.48318700	0.28508000	1.73475200
H	-0.69108700	2.04383500	1.58219900
C	-2.52316800	-0.32287000	0.17838600
O	-2.26287000	-1.30202200	0.87398500
O	-3.58819000	-0.27843800	-0.66581000
C	-4.40641900	-1.45982600	-0.70175200
H	-5.20250700	-1.23943700	-1.41254000
H	-3.82092300	-2.32119800	-1.03391300
H	-4.81981100	-1.67015900	0.28808000

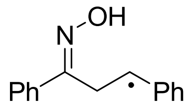
3		

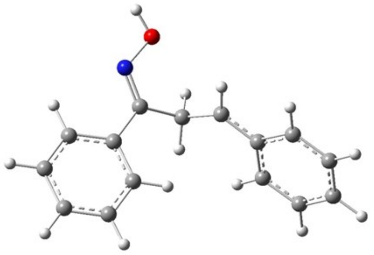
Cartesian Coordinates

C	-2.84122900	-2.09382900	-0.64676900
C	-1.87909100	-1.09041600	-0.55083900
C	-2.25182200	0.21394200	-0.16606800
C	-3.60226600	0.47872600	0.14619600
C	-4.55516700	-0.53423900	0.05332700
C	-4.18037900	-1.82258700	-0.34315100
H	-2.54613800	-3.09150500	-0.95889000
H	-0.84016200	-1.30024900	-0.78271800
H	-3.89069700	1.47992200	0.45043100
H	-5.59345500	-0.31696200	0.28710100
H	-4.92544200	-2.60942200	-0.41423900
C	-1.25789600	1.25307900	-0.02922700
N	-1.07157100	2.28212800	-0.71072900
O	-0.04528000	3.16567200	-0.24178900
H	-0.06392000	3.86523900	-0.91085900
C	0.29916000	0.83628500	1.76337700
C	0.99839600	-0.29915700	1.47342300
H	0.68417700	1.82367000	1.53972500
H	-0.53662800	0.78862500	2.45280900
H	0.62440800	-1.24422400	1.86512200
C	2.20179600	-0.39830400	0.65098700
C	2.89800400	-1.62403100	0.59439000
C	2.70314200	0.68430800	-0.10491100
C	4.05815800	-1.76184700	-0.16675000
H	2.52323300	-2.47115500	1.16401300
C	3.86131700	0.54362400	-0.86558600
H	2.17013500	1.62999700	-0.10928700
C	4.54780200	-0.67663200	-0.89949100
H	4.57936400	-2.71478000	-0.18895000

H	4.22899400	1.38751700	-1.44284600
H	5.44982800	-0.78047500	-1.49544700

4





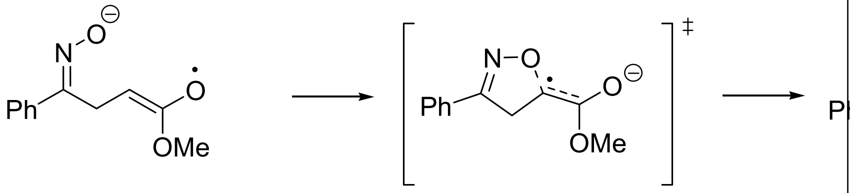
Cartesian Coordinates

C	-4.27696700	-1.23606000	0.21077100
C	-3.56558300	-0.04989700	0.04321200
C	-2.16211300	-0.06418300	-0.06331200
C	-1.49618900	-1.30044900	-0.00209400
C	-2.21219700	-2.48763600	0.16937600
C	-3.60403900	-2.46141100	0.27483500
H	-5.36040100	-1.20597900	0.28431300
H	-4.08704500	0.89915800	-0.01293200
H	-0.41381100	-1.34089900	-0.06490400
H	-1.67808500	-3.43191500	0.22252500
H	-4.16057700	-3.38538900	0.40231200
C	-1.39821900	1.19962900	-0.23506500
N	-1.98173700	2.27766300	0.15970500
O	-1.18809600	3.42483700	-0.04845500
H	-1.76024400	4.13439500	0.27335300
C	-0.00426600	1.17984900	-0.84206400
C	1.07068300	1.07151500	0.20324600
H	0.92245500	1.65816500	1.10618600
H	0.05358100	0.36067500	-1.56295400
H	0.12144200	2.11459400	-1.40640000
C	2.26903800	0.32446000	0.09582400
C	3.19968000	0.33179400	1.18053700
C	2.62113600	-0.44923300	-1.05125000
C	4.38566500	-0.38439700	1.12242700
H	2.96085000	0.91465400	2.06635200
C	3.81247700	-1.16304900	-1.09796600
H	1.95594400	-0.47807700	-1.90823700
C	4.70493500	-1.14096700	-0.01660900
H	5.07108300	-0.35847500	1.96507100
H	4.05370100	-1.74171500	-1.98548400
H	5.63378300	-1.70132300	-0.06070200

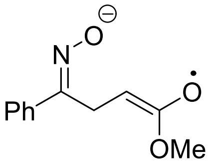
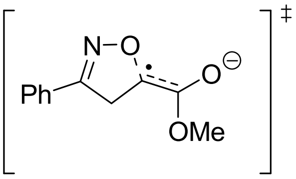
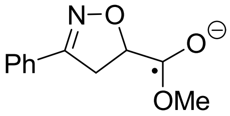
5.4 Cyclization on enol-radical

DFT Method: UB3LYP/6-31+G(d,p) [values are in Kcal mol^{-1}]

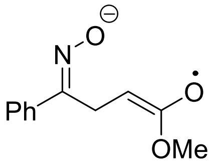
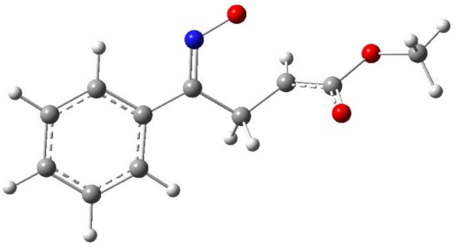
5.4.1 Activation and Reaction Energies

Entry	***Enolization Mediated Cyclisation***	**Activation Energy ($\Delta G^{\neq}$)**	**Energy of Reaction (ΔG)**
1		11.8	6.6

5.4.2 Computed Energies [values are in Hartree]

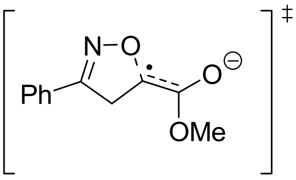
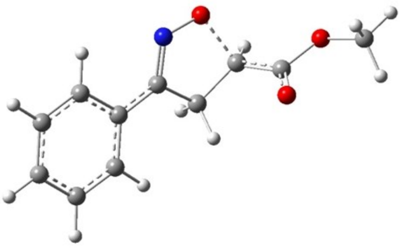
No.	Species	Total Electronic Energy	Sum of Electronic and Zero-point Energies	Gibbs Free Energy
1		-706.2278896	-706.028915	-706.072521
2		-706.2090332	-706.011021	-706.053138
3		-706.2173109	-706.017944	-706.060738

5.4.3 Optimized Structures and Cartesian Coordinates

No.	Radical	Optimized Structure
1		

Cartesian Coordinates

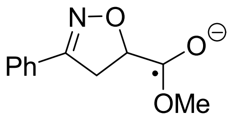
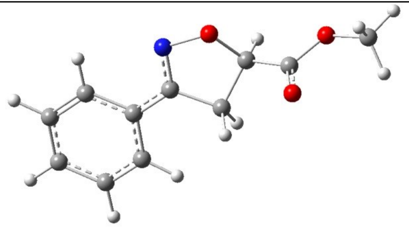
C	1.81728700	-0.12849200	-0.79602400
C	0.45497000	-0.64865100	-0.49818800
C	-0.58236800	0.42727300	-0.14665000
H	2.00838000	0.39584100	-1.72362400
H	0.52588100	-1.36918100	0.32895300
H	0.06237600	-1.20082300	-1.36823700
C	2.92625000	-0.46399300	0.01692400
O	2.93928100	-1.12679200	1.06721700
O	4.12802200	0.04626000	-0.49459900
C	5.27235000	-0.19652500	0.30941800
H	5.45977600	-1.27014900	0.43295800
H	6.11120500	0.27079300	-0.21500800
H	5.16286700	0.24524600	1.30668900
N	-0.21504500	1.65959200	0.09369600
O	1.02216100	1.99832900	0.01825000
C	-2.00693900	0.09750400	-0.04260000
C	-2.46720400	-1.23322600	-0.17342500
C	-2.98900400	1.09318900	0.19369700
C	-3.82585100	-1.54943200	-0.07728800
H	-1.75465600	-2.03351700	-0.34235900
C	-4.33856200	0.77323000	0.29005800
H	-2.65682100	2.12037700	0.29897600
C	-4.77694700	-0.55374800	0.15410900
H	-4.13832200	-2.58663500	-0.18130300
H	-5.06181700	1.56605100	0.47153500
H	-5.83314800	-0.80029700	0.22841200

No.	Radical	Optimized Structure
2		

Cartesian Coordinates

C	-1.82385400	0.21534800	0.95920400
C	-0.45157700	-0.38615400	1.19012100
C	0.51291100	0.48342300	0.39815600
H	-2.37227500	0.54414300	1.83897300
H	-0.42185300	-1.41979500	0.82963400
H	-0.20044400	-0.38927200	2.26162500
N	-0.03240800	1.59172400	-0.05766700

O	-1.29790100	1.74678500	0.39736200
C	-2.67469300	-0.41008100	-0.03920900
O	-2.32844000	-1.11365100	-1.00238000
O	-4.01983300	-0.05071100	0.14044800
C	-4.89829000	-0.50951200	-0.87567700
H	-4.90870300	-1.60500200	-0.93527900
H	-5.89194200	-0.14116900	-0.60414300
H	-4.60948300	-0.11968300	-1.85870900
C	1.88085300	0.12651600	0.09998800
C	2.43100200	-1.12532800	0.48422000
C	2.75755900	1.03930800	-0.55684600
C	3.76251300	-1.44558100	0.22642500
H	1.80118500	-1.85478000	0.98503500
C	4.08158700	0.70811300	-0.81411500
H	2.36252000	2.00491100	-0.85508200
C	4.60957900	-0.53682100	-0.42682200
H	4.14408400	-2.41731400	0.53496300
H	4.71958700	1.42913400	-1.32285500
H	5.64803300	-0.78800800	-0.62661900

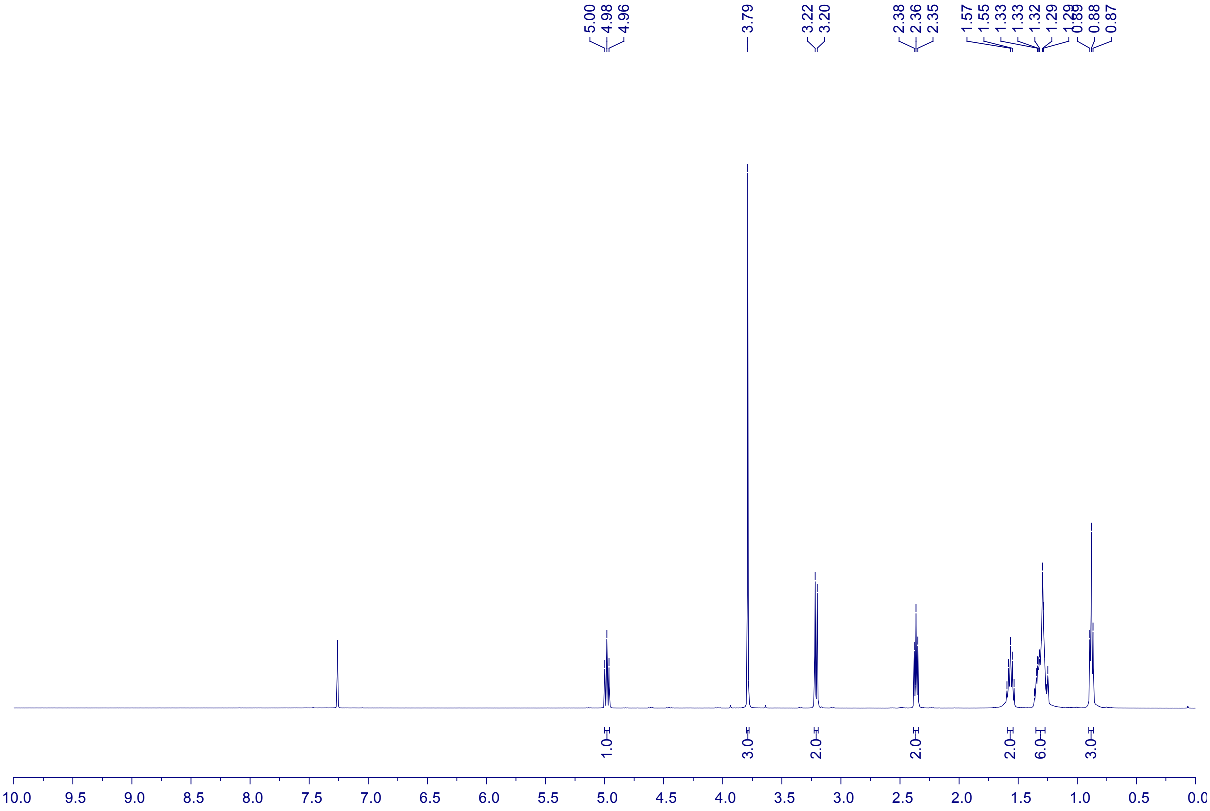
6		

Cartesian Coordinates

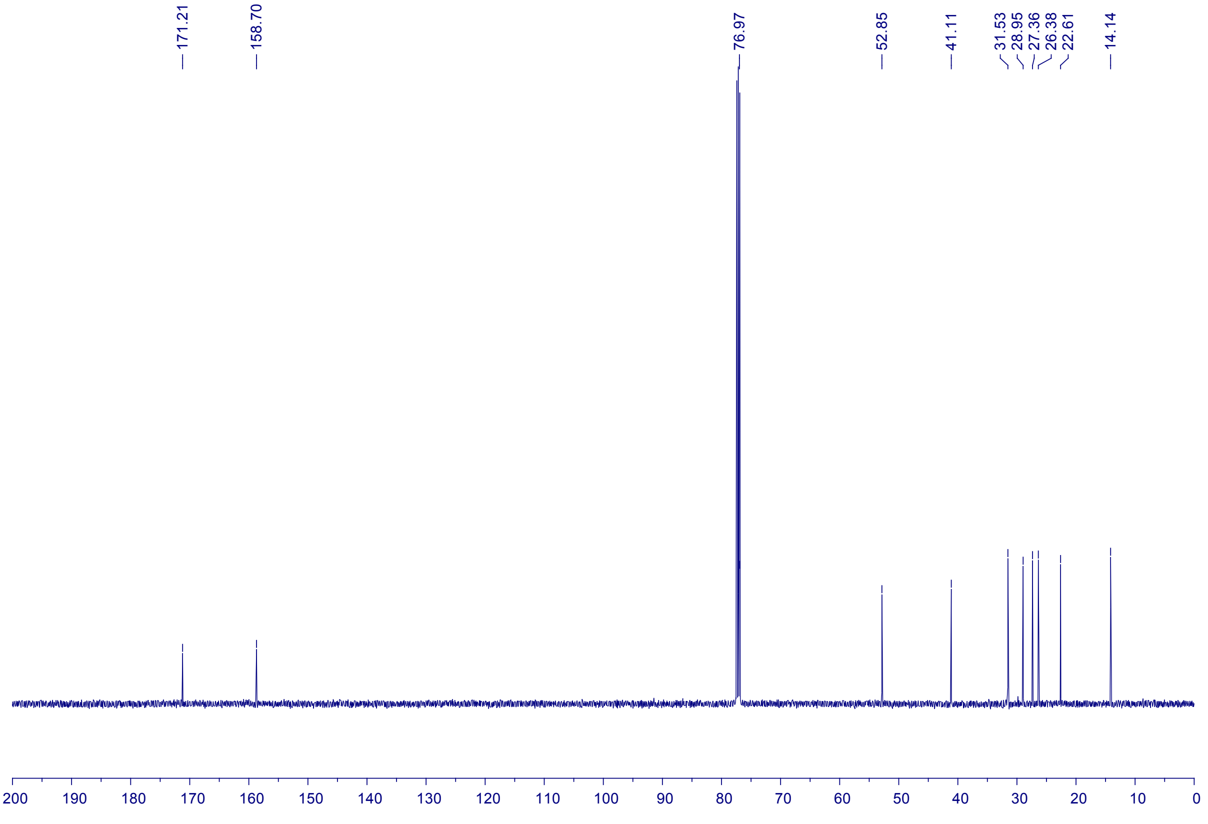
C	1.62419900	0.20521500	-0.37318000
C	0.45504900	-0.67499300	0.06880500
C	-0.64680800	0.36569800	0.07550300
H	1.67943400	0.26075000	-1.47096400
H	0.64559000	-1.09730100	1.06631300
H	0.27365700	-1.50211000	-0.62757100
N	-0.15885300	1.61680300	0.14788400
O	1.29838800	1.50004600	0.15813500
C	2.97854600	-0.20077000	0.16999700
O	3.22460000	-0.57410800	1.30088400
O	3.94794500	-0.10423100	-0.78908700
C	5.27199400	-0.44252600	-0.36156100
H	5.31615300	-1.48013000	-0.01655000
H	5.90880400	-0.30374200	-1.23681000
H	5.59354300	0.21193300	0.45391100
C	-2.03556800	0.07094800	0.00509800
C	-2.53687400	-1.27372800	-0.03928500
C	-3.02831800	1.11586200	-0.00048300
C	-3.89731400	-1.54443400	-0.09465400
H	-1.83712900	-2.10604200	-0.02204000
C	-4.38142300	0.82450000	-0.05509400
H	-2.68977300	2.14657600	0.03741900
C	-4.85404100	-0.50612000	-0.10383700
H	-4.22728100	-2.58253700	-0.12716600
H	-5.09688500	1.64691100	-0.05946300
H	-5.91826400	-0.72349600	-0.13956800

6 NMR Spectra

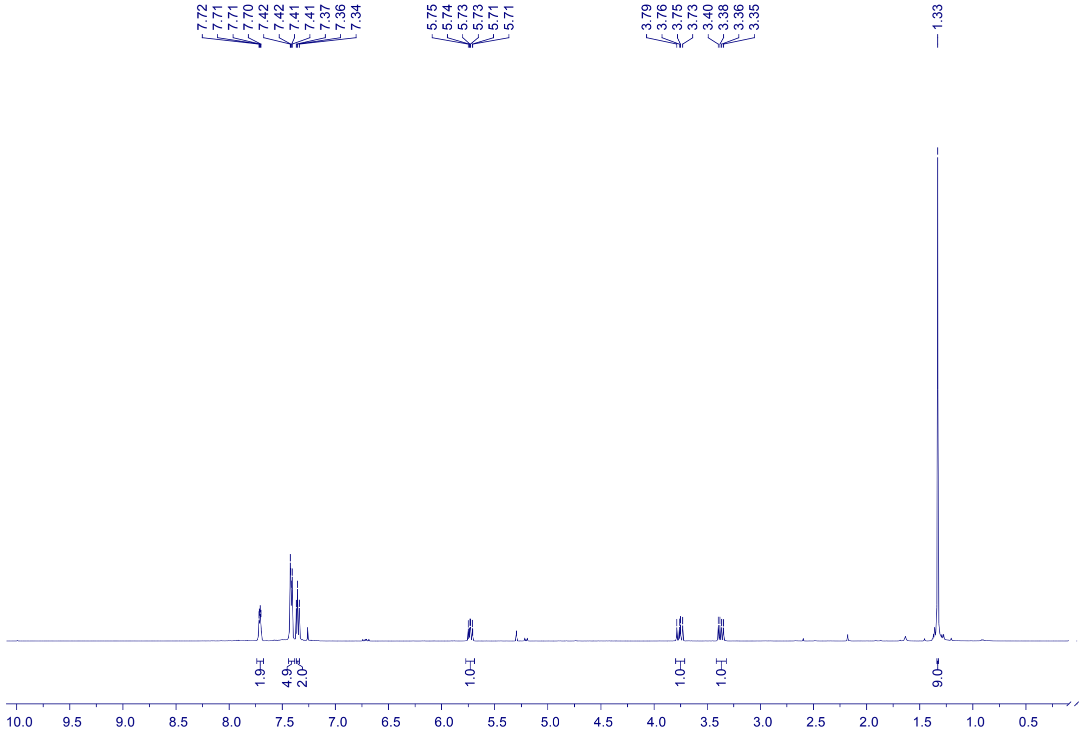
1c, ^{1}H NMR (400 MHz, CDCl$_3$)



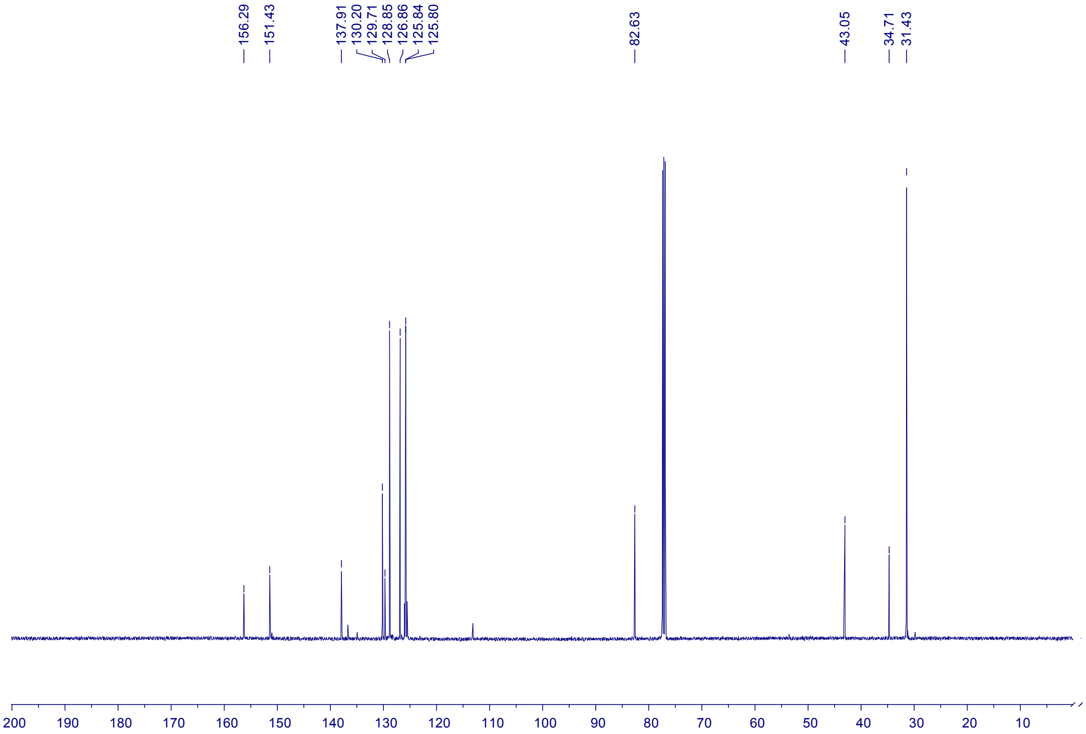
1c, ^{13}C NMR (101 MHz, CDCl$_3$)



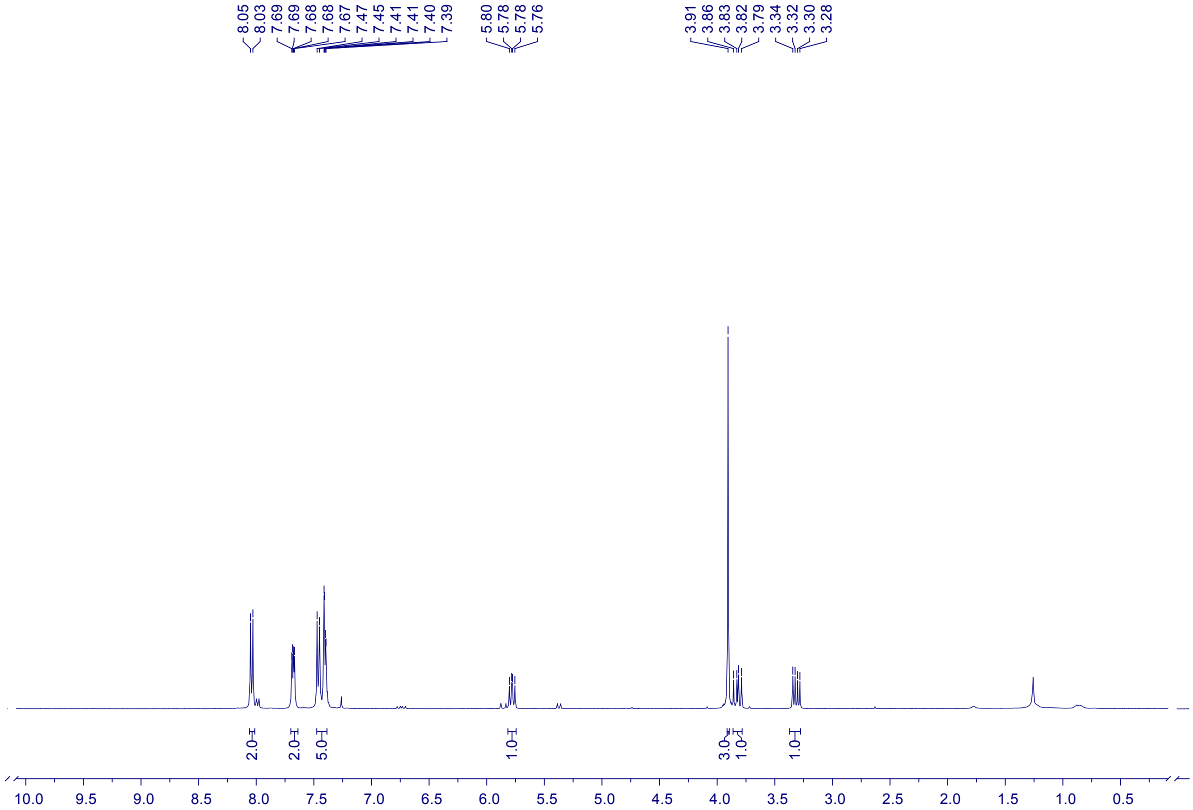
2c, ^{1}H NMR (400 MHz, CDCl$_3$)



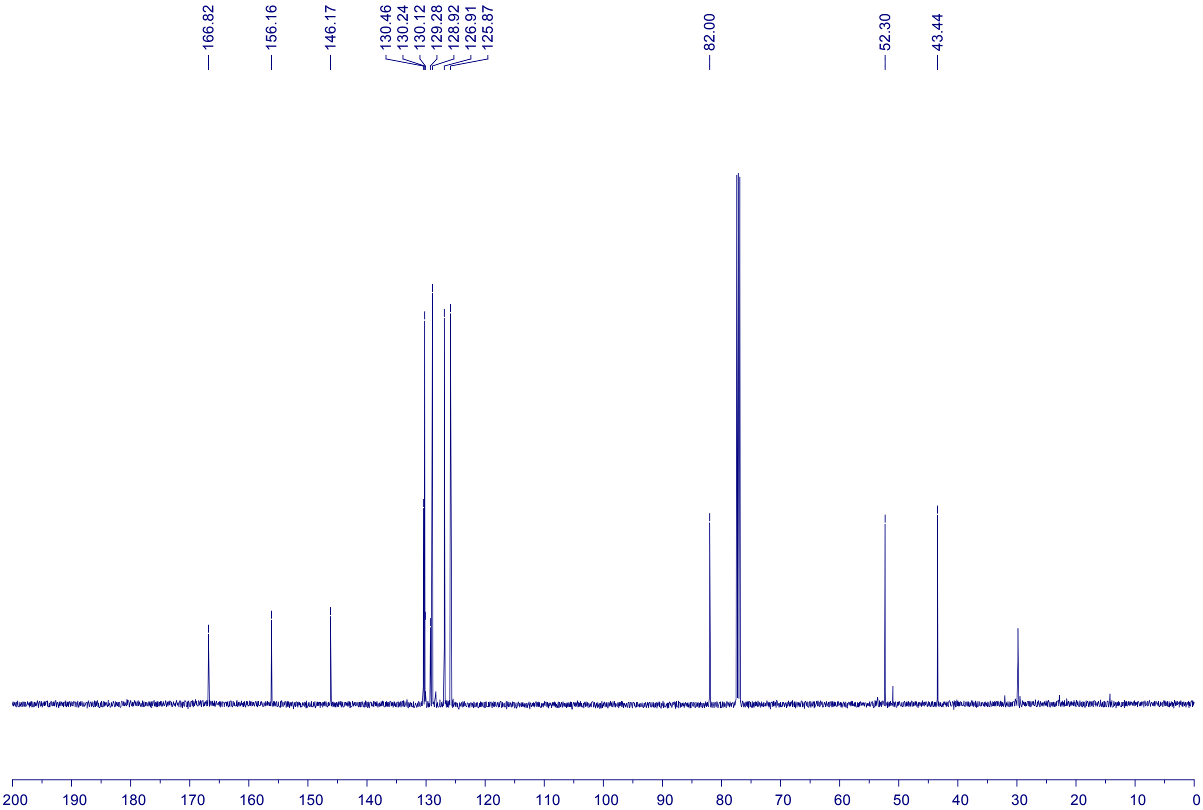
2c, ^{13}C NMR (101 MHz, CDCl$_3$)



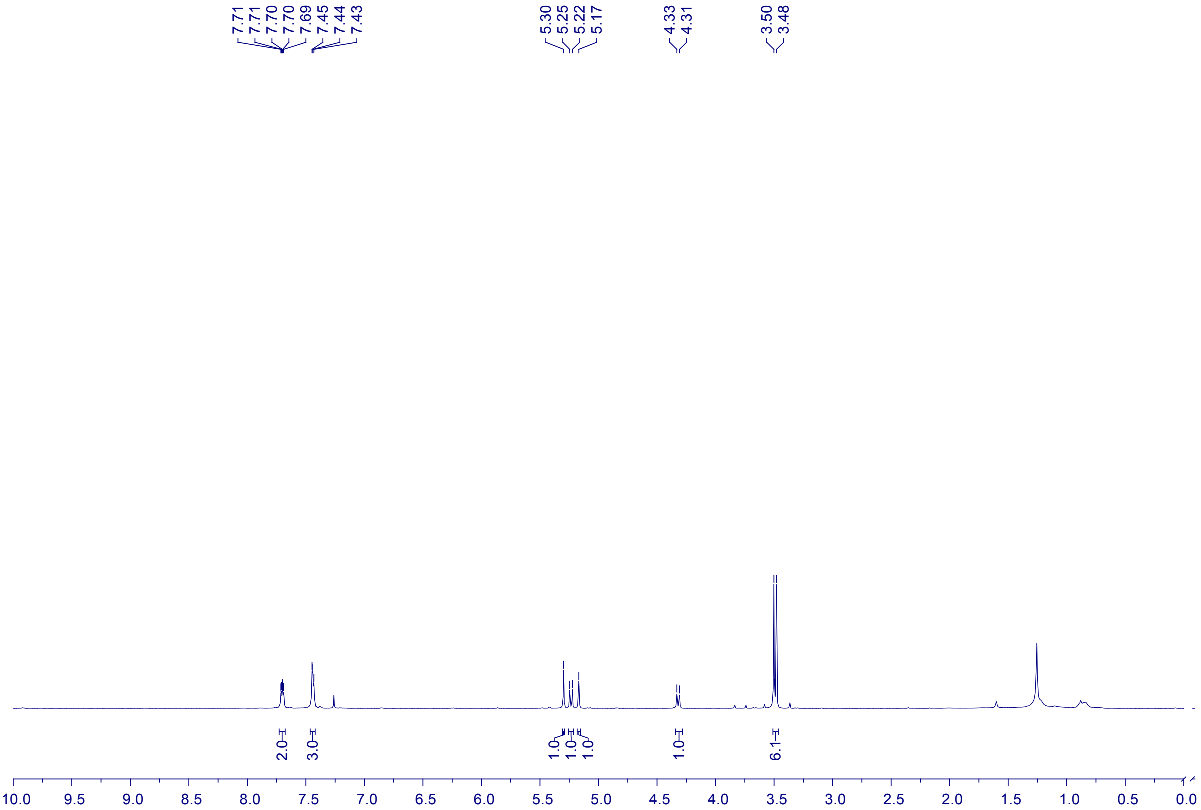
2g, ^{1}H NMR (400 MHz, CDCl$_3$)



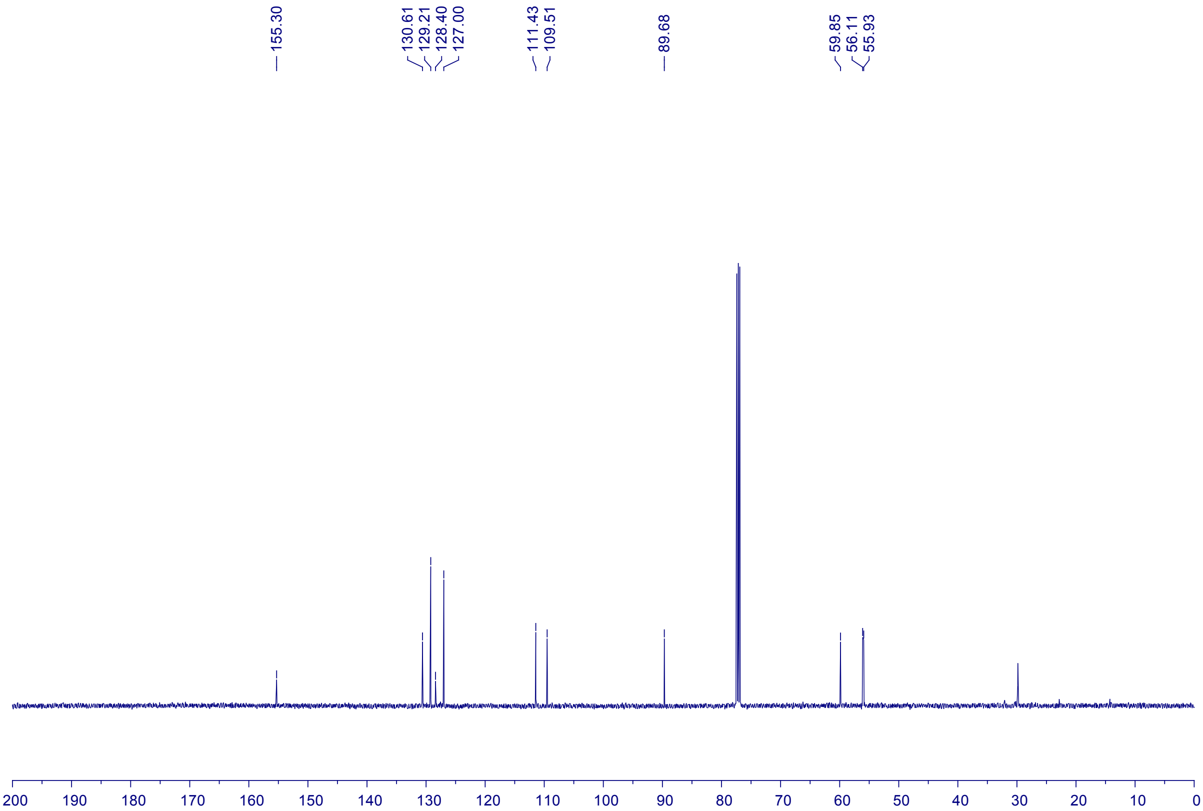
2g, ^{13}C NMR (101 MHz, CDCl$_3$)



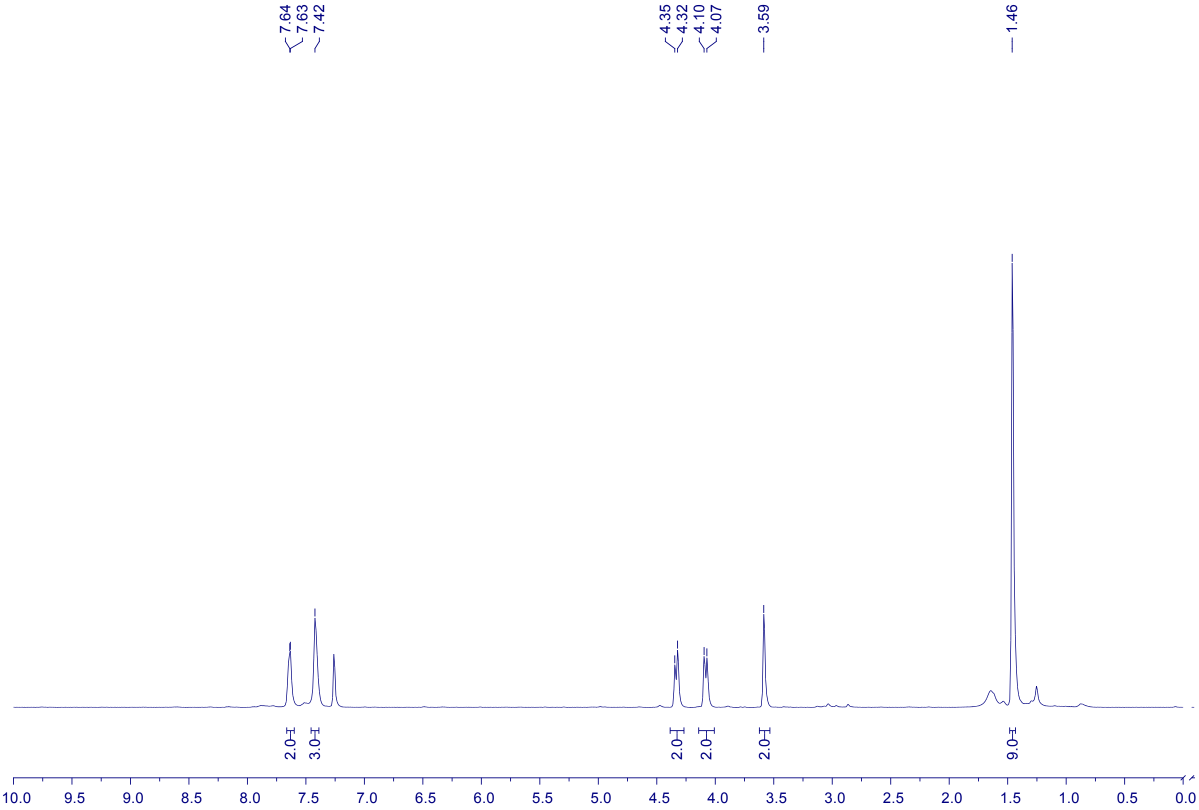
2s, ^{1}H NMR (400 MHz, CDCl$_3$)



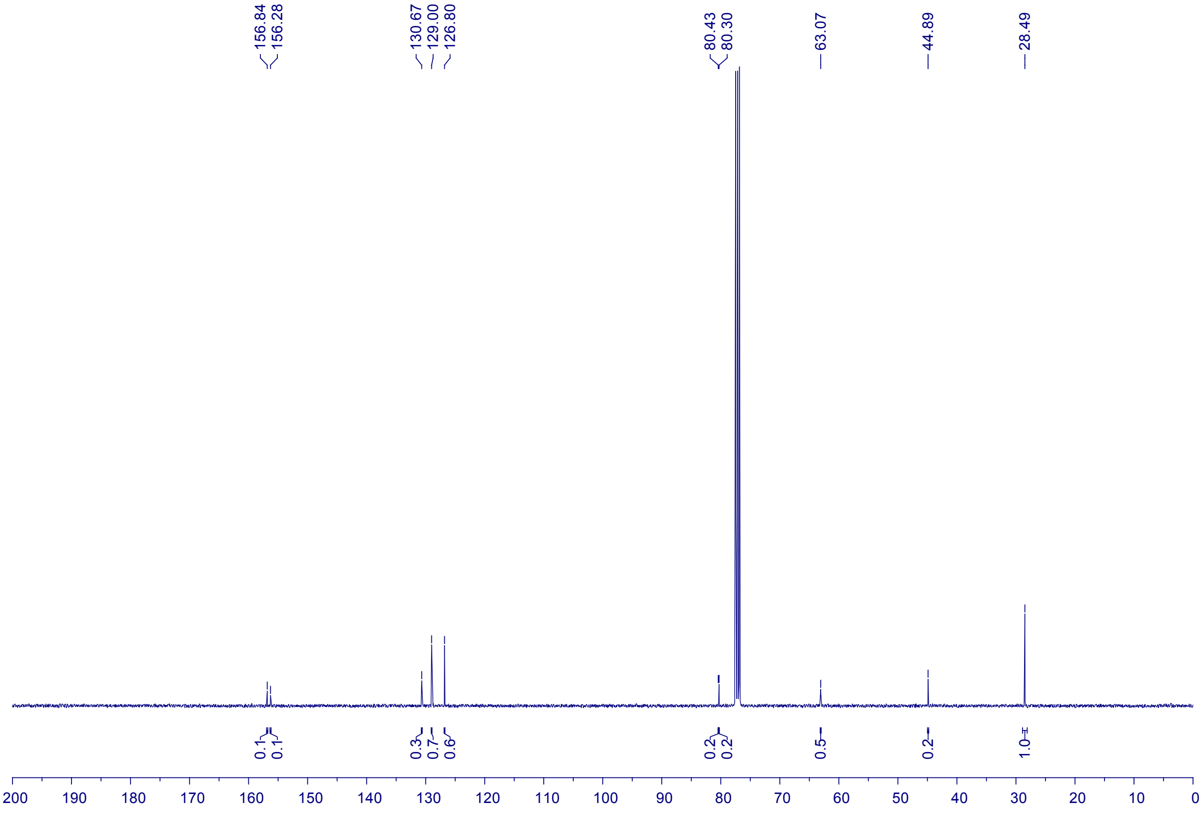
2s, ^{13}C NMR (101 MHz, CDCl$_3$)



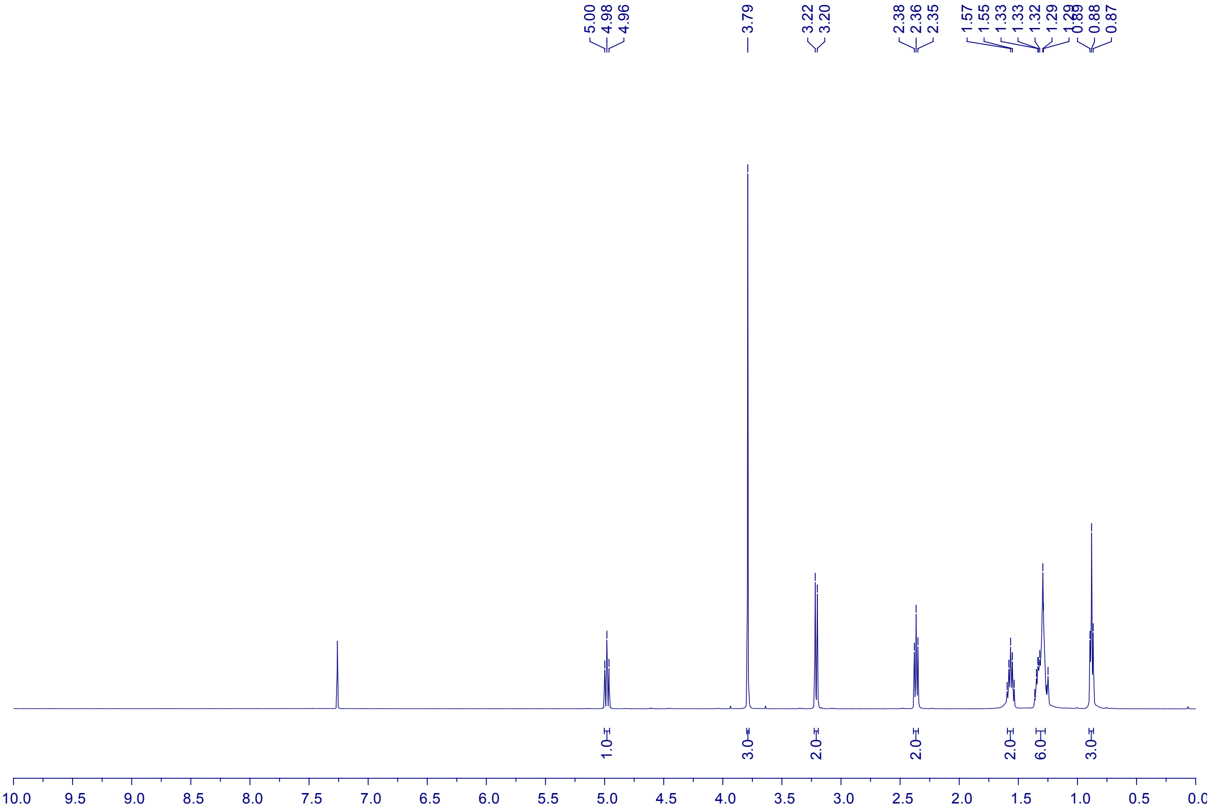
2v, ^{1}H NMR (400 MHz, CDCl$_3$)



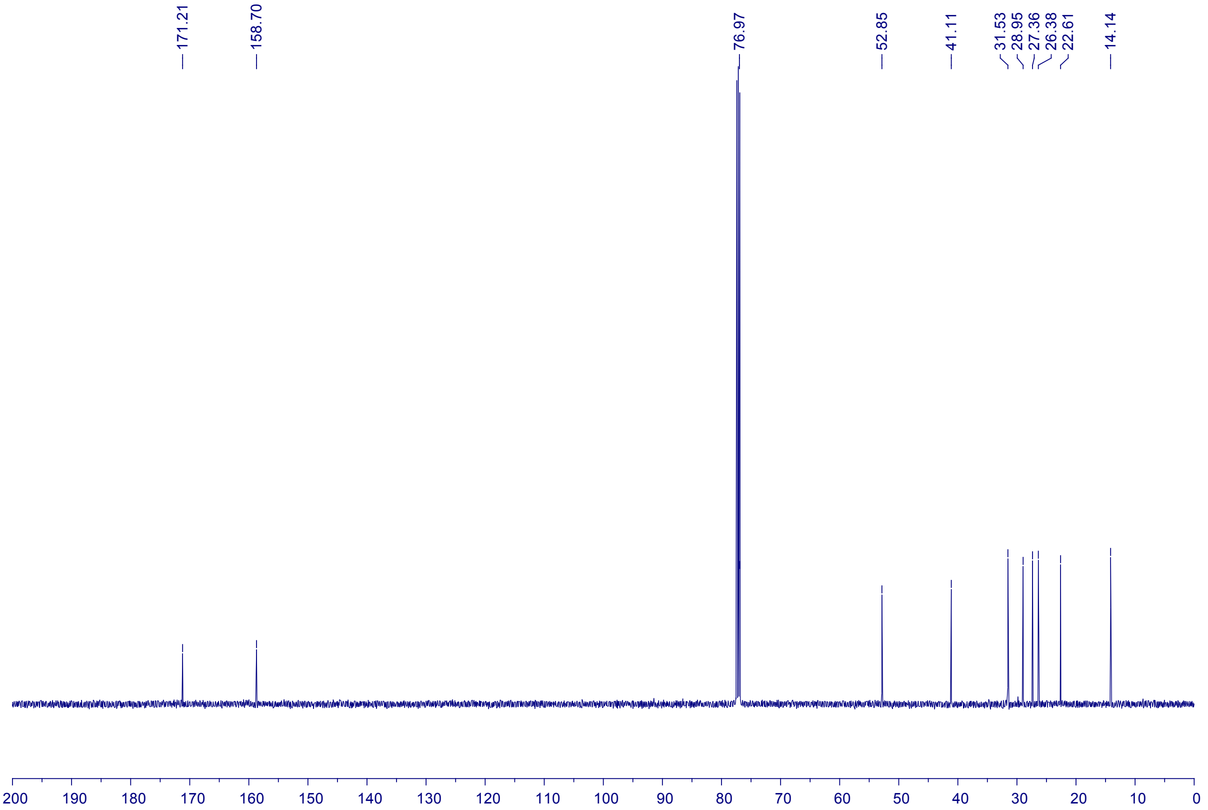
2v, ^{13}C NMR (101 MHz, CDCl$_3$)



2z, ^{1}H NMR (400 MHz, CDCl$_3$)



2z, ^{13}C NMR (101 MHz, CDCl$_3$)



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