Supporting Information

Photocatalytic N-Formylation of Amines via a Reductive Quenching Cycle in the Presence of Air

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1. General methods and material

Eosin Y disodium salt (≥ 85% dye content, catalogue number 115935-25G) was purchased from Merck Millipore. All other commercially available reagents and solvents were purchased and used without further purification. Compound **1f** was prepared according to the literature procedure.[1]

Thin-layer chromatography was performed using silica gel plates 60 F254: Visualization was accomplished with appropriate stain (basic $KMnO_4$).

Standard flash chromatography was performed on an Isolera™ Spektra Systems automated with high performance flash purification system using silica gel of particle size 40−63 μm. Macherey-Nagel silica gel 60 M (230-440 mesh) was used for column chromatography.

^1H and ^{13}C NMR spectra were recorded on Bruker Avance spectrometers (400 MHz and 101 MHz) in $CDCl_3$ solution with internal solvent signal as reference (7.26 and 77.0, respectively). Proton NMR data are reported as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, ddd = doublet of doublets of doublets, td = triplet of doublets, m = multiplet, br. s. = broad singlet), coupling constants (Hz) and numbers of proton. Data for ^{13}C NMR are reported in terms of chemical shift and no special nomenclature is used for equivalent carbons.

Gas chromatography (GC) and gas chromatography coupled to low resolution mass spectrometry (GC-MS) analyses were performed using a capillary column (length: 30 m; diam. 0.25 mm; film: 0.25 μm) using He gas as carrier. GC was equipped with a FID detector. GC-MS was performed on 5975 MSD single quadruple detector. Formylated products were identified by comparing with authentic samples (GC/FID). Quantification of the *N*-formylated products was performed by GC/FID analysis using internal standard.

UV–Vis analyses were performed with Varian Cary 50 UV/Vis spectrophotometer and Agilent 8453 UV-Vis Spectrometer. For UV measurements 10 mm Hellma fluorescence quartz cuvette (117.100F-QS) was used.

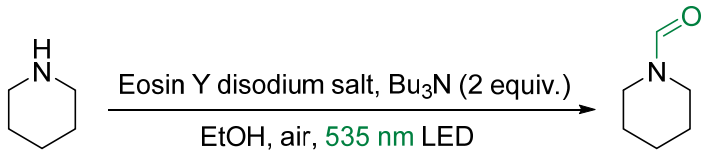
Photocatalytic reactions were performed with 535 nm LEDs (OSRAM Oslon SSL 80 green LEDs, λ_{em} = 535 nm (± 15 nm), 3.5 V, 700 mA).

2. General procedure for the formylation of amines

The amine (0.05 mmol, 1 eq.) was placed in a 5 mL vial equipped with a small PTFE stirring bar and then 2 mL solution of Eosin Y disodium salt in ethanol (0.0025 mmol, 5 mol%) was added immediately to avoid any evaporation of the amine. Then tributylamine (0.1 mmol, 2 eq.) was added (only for the formylation of secondary/primary amines, not for the formylation of tertiary amines) to the reaction mixture and the reaction vial was placed in a cooling block maintaining 23 °C in open atmosphere. The reaction mixture was stirred and irradiated through the plane bottom of the vials by 3W blue LED (λ_{em} = 535 nm) and the reaction conversion was monitored by GC analysis. After complete conversion an internal standard (4-*tert*-butylcyclohexanone, 0.5 mL, *c* = 15 mg/mL) was added to the reaction mixture and the product yield was determined by GC/FID using a calibrated method.

3. Control Experiments

All control experiments were repeated three times. For each control experiment one component of the reaction system depicted in Scheme S1 was omitted or substituted (Table S1).



Scheme S1: Typical reaction procedure

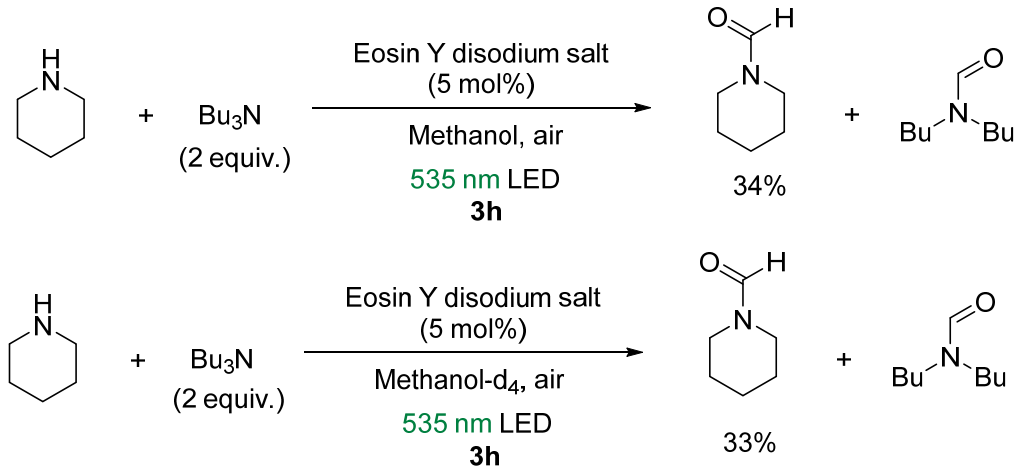
Table S1: Control experiments

Entry	Photocatalyst (mol%)	Bu_3N (equiv.)	Light (535 nm)	Reaction condition	Time (h)	Yield (%)*
1	**5**	**2**	**yes**	**EtOH, air**	**8**	**68**
2	5	2	-	EtOH, air	12	<1
3	-	2	yes	EtOH, air	12	0
4	5	-	yes	EtOH, air	12	0
5	-	2	yes	EtOH, air	12	0
6	5	2	yes	EtOH, N_2	12	0
7	5	2	yes	EtOH, $PhNO_2$, N_2	12	0

[a] GC/FID determined yield with appropriate internal standard.

4. Deuterium labeling experiment

As the reaction also works in MeOH, instead of EtOH as the solvent, we performed the deuteration experiment using MeOH as the solvent, as deuterated methanol is easily available and less expensive than deuterated ethanol.

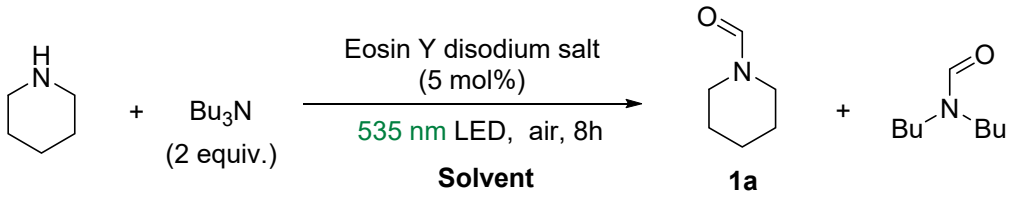


Scheme S2: No deuterium incorporation in the product.

We did not allow the reaction to go full conversion (normal reaction time is 8h) and wanted to find out if the reaction is faster in deuterated solvent and if there is any difference in the GC yield after 3 hours of irradiation. We concluded that the deuterated solvent had no effect on the reaction rate. So, singlet oxygen is not involved, as the lifetime of the singlet oxygen is much higher in deuterated solvent and the reaction should occur at a faster rate, which is not the case. Also, there was no deuterium incorporation in the product, which proves that the proton of formamide is not coming from the solvent.

5. Screening of solvents

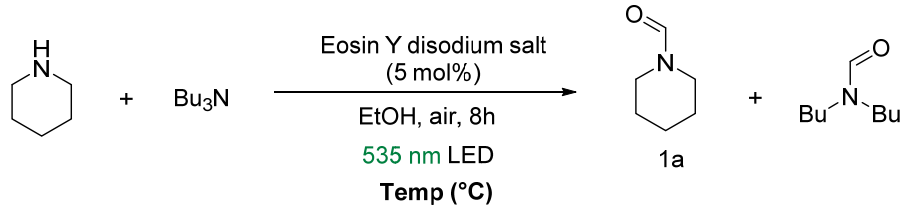
Many solvents were investigated and in our experience EtOH was the best choice. Below here, are the list of solvents screened.



Solvent	Yield of **1a** (%)
EtOH	68
MeOH	56
Isopropanol	21
MeCN (catalyst less soluble)	19
DMF	50
DMSO	17
DCM	45
MeCN/H_2O (1:1)	<5
H_2O	0

6. Screening of temperature

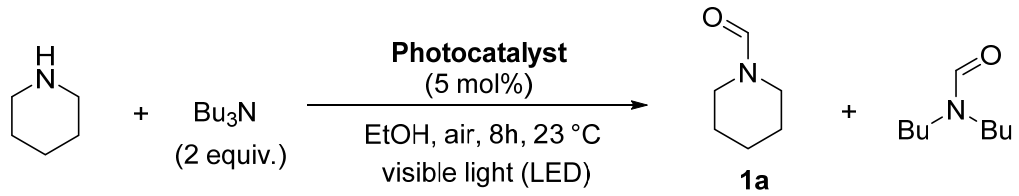
All the reactions were performed at 23 °C. The reaction works better at room temperature; increasing temperature decreases the product yield.



Temperature (°C)	Yield of 1a (%)
18	67
23	68
30	51
40	37

7. Screening of the photocatalysts

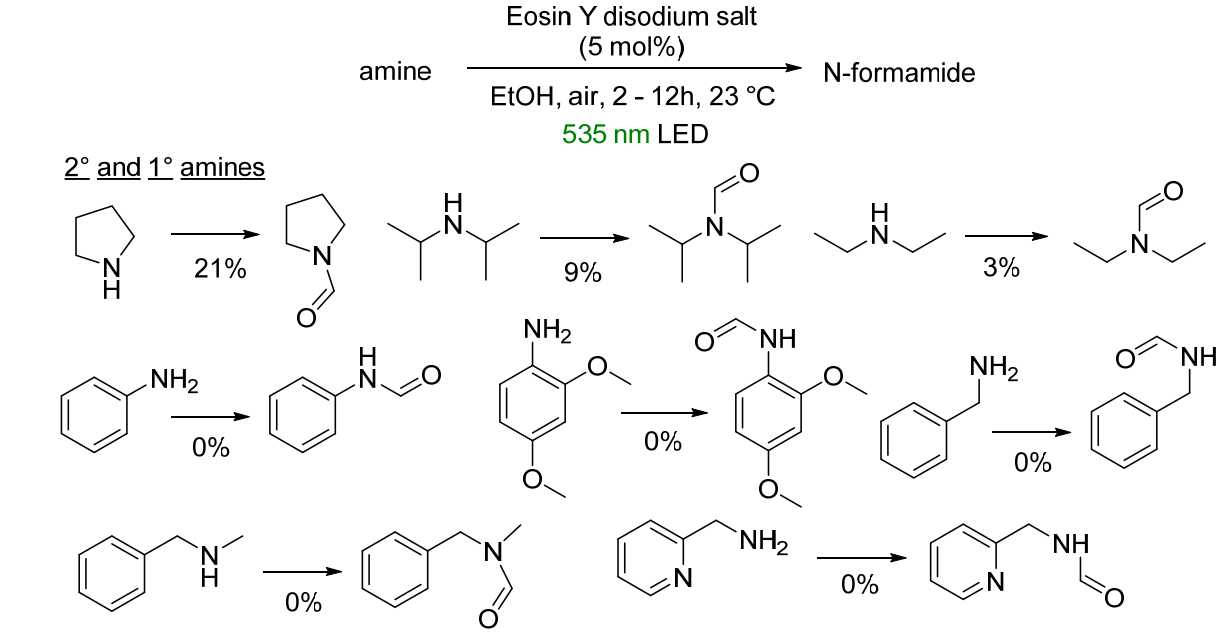
Different photocatalysts (homogeneous and heterogeneous) were screened in the reaction condition. Bodipy-I_2 gave slightly better yields compared to Eosin Y disodium salt, but Bodipy dyes are much more expensive. Therefore, commercially available, cheap Eosin Y disodium salt was used as the photocatalyst.



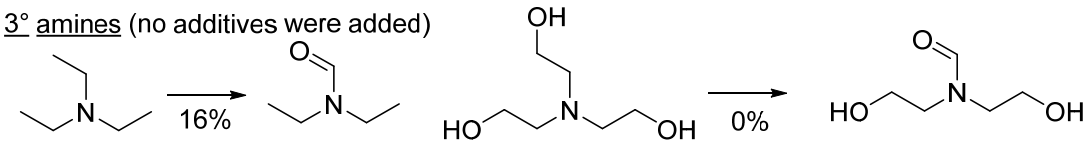
Photocatalyst	Yield of **1a** (%)
Eosin Y disodium salt	68
Eosin Y	61
Eosin B	31
Fluorescein	41
Rose Bengal	64
Erythrosin B	65
PDI	54
Rh-6G	17
$Ru(bpy)_3Cl2.6H_2O$	40
NDI	22
Bodipy-I_2	74
Acr^+-Mes	19
Riboflavin tetraacetate	7
$Cu(dap)_2Cl$	<1
$Ir(ppy)_3$	26
Methylene Blue	15
$PbBiO_2Br$	0
TiS_2	0
$YBiWO_3/RuO_2$	0

8. Scope of other amines

Several other amines were investigated, but only few gave the formylated product.



In these reactions (2° and 1° amines) 2 equiv. of Bu_3N was added for the effective quenching of the photocatalyst.



9. Photochemical reaction setup for the *N*-formylation of amines

Fig. S1: Irradiation setup

10. GC calibration curves

GC was calibrated using a four-point calibration; all calibrations were performed using 4-*tert*-butylcyclohexanone as an internal standard. The GC oven temperature program was adjusted to an initial temperature of 40 °C kept for 3 minutes, the temperature was increased at a rate of 15 °C/min over a period of 16 minutes until it reached 280 °C, then it was kept for 5 minutes at that temperature. Finally, the GC oven was heated at a rate of 25 °C/min till the final temperature (300 °C) was reached and kept for 5 minutes.

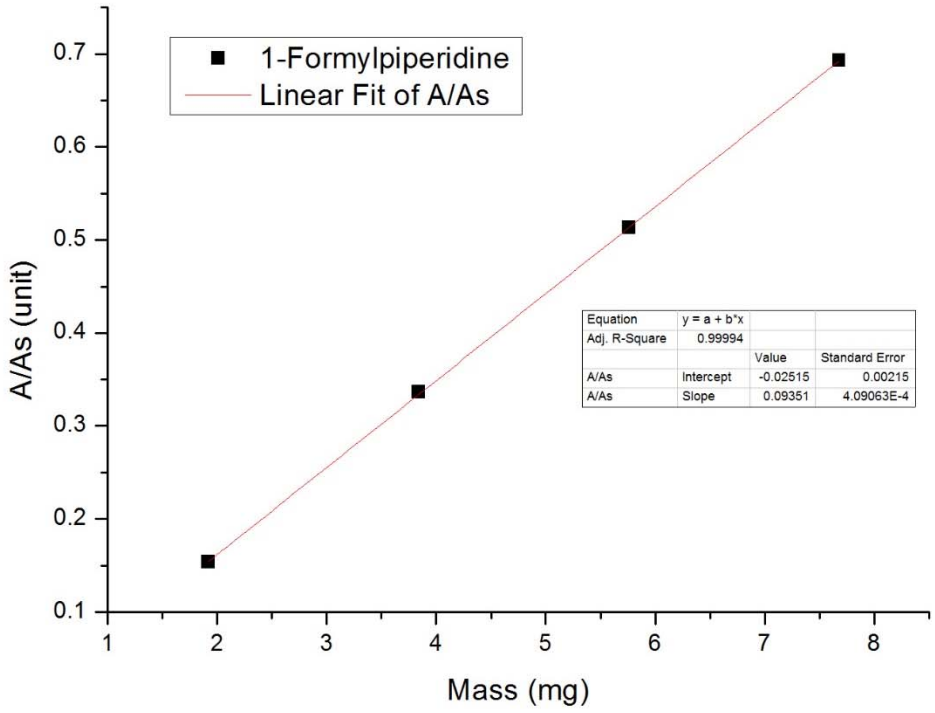


Fig. S2: Calibration curve for 1-formylpiperidine

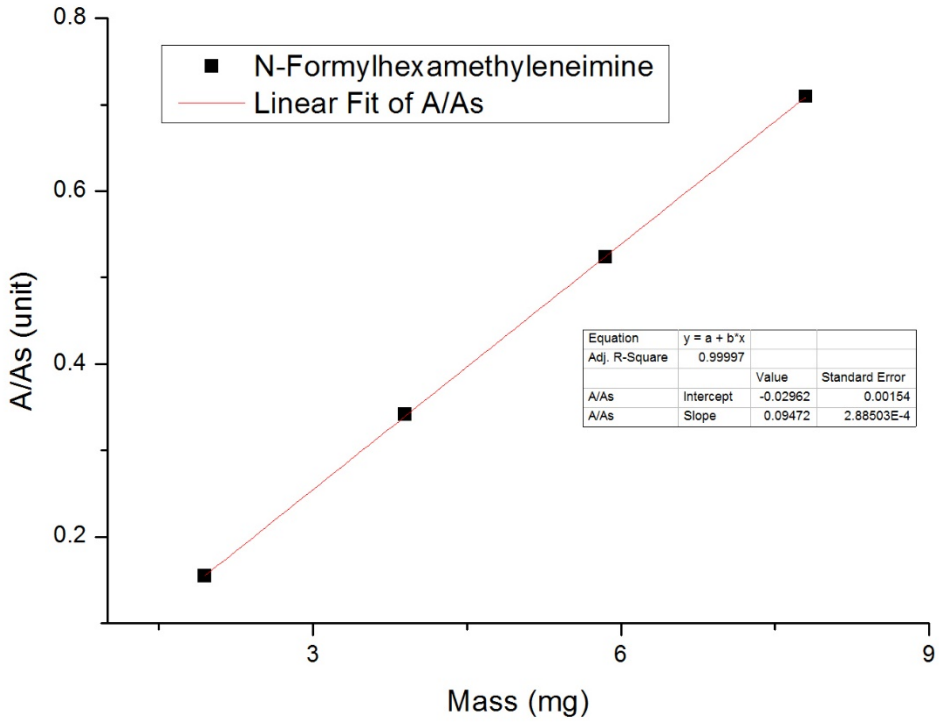


Fig. S3: Calibration curve for *N*-formylhexamethyleneimine

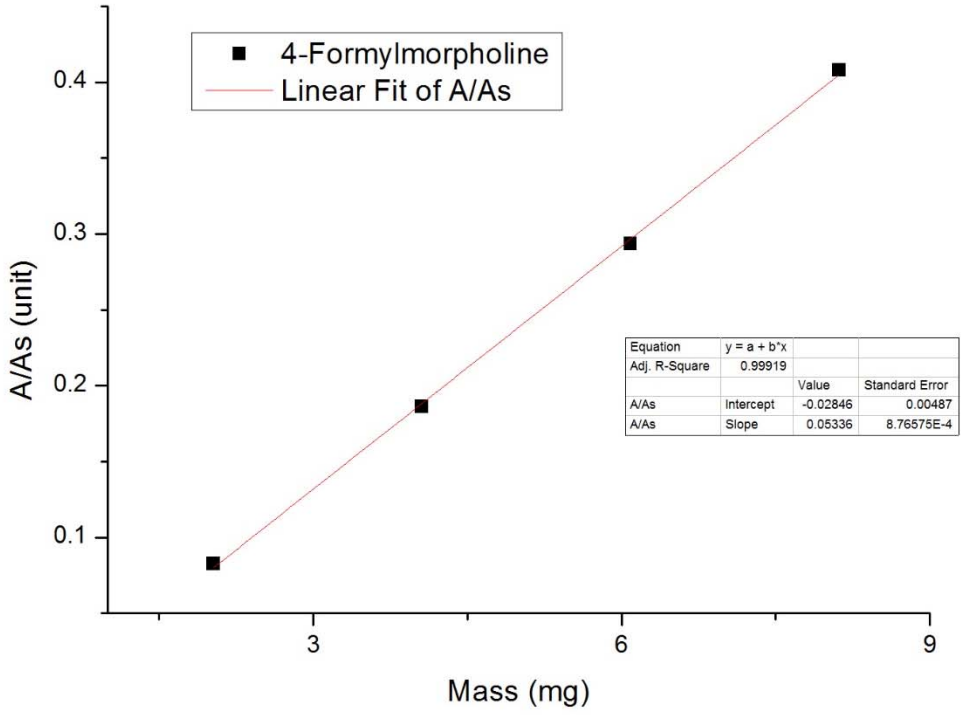


Fig. S4: Calibration curve for 4-formylmorpholine

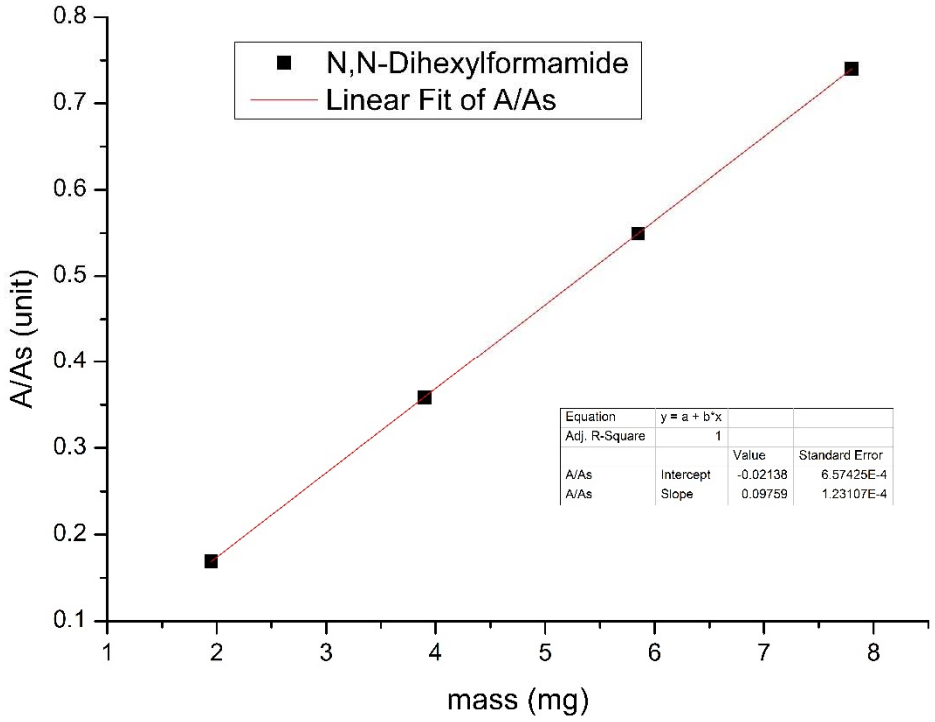


Fig. S5: Calibration curve for *N,N*-dihexylformamide

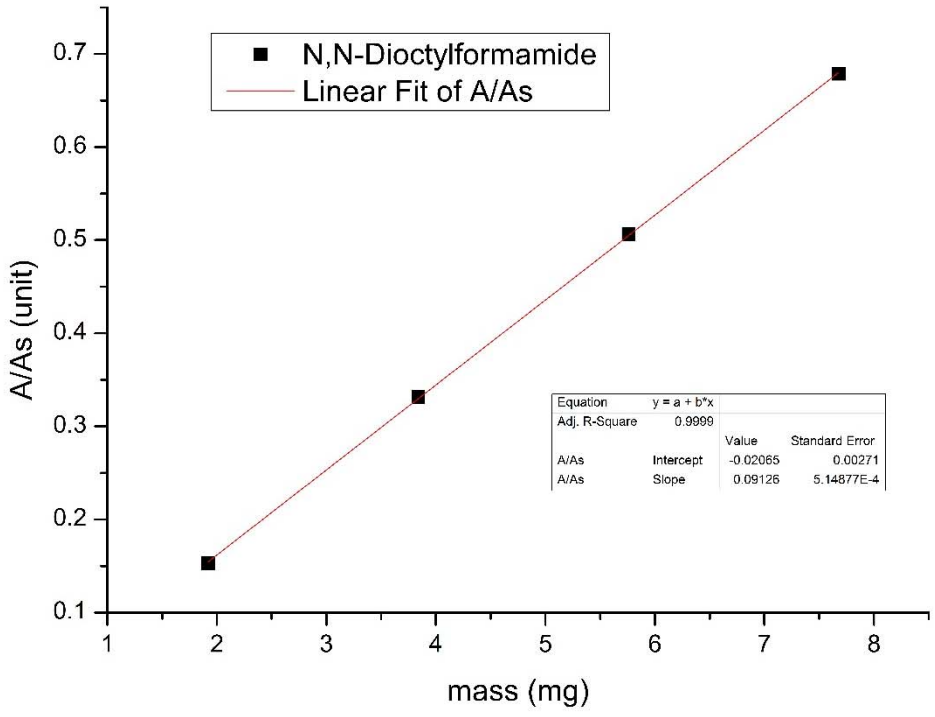


Fig. S6: Calibration curve for *N,N*-dioctylformamide

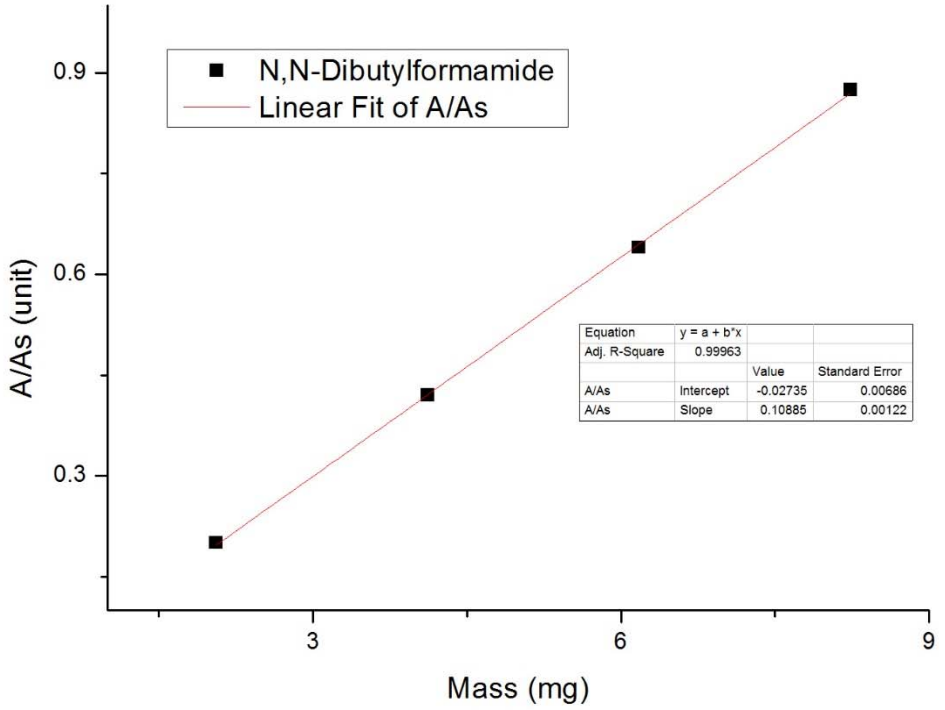


Fig. S7: Calibration curve for *N,N*-dibutylformamide

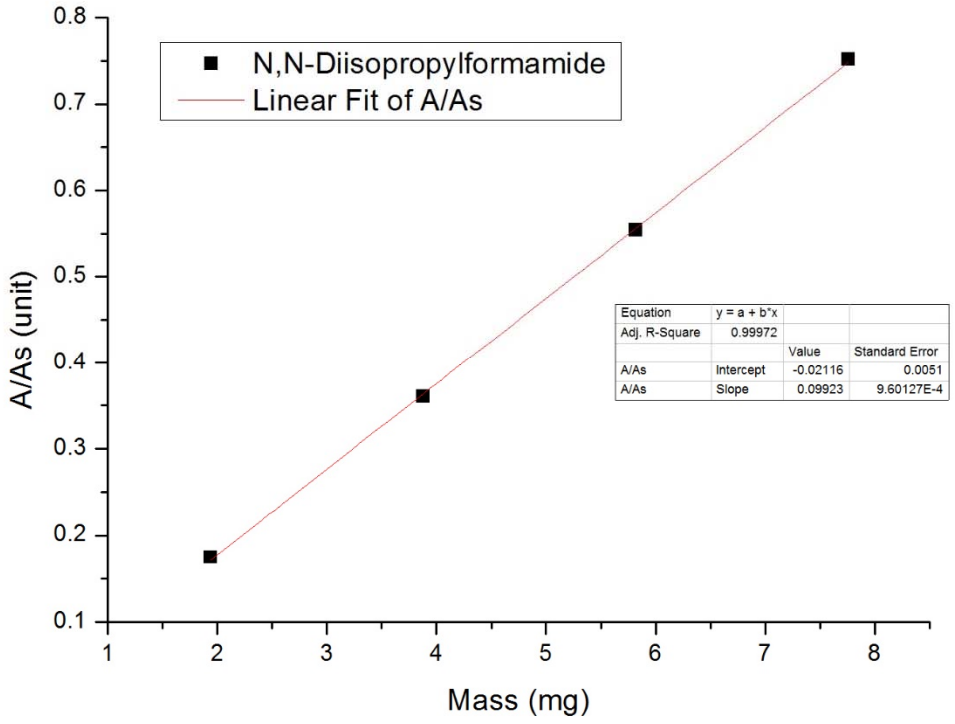


Fig. S8: Calibration curve for *N,N*-diisopropylformamide

11. Recovering the catalyst for further reactions

Eosin Y disodium salt was used 5 mol% with respect to the amine, 70% of which can be recovered after the reaction and can be used for further reaction. The formylation of piperidine gives 68% of the formylated product using 5 mol% of Eosin Y disodium salt. Using the recovered amount of photocatalyst from one reaction, the next reaction was performed using piperidine as a substrate, which gave 60% of the formylated product. The UV-Vis spectra confirmed that the recovered photocatalyst is identical to the original one.

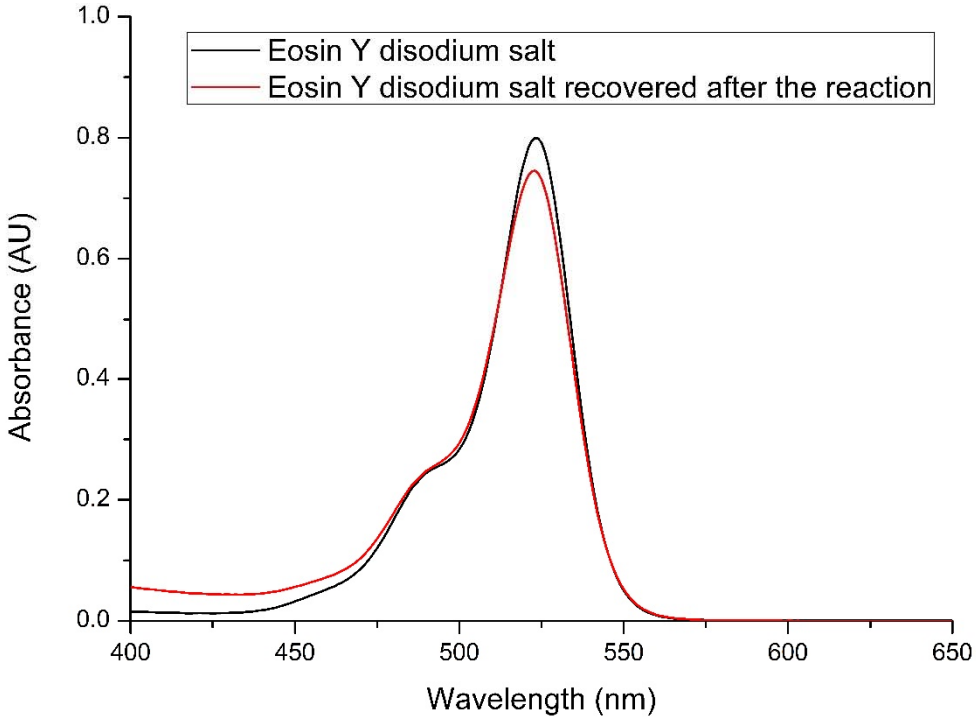


Fig. S9: Comparison of the UV-Vis spectra of Eosin Y disodium salt and the recovered Eosin Y disodium salt after the reaction

12. Alternative mechanism of the N-formylation

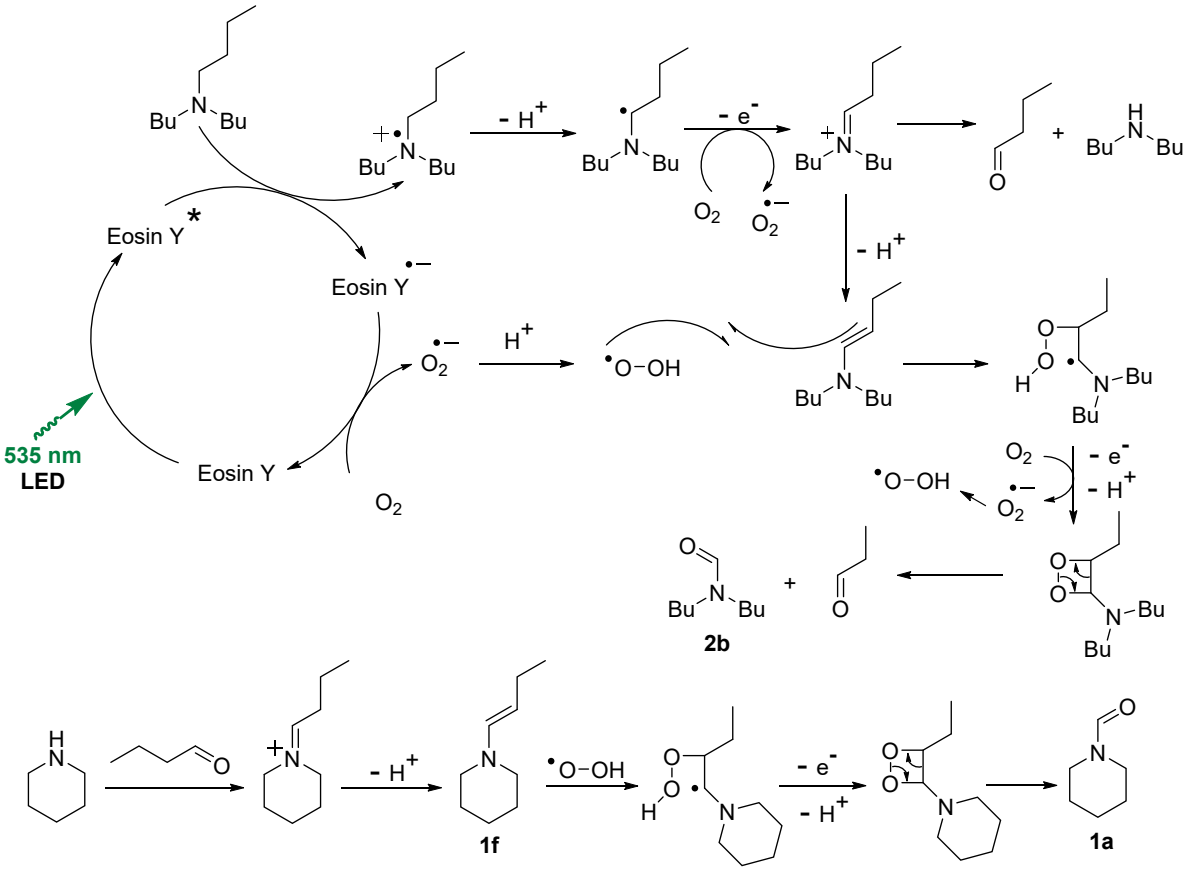
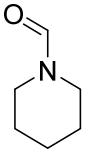


Fig. S10: Alternative mechanism for the formylation of amines where *in situ* formed enamine reacts with hydroperoxyl radical in a stepwise mechanism to form *N*-formamides.

13. Characterization of isolated *N*-formamides

Piperidine-1-carbaldehyde (**1a**):[2]



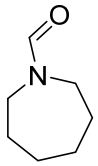
The compound was prepared according to the general procedure for the formylation of secondary/primary amines. The product was obtained by column chromatography (hexane/EtOAc, 1:1) as a colorless liquid in a yield of 54%.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.98 (s, 1H), 3.54 – 3.36 (m, 2H), 3.36 – 3.21 (m, 2H), 1.73 – 1.60 (m, 2H), 1.60 – 1.44 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 160.87, 46.93, 40.71, 26.58, 25.09, 24.70.

HRMS: calculated for M^+ $C_6H_{11}NO^+$ 113.0835; found 113.0835.

1-(formyl)-hexahydro-1H-azepine (**1b**):[3]

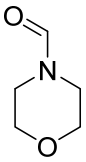


The compound was prepared according to the general procedure for the formylation of secondary/primary amines. The product was obtained by column chromatography (hexane/EtOAc, 1:1) as a colorless liquid in a yield of 44%.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (s, 1H), 3.44 (t, *J* = 5.7 Hz, 11.7 Hz, 2H), 3.37 (t, *J* = 7.2 Hz, 12 Hz, 2H), 1.73-1.69 (m, 4H), 1.57-1.55 (m, 4H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 163.1, 48.0, 43.7, 30.4, 28.1, 27.1, 27.0

N-formylmorpholine (**1c**):[3]

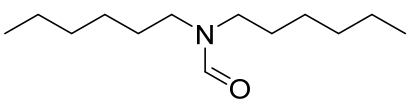


The compound was prepared according to the general procedure for the formylation of secondary/primary amines. The product was obtained by column chromatography (hexane/EtOAc, 1:1) as a pale yellow liquid in a yield of 31%.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (s, 1H), 3.70-3.63 (m, 4H), 3.58-3.66 (m, 2H), 3.48 (t, *J* = 3 Hz, 9 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 67.4, 66.6, 46.0, 40.8.

N,N-Dihexylformamide (**1d**):[2]



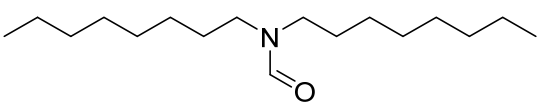
The compound was prepared according to the general procedure for the formylation of amines. The product was obtained by column chromatography (hexane/diethyl ether, 2:3) as a colorless liquid in a yield of 28%.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.04 (s, 1H), 3.36 – 3.23 (m, 2H), 3.19 (t, *J*=7.1, 2H), 1.59 – 1.45 (m, 4H), 1.36 – 1.21 (m, 12H), 0.93 – 0.83 (m, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 161.81, 46.65, 41.30, 30.50, 30.35, 27.55, 26.20, 25.58, 25.11, 21.54, 21.51, 13.00, 12.97.

HRMS: calculated for M^+ $C_6H_{11}NO^+$ 213.2087; found 213.2088.

N,N-Dioctylformamide (**1e**):[4]



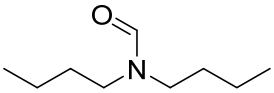
The compound was prepared according to the general procedure for the formylation of amines. The product was obtained by column chromatography (hexane/diethyl ether, 2:3) as a colorless liquid in a yield of 26%.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.05 (s, 1H), 3.34 – 3.24 (m, 2H), 3.20 (t, *J*=7.2, 2H), 1.59 – 1.44 (m, 4H), 1.35 – 1.20 (m, 20H), 0.91 – 0.84 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ = 162.94, 47.80, 42.44, 31.79, 31.75, 29.31, 29.22, 29.17, 28.65, 27.29, 26.96, 26.49, 22.64, 22.63, 14.09, 14.08.

HRMS: calculated for M^+ $C_6H_{11}NO^+$ 269.2713; found 269.2703.

N,N-dibutylformamide (**2b**):[3]



The compound was prepared according to the general procedure for the formylation of amines. The product was obtained by column chromatography (hexane/diethyl ether, 2:3) as a colorless liquid in a yield of 36%.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.03 (s, 1H), 3.28 (t, *J* = 7.5 Hz. 15 Hz, 2H), 3.30-1.53 (m, 4H), 1.48-1.23 (m, 4H), 0.95 (td, *J* = 2.1 Hz, 8.1 Hz, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.9, 47.4, 42.1, 30.8, 29.5, 20.3, 19.8, 14.0, 13.8.

14. References

[1] M. H. Norman, C. H. Heathcock, *J. Org. Chem.* 1988, *53*, 3370-3371.
[2] W. Li, X.-F. Wu, *Chem. Eur. J.* 2015, *21*, 14943-14948.
[3] H. Liu, Q. Mei, Q. Xu, J. Song, H. Liu, B. Han, *Green Chem.* 2017, *19*, 196-201.
[4] T. V. Q. Nguyen, W.-J. Yoo, S. Kobayashi, *Angew. Chem. Int. Ed.* 2015, *54*, 9209-9212.

15. ^{1}H and ^{13}C NMR spectra of the isolated *N*-formamides:

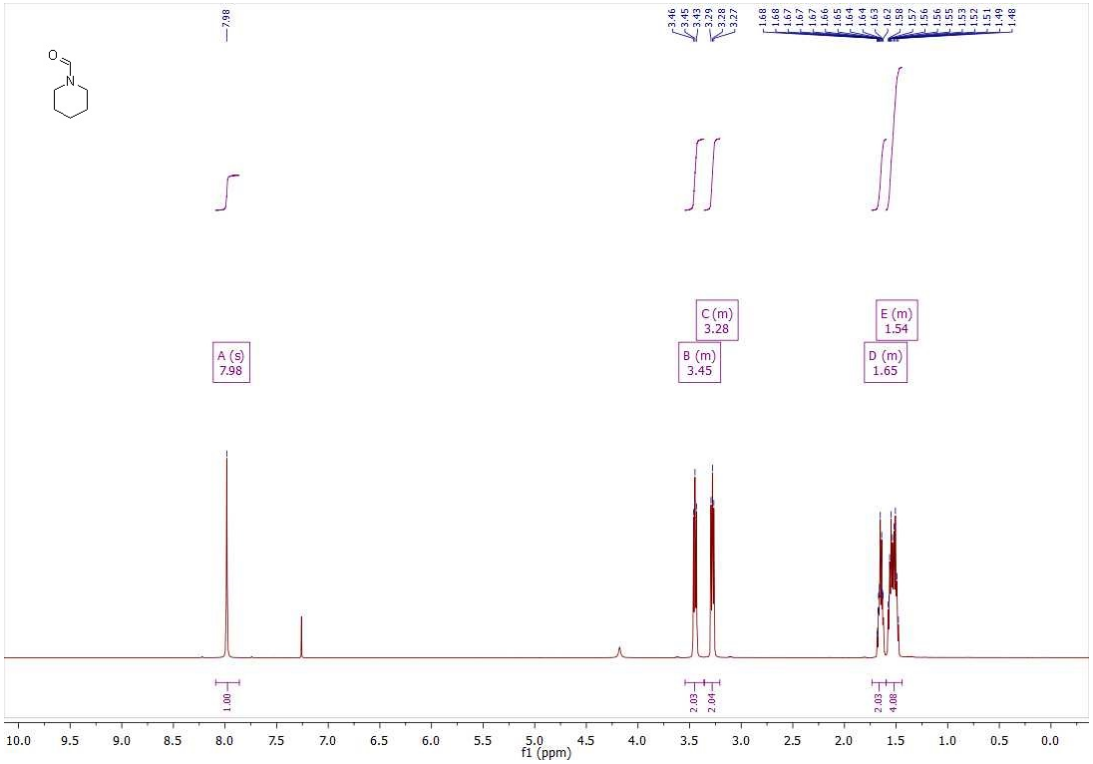


Fig. S11: ^{1}H spectrum of piperidine-1-carbaldehyde (1a)

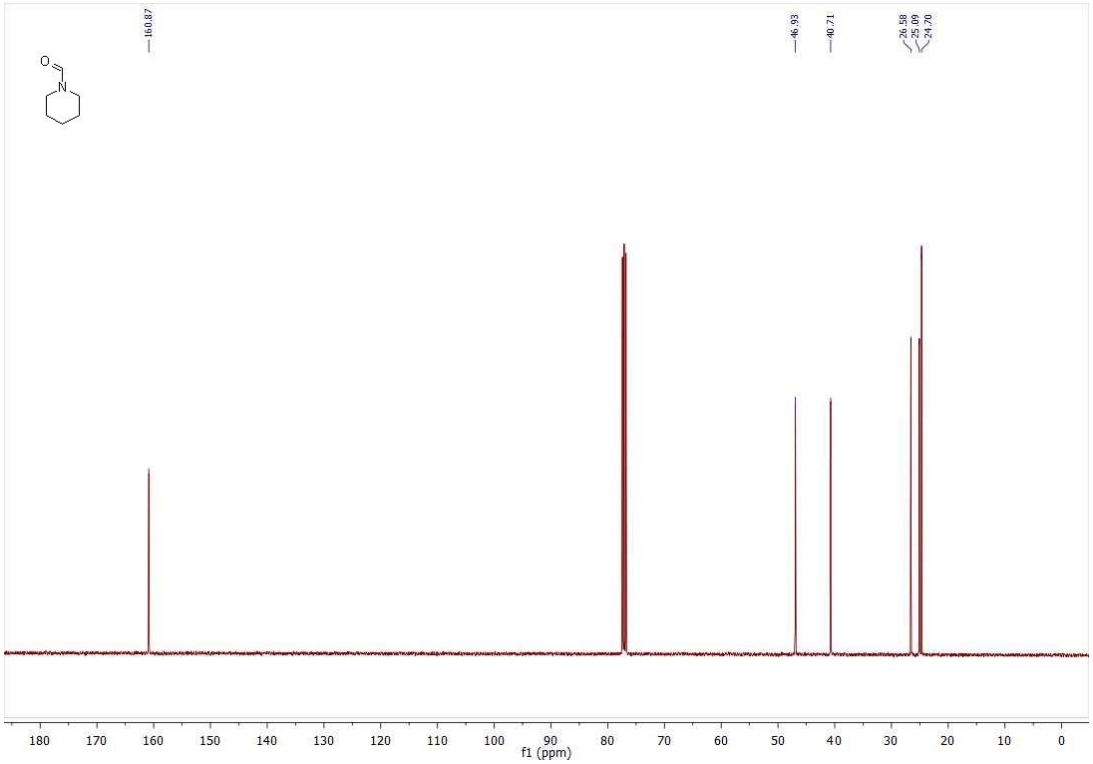


Fig. S12: ^{13}C spectrum of piperidine-1-carbaldehyde (1a)

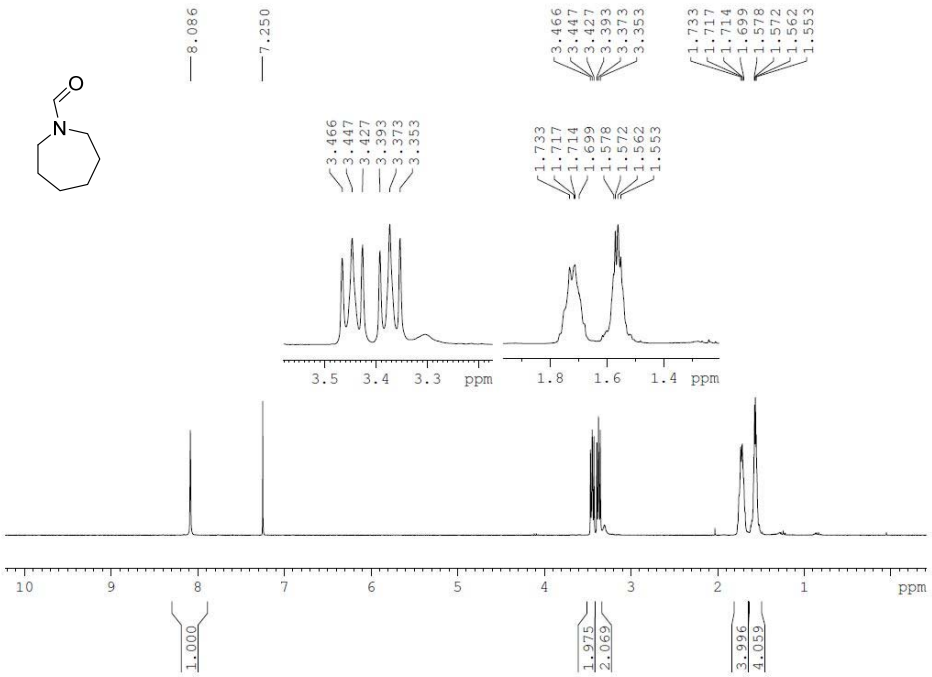


Fig. S13: ^{1}H spectrum of 1-(formyl)-hexahydro-1H-azepine (1b)

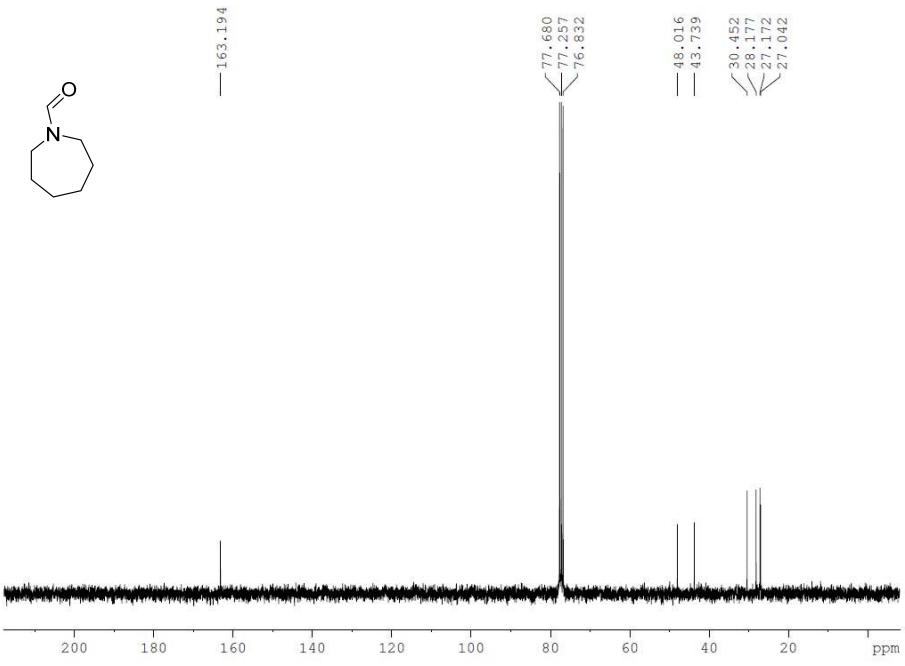


Fig. S14: ^{13}C spectrum of 1-(formyl)-hexahydro-1H-azepine (1b)

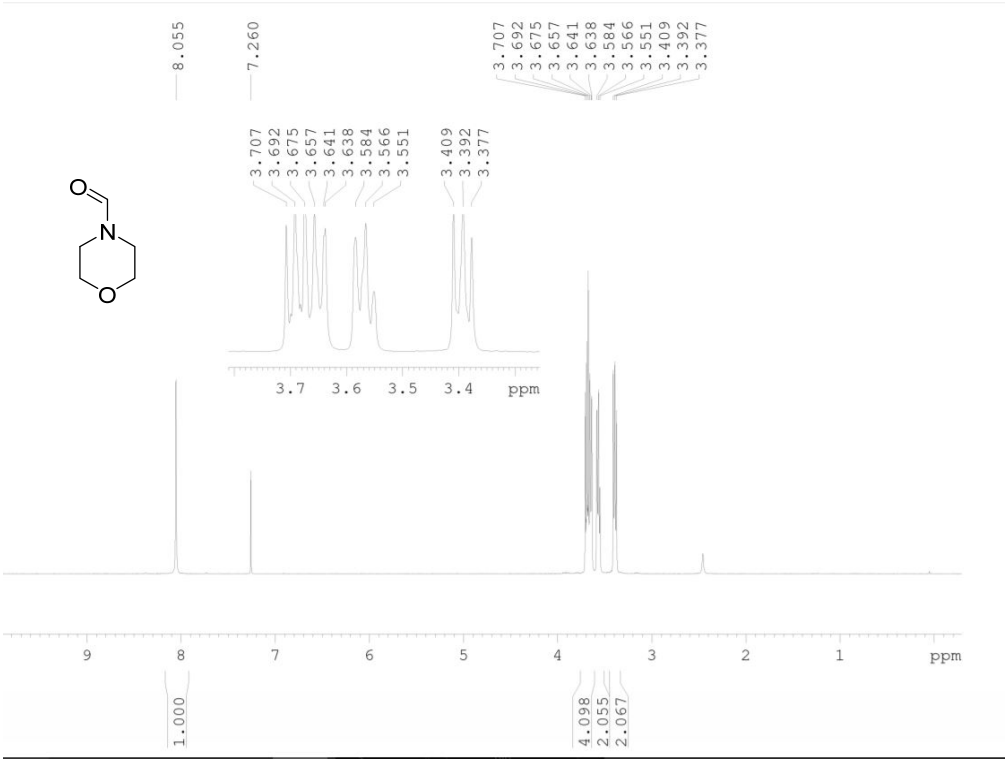


Fig. S15: ^{1}H spectrum of *N*-formylmorpholine (1c)

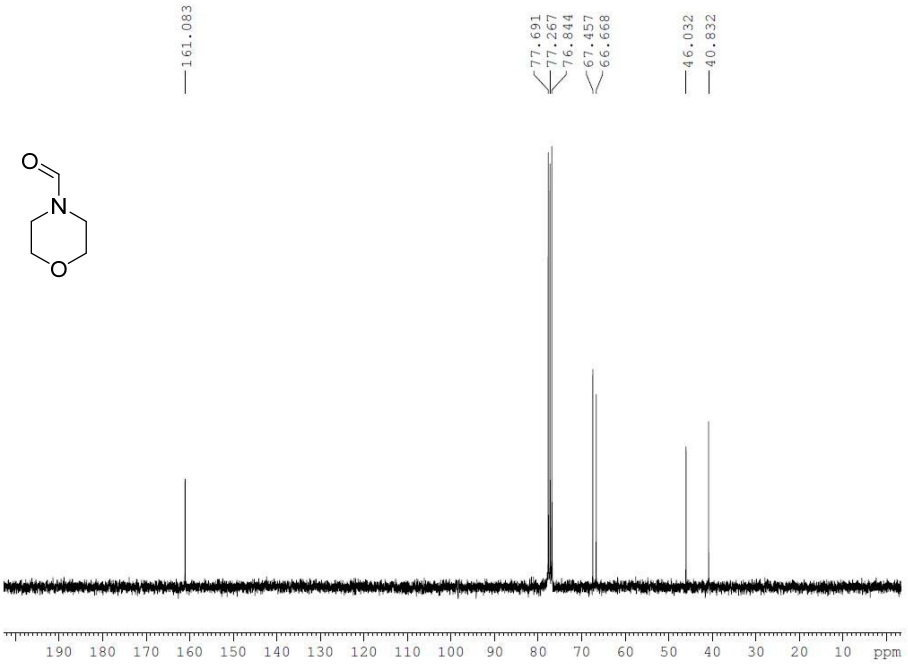


Fig. S16: ^{13}C spectrum of *N*-formylmorpholine (1c)

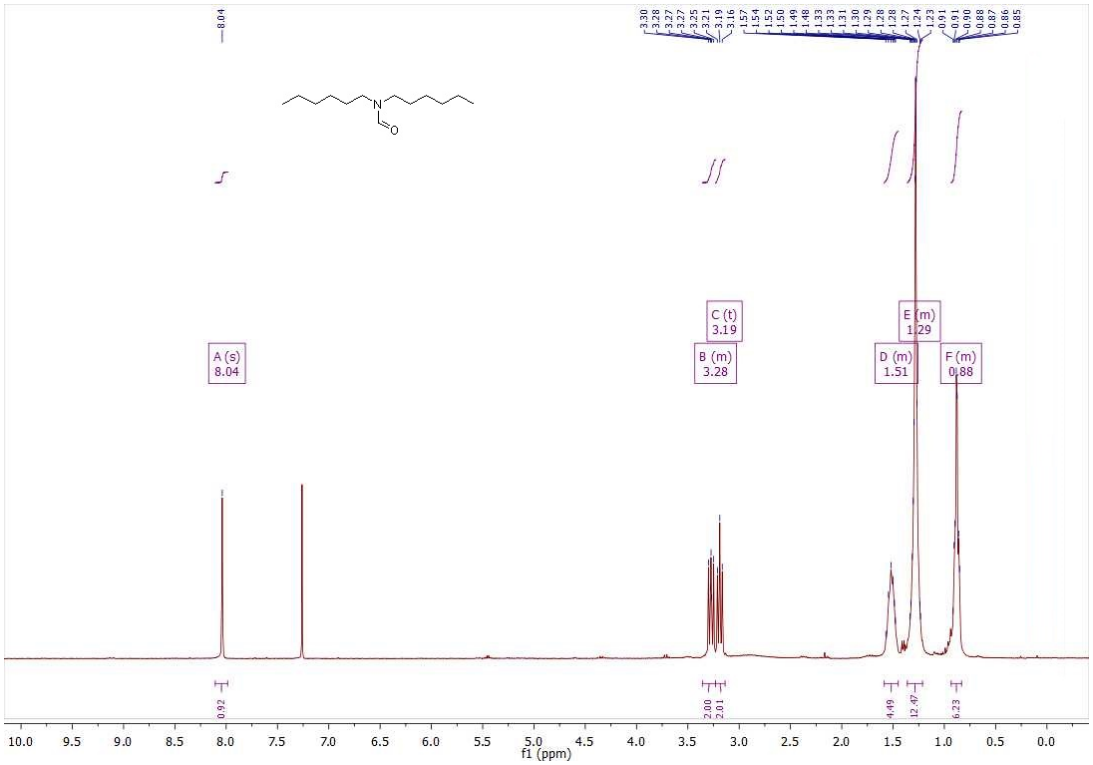


Fig. S17: ^{1}H spectrum of *N,N*-dihexylformamide (1d)

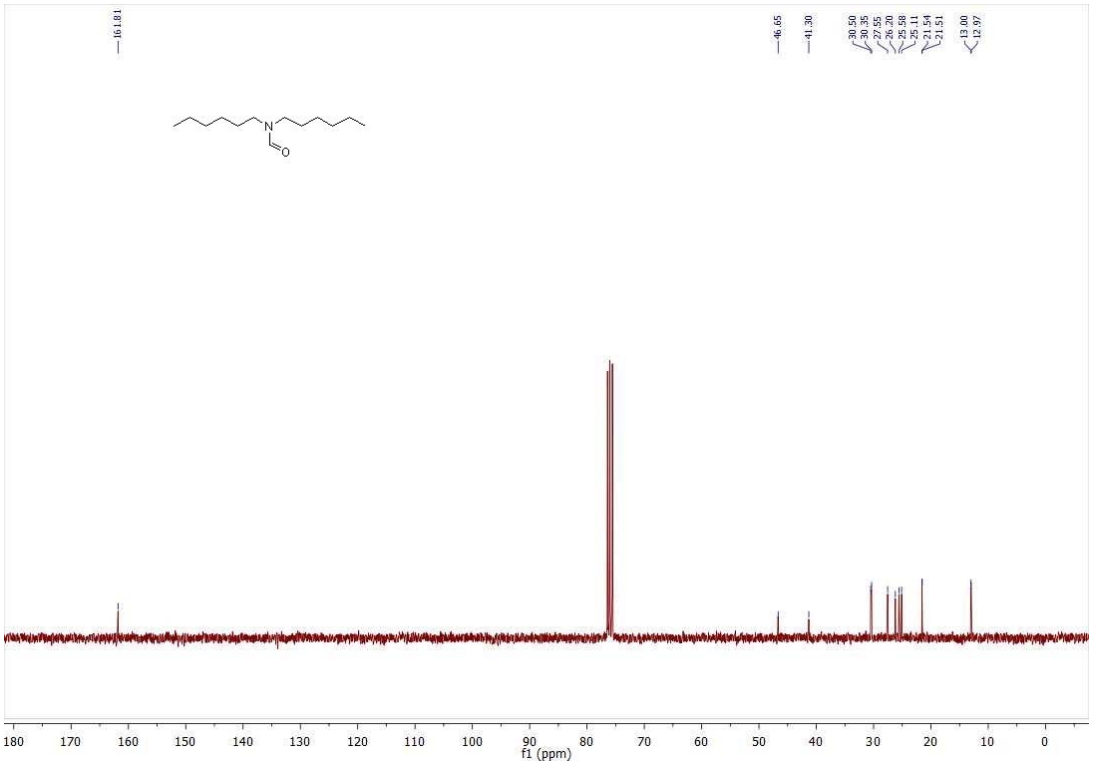


Fig. S18: ^{13}C spectrum of *N,N*-dihexylformamide (1d)

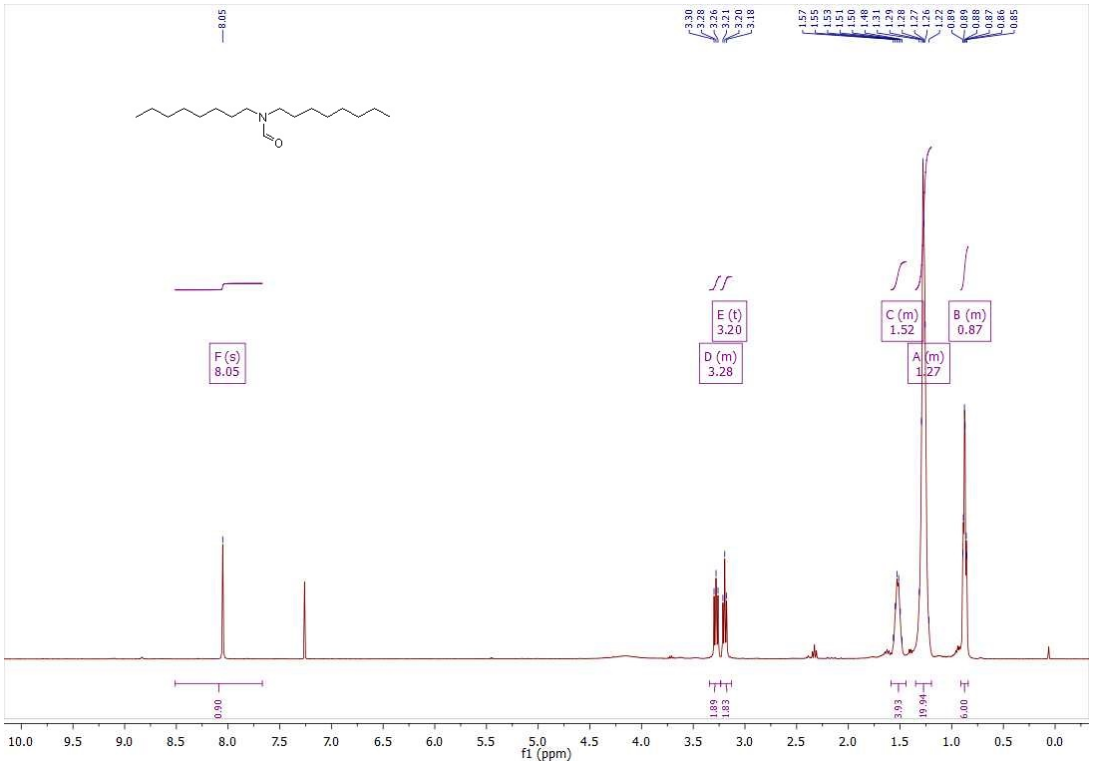


Fig. S19: ^{1}H spectrum of *N,N*-dioctylformamide (1e)

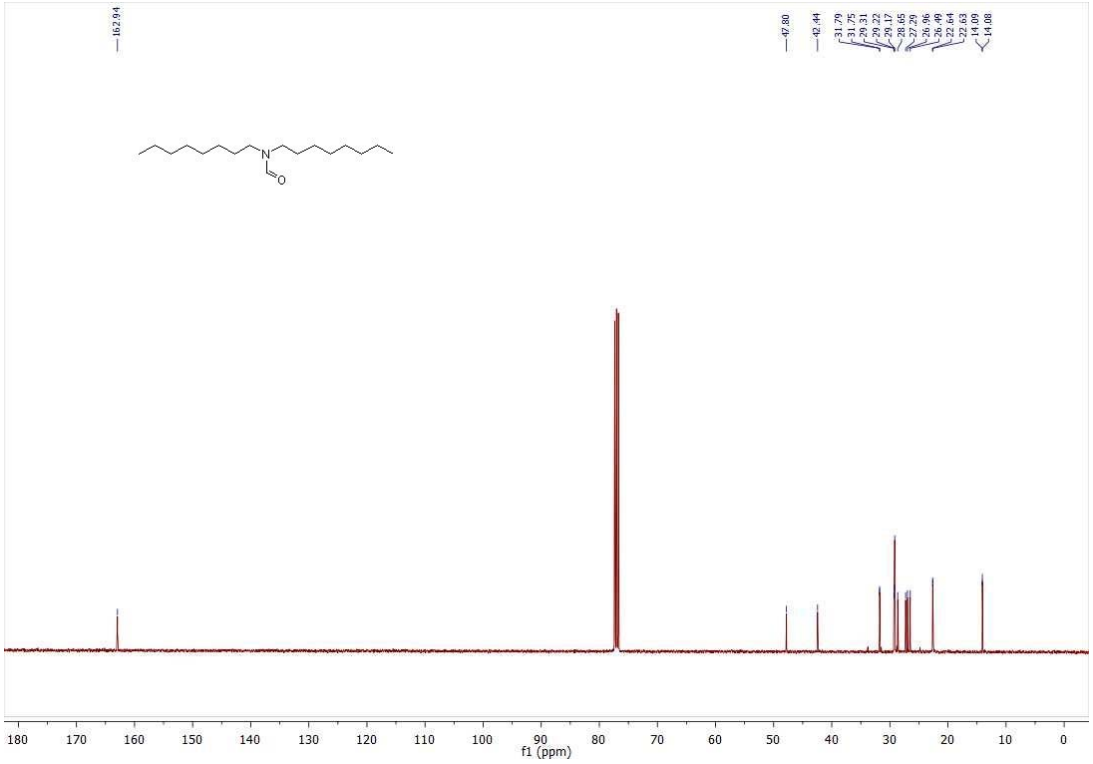


Fig. S20: ^{13}C spectrum of *N,N*-dioctylformamide (1e)

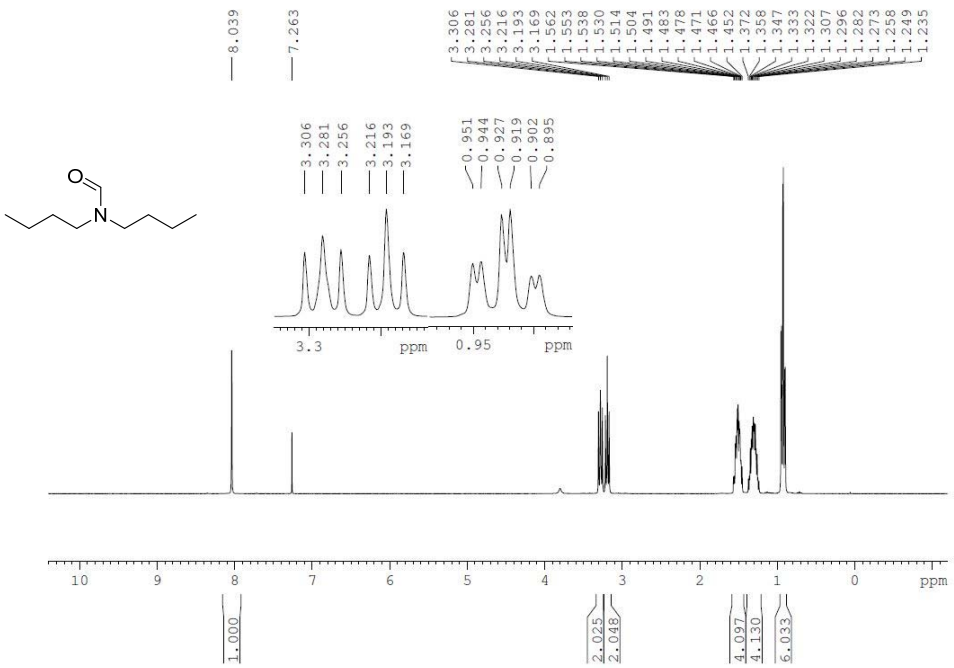


Fig. S21: ^{1}H spectrum of *N,N*-dibutylformamide (2b)

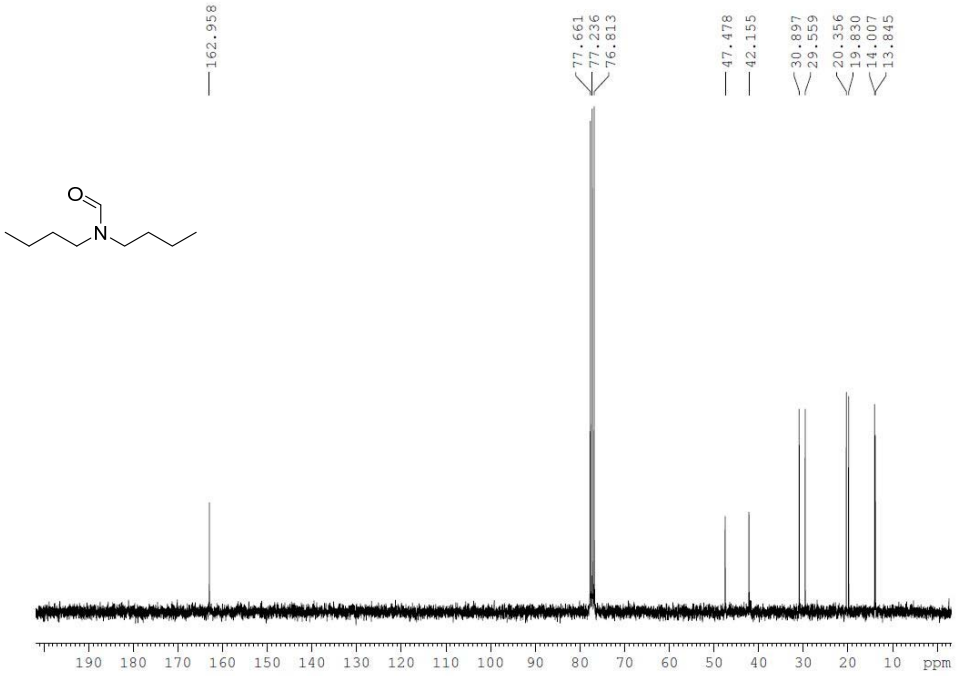


Fig. S22: ^{13}C spectrum of *N,N*-dibutylformamide (2b)