Supplementary Information (SI) for CrystEngComm.

Supplementary Information

Heating enables solid-state motion and improves the yield of a [2 + 2] cycloaddition reaction within an organic cocrystal

Gary C. George III,[a] Drew Owens,[b] Damon M. Osbourn,[c] Kristin M. Hutchins*[a,d] and Ryan H. Groeneman,*[b]

[a] Department of Chemistry, University of Missouri, Columbia, Missouri 65211, United States. Email: kristin.hutchins@missouri.edu

[b] Department of Natural Science and Mathematics, Webster University, St. Louis, Missouri 63119, United States. Email: ryangroeneman19@webster.edu

[c] Department of Chemistry, Saint Louis University, St. Louis, Missouri 63103, United States.

[d] MU Materials Science & Engineering Institute, University of Missouri, Columbia, Missouri, 65211, United States.

1. Materials, General Methods, and Synthesis of the Cocrystal

Materials

The template 4,6-dichlororesorcinol (**4,6-diCl-Res**) and ethanol were both purchased from Sigma-Aldrich Chemical (St. Louis, MO, USA) and used as received. The reactant *trans*-methyl-4-[(2-pyridin-4-yl)ethenyl]benzoate (**PEB**) was synthesized using a previously reported method.[1]

General Methods

All crystallization studies were performed in 20 mL scintillation vials and were conducted at ambient temperature and humidity. After dissolving the components as detailed below, the vials were left at room temperature, and the solvent was allowed to slowly evaporate.

Photoreactions were conducted using UV radiation from a 450 W medium-pressure mercury lamp in an ACE Glass photochemistry cabinet. The cocrystal (**4,6-diCl-Res**)·2(**PEB**) was placed between a pair of Pyrex glass plates for irradiation. The sample was heated using a Corning PC-420D hotplate (see photos of experimental setup in section 6). The photodimerization conversion for both the room temperature and heated samples of (**4,6-diCl-Res**)·2(**PEB**) were determined after UV exposure using ^{1}H NMR spectroscopy (^{1}H NMR).

The ^{1}H NMR spectra were collected using a Bruker Ascend Evo 400 MHz spectrometer with DMSO-d_6 as the solvent. Powder X-ray diffraction data was collected on a Rigaku MiniFlex 600 X-ray Powder Diffractometer acquired from Rigaku USA (The Woodlands, TX). The scan range was 3-50 degrees 2θ, the scan speed was 2 degrees/minute, and scan step was 0.01 degree. Thermal data (simultaneous TGA/DSC) was collected on a SDT Q600 acquired from TA Instruments (Newcastle, DE). The software TA Instrument Explorer 2.8.2.396 w/ Advantage for Q Series 5.5.3 was used to process the data. The sample was placed in a Tzero aluminum pan and heated from 25 to 250 °C at a rate of 20 °C/min.

Preparation of the Cocrystal

Cocrystals of (**4,6-diCl-Res**)·2(**PEB**) were synthesized by dissolving 18.7 mg of **4,6-diCl-Res** in 2 mL of ethanol that was then combined with a 2 mL ethanol solution containing 50.0 mg of **PEB** (1:2 molar ratio). The cap was removed, and then the vial was placed on the benchtop to allow for slow evaporation. Single crystals suitable for X-ray diffraction were obtained within two days.

2. X-ray Diffraction Information and Data Tables

Data were collected on a Rigaku XtaLAB Synergy-iKappa diffractometer equipped with a PhotonJet-i X-ray source operated at 50 W (50 kV, 1 mA) to generate Cu Kα radiation (λ = 1.54178 Å) and a HyPix-6000HE HPC (hybrid photon counting) detector. Crystals were transferred from the vial and placed on a glass slide in type NVH immersion oil by Cargille. A Leica optical microscope was used to identify a suitable specimen for X-ray diffraction from a representative sample of the material. The crystal and a small amount of the oil were collected on a 100-micron MiTeGen cryoloop and transferred to the instrument where it was placed under a warm nitrogen stream (Oxford) at 290 K. Data were collected at temperatures of 290 K, 310 K, 330 K, 350 K, and 370 K with a transition rate of 2 K/min between temperatures. The sample was optically centered with the aid of a video camera to ensure that no translations were observed as the crystal was rotated through all positions. The crystal was measured for size, morphology, and color.

After data collection, the unit cell was re-determined using a subset of the full data collection for each temperature. Intensity data were corrected for Lorentz, polarization, and background effects using *CrysAlisPro*.[2] A numerical absorption correction was applied based on a Gaussian integration over a multifaceted crystal and followed by a semi-empirical correction for absorption applied using the program *SCALE3 ABSPACK*.[3] The program *SHELXT*[4] was used for the initial structure solution and *SHELXL*[5] was used for the refinement of the structures. Both of these programs were utilized within the *OLEX2*[6] software. Hydrogen atoms bound to carbon and oxygen atoms were located in the difference Fourier map and were geometrically constrained using the appropriate AFIX commands.

Refinement for (4,6-diCl res)·2(PEB)

Both **PEB** molecules were disordered over two positions at each temperature. The appropriate atoms were split into sites A and B and allowed to freely refine to a stable occupancy. SIMU, RIGU, free variable DFIX, and AFIX 66 restraints and constraints were used to maintain reasonable bond lengths and ADPs. The occupancy varied throughout the temperature range, indicating dynamic motion.

Table S1. X-ray data for (**4,6-diCl res**)·2(**PEB**) at 290, 310, and 330 K.

compound formula	$C_{36}H_{30}Cl_2N_2O_6$	$C_{36}H_{30}Cl_2N_2O_6$	$C_{36}H_{30}Cl_2N_2O_6$
formula mass	657.52	657.52	657.52
crystal system	monoclinic	monoclinic	monoclinic
space group	$P2_1/n$	$P2_1/n$	$P2_1/n$
a/Å	15.67280(10)	15.69770(10)	15.72700(10)
b/Å	8.59130(10)	8.60670(10)	8.62450(10)
c/Å	23.4511(2)	23.4697(2)	23.4866(2)
α/°	90	90	90
β/°	92.6060(10)	92.6520(10)	92.6960(10)
γ/°	90	90	90
V/Å^3	3154.42(5)	3167.49(5)	3182.14(5)
ρ_{calc}/g cm^{-3}	1.385	1.379	1.372
T/K	290.0(3)	310.0(2)	330.1(2)
Z	4	4	4
radiation type	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
absorption coefficient, μ/mm^{-1}	2.271	2.261	2.251
crystal size/mm^3	0.29 x 0.174 x 0.154	0.29 x 0.174 x 0.154	0.29 x 0.174 x 0.154
no. of reflections measured	25203	24355	23462
no. of independent reflections	6654	6683	6701
no. of reflections ($I > 2\sigma(I)$)	5784	5740	5630
R_{int}	0.0306	0.0326	0.0323
R_1 ($I > 2\sigma(I)$)	0.0330	0.0338	0.0349
wR(F^2) ($I > 2\sigma(I)$)	0.0954	0.0970	0.1010
R_1 (all data)	0.0375	0.0389	0.0412
wR(F^2) (all data)	0.0993	0.1015	0.1065
Goodness-of-fit	1.080	1.064	1.085
CCDC deposition number	2486480	2486481	2486482

Table S2. X-ray data for **(4,6-diCl res)·2(PEB)** at 350 and 370 K.

compound formula	$C_{36}H_{30}Cl_2N_2O_6$	$C_{36}H_{30}Cl_2N_2O_6$
formula mass	657.52	657.52
crystal system	monoclinic	monoclinic
space group	$P2_1/n$	$P2_1/n$
a/Å	15.7598(2)	15.7987(2)
b/Å	8.64270(10)	8.66060(10)
c/Å	23.5008(2)	23.5163(3)
α/°	90	90
β/°	92.7500(10)	92.8230(10)
γ/°	90	90
V/Å^3	3197.29(6)	3213.74(7)
ρ_{calc}/g cm^{-3}	1.366	1.359
T/K	350.0(2)	370.0(3)
Z	4	4
radiation type	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
absorption coefficient, μ/mm^{-1}	2.240	2.229
crystal size/mm^3	0.29 x 0.174 x 0.154	0.29 x 0.174 x 0.154
no. of reflections measured	22494	19083
no. of independent reflections	6729	6733
no. of reflections (I > 2σ(I))	5536	5092
R_{int}	0.0338	0.0305
R_1 (I > 2σ(I))	0.0367	0.0386
wR(F^2) (I > 2σ(I))	0.1056	0.1101
R_1 (all data)	0.0443	0.0509
wR(F^2) (all data)	0.1121	0.1193
Goodness-of-fit	1.069	1.060
CCDC deposition number	2486483	2486484

3. Powder X-ray Diffraction Data

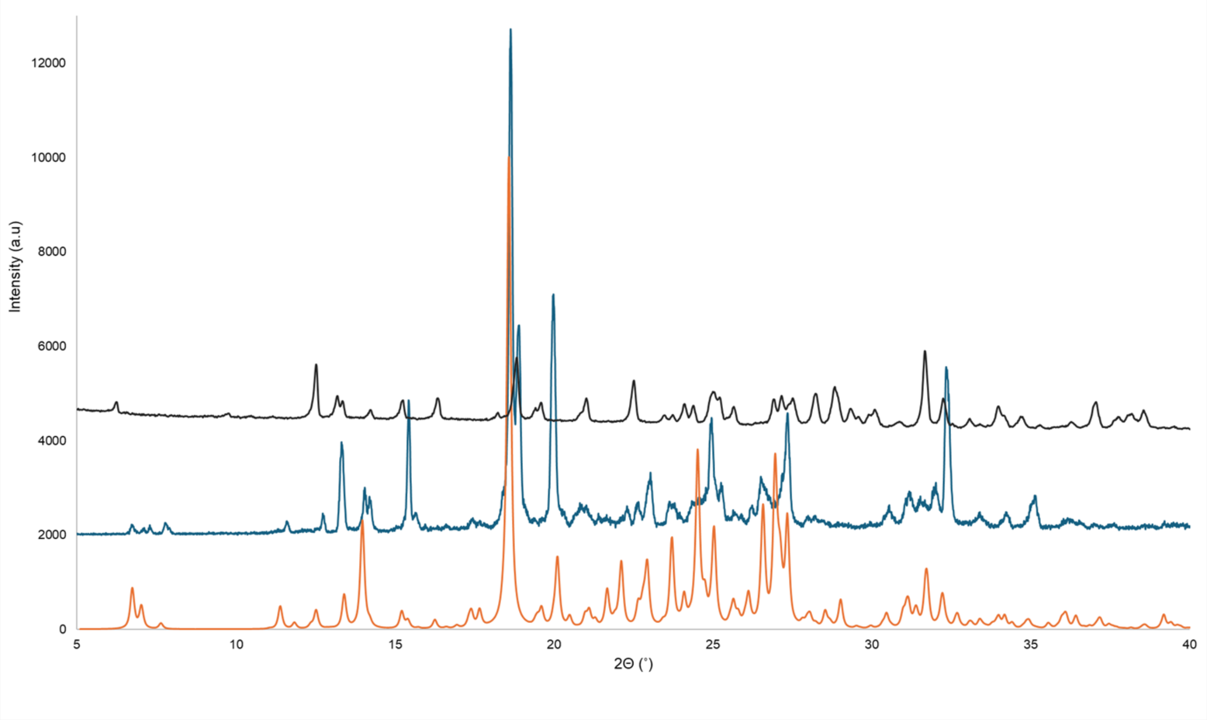

Figure S1. Powder X-ray diffraction data for (**4,6-diCl res**)·2(**PEB**). The calculated powder pattern from SCXRD data at 290 K is orange, the experimental pattern is blue, and the pattern for **4,6-diCl res** is in black (small excess present in this sample).

4. Pictures of the Experimental Setup

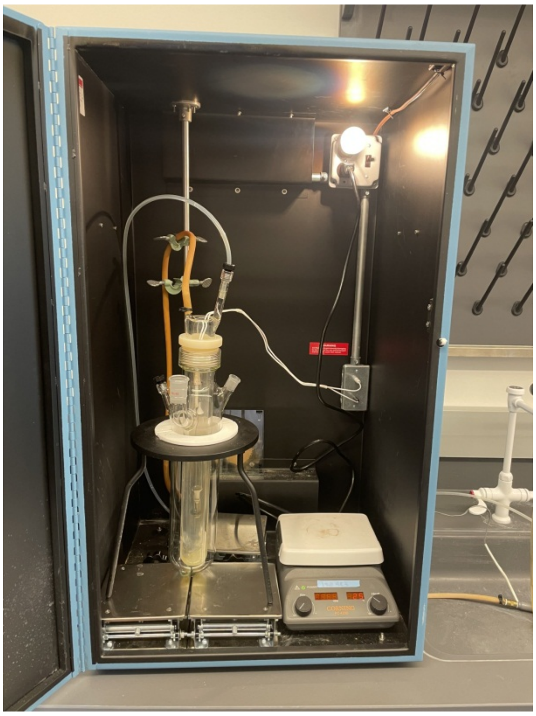

Figure S2. Experimental setup to expose (**4,6-diCl res**)·2(**PEB**) to heat and ultraviolet light simultaneously within the photoreactor.

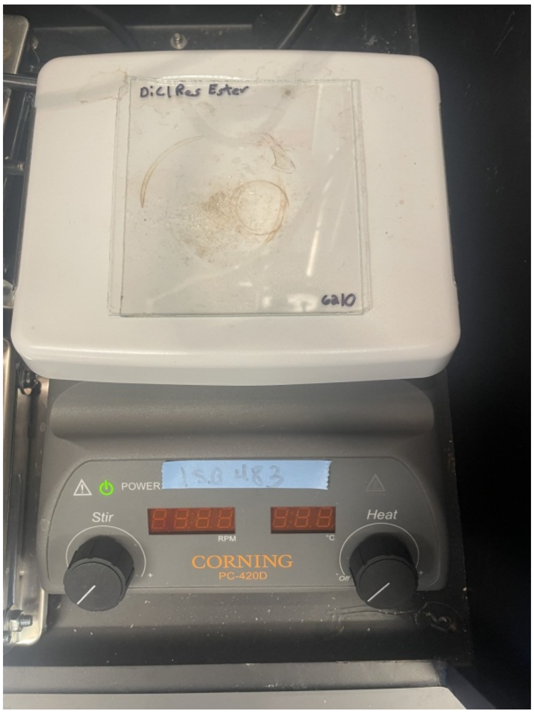

Figure S3. Location of the glass plate on the hotplate used to heat the powder sample (**4,6-diCl res**)·2(**PEB**). The top of the hot plate is a Pyroceram® Glass-Ceramic Material (from Corning®).

5. ^{1}H NMR Spectroscopic Data

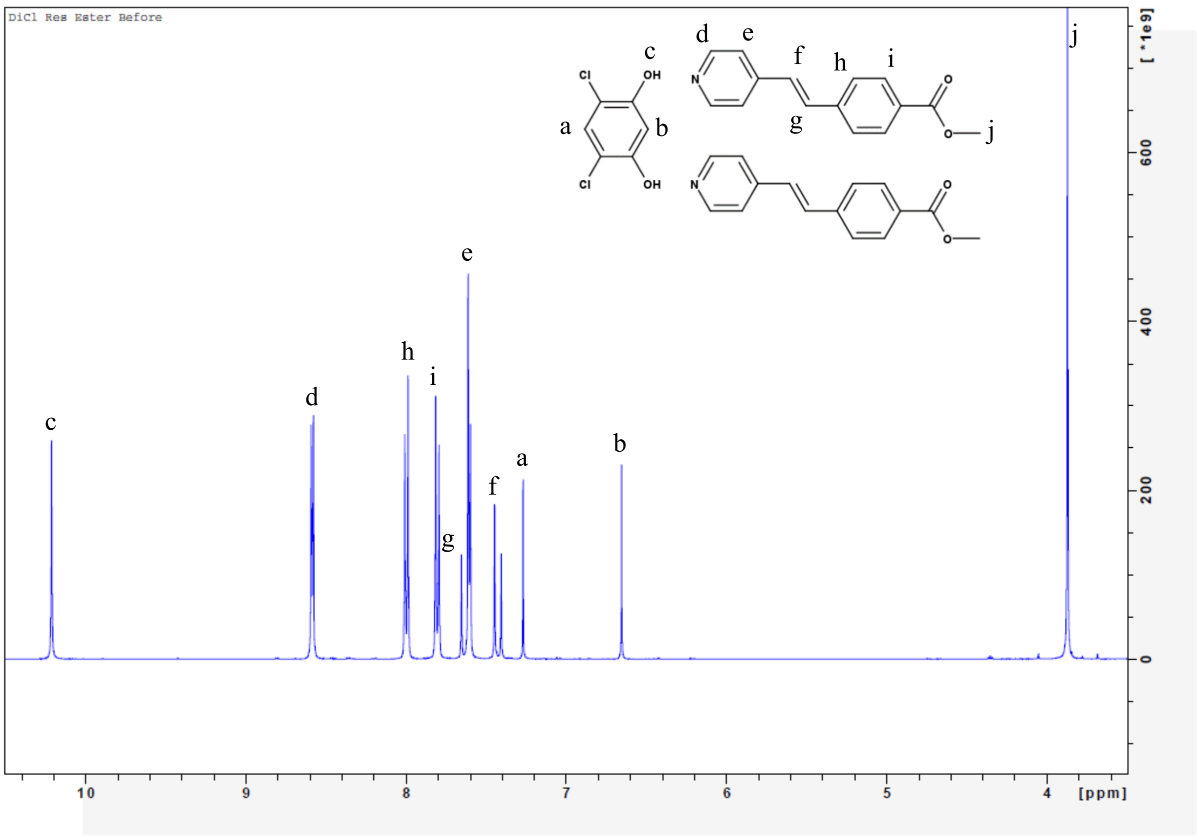

Figure S4. ^{1}H NMR spectrum of (**4,6-diCl res**)·2(**PEB**) before UV irradiation (400 MHz, DMSO-d_6).

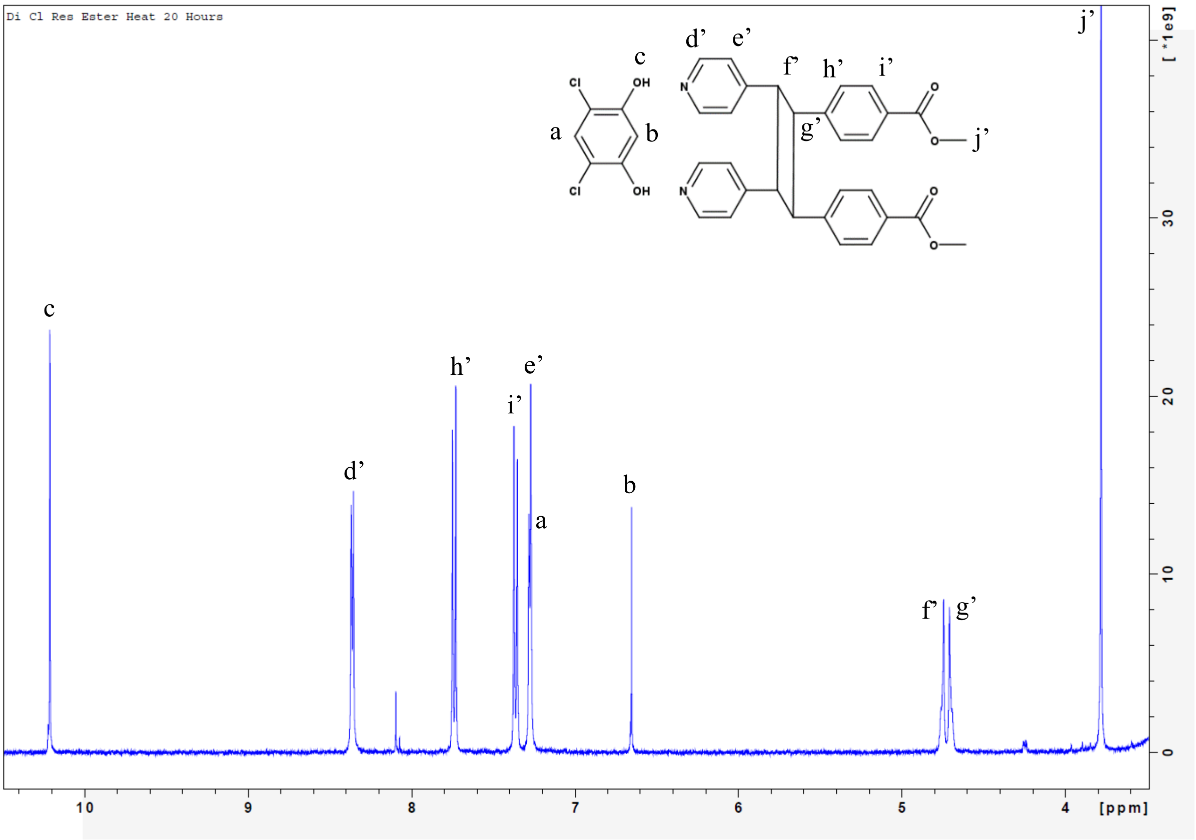

Figure S5. ^{1}H NMR spectrum of (**4,6-diCl res**)·2(**PEB**) after 20 hours of UV irradiation with simultaneous heating (400 MHz, DMSO-d_6).

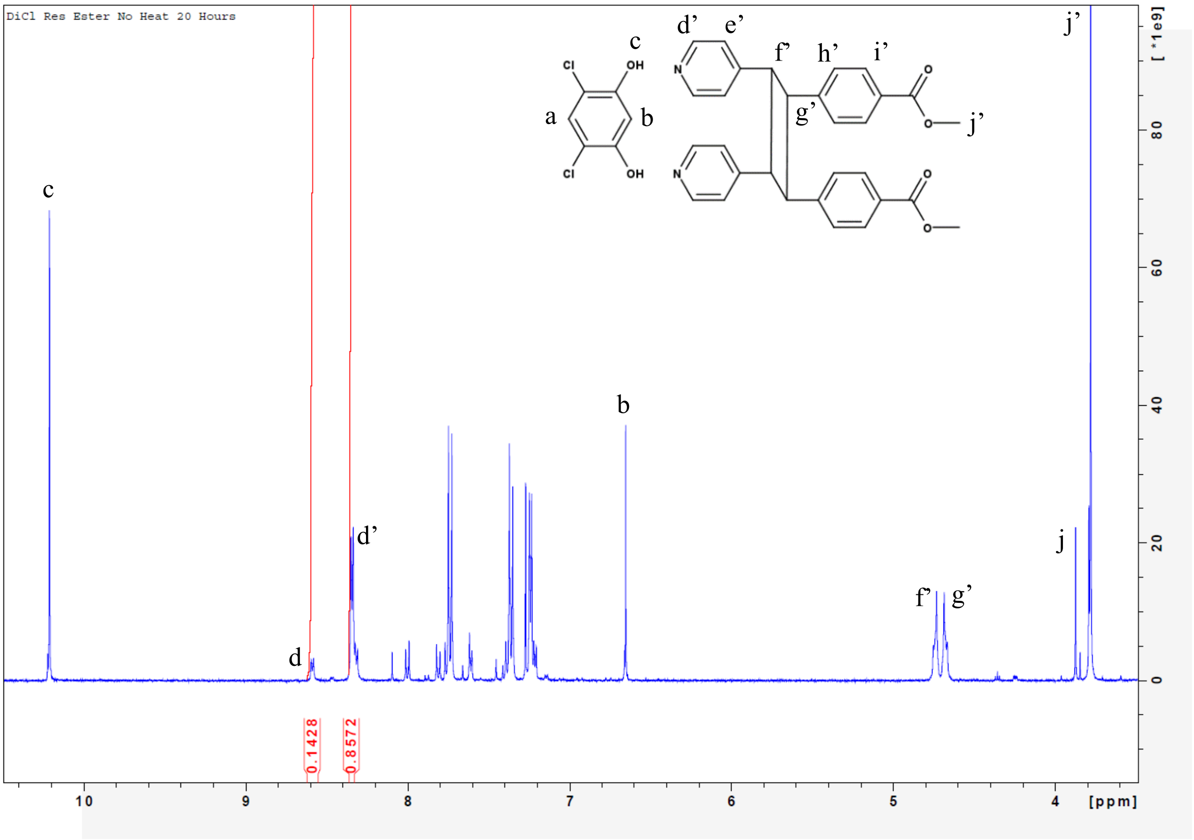

Figure S6. ^{1}H NMR spectrum of (**4,6-diCl res**)·2(**PEB**) after 20 hours of UV irradiation under ambient temperature (400 MHz, DMSO-d_6).

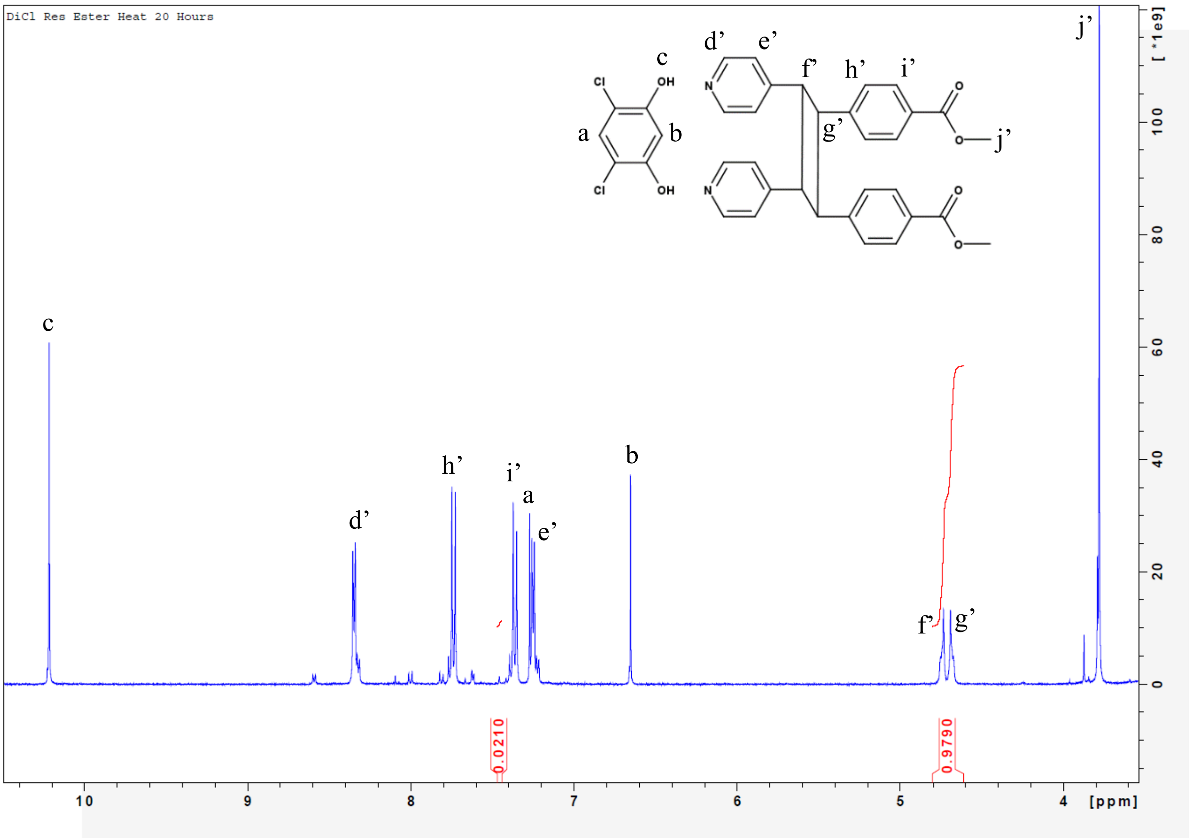

Figure S7. ^{1}H NMR spectrum of (**4,6-diCl res**)·2(**PEB**) after 20 hours of UV irradiation under ambient temperature followed by 20 hours of UV irradiation with simultaneous heating (400 MHz, DMSO-d_6).

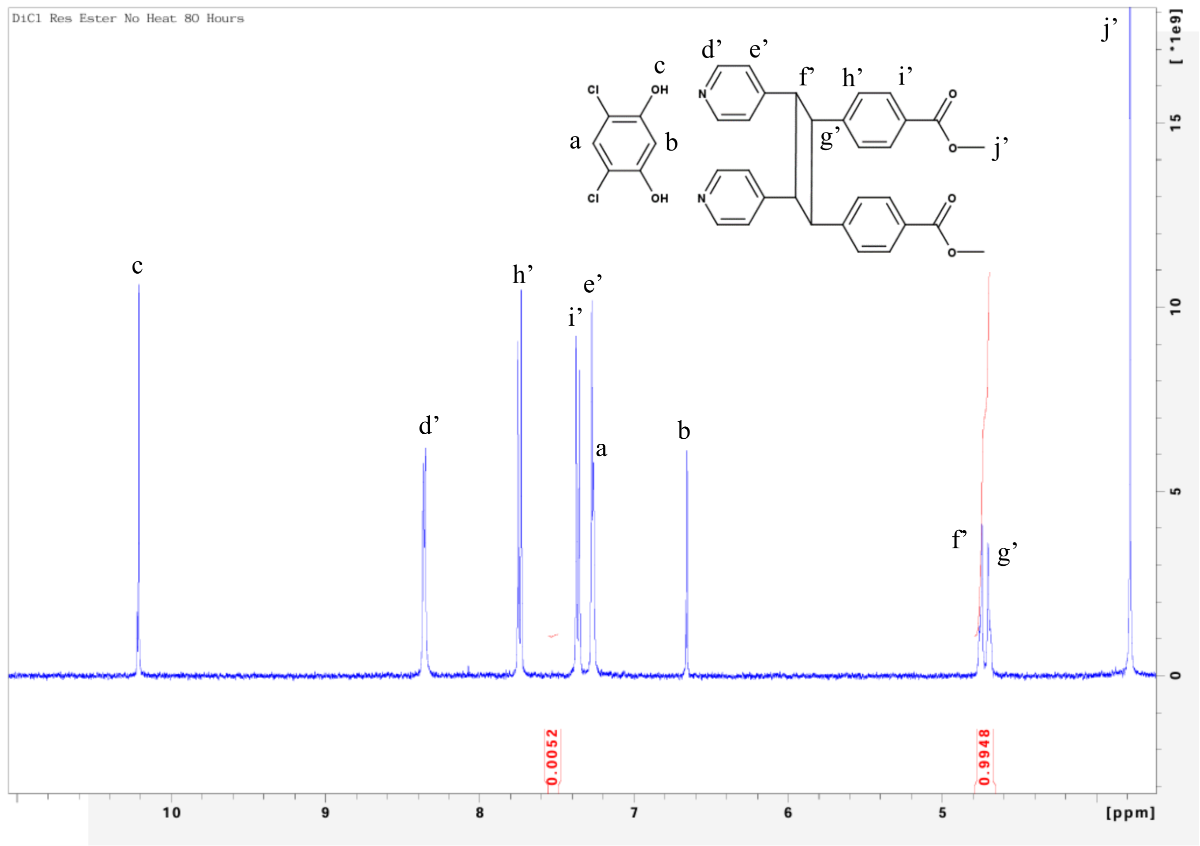

Figure S8. ^{1}H NMR spectrum of (**4,6-diCl res**)·2(**PEB**) after 80 hours of UV irradiation under ambient temperature, but with the sample placed on the hotplate surface (400 MHz, DMSO-d_6).

6. Reaction Conditions for the Various Photoreactions

Table S3. Cycloaddition yields based on ^{1}H NMR data for **(4,6-diCl res)·2(PEB)** under different conditions.

Condition	**Sample Number**	**Irradiation Time**	**^{1}H NMR Yield**
Heating at 340 K	1	10 hr 20 hr	82% 99%
	2	20 hr	99%
	3	20 hr	100%
Ambient temperature	1	20 hr	86%
	2	20 hr	86%
Ambient temperature (on hotplate surface)	1	80 hr	99%
Ambient temperature, followed by heating at 340 K	1	20 hr ambient + 20 hr heat	98%

7. Thermal Data

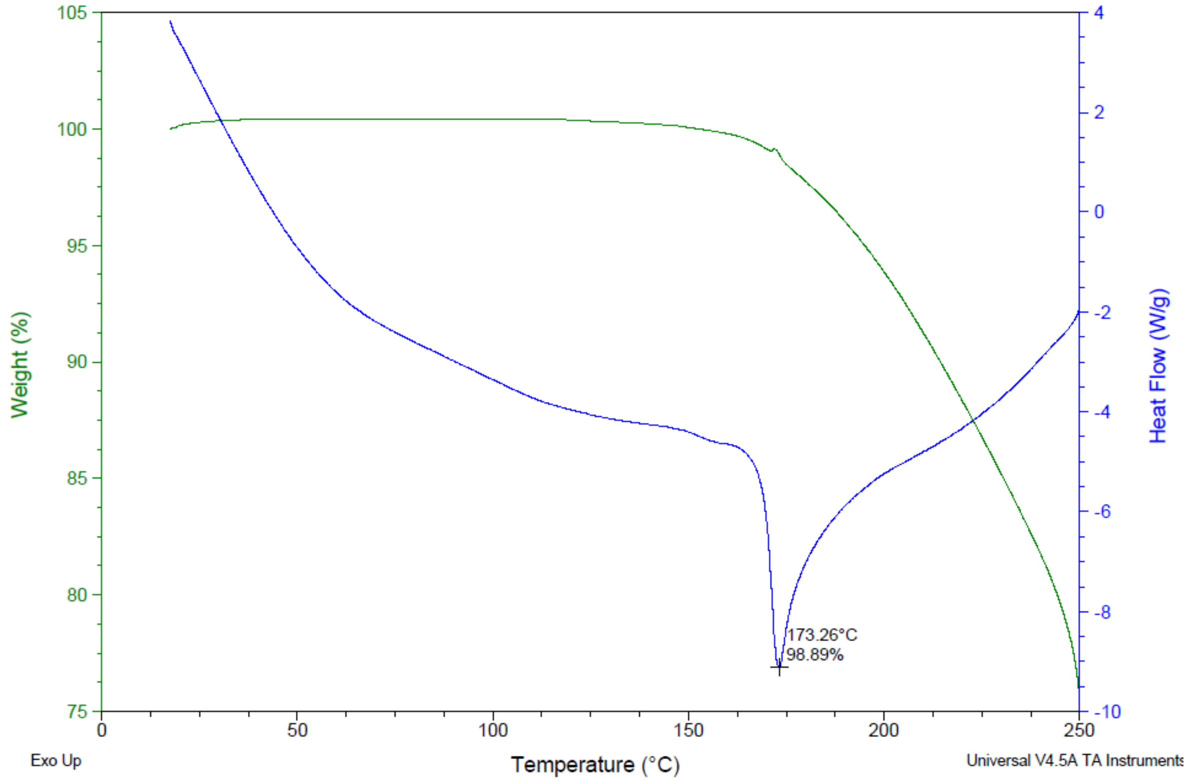

Figure S9. TGA (green) and DSC (blue) thermograms of (**4,6-diCl res**)·2(**PEB**).

8. References

1. M. L. Boilot, C. Roux, J. P. Audière, A. Dausse and J. Zarembowitch, *Inorg. Chem.*, **1996**, *35*, 3975.

2. CrysAlisPro (2018) Oxford Diffraction Ltd.

3. SCALE3 ABSPACK (2005) Oxford Diffraction Ltd

4. G. M. Sheldrick, *Acta Crystallogr., Sect. A: Found. Adv.*, **2015**, *A71*, 3.

5. G. M. Sheldrick, *Acta Crystallogr., Sect. C: Struct. Chem.*, **2015**, *C71*, 3.

6. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, and H. Puschmann. *J. Appl. Cryst.*, **2009**, *42*, 339.