Electronic Supplementary Information (ESI)

A [2+2] cross-photodimerisation of photostable olefins via a three-component cocrystal solid solution

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1. Materials

4-Bromotoluene (98%), palladium(II) chloride (99.999%), triphenylphosphine (*ReagentPlus*®, 99%), potassium carbonate (ACS reagent, ≥99.0%), 4-vinylpyridine (95%), pyridine (anhydrous, 98%), chloroform (CHROMASOLV® Plus, for HPLC, ≥99.9%), 4-chlorobenzyl chloride (purum, ≥98.0%), triethylphosphine (99%), *tert*-butanol (anhydrous, ≥99.5%), 4-pyridinecarboxaldehyde (97%), potassium *tert*-butoxide (purum, ≥97.0%), sodium hydroxide (ACS reagent, ≥97.0%) and hydrobromic acid (48 wt. % in H_2O, ≥99.99%) were purchased from Sigma-Aldrich (Saint Louis, MO). All reagents and solvents, except 4-vinylpyridine, were used as purchased. 4-Vinylpyridine was purified *via* distillation prior to use.

2. Synthesis of *trans*-1-(4-methylphenyl)-2-(4-pyridyl)ethylene (Me-PE)

Me-PE was prepared *via* a two-phase palladium-catalyzed Heck-coupling reaction. Both bromotoluene (30 mmol, 5.13 g) and 4-vinylpyridine (45 mmol, 4.73 g; 50% excess) were added to a potassium carbonate solution (c = 0.38 mol dm^{-3}, 160 ml), followed by palladium(II) chloride (0.67 mmol, 120 mg) and triphenylphosphine (2.6 mmol, 690 mg). Lastly, 1.5 ml of tri(*n*-butyl)amine were added as a phase-transfer reagent to the suspension and refluxed with stirring for 24 hours. The resulting mixture was then left to cool to room temperature. The product was subsequently extracted with 3×50 ml of chloroform. The chloroform fractions were combined, dried over anhydrous sodium sulfate and, finally, evaporated to dryness using a rotary evaporator. The crude solid contained a significant amount of both non-reacted 4-vinylpyridine and the "palladium-poisoned" product. The solid was therefore dissolved in a *minimal* amount of hot pyridine to obtain a saturated solution. The solution was subsequently refluxed to separate polymerized 4-vinylpyridine and the remaining Pd-catalyst from the solid product. The solution was then cooled (< 0 ºC) to allow precipitation of off-white **Me-PE** crystals. Yield: 3.98 g (68%).

3. Synthesis of *trans*-1-(4-chlorophenyl)-2-(4-pyridyl)ethylene (Cl-PE)

Cl-PE was prepared *via* a Horner-Wadsworth-Emmons reaction. 4-Chlorobenzyl chloride (0.0621 mol, 10.0 g) and triethylphosphite (0.0744 mol, 19.6 g) were refluxed

for 8 hours to yield 4-chloro-benzyl(diethyl)phosphonate as clear liquid. The unpurified phosphonate and crude 4-pyridinecarboxyaldehyde (0.0745 mol, 7.98 g; 20% excess) were added to 20 ml of *tert*-butanol. The obtained solution was cooled to about -15 ºC in an ice bath. Potassium *tert*-butoxide (0.0894 mol, 10.0 g) was subsequently slowly added to the vigorously stirred reaction mixture. The suspension was stirred overnight, and poured into cold water (<5 ºC, 100 ml). The precipitated bright yellow solid (*i.e.* **Cl-PE**) was filtered under vacuum, washed with 3×50 ml of water, and air-dried at in an oven overnight at 65 ºC. Overall yield: 8.93 g (71%)

4. Crystal growth

Crystals of **Cl-PE** and **Me-PE** were grown by slow solvent evaporation. For this purpose, 1 mmol of each olefin was dissolved in a minimal amount of acetonitrile, filtered through a cotton plug and left to cool and evaporate. Single crystals were obtained within 3 hours. Yield(**Cl-PE**): 52 mg (24%); yield(**Me-PE**): 104 mg (54%).

Solid solutions based on **Cl-PE** and **Me-PE** (1:1 ratio) were prepared *via* precipitation. Both **ClPE** (1 mmol, 215.7 mg) and **MePE** (1 mmol, 195.3 mg) were separately dissolved in MeCN (total volume 7 ml), refluxed for 1 hour, filtered through a cotton plug and left to cool down to room temperature. Thin crystalline plates appeared after 30 minutes. Yield: 48 mg (12%).

Single crystals of (**res**)·(**Me-PE**)$_x$·(**Cl-PE**)$_{(2-x)}$ (x ~ 1) (**1**) were obtained by solvent evaporation. Specifically, **Cl-PE** (195.2 mg, 1 mmol) and **Me-PE** (215.7 mg, 1 mmol) were refluxed together with **res** (110.1 mg, 1 mmol) in 20 ml of MeCN for 20 min. The resulting solution was left to slowly cool to room temperature. Yellow single crystals of **1** suitable for single-crystal X-ray analysis were obtained after approximately 5 h. Yield: 115 mg (22%).

Single crystals of [(H$_2$-**2x**)$^{2+}$][Br$^-$]$_2$·0.7(H$_2$O) (**3**) (where **x** = **a**-**d**) were grown from an MeCN solution of the isolated photoproducts. Upon photoreaction of **1**, the obtained homo- and heterodimers were separated form the **res** template by basic extraction using 1M NaOH and CHCl$_3$. The isolated solid was re-dissolved in MeCN. Amounts less than 0.1 ml of HBr(aq) were added dropwise to the obtained solution. Red-brown single

crystals suitable for single crystal X-ray diffraction were obtained over a period of 4 days.

5. Photoreactivity studies

In a typical photoreaction experiment, 100 mg of solid were gently ground using a mortar and pestle. The obtained powder was placed between two Pyrex glass plates. The plates were placed in a photoreactor cabinet equipped with a broad-band 450 W medium-pressure Hg-lamp. The powder distributed between the plates was mixed every 10 hours.

6. Crystallographic studies

a) Single crystal X-ray diffraction experiments.

The single-crystal diffraction data were measured on a Nonius Kappa CCD single-crystal X-ray diffractometer at both room and low temperatures using MoK_α radiation ($\lambda = 0.71073$ Å). Data collection, cell refinement and data reduction were performed using *Collect*[1] and *HKL Scalepack*/*Denzo*,[2] respectively. Structure solution and refinement were accomplished using SHELXS-97 and SHELXL-97,[3] respectively. The structures were solved using direct methods. Non-hydrogen atoms missing in the initially obtained model were indentified from the difference Fourier map within several refinement steps. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms associated with carbon atoms were refined in geometrically constrained positions (or in positions identified in the difference Fourier map, if needed to achieve a reasonable model of the investigated compound). Hydrogen atoms associated with oxygen atoms were calculated in an optimal hydrogen bonding geometry. The details of the structural analysis of all solids are summarized in Table S1.

A series of geometrical restraints (*i.e.* SADI, DFIX, FLAT) and constraints (i.e. EXYZ and EADP) were utilized to achieve reasonable models of most investigated compounds.

For the cocrystal solid solution **1**, both a low and room temperature dataset were collected using the same single crystal. The low temperature dataset was utilized to determine the composition of **1** as accurately as possible. The refined occupancy factors of **Me-PE** and **Cl-PE** were then used to refine the room temperature crystal structure.

The room temperature dataset was used to elucidate the arrangement of the olefinic C=C bonds at conditions at which the photoreaction was performed.

In the crystal structure of compound **3**, the H(N,pyridinium)-atoms (*i.e.* H1N and H2N) were located in the difference Fourier map and their H-N distances were refined using the DFIX restraint in SHELX. Likewise, two H(C)-atom positions (*i.e.* H6 and H15) were determined using the difference map since their calculated positions resulted in the appearance of unreasonably short H-H distances in the highly strained cyclobutane model. Their corresponding C-H distances were also refined using the DFIX restrain.

Table S1. Crystallographic parameters for crystal structures **Cl-PE**, **Me-PE**, **1** and **3**.

Compound reference	**Cl-PE**	**Me-PE**	**1 (150 K)**
Chemical formula	$C_{13}H_{10}ClN$	$C_{14}H_{13}N$	$C_{33\cdot34}H_{30\cdot03}Cl_{0\cdot66}N_2O_2$
M_r	215.67	195.25	514.05
Crystal system	Triclinic	Orthorhombic	Triclinic
a/Å	9.4815(10)	6.0339(7)	9.9438(11)
b/Å	9.6019(12)	7.6092(9)	10.1775(11)
c/Å	14.2885(18)	23.135(3)	14.0261(15)
α/°	71.745(5)	90	105.642(5)
β/°	76.746(6)	90	98.420(5)
γ/°	62.801(5)	90	92.492(5)
V/Å^3	1093.0(2)	1062.2(2)	1347.0(3)
T/K	298(2)	150(2)	150(2)
Space group	$P\bar{1}$	$P2_12_12_1$	$P\bar{1}$
Z	4	4	2
Radiation type	MoK_α	MoK_α	MoK_α
μ/mm^{-1}	0.312	0.071	0.142
No. of refl. measured	6753	6496	8856
No. of indep. reflections	3773	1117	4679
R_{int}	0.0641	0.0379	0.02
R_1 ($I > 2\sigma(I)$)	0.1168	0.038	0.0434
$wR(F^2)$ ($I > 2\sigma(I)$)	0.2928	0.0929	0.1079
R_1 (all data)	0.2106	0.0486	0.0585
$wR(F^2)$ (all data)	0.3451	0.0973	0.1148
GooF	1.061	1.151	1.067
CCDC deposition number	809487	809488	809484

Table S1. Crystallographic data (continued).

Compound reference	**1 (296 K)**	**3**
Chemical formula	$C_{33\cdot35}H_{30\cdot05}Cl_{0\cdot65}N_2O_2$	$C_{26\cdot93}H_{26\cdot05}Br_2Cl_{1\cdot07}N_2O_{0\cdot63}$
M_r	513.89	585.54
Crystal system	Triclinic	Monoclinic
a/Å	10.0708(11)	18.3233(19)
b/Å	10.4551(11)	9.8023(11)
c/Å	13.9967(15)	14.3984(15)
α/°	105.885(5)	90
β/°	99.037(5)	93.253(5)
γ/°	92.659(5)	90
V/Å^3	1393.6(3)	2581.9(5)
T/K	296(2)	200(2)
Space group	$P\bar{1}$	$P2_1/c$
Z	2	4
Radiation type	MoK_α	MoK_α
μ/mm^{-1}	0.136	3.271
No. of refl. measured	8611	11967
No. of indep. reflections	4843	4489
R_{int}	0.0253	0.0385
R_1 ($I > 2\sigma(I)$)	0.0674	0.0484
$wR(F^2)$ ($I > 2\sigma(I)$)	0.1941	0.1023
R_1 (all data)	0.1138	0.0733
$wR(F^2)$ (all data)	0.2142	0.1096
GooF	1.087	1.025
CCDC deposition number	809485	809486

b) Powder X-ray diffraction experiments.

XRPDs were obtained using a Siemens D5000 X-ray diffractometer (Cu$K_{\alpha1}$ radiation, λ = 1.54056 Å; scan type: locked coupled; scan mode: continuous; step size: 0.02º; scan time: 2 s/step). The samples were mounted on glass slides.

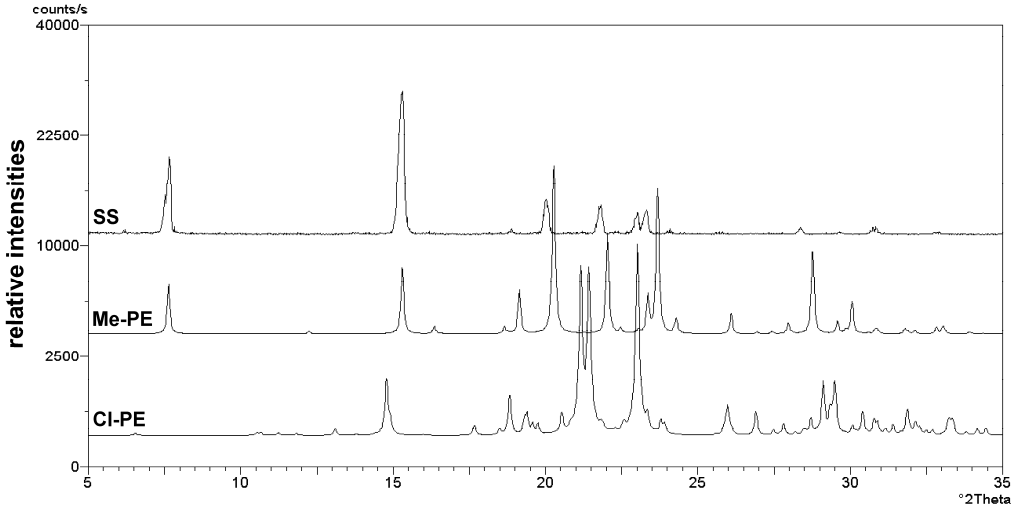

Figure S1. PXRD traces of **Cl-PE** (bottom), **Me-PE** (middle) and the **Cl-PE**/**Me-PE** solid solution (**SS**, top).

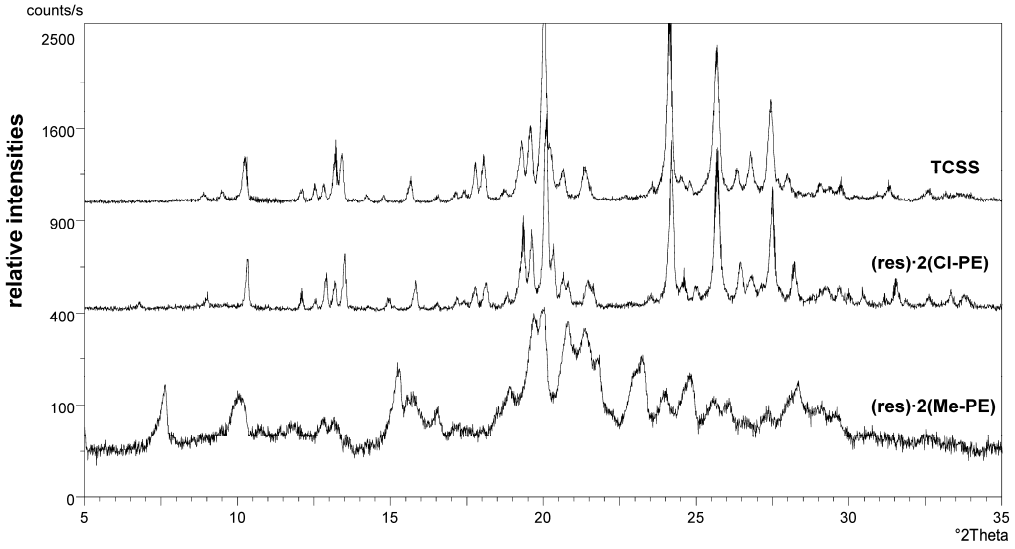

Figure S2. PXRD traces of (res)·2(**Me-PE**) (bottom), (res)·2(**Cl-PE**) (middle) and the **Cl-PE**/**Me-PE** ternary cocrystal solid solution (**TCSS**, top).

7. Separation of heterodimer 2a,b

The HPLC separation of **2a**,**b** was performed on a Beckman System Gold (model 126) HPLC, fitted with a Supelco Discovery C-18 semipreparative column (10 mm i.d. × 250 mm, 5 μm particle size). The mixture of photoproducts **2a**-**2d** was dissolved in a 0.1% formic acid solution to a final concentration of ~0.4 mg/ml, and injected onto the semipreparative column. A 20-40% linear gradient of acetonitrile (with 0.3% formic acid) over 40 min was used to elute the photoproducts in three non-overlapping peaks at 24 min (homodimer **2d**), 27 min (heterodimers **2a**,**b**) and 29.5 min (homodimer **2c**). The separation was monitored in real time by a Beckman System Gold photodiode array (PDA) detector. Each peak was collected in a 50 ml Falcon tube, frozen in liquid N_2, and lyophilized to dryness in the dark.

8. NMR studies

Products were characterized by using Avance-400 and Avance-600 Bruker NMR spectrometers (Billerica, MA) operating at 400 and 600 MHz, respectively, using deuterated dimethyl sulfoxide (DMSO-d_6) as solvent. ^{1}H and ^{13}C chemical shifts were referenced with the residual proton and carbon-13 chemical shifts of the solvent (DMSO-d_6, ^{1}H, 2.5 ppm; ^{13}C, 39.5 ppm). Fractions with milligram quantities of the product were characterized with a battery of one- and two-dimensional homonuclear and heteronuclear experiments [^{1}H, ^{13}C, correlated spectroscopy (COSY), nuclear Overhauser effect spectroscopy (NOESY), heteronuclear multiple bond correlation (HMBC) and heteronuclear single quantum coherence (HSQC)]. Gradient-assisted versions of the pulse sequences were used for all the 2D experiments. Inverse detection probe was used for all the 2D heteronuclear 2D experiments. ^{1}H and ^{13}C NMR chemical shifts for heterodimer **2a**,**b** are given in Table S2. Relaxation delay was set to 4s for all the 2D experiments. All of the NMR data were processed with TOPSPIN 1.3 suite of software programs. One-dimensional ^{1}H data were processed with zero-filling to 64k data points and 0.2 Hz exponential line broadening, whereas ^{13}C spectra were processed with zero-filling to 128k data points and 1.0 Hz of exponential line broadening. The 2D NMR data were processed with the zero-filling to 2048 points and 1024 points in acquisition and second

dimension, respectively. Relative numbers of proton signals multiplied by the integral areas were used for the quantification.

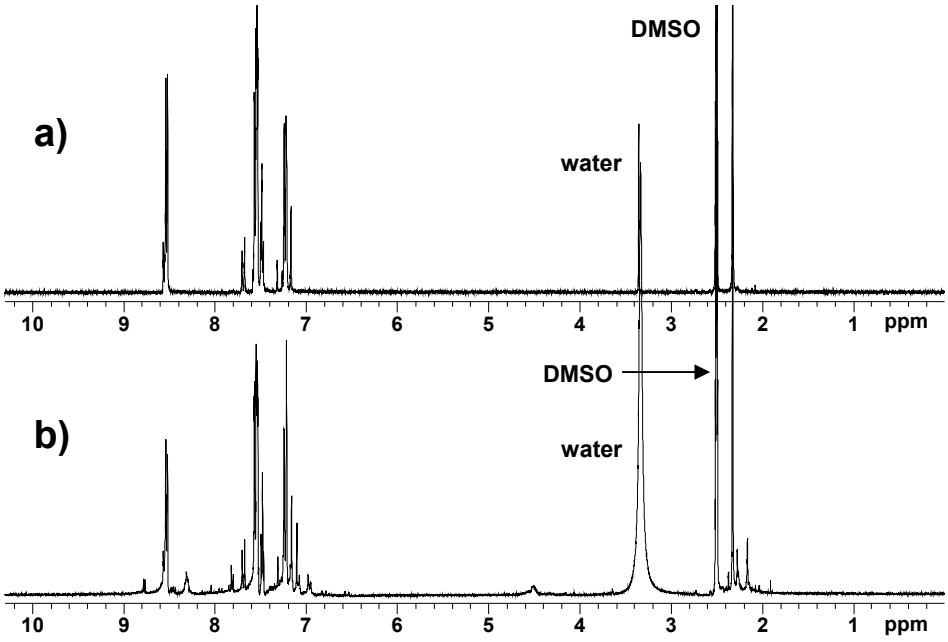

Figure S3. ^{1}H NMR spectra of the **Cl-PE**/**Me-PE** solid solution: a) before and b) after UV irradiation Peaks in the 4.3-4.8 ppm region in spectrum b) indicate the formation a mixture of cyclobutanes formed in low yields upon partial melting of the solid).

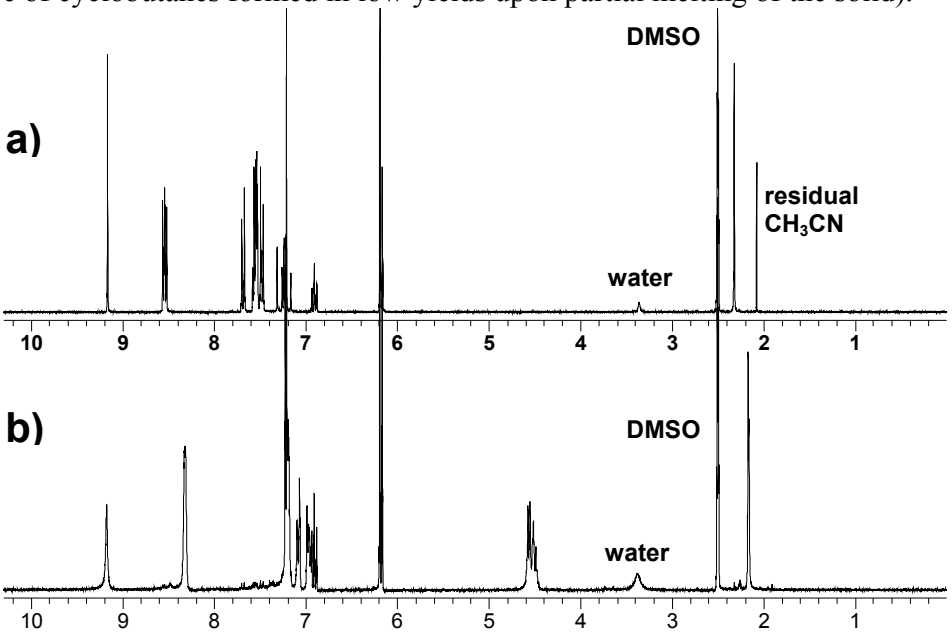

Figure S4. ^{1}H NMR spectra of cocrystal solid solution **1**: a) before and b) after UV irradiation.

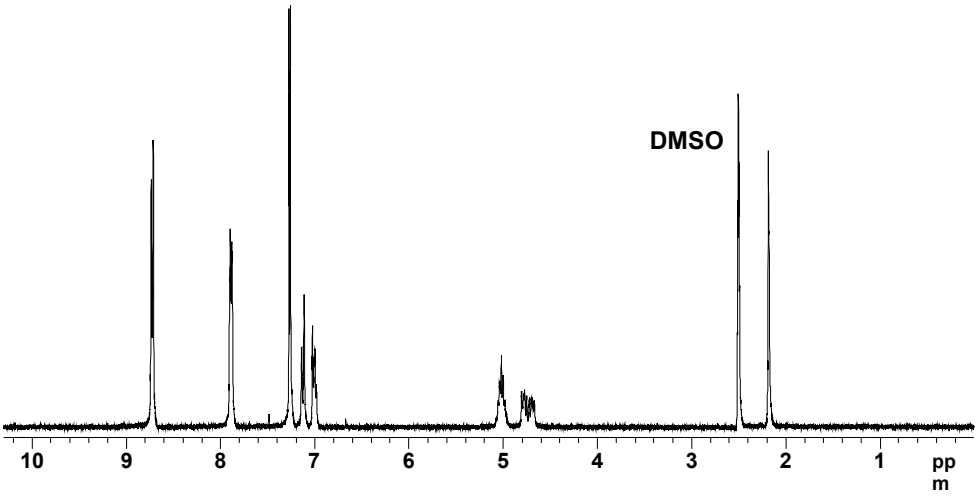

Figure S5. ^{1}H NMR spectrum of solid solution **3.**

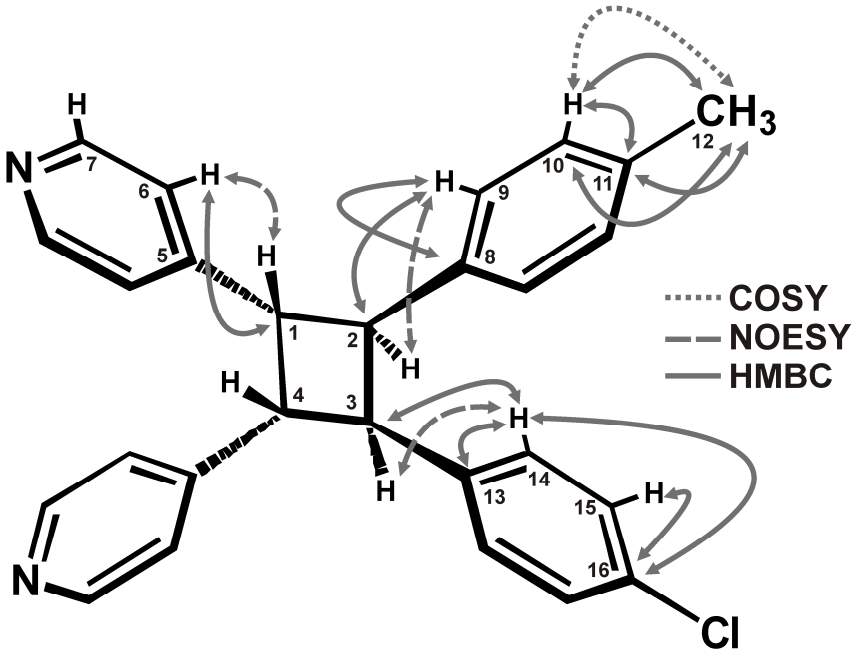

Figure S6. Selected COSY, NOESY and HMBC correlations for heterodimer **2a**,**b** (11.34-minute HPLC fraction isolated from solid **1** after UV irradiation).

Table S2. ^{1}H and ^{13}C NMR chemical shifts for heterodimer **2a**,**b**.

^{1}H nucleus	**ppm**	**^{13}C nucleus**	**ppm**
H7(pyridyl)	8.32	C7(pyridyl)	148.9
H6(pyridyl)	7.19	C6(pyridyl)	123.0
H10(toluyl)	6.98	C10(toluyl)	128.3
H9(toluyl)	7.08	C9(toluyl)	127.5
H15(chlorophenyl)	7.21	C15(chlorophenyl)	127.4
H14(chlorophenyl)	7.21	C14(chlorophenyl)	129.5
H1-4(cyclobutyl)	4.46-4.59	C1-4(cyclobutyl)	44.5-45.4
CH_3 (toluyl)	2.17	CH_3(toluyl)	20.2
		C5	149.2*
		C11	135.1
		C8	136.5
		C16	139.0*
		C13	129.9*

*^{13}C-assignments are tentative due to resonance overlap

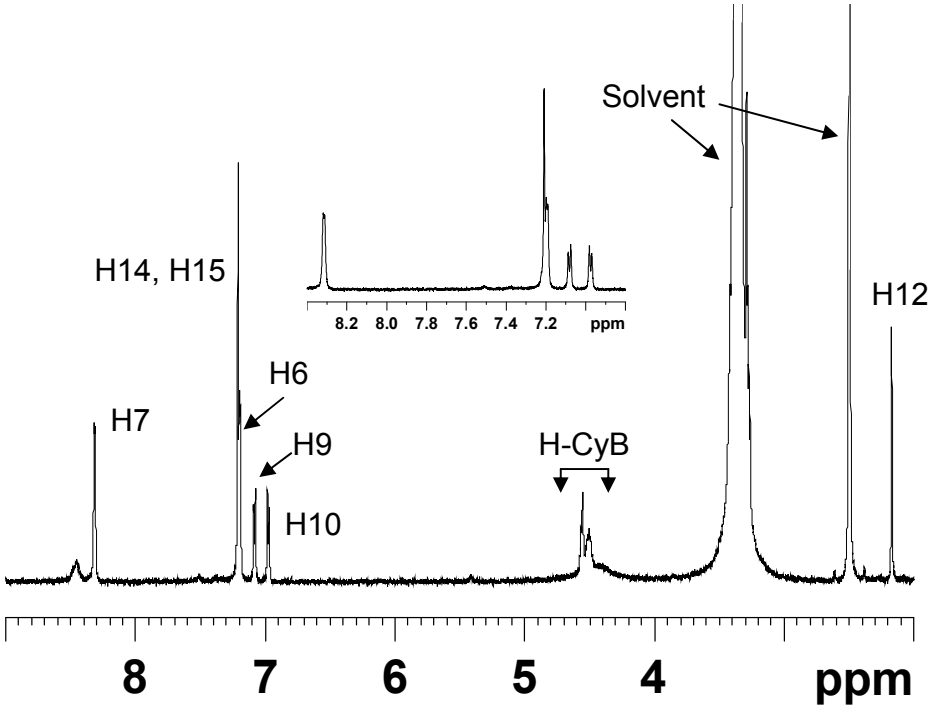

Figure S7. ^{1}H NMR spectrum of heterodimer **2a**,**b**.

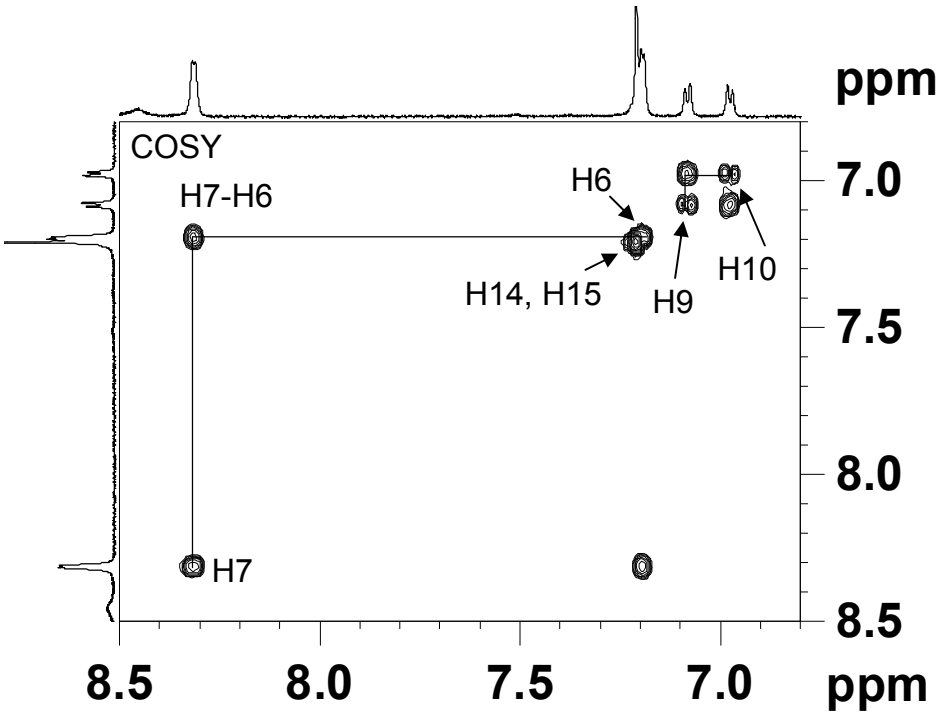

Figure S8. COSY spectrum of heterodimer **2a**,**b**.

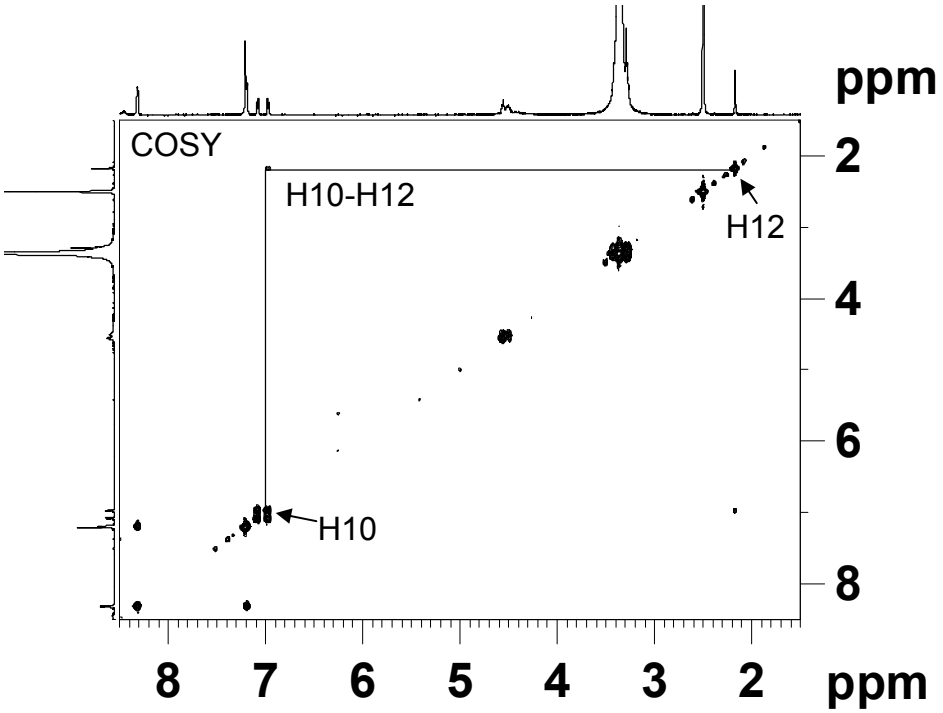

Figure S9. COSY spectrum of heterodimer **2a**,**b**.

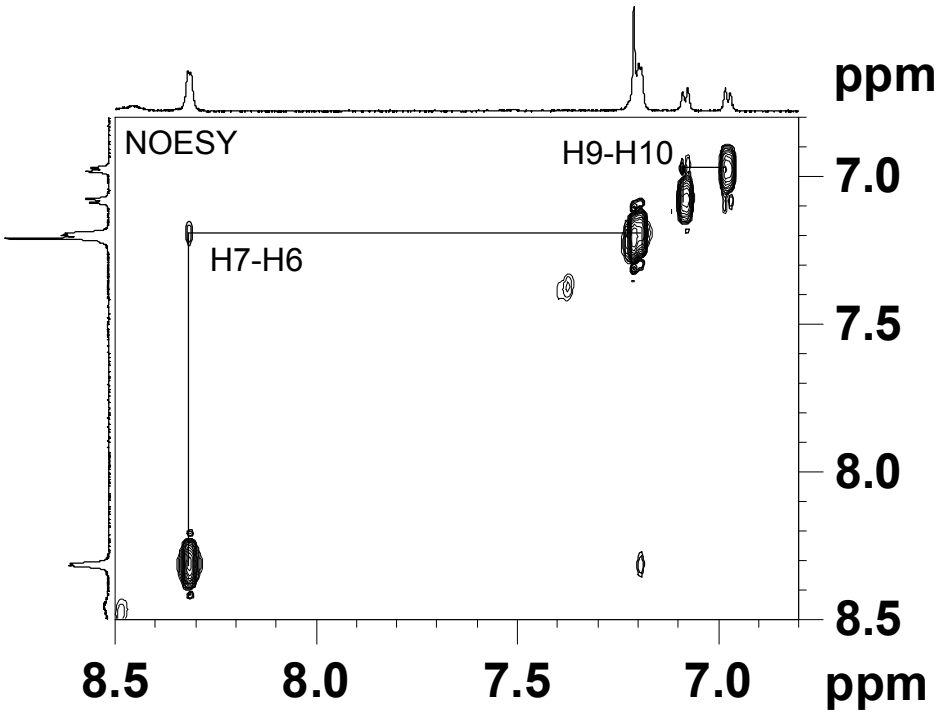

Figure S10. NOESY spectrum of heterodimer **2a**,**b**.

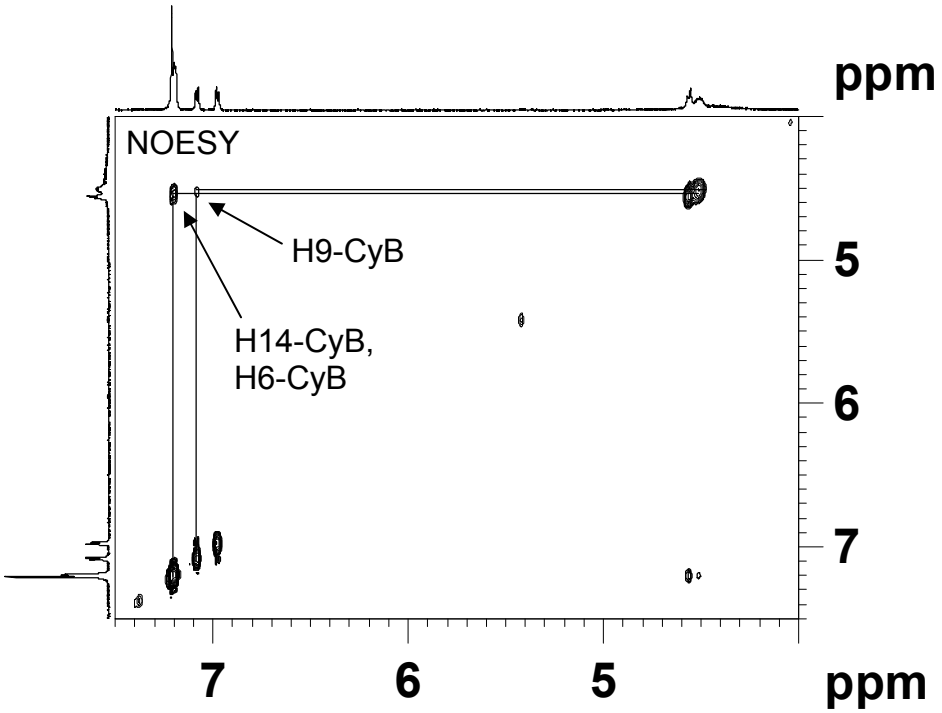

Figure S11. NOESY spectrum of heterodimer **2a**,**b**.

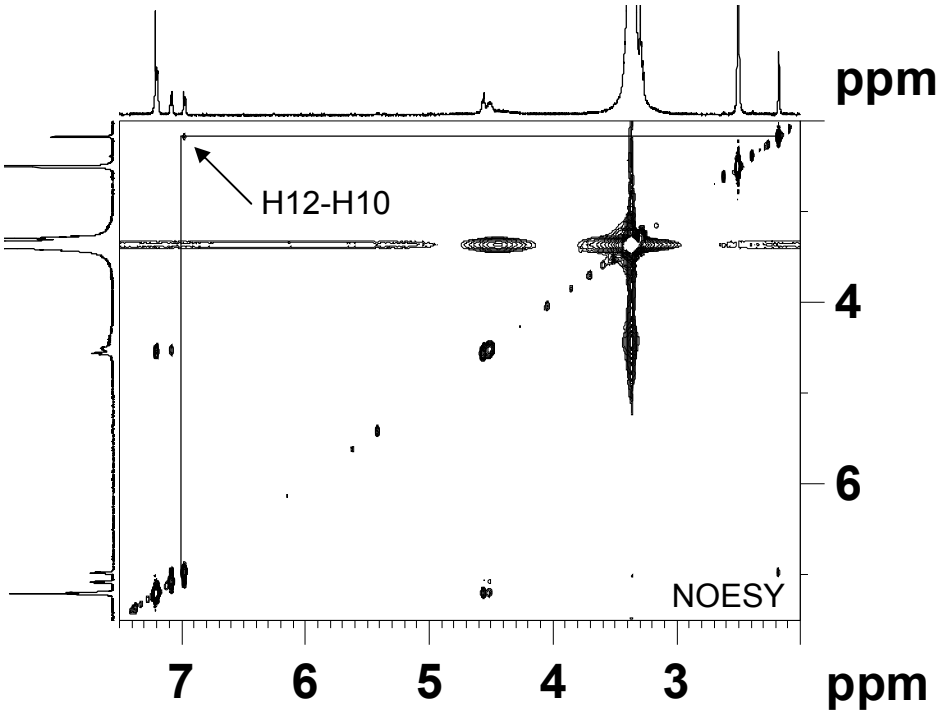

Figure S12. NOESY spectrum of heterodimer **2a**,**b**.

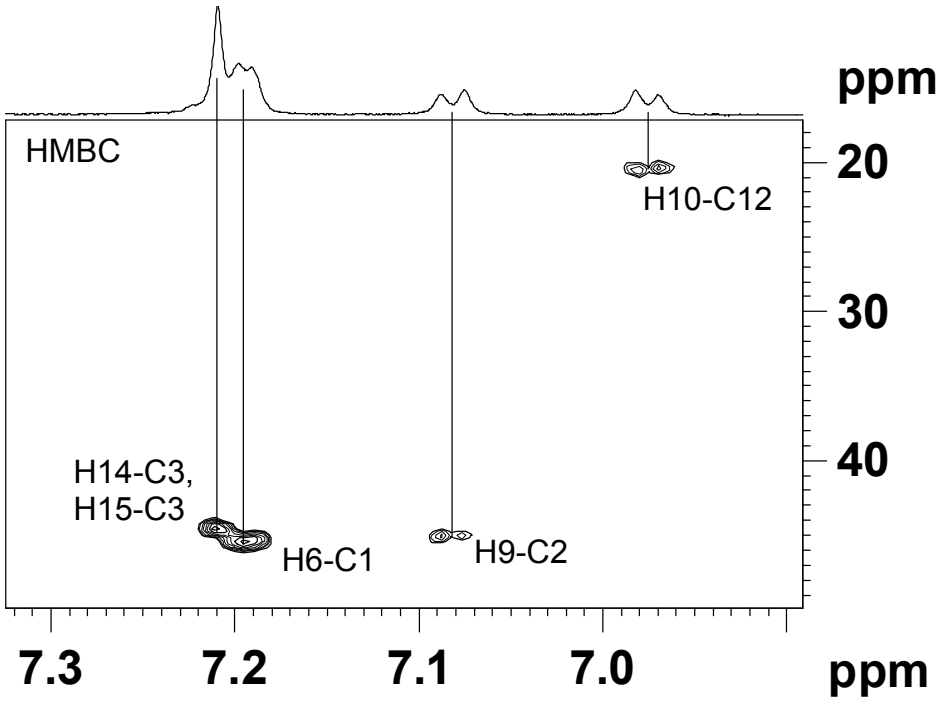

Figure S13. HMBC spectrum of heterodimer **2a**,**b**.

9. ESI-mass spectrometry

The LC-MS data was collected using a Thermo LCQ Deca mass spectrometer interfaced with a Surveyor liquid chromatograph. A Supelco Discovery C18 (15 cm × 2.1 mm, 5µm) column was used for the LCMS experiments. The solvents were 0.1% formic acid (A) and acetonitrile with 0.1% formic acid (B). The gradient started at 20% B and held for two minute then increased to 95% B by 25 minutes. The flow rate was 200 µl/min. The injection volume was 10 µl of the diluted sample. Positive electrospray was used as the ionization method. The ESI source voltage was 4.5 kV and capillary temperature was set to 275°C. The sheath and auxillary gas flow rates were 65 and 20 (arbitrary units), respectively. MS data was collected over the mass range 150-700 for 25 minutes. Thermo Xcalibur 2.0 software was used to control the LC-MS and process the data.

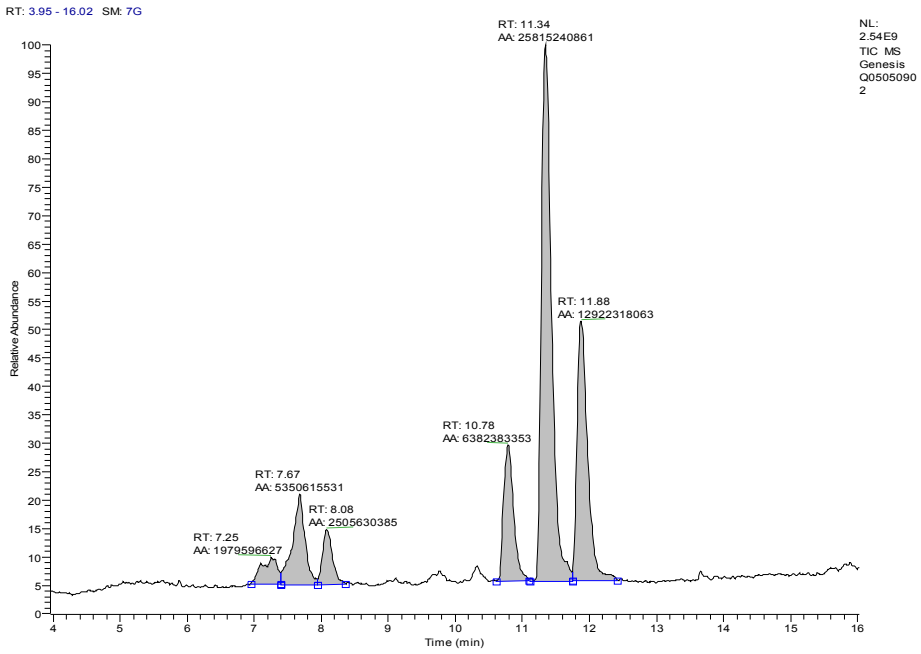

Figure S14. Chromatogram of cocrystal solid solution **1** after UV irradiation.

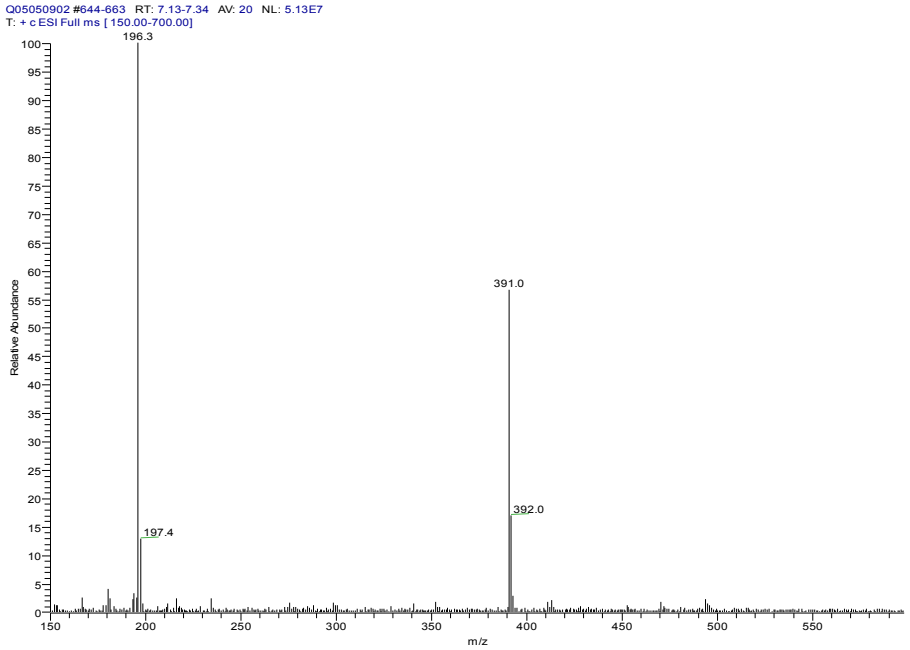

Figure S15. Mass spectrum for RT: 7.25 min

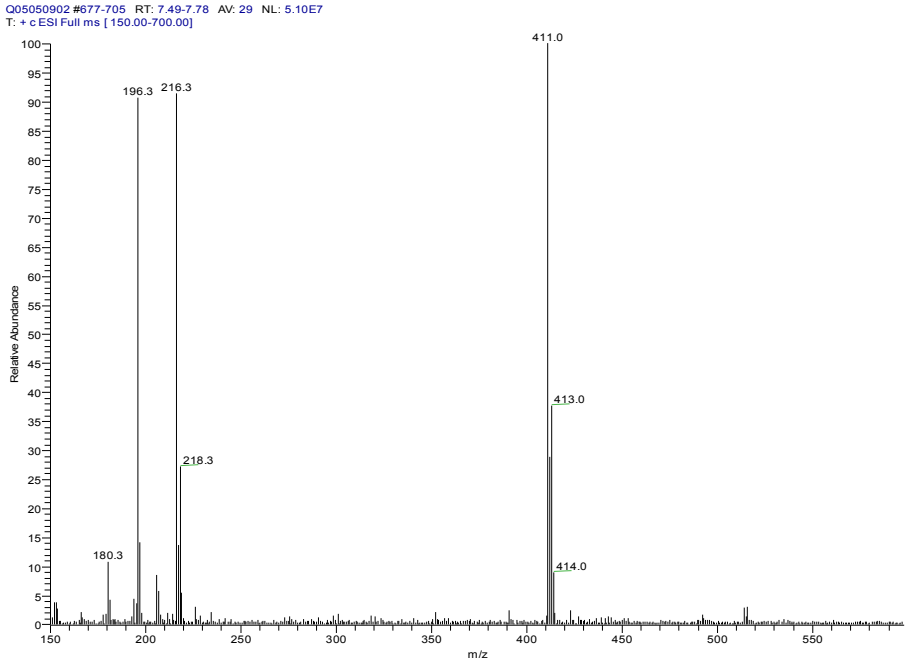

Figure S16. Mass spectrum for RT: 7.67 min.

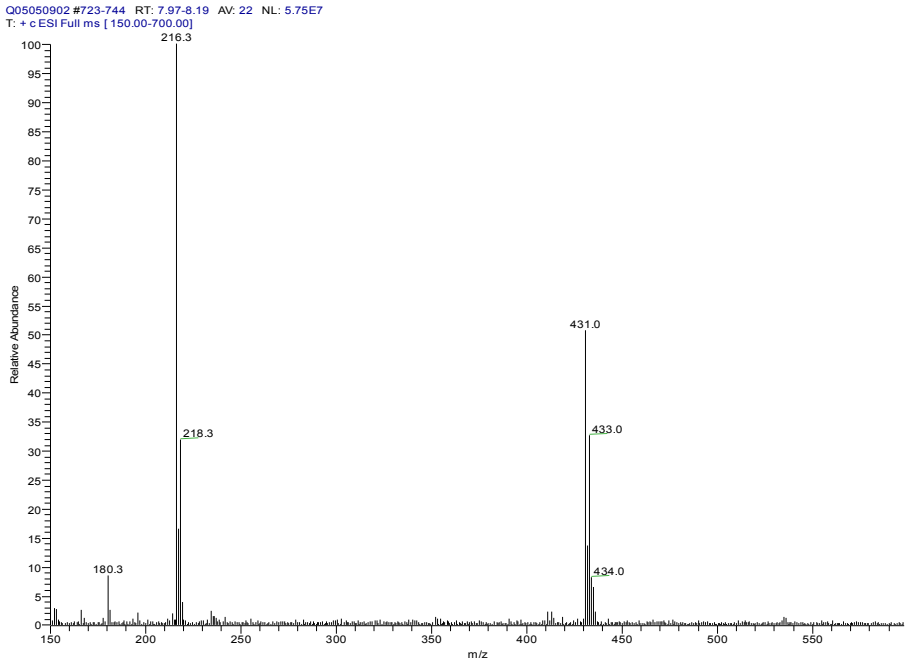

Figure S17. Mass spectrum for RT: 8.08 min.

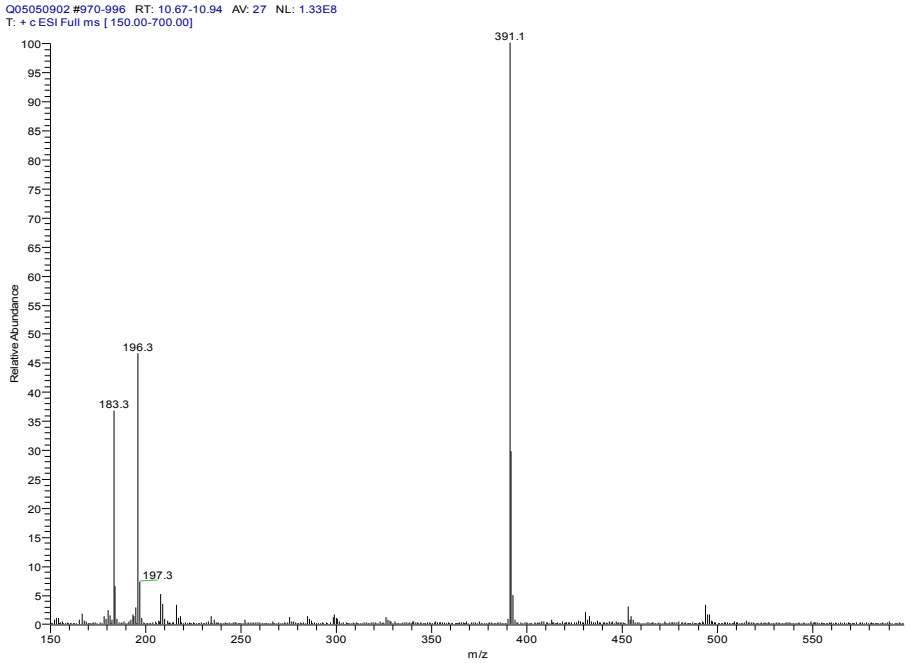

Figure S18. Mass spectrum for RT: 10.78 min.

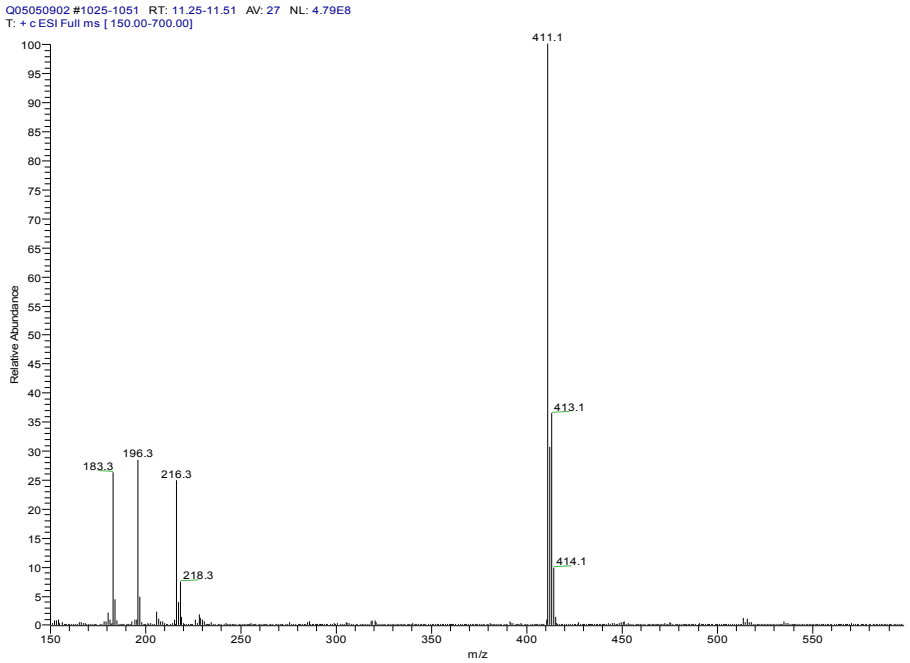

Figure S19. Mass spectrum for RT: 11.34 min.

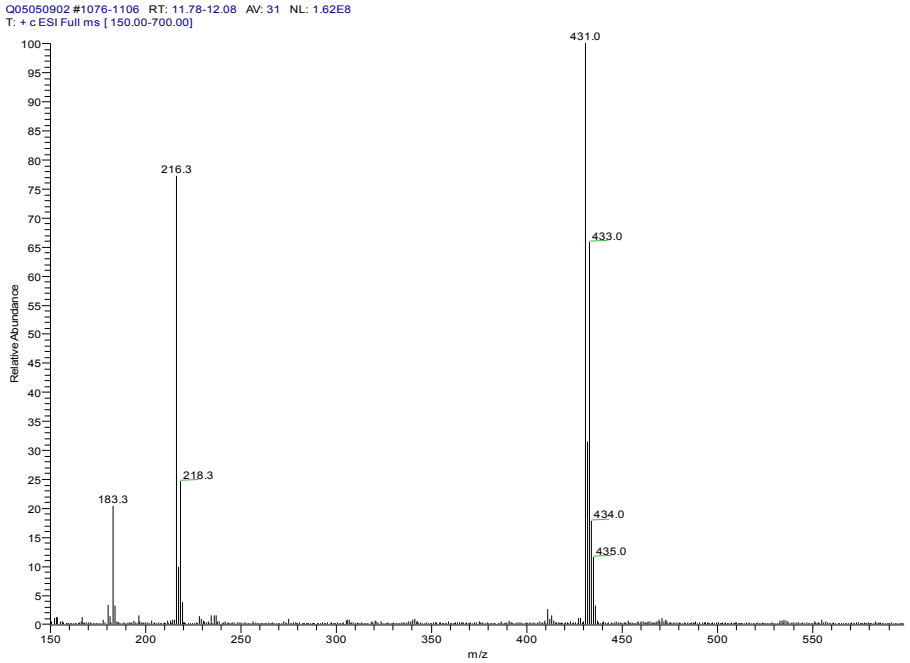

Figure S20. Mass spectrum for RT: 11.88 min.

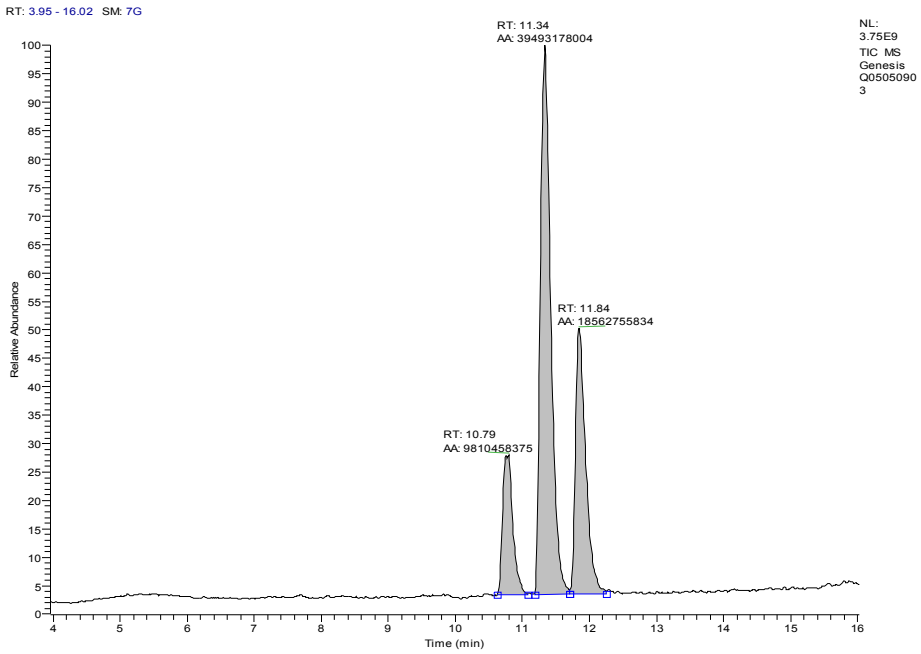

Figure S21. Chromatogram of solid solution **3**.

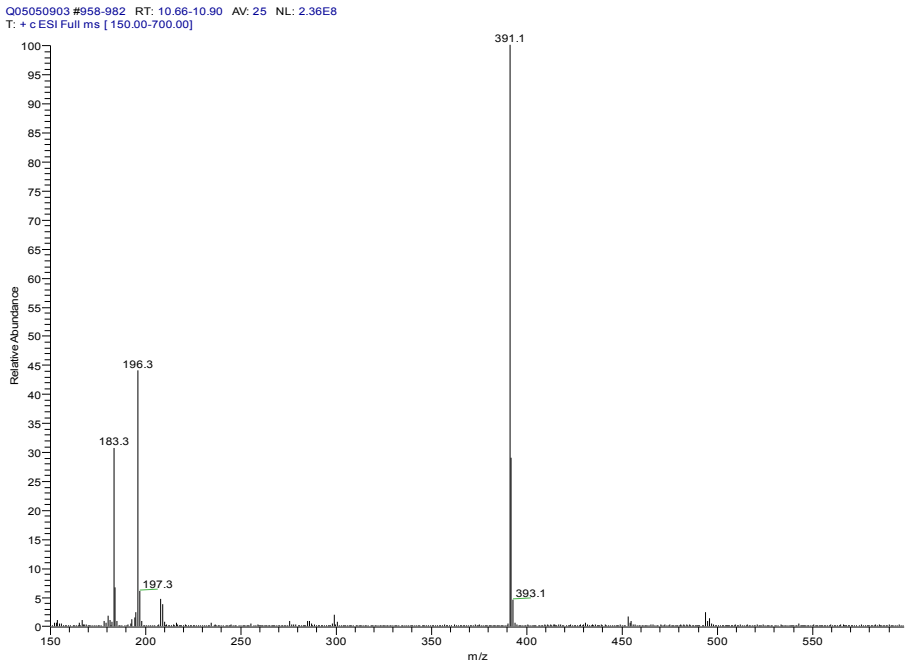

Figure S22. Mass spectrum for RT: 10.78 min.

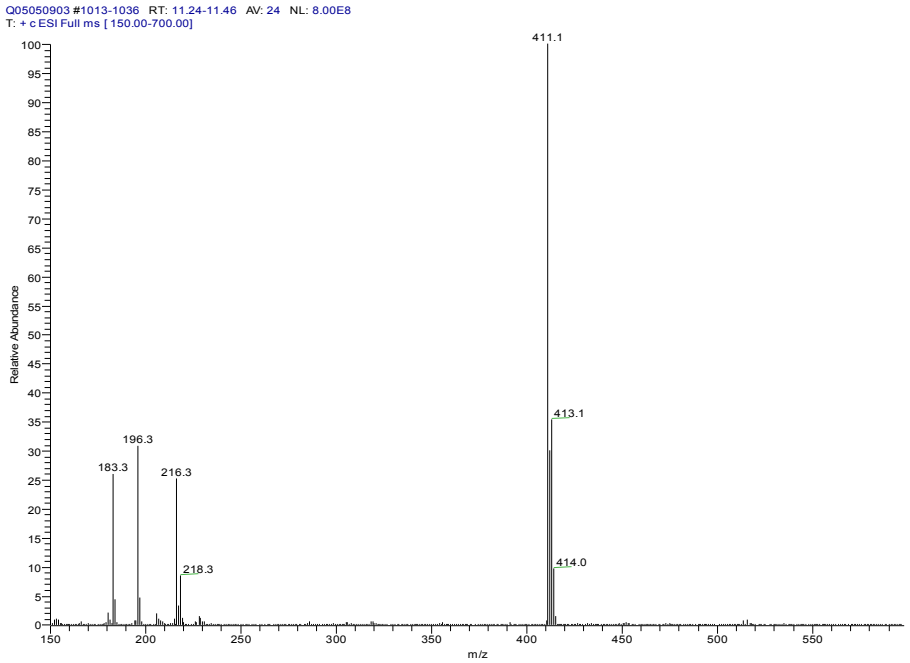

Figure S23. Mass spectrum for RT: 11.34 min.

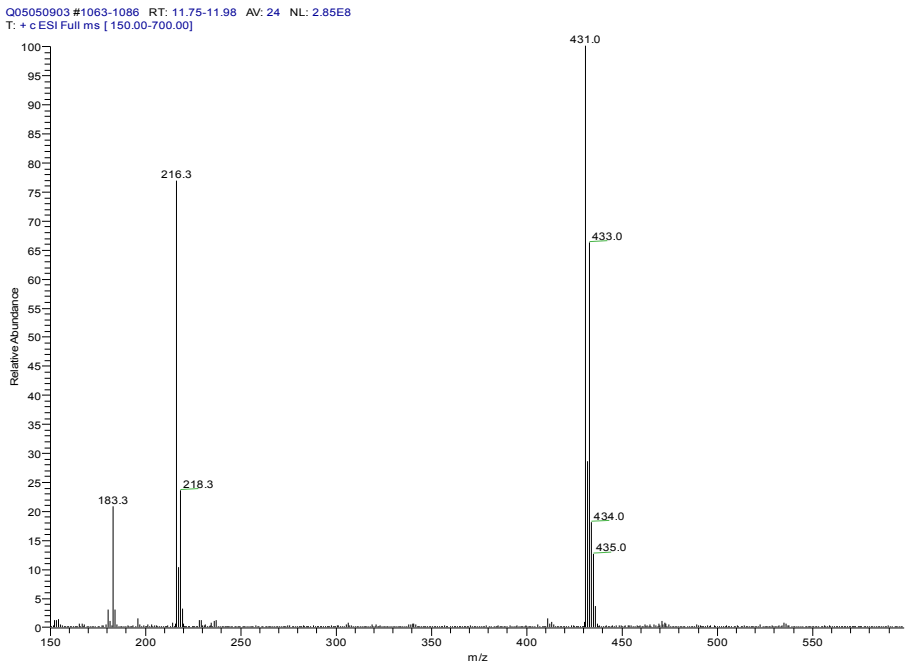

Figure S24. Mass spectrum for RT: 11.84 min.

10. References

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