Electronic supplementary information

Vapour-Induced Solid-State C–H Bond Activation for Clean Synthesis of an Organopalladium Biothiol Sensor

Andrea Monas, Krunoslav Užarević, Ivan Halasz, Marina Juribašić Kulcsár* and Manda Ćurić*

Division of Physical Chemistry, Ruđer Bošković Institute, Bijenička 54, HR−10000 Zagreb, Croatia

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EXPERIMENTAL SECTION

Aging reactions. All chemicals used for the syntheses were commercially available and were used as received. Solvents were not dried before use. The accelerated aging reactions were performed at room temperature in vapour of liquids: DMF, water or acetic acid. The mixture of solid reactants prepared by gentle grinding in an agate mortar was put in a closed vial saturated with air and liquid vapour. Complex **1A**. 30.10 mg (0.17 mmol) of azobenzene (**1**) and 37.2 mg (0.17 mmol) of $Pd(OAc)_2$ were used. Complex **2B**. 30.10 mg (0.09 mmol) of methyl orange (**2**) and 41.3 mg (0.18 mmol) of $Pd(OAc)_2$ were used. Analysis of the products by ^1H NMR and ATR-IR spectroscopies and by PXRD revealed complete conversion of reactants into the product.

Mechanochemical reactions. All grinding experiments (dry milling and LAG) were performed at room temperature in a 14 mL PMMA jars using one 10 mm stainless steel or zirconia grinding ball (4 g). A Retsch MM301 grinder mill operating at 30 Hz frequency was used for the synthesis. LAG reactions were performed in the presence of 20 μL of dimethylformamide (DMF). Complex **1A**. 60.11 mg (0.33 mmol) of azobenzene (**1**) and 149.22 mg (0.66 mmol) of $Pd(OAc)_2$ were used. Complex **2A**. 125.35 mg (0.38 mmol) of methyl orange (**2**) and 85.90 mg (0.38 mmol) of $Pd(OAc)_2$ were used. Complex **2B**. 85.58 mg (0.26 mmol) of methyl orange (**2**) and 118.0 mg (0.52 mmol) of $Pd(OAc)_2$ were used. The purity of the products was determined by ^1H NMR and ATR-IR spectroscopies and by PXRD analysis.

Solution-based reactions. Analogous solvent-based reactions were carried out by stirring of the mixture of reactants in DMF at room temperature. Complex **1A**. 50.25 mg (0.27 mmol) of azobenzene (**1**) and 123.81 mg (0.22 mmol) of $Pd(OAc)_2$ in 40 mL of DMF were used. Complex **2A**. 100.30 mg (0.31 mmol) of methyl orange (**2**) and 68.79 mg (0.31 mmol) of $Pd(OAc)_2$ were used. Complex **2B**. 50.24 mg (0.15 mmol) of methyl orange (**2**) and 137.82 mg (0.61 mmol) of $Pd(OAc)_2$ were used. The purity of the products was determined by ^1H NMR and ATR-IR spectroscopies and by PXRD analysis.

Single-crystal X-ray diffraction experiments. Single crystals of two polymorphs of *transoid* **1A** were isolated by re−crystallization of the aging product from DMF. The crystal of polymorph **1A**−I was measured on an Oxford Diffraction Xcalibur (Mo tube, CCD detector), whereas the crystal of polymorph **1A**−II was measured on an Oxford Diffraction Xcalibur Nova R (microfocus Cu tube), both at 20 °C. Program package CrysAlisPRO[1] was used for

data reduction. The structures were solved using SHELXS97[1] and refined with SHELXL97.[2] Models were refined using the full−matrix least squares refinement; all non−hydrogen atoms were refined anisotropically. Hydrogen atoms were treated as constrained entities, using the command AFIX in SHELXL97.[2] Crystallographic data and refinement details are given in Table S1. CCDC 1469187 and 1469188 contain the supplementary crystallographic data for this paper and can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk).

Powder X-ray diffraction (PXRD) experiments were performed on a PHILIPS PW 1840 X−ray diffractometer with $CuK_{\alpha 1}$ (1.54056 Å) radiation at 40 mA and 40 kV. The scattered intensities were measured with a scintillation counter. The angular range was from 3 to 50° (2θ) with steps of 0.02°, and the measuring time was 1 s per step. The data collection and analysis was performed using the program package Philips X'Pert.[3]

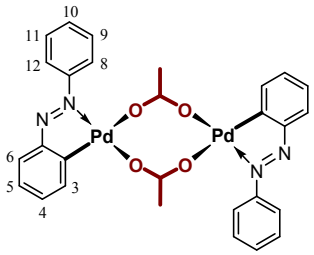
Attenuated total reflectance infrared (ATR-IR) spectra were recorded at Perkin-Elmer Spectrum Two FT-IR spectrometer with Diamond-UATR reflection cell.

NMR spectra were recorded immediately after dissolving in $CDCl_3$ and/or CD_3OD at 25 °C with Bruker AV-300 and AV−600 spectrometers operating at 300.13 and 600.13 MHz, respectively. The variable-temperature ^1H NMR experiments were recorded at 50, 25, 0 and -25 °C in $CDCl_3$ or CD_3OD. ^1H assignment is given in Table S2.

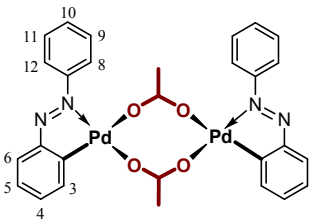
UV−vis spectra were recorded on an Agilent 8425 spectrophotometer in 20 mM sodium phosphate buffer (pH 7.4) at 20 °C.

DFT calculations were carried out using the Gaussian09.[4] Full geometry optimizations along with the vibrational frequency calculations were performed using three methods using B3LYP functional.[5] The standard 6−31G** and 6−311+G** basis sets was used for C, H, N, and O atoms, whereas Pd atoms were modelled using the Stuttgart−Dresden (SDD) pseudopotential and the accompanying SDD basis set.[6] Chloroform was modelled using the polarizable continuum model (IEF−PCM).[7]

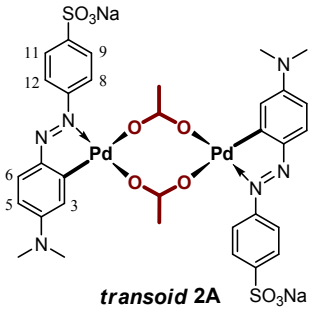
NMR SPECTROSCOPY



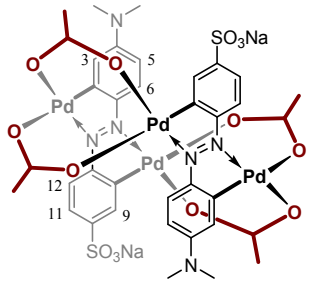
***transoid* 1A (major isomer)**
0.0 kcal/mol



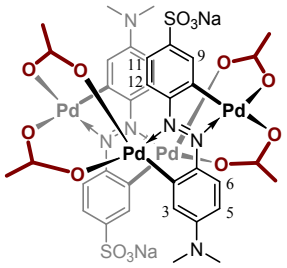
***cisoid* 1A (minor isomer)**
Gas phase (Method 1): 1.4 kcal/mol
Gas phase (Method 2): 1.2 kcal/mol
IEF-PCM, $CHCl_3$ (Method 3): 1.0 kcal/mol



***transoid* 2A**



***cisoid* 2B (major isomer)**



***transoid* 2B (minor isomer)**

Method 1: B3LYP/(SDD for Pd and 6−31G** for C, H, N, O).
Method 2: B3LYP/(SDD for Pd and 6−311+G** for C, H, N, O) with ultrafine grid.
Method 3: B3LYP/(SDD for Pd and 6−31G** for C, H, N, O) with IEF−PCM for chloroform.

Fig. S1 *Cisoid* and *transoid* isomers of products **1A**, **2A** and **2B** with denoted numeration of atoms used for NMR analysis. Calculated stabilities are given for *cisoid* and *transoid* isomers of the monocyclopalladated complex **1A**.

Table S1 ^{1}H NMR data for **1A** in $CDCl_3$ as well as **2A** and **2B** in CD_3OD in (δ / ppm, J / Hz).

	Compound						
	1A	**1A**		**2A**		**2B**	
Proton	*transoid*	*cisoid*	**Proton**	*transoid*	**Proton**	*cisoid*	*transoid*
H−3	6.49 dd J_{HH}=7.8, 1.3	6.72 dt J_{HH}=7.9, 1.2	**H−3**	5.53 d J_{HH}=2.2	**H−3**	5.94 d J_{HH}=2.3	5.95 d J_{HH}=2.4
H−4	6.80 dt J_{HH}=7.6, 1.4	6.97 dt J_{HH}=7.5, 1.2	**H−5**	6.47 dd J_{HH}=8.9, 2.3	**H−5**	6.18 dd J_{HH}=9.5, 2.3	6.21 dd J_{HH}=9.4, 2.6
H−5	7.14 dt J_{HH}=7.5, 1.1	Overlapped[a]	**H−6**	7.48 d J_{HH}=8.9	**H−6**	7.63 d J_{HH}=9.5	7.63 d J_{HH}=9.4
H−6	7.70 dd J_{HH}=7.7, 1.4	7.55 dd J_{HH}=7.7, 1.4	**H−8,12**	7.59 d J_{HH}=8.6	**H−9**	7.48 d J_{HH}=8.6	7.41 d J_{HH}=8.3
H−8,12	7.34 d J_{HH}=8.1	7.51 d J_{HH}=8.1	**H−9,11**	7.29 d J_{HH}=8.6	**H−11**	7.19 dd J_{HH}=8.4, 1.4	7.05 dd J_{HH}=8.5, 2.0
H−9,11	7.25 t J_{HH}=7.9	7.19 t J_{HH}=7.9			**H−12**	7.14 d J_{HH}=1.4	7.15 d J_{HH}=1.9
H−10	7.37 t J_{HH}=7.9	Overlapped[a]	$N(CH_3)_2$	2.93 s, br	$N(CH_3)_2$	3.21 s	Overlapped[b]
CH_3COO	2.08 s	2.34 s, 1.79 s	CH_3COO	2.04 s	CH_3COO	2.30 s, 2.11 s	2.20 s

[a] Overlapped with signals of *transoid* **1A**.
[b] Overlapped with signals of *cisoid* **2B**.

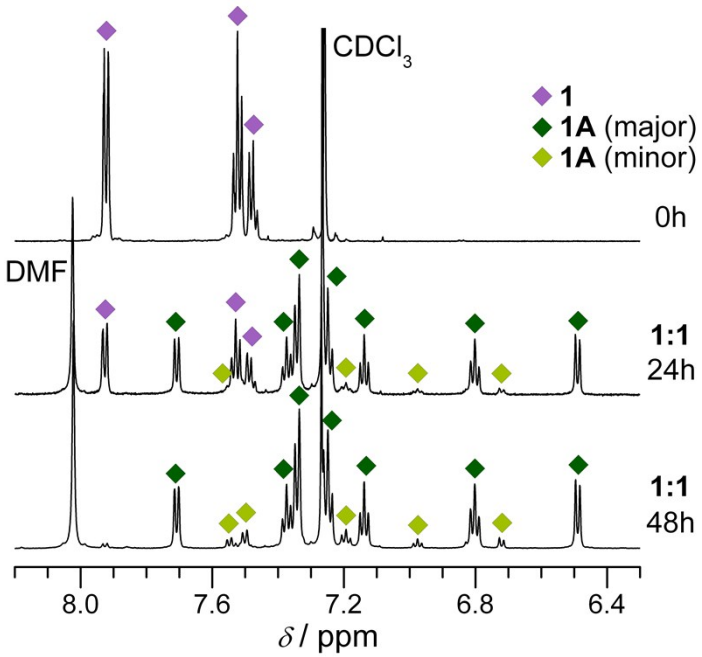


Fig. S2 Aromatic region in ^{1}H NMR spectra of reaction mixtures from aging reactions in DMF vapour of **1** and $Pd(OAc)_2$ (ratio 1:1) in $CDCl_3$ (600 MHz) recorded immediately after dissolving.

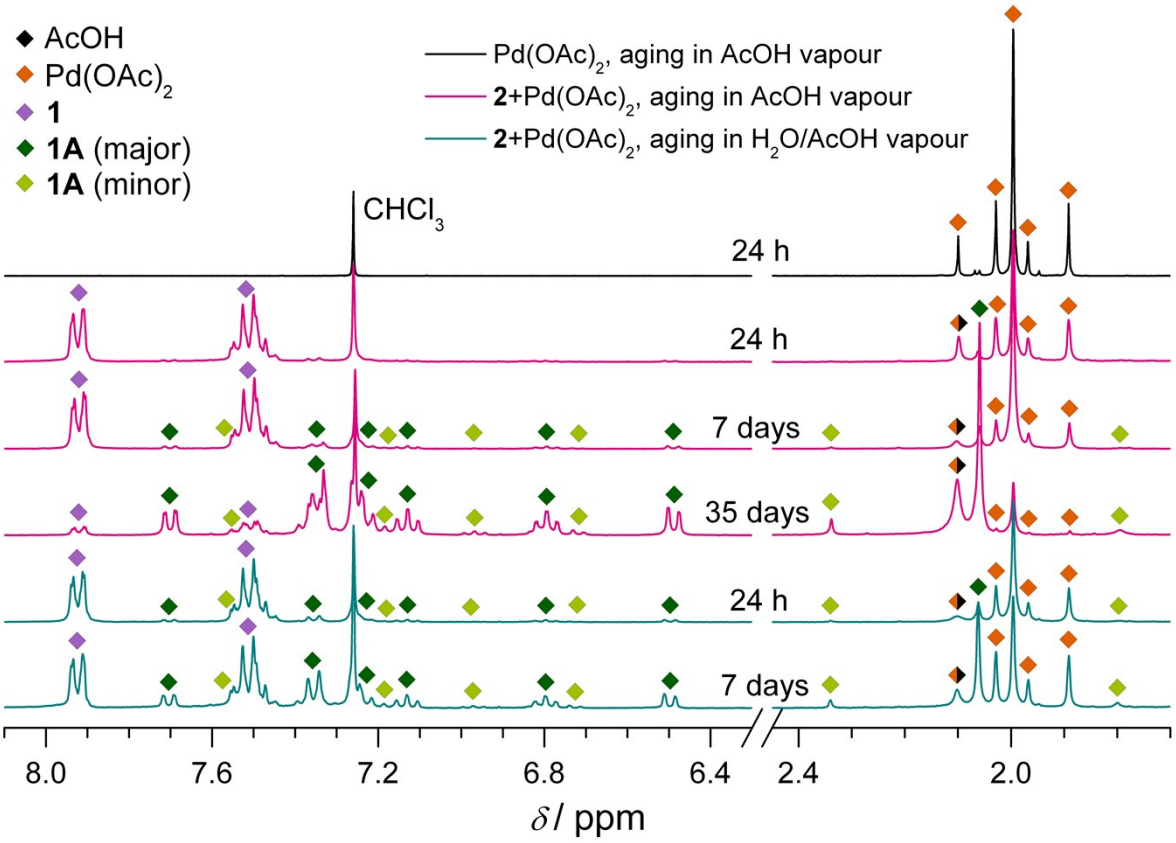
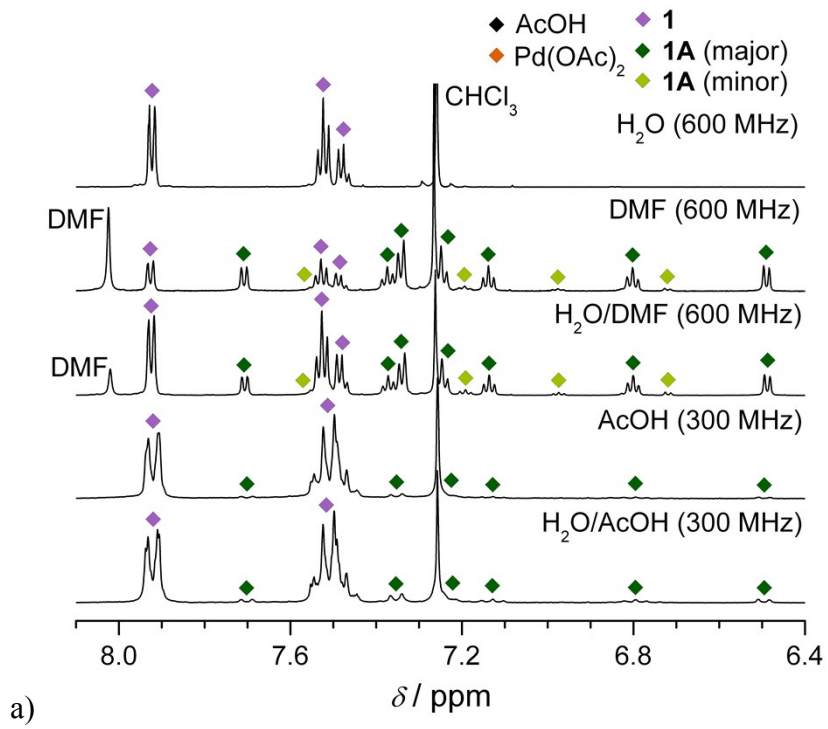
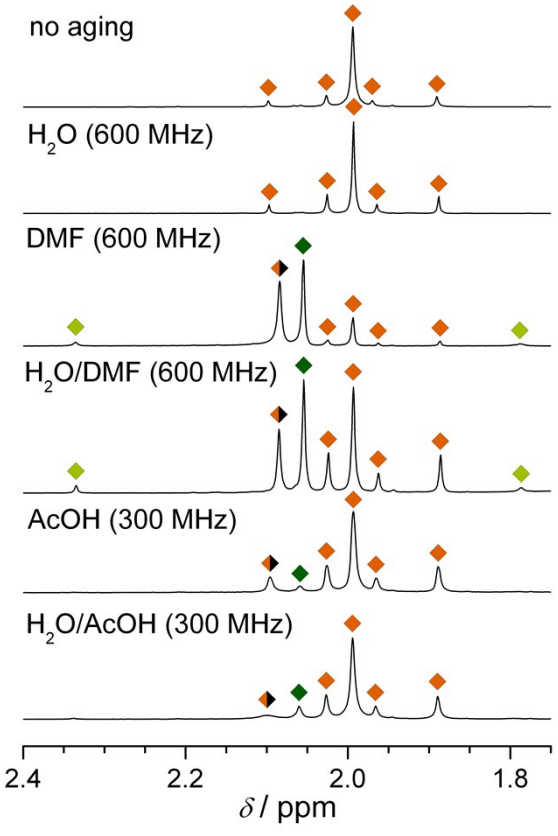


Fig. S3 ^{1}H NMR spectra (in $CDCl_3$, 300 MHz) of reaction mixtures of **1** and $Pd(OAc)_2$ (1:1) from accelerated aging in **acetic acid** (AcOH) and **water/acetic acid** vapour. Reaction times are marked along with the spectra. ^{1}H NMR spectrum of pure $Pd(OAc)_2$ after aging in AcOH for 24 hours is given as a top spectrum.



a)



b)

Fig. S4 a) Aromatic and b) aliphatic part of ^{1}H NMR spectra in $CDCl_3$ of reaction mixtures of **1** and $Pd(OAc)_2$ (1:1) from accelerated aging after **24 hours** in (from top to bottom): **water**, **DMF**, **water/DMF**, **acetic acid** (AcOH) and **water/acetic acid** vapour. ^{1}H NMR spectrum of pure $Pd(OAc)_2$ before any aging reaction is given as a top spectrum in b). Reactions in AcOH and H_2O/AcOH produced only traces of the monocyclopalladated product **1A** (see a)). Operating frequency of the NMR spectrometer (300 or 600 MHz) is given in parentheses.

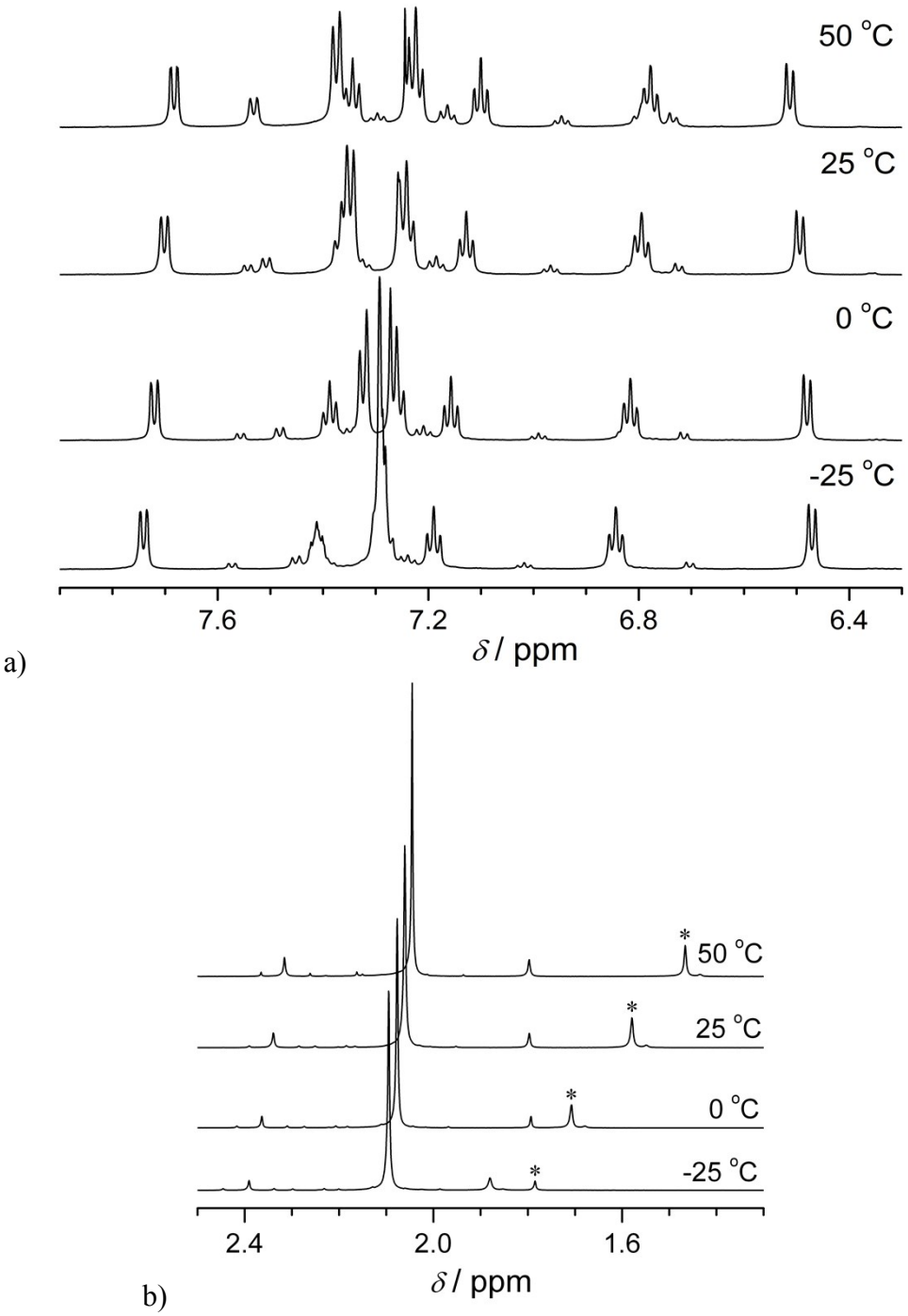


Fig. S5 a) Aromatic and b) aliphatic part of variable-temperature ^{1}H NMR spectra of **1A** recorded in $CDCl_3$ (600 MHz). Water signals are marked with an asterisk (*).

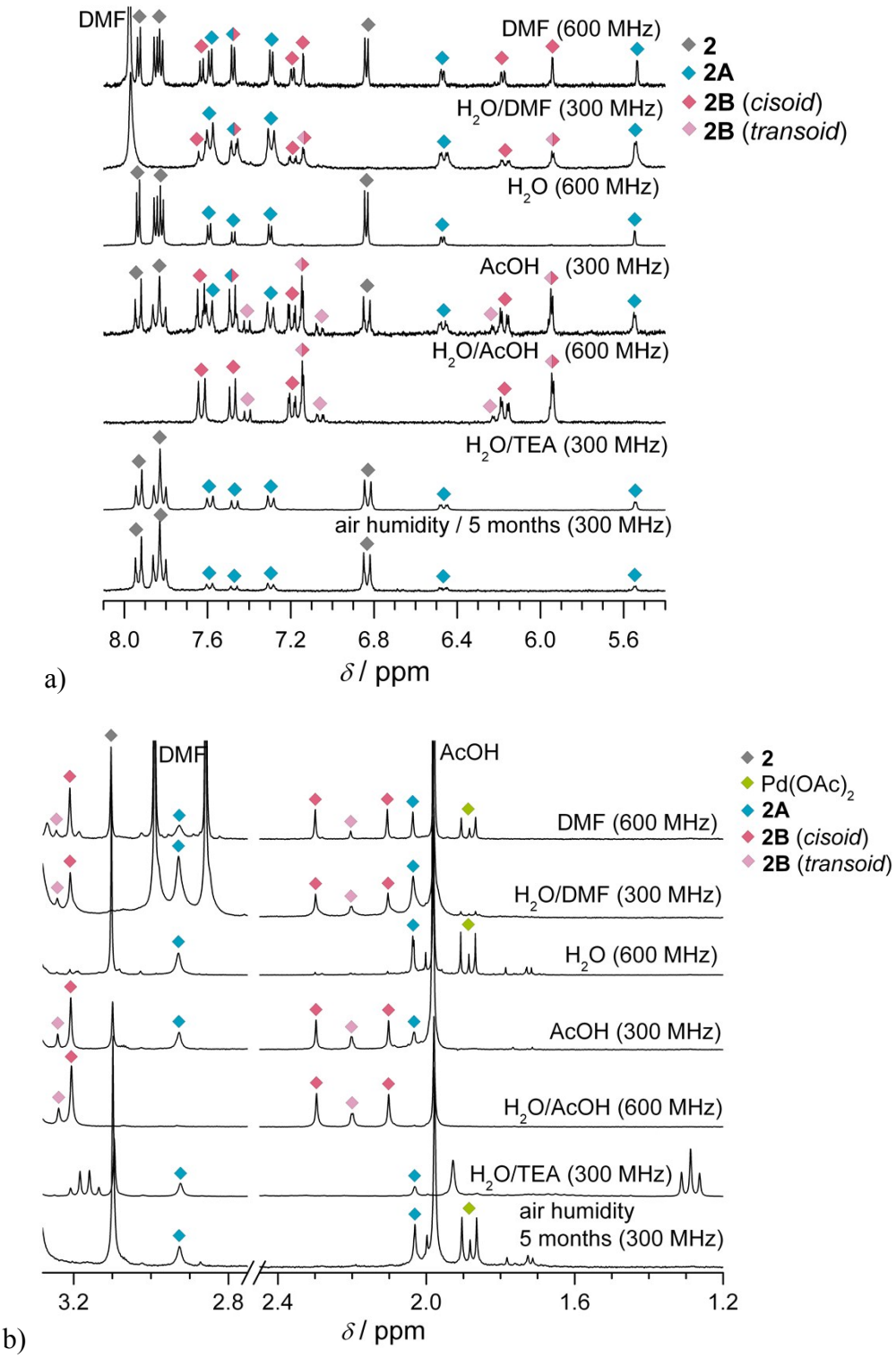


Fig. S6 a) Aromatic and b) aliphatic part of the ^{1}H NMR spectra (in CD_3OD) of reaction mixtures of **2** and $Pd(OAc)_2$ (1:2) from accelerated aging in (from top to bottom): **DMF** (after **24 hours**), **water/DMF** (after **24 hours**), **water** (after **24 hours**), **acetic acid** (AcOH, after **24 hours**), **water/acetic acid** (after **24 hours**), **water/*N*,*N*,*N*-triethylamine** (TEA, after **24 hours**) vapour and air humidity (after **5 months**). Operating frequency of the NMR spectrometer, 300 or 600 MHz, is given in parentheses.

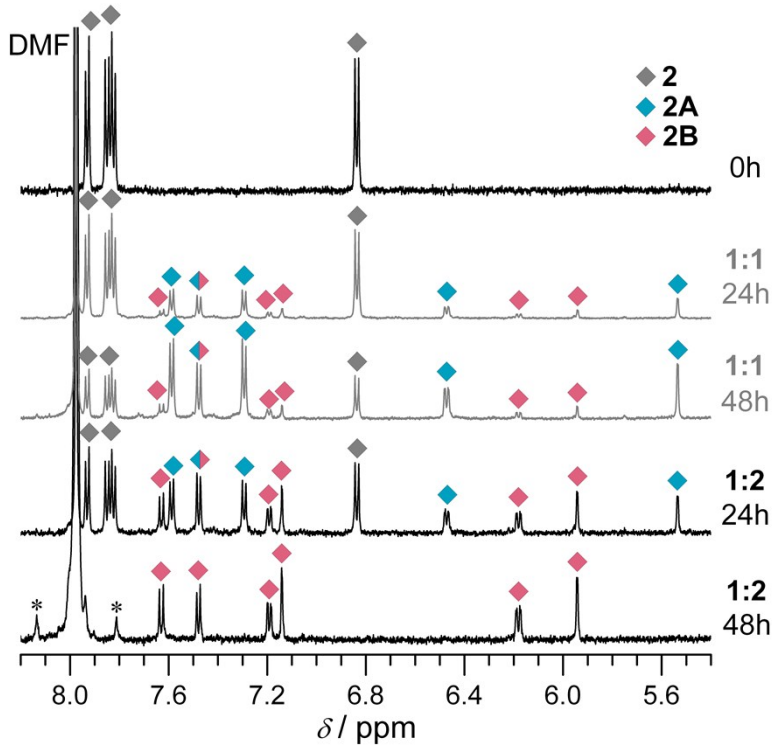


Fig. S7 Aromatic region in ^{1}H NMR spectra of reaction mixtures from aging reactions in DMF vapour of **2** and $Pd(OAc)_2$ (1:1, grey and 1:2, black) in CD_3OD (600 MHz) recorded immediately after dissolving. Side-bands are denoted by asterisks.

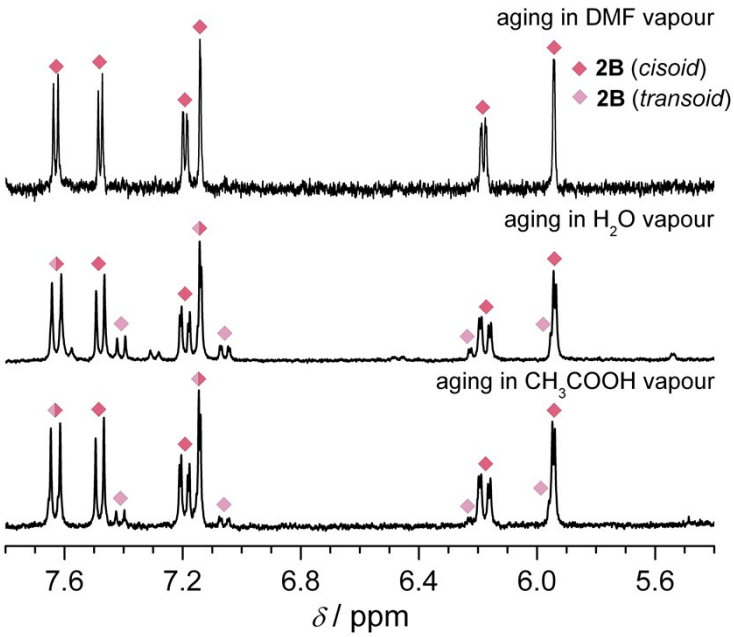


Fig. S8 Aromatic part of the ^{1}H NMR spectra (in CD_3OD, 600 MHz) of reaction mixtures of **2** and $Pd(OAc)_2$ (1:2) from accelerated aging in **DMF** (after **2 days**), **water** (after **35 days**) and **acetic acid** (after **7 days**) vapour.

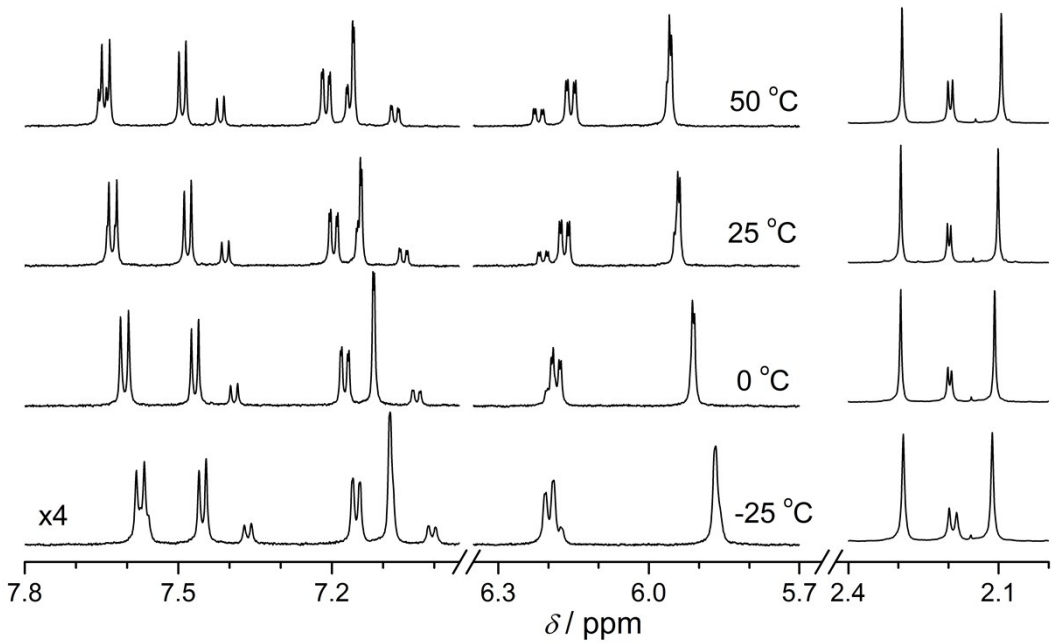


Fig. S9 Variable temperature ^{1}H NMR spectra of **2B** recorded in CD_3OD (600 MHz).

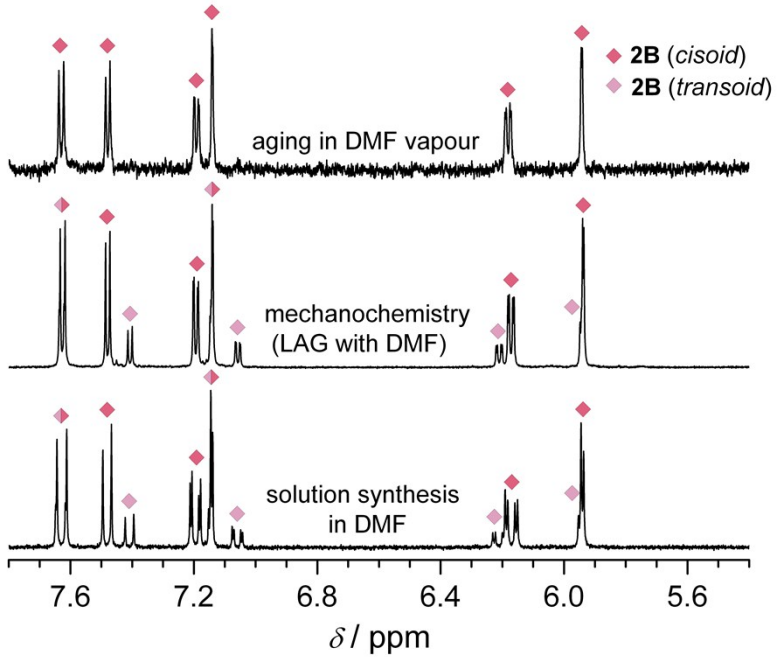


Fig. S10 Aromatic part of ^{1}H NMR spectra (in CD_3OD, 600 MHz) of reaction mixtures of **2** and $Pd(OAc)_2$ (1:2) from **accelerated aging** in DMF (after 2 days), **mechanochemical synthesis** (LAG with 20 μL DMF after 4 hours) or **solution synthesis** in DMF (after 3 weeks) vapour.

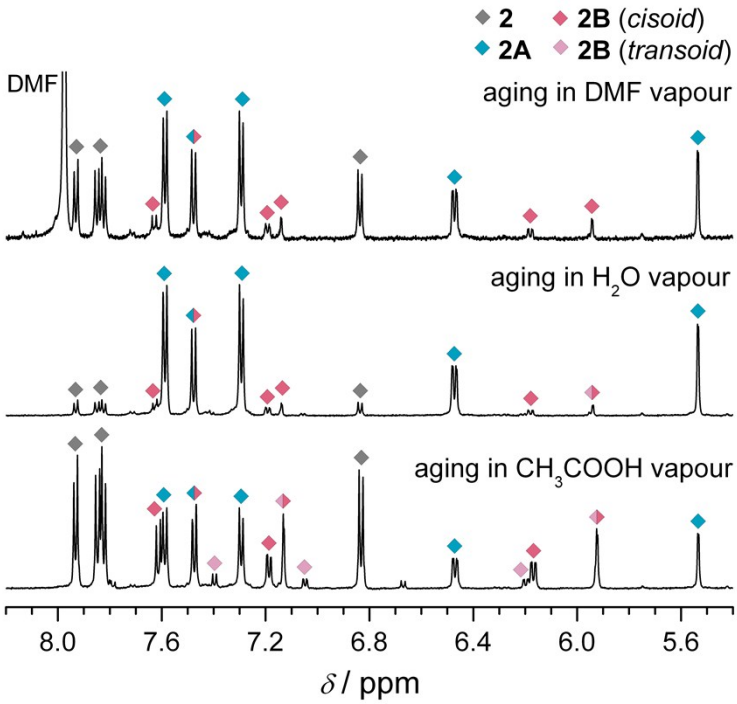


Fig. S11 Aromatic part of ^{1}H NMR spectra (in CD_3OD, 600 MHz) of reaction mixtures of **2** and $Pd(OAc)_2$ (1:1) from accelerated aging in DMF, water or acetic acid vapour after $Pd(OAc)_2$ has been consumed.

IR SPECTROSCOPY

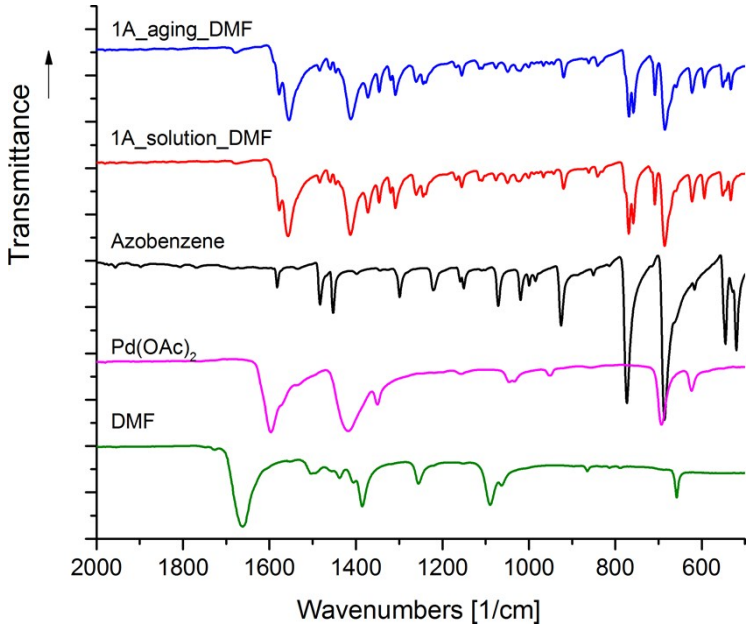


Fig. S12 ATR-IR spectra of reactants and product **1A** obtained by aging and solvent−based method.

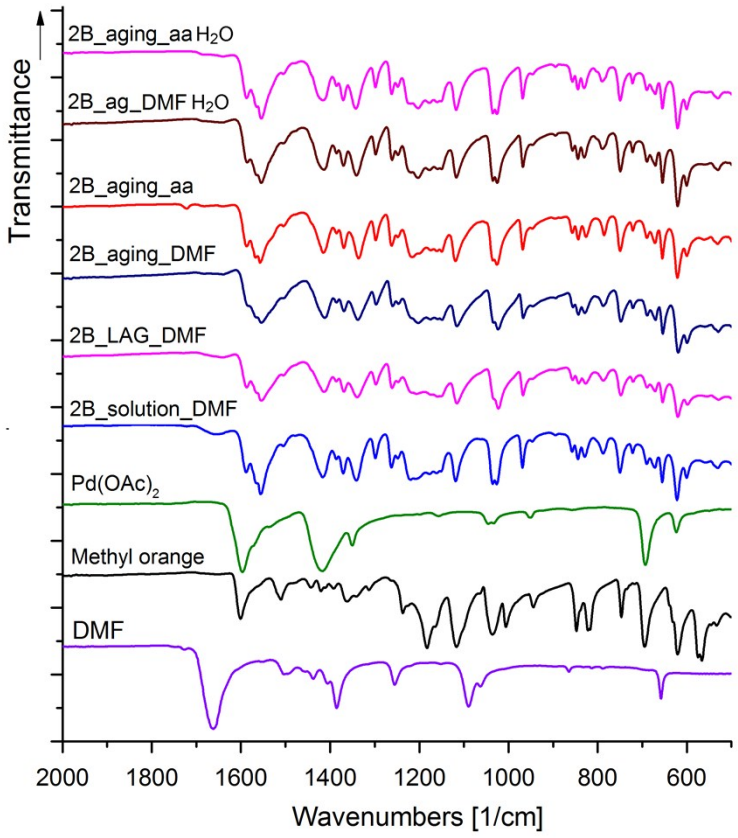


Fig. S13 ATR-IR spectra of reactants and the product (**2B**) obtained by aging, liquid−assisted grinding (LAG) and solvent−based methods. DMF stands for *N,N*-dimethylformamide, and „aa“ stands for acetic acid.

POWDER X−RAY DIFFRACTION EXPERIMENTS

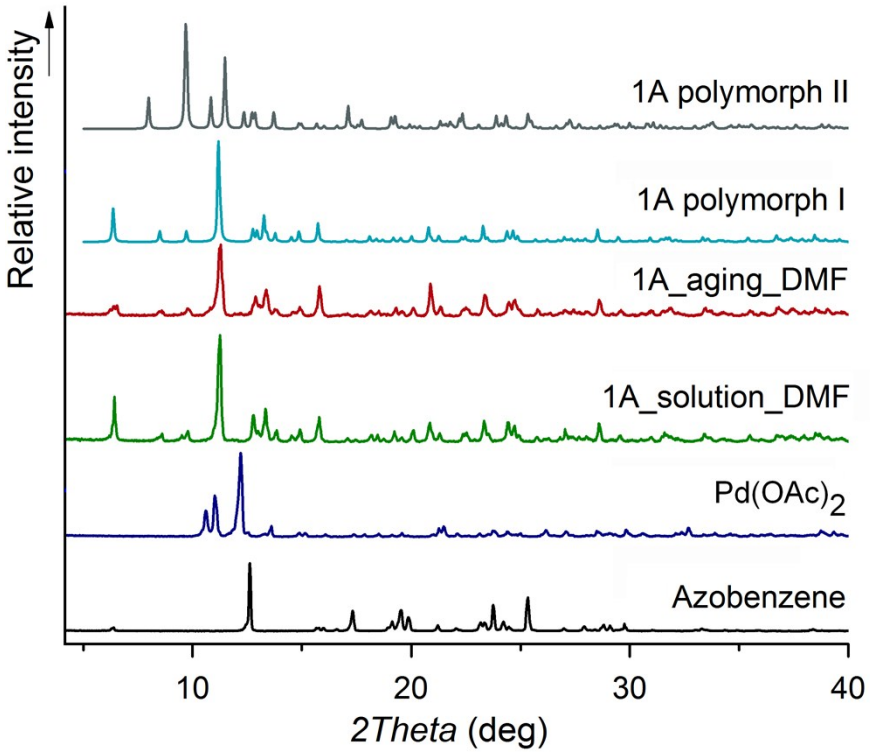


Fig. S14 PXRD patterns of reactants and the product **1A** obtained by aging and solvent−based method.

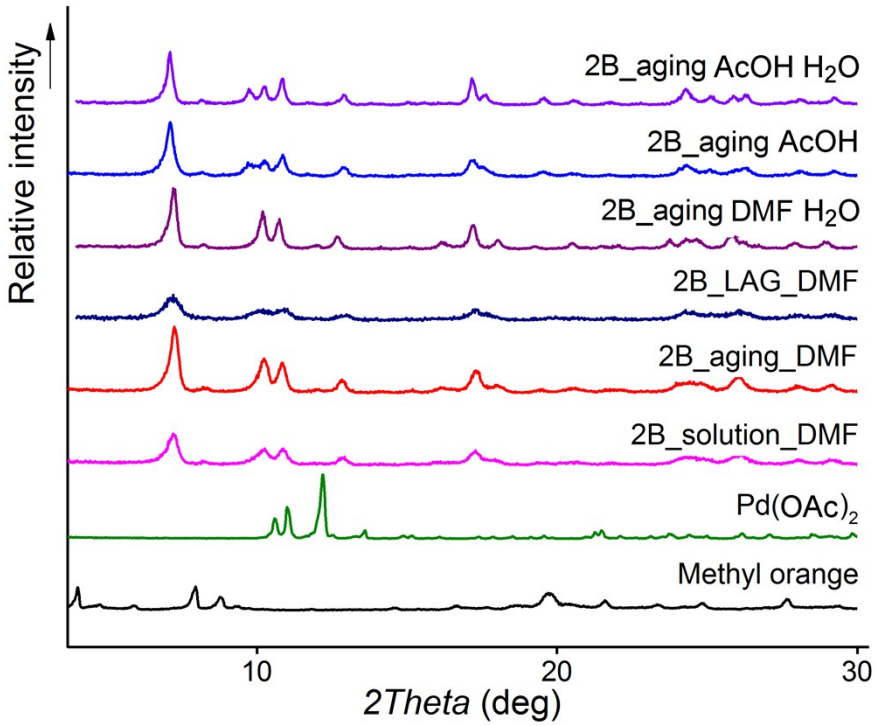


Fig. S15 PXRD patterns of reactants and the product **2B** obtained by aging, liquid-assisted grinding (LAG) and solvent−based method.

SINGLE−CRYSTAL X−RAY DIFFRACTION EXPERIMENTS

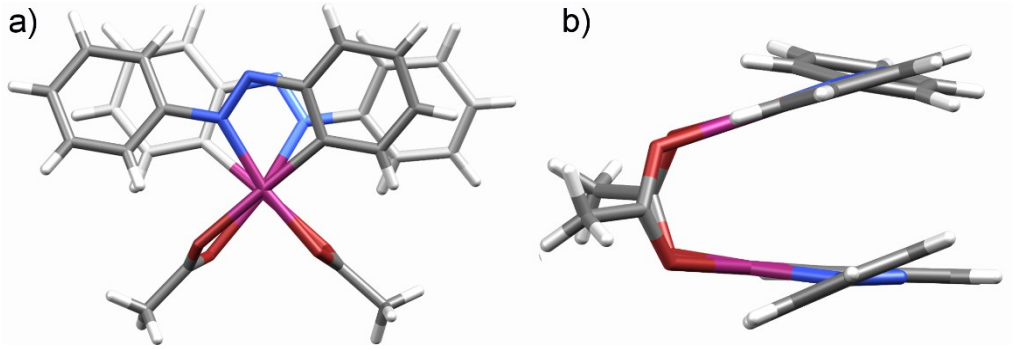


Fig. S16 Molecular structure of polymorph **1A−I** (P*bca*), (a) front view and (b) side view.

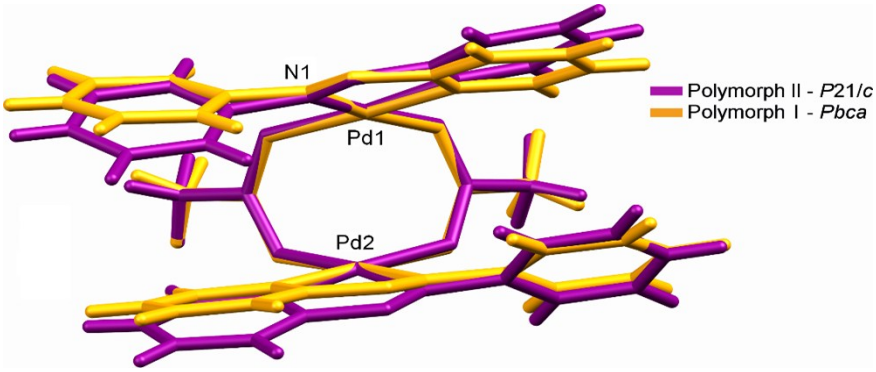


Fig. S17 Molecules of *transoid* **1A** in polymorphs **1A−I** and **1A−II** overlapped using N1−Pd1−Pd2 atoms.

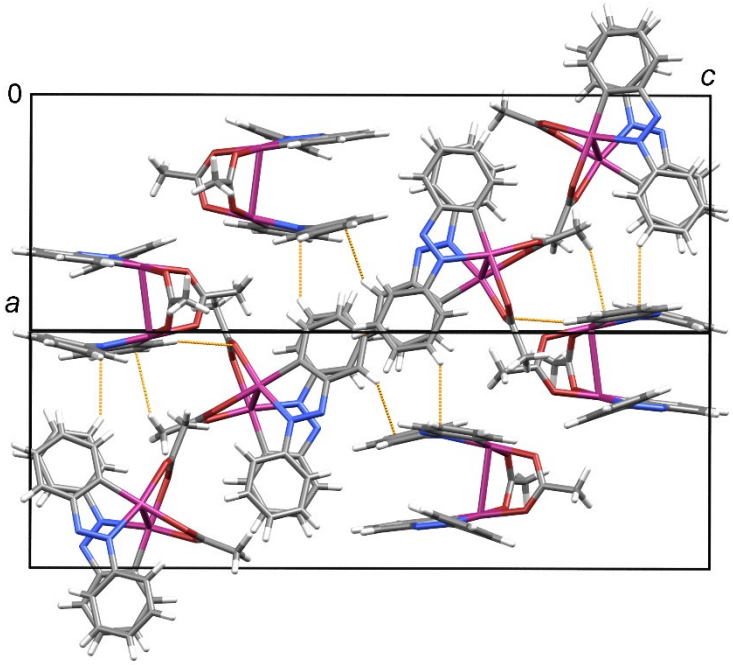


Fig. S18 Packing of polymorph **1A−I** (P*bca*) along *ab* diagonal

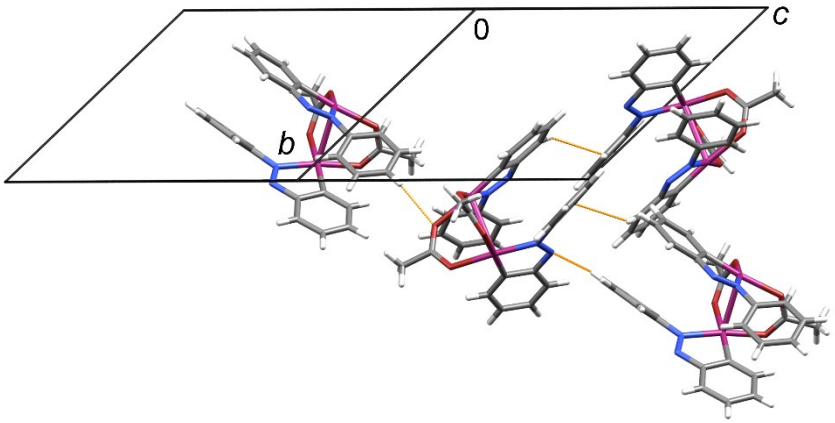


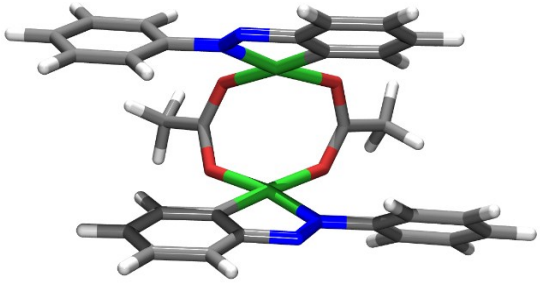
Fig. S19 Packing of polymorph **1A−II** ($P2_1/c$) along *bc* diagonal.

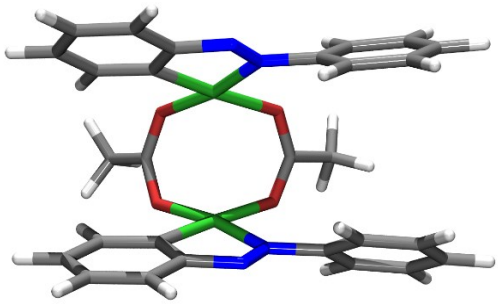
Table S2 Crystallographic data, collection and structure refinement details for complex **1A**.

Complex	**Polymorph 1A−I**	**Polymorph 1A−II**
Empirical formula	$C_{28}H_{24}N_4O_4Pd_2$	$C_{28}H_{24}N_4O_4Pd_2$
Formula wt. / g mol^{-1}	693.31	693.31
Crystal dimensions / mm	0.36 x 0.35 x 0.08	0.15 x 0.12 x 0.10
Colour	Green	Green
Solvent used for crystallization	DMF	DMF
Space group	*Pbca*	$P2_1/c$
a / Å	15.7028(3)	13.94260(10)
b / Å	12.1884(3)	18.57930(10)
c / Å	27.7307(9)	18.8456(2)
α / °	90	90
β / °	90	146.18
γ / °	90	90
Z	8	4
V / Å^3	5307.4(2)	2717.16(4)
D_{calc} / g cm^{-3}	1.735	1.695
Diffractometer type	Oxford Xcalibur Sapphire3	Oxford Xcalibur Nova
Radiation	MoK_α	CuK_α
μ / mm^{-1}	1.397	7.730
Absorption correction	Multi−scans	Multi−scans
T_{min}, T_{max}	0.776; 1.000	0.487, 1.000
Θ range / °	4.16–28.00	4.00–75.87
Range of h, k, l	$18 \geq h \geq -20$ $16 \geq k \geq -16$ $36 \geq l \geq -34$	$17 \geq h \geq -14$ $23 \geq k \geq -22$ $23 \geq l \geq -23$
Reflections collected	27470	14515
Observed reflections ($I \geq 2\sigma$)	4389	5212
Independent reflections	6376	5613
R_{int}	0.0417	0.0287
R (F)	0.0375	0.0319
R_w (F^2)	0.0887	0.0883
Goodness of fit	1.018	1.040
No. of parameters	343	345
F(000)	2752.0	1376.0
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (eÅ^{-3})	0.687, –0.539	1.158, –0.887

DFT CALCULATIONS

Calculated geometries of *transoid* and *cisoid* **1A** using *method 3*: B3LYP/(SDD for Pd and 6−31G** for C, H, N, O) with IEF−PCM for chloroform.

Transoid **1A**			
			
Pd	0.42886	1.35436	0.93340
Pd	−0.43311	−1.56928	0.54781
O	−1.14166	1.32514	2.28717
O	1.14205	−1.90433	1.85606
O	1.61024	0.25063	2.38475
O	−1.60866	−0.89334	2.24475
N	1.86221	1.68700	−0.52597
N	−1.86188	−1.47886	−0.95185
C	−0.36919	3.41173	−2.62576
H	0.24879	3.60803	−3.49641
N	1.49159	2.28784	−1.58532
C	3.83941	0.81466	−1.70211
H	3.27200	0.79759	−2.62507
C	−1.68669	3.85265	−2.55046
H	−2.12417	4.40717	−3.37443
N	−1.49101	−1.77282	−2.13347
C	3.21745	1.23997	−0.51798
C	−1.90681	2.86446	−0.32416
H	−2.51500	2.66393	0.55187
C	−3.82607	−0.29929	−1.84985
H	−3.25606	−0.03945	−2.73396
C	−3.92218	−1.37078	0.33489
H	−3.43025	−1.93170	1.11936
C	3.92303	1.25537	0.69143
H	3.42446	1.57583	1.59743
C	0.36472	−2.59291	−3.43422
H	−0.25014	−2.53923	−4.32725
C	−0.59028	2.41167	−0.37551
C	5.26119	0.86160	0.70862
H	5.81459	0.88918	1.64232
C	2.43202	−3.11084	−2.29793
C	1.67733	−3.05224	−3.47743

Cisoid **1A**			
			
Pd	0.40469	−1.69710	0.53955
Pd	0.65078	1.35831	0.98485
O	−0.94773	0.85807	2.34593
O	−0.98805	−1.39753	2.16124
O	1.98858	0.60572	2.39290
O	1.92094	−1.62423	1.96130
N	−0.89892	−1.98292	−1.04776
N	−0.38686	−2.15804	−2.20043
C	−2.32477	−1.93557	−1.01398
C	1.66061	−2.05616	−0.93439
C	−3.05268	−1.44020	−2.10778
C	0.99654	−2.20529	−2.18138
C	−4.44329	−1.44179	−2.06106
H	−5.00769	−1.05003	−2.90177
C	−2.98733	−2.42138	0.12013
H	−2.41105	−2.78549	0.96087
C	1.69709	−2.43410	−3.37784
H	1.14689	−2.54014	−4.30761
C	3.05034	−2.15645	−0.91853
H	3.59124	−2.05512	0.01670
C	−5.11231	−1.93964	−0.93741
C	−4.38197	−2.42955	0.14732
H	−4.89689	−2.82057	1.01953
C	3.08459	−2.52417	−3.33591
H	3.64787	−2.70132	−4.24643
C	3.75224	−2.39081	−2.11084
C	2.31709	−0.60234	2.60169
C	3.27179	−0.85418	3.75270
H	2.68376	−1.01059	4.66361
H	3.86310	−1.75282	3.57132
H	3.92129	0.00805	3.91022
N	0.23431	2.75224	−1.51231

H	2.11411	−3.36762	−4.41955
C	0.16973	2.69945	−1.54136
C	1.74869	−0.99659	2.51706
C	5.88681	0.43651	−0.46568
C	5.17120	0.41112	−1.66782
H	5.65160	0.07226	−2.58066
C	−3.21256	−1.03639	−0.82507
C	−2.44530	3.58204	−1.40355
C	−5.15306	0.09621	−1.70698
H	−5.62678	0.67525	−2.49387
C	1.89455	−2.70639	−1.06607
H	2.49909	−2.75742	−0.16640
C	−5.87213	−0.24409	−0.55589
C	0.58297	−2.24188	−0.99649
C	−1.74440	0.27720	2.69580
C	−0.17332	−2.19515	−2.19891
C	−5.25534	−0.97947	0.45892
H	−5.81186	−1.25223	1.35038
C	2.76401	−1.47695	3.53753
H	3.76933	−1.30063	3.14009
H	2.64524	−2.54056	3.74533
H	2.66671	−0.89882	4.45931
C	−2.75405	0.47849	3.81067
H	−2.68149	−0.33830	4.53217
H	−3.76021	0.45194	3.37827
H	−2.60834	1.43723	4.30899
H	6.92572	0.12154	−0.44558
H	−6.90711	0.06681	−0.45054
H	−3.47200	3.93396	−1.34704
H	3.45480	−3.47643	−2.33606

N	−0.42158	2.32560	−0.50772
C	1.59954	2.55852	−1.39751
C	−2.49141	2.50568	−1.82615
C	2.09758	1.92697	−0.22653
C	−1.83530	2.50939	−0.58429
C	3.47827	1.78665	−0.09967
H	3.89863	1.31978	0.78493
C	2.44931	3.02236	−2.41602
H	2.02152	3.49754	−3.29328
C	−2.55347	2.72422	0.59836
H	−2.03693	2.70645	1.54910
C	−3.86418	2.72608	−1.87566
H	−4.37412	2.71523	−2.83422
C	4.32995	2.25441	−1.11208
C	3.82319	2.86420	−2.26757
H	4.50004	3.21575	−3.03957
C	−3.92751	2.95629	0.53224
H	−4.48301	3.13623	1.44755
C	−4.58594	2.95618	−0.69902
C	−1.35259	−0.29715	2.67615
C	−2.40575	−0.37516	3.76847
H	−2.40732	0.52955	4.37787
H	−3.38942	−0.48149	3.29759
H	−2.23990	−1.25387	4.39521
H	−1.91997	2.32734	−2.72931
H	−2.52172	−1.05818	−2.97148
H	−6.19770	−1.93945	−0.90744
H	−5.65710	3.12824	−0.74381
H	4.83588	−2.46968	−2.08209
H	5.40461	2.14102	−0.99561

UV−VIS SPECTROSCOPY

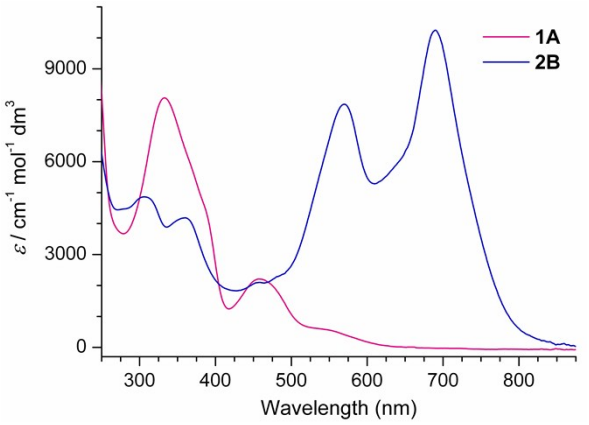


Fig. S20 UV−vis spectra of **1A** and **2B** at 20 °C in methanol.

STUDIES WITH AMINO ACIDS

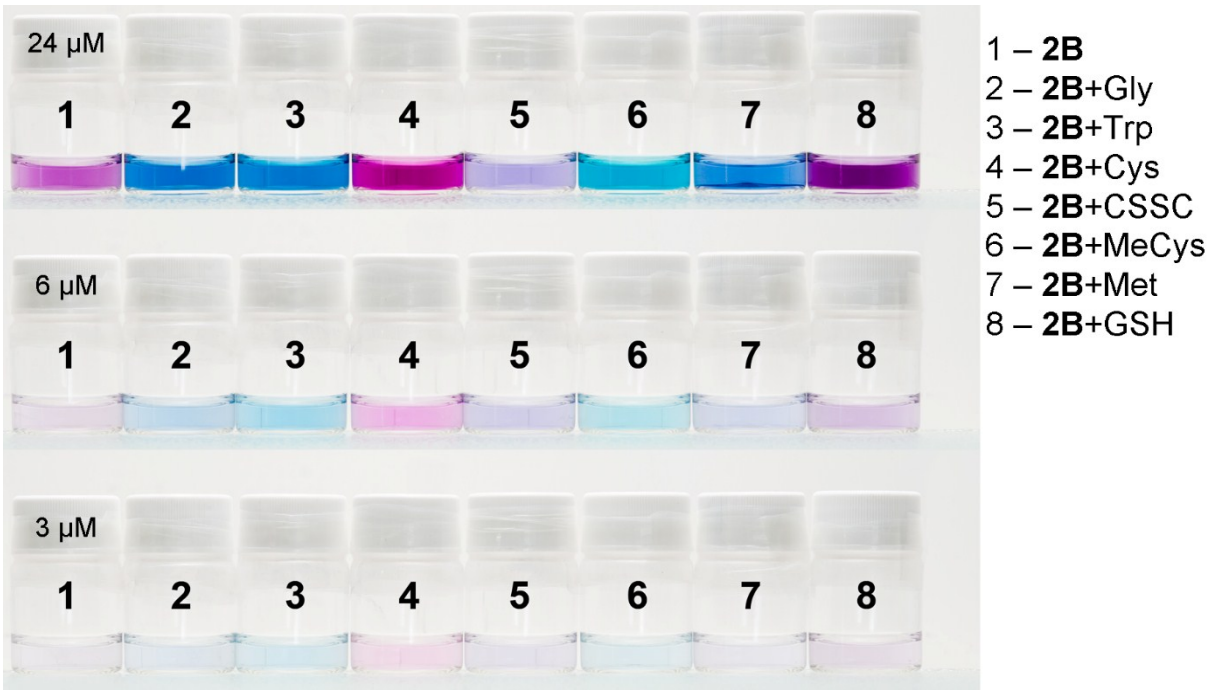


Fig. S21 Solutions with 24, 6 and 3 μM concentrations of **2B** in 20 mM sodium phosphate buffer (pH 7.4) after adding selected AA (4 eq). Due to solubility of CSSC, solutions have 10, 6 and 3 μM concentrations of **2B**.

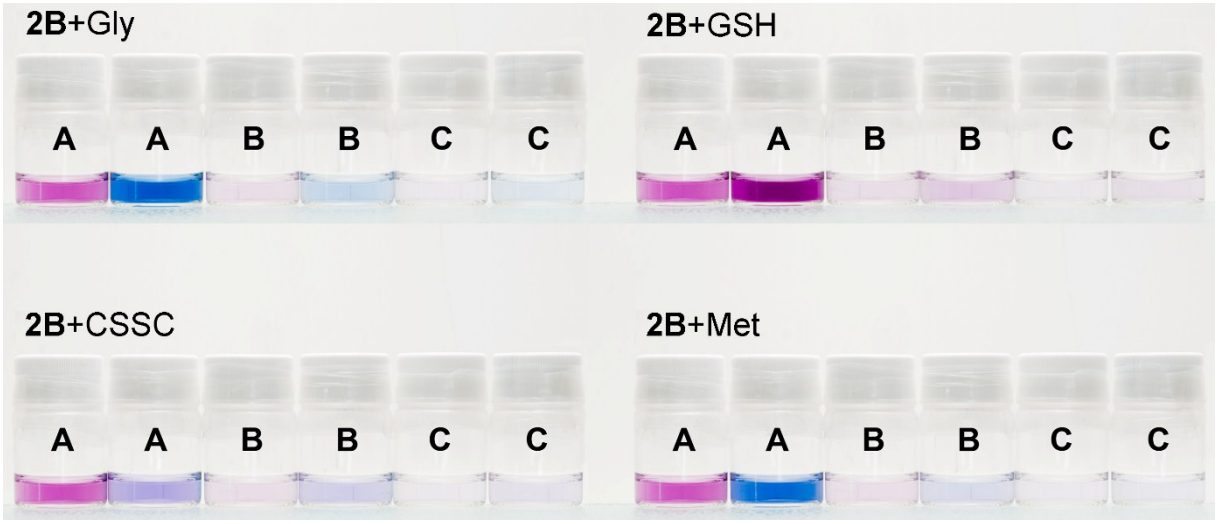


Fig. S22 Solutions of **2B** in 20 mM sodium phosphate buffer (pH 7.4) after adding selected AA (4 eq). Solutions of Gly, GSH and Met with 24, 6 and 3 μM concentrations of **2B** are marked **A**, **B**, and **C**, respectively. Solutions of CSSC with 10, 6 and 3 μM concentrations of **2B** are marked **A**, **B**, and **C**, respectively.

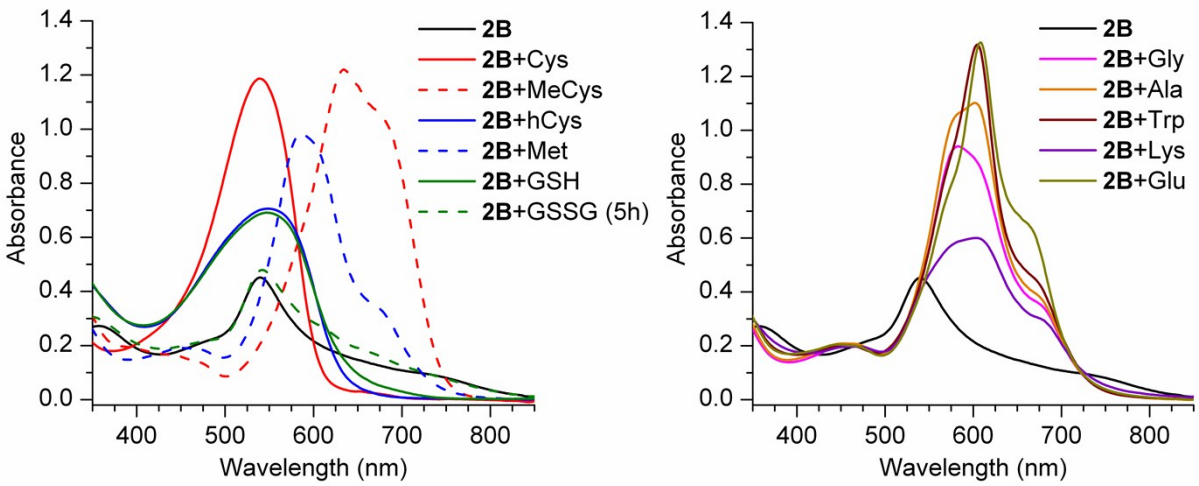


Fig. S23 Chromogenic behaviour of **2B** with AAs: (a) UV−vis spectra of **2B** (24 μM) after adding 30 equivalents of AA showing S−containing AAs separately (left) from other AAs (right). Data were collected at 20 °C in 20 mM sodium phosphate buffer (pH 7.4).

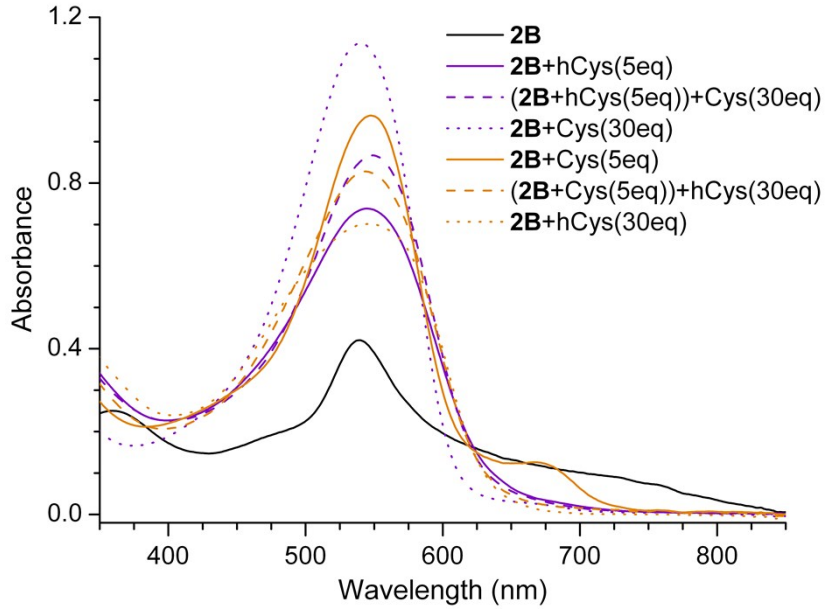


Fig. S24 UV-vis spectra of **2B** after adding Cys and/or hCys. One selected AA–SH (Cys or hCys; 5 eq) was added to the solution of **2B** (23 μM) and UV-vis spectrum was recorded after 5 hours (*coloured full lines*). Other AA-SH (Cys or hCys; 30 eq) was added to the above prepared solutions and UV–vis spectra were recorded after 20 hours (*coloured dashed lines*). UV-vis spectra of **2B** (23 μM) before (*black full line*) and after addition of one AA-SH (Cys or hCys; 30 eq) (*dotted coloured lines*). Data were collected at 20 °C in 20 mM sodium phosphate buffer (pH 7.4).

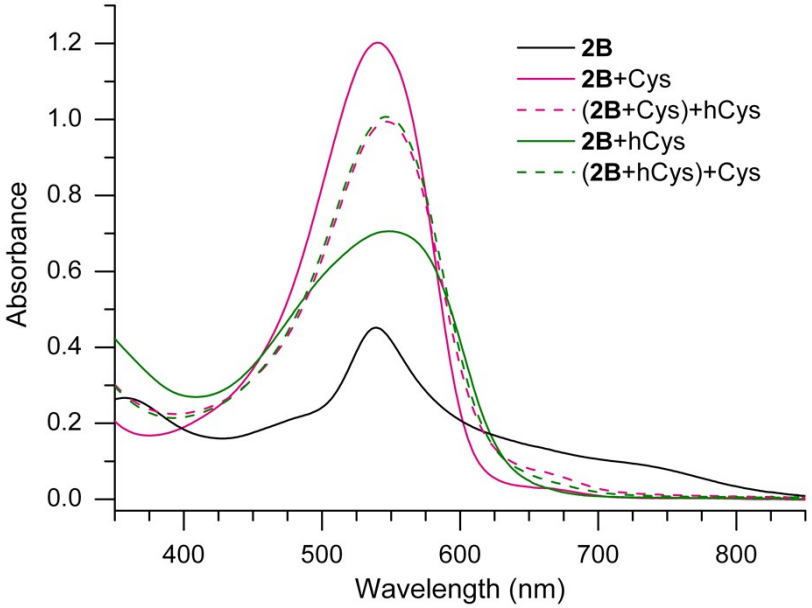


Fig. S25 UV–vis spectra of **2B** after adding Cys and/or hCys. One selected AA–SH (Cys or hCys; 30 eq) was added to the solution of **2B** (23 μM) and UV–vis spectrum was recorded after 5 hours (*coloured full lines*). Other AA-SH (Cys or hCys; 30 eq) was added to the above prepared solutions and UV–vis spectra were recorded after 25 hours at 20 °C and 5 hours at 50 °C (*coloured dashed lines*). UV–vis spectrum of **2B** (23 μM) is shown as a *black full line*. Data were collected at 20 °C in 20 mM sodium phosphate buffer (pH 7.4).

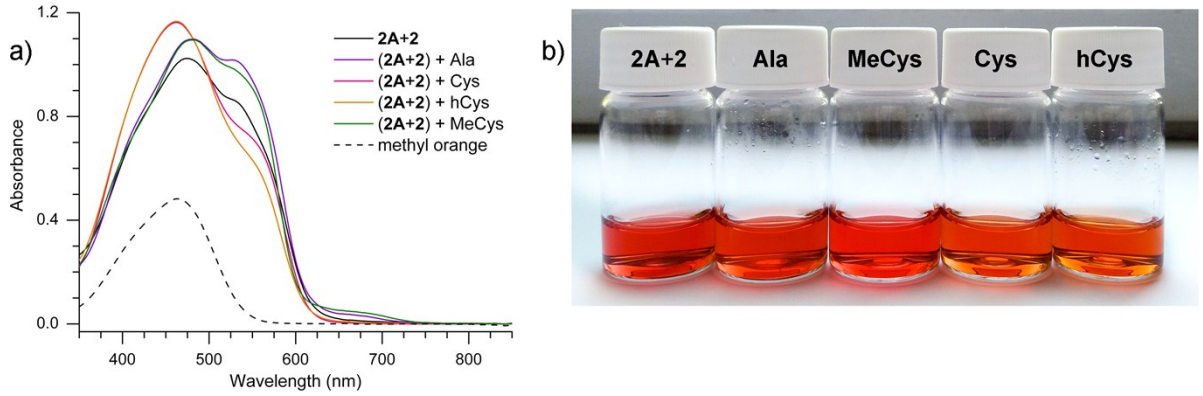


Fig. S26 a) UV–vis spectra of the isolated mixture from aging reaction of **2** and $Pd(OAc)_2$ in water vapour for 24 hours which has been washed with chloroform to remove $Pd(OAc)_2$ (**2A**+**2**, *black full line*), solutions of (**2A**+**2**) with one selected AA (Ala, MeCys, Cys or hCys) in excess (*coloured full lines*) and methyl orange (**2**, 25.8 μM, *black dashed line*); and b) photographs of the solutions of (**2A**+**2**) without and with one added AA as denoted in the photograph. Selected AA was added to the solution of (**2A**+**2**) and after 5 hours UV–vis spectrum was collected at 20 °C in 20 mM sodium phosphate buffer (pH 7.4). UV–vis spectrum of the solution of methyl orange does not change after AAs are added.

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