

## Electronic Supplementary information

### Dual stereocontrol over the Henry reaction with a light and heat triggered organocatalyst

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### **General information:**

Solvents and commercial starting materials were used as received (from Fluorochem or Sigma Aldrich). Dibromo-motor **3**,<sup>1</sup> catalyst **1**<sup>1</sup> and 2-bromo-4-pyridyl(dimethyl)amine<sup>2</sup> were prepared as described in the literature. Technical grade solvents were used for extraction and chromatography. Merck silica gel 60 (230-400 mesh ASTM) was used in flash chromatography. UV/VIS measurements were performed on a Jasco V-630 spectrophotometer. CD measurements were performed on a Jasco J-815 CD spectrophotometer. UV irradiation experiments were carried out using a Spectroline model ENB-280C/FE lamp. NMR spectra were obtained using a Varian Mercury Plus (400 MHz) and a Varian VXR-300S (300 MHz). Chemical shift values are reported in ppm with the solvent resonance as the internal standard (CHCl<sub>3</sub>:  $\delta$  7.26 for <sup>1</sup>H,  $\delta$  77.0 for <sup>13</sup>C, DCM:  $\delta$  5.32 for <sup>1</sup>H,  $\delta$  53.8 for <sup>13</sup>C). Enantiomeric ratios were determined by HPLC analysis using a Shimadzu LC 10ADVP HPLC equipped with a Shimadzu SPD10AVP diode array detector and chiral columns as indicated. Sample injections were made using an HP 6890 Series Auto sample Injector. Exact mass spectra were recorded on a LTQ Orbitrap XL (ESI+) or on a DART Xevo G2 QToF. Optical rotations were measured in CHCl<sub>3</sub> on a Perkin Elmer 241 MC polarimeter with a 10 cm cell (concentration c given in g/mL). All reactions requiring inert atmosphere were carried out under argon atmosphere using oven dried glassware and standard Schlenk techniques. Dichloromethane and toluene were used from the solvent purification system using a MBraun SPS-800 column. THF was distilled over sodium under nitrogen atmosphere prior to use. Melting points were determined using a Büchi Melting Point B-545.

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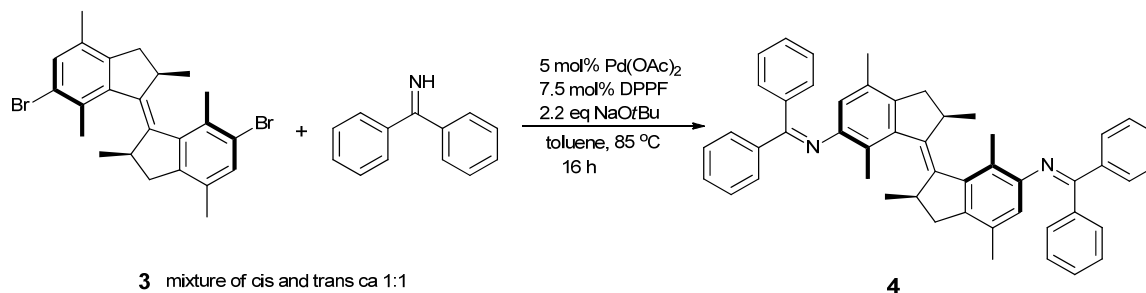
<sup>1</sup> J. Wang, B. Feringa, *Science*, 2011, **331**, 1429-1431.

<sup>2</sup> D. Cuperly, P. Gros and Y. Fort, *J. Org. Chem.*, 2002, **67**, 238-241.

## Experimental details:

### 1) Preparation of the dynamic catalyst **5** in its *(R,R)*-*(P,P)*-*trans* form:

**Compound 4** ((2*R*,2'*R*)-(*P,P*)-*E*-*N*6,*N*6'-bis(diphenylmethylene)-2,2',4,4',7,7'-hexamethyl-2,2',3,3'-tetrahydro-[1,1'-biindenylidene]-6,6'-diamine):<sup>3</sup>



In an oven dried Schlenk flask equipped with a stirring bar compound **3** (1.00 g, 2.11 mmol) (ca 1:1 *cis:trans* ratio), Pd(OAc)<sub>2</sub> (24 mg, 0.11 mmol), DPPF ligand (88 mg, 0.16 mmol) and NaOtBu (405 mg, 4.22 mmol) were dissolved in dry toluene (12 mL). Subsequently benzophenone imine (0.88 mL, 5.27 mmol) was added dropwise to the solution which was then heated to 90 °C. After stirring for 16 h the reaction mixture was cooled down and washed with water. The water layer was then extracted with (3 x 20 mL) DCM. The combined organic layers were dried over MgSO<sub>4</sub>, filtered and the solvent was evaporated. After purification via flash chromatography with pentane/Et<sub>2</sub>O=95/5 (R<sub>f</sub>=0.15), product was obtained as a yellow solid (593 mg, 0.84 mmol, Y=80% based on *trans*-**3**).

mp= 187-189 °C.

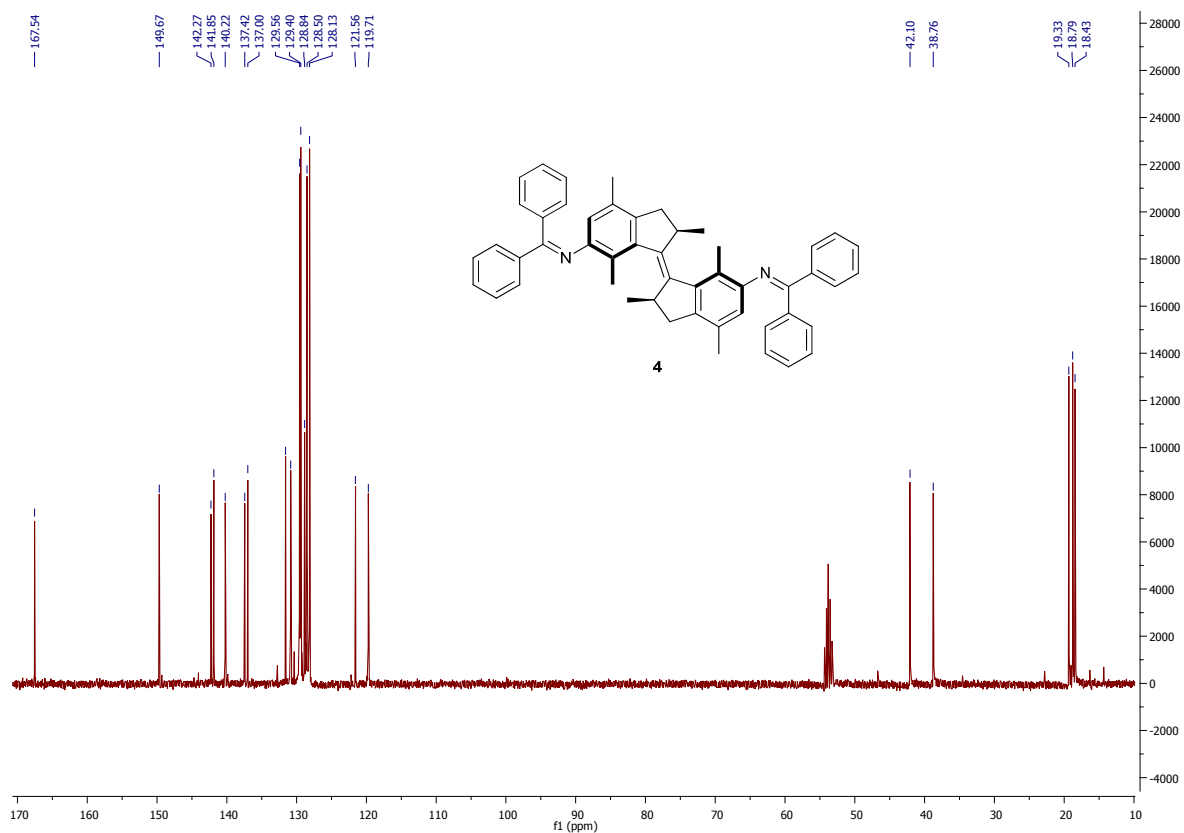
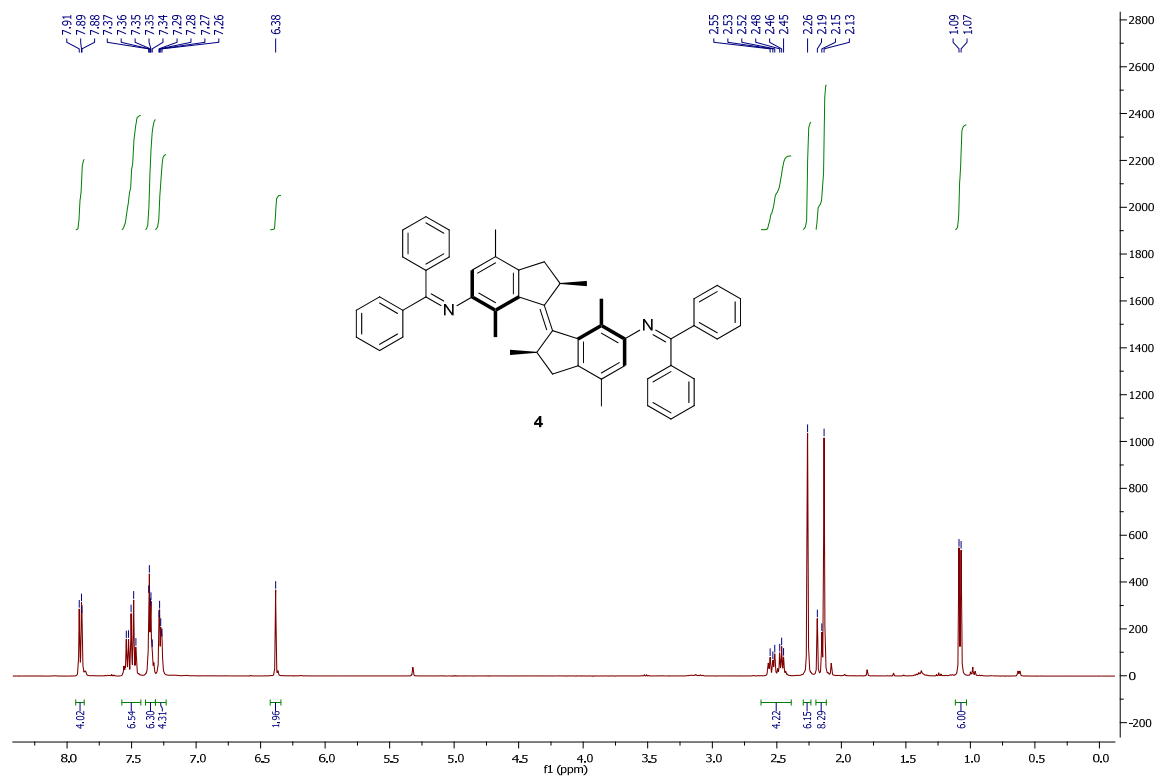
$[\alpha]_D^{20} = +134.5$  (c = 0.14 in CHCl<sub>3</sub>)

<sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 7.88-7.92 (m, 4H), 7.45-7.57 (m, 6H), 7.31-7.39 (m, 6H), 7.25-7.30 (m, 4H), 6.38 (s, 2H), 2.51-2.58 (m, 2H), 2.41-2.50 (m, 2H), 2.26 (s, 6H), 2.12-2.20 (m, 8H), 1.08 (d, J=6.4 Hz, 6H).

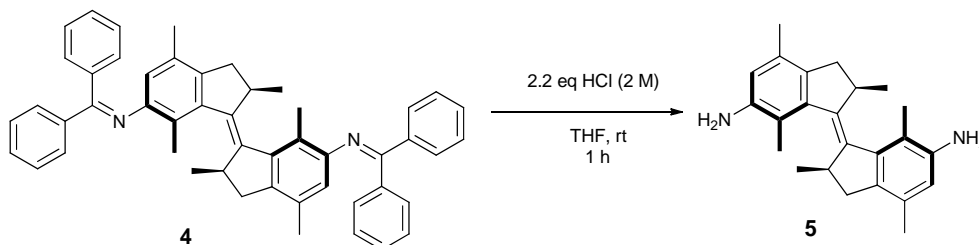
<sup>13</sup>C NMR (101 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ 167.54, 149.67, 142.27, 141.85, 140.22, 137.42, 137.00, 131.57, 130.84, 129.56, 129.40, 128.84, 128.50, 128.13, 121.56, 119.71, 42.10, 38.76, 19.33, 18.79, 18.43.

HRMS (APCI+, *m/z*): calculated for C<sub>50</sub>H<sub>47</sub>N<sub>2</sub> [M+H]<sup>+</sup>: 675.3734, found: 675.3474.

<sup>3</sup> Procedure adapted from G. Mann, J. F. Hartwig, M. S. Driver and C. Fernández-Rivas, *J. Am. Chem. Soc.*, 1998, **120**, 827.



**Compound 5 (2*R*,2'*R*,*E*) –(P,*P*) –2,2',4,4',7,7'-hexamethyl-2,2',3,3'-tetrahydro-[1,1'-bisindenylidene]-6,6'-diaminea<sup>4</sup>:**



Compound **4** (550 mg, 0.82 mmol) was dissolved in 2 mL of THF and 2 M HCl (aq) (0.90 mL, 1.80 mmol) was added via syringe to the solution. Upon addition a colour change from yellow to red-orange could be observed, followed by formation of a white precipitate. After 1 h the reaction was completed (followed by TLC pentane:Et<sub>2</sub>O=1:1, *R<sub>f</sub>*(**3**)=0.3). The reaction mixture was diluted with 20 mL of 0.5 M HCl (aq) and washed 3 times with 10 mL of diethyl ether. Subsequently the water layer was basified (pH>10) by addition of solid Na<sub>2</sub>CO<sub>3</sub> and the product was extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over MgSO<sub>4</sub> and evaporated under reduced pressure to yield product **5** as a white solid (256 mg, 0.74 mmol, Y=90%).

mp= 112- 114 °C.

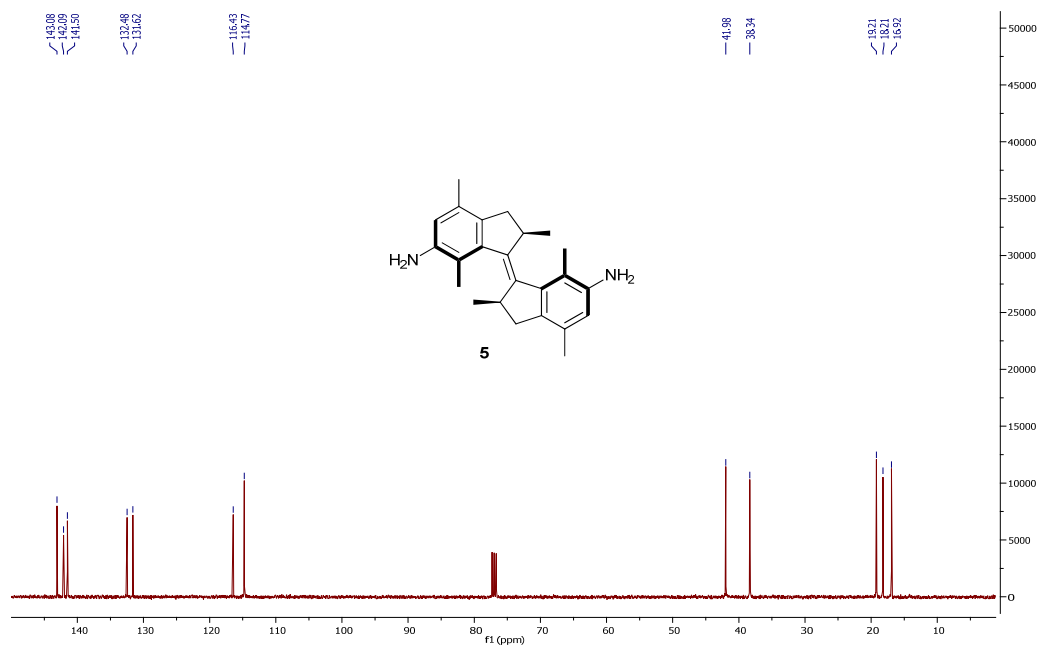
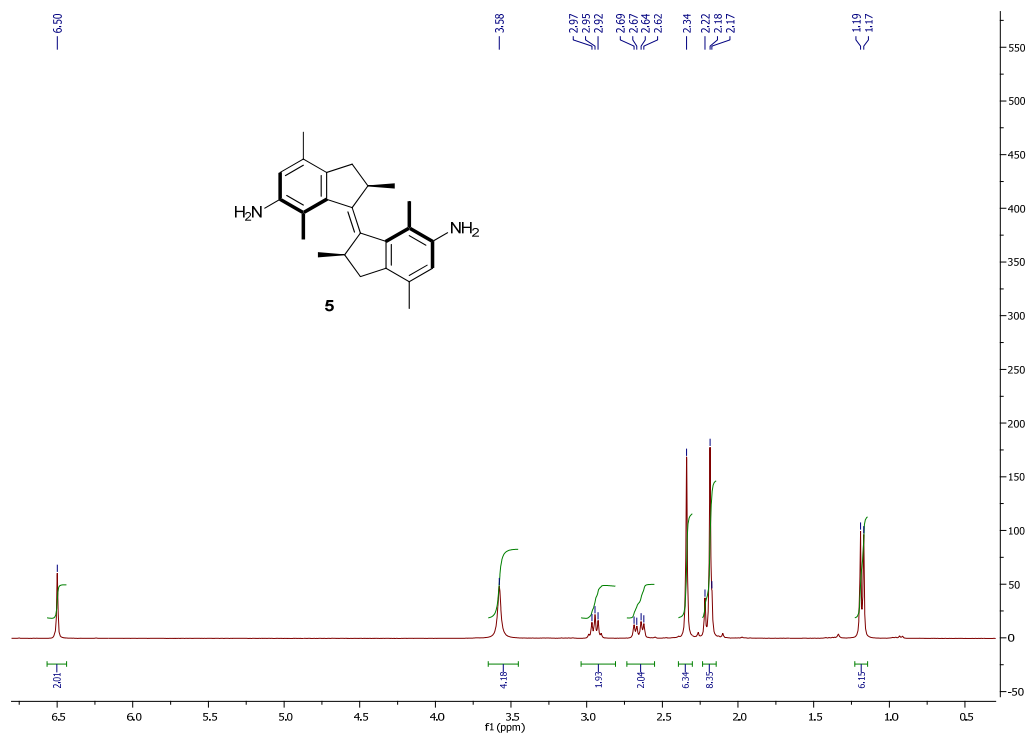
[ $\alpha$ ]<sub>D</sub><sup>20</sup> = - 221.3 (c = 0.15 in CHCl<sub>3</sub>).

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  6.50 (s, 2H), 3.58 (bs, 4H), 2.88-3.00 (m, 2H), 2.59-2.72 (m, 2H), 2.34 (s, 6H), 2.15-2.23 (m, 8H), 1.18 (d, *J*=6.4 Hz, 6H).

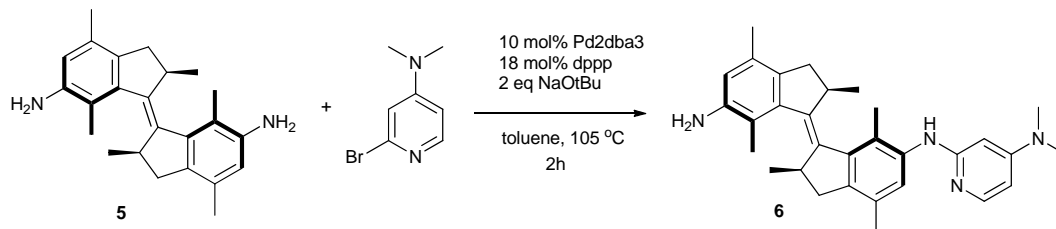
<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  143.08, 142.09, 141.50, 132.48, 131.62, 116.43, 114.77, 41.98, 38.34, 19.21, 18.21, 16.92.

HRMS (APCI+, *m/z*): calculated for C<sub>24</sub>H<sub>31</sub>N<sub>2</sub> [M+H]<sup>+</sup>: 347.2482, found: 347.2481.

<sup>4</sup> We have tried to obtain product **5** from **3** directly in one pot procedure via direct amination using copper catalyzed reaction with aqueous ammonia (*Chem. Commun.*, 2009, 3035-3037, *J. Org. Chem.* **2009**, 74, 4542–4546) but the maximum overall yield was 60%, therefore lower than the result of our 2 steps procedure.



**Compound 6** *N*<sup>2</sup>-((2*R*,2'*R*,*E*)-(P,P)-6'-amino-2,2',4,4',7,7'-hexamethyl-2,2',3,3'-tetrahydro-[1,1'-biindenylidene]-6-yl)-*N*<sup>4</sup>,*N*<sup>4</sup>-dimethylpyridine-2,4-diamine:<sup>5</sup>



2-Bromo-4-pyridyl(dimethyl)amine (182 mg, 0.91 mmol), compound **5** (314 mg, 0.91 mmol), Pd<sub>2</sub>dba<sub>3</sub> (83 mg, 0.09 mmol), 1,3-bis(diphenylphosphino)propane (74 mg, 0.17 mmol), and NaOtBu (168 mg, 1.8 mmol) were dissolved in 30 mL of dry toluene which was previously purged with argon. The mixture was heated at 105 °C under N<sub>2</sub> for 2h. Then the mixture was cooled down and filtered through celite. Subsequently the solvent was evaporated under vacuum. The residue was purified by silica gel column chromatography using ethyl acetate/triethylamine (100/3) as the eluent affording 157 mg (0.34 mmol, Y=37%) of **6** as a light yellow solid.

mp= 136-138 °C.

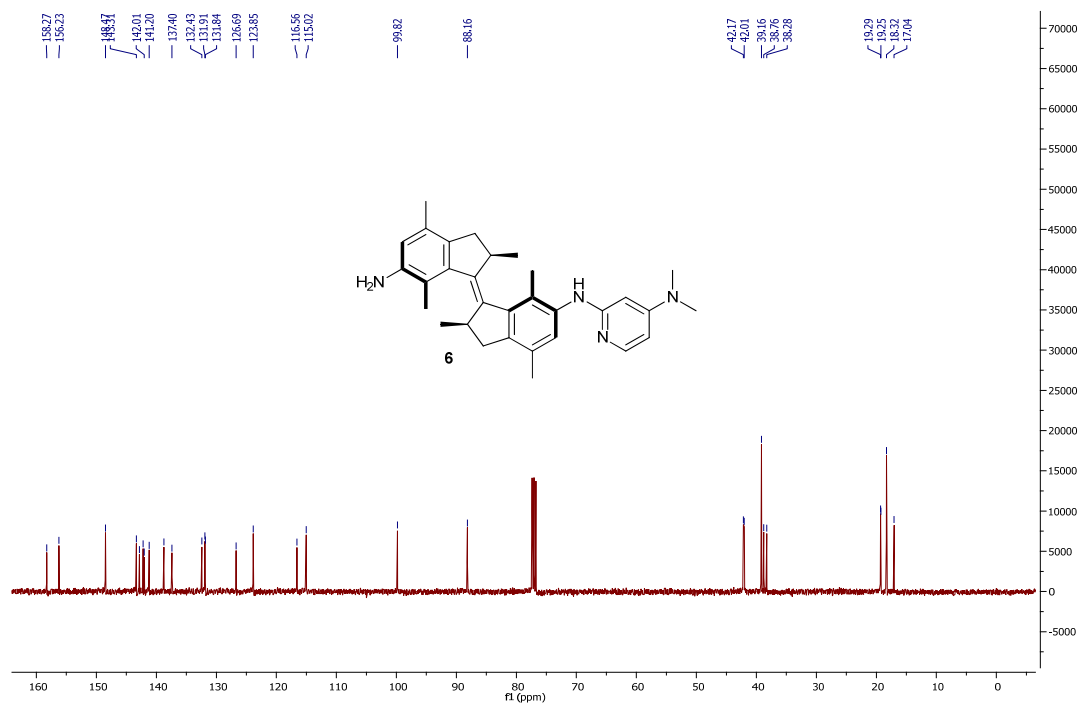
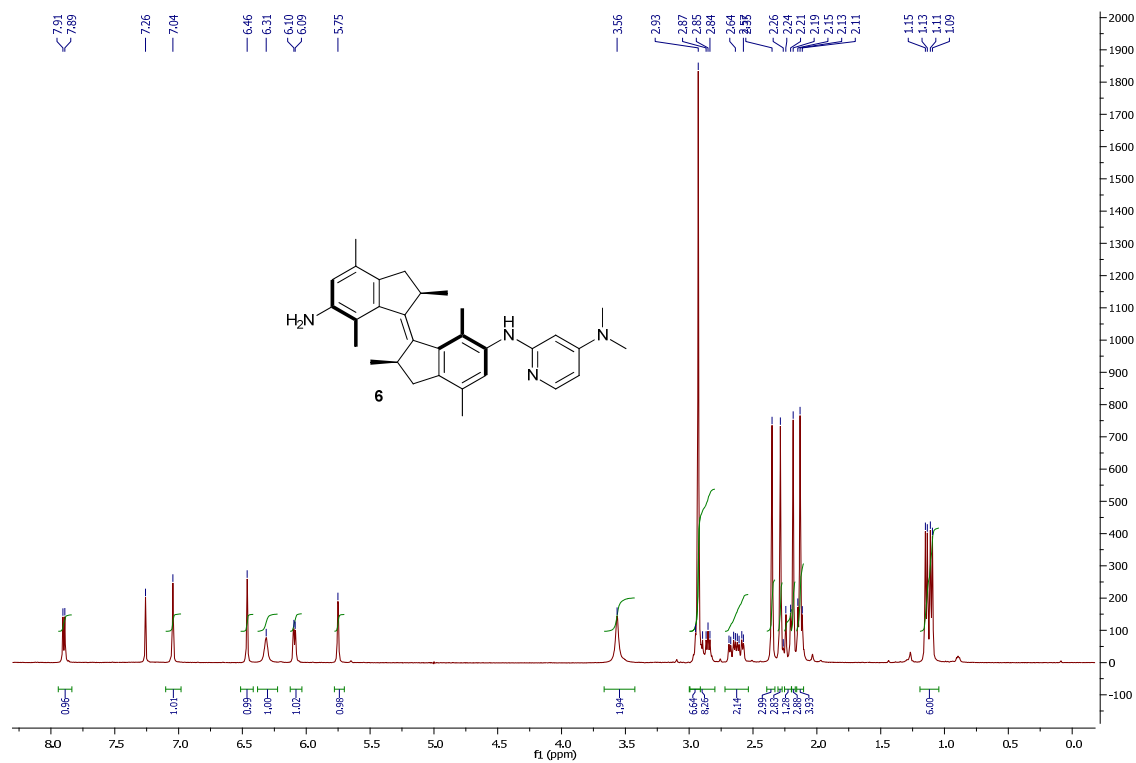
[α]<sub>D</sub><sup>20</sup> = - 164.7 (c = 0.14 in CHCl<sub>3</sub>).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 7.90 (d, *J*=6.0 Hz, 1H), 7.04 (s, 1H), 6.46 (s, 1H), 6.31 (bs, 1H), 6.10 (dd, *J*=6.0, 2.4 Hz, 1H), 5.75 (d, *J*=2.4 Hz, 1H), 3.56 (bs, 2H), 2.95 (s, 6H), 2.92-2.82 (m, 2H), 2.70-2.55 (m, 2H), 2.35 (s, 3H), 2.29 (s, 3H), 2.15 (s, 3H), 2.13 (s, 3H), 2.11-2.21 (m, 2H), 1.12 (d, *J*=6.4 Hz, 3H), 1.10 (d, *J*=6.4 Hz, 3H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 158.27, 156.23, 148.47, 143.31, 142.83, 142.20, 141.20, 138.74, 137.40, 132.43, 131.91, 131.84, 126.69, 123.85, 116.56, 115.02, 99.82, 88.16, 42.17, 42.01, 39.16, 38.76, 38.28, 19.29, 19.25, 18.32, 17.04.

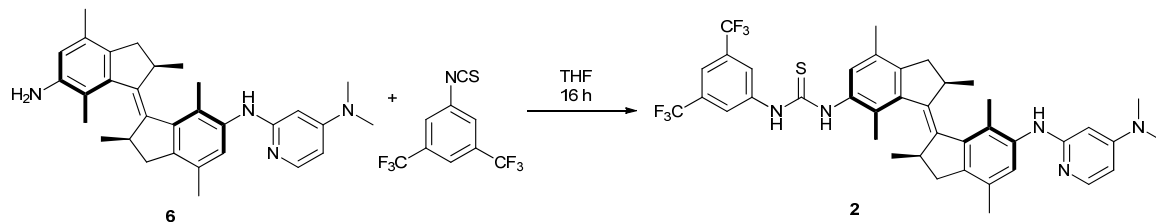
HRMS (APCI+, *m/z*): calculated for C<sub>31</sub>H<sub>39</sub>N<sub>4</sub> [M+H]<sup>+</sup>: 467.3169, found: 467.3183.

<sup>5</sup> Procedure adapted from C. Rabalakos and W. D. Wulff, *J. Am. Chem. Soc.*, 2008, **130**, 13524





**Compound 2 1-(3,5-bis(trifluoromethyl)phenyl)-3-((2*R*,2'*R*,*E*)-(P,P)-6'-((4-(dimethylamino)pyridin-2-yl)amino)-2,2',4,4',7,7'-hexamethyl-2,2',3,3'-tetrahydro-[1,1'-biindenylidene]-6-yl)thiourea:**



3,5-Bis(trifluoromethyl)phenyl isothiocyanate (68 mg, 0.25 mmol) was added dropwise to a solution of compound **6** (100 mg, 0.21 mmol) in 10 mL of dry THF which was cooled down to 0 °C . The reaction mixture was allowed to warm up to room temperature (20 °C) and stirred for 14 h. The solvent was then evaporated and the crude product purified by silica gel chromatography using first pentane/EtOAc/Et<sub>3</sub>N=50/50/3 as eluent and then increasing the polarity of the eluent to EtOAc/Et<sub>3</sub>N=100/3. Compound **2** (62 mg, 0.10 mmol, Y=40%) was isolated as a white solid.

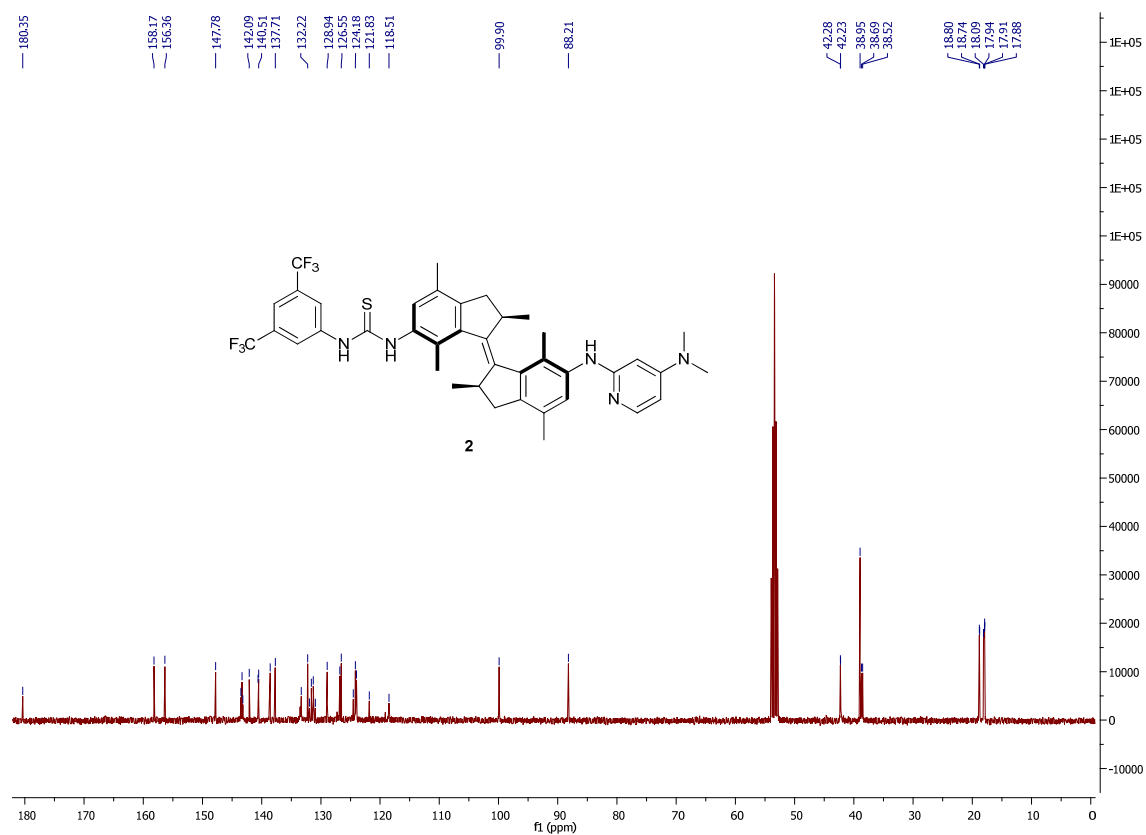
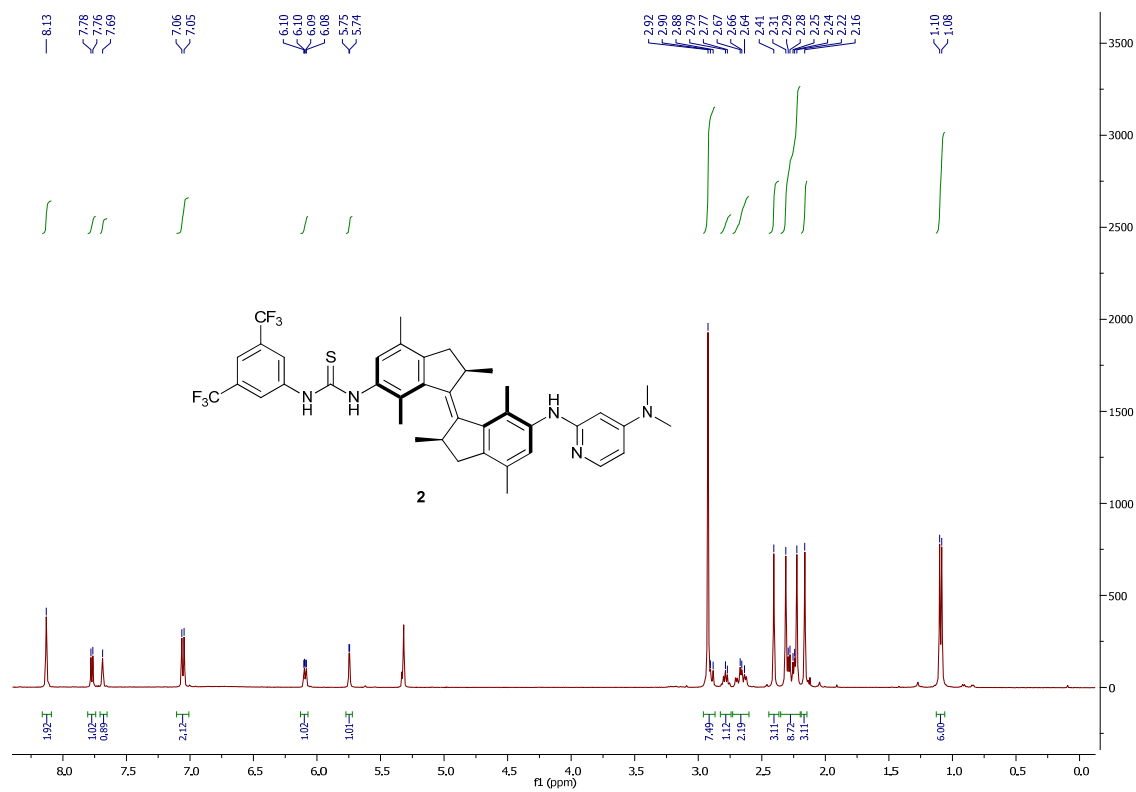
mp= 132-134 °C.

$[\alpha]_D^{20} = -59.0$  (c = 0.14 in CHCl<sub>3</sub>).

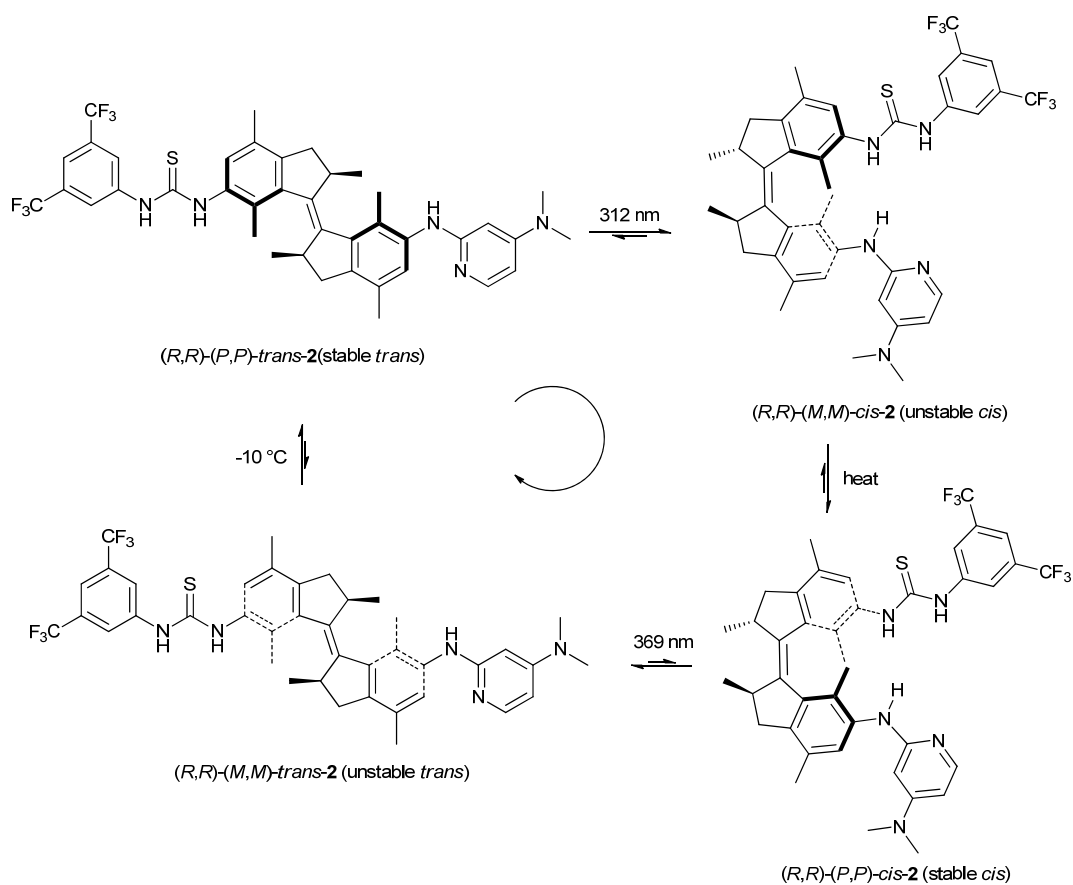
<sup>1</sup>H NMR (400 MHz, CD<sub>2</sub>Cl<sub>2</sub>)  $\delta$  8.13 (s, 2H), 7.77 (d, J=6.1 Hz, 1H), 7.69 (s, 1H), 7.07 – 7.04 (m, 2H), 6.09 (dd, J=6.0, 2.4 Hz, 1H), 5.75 (d, J=2.4 Hz, 1H), 2.95-2.87 (m, 7H), 2.74 – 2.82 (m, 1H), 2.61 - 2.72 (m, 2H), 2.41 (s, 3H), 2.33 – 2.21 (m, 2H), 2.31 (s, 3H), 2.22 (s, 3H), 2.16 (s, 3H), 1.09 (d, J = 6.4 Hz, 6H).

<sup>13</sup>C NMR (101 MHz, CD<sub>2</sub>Cl<sub>2</sub>)  $\delta$  180.35, 158.17, 156.36, 147.78, 143.50, 143.30, 143.17, 142.09, 140.51, 138.57, 137.71, 133.32, 132.22, 131.94, 131.61, 131.27, 130.94, 128.94, 126.80, 126.55, 124.54, 124.18, 123.99, 121.83, 118.51, 99.90, 88.21, 42.28, 42.23, 38.95, 38.69, 38.52, 18.80, 18.74, 18.09, 17.94, 17.91, 17.88.

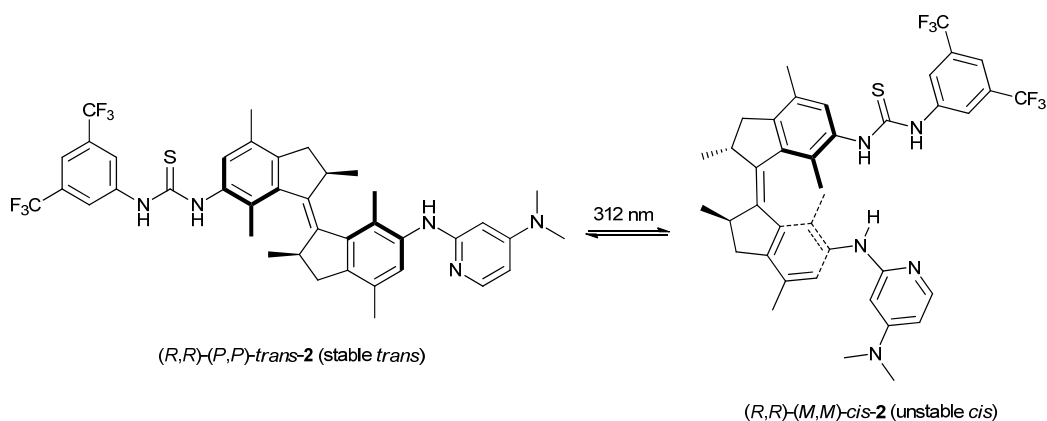
HRMS (APCI<sup>+</sup>, *m/z*): calculated for C<sub>40</sub>H<sub>42</sub>F<sub>6</sub>N<sub>5</sub>S [M+H]<sup>+</sup>: 738.3060, found: 738.3067.



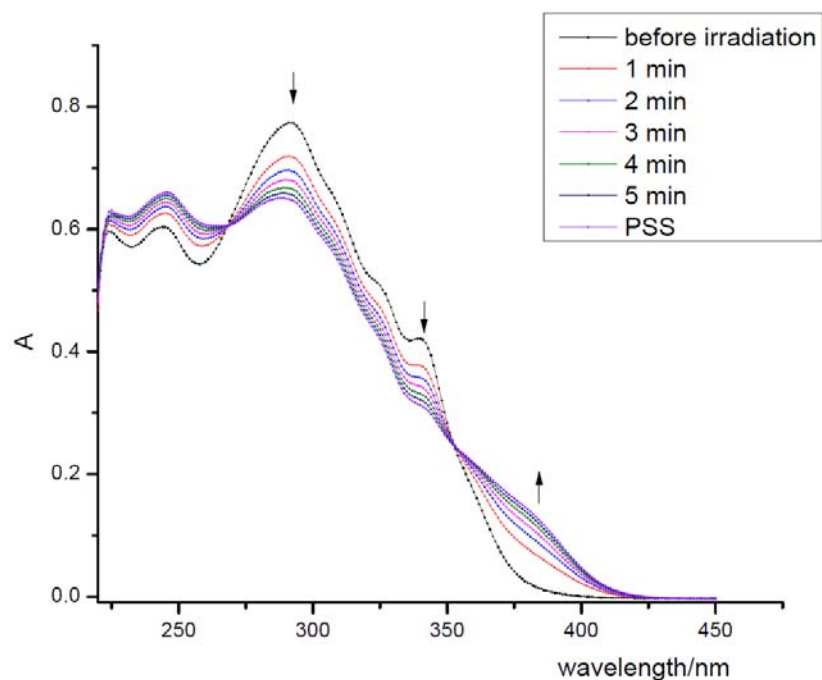
## 2) Studies of the unidirectional rotary cycle of the molecular motor based catalyst **2**:



a) UV/vis studies of the *(P,P)*-trans → *(M,M)*-cis transition upon irradiation at 312 nm.

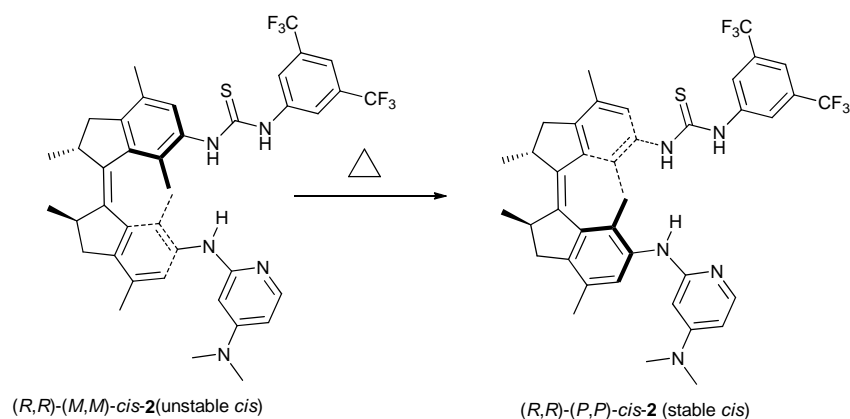


The photoisomerisation *(P,P)*-trans-**2** (stable *trans*) → *(M,M)*-cis-**2** (unstable *cis*) was followed by UV-VIS spectroscopy. A solution of *(R,R)*-*(P,P)*-trans-**2** in DCE ( $1.5 \times 10^{-5}$  M) was prepared. The changes of UV/vis absorption spectra upon photoirradiation at 312 nm were monitored (Figure S1), showing the expected red shift of the absorption of the species **2** along with the occurrence of the photoinduced isomerisation, as well as two isosbestic points at  $\lambda_1 = 275$  nm,  $\lambda_2 = 350$  nm (Figure S1).

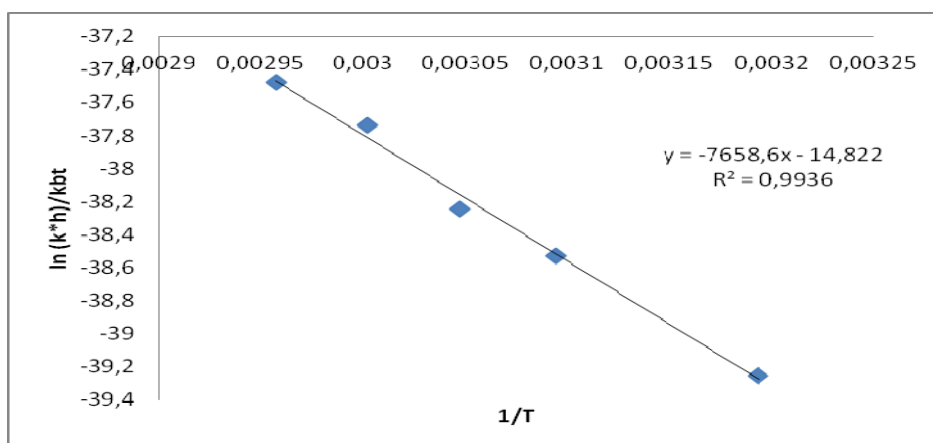


**Figure S1.** Irradiation of *trans*-motor catalyst **2** at 312 nm followed by UV/vis spectroscopy.

*b*) Thermal helix inversion (*M,M*)-*cis*  $\rightarrow$  (*P,P*)-*cis* in DCE and toluene.

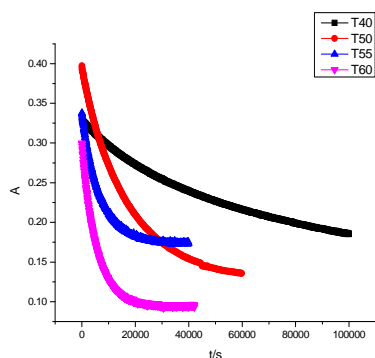


The thermal helix inversion of the unstable form of *cis*-**2** to the stable form of *cis*-**2** was followed by UV/vis spectroscopy over 5 temperatures (65, 60, 55, 50, 40 °C) in DCE (Figure S2) and over 4 temperatures (60, 55, 50, 40 °C) in toluene (Figure S3), delivering the kinetic data reported in the Figures below. Since the catalytic reactions have been made in toluene, it was decided to measure the half-life of the helix inversion transition also in this solvent. Remarkably, a significant difference has been observed between the half-lives in the above mentioned solvents (19.2 vs 149.5 h). Further investigation is in progress. Nevertheless, this study indicated that at least in toluene the half-life featured by the (*M,M*)-*cis*-**2** form is suitable for catalytic applications.

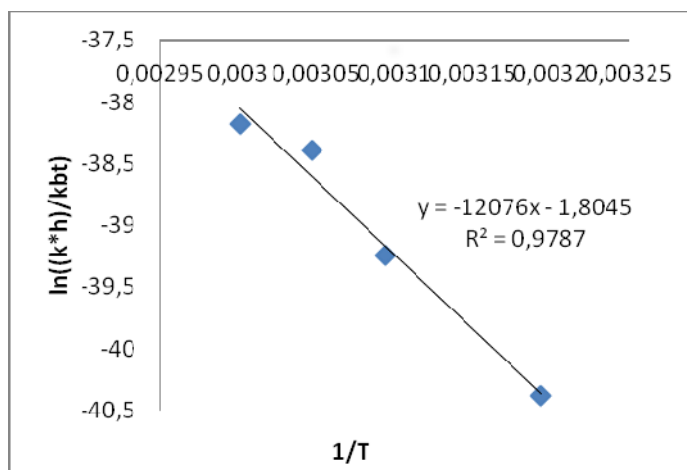


**Figure S2.** Kinetic study for the thermal isomerization from  $(2R,2'R)-(M,M)\text{-cis-2}$  in DCE, followed by absorption changes in the UV at 365 nm, at five different temperatures (65, 60, 55, 50, 40°C). The rate constants  $k$  of the first order decay at different temperatures were obtained using the equation  $A=A_0e^{-kT}$  ( $A$  and  $A_0$  are the absorbance at different time  $t$ ). By analysis of this data using the Eyring equation following data have been calculated:  $k^{20^\circ\text{C}}$  (s-1)=  $1.0 \times 10^{-5}$ ,  $t_{1/2}$ = 19.2 h,  $\Delta H^\ddagger$  = 63.9 kJ mol<sup>-1</sup>,  $\Delta G^\ddagger$  (20 °C) = 99.8 kJ mol<sup>-1</sup>,  $\Delta S^\ddagger$  = -122.6 J K<sup>-1</sup> mol<sup>-1</sup>.

A



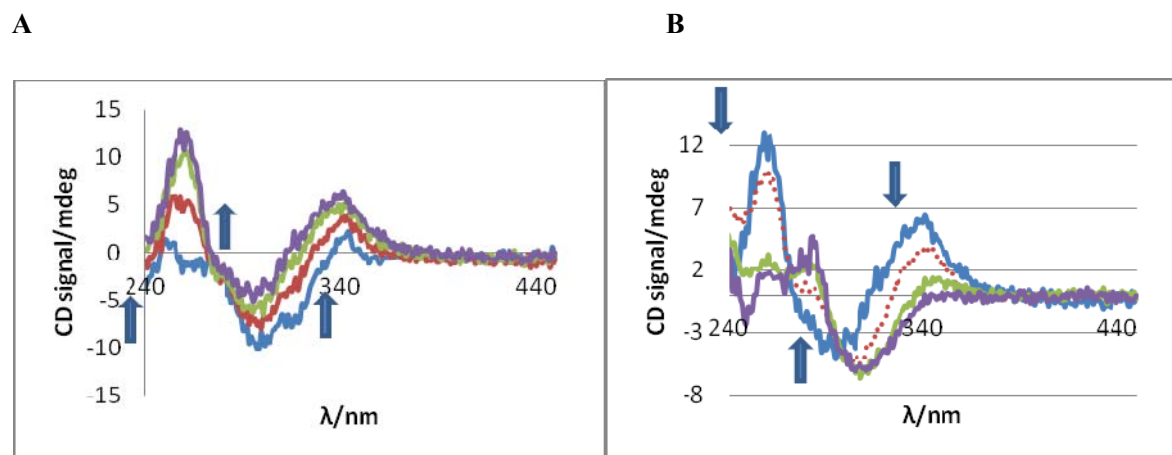
B



**Figure S3** Kinetic study for the thermal isomerization from  $(2R,2'R)-(M,M)\text{-cis-2}$  in toluene was followed by absorption changes at 365 nm at five different temperatures (65, 60, 55, 50, 40, °C). The rate constants  $k$  of the first order decay at different temperatures were obtained using the equation  $A=A_0e^{-kT}$  ( $A$  and  $A_0$  are the absorbance at different time  $t$ ). By analysis of this data using the Eyring equation following data have been calculated  $k^{20^\circ\text{C}}$  (s-1)=  $1.3 \cdot 10^{-6}$ ,  $t_{1/2}$ = 149.5 h at 20 °C,  $\Delta H^\ddagger$  = 110.5kJmol<sup>-1</sup>,  $\Delta S^\ddagger$  = 16.7 J K<sup>-1</sup> mol<sup>-1</sup>,  $\Delta G^\ddagger$  (20 °C) = 105.6 kJ mol<sup>-1</sup>.

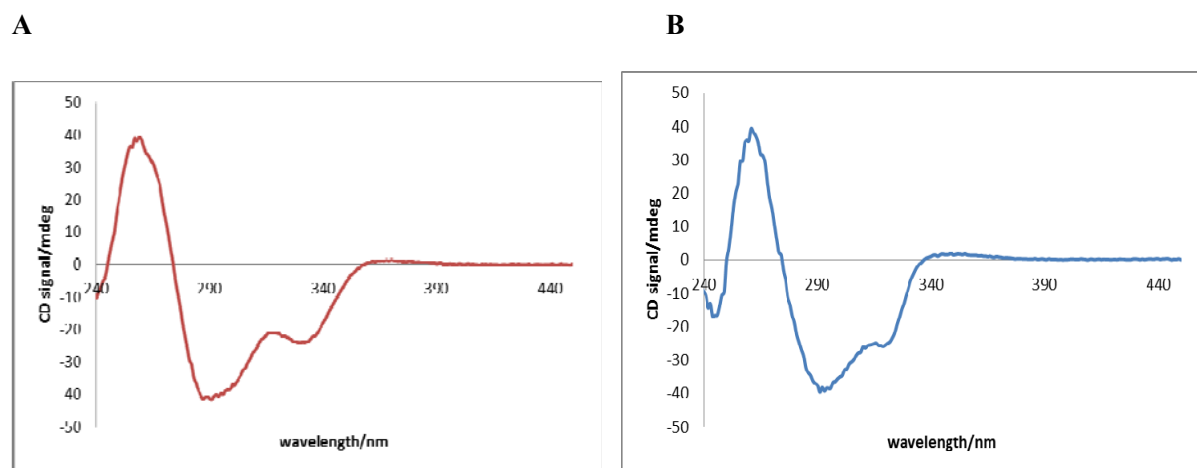
c) CD studies of the  $(P,P)$ -*trans*  $\rightarrow$   $(M,M)$ -*cis* transition upon irradiation at 312 nm, and of the thermal helix inversion  $(M,M)$ -*cis*  $\rightarrow$   $(P,P)$ -*cis*.

During both transitions, there is an inversion of the helicity of the molecule, which can be observed by following these transitions with CD spectroscopy (Figure S4).



**Figure S4.** CD spectral changes of compound **2** ( $1.5 \times 10^{-5}$  M) upon irradiation of  $(R,R)$ -( $P,P$ )-*trans*-**2** at 312 nm in DCE (A) CD spectral changes during thermal helix inversion ( $(R,R)$ -( $M,M$ )-*cis*-**2**  $\rightarrow$   $(R,R)$ -( $P,P$ )-*cis*-**2** on heating in DCE at 60 °C.

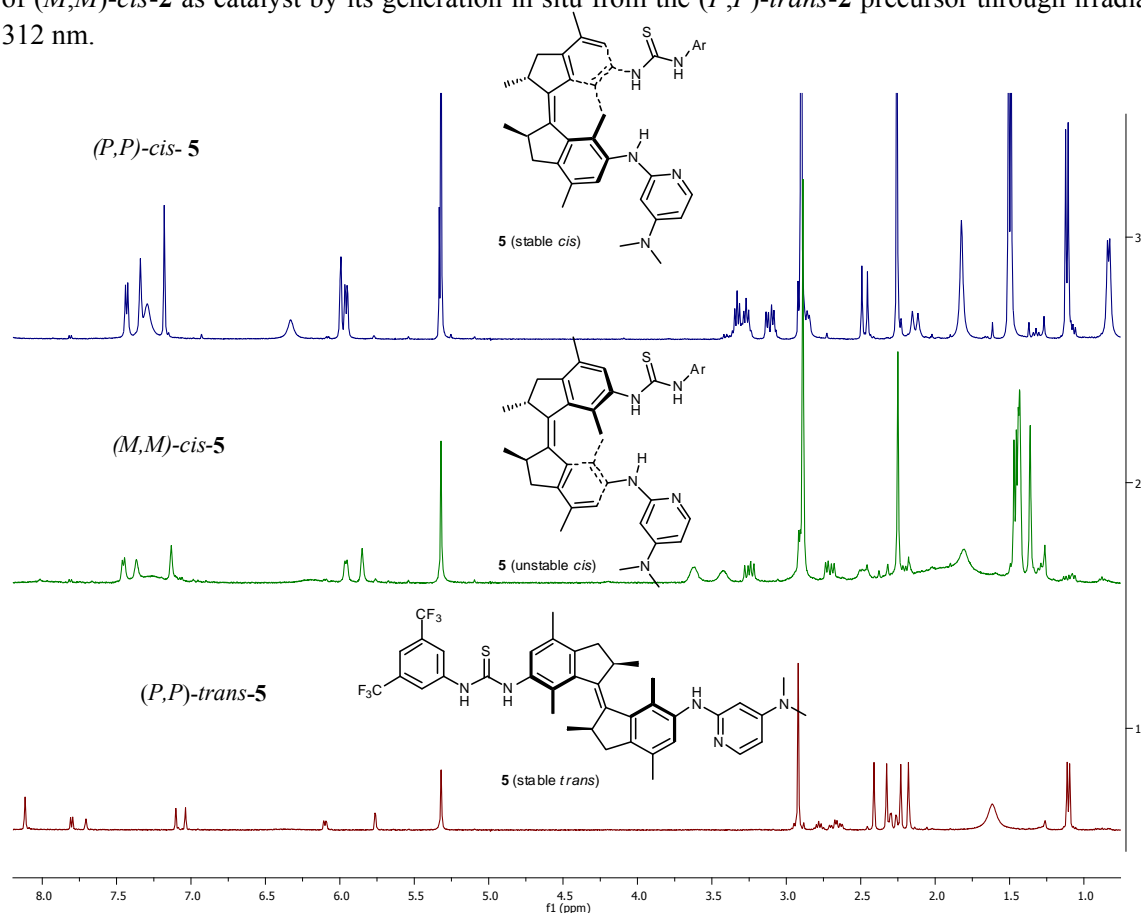
d) CD of the  $(P,P)$ -*trans* **2** at room temperature in different solvents used to prove the rotary cycle of the motor **2**



**Figure S5** CD spectra of compound **2** ( $4 \times 10^{-5}$  M) in (A) DCM and (B) DCE

e) Determination of the photostationary state (PSS) in the photoisomerisation  $(P,P)\text{-trans} \rightarrow (M,M)\text{-cis}$  through  $^1\text{H}$  NMR spectroscopy and NMR study of the thermal helix inversion  $(M,M)\text{-cis} \rightarrow (P,P)\text{-cis}$ .

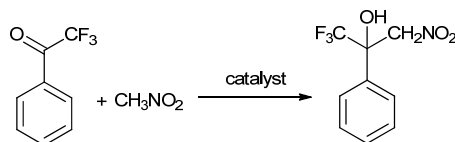
By irradiating a solution of  $(P,P)\text{-trans-2}$  in  $\text{CD}_2\text{Cl}_2$  and by following the photoisomerisation by  $^1\text{H}$  NMR spectroscopy (Figure S5), it was possible to determine accurately the PSS for this isomerisation, which was found to be 92:8 in favour of the  $(M,M)\text{-cis}$  form. Such a high PSS is thus suitable for the utilisation of  $(M,M)\text{-cis-2}$  as catalyst by its generation in situ from the  $(P,P)\text{-trans-2}$  precursor through irradiation at 312 nm.



**Figure S6** NMR changes during irradiation changes upon irradiation of  $(R,R)\text{-}(P,P)\text{-trans-2}$  at 312 nm in DCM and during thermal helix inversion  $((R,R)\text{-}(M,M)\text{-cis-2} \rightarrow (R,R)\text{-}(P,P)\text{-cis-2})$  on heating.

### 3) Catalytic enantioselective Henry reaction with the dynamic catalyst **2**:

**Table S1: Optimising conditions for the Henry reaction using (*M,M*)-*cis* : (*P,P*)-*trans* mixture at PSS (92:8)**



Catalyst loading (%mol)	Solvent (M)	t/°C	t/h	Conversion	e.r.
10	Toluene (1.0)	-25	8	full	86:14
5	Toluene (1.0)	-25	8	full	86:14
2	Toluene (1.0)	-25	16	85%	85:15
5	Toluene (1.0)	-50	8	85%	86:14
5	THF (1.0)	-25	8	full	83:17
5	DCM (1.0)	-25	8	80%	82:18
5	TBME (1.0)	-25	8	full	86:14
5	Toluene(0.001)	-25	24	90%	86:14

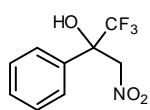
#### General procedure for the catalytic reactions:

Into a vial equipped with a magnetic stirring bar catalyst **2** (0.01 mmol, 7.4 mg, (*P,P*)-*trans*, or (*M,M*)-*cis* : (*P,P*)-*trans* mixture at PSS (92:8), or (*P,P*)-*cis*) was added and dissolved in toluene (0.10 mL). Nitromethane (10 equivalents, 120  $\mu\text{L}$ ) was added and the reaction mixture was cooled down to -25 °C. Subsequently, a solution of a trifluoroketone acceptor (0.2 mmol in 0.10 mL of toluene) was added. The mixture was stirred at the same temperature, and the reaction progress was monitored by TLC. After completion, the mixture was purified directly by column chromatography (diethyl ether:pentane=8:2). The analytical data of the obtained Henry adducts **7a-e** are in agreement with published values.<sup>6</sup> The major enantiomers of the obtained products **7** was determined by comparing the HPLC elution order with the literature values<sup>6</sup> (as the same CSP and similar eluent mixtures were employed). (*M,M*)-*cis*-**2** : (*P,P*)-*trans*-**2** PSS mixture as catalyst was found to favour the formation of the R enantiomers of products **7**, whereas (*P,P*)-*cis*-**2** as catalyst gave predominantly the S enantiomers.

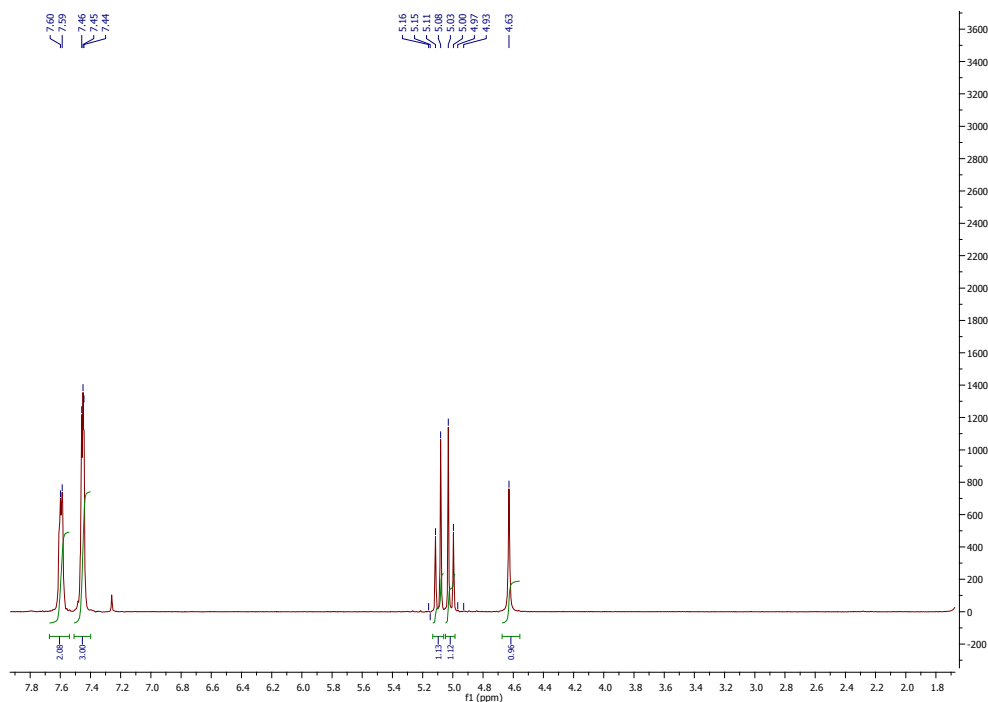
<sup>6</sup> (a) F. Tur and J. M. Saá, *Org. Lett.*, 2007, **9**, 5079-5082; (b) M. Bandini, M. Sinisi and A. Umani-Ronchi, *Chem. Commun.*, 2008, 4360-4362; (c) C. Palacio and S. Connon, *Org. Lett.*, 2011, **13**, 1298-1301.



### 1,1,1-Trifluoro-3-nitro-2-phenylpropan-2-ol (**7a**)



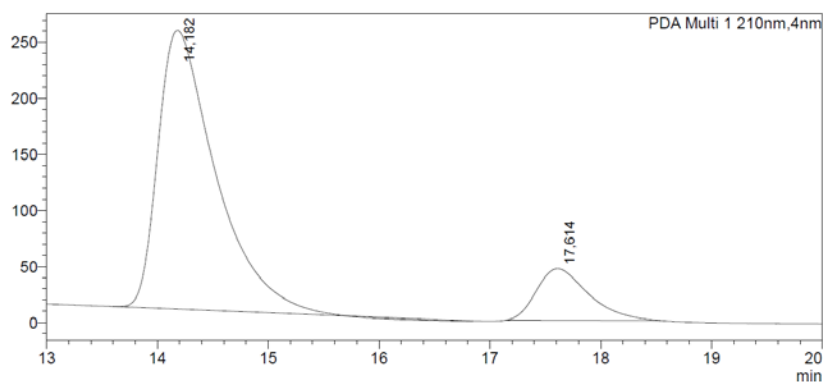
Following the general procedure the title compound was obtained as a white wax in 92% yield and 86:14 er favoring the R enantiomer using (*M,M*)-*cis*-**2** : (*P,P*)-*trans*-**2** PSS mixture (92:8) as catalyst, and in 93% yield and 79:21 er favouring the S enantiomer using (*P,P*)-*cis*-**2** as catalyst. HPLC analysis: OD-H column (210 nm), 40 °C , 0.5 mL/min method: heptane/IPA=80/20,  $t_1$ =14.2 min,  $t_2$ = 17.7 min.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.56-7.63 (m, 2H), 7.42-7.48 (m, 3H), 5.10 (d,  $J$ =13.8 Hz, 1H) , 5.01(d,  $J$ =13.8 Hz, 1H), 4.63 (s, 1H).



HPLC analysis of **7a** obtained with (*M,M*)-*cis*-**2** : (*P,P*)-*trans*-**2** PSS mixture (92:8) as catalyst:

#### <Chromatogram>

mAU



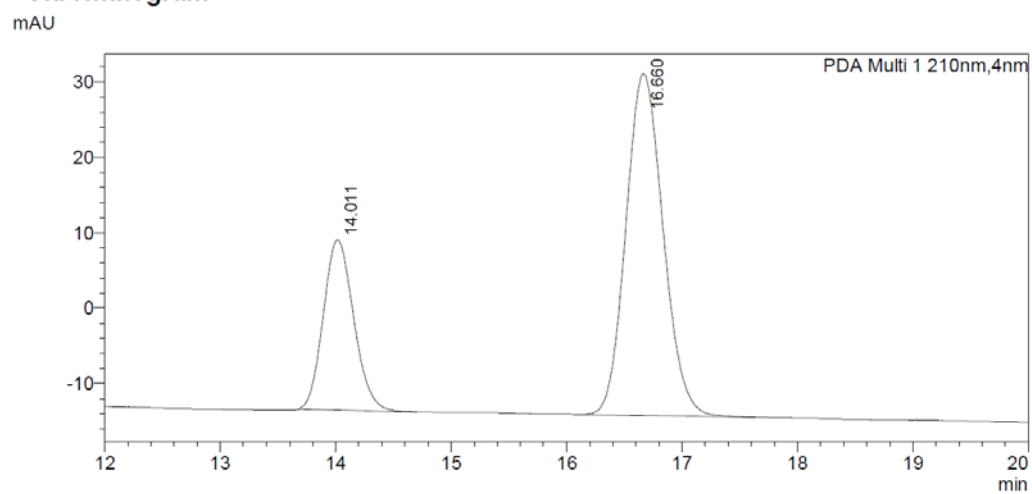
#### <Peak Table>

PDA Ch1 210nm

Peak#	Ret. Time	Area	Height	Area%
1	14.182	8980027	248681	85.632
2	17.614	1506730	46212	14.368
Total		10486757	294893	100.000

HPLC analysis of **7a** obtained with (*P,P*)-**2** as catalyst:

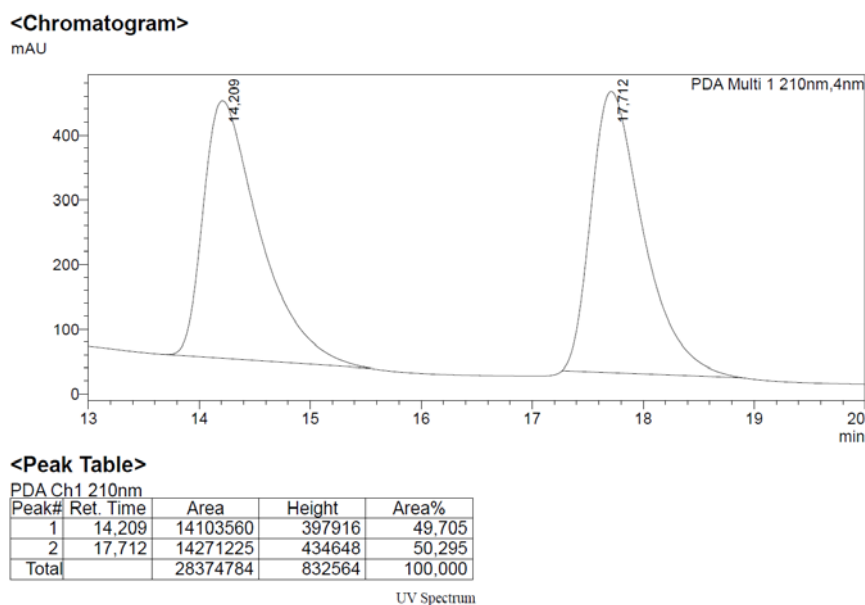
<Chromatogram>



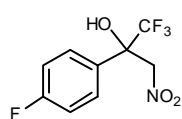
<Peak Table>

PDA Ch1 210nm				
Peak#	Ret. Time	Area	Height	Area%
1	14.011	413960	22617	28.927
2	16.660	1017103	45313	71.073
Total		1431063	67930	100.000

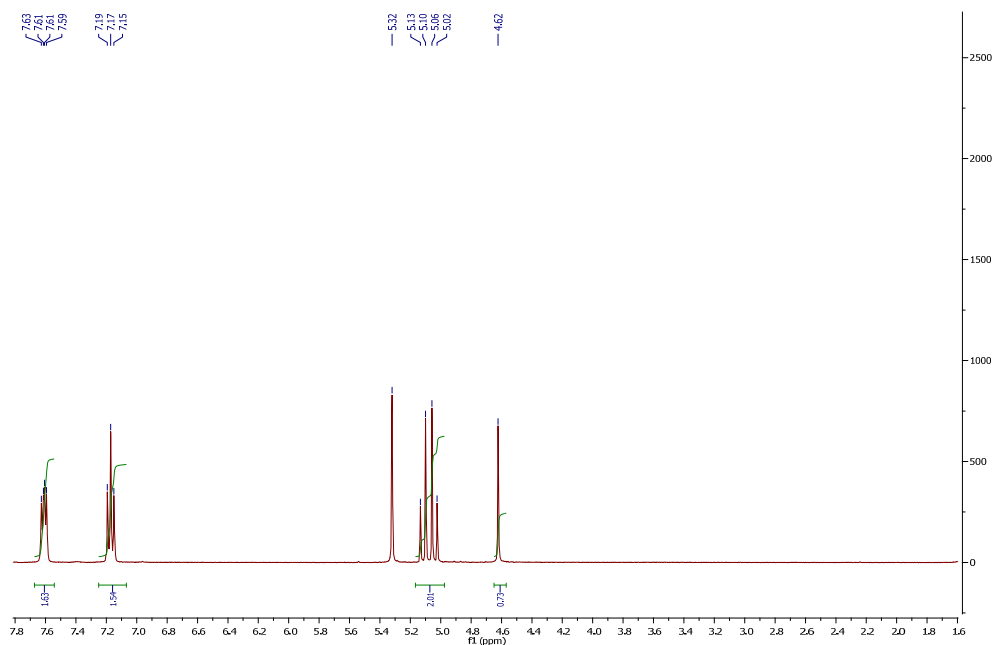
HPLC analysis of **7a** obtained with (*P,P*)-**trans-2** as catalyst:



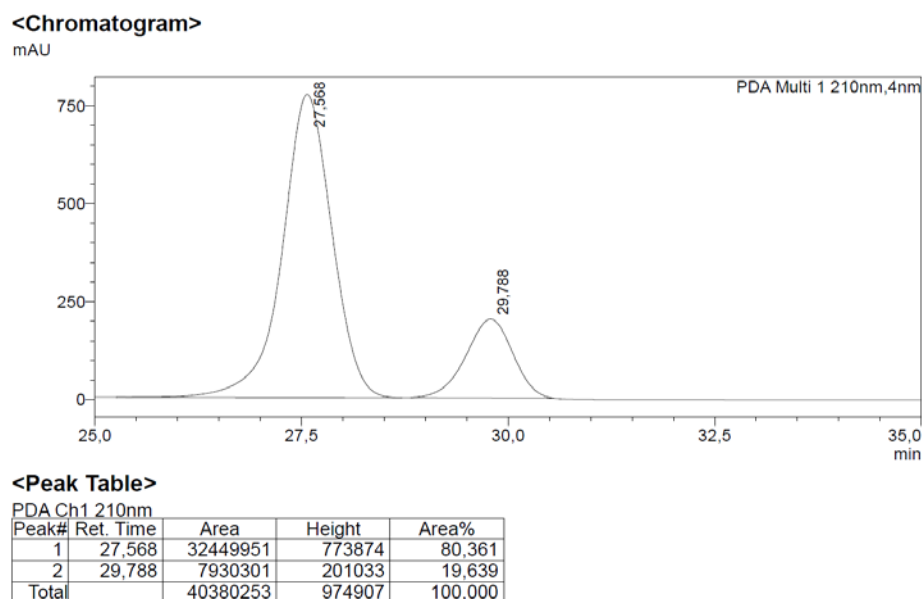
### 1,1,1-Trifluoro-2-(4-fluorophenyl)-3-nitropropan-2-ol (**7b**)



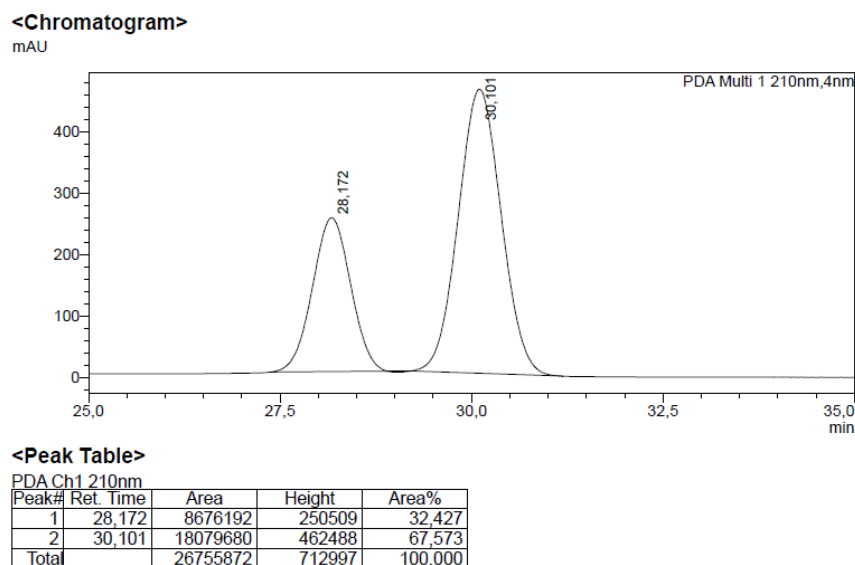
Following the general procedure the title compound was obtained as a pale yellow oil in 90% yield and 80:20 er favoring the R enantiomer using (*M,M*)-*cis-2* : (*P,P*)-*trans-2* mixture at PSS (92:8) as catalyst. HPLC analysis: OJ-H ,40 °C , 0.5 mL/min, heptane/IPA=90/10,  $t_1$ =27.6 min,  $t_2$ = 29.8 min.  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_2\text{Cl}_2$ ) 7.61 (dd,  $J$  = 8.5, 5.3, 2H), 7.17 (t,  $J$  = 8.6, 2H), 5.12 (d,  $J$  = 13.7, 1H), 5.04 (d,  $J$  = 13.7, 1H), 4.62 (s, 1H).



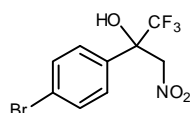
HPLC analysis of **7b** obtained with (*M,M*)-*cis*-**2** : (*P,P*)-*trans*-**2** PSS mixture (92:8) as catalyst:



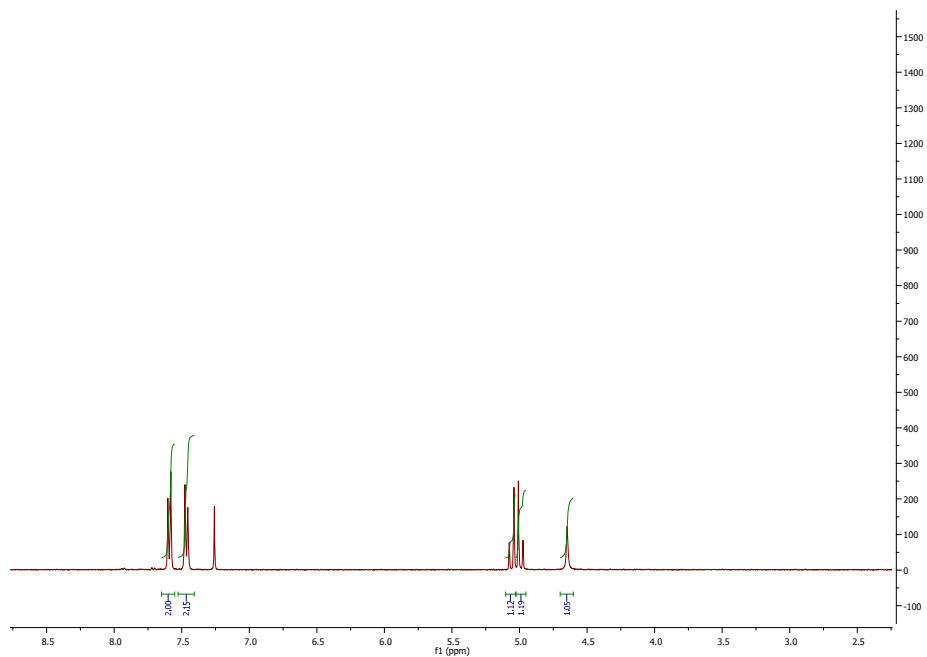
HPLC analysis of **7b** obtained with (*P,P*)-*cis*-**2** as catalyst



### 2-(4-Bromophenyl)-1,1,1-trifluoro-3-nitropropan-2-ol (**7c**)

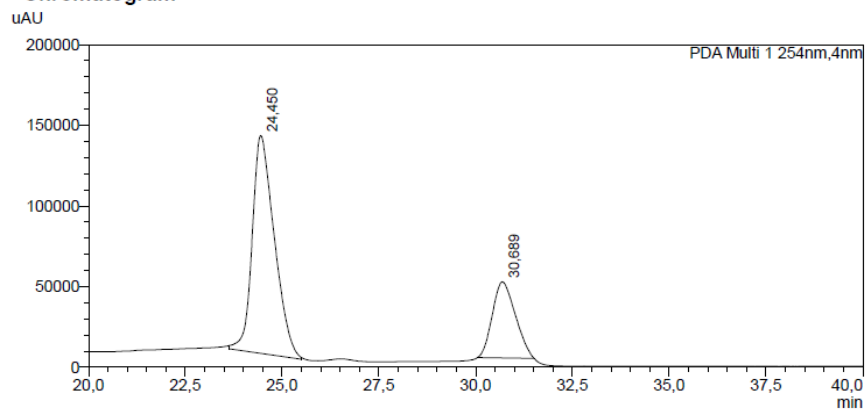


Following the general procedure the title compound was obtained as a pale yellow oil in 90% yield and 73:27 er favoring the R enantiomer using (*M,M*)-*cis*-**2** : (*P,P*)-*trans*-**2** mixture at PSS (92:8) as catalyst, and in 90% yield and 57:43 er favouring the S enantiomer using (*P,P*)-*cis*-**2** as catalyst. HPLC analysis: OJ-H ,40 °C , 0.5 mL/min, heptane/IPA=90/10,  $t_1$ =24.4 min,  $t_2$ = 30.7 min;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.59 (d,  $J$ =8.7 Hz, 1H), 7.47 (d,  $J$ =8.5 Hz, 1H), 5.02 (q,  $J$ =13.7 Hz, 1H), 4.65 (s, 1H).



HPLC analysis of **7c** obtained with (*M,M*)-*cis*-**2** : (*P,P*)-*trans*-**2** PSS mixture (92:8) as catalyst:

<Chromatogram>

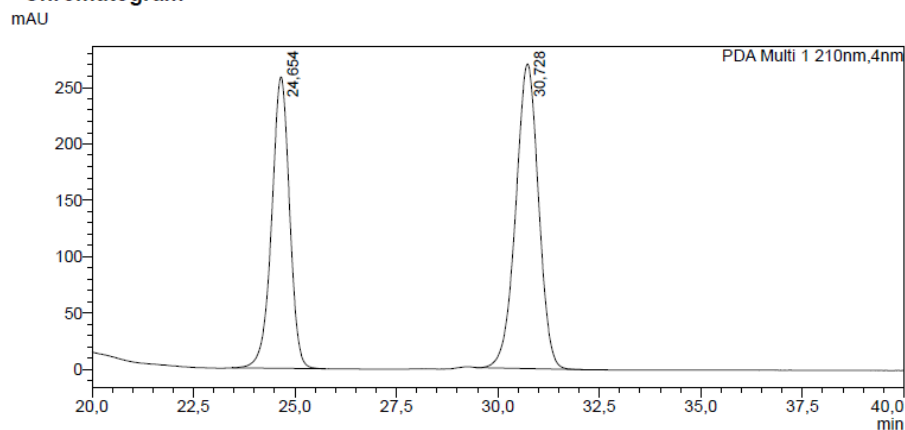


<Peak Table>

PDA Ch1 254nm				
Peak#	Ret. Time	Area	Height	Area%
1	24,450	5364864	134945	73,403
2	30,689	1943948	47152	26,597
Total		7308812	182096	100,000

HPLC analysis of **7c** obtained with (*P,P*)-**cis-2** as catalyst

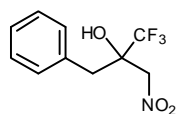
<Chromatogram>



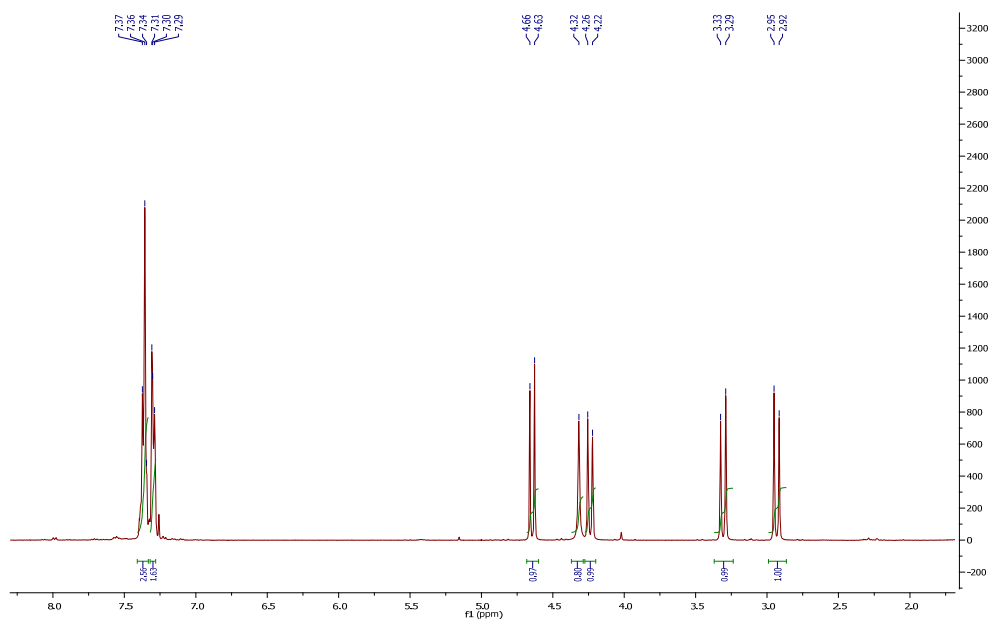
<Peak Table>

Peak#	Ret. Time	Area	Height	Area%
1	24,654	7917246	258239	42,829
2	30,728	10568344	269822	57,171
Total		18485591	528062	100,000

**2-Benzyl-1,1,1-trifluoro-3-nitropropan-2-ol (7d)**

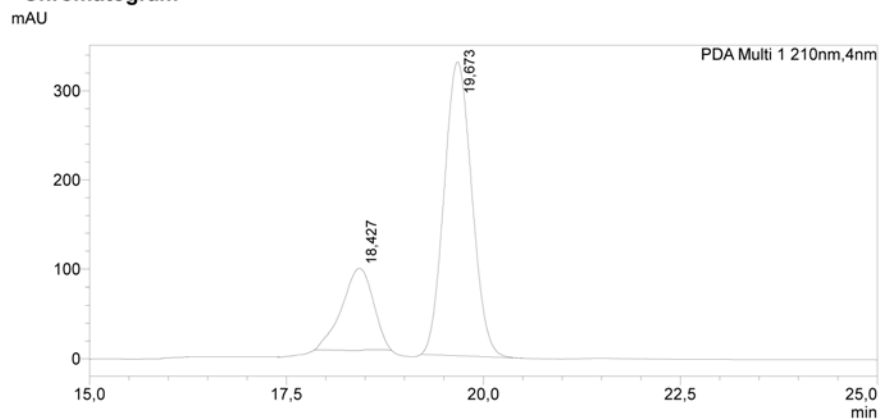


Following the general procedure the title compound was obtained as a pale yellow oil in 80% yield and 78:22 er favoring the R enantiomer using (*M,M*)-**cis-2** : (*P,P*)-**trans-2** mixture at PSS (92:8) as catalyst, and in 80% yield and 70:30 er favouring the S enantiomer using (*P,P*)-**cis-2** as catalyst. HPLC analysis: OJ-H (210 nm), 40 °C , 0.5 mL/min, heptane/IPA=90/10,  $t_1$ =18.4 min,  $t_2$ = 19.7 min.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.33-7.40 (m, 3H), 7.27-7.32 (m, 2H) , 4.64 (d,  $J$ =13.2 Hz, 1 H), 4.32 (s, 1H), 4.24 (d,  $J$ =13.2 Hz, 1H), 3.31(d,  $J$ =14.4 Hz, 1 H), 2.93 (d,  $J$ =14.4 Hz, 1H).



HPLC analysis of **7d** obtained with (*M,M*)-**cis-2** : (*P,P*)-**trans-2** PSS mixture (92:8) as catalyst:

<Chromatogram>

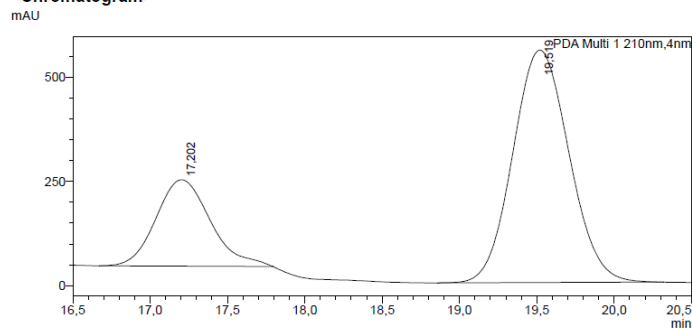


<Peak Table>

Peak#	Ret. Time	Area	Height	Area%
1	18.427	2309072	87277	22.274
2	19.673	8057655	328883	77.726
Total		10366727	416160	100.000

HPLC analysis of **7d** obtained with (*P,P*)-**cis-2** as catalyst

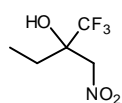
<Chromatogram>



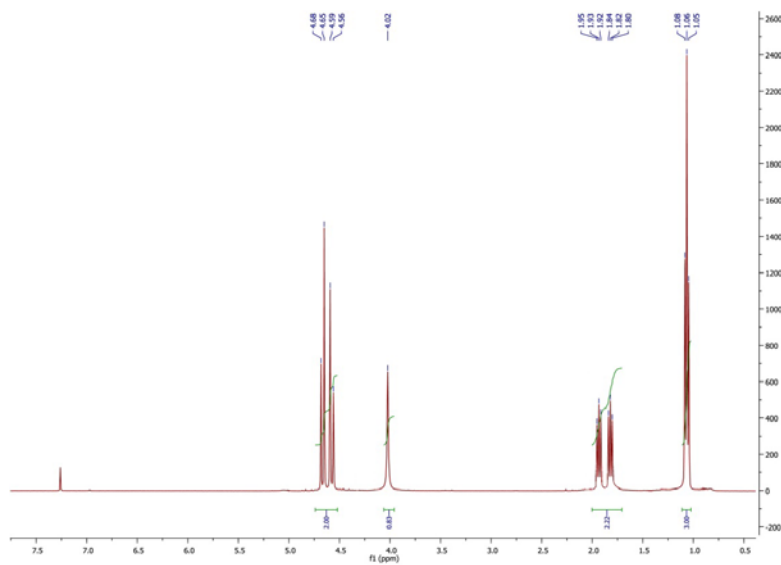
<Peak Table>

Peak#	Ret. Time	Area	Height	Area%
1	17.202	5059235	206996	26.429
2	19.519	14083160	557248	73.571
Total		19142394	764244	100.000

### 1,1,1-Trifluoro-2-(nitromethyl)butan-2-ol (**7e**)

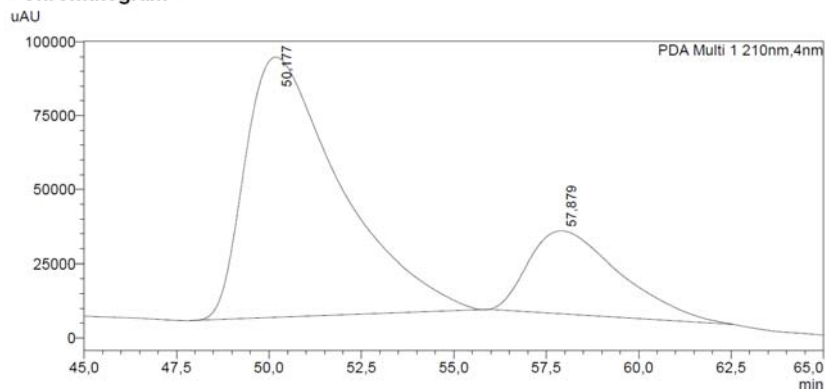


Following the general procedure the title compound was obtained as a pale yellow oil in 72% yield and 77:23 er favoring the R enantiomer using (*M,M*)-*cis*-**2** : (*P,P*)-*trans*-**2** mixture at PSS (92:8) as catalyst, and in 72% yield and 59:41 er favouring the S enantiomer using (*P,P*)-*cis*-**5** as catalyst. HPLC analysis OD-H, 40 °C , 0.5 mL/min, heptane/IPA=99/1,  $t_1$ =50.2 min,  $t_2$ = 57.9 min.  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.67 (d,  $J$ =13.6 Hz, 1H), 4.57 (d,  $J$ =13.6 Hz, 1H), 4.02 (s, 1H), 1.77-1.97 (m, 2H), 1.06 (t, 3H).



HPLC analysis of **7d** obtained with (*M,M*)-*cis*-**5** : (*P,P*)-*trans*-**2** PSS mixture (92:8) as catalyst:

#### <Chromatogram>



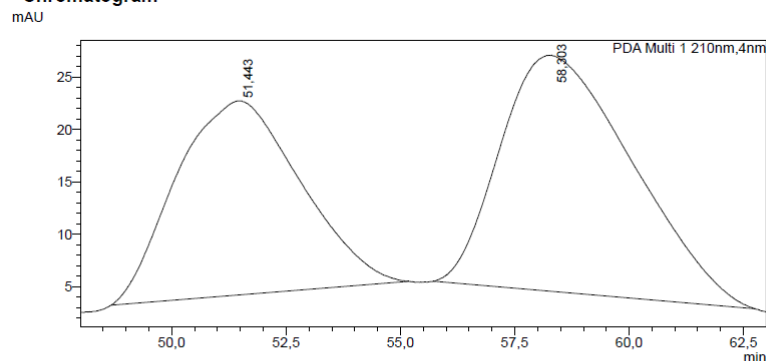
#### <Peak Table>

PDA Ch1 210nm				
Peak#	Ret. Time	Area	Height	Area%
1	50.177	15769153	87980	76.583
2	57.879	4821728	27880	23.417
Total		20590881	115860	100.000



HPLC analysis of **6e** obtained with (*P,P*)-**5** as catalyst

<Chromatogram>



<Peak Table>

PDA Ch1 210nm				
Peak#	Ret. Time	Area	Height	Area%
1	51.443	3499915	18514	43.630
2	58.303	4521825	22526	56.370
Total		8021740	41040	100.000

### X-ray crystallography

Crystals of compound **2** (CCDC 966782) could reproducibly be obtained by slow evaporation of a THF solution, but X-ray analysis of these crystals was thwarted by facile loss of co-crystallized THF from the lattice. Attempts to obtain crystalline material from different solvents failed, and thus we resorted to analysis of the crystals from THF. ‘Crystals’ of several batches were tested only to give low quality diffraction images, likely related to loss of THF from the lattice and its collapse. Ultimately, a small platelet was found that gave a sharp (but weak) diffraction pattern and this was used for the crystal structure determination using Cu K $\alpha$  (1.54178 Å) radiation. The crystal was mounted on top of a cryoloop and transferred into the cold nitrogen stream (100 K) of a Bruker-AXS D8 Venture diffractometer. Data collection and reduction was done using the Bruker software suite APEX2.<sup>7</sup> The final unit cell was obtained from the xyz centroids of 9916 reflections after integration. A multiscan absorption correction was applied, based on the intensities of symmetry-related reflections measured at different angular settings (SADABS).<sup>7</sup> The structure was solved by direct methods using SHELXS.<sup>8</sup> From subsequent refinement of the structure (SHELXL)<sup>9</sup> it was clear that one of the CF<sub>3</sub> groups was highly disordered; the density could be described by two disorder components (major fraction 56%) with restrain instructions for the C-F bond lengths applied (DFIX). All non-hydrogen atoms were refined with anisotropic displacement parameters, and hydrogen atoms were included riding on their carrier atoms. Due to the weak scattering power of the crystal, a few atoms refined to non-positive definite anisotropic displacement parameters. Ultimately, the data was cut off at 1 Å resolution and SIMU/DELU instructions were applied in the refinement. The absolute structure was identified based on anomalous dispersion, with Flack’s parameter<sup>9</sup> refining to 0.01(3). Crystal data and details on data collection and refinement are presented in Table S1

<sup>7</sup> Bruker, (2012). APEX2 (v2012.4-3), SAINT (Version 8.18C) and SADABS (Version 2012/1). Bruker AXS Inc., Madison, Wisconsin, USA.

<sup>8</sup> Sheldrick, G. M. (2008). *Acta Cryst.* **A64**, 112-122

<sup>9</sup> Flack, H. D. (1983). *Acta Cryst.* **A39**, 876-881

**Table S1.** Crystallographic data for **2**

chem formula	C <sub>44</sub> H <sub>49</sub> F <sub>6</sub> N <sub>5</sub> OS
M <sub>r</sub>	809.94
cryst syst	monoclinic
color, habit	colorless, platelet
size (mm)	0.11 x 0.08 x 0.02
space group	P2(1)
a (Å)	15.683(3)
b (Å)	16.311(3)
c (Å)	17.436(3)
β, deg	110.279(4)
V (Å <sup>3</sup> )	4183.8(14)
Z	4
ρ <sub>calc</sub> , g.cm <sup>-3</sup>	1.286
μ(Cu Kα), cm <sup>-1</sup>	1.254
F(000)	1704
temp (K)	100(2)
θ range (deg)	4.69–50.42
data collected (h,k,l)	-15:15, -16:16, -17:17
no. of rflns collected	43545
no. of indepndt rflns	8717
observed rflns	6605 (F <sub>o</sub> ≥ 2 σ(F <sub>o</sub> ))
R(F) (%)	5.90
wR(F <sup>2</sup> ) (%)	13.16
GooF	1.022
Weighting a,b	0.0797, 2.5483
params refined	1071
restraints	1126
min, max resid dens	-0.451, 0.474