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Supporting Information

DNA-Accelerated Catalysis of Carbene-Transfer Reactions by a DNA/ Cationic Iron Porphyrin Hybrid

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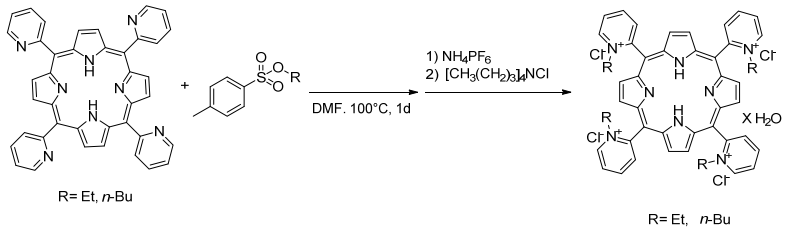
1. General remarks.

Salmon testes DNA, compounds **1**-**2**, **4**-**6** and **8**-**9** were obtained from Sigma Aldrich and used without further purifications. Fe (III)TM-4-pyP, H2T-2-PyP and H2TM-2-PyP were purchased from Frontier scientific. H-NMR were recorded on a Varian 400 (400 and 100 MHz). Chemical shifts (δ) are denoted in ppm using residual solvent peaks as internal standard (δH=7.26). High resolution mass spectra (HRMS) were recorded on an Orbitrap XL (Thermo Fisher Scientific; ESI pos. mode). Electron impact masses spectra (EI) were obtained on a GC-2010 Plus Shimadzu with a HP1 column (30 m x 250 µm x 0.25 µm). Enantiomeric excess determinations or yields were measured by HPLC analysis (Chiracel-OBH, Chiralcel-ODH or Chiralpak-OJH) using UV-detection (Shimadzu SCL-10Avp) or GC analysis (HP-5 (30 m x 250 µm x 0.25 µm) or CP Chiralsil-Dex CB (25 m x 250 µm x 0.25 µm)) using FID detection (Hewlett Packard 6890 Series II chromatograph). The injector temperature was 225ºC and the FID temperature was 250ºC. Flash chromatography was performed using silica gel 60 Å (Merck, 200-400 mesh) or a Grace Reveleris® Flash System (40 µm silica column). UPLC-MS analysis was performed on Waters Acquity H-class UPLC equipped with TUV detector and a Xevo G2 TOF mass detector from Waters Chromatography BV. An Acquity HSS T3 column with size particle 1.8 µm was used and the samples were eluted with a linear gradient from 95% of formic acid in water to 80% of 0,1% formic acid in ACN over 30 min.

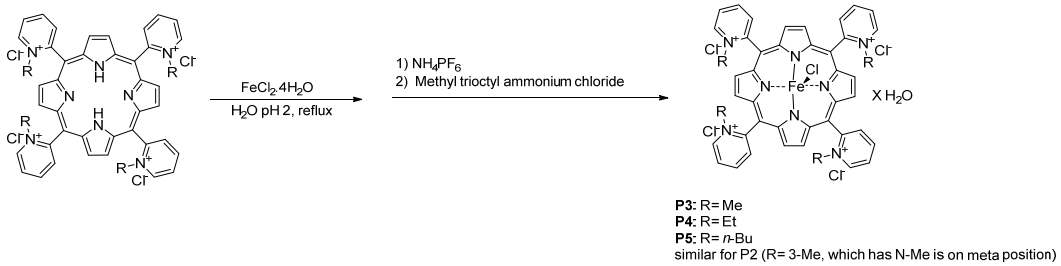
Elemental analyses were performed with a Foss-Heraeus CHN Rapid or a EuroVector Euro EA elemental analyzer. UV/Vis absorption spectra were recorded with a Jasco v-560 spectrophotometer in 1 cm path length quartz cuvettes.

2. Synthesis of Fe (III) porphyrins (Fe(III)TM-3-pyp (P2), Fe(III)TM-2-pyp (P3), Fe(III)TEt-2-pyp (P4) and Fe(III)TBu-2-pyp (P5).[3]

Alkylation:



Metalation:



Scheme S1. Synthesis of Fe(III) porphyrins.

Alkylation (representative procedure).

H2T-2-PyP (250 mg; 0.404 mmol) was dissolved in 50 mL of DMF at 100 °C and to the resulting solution 10 g (0.05 mol) of ethyl- or 11 g (0.05 mol) *n*-butyl p-toluenesulfonate were added. The course of the reaction was followed by thin-layer chromatography (TLC) on silica gel plates using acetonitrile/KNO_3(sat)/water = 8:1:1 as eluent. The reaction was completed within 24 h. Water (100 mL) and $CHCl_3$ (100 mL) were added to the mixture. The $CHCl_3$ layer was discarded and the washing with $CHCl_3$ was repeated several times (3 × 100 mL). The aqueous phase was filtered. The porphyrin was precipitated as the PF_6^- salt with saturated aqueous solution of NH_4PF_6 (2 mL). The precipitate was washed with a mixture of *i*-propanol diethyl ether (1:1) (10 mL). The dried precipitate was then dissolved in acetone, filtered, and precipitated as the chloride salt with saturated acetone solution of tetrabutylammonium chloride (2 mL). It was then dissolved in water (the smallest possible amount) and dried under vacuum. The corresponding porphyrins were purified from other partial alkylated porphyrins via automatic reverse phase column chromatography (gradient water acetonitrile, 100% water (15 min), increase of 10% ACN every ten minutes). The

different fractions were analysed using UPLC-TOF and ESI-MS. Yields (calculated based on formulation given in the literature):

H2TEt-2pyp: 159 mg (42%). UPLC-MS (H_2TE-2-pyP^{4+}): (m/z): 183, 244, 367.

HRMS calcd for $C_{48}H_{46}N_8^{3+}$ [M^{4+}]/3: 244.794, found 244.458.

H2TBu-2pyp: 143 mg (28%). UPLC-MS (H_2TBu-2-pyP^{4+}): (m/z): 211, 282.

HRMS calcd for $C_{56}H_{62}N_8^{4+}$ [M^{4+}]/3: 282.170, found 282.279.

Metalation (representative procedure): The pH of an aqueous solution of H2Tmethyl-3-PyPCl4 (100 mg; 0.147 mmol) in 60 ml water was adjusted to 2 (with 1 M HCl), and a 40-fold molar excess $FeCl_2.4H_2O$ was added and the solution was stirred and heated under reflux. The course of the metalation was followed on silica gel TLC plates using acetonitrile/KNO_3(sat)/water = 8:1:1 as a mobile phase (pH = 2, adjusted by 1 M HCl). Additionally, the decrease of the fluorescenceof the metal-free porphyrin was followed using UV light at 356 nm. The metalation was completed in 18 hours. The solution was filtered through a filter paper. The Fe porphyrin was precipitated as the PF_6^- salt with a saturated aqueous solution of NH_4PF_6 (2ml). The precipitate was thoroughly washed with diethyl ether (5 × 5 mL). The dried precipitate was then dissolved in acetone (the smallest possible amount) and precipitated as the chloride salt with saturated acetone solution of methyl-tri-noctylammonium chloride (2 mL). The precipitate was washed with acetone and dissolved in the smallest possible amount of water. The whole precipitation procedure was repeated once again to ensure high purity. The iron porphyrin **P3** was isolated in 18% yield (15 mg) (calculated based on formulation given in the literature). The metalation and purification of ortho isomeric porphyrins were similar to their meta analogues except that $FeCl_2.4H_2O$ was added in a 100-fold molar excess. The metalation of Fe(III)TBu-2-pyp was slower (4 days) due to the steric hindrance of the alkyl chains. The ortho Fe porphyrins were isolated in: Fe(III)TM-2-pyp 80% yield, Fe(III)TEt-2-pyp 91% yield and Fe(III)TBu-2-pyp 31% yield.

The corresponding iron porphyrins were characterized with UV/vis spectroscopy, elemental analysis and electrospray-ionization mass spectrometry (ESI-MS). UV/vis spectra were recorded in 0.01 M HCl at 25ºC with 0.5 nm resolution using a 1 cm quartz cuvette. At this pH (pH 2) all metalloporphyrins have two H_2O molecules as axial ligands. Samples for ESI-MS analyses were prepared in acetonitrile/H_2O mixture

(1:1, v/v) containing 0.01% v/v heptafluorobutyric acid (HFBA). The addition of an ion pairing agent to the samples made MS data easier to interpret, as the pairing of Fe(III)Talkyl-2,3-pyp^{5+} with HFBA^{-} reduced the overall charge of the analyte and brought the corresponding *m/z* MS peaks to regions of low interference from sample/solvent matrix components. It also avoids the formation of monohydroxo (OH)(H2O)Fe-pyp species.

P2

UV/vis: (Soret band) λ_{max}: 398 nm. Elemental analysis (calcd %) for $C_{44}H_{36}Cl_5FeN_8 \cdot 11H_2O$: C, 47.69; H, 5.28; N, 10.11; found: C, 47.63; H, 4.55; N, 10.82. HRMS calcd for $C_{56}H_{36}F_{21}FeN_8O_6^{2+}$ [M^{5+}+3HFBA] $^{2+}$/2: 685.588; found 685.587. HRMS calcd for $C_{48}H_{34}F_7FeN_8O_2^{2+}$ [M^{5+}+HFBA-2H^+]$^{2+}$/2: 471.602; found 471.604.

P3

UV/vis: (Soret band) λ_{max}: 395 nm. Elemental analysis (calcd %) for $C_{44}H_{36}Cl_5FeN_8 \cdot 11H_2O$: C, 47.69; H, 5.28; N, 10.11; found: C, 47.92; H, 4.81; N, 10.07. HRMS calcd for $C_{60}H_{36}F_{28}FeN_8O_8^{+}$ [M^{5+}+4HFBA]$^{+}$: 1584.156; found 1584.160. HRMS calcd for $C_{56}H_{36}F_{21}FeN_8O_6^{2+}$ [M^{5+}+3HFBA]$^{2+}$/2: 685.588; found 685.587. HRMS calcd for $C_{48}H_{34}F_7FeN_8O_2^{2+}$ [M^{5+}+HFBA-2H^+]$^{2+}$/2: 471.602; found 471.605.

P4

UV/vis: (Soret band) λ_{max}: 397 nm. HRMS calcd for $C_{52}H_{42}F_7FeN_8O_2^{2+}$ [M^{5+}+HFBA-2H^+]$^{2+}$/2: 499.64; found 499.632. HRMS calcd for $C_{52}H_{41}F_7FeN_8O_2^{3+}$ [M^{5+} +HFBA - H^+]$^{3+}$/3: 333.427; found 333.760.

P5

UV/vis: (Soret band) λ_{max}: 396 nm. HRMS calcd for $C_{60}H_{57}F_7FeN_8O_2^{+}$ [M^{5+}+HFBA-3H^+]$^{+}$: 1110.384; found 1110.383. HRMS calcd for $C_{68}H_{60}F_{21}FeN_8O_6^{2+}$ [M^{5+}+3HFBA] $^{2+}$/2: 769.682; found 769.691. HRMS calcd for $C_{60}H_{58}F_7FeN_8O_2^{2+}$ [M^{5+}+HFBA - 2H^+]$^{2+}$/2: 555.703; found 555.694.

Achieving good results for the elemental analysis of these porphyrins is known to be challenging as a result the procedure for their isolation.[1] Some common issues are the presence of solvent in the sample either as an axial ligand or crystallization solvent, and the presence of co-precipitated salts and/or different counter-ions. The porphyrins reported here exhibit physical and spectral properties in accordance with the literature.[3]

3. Additional catalysis results.

Table S1. pH optimization of the catalytic reaction.[a]

Entry	pH	Yield [%]	ee_{trans}[%]	Trans/cis	TTN[c]
1[b]	5.5	6±0	47±1	13±1	4±0
2	6.5	14±3	42±0	12±1	9±0
3	7.5	10±0	33±0	9±1	7±0

[a] The experiments were carried out with 5 mM **1**, 50 mM **2**, 6 mM base pairs of st-DNA and 75 μM of Fe (III) porphyrins in 20 mM MOPS buffer.3% v/v ACN, for 5 minutes at 5ºC, unless otherwise specified. Yields and enantioselectivities are based on areas of HPLC and GC peaks that are compared to 2-methyl anisole as internal standard. All data averages of two or more experiments. Errors are standard deviations. [b] 2-(N-morpholino)ethanesulfonic acid (MES, used as buffer). [c] TTN = total turnover numbers.

Table S2. Investigation of the scope of diazocompounds.[a]

Entry	Styrene	Diazo reagent	Product	DNA [mM]	Yield [%][b]	TTN[c]	ee_{trans} [%][b]
1	**4**	**7**	**13**	-	24±9	31	-
2	**4**	**7**	**13**	6	44±3	59	50
3	**4**	**8**	**14**	-	≤3	-	-
4	**4**	**8**	**14**	6	12±5	15	21
5	**4**	**9**	**15**	-	≤3	-	-
6	**4**	**9**	**15**	6	≤3	-	-

[a] The experiments were carried out with 5 mM substrate and 50 mM diazo compound, 6 mM base pairs of st-DNA and 37.5 μM of P3 in 20 mM MOPS buffer (pH 6.5), 3% v/v ACN, for 5 minutes at 5ºC, unless otherwise specified. Yields and enantioselectivities are based on areas of HPLC and GC peaks that are compared to 2-methyl anisole as internal standard. All data were averaged over two or more experiments. [b] of the trans isomers; reproducibility *ee*'s ±3%. [c] TTN = total turnover numbers.

4. Representative procedure for the DNA-based catalytic asymmetric cyclopropanation

Salmon testes DNA (6.0 mg/mL) was dissolved in a 20 mM solution of MOPS buffer pH 6.5 (9.0 mM in base pairs) 2 days before use. The following final concentrations were used in catalysis: 5 mM of substrate 4-methoxystyrene (**4**), 50 mM of ethyl diazoacetate (**2**), 37.5 μM of iron porphyrin and 6 mM of DNA (in base pairs). 250 μl of a 1.125 mM solution of the iron porphyrin* was added to 2.0 mL of buffer in a 15 mL Greiner tube. Then, 5 mL of st-DNA solution was added and the solution was mixed by continuous inversion at 5°C. After incubation for 30 min, 50 μL of a 750 mM solution of 4-methoxystyrene (**4**) in acetonitrile and 200 μL of a 1.875 M solution of ethyl diazoacetate (**2**) in acetonitrile were added to start the catalytic reaction. After 5 minutes the product was extracted with diethyl ether (3 × 5 mL). The organic layer was washed with brine (1 × 5 mL). After drying (Na_2SO_4) and evaporation of the solvent the crude product was analyzed by HPLC and GC, using 2-methylanisole as internal standard.

* The concetration of the stock solution of the catalyst was always checked by UV-Vis spectroscopy. The absorbance of the Soret band of the porphyrin was measured and the concentration of the solution was calculated using the corresponding extinction coefficients.[3]

HPLC and/or GC analysis

To determine the yield of the catalytic reaction, pure reference compound was analysed together with an external standard. The observed peak areas for products (P) and external standard (S) $\frac{area\ P}{area\ S}$ were plotted against the concentrations of both compounds in the analytic sample $\frac{[P]}{[S]}$. The slope of the linear fit gave the correction factor *c*.

The concentration of products in the catalysis reaction samples was calculated using the following formula:

$$[P] = \frac{area\ P}{area\ S * c} * [S]$$

Were *[P]* is the concentration of product in the catalysis reaction sample, *area P* is the addition of all products peak areas, *area S* is the peak area of the external standard, *c* is the correction factor and *[S]* is the concentration of the standard solution.

The yield of the reaction was calculated as follows:

$$\text{Yield (\%)} = \frac{[P]}{[P]max} * 100$$

Were *[P]* is the concentration of product in the catalysis reaction samples and *[P]max* is the maximal theoretical concentration of product in the catalysis reaction samples depending on the amount of substrate added to the catalytic reaction.

HPLC chromatogram of *rac*-14 and standard catalytic reaction:

(14) Chiracel-OBH *n*-heptane 100%, 0.5ml/min

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Batch Filename	: 20150502.lcb		
Vial #	: 1-61	Sample Type	: Unknown
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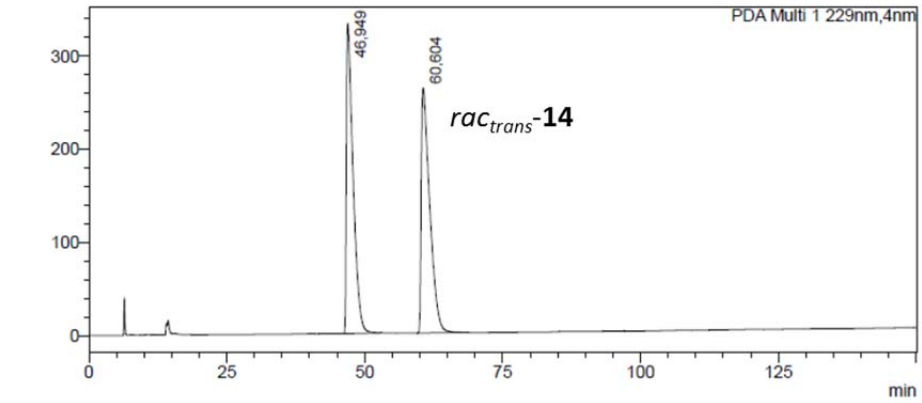

<Peak Table>

PDA Ch1 229nm

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2	60,604	28119413	262831	50,053			
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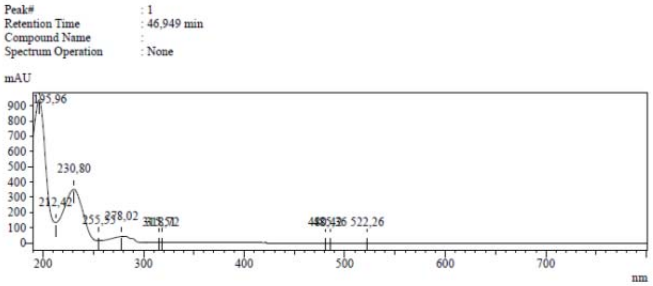

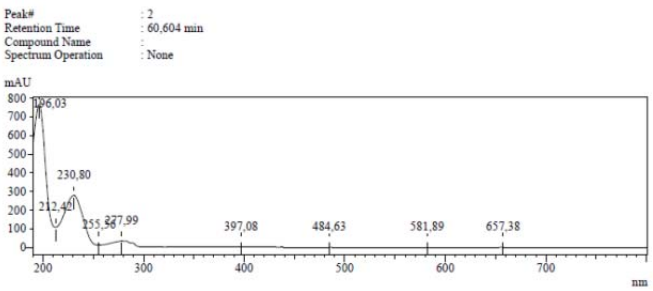

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Sample ID	: ar-341.5		
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Batch Filename	: 20150502.lcb		
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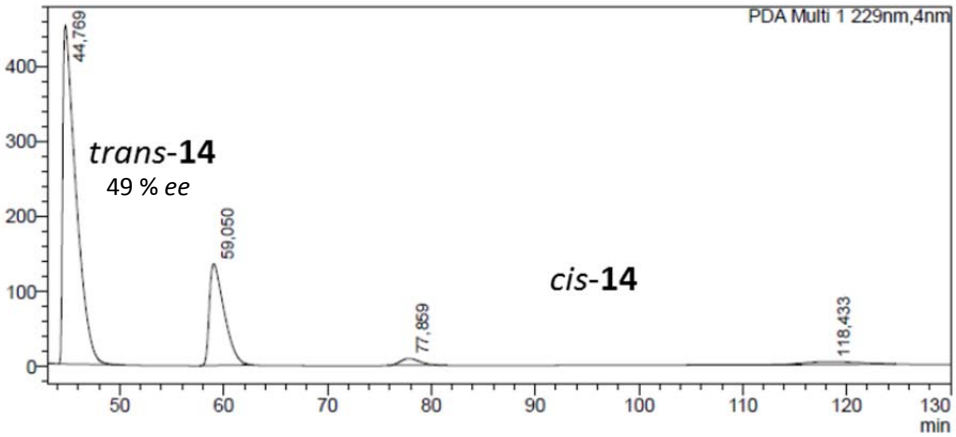

<Peak Table>

PDA Ch1 229nm

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
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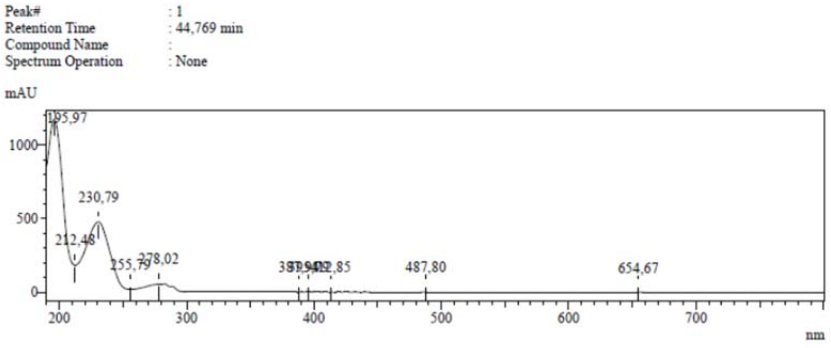
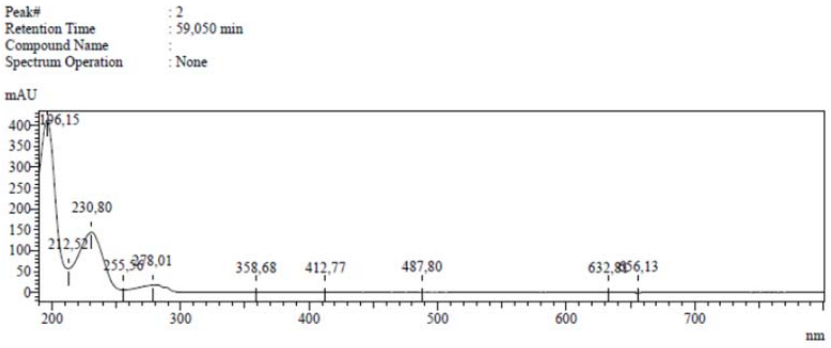
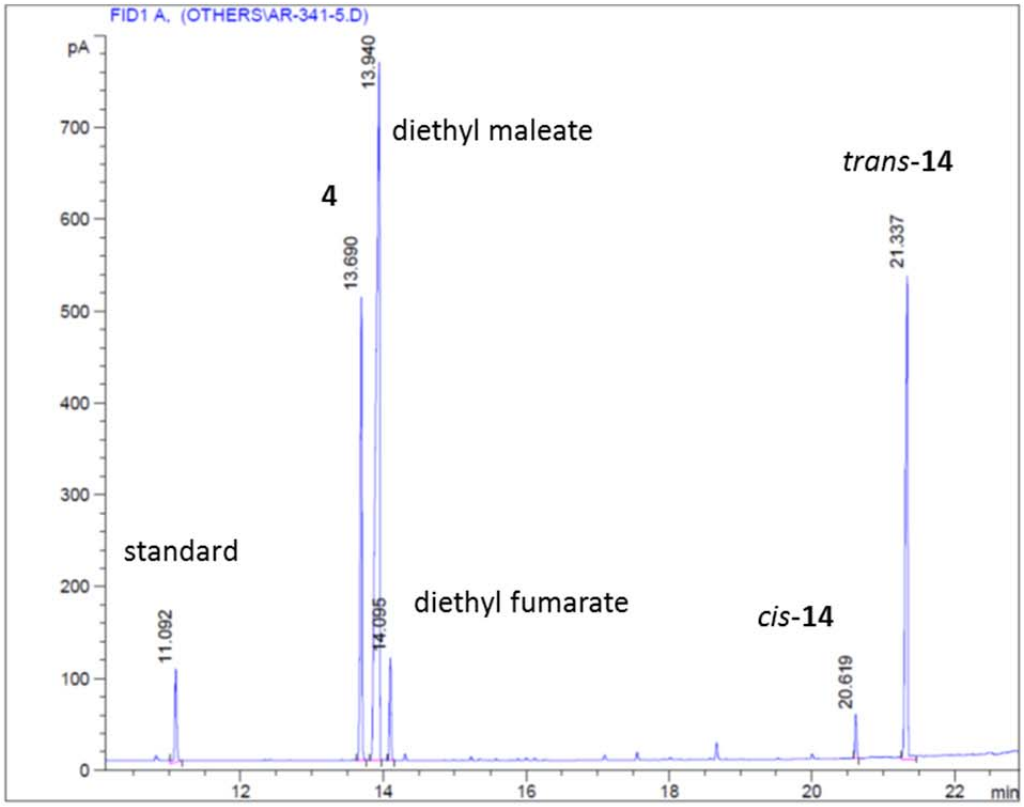
2	59,050	13482434	135516	24,159		M	
3	77,859	1206881	9150	2,163		M	
4	118,433	1322001	3777	2,369		M	
Total		55807599	599541				





GC chromatogram of the standard catalytic reaction:

14 HP-05 60ºC (5 min), 10ºC/min 260ºC.

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|   2|   13.690|MM     |  0.031|   933.451|  17.744|               |
|   3|   13.940|MM     |  0.059|  2705.179|  51.422|               |
|   4|   14.095|MM     |  0.025|   171.468|   3.259|               |
|   5|   20.619|MM     |  0.028|    81.928|   1.557|               |
|   6|   21.337|MM     |  0.037|  1178.473|  22.401|               |
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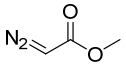
5. Synthesis and characterization

Synthesis of methyl-2-diazoacetate **7**:

The procedure was adapted from the literature.[2] To a solution of methyl acetoacetate (1.16 g, 10 mmol) in acetonitrile (12 mL) was added Et_3N (1.31g, 13 mmol). The reaction mixture was cooled in an ice bath and a solution of *p*-acetamidobenzenesulfonyl azide (2.64 g, 11 mmol) in acetonitrile (12 mL) was added slowly. The reaction mixture was allowed to warm to room temperature. After stirring for 17 h, solvent was removed under reduced pressure. The residue was dissolved in ether (60 mL) and washed with 5% aqueous KOH solution (50 mL). To a solution of the crude methyl 2-diazo-acetoacetate in ethyl ether was added 5% KOH (50 ml), and the reaction mixture was stirred for 2 h. The organic phase was separated, dried over Na_2SO_4, and concentrated under reduced pressure. Methyl diazoacetate was obtained as a yellow liquid (231 mg, 23%).



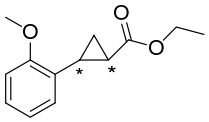
Methyl diazoacetate (7).

Yield: 231 mg (2.3 mmol, 23%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.67 (br, 1H), 3.68 (s, 3H).

Compound **7** exhibits physical and spectral properties in accord with the literature.[5]

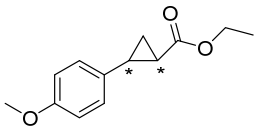
General procedure 1: Synthesis of cyclopropanes **3**, **10**, **11** and **12**:[2]

FeTPPCl (7.0 mg, 0.01 mmol, 1 mol%) was dissolved in the substrate (1.0 mmol) in an open round bottom flask under air. To this mixture was then added glycine ethyl ester hydrochloride (279 mg, 2.0 mmol, 2 eq.), water (5.0 mL) and acetic acid (10.0 mg, 0.15 mmol, 0.15 eq.). To this stirred heterogeneous mixture was added $NaNO_2$ (166 mg, 32.4 mmol, 2.4 eq.) in one portion at 40 °C. After 24 h, the mixture was diluted with water (4 mL), extracted with CH_2Cl_2 (3 × 5 mL), washed with brine (1 × 5 mL), dried over Na_2SO_4 and the solvent was evaporated in *vacuo*. The crude product was further purified by flash chromatography to afford the pure *trans* product (103 mg, 47%).



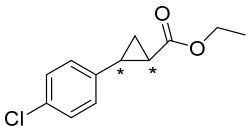
(1RS,2RS)-Ethyl 2-(2-methoxyphenyl)cyclopropane-1-carboxylate (3).

Prepared using general procedure 1, starting from (138.4 mg, 1 mmol) 2-methoxystyrene. Purified by column chromatography (SiO_2, 10% EtOAc:pentane), to afford the product as a white solid. Yield: (103 mg, 47%) of **3**. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.25-7.16 (m, 1H), 6.88-6.83 (m, 3H), 4.17 (c, *J*=8.0 Hz, 2H), 3.83 (s, 3H), 2.74-2.71 (m, 1H), 1.85-1.82 (m, 1H), 1.53-1.50 (m, 1H), 1.32-1.26 (m, 4H). MS (EI): *m*/*z* (%) = 220 (40) $[M]^+$, 174 (40), 147 (100), 91 (70). Enantiomeric excess and yields were determined by HPLC analysis (Chiralcel-ODH, *n*-heptane/iPrOH 98:2, 0.5 ml/min. Retention times: 21.6 and 48.5 min.). *c*: 1.33305 at λ=279 nm. The cis product was not isolated, the retention times are: HPLC: 14.6 and 15.5 min.



(1RS,2RS)-Ethyl 2-(4-methoxyphenyl)cyclopropane-1-carboxylate (10).

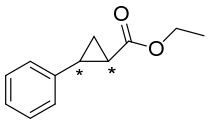
Prepared using general procedure 1, starting from (276.8 mg, 2 mmol) 4-methoxystyrene. Purified by column chromatography (SiO_2, 5% EtOAc:pentane), to afford the product as a white solid. Yield: (98.6 mg, 45%) of **10**.^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.05 (d, *J*=8.0 Hz, 2H), 6.84 (d, *J*=8.0 Hz, 2H), 4.18 (c, *J*=8.0 Hz, 2H), 3.80 (s, 3H), 2.47-2.42 (m, 1H), 1.85-1.81 (m, 1H), 1.58-1.54 (m, 1H), 1.31-1.24 (m, 4H). MS (EI): *m*/*z* (%) = 220 (34) $[M]^+$, 191 (20), 147 (100), 91 (40). Enantiomeric excess was determined by HPLC analysis (Chiralcel-OBH, *n*-heptane 100%, 0.5 ml/min. Retention times: 46.9 and 60.6 min.). Yield was determined by HPLC analysis *c*: 5.5719 at λ=229 nm or GC (HP019-60ºC (5 min), 10ºC/min 260ºC) Retention times: 21.6. *c*: 2.45255. The *cis* product was not isolated, the retention times are: HPLC: 77.9 min and 118.4 min. GC: 20.3 min.



(1RS,2RS)-Ethyl 2-(4-chlorophenyl)cyclopropane-1-carboxylate (11).

Prepared using general procedure 1, starting from (277.0 mg, 2 mmol) 4-chlorostyrene. Purified by column chromatography (SiO_2, 1% EtOAc:pentane), to afford the product as an brownish liquid. Yield: (324.6 mg, 72%) of **11**. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.21 (d, *J*=8.0 Hz, 2H), 6.99 (d, *J*=8.0 Hz, 2H), 4.15 (c, *J*=4.0 Hz, 2H), 2.47-2.44 (m, 1H), 2.02-1.82 (m, 1H), 1.60-1.48 (m, 1H), 1.27-1.21 (m, 4H). MS (EI): *m*/*z* (%) = 224 (30) $[M]^+$, 151 (70), 115 (100), 89 (20).

Enantiomeric excess was determined by HPLC analysis (Chiralpak-OJH, *n*-heptane 100%, 0.5 ml/min. Retention times: 44.1 and 48.7 min.). Yield was determined by GC analysis (Chirasil-Dex CB-40ºC (0 min), 5ºC/min 230ºC). Retention time: 29.3. *c*: 1.2249. The *cis* product was not isolated, the retention times are: HPLC: 37.0 min and 39.4 min. GC: 28.4 and 28.6 min.



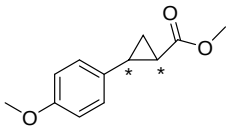
(1RS,2RS)-Ethyl 2-phenylcyclopropane-1-carboxylate (12).

Prepared using general procedure 1, starting from (208.0 mg, 2 mmol) styrene. Purified by column chromatography (SiO_2, 5% EtOAc:pentane), to afford the product as a white solid. Yield: (189 mg, 50%) of **12**. ^1H NMR (400 MHz, $CDCl_3$) δ = 7.32-7.28 (m, 2H), 7.24-7.20 (m, 1H), 7.13-7.11 (m, 2H), 4.20 (c, *J*=4.0 Hz, 2H), 2.58-2.53 (m, 1H), 1.94-1.91 (m, 1H), 1.63-1.61 (m, 1H),1.33-1.30 (m, 4H). MS (EI): *m*/*z* (%) = 190 (20) $[M]^+$, 144 (20), 117 (100), 91 (24). Enantiomeric excess and yields were determined by GC analysis (Chirasil-Dex CB-isotherm 125ºC). Retention times: 31.7 and 31.6. *c*: 1.2249. The *cis* product was not isolated, the retention times are: GC: 28.1 and 30.3 min.

These compounds exhibit spectral properties in accordance with the literature.[Error! Bookmark not defined.,2]

General procedure 2: Synthesis of cyclopropanes **13** and **14**:[3]

This procedure was adapted from the literature. Under inert atmosphere, $Rh_2(OAc)_4$ (5.2 mg, 0.01 mmol) was dissolved in CH_2Cl_2 (32 mL). 4-Methoxystyrene was added (6.0 mmol, 5 eq.) and the reaction was heated until reflux. The corresponding alkyl diazoacetate (1.2 mmol, 1eq.) was added over 3 hours to the reaction mixture using a syringe pump. Once the addition was completed, the reaction mixture was stirred one additional hour. After that, the solvent was evaporated in *vacuo*. The crude product was purified by flash column chromatography.

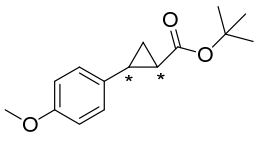


(1RS,2RS)-Methyl 2-(4-methoxyphenyl)cyclopropane-1-carboxylate (13).

Prepared using general procedure 2, starting from (802.0 mg, 6 mmol) 4-methoxystyrene. Purified by column chromatography (SiO_2, 1% EtOAc:pentane), to afford the product as a yellow liquid. Yield: (40 mg, 16%) of **13**. ^1H

NMR (400 MHz, $CDCl_3$) δ = 7.03 (d, *J*=8.0 Hz, 2H), 6.82 (d, *J*=8.0 Hz, 2H), 3.78 (s, 3H), 3.71 (s, 3H), 2.51-2.48 (m, 1H), 1.84-1.82 (m, 1H), 1.55-1.58 (m, 1H), 1.30-1.25 (m, 1H). MS (EI): *m*/*z* (%) = 206 (50) $[M]^+$, 147 (100), 91 (45), 77 (25). Enantiomeric excess was determined by HPLC analysis (Chiralpak-OJ, *n*-heptane/iPrOH 99.5:0.5, 0.5 ml/min. Retention times: 78.0 and 110.7 min. Yield was determined by GC analysis (Chirasil-Dex CB-40ºC (0 min), 5ºC/min 230ºC). Retention time: 29.2. *c*: 1.0335 . The *cis* product was not isolated, the retention times are: HPLC: 70.2 min and 83.3 min. GC: 28.1 and 28.3 min.

This compound exhibit spectral properties in accordance with the literature.[4]



(1RS,2RS)-*tert*-Butyl 2-(4-methoxyphenyl)cyclopropane-1-carboxylate (14).

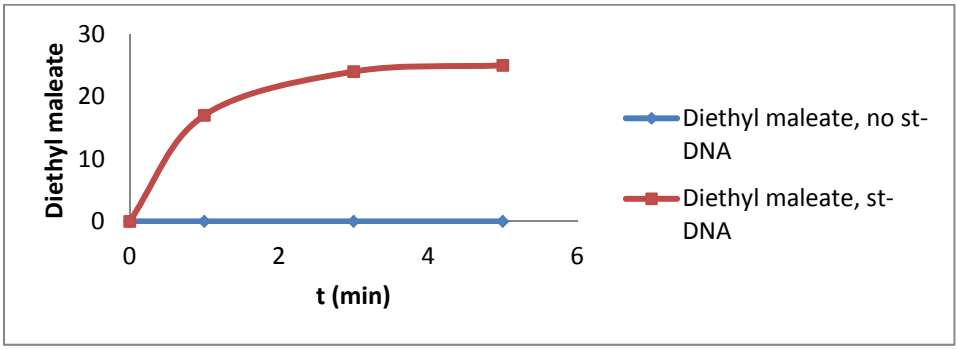
Synthesized using general procedure 2 starting from (802 mg, 6 mmol) 4-methoxystyrene. Purified by column chromatography (SiO_2, 2% EtOAc:pentane), to afford the product as a yellow oil. Yield: (128.6 mg, 9%) of **14**. ^1H NMR (400 MHz, $CDCl_3$) δ = 7.04 (d, *J*=8.0 Hz, 2H), 6.83 (d, *J*=8.0 Hz, 2H), 3.79 (s, 3H), 2.44-2.39 (m, 1H), 1.79-1.74 (m, 1H), 1.52-1.47 (m, 10H), 1.21-1.16 (m, 1H). MS (EI): *m*/*z* (%) = 248 (6) $[M]^+$, 192 (58), 147 (100), 91 (20). Enantiomeric excess was determined by HPLC analysis (Chiralpak-OJ, *n*-heptane/iPrOH 99:1, 0.5 ml/min. Retention times: 17.8 and 19.2 min.). Yield was determined by GC analysis (Chirasil-Dex CB-40ºC (0 min), 5ºC/min 230ºC). Retention time: 31.4. *c*: 1.5111.

This compound exhibit spectral properties in accordance with the literature.[5]

6. DNA-based catalytic asymmetric cyclopropanation in time

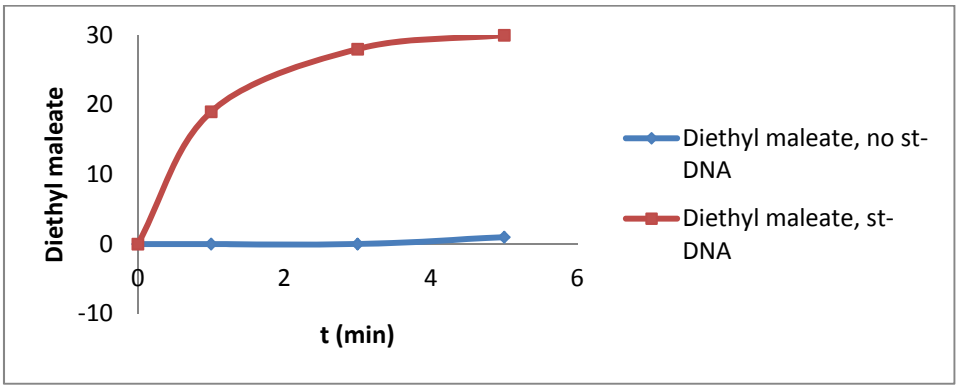
Standard protocol, at 1, 3 and 5 minutes an aliquot of 1 mL was taken and analyzed. Analysis by GC (HP-5), method 60ºC (5 min), 10ºC/min 260ºC. Retention time: 13.7 (substrate **4**), 13.9 (diethyl maleate) *c*= 0.9086.

a)



In absence of 4-methoxystyrene (**4**).

b)



In presence of 4-methoxystyrene (**4**).

Figure S1. A and **b**: Study of the formation of diethyl maleate in time.

7. Kinetic study of N_2 release

System 1: Magnetic stirring.

System 2: Orbital mixing.

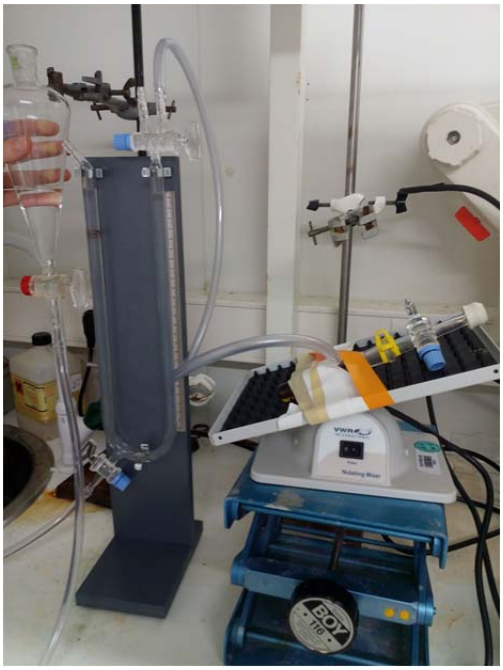


Figure S2. Set ups for the measurement of N_2 release.

In both systems the gas burette (filled with EtOH) was connected to the Schlenck vessel. The DNA-based catalytic asymmetric cyclopropanation reaction was set up as previously described. After the incubation of the reaction mixture for 30 minutes, the solution was introduced in the Schlenck vessel and connected to the gas burette, after

which the reaction was started by addition of EDA. In order to follow the reaction accurately, a video of five minutes of every experiment was recorded. In figure 1 the volume of N_2 released every 5 seconds during 5 minutes reaction is plotted. Once the reaction was finished, the work up and the analysis were performed as described in the general catalytic procedure.

Table S3. Comparison of the catalytic results between the different stirring methods.

Entry	Stirring method	st-DNA [mM]	Yield [%][b] (4)	Diethyl maleate	ee_{trans} [%][c]
1	Orbital mixing	-	5±5	17±5	-
2	Orbital mixing	6	14±1	29±0	50±0
3	Magnetic stirring	-	17±3	42±0	-
4	Magnetic stirring	6	7±1	21±0	50±0
5	Continuous inversion	-	3±3	3±0	-
6	Continuous inversion	6	32±6	30±3	50±3

The experiments were carried out with 5 mM substrate **4** and 50 mM EDA, 6 mM base pairs of st-DNA and 37.5 μM of P3 in 20 mM MOPS buffer (pH 6.5), 3% v/v ACN, for 5 minutes at 5ºC, unless otherwise specified. [b] Yields and enantioselectivities are based on areas of HPLC and GC peaks that are compared to 2-methyl anisole as internal standard. All data are averages of two or more experiments.

8. DNA-based catalytic asymmetric cyclopropanation in presence of nucleobases and amines

The procedure was similar to the standard one (without st-DNA), except for the step of the incubation. In this case, after addition of Fe(III)TM-2-pyp (P3), the corresponding nucleobase or amine were added until reaching a concentration of 37.5 μM.

Stock solutions of the nucleobases:

Adenine: 28.1 mM in DMSO.

Thymine: 9.38 mM in buffer.

Guanine: 28.1 mM in HCl (0.1 M).

Cytosine: 9.38 mM in buffer.

Stock solutions of the amines:

Pyridine: 28.1 mM in acetonitrile.

Benzylamine: 28.1 mM in acetonitrile.

9. References

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