
SUPPORTING INFORMATION

Nickel(BiPhePhos)-Catalyzed Hydrocyanation of Styrene—Highly Increased Catalytic Activity by Optimized Operational Procedures

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1. Implementation of hydrocyanations

HCN is highly volatile, toxic and can polymerize explosively in the liquid state under base catalysis. It was handled exclusively in a well-ventilated fume hood with at least two instructed persons. In addition to the general personal protective equipment for safe laboratory work, these persons were each equipped with a BW Solo HCN gas detector and Butoject butyl gloves (both from Honeywell). HCN was stored in a lockable freezer (-26 °C) to which only instructed persons have access. The volume in a single storage vessel was approximately 2 mL.

All experiments were performed using standard Schlenk techniques. Working steps in the glovebox were performed in a Labmasterpro ECO from mBRAUN under an argon atmosphere. Hydrocyanations were performed in Schlenk tubes (height: 124.5 mm, inner diameter: 23.4 mm, glass thickness: 2.6 mm) with a GL-32 closure and Young stopcock connection.

1.1. Experimental procedure of hydrocyanation reactions

Ligand was added to the reaction vessel in a glovebox according to the amounts given in the script and dissolved in dry, degassed toluene (2/3 of the amount of solvent). $\text{Ni}(\text{cod})_2$ was added next and the resulting solution was stirred for 30 minutes at room temperature. Afterwards the reaction vessel was removed from the glovebox and styrene was added through a septum (renewed for each reaction).

Dry and degassed Toluene (1/3 of the amount of solvent) was placed in another Schlenk flask, cooled to -50 °C and then dry and degassed HCN was added using an Eppendorf pipette (HCN was only thawed to the required amount and handled close to the melting point). Upon addition, the HCN froze visibly to form a white solid. Afterwards, the mixture was carefully warmed until a homogeneous solution was formed and then added to the reaction mixture using a syringe to start the reaction.

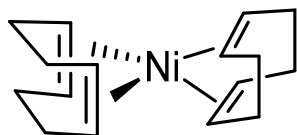
Once the reaction was complete the reaction vessel was carefully opened. A light argon stream was passed through the solution to remove remaining HCN. GC standard was added before and a sample was taken to be analyzed via GC-FID.

1.2. Procedure for conversion/time-plots

According to the previous procedure. DBE was used as an internal standard for GC-FID analysis and was added before the start of the reaction. Samples were taken with a syringe flushed with argon. Samples are quenched using wet and air-containing PhMe and are degassed using a steam of argon.

Important: Extreme caution when taking samples! The flask may be under pressure and the reaction solution contains an unknown concentration of hydrogen cyanide. Wear butyl rubber gloves, use HCN warning devices, and hold the syringe and cannula firmly. When pulling out the syringe, ensure no drops of the sample solution are splashed. Only work in a well-ventilated fume hood.

1.3. Synthesis of $\text{Ni}(\text{cod})_2$



$\text{Ni}(\text{acac})_2$ (1284.6 mg, 5 mmol, 1 eq) was added to a Schlenk flask, dried for 10 min under reduced pressure at 80 °C and then suspended in THF (4 mL) and COD (3.9 mL, 30 mmol, 6 eq). The resulting green mixture was cooled to 35 °C and $n\text{Bu}_2\text{Mg}$ (11 mL, 1 M in heptane, 11 mmol, 2.2 eq) was added over 10 min. The color changed from green to yellow/brown to red-black during this time. After additional 10 min time the stirring was stopped and a light-colored precipitate formed. The supernatant red-black solution was

carefully removed with a filter cannula. The resulting solid was washed with degassed acetone (5×1.5 mL) in the cold until all brown residues were removed. The light-yellow solid was dried under reduced pressure and $\text{Ni}(\text{cod})_2$ (628.7 mg, 2.29 mmol, 46%) was obtained as a fine yellow powder.

^1H -NMR (500 MHz, C_6D_6): $\delta = 4.30$ (s, 4H), 2.08 (s, 8H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ -NMR (126 MHz, C_6D_6): $\delta = 89.69$ (s, 4C), 30.89 (s 4C) ppm.

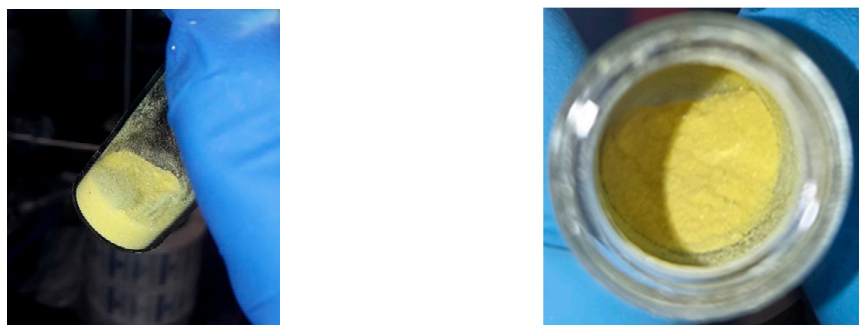


Figure S1. Yellow color of the synthesized $\text{Ni}(\text{cod})_2$ indicates high purity. (Grey or beige color indicates the presence of metallic nickel, whereas green color indicates $\text{Ni}(\text{II})$ complexes).

1.4. Synthesis of HCN

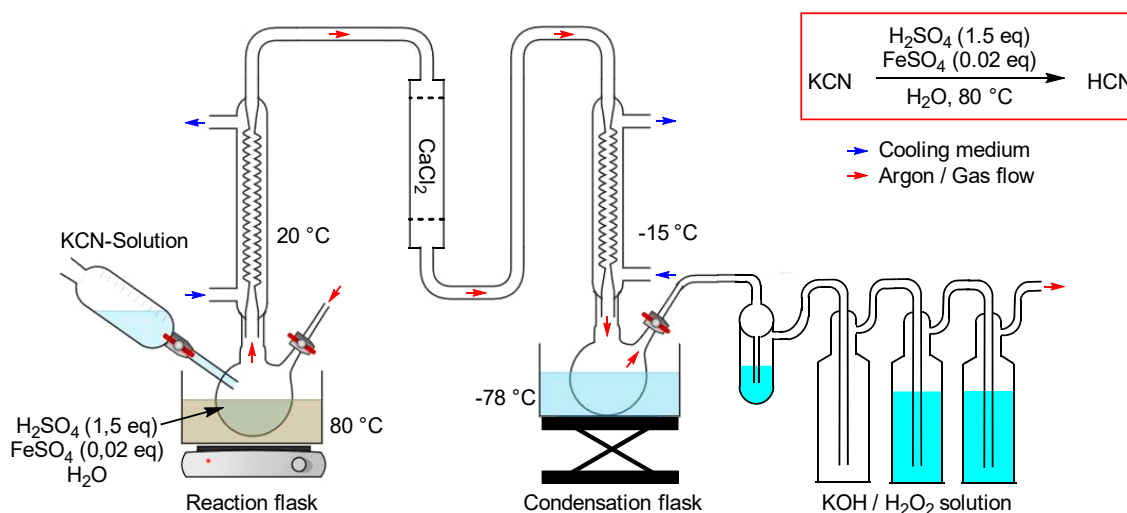


Figure S2. apparatus for hydrogen cyanide synthesis.

The apparatus was set up as shown in Figure S2 (connections via PVC tubes) and then flushed with argon for 30 min. Water (50 mL) and concentrated sulfuric acid (102 mL, 1.91 mol, 1.5 eq) were added into the reaction flask. $\text{FeSO}_4 \cdot 7 \text{H}_2\text{O}$ (8.2 g, 0.03 mol, 0.02 eq) was carefully dissolved as a catalyst while stirring vigorously. This solution was heated to 80 °C and KCN (82.0 g, 1.26 mmol, 1 eq) dissolved in water (150 mL) was slowly added via a dropping funnel while argon was continuously flowing through the apparatus.

The first 80 mL of solution were added within 30 min, but no condensation could be detected in the condensation flask. Therefore, the heating bath temperature was lowered to 40 °C, and the dropping rate and the argon flow were reduced to a minimum. Afterwards, a white solid condensed between the Schlenk stopcock and the ground joint of the condensation flask. This led to the stopcock becoming blocked, and the addition of the KCN had to be interrupted once to remove the cold bath briefly. Once the HCN had melted a little and sunk deeper into the flask, a gas flow could be observed again at the bubble counter and the synthesis was continued. This was done for a further 4 h (40 mL KCN solution). The apparatus was then sealed airtight, and the condensation flask was

stored overnight at $-26\text{ }^{\circ}\text{C}$ under lock and key. The next day, the apparatus was reconnected identically, and the remaining KCN solution was added. After another 5 h, this was completed and HCN (12.8 g, 0.48 mol, 38%) was obtained as a white solid in the cold. For further purification, it was additionally degassed using the Freeze-Pump-Thaw method (three cycles). Afterwards, HCN was stored at $-26\text{ }^{\circ}\text{C}$.

The apparatus was rinsed for 30 minutes with a strong argon stream, and then all components were carefully rinsed with a KOH/H₂O₂ solution.

2. GC

GC-samples were taken after removing the remaining hydrogen cyanide by a stream of argon. *n*-decane was added as an internal standard. About 0.7 ml of the reaction mixture is filtered through a syringe filter, placed in a GC vial and diluted with toluene.

2.1. Device

The GC analysis was performed on an Agilent 7890A equipped with an Agilent HP-5 column and an FID detector. The calibration factors were determined experimentally using *n*-decane or di-*n*-butyl ether (DBE) as internal standard.

2.2. Method

The split ratio of the method was set to 84:1 at a split flow of $184.8\text{ mL}\cdot\text{min}^{-1}$ and the temperature and gas flow profiles are listed in Table S1 and Table S2.

Table S1. Gas flow profile of the GC method.

| | Gas flow rate | End flow / $\text{mL}\cdot\text{min}^{-1}$ | Hold / min |
|--------|---------------|--|------------|
| Start | - | 2.2 | 18.0 |
| Ramp 1 | 2.0 | 4.4 | 3.0 |

Table S2. Temperature profile of the GC method.

| | Heat rate / $^{\circ}\text{C}\cdot\text{min}^{-1}$ | End temperature / $^{\circ}\text{C}$ | Hold / min |
|--------|--|--------------------------------------|------------|
| Start | - | 40.0 | 3.0 |
| Ramp 1 | 7.5 | 140.0 | 0.0 |
| Ramp 2 | 85.0 | 290.0 | 4.0 |

2.3. Calibrations

2.3.1. *n*-decane

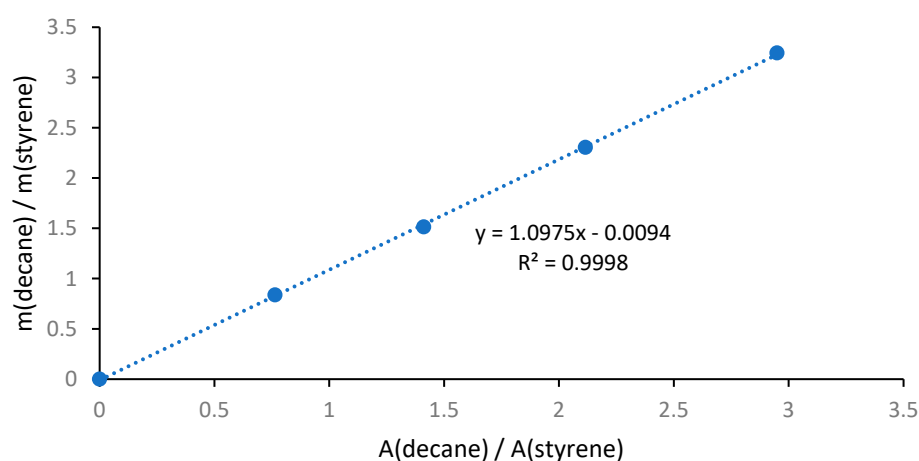


Figure S3. GC-FID Calibration of Styrene with *n*-decane as internal standard.

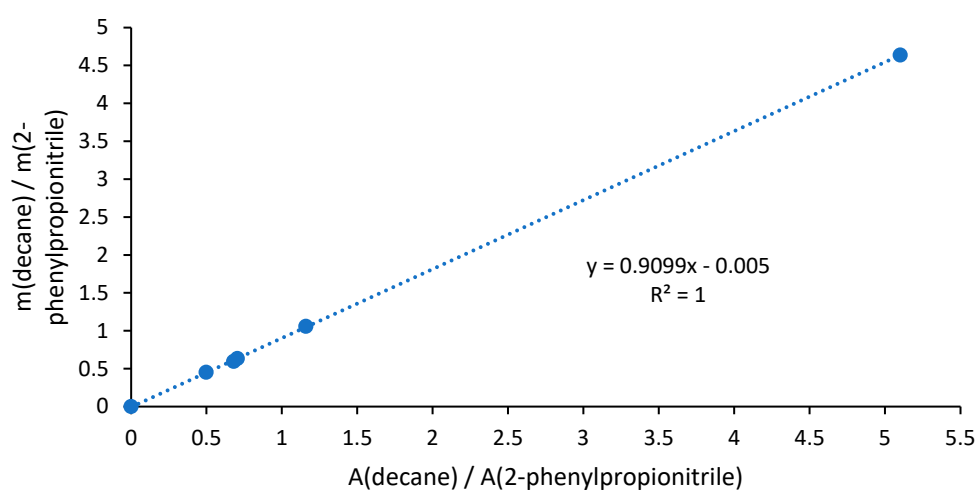


Figure S4. GC-FID Calibration of 2-phenylpropionitrile with n-decane as internal standard.

2.3.2. DBE

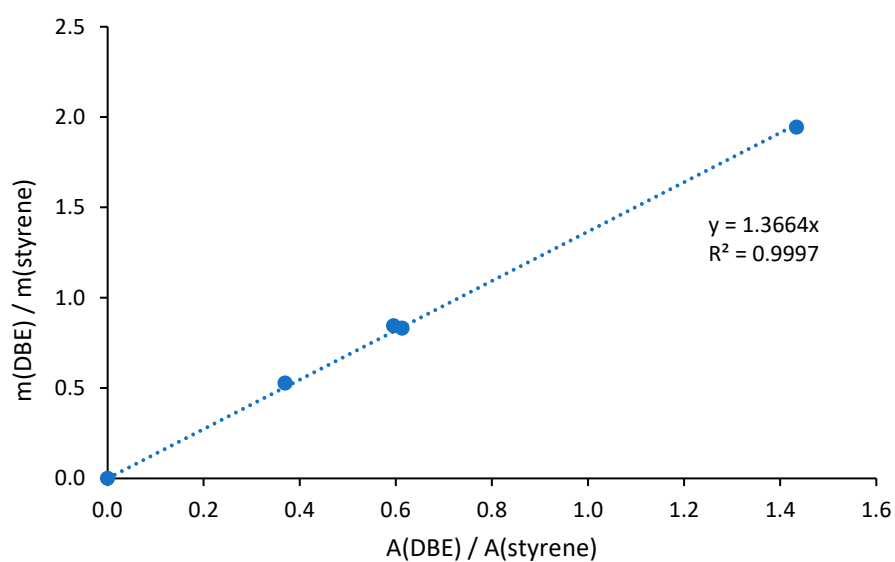


Figure S5. GC-FID Calibration of Styrene with DBE as internal standard.

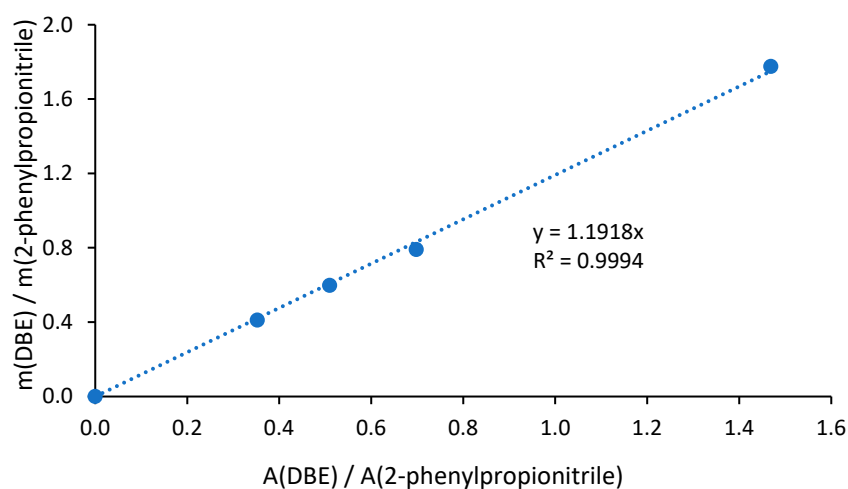


Figure S6. GC-FID Calibration of 2-phenyl propionitrile with DBE as internal standard.

2.4. Calculation of conversion (X), yield (Y), and selectivity (S)

The mass of styrene m_{Styrene} within a GC sample is calculated with the weighed mass of the n -decane m_{Decane} , the areas A of the chromatogram and the calibration factor R_f using formula (S1):

$$m_{\text{Styrene}} = \frac{m_{\text{Decane}} \cdot A_{\text{Styrene}}}{A_{\text{Decane}} \cdot R_f} \quad (\text{S1})$$

The mass was then converted into the amount of substance n via Formula (S4) in order to calculate the conversion X , the yield Y and the selectivity S of the hydrocyanation according to Formulas (S2–S5):

$$n_{\text{styrene}} = \frac{m_{\text{styrene}}}{M_{\text{styrene}}} \quad (\text{S2})$$

$$X = \frac{n_{\text{styrene}}}{n_{0,\text{styrene}}} \quad (\text{S3})$$

$$Y = \frac{n_{\text{nitriles}}}{n_{0,\text{styrene}}} \quad (\text{S4})$$

$$S = \frac{Y}{X} \quad (\text{S5})$$

2.5. Calculation of TON

$$TON = \frac{n_{\text{nitrileproduct}}}{n_{\text{catalyst}}} \quad (\text{S6})$$

2.6. Calculation of TOF_{20}

Turn-Over-Frequency was determined at a conversion of 20%. Time when conversion is exactly 20% is calculated based on a fit.

$$TOF_{20} = \frac{0.2 n_{0,\text{styrene}}}{n_{\text{catalyst}} \cdot t} \quad (\text{S7})$$

3. NMR-Analysis of Catalyst Preforming

A Magritek Spinsolve 60ultra Phosphorus was used to investigate catalyst preforming and reaction solutions via $^{31}\text{P}\{^1\text{H}\}$ -NMR analysis.

3.1. Catalyst preforming at room temperature

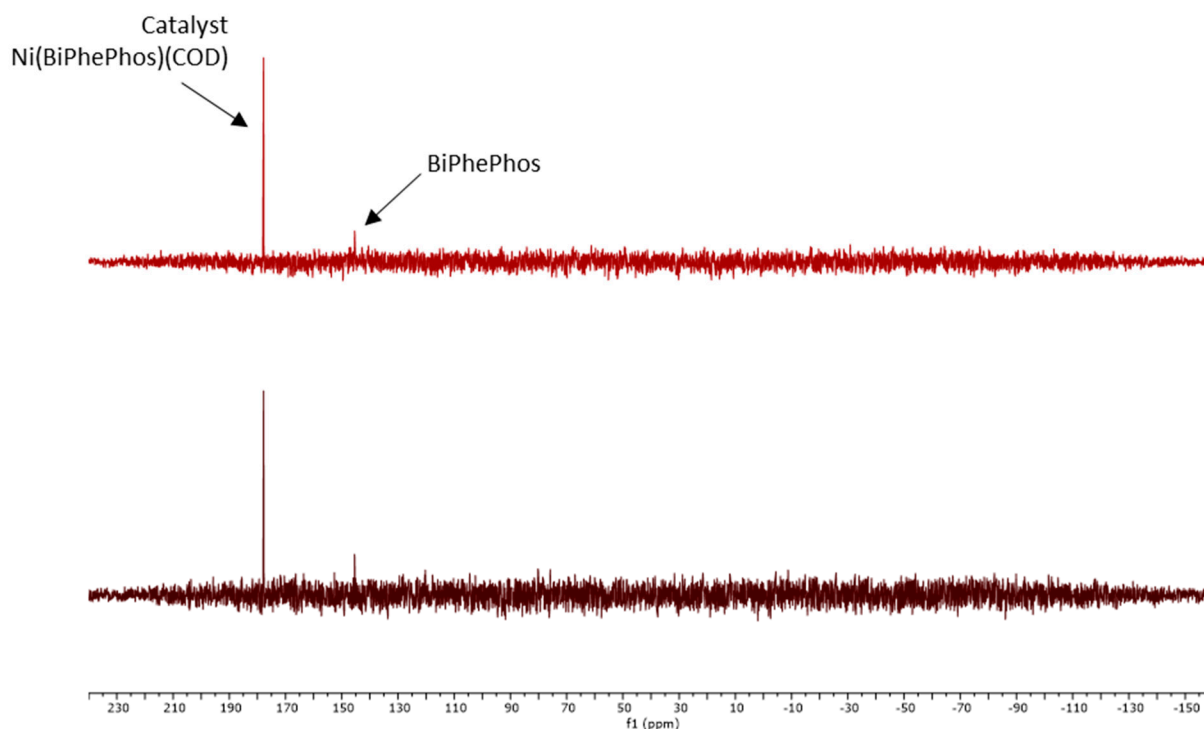


Figure S7. $^{31}\text{P}\{^1\text{H}\}$ -NMR (162 MHz, toluene) of the preformed catalyst at room temperature. Conditions: $\text{Ni}(\text{cod})_2$ (13.8 mg, 5 mmol, 1 eq) and BiPhePhos (56.8 mg, 7 mmol, 1.2 eq) were weighed out, dissolved in toluene (3 mL) and stirred. Top: 4 h, bottom: 8 h.

3.2. Catalyst preforming at 90 °C

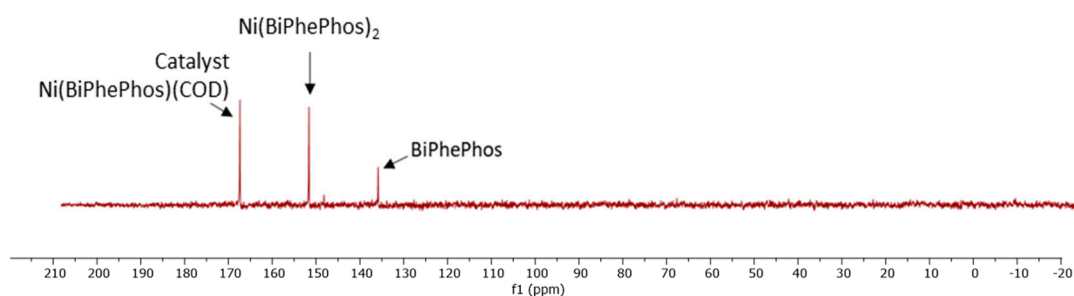


Figure S8. $^{31}\text{P}\{^1\text{H}\}$ -NMR (162 MHz, toluene) of the preforming solution at 90 °C. Reaction conditions: $\text{Ni}(\text{cod})_2$ (13.8 mg, 5 mmol, 1 eq) and BiPhePhos (48.7 mg, 6 mmol, 1.2 eq) were dissolved in toluene (3 mL) and stirred (90 °C, 4 h).

4. X/t-plots

4.1. Room temperature (22 °C)

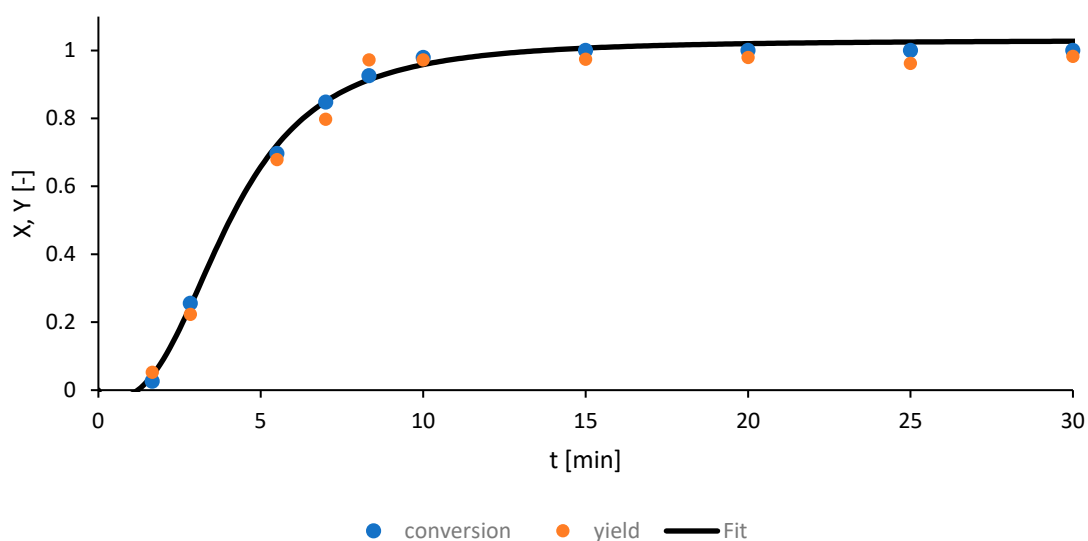


Figure S9. Conversion/time-plot of the hydrocyanation of styrene: Reaction conditions: BiPhePhos (11.8 mg, 0.015 mmol) is dissolved in toluene (5 mL) and Ni(cod)₂ (3.4 mg, 0.013 mmol, 0.5 mol%) is added. Styrene (260.5 mg, 2.5 mmol, 1 eq.) and dibutyl ether (168.6 mg) are added as internal GC standard at 22 °C. HCN (125 µL, 3.125 mmol, 1.25 eq.) is dissolved in cold toluene (2.5 mL) in a separate flask and added to the reaction mixture.

$$\text{Fit } X(t) = 1.030384 - (1.062332354) * (1 + (x/4.04457)^{-2.894674})$$

4.2. 60 °C

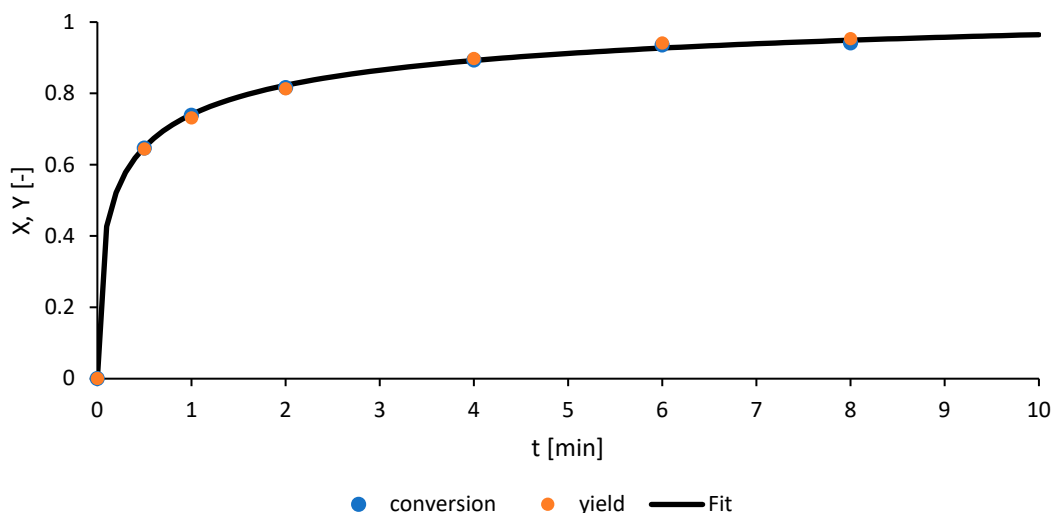


Figure S10. Conversion/time-plot of hydrocyanation of styrene with reduced amount of solvent: reaction conditions: BiPhePhos (11.8 mg, 0.015 mmol) is dissolved in toluene (0.5 mL) and Ni(cod)₂ (3.4 mg, 0.013 mmol, 0.5 mol%) is added. Styrene (260.5 mg, 2.5 mmol, 1 eq.) and dibutyl ether (174.3 mg) are added as an internal GC standard. The reaction mixture is placed inside of an oil bath at 60 °C for 5 minutes to reach 60 °C. HCN (125 µL, 3.125 mmol, 1.25 eq.) is dissolved in cold toluene (0.75 mL) in a separate flask and added to the reaction mixture. X and Y based on GC analysis with DBE as internal standard.

$$\text{Fit: } X(t) = 1.12083 - (1.12081 / (1.94729 t^{0.501044} + 1))$$

4.3. 90 °C

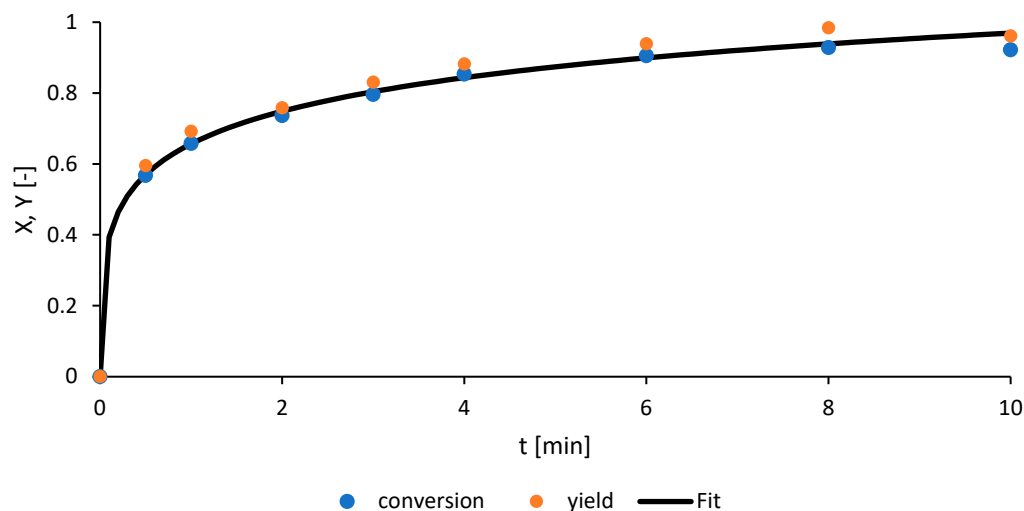


Figure S11. Conversion/time-plot of hydrocyanation of styrene with reduced amount of solvent: reaction conditions: BiPhePhos (11.8 mg, 0.015 mmol) is dissolved in toluene (0.5 mL) and Ni(cod)₂ (3.4 mg, 0.013 mmol, 0.5 mol%) is added. Styrene (260.5 mg, 2.5 mmol, 1 eq.) and dibutyl ether (174.3 mg) are added as an internal GC standard. The reaction mixture is placed in an oil bath at 90 °C for 5 minutes to reach 90 °C. HCN (125 µL, 3.125 mmol, 1.25 eq.) is dissolved in cold toluene (0.75 mL) in a separate flask and added to the reaction mixture. X and Y based on GC analysis with DBE as internal standard.

$$\text{Fit: } X(t) = 173.9178 - (173.914511644 / (1 + (t/4.83886)^{0.3170879}))$$

5. Temperature profile with toluene at r.t.

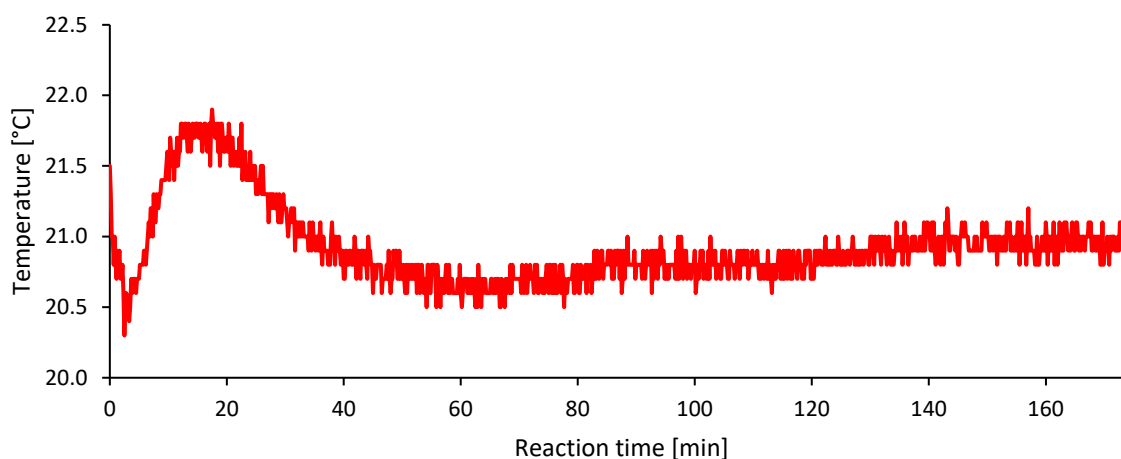


Figure S12. Temperature profile of hydrocyanation of styrene without precooling of HCN: Reaction conditions: BiPhePhos (4.7 mg, 0.006 mmol) was dissolved in toluene (2 mL) and Ni(cod)₂ (1.4 mg, 0.005 mmol, 0.5 mol%) was added. Styrene (104 mg, 1 mmol, 1 eq.) was added. HCN (50 µL, 1.25 mmol, 1.25 eq.) was dissolved in toluene (1 mL) in a separate flask and added to the reaction mixture. After the reaction time of 3 h at room temperature, n-decane was added as an internal standard after the reaction. The temperature was recorded with an EnviroPad-TC thermometer.