A Survey of Acid Catalysts for Use in Two-Step, One-Flask Syntheses of Meso-Substituted Porphyrinic Macrocycles

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Supporting Information

Experimental Section

Materials. Pyrrole (Acros) was distilled from calcium hydride and stored at –15 °C until use. The distilled pyrrole was used prior to any discoloration. CH_2Cl_2 (Fisher, ACS grade) was distilled from potassium carbonate and stored over 4-Å Linde molecular sieves. Benzaldehyde (Aldrich, 99.5%) and DDQ (Aldrich) were used as received. All acids were purchased from Aldrich and used as received except for Montomorillonite K10 which was activated for 3 h at 120 ºC at < 1 torr. No special precautions were taken to avoid contact of the acids with the atmosphere, although dispensing of acids was done as quickly as possible and containers were kept tightly closed as much as possible.

Preliminary Acid Screening Experiments. *Soluble acids.* To a 20-mL vial containing a micro stir bar, 10 mL of a freshly prepared stock solution of 10 mM pyrrole and 10 mM benzaldehyde in CH_2Cl_2 was added via a solvent pump. Reactions were initiated by addition of the acid (neat, 1 M solution, or 100 mM solution in CH_2Cl_2). Acid concentrations from 0.32 to 320 mM were typically examined, though in some cases acid concentrations as low as 0.01 mM and as high as 1 M were examined. Reactions were monitored at 15 min, 1 h, and 4 h by transferring a 50 μL aliquot to a vial containing 300 μL of a 10 mM solution of DDQ in toluene. After addition of 1 μL of triethylamine, the UV-vis spectrum was recorded of a 30 μL portion of the oxidized aliquot diluted by 3 mL of CH_2Cl_2 / EtOH (3:1). The TPP yield was calculated as reported previously.[1]

Insoluble Acids. The acids were preweighed into 20-mL vials followed by addition of a micro stir bar. The reactions were initiated by the addition via a solvent pump of 10 mL of a freshly prepared stock solution of 10 mM pyrrole and 10 mM benzaldehyde in CH_2Cl_2. The reactions were monitored as described above.

Determination of Yields of TPP, TPS, and NC-TPP. Into a 100-mL round bottom flask, CH_2Cl_2 (45 mL), pyrrole (31.2 μL, 0.45 mmol), and benzaldehyde (45.7 μL, 0.45 mmol) were added. The reaction was initiated by the addition of acid. The reactions were monitored at 1 min, 4 min, 8 min, 15 min, 30 min, 1 h, 2 h, 4 h, 8 h, and 24 h by transferring a 2-mL aliquot to a vial containing DDQ (5 mg, 0.02 mmol). Triethylamine was added (8-fold relative to acid

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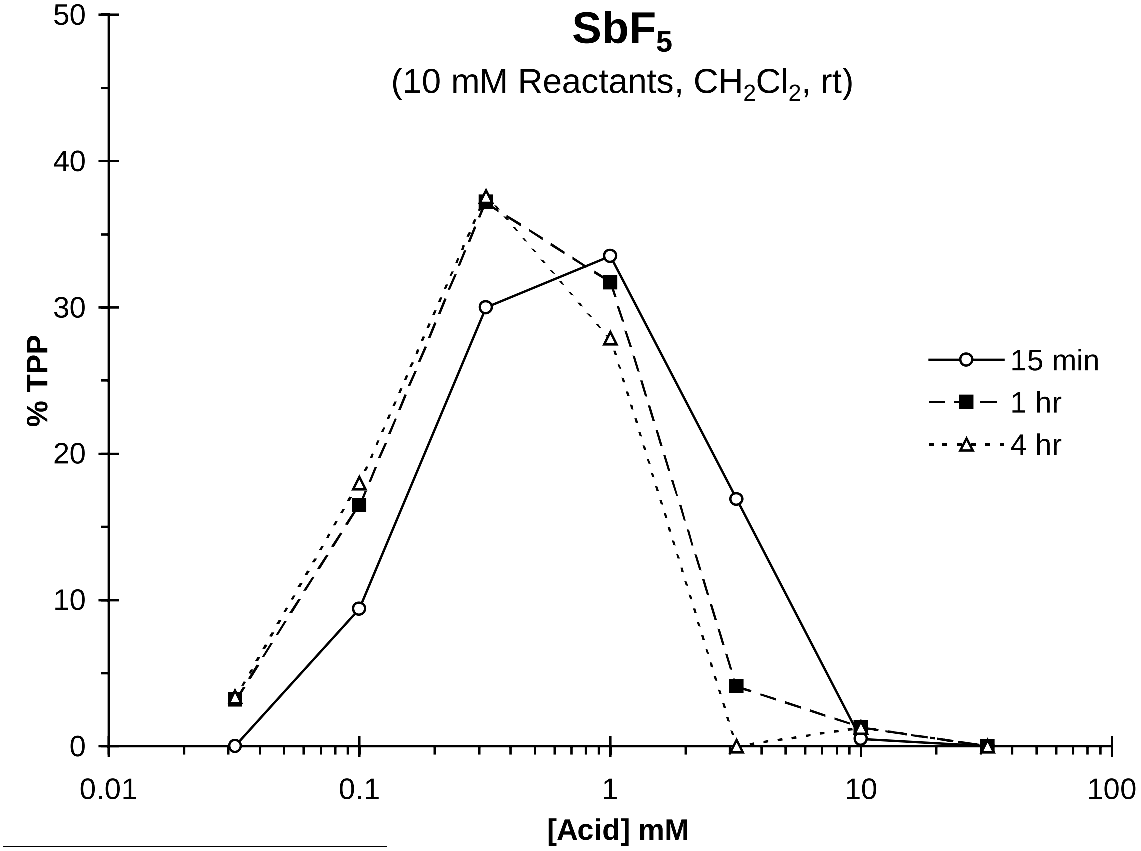
(1) Lindsey, J.S.; Schreiman, I.C.; Hsu, H.C.; Kearney, P.C.; Marguerettaz, A.M. *J. Org. Chem.* **1987**, *52*, 827-836.

concentration up to 50 μL). UV-vis and HPLC analyses were done as described previously[1,2] with only key details repeated here. Prior to HPLC analysis, an aliquot of the crude, oxidized reaction mixture (1.5 mL) was passed through a pipet column containing 1.4 g of basic alumina (activity II). The sample was eluted with three 1-mL portions of CH_2Cl_2 and 1-2 drops of TEA (to ensure all NC-TPP passes through the column). The solvent was driven off the column by application of mild pressure using a handheld pipet tool. The eluant was transferred immediately to an autosampler vial and capped. HPLC analysis was performed using a Hewlett-Packard 1100 series HPLC with a quaternary pump, an autosampler, thermostated column compartment at 25 ºC, and a diode array UV-vis detector. A silica gel analytical column was used (Alltech, Altima, 4.6 mm by 250 mm) with an isocratic solvent mixture of 92.5% hexanes and 7.5% acetone. (The hexanes was 50% water saturated by mixing equal volumes of dry hexanes and hexanes stored over water.) The solvent flow rate was controlled as follows: t = 0 to 5 min, 1 mL/min; t = 5 to 7 min, linear increase to 2.5 mL/min; t = 7 to 10.5 min, 2.5 mL/min; t = 10.5 to 11.5 min, linear decrease to 1 mL/min; and t = 11.5 to 13 min, 1 mL/min. The solvent front occurred at 2.5 min, TPP eluted at 5.0 min, TPS at 7.9 min, and NC-TPP at 9.9 min. Detection was performed at the following wavelengths: TPP, 417 nm and 590 nm; TPS, 490 nm; and NC-TPP, 438 nm.

Illustrative Data from Acid Screening Experiments

An illustrative plot of TPP yield as a function of acid concentration for SbF_5 shows that SbF_5 catalyzes the condensation leading to TPP formation, and the approximately optimal acid concentration is 0.32 mM.



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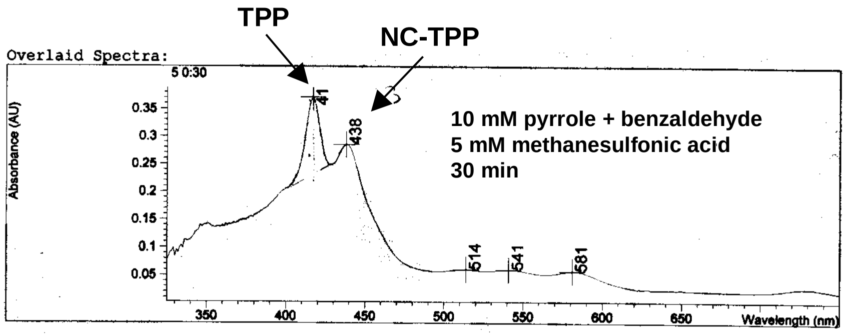
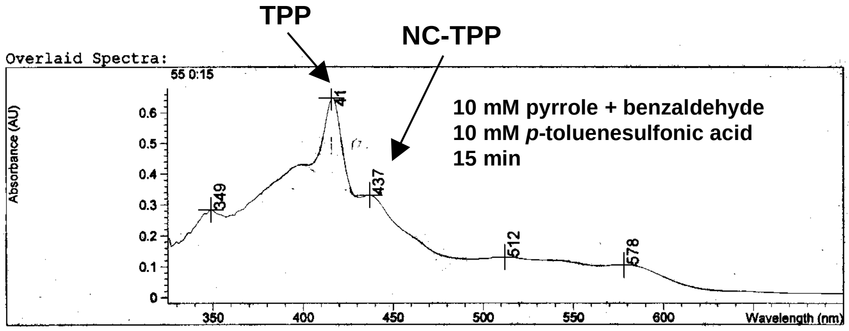
(2) Geier, G. R., III; Lindsey, J. S. *J. Org. Chem.* **1999**, *64*, 1596-1603.

Detection of NC-TPP During Preliminary Acid Screening

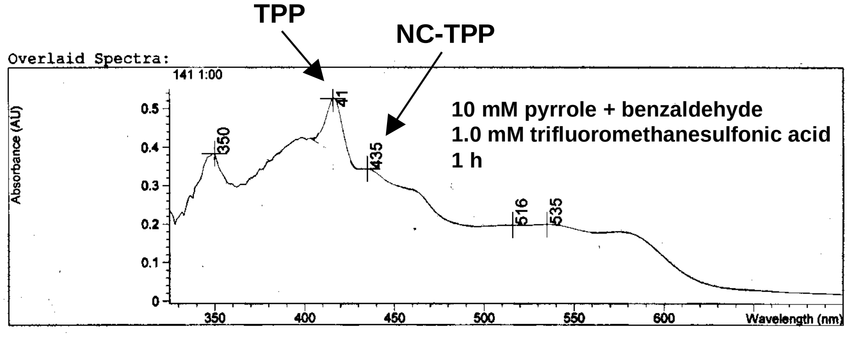
The preliminary acid experiments also allowed detection of reaction conditions providing high yields of other porphyrinic products. For example, methanesulfonic acid catalysis giving rise to significant NC-TPP produced a peak at 438 nm (characteristic of the NC-TPP Soret band) in the UV-vis spectrum of the crude, oxidized reaction mixture. Thus, prior to more detailed experiments, it was clear that methanesulfonic acid was a good catalyst for NC-TPP formation. The yield of NC-TPP could not be determined precisely from this UV-vis data alone, though a lower limit could be estimated as only samples containing at least ~10% NC-TPP provided a detectable NC-TPP Soret band. Exact NC-TPP yields were determined in subsequent experiments involving HPLC analysis. The NC-TPP Soret band was also detected in preliminary screening experiments involving *p*-toluenesulfonic acid and trifluoromethanesulfonic acid—albeit to a lesser extent. The NC-TPP Soret band was not detected for any other acids. No peaks corresponding to TPS were detected from any acids at any concentration in this preliminary screen.



10 mM pyrrole + benzaldehyde
5 mM methanesulfonic acid
30 min



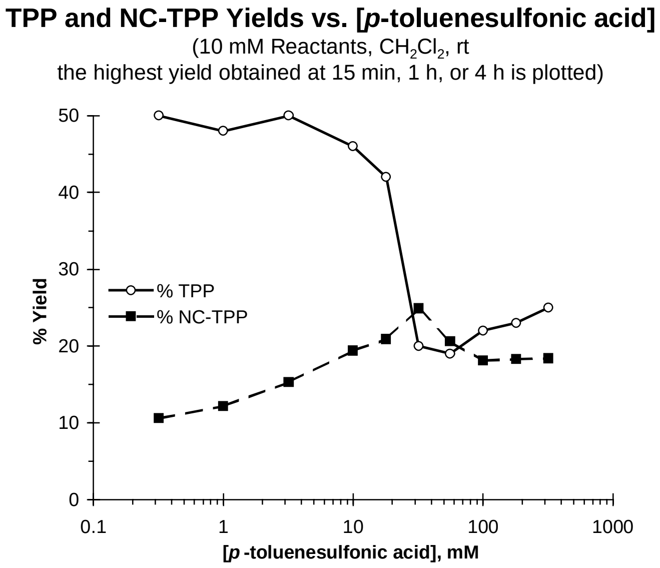
10 mM pyrrole + benzaldehyde
10 mM *p*-toluenesulfonic acid
15 min



10 mM pyrrole + benzaldehyde
1.0 mM trifluoromethanesulfonic acid
1 h

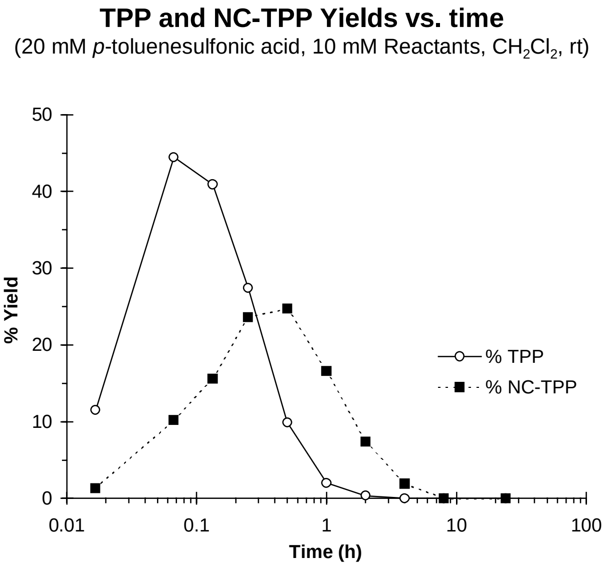
Identifying the Maximum Yield of NC-TPP from *p*-Toluenesulfonic Acid and Trifluoromethanesulfonic Acid Catalysis

Due to the ~10% yields of NC-TPP observed during experiments at acid concentrations optimal for TPP formation and to the detection of the NC-TPP Soret band in preliminary acid screening experiments, further experiments were performed to determine the maximum yield of NC-TPP from each acid. Determination of NC-TPP as a function of acid concentration showed that ~20 mM *p*-toluenesulfonic acid and ~1.0 mM trifluoromethanesulfonic acid provided the highest yields of NC-TPP. NC-TPP yield as a function of time (note the log scale) was monitored for 20 mM *p*-toluenesulfonic acid, where a maximum yield of NC-TPP (25%) was obtained at 30 min.



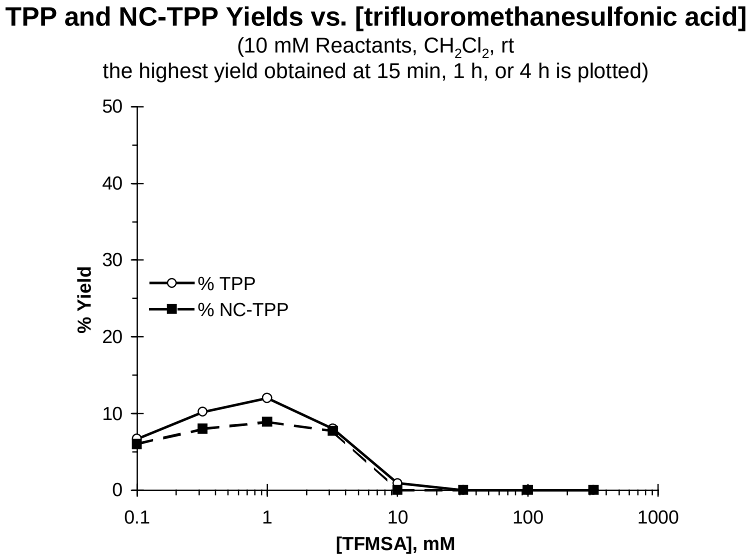
TPP and NC-TPP Yields vs. [*p*-toluenesulfonic acid]

(10 mM Reactants, CH_2Cl_2, rt
the highest yield obtained at 15 min, 1 h, or 4 h is plotted)



TPP and NC-TPP Yields vs. time

(20 mM *p*-toluenesulfonic acid, 10 mM Reactants, CH_2Cl_2, rt)



TPP and NC-TPP Yields vs. [trifluoromethanesulfonic acid]

(10 mM Reactants, CH_2Cl_2, rt
the highest yield obtained at 15 min, 1 h, or 4 h is plotted)