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Organocatalysis

A Microporous Binol-Derived Phosphoric Acid**

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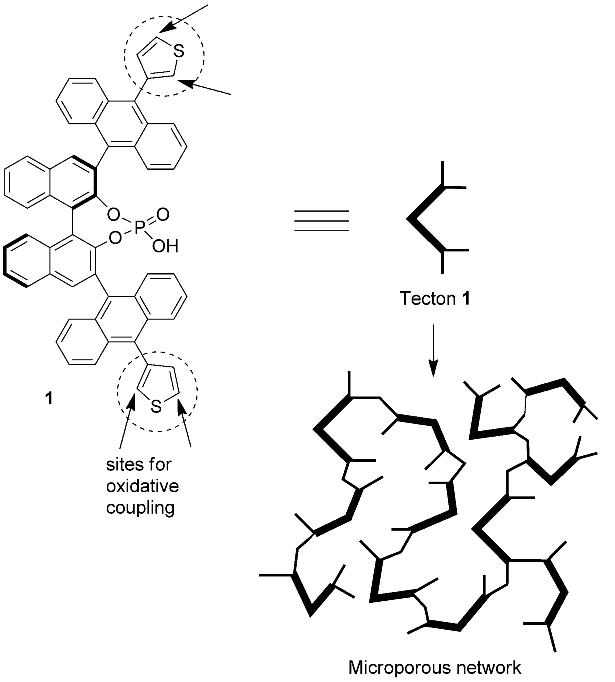
Dedicated to Professor Ekkehard Winterfeldt on the occasion of his 80th birthday

During the last decade, organocatalysis has emerged as an important tool for a rapidly expanding range of synthetic transformations.[1] Like metal catalysis, organocatalysis also provides tremendous opportunities in the field of asymmetric catalysis.[2] In particular, binol-derived phosphoric acid catalysis[3] has been applied successfully for many asymmetric reactions, such as transfer hydrogenation,[4] hydrocyanations,[5] Aldol-type[6] and Friedel–Crafts-type reactions,[7] or the Baeyer–Villiger reaction[8] in recent years. Their success in homogeneous reactions is undisputed but the drawback is still the recovery of the expensive catalysts. Therefore it is desirable to design heterogeneous catalysts,[9] especially because often up to 20 mol % of the catalyst has to be used.

Over the years, several methods have been developed to immobilize catalysts.[10] In the field of organocatalysis, several catalysts have already been immobilized successfully, such as proline[11] and diarylprolinol silyl ether.[12] Very recently, polymer-supported catalysts based on binol (1,1′-binaphthalene-2,2′-diol)-derived phosphoric acids have been prepared by the Rueping group.[13] However, these types of polymer-supported catalysts often show slower reaction rates compared to their homogeneous counterpart because of lower accessibility of the catalytic center.[14] Recently we reported on a concept using binol-derived tectons to generate a microporous polymer network.[15]

Such a polymer network, which only contains the molecular catalyst, ensures a high density and accessibility of catalytic centers and thus fast reaction rates. A variety of functional organic tectons have been applied recently to generate microporous polymers.[16] Also few examples have been applied as organocatalysts or in asymmetric catalysis.[17] To build up porous polymers from catalytically active tectons, polymerizable groups have to be introduced. Depending on the functionality, different types of polymerization, such as Sonogashira,[18] Suzuki,[19] Yamamoto,[20] or oxidative coupling can be applied.[21] We chose 1,1′-binaphthalene-2,2′-diyl hydrogenphosphate (BNPPA) with 9-anthracenyl as bulky groups in 3,3′-positions as a starting tecton. This compound is known to catalyze Strecker reactions,[9] Friedel–Crafts alkylation, and aza-ene-type reactions[22] with good selectivity. To couple BNPPA units, we decided to introduce a 3-thiophenyl group at the 10-position of the anthracene units. Thiophenes of this type can be coupled under mild oxidative coupling condition using $FeCl_3$. As the thiophene unit is connected at 3-position, it has two free sites (2,5-positions) for oxidative coupling,[23] enabling the formation of a network (Scheme 1).



Scheme 1. Strategy to assemble a chiral microporous polymer.

Starting from dimethylated (*R*)-binol, the diboronic acid **2** was synthesized as precursor for the Suzuki coupling reaction.[24] Double coupling with 3-(10-bromoanthracen-9-yl)-thiophene led to structure **4** (Scheme 2) in good yields. Subsequent cleavage of the methyl ether with BBr_3 and treatment with phophorous oxychloride gave the BNPPA chloride **5**. The corresponding phosphoric acid **1**, obtained in overall 74 % yield by hydrolysis of **5**, is not suitable for oxidative coupling owing to solubility issues. However, the $FeCl_3$-mediated reaction is successful, with the highly soluble **5** affording polymeric acid chloride **6**. Hydrolysis of **6** with

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[**] This work was supported by the Cluster of Excellence “Unifying Concepts in Catalysis” and the “Berlin International Graduate School of Natural Sciences and Engineering”. Binol = 1,1′-binaphthalene-2,2′-diol.

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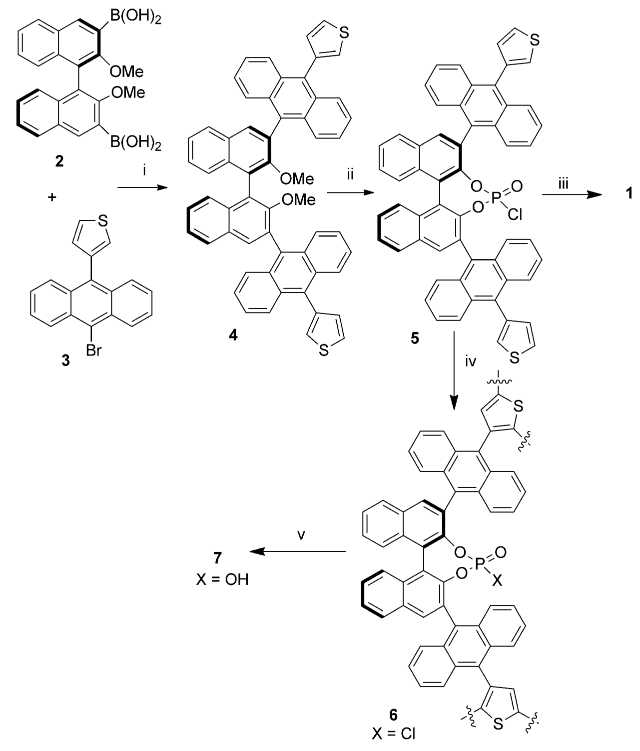


Scheme 2. Synthesis of the polymer network. Conditions: i) [Pd(PPh_3)$_4$], K_2CO_3, THF/H_2O, 80 °C; ii) a) BBr_3, CH_2Cl_2, b) poly(4-vinyl pyridine), $POCl_3$, CH_2Cl_2; iii) THF, 1 M HCl, RT; iv) $FeCl_3$, toluene, acetonitrile; v) aqueous HCl.

aqueous HCl and multiple washing with ethanol, THF, and $CHCl_3$ gave the desired iron-free material **7** as a powder, which was insoluble in solvents such as ethanol, THF, $CHCl_3$, and CH_2Cl_2 (80 % yield).

Nitrogen sorption of the polymer network **7** showed an isotherm typical for microporous materials. The surface area, calculated by the BET method, is 386 $m^2 g^{-1}$, which should enable good accessibility of the catalytically active centers (Figure 1).

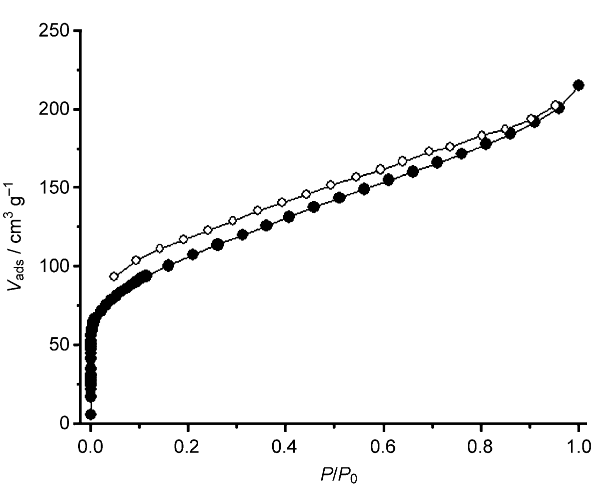
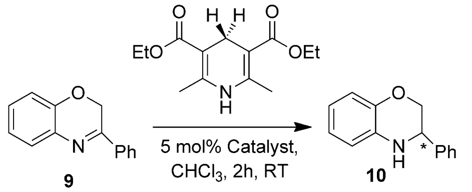


Figure 1. Nitrogen adsorption isotherm of polymer network **7**. ● Adsorption, ○ desorption.

We expected the new monomer BNPPA **1** should have similar steric effects at the phosphoric acid center like the commercially available (*R*)-3,3′-bis(9-anthracenyl)-1,1′-binaphthyl-2,2′-diyl hydrogenphosphate **8**. Therefore, we compared **1** with **8** and network **7**. The porous polymer network was first tested as a catalyst in the asymmetric transfer hydrogenation of prochiral benzoxazines. The 3,3′phenanthrenyl-substituted BNPPA catalyst has been shown to afford the best result, with 98 % enantioselectivity for asymmetric transfer hydrogenation of 3-phenyl-2*H*-1,4-benzoxazine.[25] Using the commercially available 9-anthracenyl substituted BNPPA (**8**) as a catalyst, we obtained 95 % *ee* (Table 1). Enantioselectivity of this reaction could be even increased by the new BNPPA (**1**) to 99 % *ee*. With network **7**, we achieved an *ee* of 98 %, which is comparable to the result of catalyst **1** and even better than **8**. This result shows that nearly no loss in selectivity occurs when switching over to heterogeneous catalysis.

Table 1: Asymmetric hydrogenation of 3-phenyl-2*H*-1,4-benzoxazine.



Entry	Catalyst	Conversion[a] [%]	*ee* [%][b]
1	**8**	99	95 (*S*)
2	**1**	99	99 (*S*)
3	network **7**	99	98 (*S*)

[a] Yield of isolated product 91 %; conversion checked by ^1H NMR spectroscopy. [b] *ee* determined by HPLC using an Chiracel OD-H column.

In a recent example,[13] Rueping and co-workers immobilized binol-derived phosphoric acid structure into a polymer-supported catalyst. Using 5 mol % of their polymer-supported catalyst, a 20–24 h reaction time was required to achieve full conversion and 94 % *ee* for asymmetric hydrogenation of 3-phenyl-2*H*-1,4-benzoxazine. With our catalyst, the same reaction was complete within 2 h with 5 mol % of the soluble catalyst **1** or with the same weight percentage of the insoluble network **7**. The reaction rate with heterogeneous catalyst **7** was monitored by kinetic experiments and found to be as fast as with homogeneous catalyst **1** owing to the microporous nature and high surface area of our heterogeneous catalyst.

The heterogeneous catalyst **7** can be easily separated by centrifugation and reused for further repeating runs. For each run, 99 % conversion and 98 % *ee* was observed. Even after 10 runs, the catalyst works without any loss in activity or selectivity (Figure 2). Furthermore, we performed hot extraction experiments to check if the catalysis is truly heterogeneous in nature or not. After 50 % conversion of substrate **9**, we filtered out catalyst **7**, and even after 24 h we observed no further conversion of substrate **9** to product, which shows that the catalysis is exclusively heterogeneous.

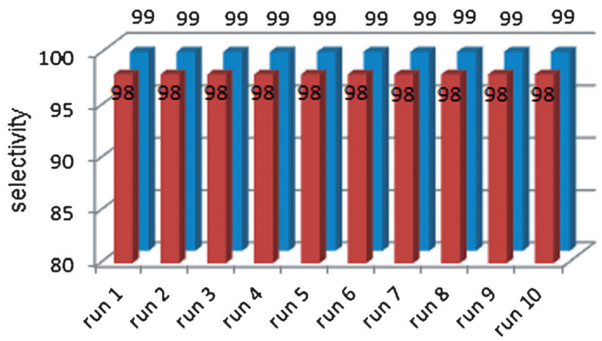
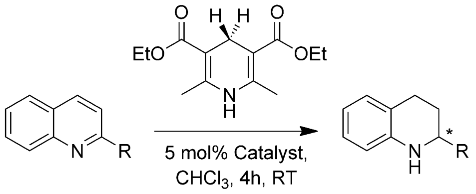


Figure 2. Repeated runs using recycled network **7** as catalyst. 🟥 % *ee*, 🟦 % conversion.

To establish the versatility of our BNPPA network, it was also used in asymmetric transfer hydrogenation reactions with other substrates. The tetrahydroquinoline structure is a very important structural motif in many natural products and bioactive molecules, and binol-derived phosphoric acids have been used in the asymmetric transfer hydrogenation reaction of 2-aryl quinolines.[26] Therefore, polymer network **7** was used as heterogeneous catalyst in the reduction of 2-aryl quinolones. The results (Table 2) show that the performance of the polymer network is again comparable to the homogeneous reaction and gives high selectivity for different aryl substituents.

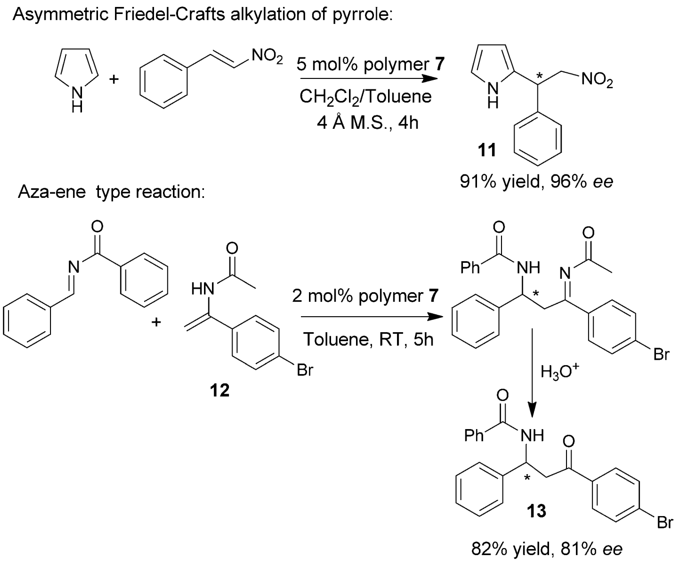
Table 2: Asymmetric hydrogenation of 2-aryl quinolines.



Entry	Catalyst	R	Conversion [%]	*ee* [%]
1	**1**	phenyl	99	98 (*S*)
2	polymer **7**	phenyl	99	97 (*S*)
3	polymer **7**	1-naphthyl	99	94 (*S*)
4	polymer **7**	3-methoxyphenyl	99	87 (*S*)

Apart from hydrogenation reactions, BNPPA-derived catalysts are extensively used for C–C bond-formation reations. Sheng and co-workers reported an efficient Brønsted acid catalyzed asymmetric Friedel–Crafts alkylation of pyrroles.[27] Pyrroles are often present as the core in many natural products and pharmaceuticals.[28] Network **7** was used for asymmetric Friedel–Crafts alkylation of unprotected pyrrole with nitroalkene. The reaction in a mixture of DCM and toluene at room temperature afforded a yield of 91% with a selectivity of 96% *ee* (*R*).

Chiral Brønsted acids are very useful in asymmetric addition of nucleophiles to imines. The imines can be activated by protonation followed by an attack of a nucleophile, resulting in chiral products. The Strecker reaction, aza-ene-type reactions, and many other reactions are catalyzed in this fashion. Terada and co-workers have reported the addition of enecarbamate and enamide to N-benzoylaldimine.[22] This is an efficient method to prepare chiral β-amino ketones. To demonstrate the broader scope of network **7**, we also carried out an aza-ene-type reaction (Scheme 3). Addition of enecarbamate **12** to freshly prepared N-benzoylaldimine and subsequent hydrolysis afforded the β-amino ketone **13** in 82% yield and 81% *ee* (*R*).



Scheme 3. Asymmetric Friedel–Crafts alkylation of pyrrole and an aza-ene-type reaction catalyzed by BNPPA-based network **7**.

In conclusion, we have synthesized a new chiral BNPPA-derived heterogeneous catalyst with high permanent surface area, which is highly active and selective in asymmetric organocatalysis, such as transfer hydrogenation, aza-ene-type reactions and the asymmetric Friedel–Crafts alkylation of pyrrole. The catalyst is stable, easily separable, and can be reused several times. This porous material is a new type of a heterogeneous phosphoric acid with a porous structure with all the benefits of heterogeneous catalysis without any loss in activity and selectivity. The reaction rates are comparable with those of the soluble catalyst.

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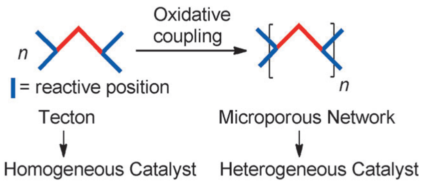
Communications

Organocatalysis

D. S. Kundu, J. Schmidt, C. Bleschke,
A. Thomas,* S. Blechert* ___ ▮▮▮▮–▮▮▮▮

A Microporous Binol-Derived Phosphoric Acid



No slow down: A microporous recyclable heterogeneous catalyst made from a 1,1′-binaphthalene-2,2′-diol (binol)-derived phosphoric acid chloride is as active as the corresponding homogeneous catalyst when using the same mass of both in different reactions. Reaction rates, yields, and enantioselectivities are comparable.