

Synthetic Nitrogen-containing Polymers and their Application as Copper Supports in Click Chemistry

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ABSTRACT

Two nitrogen-containing polymers were synthesized and used as support for CuSO₄ to evaluate their catalytic activity in 1,3-heterodipolar cycloaddition reactions (1,3-DC) of benzylazide and ethyl propiolate. Polyvinylimidazole (PVI-DVB) was obtained by vinylimidazole polymerization with divinylbenzene and polystyryl pyridine (PSP) was prepared by condensation of lutidine and terephthaldehyde and with collidine as the reticulating agent. The activity was measured by titration with standard HCl solution, and PVI-DVB showed 4.6 mEg/g and PSP 0.7 mEg/g polymer. Impregnation with copper was possible by stirring the polymers in aqueous CuSO₄ solution. PSP fixed less copper (~0.2 %) than PVI-DVB that fixed thirty times more (6.2 %). The 1,3-DC under microwave irradiation, in the presence of PSP-Cu or PVI-DVB-Cu, gave origin to quantitative yields of the triazoles, and 1,4 regioisomer was the main product. By reusing the copper supported (4X), no changes in yields were observed, only a small decrease in regioselectivity.

Keywords: Polyvinylimidazole Divinylbenzene, Polystyryl Pyridine, Copper Supported, Click Chemistry

I. INTRODUCTION

The methodology of ‘solid phase’ synthesis was first described in the literature by Merrifield and since then the use of this approach in organic preparations has expanded from laboratorial protocols to industrial processes.¹

Solid supported reagents are easily removed from reactions by filtration and recycling of recovered reagents is economical, environment-friendly and efficient.

Metal supported polymers have been successfully employed in various catalytic processes and the presence of heterochain polymers containing functional groups of electron pair donors, such as carboxyl, hydroxyl, amino derivative groups, sulfur and phosphorus can be used to attach metals onto the surface of polymers.² Nitrogen-containing heterocyclic compounds are an important class of metal ligands and polymers containing these

groups have been used as a support in the preparation of organic catalysts. Polyvinylpyridines (PVPY)³ and poly-*N*-vinylimidazole (PVI)⁴ are the most representative members of this group.

PVPY are interesting polymer ligands which can act as catalytic supports and the presence of nitrogen atoms in different positions in relation to the main chain affects their complexing ability and hence, should influence their catalytic activity.³ Kureshy *et al.* studied supported manganese salen complexes on 4-vinylpyridine reticulated with DVB and described as a powerful catalyst in the enantioselective epoxidation of styrene.⁵ Spinelli *et al.* reported the ability of poly(4-vinylpyridine) films to protect copper corrosion at acid pH. These films managed to impart a significant level of corrosion resistance to the copper samples and almost 100% efficiency was reached employing this methodology.⁶

PVI was used by Breslow *et al.* as an enzyme mimetic in

transaminase enzyme mimics with hydrophobically bound pyridoxamine derivatives to catalyze the reaction of pyridoxamine A with pyruvic acid to form alanine and pyridoxal in water, as coenzyme mimics.⁷ Other examples of PVI as a catalyst are in the ultrasound assisted aldol condensation reaction of ketones with aromatic aldehydes and allylic arylation/alkenylation of allylic esters with aryl/alkenyl boronic acids and tetraaryl borates.⁸ Rainer *et al.* compared four manufactured PVI copolymers for the solid phase extraction of selected non-steroidal anti-inflammatory drugs.⁹ Styrene-based copolymers and a methacrylate-based cross-linker were used in solid phase extraction with better results. Microwave irradiation has become an interesting alternative source of heating in polymer chemistry and the advances in microwave-assisted polymer synthesis was reviewed by Hoogenboom and Schubert.¹⁰ An example of this application in the preparation of nitrogenated resins is described by Marestin *et al.* in an one-pot polycondensation reaction to obtain poly(arylimidazole).¹¹ PVI and PVI copolymers have also shown effective corrosion inhibition for copper at elevated temperatures and recently as catalyst for dephosphorylation reactions potentiated by ionic micelles.¹²

In this study two nitrogenated polymers were synthesized and used as a support for copper sulfate to evaluate their catalyst activity in 1,3-DC of benzylazide and ethylpropiolate.¹³ Polyvinylimidazole (PVI-DVB) was obtained by vinyl imidazole polymerization with the cross-linker divinylbenzene, under microwave irradiation. The second was a pyridine derivative polymer, obtained by condensation of 2,6-lutidine and terephthalaldehyde and with 2,4,6-collidine as the reticulating agent. Evaluations of these two nitrogenated polymers also included the minimum amount of catalyst necessary, the regioselectivity of the cycloaddition reaction and the reuse of the copper (CuSO_4) support. Also the quantities of copper before and after use were evaluated. some guidelines.

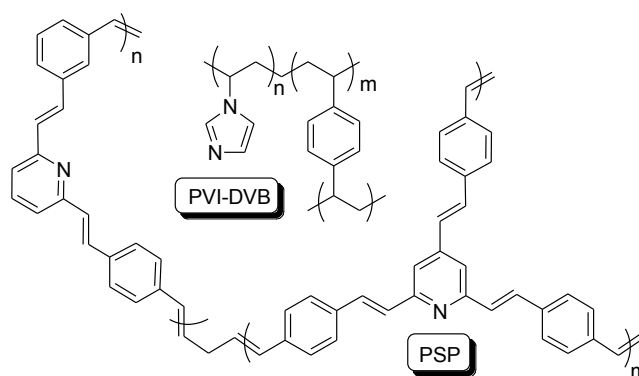


Figure 1. Synthetic Nitrogenated Polymers PSP and PVI-DVB

II. METHODS AND MATERIAL

Reagents and solvents were purchased from Fluka, Merck and Aldrich, and used without any further treatment. The Fourier transform infrared (FTIR) spectra were recorded on Perkin Elmer FTIR-FIT Spectrometer Frontier. Thermogravimetric analyses (TG) were carried out in a Mettler TG 50. The nuclear magnetic resonance (NMR) spectra were obtained on a Varian MR-400 (400 MHz) in CDCl_3 and chemical shifts reported in ppm, referenced to tetramethylsilane (TMS) as the external reference. Elemental analyses were performed using an Thermofinnigan Flash EA 1112 Series instruments. The known products were characterized by FTIR and ^1H NMR spectra. Preparation of PVI-DVB and the 1,3 DC reactions were performed on a microwave synthesis reactor model Anton-Paar Monowave 300.

Preparation of Poly (*N*-vinylimidazole-co-divinylbenzene)

PVI-DVB was prepared based on procedures described in the literature.¹⁴ A solution of 1.0 g of *N*-vinylimidazole (10.6 mmol), 200 mg of divinylbenzene (20 wt%) and 30 mg of benzoyl peroxide (0.12 mmol) as initiator was irradiated by microwave in a sealed tube with an inert atmosphere. The mixture was heated at 100°C for 60 minutes. The polymer was centrifuged and the solvent and excess of reagent were removed. Then the polymer was washed by stirring with methanol (15 ml) for 10 minutes and finally centrifuged to remove the supernatant. This process was repeated three times to remove oligomers and unreacted monomers. Then the polymer was dried in an oven for 24 hours at 50°C yielding 0.32 g of a light brown hard solid.

Preparation of Polystyryl pyridine

PSP was prepared by the condensation of 470 mg of terephthalaldehyde (3.5 mmol) with 109.1 mg of 2,4,6-collidine and (0.9 mmol) and 225.1 mg of 2,6-lutidine (2.1 mmol), in the presence of 1.9 g of acetic anhydride (18.6 mmol). The reaction was subjected to 170°C under conventional heating for 48 hours. Methanol (15 mL) was added to the reaction medium to remove residual reagents. The polymer was dried under vacuum to produced 683.0mg of a hard dark solid.

Determination of polymer activity

To determine the reactive centers of the samples, a 5.00 mL aliquot of 0.1015 M HCl was added to 50.0 mg of each sample and maintained under stirring for 24 h. After this time, the samples were analytically filtered, washed exhaustively with water and titrated with 0.1 M NaOH.

Copper impregnation (general experimental)

A mixture of an aqueous solution of CuSO₄ (100 mL, 20% w/v) and 0.5 g of polymer was maintained under stirring, at room temperature, for 24 h. After agitation the polymer was centrifuged and washed with 20 mL of methanol. The washes were repeated 3 times and then the compound was dried under high vacuum.

General procedure for copper-supported cycloaddition

250 mg of benzylazide (1.9 mmol) and 0.23 mL of ethyl propiolate (2.3 mmol) were added to a 30 mg suspension of a Cu complex (0.5 mol%) in water (5 mL). The mixture was stirred at 100°C for 60 minutes under microwave irradiation in a sealed tube. At the end of the reaction (monitored by TLC) the mixture was washed with 10 mL of methanol, filtered off and the solvent removed by vacuum to produce a white solid. The crude adduct was submitted to ¹H-NMR.

Recycling of the Catalyst

After filtering the reaction mixture, the catalyst was separated, washed with 10 mL of methanol, dried at room temperature overnight, and re-used for the other reactions. The catalyst was recycled four times without appreciable loss of its catalytic properties, Table 1.

Selected Spectral Data for Products of Table 1: ¹H NMR (400 MHz, CDCl₃): δ = 1.35 (t, 3H, J = 7.1 Hz), 4.36 (q, 2H, J = 7.1 Hz), 5.55 (s, 2H), 5.90 (s, 2H), 7.25 - 7.37 (m, 5H), 7.95 (s, 1H) ppm.

III. RESULTS AND DISCUSSION

The imidazole and pyridine polymers were chosen to develop an efficient sorbent of CuSO₄, due to their chelant features and availability of monomers. Free N donor ligands such as imidazole and pyridine have different basicities giving complexes with large differences of dissociation constants.^{3,4,15}

PVI-DVB was obtained by suspension polymerization in a high-pressure glass flask containing benzoyl peroxide (3 wt%), vinylimidazole and divinylbenzene and submitted to microwave irradiations (200 W) for 1 hour at 100°C.¹⁶ After the reaction, the light brown hard solids were chopped into pieces and washed excessively with methanol and dried. No effort was made to optimize the yields obtained and the polymer was immediately analyzed to measure the activity obtained.

PSP was prepared by condensing terephthalaldehyde and 2,6-lutidine with a small amount of 2,4,6-collidine as a crosslinking agent in acetic anhydride, according to Werner.¹⁷ After reflux, the reaction mixture was poured into water and then the resultant solid was washed excessively with methanol and dried. There are very few examples of uses for this polymer in the literature, and only two patents with few citations.¹⁸

The activity of the polymers was measured by titration with standard hydrochloric acid solution to compare the ability of each polymer to complex with copper. The imidazole polymer, PVI-DVB showed more activity than the pyridine-terephthalate copolymers, PSP giving: 4.6 mEg/g and 0.7 mEg/g polymer, respectively. The higher activity of the PVI-DVB, almost seven times more than PSP, is related to the higher basicity of the imidazole nucleus.

The polymers obtained in this work are insoluble in water, at different pHs and in most of the solvents used in a chemical laboratory.¹⁹ In view of this, the impregnations with copper were made in a

heterogeneous phase stirring the polymers in a 30% CuSO₄ water solution for 24 hour. After filtration and exhaustive washing with water and methanol, the dry supported material was used directly in the cycloaddition reactions. PVI-DVB-Cu acquired a bluish color.

PSP fixes less copper (~0.2%) than PVI-DVB that fixed it thirty times more (6.2%). This result may be associated with greater basicity of the imidazole nucleus than pyridine and the nitrogen percentage in meros.^{3,4,16} Additionally, elementary analyses of PSP and PVI-DVB displayed a nitrogen content of 4.9% and 7.3%, respectively, which shows that imidazole and pyridine were incorporated into the polymeric network.

The Fourier transform infrared spectroscopy by attenuated total reflectance (ATR-FTIR) of PSP showed aromatic C-H stretching of the aromatics rings at 3026 cm⁻¹ (Figure 2A). The bands at 1599 and 1559 cm⁻¹ corresponding to double bonds (aromatic C=C / C=N) axial strains stretching. Important bands observed at 960, 814 and 735 cm⁻¹ were related to the C-H bending of aromatic bonds. The strong band observed at 1757 cm⁻¹ was related to carbonyl stretching absorption of terephthalic aldehyde condensation intermediates that had not fully reacted. In PSP-Cu only one small new band was observed at 1774 cm⁻¹ and the rest of the spectrum was very similar to PSP.

PVI-DVB FTIR showed small broad bands between 3400 - 3200 cm⁻¹ of group vibrations associated to the imidazole ring (Figure 2B). Aromatic C-H stretching vibration appeared at 3113 cm⁻¹ as a weak band and another stretching vibration was observed at 2921 cm⁻¹, according to Zhang *et al.* Another small and narrow band observed at 1643 cm⁻¹ is characteristic of the C=C stretching vibration. The band observed at 1497 cm⁻¹ is one of the characteristic bands of the imidazole ring. A narrow peak was observed at 1226 cm⁻¹ and considered to be the C-H bending with C-N stretching of imidazole.

Bending vibrations of the backbone chain contributed to the band at 1085 cm⁻¹ together with the imidazole ring C-H bending. The characteristic band at 661 cm⁻¹ was considered to be the puckering vibration of the imidazole ring. All the bands are in agreement with the FTIR results.¹⁴ In PVI-DVB-Cu the band between 3400 - 3200 cm⁻¹ is broader and the C-H stretching vibration at 3113 cm⁻¹ moved to 3124 cm⁻¹. The most important changed could be observed between 1700 and 600 cm⁻¹. The band at 1643 cm⁻¹ was broad and superimposed the near peaks. The bands observed at 1497 and 1226 cm⁻¹ decreased significantly in intensity and two new strong bands at 1095 cm⁻¹ and 1042 cm⁻¹ appeared. The unequivocally band of imidazole ring at 661 cm⁻¹ remained unchanged in the PVI-DVB-Cu.²⁰

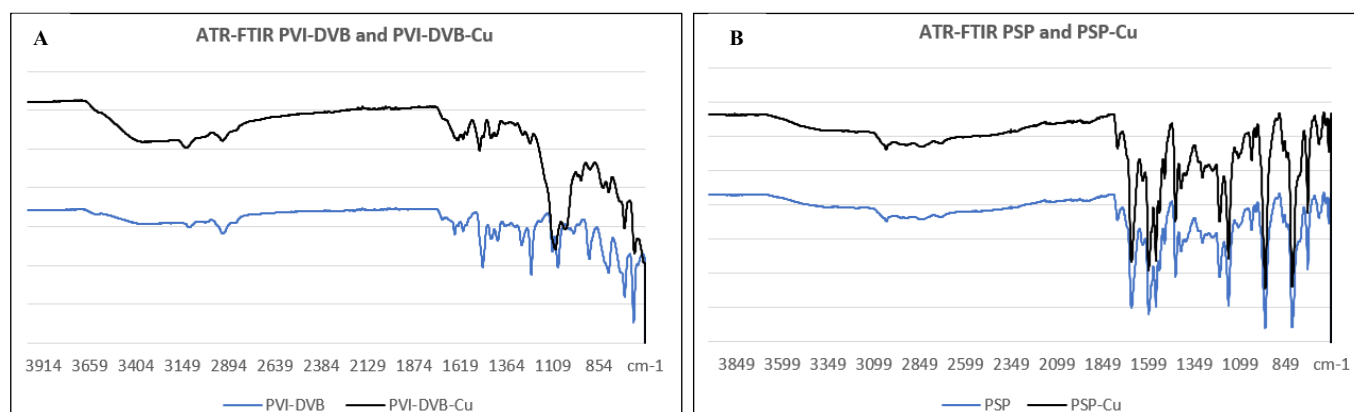


Figure 2. ATR-FTIR of PVI-DVB and PSP

Thermal Gravimetric Analysis (TGA) was performed on PVI-DVB/PVI-DVB-Cu and PSP/PSP-Cu (Figure 3). A small loss of mass was found for PVI-DVB at around 70 and 150°C. After reaching a temperature of 410°C mass loss took place due to polymer decomposition, and on reaching a maximum at 475 °C, there was almost total

mass loss. The general shape of the thermal degradation of PVI-DVB-Cu is similar to PVI-DVB with a slight increase of thermal resistance due to the copper. Mass loss was registered at around 75°C and 150°C and the mass loss related to polymer decomposition began at 380°C and a maximum at 450°C with near total loss

(Figure 3A).

PSP showed an expressive loss of mass at 110°C, which was probably related to water, and then two other mass loss observations were at 190 and 240°C. After reaching 400°C, further mass loss took place reaching a maximum at 550°C and 565°C. A significant change in the thermal degradation profile is observed in PSP-Cu,

(Figure 3B). Mass loss was observed at 60°C and a maximum registered at 305°C. After that, the main thermal degradation of PSP-Cu was observed starting at 400°C and a maximum at 550°C with a behavior similar to PSP. The presence of copper in PSP seems to increase the thermal stability of the polymer matrix slightly.²¹

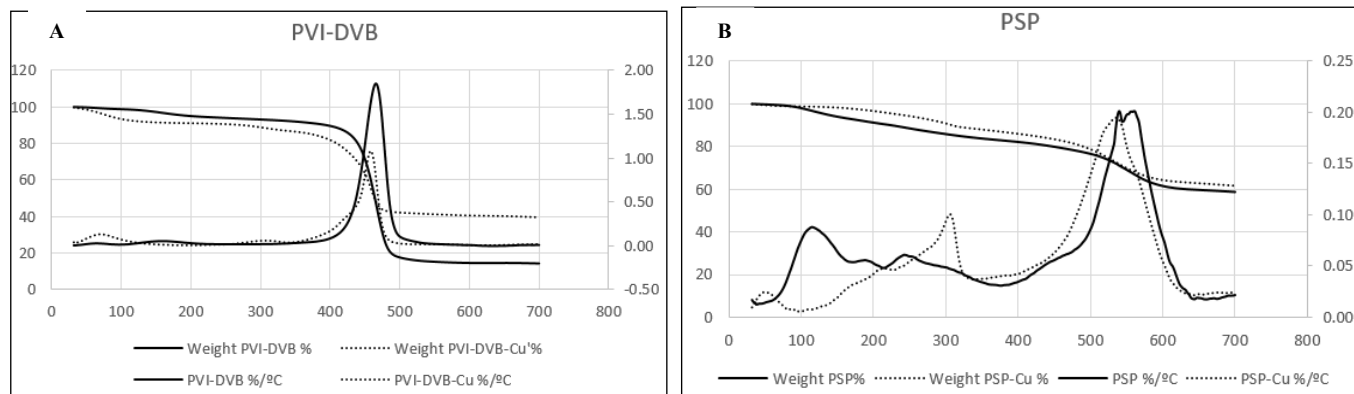
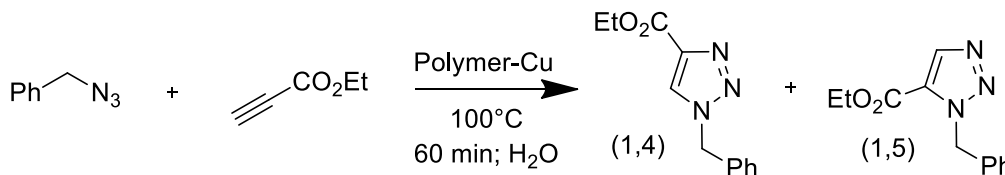


Figure 3. TGA experiments with PVI-DVB and PSP

The 1,3-cycloaddition reaction of benzylazide and ethyl propiolate was used to compare the catalytic activity of the polymers-supported CuSO_4 .²² The reactions were performed in aqueous media under microwave irradiation²³ and yields were quantitative. When using PVI-DVB-Cu (Entry 1, Table 1) the highest regioselectivity was observed and 1,4-triazol ester was the major product. The polymer supported catalyst was stable and did not show any significant change in its reaction rate when recycled. After two or four reuses, no significant loss of yield and regioselectivity were observed (Entries 2 and 3, Table 1).

Substantial leaching of metal from the support was also observed, and no doubt was related to the decrease of selectivity (Entries 1 and 3). The same yields but with less selectivity was observed when PSP-Cu was used under the same conditions (Entry 4). Regioselectivity was not affected after two reuses but after four a decrease was detected (Entries 5 and 6). Compared with PVI-DVB-Cu a minor loss of copper was observed and is probably related to the decrease of selectivity.

Table 1. Preparation of Carboxyethyl-*N*-benzyltriazoles via 1,3-DC.



Entry	Polymer	Activity mEg/g	Polymer (mg) ^a	% Cu ^c	Yield (%)	1,4:1,5 ratio ^e
1	PVI-DVB-Cu	4.6	38.5 ^b	6.20	100	93:7

2 ^c	PVI-DVB -Cu	4.6	38.5	NM	100	92:8
3 ^d	PVI-DVB -Cu	4.6	38.5	1.50	100	89:11
4	PSP-Cu	0.7	197.8 ^b	0.30	100	87:13
5 ^c	PSP-Cu	0.7	197.8	NM	98	87:13
6 ^d	PSP-Cu	0.7	197.8	0.13	98	78:22

^a For 1.9 mmol of azide and 2.3 mmol of propiolate. ^b 0.18 mEg (PVI-DVB) and 0.14 mEg (PSP) of basic centers. ^c NM=Not measured and second reuse. ^d Fourth reuse. ^e The ratio of regioisomers was determined by integrating the benzylic signs of each regioisomer at 5.51 ppm and 5.86 ppm.

Minor proportions of polymers were also tested (data not shown) but incomplete reactions and lower selectivities were obtained. We used similar molar relations of catalyst, expressed by significant mass difference of polymer employed in cycloaddition reactions, due to polymer activity differences (4.6 and 0.7 mEg/g to PVI-DVB and PSP, respectively). Part of the copper lost observed in the polymers may be associated with the complexation of the metal with triazole. The ICP analysis of triazole indicated the presence of copper, 0.06 %.²⁴ Zhu *et al.* also detected copper in triazoles, prepared from copper catalyzed cycloadditions.²⁵

IV. CONCLUSION

The polymers PSP and PVI-DVB were obtained in moderate yields and copper impregnation was possible by stirring the polymers in a aqueous solution of CuSO₄. The amount of copper supported, measured by ICP-AES, in PSP was about thirty times less than in PVI-DVB, which is probably associated with the polymer reticulation and also its activity (0.7 mEg/g versus 4.6 mEg/g). The 1,3-cycloaddition reaction between benzylazide and ethylpropiolate, in water and under microwave irradiation, in the presence of PSP-Cu or PVI-DVB-Cu, gave origin in quantitative yields to the triazols, and 1,4 regioisomer was the main product. By reusing the copper supported, no changes in yields were observed, but a small decrease in the regioselectivity was measured. After four reuses some leaching of the copper was observed and the amount remaining in PSP-Cu was about 50% of the initial content. A more expressive decrease was measured in PVI-DVB-Cu (24%), but did not affect significantly the yields or the regioselectivity.

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