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Heterocyclic Polymers as Catalysts in Organic Synthesis. Effect of Macromolecular Design and Microenvironment on the Catalytic Activity of Polymer-Supported (Dialkylamino)pyridine Catalysts

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ABSTRACT: Several new polystyrene-based resins containing (dialkylamino)pyridine pendant groups have been prepared by chemical modification of halogenated bead polymers or by suspension copolymerization of the corresponding monomers with divinylbenzene and styrene or 4-vinylpyridine. Kinetic studies on the polymeric catalysts and comparisons with low molecular weight analogues indicate that their efficiency as acylation catalysts depends on the microenvironment and the structure of the catalytic sites, the degree of functionalization, and the distance of the catalytic sites from the polymer aryl. Best results are obtained with gel-type polymers containing a three-carbon spacer group between the polystyrene rings and the catalytic site and functionalized to an extent of less than 50%, providing a hydrophobic local environment to the catalytic centers. Copolymers containing 4-vinylpyridine units in addition to the catalyst units, or high concentrations of the latter, show a strong microenvironment effect whereby activity is lowered drastically in a way that cannot be duplicated with other catalysts under homogeneous conditions.

Introduction

Polymers containing pyridine moieties have been widely studied in the preparation of polymer reagents and catalysts for general use in organic applications.[1] Some of these have found commercial applications[1,2] due to the availability of cross-linked poly(4-vinylpyridine) in various bead forms. Similarly, the emergence of commercial sources for other heterocyclic bead polymers such as poly(benzimidazole) suggests their application as simple heterogeneous hydrogenation catalysts[3] or in other types of supported chemistry.[4] Significant potential for a different kind of catalysis has recently drawn much attention to the possibilities of polymers containing 4-(dialkylamino)-pyridine heterocycles as supported functional groups.[4-11]

(Dimethylamino)pyridine (DMAP, **1a**) is a material that has found numerous important applications since it became commercially available several years ago. It is an excellent catalyst for a variety of nucleophilic addition reactions, being most notably useful in difficult acylations and silylations of tertiary and other hindered hydroxyls.[12-14] DMAP is of particular interest to the research chemist and to the pharmaceutical and fine chemicals industry as its presence increases conversion yields while reducing side-product formation in such otherwise slow reactions. Current drawbacks to this soluble catalyst include its relatively high cost and the additional treatment that may be needed to remove it during product purification. In contrast, a polymer-bound catalyst possessing an activity comparable to DMAP would at once be easier to separate[15] from reaction media and repurified for later recycling, which may favorably counterbalance the somewhat higher initial cost of such a material.

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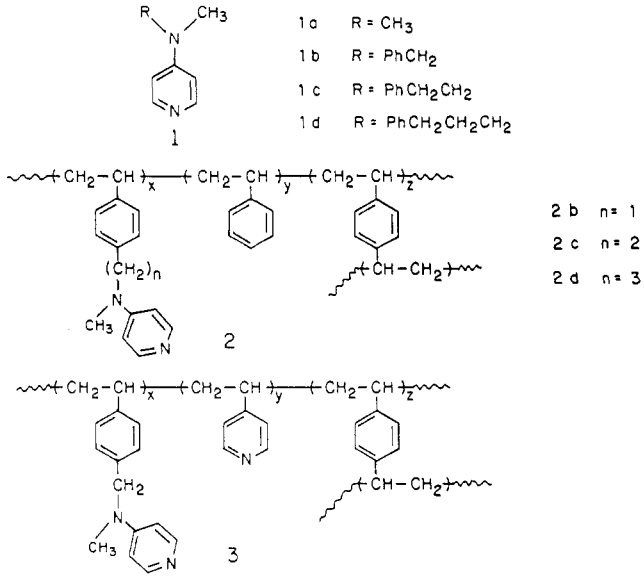


Results and Discussion

The first objective of this study was to determine which factors, other than the exact nature of the (dialkylamino)pyridine moiety, affect the reactivity of the polymer-bound catalysts. Specifically, we wanted to investigate effects of the microenvironment and of the accessibility of the reactive sites within the polymer beads. The catalytic moiety chosen for this preliminary study was 4-(*N*-benzyl-*N*-methylamino)pyridine (BMAP), **1b**, previously used by Tomoi et al.[5] The test reaction was the acetylation of 1-methylcyclohexanol at 60 °C in the presence of triethylamine and 5 mol % of the catalyst[16] in toluene.

Polymeric analogues of BMAP (e.g., **2b**) are conveniently prepared by incorporation of 4-(*N*-methyl-*N*-(*p*-vinylbenzyl)amino)pyridine[5] in various suspension copolymerization recipes. These included varying amounts of added comonomers such as styrene and cross-linking reagents such as divinylbenzene (DVB). If desired, the microenvironment of the catalytic sites can be modified by substituting 4-vinylpyridine for styrene as a comonomer to afford polymer **3**. Though 4-vinylpyridine has a higher reactivity[17] than styrene or substituted styrenes of the type used in this study, the reactivity ratios are such that somewhat random structures, initially richer in 4-vinylpyridine, are obtained. Despite this less than ideal distribution of monomers in the copolymers, it was expected that incorporation of some 4-vinylpyridine moieties in the polymeric catalyst would modify drastically the polarity of the medium in the vicinity of the reactive sites, creating a unique environment not normally achievable in classical solution chemistry. The possibility of creating a synergism by placement of acid acceptors near the catalytic centers or by using a high concentration of the latter was also attractive.

Similarly, the ease of penetration of the soluble reagents within the polymer beads, and thus the accessibility of the reactive sites, can be modified by increasing the percentage of cross-linking monomer and otherwise changing the reaction conditions during suspension polymerization. Incorporation of a low percentage of cross-linking agent (1–3% DVB) in the suspension polymerization results in the formation of swellable gel-type beads. If larger amounts of cross-linker are used in the presence of suitable porogens, rigid macroporous resins possessing significant porosities are obtained.[18]

Two families of polymers containing 8–20% of bound analogues of BMAP in a medium consisting mainly of styrene of 4-vinylpyridine cross-linked with varying amounts of divinylbenzene were prepared and tested in the acylation of 2-methylcyclohexanol in dilute solution.

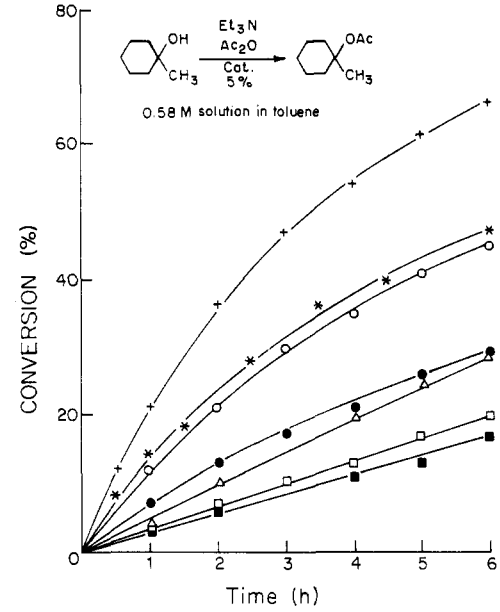


Figure 1. Activity of acylation catalysts: (+) **1a**; (*) **1b**; (○) **2b** (2% cross-linked); (●) **3** (2% cross-linked); (△) **2b** (34% cross-linked, butanol porogen); (□) **2b** (34% cross-linked, heptane porogen); (■) **3** (34% cross-linked, heptane porogen).

As can be seen in Figure 1, the incorporation of large amounts of 4-vinylpyridine in the polymer beads (structure **3**) causes a noticeable decrease in the catalytic activity of the material when compared to a similar copolymer with styrene **2b**. Analogous results are obtained with 34% DVB-cross-linked macroreticular resins **2b** and **3**: again the resin that contains 4-vinylpyridine has a lower activity than that which contains the nonpolar and chemically inert comonomer styrene. Since all reactions with the polymer catalysts are carried out in the presence of excess strongly basic triethylamine, the lower reactivity of the pyridine-containing polymers cannot be due to the permanent formation of ions within the polymer network. The lower reactivity may be explained by either a simple polarity effect or by a high local concentration of reactive sites. As 4-vinylpyridine is more reactive than styrene in radical copolymerizations,[17] there may exist within the insoluble copolymer beads areas of high concentration of 4-vinylpyridine or of the (dialkylamino)pyridine moieties. These may favor the accumulation of acetate product in the immediate vicinity of the catalytic sites, thereby causing product inhibition of the reaction. Alternately, deactivation may result from a simple increase in polarity and solvating power of the medium in the immediate environment of the site of reaction. This could destabilize the transition state[12–14] arising from the attack of nucleophile (alcohol) onto charged substrate (acyl–aminopyridinium intermediate). As will be seen later, this remarkable decrease in reactivity cannot be duplicated in solution;[19] it is likely attributable to a polymer microenvironment effect not unlike that observed by Urruti and Kilp[20] in their very interesting work with polymer-bound photosensitizers. A complementary study involving a polymer containing a high concentration of catalytic sites with no inert diluent leads to essentially the same conclusions.

The observed decrease in reactivity when changing from gel to macroporous support is typical.[21] Despite their permanent porous structure, which makes them more suitable for flow system applications than their gel counterparts, reactions within the rigid matrices of macroporous

Table I
Catalytic Activity of Model Compounds in the Acetylation of 1-Methylcyclohexanol[a]

entry	structure	% yield 2 h	% yield 6 h	rel activity[b] 2 h	rel activity[b] 6 h	chem shift[c] δ, ppm
1	**1a**	60	82	100	100	6.44
2	**1b**	38	68	63	83	6.52
3	**1c**	53	78	88	95	6.45
4	**1d**	56	82	93	100	6.38

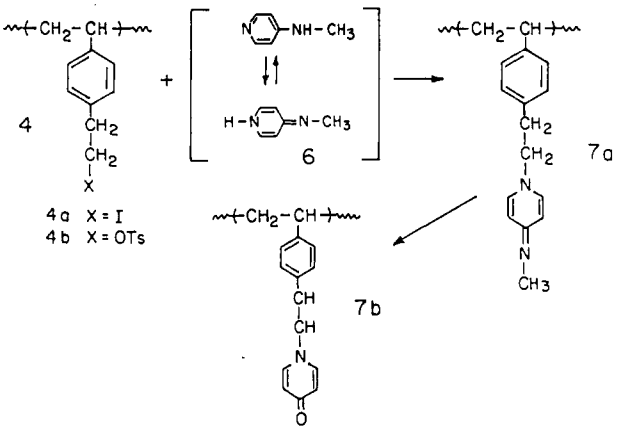
[a] Reaction with 0.9 M cyclohexanol in toluene containing 5 mol % of catalyst, 30% excess triethylamine, and 100% excess acetic anhydride at 60 °C. [b] (Dimethylamino)pyridine (**1a**) taken as reference. [c] NMR chemical shift of β-pyridine protons.

resins are more limited by restricted diffusion. It is also interesting to compare the relative reactivities of two DMAP-containing macroporous resins with identical chemical composition but prepared by suspension polymerization in the presence of different porogens. As can be seen in Figure 1 the resin prepared with butanol as porogen is significantly more reactive than that prepared with heptane, which reflects the better porogenic properties of butanol for this system.

Studies by Tomoi,[5] Verducci,[8] and others have suggested that the activities (per mole of heterocycle) of polymeric acylation catalysts generally do not exceed those of their low molecular weight analogues. This is confirmed in Figure 1 where a comparison of catalysts **1b** and **2b** shows that the low molecular weight analogue is only slightly more active than its lightly cross-linked polymeric counterpart. In view of our ability to prepare polymers containing reactive groups linked to styrene through a two-[22] or three-carbon[23] spacer, we prepared model compounds **1c** and **1d** and evaluated their performance in the above-mentioned standard acylation reaction.[16] These results (Table I) suggest that the steric and/or electronic deactivation of catalyst (per mole of heterocycle reactive site) observed in going from dimethyl-substituted **1a** (DMAP) to methylbenzyl-substituted **1b** (BMAP) and its polymer analogue **2b** can be largely remedied by simply extending the chain between the active heterocycle and the aromatic ring phenyl group (**1c**, **1d**) or polystyrene support (**2c**, **2d**). This "spacer effect", which is a well-documented observation for other kinds of polymer reagents,[6,22,31] is likely due here to the change in electronic environment of the catalytic sites. Thus, **1c** is significantly more reactive than **1b** while **1d** is essentially as reactive as DMAP itself. Table I correlates catalytic activity to the NMR chemical shift of the β-pyridinc protons for **1a–1d**. It is found that for the homologous series **1b**, **1c**, and **1d** these shifts reflect the relative order of catalytic activity of the compounds, as predicted by Hassner.[13] It would be unwise at this point to speculate on a simple pK_a–activity relationship since all reactions are carried out in the presence of triethylamine, which, despite its high pK_a, has no catalytic activity.[12,13]

An alternate route to **2b** involves the alkylation of 2-(methylamino)pyridine with readily available reticulated (chloromethyl)polystyrene (Merrifield resin[15]). In neutral medium, the reaction proceeds to give a significant amount of nitrogen-containing moieties incorporated into polymer resins as shown by elemental analysis. However, the polymer's infrared spectrum displays a large band at 1635–1650 cm^{-1}, identified as 4-pyridone.[24] This arises from alkylation of the *ring* nitrogen of the ambident heterocycle by polymer electrophile, giving a pyridonimine that is then hydrolyzed to pyridone[25] during polymer wash (Scheme I). Fortunately, in contrast to and despite suggestions to the contrary,[5] chloromethylated polystyrene can be modified readily and quantitatively to the corresponding aminopyridine resin **2b** using the sodium salt of 4-(*N*-methylamino)pyridine in dry DMF; we have observed that the same reaction in THF results in a polymer that is contaminated with 10% or more pyridone units.

Scheme I



Scheme II

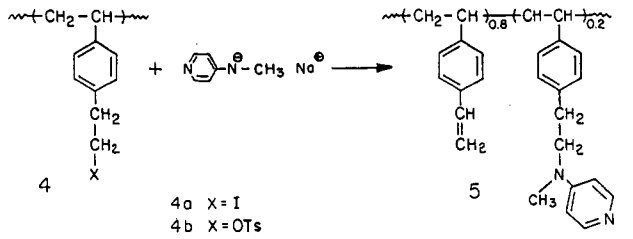


Table II
Catalytic Activity of Polymer-Bound Catalysts in the Acetylation of 1-Methylcyclohexanol[a]

entry	polymer	method of prep[b]	DF	capacity,[c] mmol/g	rel activity,[d] % 1a 2 h	rel activity,[d] % 1a 6 h
1	**2b**	A	0.08	0.67	62	80
2	**2b**	B	0.16	1.34	60	79
3	**2c**	B	*e*	0.66	14[e]	35[e]
4	**2d**	B	0.16	1.18	83	94
5	**2d**	B	0.16	1.23	87	98
6	**2d**	A	0.23	1.64	82	94
7	**2d**	A	0.30	2.10	85	100
8	**2d**	A	0.48	3.06	80	94
9	**2d**	A	0.96	3.82	65	77

[a] Reaction conditions: 5 mol % catalyst, 0.9 M 1-methylcyclohexanol in toluene at 60 °C (see Experimental Section). [b] All polymers are cross-linked with 2% divinylbenzene. (A) Suspension polymerization of active monomers; (B) chemical modification of halogenated polymers. [c] Capacity calculated from nitrogen analyses. [d] Activity using **1a** as reference (100%). [e] Polymer is contaminated by side products.

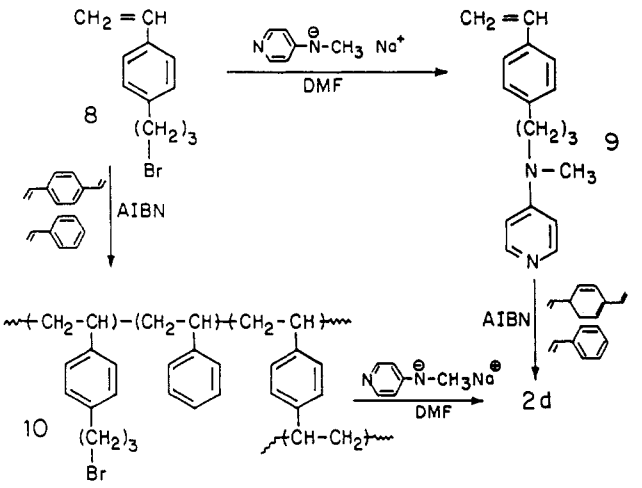
2-Iodoethyl and 2-tosyloxyethyl resins are easily prepared from polystyrene using simple modifications that have been optimized and that proceed in essentially quantitative yields.[22] Subsequent alkylation with a number of nucleophiles gives useful and stable polymers containing various functionalities attached through a bimethylene spacer to the aromatic rings of polystyrene.[22] However, treatment of these substrates with sodium 4-(*N*-methylamino)pyridine (Scheme II) leads to extensive elimination with formation of conjugated pendant olefins, while only ca. 20% functionalization is observed by nitrogen analysis. Similarly, reaction with 4-aminopyridine in neutral medium leads to extensive formation of 4-pyridinone which,

Table III
Effect to Reaction Conditions on the Catalytic Activity in the Acetylation of 1-Methylcyclohexanol

entry	catalyst struct[a]	concn alcohol, mol/L	T, °C	% yield 2 h	% yield 6 h	rel activity, % 1a 2 h	rel activity, % 1a 6 h
1	**1a**	0.58	60	35	63		
2	**2b**	0.58	60	18	40	51	63
3	**2d**	0.58	60	29	59	83	94
4	**1a**	0.90	60	60	82		
5	**2b**	0.90	60	36	65	60	79
6	**2d**	0.90	60	49	77	83	94
7	**1a**	1.47	60	77	94		
8	**2b**	1.47	60	60	87	78	93
9	**2d**	1.47	60	72	92	94	98
10	**1a**	0.90	25	39	66		
11	**2b**	0.90	25	21	45	54	68
12	**2d**	0.90	25	30	59	77	89

[a] Polymers **2b** and **2d** have DF = 0.16. Catalyst concentration is 5 mol %.

Scheme III



as seen in Table II, results in a poor polymeric catalyst. In view of these problems and of our parallel study of model compounds that predicted that **2d** would perform at least as well as **2c**, this approach was abandoned and no further attempts were made to prepare **2c**.

The difficulties encountered in the syntheses of resins with structure **2c** can be avoided in the preparation of resin **2d**, which has an additional carbon atom between the aromatic ring and the active center. Scheme III shows two routes to resin **2d**, one involving the synthesis of the corresponding monomer **9** and the other the chemical modification of the bromopropyl resin **10**. Both of these routes have as a key step the nucleophilic displacement of bromide ion by the sodium salt of 4-(*N*-methylamino)-pyridine, a reaction that we had optimized earlier with chloromethylated polystyrene. This reaction being done under strongly basic conditions in DMF is not troubled by interference from ring alkylation of (*N*-methylamino)pyridine **6** and is not accompanied by elimination in contrast with the corresponding reaction on polymer **4**.

The starting material for both routes is 1-(3-bromopropyl)-4-ethenylbenzene (**8**) which is prepared easily from (3-bromopropyl)benzene as described by Hallensleben.[23] Suspension polymerization of either **8** or **9** with styrene and 1–2% divinylbenzene affords resins **10** or **2d**, respectively, with capacities that vary depending on the composition of the monomer feed. The products that are obtained by both routes are indistinguishable as the conversion of **10** to **2d** is essentially quantitative.

Testing of the various polymers in the catalyzed acetylation of 1-methylcyclohexanol produced the results shown in Tables II and III. It should be mentioned that for all reactions involving polymer-bound catalysts, results are given as an average value for several runs with variations of ±2% observed in parallel runs. In addition, while the reactions with **1a–d** are carried out in homogeneous medium, those with the polymeric catalysts are nonhomogeneous and some detectable decrease in catalytic effect may result if small amounts of the solid catalyst are removed from the reacting mixture through being spattered onto the walls of the reaction vessel.

As can be seen in Table II, the method of preparation of the polymers, chemical modification vs. suspension copolymerization, has no noticeable effect on the activity of the catalyst provided the technique used for the chemical modification does not lead to side-product formation. However, the chemical modification route used to prepare **2c** does lead to extensive side reactions, which explains the low reactivity shown in Table II (entry 3). Because our samples of **2c** contained inactive impurities such as pyridones, the actual concentration of (dialkylamino)pyridine moieties was much lower than was calculated from simple nitrogen analyses.

As expected, **2d** is significantly more active than its benzylic analogue **2b**. It is interesting to compare the normalized activities for a series of copolymers with increasing degrees of functionalization (entries 6–9, Table II). Maximum activity per mole of heterocycle is not observed for the resin with the highest degree of functionalization but is instead achieved with resins that contain significant amounts of nonpolar styrene units. The decreased reactivity shown for entry 9 is consistent with the earlier finding with polymer **3** and with the observation that comparable homogeneous catalysts have reduced activity in highly polar media. Here again a microenvironment effect is seen and the decreased activity might well be derived from the high local concentration of catalyst sites favoring the accumulation of acetate and leading to product inhibition.

More detailed comparisons between polymers **2b** and **2d** and DMAP **1a** are shown in Table III as well as in Figure 2. While the temperature and concentration efects that are shown in Table III are quite predictable, the difference in reaction kinetics is most easily seen in Figure 2. Both polymers **2b** and **2d** afford lower initial rates than **1a** though increasing the concentration of substrate in the reaction medium reduces the difference. Both polymers **2b** and **2d** have the best performance relative to DMAP when used in fairly concentrated solutions of the alcohol to be acylated. In the case of the gel resins used through the most of this study, mass-transfer limitations can be ruled out as demonstrated by experiments involving beads of different sizes and variations in reactor stirring speed.

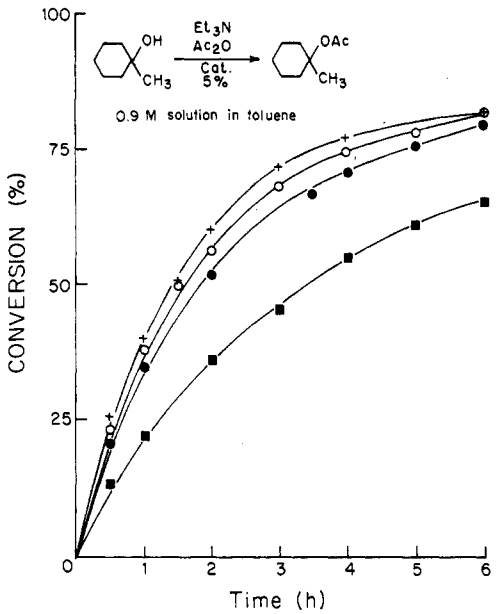


Figure 2. Activity of acylation catalysts: (+) **1a**; (○) **1d**; (●) **2d**; (■) **2b**.

For example, the reaction curve obtained with polymer **2b** is unchanged when the catalyst is ground from its original 100–150-μm average size to fine 3–5-μm particles. Similarly the kinetics appear essentially unaffected by large variations in stirring speed.

It is also worthwhile commenting on the influence of the nature of solvent on the reactivities of the polymeric catalysts and of their low molecular weight analogues. For all catalysts, the reaction in pyridine medium is much slower than in toluene. For example, in a typical series of reactions run under standard conditions[32] with a constant concentration of cyclohexanol, both catalysts **1b** and **1d** show an activity in pyridine that is only 50–55% of that in toluene. In contrast, their polymer-bound analogues **2b** and **2d** have relative activities in pyridine that are 60–65% of those in toluene. Most striking perhaps is the fact resin **3**, which has its catalytic sites surrounded by polymerized 4-vinylpyridine moieties, is only 40–45% as active in pyridine as it is in toluene. These variations in activities probably reflect the differences in the microenvironments of the various catalytic sites. Both polymers **2b** and **2d** contain approximately five styrene units for each (dialkylamino)pyridine group. Though randomly placed throughout the polymer chains, these styrene units are always held in proximity to the catalytic sites, and, through local ordering, they can maintain a lower polarity in the immediate environment of the reactive sites. In effect, the styrene moieties act as a "polarity shield", reducing somewhat the deleterious effect of the less favorable solvent and presenting the attacking nucleophile with a local medium which facilities its attack. In contrast, polymer **3**, when used in pyridine, provides an environment where all the catalytic sites are surrounded either by other catalytic sites or by pyridine units with no possibility of shielding or local ordering of less polar moieties.

It is interesting at this juncture to compare our results with those of Tomoi[5] and Menger,[11] who also prepared resins with structure **2b**. Though Tomoi et al. used 20 mol % of the polymer-bound catalyst vs. 5 mol % used in this study, the relative activities are essentially identical. In contrast, the activity reported by Menger for the acetylation of 1-methylcyclohexanol using a polymer similar to **2b** is much lower than that we observed. There may be several reasons for this apparent discrepancy. Though Menger's synthetic approach resembles ours, the starting material was linear poly(vinylbenzyl chloride) rather than the 1–2% cross-linked bead material obtained by the more desirable suspension copolymerization process. A particular problem is that linear poly(vinylbenzyl chloride) is much more difficult to handle than the corresponding bead polymer. It is also extremely light-sensitive[26,27] and cross-links readily under normal illumination to afford gels with poor mechanical properties. In addition, we have shown earlier that the chemical modification of a chloromethylated polystyrene bead polymer by reaction with sodium salt of 4-(*N*-methylamino)pyridine is best carried out in DMF as the reaction in THF is accompanied by formation of a polymer-bound pyridone side products. If a side product is also formed in the reaction with linear poly((chloromethyl)styrene), then Menger's polymer would be contaminated with nitrogen-containing moieties which possess no intrinsic catalytic activity and therefore, if unaccounted for, would lower its apparent activity. Another cause for the lower reactivity observed by Menger et al. might be the polarity of the polymeric catalyst, which, being highly functionalized with polar species, behaves in much the same way as highly loaded **2d** (Table II, entry 9).

In summary, this work shows that polymer-supported acylation catalysts such as **2d** possess a high catalytic activity and are easily prepared. The design of the polymers were based on model studies with low molecular weight analogues, though effects that are uniquely related to the microstructure of the polymeric catalysts should also be taken into consideration. Such effects dictate that the microenvironment of the catalytic sites be considered when designing the polymeric catalysts. Due to the inherent nature of polymer chains, reactive groups remain concentrated within the polymer beads despite the swelling which reduces somewhat their local concentration. As a result the local polarity within polymer beads, as opposed to the bulk polarity of the medium, takes on added importance. This may prevent the efficient use of polymers that would be constituted exclusively of catalytic units or that would contain high concentrations of polar groups such as acid acceptors. Finally, the importance of the reaction conditions used in the preparation of the reactive polymers must again be emphasized since misleading results may be obtained if care is not taken to avoid the occurrence of deleterious side reactions.

We are currently exploring other supported acylation catalysts that may be even better suited to industrial scale syntheses.

Experimental Section

General Remarks. Chloromethylated polystyrene was prepared from Bio-Beads SX1 (Bio-Rad Laboratories) as described previously.[15,28] 4-*N*,*N*-dimethylpyridinamine was a gift from Reilly Tar and Chemical Co. Styrene, 4-vinylpyridine, and 1-methylcyclohexanol (Aldrich) were distilled prior to use. Divinylbenzene (Polysciences) was 55% pure (remainder ethylstyrene) and was used without purification. Infrared spectra were measured on a Nicolet 10-DX FT-IR, NMR spectra were recorded with Varian EM 360, CFT-80, or XL-300 spectrometers, while mass spectra were obtained on a VG-7070E double-focusing mass spectrometer using chemical ionization where appropriate.

Preparation of 4-(*N*-Methyl-*N*-benzylamino)pyridine (1b). Compound **1b** was prepared by a procedure similar to that of Tomoi et al.[5] Anal. Calcd for $C_{13}H_{14}N_2$: C, 78.75; H, 7.12; N, 14.13. Found: C, 78.63; H, 6.96; N, 14.00. MS *m/e* 198 (M^+), 121, 91; ^1H NMR 3.05 (s, 3 H), 4.56 (s, 2 H), 6.54, 8.18 (2d, 4 H, pyridyl), 7.15–7.30 (m, 5 H, phenyl).

Preparation of 4-(*N*-Methyl-*N*-(phenylethyl)amino)pyridine (1c). A solution of 19.8 g (0.1 mol) of 4-(*N*-(phenylethyl)amino)pyridine[23] in 400 mL of dry DMF is treated with 2.9

g of sodium hydride. The mixture is then alkylated by dropwise addition of a solution of 6.23 mL of iodomethane in 20 mL of DMF. After standing overnight, the precipitate is filtered and the filtrate is evaporated. The residue is taken in dichloromethane and the organic solution is washed with water, dried over $MgSO_4$, and evaporated to afford crude **1c**, which is purified by vacuum distillation: bp 147–149 °C (0.1 mm), 67% yield. Anal. Calcd for $C_{14}H_{16}N_2$: C, 79.21; H, 7.60; N, 13.20. Found: C, 79.10; H, 7.58; N, 13.45. ^1H NMR 2.84 (m, 5 H), 3.56 (t, 2 H), 6.45, 8.18 (2d, 4 H, pyridyl), 7.14–7.30 (m, 5 H, phenyl); MS *m/e* 212 (M^+), 121.

Preparation of 4-(*N*-Methyl-*N*-(phenylpropyl)amino)-pyridine (1d). A solution of 2.7 g (0.025 mol) of 4-(*N*-methylamino)pyridine in 12 mL of dry DMF is treated with 0.65 g of sodium hydride. The mixture is then alkylated as above for **1c** with an equimolar amount (3-bromopropyl)benzene. After workup pure **1d** is isolated in 57% yield: bp 151–152 °C (0.1 mm). Anal. Calcd for $C_{15}H_{18}N_2$: C, 79.61; H, 8.02; N, 12.37. Found: C, 79.36; H, 7.89; N, 12.48. MS *m/e* 226 (M^+), 121; ^1H NMR: 1.90 (m, 2 H), 2.63 (t, 2 H), 2.92 (s, 3 H), 3.22 (t, 2 H), 6.38, 8.14 (2d, 4 H, pyridyl), 7.15–7.28 (m, 5 H, phenyl).

Preparation of 4-(*N*-Methyl-*N*-(*p*-vinylbenzyl)amino)-pyridine. This vinyl monomer was prepared as described by Tomoi et al.[5]

Preparation of 4-[*N*-Methyl-*N*-((*p*-vinylphenyl)-propyl)amino]pyridine (9). This monomer is prepared by alkylation (see **1d** above) of 4-(*N*-methylamino)pyridine with 1-(3-bromopropyl)-4-ethenylbenzene (**8**) prepared by the procedure of Hallensleben.[23] The crude material is purified by liquid chromatography on silica gel (ethyl acetate) and recrystallized from 1:1 ether–petroleum ether in 58% yield: mp 50–51 °C. Anal. Calcd for $C_{17}H_{20}N_2$: C, 80.91; H, 7.99; N, 11.10. Found: C, 80.60; H, 7.99; N, 11.12. MS *m/e* 252 (M^+), 121; ^1H NMR 1.88 (m, 2 H), 2.59 (t, 2 H), 2.90 (s, 3 H), 3.30 (t, 2 H), 5.16, 5.66, 6.64 (2d + m, 3 H, vinylic), 6.36, 8.11 (2d, 4 H, pyridyl) 7.08, 7.28 (2d, 4 H, phenyl).

Preparation of the Polymer-Bound Catalysts. (a) Chemical Modification. The procedure used for the modification of 2% cross-linked chloromethylated polystyrene or polymer **10** with 4-(*N*-methylamino)pyridine is similar to that described above for **1d** using however a twofold excess of the sodium salt of 4-(*N*-methylamino)pyridine. The polymers are then washed repeatedly with organic and aqueous solvents to remove all soluble contaminants. After drying, their degree of functionalization is evaluated from elemental analysis. No residual halogen is found, and, in general, the procedure leads to quantitative displacements.

(b) Preparation of Gel-Type Beads by Suspension Polymerization. The polymerizations are carried out in a Buchi BEP 280 stirred autoclave using a 250-mL thermostated vessel fitted with overhead anchor-type stirrer. The standard procedure is as follows: to 150 mL of a 1.5% solution of poly(vinyl alcohol) (Polyviol W25/140, Wacker Chemie) in degased distilled water is added a mixture of 20 g of monomers (e.g., **9**, styrene, and divinylbenzene) in 30 g of toluene containing 0.2 g of azobis(isobutyronitrile). Nitrogen is bubbled through the mixture for 10 min and polymerization is started by heating the mixture (75 °C) while stirring at 300 rpm (8 h). The polymer beads are then decanted from aqueous suspension until the supernatant is clear. The decantation procedure is reported with methanol, toluene, and methanol as the liquid phases. The filtered polymer is then dried under vacuum at 50 °C and analyzed. In typical experiments yields of up to 85% based on starting monomer are obtained.

(c) Preparation of Macroporous Beads by Suspension Polymerization. The procedure used for these preparations is identical with the above with the following exceptions: the monomer mixture contains a higher proportion of divinylbenzene and the toluene is replaced by a suitable porogen such as 1-butanol. In typical experiments yields of up to 89% are obtained.

Testing of the Catalysts. A mixture of 2 mL of 1-methylcyclohexanol (16.2 mmol), 0.81 mmol of catalyst (5 mol %), and 3 mL of triethylamine (21.6 mmol) in enough toluene (typically 10–20 mL) to adjust the concentration of the solution to an appropriate value[30] is placed in a thermostated cell at the desired reaction temperature (25 or 60 °C). After the mixture is stirred under nitrogen for 15 min, 3 mL of acetic anhydride (31.6 mmol) is added while stirring is continued. The progress of the reaction is monitored by withdrawing small aliquots for chromatographic analysis (10% SE-30 on Chromosorb G). 1-Methylcyclohexyl acetate can be purified by distillation.

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