

Synthesis and Characterization of a New Chiral Polyurea-Based Catalyst

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SYNOPSIS

A series of chiral poly(urea)s was synthesized by solution polyaddition. The polymers are characterized by NMR, FTIR, DSC, viscosimetry, and microanalysis. After deposition of the rhodium, the insoluble chiral polymers were used as catalysts in the reduction of acetophenone by hydrogen transfer. The influence of the structure of the polymers on the catalytic activity and selectivity was investigated. The enantiomeric excesses (e.e.) obtained were up to 60%, and the polymeric catalysts were reused without loss of activity and selectivity. © 1996 John Wiley & Sons, Inc.

INTRODUCTION

Chemical synthesis of enantiomerically pure compounds plays a pivotal role in the development of pharmaceuticals, agrochemicals, flavors, and fragrances, as well as certain advanced materials. The main limitations in industrial use of the already known homogeneous catalytic reactions lies in the recovery and recycling of the catalysts. Indeed, in many cases, both the cost of the transition metal and of the chiral ligand are not negligible compared with the price of the synthesized product. This problem can be solved by fixing the ligand on a solid, insoluble support such as silica, zeolite, or a polymer. The structures of the support have to be optimized to limit the decrease of selectivity, activity, and leaching of the metal. The use of polymer-supported catalysts for asymmetric catalysis has been already reported in the literature.¹⁻³ Most of the systems involve crosslinked polystyrene or polyacrylate-supported reagents.^{4,5}

Nitrogen-containing ligands are more and more used in asymmetric catalysis⁶ for reactions as different as carbonyl reduction⁷ or allylic alkylation.⁸ Recently, we reported the asymmetric homogeneous hydride transfer reduction of prochiral ketones using

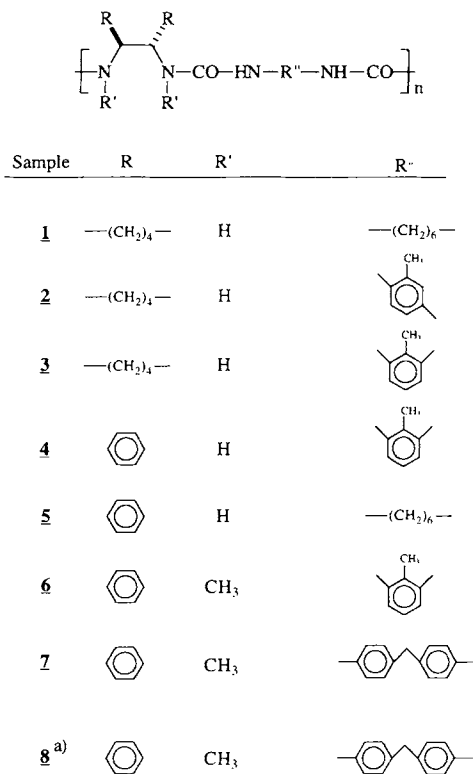
C₂-symmetric diamine ligands.⁹ Those dinitrogen chiral ligands offer an original possibility: They can be used as monomers in polyaddition with diisocyanates to form insoluble polyureas.

To study heterogeneous asymmetric catalysis by metal-containing polymers, we synthesized a series of polyureas having chiral diamine unity as part of the backbone (Fig. 1). Those polymers were complexed with rhodium and used as catalysts in asymmetric hydride transfer C=O bond reduction (Fig. 2).

EXPERIMENTAL

N,N'-Dimethyl-1,2-diphenyl-1,2-ethanediamine was synthesized as described previously.¹⁰ All other materials, including 1,2-diaminocyclohexane, 1,2-diphenyl-1,2-ethanediamine, diisocyanates, bis-(1,5-cyclooctadiene)dirhodium(*l*)dichloride, acetophenone, and solvents were reagent grade and were used without further purification. Elemental analyses were performed by Service Central d'Analyse, CNRS, BP 22, F-69390 Vernaison. FTIR spectra were recorded on a Perkin-Elmer 1720-X apparatus as KBr discs. ¹H- and ¹³C-NMR spectra of soluble polymers were recorded on a Bruker-AM200 instrument as 1% solutions in deuterated chloroform and in deuterated trifluoroacetic acid using TMS as the internal standard. Thermal properties were examined on a Perkin-Elmer DSC-7 instrument using a

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a) cross-linked

Figure 1 The structure of the polymers.

heating rate of 10°C/min. Inherent viscosities are measured at 25°C in trifluoroacetic solution with a concentration of 1 g/dL. Optical rotations were measured on a Perkin-Elmer-241 polarimeter instrument in trifluoroacetic acid solutions with concentrations $c = 5$ g/L. Conversion and enantiomeric excesses (e.e.) of the reduction of acetophenone were monitored by gaseous chromatography using a CY-DEX B chiral column (margin of error: $\pm 1\%$).

General Procedure for Preparation of Polyureas

The diamine (about 1 g) was dissolved in 2 mL of dry dichloromethane in a 25 mL three-necked round-bottomed flask under a dry argon atmosphere. While the above solution was vigorously stirred with a magnetic stirrer, a solution of the equivalent amount of diisocyanate in 2 mL of dichloromethane was added rapidly through the funnel. The polyaddition was quenched by adding propan-2-ol. All polymers precipitated. The product was filtered off, washed several times with propan-2-ol, and dried under vacuum at room temperature. All polymers were left in contact with air during 7 days and then analyzed.

MICROANAL:

1: C₁₄H₂₆N₄O₂. Calcd: C, 59.5%; N, 19.8%; O, 11.3%; H, 9.3%.

Found: C, 58.6%; N, 20.6%; O, 11.9%; H, 9.3%.

2: C₁₅H₂₁N₄O₂, 3.3H₂O. Calcd: C, 51.2%; N, 15.9%; O, 25.0%; H, 7.9%.

Found: C, 53.9%; N, 15.3%; O, 24.4%; H, 6.4%.

5: C₂₂H₂₈N₄O₂, 0.5H₂O. Calcd: C, 67.8%; N, 14.4%; O, 10.7%; H, 7.5%.

Found: C, 67.0%; N, 13.9%; O, 10.7%; H, 7.5%.

6: C₂₅H₂₆N₄O₂, 2H₂O. Calcd: C, 66.6%; N, 12.4%; O, 14.2%; H, 6.7%.

Found: C, 67.0%; N, 12.4%; O, 14.2%; H, 6.4%.

7: C₃₁H₃₀N₄O₂, 0.5H₂O. Calcd: C, 74.5%; N, 11.2%; O, 8.0%; H, 6.2%.

Found: C, 72.0%; N, 10.7%; O, 8.0%; H, 6.4%.

8: C₃₁H₃₀N₄O₂, 0.7H₂O. Calcd: C, 74.0%; N, 11.1%; O, 8.6%; H, 6.3%.

Found: C, 74.0%; N, 10.7%; O, 8.6%; H, 6.8%.

Hydride Transfer Reduction of Acetophenone

A slurry of the polymer (corresponding to 0.0127 mmol of diamine) bis(1,5-cyclooctadiene)dirhodium (I) dichloride (0.00127 mmol), and KOH (0.0762 mmol) in propan-2-ol (4 mL) was stirred overnight at room temperature. Acetophenone (0.254 mmol) was then added and the mixture heated at 70°C.

RESULTS AND DISCUSSION

Polymer Synthesis

To incorporate the chiral diamine units in the polymer, we copolymerized it with different diisocyanates. The advantage of this method is its simplicity. Polyaddition is made under mild conditions and yields are quantitative. The polymers were synthesized by uncatalyzed solution polyaddition of diamines with diisocyanates. The yields were high, and the polymers were isolated by precipitation with propan-2-ol.

To obtain the polymers with high molecular weight, we used a balanced system ($[NCO]/[NH] = 1$). The reaction of polyaddition was rapid and exothermic. All polymers precipitated during the reaction, except polymers **6** and **7**, where the polymers precipitated only after quenching by propan-2-ol. Polymer **8** was

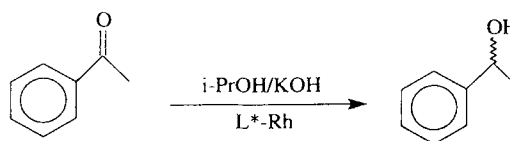


Figure 2 Reduction of acetophenone.

Table I The Main Absorption Bands in FTIR Spectra (cm⁻¹)

Entry	Polymer	$\nu_{\text{N-H}}$	$\nu_{\text{C-H}}$ Arom.	$\nu_{\text{C-H}}$ Aliph	$\nu_{\text{C=O}}$
1		3346	—	2929 2856	1636
2		3323	3030	2931 2856	1641
3		3323	3030	2931 2856	1641
4		3320	3086 3030	2950 2927	1646
5		3357	3061 3030	2929 2856	1637
6		3426 3330	3060 3029	2960 2923	1646
7		3332	3062 3030	2930 2857	1652

obtained using crude methylenediisocyanate, which is a mixture of pure MDI (60%) and different triisocyanates (30%). The crosslinking was instantaneous, giving a hard, insoluble polymer which was crushed and then washed. The properties of the polymers are given in the Tables II-IV.

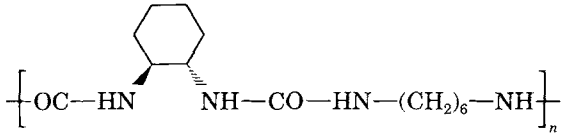
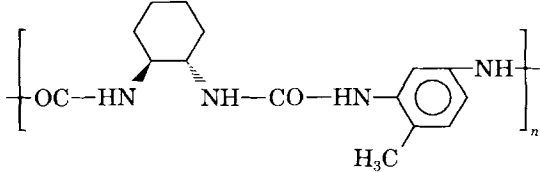
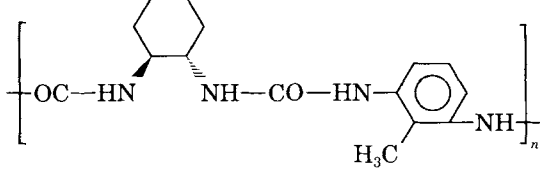
Inherent Viscosity Measurements

The inherent viscosities of the polymers were obtained from CF₃COOH solution, using the following equation:

$$\eta_{\text{inh}} = (\ln \eta_{\text{rel}}) / c$$

where $\eta_{\text{rel}} = \eta_{\text{solution}} / \eta_{\text{solvent}}$ and c is the concentration, g/dL. The values of η_{inh} are given in the Tables II-IV. They are comparable to those obtained by Zhang and Neckers¹¹ (derived from 4,4'-diamino-2,2'-bipyridine and TDI) and they are lower than those obtained by Kwolek¹² (derived from *trans*-2,5-dimethylpiperazine and MDI). The values of η_{inh} are high in the case of the polymers **1**, **2**, and **5**, indi-

Table II Characterization of Polymers: Polymers Derived from (1*S*, 2*S*)-(+)-1,2-Diaminocyclohexane

Sample	Polymer	Yield (%)	η_{inh}^a	$T_m, ^\circ\text{C}$ (DSC)	$[\alpha]_D^b$
1		95	0.414	250 (268)	-56.6°
2		98	0.389	298	-58.5°
3		98	0.147	331	-125.5°

^a Measured in trifluoroacetic acid at 25°C with $c = 1$ g/dL.

^b CF_3COOH , $c = 5$.

cating relatively high molecular weight. The others are oligomers. The difference in the molecular weights can be attributed to the reactivity of the diisocyanate used. The polymers derived from aliphatic hexamethylenediisocyanate, which is more reactive than are MDI and TDI, have higher inherent viscosities.

Solubility of the Polymers

All polymers were white or slightly colored powders, insoluble in common organic solvents. The insolubility of the polymers in propan-2-ol allows us to say that the reduction of acetophenone takes place in a really heterogeneous system. The additional proof for that is the recycling of the polymers, which will be discussed later. The solubility of the polymers in chloroform and dichloromethane increases when the spacing between the urea units increases and they became completely soluble in the case of polymers **6** and **7**. Those two polymers also contain the diamine with *N,N'*-dimethyl groups which weaken the hydrogen bonding. By quenching the polyaddition with propan-2-ol, we avoided crosslinking (except for polymer **8**) to facilitate characterization. All polymers were soluble in trifluoroacetic acid and sulfuric acid.

FTIR Analysis

FTIR spectra of the polymers were taken as a KBr disc. The main absorption bands are given in Table I. All polymers show the characteristic bands of N—H stretching vibrations (3330 cm^{-1}), aromatic (except for polymer **1**) and aliphatic C—H stretching vibrations and C=O stretching vibrations of carbonyls in the urea bond. The N—H absorption peak (stretch) was located at 3330 cm^{-1} indicates that most of the NH groups are hydrogen-bonded because the free N—H absorption peak at 3445 cm^{-1} is negligible,¹³ except in the case of polymer **6**, where its intensity is equal to the other absorption band due to the presence of a methyl group on the nitrogen atom in the urea bond. The *N*-methyl group prevents the formation of hydrogen bonds and increases solubility.

NMR Study

NMR spectra of some polymers were recorded from CDCl_3 or/and CF_3COOD solutions. The chemical shifts are given below:

Polymer **6**:

$^1\text{H-NMR}$ (CDCl_3), δ (ppm) = 6.8–7.5 (m, H_{arom}); 6.45 (m, NCH + NH); 2.68 (s, NCH_3); 2.19 (s, Ph-CH_3).

Table III Polymers Derived from (1*R*, 2*R*)-(+)-1,2-Diphenyl-1,2-ethanediamine

Sample	Polymer	Yield (%)	η_{inh}^a	$T_m, ^\circ\text{C}$ (DSC)	$[\alpha]_D^b$
4		100	0.105	273	-15.1°
5		99	0.332	(199) 223	-53.7°

^{a,b} See footnotes to Table II.

¹H-NMR (CF₃COOD), δ (ppm) = 7.05 (m, H_{arom}); 6.34 (s, NCH); 2.84 (s, N—CH₃); 2.14 (s, Ph—CH₃).

¹³C-NMR (CDCl₃), δ (ppm) = 156.1; 119.9–137.5; 55.2; 29.7; 13.1.

Polymer 7:

¹H-NMR (CDCl₃), δ (ppm) = 6.9–7.2 (m, H_{arom}); 6.45 (s, NCH + NH); 3.78 (s, Ph—CH₂—Ph); 2.68 (s, NCH₃).

¹H-NMR (CF₃COOD), δ (ppm) = 7.34 (s, H_{arom}); 6.55 (s, NCH); 4.1 (s, Ph—CH₂—Ph); 3.1 (s, NCH₃).

¹³C-NMR (CDCl₃), δ (ppm) = 29.7; 55.0; 119–137.4; 156.

Monomeric analog **9**: ((1*S*, 2*S*)-(+)-*N,N'*-dimethyl-1,2-diphenylethylenyl-diphenyl diurea):

¹H-NMR (CDCl₃), δ (ppm) = 6.99–7.37 (m, H_{arom}); 6.52 (s, NCH); 6.41 (s, NH); 2.78 (s, NCH₃).

¹H-NMR (CF₃COOD), δ (ppm) = 7.34–7.51 (m, H_{arom}); 6.53 (s, NCH); 3.1 (s, NCH₃).

¹³C-NMR (CDCl₃), δ (ppm) = 155.9; 119.6–139.5; 55.0; 29.8.

The ¹H-NMR and ¹³C-NMR spectra confirm the supposed structure of the polymers studied. We do not detect the chain ends, which means that the molecular weight of the samples is relatively high. Given the sensibility of the NMR method, we can estimate that its minimum value is 2000 g/mol. It

Table IV Polymers Derived from (1*R*, 2*R*)-(+)-*N,N'*-Dimethyl-1,2-diphenyl-1,2-ethanediamine

Sample	Polymer	Yield (%)	η_{inh}^a	$T_m, ^\circ\text{C}$ (DSC)	$[\alpha]_D^b$
6		100	0.105	277	-203°
7		95	0.147	254	-330°
8 ^c		98 ^c	—	—	—

^{a,b} See footnotes to Table II.

^c Crosslinked by excess diisocyanate (crude MDI; 60% of diisocyanate, 30% of different triisocyanates).

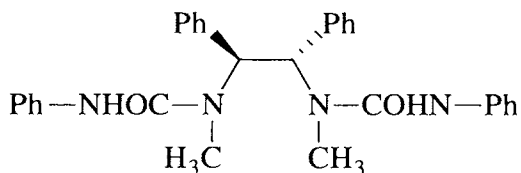


Figure 3 Monomeric analog of the polyureas (**9**).

is noticeable that the NCH protons are strongly shifted downfield ($\delta = 6.45$ ppm) which is due to deshielding by the anisotropy of the C=O group and/or phenyl group.

Optical Activity

All polymers were optically active (see Tables II–IV). It is interesting to note that in all samples the direction of rotation is reversed compared to that of corresponding diamine. The same phenomenon is observed in the case of monomeric analog of the polymers with product **9** (Fig. 3), which was synthesized from (1*S*, 2*S*)-(–)-*N,N'*-dimethyl-1,2-diphenyl-1,2-ethanediamine and phenyl isocyanate. It has $[\alpha]_D^{25} = +405^\circ$ ($c = 2$, chloroform), while the diamine has $[\alpha]_D^{25} = -20^\circ$ ($c = 1$, chloroform).

Thermal Properties

Melting points of polyureas were determined by DSC and they are above 250°C for all the samples due to existence of strong hydrogen bonding. It is important to note that heating polymers slightly above their melting points leads to degradation. In the case of **1** and **5**, there are two melting points. The multiple melting peaks are probably due to reorganization of metastable crystals from folded chains.¹⁴ The fact that melting peaks are relatively sharp shows that the polymers have a regular structure. However, X-ray diffraction did not reveal any crystallinity.

The presence of the exothermic peak at 90°C is due to the evaporation of water in the polymers. The presence of different amounts of water in the samples which were left in contact with air was also observed by microanalysis (see Experimental). The entirely aliphatic polymer **1** is hydrophobic and does not contain water, while others contain different quantities, ranging from 0.5 mol per monomer unit for **5** and **7** to 2 mol for **6** and **2**, respectively. The hydrophilicity of the polyureas is due to the urea bond and to the aromatics. It is not clear which of those two factors is more important for the hydrophilic character of the polymers. The presence of water is important for catalytic activity.

Preparation of Rh Catalysts

Rhodium-containing catalysts were prepared by complexation of the metal to the nitrogen ligands in the backbone ($[\text{diamine unit}]/[\text{Rh}] = 10$). To this end, $[\text{Rh}(\text{COD})\text{Cl}]_2$ was added to the slurry of the polymer in propan-2-ol. After 24 h of stirring at room temperature, the catalyst was filtered-off, washed thoroughly with propan-2-ol, and dried under vacuum at room temperature. The catalysts were slightly yellow. Elemental analysis confirms that rhodium is complexed quantitatively.

ANAL: calcd Rh % = 2.41.

Found: 2.01%.

Reduction of Acetophenone by Rh Catalysts

As-prepared catalysts were used in the reduction of acetophenone (Fig. 2) by hydride transfer. The results are presented in Table V.

The reduction by hydride transfer is attractive because one can avoid utilization of H_2 and high pressure. In Table V, the results obtained in the homogeneous catalytic asymmetric reduction of acetophenone (entries 1, 5, and 8)⁹ are compared with those obtained using polymers as heterogeneous catalysts. The best results in homogeneous catalysis are obtained using *N,N'*-dimethyl-1,2-diphenyl-1,2-ethanediamine (entry 8). The enantiomeric excess (e.e.) was 67% at room temperature. It was slightly lower at 70°C (55%). At room temperature in the heterogeneous catalysis, the reaction rates were low. To accelerate the conversion, the reaction temperature was increased to 70°C. The results presented in Table V were obtained at 70°C, including those in the homogeneous system. In general, the polymers keep the selectivity of monomeric analogs. In the case of polymer **1**, both selectivity and activity are increasing (entries 1 and 2). The importance of C_2 symmetry is demonstrated in entries 3 and 4. Polymer **2**, derived from disymmetric 2,4-toluenediisocyanate, gives no enantiomeric excess, while its analog, polymer **3**, preserves its C_2 -axis of symmetry and gives 13% of e.e.

The best results are obtained with polymer **8**, which is crosslinked by an excess of diisocyanate, and by using crude MDI, which is a mixture of 60% of diisocyanate and 30% of different triisocyanates (entry 11). It seems that, as in the case of the soluble ligand, the rigidity of the active site is crucial for the selectivity of the catalytic system. Polymer **6** (entry 6), which contains 2 mol of water per unit of the monomer, is unusually inactive. We think that the presence of water slows down the reduction.

Table V Reduction of Acetophenone

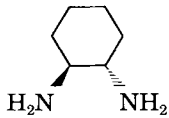
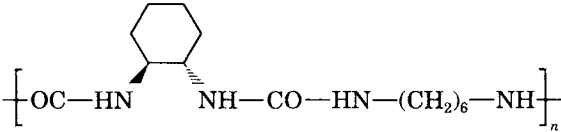
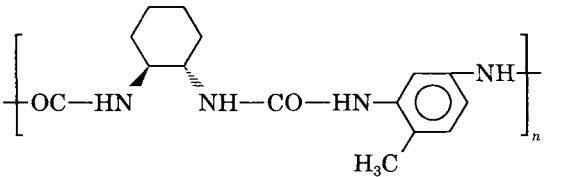
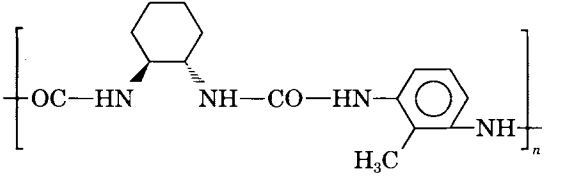
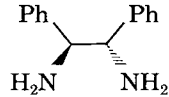
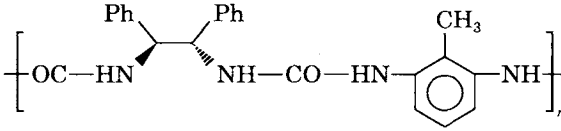
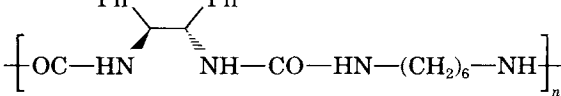
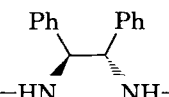
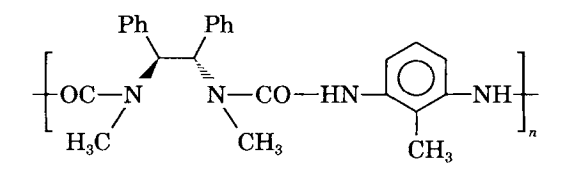
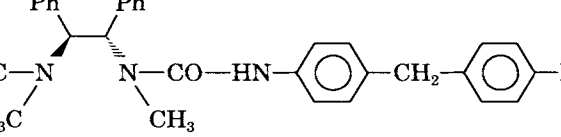
No.	Chiral Polymer-Rh Catalyst*	Conversion (%)	Time (Days)	e. e. (%) (Configuration)
1		5.5	6	12 (<i>R</i>)
2		70	5	30 (<i>S</i>)
3		80	4	0
4		50	4	13 (<i>S</i>)
5		94	8	17 (<i>S</i>)
6		54	3	10 (<i>R</i>)
7		20	4	9 (<i>R</i>)
8		94	7	55 (<i>S</i>)
9		63	17	24 (<i>R</i>)
10		97	3	39 (<i>R</i>)

Table V (Continued)

No.	Polymer-Rh Catalyst*	Conversion (%)	Time (Days)	e. e. (%) (Configuration)
11		100	1	60 (R)
12		100	1	60 (R)
13		100	1	59 (R)

Polymers containing *N,N'*-dimethyl-1,2-diphenyl-1,2-ethanediamine units give better results than those with diaminocyclohexane units.

One of the main advantage of heterogeneous catalysis is the possibility of reusing the catalyst. This is demonstrated in entries 11, 12, and 13, where the polymer was separated after completion of the reaction by simple filtration, washed, and reused twice without loss of selectivity and activity (entries 12 and 13). The elemental analysis performed on polymer **8** after three cycles shows that the metal is not leached from the catalyst.

CONCLUSION

A series of chiral polyureas with a pseudo- C_2 -axis of symmetry was synthesized by a simple and rapid method of solution polyaddition. The polymers, which are insoluble in the reaction medium complexed with rhodium, were used as chiral catalysts in the heterogeneous asymmetric reduction of acetophenone by hydride transfer. The results show that by this simple way one can obtain efficient heterogeneous catalysts. Other types of polymers and other reactions using as synthesized metal-containing chiral polymers are under investigation in our laboratory.

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