for $C_5H_{10}O_2N_2$ (M^+) 130.0742, found 130.0741.

Acknowledgment. We are grateful to Alan T. Johnson for the X-ray structure determination of the cis isomer of compound **36**. Financial support was provided by the National Science Foundation (CHE-8619029). Funds for the purchase of a Bruker AC-300 MHz NMR spectrometer were provided by the National Science Foundation (1 S10 RR 04039-01).

Supplementary Material Available: Tables listing the crystallographic data collection details, refinement procedures, bond lengths, bond angles, positional parameters, and thermal parameters of *cis*-4,5-dimethyl-1-(*o*-nitrobenzyl)-2-[2-(trimethylsilyl)ethoxycarbonyl]pyrazolidin-3-one, **36** (13 pages). Ordering information is given on on any current masthead page.

Notes

Polymer-Supported Poly(amino acids) as New Asymmetric Epoxidation Catalyst of α,β-Unsaturated Ketones

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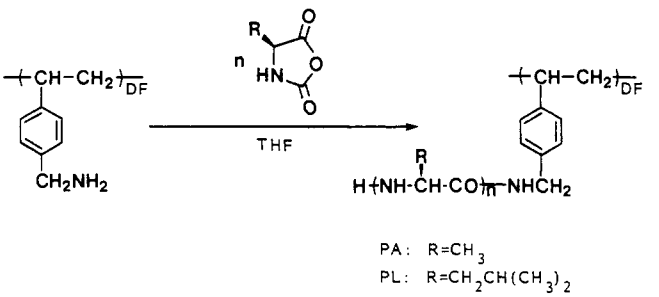
Recently there has been much work on polymer-supported asymmetric syntheses.[1] The polymers, in insoluble beads form, offer a well-documented advantage in purification since separation of chiral reaction product from the chiral auxiliary is achieved by filtration.[2] The polymers can be recycled and may provide a unique microenvironment that may result in enhanced stereoselectivities.

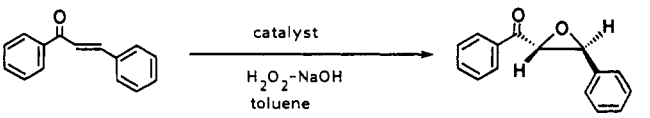
Asymmetric reactions in which peptides or poly(amino acids) take part include Michael additions of active hydrogen compounds to activated double bonds,[3] carbonylation of allylic alcohols,[4] hydrogenation,[5] oxidation,[6] and reduction.[7] Among the most interesting asymmetric syntheses using poly(amino acids) are the epoxidations of α,β-unsaturated carbonyl compounds reported by Juliá and his group.[8] Enantioselectivities higher than 90% with poly(L-alanine) as chiral catalyst have been reported. A considerable drawback to this system is the difficulty of separation and recycling of the semisolid pastelike poly(amino acid).

We have found that poly(styrene-co-divinylbenzene)-supported poly(amino acid) can act as an efficient chiral catalyst in the epoxidation of α,β-unsaturated carbonyl compounds with alkaline hydrogen peroxide to yield optically active epoxy ketones in high enantioselectivities up to 99%. Separation of the polymer-supported catalyst has been remarkably improved in this system, and they could be reused without a significant loss of activity as will be discussed in this paper.

Scheme I



Scheme II



Polymer-supported poly(amino acids) were synthesized by the following procedure. A 2% cross-linked microporous polystyrene resin incorporating aminomethyl functionality was prepared as a starting material. Utilizing this polymeric primary amine as an initiator, *N*-carboxyanhydrides (NCA) of L-alanine and L-leucine were polymerized in THF at room temperature for 40 h under a nitrogen atmosphere to obtain the polymer-supported poly(L-alanine) (PA) and poly(L-leucine) (PL), respectively, with different degrees of polymerization (n), depending upon the NCA:initiator ratio (Scheme I). The aminomethyl group of highly cross-linked macroporous polystyrene containing 20 mol % of divinylbenzene was not suited for this grafting reaction since the resin has no swellability in organic solvents (ML). We have also prepared linear polystyrene-based catalyst (LL).

The various polymer-supported poly(amino acids) (PA1-PA8, PL1-PL6, ML, and LL) were tested as chiral catalysts in the epoxidation of benzalacetophenone according to Juliá's procedure.[8] The reactions were carried out at room temperature in a triphase system with toluene, water, polymeric catalyst, and oxidant (H_2O_2–NaOH), unless otherwise stated (Scheme II). The results are summarized in Table I. Satisfactory enantioselectivities were obtained by using both PA and PL as asymmetric

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Table I. Asymmetric Epoxidation of Benzalacetophenone Catalyzed by Polymer-Supported Poly(amino acids)

				2,3-epoxy-1,3-diphenyl-1-propanone		
entry	catalyst	DF[a]	n[b]	% yield[c]	$[\alpha]^{25}_{577}$,[d] deg (CH_2Cl_2)	% ee[e]
1	PA1	0.05	14	20	−117	46
2	PA2	0.20	17	46	−126	49
3	PA3	0.30	4	50	−214	83
4	PA4	0.40	5	67	−226	88
5	PA5	0.40	15	54	−187	73
6	PA6	0.40	20	66	−240	93
7	PA7	0.40	38	52	−220	86
8	PA8	0.75	20	46	−155	60
9	PL1	0.20	20	47	−221	86
10[f]	PL1	0.20	20	43	−214	83
11	PL2	0.32	32	92	−255	99
12	PL3	0.40	9	36	−205	80
13	PL4	0.40	20	50	−225	88
14[f]	PL4	0.40	20	37	−220	86
15	PL5	0.40	33	94	−250	97
16[f]	PL5	0.40	33	82	−214	83
17	PL6	0.75	20	25	−151	59
18	ML[g]	0.20	6	10	−109	42
19	LL[h]	0.50	18	40	−103	40

[a] Degree of functionalization: see Experimental Section. [b] Degree of polymerization of poly(amino acid). [c] Based on material isolated after chromatography over silica gel. [d] $[\alpha]^{20}_{578}$ −214° (CH_2Cl_2) for (−)-(2*R*,3*S*)-1,3-diphenyl-1-propane: see ref 8b. [e] Determination of the enantiomeric excess by chiral-phase HPLC analysis using chiral column. [f] Reaction performed in CCl_4. [g] Macroporous polystyrene resin supported poly(L-leucine). [h] Linear polystyrene supported poly(L-leucine).

catalysts. In the range of DF = 0.3–0.4 for PA and DF = 0.20–0.40 for PL the product showed relatively high % ee. It is noteworthy that polymeric catalysts having a small degree of polymerization (n < 10) still have high catalytic activities (entries 3, 4, and 12). Nonsupported poly(amino acids) (n < 10) gave only poor chemical and optical yield.[8] Results obtained with PA8 and PL6 having high DF value (0.75) showed a lowering in the enantioselectivities, and handling of the polymeric catalyst was somewhat difficult because of their similarity to nonsupported poly(amino acid). The use of CCl_4 as organic phase afforded somewhat lower % ee (entries 10, 14, and 16). PL2 gave the best result in this system to obtain 92% yield with 99% ee. The polymer-supported catalysts could be recycled several times without significant loss of activity. Indeed, after 12 times of recycles of PL2 chiral epoxide was obtained in 95% yield with 94% ee. The use of the macroporous polymer-supported catalyst, ML, resulted in the lowering chemical and optical yield. The linear polystyrene-supported catalyst, LL, has also been tested in the asymmetric epoxidation. Overall, handling of the linear polystyrene-based catalyst is much more difficult than that of its cross-linked analogue, and small processing losses are harder to avoid, making quantitative recovery of the polymeric catalyst almost impossible to achieve.

The use of polymeric catalysts containing poly(L-amino acid) always results in the predominant formation of the 2*R*,3*S* epoxide determined by optical rotation measurements.[9]

The reactions of other α,β-unsaturated ketones were also examined in a similar manner using PL5. As shown in Table II, all the olefins tested afforded the corresponding epoxides with high optical yields. The broad substrate specificity enables the synthesis of a variety of optically active epoxy ketones.

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Table II. Asymmetric Epoxidation of α,β-Unsaturated Ketones Using Polymer-Supported Poly(L-leucine) (PL5)

	$R^1COCH{=}CHR^2$		product		
entry	R^1	R^2	% yield[a]	$[\alpha]^{25}_{577}$, deg (*c* 2.0, CH_2Cl_2)	% ee[b]
1	Ph	Ph	94	−249	97
2	Ph	*p*-MeOPh	89	−305	90
3	Ph	*p*-NO_2Ph	90	−274[c]	99
4	Ph	*o*-MeOPh	56	−22	76
5	Ph	*o*-EtOPh	56	+25	83
6	Ph	*p*-ClPh	98	−253[d]	99
7	*p*-MeOPh	Ph	83	−164	87
8	*p*-ClPh	Ph	98	−202	99

[a] Based on material isolated after chromatography over silica gel. [b] Enantiomeric excess determination was performed using chiral-phase HPLC analysis. [c] $[\alpha]^{20}_{578}$ −205° (CH_2Cl_2) for (−)-2,3-epoxy-3-(4-nitrophenyl)-1-phenyl-1-propane in 82% ee: see ref 8b. [d] $[\alpha]^{20}_{578}$ −148° (CH_2Cl_2) for (−)-3-(4-chlorophenyl)-2,3-epoxy-1-phenyl-1-propanone in 66% ee: see ref 8b.

Experimental Section

General Methods. ^{1}H NMR NMR spectra were recorded on a JEOL JNM-GX270 nuclear magnetic resonance spectrometer in a $CDCl_3$ solution with Me_4Si as an internal standard. Infrared spectra were recorded on JEOL JIR-40X FTIR and Jasco A-3 spectrophotometers. The melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Thin-layer chromatography was performed on silica gel 60F-254 precoated plates (Merck). Column chromatography was performed on silica gel C-200 (100–200 mesh, Wako).

Enantiomeric excess determination was performed by using chiral phase HPLC analysis (chitosan based column, 4.6 mm × 250 mm, which is a kind gift from Nippon Steel Co., hexane/2-propanol, 97/3, 0.6 mL/min) based on comparison of retention times and the areas between the asymmetric epoxidation product and the racemic ones. HPLC was effected on a Jasco Trirotar-III liquid chromatograph. Optical rotations were measured on materials isolated by column chromatography by using a Jasco DIP-140 digital polarimeter.

Capacities of the polymers determined by gravimetry and elemental analysis are expressed in millimoles of functional groups per gram of dry resin (mmol/g) or as degree of functionalization (DF). The DF of a polystyrene-based reactive polymer is a measure of the proportion of aromatic styrene rings that carry the desired functionality. For example, DF = 0.30, if 30% of the styrene units are functionalized.

The purity of all title compounds was judged to be >95% by ^{1}H NMR spectral determinations.

Materials. *N,N*-Dimethylformamide and toluene were dried on CaH_2 and distilled under vacuum prior to use. Tetrahydrofuran was distilled from sodium benzophenone ketyl immediately before use. L-Alanine, L-leucine, benzaldehyde, 4-methoxybenzaldehyde, 4-nitrobenzaldehyde, 2-methoxybenzaldehyde, 2-ethoxybenzaldehyde, 4-chlorobenzaldehyde, acetophenone, 4-methoxyacetophenone, and 4-chloroacetophenone were commercially available and used as received. 4-Vinylbenzyl chloride is a kind gift from Seimi Chemical Co.

Synthesis of Polymer-Supported Catalysts. PL5. *N*-Carboxy-L-leucine anhydride (L-leucine NCA) was prepared according to the literature[10] in 80% yield; mp 76–77 °C (lit.[11] mp 76–77 °C). The starting resin was prepared by suspension polymerization of a styrene, divinylbenzene, and 4-vinylbenzyl chloride using AIBN as an initiator at 70 °C for 24 h under nitrogen.[1a] Amination of the chloromethyl functionality was conducted by reaction with phthalimide followed by hydrazine.[12] Removing impurities from the aminomethylated resin, particularly water and amine, is required to prevent homopolymerization of NCA in the THF phase during immobilization. Soxhlet extraction with dry THF was conducted to sufficiently purify the resin. To

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the aminomethylated polystyrene resin (0.3 g, 3.46 mequiv of NH_2/g) suspended in dry THF was added a THF solution of L-leucine NCA (5.7 g, 36.3 mmol), and the solution was stirred at room temperature for 40 h. The resulting polymer beads were filtered and washed with THF and methanol. After drying in vacuo at 40 °C for 24 h, 4.20 g of polymer was obtained. Nitrogen analysis indicated an average degree of polymerization (n) of poly(L-leucine) corresponding to 33.

Preparation of α,β-Unsaturated Ketones. All α,β-unsaturated ketones were synthesized according to the literature.[13]

(*E*)-1,3-Diphenyl-2-propen-1-one: mp 57–58 °C (lit.[13a] mp 57–58 °C).

(*E*)-1-(4-Methoxyphenyl)-3-phenyl-2-propen-1-one: mp 99–102 °C. Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.70; H, 5.85.

(*E*)-3-(4-Nitrophenyl)-1-phenyl-2-propen-1-one: mp 163–165 °C (lit.[13b] mp 165 °C).

(*E*)-3-(2-Methoxyphenyl)-1-phenyl-2-propen-1-one: mp 59–61 °C (lit.[13c] mp 58–59 °C).

(*E*)-3-(2-Ethoxyphenyl)-1-phenyl-2-propen-1-one: oil. Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39 Found: C, 80.85; H, 6.30.

(*E*)-3-(4-Chlorophenyl)-1-phenyl-2-propen-1-one: mp 114–116 °C (lit.[13b] mp 115 °C).

(*E*)-3-(4-Methoxyphenyl)-1-phenyl-2-propen-1-one: mp 69–71 °C. Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.60; H, 5.95.

(*E*)-1-(4-Chlorophenyl)-1-phenyl-2-propen-1-one: mp 94–95 °C. Anal. Calcd for $C_{15}H_{11}ClO$: C, 74.23; H, 4.57; Cl, 14.61. Found: C, 74.29; H, 4.60; Cl, 14.65.

Asymmetric Epoxidation of Benzalacetophenone. The following procedure is representative of these reactions. To a stirred solution of 1.0 g of benzalacetophenone (4.8 mmol) in toluene (12 mL) was added 3.98 g of PL2 (1.0 mequiv of poly(L-leucine). Then 4.4 mL of H_2O_2 (30 wt % solution in water) and 0.35 g of NaOH in water (2 mL) were added at 0 °C. The mixture was stirred at room temperature for 2 days. The reaction was monitored by TLC. The polymeric catalyst was filtered off and toluene layer was washed with water and dried over $MgSO_4$, and the solvent was evaporated. The residue was subjected to silica gel column chromatography using toluene as eluent to obtain a white solid (0.99 g, 92%): mp 64–65 °C; $[\alpha]^{25}_{577}$ −255° (*c* 2.15, CH_2Cl_2) [lit.[8b] mp 63–65 °C; lit.[8b] $[\alpha]^{20}_{578}$ −214° (*c* 1, CH_2Cl_2)]; TLC R_f = 0.3 in toluene. The enantiomeric excess was determined by using chiral-phase HPLC to give 99% ee. The ^1H NMR and IR spectra of (−)-(2*R*,3*S*)-epoxy-1,3-diphenyl-1-propanone were essentially identical with those reported in the literature.[8b]

Epoxidations of other olefins were performed in the same manner as described above.

(−)-2,3-Epoxy-3-(4-methoxyphenyl)-1-phenyl-1-propanone: mp 60–63 °C. Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.58; H, 5.55. Found: C, 75.60; H, 5.53.

(−)-2,3-Epoxy-3-(4-nitrophenyl)-1-phenyl-1-propanone: mp 140–142 °C (lit.[8b] mp 139–141.5 °C). Anal. Calcd for $C_{15}H_{11}NO_4$: C, 66.91; H, 4.12; N, 5.20. Found: C, 66.93; H, 4.16; N, 5.18.

(−)-2,3-Epoxy-3-(2-methoxyphenyl)-1-phenyl-1-propanone: mp 90–91 °C. Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.58; H, 5.55. Found: C, 75.62; H, 5.57.

(+)-2,3-Epoxy-3-(2-ethoxyphenyl)-1-phenyl-1-propanone: mp 92–93 °C. Anal. Calcd for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 76.14; H, 5.99.

(−)-3-(4-Chlorophenyl)-2,3-epoxy-1-phenyl-1-propanone: mp 69–70 °C (lit.[8b] mp 68 °C).

(−)-2,3-Epoxy-1-(4-methoxyphenyl)-3-phenyl-1-propanone: mp 60–62 °C. Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.58; H, 5.55. Found: C, 75.62; H, 5.53.

(−)-1-(4-Chlorophenyl)-2,3-epoxy-3-phenyl-1-propanone: mp 90–91 °C. Anal. Calcd for $C_{15}H_{11}ClO_2$: C, 69.64; H, 4.29; Cl, 13.70. Found: C, 69.67; H, 4.30; Cl, 13.73.

Supplementary Material Available: ^1H NMR spectra of α,β-unsaturated ketones and epoxy ketones (16 pages). Ordering information is given on any current masthead page.

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Hydrolysis of 4-Nitrophenyl Phenyl(trichloromethyl)phosphinate: Predominance of a P–C vs P–O Bond Cleavage Reaction†

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Results of kinetic and product distribution studies in the hydrolysis of 4-nitrophenyl phenyl(trichloromethyl)-phosphinate, at pH values ranging from 1.3 to 10.2, are described. P–C (vs P–O) bond cleavage predominates at all pH levels and represents the first report of P–CCl_3 bond scission under either acidic or neutral conditions for a trichloromethyl phosphorus ester.

The carbon–phosphorus bond in dialkyl (trichloromethyl)phosphonates [$(RO)_2P(O)X$, where X = CCl_3] and other trichloromethyl-containing organophosphorus compounds undergoes P–C bond cleavage, but significant chemoselectivity results depending on the reaction conditions employed. The trichloromethyl–phosphorus bond is cleaved under strongly basic aqueous conditions;[1] following treatment with ethanolic potassium hydroxide,[2] fluoride ion,[3] strong base, sodium ethoxide, and potassium *tert*-butoxide;[4] by sodium methoxide in anhydrous methanol;[5] and photochemically.[6] In contrast, under milder conditions, the P–C bond in these same (and other) trichloromethyl-containing organophosphorus compounds is stable. Thus, treatment with dilute base or with various amines;[7] exposure to dilute acid, ethanol, or recrystallization from water;[1c,4] treatment with strong hydrochloric acid,[8] with refluxing ethanol;[9] during transesterification of aliphatic and aromatic carboxylic acids;[10] and even exposure to 0.1 N aqueous $Ba(OH)_2$(room temperature, 20 hr) of nucleoside 5′-trichloromethyl)phosphonates[4] leads to no P–C bond cleavage. Of particular note is the stability of the P–CCl_3 bond under even strongly acidic (18% aqueous HCl) conditions.

During investigations into the inhibition of cholinesterases by a variety of organophosphinates,[11] Lieske et al.[12] obtained unexpected results during characterization of one of these compounds. Routine alkaline hydrolysis studies carried out to assess the reactivity of 4-nitrophenyl phenyl(trichloromethyl)phosphinate (1) produced only 4% of the stoichiometric amount of 4-nitrophenol at pH 9.10 and 25.0 °C.[13] Evidence for the identity of 1 was conclusive, i.e., elemental analysis, IR spectrum, ^{31}P and proton NMR. Thus, it appeared possible that one or more competing, parallel reactions could be occurring during the hydrolysis to account for the low production of 4-nitrophenol. Hydrolysis of 1 to produce 4-nitrophenol is illustrated by reaction sequence a shown in Scheme I. In accord with published results for strong base cleavage of the analogous phenyl trichloromethyl chloridate,[4] P–CCL_3 cleavage during base-mediated hydrolysis of 1 might occur via pathway b.

To examine whether 1 was hydrolyzed in part via pathway b, the reaction mixture was assayed for the pro-

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† **Note.** The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting views of the Department of the Army or the Department of Defense.