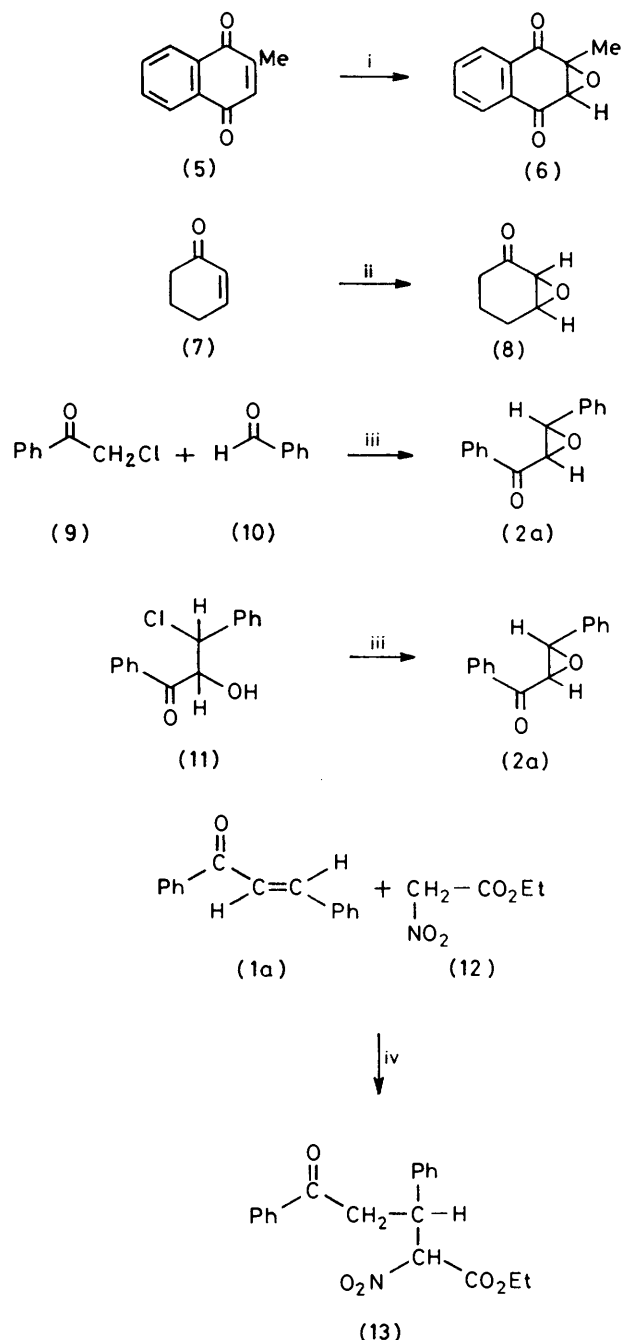
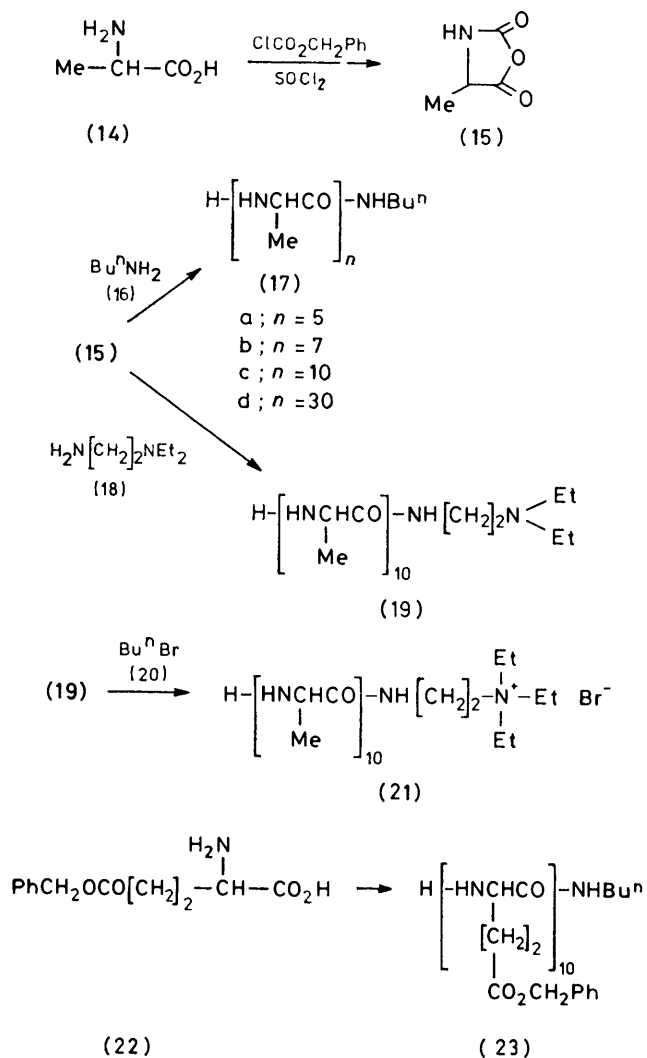


Catalyst (19) was obtained by polymerisation of (*S*)-alanine-NCA (15) with *N,N*-diethylethylenediamine (18) and catalyst (21) was prepared by reaction of catalyst (19) with *n*-butyl bromide (20).



SCHEME 2 Reagents: i, H_2O_2 - K_2CO_3 , toluene, catalyst; ii, H_2O_2 -NaOH, toluene, catalyst; iii, NaOH, toluene, catalyst; iv, toluene, catalyst

All the epoxidations were carried out at room temperature in a triphase system with toluene, water, a catalytic amount of polypeptides (17), (19), (21), or (23) and a large excess of oxidant (H_2O_2 -NaOH), unless otherwise



SCHEME 3

stated. All other reactions were performed in similar triphase systems (see Experimental section).

RESULTS

The epoxidation of substrates (1a)—(1h) in the triphase system water-toluene-poly-(*S*)-alanine (17c) occurs with good chemical yields and high optical yields (see Table 1). The stereoselectivity of the epoxidation by our method is substantially higher than that obtained by the procedure of Wynberg *et al.*^{9b} under phase-transfer conditions starting from the chalcones (1a)—(1h). In contrast, the stereoselectivity of the reaction decreases substantially with substrates (3), (5), and (7).

Structural Variations within the Catalyst.—The results obtained with the catalysts (17), (19), (21), and (23) in the epoxidation of chalcone (1a), reported in Table 2, indicate that (i) the use of catalysts (19) and (21) not only reduces the chemical yield, but also affects the asymmetric synthesis; (ii) when the catalysts (17a)—(17d), with different degrees of polymerisation, are used the enantioselectivity is

maximum with catalyst (17d) ($n = 30$) [enantiomeric excess (e.e.) 96%] and progressively decreases with lower degrees of polymerisation; (iii) among the catalysts tested poly-*S*-benzyl glutamate (23) gives the lowest asymmetric

TABLE 1

Epoxidation of substituted chalcones carried out in toluene with poly-*(S)*-alanine (17c)

Substrate ^a	Yield (%) ^b	$[\alpha]_{578}^{20}$ (°) (CH ₂ Cl ₂) ^c	E.e. (%) ^d
(1a)	78–85 ^e	–166–184 ^e	78–86 ^e
(1b)	83	–205 ^e	82 ^e
(1c)	29 ^d	–13 ^f	
(1d)	53 ^d	–230 ^f	
(1e)	96	–183	80
(1f)	30	–123	70
(1g)	54	–67	50
(1h)	47	–148	66

^a All α - β unsaturated ketones were synthesized according to ref. 15; (*E*)-alkenes were used. ^b Based on material isolated after chromatography over silica gel. ^c Results depend on chemical and optical purity of poly-*(S)*-alanine. ^d Calculated by ¹H n.m.r. spectroscopy. ^e Value after one crystallization from ethanol. ^f Rotation determined according to yield calculated by ¹H n.m.r. spectroscopy. ^g Determination of the enantiomeric excess by ¹H n.m.r. spectroscopy in the presence of Eu(hfc)₃ as chiral shift reagent.

induction; (iv) when the poly-*(S)*-alanines (17c) and (17d) ($n = 10$ and 30) are recovered from the epoxidation and recycled (see Experimental section) a decrease in chemical and optical yields is observed; (v) no reactions occur in the absence of the polypeptide; (vi) the racemic epoxide is obtained if the reaction is performed in a biphasic water-poly-*(S)*-alanine system.

TABLE 2

Epoxidation of chalcone (1a) carried out in toluene at room temperature with catalysts (17), (19), (21), and (23)

Catalyst ^a	Time (h)	Yield (%) ^b	$[\alpha]_{578}^{20}$ (°) (CH ₂ Cl ₂) ^c	E.e. (%) ^d
None	24	0	0	
(17a)	24	9	–23	11
(17b)	24	18	–59	28
(17c)	24	78	–179.6	
(17c) ^e	24	100	0	
(17c) ^{d,e}	28	85	–92.5 ^f	
(17d)	24	57	–200	93
(17d) ^{d,e}	66	75 ^f	–140 ^f	
(19)	24	52 ^f	–32	15
(21)	24	62 ^f	–43	20
(23)	144	12 ^f	–23.4 ^f	
(17d) ^e	28	96	–206 ^f	96

^a See Experimental section. ^b Calculated by ¹H n.m.r. spectroscopy. ^c Reaction performed without solvent. ^d Reaction performed with recycled poly-*(S)*-alanine. ^e Reaction performed in CCl₄. ^f Based on material isolated after chromatography over silica gel. ^g $[\alpha]_{578}^{20}$ measured in acetone.

The Solvent.—Toluene and carbon tetrachloride are the solvents of choice (see Table 3). In connection with the results reported by Wynberg and Greijdanus ¹¹ in the epoxidation of chalcones with Quibec under phase-transfer conditions, we have found that there is no direct correlation between the dielectric constant of the solvent and the e.e. of the epoxychalcone obtained; indeed, cyclohexane and hexane gave the lowest asymmetric inductions. In contrast, the rate of the reaction is highest when hexane is used.

The Temperature.—The degree of asymmetric induction in the epoxidation of chalcone (1a) in toluene using catalyst

TABLE 3

Solvent effects in the epoxidation of chalcone (1a) with catalyst (17c) at room temperature

Solvent	Time (h)	Yield (%) ^a	$[\alpha]_{578}^{20}$ (°) (acetone)
Toluene	24	77	–179.6
CCl ₄	28	75	–190
Chlorobenzene	48	83	–180.3
CH ₂ Cl ₂	50	78	–160.0
Cyclohexane	48	92	–103
Hexane	24	95	–30.6

^a Calculated by ¹H n.m.r. spectroscopy.

(17c) decreases when the temperature is raised, as shown in Table 4.

The Amount of Catalyst Employed.—There is no substantial change in the stereoselectivity of the reaction when

TABLE 4

Temperature effect in the epoxidation of chalcone (1a) with catalyst (17c) in toluene

T (°C)	Time (h)	Yield (%) ^a	$[\alpha]_{578}^{20}$ (°) (acetone)
0	67	86	–180
25	64	77	–179.6
50	22	36 ^{b,c}	–92.3

^a Calculated by ¹H n.m.r. spectroscopy. ^b This low conversion is probably due to the destruction of H₂O₂ at this temperature. ^c Based on material isolated after chromatography over silica gel.

different substrate : catalyst ratios are employed (see Table 5). This behaviour is in sharp contrast with experimental results obtained by using BSA as catalyst.⁴ Chemical conversion is more influenced than optical yield when the relative amount of catalyst decreases.

TABLE 5

Effect of the substrate : catalyst ratio in the epoxidation of chalcone (1a) with catalyst (17c) in CCl₄ at room temperature

Chalcone (g)	Catalyst (g)	Time (h)	Yield (%) ^a	$[\alpha]_{578}^{20}$ (°) (acetone)
0.5	0.4	28	100	–190
0.25	0.4	28	98	–187
0.5	0.1	71	60 ^b	–177.0
0.5	0.02	282	42.3 ^b	–167.0

^a Calculated by ¹H n.m.r. spectroscopy. ^b Based on material isolated after chromatography over silica gel.

Other Oxidising Agents.—Results obtained with catalyst (17c) in the epoxidation of chalcone (1a) using different oxidising agents (Table 6) show that (i) H₂O₂–NaOH is the best system among those tested; and (ii) the reaction

TABLE 6

Effect of the oxidant in the epoxidation of chalcone (1a) with catalyst (17c) in toluene at room temperature

Oxidant	Yield (%) ^a	E.e. (%) ^b
H ₂ O ₂ –NaOH	85 ^c	86
MCPBA–NaHCO ₃ –H ₂ O ^b	10	0
Bu ^t O ₂ H–NaOH–H ₂ O	42	18
Bu ^t O ₂ H ^d	0	
Bu ^t O ₂ H–K ₂ CO ₃ ^e	100	0

^a Calculated by ¹H n.m.r. spectroscopy. ^b MCPBA = *m*-chloroperbenzoic acid. ^c Based on material isolated after chromatography over silica gel. ^d 80%. ^e Solid.

does not occur using 80% Bu^tO₂H. If solid K₂CO₃ is added to the system, the chemical conversion is complete, but the epoxychalcone obtained is racemic. This fact shows that a triphasic system is necessary for asymmetric induction.

Epoxidation of Substrates other than Chalcones.—Epoxidation reactions of (*E*)-2-nitro-1-phenylpropene (3), 2-methyl-1,4-naphthoquinone (5), and cyclohex-2-enone (7) in a triphase system in the presence of catalysts (17c) and (23) were studied. Chemical yields and optical rotations of the products are reported in Table 7. The epoxidation of the

TABLE 7

Epoxidation of substrates other than substituted chalcones with catalysts (17c) and (23) in toluene at room temperature

Substrate ^a	Catalyst	Oxidant	Yield (%) ^b	[α] ₄₃₆ ²⁰ (°) (CH ₂ Cl ₂)	E.e. (%) ^c
(3)	(17c)	H ₂ O ₂ -NaOH	50 ^d	-1.3	7
(3)	(23)	H ₂ O ₂ -NaOH	67 ^d	-0.7	3.8
(5) ^e	(17c)	K ₂ CO ₃ -Bu ^t O ₂ H ^f	100	0	
(5)		K ₂ CO ₃ -Bu ^t O ₂ H ^f	81	0	
(5)	(17c)	K ₂ CO ₃ -H ₂ O ₂ ^f	100	0	
(5)		K ₂ CO ₃ -H ₂ O ₂ ^f	41	0	
(7)	(17c)	K ₂ CO ₃ -H ₂ O ₂ ^f	19	-0.4	

^a 2-Nitro-1-phenylpropene was synthesized according to ref. 16. ^b Calculated by ¹H n.m.r. spectroscopy. ^c The e.e. was determined by ¹H n.m.r. spectroscopy using Eu(hfc)₃ as chiral shift reagent. ^d In both cases some benzoic acid is obtained as a product of the basic decomposition of the substrate (3). ^e 2-Methyl-1,4-naphthoquinone is commercially available from Merck. ^f K₂CO₃ has been used instead of NaOH to avoid oxidations.

nitropropene (3) with poly-(*S*)-alanine (17c) gives higher optical yields than poly-(*S*)-benzyl glutamate (23) with e.e. 7% and 3.8%, respectively.

The epoxidation of 2-methyl-1,4-naphthoquinone (5) was performed either with K₂CO₃-Bu^tO₂H or with K₂CO₃-H₂O₂, but in both cases no stereoselectivity was obtained; in the absence of catalyst the chemical yields are lower. The oxidation of this substrate with NaOH-H₂O₂ in these conditions yielded phthalic acid as the main product.

Starting from cyclohex-2-enone (7), no substantial chemical and optical yield were observed. In contrast to the chalcones (1a)-(1h) Wynberg's PTC procedure affords better results for these substrates.

Other Base-catalyzed Reactions.—Both the Darzens condensation of phenacyl chloride (9) with benzaldehyde (10) and the dehydrohalogenation of chlorohydrin (11), carried out in toluene with catalyst (17c), occur with very low optical yields (see Table 8). The addition of ethyl nitroacetate (12) to chalcone (1a) affords the adduct (13) with appreciable optical yields (6.4%), but only after long reaction times (31 days).

DISCUSSION

Owing to the many factors involved in this epoxidation reaction (structure of the catalyst, degree of polymerisation, solvent, temperature, amount of catalyst employed, and nature of the starting material) it is difficult to rationalise the occurrence of asymmetric induction. Nevertheless, the following inferences can be made.

(a) Poly-(*S*)-alanine acts as chemical catalyst in the epoxidation of electron-poor olefins and is responsible for

asymmetric induction. Indeed, epoxidation reactions performed in the absence of poly-(*S*)-alanine not only give low chemical conversions, even for a longer reaction time, but also afford racemic products (Table 2). The amount and concentration of poly-(*S*)-alanine does not substantially influence the optical purity of the epoxide.

TABLE 8

Examples of base-catalyzed reactions with catalyst (17c) in toluene at room temperature

Reaction	Base	Time (h)	Yield (%) ^a	[α] ₅₇₈ ²⁰ (°) (CH ₂ Cl ₂)	E.e. (%) ^c
(9) + (10)→(2a)	NaOH (10%)	24	90	0	^c
(9) + (10)→(2a)	NaOH (10%) ^b	24	90	0	
(11) →(2a)	NaOH (10%)	0.2	100	+3.8	1.8 ^d
(11) →(2a)	NaOH (10%) ^e	0.2	53	+3.9	1.8
(11) →(2a) ^b	NaOH (10%)	2	100	0	
(1a) + (12)→(13)	NaOH	744	60	+8	6.4 ^f

^a Based on material isolated after chromatography over silica gel. ^b Reaction performed in the absence of catalyst. ^c Values reported by Wynberg in PTC: conversion 68%, optical yield 8%. ^d Values reported by Wynberg in PTC: conversion 90%, optical yield 6%. ^e Reaction performed with NaOH (50% mol equiv.). ^f Calculated after decarboxylation (see Experimental section).

(b) The prevailing enantiomer of the chalcone epoxide (2a) shows a negative optical rotation; therefore it must have, according to Wynberg,^{9a} the (2*R*,3*S*) absolute configuration. It is of note that the main stereochemical course starting from compound (19) is the same both in our triphase system and in the reaction carried out under PTC conditions with Quibec as catalyst.^{9b} The same absolute configuration has been assigned to epoxides (1e), (1f), and (1h) on the basis of the chirality induced in MBBA colestheric phase.¹²

(c) Both organic solvent and water are necessary in order to perform asymmetric epoxidation (see Table 6). This indicates that the reaction occurs only in a triphase system.*

(d) The possibility that the optical activity of the epoxide arises *via* asymmetric destruction of one of the two possible enantiomers can be ruled out. Starting from racemic epoxychalcone with poly-(*S*)-alanine, under the usual reaction conditions, the recovered epoxide (>95%) did not show any optical activity. Long reaction times do not lead to any appreciable racemisation of the epoxide (see Experimental section).

(e) In all the examined systems the highest stereoselectivity is observed in the presence of poly-(*S*)-alanine. The use of poly-(*S*)-benzyl glutamate (23) and of the modified polyalanines (19) and (21) leads to a remarkable decrease of the chemical and optical yields.

(f) The enantioselectivity reaches its maximum with catalyst (17d) (*n* = 30) and decreases with lower polymerisation (Table 2). This could possibly be attributed

* The reason for binding of the poly-(*S*)-alanine and the crucial role played by interfaces are unclear.

to conformational modifications of the polymer, caused by the change in the degree of polymerisation.¹³ In this respect it has to be mentioned that Inoue^{3a} and his co-worker have found that poly-(S)-alanines with $n = 3$ and 5 mainly assume the β -conformation, whereas in cases of higher values of n , the random and α -helical conformation are more important.

(g) Apart from the epoxidation of chalcone and related systems, poly-(S)-alanine is much less effective, as a catalyst, in the epoxidation of other systems such as 2-methyl-1,4-naphthoquinone (5), 2-nitro-1-phenylpropene (3) (Table 7), and in base-promoted reactions such as the dehydrohalogenation of halogenohydrin (9), the Darzens condensation of phenacyl chloride (9) with benzaldehyde (10), and the addition of ethyl nitroacetate (12) to the chalcone (1a). Indeed, in the Michael addition of ethyl nitroacetate (12) to the chalcone (1a), the adduct exhibits a low optical purity. The sign of its optical rotation is opposite that of the prevalent enantiomer obtained under phase-transfer conditions.¹⁴ Similarly, in the dehydrohalogenation of halogenohydrins the stereoselectivity is low and the prevalent enantiomer has an absolute configuration opposite to the enantiomer obtained in the epoxidation of chalcone.^{9a} Finally, in the Darzens condensation of phenacyl chloride (9) with benzaldehyde (10) the epoxide obtained is racemic.

Such a specific behaviour in the epoxidation of chalcones (1a)–(1h) with H_2O_2 and NaOH in triphase systems indicate that poly-(S)-alanine acts like a synthetic enzyme.

Experiments are in progress to perform stereoselective organic reactions with polypeptides other than poly-(S)-alanine and poly-(S)-benzyl glutamate and to elucidate the physicochemical properties of these particular triphase systems.

EXPERIMENTAL

Melting points are uncorrected. The optical rotations were determined with a Perkin-Elmer P-141 instrument and 241 polarimeter. I.r. spectra were recorded on a Perkin-Elmer 257 spectrophotometer. 1H N.m.r. spectra were recorded on a Hitachi Perkin-Elmer R-24 spectrometer, using tetramethylsilane as internal or external standard; chemical shifts are expressed as δ values. Enantiomeric excesses (e.e.) were determined by 1H n.m.r. spectroscopy, with $Eu(hfc)_3$, using a Varian 390 instrument. Mass spectra were determined on a Hitachi Perkin-Elmer RM-50 instrument. U.v. spectra were recorded on a Perkin-Elmer model 124 spectrophotometer. Microanalyses were performed by the Instituto de Química Bio-Orgánica (CSIC, Barcelona).

Synthesis of Substrates.—Olefins (1a)–(1h) were synthesized as described in ref. 15: (E)-1,3-diphenylprop-2-en-1-one (1a) had m.p. 55–57 °C (lit.,¹⁵ 55–57 °C); (E)-3-(4-nitrophenyl)-1-phenylprop-2-en-1-one (1b) had m.p. 163 °C (lit.,^{17a} 165 °C); (E)-3-(2-methoxyphenyl)-1-phenylprop-2-en-1-one (1c) had m.p. 61 °C (lit.,^{17b} 58–59 °C); (E)-3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one (1d) had m.p. 75–77 °C (lit.,^{17a} 79 °C); (E)-3-phenyl-1-(2-thienyl)prop-2-en-1-one (1e) had m.p. 81 °C (lit.,^{17c} 81 °C); (E)-3-phenyl-1-

(3-thienyl)prop-2-en-1-one (1f) had m.p. 104–106 °C, ν (KBr) 1 665 (C=O), 1 610 (C=C), and 980 cm^{-1} (C=CH); δ (CCl_4) 8.10–7.10 (10 H, m); λ_{max} (EtOH) 310 (log ϵ 4.41) and 226 nm (log ϵ 4.19) (Found: C, 73.2; H, 4.7; S, 14.6. $C_{13}H_{10}OS$ requires C, 72.9; H, 4.7; S, 14.9%); (E)-1-(2-methoxyphenyl)-3-phenylprop-2-en-1-one (1g) had m.p. 39–40 °C (lit.,^{17d} m.p. 41 °C); (E)-3-(4-chlorophenyl)-1-phenylprop-2-en-1-one (1h) had m.p. 114–115 °C (lit.,^{17a} 115 °C).

(E)-2-Nitro-1-phenylpropene (3) was prepared according to ref. 16 and had m.p. 65 °C (lit.,¹⁶ m.p. 64–65 °C). *trans*-3-Chloro-2-hydroxy-1,3-diphenylpropan-1-one (11) was prepared according to ref. 17e and had m.p. 104–105 °C (lit.,^{17e} 105–107 °C). 2-Methyl-1,4-naphthoquinone (5), cyclohex-2-en-1-one (7), phenacyl chloride (9), benzaldehyde (10), and ethyl nitroacetate (12) were commercial products. All products showed i.r. and 1H n.m.r. spectra in agreement with the proposed structure.

Synthesis of Catalysts.—(S)-4-Methyl-1,3-oxazolidine-2,5-dione [(S)-alanine-NCA] (15). *N*-Benzyloxycarbonyl-(S)-alanine¹⁸ (28 g, 0.134 mol) was added in small portions to freshly distilled $SOCl_2$ (200 g). The excess of $SOCl_2$ was removed under reduced pressure, hexane (100 ml, dried over Na) was added to the residue, and the solvent was distilled under reduced pressure. The resulting solid was filtered off, washed with dry hexane, and crystallized twice from anhydrous Cl_3CH -dioxan (4:1), to give (S)-alanine-NCA (15), 11.4 g (79% yield), m.p. 86–88 °C (lit.,^{3a} m.p. 92 °C); ν (KBr) 3 330 (NH), 1 869 (C=O), and 1 765 cm^{-1} (C=O); δ (Cl_3CO) 6.70br (1 H, s) and 1.58 (3 H, d).

Poly-(S)-alanine (17a). A solution of *n*-butylamine (0.637 g, 8.73 mol) in anhydrous acetonitrile (64 ml) was added, under magnetic stirring at room temperature, to a solution of *S*-alanine-NCA (5.0 g, 43.5 mmol). After 4 days, the solvent was removed under reduced pressure, the solid residue was washed with Cl_2CH_2 (50 ml), and dried under reduced pressure for 2 days to give the poly-*S*-alanine (17a), 2.82 g (78% yield); $[\alpha]_D^{20} -94.3^\circ$ (c 1.676 in CF_3CO_2H); ν (KBr) 3 270, 3 060, 1 655, 1 630, 1 540, and 1 305 cm^{-1} ; δ (CF_3CO_2H) 7.3 (NH), 6.85 (NH_2), 4.2 ($NHCHCO$), 3.0 (CH_2R), 1.1 ($CH_2CH_2CH_2Me$ and $NHCHMeCO$), and 0.50 ($[CH_2]_3Me$).

Poly-(S)-alanines (17b)–(17d). Compounds (17b)–(17d) were synthesized in a similar manner, using the correct NCA: initiator ratio. Poly-(S)-alanine (17b) (64% yield) had $[\alpha]_D^{20} -95.1^\circ$ (c 1.67 in CF_3CO_2H); poly-(S)-alanine (17c) (100% yield) had $[\alpha]_D^{20} -120.5^\circ$ (c 0.996 in CF_3CO_2H); and poly-(S)-alanine (17d) (100% yield) had $[\alpha]_D^{20} -129.6^\circ$ (c 2.041 in CF_3CO_2H).

Poly-(S)-alanine (19). (S)-Alanine-NCA (15) (7.00 g, 60.9 mmol) was dissolved in acetonitrile (120 ml, dried over P_2O_5) and *N,N*-diethylethylenediamine (0.71 g, 6.09 mmol) was added. The mixture was stirred for 12 days, the solid was filtered off, washed with Cl_2CH_2 and Et_2O , and dried under reduced pressure to give compound (19), 5.0 g (99% yield); $[\alpha]_{578}^{20} -106^\circ$ (c 1.135 in CF_3CO_2H); ν (KBr) 3 270, 3 060, 1 655, 1 630, 1 540, and 1 300 cm^{-1} ; δ (CF_3CO_2H) 7.15 (NH), 6.8 (NH_2), 4.1 ($NHCHCO$), 3.5–2.7 { $NH[CH_2]_2N(CH_2Me)_2$ }, and 1.05 (Me).

Poly-(S)-alanine (21). The polymer (19) (1.00 g) and *n*-butyl bromide (0.5 g, 3.65 mmol) were added to acetone (50 ml) dried over P_2O_5 . The mixture was stirred at room temperature for 40 days. Most of the solvent was evaporated off and the solid was filtered off, washed several times with Cl_2CH_2 , and dried under reduced pressure to afford the alanine (21) 0.95 g (81.5% yield); $[\alpha]_{578}^{20} -102^\circ$ (c 1.186 in

$\text{CF}_3\text{CO}_2\text{H}$); ν (KBr) 3 270, 3 060, 1 655, 1 630, 1 540, and 1 300 cm^{-1} ; δ ($\text{CF}_3\text{CO}_2\text{H}$) 7.60–6.20 (NH and NH_2), 4.20 (NHCHCO), 3.50–2.70 { $\text{NH}[\text{CH}_2]_2\text{N}(\text{CH}_2\text{Me})_2(\text{CH}_2\text{C}_3\text{H}_7)$ }, 1.50–0.50 ($\text{CH}_2[\text{CH}_2]_2\text{Me}$ and all other Me groups).

(S)-4-(2-Benzoyloxycarbonylethyl)-1,3-oxazolidine-2,5-dione [5-benzyl-(S)-glutamate-NCA]. A 20% phosgene solution in toluene was added to a suspension of 5-benzyl-(S)-glutamate (20.0 g, 84.4 mmol) in anhydrous tetrahydrofuran (THF) (400 ml). The mixture was stirred for 5 h at room temperature, further phosgene solution (45 ml) was added and the reaction mixture was stirred for another 3 h. The solvents were removed under reduced pressure and the solid was crystallized twice from hexane-AcOEt (1:1) to give the required glutamate, 19.6 g (88.3% yield), m.p. 92–93 °C (lit.,^{3d} m.p. 93–94 °C); ν (KBr) 3 330, 1 890, 1 865, 1 785, and 1 725 cm^{-1} ; δ (Cl_3CD) 7.25 (5 H, s), 6.90br (1 H, s), 5.10 (2 H, s), 4.35 (1 H, t), and 2.70–2.00 (4 H, m).

Poly-[5-benzyl-(S)-glutamate] (23). 5-Benzyl-(S)-glutamate-NCA (18.0 g, 0.0684 mol) was dissolved in dioxan (350 ml, dried over Na), *n*-butylamine (0.50 g, 6.84 mmol) was added, and the solution was stirred for 72 h. Most of the solvent was evaporated off, Et_2O (1 l) was added, and the precipitated polymer was filtered off and dried under reduced pressure for 2 days at 50 °C to give the glutamate (23), 12.4 g (80% yield); $[\alpha]_{\text{D}}^{20} -40.5^\circ$ (c 1.334 in $\text{CF}_3\text{CO}_2\text{H}$); ν (film from Cl_3CH) 3 270, 1 730, 1 650, 1 625, 1 545, 1 520, 1 160, 740, and 695 cm^{-1} ; δ ($\text{CF}_3\text{CO}_2\text{H}$) 7.45 (NH), 6.70 (Ph), 4.50 (CH_2Ph), 4.15 (NHCHCO), 2.70 ($\text{NHCH}_2[\text{CH}_2]_2\text{Me}$), 2.25–1.20 ($\text{CH}[\text{CH}_2]_2\text{CO}_2\text{R}$), 0.80 ($\text{NHCH}_2[\text{CH}_2]_2\text{Me}$), and 0.35 ($\text{NH}[\text{CH}_2]_3\text{Me}$).

Epoxidation of Substrates (1a)–(1h) in the Presence of Poly-(S)-alanine (17c) (24).—General procedure. Poly-(S)-alanine (400 mg, 0.5 mmol) was added to a solution of compound (1) (2.4 mmol) in toluene (6.00 g). The mixture was stirred at room temperature for 48 h. The reaction was monitored by t.l.c. and, when necessary, the alkaline solution (2.2 ml) was added after 24 h. The catalyst was filtered off and washed with Cl_2CH_2 (50 ml). The organic phase was washed with water (3 × 25 ml), dried (MgSO_4), and the solvent was evaporated off. Except when indicated, the residue was purified by column chromatography on SiO_2 using toluene or light petroleum–diethyl ether (9:1) as eluant.

(–)-2(R),3(S)-Epoxy-1,3-diphenylpropan-1-one (2a). Compound (2a) was obtained after several crystallizations from hexane and had $[\alpha]_{\text{D}}^{20} -214^\circ$ (c 1 in Cl_2CH_2), m.p. 63–65 °C [the m.p. and rotation remained unchanged after a further crystallization (lit.,^{19a} m.p. 89–90 °C for the racemic material)]; ν (KBr) 1 685 (C=O), 1 235 (C–O), 895 (C–O), 760, and 690 cm^{-1} ; δ (Cl_3CD) 8.10–7.25 (10 H, m), 4.27 (1 H, d, J 2 Hz), and 4.06 (1 H, d, J 2 Hz); λ_{max} (EtOH) 250 nm ($\log \epsilon$ 4.18); m/e 224 (M) (Found: C, 80.6; H, 5.5. $\text{C}_{15}\text{H}_{12}\text{O}_2$ requires C, 80.36; H, 5.4%).

trans-(–)-2,3-Epoxy-3-(4-nitrophenyl)-1-phenylpropan-1-one (2b). Compound (2b) had $[\alpha]_{\text{D}}^{20} -191^\circ$ (c 2.028 in Cl_2CH_2), m.p. 138–140 °C (lit.,^{19b} m.p. 149–150.5 °C for the racemic material). One crystallization from ethanol gave a product with $[\alpha]_{\text{D}}^{20} -205^\circ$ (c 1.184 in Cl_2CH_2), e.e. 82%, m.p. 139–141.5 °C. A second crystallization afforded an epoxide with $[\alpha]_{\text{D}}^{20} -220^\circ$ (c 0.517 in Cl_2CH_2), m.p. 139–141.5 °C; ν (KBr) 1 690 (C=O), 1 510 (NO_2), 1 340 (NO_2), and 1 226 (C–O); δ (Cl_3CD) 8.30–7.30 (9 H, m), 4.30 (1 H, d, J 1.5 Hz), and 4.21 (1 H, d, J 1.5 Hz); λ_{max} (EtOH) 256 nm ($\log \epsilon$ 4.32); m/e 269 (M).

(–)-2(R),3(S)-Epoxy-3-phenyl-1-(2-thienyl)propan-1-one

(2e). Compound (2e) had $[\alpha]_{\text{D}}^{20} -183^\circ$ (c 0.530 in Cl_2CH_2), m.p. 52–56 °C. One crystallization from ethanol gave a product with $[\alpha]_{\text{D}}^{20} -214^\circ$ (c 1.022 in Cl_2CH_2), m.p. 54–58 °C. A second crystallization afforded an epoxide with $[\alpha]_{\text{D}}^{20} -227^\circ$ (c 0.551 in Cl_2CH_2), m.p. 50.5–52.5 °C; ν (KBr) 1 670 (C=O), 1 240 (C–O), 885 (C–O), 750, and 697 cm^{-1} ; δ (Cl_4C) 7.88 (1 H, d), 6.53 (1 H, d), 7.18 (5 H, s), 7.03 (1 H, dd), 4.03 (1 H, d, J 2 Hz), and 3.76 (1 H, d, J 2 Hz); λ_{max} (EtOH) 292 (log ϵ 4.08) and 266 nm (4.14); m/e 230 (M) (Found: C, 67.9; H, 4.4; S, 13.8. $\text{C}_{13}\text{H}_{10}\text{O}_2\text{S}$ requires C, 67.83; H, 4.4; S, 13.91%).

(–)-2(R),3(S)-Epoxy-3-phenyl-1-(3-thienyl)propan-1-one (2f). Compound (2f) had $[\alpha]_{\text{D}}^{20} -123^\circ$ (c 1.028 in Cl_2CH_2), m.p. 88–90 °C. One crystallization from ethanol afforded a product with $[\alpha]_{\text{D}}^{20} -151^\circ$ (c 0.622 in Cl_2CH_2); ν (KBr) 1 670 (C=O), 1 242 (C–O), 872 (C–O), 745, and 690 cm^{-1} ; δ (Cl_4C) 8.35 (1 H, dd), 7.58 (1 H, dd), 7.28 (5 H, s), 7.20 (1 H, dd), 4.04 (1 H, d, J 2 Hz), and 3.80 (1 H, d, J 2 Hz); λ_{max} (EtOH) 257 nm (log ϵ 4.26); m/e 230 (M) (Found: C, 67.8; H, 4.3; S, 13.7. $\text{C}_{13}\text{H}_{10}\text{O}_2$ requires C, 67.8; H, 4.4; S, 13.9%).

trans-(–)-2,3-Epoxy-1-(2-methoxyphenyl)-3-phenylpropan-1-one (2g). Compound (2g) had $[\alpha]_{\text{D}}^{20} -67^\circ$ (c 1.735 in Cl_2CH_2), m.p. 105–108 °C (lit.,^{19c} m.p. 125 °C for the racemic compound). One crystallization from ethanol afforded a product with $[\alpha]_{\text{D}}^{20} -80.3^\circ$ (c 1.420 in Cl_2CH_2), m.p. 110–112 °C; ν (KBr) 2830 (OMe), 1 680 (C=O), 1 255 (C–O), and 895 (C–O) cm^{-1} ; δ (Cl_4C) 7.90–6.70 (9 H, m), 4.05 (1 H, d, J 1.8 Hz), 3.85 (1 H, d, J 1.8 Hz), and 3.65 (3 H, s); λ_{max} (EtOH) 313 (log ϵ 3.69) and 254 nm (4.13); m/e 254 (M) (Found: C, 75.7; H, 5.45. $\text{C}_{16}\text{H}_{14}\text{O}_3$ requires C, 75.6; H, 5.5%).

(–)-3-(4-Chlorophenyl)-2(R),3(S)-epoxy-1-phenylpropan-1-one (2h). Compound (2h) had $[\alpha]_{\text{D}}^{20} -148^\circ$ (c 5.885 in Cl_2CH_2). One crystallization from ethanol gave a product with $[\alpha]_{\text{D}}^{20} -192^\circ$ (c 0.328 in Cl_2CH_2), m.p. 68 °C; ν (film from Cl_3CH) 1 705 (C=O), 1 240 (C–O), 810, and 705 cm^{-1} ; δ (Cl_3CD) 8.20–7.20 (9 H, m), 4.21 (1 H, d, J 1.8 Hz), 4.03 (1 H, d, J 1.8 Hz); λ_{max} (EtOH) 250 nm (log ϵ 4.35); m/e 258 (M) (Found: C, 69.6; H, 4.3; Cl, 14.1. $\text{C}_{15}\text{H}_{11}\text{ClO}_2$ requires C, 69.6; H, 4.3; Cl, 13.7%).

Epoxidation of the Chalcone (1a) in Toluene at Room Temperature with Catalysts (17), (19), (21), and (23).—The reactions were performed in the same manner as described before and using the same amounts of reagents. In assay with catalyst (23), the following amounts were used: chalcone (1a) (1 g, 4.8 mmol), toluene (15 ml), catalyst (23) (625 mg), and 4.4 ml of a solution of NaOH in 30% H_2O_2 (0.08 g ml^{-1}). Results and other experimental details are explained in Table 2.

Epoxidation with MCPBA. Chalcone (1a) (0.5 g, 2.4 mmol), toluene (6 g), catalyst (17c) (400 mg), NaHCO_3 (1 g), H_2O (10 ml), and 84% MCPBA (0.5 g) were stirred for 75 h at room temperature. NaHCO_3 (0.5 g), H_2O (5 ml), and 85% MCPBA (0.25 g) were added after 24 and 48 h. Cl_2CH_2 (50 ml) and H_2O (50 ml) were added and the catalyst was filtered off. The organic layer was separated off and washed several times with water, dried (MgSO_4), and solvent evaporated off; the yield was calculated from ^1H n.m.r. data (see Table 6).

Epoxidation with $\text{Bu}^t\text{O}_2\text{H}$. Chalcone (1a) (0.5 g, 2.4 mmol), toluene (6 g), catalyst (17c) (400 mg), 10% NaOH solution (5 ml), and 80% $\text{Bu}^t\text{O}_2\text{H}$ (0.5 g) were stirred at room temperature for 58 h. 80% $\text{Bu}^t\text{O}_2\text{H}$ (0.5 g) and 10% aqueous NaOH (5 ml) were added after 26 and 50 h. The catalyst was filtered off and washed with Cl_2CH_2 . The

organic layer was separated off, washed with H₂O, 10% Na₂SO₃, and H₂O, and dried. After evaporation of the solvent, the crude product was eluted on SiO₂ (10 g), Cl₂CH₂ as eluant, to obtain a mixture (0.4396 g) of starting material and the epoxide (2a). In the absence of water and NaOH, no reaction occurred after 12 h; when K₂CO₃ (0.5 g) was added complete reaction occurred after 20 h.

Epoxidation of Substrates other than Substituted Chalcones with Catalysts (17c) and (23) in Toluene at Room Temperature.

—*Epoxidation of compound (3) with catalyst (17c).* Substrate (3) (0.78 g, 4.8 mmol), toluene (6 g), catalyst (17c) (400 mg), and 4.4 ml of a solution of NaOH in 30% H₂O₂ (0.08 g ml⁻¹) were stirred at room temperature for 24 h. The reaction mixture was worked-up as described before, and the crude product was eluted on SiO₂ (10 g), using Cl₂CH₂ as eluant, to give a mixture (0.487 g) of alkene and epoxide. Acidification of aqueous layer and extraction with diethyl ether gave benzoic acid (80 mg).

Epoxidation of compound (3) with catalyst (23). The same procedure was carried out, using catalyst (23) (652 mg). After two elutions of the crude product on SiO₂ the liquid (4) (0.5732 g) was obtained; 67% yield; $[\alpha]_{578}^{20} -0.7^\circ$ (*c* 5.732 in Cl₂CH₂); δ (Cl₃CD) 7.42 (5 H, s), 4.55 (1 H, s), 1.80 (3 H, t); no starting material was detected. Benzoic acid (45.5 mg) was obtained after acidification and extraction of the aqueous layer.

Epoxidation of compound (5) with Bu^tO₂H. 2-Methyl-1,4-naphthoquinone (5) (0.413 g, 2.4 mmol), toluene (6 g), catalyst (17c) (200 mg), K₂CO₃ (1 g), H₂O (5 ml), and 0.5 g of 80% Bu^tO₂H were stirred for 24 h. The reaction mixture was worked-up to give a solid free from starting material. A crystallization from ethanol gave a product with m.p. 93–95 °C (lit.,²¹ m.p. 95.5–96.5 °C); $[\alpha]_{436}^{20} 0^\circ$ (*c* 1.332 in acetone); ν (KBr) 1 700 (C=O) cm⁻¹; δ (Cl₄C) 7.95–7.40 (4 H, m), 3.70 (1 H, s), and 1.65 (3 H, s). The same reaction carried out without catalyst gave, after 64 h, the epoxide (6) in 81% yield.

Epoxidation of compound (5) with H₂O₂. 2-Methylnaphthoquinone (5) (0.413 g, 2.5 mmol), toluene (6 g), catalyst (17c) (200 mg), and 4 ml of a solution of K₂CO₃ in 30% H₂O₂ (0.15 g ml⁻¹) were stirred for 24 h. The reaction mixture was worked-up to give a solid free from starting material. A crystallization from ethanol gave a product with m.p. 94–96 °C; $[\alpha]_{436}^{20} 0^\circ$ (*c* 1.520 in acetone); i.r. and ¹H n.m.r. as described above. The same reaction carried out without catalyst gave, after 72 h, the epoxide (6) in 41% yield.

(–)-2,3-Epoxy-cyclohexanone (8).—Cyclohex-2-enone (1.069 g, 11.1 mmol), Cl₄C (6 ml), catalyst (17c) (400 mg) and 4.4 ml of a solution of NaOH in 30% H₂O₂ (0.08 g ml⁻¹, added slowly as drops), were stirred for 45 min at 0 °C. The reaction mixture was worked-up and the crude epoxide was purified by column chromatography (eluant: hexane–Cl₂CH₂, 1 : 1) to give the pure epoxide (0.238 g; 19% yield), $[\alpha]_{578}^{20} -0.42^\circ$ (*c* 2.380 in Cl₂CH₂); ν (film) 1 720 (C=O) and 1 250 (C–O); δ (Cl₃CD) 3.62 (1 H, m), 3.15 (1 H, d), and 2.7–1.2 (6 H, m) (lit.,²²).

Darzens Reactions.—Phenacyl chloride (9) (93 mg, 0.6 mmol), benzaldehyde (10) (91 mg, 0.86 mmol), catalyst (17c) (110 mg), toluene (1.5 g), and 10% aqueous NaOH (0.30 ml), were stirred for 24 h at room temperature. The reaction mixture was worked-up in the usual manner. The reaction performed without catalyst afforded similar results (see Table 8).

Dehydrohalogenation of Erythrochlorohydrin (11).—Com-

pound (11) (0.63 g, 2.4 mmol), toluene (6 g), catalyst (17c) (400 mg) and 10% aqueous NaOH (4.5 ml, 11.3 mmol) were used. The reaction was performed and worked-up in the usual way. The epoxide was purified by column chromatography using hexane–ether (9 : 1) as eluant. Yields and e.e. are reported in Table 8. For results of the same reaction carried out without catalyst and for the assay performed with only 50% of stoichiometric NaOH see Table 8.

Addition of Ethyl Nitroacetate to Chalcone (1a).—Chalcone (1a) (0.5 g, 2.4 mmol), ethyl nitroacetate (0.3605 g, 2.7 mmol), and catalyst (17c) (400 mg) were stirred for 31 days. The reaction mixture was worked-up and the residue chromatographed on SiO₂ (using hexane–Et₂O, 9 : 1, as eluant) to afford compound (13), $[\alpha]_{578}^{20} 8^\circ$ (*c* 1.891 in Cl₂CH) in 60% yield. Decarboxylation of compound (13) with EtOH–NaOH¹⁴ gave (+)-4-nitro-1,3-diphenylbutan-1-one, m.p. 91–92 °C; $[\alpha]_{578}^{20} 2.63^\circ$; e.e. 6.4%.

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