Synthesis of Enantio-and Diastereo-isomerically Pure β- and γ-Substituted Glutamic Acids *via* Glycine Condensation with Activated Olefins

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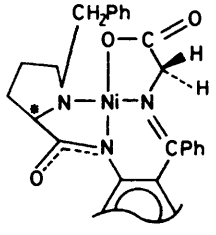
The glycine fragment in the nickel(II) complex formed from the Schiff base of glycine and (*S*)-*o*-[(*N*-benzylprolyl)amino]benzophenone undergoes base-catalysed Michael addition in methanol in the presence of MeONa to the activated olefins methyl acrylate, acrylonitrile, methyl methacrylate, acrolein, and methyl *trans*-cinnamate. Complexes of substituted (*S*)-glutamic acid or its derivatives were formed in good chemical yields with almost complete diastereoselection at the α-carbon atom of the amino acid moiety. Diastereoselection at the β- and γ-atoms was not significant, but the isomeric complexes could be easily separated chromatographically. Cleavage of the pure diastereoisomers with aqueous HCl gave, in good yields, optically pure glutamic acids and regenerated the original chiral reagent. The configurations of the amino acid β- and γ-carbon atoms were determined by ^{1}H n.m.r. spectroscopy and crystal structure *X*-ray analysis of the corresponding original complexes. The addition to acrolein, catalysed by triethylamine in methanol, leads to the 1,4-adduct exclusively. The amino acid thus obtained could be converted into (*S*)-proline by reduction with $NaBH_4$.

Glutamic acid and its derivatives are important physiologically active compounds [1] and, as is the case with other α-amino acids, the observed activity is usually associated with one optically pure isomer.[2] In view of this a general method of producing diastereo- and enantio-isomerically pure substituted glutamic acids would be synthetically useful. In spite of recent progress in the field of α-amino acid synthesis in general [3] and glutamic acid in particular,[4] such a method is as yet not available.



(1)

Earlier we developed asymmetric general methods of β-hydroxy-α-amino acid [5] and α-alkyl-α-amino acid synthesis [6] starting from chiral Schiff base Ni^{II} complexes of α-amino acids. In the present work we have applied this approach to prepare asymmetric derivatives of glutamic acids. The synthetic route consists in Michael addition of a Ni^{II} complex of a Schiff base derived from (*S*)-*o*-[(*N*-benzylpropyl)amino]benzophenone and glycine (**1**) to activated olefins.

Results

Synthesis and Reactions of Complex (**1**).—Complex (**1**) was obtained *via* condensation of *o*-[(*N*-benzylprolyl)amino]-benzophenone (**2**) with glycine in the presence of $Ni(NO_3)_2$ in methanol, as described earlier.[5]

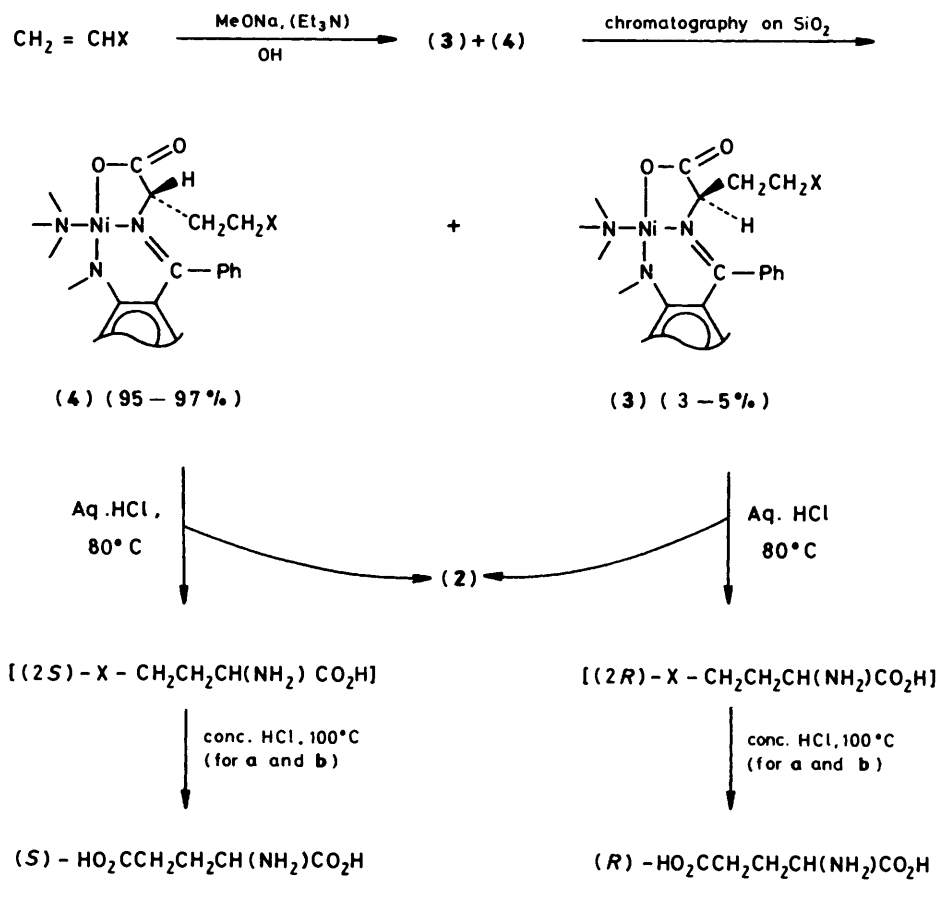
Condensation of complex (**1**) *with acrylonitrile and methyl acrylate.* Complex (**1**) adds to the title compounds in methanol in the presence of MeONa to give a mixture of the diastereoisomeric complexes (**3**) and (**4**) (5:95), as shown in Scheme 1.

The isomers could be easily separated chromatographically on SiO_2. As expected, they have the same set of proton signals, differing only in their chemical shifts and their u.v.–visible and i.r. spectra are similar. O.r.d. curves of (**3b**) and (**4a**, **b**) are presented in Figure 1.

The complexes decomposed with aqueous HCl to give initially (**2**) in 85—98% yield and 2-amino-4-cyanobutyric acid (from **b**) or the partially hydrolysed γ-methyl ester of glutamic acid (from **a**), which was further hydrolysed to the acid itself. Complex (**3b**) could also be hydrolysed to (*R*)-glutamic acid (e.e. >95%). Optically pure (*S*)-glutamic acid (according to g.l.c. analysis data [7]) could also be obtained from (**4a**). Decomposition of the initial mixture of (**3a**) and (**4a**) gives (*S*)-glutamic with an enantioisomeric excess (e.e.) of 91%, which, evidently, reflects closely the ratio of the initial isomeric complexes.

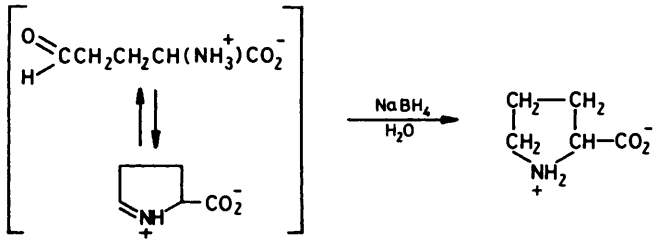
Condensation of complex (**1**) *with acrolein.* The reaction is catalysed by Et_3N and follows Scheme 1, giving diastereoisomers (**3c**) and (**4c**) (5:95) easily separable by chromatography on SiO_2. The structure of these compounds was established by physical and chemical methods (see Experimental section). Comparison of the o.r.d. curves of (**3c**) and (**4c**) with those of (**3b**) and (**4b**) showed that (**3c**) contains an amino acid of (*R*)-configuration, while (**4c**) contains an (*S*)-amino acid. This conclusion was supported by the $NaBH_4$ reduction of 2-amino-4-formylbutyric acid, obtained without isolation after the decomposition of (**3c**), to (*R*)-proline (>95 e.e.); (*S*)-proline (>95 e.e.) was prepared in this way from (**4c**) (see Scheme 2).

Addition of complex (**1**) *to methyl methacrylate.* The reaction catalysed by MeONa in MeOH was expected to produce four isomers differing in the configuration of the α- and γ-carbon atoms of the amino acid side-chain. In fact, only three isomers were detected in the reaction mixture, and these were designated (**5**), (**6**), and (**7**) (0.1:2:1), according to the order of their elution from a chromatographic column (SiO_2); the physical and chemical data for these compounds are in agreement with isomeric nature. The o.r.d. curves in the region of d–d transitions are presented in Figure 2. The difference in the shape of these curves can be mainly related to the configuration of the α-carbon of the amino acid side-chain, the chiral centres of the proline fragment being identical for all the isomers, and the



(4a) X = CO_2Me
(3b), (4b) X = CN
(3c), (4c) X = CHO

Scheme 1.



Scheme 2.

γ-carbon atom of the α-amino acid side-chain too remote from the Ni atom to influence the optical activity of d–d transitions to any significant extent.[8] Thus, comparison of the o.r.d. curves of (3) and (4) (**b** and **c**) with those of (5), (6), and (7) demonstrates that (5) contains an amino acid with an α-carbon atom of (*R*)-configuration, while (6) and (7) contain amino acids having identical (*S*)-α-carbon atoms whilst evidently differing in the configuration of their γ-carbon atoms. An *X*-ray crystal structure analysis (see Figure 3), shows that (6) contains the γ-methyl ester of (2*S*,4*R*)-4-methylglutamic acid: (7) may thus be formulated as a complex of (2*S*,4*S*)-4-methylglutamic acid. Decomposition of (5), (6), or (7) with aqueous HCl liberates (2) (90%) and produces partially hydrolysed esters of 4-methylglutamic acid.

The complete hydrolysis of the esters of 4-methylglutamic acid with concentrated aqueous HCl results in almost optically pure (g.l.c.) amino acids in yields of 40—60% (see Table 1). The amino acids obtained from (5) and (6) have identical ^{1}H n.m.r. spectra that clearly testify to the (2*R*,4*S*)-configuration of the former.

Addition of complex (1) *to the methyl ester of* trans-*cinnamic acid.* The reaction carried out in methanol in the presence of MeONa gave a mixture of isomers from which two were isolated in 80% yield: these were designated (8) for the isomer less strongly adsorbed on SiO_2, and (9) for the more strongly adsorbed one (2:1). According to the physical and chemical data, (8) and (9) are diastereoisomeric Ni^{II} complexes of the Schiff bases derived from (2) and the γ-methyl ester of 3-phenylglutamic acid. The o.r.d. curves of (8) and (9) (see Figure 2) indicate that both these isomers have the same (*S*)-configuration for the α-carbon atom. The configuration of the β-carbon atoms of (8) and (9) were assigned on the basis of an analysis of their ^{1}H n.m.r. spectra as described below.

Inspection of molecular models of (8) and (9) shows that the most stable conformation for the amino acid side-chain is the one with the α-hydrogen atom oriented roughly parallel to the C=N bond, with a 'gauche' spatial arrangement of the α- and β-hydrogens (see Figure 4 a and b). The observed $J_{vic}(H^{\alpha}–H^{\beta})$,

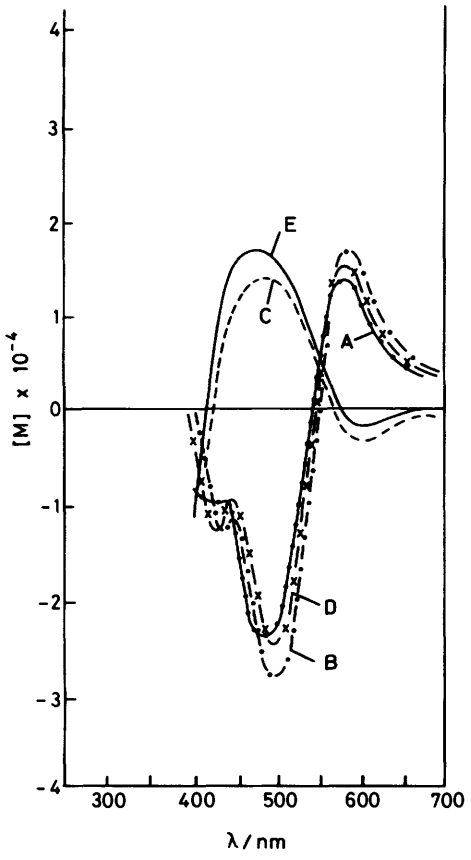


Figure 1. O.r.d. curves at 25 °C in MeOH: A = (**4a**), B = (**4b**), C = (**3b**), D = (**4c**), and E = (**3c**)

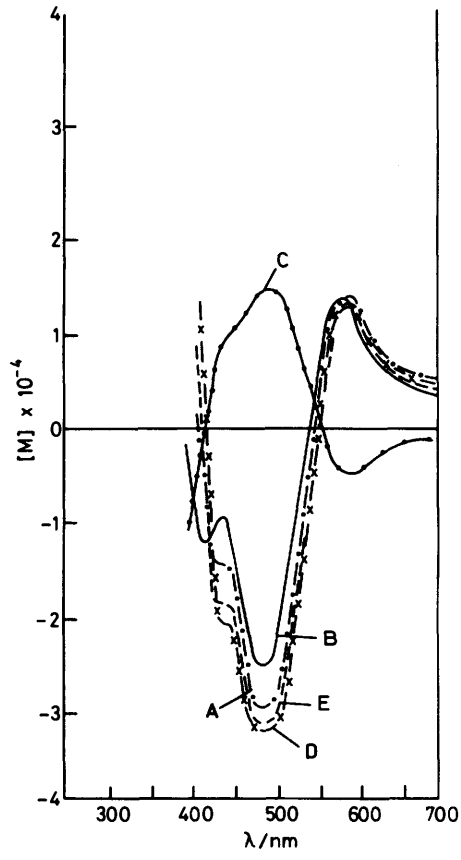


Figure 2. O.r.d. curves at 25 °C in MeOH: A = (**6**), B = (**7**), C = (**5**), D = (**8**), and E = (**9**)

equal to 3.7 Hz for (**8**), corresponds to a 90% proportion of the 'gauche' conformation, that is with a 60° torsion angle between these hydrogens. Such an arrangement of the α- and β-hydrogens for the isopropyl valine side-chain was observed earlier for the analogous Ni^{II} complexes derived from the Schiff base of (*S*)-*o*-[(benzylprolyl)amino]acetophenone.[9]

As a consequence of this conformation, the isomer containing (2*S*,3*R*)-3-phenylglutamic acid (see Figure 4a) has the 3-phenyl substituent situated under the H^{γ}_{endo} of the proline fragment. The ^1H n.m.r. signal of this proton would be expected to be shifted upfield, owing to the diamagnetic ring current of the phenyl ring, as compared with other analogous complexes. In fact, the signal of one of the H^{γ} atoms in the proline fragment was found at 1.4 p.p.m. in the spectrum of (**8**), *i.e.* 0.5 p.p.m. upfield as compared with its position in the other complexes (see ref. 9 and Experimental section). Thus, (**8**) could be assigned the configuration shown in Figure 4a. The isomer containing (2*S*,3*S*)-3-phenylglutamic acid (see Figure 4b) has one of its side chain H^{γ} substituents situated directly under the Ni^{II} atom, and, because of it, the signal of the substituent should be shifted to a weaker field.[9,10] As expected, the signal of one of the side-chain H^{γ} in (**9**) is shifted 1.8 p.p.m. downfield, as compared with (**8**).

Decomposition of the complexes, as described above, results in (**2**) and (2*S*,3*R*)-3-phenylglutamic acid [from (**8**)] or (2*S*,3*S*)-3-phenylglutamic acid [from (**9**)]. The enantioisomeric purity of the amino acids (see Table 1) was determined with the help of a chiral shift reagent and exceeds 95%.

Discussion

Until now all attempts to carry out the addition of transition-metal Schiff base glycine complexes to activated olefins have led

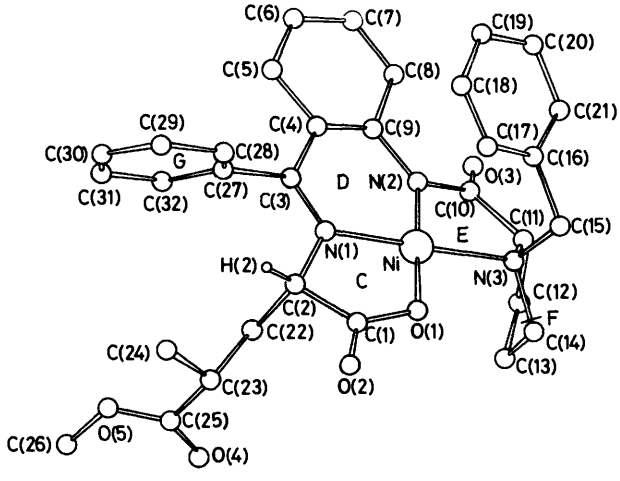


Figure 3. Structure of Ni^{II} complex of (2*S*,4*R*)-4-methylglutamic acid Schiff base with (*S*)-*o*-(*N*-benzylpropyl)aminobenzophenone (**6**) (conformer B). Selected bond lengths: Ni–O(1) = 1.84(1), Ni–N(1) = 1.86(1), Ni–N(2) = 1.86(1), and Ni–N(3) = 1.93(1) Å

to either cyclization products[12] (nonaqueous solutions) or low yields of desired compounds.[13] In the case of acrylonitrile (aqueous solution), only the product of the addition of two molecules of acrylonitrile to one molecule of glycine was formed.[14]

A probable mechanism for the reaction includes attack of the carbanion of the glycine fragment at the activated olefin double

Table 1. Michael addition of complex (1) to activated olefins[a]

Olefin	Product	Yield of pure diastereoisomers, %[b] configuration of the amino acid side-chain	Recovery of the amino acid from the complex (%)[c]	Optical purity of the amino acid
CH_2=$CHCO_2Me$	(4a)	89, 2-*S*	64 (80)[d]	>95[e] (91)[d,e]
	(3b)	3.5, 2-*R*		>95[e,h]
CH_2=CHCN	(4b)	82, 2-*S*	75	>95[f]
	(3c)	4, 2-*R*	42[g]	>95[e]
CH_2=CHCHO	(4c)	70, 2-*S*	40[g]	>95[e]
	(5)	2.5, 2*R*,4*S*	72	>95[e]
CH_2=C(Me)CO_2Me	(6)	53, 2*S*,4*R*	70	>95[e,f]
	(7)	25, 2*S*,4*S*	67	>95[e,f]
trans-PhCH=$CHCO_2Me$	(8)	51, 2*S*,3*R*	70	>95[f]
	(9)	26, 2*S*,3*S*	80	>95[f]

[a] Reaction conditions: MeOH solution, MeONa (or Et_3N) catalyst, 25 °C, under Ar, ratio of the olefin to complex (1), 1:1—1.2. [b] After chromatography on SiO_2, based on initial (1). [c] Based on the pure diastereoisomeric complex. [d] The amino acid obtained from the initial mixture of (3a) and (4a). [e] G.l.c. enantioisomeric analysis. [f] ^1H N.m.r. data for a chiral lanthanide shift reagent. [g] Calculated for (*S*)-and (*R*)-proline, no attempts were made to improve the yield. [h] Determined after hydrolysis to glutamic acid.

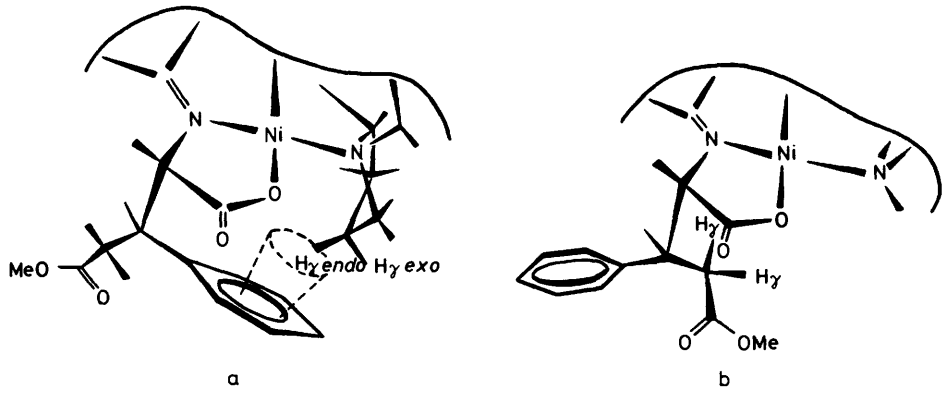


Figure 4. (a) Conformation of the amino acid side-chain in (8) and schematic representation of the shielding of H_{endo} of the Pro-fragment owing to the diamagnetic ring current of the phenyl ring in (8), and (b) conformation of the amino acid side-chain in (9)

bond with the formation of a further intermediate γ-carbanion (see Scheme 3). This entity can be stabilized either by intramolecular addition to a C=N bond, leading to cyclization (path a), or by its accepting a proton from the solution, resulting in the usual 1,4-addition product[13] (path b). In nonaqueous solutions, where the concentration of proton donors is low, the reaction follows path a.[12,14] As might be expected, cyclization *via* path a was blocked by steric hindrance. This is illustrated using the structure of (6) (Figure 3). The plane of the phenyl substituent on the C=N bond forms an angle of 100° with the plane formed by the atoms C(3), C(4), C(9), and N(2). Rotation of this substituent is restricted by the substituents at C(5) and C(2) which, in their turn, are rigidly fixed by the framework of the macrocyclic complex molecule. As a result, any nucleophilic attack at the C=N bond is sterically hindered by the phenyl group. A nonbinding steric interaction of this substituent with the amino acid side-chain makes the latter assume a pseudo-axial orientation. Such a conformation is a typical feature of many α-amino acid Schiff base transition-metal complexes.[9,15] As a consequence, the smaller α-hydrogen substituent of the amino acid takes a pseudoequatorial position. Substitution of a more bulky group for this hydrogen atom would cause severe steric strain, which in a rigid polycyclic structure of the complex could not be effectively minimized by the distortions of valency and torsion angles. This is probably the main underlying reason for the absence of any bis-adduct formation in the case of olefin addition to complex (1).

Considerable diastereoselectivity (>90%) observed in the Michael additions to complex (1) is thermodynamic in origin, the diastereoisomers formed being easily equilibrated[9] under the experimental conditions (high Et_3N concentrations of MeONA >0.1M). As in all the other complexes of a similar or analogous structure, the most stable isomer is that derived from the (*S*)-α-amino acid.[5,9]

Conclusions

In this work we have developed a simple general method of preparing enantio- and diastereo-isomerically pure substituted (*S*)-glutamic acids and their derivatives, starting from glycine. The chiral auxiliary (2) can be easily recovered and re-used. Simplicity of the experimental procedure and a broad range of activated olefins capable of entering the addition reaction of complex (1) make the method attractive.

Asymmetric addition of complex (1) to acrolein or substituted acroleins may eventually provide an easy access to enantio- and diastereo-pure prolines. At present this method is in the development stage.

Experimental

General.—Reagents were purchased from Reachim (U.S.S.R.), with the exception of *o*-aminobenzophenone and Silica Gel 60 F_{254} purchased from Merck and Sephadex LH-20 purchased

Table 2. Atomic co-ordinates ($\times 10^4$, Ni $\times 10^3$)

Atom	*x*	*y*	*z*	Atom	*x*	*y*	*z*
Ni(A)	20 830(13)	74 945(14)	66 583(8)	O(4A)	5 311(17)	6 703(20)	8 208(12)
Ni(B)	−892(13)	6 582(12)	49 351(8)	O(5A)	4 397(12)	7 468(12)	7 903(7)
C(25A)	4 560(16)	6 833(14)	8 088(8)	C(26A)	4 971(29)	8 164(19)	7 926(14)
O(1A)	2 120(7)	7 717(6)	7 464(4)	O(2A)	2 231(7)	7 145(6)	8 337(5)
O(3A)	2 293(7)	7 903(6)	4 971(5)	N(1A)	2 074(8)	6 442(6)	6 870(5)
N(2A)	1 947(8)	7 290(7)	5 859(5)	N(3A)	2 132(9)	8 604(7)	6 476(5)
C(1A)	2 262(10)	7 124(9)	7 792(7)	C(2A)	2 436(9)	6 367(9)	8 468(6)
C(3A)	1 811(9)	5 838(8)	6 554(6)	C(4A)	1 484(9)	5 940(8)	5 963(6)
C(5A)	1 047(10)	5 280(9)	5 730(7)	C(6A)	651(11)	5 325(10)	5 171(7)
C(7A)	693(11)	6 001(9)	4 857(7)	C(8A)	1 097(10)	6 630(9)	5 072(8)
C(9A)	1 547(10)	6 637(9)	5 629(7)	C(10A)	2 225(12)	7 910(10)	5 506(8)
C(11A)	2 452(11)	8 641(10)	5 847(7)	C(12A)	3 451(13)	8 737(12)	5 879(9)
C(13A)	3 628(13)	8 827(12)	6 541(9)	C(14A)	2 770(12)	9 071(10)	6 804(7)
C(15A)	1 226(12)	8 937(10)	6 528(8)	C(16A)	475(10)	8 440(10)	6 286(7)
C(17A)	82(13)	7 867(10)	6 618(8)	C(18A)	−613(13)	7 426(13)	6 388(8)
C(19A)	−855(12)	7 558(13)	5 830(8)	C(20A)	−437(12)	8 075(12)	5 475(9)
C(21A)	219(12)	8 535(11)	5 706(8)	C(27A)	1 832(9)	5 050(8)	6 828(6)
C(28A)	2 452(9)	4 513(9)	6 650(7)	C(29A)	2 440(12)	3 742(11)	6 893(8)
C(30A)	1 787(13)	3 559(11)	7 285(8)	C(31A)	1 209(12)	4 082(11)	7 462(8)
C(32A)	1 188(11)	4 846(10)	7 242(7)	C(22A)	3 430(11)	6 236(10)	7 433(7)
C(23A)	3 867(11)	6 170(10)	8 046(7)	C(24A)	4 271(16)	5 355(14)	8 183(11)
O(1B)	−631(7)	550(7)	4 213(5)	O(2B)	−402(7)	148(7)	3 284(5)
O(3B)	23(7)	603(6)	6 646(4)	O(4B)	367(9)	−2 504(10)	3 727(6)
O(5B)	1 684(9)	−2 424(9)	3 394(6)	N(1B)	949(8)	382(7)	4 556(5)
N(2B)	440(7)	772(7)	5 667(5)	N(3B)	−1 165(8)	987(7)	5 302(5)
C(1B)	−135(12)	258(10)	3 803(7)	C(2B)	789(10)	41(9)	3 968(6)
C(3B)	1 758(10)	551(9)	4 719(6)	C(4B)	1 928(10)	868(9)	5 302(6)
C(5B)	2 844(13)	1 086(10)	5 393(7)	C(6B)	3 083(12)	1 394(10)	5 944(8)
C(7B)	2 483(11)	1 476(11)	6 378(8)	C(8B)	1 614(10)	1 251(10)	6 309(7)
C(9B)	1 333(9)	941(8)	5 378(6)	C(10B)	−147(10)	719(9)	6 117(6)
C(11B)	−1 102(10)	758(9)	2 936(6)	C(12B)	−1 576(12)	−31(11)	6 022(8)
C(13B)	−1 896(13)	−224(12)	5 396(9)	C(14B)	−1 976(10)	535(10)	5 092(7)
C(15B)	−1 326(11)	1 835(10)	5 197(7)	C(16B)	−502(11)	2 332(11)	5 304(7)
C(17B)	57(12)	2 443(11)	4 833(7)	C(18B)	839(13)	2 839(11)	4 938(9)
C(19B)	1 017(14)	3 128(12)	5 494(9)	C(20B)	457(13)	3 033(12)	5 946(9)
C(21B)	−342(11)	2 622(12)	5 845(8)	C(22B)	849(11)	−854(9)	4 005(7)
C(23B)	865(11)	−1 262(10)	3 400(8)	C(24B)	1 547(15)	−938(13)	2 993(10)
C(25B)	940(13)	−2 139(11)	3 497(8)	C(26B)	1 796(18)	−3 254(16)	3 516(12)
C(27B)	2 496(9)	427(9)	4 306(6)	C(28B)	2 655(10)	1 002(9)	3 863(6)
C(29B)	3 343(11)	870(9)	3 475(7)	C(30B)	3 860(12)	236(11)	3 518(8)
C(31B)	3 705(11)	−317(11)	3 951(8)	C(32B)	3 033(10)	−220(9)	4 341(7)

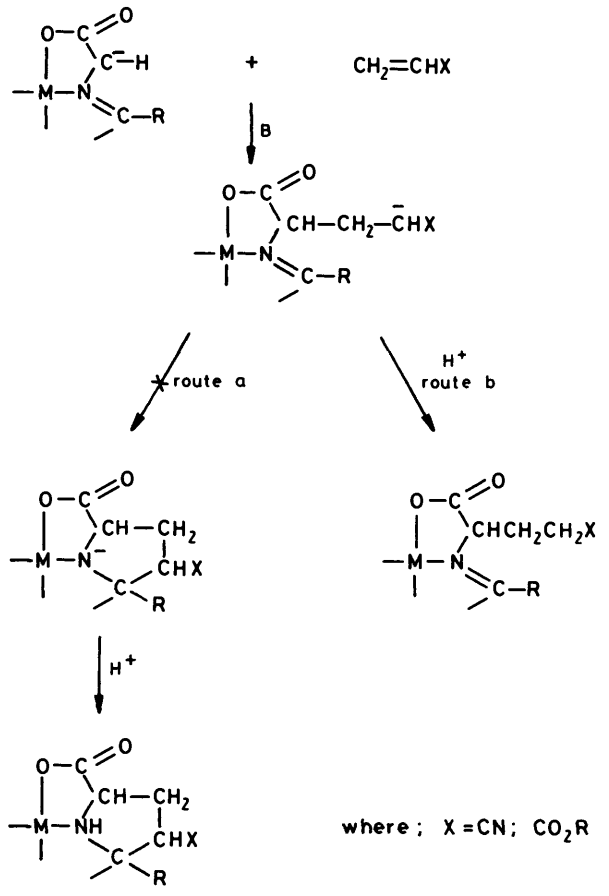
from Pharmacia. Reagents and solvents were purified in the usual way. Sodium methoxide was prepared by dissolving metallic sodium in methanol under an argon atmosphere.

Spectra were recorded with the following instruments. U.v.–visible Specord UV–vis. ^{1}H n.m.r.: Brucker WP-200 (200 MHz) and Tesla 467A. O.r.d.: Jasco ORD/UV-5, specific rotations were measured on a Perkin-Elmer 241 polarimeter. M.p.s are uncorrected and were measured with an Electrothermal melting point apparatus.

(*R*)-Propylenediaminetetra-acetic acid was obtained as described earlier.[16] Chiral lanthanide shift reagent, sodium (*R*)-(propylenediaminetetra-acetato)europiate(III), was obtained according to the procedure given for analogous complex of ethylenediaminetetra-acetic acid.[17] The shift reagent was used as described in ref. 11. Complexes (**1**) and (**2**) were prepared as described previously.[5] G.l.c. analysis was carried out as described in ref. 7.

*X-Ray Analysis.**—*Crystal data for complex* (**6**). $C_{32}H_{33}NiN_3O_5$, M = 478.2, orthorhombic, a = 15.233(1), b = 17.046(1), c = 22.700(2) Å, U = 5 894.37 Å^3, Z = 8, D_c = 1.35 g cm^{-3}, space group $P2_12_12_1$, $F(000)$ = 2 512. Crystals were obtained from hexane–acetone and contain two independent molecules of complex (**6**), differing essentially in the conformation of the amino acid side-chain (relative to C^β–C^γ bond). The unit-cell parameters and the intensities of reflections were measured with a four-circle automatic Hilger and Watts diffractometer, T = 20 °C, Mo-K_α radiation λ = 0.710 69 Å, $\theta \leqslant 27°$, $\theta/2\theta$ scan, 2 050 independent reflections with $F^2 \geqslant 2\sigma$ were used. The structure was solved by the Patterson and Fourier methods and refined by least squares in an isotropic approximation [owing to an insufficient number of reflections, only Ni(A), Ni(B), C(25A), C(26A), O(4A), and O(5A) atoms were refined anisotropically; the last four atoms have abnormally large and highly anisotropic thermal factors and seem to be disordered]. The absolute configuration of the structure was determined assuming (*S*)-configuration of the proline fragment. Anomalous scattering by the Ni atom was taken into account in the structure factor calculation.[18]

* Supplementary data available [SUP No. 56613 (12 pp.)]: full bond lengths and angles, H-atom co-ordinates, thermal parameters, and ORTEP drawing of the second (**6**) conformer (conformer A). For details of the Supplementary publications scheme see Instruction for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1986, Issue 1. The structure factors are available on request from the Editorial office.



Scheme 3.

The hydrogen atoms were placed in the geometrically calculated positions (methyl H atoms were located in the difference Fourier synthesis) and included with $B_{iso} = 7$ Å^2 in the F_{calc} as a fixed contribution. The statistical weights $w = [\sigma_F^2 + (0.015\ F_o)^2]^{-1}$ were used. The final refinement gave $R = 0.066$, $R_w = 0.062$. All calculations were carried out with the 'Eclipse S/200' minicomputer, using modified INEXTL programs.[19]

General Procedure for α-Amino Acid Synthesis by Michael Addition of Complex (**1**) *to Activated Olefins (except Acrolein).*—The olefin (3.8 mmol) in absolute methanol (2 cm^3) was added under Ar with stirring to a solution of complex (**1**) (1.62 g, 3.3 mmol) in 1M-MeONa (10 cm^3) (MeOH) at 25 °C. MeOH should be carefully dried before being used, to avoid partial hydrolysis of the reaction products in the case of acrylic acid esters. The course of reaction was monitored with t.l.c. (SiO_2). Each sample was quenched with 6% aqueous CH_3CO_2H, and the mixture of the complexes was extracted with $CHCl_3$ before being applied to the plate. After complex (**1**) had disappeared in the reaction mixture, the latter was poured into a stirred mixture of $CHCl_3$ (100 cm^3) and 6% aqueous acetic acid (100 cm^3). The chloroform layer was separated and the solvent removed under reduced pressure. The residue was subjected to flash chromatography (2 × 100 cm^3 SiO_2). The fractions containing pure diastereoisomers could be further purified on Sephadex LH-20 (C_6H_6–EtOH, 3:1). In order to obtain an α-amino acid, a solution of a pure diastereoisomer in EtOH (10 cm^3) was slowly added with stirring to 3M-aqueous HCl (15 cm^3) at 80 °C. Upon disappearance of the red colour of the complex, water was removed under reduced pressure, and then water (50 cm^3) was added to the residue; the precipitated chlorohydrate of (**2**) was then filtered off. The filtrate was neutralized with NH_3 and extracted several times with benzene. The extracts and precipitated chlorohydrate of (**2**) were combined to give, after treatment with aqueous NH_3 and evaporation of the benzene, (**2**) (1.01 g, 2.63 mmol, 80%). The filtrate was evaporated under reduced pressure to a minimal volume, and the amino acids were obtained as described for each compound. The chemical yields of the amino acids were determined by dissolving them in a solution of dioxane or Bu^{t}OH in 6M-DCl (D_2O) the concentration of which was known, and measuring the relative areas or proton signals by the ^{1}H n.m.r. method, using $(Me_2Si)_2O$ (HMDS) sealed in a glass capillary as an external standard.

(R)-2-*Amino*-4-*cyanobutyric acid from* (**3b**). The first fraction, was obtained in a yield of 3.5% (0.06 g, 0.11 mmol) using ethyl acetate as eluant; m.p. 110—112 °C (Found: C, 65.6; H, 5.2; N, 9.9. $C_{30}H_{28}N_4NiO_3$ requires C, 65.4; H, 5.1; N, 10.2%); M (25 °C, 9.7 × 10^{-4} mol dm^{-3} in MeOH, *l* 1 cm) −2 800 (578), +3 700 (546), +10 200 (436), and −8 200 (−365 nm); $\lambda_{max.}$(MeOH) 540 (log ε 2.29), 420 (3.47), 333 (3.67), and 265 nm (4.17); $\nu_{max.}$(KBr) 2 260 cm^{-1} (CN); δ ($CDCl_3$, HMDS) 1.65—2.68 (m, 9 H, amino acid 2 × β-H, 2 × γ-H, pro 2 × β-H, 2 × γ-H, δ-H), 3.62, 4.27 (AB, 2 H, *J* 12 Hz, C*H*$_2$Ph), 3.75 (m, 2 H, amino acid α-H, pro α-H), 4.17 (m, 1 H, pro δ-H), and 6.62—8.07 (m, 14 H, ArH).

The complex was decomposed as described above and, after the recovery of (**2**), the aqueous solution was subjected to cation exchange chromatography on Dowex 50 × 8 resin. Elution with 2M-ammonia and subsequent removal of water gave the α-amino acid: $\nu_{max.}$(KBr) 2 260 cm^{-1} (CN); δ(D_2O) 2.58 (m, 2 H, β-H), 3.05 (m, 2 H, γ-H), and 4.15 (t, 1 H, *J* 7 Hz, α-H).

The sample of the amino acid was too small for any meaningful optical rotation determination and was hydrolysed at 95 °C to (*R*)-glutamic acid (e.e. >95% g.l.c.) with 6M-HCl.

(S)-2-*Amino*-4-*cyanobutyric acid from* (**4b**). This was obtained in a yield of 82% (1.48 g, 2.69 mmol) as the second fraction; m.p. 220—224 °C (decomp.) (Found: C, 65.5; H, 5.1; N, 10.0. $C_{30}H_{28}N_4NiO_3$ requires C, 65.4; H, 5.1; N, 10.2%); M (25 °C, 8.3 × 10^{-4} mol dm^{-3} in MeOH, *l* 1 cm) +17 200 (578), +4 700 (546), −10 300 (436), and −480 (365 nm); $\lambda_{max.}$(MeOH) 540 (log ε 1.84), 4.18 (2.97), 333 (3.16), and 265 nm (3.65); $\nu_{max.}$(KBr) 2 250 cm^{-1} (CN); δ($CDCl_3$, HMDS) 1.75—3.73 (m, 11 H, pro 7 H, amino acid 2 × β-H, 2 × γ-H), 3.47, 4.30 (AB, 2 H, *J* 12 Hz, C*H*$_2$Ph), 3.75 (m, 1 H, amino acid α-H), 6.42—8.25 (m, 14 H, ArH). The α-amino acid was recovered in a 75% yield from (**4b**) (0.26 g, 2.0 mmol) as described above; m.p. 221—222 °C (decomp.) (lit.,[20] 220—235 °C, decomp.) (Found: C, 46.8; H, 6.5; N, 21.8. $C_5H_8N_2O_2$ requires C, 46.9; H, 6.3; N, 21.85%); $\nu_{max.}$(KBr) 2 260 cm^{-1} (CN); δ(D_2O) 2.58 (m, 2 H, β-H), 3.05 (m, 2 H, γ-H), 4.15 (t, 1 H, *J* 7 Hz, α-H), α (589 nm, 25 °C, 15.8 g dm^{-3} in D_2O, *l* 1 dm) = +25.32 [lit.,[20] α (589 nm, 25 °C, 5 g dm^{-3} in H_2O) = +27.4].

(S)-*Glutamic acid from* (**4a**). This was obtained as a second fraction (THF–C_6H_6, 1:1) in a yield of 89% (1.71 g, 2.94 mmol); m.p. 180—182 °C (Found: C, 63.7; H, 5.2; N, 7.2. $C_{31}H_{31}N_3NiO_5$ requires C, 63.7; H, 5.35; N, 7.2%); M(25 °C, 12.7 × 10^{-4} mol dm^{-3} in MeOH, *l* 1 cm) = +13 600 (578), +3 070 (546), −9 700 (436), and +3 200 (365 nm); $\lambda_{max.}$(MeOH) 530 (log ε 2.25), 408 (3.41), 330 (3.58), and 267 nm (4.10); $\nu_{max.}$(KBr) 1 740 cm^{-1} (CO, ester); δ ($CDCl_3$, HMDS) 1.75—3.45 (m, 11 H, pro 7 H, glu β-H, and γ-H), 3.50 (s, 3 H, MeO), 3.50, 4.35 (AB, 2 H, *J* 12.5 Hz, C*H*$_2$Ph), 3.80 (m, 1 H, glu α-H), and 6.50—8.15 (m, 14 H, ArH). Compound (**4a**) was decomposed as described above, and after the recovery of (**2**), concentrated HCl (10 cm^3) was added to the aqueous solution and the resulting mixture boiled for 1 h. The

Table 3. Selected bond lengths (Å) and angles (°) for A and B molecules

Bond	A	B	Bond	A	B	Bond	A	B
Ni–O(1)	1.87(1)	1.84(1)	C(4)–C(5)	1.41(2)	1.46(2)	C(12)–C(13)	1.53(3)	1.54(3)
Ni–N(1)	1.86(1)	1.86(1)	C(5)–C(6)	1.41(2)	1.40(2)	C(13)–C(14)	1.50(3)	1.47(3)
Ni–N(2)	1.86(1)	1.86(1)	C(6)–C(7)	1.36(2)	1.35(2)	C(14)–N(3)	1.46(2)	1.53(2)
Ni–N(3)	1.94(1)	1.93(1)	C(7)–C(8)	1.33(2)	1.39(2)	N(3)–C(15)	1.50(2)	1.48(2)
O(1)–C(1)	1.27(2)	1.30(2)	C(8)–C(9)	1.44(2)	1.46(2)	C(15)–C(16)	1.53(2)	1.53(2)
O(2)–C(1)	1.24(2)	1.26(2)	C(4)–C(9)	1.41(2)	1.35(2)	C(22)–C(23)	1.55(2)	1.54(2)
C(1)–C(2)	1.51(2)	1.50(2)	C(9)–N(2)	1.37(2)	1.40(2)	C(23)–C(24)	1.55(3)	1.50(3)
C(2)–N(1)	1.47(2)	1.48(2)	N(2)–C(10)	1.39(2)	1.36(2)	C(23)–C(25)	1.55(3)	1.52(2)
C(2)–C(22)	1.53(2)	1.53(2)	C(10)–O(3)	1.22(2)	1.24(2)	C(25)–O(4)	1.20(3)	1.19(2)
N(1)–C(3)	1.32(2)	1.32(2)	C(10)–C(11)	1.51(2)	1.51(2)	C(25)–O(5)	1.19(3)	1.25(2)
C(3)–C(4)	1.44(2)	1.45(2)	C(11)–N(3)	1.51(2)	1.49(2)	O(5)–C(26)	1.47(4)	1.45(3)
C(3)–C(27)	1.48(2)	1.48(2)	C(11)–C(12)	1.53(3)	1.54(2)			

Angle	A	B	Angle	A	B	Bond	A	B
O(1)–N–Ni(1)	86.7(5)	86.9(5)	C(3)–C(4)–C(5)	115(1)	113(1)	Ni–N(3)–C(11)	105(1)	106.6(9)
O(1)–Ni–N(2)	175.2(5)	178.8(5)	C(3)–C(4)–C(9)	125(1)	126(1)	Ni–N(3)–C(14)	117(1)	114(1)
O(1)–Ni–N(2)	90.6(5)	91.8(5)	C(5)–C(4)–C(9)	120(1)	121(1)	Ni–N(3)–C(15)	108.5(9)	111(1)
N(1)–Ni–N(2)	94.1(5)	94.1(5)	C(4)–C(5)–C(6)	120(1)	118(2)	C(11)–N(3)–C(14)	104(1)	103(1)
N(1)–Ni–N(3)	176.8(5)	176.8(5)	C(5)–C(6)–C(7)	120(2)	121(2)	C(11)–N(3)–C(15)	111(1)	115(1)
N(2)–Ni–N(3)	88.8(5)	87.2(5)	C(6)–C(7)–C(8)	121(2)	122(2)	C(14)–N(3)–C(15)	111(1)	108(1)
Ni–O(1)–C(1)	114.5(9)	114(1)	C(7)–C(8)–C(9)	123(2)	119(1)	C(11)–C(12)–C(13)	103(2)	103(1)
O(1)–C(1)–C(2)	124(1)	123(1)	C(4)–C(9)–C(8)	116(1)	119(1)	C(12)–C(13)–C(14)	105(2)	103(1)
O(1)–C(1)–C(2)	115(1)	117(1)	C(4)–C(9)–N(2)	121(1)	123(1)	C(13)–C(14)–N(3)	103(1)	106(2)
C(12)–C(1)–C(2)	121(1)	120(1)	C(8)–C(9)–N(2)	124(1)	117(1)	N(3)–C(15)–C(16)	117(1)	112(1)
C(1)–C(2)–N(1)	108(1)	106(1)	Ni–N(2)–C(9)	125(1)	123(1)	C(2)–C(22)–C(23)	113(1)	114(1)
C(1)–C(2)–C(22)	109(1)	108(1)	Ni–N(2)–C(10)	113(1)	112(1)	C(22)–C(23)–C(24)	115(2)	113(1)
Ni(1)–C(2)–C(22)	110(1)	109(1)	C(9)–N(2)–C(10)	122(1)	124(1)	C(22)–C(23)–C(25)	107(1)	109(1)
Ni–N(1)–C(2)	109(1)	112(1)	N(2)–C(10)–C(3)	126(2)	127(1)	C(24)–C(23)–C(25)	112(1)	114(2)
Ni–N(1)–C(3)	128(1)	128(1)	N(2)–C(10)–C(11)	114(1)	115(1)	C(23)–C(25)–O(4)	122(2)	121(2)
C(2)–N(1)–C(3)	123(1)	120(1)	O(13)–C(10)–C(11)	120(2)	118(1)	C(23)–C(25)–O(5)	120(2)	115(2)
N(1)–C(3)–C(4)	121(1)	120(1)	C(10)–C(11)–N(3)	112(1)	110(1)	O(4)–C(25)–O(5)	117(2)	123(2)
N(1)–C(3)–C(27)	118(1)	120(1)	C(10)–C(11)–C(12)	110(1)	112(1)	C(25)–O(5)–C(26)	127(2)	117(2)
C(4)–C(3)–C(27)	121(1)	120(1)	N(3)–C(11)–C(12)	105(1)	106.5(9)			

Table 4. Torsion angles in molecules A and B

Angle	A	B
Ni–N(3)–C(15)–C(16)	−41(1)	−46(1)
C(2)–C(22)–C(23)–C(25)	−121(2)	179(2)
C(22)–C(23)–C(25)–O(5)	41(2)	−105(2)
C(24)–C(23)–C(25)–O(5)	168(3)	22(2)

mixture was diluted with water (15 cm^3) and the solvent removed under reduced pressure. The residue was subjected to cation exchange chromatography on Dowex 50 × 8 resin. Elution with 2M-ammonia and subsequent removal of water gave (*S*)-glutamic acid (64%, 0.28 g, 1.88 mmol). The optical purity of the α-amino acid was determined by g.l.c.

(2R,4S)-4-*Methylglutamic acid from* (**5**). This was obtained in a 2.5% yield (0.05 g, 0.08 mmol) as the first fraction (THF, C_6H_6, hexane, EtOH 3:6:4:0.4); m.p. 197—199 °C (Found: C, 64.2; H, 5.75; N, 6.9. $C_{32}H_{33}N_3NiO_5$ requires C, 64.2; H, 5.6; N, 7.0%); M(25 °C, 12.0 × 10^{-4} mol dm^{-3} in MeOH, *l* 1 cm) −4 300 (578), +3 200 (546), +10 400 (436), and −8 900 (365 nm); $\lambda_{max.}$(MeOH) 540 nm (log ε 2.26), 420 (3.49), 333 (3.69), and 265 nm (4.21); $\nu_{max.}$(KBr) 1 750 cm^{-1} (CO, ester); δ ($CDCl_3$, HMDS) 0.79 (d, 3 H, *J* 7.5 Hz, glu γ-Me), 1.87 (m, 1 H, pro δ-*endo*-H), 1.52, 2.55 (m, 2 H, glu β-H), 2.0—2.30 (m, 2 H, pro β-H), 2.60 (m, 2 H, pro γ-H), 3.05 (m, 1 H, glu γ-H), 3.60 (s, 3 H, MeO), 3.70 (m, 1 H, pro α-H), 3.77, 4.67 (AB, 2 H, *J* 13.5 Hz, CH_2Ph), 3.88 (m, 1 H, glu α-H), 4.12 (m, 1 H, pro δ-*exo*-H), and 6.67—8.62 (m, 14 H, ArH). The α-amino acid was obtained from (**5**) as described above (72%, 0.01 g, 0.06 mmol); δ (6M-DCl, D_2O) 1.75 (d, 3 H, *J* 7 Hz, γ-Me), 2.84, 3.48 (m, 2 H, β-H), 4.20 (m, 1 H, γ-H), and 4.60 (m, 1 H, α-H). The sample of the amino acid was too small for any meaningful optical rotation determination.

(2S,4R)-4-*Methylglutamic acid from* (**6**). This was obtained in a 53% yield (1.05 g, 1.75 mmol) as the second fraction; m.p. 170—172 °C (Found: C, 64.2; H, 5.8; N, 7.2. $C_{32}H_{33}NiN_3O_5$ requires C, 64.2; H, 5.6; N, 7.0%); M(25 °C, 7.1 × 10^{-4} mol dm^{-3} in MeOH, *l* 1 cm) +15 000 (578) +1 970 (546), −13 000 (436), and +6 330 (365 nm); $\lambda_{max.}$(MeOH) 530 (log ε 2.33), 4.10 (3.64), 336 (3.66), and 268 nm (4.19); $\nu_{max.}$(KBr) 1 730 cm^{-1} (CO, ester); δ ($CDCl_3$, HMDS) 0.75 (d, 3 H, *J* 7.5 Hz, glu γ-Me), 1.50, 2.65 (m, 2 H, glu β-H), 1.90—2.20 (m, 3 H, pro 2 × β-H, δ-H), 2.27—2.77 (m, 2 H, pro γ-H), 3.10 (m, 1 H, glu γ-H) 3.25—3.65 (m, 2 H, pro-α, δ-H), 3.40, 4.30 (AB, 2 H, *J* 12.5 Hz, CH_2Ph), 3.44 (s, 3 H, MeO), 3.82 (m, 1 H, glu α-H), and 6.52—8.12 (m, 14 H, ArH). The amino acid was obtained in a yield of 70% (0.20 g, 1.22 mmol) from (**6**) as described above; δ (6M-DCl, D_2O) 1.75 (d, 3 H, *J* 7 Hz, γ-Me), 2.84, 3.48 (m, 2 H, β-H), 4.20 (m, 1 H, γ-H), 4.60 (m, 1 H, α-H); α (589 nm, 25 °C, 26.2 g dm^{-3} in 6M-DCl, *l* 1 dm) = +21.4° [lit.,[2] α (589 nm, 25 °C, 25 g dm^{-3} in 6M-HCl) = +22.7°].

(2S,4S)-4-*Methylglutamic acid from* (**7**). This was obtained in a yield of 25% (0.49 g, 0.82 mmol) as the third fraction; m.p. 183—185 °C (Found: C, 64.35; H, 5.5; N, 7.2. $C_{32}H_{33}N_3NiO_5$ requires C, 64.2; H, 5.6; N, 7.0%); M(25 °C, 5.5 × 10^{-4} mol dm^{-3} in MeOH, *l* 1 cm) +14 300 (578), +4 500 (546), −9 200 (436), and −180 (365 nm); $\lambda_{max.}$(MeOH) 530 (log ε 2.29), 408 (3.88), 333 (3.65), and 265 nm (4.20); $\nu_{max.}$(KBr) 1 730 cm^{-1} (CO, ester); δ ($CDCl_3$, HMDS) 1.07 (d, 3 H, *J* 7.5 Hz, glu γ-Me), 1.90—3.62 (m, 10 H, pro 7 H, glu α-H, β-H), 2.70 (m, 1 H, glu γ-H), 3.24 (s, 3 H, MeO), 3.45, 4.35 (AB, 2 H, *J* 13 Hz, CH_2Ph), and 6.48—8.07 (m, 14 H, ArH). The amino acid was obtained in a

yield of 67% (0.09 g, 0.55 mmol) from (**7**); δ(6M-DCl, D_2O) 1.75 (d, 3 H, *J* 7 Hz, γ-Me), 2.91 (m, 2 H, β-H), 3.10 (m, 1 H, γ-H), and 4.27 (m, 1 H, α-H); α (589 nm, 25 °C, 25.8 g dm^{-3} in 6M-HCl, *l* 1 dm) = +29.2° [lit.,[21] α (589 nm, 20 °C, 25 g dm^{-3} in 6M-HCl) = +22.2° (lit.,[2] α (589 nm, 20 °C, 25 g dm^{-3} in 6M-HCl) +36.3° [lit.,[22] α (589 nm, 20 °C, 23 g dm^{-3} in 6M-HCl) = +30.2°].

(2S,3R)-3-*Phenylglutamic acid from* (**8**). This was obtained in a yield of 51% (1.11 g, 1.68 mmol) as the first large fraction; m.p. 214—216 °C (Found: C, 67.3; H, 5.5; N, 6.5. $C_{37}H_{35}N_3NiO_5$ requires C, 67.3; H, 5.3; N, 6.4%); M (25 °C, 6.7 × 10^{-4} mol dm^{-3} in MeOH, *l* 1 cm) +15 700 (578), +567 (546), −17 000 (436), and +2 200 (365 nm); $\lambda_{max.}$(MeOH) 530 (log ε 2.41), 410 (3.52), 338 (3.71), and 268 nm (4.24); $\nu_{max.}$(KBr) 1 740 cm^{-1} (CO, ester); δ($CDCl_3$) 1.40 (m, 1 H, pro *endo* γ-H), 1.65—3.24 (m, 5 H, pro α, 2 × β-H, 2 × δ-H), 2.14 (m, 1 H, pro *exo* γ-H), 2.17 (ABX, 1 H, J_{BX} 6 Hz, J_{AB} 15 Hz, glu γ-H), 3.01 (ABX, 1 H, J_{AX} 10 Hz, J_{AB} 15 Hz, glu γ-H), 3.18 (m, 1 H, glu β-H), 3.29 (s, 3 H, MeO), 3.30, 4.12 (AB, 2 H, J_{AB} 12.8 Hz, CH_2Ph), 4.14 (d, 1 H, *J* 3.7 Hz, glu α-H), and 6.52—8.25 (m, 9 H, ArH). The α-amino acid was obtained from the complex as described above in a yield of 66% (0.25 g, 1.11 mmol); δ (6M-DCl, D_2O) 3.63 (m, 2 H, γ-H), 4.28 (m, 1 H, β-H), 4.67 (d, 1 H, *J* 5 Hz, α-H), and 7.89 (m, 5 H, ArH); α (589 nm, 25 °C, *l* 1 dm, 8.67 g dm^{-3} in 6M-DCl) +19.15°.

(2S,3S)-3-*Phenylglutamic acid from* (**9**). This was obtained in a yield of 26% (0.57 g, 0.86 mmol) as the second fraction; m.p. 278—280 °C (Found: C, 67.6; H, 5.55; N, 6.1. $C_{37}H_{35}N_3NiO_5$ requires C, 67.3; H, 5.3; N, 6.4%); M(25 °C, 9.5 × 10^{-4} mol dm^{-3} in MeOH, *l* 1 cm) +13 100 (578), −1 700 (546), −18 000 (436), and +9 600 (365 nm); $\lambda_{max.}$(MeOH) 530 (log ε 2.36) 4.10 (3.47), 333 (3.65), and 268 nm (4.17); $\nu_{max.}$(KBr) 1 740 cm^{-1} (CO, ester); δ ($CDCl_3$, HMDS) 2.19 (m, 2 H, pro γ-H and β-H), 2.65 (m, 1 H, pro β-H), 2.96 (m, 1 H, pro γ-H), 3.03 (AMX, 1 H, J_{AX} 10 Hz, J_{AM} 16.2 Hz, glu γ-H), 3.50 (m, 2 H, pro α- and δ-H), 3.52, 4.41 (AB, 2 H, *J* 12.8 Hz, CH_2Ph), 3.72 (m, 1 H, pro δ-H), 3.94 (AMX, 1 H, J_{MX} 5.2 Hz, J_{AM} 16.2 Hz, glu γ-H), 4.07 (d, 1 H, *J* 7 Hz, glu α-H), 4.54 (m, 1 H, glu β-H), and 6.03—8.13 (m, 19 H, ArH). The α-amino acid was obtained from the complex as described above in a yield of 80% (0.15 g, 0.69 mmol); δ (6M-DCl, D_2O) 3.51, 3.69 (ABX, 2 H, $J_{\gamma\beta}$ 6 and 9 Hz, $J_{\gamma\gamma}$ 17, γ-H), 4.27 (m, 1 H, β-H), 4.88 (d, 1 H, *J* 8 Hz, α-H), and 7.90 (ArH); α (589 nm, 25 °C, *l* = 1 dm, 8.1 g dm^{-3} in 6M-DCl) = +11.1°.

Michael Addition of Complex (**1**) *to Acrolein.*—Acrolein (0.3 cm^3, 4.47 mmol) was added under Ar with stirring to a solution of complex (**1**) (1.5 g, 3 mmol) in a 1M-solution of Et_3N in methanol (17 cm^3) at −10 °C. The course of the reaction was monitored with t.l.c., as described above. After complex (**1**) had disappeared from the reaction mixture, the reaction was stopped by the addition of aqueous $MeCO_2H$; subsequent treatment of the mixture was the same as in earlier described cases. The diastereoisomers were separated by flash chromatography on SiO_2 with $CHCl_3$–Me_2CO (3:1). The first fraction (**3c**) was obtained in a yield of 4.3% (0.07 g, 0.013 mmol); m.p. 98—100 °C (Found: C, 65.5; H, 5.3; N, 7.2. $C_{30}H_{29}N_3NiO_4$ requires C, 65.0; H, 5.3; N, 7.6%); M(25 °C, 10.1 × 10^{-4} mol dm^{-3} in CH_3OH, *l* 1 cm) −1 500 (578), +4 550 (546), +12 000 (436), and −14 400 (365 nm); $\lambda_{max.}$(MeOH) 530 nm (log ε 2.10), 418 (3.40), 336 (3.61), and 263 nm (4.09); $\nu_{max.}$(KBr) 1 720 cm^{-1} (CO, aldehyde); δ ($CDCl_3$, HMDS) 1.65—2.82 (m, 9 H, pro 2 × β-H, 2 × γ-H, δ-H amino acid 2 × β-H, 2 × γ-H), 3.56, 4.35 (AB, 2 H, *J* 11.2 Hz, CH_2Ph), 3.60—3.82 (m, 2 H, pro α-H, amino acid α-H), 4.17 (m, 1 H, pro δ-H), 6.57—8.60 (m, 14 H, ArH), and 9.57 (s, 1 H, CHO). The second fraction (**4c**) was obtained in a yield of 70% (1.1 g, 2.23 mmol); m.p. 195—198 °C (decomp.) (Found: C, 65.55; H, 5.6; N, 7.6. $C_{30}H_{29}N_3NiO_4$ requires C, 65.0; H, 5.3; N, 7.6%); M (25 °C, 8.7 × 10^{-4} mol dm^{-3} in MeOH, *l* 1 cm) = +14 900 (578), +5 200 (546), −8 900 (436), and +1 270 (365 nm); $\lambda_{max.}$(MeOH) 540 (log ε 2.31), 420 (3.49), 333 (3.67), and 267 nm (4.20); $\nu_{max.}$(KBr) 1 725 cm^{-1} (CO, aldehyde); δ ($CDCl_3$, HMDS) 1.79—3.76 (m, 11 H, pro 7 H, amino acid 2 × β-H, 2 × γ-H), 3.56, 4.37 (AB, 2 H, *J* 12 Hz, CH_2Ph), 3.85 (m, 1 H, amino acid α-H), 6.59—8.32 (m, 14 H, ArH), and 9.68 (s, 1 H, CHO).

After the recovery of (**2**) the aqueous solution was treated with sodium tetrahydroborate (10 equiv.) at 25 °C until effervescence stopped; a black precipitate was removed by centrifugation, and the solution was subjected to cation exchange chromatography on Dowex 50 × 8 resin. The quantitative and enantioisomeric analysis of proline were performed by g.l.c. No attempts to optimize the yield of proline were made.

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