After removal of the hydantoic acid by-product, the filtrate was concentrated to a slurry, diluted with methanol, and filtered to yield 2.45 g (26.8%) of 4,4,4-trifluorovaline (1, n = 0, R = CH_3), mp 252° dec, ir spectrum consistent with the proposed structure and nmr spectrum consistent but suggesting a 3:1 mixture of *threo* and *erythro* isomers, respectively.

Anal. Calcd for $C_5H_8F_3NO_2$: C, 35.06; H, 4.70; N, 8.18; F, 33.3. Found: C, 35.02; H, 4.75; N, 7.92; F, 34.4.

A sample of DL-4,4,4-trifluorovaline,[11] mp 248° dec, prepared by Loncrini and Walborsky,[7] was by nmr spectrum a 2:1 mixture of *threo* and *erythro* isomers, respectively. Another sample,[12] mp 239° dec, prepared by Lazar and Sheppard,[8a] was by nmr spectrum the same 2:1 mixture. The above-reported decomposition points were verified in our laboratory. The position of the α-H doublet center is pH dependent, but the relative chemical shift, *threo* to *erythro*, is τ 0.22, while that for the methyl doublet, *threo* to *erythro*, is τ −0.17. The infrared spectra of these two samples, despite the difference in decomposition point, were identical and differed only slightly in relative intensities between 650 and 950 cm^{-1} from that of the 3:1 mixture of *threo* and *erythro* isomers.

(11) Kindly supplied by Dr. D. F. Loncrini. In a personal communication he states that the melting point in ref 8a should be corrected to the one given above.

(12) Kindly supplied by Dr. J. Lazar.

Registry No.—**1** (n = 1, R = H), 23809-57-6; **1** (n = 0, R = Me) (*threo*), 23809-58-7; **1** (n = 0, R = Me) (*erythro*), 23796-83-0; **3** (n = 1, R = H), 17027-50-8; **3** (n = 0, R = Me), 23809-60-1; **4** (n = 1, R = H), 23809-61-2; **4** (n = 0, R = Me), 23809-62-3; DL-5-(3′,3′,3′-trifluoropropyl)hydantoin, 23809-63-4; DL-*threo*-N-carbamyl-4,4,4-trifluorovaline, 23809-64-5; DL-*erythro*-N-carbamyl-4,4,4-trifluorovaline, 23809-65-6.

Acknowledgment.—The authors are indebted to Dr. J. M. Chemerda and Dr. J. van de Kamp for encouragement and valued advice, to Mr. R. N. Boos and associates for microanalytical data, and to Mr. R. W. Walker and Dr. B. H. Arison for instrumental assistance.

Synthesis and Application in Peptide Chemistry of Amino Acids Possessing an Optically Active Selenohomocysteine Skeleton[1a-c]

C. S. PANDE, J. RUDICK, AND RODERICH WALTER[1d]

Departments of Surgery and Physiology, Mount Sinai Medical and Graduate Schools, New York, New York 10029, and The Medical Research Center, Brookhaven National Laboratory, Upton, New York 11973

Received October 6, 1969

The general and convenient method developed earlier in these laboratories to replace the O-tosyl moiety by selenium nucleophiles has been extended to O-tosylated homoserine derivatives and has resulted in the preparation of L-selenomethionine (**17**), L-selenoethionine (**20**), Se-benzyl-L-selenohomocysteine (**10**), and L-(+)-selenocystathionine (**23**). The specific optical rotations of **10**, **17**, and **20** were found to be higher than reported earlier for these compounds. The use of the derivatives of the foregoing selenium-containing amino acids in the synthesis of peptides was demonstrated in the case of Se-benzyl-L-selenohomocysteine. During decarbobenzoxylation of N-carbobenzoxy-L-selenomethionine and N-carbobenzoxy-L-selenoethionine with hydrogen bromide, the attack by the benzyl bromide on the selenium, which results in the displacement of the methyl or ethyl group, was prevented by the addition of the highly nucleophilic β-mercaptoethanol.

With the displacement of the O-tosyl moiety by selenium nucleophiles we introduced a general and convenient method for the preparation of selenocysteine and selenocystine derivatives which bear readily and selectively removable protecting groups[2-4] and which therefore fulfill all the prerequisites for incorporation into peptides—even those of more complex structures.[5-7] This method should also provide a versatile pathway for the synthesis of derivatives of selenohomocysteine and of amino acids possessing a selenohomocysteine skeleton as long as appropriately protected O-tosyl homoserine derivatives can be secured.

In our initial experiments we attempted to apply a synthetic route which had been successful for the conversion of L-serine into L-selenocysteine, *i.e.*, the use of O-tosylated N-carbobenzoxy-L-serine esterified with benzhydrol.[2] However, when DL-homoserine was carbobenzoxylated according to Flavin and Slaughter[8] and then allowed to react with diphenyldiazomethane,[9] the sole product was the γ-lactone of DL-N-carbobenzoxyhomoserine.[10] This result was not quite unexpected in view of the extensive lactone formation encountered when amino acids possessing a free γ-hydroxyl function are prepared, derivatized, or employed for peptide synthesis.[8,11-15] In fact, the ready formation of the γ-lactone is the basis for the selective, nonenzymatic cleavage of the peptide chain at amino acid residues which are convertible into γ-hydroxyamino acid resi-

(1) (a) This work was supported by U. S. Public Health Service Grants AM-11580 and AM-10080 and by the U. S. Atomic Energy Commission. One of us (J. R.) was a recipient of a Career Scientist Award from the New York Health Research Council (I-541). (b) Part of this work was presented before The First American Peptide Symposium, Yale University, New Haven, Conn., Aug 1968. (c) The following abbreviations have been used: Z, carbobenzoxy; Tos, *p*-toluenesulfonyl; Bzl, benzyl; DPM, diphenylmethyl; BZLN, *p*-nitrobenzyl; AcOH, acetic acid; DMF, dimethylformamide; TosBZLN, *p*-nitrobenzyl *p*-toluenesulfonate; MeOH, methanol. (d) To whom correspondence should be addressed: Department of Physiology, Mount Sinai School of Medicine of The City University of New York, 10 East 102nd St., New York, N. Y. 10029.

(2) (a) D. Theodoropoulos, I. L. Schwartz, and R. Walter, *Tetrahedron Lett.*, No. 25, 2411 (1967); (b) D. Theodoropoulos, I. L. Schwartz, and R. Walter, *Biochemistry*, **6**, 3927 (1967).

(3) R. Walter in "Peptides; Chemistry and Biochemistry" (Yale University, New Haven, Conn., 1968), B. Weinstein, Ed., Marcel Dekker, Inc., New York, N. Y., 1970, p 467.

(4) J. Roy, W. Gordon, I. L. Schwartz, and R. Walter, *J. Org. Chem.*, **35**, 510 (1970).

(5) R. Walter and V. du Vigneaud, *J. Amer. Chem. Soc.*, **87**, 4192 (1965).

(6) R. Walter and V. du Vigneaud, *ibid.*, **88**, 1331 (1966).

(7) R. Walter and W. Y. Chan, *ibid.*, **89**, 3892 (1967).

(8) M. Flavin and C. Slaughter, *Biochemistry*, **4**, 1370 (1965).

(9) J. B. Miller, *J. Org. Chem.*, **24**, 560 (1959).

(10) M. Flavin and C. Slaughter, *J. Biol. Chem.*, **235**, 1103 (1960).

(11) J. S. Morley and J. M. Smith, *J. Chem. Soc.*, 726 (1968).

(12) J. P. Greenstein and M. Winitz in "Chemistry of the Amino Acids," Vol. 3, John Wiley & Sons, Inc., New York, N. Y., 1961, p 2589.

(13) T. Wieland, *Fortsch. Chem. Org. Natur.*, **25**, 214 (1967).

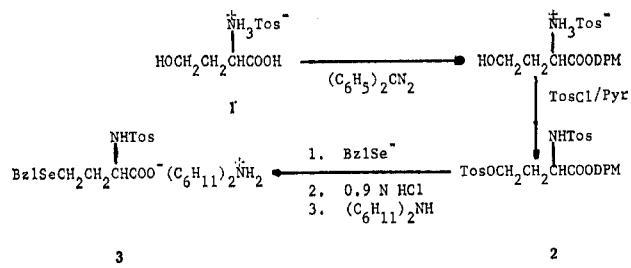
(14) Y. Fujita, J. Kollonitsch, and B. Witkop, *J. Amer. Chem. Soc.*, **87**, 2030 (1965).

(15) E. A. Bell and A. S. L. Tirimanna, *Biochem. J.*, **91**, 356 (1964).

dues, such as those of methionine[16] and aspartic acid,[17] or which already possess a γ-hydroxyl group, such as of γ,δ-dihydroxyleucine.[13] Moreover, this lactone formation has been used for the development of a N-protecting group, the γ-hydroxyisocaproyl residue.[18]

In an attempt to reduce the lactone formation we employed the poorly nucleophilic *p*-toluenesulfonate as the counterion to the NH_3^+ group of homoserine (**1**) (Scheme I). This salt, stable in dimethylformamide

SCHEME I

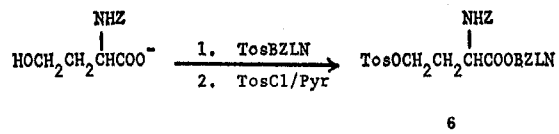


for prolonged periods of time, when treated with diphenyldiazomethane, yielded a mixture of the desired ester as well as lactone and by-products resulting from the decomposition of the diazo compound. The major by-product, as characterized by elemental analysis and ultraviolet absorption spectrum, was tetraphenylethene, which was predicted but not detected earlier.[19] Attempts to separate the ester or to acylate the amino function with carbobenzoxy chloride gave rise to additional lactone formation. However, when homoserine diphenylmethyl ester *p*-toluenesulfonate was treated with *p*-toluenesulfonyl chloride, the crystalline N,O-ditosylhomoserine diphenylmethyl ester (**2**) was secured in low yield. Both optically active and racemic **2** were converted into the corresponding Se-benzylselenohomocysteine derivatives (**3**).

From these preliminary experiments it became apparent that the most advantageous path in obtaining a fully protected O-tosylated homoserine derivative would be *via* the introduction of the amino blocking group in alkaline medium followed by the conversion of the resulting carboxylate into a suitable ester. For this purpose L-homoserine was carbobenzoxylated and the sodium N-carbobenzoxy-L-homoserinate was allowed to react with N-chloromethyl phthalimide,[20] benzyl iodide, 2,4,6-trimethylbenzyl chloride,[21] and diphenylmethyl *p*-toluenesulfonate,[22] respectively; however, in all instances the only product isolated was the α-L-carbobenzoxyaminobutyrolactone.[8] The attempt to substitute the 2,4,6-trimethylbenzyl chloride by the more reactive 2,4,6-trimethylbenzyl *p*-toluenesulfonate failed owing to the polymerization of the tosylate in the course of its preparation, a finding which is in line with the self-alkylation noticed with other tosylates.[23,24]

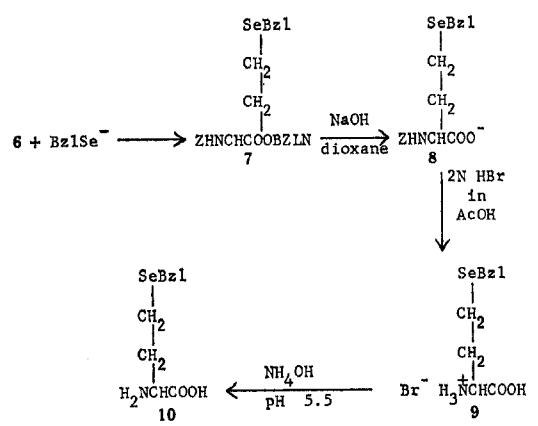
The above findings suggested that lactonization might be controlled by the use of esters, *e.g.*, *p*-nitrobenzyl, which do not readily form an intermediate carbonium ion. Indeed, the results were encouraging when N-carbobenzoxy-L-homoserine was esterified in the form of its sodium salt with *p*-nitrobenzyl tosylate[23] (Scheme II); the N-carbobenzoxy-L-homoserine *p*-nitrobenzyl ester, which readily crystallized and was stable when stored at 4° for a prolonged period of time, was obtained in high yields even in large-scale preparations. Treatment of this ester with tosyl chloride afforded N-carbobenzoxy-O-tosyl-L-homoserine *p*-nitrobenzyl ester (**6**), which proved to be a valuable intermediate for the preparation of optically active amino acids and peptides possessing a selenohomocysteine skeleton.

SCHEME II



The nucleophilic displacement of the O-tosyl moiety of **6** by the benzylselenide anion gave the corresponding Se-benzyl derivative **7** (Scheme III). Prior to saponifying **7** we established the reaction conditions to remove the *p*-nitrobenzyl group on the model compound, N-carbobenzoxy-L-alanine *p*-nitrobenzyl ester. The procedure, described by Iselin and Schwyzer,[25] which gave N-carbobenzoxy-L-alanine in high yield and without racemization, proved to be most suitable and was applied to the hydrolysis of **7** to yield N-carbobenzoxy-Se-benzyl-L-selenohomocysteine (**8**). Decarbobenzoxylation of **8** afforded the hydrobromide **9**, which was converted into Se-benzyl-L-selenohomocysteine (**10**). We observed that the specific optical rotation of **10** in hydrochloric acid is extremely temperature dependent and that it has to be read at once; the value of the specific rotation decreases as **10** is allowed to stand in the acidic solution. This may, in part, explain the lower values for the optical rotation reported for this compound by other authors. However, data presented in this paper (*vide infra*) would indicate that **10**, despite

SCHEME III

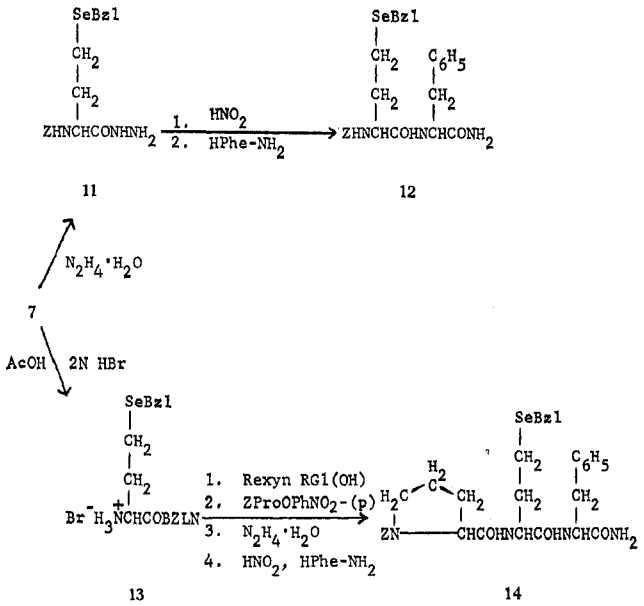


(16) B. Witkop, *Advan. Protein Chem.*, **16**, 221 (1961).
(17) E. Gross, J. L. Morrell, and P. Q. Lee, *Ann. N. Y. Acad. Sci.*, **151**, 556 (1968).
(18) T. Wieland, K. Mannes, and A. Schöpf, *Justus Liebigs Ann. Chem.*, **617**, 152 (1958).
(19) A. A. Aboderin, G. R. Delpierre, and J. S. Fruton, *J. Amer. Chem. Soc.*, **87**, 5469 (1965).
(20) G. H. L. Nefkens, G. I. Tesser, and R. J. F. Nivard, *Rec. Trav. Chim. Pays-Bas*, **82**, 941 (1963).
(21) F. H. C. Stewart, *Aust. J. Chem.*, **19**, 1067 (1966).
(22) A. Ledwith and D. G. Morris, *J. Chem. Soc.*, 508 (1964).
(23) D. Theodoropoulos and J. Tsangaris, *J. Org. Chem.*, **29**, 2272 (1964).
(24) J. K. Kochi and G. S. Hammond, *J. Amer. Chem. Soc.*, **75**, 3443 (1953).
(25) B. Iselin and R. Schwyzer, *Helv. Chim. Acta*, **45**, 1499 (1962).

the fact that it has previously been prepared by essentially two independent routes,[26,27] was not secured in an optically pure form—because selenomethionine[26-28] and selenoethionine[27] obtained after debenzylation of Se-benzyl-L-selenohomocysteine with sodium in liquid ammonia and subsequent alkylation also exhibited lower values for the optical rotation. In view of our own findings and those of others,[29,30] it is likely that, in addition to the factor of temperature sensitivity, the discrepancies may be attributed to the sodium–liquid ammonia reduction employed in these earlier studies.

It has previously been shown from this laboratory that N-carbobenzoxy-Se-benzyl-L-selenocysteine *p*-nitrobenzyl ester is ideally suited for the attachment of a Se-benzyl-L-selenocysteine residue to either the amino or the carboxyl end of an amino acid or a peptide.[2b] In the present study we explored the possibility of applying these reactions to the selenohomocysteine peptides. Therefore, on the one hand, **7** was hydrazinolyzed to yield **11**, which was then, *via* the azide method, elongated to N-carbobenzoxy-Se-benzyl-L-selenohomocysteinyl-L-phenylalanine amide (**12**) (Scheme IV).

SCHEME IV

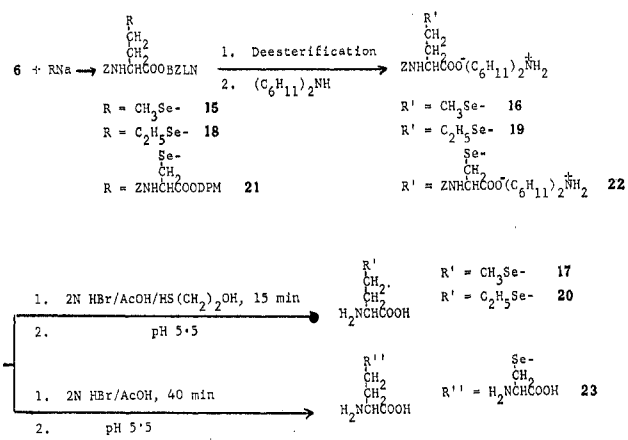


On the other, **7** was decarbobenzoxylated and the methanolic solution of the hydrobromide **13** was passed through a Rexyn RG1(OH) column to give the Se-benzyl-L-selenohomocysteine *p*-nitrobenzyl ester. Only trace amounts of *p*-nitrobenzyl alcohol were liberated during this process. The base was allowed to react with N-carbobenzoxy-L-proline *p*-nitrophenyl ester[31] and the resulting dipeptide ester was converted directly into N-carbobenzoxy-L-prolyl-Se-benzyl-L-selenohomocysteine hydrazide. This hydrazide in turn was converted in excellent yield into the protected tripeptide amide **14** *via* the azide procedure.

(26) F. Pan and H. Tarver, *Arch. Biochem. Biophys.*, **119**, 429 (1967).
(27) H.-D. Jakubke, J. Fischer, K. Jošt, and J. Rudinger, *Collect. Czech. Chem. Commun.*, **33**, 3910 (1968).
(28) G. Zdansky, *Ark. Kemi*, **29**, 437 (1968).
(29) W. H. H. Günther and H. G. Mautner, *J. Amer. Chem. Soc.*, **87**, 2708 (1965).
(30) L. B. Agenäs and B. Persson, *Acta Chem. Scand.*, **21**, 835 (1967).
(31) M. Bodansky and V. du Vigneaud, *J. Amer. Chem. Soc.*, **81**, 5688 (1959).

Next we investigated the feasibility of transforming N-carbobenzoxy-L-homoserine *p*-nitrobenzyl ester into derivatives of L-selenomethionine, L-selenoethionine, and L-(+)-selenocystathionine. First, we attempted to convert the protected ester with sodium hydrogen selenide into N-carbobenzoxy-L-selenohomocysteine *p*-nitrobenzyl ester according to the procedure introduced in this laboratory by Gordon.[3,4] However, in spite of several experimental modifications, this compound was not secured and *p*-nitrobenzyl alcohol was consistently liberated; apparently the selenol moiety of the initially formed N-carbobenzoxy-L-selenohomocysteine *p*-nitrobenzyl ester attacks the ester bond with the concomitant release of the alcohol. This difficulty was circumvented when the desired selenium nucleophile, *i.e.*, the sodium salt of methylselenol, ethylselenol,[32] or N-carbobenzoxy-L-selenocysteine diphenylmethyl ester,[2b] was allowed to react *in situ* with the ester, yielding the fully protected L-selenomethionine (**15**), L-selenoethionine (**18**), or L-(+)-selenocystathionine (**21**) derivatives, respectively, in good yields (Scheme V).

SCHEME V



In the case of **15** and **18** saponification as detailed for **8** readily yielded the N-protected amino acids, which were characterized as their dicyclohexylammonium salts. Initial attempts to decarbobenzoxylate **16** and **19** by catalytic hydrogenation or treatment with 2 *N* HBr in glacial acetic acid in the absence or presence of methyl ethyl sulfide[33,34] were unsuccessful. While in the former experiment the complete recovery of the starting material indicated that the catalyst had been poisoned, in the latter the sole product isolated was Se-benzyl-L-selenohomocysteine, a finding reminiscent of earlier experiences with N-carbobenzoxy-L-methionine.[35,36] Obviously, the nucleophilicity of methyl ethyl sulfide does not suffice to compete with the unsymmetrical dialkyl selenide for the benzyl bromide which is formed during the decarbobenzoxylation of **16** and **19** with hydrogen bromide. Therefore, in another experiment we introduced a stronger nucleophile, β-mercaptoethanol, into the reaction medium and were

(32) H. Rheinboldt in "Methoden der Organischen Chemie (Houben-Weyl)," E. Müller, Ed., Georg Thieme Velag, Stuttgart, 1955, p 952.
(33) St. Guttmann and R. A. Boissonnas, *Helv. Chim. Acta*, **41**, 1852 (1958).
(34) F. Chillemi, *Gazz. Chim. Ital.*, **93**, 1079 (1963).
(35) C. A. Dekker and J. S. Fruton, *J. Biol. Chem.*, **173**, 471 (1948).
(36) N. F. Albertson and F. C. McKay, *J. Amer. Chem. Soc.*, **75**, 5323 (1953).

able to secure L-selenomethionine (**17**) and L-selenoethionine (**20**). In fact, from qualitative experiments it emerged that the greater the quantity of added β-mercaptoethanol the higher was the yield of **17** and **20**. The specific optical rotations of L-selenomethionine and L-selenoethionine prepared by other synthetic routes[26-28] are appreciably lower than those reported in this study.

The fully protected L-selenocystathionine derivative (**21**) was deesterified stepwise; the *p*-nitrobenzyl ester was saponified and, without isolation of the intermediate, the diphenylmethyl ester group was cleaved by acidolysis and the resulting acid was then characterized as its di(dicyclohexylammonium) salt (**22**). Decarbobenzoxylation of **22** gave the hydrobromide of L-selenocystathionine, which upon adjustment of the pH to the isoelectric point, afforded the free amino acid **23**. The optical rotation of the product agreed with that reported for synthetic L-selenocystathionine[37] as well as that isolated from the South American nut, *Lecythis ollaria*.[38]

Experimental Section[39]

L-Homoserine *p*-Toluenesulfonate (1a).—*p*-Toluenesulfonic acid monohydrate (4.75 g) was added with stirring to a solution of L-homoserine (3.0 g) in water (12 ml). When the dissolution was complete, the solvent was quickly evaporated under reduced pressure. The resulting syrup was diluted with acetone (400 ml). Crystallization of the product was induced by scratching. After completion of the crystallization the salt was isolated by filtration, washed with acetone, and recrystallized from methanol–ether, yielding 5.6 g (76%), mp 124–125°, $[\alpha]^{23}D$ +6.8° (*c* 2, methanol).

Anal. Calcd for $C_{11}H_{17}NO_6S$: C, 45.4; H, 5.84; N, 4.80. Found: C, 45.1; H, 5.64; N, 4.65.

DL-Homoserine *p*-toluenesulfonate (1b) was obtained analogously, mp 141°.

Anal. Found: C, 45.3; H, 6.00; N, 4.88.

N,O-Ditosyl-L-homoserine Diphenylmethyl Ester (2a).—To a solution of L-homoserine *p*-toluene sulfonate (7.5 g) in DMF (12 ml) at 50°, diphenyldiazomethane (7.5 g) in DMF (25 ml) was added. The reaction mixture was kept at 50° for 10 min; then the solvent was removed under reduced pressure and the syrup was washed with ether to remove any excess diazomethane, benzhydrol, tetraphenylethene (*vide infra*), and other uncharacterized by-products. The resulting syrup (12 g), dried over P_2O_5 *in vacuo*, failed to crystallize. It was dissolved in dry pyridine (50 ml), the solution was cooled to −10°, and tosyl chloride (15 g) was added. After being stirred at 0° for 4 hr the reaction mixture was poured over crushed ice. The resulting oil was washed with water, dried, and extracted several times with ether. The ether-soluble fraction was applied to a column of silica gel prepared in petroleum ether (bp 90–110°). The product was eluted with ether–petroleum ether (1:1). Upon evaporation of the solvent, the desired product was isolated: yield 3.5 g (17%); mp 132–133°; $[\alpha]^{22}D$ −15.5° (*c* 1, DMF); silica gel (S_{III}) R_f 0.77.

Anal. Calcd for $C_{31}H_{31}NO_7S_2$: C, 62.7; H, 5.23; N, 2.36. Found: C, 62.8; H, 5.35; N, 2.38.

In a preliminary investigation the DL derivative **2b** was obtained in low yield, mp 118–119°.

Anal. Found: C, 63.1; H, 5.40; N, 2.28.

N-Tosyl-Se-benzyl-L-selenohomocysteine Diphenylmethyl Ester (3a).—Benzylselenol (0.48 g) was dissolved in DMF (2.5 ml), and a 13% NaOH solution (0.8 ml) was added to it. This was quickly followed by the addition of N,O-ditosyl-L-homoserine diphenylmethyl ester (1.5 g) in acetone (10 ml). The mixture was stirred for 5 min, after which it was brought to pH 5 with dilute acetic acid. Subsequently, the solvent was removed under reduced pressure and the residue was extracted with ethyl acetate, giving a syrup. The latter was taken up in benzene and chromatographed on a column of silica gel packed in the same solvent. Washing with benzene removed all the dibenzyl diselenide formed from excess benzylselenol during the isolation procedure. The product was eluted with benzene–ethyl acetate (95:5, v/v). Fractions containing the product, as tested by tlc, were combined. After removal of the solvent the resulting oil was crystallized from ether–petroleum ether–cyclohexane: yield 1.3 g (86%); mp 4°; $[\alpha]^{22}D$ +36.0° (*c* 1, chloroform); silica gel (S_{II}) R_f 0.76.

Anal. Calcd for $C_{31}H_{31}NO_4SSe$: C, 62.8; H, 5.24; N, 2.36. Found: C, 63.0; H, 5.36; N, 2.21.

The chromatographically pure, syrupy racemic compound **3b** was prepared similarly in 95% yield.

Anal. Found: C, 62.9; H, 5.31; N, 2.28.

N-Tosyl-Se-benzyl-L-selenohomocysteine Dicyclohexylammonium Salt (4a).—Compound **3a** (0.5 g) was dissolved in dry nitromethane (6 ml) containing 0.9 *N* HCl. After the solution had been left at room temperature for a period of 1 hr, the solvent was removed. The residue was triturated with dilute sodium bicarbonate solution and the insoluble portion was filtered off. From the filtrate the N-protected amino acid was extracted with ethyl acetate after acidification with dilute hydrochloric acid. The ethyl acetate solution was concentrated and the acid was isolated as its dicyclohexylammonium salt (0.4 g, 78%). On recrystallization from methanol–ether the melting point remained unchanged, mp 176–178°, $[\alpha]^{22}D$ +42.4° (*c* 1, methanol).

Anal. Calcd for $C_{30}H_{44}N_2O_4SSe$: C, 59.3; H, 7.25; N, 4.61. Found: C, 59.1; H, 7.07; N, 4.42.

The corresponding data for the racemic derivative **4b** follow: yield 80%, mp 184–186°.

Anal. Found: C, 59.1; H, 7.07; N, 4.42.

In the course of the work-up of the deesterification reaction, **3b**, **N-tosyl-Se-benzyl-DL-selenohomocysteine**, was isolated as a crystalline product, mp 113–115°.

Anal. Calcd for $C_{18}H_{21}NO_4SSe$: C, 50.7; H, 4.93; N, 3.29. Found: C, 51.1; H, 4.86; N, 3.25.

N-Carbobenzoxy-L-homoserine *p*-Nitrobenzyl Ester (5).—L-Homoserine (5 g) and sodium bicarbonate (11.1 g) were dissolved together in water (160 ml), and to the well-stirred solution carbobenzoxy chloride (7.6 ml) was added over a period of 1 hr at room temperature. After stirring for an additional 4 hr the solution was washed repeatedly with ether and the aqueous phase was evaporated to dryness under vacuum. Sodium N-carbobenzoxy-L-homoserinate was extracted from the dry residue with DMF and isolated upon removal of the solvent under vacuum as a hygroscopic powder. This was dissolved in DMF (35 ml) and acetone (70 ml), and after *p*-nitrobenzyl tosylate (15 g) had been added the mixture was gently refluxed over a water bath for 30 min. The fluffy precipitate of sodium tosylate was filtered off and the solution was concentrated under reduced pressure. On diluting the resulting syrup with water an oil separated, which was taken up in ethyl acetate. The organic layer was separated, washed with water, dried over anhydrous sodium sulfate, and concentrated. On adding an excess of ether and cooling overnight, crystals of the *p*-nitrobenzyl ester separated and were recrystallized from ethyl acetate–ether: yield 9.6 g (64%); mp 85°; $[\alpha]^{22}D$ −19.8° (*c* 2, methanol); silica gel (S_{III}) R_f 0.21.

Anal. Calcd for $C_{19}H_{20}N_2O_7$: C, 58.8; H, 5.15; N, 7.22. Found: C, 59.01; H, 5.14; N, 7.06.

(37) G. Zdansky, *Ark. Kemi*, **29**, 449 (1968).

(38) F. Kerdel-Vegas, F. Wagner, P. B. Russell, N. H. Grant, H. E. Alburn, D. E. Clark, and J. A. Miller, *Nature*, **205**, 1185 (1965).

(39) All melting points were determined with a Thomas–Hoover capillary melting point apparatus and are corrected. Optical rotations were determined with a Carl Zeiss photoelectric precision polarimeter to ± 0.005°. Elementary analyses were performed by Galbraith Laboratories, Knoxville, Tenn. The hydrogen selenide was purchased from Matheson Coleman and Bell. The following solvent systems were used for thin layer chromatography: benzene–ethyl acetate (1:2, v/v) (S_I); benzene–ethyl acetate (4:1) (S_{II}); benzene–ethyl acetate (2:1) (S_{III}); benzene–ethyl acetate–methanol (5:5:1) (S_{IV}); benzene–ethyl acetate–acetic acid (10:5:1) (S_V); and 1-butanol–water–acetic acid (4:1:1) (S_{VI}). 1-Butanol–water–acetic acid (5:5:1, upper phase) (S_{VII}) was used for paper chromatography. In the case of protected amino acids and peptides, thin layer chromatograms were run on silica gel plates and the plates were visualized by the procedure of Zahn and Rexroth.[40] Free amino acids were chromatographed on cellulose plates or Whatman #1 paper and the chromatograms were developed with ninhydrin reagent. The free amino acids were also tested for purity by chromatography on a Beckman–Spinco Model 120C amino acid analyzer according to the procedure described earlier.[41] The selenium-containing amino acids are stored at 4° and with the exclusion of light.

(40) H. Zahn and E. Rexroth, *Z. Anal. Chem.*, **148**, 181 (1955).

(41) R. Walter, D. H. Schlesinger, and I. L. Schwartz, *Anal. Biochem.*, **27**, 231 (1969).

N-Carbobenzoxy-O-tosyl-L-homoserine *p*-Nitrobenzyl Ester (6).—Compound **5** (8 g) was dissolved in dry pyridine (40 ml) at −10°, and tosyl chloride (5.4 g) was added with stirring. The reaction was allowed to continue for 3 hr at −10°, after which the mixture was poured over crushed ice. On cooling a semisolid mass was separated overnight which, after decantation of the supernatant liquid, was dissolved in ethyl acetate. The solution was washed with water, dried over anhydrous sodium sulfate, and concentrated. On adding ether and cooling, the product precipitated as crystals in 81% yield. For elemental analysis a sample was recrystallized from ethyl acetate–ether: mp 114–115°; $[\alpha]^{23}D$ −7.8° (*c* 2, DMF); silica gel (S_{III}) R_f 0.61.

Anal. Calcd for $C_{26}H_{26}N_2O_9S$: C, 57.6; H, 4.80; N, 5.17. Found: C, 57.8; H, 4.87; N, 5.24.

N-Carbobenzoxy-Se-benzyl-L-selenohomocysteine *p*-Nitrobenzyl Ester (7).—To a solution of benzylselenol (2 g) dissolved in DMF (10 ml), water (3 ml) containing NaOH (0.4 g) was added. To this mixture a solution of **6** (5.4 g) dissolved in acetone (40 ml) was quickly added. The product was worked up in the same manner as **3**, yielding 4.5 g (83%). Crystallization from ether–ethanol afforded pure product in fine needles: mp 65–66°; $[\alpha]^{21}D$ −18.4° (*c* 1, DMF); silica gel (S_{II}) R_f 0.74.

Anal. Calcd for $C_{26}H_{26}N_2O_6Se$: C, 57.7; H, 4.80; N, 5.17. Found: C, 57.9; H, 4.64; N, 4.95.

N-Carbobenzoxy-L-alanine *p*-Nitrobenzyl Ester.—N-Carbobenzoxy-L-alanine (4.46 g) and sodium methoxide (1.08 g) were dissolved in methanol (*ca.* 50 ml) and the solvent was then removed under reduced pressure. The resulting sodium N-carbobenzoxy-L-alaninate was dissolved in DMF–acetone (1:2, 22 ml), and *p*-nitrobenzyl tosylate (6.14 g) was added. The reaction mixture was gently refluxed for 30 min, after which the precipitated sodium tosylate was filtered off and the filtrate was concentrated to a syrup under vacuum. Upon addition of water (200 ml) the syrupy material crystallized readily. The crystals were collected, washed with water, and recrystallized from ethyl acetate–ether–cyclohexane: yield 4.5 g (60%); mp 100–101° (lit.[42] mp 99–100°); $[\alpha]^{22}D$ −12.9° (*c* 2, DMF); silica gel (S_{II}) R_f 0.66.

N-Carbobenzoxy-L-alanine.—N-Carbobenzoxy-L-alanine *p*-nitrobenzyl ester (1.22 g) was dissolved in dioxane (19 ml) and treated with 0.5 *N* NaOH (9 ml) added over a period of 30 min. Stirring was continued for an additional 15 min, after which the pH of the solution was brought to 7 with 1 *N* HCl. The solvent was removed under reduced pressure and the residue was shaken with ether–water to remove the *p*-nitrobenzyl alcohol. The aqueous phase was separated, washed thrice with ether, acidified to Congo red, and then extracted with ethyl acetate. The ethyl acetate solution was washed with water and dried over sodium sulfate, and the product was subsequently precipitated by the addition of petroleum ether. Recrystallization from ethyl acetate–petroleum ether afforded 0.7 g (97%) of product, mp 85–86°, $[\alpha]^{22}D$ −14.3° (*c* 2, acetic acid) [*cf.* N-carbobenzoxy-L-alanine used as a starting material in the previous experiment, mp 84–85°, $[\alpha]^{22}D$ −14.2° (*c* 2, acetic acid)].

N-Carbobenzoxy-Se-benzyl-L-selenohomocysteine (8).—Compound **7** (2 g) was dissolved in dioxane (20 ml) at room temperature and 9 ml of 0.5 *N* aqueous NaOH was added to the solution over a period of 30 min. Stirring was continued for an additional 20 min, after which the pH was lowered to 7 with 1 *N* HCl and the solution was concentrated under reduced pressure. After the dioxane had been removed, the aqueous solution was washed with ethyl acetate. The pH was lowered to 2 and the product was extracted with ethyl acetate. Crystallization from benzene–cyclohexane gave 1.2 g (50%) of the compound: mp 93–94°; $[\alpha]^{22}D$ −22.2° (*c* 1, DMF); silica gel (S_V) R_f 0.66.

Anal. Calcd for $C_{19}H_{21}NO_4Se$: C, 56.2; H, 5.17; N, 3.45. Found: C, 56.2; H, 5.28; N, 3.52.

Se-Benzyl-L-selenohomocysteine Hydrobromide (9).—Compound **8** (0.5 g) was allowed to react with 2 *N* HBr in glacial acetic acid for 1 hr. On adding a large excess of ether an oil separated which soon crystallized. The crystals were washed with ether by decantation and recrystallized from methanol–ether: yield 0.4 g (92%); mp 152–154°; $[\alpha]^{22}D$ +9.74° (*c* 1, methanol).

Anal. Calcd for $C_{11}H_{15}NO_2Se \cdot HBr$: C, 37.4; H, 4.53; N, 3.97. Found: C, 37.3; H, 4.64; N, 3.95.

Se-Benzyl-L-selenohomocysteine (10).—The hydrobromide **9** (0.2 g) was suspended in water (30 ml) and the pH was adjusted to 5.5 with ammonium hydroxide. The mixture was thoroughly stirred and left for a few hours at 4°. The crystals which had formed were separated by filtration, washed with a small amount of cold water, and recrystallized from hot water: yield 0.15 g (97%); mp 238–240° dec; $[\alpha]^{21}D$ +23.2° (*c* 0.5, 2 *N* HCl) [lit.[27] mp 213–214°; $[\alpha]^{22}D$ +19.2° (*c* 0.51, 2 *N* HCl); $[\alpha]^{27}D$ +15.1° (*c* 2, 1 *N* HCl)[26]; $[\alpha]^{25}D$ +15.5° (*c* 1, 1 *N* HCl)];[28] cellulose (S_{VI}) R_f 0.77, paper (S_{VII}) R_f 0.7.

Anal. Calcd for $C_{11}H_{15}NO_2Se$: C, 48.5; H, 5.51; N, 5.15. Found: C, 48.4; H, 4.45; N, 5.15.

N-Carbobenzoxy-Se-benzyl-L-selenohomocysteine Hydrazide (11).—Compound **7** (0.4 g) was dissolved in methanol–DMF (2:1, 1.5 ml). Hydrazine hydrate (0.3 ml) was added and the reaction was allowed to proceed at room temperature for 18 hr. At the end of this period the reaction mixture was diluted with water (100 ml) and the precipitate thus formed was filtered and washed with cold water. The product was recrystallized from methanol–ether: yield 0.25 g (81%); mp 129–130°; $[\alpha]^{23}D$ −6.5° (*c* 1.1, DMF); silica gel (S_{IV}) R_f 0.45.

Anal. Calcd for $C_{19}H_{23}N_3O_3Se$: C, 54.3; H, 5.48; N, 10.0. Found: C, 54.2; H, 5.55; N, 9.80.

N-Carbobenzoxy-Se-benzyl-L-selenohomocysteinyl-L-phenylalanine Amide (12).—The hydrazide **11** (0.3 g) was dissolved in DMF (5 ml) and the soluion was cooled to −20°. Concentrated HCl (0.8 ml) followed by a precooled solution of sodium nitrite (0.06 g in 1 ml of water) were then added. The reaction was allowed to proceed for 3 min, after which the temperature was lowered to −40°. The solution was neutralized with triethylamine. A precooled solution of L-phenylalanine amide (0.15 g) in DMF (2 ml) was then added. Subsequently, the reaction mixture was allowed to warm from −40 to −5° and was allowed to remain at this temperature for 1 hr. Stirring was continued overnight at 4°. The solvent was then removed under reduced pressure and the resulting residue was washed well with water. After drying, the product was recrystallized from 95% ethanol: yield 0.2 g (51%); mp 174–176°; $[\alpha]^{22}D$ −29.5° (*c* 2, DMF); silica gel (S_{IV}) R_f 0.57.

Anal. Calcd for $C_{28}H_{31}N_3O_4Se$: C, 60.9; H, 5.62; N, 7.61. Found: C, 60.9; H, 5.71; N, 7.52.

Se-Benzyl-L-selenohomocysteine *p*-Nitrobenzyl Ester Hydrobromide (13).—Compound **7** (1 g) was decarbobenzoxylated with 2 *N* HBr (3 ml) in glacial acetic acid over a period of 1 hr. On adding an excess of ether an oil separated, which crystallized on scratching in the presence of a drop of methanol. Recrystallization from methanol–ether afforded the pure product: yield 0.65 g (72%); mp 116°; $[\alpha]^{22}D$ +10.4° (*c* 1, methanol).

Anal. Calcd for $C_{18}H_{20}N_2O_4Se \cdot HBr$: C, 44.3; H, 4.30; N, 5.74. Found: C, 44.0; H, 4.31; N, 5.76.

N-Carbobenzoxy-L-prolyl-Se-benzyl-L-selenohomocysteine Hydrazide.—The hydrobromide **13** (1.2 g) dissolved in methanol (20 ml) was passed through a column of Rexyn RG1(OH). On evaporating the solvent 1.0 g of a gummy residue was obtained. It was dissolved in dry methylene chloride (3 ml), and N-carbobenzoxy-L-proline *p*-nitrophenyl (0.92 g) ester was added. The mixture was stirred overnight at room temperature; then the solvent was removed and the resulting residue was chromatographed on a silica gel column packed in benzene. Fractions containing the dipeptide (eluted with benzene containing 20% ethyl acetate) were collected. On removing the solvent 1.4 g (89%) of an oily residue was obtained which resisted crystallization. Therefore the ester was converted into its hydrazide according to the procedure outlined for **11**. The product was recrystallized from methanol–ether: yield 0.9 g (79%); mp 139–140°; $[\alpha]^{22}D$ −37.2° (*c* 1, DMF); silica gel (S_{IV}) R_f 0.27.

Anal. Calcd for $C_{24}H_{30}N_4O_4Se$: C, 55.8; H, 5.80; N, 10.8. Found: C, 55.8; H, 5.75; N, 10.8.

N-Carbobenzoxy-L-prolyl-Se-benzyl-L-selenohomocysteinyl-L-phenylalanine Amide (14).—The hydrazide above (0.5 g) was converted into the azide and coupled with L-phenylalanine amide under the same experimental conditions as described for the preparation of **12**. After the reaction was completed, the solvent was removed under reduced pressure and the resulting residue was washed thoroughly with water. The product was recrystallized from hot methanol: yield 0.6 g (95%); mp 196–198°; $[\alpha]^{22}D$ −40.4° (*c* 2, DMF); silica gel (S_{IV}) R_f 0.47.

Anal. Calcd for $C_{33}H_{38}N_4O_5Se$: C, 61.1; H, 5.86; N, 8.63. Found: C, 60.9; H, 5.99; N, 8.56.

(42) V. G. Debabov and V. A. Shibnev, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 1031 (1962).

N-Carbobenzoxy-L-selenomethionine *p*-Nitrobenzyl Ester (15).—Sodium (0.065 g) was dissolved in ethanol (5 ml) in a three-necked flask equipped with two dropping funnels, a magnetic stirrer, an inlet for passing the gases through the solution, and an outlet connected to a trap containing a 10% solution of NaOH. Hydrogen selenide from a tank mixed with a slow stream of hydrogen was passed under exclusion of air through the solution of sodium ethoxide. When the formation of sodium hydrogen selenide was complete, the excess of hydrogen selenide was swept away with a fast current of hydrogen. The reaction vessel was then placed in an ice bath, the current of hydrogen was slowed down, and a solution of methyl iodide (0.43 g) in DMF (2 ml) was introduced. The reaction was allowed to proceed for 10 min, after which a solution of NaOH (0.104 g) in water (2 ml) was added. This was followed by the addition of **6** (1.084 g) in DMF (3 ml). After standing for 1 hr at room temperature, the mixture was poured into 150 ml of water and extracted three times with ethyl acetate. The combined ethyl acetate extracts were washed with water, dried over sodium sulfate, and evaporated to dryness. The resulting syrup, which contained dimethyl diselenide as the major impurity, was dissolved in benzene and chromatographed through a column of silica gel packed in benzene. After removal of the solvent from fractions containing the product, it was recrystallized from ether–ethanol: yield 0.6 g (66%); mp 56–57°; $[\alpha]^{22}D$ −18.2° (*c* 1, DMF); silica gel (S_{II}) R_f 0.54.

Anal. Calcd for $C_{20}H_{22}N_2O_6Se$: C, 51.6; H, 4.73; N, 6.02. Found: C, 51.5; H, 4.70; N, 5.93.

N-Carbobenzoxy-L-selenomethionine Dicyclohexylammonium Salt (16).—The ester **15** (0.75 g) was dissolved in dioxane (7 ml), and 0.5 *N* NaOH (3 ml) was added at room temperature over a period of 30 min with stirring. The reaction was allowed to continue for an additional 30 min, at the end of which the starting material had completely disappeared, as revealed by tlc. In a manner analogous to the isolation of **8**, N-carbobenzoxy-L-selenomethionine was obtained as a syrup, converted into its dicyclohexylammonium salt, and recrystallized from methanol–ether: yield 0.8 g (97%); mp 163–164°; $[\alpha]^{22}D$ +12.7° (*c* 1, DMF).

Anal. Calcd for $C_{25}H_{40}N_2O_4Se$: C, 58.7; H, 7.83; N, 5.48. Found: C, 58.8; H, 7.93; N, 5.47.

L-Selenomethionine (17).—The salt **16** (0.3 g) was shaken with 2 *N* H_2SO_4 (10 ml) and ethyl acetate (20 ml), and the organic layer was separated, washed once with 2 *N* H_2SO_4 and twice with water, and dried with anhydrous sodium sulfate. The residue obtained on removing the solvent was dried under vacuum over P_2O_5 overnight. It was then dissolved in dry acetic acid (0.3 ml) and β-mercaptoethanol (0.7 ml). To this mixture, 4 *N* HBr (1 ml) in glacial acetic acid was added. The reaction was allowed to proceed for 15 min, after which dry ether (100 ml) was added. An oil separated, which was washed repeatedly with dry ether and finally dried under vacuum over potassium hydroxide. The dried mass was dissolved in water (5 ml) and the pH was adjusted to 5.5 with ammonium hydroxide. The solution was then concentrated to near dryness and the residue was washed several times with ethanol and recrystallized once from aqueous acetone to give 0.057 g (50%) of the product: mp 266–268° dec; $[\alpha]^{22}D$ +21.6° (*c* 0.5, 2 *N* HCl) [lit.[27] mp 275° dec; $[\alpha]^{22}D$ +17.5° (*c* 0.5, 2 *N* HCl); $[\alpha]^{27}D$ +17.8° (*c* 1, 1 *N* HCl)[26]; $[\alpha]^{25}D$ +18.1° (*c* 1, 1 *N* HCl)[28]]; cellulose (S_{VI}) R_f 0.58, paper (S_{VII}) R_f 0.39.

Anal. Calcd for $C_5H_{11}NO_2Se$: C, 30.6; H, 5.65; N, 7.14. Found: C, 30.5; H, 5.66; N, 6.62.

N-Carbobenzoxy-L-selenoethionine *p*-Nitrobenzyl Ester (18).—The method of synthesis of **18** and purification was identical with that described for **15**. Recrystallization from 95% ethanol afforded 0.8 g (82%) of the product: mp 66°; $[\alpha]^{22}D$ −19.1° (*c* 1, DMF); silica gel (S_{II}) R_f 0.6.

Anal. Calcd for $C_{21}H_{24}N_2O_6Se$: C, 52.6; H, 5.01; N, 5.85. Found: C, 52.7; H, 5.10; N, 5.83.

N-Carbobenzoxy-L-selenoethionine Dicyclohexylammonium Salt (19).—As described for the corresponding selenomethionine derivative, the *p*-nitrobenzyl ester **18** (0.55 g) was deesterified, yielding 0.35 g (89%) of the free acid. The acid was best characterized as its dicyclohexylammonium salt, which on recrysallization from methanol–ether melted at 154–155°, $[\alpha]^{22}D$ +8.2° (*c* 1.5, DMF).

Anal. Calcd for $C_{26}H_{42}N_2O_4Se$: C, 59.4; H, 8.00; N, 5.33. Found: C, 59.3; H, 8.05; N, 5.17.

L-Selenoethionine (20).—The salt **19** (0.3 g) was converted into the free acid and subsequently decarbobenzoxylated in a manner similar to the experimental procedure described for **17**. The product was recrystallized from aqueous acetone, yielding 0.08 g (67%) of compound: mp 253–256° dec; $[\alpha]^{22}D$ +21.5° (*c* 0.5, 2 *N* HCl) [lit.[27] mp 235–250° dec; $[\alpha]^{22}D$ +15.9° (*c* 0.5, *N* HCl)]; cellulose (S_{VI}) R_f 0.71, paper (S_{VII}) R_f 0.49.

Anal. Calcd for $C_6H_{13}NO_2Se$: C, 34.3; H, 6.24; N, 6.67. Found: C, 34.5; H, 6.06; N, 6.42.

N-Carbobenzoxyselenyl(β-diphenylmethoxycarbonyl-β-N′-carbobenzoxy-L-amino)ethyl-L-selenohomocysteine *p*-Nitrobenzyl Ester (21).—Sodium hydrogen selenide was prepared from sodium (0.048 g) in ethanol (5 ml) in an analogous manner as described for the preparation of **15**. Subsequently, N-carbobenzoxy-O-tosyl-L-serine diphenylmethyl ester[2b] (1.118 g) dissolved in DMF (3 ml) was introduced into the reaction vessel. After 1 hr NaOH (0.084 g) dissolved in H_2O (2 ml) was added followed by NaOH (1.084 g) in DMF (3 ml) 5 min later. The reaction flask was stored with exclusion of air and light for 3 days. For the isolation and purification of the product the same method was followed as for **15**. Two recrystallizations from 95% ethanol afforded 0.9 g (53%) of **21**, which changes its crystal contours at 58°, $[\alpha]^{21}D$ −26.3° (*c* 1, DMF), silica gel (S_{II}) R_f 0.5.

Anal. Calcd for $C_{43}H_{41}N_3O_{10}Se$: C, 61.6; H, 4.89; N, 5.01. Found: C, 61.7; H, 4.96; N, 4.89.

N,N′-Dicarbobenzoxy-L-selenocystathionine Di(dicyclohexylammonium) Salt (22).—Compound **21** (0.5 g) was saponified as described for the preparation of **8**. The acid was then converted into the dicyclohexylammonium salt, 0.3 g (56%), which on recrystallization from methanol–ether melted at 202–204°, $[\alpha]^{21}D$ +19.6° (*c* 0.5, DMF).

Anal. Calcd for $C_{47}H_{72}O_8N_4Se$: C, 62.7; H, 8.01; N, 6.23. Found: C, 63.0; H, 8.13; N, 6.34.

L-Selenocystathionine (23).—The salt **22** (0.3 g) was treated with 2 *N* H_2SO_4 and the free acid was obtained in the manner as described for **17**. The free acid was treated with 2 *N* HBr (2 ml) in glacial acetic acid for 40 min, and by diluting the reaction mixture with excess of dry ether, the hyrobromide was obtained as a gummy solid. It was dried under vacuum over KOH. The solid was then dissolved in 3 ml of water and the pH adjusted to 5.5 with ammonium hydroxide. On concentrating and cooling, L-selenocystathionine crystallized as fine needles which were collected by filtration, washed with ethanol, and recrystallized from water: yield 0.06 g (67%); mp 256–258° dec; $[\alpha]^{22}D$ +35.8° (*c* 1, 1 *N* HCl) [lit.[38] $[\alpha]D$ +36.5° (*c* 1, 1 *N* HCl); $[\alpha]^{25}D$ +36.1° (*c* 1, 1 *N* HCl)[37]], cellulose (S_{VI}) 0.07, paper (S_{VII}) 0.05.

Anal. Calcd for $C_7H_{14}N_2O_4Se$: C, 31.2; H, 5.25; N, 10.4. Found: C, 31.2; H, 5.35; N, 10.3.

Registry No.—**1a**, 23809-71-4; **1b**, 23809-72-5; **2a**, 23796-86-3; **2b**, 23809-73-6; **3a**, 23809-74-7; **3b**, 23809-75-8; **4a**, 23809-76-9; **4b**, 23796-87-4; **5**, 23809-78-1; **6**, 23809-79-2; **7**, 23809-80-5; **8**, 23809-82-7; **9**, 23809-83-8; **10**, 19635-25-7; **11**, 23809-85-0; **12**, 23796-88-5; **13**, 23809-86-1; **14**, 23809-88-3; **15**, 23796-89-6; **16**, 23809-89-4; **17**, 3211-76-5; **18**, 23796-90-9; **19**, 23809-91-8; **20**, 20999-05-7; **21**, 23809-93-0; **22**, 23809-94-1; **23**, 23809-95-2; N-tosyl-Se-benzyl-DL-selenohomocysteine, 23809-77-0; N-carbobenzoxy-L-alanine, 1142-20-7; N-carbobenzoxy-L-prolyl-Se-benzyl-L-selenohomocysteine hydrazide, 23809-87-2.

Acknowledgments.—Dr. S. Hsieh was involved in the exploratory experiments of this work and the authors thank him for his contribution. They are also grateful for the technical assistance rendered by Mrs. Bella White and Mr. Duke Kasprisin.