either 1,3- (38) or 2,3-diphenylindene (39) in the presence of oxygen in good yield.

Direct Irradiation of 1,3-Diphenyl-2-methylindenol (41). To a solution containing 407 mg of 3-phenyl-2-methylindenone[48] in 100 mL of ether at 0 °C was added 1.2 mL of 1.6 M phenylmagnesium bromide in ether. The mixture was allowed to stir for 6 h and then was quenched by the addition of a saturated ammonium chloride solution. The ether layer was washed with water and dried over anhydrous magnesium sulfate. Removal of the ether left behind 550 mg of a white foam whose spectral properties were consistent with 1,3-diphenyl-2-methylindenol (41); IR (neat) 3450, 3070, 3030, 1600, 1495, 1450, 1340, 1190, 1105, 1055, 1030, 950, 915, 785, 765 cm^{-1}; UV (95% ethanol) 280 nm (ϵ 4700), 227 (30600); NMR ($CDCl_3$, 90 MHz) δ 1.70 (s, 3 H), 2.28 (br s, 1 H), 7.0–7.53 (m, 14 H); mass spectrum, *m/e* 298 (M^+), 283, 221, 220, 189, 165, 115, 105.

Anal. Calcd for $C_{22}H_{18}O$: C, 88.56; H, 6.08. Found: C, 88.54; H, 6.11.

A solution containing 300 mg of indenol 41 in 250 mL of benzene was irradiated for 30 min, using a 450-W Hanovia medium-pressure mercury arc lamp equipped with a Vycor filter sleeve. The solvent was removed under reduced pressure and the residual oil was subjected to medium-pressure chromatography, using a silica gel column and eluting with hexane. The first fraction contained 103 mg of 1,3-diphenyl-2-methylindene (43); NMR ($CDCl_3$, 90 MHz) δ 1.86 (s, 3 H), 4.39 (br s, 1 H), 6.88–7.47 (m, 14 H). The structure of this material was verified by comparison with an authentic sample.[63] The second fraction isolated from the column contained 60 mg of a white solid, mp 105–106 °C, whose structure was assigned as 1-methyl-2,3-diphenylindene (44) by comparison with an authentic sample;[63] NMR ($CDCl_3$, 90 MHz) δ 1.08 (d, 3 H, J = 7.0 Hz), 4.02 (q, 1 H, J = 7.0 Hz), 7.05–7.38 (m, 14 H). The third fraction isolated from the column (30 mg) was a white crystalline solid, mp 90–91 °C, whose structure was assigned as 1,2-diphenyl-3-methylindene (45); NMR ($CDCl_3$, 90 MHz) δ 2.32 (d, 3 H, J = 2.0 Hz), 4.91 (q, 1 H, J = 2.0 Hz), 6.90–7.40 (m, 14 H). The structure of this material was established by comparison with an authentic sample preared according to the procedure of Koelsch and Johnson.[50]

The last material isolated from the column contained 94 mg of a white solid, mp 138–139 °C, whose structure was assigned as phenanthrene 46 on the basis of its spectral properties: IR (KBr) 1535, 1500, 1480, 1440, 1340, 1280, 1120, 940, 780, 730 cm^{-1}; UV (95% ethanol) 336 nm (ϵ 7800), 320 (7800), 313 (5300), 308 (5600), 278 (8500), 270 (12800), 263 (14000), 250 (14000), 243 (18800); NMR ($CDCl_3$, 90 MHz) δ 1.60 (d, 3 H, J = 6.5 Hz), 4.23 (q, 1 H, J = 6.5 Hz), 7.13–8.90 (m, 12 H).

Anal. Calcd for $C_{22}H_{16}$: C, 94.25; H, 5.75. Found: C, 94.18; H, 5.56.

This same material was also formed from the irradiation of either 1,3-diphenyl-2-methyl- (43) or 1-methyl-2,3-diphenylindene (44) in the presence of oxygen in good yield.

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Registry No. 4, 74272-43-8; 5, 42842-58-0; 6, 58310-20-6; 7, 36230-99-6; 8, 62907-55-5; 9, 26465-84-9; 10, 76773-25-6; 11, 76773-26-7; 12, 65086-15-9; 13, 65086-14-8; 14, 76773-27-8; 15, 76773-28-9; 16, 31366-37-7; 17, 22360-63-0; 18, 37634-53-0; 19, 3661-63-0; 20, 10425-96-4; 27, 76773-44-9; 28, 76773-29-0; 31, 76773-30-3; 32, 76773-31-4; 33, 76773-32-5; 34, 76773-33-6; 35, 76773-34-7; 36, 76773-35-8; 38, 4467-88-3; 39, 5324-00-5; 40, 201-65-0; 41, 76773-36-9; 43, 51310-26-0; 44, 51310-25-9; 45, 62747-73-7; 46, 76773-37-0; 2-methyl-3-phenylindanone, 52957-74-1; thioxanthen-9-one, 492-22-8; xanthone, 90-47-1; 3-methyl-3-phenylindanone, 26466-19-3; 7,7a-dihydro-7a-methyl-7-phenyl-2a-(phenylmethyl)spiro[indeno[2,1-*b*]oxete-2(2a*H*),9′-[9*H*]thioxanthene], 76773-38-1; 3-phenylindanone, 16618-72-7; 2-benzyl-3-phenylindanone, 76773-39-2; 3-methyl-3-phenyl-1-indanol, 76773-40-5; 3-phenyl-2-methylindanol, 65426-37-1; 1-deuterio-2-methyl-3-phenylindanol, 76773-41-6; 1-deuterio-1-methyl-3-phenylindene, 76773-42-7; 2-phenyl-3-methylindanol, 65451-65-2; 2-phenyl-1-indanone, 16619-12-8; 1-deuterio-1-methyl-2-phenylindene, 76773-43-8; 2-phenyl-1,3-indandione, 83-12-5; 2-methyl-2-phenyl-1,3-indandione, 2136-69-8; 2-methyl-2-phenyl-1,3-indandiol, 36613-96-4; 3-phenylindenone, 41916-15-8; 3-phenyl-2-methylindenone, 13304-52-4; methyl bromide, 74-83-9; phenyl bromide, 108-86-1; benzyl chloride, 100-44-7; benzyl bromide, 100-39-0.

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tert-Butyl Group as Thiol Protection in Peptide Synthesis[1]

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S-tert-Butylcysteine was obtained by a new method. A number of its N-protected derivatives and esters were synthesized. Syntheses of several peptides containing *tert*-butyl and acetamidomethyl or benzyl thioethers of cysteine were carried out. The *tert*-butyl group was removed from the thiol group of peptides by treatment with (2-nitrophenyl)sulfenyl chloride (NpsCl). The *S*-(2-nitrophenyl)sulfenyl derivatives so obtained were converted either into cysteine by reduction or into cystine derivatives by disproportionation. Owing to the mild deprotection conditions and the great stability of the *S-tert*-butyl group, the other protecting groups, particularly those of the thiols, could be easily removed from a variety of combinations.

Though about 70 protecting groups for the thiol group have hitherto been described,[2] the problem of cysteine protection has still remained unsolved. It is essential, particularly under conditions of peptide synthesis, to find a suitable protecting group which is very stable but easy to remove in the last step, which is only feasible by using specific reagents. The *S*-benzyl group, formerly a common protection in complex peptide syntheses, is practically no longer used[3] and has been replaced by the *S*-acetamidomethyl group.[4]

As far back as 1962, one of us was the first to suggest using *tert*-butyl thioether as a protecting group for cysteine.[5] A method was then reported for a direct synthesis

(1) Taken from the Ph.D. Thesis of J.J.P.; presented at the 15th European Peptide Symposium, Gdańsk, Poland, Sept 1978.

(2) See, for example, "Methoden der Organischen Chemie (Houben-Weyl)", Georg Thieme Verlag, Stuttgart, 1974, Vol. 15/1.

(3) L. Zervas, "Proceedings of 8th European Peptide Symposium, Noordwijk, 1966", North-Holland Publishing Co., Amsterdam, 1967, p 112.

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0022-3263/81/1946-1868$01.25/0

Table I. *S-tert*-Butyl-L-cysteine Derivatives (R-Cys(*t*-Bu)-OR')

compd no.	R	R'	mp, °C	yield, %
2a	CHO	H	149-150	81
2b	Pht	H	154	78
2c	Tos	H	168-170	85
2d	Boc	H	89-90	78
2e	Nps	H	159[a]	78
2f	Z	H	162-163[a]	84
3a	H	Me	120[b]	82
3b	H	Et	141-142[b]	87
3c	H	*t*-Bu	202-203[b]	41
3d	H	Bzl	166-168[c]	100
4	Tos	Me	87-88	80
5	Tos	$NHNH_2$	149-151	90
6	Z	Np	64-65	69

[a] Dicyclohexylamine salt. [b] Hydrochloride. [c] *p*-Toluenesulfonate.

of *S-tert*-butyl-L-cysteine and several of its derivatives and peptides. Callahan[6] had also obtained *S-tert*-butylcysteine derivatives. However, the *tert*-butyl group could not further be used as cysteine thiol protection in peptide syntheses because electrophilic reagents, e.g., perchloric acid and hydrogen chloride, bromide, or iodide, tested in various solvents were unable to remove it.[6] Numerous attempts to remove it with mercurium salts have to date been presented, but full experimental data have never been published either in the case of *S-tert*-butylcysteine standards[7,8] or in the case of its peptides.[8]

Quantitative removal has been accomplished on a model amino acid by the use of liquid hydrogen fluoride[9] under rather drastic conditions, but this has never been applied to peptides.

It is only after we had developed efficient and convenient conditions for an almost quantitative removal of the *S-tert*-butyl protection with (2-nitrophenyl)sulfenyl chloride (NpsCl)[10] that it appeared advisable to make a thorough study of most problems related to that protection. These problems are discussed in the present work, and the usefulness of the tested group in cysteine peptide synthesis is demonstrated.

First we present a simplified, pressureless method for synthesis of the basic substrate, i.e., *S-tert*-butyl-L-cysteine hydrochloride (**1**). It involves refluxing of cysteine with a mixture of hydrochloric acid and *tert*-butyl alcohol to obtain in nearly quantitative yield a product retaining its full optical purity. Other authors[8,11] have obtained lower yields under different conditions.

We subsequently obtained some of the most common esters **3**, *N*-acyl derivatives **2**, and the hydrazide **5** which can be used in azide synthesis. We followed typical procedures and employed **1** as a substrate. Syntheses of *N*-(2-nitrophenyl)sulfenyl derivatives **2e** should always be conducted at a properly high pH, in order to prevent cleavage of the *tert*-butyl group with the NpsCl formed in acidic medium. The fact that these conditions had not been complied with was probably the reason why attempts to obtain chemically similar *N*-[(2-nitrophenyl)-sulfenyl]-*S*-(acetamidomethyl)cysteine had failed.[12] Some data for *S-tert*-butyl-L-cysteine derivatives are given in Table I.

Table II. *S*-Nps Derivatives

no.	compd	yield, %	mp, °C
12	CHO-Cys(Nps)-Phe	100	184
13	CHO-Cys(Nps)-Phe-OMe	100	128-130
16	Z-Cys(Nps)-Cys(Bzl)-OBzl	96	152-153
19	HCl·Cys(Nps)-Cys(Nps)-OMe	92	182-183

Cysteine thiol protection is closely connected with the problem of racemization. But the racemization test[10] has shown that *S-tert*-butylcysteine derivatives **6** racemize more slowly than do *S*-benzyl and *S*-acetamidomethyl derivatives. This may be due to the positive inductive effect of the *tert*-butyl group (cf. ref 13) which is unusual among the thiol protective groups.

As it was mentioned earlier, the use of *S-tert*-butylcysteine derivatives was limited by the difficulty of removing the protective group. The splitting reagent has been chosen on the basis of the known reaction of sulfenyl chlorides with thioethers.[14-16] That reaction, which has an S_E2 mechanism, occurs, according to Moore,[14] in polar solvents, and the place of thioether bond cleavage is dictated by the greater stability of the formed carbocation.[16] We conducted our experiments on models and found that a slight excess of NpsCl in acetic acid leads to a nearly quantitative yield of *S*-Nps–Cys derivatives.[10] Now we have found equimolar amounts of splitting reagent to be sufficient. The possibility of removing the *tert*-butyl thiol protective group permitted us to test this group in the synthesis of cysteine peptides. For this purpose we obtained the following *S-tert*-butylcysteine peptides: CHO–Cys(*t*-Bu)–Phe–OMe (**7**), Z–Cys(*t*-Bu)–Cys(Bzl)–OBzl (**8**), Boc–Cys(*t*-Bu)–Cys(Acm)–OMe (**9**), and Nps–Cys(*t*-Bu)–Phe–O-*t*-Bu (**10**).

The treatment of *tert*-butyl thioethers with NpsCl under standard conditions (see the general procedure in the Experimental Section) resulted in the cleavage of the thioethers, and well crystallizing yellow *S*-Nps derivatives were thus obtained. The reaction was accompanied by the simultaneous removal of the *S*-acetamidomethyl group[17] (Table II). It must be emphasized that, as the large peptides must, as usual, be purified in the last synthesis stage, the *S*-Nps derivatives can very conveniently be isolated by gel chromatography. The counter-current isolation of the *S*-Nps peptide was described previously.[18] *S*-Nps derivatives and peptides, including Nps–glutathione and Nps–ribonuclease, were earlier obtained either from thiol compounds[19,20] or from *S*-acetamidomethyl derivatives.[17]

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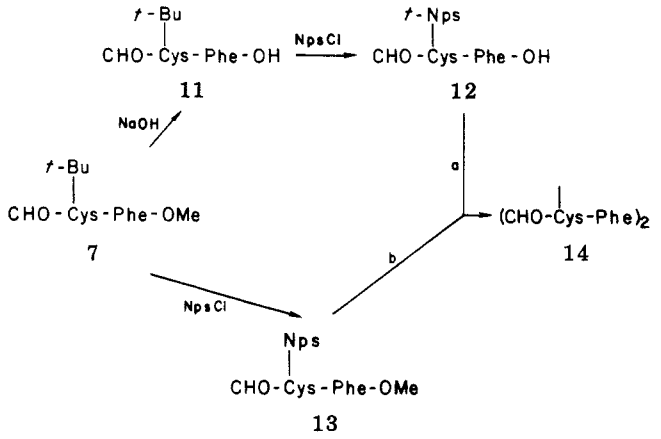
Scheme I



The last step, i.e., transformation of *S*-Nps derivatives into cysteine derivatives, does not require elaboration because, as reported earlier, *S*-Nps derivatives can easily be converted into thiols by treatment with either $NaBH_4$ or mercaptoethanol or thioglycolic acid.[20] We employed these methods followed by oxidation to obtain the cystine peptides.

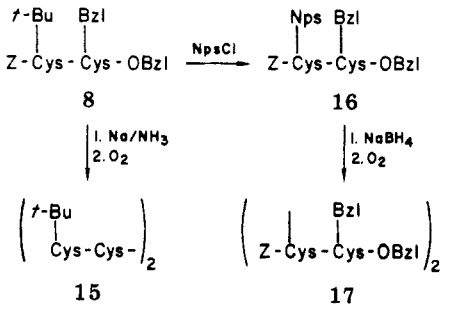
But we also found another method for such a transformation: *S*-Nps derivatives, as unsymmetrical disulfides, can be "symmetrized" to cystine derivatives and bis(2-nitrophenyl) disulfide in the presence of catalytic amounts of mercaptan at a pH value slightly exceeding 7 (see **14**, Scheme I).

The next problem studied by us was selectivity of the deprotection processes. In first attempts to remove it, the *S*-*tert*-butyl group showed that it was very resistant to acidolysis.[6] Callahan had also found that the protecting group was unaffected by hydrazine.[6] In the series of reactions described below, we found that the *S*-*tert*-butyl group was stable during alkaline hydrolysis of the ester **7** and that the *tert*-butyl thioether cleaved while both the methyl ester and the *N*-formyl group were unaffected. Moreover, simultaneous hydrolysis of the ester group and "symmetrization" of the forming salt to the cystine derivative are possible (**14b**).

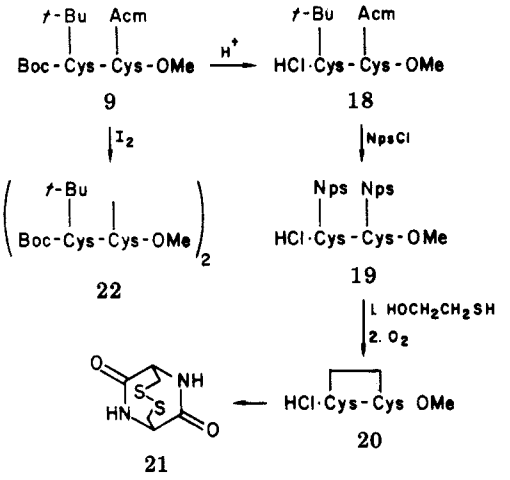
In order to investigate whether selective removal of thiol protecting groups in the presence of the *S*-*tert*-butyl group is possible, we used cysteinylcysteine peptides with two various thiol protecting groups in the molecule (**8** and **9**). This finding was of particular interest since it explains the universality of the *tert*-butyl protecting group and its usefulness in the syntheses of peptides containing more than one disulfide bridge. First we tried to remove the *S*-Bzl group in the presence of the *S*-*tert*-butyl group, and the inverse reaction was tried on the model peptide **8**. Reduction with sodium in liquid ammonia led, of course, to the removal of the *S*-benzyl and carbobenzoxyl groups and to cleavage of the benzyl ester, but the *tert*-butyl thioether remained unaffected, and after oxidation peptide **15** was obtained (Scheme II). On the other hand, treatment with NpsCl permitted us to obtain very good yields of *S*-benzyl-*S*-Nps peptide **16** which was reduced with $NaBH_4$ to thiol and then oxidized to **17**. So, the two protecting groups can be removed selectively.

We then examined a peptide containing *S*-acetoamidomethyl and *S*-*tert*-butyl groups. Their cleavage mechanisms are similar, and a reaction with NpsCl could be expected to bring about simultaneous removal of both protecting groups. Actually, treatment with 2 equiv of NpsCl led to the bis[(2-nitrophenyl)sulfenyl] derivative **19** (Scheme III). The compound was reduced with mercaptoethanol, oxidized to the ester **20**, and then cyclized to "cyclo-L-cystine" **21** according to Kamber.[21] As the *S*-*tert*-butyl group had been found stable in the presence of iodide, one could expect a successful selective removal of the *S*-acetamidomethyl group with that reagent.[21] Thus the iodolysis of **9** did afford the peptide **22** with an unaffected *S*-*tert*-butyl group. This gives a good opportunity for the synthesis of peptides with four cysteine residues.

Scheme II



Scheme III



The last reaction examined was acidolytic cleavage of the *N*-Nps group of the peptide **10** and simultaneous removal of the thiol protecting group with the NpsCl formed during the reaction to give *S*-Nps peptide **23** (eq 1). The

$$\underset{\mathbf{10}}{\text{Nps–Cys}(t\text{-Bu})\text{–Phe–O-}t\text{-Bu}} \xrightarrow{\text{HCl}} \underset{\mathbf{23}}{\text{HCl·Cys(Nps)–Phe–O-}t\text{-Bu}} \quad (1)$$

structure of the product, which was a *tert*-butyl ester, proves that the reaction proceeded under mild conditions. Selective removal of the *N*-Nps group without removal of the *tert*-butyl ester has previously been reported.[22] The facility with which the *S*-*tert*-butyl protecting group can be obtained and selectively removed, thus offering good tactic possibilities, the fact that it only causes a relatively small degree of racemization, and the fact that its crystalline derivatives can easily be handled are all qualities indicative of its usefulness in peptide synthesis.

Experimental Section

Melting points are uncorrected. TLC plates were prepared by using Merck silica gel G. The chromatograms were developed with the following solvent systems: (1) butanol–acetic acid–water

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(4:2:1), (2) chloroform–acetone–acetic acid (7:2:1), (3) benzene–acetone (3:1). ^{1}H NMR spectra were recorded on a Tesla BS-487 80-MHz apparatus with hexamethyldisiloxane (HMDSO) as a standard, and elemental analyses were performed on a Carlo Erba 1106 analyzer.

***S*-*tert*-Butyl-L-cysteine Hydrochloride (1).** A solution of L-cysteine hydrochloride (175.6 g, 1 mol) in a mixture of 450 mL of 2 N hydrochloric acid and 123 mL (97 g, 1.3 mol) of *tert*-butyl alcohol was refluxed under a long condenser for 10–12 h. Some isobutene was evolved. The solution was concentrated under reduced pressure, and the crystalline product was filtered off and washed with dry acetone: yield 209 g (90%); mp 198–200 °C. Recrystallization from 4 N hydrochloric acid gave chromatographically pure material: mp 204 °C; $[\alpha]^{20}_D$ +6.35° (*c* 2, 5 N HCl); R_f1 0.5; NMR (Me_2SO-d_6) δ 1.4 (s, 9, *t*-Bu), 3.4 (d, 2, *S*-CH_2), 4.2 (m, 1, CH) [lit.[5b] mp 203–204 °C; $[\alpha]^{20}_D$ +5.04° (*c* 2.11, 5 N HCl)].

***N*-Formyl-*S*-*tert*-butyl-L-cysteine (2a).** To a solution of 21.4 g (0.1 mol) of 1 in 200 mL of 97% HCOOH was added 100 g (ca. 0.12 mol) of CH_3COONa. The solution was cooled to 0 °C, and 70 mL of acetic anhydride was added during 45 min. The solution was stirred for 1 h, and part of the solvent was evaporated. Cold water was added to precipitate the product. A 16.5-g sample (81% yield) of crystals was obtained: mp 143–146 °C; after recrystallization from MeOH–water, mp 149–150 °C; R_f2 0.55; $[\alpha]^{20}_D$ +39° (*c* 2, MeOH); NMR (Me_2SO-d_6) δ 1.4 (s, 9, *t*-Bu), 3.2 (d, 2, *S*-CH_2), 8.8 (d, 1, CHO).

Anal. Calcd for $C_8H_{15}NO_3S$: C, 46.80; H, 7.37; N, 6.82. Found: C, 46.91; H, 7.23; N, 6.97.

***N*-Phthalyl-*S*-*tert*-butyl-L-cysteine (2b).** To a solution of 21.4 g of 1 in 200 mL of water were added 57.5 g (0.2 mol) of Na_2CO_3 and 22.5 g of *N*-(carboethoxy)phthalimide.[23] After being stirred for 20 min, the solution was acidified with 6 N hydrochloric acid and an oil precipitated. The crystals were formed after 1 day: 24.1 g (78% yield); mp 151–153 °C. After recrystallization from diethyl ether–petroleum ether: mp 154 °C; R_f2 0.8, R_f3 0.45; NMR ($CDCl_3$) δ 1.2 (s, 9, *t*-Bu), 3.3 (d, 2, *S*-CH_2), 7.6–7.9 (m, 4, C_6H_4), 10.6 (s, 1, COOH).

Anal. Calcd for $C_{15}H_{17}NO_4S$: C, 58.61; H, 5.58; N, 4.56. Found: C, 58.79; H, 5.48; N, 4.28.

***N*-Tosyl-*S*-*tert*-butyl-L-cysteine (2c).** A 24.1-g (0.1 mol) sample of 1 was dissolved in 380 mL of 1 N NaOH, and 32 g (ca. 0.17 mol) of *p*-toluenesulfonyl chloride was added with vigorous stirring. After 3 h the solution was washed with diethyl ether and acidified. A 27.2-g sample of crystals was obtained: yield 85%; mp 155–160 °C. Recrystallization from EtOH–water gave a product with the following: mp 168–170 °C; R_f2 0.8; $[\alpha]^{20}_D$ +28° (*c* 2, EtOH); NMR (Me_2SO-d_6) δ 1.4 (s, 9, *t*-Bu), 2.6 (s, 3, $C_6H_4CH_3$), 3.0 (d, 2, *S*-CH_2), 7.5–8.1 (m, 4, C_6H_4).

Anal. Calcd for $C_{14}H_{21}NO_4S_2$: C, 50.74; H, 6.39; N, 4.23. Found: C, 51.05; H, 6.21; N, 4.18.

***N*-(Carbo-*tert*-butoxy)-*S*-*tert*-butyl-L-cysteine (2d).** To a solution of 6.39 g (30 mmol) of 1 in 50 mL of water were added 21 mL (150 mmol) of triethylamine and a solution of 5.23 g (36.5 mmol) of *tert*-butyl azidoformate in 20 mL of dioxane with stirring. The solution was allowed to react for 48 h at room temperature, and the dioxane was evaporated. The residue was washed with diethyl ether, the water layer acidified with $KHSO_4$ solution, and the precipitated oil extracted with diethyl ether. The extract was washed with water, dried, and condensed to a small volume. The product was precipitated with petroleum ether. A 7.29-g (78% yield) sample of white crystals was obtained: mp 89–90 °C; R_f2 0.8; $[\alpha]^{25}_D$ −3° (*c* 2, acetone); NMR ($CDCl_3$) δ 1.2 (s, 9, *S*-*t*-Bu), 1.4 (s, 9, *O*-*t*-Bu), 3.0 (d, 2, *S*-CH_2), 11.3 (s, 1, COOH).

Anal. Calcd for $C_{12}H_{23}NO_4S$: C, 51.96; H, 8.36; N, 5.05. Found: C, 51.83; H, 8.55; N, 5.14.

The dicyclohexylamine salt of **2d** had a melting point of 184–185 °C.

Dicyclohexylamine Salt of *N*-[(2-Nitrophenyl)-sulfenyl]-*S*-*tert*-butyl-L-cysteine (2e). A 4.30-g (20 mmol) sample of 1 was dissolved in a mixture of 20 mL of 2 N NaOH and 25 mL of dioxane. To the solution were simultaneously added 4.15 g (22 mmol) of NpsCl and 12 mL of 2 N NaOH with stirring. After 30 min, 200 mL of water was added, the residue was filtered off, and the combined filtrates were acidified with $KHSO_4$ solution to pH 2–3 with simultaneous extraction with ethyl acetate. The extract was dried and condensed under reduced pressure, and then 4 mL (20.5 mmol) of dicyclohexylamine (DCHA) was added to obtain 8.0 g (78% yield) of yellow salt: mp 158–159 °C; after recrystallization from EtOH, mp 159 °C; R_f2 0.7; NMR ($CDCl_3$) δ 1.2 (s, 9, *t*-Bu), 3.0 (d, 2, *S*-CH_2), 7.4–8.4 (m, 4, C_6H_4).

Anal. Calcd for $C_{25}H_{41}N_3O_4S_2$: C, 58.67; H, 8.07; N, 8.21. Found: C, 58.85; H, 8.07; N, 8.47.

Dicyclohexylamine Salt of *N*-(Carbobenzoxy)-*S*-*tert*-butyl-L-cysteine (2f). A 21.4-g (0.1 mol) sample of 1 was treated with 33.5 mL (0.13 mol) of benzyl chloroformate according to Chimiak[5b] to yield 41.1 g (84%) of the product. Recrystallization from MeOH–diethyl ether afforded crystals: mp 162–163 °C (lit.[5b] mp 161–162 °C); R_f1 0.8.

***S*-*tert*-Butyl-L-cysteine Methyl Ester Hydrochloride (3a).** A 42.7-g (0.2 mol) sample of 1 was dissolved in 160 mL (126 g, ca. 4 mol) of MeOH and cooled to −10 °C. Then 17.4 mL (18.6 g, 0.24 mol) of $SOCl_2$ was added and the solution kept at temperature below 0 °C. Then, the solution was left for 48 h at room temperature, the solvent partly evaporated to a small volume, and diethyl ether added. A 37.5-g (82% yield) sample of hydrochloride melting at 119–120 °C was obtained. After crystallization from MeOH–diethyl ether: mp 120 °C; R_f1 0.6; $[\alpha]^{20}_D$ +18.5° (*c* 2, MeOH); NMR (CF_3COOH) δ 1.2 (s, 9, *t*-Bu), 3.8 (s, 3, OCH_3), 7.35 (br s, 3, NH_3^+).

Anal. Calcd for $C_8H_{18}NO_2SCl$: C, 42.18; H, 7.96; N, 6.15. Found: C, 42.48; H, 7.82; N, 6.01.

***S*-*tert*-Butyl-L-cysteine Ethyl Ester Hydrochloride (3b).** A 21.4-g (0.1 mol) sample of 1 was dissolved in 117 mL (92 g, 0.12 mol) of EtOH and converted to the ester by the analogous procedure as described above. A 21.0-g (87% yield) sample of the product was obtained: mp 138–139 °C; after recrystallization from EtOH–diethyl ether, mp 141–142 °C; R_f1 0.65; $[\alpha]^{20}_D$ +20.5° (*c* 2, EtOH); NMR (CF_3COOH) δ 1.2 (s, 9, *t*-Bu), 1.3 (t, 3, CH_3), 7.4 (br s, 3, NH_3^+).

Anal. Calcd for $C_9H_{20}NO_2SCl$: C, 44.70; H, 8.34; N, 5.79. Found: C, 44.37; H, 8.19; N, 6.00.

***S*-*tert*-Butyl-L-cysteine *tert*-Butyl Ester Hydrochloride (3c).** A 10.7-g (50 mmol) sample of 1 was treated with 50 mL of *tert*-butyl acetate according to Chimiak[5b] to yield 5.49 g (41%) of the product: mp 200–201 °C (lit.[5b] mp 202–203 °C); R_f2 0.4.

***p*-Toluenesulfonate of *S*-*tert*-Butyl-L-cysteine Benzyl Ester (3d).** A 21.4-g (0.1 mol) sample of 1, 57.0 g (0.3 mol) of *p*-toluenesulfonic acid monohydrate, and 51.5 mL (54 g, 0.5 mol) of benzyl alcohol were suspended in 300 mL of $CHCl_3$ and refluxed for 6 h by using a Soxhlet apparatus containing dry silica gel. $CHCl_3$ was evaporated and an equal volume of diethyl ether was added to the residue. A 44.0-g sample of a product (yield ca. 100%) melting at 148–151 °C was obtained. Recrystallization from EtOH gave a salt: mp 166–168 °C; R_f1 0.8; NMR (CF_3CO-OH) δ 1.1 (s, 9, *t*-Bu), 2.2 (s, 3, CH_3), 5.1 (s, 2, *O*-CH_2), 7.0–7.7 (m, 9, Ar).

Anal. Calcd for $C_{21}H_{29}NO_5S_2$: C, 57.38; H, 6.65; N, 3.19. Found: C, 57.39; H, 6.42; N, 3.20.

***N*-Tosyl-*S*-*tert*-butyl-L-cysteine Methyl Ester (4).** A 9.95-g (30 mmol) sample of **2c** was treated with 25 mL of MeOH and 2.6 mL (4.3 g, 36 mmol) of $SOCl_2$ by the same method as described above (for **3a**) but with petroleum ether to precipitate the product; yield 8.3 g (80%). Crystallization from ethyl acetate–petroleum ether gave crystals: mp 87–88 °C; R_f2 0.8; NMR (Me_2SO-d_6) δ 1.4 (s, 9, *t*-Bu), 2.6 (s, 3, $C_6H_4CH_3$), 3.6 (s, 3, OCH_3), 7.4–8.1 (m, 4, *p*-C_6H_4).

***N*-Tosyl-*S*-*tert*-butyl-L-cysteine Hydrazide (5).** A 5.9-g (17 mmol) sample of 4 was dissolved in 30 mL of EtOH and treated with 2.2 mL (2.2 g, 35 mmol) of 80% hydrazine hydrate. On the next day water was added, and 5.3 g (90% yield) of hydrazide crystals precipitated; mp 149–151 °C. Recrystallization from a mixture of MeOH and water (5:1) gave the product: mp 151–152 °C; R_f2 0.8, R_f3 0.3; $[\alpha]^{20}_D$ +62° (*c* 2, acetone); NMR (Me_2SO-d_6) δ 1.4 (s, 9, *t*-Bu), 2.6 (s, 3, CH_3), 4.4 (m, 2, $NHNH_2$), 7.5–8.1 (m, 4, *p*-C_6H_4), 9.5 (m, 1, $NHNH_2$).

Anal. Calcd for $C_{14}H_{23}N_3O_3S_2$: C, 48.67; H, 6.71; N, 12.16. Found: C, 48.90; H, 6.73; N, 12.36.

(23) G. H. L. Nefkens, G. I. Tesser, and R. J. F. Nivard, *Recl. Trav. Chim. Pays-Bas*, **79**, 688 (1960).

N-(Carbobenzoxy)-S-tert-butyl-L-cysteine p-Nitrophenyl Ester (6). A 22.1-g (10 mmol) sample of dicyclohexylcarbodiimide (DCC) and 1.39 g (10 mmol) of *p*-nitrophenol were dissolved in 50 mL of anhydrous ethyl acetate, the mixture was cooled to 0 °C, and then was added 3.1 g (10 mmol) of *N*-(carbobenzoxy)-*S*-*tert*-butyl-L-cysteine liberated from its DCHA salt **2f** by means of Zerolite 225,H^+. The reaction was carried out with stirring for 1 h at 0 °C and 1 h at room temperature. The urea derivative was filtered off, the solvent evaporated, and the residue crystallized from ethyl acetate–petroleum ether. A 2.98-g (98% yield) sample of product was obtained; mp 63–64 °C. Repeated recrystallization gave the product: mp 64–65 °C; $[\alpha]^{20}_D$ −14° (*c* 2, acetone), −17.5° (*c* 1, DMF); NMR ($CDCl_3$) δ 1.2 (s, 9, *t*-Bu), 5.0 (s, 2, *O*-CH_2), 7.1–8.2 (m, 4, *p*-C_6H_4), 7.2 (s, 5, C_6H_5).

Anal. Calcd for $C_{21}H_{24}N_2O_6S$: C, 58.31; H, 5.59; N, 6.47. Found: C, 58.42; H, 5.79; N, 6.38.

(N-Formyl-S-tert-butyl-L-cysteinyl)-L-phenylalanine Methyl Ester (7). To a solution of 2.05 g (10 mmol) of **2a** and 2.6 g (12 mmol) of L-phenylalanine methyl ester hydrochloride[24] in 35 mL of DMF were added 3.1 mL (22 mmol) of triethylamine in 30 mL of DMF and 2.6 mL (3.3 g, 12 mmol) of diphenylphosphoryl azide (DPPA) in 30 mL of DMF. The solution was stirred for 3 h at 0 °C and for 20 h at room temperature, diluted with 800 mL of ethyl acetate–benzene mixture (2:1), and washed with diluted hydrochloric acid, water, saturated $NaHCO_3$ solution, and saturated NaCl solution. The organic layer was dried and the solvent evaporated to obtain 3.35 g (92% yield) of peptide, mp 115–120 °C. Recrystallization from ethyl acetate–petroleum ether gave the product: mp 120–121 °C; R_f2 0.65; $[\alpha]^{20}_D$ −12° (*c* 2, acetone); NMR ($CDCl_3$) δ 1.2 (s, 9, *t*-Bu), 3.7 (s, 3, OCH_3), 7.2 (s, 5, C_6H_5), 8.2 (s, 1, HCO).

Anal. Calcd for $C_{18}H_{26}N_2O_4S$: C, 58.99; H, 7.15; N, 7.65. Found: C, 59.17; H, 7.19; N, 7.56.

[N-(Carbobenzoxy)-S-tert-butyl-L-cysteinyl]-S-benzyl-L-cysteine Benzyl Ester (8). A 14.8-g (30 mmol) sample of **2f** and 14.2 g (30 mmol) of *S*-benzyl-L-cysteine benzyl ester tosylate[25] were dissolved 150 mL of hot tetrahydrofuran each, and then the solutions were mixed. The mixture was cooled, 8.65 g (35 mmol) of 2-ethoxy-*N*-(ethoxycarbonyl)-1,2-dihydroquinoline (EEDQ) was added and the mixture stirred for 8 h at room temperature. The solvent was evaporated, and the residue was dissolved in 500 mL of ethyl acetate–benzene mixture (3:1) and then washed as described above (for **7**). The organic layer was dried and the solvent evaporated to a small volume. On addition of petroleum ether, 13.9 g (78% yield) of crystals was obtained; mp 105–108 °C. Recrystallization from ethyl acetate–petroleum ether gave the product: mp 111–112 °C; R_f3 0.7; $[\alpha]^{20}_D$ −40° (*c* 2, acetone); NMR ($CDCl_3$) δ 1.2 (s, 9, *t*-Bu), 3.5 (s, 2, *S*-$CH_2C_6H_5$), 5.0 and 5.05 (2 s, 4, *O*-CH_2), 7.0 (s, 5, *S*-$CH_2C_6H_5$), 7.1 (s, 10, $OCH_2C_6H_5$).

Anal. Calcd for $C_{32}H_{38}N_2O_5S_2$: C, 64.62; H, 6.44; N, 4.71. Found: C, 64.32; H, 6.22; N, 4.87.

[N-(Carbo-tert-butoxy)-S-tert-butyl-L-cysteinyl]-S-(acetamidomethyl)-L-cysteine Methyl Ester (9). A 4.58-g (10 mmol) sample of DCHA salt of **2d** and 2.45 g (10 mmol) of *S*-(acetamidomethyl)-L-cysteine methyl ester hydrochloride[21] were dissolved in 50 mL of DMF. The dicyclohexylammonium chloride was filtered off, the solution was cooled to 0 °C, and 1.6 g (10 mmol) of *N*-hydroxybenzotriazole and 2.27 g (11 mmol) of DCC were added. The solution was left for 1 h at 0 °C and for 1 h at room temperature. After the mixture was treated as in the procedure for **7**, a peptide was obtained and crystallized from dioxane–petroleum ether: yield 3.45 g (84%); mp 99–101 °C; R_f2 0.7; $[\alpha]^{20}_D$ −42.5° (*c* 2, acetone); NMR ($CDCl_3$) δ 1.2 (s, 9, *S*-*t*-Bu), 1.4 (s, 9, *O*-*t*-Bu), 2.0 (s, 3, $COCH_3$), 3.7 (s, 3, *O*-CH_3), 4.3 (d, 2, *S*-CH_2NH).

Anal. Calcd for $C_{19}H_{35}N_3O_6S_2$: C, 49.01; H, 7.58; N, 9.02. Found: C, 49.26; H, 7.62; N, 9.16.

[[N-(2-Nitrophenyl)sulfenyl]-S-tert-butyl-L-cysteinyl]-L-phenylalanine tert-Butyl Ester (10). A 7.68-g (15 mmol) sample of **2e** and 3.87 g (15 mmol) of L-phenylalanine *tert*-butyl ester hydrochloride[26] were dissolved with stirring in 150 mL of dioxane; precipitation of DCHA·HCl was observed. A 3.96-g (16 mmol) sample of 2-ethoxy-*N*-(ethoxycarbonyl)-1,2-dihydroquinoline (EEDQ) was then added and stirring continued for 8 h at room temperature. The salt was filtered off, the solvent was evaporated, and 7.85 g (98% yield) of the peptide was obtained; mp 130–134 °C. Recrystallization from ethyl acetate–petroleum ether gave yellow crystals: mp 136–138 °C; R_f3 0.75; $[\alpha]^{20}_D$ −12.5° (*c* 2, acetone); NMR ($CDCl_3$) δ 1.2 (s, 9, *S*-*t*-Bu), 1.4 (s, 9, *O*-*t*-Bu), 3.1 (d, 2, $CH_2C_6H_5$), 7.2 (s, 5, C_6H_5), 7.4–8.3 (m, 4, *o*-C_6H_4).

Anal. Calcd for $C_{26}H_{35}N_3O_5S_2$: C, 58.51; H, 6.61; N, 7.87. Found: C, 58.19; H, 6.40; N, 8.04.

[N-Formyl-S-tert-butyl-L-cysteinyl]-L-phenylalanine (11). A 3.7-g (10 mmol) sample of **7** was dissolved in a mixture of 50 mL of dioxane and 25 mL of water, and 5 mL of 2 N NaOH was added. The solution was left for 2 h at room temperature. Dioxane was evaporated, and the residue was diluted with 50 mL of water and then washed with ethyl acetate. The water layer was acidified with $KHSO_4$ solution, and the precipitated oil was extracted with ethyl acetate. The extracts were dried, and the solvent was evaporated to give crystals which were washed with diethyl ether: yield 3.3 g (94%); mp 143 °C; R_f2 0.75.

Anal. Calcd for $C_{17}H_{24}N_2O_4S$: C, 57.92; H, 6.86; N, 7.95. Found: C, 57.75; H, 7.00; N, 8.05.

Cleavage of the S-tert-Butyl Group. General Procedure. The *S*-*tert*-butyl derivative was dissolved in CH_3COOH, and an equimolar amount of NpsCl was added. The mixture was stirred until the dissolution of NpsCl was completed. After 2 h at room temperature a product was isolated by (A) filtration, (B) evaporation of solvent, or (C) precipitation with diethyl ether.

[N-Formyl-S-[(2-nitrophenyl)sulfenyl]-L-cysteinyl]-L-phenylalanine (12). Compound **12** was obtained from **11** according to the general procedure with isolation B. The crude product had a melting point of 173–175 °C and an R_f2 of 0.4. It was recrystallized from MeOH.

Anal. Calcd for $C_{19}H_{19}N_3O_6S_2$: C, 50.77; H, 4.26; N, 9.35. Found: C, 50.49; H, 4.59; N, 9.08.

[N-Formyl-S-[(2-nitrophenyl)sulfenyl]-L-cysteinyl]-L-phenylalanine Methyl Ester (13). Compound **13** was obtained from **7** according to the general procedure (isolation B). The crude product had the following: mp 115–120 °C; R_f3 0.45. It was recrystallized from $CHCl_3$–petroleum ether: NMR (Me_2SO-d_6) δ 2.9 (d, 2, *S*-CH_2), 3.2 (d, 2, $CH_2C_6H_5$), 3.6 (s, 3, *O*-CH_3), 7.3 (s, 5, C_6H_5), 7.5–8.6 (m, 4, C_6H_4).

Anal. Calcd for $C_{20}H_{21}N_3O_6S_2$: C, 51.82; H, 4.57; N, 9.07. Found: C, 51.92; H, 4.59; N, 9.18.

N,N-Bis(formyl-L-cystinyl)-di-L-phenylalanine (14). (a) To 0.99 g (2.2 mmol) of **12** dissolved in 10 mL of MeOH were added 5.5 mL of 0.4 N NaOH solution and 0.04 mL (0.6 mmol) of 2-mercaptoethanol. The solution was left for 3 h at room temperature. The bis(2-nitrophenyl) disulfide was filtered off, and the water layer was washed several times with ethyl acetate and then acidified with $KHSO_4$ solution. The product was extracted with ethyl acetate, the extract dried, and the solvent evaporated to yield crystals which were washed with diethyl ether: yield 0.56 g (86%); mp 192–194 °C; R_f1 0.9; $[\alpha]^{20}_D$ −80.5° (*c* 2, MeOH).

Anal. Calcd for $C_{26}H_{30}N_4O_8S_2$: C, 52.86; H, 5.11; N, 9.48. Found: C, 53.06; H, 5.40; N, 9.47.

(b) To 1.87 g (4 mmol) of **13** dissolved in 10 mL of MeOH and 10 mL of dioxane were added 10 mL of 0.4 N NaOH solution and 0.07 mL (1 mmol) of 2-mercaptoethanol. The solution was left for 4 h at room temperature. The solvents were then evaporated, and the product was extracted from the residue with water. The water layer was washed with ethyl acetate, acidified with $KHSO_4$, and extracted with ethyl acetate. The extracts were dried, and the solvent was evaporated to obtain 0.95 g (80.5%) of product, mp 182–185 °C. Recrystallization from water gave crystals: mp 190–191 °C (identical with **14a**); $[\alpha]^{20}_D$ −79.5° (*c* 2, MeOH).

Bis[(S-tert-butyl-L-cysteinyl)-L-cystine] (15). A 1.78-g (3 mmol) sample of peptide **8** was dissolved in 200 mL of liquid NH_3 and reduced with Na. The obtained blue solution was decolored with CH_3COONH_4, NH_3 was evaporated, and the dry residue was

(24) R. A. Boissonnas, S. Guttmann, P. A. Jaquenod, and J. P. Waller, *Helv. Chim. Acta*, **39**, 1421 (1956).

(25) J. A. MacLaren, W. E. Savige, and J. M. Swan, *Aust. J. Chem.*, 11, 345 (1958).

(26) R. Roeske, *J. Org. Chem.*, **28**, 1251 (1963).

immediately transferred to cold dilute hydrochloric acid. The solution was washed with ethyl acetate and the water layer oxidized with air. The sodium ions were removed by shaking the water layer with 20 mL of Amberlite IRC 50/NH_4^+, and the residue was purified by ion-exchange chromatography on a Dowex 50W-X8. After evaporation of the water, 0.60 g (71% yield) of product was obtained; mp 128–132 °C. Crystallization from water–acetone raised the melting point to 131–133 °C: $[\alpha]^{20}_D$ −36° (*c* 2, 1 N HCl); NMR (CF_3COOH) δ 1.2 (s, 9, *t*-Bu), 7.3 (br s, 3, NH_3^+), 8.0 (d, 1, CONH).

Anal. Calcd for $C_{20}H_{38}N_4O_6S_4$: C, 42.98; H, 6.85; N, 10.03. Found: C, 42.76; H, 7.06; N, 10.19.

[*N*-(Carbobenzoxy)-*S*-[(2-nitrophenyl)sulfenyl]-L-cysteinyl]-*S*-benzyl-L-cysteine Benzyl Ester (16). Compound **16** was obtained from **8** according to the general procedure (isolation A): R_f3 0.8; NMR ($CDCl_3$) δ 2.8 (d, 2, *S*-CH_2), 3.1 (d, 2, CH_2–SS), 3.5 (s, 2, *S*-$CH_2C_6H_5$), 5.0 and 5.1 (2 s, 4, *O*-$CH_2C_6H_5$), 7.3 (s, 15, C_6H_5), 7.3–8.3 (m, 4, *o*-C_6H_4).

Anal. Calcd for $C_{34}H_{33}N_3O_7S_3$: C, 59.02; H, 4.81; N, 6.07. Found: C, 59.25; H, 4.64; N, 5.98.

***N,N'*-Bis(carbobenzoxy-L-cystinyl)bis(*S*-benzyl-L-cysteine) Dibenzyl Ester (17).** To 1.11 g (1.6 mmol) of **16** in 30 mL of $CHCl_3$ was added 5 mL of MeOH, and the solution was reduced with 0.38 g (10 mmol) of $NaBH_4$. After 1 h the solution was carefully washed with water, 1 N HCl, and again with water. The cysteine peptide solution was oxidized with air, the water was evaporated, and the residue was crystallized from acetone to yield 0.59 g (68% yield) of cystine peptide: mp 147–148 °C; R_f2 0.85, R_f3 0.15; $[\alpha]^{20}_D$ −81° (*c* 2, pyridine); NMR ($CDCl_3$) δ 3.5 (s, 2, *S*-$CH_2C_6H_5$), 5.0 (s, 4, *O*-$CH_2C_6H_5$), 7.1 (s, 5, *S*-$CH_2C_6H_5$), 7.2 (s, 10, *O*-$CH_2C_6H_5$).

Anal. Calcd for $C_{56}H_{58}N_4O_{10}S_4$: C, 62.54; H, 5.43; N, 5.21. Found: C, 62.21; H, 5.69; N, 5.42.

(*S*-*tert*-Butyl-L-cysteinyl)-*S*-(acetamidomethyl)-L-cysteine Methyl Ester Hydrochloride (18). To 0.47 g (1 mmol) of protected peptide **9** in 10 mL of $CHCl_3$ was added 5 mL of a saturated solution of HCl in diethyl ether. The precipitated crystals were filtered off after 20 min: yield 0.33 g (89%); mp 110–112 °C; R_f2 0.2.

Anal. Calcd for $C_{14}H_{28}N_3O_4S_2Cl$: C, 41.83; H, 7.02; N, 10.45. Found: C, 41.97; H, 7.19; N, 10.28.

[*S*-[(2-Nitrophenyl)sulfenyl]-L-cysteinyl]-*S*-[(2-nitrophenyl)sulfenyl]-L-cysteine Methyl Ester Hydrochloride (19). Compound **19** was obtained from **18** according to the general procedure (isolation A): R_f3 0.3; NMR (Me_2SO-d_6) δ 3.75 (s, 3, OCH_3), 7.6–7.8 (m, 8, C_6H_4).

Anal. Calcd for $C_{19}H_{21}N_4O_7S_4Cl$: C, 39.27; H, 3.64; N, 9.64. Found: C, 39.14; H, 3.91; N, 9.75.

"Cyclo-L-cystine" 21. A 0.58-g (1 mmol) sample of peptide **19** was dissolved in 10 mL of MeOH and reduced with 1.4 mL (20 mmol) of 2-mercaptoethanol for 3 h, 60 mL of water was then added, and the solution was extracted several times with ethyl acetate. The peptide dissolved in the water layer was oxidized with atmospheric air, the water was then evaporated, and the residue was dried carefully. The peptide hydrochloride **20** so obtained was dissolved in 40 mL of MeOH, and 0.14 mL (1 mmol) of triethylamine was added. Cyclization was performed by heating at 45 °C for 3 h, according to Kamber.[21] Most of the MeOH was evaporated to yield 0.11 g (53% yield) of crystals: mp 230–290 °C; $[\alpha]^{20}_D$ +315° (*c* 0.8, Me_2SO) [lit.[21] mp 250–310 °C; $[\alpha]^{20}_D$ +310° (*c* 1; Me_2SO)]; NMR spectrum as reported.[21]

Bis[[*N*-(carbo-*tert*-butoxy)-*S*-*tert*-butyl-L-cysteinyl]-L-cystine Methyl Ester] (22). A solution of 0.14 g (0.55 mmol) of I_2 in 15 mL of MeOH was added with stirring to a solution of 0.21 g (0.45 mmol) of peptide **9** in 10 mL of MeOH. After 1 h the solution was cooled to 0 °C and decolored with 1 N $Na_2S_2O_3$. The solvents were evaporated, the residue was dissolved in $CHCl_3$, and the obtained solution was washed with diluted $Na_2S_2O_3$ solution and water. After the solvent was dried and evaporated, a pure, amorphous product was obtained: 0.15 g (85%); R_f3 0.6; $[\alpha]^{20}_D$ −45° (*c* 1, acetone); NMR ($CDCl_3$) δ 1.2 (s, 9, *S*-*t*-Bu), 1.4 (s, 9, *O*-*t*-Bu), 2.8 (d, 2, *S*-CH_2), 3.1 (d, 2, CH_2–SS), 3.7 (s, 3, OCH_3).

Anal. Calcd for $C_{32}H_{58}N_4O_{10}S_4$: C, 48.83; H, 7.43; N, 7.12. Found: C, 48.90; H, 7.48; N, 6.97.

[*S*-[(2-Nitrophenyl)sulfenyl]-L-cysteinyl]-L-phenylalanine *tert*-Butyl Ester Hydrochloride (23). To 2.67 g (5 mmol) in **10** in 25 mL of $CHCl_3$ was added 40 mL of HCl in diethyl ether. The product was precipitated with petroleum ether after 2 h at room temperature, and 2.15 g (94% yield) of crystals was obtained; mp 132–135 °C. Recrystallization from EtOH–diethyl ether gave the product: mp 138–140 °C; R_f1 0.8; NMR (Me_2SO-d_6) δ 1.4 (s, 9, *O*-*t*-Bu), 3.4 (d, $CH_2C_6H_5$), 7.4 (s, 5, C_6H_5), 7.6–8.2 (m, 4, *o*-C_6H_4).

Anal. Calcd for $C_{22}H_{28}N_3O_5S_2Cl$: C, 51.40; H, 5.49; N, 8.17. Found: C, 51.28; H, 5.70; N, 7.90.

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Registry No. **1**, 2481-09-6; **2a**, 65798-30-3; **2b**, 65798-31-4; **2c**, 65798-32-5; **2d**, 56976-06-8; **2d** dicyclohexylamine salt, 60143-30-8; **2e**, 65798-34-7; **2f**, 2481-12-1; **3a**, 58336-84-8; **3b**, 65798-35-8; **3c**, 2481-11-0; **3d**, 76499-06-4; **4**, 76514-48-2; **5**, 76499-07-5; **6**, 65798-38-1; **7**, 76499-08-6; **8**, 76499-09-7; **9**, 76499-10-0; **10**, 76499-11-1; **11**, 76499-12-2; **12**, 76499-13-3; **13**, 76499-14-4; **14**, 76499-15-5; **15**, 76499-16-6; **16**, 76499-17-7; **17**, 76514-49-3; **18**, 76499-18-8; **19**, 76499-19-9; **20**, 76499-20-2; **21**, 36703-44-3; **22**, 76499-21-3; **23**, 76499-22-4; L-cysteine hydrochloride, 52-89-1; *N*-(carboethoxy)-phthalimide, 22509-74-6; *tert*-butyl azidoformate, 1070-19-5; (2-nitrophenyl)sulfenyl chloride, 7669-54-7; benzyl chloroformate, 501-53-1; *N*-(carbobenzoxy)-*S*-*tert*-butyl-L-cysteine, 2640-52-0; L-phenylalanine methyl ester hydrochloride, 7524-50-7; *S*-benzyl-L-cysteine benzyl ester tosylate, 73995-16-1; *S*-(acetamidomethyl)-L-cysteine methyl ester hydrochloride, 33375-68-7; L-phenylalanine *tert*-butyl ester hydrochloride, 15100-75-1.