methyl-11-oxo-6,11-dihydrodibenzo[*b,e*]thiepin-3-carboxylate *S,S*-dioxide (**8**) in high yield.

Experimental Section

Melting points were determined with a Mel-Temp apparatus and are not corrected. The IR spectra were measured with a Perkin-Elmer Model 237B spectrophotometer in chloroform solution or as solids in potassium bromide discs. The UV spectra were recorded in methanol solution with a Cary 14 recording spectrophotometer. Proton NMR spectra were measured with a Varian HA100 spectrometer in $CDCl_3$ or Me_2SO-d_6. Chemical shifts are expressed in parts per million (δ) from internal Me_4Si. The mass spectra were obtained with an Atlas CH-4 mass spectrometer. The spectral data for all new compounds were consistent with the assigned structures. Satisfactory analytical data (±0.4%) were reported for all new compounds except for **3**, which was fully characterized as the free acid.

Methyl 11-Oxo-6,11-dihydrodibenzo[*b,e*]thiepin-3-carboxylate (1). A solution of 11-oxo-6,11-dihydrodibenzo[*b,e*]thiepin-3-carboxylic acid chloride[10] (5 g) in methanol (50 mL) was heated under reflux for 1h. The reaction mixture was cooled to 0 °C, and the product was collected by filtration: yield 4.0 g (81%); mp 150–151 °C; UV (dioxane) 246, 280, 371 nm (ϵ 27 000, 10 000, 3400); NMR ($CDCl_3$) δ 3.88 (s, 3 H), 4.03 (s, 2 H), 7.12–7.48 (m, 4 H), 7.57 (dd, J_1 = 8 Hz, J_2 = 1.5 Hz, 1 H), 7.81 (dd, J_1 = 8 Hz, J_2 = 1.5 Hz, 1 H), 7.97 (d, J = 1.5 Hz, 1 H), 8.20 (d, J = 8 Hz, 1 H). Anal. ($C_{16}H_{12}O_3S$) C, H.

Reaction of 1 with Sodium Hydride and Methyl Iodide. A mixture of the ester **1** (3.2 g) and sodium hydride (57% in oil, 0.5 g) in *N*-methylpyrrolidone (50 mL) was cooled in an ice–salt bath, stirred for 30 min, and then treated with methyl iodide (0.7 mL, 1.7 g). The reaction mixture was allowed to warm to room temperature and stirred for a further 18 h, whereupon it was diluted with ice, aqueous ammonium chloride solution, and ethyl acetate. The organic layer was separated, washed, dried, and evaporated to yield an oil which was chromatographed through silica gel (500 g) eluting with hexane–ether (20:1 → 10:1). The fractions containing pure material were evaporated to give (a) methyl 9-thiomethyl-10-methoxyanthracene-2-carboxylate (**4**; 450 mg) [mp 131–132 °C (ethyl acetate–hexane); UV (MeOH) 265, 285, 331, 352, 372, 396, 417 nm (ϵ 78 000, 67 000, 1700, 3000, 4900, 6400, 6600); IR ($CDCl_3$) 1720 cm^{-1}; NMR ($CDCl_3$) δ 2.36 (s, 3 H), 3.99 (s, 3 H), 4.10 (s, 3 H), 7.51–7.71 (m, 2 H), 8.04 (dd, J_1 = 9 Hz, J_2 = 1.5 Hz, 1 H), 8.35 (d, J = 9 Hz, 1 H), 9.00–9.16 (m, 1 H), 9.73 (brd s, 1 H). Anal. ($C_{18}H_{16}O_3S$) C, H.], (b) methyl 9-methyl-9-thiomethyl-10-oxo-9,10-dihydroanthracene-2-carboxylate (**5**; 425 mg) [mp 121 °C (methanol); UV (MeOH) 272, 313 sh nm (ϵ 21 000, 4200); IR ($CHCl_3$) 1720, 1660 cm^{-1}; NMR ($CDCl_3$) δ 1.36 (s, 3 H), 2.01 (s, 3 H), 3.96 (s, 3 H), 7.35–8.43 (m, 6 H), 8.72 (d, J = 1.5 Hz, 1 H). Mass spectrum (molecular ion) theoretical, *m/e* 312; found, *m/e* 312, 265 (100, $M^+ - 47$). Anal. ($C_{18}H_{16}O_3S$) C, H.], and (c) methyl 6-methyl-11-oxo-6,11-dihydrodibenzo[*b,e*]thiepin-3-carboxylate (**3**) as a pale yellow oil (180 mg) [UV (MeOH) 245, 280 sh, 372 nm (ϵ 2600, 10 000, 3400); IR ($CHCl_3$) 1720, 1640 cm^{-1}; NMR ($CDCl_3$) δ 1.74 (d, J = 7 Hz, 3 H), 3.88 (s, 3 H), 4.32 (q, J = 7 Hz, 1 H), 7.20–7.59 (m, 4 H), 7.81 (dd, J_1 = 8 Hz, J_2 = 1.5 Hz, 1 H), 7.97 (d, J = 1.5 Hz, 1 H), 8.20 (d, J = 8 Hz, 1 H). Mass spectrum (molecular ion) theoretical, *m/e* 298; found, *m/e* 298.].

Hydrolysis of the ester **3** with aqueous methanolic sodium hydroxide gave, after acidification and crystallization from ethyl acetate, 6-methyl-11-oxo-6,11-dihydrodibenzo[*b,e*]thiepin-3-carboxylic acid: mp 184–185 °C; NMR (Me_2SO-d_6) δ 1.67 (d, J = 7 Hz, 3 H), 4.62 (q, J = 7 Hz, 1 H), 7.32–8.27 (m, 7 H). Anal. ($C_{16}H_{12}O_3S$) C, H.

Methyl 6-Methyl-11-oxo-6,11-dihydrodibenzo[*b,e*]thiepin-3-carboxylate (3). A 9.0-mL amount of a 1 N solution of potassium *tert*-butoxide in *tert*-butyl alcohol was slowly added to a stirred solution of **1** (2.0 g) in dry *N*-methylpyrrolidone containing methyl iodide (3.0 mL, 6.9 g). During the addition the reaction mixture was cooled in a dry ice–acetone bath, the temperature of which was gradually reduced from −20 to −40 °C during the course of the reaction. The mixture was quenched by addition of saturated aqueous ammonium chloride solution (5 mL) and worked up as described above to yield the ester **3** as a pale yellow oil (1.8 g, 86%).

Methyl 11-Oxo-6,11-dihydrodibenzo[*b,e*]thiepin-3-carboxylate *S,S* Dioxide (7). A solution of the ester **1** (0.8 g) in dichloromethane (20 mL) was treated with a solution of *m*-chloroperbenzoic acid (1.2 g) in the same solvent (10 mL). After 10 min, the reaction mixture was washed with sodium bisulfite solution and then with sodium carbonate solution. The organic layer was dried and evaporated, and the residue was crystallized from ethyl acetate–hexane to yield **7**: 650 mg; mp 166–167 °C; IR 1725, 1655, 1325 cm^{-1}; NMR ($CDCl_3$) δ 3.97 (s, 3 H), 4.80 (s, 2 H), 7.22–7.63 (m, 3 H), 7.97 (d, J = 9 Hz, 1 H), 8.07 (dd, J_1 = 8 Hz, J_2 = 1.5 Hz, 1 H), 8.35 (dd, J_1 = 8 Hz, J_2 = 1.5 Hz, 1 H), 8.70 (d, J = 1.5 Hz, 1 H). Anal. ($C_{16}H_{12}O_5S$) C, H.

Methyl 6-Methyl-11-oxo-6,11-dihydrodibenzo[*b,e*]thiepin-3-carboxylate *S,S* Dioxide (8). A solution of methyl 11-oxo-6,11-dihydrodibenzo[*b,e*]thiepin-3-carboxylate *S,S*-dioxide (630 mg) in dry *N*-methylpyrrolidone was treated with sodium hydride (45 mg) and stirred for 18 h at room temperature. The solution was decolorized by addition of methyl iodide (0.14 mL) and quenched with water. The oily product was filtered and crystallized from ether–hexane to yield **8**: 480 mg; mp 151–153 °C; IR (KBr) 1725, 1655 cm^{-1}; NMR ($CDCl_3$) δ 1.53 (d, J = 7 Hz, 3 H), 3.96 (s, 3 H), 4.70 (q, J = 7 Hz, 1 H), 7.20–8.08 (m, 5 H), 8.34 (dd, J_1 = 8 Hz, J_2 = 1.5 Hz, 1 H), 8.64 (d, J = 1.5 Hz, 1 H). Anal. ($C_{17}H_{14}O_5S$) C, H.

Registry No.—**1**, 67667-05-4; **3**, 68002-09-5; **4**, 68002-10-8; **5**, 68002-11-9; **7**, 68002-12-0; **8**, 68002-13-1; 11-oxo-6,11-dihydrodibenzo[*b,e*]thiepin-3-carboxylic acid chloride, 61220-66-4; 6-methyl-11-oxo-6,11-dihydrodibenzo[*b,e*]thiepin-3-carboxylic acid, 68002-14-2.

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Studies on Sulfur-Containing Peptides: *tert*-Butyloxycarbonylsulfenyl and Benzyloxycarbonylsulfenyl Derivatives as Protecting Groups for Cysteine[1]

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Received July 20, 1978

A heterolytic fragmentation route from sulfenyl thiocarbonates to unsymmetrical disulfides was reported by Brois et al.[3]

$$R_1OCOSCl \xrightarrow{+R_2SH} R_1OCOSSR_2$$

$$\xrightarrow{+R_3SH} R_2SSR_3 + COS + R_1OH \quad (I)$$

This disulfide-forming reaction was applied by Kamber[4] to the synthesis of the disulfide-linked insulin fragment A20-B19 using the methoxycarbonylsulfenyl group[5] (R_1 = CH_3). The SCM group as a SH protecting group for cysteine has also been reported by Hiskey et al.[6]

The present report concerns our studies with two alkyloxycarbonylsulfenyl groups, *tert*-butyloxycarbonylsulfenyl (SCB) and benzyloxycarbonylsulfenyl (SZ), and their use as a thiol protection for peptide synthesis.

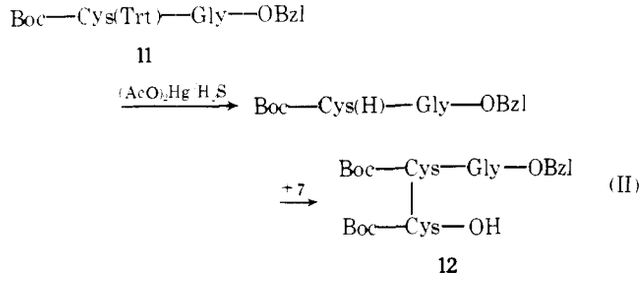
1. SCB Derivatives. Sulfenyl chloride **1** (R_1 = $(CH_3)_3C$; SCB-Cl) was synthesized from *tert*-butyl alcohol by reaction with chlorocarbonylsulfenyl chloride.[7] SCB-Cl is stable for more than 1 year at −25 °C. Unlike SMC-Cl, SCB-Cl failed to react with the *S*-Trt-cysteine derivatives Boc-Cys(Trt)-

0022-3263/78/1943-4893$01.00/0

OH[8] and Boc-Cys(Trt)-Ala-OMe. Z-Cys(SCB)-OMe (**4**) was obtained by reacting *N*-(benzyloxycarbonyl)cysteine methyl ester (**3**) with SCB-Cl in ethyl acetate according to Zervas et al.[9] The formation of the *S*-SCM derivative was similarly achieved in methanol–chloroform. The reaction mixture was purified by column chromatography. In the reaction from **3** to **4**, a considerable amount of cystine derivative [Z-Cys(−)-OMe]$_2$ (**2**) was produced. The SCB derivative **4** was shown to be unstable, being partially converted to **2** over 3 months. It was also labile to alkali. Therefore, the SCB group was judged to be not suitable for peptide synthesis.

2. SZ Derivatives. The sulfenyl chloride **5** (R_1 = $C_6H_5CH_2$; SZ-Cl) was synthesized from benzyl alcohol by analogy to Zumach et al.[7] *S*-SZ-cysteine derivatives Boc-Cys(SZ)-OH (**7**) and Boc-Cys(SZ)-Ala-OMe (**9**) were obtained by reacting the corresponding *S*-Trt derivatives **6** and **8** with **5**. Z-Cys(SZ)-OMe (**10**) was synthesized analogously to **4**. The *S*-SZ derivative **7** was coupled to alanine methyl ester by the mixed anhydride method to yield Boc-Cys(SZ)-Ala-OMe (**9**).

The unsymmetrical cystine derivative **12** was prepared from the SZ derivative **7** and a sulfhydryl cysteine peptide which was obtained from *S*-Trt derivative **11** according to Kamber[4] (eq II).



Oxidative sulfitolysis of **7** was performed in the usual manner[11] to yield Boc-Cys($SO_3^-Na^+$)-OH, which, on electrophoresis, was identical with the sulfitolysis product of *N,N'*-bis(*tert*-butyloxycarbonyl)-L-cystine.

Stability to acid and alkali treatments was studied. The SZ group is stable in trifluoroacetic acid. Derivative **7** could be selectively deprotected to *S*-SZ-cysteine by treating it with trifluoroacetic acid at room temperature for 1 h. On the other hand, the SZ group was removed by 40% hydrogen bromide in acetic acid.

The *S*-SZ derivatives **7**, **9**, and **10** were exposed to solutions of various pH values. TLC showed the existence of unchanged SZ starting material after treatment at pH 10.6 for 2 h. In the case of derivative **10**, the same treatment yielded starting material as well as the cystine derivative **2** and an unknown compound in a ratio of 1:4:3:5.

For comparison, Boc-Cys(SCM)-OMe was also treated as above. This derivative was fully converted to cystine derivatives [Boc-Cys(−)-OMe]$_2$ and [Boc-Cys(−)-OH]$_2$ in a ratio of 9:1. Thus, the SZ group is not stable enough for normal hydrazinolysis or saponification reactions, as such treatments produce symmetrical cystine derivatives as the main product.

In summary, the SZ group is stable to trifluoroacetic acid but deprotected by hydrogen bromide in acetic acid. It is more stable than the SCM group in mildly alkali conditions, but is not stable to strong alkali treatment. The SZ group may be used in peptide synthesis as a SH protecting group, as well as an intermediate for the selective conversion of cysteine to cystine in the late stage of a synthesis. The SCB group is, however, too unstable to be of value in peptide synthesis.

Experimental Section

Melting points were measured on a Bock Monoscop and are uncorrected. Optical rotations were measured using a Perkin-Elmer Model 141 polarimeter. Amino acid ratios were determined by hydrolysis of peptide in redistilled 6 N hydrochloric acid for 24 h at 110 °C, and analysis was carried out on a Biotronik Model LC-6000E. Cystine-containing peptides were converted to cysteic acid with performic acid. Thin-layer chromatograms (Merck Kieselgel 60) were performed in the following systems: CMA, chloroform–acetic acid–methanol (95:3:5); CM51, chloroform–methanol (5:1); CM91, chloroform–methanol (9:1); HEC212, *n*-hexane–ethyl acetate–chloroform (2:1:2); HEC111, *n*-hexane–ethyl acetate–chloroform (1:1:1); SBN, butan-2-ol–10% ammonia (85:15); HBP, *n*-heptane–*tert*-butyl alcohol–pyridine (75:15:15). Column chromatography was performed on Lichroprep Si60 (Merck, prepacked columns) using the above solvent systems. Unless otherwise stated, products were dried in vacuo over phosphorus pentoxide.

***tert*-Butyloxycarbonylsulfenyl Chloride (1).** Under stirring at 35–40 °C, 68 mL (0.488 mol) of triethylamine and 63.87 g (0.488 mol) of chlorocarbonylsulfenyl chloride[7] were added simultaneously to a solution of 36.20 g (0.488 mol) of *tert*-butyl alcohol in 100 mL of benzene. The mixture was stirred at 40 °C for 3 h and then cooled to 0 °C and filtered. The filtrate was washed with water, dried over Na_2SO_4, and distilled under reduced pressure to yield 50.0 g (60.8%) of a light yellow oil (**1**): n^{20}_D 1.4691; bp 50 °C (10.5 mmHg).

Anal. Calcd for $C_5H_9O_2SCl$: C, 35.61; H, 5.38; S, 19.01; Cl, 21.02. Found: C, 35.63; H, 5.37; S, 18.98; Cl, 21.10.

***N*-Benzyloxycarbonyl-*S*-*tert*-butyloxycarbonylsulfenyl-L-cysteine Methyl Ester (4).** A 2.68-g (5 mmol) amount of *N,N'*-bis(benzyloxycarbonyl)-L-cystine dimethyl ester (**2**) was treated with zinc dust and concentrated hydrochloric acid according to Zervas et al.[9] After evaporation of the solvent, the residue was dissolved in 30 mL of ethyl acetate–chloroform (1:1), which was then slowly dropped into a solution of 1.1 g (6.5 mmol) of SCB-Cl (**1**) in 20 mL of the above solvent with stirring under nitrogen at 0 °C. After 3 h, 0.52 mL (5 mmol) of diethylamine was added under stirring. The mixture was then washed with water and dried over Na_2SO_4. After evaporation of the solvent, the residue was chromatographed on Lichroprep Si60 using system HEC212 as the eluent to yield 0.33 g (16.4% calculated from the cystine derivative) of the oily product (**4**): homogeneous; system HEC212, R_f 0.78; $[\alpha]_D$ + 44.2° (*c* 1.55, $CHCl_3$).

Anal. Calcd for $C_{17}H_{23}NO_6S_2$: C, 50.85; 5.77; N, 3.51; S, 15.97. Found: C, 50.89; H, 5.96; N, 3.49; S, 16.07.

Benzyloxycarbonylsulfenyl Chloride (5). Under stirring, 12.18 g (0.1126 mol) of benzyl alcohol was added to 16.23 g (0.124 mol) of chlorocarbonylsulfenyl chloride.[7] The mixture was stirred at 50 °C for 2.5 h and then distilled under reduced pressure to yield 10.65 g (46.7%) of yellow oil (**5**): n^{20}_D 1.5639; bp 103 °C (3 mmHg).

Anal. Calcd for $C_8H_7O_2SCl$: C, 47.41; H, 3.48; S, 15.79; Cl, 17.50. Found: C, 47.54; H, 3.40; S, 15.98; Cl, 17.65.

***N*-Benzyloxycarbonyl-*S*-benzyloxycarbonylsulfenyl-L-cysteine Methyl Ester (10).** A 2.68-g (5 mmol) amount of *N,N'*-bis(benzyloxycarbonyl)-L-cystine dimethyl ester (**2**) was treated with zinc dust and concentrated hydrochloric acid according to Zervas et al.[9] After evaporation of the solvent, the residue was dissolved in 25 mL of chloroform–methanol (1:1) and slowly dropped into a solution of 1.11 g (5.5 mmol) of SZ-Cl (**5**) in 25 mL of ethyl acetate with stirring under nitrogen at 0 °C for 2 h. The mixture was allowed to stand overnight in a refrigerator at −25 °C, and then the solvent was evaporated. The residue was dissolved in 150 mL of ethyl acetate, washed with water, dried over Na_2SO_4, and evaporated to dryness. The gum was chromatographed on Lichroprep Si60 using system HEC212 as the eluent. Recrystallization of the resulting solid from ethyl acetate–*n*-hexane yielded 1.30 g (60.0%) of **10**: mp 57.5 °C; homogeneous; system HEC212, R_f 0.78; $[\alpha]_D$ +17.7° (*c* 1.02, $CHCl_3$).

Anal. Calcd for $C_{20}H_{21}NO_6S_2$: C, 55.16; H, 4.86; N, 3.22; S, 14.73. Found: C, 55.22; H, 4.90; N, 3.16; S, 14.81.

***N*-*tert*-Butyloxycarbonyl-*S*-benzyloxycarbonylsulfenyl-L-cysteine (7).** To a solution of 2.32 g (5 mmol) of *N*-*tert*-butyloxycarbonyl-*S*-trityl-L-cysteine (**6**) (obtained from the dicyclohexylammonium salt[8] by extraction into ethyl acetate from a buffer solution, pH 2.0[12]) was added 0.5 g of $CaCl_3$ and 1.11 g (5.5 mmol) of SZ-Cl (**5**) with stirring at 0 °C. After 2 h, the mixture was allowed to stand at −25 °C for 2 days. Ethyl acetate (100 mL) was then added to the organic layer, which was washed with water, dried over Na_2SO_4, evaporated to dryness, and triturated with *n*-hexane. The resulting gum was dissolved in ether, mixed with 1.3 mL of dicyclohexylamine, concentrated, and crystallized from *n*-hexane. Recrystallization from ethyl acetate–*n*-hexane provided 1.89 g (60.1%) of the dicyclohexylammonium salt of **7**: mp 122–125 °C; $[\alpha]_D$ −27.0° (*c* 1.01, $CHCl_3$).

Anal. Calcd for $C_{28}H_{44}N_2O_6S_2$: C, 59.13; H, 7.80; N, 4.93; S, 11.27. Found: C, 59.21; H, 7.98; N, 5.03; S, 11.03.

This salt was converted to the free acid in the usual manner to provide **7**: mp 36–37 °C; homogeneous; system CM51, R_f 0.56; $[\alpha]_D$ −14.7° (*c* 1.14, $CHCl_3$).

***N*-*tert*-Butyloxycarbonyl-*S*-trityl-L-cysteinyl-L-alanine Methyl Ester (8).** To a solution of 9.27 g (20.0 mmol) of **6** in 50 mL of dimethylformamide was added 2.2 mL of *N*-methylmorpholine and 2.6 mL of isobutyl chloroformate with stirring at −15 °C. After 3 min, this mixture was combined with a solution of 2.76 g (20.0 mmol) of L-alanine methyl ester hydrochloride[13] in 50 mL of dimethylformamide containing 2.2 mL of *N*-methylmorpholine at −15 °C. The mixture was stirred for 1 h at −15 °C and for 1 h at room temperature and then evaporated. A solution of the residue in ethyl acetate was washed with buffer solution (pH 2.0),[12] saturated $NaHCO_3$ solution, and water until neutral and then dried over Na_2SO_2. After removal of the solvent, the residue was crystallized from *n*-hexane. Recrystallization from hot methanol provided 8.85 g (73.3%) of the dipeptide derivative **8**: mp 184 °C; homogeneous; system CM91, R_f 0.90, and CMA, R_f 0.84; $[\alpha]_D$ +12.5° (*c* 1.03, $CHCl_3$).

Anal. Calcd for $C_{31}H_{36}N_2O_5S$: C, 67.85; H, 6.61; N, 5.11; S, 5.84. Found: C, 67.90; H, 6.70; N, 5.13; S, 5.90.

***N*-*tert*-Butyloxycarbonyl-*S*-benzyloxycarbonylsulfenyl-L-cysteinyl-L-alanine Methyl Ester (9). A. From *S*-Trityl Dipeptide 8.** To a solution of 1.60 g (2.92 mmol) of *S*-tritylcysteine derivative **8** in 30 mL of chloroform–ethyl acetate–methanol (2:2:1) was added 2.03 g (10.0 mmol) of SZ-Cl (**5**) with stirring at 0 °C. After 3 h, 2.9 mL of 1 N aqueous diethylamine was added and the mixture was stirred below 0 °C for 5 min. After evaporation of the solvent, the residue was dissolved in 200 mL of chloroform, followed by 100 mL of water to which 1 N aqueous diethylamine was added to pH 4. The organic phase was washed with water and dried over Na_2SO_4. After evaporation of the solvent, the residue was chromatographed on Lichroprep Si60 using system HEC111 as eluent to yield 0.92 g (66.6%) of oily product **9**: homogeneous; system HEC111, R_f 0.61; $[\alpha]_D$ −69.8° (*c* 1.06, $CHCl_3$).

Anal. Calcd for $C_{20}H_{28}N_2O_7S_2$: C, 50.83; H, 5.97; N, 5.93; S, 13.57. Found: C, 50.97; H, 6.02; N, 5.86; S, 13.33.

B. By the Mixed Anhydride Method. To a solution of 0.60 g (1.55 mmol) of SZ derivative **7** in 30 mL of tetrahydrofuran–dimethylformamide (5:1) was added 0.17 mL of *N*-methylmorpholine and 0.13 mL of isobutyl chloroformate with stirring at −15 °C. After 3 min, this solution was combined with a solution of 0.216 g (1.55 mmol) of L-alanine methyl ester hydrochloride[13] in 20 mL of the same solvent mixture containing 0.17 mL of *N*-methylmorpholine at −15 °C. The mixture was treated in the usual manner. Chromatography of the resulting gum provided 0.47 g (64.1%) of the dipeptide derivative **9**, identical with the material obtained in method A above.

***N*-*tert*-Butyloxycarbonyl-*S*-trityl-L-cysteinyl-L-glycine Benzyl Ester (11).** To a solution of 2.32 g (5 mmol) of **6** in 15 mL of dimethylformamide was added 0.55 mL of *N*-methylmorpholine and 0.65 mL of isobutyl chloroformate with stirring at −15 °C. After 3 min, the solution was combined with a solution of 1.69 g (5 mmol) of glycine benzyl ester toluene-*p*-sulfonate[14] in 20 mL of dimethylformamide, prepared by the addition of 0.55 mL of *N*-methylmorpholine at −15 °C. The mixture was treated in the manner previously described and crystallized from petroleum ether. Recrystallization from chloroform–*n*-hexane provided 2.55 g (83.5%) of the dipeptide derivative **11**: mp 56–57 °C; homogeneous; system CMA, R_f 0.66, and SBN, R_f 0.82; $[\alpha]_D$ +11.3° (*c* 1.08, $CHCl_3$).

Anal. Calcd for $C_{36}H_{38}N_2O_5S$: C, 70.79; H, 6.27; N, 4.59; S, 5.25. Found: C, 70.76; H, 6.36; N, 4.53; S, 5.40.

***N,N'*-Bis(*tert*-butyloxycarbonyl)-L-cystinyl-L-glycine Benzyl Ester (12).** To a solution of 611 mg (1 mmol) of the dipeptide **11** in 20 mL of ethyl acetate–methanol (2:1) was added 350 mg (1.1 mmol) of mercuric acetate with stirring. The mixture was stirred at room temperature for 4 h, and then hydrogen sulfide gas was bubbled through it for 10 min. The black precipitate was filtered off, and the filtrate was evaporated to dryness. The residue was washed four times with 10 mL of petroleum ether to provide a gum. A 385-mg (0.93 mmol) amount of **7** in 10 mL of chloroform–methanol (1:1) was added to a solution of the gum in 20 mL of the same solvent mixture with stirring at room temperature. After 2 h, the solvent was evaporated and the residue was triturated with *n*-hexane to provide a jelly-like product. This crude material was chromatographed on Sephadex LH-20 using methanol as eluent. Recrystallization from methanol–*n*-hexane provided 340 mg (62.2%) of unsymmetrical cystine derivative **12**: mp 45–47 °C; homogeneous; system CMA, R_f 0.52, HBP, R_f 0.11, and SBN, R_f 0.52; $[\alpha]_D$ −8.8° (*c* 1.12, $CHCl_3$). Amino acid ratio: cysteic acid 1.89 and glycine 1.00.

Anal. Calcd for $C_{25}H_{37}N_3O_9S_2$: C, 51.09; H, 6.35; N, 7.15; S, 10.91. Found: C, 51.18; H, 6.33; N, 6.98; S, 10.60.

Acknowledgment. We wish to thank Mr. M. Röper and Mrs. M. Sistig of the Institut für Technische Chemie, T. H. Aachen, for the ^1H NMR spectra. We thank Dr. D. J. Saunders for assistance with the manuscript and Dr. H. Zahn for his encouragement.

Registry No.—**1** (R_1 = *t*-Bu), 26555-38-4; **2**, 3693-95-6; **4**, 67951-99-9; **5**, 42734-93-0; **6**, 21947-98-8; **7**, 67952-00-5; **7** dicyclohexylamine salt, 67952-01-6; **8**, 52071-20-2; **9**, 67952-02-7; **10**, 67952-03-8; **11**, 67952-04-9; **12**, 67952-05-0; Boc-Cys(H)-Gly-OBzl, 67952-06-1; chlorocarbonylsulfenyl chloride, 2757-23-5; *tert*-butyl alcohol, 75-65-0; benzyl alcohol, 100-51-6; L-alanine methyl ester hydrochloride, 2491-20-5; glycine benzyl ester toluene-*p*-sulfonate, 1738-76-7.

References and Notes

(1) The following abbreviations have been utilized in the text: Boc = *tert*-butyloxycarbonyl; Z = benzyloxycarbonyl; Trt = trityl; SCM = methoxycarbonylsulfenyl; SCB = *tert*-butyloxycarbonylsulfenyl; SZ = benzyloxycarbonylsulfenyl; OMe = methyl ester; and OBzl = benzyl ester.
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Reaction of Organoboranes with 2,5-Dihydroxy-1,4-benzoquinone and Related Compounds, and Its Application to the Synthesis of Rapanone

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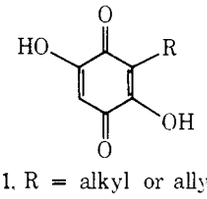
Received June 5, 1978

The wide occurrence of natural products having the 3-alkyl or 3-allyl substituted 2,5-dihydroxy-1,4-benzoquinone structure (**1**) and their application, e.g., as anthelmintic



1, R = alkyl or allyl

agents,[1] encouraged us to elaborate a general procedure for the introduction of alkyl groups into 2,5-dihydroxy-1,4-benzoquinone (**2**). Through the pioneering efforts of Hawthorne, alkylquinols may be formed by the reaction of trialkylboranes with 1,4-benzoquinone.[2] Kabalka[3] and Mikhailov[4] report that the reaction of trialkylboranes with 1,4-naphthaquinone gives the corresponding 2-alkyl-1,4-naphthalenediols. Consequently, we decided to explore the reaction of organoboranes with **2** in hope of developing a practical procedure which would

0022-3263/78/1943-4895$01.00/0