silica gel HF_{254}, thickness 0.25 mm, $CHCl_3$). The first band (R_f 0.68) gave **61** (11 mg, 20%) as a colorless oil: NMR ($CDCl_3$, 60 MHz) δ 0.0–0.85 (3 H, m), 1.13 (3 H, s), 1.73 (3 H, broad s), 4.76 (1 H, m), 4.83 (1 H, m).

The second band (R_f 0.409) gave **58** (5 mg, 8%).

7α-(1,2-Epoxy-1-methylethyl)-4aβ-methyl-1aβ-decahydrocyclopropa[*d*]naphthalene (62). A solution of **61** (15 mg, 0.073 mmol) and *m*-chloroperoxybenzoic acid (purity 85%, 20 mg, 0.099 mmol) in anhydrous CH_2Cl_2 (8 mL) was allowed to stand at room temperature for 3 h. The mixture was poured into a 1 M KI aqueous solution (50 mL) and extracted with $CHCl_3$ (4 × 15 mL). The combined extracts were washed successively with a 0.2 M $Na_2S_2O_3$ aqueous solution (30 mL), a saturated $NaHCO_3$ aqueous solution (2 × 30 mL), and a saturated NaCl aqueous solution (3 × 30 mL), dried (Na_2SO_4), and concentrated to give **62** (12 mg, 74%) as a colorless oil: NMR ($CDCl_3$, 60 MHz) δ 1.06 (3 H, s), 1.19 (3 H, s), 2.37 (1 H, d, J = 5.0 Hz), 2.72 (1 H, d, J = 5.0 Hz).

7α-(1-Hydroxy-1-methylethyl)-4aβ-methyl-1aβ-decahydrocyclopropa[*d*]naphthalene (Id). To a stirred solution of **62** (12 mg, 0.05 mmol) in anhydrous ether at 0 °C was added $LiAlH_4$ (50 mg, 1.32 mmol). The mixture was stirred at 0 °C for 1.5 h, poured into a mixture of a saturated NaCl aqueous solution (50 mL) and ice, and extracted with ethyl acetate (4 × 20 mL). The combined extracts were washed with a saturated NaCl aqueous solution (4 × 50 mL), dried (Na_2SO_4), and concentrated to give oily crude product, which was purified by TLC (Merck, silica gel HF_{254}, thickness 0.25 mm, $CHCl_3$). The band whose R_f value was 0.26 gave Id (6 mg, 50%) as a colorless oil: IR ($CHCl_3$) 3580, 3420 cm^{-1}; NMR (CCl_4, 90 MHz) δ 0.20 (1 H, dd, J = 4.5, 9.0 Hz), 0.46 (1 H, ddd, J = 2.0, 4.5, 4.5 Hz), 0.67 (1 H, m), 1.16 (6 H, s), 1.18 (3 H, s); NMR ($CDCl_3$, 200 MHz) δ 0.208 (1 H, dd, J = 4.5, 9.0 Hz), 0.475 (1 H, J = 1.8 4.5, 4.5 Hz), *ca.* 0.70 (1 H, m), 1.172 (3 H, s), 1.182 (6 H, s); MS, *m/e* (relative intensity) 222 (M^+, 0.5), 204 (54), 189 (27), 162 (23), 161 (100), 149 (45), 135 (25), 133 (18), 123 (28), 122 (34), 121 (21), 119 (16), 109 (45), 108 (18), 107 (38), 105 (45), 95 (23), 93 (39), 91 (14), 82 (37), 81 (43), 79 (21), 67 (32), 59 (95).

7α-Acetyl-4aβ-methyl-1aβ-decahydrocyclopropa[*d*]naphthalene (63). Ozone was bubbled into a solution of **61** (7 mg, 0.03 mmol) in a mixture of CH_2Cl_2 (15 mL) and methanol (10 mL) at −70 °C untill the solution became blue. The reaction mixture was worked up as usual and purified by TLC (Merck, silica gel HF_{254}, thickness 0.25 mm, $CHCl_3$) to give **63** (5 mg, 71%) as a colorless oil: NMR (CCl_4, 60 MHz) δ 0–0.67 (3 H, m), 1.12 (3 H, s), 2.08 (3 H, s).

7β-Acetyl-4aβ-methyl-1aβ-decahydrocyclopropa[*d*]naphthalene (31). A mixture of **63** (5 mg, 0.024 mmol), a 2 M KOH aqueous solution (10 mL), and methanol (10 mL) was stirred for 24 h at room temperature and worked up as usual to give oily crude product, which was purified by TLC (Merck, silica gel HF_{254}, thickness 0.25 mm, $CHCl_3$) to give **31** (4 mg, 80%) as a colorless oil: NMR ($CDCl_3$, 60 MHz) δ 0–1.0 (3 H, m), 1.14 (3 H, s), 2.15 (3 H, s); MS (13.5 eV), *m/e* (relative intensity) 206 (M^+, 59), 191 (100), 163 (75).

Acknowledgment. We wish to express our thanks to Professor E. Kurosawa for the information concerning NMR data of isocycloeudesmol. We are also grateful to Professors W. Fenical and J. J. Sims for the NMR spectra of cycloeudesmol and its derivatives. We also thank Professors S. Yamaguchi and K. Kabuto for a loan of a polarimeter and for their help in the measurement of optical rotations.

Registry No. 1, 619-02-3; 2, 4895-25-4; 3, 4895-26-5; 4, 4895-27-6; 5, 93860-75-4; 6, 93782-42-4; 7, 93860-76-5; 8, 93782-43-5; 9, 93860-77-6; 10, 93860-78-7; 11, 93782-44-6; 12, 93860-79-8; 13, 93860-80-1; 14 (isomer 1), 93860-81-2; 14 (isomer 2), 93860-82-3; 15 (isomer 1), 93782-45-7; 15 (isomer 2), 93860-83-4; 16 (isomer 1), 70037-13-7; 16 (isomer 2), 70052-22-1; 17 (isomer 1), 93860-84-5; 17 (isomer 2), 93860-85-6; 18 (isomer 1), 93782-46-8; 18 (isomer 2), 93860-86-7; 20, 93860-87-8; 21, 93782-47-9; 22, 93782-48-0; 23, 93782-49-1; 24, 93860-88-9; 25, 93782-50-4; 26, 4895-29-8; 27, 93860-89-0; 28, 93860-90-3; 29, 93860-91-4; 30, 93860-92-5; 31, 76548-22-6; 32, 93860-93-6; 33, 93782-51-5; 34, 93860-94-7; 36 (isomer 1), 93782-52-6; 36 (isomer 2), 93860-95-8; 37 (isomer 1), 93860-96-9; 37 (isomer 2), 93860-97-0; 41, 93860-98-1; 47, 65083-11-6; 48, 93860-99-2; 49, 93861-00-8; 51, 93861-01-9; 52, 93861-02-0; 53, 93861-03-1; 54, 93861-04-2; 55, 93861-05-3; 56, 93861-06-4; 57, 93861-07-5; 58, 93861-08-6; 59, 93782-53-7; 60, 93861-09-7; 61, 93861-10-0; 62 (isomer 1), 93782-54-8; 62 (isomer 2), 93861-11-1; 63, 93861-12-2; Ia, 71962-31-7; Ib, 93860-74-3; Ic, 76548-19-1; (±)-Id, 78781-34-7; III, 75744-72-8; IV, 53823-06-6; 4-chloro-2-butanone, 6322-49-2; $(CH_2{=}C(CH_3))_2CuLi$, 21329-14-6.

Notes

Kinetic Investigation of the Staphylococcal Protease Catalyzed Hydrolysis of Glutamyl Analogues: γ-Methyleneglutamic and γ-Carboxyglutamic Acid

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As characterized by Drapeau,[2] the extracellular serine protease isolated from *Staphylococcus aureus* strain V8 was shown to cleave specifically on the carboxyl side of either aspartyl or glutamyl linkages. Ensnouf and Prowse[3] found that the *S. aureus* protease did not cleave γ-carboxyglutamyl (Gla) bonds at an appreciable rate. This finding was later confirmed by Marsh,[4] who was able to isolate the Gla containing region (1–39) of the coagulation protein prothrombin by cleavage with *S. aureus* protease.

Recently, we described a procedure for the chemical modification of Gla residues in peptides[5] and proteins.[6] This conversion of Gla to γ-methyleneglutamyl (γ-mGlu) has been performed on the fragment-1 region (1–156) of prothrombin. Between two and eight out of a possible ten Gla residues have been shown to modify under various reaction conditions. Since γ-methyleneglutamic acid is

(1) Undergraduate research student.
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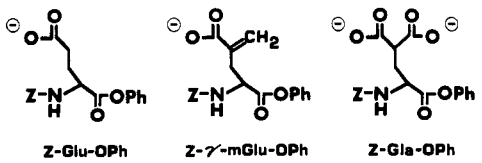
Chart I



Z-Glu-OPh Z-γ-mGlu-OPh Z-Gla-OPh

structurally and electrostatically similar to glutamic acid, we wondered if the modified residues would be recognized by *S. aureus*. A series of substrates which allowed precise measurement of enzymatic activity were synthesized and studied to address this question. These substrates were the *N*-(benzyloxycarbonyl)-α-phenyl esters of glutamic, γ-methyleneglutamic, and γ-carboxyglutamic acid (Chart I).

Preparation of Substrates

Chromophoric substrates provide a rapid and accurate spectrophotometric assay of enzyme activity. Phenyl ester compounds have been used previously for the determination of esterase and protease activities of both streptococcal[7] and staphylococcal[8] proteases. The synthetic stability and chromophoric properties of phenyl esters proved to be ideal for this investigation.

Houmard and co-workers[8] have demonstrated that *N*-(benzyloxycarbonyl)-L-glutamic acid α-phenyl ester (Z-Glu-OPh) is an acceptable substrate for *S. aureus* and, therefore, was chosen as our "reference" substrate. The previously reported syntheses of this compound have been based on the preferential nucleophilic opening of *N*-(benzyloxycarbonyl)glutamic anhydride to give the α-substituted product.[9,10] Since the properties of the corresponding γ-carboxyglutamic and γ-methyleneglutamic anhydrides are unknown, we chose a more straightforward approach to the synthesis of the α-phenyl ester analogues.

Our strategy was dictated by γ-*tert*-butyl ester protecting groups on the side chains of Z-Gla-OH and Z-Glu-OH. The introduction of an α-phenyl ester to either of these starting materials was easily accomplished with phenol and *N,N'*-dicyclohexylcarbodiimide. The resulting products resisted all crystallization attempts and remained as oils. Removal of γ-*tert*-butyl esters in the presence of α-phenyl esters has not to our knowledge beeen documented. Encourgaged by the observation of Kenner[11] that phenyl esters were stable to treatment with hydrobromic/acetic acid, we found that acidolysis with trifluoroacetic acid (TFA) selectively removed the *tert*-butyl esters.

The γ-methylene derivative was then prepared from Z-Gla-OPh by our previously described procedure: Reaction of Gla residues with a morpholine–formaldehyde mixture at pH 4.5 yields the Mannich base adduct. Fragmentation of this species occurs readily at neutral pH or in dimethylformamide to yield carbon dioxide, morpholine, and the corresponding γ-methyleneglutamyl residue.

Kinetic Measurements

The spectrophotometric measurements were performed in a standard 1.0-cm cuvette thermostated at 35 °C. To this was added 2.5 mL of tris(hydroxymethyl)aminomethane (Tris) phosphate buffer (0.20 M in Tris), pH 7.80, and 50 μL of a substrate in acetonitrile; 5 μL of enzyme was added with stirring, and recording was started within 5 s of enzyme addition. The liberation of phenol (ε 1500 M^{-1} cm^{-1}) was followed at 270 nm with a Gilford Model 260 spectrophotometer interfaced with a microprocessor-based data aquisition system. Kinetic runs were performed in triplicate, and for each substrate, corrections were made for the small but measurable nonenzymatic hydrolysis. Substrate concentrations ranged from 0.05 to 0.5 mM. Enzyme concentrations were fixed at 2.95×10^{-9} M. The concentration of enzyme stock solutions was determined by using the cited molar extinction coefficient (ε) of 11 500 M^{-1} cm^{-1} at 280 nm.[8] *Staphylococcus aureus* strain V8 protease was obtained from Miles Laboratories Inc., Elkhart, IN. The steady-state parameters k_{catal} ($V/[E_0]$) and K_M were determined by Lineweaver–Burk analysis of intital velocity measurements at the varying substrate concentrations. (Figure 1a–c). No deviation from Michaelis–Menten behavior was observed.

Table I. Kinetic Parameters of the Staphylococcal Protease Substrates[a]

substrate	K_M (mM)	k_{catal} (s^{-1})	k_{catal}/K_M (mM^{-1} s^{-1})
Z-Glu-OPh[b]	0.102	228	2260
Z-Glu-OPh	0.066	129	1960
Z-γ-mGlu-OPh	0.257	53.1	207
Z-Gla-OPh	0.078	2.34	30

[a] Experimental conditions are the same as those for Figure 1. [b] Houmard, ref 7.

Discussion

In conjunction with our method of γ-carboxyglutamyl modification, we desired a means of isolating the Gla region of modified prothrombins. The success of Marsh et al. in obtaining the 1–39 peptide by *S. aureus* cleavage at Asp-39 led us to wonder if the same procedure could be applied in the presence of γ-mGlu. The α-phenyl esters of Glu, Gla, and γ-mGlu were studied to determine the enzymatic parameters of *S. aureus* toward glutamyl analogues.

The enzymatic parameters for the esterolysis of Z-Glu-OPh in this study are roughly the same as those obtained by Houmard[8] under identical conditions (Table I). Differences may most likely be attributed to the source and purity of the enzyme preparation. As summarized in Table I the catalytic efficiency (k_{catal}/K_M) of the esterolysis of Z-γ-mGlu-OPh is approximately 10% of that obtained with Z-Glu-OPh. The cleavage rate of Z-Gla-OPh is much slower, being only 1.5% as efficient as the glutamyl standard. On the basis of these findings, it is not surprising that cleavage at Gla residues has not been detected previously.

As pointed out by Liu,[7] serine proteases generally hydrolyze specific ester substrates at a rate on the order of 10^4 times faster than the corresponding amides. Although the cleavage rates of glutamyl residue analogues in proteins will be much slower, the *relative* rates, and hence the order of selectively, is not expected to change appreciably. Therefore, it may be possible to cleave all aspartyl and glutamyl residues in a reasonably short time without interferences from γ-methyleneglutamyl and γ-carboxyglutamyl cleavages.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Optical rotations were recorded on a Perkin-Elmer Model 241 polarimeter. Ele-

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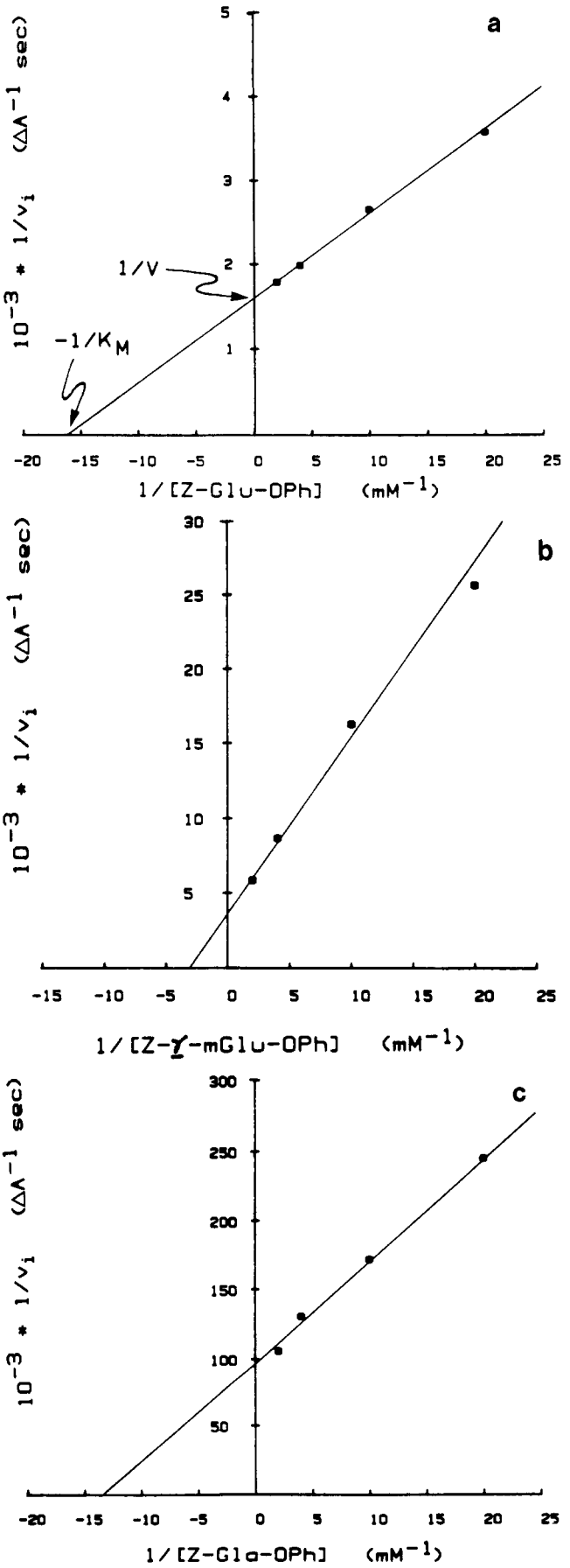

Figure 1. Lineweaver–Burk plot of *S. aureus* hydrolysis (a) of Z-Glu-OPh; (b) of Z-γ-mGlu-OPh; (c) of Z-Gla-OPh. Experimental conditions were 0.2 M Tris phosphate buffer at pH 7.8, 35 °C, 1.96% acetonitrile–water (v/v). Enzyme concentration 2.95×10^{-9} M; substrate concentrations from $0.05–0.5 \times 10^{-3}$ M. ΔA refers to a change in absorbance units.

mental Analyses were performed by Atlantic Microlabs, Atlanta, GA.

***N*-(Benzyloxycarbonyl)-γ-*tert*-butyl-L-glutamic Acid, Dicyclohexylamine Salt (1).** The salt 1 was synthesized in 20% yield (based on *N*-(benzyloxycarbonyl)-L-glutamic acid) by the methods outlined by Schwyzer et al.[12] mp 138–139.5 °C; $[\alpha]^{23}_D$ +7.2° (*c* 1.45, MeOH) [(lit. mp 140–141 °C; $[\alpha]^{23}_D$ +7.2° (*c* 1.45, MeoH)].

***N*-(Benzyloxycarbonyl)-γ-*tert*-butyl-L-glutamic Acid, α-Phenyl Ester (2).** The dicyclohexylamine salt 1 (0.40 g, 0.77 mmol) was dissolved in aqueous 20% citric acid and extracted 3 times with chloroform. The organic layers were evaporated in vacuo and combined at 0 °C in 2 mL of methylene chloride with 0.06 g (0.64 mmol) of phenol and 0.165 g (0.80 mmol) of *N,N'*-dicyclohexylcarbodiimide. The solution was stirred overnight at 0 °C and filtered to remove *N,N'*-dicyclohexylurea. The product was diluted with ethyl acetate and washed with water, 20% citric acid, water, 5% sodium bicarbonate, 20% citric acid, and water. The organic layer was dried over magnesium sulfate and evaporated to an oil. Cyrstallization from 2-propanol/water at −20 °C afforded a crude solid which was dissolved in diethyl ether and filtered to remove *N,N'*-dicyclohexylurea. Evaporation of the ether resulted in an oil which was used without further purification.

***N*-(Benzyloxycarbonyl)-L-glutamic Acid, α-Phenyl Ester (3).** A solution of 2 in 4 mL of 1:1 trifluoroacetic acid/methylene chloride was stirred at 0 °C under nitrogen for 5 h. The mixture was evaporated and dissolved in diethyl ether at 0 °C. To this solution was added 0.16 mL (0.80 mmol) of dicyclohexylamine. The resulting fluffy white precipitate was filtered, washed with ether, and dried to yield the pure dicyclohexylamine salt of 3; mp 150–153 °C (lit.[9] mp 152–153 °C).

The dicyclohexylamine salt was partitioned between chloroform and aqueous 20% citric acid and the organic layer evaporated in vacuo. Crystallization from ethyl acetate/hexane afforded pure 3: 0.05 g (18% from 1); mp 125–127.5 °C; $[\alpha]^{23}_D$ −34.4° (*c* 1.0, MeOH) [(lit.[10] mp 123–124 °C; $[\alpha]^{23}_D$ 35.7° (*c* 1.0, MeOH)].

Anal. Calcd for $C_{19}H_{19}NO_6$: C, 63.86; H, 5.36; N, 3.92. Found: C, 63.58; H, 5.41; N, 3.89.

***N*-(Benzyloxycarbonyl)-γ,γ-di-*tert*-butyl-L-γ-carboxyglutamic Acid (4).** The optically active material was obtained by resolution of D,L-4 with L-quinine as previously described.[13] The quinine salt was partitioned between ethyl acetate and aqueous 20% citric acid, and the organic layer removed by rotary evaporation. Crystallizaton from diisopropyl ether/pentane gave optically pure 4: mp 89–90 °C; $[\alpha]^{23}_D$ −12.05° (*c* 1.0, MeOH).

***N*-(Benzyloxycarbonyl)-γ,γ-di-*tert*-butyl-L-γ-carboxyglutamic Acid, α-Phenyl Ester (5).** To a stirred solution of 0.44 g (1.0 mmol) of 4 in 10 mL of methylene chloride at 0 °C was added 0.095 g (1.0 mmol) of phenol and 0.21 g (1.0 mmol) of *N,N'*-dicyclohexylcarbodiimide. The solution was stirred overnight and filtered to remove *N,N'*-dicyclohexylurea. The product was diluted with ethyl acetate and washed twice each with water, 20% citric acid, water, 5% sodium bicarbonate, and water. After evaporation, the organic residue was dissolved in 2-propanol and precipitated as an oil with water. The oily product was dried over phosphorus pentoxide and used without further purification.

***N*-(Benzyloxycarbonyl)-L-γ-carboxyglutamic Acid, α-Phenyl Ester (6).** A solution of 5 in 4 mL of 1:1 trifluoroacetic acid and methylene chloride was stirred at 0 °C under nitrogen for 5 h. The solvents were removed and the pure product was precipitated from chloroform: 0.23 g (57% from 4); mp 137–139 °C; $[\alpha]^{23}_D$ −30.3° (*c* 1.0, MeOH).

Anal. Calcd for $C_{20}H_{19}NO_8$: C, 59.85; H, 4.77; N, 3.49. Found: C, 59.59; H, 4.83; N, 3.46.

***N*-(Benzyloxycarbonyl)-L-γ-methyleneglutamic Acid, α-Phenyl Ester (7).** A solution of morpholine (50 μL, 0.57 mmol) in 4 mL of water was adjusted to roughly pH 5 with trifluoroacetic acid. To this mixture was added 0.15 g (0.37 mmol) of 6 and approxomately 2 mL of 2-propanol to give a homogeneous mixture. The pH was adjusted to 4.5 with trifluoroacetic acid and the solution cooled to 0 °C; 45 μL (0.60 mmol) of 37% formaldehyde

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was added, and after 2 h the white Mannich-base precipitate was collected by filtration and washed with water. This solid was dissolved in dimethylformamide to induce decarboxylation and stirred for 1 h. The solvent was then evaporated under reduced pressure, and the resulting oil was dissolved in ethyl acetate and washed with 20% citric acid, water, and saturated sodium chloride. The organic layer was dried over magnesium sulfate, filtered, and evaporated to an oil. Crystallization from diethyl ether/hexane afforded pure 7: 0.032 g (23%); mp 105–108 °C; $[\alpha]^{23}_D$ −34.7° (*c* 1.0, MeOH).

Anal. Calcd for $C_{20}H_{19}NO_6 \cdot {}^1/_2H_2O$: C, 63.49; H, 5.33; N, 3.70. Found: C, 63.42; H, 5.27; N, 3.66.

Acknowledgment. This research was supported by Grant HL-20161 from the National Heart, Lung and Blood Institute, U.S. Public Health Service.

Registry No. 1, 3967-21-3; 2, 70706-35-3; 3, 25126-07-2; 3·DCHA, 93255-01-7; 4, 60686-50-2; 5, 93254-98-9; 6, 93254-99-0; 7, 93255-00-6; phenol, 108-95-2; morpholine, 110-91-8; formaldehyde, 50-00-0; *Staphylococcus aureus* V_8 proteinase, 66676-43-5.

Synthesis of 3-*tert*-Alkyl-2,4-imidazolidinediones

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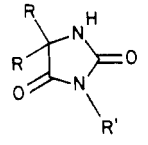
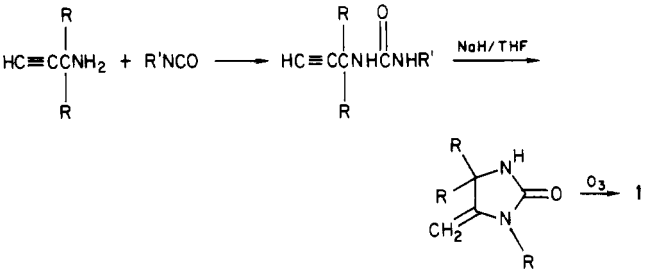
2,4-Imidazolidinediones (hydantoins 1) are widely used as anticonvulsants.[1] Specifically 5,5-diphenyl-2,4-imidazolidinedione (phenytoin or dilantin) is the major drug prescribed for grand mal seizures in epilepsy. However, no hydantoins had been reported to show any efficacy toward petit mal control until we found that 3-*tert*-butyl-5,5-dimethyl-2,4-imidazolidinedione displayed moderate activity in its initial screen.[2] Since it appeared to be a specific function of the 3-*tert*-butyl group we were interested in synthesizing 3-*tert*-butyl-5,5-diphenyl-2,4-imidazolidinedione to see if this compound might carry both grand mal and petit mal activity. In addition, we wished to extend general procedures for preparing other 3-*tert*-alkyl derivatives which are little known. Most alkylations at N-3 are accomplished by using the previously formed hydantoin anion as the nucleophile in an S_N2 displacement of an alkyl halide and thus 3-substitution is usually limited to primary alkyl groups.



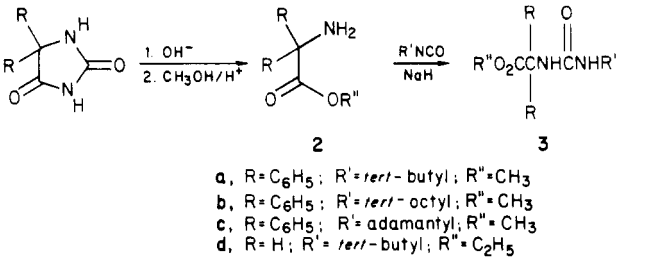
1

A procedure which we previously used, the base-catalyzed cyclization of propargylureas (Scheme I),[3,4] failed because the prerequisite α,α-diphenylpropargylamine[5] could not be prepared.

Scheme I

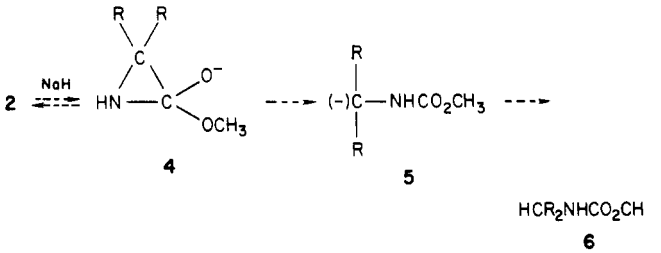


Scheme II



a, R = C_6H_5; R' = *tert*-butyl; R" = CH_3
b, R = C_6H_5; R' = *tert*-octyl; R" = CH_3
c, R = C_6H_5; R' = adamantyl; R" = CH_3
d, R = H; R' = *tert*-butyl; R" = C_2H_5

Scheme III



A method which did prove successful and, in fact, provides an alternative route to 3-substituted hydantoins is outlined in Scheme II. Starting with a 5,5-disubstituted 2,4-imidazolidinedione, hydrolysis to the amino acid and conversion to the ester allows recyclization to take place with the appropriate isocyanate.

In most cases the order of addition of amino ester **2b–d**, base, and isocyanate was not critical. However, with the diphenyl derivative **2a**, if isocyanate was not present upon the addition of sodium hydride, isomerization resulted with the formation of **6** (Scheme III). Presumably, stabilization of the anion intermediate **5** by the two phenyl groups provides the driving force for ring opening (**4**) in the forward direction as neither derivative when R = CH_3 or H behaves similarly.

Experimental Section

Diphenylglycine. In a Monel metal autoclave was placed 15 g (0.059 mol) of 5,5-diphenylhydantoin and 315 mL of 20% sodium hydroxide, and the mixture was heated at 180–185 °C for 27 h. Water was added and the mixture filtered. The filtrate was cooled in an ice bath and acidified with glacial acetic acid. The precipitate was collected, washed with water and ether, and recrystallized from ethanol–water to give 16.22 g (72%): mp 248–249 °C (lit. mp 244–245 °C).[6]

α,α-Diphenylglycine Methyl Ester. To a stirred mixture of 12.5 g (0.55 mol) of diphenylglycine in 125 mL of anhydrous methanol was bubbled anhydrous HCl gas. The addition took 1 h, during which time the mixture was kept at reflux. The excess methanol and HCl were removed in vacuo. After washing the solid with 3 × 50 mL portions of ether and 200 mL of 1 N Na_2CO_3, 200 mL of ether was added, and the mixture was stirred for 20 min. The water layer was extracted with 200 mL of ether, and the combined organics were dried ($MgSO_4$) and concentrated. The

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(5) Skelly, P. D. M.S. Thesis, The University of New Orleans, New Orleans, LA, 1981. Numerous attempts to convert 1,1-diphenyl-2-propyn-1-ol into the appropriate amine all were unsuccessful.
(6) *Chem. Abstr.* **1953**, *47*, 1190g.

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