Synthesis of Fused Hydantoins by Intramolecular Amidoalkylation

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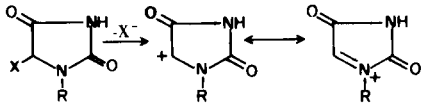
Several 1-(2-arylethyl)hydantoins **2** have been cyclized through their 5-bromo derivatives. The hydantoins **2a** and **2b**, unsubstituted in the 5-position, require stannic chloride catalysis of the cyclization to **3a** and **3b**, respectively. However, the 5-phenyl analog **2c** (n = 2) cyclizes spontaneously and essentially quantitatively to **5** during bromination. This reaction is limited to the formation of a 6-membered ring.

In 1965 it was predicted (1) that if carbonium-immonium ions (*i.e.*, B) could be generated from 5-substituted hydantoins (A), powerful electrophiles would result.

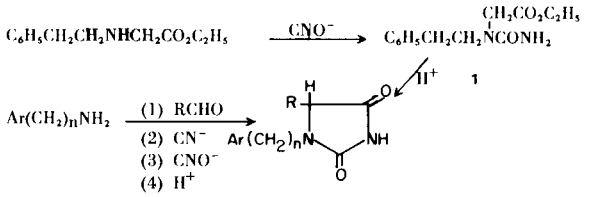


A B

In harmony with this prediction, Ben-Ishai and coworkers (2) found that 5-alkoxyhydantoins (X = OR, R = H) readily amidoalkylate aromatic compounds and olefins. Because these condensations were carried out under acid-catalyzed conditions, cation B is the probable reactive intermediate. However, Ben-Ishai and Goldstein (3) also found that these 5-alkoxyhydantoins undergo acid-catalyzed as well as thermal 1,4-addition to conjugated dienes. Hence, the corresponding uncharged, cyclic acylimine (formed by elimination of alcohol) cannot be ruled out unequivocally as a possible alternate reactive intermediate in the substitution reaction.

The present paper reports successful intramolecular amidoalkylations involving hydantoins substituted at the 1-position by 2-arylethyl groups (*i.e.*, R = $ArCH_2CH_2$ in B). Because elimination to acylimines is not possible in these instances, cation B must be the intermediate.

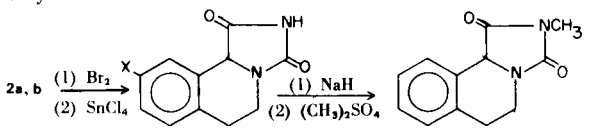
1-Phenethylhydantoin (**2a**) was prepared in two ways. The ethyl ester of *N*-phenethylglycine was converted to the urea **1** with cyanate, followed by acid catalyzed cyclization to hydantoin **2a** in an 83% over-all yield. Alternatively, phenethylamine was treated successively with formaldehyde, cyanide, cyanate, and aqueous acid to give **2a** in a 55% yield without isolation of intermediates. In the same way, 1-(*p*-chlorophenethyl)hydantoin (**2b**) was prepared (42% yield); and, by using benzaldehyde in place of formaldehyde with the appropriate arylalkylamines, the



2a, Ar = C_6H_5; n = 2; R = H
2b, Ar = *p*-ClC_6H_4; n = 2; R = H
2c, Ar = C_6H_5; n = 1, 2, 3; R = C_6H_5

three 1-arylalkyl-5-phenylhydantoins **2c** were obtained in 54 to 60% yields.

Bromination of **2a** followed by treatment of the crude product with anhydrous stannic chloride at 0° led to a 30% yield of the cyclized product **3a**, also obtained in much better yield (76%) by treatment of 3,4-dihydroisoquinoline successively with cyanide, cyanate and aqueous acid. Several other cyclization conditions that were tried (*e.g.*, aluminum chloride, concentrated sulfuric acid, polyphosphoric acid) were completely ineffective. However, the chloro-derivative **2b** gave a 66% yield of the fused hydantoin **3b** under essentially the same conditions that gave the 30% yield of **3a**.

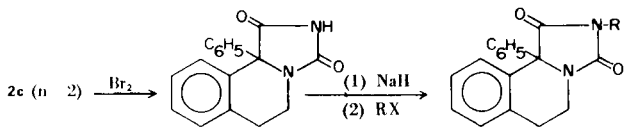


3a, X = H
3b, X = Cl

4

Surprisingly, the corresponding 5-phenylhydantoin **2c** (n = 2) underwent cyclization more readily than either **2a** or **2b**. The fused hydantoin **5** formed spontaneously in 90% yield during the bromination of **2c** (n = 2). No stannic chloride was needed. Presumably, hydrogen bromide alone serves as an autocatalyst for the reaction.

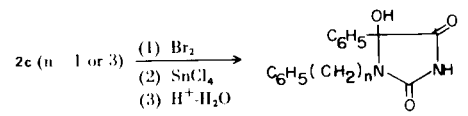
The unexpected facility of the cyclization to **5** is limited,



5

6a, R = CH_3
6b, R = $CH_2CH_2N(CH_3)_2$
6c, R = $(CH_2)_3N(CH_3)_2$·HCl
6d, R = $CH_2CH_2N(C_2H_5)_2$·HCl
6e, R = $SO_2C_6H_5$

however, to the formation of a 6-membered ring. Similar treatment of the two homologs **2c** (n = 1 and 3) led to the corresponding 5-hydroxyhydantoins **7a** and **7b** as the only identifiable products, even when stannic chloride was also used. Several other catalysts were equally unproductive (see the experimental section), as was treatment of **7a** or **7b** with concentrated sulfuric acid.



7a, n = 1
7b, n = 3

Several *N*-substituted derivatives, **4** and **6**, of the fused hydantoins, **3a** and **5**, were prepared for pharmacological testing. None showed more than weak anticonvulsant activity even though structure **5** represents a cyclized form of 5,5-diphenylhydantoin, a very useful drug in the treatment of epilepsy.

EXPERIMENTAL

Melting points were determined in capillary tubes and are uncorrected. Ir spectra were obtained on a Perkin-Elmer Model 521 spectrophotometer. Pmr spectra were recorded on a Varian T-60 (60 MHz) spectrometer. Chemical shifts are reported as δ relative to TMS (δ = 0.0 ppm), using the following abbreviations: s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet. Mass spectra were obtained in an AEI Model MS902 spectrometer. Thin-layer chromatographs (tlc) were carried out on Silic AR-7GF to a distance of 15 cm. Spots were detected by visual examination under uv light and by development in iodine vapor.

1-Carbethoxymethyl-1-phenethylurea (**1**).

To a stirred ice-cooled sample (60 g., 0.289 mole) of the ethyl ester of *N*-phenethylglycine (4) was added dropwise 35.5 ml., (0.434 mole) of concentrated hydrochloric acid. With continued stirring and cooling was added dropwise a solution of 35.2 g. (0.434 mole) of potassium cyanate in 50 ml. of water. The mixture was stirred at room temperature for 20 hours and then was taken up in a mixture of chloroform and 10% hydrochloric acid. The chloroform layer was separated, washed to neutrality with water, and dried over anhydrous magnesium sulfate. Filtration and removal of the chloroform by distillation gave a viscous oil which crystallized on trituration with a small amount of ether to give 61 g. (84%) of colorless crystals, m.p. 78-79°. Two recrystallizations of a sample from benzene-pentane gave pure **1**, m.p. 80-81°; tlc (developed with an 85:15 mixture of benzene-methanol) Rf = 0.46; ir (chloroform): 3500 and 3420 (ν NH), 1745 and 1665 (ν C=O); pmr (deuteriochloroform): δ 1.27 [t (J = 6 Hz), 3H, $C(H_2)CH_3$], δ 2.92 [t (J = 7 Hz), 2H, $ArCH_2C(H_2)$], δ 3.57 [t (J = 7 Hz), 2H, $-NCH_2-C(H_2)$], δ 3.93 [(s, 2H, $-NCH_2C=O$], δ 4.21 [q (J = 6 Hz), 2H, $-OCH_2C(H_3)$], δ 4.70 [s (broad), 2H, $CONH_2$], δ 7.30 (s, 5H, C_6H_5).

Anal. Calcd. for $C_{13}H_{18}N_2O_3$: C, 62.38; H, 7.25; N, 11.19. Found: C, 62.63; H, 7.35; N, 11.35.

1-Phenethylhydantoin (**2a**).

(a) From **1**.

A stirred mixture of 42 g. (0.168 mole) of **1** and 150 ml. of 25% hydrochloric acid was heated on the steam bath for 4 hours and then cooled in ice. The product was collected at the filter, washed with cold water and dried: yield, 34 g. (99%), m.p. 178-180°. A sample was recrystallized from ethanol to give pure **2a**, m.p. 180-181°; ir (Nujol): 1768, 1720 (ν C=O); pmr (DMSO-d_6): δ 2.76 [t (J = 7 Hz), 2H, $ArCH_2C(H_2)$], δ 3.55 [t (J = 7 Hz), 2H, $-NCH_2C(H_2)$], δ 3.90 (s, 2H, $-NCH_2CO$), δ 7.31 (s, 5H, C_6H_5), δ 10.5-10.8 (m, 1H, NH): high resolution mass spectrum (50 eV) m/e 204.0893. Calcd. for $C_{11}H_{12}N_2O_2$: 204.0898.

Anal. Calcd. for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.92; N, 13.72. Found: C, 64.64; H, 5.99; N, 13.79.

(b) Brom Phenethylamine, Formaldehyde, Cyanide, and Cyanate.

To a stirred solution of 31.2 g. (0.3 mole) of sodium bisulfate in 75 ml. of water was added 22.5 ml. of 37% aqueous formaldehyde. The solution was warmed to 60° for 15 minutes, then cooled to 35°, and 36.3 g. (0.3 mole) of phenethylamine was added. After stirring at 35° for 2 hours, a solution of 14.7 g. (0.3 mole) of sodium cyanide in 40 ml. of water was added. The temperature increased spontaneously by 10° and the clear, pale yellow solution became cloudy. Stirring at room temperature was continued for 3 hours and the mixture was allowed to separate into 2 layers. The upper layer containing the aminonitrile was taken up in a little ether, separated and concentrated in a rotary evaporator at room temperature. The residual, pale yellow oil was cooled in an ice-salt bath and a solution of 30 ml. of concentrated hydrochloric acid in 120 ml. of water was added over 15 minutes, keeping the temperature below 10°. To this stirred, cold solution was added 27.0 g. (0.333 mole) of potassium cyanate in one portion, and stirring at 0° was continued for 1.5 hours. With continued cooling and stirring, 60 ml. of concentrated hydrochloric acid was slowly added, and the reaction mixture was stirred at room temperature for 15 hours, then at 90-95° for 2 hours. After cooling in ice for 3 hours, the precipitated product was collected at the filter, washed with cold water, slurried in chloroform, filtered, and dried. There was obtained 34.0 g. (55%) of **2a**, m.p. 178-180°, identical with the material prepared from **1**.

1-(*p*-Chlorophenethyl)hydantoin (**2b**).

By substituting *p*-chlorophenethylamine (15.6 g., 0.1 mole) for the phenethylamine in the foregoing procedure, a quantity of crude product (m.p. 125-135°) was obtained which was recrystallized twice from ethanol to give 10.1 g. (42%) of pure **2b**, m.p. 139-140°; ir (Nujol): 1760, 1720 (ν C=O); pmr (DMSO-d_6): δ 2.81 [t (J = 7 Hz), 2H, $ArCH_2C(H_2)$], δ 3.52 [t (J = 7 Hz), 2H, $-NCH_2C(H_2)$], δ 3.93 (s, 2H, $-NCH_2CO$), δ 7.38 (s, 4H, C_6H_4Cl), δ 10.5-10.8 (m, 1H, NH).

Anal. Calcd. for $C_{11}H_{11}ClN_2O_2$: C, 55.36; H, 4.65; N, 11.74. Found: C, 55.23; H, 4.73; N, 11.81.

1-Phenethyl-5-phenylhydantoin (**2c**, n = 2).

To an ice-cold stirred solution of 7.35 g. (0.15 mole) of sodium cyanide in 100 ml. of 70% aqueous acetic acid was added in one

portion, a mixture of 15.9 g. (0.15 mole) of benzaldehyde and 18.2 g. (0.15 mole) of phenethylamine. The mixture was stirred at room temperature for 3.5 hours, during which time a precipitate formed. Then 13.4 g. (0.165 mole) of solid potassium cyanate was added in one portion. The mixture warmed spontaneously to 40° and everything dissolved. The resulting light yellow solution was stirred at room temperature for 1 hour, then on the steam bath for another hour. After cooling to room temperature, 50 ml. of concentrated hydrochloric acid was added and the stirred mixture was heated on the steam bath for 2.5 hours. Precipitated product was filtered from the cooled reaction mixture, washed well with water and dried, m.p. 171-172°. One recrystallization from ethanol gave 25.4 g. (60%) of pure **2c** (n = 2), m.p. 172-173° literature (5) m.p. 173-175°; ir (chloroform): 3430 (ν NH), 1785, 1740 (ν C=O); pmr 1H, ArCHCO), δ 7.0-7.7 (m, 10H, $2C_6H_5$), δ 9.0-9.5 (m, 1H, NH).

1-Benzyl-5-phenylhydantoin (**2c**, n = 1).

By substituting benzylamine for phenethylamine in the foregoing procedure, there was obtained a 54% yield of pure **2c** (n = 1), m.p. 213-215° (literature (6) m.p. 210°); ir (Nujol): 1760, 1720 (ν C=O); pmr (DMSO-d_6): δ 3.85 [d (J = 16 Hz), 1H, ArCH(H)], δ 4.85 [d (J = 16 Hz), 1H, ArCH(H)], δ 4.98 (s, 1H, ArCHCO), δ 7.0-7.7 (m, 10H, $2C_6H_5$), δ 11.0-11.2 (m, 1H, NH).

1-(3-Phenylpropyl)-5-phenylhydantoin (**2c**, n = 3).

Likewise, by using γ-phenylpropylamine in place of phenethylamine, there was secured a 60% yield of **2c** (n = 3), m.p. 133-135°. Recrystallization of a sample from a DMSO-water mixture gave pure **2c** (n = 3), m.p. 135-136°; ir (chloroform): 3430 (ν NH), 1785, 1730 (ν C=O); pmr (deuteriochloroform): δ 1.5-4.0 (m, 6H, $ArCH_2CH_2CH_2N$), δ 4.85 (s, 1H, ArCHCO), δ 7.0-7.7 (m, 10H, $2C_6H_5$), δ 9.0-9.4 (m, 1H, NH).

Anal. Calcd. for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.18; H, 6.14; N, 9.68.

2,5,6,10b-Tetrahydroimidazo[5,1-*a*]isoquinoline-1,3-dione (**3a**).

(a) From the Hydantoin **2a**.

To a solution of 2.0 g. (0.01 mole) of **2a** in 15 ml. of glacial acetic acid (in oven-dried equipment) were added 2 drops of acetic anhydride followed by 1 ml. of a saturated solution of hydrogen bromide in glacial acetic acid. To this stirred solution warmed to 55° under an atmosphere of dry nitrogen was added dropwise over a period of 2 hours 1.74 g. (0.011 mole) of bromine. After an additional 1.5-hour period of heating (55°), the solvent was removed using a rotary evaporator. The oily residue was treated successively with two portions (15-20 ml.) of dry chloroform followed by removal of each portion on the rotary evaporator. The residue was then taken up in dry chloroform (15 ml.), cooled in an ice-salt bath and the stirred solution was treated first with 1 drop of a saturated solution of hydrogen bromide in glacial acetic acid, and then dropwise over 30 minutes with 5.2 g. (0.02 mole) of anhydrous stannic chloride. The ice-cooled mixture was stirred an additional 1.5 hours, treated with 100 ml. of 6*N* hydrochloric acid and allowed to stand overnight at room temperature. The mixture was heated on the steam bath for 3 hours, cooled, and extracted with chloroform. The dried (anhydrous magnesium sulfate) extract was concentrated to dryness to give 1.5 g. of crude product (m.p. 145-150°) which was recrystallized from ethanol, yield, 0.6 g. (30%), m.p. 175-177°. A sample was recrystallized further to give pure **3a**, m.p. 181-182°; tlc (developed with an 85:15 mixture of benzene-methanol) Rf = 0.63; ir (Nujol): 1775, 1715 (ν C=O); pmr (DMSO-d_6): δ 2.6-4.3 (m, 4H, $ArCH_2CH_2N$), δ 5.34 (s, 1H, ArCHCO), δ 7.1-7.8 (m, 4H, C_6H_4), δ 10.7-11.5 (m, 1H, NH); high resolution mass spectrum (70 eV) m/e 202.0734. Calcd. for $C_{11}H_{10}N_2O_2$: 202.0742.

Anal. Calcd. for $C_{11}H_{10}N_2O_2$: C, 65.33; H, 4.98; N, 13.85. Found: C, 65.45; H, 5.13; N, 13.89.

(b) From 3,4-Dihydroisoquinoline.

A stirred, ice-cooled mixture of 7.5 g. (0.057 mole) of 3,4-dihydroisoquinoline (7) and 50 ml. of water was treated with 5.5 g. of concentrated hydrochloric acid. The clear solution was allowed to warm to room temperature and a solution of 7.44 g. (0.114 mole) of potassium cyanide in water (20 ml.) was added dropwise (30 minutes). Then 15 ml. of glacial acetic acid was added to the slightly exothermic reaction, stirring was continued for 3.5 hours and a solution of 8 ml. of concentrated hydrochloric acid in 30 ml. of water was added, followed by 5.09 g. (0.063 mole) of solid potassium cyanate. After stirring at room temperature for 1 hour, the mixture was heated to 90-95° on the steam bath and treated with 20 ml. of concentrated hydrochloric acid. After one hour at this temperature the mixture was cooled in ice, product was collected at the filter, washed with water and dried, yield, 8.75 g. (76%) of **3a**, m.p. 178-180°, identical with the material prepared by the foregoing procedure.

9-Chloro-2,5,6,10b-tetrahydroimidazo[5,1-*a*]isoquinoline-1,3-dione (**3b**).

A 23.9-g. (0.1 mole) sample of the hydantoin **2b** was submitted to the same treatment (bromine, stannic chloride) as previously described for **2a** except that the bromination was carried out at 90-95° instead of at 55°. The product crystallized from the final concentrated chloroform extract in two crops, 12.1 g., m.p. 195-197°, and 3.5 g., m.p. 188-191° (total yield, 66%). A sample was recrystallized from chloroform to give pure **3b**, m.p. 197-198°; tlc (developed with a 90:10 mixture of benzene-methanol) Rf = 0.57; ir (Nujol): 1780, 1710 (ν C=O); pmr (DMSO-d_6): δ 2.6-4.3 (m, 4H, $ArCH_2CH_2N$), δ 5.32 (s, 1H, ArCHCO), δ 7.2-7.7 (m, 3H, C_6H_3), δ 10.8-11.3 (m, 1H, NH); high resolution mass spectrum (50 eV) m/e 236.0356. Calcd. for $C_{11}H_9ClN_2O_2$: 236.0352.

Anal. Calcd. for $C_{11}H_9ClN_2O_2$: C, 55.83; H, 3.83; N, 11.84. Found: C, 55.55; H, 3.81; N, 11.75.

2-Methyl-2,5,6,10b-tetrahydroimidazo[5,1-*a*]isoquinoline-1,3-dione (**4**).

A solution of 5.06 g. (0.025 mole) of **3a** in 15 ml. of dry dimethylformamide was added dropwise to a stirred suspension of 0.66 g. (0.0275 mole) of sodium hydride in 10 ml. of dimethylformamide. After addition was complete (30 minutes) the mixture was stirred for another 1.5 hours, treated with 3.47 g. (0.0275 mole) of dimethyl sulfate and stirred at room temperature overnight. The solvent was then removed in a rotary evaporator; and the residue was taken up in chloroform, washed with water, and dried over anhydrous magnesium sulfate. Filtration and removal of the solvent by distillation gave a crude solid that was recrystallized once from ethanol to give 3.05 g. (56%) of pure **4**, m.p. 154-155°; pmr (deuteriochloroform): δ 3.05 (s, 3H) showing the presence of *N*-methyl and not *C*-methyl.

Anal. Calcd. for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.95. Found: C, 66.49; H, 5.58; N, 12.92.

10b-Phenyl-2,5,6,10b-tetrahydroimidazo[5,1-*a*]isoquinoline-1,3-dione (**5**).

To a stirred, heated (90-95°) mixture of 16.5 g. (0.059 mole) of the hydantoin **2c** (n = 2), 85 ml. of glacial acetic acid, and 0.2 ml. of acetic anhydride was added dropwise (45 minutes) a solution of 10.4 g. (0.065 mole) of bromine in 20 ml. of glacial acetic acid containing a few drops of acetic anhydride. The mixture was heated

on the steam bath for an additional 2 hours, cooled and concentrated *in vacuo* in a rotary evaporator. The residue was treated with heptane (150-200 ml.) which also was removed by distillation in the evaporator. The nearly colorless solid residue was slurried in ether, collected at the filter, washed with more ether and dried to give 14.8 g. (90%) of pure **5**, m.p. 210-211°; tlc (developed with an 88:12 mixture of benzene-methanol) R_f = 0.82; ir (chloroform): 3425 (ν NH), 1782 and 1730 (ν C=O); pmr (deuteriochloroform): δ 2.6-4.2 (m, 4H, $ArCH_2CH_2N$), δ 7.2-8.2 (m, 9H, ArH), δ 9.0-9.3 (m, 1H, NH); high resolution mass spectrum (50 eV) m/e 278.1072. Calcd. for $C_{17}H_{14}N_2O_2$: 278.1055.

Anal. Calcd. for $C_{17}H_{14}N_2O_2$: C, 73.36; H, 5.07; O, 11.49. Found: C, 73.23; H, 5.24; O, 11.39.

2-Methyl-10b-phenyl-2,5,6,10b-tetrahydroimidazo[5,1-*a*]isoquinoline-1,3-dione (**6a**).

Using compound **5** in place of compound **3a** in the procedure described above for the preparation of **4** gave a 78% yield of **6a**, m.p. 164-165.5° (from ethanol); pmr (deuteriochloroform): δ 3.17 (s, 3H, NCH_3).

Anal. Calcd. for $C_{18}H_{16}N_2O_2$: C, 73.96; H, 5.52; N, 9.58. Found: C, 74.10; H, 5.57; N, 9.64.

2-(2-Dimethylaminoethyl)-10b-phenyl-2,5,6,10b-tetrahydroimidazo[5,1-*a*]isoquinoline-1,3-dione (**6b**).

By using 2-dimethylaminoethyl chloride in place of dimethyl sulfate in the alkylation of **5**, compound **6b** was obtained in 66% yield, m.p. 116-117° (from methanol).

Anal. Calcd. for $C_{21}H_{23}N_3O_2$: C, 72.18; H, 6.63; N, 12.03. Found: C, 72.34; H, 6.75; N, 12.13.

2-(3-Dimethylaminopropyl)-10b-phenyl-2,5,6,10b-tetrahydroimidazo[5,1-*a*]isoquinoline-1,3-dione Hydrochloride (**6c**).

The product obtained by alkylation of **5** with 3-dimethylaminopropyl chloride was an oily base which was converted to a crystalline hydrochloride (**6c**), m.p. 215-216° (from ethanol-ether), obtained in a 57% yield.

Anal. Calcd. for $C_{22}H_{26}ClN_3O_2$: C, 66.07; H, 6.55; N, 10.51. Found: C, 65.81; H, 6.55; N, 10.71.

2-(2-Diethylaminoethyl)-10b-phenyl-2,5,6,10b-tetrahydroimidazo-[5,1-*a*]isoquinoline-1,3-dione Hydrochloride (**6d**).

Likewise, alkylation of **5** with 2-diethylaminoethyl chloride resulted (45% yield) in a non-crystalline base, convertible to the hydrochloride (**6d**), m.p. 194-195° (from ethanol-ether).

Anal. Calcd. for $C_{23}H_{28}ClN_3O_2$: C, 66.74; H, 6.82; Cl, 8.56; N, 10.15. Found: C, 66.55; H, 7.01; Cl, 8.79; N, 10.13.

10b-Phenyl-2-phenylsulfonyl-2,5,6,10b-tetrahydroimidazo[5,1-*a*]-isoquinoline-1,3-dione (**6e**).

Treatment of the sodium salt of **5** with benzenesulfonyl chloride in the usual manner gave **6e** (43% yield), m.p. 190-191° (from benzene).

Anal. Calcd. for $C_{23}H_{18}N_2O_4S$: C, 66.02; H, 4.34; N, 6.69; O, 15.29. Found: C, 66.02; H, 4.34; N, 6.61; O, 15.45.

1-Benzyl-5-hydroxy-5-phenylhydantoin (**7a**).

Bromination of 8.0 g. (0.03 mole) of the hydantoin **2c** (n = 1) in the usual way (see preparation of **5**) gave a viscous yellow oil (10.7 g.) which contained bromine. This was dissolved in chloroform (35 ml.) and treated with anhydrous stannic chloride (15.6 g., 0.06 mole) in the usual way (see preparation of **3a**) except that reactants were kept at room temperature overnight before hydrolytic work-up. The only material isolated was 4.10 g. (49%) of **7a**, m.p. 189-191° (from isopropyl alcohol); ir (Nujol): 3415 (ν NH), 3260 (ν OH), 1790 and 1725 (ν C=O); pmr (DMSO-d_6): no peak near δ 4.98 (ArCHCO in **2c**, n = 1).

Anal. Calcd. for $C_{16}H_{14}N_2O_3$: C, 68.08; H, 5.00; N, 9.92. Found: C, 68.01; H, 4.97; N, 9.89.

The same product was obtained when anhydrous aluminum chloride was substituted for the stannic chloride. A bromine-free product, not fully characterized, was obtained when the intermediate bromo compound was simply stirred with ethanol at room temperature for several hours.

5-Hydroxy-5-phenyl-1-(3-phenylpropyl)hydantoin (**7b**).

Bromination and attempted cyclization of the hydantoin **2c** (n = 3) likewise led to a by-product glassy material which was purified by dissolving in benzene and passing through a silica gel column: tlc (developed with a 95:5 mixture of benzene-methanol) R_f = 0.35; ir (chloroform): 3325 (broad, ν bonded OH and NH), 1785 and 1725 (ν C=O); high resolution mass spectrum (50 eV) m/e 310.1302. Calcd. for $C_{18}H_{18}N_2O_3$: 310.1317; pmr (deuteriochloroform): no peak near δ 4.85 (ArCHCO in **2c**, n = 3).

Anal. Calcd. for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; O, 15.46. Found: C, 69.49; H, 5.99; O, 14.98.

The same product was formed when anhydrous aluminum chloride either in chloroform at room temperature or in 1,2-dichloroethane at reflux temperature was used. Also treatment of the intermediate bromo compound with silver hexafluoroantimonate in hot (90-95°) nitrobenzene led to **7b** after hydrolytic work-up.

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