Derivatives of 2,3,8,9-Tetrahydro-3-oxo-1*H*-benz[*de*]isoquinoline-1,9a-(7*H*)dicarboximide (1)

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Received August 7, 1980

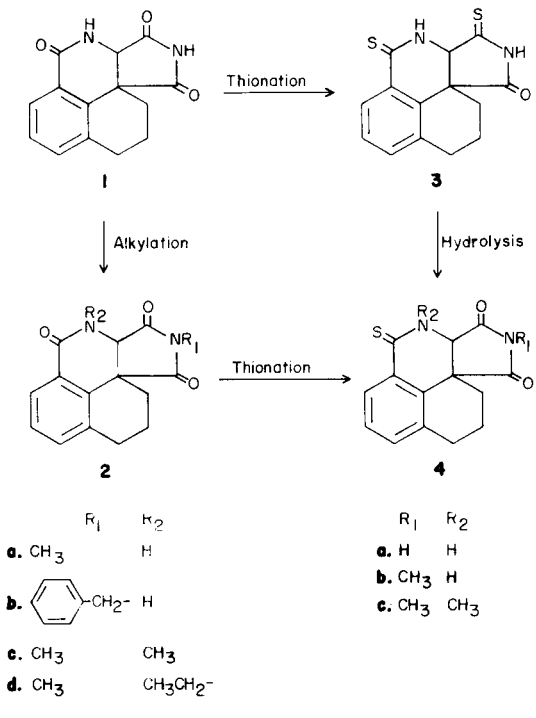
The synthesis of a series of derivatives of 2,3,8,9-tetrahydro-3-oxo-1*H*-benz[*de*]isoquinoline-1,9a-(7*H*)dicarboximide (**1**) are described. Alkylations and thionations of **1** produced a variety of interesting heterocycles. In addition, triazole and triazolone rings were fused to **1** to produce novel compounds. These structures were of interest as potential anticonvulsants.

J. Heterocyclic Chem., **18**, 79 (1981).

During the course of investigating novel succinimide heterocycles as potential anticonvusants, the isoquinoline **1** was prepared (2). While this compound itself was devoid of biological activity, further chemistry was carried out with the intent of preparing novel heterocycles of potential biological application.

Alkylation of **1** on the nitrogen of the succinimide and the lactam rings (Scheme I) produced compounds **2**.

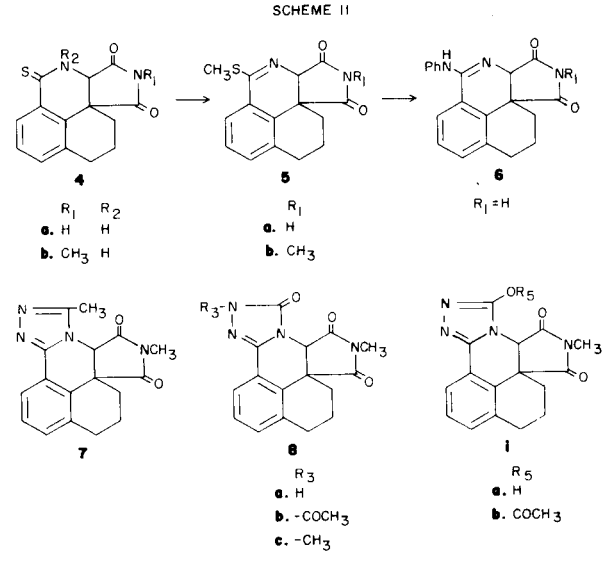
SCHEME I



Alkylation of the succinimide was accomplished utilizing potassium carbonate and the alkyl halide in dimethylformamide (3). Further alkylation of the nitrogen in the lactam ring was done using potassium hydride and the alkyl halide in anhydrous tetrahydrofuran at room temperature (4). In this manner, a series of four compounds **2a-d** were prepared which served to enhance the lipophillicity of the otherwise highly polar compound **1**.

Thionation of compound **1** was accomplished using phosphorus pentasulfide in pyridine at 90° (5) (Scheme I). The sole product isolated using these conditions was that resulting from dithionation to give compound **3** in good yield. Elemental analysis confirmed the presence of two sulfur atoms. The mass spectrum gave a base peak of M^+-87 for loss of a monothiosuccinimido fragment indicating incorporation of one sulfur on the succinimide ring and the remaining one in the lactam ring (2). The thiocarbonyl in the succinimide ring was assigned to position 3 due to the shift of the methine proton at position 3a from 4.25 ppm in compound **1** (2) to 4.48 ppm. In addition, compound **4a** (3a,4,10,11-tetrahydro-5-thioxo-9*H*-benzo[*de*]pyrrolo[3,4-*c*]isoquinoline-1,3-(2*H*)dione) has its own methine proton at 4.30 ppm indicating that removal of the thiocarbonyl in the succinimide ring produces a dramatic upfield shift which would only occur if it was adjacent to the methine proton. In fact, the methine protons at position 3a of compounds **1** and **4a** have very similar chemical shifts. Steric arguments also weigh in favor of assignments of the thiocarbonyl at position 3. The carbonyl at position 1 lies above the saturated ring and attack by the bulky pyridinium phosphorus pentasulfide complex (6) would be hindered. Position 3, however, is much more accessible.

SCHEME II



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Monothionation of compound **1** could not be accomplished; however, hydrolysis of the dithionated compound **3** using hydrazoic acid in concentrated sulfuric acid at room temperature followed by addition to ice water gave a good yield of monothionated compound **4a**. Again, elemental analysis confirmed the presence of one sulfur and the mass spectrum gave a base peak at M^{+} − 71 for loss of the succinimido group (2) indicating the sulfur was on the lactam ring. The reaction represents a novel conversion of a thiocarbonyl to a carbonyl group. The thiolactam remained uneffected by these conditions, even in the presence of excess azide.

Compounds **2a** and **c** were also thionated using the conditions described for compound **1**. In both cases, however, only monothionation occurred. Mass spectroscopy confirmed the presence of thiolactam and not thiosuccinimide which was substantiated by elemental analysis. Apparently, the presence of a methyl group on the succinimide nitrogen prevents attack of the thionating species, possibly due to steric inhibition.

Attempts to replace the sulfur in the thiolactams **4a** and **b** directly with amine nucleophiles were not successful although there are reports of similar conversions in the literature (5,7). Activation of this position was accomplished by formation of the methylthioimidates **5a** and **5b** (Scheme II) with methyl iodide in tetrahydrofuran and dimethyl sulfoxide, respectively. For **5a** no base was required in this reaction; however, for **5b** an equivalent of pyridine was necessary for complete reaction.

Replacement of the mercaptide with simple primary and secondary amines was difficult and often impossible; however, heating compound **5a** in aniline did produce the amidine **6**. Amine replacements may suffer from competition with the mercaptide leaving group which is an inherently good nucleophile. In contrast, replacement with acethydrazide or semicarbazide proceeded smoothly to give triazoles **7** and **8**. This reaction is probably driven to completion by irreversible cyclization with loss of water to produce **7** and ammonia to produce **8**.

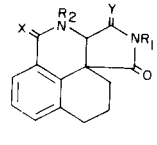
A series of 4 triazoles were prepared starting with thioimidate **5b** and condensing it with acethydrazide to produce compound **7** and semicarbazide to produce **8a**. Acetylation of **8a** with acetic anhydride gave the *N*-acetyltriazolone **8b** in good yield. Because triazolone **8a** may exist as the hydroxy tautomer **ia**, *O*-acetylation is possible to produce acetoxytriazole **ib**. However, this seems unlikely because triazoles of this type are known to prefer the triazolone tautomeric form (8). To check this, an analytical sample of triazolone **8a** was methylated (9). The methyl protons at position 2 of **8c** show a singlet at 3.34 ppm on the nmr spectrum which correlates well with literature values for these structures (8). The ultra-violet spectrum shows an absorbtion at 285 nm, close to the values for **8a** and **8b** which are 280 nm for both (see Table II). The methyl triazole **7** has 2 major absorptions at 262 and 271 nm and the tautomers **ia** and **ib** would be expected to have similar values due to the similarity of their respective chromophores. The infra-red absorption spectra for **8a** and **8b** were too complex in the carbonyl region for definitive assignment of peaks.

Mass Spectrometry.

The mass spectra were used to confirm structural assignments, based on some characteristic cleavage patterns that were obtained. Table I gives the major fragmentation modes for the substituted isoquinolines. The most diagnostic fragment obtained is that which results from loss of a succinimido fragment (M^{+} − 71), an *N*-methyl succinimido fragment (M^{+} − 85), or a thiosuccinimido fragment (M^{+} − 87) (2). The *N*-benzylated derivative (com-

Table I

Mass Spectral Fragmentation Modes for the Isoquinolinones and Isoquinolinethiones



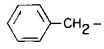
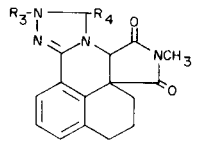
Compound Number	R_1	R_2	X	Y	Fragment (Relative Abundance)
1	H	H	O	O	256 (17.1), 255 (71.1), 185 (39.8), 184 (100.0)
2a	CH_3	H	O	O	270 (51.3), 242 (5.0), 185 (100.0)
2b		H	O	O	346 (99.7), 255 (12.2), 185 (100.0)
2c	CH_3	CH_3	O	O	284 (46.9), 199 (100.0)
2d	CH_3	$-CH_2CH_3$	O	O	298 (100), 283 (27.8), 270 (20.5), 269 (16.1), 213 (25.3)
3	H	H	S	S	288 (91.7), 201 (100.0)
4b	CH_3	H	S	O	286 (26.1), 271 (3.0), 207 (100.0), 201 (23.0)
4c	CH_3	CH_3	S	O	300 (38.8), 215 (39.5)

Table II

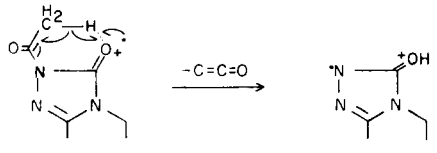
Fragmentation Modes and Ultraviolet Absorbtions for the Triazoloisoquinolines



Compound Number	R_3	R_4	Fragment (Relative Abundance)	Uv (ethanol) λ max (ε)
7	—	CH_3	308 (22.2), 223 (100.0), 154 (51.9)	262, 271 (2496)
8a	H	=O	310 (48.2), 225 (100.0)	280 (5586)
8b	CH_3OC-	=O	352 (9.6), 310 (100.0), 281 (9.9), 225 (99.8)	280 (6339)
8c	CH_3	=O	239 (100.0), 168 (70.4)	285 (9756)

pound **2b**) gives an $M^+ - 161$ for loss of an *N*-benzylsuccinimido group as its major fragment. The mass spectra were very useful for determing the thiocarbonyl position for the monothiocarbonyl compounds **4a-c**. These three compounds lose their succinimido groups, to give major fragments and none showed the loss of a thiosuccinimido fragment indicating the sulfur was part of a thiolactam ring. It is noteworthy that compound **3** loses a thiosuccinimido fragment ($M^+ - 87$) to give its base peak, indicating this is a viable fragmentation mode if it were present in the monothionated compounds.

The triazolosuccinimides **7** and **8a,b** also lose an $M^+ - 85$ fragment corresponding to an *N*-methylsuccinimido group. Compounds **7** and **8a** lose this fragment to yield their corresponding base peaks; however, the acetyltriazole **8b** loses ketene to give its base peak. This mode of fragmentation is similar to a McLafferty cleavage and probably proceeds *via* hydrogen transfer as shown below. The resulting compound then loses an *N*-methyl-



succinimido group as did the previous triazoles. If the acetoxytriazole **ib** was predominant, a fragment corresponding to loss of -$OCOCH_3$ could occur; however, no such fragment was detected, providing further evidence for the triazolone **8b** form. Structure **8a** did not show a molecular ion, but gave a base peak of $M^+ - 85$ that would correspond to loss of the *N*-methylsuccinimido group. This molecule then loses an m/e, 71 fragment that corresponds to $C_2H_3N_2O$ which is the 1,2,3 portion of the triazolo ring.

Biological Activity.

The succinimides **1, 2a-d, 3, 4a-c**, and **7** were screened for anticonvulsant activity by the National Institute of Neurological and Communicative Disorders and Stroke, under their Anticonvulsant Screening Project, using standard electroshock and Metrazole® induced seizures in mice. Compounds **3, 4c**, and **7** showed moderate protection against sc. Metrazole induced seizures. We are indebted to Dr. G. D. Gladding, Epilepsy Branch, Neurological Disorders Program, for these results.

EXPERIMENTAL

Melting points were determined on a "uni-melt" Thomas Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were obtained on a Perkin-Elmer Model 137-B infrared spectrometer. Ultraviolet spectra were obtained on a Cary 14 recording spectrophotometer. Nuclear magnetic resonance spectra were obtained on a Varian T-60A spectrometer and in certain instances on a Varian 220 MHz spectrometer. Mass spectra were obtained on a Hewlett-Packard Model 5992A GC/MS mass spectrometer or on a Varian CH7 mass spectrometer. Gas chromatographic analysis was accomplished using a Varian Model 3700 gas chromatograph equipped with a flame ionization detector. Elemental analyses were performed by Midwest Microlab, Indianapolis.

2,3,8,9-Tetrahydro-*N*-methyl-3-oxo-1*H*-benz[*de*]isoquinoline-1,9a-(7*H*)-dicarboximide (**2a**).

A mixture of 8.96 g. (0.035 mole) of **1** (2) and 5.38 g. (0.039 mole) of potassium carbonate in 125 ml. of DMF, to which was added 2.4 ml. (5.53 g., 0.039 mole) of methyl iodide, was stirred at room temperature for 12 hours. The mixture was poured into 600 ml. of water and let stand for 1 hour yielding a precipitate which was filtered, washed with water and dried to give 8.60 g. (0.0319 mole, 91%) of white crystals; m.p. 280-282°. This material is pure enough for subsequent reactions, but was recrystallized from 95% ethanol for analytical purposes; m.p. 280-281°; ir (potassium bromide): 3210 (N-H), 1800 (C=O, succinimide), 1745, 1730 (C=O, succinimide), 1670 cm^{-1} (C=O, lactam; nmr (trifluoroacetic acid): δ 2.20 (m, 4H, -$(CH_2)_2$-), 3.09 (m, 2H, -CH_2-), 3.20 (s, 3H, -CH_3-), 4.68 (s, 1H, methine), 7.60, 8.15 (m, 3H, aromatic); ms: m/e (relative abundance): M^+ 270 (51.3), 242 (5.0), 241 (21.3), 207 (12.0), 186 (100.0), 184 (37.5), 155 (10.3), 128 (15.0), 127 (13.8).

Anal. Calcd. for $C_{15}H_{14}N_2O_3$: C, 66.67; H, 5.19; N, 10.37. Found: C, 66.82; H, 5.27; N, 10.17.

2,3,8,9-Tetrahydro-*N*-benzyl-3-oxo-1*H*-benz[*de*]isoquinoline-1,9a-(7*H*)-dicarboximide (**2b**).

The reaction conditions were the same as for **2a**. The stoichiometry

was as follows: 2.56 g. (0.01 mole) of **1** and 1.52 g. (0.011 mole) of potassium carbonate, 1.31 ml. (1.88 g., 0.011 mole) of benzyl bromide, and 50 ml. of DMF. The yield of white crystals after recrystallization from ethanol was 2.91 g. (0.0084 mole, 84%), m.p. 230-231°; ir (potassium bromide): 3210 (N-H, lactam), 1780, 1730, 1720 (C=O, succinimide), 1670 cm^{-1} (C=O, lactam); nmr (deuteriochloroform/DMSO-d_6, 1.1): δ 1.92 (m, 4H, -$(CH_2)_2$-), 2.92 (m, 2H, -CH_2-), 4.39 (s, 1H, methine), 4.61 (s, 2H, -CH_2-), 7.61 (m, 3H, aromatic); ms: m/e (relative abundance) M^+ 346 (99.7), 255 (12.2), 185 (100.0), 182 (15.9), 170 (9.7), 168 (18.7), 166 (15.6), 155 (26.2).

Anal. Calcd. for $C_{21}H_{16}N_2O_3$: C, 72.83; H, 5.20; N, 8.09. Found: C, 72.81; H, 5.28; N, 8.12.

2,3,8,9-Tetrahydro-*N*,2-dimethyl-3-oxo-1*H*-benz[*de*]isoquinoline-1,9a-(7*H*)dicarboximide (**2c**).

To a stirred suspension of 10.80 g. (0.04 mole) of **2a** and 30 ml. (6.84 g., 0.048 mole) of methyl iodide in 350 ml. of dry THF was slowly added 7.63 g. (1.8 g., 0.045 mole, 23.6% oil suspension) of potassium hydride. Vigorous bubbling ensued and the reaction was complete after 2 hours at room temperature. The solvent was removed, the residue dissolved in ethyl acetate and extracted with water, saturated sodium chloride solution and dried over magnesium sulfate. The solvent was removed and the crystals were slurried in petroleum ether to remove the oil. The white crystals were filtered and dried to yield 10.34 g. (0.0364 mole, 91%) of **2c**, m.p. 215-217°. The material was recrystallized from ethanol, m.p. 216-218°; ir (potassium bromide): 1795 (C=O, succinimide), 1740, 1730 (C=O, succinimide), 1670 cm^{-1} (C=O, lactam); nmr (deuteriochloroform): δ 2.01 (m, 4H, -$(CH_2)_2$-), 2.99 (singlet superimposed on multiplet, 5H, -CH_3, -CH_2-), 3.20 (s, 5H, -CH_3), 4.11 (s, 1H, methine), 7.19, 7.99 (m, 3H, aromatic); ms: m/e (relative abundance) M^+ 284 (46.9), 255 (20.9), 199 (100.0), 198 (32.0), 155 (12.7), 149 (18.5), 137 (14.0), 136 (12.2), 135 (13.9).

Anal. Calcd. for $C_{16}H_{16}N_2O_3$: C, 67.61; H, 5.63; N, 9.86. Found: C, 67.68; H, 5.81; N, 9.58.

2,3,8,9-Tetrahydro-*N*-methyl-2-ethyl-3-oxo-1*H*-benz[*de*]isoquinoline-1,9a-(7*H*)dicarboximide (**2d**).

This procedure is similar to that utilized for the synthesis of compound **2c**, except ethyl iodide was substituted for methyl iodide. The stoichiometry was as follows: 2.70 g. (0.01 mole) of **2a**, 0.88 ml. (1.72 g., 0.011 mole) of ethyl iodide, 1.69 g. (0.4 g., 0.01 mole, 23.6% oil suspension) of potassium hydride, and 150 ml. of tetrahydrofuran. The crude yield was 2.38 g. (0.080 mole, 80%), m.p. 176-178°. Recrystallization from 95% ethanol gave white needles, m.p. 179-181°; ir (deuteriochloroform): 1800 (C=O, succinimide), 1740, 1730 (C=O, succinimide), 1670 cm^{-1} (C=O, lactam); nmr (deuteriochloroform): δ 1.19 (t, 3H, -CH_3-, ethyl), 2.0 (m, 4H, -$(CH_2)_2$-), 2.99 (singlet superimposed on multiplet, 5H, -CH_3, -CH_2-), 3.88 (q, 2H, -CH_2-, ethyl), 4.16 (s, 1H, methine), 7.25, 7.93 (m, 3H, aromatic); ms: m/e (relative abundance) M^+ 298 (100.0), 283 (27.8), 270 (20.5), 269 (16.1), 256 (10.7), 255 (10.9), 213 (25.3), 185 (32.6), 184 (14.9), 170 (25.2).

Anal. Calcd. for $C_{17}H_{16}N_2O_3$: C, 68.46; H, 6.04; N, 9.40. Found: C, 68.25; H, 5.94; N, 9.34.

3a,4,10,11-Tetrahydro-9*H*-benzo[*de*]pyrrolo[3,4-*c*]isoquinoline-1-oxo-3,5-(2*H*)dithione (**3**).

A solution of 1.75 g. (0.0068 mole) of **1** and 2.22 g. (0.01 mole) of phosphorus pentasulfide in 50 ml. of pyridine was heated under reflux in a nitrogen atmosphere for 12 hours, cooled and the pyridine removed. The yellow residue was slurried in 100 ml. of water, filtered and washed twice with water to yield 2.1 g. of crude crystals. Recrystallization from 95% ethanol gave 1.39 g. (0.0048 mole, 71%) of **3**, m.p. 284-286° dec.; ir (potassium bromide): 3200 (N-H), 1760 (C=O, succinimide), 1725 (C=O, succinimide), 1175 cm^{-1} (C=S, succinimide); nmr (DMSO-d_6/deuteriochloroform 1:1): δ 2.0 (m, 4H, -$(CH_2)_2$-), 2.98 (m, 2H, -CH_2-), 4.48 (s, 1H, methine), 7.36 (m, 3H, N-H superimposed on 2 aromatic protons), 8.18 (m, 1H, aromatic), 9.78 (s, 1H, succinimide); ms: m/e (relative abundance) 288 (91.7), 201 (100.0), 200 (23.4), 166 (8.1).

Anal. Calcd. for $C_{14}H_{12}N_2OS_2$: C, 58.33; H, 4.17; N, 9.72. Found: C, 58.23; H, 4.45; N, 9.46.

3a,4,10,11-Tetrahydro-5-thioxo-9*H*-benzo[*de*]pyrrolo[3,4-*c*]isoquinoline-1,3-(2*H*)dione (**4a**).

A solution of 8.64 g. (0.03 mole) of **3** in 225 ml. of concentrated sulfuric acid was cooled to 0° and 6.90 g. (0.031 mole) of sodium azide was added slowly. Vigorous bubbling ensued. The reaction was stirred for 2 hours, poured on ice and set for 2 hours. The yellow crystals were filtered, dried and recrystallized from acetone to give 6.90 g. (0.025 mole, 85%), m.p. 291-292° dec.; ir (potassium bromide): 3210 (N-H), 3110 (N-H), 1815 (C=O, succinimide), 1750, 1740 (C=O, succinimide), 1190 cm^{-1} (C=S, lactam); nmr (DMSO-d_6): δ 1.99 (m, 4H, -$(CH_2)_2$-), 3.91 (m, 2H, -CH_2-), 3.21 (broad singlet, 1H, N-H, lactam), 4.30 (s, 1H, methine), 7.40, 8.39 (m, 3H, aromatic), 10.68 (s, 1H, succinimide); ms: m/e (relative abundance) M^+ 272 (75.8), 256 (41.8), 201 (96.5), 200 (19.5), 192 (13.8), 185 (13.8), 166 (10.2), 160 (29.8), 128 (39.3), 96 (15.5).

Anal. Calcd. for $C_{14}H_{12}N_2O_2S$: C, 61.76; H, 4.41; N, 10.29; S, 11.76. Found: C, 61.50; H, 4.59; N, 10.25. S, 11.56.

3a,4,10,11-Tetrahydro-2-methyl-5-thioxo-9*H*-benzo[*de*]pyrrolo[3,4-*c*]isoquinoline-1,3-(2*H*)dione (**4b**).

A solution of 1.08 g. (4.0 mmoles) of **2a** and 1.00 g. (4.5 mmoles) of phosphorus pentasulfide in 50 ml. of pyridine was heated to 90° for 12 hours. The solvent was removed and the residue was triturated with 50 ml. of water. The resulting yellow crystals were filtered and washed twice with 3*N* hydrochloric acid, twice with water, and dried at 100° under vacuum for 4 hours to yield 1.08 g. (3.78 mmoles, 94.4%). Recrystallization from ethanol gave yellow crystals melting at 278-281° dec.; ir (potassium bromide): 3210 (N-H, lactam), 1800, 1740, 1725 (C=O, succinimide); nmr (DMSO-d_6): δ 1.99 (m, 4H, -CH{)}{-), 2.98 (m, 2H, -CH{-), 2.98 (s, 3H, -CH}), 4.44 (s, 1H, methine), 7.48 (m, 2H, aromatic), 8.40 (m, 1H, aromatic); ms: m/e (relative abundance) M^+ 286 (26.1), 271 (3.0), 270 (14.0), 207 (100.0), 201 (23.0), 193 (10.8).

Anal. Calcd. for $C_{15}H_{14}N_2O_2S$: C, 62.94; H, 4.90; N, 9.79. Found: C, 63.18; H, 4.88; N, 9.71.

3a,4,10,11-Tetrahydro-2,4-dimethyl-5-thioxo-9*H*-benzo[*de*]pyrrolo[3,4-*c*]-isoquinoline-1,3-(2*H*)dione (**4c**).

A solution of 1.42 g. (5.0 mmoles) of **2c** and 1.11 g. (5.0 mmoles) of phosphorus pentasulfide in 25 ml. of pyridine was heated to reflux under a nitrogen atmosphere for 12 hours. After this time, an additional 0.55 g. (2.5 mmoles) of phosphorus pentasulfide was added and the reaction was heated to reflux for an additional 4 hours. The pyridine was then removed, the residue dissolved in ethyl acetate and extracted twice with 3*N* hydrochloric acid, once with water and once with saturated sodium chloride solution. After drying over magnesium sulfate, the solvent was removed and the yellow solid recrystallized from ethanol to give 1.21 g. (4.0 mmoles, 80%) of yellow crystals; m.p. 190-192°; ir (potassium bromide): 1810, 1740, 1720 cm^{-1} (C=O, succinimide); nmr (deuteriochloroform): δ 2.00 (m, 4H, -$(CH_2)_2$-), 3.01 (m, 2H, -CH_2-), 3.03 (s, 3H, -CH_3), 3.72 (s, 3H, -CH_3), 4.25 (s, 1H, methine), 7.39 (s, 2H, aromatic), 9.33 (m, 1H, aromatic); ms: m/e (relative abundance) M^+ (38.8), 299 (5.9), 215 (39.5), 214 (14.1), 199 (22.4), 182 (11.2), 171 (10.2), 169.1 (10.9), 153 (13.5), 42 (100.0).

Anal. Calcd. for $C_{16}H_{16}N_2O_2S$: C, 64.00; H, 5.33; N, 9.33; S, 10.67. Found: C, 63.71; H, 5.08; N, 9.02; S, 10.82.

8,9-Dihydro-3-methylthio-1*H*-benz[*de*]isoquinoline-1,9a-(7*H*)dicarboximide (**5a**).

Compound **4a**, 2.72 g. (0.01 mole) was dissolved in 100 ml. of anhydrous THF, 0.93 ml. (2.13 g., 0.015 mole) of methyl iodide was added and the solution heated under reflux for 12 hours. The solvent was removed and 2.15 g. of a yellow solid was obtained, m.p. 275-279°. Recrystallization from acetone gave 1.80 g. (0.0064 mole, 64%) of **5a**, m.p. 279-280°; ir (potassium bromide): 3210 cm^{-1} (N-H, succinimide), 1800 cm^{-1} (N-H, succinimide), 1800 cm^{-1} (C=O, succinimide), 1740, 1720 cm^{-1} (C=O, succinimide); nmr (DMSO-d_6): δ 1.96 (m, 4H, -$(CH_2)_2$-), 2.34 (s, 3H, -CH_3), 2.88 (m, 2H, -CH_2-), 4.40 (s, 1H, methine), 7.39 (m, 3H, aromatic), 11.45 (s, 1H, succinimide).

Anal. Calcd. for $C_{15}H_{14}N_2O_2S$: C, 62.94; H, 4.90; N, 9.80; S, 11.19. Found: C, 62.79; H, 4.87; N, 9.86; S, 11.15.

8,9-Dihydro-*N*-methyl-3-methylthio-1*H*-benz[*de*]isoquinoline-1,9a-(7*H*)-dicarboximide (**5b**).

To a solution of 1.25 g. (0.0044 mole) of **4b** in 50 ml. of DMSO was added 0.40 ml. (0.40 g., 0.005 mole) pyridine and 0.31 g. (0.71 g., 0.005 mole) of methyl iodide. The reaction was heated to 100° with stirring for 6 hours, cooled to room temperature and poured on 100 ml. of ice water. The yellow precipitate was extracted with 50 ml. of ethyl acetate and the organic layer washed twice with water, once with saturated sodium chloride and dried over magnesium sulfate. The yield of compound **5a** after removal of solvent was 0.86 g. (0.0029 mole, 65.9%). Recrystallization from 95% ethanol gave white crystals melting at 201-202°; ir (deuteriochloroform): 1790, 1760, 1700 (C=O, succinimide), 1690 cm^{-1} (C=N, imidate); nmr (deuteriochloroform): δ 1.95 (m, 4H, -$(CH_2)_2$-), 2.41 (s, 3H, -CH_3), 3.01 (s, 3H, -CH_3), 3.05 (s, 2H, -CH_2-), 4.41 (s, 1H, methine), 7.45 (s, 3H, aromatic); ms: m/e (relative abundance) M^+ 300 (67.1), 299 (100.0), 257 (17.6), 215 (28.3), 214 (78.4), 186 (10.0), 182 (11.8), 170 (10.6), 169 (33.8), 168 (34.5), 167 (16.8), 166 (16.0).

Anal. Calcd. for $C_{16}H_{16}N_2O_2S$: C, 64.00; H, 5.33; N, 9.33; S, 10.67. Found: C, 63.91; H, 5.30; N, 9.21; S, 10.87.

8,9-Dihydro-3-anilino-1*H*-benz[*de*]isoquinoline-1,9a-(7*H*)dicarboximide (**6**).

To 1 ml. of aniline was added 100 mg. (0.35 mmole) of **5a** and the solution heated on a steam bath for 1 hour. During this time, a test for evolution of methanethiol with lead acetate paper was positive. The solution was cooled and crystals formed which were filtered and dried to give 74.9 mg. (0.23 mmole, 65%) of white crystals; m.p. 216-220°. Recrystallization from ethanol for analysis gave white crystals, m.p. 221-223°; ir (potassium bromide): 3500 (N-H, amidine), 3210 (N-H, succinimide), 1810 (C=O, succinimide), 1750, 1730 cm^{-1} (C=O, succinimide); nmr (DMSO-d_6): δ 1.99 (m, 4H, -$(CH_2)_2$-), 2.95 (m, 2H, -CH_2-), 4.28 (s, 1H, methine), 6.50-8.15 (m, 9H, N-H, amidine superimposed on aromatic).

Anal. Calcd. for $C_{20}H_{17}N_3O_2$: C, 72.51; H, 5.14; N, 12.69. Found: C, 72.36; H, 5.09; N, 12.51.

3a,5,6,11-Tetrahydro-3,*N*-dimethyltriazolo-4*H*,7*H*-[4,5-*b*]benz[*de*]isoquinoline-4,4a-dicarboximide (**7**).

To 50 ml. of DMSO was added 1.50 g. (0.005 mole) of the thioimidate **5b** and 0.41 g. (0.0055 mole) of acethydrazide. The solution was heated to 120° and the evolution of methanethiol was monitored by the yellow color obtained using lead acetate paper. After 5 hours the reaction mixture was poured into 100 ml. of water whereupon crystallization ensued. The white crystals were filtered and dried giving 1.14 g. (0.0037 mole, 74%) of **7b** which after crystallization from DMF melted at 309-310°; ir (potassium bromide): 1800, 1740, 1720 (C=O, succinimide), 1690 cm^{-1} (C=N, triazole); uv (ethanol): λ max (nm) 262,271 (ε, 2496), 283 (ε, 1604); nmr (trifluoroacetic acid): δ 2.31 (m, 4H, -$(CH_2)_2$), 3.10 (s, 3H, -CH_3), 3.11 (s, 3H, -CH_3), 3.15 (multiplet superimposed on methyl peaks, 2H, -CH_2-), 5.40 (s, 1H, methine), 7.59 (m, 2H, aromatic), 8.01 (m, 1H, aromatic); ms: m/e (relative abundance) M^+ 308 (22.2), 223 (100.0), 155 (63.0), 154 (51.9), 153 (22.2), 152 (18.5), 149 (33.3), 140 (51.9), 128 (25.9), 127 (51.9), 115 (29.6), 111 (18.5).

Anal. Calcd. for $C_{17}H_{16}N_4O_2$: C, 66.23; H, 5.19; N, 18.18. Found: C, 66.50; H, 4.91; N, 18.29.

2,3,3a,5,6,11-Hexahydro-*N*-methyltriazolo-4*H*,7*H*-[4,5-*b*]benz[*de*]isoquinoline-4,4a-dicarboximido-3-one (**8a**).

To 25 ml. of DMSO was added 1.0 g. (3.3 mmoles) of thioimidate **5b**, 0.28 ml. (0.27 g., 3.5 mmoles) of pyridine and 0.39 g. (3.5 mmoles) of semicarbazide hydrochloride. The reaction mixture was heated to 110° for 12 hours with stirring. After cooling the mixture to room temperature and pouring on ice crystals were formed. Filtration and recrystallization from DMF gave white crystals melting in excess of 320°; ir (potassium bromide): 3110 (NH, OH, tautomers, triazole), 1780, 1720, 1710 (C=O, succinimide), 1670 cm^{-1} (C=O, triazolone); uv (ethanol): λ max 280 (ε, 5586), 295 (ε, 3603); nmr (trifluoroacetic acid): δ 2.28 (m, 4H, -$(CH_2)_2$-), 3.21 (m, 5H, -CH_3 superimposed on -CH_2-), 5.22 (s, 1H, methine), 7.71 (m, 3H, aromatic); ms: m/e (relative abundance): M^+ 310 (48.2), 309 (4.0), 225 (100.0), 207 (20.5), 170 (10.9), 169 (61.4), 168 (23.8).

Anal. Calcd. for $C_{16}H_{14}N_4O_3$: C, 61.94; H, 4.52; N, 18.06. Found: C, 61.69; H, 4.53; N, 17.83.

2,3,3a,5,6,11-Hexahydro-2-acetyl-*N*-methyltriazolo-4,7*H*-[4,5-*b*]benz[*de*]-isoquinoline-4,4a-dicarboximido-3-one (**8b**).

In 2 ml. of dry pyridine was placed 0.155 g. (0.5 mmole) of **8a** and 0.1 ml. (0.102 g., 1.0 mmole) of acetic anhydride. The solution was heated to 100° for 20 minutes, then cooled in ice. White crystals formed which were filtered and washed with ether 3 times. Recrystallization from DMF gave 0.122 g. (0.35 mmole, 70%) of **8b**, m.p. 209° dec.; ir (potassium bromide): 1810, 1750, 1720 (C=O, succinimide), 1670 (C=O, triazolone), 1660 cm^{-1} (C=O, acetyl); uv (ethanol): λ max (nm) 280 (ε, 6339), 295 (ε, 2983); nmr (trifluoroacetic acid): δ 2.21 (m, 4H, -$(CH_2)_2$-), 2.75 (s, 3H, -CH_3), 3.06 (m, 5H, -CH_3 superimposed on -CH_2-), 5.15 (s, 1H, methine), 7.48 (m, 2H, aromatic), 7.90 (m, 1H, aromatic); ms: m/e (relative abundance) M^+ 352 (9.6), 310 (100.0), 281 (9.9), 225 (99.8), 207 (57.1), 169 (68.6), 154 (17.5), 153 (19.1), 127 (11.6).

Anal. Calcd. for $C_{18}H_{16}N_4O_4$: C, 61.36; H, 4.55; N, 15.91. Found: C, 60.87; H, 4.78; N, 15.90.

2,3,3a,5,6,11-Hexahydro-2,*N*-dimethyltriazolo-4*H*,7*H*-[4,5-*b*]benz[*de*]-isoquinoline-4,4a-dicarboximido-3-one (**8c**) (9).

To a solution of 10 mg. (0.032 mole) of compound **8a** in 1 ml. of DMF was added 4.45 mg. (0.032 mole) of potassium carbonate and 2 ml. (4.54 mg., 0.032 mmole) of methyl iodide. The reaction mixture was heated at 50° for 48 hours then the solvent removed under reduced pressure. The residue was stirred in 1 ml. of water and the crystals were filtered yielding 3.2 mg. (0.0099 mole, 30.9%), m.p. 249-250°; ir (potassium bromide): 1810, 1760, 1740 cm^{-1} (C=O, succinimide); uv (ethanol): λ max (nm) 285 (ε, 9756); nmr (DMSO-d_6): δ 2.04 (m, 4H, -$(CH_2)_2$-), 2.84 (s, 3H, -CH_3), 3.02 (m, 2H, -CH_2-), 3.34 (s, 3H, -CH_3), 4.91 (s, 1H, methine), 7.36 (m, 2H, aromatic), 7.66 (m, 1H, aromatic); ms: m/e (relative abundance) 239 (100.0), 168 (70.4), 167 (22.2), 166 (29.6), 154 (25.9), 153 (40.7), 141 (25.9), 140 (59.3), 127 (25.9).

REFERENCES AND NOTES

(1) Contribution No. 3554. Taken from a thesis submitted by R. Y. to Indiana University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, July 1980.

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(9) Compound **8c** was prepared from an analytical sample of **8a** and was not analyzed. However, nmr, ir and uv data are consistent with values for the other triazoles. In addition, the mass spectrum gives a base peak at m/e 239. While there is no molecular ion, the base peak corresponds to $M^+ - 85$ which is a loss of the *N*-methyl succinimido group characteristic of the succinimides in this series. For the synthesis and further physical data, see the Experimental.