Some Fused-Ring Succinimides as Potential Anticonvulsants (1)

E. Campaigne and Richard Yodice

Chemistry Laboratories, Indiana University, Bloomington, Indiana 47405

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The syntheses of two compounds, which are fused-ring succinimides, prepared as potential anticonvulsants, are described. The compounds are 3,4,5,6-tetrahydro-7-methyl-6-oxoindeno[7,1-*bc*]thiepin-4a,5-(2*H*)dicarboximide and 6,7,8,9-tetrahydro-2-oxo-1*H*-benz[*cd*]azulene-1,9a-(2*H*)dicarboximide. The spirodioxolane of the latter compound was also prepared by ketalization.

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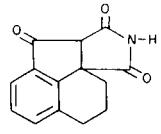
Compound **1**, 3a,4,5,6-tetrahydrosuccinimido[3,4-*b*]acenaphthen-10-one, has been shown to be a potent anticonvulsant to both electroshock and metrazole induced seizures in mice (2). Although it has very low toxicity, clinical trials have shown it to induce certain undesirable psychological side effects (3).



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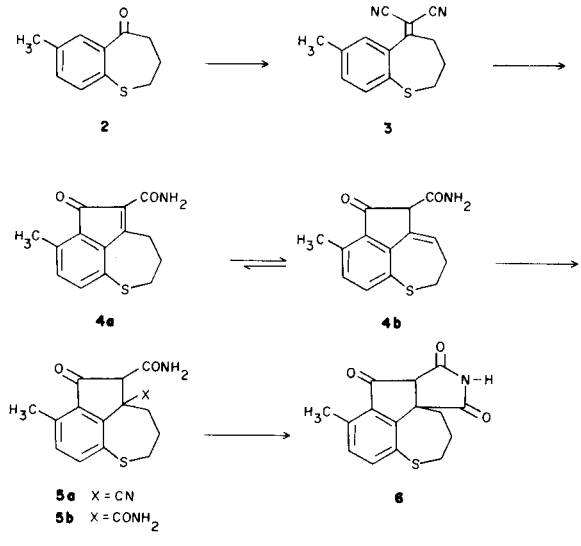
The synthesis of three related structures (compounds **6**, **11**, **12**, Schemes I and II) represent initial attempts to produce an equally potent anticonvulsant while reducing any side effects. The structural variations involve an overall one carbon homologation of the saturated ring and also introduction of a heteroatom into the ring. Compound **11** was ketalized to test the necessity for the ketone function.

The initial compound synthesized was the sulfur containing heterocycle, **6**, 3,4,5,6-tetrahydro-7-methyl-6-oxoindeno[7,1-*bc*]thiepin-4a,5-(2*H*)dicarboximide. Scheme I indicates the route which was utilized to produce this compound.

The readily available ketone **2** (4) was condensed with malononitrile in aqueous ethanol with a β-alanine catalyst according to the method of Prout (5). This method gave yields of ylidenemalononitrile **3** in the 80-90% range and was found to be superior to the procedure by Mowry (6), which utilized benzene with an ammonium acetate catalyst. The latter method had been used to synthesize compound **3** in 38% yield (7).

Treatment of ylidenemalononitrile **3** with concentrated sulfuric acid at room temperature afforded a 2:1 mixture of double bond isomers **4a** and **4b**, respectively. This result is in contrast to earlier results reported, in which only isomer **4a** was obtained (7,8). The methyl group in position 7 serves to prevent sulfonation of the ring. Recrystallization of the mixture from 95% ethanol produced exclusively the white isomer **4b**. This could be isomerized to a mixture containing 65% (measured by nmr integration) of the orange colored conjugated isomer

Scheme I



Scheme II

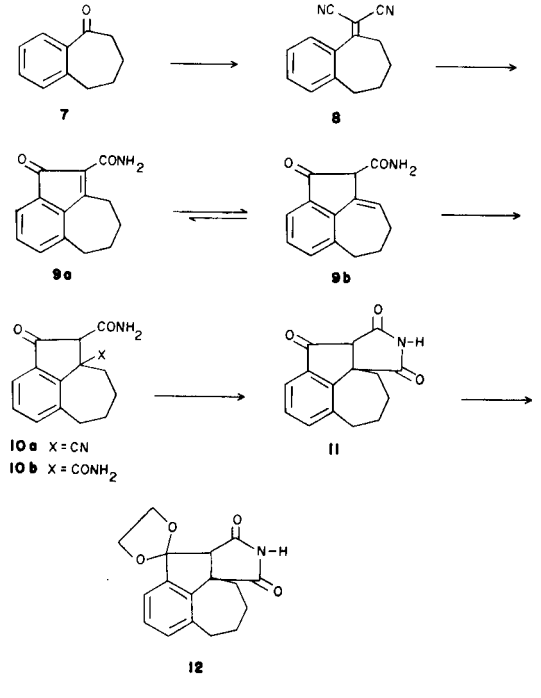


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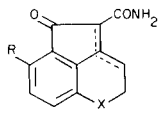
Table 1

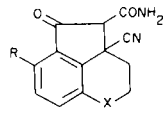
Major Fragmentation Modes of the Keto-Amides



Compound No.	X	R	Y	Fragment	Relative Abundance $M^+ - Y$
	$-CH_2-$	H	17	NH_3	100.00
			44	$CONH_2$	14.01
9	$-(CH_2)_2-$	H	17	NH_3	49.74
			44	$CONH_2$	24.88
4	$-CH_2-S-$	$-CH_3$	17	NH_3	100.00
			44	$CONH_2$	6.77

Table 2

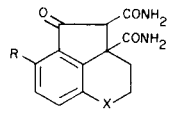
Major Fragmentation Modes of the Cyanide Addition Products



Compound No.	X	R	Y	Fragment	Relative Abundance $M^+ - Y$
	$-CH_2-$	H	17	NH_3	100.00
			27	HCN	10.59
			44	$CONH_2$	34.87
10a	$-(CH_2)_2-$	H	17	NH_3	100.00
			27	HCN	20.32
			44	$CONH_2$	85.01
5a	$-CH_2-S-$	$-CH_3$	17	NH_3	100.00
			27	HCN	3.87
			44	$CONH_2$	42.02

Table 3

Major Fragmentation Mode of the Diamides



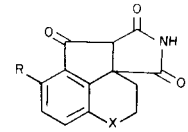
Compound No.	X	R	Y	Fragment	Relative Abundance $M^+ - Y$
	$-CH_2-$	H	44	$CONH_2$	38.18
10b	$-(CH_2)_2-$	H	44	$CONH_2$	45.89
5b	$-CH_2-S-$	$-CH_3$	44	$CONH_2$	29.99

4a by dissolving it in pyridine and allowing it to stand overnight. Addition of water and extraction with chloroform gave the mixture of isomers.

Hydrocyanation of the mixture **4a** and **4b**, which effectively trapped **4a**, was carried out in a THF/water mixture with potassium cyanide to produce **5a**. Treatment of the unconjugated isomer **4b** under the same conditions also produced the desired nitrile **5a**. This indicates an equilibration must take place in solution which produces exclusively the 1,4-addition product. An indication of isomerization to the conjugated structure **4a** is the appearance of a red color upon dissolving the white isomer **4b** in THF/water.

Table 4

Major Fragmentation Mode of the Succinimides



Compound No.	X	R	Y	Fragment	Relative Abundance $M^+ - Y$
1	$-CH_2-$	H	71	C_2HNO_2	100.00
11	$-(CH_2)_2-$	H	71	C_2HNO_2	100.00
6	$-CH_2-S-$	$-CH_3$	71	C_2HNO_2	94.55
12 (a)	$-(CH_2)_2-$	H	71	C_2HNO_2	37.05

(a) Compound **12** is the ketal, where the ketone is replaced by a $C_2H_4O_2$ group.

Hydrolysis of the nitrile **5a** to the carboxamide was readily accomplished and ring closure of the resulting diamide **5b** to the desired succinimide **6** followed the method previously reported (2). Direct conversion of **5a** to **6** resulted in overall lower yields.

Structure **11**, 6,7,8,9-tetrahydro-2-oxo-1*H*-benz[*cd*]-azulene-1,9a-(2*H*)dicarboximide, was synthesized in an analogous fashion starting from benzosuberone **7** (Scheme II). Prout's conditions afforded ylidenemalononitrile adduct **8**, which was cyclized in concentrated sulfuric acid to produce exclusively isomer **9b**. Presumably, isomer **9a** exists to a small extent in solution, which turns yellow on warming. Compound **9a** may be trapped by the addition of potassium cyanide to afford exclusively the 1,4-addition product **10a** in good yield. Attempts to isomerize compound **9b** to the conjugated isomer **9a** by dissolving it in pyridine were not successful.

Hydrolysis of nitrile **10a** to produce the dicarboxamide **10b** and subsequent ring closure to yield the desired succinimide **11** were carried out using the same procedures as those for compound **6**. Ketalization using standard conditions (9) afforded compound **12** in good yield.

Mass Spectroscopy.

The mass spectroscopic data were used to confirm structure for the compounds synthesized, due to several characteristic fragmentation patterns. Table 1 shows a competing mechanism for amide fragmentation. The major mode of fragmentation is loss of ammonia, as can be

seen by the high relative abundance of the remaining fragment. Loss of ammonia is always followed by loss of a —:C≡O: fragment. The second less favorable mode of fragmentation is loss of $CONH_2$ which is the usual fragment for most carboxamides.

Possibly the nitrogen atom removes a proton from the saturated ring and leaves as a neutral molecule of ammonia. Compound **9** (Table 1, line 2) does not exhibit as great a tendency to fragment in this mode as do the other compounds. This may be due to the preference of this compound to have the double bond exo to the 5-membered ring, thereby conformationally inhibiting this fragmentation. It should be noted that the more usual carboxamide cleavage occurs in a higher proportion for **9**.

Table 2 shows the fragmentation modes for the cyano series. Again the major mode of fragmentation is loss of ammonia. The secondary fragment in this mode is loss of m/e 27, which corresponds to loss of HCN.

A second mode of fragmentation involves the initial loss of HCN. As can be seen in Table 2, this is the least favorable mode; however, after its occurrence, the resulting molecule appears to fragment similar to the amides in Table 1. The resulting molecule after HCN loss would resemble and may in fact be identical to the amide precursor.

The third mode of fragmentation gives an m/e 44 which is likely to be the loss of a carboxamide group. This is a moderately favorable fragment as can be seen from the relative abundances.

The diamides exhibit only one fragmentation mode. As can be seen in Table 3, in all cases the predominant fragment is loss of m/e 44 corresponding to loss of the carboxamide. The resulting molecule, in all cases, then loses a fragment of m/e 17 corresponding to ammonia, to give the base peak. This is typical of the carboxamide precursor molecules. The molecule then loses a fragment of m/e 28 corresponding to the remaining carbonyl of the amide.

The succinimides shown in Table 4 all give a fragment of m/e 71 corresponding to a loss of the dicarboxamido functionality. This mode of fragmentation is the only one detected and in two out of four compounds shown, it yields the base peak. Compound **12** shows a much smaller relative abundance than the other structures due to alternate fragmentation of the ketal.

Biological Activity.

The succinimides **6, 11** and **12** 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. Only compound **11** showed weak anticonvulsant activity. 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. Nmr spectra were determined with a Varian T60A spectrometer using tetramethylsilane as an internal standard. Mass spectral analyses were performed on a Varian MAT CH7 at 70 eV ionization potential. Eastman chromatogram sheets (13181 Silica gel with fluorescent indicator No. 6060) were used for thin layer chromatography. Elemental analyses were performed by Midwest Microlab, Indianapolis.

7-Methyl-2,3,4,5-tetrahydrobenzo[*b*]thiepin-5-one (**2**).

This compound was synthesized according to a previous procedure (4). The precursor, *p*-tolythiobutyric acid, was synthesized according to the procedure by Reppe (10) and is summarized as follows. A mixture of 24.8 g. (0.2 mole) of *p*-thiocresol, 4.6 g. (0.2 mole) of sodium metal, and 16.13 ml. (18.06 g., 0.21 mole) of butyrolactone in 200 ml. of absolute ethanol afforded 31.46 g. (0.15 mole, 74.9%) of the acid as white crystals, m.p. 79-81° (lit. (10) m.p. 81°). Ring closure of 21.0 g. (0.1 mole) of this acid in 200 g. of polyphosphoric acid afforded, after distillation, 17.8 g. (0.093 mole, 93%) of ketone **2** as a colorless oil, b.p. 145-150°/5 mm (lit. (4) b.p. 138-142°/0.7 mm), ir (deuteriochloroform): 1660 cm^{-1} (C=O).

7-Methyl-2,3,4,5-tetrahydrobenzo[*b*]thiepin-5-ylidenemalononitrile (**3**).

This compound was previously reported by Schneller and Clough (7). The following procedure represents an improved yield based on a modification of the general method of Prout (5). To a solution of 15.5 g. (0.097 mole) of **2** in 50 ml. of 90% ethanol was added 7.69 g. (0.116 mole) of malononitrile and 50 mg. of β-alanine. The mixture was heated under reflux for 48 hours. The solvent was removed and the residue dissolved in 50 ml. of ether. The ethereal solution was extracted with 50 ml. of water, 50 ml. of 3*N* hydrochloric acid, 50 ml. of water and 50 ml. of saturated salt solution and dried over magnesium sulfate. The solution was filtered and the ether removed. The residue was recrystallized from ethanol to form 13.2 g. of yellow crystals, which were collected and dried. To the mother liquor was added 5 ml. of water, 2.5 g. of malononitrile and 25 mg. of β-alanine. Repeating the procedure above gave an additional 4.6 g. of product. The total yield of **3** was 17.8 g. (0.085 mole, 87.7%), m.p. 109-110° (lit (7) m.p. 109-110°); ir (potassium bromide): 2220 cm^{-1} (CN); nmr (deuteriochloroform): δ 2.38 (m, 5H, CH_3, $-CH_2-$), 2.90 (m, 4H, $-(CH_2)_2-$), 7.35 (m, 3H, aromatic).

3,4-Dihydro-2*H*-7-methyl-6-oxoindeno[7,1-*bc*]thiepin-5-carboxamide (**4a**).

This compound was also reported by Schneller and Clough (7). Due to difficulty in reproducing their procedure, a modification of the conditions was used, and is described below.

To 125 ml. of concentrated sulfuric acid was added 5.0 g. (0.021 mole) of ylidenemalononitrile **3** with stirring. The deep blue solution was stirred for 18 hours at room temperature, then poured on crushed ice. After sitting for 4 hours, the orange crystals were filtered and dried at 100° overnight. The yield was 4.63 g. (0.0179 mole, 85.9%) of product which was approximately a 2:1 mixture of double bond isomers **4a** and **4b**, 2,3-dihydro-7-methyl-6-oxoindano[7,1-*bc*]thiepin-5-carboxamide, respectively, as determined by nmr, m.p. 175-180°; ir (deuteriochloroform): 3590, 3390 (NH_2), 1710 (C=O, ketone), 1670 cm^{-} (C=O, amide); nmr (DMSO-d_6): compound **4a**, δ 3.1 (t, 2H, $-CH_2-$, area 10); compound **4b**, δ 3.98 (s, 1H, methine, area 12); ms: m/e (relative abundance) M^+ 259 (100.0), 243 (12.7), 242 (86.7), 241 (12.2), 228 (8.7), 227 (82.1), 216 (40.0), 215 (34.4), 214 (55.6), 213 (11.1), 201 (59.1), 187 (12.5), 186 (15.8), 185 (22.0), 184 (16.7), 183 (18.0), 182 (8.0), 181 (10.7), 172 (23.2), 171 (42.3), 153 (13.2), 152 (16.1).

This material was used directly in the next step. However, recrystallization of a sample from ethanol provided a high yield of the white isomer **4b**, m.p. 184-185°; nmr (deuteriochloroform): δ 2.51 (s, 3H, CH_3), 2.95 (m, 4H, $-(CH_2)_2-$), 3.98 (s, 1H, methine), 5.64 (s, 1H, NH), 6.41 (broad singlet, 1H, vinyl), 6.59 (s, 1H, NH), 6.98 (d, 1H, aromatic), 7.45 (d,

1H, aromatic). For analytical purposes, 0.45 g. of the mixture was purified on a column of 30 g. of silica gel, eluting with diethyl ether. The red crystals of structure **4a** obtained were dried and weighed 0.06 g., m.p. 168-170° (lit. (7) m.p. 175°); nmr (deuteriochloroform): δ 2.45 (m, 5H, CH_3, $-CH_2-$), 3.1 (t, 2H, $-CH_2-$), 5.8 (s, 1H, NH), 6.9 (d, 1H, aromatic), 7.3 (d, 1H, aromatic), 7.9 (s, 1H, NH).

3,4,5,6-Tetrahydro-7-methyl-4a-cyano-6-oxoindeno[7,1-*bc*]thiepin-5(2*H*)-carboxamide (**5a**).

A mixture of double bond isomers **4a,b** (2.59 g., 0.01 mole) was dissolved in 50 ml. of THF, then 20 ml. of water and 0.68 g. (0.014 mole) of potassium cyanide were added and the mixture heated under reflux for 1.5 hours. The solution was cooled to room temperature, diluted with 30 ml. of water and extracted twice with 20 ml. of chloroform. The aqueous layer, acidified with 20% sulfuric acid, produced a white precipitate, which was collected and washed twice with 50 ml. of water. The solid was dried at 100° for 12 hours yielding 2.25 g. (0.0079 mole, 79%) of white crystals, m.p. 243-246° dec. This material was used directly for the next step without further purification.

For analytical purposes, a sample was recrystallized from ethanol, m.p. 243-244°; ir (potassium bromide): 3450, 3340, (NH_2), 2250 (CN), 1670 (C=O, ketone), 1630 cm^{-1} (C=O, amide); nmr (trifluoroacetic acid): δ 2.70 (singlet superimposed on multiplet, 3H, CH_3), 2.95 (m, 6H, $-(CH_2)_3-$), 3.95 (s, 1H, methine), 7.55 (m, 2H, aromatic); ms: m/e (relative abundance) M^+ 286 (35.4), 270 (13.6), 269 (100.0), 243 (26.1), 242 (42.0), 241 (37.0), 228 (6.3), 227 (24.3), 215 (8.4), 214 (12.0), 213 (15.9), 186 (7.4), 185 (8.4).

Anal. Calcd. for $C_{15}H_{14}N_2O_2S$: C, 62.94; H, 4.89; N, 9.79; S, 11.19. Found: C, 63.20; H, 5.17; N, 10.0. S, 10.96.

3,4,5,6-Tetrahydro-7-methyl-6-oxoindeno[7,1-*bc*]thiepin-4a,5-(2*H*)dicarboxamide (**5b**).

A solution of 1.0 g. (0.0035 mole) of **5a** in 12 ml. of concentrated sulfuric acid was stirred at room temperature for 2 hours, after which time it was poured on ice and a white precipitate formed. After standing for 1 hour, the crystals were filtered and dried in an oven at 100° for 5 hour. The crude yield of **5b** was 0.92 g. (0.003 mole, 86.5%), m.p. 213-217°. Recrystallization from acetone provided white crystals, m.p. 219-220°; ir (deuteriochloroform): 3550, 3375 (NH_2), 3150 (OH of enol), 1680 (C=O, ketone), 1640 cm^{-1} (C=O, amide); nmr (DMSO-d_6): δ 2.60 (singlet superimposed on multiplet, 3H, CH_3), 2.50 (m, 6H, $-(CH_2)_3-$), 3.5 (broad multiplet, 0.25 H, enolizable methine), 6.22 (broad singlet, 0.5 H, exchangeable NH), 7.20 (d, 1H, aromatic), 7.45 (d, 1H, aromatic); ms: m/e (relative abundance) M^+ 304 (19.3), 287 (9.9), 261 (14.9), 2.60 (30.0), 244 (18.7), 243 (100.0), 216 (8.3).

Anal. Calcd. for $C_{15}H_{16}N_2O_3S$: C, 59.21; H, 5.26; N, 9.21; S, 10.53. Found: C, 58.91; H, 5.42; N, 9.06; S, 10.23.

3,4,5,6-Tetrahydro-7-methyl-6-oxoindeno[7,1-*bc*]thiepin-4a,5-(2*H*)dicarboximide (**6**).

A stirred mixture of 3.22 g. (0.0106 mole) of diamide **5b** in 30 ml. of ethylene glycol and 1 ml. of concentrated sulfuric acid was heated at 120° until all material dissolved. The mixture was stirred at 130° for 0.5 hour, then cooled to room temperature and poured on ice. After sitting for 3 hours, the crystals were filtered and air dried. Recrystallization from ethanol afforded 1.88 g. (0.0063 mole, 59.8%) of **6** as white plates, m.p. 262-263°; ir (potassium bromide): 3320 (NH), 1810 (C=O, imide), 1750 (C=O, imide), 1700 cm^{-1} (C=O, ketone); nmr (DMSO-d_6): δ 2.50 (singlet superimposed on multiplet, 3H, CH_3), 2.50 (m, 6H, $-(CH_2)_3-$), 3.82 (s, 1H, methine), 7.09 (d, 1H, aromatic), 7.65 (d, 1H, aromatic), 11.17 (broad singlet, 1H, N-H); ms: m/e (relative abundance) M^+ 287 (100.0), 217 (12.2), 216 (94.6), 201 (13.8), 183 (13.7), 160 (11.5), 115 (12.8).

Anal. Calcd. for $C_{15}H_{13}NO_3S$: C, 62.72; H, 4.53; N, 4.88; S, 11.15. Found: C, 62.44; H, 4.48; N, 5.11; S, 11.15.

Benzosuberylidenemalononitrile (**8**).

This compound was previously reported by Campaigne, Subramanya, and Maulding (11). The procedure used here is the same as that for compound **3** and represents an improved yield. A solution of 11.0 g. (0.069 mole) of benzosuberone, 5.45 g. (0.083 mole) of malononitrile, and 100 mg. of β-alanine in 40 ml. of 90% ethanol was heated under reflux. After crystallization, 2.0 g. of malononitrile, 25 mg. of β-alanine, and 5 ml. of water was added to the mother liquor and the procedure was repeated. The total yield of **8** was 12.90 g. (0.062 mole, 89.5%), m.p. 77-78° (lit. (11) m.p. 76-77°); ir (potassium bromide): 2217 cm^{-1} (CN).

2,6,7,8-Tetrahydro-2-oxo-1*H*-benz[*cd*]azulene-1-carboxamide (**9b**).

This compound was previously reported by Campaigne, Subramanya, and Maulding (11). The following modified procedure is identical to that used to synthesize compounds **4a** and **4b**. A solution of 36.0 g. (0.173 mole) of benzosuberylidenemalononitrile **8** was stirred in 400 ml. of concentrated sulfuric acid at room temperature. The yield of **9** was 30.1 g. (0.133 mole, 76.9%), m.p. 187-189° (lit. (11) m.p. 188-189°); ir (potassium bromide): 3420 (NH), 3200 (NH), 1710 cm^{-1} (C=O, amide); nmr (DMSO-d_6): δ 1.98 (m, 2H, $-CH_2-$), 2.60 (m, 2H, $-CH_2-$), 3.10 (m, 2H, $-CH_2-$), 4.10 (s, 1H, methine), 6.15 (m, 3H, NH_2, vinyl), 6.15 (deuterium oxide, t, 1H, vinyl), 7.4 (m, 3H, aromatic); ms: m/e (relative abundance) M^+ 227 (32.8), 226 (100.0), 225 (57.0), 210 (49.7), 209 (17.9), 198 (11.3), 197 (9.9), 195 (13.7), 184 (20.7), 183 (24.9), 182 (44.7), 181 (25.8), 180 (16.8), 169 (23.5), 168 (10.5), 167 (17.4), 166 (10.6), 165 (12.9), 156 (9.9), 155 (22.0), 154 (31.3), 153 (52.2), 152 (27.6), 151 (10.8). This material was used without further purification.

6,7,8,9-Tetrahydro-9a-cyano-2-oxo-1*H*-benz[*cd*]azulene-1-(2*H*)carboxamide (**10a**).

Utilizing a method developed by Koelsch (12), a mixture of 2.27 g. (0.01 mole) of **9**, 0.72 g. (0.011 mole) of potassium cyanide, 25 ml. of *t*-butyl alcohol and 25 ml. of water was heated on a steam bath for 15 minutes. After sitting at room temperature for 2 hours, the solution was made acidic to congo red with 20% sulfuric acid and diluted with 150 ml. of water. The white precipitate was collected, washed twice with 25 ml. of water and dried to yield 2.1 g. of **10a** (0.0083 mole, 83%), m.p. 211-212°. This material was used directly in the next step. For analytical purposes, recrystallization from 95% ethanol gave white crystals, m.p. 210-211°; ir (potassium bromide): 3500 cm^{-1} (N-H, amide), 3410 (N-H, amide), 3220 (O-H, enol), 2280 (C≡N), 1690 (C=O, ketone), 1650 cm^{-1} (C=O, amide); nmr (DMSO-d_6/deuteriochloroform 1:1): δ 0.6-3.40 (m, 8H, $-(CH_2)_4-$), 3.80 (s, 0.1H, methine), 6.35 (broad singlet, 2.9H, NH_2, OH of enol), 7.45 (3H, aromatic); ms: m/e (relative abundance) M^+ 254 (72.1), 238 (19.5), 237 (100.0), 227 (20.3), 211 (42.0), 210 (85.0), 209 (31.7), 208 (14.1), 196 (14.6), 195 (55.5), 184 (25.8), 183 (18.5), 182 (33.3), 181 (29.5), 169 (21.6), 167 (19.5), 155 (13.5), 154 (11.4), 153 (25.5), 152 (21.9).

Anal. Calcd. for $C_{15}H_{14}N_2O_2$: C, 70.87; H, 5.51; N, 11.02. Found: C 70.67; H, 5.75; N, 10.98.

6,7,8,9-Tetrahydro-2-oxo-1*H*-benz[*cd*]azulene-1,9a-(2*H*)dicarboxamide (**10b**).

A solution of 10.0 g. (0.0394 mole) of **10a** in 50 ml. of concentrated sulfuric acid was stirred at room temperature for 2 hours, after which time it was poured on ice and a white precipitate formed. After standing for 1 hour, the crystals were filtered and dried in an oven at 100° for 5 hours. The crude yield of **10b** was 9.9 g. (0.0364 mole, 92.4%), m.p. 216-218°. This material, recrystallized from 95% ethanol, melted at 216-217°; ir (potassium bromide): 3590 (N-H, amide), 3450 (N-H, amide), 3300 (O-H, enol), 1695 (C=O, ketone), 1630 cm^{-1} (C=O, amide); nmr (DMSO-d_6/deuteriochloroform 1:1): δ 0.6-3.2 (m, 8H, $-(CH_2)_4-$), 6.0 (s, 1H, N-H), 7.15 (s, 1H, N-H), 7.40 (m, 3H, aromatic), 7.40 (2H, NH_2, superimposed on aromatic protons); ms: m/e (relative abundance) M^+ 272 (13.1), 229 (26.8), 228 (45.9), 212 (18.6), 211 (100.0), 210.0 (5.6), 184 (10.0), 155 (10.9).

Anal. Calcd. for $C_{15}H_{16}N_2O_3$: C, 66.18; H, 5.88; N, 10.29. Found: C, 65.93; H, 5.76; N, 10.15.

6,7,8,9-Tetrahydro-2-oxo-1*H*-benz[*cd*]azulene-1,9a-(2*H*)dicarboximide (**11**).

A stirred mixture of 9.0 g. (0.0331 mole) of diamide **10b** in 90 ml. of ethylene glycol and 3 ml. of concentrated sulfuric acid was heated at 120° until all material dissolved. The mixture was stirred at 130° for 0.5 hour, then cooled to room temperature and poured on ice. After sitting for 3 hours, the crystals were filtered and air dried. Recrystallization from ethanol afforded 6.92 g. (0.0271 mole, 81.9%) of **11** as white plates, m.p. 261-262°; ir (potassium bromide): 3310 (N-H), 1800 (C=O, imide), 1740 (C=O, imide), 1700 cm^{-1} (C=O, ketone); nmr (DMSO-d_6): δ 1.0-3.2 (m, 8H, -$(CH_2)_4$-), 3.95 (s, 1H, methine), 7.58 (m, 3H, aromatic), 9.5 (s, 1H, NH); ms: m/e (relative abundance) M^+ 255 (27.7), 185 (12.9), 184 (100.0), 156 (6.5), 155 (8.1), 141 (14.1), 128 (12.9), 127 (6.0).

Anal. Calcd. for $C_{15}H_{13}NO_3$: C, 70.59; H, 5.09; N, 5.49. Found: C, 70.38; H, 5.06; N, 5.25.

Spiro[1,3-dioxolane-2,2′-6′,7′,8′,9′-tetrahydro-1′*H*-benz[*cd*]azulene-1′,9′a-(2*H*)dicarboximide] (**12**).

To a solution of 1.0 g. (0.0039 mole) of **11** and 20 mg. of *p*-toluenesulfonic acid, in 7 ml. of ethylene glycol, was added 50 ml. of benzene, forming 2 layers. The reaction vessel was equipped with a Dean-Stark trap and heated under reflux overnight. Removal of the benzene produced crystals which were collected and dissolved in ether. The ethereal solution was washed twice with sat'd. sodium bicarbonate, once with water, once with sodium chloride solution and dried over magnesium sulfate. Removal of the ether gave 0.71 g. (0.00238 mole, 60.9%) of a white powder, m.p. 220-223°. Recrystallization from THF/hexane (3:1) gave 0.55 g. (0.00184 mole, 47.2%) of white crystals, m.p. 222-224°; ir (potassium bromide): 3200 (N-H), 1790 (C=O, imide), 1745 cm^{-1} (C=O, imide); nmr (DMSO-d_6/deuteriochloroform 1:1): δ 1.0-3.0 (m, 8H, -$(CH_2)_4$-), 3.19 (s, 1H, methine), 4.19 (m, 4H, ketal), 7.21 (s, 3H, aromatic), 10.75 (s, 1H, NH); ms: m/e (relative abundance) M^+ 299 (83.3), 270 (14.1), 269 (8.0), 258 (5.8), 257 (29.5), 256 (100.0), 228 (94.6), 227 (13.0), 219 (15.9), 199 (8.1), 198 (8.7), 185 (10.8), 184 (17.1), 183 (7.9), 172 (88.0).

Anal. Calcd. for $C_{17}H_{17}NO_4$: C, 68.23; H, 5.69; N, 4.68. Found: C, 68.45; H, 5.58; N, 4.74.

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