The Schmidt Reaction on 3a,4,5,6-Tetrahydrosuccinimido[3,4-*b*]-acenaphthen-10-one and its Alkylated Derivatives

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The rearrangement of 3a,4,5,6-tetrahydrosuccinimido[3,4-*b*]acenaphthen-10-one and two methylated derivatives using Schmidt conditions is described. The ratio of the major product, 2,3,8,9-tetrahydro-3-oxo-1*H*-benz[*de*]isoquinoline-1,9a-(7*H*)dicarboximide, to the minor product, 2,3,6,7-tetrahydro-3-oxo-4*H*-benz[*ij*]-isoquinoline-4,4a-(5*H*)dicarboximide, under different acidic conditions is given. The ratios of analogous products from the methylated derivatives are similar under similar conditions.

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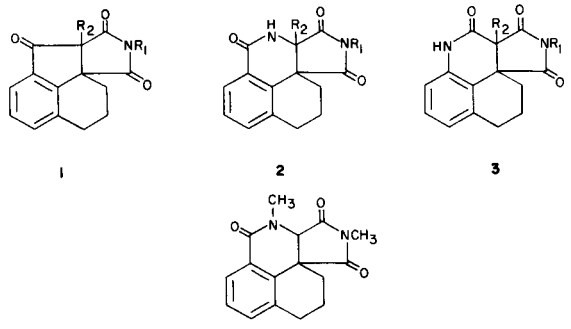
In a continuing effort to synthesize biologically active derivatives of the potent anticonvulsant, 3a,4,5,6-tetrahydrosuccinimido[3,4-*b*]acenaphthen-10-one **1a** (2,3) a study of the Schmidt Reaction of **1a** and its methyl derivatives, **1b** and **1c**, was undertaken. With the addition of hydrazoic acid to the ketone, the possibility of rearrangement to form the novel lactams **2** and/or **3** exists. The ratio of products may depend upon the migrating aptitudes of the phenyl versus the alkyl group adjacent to the ketone, the stereochemical requirements of the reaction and the reaction conditions employed (4). In this study, several reaction conditions were employed on **1a** and the isomeric ratios of **2a/3a** are reported in Table I. Compounds **1b** and **1c** (synthesized previously (5)) were then reacted using the optimum conditions found for production of isomers **2a** and **3a** from the parent ketone **1a**. The isomeric ratios of the resultant lactams **2b,c** and **3b,c** are given in Table II.



1 2 3 4

a $R_1 = R_2 = H$
b $R_1 = CH_3$, $R_2 = H$
c $R_1 = R_2 = CH_3$

When a solution of compound **1a** in concentrated sulfuric acid at room temperature was treated with sodium azide (condition 1, Table I), a single product resulting from alkyl migration, lactam **2a**, was formed. This structural assignment was confirmed by standard spectroscopic techniques including: ultraviolet, which was important in assigning the carbonyl adjacent to the phenyl ring; nuclear magnetic resonance, which indicated the methine proton (R_2 = H) was flanked by a nitrogen and a carbonyl; and ultimately an X-ray analysis, done on compound **4**, which is the *N,N*-dialkyl derivative of **2a** and was used because its crystal structure proved to be more suitable for analysis.

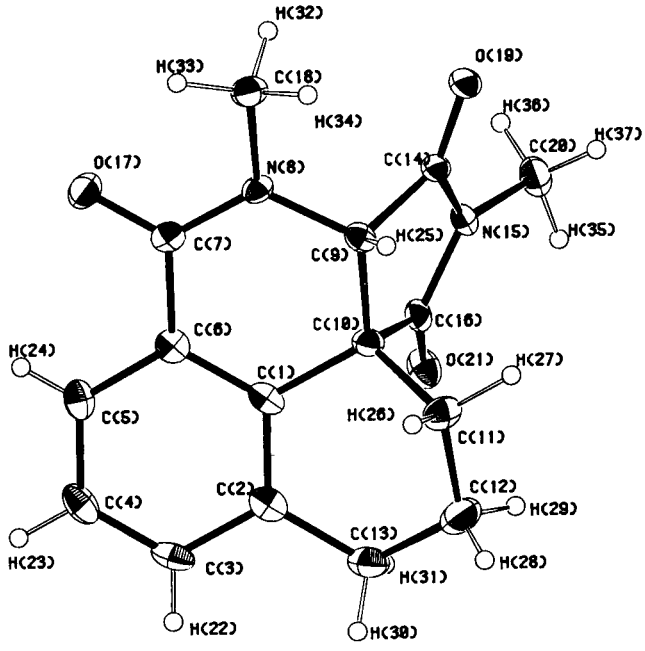


Figure 1. An ORTEP drawing of **4** showing the atomic numbering scheme used in Tables V, VI and VII. All thermal ellipsoids are shown at the 50% probability level except hydrogens, which have been given an isotropic value of 0.5 for artistic purposes.

Rearrangement of compound **1a** under several other conditions produced isomeric mixtures of **2a** and **3a**, the ratio depending on the acid employed, while the temperature only affected the overall yield of combined products.

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Table I

Schmidt Reaction Conditions for Compound **1a**

Acid (a)	Temperature °	Yield (mixture) % (c)	Product Ratio (**2a:3a**) (d)
(1) Sulfuric acid	25	91	100:0
(2) Sulfuric acid	80	68	100:0
(3) 85% Sulfuric acid	25	57	100:0
(4) Sulfuric acid	25	56	100:0
(5) 50% Ethanolic sulfuric acid	25	86	100:0
(6) PPA	80	75	60:40
(7) Methanesulfonic acid	25	77	66:34
(8) Methanesulfonic acid	100	65	64:36
(9) Methanesulfonic acid (b)	25	63	79:21
(10) Eaton's Reagent	25	72	78:22
(11) Eaton's Reagent	60	59	78:22
(12) Trichloroacetic acid	110	no reaction	
(13) Trifluoroacetic acid	72	no reaction	

(a) Solution of compound **1a** in acid and sodium azide was added. (b) Solution of excess sodium azide in acid and compound **1a** was added. (c) Yield based on crude mixture of products. (d) Ratio determined by nmr integration.

Table II

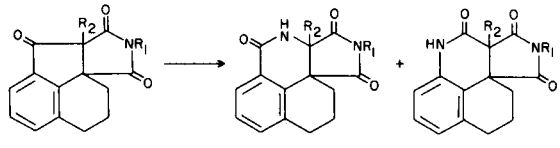
Optimum Schmidt Reaction Conditions for Compound **1**

Acid (a)	R_1	R_2	Yield (b)	Product Ratio (**2:3**) (c)
(1) Sulfuric acid	H	H	91	100:0
PPA	H	H	75	60:40
(2) Sulfuric acid	CH_3	H	87	100:0
PPA	CH_3	H	95	60:40
(3) Sulfuric acid	CH_3	CH_3	74	100:0
PPA	CH_3	CH_3	71	61:39

(a) Sulfuric acid reactions run at 25°; PPA reactions run at 80°. (b) Yield based on crude reaction mixture. (c) Ratio determined by nmr integration except item 3 which was determined by gc integration.

Table III

Major Fragmentation Modes for the Succinimides

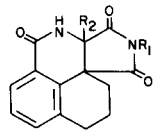


1 2 3

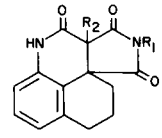
Compound No.	R_1	R_2	Y	Fragment	Relative Abundance M^+-Y
1a	H	H	71	C_2HNO_2	100.0
1b	CH_3	H	85	$C_3H_3NO_2$	100.0
1c	CH_3	CH_3	85	$C_3H_3NO_2$	100.0
2a	H	H	71	C_2HNO_2	100.0
2b	CH_3	H	85	$C_3H_3NO_2$	100.0
2c	CH_3	CH_3	85	$C_3H_3NO_2$	100.0
			15	CH_3	5.5
3a	H	H	71	C_1HNO_2	100.0
3b	CH_3	H	85	$C_3H_3NO_2$	100.0
3c	CH_3	CH_3	85	$C_3H_3NO_2$	100.0
			15	CH_3	7.1

Table IV

Ultraviolet and Chemical Shifts of the Methine Proton for Isoquinolines **2** and **3**



2



3

Compound No.	R_1	R_2	δ R_2 = H), ppm	mμ (ϵ)
2a	H	H	4.25	235 (10,401)
2b	CH_3	H	4.28	241 (10,548)
2c	CH_3	CH_3		241 (10,700)
3a	H	H	3.68	255 (12,980)
3b	CH_3	H	3.71	255 (13,291)
3c	CH_3	CH_3		253 (14,157)

Table V

Angles in Degrees

A	B	C	Angle
C(7)	N(8)	C(9)	124.5(3)
C(7)	N(8)	C(18)	118.0(3)
C(9)	N(8)	C(18)	116.3(3)
C(14)	N(15)	C(16)	113.3(3)
C(14)	N(15)	C(20)	123.4(3)
C(16)	N(15)	C(20)	123.3(3)
C(2)	C(1)	C(6)	120.8(3)
C(2)	C(1)	C(10)	118.7(3)
C(6)	C(1)	C(10)	120.4(3)
C(1)	C(2)	C(3)	118.1(4)
C(1)	C(2)	C(13)	121.9(3)
C(3)	C(2)	C(13)	120.1(4)
C(2)	C(3)	C(4)	121.0(4)
C(3)	C(4)	C(5)	120.7(4)
C(4)	C(5)	C(6)	119.8(4)
C(1)	C(6)	C(5)	119.5(4)
C(1)	C(6)	C(7)	121.9(3)
C(5)	C(6)	C(7)	118.4(4)
O(17)	C(7)	N(8)	120.2(3)
O(17)	C(7)	C(6)	121.0(3)
N(8)	C(7)	C(6)	118.8(3)
N(8)	C(9)	C(10)	116.4(3)
N(8)	C(9)	C(14)	109.2(3)
C(10)	C(9)	C(14)	104.1(3)
C(1)	C(10)	C(9)	115.2(3)
C(1)	C(10)	C(11)	108.3(3)
C(1)	C(10)	C(16)	111.6(3)
C(9)	C(10)	C(11)	109.2(3)
C(9)	C(10)	C(16)	103.4(3)
C(11)	C(10)	C(16)	108.9(3)
C(10)	C(11)	C(12)	113.5(3)
C(11)	C(12)	C(13)	115.7(4)
C(2)	C(13)	C(12)	115.1(3)
O(19)	C(14)	N(15)	125.0(4)
O(19)	C(14)	C(9)	127.3(4)
N(15)	C(14)	C(9)	107.7(3)
O(21)	C(16)	N(15)	123.7(4)
O(21)	C(16)	C(10)	128.1(3)

Table V (Continued)

A	B	C	Angle
N(15)	C(16)	C(10)	108.1(3)
C(2)	C(3)	H(22)	118.8(26)
C(4)	C(3)	H(22)	120.2(26)
C(3)	C(4)	H(23)	121.4(31)
C(5)	C(4)	H(23)	117.7(31)
C(4)	C(5)	H(24)	120.7(28)
C(6)	C(5)	H(24)	119.3(29)
N(8)	C(9)	H(25)	110.6(27)
C(10)	C(9)	H(25)	107.7(26)
C(14)	C(9)	H(25)	108.5(28)
C(10)	C(11)	H(26)	108.9(26)
C(10)	C(11)	H(27)	109.8(22)
C(12)	C(11)	H(26)	109.5(25)
C(12)	C(11)	H(27)	111.2(21)
H(26)	C(11)	H(27)	103.5(33)
C(11)	C(12)	H(28)	107.8(29)
C(11)	C(12)	H(29)	106.6(30)
C(13)	C(12)	H(28)	110.9(29)
C(13)	C(12)	H(29)	108.3(31)
H(28)	C(12)	H(29)	107.1(41)
C(2)	C(13)	H(30)	108.5(26)
C(2)	C(13)	H(31)	107.7(27)
C(12)	C(13)	H(30)	110.2(27)
C(12)	C(13)	H(31)	108.0(26)
H(30)	C(13)	H(31)	107.0(37)
N(8)	C(18)	H(32)	115.3(36)
N(8)	C(18)	H(33)	108.7(29)
N(8)	C(18)	H(34)	105.1(28)
H(32)	C(18)	H(33)	107.3(46)
H(32)	C(18)	H(34)	103.8(44)
H(33)	C(18)	H(34)	116.9(41)
N(15)	C(20)	H(35)	102.5(39)
N(15)	C(20)	H(36)	106.4(37)
N(15)	C(20)	H(37)	110.2(39)
H(35)	C(20)	H(36)	123.4(53)
H(35)	C(20)	H(37)	105.8(51)
H(36)	C(20)	H(37)	108.0(48)

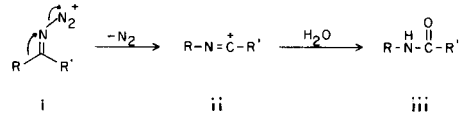
Table VI

Fractional Coordinates of Atoms

Atom	10^4x	10^4y	10^4z	$10B_{iso}$
C(1)	7738(4)	908(5)	2060(2)	13
C(2)	9096(4)	1422(5)	2053(2)	14
C(3)	9599(4)	1671(6)	2734(2)	17
C(4)	8784(4)	1384(6)	3389(2)	19
C(5)	7450(4)	875(5)	3393(2)	16
C(6)	6906(4)	663(5)	2725(2)	13
C(7)	5436(4)	334(5)	2749(2)	13
N(8)	4857(3)	444(4)	2110(2)	13
C(9)	5605(4)	797(5)	1384(2)	13
C(10)	7166(4)	724(5)	1334(2)	13
C(11)	7779(4)	2263(6)	811(2)	17
C(12)	9311(5)	2236(8)	685(3)	25
C(13)	10018(4)	1680(6)	1344(2)	20
C(14)	5251(4)	−684(6)	842(2)	14
N(15)	6408(3)	−1707(4)	642(2)	13
C(16)	7516(4)	−1122(5)	974(2)	13
O(17)	4723(3)	45(4)	3341(1)	19
C(18)	3374(4)	584(6)	2162(2)	18
O(19)	4164(3)	−954(4)	628(1)	17
C(20)	6457(5)	−3269(6)	133(2)	20
O(21)	8577(3)	−1939(4)	936(1)	18
H(22)	10432(44)	2013(55)	2735(21)	11(8)
H(23)	9096(51)	1603(69)	3840(30)	34(12)
H(24)	6910(45)	778(62)	3813(26)	21(10)
H(25)	5359(45)	1974(66)	1199(25)	25(10)
H(26)	7462(43)	3480(67)	1023(25)	24(9)
H(27)	7366(38)	2203(55)	317(22)	12(8)
H(28)	9594(46)	3352(68)	517(25)	22(10)
H(29)	9559(49)	1378(72)	294(29)	34(11)
H(30)	10696(47)	2556(64)	1426(23)	20(9)
H(31)	10488(46)	509(68)	1225(25)	25(10)
H(32)	2910(60)	−518(96)	2028(33)	57(15)
H(33)	3017(51)	888(71)	2677(30)	35(11)
H(34)	3185(52)	1543(76)	1749(30)	40(12)
H(35)	7446(73)	6606(93)	9971(37)	62(17)
H(36)	5935(56)	−4186(88)	378(32)	46(14)
H(37)	6051(60)	−2945(89)	−299(36)	56(15)

Polyphosphoric acid at 80° produced the highest proportion of **3a** (40%). However, isomer **2a** still predominated (condition 6, Table I). An analytical sample of isomer **3a** was obtained by fractional crystallization and its structure confirmed by elemental analysis (showing it to be isomeric to **2a**) and comparison of standard spectroscopic data. Under all conditions employed where a reaction occurred, the product of alkyl migration (**2a**) was either the sole or the predominant isomer formed over the product of phenyl migration (**3a**). This migratory preference is in contrast to studies on the rearrangement of indanones (6) and tetralones (6,7) which generally favor products resulting from phenyl migration. It should be noted, however, that anomalous results were reported with indenones having a carboxamido group at C-2 (8). It is therefore apparent that while compound **1** can be considered a substituted indanone, its rigid structure causes a deviation from the normal migratory aptitudes of these compounds.

Addition of hydrazoic acid to a ketone is thought to lead to formation of the transient iminodiazonium ion (**i**) which upon *trans* elimination of nitrogen, rearranges to form an iminium ion (**ii**) and reaction with water yields amide or lactam (**iii**) (4). Schmidt reactions proceeding through the iminium ion can be trapped by the addition of



i ii iii

other nucleophiles. Excess azide will add to form tetrazoles and alcohols will form imidyl esters (9). When these reactions were attempted (conditions 4, 5, and 9, Table I), no products other than the lactam were observed. There-

Table VII

Bond Distances in Angstroms

A	B	Distance
O(17)	C(7)	1.237(5)
O(19)	C(14)	1.205(4)
O(21)	C(16)	1.204(4)
N(8)	C(7)	1.362(5)
N(8)	C(9)	1.462(5)
N(8)	C(18)	1.465(5)
N(15)	C(14)	1.381(5)
N(15)	C(16)	1.383(5)
N(15)	C(20)	1.467(5)
C(1)	C(2)	1.396(5)
C(1)	C(6)	1.394(5)
C(1)	C(10)	1.508(5)
C(2)	C(3)	1.403(6)
C(2)	C(13)	1.505(6)
C(3)	C(4)	1.377(6)
C(4)	C(5)	1.372(6)
C(5)	C(6)	1.400(5)
C(6)	C(7)	1.472(5)
C(9)	C(10)	1.540(5)
C(9)	C(14)	1.533(5)
C(10)	C(11)	1.550(5)
C(10)	C(16)	1.520(5)
C(11)	C(12)	1.509(6)
C(12)	C(13)	1.517(6)
C(3)	H(22)	.86(4)
C(4)	H(23)	.93(6)
C(5)	H(24)	.88(5)
C(9)	H(25)	.96(5)
C(11)	H(26)	1.00(5)
C(11)	H(27)	1.03(4)
C(12)	H(28)	.90(5)
C(12)	H(29)	.96(5)
C(13)	H(30)	.95(5)
C(13)	H(31)	.99(5)
C(18)	H(32)	.97(7)
C(18)	H(33)	.99(5)
C(18)	H(34)	1.06(6)
C(20)	H(35)	.99(7)
C(20)	H(36)	.93(6)
C(20)	H(37)	.96(7)

fore, it is difficult to posultate the iminodiazonium ion as the intermediate in this reaction. The less commonly accepted α-azidohydrin intermediate (**iv**) would be a more favorable pathway to explain these results since there is no loss of water and hence no nucleophiles can add to it. The amide is formed instead by direct formation of carbonyl and expulsion of nitrogen and a proton.

iv

Further evidence for the lack of an iminodiazonium ion intermediate in this series of compounds was supplied by rearrangement of the alkyl derivatives **1b** and **1c**. Reaction of the *N*-methyl compound **1b** with hydrazoic acid in concentrated sulfuric acid at room temperature (reaction 2, Table II) again afforded only product **2b** resulting from alkyl migration. Use of polyphosphoric acid at 80° produced again a 60:40 mixture of isomer **2b** to **3b**, respectively. Although **3b** was not isolated, it was identified by: gc/ms, which separated and identified the parent ions and key fragmentations for **2b** and **3b**; elemental analysis of the mixture, which proved the components to be isomeric; and uv analysis, which gave key absorptions for a quinolinone system and an isoquinolinone system. The methine protons at the R_2 position provided nmr data suitable for integration to determine the isomeric ratios. The similar results obtained upon rearrangement of **1a** and **1b** is not surprising owing to the fact that the methyl substituent in **1b** is remote from the migrating centers. However, rearrangement of compound **1c** having a methyl group at a migrating center, produced the same results as those for **1a** and **1b**. Upon reaction with hydrazoid acid in concentrated sulfuric acid (condition 3, Table II), compound **2c** was the only observed isomer. Polyphosphoric acid at 80° (condition 3, Table II) gave a 60:40 mixture of **2c** to **3c**. The isomers were not separated, but were characterized by gc/ms, uv and nmr; the isomeric ratio was determined by co-injection of an original sample obtained from rearrangement of **1c** in sulfuric acid.

If the iminodiazonium ion was the intermediate, rearrangement of **1c** in polyphosphoric acid would be expected to give a lower yield of **3c**. This is because the methyl group at position R_2 should sterically interfere with the $-N_2^+$ ion and inhibit phenyl migration via *trans* elimination of nitrogen. Apparently, this does not occur, since the ratio of **2:3** for **1a, b** and **c** remains uneffected. However, if the α-azidohydrin intermediate is involved, it is not clear why the ratio of isomers would be affected by different acids.

Mass Spectroscopy (see Table III).

The compounds in this investigation all have a characteristic major fragmentation mode. The base peak is that which results from cleavage of the succinimide ring. For compounds **1a, 2a,** and **3a**, this fragment is M^+-71 (loss of $(CO)_2NH$) and for **1b,c, 2b,c,** and **3b,c,** it is M^+-85 (loss of $(CO)_2NCH_3$). For structures **1c, 2c,** and **3c**, a loss of M^+-15, corresponding to cleavage of the methyl group at R_2 is also observed. All relevant peaks are given in the experimental section under each compound listed.

Ultraviolet Spectroscopy (see Table IV).

The absorptions given in Table IV are all characteristic of the lactam structures and are in good agreement with literature values (10). Where the lactam carbonyl is in conjugation with the phenyl ring (compound **2**), the absorp-

tion is near 240 nm. When the nitrogen of the lactam is α to the phenyl ring (compound **3**), the absorption is near 255 nm. This was especially useful for characterizing compounds **2c** and **3c** where no methine proton is present at the R_2 position.

Nuclear Magnetic Resonance (see Table IV).

For compounds **2a** and **2b**, the methine proton resonates near 4.25 ppm, which is characteristic of protons on carbon α to a nitrogen and a carbonyl group. Compounds **3a** and **3b** have the methine protons near 3.70 ppm, which is typical for hydrogen atoms bound to a carbon α to two carbonyl groups and are expected to be shifted upfield with respect to the methine protons of compounds **2a** and **2b**. These values are consistent with literature values for lactams (10).

Low temperature X-ray structure of 2,3,8,9-tetrahydro-*N*,2-dimethyl-3-oxo-1*H*-benz[*de*]isoquinoline-1,9a-(7*H*)dicarboximide (**4**).

The low temperature single crystal structure analysis of **4** confirmed the structure, as shown in Figure 1 which gives the numbering scheme used. Important angles are given in Table V, and fractional coordinates of atoms are given in Table VI. Bonded distances are given in Table VII. More extensive crystallographic information is available (11).

Biological activity.

The succinimides **2a, 2b** and **4** 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® (Met.) induced seizures in mice. Compound **2a** was inactive, but compound **2b** showed inhibition of Metrazole induced seizures at 600 mg./kg., while **4** showed activity against Metrazole induced seizures at 300 mg./kg. A detailed biological evaluation of **1a** has been reported (3), while **1b** and **1c** were previously screened and were inactive as anticonvulsants (5).

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. 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.

3a,4,5,6-Tetrahydrosuccinimido[3,4-*b*]acenaphthen-10-one (**1a**).

This compound was prepared as previously reported (2).

2-Methyl-3a,4,5,6-tetrahydrosuccinimido[3,4-*b*]acenaphthen-10-one (**1b**).

This compound was originally synthesized by D. A. Templer (5) by a modification of the procedure by Calberson and Wilder (12).

A mixture of **1a** (2.41 g., 0.1 mole), potassium carbonate (13.93 g., 0.11 mole) and methyl iodide (6.85 ml., 15.6 g., 0.11 mole) in 100 ml. of dimethylformamide was stirred at room temperature for 3 hours. The mixture was poured into 800 ml. of water and the resulting solid recrystallized from 95% ethanol to give 22.5 g. (0.088 mole, 88%) of **1b**, m.p. 142-144°; ir (potassium bromide): 1770 (C=O, imide), 1730 (C=O, imide), 1710 cm^{-1} (C=O, ketone); nmr (DMSO-d_6): δ 2.57 (m, 6H, -$(CH_2)_3$-), 2.85 (s, 3H, -CH_3), 4.00 (s, 1H, methine), 7.58 (m, 3H, aromatic); ms: m/e (relative abundance) M^+ 255 (6.6), 171 (11.8), 170 (100.0), 142 (39.7), 141 (64.7), 139 (17.6), 128 (15.4), 115 (56.6).

Anal. Calcd. for $C_{15}H_{13}NO_3$: C, 70.54; H, 5.09; N, 5.49. Found: C, 70.25; H, 5.34; N, 5.47.

2,10a-Dimethyl-3a,4,5,6-tetrahydrosuccinimido[3,4-*b*]acenaphthen-10-one (**1c**).

This compound was also previously synthesized by D. A. Templer (5). Sodium hydride (0.55 g., 0.0114 mole), 50% in mineral oil, was added to a mixture of 2.55 g. (0.01 mole) of **1b** in 30 ml. of dry tetrahydrofuran in a 100 ml. roundbottom flask fitted with a drying tube (Drierite). After the evolution of hydrogen ceased, 0.69 ml. of methyl iodide (1.56 g., 0.011 mole) was added and the mixture stirred at room temperature for 2 hours. The solvent was then removed by rotary evaporation and the residue dissolved in 20 ml. of ethyl acetate. The organic layer was washed twice with water, once with 50 ml. of saturated sodium chloride solution and dried over magnesium sulfate to yield 2.22 g. (0.0083 mole, 83%) of white crystals that were washed with 50 ml. of hexane and dried, m.p. 143-144°; ir (potassium bromide): 1800 (C=O, succinimide), 1740 (C=O, succinimide), 1710 cm^{-1} (C=O, ketone); nmr (deuteriochloroform): δ 1.42 (s, 3H, -CH_3), 2.30 (m, 6H, -$(CH_2)_3$-), 3.00 (s, 3H, -CH_3), 7.55 (m, 3H, aromatic); ms: m/e (relative abundance) M^+ 269 (17.3), 184 (100.0), 183 (20.8), 169 (11.0), 155 (19.7), 153 (12.7), 152 (11.6), 141 (22.0), 128 (26.0).

Anal. Calcd. for $C_{16}H_{15}NO_3$: C, 71.37; H, 5.57; N, 5.20. Found: C, 71.66; H, 5.85; N, 5.06.

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

The procedure described in the following paragraph is condition 1, in Table I, and is representative of all the procedures used. Conditions 4 and 9 (Table I) utilized a modification which required solution of ketone **1a** in 50 ml. of acid and slow addition of a 4-fold excess of azide, in order to test for tetrazole formation.

To 150 ml. of concentrated sulfuric acid was added 9.64 g. (0.04 mole) of **1a** (2) with stirring at room temperature. Sodium azide (2.86 g., 0.044 mole) was added to the solution over a 5 minute period. Vigorous bubbling ensued and the reaction became mildly exothermic. The solution was allowed to stir for 12 hours, poured on ice and set for 1 additional hour.

Filtration of the crystals and drying at 100° for 3 hours yielded 7.7 g. (0.030 mole, 75%) of a white powder, m.p. 283-285° with decomposition. This material was pure on thin layer chromatography (ethyl acetate, Rf 0.5) but was recrystallized from 95% ethanol for analytical purposes. The solvated crystals were dried at 150° under 2 mm vacuum for 2 hours, m.p. 288-291° with decomposition; ir (potassium bromide): 3210 (N-H), 3110 (N-H), 1795 (C=O, succinimide), 1740, 1730 (C=O, succinimide), 1670 cm^{-1} (C=O, lactam); uv (ethanol): λ max (nm) 235 (ϵ, 10,401); nmr (DMSO-d_6): δ 2.08 (m, 4H, -$(CH_2)_2$O), 2.89 (m, 2H, -CH_2-), 4.25 (s, 1H, methine), 7.45-7.80 (m, 4H, aromatic, N-H, lactam), 8.67 (N-H, succinimide); ms: m/e (relative abundance) M^+ 256 (17.1), 255 (71.1), 185 (39.8), 184 (100.0), 183 (63.2), 182 (10.5), 169.0 (20.4), 155 (29.9), 128 (15.4), 127 (16.4).

Anal. Calcd. for $C_{14}H_{12}N_2O_3$: C, 65.63; H, 4.69; N, 10.94. Found: C, 65.45; H, 4.72; N, 10.78.

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

The procedure used is the same as for compound **2a**. The stoichiometry was 5.1 g. (0.02 mole) of **1b**, 75 ml. of concentrated sulfuric acid,

and 1.43 g. (0.022 mole) of sodium azide. The yield of white crystals was 4.70 g. (0.0174 mole, 87%), and was one spot by thin layer chromatography (ethyl acetate Rf 0.65), m.p. 280-282°; ir (potassium bromide): 3210 (N-H, lactam), 1800, 1745 (C=O, succinimide), 1670 cm^{-1} (C=O, lactam); nmr (DMSO-d_6): δ 1.98 (m, 4H, -$(CH_2)_2$-), 2.91 (s, 3H, -CH_3), 3.42 (m, 2H, -CH_2-), 4.28 (s, 1H, methine), 7.63 (m, 3H, aromatic); ms: m/e (relative abundance) M^+ 270 (51.3), 242 (5.0), 241 (21.3), 207 (12.0), 186 (13.5), 185 (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*,1-dimethyl-3-oxo-1*H*-benz[*de*]isoquinoline-1,9a-(7*H*)dicarboximide (**2c**).

The procedure used is the same as for compound **2a**. The stoichiometry was 5.38 g. (0.02 mole) of **1c**, 75 ml. of concentrated sulfuric acid, and 1.43 g. (0.022 mole) of sodium azide. The yield of white crystals, was 4.20 g. (0.0148 mole, 74%) and was one spot by thin layer chromatography (ethyl acetate/chloroform, 2:1, Rf 0.5); m.p. 222-224°; ir (potassium bromide): 3215 (N-H, lactam), 1800, 1745 (C=O, succinimide), 1665 cm^{-1} (C=O, lactam); nmr (deuteriochloroform): δ 1.51 (s, 3H, -CH_3), 2.00 (m, 4H, -$(CH_2)_2$-), 3.01 (m, 2H, -CH_2-), 3.05 (s, 3H, -CH_3), 7.78 (m, 3H, aromatic); ms: m/e (relative abundance) M^+ 284 (41.7), 270 (1.0), 269 (5.5), 242 (2.9), 200 (15.3), 199 (100.0), 198 (14.3), 184 (22.1), 155 (11.3).

Anal. Calcd. for $C_{16}H_{16}N_2O_3$: C, 67.61; H, 5.63; N, 9.86. Found: C, 67.72; H, 5.86; N, 10.02.

2,3,6,7-Tetrahydro-3-oxo-4*H*-benz[*ij*]isoquinoline-4,4a-(5*H*)dicarboximide (**3a**).

This procedure represents the highest isomeric ratio of **3a** relative to compound **2a**.

Over a 15 minute period, 1.3 g. (0.02 mole) of sodium azide was added to a stirred solution of 2.41 g. (0.01 mole) of **1a** in 30 g. of polyphosphoric acid at 80°. After 15 hours the mixture was cooled to room temperature and poured on ice. The mixture was stirred for 1 hour and white crystals which formed were filtered and dried to yield 1.91 g. (0.0075 mole), 75% of a mixture of Schmidt products **2a** and **3a** in a 3:2 ratio (determined by nmr integration). The mixture was fractionally recrystallized from 95% ethanol and yielded only an analytical sample of compound **3a**, m.p. 315-316° dec.; ir (potassium bromide): 3210 (N-H), 3190 (N-H), 1810 (C=O, succinimide), 1740, 1730 (C=O, succinimide), 1660 cm^{-1} (C=O, lactam); uv (ethanol): λ max (nm) 255 (ε, 12,980); nmr (DMSO-d_6): δ 1.91 (m, 4H, -$(CH_2)_2$-), 2.80 (m, 2H, -CH_2-), 3.68 (s, 1H, methine), 6.51-7.49 (m, 4H, aromatic, N-H of lactam), 11.42 (N-H, succinimide); ms: m/e (relative abundance) M^+ 256 (25.3), 186 (15.8), 185 (100.0), 184 (27.4), 183 (7.1), 156 (5.7), 155 (7.2), 128 (13.9), 127 (18.4).

Anal. Calcd. for $C_{14}H_{12}N_2O_3$: C, 65.63; H, 4.69; N, 10.94. Found: C, 65.45; H, 4.28; N, 10.88.

2,3,6,7-Tetrahydro-*N*-methyl-3-oxo-4*H*-benz[*ij*]isoquinoline-4,4a-(5*H*)-dicarboximide (**3b**).

This procedure represents the highest isomeric ratio of **3b** relative to compound **2b**. This isomer was not isolated, but was characterized by gc/ms, nmr, uv and elemental analysis of the isomeric mixture. The procedure used is the same as for compound **3a**. The yield of a 60:40 mixture of white crystals of isomers **2a** and **3b**, respectively, was 95%, m.p. 265-269° with decomposition; ir (potassium bromide): 3215 (N-H, lactam), 1810, 1750 (C=O, succinimide), 1680, 1670 (C=O, lactams); nmr (DMSO-d_6): δ 1.98 (m, 4H, -$(CH_2)_2$-), 2.91, 2.90 (2 singlets, 3H, -CH_3 of mixture), 3.42 (m, 2H, -CH_2-), 4.28, 3.71 (2 singlets in a ratio of 60:40, 1H, methine of mixture), 7.51 (m, 3H, aromatic); ms: (13) m/e (relative abundance) M^+ 270 (31.6), 185 (100.0), 184 (15.8), 156 (36.8), 129 (42.1), 128 (26.3), 127 (15.8), 115 (36.8), 76 (26.3).

Anal. Calcd. for $C_{15}H_{14}N_2O_3$: C, 66.67; H, 5.19; N, 10.37. Found: C, 66.93; H, 5.24; N, 10.48.

2,3,6,7-Tetrahydro-*N*,4-dimethyl-3-oxo-4*H*-benz[*ij*]isoquinoline-4,4a-(5*H*)-dicarboximide (**3c**).

This procedure represents the highest isomeric ratio of **3c** relative to compound **2c**. This isomer was not isolated, but was characterized by gc/ms, nmr, uv and elemental analysis of the isomeric mixture. The procedure used for the conversion of **1c** to a mixture of **2c** and **3c** is the same as that described for the preparation of compound **3a**. The yield of a 60:40 mixture of white crystals of isomers **2c** and **3c**, respectively was 71%, m.p. 214-218°; ir (potassium bromide): 3210 (N-H, lactam), 1790, 1740 (C=O, succinimide), 1675, 1673 (C=O, lactams); nmr (deuteriochloroform): δ 1.51 (2 singlets superimposed, 3H, -CH_3), 2.00 (m, 4H, -$(CH_2)_2$), 3.01 (m, 2H, -CH_2-), 3.05 (s, 3H, -CH_3), 7.52 (m, 3H, aromatic); ms: (14) m/e (relative abundance) M^+ 285 (11.2), 284 (34.5), 269 (7.1), 200 (13.4), 199 (100.0), 198 (26.1), 184 (17.2), 155 (24.1).

Anal. Calcd. for $C_{16}H_{16}N_2O_3$: C, 67.61; H, 5.63; N, 9.86. Found: C, 67.62; H, 5.82; N, 10.06.

2,3,8,9-Tetrahydro-*N*,2-dimethyl-3-oxo-1*H*-benz[*de*]isoquinoline-1,9a-(7*H*)dicarboximide (**4**).

To a stirred suspension of 10.80 g. (0.04 mole) of **2b** and 3.0 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 **4**, 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.

Single-Crystal X-Ray Structure of **4**.

All crystallographic data for **4** were obtained at $-170 \pm 5°$ using a locally designed nitrogen cooling system (15). The diffractometer used was locally constructed using a Picker goniostat and generator, and a Texas Instruments 980B mini-computer for control (16). The goniostat was equiped with a Furnas monochromator (HOG crystal).

A well-formed crystal of dimensions 0.25 x 0.35 x 0.35 mm was used for intensity data and characterization. The crystal was mounted on a glass fiber using silicone grease and cooled on the diffractometer. The space group was determined to be $P2_1/c$. Cell dimensions of a = 9.913(4), b = 7.298(3), c = 18.241(8) and β = 83.15(3), were determined by a least squares fit of angular data (22 reflections) centered in both positive and negative regions of 2θ. Centering was performed under computer control using a top/bottom-left/right slit assembly, which was also the basis of the diffractometer alignment. Based on Z = 4, the calculated density is 1.441 g./cm^3.

All non-hydrogen atoms were located by direct method phasing (17), and the hydrogen atoms were located by standard Fourier techniques. The structure was refined by full-matrix least squares techniques with isotropic thermal parameters for the hydrogen atoms, and anisotropic thermal parameters for all other atoms. In addition to thermal and positional parameters, an overall scale factor and isotropic extinction parameter were refined. Final residuals were R = .082 and Rw = .083 for the 2167 non-zero amplitudes used in the refinement. Complete

crystallographic data are available, including observed and calculated structure amplitudes (11).

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