Synthesis of Adamantane Derivatives. 54.[1] Synthesis of Novel 4-Azahomoadamantano[3,4]-Fused Heterocycles via Hydrocyanation of 4-Azahomoadamant-3-ene

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Photolysis of 1-azidoadamantane (1) in an aqueous NaCN–*n*-hexane two-phase system with Adogen 464 as a phase-transfer catalyst gave 3-cyano-4-azahomoadamantane (**3**), a hydrocyanation product of 4-azahomoadamant-3-ene (**2**). $AlCl_3$-catalyzed decomposition of **1** in the presence of trimethylsilyl cyanide also afforded **3**. **3** gave the corresponding amino acid **6** and its ester **7**. 4-Azahomoadamantano[3,4]-fused hydantoin, iminohydantoin, iminothiohydantoin, and thiohydantoin, **12**–**17**, were readily prepared by the reactions of **3** with appropriate isocyanates and isothiocyanate. The reactions of **3** with dimethyl acetylenedicarboxylate, methyl vinyl ketone, and diketene afforded the corresponding iminopyrroline (**20**), aminopyrroline (**23**), and aminopyrrolinone (**26**). Acetylation of **3** gave *N*-acetylamino derivative **27**, which was converted to Δ^2-oxazolinium perchlorate **30** via *N*-acetylamino acid **29**.

Although several 3-substituted 4-azahomoadamantanes such as 3-hydroxy, 3-alkoxy, 3-phenylthio, and 3-aryl have been prepared from the corresponding iminium cation or its equivalent[2-4] or from 4-azahomoadamant-3-ene (**2**),[5] 3-cyano derivative **3** has not been reported. We now report the synthesis of **3** from 1-azidoadamantane (**1**)[3] as well as its facile conversion to some novel 4-azahomoadamantano[3,4]-fused five-membered heterocycles, as an extension of our previous studies on the synthesis of aza-modified adamantane derivatives.[6]

Results and Discussion

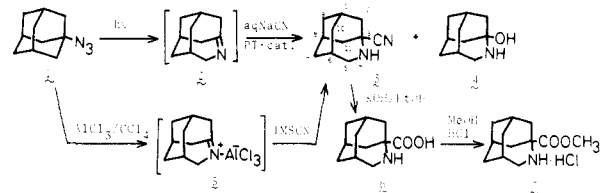
Synthesis of 3-Cyano-4-azahomoadamantane (3). In the addition of hydrogen cyanide to Schiff bases (the Strecker synthesis), the use of sodium cyanide in a phosphate buffer is known as a convenient procedure compared to the use of anhydrous hydrogen cyanide in inert solvents.[7] In view of this, 1-azidoadamantane (**1**) was irradiated in a vigorously stirred *n*-hexane–aqueous NaCN (10.2 M) two-phase system with Adogen 464 as a phase-transfer catalyst. The product from *n*-hexane was purified by sublimation to afford aminonitrile **3** as a colorless solid (64%). The ^1H NMR spectrum had a characteristic doublet for 2H at δ 3.04 (J = 4.0 Hz) due to CH_2N (two H_5), and the ^{13}C NMR spectrum exhibited eight lines in agreement with the C_s symmetry of **3**. A side product, **4**, was also isolated as an insoluble precipitate and was characterized as 3-hydroxy-4-azahomoadamantane, a hydrate of **2**, by comparison with an authentic sample.[2,3] The photolysis of **1** in the presence of KCN (10-fold molar excess with respect to **1**) and 18-crown-6 ether in THF–*t*-BuOH (5:1 v/v) required a longer irradiation time due to a lower transparency and gave a somewhat lower yield of **3** after purification.

Recently, the Lewis acid catalyzed addition of trimethylsilyl cyanide (Me_3SiCN) to Schiff bases has been developed as a modified Strecker synthesis[8] and also, the $AlCl_3$-catalyzed rearrangement of **1** to 3-aryl-4-azahomoadamantane has been reported.[4] Therefore, we examined the Lewis acid catalyzed decomposition of **1** in the presence of Me_3SiCN as a thermal route to **3**. A mixture of **1**, Me_3SiCN (22.5-fold molar excess) and $AlCl_3$ (3-fold molar excess with respect to **1**) in CCl_4 was heated under reflux for 18 h, followed by the usual workup, and chromatography afforded the aminonitrile **3** in 51% yield. However, photochemical generation of **2** in the presence of an excess of Me_3SiCN in THF did not afford **3** but only unidentified polymeric products. This fact suggests that the zwitter ionic character of the bridgehead imine **2** is not sufficient enough to cause S_E reaction of Me_3SiCN without the Lewis acid catalyst, even when the zwitter ionic character is strengthened by the electronegative nitrogen relative to the carbocyclic bridgehead alkenes.[9]

Aminonitrile **3** was converted to the corresponding amino acid **6** and its methyl ester **7** by usual procedures. All of these results are summarized in Scheme I.

Synthesis of 4-Azahomoadamantano[3,4]-Fused Heterocycles from 3. The base-catalyzed reaction of open-chain α-amino nitriles with aryl isocyanates is known

Scheme I



Scheme II

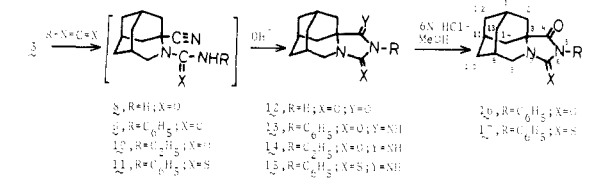


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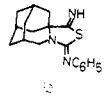
Table I. Physical Data of the Hydantoin Derivatives 12-17[a]

compd	mp,[b] °C	IR,[c] cm^{-1}	UV max,[d] nm (log ϵ)	^{1}H NMR,[e] δ
12	264-265	3200-2800, 2950, 1775, 1700, 1 1445		3.37 (d, 2, J = 4.0 Hz), 2.4-1.3 (m, 14)[f-h]
13	196-198	3300, 3060, 2920, 1725, 1645, 1420, 755, 740	220 (4.06)	7.5-7.2 (m, 6),[f] 3.61 (d, 2, J = 4.0 Hz), 2.5-1.4 (m, 13)
14	118-120	3280, 2920, 1710, 1635, 1455	226 (3.82)	5.90 (br s, 1),[f] 3.61 (q, 2, J = 7.0 (Hz), 3.53 (d, 2, J = 4.0 Hz), 2.5-1.4 (m, 13), 1.20 (t, 3, J = 7.0 Hz)
15	238-240	3240, 2925, 1660, 1445, 1298, 730	251 (4.68)	7.7-7.3 (m, 5), 6.80 (br, s, 1),[f] 3.39 (d, 2, J = 4.0 Hz), 2.6-1.5 (m, 13)
16	213-214	2920, 1770, 1710, 1405, 755	214 (4.34)	7.39 (s, 5), 3.14 (d, 2, J = 4.0 Hz), 2.5-1.2 (m, 13)
17	253-254	2920, 1740, 1465, 1285, 735	234 (4.31), 265 (4.50)	7.6-7.3 (m, 5), 3.93 (d, J = 4.0 Hz), 2.5-1.5 (m, 13)

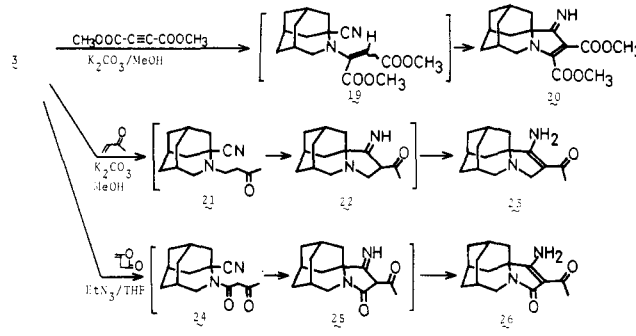
[a] See the paragraph at the end of paper about supplementary material. [b] For purification, see the Experimental Section. [c] KBr disk. [d] In MeOH. [e] In $CDCl_3$. [f] Decreased ca. 1 H or disappeared on shaking with D_2O. [g] In Me_2SO-d_6. [h] Broad singlet signal at δ 3.70 also appeared due to water.

to afford 4-iminoimidazolidin-2-ones (iminohydantoins) as cyclization products of the corresponding arylurea derivatives.[10] The amino nitrile **3**, on treatment with isocyanates or isothiocyanate, also gave hydantoin derivatives **12–15** via urea intermediates **8–11** as summarized in Scheme II and Table I. Reaction of **3** with isocyanic acid, generated from potassium cyanate and aqueous acetic acid,[11] followed by treatment with alkali gave hydantoin derivative **12** in 63% yield. On the other hand, reaction of **3** with phenyl isocyanate, ethyl isocyanate, and phenyl isothiocyanate, followed by treatment with alkali, gave the corresponding iminohydantoins **13** and **14** and iminothiohydantoin **15** in good yield. The iminohydantoin **13** and iminothiohydantoin **15** were converted to hydantoin **16** and thiohydantoin **17**, respectively, on hydrolysis in hydrochloric acid–methanol. All of these products were characterized by analytical and spectral data (Table I). The thiohydantoin structure of **17** was corroborated by UV max (MeOH) signals at 234 nm (log ϵ 4.31) and 265 (4.50), which are very similar to UV max (EtOH) 232 nm (log ϵ 4.02) and 267 (4.15) of 1-methyl-3-phenyl-2-thiohydantoin.[12] The spectral data of compound **15** supported the iminohydantoin structure to the exclusion of diiminothiazolidine **18**.



The reaction of **3** with electron-deficient alkynes and alkenes was examined as a possible route to 4-azahomoadamantano[3,4]-fused pyrroline derivatives (Scheme III). The reaction of **3** with dimethyl acetylenedicarboxylate (DMAD) in the presence of a catalytic amount of potassium carbonate afforded iminopyrroline derivative **20** in 50% yield. Although enamine intermediate **19** could not be isolated, the ^{1}H NMR spectrum of the DMAD fraction after chromatography (silica gel) revealed a singlet at δ 5.20 assignable to the vinyl proton, supporting the formation of **19**.[14] The reaction of **3** with ethyl propiolate was also

Scheme III



examined under the same conditions, but no cyclization product could be isolated.

The reaction of **3** with methyl vinyl ketone in the presence of potassium carbonate afforded a cyclization product, **23**, as colorless crystals (58%). The structure of **23** was supported by ^{1}H NMR data and a UV max (MeOH) signal at 298 nm (log ϵ 4.12).[15] The reaction of **3** with diketene in the presence of triethylamine afforded **26** in 84% yield. The facile formation of **23** and **26** could be explained by base-catalyzed cyclizations of the initial adducts **21** and **24**[16] to give **22** and **25**, followed by tautomerization to the final products **23** and **26**, respectively (Scheme III). The reactions of **3** with other Michael acceptors such as acrylonitrile, methyl acrylate, and acrolein were also examined under similar conditions, but no cyclization products were obtained because of the facile polymerization of the Michael acceptors.

Amino nitrile **32**, derived from unusually stable bridgehead imine **31**, affords the imine **31** on treatment with acetic anhydride–pyridine at room temperature.[17] However, acetylation of **3** under the same conditions gave *N*-acetyl derivative **27** in 86% yield. This is not unexpected since the bridgehead imine **2** is probably more

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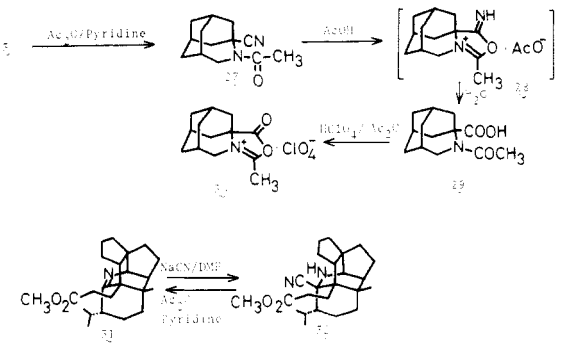
(15) Cf. UV max (heptane) 285 nm (log ϵ 3.8) of 4-amino-3-penten-2-one: Cromwell, N. H.; Watson, W. R. *J. Org. Chem.* **1949**, *14*, 411.
(16) For a recent review on the reactions of diketene, see: Kato, T. *Acc. Chem. Res.* **1974**, *7*, 265.
(17) Toda, M.; Hirata, Y.; Yamamura, S. *J. Chem. Soc., Chem. Commun.* **1970**, 1597; *Tetrahedron* **1972**, *28* 1477.

Scheme IV



strained than **31** on the basis of a comparison of the reactivity difference[5,17] and Δ-strain values of the related carbocyclic ring systems.[18] The acetylamino nitrile **27** was hydrolyzed readily to carboxylic acid **29** on heating in aqueous acetic acid, while amino nitrile **3** was stable under these conditions. The hydrolysis of **27** may be facilitated by the formation of iminooxazolinium acetate **28**, and intermediate not available in the hydrolysis of **3** (Scheme IV). The intermediacy of **28** is supported by the quantitative isolation of the oxazolium perchlorate **30** on reaction of **29** with Ac_2O–$HClO_4$.[19]

As described above, α-amino nitrile **3** is a useful intermediate for synthesis of 4-azahomoadamantano[3,4]-fused-type heterocycles, which are difficult to obtain by other routes. Furthermore, the phase-transfer-catalyzed method for conversion of azide **1** to **3** without use of hydrogen cyanide may provide a safer modification of the Strecker amino acid synthesis.

Experimental Section[20]

3-Cyano-4-azahomoadamantane (3). Method A. A vigorously stirred mixture of 1-azidoadamantane (**1**;[3] 1.77 g, 10.0 mmol), sodium cyanide (10.0 g, 204 mmol), and Adogen 464 (400 mg) in water (20 mL) and *n*-hexane (200 mL) was irradiated under argon for 3 h at room temperature through a Vycor filter with a 100-W high-pressure mercury lamp.[21] The resulting precipitate was filtered and washed with water and ether to afford 3-hydroxy-4-azahomoadamantane (**4**; 420 mg, 25.0%), which had the same IR and ^1H NMR spectra as an authentic sample.[2,3] The organic layer of the filtrate and washings was separated, and the aqueous layer was extracted with ether (3 × 10 mL). The organic layer was washed with water (3 × 10 mL) and dried (Na_2SO_4). Removal of the solvent and sublimation (180 °C, 0.4 mm) gave **3** as a colorless solid: 1.13 g (64.0%); mp. 151–153 °C; IR(KBr) 3280, 2920, 2220, 1450, 1160, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.04 (d, 2, J = 4.0 Hz), 2.5–1.3 (m, 13), 1.95 (s, 1, disappeared on shaking with D_2O); ^{13}C NMR ($CDCl_3$) δ 124.9 (s, CN), 53.9 (s, C_3), 53.1 (t, C_5), 43.0 (t, C_2, C_{11}), 36.2 (t, C_7, C_{10}), 34.6 (t, C_9), 33.2 (d, C_6), and 26.4 (d, C_1, C_8); mass spectrum, m/z (relative intensity) 177 (19), 176 (100, M^+), 175 (42), 161 (19), 149 (75), 133 (54), 119 (67), 106 (54), 81 (75), 68 (99).

Anal. Calcd for $C_{11}H_{16}N_2$: C, 74.96; H, 9.15; N, 15.89. Found: C, 75.06; H, 9.09; N, 15.90.

Compound **3** gave a picrate with a melting point of 244–246 °C dec.

Anal. Calcd for $C_{17}H_{19}N_5O_7$: C, 50.37; H, 4.72; N, 17.28. Found: C, 50.65; H, 4.57; N, 17.09.

Method B. A mixture of **1** (177 mg, 1.00 mmol), potassium cyanide (651 mg, 10.0 mmol), and 18-crown-6 (2.08 g, 5.77 mmol) in *t*-BuOH (10 mL) and THF (50 mL) was vigorously stirred for 0.5 h. After removal of some insoluble solids by decantation, the mixture was deoxygenated with argon for 0.5 h and was irradiated as above for 22 h at room temperature. The mixture was diluted with ether (100 mL) and successively washed with 2% aqueous NaOH (3 × 20 mL) water (10 mL), and saturated aqueous sodium chloride and dried (Na_2SO_4). Removal of the solvent and chromatography on a silica gel column eluted with ethyl acetate afforded **3** (100 mg, 57%).

Method C. A mixture of **1** (177 mg, 1.00 mmol), TMSCN (2.23 g, 22.5 mmol), and aluminum chloride (400 mg, 3.00 mmol) in carbon tetrachloride (20 mL) was heated to reflux under argon for 18 h. The cooled mixture was poured onto ice-cooled saturated aqueous sodium carbonate (50 mL), and the resulting precipitate was filtered through Celite 545 and washed with dichloromethane (10 mL). The organic layer from the combined filtrate and washings was separated, and the aqueous layer was extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed with water and dried (Na_2SO_4). Removal of the solvent gave crude product which was purified on a basic alumina column eluted with dichloromethane to give **3** (90 mg, 51.0%).

4-Azahomoadamantane-3-carboxylic Acid (6). A mixture of **3** (100 mg, 0.57 mmol) and potassium hydroxide (40 mg, 0.57 mmol) in ethanol (5 mL) was heated at reflux for 45 h. Removal of the solvent gave crude product which was dissolved in methanol and eluted on a silica gel column with MeOH–AcOEt to afford unreacted **3** (10.0 mg, 10.0% recovery) and the amino acid **6** as a colorless solid: 90 mg (74.0%, calculated as the monohydrate); mp 282–285 °C dec; IR(KBr) 3400–2600, 2910, 1640 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 3.36 (br s, 4), 3.19 (d, 2, J = 4.0 Hz), 2.5–1.5 (m, 13); mass spectrum, m/z (relative intensity) 196 (4), 195 (27, M^+), 150 (100), 78 (35), 44 (56).

Anal. Calcd for $C_{11}H_{17}NO_2 \cdot H_2O$: C, 61.95; H, 8.98; N, 6.57. Found: C, 61.92; H, 8.92; N, 6.51.

Methyl 4-Azahomoadamantane-3-carboxylate Hydrochloride (7). Hydrogen chloride gas was bubbled into a solution of **6** (260 mg, 1.27 mmol) in methanol (20 mL), and the mixture was heated at reflux for 6 h. Removal of the solvent under reduced pressure gave a solid residue which was recrystallized from methanol to afford the ester hydrochloride **7**: 216 mg (72.0%); mp 172–174 °C dec; IR (KBr) 3400–2400, 2940, 1740 cm^{-1}; ^1H NMR($CDCl_3$) δ 9.22 (br s, 2, disappeared on shaking with D_2O), 3.86 (s, 3), 3.72 (br s, 2), 2.7–1.2 (m, 13); mass spectrum, m/z (relative intensity) 209 (30, M^+ – HCl), 150 (100), 93 (30).

Anal. Calcd for $C_{12}H_{20}NO_2Cl$: C, 58.65; H, 8.20; N, 5.70. Found: C, 58.36; H, 8.32; N, 5.87.

5,7-Diazatetracyclo[7.3.1.1^{3,11}.0^{3,7}]tetradecane-4,6-dione (12). To a stirred solution of **3** (176 mg, 1.00 mmol) in acetic acid (2 mL) and water (4 mL) was added a solution of potassium cyanate (310 mg, 3.80 mmol) in water (6 mL) at 30 °C. The resulting mixture was stirred for 3 h at 55 °C, followed by addition of aqueous sodium hydroxide (2.00 g in 5 mL of water) and further stirring for 12 h at room temp. The mixture was diluted with water (20 mL) and concentrated under reduced pressure to afford a precipitate which was collected by filtration and recrystallized from ethanol to give the hydantoin **12** as colorless cyrstals (139 mg, 63.0%). For physical data, see Table I.

4-Imino-5-phenyl-5,7-diazatetracyclo[7.3.1.1^{3,11}.0^{3,7}]tetradecan-6-one (13). A mixture of **3** (100 mg, 0.57 mmol) and phenyl isocyanate (70 mg, 0.59 mmol) in dry dichloromethane (5 mL) was stirred at room temperature for 15 h. After removal of the solvent, the residue was dissolved in ethanol (5 mL) containing potassium hydroxide (10 mg, 0.18 mmol), and the mixture was allowed to stand at room temperature for 2 days. Addition of water (10 mL) resulted in the precipitation of crystals which were collected by filtration and recrystallized from benzene to give the iminohydantoin **13** (142 mg, 85.5%). For physical data, see Table I.

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(20) Melting points were taken in a sealed tube on a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were obtained on a JASCO IRA-1 spectrometer. UV spectra were determined on a Hitachi Model 200-10 spectrophotometer. ^1H NMR and ^{13}C NMR spectra were recorded on a JEOL JNM-C-60HL instrument at 60 MHz and a JEOL JNM-FX-60 FT NMR spectrometer at 15.04 MHz, respectively. Chemical shifts are reported in parts per million (δ) relative to Me_4Si as an internal standard in $CDCl_3$, Me_2SO-d_6, or CF_3COOD. Mass spectra were obtained with a JEOL JMS-D10 mass spectrometer at 75 eV. Microanalyses were performed with a Perkin-Elmer 240B elemental analyzer. Glc analyses were carried out by using a JEOL JGC-20K gas chromatograph on 1- or 2-m silicone SE-30 columns at 150–250 °C.

(21) The use of a quartz filter gave similar results, but the use of a Pyrex filter required a longer irradiation time.

4-Imino-5-ethyl-5,7-diazatetracyclo[7.3.1.1^{3,11}.0^{3,7}]tetradecan-6-one (14). Treatment of **3** (176 mg, 1.00 mmol) with ethyl isocyanate (180 mg, 2.52 mmol) as above and recrystallization from benzene afforded **14** as a white solid (220 mg, 89.0%). For physical data, see Table I.

4-Imino-5-phenyl-5,7-diazatetracyclo[7.3.1.1^{3,11}.0^{3,7}]tetradecane-6-thione (15). A mixture of **3** (176 mg, 1.00 mmol), phenyl isothiocyanate (135 mg, 1.00 mmol), and potassium hydroxide (10 mg, 0.18 mmol) in benzene was heated at reflux for 30 h. The mixture was concentrated to afford a precipitate which was collected by filtration and washed with water, giving **15** as a pale yellow solid (204 mg, 66.0%). For physical data, see Table I.

5-Phenyl-5,7-diazatetracyclo[7.3.1.1^{3,11}.0^{3,7}]tetradecan-4,6-dione (16). A solution of **13** (100 mg, 0.34 mmol) in methanol (5 mL) and 6 *N* hydrochloric acid (5 mL) was heated under reflux for 8 h. After concentration to ca. 6 mL, the mixture was neutralized with saturated aqueous sodium carbonate to precipitate colorless crystals which were filtered and recrystallized from carbon tetrachloride, giving **16** (82 mg, 82.0%). For physical data, see Table I.

4-Oxo-5-phenyl-5,7-diazatetracyclo[7.3.1.1^{3,11}.0^{3,7}]tetradecane-6-thione (17). The iminothiohydantoin **15** (100 mg, 0.32 mmol) was hydrolyzed as above for 20 h, followed by usual workup and recrystallization from carbon tetrachloride to give **17** as colorless crystals (78 mg, 78.0%). For physical data, see Table I.

Dimethyl 4-Imino-7-azatetracyclo[7.3.1.1^{3,11}.0^{3,7}]tetradec-5-ene-5,6-dicarboxylate (20). A mixture of **3** (100 mg, 0.57 mmol), DMAD (100 mg, 0.70 mmol), and anhydrous potassium carbonate (3 mg, 0.02 mmol) was stirred for 3 days at room temperature and 5 h at 50 °C. Removal of the solvent, followed by chromatography of the residue on a silica gel column eluted with MeOH–AcOEt (1:19 v/v) afforded unreacted DMAD (56 mg) which contained a small amount of the enamine **19** (^{1}H NMR signal at δ 5.20 s). The second fraction gave the iminopyrroline **20** as faintly yellowish crystals: 91 mg (50.0%); mp 165–167 °C; IR(KBr) 3400–3300, 2930, 1738, 1675, 1615, 1542 cm^{-1}; UV max (MeOH) 248 nm (log ϵ 4.30), 322 (4.35); ^{1}H NMR ($CDCl_3$) δ 3.96 (s, 3), 3.73 (s, 3), 3.59 (d, 2, J = 3.0 Hz), 2.4–1.2 (m, 13, decreased to ca. 12 on shaking with D_2O); mass spectrum, m/z (relative intensities) 319 (17), 318 (100, M$^+$), 287 (35), 286 (39), 271 (32)8 259 (39), 202 (66), 200 (29), 149 (92).

Anal. Calcd for $C_{17}H_{22}N_2O_4$: C, 64.13; H, 6.97; N, 8.80. Found: C, 64.28; H, 7.09; N, 8.52.

4-Amino-5-acetyl-7-azatetracyclo[7.3.1.1^{3,11}.0^{3,7}]tetradec-4-ene (23). A mixture of **3** (176 mg, 1.00 mmol), methyl vinyl ketone (346 mg, 4.93 mmol), and anhydrous potassium carbonate (10 mg, 0.07 mmol) in methanol (5 mL) was allowed to stir for 5 days at room temperature. The mixture was concentrated to ca. 1 mL and diluted with water to afford a brownish solid which was collected by filtration and recrystallized from methanol, giving **23** as colorless crystals: 143 mg (58.0%); mp 229–231 °C; IR(KBr) 3310, 3170, 2920, 2885, 1640, 1540 cm^{-1}; UV max (MeOH) 221 nm (sh), 298 (log ϵ 4.12); ^{1}H NMR (Me_2SO-d_6) δ 7.62 (br s, 2, disappeared on shaking with D_2O), 3.67 (s, 3), 2.89 (d, 2, J = 4.0 Hz), 1.89 (s, 3), 2.2–1.3 (m, 13); mass spectrum, m/z (relative intensity) 247 (14), 246 (65, M$^+$), 245 (100), 203 (38), 43 (63).

Anal. Calcd for $C_{15}H_{22}N_2O{\cdot}H_2O$: C, 68.15; H, 9.15; N, 10.60. Found: C, 68.35; H, 9.19; N, 10.60.

4-Amino-5-acetyl-7-azatetracyclo[7.3.1.1^{3,11}.0^{3,7}]tetradec-4-en-6-one (26). A mixture of **3** (100 mg, 0.57 mmol), diketene (110 mg, 1.30 mmol) and triethylamine (73 mg, 0.72 mmol) in anhydrous THF (5 mL) was allowed to stir for 2 days at room temperature. The resulting crystals were filtered and washed with ether, giving **26**: 122 mg (84.0%); UV max (MeOH) 234 nm (log ϵ 4.48), 292 (4.27); ^{1}H NMR (CF_3COOD) δ 3.88 (d, 2, J = 3.0 Hz), 2.72 (s, 3), 2.6–1.5 (m, 13); mass spectrum, m/z (relative intensity) 261 (25), 260 (100, M$^+$), 259 (29), 245 (30).

Anal. Calcd for $C_{15}H_{20}N_2O_2$: C, 69.20; H, 7.74; N, 10.76. Found: C, 69.21; H, 7.78; N, 10.72.

3-Cyano-4-acetyl-4-azahomoadamantane (27). A mixture of **3** (176 mg, 1.00 mmol) and acetic anhydride (1.02 g, 10.0 mmol) in pyridine (2 mL) was stirred for 15 h at room temperature. The mixture was poured onto saturated aqueous sodium carbonate (10 mL) and extracted with chloroform (4 × 5 mL). The combined extracts were washed with saturated aqueous sodium carbonate, dried (Na_2SO_4), and evaporated to afforded a solid residue which was recrystallized from carbon tetrachloride, giving **27** as colorless crystals: 188 mg (86.0%); mp 131–132 °C; IR(KBr) 2920, 2205, 1635, 1540 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.62 (d, 2, J = 4.0 Hz), 2.18 (s, 3), 2.7–1.3 (m, 13); mass spectrum, m/z (relative intensity) 210 (10), 218 (68, M$^+$), 203 (14), 176 (100), 175 (98), 134 (33).

Anal. Calcd for $C_{13}H_{18}N_2O$: C, 71.53; H, 8.31; N, 12.83. Found: C, 71.64; H, 8.38; N, 12.64.

4-Acetyl-4-azahomoadamantane-3-carboxylic Acid (29). A solution of **3** (176 mg, 1.00 mmol) in acetic anhydride (10 mL) was heated to reflux for 5 h. The solution was diluted with water (3 mL) and heated to reflux for 10 h. Removal of the solvent under reduced pressure gave a solid residue which was crystallized from ethanol to afford **29**: 106 mg (45.0%): mp 225–228 °C dec; IR (KBr) 3500–2600, 2920, 1735, 1600 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 11.5 (br s, 1, disappeared on shaking with D_2O), 3.18 (d, 2, J = 4.0 Hz), 1.99 (s, 3), 2.4–1.2 (m, 13); ^{13}C NMR (Me_2SO-d_6) δ 174.7 (s, COOH), 168.2 (s, $NCOCH_3$), 62.5 (s, C_3), 52.2 (t, C_5), 36.0 (t, C_2, C_{11}),[22] 35.0 (t, C_7, C_{10}),[22] 34.8 (t, C_9), 30.3 (d, C_6), 26.3 (d, C_1, C_8), 23.0 (q, CH_3); mass spectrum, m/z (relative intensities) 237 (25, M$^+$), 219 (74), 191 (67), 150 (99), 149 (100), 148 (81), 93 (63).

Anal. Calcd for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07; N, 5.90. Found: C, 65.52; H, 8.03; N, 5.82.

4-Oxo-6-methyl-5-oxa-7-azatetracyclo[7.3.1.1^{3,11}.0^{3,7}]tetradec-6-enium Perchlorate (30). To an ice-cooled and stirred mixture of **29** (25 mg, 0.11 mmol) in acetic anhydride (1 mL) was added perchloric acid (70%, 0.1 mL), and the resulting clear solution was diluted with anhydrous ether. The resulting crystals were filtered, washed with ether, and dried to afford the salt **30**: 34 mg (100%); mp 221–223 °C; IR (KBr) 2925, 1873, 1860, 1643, 1100 cm^{-1}; ^{1}H NMR (CF_3COOD) δ 4.26 (br s, 2), 2.85 (s, 3), 2.7–1.8 (m, 13).

Anal. Calcd for $C_{13}H_{18}NO_6Cl$: C, 48.84; H, 5.67; N, 4.38. Found: C, 48.82; H, 5.72; N, 4.35.

Registry No. **1**, 24886-73-5; **3**, 78837-35-1; **3** picrate, 78837-36-2; **4**, 55086-02-7; **6**, 78822-91-0; **7**, 78822-92-1; **12**, 78822-93-2; **13**, 78822-94-3; **14**, 78822-95-4; **15**, 78822-96-5; **16**, 78822-97-6; **17**, 78822-98-7; **19**, 78822-99-8; **20**, 78823-00-4; **23**, 78823-01-5; **26**, 78823-02-6; **27**, 78823-03-7; **29**, 78823-04-8; **30**, 78823-06-0; methyl vinyl ketone, 78-94-4; phenyl isocyanate, 103-71-9; ethyl isocyanate, 109-90-0; phenyl isothiocyanate, 103-72-0; diketene, 674-82-8; potassium cyanate, 590-28-3; DMAD, 762-42-5.

Supplementary Material Available: Tables of mass spectral and analytical data of the hydantoin derivatives **12–17** (Table II) and ^{13}C NMR data of **13** and **15–17** (Table III) (2 pages). Ordering information is given on any current masthead page.

(22) These assignments may be interchangeable.