reaction mixture basic, and the time was recorded when the indicator changed back to the acidic form. Repetition of this process gave between 10 and 34 points through the course of the reaction. Reactions were followed for up to 8–10 half-lives; however, only the first 1–3 half-lives were taken for calculations. The titrant volume at 8–10 half-lives was taken as the infinity titer.

GLC analyses were carried out by injection of reaction solution samples on the instument indicated above (flow rate 60–100 mL/min, and injector, column, and detector temperatures ~230, 180, and 260 °C). Integration was by "cut and weigh", with adamantane as an internal standard.

In a reaction followed by NMR, aliquots of reaction solution were added to a mixture of methylene chloride and aqueous sodium bicarbonate. After additional extraction with methylene chloride, the organic layer was washed, dried, and evaporated under vacuum, and the residue was analyzed by NMR in deuteriochloroform. The extent of reaction was determined by comparison of the integral of the signal for CH_2O protons with that for the N–CH protons of both reactant and product.

Rate constants and activation parameters were calculated, using a least-squares program on a Wang 700 calculator.

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Registry No. **1a**, 935-56-8; **1b**, 3632-95-9; **1c**, 3148-17-2; **1d**, 768-90-1; **1e**, 3049-61-4; **1f**, 16200-57-0; **1g**, 58373-13-0; **1h**, 3015-19-8; **1i**, 3015-18-7; **1j**, 71265-13-9; **1k**, 71265-14-0; **2a**, 59223-60-8; **2b**, 59223-59-5; **2c**, 59223-58-4; **3a**, 57422-54-5; **3b**, 40213-45-4; **3c**, 57422-55-6; **4a**, 15158-55-1; **4b**, 51209-45-1; **4c**, 40164-34-9; 4 (Y = Cl, X = S), 71265-15-1; **5a**, 27011-47-8; **5d**, 71265-16-2.

Synthesis of Adamantane Derivatives. 47.[1] Photochemical Synthesis of 4-Azahomoadamant-4-enes and Further Studies on Their Reactivity in Some Cycloadditions

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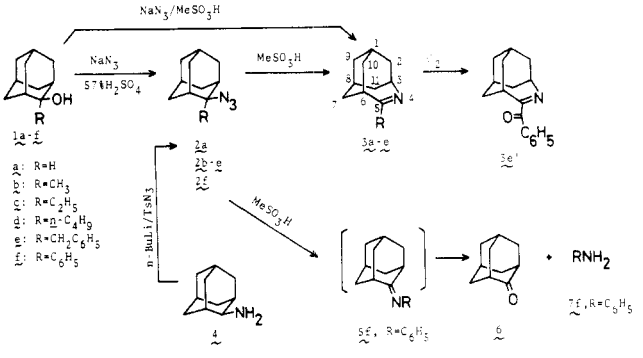
Direct photolysis of 2-azidoadamantanes (**2a,b,e,f**) in cyclohexane and/or in benzene afforded predominantly ring-expanded 4-azahomoadamant-4-enes (**3a,b,e,f**) and *N*-adamantylideneamines (**5a,b,e,f**) resulting from migration of H or a nonring carbon atom as minor products. The benzyl derivative **3e** was particularly air-sensitive and was isolated as the 5-benzoyl derivative **3e'**. The ^{13}C NMR spectra of **3a,b,e',f** are reported. The reactions of imines **3** with diphenylketene, benzonitrile oxide, diphenylnitrilimine, and tosylmethyl isocyanide afforded the corresponding cycloadducts **11**, **14a–c**, **15a,b**, and **17**, respectively.

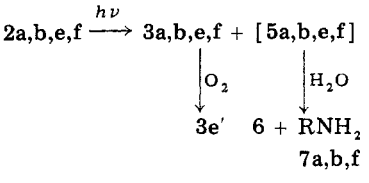
We have recently reported[2,3] that 2-azidoadamantanes **2b–f** and 4-azahomoadamant-4-enes **3a–e** are obtained in good yields from the corresponding 2-hydroxyadamantanes **1a–f** by treatment with sodium azide in 57% H_2SO_4 and in CH_3SO_3H, respectively (Scheme I). The parent **2a** could not be prepared by this simple method but was obtained by the diazo-transfer method[4] from 2-aminoadamantane (**4**). In contrast, rearrangement of **2f**, readily obtainable from **1f**, gave only adamantanone (**6**) and aniline (**7**), products of phenyl migration.

To extend these studies, we have examined the photolysis of 2-azidoadamantanes as a possible route to 4-azahomoadamant-4-enes. In this paper, we describe the results of photolysis of **2a,b,e,f**, which provided a better method for synthesis of **3f**. The carbon-13 nuclear magnetic resonance spectra of **3a,b,e',f** and cycloadditions of **3a,b,f** with ketenes and 1,3-dipoles are also reported.

Scheme I



Scheme II



Results and Discussion

Photolysis of 2-Azidoadamantanes. The photolysis of bridgehead azides such as 1-azidonorbornane,[5] 1-azidoadamantane,[6] and 1-azidotriptycene[7] is an elegant method for generation of the corresponding bridgehead imines. However, photolysis of azide derivatives at nonbridgehead positions of bi- and tricyclic compounds such as 2-azidoadamantanes has not been investigated extensively. Results of photolysis of **2a,b,e,f** in cyclohexane and/or in benzene are summarized in Scheme II and Table I. For all azides examined, preferential formation of the ring-expanded 4-azahomoadamant-4-enes **3** rather than imine **5**, the H or substituent migration product, was observed. Imines **5a**, **5b**,[8] and **5f**[9] were unstable in the

(1) Part 46: T. Sasaki, S. Eguchi, and T. Suzuki, *J. Chem. Soc., Chem. Commun.*, 506 (1979).
(2) T. Sasaki, S. Eguchi, and N. Toi, *Heterocycles*, **7**, 315 (1977).
(3) T. Sasaki, S. Eguchi, and N. Toi, *J. Org. Chem.*, **43**, 3810 (1978).
(4) For a review, see M. E. C. Biffin, J. Miller, and D. B. Paul in "The Chemistry of the Azido Group", S. Patai, Ed., Interscience, New York, 1971, pp 168–71.
(5) J. O. Reed and W. Lowski, *J. Org. Chem.*, **36**, 2864 (1971).
(6) H. Quast and P. Eckert, *Justus Liebigs Ann. Chem.*, 1727 (1974).
(7) H. Quast and P. Eckert, *Angew. Chem., Int. Ed. Engl.*, **15**, 168 (1976).

0022-3263/79/1944-3711$01.00/0

Scheme III

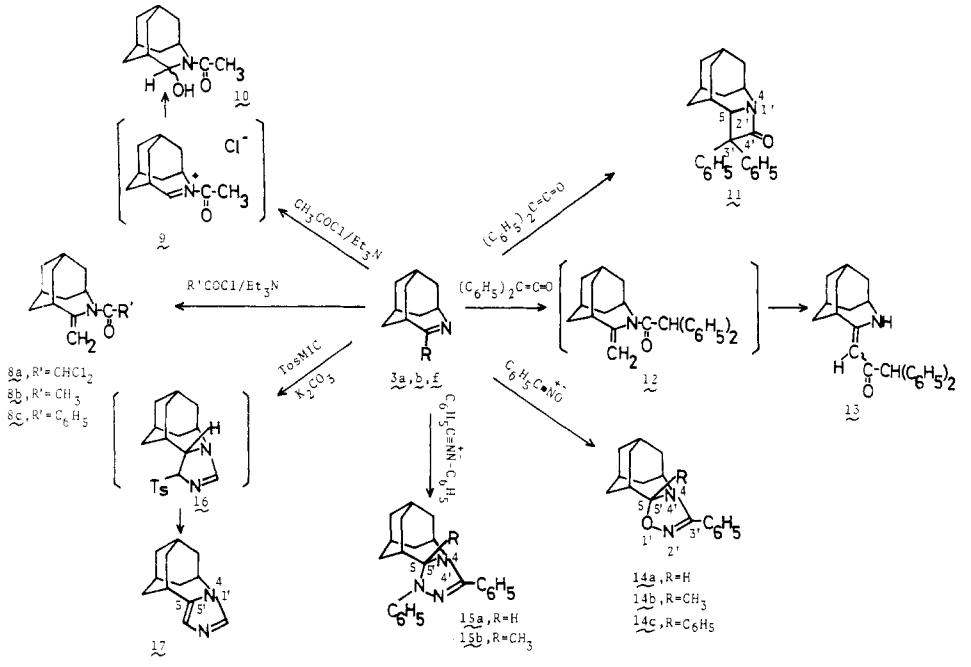
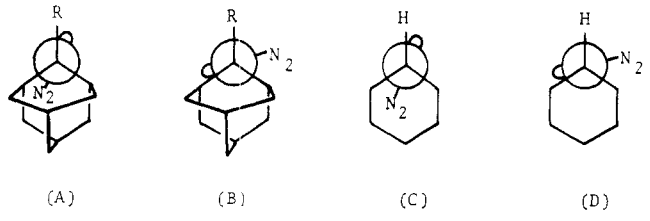


Table I. Photolysis of 2-Azidoadamantanes[a]

azide	solvent	concn, mM	products (yield, %)	
2a	cyclohexane	4.41	3a (61.5)[b]	6 (38.5)[b]
2a	benzene	4.41	3a (57.0)[b]	6 (43.0)[b]
2b	cyclohexane	10.4	3b (57.7)[c]	6 (12.8)[c]
2b	benzene	10.4	3b (53.3)[c]	6 (35.5)[c]
2e	cyclohexane	3.17	3e (55.0)[b,d]	5e (45.0)[b]
2f	cyclohexane	7.94	3f (35.7)[c,e]	6 (22.7)[c,e]
2f	benzene	7.94	3f (35.1)[c,f]	6 (26.3)[c,f]

[a] Photolysis was carried out through a quartz filter with a 100-W high-pressure mercury lamp for 2 h. [b] Relative yields on GLC analysis. [c] Isolated yields. [d] Isolated as air-oxidation product 3e′ in 21.1% yield. [e] A 10.3% amount of 2f was recovered. [f] A 11.1% amount of 2f was recovered.

atmosphere and were hydrolyzed quantitatively to amine RNH_2 (7) and adamantanone (6) which was analyzed or isolated (Table I). Preferential formation of **3a** from **2a** is unexpected even if the statistical factor is considered, in view of the fact that only H migration was observed for cyclohexyl azide,[10] in which migration ratios of 5:1–2 for H/R and 1:1 for R/C_6H_5 are reported.[10,11] These migratory ratios are correlated reasonably with the conformations of alkyl azides in the ground state.[10,11] The present results can also be rationalized in terms of the conformational factors of **2**. The relative population of A (R = H, favorable for H migration) to B (R = H, favorable for



(A) (B) (C) (D)

ring expansion) may be much less compared with that of C to D for cyclohexyl azide due to the steric interaction between $-N_2$ and adamantane ring.[12] For other substituents, R, the same factor may operate more or less in favor of the conformation B, which explains the observed relatively higher yields of **3b,e,f**.[13] Previously, we assigned structure **3e** tentatively for the ring-expanded product of **2e** despite the absence of the benzylic protons at the normal region in the ^1H NMR spectrum,[2] but this product, isolated after chromatography, turned out to be 5-benzoyl derivative **3e′**, an air-oxidation product of **3e**,[14] on the basis of the ^{13}C NMR spectrum which revealed a carbonyl carbon signal at δ 195.0 (Table II). The UV and mass spectral data also supported structure **3e′** (see Experimental Section). The ^{13}C NMR data of **3a, 3b** and **3f** as well as **3e′** are summarized in Table II. The assignments were based on the chemical shifts, peak intensities, and proton off-resonance spectral data.[15] All of these compounds had the characteristic seven peaks due to the skeletal carbons which attested to the inherent C_s symmetry of **3** and the assigned structures. From the synthetic point of view, the isolation of **3f** in 35.7% yield is worthy of note since no trace of **3f** was obtained from the acidolysis route.[2]

Further Studies on Some Cycloadditions of 4-Azahomoadamant-4-enes (3a,b,f). We have reported

(8) For **5b** and **5e**, see E. Oliveros-Desherces, M. Riviere, J. Parello, and A. Lattes, *Synthesis*, 812 (1974).

(9) For **5f**, see T. Sasaki, S. Eguchi, and Y. Hirako, *Tetrahedron*, **32**, 437 (1976)

(10) R. M. Moriarty and R. C. Reardon, *Tetrahedron*, **26**, 1379 (1970).

(11) For reviews, see (a) R. A. Abramovitch and E. P. Kyba, ref 4, pp 297–308; (b) W. Lwowski in "Reactive Intermediates", Vol. 1, M. Jones, Jr., and R. A. Moss, Eds., Wiley-Interscience, New York, 1978, pp 198–201.

(12) (a) For cyclohexyl azide, we assume, reasonably, an equatorial azido conformation as the prefered conformation at the ground state. (b) We examined the photolysis of 1-phenylcyclohexyl azide where an axial azido and equatorial phenyl conformation may be prefered at the ground state, and hence, the ring expansion may become preferential by the same steric reason to **2**. In fact, preliminary results indicated that cyclohexanone anil was produced only in 27.1% yield (isolated as the 2,4-DNP of cyclohexanone after hydrolysis) but isolation of the ring-expanded product was unsucessful. Further details of the photolysis of 1-substituted cyclohexyl azides will be reported in future.

(13) Although both ground-state conformation and intrinsic migration aptitudes are postulated to be important factors for determining the migration tendencies of tertiary alkyl azides in the photorearrangements, the conformational factor may be more important for the present very hindered 2-azidoadamantane system: F. C. Montgomery and W. H. Saunders, Jr., *J. Org. Chem.*, **41**, 2368 (1976).

(14) For examples of air oxidation of imines, see O. Cervinka, *Enamines: Synth. Struct. React.*, 285–6 (1969).

(15) (a) L. F. Johnson and W. C. Jankowski, "Carbon-13 NMR Spectra", Wiley, New York, 1972. (b) For ^{13}C NMR data of 5-methylene-4-azahomoadamantanes, see ref 3.

Table II. Chemical Shifts (δ) of 4-Azahomoadamant-4-enes[a]

compd	$C_{1,8}$	$C_{2,11}$[b]	C_3	C_5	C_6	$C_{7,10}$[b]	C_9	other carbons
3a	27.1 (d)	28.3 (t)	55.8 (d)	171.5 (d)	37.6 (d)	32.6 (t)	35.7 (t)	
3b	28.0 (d)	31.0 (t)	54.5 (d)	178.3 (s)	40.7 (d)	33.3 (t)	35.7 (t)	29.4 (q)[c]
3e′	28.0 (d)	31.4 (t)	56.1 (d)	176.1 (s)	35.7 (d)	32.6 (t)	35.4 (t)	195.0 (s),[d] 135.5 (s), 133.0 (d), 130.7 (d), 128.2 (d)[e]
3f	28.1 (d)	31.6 (t)	55.3 (d)	177.1 (s)	38.1 (d)	33.1 (t)	35.7 (t)	142.6 (s), 129.0 (d), 128.1 (d), 126.6 (d)[e]

[a] Downfield from internal tetramethylsilane in $CDCl_3$, and see the structural formula in Scheme I for numbering of the carbon atoms. [b] These assignments may be interchangeable. [c] CH_3. [d] C=O. [e] Phenyl carbons.

recently[3] that the reactions of **3b** with acyl chloride and dichlorocarbene afford 5-methylene-4-azahomoadamantane derivatives (**8a–c** and **8**, R = H). As an extension of this study, we have investigated the reactions of **3a**, **3b**, and **3f** with acetyl chloride, diphenylketene, some 1,3-dipoles, and tosylmethyl isocyanide, and these results are summarized in Scheme III.

Treatment of **3a** with acetyl chloride in the presence of triethylamine (one of the conditions for the generation of ketene) in ether under reflux for 10 h afforded **10** as colorless crystals (31%) after chromatography. In the ^1H NMR spectrum ($CDCl_3$), **10** revealed characteristic signals at δ 5.48 (dd, 1 H) and 4.72 (d, 1 H). The former signal assignable to C_5H changed to a doublet (J = 4.2 Hz), and the latter signal due to OH disappeared on shaking with D_2O, supporting structure **10**.

The reaction of **3a** with diphenylketene at room temperature for 2 days afforded an adduct **11**, mp 133–137 °C (84%), which was determined to be a [2 + 2] cycloadduct on the basis of analytical and spectral data. Appearance of a strong IR (KBr) absorption at 1735 cm^{-1} ($\nu_{C=O}$) and ^1H NMR ($CDCl_3$) signals at δ 8.0–7.1 (m, 10 H), 4.26 (s, 1 H), 4.15 (br s, 1 H), 2.45 (br s, 1 H), and 2.3–0.9 (m, 12 H) were compatible with the assigned structure **11**.[16,17]

The reaction of **3b** with diphenylketene under similar conditions (room temperature, 2 days), however, did not afford the corresponding [2 + 2] cycloadduct but afforded compound **13** in 40% yield (Scheme III). The assigned vinylogous amide structure of **13** was supported by the UV absorption (MeOH) at λ_{max} 300 nm (ε 26 800)[18–20] and the ^1H NMR signals at δ 11.4 (br s, 1 H, disappeared on addition of D_2O, NH) and 4.99 and 4.92 (each s and 1 H, C=CH and COCH). The formation of **13** was surprising because enamides are known to be thermally stable under neutral or basic conditions,[21] although their photochemical 1,3-acyl shifts (symmetry-allowed as suprafacial) are well-known.[18] In the present system **8a–c** are, in fact, stable and isolated as reported previously.[3] Therefore, **13** may be formed by further reaction of an initially produced enamide **12** with diphenylketene[21a] or via a stepwise rearrangement of **12** due to instability by severe steric hindrance.[20]

The 1,3-dipolar cycloadditions of **3a–c** were examined by using benzonitrile oxide, *C,N*-diphenylnitrone, diphenylnitrilimine, and diazomethane as a facile route to some 4-azahomoadamantano[4,5]-fused five-membered heterocycles (Scheme III).[22,23]

The reaction of **3a** with benzonitrile oxide at room temperature for 3 days afforded regioselectively $\Delta^{2'}$-oxadiazoline **14a** as colorless crystals in 67% yield. The assigned regiochemistry was supported by the appearance of a characteristic ^1H NMR doublet signal at δ 5.70 (J = 3.0 Hz, 1 H, C_5H). Similarly, the reaction of **3b** and **3f** with benzonitrile oxide yielded **14b** and **14c** in 98 and 80% yields, respectively. The observed regiochemistry is that expected from frontier molecular orbital (FMO) theory, considering LUMO (1,3-dipole)/HOMO (dipolarophile) interaction.[24,25]

The reaction of **3a** with diphenylnitrilimine at room temperature for 6 days afforded $\Delta^{2'}$-triazoline **15a** as yellowish crystals in 37% yield. The assigned regiochemistry was corroborated by the appearance of a characteristic ^1H NMR doublet signal at δ 5.00 (J = 1.5 Hz, 1 H, C_5H). Similarly, the reaction of **3b** with diphenylnitrilimine gave triazoline **15b** in 50% yield. The regiochemistry of **15a** and **15b** was also in accord with that theoretically expected.[25,26] Triazolines **15a** and **15b** had very similar UV absorptions and are strongly fluorescent compounds.

Diphenylnitrone did not afford any adducts with **3a** and **3b**, probably because of a severe steric hindrance.[27] The reaction of **3b** with a large excess (20 times) of diazomethane in 1% aqueous dioxane[28] at room temperature for 1 month did not afford any adducts, though benzalaniline is known to react with diazomethane[28] via a HOMO-controlled-type cycloaddition.[26] The lower dipolarophilicity of **3b** for diazomethane may be due to a higher LUMO energy compared with benzalaniline.

A useful method for synthesis of imidazoles via two-step anionic 1,3-dipolar cycloadditions of tosylmethyl isocyanide (TosMIC) to the C=N double bond has been reported recently.[29] We examined, therefore, the reaction of **3a** and **3b** with TosMIC in the presence of potassium carbonate

(16) The higher reactivity of diphenylketene to the C=N double bond than ketene itself is well-known. For reviews, see A. K. Mukerjee and R. C. Srivastava, *Synthesis*, 327 (1973); N. S. Isaacs, *Chem. Soc. Rev.*, 5, 181 (1976).

(17) The observed regiochemistry is in accord with the expected one from FMO theory: I. Fleming, "Frontier Orbitals and Organic Chemical Reactions", Wiley, 1976, pp 143–8.

(18) For a recent review on photochemical synthesis of vinylogous amides, see G. R. Lenz, *Synthesis*, 489 (1978).

(19) Previously prepared enamides **8a–c**[3] had UV (MeOH) absorptions at λ_{max} 222 nm (ε 14 800) (**8a**), 278 (6900) (**8b**), and 216 (12 100) and 256 (4000) (**8c**), respectively.

(20) The photorearrangement of **3b** gave 5-(acetylmethylene)-4-azahomoadamantane which also had a very similar UV (MeOH) absorption to that of **13**: λ_{max} 302 nm (ε 23 400). The stereochemistry of **13** remains undetermined. Further studies on reactions of **8** are in progress, and these results will be published in future.

(21) 1-Methylene-2-arylcarbamoyl- (or -thiocarbamoyl-) -1,2,3,4-tetrahydroisoquinolines are known to rearrange to the corresponding vinylogous amides when refluxed in toluene: (a) R. Richter, *Chem. Ber.*, 105, 82 (1972); (b) M. D. Nair and S. R. Mehta, *Indian J. Chem.*, 7, 484 (1969).

(22) For synthesis of 4-azahomoadamantano[5,4]pyrimidines and -quinazolines from 4-azahomoadamantan-5-one, see V. G. Keizer and J. G. Korsloot, *J. Med. Chem.*, 14, 411 (1971).

(23) For synthesis of some homoadamantano[4,5]-fused heterocycles via 1,3-dipolar cycloadditions to homoadamant-4-ene, see T. Sasaki, S. Eguchi, and S. Hattori, *Heterocycles*, 11, 235 (1978).

(24) The LUMO/HOMO interaction also leads the same prediction in this case.

(25) K. N. Houk, J. Sims, C. R. Watts, and L. J. Luskus, *J. Am. Chem. Soc.*, 95, 7301 (1973).

(26) See ref 17, pp 148–61.

(27) Homoadamant-4-ene also did not react with diphenylnitrone.[23]

(28) P. K. Kadaba, *Tetrahedron*, 22, 2453 (1966).

(29) A. M. van Leusen, J. Wildeman, and O. Oldenziel, *J. Org. Chem.*, 42, 1153 (1977).

as a facile route to 4-azahomoadamantanoimidazoles. **3a** afforded the corresponding imidazole derivative **17** as colorless crystals in 49% yield, whose structure was supported by analytical and spectral data. However, the reaction of **3b** with TosMIC under similar conditions gave no adducts, and only **3b** was recovered. All of these results are summarized in Scheme III.

As described above, 5-unsubstituted as well as 5-alkyl- or -phenyl-substituted 4-azahomoadamant-4-enes are now readily obtainable via acidolysis or photolysis of the corresponding 2-azidoadamantanes. The cycloaddition reactivity of **3** depended considerably on the substituent R, but the reaction with appropriate ketene and 1,3-dipoles provided a convenient route to some 4-azahomoadamantano[4,5]-fused heterocycles.

Experimental Section[30]

Photolysis of 2-Azidoadamantanes. General Procedure. A stirred solution of 2-azidoadamantanes (**2a,b,e,f**)[2] in cyclohexane or in benzene (for the concentration, see Table I) under an argon atmosphere was irradiated for 2 h through a quartz filter with a 100-W high-pressure mercury lamp. Removal of the solvent gave crude products which were analyzed on GLC or purified by chromatography on alumina (Wako, basic, grade I), eluting with *n*-hexane–CH_2Cl_2. For identification of the photoproducts, authentic samples of **3a**, **3b**, **3e′**, and **5e** were prepared by the reported methods.[2,38] The results are shown in Table I.

5-Benzoyl-4-azahomoadamant-4-ene (3e′). A stirred solution of **2e**[2] (90.0 mg, 0.337 mmol) in cyclohexane (106 mL) was irradiated as above. Removal of the solvent gave a crude product as a brownish oil which was purified on a silica gel column (CH_2Cl_2–MeOH) to afford adamantanone (10.0 mg, 19.8%) and **3e′** (18.0 mg, 21.1%) as well as many uncharacterized side products. **3e′** was identical with the sample obtained from the acidolysis route (46.9%)[2] and had the following physical properties: mp 84–88 °C; IR (KBr) 1660, 1655 (sh), 1600, 1280, 910, 740, 680 cm^{-1}; UV (MeOH) λ_{max} 252 (ϵ 20 400), 350 (423); ^1H NMR (CCl_4) δ 8.2–7.0 (m, 5 H), 4.28 (t, J = 3.0 Hz, 1 H), 3.32 (t, J = 3.0 Hz, 1 H), 2.4–1.5 (m, 12 H); ^{13}C NMR, see Table II; mass spectrum, m/e 253 (M^+), 252, 225, 148, 107, 77 (base).

Anal. Calcd for $C_{17}H_{19}NO$: C, 80.57; H, 7.56; N, 5.53. Found: C, 80.58; H, 7.60; N, 5.48.

3e′ gave the corresponding hydrochloride as hygroscopic crystals: mp 167–170 °C dec; IR (KBr) 3400–2400, 1680, 1600, 1450, 1070, 750, 690 cm^{-1}; ^1H NMR ($CDCl_3$–D_2O) δ 8.1–7.1 (m, 5 H), 4.60 (br s, 1 H), 3.11 (br s, 1 H), 2.5–1.5 (m, 12 H).

Anal. Calcd for $C_{17}H_{20}NOCl\cdot H_2O$: C, 66.33; H, 7.20; N, 4.55. Found: C, 66.45; H, 7.39; N, 4.25.

5-Phenyl-4-azahomoadamant-4-ene (3f). A stirred solution of **2f**[2] (127 mg, 0.500 mmol) in cyclohexane (63 mL) was irradiated for 2 h as above. Removal of the solvent gave a crude product which was purified on an alumina column (*n*-hexane–CH_2Cl_2) to afford adamantanone (17.0 mg, 22.7%), unreacted azide (36.0 mg), and the ring-expanded product **3f** as a viscous oil (36.0 mg, 35.7%): IR (film) 3065, 1635, 1580, 1450, 1220, 1110, 1055, 795, 690 cm^{-1}; UV (MeOH) λ_{max} 239 nm (ϵ 12 500), 280 (1630); ^1H NMR ($CDCl_3$) δ 8.0–7.1 (m, 5 H), 4.32 (br s, 1 H), 3.38 (br s, 1 H), 2.6–1.0 (m, 12 H); ^{13}C NMR, see Table II.

Anal. Calcd for $C_{16}H_{19}N$: C, 85.28; H, 8.50; N, 6.22. Found: C, 85.50; H, 8.21; N, 6.01.

5-Hydroxy-4-acetyl-4-azahomoadamantane (10). To a stirred and refluxing mixture of **3a** (145 mg, 1.00 mmol) and triethylamine (151 mg, 1.50 mmol) in anhydrous ether (6 mL) was added acetyl chloride (118 mg, 1.50 mmol) in ether (3 mL) during 0.5 h under an argon atmosphere. After the refluxing was continued for 10 h, the cooled mixture was washed with water (5 mL) and dried (Na_2SO_4). Removal of the solvent gave a crude product which was purified on an alumina column (CH_2Cl_2) to afford **10** as colorless crystals (65 mg, 31.0%): mp 128–132 °C; IR (KBr) 3300, 1620, 1450, 1045 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.48 (dd, J = 3.4 and 4.2 Hz, 1 H; d, J = 4.2 Hz, on addition of D_2O), 4.72 (d, J = 3.4 Hz, 1 H, disappeared on addition of D_2O), 4.00 (br s, 1 H), 2.16 (s, 3 H), 2.5–1.35 (m, 13 H); mass spectrum, m/e 209 (M^+), 191, 166, 151, 136, 80 (base).

Anal. Calcd for $C_{12}H_{19}NO_2$: C, 68.86; H, 9.15; N, 6.69. Found: C, 68.59; H, 8.81; N, 6.93.

3′,3′-Diphenyl-4-azahomoadamantano[4,5-*a*]azetidin-4′-one (11). To a stirred solution of **3a** (75 mg, 0.50 mmol) in anhydrous benzene (6 mL) was added diphenylketene (145 mg, 0.75 mmol) in benzene (6 mL) at room temperature (18–25 °C). After the stirring was continued for 2 days, the solvent was removed to afford crude product which was purified on an alumina column (CH_2Cl_2) to give **11** (146 mg, 84.0%): mp 133–137 °C; IR (KBr) 3060, 1735, 1390, 700 cm^{-1}; UV (MeOH) λ_{max} 250 nm (ϵ 3000); ^1H NMR, see text.

Anal. Calcd for $C_{24}H_{25}NO$: C, 83.93; H, 7.34; N, 4.09. Found: C, 83.85; H, 7.49; N, 3.85.

5-(Diphenylacetyl)methylene-4-azahomoadamantane (13). A mixture of **3b** (162 mg, 1.00 mmol) and diphenylketene (291 mg, 1.50 mmol) in anhydrous benzene (8 mL) was stirred for 2 days at room temperature. Removal of the solvent afforded a brownish residue which was purified on an alumina column (*n*-hexane–CH_2Cl_2) to give **13** as colorless crystals (142 mg, 40.3%) mp 99–94 °C; IR (KBr) 3400, 3080, 3040, 1600, 1570, 1440, 1110, 740, 690 cm^{-1}; UV (MeOH) λ_{max} 300 nm (ϵ 26 800); ^1H NMR ($CDCl_3$) δ 11.4 (br s, 1 H, disappeared on shaking with D_2O), 7.55–7.1 (m, 10 H), 4.99 (s, 1 H), 4.92 (s, 1 H), 3.55 (br s, 1 H), 2.35 (br s, 1 H, 2.2–1.3 (m, 12 H).

Anal. Calcd for $C_{25}H_{27}NO$: C, 83.99; H, 7.61; N, 3.92. Found: C, 84.13; H, 7.47; N, 3.93.

3′-Phenyl-4-azahomoadamantano[4,5-*d*]-1′,2′,4′-Δ²′-oxadiazoline (14a). To an ice-cooled and stirred solution of phenylhydroximic acid chloride (100 mg, 0.65 mmol) in ether (14 mL) was added triethylamine (71 mg, 0.70 mmol), and after 3 min, the mixture was washed with water (2 × 10 mL) and dried (Na_2SO_4). To thusly prepared benzonitrile oxide solution[31] was added **3a** (74 mg, 0.50 mmol) in ether (5 mL). After stirring for 3 days at room temperature, removal of the solvent gave crude product which was purified by preparative TLC (alumina, CH_2Cl_2) to afford **14a** as crystals (90 mg, 67%): mp 108–111 °C; IR (KBr) 3070, 1585, 1400, 1185, 760, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.7–7.2 (m, 5 H), 5.70 (d, J = 3.0 Hz, 1 H), 3.70 (br s, 1 H), 2.5–1.30 (m, 13 H); mass spectrum, m/e 268 (M^+), 148, 103, 93, 77 (base).

Anal. Calcd for $C_{17}H_{20}N_2O$: C, 76.09; H, 7.51; N, 10.44. Found: C, 75.96; H, 7.47; N, 10.61.

3′-Phenyl-5-methyl-4-azahomoadamantano[4,5-*d*]-1′,2′,4′-Δ²′-oxadiazoline (14b). The reaction of **3b** (81 mg, 0.50 mmol) with benzonitrile oxide prepared as described above under the same conditions gave **14b** after chromatography (alumina, CH_2Cl_2) as crystals (139 mg, 98.0%): mp 130–133 °C; IR (KBr) 3080, 1590, 1190, 760, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.7–7.2 (m, 5 H), 3.65 (br s, 1 H), 1.55 (s, 3 H), 2.6–1.4 (m, 13 H): mass spectrum, m/e 282 (M^+), 267, 148, 121, 93, 79 (base), 77.

Anal. Calcd for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85; N, 9.92. Found: C, 76.45; H, 7.96; N, 9.92.

3′,5-Diphenyl-4-azahomoadamantano[4,5-*d*]-1′,2′,4′-Δ²′-oxadiazoline (14c). The reaction of **3f** (148 mg, 0.583 mmol) with benzonitrile oxide prepared as above under the same conditions gave **14c** after chromatography (alumina, *n*-hexane–CH_2Cl_2) as crystals (160 mg, 80.0%): mp 175–179 °C; IR (KBr) 3060, 1590, 1560, 1160, 750, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.0–7.1 (m, 10 H), 3.90 (br s, 1 H), 2.8–2.3 (m, 2 H), 2.3–1.0 (m, 11 H);

(30) Microanalyses were performed with a Perkin-Elmer 240 elemental analyzer. Melting points were determined in a sealed tube with a Yanagimoto micromelting point apparatus (hot-stage type) and are uncorrected. IR spectra were obtained with a Jasco IRA-1 spectrometer and UV spectra with a Hitachi Model 200–10 spectrophotometer. ^1H NMR spectra were recorded on a JEOL JNM-C-60HL instrument at 60 MHz, while ^{13}C NMR spectra were recorded on a JEOL JNM-FX 60 FT NMR spectrometer at 15.04 MHz in $CDCl_3$. All NMR spectral peak positions are given in parts per million (δ) downfield from tetramethylsilane as an internal standard. Mass spectra were obtained with a Hitachi RMS-4 mass spectrometer at 70 eV. GLC analyses were performed with a JEOL JGC-20K gas chromatograph on a 1- or 2-m Silicone SE-30 column at 80–250 °C.

(31) For a review on nitrile oxide, see C. Grundmann and P. Grünanger, "The Nitrile Oxides", Springer-Verlag, Berlin, 1971.

mass spectrum, m/e 344 (M^+), 267, 148, 103 (base), 80, 79, 77.

Anal. Calcd for $C_{23}H_{24}N_2O$: C, 80.20; H, 7.02; N, 8.13. Found: C, 80.42; H, 7.20; N, 7.87.

1′,3′-Diphenyl-4-azahomoadamantano[4,5-*d*]-1′,2′,4′-$\Delta^{2'}$-triazoline (15a). To a stirred mixture of **3a** (75 mg, 0.50 mmol) and (α-chlorobenzylidene)phenylhydrazine[32] (58 mg, 0.25 mmol) in benzene (3 mL) was added triethylamine (51 mg, 0.50 mmol) in benzene (3 mL) at room temperature. After the stirring was continued for 6 days, the precipitates were filtered and washed with benzene. The combined filtrate and washings were evaporated to dryness to afford an oily product which was purified on an alumina column (n-hexane–CH_2Cl_2) to give unreacted **3a** (20 mg) and **15a** as yellowish crystals (32 mg, 37.3%): mp 176–179 °C dec; IR (KBr) 3080, 3040, 1600, 1570, 1500, 1030, 750, 690 cm^{-1}; UV (MeOH) λ_{max} 220 (ϵ 11 900), 258 (8100), 346 (7800); ^1H NMR ($CDCl_3$) δ 7.7–7.0 (m, 10 H), 5.00 (d, J = 1.5 Hz, 1 H), 4.00 (br s, 1 H), 2.50 (br s, 1 H), 2.3–1.0 (m, 12 H).

Anal. Calcd for $C_{23}H_{25}N_3$: C, 80.43; H, 7.34; N, 12.23. Found: C, 80.35; H, 7.60; N, 12.06.

1′,3′-Diphenyl-5-methyl-4-azahomoadamantano[4,5-*d*]-1′,2′,4′-$\Delta^{2'}$-triazoline (15b). The reaction of **3b** (81 mg, 0.50 mmol) with (α-chlorobenzylidene)phenylhydrazine (58 mg, 0.25 mmol) as described above under the same conditions and after chromatography (alumina, n-hexane–CH_2Cl_2) afforded unreacted **3b** (26 mg) and **15b** as yellowish crystals (45 mg, 50.3%): mp 176–180 °C dec; IR (KBr) 3060, 1590, 1495, 1400, 760, 695 cm^{-1}; UV (MeOH) λ_{max} 227 nm (ϵ 11 800), 270 (7300), 347 (7600); ^1H NMR ($CDCl_3$) δ 7.7–7.0 (m, 10 H), 3.92 (br s, 1 H), 1.67 (s, 3 H), 2.8–0.8 (m, 13 H).

Anal. Calcd for $C_{24}H_{27}N_3$: C, 80.63; H, 7.61; N, 11.75. Found: C, 80.42; H, 7.90; N, 11.69.

4-Azahomoadamantano[5,4-*e*]imidazole (17). To a stirred mixture of **3a** (75 mg, 0.50 mmol) and TosMIC[29] (162 mg, 0.80 mmol) in methanol (3 mL) and dimethoxyethane (1.5 mL) was added solid potassium carbonate (137 mg, 1.00 mmol). After the stirring was continued for 12 h at room temperature, the mixture was heated under reflux for 5 h. The solvent was removed, and the residue was treated with aqueous saturated NaCl solution (6 mL) and extracted with CH_2Cl_2 (3 × 6 mL). The combined extracts were dried (Na_2SO_4) and evaporated to dryness, affording a brownish solid which gave **17** as crystals (46 mg, 48.8%) after chromatography (alumina, CH_2Cl_2): mp 107–110 °C; IR (KBr) 3080, 1610, 1490, 1240, 1212, 927, 800 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.27 (s, 1 H), 6.67 (s, 1 H), 4.30 (br s, 1 H), 3.15 (br s, 1 H), 2.5–1.3 (m, 12 H); mass spectrum, m/e 188 (M^+, base), 173, 131, 41.

Anal. Calcd for $C_{12}H_{16}N_2$: C, 76.55; H, 8.57; N, 4.88. Found: C, 76.63; H, 8.48; N, 4.80.

The reaction of **3b** with TosMIC under the same conditions gave only recovered **3b**.

Registry No. 2a, 34197-88-1; **2b**, 65218-92-0; **2e**, 65218-95-3; **2f**, 65218-96-4; **3a**, 65218-91-9; **3b**, 65218-97-5; **3e**, 65219-00-3; **3e′**, 71302-50-6; **3e′**·HCl, 71250-91-4; **3f**, 71250-92-5; **5e**, 54530-05-1; **6**, 700-58-3; **10**, 71250-93-6; **11**, 71250-94-7; **13**, 71250-95-8; **14a**, 71250-96-9; **14b**, 71250-97-0; **14c**, 71250-98-1; **15a**, 71250-99-2; **15b**, 71251-00-8; **17**, 71251-01-9; diphenylketene, 525-06-4; phenylhydroximic acid chloride, 698-16-8; benzonitrile oxide, 873-67-6; (α-chlorobenzylidene)phenylhydrazine, 15424-14-3.

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Notes

Facile Preparation of 2- and 3-Fluoro-7,12-dimethylbenz[*a*]anthracene

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In order to elicit mutagenicity and carcinogenicity, polycyclic aromatic hydrocarbons undergo bioactivation and covalent linkage with DNA.[1] It has been shown that microsomally activated 7,12-dimethylbenz[*a*]anthracene (DMBA) binds with poly(G) to furnish products similar to the ones generated by the chemical reaction of DMBA 5,6-oxide[2,3] with poly(G). It has, however, recently been proposed that DNA binding primarily occurs[4] through the generation of a reactive diol epoxide and that the DMBA *trans*-3,4-dihydrodiol[5,6] is the most mutagenic and carcinogenic DMBA metabolite. If indeed DMBA ring A activated metabolites are primarily responsible for DNA damage and subsequent cell transformation, then the introduction of fluorine at any of positions 1, 2, 3, or 4 should considerably inhibit carcinogenicity. It has been observed that 1F- and 2F-DMBA do not produce sarcomas in long-Evans rats[7] and do not initiate tumors in mouse skin.[8] Furthermore, comparison of mutagenic and carcinogenic activities with DNA binding in Syrian hamster embryo cell culture for the 11-, 5-, and 2F analogues of DMBA showed a remarkable parallelism.[9] In connection with our research program on chemical carcinogenesis, we required relatively large amounts of the 2- and 3F-DMBA analogues for biological testing and biochemical studies.

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