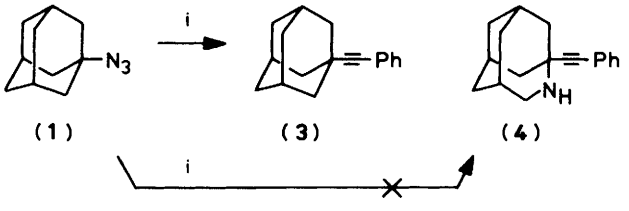
Bridgehead Substitution Reactions of 3-Methoxy-4-azahomoadamantane *via* *N*-Acyliminium Ions. A Novel Route to some [3,4]-Fused 4-Azahomoadamantane Heterocycles [1]

Tadashi Sasaki,* Shoji Eguchi, Takashi Okano, and Norihiro Nakamura
Institute of Applied Organic Chemistry, Faculty of Engineering, Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464, Japan

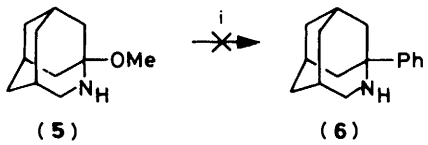
Treatment of 3-methoxy-4-methoxycarbonyl- (**9**) and 4-acetyl-3-methoxy-4-azahomoadamantane (**10**) with $AlCl_3$ in benzene afforded the corresponding 3-phenyl derivatives (**12**) and (**17**) accompanied by considerable amounts of the ring-opened products (**13**) and (**18**), respectively. The reaction of compound (**9**) with phenylethynyltrimethylsilane (**2**) and $AlCl_3$ gave the 3-phenylethynyl substitution product (**19**), while the same reaction of (**10**) gave the 3-phenylacetyl product (**21**). The cyclization of compound (**19**) with partially hydrated $AlCl_3$ afforded the oxazinone (**23**), the oxazolidinone (**24**), and the hydrochlorinated product (**25**); the base-catalysed cyclization of (**21**) gave the 3-pyrrolin-2-one (**26**). Intramolecular substitution of the 3-methoxy group with the aryl group of the arylureas (**28a**—**c**) took place smoothly with $AlCl_3$ to give the corresponding quinazolinones (**29a**—**c**) in good yields.

The nitrogen extrusion reaction of 1-azidoadamantane (**1**) with ring expansion has provided a useful synthetic methodology for some 3-substituted 4-azahomoadamantane derivatives,[2-4] which are potentially useful precursors for novel [3,4]-fused 4-azahomoadamantane heterocycles. We have reported the synthesis of some heterocycles using the hydrocyanation product of 4-azahomoadamant-3-ene, a reactive bridgehead imine.[5] As an extension of these studies, we have examined the reaction of compound (**1**) with phenylethynyltrimethylsilane (**2**) in the presence of aluminium chloride; however, only simple bridgehead substitution occurred to afford phenylethynyladamantane (**3**) and none of ring expansion product (**4**) was obtained. This result is different from the reactions of (**1**) with



Reagents: i, $PhC{\equiv}CSiMe_3$ (**2**), $AlCl_3$

trimethylsilyl cyanide [5] and with arenes,[4] both of which gave the corresponding 3-substituted 4-azahomoadamantanes. We were therefore interested in the bridgehead substitution route to appropriately functionalized 4-azahomoadamantanes in order to avoid the problems associated with the acid-catalysed ring-expansion route.[6] Direct treatment of 3-methoxy-4-azahomoadamantane (**5**) with a variety of Lewis acids, such as $AlCl_3$, $TiCl_4$, and $BF_3{\cdot}OEt_2$, in benzene gave none of the phenyl substituted product (**6**) because both extensive complexation of the catalyst by nitrogen and decomposition occurred.

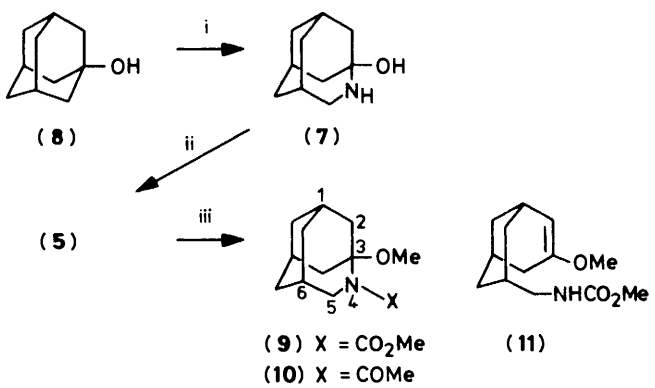


Reagents: i, Lewis acid, C_6H_6

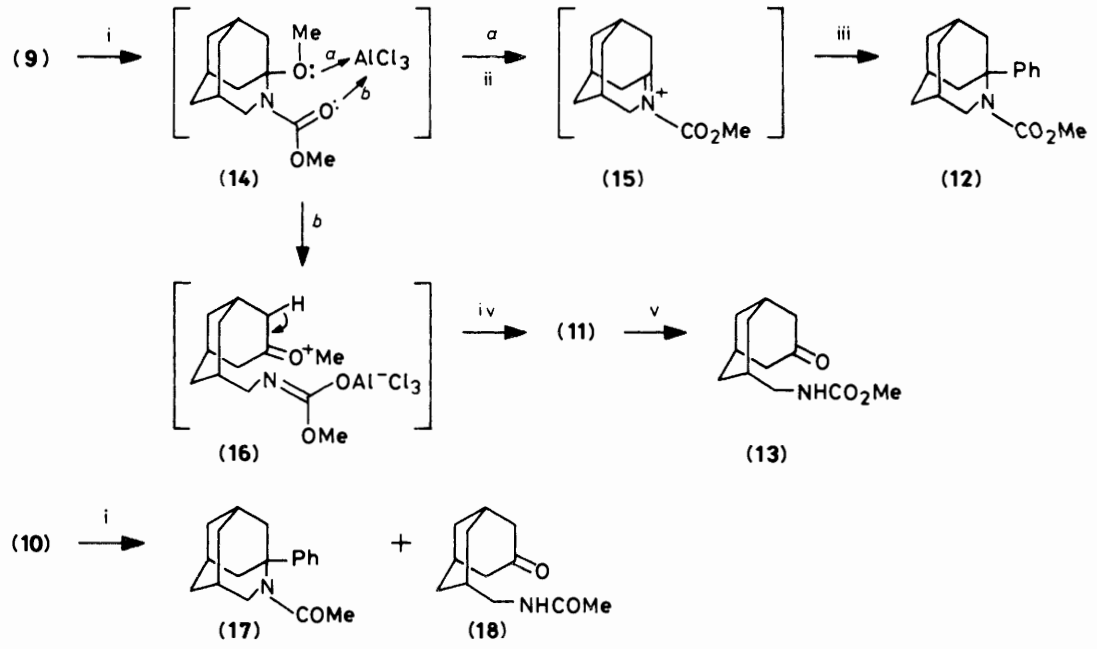
However, electrophilic addition and substitution by *N*-acyliminium ions of non-bridgehead positions with activated and non-activated unsaturated compounds have recently been reported as useful routes to the synthesis of nitrogen heterocycles.[7] *N*-Acyliminium bridgehead ions may be also useful for bridgehead substitutions, although these iminium ions should have less mesomeric stabilization because of $C{=}N^+$ bond distortion. We report here the results of such an approach to some 3-functionalized 4-azahomoadamantanes and some novel [3,4]-fused 4-azahomoadamantane heterocycles.

Results and Discussion

The methoxy amine (**5**) was prepared previously by photolysis of the azide (**1**) in methanol [2] or by treatment of the hydroxy amine (**7**) with H_2SO_4–MeOH.[8] Because these methods were not convenient for a large-scale preparation, we prepared compound (**5**) in 70% yield by treatment of the readily available alcohol (**7**) [from (**8**) [3]] with refluxing methanol in the presence of toluene-*p*-sulphonic acid as catalyst. Treatment of (**5**) with NaH–MeO_2CCl and NaH–Ac_2O in anhydrous ether gave the urethane (**9**) and the amide (**10**) in 49 and 74% yields, respectively; however, the same methoxycarbonylation in dry tetrahydrofuran often afforded a considerable amount of the enol ether derivative (**11**) *via* ring-cleavage (Scheme 1).



Scheme 1. *Reagents:* i, NaN_3, H_2SO_4–$CHCl_3$; ii, MeOH, TsOH; iii, NaH, $ClCO_2Me$ or Ac_2O–Et_2O



Scheme 2. *Reagents:* i, $AlCl_3$, C_6H_6; ii, $-AlCl_3OMe$; iii, C_6H_6, $^-H^+$; iv, H^+; v, H^+/H_2O

Treatment of compound (**9**) with aluminium chloride in benzene at room temperature afforded a phenyl substituted product (**12**) (24%) as expected, but a ring-cleaved product (**13**) was also obtained in 52% yield (Scheme 2).

The structural assignments of the ring-retained and -cleaved products were based on ^1H n.m.r. spectroscopy. For the ring-retained 4-azahomoadamantane derivatives such as (**12**), the methylene protons adjacent to the N atom appear at δ 3—4 as a characteristic doublet (*J* 3—4.5 Hz),[2,5] while for the ring-opened bicyclic products, *e.g.* (**13**), they appear at δ *ca.* 2.5—3.5 as a triplet (*J* 6—7 Hz). Formation of the product (**12**) is rationalized by the addition of benzene to an *N*-acyliminium ion (**15**) (path a); the formation of the bicyclic product (**13**) can be explained by a competitive complexation of the catalyst with the carbonyl oxygen *via* path b, followed by ring-cleavage and deprotonation to give the enol ether (**11**) which is then hydrolysed to afford (**13**). The formation of compound (**11**) was, in fact, confirmed by t.l.c.

Similar treatment of the *N*-acetyl derivative (**10**) with aluminium chloride in benzene afforded also the 3-phenyl derivative (**17**) (36%) as the ring-retained product and the ketoamide (**18**) (64%) as the ring-opened product.[9] The reactions of the urethane (**9**) with other Lewis acids ($TiCl_4$, $SnCl_4$, $BF_3{\cdot}OEt_2$) in benzene gave no better results.

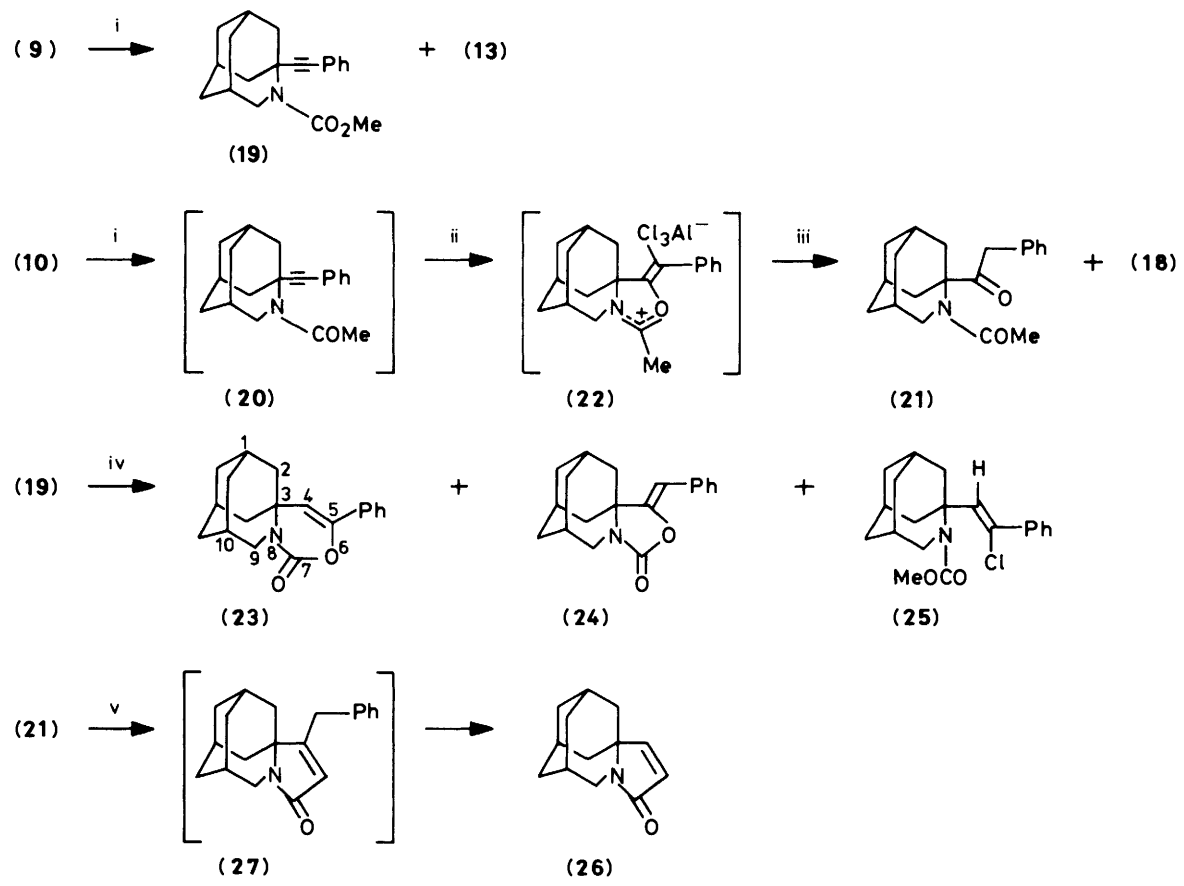
Because of the versatile properties of the acetylenic function, we attempted to introduce a phenylethynyl group at the 3-position of 4-azahomoadamantane. The electrophilic bridgehead substitution of adamantane with phenylethynyltrimethylsilane (**2**) *via* the Lewis acid-catalysed generation of an adamantyl cation has been reported.[10] Treatment of compound (**9**) and the silane (**2**) (three-fold excess) with $AlCl_3$ in dry CH_2Cl_2 at room temperature followed by work-up and chromatography afforded the ethynyl derivative (**19**) (32%) and the oxourethane (**13**) (29%) along with other uncharacterized side-products; the assigned structure of the product (**19**) was supported by the ^{13}C n.m.r. spectrum which showed two characteristic singlets due to the substituted acetylene (δ 95.3 and 77.2). However, similar treatment of the acetamide (**10**) afforded none of the ethynyl derivative (**20**), but gave the benzyl ketone derivative (**21**) (27%) as well as compound (**18**) (68%) (Scheme 3). The structure of compound (**21**) was supported by the ^1H n.m.r. spectrum which had a broad singlet (δ 3.72 for 4 H) assignable to the benzylic protons and the methylene protons adjacent to N, and also by the mass spectrum which showed a strong ion peak of *m/z* 220 ($M^+ - PhCH_2$). The facile formation of the ketone (**21**) could be explained by the conversion of (**20**) into (**22**) *via* the addition of $AlCl_3$ and the neighbouring group participation of the *N*-acetyl group, followed by hydrolysis.

Such neighbouring group participation was also useful for the heterocyclization of the phenylethynyl derivative (**19**). Thus, treatment of compound (**19**) with partially hydrated aluminium chloride (1:1 mol/mol, $AlCl_3$–$AlCl_3{\cdot}6H_2O$) in CH_2Cl_2, followed by work-up, afforded the oxazinone (**23**) (35%), the oxazolidinone (**24**) (32%), and the hydrochlorinated product (**25**) (24%). Compounds (**23**) and (**24**) exhibited carbonyl absorptions at 1 688 and 1 770 cm^{-1} in their i.r. spectra which were compatible with the assigned 6- and 5-membered ring structures, respectively. The assigned stereochemistry of the benzylidene moiety in compound (**24**) was based on the assumed *trans* addition and consideration of steric factors; the stereochemistry of (**25**) was tentatively assigned on the basis of the chemical shift (δ 6.27) of the olefinic proton.[11]

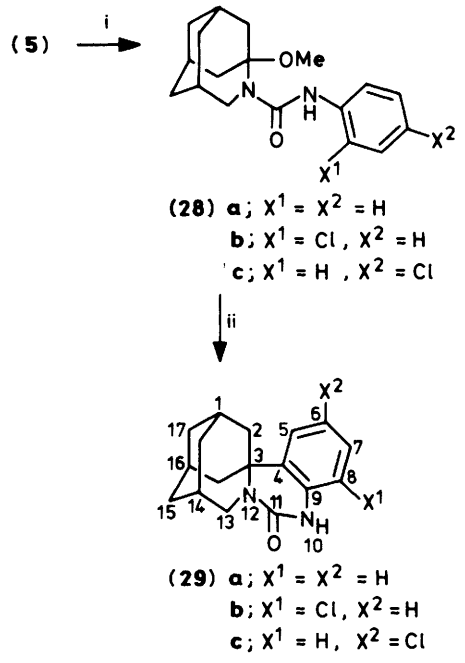
The benzyl ketone (**21**) was treated with potassium t-butoxide in dioxane under reflux for 8 h, and work-up afforded unexpectedly the unsaturated γ-lactam (**26**) in 92% yield; however, the detailed mechanism of such a novel debenzylation, which presumably occurs *via* the intermediate (**27**), is not clear at present.

The reactions of compound (**9**) with n-heptynyltrimethylsilane and acetophenone trimethylsilyl enol ether in the presence of $AlCl_3$ in CH_2Cl_2 were also examined, but ring-retained substitution products could not be obtained.

Finally, the intramolecular version of this bridgehead substitution, with appropriately *N*-substituted substrates, was investigated in order to obtain directly some [3,4]-fused 4-azahomoadamantane heterocycles. The phenylurea derivative (**28a**) was readily prepared in 69% yield from the methoxy amine (**5**) by treatment with phenyl isocyanate, while treatment of (**28a**) with $AlCl_3$ in CH_2Cl_2, followed by work-up afforded



Scheme 3. *Reagents:* i, (2), $AlCl_3$, CH_2Cl_2; ii, $AlCl_3$; iii, H_2O; iv, $AlCl_3$–$AlCl_3 \cdot 6H_2O$, CH_2Cl_2; v, $KOBu^t$, dioxane



Scheme 4. *Reagents:* i, ArNCO; ii, $AlCl_3$, CH_2Cl_2

the pentacyclic quinazolinone derivative (**29a**) in 79% yield. Similarly, the chloro substituted quinazolinones (**29b**) and (**29c**) were obtained in 90 and 46% yields respectively by treatment of the amine (**5**) with *o*- and *p*-chlorophenyl isocyanates followed by $AlCl_3$, without isolation of the ureas (**28b**) and (**28c**) (Scheme 4).

The above bridgehead substitutions *via* bridgehead *N*-acyliminium ions provide a novel route to some [3,4]-fused 4-azahomoadamantane heterocycles; however, the relatively facile decomposition of the acid-sensitive precursors, which is probably favoured thermodynamically by the release of strain on ring-opening, seems to limit the wide application of the method.

Experimental

M.p.s were taken in a sealed tube on a Yanagimoto micro melting point apparatus and are uncorrected. I.r. spectra were obtained on a Jasco IRA-1 spectrometer. ^1H and ^{13}C N.m.r. spectra were recorded on a Jeol JNM-C-60HL instrument at 60 MHz and a JEOL JNM-FX-60 FT n.m.r. spectrometer at 15.04 MHz, respectively. Chemical shifts are reported in p.p.m. (δ) relative to $SiMe_4$ as internal standard, in $CDCl_3$ or $(CD_3)_2SO$. Mass spectra were obtained with a JEOL model JMS-D10 mass spectrometer at 75 eV. Microanalyses were carried out using a Perkin-Elmer 240B elemental analyser.

3-Methoxy-4-azahomoadamantane (**5**).—3-Hydroxy-4-azahomoadamantane[3] (**7**) (5.00 g, 29.9 mmol) and *p*-TsOH·H_2O (200 mg, 1.05 mmol) in anhydrous methanol (50 ml) were heated under reflux for 2 h. The cooled mixture was stirred with anhydrous Na_2CO_3 (3 g) for 2 h and filtered. The filtrate was evaporated under reduced pressure to give an oily residue which was purified on a short column of neutral alumina (Woelm N,

activity grade III), with CH_2Cl_2 as eluant, to afford the methoxy amine (**5**) as a colourless solid (3.81 g, 70.3%), m.p. 77—79 °C (lit.,[8] 77—78 °C).

3-Methoxy-4-methoxycarbonyl-4-azahomoadamantane (**9**).—To a stirred and ice-cooled suspension of NaH (60% dispersion in oil; 1.06 g, 40.0 mmol) in dry diethyl ether (70 ml) was added the amine (**5**) (1.81 g, 10.0 mmol) under nitrogen and the mixture was stirred for 4 h at room temperature. Methyl chloroformate (1.89 g, 20.0 mmol) was then added and the stirring was continued for a further 4 days at room temperature. The ice-cooled mixture was treated with methanol (2 ml) in order to decompose the excess of NaH, and poured onto ice–water (200 ml). The organic layer was separated and the aqueous layer was extracted with diethyl ether (50 ml × 3). The combined organic layer and extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give an oily residue which was chromatographed on a short column of silica gel with n-hexane–CH_2Cl_2 as eluant to afford the *urethane* (**9**) as a colourless solid (1.17 g, 48.9%), m.p. 105—108 °C (Found: 65.1; H, 8.9; N, 5.8. $C_{13}H_{21}NO_3$ requires C, 65.24; H, 8.85; N, 5.85%); $\nu_{max.}$(KBr) 2 920, 1 695, 1 430, 1 380, 1 225, and 1 090 cm^{-1}; δ_H($CDCl_3$) 3.74 (2 H, d, *J* 3.0 Hz), 3.72 (3 H, s), 3.15 (3 H, s), and 2.7—0.9 (13 H, m); *m/z* 239 (M^+, 48%), 224 (40), 209 (32), 208 (34), 156 (70), 109 (100), 91 (36), 79 (42), and 41 (48).

4-Acetyl-3-methoxy-4-azahomoadamantane (**10**).—Treatment of the amine (**5**) (362 mg, 2.00 mmol) with NaH (60% dispersion in oil; 200 mg, 5.00 mmol) and acetic anhydride (408 mg, 4.00 mmol) in dry diethyl ether (20 ml) as described above and work-up gave the amide (**10**) as a colourless solid (330 mg, 73.9%), m.p. 98—99 °C (lit.,[9] 97—99 °C).

7-Methoxy-3-endo-(N-methoxycarbonylaminomethyl)bicyclo[3.1.1]*non-6-ene* (**11**).—When the above methoxycarbonylation of (**5**) was carried out in dry THF, a mixture of the urethane (**9**) and the enol ether (**11**) was produced, which was purified on a neutral alumina column (activity grade III, CH_2Cl_2) to afford products (**9**) (27—76%) and (**11**) (37—0%). The *enol ether* (**11**) was obtained as a colourless solid, m.p. 72—75 °C (Found: C, 65.5; H, 8.9; N, 6.1. $C_{13}H_{21}NO_3$ requires C, 65.25; H, 8.85; N, 5.85%); $\nu_{max.}$(KBr) 3 352, 2 940, 1 698, 1 684, 1 525, 1 260, and 1 242 cm^{-1}; δ_H($CDCl_3$) 4.73 (2 H, 1 H, br d, *J* 7.0 Hz, after shaking with D_2O), 3.64 (3 H, s), 3.49 (3 H, s), 3.2—2.7 (2 H, m), and 2.6—1.3 (11 H, m); *m/z* 239 (M^+, 3.0%), 207 (75), 138 (38), 109 (100), 95 (70), and 88 (68).

4-Methoxycarbonyl-3-phenyl-4-azahomoadamantane (**12**).—To a stirred solution of (**9**) (120 mg, 0.50 mmol) in dry benzene (5 ml) was added powdered $AlCl_3$ (133 mg, 1.00 mmol) in one portion under nitrogen and the stirring was continued overnight at room temperature. The mixture was cooled with ice and treated with Na_2CO_3 (0.50 g) and a few drops of water. The resulting suspension was filtered and washed with benzene (5 ml). The combined filtrate and washings were evaporated under reduced pressure to give a residue which was chromatographed on a column of silica gel with CH_2Cl_2–AcOEt (2:1 v/v) as eluant to afford the *product* (**12**) as a colourless solid (36 mg, 24.0%), m.p. 116—117 °C (Found: C, 75.8; H, 8.2; N, 4.8. $C_{18}H_{23}NO_2$ requires C, 75.76; H, 8.12; N, 4.91%); $\nu_{max.}$(KBr) 3 050, 3 010, 2 900, 1 700, 1 685, 1 435, 1 380, 750, and 695 cm^{-1}; δ_H($CDCl_3$) 7.5—6.9 (5 H, m), 3.96 (2 H, d, *J* 4.0 Hz), 3.42 (3 H, br s), and 2.7—0.9 (13 H, m); *m/z* 286 (M^+ + 1, 28%), 285 (M^+, 100), 270 (38), 228 (32), 226 (45), 215 (42), 202 (94), 167 (37), 155 (44), 149 (57),* 118 (30), 91 (60), 79 (35), 77 (50), 57 (32), 43 (39), and 41 (45).

Elution with AcOEt afforded 3-endo-(N-*methoxycarbonylaminomethyl)bicyclo*[3.3.1]*nonan-7-one* (**13**) as a colourless solid (58 mg, 51.5%), m.p. 97—99 °C (Found: C, 64.0; H, 8.5; N, 6.2. $C_{12}H_{19}NO_3$ requires C, 63.98; H, 8.50; 6, 6.22%); $\nu_{max.}$(KBr) 3 330, 2 920, 1 720, 1 700, 1 525, 1 455, and 1 225 cm^{-1}; δ_H($CDCl_3$) 5.0 (1 H, br s, D_2O exchangeable), 3.63 (3 H, s), 2.89 (2 H, t, *J* 6.0 Hz), and 2.7—0.5 (13 H, m); *m/z* 225 (M^+, 2.0%), 207 (31), 138 (48), 95 (100), and 88 (47).

4-Acetyl-3-phenyl-4-azahomoadamantane (**17**).—Treatment of the amide (**10**) (112 mg, 0.50 mmol) with $AlCl_3$ (133 mg, 1.00 mmol) in dry benzene (5 ml) as above and chromatography afforded *compound* (**17**) as a colourless solid (48 mg, 35.6%), m.p. 98—99 °C (Found: C, 80.3; H, 8.8; N, 5.0. $C_{18}H_{23}NO$ requires C, 80.25; H, 8.61; N, 5.20%); $\nu_{max.}$(KBr) 3 050, 3 020, 2 910, 1 645, 1 490, 1 450, 1 410, 1 245, 750, and 700 cm^{-1}; δ_H($CDCl_3$) 7.5—7.0 (5 H, m), 3.81 (2 H, d, *J* 4.0 Hz), 2.16 (3 H, s), and 2.7—0.9 (13 H, m); *m/z* 269 (M^+, 99%), 226 (64), 210 (99), 170 (59), 168 (51), 167 (46), 156 (53), 155 (100), 150 (37), 144 (45), 141 (47), 123 (59), 119 (43), 118 (33), 115 (46), 109 (63), 105 (50), 104 (41), 95 (34), 93 (41), 92 (46), 91 (93), 83 (31), 81 (46), 79 (50), 77 (80), 71 (46), 57 (82), 55 (63), and 51 (77).

The second fractions gave the keto amide (**18**) as a colourless solid (67 mg, 64.0%), m.p. 111—113 °C, which was identical with a sample obtained by the acetylation of (**7**).[9]

4-Methoxycarbonyl-3-phenylethynyl-4-azahomoadamantane (**19**).—To a mixture of (**9**) (239 mg, 1.00 mmol) and phenylethynyltrimethylsilane (**2**) (523 mg, 3.00 mmol) in dry CH_2Cl_2 (5 ml) was added powdered $AlCl_3$ (267 mg, 2.00 mmol) and the mixture was stirred at room temperature for 4 h under nitrogen. The mixture was cooled with ice and treated with powdered Na_2CO_3 (1.0 g) and water (0.1 ml) with stirring for 0.5 h. The precipitate was filtered off and washed with CH_2Cl_2 (5 ml). The combined filtrate and washings were evaporated under reduced pressure to give an oil which was chromatographed on a silica gel column (n-hexane–CH_2Cl_2–AcOEt) to afford *compound* (**19**) as a viscous oil (100 mg, 32.3%) (Found: C, 77.8; H, 7.4; N, 4.4. $C_{20}H_{23}NO_2$ requires C, 77.64; H, 7.49; N, 4.53%); $\nu_{max.}$ (neat film) 3 040, 3 000, 2 900, 2 220, 1 700, 1 685, 1 590, 1 485, 1 440, 1 380, 755, and 685 cm^{-1}; δ_H($CDCl_3$) 7.6—7.1 (5 H, m), 3.77 (2 H, d, *J* 4.0 Hz), 3.73 (3 H, s), and 2.8—0.9 (13 H, m); δ_C($CDCl_3$) 156.4 (1 C, s), 131.4 (2 C, d), 128.0 (2 C, d), 127.5 (1 C, d), 123.8 (1 C, s), 95.3 (1 C, s), 77.2 (1 C, s), 55.3 (1 C, s), 52.3 (1 C, q), 51.2 (1 C, t), 42.1 (2 C, t), 35.6 (1 C, t), 35.3 (2 C, t), 31.4 (1 C, d), and 27.3 p.p.m. (2 C, d); *m/z* 309 (M^+, 71%), 294 (100), and 91 (30).

The second fractions gave the oxourethane (**13**) (66 mg, 29.3%).

4-Acetyl-3-phenylacetyl-4-azahomoadamantane (**21**).—Treatment of compounds (**10**) (223 mg, 1.00 mmol) and (**2**) (523 mg, 3.00 mmol) in dry CH_2Cl_2 (5 ml) with $AlCl_3$ (267 mg, 2.00 mmol) as above, followed by work-up and chromatography (silica gel, n-hexane–CH_2Cl_2–AcOEt) afforded the *ketone* (**21**) as a colourless solid (85 mg, 27.3%), m.p. 184—186 °C (Found: C, 77.2; H, 8.0, N, 4.4. $C_{20}H_{25}NO_2$ requires C, 77.14; H, 8.09; N, 4.50%); $\nu_{max.}$(KBr) 3 060, 3 015, 2 910, 1 705, 1 615, 1 495, 1 420, 1 345, 1 232, and 715 cm^{-1}; δ_H($CDCl_3$) 7.25 (5 H, br s), 3.72 (4 H, br s), 2.5—1.3 (13 H, m), and 2.13 (3 H, s); *m/z* 220 (M^+ – $PhCH_2$, 100%) and 192 (76).

The second fractions gave the amide (**18**) (142 mg, 67.8%).

Aluminium Chloride-catalysed Cyclization of Compound (**19**).—To a stirred solution of (**19**) (100 mg, 0.32 mmol) in CH_2Cl_2 (5 ml) was added a mixture of anhydrous $AlCl_3$ (65 mg, 0.49 mmol) and $AlCl_3 \cdot 6H_2O$ (120 mg, 0.50 mmol) and the resulting mixture was stirred for 2 h at room temperature. After

* Overlapped with a background peak.

the addition of anhydrous Na_2CO_3 (1.0 g) to the mixture, the stirring was continued for 0.5 h, and the precipitate was filtered off and washed with CH_2Cl_2. The combined filtrate and washings were evaporated under reduced pressure to give a residue which was purified on a silica gel preparative t.l.c. plate (Wako gel B) with CH_2Cl_2 as eluant. The most polar product (R_F 0.11) was *5-phenyl-6-oxa-8-azatetracyclo*[8.3.1.1^{3,12}.0^{3,8}]*pentadec-4-en-7-one* (**23**), obtained as a colourless solid (33 mg, 34.9%), m.p. 186—188 °C (Found: C, 77.3; H, 7.1; N, 4.7. $C_{19}H_{21}NO_2$ requires C, 77.26; H, 7.17; N, 4.74%); $\nu_{max.}$(KBr) 3 070, 2 905, 1 688, 1 495, 1 382, 1 325, 1 283, 750, and 685 cm^{-1}; δ_H($CDCl_3$) 7.8—7.2 (5 H, m), 5.30 (1 H, s), 3.84 (2 H, d, *J* 4.0 Hz), and 2.5—1.4 (13 H, m); *m/z* 295 (M^+, 100%), 238 (90), 212 (80), 179 (39), and 105 (75).

The second most polar product (R_F 0.17) gave *4-benzylidene-5-oxa-7-azatetracyclo* [7.3.1.1^{3,11}.0^{3,7}]*tetradecan-6-one* (**24**) as a colourless solid (30 mg, 31.7%), m.p. 141—143 °C (Found: C, 77.4; H, 7.2; N, 4.6. $C_{19}H_{21}NO_2$ requires C, 77.26; H, 7.17; N, 4.74%); $\nu_{max.}$(KBr) 3 052, 3 020, 2 905, 1 770, 1 683, 1 600, 1 440, 1 383, 1 068, 1 000, 750, and 685 cm^{-1}; δ_H($CDCl_3$) 7.7—7.1 (5 H, m), 5.44 (1 H, s), 3.51 (2 H, d, *J* 4.0 Hz), and 2.5—1.4 (13 H, m); *m/z* 295 (M^+, 100%) and 242 (30).

The third product (R_F 0.25) was *3-(α-chlorostyryl)-4-methoxycarbonyl-4-azahomoadamantane* (**25**), obtained as a colourless solid (27 mg, 24.4%), m.p. 83—86 °C (Found: C, 69.7; H, 6.9; N, 3.75. $C_{20}H_{24}ClNO_2$ requires C, 69.45; H, 6.99; N, 4.05%); $\nu_{max.}$(KBr) 3 050, 3 015, 2 905, 1 685, 1 598, 1 438, 1 380, 1 225, 762, and 695 cm^{-1}; δ_H($CDCl_3$) 7.5—7.1 (5 H, m), 6.27 (1 H, s), 3.66 (3 H, s), 3.17 (2 H, d, *J* 4.0 Hz), and 2.4—1.1 (13 H, m); *m/z* 347, 345 (M^+, 2.0 and 5.0%), and 310 (100).

7-Azatetracyclo[7.3.1.1^{3,11}.0^{3,7}]*tetradec-4-en-6-one* (**26**).—A mixture of (**21**) (35 mg, 0.11 mmol) and potassium t-butoxide (30 mg, 90% Wako's reagent; 0.24 mmol) in dry dioxane (3 ml) was heated under reflux for 8 h under nitrogen. The cooled mixture was poured onto ice–water (10 ml) and extracted with chloroform (10 ml × 4). The combined extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give a residue which was purified on a preparative t.l.c. (Wako gel B5, CH_2Cl_2–AcOEt, 1:1 v/v) to afford *compound* (**26**) as a colourless solid (21 mg, 91.9%), m.p. 95—97 °C (Found: C, 76.7; H, 8.6; N, 6.6. $C_{13}H_{17}NO$ requires C, 76.81; H, 8.43; N, 6.89%); $\nu_{max.}$(KBr) 2 905, 1 675, 1 590, 1 383, 1 345, 1 270, 1 185, 1 100, 810, and 670 cm^{-1}; δ_H($CDCl_3$) 6.80 (1 H, d, *J* 6.0 Hz), 6.01 (1 H, d, *J* 6.0 Hz), 3.53 (2 H, d, *J* 4.0 Hz), and 2.5—0.9 (13 H, m); *m/z* 204 (M^+).

3-Methoxy-4-phenylcarbamoyl-4-azahomoadamantane (**28a**).—A mixture of (**5**) (100 mg, 0.55 mmol) and phenyl isocyanate (131 mg, 1.10 mmol) in dry benzene (1 ml) was stirred overnight at room temperature under nitrogen. The mixture was evaporated under reduced pressure to give a solid residue which was recrystallized from benzene to afford the *urea* (**28a**) as a colourless crystals (114 mg, 68.8%), m.p. 136—139 °C (Found: C, 71.7; H, 7.9; N, 9.2. $C_{18}H_{24}N_2O_2$ requires C, 71.97; H, 8.05; N, 9.33%); $\nu_{max.}$(KBr) 3 290, 3 050, 2 910, 2 860, 1 685, 1 590, 1 535, 1 505, 1 440, 1 310, 1 210, 1 150, 1 045, 745, and 690 cm^{-1}; δ_H($CDCl_3$) 9.12 (1 H, br s, D_2O exchangeable), 7.7—6.7 (5 H, m), 3.88 (2 H, d, *J* 4.0 Hz), 3.32 (3 H, s), and 2.7—1.2 (13 H, m); *m/z* 300 (M^+, 20%), 268 (100), 208 (65), 170 (46), 165 (32), 119 (53), 105 (46), 93 (90), 91 (74), and 77 (76).

10,12-Diazapentacyclo[12.3.1.1^{3,16}.0^{3,12}.0^{4,9}]*nonadeca-4(9),5,7-trien-11-one* (**29a**).—A mixture of (**28a**) (44 mg, 0.15 mmol) and anhydrous $AlCl_3$ (58 mg, 0.44 mmol) in dry CH_2Cl_2 (2 ml) was stirred for 14 h at room temperature under nitrogen. The mixture was cooled with ice and treated with Na_2CO_3 (1.0 g) and wet CH_2Cl_2 (10 ml) for 0.5 h with stirring. The mixture was filtered and the precipitates were washed with CH_2Cl_2 (5 ml). The combined filtrate and washings were evaporated under reduced pressure to give a solid residue which was recrystallized from $CHCl_3$–CCl_4 to afford the *quinazolinone* (**29a**) as colourless crystals (31 mg, 78.9%), m.p. 279—282 °C (Found: C, 76.3; H, 7.8; N, 10.15. $C_{17}H_{20}N_2O$ requires C, 76.09; H, 7.51; N, 10.44%); $\nu_{max.}$(KBr) 3 300, 3 180, 3 045, 2 910, 1 670, 1 595, 1 510, 1 425, and 745 cm^{-1}; δ_H($CDCl_3$) 7.67 (1 H, br s, D_2O exchangeable), 7.5—6.5 (4 H, m), 3.91 (2 H, d, *J* 4.0 Hz), and 2.7—1.3 (13 H, m); *m/z* 268 (M^+, 68%), 267 (32), 212 (30), 211 (70), 185 (100), 174 (34), 159 (67), 93 (47), and 77 (31).

p-Chloro-10,12-diazapentacyclo[12.3.1.1^{3,16}.0^{3,12}.0^{4,9}]*nonadeca-4(9),5,7-trien-11-one* (**29b**).—A mixture of (**5**) (100 mg, 0.55 mmol) and *o*-chlorophenyl isocyanate (85 mg, 0.57 mmol) in dry CH_2Cl_2 (10 ml) was stirred for 1 h at room temperature under nitrogen. To this mixture was added anhydrous $AlCl_3$ (170 mg, 1.27 mmol) and the stirring was continued for a further 36 h at room temperature. Work-up with Na_2CO_3 and wet CH_2Cl_2 as above and recrystallization from benzene–n-hexane afforded the *chloroquinazolinone* (**29b**) as colourless crystals (150 mg, 89.8%), m.p. 147—150 °C (Found: C, 67.6; H, 6.3; N, 9.2. $C_{17}H_{19}ClN_2O$ requires C, 67.43; H, 6.32; N, 9.25%); $\nu_{max.}$(KBr) 3 195, 2 900, 1 655, 1 598, 1 482, 1 410, 1 245, 1 155, 755, and 722 cm^{-1}; δ_H($CDCl_3$) 7.4—6.7 (4 H, 3 H, m, after shaking with D_2O), 3.94 (2 H, d, *J* 4.0 Hz), and 2.6—1.5 (13 H, m); *m/z* 304, 302 (M^+, 27 and 70%), 221 (32), 219 (100), 208 (42), 195 (30), 150 (68), 149 (55), 127 (46), and 95 (30).

6-Chloro-10,12-diazapentacyclo[12.3.1.1^{3,16}.0^{3,12}.0^{4,9}]*nonadeca-4(9),5,7-trien-11-one* (**29c**).—Treatment of (**5**) (100 mg, 0.55 mmol) with *p*-chlorophenyl isocyanate (85 mg, 0.57 mmol) in dry CH_2Cl_2 (10 ml), followed by treatment with $AlCl_3$ (147 mg, 1.10 mmol) as above afforded the *chloroquinazolinone* (**29c**) as colourless crystals after work-up and recrystallization from CCl_4–MeOH (76 mg, 45.5%), m.p. 170—173 °C (Found: C, 67.1; H, 6.5; N, 9.3. $C_{17}H_{19}ClN_2O$ requires C, 67.43; H, 6.32; N, 9.25%); $\nu_{max.}$(KBr) 3 315, 3 190, 3 070, 2 915, 1 658, 1 590, 1 568, 1 495, 1 432, 1 302, 1 092, and 832 cm^{-1}; δ_H[$(CD_3)_2SO$] 8.50 (1 H, br s, D_2O exchangeable), 7.5—6.7 (3 H, m), 3.78 (2 H, d, *J* 4.0 Hz), and 2.9—1.5 (13 H, m); *m/z* 304, 302 (M^+, *ca.* 2 * and 4%), 219 (100), 218 (32), 204 (53), 202 (41), 201 (33), and 91 (39).

* Overlapped with a weak background peak.

References

1 Synthesis of Adamantane Derivatives, Part 69. For Part 68, see T. Sasaki, K. Shimizu, and M. Ohno, *Chem. Pharm. Bull.*, 1984, **32**, 1433.
2 H. Quast and P. Eckert, *Liebigs Ann. Chem.*, 1974, 1727.
3 T. Sasaki, S. Eguchi, T. Katada, and O. Hiroaki, *J. Org. Chem.*, 1977, **42**, 3741.
4 D. Margosian and P. Kovacic, *J. Org. Chem.*, 1981, **46**, 877; D. Margosian, D. Sparks, and P. Kovacic, *J. Chem. Soc., Chem. Commun.*, 1980, 275.
5 T. Sasaki, S. Eguchi, and T. Okano, *J. Org. Chem.*, 1981, **46**, 4474.
6 D. Margosian, J. Speier, and P. Kovacic, *J. Org. Chem.*, 1981, **46**, 1346.
7 (*a*) J. C. Hubert, J. B. P. A. Wijnberg, and W. N. Speckamp, *Tetrahedron*, 1975, **31**, 1437; (*b*) H. E. Schoemaker, J. Dijkink, and W. N. Speckamp, *Tetrahedron*, 1978, **34**, 163; J. Dijkink and W. N. Speckamp, *ibid.*, 1978, **34**, 173; (*c*) D. J. Hart, *J. Am. Chem. Soc.*, 1980, **102**, 397; (*d*) M. Okita, T. Wakamatsu, M. Mori, and Y. Ban, *Heterocycles*, 1980, **14**, 1089; (*e*) S. Danishefsky, M. Guingant, and M. Prisbylla, *Tetrahedron Lett.*, 1980, **21**, 2033; (*f*) T. Shono, A. Matsumura, and K. Tsubata, *J. Am. Chem. Soc.*, 1981, **103**, 1172; (*g*)

H. Hiemstra and W. N. Speckamp, *Tetrahedron Lett.*, 1983, **24**, 1407 and refs. cited therein.
8 P. Kovacic, J.-H. Liu, E. M. Levi, and P. D. Roskos, *J. Am. Chem. Soc.*, 1971, **93**, 5801.
9 S. J. Padegimas and P. Kovacic, *J. Org. Chem.*, 1972, **37**, 2672.
10 T. Sasaki, A. Usuki, and M. Ohno, *Tetrahedron Lett.*, 1978, 4925; T. Sasaki, A. Usuki, and M. Ohno, *J. Org. Chem.*, 1980, **45**, 3559.
11 C. Pascual, J. Meier, and W. Simon, *Helv. Chim. Acta*, 1966, **49**, 164.

Received 31*st October* 1983; *Paper* 3/1934