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SCHMIDT REACTION OF 4-SUBSTITUTED ADAMANTANONES

Helmut Duddeck*, Dino Brosch and Gudrun Koppetsch

Ruhr-Universität Bochum, Abteilung für Chemie
Postfach 10 21 48, D-4630 Bochum 1, FRG

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Abstract - The Schmidt reaction of various 4^a- and 4^e-substituted adamantanones has been investigated. It is shown that the direction of the nitrogen insertion is not dominated by inductive substituent influences. The main reaction pathway involves the diazoiminium ion **3** and the intermediates **4** and **5** which prefer different reactions: **4** undergoes mainly fragmentation (**8** and **9**) whereas **5** gives mainly water addition products (**7**). The recyclisation of **8** and **9** is highly regioselective. The structure determinations of the products are based on their ^1H and ^{13}C NMR data.

In the course of our NMR spectroscopic investigations of substituted adamantanes[1] we wanted to prepare adamantanones with two monovalent substituents in β position to the carbonyl group. Several synthetic routes may lead to compounds of this class. In this paper we describe the Schmidt reaction of monosubstituted adamantanones; in another we report our results obtained by HBr-treatment of 2-bromooxahomoadamantanones[2]. A third route published very recently by Tříska et al. is the Beckmann rearrangement of adamantanone oximes[3].

The Schmidt reaction (SR) is a convenient method to convert carbonyl compounds into nitrogen-containing analogues[4-7]. Thus, e.g. amides and lactams can be obtained from acyclic and cyclic ketones, respectively. Several research groups found[8-13] that the Schmidt reaction of adamantanone (**1H**) with sodium azide in methanesulfonic acid affords the corresponding lactam **7H** as a side product only, the main product being 4^e-methanesulfonoxyadamantanone (**12H**)[14]. In addition, it was reported that a small amount of 4^a-methanesulfonoxyadamantanone (**16H**)[14] was isolated in this reaction, too[11,13]. These results encouraged us to use this method for the preparation of disubstituted adamantanones and monosubstituted azahomoadamantanones.

RESULTS

According to earlier reports[10-13] the first step of the SR of adamantanone (**1**, X=H) is the addition of H^+ and hydrogen azide to give **2** (Scheme 1, X=H). Via the conceivable intermediates **3**, **3'**, **3''**, **4** and/or **5** (**3'** and **3''** as well as **4** and **5** are identical pairwise if X=H) the products **6/7** of the "normal" SR is obtained[10]. The intermediates **4/5**, however, may also undergo the "anomalous" SR, i.e. a fragmentation to the bicyclononene carbonitriles **8-11**[10]. These afford the equatorially substituted mesyloxyadamantanones **12-15** which may isomerize to their epimers **16-19** under the reaction conditions to a small extent[13]. The structures **8-11**, **12-15** and **16-19** are identical or enantiomeric within each group if X is hydrogen.

Scheme 1: Reaction scheme

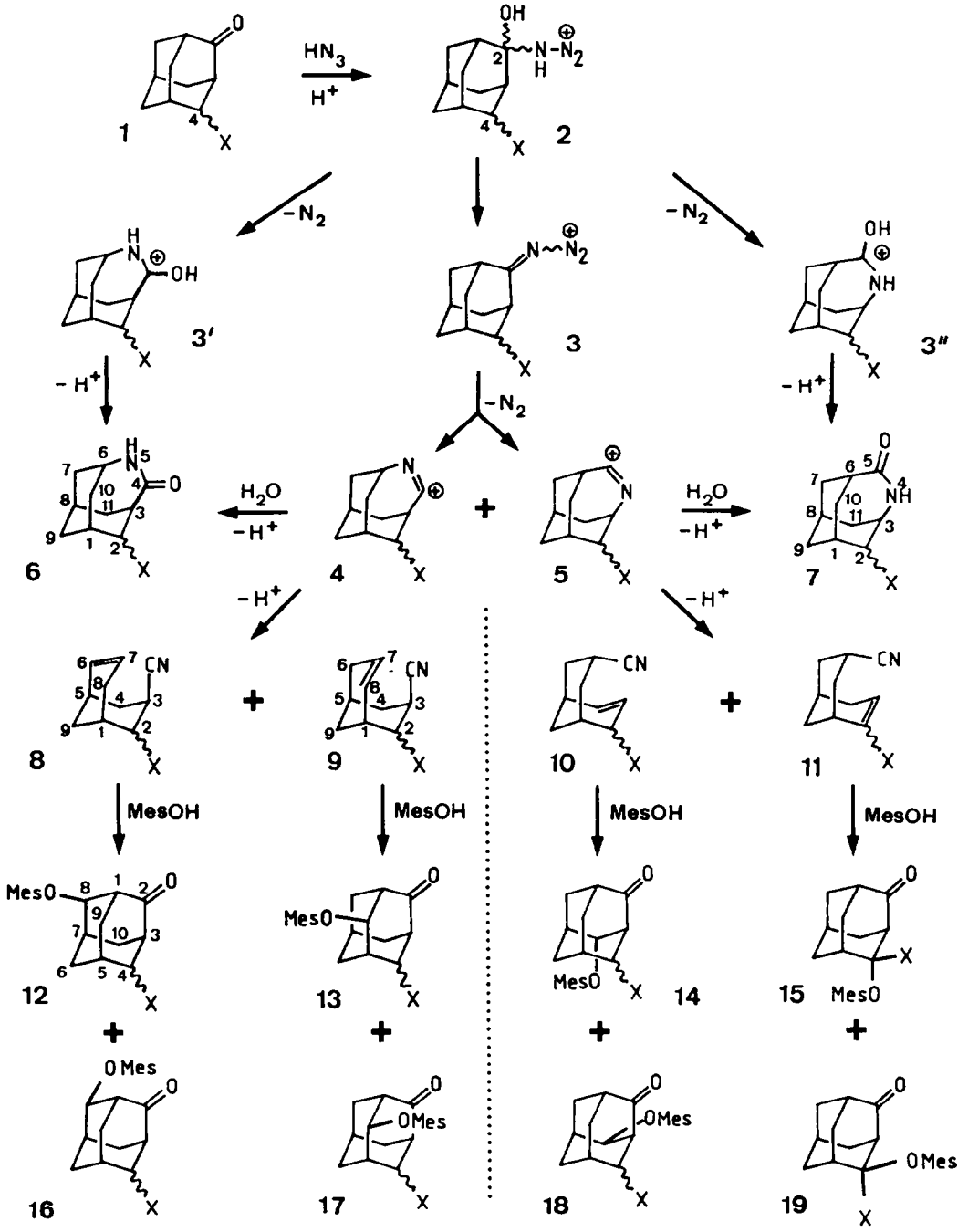
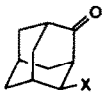
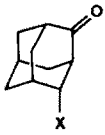


Table 1: Reaction products of the Schmidt reaction (SR) of adamantanone[a] and some 4-axially and 4-equatorially substituted derivatives[b,c,d].

Educts[e]		Products[e] "normal" SR (rearrangement)	"anomalous" SR (fragmentantion)
	1H	7H (11%)	12H (88%)
	1Aa	7Aa (33%)	12Aa (35%) + 13Aa (7%)
	1Ba	7Ba (36%)	12Ba (31%) + 13Ba (8%)
	1Ca	7Ca (29%)	12Ca (28%) + 13Ca (7%)
	1Da	7Da (35%)	12Da (22%) + 13Da (5%)
	1Ea	7Ea (14%)	12Ea (29%)
	1Ab	7Ab (44%)	12Ab (18%) + 16Ab (5%)
	1Bb	7Bb (28%)	12Bb (25%)
	1Cb	7Cb (29%)	12Cb (21%) + 16Cb (4%)
	1Db		12Db (6%)
		6Db (15%)	+1Ab (61%)
	1Eb	7Eb (39%)	12Eb (16%) + 16Eb (3%)

a Taken from ref. 10; yields are based on g.l.p.c. analysis.

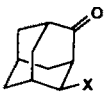
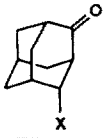
b Reaction conditions: 500-1000mg 1+ small excess of NaN_3+ 5ml CH_3SO_3H, room temperature 1hr.

c The yields correspond to isolated material and were reproducible under identical reaction conditions. The ratios in unseparable mixtures were determined by NMR.

d For details on the structure determinations of these compounds see "Experimental" section.

e Capital letters denote substituents (H=H; A= OMes; B=Cl; C=Br; D=I; E=CN); a and b refer to the stereochemical position of the substituent: a denotes the axial position in the adamantanones with respect to the substituent-bearing cyclohexanone subunit) and the endo position in the bicyclononenes, b denotes equatorial and exo positions, respectively.

Table 2: Reaction products in the modified Schmidt reaction of adamantanone[a] and some 4-axially and 4-equatorially substituted derivatives[b,c,d].

Educts[e]		Products[e] "normal" SR (rearrangements)	"anomalous" SR (fragmentation)	
	1H	7H (33%)	8H (61%)	12H (3%)
	1Aa	6Aa (9%) + 7Aa (18%)	8Aa + 9Aa (45%, 4:1)	
	1Ba	6Ba (8%) + 7Ba (13%)	8Ba + 9Ba (39%, 3:2)	12Ba (2%)
	1Ca	6Ca (12%) + 7Ca (25%)	olefin mixture (39%)	
	1Da	6Da (10%) + 7Da (26%)	8Da + 9Da (42%, 1.2:1)	
	1Ab	6Ab (8%) + 7Ab (42%)	8Ab + 9Ab (19%, 6:1)	
	1Bb	6Bb (7%) + 7Bb (28%)	8Bb + 9Bb (23%, 3:2) + 10Bb (5%) +	12Bb (1%)
	1Cb	6Cb (7%) + 7Cb (19%)	olefin mixture (21%) + 10Cb (23%)	
	1Db	6Db (8%) + 7Db (2%)	olefin mixture (16%) + 8H (15%) +	1Ab(10%)

a Taken from ref. 10; yields are based on g.l.p.c. analysis.

b Reaction conditions: 500-1000mg 1+ small excess of NaN_3+ 14ml CH_3SO_3H/CH_3COOH (3:4), room temperature, 1hr.

c The yields correspond to isolated material and were reproducible under identical reaction conditions. The ratios in unseparable mixtures were determined by NMR.

d For details on the structure determinations of these compounds see "Experimental" section.

e For the compound number code see footnote e of Table 1.

In Table 1 the results of our experiments with 4-substituted adamantanones (X=OMes, Cl, Br, I and CN in both stereochemical positions) are summarized; for the explanation of the compound codes see footnote e in Table 1.

The most surprising evidence from Table 1 is that both the "normal" and the "anomalous" SR pretend to be highly selective. In the "axial" series **1Aa**-**1Ea** we found only one lactam (**7**). From the eight isomeric disubstituted adamantanones only two (**12** and **13**) were produced, and among these **12** was clearly prevailing. Derivatives of the type **7** and **12** were the main products in the "equatorial" series, too. The only exception is the iodide **1Db** where we found the other lactam **6Db** exclusively. The side products, however, were the ketones **16** which are stereoisomers of **12**, but in no instance an isomer **13** could be traced.

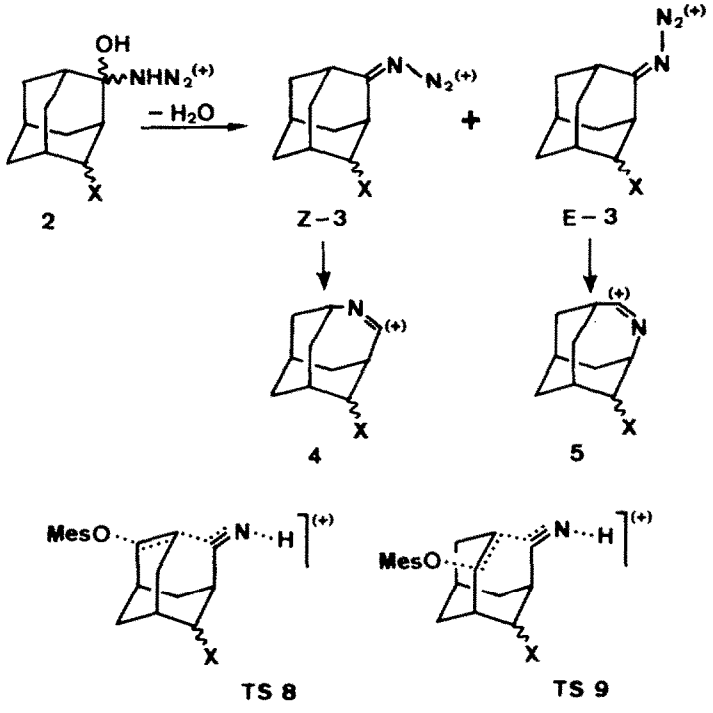
In order to rationalize the unexpected results we decided to investigate this reaction in more detail. To that end, we modified the reaction conditions in a way already reported by Sasaki et al.[10]. By changing the solvent from pure methanesulfonic acid to a 3:4-mixture of methanesulfonic and acetic acid the recyclisation step (e.g. **8** → **12**) is retarded so that the nitriles can be isolated[10]. The results of this modified SR are summarized in Table 2.

Under this conditions we also found a preponderance of the lactam **7** over **6**, the yields of **6**, however, are not negligible. Again **1Db** is an exception. Among the fragmentation products **8** and **9** the isomers **8** were found in higher yields. For both bromo and for the equatorial iodoadamantanones we obtained mixtures of the respective halogen-containing bicyclononene carbonitriles from which **8Ca**, **9Ca**, **8Cb**, **9Cb**, **8Db** and **9Db** could not be traced safely, but all their spectra, however, indicate their existance. In the case of the reaction with **1Da** we were able to separate the nitriles **8Da** and **9Da** chromatographically so that they could be characterized unequivocally by two-dimensional ^{1}H and ^{13}C NMR[15]. The ^{13}C chemical shifts of their sp^2 carbon atoms are significantly dependent on the position of the iodo atom[15] (δ and ε in **8Da** and γ and δ in **9Da**). Analogous signal patterns were observed in all other **8**/**9**-mixtures which, however, could not be separated. Thus, their ratios given in Table 2 have been determined on the basis of the sp^2 carbon signals. Isomeric carbonitriles of the type **10** and recyclisation products could be detected only in a few instances (**10Db**, **10Cb**, **12Ba** and **12Bb**). The reaction with **1Db** afforded reduction products (**8H** and **1Ab**) in considerable yields.

DISCUSSION

The difference in the formation of the lactams **6** and **7** may be interpreted as follows (see Scheme 1): The main reaction pathway involves the diazoiminium ion **3** which undergoes a rearrangement to **4** and **5**. Isomer **4** gives the fragmentation products **8**, **9**, **12**, **13** and **16**, respectively, and only small amounts of the lactams **6** are produced. On the other hand, the iminium ion **5** with axial X strongly prefers the addition of water to form **7** so that carbonitriles of type **10** and **11** and corresponding ketones (**14**, **15**, **18** and **19**) do not occur. If X is equatorial, however, the reaction of **5** is less selective so that in some instances carbonitriles **10** can be isolated. The reaction of the equatorial iodoadamantanone **1Db** does not follow this scheme since reduction and decomposition reactions dominate. Thus, there is no pronounced regioselectivity of the nitrogen insertion (**3** → **4**/**5**). The intermediates **4** and **5** react differently so that different amounts of the isomeric lactams (**6** and **7**) and nitriles (**8**-**11**) result. The lack of a clear regioselectivity is plausible if one considers that the nitrogen insertion is controlled by the stereochemistry of **3** (Scheme 2). The rearrangement involves the methine group antiperiplanar to the diazo group[4,5] only so that **Z-3** gives **4** and **E-3** gives **5**, and there is no obvious reason why **2** should favour the formation of one stereoisomer of **3**. A corresponding domination of a stereocontrol over inductive effects of X was observed in the rearrangement of Z- and E-methoximes of the bromoadamantanones **1Ca** and **1Cb**[16].

Scheme 2



An alternative explanation for the **6**/**7** ratios is a regioselectivity in the rearrangement of **2** to **3'** and **3''**, respectively, i.e. the origin of this selectivity rests in inductive effects of X. This, however, should result in a strong preference of **6** in analogy to the Baeyer-Villiger oxidation of the same starting materials[17] which is in contrast to the experimental results. On the basis of this contradiction we conclude that **3'** and **3''** do not play a significant role in the SR of 4-substituted adamantanones.

As shown in Table 1 the "anomalous" SR is highly regioselective. On the whole, the selectivity in the formation of the carbonitriles **8**/**9** under modified conditions (Table 2), however, is much less pronounced. Moreover, it is beyond question that **8** and **9** are interconverting under the strongly acidic reaction conditions and this was proven by the following experiment: Both iodonitriles **8Da** and **9Da** were subjected separately to the original SR conditions (pure methanesulfonic acid, room temperature, however without NaN_3). Whereas **8Da** afforded only the corresponding ketone **12Da**, a 2:1-mixture of **13Da** and **12Da** was obtained from **9Da**. Therefore, we conclude that the regioselectivity does not originate in the fragmentation step (**4** → **8**/**9**) but in different, reactivities of **8** and **9** in their transition states **TS 8** and **TS 9**, respectively (Scheme 2). The sp^2-^{13}C chemical shifts of **8** differ significantly from those of **9**, indicating a strong influence of X - sterically and/or electronically - on the electron density in the double bonds[15,18]. So it is reasonable that the energies of the transition states are effected as well, and this leads to the conclusion that the reaction **8** → **12** is apparently faster than **9** → **13**. The fact that in the "anomalous" SR (Table 1) the structural type of the side products is dependent on the stereochemical position of X (**13** in the axial/endo, **16** in the equatorial/exo case) cannot be explained satisfactorily, but seems to indicate different mechanisms of the perturbation by X and hence diverging relative reaction rates.

Table 3: ^{13}C chemical shifts of monosubstituted azahomoadamantanones (**6** and **7**) as well as of disubstituted adamantanones (**12**, **13** and **16**)[a]

	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	Others
6Aa	32.9	79.6	47.6	176.3	-	45.8	36.6	27.1	34.8	36.6	30.9	39.5 (OMes)
6Ba	35.4	60.1	50.5	177.0	-	45.0	36.6	26.2	35.8	30.3	31.8	
6Ca	36.0	52.8	50.9	177.1	-	45.1	36.7	26.1	36.2	31.1[b]	32.3[b]	
6Da	37.2	37.2	52.0	178.3	-	44.9	36.7	26.1	36.1	32.9[b]	32.5[b]	
6Ab	32.7	79.2	47.8	175.7	-	45.1	36.4	25.8	28.0	35.4	26.6	38.6 (OMes)
6Bb	35.2	60.1	50.3	177.3	-	45.2	36.5	26.5	28.3	37.2	25.8	
6Cb	35.8	53.3	51.0	177.9	-	45.2	36.5	26.6	29.1	37.4	26.1	
6Db	37.4	33.0	52.6	177.5	-	45.1	37.2	26.8	30.7	36.2	26.1	
7Aa	32.5	79.0	49.4	-	181.2	40.6	30.0	25.7	34.1	24.6	35.8	38.9 (OMes)
7Ba	35.2	63.5	51.7	-	181.7	40.7	30.4	25.9	35.8	24.5	36.9	
7Ca	35.6	58.1[b]	51.9	-	181.0	40.5[b]	30.4	25.9	36.2	25.3	37.1	
7Da	36.9	40.6[b]	53.0	-	180.9	40.5[b]	30.7	26.1	36.3	26.9	36.8	
7Ea	28.9	37.4	46.4	-	181.0	40.7	30.0	25.7	34.0	26.8	35.8	119.7 (CN)
7Ab	36.2	81.4	48.4	-	181.0	40.8	31.7[b]	25.9	28.2	29.7[b]	30.3[b]	38.7 (OMes)
7Bb	34.6	62.8	51.2	-	180.7	40.9	30.6[b]	26.4	28.0	31.4[b]	35.5[b]	
7Cb	35.3[b]	55.9[b]	51.3	-	181.4	41.1	30.6[b]	26.5	28.9	31.9[b]	30.5[b]	
7Db	36.5[b]	36.8[b]	52.6	-	181.7	41.1	30.6[b]	26.7	30.4[b]	32.0[b]	30.5[b]	
7Eb	29.9	37.2	46.8	-	181.6	41.0	29.9	26.0	30.4[b]	32.0[b]	33.2	120.4 (CN)
12Aa	51.5	207.1	49.8	85.1	31.8	29.0	30.8	79.8	27.3	30.7	-	38.8 (OMes)
12Ba	51.5	207.2	51.8	66.2	33.9	30.4	30.6	80.2	27.3	32.3	-	
12Ca	51.4	206.9	53.1	58.9	34.4	30.8	30.9	80.2	28.3	33.4	-	
12Da	51.3	206.9	54.3	38.7	35.3	30.8[b]	31.1	80.4	30.0[b]	34.5	-	
12Ea	51.3	206.5	46.4	39.2	29.2	29.2[b]	30.6	79.5	29.6[b]	30.6	-	118.3 (CN)
12Ab[c]	49.8	206.0	49.8	79.3	30.3	23.3	30.3	79.3	25.5	25.5	-	37.7 (OMes)
12Bb	50.5	206.9	52.5	62.2	33.5	23.3	31.5	80.0	29.4	26.2	-	
12Cb	50.6	206.5	53.0	55.0[b]	33.8[b]	24.0	31.6	80.1	30.5	27.1	-	
12Db	51.2	205.7	54.3	35.0[b]	34.8[b]	25.8	31.9	80.9	31.9	28.9	-	
12Eb	51.0	206.3	45.8	37.1	29.1	25.7	31.3	79.3	31.3	28.3	-	118.4 (CN)
13Aa	50.6	208.1	51.8	81.4	37.8	29.2	25.0	33.4	76.7	37.9	-	39.5 (OMes)
13Ba	51.8	208.1	53.4	61.6	39.7	30.4	25.0	33.6	77.4	39.6	-	
13Ca	51.4	208.2	53.9	51.7	39.8	31.5	25.1	33.8	78.2	40.7	-	
13Da[c]	51.7	208.2	55.0	31.9	40.5	30.0	25.2	34.0	79.9	41.8	-	
16Ab	50.9	206.0	49.6	85.9	37.7	28.1	31.0	79.5	26.8	29.9	-	37.7 (OMes)
16Cb	50.1	-	54.1	54.8	34.8	29.5	39.2	85.5	34.6	27.8	-	
16Eb	50.5	-	46.8	37.1	29.0	31.7	37.1	84.8	35.6	28.6	-	

[a] In $CDCl_3$, relative to internal TMS ($\delta = 0$).

[b] May be interchanged pairwise.

[c] In d_6-DMSO, relative to internal TMS ($\delta = 0$).

EXPERIMENTAL

General

The ^1H NMR measurements were carried out in $CDCl_3$ solutions at 60 MHz and/or 80 MHz using Varian EM-360 and/or Bruker WP 80 spectrometers. ^{13}C NMR spectra were recorded at 22.64 MHz and/or 62.63 MHz on Bruker WH-90 and/or WM-250 spectrometers in $CDCl_3$ solutions. All chemical shifts are given relative to tetramethylsilane as internal standard. Infrared spectra were obtained on either a Perkin-Elmer 223 or a Shimadzu IR-400 spectrometer in $CHCl_3$ solutions. The mass spectra were measured on Varian MAT CH-5 and/or CH-7 spectrometers. High resolution mass spectra (HRMS) were recorded on a Varian MAT 731 spectrometer. Chromatographic separations were carried out under medium pressure on a Merck Lobar B column filled with silicagel (40-63μm). Various ligroin/acetone mixtures were used as eluents.

The structure of the lactams **6/7** could be assigned by inspecting the signals of the bridge-head hydrogen atoms at C-3 and C-6 (cf. Scheme 1): H-6 resonates at δ=3.3-3.4 in **6** but only at δ=2.6-2.7 in **7**; H-3 signals in **6** appear at δ=3.0-3.1 and in **7** at δ=3.4-3.5. All signals can be identified easily even at low magnetic fields (e.g. 60 MHz) The estimation of the ^{13}C chemical shifts of the lactams by appropriate addition of X-substituent effects (taken from 2-X-adamantanes[1]) to the values of **6H** (≡**7H**) and comparison of these data with the experimental spectra (Table 3) led to the same structural assignment.

The ^{13}C chemical shifts of the disubstituted adamantanones (**12**, **13** and **16**) are also collected in Table 3. In a way similar to that used for the lactams ^{13}C chemical shifts can be calculated assuming additivity of individual substituent effects including interaction effects. This procedure was shown to be effective in various instances[1,2,19]. A comparison of these data with the experimental values allows unequivocal structural assignment. Structure determinations of the carbonitriles **8** and **9** are based on two-dimensional NMR experiments carried out in one example (**8Da** and **9Da**)[15].

Syntheses

General procedure of the Schmidt reaction[10]:
Ca. 500-1000mg of the respective 4-substituted adamantanone **1** were dissolved in 5ml methanesulfonic acid and cooled to 0°C. Then a small excess of NaN_3 was added in small portions under cooling with ice water and permanent stirring. After a further 1h stirring at room temperature the reaction mixture was poured onto ice and neutralized with solid $NaHCO_3$. This solution was saturated with NaCl and extracted with methylene chloride (4 x 50ml). The combined organic layers were washed with water (2 x 200ml), dried over anhydrous $MgSO_4$ and evaporated. The product mixtures were separated by medium-pressure chromatography. Starting materials and yields are summarized in Table 1.

2-exo-Iodo-5-azahomoadamantan-4-one (**6Db**)

IR: 3600-3200, 3430, 2930, 1665 cm^{-1}. NMR: 7.97-7.28 (br, 1H), 4.94 (m, 1H), 3.30 (m, 1H), 3.00 (m, 1H), 2.80-1.45 (m, 10H). MS (m/e): 291 (<1, M^+), 165 (58), 164 (100), 121 (24), 93 (44), 79 (87).

2-endo-Methanesulfonoxy-4-azahomoadamantan-5-one (**7Aa**)

IR: 3600-3200, 2900, 1665, 1335, 1170 cm^{-1}. NMR: 6.91-6.58 (br, 1H), 4.84 (t, 1H), 3.61 (m, 1H), 3.10 (s, 3H), 2.69 (m, 1H), 2.53-1.48 (m, 10H). MS (m/e): 259 (35, M^+), 180 (55), 164 (13), 163 (20), 152 (100), 136 (13), 135 (15), 134 (39), 121 (9), 108 (10), 93 (14), 91 (20), 79 (63). HRMS (m/e): 259.0895 (calcd. for $C_{11}H_{17}NO_4S$: 259.0874). M.p. 173°C.

2-endo-Chloro-4-azahomoadamantan-5-one (**7Ba**)

IR: 3550-3100, 3400, 2900, 1650 cm^{-1}. NMR: 7.36-6.64 (br, 1H), 4.27 (t, 1H), 3.44 (m, 1H), 2.68 (m, 1H), 2.53-1.47 (m, 10H). MS (m/e): 201/199 (13/40, M^+), 164 (100), 136 (53), 108 (20), 79 (33). HRMS (m/e): 201.0765/199.0777 (calcd. for $C_{10}H_{14}NOCl$: 201.0731/199.0761). For $C_{10}H_{14}NOCl$ calcd.: 60.15% C, 7.0% H, 7.0% N; found: 60.05% C, 7.05% H, 6.95% N. M.p. 285°C (dec.).

2-endo-Bromo-4-azahomoadamantan-5-one (**7Ca**)

IR: 3600-3100, 3430, 2940, 1655 cm^{-1}. NMR: 7.06-6.68 (br, 1H), 4.49 (t, 1H), 3.43 (m, 1H), 2.62 (m, 1H), 2.43-1.41 (m, 10H). MS (m/e): 245/243 (24/24, M^+), 164 (100), 136 (18), 121 (19), 108 (18), 93 (18), 91 (18), 79 (29). HRMS (m/e): 245.0222/243.0250 (calcd. for $C_{10}H_{14}NOBr$: 245.0235/243.0255). For $C_{10}H_{14}NOBr$ calcd.: 49.2% C, 5.7% H, 5.7% N; found: 50.4% C, 6.05% H, 5.6% N. M.p. 225-226°C.

2-endo-Iodo-4-azahomoadamantan-5-one (**7Da**)

IR: 3350-3100, 3430, 2940, 1660 cm^{-1}. NMR: 7.58-7.05 (br, 1H), 4.78 (t, 1H), 3.43 (m, 1H), 2.64 (m, 1H), 2.43-1.48 (m, 10H). MS (m/e): 291 (10, M^+), 164 (100), 121 (27), 93 (21), 91 (21), 79 (24). HRMS (m/e): 291.0102 (calcd. for $C_{10}H_{14}NOI$: 291.0116). For $C_{10}H_{14}NOI$ calcd.: 41.2% C, 4.8% H, 4.8% N; found: 41.45% C, 4.75% H, 4.3% N. M.p. 151-153°C.

2-endo-Cyano-4-azahomoadamantan-5-one (**7Ea**)

IR: 3400-3200, 2925, 2250, 1665 cm^{-1}. NMR: 7.1 (br, 1H), 3.50 (m, 1H), 3.35-2.68 (m, 3H), 2.55-1.72 (m, 9H). MS (m/e): 190 (100, M^+), 150 (26), 122 (54), 108 (42), 96 (47), 79 (47).

2-exo-Methanesulfonoxy-4-azahomoadamantan-5-one (**7Ab**)

IR: 3400-3100, 3375, 2900, 1640, 1340, 1160 cm^{-1}. NMR: 6.99-6.53 (br, 1H), 4.76 (m, 1H), 3.46 (m, 1H), 3.05 (s, 3H), 2.70 (m, 1H), 2.50-1.54 (m, 10H). MS (m/e): 259 (24, M^+), 180 (52), 164 (18), 163 (18), 162 (10), 152 (100), 136 (13), 135 (15), 134 (35), 121 (6), 91 (21), 79 (71).HRMS (m/e): 259.0886 (calcd. for $C_{11}H_{17}NO_4S$: 259.0874). For $C_{11}H_{17}NO_4S$ calcd.: 51.0% C, 6.6% H, 5.4% N; found: 51.05% C, 6.3% H, 5.4% N. M.p. 181°C.

2-exo-Chloro-4-azahomoadamantan-5-one (**7Bb**)

IR: 3600-3100, 3370, 2900, 1650 cm^{-1}. NMR: 8.18-7.57 (br, 1H), 4.19 (m, 1H), 3.36 (m, 1H), 2.70 (m, 1H), 2.59-1.30 (m, 10H). MS (m/e): 201/199 (15/42, M^+), 164 (100), 136 (70), 108 (20), 91 (14), 79 (33). HRMS (m/e): 201.0725/199.0758 (calcd. for $C_{10}H_{14}NOCl$: 201.0731/199.0761). M.p. 230-231°C.

2-exo-Bromo-4-azahomoadamantan-5-one (**7Cb**)

IR: 3600-3150, 3420, 2960, 1655 cm^{-1}. NMR: 7.83-7.30 (br, 1H), 4.38 (m, 1H), 3.56 (m, 1H), 2.65 (m, 1H), 2.50-1.30 (m, 10H). MS (m/e): 245/243 (19/19, M^+), 164 (100), 136 (14), 121 (17), 108 (14), 93 (17), 91 (26), 79 (32). HRMS (m/e): 245.0251/243.0268 (calcd. for $C_{10}H_{14}NOBr$: 245.0235/243.0255). M.p. 189-191°C.

2-exo-Cyano-4-azahomoadamantan-5-one (**7Eb**)

IR: 3400-3200, 2990, 2240, 1665 cm^{-1}. NMR: 7.73 (br, 1H), 3.46 (m, 1H), 3.00 (m, 1H), 2.65 (m, 1H), 2.40-1.50 (m, 10H). MS (m/e): 190 (100, M^+), 162 (8), 150 (21), 122 (42), 108 (42), 80 (41), 79 (51).

$4^a,8^e$-Di(methanesulfonoxy)-adamantan-2-one (**12Aa**)

IR: 2905, 2860, 1715, 1340, 1150 cm^{-1}. NMR (DMSO): 5.20 (m, 1H), 4.80 (m, 1H), 3.20 (s, 3H), 3.12 (s, 3H), 2.76-1.60 (m, 8H). MS (m/e): 338 (1, M^+), 242 (20), 163 (13), 146 (90), 118 (61), 91 (66), 79 (100).

4^a-Chloro-8^e-methanesulfonoxyadamantan-2-one (**12Ba**)

IR: 2900, 2850, 1710, 1340, 1150 cm^{-1}: NMR: 4.70 (m, 1H), 4.51 (m, 1H), 3.05 (s, 3H), 2.81 (m, 2H), 2.50-1.69 (m, 8H). MS (m/e): 280/278 (< 1/2, M^+), 184/182 (18/53), 154 (15), 147 (25), 121 (56), 79 (100).

4^a-Bromo-8^e-methanesulfonoxyadamantan-2-one (**12Ca**)

IR: 2910, 2860, 1710, 1340, 1155 cm^{-1}. NMR: 4.69 (m, 2H), 3.05 (s, 3H), 2.89 (m, 2H), 2.76-1.67 (m, 8H). MS (m/e): 324/322 (1/1, M^+), 243 (8), 228/226 (11/11), 147 (100), 119 (59), 91 (65), 79 (36).

4^a-Iodo-8^e-methanesulfonoxyadamantan-2-one (**12Da**)

IR: 2900, 2850, 1715, 1340, 1140 cm^{-1}. NMR: 4.83 (m, 2H), 3.10 (s, 3H), 2.97 (m, 2H), 2.69-1.63 (m, 8H). MS (m/e): 370 (2, M^+), 243 (17), 147 (100), 119 (28), 91 (45), 79 (37).

4^a-Cyano-8^e-methanesulfonoxyadamantan-2-one (**12Ea**)

IR: 2980, 2900, 2850, 2225, 1720, 1350, 1180 cm^{-1}. NMR: 4.80 (m, 1H), 3.25 (m, 1H), 3.05 (s, 3H), 3.00-2.71 (m, 2H), 2.59-1.70 (m, 8H). MS (m/e): 269 (1, M^+), 173 (57), 79 (100).

$4^e,8^e$-Di(methanesulfonoxy)-adamantan-2-one (**12Ab**)

IR: 2910, 2855, 1710, 1350, 1150 cm^{-1}. NMR (DMSO): 4.84 (m, 1H), 3.25 (s, 3H), 3.22 (s, 3H), 2.76 (m, 2H), 2.60-1.70 (m, 8H). MS (m/e): 338 (< 1, M^+), 243 (4), 242 (10), 147 (48), 146 (100), 118 (38), 91 (40), 79 (53).

4^e-Chloro-8^e-methanesulfonoxyadamantan-2-one (**12Bb**)

IR: 2900, 2850, 1710, 1360, 1160 cm^{-1}. NMR: 4.79 (m, 1H), 4.33 (m, 1H), 3.10 (s, 3H), 3.01-1.62 (m, 10H). MS (m/e): 280/278 (< 1/2, M^+), 243 (1), 201/199 (1/4), 184/182 (25/71), 147 (78), 119 (69), 91 (75), 79 (100).

4^e-Bromo-8^e-methanesulfonoxyadamantan-2-one (**12Cb**)

IR: 2915, 2860, 1710, 1340, 1160 cm^{-1}. NMR: 4.75 (m, 1H), 4.45 (m, 1H), 3.05 (s, 3H), 2.80 (m, 2H), 2.65-1.50 (m, 8H). MS (m/e): 324/322 (< 1/ < 1, M^+), 243 (13), 229/227 (1/1), 147 (100), 119 (31), 91 (48), 79 (31).

4^e-Iodo-8^e-methanesulfonoxyadamantan-2-one (**12Db**)

IR: 2920, 2855, 1710, 1340, 1155 cm^{-1}. NMR: 4.76 (m, 2H), 3.05 (s, 3H), 2.75 (m, 2H), 2.60-1.70 (m, 8H). MS (m/e): 370 (< 1, M^+), 243 (14), 147 (100), 119 (18), 91 (55), 79 (36).

4^e-Cyano-8^e-methanesulfonoxyadamantan-2-one (**12Eb**)

IR: 2920, 2865, 2240, 1720, 1340, 1160 cm^{-1}. NMR: 4.80 (m, 1H), 3.05 (m, 1H), 3.00 (s, 3H), 2.90-1.80 (m, 10H). MS (m/e): 269 (< 1, M^+), 190 (5), 175 (56), 145 (16), 79 (100).

4^{e},9^{e}-Di(methanesulfonoxy)-adamantan-2-one (**13Aa**)

IR: 2930, 2865, 1725, 1340, 1170 cm^{-1}. NMR: 5.15 (m, 2H), 3.05 (s, 6H), 2.95 (m, 2H), 2.75-1.70 (m, 8H). MS (m/e): 338 (1, M^{+}), 242 (19), 163 (20), 146 (91), 118 (55), 91 (63), 79 (100).

4^{e}-Chloro-9^{e}-methanesulfonoxyadamantan-2-one (**13Ba**)

IR: 2905, 2855, 1705, 1340, 1160 cm^{-1}. NMR: 5.15 (m, 1H), 4.50 (m, 1H), 3.05 (s, 3H), 2.80 (m, 2H), 2.55-1.65 (m, 8H). MS (m/e): 280/278 (1/3, M^{+}), 184/182 (19/56), 154 (12), 147 (28), 121 (54), 79 (100).

4^{e}-Bromo-9^{e}-methanesulfonoxyadamantan-2-one (**13Ca**)

IR: 2910, 2855, 1715, 1340, 1150 cm^{-1}. NMR: 5.30 (m, 1H), 4.75 (m, 1H), 3.04 (s, 3H), 2.85 (m, 2H), 2.70-1.58 (m, 8H). MS (m/e): 324/322 (1/1, M^{+}), 228/226 (15/15), 147 (100), 119 (55), 91 (63), 79 (43).

4^{e}-Iodo-9^{e}-methanesulfonoxyadamantan-2-one (**13Da**)

IR: 2905, 2855, 1715, 1340, 1150 cm^{-1}. NMR: 5.41 (m, 1H), 4.85 (m, 1H), 3.05 (s, 3H), 2.90 (m, 2H), 2.63-1.70 (m, 8H). MS (m/e): 370 (2, M^{+}), 243 (16), 147 (100), 119 (30), 91 (47), 79 (38).

4^{e},8^{a}-Di(methanesulfonoxy)-adamantan-2-one (**16Ab**)

IR: 2905, 2860, 1715, 1345, 1150 cm^{-1}. NMR (DMSO): 5.15 (m, 1H), 4.85 (m, 1H), 3.23 (s, 3H), 3.16 (s, 3H), 2.76 (m, 2H), 2.60-1.65 (m, 8H). MS (m/e): 338 (< 1, M^{+}), 243 (5), 242 (16), 147 (48), 146 (100), 118 (43), 91 (45), 79 (63).

4^{e}-Bromo-8^{a}-methanesulfonoxyadamantan-2-one (**16Cb**)

IR: 2920, 2855, 1715, 1340, 1160 cm^{-1}. NMR: 5.15 (m, 1H), 4.40 (m, 1H), 3.09 (s, 3H), 2.80-1.65 (m, 10H). MS (m/e): 324/322 (< 1/ < 1, M^{+}), 243 (30), 147 (18), 119 (100), 91 (58), 79 (44).

4^{e}-Cyano-8^{a}-methanesulfonoxyadamantan-2-one (**16Eb**)

IR: 2915, 2865, 2240, 1715, 1340, 1155 cm^{-1}. NMR: 5.15 (m, 1H), 3.05 (m, 1H), 3.02 (s, 3H), 2.90-1.75 (m, 10H). MS (m/e): 269 (1, M^{+}), 173 (54), 145 (15), 79 (100).

General procedure of the "modified" Schmidt reaction[10]:
To a stirred solution of ca. 500-1000mg of the respective 4-substituted adamantanone **1** in 6 ml methanesulfonic acid and 8ml glacial acetic acid a small excess of NaN_3 was added portionwise. After a further 1h stirring at room temperature the reaction mixture was poured onto ice and worked up in the usual way (vide supra). Starting materials and yields are summarized in Table 2.

2-endo-Methanesulfonoxy-5-azahomoadamantan-4-one (**6Aa**)

IR: 3550-3150, 2940, 1665, 1350, 1170 cm^{-1}. NMR: 7.15-6.75 (br, 1H), 4.94 (dd, 1H), 3.53-2.90 (m+s, 5H), 2.60-1.52 (m, 10H). MS (m/e): 259 (15, M^{+}), 180 (30), 164 (12), 163 (52), 152 (6), 136 (11), 135 (19), 121 (21), 120 (15), 93 (34), 91 (15), 79 (100). HRMS: (m/e): 259.0874 (calcd. for $C_{11}H_{17}NO_4S$: 259.0874). For $C_{11}H_{17}NO_4S$ calcd.: 51.0% C, 6.6% H, 5.4% N; found: 51.0% C, 7.0% H, 5.4% N. M.p. 152-153°C.

2-endo-Chloro-5-azahomoadamantan-4-one (**6Ba**)

IR: 3600-3100, 3400, 2910, 1650 cm^{-1}. NMR: 7.18-6.61 (br, 1H), 4.28 (m, 1H), 3.36 (m, 1H), 3.07 (m, 1H), 2.65-1.45 (m, 10H). MS (m/e): 201/199 (9/30, M^{+}), 164 (18), 163 (29), 136 (14), 135 (14), 108 (13), 94 (35), 93 (13), 91 (13), 79 (100). HRMS (m/e): 201.0743/199.0771 (calcd. for $C_{10}H_{14}NOCl$: 201.0731/199.0761). For $C_{10}H_{14}NOCl$ calcd.: 60.15% C, 7.0% H, 7.0% N; found: 60.25% C, 6.75% H, 7.1% N. M.p. 277-279°C.

2-endo-Bromo-5-azahomoadamantan-4-one (**6Ca**)

IR: 3600-3150, 3430, 2940, 1660 cm^{-1}. NMR: 7.08-6.69 (br, 1H), 4.43 (m, 1H), 3.35 (m, 1H), 3.08 (m, 1H), 2.71-1.60 (m, 10H). MS (m/e): 245/243 (23/23, M^{+}), 164 (100), 136 (17), 121 (95), 108 (10), 93 (36), 91 (16), 79 (69). HRMS: (m/e): 245.0232/243.0269 (calcd. for $C_{10}H_{14}NOBr$: 245.0235/ 243.0255). For $C_{10}H_{14}NOBr$ calcd.: 49.2% C, 5.7% H, 5.7% N; found: 49.45% C, 5.7% H, 5.7% N. M.p. 225°C.

2-endo-Iodo-5-azahomoadamantan-4-one (**6Da**)

IR: 3600-3150, 3430, 2935, 1665 cm^{-1}. NMR: 6.99-6.55 (br, 1H), 4.65 (m, 1H), 3.33 (m, 1H), 3.04 (m, 1H), 2.66-1.62 (m, 10H). MS (m/e): 291 (6, M^{+}), 164 (100), 136 (13), 121 (95), 93 (46), 91 (16), 79 (72). HRMS: (m/e): 291.0089 (calcd. for $C_{10}H_{14}NOI$: 291.0116). For $C_{10}H_{14}NOI$ calcd.: 41.2% C, 4.8% H, 4.8% N; found: 41.55% C, 4.7% H, 4.8% N. M.p. 192-193°C (dec).

2-exo-Methanesulfonoxy-5-azahomoadamantan-4-one (**6Ab**)

IR: 3600-3150, 3420, 2930, 1660, 1345, 1160 cm^{-1}. NMR: 7.04-6.66 (br, 1H), 4.97 (m, 1H), 3.35 (m, 1H), 3.05 (s, 3H), 2.99 (m, 1H), 2.48-1.51 (m, 10H).

2-exo-Chloro-5-azahomoadamantan-4-one (**6Bb**)

IR: 3530-3150, 3380, 2900, 1650 cm^{-1}. NMR: 7.47-6.89 (br, 1H), 4.52 (m, 1H), 3.36 (m, 1H), 2.97 (m, 1H), 2.60-1.43 (m, 10H). MS (m/e): 201/199 (25/79, M^+), 173/171 (8/27), 164 (100), 136 (52), 121 (38), 108 (27), 93 (40), 91 (26), 79 (88). HRMS: (m/e). 201.0761/199.0787 (calcd. for $C_{10}H_{14}NOCl$: 201.0731/199.0761). M.p. 234°C.

2-exo-Bromo-5-azahomoadamantan-4-one (**6Cb**)

IR: 3550-3150, 3400, 2900, 1650 cm^{-1}. NMR: 7.84-7.29 (br, 1H), 4.67 (m, 1H), 3.32 (m, 1H), 3.01 (m, H), 2.65-1.48 (m, 10H). MS (m/e): 245/243 (20/20, M^+), 164 (100), 79 (68).

2-exo-Iodo-4-azahomoadamantan-5-one (**7Db**)

IR: 3600-3150, 3420, 2900, 1650 cm^{-1}. NMR: 7.45-6.99 (m, 1H), 4.61 (m, 1H), 3.50 (m, 1H), 2.62 (m, 1H), 2.45-1.35 (m, 10H). MS (m/e): 291 (< 1, M^+), 164 (100), 121 (30), 79 (31).

2-endo-Iodobicyclo[3.3.1]non-6-ene-3-carbonitrile (**8Da**)

IR: 2900, 2220 cm^{-1}. NMR: 5.89 (m, 2H), 4.51 (m, 1H), 3.34 (m, 1H), 2.75-1.61 (m, 8H). MS (m/e): 273 (21, M^+), 146 (100), 119 (33), 91 (24), 79(18). ^{13}C NMR: 131.0 (d), 128.4 (d), 120.8 (s), 35.9 (d), 33.4 (d), 32.6 (d), 32.4 (t), 31.6 (t), 28.6 (t), 26.1 (d).

2-endo-Iodo-bicyclo[3.3.1]non-7-ene-3-carbonitrile (**9Da**)

IR: 2910, 2230 cm^{-1}. NMR: 5.98 (m, 2H), 4.23 (m, 1H), 3.32 (m, 1H), 2.80-1.86 (m, 8H). MS (m/e): 273 (20, M^+), 146 (100), 119 (33), 91 (44), 79 (25). ^{13}C NMR: 133.8 (d), 126.3 (d), 121.0 (s), 37.0 (d), 36.2 (t), 33.4 (d), 32.7 (t), 31.9 (t), 27.2 (d), 24.6 (d).

Bicyclo[3.3.1]non-6-ene-3-carbonitrile (**8H**)

IR: 2910, 2220 cm^{-1}. NMR: 5.77 (m, 2H), 2.89 (m, 1H), 2.60-1.20 (m, 10H). MS (m/e): 147 (46, M^+), 132 (36), 93 (25), 91 (21), 79 (100). ^{13}C NMR: 131.1 (d), 128.9 (d), 123.6 (s), 33.9 (t), 31.4 (t), 29.9 (t), 29.7 (t), 27.0 (d), 25.1 (d), 20.5 (d).

2-exo-Chlorobicyclo[3.3.1]non-3-ene-7-carbonitrile (**10Bb**)

IR: 2910, 2220 cm^{-1}. NMR: 6.05 (m, 2H), 4.68 (m, 1H), 2.97 (m, 1H), 2.72-1.69 (m, 8H). MS (m/e): 183/181 (17/50, M^+), 146 (100), 119 (31), 91 (63), 79 (35), 77 (39). ^{13}C NMR: 132.6 (d), 132.2 (d), 123.2 (s), 58.2 (d), 35.6 (d), 31.9 (t), 29.1 (t), 27.3 (d), 25.6 (t), 20.6 (d).

2-exo-Bromobicyclo[3.3.1]non-3-ene-7-carbonitrile (**10Cb**)

IR: 2910, 2220 cm^{-1}. NMR: 6.30-5.70 (m, 2H), 4.86 (m, 1H), 2.93 (m, 1H), 2.75-1.22 (m, 8H). MS (m/e): 227/225 (1/1, M^+), 146 (100), 119 (23), 91 (32), 79 (20), 77 (20). ^{13}C NMR: 133.2 (d), 131.9 (d), 51.1 (d), 35.7 (d), 32.1 (t), 29.4 (t), 27.0 (d), 25.7 (t), 20.4 (d).

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