SYNTHESIS OF ADAMANTANE DERIVATIVES. 39.[1] SYNTHESIS AND ACIDOLYSIS OF 2-AZIDOADAMANTANES. A FACILE ROUTE TO 4-AZAHOMOADAMANT-4-ENES

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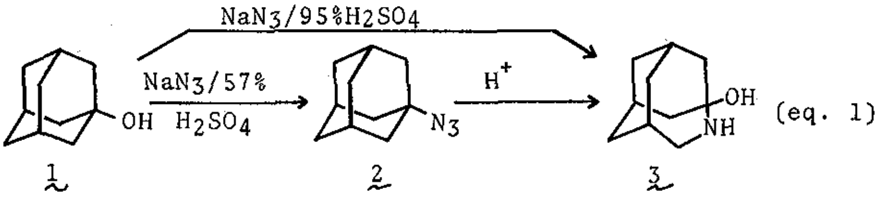
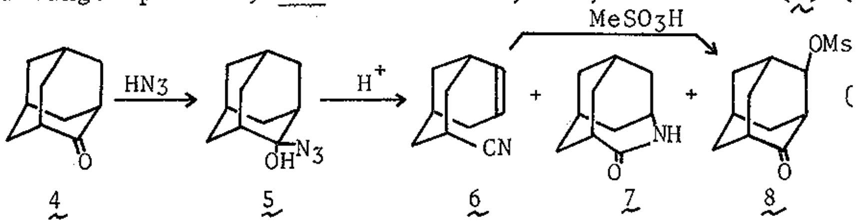
2-Azidoadamantanes 10b-f and 4-azahomoadamant-4-enes 11a-e were obtained in good yields on treatment of the corresponding alcohols 9a-f with NaN_3 in 57%-H_2SO_4-CH_2Cl_2 and in CH_3SO_3H-$CHCl_3$, respectively. Azides 10a-e gave also 11a-e on decompositions in CH_3SO_3H-$CHCl_3$, while 10f afforded only adamantylideneaniline.

We have recently reported an efficient and convenient synthesis of 1-azidoadamantane (2) and 3-hydroxy-4-azahomoadamantane (3) from 1-hydroxyadamantane (1).[2] This procedure consists of substitution of a hydroxyl group with azide function *via* carbocation, followed by acidolysis of the produced azides (eq.1).[3] On the other hand, the



(eq. 1)

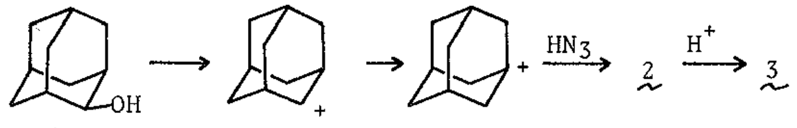
Schmidt reaction of adamantanone (4) is known to afford 6 or 8 (fragmentation and π-route cyclization products) and 7 (rearranged product) *via* 2-azido-2-hydroxyadamantane (5) (eq.2).[4]



(eq. 2)

In view of above interesting behaviors of azidoadamantanes on acidolysis, we have examined the reactions of 2-hydroxyadamantanes 9a-f with hydrazoic acid under acidic conditions.

Secondary alcohol 9a did not react with *in situ* generated hydrazoic acid (4-fold excess to 9a) in 57%H_2SO_4-CH_2Cl_2 but in 97%H_2SO_4-$CHCl_3$, 9a afforded 3 in *ca*. 30% yield accompanied with several side products. The results could be rationalized by consideration of the well known intermolecular hydride transfer to afford 1-adamantylcation which reacted with HN_3 (Scheme I).[2,5] However, when 9a was added to an

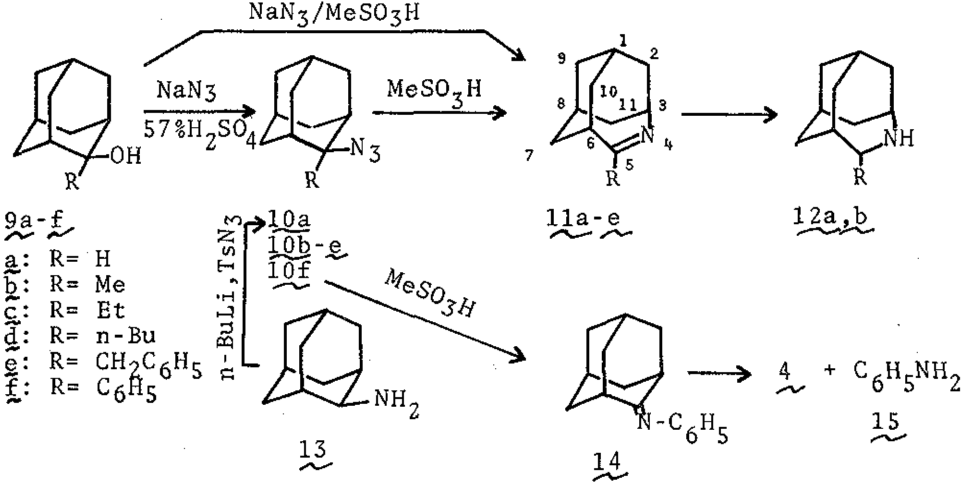


9a

Scheme I

ice-cooled and stirred mixture of HN_3 (5-fold excess) in CH_3SO_3H-$CHCl_3$ and the mixture was stirred for 5 hr at 20-25°, 4-azahomoadamant-4-ene (11a) was obtained as a very sublimable solid (61% yield). The structure was assigned on the basis of analysis, mass spectral molecular weight (*m/e* 149, M^+), ir and pmr spectral data (Table III) as well as $NaBH_4$ reduction to known 4-azahomoadamantane (12a)[6] (Scheme II). Furthermore, 2-azidoadamantane (10a) was prepared in 32% yield from 2-aminoadamantane (13) by treatment with *n*-BuLi, followed by the reaction with *p*-toluenesulfonyl azide,[3] and the decomposition of 10a in CH_3SO_3H-$CHCl_3$ afforded also exclusively the imine 11a (Table II).

Tertiary alcohols 9b-f afforded azides 10b-f in good yields on treatment with NaN_3 in 57%H_2SO_4-CH_2Cl_2 as shown in Scheme II and Table I.



Scheme II

On decomposition in CH_3SO_3H-$CHCl_3$, azides 10b-e afforded also 5-alkyl-4-azahomoadamant-4-enes 11b-e in good yields as summarized in Table II. The structures of 11b-e were supported by anlytical and spectral data (Table III) as well as reduction of 11b to 12b. Imine 11b, on refluxing with $NaBH_3(OAc)$ in dioxane for 7 hr, gave 12b which was characterized as hydrochloride (46% yield): mp 295-8°(dec);[7] ir (KBr) 3200-2400 cm^{-1}; pmr ($CDCl_3$-D_2O) δ 4.0-3.3 (m, 2H), 2.66-1.30 (m, 16H) and 1.53 (d, J=7.0Hz, 3H). Imines 11a-e gave the corresponding hydrochlorides, all of which revealed characteristic ir absorptions at 1675-1680 cm^{-1} due to $\nu_{C=N^+H}$ (Table III). Since the formation of 11a-e depends on the larger migratory aptitude of C_1-C_2 bond of adamantane nucleus than R group in 10a-e, decomposition of 10f, R=C_6H_5 is

Table I. Synthesis of 2-Azidoadamantanes 10a-f[a]

Precursor	Azide (Yield, %)	Mp, °C or n_D (temp, °C)	Ir (film) cm^{-1}	Pmr ($CDCl_3$, 60MHz) δ	Formula	Analysis[b]			
							C	H	N
13	10a (32.7)	30-35	2100	3.79(s,1), 2.5-0.5 (m,14)	$C_{10}H_{15}N_3$	F C	67.76 67.76	8.71 8.53	23.53 23.71
9b	10b (92.4)	35-36	2120 2090	2.4-1.5 (m,14), 1.46(s,3)	$C_{11}H_{17}N_3$	F C	68.95 69.07	8.81 8.96	22.23 21.97
9c	10c (91.1)	1.5252 (30.0)	2090	2.4-1.2 (m,16), 0.94(t, 7.5Hz,3)	$C_{12}H_{19}N_3$	F C	70.36 70.20	9.29 9.33	20.34 20.47
9d	10d (75.0)	1.5172 (29.3)	2090	2.4-0.7 (m,20), 0.95(t, 5.5Hz,3)	$C_{14}H_{23}N_3$	F C	72.23 72.06	9.66 9.93	18.10 18.01
9e	10e (70.8)	1.5767 (23.2)	2100	7.17(s,5), 3.05(s,2), 2.4-1.3 (m,14)[c]	$C_{17}H_{21}N_3$	F C	76.30 76.37	8.16 7.92	15.54 15.71
9f	10f (89.7)	44.5-45.6	2090	7.8-7.3 (m,5), 3.0-1.46 (m,14)	$C_{16}H_{19}N_3$	F C	76.05 75.85	7.49 7.56	16.72 16.59

[a] Azide 10a was prepared by the diazo-transfer method, while 10b-f were obtained by stirring 9b-f with NaN_3 (4-fold excess) in 57%H_2SO_4-CH_2Cl_2(1:1,v/v) for 3-5 hr at 20-25°, followed by usual work-up and chromatography (silica gel, n-pentane-CH_2Cl_2).
[b] F=Found and C=Calcd. [c] In CCl_4.

Table II. Synthesis of 4-Azahomoadamant-4-enes 11a-e from 2-Hydroxyadamantanes 9a-e and Azides 10a-e

Precursor	Mol.ratio of NaN_3 to alcohols	$CHCl_3$: CH_3SO_3H (v/v)	React. time, hr	Imine	Yield, %	Purification Method
9a	5.0	1:1	5.0	11a	60.9	sublimation (90°, 20 mm)
10a	0	3:2	0.5	11a	65.0	
9b	4.0	1:1	1.5	11b	75.3	Kugel rohr distln. (70-80°, 0.4 mm)
10b	0	4:5	0.8	11b	68.8	
9c	4.0	1:1	4.0	11c	67.7	Kugel rohr distln. (88-95°, 0.4 mm)
10c	0	1:1	2.0	11c	81.8	
9d	10.0	1:2	20.0	11d	89.3	Kugel rohr distln. (90-95°, 0.4 mm)
10d	0	1:2	1.0	11d	74.5	
9e	10.0	1:2	19.0	11e[a]	44.6	chromatography (alumina, CH_2Cl_2)
10e	0	1:2	2.0	11e[a]	46.9	

[a] Adamantylidenebenzylamine was also produced in ca. 45% yield.

Table III. Physical and Analytical Data of Cyclic Imines 11a-e and Their Hydrochlorides

Imine (mp,°C or n_D, temp)	Ir,[a] cm^{-1}	Pmr ($CDCl_3$, 60MHz),[b] δ	Formula	Analysis[c]			
					C	H	N
11a (215-8)	1650	8.07(d,6.0Hz,1), 4.33-3.90(m,1), 3.0-2.4(m,1) 2.35-1.35(m,12)	$C_{10}H_{15}N$	F	80.34	10.03	9.63
				C	80.48	10.13	9.39
11aHCl (276-9, dec)	3200-2400, 1680	9.00(d,6.0Hz,1), 4.5-4.15(m,1), 3.5-3.0(m,1), 2.5-1.4(m,12)	$C_{10}H_{16}NCl$	F	64.61	8.86	7.44
				C	64.68	8.69	7.54
11b (1.5155, 22.0)	1660	3.97(t,4.0Hz,1), 2.57(t,4.0Hz,1), 2.00(s,3), 1.9-1.5(m,12)	$C_{11}H_{17}N$	F	81.20	10.33	8.47
				C	80.92	10.50	8.58
11bHCl (278-280,dec)	3200-2400, 1680	4.27(bs,1), 2.92(bs,1), 2.75-1.5(m,15)	$C_{11}H_{18}NCl$	F	66.15	8.94	6.92
				C	66.16	9.08	7.01
11c (1.5154, 29.5)	1665	4.2-3.8(m,1), 2.78-2.45(m,1), 2.23(q,7.0Hz,2), 2.44-1.5(m,14), 1.07(t,7.0Hz,3)	$C_{12}H_{19}N$	F	81.60	10.58	7.82
				C	81.30	10.80	7.90
11cHCl (160-2)	3300-2400, 1675	4.35(bs,1), 3.2-2.7(m,3), 2.5-1.5(m,12), 1.32(t,7.0Hz,3)	$C_{12}H_{20}NCl$	F	67.61	9.65	6.42
				C	67.43	9.43	6.55
11d (1.5074, 30.0)	1660	4.01(t,3.0Hz,1), 2.62(t,3.0Hz,1), 2.45-1.15(m,18), 0.95(t,5.3Hz,3)	$C_{14}H_{23}N$	F	81.61	11.46	6.95
				C	81.89	11.29	6.82
11dHCl (148-153)	3200-2400, 1680	4.31(bs,1), 2.94(bs,3), 2.5-0.8(m,19)	$C_{14}H_{24}NCl$	F	69.53	9.91	5.64
				C	69.54	10.00	5.79
11e (84-8)	1660, 1600, 740, 680	8.2-7.1(m,5), 4.28(t,3.0Hz,1), 3.32(t,3.0Hz,1), 2.4-1.6(m,14)	$C_{17}H_{21}N$	F	85.61	8.59	6.14
				C	85.31	8.84	6.85
11eHCl (167-170)	3400-2400, 1685, 1600, 750, 690	8.1-7.1(m,5), 4.60(bs,1), 3.11(bs,1), 2.5-1.5(m,14)	$C_{17}H_{22}NCl$	F	74.03	7.92	4.79
				C	74.03	8.04	5.08

[a] In KBr for solids and film for oils. [b] Hydrochlorides were measured in $CDCl_3$-D_2O, and bs =broad singlet. [c] F=Found and C=Calcd.

expected to afford a phenyl migration product rather than a ring-expanded product by considering the well known larger migratory tendency of a phenyl group.[3] In fact, **10f** decomposed in CH_3SO_3H-$CHCl_3$ to afford only adamantanone (**4**) and aniline (**15**), which indicated the formation of adamantylideneaniline (**14**),[8] the phenyl migration product. Also, in the decomposition of **10e**, a considerable amount (*ca*.45%) of adamantylidenebenzylamine was produced as well as **11e**.[9]

The imines **11b**-**e** were obtained also directly from alcohols **9b**-**e** on treatment with NaN_3 in CH_3SO_3H-$CHCl_3$ (Table II). Therefore, above described procedures provide facile synthesis of 2-alkyl- or 2-aryl-2-azidoadamantanes and 5-unsubstituted and 5-alkyl-4-azahomoadamant-4-enes.

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7 All mps were measured in a sealed tube and are uncorrected. All new compounds gave correct combustion analyses. Alcohols **9a**-**d** were prepared by the known procedures, and **9e**, mp 54-7°, and **9f**, mp 75-8°, were prepared by the Grignard reaction of **4** and had satisfactory spectral data.

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9 The structural analysis of **11e** should be considered as tentative because of appearance of benzylic methylene at abnormally higher field in the pmr spectrum.

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