SYNTHESIS OF ADAMANTANE DERIVATIVES. 57.[1] FACILE GENERATION AND CYCLOADDITION REACTIVITY OF N-PHENYLSULFONYL-1- AND -2-ADAMANTYL-NITRILIMINES VIA BASE-INDUCED DEHYDROCHLORINATION OF N-(PHENYL-SULFOMYL)-1- AND -2-ADAMANTANECARBOHYDRAZONOYL CHLORIDES

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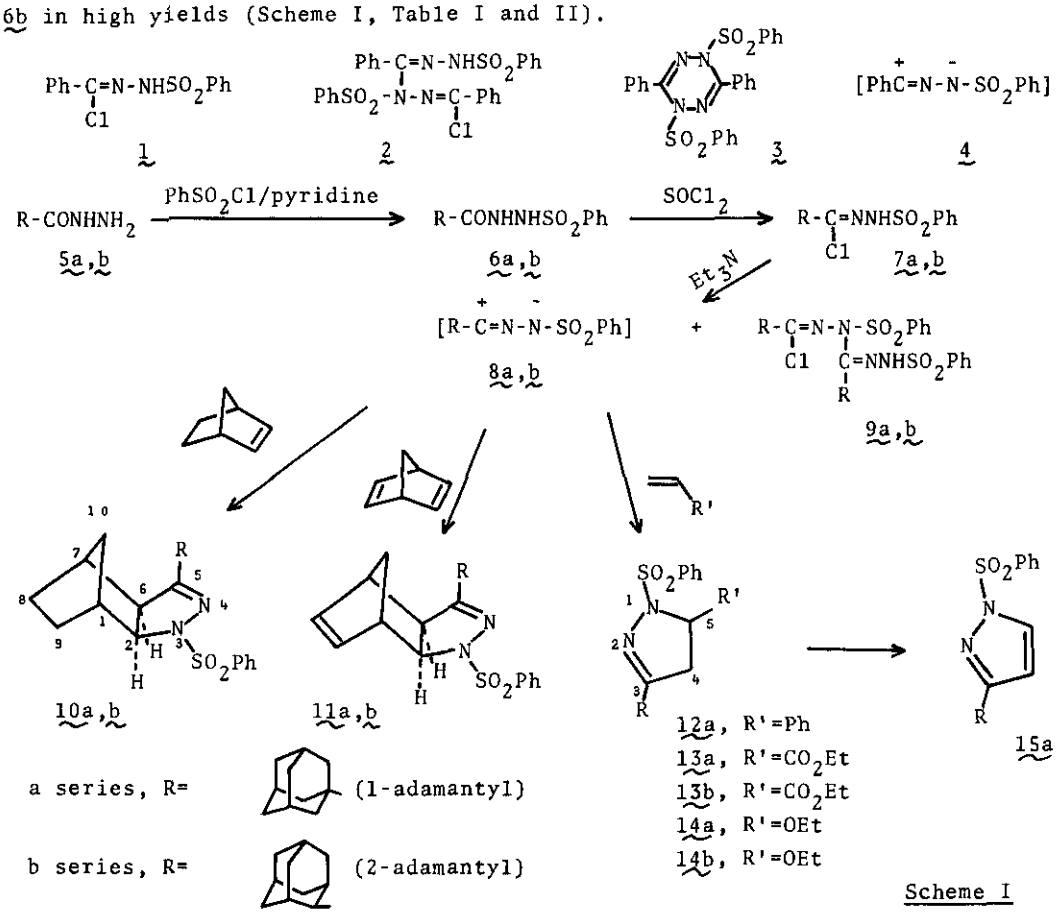
Abstract – Dehydrochlorination of N-(phenylsulfonyl)-1- and -2-adamantanecarbohydrazonoyl chlorides (7a and 7b) with triethylamine in the presence of dipolarophiles afforded the corresponding 1,3-dipolar cycloadducts (10a, 10b, 11a, 11b, 12a, 13a, 13b, 14a, 14b, and 15a) in 22-76% yields accompanied by the formation of linear dimer 9a and 9b, respectively.

The base-induced dehydrochlorination of N-(phenylsulfonyl)benzohydrazonoyl chloride (1) in the presence of dipolarophiles is known to afford only linear dimer 2 and dihydrotetrazine derivative 3 but no 1,3-dipolar cycloadducts[2] in contrast to N-phenylbenzohydrazonoyl chloride.[3] Recently, both zinc-oxide induced[4] and thermal[5] dehydrochlorinations of 1 in the presence of dipolarophiles have been shown to afford 1,3-dipolar cycloadducts of N-phenylsulfonylbenzonitrilimine (4) by us. As an extension of these studies, we wish to report here a facile generation of N-phenylsulfonyl-1- and -2-adamantylnitrilimines (8a and 8b) and their 1,3-dipolar cycloaddition reactivity via the usual base-induced dehydrochlorination of N-(phenylsulfonyl)-1- and -2-adamantanecarbohydrazonoyl chlorides (7a and 7b).

Treatment of 1-adamantanecarbonylhydrazide 5a[6] with benzenesulfonyl chloride in pyridine gave the corresponding phenylsulfonyl hydrazide 6a, which was converted to the required N-(phenylsulfonyl)-1-adamantanecarbohydrazonoyl chloride 7a by the reaction with an excess of thionyl chloride under refluxing for 1.5h. Similarly, the corresponding 2-adamantanecarbohydrazonoyl chloride 7b was prepared

from methyl 2-adamantanecarboxylate[7] via hydrazide 5b and phenylsulfonylhydrazide 6b in high yields (Scheme I, Table I and II).



Scheme I

To a stirred mixture of 7a (0.50 mmol) and norbornene (0.50 mmol) in anhydrous benzene (15 mL) was added slowly a solution of Et_3N (0.50 mmol) in benzene (5 mL) and the stirring was continued for 2h at room temperature (20-25°C). Removal of the solvent and purification of the residue on a silica gel column (benzene) gave 3-phenylsulfonyl-5-adamantyl-3,4-diazatricyclo[5.2.1.$0^{2,6\text{-exo}}$]deca-4-ene (10a), a 1,3-dipolar cycloadduct of 8a to norbornene, and a linear dimer 9a in 64 and 8% yields, respectively. The structural assignments of 10a and 9a were based on the analytical and spectral data. The dehydrochlorination of 7a with Et_3N in the presence of other dipolarophiles such as norbornadiene, styrene, ethyl acrylate and ethyl vinyl ether were carried out under the same conditions as above. Each reaction gave the corresponding 1,3-dipolar cycloadduct 11a, 12a, 13a, and 14a, respectively, accompanied by the formation of the dimer 9a (Table I). The

Table I. N-Phenylsulfonyl-1- and -2-adamantanecarbohydrazonoyl chlorides (7a and 7b) and related adamantane derivatives

Reactants (mmol)	Reagents (mmol)	Reaction temp, °C (time, h)	Products (yield, %)[b]	Mp, °C (recrystallization solvents)
5a (30)	$PhSO_2Cl$[a] (30)	rt[d] (2.0)	6a (95.0)	230-231 (MeOH)
6a (10)	$SOCl_2$ (300)	refl (1.5)	7a (100)	114-116 (C_6H_6-n-hexane)
7a (0.5)	Et_3N + norbornene[c] (0.5) (10)	rt (2.5)	10a (64.0)	174-175 (C_6H_6-n-hexane)
			9a (8.0)	198-199 (Me_2CO)
7a (0.5)	Et_3N + norbornadiene[c] (0.5) (10)	rt (2.5)	11a (59.0)	173-174 (C_6H_6-n-hexane)
			9a (17.0)	
7a (0.5)	Et_3N + styrene[c] (0.5) (10)	rt (2.5)	12a (22.0)	195-197 (C_6H_6-n-hexane)
			9a (29.0)	
7a (0.5)	Et_3N + ethyl acrylate[c] (0.5) (10)	rt (2.5)	13a (56.0)	130-131 (C_6H_6-n-hexane)
			9a (11.0)	
7a (0.5)	Et_3N + ethyl vinyl ether[c] (0.5) (10)	rt (2.5)	14a (66.0)	oil
			15a (34.0)	116-117 (C_6H_6-n-hexane)
5b (30)	$PhSO_2Cl$[a] (30)	rt (2.0)	6b (93)	221-222 (MeOH)
6b (10)	$SOCl_2$ (300)	refl (1.5)	7b (100)	144-146 (C_6H_6)
7b (0.5)	Et_3N + norbornene[c] (0.5) (10)	rt (2.0)	10b (59.0)	166-167 (C_6H_6-n-hexane)
			9b (11.0)	200-202 (Me_2CO)
7b (0.5)	Et_3N + norbornadiene[c] (0.5) (10)	rt (2.0)	11b (56.0)	152-154 (MeOH)
			9b (5.0)	
7b (0.5)	Et_3N + ethyl acrylate[c] (0.5) (10)	rt (2.5)	13b (33.0)	183-185 (C_6H_6-n-hexane)
			9b (24.0)	
7b (0.5)	Et_3N + ethyl vinyl ether[c] (0.5) (10)	rt (2.0)	14b (76.0)	oil
			9b (6.0)	

[a] Pyridine (60 mL) was used as the solvent. [b] The crude products were purified on a silica gel column eluting with benzene, followed by recrystallizations. [c] Benzene (15 mL) was used as the solvent. [d] rt = 20-25°C.

Table II. Analytical and spectral data of N-phenylsulfonyl-1- and -2-adamantanecarbohydrazonoyl chlorides 7a and 7b and related adamantane derivatives

Compd	Ir,[a] cm^{-1}	^1H Nmr($CDCl_3$,60MHz),[b] δ	Formula	Analysis[c]	C	H	N
6a	3305,3190,2920, 2860,1638,1375, 1348,1185,1178	1.6-2.0(m,15,Ad), 7.4-8.0 (m,5,Ph), 8.54(s,1,NH),[d] 9.64(s,1,NH)[d]	$C_{17}H_{22}N_2O_3S$	f	59.80	6.56	8.54
				c	61.05	6.63	8.38
7a	3200,2910,2855, 1620,1390,1346, 1175	1.5-2.1(m,15,Ad), 7.4-8.1 (m,5,Ph), 7.98(s,1,NH)[d]	$C_{17}H_{21}N_2O_2SCl$	f	57.52	5.89	8.20
				c	57.86	6.00	7.94
9a	3200,2910,2860, 1615,1360,1175	1.5-2.2(m,30,Ad), 7.4-8.0 (m,10,Ph), 8.15(s,1,NH)[d]	$C_{34}H_{41}N_4O_4S_2Cl$	f	61.30	6.18	8.36
				c	61.02	6.17	8.37
10a	2920,2860,1600, 1360,1175	1.0-2.0(m,21,Ad+CH_2x3), 2.51(s,1,H_7), 2.67(s,1,H_1), 2.59(d,1,J=9.0Hz,H_6), 3.55(d,1,J=9.0Hz,H_2), 7.4-7.9(m,5,Ph)	$C_{24}H_{30}N_2O_2S$	f	70.04	7.25	7.02
				c	70.21	7.36	6.82
11a	2920,2860,1600, 1360,1180	1.5-2.1(m,17,Ad+CH_2), 2.90 (d,1,J=9.0Hz,H_6), 3.95(d, 1,J=9.0Hz,H_2), 3.13(bs,1, H_7), 3.28(bs,1,H_1), 6.11 (m,2,H_8,H_9), 7.4-8.0(m,5, Ph)	$C_{24}H_{28}N_2O_2S$	f	70.83	6.79	7.11
				c	70.56	6.91	6.86
12a	2920,2860,1605, 1345,1170	1.6-2.1(m,15,Ad), 2.60(dd, 1,J=17.7&9.0Hz,H_4), 3.05(dd,1,J=17.7&10.5Hz,H_4), 4.68(dd,1,J=10.5&9.0Hz,H_5), 7.2-8.0(m,10,Ph)	$C_{25}H_{28}N_2O_2S$	f	71.23	6.79	6.79
				c	71.40	6.71	6.66
13a	2920,2860,1743, 1612,1367,1200, 1175	1.31(t,3,J=7.2Hz,CH_2CH_3), 1.5-2.1(m,15,Ad), 2.85(d, 2,J=10.2Hz,H_4x2), 4.05(t,1, J=10.2Hz,H_5), 4.25(q,2,J= 7.2Hz, CH_2CH_3), 7.4-8.0 (m,5,Ph)	$C_{22}H_{28}N_2O_4S$	f	63.38	6.70	6.86
				c	63.44	6.78	6.73
14a	2920,2860,1605, 1380,1180	1.16(t,3,J=7.2Hz,CH_2CH_3), 1.5-2.1(m,15,Ad), 2.38-2.57(m,2,H_4x2), 3.72(q,2, J=7.2Hz,CH_2CH_3), 5.52-5.54 (m,1,H_5), 7.3-8.0(m,5,Ph)	$C_{21}H_{28}N_2O_3S$	f	65.05	7.15	7.32
				c	64.92	7.26	7.21
15a	3070,2920,2860, 1385,1180	1.6-2.2(m,15,Ad), 6.25(d, 1,J=2.7Hz,H_4), 7.95(d,1, J=2.7Hz,H_5), 7.4-8.1(m,5, Ph)	$C_{19}H_{22}N_2O_2S$	f	66.41	6.44	8.06
				c	66.64	6.47	8.18

6b	3275,3205,2920, 2850,1646,1373, 1340,1176,1167	1.4-2.4(m,15,Ad), 7.4-8.2 (m,5,Ph), 8.45(d,1,J=5.6Hz, NH),[d] 9.81(d,1,J=5.6Hz,NH)[d]	$C_{17}H_{22}N_2O_3S$	f61.14 6.50 8.18 c61.05 6.63 8.38
7b	3180,2920,2860, 1630,1380,1355, 1180	1.4-2.7(m,15,Ad), 7.3-8.0(m, 5,Ph), 8.95(s,1,NH)[d]	$C_{17}H_{21}N_2O_2SCl$	f57.75 6.10 8.12 c57.86 6.00 7.94
9b	3205,2915,2865, 1615,1370,1177	1.2-2.7(m,30,Ad), 7.4-8.1 (m,10,Ph), 8.95(s,1,NH)[d]	$C_{34}H_{41}N_4O_4S_2Cl$	f61.23 6.23 8.34 c61.02 6.17 8.37
10b	2920,2860,1600, 1360,1175	1.0-2.1(m,18,Ad+CH_2x3), 2.30(bs,3,AdCHx2+H_7),[e] 2.42 (bs,1,H_1), 2.65(d,1,J=9.0 Hz,H_6), 2.72(bs,1,AdCH),[e] 3.72(d,1,J=9.0Hz,H_2), 7.4-8.0(m,5,Ph)	$C_{24}H_{30}N_2O_2S$	f70.07 7.40 7.05 c70.21 7.36 6.82
11b	2910,2850,1603, 1355,1170	1.1-2.5(m,17,Ad+CH_2), 2.87 (bs,1,H_7), 2.96(d,1,J=8.4 Hz,H_6), 3.80(bs,1,H_1), 4.08(d,1,J=8.4Hz,H_2), 6.15 (m,2,H_8,H_9), 7.3-8.1(m,5, Ph)	$C_{24}H_{28}N_2O_2S$	f70.47 6.98 6.92 c70.56 6.91 6.86
13b	2920,2860,1740, 1615,1367,1205, 1175	1.33(t,3,J=7.05Hz,$CH_2\underline{CH_3}$), 1.5-2.3(m,14,Ad), 2.80(bs, 1,AdCH),[e] 2.97(d,2,J=10.5Hz, H_4x2), 4.28(t,1,J=10.5Hz,H_5), 4.28(q,2,J=7.05Hz,$\underline{CH_2}CH_3$), 7.4-8.1(m,5,Ph)	$C_{22}H_{28}N_2O_4S$	f63.52 6.65 6.60 c63.44 6.78 6.73
14b	2920,2865,1610, 1360,1175	1.17(t,3,J=7.0Hz,$CH_2\underline{CH_3}$), 1.4-2.3(m,15,Ad), 2.57(d, 2,J= 4.2Hz,H_4x2), 3.80(q,2,J= 7.0Hz, $\underline{CH_2}CH_3$), 5.49(t,1, J=4.2Hz,H_5), 7.4-8.1(m,5, Ph)	$C_{21}H_{28}N_2O_3S$	f65.11 7.06 7.30 c64.92 7.26 7.21

[a] In KBr for solids and film for oils. [b] bs = broad singlet. [c] f = Found. c = Calcd. [d] Disappeared on shaking with D_2O. [e] AdCH = CH of adamantane ring.

reaction with ethyl vinyl ether gave also a pyrazole derivative 15a via an elimination of EtOH from 14a. The given stereo- (10 and 11) and regiochemistry (12-14) were supported by the ^{1}H nmr data (Table II).

The reaction of 7b with Et_3N in the presence of norbornene, norbornadiene, ethyl acrylate and ethyl vinyl ether afforded also the corresponding 1,3-dipolar cycloadducts, 10b, 11b, 13b, and 14b, respectively, accompanied by the formation of a linear dimer 9b (Scheme I, Table I and II).

From the observed reactivity and regioselectivity, the above 1,3-dipolar cycloadditions of 8a and 8b could be rationalyzed in terms of dipole-LUMO controlled type reactions.[8] A lower cycloaddition reactivity of 8b than 8a is explained by considering the steric hindrance of 2-adamantyl group.[9] The above described facile generation of 8a and 8b and their cycloaddition reactivity may be useful for synthesis of other adamantane-substituted pyrazoline and pyrazole derivatives.

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