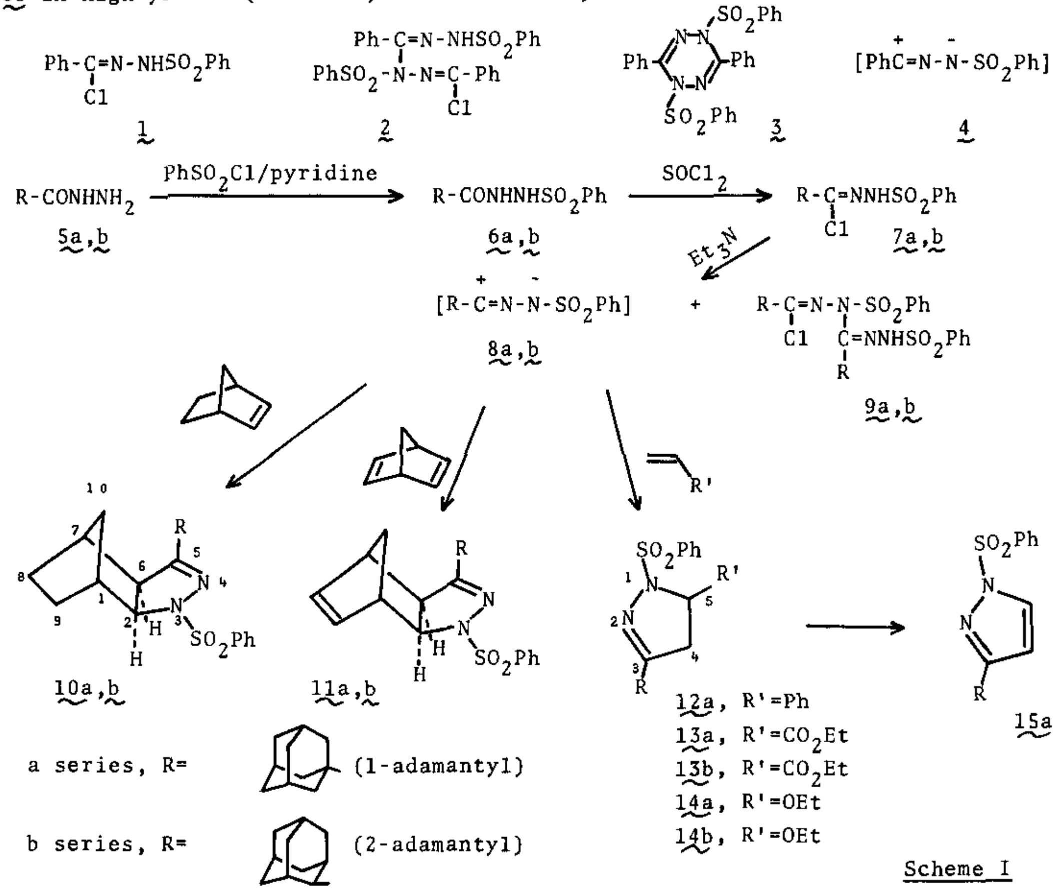
SYNTHESIS OF ADAMANTANE DERIVATIVES. 57.[1] FACILE GENERATION AND CYCLOADDITION REACTIVITY OF N-PHENYLSULFONYL-1- AND -2-ADAMANTYLNITRILIMINES VIA BASE-INDUCED DEHYDROCHLORINATION OF N-(PHENYLSULFOMYL)-1- AND -2-ADAMANTANECARBOHYDRAZONOYL CHLORIDES

Tadashi Sasaki,* Shoji Eguchi, and Yumo Tanaka
Institute of Applied Organic Chemistry, Faculty of Engineering,
Nagoya University, Furo-cho, Chikusa-ku, Nagoya 464, Japan

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$_3$N (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$_3$N 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}	^{1}H 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]	$C_{17}H_{22}N_2O_3S$	f59.80 c61.05	6.56 6.63	8.54 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]	$C_{17}H_{21}N_2O_2SCl$	f57.52 c57.86	5.89 6.00	8.20 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]	$C_{34}H_{41}N_4O_4S_2Cl$	f61.30 c61.02	6.18 6.17	8.36 8.37
10a	2920,2860,1600,1360,1175	1.0-2.0(m,21,Ad+CH$_2$x3), 2.51(s,1,H$_7$), 2.67(s,1,H$_1$), 2.59(d,1,$\underline{J}$=9.0Hz,H$_6$), 3.55(d,1,$\underline{J}$=9.0Hz,H$_2$), 7.4-7.9(m,5,Ph)	$C_{24}H_{30}N_2O_2S$	f70.04 c70.21	7.25 7.36	7.02 6.82
11a	2920,2860,1600,1360,1180	1.5-2.1(m,17,Ad+CH$_2$), 2.90 (d,1,$\underline{J}$=9.0Hz,H$_6$), 3.95(d,1,$\underline{J}$=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)	$C_{24}H_{28}N_2O_2S$	f70.83 c70.56	6.79 6.91	7.11 6.86
12a	2920,2860,1605,1345,1170	1.6-2.1(m,15,Ad), 2.60(dd,1,$\underline{J}$=17.7&9.0Hz,H$_4$), 3.05(dd,1,$\underline{J}$=17.7&10.5Hz,H$_4$), 4.68(dd,1,$\underline{J}$=10.5&9.0Hz,H$_5$), 7.2-8.0(m,10,Ph)	$C_{25}H_{28}N_2O_2S$	f71.23 c71.40	6.79 6.71	6.79 6.66
13a	2920,2860,1743,1612,1367,1200,1175	1.31(t,3,$\underline{J}$=7.2Hz,CH$_2$C$\underline{H}_3$), 1.5-2.1(m,15,Ad), 2.85(d,2,$\underline{J}$=10.2Hz,H$_4$x2), 4.05(t,1,$\underline{J}$=10.2Hz,H$_5$), 4.25(q,2,$\underline{J}$=7.2Hz, C$\underline{H}_2$CH$_3$), 7.4-8.0 (m,5,Ph)	$C_{22}H_{28}N_2O_4S$	f63.38 c63.44	6.70 6.78	6.86 6.73
14a	2920,2860,1605,1380,1180	1.16(t,3,$\underline{J}$=7.2Hz,CH$_2$C$\underline{H}_3$), 1.5-2.1(m,15,Ad), 2.38-2.57(m,2,H$_4$x2), 3.72(q,2,$\underline{J}$=7.2Hz,C$\underline{H}_2$CH$_3$), 5.52-5.54 (m,1,H$_5$), 7.3-8.0(m,5,Ph)	$C_{21}H_{28}N_2O_3S$	f65.05 c64.92	7.15 7.26	7.32 7.21
15a	3070,2920,2860,1385,1180	1.6-2.2(m,15,Ad), 6.25(d,1,$\underline{J}$=2.7Hz,H$_4$), 7.95(d,1,$\underline{J}$=2.7Hz,H$_5$), 7.4-8.1(m,5,Ph)	$C_{19}H_{22}N_2O_2S$	f66.41 c66.64	6.44 6.47	8.06 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 c61.05	6.50 6.63	8.18 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 c57.86	6.10 6.00	8.12 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 c61.02	6.23 6.17	8.34 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*=9.0Hz,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 c70.21	7.40 7.36	7.05 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*=8.4Hz,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 c70.56	6.98 6.91	6.92 6.86
13b	2920,2860,1740,1615,1367,1205,1175	1.33(t,3,*J*=7.05Hz,$CH_2C\underline{H}_3$), 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,$C\underline{H}_2CH_3$), 7.4-8.1(m,5,Ph)	$C_{22}H_{28}N_2O_4S$	f63.52 c63.44	6.65 6.78	6.60 6.73
14b	2920,2865,1610,1360,1175	1.17(t,3,*J*=7.0Hz,$CH_2C\underline{H}_3$), 1.4-2.3(m,15,Ad), 2.57(d,2,*J*=4.2Hz,H_4x2), 3.80(q,2,*J*=7.0Hz, $C\underline{H}_2CH_3$), 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 c64.92	7.06 7.26	7.30 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.

REFERENCES AND FOOTNOTES

1. Part 56: T. Sasaki, M. Ohno and A. Nakanishi, submitted for publication.
2. (a) S. Ito, Y. Tanaka and A. Kakehi, *Bull. Chem. Soc. Jpn.*, 1976, **49**, 762; (b) S. Ito, Y. Tanaka, A. Kakehi and H. Miyazawa, *ibid.*, 1977, **50**, 2969; (c) S. Wawzonek and J. N. Kellen, *J. Org. Chem.*, 1973, **38**, 3627.
3. (a) R. Huisgen, M. Seidel, J. Sauer, J. W. McFarland and G. Wallbillich, *J. Org. Chem.*, 1959, **24**, 892; (b) R. Huisgen, M. Seidel, G. Wallbillich and H. Kupfer, *Tetrahedron*, 1962, **17**, 3; (c) D. Mukherjee, C. R. Watts and K. N. Houk, *J. Org. Chem.*, 1978, **43**, 817.
4. S. Ito, A. Kakehi, T. Matsuno and T. Sasaki, *Chem. Lett.*, 1979, 733.
5. T. Sasaki, S. Eguchi and Y. Tanaka, *Tetrahedron*, 1980, **36**, 1565.
6. H. Stetter and E. Rauscher, *Ber.*, 1960, **93**, 1161.
7. This compound [bp 98-100°C/2 mmHg; ir(neat) 1730 (ν_{CO}) cm^{-1}] was prepared by usual acid catalyzed esterification (MeOH + H_2SO_4) of 2-adamantanecarboxylic acid: H. Oldenziel and D van Leusen, *J. Org. Chem.*, 1977, **42**, 3114.
8. K. N. Houk, J. Sims, C. R. Watts and L. J. Luskus, *J. Am. Chem. Soc.*, 1973, **95**, 7301. For a recent review, see I. Fleming, "Frontier Orbitals and Organic Reactions", Wiley, New York (1976).
9. For a linear array of the CNN atoms of nitrilimine, see N. H. Toubro and A. Holm, *J. Am. Chem. Soc.*, 1980, **102**, 2903 and references cited therein.

Received, 31st July, 1981