The upper band afforded 144 mg of VII: mp 128–130° (from ethanol); ir 3400, 2250, 1710, 1690, and 1670 cm^{-1}; nmr ($CDCl_3$) δ 2.2–3.0 (m, 4), 3.19 (s, 2), 3.32 (s, 2), 6.7–7.3 (m, 8), and the two exchangeable NH protons; mass spectrum m/e 388 (M^+ $C_{20}H_{18}{}^{35}Cl_2N_2O_2$).

Anal. Calcd for $C_{20}H_{18}Cl_2N_2O_2$: C, 61.72; H, 4.66; Cl, 18.22; N, 7.20. Found: C, 61.51; H, 4.75; Cl, 18.36; N, 7.14.

From the lower band there was obtained 74 mg of VI: mp 121° (from ethanol); ir 3475, 3370, 2250, 1710, 1660, and 1605 cm^{-1}; mass spectrum m/e 264 (M^+ $C_{13}H_{13}{}^{35}ClN_2O_2$).

Anal. Calcd for $C_{13}H_{13}ClN_2O_2$: C, 58.99; H, 4.95; Cl, 13.4; N, 10.59. Found: C, 58.86; H, 4.98; Cl, 13.25; N, 10.52.

Registry No.—III, 564-00-1; IV, 35159-06-9; VI, 35159-07-0; VII, 35159-08-1; IX, 35159-09-2.

Acknowledgment.—We thank Dr. L. Shadoff for the high-resolution mass spectral measurements and Dr. F. Johnson and Mr. A. A. Carlson for the initial isolation of IX.

Synthesis and Reactivity of Adamantane-1-carbonitrile *N*-Oxide

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The functionalization of adamantane has received considerable attention in recent years and several 1-substituted and some 2-substituted derivatives have been prepared.[1] Although most of the available data pertains to the unusual properties of adamantanes in polar and free-radical reactions involving the bridged ring system,[1,2] considerable interest on the internal reactivity of functional groups linked to the adamantyl moiety has arisen.[3]

We wish to report the first preparation of an adamantylfulmide and to describe some typical reactions at the CNO function in this compound. The present work enlarges the number of adamantane derivatives and provides information on the reactions of nitrile oxides[4] in general. We are currently investigating the chemistry of nitrile oxides.[5]

Adamantane-1-carbonitrile *N*-oxide (**1**) was prepared in good yield from adamantane-1-carboxaldehyde oxime (**1a**) and *N*-bromosuccinimide as outlined by Grundmann[6] for other nitrile oxides. Nitrile oxide **1** was practically unchanged after several days at room temperature, but in carbon tetrachloride solution at 50° it readily dimerized to di[adamantyl-(1)]furazan *N*-oxide (**2**) (*ca.* 80% yield). The structure of **2** is supported by the mass spectrum. Compound **2** gives the parent peak at m/e 354 (M^+) and on electron impact behaves in the characteristic manner[7] of furazan *N*-oxides, giving $(M - O)^+$, $(M - N_2O_2)^+$, $(AdCN)^+$, and $(AdCNO)^+$ as the major fragments ions. The peaks at m/e 338, corresponding to the loss of one oxygen, and at m/e 294, from the loss of N_2O_2, and the absence of absorption corresponding to $(AdCO)^+$ at m/e 163 are compatible only with the furoxan structure **2** and rule out other possible five- or six-membered isomers.

When heated at reflux in carbon tetrachloride, nitrile oxide **1** yielded, in addition to dimer **2**, the isomer 1-adamantylisocyanate (**3**) in variable amounts depending on the time of heating. Typically, after 8 hr of reflux **3** was only present in small amounts with respect to furoxan **2**, but, when heating was prolonged to 10 days, the ratio **2**:**3** was *ca.* 1:2. In the latter experiment, the infrared spectrum of the reaction mixture, taken at intervals, showed that, after the complete disappearance of the 2285- (CN) and 1335-cm^{-1} (NO) bands[8] of **1**, the absorption of the NCO group[9] at 2255 cm^{-1} gradually increased. These facts suggest that on prolonged heating the isocyanate **3** was the major reaction product because a part of it could possibly form from the furazan *N*-oxide **2** *via* a retrocycloaddition to **1** (Scheme I). The formation of isocyanate **3** and trapping of the transient nitrile oxide **1** by cycloaddition with styrene from a sample of **2** heated at reflux in carbon tetrachloride indicate that this possibility is real. Therefore, in spite of the initial formation of **2**, the isomerization of **1** to **3** can still occur directly *via* the mechanism outlined by Grundmann and Kochs.[10] However, it must be noted that an alternative route from the furazan *N*-oxide **2**, in equilibrium with the nitrile oxide **1**, is also conceivable.[11]

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[1] R. C. Fort, Jr., and P. v. R. Schleyer, *Chem. Rev.*, **64**, 277 (1964); *Advan. Alicycl. Chem.*, **1**, 283 (1966).

[2] Recent references include Z. Majerski, P. v. R. Schleyer, and A. P. Wolf, *J. Amer. Chem. Soc.*, **92**, 5731 (1970); I. Tabushi, Z. Yoshida, and N. Takahashi, *ibid.*, **92**, 6670 (1970); C. Rüchardt, *Angew. Chem., Int. Ed. Engl.*, **9**, 830 (1970); J. K. Chakrabarti and A. Todd, *Chem. Commun.*, 556 (1971); M. O. Luke and J. G.-Atkinson, *Tetrahedron Lett.*, 117 (1971).

[3] J. Strating, A. H. Alberts, and H. Wynberg, *Chem. Commun.*, 818 (1970); J. Scharp, H. Wynberg, and J. Strating, *Recl. Trav. Chim. Pays-Bas*, **89**, 18, 23 (1970); W. V. Curran and R. B. Angier, *J. Org. Chem.*, **34**, 3668 (1969); A. Kreutzberger and H.-H. Schroders, *Tetrahedron Lett.*, 4921 (1970); H. Stetter and E. Smulders, *Chem. Ber.*, **104**, 917 (1971).

[4] Reviews: (a) C. Grundmann, *Synthesis*, 344 (1970); (b) A. Quilico, *Chim. Ind.* (*Milan*), **53**, 157 (1971); (c) C. Grundmann and P. Grünanger, "The Nitrile Oxides," Springer-Verlag, Berlin, Heidelberg, New York, 1971.

[5] G. Barbaro, A. Battaglia, and A. Dondoni, *J. Chem. Soc. B*, 588 (1970); A. Battaglia, A. Dondoni, and A. Mangini, *ibid.*, 554 (1971); A. Battaglia, A. Dondoni, G. Maccagnani, and G. Mazzanti, *ibid.*, 2096 (1971).

[6] C. Grundmann and R. Richter, *J. Org. Chem.*, **33**, 476 (1968).

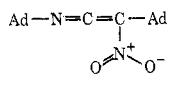
[7] (a) C. Grundmann, H.-D. Frommeld, K. Flory, and S. K. Datta, *ibid.*, **33**, 1464 (1968); (b) A. J. Boulton, P. Hadjimihalakis, A. R. Katritzky, and A. Majid Hamid, *J. Chem. Soc. C*, 1901 (1969).

[8] A. Battaglia, A. Dondoni, G. Galloni, and S. Ghersetti, *Spectrosc. Lett.*, **3**, 207 (1970).

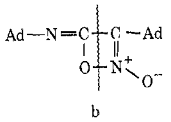
[9] W. H. T. Davidson, *J. Chem. Soc.*, 3712 (1953). For the reliability of the 2290- and 2255-cm^{-1} bands to distinguish nitrile oxides from isocyanates, see also R. H. Wiley and B. J. Wakefield, *J. Org. Chem.*, **25**, 546 (1960).

[10] C. Grundmann and P. Kochs, *Angew. Chem., Int. Ed. Engl.*, **9**, 635 (1970).

[11] A referee has drawn our attention to a variant of Scheme I, *i.e.*, $\mathbf{1} \leftrightarrows \mathbf{2} \rightarrow \mathbf{3} + \mathbf{1}$. The ring opening of **2** can take place *via* initial migration of the adamantyl group onto the imino nitrogen to give the open-chain intermediate a which in turn forms the four-membered ring compound b by



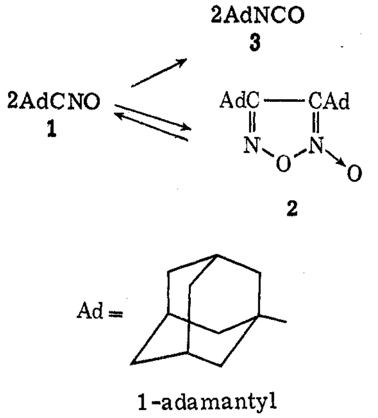
a



b

an electrocyclic rearrangement of the butadiene–cyclobutene type. The latter product leads to **3** and **1** by ring opening as indicated. This route, which is also compatible with the data reported in ref 10, needs to be considered in a more extensive study.

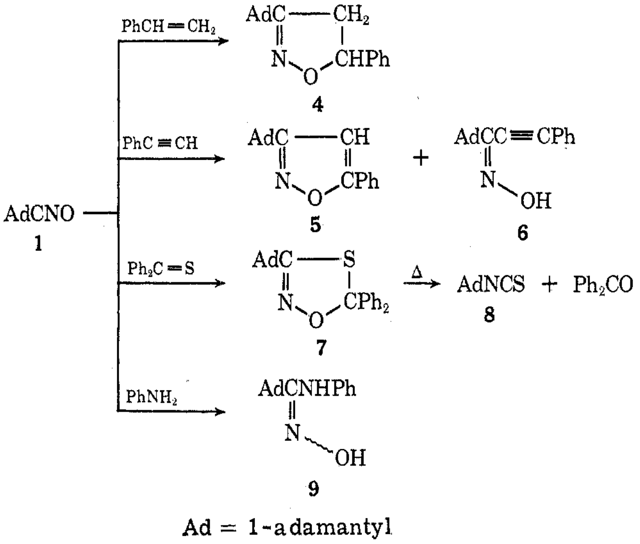
Scheme I



These results indicate that, in the case of **1**, the formation of furazan *N*-oxide **2** and isocyanate **3** is governed by a kinetic and thermodynamic control, respectively. Of the several sterically hindered nitrile oxides which have been reported[10,12] to rearrange to the corresponding isocyanates, only in the case of mesitonitrile *N*-oxide have both dimerization and isomerization products been observed under controlled temperature conditions.[7a] In the other cases, on heating at reflux in an inert high-boiling solvent such as toluene or xylene, the transient formation of furazan *N*-oxide was not noticed or was neglected. With respect to the results reported here and in view of the large steric requirements of the adamantyl group, a reconsideration of the behavior of nitrile oxides with a bulky group around to the CNO function would be of interest.

Kinetic data[5,13] and a number of syntheses[4,12] with sterically hindered nitrile oxides have shown that the steric hindrance around the CNO function decreases the tendency of nitrile oxides to dimerize, but reduces the rate of 1,3-addition reactions to only a small extent. Thus, adamantane-1-carbonitrile *N*-oxide (**1**) was quite reactive toward typical reagents of the CNO function, yielding a number of compounds, some of which were hitherto unknown, containing the adamantyl moiety (Scheme II). 1,3-Dipolar cycloadditions of **1** with styrene, phenylacetylene, and thiobenzophenone occurred readily at room temperature to yield the corresponding five-membered heterocycles **4**, **5**, and **7**, while the 1,3 additions of aniline and phenylacetylene gave the oximes **9** and **6**, the latter being the by-product of the isoxazole **5**. According to previous reports,[14] the α-acetylenic oxime **6** is assigned the configuration in which the hydroxyl group is anti with respect to the adamantyl function, whereas for amidoxime **9** the assignment is currently being studied. The oxime **6** was stable under the reaction conditions of **1** with phenylacetylene,[15] thus excluding the formation of **5** *via* a partial rearrangement of **6**.

Scheme II



Experimental Section

All melting points are uncorrected. Reagents and solvents, commercially available unless otherwise stated, were purified by standard procedures. All tlc was done using silica gel plates, benzene as eluent, and an iodine chamber to develop the spots. Nmr spectra were recorded on a JNM-PS-100 instrument with TMS as internal reference (δ 0 ppm); ir spectra were determined with a Perkin-Elmer 257 grating spectrophotometer.

Adamantane-1-carboxaldehyde Oxime (**1a**).—A mixture of adamantane-1-carboxaldehyde[16] (from reduction of 9.0 g of adamantane-1-carboxylic acid chloride), hydroxylamine hydrochloride (10.5 g), and sodium hydroxide (7.2 g) in 80 ml of ethanol–water (1:2, v/v) was heated on a steam bath for 2 hr. Dilution of the reaction mixture with 100 ml of water produced a solid, which was collected and recrystallized from ethanol–water (1:1, v/v) to yield 4.8 g of **1a**: mp 144–145°; ir (CCl_4) 3600 and 3300 cm^{-1} (OH); nmr (CCl_4) δ 8.6 (s, 1, OH, disappeared on treatment with D_2O), 6.9 (s, 1, $CH{=}N$), 2.1–1.6 (m, 15, adamantyl protons).

Anal. Calcd for $C_{11}H_{17}NO$: C, 73.70; H, 9.56; N, 7.81. Found: C, 73.85; H, 9.42; N, 7.63.

This oxime appears to have a syn configuration on the basis of further nmr data[17] in Me_2SO, δ 9.93 (OH), 6.87 ($CH{=}N$).

Adamantane-1-carbonitrile *N*-Oxide (**1**).—To a stirred solution of 0.54 g (3 mmol) of oxime **1a** and 0.53 g (3 mmol) of *N*-bromosuccinimide in 15 ml of DMF was added dropwise a solution of 0.30 g (3 mmol) of triethylamine in 5 ml of DMF at *ca.* 10°. After the mixture had been stirred for 30 min at room temperature, dilution with 50 ml of ice water gave a white solid which was collected, washed with water, and recrystallized from ethanol to yield 0.32 g (66%) of **1**: mp 160–161°; ir (CCl_4–CS_2) 2285 ($C\equiv N$), 1335 cm^{-1} (NO); nmr (CCl_4) δ 2.1–1.4 (m, adamantyl protons).

Anal. Calcd for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.86; H, 8.38; N, 7.91.

The melting point of **1** was unchanged after 6 days at room temperature.

Thermal Dimerization and Isomerization of 1.—A solution of 1.35 g of nitrile oxide **1** in 120 ml of CCl_4 was heated at 50°. The ir spectrum of the solution showed that the 2285-cm^{-1} band of nitrile oxide had disappeared after 5 days. Removal of the solvent *in vacuo* gave a residue which was recrystallized twice from isopropyl alcohol to yield 1.06 g (78%) of di[adamantyl-

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[12] C. Grundmann and J. M. Dean, *J. Org. Chem.*, **30**, 2809 (1965); C. Grundmann and S. K. Datta, *ibid.*, **34**, 2016 (1969); S. Ranganathan, B. B. Singh, and C. S. Panda, *Tetrahedron Lett.*, 1225 (1970).

[13] P. Beltrame and C. Vintani, *J. Chem. Soc. B*, 873 (1970).

[14] S. Morocchi, A. Ricca, A. Zanarotti, G. Bianchi, R. Gandolfi, and P. Grünanger, *Tetrahedron Lett.*, 3329 (1969); Z. Hamlet, M. Rampersad, and D. J. Shearing, *ibid.*, 2101 (1970); Z. Hamlet and M. Rampersad, *Chem. Commun.*, 1230 (1970).

[15] No appreciable isomerization of oxime **6** (0.004 *M* in CCl_4) to isoxazole **5** was noticed after 12 hr at 25°, whereas the reaction of **1** (0.01 *M*) with a tenfold excess of phenylacetylene has $t_{0.5}$ of 2.5 hr under the same conditions.

[16] The aldehyde was prepared as described [D. E. Applequist and L. Kaplan, *J. Amer. Chem. Soc.*, **87**, 2194 (1965)] from adamantane-1-carboxylic acid chloride and tri-*tert*-butoxyaluminum hydride, but was not purified because of its tendency to polymerize on handling [F. N. Stepanov and N. L. Dovgan, *Zh. Org. Khim.*, **4**, 277 (1968)]. The aldehyde was characterized as the 2,4-dinitrophenylhydrazone, mp 225–226° (from acetonitrile) [lit. mp 225°: H. Stetter and E. Rauscher, *Chem. Ber.*, **93**, 1161 (1960)].

[17] G. G. Kleinspehn, J. A. Jung, and S. A. Studniarz, *J. Org. Chem.*, **32**, 460 (1967).

(1)]furazan *N*-oxide (**2**): mp 179–180°; ir (CCl_4–C_2Cl_4) 1550 cm^{-1}; mass spectrum[18] *m/e* 354 (M^+), 338 $(M - 16)^+$, 294 $(M - 60)^+$, 177 $(AdCNO)^+$, 161 $(AdCN)^+$, 135 (Ad^+).

Anal. Calcd for $C_{22}H_{30}N_2O_2$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.75; H, 8.43; N, 8.05.

An identical reaction mixture of **1** in CCl_4 was heated at reflux for 8 hr. The ir spectrum of the solution showed an absorption at 2255 cm^{-1}. The solvent was removed at reduced pressure and the residue was subjected to vacuum sublimation in a cold finger apparatus. At 0.2 mm and 85–95° bath temperature, 0.12 g (9%) of 1-adamantyl isocyanate (**3**) collected on the condenser, mp 139–141°, ir (CCl_4) 2255 cm^{-1}. The specimen was identical with an authentic sample[19] by ir and mixture melting point. The residue of the sublimation, which contained a small quantity of **3**, was recrystallized from isopropyl alcohol, yielding 0.86 g (64%) of furazan *N*-oxide **2**.

In another experiment the same amounts of **1** and solvent were heated for 10 days. The reaction mixture, worked up as detailed above, gave 0.80 g (59%) of isocyanate **3** and 0.42 g (31%) of furoxan **2**.

Retro Cycloaddition of Di[adamantyl-(1)]furazan *N*-Oxide (2).—A solution of 0.50 g (1.4 mmol) of **2** in 50 ml of dry CCl_4 was heated at reflux and the transformations were monitored by ir analysis in the 2300–2200-cm^{-1} region. After 15 hr the ir spectrum showed a broad absorption with the maximum at 2280 cm^{-1}, but after 40 hr two overlapping bands at 2285 and 2255 cm^{-1} could be clearly distinguished. On heating for a total of 10 days, the ir spectrum showed a gradual increase of the isocyanate band at 2255 cm^{-1}. Removal of the solvent *in vacuo* and sublimation of the residue at 0.2 mm and 85–95° bath temperature gave 0.21 g (42%) of 1-adamantyl isocyanate (**3**), mp 138–140°, identical with an authentic sample.[19] The residue of the sublimation, 0.26 g (52%), was the unaltered furazan *N*-oxide **2**.

The same amount of furazan *N*-oxide **2** and 1.46 g (14 mmol) of styrene were heated to reflux in 50 ml of CCl_4 for 10 days. Removal of the solvent *in vacuo* gave an oil from which, on addition of petroleum ether (bp 30–60°) and chilling, fractionally separated 71 mg of unchanged **2**, mp 175–179°, and 0.28 g of a product, mp 66–67°, which upon recrystallization from ethanol–water melted at 72–73° and was identical by mixture melting point and ir with an authentic sample of 3-[adamantyl-(1)]-5-phenyl-4,5-dihydro-1,2-oxazole (**4**). The petroleum ether filtrate, after distillation of the solvent, gave an oil which chromatographed through a column of silica, benzene as eluent, yielded a fraction containing the isocyanate **3** with styrene as an impurity, and two fractions containing 65 mg of **2** and 0.17 g of **4**.

Addition Reactions to Nitrile *N*-Oxide 1.—To a stirred solution of **1** (0.62 g, 3.5 mmol) in 25 ml of dry CCl_4 was added dropwise 20–30 mmol of reactant in an equal volume of carbon tetrachloride at 25°. Only thiobenzophenone was used in a quantity equimolar to **1**. After overnight additional stirring, the solvent and the excess of reactant were removed *in vacuo* and the residue was worked up as detailed in each case. The following compounds were obtained.

3-[Adamantyl-(1)]-5-phenyl-4,5-dihydro-1,2-oxazole (4).—The residue was an oil which on treatment with petroleum ether and chilling yielded 0.87 g (89%) of **4**, mp 68–72°. After recrystallization from ethanol–water, **4** had mp 72.5–73.5°; nmr[20] (CCl_4) δ 7.0–6.8 (m, 5, aromatic protons), 5.15 (2 d, 1, CHPh), 3.15 and 2.65 (2 q, 2, CH_2 isoxazoline ring), 2.1–1.6 (m, 15, adamantyl protons).

Anal. Calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.98. Found: C, 81.50; H, 8.30; N, 5.10.

1-[Adamantyl-(1)]-5-phenyl-1,2-oxazole (5) and 1-[Adamantyl-(1)]-3-phenylprop-2-ynone Oxime (6).—The residue was an oil which on tlc showed the presence of two main components at R_f 0.47 and 0.20. The residue was chromatographed on a silica gel column. Elution with benzene, after initial fractions containing unchanged phenylacetylene, gave 0.67 g (69%) of isoxazole **5**: mp 102–103° after recrystallization from ethanol–water; ir (CCl_4–C_2Cl_4) 1630 cm^{-1}; nmr[21] (CCl_4–$CDCl_3$) δ 7.5–6.9 (m, 5, aromatic protons), 6.0 (s, 1, CH isoxazole ring), 2.1–1.6 (m, 15, adamantyl protons). *Anal.* Calcd for $C_{19}H_{21}NO$: C, 81.68; H, 7.58; N, 5.01. Found: C, 81.95; H, 7.47; N, 5.21.

Subsequent elution with benzene–ether (8:2, v/v) gave 0.20 g (21%) of oxime **6**: mp 134–135° (benzene–petroleum ether); ir (CCl_4) 3580, 3250 (OH), 2220 cm^{-1} ($C{\equiv}C$); nmr (CCl_4–$CDCl_3$) δ 8.9 (s, 1, OH, disappeared on treatment with D_2O), 7.2–6.7 (m, 5, aromatic protons), 2.1–1.6 (m, 15, adamantyl protons). *Anal.* Calcd for $C_{19}H_{21}NO$: C, 81.68; H, 7.58; N, 5.01. Found: C, 81.48; H, 7.46; N, 5.20.

The α-acetylenic oxime **6** was satisfactorily stable at room temperature.[16] However, when the reaction solution of **1** with phenylacetylene, obtained as described, was kept at 50° for 5 days, the oxime **6** was not longer detectable on tlc. After evaporation of the solvent, the residue, dissolved in ethanol–water and kept at −10° overnight, gave 0.92 g of isoxazole **5**.

3-[Adamantyl-(1)]-5,5-diphenyl-1,4,2-oxathiazole (7).—After careful[22] evaporation of the solvent *in vacuo*, the residue was recrystallized from methanol to yield 0.97 g (75%) of **7**, mp 109–110°, ir (CCl_4–C_2Cl_4) 1660 cm^{-1} ($C{=}N$).

Anal. Calcd for $C_{24}H_{25}NOS$: C, 76.76; H, 6.71; N, 3.73; S, 8.54. Found: C, 76.68; H, 6.80; N, 3.94; S, 8.76.

The structure of **7** is supported by its thermal decomposition products (see below).

***N*-Phenyladamantane-1-carboxamide Oxime (9).**—The white solid precipitated from the reaction solution was collected and washed with two 5-ml portions of CCl_4. Recrystallization from ethanol gave 0.82 g (86%) of **9**: mp 216–217°; ir (Nujol) 3380 (NH), 3250 (br), 1660 cm^{-1} ($C{=}N$); nmr (DMSO-d_6) δ 9.75 (s, 1, OH, disappeared on treatment with D_2O), 7.20–6.50 (m, 6, NH and aromatic protons), 2.1–1.6 (m, 15, adamantyl protons).

Anal. Calcd for $C_{17}H_{22}N_2O$: C, 75.51; H, 8.20; N, 10.36. Found: C, 75.81; H, 8.39; N, 10.31.

Thermal Decomposition of 1,4,2-Oxathiazole (7).—The oxathiazole (0.6 g, 1.6 mmol) was heated at 185° for 1 hr as described.[22] Chromatography of the reaction mixture on a silica gel column using benzene as eluent afforded 0.28 g (96%) of benzophenone, mp 48–50°, and 0.24 g (78%) of 1-adamantyl isothiocyanate[19] (**8**), mp 166–167°. These products were identical with authentic samples by infrared spectra and mixture melting points.

Registry No.—**1**, 35105-43-2; **1a**, 35099-47-9; **2**, 35147-20-7; **3**, 4411-25-0; **4**, 35105-45-4; **5**, 35105-46-5; **6**, 35147-21-8; **7**, 35105-47-6; **9**, 35105-48-7.

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[18] Determined with a low-resolution gas chromatograph–mass spectrometer, Perkin-Elmer 270, at 70 eV, chamber temperature 200°, through the courtesy of Dr. A. Giumanini of the University of Bologna.

[19] H. Stetter and C. Wulff, *Chem. Ber.*, **95**, 3202 (1962).

[20] A. Dondoni and F. Taddei, *Boll. Sci. Fac. Chim. Ind., Bologna*, **25**, 145 (1967).

[21] A. Battaglia, A. Dondoni, and F. Taddei, *J. Heterocycl. Chem.*, **7**, 721 (1970).

[22] A. Battaglia, A. Dondoni, and G. Mazzanti, *Synthesis*, 378 (1971).