Chemistry of 2-Substituted Adamantanes. V.[1] Photolysis of 2-Adamantyl Azidoformate

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Received March 6, 1973[2]

In an attempt to prepare adamanto[1,2-*d*]oxazolidin-2-one (**2**), 2-adamantyl azidoformate was subjected to photolysis in cyclohexane. The main product **8** (yield 41%) is formed by intermolecular insertion of the nitrene in the solvent. The only other pure compound isolated (yield 15%) is a product of intramolecular insertion. The i.r. spectrum of the latter supports the presence of a five-membered cyclic carbamate. The fact that intermolecular insertion is the main reaction is unexpected in view of the results reported by others.

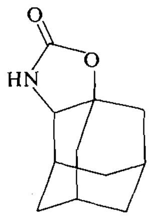
Afin de préparer l'adamantano [1,2-*d*]oxazolidinone-2 (**2**) on a soumis l'azydoformate d'adamantyle-2 en solution dans le cyclohexane à une photolyse. Le produit principal de la réaction, **8**, (rendement 41%) est formé par une insertion intermoléculaire du nitrène dans le solvant. Le seul autre produit pur isolé (rendement 15%) est un produit d'insertion intramoléculaire. Le spectre infrarouge de ce dernier indiquerait la présence d'un carbamate dans un cycle à cinq membres. Le fait que l'insertion intermoléculaire est la réaction principale est inattendue considérant les résultats rapportés par d'autres autours. [Traduit par le journal]

Can. J. Chem., 52, 1062 (1974)

Insertion reactions of nitrene intermediates, especially of carbonylnitrenes, can lead to synthetically useful processes and the topic has been thoroughly reviewed (1). The photolytic decomposition of 1-adamantyl azidoformate in cyclohexane (2,3) gives a 45% yield of adamanto-[2,1-*d*]oxazolidin-2-one (**1**). Intermolecular insertion of the intermediate carbalkoxynitrene into the solvent is a minor process giving only 4% of 1-adamantyl *N*-cyclohexylcarbamate and the three methylene groups adjacent to the substituted bridgehead in the azidoformate compete effectively with those in cyclohexane for the nitrene.

We were interested in the isomeric adamanto-[1,2-*d*]oxazolidin-2-one (**2**) and decided to attempt its synthesis in a way completely analogous to that used for **1** (2,3). Solely on statistical grounds the chances for the formation of **2** are one-third those for the cyclization leading to **1** (assuming that **3** is not formed).

Cyclization of the intermediate nitrene to the tetrahydro-1,3-oxazin-2-one derivative **3** is also a possibility, as several examples of the formation of this ring system by acylnitrene insertion have been reported (4). The considerable preference of ethoxycarbonylnitrene for insertion into the bridgehead C—H bond of adamantane has been demonstrated clearly[3] and it was hoped that this would be the dominant factor and would result in a good yield of **2**.



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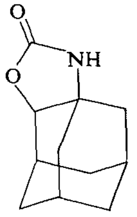

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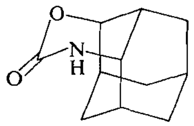

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As will be shown below, the photolysis of 2-adamantyl azidoformate was highly disappointing from the standpoint of satisfactorily preparing **2**.

Results

The compound 2-adamantyl *p*-nitrophenyl carbonate (**4**) and the carbazate **5** were prepared

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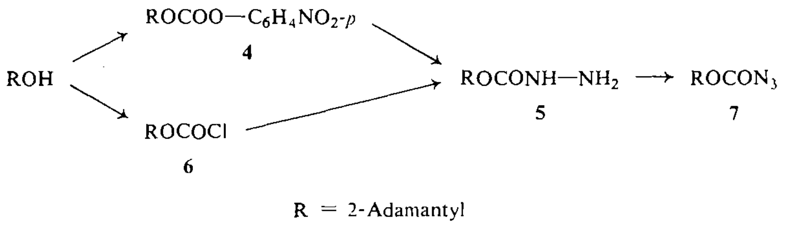
[1] For Part IV see ref. 15.

[2] Revision received November 12, 1973.

[3] The relative reactivity of the tertiary C—H bond in adamantane was found to be more than six times that of a secondary C—H bond in its reaction with ethoxycarbonylnitrene (5).



SCHEME 1

(yields, respectively, 66 and 89%) following the procedures reported for the corresponding 1-adamantyl isomers (3) but with some experimental modifications. The carbazate **5** could also be prepared (yield 82%) from 2-adamantyl chloroformate (**6**). The crude chloroformate **6** was obtained from 2-adamantanol and phosgene[4] but the yields were variable and low (28–42%).

The carbazate **5** was treated with nitrous acid and gave 2-adamantyl azidoformate (**7**), as shown in Scheme 1, with a yield of 78%.[5] The photolysis of **7** was carried out in a quartz tube at 253.7 nm and was found to be complete after 90–100 min.

Two pure products could be isolated. The first and most easily obtained product $C_{11}H_{15}NO_2$, m.p. 135–136°, has like its isomer **1** a rather low solubility in cyclohexane (3) and is obtained by filtration with a maximum yield of 15%. Although its i.r. spectrum seems to indicate the presence of a five-membered cyclic carbamate we cannot at this stage assign structure **2** to it with certainty (see Discussion).

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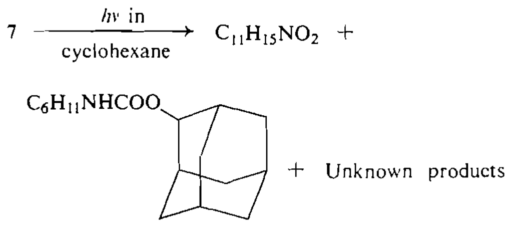

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Insertion of the nitrene intermediate into the solvent appeared to be the main reaction, giving a 41% yield of 2-adamantyl *N*-cyclohexylcarbamate (**8**), isolated after chromatography on alumina (eluent benzene). Continued elution with more polar solvents gave a variety of small and mostly very viscous residues, the i.r. spectra of which indicated the presence of amide-like compounds as well as some 2-adamantanol. These were not further investigated.

Discussion

In the absence of skeletal rearrangements[6] intramolecular insertion of the nitrene intermediate from **7** will give rise to a 2-oxazolidinone ring, as in **2**, or to a tetrahydro-1,3-oxazin-2-one ring, as in **3**.[7]

A photolysis product $C_{11}H_{15}NO_2$ resulting from intramolecular nitrene insertion and isolated with a yield of 15%, shows in its i.r. spectrum a split carbonyl absorption band with maxima at 1715 and 1755 cm^{-1} (both very strong). Compound **1** shows also two maxima, at 1724 and 1754 cm^{-1} (3), and a double band has been reported for other five- and six-membered cyclic carbamates (9,10). The carbonyl absorption in five-membered carbamate rings occurs about 40 wavenumbers higher than in six-membered rings (9–11). In the case of 2-oxazolidinone, the values 1724 (12) and 1730 cm^{-1} (10) have been reported; the six-membered cyclic carbamate tetrahydro-1,3-oxazin-2-one absorbs at 1699 cm^{-1}, while 2-oxa-4-azabicyclo[3.3.1]nonan-3-one absorbs at 1686 and 1646 cm^{-1} (10). The last compound, especially, is of interest as its bicyclic structure is part of **3**. A

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[4] Compare with the preparation of 1-adamantyl chloroformate (6,7).

[5] It is not necessary to isolate **7** for the next photolysis step (compare with ref. 3) but we often did so in order to get more accurate information about the yield of the photolysis products.

[6] The possibility of a skeletal rearrangement has been suggested by one of the referees and can of course not be ruled out, although it seems unlikely to the present author. 1-Adamantyl cations and free radicals appear to have considerable stability and skeletal isomerizations of adamantane compounds (including degenerate isomerizations) are interpreted as reactions of the 2-adamantyl carbonium ion (8).

[7] The author is not aware of any intramolecular carbalkoxynitrene insertion leading to a four-membered cyclic carbamate and considers its formation from **7** also very unlikely.

five-membered ring is indicated by the i.r. spectrum of $C_{11}H_{15}NO_2$.

Compound **3** should show two one-proton absorptions in its n.m.r. spectrum for hydrogen at C-2 and -4. The n.m.r. spectrum of the product $C_{11}H_{15}NO_2$ ($CDCl_3$) does not show these peaks but neither does it all by itself prove structure **2**. In addition to a massive multiplet (δ 1.1–2.6, 13 protons) four minor peaks occur at δ 6.22, 5.14, 4.78, and 4.11, together representing two protons. The peaks at δ 6.22 and 5.14 amount together to one proton, they can be removed by exchange with D_2O–NaOD, have the broad shape of an amide proton, and appear to have aromatic solvent-induced shifts of opposite sign in perdeuteriobenzene. These data would be compatible with structure **2** only if we were dealing with a mixture of invertomers. As the barrier to nitrogen inversion in amides is generally low,[8] this explanation would be sufficiently unusual to require confirmation which is outside the scope of the original project and at present not yet available.

Our finding that intermolecular insertion of the nitrene intermediate into the solvent cyclohexane competes so effectively with intramolecular insertion in the photolysis of 2-adamantyl azidoformate is unexpected in view of the behavior of its 1-adamantyl isomer under identical reaction conditions (3) and because of the observation (5) that, in its reaction with ethoxycarbonylnitrene, the tertiary C—H bond in adamantane is much more reactive than the secondary.

Intermolecular insertion of nitrene in cyclohexane appeared to be the main reaction in the photolysis of 1-adamantyl carbamoyl azide (14) and it is clear that the conditions for successful intramolecular nitrene insertion in adamantane derivatives are not well understood and will require further investigation.

Experimental

Photolyses were carried out in a quartz reaction tube in a Rayonet photochemical reactor equipped with eight low-pressure mercury lamps giving 84% of their emission at 253.7 nm. Melting points were determined in sealed capillary tubes and are uncorrected. The i.r. spectra were run in KBr pellets unless otherwise specified and were recorded on a Perkin-Elmer spectrophotometer, model 337, or a Unicam SP 200G instrument. Mass spectral data were obtained with a Varian-Mat CH-15 instrument at an ionization energy of 70 eV. The n.m.r. spectra were recorded on Varian A-60 and HA-100 spectrometers of the Department of Chemistry, University of Calgary and on the Varian A-60 D instrument of the National Council for Scientific Research of Zambia in the Chemistry Department of the University of Zambia. Tetramethylsilane was used as an internal standard (δ = 0 p.p.m.) in the indicated solvent. Elemental analyses were carried out by the Analytical Laboratory of the Department of Chemistry or the Analytical Service of the Department of Chemical Engineering, both of the University of Calgary.

2-Adamantyl p-Nitrophenyl Carbonate (4)

A solution of *p*-nitrophenyl chloroformate (24.0 g, 119 mmol) in dichloromethane (60 ml) was added dropwise in 1 h to a well-stirred solution of 2-adamantanol (18.0 g, 118 mmol) and quinoline (15.5 g, 120 mmol) in dichloromethane (180 ml). The reaction mixture was left standing at 25° for 3 days, extracted with water (twice, 600 ml), with 0.25 *N* HCl (twice, 600 ml), and dried (anhydrous $MgSO_4$). After evaporation of the solvent the residue (38.4 g) was redissolved in boiling dichloromethane (100 ml), treated with charcoal, and filtered. Petroleum ether (150 ml) was added to the filtrate and after cooling to 0° 2-adamantyl *p*-nitrophenyl carbonate (**4**) (24.6 g, 65.5%), m.p. 124–127°, was obtained. After repeated recrystallization the m.p. was unchanged.

Anal. Calcd. for $C_{17}H_{19}NO_5$: C, 64.35; H, 6.04; N, 4.41. Found: C, 63.99; H, 6.01; N, 4.47.

The i.r. spectrum ν_{max}: 1765 (C═O), and 1525 and 1350 cm^{-1} (NO_2), all very strong; n.m.r. δ ($CDCl_3$): 7.86 (4H, center of aromatic quartet), 4.96 (broad singlet, 1H at C-2), 1.45–2.35 (massive multiplet, 14H).

2-Adamantyl Carbazate (5)

Procedure A. 2-Adamantyl *p*-nitrophenyl carbonate (32.2 g, 101 mmol) was added to a mixture of hydrazine (20.0 g, 0.62 mol) and dry methanol (800 ml). The reaction mixture was stirred for 65 h, then heated to reflux for 3 h. After removal of the solvent (under reduced pressure), ether (900 ml) was added which dissolved part of the red oily residue. The ethereal solution was extracted with 10% NaOH (six times, 600 ml) and water (three times, 600 ml), dried (anhydrous $MgSO_4$), and after evaporation gave a residue of 2-adamantyl carbazate (18.9 g, 89%), m.p. 69–70°. Recrystallization from ether–hexane (1:2) gave an analytical sample with unchanged m.p.

Anal. Calcd. for $C_{11}H_{18}N_2O_2$: C, 62.83; H, 8.63; N, 13.32. Found: C, 63.03; H, 8.79; N, 13.00.

The i.r. spectrum ν_{max}: 1720 cm^{-1} (C═O); n.m.r. δ ($CDCl_3$): 6.16 (1H, broad singlet, —NH—), 4.87 (1H at C-2), 3.55 (2H, broad singlet, —NH_2), 1.30–2.85 (massive multiplet, 14H).

Procedure B. Following a published method for the preparation of 1-adamantyl chloroformate (6), 2-adamantanol (8.0 g, 53 mmol) was allowed to react at 0–5° with a mixture of liquid phosgene (30 g, 0.3 mol) and benzene (200 ml) in the presence of pyridine. After washing, drying, and evaporation of the solvent at 25° under reduced pressure (CAUTION: large quantities of excess phosgene escape), crude 2-adamantyl chlorofor-

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[8] Ring strain and a hetero atom bonded to nitrogen are normally required for the stabilization of the nitrogen pyramid in order to give stable invertomers (13).

mate (**6**) (7.2 g) was obtained, m.p. 40–42°. After recrystallization from petroleum ether at −20°, 4.8 g (42%), m.p. 42–44° was obtained. A small sample of **6**, repeatedly recrystallized, had a m.p. 44–45°, but no fully satisfactory elemental analysis could be obtained for this chloroformate for which the following spectral data were recorded; i.r. ν_{max}: 1775 (C═O) and 1170 cm^{-1} (broad, C—O); n.m.r. δ (CCl_4): 4.95 (singlet, 1H at C-2), 1.3–2.4 (massive multiplet, 14H).

Reaction of **6** with anhydrous hydrazine in *tert*-butyl alcohol – benzene according to the published procedure (6) for 1-adamantyl carbazate gave an 82% yield of **5**, identical with the product obtained in Procedure A.

2-Adamantyl Azidoformate (7)

2-Adamantyl carbazate (1.05 g, 5.0 mmol) was dissolved in a mixture of acetic acid (15 ml), water (50 ml), and concentrated hydrochloric acid (3.3 ml). To this solution, cooled to 0°, was added dropwise a solution of sodium nitrite (0.37 g, 5.4 mmol) in cold water (4 ml). The reaction mixture was extracted with cyclohexane (three times, 50 ml). The extract was washed with water, 5% aqueous $NaHCO_3$, water again, and dried ($MgSO_4$). Evaporation of the solvent at 20° gave a residue of 2-adamantyl azidoformate (0.86 g, 78%), m.p. 52–54°. Two recrystallizations from ethanol (at −20°) raised the m.p. to 55–56°.

Anal. Calcd. for $C_{11}H_{15}N_3O_2$: C, 59.71; H, 6.83; N, 18.99. Found: C, 59.58; H, 7.05; N, 18.68.

The i.r. spectrum ν_{max}: 2420(w), 2200(s), and 2145 (s, —N_3), 1730(vs, C═O), 1238 cm^{-1} (vs, C—O in ester); n.m.r. δ ($CDCl_3$): 5.09 (s, 1H at C-2), 1.40–2.20 (massive multiplet, 14H).

Photolysis of 2-Adamantyl Azidoformate (7) in Cyclohexane

A solution of 2-adamantyl azidoformate (3.51 g, 15.9 mmol) in cyclohexane was subjected to photolysis for 100 min, when it was found that no azidoformate was present any more. Most of the solvent was evaporated under reduced pressure (rotary evaporator) and an oily semisolid residue (4.6 g) was obtained. When some cyclohexane (15 ml) was added to this material not all redissolved at 20° and after filtration 473 mg of product with m.p. 133–134.5° was obtained. Recrystallization from ethyl acetate gave an analytical sample (m.p. 135–136°) of $C_{11}H_{15}NO_2$.

Anal. Calcd. for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.30; H, 8.07; N, 7.27.

The i.r. spectrum ν_{max}: 3400(m), 3320(w), 3255(m) with weak shoulder at 3130 (NH, free and bonded), 1755 and 1715 (vs, C═O), and the following major peaks below 1700 cm^{-1}: 1625(m), 1465(m), 1412(s), 1375(s), 1340(s), 1248(m), 1213(m), 1142(s), 1100(m), 1060(s), 1030(m), 980(m), and 948(m) cm^{-1}. Mass spectrum *m*/*e* 193 (M^+). For the n.m.r. spectrum (10% solution in $CDCl_3$) see text.

The concentrated filtered solution from which the product $C_{11}H_{15}NO_2$ had been obtained was subjected to chromatography on an alumina column. Elution with benzene yielded 2-adamantyl *N*-cyclohexylcarbamate (**8**) (1.81 g, 41%), m.p. 119–120.5°. After crystallization from 95% aqueous methanol m.p. 121–122°.

Anal. Calcd. for $C_{17}H_{27}NO_2$: C, 73.61; H, 9.81; N, 5.05. Found: C, 73.75; H, 9.49; N, 5.18.

The i.r. spectrum ν_{max}: 3310(s) and 3060(w, NH), 1695(vs, C═O), 1545(s, "amide II"); n.m.r. δ ($CDCl_3$): 4.80(s, 1H at C-2 of adamantane), 4.54(s, broad, 1H, NH, exchangeable), 3.48(s, broad, 1H, adjacent to NH), 1.0–2.4(massive multiplet, 24H).

The author thanks the Central Research Fund of the University of Zambia for financial support. During the early stages of this investigation at the University of Calgary he received a grant from the National Research Council of Canada which enabled him to employ Mr. B. Jennings (Summer Research Assistant, 1970), whose skillful and enthusiastic assistance he is pleased to acknowledge.

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