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ORGANOBORON COMPOUNDS

CDVI *. CONVERSION OF 1-BORAADAMANTANE TO 1-AZAADAMANTANE

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Summary

The reaction between 1-boraadamantane and ethyldichloramine results in the formation of 3-ethyl-3-azabicyclo[3.3.1]nonane, which is converted to 1-ethyl-1-azoniumadamantane chloride by reaction with $SOCl_2$. Hofmann degradation of the quaternary salt leads to 1-azaadamantane.

Introduction

The boron atom in 1-boraadamantane can be replaced by carbon through reaction with carbon monoxide [1,2] or potassium cyanide [3] to give an adamantane compound. The synthesis of derivatives of adamantane has been achieved starting from 1-boraadamantane derivatives [1,2].

It seemed very interesting to attempt the replacement of the boron atom in 1-boraadamantane by nitrogen, thus obtaining 1-azaadamantane. This problem has been solved through the reaction of 1-boraadamantane with alkyldichloramines, giving rise to 3-alkyl-7-hydroxymethyl-3-azabicyclo[3.3.1]nonanes [4], which are capable, after substitution of the hydroxy group by halogen, of undergoing cyclization with the formation of an ammonium structure.

It seemed expedient, from the preparative viewpoint, to use 3-ethyl-7-hydroxymethyl-3-azabicyclo[3.3.1]nonane (II) as the starting compound because the presence of the ethyl group (as compared with propyl or butyl groups) at the nitrogen atom should facilitate Hofmann degradation of the "onium" salt on treatment with a base.

* For part CDV see ref. 18.

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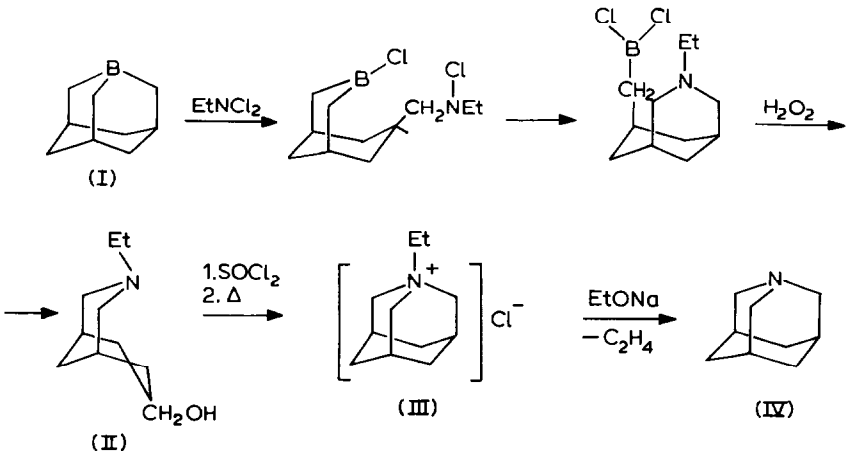
Results and discussion

Compound II was prepared by the action of ethyldichloramine on 1-boraadamantane at −40 to −70°C, followed by oxidation of the boron-containing reaction product with hydrogen peroxide in an alkaline medium. The product yield varied from 37 to 60%, with the best yield being obtained with smaller amounts of starting reagents. Compound II is a colourless, viscous liquid whose structure was confirmed by elemental analysis, and by IR and ^{1}H NMR spectroscopy. The ^{1}H NMR spectrum of compound II contains sharp signals for the following proton groups: a triplet at 1.00 ppm and a quadruplet at 2.31 ppm, with the same constant $J = 7.5$ Hz (CH_3CH_2N group); a doublet at 2.73 ppm (ring CH_2 protons) ($J = 10$ Hz); a doublet at 3.43 ppm (CH_2OH protons) ($J = 4.5$ Hz) and a singlet at 5.07 ppm (OH).

Compound II has an *endo*-hydroxymethyl group in the 7 position, and so it can be assigned a chair-boat conformation on the basis of previously cited data [5].

Both the synthesis of II and the further stages of its conversion to 1-azaadamantane (IV) are represented in Scheme 1.



SCHEME 1

Substitution of the OH group in II by chlorine takes place upon treatment of a benzene solution of II with thionyl chloride; a large temperature increase is observed, and a heavy oil-like product is formed, which is apparently 3-ethyl-7-chloromethyl-3-azabicyclo[3.3.1]nonane. When this substance is heated, quaternization of the amino group takes place with the formation of crystalline *N*-ethylazoniumadamantane chloride (III). If the reagents are mixed fast enough, the reaction occurs so energetically that no additional heating is needed for the formation of the quaternary salt, crystals of which precipitate immediately. The quaternary salt thus obtained may be either isolated and dried or used in a following stage without being isolated.

In the ^{1}H NMR spectrum of III, signals from protons on the C atoms neighbouring the N^+ centre show a considerable downfield shift (3.56 ppm), as compared with the signals of the analogous protons in 3-ethyl-7-hydroxymethyl-3-azabicyclo[3.3.1]-nonane (II) (2.73 ppm) and in azaadamantane (3.06 ppm), as a result of the presence of the positive charge on the nitrogen atom. Besides this downfield shift of signals

from N^+CH_2 ring protons, the spectrum of III also presents other evidence for the "onium structure", particularly the splitting of the methyl group signal. The methyl group in compound II produces the upfield triplet (1.00 ppm), which results from coupling of the protons of this group with the two methylene protons (J 7.5 Hz). The quadrupole moment of the nitrogen nucleus, conditioned by a non-spherical distribution of the nuclear charge, prevents observation of the coupling of the methyl group protons with the nitrogen nucleus. In the presence of the charge on nitrogen (compound III), the effect of the quadrupole interaction vanishes, so that one may observe resonance interaction of the CH_3 group protons, not only with a CH_2 group, but also with the nitrogen nucleus, whose spin is equal to 1; as a result of this, each component of the triplet is split additionally into three signals. Thus, the observed methyl group signal (1.37 ppm) in the spectrum of III is a triplet of triplets, with a vicinal constant, J 7.5 Hz, and a long range constant, J 2 Hz (Fig. 1). In addition, the spectrum of III contains signals for the protons of the CH_2 group of the ethyl radical centered at 3.25 ppm (J 7.5 Hz), signals of the methyne protons at 2.29 ppm, and also for the CH_2 protons of the cyclohexane ring (1.97 ppm). (In Fig. 1, the signal is slightly distorted due to superposition of the CH_3 protons of deuteromethanol.)

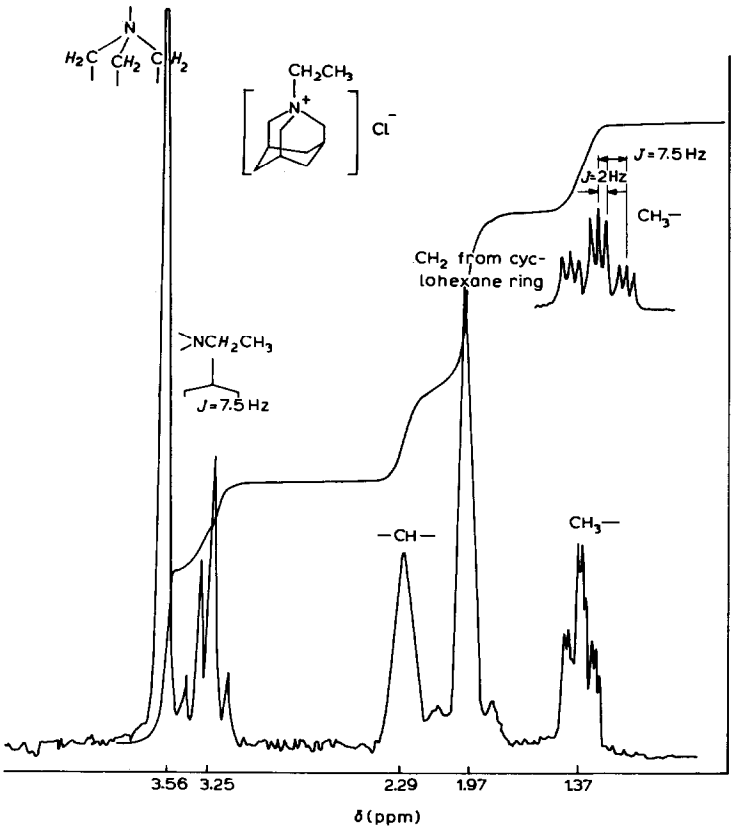


Fig. 1. ^1H NMR spectrum of 1-ethyl-1-azoniumadamantane chloride (III) in CD_3OD.

The 1-ethyl-1-azoniumadamantane salt (III) was converted to 1-azaadamantane (IV) by Hofmann degradation. For this purpose, an alcoholic solution of III was treated with an excess of sodium ethoxide, with subsequent concentration and evaporation to dryness, followed by pyrolysis. The decomposition of III under the action of sodium ethoxide proceeded at 80–100°C with the evolution of ethylene. This mode of decomposition, however, gives IV in a yield of only 28%. More complete decomposition of III takes place when the quaternary salt is heated in vacuum: 40–50% of IV is obtained by sublimation at 80°C (1.5 mmHg) for 1–2 h. Further heating at higher temperatures (140–170°C) results in an increase in the yield to 65%.

The structure of IV was confirmed by elemental analysis, m.p. (262–265; lit.: 265–267 [6], 265–269°C [7]), and by its IR, ^1H, and ^{13}C NMR spectra. The NMR spectra contain three signals, corresponding to three types of hydrogen and carbon atoms, respectively. The ^1H NMR spectrum is identical with that described in [6], whereas the ^{13}C NMR spectrum does not show complete accord with the carbon atom chemical shift values cited in [8]. The chemical shifts, observed here for $CDCl_3$ solutions (with an internal standard), were 58.37 (C(1)), 26.91 (C(2)) and 36.17 ppm (C(3)), while those in benzene solution were 59.44, 28.07 and 37.20 ppm, respectively. The literature values are: 59.7 (C(1)), 33.7 (C(2)) and 37.2 (C(3)) (with an external standard [8]).

1-Azaadamantane has not been obtained so easily before. It has been prepared so far mainly by two routes: (1) the cyclization of *cis*-symmetrically trisubstituted cyclohexane, and (2) the cyclization of 3-azabicyclo[3.3.1]nonane derivatives. The first route usually involves the catalytic reduction of ethyl trimesinoate (obtained by oxidation of mesitylene) to ethyl cyclohexanetricarboxylate. This reacts with $LiAlH_4$ to form 1,3,5-tris(hydroxymethyl)cyclohexane, which is converted, by the action of HBr, into 1,3,5-tris(bromomethyl)cyclohexane. Heating this last compound with NH_3 produces 1-azaadamantane, in small amounts (no yields being quoted) [9–11].

This method was later modified somewhat [12]: 1,3,5-tris(hydroxymethyl)cyclohexane, obtained in the previous way, was converted directly, with no bromination stage, into 1-azaadamantane by passing it over Al_2O_3 in a stream of ammonia at 375°C. In this method the yield did not exceed 9.5% [12].

According to the second method, 7-carbethoxy-3-azabicyclo[3.3.1]nonan-9-one, obtained by the condensation of an α-bromomethylacrylate (or β,β-dibromoisobutyrate) with *N*-tosyl-4-piperidone enamine, was detosylated after reduction of the ester function to give 1-azaadamantane in 78% yield [6,13,14]. In this synthetic method, the principal difficulty lies in the synthesis of azabicyclo[3.3.1]nonane compounds.

We have worked out a novel way of the synthesis of 1-azaadamantane, which is based on intramolecular migrations taking place in the initially-formed complex of chloramine with 1-boraadamantane. Closing of the 3-azabicyclo[3.3.1]nonane system, thereby obtained, has been achieved *via* quaternization of the amino group and Hofmann degradation of the quaternary compound.

Experimental

All operations with organoboron compounds were performed in an atmosphere of dry argon. Ethyldichloramine was obtained by chlorination of ethylamine with

chlorine, as described in [15]. 1-Boraadamantane was synthesized in accordance with a published method [16,17].

IR spectra were recorded on a UR-20 spectrometer, ^1H NMR spectra were obtained on VARIAN DA-60-IL and TESLA BS-497(100) instruments, and the ^{13}C NMR spectra were recorded on a BRUKER WM-250 spectrometer (62.89 MHz for carbon). The chemical shifts were determined relative to TMS.

3-Ethyl-7-hydroxymethyl-3-azabicyclo[3.3.1]nonane (II)

To a solution of 24.85 g (217.5 mmol) of $EtNCl_2$ in CH_2Cl_2 was slowly added dropwise with vigorous stirring at −50 to −70°C a solution of 29.16 g (217.5 mmol) of 1-boraadamantane in CH_2Cl_2. After the addition was complete, the reaction was gradually brought to room temperature, and the mixture was allowed to stand overnight. The solvent was removed in vacuum and the crystalline residue was washed with hexane, and then with ether, and oxidized using 75.5 ml of 30% H_2O_2 and 217 ml of 3 *M* NaOH. Distillation of the ethereal solution gave 22.94 g (57.5%) of II, b.p. 107–108°C (2 mmHg). This substance contained 3% of an impurity (GLC) and so it was purified on a column packed with Al_2O_3 using a mixture of benzene, ether and methanol (in a ratio of 12.5/2.5/1) as the eluent, Found: C, 71.93; H, 11.43; N, 7.04. $C_{11}H_{21}NO$ calcd.: C, 72.08; H, 11.55; N, 7.64%; n_D^{20} 1.4955.

1-Ethyl-1-azoniumadamantane chloride (III)

To a solution of 3.53 g (19.27 mmol) of II in benzene, which was being shaken and cooled with cold water, was carefully added, dropwise, a benzene solution of 4 ml of freshly distilled $SOCl_2$. (In this process, much heat is evolved, along with the formation of a heavy oil.) After the addition was completed, the mixture was boiled for 20 min: the oil then crystallized on cooling. The crystals were washed on a filter with benzene and dried, to afford 3.12 g (80%) of III, which crystallizes from a mixture of benzene and methylene chloride, Found: C, 64.96; H, 10.08; Cl, 17.28; N, 7.05. $C_{11}H_{20}ClN$ calcd.: C, 65.49; H, 9.99; Cl, 17.57; N, 6.94%. The substance is hygroscopic and decomposes above 300°C.

1-Azaadamantane (IV)

To a solution of 0.93 g (4.62 mmol) of III in 5 ml of EtOH was added an alcoholic solution of EtONa, prepared from 0.3 g of Na and 4 ml of EtOH. The temperature of the reaction mixture increased slightly and precipitation of NaCl took place. After the precipitate had been filtered off, the filtrate was evaporated in vacuum. The residue was sublimed at 80°C (1 mmHg) to yield 0.40 g (63%) of 1-azaadamantane, m.p. 262–265°C (hexane), Found: C, 78.93; H, 11.00; N, 10.16. $C_9H_{15}N$ calcd.: C, 78.77, H, 11.02; N, 10.21%. ^1H NMR (δ, ppm, C_6D_6): 1.41 s (CH), 1.76 s ($C-CH_2-C$), 3.05 s ($N-CH_2$); integrated intensities ratio, 1/2/2.

References

1 B.M. Mikhailov and V.N. Smirnov, Izv. Akad. Nauk SSSR, Ser. Khim., (1980) 1137.
2 B.M. Mikhailov, V.N. Smirnov and V.A. Kasparov, Izv. Akad. Nauk SSSR, Ser. Khim., (1976) 2302.
3 B.M. Mikhailov and K.L. Cherkasova, Izv. Akd. Nauk SSSR, Ser. Khim., (1976) 2056.
4 B.M. Mikhailov, E.A. Shagova and M.Yu. Etinger, J. Organometal. Chem., 220 (1981) 1.
5 Th. Reints Bok and W.N. Speckamp, Tetrahedron, 35 (1979) 267.

6 W.N. Speckamp, J. Dijkink and H.O. Huisman, J. Chem. Soc., Chem. Commun., (1970) 197.
7 W.N. Speckamp, J. Dijkink and H.O. Huisman, Tetrahedron Lett., (1974) 1853.
8 I. Morishima, K. Okada, T. Yonezawa and K. Goto, J. Am. Chem. Soc., 93 (1971) 3922.
9 R. Fusco and G. Biancetti, Atti Acad. Lincei, (8), XV, (1953) 420, Gazz. Chim. Ital., 86 (1956) 500.
10 R. Lukeš and V. Galik, Collect. Czech. Chem. Commun., 19 (1954) 712.
11 R. Lukeš and V. Galik, Chem. Listy, 48 (1954) 858.
12 V. Galik, Z. Kafka, M. Safar and S. Landa, Collect. Czech. Chem. Commun., 39 (1974) 895.
13 W.N. Speckamp, J. Dijkink, A.W.D. Dekkers and H.O. Huisman, Tetrahedron, 27 (1971) 3143.
14 A.W.D. Dekkers, W.N. Speckamp and H.O. Huisman, Tetrahedron Lett., (1971) 489.
15 L.K. Jackson, G.N.R. Smart and G.F. Wright, J. Am. Chem. Soc., 69 (1947) 1539.
16 B.M. Mikhailov and T.K. Baryshnikova, Izv. Akad. Nauk SSSR, Ser. Khim., (1978) 929.
17 B.M. Mikhailov, T.K. Baryshnikova, V.G. Kiselev and A.S. Shashkov, Izv. Akad. Nauk SSSR, Ser. Khim., (1979) 2544.
18 B.M. Mikhailov, T.A. Shchegoleva, E.M. Shashkova and V.G. Kiselev, J. Organometal. Chem., 250 (1983) 23.