Cyclic Boron Derivatives of Biurets [1]

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Boron Compounds, 1,3,5-Triaza-2-boracyclohexa-4,6-diones, Bis(N,N,N'-trimethylbiuret-1,5-diyl)borates(1-), NMR Spectra

Several 1,3,5-triaza-2-boracyclohexa-4,6-diones have been prepared by condensation reactions of boranes with biurets; N-methylated species could be characterized by their \(^1\)H, \(^13\)C NMR spectra. Some data are also reported on bicyclic bis(N,N,N'-trimethylbiuret-1,5-diyl)borate(1-) salts and on a betaine consisting of two N,N,N'-tri-methylbiuret moieties bonded to a central four-coordinate boron atom.

Introduction

Within the framework of a study of boron-nitrogen systems that are isoelectronic with organic species it is appealing to synthesize boron-nitrogen analogs of biologically active compounds.

Uracil is an important constituent of nucleic acids. However, boron-nitrogen analogs of uracil containing the skeleton 1 have received very little attention. A patent [2] reports the preparation of 1b to 1h by reaction of (-BR-NH-)_2 with R'NCO or by treating a biuret with RB(NR')_2 or RB(SR')_2, respectively, and the synthesis of the parent compound 1a by the condensation of BH_2 (generated in situ) with biuret has recently been claimed in a brief note [3]. However, only scant experimental details are available and the cited products were characterized by elemental analysis only.

\[
\begin{align*}
& \text{a: } \text{R} = \text{R'} = \text{R}^2 = \text{R}^3 = \text{H} \\
& \text{b: } \text{R} = \text{CH}_3, \text{R'} = \text{R}^2 = \text{R}^3 = \text{H} \\
& \text{c: } \text{R} = \text{CH}_3, \text{R'} = \text{H}, \text{R}^2 = \text{R}^3 = \text{C}_6\text{H}_5 \\
& \text{d: } \text{R} = \text{CH}_3, \text{R'} = \text{H}, \text{R}^2 = \text{R}^3 = \text{C}_6\text{H}_5 \\
& \text{e: } \text{R} = \text{CH}_3, \text{R'} = \text{H}, \text{R}^2 = \text{R}^3 = \text{C}_6\text{H}_5 \\
& \text{f: } \text{R} = \text{C}_6\text{H}_5, \text{R'} = \text{R}^2 = \text{R}^3 = \text{H} \\
& \text{g: } \text{R} = \text{C}_6\text{H}_4-3,4-\text{CH}_3, \text{R'} = \text{R}^2 = \text{H}, \text{R}^3 = \text{C}_6\text{H}_5 \\
& \text{h: } \text{R} = \text{C}_6\text{H}_4-4,5-\text{CH}_3, \text{R'} = \text{H}, \text{R}^2 = \text{R}^3 = \text{C}_6\text{H}_4-3-\text{Cl}. \\
\end{align*}
\]

All attempts to reproduce 1a by the described procedure as well as many variations thereof have failed. This is not surprising since in such a condensation of a carbonyl derivative with borane(3) complications are to be expected. As a matter of fact, the only clearly identified product obtained in any of the reactions studied was biuret hydrate. Therefore, we have directed our initial efforts to verify the existence of the framework of 1 by working with a trigonal borane containing no active hydrogen. Even in this approach, the insolubility of biuret in aprotic media (which are generally required when working with trigonal boranes) is a major obstacle. However, a heterogeneous-phase condensation has recently been employed for the reaction of carbohydrazide with bis(dimethylamino)phenylborane as well as borane(3) and was found to yield the desired heterocyclic species containing a carbonyl group [4]. In an extension of this work, the interaction of bis(dimethylamino)phenylborane with biuret and some related reactions have been studied.

Results and Discussion

When a benzene solution of bis(dimethylamino)phenylborane is heated to reflux with solid biuret, 2-phenyl-1,2-azaborauracil (1f) is formed according to:

\[
\text{C}_6\text{H}_5\text{B}(\text{CH}_3)_2\text{N} + \text{HN}(\text{CONH})_2 \rightarrow 1f + 2 (\text{CH}_3)\text{NH}
\]

(1)

It is difficult to separate the desired product from unreacted biuret; hence, it is best to employ an excess of bis(dimethylamino)phenylborane in the reaction. Secondly, the preparation of 1f by the outlined procedure is usually accompanied by the formation of some B-triphenylboroxine, (-BC_6H_5-O-)_2. This latter impurity is readily detected in the mass spectrum of the crude product and is best removed by washing with tetrahydro-
furan and then hexane or, better, hot toluene. The mass spectrum of the thus purified material shows the parent ion at M/z 189 as the base peak of the spectrum. A doubly charged ion of low relative abundance is observed at M/z 94.5; in general, the spectrum is characterized by very little fragmentation. The compound 11 hydrolyzes in water and due to its lack of solubility, no NMR data could be recorded. The infrared spectrum of the material shows a very strong absorption at 1463 cm\(^{-1}\) which is not observed in the spectrum of biuret and is tentatively assigned to a B–N stretching mode. A medium-to-strong intensity and fairly sharp band at 3380 cm\(^{-1}\) is indicative of N–H stretching. An extremely broad carbonyl band ranging from 1735 to 1650 cm\(^{-1}\) shows three maxima at 1726, 1702 and 1685 cm\(^{-1}\), respectively.

The structure of 11 is further substantiated by the successful synthesis of 1 with \(R = \text{C}_6\text{H}_5\) and \(R^1 = R^2 = R^3 = \text{CH}_3\) (11) by condensation of bis(dimethylamino)phenylborane with \(N,N',N''\)-trimethylbiuret; 1j (\(1, R = R^1 = R^2 = R^3 = \text{CH}_3\)) was obtained in similar fashion from bis(dimethylamino)methylborane. Since both 11 and 1j are soluble in aprotic solvents, NMR data on these species could be obtained and are in consonance with the assigned structures.

The interaction of NaBH\(_4\) with biuret in aqueous media has recently been claimed to yield the anion 2 with \(R = \text{H}\) [3]; the same anion is said to be formed on thermolysis of a mixture of biuret and boric acid at 100 to 110 °C [5]. Neither of the two cited procedures could be repeated. In the first case, biuret hydrate was the only product that could be identified. In the second case, no noticeable reaction occurred at the indicated temperature. However, at higher temperatures (near 150 °C) reaction did occur and a new species was obtained; the properties of the latter did not concur with those given for 2 [5] and the material was not further identified.

Again, employment of \(N,N',N''\)-trimethylbiuret shed some light on the processes. Reaction to tris-(dimethylamino)borane with the former was found to provide the dimethylammonium salt of 2 with \(R = \text{CH}_3\) in high yield. This event established the existence of the principal framework of 2. Reaction of trimethylamine-borane with \(N,N',N''\)-trimethyl-biuret was found to give the betaine 3.

The existence of this compound in the betaine structure 3 rather than as acid derived from the anion 2 is substantiated by NMR data. In particular, the \(^{11}\)B resonance signal is very broad indicating an unsymmetrical environment about the boron atom, and the localization of the N-bonded proton is confirmed by HNCH coupling with the adjacent N-methyl protons. It is noteworthy that under the reaction conditions (refluxing toluene) the initial product is a mixture of 3 with a second species, identified as the trimethylammonium salt of 2. However, on thermal treatment of the mixture under vacuum, trimethylamine is released and 3 is obtained exclusively.

**Experimental**

Reactions and transfers were carried out under a dry argon atmosphere. Biuret was a commercial product and was purified by recrystallization. Tris-(dimethylamino)borane [6], bis(dimethylamino)methylborane [7] and bis(dimethylamino)phenylborane [8] were prepared by the literature procedures. \(N,N',N''\)-Trimethylbiuret was prepared by a modified [9] procedure through the reaction of \(\text{CO}_2\) with \(\text{CH}_3\text{NCO}\) [10]. Elemental analyses were performed by the Schwarzkopf Microanalytical Laboratory, Woodside, NY. Melting points were determined in sealed capillaries on a Mel-Temp block and are uncorrected.

Infrared spectra were recorded on a Perkin-Elmer Model 621 spectrometer under standard operating conditions. Wavenumbers are given in cm\(^{-1}\), abbreviations of intensities are: \(s = \) strong, \(m = \) medium, \(w = \) weak, \(b = \) broad, \(v = \) very, \(sh = \) shoulder. Mass spectral data were obtained on a Hitachi-Perkin-Elmer RMU-7 instrument. Only ions of relative abundances (in parentheses) of 5\% or higher are listed. Proton NMR spectra were recorded on a Varian Model EM-390 spectrometer, \(^{11}\)B (reference: (\(\text{C}_2\text{H}_5\))\(_2\)OB\(_3\)) and \(^{13}\)C spectra.
were obtained on a Varian Model FT-80A instrument. Chemical shift data are given in ppm with positive values indicating downfield from the reference (unless otherwise noted: external) signal; abbreviations: s = singlet; d = doublet; t = triplet; as asterisk denotes a broad signal.

2-Phenyl-1,2-azaborauracil (2-phenyl-1,3,5-triazaboryclohexa-4,6-dione) (11)
A mixture of 5.15 g (50 mmol) of carefully dried biuret, 9.69 g (55 mmol) of bis(dimethylamino)phenylborane and 200 ml of benzene (dried over metallic sodium) is refluxed under argon cover and with vigorous stirring for 20 h. Colorless solids are filtered off the hot solution and are slurried with 200 ml of hot tetrahydrofuran. Solids are again collected and washed in portions with a total of 200 ml of hot dry toluene. After drying the solids under vacuum for 5 h at 70 °C, 6.3 g (66%) of product are obtained, decomposing at 336 to 340 °C (lit. [2]: 328 °C). The product can also be purified by dissolving it in dry tetramethylurea and subsequent precipitation with cyclohexane. It can be sublimed at <10⁻⁴ Torr and a bath temperature of 180 °C.

Analysis for C₆H₁₂O₃N₃B (189.00)
Found C 50.43 H 4.73 N 22.11 B 5.42.
Caled C 50.85 H 4.26 N 22.23 B 5.42.

Mass spectrum: M/z = 190(8), 189(100), 188(42), 187(7), 145(7), 130(5), 112(6), 104(7), 103(23), 102(8), 78(8), 77(9), 76(6), 69(11), 51(5). - Infrared spectrum (KBr pellet): 1785 (w), 1735 to 1651 (vs, vb), 1463 (vs, b, stretching).

1,2,3,5-Tetramethyl-1,2-azaborauracil (1,2,3,5-tetramethyl-1,3,5-triazaboryclohexa-4,6-dione) (11)
A mixture of 8.75 g (76.75 mmol) of bis(dimethylamino)methylborane, 11.13 g (76.75 mmol) of N,N′,N″-trimethylbiuret and 50 ml of toluene is refluxed with stirring for 2 h. A small amount of insoluble material is discarded and toluene is stripped of the insoluble material is filtered off and toluene is stripped of the clear solution to give 9.7 g (75%) of the crude product, m.p. (after recrystallization from hexane) 96 to 98 °C.

Analysis for C₆H₁₂O₃N₃B (168.99)
Found C 42.78 H 7.19 N 25.01 B 6.51.
Caled C 42.65 H 7.16 N 24.87 B 6.40.

NMR data (in CDCl₃): δH = 3.32 (s, 3H), 3.13 (s, 6H), 0.70 (s, 3H); δ₁₁B = 35.6; δ₁³C (proton-decoupled) = 154.3, 31.3, 29.3. (The BCH₂ signal was not observed.) - Mass spectrum: M/z = 170(6), 169(100), 168(22), 141(32), 140(9), 113(13), 112(52), 111(23), 84(11), 83(17), 71(7), 70(12), 69(8), 68(11), 67(5), 56(11), 55(23), 54(46), 53(13), 43(6), 42(9), 32(17), 28(47), 27(14), 26(6). - The infrared spectrum (KBr pellet) shows a broad carbonyl band near 1625 cm⁻¹ and another broad strong band near 1425 cm⁻¹ which is tentatively assigned to B–N stretching.

N,N′,N″-Trimethylbiuret
NMR data (in CDCl₃): δH = 7.38* (s, NH, 2H), 3.23 (s, 3H), 2.85 (d due to HNCH coupling, J = 4 to 5 Hz, 6H); δ₁³C (proton-decoupled) = 157.0, 29.7, 27.0.

Analysis for C₁₁H₁₄N₃BO₂ (231.06)
Found C 56.96 H 6.15 B 4.60 N 18.04.
Caled C 57.18 H 6.11 B 4.68 N 18.19.

NMR data (in CDCl₃): δH = 7.42 (s, 5H), 3.39 (s, 3H), 2.95 (s, 6H); δ₁₁B = 33.6; δ₁³C (proton-decoupled) = 154.9, 130.9, 129.3, 128.4, 32.9, 29.7. - Mass spectrum: M/z = 231(30), 230(100), 229(17), 173(8), 116(4), 114(16), 89(16), 88(6). - The infrared spectrum of the compound (KBr pellet) shows a very strong and broad carbonyl band centered near 1650 cm⁻¹ and a very strong and broad band near 1450 cm⁻¹ which is tentatively assigned as a B–N stretching mode.

Dimethylammonium bis(N,N′,N″-trimethylbiuret-1,3-diyl)diborate (1) (salt of anion 2 with $R = CH_3$)
A mixture of 6.5 g (45 mmol) of N,N′,N″-trimethylbiuret, 6.3 g (44 mmol) of tris(dimethylamino)borane and 50 ml of toluene is refluxed with stirring for 4 h. Insolubles are collected, washed with toluene and then hexane to give 7.55 g (99.7% calcd. for biuret) of the desired compound, m.p. 232 °C, soluble in tetramethylurea or chloroform.

Analysis for C₁₂H₁₆N₃BO₄ (343.20)
Found C 41.92 H 7.57 N 28.66 B 3.01.
Caled C 41.99 H 7.64 N 28.57 B 3.15.

NMR data (in CDCl₃): δH = 9.2² (s, 2H), 3.03 (s, 6H), 2.69 (s, 6H), 2.36 (s, 12H); δ₁₁B = −1.0; δ₁³C (proton-decoupled) = 156.3, 35.5, 28.8, 28.3. - Mass spectrum: M/z = 299(5), 298(37), 297(10), 211(11), 185(10), 184(23), 183(14), 172(35), 171(13), 126(5), 115(15), 114(6), 97(9), 91(15), 83(5), 81(5), 71(21), 70(6), 69(18), 68(6), 67(5), 58(12), 57(6), 56(8), 55(6), 45(57), 44(100), 42(19), 42(26), 41(9), 40(8), 39(7), 30(10), 28(38), 27(6). - The infrared spectrum features a broad carbonyl band near 1630 cm⁻¹ and three very strong and broad absorptions near 1475, 1400 and 1325 cm⁻¹.
The reaction of \(N,N',N''\)-trimethylbiuret with trimethylamine-borane

A mixture of 6.04 g (41.7 mmol) of \(N,N',N''\)-trimethylbiuret, 3.04 g (41.7 mmol) of trimethylamine-borane and 50 ml of toluene is refluxed overnight. The precipitate is collected, washed with toluene and then hexane and is dried under vacuum to yield 6.15 g of material (fraction 1). On subsequent heating of the dry product at 130 to 140 °C/10⁻³ Torr, gas evolution is observed for about 3 h; a colorless material, m.p. 276 to 278 °C, remains (fraction 2).

NMR data (in CDCl₃) on fraction 2 indicate the species to be the betaine 3: \(^1\)H = 8.42* (s, 1H), 3.34 (s, 3H), 3.17 (s, 3H), 2.91 (d, 3H), 2.60 (s) + 2.58 (s) (9H); \(^13\)C (proton-decoupled) = 157.5, 155.8, 151.7, 29.1, 29.0, 28.4. The broad signal \(^1\)H = 8.42 ppm is readily assigned to the nitrogen-bonded proton and those \(^1\)H = 3.34 and 3.17 ppm, respectively, to the \(NCH₃\) groups farthest from the boron. The doublet \(^1\)H at 2.91 ppm is due to HNCH coupling (\(\delta J = 4 \text{ Hz}\)) as is confirmed by a decoupling experiment. Based on intensity considerations the \(^13\)C = 155.8 ppm signal is due to that the carbonyl carbon atoms of that ring containing only trigonal nitrogen. The broadness of \(^11\)B resonance signal (half-maximum height band width approximately 600 Hz) is readily interpreted by the unsymmetrical environment of the boron atom, since the NH proton does not readily exchange (note the decoupling experiment cited above!). The mass spectrum of the material shows the parent ion M/z 298 as the base peak of the spectrum.

Analysis for \(C_{10}H_{19}N_6BO_4\) (298.00)

Found C 40.19 H 6.46 N 28.00 B 3.60,
Caled C 40.29 H 6.42 N 28.19 B 3.63.

Fraction 1 (see above) is not a uniform product. Rather it appears to be a mixture of 3 and the trimethylammonium salt of 2 with \(R = CH_3\). For example, \(^1\)H NMR signals for 3 are observed with \(^1\)H near 8.5*, 3.32 (s), 3.16 (s), 2.86 (d) and 2.54* (s) ppm. An additional very broad NH resonance signal is observed with \(^1\)H near 10.6 ppm and three singlets \(^1\)H = 3.11 (6H), 2.98 (9H), and 2.42 (12H) ppm are in good agreement with the corresponding methyl resonances of the dimethylammonium salt of the anion 2 with \(R = CH_3\) (see above). The same holds true for the \(^13\)C resonance signals with \(\delta = 156.7, 45.6, 29.1, 28.6 \text{ ppm}\), respectively, observed in addition to those of the betaine 3. The \(^11\)B NMR spectrum of fraction 1 features a sharp resonance line, \(\delta = -1.0 \text{ ppm}\), camouflaging a very broad second line near 4 ppm.

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