Electrochemical thiocyanation of dodecahydro-7,8-dicarba-*nido*-undecaborate and 7,8-dimethyldecahydro-7,8-dicarba-*nido*-undecaborate monoanions

D. A. Rudakov,[a] V. L. Shirokii,[a]★ V. I. Potkin,[a] N. A. Maier,[a] V. I. Bragin,[b,c] P. V. Petrovskii,[b] I. B. Sivaev,[b]★ V. I. Bregadze,[b] and A. V. Kisin[c]

[a]*Institute of Physical Organic Chemistry, National Academy of Sciences of Belarus, 13 ul. Surganova, 220072 Minsk, Belarus. E-mail: shirokii@ifoch.bas-net.by*

[b]*A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 28 ul. Vavilova, 119991 Moscow, Russian Federation. E-mail: sivaev@ineos.ac.ru*

[c]*State Research Institute of Chemistry and Technology of Organoelement Compounds, 38 sh. Entuziastov, 111123 Moscow, Russian Federation. E-mail: kiso@nmr.eos.incotrade.ru*

Electrochemical thiocyanation of the dodecahydro-7,8-dicarba-*nido*-undecaborate and 7,8-dimethyldecahydro-7,8-dicarba-*nido*-undecaborate monoanions afforded thiocyanate derivatives of these compounds, which were isolated as alkylammonium salts. The structures of the synthesized compounds were determined by the data from IR, ^{1}H and ^{11}B NMR, and ^{11}B—^{11}B NMR COSY spectroscopy.

Key words: carboranes, potassium dodecahydro-7,8-dicarba-*nido*-undecaborate, potassium 7,8-dimethyldecahydro-7,8-dicarba-*nido*-undecaborate, thiocyanation, electrochemistry.

7,8-Dicarba-*nido*-undecaborate anion $[7,8\text{-}C_2B_9H_{12}]^-$ is of interest for the development of agents for boron neutron capture therapy for cancer[1—3] and radionuclide diagnostics and therapy.[4,5] The introduction of substituents containing functional groups (for instance, isothiocyanate group) into the 7,8-dicarba-*nido*-undecaborate anion makes it possible to bind this anion with different compounds that provide selective delivery of the agent to a tumor, for example, to monoclonal antibodies.[6,7]

The chemical[6,8—12] and electrochemical[13] iodination and bromination[8,11,13,14] of the 7,8-dicarba-*nido*-undecaborate anion have been described earlier. The introduction of substituents of the pseudo-halogen type into the *nido*-carborane framework was unknown. At the same time, the thiocyanate derivative of the *closo*-dodecaborate anion $[B_{12}H_{11}SCN]^{2-}$ (see Refs 15 and 16) is a promising agent for boron neutron capture therapy for cancer.[17] The electrochemical method of thiocyanate group introduction into the $[B_{12}H_{12}]^{2-}$ anion was described.[18] In this work, we studied a possibility of electrochemical synthesis of thiocyanate derivatives of the [*nido*-7,8-$C_2B_9H_{12}]^-$ (**1a**) and [*nido*-7,8-Me_2-7,8-$C_2B_9H_{10}]^-$ (**2a**) anions.

Results and Discussion

Electrochemical thiocyanation of salt **1a** was carried out with dithiocyanogen formed by the anodic oxidation of the thiocyanate ion. Thiocyanation was less smooth compared to electrochemical iodination[13] and afforded thiocyano-substituted product **1b** in a yield <50%. The ^{1}H NMR spectrum of compound **1b** contains signals from two nonequivalent hydrogen atoms bonded to the carbon atoms of the carborane cage (CH_{carb}), which indicates the nonsymmetric structure of compound **1b**. The ^{11}B NMR spectrum of tetramethylammonium salt **1b** is almost the same as the spectrum of the [*nido*-9-SCN-7,8-$C_2B_9H_{11}]^-$ anion presented as a stick diagram in the review[19] (no other data on the synthesis and properties of this compound are reported). Thus, the structure (Me_4N)[9-SCN-*nido*-7,8-$C_2B_9H_{11}$] can be attributed to electrochemically synthesized compound **1b**.

Similarly, electrochemical thiocyanation of **2a** affords thiocyano-substituted product **2b**. The ^{1}H NMR spectrum of compound **2b** exhibits signals from two nonequivalent Me groups linked to the carbon atoms of the carborane cage, which indicates the nonequivalent effect of the SCN group on these Me

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 7, pp. 1553—1556, July, 2005.

1066-5285/05/5407-1599

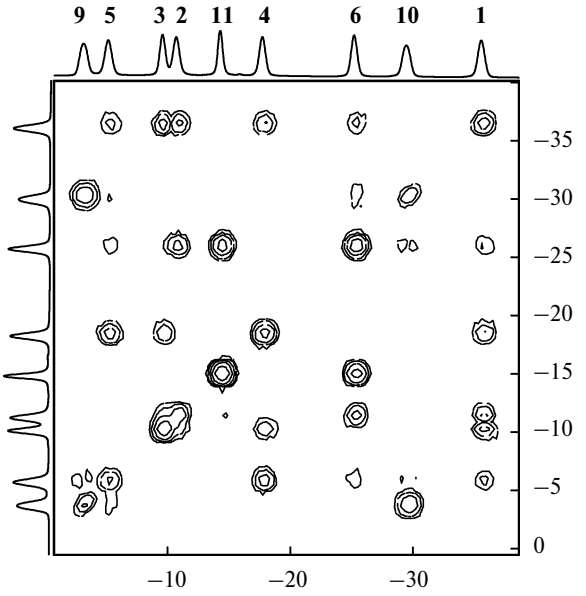


Fig. 1. $^{11}B—^{11}B$ NMR COSY spectrum of the [9-SCN-7,8-Me_2-7,8-$C_2B_9H_9]^-$ anion (**2b**).

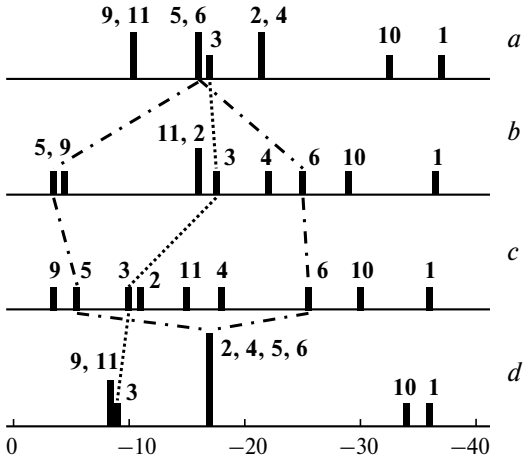


Fig. 2. Stick diagram of ^{11}B NMR chemical shifts for compounds [7,8-$C_2B_9H_{12}]^-$ (**1a**) (*a*), [9-SCN-7,8-$C_2B_9H_{11}]^-$ (**1b**) (*b*), [9-SCN-7,8-Me_2-7,8-$C_2B_9H_9]^-$ (**2b**) (*c*), and [7,8-Me_2-7,8-$C_2B_9H_{10}]^-$ (**2a**) (*d*).

groups and, hence, the nonsymmetric structure of compound **2b**.

An unambiguous conclusion about the structure of **2b** was made on the basis of analysis of the ^{11}B NMR and $^{11}B—^{11}B$ NMR COSY spectra (Fig. 1). The assignment of signals in the ^{11}B NMR spectrum is given in Table 1. Thus, compound **2b** has the structure (Me_3NH)[9-SCN-7,8-Me_2-*nido*-7,8-$C_2B_9H_9$].

It seemed of interest to compare the influence of the Me substituents on the ^{11}B NMR spectral characteristics of thiocyanate derivatives [9-SCN-7,8-X_2-*nido*-7,8-$C_2B_9H_9]^-$ (X = H, Me). The comparative stick diagram of chemical shifts for compounds **1a,b** and **2a,b** is presented in Fig. 2 (signals in the ^{11}B NMR spectra of compounds **1a,b** were assigned on the basis of previously published data,[19,20] and signals for **2a** were assigned using an additional $^{11}B—^{11}B$ NMR COSY experiment).

Methyl substituents at the carbon atoms in the carborane cage exert the greatest effect on the B(3) atom linked to two carbon atoms (difference of chemical shifts of B(3) in **2b** and **1b** ($\Delta\delta$) is +7.6 ppm). Somewhat lower difference of chemical shifts is observed for the B(2) and B(4) atoms, each of which is linked to one carbon atom ($\Delta\delta$ = +4.6 and +3.6, respectively). At the same time, the Me substituents at the carbon atoms have only insignificant effects on the difference of chemical shifts of the B(5) and B(6) atoms $\Delta = \delta_{B(5)}—\delta_{B(6)}$, which reflects the position of the bridging hydrogen atom relatively to the substituted boron atom.[19] For **1b**, this value is 21.4 ppm, and for **2b** it is 20.1 ppm. A similar change has been observed previously[21] for the introduction of Ph groups into [9-Me_2S-7,8-$C_2B_9H_{11}$].

A comparison of the IR spectra of compounds **1b** and **2b** with the spectra of unsubstituted salts **1a** and **2a** showed that the spectra of the thiocyanate derivatives contain no changes (compared to the unsubstituted compounds) related to an increase in the number of absorption bands and shifts of their maxima in the 400—1300 cm^{-1} region caused by the introduction of the SCN group into the dicarbaundecaborate system. The only additional feature

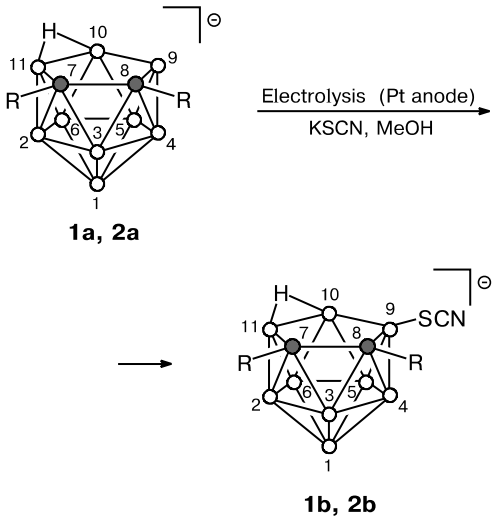
Table 1. Data of ^1H and ^{11}B NMR spectra of thiocyanate derivatives of the 7,8-dicarba-*nido*-undecaborate anion

Compound	δ ^1H	δ ^{11}B ($J_{B,H}$/Hz)
1b	3.45 (s, 12 H, $\underline{Me}_4N^+$), 2.46 (s, 1 H, $C\underline{H}_{carb}$), 1.89 (s, 1 H, $C\underline{H}_{carb}$), 2.00—0.00 (m, 9 H, B$\underline{H}$)	−3.7 (d, 1 B, B(5), J = 144); −4.3 (s, 1 B, B(9)); −15.8 (d, 2 B, B(2), B(11), J = 148); −17.7 (d, 1 B, B(3), J = 161); −21.8 (d, 1 B, B(4), J = 152); −25.1 (d, 1 B, B(6), J = 141); −29.0 (d, 1 B, B(10), J = 133); −36.6 (d, 1 B, B(1), J = 143)
2b	3.21 (s, 9 H, Me_3NH^+), 1.54 (s, 3 H, CMe_{carb}), 1.48 (s, 3 H, CMe_{carb}), 2.00—0.00 (m, 9 H, BH)	−3.6 (s, 1 B, B(9)); −5.6 (d, 1 B, B(5), J = 139); −10.1 (d, 1 B, B(3), J = 155); −11.2 (d, 1 B, B(2), J = 144); −14.8 (d, 1 B, B(11), J = 137); −18.2 (d, 1 B, B(4), J = 150); −25.7 (d, 1 B, B(6), J = 142); −29.9 (d, 1 B, B(10), J = 137); −36.0 (d, 1 B, B(1), J = 144)

in the IR spectrum was presented by intense absorption bands at 2138 cm^{-1} for **1b** and 2158 cm^{-1} for **2b** corresponding to vibrations of the SCN group. Absorption bands at 3030 cm^{-1} correspond to stretching vibrations of the C—H bonds, and high-intensity bands at 2530 cm^{-1} are assigned to stretching vibrations of the B—H bonds.

Thiocyanation of the 7,8-dicarba-*nido*-undecaborate and 7,8-dimethyl-7,8-dicarba-*nido*-undecaborate anions can be presented by Scheme 1.

Scheme 1



Experimental

IR spectra were recorded on a Protege-460 spectrometer (KBr pellets). ^1H and ^{11}B NMR spectra were obtained on Bruker AMX-400 and Bruker AM-360 spectrometers. Chemical shifts are presented relatively to Me_4Si and $Et_2O \cdot BF_3$, respectively.

Thiocyanation was carried out in an undivided electrochemical cell, whose temperature was maintained constant and which was equipped with a platinum anode, nickel cathode, and magnetic stirrer. The surface area of each electrode was 6 cm^2, and the distance between electrodes was 1 cm. Potassium dodecahydro-7,8-dicarba-*nido*-undecaborate (salt **1a**) and potassium 7,8-dimethyldecahydro-7,8-dicarba-*nido*-undecaborate (salt **2a**) were synthesized according to a previously[22] described procedure.

Synthesis of tetramethylammonium 9-thiocyanatoundecahydro-7,8-dicarba-*nido*-undecaborate [Me_4N][9-SCN-7,8-$C_2B_9H_{11}$] (1b). A solution of salt **1a** (2.00 g, 12 mmol) and potassium thiocyanate (2.95 g, 30 mmol) in anhydrous methanol (30 mL) was subjected to electrolysis with a dc density of 0.1 A cm^{-2} for 3 h at 50 °C. The quantity of passed electricity was 67 mF. After the end of electrolysis, the reaction mixture was evaporated to dryness, the residue was dissolved in water, and an aqueous solution of tetramethylammonium iodide was added. A precipitate formed was separated and washed with small amounts of water and ether (4×40 mL). The residue, being the unreacted salt, was dried. Compound **1a** was isolated in 18.9% yield (0.47 g). The filtrate was evaporated to dryness, washed with water, and dried in a Fischer injection system over $CaCl_2$. Compound **1b** (1.48 g, 5.6 mmol) was isolated in 47% yield of the starting salt.

Synthesis of trimethylammonium 7,8-dimethyl-9-thiocyanatononahydro-7,8-dicarba-*nido*-undecaborate [Me_3NH][9-SCN-7,8-Me_2-7,8-$C_2B_9H_9$] (2b). A solution of salt **2a** (0.60 g, 3 mmol) and potassium thiocyanate (1.76 g, 18 mmol) in anhydrous methanol (30 mL) was subjected to electrolysis with a dc density of 0.025 A cm^{-2} for 3 h and 13 min at 50 °C. The quantity of passed electricity was 18 mF. After the end of electrolysis, the reaction mixture was evaporated to dryness, the residue was dissolved in water, and an aqueous solution of trimethylammonium chloride was added. The precipitate formed was separated, washed with a small amount of water, and recrystallized from aqueous ethanol. Compound **2b** was obtained in 24% yield (0.20 g, 0.72 mmol).

The data of elemental analysis and ^1H and ^{11}B NMR spectra of thiocyanate derivatives **1b** and **2b** are given in Table 1. Their IR spectral data are presented in Table 2.

Table 2. Data of elemental analysis and IR spectra of thiocyanate derivatives of the 7,8-dicarba-*nido*-undecaborate anion

Compound	Found / Calculated (%)					Molecular formula	IR, ν/cm^{-1}
	C	H	B	S	N		
1b	32.0 31.8	9.7 8.7	36.2 36.8	11.1 12.1	10.6 10.6	$C_7H_{23}B_9SN_2$	3440 m, 3033 s, 2958 w, 2920 w, 2835 w, 2530 s, 2138 s, 1640 w, 1481 s, 1416 m, 1288 w, 1256 w, 1170 w, 1091 w, 1025 m, 990 m, 949 s, 915 m, 880 w, 858 m, 836 m, 794 w, 753 m, 739 w, 710 w, 655 w, 626 w, 576 w, 530 w, 495 w, 462 w, 445 w, 423 w
2b	34.5 34.5	10.0 9.0	34.6 34.9	11.5 11.5	9.6 10.1	$C_8H_{25}B_9SN_2$	3433 m, 3048 s, 2966 m, 2930 m, 2866 m, 2782 s, 2528 vs, 2158 vs, 1630 w, 1479 s, 1456 s, 1426 w, 1416 w, 1336 w, 1370 w, 1250 m, 1200 w, 1150 w, 1094 w, 1063 w, 1010 m, 983 s, 950 w, 923 w, 906 w, 883 w, 835 s, 763 w, 736 w, 660 m, 640 w, 610 w, 520 m, 456 w, 436 w, 426 w

This work was financially supported by the INTAS (Grant No. 99-00806).

References

1. M. F. Hawthorne, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 950.
2. A. H. Soloway, W. Tjarks, B. A. Barnum, F.-G. Rong, R. F. Barth, I. M. Codogni, and J. G. Wilson, *Chem. Rev.*, 1998, **98**, 1515.
3. I. B. Sivaev and V. I. Bregadze, *Ross. Khim. Zh.*, 2004, **48**, No. 4, 109 [*Mendeleev. Chem. J.*, 2004, **48**, No. 4, (Engl. Transl.)].
4. M. F. Hawthorne and A. Maderna, *Chem. Rev.*, 1999, **99**, 3421.
5. V. Tolmachev and S. Sjöberg, *Collect. Czech. Chem. Commun.*, 2002, **67**, 913.
6. E. A. Mizusawa, M. R. Thompson, and M. F. Hawthorne, *Inorg. Chem.*, 1985, **24**, 1911.
7. K. J. Winberg, M. Persson, P.-U. Malmström, S. Sjöberg, and V. Tolmachev, *Nucl. Med. Biol.*, 2004, **31**, 425.
8. F. P. Olsen and M. F. Hawthorne, *Inorg. Chem.*, 1965, **4**, 1839.
9. L. I. Zakharkin, G. G. Zhigareva, and V. A. Antonovich, *Zh. Obshch. Khim.*, 1980, **22**, 1026 [*J. Gen. Chem. USSR*, 1980, **22** (Engl. Transl.)].
10. R. H. Pak, R. R. Kane, C. B. Knobler, and M. F. Hawthorne, *Inorg. Chem.*, 1994, **33**, 5355.
11. G. K. Semin, L. I. Zakharkin, S. I. Kuznetsov, G. G. Zhigareva, and E. V. Bryukhova, *Zh. Obshch. Khim.*, 1998, **68**, 969 [*Russ. J. Gen. Chem.*, 1998, **68**, 919 (Engl. Transl.)].
12. E. C. Santos, A. B. Pinkerton, S. A. Kinkead, P. K. Hurlburt, S. A. Jasper, C. W. Sellers, J. C. Huffman, and L. J. Todd, *Polyhedron*, 2000, **19**, 1777.
13. V. L. Shirokii, D. A. Rudakov, A. V. Bazhanov, E. G. Zalesskaya, V. I. Potkin, N. A. Maier, S. V. Timofeev, P. V. Petrovskii, and V. I. Bregadze, *Elektrokhimiya*, 2004, **40**, 242 [*Russ. J. Electroctrochem.*, 2004, **40**, 212 (Engl. Transl.)].
14. L. I. Zakharkin, V. V. Kobak, A. I. Kovredov, and V. A. Antonovich, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1979, 2122 [*Bull. Acad. Sci. USSR. Div. Chem. Sci.*, 1979, **28** (Engl. Transl.)].
15. H.-G. Srebny and W. Preetz, *Z. Anorg. Allg. Chem.*, 1984, **513**, 7.
16. I. B. Sivaev, S. B. Katser, K. A. Solntsev, and N. T. Kuznetsov, *Zh. Neorg. Khim.*, 1995, **40**, 807 [*Russ. J. Inorg. Chem.*, 1995, **40**, 779 (Engl. Transl.)].
17. R. A. Spryshkova, E. Yu. Grigor´eva, and V. A. Brattsev, *Voprosy onkologii* [*Problems of Oncology*], 1997, **41**, 106 (in Russian).
18. J. H. Morris, V. A. Brattsev, and D. F. Gaines, in *Advances in Boron Chemistry*, Ed. W. Siebert, Cambridge, The Royal Society of Chemistry, 1997, p. 434.
19. S. Hermanek, *Chem. Rev.*, 1992, **92**, 325.
20. S. Hermanek, *Inorg. Chim. Acta.*, 1999, **289**, 20.
21. G. M. Rosair, A. J. Welch, A. S. Weller, and S. K. Zahn, *J. Organomet. Chem.*, 1997, **536—537**, 299.
22. M. F. Hawthorne, D. C. Young, P. M. Garrett, D. A. Owen, S. G. Schwerin, F. N. Tebbe, and P. A. Wegner, *J. Am. Chem. Soc.*, 1968, **90**, 862.

Received March 16, 2005