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Nucleophilic Substitution at α-Methylene Group Attached to *o*-Carboranes. Synthesis of Carboranylmethylthiopyridines.

Andrei A.Semioshkin*, Gennadii M.Ptashits*, Vladimir L.Ivanov, Vasilii A.Artyomov**, Anatolii M.Shestopalov**, Vladimir I.Bregadze*, Viktor P.Litvinov****

*A.N.Nesmeyanov Institute of Organoelement Compounds, 117813, Moscow, Russia, E-mail: bre@ineos.ac.ru

**N.D.Zelinsky Institute of Organic Chemistry, 117913, Moscow, Russia, E-mail dva@nmr1.ioc.ac.ru

Abstract: The S_N2-type substitution on bromomethyl-*o*-carborane was never reported earlier. It was found that pyridine-2(1H)-thiones react with bromomethyl-*o*-carborane in the presence of triethylamine. This reaction leads to the *o*-carboranylmethylthiopyridines with high yields. A series of the novel *o*-carboranylmethylthiopyridines was synthesized and characterized by various spectral methods. © 1997 Elsevier Science Ltd.

Introduction.

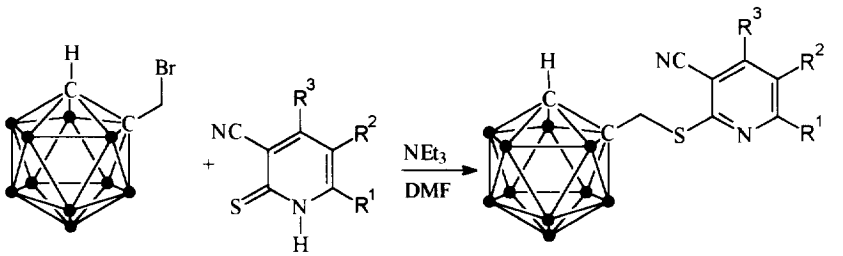
Bromomethyl-*o*-carboranes are among the most easy prepared starting material for the synthesis of functionally substituted carboranes[1]. So far, only the electrophilic substitution of bromine atom by metals (e.g., Mg, Li) was used in the synthetic ways starting from these compounds[2, 3]. No examples of preparative S_N-reactions of ones were described. Moreover, it was reported that the reactions of bromo- and chloromethyl-*o*-carboranes with various nucleophiles (Na_2S/EtOH, NaI/acetone, potassium phthalimide/DMF) do not take place and result in the recovering of starting materials[4].

By the way deprotonated 3-cyanopyridine-2(1H)-thiones[5] are known as the strong nucleophiles and very weak bases. Therefore they are widely used for the preparation of different heterocyclic compounds[5]. The methods of their preparation are also described in detail[5].

We found that 3-cyanopyridine-2(1H)-thiones react with bromomethyl-*o*-carborane in the presence of Et_3N giving novel carboranylmethylthiopyridines.

Results and discussion.

Various 3-cyanopyridine-2(1H)-thiones (**2a-d**) react with bromomethyl *o*-carborane (**1**) in DMF in the presence of Et_3N. This reaction results in the novel *o*-carboranylmethylthiopyridines (**3a-d**) with high yields (70-85%) (Table 1).



2,3	R^1	R^2	R^3
a	Me	H	Me
b	Ph	H	Ph
c	Ph	H	4-BrC_6H_4
d	NH_2	CN	H

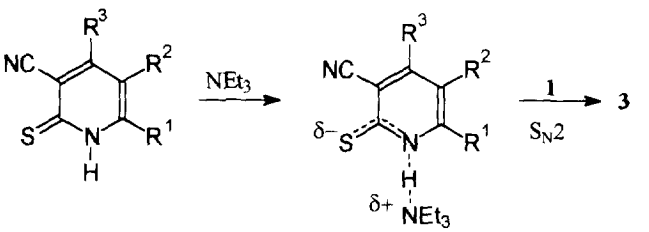
Table 1. *o*-Carboranylmethylthiopyridines

Compound	m.p., °C	Formula	Microanalysis data, found/calculated, %			Yield, %
			C	H	N	
3a	117	$C_{11}H_{20}B_{10}N_2S$	41.12 41.09	6.64 6.58	8.73 8.71	83
3b	213-215	$C_{21}H_{24}B_{10}N_2S$	56.55 56.60	5.71 5.65	6.20 6.29	72
3c	201	$C_{21}H_{23}B_{10}BrN_2S$	48.02 48.09	4.58 4.61	5.30 5.34	77
3d*	159	$C_{10}H_{16}B_{10}N_4S$- C_3H_7NO	38.06 38.50	5.83 5.72	17.33 17.27	73

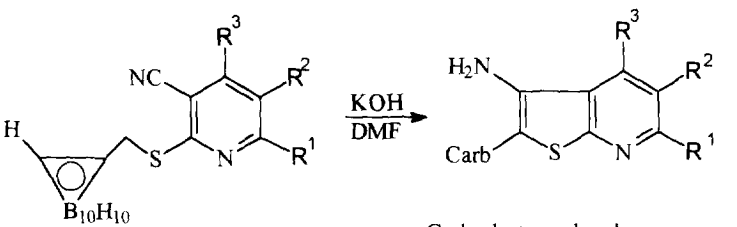
*Contains DMF

The spectral data (NMR, IR, Mass spectra) completely confirm the structure (**3**) (Table 2). In the IR-spectra appear absorption bands of B-H, C≡N groups, and pyridine moiety. In the ^{1}H NMR spectra of (**3a-d**) the signal of CH_2-S protons is about 4.5 ppm and carborane CH is about 4.8-5.3 ppm. Latter signal is shifted downfield in comparison with starting material (**1**). In the ^{11}B NMR spectra (Table 2) the signals are typical for the monosubstituted carborane. Moreover, all of these signals are doublets in the ^{11}B-^{1}H coupled spectrum, therefore no substitution on boron takes place. Finally, ^{13}C NMR spectral data of (**3a,b**) show the presence of both carborane carbons, S-CH_2-group, pyridine ring and C≡N group in these compounds.

We have already mentioned that (**1**) seems to be an inert substrate for the nucleophilic substitution reactions. We found that potassium salts of the pyridinethiones (**2**) did not react with (**1**) at all. Therefore, we suppose that the electrophilic assistance of the cation at the S_N2-substitution decreases the rate of the reaction in the case (**1**) due to of σ-acceptor properties of the *o*-carborane substituent. Pyridinethiones (**2**) do not form a real ionic pair with triethylamine. The negative charged sulfur atom becomes free and it makes substitutions easier:



The compounds (**3**) are also interesting because they can be introduced into Thorpe-Ziegler reaction because of strong -I effect of the carborane. We found that the classical Thorpe-Ziegler reaction takes place, but according to ^{11}B NMR data the carborane cage is destroyed:



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Carb=destroyed carborane cage

Table 2. Spectral data of *o*-carboranylmethylthiopyridines (**3**)

Compound	^{1}H NMR[1], δ(ppm.)	^{13}C NMR[1], δ(ppm.)	^{11}B NMR[1], δ(ppm.)	IR, ν(cm^{-1})	Mass, M$^+$ (m/e)
3a	7.17(s.,1H,H5), 4.81(br.s.,1H, CH-carb.), 4.40(s.,2H,CH_2-S), 2.51(s.,3H,6-CH_3), 2.48(s.,3H, 4-CH_3), 3.8-1.1(br.m.,10H, BH-carb.)	162.1(C2), 158.5(C6), 153.5(C4), 120.9(C5), 114.5(CN), 104.9(C3), 75.7(C-carb.), 62.6(CH-carb.), 34.9(CH_2-S), 23.9(6-CH_3), 19.5(4-CH_3)	-2.4(1B,151Hz), -5.2(1B,152Hz), -9.3(2B[3]), -10.6(2B[3]), -11.5(2B[3]), -12.5(2B[3])	2603(BH), 2215(CN), 1584(Py)	320
3b	8.33(m.,2H,*o*-H 6-Ph), 8.04 (s.,1H,H5), 7.79(m.,2H,*o*-H 5-Ph), 7.61(m.,6H,*m*-and *p*-H Ph), 5.31(br.s.,1H, CH-carb.), 4.58(s.,2H,CH_2-S), 3.8-1.0 (br.m.,10H,BH-carb.)	161.2(C2), 160.1(C6), 156.5(C4), 138.1 and 137.2(*i*-C Ph), 132.2 and 131.5(*o*-C Ph), 130.3 and 130.2(*m*-C Ph), 129.9 and 129.0(*p*-C Ph), 118.9(C5), 116.1(CN), 108.2(C3), 76.5(C-carb.), 63.4(CH-carb.), 35.9(CH_2-S)	-2.1(1B,162Hz), -5.0(1B,167Hz), -8.8(2B[3]), -10.6(4B[3]), -12.25(2B[3])	2586(BH), 2215(CN), 1573(Py)	444
3c	8.30(m.,2H,*o*-H Ph), 8.02(s., 1H,H5), 7.78(AA'XX'(A-part),2H,*o*-H 4-Ar), 7.59(m., 5H,another H of aryls), 5.28 (br.s.,1H,CH-carb.), 4.56(s., 2H,CH_2-S), 3.8-1.0(br.m., 10H,BH-carb.)	[2]	-2.5(1B,150Hz), -5.1(1B[3]), -9.1(2B[3]), -10.8(4B[3]), -12.3(2B[3])	2571(BH), 2221(CN), 1576(Py)	523
3d[4]	8.38(s.,1H,H4), 8.17(br.s.,2H, NH_2), 5.24(br.s.,1H,CH-carb.), 4.22(s.,2H,CH_2-S), 3.8-1.0(br.m.,10H,BH-carb.)	[2]	-2.2(1B, 147Hz), -5.5(1B[3]), -8.9(2B[3]), -10.7(4B[3]), -12.2(2B[3])	3204(NH), 2572(BH), 2218,2217(CN), 1581(Py)	332

[1]Acetone-d_6 for (**3a**) and DMSO-d_6 for (**3b-d**), [2]Dramatical low solubility, [3]J_{BH} is not resolved, [4]Containes DMF

EXPERIMENTAL

All chemicals were reagent grade and were received from standard commercial vendors. Bromomethyl-*o*-carborane (**1**) was prepared by refluxing of sublimated decaborane ($B_{10}H_{14}$) and propargyl bromide in CH_3CN[1]. Pyridinethiones (**2**) were prepared by described methods: (**2a**)[6], (**2b,c**)[7], (**2d**)[8], respectively. DMF was distilled under CaH_2. ^1H and ^{13}C NMR Spectra were recorded on a Bruker-AMX-400 (400MHz for ^1H and 104MHz for ^{13}C). ^{11}B NMR Spectra were recorded on a Bruker-AC-200 (at 64MHz). Lock was mountained with deuterated solvents. Chemical shifts were referred to external standarts (TMS for ^1H, ^{13}C and BF_3-Et_2O for ^{11}B). IR-Spectra were registred for KBr tablets on Specord-M80. Mass-spectra were recorded on a KRATOS MS-890 spectrometer (70eV). Microanalysis was obtained on a Perkin-Elmer C,H,N-analyser (obtained data agreed with calculated). Melting points were measured in sealing capillars. Yields and characteristics of the obtained compounds are presented in tables 1,2.

2-(o-Carboranylmethylthio)-3-cyanopyridines (3a-d)

Bromomethyl-*o*-carborane (**1**, 0.6g, 2.5mmol), pyridinethione (**2**, 2.5mmol), and triethylamine (0.7ml, 5mmol) were held in 15ml of abs. DMF for 2.5-3h at 95-100°C. The resulting mixture was cooled and the product was precipitated by the excess of water. Precipitate was filtred off, washed with 2x5ml EtOH, 2x5ml H_2O, again 2x5ml EtOH, 2x5ml hexane, and dried in the air.

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