CONSTITUTION AND HPLC RESOLUTION OF ENANTIOMERS OF THE [8,4′-μ-R_2N-*commo*-(1,2-$C_2B_9H_{10}$)$_2$-3-Co] COMPLEX – THE THIRD ISOMER OF NITROGEN-BRIDGED BISICOSAHEDRAL COBALTACARBORANE

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A fully asymmetric structure of the [4,8′-μ-R_2N-*commo*-(1,2-$C_2B_9H_{10}$)$_2$-3-Co] (R = H and Me) cobaltacarborane complexes with a monoatomic nitrogen bridge between both ligands was determined by high resolution mass spectrometry and ^1H, ^{11}B NMR, [^{11}B-^{11}B] COSY NMR spectroscopy. Their structures have been also supported by the resolution of both compounds into enantiomers on the β-cyclodextrin HPLC column. A complex reaction of the [3-Co-*commo*-(1,2-$C_2B_9H_{11}$)$_2$]$^-$ ion with the NO^+ cation is briefly discussed and the tentative structure of the second main product is also suggested.

As reported earlier[1], on treatment of the [3-Co-*commo*-(1,2-$C_2B_9H_{11}$)$_2$]$^-$$Cs^+$ salt[2] with sodium nitrite and concentrated sulfuric acid in benzene, three uncharged species have been obtained according to TLC monitoring[1]. The red spot (R_F 0.44, Silufol, benzene) was identified as that belonging to the symmetric [8,8′-μ-H_2N-*commo*-(1,2-$C_2B_9H_{10}$)$_2$-3-Co] (*I*) cobaltacarborane – a unique species with an intramolecular monoatomic bridge between both carborane ligands. Its molecular structure was confirmed subsequently by an X-ray diffraction study[3]. The minor product, identified as a yellow spot of R_F 0.17, was isolated as well, but it has been characterized only incompletely as an asymmetric isomer of *I* by mass spectrometry. However, due to its asymmetry and low resolution of the NMR resonances, we were unable to establish its constitution reliably at that time.

Repaying our sixteen-year old debt, we have identified the yellow compound as the asymmetric [4,8′-μ-H_2N-*commo*-(1,2-$C_2B_9H_{10}$)$_2$-3-Co] (*IIa*) (Fig. 1) N-bridged cobaltadicarbaborane, the constitution of which has been confirmed by conversion of *IIa* into its *N*,*N*-dimethyl derivative (*IIb*) followed by investigation of this derivative by high-field NMR spectroscopy. The NMR results were then complemented by resolution of *IIa* and *IIb* into enantiomers via HPLC on a chiral β-cyclodextrin column. This efficient

combination of the two newly available methods allows for solution of subtle stereochemical problems that were hardly to solve until recently[4,5].

The structure in Fig. 1 is consistent with the NMR data (see Table I) and the similar inclination of the deltahedral ligands as found by X-ray diffraction study[3] in an N-substituted derivative of *I* should be expected.

The seemingly complex numbering scheme (see also ref.[4]) is consistently based on usual numbering convention for icosahedral carboranes combined with the earlier re-

TABLE I
^{1}H and ^{11}B NMR spectra (δ, ppm) of compounds *IIa* and *IIb*

Species	^{1}H NMR (500 MHz)[a]	^{11}B NMR (160.4 MHz)[a,b]
IIa	3.56 (CH); 3.67(2) (CH); 5.27 (CH); 4.75 (NH)	3.05; 0.31; –0.76 (d, s); –6.34 (d, s); –7.57(2); –8.22(2); –8.85; –9.53(2); –15.40; –18.15; –20.08; –21.60; –23.24
IIb	3.52 (CH); 3.57 (CH); 3.64 (CH); 4.99 (CH); 2.62 (CH_3); 2.88 (CH_3)	5.27 (s); 2.53 [4.00]; –0.91 (s, d) [3.05]; –2.05 [2.95]; –6.15 [2.21, 4.02]; –8.62 [2.36]; –9.19 [2.15, 2.26]; –9.95 [2.15, 2.529]; –10.82 [2.08]; –15.55 [1.988]; –18.29 [1.791]; –21.16, –21.56 [1.83, 1.68]; –22.32 [1.93]; –23.14 [1.95]

[a] Additional NMR spectra are available on request. [b] Followed by cluster proton chemical shifts (in square brackets).

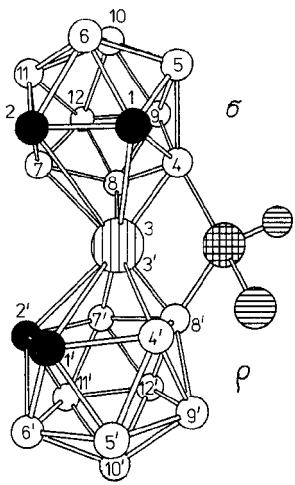


FIG. 1
Schematic drawing of the proposed structure of the [ρ-, 4,8′-μ-Me_2N-*commo*-(1,2-$C_2B_9H_{10})_2$-3-Co] enantiomer; its mirror image will represent the σ-antipode

ported[4] principle of least locant numbers and σ-, ρ-convention for chiral deltahedral species[6].

Stereochemical relation between the symmetric *I* and asymmetric *II* is apparent from Fig. 2, where only the conformations of the ligand planes associated with the metal vertex are shown (other upper and lower B–H vertices B(5,6,9 – 12) are omitted for clarity). Some properties of the parent species *IIa* and its *N*,*N*-dimethyl derivative *IIb* are presented in the experimental part, while those relevant to the determination of their constitutions are summarized in Table I.

The unambiguous structural evidence of structure *IIb* (see Fig. 1), consistent with a $Me_2N<^{+}$ bridge replacing two terminal hydrogen atoms in the parent cobaltacarborane ion, is based on high resolution mass spectrum which is in agreement with $[^{12}C_6{}^{11}B_{18}{}^{1}H_{26}{}^{14}N^{57}Co]^{+}$ high mass molecular cut-off and on four different C–H carborane signals along with two signals assigned to two nonequivalent Me_1NMe_2 methyl groups in the ^{1}H NMR spectra. Moreover, as it is evident from Fig. 2, there is no other conformation allowing for an interligand B–(R_2N)–B bridge with the formation of an asymmetric structure.

The very complex ^{11}B NMR spectrum shows fifteen signals out of eighteen expected for a completely asymmetric structure, three of them being coincidentally overlapped. However, both well resolved singlets of the bridgehead B-vertices can be readily assigned by comparison with corresponding resonances in the ^{11}B spectrum of the symmetric species[1] *I*. Thus the singlet at –0.91 ppm belongs to B(4), and the other at 5.27 ppm corresponds to B(8′). Detailed assignments of other signals are still not possible due to the extreme complexity of the [^{11}B-^{11}B] COSY NMR spectrum.

Further support for this constitution is afforded by the resolution of *IIa* and *IIb* into enantiomers, carried out via HPLC on β-cyclodextrin column, following the procedure which has become routine only recently for a similar class of compounds[4,5]. However, outstandingly high values of resolution and selectivity were observed for enantiomers

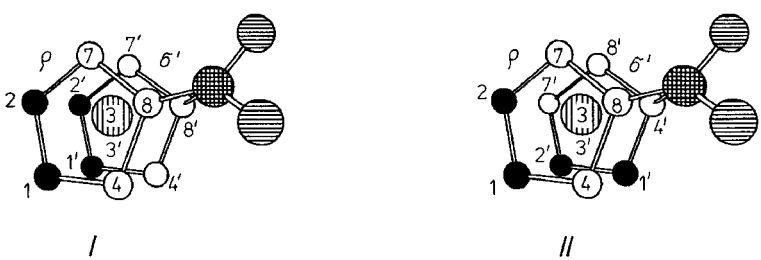


FIG. 2
Conformation of the pentagonal ligand planes associated with the metallaborane isomers *I* and *II*. Other {B-H} vertices B(5,6,9 – 12) are omitted for clarity

of $H_2N<$ bridged compound *IIa* (Table II). Furthermore, the selectivity (α) and the resolution (*Rs*) values of *IIa* are much less affected by increasing methanol content in the mobile phase in comparison with an other asymmetrically bridged compound [6,6′-μ-H_2N-*commo*-(1,7-$C_2B_9H_{10})_2$-2-Co], previously reported[5]. The enantiomers of compound *IIb* exhibit slightly higher values of capacity factor *k′*, α and *Rs* in 85% aqueous methanol than do the enantiomers of the structurally related compound[5] [6,6′-μ-Me_2N-*commo*-(1,7-$C_2B_9H_{10})_2$-2-Co]. In contrast to the last compound, the *Rs* values of *IIb* exhibit increasing trend with the increasing methanol content in the mobile phase (Table II). This effect should be ascribed to the decrease of the solubility of the *IIb* as the water content in the mobile phase increases. Therefore, the faster separation of the both compounds under discussion is thus possible using mobile phases with high methanol content (95 – 100%) with still good *Rs* values (above 1.5). Furthermore, using these conditions, the sample loading on the semipreparative column (8 × 250 mm) could be increased up to 1 mg per single injection, i.e. approximately fivefold greater amount of the sample than have been recently reported[5] for another bridged compounds. Observed differences in the chromatographic behaviour of the closely related compounds [6,6′-μ-R_2N-*commo*-(1,7-$C_2B_9H_{10})_2$-2-Co] (R = H, Me) and *IIa*, *IIb* should be probably ascribed to the higher dipole moment of the latter species. The examples of the analytical and semipreparative enantiomeric separations of the compounds *IIa* and *IIb* by HPLC on β-cyclodextrin are given in Figs 3 and 4.

The enantiomers of both compounds *IIa* and *IIb* eluting first on this type of β-cyclodextrin material exhibited identical orientation of the Cotton effects in their circular dichroism spectra (CD). CD spectra of the enantiomers of *IIb* are shown in Fig. 5.

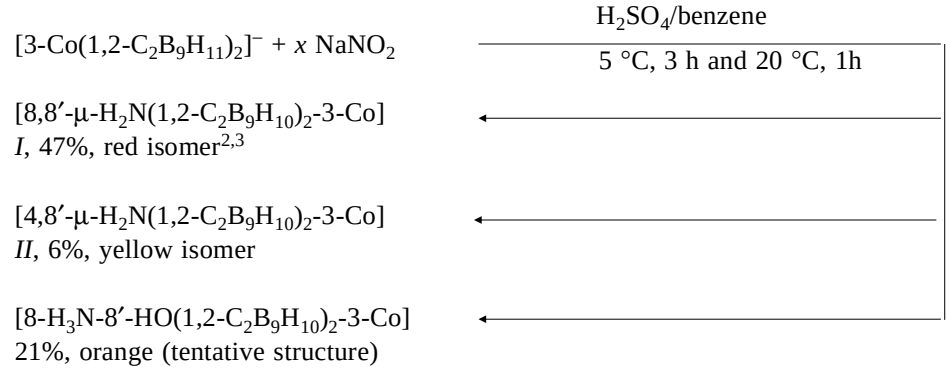
TABLE II

Effect of the methanol content in the mobile phase on the capacity factors (*k′*), selectivity (α) and the resolution (*Rs*) values of the enantiomers of the compounds *IIa* and *IIb* (flow rate 1.6 ml/min, detection at 280 nm, injections 2 μl of a solution in methanol (1 mg/ml))

Methanol %	*IIa*			*IIb*		
	k_1'	α	*Rs*	k_1'	α	*Rs*
70	4.77	1.46	3.80	–	–	–
80	3.77	1.42	3.60	9.42	1.20	1.38
85	2.05	1.41	3.60	6.11	1.21	1.60
90	1.61	1.35	3.64	4.28	1.21	1.68
95	1.33	1.29	2.89	3.00	1.20	1.95
100	1.17	1.19	2.63	2.33	1.19	2.00

Noteworthy is relatively great difference in the melting points of the racemate and pure enantiomers of *IIb*. While racemate melts at 237 °C, melting points of the first and second eluting enantiomers were 270 °C and 268 °C, respectively.

The results presented above now permit to complement the reaction scheme for the reaction of the $[3\text{-Co-}commo\text{-}(1,2\text{-}C_2B_9H_{11})_2]^-$ ion with the NO^+ cation, on which the formation of complexes of the type *II* is evidently based:



The second most abundant product of this reaction[1] – the orange species (R_F 0.02, Silufol, benzene) still awaits a more reliable structural characterization, although NMR evidence so far available is best compatible with the $[8\text{-}H_3N\text{-}8'\text{-HO-}commo\text{-}(1,2\text{-}C_2B_9H_{10})_2\text{-3-Co}]$ cobaltacarborane. Though this entirely asymmetric species is much less stable than both congeners *I* and *IIa*, we still hope to elucidate its definitive structure in the near future.

EXPERIMENTAL

TLC was performed on silica gel sheets Silufol (Kavalier, Votice). The chemicals used were of reagent grade (Lachema, Brno), unless stated otherwise and were used as purchassed.

The ^1H and ^{11}B NMR spectra (δ, ppm) were measured with Varian XL-500 spectrometer at 500 MHz (^1H) and 160.4 MHz (^{11}B) (compound *IIb*) and with Varian XL-200 spectrometer at 200 MHz (^1H) and 64.18 MHz (^{11}B) (compound *IIa*), in deuteriochloroform (relative to $B(OCH_3)_3$ as internal standard, –18.2 ppm). Mass spectra were recorded with Jeol HP-5985 by electron impact ionization at 70 eV. Circular dichroism spectra were recorded on Auto Dichrographe Mark V (Jobin Yvon, France), driven by a microcomputer (Silex, France) loaded with our own software. The measurements were performed in methanol (Uvasol, Merck) in quartz cells with the optical path length 0.1 cm.

The simple isocratic chromatographic system was described elsewhere[5]. The chromatographic separations were performed on a stainless steel semipreparative column packed with β-cyclodextrin chiral stationary phase (high loading of β-CD, 250 × 8 mm i.d., Institute of Organic Chemistry and Biochemistry, AS CR, Prague) having β-CD molecules directly bonded[7] to the silica gel support Se-

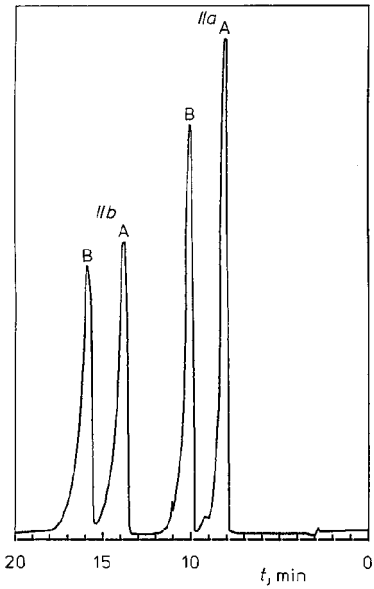


FIG. 3
Analytical HPLC separation of enantiomers A and B of *IIa* and *IIb* on a β-cyclodextrin column (250 × 8 mm) in 85% aqueous methanol (flow rate 1.6 ml/min, detection at 280 nm, sensitivity 0.04 a.u.f.s., injection 2 μl of the mixture of compounds *IIa* and *IIb* (0.5 mg/ml of each)

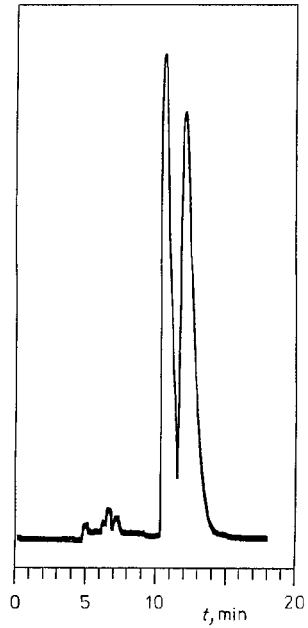


FIG. 4
Semipreparative separation of enantiomers of compound *IIb* on a β-cyclodextrin column (250 × 8 mm) in 95% aqueous methanol (flow rate 1.6 ml/min, injection 100 μl of methanolic solution of the *IIb* (5 mg/ml) detection at 290 nm, sensitivity 1.28 a.u.f.s)

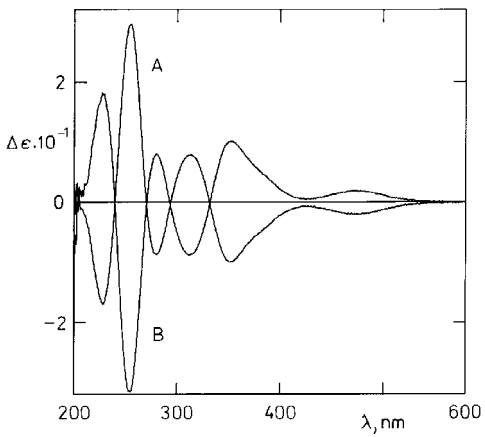


FIG. 5
Circular dichroism spectra of the enantiomers of compound *IIb* in methanolic solution of concentration 1.36 . 10^{-3} mol/l. Curves A and B represent those of the earlier and later eluted enantiomer

paron SGX 7 μm (TESSEK Ltd., Prague). The chromatographic conditions used for separation of enantiomers of *IIb* are described in Fig. 3 caption. Pure enantiomers in 3 mg amounts were isolated according the previously reported semipreparative HPLC method[5].

[8,4′-μ-H_2N-*commo*-(1,2-$C_2B_9H_{10}$)2-3-Co] (*IIa*)

The reaction of the [3-Co-*commo*-(1,2-$C_2B_9H_{11})_2$]$^-Cs^+$ salt (4.6 g, 0.01 mol) with $NaNO_2$ (H_2SO_4/benzene) has been carried out as described previously[2] and the products were isolated by chromatography on silica gel column. Elution with benzene developed a yellow band from which compound *IIa* was isolated upon evaporation of the benzene as an orange powder, 0.20 g (6%), R_F (benzene) 0.17, m.p. 289 – 290 °C, m.p. of pure enantiomers 290 – 291 °C, R_F (benzene) 0.17. Mass spectrum (*m*/*z*): 341. For the ^1H NMR and ^{11}B NMR data see Table I.

N,*N*-Dimethyl Derivative *IIb*

To a solution of compound *IIa* (0.50 g, 1.5 mmol) and KOH (2.0 g, 35 mmol) in ethanol (50 ml), dimethylsulfate (2 ml) was added and left to stand at 20 °C (until the starting species disappeared on TLC monitoring); aqueous NH_3 (5 ml of 15% solution) was added and after 5 min the mixture was evaporated to dryness in vacuum. The residue was extracted with benzene (2 × 10 ml), the combined extracts were filtered through a short silica gel column and the TLC pure eluate was evaporated in vacuum to yield 0.52 g (98%) of product as a coarse orange mass sublimable without decomposition over 200 °C (bath) at 13 Pa; R_F 0.26 (benzene–hexane 1 : 2), m.p. 237 °C , m.p. of the first and second eluted enantiomer 270 and 268 °C, respectively. Mass spectrum (*m*/*z*): 369; for [$^{12}C_6{}^{11}B_{18}{}^1H_{26}{}^{14}N^{57}Co$]$^+$ calculated 369; UV-VIS (CH_2Cl_2), (λ_{max} in nm (ε)): 217 (28 180), 320 (7 680), 430 (1 938); other properties are summarized in Table I.

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