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Synthesis of *o*(*m*)-Carborane-Containing Azomethines

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Abstract—A method of preparative synthesis of *o*(*m*)-carborane-containing azomethines via the condensation of *o*(*m*)-carboranyl-*C*-methylene-4-formylbenzoates with aliphatic, cycloaliphatic, and aromatic amines was developed.

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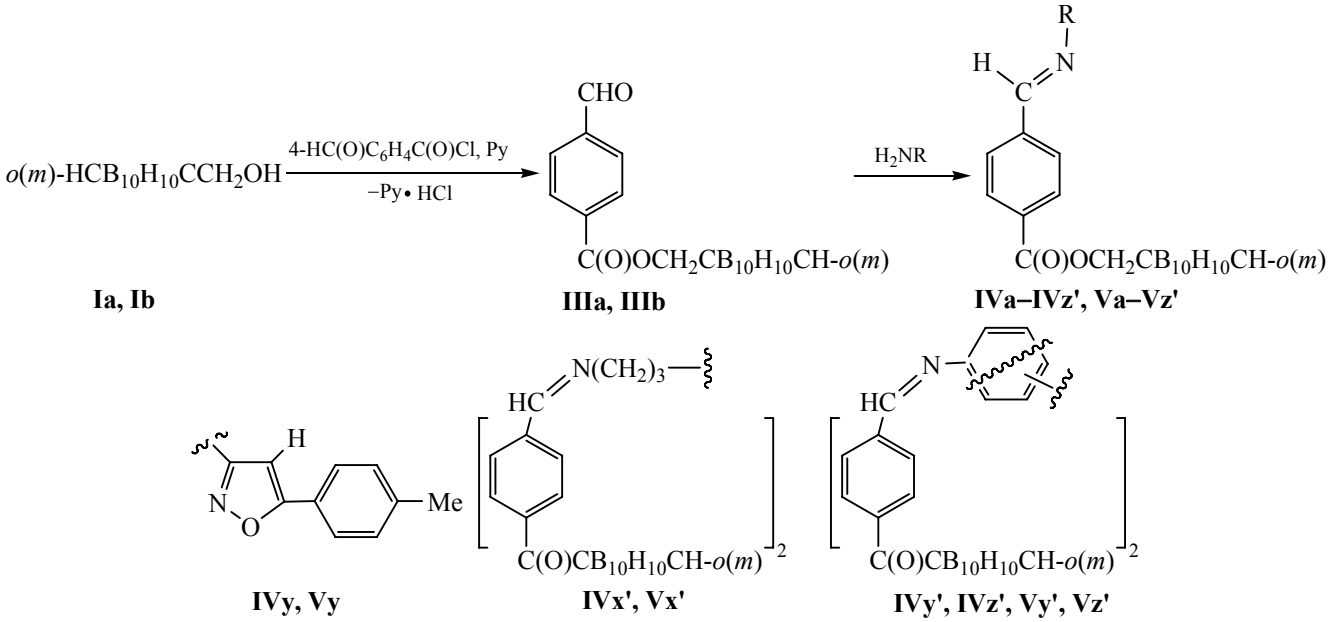
Previously we have reported on the synthesis of *o*(*m*)-carborane-containing Schiff bases via the condensation of vanillin esters of *o*(*m*)-carborane-*C*-carboxylic acid and vanillin with amines [1–4]. The carborane nitrogen-containing derivatives are of interest for research in the field of the boron neutron capture therapy of the tumor diseases, radionuclide diagnostics and therapy [5, 6].

In this work we describe the method of preparative synthesis of new *o*(*m*)-carborane azomethines **IVa**–**IVz'** and **Va**–**IVz'** by the condensation of *o*(*m*)-



Ia, **IIIa**, **IVa**– **IVz'** are *o*-carborane derivatives; **Ib**, **IIIb**, **Va**–**Vz'** are *m*-carborane derivatives; **IV**, **V**: R = *n*-$C_{16}H_{33}$ (**a**), *n*-$C_{18}H_{37}$ (**b**), cyclo-C_6H_{11} (**c**), CH(1-Ad)Me (**d**), *L*-CH(CHMe$_2$)CO$_2$Me (**e**), *L*-CH(CHCH$_2$Me$_2$)CO$_2$Me (**f**), *L*-CH(CHMeEt)CO$_2$Me (**g**), *L*-CH(CH$_2$Ph)CO$_2$Me (**h**), 4-MeC_6H_4 (**i**), 2-biphenyl (**j**), 4-biphenyl (**k**), 1-naphthyl (**l**), 2-naphthyl (**m**), 3-BrC_6H_4 (**n**), 4-BrC_6H_4 (**o**), 4-IC_6H_4 (**p**), 1-bromo-2-naphthyl (**q**), 2-hydroxyphenyl (**r**), 4-phenoxyphenyl (**s**), 4-EtC(O)C_6H_4 (**t**), 3-HO$_2$CC_6H_4 (**u**), 4-HO$_2$CC_6H_4 (**v**), 4-EtO$_2$CC_6H_4 (**w**), 4-BuO$_2$CC_6H_4 (**x**); **IVx'**, **Vx'** are 1,6-hexamethylene diamine derivatives; **IVy'**, **IVz'** , **Vy'**, **Vz'** are 1,3- and 1,4-phenylene diamine derivatives.

carborane-*C*-methyl-4-formylbenzoates **IIIa** and **IIIb** with aliphatic, cycloaliphatic, and aromatic amines **IIa**–**IIz'**. The yields of compounds **IVa**– **IVz'** and **Va**–**IVz'** were 82–88%.

The starting *o*(*m*)-carborane-*C*-methylene-4-formylbenzoates **III** were synthesized by the esterification of *o*(*m*)-carborane-*C*-methanols **I** with 4-formylbenzoyl chloride in the presence of pyridine [7]. The yields of compounds **IIIa** and **IIIb** were 88–90%.

The obtained carborane-containing compounds **III**, **IV**, and **V** are crystalline or amorphous glassy substances, which are soluble in DMF, DMSO, and $CHCl_3$. The structure of the obtained compounds was confirmed by the elemental analysis, IR and NMR spectroscopy (see the table).

Yields, melting points, and elemental analysis data for compounds **III**, **IV** and **V**

Comp. no.	Yield, %	mp, °C	Found, %				Formula	Calculated, %				*M*	
			C	H	B	N		C	H	B	N	found	calculated
IIIa	88	77–78	43.38	6.14	35.02	–	$C_{11}H_{18}B_{10}O_3$	43.12	5.92	35.29	–	299.0	306.4
IIIb	90	85–86	43.44	6.99	34.96	–	$C_{11}H_{18}B_{10}O_3$	43.12	5.92	35.29	–	297.5	306.4
IVa	83	37–38	61.65	9.87	20.05	2.19	$C_{27}H_{51}B_{10}NO_2$	61.21	9.70	20.41	2.64	504.7	529.8
IVb	84	38–39	62.73	10.08	18.95	2.04	$C_{29}H_{55}B_{10}NO_2$	62.44	9.94	19.38	2.51	538.4	557.9
IVc	87	–	52.99	7.67	27.60	3.21	$C_{17}H_{29}B_{10}NO_2$	52.69	7.54	27.90	3.61	359.6	387.5
IVd	88	–	59.52	8.14	22.76	2.88	$C_{23}H_{37}B_{10}NO_2$	59.07	7.97	23.12	3.00	460.0	467.7
IVe	88	–	48.98	7.19	25.38	3.05	$C_{17}H_{29}B_{10}NO_4$	48.67	6.97	25.77	3.34	404.2	419.5
IVf	86	–	50.17	7.42	24.65	2.90	$C_{18}H_{31}B_{10}NO_4$	49.87	7.21	24.94	3.23	409.6	433.6
IVg	86	–	50.08	7.39	24.61	2.99	$C_{18}H_{31}B_{10}NO_4$	49.87	7.21	24.94	3.23	412.8	433.6
IVh	87	–	54.23	6.41	22.86	2.80	$C_{21}H_{29}B_{10}NO_4$	53.94	6.25	23.12	3.00	448.3	467.6
IVi	82	81–82	54.94	6.53	27.01	3.28	$C_{18}H_{25}B_{10}NO_2$	54.66	6.37	27.33	3.54	382.2	395.5
IVj	85	143–144	60.72	6.18	23.10	2.86	$C_{23}H_{27}B_{10}NO_2$	60.37	5.95	23.63	3.06	441.4	457.6
IVk	88	172–173	60.80	6.22	23.28	2.90	$C_{23}H_{27}B_{10}NO_2$	60.37	5.95	23.63	3.06	448.1	457.6
IVl	86	107–108	58.75	6.00	24.81	2.92	$C_{21}H_{25}B_{10}NO_2$	58.45	5.84	25.05	3.25	420.3	431.5
IVm	86	164–165	58.89	6.08	24.73	2.99	$C_{21}H_{25}B_{10}NO_2$	58.45	5.84	25.05	3.25	418.7	431.5
IVn[a]	84	–	44.62	4.97	23.11	2.63	$C_{17}H_{22}B_{10}BrNO_2$	44.35	4.82	23.48	3.04	443.7	460.4
IVo[b]	86	150–151	44.70	5.03	23.07	2.85	$C_{17}H_{22}B_{10}BrNO_2$	44.35	4.82	23.48	3.04	451.9	460.4
IVp[c]	85	175–176	40.25	3.51	10.96	2.46	$C_{17}H_{22}B_{10}INO_2$	40.24	4.37	21.31	2.76	484.2	507.4
IVq[d]	84	126–127	49.12	4.94	20.85	2.30	$C_{21}H_{24}B_{10}BrNO_2$	49.41	4.74	21.18	2.74	497.6	510.4
IVr	88	171–172	51.64	5.98	26.76	3.13	$C_{17}H_{23}B_{10}NO_3$	51.37	5.83	27.20	3.52	381.0	397.5
IVs	87	86–87	58.51	5.90	22.53	2.40	$C_{23}H_{27}B_{10}NO_3$	58.33	5.75	22.83	2.96	458.4	473.6
IVt	86	–	55.43	6.50	24.28	2.83	$C_{20}H_{27}B_{10}NO_3$	54.90	6.22	24.71	3.20	418.8	437.5
IVu	85	168–169	51.15	5.62	25.03	2.87	$C_{18}H_{23}B_{10}NO_4$	50.81	5.45	25.41	3.29	446.2	425.5
IVv	88	272–273	51.19	5.71	25.20	2.94	$C_{18}H_{23}B_{10}NO_4$	50.81	5.45	25.41	3.29	451.0	425.5
IVw	83	–	53.32	6.24	23.51	2.86	$C_{20}H_{27}B_{10}NO_4$	52.96	6.00	23.84	3.09	436.1	453.5
IVx	84	164–165	55.15	6.72	22.07	2.56	$C_{22}H_{31}B_{10}NO_4$	54.87	6.49	22.45	2.91	460.3	481.6
IVy	87	218–219	54.83	5.66	22.88	5.83	$C_{21}H_{26}B_{10}N_2O_3$	54.53	5.67	23.37	6.06	448.3	462.6
IVx'	83	–	48.87	7.19	30.79	3.75	$C_{28}H_{48}B_{20}N_2O_4$	48.53	6.98	31.20	4.04	667.5	692.9
IVy'	83	–	49.19	6.00	31.23	3.76	$C_{28}H_{40}B_{20}N_2O_4$	49.11	5.89	31.57	4.09	655.9	684.9
IVz'	85	264–265	49.49	6.07	31.20	3.88	$C_{28}H_{40}B_{20}N_2O_4$	49.11	5.89	31.57	4.09	668.3	684.9
Va	85	37–38	61.66	9.74	20.22	2.35	$C_{27}H_{51}B_{10}NO_2$	61.21	9.70	20.41	2.64	512.5	529.8
Vb	82	39–40	62.59	10.27	18.90	2.25	$C_{29}H_{55}B_{10}NO_2$	62.44	9.94	19.38	2.51	543.2	557.9
Vc	84	–	52.14	7.67	27.51	3.30	$C_{17}H_{29}B_{10}NO_2$	52.69	7.54	27.90	3.61	364.4	387.5
Vd	88	–	59.60	8.21	22.72	2.50	$C_{23}H_{37}B_{10}NO_2$	59.07	7.97	23.12	3.00	458.1	467.7
Ve	84	–	48.92	7.15	25.65	2.98	$C_{17}H_{29}B_{10}NO_4$	48.67	6.97	25.77	3.34	412.2	419.5
Vf	86	–	50.30	7.23	24.45	2.90	$C_{18}H_{31}B_{10}NO_4$	49.87	7.21	24.94	3.23	414.5	433.6
Vg	85	–	50.17	7.44	24.63	2.76	$C_{18}H_{31}B_{10}NO_4$	49.87	7.21	24.94	3.23	423.4	433.6
Vh	85	–	54.42	6.48	22.70	2.67	$C_{21}H_{29}B_{10}NO_4$	53.94	6.25	23.12	3.00	451.6	467.6

(Contd.)

Comp. no.	Yield, %	mp, °C	Found, %				Formula	Calculated, %				*M*	
			C	H	B	N		C	H	B	N	found	calculated
Vi	86	127–128	54.23	6.48	27.01	3.18	$C_{18}H_{25}B_{10}NO_2$	54.66	6.37	27.33	3.54	385.2	395.5
Vj	84	–	60.66	6.21	23.17	2.50	$C_{23}H_{27}B_{10}NO_2$	60.37	5.95	23.63	3.06	449.0	457.6
Vk	85	191–192	60.75	6.17	23.06	2.84	$C_{23}H_{27}B_{10}NO_2$	60.37	5.95	23.63	3.06	447.4	457.6
Vl	87	171–172	58.86	6.02	24.75	2.92	$C_{21}H_{25}B_{10}NO_2$	58.45	5.84	25.05	3.25	422.8	431.5
Vm	88	124–125	58.90	5.88	24.92	3.03	$C_{21}H_{25}B_{10}NO_2$	58.45	5.84	25.05	3.25	416.4	431.5
Vn[e]	83	–	44.58	5.05	23.40	2.82	$C_{17}H_{22}B_{10}BrNO_2$	44.35	4.82	23.48	3.04	444.2	460.4
Vo[f]	85	136–137	44.69	5.01	23.00	2.81	$C_{17}H_{22}B_{10}BrNO_2$	44.35	4.82	23.48	3.04	454.7	460.4
Vp[g]	85	146–147	40.40	4.57	20.91	2.40	$C_{17}H_{22}B_{10}INO_2$	40.24	4.37	21.31	2.76	488.2	507.4
Vq[h]	84	–	49.85	5.02	20.73	2.44	$C_{21}H_{24}B_{10}BrNO_2$	49.41	4.74	21.18	2.74	494.3	510.4
Vr	85	163–164	51.24	6.10	26.84	3.12	$C_{17}H_{23}B_{10}NO_3$	51.37	5.83	27.20	3.52	381.9	397.5
Vs	86	108–109	58.57	5.81	22.48	2.56	$C_{23}H_{27}B_{10}NO_3$	58.33	5.75	22.83	2.96	456.2	473.6
Vt	86	–	55.36	6.28	24.25	2.78	$C_{20}H_{27}B_{10}NO_3$	54.90	6.22	24.71	3.20	428.7	437.5
Vu	86	187–188	51.19	5.64	25.08	2.90	$C_{18}H_{23}B_{10}NO_4$	50.81	5.45	25.41	3.29	443.4	425.5
Vv	84	275–276	50.99	5.63	25.30	3.14	$C_{18}H_{23}B_{10}NO_4$	50.81	5.45	25.41	3.29	454.2	425.5
Vw	84	–	53.50	6.21	23.25	2.61	$C_{20}H_{27}B_{10}NO_4$	52.96	6.00	23.84	3.09	445.4	453.5
Vx	85	–	55.16	6.58	22.13	2.56	$C_{22}H_{31}B_{10}NO_4$	54.87	6.49	22.45	2.91	468.8	481.6
Vy	86	229–230	54.91	5.80	23.05	5.67	$C_{21}H_{26}B_{10}N_2O_3$	54.53	5.67	23.37	6.06	449.5	462.6
Vx'	82	–	48.98	7.34	30.72	3.78	$C_{28}H_{48}B_{20}N_2O_4$	48.53	6.98	31.20	4.04	675.1	692.9
Vy'	83	–	49.49	5.94	31.16	3.76	$C_{28}H_{40}B_{20}N_2O_4$	49.11	5.89	31.57	4.09	668.6	684.9
Vz'	84	252–253	49.19	5.80	31.27	4.02	$C_{28}H_{40}B_{20}N_2O_4$	49.11	5.89	31.57	4.09	677.2	684.9

[a] Found Br, %: 16.92. Calculated Br, %: 17.36. [b] Found Br, %: 16.99. Calculated Br, %: 17.36. [c] Found I, %: 24.76. Calculated I, %: 25.01. [d] Found Br, %: 15.23. Calculated Br, %: 15.65. [e] Found Br, %: 16.84. Calculated Br, %: 17.36. [f] Found Br, %: 16.90. Calculated Br, %: 17.36. [g] Found I, %: 24.73. Calculated I, %: 25.01. [h] Found Br, %: 15.36. Calculated Br, %: 15.65.

The IR spectra of carborane-containing aldehydes **IIIa** and **IIIb** and azomethines **IVa**–**IVz'** and **Va**–**Vz'** contain the following characteristic absorption bands (ν, cm^{-1}): 3060±4 ($C–H_{carb}$), 2590±15 (B–H), 1730±5 ($C=O_{ester}$), 1615±5, 1580±5, 1415±5 ($C=C_{Ar}$), 1265±5, 1105±5, 1015±5 (C–O), 840±5, 755±5, 720±5 ($C–H_{Ar}$), 1706±1 ($C=O_{ald}$), 1633±13 (C=N).

The ^{1}H NMR spectra of *o*-carborane derivatives **IIIa** and **IVa**–**IVz'** contain the characteristic proton signals at δ 4.9±0.2 (s, CH_2O) and 5.4±0.1 ppm (br.s , CH_{carb}), of *m*-carborane derivatives **IIIb** and **Va**–**Vz',** at 4.1±0.1 (br.s , CH_{carb}) and 4.6±0.3 ppm (s, CH_2O). The aromatic protons appear in the range of 7.9–8.2 ppm (m, C_6H_4). In the spectra of carborane-containing aldehydes **IIIa** and **IIIb** there is a singlet signal of aldehyde group at δ 10.1 ppm. The azomethine moiety appears as a signal at δ 8.6±0.3 ppm, which is characteristic for *E*-configuration of azomethines [8].

EXPERIMENTAL

The IR spectra were recorded on a Nicolet Protégé-460 Fourier-spectrometer (from film or pellets with KBr). The ^{1}H NMR spectra were registered on a Tesla BS-587A spectrometer (100 MHz) for 5% DMSO-d_6 solutions relative to internal TMS (**IV**, **V**); the ^{1}H and ^{11}B NMR spectra (**IVo**, **Vo**), on a Bruker Avance-500 spectrometer (^{1}H at 500 MHz and ^{11}B at 160.46 MHz) for 15% $CDCl_3$ solutions. The molecular mass was determined by cryoscopy in benzene.

4-Formylbenzoyl chloride [bp 282–283°C (760 mm Hg), mp 54–55°C] was prepared by the reaction of 4-formylbenzoic acid with 1.5 mol of $SOCl_2$ in the presence of catalytic amount of DMF.

4-Formylbenzoyloxymethylene-(*o*,*m*)-*C*-carboranes (IIIa, IIIb). To a solution of 0.1 mol (*o*, *m*)-*C*-

carboranylmethanol **I** and 0.1 mol of 4-formylbenzoyl chloride in 300 ml of anhydrous diethyl ether was added 0.1 mol of anhydrous pyridine in 50 ml of diethyl ether within 30 min with cooling to 10–15°C while vigorous stirring. The mixture was stirred for 1 h and diluted with 500 ml of water. The ether layer was separated, washed with water (3×200 ml) and saturated $NaHCO_3$ solution (2×200 ml), dried over $MgSO_4$, and concentrated. The residue was crystallized from hexane.

(*o*,*m*)-Carborane-containing azomethines (IVa–IVy, Va–Vy). A mixture of 5 mmol of 4-formylbenzoyloxymethylene-(*o*,*m*)-*C*-carborane **III** and 5 mmol of the corresponding secondary amine **IIa–IIx'** in 40 ml of anhydrous methanol was refluxed for 30–45 min and then cooled to 0–5°C. The crystalline azomethines were filtered off through the glass porous filter, washed with cold methanol and dried in air for 6–8 h. The glassy azomethines were decanted and purified by the column chromatography on a neutral alumina (40–100 μm, Brockman activity degree II) eluting with dichloromethane.

(*o*,*m*)-Carborane-containing bisazomethines (IVx'–IVz' , Vx'–Vz'). A solution of 10 mmol of 4-formylbenzoyloxymethylene-(*o*,*m*)-*C*-carborane **III** and 5 mmol of the corresponding primary amine **IIx'–IIz'** in 50 ml of anhydrous methanol was refluxed for 45 min. The target products were isolated similarly to azomethines (**IVa–IVy, Va–Vy**).

(*E*)-*o*-Carboranyl-*C*-methylene-4-[(4^1-bromophenyl)iminomethyl]benzoate (IVo). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.2–1.4 m ($B_{10}H_{10}$), 3.91 br.s (CH_{carb}), 4.81 s (CH_2O), 7.11 d ($J_{2',3'}$ 8.0 Hz), 7.51 d ($J_{2',3'}$ 8.0 Hz), 7.99 d ($J_{2,3}$ 7.7 Hz), 8.11 d ($J_{2,3}$ 7.7 Hz), 8.48 s (HC=N). ^{11}B NMR spectrum ($CDCl_3$), δ_B, ppm: –1.2 d (1B, $B^{12/9}$, *J* 150 Hz), –3.8 d (1B, $B^{9/12}$), *J* 144 Hz), –8.8 d (2B, $B^{8,10}$, *J* 151 Hz), –11.0 d (2B, $B^{4,5}$, *J* 147 Hz), –12.4 d (4B, $B^{3,6,7,11}$, *J* 144 Hz).

(*E*)-*m*-Carboranyl-*C*-methylene-4-[(4^1-bromophenyl)iminomethyl]benzoate (Vo). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.6–1.4 m ($B_{10}H_{10}$), 3.00 br.s (CH_{carb}), 4.55 s (CH_2O), 7.11 d ($J_{2',3'}$ 7.1 Hz), 7.51 d ($J_{2',3'}$ 7.1 Hz), 7.99 d ($J_{2,3}$ 7.1 Hz), 8.13 d ($J_{2,3}$ 7.1 Hz), 8.48 s (HC=N). ^{11}B NMR spectrum ($CDCl_3$), δ_B, ppm: –3.8 d (1B, B^5, *J* 163 Hz), –8.0 d (1B, B^{12}, *J* 165 Hz), –10.0 d (2B, $B^{9,10}$, *J* 148 Hz), –11.0 d (2B, $B^{4,6}$, *J* 159 Hz), –12.6 d (2B, $B^{8,11}$, *J* 168 Hz), –15.1 d (2B, $B^{2,3}$, *J* 180 Hz).

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