ORGANOBORON COMPOUNDS.

379. BORON CHELATES BASED ON 7-METHOXYMETHYL-3-BORABICYCLO[3.3.1]NON-6-ENE DERIVATIVES

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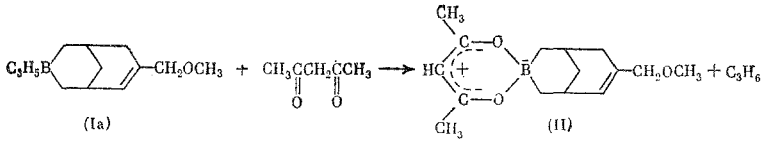
Many organoboron chelates, resistant to moisture and air, have potential biological activity [1].

The reaction of 3-allyl-7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene (Ia) and 3-methoxy-7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene (Ib) [2], synthesized via allylboracetylenic condensation, with various complexing agents was studied in the present paper. It was shown that either an allyl or methoxyl group on the B atom is easily replaced when (Ia) and (Ib) are reacted with amines and alcohols.

The reaction of (Ia) with acetylacetone is exothermic and proceeds with the liberation of propylene and the formation of the inner complex 3-(4-oxopent-2-en-2-yloxy)-7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene (II) in 82.6% yield

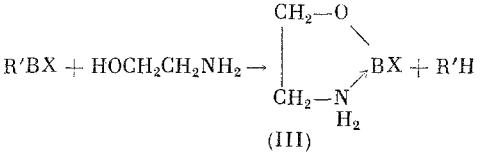


(Ia) (II)

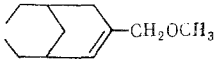
The pale yellow crystals in (II) are stable in an inert atmosphere, but they gradually hydrolyze in the air. The IR spectrum of (II) has the characteristic bands of cyclic acetylacetonates at 1545 (C=C) and 1595 cm^{-1} (C=O) [3, 4] and lacks the bands of the free acetylacetone in the 1600-1700 cm^{-1} (1630, 1675, 1690 cm^{-1}) region. The structure of (II) is also confirmed by the PMR spectral data ($CHCl_3$, δ, ppm): 5.73 m (HC=C of bicycle), 5.51 (HC acac), 3.45 m (CH_2O), 3.33 s (OCH_3), 2.04 s and 1.97 s (CH_3 acac) [5]. The ^{13}C NMR spectrum corresponds to the structure of (II) and has the signals ($CDCl_3$, δ, ppm): the two CH_3 and CH groups of the acetylacetone fragment (respectively 24.1, 24.2, and 100.2), the CH_3O and CH_2O groups (57.5 and 78.2), the C^6 and C^7 atoms of the bicycle (131.7 and 132), and the C—O→B fragments (189.9 and 190.1). Based on the ^1H and ^{13}C NMR spectral data, the CH_3 groups of the chelate ring are not equivalent.

The reaction of (Ia) and (Ib) with amino alcohols gives the aminooxy derivatives of 7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene, which contain an inner complex N→B bond and whose resistance to moisture and air depends on the structure of the amino alcohol.

Thus, in the case of monoethanolamine the air-stable 3-(β-aminoethoxy)-7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene (III) was obtained in 86-92% yield



(III)

R′=C_3H_5, CH_3O. Here and subsequently X = 

The inner complex character of compound (III) is confirmed by the IR spectrum, which has the bands of an NH_2 group, coordinated with the B atom: 3340, 3290, 3165 (on the background of a broad band, characteristic for an associated NH_2), and 1590 cm^{-1}; the spectrum

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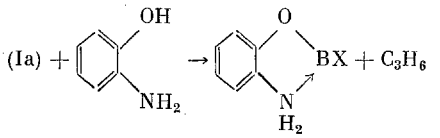
lacks the band of a free NH_2 group in the high-frequency portion of the spectrum (3500-3400 cm^{-1}) [6]. The following signals were detected in the PMR spectrum of (III) ($CHCl_3$, δ, ppm): 5.44 m (HC=C of bicycle), 3.33 s (CH_3O), and 2.88 br.t (CH_2N).

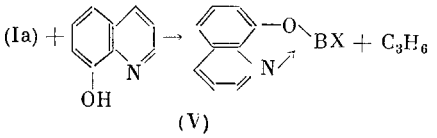
The reaction of (Ia) with o-aminophenol leads to the very air-unstable 3-(2-aminophenyloxy)-7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene (IV) in 92.5% yield:



(IV)

Previously it was mentioned on the example of diarylboric acid derivatives [7] that the o-aminophenol derivatives are less stable than the ethanolamine derivatives. The IR spectrum of (IV) has the bands of an associated NH_2 group: 3300, 3268 (on the background of a broad band), 3060, and 1575 cm^{-1}, and also the bands of the stretching vibrations of a free NH_2 group: 3500 and 1623 cm^{-1}, i.e., a mixture of the inner complex and open form of compound (IV) is probably formed. In the PMR spectrum of (IV) were recorded the signals ($CDCl_3$, δ, ppm) of the phenyl protons in the 6.56-7.20 region; 5.84 m (HC=C of bicycle), 5.26 br. (NH_2), 3.76 m (CH_2O), and 3.47 s (CH_3O).

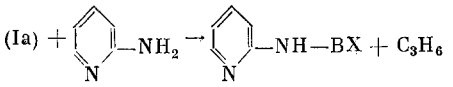
The reaction of (Ia) with 8-hydroxyquinoline proceeds easily at 20° and the stable inner complex 3-(quinolinyl-8-oxy)-7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene was obtained as yellow crystals in 89% yield.



(V)

The IR spectrum of (V) has bands that are characteristic for coordination compounds: 1590, 1623 cm^{-1} (quinoline ring). In the PMR spectrum ($CDCl_3$, δ, ppm) were detected the signals of 6 quinoline protons in the 8.25-6.73 region, and also at 4.87 m (HC=C of bicycle), 3.95 m (CH_2O) and 3.74 s (CH_3O).

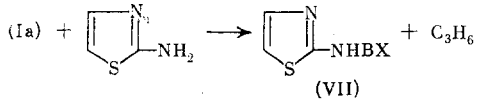
The reaction of (Ia) with 2-aminopyridine at 50-60° gave 3-(2-pyridylamino)-7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene (VI):



(VI)

The structure of (VI) is confirmed by the IR and PMR spectral data. The IR spectrum of (VI) (in CH_2Cl_2) resembles the IR spectra of the 2-pyridylaminodialkylboranes [8]; it has bands at 3385 cm^{-1} (NH group), 1630 cm^{-1} (C=N of pyridine), and also a band at 3450 cm^{-1}, caused by the partial hydrolysis of the compound. The PMR spectrum ($CDCl_3$, δ, ppm) has the signals: 8.16 m, 7.60-7.30 m, 6.90-6.60 m (pyridine protons and NH), 5.68 m (HC=C of bicycle), (ratio of intensities = 5.1:1.0), 3.72 m (CH_2O) and 3.17 s (CH_3O).

The reaction of (Ia) with 2-aminothiazole proceeds in a similar manner under somewhat more drastic conditions (80-90°), and 3-(2-thiazolylamino)-7-methoxymethyl-3-borabicyclo-[3.3.1]non-6-ene (VII) is obtained here:

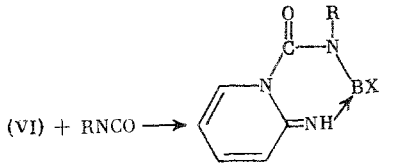


(VII)

The IR spectrum of (VII) (CH_2Cl_2) has a band of the NH group at 3370 cm^{-1} and a band at 3480 cm^{-1}, caused by the partial hydrolysis of the compound. The PMR spectrum has the signals ($CDCl_3$, δ, ppm): 7.07 d (J = 4 Hz) (H^5 of thiazole), 6.49 d (H^4 of thiazole + NH), 5.70 m (HC=C of bicycle), (ratio of intensities = 2.9:1.0), 3.68 m (CH_2O) and 3.19 s (CH_3O).

As was shown in [9, 10], the 2-pyridylaminoboranes react with unsaturated oxygen- and nitrogen-containing compounds (isocyanates, isothiocyanates, carbodiimides) to give cyclic chelates. It seemed of interest to obtain the chelates from the 2-pyridylamine derivatives

of 3-borabicyclo[3.3.1]non-6-ene with isocyanates and isothiocyanates. It proved that (VI) adds to the C=N bond of either phenyl or naphthyl isocyanate, with a tautomeric rearrangement of the 2-aminopyridine fragment of (VI) to the 2-pyridonimine fragment, and the chelates N_1-[N-(7-methoxymethyl-3-borabicyclo[3.3.3]non-6-en)-3-yl]-(N-phenylcarbamoyl)pyridon-2-iminate (VIIIa) or N_1-[N-(7-methoxymethyl-3-borabicyclo[3.3.1]non-6-en)-3-yl]-(N-α-naphthylcarbamoyl)-pyridon-2-iminate (VIIIb) are formed, in which the ligands are the 1-carbamoylpyridone-2-imines (in respective yields of 80 and 91.5%).



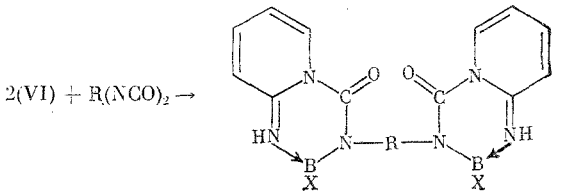
(VI) + RNCO →

(VIII)

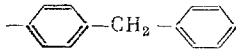
R = C_6H_5(a), α-$C_{10}H_7$(b).

The structure of (VIIIa) and (VIIIb) was confirmed by the spectral data. The IR spectra have ν C=N (1665 cm^{-1}) and ν C=O [1716 cm^{-1} for (VIIIa) and 1715 cm^{-1} for (VIIIb)], and the band of a coordinated NH [3360 cm^{-1} for (VIIIa) and 3365 cm^{-1} for (VIIIb)]. The following signals were recorded in the PMR spectra ($CDCl_3$, δ, ppm): (VIIIa) = 8.37-8.19 m, 7.61-6.94 m, 6.63-6.44 m, 6.27-6.07 m (pyridine and phenyl protons and NH), 5.96 m (HC=C of bicycle), and 3.25 s (CH_3O); (VIIIb) = signals in the 8.37-6.06 region (aromatic protons and NH), 5.97 m (HC=C of bicycle), and 3.48 s (CH_3O).

When (VI) is reacted with diisocyanates the (VI) adds to both O=C=N groups, and binary chelates (IX) or (X) are formed. (N,N'-hexamethylenyl-1,6)-di-[7-methoxymethyl-3-borabicyclo-[3.3.1]non-6-en-3-yl-(N-carbamoylpyridon-2-iminate)] is formed in 98% yield from hexamethylene diisocyanate, while chelate (X) was obtained in 75% yield by the reaction of (VI) with diisocyanodiphenylmethane:

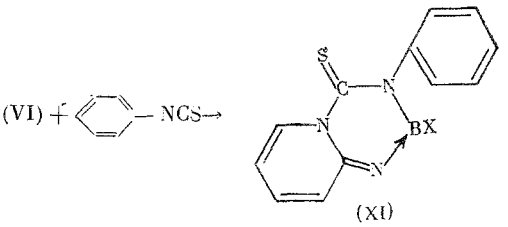


2(VI) + $R(NCO)_2$ →

R = $(CH_2)_6$ (IX),  (X)

The IR and PMR spectral data confirm the structure of (IX) and (X). The IR spectra have the distinct bands of C=N (1665 cm^{-1}) and C=O [1720 cm^{-1} for (IX), and 1715 cm^{-1} for (X)]. In the PMR spectra were found the signals ($CDCl_3$, δ, ppm): for (IX) 8.44-8.18 m, 7.14-5.85 m (pyridine protons and NH), 5.71 m (HC=C of bicycle), and 3.43 s (CH_3O); for (X) = signals of aromatic protons in 8.38-6.07 region, 5.95 m (HC=C of bicycle), 3.96 m (CH_2O), and 3.41 s (CH_3O).

In the case of phenyl isothiocyanate the reaction with (VI) leads to N_1-[N-(7-methoxymethyl-3-borabicyclo[3.3.1]non-6-en)-3-yl]-(N-phenylthiocarbamoyl)pyridon-2-iminate (XI).



(VI) + — NCS →

(XI)

Compound (XI) is unstable in the air. Its IR spectrum has a characteristic band at 1665 cm^{-1} (νC=N). In the PMR spectrum of (XI) ($CHCl_3$, δ, ppm) were detected the signals of aromatic protons, 5.47 m (HC=C of bicycle), 3.55 m (CH_2O), and 3.25 s (CH_3O).

EXPERIMENTAL

The operations were run in a dry argon atmosphere, and freshly distilled dry solvents were used. The PMR spectra were recorded on Varian DA-60-IL and Tesla BS 497-100 instruments, the ^{13}C NMR spectra were recorded on a Bruker WP-60 instrument, using TMS as the internal standard, the IR spectra were recorded on a UR-20 spectrometer, and the mass spectra were recorded on a Varian MAT CH-6 mass spectrometer, with direct insertion of the sample into the ion source, varying the temperature as a function of the volatility of the samples in the range 50-150°, and using an ionizing voltage of 70 eV and an emission current of 100 μA.

3-Allyl-7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene (Ia) was synthesized as described in [2], by the condensation of methoxypropyne with triallylborane at 130-140°. Yield 83.5%. The methanolysis of (Ia) leads to 3-methoxy-7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene (Ib) in 95% yield. ^{13}C NMR spectrum of (Ib) ($CDCl_3$, δ, ppm): 25.4, 26.0, 27.4, 29.5, 33.4, 35.2 (signals of C_{sp^3}, atoms of bicycle), 52.9 (CH_3OB), 5.69 (CH_3O), 77.2 (CH_2O), 131.4 (C^6), 131.7 (C^7). The PMR spectra of (Ia) and (Ib) have the signals: 5.58 d (HC=C of bicycle), 3.50 s (CH_3OB), and 3.10 s (CH_3O).

3-(4-Oxopent-2-en-2-yloxy)-7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene (II). With stirring, to 1.8 g of (Ia) at 20° was added in 5 min 1 g of acetylacetone, in which connection heat was evolved and the mixture turned yellow. The mixture was heated for 30 min at 85-90°, the low-boiling compounds were vacuum-distilled, and the yellow residue was recrystallized from pentane to give 1.9 g (82.6%) of (II) as pale yellow crystals, mp 54.5-55.5°. Found: C 68.85; H 8.79; B 4.11%. $C_{15}H_{23}BO_3$. Calculated: C 68.72; H 8.74; B 4.13; O 18.31%.

3-(β-Aminoethoxy)-7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene (III). To 2.1 g of (Ia) was added a solution of 0.9 g of ethanolamine in 6 ml of abs. benzene and the mixture was refluxed for 3 h, in which connection 190 ml of propylene (83% yield) was evolved. Then 3 ml of benzene was distilled off, the residue was cooled, and the obtained white precipitate was filtered and washed thrice with cold abs. ethanol. We obtained 2.05 g (92%) of chelate (III) with mp 115-116°.

In the case of (Ib) the reaction was run in toluene, and the methanol and toluene were distilled from the reaction mixture. We obtained (III) in 86% yield. Found: C 63.77; H 10.01; B 4.70%. $C_{12}H_{22}BNO_2$. Calculated: C 64.59; H 9.94; B 4.85%.

3-(2-Aminophenyloxy)-7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene (IV). To 1.03 g of (Ia) was added a solution of 0.55 g of 2-aminophenol in 10 ml of THF. The mixture was heated for 30 min at 60-65°, and here the calculated amount of propylene was evolved. The solvent was distilled off, the viscous residue was washed thrice with freshly distilled hexane, and the pale yellow crystals were dried in vacuo. We obtained 1.25 g (92.5%) of (IV), a substance that is very sensitive to moisture and air. Found: C 71.53; H 8.82; B 3.66%. $C_{16}H_{22}BNO_2$. Calculated: C 70.86; H 8.18; B 3.99%.

3-(Quinolinyl-8-oxy)-7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene (V). To a solution of 1.85 g of (Ia) in 2 ml of benzene at 20° was added 1.32 g of 8-hydroxyquinoline in 10 ml of benzene. Then the benzene was vacuum-distilled and the oily residue was dissolved in 15 ml of hexane at the boil. The mixture was then cooled and rubbed at −70°, followed by decantation, to give a bright yellow crystalline product, which was washed twice with chilled hexane. We obtained 2.45 g (89%) of (V), mp 77.5-78.5°. The chelate is stable in the air. Found: C 74.50; H 7.31; B 3.45%. $C_{19}H_{22}BNO_2$. Calculated: C 74.28; H 7.22; B 3.52%.

3-(2-Pyridylamino)-7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene (VI). With stirring, to 8.3 g of (Ia) was added a solution of 3.67 g of 2-aminopyridine in 20 ml of THF, after which the mixture was heated for 1 h at 50-60° until the propylene evolution ceased. The solvent was distilled off and the residue was distilled. We obtained 7.55 g (76%) of (VI) with bp 168-170° (0.5 mm). Found: C 70.59; H 8.40; B 4.34%. $C_{15}H_{21}BN_2O$. Calculated: C 70.33; H 8.26; B 4.22%.

3-(2-Thiazolylamino)-7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene (VII). To 3.55 g of (Ia) in 15 ml of THF was added a solution of 1.66 g of 2-aminothiazole in 12 ml of THF, and the mixture was heated at 80-90° until the propylene evolution ceased. The solvent was vacuum-distilled and the residue was distilled. We obtained 3.07 g (71%) of (VII), bp 170-180° (1 mm), mp 39-42°. Found: C 59.04; H 7.35; B 3.92; S 11.78%. $C_{13}H_{19}BN_2OS$. Calculated: C 59.55; H 7.30; B 4.13; S 12.33%.

N_1-[N-(7-Methoxymethyl-3-borabicyclo[3.3.1]non-6-en)-3-yl]-(N-phenylcarbamoyl)pyridon-2-iminate (VIIIa). To a solution of 2.3 g of (VI) in 5 ml of hexane at 20° was added a solution of 1.1 g of phenyl isocyanate in 3 ml of hexane. From the obtained bright yellow solution we isolated 2.6 g (80%) of (VIIIa) with mp 118-119°. The mass spectrum has the molecular ion $[M]^+$ with m/e 375 and the ion $[M-CH_3O]^+$ with m/e 344. Found: C 70.06; H 7.20; B 2.95%. $C_{22}H_{26}BN_3O_2$. Calculated: C 70.41; H 6.98; B 2.88%.

N_1- [N-(7-Methoxymethyl-3-borabicyclo[3.3.1]non-6-en)-3-yl]-(N-α-naphthylcarbamoyl)pyridon-2-iminate (VIIIb). The same as the preceding, from 1.4 g of (VI) and 0.85 g of α-naphthyl isocyanate we obtained 2.05 g (91.5%) of (VIIIb) with mp 144-145° (alcohol). In the mass spectrum was recorded the molecular ion $[M]^+$ with m/e 425 and the ion $[M-CH_3O]^+$ with m/e 394. Found: C 73.59; H 6.28; B 2.40%. $C_{26}H_{28}BN_3O_2$. Calculated: C 73.42; H 6.63; B 2.54%.

(N,N'-Hexamethylenyl-1,6)-di[7-methoxymethyl-3-borabicyclo[3.3.1]non-6-en-3-yl-(N-carbamoylpyridon-2-iminate)] (IX). To a solution of 2.1 g of (VI) in 10 ml of hexane at 20° was added a solution of 0.65 g of hexamethylene diisocyanate in 4 ml of hexane. After 10 h the obtained precipitate was filtered and dried in vacuo. We obtained 2.7 g (98%) of (IX) with mp 146-149°. Found: C 67.19; H 8.61; B 2.90%. $C_{38}H_{54}B_2N_6O_4$. Calculated: C 67.06; H 8.00; B 3.18%.

Chelate (X). To 2.25 g of (VI) at 20° was added a solution of 1.1 g of 4,4'-diisocyanodiphenylmethane in 10 ml of benzene and the mixture was let stand for a day. The yellow crystals were filtered, washed thrice with cold benzene, and dried in vacuo. We obtained 2.5 g (75%) of (X) with mp above 260°. Found: C 70.92; H 6.31; B 1.68%. $C_{45}H_{52}B_2H_6O_4$. Calculated: C 70.87; H 6.87; B 1.84%.

N_1-[N-(7-Methoxymethyl-3-borabicyclo[3.3.1]non-6-en)-3-yl]-(N-phenylthiocarbamoyl)pyridon-2-iminate (XI). To 1.7 g of (VI) in 10 ml of benzene at 20° was added 0.9 g of phenyl isothiocyanate and the mixture was let stand for a day. The benzene was vacuum-distilled using an oil pump, and the residue was treated five times with freshly distilled hexane. We obtained 2.1 g (83.5%) of viscous dark yellow (XI), which is decomposed by moisture and air. Found: C 68.29; H 7.54; B 2.67; S 7.76%. $C_{22}H_{26}N_3BOS$. Calculated: C 67.52; H 6.70; B 2.67; S 8.19%.

CONCLUSIONS

1. The reaction of 3-allyl-7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene and 3-methoxy-7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene with acetylacetone, monoethanolamine, 2-aminophenol, and 8-hydroxyquinoline gives, as a result of replacing the allyl or methoxyl group on the boron atim, the corresponding amino or hydroxy derivatives, which have an inner complex structure.

2. The reaction of 2-aminopyridine or 2-aminothiazole with 3-allyl-7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene gave the corresponding 2-pyridylamino- or 2-thiazolylamino-B-substituted compounds.

3. The reaction of 3-(2-pyridylamino)-7-methoxymethyl-3-borabicyclo[3.3.1]non-6-ene with isocyanates or phenyl isothiocyanate leads to chelates in which the ligands are 1-carbamoylpyridon-2-imine derivatives.

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