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Heteroaromatic Boron Compounds. XI. On the Nitration of 3,2-Borazaropyridines under Non-acidic Conditions

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Derivatives of 3,2-borazaropyridines, *i.e.* 6,7-dimethyl-7,6-borazarothieno[3,2-*c*]pyridine (IIa), 3,4-dimethyl-4,3-borazoisoquinoline (IVa) 2,3-dimethyl-4-ethyl-3,2-borazaropyridine (Ia) and 2,3-dimethyl-5-ethyl-3,2-borazaropyridine (Ib), were conveniently nitrated in high yield, when *N*-nitropicolinium tetrafluoroborate in acetonitrile was used as nitrating agent. Substitution occurred exclusively in the position α to the pyridinic nitrogen, except in Ib where 82 % of the 6-nitro and 18 % of the 4-nitro derivatives were formed. No oxidation of the $B-CH_3$ groups occurred. The nitro derivatives could be reduced to the corresponding amino derivatives, using hydrazine and palladium on charcoal.

It has previously been demonstrated that 3,2-borazaropyridines such as Ia and Ib [1,2] and their thiophene-fused derivatives (IIa) and (III),[3,4] from which they are prepared, are stable aromatic systems. They can be halogenated and nitrated.[1,2,4–6] In our previous investigations, fuming nitric acid in acetic anhydride-acetic acid was used as nitrating agent.[2,4] With this reagent IIa and III were nitrated in the boron-nitrogen containing ring (the 4-position of IIa and the 7-position of III, respectively), while Ia was nitrated in the 6-position and Ib gave a mixture of the 6- (predominantly) and the 4-nitro derivative.[2] The great disadvantage of this reagent was that it caused partial oxidation of the $B-CH_3$ groups to yield the $B-OH$ derivatives, which made purification and characterization more difficult. It was therefore of interest to find a milder and less oxidative nitrating agent. Dewar and von Rosenberg [7] attempted the nitration of 4-methyl-4,3-borazaroisoquinoline with nitronium tetrafluoroborate in tetramethylene sulfone, but could only recover starting material. However, Cupas and Pearson [8] reported in 1968 that *N*-nitro-pyridinium tetrafluoroborates could be used as nitrating agents for benzene and toluene. These authors recommended 2-picoline as pyridine base. It is possible that the failure in the nitration with nitronium tetrafluoroborate is due to complexation with the pyridinic nitrogen of the borazaropyridine and that this can be avoided by using the 2-picoline complex. The base strength of 2-picoline is much greater than that of borazaropyridines.[2] Our hope that borazaropyridines could be nitrated with *N*-nitro-2-picolinium tetrafluoroborate was also strengthened by the fact that the former compounds are smoothly brominated in pyridine-carbon tetrachloride.[6]

Our expectations were fulfilled, as 3,4-dimethyl-4,3-borazaroisoquinoline (IVa) [9] gave 3,4-dimethyl-1-nitro-4,3-borazaroisoquinoline (IVb) in 82 % yield as the only isomer. The structure was established by elemental analyses and oxidative degradation to benzoic acid. Dewar and von Rosenberg [7] have shown that under strongly acidic conditions (fuming nitric acid in conc. sulfuric acid), 4-methyl-4,3-borazaroisoquinoline is substituted in the benzene ring, yielding 8-nitro-4-methyl-4,3-borazaroisoquinoline. 6,7-Dimethyl-7,6-borazarothieno-[3,2-*c*]pyridine (IIa) with *N*-nitro-2-picolinium-tetrafluoroborate gave exclusively 6,7-dimethyl-4-nitro-7,6-borazarothieno[3,2-*c*]pyridine (IIb).

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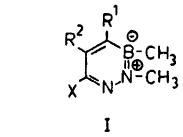
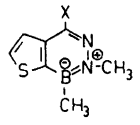


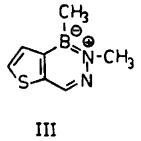
I

a. $R^1 = C_2H_5$; $R^2 = H$; X = H
b. $R^1 = H$; $R^2 = C_2H_5$; X = H
c. $R^1 = C_2H_5$; $R^2 = H$; $X = NO_2$
d. $R^1 = H$; $R^2 = C_2H_5$; $X = NO_2$
e. $R^1 = NO_2$; $R^2 = C_2H_5$; X = H
f. $R^1 = H$; $R^2 = C_2H_5$; $X = NH_2$

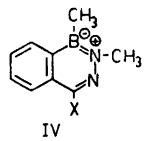


II

a. X = H
b. $X = NO_2$
c. $X = NH_2$



III



IV

a. X = H
b. $X = NO_2$

The structure followed directly from the NMR spectrum, as it still shows two thiophenic doublets, with the characteristic coupling constant of 5.0 Hz.[1a] Also 2,3-dimethyl-4-ethyl-3,2-borazaropyridine (Ia) gave only one nitro derivative, which by NMR was shown to be 2,3-dimethyl-4-ethyl-6-nitro-3,2-borazaropyridine (Ic). Compared to the parent compound,[2] the 5-hydrogen resonance is shifted 0.97 ppm towards lower field, which is of the expected order for nitro-caused *ortho* shifts in aromatic systems.[10] An assignment of the structure to the 5-nitro isomer would lead to an unreasonable *ortho*-nitro-caused shift of 0.12 ppm.

The nitration of Ib led, according to combined GLC-mass spectrometry, to two mononitro derivatives. It was not possible to separate these isomers by fractional distillation. NMR spectrometry showed that the mixture consisted of 80 % of 2,3-dimethyl-5-ethyl-6-nitro-3,2-borazaropyridine (Id) and 20 % of 2,3-dimethyl-5-ethyl-4-nitro-3,2-borazaropyridine (Ie). The structure assignments could easily be carried out with the aid of chemical shift considerations, as mentioned above. In addition, the 6-nitro isomer could also be identified by the presence of the characteristic long-range coupling $J_{CH_3\text{-}H\text{-}4}$.[2]

It is thus evident that for nitration, as well as for bromination [6] under non-acidic conditions, the order of reactivity of the three carbon positions of 3,2-borazaropyridine is $6 > 4 \gg 5$. It also appears that nitration is somewhat more selective than bromination. A more detailed discussion of the possible mechanisms of these substitution reactions will be given in a following, paper where also some other examples of substitution reactions will be presented.

No nitro derivatives were obtained when the isoelectronic 2,3,4-trimethyl- and 2,3,5-trimethylpyridine were reacted with *N*-nitro-2-picolinium tetrafluoroborate under the same conditions. However, as starting material was not recovered it is probable that ring-opening to glutacone aldehyde derivatives occurred, similar to that described by Olah and coworkers [11] for the reaction of *N*-nitropyridinium fluoroborate with excess pyridine.

The nitro derivatives described above could be transformed to amino derivatives, which constitute starting materials of great utility. We found that hydrazine in the presence of palladium on charcoal,[12,13] which has also been used by Dewar and Kubba [14] for the reduction of various nitro-9,10-borazaraphenantrenes, was an excellent reagent for this purpose. Thus IIb gave 4-amino-6,7-dimethyl-7,6-borazarothieno-[3,2-c]pyridine (IIc) in high yield. It is also interesting to note that the mixture of Id and Ie gave pure 6-amino-2,3-dimethyl-5-ethyl-2,3-borazaropyridine (If) in 52 % yield. This could indicate that 4-amino-2,3-dimethyl-5-ethyl-3,2-borazaropyridine is an unstable compound, which decomposed after formation. For comparative purposes 6-nitro-2,3,5-trimethylpyridine [2] was also reduced to the 6-amino derivative.

EXPERIMENTAL

6,7-Dimethyl-4-nitro-7,6-borazarothieno[3,2-c]-pyridine (IIb). 1.32 g (0.010 mol) of nitronium tetrafluoroborate (weighed under dry nitrogen atmosphere in a glove box) was suspended in 20 ml of dry acetonitrile under nitrogen. To this mixture, 0.93 g (0.010 mol) of dry 2-picoline, distilled over barium oxide and stored over molecular sieves, was addded dropwise. The pale yellow solution, maintained at about 0 °C, was pressed into a dropping funnel by dry nitrogen. The solution of *N*-nitro-picolinium tetrafluoroborate was added dropwise to a stirred solution of 1.04 g (0.010 mol) of 6,7-dimethyl-7,6-borazarothieno[3,2-c]pyridine [2] in 20 ml of dry acetonitrile, at 0 °C. When the addition was complete,

the cooling bath was removed and the mixture was allowed to reach room temperature. The mixture was then stirred for an additional 4 h. The solvent was removed under reduced pressure and to the remaining red-brown crystalline cake water was added. The water solution was extracted four times with ether. The combined ether fractions were dried and the ether removed under reduced pressure. The resulting crystalline cake was recrystallized from 60 % ethanol-water. These crystals contained about 10 % of starting material according to GLC. A second recrystallization gave analytically pure material as white needles. Yield: 1.42 g (68 %) of the title compound. M.p. 129.0–131.0 °C. NMR [$(CD_3)_2CO$]: δ 8.23 and 7.93 (thioph., $J_{2,3}$ 5.0 Hz), 3.87 (NCH_3), 1.05 (BCH_3). [Found: C 40.12; H 3.90; B 5.11; N 20.14; S 15.46. Calc. for $C_7H_8BN_3O_2S$ (209.0): C 40.22; H 3.86; B 5.17; N 20.10; S 15.33.]

3,4-Dimethyl-1-nitro-4,3-borazaroisoquinoline (IVb). 1.58 g (0.010 mol) of 3,4-dimethyl-4,3-borazaroisoquinoline [9] was treated with *N*-nitropicolinium tetrafluoroborate as described above. The mixture was worked up according to the procedure above. The crude product (2.33 g) was recrystallized from 50 % ethanol-water, leaving 1.66 g (82 %) of the title compound; m.p. 152–153 °C. NMR [$(CD_3)_2CO$]: δ 8.08 (m, arom.), 3.80 (NCH_3), 1.07 (BCH_3). [Found: C 53.56; H 5.08; B 5.13; N 20.21. Calc. for $C_9H_{10}BN_3O_2$ (203.0): C 53.25; H 4.97; B 5.32; N 20.70.]

Degradation of the nitro product. 3,4-Dimethyl-1-nitro-4,3-borazaroisoquinoline (IVb) was oxidized with $KMnO_4$ in alkaline medium as described for 1-bromo-4-methyl-4,3-borazaroisoquinoline.[15] This oxidation gave after work-up 35 % of benzoic acid identical with authentic material.

2,3-Dimethyl-4-ethyl-6-nitro-3,2-borazaropyridine (Ic). 1.36 g (0.010 mol) of 2,3-dimethyl-4-ethyl-3,2-borazaropyridine was treated with *N*-nitropicolinium tetrafluoroborate as described above. The mixture was worked up according to the procedure above. The crude product was fractionated, yielding 1.05 g (58 %) of the title compound; b.p. 79–82 °C/2 mmHg. NMR ($CDCl_3$): δ 1.20 (CH_3CH_2), 2.70 (CH_3CH_2), 3.85 (NCH_3), 7.88 (H-5), 0.86 (BCH_3). [Found: C 46.54; H 6.79; B 5.80; N 23.09. Calc. for $C_7H_{12}BN_3O_2$ (181.0): C 46.45; H 6.68; B 5.97; N 23.21.]

2,3-Dimethyl-5-ethyl-6-nitro-3,2-borazaropyridine (Id) and 2,3-dimethyl-5-ethyl-4-nitro-3,2-borazaropyridine (Ie). 1.36 g (0.010 mol) of 2,3-dimethyl-5-ethyl-3,2-borazaropyridine [2] was treated with *N*-nitropicolinium tetrafluoroborate as described above. The mixture was worked up according to the procedure above. The crude product contained two isomers according to combined GLC-mass spectroscopy in the proportion 18:82. NMR showed that 20 % consisted of 2,3-dimethyl-5-ethyl-4-nitro-3,2-borazaropyridine (Ie) and 80 % of 2,3-dimethyl-5-ethyl-6-nitro-3,2-borazaropyridine (Id). Fractional distillation gave 1.16 g (64 %) of a mixture of Id and Ie; b.p. 74–77 °C/1.8 mmHg. NMR ($CDCl_3$) of Id: δ 1.21 (CH_3CH_2), 2.63 (CH_3CH_2), 3.73 (NCH_3), 7.18 (H-4), 0.78 (BCH_3), J_{CH_2-H-4} 1.0 Hz. NMR ($CDCl_3$) of Ie: δ 1.21 (CH_3CH_2), 2.63 (CH_3CH_2), 3.80 (NCH_3), 7.92 (H-6), 0.72 (BCH_3). [Found: C 46.50; H 6.73; B 5.86; N 23.16. Calc. for $C_7H_{12}BN_3O_2$ (181.0): C 46.45; H 6.68; B 5.97; N 23.21.]

4-Amino-6,7-dimethyl-7,6-borazarothieno[3,2-c]pyridine (IIc). 3.35 g (0.016 mol) of 6,7-dimethyl-4-nitro-7,6-borazarothieno[3,2-*c*]pyridine (IIb) was dissolved in 100 ml abs. ethanol and 0.5 g of palladium (10 %) on charcoal was added. The mixture was refluxed and stirred and 10 ml of hydrazine hydrate (99–100 %) carefully added. During this addition, the reaction became rather exothermic and the yellow colour of the solution disappeared. After the addition of hydrazine hydrate the reaction mixture was refluxed for 30 min. After cooling, the catalyst was filtered off and washed with abs. ethanol. The solvent was evaporated and the residue was extracted with ether. The combined ether fractions were dried over magnesium sulfate and the ether was evaporated. The residue, a white crystalline cake, was recrystallized from 30 % ethanol-water. Yield after recrystallization: 2.4 g (84 %) of the title compound; m.p. 121.0–122.0 °C. NMR ($CDCl_3$): δ 7.68 and 7.47 (thioph., $J_{2,3}$ 4.8 Hz), 3.58 (NCH_3), 0.85 (BCH_3). [Found: C 47.00; H 5.67; N 23.38; B 5.99. Calc. for $C_7H_{10}N_3BS$ (179.0): C 46.96; H 5.63; N 23.47; B 6.04.]

6-Amino-2,3-dimethyl-5-ethyl-3,2-borazaropyridine (If). 1.81 g (0.010 mol) of 2,3-dimethyl-5-ethyl-6-nitro-3,2-borazaropyridine (Id) (containing 18 % of the 4-isomer) was dissolved in 100 ml of abs. ethanol, and 0.25 g of palladium (10 %) on charcoal was added. The mixture was treated as mentioned above and 6 ml of hydrazine hydrate was added. The mixture was worked up according to the last procedure. The crude product was distilled at reduced pressure; b.p. 69–72 °C/1 mmHg. The product crystallized in the receiver. GLC (BDS 10 %, 90–200 °C 10°/min) showed only one peak in addition to solvent. The product was recrystallized from 10 % ethanol-water, yielding 0.79 g (52 %) of the title compound, m.p. 70.0–71.5 °C. NMR ($CDCl_3$): δ 1.22 (CH_3CH_2), 2.41 (CH_3CH_2), 3.50 (NCH_3), 6.78 (H-4), 0.62 (BCH_3), 3.67 (NH_2), J_{CH_2-H-4} = 1.0 Hz. [Found: C 55.54; H 9.42; N 27.76; B 7.18. Calc. for $C_7H_{14}N_3B$ (151.0): C 55.67; H 9.34; N 27.82; B 7.26.]

6-Amino-2,3,5-trimethylpyridine. 1.00 g (0.006 mol) of 6-nitro-2,3,5-trimethylpyridine was dissolved in 150 ml of ethanol. To this solution 0.2 g of palladium (10 %) on charcoal and 10 ml of hydrazine hydrate were added as described above. The mixture was worked up as described above. The crystalline product was recrystallized from ligroin (80–120 °C), yielding 0.81 g (99 %) of the title compound, m.p. 105.0–

105.5 °C. NMR ($CDCl_3$): δ 6.98 (H-4), 4.38 (NH_2), 2.05, 2.10 and 2.30 [CH_3(2,3,5)]. [Found: C 70.4; H 9.0; N 20.7. Calc. for $C_8H_{12}N_2$ (136.2): C 70.55; H 8.88; N 20.57.]

GLC analyses were carried out with a Varian model 1400 gas chromatograph. NMR spectra were recorded with a Varian A 60 NMR spectrometer and mass spectra were obtained with a LKB A-9000 mass spectrometer. Elemental analyses were carried out by Dornis und Kolbe, Mikroanalytisches Laboratorium, Mülheim/Ruhr.

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