Tetrahedron Letters No.26, pp. 2967-2970, 1966. **Pergamon Press Ltd.**
Printed in Great Britain.

ON THE NITRATION AND BROMINATION OF 4-METHYL-4,5-BORAZAROTHIENO[2,3-c]PYRIDINE

Salo Gronowitz* and Johannes Namtvedt
Chemical Institute, University of Oslo, Norway

(Received 25 April 1966)

A recent publication by Dewar and Rosenberg (1) on the bromination and nitration of 4-methyl-4,3-borazaroisoquinoline (I) has prompted us to report our results on the bromination and nitration of the thiophene analogue of I, 4-methyl-4,5-borazarothieno[2,3-c]pyridine (IIa; $R=CH_3$, $R'=H$). This is only a small part of our work on the synthesis and reactions of new heteroaromatic boron compounds of type II and III, the result of which will be published elsewhere.

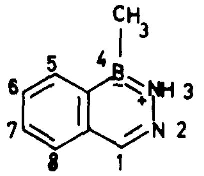
IIa was obtained in 82 % yield by refluxing 4-hydroxy-4,5-borazarothieno[2,3-c]pyridine (2) (IIb; $R=OH$, $R'=H$) with butyl alcohol using a Dean-Stark trap, removing excess butyl alcohol in vacuo and reacting the remaining butyl ester dissolved in ether with an excess of methyl magne-

---

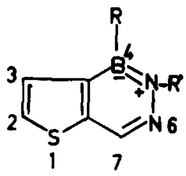
* Present address: Chemical Institute, University of Lund, Lund, Sweden.

sium iodide. Pale yellow needles from ethanol/water, m.p. 62-63°C. Anal. Calcd. for $C_6H_7BN_2S$: C 48.04; H 4.71; N 18.67. Found C 48.07; H 4.57; N 18.87.

Dewar and Rosenberg (1) claim that bromination and nitration of I occurs in the 8-position of the benzenic ring. Their proof consists of NMR-spectroscopical data, which, due to the complex pattern of the phenyl hydrogen resonances, is not too easily interpreted. On the other hand, the claim that the bromination product of I gives orthobromobenzoic acid upon oxidation with alkaline permanganate strengthens their structure proposals, although the possibility for rearrangements during reactions should be kept in mind.

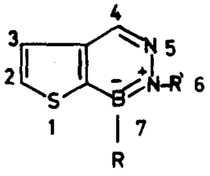


I

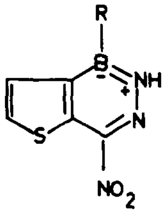


IIa R=CH_3, R'=H

IIb R=OH, R'=H



III



IVa R=CH_3

IVb R=OH

We found that bromination and nitration of IIa led to substitution in the 7-position of the boron-nitrogen containing ring. The evidence is quite clear cut. The NMR-spectrum of IIa in dimethyl sulphoxide is completely resolved, showing the NH resonance at -1.45 τ, the 7-hydrogen resonance at 1.38 τ, and the two thiophenic hydrogen resonances occurring as doublets at 2.11 τ and 2.49 τ with a coupling of 5.0 c/s characteristic of 2,3-disubstituted thiophenes (3). Finally, the B-CH_3 resonance occurs at 9.10 τ. Bromination of IIa in acetic acid at room temperature yielded in 47 % 7-bromo-4-methyl-4,5-borazarothieno[2,3-c]-pyridine, m.p. 115-122°. Anal. Calcd. for $C_6H_6BBrN_2S$: C 31.48; H 2.64; N 12.23. Found C 30.73; H 2.61; N 11.88.

In the NMR-spectrum (DMSO) of this product the 7-hydrogen resonance has disappeared, but the two thiophenic resonances are present and appear again as doublets with a coupling of 5.1 c/s at 1.91 τ and 2.18 τ. The NH resonance appears at -1.65 τ and the B-CH_3 resonance at 9.10 τ. Chemical proof was obtained by oxidation at 0°C with alkaline potassium permanganate, which yielded 2-carboxy-3-thiopheneboronic acid identical with an authentical sample (4). On heating with 2 N sodium hydroxide the 2-carboxy-3-thiopheneboronic acid was transformed to 2-thiophenecarboxylic acid. The combined physical and chemical evidence, thus, leave no doubt that the brominated product is 7-bromo-4-methyl-4,5-borazarothieno[2,3-c]-pyridine.

Nitration of IIa in acetic acid with fuming nitric acid in acetic anhydride at room temperature yielded two products which were separated through fractionated crystallisation from ethanol. One was 4-methyl 7-nitro-4,5-borazarothieno[2,3-c]pyridine (IVa) obtained as yellow needles, m.p. 230-234°C. Calcd. for $C_6H_6BN_3O_2S$: C 36.95; H 3.10; N 21.54. Found C

37.13; H 3.03; N 21.42. The other compound was 4-hydroxy-7-nitro-4,5-borazarothieno[3,2-c]pyridine (IVb), identical (IR) with the product obtained in the nitration of IIb under the same conditions. The NMR-spectrum (DMSO) of both compounds showed the absence of the 7-hydrogen and the presence of two thiophenic hydrogens (IVa: $\tau_{2,3}$ 1.80, 2.20; J_{23} = 5.1 c/s, τ_{NH} = -2.18, τ_{B-CH_3} = 8.97, IVb: $\tau_{2,3}$ 1.95, 2.17, J = 5.2 c/s, τ_{NH} = -1.33). Further evidence is obtained from the fact that IVb upon alkaline hydrolysis yields 2-thiophenecarboxylic acid confirming that the nitro group is in the 7-position.

That I and IIa have different substitution pattern is of some interest, for it is very seldom observed in a condensed ring-system where substitution occurs in the benzenic ring-part, that change to a thiophene analogue could cause reaction to occur in the less reactive ring. We are pursuing our investigations in this field.

NMR-spectra were recorded on a Varian A-60 spectrometer. The authors are indebted to Dr. Anna-Britta Hörnfeldt for recording the NMR-spectra.

REFERENCES

1. M.J.S. Dewar and J.L. von Rosenberg, J. Amer. Chem. Soc. **88**, 358 (1966).
2. S. Gronowitz and A. Bugge, Acta Chem. Scand. **19**, 1271 (1965).
3. R.A. Hoffman and S. Gronowitz, Arkiv Kemi **16**, 563 (1960).
4. S. Gronowitz and A. Bugge, Acta Chem. Scand. **20**, 261 (1966).