When fresh pepsin was added to the material which gave the pattern *c* and the mixture kept at +40°C, the pattern changed successively to *d* (after 30 min), *e* (60 min), and *g* (120 min). Finally a pattern A-G similar to that of soluble collagen was obtained.

The *y*-fractions were in some cases very large and differed clearly from the *x*-fractions, which correspond to the *γ*- and *δ*-fractions mentioned previously by several authors.[6] The *y*-fractions become less prominent after continued action of pepsin but their mobility does not change. These fractions deserve special attention because they contain the intermolecular linkages of insoluble collagen within the soluble aggregates of tropocollagen.

Fig. 2 shows schematically the progress of degradation of soluble collagen as revealed by the starch gel-electrophoretic patterns. In the denatured peptide chains there seem to be certain linkages which are broken almost immediately after the addition of pepsin. Further degradation occurs first after a definite time interval. Most interesting to us seem the fractions which are constant (A, B-C) and those which migrate close to the original components (D,E,F,G). From preliminary gel-filtration experiments we know that the particle weights of the latter fractions are between those of albumin and the α-chains of collagen. The fractions designated α1′ and α2′ are believed to resemble the α-chains; *cf.* Ref. 7.

Acknowledgements. This work is a part of a program supported by institutional grants from the *U.S. Department of Agriculture*, Foreign Research and Technical Programs Division, and from the *Sigrid Jusélius Foundation.*

1. Penttinen, R., Kari, A. and Kulonen, E. *Acta Chem. Scand.* **20** (1966) 1304.
2. Heikkinen, E. and Kulonen, E. *Acta Physiol. Scand.* (1966). *In press.*
3. Näntö, V., Maatela, J. and Kulonen, E. *Acta Chem. Scand.* **17** (1963) 1604.
4. Näntö, V., Pikkarainen, J. and Kulonen, E. *J. Am. Leather Chemists' Assoc.* **60** (1965) 63.
5. Kulonen, E., Hollmén, T., Näntö, V. and Pikkarainen, J. In *Structure and Function of Connective and Skeletal Tissue*, (Ed. by S. Fitton-Jackson *et al.*), Butterworths, London 1965, p. 216.
6. Veis, A. and Anesey, J. *J. Biol. Chem.* **240** (1965) 3899.
7. Kühn, K. and Eggl, M. *Biochem. Z.* **344** (1966) 215.

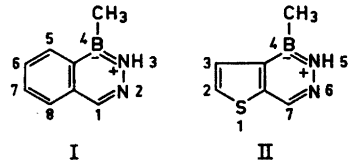
Received May 23, 1966.

On the Structure of the Bromination Product of 4-Methyl-4,3-borazaroisoquinoline

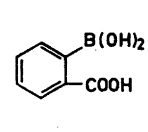
JOHANNES NAMTVEDT and SALO GRONOWITZ*

Chemical Institute, University of Oslo, Oslo, Norway

In a recent publication by Dewar and von Rosenberg [1] it is claimed that the bromination and nitration of 4-methyl-4,3-borazaroisoquinoline (I) occurs in the 8-position of the benzenic ring. On the other hand the present authors have found that the thiophene analogue of (I), 4-methyl-4,5-borazarothieno[2,3-c]pyridine (II) is brominated and nitrated in the 7-position of the boron-nitrogen containing ring.[2] Our structural proof was based on completely resolved NMR-spectral data and on chemical degradation.



III



IV

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

The different substitution pattern of I and II is rather unexpected, for it is very seldom, if at all, 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 have therefore reinvestigated the structure of the bromination product of I. Dewar's and von Rosenberg's main evidence for the structure of the bromination product of I was that oxidation with alkaline permanganate followed by acidic hydrolysis yielded *ortho* bromobenzoic acid. Furthermore quantum chemical calculations indicated that the 8-position should be most reactive followed by the 5-position. The NMR-spectra of the bromination product, published by Dewar and von Rosenberg, give no indication of its structure due to the complex pattern of the phenyl hydrogen resonances. However, a route is possible through which *ortho* bromobenzoic acid could be derived from the 1-bromo derivative (III). During the acidic hydrolysis, excess permanganate and also manganese dioxide could oxidize the bromine ion formed to free bromine, which then rapidly gives *ortho* bromobenzoic acid in the bromodeboronation reaction with *ortho* carboxybenzeneboronic acid (IV).

We found when excess permanganate was destroyed by ethanol and the manganese dioxide filtered off, followed by alkaline hydrolysis to complete deboronation, *benzoic acid* was isolated. We could also confirm that *ortho* bromobenzoic acid was indeed isolated when the oxidation was carried out according to Dewar and von Rosenberg.

It appears therefore highly probable that the bromination product of I is 1-bromo-4-methyl-4,3-borazaroisoquinoline (III) and not the 8-isomer.

With regard to the nitration product of I, the NMR-spectrum published by Dewar and von Rosenberg could possibly be interpreted to be that of the 8-isomer. It is not unusual in isoquinoline that electrophilic aromatic substitution occurs in different positions. While sulfonation and nitration occurs mainly at position 5, bromination and mercuration takes place mainly at position 4. However, due to some inconsistencies between figure and text in their paper, it is difficult to come to a definite conclusion.

In regard to the above mentioned results the structure of the nitration product of I should therefore also be reinvestigated.

Experimental. Bromination of 4-methyl-4,3-borazaroisoquinoline[3] according to the procedure of Dewar and von Rosenberg yielded 74 % of 1-bromo-4-methyl-4,3-borazaroisoquinoline, m.p. 130–131°C. (Literature value: yield 84 %, m.p. 133–134°C).

Degradation of the bromination product. To a suspension of 0.30 g of the bromination product in 50 ml of 1 N sodium hydroxide solution was added at 0°C 1.2 g of potassium permanganate in small portions. After stirring at 0°C for 3 h, excess potassium permanganate was destroyed by addition of ethanol. The mixture was filtered and the filtrate acidified to pH 1 with 2 N sulfuric acid, and extracted with ether. The ether solution was dried and evaporated *in vacuo*. The residue was refluxed for 2 h with 50 ml of 2 N sodium hydroxide solution, acidified to pH 1 with 2 N sulfuric acid and extracted with ether. The ether solution was dried and evaporated *in vacuo* yielding 0.050 g (30 %) of benzoic acid with an IR-spectrum identical to that of an authentic sample. M.p. after recrystallization from water 115–119°C.

Following the oxidation procedure of Dewar and von Rosenberg in detail yielded 27 % of *ortho* bromobenzoic acid with an IR-spectrum identical to that of an authentic sample. M.p. 145–148°C after recrystallization from benzene and sublimation.

1. Dewar, M. J. S. and von Rosenberg, Jr., J. L. *J. Am. Chem. Soc.* **88** (1966) 358.
2. Gronowitz, S. and Namtvedt, J. *Tetrahedron Letters.* **1966** 2967.
3. Dewar, M. J. S. and Dougherty, R. C. *J. Am. Chem. Soc.* **86** (1964) 433.

Received June 1, 1966.