

RING FISSIONS DURING REACTIONS OF AMINOBROMOISOQUINOLINES

WITH POTASSIUM AMIDE IN LIQUID AMMONIA (1)

Formation of 1-cyanoisocindole from 3-amine-4-bromoisoquinoline

Georgine M.Sanders, M.van Dijk and H.J.den Hertog

(Laboratory of Organic Chemistry of the Agricultural University, Wageningen, the Netherlands)

(Received in UK 2 October 1972; accepted for publication 11 October 1972)

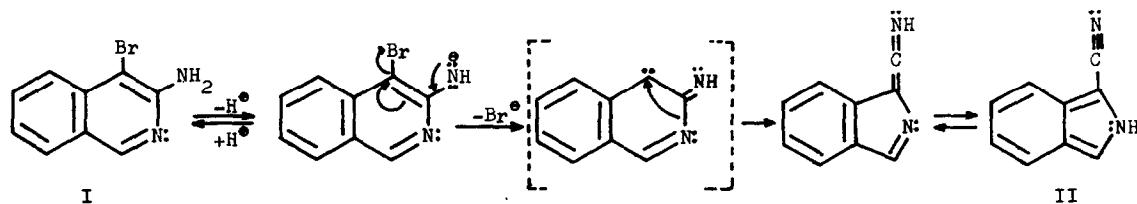
When investigating reactions of halogeno derivatives of isoquinoline with potassium amide in liquid ammonia under conditions as used previously (2), we found that 3-amine-1-bromoisoquinoline and 1-amino-3-bromoisoquinoline (m.p. 182-183°C) change rapidly and in high yield into o-cyanobenzyl cyanide (3). These reactions affirm the course of the ring fission in 2-amino-6-bromopyridine, yielding 1,3-dicyanopropene in poor yield only (4).

4-Amine-3-bromoisoquinoline (m.p. 140-141°C) is converted into o-cyanobenzyl isocyanide in excellent yield analogously to the amination of 3-amine-2-bromoquinoline producing o-cyanomethylphenyl isocyanide and as a secondary product 3-cyanoisocindole (2).

An interesting new type of ring transformation was found with 3-amine-4-bromoisoquinoline (I), which was converted into 1-cyanoisocindole (II).

Upon reacting 4 mmoles of I with 20 mmoles of KNH_2 in 100 ml liquid NH_3 for 24 h, two main products were obtained in moderate yields, i.e. 3-amineisoquinoline and a slightly brownish crystalline substance (m.p. 125-132°C, dec.). The latter compound was shown to be II on account of its reaction with Ehrlich's reagent, its PMR, IR, UV and M spectrum; the spectroscopic properties agree well with these published recently (5), our measurements also indicating the absence of the tautomeric isocindolenine form in benzene and chloroform.

The type of ring transformation found with I is unprecedented, 2-amine-3-bromopyridine and 2-amine-3-bromoquinoline reacting via an EA mechanism (6,2) and 2-amine-3-bromo-4-methylpyridine (m.p. 119-120°C) remaining practically unchanged when reacted for 48 h. Direct evidence for the mechanism of the conversion I-II lacking, the subsequent route shewing some relation to the Welff rearrangement (7) is suggested:



A similar mechanism has been proposed by Reelfsema for the conversion of 2-bromo-3-hydroxypyridine into pyrrole-2-carboxamide (8). In this connection we also point to the fact that 1-amine-4-bromoquinoline (m.p. 150-151°C) was not converted by KNH_2 in liquid NH_3 in 6 h, a similar rearrangement being possibly prevented due to the position of the two substituents.

The formation of 3-aminopyridine from I was not unexpected as we had found previously that bromine at C-4 is rather easily removed in the basic medium, c.f. the conversion of 4-bromoquinoline into isoquinoline (together with 4,4'-biisoquinoline, 1-amine-4,4'-biisoquinoline, 1-aminopyridine and 1-amine-4-bromoquinoline) in 10 min (3). The formation of isoquinoline and the dimeric compounds in this case is thought to occur, probably partly by a radical anion mechanism (9), via a C-4 carbanion, arising from Br^\ominus abstraction by the amide ion. Thus, it seems likely that the dehalogenation of I occurs in the same way via a C-4 carbanion but is slowed down considerably due to the fact that most of the starting material is present as $\text{R-NH}^\ominus \text{K}^\oplus$ in the strongly basic medium.

Acknowledgement We are indebted to Dr.P.Smit and Mr.A.van Veldhuizen for the interpretation and recording of the PMR and IR spectra, to Drs.C.A.Landheer for determination of the mass spectra and to Mr.W.P.Combé for carrying out the microanalyses.

References

- (1) Part XXIX in the series Ring Transformations; part XXVIII from this laboratory: P.J.Lent and H.C.van der Plas, *Rec.Trav.Chim.Pays-Bas*, in press.
- (2) H.J.den Herteg and D.J.Buurman, *Rec.Trav.Chim.* 91, 841 (1972).
- (3) The detailed results of our investigations will shortly be published in *Rec.Trav.Chim.Pays-Bas*.
- (4) J.W.Streef and H.J.den Herteg, *Rec.Trav.Chim.* 88, 1391 (1969).
- (5) R.F.C.Brown and R.J.Smith, *Aust. J.Chem.* 25, 607 (1972).
- (6) J.W.Streef and H.J.den Herteg, *Rec.Trav.Chim.* 85, 803 (1966).
- (7) W.Kirmse, "Carbene, Carbeneide, Carbenanaloge", Verlag Chemie, 1969, p. 166.
- (8) W.A.Reelfsema, Thesis, Wageningen 1972, p. 34.
- (9) J.F.Garst and J.T.Barbas, *Tetrahedron Letters* 1969, 3125.