Ring Transformation of 8-Bromo-1,7-phenanthroline in Reaction with Potassium Amide/Liquid Ammonia

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Reaction of 8-bromo-1,7-phenanthroline with potassium amide in liquid ammonia gives besides the corresponding 8-amino compound 2-methyl-1,3,5-triazaphenanthrene. In this ring transformation 7-ethynylaminoquinoline-8-aldimine is involved as intermediate, as proved by nmr spectroscopy.

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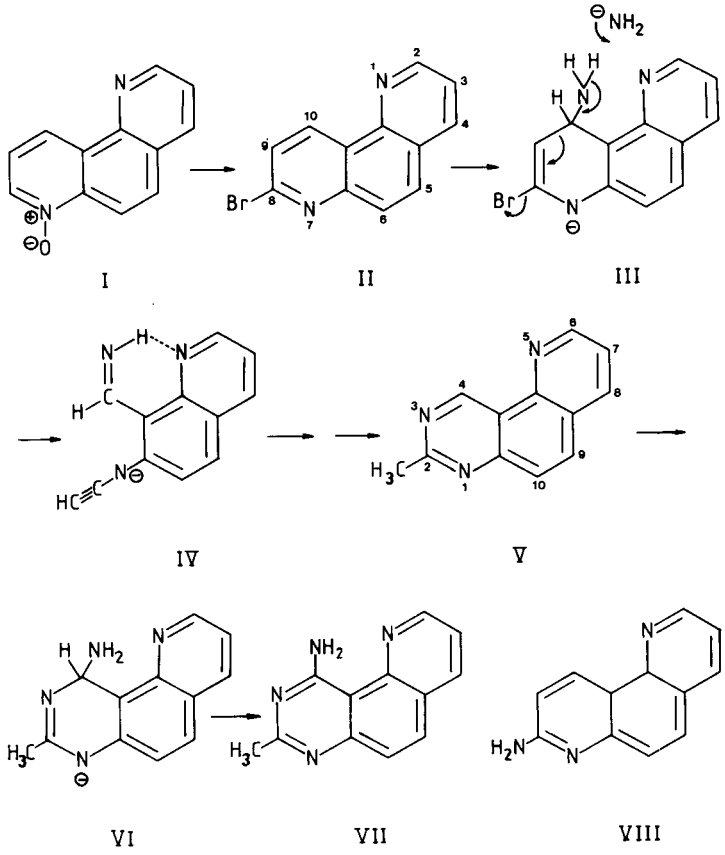
Our ongoing interest in the occurrence of telesubstitutions (3) in heterocyclic aryl halides induced us to study the behaviour of 8-bromo-1,7-phenanthroline (II) towards potassium amide in liquid ammonia. Compound II was prepared by reaction of 1,7-phenanthroline 7-oxide (I) with acetic anhydride and subsequent treatment of the product with phosphorus oxybromide. Reaction of II with potassium amide/liquid ammonia for 4 hours gave no trace of a telamination product, but nearly exclusively ring transformation products, *i.e.*, 2-methyl-1,3,5-triazaphenanthrene (V) and a trace of its 4-amino derivative VII, together with some 8-amino-1,7-phenanthroline (VIII). The latter was identical to the product obtained by reaction of II with ethanolic ammonia.

The structure of V could unequivocally be assigned from its nmr spectrum. Alongside the expected chemical shifts and splitting patterns of H−6, H−7, H−8, H−9 and H−10 (see the experimental part) a singlet at a very low field (δ = 10.44 ppm, 1−H, H−4) and a singlet at a high field (δ = 2.96 ppm, 3−H, CH_3) were detected. They are characteristic of the presence of the 2-methyl group and the pyrimidine ring in V.

Compound V crystallizes with 1 mole of water. The nmr spectrum in deuteriochloroform shows that this molecule of water has not been added to the 3,4−C=N bond, forming a covalent hydrate. However, in an aqueous solution of deuterio sulfuric acid V easily undergoes covalent hydration, as shown by nmr spectroscopy, analogous to the covalent hydration reported for quinazoline (4). As a consequence of the rehydridization of C−4, ($sp^2 \rightarrow sp^3$) H−4 had undergone an upfield shift of 3.32 ppm (see the experimental part). When dissolving V in potassium amide/liquid ammonia, σ-adduct formation took place at position 4, leading to the anion of 4-amino-2-methyldihydro-1,3,5-triazaphenanthrene (VI), as indicated by the occurrence of a triplet at 6.21 ppm showing that H−4 has undergone a large upfield shift of $\Delta\delta$ = 4.23 ppm (see experimental). Oxidation of VI with potassium permanganate — a procedure which has been described previously (5,6) for converting amino σ-adducts into amino compounds gave VII.

The mechanism of the ring transformation of II into V can be described to occur by an initial attack of the amide



anion at C−10 of II, leading to 10-amino-8-bromodihydrophenanthrolinide (III). Ring opening as indicated gave *via* IV product V. In an attempt at obtaining experimental evidence for the formation of this C−10 adduct we measured the ^1H nmr spectrum of a solution of II in potassium amide/liquid ammonia.

However, the spectrum did not exhibit signals of III, but signals which could only be assigned to the presence of the anion of 7-ethynylaminoquinoline-8-aldimine (IV). Along side the proton signals which are characteristic of a 7,8-disubstituted quinoline (see table), we found that the C−H of the aldimino side chain is present as a doublet at 9.56 ppm and the NH as a doublet at 11.54 ppm. That the NH doublet is found at such a low field, compared to the NH in other imines (7) is certainly due to the influence of the

lone pair of the nitrogen atom in the quinoline ring (see IV) (8).

Table

^{1}H-NMR Data of 7-Ethynylaminoquinoline-8-aldimine (IV) in Potassium Amide/Liquid Ammonia

H−2	H−3	H−4	H−5	H−6	H−10	NH
8.24	6.68	7.57	7.83	7.07	9.56	11.54

$J_{2,3}$ = 4.6 Hz, $J_{2,4}$ = 1.6 Hz, $J_{3,4}$ = 8.0 Hz, $J_{5,6}$ = 10.0 Hz, $J_{NH,H}$ = 22.8 Hz.

The ^{1}H nmr signal of the ethynyl proton in IV is absent, being abstracted in the potassium amide/liquid ammonia system. However, the presence of the ethynyl group was proven by ^{13}C-nmr signals at 110.4 ppm and 118.3 ppm. These values are quite in agreement with those reported for the ethynyl part of the product obtained by ring opening of pyrimidines with potassium amide (9). The quinoline-8-aldimine (IV) was found to be stable in liquid ammonia, but to cyclise into V during work-up. Although the conversion of a pyridine ring into a pyrimidine ring is not unprecedented (10,11), it has never been possible to obtain sound nmr evidence for the structure of intermediates formed in this ring transformation reaction. The data mentioned above provide us with the first evidence for the ethynylamino structure of the open-chain intermediate, being formed when the pyridine ring is opened by potassium amide. In earlier studies the structure of the open-chain intermediates being obtained during the ring transformation of pyrimidines into *s*-triazines was also established (9) by ^{13}C-nmr spectroscopy.

EXPERIMENTAL

Melting points are uncorrected. The nmr spectra were recorded on a Varian XL−100−15, a Hitachi Perkin Elmer R24 B or a Bruker CXP−300 spectrometer.

8-Bromo-1,7-phenanthroline (II).

A mixture of 2.1 g (10.7 mmoles) of 1,7-phenanthroline-7-oxide (I) (12,13) and 15 ml of acetic anhydride was refluxed during 2 hours. The mixture was then poured onto 150 g of ice and stirred for 3 hours. Solid sodium carbonate was added to neutralize the mixture. The precipitate was filtered off and dried *in vacuo* over phosphorus pentoxide. A mixture of this product and 7.9 g (27.5 mmoles) of phosphorus oxybromide was heated at 140° in a stoppered flask for 4 hours. The reaction mixture was then poured onto ice and neutralized with concentrated ammonia; the solution was continuously extracted with chloroform. Evaporation of the solvent and purification of the residue by column chromatography on silica gel with chloroform as eluent gave 640 mg of II (23%) mp 146−147°; ^{1}H nmr (deuteriochloroform): δ 9.14 ppm (H−10, d, J = 8.5 Hz), 8.86 ppm (H−2, dd, J = 5.5 Hz and 2 Hz), 8.17 ppm (H−4, dd, J = 8 Hz and 2 Hz), 7.81 ppm (H−5 and H−6, s), 7.63 ppm (H−9, d, J = 8.5 Hz), 7.53 ppm (H−3, dd, J = 5.5 Hz and 8 Hz).

Anal. Calcd. for $C_{12}H_7BrN$: C, 55.62; H, 2.72. Found: C, 55.62; H, 2.80.

Amination of 8-Bromo-1,7-phenanthroline (II).

The amination of II with 4 equivalents of potassium amide was carried out as described before (14). The reaction time was 4 hours. The reaction mixture was separated by column chromatography on silica gel with chloroform/ethanol as eluent, yielding the following compounds:

2-Methyl-1,3,5-triazaphenanthrene (V).

This compound was obtained in a yield of 55% mp 129−130°; ^{1}H nmr (deuteriochloroform): δ 10.44 ppm (H−4, s), 9.98 ppm (H−6, dd, J = 4 Hz and 2 Hz), 8.17 ppm (H−8, dd, J = 8 Hz and 2 Hz), 8.04 ppm (H−9 or H−10, d, J = 9 Hz), 7.81 ppm (H−10 or H−9, d, J = 9 Hz), 7.52 ppm (H−7, dd, J = 8 Hz and 4 Hz), 2.96 ppm (CH_3, s); (deuterium oxide/deuteriosulfuric acid): δ 9.20 ppm (H−8, dd, J = 1.5 Hz and 8.5 Hz), 9.15 ppm (H−6, dd, J = 1.5 Hz and 5.5 Hz), 8.45 ppm (H−10, d, J = 9 Hz), 8.16 ppm (H−7, dd, J = 5.5 Hz and 8.5 Hz), 7.79 ppm (H−9, d, J = 9 Hz), 7.12 ppm (H−4, s), 2.68 ppm (CH_3, s); (potassium amide/liquid ammonia); δ 8.55 ppm (H−6, dd, J = 2 Hz and 4.5 Hz), 7.92 ppm (H−8, dd, J = 2 Hz and 7.5 Hz), 7.41 ppm (H−10, d, J = 9 Hz), 7.01 ppm (H−9, d, J = 9 Hz), 6.98 ppm (H−7, dd, J = 4.5 Hz and 7.5 Hz), 6.21 ppm (H−4, t, J = 6.5 Hz). The signal of the methyl group lies under the broad peak of ammonia.

Anal. Calcd. for $C_{12}H_9N_3 \cdot H_2O$: C. 67.59; H, 5.20. Found: C, 67.38; H, 5.37.

8-Amino-1,7-phenanthroline (VIII).

This compound was obtained in a yield of 19%, mp 206−208° (picrate mp 307−310° dec; ^{1}H nmr: δ 9.18 ppm (H−10, d, J = 9 Hz), 8.97 ppm (H−2, dd, J = 2 Hz and 4.5 Hz), 8.06 ppm (H−4, dd, J = 2 Hz and 9 Hz), 7.73 ppm (H−5 and H−6, s), 7.36 ppm (H−3, dd, J = 9 Hz and 4.5 Hz), 6.83 ppm (H−9, d, J = 9 Hz), 5.40 ppm (NH_2, b).

Anal. Calcd. for $C_{12}H_9N_3 \cdot C_6H_3N_3O_4$: C, 51.34 H, 2.79. Found: C, 50.95; H, 2.85.

4-Amino-2-methyl-1,3,5-triazanapthalene (VII).

This compound was obtained only in trace amounts, mp 218−220°; ^{1}H nmr: δ 8.82 ppm (H−6, dd, J = 2 Hz and 5 Hz), 8.14 ppm (H−8, dd, J = 2 Hz and 7 Hz), 7.90 ppm (H−9 or H−10, d, J = 8 Hz), 7.65 ppm (H−10 or H−9, d, J = 8 Hz), 7.41 ppm (H−7, dd, J = 5 Hz and 8 Hz), 3.20 ppm (NH_2, b), 2.64 ppm (CH_3, s).

Anal. Calcd. for $C_{12}H_{10}N_4 \cdot \frac{1}{2}H_2O$: C, 65.74; H, 5.06. Found: C, 65.63; H, 5.28.

Amination of 2-Methyl-1,3,5-triazanaphthalene (V).

To a solution of potassium amide prepared from 0.2 g of potassium and 10 ml of liquid ammonia, 0.5 of V was added. After 5 minutes 2.0 g of potassium permanganate were added in small portions. The mixture was stirred for 15 minutes, then quenched with 1 g of ammonium sulphate. After evaporation of the ammonia, concentrated ammonia was added and the mixture was continuously extracted with chloroform. The residue obtained on evaporation of the chloroform was separated on four plates (20 × 20 cm) covered with 0.5 mm of silica gel, chloroform/ethanol being used as eluent (9:1). Extraction of the upper bond yielded 0.42 g of unreacted V. Extraction of the lower bond gave 0.04 (7%) g of VII, mp 218−220°.

8-Amino-1,7-phenanthroline (VIII).

In a Carius tube a solution of 0.1 g of II in 10 ml of absolute ethanol was saturated with ammonia at 0°. The tube was sealed and heated at 160° for 63 hours. The tube was cooled, opened and the contents were continuously extracted with chloroform. After evaporation of the chloroform the product was recrystallized from chloroform, yielding 0.04 g (53%) of VIII mp 205−208°.

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