potassium hydroxide", which describes a reinvestigation of Sadykov's first paper.[2] Rubtsov realized that compound *1*, described by Sadykov as a high melting solid, was in fact identical with compound *6*. As might have been expected the change of solvent to methanol (*cf.* Ref. 1) in the Hofmann degradation of compound *6* had no marked effect on the outcome of the reaction; the main product was still compound *7* together with minor amounts of compound *4* and piperidine.

Some results obtained during a recent investigation (*cf.* Ref. 5) caused me to repeat the experiment described in Sadykov's second paper.[2] The free base *8*, an oil, seemed fairly stable and showed less tendency to dimerize than did compound *1*. Thus on treatment of *8* with methanolic potassium hydroxide, ether formation could be expected to occur as the main reaction in analogy with Knorr's findings.[1] In fact, compound *9*, *N*-(β-methoxyethyl)-anabasine, was obtained in about 80 % yield. B.p. 100°/0.1 mm (bath temp.). IR: (instruments and technique used in IR and NMR: *cf.* Ref. 5) 2820 (m) and 1120 (s, broad) cm^{-1}. NMR: three-proton singlet at δ 3.15 ppm). For comparison compound *9* was prepared independently by alkylation of anabasine with β-methoxyethyl *p*-toluenesulphonate. Identity was confirmed by GLC, IR, and a mixed melting point determination of the picrates (m.p. and mixed m.p. 174–175°).

The experiments described in Sadykov's last paper [3] have not been repeated. It must, however, be considered unlikely that the products described possessed structures *12* and *14*. As primary structural evidence Sadykov used a comparison of the IR spectrum of the alleged product *11* (actually structure *7*) with that of *12* as well as that of *13* (actually structure *9*) with *14*.

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Synthesis of Tricyclic Homologues of 1,6- and 2,7-Naphthyridine

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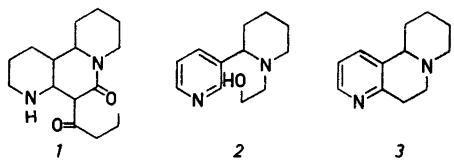
Hydrogenated pyrrolo- and pyrido-naphthyridines of the types represented by the structural formulae *7*, *11*, and *15* were required for pharmacological investigations (*cf.* Ref. 1). Recently the alkaloid haloxine [2,3] was found to possess structure *1* embodying the skeleton *7*.



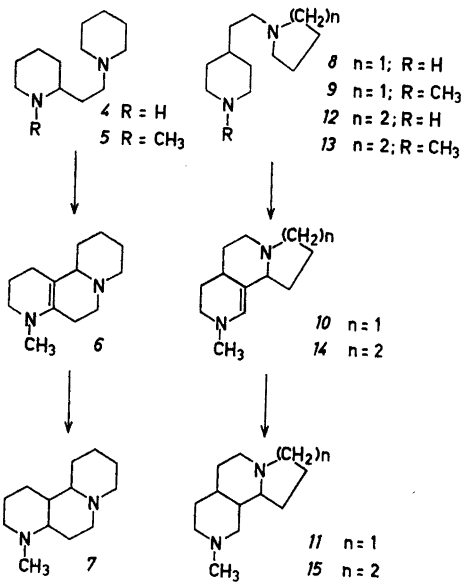
1 *2* *3*

Fig. 1.

It has been claimed [4] that a compound supposed to possess structure *3* is formed simply by heating the alcohol *2* with phosphorus pentoxide.

I have repeated this experiment but except for intractable resins only small amounts of unchanged starting material could be isolated. After several other attempts to synthesise compounds of type *7*, *11*, and *15* the reactions summarized in Scheme 1 led to the required bases.

The aminoethylpiperidines *4*, *8*, and *12*, obtained by catalytic hydrogenation of the corresponding piperidino- and pyrrolidino-ethylpyridines,[5] were methylated to compounds *5*, *9*, and *13*, respectively. When these tertiary diamines (*5*, *9*, and *13*) were oxidized with mercuric acetate,[6] mercurous acetate was formed in amounts roughly



Scheme 1

corresponding to the introduction of one double bond in each heterocyclic ring. The double enamines formed, underwent intramolecular condensation under the prevailing weakly acid conditions with the formation of *6*, *10*, and *14*, respectively. Evidence that this interpretation of the reactions is correct is given below (*cf.* Table 1).

The free bases *6*, *10*, and *14* exhibited a strong double bond stretching maximum in the 1660 cm^{-1} infrared region, which in the corresponding perchlorates was shifted to around 1700 cm^{-1} (*cf.* Ref. 6). In the NMR spectra of *6*, *10*, and *14* the protons of the N-methyl groups appeared as sharp singlets around δ 2.50 ppm and the olefinic protons in *10* and *14* as near-doublets at 5.74 and 5.61 ppm, respectively (*cf.* dimethyl-tetrahydroanabasine:[7] enamine-methyl 2.55 and olefinic H at 5.75 ppm). The three products exhibited great similarities in their mass spectra (MS). The peak from the $(M-1)^+$ ion was very strong (in *6* and *10* the base peak) and is possibly due to the conjugated immonium ion formed by loss of the allylic proton adjacent to the bridge-head nitrogen.

When the solid perchlorates of *6*, *10*, and *14* were reduced with sodium borohydride, the saturated compounds *7*, *11*, and *15* were obtained. In the NMR-spectra of *7*, *11*, and *15* the signals of the protons of the *N*-methyl groups appeared at 2.2 ppm, which is normal for a methyl group of a saturated amine. Their mass spectra were similar to those of their unsaturated precursors and all exhibited a pronounced $(M-3)^+$ peak, possibly resulting by the same type of fragmentation as suggested above.

The configuration of the above tricyclic products has not yet been investigated. No information could be adduced from the 2700–2800 cm^{-1} region of their IR spectra.[8] In this region all the spectra show a strong peak (*N*–Me) together with groups of minor bands, which are hardly distinguishable from those in the spectra of the starting materials *5*, *9*, and *13*. Minor products formed in the reactions in scheme 1 have not been investigated.

Experimental. Melting and boiling points are uncorrected. IR spectra were recorded on a Perkin-Elmer No. 237 grating instrument (sample as liquid film or for solids in KBr), NMR spectra on a Varian A 60 instrument operating at 60 Mc/s (solvent carbon tetrachloride, internal standard tetramethylsilane), and mass spectra on a LKB 9000 instrument. The reported compounds gave satisfactory elementary analyses.

Aminoethylpiperidines, *4*, *8*, and *12*. 2- or 4-Piperidinoethylpyridine or 4-pyrrolidinoethylpyridine [5] (0.1 mole), glacial acetic acid (50 ml) and platinum oxide (300 mg) were shaken with hydrogen under 5 atm pressure at room temperature. After the uptake of 3 moles of hydrogen (10–15 h) the mixtures were filtered and excess acetic acid evaporated under reduced pressure. The isolated bases were distilled affording the aminoethylpiperidines in 75–85 % yield. (B.p. of *4*: 90–92°/0.8 mm; of *8*: 68–72°/0.2 mm; and of *12*: 83–84°/0.4 mm).

Aminoethyl-N-methylpiperidines, *5*, *9*, and *13*. Compounds *4*, *8*, and *12* (0.1 mole) were methylated by heating with 90 % formic acid (25 ml) and 37 % aqueous formaldehyde (12 ml) for 8 h on a steam bath. Excess 2 N hydrochloric acid was added and the mixtures were concentrated to viscous syrups under reduced pressure. The isolated bases were distilled yielding the aminoethyl-*N*-methylpiperidines in 90–96 % yield. (B.p. of *5*: 95–97°/0.9 mm; of *9*: 80–82°/0.5 mm; and of *13*: 91–92°/0.6 mm).

Mercuric acetate oxidations of *5*, *9*, and *13* to *6*, *10*, and *14*, respectively. The diamines *5*, *9*, and *13* (0.01 mole) dissolved in 5 % aqueous

Table 1. Yields and properties of compounds *6*, *10*, and *14*.

Compound	*6*	*10*	*14*
Emp.form.	$C_{13}H_{22}N_2$	$C_{12}H_{20}N_2$	$C_{13}H_{22}N_2$
Yield, %	34	53	75
Hg(I)-OAc % of theor.	114	72	88
B.p., °C/mm	120/0.3	100/0.2	125/0.5
IR, cm^{-1}	1656	1660	1658
NMR, δ ppm *N*-Me	2.51	2.50	2.44
Vinyl-H	—	5.74	5.61
MS, *m/e* M^+	206 (40 %)	192 (36 %)	206 (100 %)
$(M-1)^+$	205 (100 %)	191 (100 %)	205 (80 %)
Diperchlorate m.p. °C	210–212	203–205	173–176
IR, cm^{-1}	1688	1705	1697

Table 2. Properties of compounds *7*, *11*, and *15*.

Compound	*7*	*11*	*15*
Emp.form.	$C_{13}H_{24}N_2$	$C_{12}H_{22}N_2$	$C_{13}H_{24}N_2$
B.p., °C/mm	100/0.05	85/0.05	105/0.1
Dipicrate m.p., °C (decomp.)	279–281	263–265	246–250
NMR, δ ppm *N*-Me	2.20	2.17	2.16
MS, *m/e* M^+	208 (43 %)	194 (41 %)	208 (48 %)
$(M-3)^+$	205 (14 %)	191 (13 %)	205 (34 %)
Base peak	83	136	150

acetic acid (50 ml) were added to a hot, stirred solution of mercuric acetate (28.7 g, 0.09 mole) in 5 % acetic acid (150 ml). The heating was continued on a steam bath for 4–8 h. A white precipitate of mercurous acetate appeared in 10–30 min. At the end of the heating period the mixtures were cooled and the precipitates collected (yields *cf.* Table 1). The filtrates were heated to 90° and freed from mercury by excess of hydrogen sulphide. The solutions were concentrated to a volume of 50 ml under reduced pressure, cooled in an ice bath and excess potassium carbonate added. The bases were extracted with ether and finally distilled (oil bath, bath temperature given in Table 1). The distillates were dissolved in dry ether containing absolute ethanol (5 %), 50 % ethanolic perchloric acid was then added dropwise with swirling to the solutions until acid. Oils separated which slowly crystallized. The salts were recrystallized from mixtures of methanol-dry ether. The bases isolated from these recrystallized perchlorates were submitted to GLC [9] and gave single peaks (spectral properties *cf.* Table 1).

Borohydride reduction of the perchlorates of *6*, *10*, and *14* to *7*, *11*, and *15*, respectively. The finely powdered perchlorates *6*, *10*, and *14* were slowly added to a stirred solution of an excess of sodium borohydride in methanol at 0°. After 1 h the mixtures were worked up in the usual way and the bases distilled (oil bath, bath temperature given in Table 2). The yields were high (*ca.* 90 %). The distilled bases were converted to their picrates and recrystallized from ethanol-acetic acid. The bases isolated from these recrystallized picrates were investigated by GLC and gave single peaks (spectral properties *cf.* Table 2).

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