## Heterocycles with a bridgehead nitrogen atom. 16.\* Assembly of a *peri*-fused system from an angular tricycle by recyclization of an oxazole ring into pyrrole one

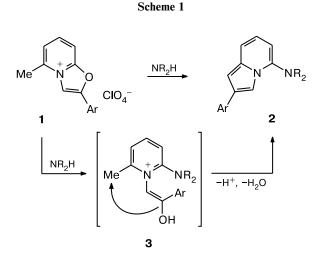
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An unusual example of the recyclization of the tricyclic 6,7,8,9-tetrahydrooxazolo[3,2-*a*]quinolinium system into the 8,9-dihydro-7*H*-pyrrolo[3,2,1-*ij*]quinoline system was discovered. The reaction is a topological modification of the known conversion of oxazolo[3,2-*a*]pyridinium salts into indolizines. The structural feature of this transformation is a change of the annelation type in the tricycle from the angular one to *peri*-fusion of three rings.

**Key words:** recyclization, oxazole, pyrrole, indolizine, annelation, *peri*-fused rings, X-ray diffraction analysis.

Earlier,<sup>2,3</sup> we discovered a new family of recyclization reactions of the oxazole ring into the pyrrole one, through which fused oxazolo[3,2-*a*]pyridinium salts 1 were converted to 5-substituted indolizines 2 virtually inaccessible in any other ways (Scheme 1).



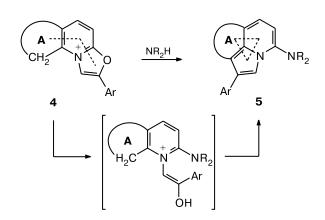
Most likely, the conversion proceeds<sup>4</sup> through the formation of pyridinium intermediate 3, in which cyclocondensation of a new pyrrole ring involves the  $\alpha$ -methyl group of the salt 3.

An interesting topological modification of this transformation could be conversion of tricyclic systems **4** containing a methylene fragment (as in cation **4**) as part of an

\* For Part 15, see Ref. 1.

additional ring A instead of the methyl group (as in salts 1 and 3) (Scheme 2). In this case, the ring A originally fused only with the pyridine ring of salt 4 would become additionally fused with a newly formed pyrrole ring to give system 5. Therefore, the overall structural reconstruction of tricycles  $4\rightarrow 5$  would be an example of an extremely rare mode of transformation of an angular structure (three rings with two fused sides) into a *peri*-fused system (three rings are all fused in pairs).

Scheme 2

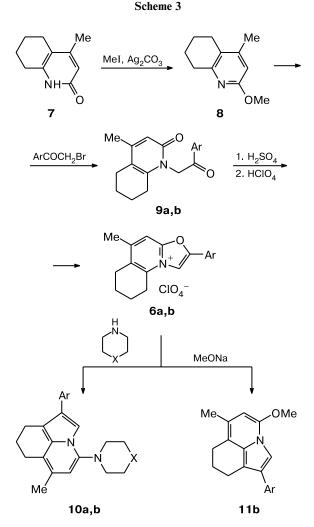


We experimentally performed this unusual topological transformation with 6,7,8,9-tetrahydrooxazolo[3,2-a]quinolinium salt **6** as a tricyclic system of the type **4** (Scheme 3).

Tricycle 6 was synthesized in three steps starting from available tetrahydroquinolone 7. To construct the oxazole

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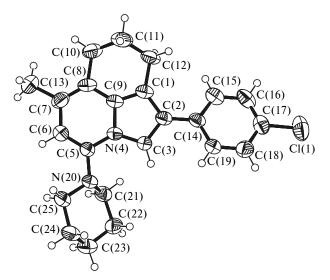
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**8—11:** Ar = *p*-Cl—Ph (**a**), *p*-NO<sub>2</sub>—Ph (**b**) **10:** X = CH<sub>2</sub> (**a**), O (**b**)

ring of system **6**, selective *N*-phenacylation in the pyridone fragment of compound **7** was required. Using Bradsher's known methodology,<sup>5</sup> which employs a protective methyl group to prevent *O*-phenacylation, we obtained 2-methoxy derivative **8**. Reactions of the latter with halogen ketones yielded, *via* simultaneous *N*-phenacylation and *O*-demethylation, the desired intermediate products **9a,b**. Their cyclodehydration into tricycles **6a,b** was carried out by successive treatment with sulfuric and perchloric acids. The <sup>1</sup>H NMR spectra of perchlorates **6** contain no signals for two methylene protons; instead, a low-field aromatic singlet for the oxazole ring appears at  $\delta$  9.4–9.6. Earlier, compounds **6a, 8**, and **9a** were synthesized and characterized by X-ray diffraction data.<sup>6</sup>

In reactions with secondary amines or sodium methoxide, the obtained representatives of the angular tricyclic system **6** smoothly underwent recyclization to give amino or methoxy derivatives of 8,9-dihydro-7*H*-pyrrolo[3,2,1-*ij*]quinolines **10** and **11** with the *peri*-fused



**Fig. 1.** Structure **10a** (from X-ray diffraction data). The selected bond lengths in the tricycle are:

Bond	$d/\text{\AA}$	Bond
C(1) - C(2)	1.455 (3)	C(5) - N(20)
C(1) - C(9)	1.357 (3)	C(6) - C(7)
C(1) - C(12)	1.526 (3)	C(7) - C(8)
C(2) - C(3)	1.386 (3)	C(7)–C(13)
C(2)-C(14)	1.455 (3)	C(8) - C(9)
C(3) - N(4)	1.360 (2)	C(1) - C(10)
N(4) - C(9)	1.410 (3)	C(10)-C(11)
N(4) - C(5)	1.378 (3)	C(11)-C(12)
C(1) - C(6)	1.352 (3)	

rings. The <sup>1</sup>H NMR spectra of heterocycles **10** and **11** contain no signals for one of the methylene units (as distinct from salts **6**), while the low-field singlet for the oxazole ring is replaced by a singlet for the pyrrole ring at  $\delta$  7.2–7.4. The structure of the tricycle obtained was unambiguously proved by X-ray diffraction analysis for compound **10a** (Fig. 1); the structure will be extensively discussed elsewhere\*.

The discovered transformation opens up a new strategy of the synthesis of the pyrrolo[3,2,1-ij]quinoline system. Compounds of this class first obtained in the 1980s<sup>7,8</sup> attracted attention as agonists of dopamine receptors.<sup>9</sup> Note that amino or alkoxy derivatives of this system have been unknown hitherto. Our subsequent studies will be devoted to the effects of the substituent nature in the pyridine ring and the size of the saturated fragment in system **6** on the recyclization in question.

## Experimental

<sup>1</sup>H NMR spectra were recorded on a Bruker AC 400 instrument. The syntheses and X-ray diffraction analysis of compounds

<sup>\*</sup> The material is being prepared for publication.

**6a** and **9a** were described earlier.<sup>6</sup> Compound **7** was prepared according to a known procedure.<sup>10</sup>

**2-Methoxy-4-methyl-5,6,7,8-tetrahydroquinoline (8).** A mixture of 4-methyl-5,6,7,8-tetrahydroquinolin-2-one (7) (57 mmol), CH<sub>3</sub>I (72 mmol), and freshly prepared and well dried  $Ag_2CO_3$  (28.5 mmol) in 90 mL of benzene was refluxed for 50 to 60 h in a light-protected flask. The precipitate was filtered off, the solvent was removed from the mother liquor, and the residue was distilled *in vacuo* while collecting a fraction with b.p. 147 °C (20 Torr). The yield of compound **8** was 3.8 g (38%), m.p. 40–41 °C (*cf.* Ref. 6: m.p. 35–40 °C).

**4-Methyl-1-(4-nitrophenacyl)-5,6,7,8-tetrahydroquinolin-2one (9b).** A solution of compound **8** (25 mmol) and 4-nitrophenacyl bromide (20 mmol) in 40 mL of MeCN was refluxed for 40 h. The precipitate was filtered off and recrystallized from acetonitrile. The yield of compound **9b** was 3.56 g (55%), m.p. 194–196 °C. Found (%): N, 5.50.  $C_{18}H_{18}N_2O_4$ . Calculated (%): N, 5.56. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>),  $\delta$ : 8.33 (m, 4 H, ArH); 6.14 (s, 1 H, H(3)); 5.52 (s, 2 H, NCH<sub>2</sub>); 2.47 (m, 4 H, CH<sub>2</sub>); 2.12 (s, 3 H, CH<sub>3</sub>); 1.74 (m, 4 H, CH<sub>2</sub>).

**5-Methyl-2-(4-nitrophenyl)-6,7,8,9-tetrahydrooxazolo[3,2-***a***]<b>quinolinium perchlorate (6b).** Compound **9b** (5 mmol) was carefully dissolved in 30 mL of conc.  $H_2SO_4$  and left at room temperature for 16 h. The mixture was carefully poured into 300 mL of water and allowed to cool. Then 70% HClO<sub>4</sub> (15 mL) was added dropwise. The precipitate was filtered off, washed with water to a neutral reaction, and dried. The yield of compound **6b** was 1.93 g (95%), m.p. 283–285 °C. Found (%): N, 6.75.  $C_{18}H_{17}N_2O_3 \cdot ClO_4$ . Calculated (%): N, 6.85. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>), & 9.62 (s, 1 H, H(1)); & 50, & 28 (both m, 2 H each, ArH); & 23 (s, 1 H, H(4)); 3.13, 2.82 (both m, 2 H each, CH<sub>2</sub>); 2.60 (s, 3 H, CH<sub>3</sub>); 1.90, 1.99 (both m, 2 H each, CH<sub>2</sub>).

Recyclization of salts 6 in the presence of secondary amines (general procedure). A secondary amine (1 mL,  $\sim$ 20-fold excess) was added to a solution of perchlorate 6 (0.5 mmol) in 10 mL of acetonitrile. The mixture was refluxed to give a crimson solution, which rapidly turned greenish yellow. The resulting solution was poured into water. The precipitate was filtered off, dried, and recrystallized from acetonitrile.

1-(4-Chlorophenyl)-6-methyl-4-piperidino-8,9-dihydro-7*H*pyrrolo[3,2,1-*ij*]quinoline (10a) was obtained from perchlorate 6a and piperidine. The reaction duration was 2 min. The yield of compound 10a was 98%, m.p. 138–139 °C (yellow prismatic crystals). X-ray diffraction data are shown in Fig. 1. Found (%): N, 7.61.  $C_{23}H_{25}CIN_2$ . Calculated (%): N, 7.68. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>),  $\delta$ : 7.51, 7.33 (both m, 2 H each, ArH); 7.18 (s, 1 H, H(3)); 5.76 (s, 1 H, H(6)); 3.00 (m, 4 H, CH<sub>2</sub>); 2.95, 2.74 (both m, 2 H each, CH<sub>2</sub>); 2.15 (s, 3 H, CH<sub>3</sub>); 2.00 (m, 2 H, CH<sub>2</sub>); 1.80, 1.67 (both m, 4 H each, CH<sub>2</sub>).

**6-Methyl-4-morpholino-1-(4-nitrophenyl)-8,9-dihydro-7***H***pyrrolo[3,2,1-***ij***]quinoline (10b)** was obtained from perchlorate **6b** and morpholine. The reaction duration was 4 h. The yield of compound **10b** was 40%, m.p. 218–220 °C. Found (%): N, 11.05.  $C_{22}H_{23}N_3O_3$ . Calculated (%): N, 11.13. <sup>1</sup>H NMR (CDCl<sub>3</sub>),  $\delta$ : 8.25, 7.73 (both m, 2 H each, ArH); 7.40 (s, 1 H, H(3)); 5.88 (s, 1 H, H(6)); 3.95, 3.10 (both m, 4 H each, CH<sub>2</sub>); 3.03, 2.80 (both m, 2 H each, CH<sub>2</sub>); 2.19 (s, 3 H, CH<sub>3</sub>); 2.06 (m, 2 H, CH<sub>2</sub>).

**4-Methoxy-6-methyl-1-(4-nitrophenyl)-8,9-dihydro-7***H***-<b>pyrrolo**[**3**,**2**,**1**-*ij*]**quinoline (11b).** Perchlorate **6b** (0.5 mmol) was added to a solution of MeONa in methanol (prepared from Na metal (7.4 mmol) and anhydrous MeOH (10 mL)). The reaction mixture was left for 16 h. The precipitate that formed was filtered off and recrystallized from acetonitrile. The yield of compound **11b** was 0.10 g (62%), m.p. 183–185 °C. Found (%): N, 8.50. C<sub>19</sub>H<sub>18</sub>N<sub>2</sub>O<sub>3</sub>. Calculated (%): N, 8.69. <sup>1</sup>H NMR (CDCl<sub>3</sub>),  $\delta$ : 8.23, 7.72 (both m, 2 H each, ArH); 7.48 (s, 1 H, H(3)); 5.56 (s, 1 H, H(6)); 4.02 (s, 3 H, OCH<sub>3</sub>); 3.02, 2.77 (both m, 2 H each, CH<sub>2</sub>); 2.19 (s, 3 H, CH<sub>3</sub>); 2.05 (m, 2 H, CH<sub>2</sub>).

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