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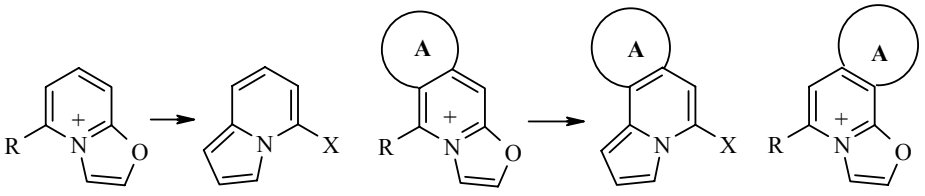
HETEROCYCLES WITH A BRIDGING NITROGEN ATOM. 19.* DEVELOPMENT OF ROUTES FOR THE SYNTHESIS OF OXAZOLOISOQUINOLINIUM SALTS BASED ON PHENACYLATION OF α-METHYL-1(3)-ISOQUINOLONES**

E. V. Babaev[1]*, **A. A. Nevskaya[1]**, **I. V. Dlinnykh[1]**, **and V. B. Rybakov[1]**

Alkylation of 3-methyl-1-isoquinolone and 1-methyl-3-isoquinolone with phenacyl bromides proceeds regioselectively with the formation in the first case of only an N-phenacyl derivative and in the second only the O-derivative. The 5-methyl[1,3]oxazolo[3,2-a]isoquinolinium salt has been synthesized and its reactions with ammonia, morpholine, and sodium methylate have been investigated.

Keywords: 1-isoquinolone, isoquinol-3-one, bridging oxazoloquinolines, O,N-alkylation.

In reactions of oxazolopyridinium salts **1** with nucleophiles both the six- and five-membered fragments of the bicycle may be subject to opening, see the review [2]. The recyclization discovered by us of the oxazole nucleus into a pyrrole in 5-methyloxazolopyridinium salts (**1**, R = Me) leading to 5-substituted indolizines **2** is of the greatest interest [2-5].



1 **2** **3** **4**

* For Communication 18 see [1].

** Dedicated to Academician B. A. Trofimov on his 70th jubilee

*** To whom correspondence should be addressed, e-mail: babaev@org.chem.msu.ru.

[1]Chemical Faculty, M. V. Lomonosov Moscow State University, Moscow 119992, Russia.

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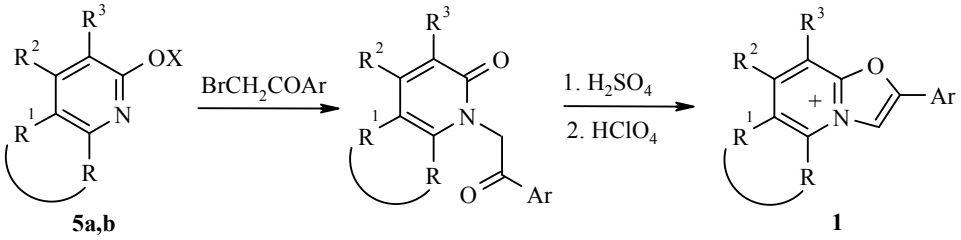
We have attempted to broaden the circle of substrates capable of an analogous conversion using the tricyclic systems **3** and **4**. We previously succeeded in synthesizing oxazolopyridinium salt **3** (R = Me), in which the annelated ring **A** is cyclohexane. Such a linear tricycle is readily converted into angular tricyclic indolizines on reaction with secondary amines [6] or alcoholates [7]. The present work is devoted to the problem of synthesizing and investigating the possibility of recyclizing tricyclic benzo analogs, linear of type **3** and angular of type **4** (R = Me, **A** is benzo) in which the oxazole nucleus is linked with an isoquinoline ring by various means.

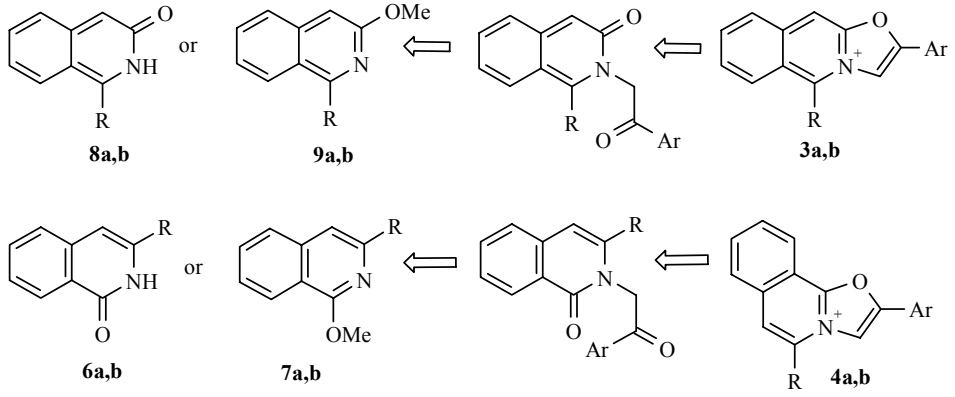
The standard route of building up an oxazole ring on a pyridine at the C–N bond comprises N-phenacylation of alkaline salts of pyridone **5a** [8, 9] or methoxypyridines **5b** [2, 10] (according to Bradsher) with subsequent acid cyclocondensation.



5 a X = Na, **b** X = Me

It is possible to obtain bicyclic salts **1** and their (cyclo)homologs (R = H, Me, RR^1 is the cycloalkane fragment) [2]. A tricyclic oxazoloquinoline was synthesized on using 2-methoxyquinoline [10].

The use of an analogous strategy for the synthesis of oxazoloisoquinolinium salts **3, 4** has been investigated to a small extent. The sole described example is the synthesis of angular salt **4a** on using 1-methoxyisoquinoline (**7a**) [10]. The homologous salt **4b** is unknown, and information on linear tricyclic system **3** is generally absent from the literature.

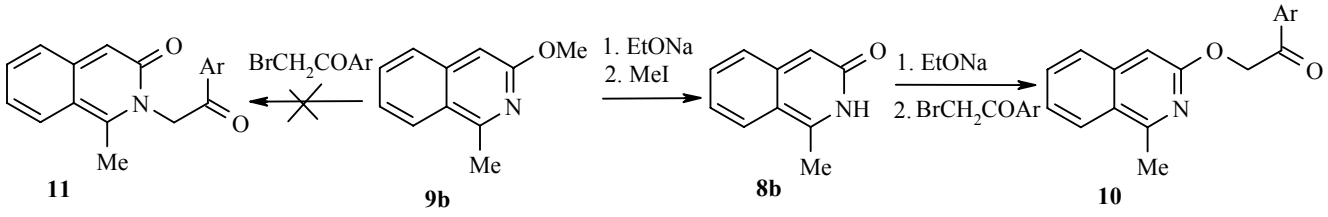


3, 4, 6–9 a R = H, **b** R = Me

For the synthesis of salts **3b**, **4b** by such a scheme it is evidently necessary to effect a regioselective N-phenacylation of methylisoquinolones **8b** and **6b** (or their alkaline salts) or of the corresponding α-methyl-α'-methoxy derivatives **9b**, **7b**. There are data in the literature on the N-alkylation of 1(3)-methoxyisoquinolines **7a**, **9a** and the simplest 1(3)-isoquinolones **6a**, **8a**, however information on analogous reactions of their homologs **6b-9b** is extremely scanty.

It is known that the alkaline salts of 1-isoquinolone **6a** may be subject to selective N-alkylation by various alkylating agents [11-13], including phenacyl bromide [14]. The N-phenacylation of 1-methoxy-

isoquinoline **7a** in low yield (~8%) has been described [10]. Examples of the N-alkylation of the homologous isoquinolone **6b** or the methoxy derivative are unknown, although an unusual intramolecular N-alkylation, accompanying O-demethylation, for the structurally analogous 1-methoxy-3-(ω-bromopropyl)isoquinoline has been described [15].



11 **9b** **8b** **10**

Ar = *p*-BrC_6H_4

There are few examples of N-alkylation among derivatives of 3-isoquinolone **8a** and also of 3-methoxyisoquinoline **9a**. Strangely, alkylation reactions of the simplest 3-isoquinolones **8a,b**, were not studied in detail (because it is possible that such N-alkyl derivatives are obtained more conveniently by recyclization of benzopyrones), although examples of O-acylation [16] (and also of O-silylation and O-tosylation) of compounds **8a,b** are described in the literature. 3-Ethoxyisoquinoline (with additional substituents in the benzene ring) successfully undergo N-alkylation [17]. It is interesting that on methylation of the sodium salt of 3-oxopapaverine (a derivative of 1-benzyl-3-isoquinolone), in which the nitrogen atom is sterically hindered, a mixture was obtained of the products of N- and O-alkylation (43:10) with a clear preference for the N-isomer [18]. There is mention of a regioselective N-methylation of a 1,4-disubstituted 3-isoquinolone in [19].

TABLE 1. Crystallographic Characteristics, Details of the X-ray Diffraction Experiment, and Stuctural Refinement for Compounds **10**, **13**, and **14**

Compound	**10**	**13**	**14**
Empirical formula	$C_{18}H_{14}BrNO_2$	$C_{19}H_{13}ClN_2O_2$	$C_{21}H_{15}Cl_2N_3O_5$
M	356.21	336.76	460.26
System	Triclinic	Triclinic	Triclinic
Space group	*P*-1	*P*-1	*P*-1
a, Å	8.285(4)	4.6601(18)	7.5329(10)
b, Å	8. 11.559(3)	11.786(3)	9.6985(14)
c, Å	11.559(3)	14.764(5)	14.521(4)
α, deg	83.015(18)	82.91(2)	98.165(16)
β, deg	86.40(3)	81.09(4)	101.181(17)
γ, deg	69.59(3)	83.51(3)	95.752(11)
V, Å^3	752.7(5)	791.3(4)	1021.2(4)
Z	2	2	2
ρ_{calc}, mg/m^3	1.572	1.413	1.497
Absorption coefficient, mm^{-1}	3.775	2.252	3.215
Crystal dimensions, mm	0.2 × 0.2 × 0.2	0.2 × 0.2 × 0.2	0.2 × 0.2 × 0.2
Range of angles θ, deg	3.85–74.91	3.04–74.73	3.15–73.97
Range of indexes	-10≤*h*≤10, -10≤*k*≤10, 0≤*l*≤14	-5≤*h*≤5, -14≤*k*≤14, 0≤*l*≤18	-9≤*h*≤9, -12≤*k*≤11, 0≤*l*≤17
Size of experiment	3161	3261	4163
Number			
independent reflections	2995	3261	3987
parameters refined	200	218	282
GOOF	1.009	0.899	0.820
R-factor [*I*>2σ(*I*)], R_1/wR_2	0.0379/0.0916	0.0436/0.1012	0.0635/0.0857
R-factor from all data R_1/wR_2	0.0408/0.0936	0.0473/0.1020	0.2569/0.1494
$\Delta\rho_{max}/\Delta\rho_{min}$, e/ Å^3	0.268/-0.481	0.235/-0.201	0.262/-0.251

Study of the Phenacylation of Derivatives of 1-Methyl-3-isoquinolones 8b, 9b and Attempts to Synthesize the Linear System 3b. We discovered that heating equimolar amounts of the sodium derivative of 1-methyl-3-isoquinolone **8b** and *p*-bromophenacyl bromide in DMF leads to the formation of a single product of O-alkylation **10**, the structure of which was established unequivocally by X-ray structural analysis (Fig. 1, Tables 2 and 3).

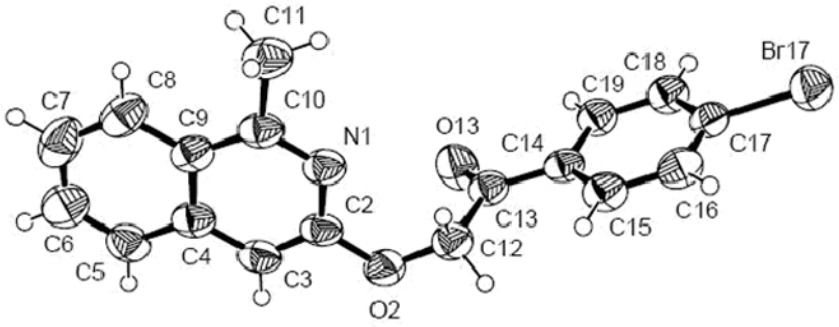


Fig. 1. Numbering of atoms and spatial structure of compound **10**. Ellipsoids of thermal vibrations are given with a probability of 50%. The numbering of atoms does not correspond to IUPAC nomenclature.

TABLE 2. Bond Lengths (*d*) in Structure **10**

Bond	*d*, Å	Bond	*d*, Å
Br(17)–C(17)	1.886(2)	C(8)–C(9)	1.413(3)
N(1)–C(10)	1.323(2)	C(9)–C(10)	1.416(3)
N(1)–C(2)	1.357(2)	C(10)–C(11)	1.500(2)
C(2)–C(3)	1.360(3)	C(12)–C(13)	1.505(3)
C(2)–O(2)	1.363(2)	C(13)–O(13)	1.211(3)
O(2)–C(12)	1.411(3)	C(13)–C(14)	1.482(3)
C(3)–C(4)	1.399(3)	C(14)–C(19)	1.391(3)
C(4)–C(9)	1.426(2)	C(14)–C(15)	1.396(3)
C(4)–C(5)	1.433(3)	C(15)–C(16)	1.398(3)
C(5)–C(6)	1.343(4)	C(16)–C(17)	1.372(3)
C(6)–C(7)	1.394(4)	C(17)–C(18)	1.371(3)
C(7)–C(8)	1.373(4)	C(18)–C(19)	1.391(3)

Attempts at selective N-phenacylation according to Bradsher of the 3-methoxy derivative **9b** proved to be unsuccessful. The initial compounds were recovered from the reaction mixture even after boiling for many hours in acetonitrile or heating in DMF.

Selective O-alkylation of isoquinolone **8b** may be explained not only by the steric effect of the two substituents in the positions α to the nitrogen atom. It is extremely probable that the formation of the N-isomer **11** may be hindered further by a thermodynamic factor linked with the quinonoid type of structure of the whole class of N-alkyl-3-isoquinolones.

Theoretically isoquinoline **10** might serve as the precursor of the desired tricycle **3b**. (An example of a similar process is known, the synthesis of the thioanalog of system **3** by the acid cyclization of 3-(phenacylthio)isoquinoline [20]). Meanwhile, all attempts to close the oxazolium ring in O-phenacyl derivative **10** by the action of conc. H_2SO_4 or oleum proved to be unsuccessful and led only to salts of the initial isoquinoline **10**.

TABLE 3. Valence Angles (ω) in Structure **10**

Angle	ω, deg	Angle	ω, deg
C(10)–N(1)–C(2)	118.21(18)	N(1)–C(10)–C(11)	115.64(19)
N(1)–C(2)–C(3)	124.68(17)	C(9)–C(10)–C(11)	121.83(18)
N(1)–C(2)–O(2)	117.78(18)	O(2)–C(12)–C(13)	112.92(17)
C(3)–C(2)–O(2)	117.53(15)	O(13)–C(13)–C(14)	121.84(17)
C(2)–O(2)–C(12)	119.42(14)	O(13)–C(13)–C(12)	120.94(19)
C(2)–C(3)–C(4)	118.10(16)	C(14)–C(13)–C(12)	117.22(16)
C(3)–C(4)–C(9)	118.75(18)	C(19)–C(14)–C(15)	119.03(18)
C(3)–C(4)–C(5)	122.21(17)	C(19)–C(14)–C(13)	118.94(17)
C(9)–C(4)–C(5)	119.02(18)	C(15)–C(14)–C(13)	122.03(16)
C(6)–C(5)–C(4)	119.6(2)	C(14)–C(15)–C(16)	119.70(17)
C(5)–C(6)–C(7)	122.3(3)	C(17)–C(16)–C(15)	119.98(18)
C(8)–C(7)–C(6)	119.7(2)	C(18)–C(17)–C(16)	121.10(19)
C(7)–C(8)–C(9)	121.0(2)	C(18)–C(17)–Br(17)	119.44(15)
C(8)–C(9)–C(10)	123.95(17)	C(16)–C(17)–Br(17)	119.44(16)
C(8)–C(9)–C(4)	118.3(2)	C(17)–C(18)–C(19)	119.46(17)
C(10)–C(9)–C(4)	117.70(17)	C(14)–C(19)–C(18)	120.71(18)
N(1)–C(10)–C(9)	122.52(16)		

Synthesis of the Angular System 4b by Phenacylation of the 3-Methyl-1-isoquinolone Derivative 6b. The most available* representative of the 3-methyl-1-isoquinolone series is the 4-cyano derivative **12**, which was synthesized from accessible reactants in three steps according to the known methods. We carried out alkylation of it with *p*-chlorophenacyl bromide under conditions analogous to the phenacylation of compound

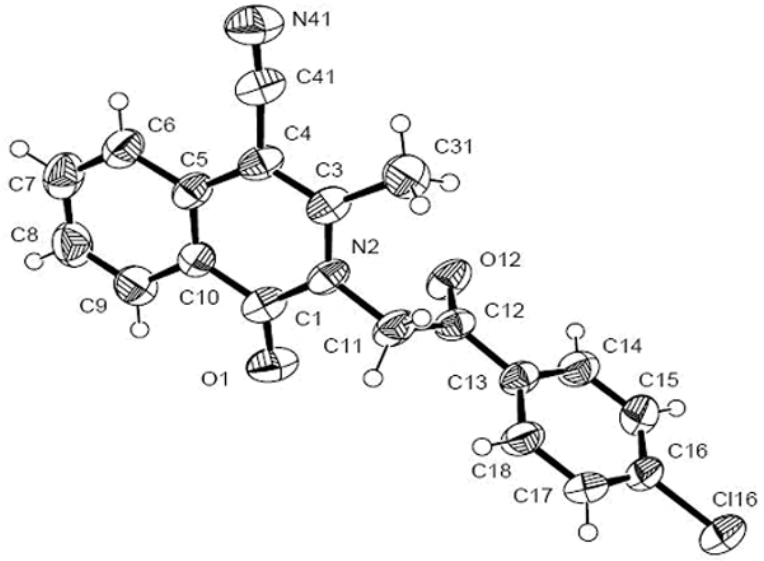


Fig. 2. Numbering of atoms and spatial structure of compound **13**. Ellipsoids of thermal vibrations are given with a probability of 50%. The numbering of atoms does not correspond to IUPAC nomenclature.

* Synthesis of the simplest isoquinolone **6b** by hydrolysis of nitrile **12** in sulfuric acid is described in [21]. We discovered however, that a significant amount of sulfonation byproduct is formed in this reaction, consequently compound **12** was used in later experiments.

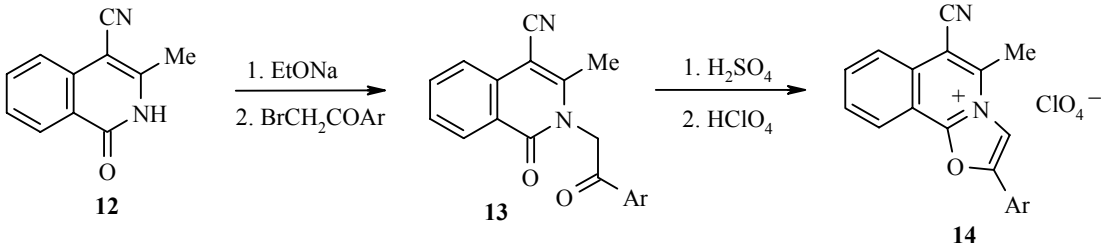
TABLE 4. Bond Lengths (*d*) in Structure **13**

Bond	*d*, Å	Bond	*d*, Å
C(1)–O(1)	1.2294(18)	C(7)–C(8)	1.403(3)
C(1)–N(2)	1.414(2)	C(8)–C(9)	1.363(3)
C(1)–C(10)	1.439(2)	C(9)–C(10)	1.410(2)
N(2)–C(3)	1.389(2)	C(11)–C(12)	1.509(2)
N(2)–C(11)	1.4614(18)	C(12)–O(12)	1.2243(18)
C(3)–C(4)	1.368(2)	C(12)–C(13)	1.4837(19)
C(3)–C(31)	1.493(2)	C(13)–C(14)	1.382(2)
C(4)–C(41)	1.432(2)	C(13)–C(18)	1.401(2)
C(4)–C(5)	1.444(2)	C(14)–C(15)	1.373(2)
C(41)–N(41)	1.142(2)	C(15)–C(16)	1.386(3)
C(5)–C(10)	1.375(2)	C(16)–C(17)	1.345(3)
C(5)–C(6)	1.416(2)	C(16)–Cl(16)	1.7321(16)
C(6)–C(7)	1.371(3)	C(17)–C(18)	1.386(2)
C(7)–C(8)	1.403(3)		

TABLE 5. Valence Angles (ω) in Structure **13**

Angle	ω, deg	Angle	ω, deg
O(1)–C(1)–N(2)	117.51(14)	C(8)–C(9)–C(10)	118.47(17)
O(1)–C(1)–C(10)	125.58(15)	C(5)–C(10)–C(9)	121.05(14)
N(2)–C(1)–C(10)	116.91(13)	C(5)–C(10)–C(1)	120.90(14)
C(3)–N(2)–C(1)	123.16(12)	C(9)–C(10)–C(1)	118.05(14)
C(3)–N(2)–C(11)	121.59(13)	N(2)–C(11)–C(12)	113.16(12)
C(1)–N(2)–C(11)	115.19(13)	O(12)–C(12)–C(13)	122.01(14)
C(4)–C(3)–N(2)	118.29(14)	O(12)–C(12)–C(11)	120.47(13)
C(4)–C(3)–C(31)	123.46(15)	C(13)–C(12)–C(11)	117.52(12)
N(2)–C(3)–C(31)	118.17(13)	C(14)–C(13)–C(18)	119.16(14)
C(3)–C(4)–C(41)	118.26(15)	C(14)–C(13)–C(12)	119.00(13)
C(3)–C(4)–C(5)	121.74(14)	C(18)–C(13)–C(12)	121.83(14)
C(41)–C(4)–C(5)	119.99(14)	C(15)–C(14)–C(13)	121.15(16)
N(41)–C(41)–C(4)	175.1(2)	C(14)–C(15)–C(16)	118.71(16)
C(10)–C(5)–C(6)	118.90(15)	C(17)–C(16)–C(15)	121.12(15)
C(10)–C(5)–C(4)	118.88(13)	C(17)–C(16)–Cl(16)	119.49(14)
C(6)–C(5)–C(4)	122.22(15)	C(15)–C(16)–Cl(16)	119.28(14)
C(7)–C(6)–C(5)	120.75(17)	C(16)–C(17)–C(18)	120.88(16)
C(6)–C(7)–C(8)	118.74(16)	C(17)–C(18)–C(13)	118.81(15)
C(9)–C(8)–C(7)	122.08(17)		

8b. The N-alkyl derivative **13** was isolated in 25% yield as the sole reaction product. A combination of ^{1}H NMR and IR spectroscopy was carried out to establish the direction of alkylation. Structural investigation of a monocrystal of compound **13** by X-ray structural analysis (Fig. 2, Tables 4 and 5) finally confirmed these conclusions.



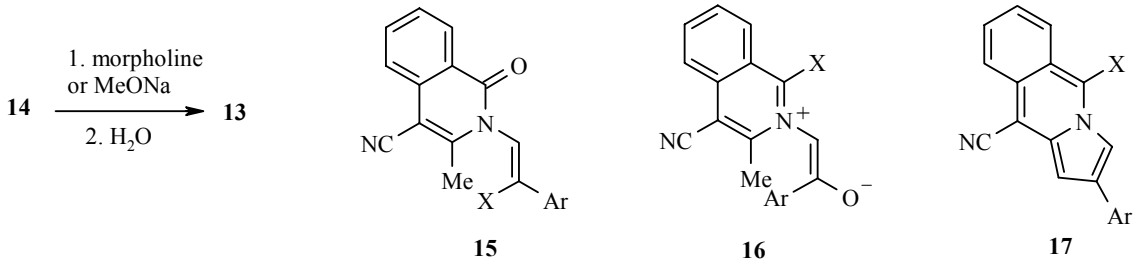
12 **13** **14**

Ar = *p*-ClC$_6$H$_4$

Cyclization of the obtained N-phenacyl-1-isoquinolone **13** was effected by the action of conc. H_2SO_4, the reaction product was isolated as the perchlorate.

We discovered that cyclization did not take place with a brief (15 min) action of acid, however it was fully complete after 1 day. Under these conditions hydrolysis of the cyano group did not occur and the perchlorate of the tricyclic oxazoloisoquinoline **14** was formed in 72% yield. The results of X-ray structural analysis of a monocrystal of this compound obtained from solution in acetonitrile are given in Fig. 3 and Tables 6 and 7.

Reaction of Salt 14 with Nucleophiles. The reaction of perchlorate **14** with morpholine proceeded completely in 15 min. After treating the reaction mixture with water a compound was isolated which had the structure of N-phenacyl-1-isoquinolone **13** according to spectral data. The interaction of salt **14** with a methanolic solution of sodium methylate led to the same compound **13**.



13–17 Ar = *p*-ClC_6H_4, X = OMe, morpholine

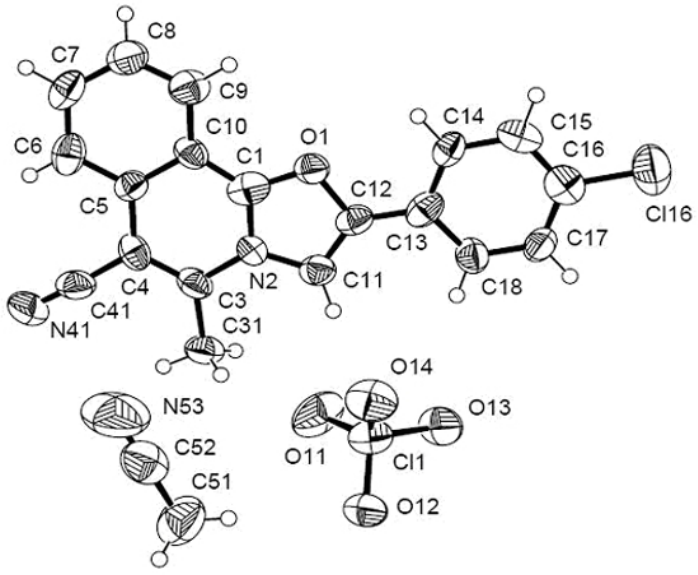


Fig. 3. Numbering of atoms and spatial structure of compound **14**. Ellipsoids of thermal vibrations are given with a probability of 50%. The numbering of atoms does not correspond to IUPAC nomenclature.

In both cases no formation of the benzoindolizine structure **17** was observed. Since the isoquinoline fragment remains unchanged, the observed conversion is evidently linked with attack of nucleophile at the oxazole ring, for example, at position 2. The resulting opening form **15** subsequent treatment with water

converts into N-phenacylisoquinolone **13**. Clevage of the C(2)–O bond under the action of sodium methylate was observed by us previously for oxazolopyridinium salt **1** (R = H) [22]. An analogous direction of opening the azole ring was also observed for the reaction of a thiazoloisoquinolinium salt (isostructure of salt **14**) with a secondary amine [20].

Interaction of salt **14** with ammonia in anhydrous medium leads to the formation of a new compound, imidazoisoquinoline **18**.

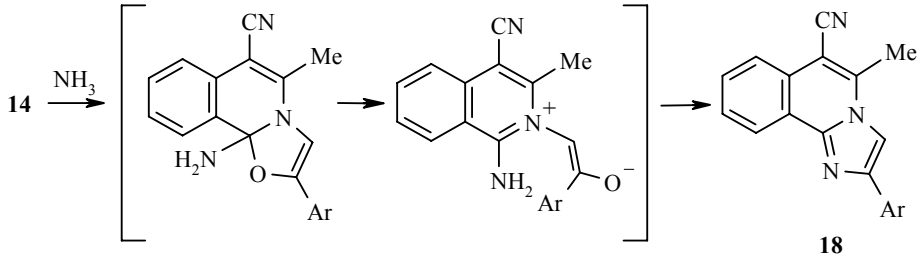
TABLE 6. Bond Lengths (*d*) in Structure **14**

Bond	*d*, Å	Bond	*d*, Å
C(1)–O(1)	1.341(9)	C(9)–C(10)	1.414(9)
C(1)–N(2)	1.353(9)	C(13)–C(14)	1.381(10)
C(1)–C(10)	1.371(10)	C(13)–C(18)	1.390(9)
O(1)–C(12)	1.381(8)	C(13)–C(12)	1.422(10)
N(2)–C(11)	1.382(9)	C(11)–C(12)	1.332(9)
N(2)–C(3)	1.389(9)	C(14)–C(15)	1.403(10)
C(3)–C(4)	1.384(10)	C(15)–C(16)	1.374(10)
C(3)–C(31)	1.513(9)	C(16)–C(17)	1.389(10)
C(4)–C(41)	1.422(10)	C(16)–Cl(16)	1.722(9)
C(4)–C(5)	1.454(9)	C(17)–C(18)	1.366(10)
C(41)–N(41)	1.119(10)	Cl(1)–O(14)	1.444(5)
C(5)–C(6)	1.412(9)	Cl(1)–O(11)	1.464(5)
C(5)–C(10)	1.413(9)	Cl(1)–O(12)	1.498(5)
C(6)–C(7)	1.388(10)	Cl(1)–O(13)	1.561(5)
C(7)–C(8)	1.404(10)	C(51)–C(52)	1.446(12)
C(8)–C(9)	1.361(10)	C(52)–N(53)	1.158(12)

TABLE 7. Valence Angles (ω) in Structure **14**

Angle	ω, deg	Angle	ω, deg
O(1)–C(1)–N(2)	107.7(8)	C(9)–C(10)–C(5)	120.6(8)
O(1)–C(1)–C(10)	126.9(8)	C(14)–C(13)–C(18)	117.2(8)
N(2)–C(1)–C(10)	125.4(9)	C(14)–C(13)–C(12)	121.0(8)
C(1)–O(1)–C(12)	108.2(6)	C(18)–C(13)–C(12)	121.6(8)
C(1)–N(2)–C(11)	108.5(7)	C(12)–C(11)–N(2)	107.1(7)
C(1)–N(2)–C(3)	120.3(8)	C(11)–C(12)–O(1)	108.4(7)
C(11)–N(2)–C(3)	131.0(7)	C(11)–C(12)–C(13)	134.5(8)
C(4)–C(3)–N(2)	118.5(7)	O(1)–C(12)–C(13)	117.1(7)
C(4)–C(3)–C(31)	125.5(8)	C(13)–C(14)–C(15)	121.8(8)
N(2)–C(3)–C(31)	116.0(7)	C(16)–C(15)–C(14)	118.7(8)
C(3)–C(4)–C(41)	119.5(8)	C(15)–C(16)–C(17)	120.4(8)
C(3)–C(4)–C(5)	120.2(8)	C(15)–C(16)–Cl(16)	119.9(7)
C(41)–C(4)–C(5)	120.3(8)	C(17)–C(16)–Cl(16)	119.5(7)
N(41)–C(41)–C(4)	176.1(10)	C(18)–C(17)–C(16)	119.4(8)
C(6)–C(5)–C(10)	120.0(7)	C(17)–C(18)–C(13)	122.3(8)
C(6)–C(5)–C(4)	120.3(9)	O(14)–Cl(1)–O(11)	113.7(4)
C(10)–C(5)–C(4)	119.7(8)	O(14)–Cl(1)–O(12)	110.8(3)
C(7)–C(6)–C(5)	118.7(9)	O(11)–Cl(1)–O(12)	111.3(4)
C(6)–C(7)–C(8)	119.9(9)	O(14)–Cl(1)–O(13)	109.0(3)
C(9)–C(8)–C(7)	123.0(8)	O(11)–Cl(1)–O(13)	105.7(3)
C(8)–C(9)–C(10)	117.8(8)	O(12)–Cl(1)–O(13)	105.8(3)
C(1)–C(10)–C(9)	123.4(8)	N(53)–C(52)–C(51)	179.1(14)
C(1)–C(10)–C(5)	115.9(7)		

In this case the mechanism of recyclization probably includes attack of an ammonia molecule at the bridging position of the oxazoloisoquinolinium cation, the opening of the ring, and its subsequent closing onto the incoming amino group.



18

Ar = *p*-ClC_6H_4

The result obtained in the reaction with ammonia does not exclude the alternative explanation of the conversaion of salt **14** under the action of morpholine and alcoholate. The unstable ylid **16**, which readily undergoes subsequent hydrolysis, may serve in the intermediate opening of the tricycle under the action of secondary amine or alcoholate. The closing of the pyrrole ring in ylid **16** (analogous to the recyclization of salt **1**) expected by us should lead to the tricyclic indolizine **17**. Possibly such recyclization did not occur due to the low aromaticity of indolizine **17**, which has a clear quinonoid structure.

In this way attempts to generalize the strategy of recyclization of the oxazole nucleus into a pyrrole (**1** →**2**) by transfer from the oxazolopyridinium system **1** to its benzenologs **3b**, **4b** (containing an isoquinoline fragment in the tricycle) encounter two inherent difficulties. The angular tricyclic cation **4b** was synthesized, however it proved not to have the capacity of recyclization into linear tricyclic indolizines **17**. The linear tricyclic cation **3b** generally was not obtained (in the standard strategy for the synthesis of salt **1**), since the isomeric O-alkyl derivative **10** is formed in place of the key intermediate **11**. It is interesting that in both cases the key factor distinguishing the isoquinoline system from the pyridine may be the instability of derivatives **11**, **17**, having a quinonoid motif in the isoquinoline fragment.

EXPERIMENTAL

The IR spectra were recorded on a UR 20 instrument in nujol. The ^1H and ^{13}C NMR spectra were recorded on a Bruker AC 400 instrument (400 and 90 MHz) in DMSO-d_6, internal standard was TMS. The mass spectra were obtained on a Finnigan MAT Incos 50 spectrometer with direct insertion of sample into the ion source, ionization energy was 70 eV.

X-Ray Structural Investigation of Compounds 10, 13, and 14. The experimental intensities of the diffraction patterns were obtained on a CAD4 diffractometer [23] (Cu*K*α radiation, λ = 1.5418 Å, graphite monochromator, ω-scanning). The parameters of the unit cells were determined and refined according to 25 reflections in the angle intervals θ 34.97-36.74°, 30.03-31.91°, and 25.05-26.60°. An absorption correction was introduced for compound **10** in accordance with North–Phillips–Mathews [24]. For compounds **13** and **14** no absorption correction was introduced, since they have low absorption coefficients and small linear dimensions. Primary processing of the masses of diffraction data was carried with the WinGX set of programs [25]. All the subsequent calculations were carried out with the SHELX97 set of programs [26]. The crystal structures were determined by direct methods with subsequent refinement of the positional and thermal parameters in an anisotropic approximation for all the non-hydrogen atoms. The hydrogen atoms were calculated from geometric

considerations and were refined within the framework of the "rider-atom" model. Individual crystallographic characteristics and experimental parameters, interatomic distances, and valence angles in the investigated compounds are set out in Tables 1-7. The spatial disposition of atoms in the molecules of compounds **10**, **13**, and **14**, and their numbering are shown in Figs. 1-3, and were obtained using the ORTEP-3 program [27]. The crystallographic information on compounds **10**, **13**, and **14** is deposited in the Cambridge structural data bank (deposit CCDC Nos. 687065, 687066, and 687067 respectively) [28].

1-Methyl-3-isoquinolone (8b). Ethyl diethoxyacetate (27 ml, 150 mmol) was added to a solution of sodium hydroxide (6.2 g, 155 mmol) in ethanol. The mixture was boiled for 1 h and the solvent removed in vacuum. The sodium diethoxyacetate obtained was suspended in anhydrous ether (120 ml), and thionyl chloride (11 ml, 150 mmol) was added to it in portions with stirring and cooling, maintaining the reaction temperature below 0°C. After the end of the addition the reaction mixture was boiled for 40 min, then poured into a mixture of benzene (75 ml), pyridine (45 ml), and α-methylbenzylamine (19 ml, 150 mmol) cooled in an ice bath. The mixture obtained was once again boiled for 40 min, then cooled to room temperature, and poured into water. The organic layer was separated and the aqueous layer was additionally extracted with benzene. The combined organic extracts were washed with 2% hydrochloric acid solution (1 liter), and evaporated in vacuum. Yield of **N-(1-Phenylethyl)-2,2-diethoxyacetamide** was 16 g (42%), n_D^{19} 1.5016. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.72 (1H, d, *J* = 7.96, NH); 7.18-7.32 (5H, m, C_6H_5); 4.98 (1H, m, CH); 4.68 (1H, s, $CH(OEt)_2$); 3.58 (4H, m, $C\underline{H}_2CH_3$); 1.45 (3H, d, *J* = 7.08, CH_3); 1.20 (6H, m, $CH_2C\underline{H}_3$).

N-(1-Phenylethyl)-2,2-diethoxyacetamide without further purification was induced into acid cyclization by the procedure of [29]. **1-Methyl-3-isoquinolone (8b)** was obtained in this way in 64% yield.

3-Methoxy-1-methylisoquinoline (9b). Compound **8b** (0.5 g, 3.14 mmol) was boiled for 30 min with a solution of sodium ethylate (3.14 mmol) in ethanol. The solvent was evaporated in vacuum. Methyl iodide (0.6 ml, 9.4 mmol) and absolute DMF (10 ml) were added to the obtained dry sodium salt. The mixture was maintained at 40°C for 16 h, then poured into water, and the mixture extracted with carbon tetrachloride. The solvent was removed in vacuum, and the residue chromatographed on a column of silica gel (eluent chloroform). Yield was 0.12 g (22%), R_f 0.6, oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.01 (1H, d, *J* = 8.85, H-8); 7.68 (1H, d, *J* = 7.96, H-5); 7.54 (1H, m, H-6); 7.34 (1H, m, H-7); 6.85 (1H, s, H-4); 3.96 (3H, s, OCH_3); 2.87 (3H, s, CH_3).

4-Cyano-3-methylisoquinol-1-one (12) was obtained by the procedure of [30].

1-(4-Bromophenyl)-2-[(1-methylisoquinolin-3-yl)oxy]ethanone (10). 1-Methylisoquinol-3-one (2 g, 13 mmol) was boiled for 30 min with a solution of sodium ethylate (13 mmol) in ethanol. The solvent was removed in vacuum. 4-Bromophenacyl bromide (3.6 g, 13 mmol) and absolute DMF (50 ml) were added to the obtained sodium salt. The reaction mixture was heated on a water bath for 4 h, then cooled to room temperature, and poured into water. The reaction product was extracted with chloroform, the extract washed with water, and evaporated in vacuum. The dry residue was crystallized from ethanol. Yield was 3.6 g (78%). Mp 123-125°C (ethanol). IR spectrum, ν, cm^{-1}: 1700, 1630, 1590. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.00 (1H, d, *J* = 7.96, H-8); 7.94 (2H, d, *J* = 8.0, ArH); 7.73 (1H, d, *J* = 8.84, H-5); 7.69 (2H, d, *J* = 8.0, ArH); 7.56 (1H, m, H-6); 7.36 (1H, m, H-7); 7.03 (1H, s, H-4); 5.62 (2H, s, CH_2); 2.74 (3H, s, CH_3). Found, %: C 60.75; H 3.91; N 4.02. $C_{18}H_{14}BrNO_2$. Calculated, %: C 60.69; H 3.96; N 3.93. X-ray structural analysis see Fig. 1, monocrystal was grown from acetonitrile.

2-[2-(4-Chlorophenyl)-2-oxoethyl]-4-cyano-3-methyl-1-isoquinolone (13) was obtained analogously to compound **10** from 4-cyano-3-methyl-1-isoquinolone (**12**) (1 g, 5 mmol) and *p*-chlorophenacyl bromide (1.3 g, 5 mmol). Reaction time was 5 h. Yield was 0.63 g (32%). Mp 247-249°C (ethanol). IR spectrum, ν, cm^{-1}: 2260, 1680 (1660 sh), 1600. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.24 (1H, d, *J* = 7.96, H-8); 8.14 (2H, d, *J* = 7.96, ArH); 7.86 (1H, m, H-7); 7.78 (1H, d, *J* = 7.96, H-5); 7.56-7.61 (3H, m, H-6, ArH); 5.77 (2H, s, CH_2); 2.63 (3H, s, CH_3). Found, %: C 67.64; H 3.78; N 8.34. $C_{19}H_{13}ClN_2O_2$. Calculated, %: C 67.76; H 3.89; N 8.32. X-ray structural analysis see Fig 2, monocrystal was grown from acetonitrile.

2-(4-Chlorophenyl)-6-cyano-5-methyl[1,3]oxazolo[2,3-*a*]isoquinolin-4-ium Perchlorate (14). Conc. H_2SO_4 (20 ml) was added to compound **13** (0.5 g, 1.5 mmol) and the mixture left overnight. The reaction mixture was poured into water, and an insoluble contaminant was filtered off. Perchloric acid (70%; 3 ml) was added to the filtrate. The resulting solid was filtered off, dried in vacuum, and crystallized from acetonitrile. Yield was 0.68 g (72%). Mp 298-299°C (acetonitrile. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 9.79 (1H, s, H-3); 9.00 (1H, d, *J* = 7.96, H-10); 8.36 (2H, m, H-7,8); 8.25 (2H, d, *J* = 7.96, ArH); 8.21 (1H, m, H-9); 7.71 (2H, d, *J* = 7.96, ArH); 3.20 (3H, s, CH_3). Found, %: C 54.60; H 3.16; N 8.99. $C_{21}H_{15}Cl_2N_3O_5$. Calculated, %: C 54.80; H 3.28; N 8.99. X-ray structural analysis see Fig. 3 (solvate with acetonitrile), monocrystal grown from acetonitrile.

2-(4-Chlorophenyl)-5-methylimidazo[2,1-*a*]isoquinoline-6-carbonitrile (18). A current of dry ammonia was passed through a suspension of oxazoloisoquinolinium perchlorate **14** (60 mg, 0.13 mmol) in acetonitrile (3 ml) for 2 h. The suspension rapidly passed into solution, and then a white precipitate formed. The mixture was allowed to stand for 5 days without access to air. The solvent was removed in vacuum, the solid residue extracted with chloroform, and the extract evaporated. Yield was 20 mg (40%). Mp 222-225°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.58 (1H, d, *J* = 7.05, H-10); 8.29 (1H, s, H-3); 8.10 (2H, d, *J* = 7.58, ArH); 7.90 (1H, m, H-8); 7.80 (2H, m, H-9,7); 7.54 (2H, d, *J* = 7.58. ArH); 2.93 (3H, s, CH_3). Mass spectrum, *m/z* (I_{rel}, %): 317/319 $[M]^+$ (100/35), 282 (6), 153 (8), 140 (32), 126 (12), 113 (16), 101 (13), 87 (14), 75 (40). Found, %: C 1.64; H 3.65; N 13.44. $C_{19}H_{12}ClN_3$. Calculated, %: C 71.81; H 3.81; N 13.22.

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