SYNTHESIS OF INDOLES FROM PYRIDINIUM SALTS.

6.* REACTION OF 3-NITROQUINOLINIUM SALTS WITH KETONES IN THE PRESENCE OF AMINES

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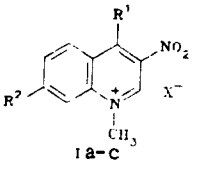
It is shown that in the reaction of 3-nitroquinolinium salts with aliphatic ketones and amines the ketone adds to the 2 and 4 positions with the formation of tricyclic adducts — benzazabicyclononane derivatives. Their conformational analysis was carried out on the basis of the NMR spectral data. Intermediate products of the monoaddition of ketones in the 4 position of the heteroring were isolated for the unsubstituted 3-nitroquinolinium salt.

We have recently established [1] that the diaddition of a ketone component to the 4 and 6 positions of the starting salt is necessary for the formation of indoles from 3-nitropyridinium salts. When 3-nitroquinolinium salts are used instead of 3-nitropyridinium salts this addition becomes impossible, which should lead to the realization of new reaction directions.

It is generally known that the ketone—amine system is the source of both N- and C-nucleophiles; an aliphatic ketone may act as both a mono- and a 1,3-bis-C,C-nucleophile. The addition of nucleophiles to nitro azines proceeds readily in the case of additional activation of the molecule by quaternization [2], by the introduction of a second nitro group [3, 4], or by benzannelation [4, 5]. The monoaddition of nucleophiles takes place primarily in the 4 position [2, 5]. The reaction with 1,3-bisnucleophiles leads to the formation of bicyclic adducts via meta bonding [4]. The only examples of meta bonding for 3-nitroquinoline are the reactions of the base and its N-oxide with 1,3-bis-C,N-nucleophile — phenylacetamidine [4]. The reaction of 3-nitroquinolinium salts with 1,3-bis-C,C-nucleophiles has not been previously studied. In this case one should also have expected both monoaddition of the ketone in the 4 position and its meta bonding in the 2 and 4 positions. To verify this assumption we selected the 1-methyl-3-nitroquinolinium cation (Ia) itself, as well as cations that contain substituents in the 4 (Ib) and 7 (Ic) positions, as starting 3-nitroquinolinium salts.



I a-c

I a $R^1=R^2=H$, $X=MeSO_4^-$; b $R^1=CH_3$, $R^2=H$, $X=MeSO_4^-$, c $R^1=H$, $R^2=OCH_3$, $X=PhSO_3^-$

The starting 3-nitroquinoline base and its 7-methoxy derivative were obtained by the methods in [6] and [7], respectively. To obtain 4-methyl-3-nitroquinoline we used replacement of the chlorine atom in 4-chloro-3-nitroquinoline by a methyl group, which was previously used only in the pyridine series [8] and consists in replacement of the chlorine atom by a malonic ester residue with subsequent hydrolysis and decarboxylation.

Both pathways, which lead to the formation of 4-acetonyl-1-methyl-3-nitro-1,4-dihydroquinoline (II) and two isomeric tricyclic products of meta bonding IIIa, b, are realized in the reaction of salt Ia with acetone and piperidine under mild conditions.

*See [1] for Communication 5.

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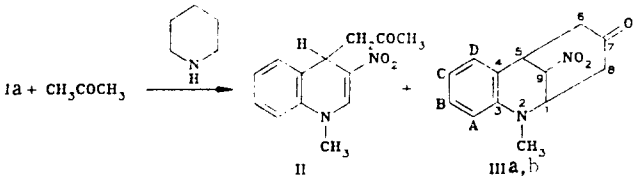
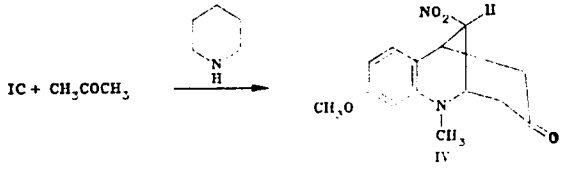


According to the NMR spectral data (see the subsection "Establishment of the Structures and Conformations"), 2-methyl-9-nitro[3,4]benz-2-azabicyclo[3.3.1]nonan-7-ones IIIa, b were found to be isomers with different orientations of the nitro group in the 9 position; isomer IIIa with an equatorial orientation of the nitro group relative to the cyclohexane ring is the predominant isomer (IIIa:IIIb = 7.4). Isomer IIIb is thermodynamically less stable, since we observed from the TLC and NMR spectral data that upon prolonged standing for a few months in solution in $CDCl_3$ it undergoes almost complete isomerization to the more stable IIIa isomer. Isomers IIIa, b differ substantially with respect to chromatographic mobilities and mass-spectral behavior (see the experimental section and the subsection on mass spectrometry). These differences, together with the NMR spectral data, assisted us in establishing the conformation of the nitro group in the remaining tricyclic structures.

Open form II is an intermediate form, and it was shown by chromatography that under the reaction conditions it is gradually converted to tricyclic III.

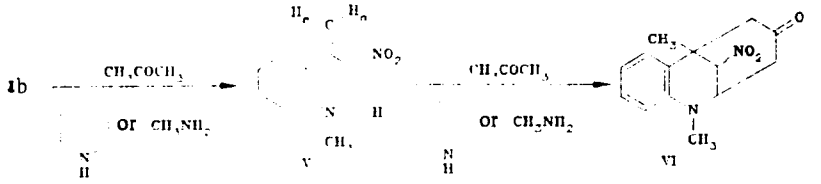
Bands of stretching vibrations of carbonyl (1725 cm^{-1}) and nitro groups are observed in the IR spectra of both structures II and III; the bands of symmetrical vibrations of the NO_2 group lie in the same region (1380 cm^{-1}), whereas the bands of asymmetrical vibrations differ markedly (1495 cm^{-1} for II and 1555 cm^{-1} for III). The UV spectra of II and III also differ substantially. As one should have expected, the presence of a nitro enamine conjugated fragment in II leads to the development of an intense long-wave maximum at 417 nm (log ε 4.22). Signals of 2-H and 4-H protons and an acetonyl residue are characteristic for structure II in the ^1H NMR spectrum. The signal of the 2-H proton (8.13 ppm, d, J_{24} = 0.7 Hz) is the weakest-field signal in the spectrum. The signals of the protons of the CH_2 group of the acetonyl residue and the 4-H proton constitute an ABX system with J_{AB} = 17.5 Hz, J_{AX} = 3.6 Hz, and J_{BX} = 6.2 Hz.

In contrast to unsubstituted salt Ia, salt Ic, which has a donor methoxy group in the 7 position of the nitroquinolinium cation, reacts with acetone with the formation of a single reaction product — azabicyclononane IV.



An open structure and a conformer with an axial nitro group were not detected in this case even in trace amounts.

Since it is known [9] that pyridinium cations that contain α- or γ-alkyl substituents are capable of undergoing facile deprotonation with the formation of neutral anhydro bases, we investigated a 4-methyl-3-nitroquinolinium salt (Ib) in the hope of isolating an anhydro base that is additionally stabilized by benzannelation and studying its reactivity.



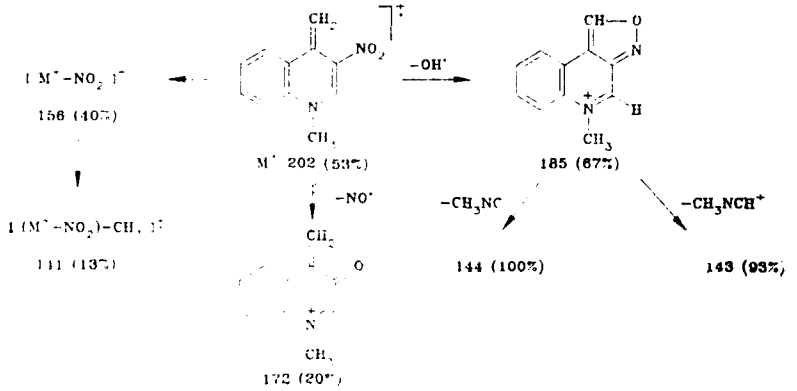
In fact, slightly soluble anhydro base V, the IR spectrum of which confirms the presence of a nitro group (1380 (sym) and 1520 (as) cm^{-1}), is readily formed in the action on salt Ib of both secondary (piperidine) and primary (methylamine) amines. In the ^1H NMR spectrum the weakest-field signal is the doublet of the 2-H proton (8.28 ppm), the multiplicity of which is due to spin-spin coupling with the β-H proton ($J_{2\beta}$ = 1 Hz) in conformity

TABLE 1. ^{1}H NMR Spectra of Benzazabicyclononanes in $CDCl_3$

Protons	Compound								
	IIIa	IIIb	IIIb*[1]	IV*[1]	VI	VIIIa	VIIIb	IXa	IXb
	Chemical shifts, δ, ppm								
1-H	4.51	4.52	3.74	4.23	4.29	4.49	4.55	4.19	4.49
5-H	4.03	4.10	3.42	3.94	1.66[5]*	3.76	3.90	4.01	4.07
6*a*-H	2.81	2.84	1.90	2.74	2.64	1.38[5]*	2.83	2.98	2.85
6*e*-H	2.69	2.56	2.31	2.58	2.55	2.84	1.09[5]*	2.60	2.74
8*a*-H	2.55	2.70	1.54	2.47	2.59	2.75	2.60	1.31[5]*	2.67
8*e*-H	2.77	2.70	2.23	2.68	2.80	2.68	2.81	2.81	1.18[5]*
9-H	5.11	5.14	3.86	5.08	5.20	5.22	5.22	5.22	5.18
N-CH_3	2.92	2.96	2.23	2.88	2.92	2.94	2.93	2.94	3.06
J	SSCC, Hz								
15	2.7	3.3	3.0	2.6	3*, 6*	3.0	2.8	2.7	3.0
18*a*	4.3	5*	4.2	4.2	4.3	4.0	3.8	3*, 6*	3.8
18*e*	2.7	5*	2.6	2.6	2.6	2.9	3.0	2.0	3*, 6*
19	3.0	3.0	3.0	3.2	2.7	3.0	3.0	3.2	2.8
56*a*	4.6	4.4	4.5	4.4	3*, 6*	3*, 6*	4.2	4.7	4.3
56*e*	3.2	2.7	3.2	3.2	3*, 6*	2.4	6*	3.2	3.4
59	2.6	3.0	2.6	2.5	3*, 6*	2.8	2.7	2.5	3.0
6*a*6*e*	−15.6	−15.8	−15.3	−15.4	−15.1	7.6[3]*	6.8[3]*	−15.8	−14.8
6*a*8*a*	(−)0.8[4]*	6*	(−)0.8[4]*	(−)0.7[4]*	(−)1.0[4]*	3*, 6*	(−)1.2[4]*	3*, 6*	(−)1.2[4]*
6*e*8*e*	2.6	3.0	2.7	2.8	2.5	1.8	3*, 6*	1.9	3*, 6*
8*a*8*e*	−16.3	6*	−16.2	−16.2	−16.0	−16.5	−15.5	7.5[5]	6.8[3]*

*[1]The spectrum was recorded in C_6D_6.
*[2]The chemical shift of the protons of the OCH_3 group was 3.72 ppm.
*[3]The parameter for the corresponding methyl group.
*[4]The sign of the constant is postulated (see the text).
*[5]$|J_{18a} + J_{18e}| = 6.5$ Hz.
*[6]Does not appear in the spectrum.

with the "zigzag rule" [10]. Signals of methylene protons are also characteristic for this system: the signal of the α-H proton lies at weaker field (6.03 ppm) than that of the β-H proton (5.47 ppm, d, J_{β_2} = 1 Hz), while the geminal spin-spin coupling constant (SSCC) is very small and does not show up in the spectrum. A characteristic signal of an exocyclic methylene group at 100.50 ppm is also observed in the ^{13}C NMR spectrum. The mass-spectral fragmentation of anhydro base V can be represented by the following scheme:



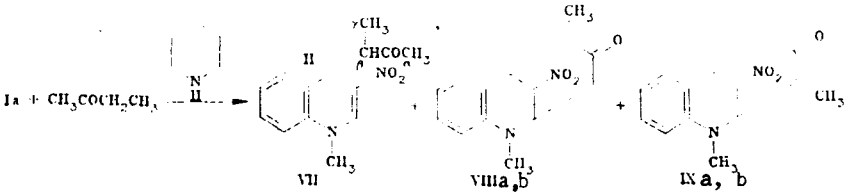
The isolated anhydro base was once again subjected to reaction with acetone and methylamine; this led to the formation of 2,5-dimethyl-9-nitro[3,4]-benz-2-azabicyclo[3.3.1]-nonan-7-one (VI). When a more basic amine – piperidine — is used, anhydro base V is formed in high yield, whereas meta bonding, which lead to tricyclic VI, takes place more slowly.

In the case of unsubstituted salt Ia we also investigated the possibility of a different regioorientation of addition in the case of an unsymmetrical ketone — methyl ethyl ketone.

TABLE 2. ^{13}C NMR Spectra (chemical shifts, δ, ppm) of the Benzazabicyclononanes in $CDCl_3$

Carbon atom	Compound			
	IIIa	IIIb	IV*	VI**
$C_{(1)}$	58.2	58.1	58.0	59.9
$C_{(3)}$	141.6	142.5	142.6	141.4
$C_{(4)}$	119.9	121.2	112.6	124.0
$C_{(5)}$	37.5	39.0	36.7	39.1
$C_{(6)}$	48.8	45.8	48.9	57.3
$C_{(7)}$	204.9	205.7	205.9	205.0
$C_{(8)}$	44.2	40.9	44.0	44.7
$C_{(9)}$	79.9	80.7	79.8	87.3
$N-CH_3$	37.2	37.4	37.2	37.7
A	111.3	111.6	97.6	111.4
B	128.8	128.8	160.3	128.5
C	118.2	118.4	102.9	118.4
D	129.1	129.4	129.6	125.0

*55.1 ppm ($7-OCH_3$).
**24.1 ppm ($5-CH_3$).



Of the two expected open forms under the selected conditions we were able to isolate only one — the product of attack of the methylene group of methyl ethyl ketone in the 4 position of the salt molecule (VII). Its IR and UV spectra are similar to the spectra of II. In addition to the characteristic signals of 2-H (8.21 ppm, d, J_{24} = 1.1 Hz) and 4-H (4.90 ppm, dd, J_{42} = 1.1 Hz, $J_{4\beta}$ = 4.2 Hz) protons, in the ^1H NMR spectrum of dihydroquinoline VII ($CDCl_3$) one observes signals of a methyl ethyl ketone residue: 2.18 (3H, d, α-CH_3, $J_{\beta\alpha}$ = 0.37 Hz), 2.73 (1H, dqd, β-H, $J_{\beta\alpha}$ = 0.37 Hz, $J_{\beta\gamma}$ = 7.0 Hz, $J_{\beta 4}$ = 4.2 Hz), 0.94 ppm (3H, d, γ-CH_3, $J_{\gamma\beta}$ = 7.0 Hz). A multiplet of four aromatic protons shows up at 6.96-7.42 ppm, while a singlet of protons of an $N-CH_3$ group appears at 3.48 ppm.

According to the spectral data and the results of elementary analysis, the benzazabicyclononane fraction isolated from the reaction is a mixture of four isomers. As one should have expected, when an unsymmetrical ketone is used, both possibilities of regioorientation of its diaddition are realized. In addition, each of the regiomers exists in the form of two isomers due to different orientations of the methyl group at the $C_{(6)}$ and $C_{(8)}$ centers. By means of high-performance flash chromatography [11] we were able to separate this fraction into three, two of which are individual VIIIb and IXa, the third of which is a mixture of regiomers VIIIa and IXb.

Establishment of the Structures and Conformations of the Benzazabicyclononanes

The structures of tricyclic III, IV, VI, VIII, and IX were established on the basis of a combination of data from the ^1H and ^{13}C NMR spectra (Tables 1 and 2). Characteristic signals for an o-disubstituted aromatic ring at 6.4-7.2 ppm are observed in the ^1H NMR spectra. A three-spin system of aromatic protons is characteristic for IV, and the aliphatic part of its spectrum contains a signal of protons of a methoxy group. Signals of $N-CH_3$ groups appear at 2.88-3.06 ppm ($CDCl_3$).

We made a detailed analysis of the multiplet structure of the aliphatic part of the spectra of the investigated compounds obtained with an instrument with an operating frequency of 360 MHz using the double-resonance technique; this enabled us to determine quite accurate values of virtually all of the SSCC. In the case of IIIb, because of the virtually complete coincidence of the chemical shifts of the 8a-H and 8e-H protons, the spectra of

TABLE 3. Mass Spectra of Benzazabicyclononanes

Compound	M⁺	F_1	F_2	F_3	F_3'	F_4	F_4'	F_5
IIIa	246 (43)	200 (18)	144 (100)	158 (41)	—	157 (19)	—	198 (35)
IIIb	246 (36)	200 (38)	144 (100)	158 (53)	—	157 (13)	—	198 (2)
IV	276 (100)	230 (57)	174 (97)	188 (42)	—	187 (14)	—	219 (23)
VI	260 (90)	214 (30)	158 (100)	172 (46)	—	157 (19)	—	203 (38)
VIIIa +IXb	260 (24)	214 (11)	144 (100)	172 (13) 158 (12)		171 (4) 157 (10)		189 (40)
VIIIb	260 (27)	214 (13)	144 (100)	172 (16)	158 (10)	171 (4)	157 (7)	189 (11)
IXa	260 (17)	214 (9)	144 (100)	158 (12)	172 (11)	157 (14)	171 (3)	189 (64)

solutions in $CDCl_3$ have an apparent simple structure, which does not make it possible to obtain complete information regarding all of the SSCC. In this case we used the specific solvation of C_6D_6, as a result of which we obtained sufficiently informative spectra (Table 1).

In all cases we assumed negative values for the geminal SSCC in the ^1H NMR spectra of the investigated tricyclic structures. The greater (with respect to the standard) values of these constants (from −14.8 to −16.5 Hz) indicate that the CH_2 groups are adjacent to the carbonyl fragment [12]. The signals of the 9-H proton attached to the carbon atom bonded to the nitro group [4], the multiplet structure of which constitutes evidence for spin-spin coupling with the 1-H and 5-H protons (a triplet for III, IV, VIII, and IX and a doublet for 5-methyl-substituted VI), are found in the characteristic region (5.08-5.22 ppm, $CDCl_3$). The assignment of the signals of the methylidyne 1-H and 5-H protons in the case of IIIa was made on the basis of $^{13}C\{^1H\}$ two-dimensional correlation spectra by coupling of the corresponding signals in the carbon spectra, which have characteristic differences in the chemical shifts (see Table 2). The mutual assignment of the signals of the 6-H and 8-H protons was made on the basis of experiments involving double resonance at the frequency of the 1-H and 5-H protons for each investigated structure.

The entire set of data obtained provides evidence that the investigated structures are benzazabicyclononane derivatives in which cis fusion of the saturated rings is realized.

A common problem for all of the investigated structures is the determination of the conformation of the NO_2 group in the 9 position. High stereospecificity of the reaction is observed for all cases of the reaction of 3-nitroquinolinium salts Ib, c with acetone, since it leads only to one conformer; we were able to isolate a second conformer (IIIb) in small amounts only for unsubstituted salt Ia. It should be noted in this case that closeness of the parameters of the ^1H and ^{13}C NMR spectra is observed for structures IV, VI, and major conformer IIIa. By means of the two-dimensional ^{13}C NMR J spectra with selective excitation of the 9-H proton we were able to determine for IIIa the constants of spin-spin coupling of the 9-H proton with the $C_{(6)}$ and $C_{(8)}$ carbon atoms, which were found to be 2.2 and 1.1 Hz, respectively (see [13] for a description of the method). These SSCC undoubtedly constitute evidence for an axial orientation of the 9-H proton in the cyclohexanone ring [14]. Furthermore, in comparing the chemical shifts in the ^{13}C NMR spectra of IIIa and IIIb one may note that a strong-field shift of the $C_{(6)}$ and $C_{(8)}$ signals of ∿3 ppm is observed for conformer IIIb (Table 2); this is normal for the manifestation of the γ NO_2 group in the cyclohexanone fragment [15]. Thus isomer IIIb can be considered to be the conformer with an axial NO_2 group.

Let us note that, up until now, the question of the conformation of the nitro group in such structures has remained open (for example, see [4]). We have been able to solve this problem for the first time on the basis of the spectral method set forth above.

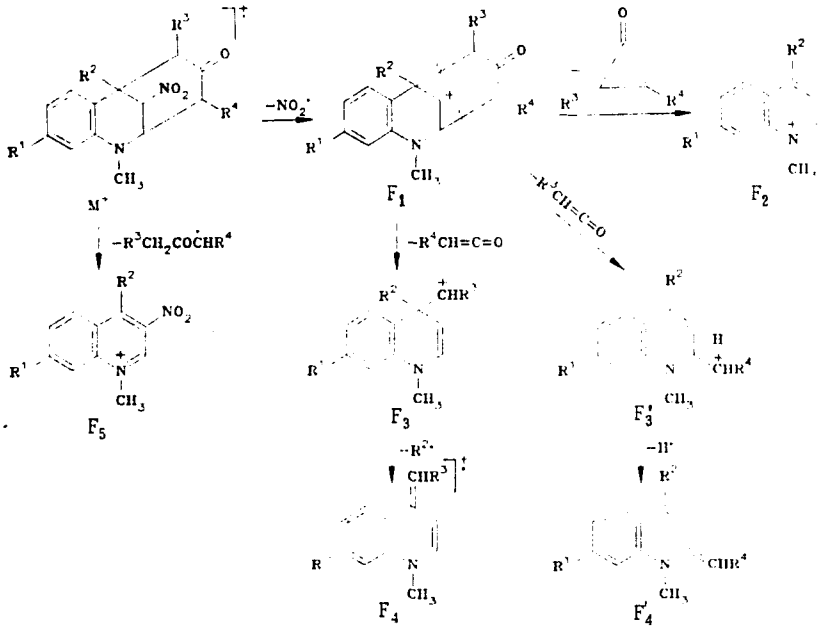
Four isomeric tricyclic compounds VIIIa, b and IXa, b, which, according to the ^1H NMR spectral data, are homologs of IIIa that contain methyl groups in the 6 or 8 position, are formed in the reaction of 3-nitroquinolinium salt Ia with methyl ethyl ketone. Signals of all three methylidyne protons — 1-H, 5-H, and 9-H — and a doublet signal of the CH_3 group with a splitting of 6.8-7.6 Hz are observed in the aliphatic part of the spectra of VIII and IX.

We interpreted the multiplet structure of the aliphatic part of the spectra of these compounds using the double-resonance technique for each isomer (Table 1). The position of the CH_3 group follows directly from the character of the multiplicity of the signals of the

6-H or 8-H proton: in VIIIa, b the methyl group is in the 6 position, whereas it is in the 8 position in IXa, b. To determine the conformation of the CH_3 groups we used the constants of long-range spin-spin coupling through four bonds; we assumed that such constants in structures of our type can have large values (on the order of 2-3 Hz) only in the case of an equatorial-equatorial orientation of the coupled protons, while for all of the remaining types of orientation such constants should have small (in absolute value) negative values [16]. In fact, for III, IV, and VI (Table 1) the $^4J_{8e6e}$ values are 2.5-3.0 Hz, while the $^4J_{6a8a}$ values, for which we postulated a negative sign, are small in absolute value (0.7-1.0 Hz), whereas $^4J_{6e8a}$ and $^4J_{6a8e}$ for all of the investigated compounds have negligibly small values. As criteria for establishing the conformation of the methyl group in VIII and IX one can also use the $^3J_{1a}$, $^3J_{1e}$, $^3J_{5a}$, and $^3J_{5e}$ constants, for which in the series of compounds III, IV, and VI a stable dependence is observed: the constant with the axial proton is ~1.6-1.7 Hz greater than the corresponding constant with the equatorial proton. Thus it follows from the data that we obtained that the CH_3 group in VIIIa and IXa is axially oriented, whereas in VIIIb and IXb it is equatorially oriented.

Mass-Spectral Investigation of the Compounds Obtained

The principal pathway of fragmentation of the molecular ions of benzazabicyclononanones III, IV, VI, VIII, and IX is elimination of an NO_2 radical (F_1) with the subsequent splitting out of a ketone fragment, which leads to a stable quinolinium ion (F_2), the peak of which is, as a rule, the maximum peak in the spectrum. In addition, the F_1 ion can eliminate ketene molecules via two possible pathways with the formation of F_3 and F'_3 fragments. The second pathway of the dissociative ionization of the molecular ions of these structures is due to the initial splitting out of a ketone fragment with retention of the nitro group (the F_5 ion). In the case of a pair of conformers with a different orientation of the nitro group — IIIa (e-NO_2) and IIIb (a-NO_2) — we observed a substantially different contribution of this fragmentation pathway: the intensities of the peaks of the F_5 ions are 35% and 2%, respectively. This makes it possible to propose a mass-spectrometric method for the determination of the conformation of the nitro group in such compounds. It is apparent from the data in Table 3 that the nitro group occupies an equatorial orientation in all of the remaining benzazabicyclononanes IV, VI, VIII, and IX.



In contrast to this, mass spectrometry does not reveal the principles of the dissociative ionization of the isomeric VIIIa, b and IXa, b structures (Table 3).

A characteristic peculiarity of the fragmentation of the molecular ions of open structures II and VII under the influence of electron impact is the lower (as compared with the tricyclic compounds) intensity of the peak of the molecular ion and the development of a new fragmentation pathway due to elimination of an OH group (see the experimental section).

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were obtained with a UR-20 spectrometer. The UV spectra of solutions in alcohol were recorded with a Cary-219 spectrophotometer. The NMR spectra were recorded with T-60, Jeol FX-100, and Bruker AM-360 spectrometers with TMS as the internal standard. The mass spectra were recorded with an MKh-1303 spectrometer with direct introduction of the samples into the ion source at an ionizing-electron energy of 70 eV at 90-110°C. The course of the reactions and the purity of the compounds obtained were monitored by TLC on Silufol in a benzene–ethyl acetate system (4:1).

See above for the preparation of the starting 3-nitroquinoline base and its 7-methoxy derivative, as well as 4-methyl-3-nitroquinoline.

1-Methyl-3-nitroquinolinium Methylsulfate (Ia). A mixture of 1.24 g (7 mmole) of 3-nitroquinoline, 10 ml of acetonitrile, and 1 ml (10 mmole) of dimethyl sulfate was refluxed for 12 h, after which the precipitate was removed by filtration to give 1.77 g (88%) of a product with mp 159-160°C (from acetonitrile). Found: C 44.1; H 3.9%. $C_{11}H_{12}N_2O_6S$. Calculated: C 40.0; H 4.0%.

1,4-Dimethyl-3-nitroquinolinium Methylsulfate (Ib). A 31-ml (210 mmole) sample of malonic ester was added to a solution of 5 g (210 mmole) of sodium in 100 ml of methanol, after which the methanol was removed by vacuum distillation to dryness, and the residue was dissolved in 150 ml of dry DMF. A solution of 17 g (80 mmole) of 4-chloro-3-nitroquinoline [17] in 200 ml of dry DMF was added dropwise in the course of 30 min at 70°C to the resulting solution, and the DMF was removed by vacuum distillation on a water bath. A 300-ml sample of 18% HCl was added to the residue, and the mixture was refluxed for 3 h and filtered. The filtrate was neutralized with 30% aqueous NaOH. After 1 h, the precipitated 4-methyl-3-nitroquinoline was removed by filtration, washed with water, and air dried to give 10 g (62%) of a product with mp 116-117°C (from aqueous acetone) (mp 116.5-118.5°C [18]).

The method used to obtain salt Ia was used to obtain 1.2 g (77%) of salt Ib, with mp 176-178°C (dec., from acetonitrile), from 0.94 g (5 mmole) of 4-methyl-3-nitroquinoline and 0.52 ml (5.5 mmole) of dimethyl sulfate after reaction for 15 h. Found: C 45.8; H 4.8%. $C_{12}H_{24}N_2O_6S$. Calculated: C 45.8; H 4.5%.

1-Methyl-7-methoxy-3-nitroquinolinium Benzenesulfonate (Ic). A mixture of 2.5 g (12 mmole) of 7-methoxy-3-nitroquinoline and 2.9 ml (22 mmole) of methyl benzenesulfonate was heated for 40 min at 140°C, after which the reaction mass was triturated with dry ether and filtered to give 4.35 g (96%) of salt Ic with mp 246-248°C. Found: C 54.2; H 4.4%. $C_{17}H_{19}N_2O_6S$. Calculated: C 54.2; H 4.4%.

Reaction of 3-Nitroquinolinium Methylsulfate (Ia) with Acetone and Piperidine. A 0.4 ml (4 mmole) sample of piperidine was added with stirring to a mixture of 0.6 g (2 mmole) of salt Ia and 7 ml of acetone. After 2 days, the mixture was evaporated in vacuo, and the residue was chromatographed with a column packed with silica gel (40/100 μm) with a successive increase in the polarity of the benzene–ethyl acetate eluent by changing the ratio from 10:1 to 4:1. The residue from evaporation of the fraction with R_f 0.80 was recrystallized from benzene–hexane (1:1) to give 27 mg (6%) of 2-methyl-9a-nitro[3, 4]benz-2-azabicyclo[3.3.1]nonan-7-one (IIIb) with mp 127-129°C.

Subsequent elution gave 200 mg (44%) of 9e-nitro isomer IIIa with R_f 0.42 and mp 173-175°C. Found: C 63.7; H 5.8%. $C_{13}H_{14}N_2O_3$. Calculated: C 63.4; H 5.7%.

Further elution gave (1-methyl-3-nitro-1,4-dihydro-4-quinoly)propan-2-one (II) with R_f 0.35 and mp 125-127°C; the yield was 42 mg (9%). ^{1}H NMR spectrum ($CDCl_3$): 2.04 (3H, s, $COCH_3$); 2.84 (A) and 3.03 (B) (2H, AB part of an ABX system, J_{AB} = 17.5 Hz, J_{AX} = 3.6 Hz, J_{BX} = 6.2 Hz, $COCH_2$); 3.50 (3H, s, N–CH_3); 4.85 (1H, X part of the ABX system, J_{AX} = 3.6 Hz, J_{BX} = 6.2 Hz, 4-H); 7.15 (4H, m, aromatic); 8.13 ppm (1H, d, J_{24} = 0.7 Hz, 2-H). ^{13}C NMR spectrum: 30.51 ($\underline{C}H_3CO$); 33.05 ($\underline{C}H_2CO$); 40.04 (N–CH_3); 50.60 [$C_{(4)}$]; 113.92 [$C_{(8)}$]; 125.59, 127.99 and 128.63 [$C_{(5)}$, $C_{(6)}$, $C_{(7)}$]; 142.57 [$C_{(2)}$]; 206.18 ppm (C=O). Mass spectrum*: 246 (20), 229 (22) [M^+ – OH], 200 (7.5), 199 (5), 198 (7), 190 (13), 189 (100), 186 (28), 185 (14.5), 184 (8.5), 159 (5), 158 (16), 157 (27), 156 (5), 144 (39), 143 (92), 141 (15), 131 (11.5), 130 (6.5), 128 (12) 117 (6), 115 (27.5).

*The peaks of ions with intensities >5% are presented. Here and subsequently, the m/z values (intensities in percent) are given for the ion peaks.

2-Methyl-9-nitro[3,4]-(3-methoxybenz)-2-azabicyclo[3.3.1]nonan-7-one (IV). A 0.39 ml (3.9 mmole) sample of piperidine was added to a mixture of 0.5 g (1.3 mmole) of salt Ic and 3 ml of acetone. After 2 days, the reaction mixture was evaporated in vacuo, and the residue was chromatographed with a column packed with silica gel (40/100 μm) in a benzene–ethyl acetate system (4:1) to give 0.25 g (68%) of tricyclic compound IV with mp 160-161°C (from benzene–hexane). Found: C 61.0; H 6.0%. $C_{14}H_{16}N_2O_4$. Calculated: C 60.9; H 5.8%.

1-Methyl-4-methylene-3-nitro-1,4-dihydroquinoline (Anhydro Base V). A 0.4-ml (4 mmole) sample of piperidine was added to a mixture of 0.65 g (2.1 mmole) of salt Ib and 4 ml of acetone, and the mixture was stirred for 2 days at 20°C. The bright-red crystals of anhydro base V were removed by filtration to give 0.18 g (43%) of a product with mp 195-196°C. ^{1}H NMR spectrum: 3.56 (3H, s, N–CH_3), 5.47 (1H, d, $J_{\beta 2}$ = 1 Hz, β-H), 6.03 (1H, s, α-H), 7.05-7.83 (4H, m, aromatic), 8.28 ppm (1H, d, $J_{2\beta}$ = 1 Hz, 2-H). ^{13}C NMR spectrum: 40.77 (N–CH_3); 100.50; (4-CH_2); 115.07 [$C_{(8)}$]; 124.89, 125.96 and 129.20 [$C_{(5)}$, $C_{(6)}$, $C_{(7)}$]; 142.68 ppm [$C_{(2)}$].

2,5-Dimethyl-9-nitro[3,4]benz-2-azabicyclo[3.3.1]nonan-7-one (VI). A) The mother liquor from the filtration of anhydro base V was evaporated in vacuo, and the residue was chromatographed with a column under the conditions used to isolate tricyclic compound IV to give 0.15 g (28%) of VI with mp 189-190°C.

B) A 4-ml sample of acetone and 4 ml of a 22% solution of methylamine in alcohol were added to 0.08 g (0.4 mmole) of anhydro base V, and the mixture was maintained at 20°C for 2 days. It was then evaporated in vacuo, and the reaction product was isolated as in the preceding experiment to given 0.064 g (65%) of VI, which was identical to the sample obtained by method A.

Reaction of 3-Nitroquinolinium Methylsulfate (Ia) with Methyl Ethyl Ketone and Piperidine. A 0.4-ml (4 mmole) sample of piperidine was added with stirring to a mixture of 0.6 g (2 mmole) of salt Ia and 4 ml of methyl ethyl ketone. After 2 days (see the preceding method), workup gave a mixture of approximately equal amounts of azabicyclononanes VIIIa, b and IXa, b (with an average R_f value of 0.52) [overall yield 238 mg (44%)] and 3-(1-methyl-3-nitro-1,4-dihydro-4-quinolyl)-2-butanol (VII) [82 mg (16%), mp 132-133°C, R_f 0.30]. ^{1}H NMR spectrum ($CDCl_3$): 0.94 (3H, d, J = 7.08 Hz, $CHCH_3$), 2.18 (3H, d, $COCH_3$, J_{CH_3CH} = 0.37 Hz), 2.73 (1H, m, $CHCH_3$), 3.48 (3H, s, N–CH_3) 4.90 (1H, dd, 4-H, J_{42} = 1.1 Hz, $J_{4-H,CH}$ = 4.2 Hz), 6.96-7.42 (4H, m, aromatic), 8.21 ppm (1H, d, 2-H, J_{24} = 1.1 Hz). ^{13}C NMR spectrum: 11.35 (CH_3CH), 29.03 (CH_3CO), 39.80 (N–CH_3), 39.94 (CHCO), 54.92 [$C_{(4)}$], 113.73 [$C_{(8)}$], 125.61, 128.12 and 129.73 [$C_{(5)}$, $C_{(6)}$, $C_{(7)}$], 142.75 [$C_{(2)}$], 208.88 ppm (CO). Mass spectrum*: M^+ 260 (10), 243 (3) [$M^+ - OH$], 191 (22), 190 (23), 189 (100), 185 (6), 183 (3), 173 (3), 170 (5), 144 (17), 143 (83), 142 (20), 141 (4), 131 (7), 130 (4), 129 (3), 128 (11), 127 (3), 117 (5), 116 (7), 115 (21).

The mixture of azabicyclononanes VIIIa, b and IXa, b was separated by means of high-performance flash chromatography [11] with a column packed with Silpearl adsorbent for TLC in a benzene–ethyl acetate system (3:1); the column was 200 by 20 mm, and the air pressure was 0.25 atm. Because of the extremely slight differences in the R_f values (ΔR_f 0.04-0.05) of the regioisomers and conformers of VIII and IX we used a single charge of no more than 50 mg in the column, thereby accumulating the amounts necessary for recording of the NMR spectra. The spectral samples were additionally crystallized from benzene–hexane. The 1,6e-dimethyl (VIIIb) and 1,8a-dimethyl (IXa) isomers were isolated in individual form, while 1,6a-dimethyl- (VIIIa) and 1,8e-dimethyl-9-nitro[3,4]-benz-2-azabicyclo[3.3.1]nonan-7-one (IXb) were isolated in the form of a mixture.

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ACYLATION OF PHENACYLPYRIMIDINES

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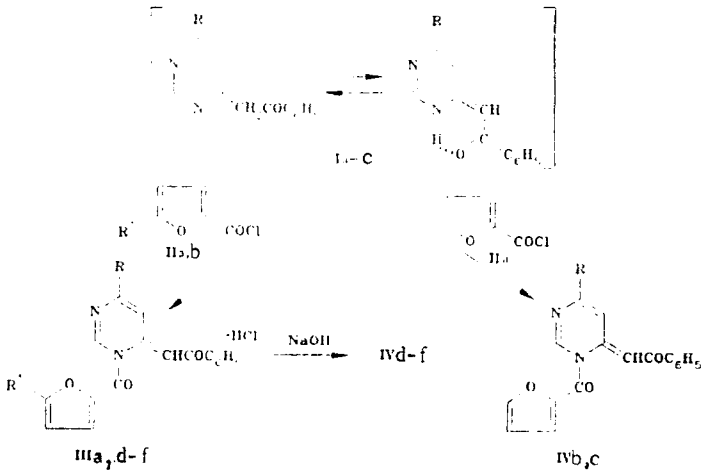
The reaction of phenacylpyrimidines with 2-furancarboxylic chlorides was studied. 1-Furoylphenacylidenepyrimidines were obtained.

For further study of the chemical properties of the pyrimidine-series ketones that we prepared previously [1, 2], we investigated the acylation of phenacylpyrimidines by 2-furancarboxylic chlorides.

In the reaction of phenacylpyrimidines Ia-c with acid chlorides IIa and IIb, we obtained the corresponding 1-furoylphenacylidenepyrimidines IVa-f:



I a $R=N(CH_3)_2$, b $R=OCH_3$, c $R=CH_2COC_6H_5$; II a $R^1=H$, b $R^1=NO_2$; III a, IV a $R=N(CH_3)_2$, $R^1=H$; IV b $R=OCH_3$, $R^1=H$; IV c $R=CH_2COC_6H_5$, $R^1=H$; III d, IV d $R=N(CH_3)_2$, $R^1=NO_2$; III e, IV e $R=OCH_3$, $R^1=NO_2$; III f, IV f $R=CH_2COC_6H_5$, $R^1=NO_2$

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