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17a-ACETOXY-16,16-DIMETHYL-8-AZA-D-HOMOGONA-1,3,5(10),9(11),13,17-HEXAEN-12-ONE, THE PRODUCT OF ACYLOTROPIC REARRANGEMENT AT INTERACTION OF 16,16-DIMETHYL-8-AZA-D-HOMOGONA-1,3,5(10),9(11),13-PENTAENE-12,17a-DIONE WITH ACETIC ANHYDRIDE

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On interaction of 16,16-dimethyl-8-aza-D-homogona-1,3,5(10),9(11),13-pentaene-12,17a-dione with acetic anhydride acylotropic rearrangement occurs with the formation of a single product, viz. 17a-acetoxy-16,16-dimethyl-8-aza-D-homogona-1,3,5(10),9(11),-13,17a-hexaen-12-one. The effect of sodium acetate and of acetic acid concentration on the result of the reaction has been studied. The structure of the product was confirmed by data of elemental analysis, IR, UV, ^1H, and ^{13}C NMR spectroscopy, mass spectrometry, and also X-ray structural analysis.

The oxidation–reduction deoxogenation of 8-aza-D-homogona-1,3,5(10),13-tetraene-12,17a-diones {or 1,13(2H),2,3,4,6,6,11b,12-heptahydrodibenzo[a,f]-quinolizine-1,13-diones} by the action of acetic anhydride has been reported recently [1,2]. The reaction leads to the unavailable by known methods 8-azasteroid derivatives, which belong to the group of low-molecular nonantigenic immunomodulators [3]. This reaction is of theoretical and practical interest as a model process in investigations of new chemical and biochemical conversions of condensed azinones, widely represented by natural [4] and synthetic analogs [5].

To clarify some aspects of the mechanism and scope of this reaction we investigated its application to 9,11-dehydro derivatives of 8-aza-D-homogonane having no active benzyl protons at the $C_{(9)}$ atom, the presence of which we considered to be a necessary prerequisite for the oxidation–reduction process [1,2]. 8-Aza-D-homogonane (I), obtained by annelation of 3,4-dihydroisoquinoline with 2-chloroacetyldimedone, was selected as the model [6]. The reaction of compound I with acetic anhydride was carried out with and without addition of acetic acid both in the presence and in the absence of fused sodium acetate, which possesses catalytic activity in acylation reactions and in O,C or O,O' isomerization. The results of the investigation showed that regardless of the presence of sodium acetate and the reaction conditions, the deoxogenation of homogonane I did not occur and the sole product in all cases was the enol acetate II. This indicates the correctness of our hypothesis on the need for the presence of benzyl hydrogen atoms in position 9 for oxidative–reductive deoxogenation [1,2]. It is important to note that in several cases complete conversion of the initial diketone I to enol acetate II was not reached probably due to the equilibrium character of this process.

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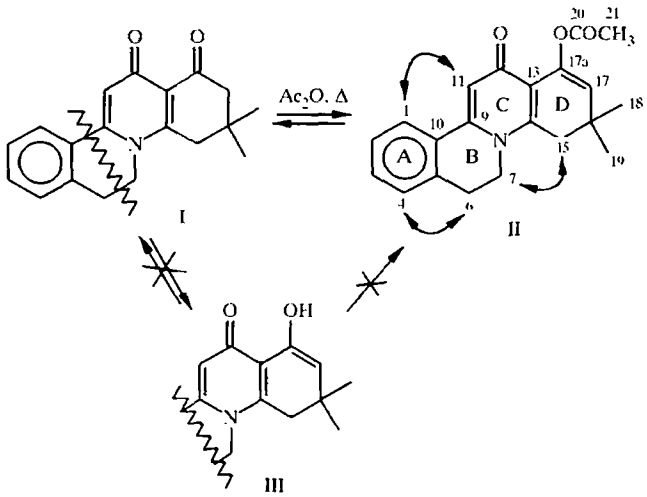
The effect of acetic acid concentration on the formation of compound II and acidolysis of the latter to homogonane I were studied in a more detailed investigation of the conversion. As a result of carrying out the reaction in acetic anhydride containing 10% (by volume) of acetic acid (Ac_2O : AcOH = 9 : 1), the amount of product II on reaching the equilibrium was 11% of the unreacted substrate I according to GLC data. Increase in the acetic acid concentration to 50% (Ac_2O : AcOH = 1 : 1) led to the formation of product II in trace amounts only (approximately 0.5-1%). On the other hand, removal of acetic acid formed in the course of the reaction enabled the equilibrium to be displaced practically completely toward the formation of enol acetate II.

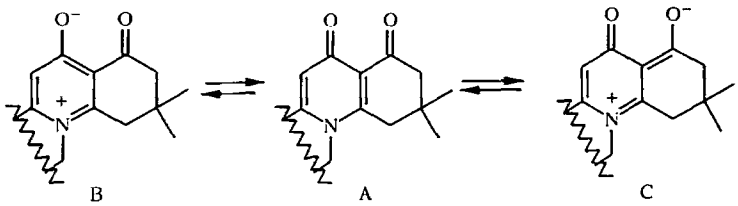
Scheme 1



The formation of enol acetate II may be represented as the result of acylation of enol III, since the keto–enol tautomerization I ⇄ III is possible for the 17a-carbonyl group of substrate I. To clarify the possibility of this route an investigation was undertaken of the H/D isotope exchange of the 8-aza-D-homogonane I by ^{1}H NMR method in various solvents (1. $CDCl_3$–D_2O–heterophase/20°C/240 h; 2. Py-d_5–D_2O/20°C/72 h; 3. CD_3COOD–D_2O/20°C/48 h). No reduction of the integrated intensity of the signal at 2.39 ppm for the protons of the $C_{(17)}H_2$ fragment was observed in any of the experiments. This indicates the absence of isotope exchange in the latter and permits exclusion of keto–enol tautomerism and the formation of product II through the enol III.

Another explanation of the investigated reaction is based on the mesomeric nature of 8-aza-D-homogonane (I) which may be represented by the set of limiting structures A, B, and C.

Scheme 2

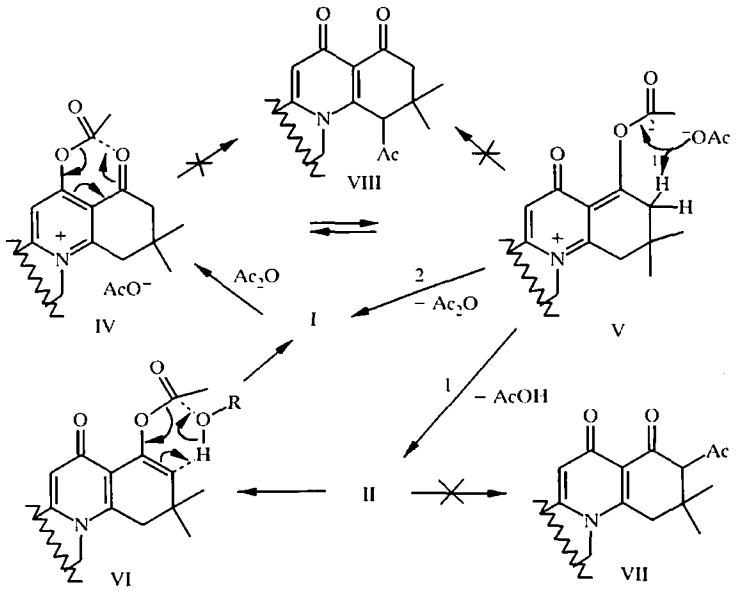


I

Evidently the oxygen atoms of both the $C_{(12)}$=O and the $C_{(17a)}$=O groups may be subjected to electrophilic attack by the acetic anhydride carbonyl group. On the basis of data for γ-pyridone rings the $C_{(12)}$=O bond length in the compound I is 1.236-1.249 Å [1,2,7] and that of $C_{(17)}$=O 1.218-1.222 Å [8], which together with data on protonation of 8-aza-D-homogonanes of type (I) enables the oxygen atom of the $C_{(12)}$=O group to be considered the

more preferred nucleophilic center. Consequently the formation of iminium salt IV (Scheme 3) may be the first step in the interaction of 8-aza-D-homogonane I with acetic anhydride. Due to the spatial proximity of the $C_{(12)}OAc$ and $C_{(17)}=O$ groups (2.0-2.5 Å) the compound IV undergoes O,O'-isomerization similar to the migration of acyl groups in the enol acylates of β-di- and β,β'-tricarbonyl compounds, known as the phenomenon of acylotropy [9], with the formation of the isomeric iminium salt (V) (intramolecular acylotropy). It should be mentioned that the formation of salts of 8-azasteroids was described previously in [6]. The conversion of salt V into enol acetate II was achieved by removal of proton from the $C_{(17)}H_2$ unit and subsequent migration of double bonds (route 1). On the other hand, nucleophilic attack of acetate anion at the $C_{(17)}OAc$ group enables regeneration of the initial compound I and acetic anhydride (route 2, intermolecular acylotropy).

Scheme 3



Enol acetate II is stable at room temperature in protic solvents (water, alcohols, glacial acetic acid). Monocrystals of it for X-ray crystallographic analysis were obtained by crystallization from ether–alcohol solution (95% alcohol, 128 h, 20°C) as crystal hydrate containing 0.5 moles of water. Keeping these crystals for 7 days in glacial acetic acid caused no changes in the reaction medium (TLC control). However, boiling the compound II in glacial acetic acid or aqueous alcohol solution leads to quantitative regeneration of ketone I. These results, together with the data on the effect of acetic acid concentration on the formation of enol acetate II indicate that on carrying out the reaction in the absence of sodium acetate the resulting product II is converted into the initial diketone I by acidolysis through the six-membered transition state VI (R = Ac). Hydrolysis of enol acetate II also occurs under the influence of strong acids (toluene-*p*-sulfonic, trifluoroacetic, and hydrochloric acids) or bases (sodium hydroxide) at room temperature, however under these conditions evidently other routes based on acidic and basic mechanisms are put into effect. Reaction in the presence of sodium acetate also represents a case of basic catalysis.

The structure of enol acetate II was confirmed by physicochemical methods, including X-ray structural analysis. Absorption bands were observed in its IR spectrum at 1755 and 1220-1245 cm^{-1} corresponding to C=O and C–O vibrations of the ester substituent and also at 1662 cm^{-1} characteristic of C=O vibrations of γ-pyridone fragment [10]. The UV spectrum of compound II was characterized by a broad intense absorption band at 275 nm which, according to literature data, must be assigned to absorption caused by π-π* electronic transitions of the γ-pyridone chromophore.

In the ^1H NMR spectrum of enol acetate II an additional three-proton singlet was present at 2.29 ppm for the acetoxy group in difference to the spectrum of the initial diketone I [12]. In place of the two-proton signal from $C_{(17)}H_2$ at 2.39 ppm for the initial diketone I an one-proton singlet was observed at 5.29 ppm assigned to the 17-H vinyl proton. The signals of the other structural fragments of compounds I and II were extremely similar. Complete assignment of the signals in the ^1H NMR spectrum of enol acetate II was performed with the aid of double resonance experiments and the nuclear Overhauser effect (NOE). Spin-spin coupling was established between two-proton triplets at 3.07 and 4.08 ppm which enabled assignment of these signals to protons in positions 6 and 7. The interaction of one-proton multiplets at 7.26 and 7.69 ppm with the two-proton multiplet at 7.39 ppm indicates that they are signals from the 1-, 2-, 3-, and 4-H aromatic protons. Consideration of the proposed structure of compound II with the aid of Dreiding models showed that three groupings of protons were sufficiently adjacent for observing NOE significant in value. In reality sequential saturation of the one-proton singlet at 6.88, the two-proton singlet at 2.80 and the two-proton triplet at 3.07 ppm led to the appearance of the corresponding signals in the differential NOE spectra, *viz.* multiplet at 7.69, triplet at 4.08, and multiplet at 7.26 ppm. Reverse experiments also confirmed the presence of NOE for these groupings and enabled assignment of the signals indicated to the protons at positions 11 and 1, 15 and 7, 6, and 4 respectively.

The ^{13}C $\{^1H\}$ NMR spectrum in combination with the DEPT spectrum of the compound II contains 21 signals from 21 ^{13}C atoms in the molecule. In character three of them were methyl, three methylene, and six methine group carbon atoms, but eight were quaternary carbons. Compared to the spectrum of diketone I additional signals were observed in the spectrum of enol acetate II at 21.006 and 169.809 ppm corresponding to ^{13}C atoms of CH_3 and COO groups. In place of the signal of the $^{13}C_{(17)}$ of methylene unit (51.589 ppm) a signal was observed for vinyl carbon atom at the same position at 115.513 ppm, and in place of the signal for the $C_{(17a)}$ carbonyl group atom (194.370 ppm) there was a signal for the $^{13}C_{(17a)}$ atom forming part of the vinyl grouping at 147.645 ppm. The assignment of signals in the ^{13}C NMR spectra of compounds I and II was made on the basis of literature data using the additivity principle [12,13].

Data of mass spectroscopy confirmed the structure of compound II showing the presence of molecular ion peak and fragmentation pattern characteristic of enol acetates [14].

The molecular and crystal structure of enol acetate II was established by X-ray structural analysis. This compound was shown to crystallize with a molecule of water. In the symmetrically independent part of the unit cell there were two chemically identical but crystallographically nonequivalent molecules (conformers) subsequently designated by us as a and b (in conformers a and b the rings are denoted as A', B', C', D', and A", B", C", D" respectively). Projections of both conformers are represented in Fig. 1, the plane of the aromatic ring being perpendicular to the plane of Fig. 1. Also a picture of the superposition of the conformers to one another is shown. As is seen the superimposed rings A' and A", B' and B" are not different practically. The conformational features of the molecules of the compound studied are as follows. The aromatic rings A' and A" are planar. The mean deviation of atoms forming the corresponding ring from the mean square plane was 0.004 (ring A') and 0.006 Å (ring A"). Rings B' and B" have the conformations of a half-bath, i.e., the $C_{(7)}$, $N_{(8)}$ atoms in B' and $C_{(7')}$, $N_{(8')}$ atoms in B", lying out of the plane of the ring are displaced to one side of it. The mean deviation of the atoms from the mean-square plane were 0.010 and 0.011 Å for B' and B" respectively. The dihedral angles between the planes of rings φ(A',B') and φ(A", B") were 2.7(3) and 3.7(2)°. Rings C' and C" were planar with mean deviation of atoms from the plane of 0.013 and 0.017 Å; dihedral angles were φ(B'C') = 20.7(2), φ(B"C") = 15.3(2)°. Rings D' and D" have the half-chair conformation, which is usual for 1,3-cyclohexadienes. It should however be mentioned that the torsion angle $C_{(14)}C_{(13)}C_{(17a)}C_{(17)}$ in the diene fragment of ring D' is 17.8(4)° and agrees with that for 1,3-cyclohexadiene molecule. In ring D" the analogous angle is 6.4(5)° so indicating a significant deformation of this ring. The structure of the tetracyclic molecular skeletons of both conformers are therefore mainly similar although it is possible to notice some flattening of the conformer b due to the significant torsional deformation of ring D" (Fig. 1). The bond lengths and valence angles in the molecules of both conformers do not differ within the limits of error (Tables 1, 2) and are usual for such a series of systems [8,15]. The significant distinction between the conformers is the different disposition of the acetyl fragment relative to the tetracyclic skeleton of the molecule (Fig. 1c). This is probably explained by the requirement for the most dense packing of molecules in the crystal. The latter is achieved firstly by the fact that a molecule of water links the conformers into trimolecular complex due

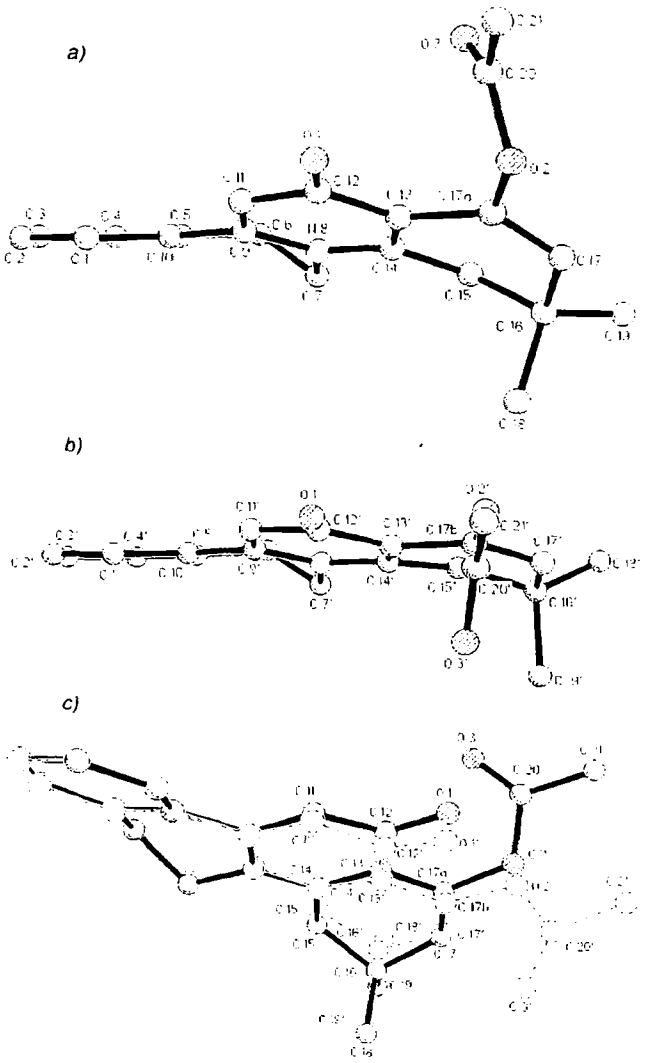


Fig. 1. Structure of the conformers of enol acetate (II): a) conformer a; b) conformer b; c) superposition of the structures of conformers a and b (dotted lines depict the atoms and bonds of conformer b).

to the formation of fairly strong hydrogen bonds; $d(O_{(1w)}\cdots O_{(1)})$ = 2.898(4), $d(O_{(1w)}-H_{(2w)})$ = 0.93(5), $d(H_{(2w)}\cdots O_{(1)})$ = 1.99(5) Å, $\omega(O_{(1w)}-H_{(2w)}\cdots O_{(1)})$ = 166(4)°; $d(O_{(1w)}\cdots O_{(1')})$ = 2.823(4), $d(O_{(1w)}-H_{(1w)})$ = 0.87(5), $d(H_{(1w)}\cdots O_{(1')})$ = 1.95(5) Å, $\omega(O_{(1w)}-H_{(1w)}\cdots O_{(1')})$ = 177(5)° (Fig. 2), and secondly the interaction between such aggregates in the structure is effected by means of van der Waals forces.

On the basis of the results of previous studies [1,2] it was presumed that 17- and/or 15-acetyl-substituted compounds VII or VIII – the products of α- or γ-O,C-isomerization of acetates II and/or compounds IV, V respectively – were obtained initially. However, regardless of the temperature of the reaction and its duration only the initial diketone I and enol acetate II were isolated from the reaction mixture. No formation of products of oxidation-reduction deoxogenation of substrate I [1,2] was observed in any experiment. This is possibly explained, on the one hand, by the steric hindrance to both α- and γ-O,C-isomerization linked with the presence of the *gem*-dimethyl grouping at the $C_{(16)}$ atom and by the absence of benzyl protons in position 9, and on the other hand by the thermodynamic preference for acylotropy compared with isomerization processes.

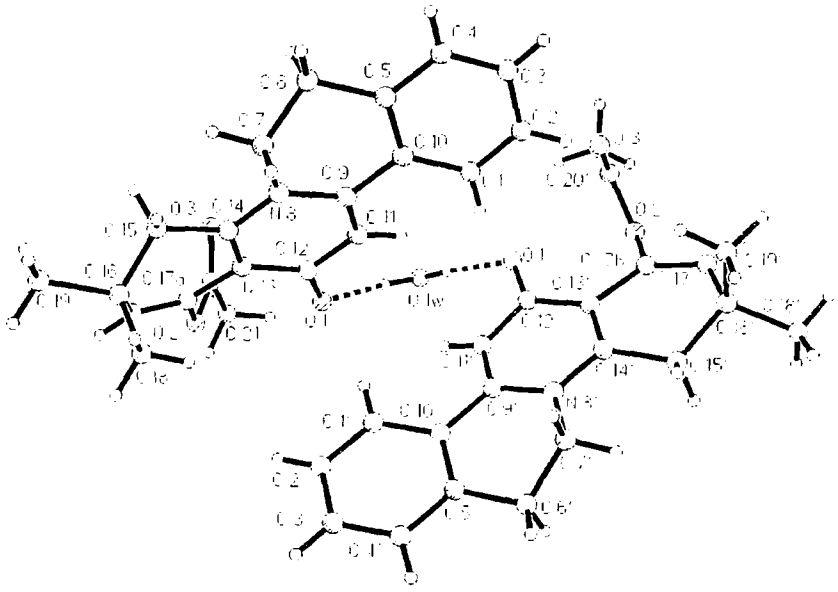


Fig. 2. Trimolecular complex in the crystal structure of enol acetate II (the hydrogen bonds are shown by dotted lines).

TABLE 1. Bond Lengths in Molecules of Conformers a and b of Enol Acetate II

Bond	*d*, Å	
	conformer a	conformer b
$C_{(1)}$–$C_{(2)}$	1.378(5)	1.374(5)
$C_{(1)}$–$C_{(10)}$	1.398(5)	1.393(5)
$C_{(2)}$–$C_{(3)}$	1.381(5)	1.371(6)
$C_{(3)}$–$C_{(4)}$	1.371(5)	1.368(6)
$C_{(4)}$–$C_{(5)}$	1.397(5)	1.393(5)
$C_{(5)}$–$C_{(10)}$	1.381(4)	1.389(4)
$C_{(5)}$–$C_{(6)}$	1.485(5)	1.496(5)
$C_{(6)}$–$C_{(7)}$	1.492(5)	1.472(5)
$C_{(7)}$–$N_{(8)}$	1.490(4)	1.491(4)
$N_{(8)}$–$C_{(14)}$	1.372(4)	1.381(4)
$N_{(8)}$–$C_{(9)}$	1.387(4)	1.376(4)
$C_{(9)}$–$C_{(11)}$	1.359(4)	1.357(4)
$C_{(9)}$–$C_{(10)}$	1.492(4)	1.487(4)
$C_{(11)}$–$C_{(12)}$	1.427(4)	1.428(4)
$C_{(12)}$–$O_{(1)}$	1.257(3)	1.262(3)
$C_{(12)}$–$C_{(13)}$	1.446(4)	1.436(4)
$C_{(13)}$–$C_{(14)}$	1.382(4)	1.380(4)
$C_{(13)}$–$C_{(17a)}$	1.474(4)	1.484(4)
$C_{(14)}$–$C_{(15)}$	1.515(4)	1.506(5)
$C_{(15)}$–$C_{(16)}$	1.522(5)	1.525(5)
$C_{(16)}$–$C_{(17)}$	1.497(4)	1.494(5)
$C_{(16)}$–$C_{(18)}$	1.534(5)	1.522(5)
$C_{(16)}$–$C_{(19)}$	1.541(5)	1.532(6)
$C_{(17)}$–$C_{(17a)}$	1.320(4)	1.324(4)
$C_{(17a)}$–$O_{(2)}$	1.407(3)	1.404(4)
$C_{(20)}$–$O_{(3)}$	1.198(4)	1.187(4)
$C_{(20)}$–$O_{(2)}$	1.354(4)	1.354(4)
$C_{(20)}$–$C_{(21)}$	1.480(5)	1.487(5)

TABLE 2. Valence Angles in Molecules of Conformers a and b of Enol Acetate II

Angle	ω, deg	
	conformer a	conformer b
$C_{(2)}$–$C_{(1)}$–$C_{(10)}$	120.2(3)	121.1(4)
$C_{(1)}$–$C_{(2)}$–$C_{(3)}$	119.8(4)	120.5(4)
$C_{(4)}$–$C_{(3)}$–$C_{(2)}$	120.4(3)	119.3(4)
$C_{(3)}$–$C_{(4)}$–$C_{(5)}$	120.4(4)	121.2(4)
$C_{(10)}$–$C_{(5)}$–$C_{(4)}$	119.4(3)	119.6(3)
$C_{(10)}$–$C_{(5)}$–$C_{(6)}$	118.4(3)	117.6(3)
$C_{(4)}$–$C_{(5)}$–$C_{(6)}$	122.2(3)	122.5(3)
$C_{(5)}$–$C_{(6)}$–$C_{(7)}$	112.7(3)	111.7(3)
$N_{(8)}$–$C_{(7)}$–$C_{(6)}$	111.4(3)	113.2(3)
$C_{(9)}$–$N_{(8)}$–$C_{(14)}$	120.0(2)	120.2(2)
$C_{(14)}$–$N_{(8)}$–$C_{(7)}$	121.1(2)	121.2(2)
$C_{(9)}$–$N_{(8)}$–$C_{(7)}$	119.0(3)	118.4(3)
$C_{(11)}$–$C_{(9)}$–$N_{(8)}$	119.2(3)	119.5(3)
$C_{(11)}$–$C_{(9)}$–$C_{(10)}$	122.2(3)	121.8(3)
$N_{(8)}$–$C_{(9)}$–$C_{(10)}$	118.5(2)	118.7(3)
$C_{(5)}$–$C_{(10)}$–$C_{(1)}$	119.8(3)	118.3(3)
$C_{(5)}$–$C_{(10)}$–$C_{(9)}$	119.6(3)	120.8(3)
$C_{(1)}$–$C_{(10)}$–$C_{(9)}$	120.5(3)	120.9(3)
$C_{(9)}$–$C_{(11)}$–$C_{(12)}$	124.1(3)	123.6(3)
$O_{(1)}$–$C_{(12)}$–$C_{(11)}$	121.6(3)	120.7(3)
$O_{(1)}$–$C_{(12)}$–$C_{(13)}$	123.9(3)	124.5(3)
$C_{(11)}$–$C_{(12)}$–$C_{(13)}$	114.5(2)	114.8(3)
$C_{(14)}$–$C_{(13)}$–$C_{(12)}$	120.3(3)	120.6(3)
$C_{(14)}$–$C_{(13)}$–$C_{(17a)}$	116.6(3)	116.7(3)
$C_{(12)}$–$C_{(13)}$–$C_{(17a)}$	123.1(3)	122.6(3)
$N_{(8)}$–$C_{(14)}$–$C_{(13)}$	121.8(3)	121.1(3)
$N_{(8)}$–$C_{(14)}$–$C_{(15)}$	118.9(3)	117.6(3)
$C_{(13)}$–$C_{(14)}$–$C_{(15)}$	119.2(3)	121.0(3)
$C_{(14)}$–$C_{(15)}$–$C_{(16)}$	113.7(3)	116.6(3)
$C_{(17)}$–$C_{(16)}$–$C_{(15)}$	109.4(3)	112.2(3)
$C_{(17)}$–$C_{(16)}$–$C_{(18)}$	110.3(3)	110.9(3)
$C_{(15)}$–$C_{(16)}$–$C_{(18)}$	109.0(3)	108.8(3)
$C_{(17)}$–$C_{(16)}$–$C_{(19)}$	109.5(3)	107.6(3)
$C_{(15)}$–$C_{(16)}$–$C_{(19)}$	108.3(3)	108.3(4)
$C_{(18)}$–$C_{(16)}$–$C_{(19)}$	110.3(3)	108.9(4)
$C_{(17a)}$–$C_{(17)}$–$C_{(16)}$	120.6(3)	121.9(3)
$C_{(17)}$–$C_{(17a)}$–$O_{(2)}$	117.7(3)	117.8(3)
$C_{(17)}$–$C_{(17a)}$–$C_{(13)}$	123.6(3)	124.4(3)
$O_{(2)}$–$C_{(17a)}$–$C_{(13)}$	118.6(2)	117.6(3)
$O_{(3)}$–$C_{(20)}$–$O_{(2)}$	123.0(3)	123.2(3)
$O_{(3)}$–$C_{(20)}$–$C_{(21)}$	126.7(3)	125.4(3)
$O_{(2)}$–$C_{(20)}$–$C_{(21)}$	110.4(3)	111.4(3)
$C_{(20)}$–$O_{(2)}$–$C_{(17a)}$	117.9(2)	117.2(2)

On the basis of the obtained results we have reached the conclusion that on interaction of 8-aza-D-homogonane I with acetic anhydride, a cyclic acylotropic process is effected in which the acetate II and 8-aza-D-homogonane I are in equilibrium. The oxidation-reduction deoxogenation of azines under the action of acetic anhydride described previously [1,2] is caused by the presence of active benzyl protons at position 9 of these molecules. The observed process of intra- and intermolecular acylotropy is of considerable theoretical interest as a model process for the transfer of acyl groups in chemical and biological systems.

TABLE 3. Coordinates ($\times 10^4$) and Equivalent Isotropic Thermal Parameters ($Å^2 \times 10^3$) of Atoms in the Structure of Enol Acetate II

Atom	*x/a*	*y/b*	*z/c*	*U*(eq)
		Conformer a		
$C_{(1)}$	-2194(2)	3037(3)	1125(2)	62(1)
$C_{(2)}$	-2828(2)	3114(4)	714(2)	73(1)
$C_{(3)}$	-3372(2)	3965(4)	894(2)	76(1)
$C_{(4)}$	-3282(2)	4742(4)	1474(2)	73(1)
$C_{(5)}$	-2642(2)	4672(3)	1896(2)	59(1)
$C_{(6)}$	-2528(2)	5477(4)	2538(2)	70(1)
$C_{(7)}$	-1742(2)	5817(3)	2670(2)	67(1)
$N_{(8)}$	-1263(1)	4663(2)	2662(1)	50(1)
$C_{(9)}$	-1438(2)	3676(3)	2197(2)	48(1)
$C_{(10)}$	-2101(2)	3813(3)	1723(2)	51(1)
$C_{(11)}$	-1019(2)	2602(3)	2205(2)	47(1)
$C_{(12)}$	-393(2)	2416(3)	2663(2)	48(1)
$C_{(13)}$	-228(2)	3479(3)	3130(2)	47(1)
$C_{(14)}$	-652(2)	4573(3)	3099(2)	50(1)
$C_{(15)}$	-452(2)	5692(3)	3575(2)	62(1)
$C_{(16)}$	369(2)	5819(3)	3729(2)	60(1)
$C_{(17)}$	680(2)	4538(3)	3921(2)	58(1)
$C_{(17a)}$	398(2)	3486(3)	3639(2)	51(1)
$C_{(18)}$	738(2)	6347(4)	3070(2)	80(1)
$C_{(19)}$	481(3)	6743(4)	4358(2)	94(1)
$C_{(20)}$	348(2)	1361(3)	4062(2)	60(1)
$C_{(21)}$	777(3)	161(3)	4085(2)	86(1)
$O_{(1)}$	-18(1)	1408(2)	2645(1)	60(1)
$O_{(2)}$	754(1)	2323(2)	3795(1)	58(1)
$O_{(3)}$	-268(2)	1505(2)	4253(1)	74(1)
		Conformer b		
$C_{(1')}$	-749(2)	-3105(4)	-1176(2)	72(1)
$C_{(2')}$	-1334(2)	-3861(4)	-1377(2)	86(1)
$C_{(3')}$	-1717(2)	-4524(4)	-881(2)	81(1)
$C_{(4')}$	-1522(2)	-4399(4)	-180(2)	76(1)
$C_{(5')}$	-935(2)	-3629(3)	37(2)	60(1)
$C_{(6')}$	-743(2)	-3392(4)	801(2)	78(1)
$C_{(7')}$	48(2)	-3166(4)	915(2)	77(1)
$N_{(8')}$	344(1)	-2166(2)	437(1)	52(1)
$C_{(9')}$	68(2)	-2095(3)	-247(2)	48(1)
$C_{(10')}$	-544(2)	-2961(3)	-465(2)	51(1)
$C_{(11')}$	353(2)	-1233(3)	-701(2)	50(1)
$C_{(12')}$	974(2)	-450(3)	-531(2)	50(1)
$C_{(13')}$	1243(2)	-556(3)	189(2)	48(1)
$C_{(14')}$	923(2)	-1395(3)	653(2)	54(1)
$C_{(15')}$	1141(2)	-1404(5)	1427(2)	88(1)
$C_{(16')}$	1903(2)	-894(3)	1622(2)	62(1)
$C_{(17')}$	2141(2)	130(3)	1126(2)	62(1)
$C_{(17b)}$	1850(2)	249(3)	480(2)	54(1)
$C_{(18')}$	1903(3)	-405(5)	2381(2)	106(2)
$C_{(19')}$	2452(3)	-1997(5)	1574(3)	107(2)
$C_{(20')}$	2623(2)	985(3)	-413(2)	61(1)
$C_{(21')}$	2796(2)	2115(4)	-856(2)	85(1)
$O_{(1')}$	1262(1)	237(2)	-997(1)	70(1)
$O_{(2')}$	2098(1)	1258(2)	58(1)	59(1)
$O_{(3')}$	2913(2)	-28(3)	-446(2)	84(1)
		Water molecule		
$O_{(1w)}$	-517(2)	-1121(3)	2232(2)	89(1)

EXPERIMENTAL

Melting points were determined on a Boetius heating block. The IR spectra were obtained on a UR 20 instrument in KBr disks. The UV spectra were taken on a Specord M 400 spectrophotometer for solutions in ethanol. The ^{1}H and ^{13}C NMR spectra were obtained on a Bruker AC 200 spectrometer, resonance frequencies were 200 and 90.54 MHz respectively, internal standard was TMS. Experiments on double resonance and NOE were effected using programs provided with the instrument. Chromato-mass spectra of enol acetate II were obtained on a Shimadzu GC 17A/QP 5000 chromato-mass spectrometer using a capillary column (50 m × 0.3 mm, universal phase SE-54), carrier gas was helium (30 m/sec), temperature program 5-300°C, 5°C/min, evaporator temperature 210°C; ionizing voltage 70 eV. A check on the progress of reactions and the purity of products was effected using GLC and TLC. The TLC was carried out on Silufol UV-254 plates (chloroform–methanol, 9.5 : 0.5), visualizing with UV light and iodine vapor, with subsequent calcining at 250-350°C. The GLC analysis was carried out on a Chrom-4 chromatograph with a flame-ionization detector, using a quartz capillary column (length 25 m, internal diameter 0.25 mm, stationary phase SE-3C, 0.3 μm), carrier gas was helium (28 cm/sec); stream division of carrier gas 1/30; temperature program 35-310°C, 5°C/min; evaporator temperature 180°C; test sample 0.5 μl 3% solution of reaction mixture in chloroform. Distillation of solvents was carried out at reduced pressure on a rotary evaporator.

X-Ray Structural Analysis of Compound II Solvate was carried out on a prismatic crystal of size of 0.85 × 0.50 × 0.25 mm. A three-dimensional set of X-ray diffraction data was obtained on a Nicolet R3m automatic four-circle diffractometer, MoKα radiation, graphite monochromator, θ/2θ scanning (2θ max = 55°). Total number of reflections measured was 6388, of which 5580 were independent ($R_{(int)}$ = 0.0456). The compound crystallizes in monoclinic form, space group $P2_{1/n}$. Unit cell parameters: a = 18.233(6); b = 10.463(2); c = 18.880(5) Å; β = 91.48(2)°; V = 3601(2) Å^3; Z = 8; $d_{(roentg.)}$ = 1.271 g/cm^3; μ = 0.86 cm^{-1}. The structure of the compound was solved by the direct method. The positions of hydrogen atoms (except for the hydrogen atoms of the water molecule located from a Fourier differential synthesis) were calculated geometrically. Refinement was carried out with a full-matrix least-squares method taking into account the anisotropy of the thermal vibrations of the nonhydrogen atoms. The hydrogen atoms were refined with a rider model (hydrogen atoms of the water molecule were refined in isotropic mode). Final values of the uncertainty factors: R_1 = 0.0622, wR_2 = 0.1720 [$I > 2\sigma(I)$]; R_1 = 0.0817, wR_2 = 0.1995 (all data). All calculations were carried out with the aid of the SHELX-97 (PC version) programs [16-18]. The coordinates and equivalent isotropic thermal parameters of atoms are given in Table 3.

17a-Acetoxy-16,16-dimethyl-8-aza-D-homogona-1,3,5(10),9(11),13,17-hexaen-12-one (II). A. Synthesis in the Presence of Sodium Acetate. Mixture of 8-aza-D-homogonane (I) (1.47 g, 5 mmol) and fused sodium acetate (0.41 g, 5 mmol) in acetic anhydride (8 ml) was boiled in atmosphere of argon. After 3.5 h the ratio of initial compound I and product II in the reaction mixture became constant (TLC data). Boiling was continued for 15 h, the reaction mixture was then evaporated under reduced pressure, and the residue dissolved in chloroform. The solution obtained was washed with water, dried over sodium sulfate, and separated into two fractions by flash chromatography on silica gel (15 g; 5/40 μ, eluent chloroform–methanol, 9.5 : 0.5). Enol acetate II (0.7 g) was obtained from the first fraction after evaporation and crystallization of the residue from chloroform–hexane mixture. Compound II formed fine plate-like crystals; yield 41.7%; mp 108-111°C. IR spectrum: 1755, 1662, 1605, 1585, 1551, 1495, 1366, 1200-1245, 1175, 1093, 780 cm^{-1}. UV spectrum, λ_{max}, nm (ε): 205 (23290), 275 (33540), 304 (11645), λ_{min}, (ε): 238 (9320). ^{1}H NMR spectrum: 1.16 (6H, s, $C_{(18)}H_3$, $C_{(19)}H_3$); 2.29 (3H, s, $C_{(21)}H_3$); 2.80 (2H, s, $C_{(15)}H_2$); 3.07 (2H, t, J = 6.3 Hz, $C_{(6)}H_2$); 4.08 (2H, t, J = 6.3 Hz, $C_{(7)}H_2$); 5.29 (1H, s, $C_{(17)}H$); 6.88 (1H, s, $C_{(11)}H$); 7.26 (1H, d, J = 7.7 Hz, $C_{(4)}H$); 7.39 (2H, m, $C_{(2)}H$ and $C_{(3)}H$); 7.69 ppm (1H, m, $C_{(1)}H$). ^{13}C NMR spectrum: 21.006 ($C_{(21)}$); 27.952 ($C_{(18)}$ and $C_{(19)}$); 28.34 ($C_{(6)}$); 31.211 ($C_{(16)}$); 39.796 ($C_{(15)}$); 44.715 ($C_{(7)}$); 115.513 ($C_{(17)}$); 117.183 ($C_{(13)}$); 120.394 ($C_{(11)}$); 125.784 ($C_{(4)}$); 127.378 ($C_{(2)}$); 128.087 ($C_{(3)}$); 129.357 ($C_{(10)}$); 130.304 ($C_{(1)}$); 133.769 ($C_{(5)}$); 143.821 ($C_{(14)}$); 144.035 ($C_{(9)}$); 147.645 ($C_{(17a)}$); 169.809 ($C_{(20)}$); 179.971 ppm ($C_{(12)}$). Mass spectrum, m/z (I_{rel}, %): 336.30 $[M + 1]^{+\cdot}$ (0.95); 335.30 $[M]^{+\cdot}$ (4.11); 294.25 $[M + 1 - CH_2OH]^{+\cdot}$ (1.33); 293.25 $[M - CH_2CO]^{+\cdot}$ (5.61); 292.25 $[M + 1 - CH_3CO]^{+\cdot}$ (2.26); 280.25 $[M + 1 - CH_2CO - CH_2]^{+\cdot}$ (2.54); 279.25 $[M + 1 - CH_2CO - Me]^{+}$ (19.63); 278.20 $[M - CH_2CO - Me]^{+}$ (100); 276.20

(1.87); 264.20 (2.61); 263.20 (6.23); 262.15 (3.57); 250.20 (2.56); 249.20 (1.82); 248.20 (6.36); 235.20 (2.36); 234.15 (4.30); 233.15 (2.10); 220.15 (3.18); 218.20 (1.47); 217.15 (1.67); 206.15 (1.94); 181.15 (1.62); 180.15 (1.66); 115.05 (3.77); 102.05 (1.58); 77.05 (3.95). Found, %: C 75.24; H 6.35; N 4.11. $C_{21}H_{21}NO_3$. M^+ 335. Calculated, %: C 75.20; H 6.31; N 4.18. M 335.40.

The starting material I (0.75 g: 51%) was obtained from the second fraction after evaporation and crystallization of the residue (ethanol–ether). It was identical with an authentic specimen of 8-aza-D-homogonane (I) (TLC, mp of a mixed test sample); mp 247-250°C. Lit. mp 247-250°C [6]; 247-249°C [12].

B. Synthesis in the Absence of Sodium Acetate. 8-Aza-D-homogonane (I) (0.88 g, 3 mmol) was boiled in acetic anhydride (5 ml) in atmosphere of argon. After 3.5 h the ratio of compounds I and II in the reaction mixture remained unchanged. Boiling was continued for 6.5 h, acetic anhydride was then evaporated, the residue was kept in a vacuum desiccator over KOH for 24 h, then dissolved in chloroform, and separated into two fractions by flash chromatography. The enol acetate II (0.51 g, 51%) was obtained from the first fraction as yellow prismatic crystals after evaporation and crystallization of the residue from ethanol–ether. A monocrystal was taken for X-ray structural analysis. Mp 115.0-117.5°C. The compound II obtained was identical with a sample synthesized by method A (TLC, IR, UV spectra, mp of mixed sample). The diketone I (0.37 g, 42%) was obtained from the second fraction by evaporation and crystallization from ethanol–ether; mp 247-249°C. Found, %: C 73.18; H 6.39; N 4.00. $C_{21}H_{21}NO_3 \cdot 0.5\ H_2O$. M^+ 335. Calculated, %: C 73.24; H 6.44; N 4.07. M 344.41.

C. Synthesis with Distillation of Acetic Acid. 8-Aza-D-homogonane (I) (0.74 g, 2.5 mmol) was boiled in acetic anhydride (10 ml) in atmosphere of argon, distilling off acetic acid formed in the course of the reaction. After 7 h the reaction mixture, the volume of which was reduced by approximately half, was evaporated to dryness. The residue was kept over KOH in a vacuum desiccator, then dissolved in chloroform, and the solution filtered through silica gel (5 g). After evaporation of the filtrate and crystallization of the residue (chloroform–hexane), enol acetate II (0.8 g, 96%) was isolated as yellow plate-like crystals, identical (TLC, IR, and UV spectra) with that obtained by methods A and B; mp 108-111°C.

Acidolysis of Enol Acetate II. Solution of enol acetate II (0.5 g) in glacial acetic acid (5 ml) was kept at 20°C for 7 days (according to TLC no changes were occurring at this time). The reaction mixture was then boiled and after 3 h complete conversion of enol acetate II into diketone I had occurred (according to TLC data). Boiling was continued for 1 h further, after which the reaction mixture was evaporated, the residue kept for 24 h over KOH in a vacuum desiccator, and crystallized (ethanol–ether). 8-Aza-D-homogonane (I) (0.42 g, 95%) was obtained as fine colorless prismatic crystals of mp 247-250°C. The compound obtained was identical to a known specimen of 8-aza-D-homogonane (I) (TLC, no depression of mp of a mixed sample). ^{13}C NMR spectrum: 28.353 ($C_{(6)}$); 28.548 ($C_{(18)}$, $C_{(19)}$); 31.72 ($C_{(16)}$); 41.495 ($C_{(15)}$); 45.002 ($C_{(7)}$); 51.589 ($C_{(17)}$); 117.874 ($C_{(11)}$); 119.994 ($C_{(13)}$); 125.806 ($C_{(4)}$); 127.575 ($C_{(2)}$); 128.056 ($C_{(3)}$); 128.575 ($C_{(10)}$); 130.744 ($C_{(1)}$); 134.417 ($C_{(5)}$); 144.811 ($C_{(9)}$); 157.244 ($C_{(14)}$); 175.637 ($C_{(12)}$); 194.307 ($C_{(17a)}$).

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