ANGULARLY ALKYLATED 8-AZA-D-HOMOGONANES

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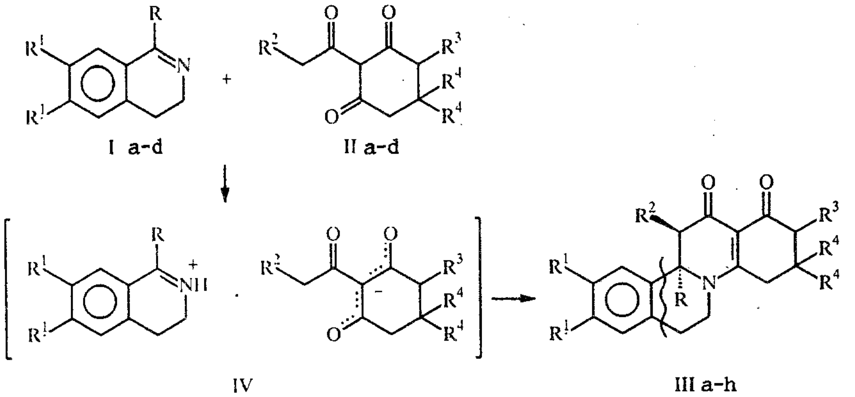
We have established that cyclic azomethines (1-alkyl-substituted 3,4-dihydroisoquinolines) enter into the annelation reaction with cyclic β-triketones (2-acyl-1,3-cyclohexanediones) with formation of C-9 angularly alkylated 8-aza-D-homogonanes. We have shown that the reaction of asymmetric β-triketones (2-acetyl-5,5-dimethyl-4-methoxycarbonyl-1,3-cyclohexanedione) is accomplished regioselectively, leading to the 17-methoxycarbonylated 8-aza-D-homogonane derivative, existing in solutions in the form of a mixture of stereiosomers with respect to C-17 (due to keto-enol tautomerism) and in crystals in the form of a single stereoisomer. The structure of the 8-azo-D-homogonanes has been proven by UV, IR, and PMR spectra.

Annelation of cyclic Schiff bases by β-di- and tricarbonyl compounds is a key step AB + D → ABCD in the synthesis scheme for a new class of low-molecular nonantigenic immunomodulators of the 8-azasteroid series, which are of interest as base material for creation of drugs with a specified set of biological properties [1-4]. However, the mechanisms and range of applicability of this reaction has been little studied, which limits the efficacy of its use. Thus there is no information in the literature about including 1-alkyl-substituted 3,4-dihydroisoquinolines in this reaction, and available data on the reaction of 1-methyl-substituted 3,4-dihydroisoquinolines with carbonyl compounds suggest that the reaction is oriented at the methyl group [5-6], which does not allow us to make any justifiable prediction about their inclusion in the reaction of annelation with β-triketones. Nevertheless, these questions acquire fundamental importance in the development of approaches to compounds of a specified structure and in connection with the need to obtain the broadest possible series of biologically active 8-azasteroids, required for analysis of the interconnection between the structure and the biological function of this class of compounds.

1-Alkyl-substituted 3,4-dihydroisoquinolines (Ia-d) were obtained by the Bishler–Napiral'skii reaction [7], condensation of phenethylamine acetamide under the action of polyphospheric acid (Ia) and condensation of the corresponding amides of 3,4-dimethoxyphenethylamine under the action of phosphorus oxychloride (Ib-d). 2-Acetyldimedone (IIa) was obtained by the previously described O,C-rearrangement of the enol acetate of dimedone under the action of aluminum chloride in dichloroethane [8]. 2-Propionyldimedone (IIb) and 2-acetyldihydroresorcinol (IIc) were obtained analogously using zinc chloride as the catalyst for O,C-isomerization. 2-Acetyl-4-methoxycarbonyldimedone (IId) was obtained by isomerization of the regioisomeric mixture of enol acetates of carbomethoxydimedone under the action of 4-dimethylaminopyridine [9], since the use of aluminum and zinc chlorides as isomerization catalysts did not yield the desired β-triketone. The structure of the 3,4-dihydroisoquinolines (Ia-d) and 2-acyl-1,3-cyclohexanediones (IIa-d) obtained was proved by physicochemical data, and also by comparison of the latter with literature data and data obtained for unsubstituted 3,4-dihydroisoquinolines and related β-triketones.

Annelation of azomethines (Ia-d) by β-triketones (IIa-d) was accomplished by boiling their equimolar mixtures in alcohol solutions and also without heating, which as mentioned earlier is a necessary condition for the reaction, which occurs through the intermediate salt complex (IV) and remains in this stage when there is no heating. We should note that we could not detect the formation of the salt complex (IV) in any of the experiments performed, which raises doubts concerning the claims made earlier concerning its role in the reaction mechanism [10]. The data obtained indicate that the salt intermediates (IV) formed in the first stage of the reaction between azomethines (Ia-d) (bases) and β-triketones (IIa-d) (acids) are probably short-lived and do not determine the orientation or rate of the reaction. Thus, as a result of reaction of azomethines (Ia-d) with β-triketones (IIa-d), we obtained the angularly alkylated 9-alkyl-substituted 8-aza-D-homogonanes (IIIa-h).

Institute of Bioorganic Chemistry, Belorussian Academy of Sciences, Minsk 220067. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 86-93, January, 1993. Original article submitted August 26, 1991.



Ia-b IIIa-f R = Me; Ic IIIg R = Et; Id, IIIh R = *i*-Pr; Ia IIIa-c R^1 = H; Ib-d IIId-h R^1 = =OMe; IIa,b-d IIIa-b,d-h R^2 = H; IIb IIIc R^2 = Me IIa-c, III a-e, g-h R^3 = H; IId IIIf R^3 = =COOMe; IIc IIIa,d,h R^4 = H; IIa,b,d IIIb-c,d-g R^4 = Me

A distinguishing feature of the PMR spectra of all the 9-alkyl derivatives (IIIa-h) obtained is the absence of resonance signals from the benzyl proton at C-9 at 4.7-5.0 ppm, characteristic for the previously described C-9 unsubstituted 8-azasteroids; and for the compounds which are unsubstituted at C-11 (IIIa-b, d-h), the presence of resonance signals from the methylene group C-11 as an AB-spin system at 2.8-3.1 and 2.6-2.8 ppm (J = 15-16 Hz) instead of the ABX-spin system characteristic for C-9-C-11 unsubstituted analogs [10-12]. In the case of the 9,11-dimethyl-substituted derivative (IIIc), in the PMR spectrum we observe only one set of resonance signals, which indicates formation of a single stereoisomer. Based on assignments made previously for the C-11-methyl-substituted derivatives of 8-azasteroids, this isomer is assigned as the one with trans methyl groups.

The 9-methyl-17-methoxycarbonyl derivative (IIIf) was obtained as a mixture of stereoisomers (VIa, b), interconverting through the enol derivative (V), whose ratio changes depending on the conditions. Thus when we record the PMR spectrum of the derivative (IIIf) immediately after preparation of the sample, we observe only one set of resonance signals from the protons, indicating that only one stereoisomer is present in the crystals, which after 6-12 h exposure is partially (by 25-30%) converted to its antipode (VI). We also detected this process using TLC. We should note that the enol form (V) was not detected in the IR or PMR spectra, which probably is explained by its extremely low population.

Study of the process of stereoisomerization of the methoxycarbonyl derivative (IIIf) in the presence of acids, with the goal of increasing the population of the enol tautomer (V) and accordingly simplifying the PMR spectrum, led to an unexpected result. In this case, instead of the expected enol tautomer (V), we observed the enol-immonium tautomer (VII). Such an assignment was made because in the PMR spectrum there are resonance signals from the enol proton at 15.65 ppm and from the C-17 methine proton at 3.25 ppm, which in the absence of acid catalysis is observed at 3.21 ppm (predominant isomer VIa) and 3.24 ppm (VIb), or only at 3.21 ppm when the spectrum is recorded immediately after preparation of the sample. Simplification of the PMR spectrum of the derivative (IIIf) in the presence of acids is probably a consequence of steric interactions between the methoxycarbonyl substitute at C-17 and C-16 of the *gem*-dimethyl group, enhanced by

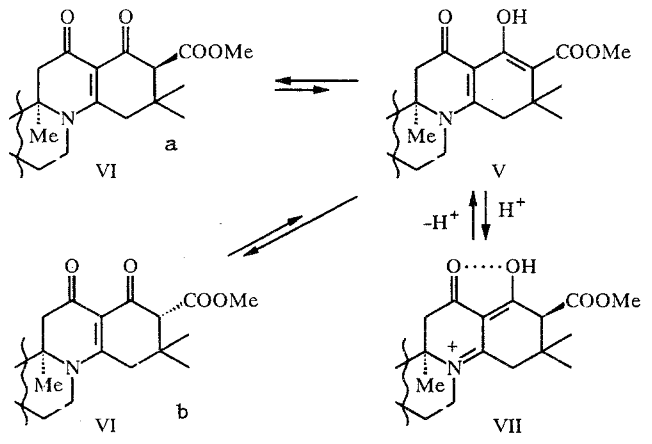


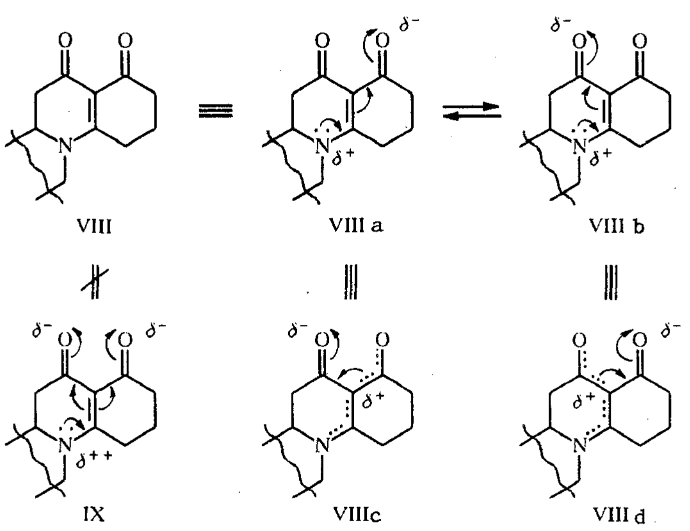
TABLE 1. Characteristics of 8-Aza-D-Homogonanes (IIIa-h)

Compound	Empirical formula	mp, °C (solvent)	IR spectrum (KBr, ν, cm^{-1})	UV spectrum (ethanol, λ_{max}, nm, lg ε)	PMR spectrum (CDCl$_3$, δ, ppm; J Hz)	Yield, %
IIIa	$C_{18}H_{19}NO_2$	213...215 (acetone–ether)	1676, 1593, 1525	265 (3,97), 306 (3,96)	1,60 (3H, s, C^9CH_3); 1,98 (1H, m $C^{16}H_B$); 2,09 (1H, m, $C^{16}H_A$); 2,32 (1H, d, t, d, $C^{15}H_B$; 15,6; 12,0; 4,8); 2,44 (1H, t, t, $C^{15}H_A$; 15,6; 4,8; 3,6); 2,58 (1H, d, $C^{11}H_B$; 15,6); 2,61 (1H, d, t, d, $C^{17}H_B$; 15,6; 12,0; 4,8); 2,75 (1H, d, $C^{11}H_A$; 15,6); 2,87 (1H, t, t, $C^{17}H_A$; 15,6; 4,8; 4,8); 2,97 (1H, t, t, C^6H_e; 16,8; 3,0; 3,0); 3,12 (1H, d, t, d, C^6H_a; 16,8; 12,0; 4,8); 3,39 (1H, d, d, d, C^7H_a; 13,2; 12,0; 3,0); 4,28 (1H, q, q, C^7H_e; 13,2; 14,8; 3,0); 7,15...7,31 (4H, m, arom.)	60
IIIb	$C_{20}H_{23}NO_2$	232...234 (alcohol–ether)	1340, 1442, 1490, 1520, 1610, 1685	266 (4,18), 307 (4,27)	1,09 (3H, s $C^{16}CH_3$); 1,15 (3H, s, $C^{16}CH_3$); 1,59 (3H, s, C^9CH_3); 2,27 (2H, s, $C^{15}H_2$); 2,58 (2H, s, $C^{17}H_2$); 2,68 (1H, d, $C^{11}H_B$; 15,6); 2,78 (1H, d, $C^{11}H_A$; 15,6); 2,97 (1H, t, t, C^6H_e; 15,6; 3,6; 3,6); 3,11 (1H, d, t, d, C^6H_a; 15,6; 12,0; 4,8); 3,39 (1H, d, d, d, C^7H_a; 13,2; 12,0; 3,6); 4,28 (1H, t, t C^7H_e; 13,3; 4,8; 3,6); 7,15...7,30 (4H, m, arom.)	81
IIIc	$C_{21}H_{25}NO_2$	247...250 (alcohol–ether–hexane)	1442, 1490, 1505, 1513, 1610, 1680	200 (4,50), 264 (4,28), 308 (4,25)	0,64 (3H, d, $C^{11}CH_3$; 8,4); 1,09 (3H, s, $C^{16}CH_3$); 1,15 (3H, s, $C^{16}CH_3$); 1,61 (3H, s, C^9CH_3); 2,29 (2H, s, $C^{15}H_2$); 2,56 (3H, m, $C^{11}H$, $C^{17}H_2$); 2,93 (1H, t, t, C^6H_e; 15,6; 4,2, 4,2); 3,05 (1H, d, t, d, C^6H_a; 15,6; 12,6; 4,2); 3,35 (1H, d, d, d, C^7H_a; 12,6; 12,6; 3,6); 4,29 (1H, t, t, C^7H_e; 12,6; 3,6; 3,6); 7,12...7,31 (4H, m, arom.)	32
IIId	$C_{20}H_{23}NO_4$	232...234 (alcohol–ether)	1510, 1520, 1613, 1683	203 (4,55), 228 (3,71), 267 (4,09), 306 (4,11)	1,58 (3H, s, C^9CH3); 1,98 (1H, m, $C^{16}H_e$); 2,08 (1H, m, $C^{16}H_a$); 2,31 (1H, d, t, d, $C^{15}H_B$; 15,6; 12,0; 4,8); 2,46 (1H, t, t, $C^{15}H_A$; 15,5; 4,8; 4,8); 2,65 (1H, d, t, d, $C^{17}H_B$; 15,6; 9,6; 6,0); 2,67 (1H, d, $C^{11}H_B$; 15,6); 2,77 (1H, d, $C^{11}H_A$; 15,6); 2,84 (1H, t, t, $C^{17}H_A$; 15,6; 2,4; 2,4); 2,84 (1H, t, t, C^6H_e; 15,6; 2,4; 2,4); 3,05 (1H, d, t, d, C^6H_a; 15,6; 12,0; 4,2); 3,38 (1H, d, d, d, C^7H_a; 13,8; 12,0; 2,4); 3,84 (3H, s, OCH_3); 3,88 (3H, s, OCH_3); 4,25 (1H, t, t, C^7H_e; 13,8; 4,2; 2,4); 6,59 and 6,63 (2H, s, arom.)	72

IIIe	$C_{22}H_{27}NO_4 \cdot C_2H_6O$	269 (alcohol–ether–hexane)	1503, 1615, 1680	303 (4,72), 228 (3,90), 267 (4,20), 306 (4,27)	1.03 (3H, s, $C^{16}CH_3$); 1.15 (3H, s, $C^{16}CH_3$); 1,58 (3H, s, C^9CH_3); 2,30 (2H, s, $C^{15}H_2$); 2.59 (2H, s, $C^{17}H_2$); 2,68 (1H, d, $C^{11}H_B$; 15,6) ; 2,79 (1H, d, $C^{11}H_A$; 15,6); 2.86 (1H, t,t, C^6H_e; 15,6; 3,6; 2,4); 3,05 (1H, d,t,d, C^6H_a; 15,6; 12.0; 4.2); 3.38 (1H, d,d,d, C^7H_a; 12,0; 12,0; 3.6); 3,85 (3H, s, OCH_3); 3.88 (3H, s, OCH_3); 4,27 (1H, q,q, C^7H_e; 12,0 4,2; 2,4); 6.59 and 6.63 (2H, s, arom.)	57
IIIf	$C_{24}H_{29}NO_6$	178...180 (chloroform–ether–hexane)	1145, 1263, 1335, 1445, 1505, 1516, 1615, 1682, 1735	204 (4,43), 227 (3,78), 271 (4,00), 296 (4,01), 307 (4,08)	1,16 (3H, s, $C^{16}CH_3$); 1,17 (3H, s, $C^{16}CH_3$); 1,21 (3H, s, C^9CH_3); 2,41 (1H, d, $C^{11}H_B$; 18,0); 2,67 (1H, d, $C^{15}H_B$; 15,6); 2,79 (1H, d, $C^{15}H_A$; 15,6); 2,85 (1H, m, C^6H_e); 3,05 (1H, d,d,d C^6H_a; 15,6; 4,8; 4,8); 3,15 (1H, d, $C^{11}H_A$; 18,0); 3,21 (1H, s, $C^{17}H$); 3,37 (1H, d,d,d C^7H_a; 15,6; 3,6; 3,6); 3,68 (3H, s, $C^{17}COOCH_3$); 3,85 (3H, s, OCH_3); 3,89 (3H, s, OCH_3); 4,27 (1H, t,t, C^7H_e; 15,6; 3,6; 3,6); 6,59 and 6,63 (2H, s, arom.)	25
IIIg	$C_{23}H_{29}NO_4$	232...234 (alcohol–ether)	1130, 1145, 1230, 1257, 1335, 1445, 1465, 1510, 1617, 1690	204 (4,60), 231 (3,96), 269 (4,21), 294 (4,10), 312 (4,20)	0,83 (3H, t, $C^9CH_2C\underline{H}_3$; 7,2); 1,09 (3H, s, $C^{16}CH_3$); 1,12 (3H, s, $C^{16}CH_3$); 1,95 (1H, m, $C^9C\underline{H}_2CH_3$; 15,6; 7,2); 2,27 (2H, s, $C^{15}H_2$); 2,32 (1H, m, $C^9C\underline{H}_2CH_3$; 15,6; 7,2); 2,60 (2H, s, $C^{17}H_2$); 2,65 (1H, d, $C^{11}H_B$; 15,6); 2,77 (1H, d, $C^{11}H_A$; 15,6); 2,91 (1H, t,t, C^6H_e; 15,6; 4,8; 4,8); 3,00 (1H, d,t,d, C^6H_a; 15,6; 10,8; 4,8); 3,57 (1H, d,t,d, C^7H_a; 12,6; 10,8; 3,6); 4,24 (1H, t,t, C^7H_e; 12,6; 3,6; 3,6); 6,61 and 6,65 (2H, s, arom.)	50
IIIh	$C_{22}H_{27}NO_4$	166...168 (ether–hexane)	1262, 1343, 1447, 1462, 1500, 1525, 1603, 1615, 1675	206 (4,52), 229 (3,90), 268 (4,18), 294 (4,04), 311 (4,15)	0,95 and 1,00 (3H and 3H, s,d,d, $C^9CH(C\underline{H}_3)_2$; 7,0); 2,02 (2H, m, $C^{16}H_2$); 2,36 (2H, m, $C^{15}H_2$); 2,49 (1H, m, $C^9C\underline{H}(CH_3)_2$; 7,0); 2,75 (2H, m, $C^{17}H_2$); 2,77 (1H, d, $C^{11}H_B$; 16,0); 2,98 (2H, m, $C^6H_aH_e$); 3,05 (1H, d, $C^{11}H_A$; 16,0); 3,84 (4H, m, OCH_3, C^7H_a); 3,87 (3H, s, OCH_3); 4,08 (1H, t,t. C^7H_e; 13,5; 6,0; 6,0); 6,62 and 6,67 (2H, s,s, arom.)	7

flattening of the D ring upon realization of the enol-immonium tautomer (VII). In this case, it is energetically more favorable for the C-17 methoxycarbonyl substituent to occupy the *trans* axial position relative to one of the C-16 methyl groups, since for an equatorial position it will undergo significant diequatorial repulsion by one of the C-16 methyl groups.

In the electronic spectra of derivatives (IIIa-h), we observe two absorption bands that are characteristic for this series of compounds, at 264-270 nm (ε 15,000-19,000) and 306-312 nm (ε 14,000-18,000), corresponding to chromophores of the α-acyl-β-aminovinylcarbonyl moiety of molecule VIII or the A moiety. The low-frequency absorption band (306-312 nm) is due to $\pi-\pi^*$ electronic transitions of the β-aminovinylcarbonyl chromophore of VIIIa molecule or the B moiety, while the broadened high-frequency band at 264-270 nm is the result of a $\pi-\pi^*$ transition of the B-chromophore (VIIIb) and the α-acyl moieties, conjugated with the B moieties (VIIIc-d). Such an assignment of the bands agrees well with our data on the electronic spectroscopy of different 8-aza-D-homogonanes modified at the carbonyl group, in particular derivatives lacking chromophore properties (ethylene ketals, acetals) or derivatives with quite distinctive chromophore characteristics (hydroxyimino derivatives). Both of the indicated absorption bands are charge-transfer bands. [The low-frequency band involves charge transfer from the nitrogen atom to the oxygen atom of the B-moiety of (VIIIa), while the high-frequency band involves charge transfer from the nitrogen atom to the oxygen atom of the B moiety of (VIIIb) and from the B-moieties to the oxygen atom of the α-acyl carbonyl groups (VIIIc-d)]. Thus the A-moiety of the 8-aza-D-homogonanes (IIIa-h) obtained in this investigation and described earlier [10-14] is not cross conjugated (IX), for which we probably should observed the presence of only one band due to the $\pi-\pi^*$ transition of the single A-chromophore.



In the vibrational spectra of compounds (IIIa-h), there is a system of bands in the 1480-1695-cm^{-1} region which is quite characteristic for this series of compounds. The broad and complex band at 1480-1525 cm^{-1} belongs to the $\nu_{C=C}$ stretching vibrations of the aromatic nuclei and the A moieties. The group of bands with frequency 1580-1620 cm^{-1} is due to the $\nu_{C=O}$ and $\nu_{C=C}$ stretching vibrations of the B moieties (VIIIa-b) and the aromatic nuclei respectively, while in the 1675-1690-cm^{-1} region they are due to the α-acyl C=O groups (VIIIc-d). The observed shift in the vibrational frequency of the α-acyl moieties by $\approx$20-35 cm^{-1} in the low-frequency region indicates the conjugated character of the α-acyl carbonyl groups, similar to the conjugation in aromatic, α,β-unsaturated and α-cyclopropane-substituted carbonyl compounds [15]. The assignment of the indicated bands in the IR spectra (as in the case of the electronic spectra) of compounds IIIa-h is in good agreement with data obtained for 8-aza-D-homogonanes modified at the carbonyl groups.

EXPERIMENTAL

To monitor the course of the reactions and the purity of the 8-aza-D-homogonanes obtained (IIIa-h), we used TLC on Silufol UV-254 plates, eluting agent 9.5:0.5 chloroform–methanol; visualization in UV light or with iodine vapor. The melting points were determined on a Boetius heating stage. The IR spectra were obtained on the UR-20 in KBr disks. The electronic spectra were taken on the Specord UV-VIS spectrophotometer in ethanol solutions. The mass spectra were obtained on the MAT-311 Varian spectrometer, electron ionizing energy 70 eV, direct injection of the sample. The PMR spectra were obtained on the Bruker WM-360 (360 MHz) and the Bruker AC-200 (200 MHz) in $CDCl_3$ with TMS as the internal standard, digital resolution 0.5 Hz. The yields, melting points, IR, UV, and PMR spectroscopy and mass spectrometry data for the obtained compounds (IIIa-h) are presented in Table 1.

9-Methyl-8-aza-D-homogona-1,3,5(10),13-tetraene-12,17a-dione (IIIa). A mixture of 1.45 g (10 mmole)of 1-methyl-3,4-dihydroisoquinoline (Ia of and 1.54 g (10 mmoles) of 2-acetyl-1,3-cyclohexanedione (IIc) in 20 ml of absolute ethanol was allowed to stand at room temperature under an argon atmosphere for 72 h. When the reaction was complete, the solvent was evaporated, the residue was recrystallized from a 2:3 mixture of acetone–ether; 1.7 g IIIa was obtained.

9,16,16-Trimethyl-8-aza-D-homogona-1,3,5(10),13-tetraene-12,17a-dione (IIIb). A mixture of 1.45 g of (10 mmoles) of azomethine (Ia) and 1.82 g (10 mmoles) of 2-acetyl-5,5-dimethyl-1,3-cyclohexanedione (IIa) in 20 ml of ethanol was boiled for 10 h. Then the solvent was evaporated, the residue was ground with ether and recrystallized from a 3:7 ethanol–ether mixture. 2.5 g compound IIIb was obtained.

9,11,16,16-Tetramethyl-8-aza-D-homogona-1,3,5(10),13-tetraene-12,17a-dione (IIIc). A mixture of 1.45 g of azomethine (Ia) and 1.96 g (10 mmoles) of 2-propionyl-5,5-dimethyl-1,3-cyclohexanedione (IIb) in 30 ml of ethanol was boiled for 14 h. Then the solvent was evaporated, the residue was dissolved in chloroform and filtered through 10 g of silica gel 5/40μ. The collected eluates were evaporated, the residue was recrystallized from a 1:2:2 ethanol–ether–hexane mixture. 1.02 g of 8-azasteroid IIIc was obtained.

9-Methyl-2,3-dimethoxy-8-aza-D-homogona-1,3,5(10),13-tetraene-12,17a-dione (IIId). A. A mixture of 2.05 g (10 mmoles) of 1-methyl-6,7-dimethoxy-3,4-dihydroisoquinoline (Ib) and 1.54 g (10 mmoles) of β-triketone (IIa) in 20 ml of ethanol was allowed to stand at room temperature for 48 h. Then the solvent was evaporated, and the residue was recrystallized from a 1:2.5 ethanol–ether mixture. 2.47 g of 8-azasteroid IIId was obtained.

B. An equimolar mixture of 10 mmoles of azomethine (Ib) and 10 mmoles of β-triketone (IIa) was boiled with a reflux condenser for 9 h. Then the solvent was evaporated, the residue was dissolved in chloroform and filtered through 10 g silica gel 5/40μ. After evaporation and recrystallization from a 1:2:4 ethanol–acetone–ether mixture, 2.03 g of 8-azasteroid IIId was obtained, identical to the sample obtained according to method A.

9,16,16-Trimethyl-2,3-dimethoxy-8-aza-D-homogona-1,3,5(10),13-tetraene-12,17a-dione (IIIe). A mixture of 4.1 g (20 mmoles) of azomethine (Ib) and 3.64 g (20 mmoles) of β-triketone (IIa) in 25 ml of ethanol was boiled for 2 h, evaporated to 1/3 of the initial volume of the reaction mixture, diluted with ether until weak turbidity and allowed to stand to crystallize at 5°C. The precipitated crystals were filtered from a 2:3:2 ethanol–ether–hexane mixture. 4.2 g of compound IIIe were obtained.

9,16,16-Trimethyl-2,3-dimethoxy-17-methoxycarbonyl-8-aza-D-homogona-1,3,5(10),13-tetraene-12,17a-dione (IIIf). A mixture of 2.05 g (10 mmoles) of azomethine (Ib) and 2.4 g (10 mmoles) of 2-acetyl-5,5-dimethyl-4-methoxycarbonyl-1,3-cyclohexanedione (IId) in 40 ml of ethanol was boiled for 40 h. Then the solvent was evaporated, the residue was dissolved in 10 ml of chloroform and chromatographed on a column (15 cm) with silica gel 100/250μ (100 g). The substance isolated from the eluates was recrystallized from a 1:2:2 chloroform–ether–hexane mixture. 1.07 g of compound IIIf was obtained.

16,16-Dimethyl-2,3-dimethoxy-9-ethyl-8-aza-D-homogona-1,3,5(10),13-tetraene-12,17a-dione (IIIg). A mixture of 2.19 g (10 mmoles) of 6,7-dimethoxy-1-ethyl-3,4-dihydroisoquinoline (Ic) and 1.81 g (10 mmoles) of 2-acetyldimedone (IIa) in 50 ml of ethanol was boiled for 40 h. Then the solvent was evaporated, the residue was dissolved in chloroform and chromatographed on a column (10 cm) with silica gel 40/100μ (eluting agent, chloroform). The result was crystallized from a 1:2.5 ethanol–ether mixture. 1.93 g of compound IIIf was obtained.

2,3-Dimethoxy-9-isopropyl-8-aza-D-homogona-1,3,5(10),13-tetraene-12,17a-dione (IIIh). A mixture of 2.33 g (10 mmoles) of 6,7-dimethoxy-1-isopropyl-3,4-dihydroisoquinoline (Id) and 1.64 g (10 mmoles) of β-triketone (IIc) in 40 ml of ethanol was boiled for 72 h. Then the reaction mixture was evaporated, the residue was dissolved in chloroform and filtered through 10 g of silica gel 5/40μ (chloroform). The eluates were evaporated and the residue was crystallized from a 2:5 ether–hexane mixture. 0.25 g of compound IIIh was obtained.

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