Table 2. CI mass spectra of 1,1-dinitroethane and 1-halo-1,1-dinitroethanes $MeCX(NO_2)_2$ (with tetramethylsilane as the reagent gas)

Compound	m/z (I_{rel} (%))		
	$[M+SiMe_3]^+$	$[M+SiMe_3-NO_2]^+$	$[M+SiMe_3-XNO_2]^+$
1,1-Dinitroethane	193 (45.5)	147 (40.5)	146 (100)
1-Fluoro-1,1-dinitroethane	211 (99.5)	165 (61.8)	146 (100)
1-Chloro-1,1-dinitroethane	227 (67.9)	181 (100)	146 (67.5)
	229 (24.4)	183 (42.7)	—

Other routes of fragmentation, analogous to the reactions of decomposition of the protonated molecular ions of nitroalkanes (elimination of H_2O and HNO),[2] were not observed in the case of ion-adducts of mononitroalkanes with the trimethylsilyl cation.

Unlike those of mononitroalkanes, the CI mass spectra of dinitroethanes contain ion-adducts of only one type, $[M+SiMe_3]^+$ (Table 2), which decompose with the loss of a stable $NO_2^{\cdot}$ radical similarly to the corresponding protonated molecular ions (*cf.* Ref. 1). By analogy with the $[M+H-NO_2]^+$ ions, the structure of $MeC^{\cdot}XN^+O_2 \cdot SiMe_3$ can be ascribed to the $[M+SiMe_3-NO_2]^+$ ions.

The another reaction path of fragmentation of the $[M+SiMe_3]^+$ ions of dinitroethanes, with the loss of an XNO_2 (X = H, F, or Cl) molecule, has no analogs among the fragmentation processes of their protonated molecular ions.

This work was financially supported by the Russian Foundation for Basic Research (Project No. 96-03-33398).

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Received January 9, 1997

Synthesis of 6α-methyl-16α,17α-cyclohexanoprogesterone *via* γ-methylenation of 16α,17α-cyclohexanopregn-4-ene-3,20-dione

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6-Methylene-16α,17α-cyclohexanopregn-4-ene-3,20-dione **2** has been synthesized by the reaction of Δ^4-3-ketone **1** with $CH_2(OEt)_2$ and $POCl_3$ in the presence of AcONa in 55% yield. Reduction of the product **2** in the presence of 5% Pd/C gives 6α-methyl-16α,17α-cyclohexanoprogesterone **3** in a yield exceeding 70%.

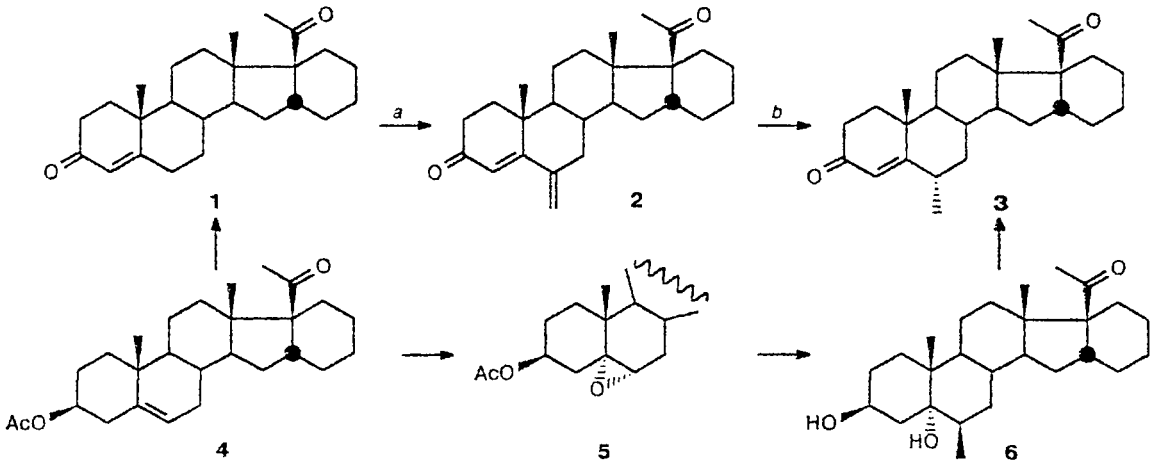
Key words: methylenation, pentarane, progestin.

6α-Methyl-16α,17α-cyclohexanoprogesterone (6α-methyl-D_6^6-pentarane) (**3**) (Scheme 1) is a synthetic progestin that exhibits high progestational and contraceptive activities.[1] Earlier for the synthesis of compound **3**, the succession of transformations **4** → **5** → **6** → **3** (see Scheme 1) was used,[2,3] in which the key step was the

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 6, pp. 1234—1236, June, 1997.

1066-5285/97/4606-1185 $18.00

Scheme 1



Reagents and conditions: *a*. $CH_2(OEt)_2$, $CHCl_3$, $POCl_3$, NaOAc; 60—75 °C; yield 55%; *b*. 5% Pd/C, *cyclo*-C_6H_{10}, EtOH; 28 h; dilute HCl; yield 73%.

ring opening of 5α,6α-oxide **5** with methylmagnesium iodide; in this case, the reaction gave exclusively 6β-methyldiol **6** while the sterically hindered 20-carbonyl group in molecule of **5** was not involved in the reaction.[2] However, this method of introducing the 6-methyl group required the preliminary protection of the 20-carbonyl group when it was used for other progestins of the D′-pentarane series, for example, 16α,17α-cyclobutanoprogesterone.[4]

In this communication we report an alternative synthesis of 6α-methyl-16α,17α-cyclohexanoprogesterone **3**. The key intermediate in this synthesis is 6-methylene derivative **2**, which was obtained by γ-methylenation of Δ^4-3-oxopentarane **1** by the Wiechert method.[5] It should be noted that such a one-step procedure for introducing a methylene group into steroid conjugated ketones has been rather widely used for the synthesis of methylene steroids of various classes,[5—7] and the yields of the final product were 60—65%. The starting conjugated ketone **1** was obtained by Oppenauer oxidation of the corresponding 3β-hydroxy-Δ^5-derivative.[2] The interaction of compound **1** with reagents X—CH_2OR (X = OR, Cl, OAc, R = Me, Et) and $POCl_3$ in the presence of AcONa led directly to 6-methylene derivative **2**. Formaldehyde diethylacetal (ethylal) proved to be the best reagent in this case. When a mixture of ketone **1** with an excess of ethylal, $POCl_3$, and AcONa in anhydrous $CHCl_3$ was boiled, compound **2** was obtained; the yield was 55% after chromatographic purification. When ethylal was replaced by methylal, the yield of dione **2** decreased to 20—25%; when chloromethyl methyl ether was used, the obtained compound **2** was contaminated by chlorinated unidentified by-products.

Reduction of the 6-methylene group of dione **2** to the target product **3** in the presence of 5% Pd/C and cyclohexene as a hydrogen donor proceeds *via* the step of isomerization of the exocyclic double bond in molecule **2** into ring *B* to give the intermediate $\Delta^{4,6}$-6-methyl derivative.[8] The latter is further reduced into a mixture of stereoisomeric 6α,β-Δ^4-3-ketones, which are easily transformed into 6α-methylpentarane **3** by treatment with an acid. The course of the reaction was monitored by UV spectroscopy: λ_{max} changed from 260 nm (6-methylene-Δ^4-3-ketone) *via* λ_{max} = 285 nm ($\Delta^{4,6}$-3-ketone) to λ_{max} = 245 nm (Δ^4-3-ketone).

Thus, this communication describes a two-step method for the synthesis of 6α-methyl-16α,17α-cyclohexanoprogesterone from its 6-desmethyl precursor. In many cases this method can compete with the alternative methods for the introduction of a 6-methyl group into pentaranes.

Experimental

Melting points were determined on a Boetius heating plate. ^{1}H NMR spectra were recorded in $CDCl_3$ on a Bruker WM-250 spectrometer. UV spectra were obtained on a Unicam SP-700 instrument. The qualitative analysis of the mixtures was carried out by TLC on Silufol L UV-254 plates (Czech Republic). Columns with Woelm silica gel were used for preparative chromatography.

6-Methylene-16α,17α-cyclohexanopregn-4-ene-3,20-dione (2). A suspension of compound **1** (1 g), anhydrous AcONa (1 g), and freshly distilled $POCl_3$ (30 mL) in 25 mL of anhydrous $CHCl_3$ was stirred under argon for 45 min at 65—70 °C. A saturated aqueous solution of sodium carbonate (100 mL) was then added dropwise to the reaction mixture cooled to 18—20 °C and stirred for an additional 1.5 h. The aqueous layer was separated, and the organic layer was thoroughly washed with water until the reaction became neutral and dried with Na_2SO_4. The crystalline residue obtained after removal of the solvent was chromatographed on a column. Dienedione **2** (0.57 g, 55%), m.p. 181—185 °C (ether—hexane) was isolated by elution with a heptane—ether mixture (4 : 1). UV, λ_{max}/nm: 260 (ε 11200). ^{1}H NMR, δ: 0.72 (s, 3 H, 18-Me); 1.09 (s, 3 H, 19-Me); 2.14 (s, 3 H, 21-Me); 3.0 (m, 1 H, C(16)H); 4.94, 5.06 (2 m, 2 H, C(6)CH_2); 5.92 (s, 1 H, C(4)H). Further elution gave the starting ketone **1** (0.22 g).

6α-Methyl-16α,17α-cyclohexanopregn-4-ene-3,20-dione (3). A mixture of a solution of product **2** (0.45 g) in 25 mL of EtOH, 5% Pd/C (0.3 g), and 2.5 mL of freshly distilled cyclohexene was boiled with stirring for 28 h. During this period cyclohexane was added three times (3×1.5 mL). The catalyst was filtered off and washed with ethanol. The filtrate was acidified with dilute HCl, and most of the ethanol was removed *in vacuo*. Ice was added to the residue, and the white powder that precipitated was filtered off, washed with water on a filter, and air dried. Chromatographic purification afforded enedione **3** (0.33 g, 73%), m.p. 175—178 °C, which gave no melting point depression with an authentic sample.[9]

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Received January 29, 1997

Bis-*para*-semiquinoid type double cyclopalladation in the series of six-membered two-nitrogen bridged annulene-dihydroannulene ligands

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The cyclometallation reaction known in the series of annulene heteroorganic ligands was extended to six-membered dihydroannulenes with a dinitrogen bridge. Double cyclopalladation of 4-methyl-4-trichloromethylcyclohexa-2,5-dien-1-one azine yielded the first representative of a new class of cross-conjugated diazadipalladatetracycles, *viz.*, 5,10-bis(acetylacetonato)-2,7-dimethyl-2,7-bis(trichloromethyl)-2,7-dihydro-4b,9b-diaza-5,10-dipalladaindeno[2,1-*a*]indene, isolated as a diastereomer mixture of the achiral *meso*-form (*E*-isomer) and a racemate (*Z*-isomer). This reaction offers a method for transition metal-mediated activation of non-reactive C—H bonds at position 2 of cyclohexa-2,5-dienylidene systems and a route toward the very rare chiral polyheteroelement system with rotational symmetry.

Key words: azines of α,β-unsaturated carbonyl compounds, 2,5-cyclohexadienones, use of Pd^{II} derivatives in fine organic synthesis, double cyclopalladation, unsaturated metallaheterocycles, organometallic compounds, stereoisomerism, chirality.

The reaction of cyclometallation (also known as *ortho*-metallation) producing π,π-conjugated diaza-metalladi- and tetracycles (**1**[1], **2**[2]; *cf.* also Ref. 3) was discovered at the end of the 1960s for the benzenoid compound, azobenzene **3**, in which both six-membered rings are aromatic and the N atoms are linked by a π-bond (*cf.* the recently discovered reaction of double cyclometallation of azines of benzaldehyde[4] and benzophenone[5]). In the present work we for the first time extended the annulene type of transformation to a series of six-membered two-nitrogen bridged dihydroannulenes, azines of 4,4-disubstituted 2,5-cyclohexadienones (**4**),

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 6, pp. 1236—1239, June, 1997.