LITERATURE CITED

1. Nguen Kong Khao, M. V. Mavrov, and É. P. Serebryakov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 5, 1142 (1988).
2. M. Mori, T. Chuman, K. Kato, and K. Mori, Tetrahedron Lett., 23, 4593 (1982).
3. K. Mori, H. Nomi, T. Chuman, et al., Tetrahedron, 38, 3705 (1982).
4. R. Baker and J. A. Devlin, Chem. Communs., 147, (1983).
5. Y. Takeda, Y. Kobayashi, and F. Sato, Chem. Lett., 471, (1985).
6. K. Mori and H. Watanabe, Tetrahedron, 41, 3423 (1985).
7. Y. Kobayashi, Y. Kitano, and F. Sato, Chem. Communs., 1329 (1984).
8. Nguen Kong Khao, M. V. Mavrov, and É. P. Serebryakov, Zh. Org. Khim., 23, 1649 (1987).
9. Nguen Kong Khao, M. V. Mavrov, and É. P. Serebryakov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 8, 1792 (1987).
10. D. Seebach, A. K. Beck, M. Schiess, et al., Pure Appl. Chem., 55, 1807 (1983).
11. P. A. Bartlett, D. P. Richardson, and J. Meyerson, Tetrahedron, 40, 2317 (1984).
12. B. Wiedemann and D. Seebach, Helv. Chim. Acta, 63, 2451 (1980).

TRANSFORMED STEROIDS.

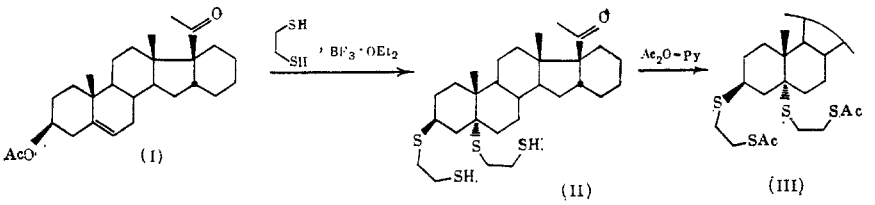
176. REACTION OF Δ^5-3β-SUBSTITUTED 16α,17α-CYCLOHEXANOPREGNEN-20-ONES WITH THIOLS: SYNTHESIS OF 3-MONO- AND 3,5-BIS-SULFUR-CONTAINING STEROIDS

I. S. Levina, L. E. Kulikova, E. G. Cherepanova, and V. S. Bogdanov

UDC 542.91:547.92

In continuation of studies of the synthesis and chemical transformations of pregna-D_6'-pentaranes – 16α,17α-cyclohexanopregnen-20-ones, we investigated one of the methods for the reductive removal of the hindered 20-keto group in (I) by desulfurization of the corresponding thioketal derivative. In attempts to obtain a 20-thioketal by the standard procedure of ethanedithiol acting on the ketone in the presence of catalytic amounts of $HClO_4$ [1] or BF_3 etherate in AcOH [2], only the initial pentarane (I) was separated. However, the sulfur-containing product was obtained in up to 50% yield by the action of a threefold excess of BF_3 etherate on a solution of (I) in ethanedithiol at 20°C. Based on the combined physicochemical data, the structure of a bismercaptoethyl derivative (II) was ascribed in this compound (Scheme 1)

Scheme 1



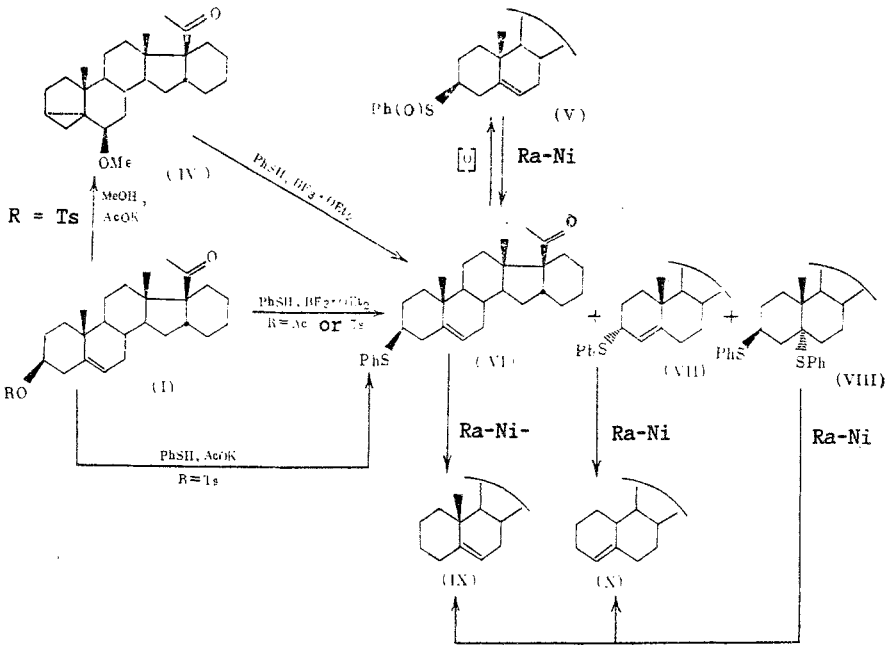
In fact, in the IR spectrum there is an absorption band of the 20-ketone with ν 1688 cm^{-1} and in the region with ν 2560-2570 cm^{-1}, a band corresponding to the stretching vibrations of the SH group. The PMR spectrum of (II) contains two partially overlapping multiplets of the methylene protons of the $-CH_2SH$ group in the 2.4-2.8 ppm region. In the ^{13}C NMR spectrum with proton coupling, a singlet at 59.7 ppm and a doublet at 38.9 ppm indicate the substitution of the steroid by the SCH_2 groups at the 3- and 5-positions (compare ^{13}C signal in androstane), while the chemical shift on C^1 (30.9 ppm) indicates the presence of only one γ-gauche effect at C^1 (the effect of the 5α-SCH_2CH_2SH group), from which it follows

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow.
Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 6, pp. 1364-1369, June, 1989. Original article submitted December 22, 1987.

 0568-5230/89/3806-1246$12.50

that the substituent at the 3-position has a β-orientation.* During the acetylation of (II), a diacetate (III) was obtained, the structure of which was confirmed by the PMR spectrum. The fundamental peak in the mass spectra of dithiol (II) and its diacetate (III) is that having m/z 353, corresponding to the splitting of dithiol or dithioacetate groups from M^+: $[M-SCH_2CH_2SH-(CH_2SH)_2]^+$ and $[M-SCH_2CH_2SAc-HSCH_2CH_2SAc]^+$. The above result was somewhat surprising in view of the information available in the literature on the occurrence of the reaction under consideration in the androstane [2] or sapogenin series [3]. In this connection, and for a more thorough examination of this reaction, we studied the reaction of (I) with thiophenol in the presence of BF_3 etherate. It could therefore be expected that the products formed by the action of thiophenol will have structures with more easily interpretable spectral data (Scheme 2) .

Scheme 2



It was found that holding of (I) with thiophenol (in CH_2Cl_2 or without a solvent) in the presence of 2-10 mole equivalents of $BF_3 \cdot OEt_2$ leads to an overall yield of 70% to a mixture of three compounds which were separated chromatographically and by fractional crystallization: two chromatographically coinciding mono- (VI) and (VII) and 3,5-bisphenylthio derivatives (VIII) in a ratio of ~1:3. The structure of these products can be seen from the data on their physicochemical analysis. Thus, in the PMR spectra of the mono-derivatives (VI) and (VII), there is a methine proton multiplet at C^3, carrying a thiophenyl group, with δ 3.00 and 3.84 ppm, respectively, and a multiplet of aromatic protons with a center at δ 7.35 ppm. The characteristic chemical shifts of C^8 and C^9 in the ^{13}C NMR spectra determine the position of the double bond – Δ^5 in (VI) (32.0 and 50.7 ppm) and Δ^4 in (VII) (35.9 and 54.4 ppm). The orientation of the 3-SPh-group is confirmed by the value of δ C^1 which indicates the absence of a strong field γ-gauche effect of 3-SPh in (VI) (39.8 ppm) and its presence in (VII) (32.4 ppm), i.e., a 3β- and 3α-orientation, respectively. In the PMR spectrum of the 3,5-bisphenylthio derivative (VIII), a weak-field shift of 0.14 ppm of the 19-CH_3 group singlet and a 0.15 ppm strong field shift of the H–C^3 signal are observed, compared with the monosubstituted derivative (VI). Its ^{13}C NMR spectrum indicates the same position and orientation of sulfur-containing substituents, as in steroid (II), i.e., a 3β- and 5α-SPh (δ C^3 and C^5 42.8 and 63.5 ppm, respectively, and δ C^1 30.9 ppm). In the mass spectra of compounds (VI)-(VIII) there are low-intensity M^+; the main path of their fragmentation consists in the splitting of one (or two) sulfur-containing groups with the formation of ions with m/z 353 ($[M - PhS]^+$, $[M - PhS - PhSH]^+$).

During desulfurization of (VI)-(VIII) with Ra-Ni in dioxane, Δ^5-(IX), Δ^4-(X) respectively were obtained, and a mixture (1:1) of Δ^5- and Δ^4-olefins, as confirmed by comparison of

*The ^{13}C NMR spectra of (II) and of the compounds described below will be published in a separate report.

the ^{13}C NMR spectra of (IX) and (X) with the ^{13}C spectra of Δ^5- and Δ^4-cholestanes (rings A and B) [4] and with the spectrum of (I) (rings C, D, and D').

It is of interest to note that the 3β-SPh-derivatives (VI) and (VII) were found to be very labile, and were readily oxidized during chromatography or crystallization and on standing. In particular, during the chromatography of (VI), a 1:1 mixture of erythro-threo isomers of sulfoxide (V) was separated, by fractional crystallization of which the individual isomers of (V) were isolated. The existence of an equivalent mixture of diasteromers at the S atom in (V) is indicated by a double set of signals of the C^1, C^2, C^3, C^4, and C^6 atoms in the ^{13}C NMR spectrum, whereby the difference in the chemical shifts is 0.29; 2.90; 0.26; 3.01; and 0.06 ppm, respectively. From the desulfurization of (V) on Ra-Ni, compound (IX) was obtained via the intermediate formation of (VI).

In the reaction of the tosylate (I, R = Ts) with thiophenol in the presence of 5 mole equivalents of $BF_3 \cdot OEt_2$ in CH_2Cl_2, the same mixture of products (VI)-(VIII) was obtained in 76% yield with a ratio of ((VI) + (VII)):(VIII) ≈ 5:1. It should be noted that with increase in the amount of $BF_3 \cdot OEt_2$, the fraction of the bis-product (VIII) increases, and when a tenfold excess is used, this ratio becomes 1:1.

The above results for the synthesis of the mercapto compounds (VI)-(VIII) can be explained as follows: as a result of a Lewis acid catalyzed splitting of the C–O bond in the molecules of the acetate (I, R = Ac) or tosylate (I, R = Ts), an intermediate carbonium ion is generated at C^3, and is stabilized by the homoallyl Δ^5-bond, which is further attacked from the α- or β-side by the thiol reagent, with a retention of the shift of the C=C bond. The presence of excess reagent in the reaction mixture can lead to the formation of bisthio-products (II), (VIII) also via the carbonium ion intermediate at C^5.

The formation of products of the reaction of the ethanedithiol with Δ^4-3-keto-6- or Δ^4-6-keto-3-acetates of cholesterol in the presence of BF_3 etherate, leading primarily to the splitting of the allylic C–O bond [5] has been explained in the same way.

The above explanation fully agrees with the observed result with respect to the regio- and stereochemically pure solvolysis of tosylate (I, R = Ts) by thiophenol in the presence of AcOK, leading in high yield to the 3β-thiosubstituted product (IV) only. In this case the reaction can proceed via the intermediate unstable i-steroid thiophenyl derivatives of type (IV). As a proof for the occurrence of this intermediate, we can cite the fact that the solvolysis of the i-steroid (IV), specifically prepared for this purpose, with thiophenol in the presence of 2.0 mole equivalents of BF_3 etherate in CH_2Cl_2 smoothly gives the 3β-thio-substituted product (VI) only. The structure of the 3,5α-cyclosteroid (IV) was confirmed by its ^1H and ^{13}C NMR spectra. Thus, in the ^{13}C NMR spectrum, the strong-field signals from the methylene (13.0 ppm, $^1J_{CH}$ = 157 Hz), methine (21.5 ppm) and quaternary C atoms indicate the presence of C^3–C^4–C^5 cyclopropane fragment. The presence of a doublet at 82.2 ppm, the shift of the signal from C^7 to 35.1 ppm, and a 5.6 ppm strong-field shift of the signal from C^8 relative to the position of these signals in the spectrum of androstane [4], indicate a 6β-disposition of the OMe group (the presence of the OMe substituent is confirmed by a quartet at 56.4 ppm).

We should note in conclusion that the participation of the Δ^5-3β-acyloxy group in the reaction with thiols in the presence of $BF_3 \cdot OEt_2$, described using the example of 16α,17α-cyclohexanopregnane, is general in character, as confirmed by the purposely specially carried out reaction of cholest-5-en-3β-ol acetate with PhSH and 6 mole equivalents of $BF_3 \cdot OEt_2$. 3β,5α-Bisphenylthiocholestane (XI) was thus separated. In the spectrum of the latter, the singlet at 60.7 ppm and a doublet at 43.0 ppm indicate unequivocally the substitution of rings A and B by the SPh groups at positions 3 and 5, while the chemical shift of C^1 of 32.4 ppm indicates an α-orientation of SPh at C^5 and β-orientation at C^3.

EXPERIMENTAL

The melting points were determined on a Koffler block. The IR spectra (KBr tablets) were measured on a UR-20 spectrophotometer. The PMR and ^{13}C NMR spectra were obtained in $CDCl_3$ on a Bruker WM-250 spectrometer with the working frequencies of 250 and 62.89 MHz, respectively. The electron impact mass spectra were obtained using an LKB-9000 spectrometer with an ionizing voltage of 70 eV, the ionic source temperature of 250°C, and the exposure temperature of 30-40°C. The chemical ionization mass spectra were obtained using a Kratos MS-30 spectrometer, the gaseous reagents being methane and isobutane, with the ionization cham-

ber temperature of 150°C and ionizing voltage of 100 eV. The TLC was carried out on microplates with Woelm brand silica gel (5-40 μm). Woelm brand silica gel was used for the columns.

Reaction of Acetate (I, R = Ac) with Ethanedithiol. a) A solution of 3 g (7.2 mmoles) of (I, R = Ac) and 3 ml (24.3 mmoles) of $BF_3 \cdot OEt_2$ in 8 ml of $(CH_2SH)_2$ was held in Ar for 24 h, then treated with H_2O, extracted with ether, the extract was washed with H_2O, and the solvent was removed in vacuo. The residue obtained was chromatographed on 150 g of SiO_2. The elution with a hexane–ether (95:5) mixture gave 1.97 g (50%) of 3β,5α-bis-2'-mercaptoethyl derivative (II); an analytical sample had mp 205-211°C (ether–hexane). IR spectrum (ν, cm^{-1}): 1688 (C=O), 2560-2570 (SH). PMR spectrum (δ, ppm): 0.64 s (3H, 18-CH_3), 1.04 s (3H, 19-CH_3), 2.10 s (3H, 21-CH_3), 2.40-2.80 m (8H, CH_2CH_2SH), 2.92 m (1H, H–C^{16}), 3.55 m (1H, H–C^3). Mass spectrum, m/z (rel. intensity, %): M^+ 540 (2.2), 447 (33.8), 403 (7.5), 387 (28.5), 353 (100).

b) A solution of 0.25 g (0.6 mmole) of (I, R = Ac), 0.5 ml (4 mmoles) of $BF_3 \cdot OEt_2$ and 0.5 ml of $(CH_2SH)_2$ in 2 ml of CH_2Cl_2 was held for 24 h at 20°C. After the above-described treatment, 0.13 g (40%) of (II) were obtained, mp 206-211°C.

Acetate (III) – colorless prisms, mp 136-137°C (ether–hexane). IR spectrum (ν, cm^{-1}): 1695 (C=O). PMR spectrum (δ, ppm): 0.64 s (3H, 18-CH_3), 1.05 s (3H, 19-CH_3), 2.11 s (3H, 21-CH_3), 2.35 s (6H, SAc), 2.43-2.55, 2.68-2.78, 2.90-3.18 m (9H, $-CH_2CH_2S-$ and H–C^{16}), 3.62 m (1H, H–C^3). Mass spectrum, m/z (rel. intensity, %): M^+ 624 (4.1), 5.48 (10.9), 4.89 (84.9), 447 (13.7), 412 (13.7), 353 (100). Found, %: C 63.18; H 8.44; S 20.43. $C_{33}H_{52}O_3S_4$. Calculated, %: C 63.43; H 8.41; S 20.52.

16α,17α-Cyclohexanopregn-5-en-3β-ol-20-one Tosylate (I, R = Ts). A solution of 4.51 g (12.2 mmoles) of (I, R = H) and 6.3 g of TsCl in 150 ml of Py was held at 5°C for 24 h. It was then poured onto ice, the precipitate that separated was filtered, washed on the filter with H_2O, and dried in air. Crystallization from a CH_2Cl_2–hexane mixture gave 6.59 g (a quantitative yield) of (I, R = Ts), mp 164-166°C. PMR spectrum (δ, ppm): 0.66 s (3H, 18-CH_3), 0.96 s (3H, 19-CH_3), 2.12 s (3H, 21-CH_3), 2.43 s (3H, Ts), 2.95 m (1H, H–C^{16}), 4.32 m (1H, H–C^3).

6β-Methoxy-16α,17α-cyclohexano-3,5α-cyclopregnan-20-one (IV). A solution of 3.3 g (6.1 mmoles) of (I, R = Ts) and 3.3 g of AcOK in 250 ml of MeOH was boiled for 2 h, MeOH was removed, and the residue was extracted with ether. The extract was washed with 5% $KHCO_3$ and H_2O, and dried over anhydrous K_2CO_3. The ether was evaporated and the oil obtained was chromatographed on 100 g of fluorosil. Elution with a hexane–ether (94:6) mixture gave 1.92 g (82%) of (IV) in the form of an oil; holding of the solution of (IV) in petroleum ether at 5°C gave 0.43 g of (IV), mp 100-102°C. PMR spectrum (δ, ppm, J, Hz): 0.43 d.d ($^2J_{H\alpha^4,He^4}$ = 5, $^3J_{H\alpha^4,H^3}$ = 8), 0.64 d.d ($^2J_{He^4,H\alpha^4}$ = 5, $^3J_{He^4,H^3}$ = 4), 0.73 s (3H, 18-CH_3), 1.02 s (3H, 19-CH_3), 2.11 s (3H, 21-CH_3), 2.77 m (1H, H–C^6), 2.95 m (1H, H–C^{16}), 3.31 s (3H, OCH_3).

Reaction of (I, R = Ac) with Thiophenol. A solution of 3 g (7.2 mmoles) of (I, R = Ac), 8 ml of PhSH and 6 ml (48.7 mmoles) of $BF_3 \cdot OEt_2$ in 25 ml of CH_2Cl_2 was held in Ar for 24 h at 20°C. The oily residue obtained after standard treatment was chromatographed on 150 g of SiO_2. Elution with a hexane–ether (97:3) mixture gave: 1) 0.62 g of the 3,5-bis-phenylthio derivative (VIII), mp 208-209°C (acetone). IR spectrum (ν, cm^{-1}): 1570-1585 (C=C), 1690 (C=O). PMR spectrum (δ, ppm): 0.65 s (3H, 18-CH_3), 1.14 s (3H, 19-CH_3), 2.12 s (3H, 21-CH_3), 2.95 m (1H, H–C^{16}), 3.97 m (1H, H–C^3); 7.30-7.42 m (arom. H). Mass spectrum, m/z (rel. intensity, %); M^+ 572 (0.89), 463 (90), 419 (11.7), 354 (37), 353 (100), 309 (30). Calculated for $C_{37}H_{48}OS_2$, mol. wt. 572.80.

2) 2.47 g of a crystalline mixture of (VI)-(VIII). Its repeated chromatography gave: a) 0.76 g of a mixture (1:1) of (VI) and (VII) (18%). Compounds (VI) and (VII) were isolated by crystallization from acetone. Compound (VI), mp 188-190°C. IR spectrum (ν, cm^{-1}): 1575-1585 (C=C), 1695 (C=O). PMR spectrum (δ, ppm): 0.72 s (3H, 18-CH_3), 1.01 s (3H, 19-CH_3), 2.14 s (3H, 21-CH_3), 3.00 m (2H, H–C^3 and H–C^{16}), 5.33 m (1H, H–C^6), 7.29-7.42 m (arom. H). Mass spectrum, m/z (rel. intensity, %): M^+ 462 (1.1), 353 (100), 335 (15), 309 (15). Calculated for $C_{31}H_{42}OS$, mol. wt. 462.75. Compound (VII), mp 206-209°C. IR spectrum (ν, cm^{-1}): 1575-1585 (C=C), 1695 (C=O). PMR spectrum (δ, ppm): 0.69 s (3H, 18-CH_3), 1.00 s (3H, 19-CH_3), 2.12 s (3H, 21-CH_3), 2.95 m (1H, H–C^{16}), 3.84 br. s (1H, H–C^3), 5.45 m (1H, H–C^4), 7.29-7.42 m (arom. H). Mass spectrum, m/z (rel. intensity, %): M^+ 462 (1.4), 353 (100), 335 (3.7), 309 (15.7). Calculated for $C_{31}H_{42}OS$, mol. wt. 462.75.

b) 1.5 g of (VIII) (overall yield 51%).

Reaction of (I, R = Ts) with Thiophenol. a) A solution of 0.89 g (1.64 mmoles) of (I, R = Ts), 1.2 ml of PhSH and 1.0 ml (8.1 mmoles) of $BF_3 \cdot OEt_2$ in 20 ml of CH_2Cl_2 was held for 24 h at 20°C. After a treatment similar to that described above and chromatography of the products, 0.48 g (64%) of a mixture (1:1) of (VI) and (VII) and 0.11 g (12%) of (VIII) were obtained.

b) A solution of 0.16 g (0.3 mmole) of (I, R = Ts) and 0.22 g of AcOK in 1.3 ml of PhSH was heated for 5 min at 60°C. The mixture was then diluted with ether, washed with 5% $KHCO_3$, H_2O, and dried over anhydrous K_2CO_3, and the solvents were evaporated in vacuo. The residue was chromatographed on 30 g of SiO_2. Elution with a hexane–ether (97:3) mixture gave 0.1 g (73%) of (VI), mp 178-186°C.

Reaction of 3,5-cyclosteroid (IV) with Thiophenol. a) A solution of 0.46 g (1.2 mmoles) of (IV), 1.2 ml of PhSH, and 0.3 ml (2.4 mmoles) of $BF_3 \cdot OEt_2$ in 25 ml of CH_2Cl_2 was held for 24 h at 20°C. After a standard treatment, 0.34 g (74%) of (VI) was isolated, mp 187-189°C (MeOH).

b) In a similar way, the reaction of 1.4 g (3.64 mmoles) of (IV), 3.8 ml of PhSH, and 2.7 ml (22.6 mmoles) of $BF_3 \cdot OEt_2$ in 25 ml of CH_2Cl_2 gave 0.30 g of (VI) and 0.76 g of the polar product (V) [elution with an acetone–hexane (20:80) mixture], mp 181-188°C (acetone–hexane) in the form of a chromatographically homogeneous mixture (1:1) of erythro-threo isomers. Repeated chromatography and fractional crystallization gave the individual isomers of (V): 1) (V), mp 199-201°C. PMR spectrum (δ, ppm): 0.68 s (3H, 18-CH_3), 0.88 s (3H, 19-CH_3), 2.13 s (3H, 21-CH_3), 2.95 m (1H, H–C^{16}), 5.29 m (1H, H–C^6), 7.57 m (arom. H). Mass spectrum, m/z: (M^+ + 1) 479. Calculated for $C_{31}H_{42}O_2S$, mol.wt. 478.75.

2) (V), mp 203-205°C. PMR spectrum (δ, ppm): 0.68 s (3H, 18-CH_3), 0.97 s (3H, 19-CH_3), 2.12 s (3H, 21-CH_3), 2.95 m (1H, H–C^{16}), 5.34 m (1H, H–C^6), 7.55 m (arom. H). Mass spectrum, m/z: (M^+ + 1) 479. Calculated for $C_{31}H_{42}O_2S$, mol. wt. 478.75.

Desulfurization by Ra-Ni. a) A solution of 0.1 g of (VI) in 15 ml of dioxane was boiled with 1 g of Ra-Ni for 8 h. The catalyst was filtered, washed on the filter with dioxane, the filtrate was evaporated, and the residue was chromatographed. Elution with petroleum ether gave 0.07 g of (IX), mp 195-198°C (MeOH). PMR spectrum (δ, ppm): 0.70 s (3H, 18-CH_3), 1.01 s (3H, 19-CH_3), 2.14 s (3H, 21-CH_3), 2.95 m (1H, H–C^{16}), 5.28 m (1H, H–C^6). Mass spectrum, m/z: M^+ 354. Calculated for $C_{25}H_{38}O$, mol. wt. 354.58.

b) In a similar way, from 0.2 g of (V), 0.08 g of (IX), mp 196-198°C, was obtained.

c) From 0.09 g of (VII), 0.05 g of (X) was obtained, mp 164-167°C (MeOH). PMR spectrum (δ, ppm): 0.70 s (3H, 18-CH_3), 1.03 s (3H, 19-CH_3), 2.13 s (3H, 21-CH_3), 2.95 m (1H, H–C^{16}), 5.30 m (1H, H–C^4). Mass spectrum, m/z: (M^+) 354. Calculated for $C_{25}H_{38}O$, mol. wt. 354.58.

d) From 0.2 g of (VIII), 0.075 g of a mixture of (IX) and (X) was obtained, mp 149-157°C. Crystallization from MeOH gave the individual (IX), mp 196-200°C and (X), mp 163-167°C.

Reaction of Cholest-5-en-3β-ol Acetate with Thiophenol. From 0.61 g (1.5 mmoles) of cholest-5-en-3β-ol acetate, 1.6 ml PhSH and 1.12 ml (9 mmoles) of $BF_3 \cdot OEt_2$ in 10 ml of CH_2Cl_2, under the above-described conditions, after chromatography, 0.60 g of a mixture of mono- and bisphenylthio-adducts was obtained, from which 0.1 g of 3β,5α-bisphenylthiocholestane (XI), mp 184-188°C (ether–MeOH) was isolated, mp 184-188°C (ether–MeOH). PMR spectrum (δ, ppm): 0.67 s (3H, 18-CH_3), 0.90 t (6H, CH–CH_3), 1.16 s (^{3}H, 19-CH_3), 3.97 m (1H, H–C^3), 7.30-7.42 m (arom. H).

CONCLUSIONS

1. The reaction of Δ^5-3β-substituted pentaranes with ethanedithiol and thiophenol in the presence of BF_3 etherate results in the formation of a mixture of 3-mono- and 3,5-bisalkylthio products.

2 A convenient method for the introduction of a mercapto substituent into the 3β-position of the steroid molecule was developed.

LITERATURE CITED

1. G. R. Pettit and J. Bowyer, J. Org. Chem., 25, 84 (1960).
2. L. F. Fieser, J. Am. Chem. Soc., 76, 1945 (1954).
3. C. Djerassi, O. Halpern, G. R. Pettit, and G. H. Thomas, J. Org. Chem., 24, I. (1959).
4. J. W. Blunt and J. B. Stothers, Org. Magn. Reson., 9, 439 (1977).
5. L. F. Fieser, Ch. Yuah, and T. Goto, J. Am. Chem. Soc., 82, 1996 (1960).

THREE-DIMENSIONAL STRUCTURES OF PHOSPHORUS-CONTAINING HETEROCYCLES.

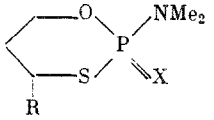
50. 2-DIMETHYLAMINO-2-OXO- AND -2-THIONO-1,3,2-OXATHIAPHOSPHORINANES

B. A. Arbuzov, R. P. Arshinova, O. A. Bulgakova, O. N. Nuretdinova, F. F. Guseva, I. Kh. Shakirov, Sh. K. Latynov, and A. V. Il'yasov

UDC 541.63:547.1'118:547.87

A previously conducted conformational analysis of 1,3,2-dioxaphosphorinane systems [1] showed that the presence of a dialkylamino group at the phosphorus atom promotes stabilization of the chair (C) conformation with an equatorial orientation of the exocyclic P–N bond (e-C). A study of the effect of the nature of endocyclic substituents attached to the phosphorus atom on the conformation of the six-membered rings seems of interest. For this purpose we previously examined 2-aroxy-2-oxo-1,3,2-oxathiaphosphorinanes (1,3,2-OTP) [2], in which the aroxy group, as in the corresponding 1,3,2-dioxaphosphorinanes, is preferably axially oriented.

In the present research we investigated the three-dimensional structures of 2-dimethylamino-2-oxo- and -2-thiono-1,3,2-OTP and their 4-methyl derivatives I-IV by Raman and ^1H and ^{31}P NMR spectroscopy and the method of dipole moments (DM).



(I), (II), (III), (IV)

R = H, X = O (I); R = Me, X = O (II); R = H, X = S (III); R = Me, X = S (IV).

The configurational homogeneity of the 2-methyl derivatives was monitored by means of the chemical shifts due to the phosphorus nuclei. Oxide II is characterized by a shift of 26 ppm. Carrying out the reaction with P_2S_5 leads to two products that have shifts of 85 and 88 ppm. The presence of two signals of unequal intensity constitutes evidence for the nonstereospecific character of replacement of the phosphoryl group by a thiophosphoryl group. The two geometrical isomers also differ with respect to their aggregate states under normal conditions: the minor isomer (88 ppm) is a liquid, while the more stable isomer is a crystalline substance; gradual conversion to the crystal state on standing is observed for a mixture of the geometrical isomers.

The conformational and configurational homogeneities of thio derivatives III and IV were investigated by means of the vibrational spectra recorded for 1,3,2-OTP in various aggregate states and in solutions with variation of the polarity of the medium. The most informative frequencies are presented in Table 1. Also given in Table 1 are the corresponding values previously obtained for 2-dimethylamino-2-thiono-1,3,2-dioxaphosphorinane (V) and two geometrical isomers of the 4-methyl derivatives, viz., the cis isomer with an e,e orientation of the 4-methyl and dimethylamino groups and the trans isomer with an *a*,e orientation

A. M. Butlerov Chemical Institute, V. I. Ul'yanov-Lenin Kazan State University. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 6, pp. 1369-1374, June, 1989. Original article submitted March 22, 1988.

0568-5230/89/3806-1251$12.50