Notes

Chem. Pharm. Bull. 17(6)1255—1260(1969)

UDC 547.92.04 : 546.185-325

Polyphosphoric Acid-catalyzed Beckmann Rearrangement of 3-Keto-steroid Oximes

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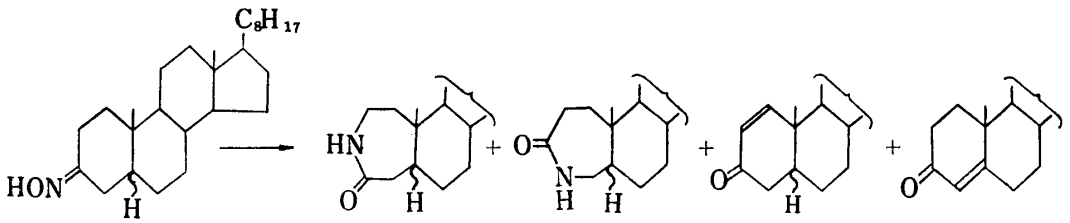
(Received May 15, 1968)

It was reported that the treatment of 5α-cholestan-3-one oxime (I) with thionyl chloride or polyphosphoric acid (PPA) gave the corresponding lactams which had been regarded as the pure 3-aza-lactam[2,3] (II) but later suggested to be a mixture of II and isomeric 4-aza-lactam (III).[4] Similarly, 5β-cholestan-3-one oxime (VI) gave an apparently pure product which is also regarded now as a mixture of isomeric lactams, VII and VIII.[2-4]

In the course of the reinvestigation of this reaction using PPA, it has been found that the oxime (I) gave an appreciable amount of two by-products. These by-products were identified by their physical constants and comparison with authentic specimens as 5α-cholest-1-en-3-one[5] (IV) (yield, 1.9—3.4%) and cholest-4-en-3-one[5] (V) (yield, 1.6—3.4%). The oxime (VI) was also found to give 5β-cholest-1-en-3-one[6] (IX) (yield, 0.5—1.9%) and cholest-4-en-3-one (V) (yield, 2.5—5.4%).



I: 5α VI: 5β — II: 5α VII: 5β — III: 5α VIII: 5β — IV: 5α XI: 5β — V

Chart 1

The formation of unsaturated ketones was observed only when PPA was used as a dehydration reagent. Thus, treatment of the oxime (I) with either 90% sulfuric acid, phosphorus pentoxide, thionyl chloride, or *p*-toluenesulfonyl chloride affords lactams, and no trace of the unsaturated ketones could be detected. It is well known that the oximes of α,α-disubstituted cyclic ketones give unsaturated nitriles when treated with thionyl chloride,[7] *p*-toluenesulfonyl chloride,[8] or PPA,[9,10] and that the acid treatment of certain unsaturated nitriles leads to

1) Location: *Kita-12-jo, Nishi-5-chome, Sapporo, Hokkaido.*
2) C.W. Shoppee and J.C. Sly, *J. Chem. Soc.*, **1958**, 3458.
3) N.J. Doorenbos and M.T. Wu, *J. Org. Chem.*, **26**, 2585 (1961).
4) C.W. Shoppee, G. Kruger and R.N. Mirringhton, *J. Chem. Soc.*, **1962**, 1050.
5) C. Djerassi and C.R. Scholz, *J. Am. Chem. Soc.*, **69**, 2404 (1947).
6) M. Rubin and B.H. Armbrecht, *J. Am. Chem. Soc.*, **75**, 3513 (1953).
7) C.W. Shoppee, Ruth. E. Lack and S.K. Roy, *J. Chem. Soc.*, **1963**, 3767.
8) J. Klinot and A. Vystrčil, *Collection Czech. Chem. Commun.*, **27**, 377 (1962).
9) R.K. Hill and R.T. Conley, *Chem. Ind.* (London), **1956**, 1314.
10) R.K. Hill and R.T. Conley, *J. Am. Chem. Soc.*, **82**, 645 (1960).

corresponding unsaturated ketones.[9,11] Unsubstituted cyclic keto oximes also afford unsaturated nitriles when treated with silica gel or boric acid-alumina catalyst at a high temperature.[12] From these examples, the following process, which involves fragmentation and recyclization, was assumed for the mechanism.

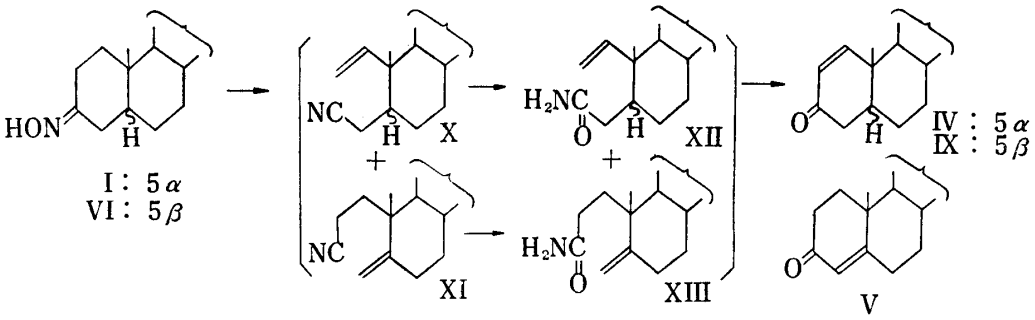


Chart 2

In connection with this assumption, two unsaturated nitriles were prepared and tested for the cyclization. 4,4-Dimethyl-5α-cholestan-3-one oxime (XIV), when refluxed with *p*-toluenesulfonyl chloride in pyridine gave 8.5% of 4-aza-A-homo-4a,4a-dimethyl-5α-cholestan-3-one (XV) and 85% of 3,4-*seco*-4-methyl-4-methylene-5α-cholestano-3-nitrile (XVI). The 4-aza structure of XV was confirmed by the nuclear magnetic resonance (NMR) which showed a broad signal of C–2 methylene adjacent to carbonyl group between τ 7.28 and τ 7.70. Formulation of unsaturated nitrile as XVI was supported by its infrared (IR) spectrum which showed absorptions at 2260 cm^{-1} (CN), 1635, and 895 cm^{-1} (exocyclic methylene) and by the NMR which showed a vinylic methyl signal at τ 8.22 as a broad singlet and multiplets of two vinylic protons centered at τ 5.05 and τ 5.27. When treated at room temperature, the oxime (XIV) gave 60% of the ε-lactam (XV).

In the same manner, 3β-acetoxy-5α-androstan-17-one oxime (XVII) gave 45% of known 3β-acetoxy-17a-aza-D-homo-5α-androstan-17-one[13] (XVIII), NMR τ: 9.17 (19-Me), τ: 8.84 (18-Me), τ: 7.35—7.8 (C–16 methylene), and 9% of oily 3β-acetoxy-13,17-*seco*-5α-androst-13-(18)-eno-17-nitrile (XIX), IR ν_{max}^{Nujol} : 2265, 1643, 893 cm^{-1}. However, treatment of the un-

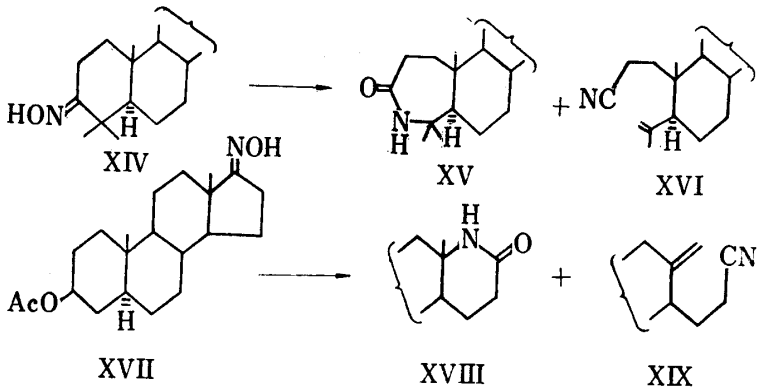


Chart 3

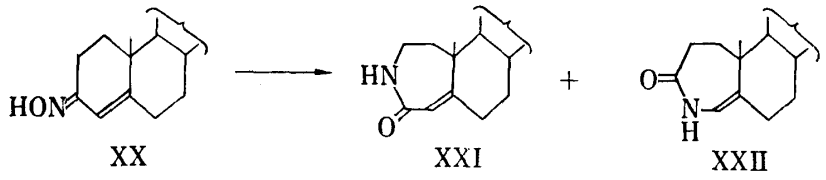
saturated nitriles (XVI or XIX) with PPA at 125—135° for 5—30 min only furnished an intractable mixture and attempted isolation of the cyclization products was unsuccessful. The failure of the enone formation can be attributed to the fact that the double bond was

11) C.F. Koelsch, *et al.*, *J. Am. Chem. Soc.*, **72**, 346 (1950).
12) *a*) O. Wallach, *Ann.*, **309**, 1 (1889); *b*) V. Davydov, *Chem. Tech.* (Berlin)., **7**, 647 (1955) [*C.A.*, **50**, 10678 (1956)].
13) H. Wolf, *Tetrahedron Letters*, **1965**, 1075.

located on the position where migration can easily occur and the condition used was too drastic for a double bond or acetoxyl group.

The observed anomaly of the Beckmann rearrangement led us to reinvestigate the reaction with oximes of cholest-4-en-3-one and 5α-cholest-1-en-3-one which have been known to afford only α,β-unsaturated lactams, XXI[4] and XXV,[14] respectively. This time, the unsaturated keto-oximes afforded the normal products, namely, the unsaturated lactams corresponding to *syn* form and the enamine lactams corresponding to *anti* form. The formation of enamine lactams has not been reported in the cholestenone series and the *anti* oximes are known to resist the rearrangement.[4,15]

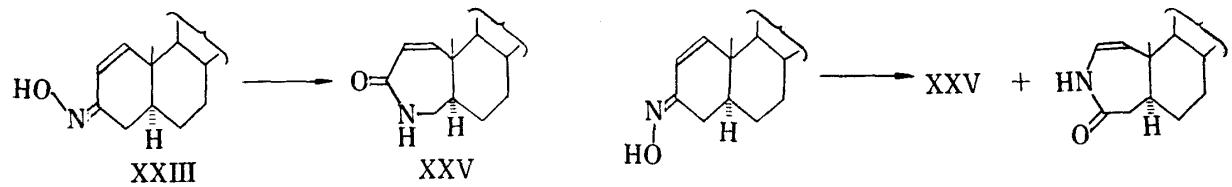
Cholest-4-en-3-one oxime (XX), containing 75% of the *syn* form and 25% of the *anti* form[15] was treated with PPA at 125—135° for 10 min and gave 10% of the known 3-aza-A-homo-cholest-4a-en-4-one (XXI)[4] and 11% of 4-aza-A-homo-cholest-4a-en-3-one (XXII) after purification by preparative thin-layer chromatography (TLC). The enamine lactam structure of XXII was supported by its ultraviolet (UV) absorption at 243.5 mμ (log ε 4.19)[16] and by the NMR spectrum which showed one vinylic proton at τ 4.58 as a slightly broad doublet (J=6 cps) coupled with the proton bound to the nitrogen and a broad signal of a methylene adjacent to carbonyl group between τ 7.4 and 7.9. The doublet at τ 4.58 changes to a singlet upon treatment with D_2O, showing the presence of a coupling with the NH proton.



XX XXI XXII

Chart 4

The oximes of 5α-cholest-1-en-3-one was separated into the *syn* form (16%) and the *anti* form (84%) by preparative TLC after repeated developments. The *syn* oxime (XXIII), mp 77—78°/144.5—147.5°, partly turns into *anti* form when heated or exposed to light for a few days. The NMR spectrum of the *syn* oxime (XXIII) showed C–1 proton at τ 3.53 as a doublet (J=11 cps) and C–2 proton deshielded by hydroxyl group at τ 3.35 as a doublet (J=11 cps) (reported,[14] C–1 proton: τ 3.58, J=10 cps, C–2 proton: τ 3.44, J=10 cps). Treatment of the *syn* oxime (XXIII) with PPA gave 44% of the corresponding 4-aza-A-homo-5α-cholest-1-en-3-one (XXV) as a sole product. In the same way, the *anti* oxime (XXIV) gave 32% of 3-aza-A-homo-5α-cholest-1-en-4-one (XXVI) and 19% of the unsaturated lactam (XXV) which was possively derived by partial isomerization of the starting *anti* oxime to the *syn* oxime (XXIII).



XXIII XXV XXIV XXVI

Chart 5

The enamine lactam structure of XXVI was confirmed by the UV absorption at 237 mμ (log ε, 4.03)[16] and by the NMR spectrum which showed C–1 proton at τ 5.12 as a doublet (J=10.6 cps) and C–2 proton at τ 4.50 as a quartet ($J_{2,1}$=10.6 cps, $J_{2,NH}$=5.8 cps). Deuterium

14) C.W. Shoppee, R. Lack, R.N. Mirringhton and L.R. Smith, *J. Chem. Soc.*, **1965**, 5868.
15) F. Kohen, *Chem. Ind.* (London), **32**, 1378 (1966).
16) R.H. Mazur, *J. Org. Chem.*, **26**, 1289 (1961).

exchange changed the quartet at τ 4.50 to a doublet at τ 4.50 (J=10.6 cps). The unsaturated lactam (XXV), derived from both *syn* and *anti* isomers, showed different physical constants from that described by Shoppee (reported,[14] mp 253—255°/276—278° (decomp.), ν_{max}^{Nujol}: 1700, 1650, 1600 cm^{-1}). The UV absorption was reported to have a maximum at 219 mμ with an abnormally low extinction (log ε 2.9). Our substance showed mp 230—232° and repeated recrystallizations failed to raise the melting point. It showed IR absorptions at 3165, 3055, 1665, 1642, 1609, and 1600 cm^{-1} (Nujol), UV absorption at 217.5 mμ (log ε 4.14), and NMR signals at τ 9.37 (18-Me), τ 9.01 (19-Me), τ 4.37 (C-2 proton, slightly broad doublet, J=13.5 cps), τ 3.79 (C-1 proton, doublet, J=13.5 cps). The broadness of the doublet at τ 4.37 is due to the long-range coupling with NH proton, thus changing to a sharp doublet by treatment with D_2O. All these data support the correct structure of XXV.

Experimental[17]

5α-Cholestan-3-one, mp 128—129°, and 5β-cholestan-3-one, mp 61—62°, were carefully checked by the UV spectrum before use to avoid contamination with unsaturated ketones.

Beckmann Rearrangement of 5α-Cholestan-3-one Oxime (I)——A mixture of 2.72 g of 5α-cholestan-3-one oxime (I) and 80 g of PPA was heated with manual stirring at 125—130° for 30 min and then poured into 400 g of ice-water. The aqueous solution was neutralized with cold 50% NaOH and extracted with ether. The ether layer was washed with H_2O and saturated NaCl solution; after being dried over Na_2SO_4, the solution was concentrated to give 1.5 g of a lactam mixture. The mother liquor was concentrated and chromatographed on silicagel (15 g). Elution with benzene gave 56 mg of a solid and further elution with benzene gave 47 mg (1.6%) of cholest-4-en-3-one (V). mp and mixed mp 81—82°. $[\alpha]_D$ +88.7° (c=0.71, $CHCl_3$). UV λ_{max}^{EtOH} mμ (log ε): 242 (4.23). IR ν_{max}^{Nujol} cm^{-1}: 1675, 1613, 865.

Purification of the sticky solid (56 mg) using preparative TLC afforded 47 mg (1.6%) of 5α-cholest-1-en-3-one (IV). mp 99.5—100.5°, mixed mp 100—100.5°. $[\alpha]_D$ +53.8° (c=0.38, $CHCl_3$). UV λ_{max}^{EtOH} mμ (log ε): 231 (4.00). IR ν_{max}^{Nujol} cm^{-1}: 1680, 1605, 778.

Beckmann Rearrangement of 5β-Cholestan-3-one Oxime (VI)——A mixture of 3.0 g of the oxime (VI) and 95 g of PPA was treated by the same procedure as above. Concentration of the ether extract afforded 2.74 g of a lactam mixture. The mother liquor was submitted to preparative TLC and developed twice using benzene–ether (19:1). Elution of the adsorbent corresponding to the bands of *Rf* 0.77 and 0.58 with EtOAc gave two compounds.

a) Upper band (15 mg, 0.5%), 5β-cholest-1-en-3-one (IX). mp 105.5—106.5°. $[\alpha]_D$ +107.6° (c=0.79, $CHCl_3$). UV λ_{max}^{EtOH} mμ (log ε): 232 (3.91). IR ν_{max}^{Nujol} cm^{-1}: 1678, 1610, 843, 785.

b) Lower band (76 mg, 2.5%), cholest-4-en-3-one, mp and mixed mp 82—83°. $[\alpha]_D$ +87.1° (c=1.17, $CHCl_3$). UV λ_{max}^{EtOH} mμ (log ε): 242 (4.22). IR ν_{max}^{Nujol} cm^{-1}: 1675, 1613, 865.

Beckmann Rearrangement of the Oxime (I) by Various Catalysts——a) By Thionyl Chloride: The oxime (200 mg) in 6 ml of dry dioxan was treated with $SOCl_2$ as described by Shoppee.[2] TLC of the crude products showed it to consist of only lactams, and no trace of unsaturated ketone or unsaturated nitrile was detected.

b) By 90% H_2SO_4: A mixture of 200 mg of the oxime (I) and 3 ml of 90% H_2SO_4 was heated at 100° for 20 min and left to cool. The mixture was then poured into ice-water, extracted with ether, and worked up as usual. TLC and IR spectrum of the crude product showed it to consist of only lactams. IR ν_{max}^{Nujol} cm^{-1}: 3180, 3050, 1660.

c) By P_2O_5: A mixture of 200 mg of the oxime (1) and 350 mg of P_2O_5 in 10 ml of dry benzene was refluxed for 20 min and worked up as usual. TLC and IR spectrum of the crude product was almost identical with those of the products obtained by conc. H_2SO_4.

d) By *p*-Toluenesulfonyl Chloride: A solution of 100 mg of the oxime (1) and 200 mg of TsCl in 3 ml of dry pyridine was refluxed for 30 min and poured into ice-water. Extraction with $CHCl_3$ and the usual working up gave a solid residue whose TLC showed it to consist of only lactams. IR ν_{max}^{Nujol} cm^{-1}: 3180, 3060, 1665, 1635.

4,4-Dimethyl-5α-cholestan-3-one Oxime (XIV)——4,4-Dimethyl-5α-cholestan-3-one (125 mg) in 1 ml of pyridine was treated with 50 mg of $HONH_2 \cdot HCl$ at 100° for 15 min. The solution was poured into water, filtered, and the solid was washed with water. The oxime thus obtained was an amorphous powder which melted at 207—209° (120 mg). $[\alpha]_D$ −46.3° (c=1.14, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 3280, 942, 925. *Anal.* Calcd. for $C_{29}H_{51}ON$: C, 81.05; H, 11.96. Found: C, 81.03; H, 11.94.

17) Melting points were measured on a Kofler's hot stage and are not corrected. NMR spectra were measured in $CDCl_3$ solution.

Beckmann Rearrangement of 4,4-Dimethyl-5α-cholestan-3-one Oxime (XIV)——a) A solution of 200 mg of the oxime (XIV) in 3.5 ml of dry pyridine was treated with 400 mg of TsCl under reflux for 3 hr. The mixture was then poured into water and extracted with $CHCl_3$. The residue was adsorbed on 1 g of silicagel and eluted with benzene and ether. The eluate with benzene gave 170 mg of 3,4-*seco*-4-methyl-4-methylene-5α-cholestano-3-nitrile (XVI) mp 70.5—72° (from MeOH). $[\alpha]_D$ +11.3° (c=2.70, $CHCl_3$). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3075, 2260, 1635, 895. NMR τ: 9.30 (18-Me), 9.04 (19-Me), 8.22 (broad singlet), 5.05 (singlet), 5.27 (singlet) (isopropenyl). *Anal.* Calcd. for $C_{29}H_{49}N$: C, 84.60; H, 12.00. Found: C, 84.49; H, 11.90. The eluate with ether gave 17 mg of 4-aza-A-homo-4a,4a,-dimethyl-5α-cholestan-3-one (XV), mp 230°, recrystallized from MeOH, IR ν_{max}^{Nujol} cm^{-1}: 1660, 1635 (shoulder).

b) The oxime (XIV) (100 mg) in 1.2 ml of dry pyridine was treated with 200 mg of TsCl at room temperature over night and worked up as above. Chromatography of the product on silicagel furnished 60 mg of a lactam (XV) which crystallized from $CHCl_3$–ether as needles. mp 228—229°. $[\alpha]_D$ +7.8° (c=0.51, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 3240, 1665, 1632, 1215, 1170. NMR τ: 9.35 (18-Me), 8.95 (19-Me), 7.28—7.70 (2H, broad, C_2-2H), 4.34 (broad, –NH–C–). *Anal.* Calcd. for $C_{29}H_{51}ON$: C, 81.05; H, 11.96; N, 3.26. Found: C, 80.57; H, 11.87; N, 3.34.

Beckmann Rearrangement of 3β-Acetoxy-5α-androstan-17-one Oxime (XVII)——A solution of 300 mg of oxime (XVII) in 6 ml of dry pyridine was treated with 600 mg of TsCl refluxing for 10 min and worked up as usual. Concentration of the solvent gave 135 mg of crude lactam (XVIII), mp 262—268° (45%). One recrystallization from ether raised the mp to 270—272°. $[\alpha]_D$ +0.7° (c=2.52, $CHCl_3$). IR ν_{max}^{Nujol} cm^{-1}: 3160, 3035, 1743, 1675, 1250, 1163, 1025. NMR τ: 9.17 (19-Me), 8.84 (18-Me), 7.96 (–OAc), 7.35—7.8 (2H, broad, C_{16}-2H), 5.25 (broad, 3α-H), 3.48 (broad, –NH–C–). *Anal.* Calcd. for $C_{21}H_{33}O_3N$: C, 72.58; H, 9.57; N, 4.03. Found: C, 72.69; H, 9.60; N, 4.03.

The mother liquor was then submitted to preparative TLC using benzene as a developing solvent. Elution of the adsorbent corresponding to the band of *Rf* 0.3 with $CHCl_3$ and evaporation of the solvent furnished 27 mg of oily 3β-acetoxy-13,17-*seco*-5α-androst-13(18)-eno-17-nitrile (XIX). $[\alpha]_D$ −35.2° (c=2.7, $CHCl_3$). IR $\nu_{CCl_4}^{CN}$ cm^{-1}: 3075, 2265, 1742, 1643, 1240, 1032, 893.

Treatment of the Unsaturated Nitriles (XVI and XIX) with PPA——Treatment of the unsaturated nitriles (XVI and XIX) with PPA at 125—135° for 5—30 min furnished only inseparable mixture and isolation of cyclization products was unsuccessful.

Beckmann Rearrangement of Cholest-4-en-3-one Oxime (XX)——A mixture of 500 mg of the oxime (XX) and 15 g of PPA was heated with manual stirring at 125—135° for 10 min and then poured into ice–water. The mixture was extracted with ether and washed with H_2O and saturated aqueous NaCl solution. The dried product thus obtained was submitted to preparative TLC using ether as a developing solvent. Elution of the adsorbent corresponding to two bands at *Rf* 0.76 and 0.33 with ether and $CHCl_3$ afforded two compounds.

a) Upper band, (55 mg, 11%), 4-aza-A-homo-cholest-4a-en-3-one (XXII). mp 234—236°. $[\alpha]_D$ −11.5° (c=1.65, $CHCl_3$). UV λ_{max}^{EtOH} mμ (log ε): 243.5 (4.19). IR ν_{max}^{Nujol} cm^{-1}: 3330, 3180, 1683, 1660, 1632. NMR τ: 9.31 (18-Me), 8.89 (19-Me), 7.4—7.9 (C_2-2H), 4.58 (slightly broad doublet, $J_{4a,NH}$ =6 cps), 3.02 (broad. –C(=O)–NH–). *Anal.* Calcd. for $C_{27}H_{45}ON$: C, 81.14; H, 11.35; N, 3.51. Found: C, 80.50; H, 11.18; N, 3.58.

b) Lower band, (52 mg, 10%), 3-aza-A-homo-cholest-4a-en-4-one. mp 253—255°. UV λ_{max}^{EtOH} mμ (log ε): 222.5 (4.07) [reported,[4] mp 252—256°. UV ν_{max} mμ (log ε): 222 (4.1)]; identical IR spectrum with that of the product obtained by TsCl in dimethylformamide.[15]

Oximes (XXIII and XXIV) of 5α-Cholest-1-en-3-one——Cholest-1-en-3-one (90 mg) in 5 ml of MeOH was mixed with a warm solution of $HONH_2 \cdot HCl$ (100 mg) and anhydrous NaOAc (100 mg) in dil. MeOH. After boiling 1.5 hr, the mixture was poured into water, extracted with $CHCl_3$, and the product submitted to preparative TLC using benzene–ether (97:3) as a solvent system. After developing five times and detecting with UV lamp, two bands were eluted with $CHCl_3$.

a) Upper band (67 mg, *anti* oxime, XXIV). mp 148—149°. UV λ_{max}^{EtOH}: 235 mμ (reported,[14] mp 149—150°). NMR τ: 3.58 (C_1-H, doublet, J=10 cps), 4.00 (C_2-H, doublet, J=10 cps).

b) Lower band (13 mg, *syn* oxime, XXIII). mp 77—78°/144.5—147.5° from MeOH. UV λ_{max}^{EtOH}: 237 mμ. IR ν_{max}^{Nujol} cm^{-1}: 3260, 975, 950, 775. NMR τ: 9.31 (18-Me), 9.09 (19-Me), 3.53 (C_1-H doublet, J=11 cps), 3.35 (C_2-H doublet, J=11 cps), (reported,[14] C_1-H: 3.58, J=10 cps, C_2-H: 3.44, J=10 cps). *Anal.* Calcd. for $C_{27}H_{45}ON \cdot \frac{1}{2}H_2O$: C, 79.35; H, 11.35. Found: C, 79.33; H, 11.28.

Beckmann Rearrangement of 5α-Cholest-1-en-3-one Oxime——a) *Syn* Oxime (XXIII): A mixture of 27 mg of the oxime (XXIII) and 1 g of PPA was heated with mannual stirring at 125—135° for 15 min and then poured into ice–water. Extraction with ether and the usual working up furnished a solid residue which was further purified by TLC using ether as a developing solvent. Elution of the UV-absorbing portion with ether and $CHCl_3$ afforded 12 mg (44%) of slightly impure 4-aza-A-homo-5α-cholest-1-en-3-one, mp 228—232° (from MeOH). UV λ_{max}^{EtOH}: 216 mμ. IR ν_{max}^{Nujol} cm^{-1}: 3150, 3045, 1668, 1641, 1609, 1600, 832.

b) *Anti* Oxime (XXIV): A mixture of 110 mg of the oxime (XXIV) and 3 g of PPA was treated by the same procedure as above. The product was then submitted to preparative TLC using ether as a solvent.

Elution of the adsorbent corresponding to two bands at *Rf* 0.77 and 0.58 with $CHCl_3$ and ether gave two compcunds.

a) Upper band (35 mg, 32%), 3-aza-A-homo-5α-cholest-1-en-4-one (XXVI) as needles, mp 224—225° from MeOH. $[\alpha]_D$ +5.8° (c=1.53, $CHCl_3$). UV λ_{max}^{EtOH} mμ (log ε): 237 (4.03). IR ν_{max}^{Nujol} cm^{-1}: 3330, 1690, 1658, 1643, 1072, 755. NMR τ: 9.32 (18-Me), 9.05 (19-Me), 5.12 (C_1-H, doublet, $J_{1,2}$=10.6 cps), 4.50 (quartet, C_2-H, $J_{2,1}$=10.6 cps, J=5.8 cps), 2.75 (broad, –NH–C(=O)–). *Anal.* Calcd. for $C_{27}H_{45}ON$: C, 81.14; H, 11.35; N, 3.51. Found: C, 81.08; H, 11.42; N, 3.46.

b) Lower band (21 mg, 19%), 4-aza-A-homo-5α-cholest-1-en-3-one (XXV) as needles, mp 230—232°, from MeOH. UV λ_{max}^{EtOH} mμ (log ε): 217.5 (4.14). IR ν_{max}^{Nujol} cm^{-1}: 3165, 3055, 1665, 1642, 1609, 1600, 835. NMR τ: 9.37 (18-Me), 9.01 (19-Me), 6.5—7.0, 7.0—7.6 (broad, 4a-α, β-H), 4.37 (C_2-H, slightly broad doublet, J=13.5 cps), 3.79 (C_1-H, doublet, J=13.5 cps), 3.05 (broad, –NHC(=O)–). *Anal.* Calcd. for $C_{27}H_{45}ON$: C, 81.14; H, 11.35; N, 3.51. Found: C, 80.97; H, 11.31; N, 3.55.

[Chem. Pharm. Bull. 17(6)1260—1263(1969)]

UDC 547.72.07 : 547.379.2.04

Synthesis of the Furan Derivatives. XLIV.[1] Oxidation of Dimethyl Sulfonium Bromides in Dimethyl Sulfoxide Solution

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(Received May 30, 1968)

It was shown that the oxidation of seven halides to the corresponding aldehydes could be achieved simply by dissolving the halides in dimethyl sulfoxide[3] (DMSO). In addition, other several papers[4] concerning the reaction of this type which yielded phenyl glyoxal and glyoxalic acid have been reported. In our laboratory,[5] it was found that the oxidation of halides (Ib, Ic, Id) with DMSO at room temperature gave the corresponding glyoxals (IIIb, IIIc, IIId) and thiolformates (IVb, IVc, IVd).

In connection with these experiments, phenacyl dimethylsulfonium bromide (IIa) was isolated unexpectedly from the reaction of phenacyl bromide (Ia) with DMSO under mild condition. This fact suggested that this compound (IIa) wolud be one of the isolable intermediates of this reaction and can be used as starting material, because IIa is readily prepared by the reaction of Ia with dimethyl sulfide.

The object of this work is to investigate the reaction of phenacyl-(IIa),[6a] 4-bromophenacyl-(IIb),[6b] 2-furoylmethyl-(IIc) and 5-nitro-2-furoylmethyl-(IId) dimethylsulfonium bromide with DMSO.

No reaction took place between IIa and DMSO at room temperature (about 15—20°) even after 10 hours. Heating at 40° for 5 hours in a nitrogen atmosphere yielded two com-

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