Anal. Calcd for $C_{11}H_{15}N_5O_4$: C, 46,96; H, 5.41; N, 24.90. Found: C, 47.11; H, 5.65; N, 24.59.

Periodate Uptake. The spectrophotometric procedure of Rammler and Rabinowitz[27] was used to determine the consumption of periodate. 9-(6-Deoxy-β-D-gulofuranosyl)adenine (**14**) consumed a total of 0.93 molar equiv of periodate in under 0.5 hr, whereas it took 9-(6-deoxy-α-D-idofuranosyl)adenine (**16**) 160 hr to consume 0.90 molar equiv.

Polarimetric Studies. Between 10 and 13 mg of each nucleoside was dissolved in 0.75 ml of hot water in a 2-ml volumetric flask and then cooled to room temperature. To the solution was added 0.5 ml of 0.25 *M* sodium periodate. The reaction mixture was kept in the dark at room temperature, the time of reaction being 1 day for **14** and 5 days for **16**. At the end of the reaction time, 60 mg of sodium borohydride was added and after 1 hr, the excess hydride was destroyed by slow addition of 0.4 ml of 20% acetic acid solution. When effervescence stopped (1–2 hr) the volume was adjusted with water to 2 ml and the optical rotation was measured. The results are shown in Table II.

Deamination of 8 with Adenosine Deaminase. The enzyme reaction was followed spectrophotometrically[28] at 265 nm at 25° in 0.5 *M* phosphate buffer (pH 7.6). The concentration of **8** was 6×10^{-6} *M* and 3 ml of this solution was added to a cuvette. A solution of buffer containing the enzyme (0.1 ml, 2.1 units) (Sigma Chemical Co.) was added to start the reaction and this was mixed thoroughly. The uv absorption leveled off at a constant value after 5 min. The uv absorption spectrum had a maximum at 249 nm. An identical reaction using adenosine gave an almost instantaneous leveling off of the optical density and a shift in the uv to λ_{max} 248 nm.

Registry No.—**1**, 50692-25-6; **2**, 50692-26-7; **4**, 57207-09-7; **5**, 57207-10-0; **8**, 57237-22-6; **9**, 57207-11-1; **14**, 57237-23-7; **15**, 57237-24-8; **16**, 57237-25-9; benzoyl chloride, 98-88-4; 6-benzamidochloromercuripurine, 17187-65-4.

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Reaction of 4,5-Diamino-1,3-dimethyluracil with Diketones

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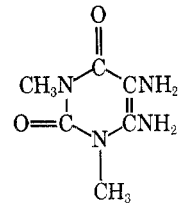
4,5-Diamino-1,3-dimethyluracil when treated with acetylacetone and with dibenzoylmethane formed 4-(4-amino-1,3-dimethyluracil-5-amino)-3-buten-2-one and β-(4-amino-1,3-dimethyluracil-5-amino)chalcone, respectively. The reaction of the diamine with *trans*-1,2-di-*p*-toluylethylene in ethanol gave 3-*p*-tolyl-5,7-dimethyl-6,8-dioxo-5,6,7,8-tetrahydropteridine and 1,3-dimethyl-8-*p*-tolylxanthine. The same reaction in acetic acid gave the isomeric pteridines and a diazepine. Condensation of the diamine with 1,2-di-*p*-toluylethane in ethanol formed a pyrrole.

The reaction of 4,5-diamino-1,3-dimethyluracil (**1**) with acetylacetone, dibenzoylmethane, *trans*-di-*p*-toluylethylene, and 1,2-ditoluylethane has been studied to determine whether this diamine **1** would behave in a similar manner to that found for *o*-phenylenediamine with similar compounds.

4,5-Diamino-1,3-dimethyluracil (**1**) gave with acetylacetone and dibenzoylmethane in ethanol containing a trace of acetic acid the corresponding substituted unsaturated ketones (**2**, R = CH_3 or C_6H_5). Evidence for these structures was the elemental analysis and spectral data; the NMR spectra showed three exchangeable protons in the presence of deuterium oxide.

Attempts to convert **2** (R = CH_3) to the diazepine were



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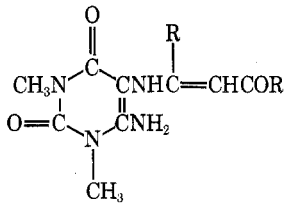

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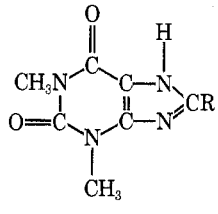
not successful; thermolysis at its decomposition point proceeded with the elimination of acetone and formation of the xanthine **3** (R = CH_3). Heating **2** (R = CH_3) with acetic anhydride gave a mixture of 5-acetylamino-4-amino-1,3-dimethyluracil and the xanthine **3** (R = CH_3). Using acetic



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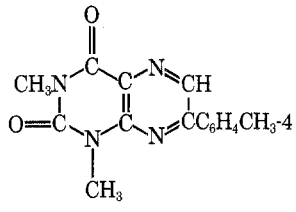
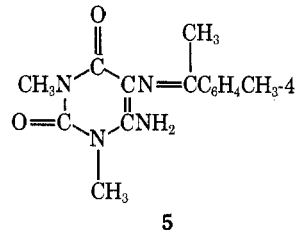


4

acid as a solvent for the condensation of **1** and acetylacetone gave a similar mixture of compounds. These conditions when applied to *o*-phenylenediamine are reported to form the diazepine.[1] Compound **2** (R = C_6H_5) upon heating behaved in a similar fashion to the methyl derivative **2** (R = CH_3); softening occurred at 370° with a final melting at 389–395°, which is the melting point of the xanthine **3** (R = C_6H_5). This xanthine **3** (R = C_6H_5) was also isolated in a small amount in the condensation of **1** with dibenzoylmethane.

Condensation of the diamine **1** with *trans*-di-*p*-toluylethylene in absolute ethanol under nitrogen gave the pteridine **4**, small amounts of the xanthine **3** (R = 4-$CH_3C_6H_4$), and 1,2-di-*p*-toluylethane. This reaction parallels that reported between *o*-phenylenediamine and *trans*-dibenzoylethylene[2] except that the by-product from the formation of the pteridine **4**, *p*-methylacetophenone, was not isolated. This ketone may be the precursor of the xanthine **3** (R = 4-$CH_3C_6H_4$), since the condensation product **5**



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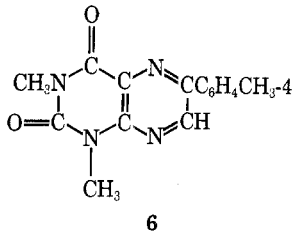

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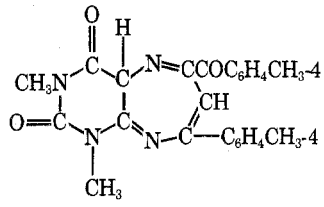
from the diamine **1** and *p*-methylacetophenone upon melting forms **3** (R = $C_6H_4CH_3$-4). This behavior resembles that reported for the thermolysis of ketone derivatives of *o*-phenylenediamine.[3]

The reaction between the diamine **1** and *trans*-di-*p*-toluylethylene in acetic acid gave a mixture of products from which the following were isolated and characterized: the pteridine **4**, the isomeric pteridine **6**, diazepine **7**, *p*-methylacetophenone, 2,5-di-*p*-tolylfuran, *trans*-di-*p*-toluylethylene, 1,2-di-*p*-toluylethane, and 5-acetylamino-4-amino-1,3-dimethyluracil. In contrast to the reaction of *o*-phenylenediamine with *trans*-dibenzoylethylene under similar conditions,[2] none of the pyrrole **8** was isolated. This compound (**8**) was prepared, however, by the condensation of the diamine **1** with 1,2-di-*p*-toluylethane in absolute ethanol under nitrogen. The equivalency of the vinyl hydrogens and the *p*-tolyl groups in the NMR spectrum eliminated a dihydrodiazocine structure as a possibility for this compound.



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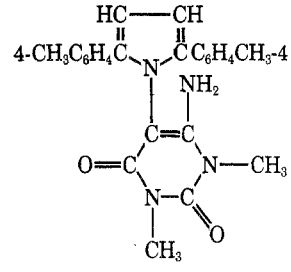

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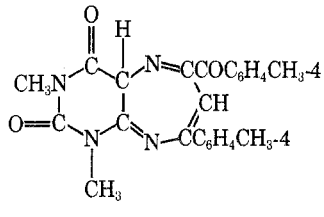
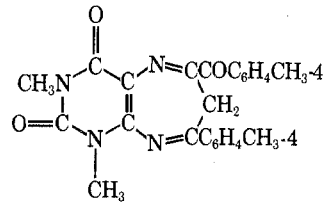
The structure of the isomeric pteridine **6** was indicated by elemental analysis and spectral data. The NMR spectrum was similar to that for the pteridine **4** with slight variations in the chemical shifts; the largest differences occurred for the ortho hydrogens in the *p*-tolyl group and the 3 hydrogen. Similarities occurred in the infrared spectrum with the exception of the 12–12.5-μ region. The pteridine **4** showed two absorptions at 12 and 12.4 μ whereas the isomer **6** showed only one at 12.1 μ. The mass spectra showed similar fragmentations but the intensities of some of the peaks varied.

The formulation of the diazepine **7** was based on the infrared and NMR spectra. The former showed no absorption for a NH group. The NMR spectra in trifluoroacetic acid and deuterionitrobenzene showed two singlets for the vinyl hydrogen and the bridgehead hydrogen. Both of these singlets disappeared in deuterated trifluoroacetic acid. Exchange would occur through an equilibrium between the following tautomeric forms.





Such an equilibrium may also account for the unequal heights observed for the methyl peaks in the NMR spectrum in trifluoroacetic acid. These heights were likewise temperature dependent.

Solutions of diazepine **7** in trifluoroacetic acid were dark red in color; a similar color is reported for the diazepines from *o*-phenylenediamine.[1] In contrast to the latter, addition of water caused precipitation of the diazepine **7**; no contraction in the diazepine ring occurred comparable to that observed with *o*-phenylenediamine derivatives.[4] This compound **7** was also thermally stable in contrast to 1-phenyl-2-(3-phenyl-1,2-dihydroquinoxaline-2-ylidene)ethan-

one isolated from *o*-phenylenediamine and *trans*-dibenzoylethylene,[2] which had been formulated previously as a diazepine.[5]

Experimental Section

Melting points are not corrected. Infrared spectra were recorded on a Model 185 Perkin-Elmer spectrometer and a Beckman Model 1R-20A spectrometer and the NMR spectra were obtained with a Varian A-60 spectrometer. Mass spectra were obtained with a Hitachi RMUGE spectrometer.

4,5-Diamino-1,3-dimethyluracil (1). A suspension of 5-nitroso-4-amino-1,3-dimethyluracil (18.4 g) in absolute ethanol (150 ml) was reduced with hydrogen (45 psi) in the presence of platinum oxide (0.1 g). The reduction was terminated when the red-colored suspension became a pale tan precipitate. The liquid was decanted and the solid was recrystallized from ethanol, yield 9.0 g, mp 211–214° (lit.[6] 209°). Concentration of the filtrate gave an additional 1.57 g which melted at 190–211°.

4-Methyl-4-(4-amino-1,3-dimethyluracil-5-amino)-3-buten-2-one (2, R = CH_3). A solution of the diamine 1 (1.7 g) and acetylacetone (1.0 g) in absolute ethanol (30 ml) containing 1 drop of glacial acetic acid was heated at reflux for 7 hr. The resulting solid (2.26 g) upon heating darkened and softened between 209 and 219° and then melted at 327–330°. Recrystallization from ethanol did not change this behavior: ir (Nujol) 3333, 3125 (NH), 1695, 1623 cm^{-1} (CO); NMR (Me_2SO-d_6, 135°) δ 1.7 (s, 3, CH_3CO), 1.93 (s, 3, $CH_3C{=}C$), 3.13 (s, 3, CH_3N), 3.33 (s, 3, CH_3N), 5.17 (s, 1, CH), 6.40 (broad s, 2, NH_2), 10.7 (broad s, 1, NH).

Anal. Calcd for $C_{11}H_{16}O_3N_4$: C, 52.38; H, 6.35; N, 22.22. Found: C, 52.35; H, 6.38; N, 22.43.

Thermolysis of 2 (R = CH_3). Compound 2 (R = CH_3) (0.6 g) was heated at 225–235° for 30 min and the resulting solid was extracted with hot water (12 ml) and filtered. The solution on cooling gave 1,3,8-trimethylxanthine 3 (R = CH_3) (0.10 g), mp 330–335° (lit.[7] 325°).

Reaction of 2 (R = CH_3) with Acetic Anhydride. Compound 2 (R = CH_3) (1.26 g) was dissolved in a mixture of acetic anhydride (1 ml) and acetic acid (10 ml) by heating at 90° and the resulting solution was allowed to stand for 22 hr at room temperature. Addition of water followed by removal of the solvent under reduced pressure gave a solid which upon fraction crystallization from methanol gave 1,3,8-trimethylxanthine 3 (R = CH_3) (0.02 g) and 5-acetylamino-4-amino-1,3-dimethyluracil (0.67 g): mp 272–282°, solidified and remelts at 330° (lit.[8] 275–276°); NMR (D_2O) δ 2.62 (s, 3, CH_3CO), 3.68 (s, 3, CH_3N) 3.85 (s, 3, CH_3N).

Reaction of 1 with Acetylacetone in Acetic Acid. The diamine 1 (1.7 g) and acetylacetone (1.0 g) were heated at reflux in acetic acid (25 ml) for 7.5 hr. Addition of water followed by evaporation to dryness under reduced pressure gave a solid which upon fractionation from methanol gave 1,3,8-trimethylxanthine 3 (R = CH_3) (1.28 g) and 5-acetylamino-4-amino-1,3-dimethyluracil (0.3 g).

β-(4-Amino-1,3-dimethyluracil-5-amino)chalcone (2, R = C_6H_5). A solution of the diamine 1 (1.70 g) and dibenzoylmethane (2.24 g) in absolute ethanol (75 ml) containing 3 drops of acetic acid was heated at reflux for 17 hr. The solution upon cooling gave a yellow solid (1.67 g). Recrystallization from ethanol gave 8-phenyl-1,3-dimethylxanthine (3, R = C_6H_5) (0.11 g): mp 388–394° (lit.[9] >300°); NMR (CF_3COOH) δ 3.63 (s, 3, NCH_3), 3.88 (s, 3, NCH_3), 7.5–7.9 (m, 3, meta and para aromatic H), 7.9–8.2 (m, 2, ortho aromatic H), 10.97 (broad s, 1, NH).

Concentration of the alcohol filtrate gave 2 (R = C_6H_5) (1.38 g) which upon recrystallization from ethanol gave yellow needles (1.05 g) that softened at 370° and melted at 389–395°; ir (Nujol) 3333, 3150 (NH), 1705 (CO), 1665 (CO), 1580 cm^{-1} (broad) (C=N, C=C); NMR (Me_2SO-d_6) δ 2.93 (s, 3, CH_3N), 3.17 (s, 3, CH_3N), 6.03 (s, 1, C=CH), 7.28–7.65 (m, 6, C_6H_5, meta and para aromatic H), 7.65–8.1 (m, 4, ortho aromatic H), 7.20 (broad s, 2, NH_2), 11.37 (s, 1, NH). Treatment with D_2O caused the singlets at δ 7.20 and 11.37 to disappear.

Anal. Calcd for $C_{21}H_{20}N_4O_3$: C, 67.02; H, 5.32; N, 14.89. Found: C, 67.20; H, 5.15; N, 14.90.

3-*p*-Tolyl-5,7-dimethyl-6,8-dioxo-5,6,7,8-tetrahydropteridine (4). The diamine 1 (1.70 g) and *trans*-di-*p*-toluylethylene (2.64 g) in absolute ethanol (100 ml) were heated at reflux under nitrogen for 24 hr. The solid (0.66 g) obtained upon cooling was treated with chloroform and the soluble portion after removal of the chloroform and recrystallization from ethyl acetate melted at 250–252°, yield 0.33 g. Successive crystallizations from ethanol and methanol gave the pteridine 4 melting at 255–258° (lit.[10] 257°); NMR ($CDCl_3$) δ 2.44 (s, 3, CH_3), 3.50 (s, 3, CH_3N), 3.76 (s, 3, CH_3N), 7.33 (d, 2, meta H, J = 8 Hz), 8.03 (d, 2, ortho H, J = 8 Hz), 8.95 (s, 1, CH).

The insoluble portion (0.03 g) from the chloroform extract was 8-*p*-tolyl-1,3-dimethylxanthine (3, R = *p*-$CH_3C_6H_4$): mp 375–380°; ir (Nujol) 3125 (NH), 1689, 1639 cm^{-1} (CO); NMR (CF_3COOH) δ 2.52 (s, 3, CH_3), 3.62 (s, 3, NCH_3), 3.85 (s, 3, NCH_3), 7.52 (d, 2, meta ArH, J = 8 Hz), 7.97 (d, 2, ortho ArH, J = 8 Hz).

Anal. Calcd for $C_{14}H_{14}N_4O_2$: C, 62.22; H, 5.19; N, 20.74. Found: C, 62.08; H, 5.22; N, 20.37.

The filtrate from the reaction was evaporated to dryness and the resulting highly colored residue was extracted with hexane; no *p*-methylacetophenone was found by GLC analysis. The residue was taken up in benzene and chromatographed on silica gel. Elution with benzene gave 1,2-di-*p*-toluylethane (0.34 g). Identification was made by comparison with an authentic sample.[11] Further elution with chloroform and with ethyl acetate gave glassy materials which were not investigated.

Reaction of Diamine 1 with *trans*-Di-*p*-toluylethylene in Acetic Acid. A solution of the diamine 1 (3.18 g) and *trans*-di-*p*-toluylethylene (4.94 g) in acetic acid (70 ml) was heated at reflux for 21 hr. Addition of water followed by removal of the solvent under reduced pressure gave a solid which was heated with methanol (100 ml) and the resulting mixture was cooled. The solid present was filtered and washed with methanol (50 ml), yield 1.53 g. Extraction with hot ethyl acetate gave the insoluble diazepine 7, yield 1.04 g, mp 245–250°. Recrystallization from chloroform gave a sample (0.92 g) melting at 253–255°; ir (Nujol) 1709 (CON), 1667 (COAr), 1604 cm^{-1} (C=C); NMR ($C_6D_5NO_2$, 150°) δ 2.28 (s, 2.35, CH_3), 2.38 (s, 3.65, CH_3), 3.53, 3.55 (two singlets, 4.3, NCH_3), 3.68 (s, 1.7, NCH_3), 4.78 (s, 1, COCH), 6.55 (s, 1, =CH), 7.0–8.12 (m, aromatic H); NMR (CF_3COOH) δ 2.42 (s, 4.6, CH_3), 2.56 (s, 1.4, CH_3), 3.56, 3.63 (two s, 3, CH_3N), 3.80, 3.88 (two s, unequal height with a ratio of 3:4, 3, CH_3N), 4.92 (s, 1, COCH), 6.75 (s, 1, =CH), 7.28 (d, 2, meta ArH, J = 8 Hz), 7.35 (s, 2, meta ArH), 7.58 (s, 2, ortho ArH), 7.80 (d, 2, ortho ArH, J = 8 Hz); NMR (CF_3COOD, room temperature) same spectrum except that the peaks at δ 4.92 and 6.75 were absent. At 70° the peak at δ 2.42 increased at the expense of the peak at δ 2.57; the two peaks at δ 3.56 and 3.63 coalesced into one at δ 3.63 and the two singlets at δ 3.80 and 3.88 appeared at δ 3.80 and 3.92 in a ratio of 2.4:1. The aromatic region showed very little change, *m/e* 414.

Anal. Calcd for $C_{24}H_{22}N_4O_3$: C, 69.60; H, 5.31; N, 13.52. Found: 69.30; H, 5.20; N, 13.30.

The ethyl acetate extract upon concentration gave 0.24 g of a solid which after crystallization from benzene gave 0.13 g of the pteridine 4, mp 253–255°. Further concentration of the ethyl acetate gave 0.1 g of a solid which after two crystallizations from benzene gave the isomeric pteridine 6 melting at 235–237°; ir (Nujol) 1739, 1661 cm^{-1} (CO); NMR (CF_3COOH) δ 2.45 (s, 3, CH_3), 3.65 (s, 3, NCH_3), 3.87 (s, 3, NCH_3), 7.35 (d, 2, meta ArH, J = 8 Hz), 7.83 (d, 2, ortho ArH, J = 8 Hz), 8.65 (s, 1, =CH); *m/e* 282.

Anal. Calcd for $C_{15}H_{14}N_4O_2$: C, 63.83; H, 4.96; N, 19.86. Found: C, 63.89; H, 5.12; N, 19.72.

The methanol extracts were evaporated to dryness under reduced pressure and the solid obtained was treated with benzene. The insoluble portion (0.99 g) when recrystallized from ethanol gave 0.50 g of 5-acetylamino-4-amino-1,3-dimethyluracil melting at 278° with decomposition.

The benzene filtrate was chromatographed on silica gel. Elution with benzene gave 2,5-di-*p*-tolylfuran which after crystallization from methanol melted at 162–165°, yield 0.12 g. Identification was made by comparison with an authentic sample.[12] Further elution with benzene gave 0.56 g of a mixture of *trans*-1,2-*p*-toluylethylene and 1,2-toluylethylene melting at 124–137°. Analysis by NMR indicated that the ratio of unsaturated diketone to the saturated diketone was 65:35.

Elution further with benzene and then with chloroform gave a mixture of the isomeric pteridines (4, 6) (0.16 g) (by ir spectral analysis) and the pteridine 4 (0.11 g).

In a separate run the solid obtained by evaporating the methanol extract was extracted with hexane and gave 0.16 g of *p*-methylacetophenone. Identification and quantification were made by gas–liquid chromatography using a 5% SE-30 on 100–120 mesh Chromosorb P column at 119°.

5-(1-Methyl-*p*-tolylidene)amino-4-amino-1,3-dimethyluracil (5). The diamine 1 (0.85 g) was heated with *p*-methylacetophenone (2 ml) under nitrogen at 100° for 17 hr. Addition of chloroform to the product gave a solid (1.1 g) which after two crystalliza-

tions from ethanol when heated softened at 217° and melted with gas evolution at 221°: ir (Nujol) 3266 (NH_2), 1681 (CO), 1600 cm^{-1} (C=N).

Anal. Calcd for $C_{15}H_{18}N_4O_2$: C, 62.94; H, 6.29; N, 19.58. Found: C, 63.03; H, 6.04; N, 19.81.

Thermolysis of 5. Compound **5** (1.09 g) was heated at 220–230° for 15 min and the resulting solid was treated with water. Filtration gave 0.47 g of a solid which was extracted with chloroform and recrystallized twice from ethanol, mp 372–384°. The ir spectrum was similar to that of the compound isolated in the reaction of the diamine **1** with *trans*-di-*p*-toluylethylene in ethanol.

Condensation of Diamine 1 with 1,2-Di-*p*-toluylethane. The diamine **1** (0.85 g) was heated at reflux with 1,2-di-*p*-toluylethane (1.33 g) in absolute ethanol (50 ml) under nitrogen for 31 hr. The solution upon filtration gave 1.50 g of the pyrrol **8** which after recrystallization successively from ethyl acetate and methanol melted at 303–309° dec; ir (Nujol) 3333 (NH), 1701 (CO), 1600 cm^{-1} (C=C); NMR (Me_2SO-d_6) δ 2.23 [s, 6, $(CH_3)_2$], 3.13 (s, 3, NCH_3), 3.18 (s, 3, NCH_3), 6.26 (broad s, 2, NH_2), 6.39 (s, 2, =CH), 7.03 (d, 4, meta ArH, J = 8 Hz), 7.30 (d, 4, ortho ArH, J = 8 Hz). Upon the addition of D_2O the peak at δ 6.26 disappeared, *m/e* 400.

Anal. Calcd for $C_{24}H_{24}N_4O_2$: C, 72.0; H, 6.0; N, 14.0. Found: C, 71.86; H, 6.00; N, 13.82.

Registry No.—**1**, 5440-00-6; **2** (R = CH_3), 57196-68-6; **2** (R = C_6H_5), 57196-69-7; **3** (R = CH_3), 830-65-9; **3** (R = C_6H_5), 961-45-5; **3** (R = *p*-$CH_3C_6H_4$), 57196-70-0; **4**, 51445-58-0; **5**, 57196-71-1; **6**, 57196-72-2; **7**, 57196-73-3; **8**, 57196-74-4; 5-nitroso-4-amino-1,3-dimethyluracil, 6632-68-4; acetylacetone, 123-54-6; 5-acetylamino-4-amino-1,3-dimethyluracil, 10184-41-5; dibenzoylmethane, 120-46-7; *trans*-di-*p*-toluylethylene, 17342-09-5; 2,5-di-*p*-tolylfuran, 57196-75-5; *p*-methylacetophenone, 122-00-9; 1,2-di-*p*-toluylethane, 13145-56-7.

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Synthesis of β,γ-Acetylenic 3-Oxo Steroids of the 5,10-Seco Series[1]

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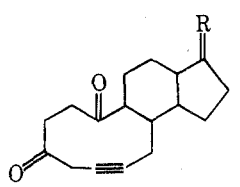
The synthesis is reported of 5,10-seco-19-norcholest-5-yne-3,10-dione (**1a**) and its estryne and 19-norpregnyne analogues (**1b** and **1c**, respectively). The key $\Delta^{5(10)}$-6-oxo intermediates (**3a–c**), prepared by direct chromium trioxide–pyridine oxidation of the corresponding Δ^5-19-hydroxy steroids (**2a–c**), were converted to the 5β,10β-oxido-6-oxo steroids (**4a–c**) using alkaline hydrogen peroxide or *m*-chloroperbenzoic acid. Compounds **4a–c** gave, after Tanabe–Eschenmoser fragmentation, the 3β-acetoxy-5,10-seco-5-yne derivatives (**5a–c**), which in turn yielded **1a–c**, after hydrolysis of the acetoxy groups followed by Jones oxidation. The 5β,10β configuration in the 5,10-oxido-6-oxo steroids was assigned on the basis of CD and of chemical evidence. Another route to the 5β,10β-oxido-6-ketone grouping was found in treatment of the $\Delta^{5(10)}$-6β-acetoxy compound **10** with Jones reagent to give directly the 5β,10β-oxido-6-ketone **4b**.

Studies concerned with the design and synthesis of specific enzyme-generated inhibitors of the Δ^5-3-keto steroid isomerase of *P. testosteroni* required the synthesis of 5,10-seco acetylenic steroids with the structures **1a–c.**



1a, R = β-C_8H_{17}, α-H
b, R = O
c, R = β-CH_3CO, α-H

These compounds were designed as substrates for Δ^5-3-keto steroid isomerase[2] with the hope that the enzyme, through its normal mode of action,[2,3] would convert the β,γ-acetylenic ketone system to the conjugated allenic ketone grouping. Thus, the enzyme converts Δ^5-3-oxo steroids to the corresponding Δ^4-3-oxo steroids by removing the 4β proton which is transferred intramolecularly to the 6β position, most plausibly via an enol intermediate. If compounds such as **1** proved to be substrates for the enzyme, the same process should generate the reactive $\Delta^{4,5}$-dien-3-one system. It was hoped that the latter would then react with a nucleophilic amino acid residue at or near the active site.

Examination of models suggested that these 5,10-seco steroids, with the ten-membered ring partly rigidified by the constraints of the acetylenic and carbonyl groupings, as well as by the ring junction at C-8 and C-9, might approximate conformationally to the natural tetracyclic Δ^5-3-oxo steroid system. In the event, seco steroids **1b** and **1c** indeed proved[4] to be excellent substrates for, and potent irreversible inhibitors of, the enzyme.

We report here the synthetic routes leading to compounds **1a–c**, as illustrated in Chart I, initially carried out in the cholestane series for calibration purposes.

The critical part of the route involved generation of the key $\Delta^{5(10)}$-6-oxo intermediate (**3a**) with subsequent fragmentation of the derived 5β,10β-oxido-6-ketone (**4a**) to **5a** by the Tanabe–Eschenmoser[5,6] procedure. It was necessary to accumulate large quantities of the $\Delta^{5(10)}$-6-ketone (**3a**) and we first tried the known procedure[7] shown below.

This involved lead tetraacetate induced fragmentation of 3β-acetoxy-19-hydroxycholest-5-ene (**2a**) followed by cleavage of the acetoxy groups (lithium aluminum hydride) and selective oxidation at C-6 with manganese dioxide. In