seemed important to ascertain whether the spectrum of this compound was indeed anomalous we undertook its preparation by an unambiguous route.

3β-Chloro-Δ⁵-pregnen-20-one was prepared from Δ⁵-pregnen-3β-ol-20-one with phosphorus pentachloride and reduced with sodium and propanol. The resulting mixture of the two Δ⁵-pregnen-20-ols was oxidized according to the method of Bladon, *et al.*,[6] which proved superior to the customary procedure with bromination of the 5–6 double bond. The reaction product was identified as Δ⁵-pregnen-20-one by its composition, its rotation, and by its conversion to the known allopregnan-20-one. It is clearly different from the product described by the Swiss workers as shown by a comparison of the infrared spectra and the melting points. The absorption maxima of our preparation (12.54 (v.s.), 12.36 (w), and 12.02 (v.s.) μ (798, 809, 832 cm.$^{-1}$) in carbon disulfide, and near 12.50, 12.34 and 11.95 μ (800, 811, 837 cm.$^{-1}$) in Nujol) were in close accord with the corresponding peaks of Δ⁵-cholestene[5] and of 20α-acetoxy-Δ⁵-pregnene. Since no peaks of comparable height were seen in the reduction products[7] cholestane[6] and allopregnan-20-one it is probable that all three frequencies are characteristic of Δ⁵-unsaturated steroids that lack a substituent at C-3 and are not subject to disturbing influences from other vicinal groups.

The results serve to re-emphasize that the presence even of a strong maximum in the 12 μ range is insufficient proof for the presence of a trisubstituted double bond and indicate the greater reliability of a spectral comparison with closely related structures.

Experimental[8]

Δ⁵-Pregnen-20-one.—A solution of 62 mg. of phosphorus pentachloride in 2.8 cc. of dry chloroform was added dropwise to a stirred solution of 37 mg. of Δ⁵-pregnen-3β-ol-20-one in 4.6 cc. of the same solvent (50 minutes at −15°). The mixture was stirred at 0° for 10, and at room temperature for 60 minutes and worked up in the usual manner.[9] The resulting 3β-chloro-Δ⁵-pregnen-20-one which was purified by chromatography on alumina and by recrystallization from dilute methanol and from petroleum ether melted at 148.5–150.5°; lit.[10] m.p. 146.5° uncor. The absorption peaks at 13.15, 12.51 and 12.18 μ (760, 799, 821 cm.$^{-1}$) are in good accord with the corresponding maxima of other Δ⁵-3β-chlorosteroids.[11] Another strong peak was at 12.10 μ (827 cm.$^{-1}$). A solution of 46.8 mg. of 3β-chloro-Δ⁵-pregnen-20-one in 8 cc. of propanol was reduced with 540 mg. of sodium as described for other 3-chlorosteroids.[9] The crude diols (42.3 mg.) in 6 cc. of acetone were oxidized with 0.13 cc. of 8 *N* chromic acid reagent[6] for 5 minutes at 34°. The excess oxidant was reduced by adding immediately a mixture of 110 mg. sodium bisulfite, 1.2 cc. of *N* sulfuric acid and 6.4 cc. of acetone. The reaction mixture was distributed between ether and water. The ether layer was washed with potassium carbonate and water. The ether residue (35.7 mg.) was freed of a high melting impurity which was rather insoluble in petroleum ether and recrystallized from this solvent and from methanol; yield of Δ⁵-pregnen-20-one 16.2 mg., m.p. 133–135°, $[\alpha]^{27}D$ +6° (*c* 0.5, chloroform) [M]D +18° ([M]D calcd. +26° from [M]D for cholesterol[12] −154°, Δ⁵-cholestene[12] −207° and of Δ⁵-pregnen-3β-ol-20-one[12] +79°); carbonyl peak at 5.86 μ (1706 cm.$^{-1}$).

Anal. Calcd. for $C_{21}H_{32}O$: C, 83.94; H, 10.74. Found: C, 83.81; H, 10.72.

Allopregnan-20-one.—A mixture of 8.7 mg. of Δ⁵-pregnen-20-one, 200 mg. of prereduced palladium–calcium carbonate catalyst and 8.5 cc. of 95% ethanol were shaken in an atmosphere of hydrogen. The uptake of gas ceased after 15 minutes. The reduction product was isolated in the usual manner[9] and recrystallized from methanol to give 5.3 mg. of allopregnan-20-one. The m.p. (136.5–137.5°) remained unchanged by admixture with a specimen[13] prepared from allopregnane-3,20-dione. The infrared spectra of both preparations were in good agreement. In the 12 μ region allopregnan-20-one showed very weak peaks near 12.56 and 12.09 μ (796, 827 cm.$^{-1}$). The ketone peak was at 5.86 μ (1706 cm.$^{-1}$). The compound has been prepared by a variety of methods. Several of these are cited by Mancera, *et al.*[14]

(6) P. Bladon, J. M. Fabian, H. B. Henbest, H. P. Koch and G. W. Wood, *J. Chem. Soc.*, 2402 (1951).

(7) This is in contrast to the peaks seen near 12.0 μ in many Δ⁵-3β-acetoxy steroids. These weaker maxima were considered to be unrelated to the presence of the double bond since reduction caused little or no spectral change (*cf.* Fig. 1 in ref. 5).

(8) All m.p.'s reported are corrected. Details on spectrographic technique have been given previously.[5] The solvent was carbon disulfide unless indicated otherwise. Weak bands are designated as (w), very strong ones as (v.s.). The analysis is by Dr. E. W. D. Huffman, Wheatridge, Colorado.

(9) H. Hirschmann and F. B. Hirschmann, *J. Biol. Chem.*, **184**, 259 (1950).

(10) A. Butenandt and W. Grosse, *Ber.*, **70**, 1446 (1937).

(11) H. Hirschmann, *Ciba Foundation Colloquia*, in press.

(12) D. H. R. Barton and J. D. Cox, *J. Chem. Soc.*, 783 (1948).

(13) H. Hirschmann, F. B. Hirschmann and M. A. Daus, *J. Biol. Chem.*, **178**, 751 (1949).

(14) O. Mancera, G. Rosenkranz and C. Djerassi, *J. Org. Chem.*, **16**, 192 (1951).

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β-Fattyalkylaminopropionaldehydes[1]

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It has been found that aliphatic amines having long chain (twelve or more carbon atoms) alkyl groups undergo the Mannich reaction[2] with formaldehyde and other lower aldehydes which contain α-hydrogen atoms in much the same manner as do the lower alkylamines. The products are obtained in good yields (81–92%) in every case except those involving primary fatty amines and acetaldehyde; in such cases mixtures are obtained which are difficult if not almost impossible to separate.

The aldehyde function of the β-fattyalkylaminopropionaldehydes is singularly unreactive for an aldehydo group. It is noteworthy that all attempts to prepare the usual aldehyde derivatives (2,4-dinitrophenylhydrazone, semicarbazone and oxime) were unsuccessful, although positive Tollens tests[3] were obtained. However, the elemental analyses, the mode of formation, and the infrared spectrum of one of the compounds (α,α-dimethyl-β-didodecylaminopropionaldehyde; bands at 880, 1100, 1310, 1730 and 2700 cm.$^{-1}$) constitute strong evidence in favor of the β-alkylaminopropionaldehyde structure.

Experimental

α,α-Dimethyl-β-didodecylaminopropionaldehyde.—Didodecylamine (71 g.) was dissolved in 95% ethanol (100 ml.)

(1) Paper No. 148, Journal Series, General Mills Research Laboratories.

(2) C. Mannich, U. S. Patent 1,824,676; Blicke, in "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 303.

(3) S. M. McElvain, "The Characterization of Organic Compounds," The Macmillan Co., New York, N. Y., 1945, p. 133.

and formalin (16.2 g.) was added. The resulting solution was stirred for a few minutes and isobutyraldehyde (14.4 g.) was added and the resulting reaction mixture was refluxed for a period of one hour. After cooling the reaction mixture separated into two distinct phases. The lower (ethanol) phase was removed, leaving a slightly cloudy, colorless liquid (93 g.). The volatile impurities were removed by evacuation at 0.2 mm. for three hours at 40°. A small amount of finely divided solid material was removed by filtration, yielding 81 g. (92%) of a clear, colorless liquid, $n^{30}D$ 1.4544, neutral equivalent, 422.

An analytical sample was prepared by adding 0.108 g. of oxalic acid (in 50 ml. of ether) to 5 g. of the above material in 30 ml. of ether. The ether was removed by evaporation, and the residue was extracted with Skellysolve B in which the Mannich base was soluble but didodecylammonium oxalate was insoluble. Filtration and removal of the solvent left 4.8 g. of a clear, colorless liquid, $n^{30}D$ 1.4547.

Anal. Calcd. for $C_{29}H_{59}NO$: C, 79.56; H, 13.58; N, 3.20; neut. equiv., 438. Found: C, 80.01; H, 13.38; N, 3.62; neut. equiv., 428.

α,α-Dimethyl-β-dodecylaminopropionaldehyde.—Dodecylamine (74 g.) was dissolved in 95% ethanol (100 ml.). The resulting solution was warmed to 50° and formalin (32.4 g.) was added over a period of 15 minutes. Isobutyraldehyde (28.8 g., 0.40 mole) was then added, and the solution was refluxed for one hour, and finally allowed to cool to 25°. The lower phase, 102 g., was removed and combined with an additional 5 g. obtained by adding water to the ethanol layers. The product was evacuated at 0.35 mm. for 4 hours at 40° leaving a clear, colorless oil, wt. 101 g. (88%), $n^{30}D$ 1.4568.

Anal. Calcd. for $C_{17}H_{35}NO$: N, 5.20; neut. equiv., 270. Found: N, 5.18; neut. equiv., 273.

A portion (20 g.) of this material was dissolved in 150 ml. of dioxane, 0.20 g. of Adams catalyst was added, and the mixture was placed in a low pressure hydrogenation shaker at 45 lb. p.s.i. and 30°. No pressure drop occurred during 2.5 hours. The mixture was heated to 80°, but no pressure drop occurred during 2 hours. No further attempt was made to reduce the compound to the amino alcohol.

β-Didodecylaminopropionaldehyde.—This compound was prepared from didodecylamine, formalin and acetaldehyde by a procedure similar to those described above; yield 81%, $n^{30}D$ 1.4661.

Anal. Calcd. for $C_{27}H_{55}NO$: N, 3.42; neut. equiv., 410. Found: N, 3.32; neut. equiv., 416.

α-Methyl β-Octadecylaminopropionaldehyde.—This compound was prepared from octadecylamine, formaldehyde and propionaldehyde by a procedure similar to those described above. The product crystallized from the reaction mixture; m.p. 32–33°, yield 88%.

Anal. Calcd. for $C_{22}H_{45}NO$: N, 4.16; neut. equiv., 340. Found: N, 4.46; neut. equiv., 342.

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The Permanganate Oxidation of Uracil and 5-Nitrouracil

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The reaction of uracil with potassium permanganate in slightly acidic solution to yield carbon dioxide and oxaluric acid has been of considerable use in the degradation of the pyrimidine ring.[1,2] Edmonds, Delluva and Wilson have presented good evidence, although somewhat indirect in nature, suggesting that neither the carbon dioxide nor the oxaluric acid represent specific carbon atoms of the uracil. In this work synthetic orotic acid-4-C^{14} was supplied to a yeast and after a period of metabolic activity radioactive uracil was isolated.[3] The logical assumption was made that the conversion of the orotic acid to uracil by the yeast involved only the loss of the carboxyl group, resulting in uracil labeled only in the 4-position. Reaction of the uracil with permanganate, however, led to the finding that radioactivity was present in both the carbon dioxide and oxaluric acid fractions, indicating the lack of specificity of the oxidation.

Behrend and Offe[4] have described experiments, however, which have been interpreted as indicating that the course of the reaction varies with the nature and position of the substituent groups, and that 5-nitrouracil reacts in such fashion that the carbon atoms of the oxalic acid portion of the oxaluric acid fragment are derived from carbons 4 and 5 of the pyrimidine.

Lagerkvist[5] has applied these conclusions to the interpretation of the data resulting from experiments on the biosynthesis from radioactive bicarbonate of the nucleic acid pyrimidines of the rat. In this work the isolated uracil was converted to 5-nitrouracil prior to permanganate oxidation. It was concluded from the observed radioactivity of the reaction products and the assumption that carbons 4 and 5 of the nitrouracil gave rise to the oxaluric acid that bicarbonate was a direct precursor of carbon 6 of nucleic acid pyrimidines.

In view of the current interest in the biosynthesis of the nucleic acid components and the potential importance of Lagerkvist's results, it was felt that the course of the reaction of 5-nitrouracil with permanganate should be re-examined. It was deemed desirable at the same time to attempt a direct test of the conclusions of Edmonds, *et al.*,[2] concerning the oxidation of uracil.

Accordingly, both uracil-4-C^{14} and 5-nitrouracil-4-C^{14} were synthesized and subjected to permanganate oxidation. The distribution of radioactivity in the carbon dioxide and oxaluric acid fractions was then determined. The results, presented in Table I for typical experiments, were very similar for both pyrimidines and were in excellent agreement with those of Edmonds, *et al.*,[2] for uracil. High percentages of the isotope were found in both fractions, indicating that ring cleavage had occurred rather indiscriminately between carbons 4 and 5 and between carbons 5 and 6 of the pyrimidine ring.

TABLE I

PERMANGANATE OXIDATION OF URACIL-4-C^{14} AND 5-NITROURACIL-4-C^{14}

Compound	Amt. used, mg.	Amt. recovered (as $BaCO_3$), mg.	Total activity, c./min.
Uracil-4-C^{14}	75		24.7×10^5
Carbon dioxide		115	9.1×10^5
Oxalic acid		160	10.6×10^5
5-Nitrouracil-4-C^{14}	47.5		21.6×10^4
Carbon dioxide		53	7.1×10^4
Oxalic acid		72	8.2×10^4

(1) M. R. Heinrich and D. W. Wilson, *J. Biol. Chem.*, **186**, 447 (1950).

(2) M. Edmonds, A. M. Delluva and D. W. Wilson, *ibid.*, **197**, 251 (1952).

(3) The numbering of the pyrimidine ring throughout this article is in conformance with the current usage of *Chemical Abstracts*.

(4) R. Behrend and G. Offe, *Ann.*, **353**, 267 (1907).

(5) U. Lagerkvist, *Acta Chem. Scand.*, **4**, 1151 (1950).