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).

It must be concluded that the oxidation with permanganate of 5-nitrouracil, as well as of uracil itself, under the conditions used does not yield fractions representing specific carbon atoms of the ring system. The conclusions of Lagerkvist,[5] therefore, concerning the role of bicarbonate as a precursor of carbon 6 of uracil must be viewed with considerable doubt.

Experimental

Uracil-4-C^{14}.—The method of Davidson and Baudisch[6] was used for the synthesis of uracil from urea and a sample of malic acid-4-C^{14} prepared in this Laboratory by methods recently described.[7] The identity and purity of the twice-recrystallized uracil-4-C^{14} were established by the determination of the ultraviolet absorption spectrum in 0.01 *N* hydrochloric acid. Both the ϵ_{max} and the ratio of optical densities at 260 and 280 mμ agreed to within 1% with published data.[8]

5-Nitrouracil-4-C^{14}.—The isotopic nitrouracil was prepared by the method of Johnson and Matsuo[9] from a portion of the uracil-4-C^{14} diluted somewhat with non-radioactive uracil. The increase in weight during this process was 94% of that required by theory. The material was recrystallized once from water.

Oxidation of Uracil-4-C^{14}.—The procedures described by Heinrich and Wilson[1] for the cleavage of the pyrimidine ring, collection of the carbon dioxide, hydrolysis of the oxaluric acid, separation of the calcium oxalate and its subsequent oxidation to carbon dioxide were followed closely, except that the *p*H was maintained between 5 and 7 with the aid of a *p*H meter.

Oxidation of 5-Nitrouracil.—The method of Behrend and Offe[4] was followed for the oxidation step, followed by procedures similar to those mentioned above for uracil.

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(10) The work described in this paper was sponsored by the Atomic Energy Commission.

A Convenient Preparation of Ethyl 2-Pyridylacetate

BY NEWTON N. GOLDBERG, BRUNO M. PERFETTI AND ROBERT LEVINE

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The following three methods are reported in the literature for the preparation of ethyl 2-pyridylacetate (I): (1) the alcoholysis of 2-pyridylacetanilide, which was prepared by the Beckmann rearrangement of 2-phenacylpyridine oxime,[1,2] (2) in 25% yield by the reaction of the potassium derivative of 2-picoline (prepared from the tar base and potassium amide) with diethyl carbonate[3] and (3) in 35–40% yield by the esterification of the lithium salt of 2-pyridylacetic acid, which was prepared by the carbonation of 2-lithiopyridine, which was in turn prepared from phenyllithium and 2-picoline.[4] These three methods have the common disadvantage that they are lengthy processes.

We have now found that by modifying the method developed in this Laboratory for the acylation of the lithium derivatives of methylated tar bases,[5,6] I may be prepared in 44.5% yield by the addition of a dilute ethereal solution of 2-picolyl lithium to a dilute ethereal solution of diethyl carbonate over a five-hour period. In addition to I, a small amount of di-2-picolyl ketone was isolated as its dipicrate.

Procedure.—2-Picolyllithium (0.4 mole) in 800 ml. of absolute ether was prepared as described previously[5] by the interaction of 0.4 mole of phenyllithium (prepared from 0.8 mole of lithium ribbon[7] and 0.4 mole (62.8 g.) of bromobenzene) and 0.4 mole (37.2 g.) of 2-picoline and was added over a five-hour period to a rapidly stirred cold (ice–salt-bath) solution of diethyl carbonate (0.2 mole, 23.6 g.) in 700 ml. of anhydrous ether. The ether was not allowed to reflux during the addition of the 2-picolyllithium. After the addition of the 2-picolyllithium was complete, the cooling bath was removed. The reaction mixture was heated to reflux, poured onto 200 g. of ice and extracted with several 200-ml. portions of ether. The combined ethereal phases were dried and concentrated and the residue fractionated to give 14.7 g. (44.5%) of ethyl 2-pyridylacetate, b.p. 110–113° (6 mm.); picrate, m.p. 138.8–139.2°.[5] The tarry residue was extracted for 18 hours with petroleum ether, b.p. 60–70°, in a Soxhlet extractor to give a small amount (< 0.1 g.) of a semi-solid material, which contained di-2-picolyl ketone, as indicated by the analysis of its dipicrate, m.p. 190–191° (from 95% ethanol) (undepressed by the dipicrate of the ketone obtained by the carbonation of 2-picolyllithium).

Anal. Calcd. for $C_{25}H_{18}O_{15}N_8$: N, 16.72. Found: N, 16.51.

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(7) The lithium ribbon was generously supplied by the Metalloy Corporation.

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Some Brominated Dibenzothiophene Derivatives

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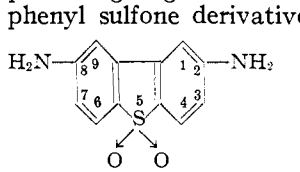
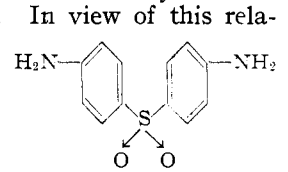
Dibenzothiophene derivatives, especially the substituted 5-dioxides, are closely related to substituted diphenyl sulfones; several compounds possessing high antituberculous activity are diphenyl sulfone derivatives. In view of this relationship and the demonstrated activity of 2-halo-7-aminodibenzofurans[1] the preparation of 2-bromo-



2,8-Diaminodibenzothiophene-5-dioxide



p,p'-Diaminodiphenyl sulfone

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