Biological testing of these compounds will be carried out by Drs. H. P. Morris and Helen Dyer at the National Cancer Institute. The results will be published elsewhere.

EXPERIMENTAL

Preparation of 100% nitric acid. (a) Isotopic nitric acid,[7] (6.79 g.; 0.108 mole as 52.72 g. of a 12.88% solution containing 62.8 atom % nitrogen-15) was carefully neutralized, with cooling, by addition of 4.32 g. (0.108 mole) of sodium hydroxide dissolved in the minimum amount of water. The water was removed by distillation and the dry salt was treated with concentrated sulfuric acid (18 ml., 0.32 mole). Distillation at atmospheric pressure gave 5.6 g. (0.089 mole) of 100% nitric acid-N^{15} b.p. 80–83° (82% recovery).

(b) Potassium nitrate (14.2 g.; 0.07 mole) containing 97.0 atom % nitrogen-15[7] and 31.1 ml. (0.56 mole) of concentrated sulfuric acid gave, upon distillation, 7.1 g. of 100% nitric acid-N^{15} b.p. 78–82° (81% recovery).

4'-Fluoro-4-nitrobiphenyl-N^{15}. A solution of 100% nitric acid-N^{15} (5.6 g.; 0.09 mole containing 62.8 atom % nitrogen-15) in 5.6 g. of glacial acetic acid was added dropwise with stirring to molten 4-fluorobiphenyl (18.4 g.; 0.107 mole, 20% excess), keeping the temperature between 75–82°. Acetic anhydride (12 ml., 0.13 mole) was then added slowly to remove water of reaction. The mixture was kept at 80° for 4 hr., then poured into ice water. After standing overnight the solid was removed by filtration, washed several times with water and then three times with 100-ml. portions of hexane. Crude yield of 4'-fluoro-4-nitrobiphenyl-N^{15} was 9.8 g. (50% based on the nitric acid used). Recrystallization from 175 ml. of ethanol gave 5.5 g. (28%) m.p. 125–126° (lit.,[8] m.p. 123°).

4'-Fluoro-4-acetylaminobiphenyl-N^{15}. 4'-Fluoro-4-nitrobiphenyl-N^{15} (5.5 g.; 0.025 mole) in 150 ml. of warm ethanol was hydrogenated at low pressure using 0.05 g. Adams' platinum oxide catalyst. The yellow solution was filtered free of catalyst into 20 ml. of concentrated hydrochloric acid. The ethanol was removed by distillation, the residue was taken up in hot water containing a little hydrochloric acid, and the solution filtered through a thin mat of charcoal. Potassium acetate was added to the solution just to turbidity, then acetic anhydride (25 ml.) was added, followed by potassium acetate to *p*H 5–6. Stirring was continued for 2 hr. and after standing overnight the 4'-fluoro-4-acetylaminobiphenyl-N^{15} which had precipitated amounted to 2.65 g. (46.5%) m.p. 206° (lit.[9], m.p. 205–206°).

4-Nitrobiphenyl-N^{15}. To molten biphenyl (15.9 g.; 0.103 mole) at 75° was added dropwise with stirring a solution of 5.4 g. (0.086 mole) of 100% nitric acid containing 97.0 atom % nitrogen-15 in 5.4 g. of glacial acetic acid, keeping the temperature below 80°. When the addition had been completed acetic anhydride (12 ml., 0.13 mole) was slowly added to remove water of reaction, then the mixture was kept at 75–80° for 4 hr. After pouring into ice water and leaving overnight, the water was decanted from the semisolid yellow residue, the residue was triturated three times with 50-ml. portions of hexane to remove unchanged biphenyl and 2-nitrobiphenyl and recrystallized from ethanol, giving 6.0 g. of 4-nitrobiphenyl-N^{15} (35.3% based on the nitric acid consumed), m.p. 113–114° (lit.,[10] m.p. 114°).

4-Aminobiphenyl-N^{15}. A mixture of 4-nitrobiphenyl-N^{15} (6.0 g., 0.03 mole), 175 ml. of ethanol, 2.1 g. of calcium chloride dissolved in 41 ml. of water, 63.6 g. of zinc dust, and 2.0 g. of Norit were refluxed for 3 hr., 1.0 ml. of 85% hydrazine hydrate was added and the mixture filtered to remove the zinc, the residue being washed twice with 25-ml. portions of hot ethanol. The alcoholic filtrates were poured into 2 l. of water and allowed to stand overnight. The white precipitate of 4-aminobiphenyl-N^{15} was filtered off and washed well with water, then air-dried. Yield was 4.6 g. (90%) m.p. 53–54° (lit.,[11] m.p. 50–52°).

4-Acetylaminobiphenyl-N^{15}. 4-Aminobiphenyl-N^{15} (4.6 g.; 0.027 mole) was dissolved with heating in 60 ml. of benzene, decanted from a little insoluble material and treated with 5 ml. of acetic anhydride. A precipitate began to form immediately. After refluxing for 15 min. the clear solution was allowed to cool slowly to room temperature. The white crystals which formed were filtered and washed several times with water, giving 5.2 g. (91%) of 4-acetylaminobiphenyl-N^{15} m.p. 171° (lit.[12], m.p. 171–172°) and containing 97.0 atom % nitrogen-15.

2-Nitro-7-acetoxyfluorene-N^{15}. The literature procedure[6] was modified as follows: A mixture of 5.6 g. (0.025 mole) of 2-acetoxyfluorene and 22.5 g. (0.375 mole) of glacial acetic acid was heated to 80° to effect solution, then allowed to cool to 50°. A solution prepared by adding 1.6 g. (0.025 mole) of 100% nitric acid containing 97.0 atom % nitrogen-15 to 12.8 g. (0.125 mole) acetic anhydride in an ice bath (exothermic reaction) was then added to the 2-acetoxyfluorene solution and an exothermic reaction set in. When the temperature reached 75° the mixture was cooled in an ice bath. After the initial exothermic reaction had subsided the mixture was kept at 70–75° for 5 min., then allowed to stand overnight. The yellow solid was filtered, washed with water until the filtrate was no longer acidic and dried, giving 5.4 g. (80.6%) of 2-nitro-7-acetoxyfluorene-N^{15} m.p. 192–193° (lit.[6], 191–192°).

N-(7-Hydroxy-2-fluorenyl)acetamide-N^{15}. To a boiling solution of 2-nitro-7-acetoxyfluorene-N^{15} (5.4 g.; 0.02 mole) in 1 l. of ethanol was added slowly over a period of 1 hr. a solution of 41.7 g. (0.22 mole) of stannous chloride dissolved in 350 ml. of concentrated hydrochloric acid. The solution was concentrated to one-third its volume, then brought up to one-half its original volume with concentrated hydrochloric acid and allowed to stand overnight. The precipitate was filtered and dissolved in 200 ml. of hot water containing a few drops of stannous chloride–hydrochloric acid solution. The solution was filtered through a mat of charcoal and then brought to *p*H 5–6 with potassium acetate. After addition of 40 ml. of acetic anhydride the mixture was allowed to stand overnight. The precipitate of *N*-(7-hydroxy-2-fluorenyl)acetamide-N^{15} containing 97.0 atom % nitrogen-15 amounted to 2.8 g. (48%) m.p. 229–231° (lit.,[13] m.p. 230–232°).

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A Preparation of 10-Hydroxydecanoic Acid

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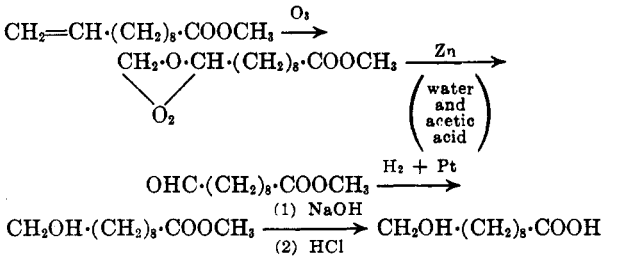
The synthesis of 10-hydroxydecanoic acid has been accomplished by three methods.[2–4] The one

reported by Lycan and Adams is the most direct but requires four steps:



The method reported herein eliminates two of these steps, conversion of methyl undecenoate ozonide to the aldehydo ester, and catalytic hydrogenation of the hydroxy ester. Instead, the ozonide is reduced directly to methyl 10-hydroxydecanoate with sodium borohydride. 10-Hydroxydecanoic acid is then obtained in an overall yield of nearly sixty per cent by saponification of the ester. Although reduction of ozonides has been accomplished with lithium aluminum hydride,[5] sodium borohydride was employed to avoid concomitant reduction of the ester moiety.[6]

EXPERIMENTAL

10-Hydroxydecanoic acid. A solution of 20.0 g. of methyl 10-undecenoate in 60 ml. of ethyl acetate, maintained at a temperature of −50 to −60°, was treated approximately for 1¼ hr. with a slow stream of ozone in oxygen until ozone was detected in the exit gases. The solution of ozonide[7] was then added rapidly (within 2 min.) to a vigorously stirred ice cold mixture of 6.0 g. of sodium borohydride and 120 g. of tetraethylene glycol dimethyl ether. The mixture was stirred for 2 hr. at ice-bath temperature and an additional hour at room temperature after which it was poured into 1 l. of water containing 30 ml. of concentrated hydrochloric acid. The hydrolysis mixture was saturated with salt; the oil which formed was separated and the aqueous fraction extracted with three 100-ml. portions of diethyl ether. The combined oil and ether extracts was washed successively with water, aqueous sodium carbonate, and water and dried over anhydrous magnesium sulfate. After removal of ether by evaporation under reduced pressure, the residual oil was heated at reflux temperature for 30 min. with 50 ml. of 20% aqueous sodium hydroxide. The saponification mixture was then steam distilled until turbidity and odor were no longer detected in the distillate, after which it was cooled in an ice bath and acidified with 1:1 aqueous hydrochloric acid. The resulting precipitate was filtered, washed with water until free from mineral acid, and dried. It was dissolved in hot ethylene dichloride, filtered to remove a small amount of insoluble material, and allowed to recrystallize. In this manner, 12.0 g. (59%) of a colorless crystalline product, m.p. 75–76°, was obtained.

Anal.[8] Neut. equiv. Calcd.: 188.2. Found: 189.2. Hydroxyl value. Calcd.: 9.02. Found: 9.15.

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(8) The authors are indebted to Mr. L. D. Metcalfe for these analyses.

Conformational Analysis of the Prins Reaction

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It has been shown that the Prins reaction gives stereospecifically *trans*-2-hydroxymethylcyclohexanol when cyclohexene is employed as the olefin.[2,3] In an effort to elucidate the initial conformation of the products of this reaction we have employed the rigid *trans*-Δ^2-octalin[4] system (I).

It is generally agreed[3,5,6] that the first step in a Prins reaction involves the addition of a proton to a neutral formaldehyde molecule. The stereospecific *trans* addition of the hydroxy and the hydroxymethylene groups to the double bond of a cyclic olefin argues against a free carbonium ion but can be rationalized on the basis of a solvated cyclic intermediate. By comparison with other addition reactions involving cyclic intermediates, *i.e.* bromination, the product would be predicted to exhibit a diaxial conformation[7] of the hydroxy and hydroxymethylene groups. Our results confirm the above postulation.

Under the conditions of the Prins reaction, *trans*-Δ^2-octalin, I, gave *trans*-2-hydroxymethyl-3-hydroxy-*trans*-decalin, II. The conformation of this compound was proved in the following manner: The *mono*-tosylate, III, was prepared and subsequently displaced by cyanide ion. The latter re-

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