poured into ice-water to decompose the remaining phosphorus oxychloride. The water solution was extracted three times with ether; after the ether was dried over magnesium sulfate and evaporated, leaving crude 2-chloro-3-methylquinoxaline, the chloro compound was recrystallized from ethanol–water (1:1) to give 1.1 g. (54% yield) of light pink platelets of 2-chloro-3-methylquinoxaline melting at 90–92°.

Anal. Calcd. for $C_9H_7N_2Cl$: N, 15.7. Found: N, 15.7, 15.5.

***dl*-2-Methyl-1,2,3,4-tetrahydroquinoxaline.**—A solution of 2.0 g. of 2-chloro-3-methylquinoxaline and 0.5 g. of anhydrous sodium acetate in 25 ml. of glacial acetic acid was reduced over 0.2 g. of 5% palladium chloride–charcoal catalyst[5] at 60° and 2 atm. of hydrogen for four hours. After the catalyst was removed, the solution was evaporated to 10 ml. on a steam-bath. Fifty per cent. sodium hydroxide solution was added in excess, and the solid mass was triturated with ether three times; the ether solution was then dried over solid sodium hydroxide, evaporated, and the residue was recrystallized twice from petroleum ether (b.p. 60–90°) to give 1.1 g. (65% yield) of *dl*-2-methyl-1,2,3,4-tetrahydroquinoxaline melting at 70–71°. Ris[4] obtained a melting point of 72° for *dl*-2-methyl-1,2,3,4-tetrahydroquinoxaline prepared by a different method. *dl*-2-Methyl-1,2,3,4-tetrahydroquinoxaline melting at 71–72° was also prepared in this Laboratory by reduction of 2-methylquinoxaline[6] over palladium–charcoal catalyst. There was no depression of the melting point when the *dl*-2-methyl-1,2,3,4-tetrahydroquinoxalines prepared by the two different methods were mixed.

N-(2-Nitro-5-methylphenyl)-*dl*-α-alanine.—Seven and six-tenths grams of α-bromopropionic acid and 15 g. of 3-amino-4-nitrotoluene[7] were heated on a steam-bath for 96 hours in a flask fitted with a cold finger condenser. The reaction mixture was cooled and extracted three times with 40-ml. portions of 15% ammonium hydroxide solution. The red, basic solution was heated with 1.0 g. of charcoal and filtered to clarify the solution. This basic solution was brought to *p*H 4 with 10% hydrochloric acid, giving an orange precipitate which was filtered off. The above process was repeated twice again to give 4.4 g. (39% yield) of N-(2-nitro-5-methylphenyl)-*dl*-α-alanine melting at 127–128°.

Anal. Calcd. for $C_{10}H_{12}O_4N_2$: N, 12.5. Found: N, 12.4, 12.3.

2-Hydroxy-3,6-dimethylquinoxaline.—A solution of 2.5 g. of N-(2-nitro-5-methylphenyl)-*dl*-α-alanine in 40 ml. of ethanol was reduced over a 5% palladium chloride–charcoal catalyst at 30° and 2 atm. of hydrogen for four hours. After the catalyst was removed, the ethanol was evaporated from a steam-bath. The residue was taken up in 25 ml. of 8% hydrogen peroxide and 25 ml. of 8% sodium hydroxide solutions and heated on a steam-bath for two hours. After the basic solution was brought to *p*H 4 with acetic acid, the precipitate was filtered off and recrystallized from ethanol–water (4:1) to give 1.6 g. (82% yield) of 2-hydroxy-3,6-dimethylquinoxaline melting at 248–249°. The product prepared by Marks and Schultz[3] melted at 248–249° after recrystallization; 254° after sublimation. A mixed melting point of these compounds gave no depression.

2-Chloro-3,6-dimethylquinoxaline.—2-Hydroxy-3,6-dimethylquinoxaline was transformed into 2-chloro-3,6-dimethylquinoxaline by the method described above under 2-chloro-3-methylquinoxaline in 66% yield, m.p. 76–77°.

Anal. Calcd. for $C_{10}H_9N_2Cl$: N, 14.5. Found: N, 14.4, 14.5.

***dl*-2,7-Dimethyl-1,2,3,4-tetrahydroquinoxaline.**—This was prepared in 72% yield by reduction of 2-chloro-3,6-dimethylquinoxaline, m.p. 118–118.5°.

Anal. Calcd. for $C_{10}H_{14}N_2$: N, 17.3. Found: N, 17.0, 17.1.

2-Chloro-3,7-dimethylquinoxaline.—2-Hydroxy-3,7-dimethylquinoxaline[3] gave 2-chloro-3,7-dimethylquinoxaline in 72% yield, m.p. 86–87°.

Anal. Calcd. for $C_{10}H_9N_2Cl$: N, 14.5. Found: N, 14.4, 14.3.

***dl*-2,6-Dimethyl-1,2,3,4-tetrahydroquinoxaline.**—This was prepared by reduction of 2-chloro-3,7-dimethylquinoxaline in 60% yield, m.p. 115–115.5°.

Anal. Calcd. for $C_{10}H_{14}N_2$: N, 17.3. Found: N, 17.1, 17.1.

A 1:1 mixture of *dl*-2,6- and 2,7-dimethyl-1,2,3,4-tetrahydroquinoxaline was found to melt at 88–89°.

Hinsberg's Mixture of 2,6- and 2,7-Dimethylquinoxaline.—3,4-Diaminotoluene was condensed with chloroacetone according to Hinsberg's procedure,[2] the reaction product fraction boiling between 265–285° finally being collected. Hinsberg collected the fraction boiling 265–270°. The Hinsberg mixture was reduced over 5% palladium chloride–charcoal at 60° and 2 atm. of hydrogen for four hours. The reduction product was worked up in a manner similar to those procedures cited above, giving a 48% yield of a mixture of *dl*-2,6- and -2,7-dimethyl-1,2,3,4-tetrahydroquinoxaline which melted at 88–89°. No change of the melting point was observed when this was mixed with a synthetic 1:1 mixture of the pure isomers. Repeated recrystallizations from petroleum ether (b.p. 60–90°) did not change the melting point.

Anal. Calcd. for $C_{10}H_{14}N_2$: N, 17.3. Found: N, 17.2, 17.2.

Spectrophotometric Data.—The ultraviolet absorption spectra were obtained on a Beckman model DU quartz spectrophotometer. All curves were run on analytical samples at concentrations of 10 mg./l. of solvent.

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Synthesis of Fumaric Acid-2-C^{14} and Maleic Anhydride-2-C^{14} [1]

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In the course of our work on organic and biochemical reaction mechanisms, it was found necessary to develop a useful method for synthesizing fumaric acid-2-C^{14} and maleic anhydride-2-C^{14} on a small scale.

The synthesis of methine-labeled fumaric acid is a six-step process. When the reaction is carried out on a 10-millimole scale the yield of fumaric acid-2-C^{14} is 76% based on $C^{14}O_2$, whereas on a 2-millimole scale the yield of acid is 63%. Briefly outlined the procedure is: (a) conversion of $C^{14}O_2$ to methylene-labeled succinic acid (four steps) in an 89% yield by modification[2] of the method recently described by Kushner and Weinhouse[3]; (b) dibromination of succinic acid-2-C^{14}; and (c) reaction of *meso*-dibromosuccinic acid-2-C^{14} with an acetone solution of sodium iodide to furnish fumaric acid-2-C^{14}.

Maleic anhydride-2-C^{14} is readily obtained from fumaric acid-2-C^{14} and phosphorus pentoxide in 96% yield under carefully controlled conditions. In a forthcoming paper the preparation of ring-labeled benzoic acid from maleic anhydride-2-C^{14} and butadiene will be described.

Fumaric acid-1-C^{14} and maleic anhydride-1-C^{14} can be made from carboxyl-labeled succinic acid[3] by use of the procedure described above.

The *meso*-dibromosuccinic acid-2-C^{14} should also be a useful intermediate in the synthesis of such

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compounds as acetylene dicarboxylic acid-2-C^{14} and *meso*-tartaric acid-2-C^{14}.

Experimental[4]

***meso*-Dibromosuccinic Acid-2-C^{14}.**—By modification of the excellent method of Hughes and Watson,[5] the yield of the dibromosuccinic acid was increased to 90–96%. Bromination of succinic acid-2-C^{14} was carried out on a 2.5-millimole scale and after the reaction was complete the contents of four tubes were combined. When the bromination was carried out on a 10-millimole scale in a single tube, unsafe pressures developed during the reaction. Each Pyrex combustion tube (15 × 20 × 250 mm.) was charged with 295 mg. (2.5 millimoles) of succinic acid-2-C^{14}, 0.24 cc. of water, 0.06 cc. of 48% hydrobromic acid and 0.28 cc. of bromine. Then the tubes were sealed, placed in a steel jacket, heated at 95–100° for 96 hours, cooled to room temperature, and opened. After placing the tubes in a vacuum desiccator containing calcium hydride, the system was evacuated (1 mm.) for two hours.

Fumaric Acid-2-C^{14}.—The *meso*-dibromosuccinic acid-2-C^{14} in each tube was removed by adding three 4-cc. portions of acetone, and the extracts from the four tubes combined. Next the acetone solution containing the bromoacid was heated under reflux with a solution of 4.5 g. (30 millimoles) of sodium iodide in 20 cc. of acetone for 75 minutes. After cooling the mixture to room temperature the liberated iodine was titrated with 1 *N* sodium thiosulfate. Five cc. of glacial acetic acid was added and the solution continuously extracted with ether for 24 hours. This solution was evaporated to dryness on a boiling water-bath by sweeping a stream of air over the surface of the liquid. The residue was dissolved in boiling water and the water extracts acidified with 5 cc. of glacial acetic acid before continuously extracting with ether for 24 hours. Following removal of the solvent, the product was dried *in vacuo* over calcium hydride. Then the crude product was dissolved in 50 cc. of boiling water, 50 mg. of Darco S-51 added, and after 20 minutes the solution heated to boiling, and the charcoal removed by suction filtration. After concentrating the solution to 9 cc., the tube was allowed to stand at 0° for 8 hours, and then the crystals of fumaric acid were collected by filtration through a sintered glass funnel. This material was dried *in vacuo* over calcium hydride and weighed 935 mg. The mother liquor was concentrated to 2 cc. and the second crop of fumaric acid-2-C^{14} collected which weighed 60 mg. The over-all yield was 86% based on succinic acid-2-C^{14} and the material melted at 268°.[4] However, the melting point of fumaric acid-2-C^{14} determined in a sealed tube and in the conventional way was 287°. A semi-micro quantitative hydrogenation was carried out with an 83-mg. sample (0.715 millimole) of fumaric acid-2-C^{14} and it was found that 0.72 millimole of hydrogen was consumed. The dimethyl fumarate derivative was prepared and melted at 104°.[6] Another check on the purity of the fumaric acid-2-C^{14} involved the preparation of a paper chromatogram using a 70% phenol–water–formic acid system.[7] By use of an alkaline brom cresol green spray and a radioautograph only fumaric acid-2-C^{14}, $R_f = 0.62$, was found.

Maleic Anhydride-2-C^{14}.[8]—A 50-ml. round-bottom flask equipped with a 24/40 male joint was attached to an apparatus containing a 24/40 female joint, a small U-type trap, a small collection trap, and finally a high-vacuum stopcock. A layer of 4 g. of phosphorus pentoxide was placed in the flask, then 804 mg. (6.93 millimoles) of fumaric acid-2-C^{14} added, and next 4 g. of phosphorus pentoxide were placed over the fumaric acid. The system was evacuated to 1 mm. and then isolated. The entire reaction flask was immersed in an oil-bath and the bath temperature raised to 155–160° and held there for three hours. The liberated maleic anhydride-2-C^{14} was collected by cooling the small U-type trap with liquid nitrogen. After the collection was complete the reaction vessel was sealed off from the traps. The U-type trap containing the product was allowed to warm to room temperature and then immersed in an oil-bath at 100° and the maleic anhydride vacuum-distilled into the small collection trap which was cooled by liquid nitrogen. Dry air was then admitted to the system and the maleic anhydride collected. A 651-mg. yield of maleic anhydride-2-C^{14} was obtained (96% based on fumaric acid-2-C^{14}), m.p. 53.5–54°. A sample of this material was titrated with alkali and furnished a neutral equivalent of 49.5 (theoretical 49.0). Another sample was converted to *cis*-Δ^4-tetrahydrophthalic anhydride in almost quantitative yield, m.p. 104.5–105.5°.[9] This material was recrystallized until the assay for C^{14} gave a constant specific activity.

Radioactive and Chemical Assays.—The compounds listed in Table I were burned to carbon dioxide and the radioactive gas collected in traps cooled by liquid nitrogen. After the oxidation was complete, the amount of carbon dioxide was determined manometrically (the carbon content of all compounds was within 0.3% of the theoretical values) and then transferred to an evacuated ionization chamber using vacuum-line technique. All radioactivity measurements were made by using an ion-chamber in conjunction with a vibrating reed electrometer.[10]

TABLE I

Compound	Microcuries of C^{14} per millimole of compound
Succinic acid-2-C^{14}	3.33
Fumaric acid-2-C^{14}	3.34
Maleic anhydride-2-C^{14}	3.35
cis-Δ^4-Tetrahydrophthalic anhydride-1-C^{14}	3.34

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[4] All melting points were obtained using polarized light and the Kofler micro melting point technique.

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The Heats of Solution of Erythritol, Mannitol and Dulcitol; Combustion Values for Liquid Polyhydroxy Alcohols

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The heats of solution of crystalline *i*-erythritol, *d*-mannitol and dulcitol in water at 25° constitute thermal data of considerable intrinsic interest. Moreover, the presence of the hydroxyl group in both solute and solvent is conducive to solutions which are almost "perfect." Hence, the heats of solution in these cases should approximate the theoretical heats of fusion of the crystalline substances at the temperature of the solution process.[1]

Thermal data of this sort can then be combined with the heats of combustion and enthalpies of formation of the crystalline substances so as to yield corresponding values at 25° for the hypothetical liquid state. Such a procedure is frequently advantageous, since regularities are more pronounced in any homologous series, or related group, of organic compounds if the comparisons are based upon the liquid state rather than upon the more individualistic crystalline forms.

Experimental

Method and Materials.—The calorimeter and method which Rowe and Parks[2] developed for measuring the heats of solution of various forms of glucose in water were used for the present determinations.

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