and the resulting white, granular, ether-insoluble material was filtered and air-dried to give 4.70 g. (70%) of product melting at 250.5–253°. A crystallization from ethanol gave 4.30 g. (64%) of material melting at 253–255°. Two recrystallizations from the same solvent resulted in a product melting at 255.5–256.5°. The melting point of the benzophenone adduct has been reported by earlier workers to be 253°.[12,13]

2,2′-Dilithiobiphenyl and Diphenyldichlorosilane.—To a rapidly stirred solution of 10 g. (0.032 mole) of 2,2′-dibromobiphenyl in 50 ml. of ether was added slowly 47 ml. of a 1.31 *N* *n*-butyllithium solution. The reaction mixture was stirred at room temperature for 4.5 hours after which time Color Test II[14] was negative. To the refluxing organolithium solution was added, over a 15-minute period, a solution of 8.10 g. (0.032 mole) of diphenyldichlorosilane in 35 ml. of ether. Shortly after the addition was begun, a large amount of salt formation was noted. The refluxing was continued for one hour after which time Color Test I was strongly positive. Subsequently, 90 ml. of sodium-dried benzene was added to the reaction mixture and the ether was distilled until a temperature of 59° was reached. After stirring at this temperature for 0.5 hour, more ether was distilled until a temperature of 63° was attained. Subsequent to refluxing 30 minutes at this temperature, Color Test I began to decrease in intensity and in another 30 minutes it was negative. The reaction mixture was hydrolyzed with water and the two resulting phases were separated. After washing the aqueous layer twice with ether, the combined organic layer was dried over anhydrous sodium sulfate, and the solvents removed; upon cooling, the residue solidified. Most of the crude material was dissolved in refluxing petroleum ether (b.p. 60–70°).[15] The material which did not dissolve after several minutes of refluxing was decanted and dried to give 0.50 g. of material melting over the range 210–215°. From the petroleum ether there crystallized 4.33 g. (49%) of slightly impure 5,5-diphenyldibenzosilole melting at 142–145°. The presence of a second compound was quite evident when the mixture was recrystallized from ethanol since from this solvent there were obtained two distinct crystalline types. Two different crystal types were also obtained from petroleum ether but in this case the difference was not so obvious.

Further purification was achieved by dissolving most of the impure cyclic silicon compound in warm but not refluxing petroleum ether. The petroleum ether solution was decanted from the insoluble solid and allowed to cool. The cyclic silicon compound crystallized first and as soon as the second type of crystals began to appear the solution was filtered to give, after drying, 2.10 g. of product melting at 147–148°. Two subsequent recrystallizations from petroleum ether and ethanol, respectively, gave a material melting at 148–149°.

The material melting over the range 210–215° was crystallized twice from ethanol to give white needles melting at 228–229°. More of this same material was obtained by fractionally crystallizing the residue resulting on removal of the solvent from the filtrates of the cyclic silicon compound. The combined residues were first crystallized from ethanol to give a material melting over the range 145–170°. The material was placed in warm petroleum ether and the insoluble needles were filtered. The needles were recrystallized from ethanol to give additional product melting at 229–230°. By repeating this process several times with the impure cyclic silicon compound there was finally obtained a total yield of 0.5 g. of material melting at 229–230° and an additional 1.1 g. of 5,5-diphenyldibenzosilole. The total yield of pure cyclic silicon compound was 3.1 g. (31%).

Anal. Calcd. for $C_{24}H_{18}Si$: C, 86.19; H, 5.43; Si, 8.39; mol. wt., 334. Found: C, 86.06, 85.91; H, 5.58, 5.77; Si, 8.38; mol. wt., 318, 326, 315 (Rast), 321 (Signer).

In another run employing *n*-heptane rather than benzene as one of the solvents to obtain an elevated temperature, the yield of 5,5-diphenyldibenzosilole was comparable to the yield mentioned above. In this particular run an attempt was made to separate the high melting compound by chromatographing the material on a column of alumina. This procedure did not result in any clean-cut separation of the two compounds.

Anal. of the high-melting, silicon-containing compound. Found: C, 88.68, 88.60; H, 5.53, 5.42; Si, 5.6; mol. wt., 462, 447.

The above analyses together with the molecular weight determinations indicated that the compound might be bis-(2-biphenylyl)-diphenylsilane, a compound which could quite possibly be formed in the reaction. However, the latter compound has been synthesized from 2-biphenylyllithium and diphenyldichlorosilane and has been reported to melt at 137–137.5°.[16] A comparison of the infrared spectra also indicated the compounds to be different. This compound is being investigated further.

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[12] A. E. Tschitschibabin and P. G. Sergejeff, *Ber.*, **59**, 654 (1926).

[13] G. Wittig and M. Leo, *ibid.*, **64**, 2395 (1931).

[14] H. Gilman and J. Swiss, THIS JOURNAL, **62**, 1847 (1940).

[15] Throughout the remaining text the petroleum ether referred to is that which boils over the range 60–70°.

[16] H. Gilman and K. Oita, *J. Org. Chem.*, **20**, 862 (1955).

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Synthesis of Thymine (Methyl-C^{14})[1]

BY ROBERT B. HENDERSON, R. M. FINK AND KAY FINK

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Labeled thymine has been prepared with N^{15} in the 1- and 3-positions[2] and with C^{14} in the 2-position[3] and this note describes the synthesis of thymine (methyl-C^{14}). Because this compound was to be used in biological experiments in which filter paper chromatography was the analytical procedure, thymine with a high specific activity was desired in order to facilitate detection of spots representing only a few micrograms of metabolites. To avoid the expedient of diluting the radioactive starting material with inactive compound, a synthesis[4] was adapted for use on a milligram scale to give acceptable yields of radiothymine (5-methyl-C^{14}-uracil) starting with sodium propionate-3-C^{14}. The propionate, as ethyl propionate, was condensed with diethyl oxalate; the oxalopropionate was hydrogenated to β-methyl malate; and saponification gave β-methylmalic acid, which was condensed with urea to produce thymine. In the case of the small scale runs, all reactions from the ester condensation step onward were carried out in one flask with the only purification of reaction products being the pumping off of volatiles.

Using gram quantities of materials and purifying at some steps an over-all yield of about 30% was obtained—governed by the ester condensation and urea–methylmalic acid reactions, which resulted in 60–70% and 50–55% yields, respectively—but on a milligram scale the net yield was only about 10%.

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[1] This investigation was aided by Cancer Research Funds of the University of California and by research grant No. C-1669 from the National Cancer Institute, National Institutes of Health, U. S. P. H. S.

[2] A. A. Plentl and R. Schoenheimer, *J. Biol. Chem.*, **153**, 203 (1944).

[3] L. L. Bennett, Jr., THIS JOURNAL, **74**, 2432 (1952).

[4] (a) D. Davidson and O. Baudisch, *ibid.*, **48**, 2379 (1926); (b) H. M. Scherp, *ibid.*, **68**, 912 (1946).

At the end of some "cold" runs, the thymine was isolated as crystalline material but the radiothymine, after chromatographic purification, was handled in solution with less loss. Chromatographic behavior and ultraviolet absorption were relied upon for identification and assay. The specific activity of the product was identical, within the limits of error, to that of the propionate as reported by the supplier, ORNL.

Experimental

Ethyl propionate-3-C^{14} was prepared from 26.7 mg. (0.278 mmole) of powdered sodium propionate-3-C^{14} (0.452 μc./μmole) by reaction with 2.0 ml. of triethyl phosphate at 170–185° in an apparatus similar to that described by Melville, *et al.*,[5] and collected in a spiral trap with a sintered glass plate.[6]

Subsequent reactions were carried out in a 50-ml. spherical flask having a stoppered 8-mm. side-arm. The neck of the flask included a 3-mm. bore stopcock and terminated in a ball joint for attachment to the vacuum line.

Sodium Diethyl Methyl-C^{14}-oxosuccinate.—The ethyl propionate was condensed into the reaction flask which contained 0.48 mmole of dry sodium ethoxide, 0.49 mmole of diethyl oxalate and 0.3 ml. of diethyl ether. The flask was removed from the vacuum line, shaken mechanically for two hours, and then heated for a few minutes in a boiling water-bath while vented to the atmosphere through a liquid nitrogen-cooled trap. An orange-red solid, presumably sodium diethyl methyl-C^{14}-oxosuccinate, remained.

Diethyl β-Methyl-C^{14}-malate.—To the above solid in the reaction flask cooled to 0° was added a slurry of 10–20 mg. of Adams platinum oxide catalyst in 0.5 ml. of dil. acetic acid (0.63 meq.) and 1.5 ml. of ethanol. The flask side-arm was sealed off and the flask returned to the vacuum line. While immersed in liquid nitrogen to the level of the stopcock plug the flask was evacuated, flushed with hydrogen and then filled with one atmosphere of hydrogen. The stopcock was closed and secured and the flask placed on a shaker to warm to room temperature and to shake for two hours.[7] In large scale runs the yields were 85–95%.[4b]

Sodium β-Methyl-C^{14}-malate.—The flask was vented to release excess hydrogen, 1.0 ml. of 2.34 N sodium hydroxide was added, and the reaction mixture was shaken two hours at room temperature.[8] Volatile materials were removed at room temperature by pumping the flask slowly down to 50 μ to leave a white solid.

Thymine (Methyl-C^{14}).—Four ml. of 20% fuming sulfuric acid was cooled in an ice-salt-bath and one g. of urea was dissolved in portions so that the temperature remained below 10°. Two ml. of this solution was transferred to the reaction flask which then was heated on a steam-bath with occasional swirling for 2.5 hours. The product was taken up in water. Ultraviolet assay indicated the presence of 4.85 mg. of thymine (0.038 mmole, 14%). The solution was brought to *p*H 4.0 by adding anion exchange resin (Amberlite IRA-400, OH$^-$ form). After removal of resin on a büchner funnel, assay of the filtrate gave 3.12 mg. of thymine. The resin was re-extracted by stirring with water and filtering again. These two filtrates were concentrated to small volumes and chromatographed in butanol-2 saturated with water on filter paper which had previously been chromatographically washed with butanol–water. The thymine-containing areas were cut from the paper and extracted with abs. ethanol. The thymine solutions thus obtained from the two resin filtrates exhibited good absorption curves so the solutions were combined; yield 2.24 mg. (0.018 mmole, 6.4%); radioactivity: 0.46 μc./μmole; yields ranged from 3.3 to 17.0%.

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[5] C. Melville, J. Rachele and E. Keller, *J. Biol. Chem.*, **169**, 419 (1947).

[6] M. Calvin, C. Heidelberger, J. C. Reid, B. M. Tolbert and P. E. Yankwich, "Isotopic Carbon," John Wiley and Sons, Inc., New York, N. Y., 1949, p. 133.

[7] Neither in macro-scale reductions, where the diethyl β-methylmalate was isolated by fractionation, nor in some micro-scale reactions, where aliquots of the reaction product after hydrolysis were chromatographed, was evidence obtained for the presence of diethyl α-methylsuccinate: *cf.* E. C. Jorgensen, J. A. Bassham, M. Calvin and B. M. Tolbert, THIS JOURNAL, **74**, 2418 (1952).

[8] Experiments using pure diethyl β-methylmalate indicated that hydrolysis was 98-100% complete in this time.

Pentaerythritol Derivatives. I. The Preparation of Pentaerythritol Monomethyl Ether[1]

BY C. H. ISSIDORIDES AND A. I. MATAR

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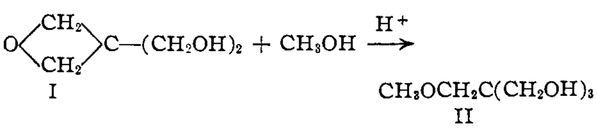
In a previous work on the preparation of pentaerythritol ethers[2] it was found that the trimethylene oxide ring of 3,3-bis-(hydroxymethyl)-oxetane (I) can be opened by the sodium salt of ethylene glycol to give pentaerythritol β-hydroxyethyl ether in satisfactory yield. Recently, Searles and Butler[3] have shown that trimethylene oxide reacts with alcohols in the presence of catalytic amounts of strong acids or bases or in the presence of water to give the corresponding monoalkyl ethers of trimethylene glycol. These reactions indicate that the behavior of 1,3-epoxides toward alcohols is similar to that of 1,2-epoxides.

The present paper describes the preparation of pentaerythritol monomethyl ether (II) from 3,3-bis-(hydroxymethyl)-oxetane (I) and methyl alcohol in the presence of catalytic amounts of sulfuric acid. This method, in contrast to the ones previously described in the literature,[4–6] gives II in good yield (80%).



A small amount of a side-product (probably a mixture of pentaerythritol and a higher polyether) which is also formed during this reaction can be separated easily from the main product by continuous extraction of the latter with dry ether. The monomethyl ether of pentaerythritol obtained by this method was further characterized as the triacetate and the tritrityl ether.

The starting material I in this investigation was obtained by the action of alcoholic potassium hydroxide on pentaerythrityl monobromide (III) according to the method of Govaert and Beyaert.[7] This procedure gives I in good yield, also small amounts of a side-product which we identified as 2-methylene-1,3-propanediol (IV) by its physical constants and by conversion to the corresponding diacetate and dichloride. The formation of IV is probably the result of an elimination reaction op-

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[1] Abstracted in part from the M.S. thesis of Afaf I. Matar, American University of Beirut, June, 1955.

[2] S. Wawzonek and C. H. Issidorides, THIS JOURNAL, **75**, 2373 (1953).

[3] S. Searles and C. F. Butler, *ibid.*, **76**, 56 (1954).

[4] L. Orthner and G. Freyss, *Ann.*, **484**, 131 (1930).

[5] S. Wawzonek and D. A. Rees, THIS JOURNAL, **70**, 2433 (1948).

[6] S. Wawzonek and J. P. Henry, *ibid.*, **75**, 1258 (1953).

[7] F. Govaert and M. Beyaert, *Proc. Acad. Sci. Amsterdam*, **42**, 790 (1939).