is in agreement with that reported by Hackspill and Wolfe. The solubility of BaO in $BaCO_3$ is approximately 4%.

MURRAY HILL, NEW JERSEY RECEIVED MAY 18, 1951

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o-Toloxypropyl Carbamates

BY B. J. LUDWIG AND E. C. PIECH

In view of the marked anticonvulsant activity exhibited by carbamate esters of certain 2,2-disubstituted 1,3-propanediols,[1] it appeared of interest to prepare some carbamate derivatives of the muscle relaxant drug mephenesin (3-*o*-toloxy-1,2-propanediol) and the closely related *o*-toloxypropanols for pharmacological screening.

Employing the procedure described earlier for the carbamylation of substituted propanediols,[2] we have prepared the compounds described in Table I. While this work was in progress there appeared the publication of Yale, *et al.*,[3] describing a monocarbamate ester of mephenesin. These authors ascribed to their compound the primary ester structure on the basis of greater reactivity of the primary hydroxyl group of mephenesin with phosgene. It was of interest that the monocarbamate prepared by us, by ammonolysis of the cyclic carbonate of mephenesin, proved to be identical to that obtained by Yale, *et al.*

The results of the pharmacological studies carried out on these compounds will be published elsewhere.

Experimental[4]

1-*o*-Toloxy-2-propanol and **3-*o*-toloxy-1-propanol** were prepared by the condensation of *o*-cresol with propylene chlorohydrin and trimethylene chlorohydrin, respectively.

3-*o*-Toloxy-1-isopropoxy-2-propanol.[5]—Thirty-four grams (0.25 mole) of 1-chloro-3-isopropoxy-2-propanol[6] was added with stirring to a solution of 27 g. (0.25 mole) of *o*-cresol and 11.2 g. (0.28 mole) of sodium hydroxide in 100 ml. of water. The solution was heated to boiling and refluxed for two hours. The cooled solution was extracted with chloroform and the chloroform extract washed free of alkali. Upon removal of solvent, the crude ether was obtained as a thick oil. Distillation under reduced pressure gave 39 g. (70%) of 3-*o*-toloxy-1-isopropoxy-2-propanol; b.p. 132–134° (3 mm.), n^{25}_D 1.4979.

Anal. Calcd. for $C_{13}H_{20}O_3$: C, 69.61; H, 8.92. Found: C, 69.52; H, 8.91.

Conversion of these toloxy propanols to the corresponding carbamate esters was accomplished using a slight modification of the general procedure described earlier.[2] The phosgene reaction mixture after standing overnight was treated directly with gaseous ammonia until alkaline, and the water soluble components removed by extracting with water. The crude amides obtained by evaporation of the solvent under reduced pressure solidified on cooling, and were purified by recrystallization from benzene–ligroin mixture and finally from water. Over-all yields of 60–80% were obtained.

4-*o*-Toloxymethyl Dioxolone-2.—This compound was prepared by the phosgenation of mephenesin in the presence of antipyrine according to the procedure described earlier for the preparation of cyclic carbonates of 2,2-disubstituted-1,3-propanediols.[2] From 18.2 g. of mephenesin there was obtained 15 g. (72%) of 4-*o*-toloxymethyl dioxolone-2. The product, purified by crystallization from water, melted at 96–97°.

Anal. Calcd. for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81. Found: C, 63.50; H, 5.81.

3-*o*-Toloxy-2-hydroxypropyl carbamate was obtained by ammonolysis of the above cyclic carbonate of mephenesin with an excess of liquid ammonia in a steel vessel at room temperature. Purification was effected by crystallization from water.

3-*o*-Toloxy-1,2-propanediol Dicarbamate.—Using the procedure described earlier for the preparation of 2,2-disubstituted-1,3-propanediol dicarbamates,[2] 36.4 g. (0.2 mole) of mephenesin yielded 32 g. of crude dicarbamate. This product was purified by crystallization first from water, then from ethanol.

The physical constants and analytical data for these compounds are summarized in Table I.

TABLE I

Compound	Yield, %	M.p., °C.	Formula	Nitrogen, % Calcd.	Nitrogen, % Found
3-*o*-Toloxy-2-propyl carbamate	67	73–73.5	$C_{11}H_{15}NO_3$	6.71	6.59
3-*o*-Toloxy-1-propyl carbamate	78	96–97	$C_{11}H_{15}NO_3$	6.71	6.60
3-*o*-Toloxy-1-isopropoxy-2-propyl carbamate	60	68.5–69	$C_{14}H_{21}NO_4$	5.24	5.28
3-*o*-Toloxy-2-hydroxypropyl carbamate	65	93–94	$C_{11}H_{15}NO_4$	6.22	6.29
3-*o*-Toloxy-1,2-propanediol dicarbamate	55	168–169	$C_{12}H_{16}N_2O_5$	10.45	10.59

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[1] Unpublished data by Dr. F. M. Berger of these laboratories.

[2] B. J. Ludwig and E. C. Piech, THIS JOURNAL, **73**, 5779 (1951).

[3] H. L. Yale, E. J. Pribyl, W. Braker, F. H. Bergeim and W. A. Lott, *ibid.*, **72**, 3710 (1950).

[4] All temperatures reported are uncorrected. Microanalyses were performed by Schwarzkopf Microanalytical Laboratory, Middle Village, Long Island, N. Y.

[5] Some pharmacological properties of this compound have been described by C. H. Hine, H. E. Christensen, F. J. Murphy and H. Davis, *J. Pharmacol. Exptl. Therap.*, **97**, 414 (1949). The preparation and physical constants of this compound were not described by these authors.

[6] Generously supplied by Shell Development Company, Emeryville, California.

Synthesis of Butadiene-2,3-C^{14} [1]

BY KINGSLEY M. MANN[2] AND ROBERT F. NYSTROM

In connection with polymerization studies and the preparation of more complex compounds by the Diels–Alder reaction, it was necessary to develop a small-scale preparation for high-purity butadiene-2,3-C^{14}.

The synthesis of tagged butadiene is an eight-step process, furnishing an over-all yield of 49% based on radioactive carbon dioxide. The method briefly outlined is: (a) conversion of $C^{14}O_2$ to methylene-labeled succinic acid (four steps) in an 89% yield by modification of the procedure recently described by Kushner and Weinhouse[3]; (b) esterification of the acid; (c) reduction of the ester to 1,4-butanediol-2,3-C^{14} by lithium aluminum hydride; (d) conversion of the diol to 1,4-dibromobutane-2,3-C^{14}; and (e) reaction between the dibromide and trimethylamine to give the di-

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[1] This work was performed under Atomic Energy Commission Contract AT-(40-1)-282.

[2] The Upjohn Co., Kalamazoo, Mich.

[3] Kushner and Weinhouse, THIS JOURNAL, **71**, 3558 (1949).

quaternary salt which upon treatment with silver oxide and heating furnishes butadiene-2,3-C^{14}.

Terminal-labeled butadiene-1,4-C^{14} can be made from carboxyl-labeled succinic acid[3] utilizing steps (b) through (e) described above.

Experimental

Tetramethylene-2,3-C^{14}-bis-[trimethylammonium Bromide].—To 1.18 g. (10 millimoles) of succinic acid-2,3-C^{14} were added 10 ml. of absolute ethanol, which previously had been saturated with dry hydrogen chloride at 10°, and then 40 ml. of benzene. The reaction mixture was heated to boiling and the water removed with the aid of a "moisture test receiver." After refluxing 15 hours the excess ethanol and a trace of water were removed by distillation, whereas the bulk of the benzene was taken off under vacuum (15 mm.) at room temperature. The ester was transferred to a dropping funnel with 25 ml. of absolute ether. Reduction of the ester was accomplished by adding it dropwise to a well-stirred solution of one gram of lithium aluminum hydride in 150 ml. of absolute ether. After the last addition, the mixture was refluxed one hour before the excess hydride was decomposed by the dropwise addition of water. Sufficient 6 N hydrochloric acid now was added to obtain a clear solution and then the 1,4-butanediol-2,3-C^{14} was removed by a 74-hour continuous ether extraction. The ether extract containing the diol was transferred to a Cheronis micro porous disperser apparatus and the solvent removed in a stream of nitrogen. Ten milliliters of water was added and the mixture saturated with gaseous hydrogen bromide at 10°. Upon heating the solution to 90–95° while still passing in hydrogen bromide, a cloudiness developed and gradually the heavy 1,4-dibromobutane-2,3-C^{14} settled out. After two hours, heating was discontinued, the solution cooled, and the dibromide extracted with ether (five 30-ml. portions). The ethereal solution was washed with brine containing sodium bicarbonate and then dried over calcium sulfate.

Following removal of the drying agent the solution was evaporated at 60° under anhydrous conditions in a 250-ml. ground-glass erlenmeyer flask. To the 1,4-dibromobutane-2,3-C^{14} were added 25 ml. of absolute ethanol which had previously been saturated at 10° with anhydrous trimethylamine. The mixture was refluxed for one hour under anhydrous conditions and the excess trimethylamine was allowed to escape through a mercury bubbler. After cooling the mixture, 200 ml. of absolute ether was added and the white precipitate allowed to settle overnight at 4°. The solid was collected by filtration through a sintered glass funnel, followed by extensive washing with absolute ether. The yield of diquaternary salt was 2.16 g. or 65% based on succinic acid.

Butadiene-2,3-C^{14}.[4]—One and eight-tenths grams of the diquaternary salt was dissolved in 15 ml. of water, and silver oxide from 2.5 g. of silver nitrate and 10 ml. of 8% potassium hydroxide was added. After vigorous stirring the precipitate was filtered off. The decomposition of the substituted ammonium hydroxide was carried out by heating the aqueous solution to boiling (Glas-Col heater temperature—160°) in a stream of helium. Some of the water vapor in the gas stream was removed by a cold-water condenser and the trimethylamine absorbed by bubbling through 3 N sulfuric acid. The butadiene-2,3-C^{14} was collected in traps cooled by liquid nitrogen. As the decomposition proceeded the temperature was allowed to rise and as the reaction went to completion the temperature of the Glas-Col heater rose to 250°. The butadiene-2,3-C^{14} was dried by vacuum distillation (10^{-4} mm.) through "indicating" drierite (fifteen passes). A yield of 4.55 millimoles (84%) of butadiene-2,3-C^{14} based on the diquaternary salt was obtained. The vapor pressure of the product was 9.65 cm. at −46°, as compared with 9.50 cm. for a sample of ordinary butadiene (99% pure). The over-all yield of butadiene-2,3-C^{14} from radioactive carbon dioxide was 49%.

Establishment of Purity of Butadiene-2,3-C^{14}.—In addition to determining the purity of the tagged butadiene by vapor pressure determination of successive fractions, the specific activity was found of various intermediates in the synthesis, of a derivative, and of a degradation product of butadiene-2,3-C^{14}.

By use of the reaction between labeled butadiene and maleic anhydride,[5] *cis*-Δ^4-tetrahydrophthalic anhydride-4,5-C^{14} was prepared in almost quantitative yield. The material was recrystallized until the assay for C^{14} gave a constant specific activity.

TABLE I

Compound	Microcuries of C^{14} per millimole of compound
Ethylene-1,2-C^{14}	1.63
Succinic acid-2,3-C^{14}	1.63
Tetramethylene-2,3-C^{14}-bis-[trimethylammonium bromide]	1.64
Butadiene-2,3-C^{14}	1.64
cis-Δ^4-Tetrahydrophthalic anhydride-4,5-C^{14}	1.65
Glyoxal-1,2-C^{14}-2,4-dinitrophenylosazone	1.64

Another check on the purity and also the position of labeling of butadiene-2,3-C^{14} was obtained when the diene was degraded by use of ozone. Radioactive glyoxal was isolated as the glyoxal-1,2-C^{14}-2,4-dinitrophenylosazone, m.p. 320–322° (dec.), which was purified by repeated crystallization.

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.[6]

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[4] Willstätter and Heubner, *Ber.*, **40**, 3869 (1907).

[5] Farmer and Warren, *J. Chem. Soc.*, 897 (1929).

[6] Palevsky, Swank and Grenchik, *Rev. Sci. Instruments*, **18**, 298 (1947).

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Some Observations on Ammonium Tetrafluoborate

BY DONALD RAY MARTIN[1] AND JAMES KIRK RIECKE

In a research project involving the use of ammonium tetrafluoborate, the following physical and chemical properties were observed. These properties are reported inasmuch as most of them have not appeared in the literature and the others are not in accord with previous observations.[2]

The ammonium tetrafluoborate was obtained as the technical grade supplied by the General Chemical Company. Only ammonium tetrafluoborate which had been purified by four crystallizations from water solutions was used in these studies. The purified salt was analyzed by the usual microanalytical procedures and found to contain 3.91% hydrogen and 13.12% nitrogen compared with the theoretical values of 3.85 and 13.36, respectively.

The presence of the tetrafluoborate ion in the purified salt was established by its precipitation as the grayish-white compound, nitron tetrafluoborate. It was impossible to obtain the fine green needles (which upon standing for some time turn yellow) described by Lange.[3] In order to check the procedure, aqueous solutions of different concentrations of tetrafluoboric acid, hexamminechromium(III) tetrafluoborate, hexamminecobalt(II) tetrafluoborate and hexam-

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[1] Naval Research Laboratory, Washington, D. C.

[2] H. S. Booth and D. R. Martin, "Boron Trifluoride and Its Derivatives," John Wiley and Sons, Inc., New York, N. Y., 1949, pp. 108-111.

[3] W. Lange, *Ber.*, **59**, 2107, 2432 (1926).