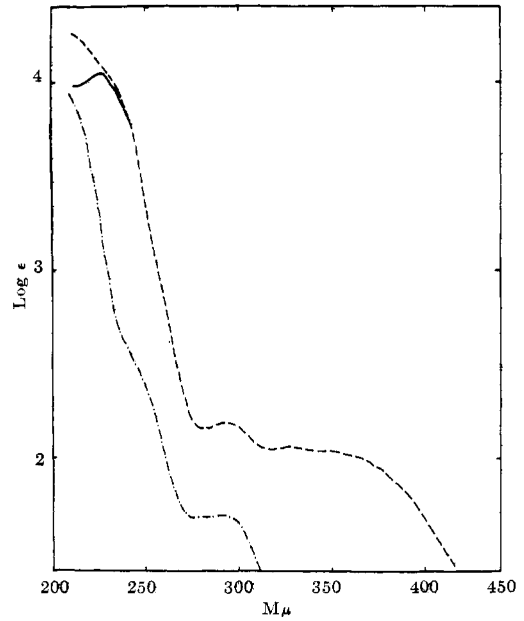


Fig. 1.—Evaluation of enedione chromophore absorption maximum in spectra of bicyclohexenyl-*p*-benzoquinone adducts
(– – – –) Spectrum of $\Delta^{2,14}$ tetradecahydrotriphenylene-1,4-dione (Ia) (in ethanol)
(- · – · –) Spectrum of Δ^{14} hexadecahydrotriphenylene-1,4-dione (IVa) (in ethanol)
(———) Curve obtained by subtracting IVa from Ia

high absorption in the 210–225 mμ region ($\epsilon_{210\ m\mu}$ 8700, $\epsilon_{220\ m\mu}$ 4400).

On the assumption that this high absorption of 14:15 double bond might mask the maximum due to the enedione chromophore, the intensity values of the reduced adducts IV in the 210–240-mμ region were subtracted from those of the adducts I. When the resulting intensity values were plotted against the respective wave lengths (Fig. 1), there was obtained for adducts Ia, Ib, and Ic the expected maximum of the enedione chromophore (Table I).

Experimental

The absorption spectra were measured with a Unicam SP 500 spectrophotometer. Melting points were measured in a capillary and are uncorrected.

6,7-Dimethyl-5,8,9,10-tetrahydronaphthoquinone (Table I).—A mixture of 2,3-dimethylbutadiene (4 g., 0.049 mole) and *p*-benzoquinone (4 g., 0.037 mole) was kept for 1 week at room temperature. Trituration with ethanol (15 ml.) yielded yellow crystals (6.75 g., 96%), m.p. (from ethanol) 115–117° (lit.[5] m.p. 113–115°) $\nu_{C=O}^{CHCl_3}$ 1690 cm.$^{-1}$. λ_{max} 228 mμ, ε 9800.

6,11-Dimethyl-Δ^{14}-hexadecahydrotriphenylene-1,4-dione (IVb).—A solution of 6,11-dimethyl-$\Delta^{2,14}$-tetradecahydrotriphenylene-1,4-dione Ib (4.5 g.) in acetic acid (70 ml.) was shaken with powdered zinc (15 g.) for 15 min. The mixture was then filtered, and the filtrate was poured into cold water (1.5 l.), shaken for 15 min., and kept in the refrigerator overnight. A white precipitate was obtained which upon crystallization from methanol yielded white crystals (3.3 g.), m.p. 107–110°. Recrystallization from methanol gave the analytical sample, m.p. 133.5–135°.

Anal. Calcd. for $C_{20}H_{18}O_2$: C, 79.95; H, 9.39; O, 10.65. Found: C, 79.69; H, 9.39; O, 10.67.

Acknowledgment.—This research was supported by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is hereby made to the donors of said fund.

---

[5] L. F. Fieser, W. P. Campbell, and E. M. Fry, *J. Am. Chem. Soc.*, **61**, 2217 (1939).

A Method of Tritium Labeling

M. W. LINDAUER AND H. A. SMITH

Department of Chemistry, University of Tennessee, Knoxville, Tenn.

Received November 29, 1961

The use of tritium as a tracer in reactions of various organic compounds is of growing interest. Much of the labeling is accomplished by the Wilzbach method which involves the exposure of such compounds to curie quantities of tritium gas for periods of hours or days.[1] In general, the labeling process is accompanied by the appearance of a number of labeled by-products often with specific activities 10–100 times greater than that of the desired material.[2] The presence of these by-products which arise from such processes as polymerization,[3] replacement of substituents,[4] isomerization,[3] and addition of tritium to unsaturated linkages[5] requires careful purification procedures. The times necessary for labeling by the Wilzbach method may be greatly reduced if an electric discharge is employed during the period of gas exposure.[6] Labeling in the presence of uranium hydride containing tritium has also been carried out with certain advantages over the usual procedure.[7]

It is well known that rapid exchange between deuterium gas and the active hydrogen in organic compounds such as acids and alcohols occurs in the presence of certain metal catalysts.[8] The same

---

[1] K. E. Wilzbach, *J. Am. Chem. Soc.*, **79**, 1013 (1957).

[2] K. E. Wilzbach, "Proceedings of the International Atomic Energy Agency Symposium on the Detection and Use of Tritium in the Physical and Biological Sciences," Vienna, Austria, 1961, paper 83.

[3] P. Riesz and K. E. Wilzbach, *J. Phys. Chem.*, **62**, 6 (1958).

[4] L. Dorfman and K. E. Wilzbach, *ibid.*, **63**, 799 (1959).

[5] H. J. Dutton, E. P. Jones, L. H. Mason, and R. F. Nystrom, *Chem. Ind.* (London), 1176 (1958).

[6] F. L. Jackson, G. W. Kittinger, and F. P. Krause, *Nucleonics*, **18**, 102 (1960).

[7] R. E. Felter and L. A. Currie, "Proceedings of the International Atomic Energy Agency Symposium on the Detection and Use of Tritium in the Physical and Biological Sciences," Vienna, Austria, 1961, paper 121.

[8] L. E. Line, Jr., B. Wyatt, and H. A. Smith, *J. Am. Chem. Soc.*, **74**, 1808 (1952); H. A. Smith and E. L. McDaniel, *ibid.*, **77**, 583 (1955); E. L. McDaniel and H. A. Smith in "Advances in Catalysis and Related Subjects," Vol. IX, Academic Press, Inc., New York, 1957, p. 76; H. A. Smith and B. B. Stewart, *J. Am. Chem. Soc.*, **82**, 3898 (1960).

behavior is expected when tritium gas is employed. The labeling of a compound at the position of an active hydrogen is of little value since the labeled atom is readily lost under mild conditions. However, when the tritium atom can be easily transferred to a position where it is not labile, a satisfactory tagging process results. Furthermore, the position which the tritium atom assumes in the molecule should be reasonably well established by the synthetic route employed. The method has been applied to the synthesis of tritiated acetic acid and tritiated *N*-methylpyrrole.

Experimental

Materials.—Malonic acid was Eastman White Label grade and was used without further purification. *N*-Methylpyrrole-2-carboxylic acid was prepared by metalation of *N*-methylpyrrole with *n*-butyllithium followed by carbonation.[9] C. P. dioxane (Matheson, Coleman, and Bell) was used as solvent. No purification was necessary. The tritium gas of 99+ % purity was obtained from the Oak Ridge National Laboratory. One curie of this isotope (0.45 standard cc.) was added to 4000 standard cc. of hydrogen and the mixture stored in a small metal tank. The isotopic mixture remained in the tank for more than a year before use in the labeling experiments; at this time, gas chromatographic analysis showed that 95% of the tritium was in the form of tritium hydride.[10] The activity was about 0.3 mc. per standard cc.

The catalyst employed in the exchange process was 5% rhodium supported on alumina and was obtained from Baker and Co., Inc., of Newark, N. J.

Exchange Procedure.—All exchange reactions were carried out in heavy-walled 50-ml. Erlenmeyer flasks each fitted with a 6-mm., straight-bore stopcock terminating in a ball and socket joint. The catalyst, substrate, and solvent, in that order, were introduced into the flask through a long-stemmed funnel. The flask was then attached by means of the ball and socket joint to a manifold which contained (1) a source of tritium hydride, (2) a gas sampling chamber of known volume, (3) a mercury manometer, (4) a source of helium, and (5) a 50-ml. Berkowski ionization chamber attached to a Cary Model 31 vibrating reed electrometer equipped for continuous recording. The latter two were used in the analyses of the residual gas after the exchange. The flask was cooled in liquid nitrogen, evacuated, and filled with the hydrogen–tritium hydride mixture to the desired pressure. The exchange vessel was removed from the manifold, warmed to room temperature, and shaken for at least 10 min. The solution was again attached to the manifold, cooled in liquid nitrogen, and the gas sample removed for analysis by gas chromatography.

The flask was taken from the manifold and warmed to room temperature. After removal of the catalyst by filtration through a fritted glass funnel, the solution was concentrated by evaporation of most of the solvent, then transferred to a semimicro distillation apparatus for evaporation of the remaining solvent and decarboxylation.

Decarboxylation Procedure.—The tritiated acids were decomposed by heating followed by product distillation. The distillates were sampled, and the samples diluted with appropriate solvents for counting.

Tritium Analysis of Products.—All tritium activities of labeled compounds were obtained by the liquid scintillation method employing a Baird-Atomic Model 745 system. The scintillation solution contained 4 g./l. of 2,5-diphenyloxazole (PPO) and 50 mg./l. of 2,2′-*p*-phenylenebis(5-phenyloxazole) (POPOP) in toluene.

Elimination of Labile Tritium.—In the preparation involving exchange with malonic acid, the acetic acid produced contained both unlabile tritium (in the methyl group) and labile tritium (in the carboxyl group). The latter type was eliminated by neutralization with sodium hydroxide followed by removal of tritiated water from the salt formed, and acidification to regenerate the organic acid.

Experimental Calculations and Results

As expected, tritium in the presence of rhodium catalyst exchanges rapidly with the hydrogen atom of a carboxyl group. Under the experimental conditions employed, some 60% of the gas phase tritium atoms were exchanged in 10 min. Apparently, equilibrium had been established, since continued shaking for 90 min. gave virtually the same result. The details of three exchange reactions are shown in Table I.

TABLE I

EXCHANGE REACTIONS OF TRITIUM HYDRIDE WITH CARBOXYLIC ACIDS IN THE PRESENCE OF 0.1 G. OF RHODIUM CATALYST AND 25 ML. OF DIOXANE SOLVENT

Acid	Gas Pressure, Cm. Hg at 77°K.	Tritium, Mc.	Acid Concentration, Moles/L.	Exposure Time, Min.	Fraction of tritium Exchanged
Malonic	26	8	0.2	10	0.61
Malonic	43	13	0.2	90	0.63
N-Methylpyrrole-2-carboxylic acid	25	7.5	0.17	90	0.59

The activity of the acetic acid obtained by decomposition of the labeled malonic acid was 36 mc. per mole while that of the *N*-methylpyrrole obtained by decarboxylation of the *N*-methylpyrrole-2-carboxylic acid was 8 mc. per mole. In each case, there appeared to be some loss of tritium activity by exchange of the tritium in the carboxyl group with hydrogen adsorbed on the glass surface of the container. This could undoubtedly be reduced by pretreatment procedures.

Discussion

The success of the method of labeling reported here depends upon the rapid exchange of tritium with carboxyl hydrogen atoms in the presence of a noble metal catalyst such as rhodium. The specific activities of the product obtained are dependent on the fraction of tritium in the hydrogen gas employed in the exchange reaction. With the mole fraction of tritium only around 10^{-4}, the specific activities were about 10% of the 3–90 mc. per gram reported for the Wilzbach gas exposure method[2] when the mole fraction of tritium was essentially

---

(9) D. A. Shirley, B. H. Gross, and P. A. Roussel, *J. Org. Chem.*, **20**, 225 (1955).

(10) H. A. Smith and E. H. Carter, "Proceedings of the International Atomic Energy Agency Symposium on the Detection and Use of Tritium in the Physical and Biological Sciences," Vienna, Austria, paper 109. in press.

unity. If one expresses the efficiency of tritium labeling in terms of millicuries of incorporated activity per curie-hour of tritium exposure, the efficiency of the exchange-decarboxylation method is some 10^5 times that found when the Wilzbach method is applied to the labeling of toluene.[11]

Because of the low level of tritium activity and short exposure times, the products formed are not contaminated to any appreciable extent by high specific activity materials resulting from side reactions. In addition, the decarboxylation-distillation procedure may be expected to produce some purification. The rhodium catalyst employed in the exchange process is an excellent hydrogenation catalyst, and might be expected to accelerate hydrogenation of unsaturated linkages thus producing saturated by-products. However, the hydrogenation is ordinarily much slower than the desired exchange reaction, so that little contamination results. The tritiated *N*-methylpyrrole prepared by exchange and decarboxylation of *N*-methylpyrrole-2-carboxylic acid was examined for contamination by gas chromatography. This examination revealed the presence of a very small amount (3% or less) of a lower boiling contaminant, probably *N*-methylpyrrolidine. This contaminant can be readily removed by chromatographic processes. Incidentally, the problem of hydrogenation of unsaturated linkages is also present when the Wilzbach method is employed.[5]

While the method of labeling which has been described is not as general as that of Wilzbach, it should be applicable to any compound containing a carboxyl group which can be readily decarboxylated. It has the advantage of employing low activities of tritium and short exposure times and producing products of high purity labeled in specific positions.

A similar method has been used for producing nicotinic acid-2-*t*-through decarboxylation of tritiated quinolinic acid.[12] However, the latter compound was prepared through exchange with tritium oxide rather than the readily available tritium gas.

Acknowledgment.—The authors are indebted to the National Science Foundation for aid through its Research Participation for College Teachers Program and the United States Atomic Energy Commission for support of this work. They are also indebted to Drs. D. A. Shirley and R. G. Thompson for the sample of *N*-methylpyrrole-2-carboxylic acid used in the exchange experiments and to Mr. E. H. Carter, Jr., for the gas chromatographic analyses.

[11] H. J. Ache, W. Herr, and A. Theimann, Proceedings of the Symposium on the Detection and Use of Tritium in the Physical and Biological Sciences, Vienna, Austria, 1961, paper 10, in press.

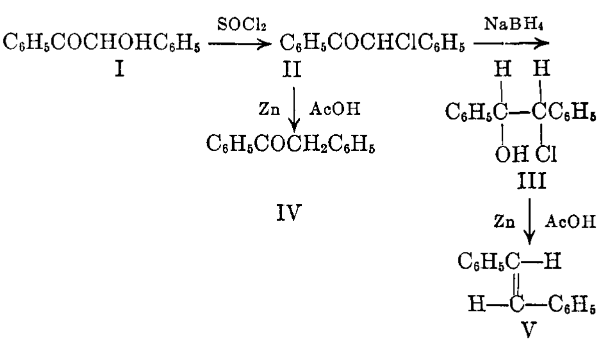
[12] R. F. Dawson, D. R. Christman, A. D'Adamo, M. L. Solt, and A. P. Wolf, *J. Am. Chem. Soc.*, **82**, 2628 (1960). *Cf.* A. P. Holemann and K. Clusius, *Ber.*, **70**, 819 (1937).

Preparation of *trans*-Stilbene from Benzoin

Louis F. Fieser and Yasuaki Okumura

Harvard Chemical Laboratory, Harvard University, Cambridge, Mass.

Received December 1, 1961



A procedure for the preparation of *trans*-stilbene developed by one of us[1] calls for reaction of benzoin with thionyl chloride to produce desyl chloride (II), reduction with sodium borohydride to give a product rich in the *erythro* chlorohydrin III, and reaction with zinc dust and acetic acid. The two reduction steps are run consecutively in the same ethanol solution. If deteriorated sodium borohydride is used (University of Illinois), the low-melting product is desoxybenzoin (IV). At the Massachusetts Institute of Technology most members of the class obtained *trans*-stilbene but a few encountered desoxybenzoin. After trying all conceivable variations in the second and third steps to no avail, the author of the manual considered the possibility for variable interpretation of the following direction: "Place four grams of benzoin (crushed to a powder) in a one hundred-milliliter round-bottomed flask, cover it with four milliliters of thionyl chloride, warm gently on the steam bath (hood) . . . . " The comma after "thionyl chloride" represents a pause in operation, as in reading. The pause is ordinarily not more than a second or two, but it could be long, as over the lunch hour or overnight. Trial indeed showed that if the mixture of reagents is let stand at room temperature until reaction is complete and the subsequent steps are then applied, the final product that crystallizes from ethanol is desoxybenzoin. The yield is low; a major product, retained in the mother liquor, is *meso*-hydrobenzoin. For avoidance of trouble at this stage, and to insure removal of all excess thionyl chloride which otherwise affords sulfur in the next step, the present procedure is as follows: "Put four grams of benzoin into a tared one hundred-milliliter flask and mount the

---

[1] L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed., revised, D. C. Heath, 1957, pp. 178–180. For an interpretation of the stereochemistry, see L. F. Fieser and M. Fieser, "Advanced Organic Chemistry," Reinhold Publishing Corp., 1961, pp. 165–170.