

Mechanism of the Friedel-Crafts Reaction of 1-Benzenesulfonyl-2-bromomethylethyleneimine with Benzene¹

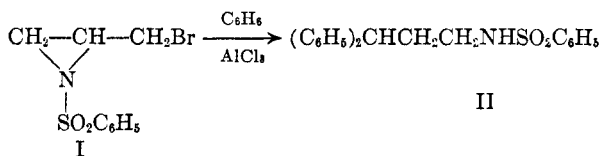
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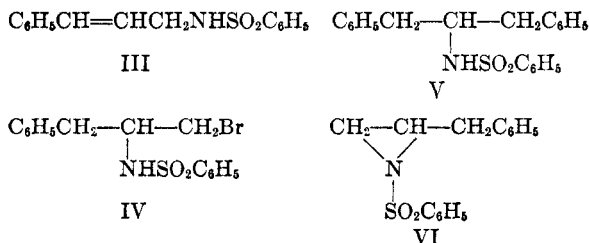
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In its aluminum chloride-catalyzed reaction with benzene, 1-benzenesulfonyl-2-phenylazetidine (from the action of benzenesulfonyl chloride and alkali with 3-amino-3-phenylpropanol) produces *N*-(3,3-diphenylpropyl)benzenesulfonamide (II) in good yield. Accordingly, the possibility that the azetidene is an intermediate in the Friedel-Crafts reaction of 1-benzenesulfonyl-2-bromomethylethyleneimine (I) with benzene to give II receives support. To establish the relation of one of the ring carbon atoms of ethyleneimine I with the propyl carbon atoms of II, ethyleneimine I with carbon-14 at its 3-position was converted to the Friedel-Crafts product II. Here, the activity was shown to be wholly at the 1-position. Accordingly, the extensive shuffling of positions encountered in reactions of cyclopropylcarbonium ions finds no counterpart in this Friedel-Crafts reaction with I. The radioactive ethyleneimine I was prepared from acrylic-1-¹⁴C acid, obtained by carbonating the Grignard reagent from vinyl bromide with radioactive carbon dioxide. The anthracene adduct of the acrylic acid was converted by reducing the corresponding amide to the aminomethyl derivative. Pyrolysis produced allylamine, which with benzenesulfonyl chloride gave *N*-(allyl-1-¹⁴C)-benzenesulfonamide. Bromination and alkali-cyclization completed the preparation of the labeled ethyleneimine. Appropriate degradations proved that the *N*-(allyl)benzenesulfonamide contained activity only at its 1-position. The degradation of the radioactive Friedel-Crafts product proceeded by its conversion to 3,3-diphenylpropene-1-¹⁴C, which on cleavage by ozonolysis gave radioactive formaldehyde and nonradioactive diphenylacetaldehyde.

1-Benzenesulfonyl-2-phenylazetidine (X) as an Intermediate in the Friedel-Crafts Reaction of 1-Benzenesulfonyl-2-bromomethylethyleneimine (I) with Benzene.—1-Benzenesulfonyl-2-bromomethylethyleneimine (I) reacts with benzene



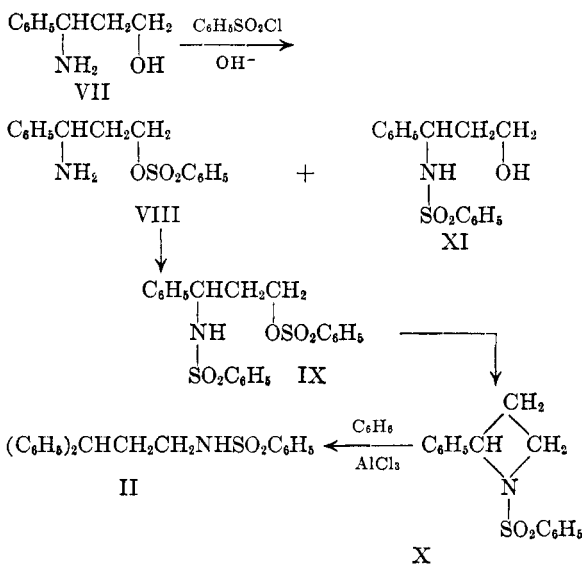
in the presence of aluminum chloride to give *N*-(3,3-diphenylpropyl)benzenesulfonamide (II).² In an effort to define the reaction path, several related compounds—*viz.*, *N*-(cinnamyl)benzenesulfonamide (III), 1-bromo-2-benzenesulfonamido-3-phenylpropane (IV), 1,3-diphenyl-2-benzenesulfonamidopropane (V), and 1-benzenesulfonyl-2-benzylethyleneimine (VI)—were considered as possible intermediates. However, because none of



these compounds on exposure to benzene and aluminum chloride gave *N*-(3,3-diphenylpropyl)benzenesulfonamide (II), they were excluded as inter-

mediates.³ 1-Benzenesulfonyl-2-phenylazetidine (X), another possibility,³ has now been prepared and tested in the same way.

Azetidine X could be obtained directly, although in low yield, by treating 3-amino-3-phenylpropanol (VII)³ with benzenesulfonyl chloride in aqueous sodium hydroxide. The azetidene is formed from



the dibenzenesulfonyl derivative IX which, as its anion, cyclizes with displacement of the benzenesulfonate group. Formation of this intermediate IX proceeds evidently by reaction first at the hydroxyl group (to give the *O*-benzenesulfonyl derivative VIII) and only then at the amino group. Because a faster action is expected at the nitrogen than at the oxygen, more *N*-benzenesulfonyl deriva-

(1) Abstracted from the dissertation submitted by Walter R. Koehler to the Graduate School of Boston University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, 1960.

(2) W. J. Gensler and J. C. Rockett, *J. Am. Chem. Soc.*, **77**, 3262 (1955).

(3) E. L. Jenner, *Chem. Abstr.*, **46**, 9603 (1962) [U.S. Patent 2,584,589 (1952)].

tive XI will be formed than O-benzenesulfonyl derivative VIII. Once formed, the N-benzenesulfonyl derivative, as an anion, will resist combination with a second molecule of benzenesulfonyl chloride. Actually, the major product in the reaction was found to be the N-benzenesulfonyl derivative XI. Treatment of amino alcohol VII with benzenesulfonyl chloride in dry pyridine and only then with aqueous sodium hydroxide gave azetidine X in better yield. In pyridine solution, the first-formed N-benzenesulfonyl derivative would not ionize and therefore should react further with less difficulty to give the necessary dibenzenesulfonyl compound IX.

Positive results were obtained when azetidine X was tried in the Friedel-Crafts reaction; N-(3,3-diphenylpropyl)benzenesulfonamide (II) could be isolated in good yield. This fact lends support to the postulation of azetidine X as an intermediate in the I to II process.

The conversion of three-membered ring-compound I to four-membered ring-intermediate X is reminiscent of the rearrangements of cyclopropylcarbinyl to cyclobutyl compounds.⁴ 1-Benzenesulfonyl-2-bromomethylethyleneimine (I) is, in fact, a heterocyclic analog of cyclopropylcarbinyl bromide. To ascertain whether there is more here than just a formal parallelism and to gain further insight into the mechanism, the I to II process was examined more carefully. The interchange of skeletal positions in the cyclopropylcarbinyl reactions⁴ suggested that a related scrambling might occur in the heterocyclic process. To check this point, 1-benzenesulfonyl-2-bromomethylethyleneimine-3-¹⁴C (XVIII) was prepared and put through the Friedel-Crafts reaction. The resulting labeled N-(3,3-diphenylpropyl)benzenesulfonamide was then systematically degraded to locate the radioactivity.

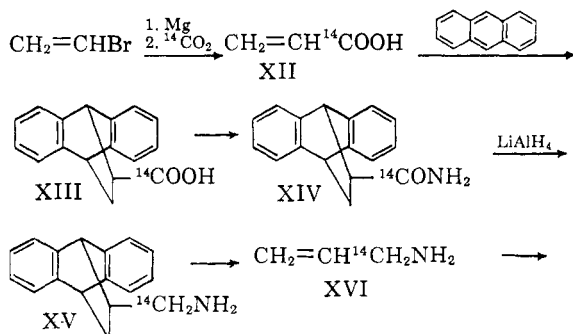
Preparation of 1-Benzenesulfonyl-2-bromomethylethyleneimine-3-¹⁴C (XVIII).—Allylamine-1-¹⁴C (XVI) was required for the preparation of the labeled ethyleneimine XVIII. An allylamine syn-

thesis was utilized that removed all concern about possible complications involving either ethylenic unsaturations or allylic rearrangements.

Acrylic-1-¹⁴C acid (XII), from the reaction of the Grignard derivative⁵ of vinyl bromide with radioactive carbon dioxide,⁶ was combined with anthracene⁷ to give 9,10-dihydro-9,10-ethanoanthracene-11-(carboxylic-¹⁴C acid) (XIII). Reduction of the corresponding amide XIV with lithium aluminum hydride furnished amine XV, which decomposed on heating to anthracene and allylamine-1-¹⁴C (XVI).^{8,9} The benzenesulfonyl derivative XVII of this allylamine was brominated and then cyclized with alkali¹⁰ to the desired labeled ethyleneimine XVIII.

To confirm the assigned location of activity, N-(allyl-1-¹⁴C)benzenesulfonamide (XVII) was treated first with ozone and then with silver oxide in aqueous alkali. The resulting N-(benzenesulfonyl)-glycine-2-¹⁴C (XIX) was esterified with diazomethane and then treated with phenyl Grignard reagent to give benzenesulfonamide derivative XX. This material, which incorporates the carbon originally at positions 1 and 2 of the N-(allyl-1-¹⁴C)-benzenesulfonamide (XVII) also contained all the original activity. Cleavage of benzenesulfonamide XX with lead tetraacetate furnished benzophenone (XXI), derived from position 2 of allyl compound XVII, and formaldehyde (XXII), derived from position 1 of allyl compound XVII. The formaldehyde fragment XXII contained all, the benzophenone fragment XXI none, of the original activity. From these results, all the activity of the N-(allyl)benzenesulfonamide (XVII) is, as indicated, at the 1-position, and accordingly all the activity of the 1-benzenesulfonyl-2-bromomethylethyleneimine (XVIII) is at its 3-position.

A different result was found when the ozonolysis mixture from the radioactive N-(allyl)benzenesulfonamide (XVII) was decomposed with zinc and the cleavage formaldehyde XXIII isolated. If the first degradation scheme is valid, this formaldehyde should have been devoid of activity;



(4) For leading references see, R. H. Mazur, W. N. White, D. A. Semelow, C. C. Lee, M. S. Silver, and J. D. Roberts, *J. Am. Chem. Soc.*, **81**, 4390 (1959); S. Winstein and E. M. Kosower, *ibid.*, **81**, 4399 (1959); R. A. Sneen, K. M. Lewandowski, and I. A. I. Taha, *ibid.*, **83**, 4843 (1961); E. Renk and J. D. Roberts, *ibid.*, **83**, 878 (1961).

(5) H. Normant, *Bull. soc. chim. France*, 728 (1957).

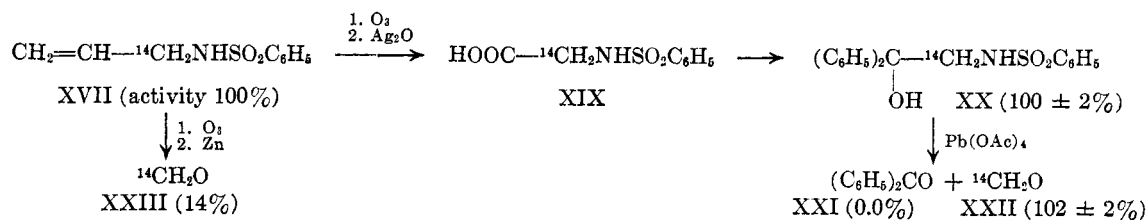
(6) Acrylic acid from the carbonation of the Grignard reagent from vinyl chloride with solid carbon dioxide in large excess has been reported [H. E. Ramsden, J. R. Leebrick, S. D. Rosenberg, E. H. Miller, J. J. Walburn, A. E. Balint, and R. Cserr, *J. Org. Chem.*, **22**, 1602 (1957)]. No excess of carbon dioxide was used in our work.

(7) H. Scheibler and V. Scheibler, *Chem. Ber.*, **87**, 379 (1954), use acrylic acid as solvent for the diene reaction. We find that xylene is a convenient solvent and that a large excess of acrylic acid is unnecessary.

(8) K. Alder has mentioned the production of allylamine by pyrolysis of its anthracene adduct, but without details ("Newer Methods of Preparative Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1948, p. 489).

(9) Allylamine-1-¹⁴C has also been prepared from sodium cyanide-¹⁴C by way of 3-hydroxypropionitrile-1-¹⁴C and acrylonitrile-1-¹⁴C (private communication from Robert F. Nystrom, Director, Radio-carbon Laboratory, University of Illinois). Also, cf. C. R. A. Berger, J. C. Leak, C. Costa Neto, and R. F. Nystrom, Abstracts American Chemical Society Meeting, April, 1960, p. 48-O.

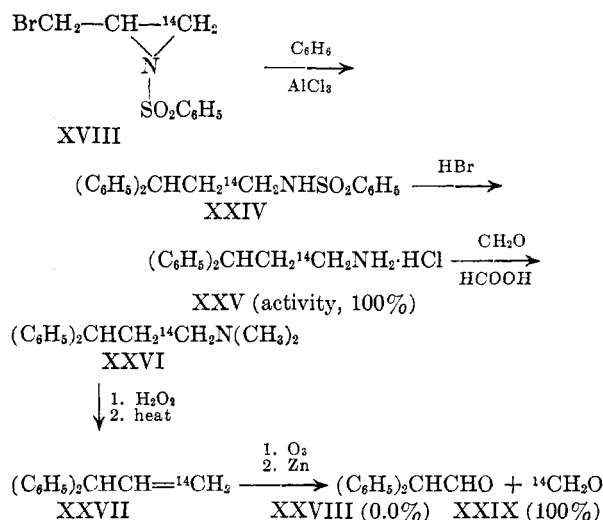
(10) J. Gensler, *J. Am. Chem. Soc.*, **70**, 1843 (1948).



in fact, it contained appreciable activity. However, ozonolysis of allyl systems attached to electronegative groups has been known to give products arising from cleavage not only at the double bond but also at the single bond.¹¹ If this kind of cleavage occurs here, some of the labeled 1-position of N-(allyl-1-¹⁴C)-benzenesulfonamide (XVII) will emerge as labeled formaldehyde. We believe that this is the correct interpretation, and that the presence of activity in the cleavage-formaldehyde XXIII should not be taken as indicating activity in the 3-position of allyl derivative XVII. The conclusion that there is only a single labeled position in XVII is supported not only by the above mentioned results with glycine XIX but also by the distribution of activity in the subsequently derived N-(3,3-diphenylpropyl)benzenesulfonamide (XXIV).

Location of Activity in the N-(3,3-Diphenylpropyl)-benzenesulfonamide (XXIV) from 1-Benzenesulfonyl-2-bromomethylethyleneimine-3-¹⁴C (XVIII).—Radioactive N-(3,3-diphenylpropyl)benzenesulfonamide (XXIV) was prepared from the labeled ethyleneimine XVIII and was degraded to find the amount of activity at each of the three propyl positions. Treatment with hot concentrated hydrobromic acid and phenol¹² removed the benzenesulfonyl group and gave 3,3-diphenylpropylamine (XXV). This was dimethylated with formaldehyde and formic acid to the tertiary amine XXVI, which was converted through the N-oxide to 3,3-diphenylpropene (XXVII).^{13,14} The carbon atoms of the propene chain were separated first by ozonolysis to formaldehyde (XXIX) and diphenylacetaldehyde (XXVIII), and then by permanganate oxidation of diphenylacetaldehyde semicarbazone—the form in which diphenylacetaldehyde was isolated—to benzophenone. With this sequence, the activity at the N-(3,3-diphenylpropyl)benzenesulfonamide (XXIV) 1-position (as formaldehyde XXIX), at its 3-position (as benzophenone), and at

its 2-position [as the difference between diphenylacetaldehyde (XXVIII) and benzophenone] could be determined. Application of this procedure showed that the radioactivity in benzenesulfonamide XXIV is concentrated at the 1-position. Accordingly, in the Friedel-Crafts process, the methylene group at position 3 of 1-benzenesulfonyl-2-bromomethylethyleneimine (I) provides all the carbon for position 1 of the N-(3,3-diphenylpropyl)benzenesulfonamide product (II), and none of the carbon for positions 2 and 3.



Discussion

In the Friedel-Crafts reaction with ethyleneimine I, two reaction paths consistent with the data and involving azetidinium X as an intermediate can be written. In both paths, the postulated initial coordination of aluminum chloride with the bromine atom of I, by ionizing or polarizing the carbon-to-bromine bond, makes the exocyclic carbon electron-deficient. One sequence¹⁵ calls for ring expansion of ion XXX to XXXI. Alkylation of benzene by the new carbonium ion XXXI gives the 2-phenylazetidinium intermediate, which reacts with another molecule of benzene to give the final product XXIV.

An alternate sequence involves XXXII, a non-classical bicyclobutonium ion analog—but only with the proviso that XXXII combines with benzene to furnish the 2-phenylazetidinium faster than it isomerizes to any of the five other possible non-classical ions. Both pathways accommodate the

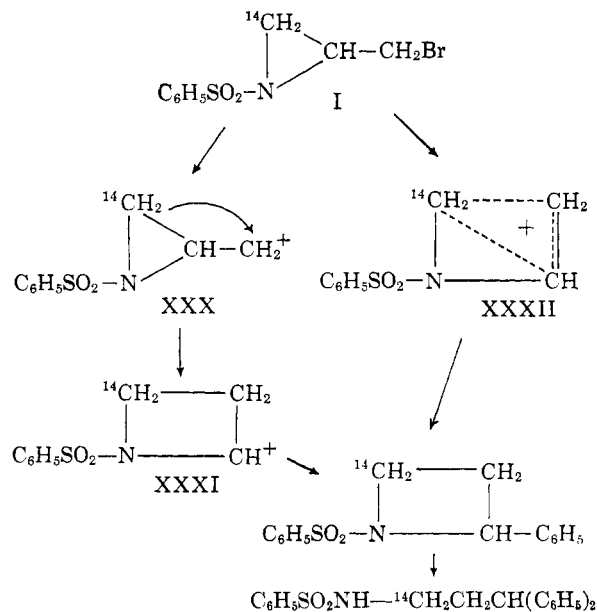
(11) Cf. P. S. Bailey, *Chem. Rev.*, **58**, 925 (1958). Rearrangements in simple allyl systems have been reported by W. P. Crain and R. M. Noyes, *J. Am. Chem. Soc.*, **81**, 2031 (1959) and by R. Raulins and L. A. Sibert, Abstracts American Chemical Society Meeting, September, 1959, p. 79-P; S. J. Rhoads, R. Raulins, and R. D. Reynolds, *J. Am. Chem. Soc.*, **76**, 3456 (1954). No rearrangements were observed by R. F. Nystrom and J. C. Leak, *ibid.*, **75**, 3039 (1953); R. F. Nystrom and C. R. A. Berger, *Chem. Ind. (London)*, 559 (1958); J. Segers, F. Kalberer, and H. Schmid, *Helv. Chim. Acta*, **41**, 1198 (1958); S. H. Sharman, F. F. Caserio, R. F. Nystrom, J. C. Leak, and W. G. Young, *J. Am. Chem. Soc.*, **80**, 5965 (1958).

(12) H. R. Synder and R. E. Heckert, *ibid.*, **74**, 2006 (1952).

(13) A. C. Cope and C. L. Baumgardner, *ibid.*, **79**, 960 (1957).

(14) C. L. Baumgardner, *ibid.*, **83**, 4423 (1961).

(15) The formulations are given as free ions only for convenience.



fact that the carbon atom at position 3 of ethyleneimine I retains its individuality. In this respect, the aluminum chloride reaction of I is clearly different from the reactions of cyclopropylcarbonyl ions.⁴ Both pathways predict that the exocyclic carbon of the ethyleneimine will appear at the 2-position of the product XXIV. A tracer experiment, with the exocyclic position of I labeled, should provide a means of checking the acceptability of these mechanisms.

The conversion of azetidine X to benzenesulfonamide II is essentially a Friedel-Crafts alkylation of benzene with an N-(benzyl)benzenesulfonamide. Although we are not aware of other alkylations with N-(benzyl)sulfonamides, the process fits the general pattern. Thus, coordination of aluminum chloride to the oxygen or nitrogen of the sulfonamido group would develop a relatively stable, electron-deficient center at the azetidine 2-position. Combination with benzene at this point leads directly to the product II.

Experimental¹⁶

3-Amino-3-phenylpropanol (VII). A. From 3-Amino-3-phenylpropanoic Acid.—The lithium aluminum hydride reduction of 3-amino-3-phenylpropanoic acid to 3-amino-2-phenylpropanol (VII) was adapted from the general directions of Vogl and Pöhm.¹⁷ After our work was completed, the preparation was described in its essentials by Rodionov and Kiseleva.¹⁸ We found that 3-amino-3-phenylpropanol (VII), melting at 73–75°¹⁹ after one crystallization from

(16) Melting points are uncorrected. The elementary analyses were performed by Carol K. Fitz, 115 Lexington Avenue, Needham Heights 94, Mass. Ultraviolet absorption curves were determined with a Beckman DK-1 recording instrument. Infrared curves were obtained with a Perkin-Elmer Model 21 double-beam spectrophotometer.

(17) O. Vogl and M. Pöhm, *Monatsh.*, **83**, 541 (1952); **84**, 1097 (1953).

(18) V. M. Rodionov and V. V. Kiseleva, *Chem. Abstr.*, **51**, 1885 (1957) [*Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 575 (1956)].

benzene-petroleum ether, was obtained in 88% yield when a mixture of 5.1 g. of 3-amino-3-phenylpropanoic acid²⁰ and 4.0 g. of lithium aluminum hydride in 130 ml. of tetrahydrofuran was boiled for 7 hr. A mixture of the product with the same material (m.p. 70–72°) prepared from styrene as described below melted at 71–73°.

B. From Styrene.—A procedure essentially that of Jenner³ led to 3-amino-3-phenylpropanol, m.p. 70–72°, from the reaction of styrene, paraformaldehyde, and acetonitrile followed by alkaline hydrolysis of the first-formed diacetyl derivative.

1-Benzenesulfonyl-2-phenylazetidine (X). A. From 3-Amino-3-phenylpropanol (VII) in One Stage.—A vigorously stirred mixture of 0.75 g. (5.0 mmoles) of 3-amino-3-phenylpropanol (VII) and 10 ml. of water was treated first with 2.0 ml. (16 mmoles) of freshly distilled benzenesulfonyl chloride and immediately thereafter with a solution of 1.0 g. (25 mmoles) of sodium hydroxide in 10 ml. of water. After 70 min. of stirring, the mixture was filtered, and the solids were dried overnight in a vacuum desiccator. Crystallization from 95% ethanol gave 92 mg. (7%) of 1-benzenesulfonyl-2-phenylazetidine (X), m.p. 120–122°. Another crystallization brought the melting point to 123.5–124°.

Anal. Calcd. for $\text{C}_{15}\text{H}_{15}\text{NO}_2\text{S}$: C, 65.92; H, 5.53; mol. wt., 273. Found: C, 66.0; H, 5.6; mol. wt., 297.

This compound, either pelleted with potassium bromide or dissolved in carbon disulfide, showed no infrared absorption peaks below 3.2 μ .

The clear alkaline filtrate from which azetidine X had been removed was acidified with hydrochloric acid. The white precipitate that formed immediately was collected, washed with several small portions of water, and dried in a desiccator. The solid (1.1 g. or 76%; m.p. 130–131°) was crystallized twice from absolute alcohol to give 0.25 g. of 3-benzenesulfonamido-3-phenylpropanol (XI), m.p. 131–132°.

Anal. Calcd. from $\text{C}_{15}\text{H}_{17}\text{NO}_3\text{S}$: C, 61.9; H, 5.9; mol. wt., 291. Found: C, 62.0; H, 5.5; mol. wt., 270.

B. From 3-Amino-3-phenylpropanol (VII) in Two Stages.—Directions for the benzenesulfonylation was adapted from the general procedure of Tipson.²¹ Benzenesulfonyl chloride (42 ml., 0.33 mole) was added in one portion to a solution of 20.9 g. (0.138 mole) of 3-amino-3-phenylpropanol (VII) in 400 ml. of pyridine at –2°. The solvent had been dried for several days over barium oxide and was filtered just before use. The inside temperature rose to 20°, but ice-salt cooling brought the temperature below 5°. The mixture was kept in the refrigerator overnight.

The resulting dark brown solution was poured over 700 g. of crushed ice and 1 l. of water. The mixture, in which a heavy, dark oil was present, was extracted with ether. The combined ether extracts (2 l.) were washed twice with water and then dried with magnesium sulfate. The solution was treated with decolorizing carbon (Norit), and the clear solution was distilled to remove most of the solvent.

The residue, dissolved in approximately 90 ml. of acetone, was added to 3.8 l. of water containing 8.4 g. (0.21 mole)

(19) J. English, Jr., and A. D. Bliss [*J. Am. Chem. Soc.*, **78**, 4057 (1956)] report m.p. 74.5–75°; L. Birkofer and L. Erlenbach [*Chem. Ber.*, **91**, 2383 (1958)] report m.p. 73°.

(20) R. E. Steiger, "Organic Syntheses," Coll. Vol. III, Wiley, New York, N. Y., 1955, p. 91. The preparation calls for boiling an alcohol solution of hydroxylamine and cinnamic acid for 9 hr. During this period, a white solid deposited in the condenser. The following properties indicate that this solid is a saltlike combination of hydroxylamine and carbon dioxide: insoluble in absolute alcohol or ether but soluble in water to give a solution alkaline to litmus; contains no halogen; reduces Tollen's reagent; has no odor but produces an ammoniacal odor when warmed with alkali; evolves an odorless gas when treated with cold dilute hydrochloric acid; gives a white precipitate with aqueous calcium chloride.

(21) R. S. Tipson, *J. Org. Chem.*, **9**, 235 (1944).

of sodium hydroxide. The alkaline mixture was allowed to stand overnight at room temperature.

The silky, tan needles were separated from an amorphous mass in the mixture by careful decantation through a Büchner funnel. The needles, still slightly moist, were crystallized from aqueous ethanol, the white crystals were washed in the funnel with 50% ethanol, and were finally dried *in vacuo*. The 1-benzenesulfonyl-2-phenylazetidide (X) so obtained weighed 6.1 g. (16%) and melted at 123.5–125°. Another 0.25 g. (0.7%) of product, m.p. 123.5–124.5°, could be isolated from the amorphous mass.

N-(3,3-Diphenylpropyl)benzenesulfonamide (II) from the Reaction of 1-Benzenesulfonyl-2-phenylazetidide (X), Benzene, and Aluminum Chloride.—A mixture of 3.48 g. (0.0128 mole) of 1-benzenesulfonyl-2-phenylazetidide (X), 2.6 g. (0.195 mole) of aluminum chloride taken from a freshly opened bottle of reagent grade material, and 50 ml. of sodium-dried benzene was treated essentially according to the procedure for the analogous reaction with 1-benzenesulfonyl-2-bromomethylethyleneimine (I).² Instead of crystallization from alcohol, addition of a small volume of ether to the viscous, oily product led to the spontaneous appearance of 1.95 g. of white, crystalline N-(3,3-diphenylpropyl)benzenesulfonamide (II), m.p. 127–128°. The melting point of a mixture with the same material (m.p. 127–128°) prepared from 1-benzenesulfonyl-2-bromomethylethyleneimine was 127–128.5°.

Further processing of the mother liquor afforded an additional 0.60 g. of benzenesulfonamide II with m.p. 126–127.5° and 0.74 g. with m.p. 124–126°. Accordingly, the yield was 3.29 g. or 73%.

When a parallel reaction was carried out according to the above method with 3.52 g. (0.0127 mole) of 1-benzenesulfonyl-2-bromomethylethyleneimine (I) in place of the azetidide X, the yield of twice-crystallized sulfonamide II, which was still faintly yellow and which showed m.p. 127–128°, was 0.67 g. (15%). This material, mixed with an earlier sample of II (m.p. 129–129.5°),¹⁰ melted at 128–129°.

Radioactivity Measurements.—A windowless flow-counter was used in the proportional region with the center-wire at a potential close to the middle of the counting plateau at 1750–2050 v. The measurements were made with solutions of the radioactive materials in formamide or dimethylformamide.^{22,23} The solution, a fixed standard of barium carbonate-¹⁴C, and an empty planchet (for background) were counted over successive, equal periods and in random order. The counts for solution and standard were corrected for background, and the ratio of the solution-to-standard counts was determined. Seven repetitions of this counting process furnished an average ratio with a standard deviation of approximately 1%. The ratio, corrected for the self-absorption of the solution and divided by the millimoles of compound in the measured solution, gave the *relative molar activity*, which served as the basis for all activity comparisons. The relative molar activity for each substance was determined in duplicate. Then, after another crystallization, the relative molar activity was determined again in duplicate. Student *t*-values showed that the relative molar activities before and after crystallization were the same. For all the measurements, the over-all standard deviation of the relative molar activities was ca. 2%.

Acrylic-1-¹⁴C Acid (XII).—The following were connected to a vacuum manifold: a reaction flask provided with a small, graduated dropping funnel and a short, vertical, water-cooled condenser (the connection to the manifold was from the top of the condenser through a stopcock); a small pear-shaped flask with a stopcock; and, through a

three-way stopcock, (a) a round-bottomed flask containing 5 g. of potassium hydroxide in 60 ml. of *n*-propyl alcohol, and (b) a flask containing barium carbonate (0.213 g. incorporating about 2.2 mc. of carbon-14 plus 11.40 g. of Baker's Analyzed material dried at 110° for 3 days; total amount, 0.0588 mole) and provided with a dropping funnel holding 35 ml. of concentrated sulfuric acid. The manifold also had outlets for a mercury U-tube manometer, and for nitrogen, which was dried by exposure in succession to concentrated sulfuric acid, calcium sulfate (Drierite) and soda-lime. All parts of the apparatus were scrupulously dried just before use.

The solution of potassium hydroxide in propanol at –80° was degassed by exposure to a mercury diffusion-pump vacuum and then disconnected from the system by closing the single stopcock just above the flask as well as the three-way stopcock. These stopcocks were not opened until the end of the reaction.

Magnesium turnings (1.45 g. or 0.0597 g.-atom of Dow resublimed material) were placed in the reaction flask, the entire system was then evacuated, filled with dry nitrogen, and re-evacuated. The flask with magnesium was flamed lightly with a yellow flame and allowed to cool. Nitrogen was bled in, removed by pumping, and again introduced until the system was under a slight positive pressure.

The dropping funnel above the reaction flask was removed, and a small crystal of iodine followed by 20 ml. of tetrahydrofuran was added to the magnesium against a stream of dry nitrogen. The tetrahydrofuran had been allowed to stand over pellets of potassium hydroxide for a day and then distilled from lithium aluminum hydride. The dropping funnel was replaced without delay. In the dropping funnel was placed a solution of 7.6 g. (0.071 mole) of freshly distilled vinyl bromide (Matheson) with 12 ml. of tetrahydrofuran. This solution was added by drops over a period of 40 min. to the stirred magnesium suspension while applying a water bath maintained at 30–35° by occasional addition of ice. After an additional 15 min. at room temperature, no magnesium remained. The yellow solution of the vinyl Grignard reagent was diluted with 50 ml. of sodium-dried ether, and the dropping funnel over the reaction flask replaced with a glass stopper.

The flow of nitrogen was interrupted, the reaction mixture was brought to liquid nitrogen temperatures, and the entire system was evacuated. With the stopcocks to the pump and to the flask containing barium carbonate closed, the Grignard solution was allowed to melt and was then stirred. When the internal pressure was approximately 25 cm., the Grignard solution was again cooled in liquid nitrogen and the entire system evacuated to a pressure of 10^{–4} mm. The stopcocks to the pump and to the Grignard solution were closed, and the liquid nitrogen bath was transferred to the small pear-shaped flask.

Addition of concentrated sulfuric acid over a period of 1 hr. to the barium carbonate released carbon dioxide, which condensed in the pear-shaped flask. Careful warming of the mixture in the carbon dioxide generator ensured the liberation of all the carbon dioxide, after which treatment the stopcock to the generator was closed.

Carbon dioxide was allowed to flow into the stirred Grignard mixture, which was held at –20 to –25°. The transfer was easily controlled by replacing the liquid nitrogen bath around the pear-shaped flask with an acetone-solid carbon dioxide bath. After completion of the transfer, the reaction mixture was stirred at –20 to –25° for 30 min. and then at –80° for another 30 min.

All residual carbon dioxide in the system was condensed in the reaction flask with the help of liquid nitrogen. The cold bath was removed, the stopcocks to the alkaline propanol flask were opened and, as the reaction mixture approached room temperature, whatever carbon dioxide that was evolved was absorbed in the alkaline propanol held at 0°. Finally, a small amount of solvent was distilled from

(22) A. Schwebel, H. S. Isbell, and J. D. Moyer, *J. Res. Natl. Bur. Std.*, **53**, 221 (1954).

(23) J. E. Stouffer, doctoral dissertation, Boston University, 1957, p. 48.

the reaction vessel to the alkaline propanol. The appropriate stopcock was closed and the flask containing the recovered carbon dioxide was removed.

An ether solution (5 ml.) containing 0.1 g. of hydroquinone was added to the carbonation mixture followed by 10 ml. of water. Solvent was removed by distillation on the steam bath at 200 mm. A solution of 8 g. of citric acid in 20 ml. of water was added, and the mixture was extracted with five 100-ml. portions of pure ether containing a trace of hydroquinone. Pilot runs had shown that acrylic acid is completely removed by this extraction. After the combined ether extracts had been dried with magnesium sulfate, most of the solvent was removed by distillation through a 25-cm. Vigreux column at bath temperatures up to 100°. More solvent was removed by reducing the pressure to 200 mm. The yellow, residual acrylic-1-¹⁴C acid (XII) was used in the reaction with anthracene without further treatment.

9,10-Dihydro-9,10-ethanoanthracene-11-(carboxylic-¹⁴C Acid) (XII).—The procedure of Scheibler and Scheibler⁷ was modified as follows.

A mixture of the above-mentioned acrylic-1-¹⁴C acid (XII), 0.2 g. of precipitated copper,²⁴ 0.1 g. of hydroquinone, 20 g. (0.112 mole) of anthracene (m.p. 211–212°), and 60 ml. of xylene was stirred and boiled for 17 hr. The mixture was filtered at room temperature, and the solids were washed with two 50-ml. portions of benzene and then with several 50-ml. portions of methanol. Volatile material was removed from the combined filtrate and washings by distillation on the steam bath, first at atmospheric pressure and then at 2 mm. Acidic material was dissolved by treating the solid residue with 200 ml. of boiling 5% aqueous sodium hydroxide and filtering the continuously stirred mixture through a steam-heated, sintered-glass funnel. The solids were rinsed on the funnel with two 100-ml. portions of hot 5% sodium hydroxide solution and then with three 100-ml. portions of hot water.

The hot, combined alkaline filtrates were acidified with concentrated hydrochloric acid and the mixture allowed to stand in the cold overnight. Filtration afforded a brown solid, which was washed with cold water and then dried at 110°. This crude product XIII, (4.0 g., m.p. 174–179°) treated with 1 g. of decolorizing carbon (Norit) in 25 ml. of ethanol and then crystallized from aqueous alcohol, gave 3.5 g. of 9,10-dihydro-9,10-ethanoanthracene-11-(carboxylic-¹⁴C acid) (XIII), m.p. 183–185°. Reworking the mother liquor after addition of 2 g. of nonradioactive material, m.p. 186–187°, afforded 1.96 g. of product, 184–186°, containing most of the remaining radioactive material. Melting points of 187–188°²⁵ and 189°²⁷ were reported before.

The conversion to product XIII from barium carbonate was approximately 25%. Approximately 13% of the carbonate could be recovered as barium carbonate, so that the corrected yield is a little higher. Pilot runs of the entire process starting with vinyl bromide resulted in conversions of 25–40%. Since pilot runs in the diene reaction starting with pure acrylic acid gave acid XIII in 85% yield, evidently the carbonation is the limiting step.

9,10-Dihydro-9,10-ethanoanthracene-11-(carboxamide-¹⁴C) (XIV).—Radioactive acid XIII (5.45 g. or 0.0218 mole, containing ca. 0.57 mc. of activity) was treated with a boiling mixture of 37 ml. of pure benzene and 8.8 g. (0.074 mole) of thionyl chloride (Eastman Kodak White Label) for 2 hr. The reaction flask was provided with a vertical condenser protected from atmospheric moisture. About 25 ml. of volatile material was removed by distillation, and the concentrated, hot solution was poured slowly into 200 ml. of vigorously stirred, concentrated aqueous am-

monia at –10°. After 15 min., the solids were collected, washed with cold water, and crystallized. A first crop (4.12 g.) was taken from *n*-butyl alcohol, a second (0.85 g.) and third crop (0.17 g.) from aqueous alcohol. Recrystallization of the combined solids from 250 ml. of xylene afforded 5.06 g. (93%) of amide XIV, which after drying showed m.p. 236–237°.

In pilot runs, several crystallizations brought the melting point of amide XIV to 238–239°.

Anal. Calcd. for C₁₇H₁₅NO: C, 81.90; H, 6.06; N, 5.62. Found: C, 82.1; H, 6.1; N, 5.6.

11-(Aminomethyl-¹⁴C)-9,10-dihydro-9,10-ethanoanthracene (XV).—The dioxane used for this preparation was boiled over sodium for 3 days, decanted from the solids, and distilled at 100–101° from lithium aluminum hydride.

A mixture of carboxamide XIV (5.06 g. or 0.0203 mole, ca. 0.53 mc.) and dioxane (500 ml.) was warmed and stirred until no solid remained. The reaction vessel was a 1000-ml. flask provided with a stirrer and a vertical condenser topped with a drying tube. A suspension of 3.0 g. (0.08 mole) of lithium aluminum hydride with 100 ml. of dioxane was added rapidly to the vigorously stirred mixture, which was then boiled and stirred for 1 hr. Stirring was continued until the mixture came to room temperature. The flask was allowed to stand overnight.

A solution of 60 ml. of concentrated hydrochloric acid plus 60 ml. of water was added by drops to the stirred mixture. The two-phase solution, free of solid, was distilled under water-pump vacuum at temperatures no higher than 100° until a thick, white semisolid remained. This was dissolved in 200 ml. of boiling water, and the solution was stored in the refrigerator. Filtration afforded the white, crystalline hydrochloride of the product XV, which was washed twice with cold 1% hydrochloric acid and then dried over sodium hydroxide pellets. This first crop, m.p. 298–301°, weighed 4.42 g. A second crop, m.p. 291–293°, could be isolated from the mother liquors (0.91 g.). Both crops were shaken with 500 ml. of cold water, 250 ml. of ether, and 20 ml. of 10% sodium hydroxide solution. The clear, aqueous layer was separated and extracted with another 200 ml. of ether. The combined ether extracts were washed twice with water, dried with magnesium sulfate, and warmed to remove solvent. Crystallization of the residue from 15 ml. of hexane afforded 4.14 g. (87%) of radioactive 11-aminomethyl-9,10-dihydro-9,10-ethanoanthracene (XV), m.p. 116.5–117°. After 0.17 g. of nonradioactive amine XV had been added to the mother liquors, further processing gave another 0.20 g. of product, m.p. 113–115°, which was combined with the main crop.

In preliminary experiments with nonradioactive materials, recrystallizations from *n*-heptane furnished a sample of amine XV, m.p. 116.5–117°, for analysis.

Anal. Calcd. for C₁₇H₁₇N: C, 86.77; H, 7.28; N, 5.95. Found: C, 86.19; H, 7.2; N, 5.9.

The corresponding hydrochloride was prepared by treating 0.1 g. of the pure amine in 10 ml. of ether with 0.13 ml. of concentrated hydrochloric acid plus 3 ml. of ethanol. After 1 hr., the mixture was filtered, and the solid was washed twice and then dried at 75–80° (0.025 mm.). The hydrochloride of aminomethyl compound XV showed m.p. 310–310.5°.

Anal. Calcd. for C₁₇H₁₈ClN: C, 75.12; H, 6.67; Cl, 13.05; N, 5.15. Found: C, 74.9; H, 6.9; Cl, 13.0; N, 5.2.

N-(Allyl-1-¹⁴C)-benzenesulfonamide (XVII).—A finely ground mixture of 11 g. of anthracene and 4.34 g. (0.0185 mole) of 11-(aminomethyl-¹⁴C)-9,10-dihydro-9,10-ethanoanthracene (XV) was placed in a 50-ml. pear-shaped flask together with 0.5 g. of finely ground clay plate. The reaction flask had a side arm through which nitrogen could be passed. The flask was provided with a short air condenser connected to an exit tube which carried escaping gases first to the bottom of a tube containing 50 ml. of water at 0° and then into a solution of 1.5 ml. of concentrated hydro-

(24) A. I. Vogel, "Practical Organic Chemistry," Longmans, Green, & Co., New York, N. Y., 1956, p. 192.

(25) A. Ya. Berlin, *Chem. Abstr.*, **47**, 8712 (1953) [*Zh. Obshch. Khim.*, **22**, 1656 (1952)].

chloric acid plus 25 ml. of water. After the system had been thoroughly flushed with nitrogen, the nitrogen flow was adjusted to *ca.* 25 bubbles per min., and a Wood's metal bath at 320° was raised under the flask. Immediate evolution of gas was noted. The bath temperature was raised to 350° over a period of 30 min.

The combined contents of the two receiving vessels in a tightly stoppered flask were vigorously shaken with 55 ml. of 10% sodium hydroxide solution and 4.8 g. (0.027 mole) of redistilled benzenesulfonyl chloride for 20 min. The reaction mixture was filtered first through fluted filter paper and then through a mat of filter aid (Hyflo-Supercel). Acidification of the chilled, clear filtrate with 12.5 ml. of concentrated hydrochloric acid gave a cloudy solution, which after standing cold overnight changed to a crystalline precipitate. The solids were collected, washed on the funnel with three portions of cold water, and dried overnight *in vacuo* over sodium hydroxide pellets. The white, crystalline *N*-(allyl-1-¹⁴C)benzenesulfonamide (XVII) so obtained weighed 2.46 g. (67%) and melted at 40–40.5°. In a pilot experiment, a sample of the sulfonamide prepared in this way (m.p. 39.5–40.5°), when mixed with authentic material (m.p. 39.0–41.0°), showed m.p. 39.5–41.0°.

Duplicate determinations of the relative molar activity gave values of 25.64 and 26.07 (average, 25.85). Recrystallization of the radioactive product from aqueous alcohol afforded 2.04 g. of sulfonamide XVII, m.p. 40–40.5°, with a relative molar activity of 25.68 and 25.76 (average, 25.72).

Formaldehyde (XXIII) from the Ozonolysis of *N*-(Allyl-1-¹⁴C)benzenesulfonamide (XVII).—A solution of 17.79 mg. of radioactive sulfonamide XVII plus 224.7 mg. of the same nonradioactive sulfonamide (total amount: 0.00123 mole with relative molar activity, 1.886) in 70 ml. of methylene dichloride that had been distilled from calcium hydride was treated with oxygen and ozone at a rate of 6.06×10^{-5} moles of ozone per min. The methylene dichloride solution was held at acetone–Dry Ice temperatures. After 21 min., at which time 0.00127 mole of ozone had been added, the solution became blue. The stream of ozonized oxygen was replaced with one of nitrogen while the temperature was allowed to reach room temperature. Nitrogen was bubbled through the solution placed in a 35–45° bath until the volume was *ca.* 10 ml. This concentrated solution was added dropwise to a vigorously stirred suspension of 1.5 g. of zinc dust in 50 ml. of water. The mixture was stirred further for 30 min. and then allowed to stand overnight.

After solids were removed by filtration and rinsed with water and ether, the aqueous phase was treated with 20 g. of sodium chloride and was extracted with six 25-ml. portions of ethyl acetate. The aqueous phase was diluted to 400 ml. with water, a solution of 0.5 g. (0.0036 mole) of methone in 10 ml. of alcohol was added, and the mixture was allowed to stand in the cold overnight. The white, crystalline precipitate of formaldehyde dimethone was collected, washed several times with cold water, and dried over sodium hydroxide pellets at 30 mm. This material, m.p. 186–187°, weighed 181 mg. (50%) and showed relative molar activities of 0.2581 and 0.2488. Recrystallization from a mixture of 10 ml. of alcohol and 6 ml. of water gave 134 mg. of formaldehyde dimethone, m.p. 187.5–188°, with relative molar activity values of 0.2594 and 0.2507. Accordingly, approximately 14% of the activity of allyl derivative XVII appears in the formaldehyde formed by ozonolysis.

***N*-(benzenesulfonyl)glycine-2-¹⁴C (XIX) from the Ozonolysis of *N*-(Allyl-1-¹⁴C)benzenesulfonamide (XVII).**—A solution of 0.0936 g. of radioactive sulfonamide XVII and 1.81 g. of the same nonradioactive material (total amount, 0.0096 mole with relative molar activity, 1.266) in 71 ml. of methylene dichloride was treated with a molar proportion of ozone essentially as described above. After excess ozone had been removed in a stream of nitrogen, the solution, at room temperature, was added dropwise to a

hot, vigorously stirred suspension of silver oxide²⁶ in 300 ml. of 10% aqueous sodium hydroxide. The mixture was then stirred at 90–95° for 3 hr. and allowed to stand overnight.

Filtration removed the solids, which were rinsed with some 10% sodium hydroxide solution. The filtrate and washings were acidified with 70 ml. of concentrated hydrochloric acid, filtered, and then concentrated by distillation from a 100° bath under 120 mm. until salt began to separate. After addition of just enough water to dissolve the salt in the cold mixture, it was extracted with six 50-ml. portions of ethyl acetate. The combined extracts were washed with two 20-ml. portions of cold water, and the almost colorless solution was concentrated to 15 ml. Cooling caused crystals to appear. Small portions of petroleum ether (b.p. 30–60°), 30 ml. in all, were added as the product crystallized, and finally the mixture was stored in the cold overnight.

The precipitate was collected, recrystallized from 12 ml. of water, and the purified material dried in a vacuum desiccator over concentrated sulfuric acid. The *N*-(benzenesulfonyl)glycine-2-¹⁴C (XIX) so obtained weighed 0.99 g. (48%) and showed m.p. 165–167°. Cocker and Lapworth²⁷ reported m.p. 165°.

Methyl Ester of *N*-Benzenesulfonylglycine-2-¹⁴C (XIX).—Diazomethane in large excess (0.8 g. in 25 ml. of ether) was added to a stirred, cold suspension of 0.99 g. (0.0046 mole) of *N*-benzenesulfonylglycine-2-¹⁴C (XIX) in 50 ml. of ether. After 4 hr. of stirring at 0°, the solution was treated with a few drops of ethereal acetic acid and then washed with two 10-ml. portions of 10% aqueous sodium bicarbonate followed by one 10-ml. portion of water. After all solvent had been removed from the dried (magnesium sulfate) solution, crystallization of the viscous residue from a mixture of 6 ml. of chloroform and 40 ml. of petroleum ether afforded the desired ester. This material, after careful drying, weighed 0.74 g. (70%) and showed m.p. 65–65.5°. In similar pilot experiments yields as high as 86% were obtained. Esterification by boiling glycine XIX in 10:1 methanol–benzene containing a small amount of concentrated sulfuric acid gave the same product, which after several recrystallizations showed m.p. 64.5–65°.

Anal. Calcd. for C₉H₁₁NO₄S: C, 47.16; H, 4.84. Found: C, 47.2; H, 4.9.

***N*-(2-Hydroxy-2,2-diphenylethyl-1-¹⁴C)benzenesulfonamide (XX).**—An earlier set of directions²⁸ was modified as follows. The methyl ester of *N*-benzenesulfonylglycine-2-¹⁴C (XIX) (0.74 g. or 0.0032 mole) in 25 ml. of sodium-dried ether was added over a 5-min. period to a vigorously stirred Grignard reagent prepared from 10 g. (0.0063 mole) of bromobenzene, 1.25 g. (0.0051 g.-atom) of Dow sublimed magnesium, and 75 ml. of sodium-dried ether. An atmosphere of nitrogen was maintained over the reaction mixture during the addition and the subsequent 6-hr. period of stirring.

The mixture was allowed to stand overnight and was then poured over a mixture of 240 g. of ice and water containing 12 ml. of concentrated hydrochloric acid. The aqueous layer was extracted with 75 ml. of ether, and the combined ether solutions were washed in succession with 30 ml. portions of water, 10% aqueous sodium bicarbonate, and water. The solution was dried with magnesium sulfate and the solvent was removed.

The yellow, residual oil in 25 ml. of benzene was placed on a 2.5 × 13 cm. column of alumina (60 g. of Merck material). The following solvents were then passed through the column: (a) 250 ml. of benzene, (b) 350 ml. of ether, and (c) 660 ml. of a mixture of 10 volumes of ether and 1 volume of absolute ethanol. The material in the ether–ethanol eluate was freed of all solvent and then dissolved in a solution of 10 ml. of acetic acid and 10 ml. of water. After

(27) W. Cocker and A. Lapworth, *J. Chem. Soc.*, 1894 (1931).

(28) F. Bettzieche, R. Menger, and K. Wolf, *Z. physiol. Chem.*, 160, 270 (1926).

treatment with a small amount of decolorizing carbon (Norit), the solution was allowed to stand cold for 4 hr. The crystals of N-(2-hydroxy-2,2-diphenylethyl-1-¹⁴C)benzenesulfonamide (XX) were collected, washed, and dried *in vacuo* over sodium hydroxide. This product (0.53 g. or 47%), m.p. 135–136°, was analyzed for radioactivity and then recrystallized from a mixture of benzene (10 ml.) and *n*-hexane (20 ml.). The white, needlelike crystals of hydroxysulfonamide XX (0.47 g.), m.p. 136–137°, were reanalyzed.

Relative molar activity of XX before final crystallization: 1.371, 1.238 (average, 1.304); after final crystallization: 1.257, 1.263 (average, 1.260).

Formaldehyde (XXII) and Benzophenone (XXI) by Cleavage of N-(2-Hydroxy-2,2-diphenylethyl-1-¹⁴C)benzenesulfonamide (XX) with Lead Tetraacetate.—A mixture of 0.440 g. (0.00125 mole) of hydroxysulfonamide XX, 1.3 g. (0.0019 mole) of lead oxide (Pb₂O₄),²⁹ and 4.7 ml. of acetic acid was stirred and heated on the steam bath until the lead oxide had dissolved. After an additional 1.5 hr. on the steam bath, 20 ml. of hot water was added, and the mixture was boiled for a few seconds. After further dilution with 55 ml. of cold water, the benzophenone product was removed by extraction with two 55-ml. portions of ether.

The aqueous layer, containing the formaldehyde product XXII, was filtered through a mat of filter aid (Hyflo-Supercel). After addition of 10% sodium acetate solution until the pH was 4.5, 10 ml. of alcoholic methone (0.55 g. or 0.0039 mole) was added, and the cloudy mixture was allowed to stand overnight. The solids were collected, washed with water, dried, and finally recrystallized from 6 ml. of 95% alcohol. The resulting formaldehyde dimethone (0.214 g. or 58%; m.p. 187.5–188.5°), after analysis for radioactivity was crystallized again from 95% alcohol to give the same product (0.116 g.), m.p. 187.5–188°.

Relative molar activity of the formaldehyde dimethone before final crystallization: 1.315, 1.243 (average, 1.279); after final crystallization: 1.292, 1.284 (average, 1.288).

The ether solution containing the benzophenone was washed with three 30-ml. portions of 1% aqueous sodium hydroxide, followed by two small portions of water. The ether solution was dried with magnesium sulfate and then concentrated. The almost colorless, oily residue on treatment with freshly distilled phenylhydrazine in methanol afforded benzophenone phenylhydrazone (0.032 g., m.p. 134–135.5° after two crystallizations). A final crystallization from methanol-water-dimethylformamide solvent gave the same material with m.p. 135–135.5°.

Relative molar activity of the benzophenone phenylhydrazone before final crystallization: -0.003; after final crystallization: 0.003. Because of the low activity, the standard deviations of the actual counts were 44 and 60%, respectively.

1-Benzenesulfonyl-2-bromomethylethyleneimine-3-¹⁴C (XVIII).—N-(Allyl-1-¹⁴C)benzenesulfonamide (XVII) was diluted with nonradioactive material until the weight was 4.00 g. (0.0203 mole). This material was first brominated and then treated with aqueous sodium hydroxide³⁰ to give 5.34 g. (97%) of 1-benzenesulfonyl-2-bromomethylethyleneimine-3-¹⁴C (XVIII), m.p. 87.5–88°.

N-(3,3-Diphenylpropyl-1-¹⁴C)-benzenesulfonamide (XXIV).—A mixture of 5.34 g. (0.0193 mole) of 1-benzenesulfonyl-2-bromomethylethyleneimine-3-¹⁴C (XXIV) and 4.0 g. (0.030 mole) of aluminum chloride in 80 ml. of pure benzene was treated essentially as described before.² Three crystallizations of the product from 95% alcohol gave 1.52 g. (22%) of N-(3,3-diphenylpropyl-1-¹⁴C)benzenesulfonamide (XXIV), m.p. 126–127°. Further processing of the mother liquors, including addition of a total of 2.18 g. of nonradioactive material as scavenger, furnished another 2.21 g. of product

XXIV, m.p. 126.5–127.5°. The two fractions were combined.

3,3-Diphenylpropylamine-1-¹⁴C Hydrochloride (XXV).—A mixture of N-(3,3-diphenylpropyl-1-¹⁴C)benzenesulfonamide (XXIV) with enough nonradioactive material to bring the total weight to 4.00 g. (0.0116 mole), 8 g. of pure phenol, and 60 ml. of freshly distilled 48% aqueous hydrobromic acid was stirred and boiled for 3 hr. according to the general directions of Snyder and Heckert.¹² The cooled mixture was poured into 600 ml. of water. The aqueous layer as well as the heavy, red oil was washed with 350 ml. of ether in several portions. The ether was rinsed with 100 ml. of water, which was returned to the aqueous system. The ether layer was discarded.

Sodium hydroxide solution (250 ml. of 10%) was added to the aqueous system, which was then extracted with 200 ml. of ether. Nonradioactive 3,3-diphenylpropylamine hydrochloride (1.00 g.) was added to the alkaline aqueous solution, and the extraction was repeated with 100 ml. of ether. After the combined ether extracts were dried with magnesium sulfate, they were treated with 1.3 ml. of concentrated hydrochloric acid plus 50 ml. of ether. The crystalline solids that formed when this mixture was allowed to stand in the cold overnight were collected, washed twice on the funnel with ether, and dried over sodium hydroxide pellets. The 3,3-diphenylpropylamine-1-¹⁴C hydrochloride (XXV) so obtained weighed 3.06 g. (71%) and showed m.p. 212.5–213.5°.

Relative molar activity: 4.992, 4.947 (average, 4.970).

The radioactive hydrochloride, mixed with an equal weight of pure nonradioactive material, was recrystallized from absolute alcohol-petroleum ether (m.p. 30–60°). The hydrochloride was recovered in three crops (total weight, 5.99 g.), m.p. 213–214°. The first and main crop was analyzed for radioactivity.

Relative molar activity: 2.454, 2.410 (average, 2.432).

N,N-Dimethyl-3,3-diphenylpropylamine-1-¹⁴C (XXVI).³⁰—A mixture of 5.75 g. (0.0232 mole) of 3,3-diphenylpropylamine-1-¹⁴C (XXV) hydrochloride (relative molar activity, 2.432), and 100 ml. of 2.5% cold aqueous sodium hydroxide was extracted with 200 ml. of ether in three portions. The combined ether solutions were dried (magnesium sulfate), and all solvent was removed at 100° under water-pump vacuum. The residual oil, cooled to 0°, was treated with 5.0 ml. of 98–100% formic acid, and the mixture was stirred at room temperature until all solids dissolved. After 5.5 ml. of 37% aqueous formaldehyde had been added (cooling and swirling), the solution was heated on the steam bath under a vertical condenser for 5 hr.

Cold 4% sodium hydroxide solution (125 ml.) was added, and the alkaline mixture was extracted with 200 ml. of ether in three portions. The combined etheral extracts were dried with magnesium sulfate. Removal of solvent and distillation of this residual oil afforded 4.31 g. of product, b.p. 118–121° (0.4 mm.). Crystallization of this material from petroleum ether (b.p. 30–60°) at -23° gave 3.39 g. (61%) of white, crystalline N,N-dimethyl-3,3-diphenylpropylamine-1-¹⁴C (XXVI), m.p. 43–44°. The melting points reported before for this material range from 42 to 46°.³¹

3,3-Diphenylpropene-1-¹⁴C (XXVII).¹⁴—The radioactive N,N-dimethyl-3,3-diphenylpropylamine (XXVI) (3.39 g.) in methanol (8 ml.) was converted to its N-oxide with 6.5 ml. of 30% hydrogen peroxide solution. Pyrolysis of the methanol-free N-oxide at 70–170° followed by redistillation of the crude product through a 2-in. Vigreux column gave

(30) Cf. R. N. Icke and B. B. Wisegarver, "Organic Synthesis," Coll. Vol. III, Wiley, New York, N. Y., 1955, p. 723; M. L. Moore, *Org. Reactions*, **5**, 307 (1949).

(31) D. W. Adamson, *J. Chem. Soc.*, **1949**, S144; A. W. Ruddy, *J. Am. Chem. Soc.*, **73**, 4096 (1951); N. Sperber, M. Sherlock, and D. Papa, *ibid.*, **75**, 1122 (1953).

(29) J. G. N. Drewitt, *Chem. Abstr.*, **40**, 1537 (1946) [U. S. Patent 2,389,187 (1945)].

2.27 g. (82%) of 3,3-diphenylpropene-1-¹⁴C (XXVII), b.p. 89–92° (0.5 mm.).

In preliminary work, nonradioactive 3,3-diphenylpropene b.p. 105–107° (0.7 mm.), n_D^{20} 1.5777, n_D^{25} 1.5756, was prepared in the same way.

Anal. Calcd. for C₁₅H₁₄: C, 92.74; H, 7.26. Found: C, 92.6; H, 7.2.

The neat liquid showed infrared absorption peaks at 10.03 and 10.88 μ . A 2.26×10^{-3} M solution in carbon tetrachloride showed ultraviolet absorption maxima at 270.5 m μ (log ϵ 2.67) and 262 m μ (log ϵ 2.82). The spectrum is similar to that of diphenylmethane,³² which has maxima at 269 m μ (log ϵ 2.6) and 259 m μ (log ϵ 2.7), but is different from that of 1,1-diphenylpropene,³² which has maxima at 294 m μ (log ϵ 2.5) and 250 m μ (log ϵ 4.1).

3,3-Diphenylpropene-1 has been reported before¹⁴ with n_D^{25} 1.5754 and with absorption maxima in 95% alcohol at 270 m μ (log ϵ 2.55), 260 (2.72), 255 (2.68), and 250 (2.59).

Formaldehyde (XXIX) and Diphenylacetaldehyde (XXVIII) from the Ozonolysis of 3,3-Diphenylpropene-1-¹⁴C (XXVII).—A solution of 0.768 g. (0.00395 mole) of 3,3-diphenylpropene-1-¹⁴C (XXVII) in 70 ml. of methylene chloride at Dry Ice–acetone temperatures was treated with ozone–oxygen until, after 14 min., 0.00390 mole of ozone had been absorbed. Excess ozone was removed in a stream of nitrogen.

Zinc dust (5 g.) was treated with 20 ml. of 10% acetic acid for 5 min. The acid was removed by decantation, and the zinc was rinsed by slurring with water and decanting.

After addition of the moist zinc and 25 ml. of precooled absolute alcohol to the methylene chloride solution, the mixture was stirred at Dry Ice–acetone temperatures for a short time. The cold bath was removed, and the stirred mixture was allowed to warm to 0°. Ice water (25 ml.) was added and stirring was continued for 2 hr. at room temperature. Solids were removed by filtration and were rinsed once with water and once with methylene chloride. The organic layer in the filtrate was shaken with two 25-ml. portions of water, one 25-ml. portion of 10% sodium bicarbonate solution, and two 25-ml. portions of water. All the aqueous phases were combined.

Solvent was removed from the methylene chloride solution by distillation on the steam bath under water-aspirator vacuum. A mixture of the oily residue in 20 ml. of methanol

with 0.74 g. of semicarbazide hydrochloride and 1.10 g. of sodium acetate crystals in 7.5 ml. of water was warmed at 100° to dissolve all solids and was allowed to stand at room temperature overnight. Two crops of solids were collected, combined, and recrystallized from methanol–water (2:1) to give 0.73 g. (73%) of crystalline diphenylacetaldehyde (XXVIII) semicarbazone, m.p. 162–163°.

Relative molar activity: 0.0042, 0.0026 (average, 0.0034).

Authentic diphenylacetaldehyde was prepared by rearrangement of hydrobenzoin,³³ purified through the bisulfite addition compound,³⁴ and converted as above to the semicarbazone, m.p. 161–162°. The diphenylacetaldehyde obtained in preliminary ozonolysis experiments gave a semicarbazone with m.p. 161.5–162.5°. A mixture with authentic material melted at the same temperature; a mixture with benzophenone semicarbazone (m.p. 164–165°) melted at 127–149°.

The aqueous solution of formaldehyde (XXIX) was adjusted to pH 4.5 by addition of acetic acid, was rinsed once with methylene chloride and once with ether, and was treated as before with methone (1.75 g. or 0.0125 mole) in alcohol (35 ml.). The radioactive formaldehyde dimethone obtained here (1.01 g., 87%) showed m.p. 187–188°. Recrystallization from 95% alcohol brought the melting point to 187.5–188°.

Relative molar activity of the formaldehyde dimethone before final crystallization: 2.409, 2.445 (average, 2.427); after final crystallization: 2.399, 2.446 (average, 2.423).

Benzophenone from Diphenylacetaldehyde Semicarbazone.—A mixture of diphenylacetaldehyde semicarbazone (0.25 g. or 0.001 mole), pyridine (5 ml.,³⁵ potassium permanganate (1.0 g.), sodium hydroxide (2.5 g.), and water (45 ml.) was boiled for 1 hr. Addition of solid sodium bisulfite both before and after acidification with 10% sulfuric acid decomposed all permanganate and manganese dioxide. Cooling the resulting mixture for 18 hr. resulted in the precipitation of 0.14 g. (77%) of still yellow benzophenone, m.p. 46–47°. A mixture with authentic material (m.p. 47.5–49°) showed m.p. 46.5–48°.

The semicarbazone of the oxidation product melted at 163.5–164.5°; the semicarbazone of benzophenone has been reported with m.p. 164–165°.³⁶

(33) W. G. M. Weise, *Ann.*, **248**, 34 (1888).

(34) A. Breuer and T. Zincke, *ibid.*, **198**, 141 (1879).

(35) Cf., J. T. Eaton, D. B. Black, and R. C. Fuson, *J. Am. Chem. Soc.*, **56**, 687 (1934).

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