Sulfonanilide.—White crystals (89%) from isoöctane, m. p., 133.5–134.2°.

Anal. Calcd. for $C_{16}H_{18}O_4N_2S$: C, 58.0; H, 5.3. Found: C, 57.8; H, 5.1.

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Production of Radioactive Carbon Monoxide from Barium Carbonate

BY JOSEPH T. KUMMER[1]

It has been found possible to prepare conveniently a supply of radioactive carbon monoxide of a specific activity and sufficient in quantity for use in the study of many catalytic reactions. This is done by exchanging, over a hot tungsten filament, the C^{14} in a small amount of carbon dioxide obtained from barium carbonate of high specific activity (about 0.5% of the carbon in the barium carbonate was C^{14}) with the carbon in a large amount of normal carbon monoxide. Since the apparatus and procedure are extremely simple, and since such exchange experiments have not previously been described for a tungsten surface,[2] they are described below in conjunction with Fig. 1. It is hoped that the method will be useful to those wishing to employ carbon monoxide for tracer studies.

The system is completely evacuated, before the exchange run, to 10^{-5} mm. or better. Then, with stopcock A closed, the bulb containing 85% H_3PO_4 is rotated and the acid allowed to react with a few mg. of the radioactive barium carbonate. When stopcock A is opened, the carbon dioxide is allowed to pass through the Dry Ice trap into trap X, cooled in liquid nitrogen. The acid–carbonate mixture is evacuated and warmed to drive all of the carbon dioxide out of the solution and into trap X. This carbon dioxide is next allowed to evaporate into the electric light bulb and is diluted with the required amount of carbon monoxide, manometer C being used for estimating approximately the amount of carbon monoxide added. If the light bulb is run at 60–80 volts overnight (sixteen hours) the exchange will be complete. No experiments have been made as to the rate of exchange or length of time it would take if the bulb were run at 110 volts. Carbon filament bulbs were originally tried but were found to be unsatisfactory because their filaments burned out in an atmosphere of carbon monoxide within a few hours. After a year of use, the tungsten filament showed no deterioration. When the exchange is complete, the radioactive carbon monoxide is pumped into the storage reservoir by means of a Töpler pump through

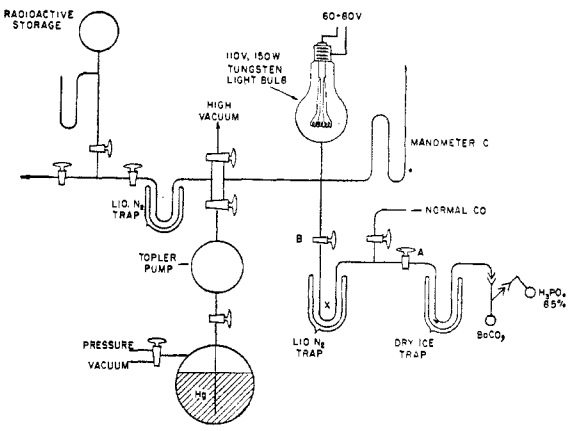

Fig. 1.

a liquid nitrogen trap, to remove the carbon dioxide.

Below are data for a particular test run using a new, 150-watt, 110-volt Westinghouse tungsten filament light bulb.

A sample of 2.6 mg. of BaC^*O_3[3] was taken; it was capable of producing approximately 10^7 disintegrations per minute. The C^*O_2 in trap X was flushed into the light bulb by 200 cc. of normal carbon monoxide (to a total pressure of about 300 mm.) after the liquid nitrogen was removed from trap X. After the C^*O_2 and carbon monoxide had been mixed by a few strokes of the Töpler pump, a 1-cc. sample was removed for analysis (*without* interposing a liquid nitrogen trap); this sample showed 42,000 disintegrations per minute per cc. of gas.

A similar sample taken *through* a liquid nitrogen trap for removing carbon dioxide showed 190 disintegrations per minute per cc. of gas.

After the filament in the bulb had been operated at 70 volts for sixteen hours, a 1-cc. sample removed *through* a liquid nitrogen trap showed a count of 42,100 disintegrations per minute per cc. of gas. Apparently, therefore, the exchange over the tungsten filament was complete in this period of time.

(1) Gulf Research & Development Company Fellowship, Mellon Institute of Industrial Research, Pittsburgh, Pa.

(2) Brandner and Urey, *J. Chem. Phys.*, **13**, 351 (1945), have studied the kinetics of C^{13} exchange between CO and CO_2 over quartz, Au, and Ag.

(3) An asterisk is used to designate C^{14}.

RECEIVED JULY 10, 1947

Thiophene-Containing Antihistaminic Agents

BY L. P. KYRIDES, F. C. MEYER AND F. B. ZIENTY

The high order of antihistaminic activity recently reported for the thiophene analog (I)[1,2,3] of Pyribenzamine was observed[4] on (I) prepared in this Laboratory and tested prior to Dr. Weston's disclosure. In addition, several other

(1) Weston, THIS JOURNAL, **69**, 980 (1947).

(2) Clapp, Clark, Vaughan, English and Anderson, *ibid.*, **69**, 1549 (1947).

(3) Roth, Richards and Shepperd, *Federation Proc.*, **6**, 366 (1947).

(4) Lee, Dinwiddie and Chen, *J. Pharmacol. Exptl. Therap.*, **90**, 83 (1947).

analogs of known antihistaminic agents have been prepared and evaluated.

Whereas N,N-dimethyl-N′-phenyl-N′-(2-thenyl)-ethylenediamine (2740 R. P.) (II), the thiophene analog of Antergan,[5] recently was reported to be devoid of antihistaminic activity,[6] our compound proved to be approximately two-thirds as active as Antergan. The diethyl analog (III) of (II) is only one-fifth as active as Antergan; (I) is more active than (II) and has given encouraging results in man.

2-[N-(2′-Thenyl)-anilinomethyl]-2-imidazoline (IV), the thiophene analog of Antistine,[7] 2-(N-benzylanilinomethyl)-2-imidazoline, was found to be only 5% as active as Antergan, and the thiophene analog (V) of N-(2-pyridyl)-benzamide[8] proved to be inactive.

The products were tested for pharmacologic and therapeutic activity in the Lilly Research Laboratories.

Experimental[9]

N,N-Dimethyl-N′-phenyl-N′-(2-thenyl)-ethylenediamine (II).—N,N-Dimethyl-N′-phenylethylenediamine (VI)[10] (26.6 g.) in 100 cc. of benzene was converted to the monohydrochloride, 10.7 g. of 2-thenyl chloride in 35 cc. of benzene was added, and the mixture was stirred at 65–70° for six hours. The mixture was agitated with 80 g. of 25% sodium hydroxide solution at 60° for one hour, and the benzene layer was separated. A dark-colored liquid, weight 15 g., was present between the aqueous and benzene layers; this probably was a quaternary compound resulting from reaction of 2-thenyl chloride with the dimethylamino group. The benzene layer yielded upon distillation 15.8 g. of recovered (VI) and 7.0 g. (42.5%) of (II), a yellow oil, b. p. 185–186° (8 mm.).

The base (II), dissolved in a 3:1 solution of carbon tetrachloride and acetone, upon treatment with hydrogen chloride yielded the monohydrochloride, which was recrystallized from acetone containing a small amount of water; m. p. 183–184°.

Anal. Calcd. for $C_{15}H_{20}N_2S\cdot HCl$: Cl, 11.9. Found: Cl, 11.9.

When it was endeavored to prepare (II) by the procedure used for (III), the quaternary salt was the chief product. Attempts to prepare (II) by the reaction of N-(2-thenyl)-aniline (VII) and N,N-dimethyl-β-chloroethylamine hydrochloride proved unsuccessful, since none of the high boiling amines obtained corresponded in properties with those of (II).

N,N-Diethyl-N′-phenyl-N′-(2-thenyl)-ethylenediamine (III).—A solution of 6.6 g. (0.05 mole) of 2-thenyl chloride in 65 cc. of benzene was dropped into a solution of 19.2 g. (0.10 mole) of N,N-diethyl-N′-phenylethylenediamine (VIII)[11] in 100 cc. of butanol at 25° during two hours. The mixture was stirred at 25° for twenty hours, treated with excess aqueous alkali, and the organic layer was separated and distilled. Nine grams of (VIII) was recovered and 9 g. (59%) of (III)[12] was obtained; b. p. 157–160° (2 mm.).

When (III) was treated with hydrogen chloride as under (II), the dihydrochloride was precipitated as an oil which soon solidified. After recrystallization from aqueous acetone, the salt melted at 144–145°.

Anal. Calcd. for $C_{17}H_{24}N_2S\cdot 2HCl$: Cl, 19.6. Found: Cl, 19.7.

N-(2-Thenyl)-aniline (VII).—One mole (93 g.) of aniline was heated with agitation at 95–100° as 39.8 g. (0.3 mole) of 2-thenyl chloride was added in one and one-half hours. The mixture was maintained at 95–100° for four hours, cooled and treated with aqueous sodium hydroxide (0.3 mole). The oil layer was separated, washed with water, and dried over sodium sulfate. The crude product was fractionated under reduced pressure. After a forerun of recovered aniline, there was obtained 43 g. (76%) of (VII); b. p. 150–155° (4 mm.), $n^{20}D$ 1.6295.

Anal. Calcd. for $C_{11}H_{11}NS$: N, 7.4. Found: N, 7.8.

Ethyl N-Phenyl-N-(2-thenyl)-aminoacetate (IX).—A mixture of 30 g. (0.16 mole) of (VII) and 9.8 g. (0.08 mole) of ethyl chloroacetate was heated at 120° for six hours. The mixture was cooled, treated with aqueous sodium hydroxide (0.1 mole), benzene was added, and the organic layer was separated, washed with water and dried. After removal of the solvent, the crude product was fractionated; yield, 10 g. (45%) of (IX), b. p. 155–165° (0.3 mm.).

Anal. Calcd. for $C_{15}H_{17}NO_2S$: N, 5.1. Found: N, 5.1.

2-[N-(2′-Thenyl)-anilinomethyl]-2-imidazoline (IV).—A mixture of 13 g. (0.047 mole) of (IX) and 25 g. of ethylenediamine (97.4% assay) was heated at the boiling point as ethanol, water, and some ethylenediamine were removed slowly through a small fractionating column over a period of twenty hours. The vapor temperature at the end was 116° and the batch temperature rose to 130–135°. After removing the excess ethylenediamine, the residue was fractionated to yield 7 g. (55%) of (IV), b. p. 190–200° (0.4 mm.). The base was converted to the monohydrochloride, which was recrystallized from acetone-ethanol; m. p. 219–220°.

Anal. Calcd. for $C_{15}H_{17}N_3S\cdot HCl$: Cl, 11.5. Found: Cl, 11.8.

N-(2-Pyridyl)-2′-thiophenecarboxamide (V).—To a solution of 47 g. (0.5 mole) of 2-aminopyridine in 250 cc. of dry toluene 12 g. (0.5 mole) of sodium hydride was added, and the mixture was warmed slowly to reflux as hydrogen was evolved. After refluxing for one and one-half hours, the resulting slurry of the sodium derivative of 2-aminopyridine was cooled to 80° and 73.3 g. (0.5 mole) of 2-thenoyl chloride[13] was added dropwise in one hour. The mixture then was refluxed for two hours, cooled, filtered and the salt cake was washed with toluene. The filtrate upon distillation yielded 87 g. (85%) of (V), b. p. 165–170° (2 mm.). The product, which solidified on cooling, was converted to the monohydrochloride in methyl ethyl ketone–ethanol mixture and the salt was allowed to crystallize; m. p. 215–217°, with slight previous softening.

Anal. Calcd. for $C_{10}H_8N_2OS\cdot HCl$: Cl, 14.7. Found: Cl, 14.6.

(5) Halpern, *Arch. intern. pharmacodynamie*, **68**, 339 (1942).

(6) Viaud, *Produits Pharmaceutiques*, **2**, 53 (1947).

(7) Meier and Bucher, *Schweiz. med. Wochschr.*, **76**, 294 (1946); Schindler, *ibid.*, **76**, 300 (1946); abstract in *J. Am. Med. Assoc.*, **131**, 1536 (1946).

(8) Mayer, *J. Allergy*, **17**, 153 (1946).

(9) All melting points are corrected.

(10) Huttrer, Djerassi, Beears, Mayer and Scholz, THIS JOURNAL, **68**, 2001 (1946).

(11) Dewar, *J. Chem. Soc.*, 622 (1944).

(12) A sample of this base was prepared by Mr. D. G. Sheets.

(13) Blicke and M. F. Zienty, THIS JOURNAL, **63**, 2945 (1941); Jones and Hurd, *ibid.*, **43**, 2444 (1921).

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The Vibration Spectrum of Nitric Acid

BY OTTO REDLICH

The fairly weak Raman line 1538 cm.$^{-1}$ in the Raman spectrum of pure nitric acid was interpreted[1] as due to the out-of-plane vibration for

(1) O. Redlich and L. E. Nielsen, THIS JOURNAL, **65**, 654 (1943).