Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.3; H, 9.2. Found: C, 76.0; H, 9.2.

***allo*-Pregnan-3,12,20-trione from Desoxycholic Acid.**—Using essentially the procedures described in the literature,[4-7] desoxycholic acid was converted to 3(α)-hydroxy-12(α)-acetoxypregnan-20-one, m. p. 205–206°, $[\alpha]^{25}D$ +150° in acetone (literature[7]: m. p. 208–210°, $[\alpha]D$ +151 ± 6° in acetone) and then to 12(α)-acetoxyprogesterone,[6] m. p. 181°, $[\alpha]^{26}D$ +215° and $[\alpha]^{26}_{5461}$ +259° in chloroform, absorption maximum at 240 mμ (log ε 4.14 in ethanol).

To 500 mg. of 12(α)-acetoxyprogesterone dissolved in 60 ml. of absolute ethanol was added 6 g. of sodium during fifty minutes at steam-bath temperature. The reaction mixture was diluted with ether and the ethereal solution was washed and evaporated to dryness. The residue was then oxidized with 1.14 g. of chromic anhydride in 114 ml. of acetic acid at room temperature for twelve hours. The reaction mixture was processed as described above for the product from hecogenin to give crude material from ether, m. p. 185–194°, wt. 120 mg. Recrystallization from aqueous methanol gave *allo*-pregnan-3,12,20-trione as needles, m. p. 206–208°, $[\alpha]^{23}D$ +184° and $[\alpha]^{23}_{5461}$ +224° (chloroform), no maximum at λ 240 mμ.

Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.3; H, 9.2. Found: C, 76.0; H, 8.9.

The reduction was also accomplished with hydrogen and Adams catalyst in acetic acid at room temperature and three atmospheres for five hours. After hydrolyzing with 2% alcoholic potash and oxidizing with chromic acid as described above, the product was crystallized from ether, m. p. and mixed m. p. with above, 206–208°.

Pregnan-3,12,20-trione.—For purposes of comparison with the above isomeric substance, this compound was prepared by the oxidation of pregnan-3(β)-ol-12,20-dione with chromic anhydride in acetic acid at room temperature for forty minutes. The product was crystallized successively from ether, aqueous methanol and then acetone, m. p. 204–206°, $[\alpha]^{26}D$ +181°, and $[\alpha]^{26}_{5461}$ +225° in chloroform (literature for pregnan-3,12,20-trione[7]: m. p. 201–202°; $[\alpha]^{17}D$ +182 ± 7°, $[\alpha]^{17}_{5461}$ +218 ± 8° in acetone). A mixture with the above isomeric substance showed a melting point depression of 36°.

(4) Hoehn and Mason, THIS JOURNAL, **60**, 1493 (1938).

(5) Miescher, *et al.*, *Helv. chim. Acta*, **27**, 1815 (1944); **28**, 1252 (1945).

(6) Shoppee and Reichstein, *ibid.*, **24**, 351 (1941).

(7) Reichstein and von Arx, *ibid.*, **23**, 747 (1940).

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Identification of Free Radicals by Radio-halogens in the Radiolysis of Hydrocarbons[1]

BY RUSSELL R. WILLIAMS, JR., AND WILLIAM H. HAMILL

Recent work in these laboratories on the photolysis and radiolysis of alkyl iodides,[2] in which radioactive iodine was used to demonstrate the high efficiency of reactions of the type

$$R\cdot + I_2 \longrightarrow RI + I$$

has suggested the use of radioactive halogens as a general method of detecting and identifying free radicals. By using molecular halogens of high specific activity in systems where such radicals are generated one may expect to be able to observe unweighable but radiochemically detectable amounts of the halides corresponding to the free radicals formed. Subsequent addition and fractionation of appropriate carrier substances, followed by activity determinations, will give an estimate of the types and relative amounts of radicals formed.

We have tested this procedure in a number of systems, producing free radicals both by absorption of light and ionizing radiations. The accompanying figure shows the result of gamma irradiation of a solution of approximately 4 mg. of highly active[3] iodine in 5 cc. of purified *n*-pentane. After exposure, excess iodine was extracted and 10 cc. each of methyl, ethyl, *n*-propyl, *n*-butyl and *n*-amyl iodides added. These carriers were fractionated in a glass-packed Todd column, taking 2-cc. cuts. The activity of each fraction was measured in a liquid cell Geiger counter. Both the activity and boiling point of each fraction are indicated in the figure. The purest fractions corresponding to each carrier are labeled.

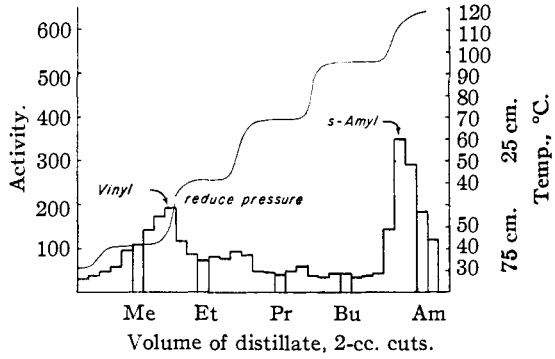

Fig. 1.—Radiolysis of *n*-pentane (liquid) + I_2*.

It is apparent from the data that considerable proportions of the lower alkyl iodides were formed, corresponding to rupture of the pentane molecule, radical or ion. At least two intermediate peaks appear. These must correspond to active species for which no carrier was added. From the sequence of these in the distillation curve they have been tentatively identified as vinyl iodide and *s*-amyl iodide.

This technique is also being applied to the photobromination of hydrocarbons and here again fragmentation of the carbon chain appears to be significant. In the photobromination of gaseous *n*-pentane with visible light at 80°, the ratio of all lower bromides to amyl bromides appears to be approximately 30:70. This ratio remains unchanged over a thirty-fold change in the ratio of bromine and pentane pressures, which indicates that the production of the lower bro-

(1) Reported at the 116th meeting of the American Chemical Society, Atlantic City, N. J., September 19–23, 1949.

(2) R. H. Schuler, Dissertation, University of Notre Dame, 1949.

(3) Activity due to 8-day I^{131}, obtained from U. S. Atomic Energy Comm., Oak Ridge, Tenn.

mides cannot be ascribed to reaction of bromine with impurities.

This method of detecting and identifying free rad cals should be widely applicable in both liquid and gaseous systems. Iodine and bromine have their respective advantages, both chemically and radiochemically. The interpretation of the results of these experiments must await the accumulation of further data.

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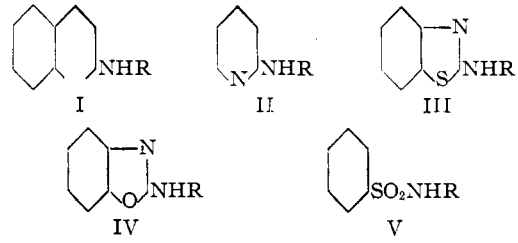
Certain Heterocyclic and Benzenesulfonyl Derivatives of γ-Diethylaminopropylamine[1]

BY MARTIN J. WEISS[2] AND CHARLES R. HAUSER

Various 2-methoxy-6-chloro-9-alkylaminoacridine derivatives having variations in the side chain[3] have been found to exhibit antitubercular activity. Since the derivative having the γ-diethylaminopropylamine side chain was one of the most active,[4] we have attached this side chain to several other heterocyclic nuclei and to the benzenesulfonyl group to form compounds I–V, R = $-(CH_2)_3N(C_2H_5)_2$. Although none of these compounds showed antitubercular activity under the conditions employed with the acridine,[4] their syntheses seemed worthy of reporting.



Compounds I to IV inclusive were prepared by heating halogen derivatives of the appropriate heterocyclic compounds with two molecular equivalents of γ-diethylaminopropylamine in the absence of a solvent. The extra equivalent of the diamine served to neutralize the hydrogen halide formed in the coupling reaction. The results are summarized in Table I. An attempt to couple 2-bromothiophene with the diamine was unsuccessful. Compound (V) was prepared from benzenesulfonyl chloride and the diamine in pyridine.

Compound (II) was prepared by Whitmore and co-workers[5] by heating a pyridine solution of 2-bromopyridine and the diamine in a sealed tube. Compound (III) has also been reported previously but no yield was given.[6]

TABLE I

COUPLING OF γ-DIETHYLAMINOPROPYLAMINE WITH HALOGEN COMPOUNDS

Halogen compound	Time, hr.	Product	B. p.[a] °C.	Mm.	Yield, %	Picrate M. p., °C.
2-Chloroquinoline	8[b]	2-(γ-Diethylaminopropylamino)-quinoline (I)	181–185	2	49	*ca.* 280[c] dec.
2-Bromopyridine[d]	6[b]	2-(γ-Diethylaminopropylamino)-pyridine (II)	136–138[e]	3.5	68	165–166[f]
2-Chlorobenzothiazole	4[g]	2-(γ-Diethylaminopropylamino)-benzothiazole (III)	216–218	6.5	85	195–196[h]
2-Chlorobenzoxazole	3.5[g]	2-(γ-Diethylaminopropylamino)-benzoxazole (IV)	170	1.5	71	168–169[i]

[a] The boiling points listed were obtained on redistillation of the product; the yield is based on the product obtained after the initial distillation. [b] At refluxing temperature. [c] After six recrystallizations from a mixture of methyl cellosolve and isopropyl ether, followed by several washings with ethyl ether. *Anal.* Calcd. for $C_{22}H_{26}N_6O_7$: C, 54.31; H, 5.39. Found: C, 54.55; H, 4.96. [d] Only 0.063 mole of 2-bromopyridine and 0.127 mole of diamine were used. [e] Reported b. p. 105–107° at 0.8 mm.[5] [f] After five recrystallizations from a mixture of methyl cellosolve and isopropyl ether; reported m. p. 163.5–164°.[5] [g] This reaction was carried out in a bath maintained at about 120°. [h] After one recrystallization from dioxane; reported m. p. 195–197°.[6] [i] After four recrystallizations from a mixture of acetone and isopropyl ether. The substance analyzed correctly for the dipicrate. *Anal.* Calcd. for $C_{26}H_{27}N_9O_{15}$: C, 44.26; H, 3.86. Found: C, 43.94; H, 3.64.

Experimental[7]

Compounds I–IV (Table I).—The halogen compound (0.10 mole) and γ-diethylaminopropylamine (0.20 mole) were mixed in the absence of a solvent and heated. With the highly reactive 2-chlorobenzoxazole, the diamine was added dropwise to the halogen compound. After the reaction had been allowed to cool to room temperature, it was poured into a potassium carbonate solution. The mixture was extracted several times with ether and the combined ether extracts were dried over Drierite. The solvent was removed and the residue was distilled *in vacuo* through an 11-cm. Vigreux column and then redistilled. Since 2-(γ-diethylaminopropylamino)-quinoline is not very soluble in ether, extraction with ether gave three layers. The aqueous layer was separated from the two organic layers, which were made homogeneous by the addition of commercial absolute ethanol. The ether–ethanol solution was then treated as above.

N-(γ-Diethylaminopropyl)-benzenesulfonamide (V).—To a solution of 13.0 g. (0.10 mole) of γ-diethylaminopropylamine in 50 ml. of anhydrous pyridine was slowly

(1) Paper II on antitubercular drugs; paper I, THIS JOURNAL, **70**, 4020 (1948).

(2) Eli Lilly Fellow, 1947–1948; present address: Hickrill Chemical Research Foundation, Katonah, New York.

(3) These compounds were prepared as potential antimalarial drugs; see Breslow, Walker, Yost, Shivers and Hauser, THIS JOURNAL, **68**, 100 (1946), and earlier papers.

(4) This compound showed antitubercular activity at a minimum dosage of 0.02 mg. per 10 ml. of culture, when tested by an *in vitro* method carried out at the laboratories of Eli Lilly and Company, Indianapolis, Indiana, using avirulent human strain no. 599 organism.

(5) Whitmore, Mosher, Goldsmith and Rytina, THIS JOURNAL, **67**, 393 (1945).

(6) Tsuda, Sakamoto, Mutsuda and Kanno, *J. Pharm. Soc. Japan*, **462** (1940); German abstract, p. 184.

(7) Analyses by the Clark Microanalytical Laboratories, Urbana, Illinois.