

dithiohydantoin<sup>3</sup> and 5-hexyl-5-methyl-2,4-dithiohydantoin (m.p. 98.5–99.6°. *Anal.* Calcd.: N, 12.16; S, 27.83. Found: N, 12.20; S, 27.83.)

Doses of the order of 200–300 mg./kg./day of 5-*n*-heptyl-2-thiohydantoin were required to protect all mice infected intravenously with *M. tuberculosis* H37Rv from the lethal effects of the disease. This was true also when a strain highly resistant to streptomycin was used to infect the animals. In both cases postmortem examination of the surviving mice revealed little if any tuberculous pathology. When this drug was fed to hamsters infected with the H37Rv strain at a concentration of 0.1% in the diet a therapeutic effect equivalent to that obtained with a fourfold concentration of *p*-aminosalicylic acid was achieved. In this species, too, the tuberculous pathology in the survivors was quite small. Extensive acute and chronic toxicity studies in rodents, dogs and monkeys showed that the drug is well tolerated by these species. In view of these results it is felt that 5-*n*-heptyl-2-thiohydantoin is worthy of clinical trial as an antitubercular drug.

It seems more than a coincidence that the group-

ing,  $\text{—NH—}\overset{\text{S}}{\underset{\text{||}}{\text{C}}}\text{—NH—}$  or a tautomeric form thereof occurs so frequently in *in vivo* tuberculostatically active drugs. The thiosemicarbazones, the thioureas reported by Huebner,<sup>4</sup> the mercaptotriazinones of Hagenbach<sup>5</sup> and now the thiohydantoin all have in common the thioureido function.

(3) H. C. Carrington, *J. Chem. Soc.*, 681 (1947).

(4) C. F. Huebner, *et al.*, *THIS JOURNAL*, **75**, 2274 (1953).

(5) R. E. Hagenbach, E. Hodel and H. Gysin, *Experientia*, **10**, 620 (1954).

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#### DIRECT PRODUCTION OF RADIOACTIVE ALIPHATIC HYDROCARBONS BY PILE IRRADIATION<sup>1</sup>

Sir:

Study of the hot atom chemistry of carbon-14 by the irradiation of nitrogenous organic materials in the heavy water pile at the Argonne National Laboratory (CP-3') has led us to observe a method of producing saturated aliphatic hydrocarbons in radioactive form in high yield and high specific activity.

A 5 mole per cent. solution of aniline in normal pentane, 20 cc. of which was enclosed in a quartz tube and irradiated for one week in the CP-3' pile at a flux of  $10^{11}$  neutrons per cm.<sup>2</sup> per second, proved to yield about 25% of the radiocarbon in the form of radioactive normal pentane, with less than 1% as iso- or neo-pentane; about 15% in the form of radioactive hexane, which apparently is about two-thirds normal hexane; and the remainder in heavier hydrocarbons. The distribution is given in Table I.

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TABLE I

COMPOSITION OF THE RADIOACTIVE HYDROCARBONS FORMED BY THE IRRADIATION OF A 5 MOLE PER CENT. SOLUTION OF ANILINE IN NORMAL PENTANE

5% of total C<sup>14</sup> was extractable into 12 N HCl

Chemical form	Per cent. of the total radiocarbon
Gases (Boiling up to room temperature)	12
<i>n</i> -Pentane	25
<i>i</i> -Pentane	1
<i>n</i> -Hexane	12
Other hexanes	6
Heptane and heavier hydrocarbons, boiling according to following ranges, °C.	
95–125°	8
125–155°	5
155–175°	6
175–215°	5
215–245°	3
245–290°	3
Residue	9

It is clear from these preliminary results, which were duplicated by a second run in which ethylamine was substituted for aniline, that a high velocity carbon-14 on colliding with the liquid aliphatic hydrocarbon has a very good chance of entering the chain. The reasons for this may be debatable, but the facts seem to be clear. It should be realized that the hexane and heavier hydrocarbons produced in the above-described bombardment were essentially carrier free except for any which may have been produced by gamma and fast neutron radiation. It would seem therefore that the process described can produce radioactive hydrocarbons of high specific activity. It is further clear that as far as neutron economy is concerned, this process could well compete with any organic synthesis, for the sole labor involved is the purification of the original chemical, the preparation of the samples for irradiation, and the subsequent distillation and separation. There is reason to believe that the procedure outlined would also serve to introduce radiocarbon into heavy lubricating oils.

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#### ENZYMATIC REDUCTION OF CORTISONE<sup>1</sup>

Sir:

Previous *in vivo* and *in vitro* studies reveal that the major pathway of cortisone metabolism is the reduction of the  $\Delta^4$ -3 ketone group to the saturated 3-alcohol by the liver.<sup>2,3,4</sup> We should like to report the presence of an enzyme system in rat liver

(1) Abbreviations as used in this communication are: cortisone ( $\Delta^4$ -pregnene-17 $\alpha$ ,21-diol-3,11,20-trione), dihydrocortisone (pregnane-17 $\alpha$ ,21-diol-3,11,20-trione), tetrahydrocortisone (pregnane-3 $\alpha$ ,17 $\alpha$ ,21-triol-11,20-dione), TPNH and TPN (reduced and oxidized triphosphopyridine nucleotide, respectively), DPNH and DPN (reduced and oxidized diphosphopyridine nucleotide, respectively).

(2) J. J. Schneider, *J. Biol. Chem.*, **194**, 337 (1952).

(3) J. J. Schneider and P. M. Horstmann, *ibid.*, **196**, 629 (1952).

(4) E. V. Caspi, H. Levy and O. M. Hechter, *Arch. Biochem.*, **45**, 169 (1953).