

	Coups/minute
Acide L- $\alpha$ -aminoadipique	800 000
Acide chloracétyl-D- $\alpha$ -aminoadipique	9 200 000

### 3<sup>o</sup> — ACIDE D- $\alpha$ -AMINOADIPIQUE <sup>14</sup>C-6.

L'acide chloracétyl-D- $\alpha$ -aminoadipique est hydrolysé pendant 2 heures par de l'acide chlorhydrique 2 N à reflux. Après concentration, l'acide D- $\alpha$ -aminoadipique est purifié par électrophorèse préparative sur papier.

### 4<sup>o</sup> — PURIFICATION

Les isomères optiques obtenus sont finalement passés sur une colonne de résine Amberlite CG 120, forme chlorure (120  $\times$  10 mm). L'élution, réalisée par un gradient de concentration croissante en acide chlorhydrique, permet d'obtenir des acides aminés marqués ne donnant qu'une seule tache radio-active par autoradiographie d'un chromatogramme bidimensionnel sur papier dans les solvants : *n*.butanol/acide acétique/eau (4 : 1 : 5; v/v) et phénol aqueux à 10 p. 100/eau (1 : 1; v/v).

J. MIZON

Institut de Recherches sur le Cancer et Laboratoire de Chimie Biologique  
de la Faculté de Médecine et de Pharmacie, Lille

### BIBLIOGRAPHIE

GREENSTEIN, J. P., BIRNBAUM, S. M. et OTEY, M. C. — *J. Amer. Chem. Soc.*, **75**, 1994 (1953).

## Synthesis of 2,4-Dinitrochlorobenzene-3,5-<sup>3</sup>H

Received on April 5, 1968

In a study of the metabolism of 2,4-dinitrochlorobenzene-3,5-<sup>3</sup>H (III) in epidermis by autoradiography it was necessary to prepare highly tritiated III. An attempt <sup>(1)</sup> to synthesize III through reduction of 1-bromo-3-chlorobenzene (I) failed, although this procedure succeeded for the synthesis of 2,4-dinitrofluorobenzene-3,5-<sup>3</sup>H. In course of the present work, this way was employed and proved to be successful for the preparation of III. As shown in Figure 1, III was synthesized by reduction of I with a palladium catalyst to chlorobenzene-3,5-<sup>3</sup>H (II) followed by nitration.

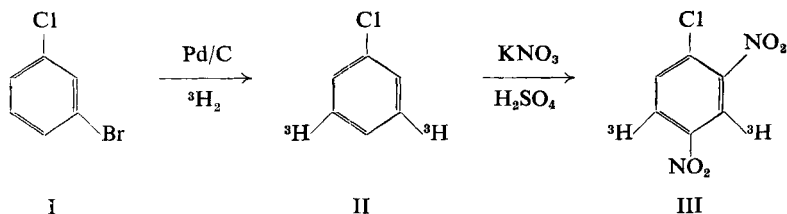


FIG. 1

We report the synthesis of III, with a specific activity of 643 millicuries per millimole, starting from tritium gas having a total activity of 4 curies.

#### EXPERIMENTAL AND RESULTS

##### *Materials.*

1-Bromo-3-chlorobenzene was commercially available and purified by distillation. 5% Palladium on charcoal catalyst was purchased from Nakarai Chemicals Ltd., Kyoto, and used without additional purification. The Radiochemical Centre Amersham tritium gas (98 % purity) was employed.

##### *Chlorobenzene-3,5-<sup>3</sup>H (II).*

A mixture of 200 mg of 5 % palladium on charcoal catalyst, 281 mg (5 millimoles) of potassium hydroxide (in the prior synthesis <sup>(1)</sup> excess of potassium hydroxide was used), and 1.5 ml of methanol in a 5 ml round-bottom flask was activated at room temperature by bubbling with hydrogen gas for a few min. To the mixture was added 0.6 ml (5 millimoles) of I. The flask was connected to a vacuum manifold, equipped with a Toepler pump, and the mixture was stirred magnetically at room temperature with 70 ml (3.1 millimoles) of hydrogen gas containing tritium gas having a total activity of 4 curies. After absorption of the tritium gas was complete, the reaction mixture was distilled in vacuum to yield crude product. The distillate was separated into its components by gas chromatography on Silicon DC 550 (1 × 100 cm), and that containing pure II was collected into a trap cooled by liquid nitrogen; 135 mg, 40 % of theory, specific activity : 640 mC/mmole.

##### *2,4-Dinitrochlorobenzene-3,5-<sup>3</sup>H (III).*

To a mixture of 135 mg (1.2 millimoles) of the above tritiated chlorobenzene, 0.8 ml of carbon tetrachloride, and 1.2 ml of concentrated sulfuric acid, maintained below 5° C, was added 292 mg (2.9 millimoles) of potassium nitrate under stirring during 1 hour and then stirred at 45° C for 2.5 hours. The mixture was poured onto ice, extracted with four 10 ml portions of

ether, washed with water, and dried with Drierite. Ether was removed, and the residue recrystallized from methanol to give III; yield : 140 mg, 58 % of theory, m.p. 49-50.5° C (lit. m.p. 50° C), specific activity : 643 mC/mmole, radioactive yield based on tritium gas : 22 %.

A thin layer chromatogram, developed in a system of benzene-*n*-hexane (2 : 1 v/v), shows only one radioactive peak, and the infrared spectrum was consistent with the expected structure.

#### DISCUSSION

Although Hesselbo has reported exchange of hydrogen atoms of fluoro-benzene-3,5-<sup>3</sup>H at the stage of nitration to significant degree, no exchange of hydrogen atoms of II under this experimental condition was found, and Melander <sup>(2)</sup>, also, has described that 2,4-dinitrotoluene-3,5-<sup>3</sup>H was synthesized by nitration of toluene-3-<sup>3</sup>H without decrease of the radioactivity. This discrepancy is due to the difference among the electronegativities of methyl, chloro, and fluoro groups. The low yield of II is a result of formation of benzene-<sup>3</sup>H and cyclohexane-<sup>3</sup>H, which were identified by gas chromatography. During reduction of I, it was required to use equimolecular amounts of potassium hydroxide and I, since formation of biphenyl was found by gas chromatography with excess of potassium hydroxide.

In this synthesis, III, with a specific activity of 643 mC/mmole, was obtained starting from tritium gas having a specific activity of 4 C/3.1 mmoles. Therefore, it is concluded that the use of a larger amount of tritium gas can give III with a specific activity of several curies per millimole.

KEN-ICHI KUDO, TAKAYOSHI ADACHI

Central Research Laboratory  
Sumitomo Chemical Co., Ltd.  
Takatsuki, Osaka, Japan.

MICHIO ENDO

Pharmaceutical Division  
Sumitomo Chemical Co., Ltd.  
Takarazuka, Hyogo, Japan.

#### REFERENCES

1. HESSELBO, T. — *Int. J. Appl. Rad. Isotopes*, **16** : 329 (1965).
2. MELANDER, L. — *Arkiv Kemi*, **2** : 270 (1950).