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The Synthesis of 2-Chloro-4,6-bis-(ethyl-[1-^{14}C]-amino)-*s*-triazine-(Simazine)

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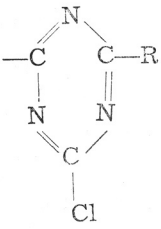
The herbicide 2-chloro-4,6-bis-(ethylamino)-*s*-triazine (Simazine), (III) labeled with ^{14}C in the ring was prepared by the Geigy Agricultural Chemicals Co.[1] We nedeed III labeled in the side chain, and the present note reports its synthesis according to the scheme:

$$Na^{14}CN \longrightarrow \underset{\text{I}}{CH_3{}^{14}CN} \longrightarrow \underset{\text{II}}{CH_3{}^{14}CH_2NH_2xHCl} \longrightarrow$$



III

R = $CH_3{}^{14}CH_2NH$—

In the literature[2,3] the synthesis of II by catalytic hydrogenation of I with Raney nickel is described. However, by this reaction some diethylamine-[1,1'-^{14}C] is also formed. Therefore, the preparation of I[3,4] was modified in order to obtain a waterfree product, which was then reduced by $LiAlH_4$, yielding very pure II.

Simultaneous addition of II and sodium hydroxide[5] into a suspension of cyanuric chloride in water, in a 2:4:1 molar ratio, under controlled conditions[6], afforded III in a fairly high chemical (46.3%) and radiochemical (41.8%) yield, based on $Na^{14}CN$.

EXPERIMENTAL

Melting points are uncorrected.

Acetonitrile -[1-^{14}C] (I)

Inactive sodium cyanide (Mallinckrodt, AR) used in this experiment was found to be 88.5% pure. To 2.7720 g. (50 mmoles calc'd. on pure salt) of this product, $Na^{14}CN$ (Radiochemical Centre Amersham, 1 mc, 3 mg.) dissolved in water (total volume 4 ml.) and freshly distilled methyl iodide (3.45 ml., 7.885 g., 50 mmoles plus 10% excess) were added under cooling. After shaking[3] (48 hrs.), the flask was rinsed with abs. ether (5 ml.), and the mixture distilled until the temperature of vapours reached 80°. The flask was then cooled to 0°, abs. ether (10 ml.) added and the fractionation repeated until the temperature reached 90°; the same process was repeated once again. The distillate (about 35 ml.) was dried (48 hrs.) by subsequent addition of calcium chloride.

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Ethylamine-[1-^{14}C] (II)

In a three-necked, 200 ml. flask, equipped with a stirrer, a dropping funnel and a reflux condenser protected from moisture, $LiAlH_4$ (2.015 g., 54 mmoles) and abs. ether (60 ml.) were placed. Under stirring and cooling (0°) the ethereal solution of I was dropped in (1 hr.) and the stirring of the mixture continued at room temperature (2 hrs.) and at 35° (2 hrs.). The mixture was then cooled to 0°, and the reflux condenser was connected, through a soda lime tube filled with glass-wool and a bent glass tube with two washing bottles containing 35 and 10 ml. of 2.5 *N* HCl. The complex was successively decomposed with water (2.5 ml.), 20% NaOH (1.6 ml.) and water (5 ml.). The dropping funnel was replaced by a gas inlet tube and nitrogen bubbled through the mixture under stirring and heating (bath temp. 45—50°) for 5 hours. The solution in the washing bottles, containing II and some ether was evaporated *in vacuo*, the residue re-evaporated with water and ethanol, and dried in a vacuum desiccator. 3.1754 g. of II (77.87% calc'd. on $Na^{14}CN$) as white needles were obtained.

2-Chloro-4,6-bis-(ethyl-[1-^{14}C]-amino)-s-triazine (*Simazine*, III)

Cyanuric chloride (3.5754 g., 19.45 mmoles, m. p. 145—146°) and 25 ml. of water were placed in a three-necked flask immersed in an ice-bath and equipped with a stirrer and two loosely attached dropping funnels. II (3.1754 g., 38.9 mmoles) and sodium hydroxide (3.1120 g., 77.8 mmoles) were separately dissolved in an equal volume of water (22 ml.) and under stirring and cooling the halves of the volumes were simultaneously dropped into the suspension for 1 hour. The mixture was kept at 0° for additional 2 hours, then at 35—40° the remaining halves of II and NaOH were added during 1 hour, and finally the mixture was kept at this temperature for further 2 hours. The precipitate was filtered off, washed with 50 ml. of ice-water and dried. The crude product (3.5468 g., m. p. 202—206°) was dissolved in boiling ethanol (280 ml.) and filtered through a charcoal layer. From the colourless solution 2.3319 g. of III with m. p. 225—226°.[6] were obtained. Yield: 46.25% (calc'd. on $Na^{14}CN$). Specific activity: 0.1794 μc/mg., 36.17 μc/mmole, which did not change after a further recrystallization of a small sample. Radiochemical yield based on $Na^{14}CN$: 41.84%.

The radioactivity determinations were made on samples of »infinite thickness« and compared with the ^{14}C Amersham standard of the same size.

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IZVOD

Sinteza 2-klor-4,6-bis-(etil-[1-^{14}C]-amino)-*s*-triazina (Simazina)

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Herbicid Simazin (III) markiran u lancu priređen je iz etilamin-[1-^{14}C] hidroklorida (II) i cijanurne kiseline. Kao ishodni produkt služio je $Na^{14}CN$ (1 mc) koji je preveden u acetonitril-[1-^{14}C] (I) te preko II u dvostruko markirani III. Iskorištenje, kemijsko: 46.3% i radiokemijsko: 41.8%, obzirom na ishodni $Na^{14}CN$.

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