Desulfuration of 2-(2',4'-dinitrophenylthio) Indoles, a general Method for the Introduction of H Isotopes in Position 2 of naturally occurring Indoles: 3-Indoleacetic Acid-2D*

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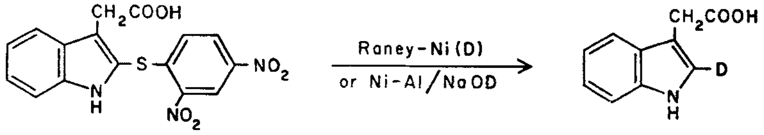
Procedures for the preparation of specifically labelled natural indoles usually involve synthetic routes *via* specifically labelled indoles or indole precursors. For the introduction of tritium in position 2 of the indole ring of tryptophan and tryptamine for example, indole-[2-T] was prepared and the natural indole synthesized subsequently (1).

We wish to describe a general method for the introduction of H isotopes into the 2-position of 3-substituted indoles based on desulfuration of DNPS **-indole derivatives. The latter can easily be prepared in high yield from the 3-substituted indole to be labelled and 2, 4-dinitrophenylsulfenyl chloride (2).

Two methods for the preparation of 3-indoleacetic acid **-2D are described below. Deuterium, derived from D_2O, is introduced in the last step of the procedure and high percentage of label incorporation is observed. Previous results indicate (2) that most naturally occurring indoles can be labelled in a similar way.



PREPARATION OF 3-INDOLEACETIC ACID-[2-D] FROM 2-(2',4'-DINITROPHENYLTHIO)-3-INDOLEACETIC ACID.

The labile hydrogen atoms in the starting material were exchanged with D_2O-dioxane.

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** Abbreviations used : IAA : 3-indoleacetic acid; DNPS : 3,4-dinitrophenylthio.

(i) *By desulfuration with deuterium-Raney nickel*:

Deuterium-Raney nickel was prepared from active catalyst in water (No. 28; W. R. Grace & Co.) by three successive equilibrations with 99 % D_2O (3). Deuterium-Raney nickel (3 g) (*ca.* 5 ml settled catalyst in D_2O) was added to a solution of 2-DNPS-IAA (250 mg, *cf.* ref. 2) in dioxane (75 ml) and water (25 ml). After the mixture had been stirred vigorously at 25° C until the solution was colorless (1-5 min) the catalyst was removed by filtration and washed with warm dioxane.* The filtrate was evaporated to dryness and the residue recrystallized from benzene-hexane to give 44 mg (38 %) 3-indoleacetic acid-[2-D] m.p. 167° C.

(ii) *By desulfuration with nickel-aluminium alloy and NaOD*:

2*N* NaOD was added, dropwise, to a stirred suspension of 2-DNPS-IAA (250 mg) and nickel aluminium alloy [500 mg; British Drug Houses; (50 : 50)] in D_2O (4 ml). The mixture was filtered as soon as the yellow-orange color was discharged (*ca.* 5 min). The alkaline filtrate was then extracted with ether (50 ml) and the aqueous phase of this extraction acidified (HCl; pH 2.5) and reextracted with ether (2 × 30 ml). This ether layer, after washing with water and drying (Na_2SO_4) was evaporated to dryness. 3-Indoleacetic acid-[2-D] m.p. 167-8° C was obtained (78 mg, 66.5 %) without further purification.

The incorporation of deuterium was > 95 % in both cases, as determined by p.m.r. spectroscopy.

Attempts to prepare IAA-[2-D] by desulfuration of di-(3-indoleacetic acid)-2-disulfide (4) by the two methods described above were unsuccessful.

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* Because of the pyrophoric nature of Raney nickel the catalyst should not be allowed to become dry.

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