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# PHOTOCHEMICAL SYNTHESIS OF 2-(2-AMINOETHYL)INDOLE (ISOTRYPTAMINE) DERIVATIVES[1]

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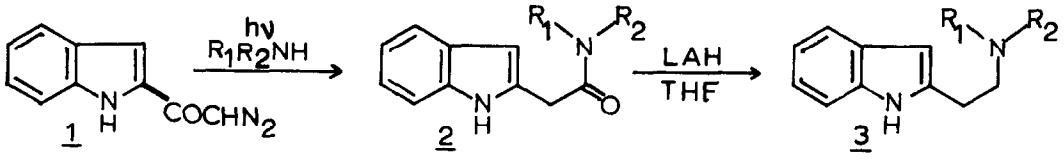
Unlike tryptamine derivatives which have, by virtue of their central position in Nature (1), numerous versatile and dependable routes available for their synthesis (2), the related 2-(2-aminoethyl)indole (isotryptamine) systems 3 have remained virtually unknown and the recorded routes to these systems are far from satisfactory (3,4). We wish to report a facile synthesis of isotryptamines 3 which involves a photochemical Wolff rearrangement (5) as the key step and which, for the first time, makes these compounds available in preparative quantities. Irradiation of the known indole-2-diazoketone 1 (6) in the presence of an excess of primary or secondary amines yields the corresponding amides 2 (7,8) which, upon reduction with lithium aluminum hydride in refluxing tetrahydrofuran, produces the isotryptamine derivatives. Table I lists the compounds which have been prepared by this efficient synthetic sequence (9).




1 2 3

The potential utility of these new isotryptamines in heterocyclic synthesis is readily recognized (10). Exploratory work in this direction is in progress.

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TABLE I

Synthesis of Indole-2-Acetamide (2) and Isotryptamine (3) Derivatives.

| | $R_1$ | $R_2$ | 2 Yield % | 2 m.p. °C | 3 Yield % | 3 m.p. °C |
|---|---|---|---|---|---|---|
| a | H | H | 98 | 174-175 | 71 | 98-99[a] |
| b | H | $CH_3$ | 92 | 122-123 | 73 | 95-96 |
| c | $CH_3$ | $CH_3$ | 94 | 157-158 | 82 | 94-95 |
| d | $C_2H_5$ | $C_2H_5$ | 97 | 88-90 | 72 | 180-181[b] |
| e | $-(CH_2)_4-$ | | 89 | 189-190 | 86 | 140-141 |
| f | $-(CH_2)_5-$ | | 82 | 127-128 | 87 | 96-97 |
| g | $-(CH_2)_2-O-(CH_2)_2-$ | | 93 | 180-181 | 83 | 122-123 |

[a] lit. m.p. 100-101° (3a).

[b] m.p. of hydrochloride salt.

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(4) A recent report describes a novel entry into the system 3. However, this method is only applicable to the synthesis of 3-substituted isotryptamines: A. Ebnother, P. Niklaus and R. Suess, Helv. Chim. Acta, 52, 629 (1969).

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(7) The following procedure is typical: a 0.2% solution of 1 in EtOH-piperidine mixture (8:1 v/v) is photolyzed (10-20°, Rayonet reactor, 3500 Å) for 2-3 hours and the amide 2f is isolated by evaporation to dryness and recrystallization from $CH_2Cl_2$-cyclohexane.

(8) We have also found that photolysis of 1 in ethanol yields ethyl 2-indolylacetate (quantitative) and in THF-water the hitherto elusive indole-2-acetic acid (64%) (3b, 3c).

(9) All new compounds gave elemental analysis within 0.3% of theory and exhibited ir, uv and nmr spectra consistent with the assigned structures.

(10) For example, substituted γ-carboline derivatives which have been previously unavailable (11) or laboriously obtained (12) should now be accessible by the normal Pictet-Spengler or Bischler-Napieralski routes (3d).

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