Tetrahedron Letters No. 5, pp 461 - 462, 1974. Pergamon Press. Printed in Great Britain.

1-AMINOINDOLES

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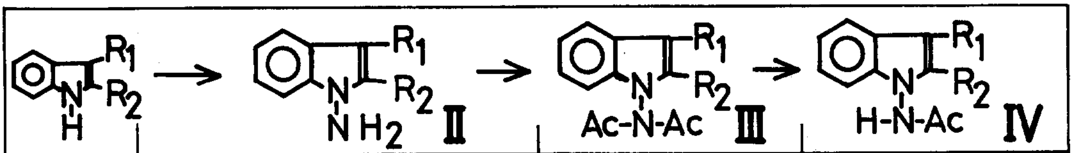
(Received in Japan 26 November 1973; received in UK for publication 28 December 1973)

In a previous paper we reported[1] that many kinds of 3-, 4-, and 6-substituted indole derivatives can be obtained directly from the corresponding 1-substituted indoles by irradiation with U. V. light. In order to attempt our reaction on indoles in which the 1-substituent is a nitrogen function, we needed 1-aminoindole derivatives. Though various 1-aminoindole derivatives are known, their preparation by known methods is not straightforward[2]. To meet our need, therefore, we developed a new general method for the facile synthesis of 1-aminoindole derivatives by the reaction of indoles with hydroxylamine-O-sulfonic acid. We wish to report this method here.

General procedure

Hydroxylamine-O-sulfonic acid (6.152g, 54.4mmole) was added in several portions to a chilled suspension of indole (3.201g, 27.3mmole) and crushed KOH (24.551g, 438.4mmole) in abs. dimethylformamide (50ml). After the mixture had been stirred for 1 hr at room temperature, water was added and then the mixture was extracted with benzene. The benzene extract was washed with water, dried, and concentrated in vacuo to leave an oil, which was chromatographed on silica gel. Elution with CH_2Cl_2-hexane (1:1) first gave 2.130g of indole. Further elution with the same solvent system produced 1.162g of 1-aminoindole[3] (yield: 32.1%, 96.3% corrected for unreacted starting material). Recrystallization from hexane gave colorless prisms: mp 41-41.5°; ir(KBr) 3340 and 1618 cm^{-1}; nmr($CDCl_3$) δ 4.46(2H, s.), 6.33(1H, d. J=3.5), 7.55(1H, m.), 7.33-7.00(4H, m.): Mass Spectrum; m/e 132(M^+): Anal. Calcd. for $C_8H_8N_2$: C, 72.70; H, 6.10; N, 21.20. Found: C, 72.66; H, 6.08; N, 21.16.

This is the first synthesis of 1-aminoindole (IIa). The 1-aminoindoles (IIb-IIe) shown in Table I were also prepared in the same way. Their structures were confirmed by their nmr spectra, in which the 1-amino proton signal appeared as a broad singlet at δ 4.04-4.26 (2H) in addition to signals of the 2- and 3-substituents. Further proof was obtained from reaction of the 1-aminoindoles (IIa-IIe) with acetic anhydride to afford the corresponding 1-diacetylimidoindoles (IIIa-IIIe). These diacetyl derivatives showed an absorption band at 1714-1734 cm^{-1} in the infrared spectra, while in the nmr spectra an acetyl proton was observed as a singlet at δ 2.28-2.30 (6H), showing that both the acetyl groups are equivalent. 1-acetamidoindoles (IVa-IVe) were obtained in quantitative yield by hydrolysis of the corresponding diacetyl compounds (IIIa-IIIe) with dilute alkali. They showed an amide band at 1674-1679 cm^{-1}, and their nmr spectra suggested the existence of two restricted rotational isomers in $CDCl_3$ whereas only one isomer existed in d_6-DMSO. Investigation of various reactions of 1-aminoindoles is now in progress.



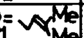
I	II			III		IV	
	mp(°C)	yield(%)	NH_2 signal δ.(CDCl3)	mp(°C)	Ac.signal δ.(CDCl3)	mp(°C)	IR(KBr)
a) $R_1=R_2=H$	41 - 41.5	32.1 (96.3)	4.46	98.5-99.5	2.30	141 - 142	1678
b) $R_1=CH_2Ø$ $R_2=H$	oil	39.5(84.2)	4.16	96.5-97.5	2.30	139-140	1677
c) $R_1=Me$ $R_2=H$	59.5-60.5	39.8(85.6)	4.30	138-139	2.28	174.5-175.5	1679
d) $R_1=$  $R_2=H$	oil	33.7(66.6)	4.13	oil *	2.30	103-104	1674
e) $R_1=H$ $R_2=Me$	114-115	17.1 (33.2)	4.04	oil *	2.29	133.5-134.5	1678

Table I ( ) =yield,corrected for unreacted starting material

* Spectral properties were completely in accord with the structures IIId and IIIe. Analysis was not conducted because these compounds were easily hydrolyzed during purification and contained small amounts of the corresponding monoacetyl compounds (IVd, IVe), detected by thin layer chromatography.

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