Synthesis of Isoindole by Retro-Diels–Alder Reaction

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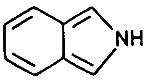
Summary Thermal fragmentation of 1,2,3,4-tetrahydro-1,4-epiminonaphthalene at reduced pressure affords pure isoindole in essentially quantitative yield.

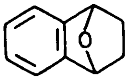
The first isolation of isoindole (I) was reported recently by Bonnett and Brown,[1] who prepared it by pyrolysis of 2-(methoxycarbonyloxy)isoindoline at 500° and 0·01 mmHg. At about the same time, Wiersum and Mijs described[2] a simple route to isobenzofuran involving the thermal fragmentation at reduced pressure of the epoxynaphthalene (II); ethylene is formed as coproduct in this 4 + 2 retro-cyclo-addition. Since the preparative work of Bonnett and Brown demonstrated that isoindole can tolerate short exposure to elevated temperature *in vacuo*, it seemed reasonable that this elusive molecule could also be synthesized by vacuum thermolysis of the epiminonaphthalene (III)[3], the nitrogen analogue of (II). We now report that this is, indeed, the case.

Sublimation of (III) (*ca.* 1 g per 20 min) from a glass tube at 80° and 0·5 mmHg through an unpacked quartz tube

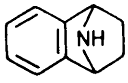
(300 mm; 24 mm diam.) at 600° afforded isoindole (I) and ethylene. The products were collected in a trap cooled by liquid nitrogen. Subsequent replacement of the nitrogen coolant by a solid CO_2–acetone bath caused the ethylene to distil leaving only the white crystals of isoindole (I) in essentially quantitative yield. Ethylene was characterized by passing it into a solution of bromine in CCl_4. The resulting ethylene dibromide was shown by i.r. and n.m.r. spectroscopy to be identical with an authentic specimen. Evidence that the isoindole (I) was pure and had, therefore, successfully survived the conditions of its production was obtained by both spectral and chemical means. The n.m.r., i.r., u.v., and mass spectra of (I) were identical with those reported by Bonnett and Brown.[1] As expected, (I) gives a colour (magenta) with Ehrlich's reagent and decomposes rapidly at room temperature.



(I)



(II)



(III)

Treatment of cold crystals of (I) with ethereal *N*-phenylmaleimide afforded, after recrystallization from ethanol, the *exo*-adduct, m.p. 208—209° (70%), shown by t.l.c., m.p., mixed m.p., and n.m.r. analysis to be identical with a specimen prepared by the method of Kreher and Seubert.[4]

This preparation of isoindole appears to have some advantage over that employing 2-(methoxycarbonyloxy)-isoindoline since it affords (I) free of coproducts.

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