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Treatment of two isatin-3-imines, 3-isopropylamino-1-methylindoline-2-one and 3-cyclohexylamino-1-methylindolin-2-one with sodium borohydride produced the fully-reduced anilines 2-isopropylamino-2-(2-methylaminophenyl)ethanol and 2-cyclohexylamino-2-(2-methylaminophenyl)ethanol, respectively. Reductive ring-opening of derivatives of isatin is not observed in related examples when either catalytic or lithium aluminum hydride reduction are employed and it is concluded that the present effect is dependant upon the softness of sodium borohydride as a reducing agent.

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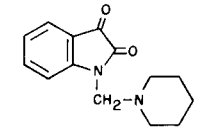
The literature relating to the reduction of derivatives of isatin or oxindole with lithium aluminum hydride (2) or diborane (3,4,5) is somewhat conflicting, however, the production of either the corresponding indole or indoline is usually observed. In contrast, reduction of the isatin (**1**) with sodium borohydride was recently shown to produce a mixture of two complex products both of which retained the amidic (2-position) carbonyl intact (6). These results prompted us to describe the total reduction and ring opening of the related isatin-3-imines (**2**) with sodium borohydride to give the anilines (**3**). The imines (**2**) were prepared by the condensation of *N*-methylisatin with the appropriate amine in ethanol and were reduced with an excess of sodium borohydride in boiling ethanol giving the anilines (**3**) in yields of 38% and 27%, respectively.

The structures of the anilines were supported by their elemental analysis and nmr spectra, although the most conclusive proof of structure was afforded by their mass spectra each of which showed a molecular ion six mass units higher than that of the starting material, clearly consistent with a three point reduction.

It would be expected (7) that initial reduction of **2** would occur at the imino function yielding the corresponding 3-aminoindolin-2-one followed by amide reduction and base induced ring opening by attack at C-2. This sequence, however, is somewhat at variance with the observation of Hudson and Roberts (8) that reduction of the related indolin-2-one (**4**) with lithium aluminum hydride in refluxing tetrahydrofuran gave a mixture of the derived 3-aminoindole and 3-aminoindoline. This difference in behaviour is probably associated with the specific use of sodium borohydride in our examples. Reductive ring opening of related cyclic amides is known to occur with sodium borohydride (9,10), for example, the imide (**5**) is ring opened to **6** under these conditions (9). Further, *N*-carbethoxyaziridine (**7**) is reductively ring opened in the presence of borohydride (to give **8** (11)) whilst the related *N*-acylaziridine (**9**) is reduced by lithium aluminum hydride with a retention of the aziridine ring (12). These effects can be associated with the relative soft and hard properties of sodium borohydride and lithium aluminum hydride, respectively, and are consistent with the findings of the present study.



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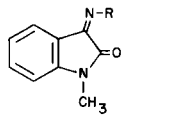

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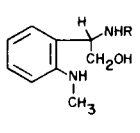
b) R = cyclohexyl



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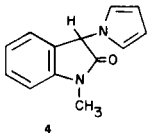

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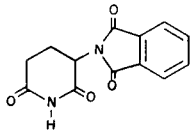

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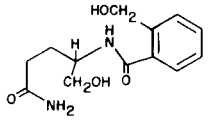

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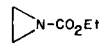

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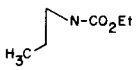

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EXPERIMENTAL

Nmr spectra were measured using a Perkin Elmer A60A spectrometer with deuteriochloroform as solvent and TMS as internal standard. Mass spectra were determined on an MS9 spectrometer operating at 70 ev.

3-Isopropylamino-1-methylindolin-2-one (**2a**).

Isopropylamine (14.75 g., 0.25 mole) was added to a solution of *N*-methylisatin (4.0 g., 0.025 mole) in ethanol (100 ml.) and the resulting solution refluxed for 0.5 hour. The solution was

allowed to stand overnight at room temperature. Removal of the solvent gave an oily solid which was crystallized from light petroleum (b.p. 60-80°) yielding the product as yellow needles, (3.0 g., 60%), m.p. 85-87°).

Anal. Calcd. for $C_{12}H_{14}N_2O$: C, 71.2; H, 6.9; N, 13.9 (M^+ 202). Found: C, 71.3; H, 7.1; N, 13.8 (M^+ 202).

3-Cyclohexylimino-1-methylindolin-2-one (**2b**).

This compound was prepared as in the above example from *N*-methylisatin and cyclohexylamine (39%), m.p. 74-76°.

Anal. Calcd. for $C_{15}H_{18}N_2O$: C, 74.4; H, 7.4; N, 11.6 (M^+ 242). Found: C, 74.1; H, 7.5; N, 11.5 (M^+ 242).

2-Isopropylamino-2-(2-methylaminophenyl)ethanol (**3a**).

Sodium borohydride (2.2 g., 0.06 mole) was added to a solution of **2a** (2.02 g., 0.01 mole) in absolute ethanol (100 ml.) and the mixture refluxed for 2 hours when it was poured into water (50 ml.). The aqueous reaction solution was extracted with ether (2 x 150 ml.) and the combined extracts washed with water, dried (magnesium sulfate) and evaporated yielding the product as an oil which was crystallized twice from ethyl acetate (0.8 g., 38%), m.p. 124-125°; nmr: δ 0.98 and 1.09 (two doublets J = 7 Hz due to asymmetry of adjacent carbon, NH-*iso*-Pr-CH_3's), 2.9 (septet, J = 7 Hz, *iso*-Pr), 2.81 (s, N-CH_3), 3.0-4.0 (2H exchangeables), 3.9 (m, $CHCH_2OH$, 3H) and 6.6-7.4 (m, aromatics); ms: m/e 208 (M^+), 190 (M^+-H_2O) and 177 (M^+-CH_2OH).

Anal. Calcd. for $C_{12}H_{20}N_2O$: C, 69.2; H, 9.6; N, 13.46. Found: C, 69.1; H, 9.9; N, 13.4.

2-Cyclohexylamino-2-(2-methylaminophenyl)ethanol (**3b**).

This compound was prepared from **2b** exactly as described for **3a**. The pure product was obtained after two crystallizations from ethyl acetate (27%), m.p. 122-124°; nmr: δ 1.0-2.0 (m, cyclohexyl CH_2's), 2.8 (s, N-CH_3), 3.4 (broad m, exchangeables), 3.8-4.2 (m, $CHCH_2OH$, 3H) and 6.5-7.5 (m, aromatics); ms: m/e 248 (M^+), 230 (M^+-H_2O) and 217 (M^+-CH_2OH).

Anal. Calcd. for $C_{15}H_{24}N_2O$: C, 72.6; H, 9.7; N, 11.3. Found: C, 72.9; H, 9.9; N, 11.3.

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