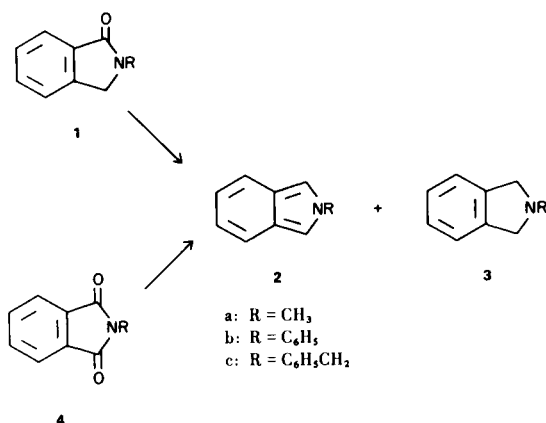


## The Direct Conversion of Phthalimides to Isoindoles

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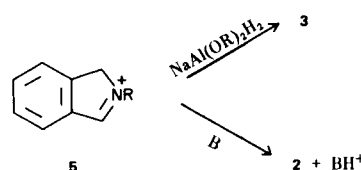
In 1955, Wittig (1) described the preparation of *N*-methyl- (2a) and *N*-phenylisoindole (2b) by treatment of the corresponding phthalimidines (1) with 0.25 molar equivalent of lithium aluminum hydride in ether, followed by pyrolysis of the (presumed) intermediate lithium alcoholate. We found that similar treatment of *N*-benzylphthalimidine (1c) gave essentially *N*-benzylisoindoline (3c) with only trace amounts of the isoindole. Replacement of LAH by sodium bis-(2-methoxyethoxy)aluminum hydride (2) ("SDMA") resulted in the formation of the isoindole 2c in 60% yield. It was then observed that 2c (along with some isoindoline, 3c) could be prepared directly from *N*-benzylphthalimide (4c) by treatment with SDMA for 30 minutes at room temperature in benzene solution, whereas reduction of 4c with LAH yields only the isoindoline.



Optimum yields of 2c were obtained using 3 moles of SDMA per mole of 4c at a reaction temperature of 15-20°; increasing the excess of SDMA or raising the temperature favored isoindoline formation. Compounds 2c and 3c were separated on the basis of the relative insolubility of 2c in cold ethanol.

The distinctive UV peak of the isoindole at 327 nm appeared in the reaction solution shortly after the reagents were mixed, and was unaffected by the addition of water. When 2c was treated with SDMA in benzene at room temperature or with LAH under the conditions described by Wittig (1), it was recovered unchanged. It is apparently not an intermediate in the reduction of 4c to 3c. It

appears reasonable to assume that the isoindole and the isoindoline arise from competing reactions; at some stage in the reduction, a precursor, possibly 5, may be either reduced further to give 3 or may liberate a proton to yield 2. If there is sufficient excess of reducing agent, the



formation of 2 can be virtually suppressed. The reason for the observed differences in behaviour between SDMA and LAH remains to be clarified.

## EXPERIMENTAL

*N*-Benzylphthalimide (12.2 g., 0.05 mole) was added in portions with vigorous stirring to sodium bis-(2-methoxyethoxy)aluminum hydride (41.9 ml. of 70% benzene solution, equivalent to 0.3 g-atoms of hydrogen) in 50 ml. benzene. The temperature was maintained at 15-20° during the addition period of 30 minutes. The reaction mixture was stirred at room temperature for 15 minutes and 25% sodium hydroxide (20 ml.) was then added dropwise. The benzene layer was separated and washed with water, dried and evaporated. The residue was crystallized from absolute ethanol giving *N*-benzylisoindole, m.p. 117-118°, yield 3.0 g. (29%) [lit. (3) m.p. 119-120°],  $\lambda$  max 327 nm ( $\log \epsilon = 3.65$ ).

Anal. Calcd. for C<sub>15</sub>H<sub>13</sub>N: C, 86.91; H, 6.33; N, 6.76. Found: C, 86.44; H, 6.51; N, 7.19.

The U.V. spectrum of the ethanolic filtrate indicated the presence of an additional 20% yield of the isoindole, but this could not be isolated. Evaporation and distillation of the residue gave *N*-benzylisoindoline, b.p. 135°/0.1 mm., yield 1.8 g. The product was isolated as the hydrochloride, m.p. 210-211°, from chloroform-ether [lit. (4) m.p. 198°].

Anal. Calcd. for C<sub>15</sub>H<sub>16</sub>ClN: C, 73.41; H, 6.56; Cl, 14.43; N, 5.70. Found: C, 73.40; H, 6.79; Cl, 14.38; N, 5.49.

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