Reduction of Indolic Imides with Sodium Borohydride

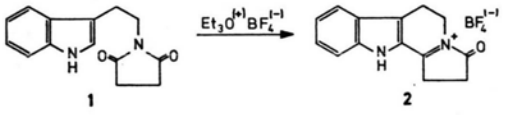
ATTA-UR-RAHMAN and NIGHAT WAHEED
H. E. J. Postgraduate Institute of Chemistry, University of Karachi, Karachi-32, Pakistan

(Z. Naturforsch. **31 b**, 287–288 [1976]; received September 23, 1975)

Reduction, Imides, Cyclization, Indole Alkaloids, Sodium Borohydride

The reduction of imides with sodium borohydride affords ring cleaved products instead of the corresponding carbinol lactams suggested previously.

We have previously described[1] a new procedure for the cyclization of the imide (**1**) using triethyl oxonium tetrafluoroborate to the corresponding indole (3.2 g) indolizine derivative (**2**) in high yields. Conventional procedures had earlier failed to affect such a cyclization[2]. A recent report[3,4] in the literature demonstrated an alternative mode of cyclization by the reduction of imides with sodium borohydride to the corresponding carbinol amides which could be subsequently cyclized under acid catalysed conditions.

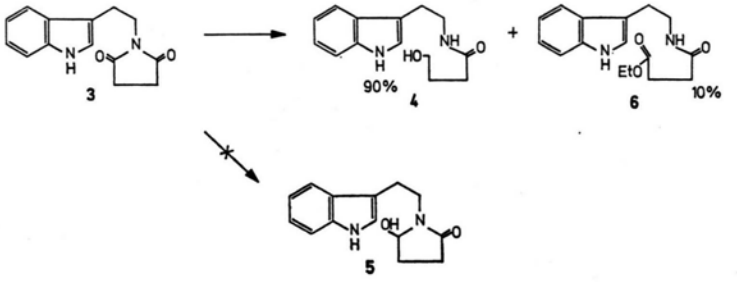


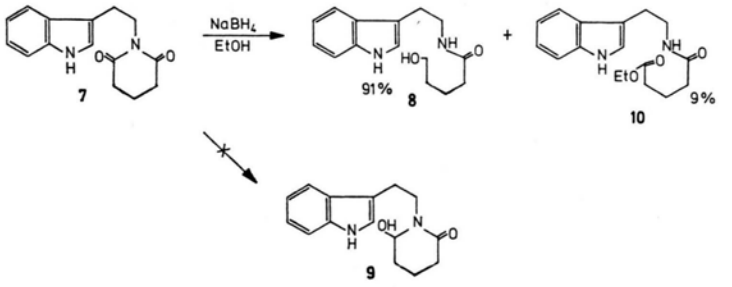
Requests for reprints should be sent to Dr. ATTA-UR-RAHMAN, H.E.J Postgraduate Institute of Chemistry, University of Karachi, *Karachi-32*, Pakistan.

Since the reduction/cyclization procedure appeared to offer attractive possibilities for the synthesis of alkaloidal intermediates, we have examined the applicability of this reaction in some indolic imides. N-succinimido tryptamine (**3**) was reduced under buffered pH-controlled conditions[3] with varying amounts of sodium borohydride but the product obtained was identified as the amide alcohol (**4**), m.p. 68 °C.

The substance possessed a normal indolic chromophore, and showed the amide carbonyl absorption at 1630 cm^{-1}. The mass spectrum showed the molecular ion at 246 with other major peaks at 228, 200, 143, 130, 130, and 103. No carbinol amide (**5**) was detectable. When the same reduction was carried out in pure ethanol, the amide ester (**6**) was also detectable in addition to the major amide alcohol (**4**).

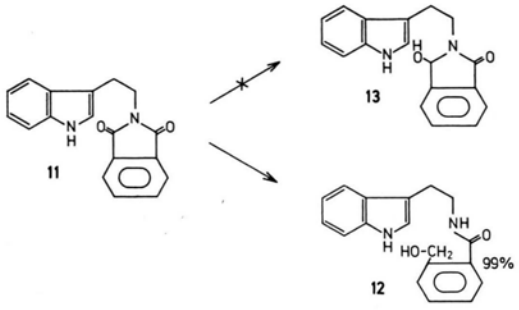
N-Glutarimido tryptamine (**7**), when similarly reduced with sodium borohydride under pH controlled conditions, afforded a new slower moving product m.p. 68 °C. The compound possessed an indolic UV spectrum and showed the presence of an amide carbonyl at 1632 cm^{-1} in its IR spectrum. The mass spectrum afforded the molecular ion at $m/e = 260$ and other major peaks appeared at $m/e = 240$, 160, 143, 130, and 103. It was thus clear that here again ring cleavage of the product had





occurred resulting in the formation of the amide (**8**). A minor faster moving crystalline product, m.p. 90 °C, of this reaction was also found to be indolic and afforded the molecular ion at $m/e = 302$. This was identified as the amide ester (**10**).

N-Phthalimidotryptamine (**11**) was also subjected to reductions with varying quantities of sodium borohydride in buffer media[3].



Substance **11** was found to be converted quantitatively to a new slower running material, m.p. 130 °C. Structure **12** was assigned to the product based on its indolic UV, amide absorption at 1632 cm^{-1} and mass spectrum ($M^+ = 294$, major peaks at 276, 200, 188, 160, 143, 130, 105, and 103).

It is evident from these experiments that the when imides are reduced with sodium borohydride, the predominant tendency is for ring opening to occur. This observation is in agreement with the results of other workers[5–8] who have observed similar cleavages of imides. Since many of the substances examined by SPECKAMP and coworkers[4] possessed α-substituents to the imide carbonyl groups, it is possible that the presence of such substituents results in sufficient ring stabilization so as to afford significant quantities of the intermediate hydroxylactams. The scope of applicability of the reaction appears, however, to be rather limited because of the facile ring opening of the carbinol amides.

[1] ATTA-UR-RAHMAN, J. Chem. Soc. (Perkin I) **1972,** 736.
[2] E. WENKERT, S. GARRAT, and K. E. DAVE, Canad. J. Chem. **42,** 489 [1964].
[3] J. C. HUBERT, W. N. SPECKAMP, and H. O. HUISMAN, Tetrahedron Letters **44,** 4493 [1972].
[4] J. B. P. A. WIJNBERG, W. N. SPECKAMP, and H. E. SCHOEMAKER, Tetrahedron Letters **46,** 4073 [1974].
[5] Z. HORI, C. IWATA, and Y. TAMURA, J. Org. Chem. **26,** 2273 [1961].
[6] F. C. UHLE, J. Org. Chem. **26,** 2998 [1961].
[7] Y. KONDO and B. WITKOP, J. Org. Chem. **33(1),** 206 [1968].
[8] T. WATANABE, F. HANAGUCHI, and S. OHKI, Yakugaku Zasshi **93(7),** 845 [1973].

Satz und Druck: Allgäuer Zeitungsverlag GmbH, Kempten