# Titanium(0) Reagents; 2. A Selective and Efficient Deoxygenation of Halogen Containing Heteroaromatic *N*-Oxides

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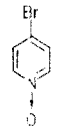
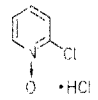
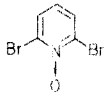
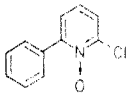
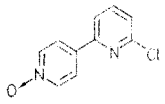
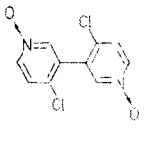
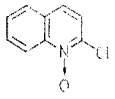
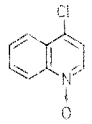
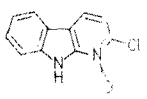
Following successful reductions of unfunctionalized heteroaromatic *N*-oxides by titanium(0), we applied this method to halogenated aromatic *N*-oxides to give the deoxygenated halogeno derivatives in 90–95% yield.

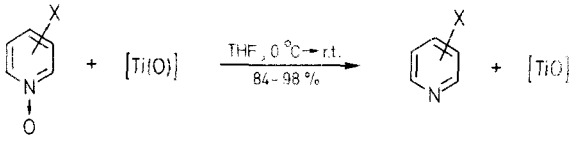
Recently,[1] we have described the use of low-valent titanium for the deoxygenation of unfunctionalized heteroaromatic *N*-oxides to give, under mild conditions, almost quantitative yields of deoxygenated products. We have now applied this for selective deoxygenation to substituted heteroaromatic *N*-oxides, having labile halogen atoms *ortho* or *para* to the ring nitrogen, which are susceptible to simultaneous dehalogenation reactions.[2]

We found, that titanium(0) slurry, easily accessible by the reduction of titanium tetrachloride with lithium aluminium hydride or magnesium in tetrahydrofuran,[1] is an excellent reagent for selective deoxygenation of halogen containing heteroaromatic *N*-oxides.

**Table.** Deoxygenation of Halogen Containing Heteroaromatic *N*-Oxides by a Titanium(0) Reagent

| Substrate **1** | | Titanium(0)/ Substrate Molar Ratio | Product **2** | Yield (%) | m.p. (°C) | (solvent) |
|---|---|---|---|---|---|---|
| | | | | | found | reported |
| **a**[a] |  | 1:1 | **a**[a,b] | 90[c] | – | – |
| **b**[3] |  | 1:1 | **b**[a,b] | 84[c] | – | – |
| **c**[a] |  | 1:1 | **c**[a,b] | 96[c] | – | – |
| **d**[a] |  | 1:1 | **d**[a,b] | 97[c] | – | – |
| **e**[4] |  | 1:1 | **e**[a,b] | 98[c] | – | – |
| **f**[e] |  | 1:1 | **f**[b,5] | 95[c] | 30–32 (hexane) | 34[5] (petroleum ether) |
| **g**[f] |  | 1:1 | **g**[g] | 98[c] | 118–120 (hexane) | – |
| **h**[6] |  | 2:1 | **h**[b,6] | 98[c] | 110–111 (hexane) | 110[6] |
| **i**[7] |  | 1:1 | **i**[a,b] | 97[c] | – | – |
| **j**[8] |  | 1:1 | **j**[a,b] | 92[c] | – | – |
| **k**[9] |  | 1:1 | **k**[b,10] | 88[d] | 258–260 (BuOAc) | 271–273[10] (BuOAc) |

[a] Commercially available.
[b] Products identified by comparison of TLC, IR and MS with those of authentic samples.
[c] Yield of product purified by flash chromatography on silica gel with hexane/ethyl acetate 10/1.
[d] Yield of product recrystallized.
[e] Prepared from **2f** by known procedure;[7] m.p. 141–142°C from hexane/$CHCl_3$; satisfactory microanalysis obtained: C, H, N ± 0.23.
[f] Prepared from **2g** by known procedure;[11] m.p. 157–159°C from hexane/$CHCl_3$; satisfactory microanalysis obtained: C, H, N ± 0.29.
[g] Prepared by hydrolysis, decarboxylation and chlorination of 2-hydroxy-[2,4′-bipyridine]-3-carbonitrile;[12] m.p. 120–122°C from hexane satisfactory microanalysis obtained: C, H, N ± 0.18.




1 2

X = 2- or 4-Br(Cl)

The reaction proceeds smoothly and quickly at room temperature, affording in most cases the deoxygenated product in over 90% yield. The results are presented in the Table.

All reactions were carried out in a nitrogen atmosphere, using standard techniques for the exclusion of air and moisture.

All solvents were distilled prior to use. THF was dried over sodium and lithium aluminum hydride (LAH) and redistilled under nitrogen. Unless otherwise noted, all chemicals were purchased from Aldrich Chemical Co. and were used without further purification. Flash chromatography was performed on silica gel (Merck), 230–400 mesh by eluting with hexane/ethyl acetate 10/1. IR spectra were recorded on a Beckman 4240 spectrometer. Mass spectra were recorded on a LKB-9000A instrument. Melting points are uncorrected.

**Preparation of the Titanium(0) Reagent:**
LAH (0.46 g, 0.013 mol) is added portionswise to a stirred, yellow suspension obtained by the addition of $TiCl_4$ (2 mL, 0.018 mol) to dry THF (50 mL), and the black slurry is stirred at room temperature for 15 min.

**Deoxygenation of Heteroaromatic *N*-Oxides; General Procedure:**
Halogen-substituted heteroaromatic *N*-oxide **1** (0.02 mol for monooxides or 0.01 mol for dioxides) is added portionwise at 0 °C to the stirred slurry of the titanium(0) reagent prepared above. The reaction mixture is stirred for 15 min at room temperature and then decomposed with water (50 mL) and 25% ammonia solution (50 mL). The mixture is extracted with ether (5 × 50 mL) or continously with $CHCl_3$; the organic layer is dried ($MgSO_4$) and evaporated. The residue is flash-chromatographed on silica gel or recrystallized to give pure product **2** (Table).

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