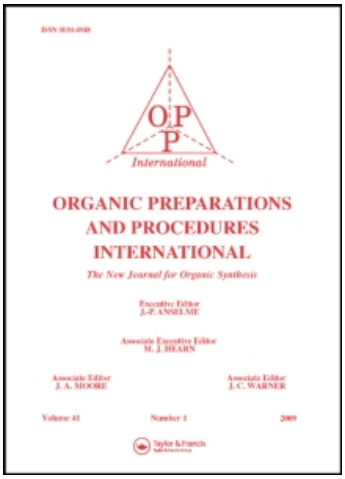

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3-NITRO-7-CHLOROQUINOLINE

Ned D. Heindel[a]; Stephen A. Fine[a]
[a] Department of Chemistry, Lehigh University, Bethlehem, Penna.

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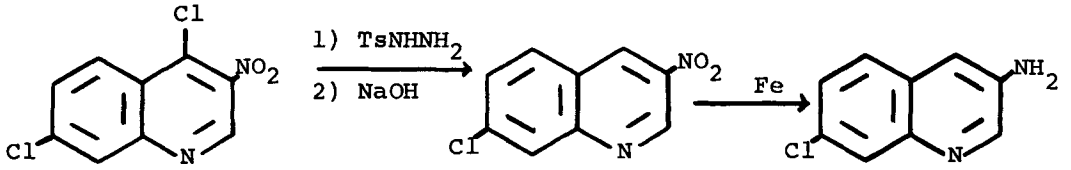
3-NITRO-7-CHLOROQUINOLINE[1]

Ned D. Heindel and Stephen A. Fine
Department of Chemistry
Lehigh University
Bethlehem, Penna. 18015



The difficulty of synthesizing 3-nitroquinolines lacking substituents in the pyridine ring is attested to by the scarcity of these substances in the chemical literature. The only sequences of generality involve the low yield nitration of quinolines at C-3 or the cyclization of unsaturated nitro-containing precursors.[2,3]

One of the best methods to incorporate a nitro function at C-3 involves treatment of the 4(1H)-quinolone with concentrated nitric acid in a technique which, while providing only moderate yields of the 3-nitro-4(1H)-quinolones, is the essence of simplicity to execute.[2,4] Obviously, the removal of the oxygen moiety at C-4 must be accomplished by a reduction which leaves the 3-nitro group untouched.

We wish to report that this operation can be carried out through the 4-chloro-3-nitroquinoline (obtained by $POCl_3$ reaction on the 3-nitro-4(1H)-quinolone) by dehalogenation with p-toluene-sulfonylhydrazine. Although dechlorinations with this reagent were first demonstrated to be of synthetic merit two decades ago, no procedures have appeared describing its application in the 4-haloquinoline series.[5]

Since 3-amino-7-chloroquinoline has been previously prepared in apparently only a low yield by hydrogenolysis-hydrogenation of 4,7-dichloro-3-nitroquinoline,[4] we have reduced 3-nitro-7-chloroquinoline to this corresponding aminoquinoline in 65% yield. Not only does this reaction serve to confirm the original site of nitration in the quinolone but it also demonstrates that this nitration-dechlorination-reduction pathway can provide an excellent route to 3-amino-quinolines.

EXPERIMENTAL[6]

7-Chloro-3-nitroquinoline: A solution of 4,7-dichloro-3-nitro-quinoline[4] (28.0 g, 0.115 moles) in 560 ml of $CHCl_3$ was mixed with a solution of 23.4 g, 0.120 moles, of p-toluene-sulfonylhydrazine in 600 ml of $CHCl_3$. The solution was stirred at room temperature for 24 h and filtered to collect the cream-colored hydrazino intermediate. The precipitate, 45.3 g, m.p. approximately 185°C with decomposition, was washed with cold $CHCl_3$ and air dried.

The intermediate was dissolved in 2ℓ of 0.5 N NaOH, heated to 80°C and maintained at that temperature for 1 h. The dark red mixture was cooled to room temperature, filtered, and the brown solid was washed thoroughly with water. Recrystallization of the crude product from petroleum ether (60-110°) gave 14.9 g, 62%, of orange needles, m.p. 145-147°. The analytical sample was prepared by recrystallization from 1:2 $CHCl_3$: n-hexane, m.p. 145.5-147.5°.

Anal. Calcd for $C_9H_5ClN_2O_2$: C, 51.82; H, 2.41; N, 13.43. Found: C, 51.98; H, 2.48; N, 13.21.

NMR($CDCl_3$) τ, ppm: 0.33 (d, 1, J = 2 Hz), 0.96 (d, 1, J = 2Hz), 1.76 (d, 1, J = 2 Hz), 1.98 (d, 1, J = 9 Hz), 2.30 (q, 1, J_o = 9 Hz, J_m = 2 Hz).

3-Amino-7-chloroquinoline: "Activated" iron was prepared according to the method of Hazlet[7] from powdered iron (135 g) and 27 ml of concentrated HCl. A mixture of 7-chloro-3-nitroquinoline (13.7 g) and 400 ml of benzene was heated to reflux and agitated with a vigorous mechanical stirrer. The "activated" iron was introduced

and vigorous stirring and reflux maintained for an additional 0.5 h whereupon the portionwise addition of 55 ml of water was initiated. Water addition required six h and upon completion the mixture was refluxed for an additional 0.5 h, filtered hot, and the iron residue washed thoroughly with benzene. The cooled solution was extracted with four 100 ml portions of 2% HCl. The extracts were filtered and carefully neutralized to pH 6 with 10% NaOH. After 20 min the aqueous layer was filtered again to remove a trace of precipitated solid, made strongly basic with NaOH and extracted thoroughly with ether. The ether layer was dried ($MgSO_4$) and evaporated to yield 7.60 g (65%) of an off-white solid, m.p. 130-143°. Vacuum sublimation gave silky white needles, m.p. 140-141.5°, lit m.p. 143-5° [4]

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