

Transition Metal Catalyzed Oxidations. 13 [1]

Oxidative *N*-Dealkylation of Secondary *N*-Aryl-*N*-alkyl Amines and Cleavage of Nitrones with $Zr(O-t-Bu)_4$ /tert-Butyl Hydroperoxide

Karsten Krohn* and Jochen K pke

Paderborn, Universit t-GH, FB 13-Fachbereich Chemie und Chemietechnik

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Dedicated to Prof. Jan Thiesing on the Occasion of his 75th Birthday

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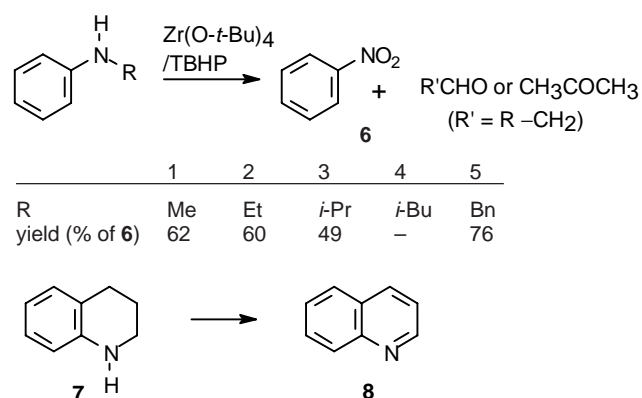
Abstract. The secondary *N*-aryl-*N*-alkyl amines **1–3** and **5** are oxidized by the $Zr(O-t-Bu)_4$ /TBHP system to nitrobenzene (**6**) and the corresponding carbonyl compounds with cleavage of the *C–N* bond. Nitrones are postulated as reac-

tion intermediates as demonstrated by the cleavage of **9–11** to nitrobenzene (**6**) and the benzaldehydes **12–14** by the same catalytic oxidation system.

In connection with the zirconium alkoxide-catalyzed oxidation of primary aromatic [2] and aliphatic [3] amines to nitro compounds, we also investigated the reaction of secondary *N*-aryl-*N*-alkyl amines with the system $Zr(O-t-Bu)_4$ /tert-butyl hydroperoxide (TBHP). Surprisingly, and in contrast to most other oxidations of secondary amines, a *C–N*-cleavage was observed in the reaction of *N*-methylaniline (**1**), and nitrobenzene (**6**) was isolated in 62% yield. There are only few reports in the literature on this interesting oxidative degradation of secondary amines. Very strong oxidation reagents such as peroxotrifluoroacetic acid [4] are able to cleave the *C–N* bond of secondary amines such as **1** to nitrobenzene (84%). In tungsten-catalyzed oxidations with hydrogen peroxide only 11% nitrobenzene was detected in the oxidation of *N*-benzylaniline along with other degradation products [5].

To test the scope and limitations of the reaction, we selected *N*-alkylanilines with primary, secondary, tertiary, and benzylic *N*-alkyl groups in addition to the cyclic tetrahydroquinoline (**7**). The experiments showed in fact that the oxidative cleavage of secondary *N*-aryl-*N*-alkyl amines with the system $Zr(O-t-Bu)_4$ /TBHP was not limited to *N*-methylanilines. The corresponding *N*-ethyl (**2**), *N*-2-propyl (**3**), and *N*-benzyl anilines (**5**) were oxidized to nitrobenzene in 60, 49, and 76% isolated yield, respectively (Scheme 1). The alkyl group was converted to the corresponding carbonyl compound and formaldehyde, acetone, and benzaldehyde were detected by gas chromatography in the crude reaction mixture. Interestingly, *N*-tert-butylaniline (**4**) was not cleaved to nitrobenzene. Tetrahydroquinoline (**7**), which is known to undergo easy dehydrogenation to an aro-

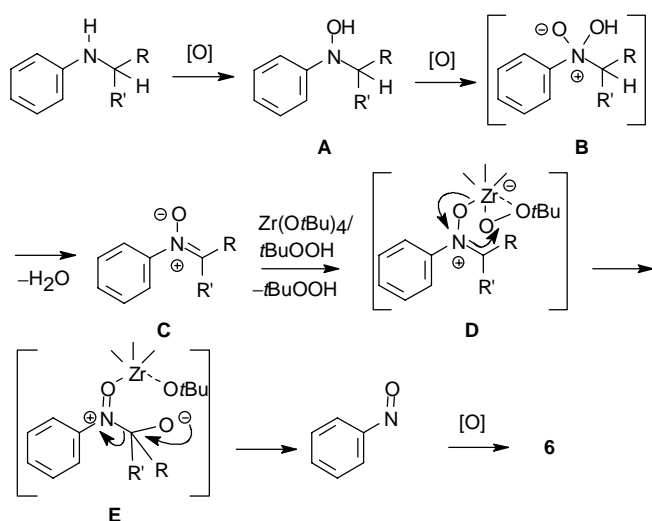
matic heterocyclic system, was smoothly converted to quinoline (**8**).



Scheme 1 Oxidative cleavage of primary and secondary *N*-alkyl-*N*-aryl amines

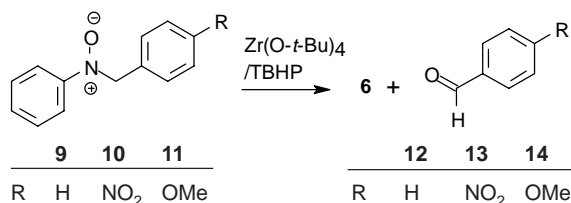
The question arose how the *C–N* bond in the *N*-alkylanilines was cleaved under these mild oxidative conditions. Based on the experience with primary amines [3, 6], we postulated the initial oxygenation of the secondary amine to the hydroxylamine **A** and then via **B** to the nitrone **C** as shown in Scheme 2. The crucial step in nitrone formation is water elimination from **B**. This step cannot proceed in *tert*-alkylanilines, and the failure of *tert*-butylaniline to form nitrobenzene supports this step of the mechanism. *N*-Aryl-*N*-benzyl secondary amines react most easily presumably because water elimination to form the intermediate nitrones is much more rapid than in the corresponding *N*-aryl-*N*-alkyl derivatives. The nitrone thus formed can then coordinate with the

zirconium metal as shown in **D**, and the O–O double bond of the hydroperoxide ligand is then attacked by the nitron double bond as the nucleophile. This is another example of the oxygenation of the *vinyl*ic double bond in transition metal peroxo complexes as previously observed in phenols [7] or enolates [8, review 9]. The resultant oxygenation product then decomposes with C–N bond cleavage as depicted in **E** to yield nitrosobenzene that is easily oxidized by the Zr(O-*t*-Bu)₄/TBHP system to nitrobenzene, as was demonstrated in a previous investigation [2].



Scheme 2 Mechanistic proposal for C–N bond cleavage in *N*-alkyl-*N*-aryl amines

It was not possible to directly detect nitrones as reaction intermediates nor could they be trapped in 1,3-dipolar cycloadditions with olefins. However, the three nitrones **9**–**11** with electronically different substituents on the aromatic ring could be quantitatively cleaved to nitrobenzene and the corresponding benzaldehydes **12**–**14** as detected by GC. The nitrones reacted rapidly at room temperature, and there was no obvious difference in reaction rate as observed by TLC monitoring.



Scheme 3 Oxidative cleavage of nitrones to nitrobenzene and aldehydes

In summary, a novel C–N cleavage of secondary *N*-aryl-*N*-alkyl amines under mild oxidative conditions with the Zr(O-*t*-Bu)₄/TBHP system is reported. The

corresponding nitrones, postulated as reaction intermediates, are also cleaved by the same catalytic oxidation system to nitrobenzene and benzaldehydes.

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Experimental

For general methods and instrumentation see [10].

Oxidative Cleavage of Secondary *N*-Alkylanilines (General Procedure)

All reactions were conducted in a dry 50 ml two necked flask with magnetic stirrer, gas inlet, and septum. To a solution of the *N*-alkylanilines (**1**–**5** and **7**; 10 mmol) in dry CH₂Cl₂ (20 ml) was added freshly activated powdered molecular sieves (3 A, 1.5 g). Zirconium tetra-*tert*-butylate (0.4 ml, 1.0 mmol) was then added, the mixture was stirred for 30 min, and the *N*-alkylanilines were added within 5 min. The suspension was refluxed (ca. 5 h, TLC monitoring), and water (15 ml) was then added to quench the reaction. The mixture was filtered, and the molecular sieves were carefully washed with CH₂Cl₂ (20 ml). A 5% aqueous solution of sodium sulfite (100 ml) was added, and the mixture was stirred overnight to reduce excess TBHP. The organic phase was separated, washed with water (10 ml), dried (Na₂SO₄), and analyzed by GC. Nitrobenzene was isolated by removal of the solvent under reduced pressure and bulb to bulb distillation of the residue. For yields of **6** see Scheme 1. The volatile aldehydes corresponding to **1**, **2** and **5** were detected qualitatively by GC. 35% pure quinoline (**8**) was isolated in the reaction of tetrahydroquinoline.

Oxidative Cleavage of Nitrones (General Procedure); Formation of Nitrobenzene (**6**) and Benzaldehydes **12**–**14**

The nitrones were prepared by condensation of phenylhydroxylamine with the corresponding benzaldehydes as described in the literature (**9**, **10**: [11], **11**: [12]). Powdered molecular sieves (3 A, 600 mg) were added to a solution of the nitron (1 mmol) in CH₂Cl₂ (10 ml), and the suspension was stirred for 30 min. Zr(O-*t*-Bu)₄ (0.04 ml, 0.1 mmol) and TBHP (1.0 ml in CH₂Cl₂, 3.1 mmol) were added, and the mixture was stirred for ca. 5 h at 20 °C (TLC monitoring). Yields of nitrobenzene (**6**) and benzaldehydes **12**–**14** were quantitative by GC.

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Address for correspondence:
Prof. K. Krohn
Fachbereich Chemie und Chemietechnik
der Universität – GH Paderborn
Warburger Str. 100
D-33098 Paderborn
Fax: Internat. code (0) 5251-60-3245
e-Mail: kk@chemie.uni-paderborn.de