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A Novel Synthesis of Aromatic *N*-Chloro Aldimines

René Kupfer and Udo H. Brinker*

Department of Chemistry, State University of New York at Binghamton, Binghamton, New York, 13902-6016

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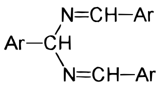
Introduction

A new synthesis of *N*-chloro aldimines (*N*-chlorobenzenemethanimines) **1** from hydrobenzamides (1-phenyl-*N*,*N'*-bis(phenylmethylene)methanediamines) **2** has been developed. The starting materials **2** are readily available from the reaction of the corresponding aromatic aldehydes and ammonia.[1] In general, hydrobenzamides **2** are crystalline compounds which can be stored without decomposition and, therefore, should be convenient precursors for the synthesis of *N*-chloro aldimines.

$Ar{-}CH{=}NCl$

1



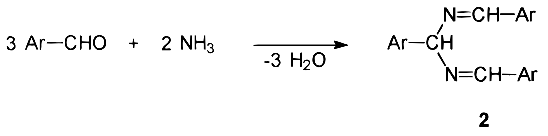
$$Ar{-}CH(N{=}CH{-}Ar)_2$$

2

N-Chloro ketimines have been used for the synthesis of substituted imines[2a] and diaziridines[3] from which diazirines[4] are made, but not much is known about the corresponding *N*-chloro aldimines. This is due to their instability when compared with the *N*-chloro ketimines.[2] Elimination of hydrogen chloride to produce the corresponding nitriles is facile, and decomposition can occur even violently. *N*-Chloro ketimines could be obtained by different methods, such as the elimination of hydrogen chloride from secondary *N*,*N*-dichloroamines[5] or chlorination of imines.[6] In contrast, only one convenient method for the preparation of *N*-chloro aldimines has been reported thus far. According to Forster[7] and Raschig,[8] aldehydes are treated with chloramine in aqueous solution. Later this method was developed into a general synthesis for the preparation of substituted *N*-chlorobenzenemethanimines **1** by Hauser and co-workers.[9] The parent compound, the unsubstituted *N*-chlorobenzenemethanimine (**1a**), however, could not be isolated and identified, since it readily decomposed into benzonitrile and hydrogen chloride.[10]

Results and Discussion

Hydrobenzamides **2**, the starting materials for the synthesis of *N*-chloro aldimines, are easily obtained from the reaction of the corresponding aromatic aldehydes with aqueous ammonia[1] in nearly quantitative yields.



$$3\,Ar{-}CHO + 2\,NH_3 \xrightarrow[-3\,H_2O]{} Ar{-}CH(N{=}CH{-}Ar)_2$$

Ar = **a** phenyl **b** *p*-anisyl **c** *p*-tolyl

We have found that hydrobenzamides **2** react with *tert*-butyl hypochlorite in methanol to form a mixture of the corresponding *N*-chloro aldimines **1** and dimethyl acetals **4**. According to the mechanism depicted below, the assumed intermediate **3** can either solvolyze completely in the alcoholic solution (Scheme 1, path a) or react again with *tert*-butyl hypochlorite to form an equimolar mixture of *N*-chloro aldimine **1** and acetal **4** (path b).

If methanol is replaced by nonprotic solvents such as methylene chloride, the reaction starts very slowly even at room temperature but gets vigorous after a few seconds to a few minutes. In this case, *N*-chloro aldimines **1** are obtained, albeit in low yield. Instead of acetals, aldehydes are produced as side products after aqueous workup. The vigorous reaction might be due to the hydrogen chloride evolved from the decomposition of the *N*-chloro aldimine formed. The observation that added acetic acid initiates the exothermic reaction supports this. The mechanism of the reaction in nonprotic solvents needs to be studied in more detail.

N-Chlorobenzenemethanimine (**1a**), *N*-chloro-4-methoxybenzenemethanimine (**1b**), and *N*-chloro-4-methylbenzenemethanimine (**1c**) were synthesized according to the new procedure (Table 1).

For the synthesis of **1a** and **1c**, it is possible to carry out the reaction at room temperature. This causes only slightly lower yields of *N*-chloro aldimines **1a** and **1c**. In the reaction with hydroanisamide (1-(4-methoxyphenyl)-*N*,*N'*-bis[(4-methoxyphenyl)methylene]methanediamine) (**2b**), however, at room temperature, instead of *N*-chloro-4-methoxybenzenemethanimine (**1b**), *p*-chloroanisole was obtained.

Experimental Section

^1H and ^{13}C NMR spectra were recorded on a 360 (90.6)-MHz spectrometer. IR spectra were obtained on a FT-IR instrument. Analytical gas chromatography was performed using a 25 m × 0.272 mm (i.d.) OV 101 glass capillary column. Preparative chromatography was done on a short column using silica gel 60 (230−400 mesh).

tert-Butyl hypochlorite was prepared according to *Organic Syntheses*.[11]

Synthesis of Hydrobenzamides 2a−c (General Procedure).[1] Freshly distilled aldehyde was added to a *ca*. 10-fold excess of an aqueous solution of NH_3 (∼29%). After the solution was stirred for 1 day, the liquid was poured off and the clumps were crushed and dried in a desiccator. The products **2a−c** can be recrystallized from ethanol which is, however, not necessary for the next step.

Synthesis of *N*-Chloro Aldimines 1a−c (General Procedure). Hydrobenzamides **2a−c** (10 mmol) were suspended in 15 mL of methanol. After the solution was cooled to −65 °C, 2.2 g (20 mmol) of *tert*-butyl hypochlorite was added within ca. 5 min with stirring (exothermic reaction). Over the next 10 min, the mixture was allowed to warm up to almost room temperature. The solution was poured into ca. 60 mL of aqueous

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[1] (a) Laurent, M. A. *Ann. Chim. Phys.* **1836**, *62*, 23. (b) Laurent, M. A. *Liebigs Ann. Chem.* **1837**, *21*, 130. (c) Francis, F. *Ber.* **1909**, *42*, 2216. (d) Hunter, D. H.; Sim, S. K. *Can. J. Chem.* **1972**, *50*, 669, 678.

[2] (a) Pawlenko, S. In *Houben-Weyl, Methoden der Organischen Chemie;* Thieme Verlag: Stuttgart, 1990; Vol. E14b, p 282. (b) Theilacker, W.; Wegner, E. *Angew. Chem.* **1960**, *72*, 127.

[3] Fuchs, J. J. U.S. Patent 1966, 3287354.

[4] (a) *Chemistry of Diazirines*; Liu, M. T. H., Ed.; CRC: Boca Raton, 1987; Vol. 1, p 2. (b) Kupfer, R.; Poliks, M. D.; Brinker, U. H. *J. Am. Chem. Soc.* **1994**, *116*, 7393.

[5] Eichenhofer, K.-W.; Schliebs, R. *Naturwissenschaften* **1977**, *64*, 529.

[6] Curtin, D. Y.; Crubbs, E. J.; McCarty, C. G. *J. Am. Chem. Soc.* **1966**, *88*, 2775.

[7] Forster, M. O. *J. Chem. Soc. Trans.* **1915**, *107*, 260.

[8] Raschig, F. In *Schwefel- und Stickstoffstudien*; Verlag Chemie G.m.b.H.: Leipzig-Berlin, 1924; p 68, 78.

[9] (a) Hauser, C. R.; Hauser, M. L. *J. Am. Chem. Soc.* **1930**, *52*, 2050. (b) Hauser, C. R. *J. Am. Chem. Soc.* **1930**, *52*, 1108. (c) Hauser, C. R.; Hauser, M. L.; Gillaspie, A. G. *J. Am. Chem. Soc.* **1930**, *52*, 4158. (d) Hauser, C. R.; Gillaspie, A. G.; LeMaistre, J. W. *J. Am. Chem. Soc.* **1935**, *57*, 567.

[10] Luxmoore, C. M. *J. Chem. Soc.* **1896**, *69*, 177.

[11] Mintz, M. J.; Walling, C. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. V, p 184.

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Scheme 1

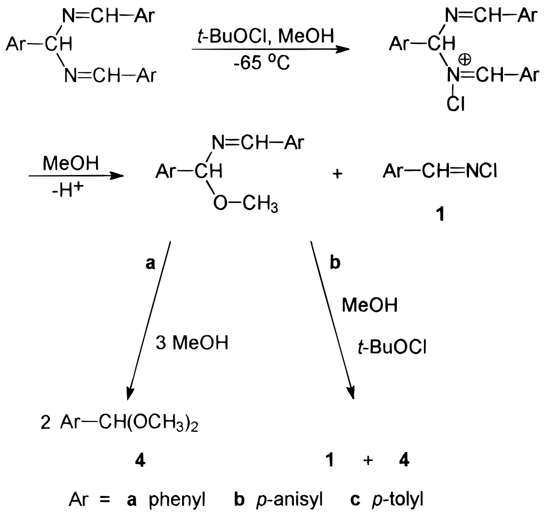
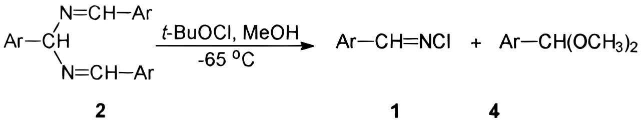


Table 1



2	1[a]	4[a]
a	1.06 mol (53%)[b]	1.28 mol
b	0.82 mol (41%)[b]	1.30 mol
c	1.50 mol (79%)[b]	0.64 mol

[a] total isolated yield based on one mole of hydrobenzamide **2**

[b] percent yield, if assumed that two moles of chlorimine are formed from one mole of starting material

ammonia (5%), and the product was extracted with ether. After the solution was dried over Na_2SO_4, it was decanted and evaporated under reduced pressure. The residue consisted of a mixture of *N*-chloro aldimine and dimethyl acetal. Pure *N*-chloro aldimine was obtained by column chromatography using hexanes as eluent.

The acetals can be washed out with polar solvents such as ethyl acetate. These compounds are usually contaminated with their hydrolysis products, i.e., hemiacetals and aldehydes.

a. Reaction with hydrobenzamide (2a) to give *N*-chlorobenzenemethanimine (1a): yield; 1.5 g (10.6 mmol), yellowish liquid; ^{1}H NMR ($CDCl_3$) δ 7.37–7.53 (m, 3 H), 7.66 (d, 2 H), 8.78 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 128.0 (2 C), 129.0 (2 C), 132.1 (1 C), 133.2 (1 C), 172.7 (1 C); IR (neat, cm^{-1}) 1599, 1563, 1215.

Benzaldehyde dimethyl acetal (4a): yield 2 g (12.8 mmol).

b. Reaction with *p*-hydroanisamide (2b) to give *N*-chloro-4-methoxybenzenemethanimine (1b): yield 1.4 g (8.2 mmol) (this compound was already prepared by Hauser[9a]); ^{1}H NMR ($CDCl_3$) δ 3.83 (s, 3 H), 6.92 (d, 2 H), 7.59 (d, 2 H), 8.68 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 55.4 (1 C), 114.4 (2 C), 129.3 (1 C), 129.7 (2 C), 162.7 (1 C), 171.8 (1 C); IR (neat, cm^{-1}) 1607, 1260.

***p*-Anisaldehyde dimethyl acetal (4b):** yield 2.4 g (13 mmol).

c. Reaction with *p*-hydrotoluamide (1-(4-methylphenyl)-*N*,*N*′-bis[(4-methylphenyl)methylene]methanediamine) (2c), to give *N*-chloro-4-methylbenzenemethanimine (1c): yield 2.44 g (15.8 mmol) (this compound was already prepared by Hauser *et al.*[9d]); ^{1}H NMR ($CDCl_3$) δ 2.37 (s, 3 H), 7.21 (d, J = 8.0 Hz, 2 H), 7.54 (d, J = 8.0 Hz, 2 H), 8.73 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 21.6 (1 C), 128.0 (2 C), 129.6 (2 C), 130.6 (1 C), 142.7 (1 C), 172.5 (1 C); IR (neat, cm^{-1}) 1607, 1593, 812.

***p*-Tolualdehyde dimethyl acetal (4c):** yield 1.1 g (6.4 mmol).

Caution: *N*-chloro aldimines (*N*-chlorobenzenemethanimines) can decompose suddenly, evolving a cloud of hydrogen chloride. This decomposition happens upon heating,[9a,d] or might even take place upon standing at room temperature (*N*-chloro-4-methoxybenzenemethanimine, **(1b)**!). In hydrocarbon solution, however, *N*-chloro aldimines seem to be safe to work with.

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CAS Registry Numbers (supplied by author): **1a** [112129-04-1]; **2a** [92-29-5]; **2b** [644-03-1]; **2c** [35779-32-9].

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Additions and Corrections

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G. Capozzi, R. W. Franck, M. Mattioli, S. Menichetti,* C. Nativi, and G. Valle. Phthalimidesulfenyl Chloride. 9. A Simple Access to α,α′-Dioxothiones, a New Class of Bis-heterodienes. Synthesis of 1,4-Oxathiin Systems.

Page 6426. The following sentence was inadvertently omitted from the Acknowledgment. The authors wish to thank Angeles Dios (Hunter College) for the experimental details of the optimized preparation of glucal cycloadduct **7e**.

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