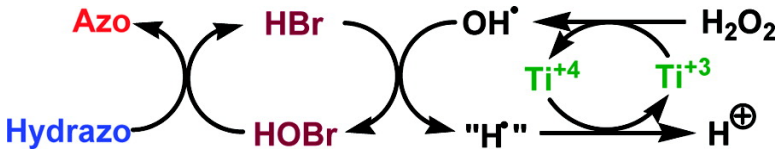
Communication

Catalytic Oxidation of Hydrazo Derivatives Promoted by a TiCl/HBr System

Eyal Drug, and Michael Gozin

J. Am. Chem. Soc., **2007**, 129 (45), 13784-13785• DOI: 10.1021/ja074413c • Publication Date (Web): 24 October 2007



More About This Article

Additional resources and features associated with this article are available within the HTML version:

- Supporting Information
- Links to the 1 articles that cite this article, as of the time of this article download
- Access to high resolution figures
- Links to articles and content related to this article
- Copyright permission to reproduce figures and/or text from this article

View the Full Text HTML

J|A|C|S
COMMUNICATIONS

Published on Web 10/24/2007

Catalytic Oxidation of Hydrazo Derivatives Promoted by a $TiCl_3$/HBr System

Eyal Drug and Michael Gozin*

School of Chemistry, Raymond and Beverly Sackler Faculty of Exact Sciences, Tel-Aviv University, Ramat Aviv, Tel-Aviv 69978, Israel

Received June 18, 2007; E-mail: cogozin@mgchem.tau.ac.il

Development of efficient processes for preparation of azo derivatives is very important as these compounds are commonly used as organic dyes,[1] indicators,[2] radical reaction initiators,[3] and therapeutic agents.[4] In addition, azo compounds have potential for use in electronic[5] and drug delivery applications.[6]

Presently known synthetic strategies to obtain these materials include a very broad range of stoichiometric processes such as electrophilic reactions of diazonium salts,[7a] coupling of primary arylamines with aromatic nitroso[7b] and nitro[7c] compounds, Wallach rearrangements of azoxy derivatives,[7d] rearrangements of aryl triazenes,[7e] and reduction of azoxy and nitro aromatics.[7f]

Additional important methods for obtaining azo derivatives involve hydrazine oxidation. Most of these methods are based on stoichiometric processes and require use of $Pb(CH_3CO_2)_4$,[8a] HgO,[8b,c] $(NH_4)_2S_2O_8$,[8d] *N*-bromosuccinimide in pyridine,[8e,f] tetrabutylammonium cerium(IV) nitrate[8g] and arylsulfonyl peroxide reagents,[8h] $NaNO_2$ in acetic anhydride,[8i] and $NaNO_2$/$NaHSO_4$ on silica support.[8j]

There are only a few known examples of catalytic oxidation of hydrazo compounds to the corresponding azo derivatives. Utilizing oxygen or H_2O_2 as oxidants, NH_4VO_3,[9a] $CuCl_2$,[9b] and Co(II) complexes[9c,d] were reported to catalyze this transformation. Also, $FeSO_4$ was shown to function as hydrazo oxidation catalyst when a mixture of $KClO_3$/H_2SO_4 was used as an oxidant.[9e]

Here we report the discovery of a novel catalytic system, with a conceptually new mechanism of action, capable of highly efficient and selective oxidation of hydrazo compounds into the corresponding azo derivatives. This new process is compatible with a range of substituents, including aryl, methoxyaryl, nitroaryl, and acetyl, on the hydrazo functional group.

In the present study, a series of hydrazo compounds (entries 1−6, Table 1) were treated with H_2O_2 and a catalyst mixture comprising $TiCl_3$ and HBr (Figure 1). The reported reactions proceed under ambient conditions with fast kinetics and are compatible with a series of solvents, including alcohols and DMSO. For all evaluated hydrazo starting materials, high yields of the corresponding azo products were observed within a short period of time after completion of the H_2O_2 addition. Furthermore, versatility and selectivity of the $TiCl_3$/HBr system was compared to the known NH_4VO_3 catalyst, used for H_2O_2-based oxidation of hydrazo compounds. Therefore, in a comparative investigation, previously investigated substrates (entries 1−6, Table 1) were treated with H_2O_2, using NH_4VO_3 as a catalyst.[9a]

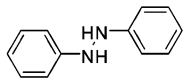
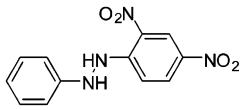
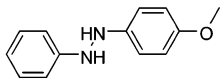
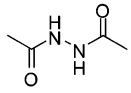
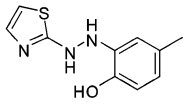
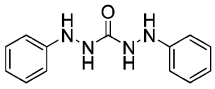
Attempts to perform the reaction using a catalyst composed of $TiCl_3$ and HCl (instead of HBr) were not successful, and no oxidation products were observed.

The $TiCl_3$/HBr system is likely to function via two separate and distinctive catalytic cycles, which are linked by radical species (Figure 2). The first cycle involves a single-electron redox transformation between Ti^{3+} and Ti^{4+} complexes. This reaction is initiated by the well-described process in which $TiCl_3$ reacts with H_2O_2 under acidic conditions, generating hydroxyl radicals, water, and the Ti^{4+} species.[10]

Under investigated reaction conditions, we propose that the formed hydroxyl radicals oxidize HBr into the corresponding hypobromous acid. Subsequently, formed HOBr is reduced back to the HBr and water by the hydrazo substrate, concurrently producing the desired azo derivative and thus closing the HBr−HOBr catalytic cycle (Figure 2).

Although formation of the hydroxyl radical is well-documented, the formation of the hydrogen radical species could not be easily proven, due to very high reactivity and short lifetime. Yet, strong

Table 1. Hydrogen Peroxide Based Oxidation of Various Hydrazines Using $TiCl_3$/HBr Catalyst and, For Comparison, NH_4VO_3 Catalyst (Isolated Yields of the Corresponding Azo Products Are Presented)

Entry	Substrate	$TiCl_3$/HBr Yields(%)[a]	NH_4VO_3 Yields (%)[b]
1		95	96
2		88	47
3		95	82
4		90	24
5		88	16
6		85	38

[a] Experimental conditions: $TiCl_3$ solution (15% in HCl aqueous solution, 0.2−0.25 mol %); HBr solution (33% in acetic acid solution, 1.0−1.5 mol %); H_2O_2 solution (30% in water, ∼1.5 mol %). [b] Experimental conditions: NH_4VO_3 solution (1.0% in 1.0 M HCl solution, 0.4 mol %); H_2O_2 solution (30% in water, ∼1.5 mol %).

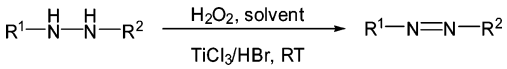


Figure 1. General procedure for the catalytic oxidation of hydrazo compounds to the corresponding azo derivatives. Catalyst: $TiCl_3$/HBr.

10.1021/ja074413c CCC: $37.00

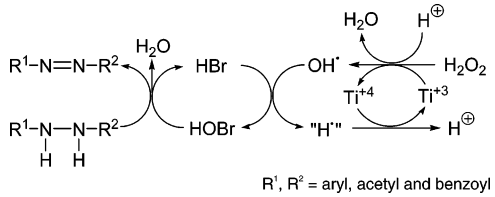


Figure 2. Proposed mechanism for the catalytic oxidation of the hydrazo compounds using H_2O_2 and $TiCl_3$/HBr catalyst.

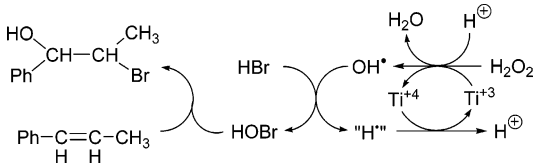


Figure 3. Proposed mechanism of olefin hydrobromination process, based on HBr, H_2O_2, and $TiCl_3$ catalyst.

support for the suggested mechanism was provided by the work of Nenadovic and co-workers who have shown that, in ethanol, Ti^{4+} could be effectively reduced by hydrogen radicals to Ti^{3+} complexes with a rate of 5.95×10^7 dm^3 mol^{-1} s^{-1}.[11]

The mechanistic studies of the discovered process were begun with the evaluation of the HBr−HOBr cycle, starting with validation of the hypobromous acid formation. On the basis of the olefin hydrobromination reaction reported by Saint and others,[12] we used *trans*-methylstyrene as a HOBr-trapping substrate (Figure 3). The reaction was performed with catalytic and stoichiometric amounts (as compared to *trans*-methylstyrene starting material) of HBr reagent. In each case, a corresponding amount of hydrobromination product was observed, clearly indicating the formation of HOBr species in our process.

We have performed stoichiometric oxidations of hydrazo starting materials (entries 1−3, Table 1) by using an in situ generated hypobromous acid from *N*-bromoacetamide and HOCl.[13a] These oxidation reactions produced the same yields of the azo products as our catalytic process, providing a strong support to our claim that HOBr is indeed the oxidant of the hydrazo compound in the reaction. It should be mentioned that no azo products were detected when we attempted to react stoichiometric amounts of hydrazo derivatives with HOCl or directly with H_2O_2.

Additional studies included evaluation of other metal-containing compounds as potential cocatalysts in our system. Specifically, VO(acac)$_2$[13] and CuI,[14] both capable of single-electron redox transformation, were used instead of $TiCl_3$; however, no hydrazo oxidation was observed with these compounds.

In summary, a novel method for preparing azo compounds via catalytic oxidation of corresponding hydrazo precursors has been discovered. This oxidation process was highly efficient and selective and represents a valuable addition to the chemistry of azo compounds. Further investigations to expand the scope of this reaction are currently under active investigation in our laboratories.

Acknowledgment. The authors thank Bogdan Belgorodsky, Dr. Shlomit Gali, Dr. Dan Grinstein, and Sharon Gil-Chaimov for their contributions, and Tel-Aviv University for its generous financial support.

Supporting Information Available: Synthetic procedures and characterization of compounds **2** and **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) *Industrial Dyes: Chemistry, Properties, Applications*; Hunger, K., Ed.; Wiley-VCH: Weinheim, Germany, 2003.
(2) (a) Anderson, R. G.; Nickless, G. *Analyst* **1967**, *92*, 207−238. (b) Ashutosh, P. N. D.; Mehrotra, J. K. *Colourage* **1979**, *26*, 25.
(3) (a) Athey, R. D., Jr. *Eur. Coatings J.* **1998**, *3*, 146−149. (b) Sheppard, C. S. *Encycl. Polym. Sci. Eng.* **1985**, *2*, 143−157.
(4) (a) Hoult, J. R. S. *Drugs* **1986**, *32* (Suppl. 1), 18−26. (b) Sandborn, W. J. *Am. J. Gastroenterol.* **2002**, *97*, 2939−2941.
(5) (a) Cisnetti, F.; Ballardini, R.; Credi, A.; Gandolfi, M. T.; Masiero, S.; Negri, F.; Pieraccini, S.; Spada, G. P. *Chem.—Eur. J.* **2004**, *10*, 2011−2021. (b) Tripathy, S.; Kim, D. Y.; Li, L.; Kumar, J. *Pure Appl. Chem.* **1998**, *70*, 1267−1270.
(6) (a) Jain, A.; Gupta, Y.; Jain, S. K. *Crit. Rev. Ther. Drug Carrier Syst.* **2006**, *23*, 349−400. (b) Van den Mooter, G.; Maris, B.; Samyn, C.; Augustijns, P.; Kinget, R. *J. Pharm. Sci.* **1997**, *86*, 1321−1327.
(7) (a) Szele, I.; Zollinger, H. *Top. Curr. Chem.* **1983**, *112*, 1−66. (b) Boyer, J. H. *The Chemistry of the Nitro and Nitroso Groups*; Feuer, H., Ed.; Interscience: New York, 1969; Part 1, p 278. (c) Stern, M. K.; Hileman, F. D.; Bashkin, J. K. *J. Am. Chem. Soc.* **1992**, *114*, 9237−9238. (d) Buncel, E. *Acc. Chem. Res.* **1975**, *8*, 132−139. (e) Williams, D. L. H.; Buncel, E. *Isot. Org. Chem.* **1980**, *5*, 147−230. (f) Newbold, B. T. *The Chemistry of the Hydrazo, Azo and Azoxy Groups*; Patai, S., Ed.; Interscience: New York, 1975; Part 2, p 602.
(8) (a) Billera, C. F.; Dunn, T. B.; Barry, D. A.; Engel, P. S. *J. Org. Chem.* **1998**, *63*, 9763−9768. (b) Cohen, S. G.; Zand, R. *J. Am. Chem. Soc.* **1962**, *84*, 586−591. (c) LeFevre, G. N.; Crawford, R. J. *J. Am. Chem. Soc.* **1986**, *108*, 1019−1027. (d) Whalley, B. J. P.; Evans, H. G. V.; Winkler, C. A. *Can. J. Chem.* **1956**, *34*, 1154−1162. (e) Wang, C.; Wang, X.; Wang, Y. *Indian J. Chem., Sect. B* **1999**, *38B*, 964−965. (f) Li, J.-P.; Liu, P.; Wang, Y. *J. Chem. Res. (S)* **2003**, 109−110. (g) Muathen, H. A. *Indian J. Chem.* **1991**, *30B*, 522−524. (h) Hoffman, R. V.; Kumar, A. *J. Org. Chem.* **1984**, *49*, 4014−4017. (i) Li, X.; Wang, Y.; Wang, J. *Indian J. Chem.* **2004**, *43B*, 677−678. (j) Li, X.; Wang, Y.; Wang, J. *J. Chem. Res. (S)* **2002**, 540−541.
(9) (a) Trischler, F. J. *Therm. Anal.* **1979**, *16*, 119−122. (b) Blackadder, D. A.; Hinshelwood, C. *J. Chem. Soc.* **1957**, 2904−2906. (c) Nemeth, S.; Szeverenyi, Z.; Simandi, L. I. *Inorg. Chim. Acta* **1980**, *44*, L107−L109. (d) Kim, S. S. B.; Hommer, R. B.; Cannon, R. D. *Bull. Korean Chem. Soc.* **2006**, *27*, 255−265. (e) Shi, L.; Pan, F.; Jia, X.-S.; Wang, Y. *Synth. Commun.* **2001**, *31*, 1691−1695.
(10) (a) Dixon, W. T.; Norman, R. O. C. *J. Chem. Soc.* **1963**, 3119−3124. (b) Cocivera, M.; Fyfe, C. A.; Vaish, S. P.; Chen, H. E. *J. Am. Chem. Soc.* **1974**, *96*, 1611−1613. (c) Cannella, R.; Clerici, A.; Panzeri, W.; Pastori, N.; Punta, C.; Porta, O. *J. Am. Chem. Soc.* **2006**, *128*, 5358−5359.
(11) Mićić, O. I.; Nenadović, M. T. *J. Chem. Soc., Dalton Trans.: Inorg. Chem.* **1979**, *12*, 2011−2014.
(12) (a) Marples, B. A.; Saint, C. G. *Synth. Commun.* **1982**, *12*, 545−555. (b) Kocovsky, P.; Stary, I.; Zajicek, J.; Turecek, F.; Vasickova, S. *J. Chem. Soc., Perkin Trans. 1* **1988**, *8*, 2297−2303.
(13) Maurya, M. R. *Coord. Chem. Rev.* **2003**, *237*, 163−181.
(14) Goodgame, D. M. L.; Goodgame, M.; Rayner, G. W. *Nature* **1969**, *222*, 866.

JA074413C