JOC*Note*

A Fast, High-Yield Preparation of Vicinal Dinitro Compounds Using HOF·CH_3CN

Elizabeth Golan and Shlomo Rozen*

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

rozens@post.tau.ac.il

Received July 7, 2003

Abstract: HOF·CH_3CN, a very efficient oxygen-transfer agent, was reacted with various aliphatic and aromatic vicinal diamino compounds. The products were the rare, vicinal dinitro derivatives formed in excellent yields and short reaction times. This is in contrast to other oxygen-transfer agents which tend to break the central C−C bond of the diamino precursor. This reaction was also used for making dinitro compounds with all four oxygens, being the [18]O isotope.

Nitro compounds have found numerous uses in organic chemistry. More than 25 years ago, Seebach had already dubbed them "ideal intermediates in organic synthesis".[1] However, the difficulties associated with the preparation of 1,2-dinitro derivatives limited their use to being only precursors for tetrasubstituted olefins[2] and electronic switching devices.[3]

In aliphatic chemistry, two main methods were usually employed. The first was fusing two molecules, each containing an oxime[4] or a nitro group,[5] while the second was based on reacting olefins with the highly toxic dinitrogen tetroxide (N_2O_4). The latter resulted, in most cases, in low yields of the 1,2-dinitro products.[6] To obtain 1,2-dinitro aromatic compounds is even more challenging since nitration of nitroaromatics tends to give mainly *m*-dinitro derivatives. These limited methods have nevertheless been used, since conventional oxidation of vicinal diamino groups could not have been employed due to the "push−pull" effect generated during the oxidation process which tends to break the central C−C bond.[7]

Some years ago, we developed the HOF·CH_3CN complex, which is conveniently generated in situ by bubbling diluted fluorine (commercially available) through aqueous acetonitrile.[8] This oxygen-transfer agent was used for epoxidations of various types of olefins,[9] converting alcohols[10] and methyl ethers[11] to ketones, preparing *N*-oxides,[12] oxidizing sulfides, including electron depleted ones to sulfones,[13] transforming primary amines to the corresponding nitro compounds,[14] and much more.[15] HOF·CH_3CN is unique among all oxidants since it possesses a very strong electrophilic oxygen atom which can be transferred to nucleophilic centers under very mild conditions (0 °C, few seconds). Such conditions help to avoid many side reactions usually associated with elevated temperatures and long reaction times. This was indeed the main factor responsible for the successful reaction of amino acids with HOF·CH_3CN that yielded the corresponding α nitro acids with no decarboxylation or deamination.[16] We found that these properties also enabled the oxidation of vicinal diamino compounds to the corresponding dinitro derivatives without breaking the central C−C bond as other reagents do.

It took 3 min for HOF·CH_3CN to convert 1,2-diaminopropane (**1**) to 1,2-dinitropropane (**2**) in 82% yield. For comparison, this product was previously prepared from propene and N_2O_4 in 20% yield,[17] so even the common spectral properties of **2** and similar compounds could not be found in the literature until today. The reaction also proceeded well with tertiary amines, and it took only a minute to transform 1,2-diamino-2-methylpropane (**3**) to 1,2-dinitro-2-methylpropane (**4**) in 90% yield. Cyclic diamino compounds were also subjected to reaction with HOF·CH_3CN, and *trans*-1,2-diaminocyclohexane (**5**) produced the *trans*-1,2-dinitrocyclohexane (**6**) in 95% yield. Again, this product was obtained in the past by using N_2O_4,[6] but in 25% yield only. *cis*-1,2-Diaminocyclohexane (**7**) behaved somewhat differently, and while we could detect the corresponding dinitro derivative **8**, we were unable to purify it since upon workup it spontaneously eliminated the elements of HNO_2, producing 1-nitrocyclohexene (**9**) isolated in 71% yield.[18]

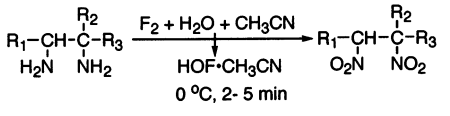
Although it is reasonable to assume a direct attack of the electrophilic oxygen atom of the HOF·CH_3CN on the nucleophilic nitrogen, we have observed in the past attacks of this reagent on the carbon atom α to electron-donating heteroatoms.[10,11] This, however, is not the case with the family of the vicinal diamines. The stereochemistry around the nitrogen-bonded carbons is fully retained as evident from the reaction of (1*S*,2*S*)-(−)-1,2-diphenyl-

* Author to whom correspondence may be addressed. Fax: 972-3-6409293.

(1) Seebach, D.; Colvin, E. W.; Lehr, F.; Weller, T. *Chimia* **1979**, *33*, 1.
(2) Korenblum, N. *Aldrichimica Acta* **1990**, *23* (3), 71.
(3) Chen, J.; Reed, M. A.; Rawlett, A. M.; Tour, J. M. *Science* **1999**, *286*, 1550.
(4) Camps, P.; Munoz-Torrero, D. *Tetrahedron Lett.* **1994**, *35*, 3187.
(5) Wade, P. A.; Kondracki, P. A.; Carrol, P. J. *J. Am. Chem. Soc.* **1991**, *113*, 8807.
(6) Baldock, H.; Levy, N.; Scaife, C. W. *J. Chem. Soc.* **1949**, 2627.
(7) Dave, P. R.; Axenrod, T.; Qi, L.; Bracuti, A. *J. Org. Chem.* **1995**, *60*, 1895 and references therein.
(8) Rozen, S.; Brand, M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 554.
(9) (a) Rozen, S.; Kol, M. *J. Org. Chem.* **1990**, *55*, 5155. (b) Hung, M. H.; Smart, B. E.; Feiring, A. E.; Rozen, S. *J. Org. Chem.* **1991**, *56*, 6, 3187. (c) Rozen, S.; Bareket, Y.; Dayan, S. *Tetrahedron Lett.* **1996**, *37*, 531. (d) Dayan, S.; Ben-David, I.; Rozen, S. *J. Org. Chem.* **2000**, *65*, 8816.
(10) Rozen, S.; Bareket, Y.; Kol, M. *Tetrahedron* **1993**, *49*, 8169.
(11) Rozen, S.; Dayan, S.; Bareket, Y. *J. Org. Chem.* **1995**, *60*, 8267.
(12) Dayan, S.; Kol, M.; Rozen, S. *Synthesis* **1999**, 1427.
(13) (a) Rozen, S.; Bareket, Y. *J. Org. Chem.* **1997**, *62*, 1457. (b) Toyota, A.; Ono, Y.; Chiba, J.; Sugihara, T.; Kaneko, C. *Chem. Pharm. Bull.* **1996**, *44*, 703.
(14) (a) Kol, M.; Rozen, S. *J. Chem. Soc., Chem. Commun.* **1991,** 567. (b) Rozen, S.; Kol, M. *J. Org. Chem.* **1992**, *57*, 7342. (c) Dirk, S. M.; Mickelson, E. T.; Henderson, J. C.; Tour, J. M. *Org. Lett.* **2000**, *2*, 3405.
(15) (a) Rozen, S. *Acc. Chem. Res.* **1996,** *29*, 243. (b) Rozen, S. *Pure Appl. Chem.* **1999**, *71*, 481.
(16) Rozen, S.; Bar-Haim, A.; Mishani, E. *J. Org. Chem.* **1994**, *59*, 1208.
(17) Levy, N.; Scaife, C. W. *J. Chem. Soc.* **1946**, 1093.
(18) Sreekumar, R.; Padmakumar, R.; Rugmini, P. *Tetrahedron Lett.* **1998**, 39, 2695.

10.1021/jo030217m CCC: $25.00
Published on Web 10/18/2003

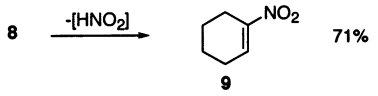
ethylenediamine (**10**), $[\alpha]_D = -102°$ (EtOH), with HOF·CH_3CN, resulting in 95% yield of (1*S*,2*S*)-(−)-1,2-dinitro-1,2-diphenylethane (**11**), $[\alpha]_D = -414°$ (EtOH).[19]



1	$R_1 = CH_3$; $R_2 = R_3 = H$	**2**	82%
3	$R_1 = H$; $R_2 = R_3 = CH_3$	**4**	90%
10	$R_1 = R_3 = Ph$; $R_2 = H$ (1S, 2S)	**11**	95%

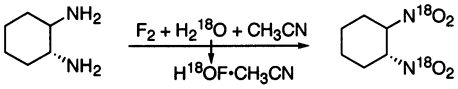
5 $R_1 = NH_2$; $R_2 = H$ **6** $R_1 = NO_2$; $R_2 = H$ 95%

7 $R_1 = H$; $R_2 = NH_2$ **8** $R_1 = H$; $R_2 = NO_2$



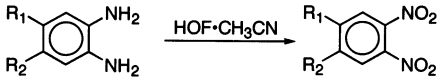
8 → **9** 71%

One of the advantages of HOF·CH_3CN is that its electrophilic oxygen originates in water, which is the most convenient source for all oxygen isotopes. We have passed fluorine through a solution of acetonitrile and $H_2{}^{18}O$ and obtained $H^{18}OF{\cdot}CH_3CN$, which was reacted with *trans*-1,2-diaminocyclohexane (**5**). The ^{18}O content of the product was difficult to quantitate using conventional EI or CI techniques. Even Amirav's supersonic GC/MS,[20] which usually solves such problems,[21] was not fully successful with this family of compounds. Fortunately, however, Amirav developed a new ionization method named cluster chemical ionization, which is based on electron ionization of clusters formed from the sample and a solvent such as MeOH, both in the supercooled supersonic expansion stage.[22] This mass spectrum (cluster CI with MeOH, $m/z = 183$ $(M + 1)^+$) clearly confirms that all four oxygen atoms of all ^{18}O-*trans*-1,2-dinitrocyclohexane **12** (94% yield) are the expected ^{18}O isotope. To the best of our knowledge this is the first time that a compound containing four ^{18}O atoms is described.



5 → **12** 94%

This oxidation also proceeds well with aromatic diamines. We reacted 4,5-dimethyl-1,2-phenylenediamine (**13**) with HOF·CH_3CN for 4 min at −15 °C and obtained 4,5-dimethyl-1,2-dinitrobenzene (**14**) in 87% yield. This compound was previously described as a low-yield byproduct during the nitration of 1,2-dimethyl-4-nitrobenzene.[23] The presence of an electron-withdrawing group on the aromatic ring reduces the nucleophilicity of the amino nitrogen atoms, and the reaction of 3,4-diaminobenzophenone (**15**) proceeded with 55% yield only to give 3,4-dinitrobenzophenone (**16**).[24] An additional factor contributing to the reduced yield of this particular reaction is the slower, but still noticeable, competitive Baeyer−Villiger reaction with the HOF·CH_3CN.[10]



13	$R_1 = R_2 = CH_3$	**14**	87%
15	$R_1 = PhCO$; $R_2 = H$	**16**	55%

In conclusion, it was demonstrated that the HOF·CH_3CN, probably the best oxygen-transfer agent chemistry has to offer, is capable of oxidizing vicinal diamino compounds to their vicinal dinitro counterparts, a transformation that could not be carried out before. The only "problem" with this agent is that some chemists are reluctant to work with F_2. They should not be. Today, prediluted fluorine is commercially available and working with it is as easy as turning a valve *on* and *off*. All reaction vessels are standard glassware, and a simple basic trap removes small amounts of F_2 that did not react with the water. Twenty years ago, only a handful of organic laboratories were working with this element. Today, there are more than a hundred. We hope that this work will contribute to increase this number.

Experimental Section

^1H NMR and ^{13}C NMR spectra were obtained at 200 and 50.2 MHz, respectively, with Me_4Si as an internal standard. The mass spectra were recorded on a homemade GC/MS with a supersonic molecular beam (refs 20 and 22). All clusters CI were obtained with MeOH.

General Procedure for Working with Fluorine. Fluorine is a strong oxidant and a very corrosive material. It should be used only with an appropriate vacuum line such as the one described in ref 12. For the occasional user, however, various premixed mixtures of F_2 in inert gases are commercially available, simplifying the process. If elementary precautions are taken, work with fluorine is relatively simple and we have had no bad experiences working with it.

General Procedure for Producing HOF·CH_3CN Complex. Mixtures of 10−15% F_2 with nitrogen were used in this work. They were passed at a rate of about 400 mL min^{-1} through a cold (−10 °C) mixture of 60 mL of CH_3CN and 6 mL of H_2O. The development of the oxidizing power was monitored by reacting aliquots with acidic aqueous solution of KI. The liberated iodine was then titrated with thiosulfate. Typical concentrations of the oxidizing reagent were around 0.4−0.6 M. The diamino compound (1−2 g) was dissolved in about 20 mL of CH_2Cl_2, cooled to 0 °C, and added in one portion to 6 mol/equiv of the reagent. About 2−3 g of NaF was added to all aliphatic diamino derivatives to absorb the HF found in the reagent and minimize the formation of amino/HF salts. The reaction was quenched with dilute bicarbonate and extracted with CH_2Cl_2, and the organic layer was dried over $MgSO_4$.

(19) The racemic **11** has been made by Korenblum nitro synthesis: Crombie, L.; Roughley, B. S. *Tetrahedron* **1986**, *42*, 3147. Obviously, such synthesis is bound to lead to racemic compounds only.

(20) (a) Dagan, S.; Amirav, A. *J. Am. Soc. Mass Spectrom.* **1995**, *6*, 120. (b) Amirav, A.; Gordin, A.; Tzanani, N. *Rapid Commun. Mass Spectrom.* **2001**, *15*, 811.

(21) Rozen, S.; Golan, E. *Eur. J. Org. Chem.* **2003**, 1915.

(22) (a) Dagan, S.; Amirav, A. *J. Am. Soc. Mass Spectrom.* **1996,** *7*, 550. (b) Fialkov, A. B.; Amirav, A. *Rapid Commun. Mass Spectrom.* **2003**, *17*, 1326.

(23) Fischer, A.; Henderson, G. N.; Iyer, L. M. *Can. J. Chem.* **1985**, *63*, 2390.

(24) Kametani, T.; Shio, M. *J. Heterocycl. Chem.* **1971**, *8*, 545.

Evaporation of the solvent followed by purification by either flash chromatography or recrystallization gave the target dinitro product. With the exception of the chiral compound **11** and the [18]O labeled **12**, the final dinitro products are known. Their spectral properties are in full agreement with the corresponding structures.

1,2-Dinitropropane (2)[17] was prepared from **1** as described above in 82% yield: yellow oil; ^{1}H NMR 5.25−5.22 ppm (1 H, m), 5.11 ppm (1 H, dd, $J1 = 16$ Hz, $J2 = 9$ Hz), 4.62 ppm (1 H, dd, $J1 = 16$ Hz, $J2 = 2.5$ Hz), 1.68 ppm (3 H, d, $J = 7$ Hz); ^{13}C NMR 77.94, 74.66, 16.41 ppm. Cluster CI MS: $m/z = 135$ $(M + 1)^+$.

1,2-Dinitro-2-methylpropane (4) was prepared from **3** as described above in 90% yield: mp 50 °C (from MeOH); ^{1}H NMR 4.96 (2 H, s), 1.74 ppm (6 H, s); ^{13}C NMR 84.02, 79.79, 23.68 ppm. Cluster CI MS: $m/z = 149$ $(M + 1)^+$.

***trans*-1,2-Dinitrocyclohexane (6)**[6] was prepared from **1** as described above in 95% yield: yellow oil; ^{1}H NMR 5.04−4.98 (2 H, m), 2.64−2.61 (2 H, m), 1.98−1.95 (2 H, m), 1.80−1.77 (2 H, m), 1.49−1.44 ppm (2 H, m); ^{13}C NMR 83.84, 30.35, 23.35 ppm. Cluster CI MS: $m/z = 175$ $(M + 1)^+$. For trans (all [18]O-1,2-dinitrocyclohexane (**12**)), cluster CI MS: $m/z = 183$ $(M + 1)^+$.

1,-Nitrocyclohexene (9)[18] was prepared from **5** as described above in 71% yield: yellow oil; ^{1}H NMR 7.35−7.30 (1 H, m), 2.61−2.54 (2 H, m), 2.37−2.32 (2 H, m), 1.82−1.73 (2 H, m), 1.66−1.61 ppm (2 H, m); ^{13}C NMR 134.25, 29.59, 24.70, 23.82, 21.70, 20.58 ppm. Cluster EI MS: $m/z = 127$ $(M)^+$.

(1*S*,2*S*)-(−)-1,2-Dinitro-1,2-diphenylethane (11)[19] was prepared from **10** as described above in 95% yield: mp 147 °C (from MeOH); $[a]_D = -414°$ (EtOH); ^{1}H NMR 7.27 (10 H, m), 6.42 ppm (2 H, s); ^{13}C NMR 130.63, 129.34, 127.80, 90.24 ppm.

4,5-Dimethyl-1,2-dinitrobenzene (14)[22] was prepared from **13** as described above in 87% yield: mp 116 °C (from EtOH); ^{1}H NMR 7.68 (2 H, s), 2.42 ppm (6 H, s); ^{13}C NMR 143.31, 140.38, 125.49, 19.63 ppm.

3,4-Dinitrobenzophenone (16)[23] was prepared from **15** as described above in 54% yield: mp 80 °C (from MeOH); ^{1}H NMR 8.33−8.32 (1 H, m), 8.18−8.01 (2 H, m), 7.82−7.67 (3 H, m), 7.61−7. 53 ppm (2 H, m); ^{13}C NMR 191.79, 141.83, 134.90, 134.05, 133.93, 129.78, 128.81, 125.94, 125.03 ppm; MS (EI): $m/z = 272$ $(M)^+$.

Acknowledgment. This work was supported by the Israel Science Foundation founded by the Israel Academy of Sciences and Humanities.

JO030217M