Oxidation of Alkynes by the HOF·CH_3CN Complex

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The HOF·CH_3CN complex discovered over a decade ago[1] is probably the best oxygen transfer agent organic chemistry has to offer. It is simply prepared by bubbling nitrogen-diluted fluorine into aqueous acetonitrile and is stable at 0 °C for a few hours. It reacts very efficiently with a large variety of organic compounds resulting either in their oxidation or in transferring an oxygen atom from the reagent to the substrate.[2] One of the most useful reactions of this complex is with olefins resulting in their epoxidation,[3] but its reactions with triple bonds has not yet been investigated.

Several methods for the oxidation of alkynes are described in the literature involving different types of reagents such as metal oxidants,[4] hydrogen peroxide catalyzed by metal complexes,[5] [fluoro(trifluoromethanesulfonyloxy)iodo]benzene,[6] and dimethyldioxirane,[7] each used for a specific substrate. We found that the HOF·CH_3CN complex is able to replace all the above reagents, usually in better yields and always under much milder conditions.

The reaction of diphenylacetylene (**1**) with 2.5 equiv[8] of HOF·CH_3CN gave both benzil (**2**) as the main product (55% yield) and benzophenone (**3**) (35% yield), a product resulting from a loss of a carbon atom. A small amount of α-fluoro-α-phenyl acetophenone (**4**)[9] was also formed. Aliphatic acetylenes such as 4-octyne (**5**) on the other hand formed a mixture of *cis* and *trans* isomers of the α,*β*-epoxy-4-octanone (**6**) as the major product (83% yield).[5a] Small amounts (<10%) of 4-heptanone (**7**) (again as a result of loss of a carbon) and 4,5-octane-dione (**8**)[5b] were also detected. Working with less than 1 mol equiv resulted in *cis*- and *trans*-3-octen-4-one (2:3 ratio) **9**[5a] as the major product, indicating that the epoxides **6** result from epoxidation of the respective unsaturated ketones (Scheme 1).

Oxidation of alkynes has been attempted several times in the past resulting in a commonly suggested mechanism.[10] This mechanism (Scheme 2) involves an oxirene **A** which, although never isolated, was assumed to be the first step. It has been also assumed that **A** can either undergo an additional oxidation to give a double epoxide **B** or lead via concerted rearrangement to an intermediate **C** and a ketene of type **D**. These intermediates give rise to all products described as shown in Scheme 1.

It was interesting to study the case of 1-pheny-1-pentyne (**10**), an acetylene possessing both an aromatic and an aliphatic side chain. The reaction with HOF·CH_3CN produces indeed a combination of all expected products with the diketone **11**[11] and 1-phenyl-1-butanone (**12**) (22% yield) being the major components. The enone **13**[12] (cis:trans = 2:3), its epoxide **14**,[12] and the α-fluoro ketone **15**[11] were also obtained in small quantities.

Using substrates bearing electron-withdrawing substituents on the triple bond, such as 4-phenyl-3-butyne-2-one (**16**) and methyl phenylpropyolate (**17**), gave a narrower product distribution. The ynone **16** required a 10-fold excess of the HOF·CH_3CN complex in order to achieve a full conversion. The product which proved to be 1-phenyl-1,2-propanedione (**18**), obtained in nearly quantitative yield, resulted from the rearrangement of the respective intermediate **D** (Scheme 2). In the case of **17** where such a rearrangement is less favorable, the diketo ester **19**[13] was obtained (in its hydrate from) as the only product in very high yield.

Symmetrical acetylenes with electron-withdrawing groups also react well. 2,5-Dimethyl-2,5-diacetoxy-3-hexyne (**20**), gave a single product identified as 2,5-dimethyl-2,5-diacetoxy-3,4-hexanedione (**21**),[14] a product formed via the bis epoxide **B** (Scheme 2).

Terminal arylacetylenes react quickly with the oxidizing complex to produce benzaldehydes. Small amounts of further oxidation to the corresponding acids could also be detected. Thus, the reaction of phenyl acetylene (**22**) with 5 mol equiv of the oxidizing complex yielded 85% of benzaldehyde (**23**) and 5% of benzoic acid (**24**). Electron-donating or -withdrawing substituents on the aromatic ring do not affect the outcome. The oxidation of 4-methyl phenyl acetylene (**25**) gave 80% 4-methyl benzaldehyde (**26**) and 9% of 4-methylbenzoic acid (**27**), and 4-chlorophenylacetylene (**28**) was likewise converted to 4-chlorobenzaldehyde (**29**) accompanied by a small amount of 4-chlorobenzoic acid (**30**) (Scheme 1).

The reaction of terminal aliphatic alkynes is less efficient than the ones described above. 1-Heptyne (**31**) and 1-octyne (**32**), for example, require a considerable excess of the oxidizing agent in order to achieve a full

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[1] Rozen, S.; Brand, M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 554.

[2] Rozen, S. *Acc. Chem. Res.* **1996**, *29*, 243.

[3] Rozen, S.; Kol, M. *J. Org. Chem.* **1990**, *55*, 5155. Rozen, S.; Bareket, Y.; Dayan, S *Tetrahedron Lett.* **1996**, *37*, 531.

[4] Wolfe, S.; Ingold, C. F. *J. Am. Chem. Soc.* **1983**, *105*, 7755.

[5] (a) Sakaguchi, S.; Watase, S.; Katayama, Y.; Sakata, Y.; Nishiyama, Y.; Ishii, Y. *J. Org. Chem.* **1994**, *59*, 5681. (b) Zhu, Z.; Espenson, J. H. *J. Org. Chem.* **1995**, *60*, 7728.

[6] Pirguliyev, N. S.; Brel, V. K.; Zefirov, N. S.; Stang, P. J. *Mendeleev Commun.* **1999**, 189.

[7] Murray, R. W.; Singh, M. *J. Org. Chem.* **1993**, *58*, 5076.

[8] Such a concentration constitutes of up to 50% excess of the reagent since 2 mol/equiv is the minimum needed for the oxidation of a triple bond. Using less reagent does not change the distribution of the products but lowers the conversion of the acetylenic substrate.

[9] Merritt, R. F.; Ruff, J. K. *J. Org. Chem.*, **1965**, *30*, 328.

[10] E. G. Lewars, *Chem. Rev.* 1983, *83*, 519.

[11] Stavber, S.; Zupan, *M. J. Org. Chem.* **1987**, *52*, 5022.

[12] Enders, D.; Zhu, J.; Raabe, G. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 5, 1725.

[13] Wasserman, H. H.; Baldino, C. M.; Coats, S. J. *J. Org. Chem.* **1995**, *60*, 8231.

[14] Although previously mentioned in the literature: Lehmann, A. Oertel, M. *Chem. Tech.* **1959**, *11*, 453 (*Chem. Abstr.* **1960**, *54*, 4377b)—compound **21** has never been properly identified. Its physical properties are as following: oil, IR (in CH_2Cl_2 solution): 1724, 1742 (sh) cm^{-1}; ^1H NMR: 1.59 (s, 12H), 2.06 ppm (s, 6H); ^{13}C NMR: 20.7, 24.1, 82.1, 170.8, 194.5 ppm; MS (CI): *m/e* 259.117195 $(M + 1)^+$, calcd for $C_{12}H_{19}O6$ 259.118164.

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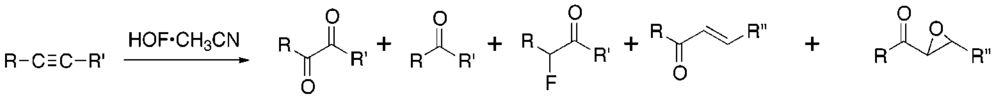
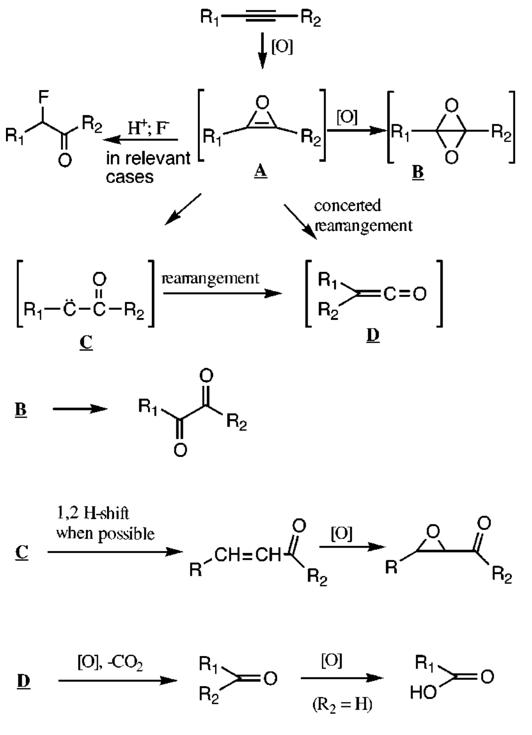
Scheme 1



1	R = R' = Ph	**2** (55%)	**3** (35%)	**4** (6%)			
5	R = R' = Pr	**8** (6%)	**7** (10%)		**9**	R = Pr; R'' = Et	**6** (83%)
10	R = Ph; R' = Pr	**11** (50%)	**12** (22%)	**15** (6%)	**13** (7%)	R = Ph; R'' = Et	**14** (10%)
16	R = Ph; R' = COMe		**18** (95%)				
17	R = Ph; R' = COOMe	**19** (95%)					
20	R = R' = $\underset{OAc}{Me_2C}$	**21** (73%)					
22	R = Ph; R' = H		**23** (85%) + **24** R' = OH (5%)				
25	R = *p*-MeC_6H_4; R' = H		**26** (80%) + **27** R' = OH (9%)				
28	R = *p*-ClC_6H_4; R' = H		**29** (85%) + **30** R' = OH (5%)				
31	R = H; R' = C_5H_{11}	**37** (12%)	**39** (20%) + **41** R = OH (5%)		**35** (15%)	R = H; R'' = Bu	**33** (45%)
32	R = H; R' = C_6H_{13}	**38** (12%)	**40** (20%) + **42** R = OH (5%)		**36** (15%)	R = H; R'' = C_5H_{11}	**34** (45%)
43	R = $C_5H_{11}\overset{H}{\underset{OAc}{C}}$; R' = H	No significant reaction					

Scheme 2



conversion, resulting in a complex mixture of products composed of the corresponding α,β-epoxy aldehydes **33**[15] and **34**,[16] α,β-unsaturated ones **35** and **36**,[17] α-keto aldehydes **37**[18] and **38**,[19] one carbon smaller aldehydes **39** and **40**, and additional small amounts of the corresponding acids **41** and **42**.

Terminal aliphatic alkynes containing an adjacent electron-withdrawing group are even less reactive with the electrophilic HOF•CH_3CN, and 3-acetoxy-1-octyne (**43**) with its acetoxy group does not react even after prolonged treatment with a large excess of the oxidant.

In conclusion, it was found that the HOF•CH_3CN complex efficiently oxidizes internal carbon−carbon triple bonds. In contrast to some previous reports of the oxidation of alkynes,[4] the HOF•CH_3CN complex, being a strong electrophile, reacts more rapidly with aromatic alkynes than with aliphatic ones. All products obtained can be explained by assuming a primary formation of an “oxirene species” which undergoes further rearrangement or oxidation reactions (Scheme 2).

Experimental Section

^1H NMR spectra were recorded using Bruker AC-200 with $CDCl_3$ as a solvent and Me_4Si as an internal standard. The proton broad band decoupled ^{13}C NMR spectra were recorded at 90.5 MHz. Here too, $CDCl_3$ served as a solvent with TMS as an internal standard. GC-MS spectra were measured with a VG

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[15] Miiyashita, M.; Suzuki, T.; Hoshino, M.; Yoshikoshi, A. *Tetrahedron* **1997**, *53*, 12469.

[16] Corey, E. J.; Mehrotra, M. M.*Tetrahedron Lett.* **1986**, *27*, 5173.

[17] Choudary, B. M.; Prasad, D.; Valli, V. L. K. *Tetrahedron Lett.* **1990**, *31*, 7521. As with compound **13**, these minor enones were obtained as mixtures of cis:trans = 2:3.

[18] Verhe, R.; Courthein, D.; Kimpe, N.; Buyck, L.; Schamp, N. *Synthesis* **1982**, 667.

[19] Rosowsky, A.; Chen, K. K. N. *J. Org. Chem.* **1973**, *38*, 2073.

micromass 7070H instrument. IR spectra were recorded as neat films, in $CHCl_3$ solution or in KBr pellets on a Bruker Vector22 FTIR spectrophotometer. The spectral properties of all products presented in this work are in excellent agreement with the literature. With the exception of the commercial compounds, they all have been referenced in the previous section.

General Procedure for Working with Fluorine and Producing $HOF \cdot CH_3CN$. Fluorine is a strong oxidant and a corrosive material. It should be used only with an appropriate vacuum line constructed in a well-ventilated area. If elementary precautions are taken, work with fluorine is relatively simple, and we have had no bad experiences working with it. A proposed detailed setup for working with pure fluorine and details for producing the $HOF \cdot CH_3CN$ complex have been published recently.[20] For the occasional user, prediluted 10% fluorine in nitrogen, which is commercially available, simplifies the whole process.

General Oxidation Procedure. About 2.5 mmols of an alkyne were dissolved in 10−20 mL of $CHCl_3$. The mixture was then cooled to 0 °C and added to 3−10-fold excess of the $HOF \cdot CH_3CN$ complex. After about 5−10 min, the reaction mixture was warmed to room temperature, neutralized with sodium bicarbonate, filtered, evaporated almost to dryness, extracted with $CHCl_3$, and dried over $MgSO_4$. When necessary, the products were isolated and purified by flash chromatography using Merck Silicagel 60 H, P.E/EtOAc serving as eluent. The outcome of the reaction was analyzed by NMR (^1H, ^{13}C, and ^{19}F), IR, and GCMS. The spectral data of the noncommercial known products were compared with the literature reports, and in every case an excellent agreement was obtained.

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Supporting Information Available: IR, HRMS, ^1H and ^{13}C spectra of compound **21**. This material is available free of charge via the Internet at http://pubs.acs.org..

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[20] Dayan, S.; Kol, M.; Rozen, S. *Synthesis* **1999**, 1427. Rozen, S.; Dayan, S. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 3471.