conjugation when compared to acyclic *Z,s-Z* enaminones. This would increase the electron density on nitrogen and thus favor reaction at this site. On the other hand, attack at the C_α carbon position might be slowed down because of the development of substantial 1,3-diaxial interaction in the transition state, which we expect to be important for the volumous diphenylketene. Further information has been obtained using AM1 geometric optimization,[17] which shows that while *Z,s-Z* acyclic enaminones have a planar nitrogen, it is not planar in cyclic enamino ketones, which is an indication of the decrease in conjugation. In agreement with this supposition, shorter bond lengths for C=O and C=C bonds and longer bond lengths for OC–C and C–N bonds were obtained.

The HOMO energies obtained by HAM/3 and AM1 (Figure 1, Table II) do not show as much agreement with the reactivity observed as did the acyclic enaminones. An interesting result of the HAM/3 calculations for the cyclic enaminones is the high energy of the second HOMO which corresponds to a nonbonded electron pair on oxygen. Thus, this orbital would also have to be considered in any analysis of reactivity. In fact, this might explain the greater tendency for cyclic *E,s-E* enamino ketones to give high yields of O-alkylated salts upon alkylation when compared to acyclic enaminones[21] and to give O-acylated products[22] or C_α-acyl derivatives via unstable O-acylated intermediate salts[23] upon acylation. Calculations on compound **2a** using standard geometric models[18] and fixed in the four possible geometric forms show that the high energy of the second HOMO (Table IV) is a function of the *s-E* conformation. Thus to explain the reaction of the cyclic enaminones **4**, the possibility of prior reaction of the diphenylketene on oxygen to form an unstable intermediate that then reacts further with another molecule of enaminone cannot be dismissed. However at some point during the reaction a greater preference for reaction at nitrogen would have to be explained.

Conclusion

In conclusion, we can see that molecular orbital considerations clarify the reactivity of this system, especially when HAM/3 is used for calculating frontier-orbital energies. Although this method, which has been developed for first row elements, is readily available,[24] it has not been explored by organic chemists. Considering the importance of frontier orbitals in understanding reactivity, we should see more use of HAM/3 in the future.

Experimental Section

The ^1H NMR spectra were recorded with a Varian T-60 or Bruker AW-80 spectrometer using tetramethylsilane as internal reference. IR spectra were recorded on a Perkin-Elmer 399B spectrometer. Electron-impact mass spectra were obtained with a Varian MAT 311A mass spectrometer at 70 eV. Melting points were obtained on a Reichert apparatus and are uncorrected.

Enaminones **2**, **3**, and **4**[21] and diazo ketone **1**[25] were prepared according to reported methods.

Reactions of Diazodiphenylethanone (1) with Enaminones 2 and 3. A solution of **1** (222 mg, 1.00 mmol) and the enaminone (1.00 mmol) in ethanol-free methylene chloride (5 mL) was left at room temperature (22–23 °C) in the absence of light for 7 days. After evaporation of the solvent, the products were separated by column chromatography with neutral aluminum oxide using mixtures of hexane, methylene chloride, and methanol as eluents. Solid products were recrystallized with methylene chloride–hexane.

Reactions of 1 with Enaminones 4. A solution of **1** (222 mg, 1.00 mmol) and the enaminone **4** (1.00 mmol) in ethanol-free methylene chloride [50 mL (200 mL for **4c**)] was left at reflux for 1 day. The products were separated and purified by the same procedure as for enaminones **2** and **3**.

For elution solvents, yields and physical data of the products see Table V.

Acknowledgment. We thank FINEP (Financiadora de Estudos e Projetos) for financial support, Rhodia S/A-Brasil for elemental analysis, and Prof. R. E. Bruns for his helpful discussions.

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(21) Greenhill, J. V. *Chem. Soc. Rev.* **1977**, 277.
(22) Walter, W.; Saha, C. R. *Chem. Ber.* **1986**, *119*, 1095.
(23) Alt, G. H.; Speziale, A. J. *J. Org. Chem.* **1964**, *29*, 798.
(24) Quantum Chem. Program Exchange, Prog. No. 393; Department of Chemistry, Indiana University.
(25) Muchowski, J. M. *Tetrahedron Lett.* **1966**, 1973.

Olefin Epoxidation Using Elemental Fluorine

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F_2 reacts with water and CH_3CN, apparently to produce the relatively stable complex $HOF{\cdot}CH_3CN$. This is probably the best known oxygen-transfer reagent and can epoxidize olefins quickly and efficiently. Various types of alkenes including aliphatic, benzylic, enones, dienones, maleates, and fumarates have been examined, and all react with the reagent to produce the corresponding mono- or diepoxides in good to excellent yields. This epoxidation is fully stereospecific, and the configuration of the starting olefin is fully retained in the resulting oxirane. In cases where exceptionally stable oxocarbocations can be formed as in 1,1-diphenylethene, the reaction produces vicinal glycols in good yields. Since the origin of the epoxides' oxygen is in the water, this method is very suitable for introducing the isotopes ^{17}O and ^{18}O into various molecules.

Although F_2 has been known for more than a century, it was widely assumed to be unsuitable for organic synthesis. Most of the usual organic substrates were considered to be too fragile and vulnerable for this powerful and corrosive element. Only a few sporadic attempts to use it were thus recorded, most of them with highly stable polyhalogenated compounds.[1]

About 10 years ago we started to demonstrate systematically that, properly handled, fluorine can be a very helpful fluorinating agent, which not only does not destroy

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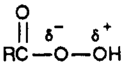
[1] See for example: Miller, W. T.; Staffer, J. O.; Fuller, J.; Currie, A. C. *J. Am. Chem. Soc.* **1964**, *86*, 51. But see however, also: Merritt, R. F.; Stevens, T. E. *J. Am. Chem. Soc.* **1966**, *88*, 1822.

organic substances but can be employed even in highly stereo- and regioselective reactions.[2] It has been also shown that under proper conditions this versatile element can be a source of radical,[3] electrophilic,[4] and nucleophilic[5] fluorine species.

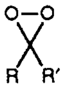
Despite fluorine's rare use, it is not surprising to find it in the service of the organofluorine chemistry. It is more surprising to discover, however, that this element can also be an important tool in general organic synthesis for difficult chemical transformations leading eventually to fluorine-free derivatives. We have recently started to develop this trend by using F_2 for turning deactivated alkanes into alkenes,[6] for acetoxylation[7] and chlorination[8] of heterocyclic systems, for aromatic brominations[9] and iodinations[10] and for the hydroxylation of remote tertiary sites of deactivated organic molecules.[11] We describe here yet another unexpected transformation, where fluorine is used for unprecedented fast and efficient epoxidation of olefins.[12]

Synthesis of epoxides is a very active field in organic chemistry. It seems that for almost every type of double bond a special epoxidation reagent has been developed. One can find quite a few cases of peroxy acids reacting for hours at elevated temperatures with simple alkenes in order to form regular epoxides. More deactivated olefins require lengthy treatment with strongly basic hydrogen peroxide solutions, while in other cases a halohydrin has to be prepared first, followed by basic HX elimination. There are many other reactions devised for oxygen transfer such as various oxidants combined with transition metals[13] with or without macrocyclic hosts and industrial specific epoxidations using oxygen,[14] to name just a few. It would be of a considerable interest therefore to develop a single general epoxidizing agent that would react very rapidly and in good yields with most types of double bonds.

Practically all current direct epoxidation methods use reagents possessing the peroxy bond. The reason for this is the high electronegativity of the oxygen and hence the relatively easily induced small positive pole on the adjacent oxygen atom especially if helped by additional factors, such as resonance stability of a leaving carboxylic group (**A**) or strain relief in the small dioxirane ring (**B**).[15]



A



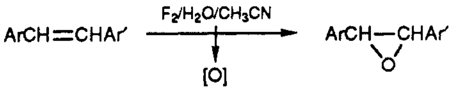
B

There is, however, another approach to generate a positive pole on the epoxidizing oxygen that involves attaching it to an even stronger electronegative atom. Fluorine is, of course, the only candidate that can fulfill this requirement.

Passing fluorine diluted with nitrogen through acetonitrile does not produce any oxidative product. Passing the same F_2/N_2 mixture through water at 0 °C also does not result in any long-lasting oxidant other than H_2O_2. It is well-known that the last reaction produces HOF as a transient oxidant that is stable only at very low temperatures,[16] a fact that considerably reduces its usefulness in organic chemistry.

When, however, nitrogen-diluted fluorine is passed through a cold (-10 °C) mixture of acetonitrile and water, an oxidizing solution persistent at temperatures of up to 25 °C for several hours, is formed. Although our studies of the exact constitution of this oxidizing material have not yet been completed,[17] there are some indications that we are producing a complex of HOF and CH_3CN that derives its stability from the donor–acceptor relationship of these components.[18] In any event, the oxygen atom of the active agent proves to be electrophilic in nature and reacts quickly and smoothly with almost any type of olefin.

It takes less than 1 min for *trans*-stilbene (**1**) to react with the oxidizer at 0 °C, producing *trans*-stilbene oxide (**2**) in higher than 90% yield. The physical constants of the oxide show a full retention of the starting material configuration. Similar results were observed with *cis*-stilbene (**3**), which was converted to *cis*-stilbene oxide (**4**) without any traces of the trans isomer (**2**). Substituted stilbenes react as well, as evidenced by the transformation of *trans*-4-chlorostilbene (**5**) to the corresponding epoxide **6** in 90% yield. Even the electron-deficient double bond of *trans*-4,4′-dinitrostilbene (**7**) was successfully epoxidized, although a 2-fold excess of the reagent was needed. Since the solubility of **7** is low, the reaction time had to be extended to 30 min, but eventually the solid suspension was converted to the much more soluble epoxide **8** in 70% yield.[19]



1	Ar = Ar′ = Ph (trans)	**2**
3	Ar = Ar′ = Ph (cis)	**4**
5	Ar = *p*-ClC_6H_4; Ar′ = Ph (trans)	**6**
7	Ar = Ar′ = *p*-$O_2NC_6H_4$ (trans)	**8**

While some of the above epoxides can also be obtained by prolonged treatment with conventional peroxy acids, conjugated benzylic enones are much more resistant and usually require treatment with basic H_2O_2. The oxidizing agent made from fluorine, however, is fully capable of epoxidizing such enones without the need for drastic conditions of temperature, reaction time, or pH. The only concession made was increasing the ratio of reagent to alkene to nearly 3:1. Thus, α,β-unsaturated esters, specifically ethyl cinnamate (**9**), or ketones such as benzal acetone (**11**), were converted to the corresponding epoxides (**10**[20] and **12**[21]) in about 85% yield each.

This epoxidation method is not confined to benzylic olefins only. The synthesis of cyclooctene oxide from the

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(2) Rozen, S. *Acc. Chem. Res.* **1988**, *21*, 307. Purrington, S. T.; Kagen, B. S.; Patrick, T. B. *Chem. Rev.* **1986**, *86*, 997.

(3) See for example: Persico, D. F.; Gerhardt, E.; Lagow, R. J. *J. Am. Chem. Soc.* **1985**, *107*, 1197. Adcock, J. L.; Cherry, M. L. *Ind. Eng. Chem. Res.* **1987**, *26*, 208.

(4) Rozen, S.; Lerman, O.; Kol, M.; Hebel, D. *J. Org. Chem.* **1985**, *50*, 4753.

(5) Rozen, S.; Brand, M. *J. Org. Chem.* **1985**, *50*, 3342.

(6) Rozen, S.; Gal, C. *J. Org. Chem.* **1987**, *52*, 2769.

(7) Rozen, S.; Hebel, D. *Heterocycles* **1989**, *28*, 249.

(8) Hebel, D.; Rozen, S. *J. Org. Chem.* **1988**, *53*, 1123.

(9) Rozen, S.; Brand, M.; Lidor, R. *J. Org. Chem.* **1988**, *53*, 5545.

(10) Rozen, S.; Zamir, D.; Menahem, Y.; Brand, M. *J. Org. Chem.* **1988**, *53*, 1123.

(11) Rozen, S.; Brand, M.; Kol, M. *J. Am. Chem. Soc.* **1989**, *111*, 8325.

(12) For preliminary communication: Rozen, S.; Brand, M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 554.

(13) Jorgensen, K. A. *Chem. Rev.* **1989**, *89*, 431.

(14) Feiring, A.; Smart, B. *Ullmann's Encyclopedia of Industrial Chemistry*, 5th ed.; VCH: New York, 1988; Vol. A 11.

(15) Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res.* **1989**, *22*, 205.

(16) Appelman; E. H. *Acc. Chem. Res.* **1973**, *6*, 113. Appelman; E. H.; Jache, A. W. *J. Am. Chem. Soc.* **1987**, *109*, 1754.

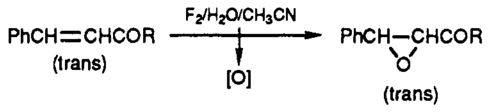
(17) We are in the process of isolating the oxidative material and measuring its various spectral properties. A full report on this work will be published later.

(18) Zuchner, K.; Richardson, T. J.; Glemser, O.; Bartlett, N. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 944.

(19) Usually this epoxide is made by indirect epoxidation methods: Ramirez, F.; Gulati, A. S.; Smith, C. P. *J. Org. Chem.* **1968**, *33*, 13.

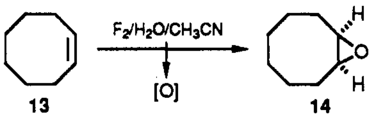
(20) Baldas, J.; Parter, Q. N. *Austr. J. Chem.* **1967**, *20*, 2655.

(21) Temple, R. D. *J. Org. Chem.* **1970**, *35*, 1275.

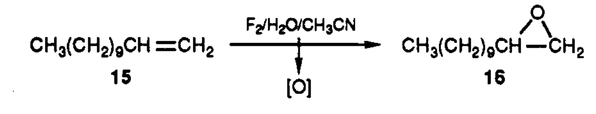


9 R = OEt **10**
11 R = Me **12**

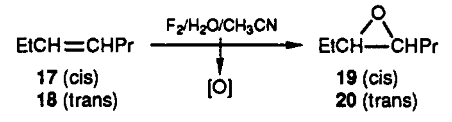
olefin and H_2O_2/CH_3CN has been described in *Organic Synthesis*. Long reaction times at elevated temperatures were required for this reaction.[22] Our oxidizing solution, which can also be made quickly from commercially available F_2/N_2 mixtures, reacts with cyclooctene (**13**) at 0 °C in less than 1 min to form cyclooctane oxide (**14**) in 85% yield. Straight-chain olefins gave similar results. 1-Dodecene (**15**) was instantaneously converted to epoxide **16** in higher than 90% yield and the more substituted cis- (**17**) and *trans*-hepta-3-enes (**18**) were converted to the respective *cis*- and *trans*-3,4-epoxyheptanes (**19** and **20**)[23] in 95% and 75% yields, respectively. These epoxides fully retain the original configuration of the parent alkenes. Trisubstituted olefins react a bit slower, and in the case of the cis rose oxide (**21**) a full conversion was achieved after 5 min, producing epoxide **22** (as a diastereomeric mixture) in 85% yield.[24] β-Citronellol (**23**) also reacted, but although the oxidizing solution seems to react faster with double bonds than with primary alcohols, the latter affects the reaction and the yield of 6,7-epoxy-3,7-dimethyl-1-octanol (**24**) dropped to 45%.[25] With the smaller, more water-soluble methallyl alcohol (**25**), the results were even worse, and although a full conversion was achieved in less than 1 min, only a few percent of the epoxide could be detected. A free hydroxyl group can also cause other types of problems as demonstrated by linalool (**26**), which gave a complicated mixture apparently due to various cyclization processes. These problems can be addressed by first protecting the alcohol moiety with acetate or the easily removed trichloroacetate (**27–29**). Thus, the two unknown epoxides of β-citronellol trichloroacetate (**30**)[26] and methallyl alcohol trichloroacetate (**31**),[27] along with the known epoxide of the linalyl acetate (**32**),[28] were obtained and isolated in 70%, 85%, and 75% yields, respectively.



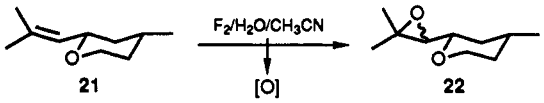
13 **14**



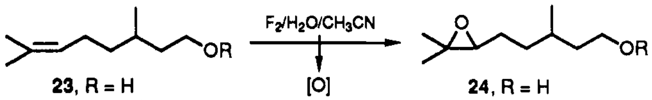
15 **16**



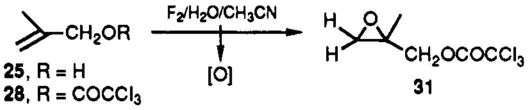
17 (cis) **19** (cis)
18 (trans) **20** (trans)



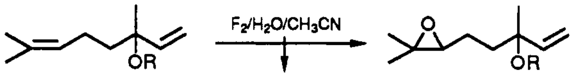
21 **22**



23, R = H **24**, R = H
27, R = $COCCl_3$ **30**, R = $COCCl_3$

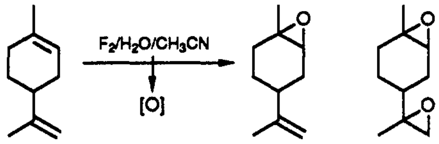


25, R = H **31**
28, R = $COCCl_3$

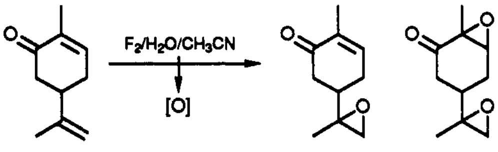


26, R = H **32**, R = Ac
29, R = Ac

The last case of the selective epoxidation of the more electron-rich trisubstituted double bond of linalyl acetate demonstrates the electrophilic nature of the epoxidizing agent. Similarly, when limonene (**33**) was reacted with an equimolar amount of oxidant, the epoxidation took place again on the more electron-rich endocyclic double bond, producing 1,2-epoxylimonene (**34**)[29] in 35% yield, along with a small amount of the diepoxide. Using an excess of 2.5 mole equiv of oxidant resulted mainly in the formation of limonene dioxide (**35**)[30] in 35% yield. With dienes having more differentiated double bonds, such as (*R*)-(−)-carvone (**36**), the results were even clearer. Reacting 1 mole equiv of the oxidant for 1 min at 0 °C resulted in clean monoepoxidation (two diastereoisomers) of the unconjugated double bond, forming 2-methyl-5-(2-methyloxiranyl)-2-cyclohexen-1-one (**37**)[29] in 60% yield. This monoepoxide, or the starting carvone itself, can be subjected to further epoxidation with a large excess of the reagent (up to 4 equiv) for 1 h at 0 °C to produce the diastereoisomeric mixture of the corresponding diepoxide **38**[31] in greater than 50% yield.



33 **34** **35**



36 **37** **38**

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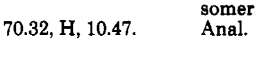
[22] Bach, R. D.; Knight, J. W. *Org. Synth.* **1981**, *60*, 63.

[23] Schneider, H. J.; Agrawal, P. K. *Magn. Reson. Chem.* **1986**, *24*, 718.

[24] Two diastereoisomers were obtained in a ratio of 3.6:1, but at this point we do not know their respective configurations: ^1H NMR (major diastereoisomer) 4.04 (1 H, ddd, J_1 = 9 Hz, J_2 = 4.5 Hz, J_3 = 1 Hz), 3.42 (1 H, dt, J_1 = 12 Hz, J_2 = 2 Hz), 3.14 (1 H, ddd, J_1 = 12 Hz, J_2 = 8 Hz, J_3 = 2 Hz), 2.7 (1 H, d, J_1 = 8 Hz), 1.32 (3 H, s), 1.31 (3 H, s), 0.97 (3 H, d, J_1 = 6 Hz), (minor diastereoisomer) 4.02 (1 H, ddd, J_1 = 9 Hz, J_2 = 4.5 Hz, J_3 = 1 Hz), 3.42 (1 H, dt, J_1 = 12 Hz, J_2 = 2 Hz), 3.10 (1 H, ddd, J_1 = 12 Hz, J_2 = 8 Hz, J_3 = 2 Hz), 2.64 (1 H, d, J_1 = 8 Hz), 1.34 (6 H, s), 0.96 (3 H, d, J_1 = 6 Hz); MS, *m/e* 170 (M^+), 140 [$(M - CH_2O)^+$], 112 [$(M - Me_2CO)^+$], 99



$$[(M{-}Me_2C\underset{O}{—}CH)^+]$$

Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.59, H, 10.59. Found: C, 70.32, H, 10.47.

[25] The yield of **24** obtained by the usual reaction with MCPBA is even lower, 30%: Robinson, P. L.; Barry, C. N.; Kelly, J. W.; Evans, S. A., Jr. *J. Am. Chem. Soc.* **1987**, *107*, 5210.

[26] IR, 1765, 1250 cm^{-1}; ^1H NMR, 4.42 (2 H, t, J = 6.5 Hz), 2.70 (1 H, t, J = 6.5 Hz), 1.95–1.35 (7 H, m), 1.31 (3 H, s), 1.27 (3 H, s), 0.98 (3 H, d, J = 6 Hz); MS, *m/e* 59 $(Me_2COH)^+$ (a characteristic peak for dimethyl epoxides). Anal. Calcd for $C_{12}H_{19}Cl_3O_3$: C, 45.38; H, 5.99. Found: C, 45.70; H, 6.20.

[27] IR, 1765 cm^{-1}; ^1H NMR, 4.5, 4.25 (2 H, AB system, J = 11.5 Hz), 2.87, 2.74 (2 H, AB system, J = 4.5 Hz), 1.46 (3 H, s); MS, *m/e* 202, 204, 206 [$(M - CH_2O)^+$], 117, 119, 121 $(CCl_3)^+$, 43 $(CH_3CO)^+$. Anal. Calcd for $C_6H_7Cl_3O_3$: C, 30.85; H, 3.00. Found: C, 30.58; H, 3.18.

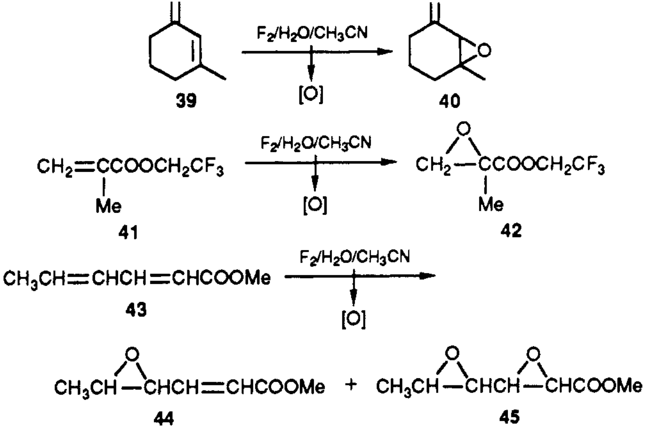
[28] Williams, P. J.; Strauss, C. R.; Wilson, B. *Phytochemistry* **1980**, *19*, 1137.

[29] Kim, Y. H.; Chung, B. C. *J. Org. Chem.* **1983**, *48*, 1562.

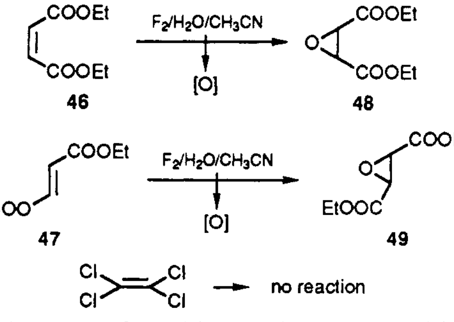
[30] Mori, K.; Kato, M. *Tetrahedron* **1986**, *42*, 5895.

[31] IR, 1715 cm^{-1}; ^1H NMR, 3.48 (1 H, d, J = 4 Hz), 2.1–2.7 (5 H, m), 1.78–2.02 (2 H, m), 1.41 (3 H, s), 1.3 (3 H, two s for the two diastereoisomers); MS, *m/e* 182 (M^+), 167 [$(M - Me)^+$], 139 [$(M - Me - CO)^+$]. Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.93; H, 7.69. Found: C, 66.14; H, 7.96.

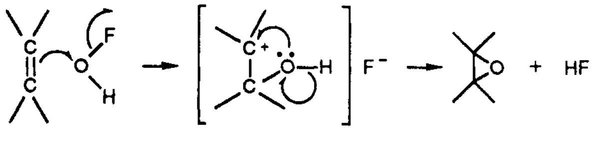
This epoxidation works also with enones substituted at the β-position as with 3-methylcyclohexenone (**39**). When this compound was mixed with a slight excess of the reagent at 0 °C for less than 1 min, 2,3-epoxy-3-methylcyclohexanone (**40**) was obtained in 70% yield. The somewhat more electron-deficient 1,1,1-trifluoroethyl methacrylate (**41**) was also converted to epoxide **42**[32] in 85% yield although in this case 30 min of reaction time was allowed. The regioselectivity of this electrophilic epoxidation could be clearly demonstrated when the conjugated diene in methyl sorbate (**43**) was reacted with the oxidized agent. With only a slight excess of the reagent the γ,δ-position was immediately epoxidized, producing methyl 4,5-epoxy-2-hexenoate (**44**) in 90% yield. Increasing the oxidant concentration 3-fold forced also the second double bond to react, forming a mixture of the mono- and diepoxides (**44** and **45**) in a 2:1 ratio. Using 10-fold excess reversed the ratio in favor of the methyl 2,3:4,5-diepoxyhexanoic acid (**45**)[33] obtained in 60% yield. It should be mentioned that to the best of our knowledge this type of vicinal diepoxide has never been made before by any direct epoxidation procedure.



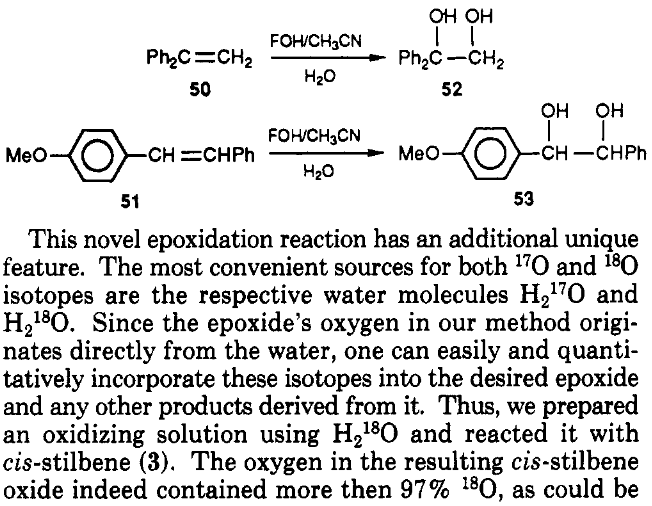
The double bonds in diethyl maleate (**46**) and fumarate (**47**) are the most electron-deficient olefins mentioned in this work so far. These were indeed the most difficult compounds to epoxidize. The usual treatment with a slight excess of oxidant for short periods of time did not result in any reaction. With a large excess, however (5–10 mol equiv), progress could be monitored and after 12 h at room temperature about 90% conversion was achieved. Thus, *cis*- (**48**) and *trans*-diethyl epoxysuccinate (**49**) were obtained in 65% and 50% yields, respectively.[34] As in the previous cases, a full retention of configuration was observed, and neither **48** nor **49** was contaminated with the other. Trying an even more hindered and electron-deficient olefin such as tetrachloroethene failed to produce anything but the starting material.



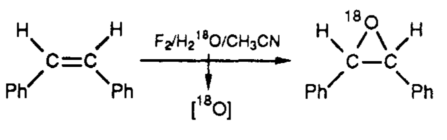
The strong electrophilicity of this reagent, the speed of the reaction, and the full retention of configuration suggest a fast two-step process involving formation of the highly unstable β-oxocarbocation, helped by the eventual formation of HF. Similar tight cages of highly energetic carbocations are well-known in electrophilic fluorinations.[35]



Olefins producing exceptionally stable β-oxocarbocations are usually transformed to vicinal glycols. Such is the case with 1,1-diphenylethene (**50**) and 4-methoxystilbene (**51**), which form **52**[36] and **53**[37] in 80% and 65% yields even at −15 °C. At this stage we do not know whether the glycols are obtained by direct means through nucleophilic attack of the water on the oxocarbocation or via the corresponding epoxides, which are easily opened under the reaction conditions.[38]



This novel epoxidation reaction has an additional unique feature. The most convenient sources for both ^{17}O and ^{18}O isotopes are the respective water molecules $H_2{}^{17}O$ and $H_2{}^{18}O$. Since the epoxide's oxygen in our method originates directly from the water, one can easily and quantitatively incorporate these isotopes into the desired epoxide and any other products derived from it. Thus, we prepared an oxidizing solution using $H_2{}^{18}O$ and reacted it with *cis*-stilbene (**3**). The oxygen in the resulting *cis*-stilbene oxide indeed contained more then 97% ^{18}O, as could be determined by high-resolution mass spectrometry.



In conclusion, we are presenting a novel, easy, and general way for epoxidation of many types of alkenes. Although the reaction medium is always weakly acidic, the low temperatures and the very short reaction times allow epoxidation of molecules sensitive to bases and acids. A second major point in which we are particularly interested is the fact that elemental fluorine, which was in "deep

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[32] ^{1}H NMR, 4.55 (2 H, m), 3.13 (1 H, d, J = 6 Hz), 2.82 (1 H, d, J = 6 Hz), 1.61 (3 H, s); MS, *m/e* 184 (M$^+$). Anal. Calcd for $C_6H_7F_3O_3$: C, 39.13; H, 3.80. Found: C, 38.84; H, 3.86.

[33] A mixture of two diastereoisomers. IR, 1700 cm^{-1}; ^{1}H NMR, 3.79, 3.78 (3 H, s), 3.45, 3.44 (1 H, d, J = 5 Hz), 3.22 (1 H, dd, J_1 = 4 Hz, J_2 = 5 Hz), 3.21 (1 H, t, J = 5 Hz), 3.02 (1 H, m), 2.76 (1 H, t, J = 5 Hz), 2.75 (1 H, dd, J_1 = 4 Hz, J_2 = 5 Hz), 1.35 (3 H, d, J = 5 Hz); ^{13}C NMR (H decoupled) 168.27, 55.63, 16.65 (C_1, C_6, C_7), 56.36, 52.89, 52.20, 51.88, 50.48, 50.01 (C_2, C_3, C_4, C_5); MS, *m/e* 99 [(M − COOMe)$^+$]. Anal. Calcd for $C_7H_{10}O_4$: C, 53.16; H, 6.33. Found: C, 53.48; H, 6.24.

[34] These epoxides are important intermediates in many syntheses, immunopharmacological studies, and polymerization processes. They are always made indirectly, usually by elimination in 2,3-disubstituted succinic acid derivatives.

[35] Rozen, S.; Lerman, O. *J. Org. Chem.* **1980**, *45*, 672.

[36] Newbold, G. T.; Spring, F. S. *J. Chem. Soc.* **1945**, 247.

[37] Imuta, M.; Ziffer, H. *J. Org. Chem.* **1978**, *43*, 3319.

[38] We have prepared the two epoxides by alternative routes. After being subjected to our reaction conditions, the epoxides were fully consumed and we were able to isolate the corresponding glycols **52** and **53**.

freeze" for most of its known existence, is proving to be a very versatile reagent with a broad spectrum of uses in both fluorine and general organic chemistry.

Experimental Section

^{1}H NMR spectra were recorded with Bruker WH-360 and AC200E spectrometers at 360 and 200 MHz, respectively, with $CDCl_3$ as solvent and Me_4Si as an internal standard. The ^{19}F NMR spectra were measured at 338.8 MHz and are reported in parts per million upfield from $CFCl_3$, which served as both solvent and internal standard. The proton broad-band-decoupled ^{13}C NMR spectra were recorded on the Bruker AC200E spectrometer at 50.30 MHz; $CDCl_3$ served as solvent and TMS as internal standard. Mass spectra were measured with a Du Pont 21-491B spectrometer. IR spectra were recorded as neat films, in $CHCl_3$ solution or as KBr pellets on a Perkin-Elmer 177 spectrophotometer.

General Procedure for Working with Fluorine. Fluorine is a strong oxidizer and a very corrosive material. An appropriate vacuum line made from copper or monel in a well-ventilated area should be constructed for working with this element. For more experimental details, see for example ref 28. For the occasional user, however, various premixed mixtures of F_2 in inert gases are commercially available, simplifying the whole process. The reactions themselves can be carried out in glass vessels. If elementary precautions are taken, work with fluorine is relatively simple and we have had no bad experiences working with this element.

General Procedure for Producing the Oxidizing Reagent. Mixtures of 10% F_2 with nitrogen were used in this work. The gas mixture was prepared in a secondary container before the reaction was started. This mixture was then passed at a rate of about 400 mL/min through a cold (−10 °C) and vigorously stirred mixture of 400 mL of CH_3CN and 40 mL of H_2O. The formation of the oxidizing power was monitored by reacting aliquots with an acidic aqueous solution of KI. The liberated iodine was then titrated with thiosulfate. We have thus achieved concentrations of more then 1 mol/L of the oxidizing reagent.

General Epoxidation Procedure. An appropriate amount of olefin (see discussion) was dissolved in about 50 mL of CH_2Cl_2, and the resultant mixture was cooled to 0 °C and added in one portion to the reaction vessel in which the oxidizing agent had been prepared. With the exception of the more resistant olefins mentioned earlier, the reaction was stopped after 1 min by neutralizing with saturated sodium bicarbonate solution. The mixture was then poured into 1500 mL of water, extracted with CH_2Cl_2, and washed with $NaHCO_3$ and water until neutral. The organic layer was dried over $MgSO_4$ and the solvent evaporated, preferably at room temperature. The crude product was usually purified by vacuum flash chromatography using silica gel 60-H (Merck) and if needed also by HPLC (Waters) on Merck's LiChrosorb Si-100. The purity was also confirmed by GC on 20% SE-30 or 10% OV-17 columns. The spectral and physical properties of the known products thus obtained were compared either with those of authentic samples or with the properties reported in the literature. In every case excellent agreement was obtained. All new compounds were properly identified by ^{1}H NMR, ^{13}C NMR, IR, MS, and microanalysis. Some of the spectral properties of these compounds can be found in the appropriate footnotes.

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Notes

A Tandem Denitration–Deoxygenation of α-Nitro Ketones via (*p*-Tolylsulfonyl)hydrazones with Lithium Aluminum Hydride: A Practical Synthesis of (*Z*)-9-Tricosene, the Sex Pheromone of the Housefly (*Musca domestica*)

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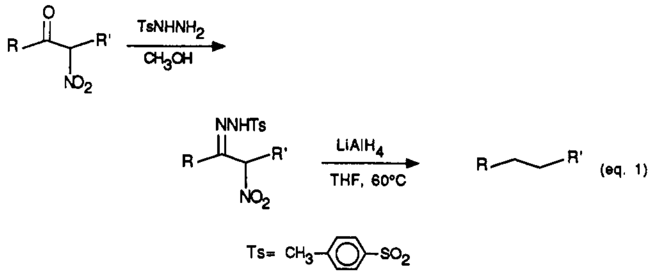
The utilization of α-nitro ketones in organic synthesis has been increased by the discovery of efficient procedures to affect the substitution of the nitro group with hydrogen or deuterium. Procedures and examples of the utilization of functionalized nitroalkanes as reagents for alkyl anion synthons to build structures in a convenient and predictable way[1,2] have been reviewed.

Now, we report a tandem denitration–deoxygenation sequence performed by reduction of (*p*-tolylsulfonyl)hydrazones of α-nitro ketones 1 with lithium aluminum hydride in tetrahydrofuran (THF) at 60 °C (eq 1). On the basis of our indirect method to effect the denitrohydrogenation of α-nitro ketones[1,3] and on the Caglioti reaction[4,5] for the carbonyl to methylene conversion, this procedure provides the corresponding alkanes in good to high yields (Table I).



Linear α-nitro ketones can be easily prepared by classical chain-lengthening sequences such as acylation of primary nitroalkanes[6,7] and nitro aldol reaction (Henry reaction)

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[1] (a) Rosini, G.; Ballini, R. *Synthesis* **1988**, 833. (b) Ono, N.; Kaji, A. *Synthesis* **1986**, 693. (c) Seebach, D.; Colvin, E. W.; Lehr, F.; Weller, T. *Chimia* **1979**, *33*, 1.

[2] Kamimura, A.; Kurata, K.; Ono, N. *Tetrahedron Lett.* **1989**, 4819.

[3] Rosini, G.; Ballini, R.; Zanotti, V. *Synthesis* **1983**, 137. Rosini, G.; Ballini, R. *Synthesis* **1983**, 228.

[4] Caglioti, L.; Grasselli, P. *Chem. Ind.* (*London*) **1964**, 153. Caglioti, L. *Tetrahedron* **1966**, *22*, 487. Caglioti, L. *Org. Synth.* **1972**, *52*, 122.

[5] Other reducing agents may be used. (a) $NaBH_3CN/H^+$: Hutchins, R. O.; Maryanoff, B. E.; Milewski, C. A. *J. Am. Chem. Soc.* **1971**, *95*, 3662. Rosini, G.; Medici, A.; Soverini, M. *Synthesis* **1979**, 789. (b) Catecholborane: Kabalka, G. W.; Baker, J. D., Jr. *J. Org. Chem.* **1975**, *40* 1834.

[6] Crumbie, R. L.; Nimitz, J. S.; Mosher, H. S. *J. Org. Chem.* **1982**, *47*, 4040.

[7] Ono, N.; Fuji, M.; Kaji, A. *Synthesis* **1987**, 532.

0022-3263/90/1955-5159$02.50/0