Table I. α-Fluorocarbonyl Compounds Prepared with CF_3OF

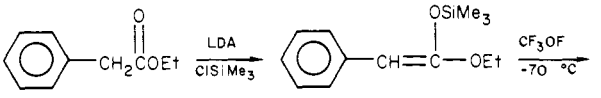
compound[a]	yield, %	mp, °C (recrys solv) [bp (mm), °C]	^{19}F NMR ($CDCl_3$), δ, ppm
esters			
ethyl α-fluorobenzeneacetate (3)	77	[96-98 (4.8)]	-180.1 (d, J = 48 Hz)
ethyl α-fluoro-4-isobutyl-α-methylbenzeneacetate	85	[88-89 (0.4)]	-150.9 (q, J = 22 Hz)
ketones			
α-fluoroacetophenone	70	25-26 [93 (7)]	-231.9 (t, J = 47 Hz)
α,4-difluoroacetophenone	70	48-50 [75 (1.4)]	-232.0 (d, J = 47 Hz) -105.0 (m)
2-fluorocyclohexanone	74	[46 (2.8)]	-188.8 (d, m, J = 51 Hz)
exo-3-fluoronorcamphor	83	99-101 [80 (17)]	-190.0 (d, J = 53 Hz)
α-fluoro-α-phenylacetophenone	72	50-51 (heptane)	-176.5 (d, J = 49 Hz)
aldehyde			
α-fluorobenzeneacetaldehyde[b]	70	[35-36 (1.0)]	-178.8 (d, d, J = 49, 24 Hz)
amides			
α-fluoro-*N*,*N*-dimethylbenzeneacetamide	65	[98-100 (0.45)]	-175.9 (d, J = 50 Hz)
3-fluorodiazepam	80	149-151 (ethanol)	-161.7 (d, J = 57 Hz)
acids			
α-fluorobenzeneacetic acid	90	75-77 (hexane)	-181.4 (d, J = 48 Hz)
α-fluoro-4-isobutylbenzeneacetic acid (6)	80	64-66 (pentane)	-179.9 (d, J = 48 Hz)
3-chloro-α-fluorobenzeneacetic acid	72	61-63 (hexane)	-179.8 (d, J = 47 Hz)
4-chloro-α-fluorobenzeneacetic acid	70	66-68 (hexane)	-182.6 (d, J = 47 Hz)
2-fluoro-2-phenoxyacetic acid	71	61-63 (heptane)	-130.1 (d, J = 59 Hz)
2-fluoro-2-(2,4-dichlorophenoxy)acetic acid	70	89-91 (chlorobutane)	-131.5 (d, J = 59 Hz)
2-fluoro-2-(2,4,5-trichlorophenoxy)acetic acid	76	132 (chlorobutane)	-132.9 (d, J = 59 Hz)
2-fluoro-2-(2-naphthoxy)acetic acid	70	>100 dec	-130.7 (d, J = 60 Hz)

[a] All new compounds gave satisfactory (±0.4%) elemental analysis (C, H, F). [b] Polymerizes on standing.

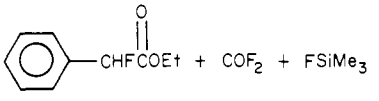
disadvantage in that sometimes a vigorous hydrolysis step is needed to generate the α-fluoro ketones, and yields can be low.

These disadvantages can be overcome by use of trimethylsilyl enol ethers as the fluorinating substrate. In general, trimethylsilyl enol ethers are easy to prepare from most carbonyl compounds, including esters[2] and amides[3] as well as aldehydes and ketones.[4] Silyl enol ethers of all classes of carbonyl compounds react rapidly with CF_3OF at -70 °C in an inert solvent such as CCl_3F to give directly the corresponding α-fluorocarbonyl compound. Workup is simple; no hydrolysis step is required. Since the byproducts of the reaction are all gaseous (carbonyl fluoride and fluorotrimethylsilane), the α-fluorocarbonyl product can be obtained in nearly pure form by a simple evaporation of the reaction mixture.

A sample procedure follows: Ethyl benzeneacetate (**1**) was



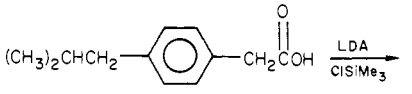
1 2



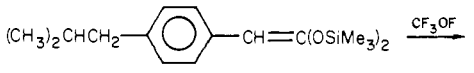
3

converted to its silyl enol ether (**2**) by treatment with lithium diisopropylamide (LDA) and chlorotrimethylsilane.[2] A solution of 21.28 g (0.09 mol) of this enol ether (**2**) in 200 mL of CCl_3F was cooled to -70 °C, and 9.4 g (0.09 mol) of CF_3OF[5] was passed into the solution for 3 h. The reaction mixture was warmed to room temperature and distilled to give 12.52 g (77%) of ethyl α-fluorobenzeneacetate (**3**).

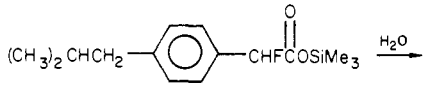
This same chemistry can also be used to convert carboxylic acids to their corresponding α-fluoro derivatives, but an extra hydrolysis step is necessary. The acids are first converted to bis(trimethylsilyl)ketene acetals[6] by reaction with LDA and chlorotrimethylsilane. For example, **5**, bp 128-130 °C (0.4 mm), was prepared from ibufenac (**4**). The ketene acetals are then treated

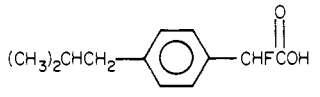


4



5





6

with CF_3OF to give trimethylsilyl α-fluoro esters, which can be easily hydrolyzed to the free α-fluoro acids. Table I shows α-fluorocarbonyl compounds prepared by this new procedure.

(2) Ainsworth, C.; Chen, F.; Kuo, Yu-N. *J. Organomet. Chem.* **1972**, *46*, 59-72.
(3) Woodbury, R. P.; Rathke, M. W. *J. Org. Chem.* **1978**, *43*, 881-884.
(4) House, H. O; Czuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324-2336.
(5) P.C.R. Inc., Gainesville, FL 32602. CF_3OF is an extremely reactive and toxic gas, and proper safety precautions should be followed in its use.
(6) Ainsworth, C.; Kuo, Yu-N. *J. Organomet. Chem.* **1972**, *46*, 73-83.

W. J. Middleton,* E. M. Bingham
Central Research and Development Department
E. I. du Pont de Nemours and Co.
Experimental Station, Wilmington, Delaware 19898
Received March 7, 1980

^1H and ^{14}N Electron-Nuclear Double Resonance of Oxovanadium(IV) Porphyrin in Solid Solution

Sir:

The oxovanadium(IV) ion, VO^{2+}, is used extensively in ESR studies of metal ion complexes.[1-4] The information derived in

0002-7863/80/1502-4846$01.00/0

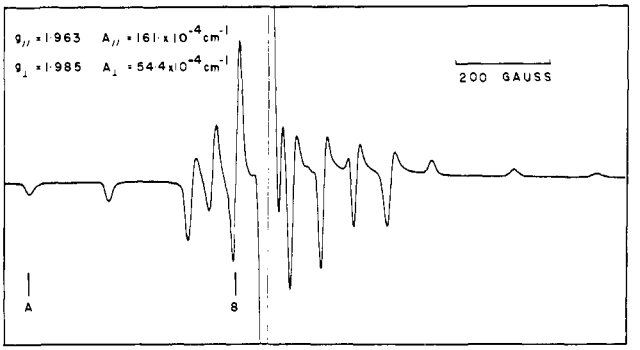


Figure 1. Room-temperature ESR spectrum of phosphate mineral extract recorded with a Varian E-9 spectrometer. Conditions: microwave frequency 9.172 GHz, power 5 mW, amplification 2.5 × 10^2, time constant 0.3 s, field modulation 5 G.

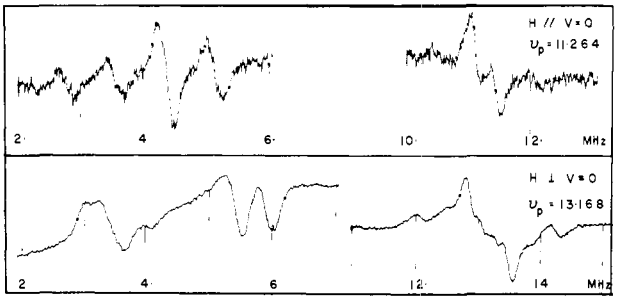


Figure 2. ENDOR spectra of phosphate mineral extract recorded with a Varian E-9 spectrometer with home-built ENDOR attachment.[6] Conditions: ~170 °C, microwave frequency 8.961 GHz, microwave power 5 mW, rf power ~200 W, 10-kHz FM with 90-kHz deviation. Top spectrum: field position A (cf. Figure 1), amplification 1 × 10^4, time constant 1 s. Bottom spectrum: field position B, amplification 2.5 × 10^3, time constant 1 s.

these studies is limited since the spectra rarely display ligand hyperfine structure.[1] It has been shown previously[5,6] that information on proton hyperfine splitting constants (hfsc) of VO^{2+} complexes in solid solution can be obtained with ENDOR.[7] The experimental results presented here illustrate that data on hfsc of ligand nuclei with low ENDOR sensitivity (such as ^{14}N) are readily accessible as well. As a consequence, the technique can make valuable contributions to the understanding of biochemical systems involving the VO^{2+} ion that are currently of interest.[4,8-11]

Figure 1 shows the ESR spectrum of a black solid obtained by chloroform extraction of a phosphate mineral sample from Youssoufia in Morocco.[12] The g value and ^{51}V hfsc data given in the figure are virtually identical with those reported for oxovanadium porphyrins.[14] Figure 2 shows the ENDOR spectrum

Table I. ^{14}N Hyperfine (A) and Quadrupole[a] (P) Coupling Constants

	hyperfine, MHz[b]			quadrupole, MHz		
	A_{xx}	A_{yy}	A_{zz}	P_{xx}	P_{yy}	P_{zz}
extract	9.7	4.3	7.93	±0.2	±0.1	∓0.38
VOTPP[c]	9.6	4.2	7.92	±0.2	±0.1	∓0.38

[a] Signs have been chosen so that the trace "vanishes". [b] The uncertainty in the values of the principal components is estimated to be ±0.05 MHz. [c] A full discussion of the data obtained in the ^{14}N and ^{1}H ENDOR study of VOTPP will be presented elsewhere.[15]

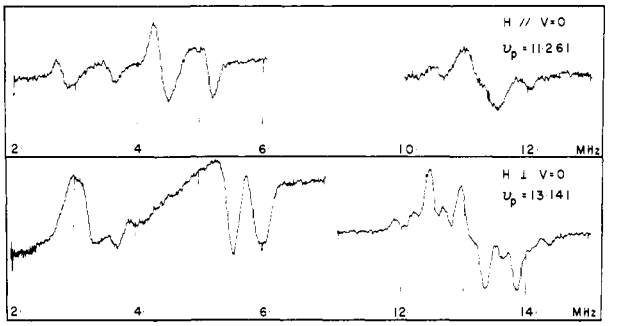


Figure 3. ENDOR spectra of VOTPP (~1%) in ZnTPP. Top spectrum: field position A, amplification 4 × 10^3. Bottom spectrum: field position B, amplification 4 × 10^3. Other conditions as noted in Figure 2.

obtained with field setting A (cf. Figure 1) and gives the ligand hfsc components along the VO bond axis. Figure 2 also gives the ENDOR spectrum for field setting B; this spectrum reflects the ligand hyperfine structure in the plane perpendicular to the VO bond.

The ENDOR lines between 2 and 7 MHz must be attributed to ^{14}N. The positions of the ^{14}N lines in the "single crystal" type spectrum in Figure 2 (top) are given by $^1/_2A_{zz} \pm \nu_N \pm P_{zz}$.[7] Here A_{zz} and P_{zz} are the ^{14}N hyperfine and quadrupole splittings along the VO axis, and ν_N is the nuclear Zeeman splitting. The ^{14}N spectrum in Figure 2 (bottom) represents a two-dimensional powder spectrum. Computer simulations of the ENDOR spectra[15] show that the position of the pair of lines between 5 and 6 MHz is given by $^1/_2A_{xx} + \nu_N \pm P_{xx}$ (where the x axis is a principal axis of the ^{14}N hyperfine and quadrupole tensors in the plane perpendicular to VO) and the incompletely resolved pair at about 3 MHz by $^1/_2A_{yy} + \nu_N \pm P_{yy}$. Table I summarizes the ^{14}N hyperfine and quadrupole data.

A comparison of the ^{14}N ENDOR spectrum obtained from the mineral extract with the spectrum of vanadyl tetraphenylporphyrin (VOTPP) doped in ZnTPP (Figure 3) provides evidence that the VO complex is indeed a metal porphyrin. The ^{14}N hyperfine and quadrupole data for VOTPP are given for comparison in Table I.

The presence of oxovanadium porphyrins in the geochemical environment has been noted previously in numerous publications.[8] However, their origin still is a matter of speculation. While we have not yet completed the analysis of the proton ENDOR spectra, they clearly provide a relatively simple and sensitive method of characterizing naturally occurring oxovanadium porphyrins and thereby may contribute to the understanding of their origin.

Two other fields of applications where the ENDOR technique may prove useful are the following. The oxovanadium(IV) ion has found use in recent years as a probe of the structure of metal proteins.[2,16-18] The finding that ENDOR on VO^{2+} in solid solution gives access to data on hfsc of ligand nuclei such as protons and

(1) B. A. Goodman and J. B. Raynor, *Adv. Inorg. Chem. Radiochem.*, **13**, 135 (1970).
(2) N. D. Chasteen, *Coord. Chem. Rev.*, **22**, 1 (1977).
(3) R. A. Peckauskas, J. D. Termine, and I. Pullman, *Biopolymers*, **15**, 569 (1976).
(4) L. C. Cantley, Jr., and P. Aisen, *J. Biol. Chem.*, **254**, 1781 (1979).
(5) H. van Willigen, *Chem. Phys. Lett.*, **65**, 490 (1979).
(6) H. van Willigen, *J. Magn. Reson.*, in press.
(7) G. H. Rist and J. S. Hyde [*J. Chem. Phys.*, **52**, 4633 (1970)] give a general description of the principles involved.
(8) G. W. Hodgson, *Ann. N.Y. Acad. Sci.*, **206**, 670 (1973), and references cited therein.
(9) J. L. Johnson, H. J. Cohen, and K. V. Rajagopalan, *Biochem. Biophys. Res. Commun.*, **56**, 940 (1974).
(10) R. L. Post, D. P. Hunt, M. O. Walderhaug, R. C. Perkins, J. H. Park, and A. H. Beth, *Na,K-ATPase: Struct. Kinet.* [*Proc. Int. Conf. Prop. Funct. Na,K-ATPase*], **2** (1978).
(11) T. J. B. Simons, *Nature* (*London*), **281**, 337 (1979).
(12) This study is part of an effort to identify the organic matter affecting the industrial use of this phosphate ore.[13] A complete report will be published elsewhere.
(13) A. B. Soulami, V. Pellegrin, and P. Viallefont, *Mines Geol.*, **38**, 43 (1975).
(14) D. Kivelson and S. K. Lee, *J. Chem. Phys.*, **21**, 1896 (1964).
(15) C. F. Mulks and H. van Willigen, to be published.
(16) N. D. Chasteen, R. J. DeKoch, B. L. Rogers, and M. W. Hanna, *J. Am. Chem. Soc.*, **95**, 1301 (1973).
(17) N. D. Chasteen and J. Francavilla, *J. Phys. Chem.*, **80**, 867 (1976).
(18) D. C. Harris, *Biochemistry*, **16**, 560 (1977).

nitrogens suggests that the technique will be valuable in this field of research. Finally, it has been suggested that the vanadate and oxovanadium(IV) ions may play a role in regulating enzyme activity.[4,10,11] Already ESR has been applied to study the fate of the vanadate ion transported into the human red cell.[4] Here also ENDOR could provide valuable complementary information. It is of interest that information on ligand hfsc's in VO^{2+} complexes can be derived also from modulation effects on electron spin-echo decay curves.[19] Whether or not this method can give access to the detailed information presented here remains to be seen. In any case, the method of analysis used by Dikanov et al.[19] does not lend itself for this purpose.

Acknowledgments. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for the support of this research.

(19) S. A. Dikanov, V. F. Yudanov, and Y. D. Tsvetkov, *J. Magn. Reson.*, **34**, 631 (1979).

(20) (a) Department of Chemistry, Faculty of Sciences, Rabat, Morocco; (b) Harvard Medical School, Boston, Massachusetts, and Institut National Polytechnique de Toulouse, France

H. van Willigen,* C. F. Mulks, A. Bouhaouss[20a]
M. Ferhat,[20a] A. H. Roufosse[20b]

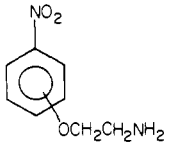
Department of Chemistry, University of Massachusetts
Boston, Massachusetts 02125

Received February 4, 1980

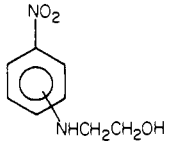
Thermal and Photochemical Smiles Rearrangements of β-(Nitrophenoxy)ethylamines

Sir:

Our interest in aromatic photosubstitution reactions prompted us to search for intramolecular photosubstitutions analogous to the extensively reported intermolecular reactions.[1] Ground-state intramolecular nucleophilic aromatic substitutions are known as Smiles rearrangements or, when carbon nucleophiles are involved, as Truce-Smiles rearrangements.[2] We wish to report that we have successfully synthesized, as prospective Smiles rearrangement precursors, the hydrochlorides of the ortho, meta, and para isomers of β-(nitrophenoxy)ethylamine, I, II, and III, and have examined their thermal and excited-state reactions.



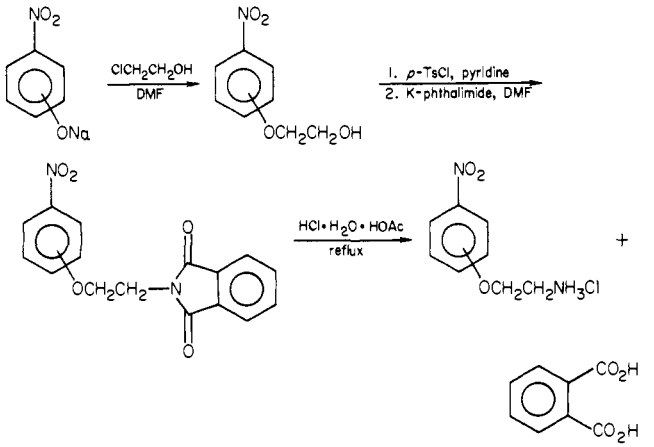
I, ortho
II, meta
III, para



IV, ortho
V, meta
VI, para

The hydrochlorides of I, II, and III were synthesized by the sequence outlined in Scheme I.[3] Hydrochlorides were selected as the synthetic targets because previous attempts to isolate the neutral forms of I and III[4-6] had failed due to their facile rearrangements.[7]

Scheme I



As expected, I and III underwent smooth Smiles rearrangements in aqueous sodium hydroxide to give the corresponding β-(nitroanilino)ethyl alcohols, IV and VI. First-order rate constants for the rearrangements of I and III in aqueous sodium hydroxide (0.01 M) at 33 °C are 1.5×10^{-4} s^{-1} and 4.2×10^{-5} s^{-1}, respectively.[8]

I and III at 0 °C in aqueous sodium hydroxide had half-lives on the order of days. We were able, therefore, to examine the photochemical reactions of I and III with little interference by the thermal reaction by keeping the photolysis temperatures near 0 °C. Photolysis of I (1.6×10^{-4} M) with Pyrex-filtered light from a medium-pressure Hg lamp (1200 W General Electric UA-11) in a cuvette in aqueous sodium hydroxide (0.01 M) at 0-5 °C caused complete loss of reactant absorptions in 2 min and gradual thermal changes in the UV spectrum over 15 min, leading to product absorptions at 335, 300, and 229 nm. Absorption by a thermally reactive intermediate was observed at 287 nm. A scarcely noticeable shoulder absorption appeared in the 400-450-nm range, a region in which the Smiles product IV absorbs strongly (λ_{max} 441 nm (ε 6140)); IV was stable thermally and photochemically in the reaction medium. Though we have not isolated the photoproducts, the observations are sufficient to conclude that I does not undergo Smiles rearrangement in the excited state.

Photolysis of III under the same conditions used for I also caused little or no absorption attributable to the Smiles rearrangement product VI (λ_{max} 404 nm (ε 13300)). In this case also, the Smiles product VI was shown to be stable under the irradiation conditions. A preparative photoreaction of III (600 mg) in aqueous 0.04 M Na_2CO_3 (550 mL) was carried out by irradiating the solution for 2 h at 2-18 °C with a 450-W Hanovia immersion lamp. UV spectra of diluted aliquots of the reaction mixture showed that III (λ_{max} 318 nm (ε 8000)) had almost completely reacted in this time. Workup was performed by neutralization, extraction with ethyl acetate, and concentration of the extract to a brown oil. Chromatography of a portion of the extracted products (392 mg) on activated alumina (15 g) gave a red solid (67 mg) identified as 3,4-dihydro-6-nitro-2*H*-1,4-benzoxazine (VII, 14%),[9] a yellow solid (55 mg) identified as *N*-(2-hydroxyethyl)-4-nitroaniline (VI, 11%),[7] and a red salt (148 mg), recovered by washing the alumina with water, which was identified as the sodium salt of *N*-(2-hydroxyethyl)-2-hydroxy-5-nitroaniline (VIII, 25%).[10] These substances were identified by spectral and chromatographic comparisons with authentic samples. Additional study revealed that VII is stable under the irradiation conditions and could not be an intermediate in the formation of VIII. The elimination of atmospheric oxygen by flushing the reaction solution

(1) Cornelisse, J.; Havinga, E. *Chem. Rev.* **1975**, *75*, 353-88.
(2) Truce, W. E.; Kreider, E. M.; Brand, W. W. *Org. React. (N.Y.)* **1970**, *18*, 99-215.
(3) Satisfactory spectral data and elemental analyses were obtained for all new compounds.
(4) Kleb, G. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 291.
(5) Bernasconi, C. F.; de Rossi, R. H.; Gehriger, C. L. *J. Org. Chem.* **1973**, *38*, 2838-42.
(6) Caldwell, W. T.; Schweiker, G. C. *J. Am. Chem. Soc.* **1952**, *74*, 5187-89.
(7) Knipe has synthesized III by β-aminoethoxide displacement on *p*-chloronitrobenzene; see Knipe, A. C.; Sridhar, N. *Synthesis* **1976**, 606-7.
(8) The kinetics of Smiles rearrangement of III have been reported: Knipe, A. C.; Lound-Keast, J.; Sridhar, N. *J. Chem. Soc., Chem. Commun.* **1976**, 765-6.
(9) Bugaut, A.; Estradier, F.; Ger. Offen. 1 940085; *Chem. Abstr.* **1970**, *73*, 36576P.
(10) Eckhardt, W. German Patent 928 909; *Chem. Abstr.* **1958**, *52*, 4197f.

0002-7863/80/1502-4848$01.00/0