structure, and by strategic employment of selective isotopic labeling, we have shown that the problem of assigning chemically similar resonances in the solid is by no means an intractable one. This is exemplified by our almost-complete assignment of a series of 17 retinal derivatives, many of which have provided problems even in solution. The fruits of the endeavor are several. First, we have acquired a much deeper understanding of the chemical shielding tensors of polyene derivatives and the factors which influence them, particularly the quite clear distinction between steric effects, which perturb the out-of-plane tensor element almost exclusively, and π-electron perturbations, which affect the in-plane elements. This distinction probably applies equally to other π-electron systems such as aromatics, purines, pyrimidines, and other heterocycles. Second, we have been able to distinguish between molecular conformations which rapidly equilibrate in solution. In our case, we have shown that the 6-s-trans and 6-s-cis conformers in retinal derivatives are demarked by quite different chemical shifts at the C-5 position, enabling us to determine this conformation in molecules of unknown structure. Third, we have demonstrated that the counterion effects noted by us for ^{15}N-labeled retinal Schiff bases penetrate quite deeply along the carbons of the conjugated system but are considerably weaker for ^{13}C than they are for nitrogen. Finally, we have obtained a comprehensive set of shielding tensor data for all positions of a variety of retinal derivatives, which should greatly aid continuing research on retinal containing proteins like rhodopsin and bacteriorhodopsin.[10-12]

Acknowledgment. We thank Drs. D. J. Ruben, M. G. Munowitz, W. P. Aue, and S. K. Das Gupta for their valuable assistance with various parts of this work. The research was supported by the National Institutes of Health (GM-23316, GM-23289, and RR-00995), the National Science Foundation (DMR-8211416), the Netherlands Foundations for Chemical Research (SCN), and the Netherlands Organization for the Advancement of Pure Research (ZWO). J. H. is a recipient of an American Cancer Society Faculty Research Award.

Registry No. *all-trans*-Retinal, 116-31-4; 13-*cis*-retinal, 472-86-6; methylamine, 74-89-5; ethylamine, 75-04-7; propylamine, 107-10-8; butylamine, 109-73-9; pentylamine, 110-58-7; hexylamine, 111-26-2; cyclohexylamine, 108-91-8; retinal methylimine Schiff base, 51424-44-3; retinal ethylimine Schiff base, 96998-37-7; retinal propylimine Schiff base, 53633-90-2; retinal butylimine Schiff base, 36076-04-7; retinal pentylimine Schiff base, 82628-41-9; retinal hexylimine Schiff base, 34882-02-5; retinal cyclohexylimine Schiff base, 96949-06-3; 2,4,6-octatrienal, 17609-31-3; 2,4,6-octatrienal butylimine Schiff base, 96949-07-4; *N*-butylretinylideneimine hydrochloride, 28448-64-8; *N*-butylretinylideneimine hydrobromide, 28448-68-2; *N*-butylretinylideneimine dichloroacetate, 96949-08-5; *N*-butylretinylideneimine trichloroacetate, 28448-65-9; *all-trans*-retinoic acid, 302-79-4; retinol acetate, 127-47-9; β-carotene, 7235-40-7.

Nuclear Spin–Spin Coupling via Nonbonded Interactions. 5. N–F Coupling[1]

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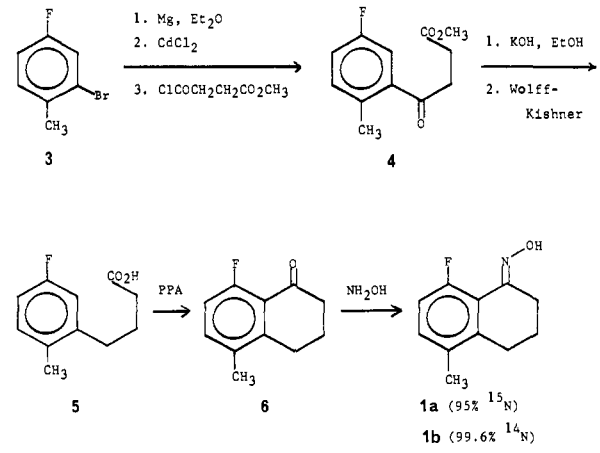
Abstract: On the basis of the lone-pair orbital overlap theory that was developed earlier to account for the phenomenon of "through-space" F–F nuclear spin–spin coupling between intramolecularly crowded fluorine atoms, the existence of "through-space" N–F coupling is predicted. This previously untested prediction is verified experimentally through the observation of a much larger ^{15}N–^{19}F coupling constant for ^{15}N-enriched 3,4-dihydro-8-fluoro-5-methyl-1(2*H*)-naphthalenone oxime (J_{NF} = 22.4 Hz) than for ^{15}N-enriched *o*-fluorobenzaldehyde oxime (J_{NF} = 3.2 Hz).

The phenomenon of "through-space" nuclear spin–spin coupling between fluorine atoms that are crowded against one another intramolecularly is well documented;[3] some extraordinarily large "through-space" F–F coupling constants in the range of 170–200 Hz have been reported.[3a,b,e] Such coupling has been attributed theoretically to direct orbital overlap interactions of the type illustrated in Figure 1.[4] In this particular theoretical formulation,[5] the overlap of two nominally one-center $2p_F$ lone-pair orbitals is imagined to generate two nominally two-center orbitals, a σ_{FF} bonding orbital and a σ^*_{FF} antibonding orbital. Although this overlap interaction would not lead to net *chemical bonding* between the two fluorine atoms, it has been argued[4] that it should provide a four-electron linkage for the transmission of spin information between the two fluorine nuclei.

Scheme I



On the basis of the lone-pair overlap picture[4] of "through-space" F–F coupling presented in Figure 1, we predicted the existence

(1) For Part 4, see: Mallory, F. B.; Mallory, C. W.; Ricker, W. M. *J. Org. Chem.* **1985**, *50*, 457–461.
(2) (a) Bryn Mawr College. (b) University of Pennsylvania.
(3) (a) Servis, K. L.; Fang, K.-N. *J. Am. Chem. Soc.* **1968**, *90*, 6712–6717. (b) Chambers, R. D.; Sutcliffe, L. H.; Tiddy, G. J. T. *Trans. Faraday Soc.* **1970**, *66*, 1025–1038. (c) Mallory, F. B.; Mallory, C. W.; Fedarko, M.-C. *J. Am. Chem. Soc.* **1974**, *96*, 3536–3542 and references cited therein. (d) Hilton, J.; Sutcliffe, L. H. *Prog. Nucl. Magn. Reson. Spectrosc.* **1975**, *10*, 27–39. (e) Mallory, F. B.; Mallory, C. W.; Ricker, W. M. *J. Am. Chem. Soc.* **1975**, *97*, 4770–4771 and references cited therein. (f) Matthews, R. S.; Preston, W. E. *Org. Magn. Reson.* **1980**, *14*, 258–263. (g) Matthews, R. S. *Ibid.* **1982**, *18*, 226–230.
(4) Mallory, F. B. *J. Am. Chem. Soc.* **1973**, *95*, 7747–7752.
(5) Numerous other theoretical approaches have been suggested as well: see ref 3–18 cited by Schaefer and co-workers.[6b]

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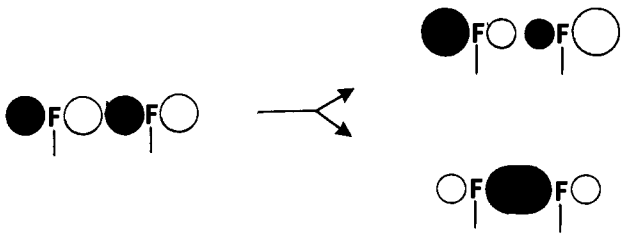


Figure 1. Bonding (σ_{FF}) and antibonding (σ^*_{FF}) orbitals generated by overlap of lone-pair orbitals ($2p_F$) on intramolecularly crowded fluorine atoms.

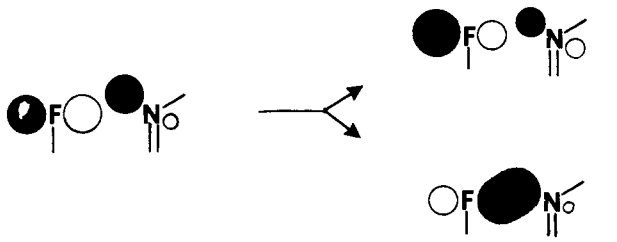


Figure 2. Bonding (σ_{NF}) and antibonding (σ^*_{NF}) orbitals generated by overlap of lone-pair orbitals ($2p_F$ and $2sp^2_N$) on intramolecularly crowded fluorine and nitrogen atoms.

of "through-space" N–F coupling for molecules having spatially proximate nitrogen and fluorine atoms with lone-pair orbitals oriented for overlap as illustrated in Figure 2.[6]

To test this prediction, we synthesized the ^{15}N-enriched oxime **1a** (and also, as a reference compound, the unenriched oxime **1b**) by the sequence of reactions outlined in Scheme I. The ^{19}F and ^1H NMR spectra of oximes **1a** and **1b** were measured at 188.3 and 200.1 MHz, respectively.[7] Complete analyses of these spectra yielded the chemical shifts and coupling constants listed in Table I. The ^{19}F spectra of oximes **1a** and **1b** are given in Figure 3. The ^{19}F spectrum of the ^{14}N-oxime **1b** shows a set of four 1:3:3:1 quartets centered 0.11 ppm upfield from TTC.[7] From the splitting within each quartet a coupling constant of 1.2 Hz was determined for the interaction of F-8 with the C-5 methyl protons. The midpoints of these four quartets were treated[8] as the four main lines of the X part of an ABX system consisting of H-6, H-7, and F-8, respectively. The two characteristic splittings within this four-line pattern for oxime **1b** are 5.4 Hz and 11.9 Hz.[9] The ^{19}F spectrum of the ^{15}N-oxime **1a** (Figure 3) shows a set of *eight* 1:3:3:1 quartets, each with 1.2-Hz internal splittings, centered 0.11 ppm upfield from TTC.[7] The midpoints of these eight quartets were treated as the eight main lines of the X part of an ABXZ system consisting of H-6, H-7, F-8, and the ^{15}N nucleus, respectively. Two of the three characteristic splittings within this eight-line pattern for oxime **1a** are 5.4 and 11.9 Hz,[9] identical in magnitude with the splittings observed for the ^{14}N-oxime **1b**; the third of the characteristic splittings is 22.4 Hz, which clearly is a measure of the coupling between the ^{15}N and ^{19}F nuclei in oxime **1a**.

To establish that "through-space" interactions contribute importantly to the 22.4-Hz N–F coupling found for oxime **1a**, one

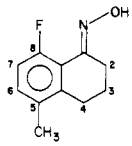
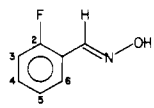
(6) Evidence for "through-space" P–F coupling in some *o*-(trifluoromethyl)phenylphosphine derivatives has been reported: (a) Miller G. R.; Yankowsky, A. W.; Grim, S. O. *J. Chem. Phys.* **1969**, *51*, 3185–3190. (b) Schaefer, T.; Marat, K.; Lemire, A.; Janzen, A. F. *Org. Magn. Reson.* **1982**, *18*, 90–91.

(7) NMR spectra were determined in $CDCl_3$ solution at 17 °C unless specified otherwise. Chemical shifts were measured in ppm downfield from tetramethylsilane (Me_4Si) for ^1H and in ppm downfield from 1,1,2,2-tetrachloro-3,3,4,4-tetrafluorocyclobutane (TTC) for ^{19}F. We estimate that our reported values for chemical shifts and coupling constants are reliable to about ±0.005 ppm and about ±0.2 Hz, respectively.

(8) Pople, J. A.; Schneider, W. G.; Bernstein, H. J. "High-resolution Nuclear Magnetic Resonance"; McGraw-Hill: New York, 1959; p 134.

(9) This ^{19}F pattern is very close to that for a first-order AMX system, as indicated by the almost exact correspondence of the spectral splittings of 5.4 and 11.9 Hz with the H–F coupling constants of 5.3 and 12.0 Hz, the latter being determined from an ABX analysis of the eight-line pattern for H-6 and H-7 in the low-field region of the ^1H spectrum.

Table I. Parameters from the ^{19}F and ^1H NMR Spectra of Oximes **1a**, **1b**, **2a**, and **2b**[a]

oxime	chem shifts, ppm		coupling const, Hz	
	F–8	−0.11	^{15}N, F	22.4
	H–7	6.90	H–7, F	12.0
	H–6	7.09	H–6, F	5.3
	CH_3	2.25	CH_3, F	1.2
	H–4	2.68	H–7, H–6	8.3
	H–3	1.86	H–4, H–3	6.1
	H–2	2.89	H–3, H–2	6.7
1a(^{15}N), 1b(^{14}N)	OH	10.4	H–2, ^{15}N	1.8
	F–2	−4.44	^{15}N, F	3.2
	H–3	7.09	H–3, F	10.4
	H–4	7.37	H–4, F	5.3
	H–5	7.16	H–6, F	7.2
	H–6	7.77	H–3, H–4	8.2
2a(^{15}N), 2b(^{14}N)	–CH=	8.38	H–3, H–5	1.2
	OH	9.2	H–4, H–5	7.4
			H–4, H–6	1.8
			H–5, H–6	7.6
			–CH=, ^{15}N	2.3

[a] See ref 7 and the Experimental Section for further details.

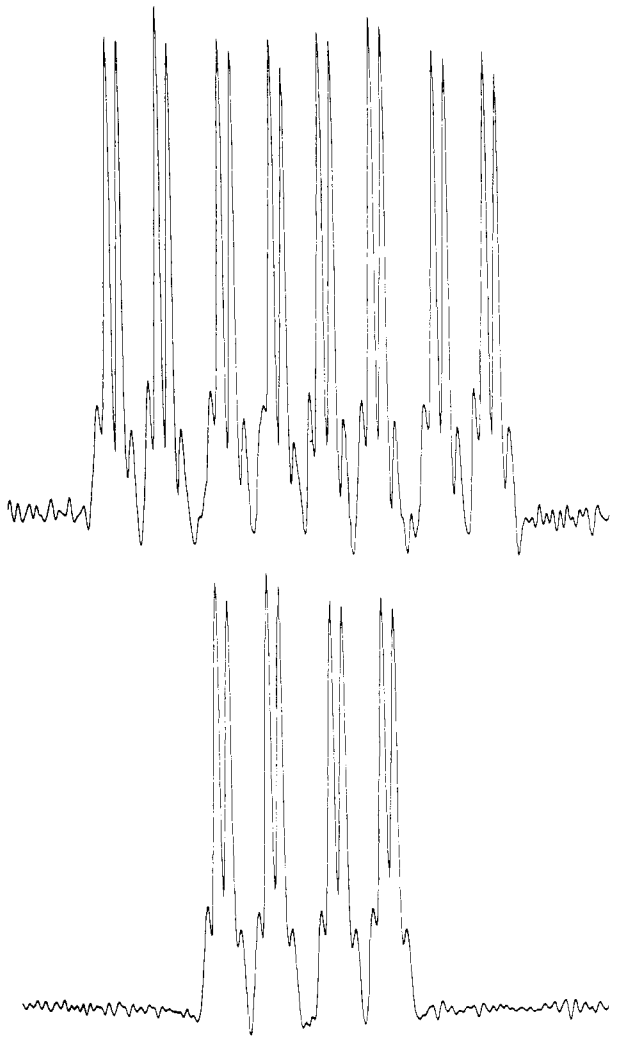
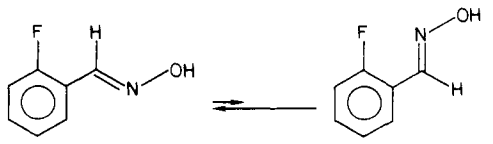


Figure 3. Reproductions of the 188.3-MHz ^{19}F NMR spectra of the ^{15}N-oxime **1a** (upper trace) and the ^{14}N-oxime **1b** (lower trace) in $CDCl_3$ solution. The pre-induction decays for these spectra were subjected to Gaussian line-narrowing multiplication before Fourier transformation. Line positions in Hz relative to TTC[7] for **1a**: −0.4, 0.8, 2.0, 3.2, 5.0, 6.2, 7.4, 8.6, 11.5, 12.7, 13.9, 15.1, 16.9, 18.1, 19.3, 20.5, 22.0, 23.2, 24.4, 25.6, 27.4, 28.6, 29.8, 31.0, 33.9, 35.1, 36.3, 37.5, 39.3, 40.5, 41.7, and 42.9. Line positions in Hz relative to TTC[7] for **1b**: 10.3, 11.5, 12.7, 13.9, 15.7, 16.9, 18.1, 19.3, 22.2, 23.4, 24.6, 25.8, 27.6, 28.8, 30.0, and 31.2.

must be able to argue that "through-bond" interactions make only a small contribution to the observed coupling. In fact, Sibi and Lichter[10] report values of less than 1 Hz for various four-bond (and also three-bond!) $^{15}N-^{19}F$ coupling constants in their systematic studies of fluoropyridines and fluoroanilines. As a closer model system for the "through-bond" component of the N–F coupling in oxime **1a**, however, we have chosen the ^{15}N-enriched *o*-fluorobenzaldehyde oxime **2a**. For this oxime, we expect an overwhelming preference at equilibrium for conformer **2a** over conformer **2a′** on the basis of two factors: greater van der Waals crowding and also greater electrostatic repulsion between C—F and C=N bond dipoles in conformer **2a′**.



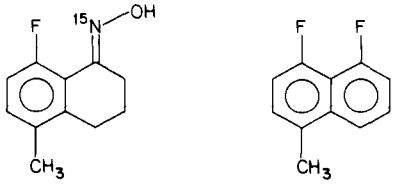
2a (95% ^{15}N)
2b (99.6% ^{14}N)

2a′
2b′

The ^{15}N and ^{19}F nuclei in conformer **2a** are too remote from one another spatially for "through-space" interactions, so spin–spin coupling between these two nuclei must occur entirely by "through-bond" interactions. Because the four-bond pathway for N–F coupling in oxime **2a** has the same connectivity as that in oxime **1a**, we believe the value of J_{NF} for **2a** should provide a reasonable estimate of the magnitude of the "through-bond" component of the overall 22.4-Hz N–F coupling in **1a**. Accordingly, we prepared the ^{15}N-enriched oxime **2a** and its unenriched counterpart **2b** and measured the ^{19}F and ^{1}H spectra of both oximes at 188.3 and 200.1 MHz, respectively. Complete analyses were achieved for all four spectra; the resulting chemical shifts and coupling constants are listed in Table I. The observed magnitude of 2.3 Hz for the $^{15}N-^{1}H$ coupling constant for the CH=N proton in oxime **2a** demonstrates unequivocally that the C=N double bond in this oxime has the *E* configuration.[11] The peak assignments for the ring protons in the ^{1}H spectra of oximes **2a** and **2b** were confirmed by homonuclear decoupling experiments. The eight-line ^{19}F spectrum of the ^{14}N-oxime **2b** has characteristic splittings of 5.3, 7.2, and 10.4 Hz arising from H–F coupling. The sixteen-line ^{19}F spectrum of the ^{15}N-oxime **2a** has the identical three H–F splittings of 5.3, 7.2, and 10.4 Hz, plus a fourth splitting of 3.2 Hz that clearly arises from $^{15}N-^{19}F$ coupling. This ^{19}F spectrum of oxime **2a** exhibits only a slight dependence on temperature: J_{NF} increases linearly from 3.2 to 3.7 Hz and the ^{19}F chemical shift moves downfield linearly by 0.6 ppm as the temperature is decreased from +17 to −33 °C.

From our observation that the value of J_{NF} for oxime **1a** is much larger than that for oxime **2a** (22.4 Hz compared to 3.2–3.7 Hz) we conclude that "through-space" interactions are indeed primarily responsible for the observed 22.4-Hz N–F coupling in oxime **1a**. This represents the first experimental demonstration, to our knowledge, of the existence of "through-space" N–F coupling, in confirmation of our theoretical prediction.

It is interesting to compare the magnitude of the N–F coupling in oxime **1a** with the magnitude of the roughly analogous F–F coupling in 1-methyl-4,5-difluoronaphthalene (**7**).[3c]



1a: J_{NF} = 22.4 Hz

7: J_{FF} = 65 Hz[3c]

The proper comparison here is not the ratio of coupling constants, J_{NF}/J_{FF}, but rather the ratio of reduced coupling constants, K_{NF}/K_{FF}, in which account is taken of the fact that the absolute value of the magnetogyric ratio for ^{15}N is only about $^{1}/_{9}$ that for ^{19}F. Thus K_{NF} for oxime **1a** is about three times as large (i.e., $9 \times 22.4/65$) as K_{FF} for naphthalene **7**. As a very preliminary speculation, this apparently greater effectiveness of "through-space" N–F coupling as compared to "through-space" F–F coupling might arise because the relevant lone-pair electrons on nitrogen are in a hybrid orbital with some s character, which allows them to make direct Fermi contact with the N nucleus, whereas the relevant lone-pair electrons on fluorine are in a 2p orbital such that Fermi contact with the F nucleus requires indirect spin-polarization of the fluorine 1s and 2s electrons by the fluorine 2p electrons.

Experimental Section

Melting points were measured with a Thomas-Hoover oil-bath apparatus and are uncorrected. Elemental analyses were performed by M-H-W Laboratories. ^{1}H NMR spectra[7] were obtained with an IBM WP-200 SY (200.1 MHz) or a Perkin-Elmer R-32 (90 MHz) spectrometer. ^{19}F NMR spectra[7] were obtained with an IBM WP-200 SY (188.3 MHz) spectrometer. Mass spectra were determined with a VG 70-70 Micromass double-focusing spectrometer. Sublimations at reduced pressure were carried out as described previously.[12]

2-Bromo-4-fluorotoluene (3). Treatment of 4-nitrotoluene with Br_2 and iron powder at 95–100 °C gave 2-bromo-4-nitrotoluene (74%).[13] Reduction of this material with iron and hydrochloric acid gave 3-bromo-4-methylaniline (97%).[13,14] A Schiemann reaction of this amine gave 2-bromo-4-fluorotoluene (75%),[15] bp 167–172 °C (lit.[15] bp 170–172 °C).

Methyl 3-(5-Fluoro-2-methylbenzoyl)propionate (4). A previously described general procedure[16] was followed. To the Grignard reagent prepared from 59 g (0.3 mol) of 2-bromo-4-fluorotoluene (**3**) and 7.6 g (0.3 mol) of magnesium turnings in 250 mL of dry diethyl ether and 50 mL of dry, thiophene-free benzene was added 33.6 g (0.18 mol) of cadmium chloride in one portion. The mixture was stirred mechanically and heated at reflux for 45 min. Then the reflux condenser was replaced by a small fractionating column and the ether was removed by distillation. During the distillation, a total of 350 mL of benzene was added to the reaction mixture in several portions. When the head temperature reached 77 °C and 400 mL of distillate had been collected, the reaction mixture suddenly became quite viscous. To facilitate stirring, another 25 mL of benzene was added. Next a solution of 41 mL (50 g, 0.3 mol) of carbomethoxypropionyl chloride in 30 mL of benzene was added dropwise to the cadmium reagent over 10 min, after which the reaction mixture was stirred and heated at reflux for 1.5 h and finally let stand overnight at room temperature. The cadmium complex was decomposed by the addition of 40 mL of concentrated hydrochloric acid followed by 200 mL of water. The layers were separated, and the organic layer was washed three times with aqueous $NaHCO_3$ and finally with saturated aqueous NaCl. The solution was dried over anhydrous $MgSO_4$ and filtered and the solvent removed on a rotary evaporator to give a red liquid. Distillation at reduced pressure gave 42.3 g (61%) of methyl 3-(5-fluoro-2-methylbenzoyl)propionate (**4**) as a colorless oil, bp 95–98 °C at 0.08 torr: ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.34 (dd, 1 H, H-6′, $J_{5',6'}$ = 9 Hz, $J_{4',6'}$ = 2 Hz), 7.24–6.91 (m, 2 H, H-3′ and H-4′), 3.67 (s, 3 H, OCH_3), 3.16 (t, 2 H, H-3 or H-2, J = 7 Hz), 2.70 (t, 2 H, H-2 or H-3, J = 7 Hz), 2.40 (br s, 3 H, $ArCH_3$).

4-(5-Fluoro-2-methylphenyl)butyric Acid (5). Saponification of ester **4** with potassium hydroxide in 95% ethanol gave, after recrystallization of the crude product from a mixture of toluene and hexane, 3-(5-fluoro-2-methylbenzoyl)propionic acid (76%) as small white crystals, mp 83.5–85.7 °C: ^{1}H NMR (90 MHz, $CDCl_3$) δ 10.5 (br s, 1 H, CO_2H), 7.35 (dd, 1 H, H-6′, $J_{5',6'}$ = 9 Hz, $J_{4',6'}$ = 2 Hz), 7.27–6.94 (m, 2 H, H-3′ and H-4′), 3.17 (t, 2 H, H-3 or H-2, J = 8 Hz), 2.77 (t, 2 H, H-2 or H-3, J = 8 Hz), 2.42 (s, 3 H, CH_3); MS, m/z 210 (M^+).

Wolff–Kishner reduction[17] of this keto acid (9.8 g, 0.05 mol) with hydrazine hydrate (85% in water, 8 mL, 0.14 mol) and potassium hydroxyde (9.0 g, 0.14 mol) in 65 mL of diethylene glycol at 200 °C gave, after acidification of the reaction mixture, an orange oil that partially solidified on standing. Sublimation of this material at 57 °C and 0.005 torr gave 5.0 g (55%) of 4-(5-fluoro-2-methylphenyl)butyric acid (**5**), mp 65.0–66.8 °C: ^{1}H NMR (90 MHz, $CDCl_3$) δ 9.07 (br s, 1 H, CO_2H),

(10) Sibi, M. P.; Lichter, R. L. *Org. Magn. Reson.* **1980**, *14*, 494–496.
(11) Crêpaux, D.; Lehn, J.-M. *Org. Magn. Reson.* **1975**, *7*, 524–526.
(12) Mallory, F. B. *J. Chem. Educ.* **1962**, *39*, 261.
(13) Higginbottom, A.; Hill, P.; Short, W. F. *J. Chem. Soc.* **1937**, 263–266.
(14) West, R. W. *J. Chem. Soc.* **1925**, 494–495.
(15) Dewar, M. J. S.; Grisdale, P. J. *J. Org. Chem.* **1963**, *28*, 1759–1762.
(16) Dauben, W. G.; Tilles, H. *J. Org. Chem.* **1950**, *15*, 785–789.
(17) Huang-Minlon, *J. Am. Chem. Soc.* **1946**, *68*, 2487–2488.

7.10–6.61 (m 3 H, H-3′,4′,6′), 2.62 (t, 2 H, H-2 or H-4, J = 7 Hz), 2.41 (t, 2 H, H-4, or H-2, J = 7 Hz), 2.23 (s, 3 H, CH_3), 1.88 (pentet, 2 H, H-3, $J_{2,3} = J_{3,4}$ = 7 Hz); MS, m/z 196 (M^+).

3,4-Dihydro-8-fluoro-5-methyl-1(2*H*)-naphthalenone (6). Treatment of 4.9 g (0.025 mol) of carboxylic acid **5** with polyphosphoric acid at 90–94 °C for 8 min, followed by aqueous workup, gave a pale yellow solid. Sublimation of this material at 50 °C and 0.005 torr gave 3.7 g (83%) of ketone **6** as colorless prisms, mp 54–57 °C. Recrystallization of the sublimate from hexane gave colorless needles of **6** with mp 56.3–57.2 °C: ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.22 (dd, 1 H, H-6, $J_{6,7}$ = 8 Hz, $J_{6,8}$ = 5 Hz), 6.80 (dd, 1 H, H-7, $J_{6,7}$ = 8 Hz, $J_{7,8}$ = 11 Hz), 2.82 (t, 2 H, H-2 or H-4, J = 6 Hz), 2.62 (t, 2 H, H-4 or H-2, J = 6 Hz), 2.24 (br s, 3 H, CH_3), 2.10 (pentet, 2 H, H-3, $J_{2,3} = J_{3,4}$ = 6 Hz); ^{19}F NMR (188.3 MHz, 0.30 M in $CDCl_3$) 2.34 ppm upfield from TTC[7] (dd of q, $J_{7,8}$ = 11.4 Hz, $J_{6,8}$ = 5.3 Hz, $J_{CH_3,8}$ = 1.1 Hz). Anal. ($C_{11}H_{11}FO$) C, H.

3,4-Dihydro-8-fluoro-5-methyl-1(2*H*)-naphthalenone Oximes (1a and 1b). Treatment of 0.50 g (2.8 mmol) of ketone **6** with 0.42 g (6.0 mmol) of hydroxylamine hydrochloride, 5 mL of pyridine, and 10 mL of 95% ethanol gave, after one recrystallization from 95% ethanol, 0.50 g (93%) of oxime **1b**, mp 193–196 °C. A second recrystallization from 95% ethanol gave long, colorless needles of **1b** with mp 197.5–199.0 °C: ^{1}H NMR (200.1 MHz, $CDCl_3$) δ 10.4 (br s, 1 H, OH), 7.09 and 6.90 (AB part of ABX, 2 H, H-6 and H-7, respetively, $J_{6,7}$ = 8.3 Hz, $J_{6,8}$ = 5.3 Hz, $J_{7,8}$ = 12.0 Hz), 2.89 (t, 2 H, H-2, $J_{2,3}$ = 6.7 Hz), 2.68 (t, 2 H, H-4, $J_{3,4}$ = 6.1 Hz), 2.25 (br s, 3 H, CH_3), 1.86 (pentet, 2 H, H-3, apparent J = 6.4 Hz); ^{19}F NMR (188.3 MHz, 0.27 M in $CDCl_3$) see Figure 3 and Table I. Anal. ($C_{11}H_{12}FNO$) C, H.

Similar treatment of 0.64 g (3.6 mmol) of ketone **6** with 0.30 g (4.3 mmol) of (^{15}N)hydroxylamine hydrochloride (Cambridge Isotope Laboratories, Inc., 95% ^{15}N), 7 mL of pyridine, and 14 mL of 95% ethanol gave, after recrystallization of the crude product from 95% ethanol, 0.63 g (90%) of oxime **1a**, mp 196.8–198.4 °C: ^{1}H NMR (200.1 MHz, $CDCl_3$) δ 10.4 (br s, 1 H, OH), 7.09 and 6.90 (AB part of ABX, 2 H, H-6 and H-7, respectively, $J_{6,7}$ = 8.3 Hz, $J_{6,8}$ = 5.3 Hz, $J_{7,8}$ = 12.0 Hz), 2.89 (t of d, 2 H, H-2, $J_{2,3}$ = 6.7 Hz, $J_{2,N}$ = 1.8 Hz), 2.68 (t, 2 H, H-4, $J_{3,4}$ = 6.1 Hz), 2.25 (br s, 3 H, CH_3), 1.86 (pentet, 2 H, H-3, apparent J = 6.4 Hz); ^{19}F NMR (188.3 MHz, 0.27 M in $CDCl_3$) see Figure 3 and Table I; MS, m/z 194 (M^+).

***o*-Fluorobenzaldehyde Oximes (2a and 2b).** A mixture of 0.30 g (2.4 mmol) of *o*-fluorobenzaldehyde, 0.23 g (3.3 mmol) of hydroxylamine hydrochloride, 1 mL of water, 1 mL of 10% aqueous sodium hydroxide, and about 10 drops of 95% ethanol (to bring the aldehyde into solution) was heated in a boiling water bath for 15 min. Then the solution was cooled thoroughly in ice, and 0.2 g (59%) of oxime **2b** was collected by filtration. Recrystallization from hexane gave 0.13 g of **2b** as white needles, mp 61.8–62.3 °C (lit.[18] mp 63 °C): ^{1}H NMR (200.1 MHz, $CDCl_3$) δ 9.2 (br s, 1 H, OH), 8.38 (s, 1 H, CH=N), 7.77 (t of d, 1 H, H-6, apparent J = 7.4 and 1.8 Hz), 7.37 (t of dd, 1 H, H-4, apparent J = 7.8, 5.3, and 1.8 Hz), 7.16 (br t, 1 H, H-5, apparent J = 7.5 Hz), 7.09 (ddd, 1 H, H-3, $J_{2,3}$ = 10.4 Hz, $J_{3,4}$ = 8.2 Hz, $J_{3,5}$ = 1.2 Hz); ^{19}F NMR (188.3 MHz, 0.63 M in $CDCl_3$) 4.44 ppm upfield from TTC[7] (ddd, $J_{2,3}$ = 10.4 Hz, $J_{2,4}$ = 5.3 Hz, $J_{2,6}$ = 7.2 Hz).

An identical procedure, except for the use of (^{15}N)hydroxylamine hydrochloride (Cambridge Isotope Laboratories, Inc., 95% ^{15}N), was employed to prepare 0.14 g of oxime **2a**, mp 62.0–63.2 °C: ^{1}H NMR (200.1 MHz, $CDCl_3$) δ 9.2 (br s, 1 H, OH), 8.38 (d, 1 H, CH=N, J_{HN} = 2.3 Hz), 7.77 (t of d, 1 H, H-6, apparent J = 7.4 and 1.8 Hz), 7.37 (t of dd, 1 H, H-4, apparent J = 7.8, 5.3, and 1.8 Hz), 7.16 (br t, 1 H, H-5, apparent J = 7.5 Hz), 7.09 (ddd, 1 H, H-3, $J_{2,3}$ = 10.4 Hz, $J_{3,4}$ = 8.2 Hz, $J_{3,5}$ = 1.2 Hz); ^{19}F NMR (188.3 MHz, 0.63 M in $CDCl_3$) 4.44 ppm upfield from TTC[7] (dddd, $J_{2,3}$ = 10.4 Hz, $J_{2,4}$ = 5.3 Hz, $J_{2,6}$ = 7.2 Hz, $J_{2,N}$ = 3.2 Hz); MS, m/z 140 (M^+).

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Registry No. 1a, 97072-88-3; **1b**, 97072-89-4; **2a**, 97072-90-7; **2b**, 24652-66-2; **3**, 1422-53-3; **4**, 97072-91-8; **5**, 97072-92-9; **6**, 97072-93-0; (^{15}N)-hydroxylamine hydrochloride, 40711-48-6; *o*-fluorobenzaldehyde, 446-52-6; 3-(5-fluoro-2-methylbenzoyl)propionic acid, 97072-94-1; 4-nitrotoluene, 99-99-0; 2-bromo-4-nitrotoluene, 7745-93-9; 3-bromo-4-methylaniline, 7745-91-7; carbomethoxypropionyl chloride, 1490-25-1; hydroxylamine hydrochloride, 5470-11-1.

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Transient Absorption and Two-Step Laser-Excitation Fluorescence Studies on the Proton Transfer in the Ground and Excited States of 3-Hydroxyxanthone in Alcohols

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Abstract: The alcoholic solutions of 3-hydroxyxanthone (3-HX) exhibit considerably large Stokes-shifted fluorescence in the 430–530-nm region at room temperature. In the deaerated methanol solution, the 450-nm fluorescence decays almost single exponentially with a lifetime of 5.9 ns, while the longer wavelength fluorescence (470–530 nm) shows double exponential (τ = 0.5 and 5.8 ns). The long and short decay fluorescences were ascribed to anion and tautomer simultaneously generated by the excited-state proton transfer in 3-HX, respectively. The transient absorption of the deaerated methanol solution of 3-HX shows a strong absorption band with a rise at 355 nm and broad bands at 370–460 nm. These absorption bands were ascribed to the ground-state anion and tautomer formed in the relaxation of their excited states. The two-step laser-excitation (TSLE) fluorescence by the second laser excitation of the transient absorption was measured at room temperature. The second laser excitations at 440 and 457 nm exhibit the short lived fluorescence spectra (τ = ~0.6 ns) at 470–530 nm, which is ascribed to the tautomer fluorescence. The second laser excitations of 406 and/or 420 nm at several delay times afford the TSLE time-resolved fluorescence spectra. The TSLE fluorescence at 470–530 nm decreases rapidly in intensity with increasing delay time, while the intensity in the 460-nm region gradually increases at long delay times. The former and latter were ascribed to the tautomer and anion of 3-HX, respectively. The rise and decay of the ground-state anion and tautomer obtained by TSLE variable delay are consistent with those obtained by transient absorption spectra. This fact suggests that the ground-state anion may be generated at the expense of the ground-state tautomer in addition to the formation from its excited state, and this anion relaxes to the parent molecule by the reverse proton transfer in the ground state.

Two-step laser-excitation fluorescence or two-step laser-induced fluorescence spectra have been reported for the investigations of unstable molecules[1-3] and/or transient states.[4] We have reported in several papers of the transient absorption and TSLE fluores-

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