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THROUGH-SPACE HYDROGEN-FLUORINE AND CARBON-FLUORINE SPIN-SPIN COUPLING IN 5-FLUORO-3,3-DIMETHYL-1,2,3,4-TETRAHYDROPHENANTHRENE

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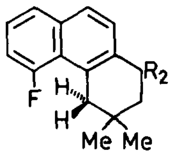
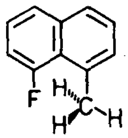
Summary: The ^{1}H and ^{13}C NMR spectra of the title compound (1) reveal through-space couplings between the fluorine and the C-4 methylene group (^{1}H and ^{13}C), as well as coupling between the fluorine and the C-3 methine carbon and the C-2 methylene carbon.

"Through-Space" or "proximate" spin-spin coupling between fluorine and other magnetic nuclei (^{1}H, ^{13}C, ^{19}F) is firmly established as an NMR phenomenon.[1] Although it is clear from theoretical studies[2] that these interactions--particularly H-F coupling--depend both on proximity and bond orientation effects, very few experimental systems have been designed in which both factors can be studied. One such, recent example is the elegant work of Ōki[3] who observed through-space coupling between fluorine and the individual protons in a "frozen" methyl group at low temperature in 8,13-dichloro-1,2,3,4-tetrafluoro-9-methyltriptycene.

In this Letter we describe the synthesis and NMR spectra of 5-fluoro-3,3-dimethyl-1,2,3,4-tetrahydrophenanthrene (1), a system designed to approximate[4] the corresponding "frozen" methyl rotamer in 8-fluoro-1-methylnaphthalene (2)[5] and 8-fluoro-N-methylquinolinium salts (3),[2] molecules for which pronounced through-space H-F and C-F couplings are observed, as shown below.

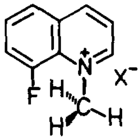


1 (R=H,D)



$^5J_{HF}$ = ± 7.5 Hz[5]
$^4J_{CF}$ = ± 12.0 Hz[5b]

2

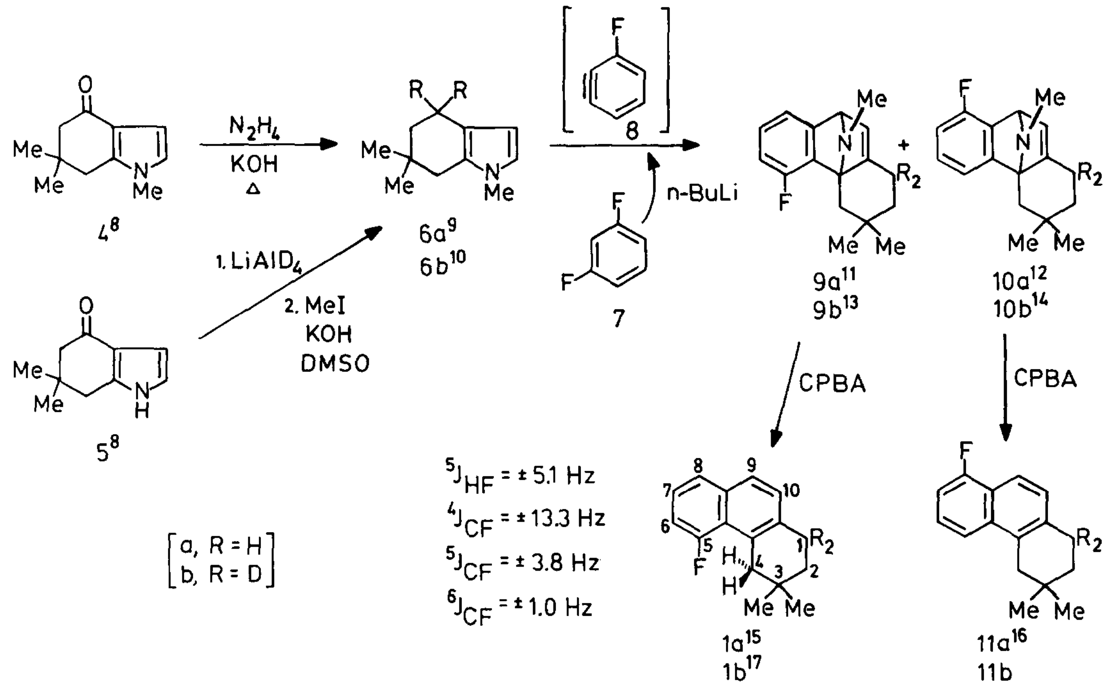


$^5J_{HF}$ = +8.8 Hz[2]
$^4J_{CF}$ = +16.3 Hz[2]

3

Our syntheses of 1 and the 8-fluoro isomer 11 are summarized in Scheme I, the key steps being a Diels-Alder reaction between pyrrole 6 and 3-fluorobenzyne (8), and the oxidative deamination with *m*-chloroperbenzoic acid (CPBA)[6] of the easily separated and distinguishable[7] imines 9 and 10. We chose to study the compound having dimethyl and deuterium substitution at C(3) and C(1), respectively, in order to simplify the NMR spectra of 1.

Scheme I



The ^{1}H and ^{13}C NMR spectra of 11a reveal no observable coupling between the fluorine atom and any of the aliphatic protons or carbons.[16] However, the corresponding spectra of 1a (and 1b) indicate several through-space couplings involving the fluorine atom. Thus, the C(4) methylene protons are coupled to ^{19}F: $^5J_{HF}$ = ±5.1 Hz, a value which is comparable to the ±6.1 Hz observed by Oki[3] for the corresponding syn-clinal protons in a frozen methyl rotor, and to the ± 4.8 Hz observed by Heaney[18] in a related system. The sign of $^5J_{HF}$ in 1a is assumed to be positive based on the positive $^5J_{HF}$ determined[2] for 3 and the results of Oki who showed that all three protons in a frozen methyl rotor are coupled to the fluorine atom with the *same* sign. Theoretical arguments, based on the INDO-FPT method,[2] predict *opposite* signs for the coupling involving syn and anti protons in a frozen methyl system. The origin of this discrepancy between theory and experiment remains unknown.[19]

Of particular interest are the ^{13}C-^{19}F splittings observed in the ^{13}C NMR spectrum of 1. In addition to the expected coupling to the C(4) methylene group: $^{4}J_{CF}$ = ±13.3 Hz, there is observed coupling between the fluorine and C(3): $^{5}J_{CF}$ = ±3.8 Hz; and C(2): $^{6}J_{CF}$ = ±1.0 Hz. These latter through-space "zig-zag" couplings are apparently unprecedented[20] and may result from favorable non-bonded interactions between the fluorine and molecular orbitals associated with the C(4)-C(3)-C(2) carbon framework. In accord with this "zig-zag" mechanism we observe no splitting of the methyl carbons by the fluorine. A similar zig-zag angular dependence has been observed for vicinal C-C couplings ($^{3}J_{cc}$) in alkanes.[21]

We believe that these coupling constants further illustrate the importance of nonbonded interactions between a fluorine and a proximate carbon atom (i.e., C(4) in 1) in through-space H-F and C-F coupling, as suggested by Servis[22] and later extended by Mallory.[23] Finally, these data would appear to contradict the "converging-vector rule" for through-space H-F coupling.[24]

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3. (a) G. Yamamoto and M. Oki, Tetrahedron Lett., 26, 457 (1985); (b) G. Yamamoto and M. Oki, J. Org. Chem., 49, 1913 (1984).
4. The cyclohexene ring in 1 is, of course, nonplanar but presumably undergoes rapid ring-flipping between two equivalent half-chain conformers at room temperature.
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7. This was accomplished using medium pressure liquid chromatography and the cycloadducts were distinguished by the characteristic five-bond zig-zag H-F coupling in 9 but not in 10: cf., G.W. Gribble and W.J. Kelly, Tetrahedron Lett., 22, 2475 (1981).
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9. 6a: (83%) bp 77-85°/0.15 torr; ^{1}H-NMR ($CDCl_3$) δ 6.40 (d, J = 3.0, 1H), 5.85 (d, J = 3.0, 1H), 3.35 (s, 3H), 2.50 (t, J = 6.0, 2H), 2.20 (s, 2H), 1.50 (t, J = 6.0, 2H), 1.00 (s, 6H); ms m/e 163.1361 (M^+, calcd for $C_{11}H_{17}N$, 163.1365).
10. 6b: (70% from 5) bp 63-66°/0.1 torr; ^{1}H NMR ($CDCl_3$) δ 6.40 (d, J = 2.5, 1 H), 5.85 (d, J = 2.5, 1H), 3.35 (s, 3H), 2.25 (s, 2H), 1.50 (s, 2H), 1.05 (s, 6H); ms m/e 165.1483 (M^+, calcd for $C_{11}H_{15}D_2N$, 165.1487).
11. 9a: (17%) mp 59-60° (Et_2O); ^{1}H NMR ($CDCl_3$) δ 6.9-6.65 (m, 3H), 6.45 (br s, 1H), 4.20 (t, J = 2.0, 1H), 2.30 (m, 2H), 1.90 (s, 3H), 1.50 (m, 2H), 1.20 (s, 2H), 1.10 (s, 6H); ms m/e 257.1579 (M^+, calcd for $C_{17}H_{20}NF$, 257.1579); Anal. Calcd C, 79.34; H, 7.83; N, 5.44; found: C, 79.34; H, 7.83; N, 5.40.

12. *10a*: (12%) mp 84-85° (Et_2O); ^1H NMR ($CDCl_3$) δ 7.2-6.75 (m, 3H), 6.5 (br s, 1H), 4.60 (d, J = 2.0, 1H), 2.40 (t, J = 5, 2H), 1.95 (s, 3H), 1.50 (t, J = 5.0, 2H), 1.10 (s, 6H); ms *m/e* 257.1566 (M^+, calcd for $C_{17}H_{20}NF$, 257.1579.

13. *9b*: (19%) mp 64-65° (Et_2O); ^1H NMR ($CDCl_3$) δ 6.90 (m, 3H), 6.46 (m, 1H), 4.26 (t, J = 2.6, 1H), 1.95 (s, 3H), 1.46 (s, 2H), 1.15 (s, 2H), 1.07 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 159.8 (d, J = 247), 159.5 (d, J = 3.4), 132.4, 127.1 (d, J = 6), 117.9 (d, J = 1.2), 113.8 (d, J = 24.8), 75.4 (d, J = 2.6), 70.7, 38.5, 36.3, 33.1, 32.9, 30.5, 25.9 (d, J = 7.7); ms *m/e* 259.1708 (M^+, calcd for $C_{17}H_{18}D_2NF$, 259.1705).

14. *10b*: (14%) mp 88.5-89° (Et_2O); ^1H NMR ($CDCl_3$) δ 7.2-6.7 (m, 3H), 6.6 (br s, 1H), 4.65 (d, J = 2.6, 1H), 1.95 (s, 3H), 1.55 (s, 2H), 1.20 (s, 8H); ms *m/e* 259.1709 (M^+, calcd for $C_{17}H_{18}D_2NF$, 259.1705).

15. *1a*: (92%) bp 114-118°/0.15 torr; ^1H NMR ($CDCl_3$) δ 7.5-6.8 (m, 5H), 3.10 (d, J = 5.1, 2H), 2.90 (t, J = 7.0, 2H), 1.50 (t, J = 7.0, 2H), 1.00 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 160.7 (d, J = 254), 135.2 (d, J = 6.0), 134.2 (d, J = 1.7), 130.7 (d, J = 4.9), 129.1 (d, J = 1.7), 125.4 (d, J = 2.6), 124.9 (d, J = 2.6), 124.4 (d, J = 2.8), 124.1 (d, J = 11.5), 111.6 (d, J = 24.8), 42.7 (d, J = 13.3), 35.0 (d, J = 1.0), 29.5 (d, J = 3.8), 28.7, 28.3; ms *m/e* 228.1314 (M^+, calcd for $C_{16}H_{17}F$, 228.1314).

16. *11a*: (93%) bp 155-165°/0.4 torr; ^1H NMR ($CDCl_3$) δ 7.95-7.0 (m, 5H), 2.92 (t, J = 7.3, 2H), 2.82 (s, 2H), 1.61 (t, J = 7.3, 2H), 1.06 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 159.4 (d, J = 252), 134.7 (d, J = 4.3), 134.1 (d, J = 1.1), 131.0 (d, J = 2.7), 128.4 (d, J = 1.7), 125.6 (d, J = 10.3), 123.3 (d, J = 12.0), 118.8 (d, J = 3.4), 117.9 (d, J = 7.0), 108.3 (d, J = 21.7), 40.1, 35.5, 29.6, 28.75, 27.8; ms *m/e* 228.1323 (M^+, calcd for $C_{16}H_{17}F$, 228.1314.

17. *1b*: (97%) oil; ^1H NMR ($CDCl_3$) δ 7.75-6.8 (m, 5H), 3.10 (d, J = 5.1, 2H), 1.55 (s, 2H), 1.00 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 160.8 (d, J = 253), 135.2 (d, J = 5.1), 134.1 (d, J = 1.7), 130.8 (d, J = 5.5), 129.2 (d, J = 1.7), 125.4 (d, J = 2.9), 124.9 (d, J = 2.6), 124.5 (d, J = 3.8), 123.7 (d, J = 10.3), 111.6 (d, J = 23.4), 42.3 (d, J = 13.7), 34.6 (d, J = 1.1), 29.2 (d, J = 3.5), 28.5.

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