

5-Trifluoromethyl-1,7-phenanthroline

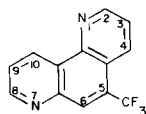
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While preparing a series of 7-aminoquinolones in order to determine the effect of kind and position of substituents on the fluorescence (1), the synthesis of 7-amino-4-methyl-5-trifluoromethyl-2-quinolone was attempted. Heating equimolar amounts of 3,5-diaminobenzotrifluoride and ethyl acetoacetate at 150-160° (reaction conditions similar to those employed by Woods and Fooladi (2) for making 7-amino-4-substituted-2-quinolones) yielded a red-brown gum, from which none of the desired product could be isolated. When this gum was heated in 96% sulfuric acid at 90-100° for 1 hour on the assumption that it was the acetoacetanilide (Knorr synthesis of carbostyrils (3)), the quinolone was still not formed. Rather, substantial amounts of 5-trifluoromethyl-1,7-phenanthroline (1) were recovered.

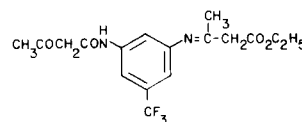


This structure is assigned on the basis of elemental analysis and mass spectrum, and an analysis of its nmr spectra. Table I summarizes the chemical shift and spin-coupling parameters which were observed. Comparable values have been reported for substituted quinolines by Brügel (4), and for 1,7-phenanthrolines by Mlochowski (5). The observed proton spin-coupling constants are typical of pyridine derivatives, in which the $J_{2,3}$ interaction is only 4.5 Hz compared with typical values of 8.0 Hz in phenyl rings. In addition, a weak five-bond coupling between protons 6 and 10 serves to identify the manner in which the corresponding rings are fused. The relative orientation of the first and second rings is clearly indicated by the ^{19}F nmr spectrum (pulsed FT, 94.1 MHz, deuteriochloroform) in which the stronger proton-fluorine spin-coupling interaction (1.9 Hz) is with H-4, and the weaker (0.8 Hz) coupling is with H-6. Even though the proton in the 4-position is five bonds removed from the fluorines and the 6-position proton is only four bonds away, the possibility of the fluorine atoms actually being in closer proximity to H-4 permits a stronger through-space spin-coupling with this proton.

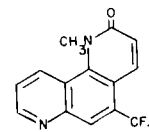
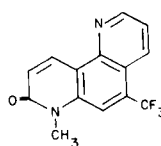
Proton-fluorine spin-coupling through five or more bonds is not generally observed unless the separation

between the nuclei is comparable to the sum of their van der Waal's radii (6).

The mechanism of formation of 1 is obscure, especially since the product does not contain the methyl groups one would expect if either the acetoacetanilide or the anil were intermediates.



The trifluoromethylphenanthroline was converted to the monoquaternary salt by reaction with methyl *p*-toluenesulfonate; the salt in turn was oxidized by basic ferricyanide to an *N*-methyl phenanthroline. Two isomers, 2 and 3, are possible:



The structural evidence provided by the ^1H nmr spectrum (100.1 MHz, swept mode, deuteriochloroform) indicated that the isolated oxidation product was 2:

(1) A relatively strong spin-coupling exists between the fluorine nuclei and the proton at position-4 in the

Table I

Nmr Parameters for Compounds 1 and 2

^1H Chemical Shifts, ppm		^1H Coupling Constants, Hz			
	1	2		1	2
H-2	9.13	8.95	$J_{2,3}$	4.39	4.3
H-3	7.67	7.47	$J_{2,4}$	1.83	1.8
H-4	8.58	8.39	$J_{3,4}$	8.54	8.5
H-6	8.51	7.90	$J_{6,10}$	0.73	--
H-8	9.09	--	$J_{8,9}$	4.39	--
H-9	7.74	6.92	$J_{8,10}$	1.77	--
H-10	9.59	9.04	$J_{9,10}$	8.36	9.6
CH ₃	--	3.85			
^{19}F Chemical Shifts, ppm		^{19}F - ^1H Coupling Constants, Hz			
CF ₃	60.87	60.5	$J_{4-\text{CF}_3}$	1.92	1.8
			$J_{6-\text{CF}_3}$	0.82	~ 0.5

(relative to tri-chlorofluoromethane)

ring adjacent to the CF_3 group. If this proton were in a pyridone ring (isomer **3**), it would show spin-coupling to only one other proton, but the fact that it shows two proton-proton splittings, $J_{3,4}$ and $J_{2,4}$, indicates that it is in a pyridine ring.

(2) Similarly, H-9 and H-10 appear as a simple AB quartet as expected in the pyridone ring system.

(3) The chemical shifts of H-2, -3, and -4 are in good agreement with the corresponding protons in the parent compound.

EXPERIMENTAL

3,5-Diaminobenzotrifluoride.

This compound was prepared in quantitative yield from 3,5-dinitrobenzotrifluoride (7).

The *sulfate* after one recrystallization from 95% ethanol and one from 2-propanol decomposed 249-256°.

Anal. Calcd. for $\text{C}_{14}\text{H}_{16}\text{F}_6\text{N}_4\text{O}_4\text{S}$: N, 12.44; S, 7.12. Found: N, 12.33; S, 7.68.

5-Trifluoromethyl-1,7-phenanthroline (1).

3,5-Diaminobenzotrifluoride (3.96 g., 0.0225 mole) and 2.92 g. (0.0225 mole) of ethyl acetoacetate were mixed and heated at 150-160° for 41 hours under an air condenser. (The results were similar with an 18-hour heating.) The dark amber, viscous mass was cooled, dissolved in 20 ml. of ethanol and chilled at -16° for several days. A trace of solid crystallized and was removed (although this material had a blue-green fluorescence in ethanol, its ^1H nmr spectrum in DMSO-d_6 was not in agreement with that expected for 7-amino-4-methyl-5-trifluoromethyl-2-quinolone). Evaporation of the alcoholic solution left 5.1 g. of red-brown gum which was dissolved in 16 ml. of 96% sulfuric acid, preheated to 85°; the latter solution was then heated in an oil bath at 90-100° for 1 hour. The cold acid solution was poured over 75 g. of ice; any solid which separated was removed and washed with cold water. With cooling, the acid solution was made basic with 25% aqueous sodium hydroxide; the solid was filtered and washed with 50 ml. of chloroform, which in turn was used to extract the aqueous phase. This operation was repeated three times. There was left 0.3 g. of yellow solid, m.p. 195-210°, not characterized further.

The combined chloroform extracts were dried, then evaporated to leave 2.9 g. of dark oil which soon crystallized. (Upon standing, hair-like needles, several inches long, slowly sublimed; m.p. 83-84°.) The crude product was extracted with three 20-ml. portions of

boiling cyclohexane, carefully separating each time from the insoluble black tar. Evaporation of the cyclohexane left 1.9 g. (34%) of pale yellow solid. Recrystallization from cyclohexane gave flat needles, m.p. 86-87°; ir (Mull), NH and CO stretching frequencies were absent.

Anal. Calcd. for $\text{C}_{13}\text{H}_7\text{F}_3\text{N}_2$: C, 62.90; H, 2.84; N, 11.29; F, 22.96; mol. wt. 248.2. Found: C, 62.77; H, 2.86; N, 11.28; F, 22.83; mol. wt. (mass spec.) 248.

7-Methyl-8-oxo-7,8-dihydro-5-trifluoromethyl-1,7-phenanthroline (2).

A solution of 2.1 g. of the previous compound and 1.6 g. of methyl *p*-toluenesulfonate in 20 ml. of dry acetonitrile was refluxed for 16 hours. The cooled solution was diluted with a large volume of ether to precipitate the salt; the supernatant was decanted and the red-brown gum triturated several times with more ether. The crude salt was dissolved in 150 ml. of water, filtered from some insoluble tar, and added with stirring during 1.5 hours to a solution of 2.4 g. of sodium hydroxide and 9.5 g. of potassium ferricyanide in 250 ml. of water at 15-20°. Stirring was continued for 6 hours at 25°. The gummy product was extracted into ether, washed twice with cold water, dried over sodium sulfate, and the solvent removed; 0.8 g. (34%) of brown solid plus gum. Recrystallization from cyclohexane gave a tan solid, from which most of this color could be removed by washing with very cold ether, m.p. 186-189°; ir (Mull): 1660 cm^{-1} (CO).

Anal. Calcd. for $\text{C}_{14}\text{H}_9\text{F}_3\text{N}_2\text{O}$: C, 60.43; H, 3.26; N, 10.07. Found: C, 60.49; H, 3.24; N, 10.39.

An attempt to methylate further this compound by refluxing overnight with methyl toluenesulfonate in acetonitrile was unsuccessful; starting compound was recovered.

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