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The Preparation and Infrared Spectra of *o*-, *m*-, and *p*-Fluoroanilides

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Ortho-, *meta*-, and *para*-fluoroanilides were prepared from the following carboxylic acids: acetic, 4-chlorobutanoic, isovaleric, isocaproic, lauric, benzoic, *p*-toluic, phenylacetic, 3-phenylpropionic, 4-phenylbutanoic, and *o*-methoxybenzoic acid. The melting points of the derivatives are given. It is difficult to purify fluoroanilides by recrystallization, and they are consequently not convenient to use for the purpose of identifying carboxylic acids.

Infrared spectra of the prepared fluoroanilides were recorded, using potassium bromide discs as well as solutions in acetonitrile. Strong absorption bands were observed which are assumed to result from the carbon-fluorine stretching vibrations; in acetonitrile the bands for the *o*-, *m*-, and *p*-compounds occurred at 1193 ± 4 cm^{-1}, 1144 ± 4 cm^{-1}, and 1210 ± 1 cm^{-1}, respectively.

Gas chromatographic data and infrared spectra (1000–1400 cm^{-1}) are given for *o*-, *m*-, and *p*-fluoroaniline.

For the identification of carboxylic acids anilides and substituted anilides, *e.g.* *p*-bromoanilides and *p*-toluidides, have often been used. It was therefore natural to investigate whether fluoroanilides had particular merits when the identification depends on infrared spectra as proposed in a previous article [1] and not — as is usually the case — on melting point determinations.

It was furthermore of interest to utilize the infrared spectra of fluoroanilides — if possible — to determine the location and intensity of the carbon-fluorine stretching vibrations in compounds of this type. Since the mass of the fluorine atom is low, and since we are considering a single-bond skeletal mode, considerable frequency alterations are observed as a result of interactions with neighbouring groups. But if the C—F group is placed in uniform surroundings, as is the case with regard to the three fluoroanilides, it should be possible to assign a certain frequency to it. There is not much information available in the literature as regards this problem, but it appears that the absorption band in question should be very strong [2] and expected in the range 1000— 1400 cm^{-1}.

PREPARATION OF FLUOROANILIDES

Fluoroanilides were prepared from eleven carboxylic acids. The yields varied from 5 to 50 %. Efforts were concentrated on the preparation of substances in the highest possible stage of purity.

The corrected melting points found are listed in Table 1 together with nitrogen analyses (by P. Hansen, The Microanalytical Laboratory, University of Copenhagen) and melting points of previously described fluoroanilides.

To ascertain that the three fluoroanilines were not contaminated by isomers the compounds were subjected to gas chromatography on a silicone elastomer column as well as on a poly(ethylene glycol succinate) column. On the former poor separations of the *ortho*- and *meta*-compounds were obtained, but on the polyester column a good separation of all three fluoroanilines was achieved within 6 min. The retention times, relative to aniline, on the polyester column at 194° were 0.78, 1.35, and 1.20 for *o*-, *m*-, and *p*-fluoroaniline, respectively. — The chromatography showed that the purity of the *o*- and *m*-compounds was satisfactory, as they contained less than 1 % of isomeric forms, whereas the *p*-compound contained about 7 % of *o*-fluoroaniline. Some of the *p*-fluoroanilides prepared were hydrolyzed by refluxing with strong hydrochloric acid for 16 h, and the fluoroaniline produced was subjected to gas chromatography. This showed that the *p*-fluoroanilides contained 2—3 % of the *o*-compounds. Additional purification of the products was considered unnecessary for the purpose of the spectroscopic examinations, but the melting points of the pure *p*-fluoroanilides are presumably slightly higher than the values given here.

Incidentally, it was later found that it is comparatively easy to prepare pure *p*-fluoroaniline from the commercial product by preparative gas chromatography.

The fluoroanilides were frequently obtained in the form of oils and — as shown in Table 1 — in some cases it proved impossible to obtain crystalline products. In many cases the melting points are between 50 and 100°C which makes recrystallization difficult. The *para*-compounds, which have the highest melting points gave just as much trouble as the *ortho*- and *meta*-compounds. Therefore none of the three fluoroanilide types are particularly useful derivatives for the purpose of identifying carboxylic acids. The infrared spectra of the fluoroanilides are quite suitable for the identification of the acids concerned, but they do not have any advantages over the spectra of *e.g.* non-substituted anilides, the preparation and purification of which generally involve fewer difficulties.[8]

THE INFRARED SPECTRA OF FLUOROANILIDES

The infrared spectra of the prepared derivatives were recorded by means of a grating spectrophotometer (Perkin-Elmer, model 421) in the range 550—4000 cm^{-1}, using the potassium bromide disc technique which has been described in detail in a previous article.[1] All *p*-compounds showed a strong absorption band in the range 1206—19 cm^{-1}. In the case of the *o*- and *m*-compounds it was more difficult to assign a probable location to the C—F stretching vibra-

Table 1. Melting points and analysis of the *o*-, *m*-, and *p*-fluoroanilides.

Acid	% N in anilide (calc.)	*o*-Fluoroanilide		*m*-Fluoroanilide		*p*-Fluoroanilide	
		% N	m.p.	% N	m.p.	% N	m.p.
Acetic			75.3—6.1°[a]		85.2—5.7°[b]		153.1—3.3°[c]
4-Chlorobutanoic	6.49	6.75	55.6—5.9°	—	oil	—[d]	56.0—6.2°
Isovaleric	7.18	[e]	68.7—8.9°	7.22	94.9—5.1°	7.10	110.6—1.0°
Isocaproic	6.69	6.85	63.7—3.9°	6.74	76.1—6.3°	6.95	80.7—1.0°
Lauric	4.77	4.96	64.8—5.0°	4.89	63.7—4.3°	—[d]	73.2—3.6°
Benzoic	6.51		113.6—3.7°[f]	6.44	143.7—3.8°		184.0—4.3°[g]
Phenylacetic	6.11	6.31	98.8—9.2°	6.07	105.5—5.7°	—[d]	136.2—6.5°
p-Toluic	6.11	5.78	116.4—7.2°	6.24	132.2—2.6°	6.10	182.9—3.4°
3-Phenylpropionic	5.76	5.81	102.8—3.0°	5.93	86.2—6.7°	—[d]	114.2—5.0°
4-Phenylbutanoic	5.44	—	oil	—	oil	5.49	86.8—7.2°
o-Methoxybenzoic	5.71	5.84	68.9—9.3°	5.86	65.3—5.7°	5.60	81.4—1.7°

[a] 78—79° [3]. [b] 86—87° [3]; 84° [4]. [c] 152—153° [3]. [d] Identity only determined from the IR-spectrum. [e] Anal.C 67.67; H 7.23. Found: C 67.65; H 7.28. [f] 113° [5].[g] 181° [6]; 182—184° [7].

Table 2. Position of the C—F stretching vibration of *o*-, *m*-, and *p*-fluoroanilides in potassium bromide and acetonitrile (given in cm^{-1}).

Acid	*o*-Fluoroanilide		*m*-Fluoroanilide		*p*-Fluoroanilide	
	KBr	CH_3CN	KBr	CH_3CN	KBr	CH_3CN
Acetic	1196	1196.5	1139	1144.5	1206	1210
4-Chlorobutanoic	1195	1194	—	—	1212	1210
Isovaleric	1202	1192.5	1137	1141.5	1213	1210
Isocaproic	1195	1193	1140	1141	1217	1211
Lauric	1200	1193.5	1142	1140.5	1219	1210
Benzoic	1199	1193	1147	1146.5	1213	1211
Phenylacetic	1197	1193.5	1134	1147	1214	1209
p-Toluic	1205	1189	1149	1146.5	1213	1211
3-Phenylpropionic	1188	1193	1148	1145	1218	1209
4-Phenylbutanoic	—	—	—	—	1216	1211
o-Methoxybenzoic	1193	1193.5	1148	1148	1211	1210.5

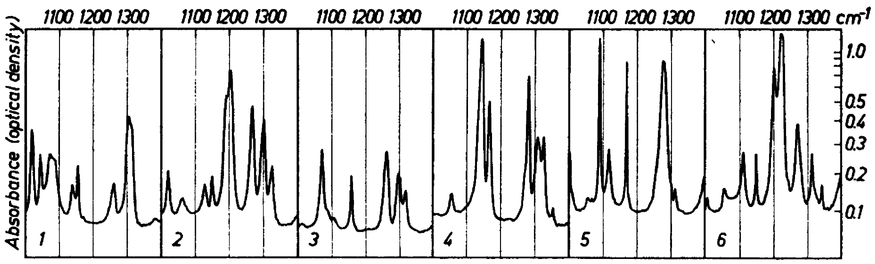

Fig. 1. IR-Spectra of chloroanilines and fluoroanilines. 1, *o*-Chloroaniline. 2, *o*-Fluoroaniline. 3, *m*-Chloroaniline. 4, *m*-Fluoroaniline. 5, *p*-Chloroaniline (in CS_2). 6, *p*-Fluoroaniline (in CS_2).

tion as the region of interest is a pronounced finger-print region. For reasons of space it is impossible to include the spectra of the fluoroanilides here; see Ref. 8.

Since isotopic methods for the identification of the desired vibration could not be used in this case, spectra were recorded of a number of analogous chlorine compounds. The spectra of the three chloroanilines, *ortho*-, *meta*-, and *para*, as well as those of the corresponding fluorine compounds in the range 1000—1400 cm^{-1} are recorded in Fig. 1 (correction: $+3$ cm^{-1} at 1000 cm^{-1}; $+2$ cm^{-1} at 1400 cm^{-1}); the *ortho*- and *meta*-compounds are in liquid form, while the *para*-compounds are dissolved in carbon disulfide. A comparison was also made between the three chloroanilides and the three fluoroanilides of acetic acid.

This procedure showed that it would be reasonable to look for the C—F absorption slightly above 1200 cm^{-1} in the *para*-compounds, near 1200 cm^{-1} in the *ortho*-compounds, and about 50 cm^{-1} further down in the *meta*-compounds. The various types of fluoroanilides were found to exhibit absorption bands at these wave numbers. The exact location of the bands appears in Table 2.

Since the range of absorption values observed using potassium bromide discs may be up to ten times that observed using a solvent, it would be of interest to try the latter method. Solvents suitable for spectral studies are carbon disulfide, benzene, and acetonitrile. *Para*-fluoroanilides are insoluble in the former two, but in acetonitrile they are soluble to the extent of 0.05 M. The *o*-, *m*-, and *p*-fluoroanilides consequently were examined in acetonitrile. The results obtained appear in Table 2.

In summary it may be said that the *o*-, *m*-, and *p*-fluoroanilides in acetonitrile absorb at 1193 ± 4 cm^{-1}, 1144 ± 4 cm^{-1}, and 1210 ± 1 cm^{-1}, respectively. The above absorption bands are assumed to refer to carbon-fluorine stretching vibrations.

EXPERIMENTAL

Preparation of derivatives. The carboxylic acids used were supplied by "Fluka" (puriss. or purum); the fluoroanilines were also from this firm (purum). Five mmoles of fluoroaniline were dissolved in about 4 ml of pyridine and the solution was cooled in an ice bath. To the solution was added 5 mmoles of acid chloride which was prepared from the carboxylic acid by refluxing with thionyl chloride and subsequent distillation through a 5 cm packed column. The reaction mixture was allowed to stand for one hour or more, and during this time pyridine hydrochloride precipitated. The pyridine was removed by extraction with dilute hydrochloric acid, causing the anilide to separate — usually in the form of an oil. The products were crystallized and recrystallized two or three times from dilute ethanol and dried *in vacuo* at 45°C.

In a few cases it proved impossible to crystallize the prepared substance. The oil was then dissolved in ether, washed with dilute hydrochloric acid and with water. The ether phase was dried over anhydrous magnesium sulfate, and the ether was evaporated. In three cases the resulting products were oils which refused to crystallize. These oils were not used for the spectroscopic examination.

Gas chromatographic examinations. The analytical chromatograph used was a Perkin-Elmer Fraktometer Model 116 E with katharometer detector. The columns were copper tubes (2 m in length) with an inner diameter of 4 mm, packed with 20 % of stationary phase on Celite support. A silicone elastomer (E 301) was used as non-polar stationary phase and a poly(ethylene glycol succinate) prepared according to Ref. 9 was used as a polar stationary phase. In the latter case the column temperature was 194°C, the carrier gas was helium (flow rate: 66 ml/min, calculated at 21°C), and the sample size was 0.5 μl.

The preparative chromatograph used was an Autoprep model A 700 equipped with katharometer detector. The column was a 6 m copper tube (diameter 10 mm) with the same polar stationary phase as the one described above. Temperature programming was used (maximum 185°C); hydrogen was used as carrier gas, and the sample size was about 300 μl.

Spectroscopic examinations. The spectra were recorded using a Perkin-Elmer Infracord model 137 and Perkin-Elmer Spectrophotometers models 21 and 421. The spectra reproduced in the present article were recorded using the latter instrument. The adjustment was as follows: slit program, 1000; gain, 2.8; attenuator speed, 1100; scan rate, 100 cm^{-1}/min; automatic suppression, 1; source current, 0.35 A.

The solutions of *p*-fluoroanilides in acetonitrile (0.05 M) were examined in the range 1130—1310 cm^{-1} (Perkin-Elmer Spectrophotometer model 21 with NaCl prism; scan rate: 40 cm^{-1}/min; cuvette: 0.11 mm). The *ortho-* and *meta*-fluoroanilides were examined in the range 1100—1300 cm^{-1} (Perkin-Elmer Grating Spectrophotometer model 421; scan rate: 60 cm^{-1}/min; concentration: 0.10 M; cuvette: 0.45 mm). The acetonitrile was previously dried over calcium hydride.[10]

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