OTHER AVAILABLE STUDY SUMMARIES FOR N-EtFOSE ALCOHOL

TEST SUBSTANCE

Identity: N-ethylperfluorooctane sulfonamidoethanol; may also be referred to as N-EtFOSE Alcohol or FM-3422. (1-Octanesulfonamide, N-ethyl-1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-N-(2-hydroxyethyl)-, CAS # 1691-99-2)

Remarks: Material is an off-white, waxy solid of uncharacterized purity.

The attached are overviews created from 1983 and before. Robust summaries are being submitted for many of the individual studies covered in these reviews. Others have not been summarized due to the fact new studies exist that supercede these, the original study cannot be found, or they are being repeated.

OTHER

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TECHNICAL REPORT SUMMARY

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To: D. L. Bacon	
Author(s): A. Mendel	Employee Number(s): 43939
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Progress Report

REPORT ABSTRACT: (200-250 words) This abstract information is distributed by the Technical Communications Center to alert 3M'ers to Company R&D. It is Company confidential material.

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INTRODUCTION

This portion of the report was concerned with the analytical aspects of FM 3422. It was quantitated by gas chromatography (GC) using electron capture detection. Before analyses could be conducted, however, many variables had to be resolved and some experimental observations needed clarification. These are discussed below and detailed in the experimental section.

DISCUSSION AND RESULTS

The solvent of choice for extraction of FM 3422 from water was ethyl acetate, since recent literature studies have indicated ethyl acetate to be superior in general to ether. The recovery of FM 3422 by ester extraction was quantitative from water and from water to which salt (salt-out technique) was added respectively. FM 3422 can be quantitated up to at least 125 ppm (region of linearity; see Figure 1). Solutions of FM 3422 above this concentration (e.g., 250 ppm), gave responses beyond the integrator's range. The limit of detection was found to be 0.05 ppm which represents 0.25 ng absolute. Naturally, solutions of FM 3422 higher or lower in concentration can be diluted or concentrated respectively for analysis in the range of linearity.

The gas chromatographic pattern for FM 3422 was examined briefly and is shown in Figure 2. While the Carbowax 20M column used in this study resolves the product into three peaks, other columns (e.g., OV101, SE52, W982) may not all resolve FM 3422 into three components (1).

The solubility of FM 3422 in water was determined to be 0.05 ppm using a recently designed apparatus for continuously saturating water with hydrophobic organic chemicals (2).

Concentration of FM 3422 from water (rotary evaporator) gave low recoveries. Concentrations can be conducted successfully from organic solvents provided water is absent or that water has been removed previously by forming an azeotrope. This same observation was noted independently for another fluorine-containing compound(3).

It was also necessary to determine the kind of containers that could be used to hold FM 3422 containing samples which would be generated in soil and aquatic testing studies. Plastics such as polyethylene and polycarbonate were unsatisfactory, while glass was satisfactory at the 0.05 ppm concentration of FM 3422 in water. These results are shown in Table IV.

Stability of FM 3422 to alkali was also studied. In 20% alcoholic potassium hydroxide at 50°, thirty percent of the FM 3422 hydrolyzed after seven hours and after twenty-four hours, only eight percent FM 3422 remained (see Table V). TLC and IR studies of these products showed that FM 3422 was converted to FC-95 as expected.

The ability of sludge (bacteria) to biodegrade FM 3422 was also investigated. If FM 3422 biodegrades, theoretically, it might degrade to perfluorooctane sulfonamide and/or to FC-128 (N-perfluorooctanesulfonyl-N-ethylglycine or a salt thereof). It was necessary to show that neither of these materials interfered with the GC analysis of FM 3422. This was the case.

Radioactive FM 3422 (labeled in the R_f group) was also used in biodegradation studies described elsewhere in this report. Preliminary TLC (thin-layer chromatography) and subsequent autoradiography revealed the sample to be impure. Accordingly, it was purified by a combination of preparative TLC and column adsorption chromatography to give FM 3422-^{14}C whose autoradiogram showed one spot only.

Die-away studies to measure the biodegradation, if any, of FM 3422 are discussed in a different section of this report. In this section of the report, however, the ethyl acetate extracts from these die-away studies were routinely examined by TLC, which showed a second spot in addition to expected FM 3422. Scaleup (preparative TLC) afforded enough of this second component for IR, mass spectroscopy (MS) and GC studies. IR indicated a fluorocarbon species complexed possibly with a nitrogen-containing compound. MS showed FM 3422 plus carbon dioxide and ammonia and GC revealed only FM 3422. This second component was not further characterized.

Analytical methods to quantify FC-95 directly are not known. Some scouting time was devoted to try to derivatize FC-95 so that the derivative could be analyzed. Summarized below are methods which have failed.

Sulfonates are known to form complexes with benzyl isothiourea hydrochloride by displacement of the chloride with the sulfonate anion. Accordingly, the crystalline trifluoromethanesulfonate of the UV-absorbing benzyl isothiourea was synthesized (41433-49). Unfortunately, this complex was not stable in aqueous solution (sulfide odors) and it did not lend itself to analysis by HPLC using UV detection, or by fluorescence (very weak fluorescence).

FC-95 could not be caused to react with 2,4-dinitrofluorobenzene (44191-25) nor could the phenyl ester be made by esterification with phenol-boric acid-sulfuric acid (44191-33). FC-95 could not be converted to the sulfonyl chloride using phosphorus oxytrichloride in pyridine (44191-35).

Perfluorooctane sulfonic acid could not be caused to condense with aniline in the presence of dicyclohexyl carbodiimide, a potent water scavenger (44191-36, -38).

EXPERIMENTAL (4)

This work is recorded in notebooks 41433, 41947, 44191, and 46269, and filed under Environmental Laboratory Request 3645.

FM 3422 (labeled E788, CG745-2 and received from D. Ricker, Commercial Chemicals) was off color and accordingly was sublimed (60°/<1 mm Hg) to give white solid which was used in subsequent work unless indicated otherwise. All solvents used were reagent grade. Thin-layer chromatography was performed on silica gel coated on glass plates (E. Merck) and plate visualization was performed according to the "Wong" technique, described in notebook 44191-16, -17-20, -21, -22.

FM 3422 was gas-chromatographed using the HP Model 5713 GC with the Model 3380A integrator-printer. GC conditions were: Carbowax 20M column, 6% loading on Q support (column 0.18m x 3.18mm; 6 foot x 1/8 inch O.D.): injection port, 200°C; detector, 300°C; column isothermal, 170°; argon/methane flow rate about 40 ml/min.

GAS CHROMATOGRAPHY OF FM 3422

Comparison of Nonsublimed with Sublimed FM 3422 (41947-26)

A 10 ppm solution in 1-octanol of FM 3422, crude and sublimed respectively, was gas chromatographed. The area percents were compared and the sublimed material was shown to be purer, i.e., the nonsublimed material was 9.94 ppm, based on the sublimed material being 10 ppm. GC program: initial temperature, 170°; final temperature, 210° at 8°/min.

Determination of Linear Range of Detection of FM 3422 by EC/GC

A standard solution of 1000 ppm of FM 3422 was diluted to give 250-, 125-, 100-, 50-, 25-, 20-, and 10- ppm solutions. Five microliter aliquots were then injected into the GC and the RESPONSE (area) was recorded. The data are given in TABLE I and illustrated in Figure 1.

TABLE I

DETECTION LIMITS OF FM 3422

Standard Solution (ppm)	RESPONSE (Area)	Area x 10^6
1000	*	
250	*	
125	18,534,286	18.5
100	14,741,274	14.7
50	7,502,012	7.5
25	3,819,671	3.8
20	3,138,201	3.1
10	1,598,396	1.6

*Beyond signal response of integrator.

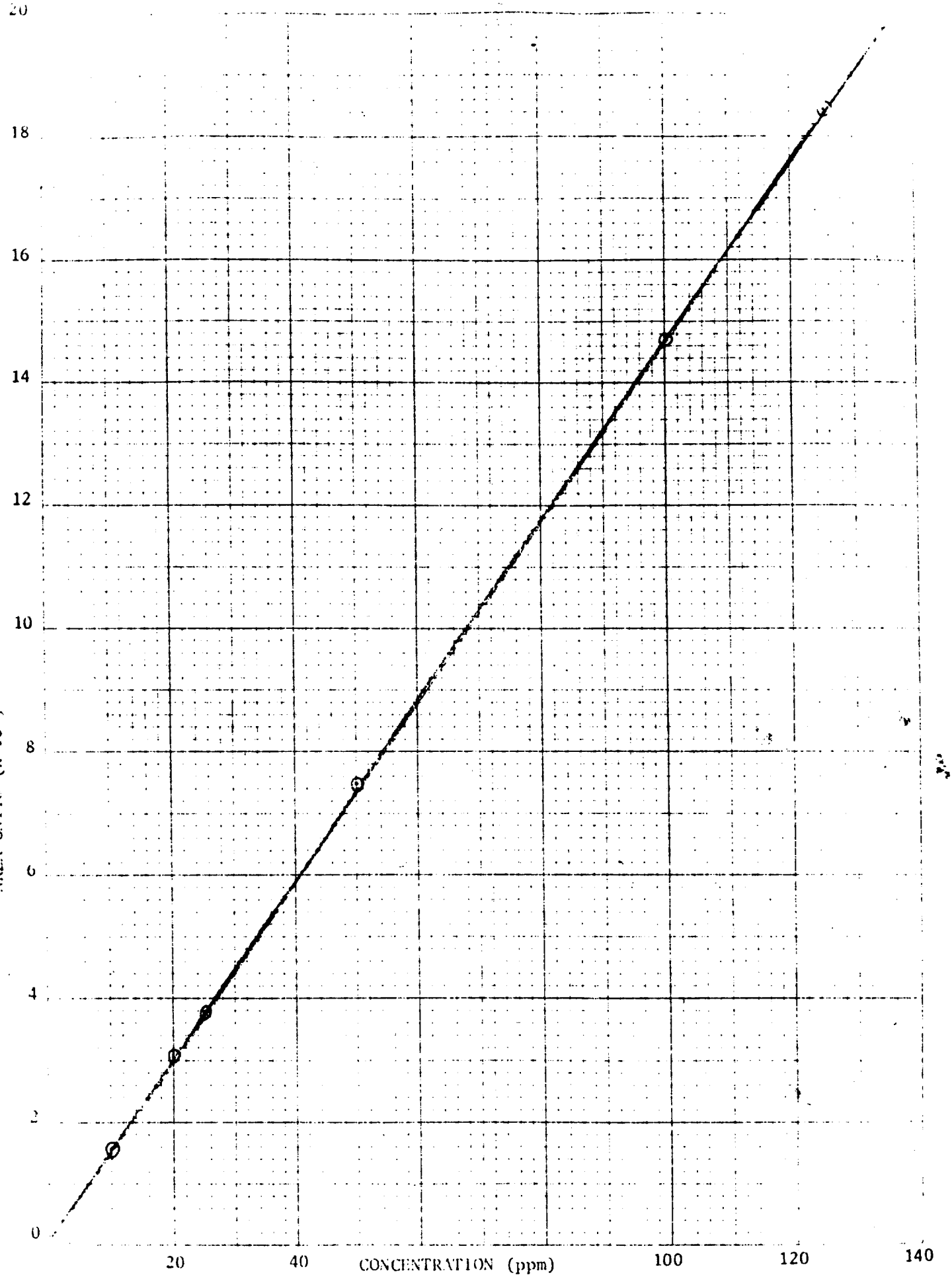

Figure 1 - Range of Detection of FM 3422

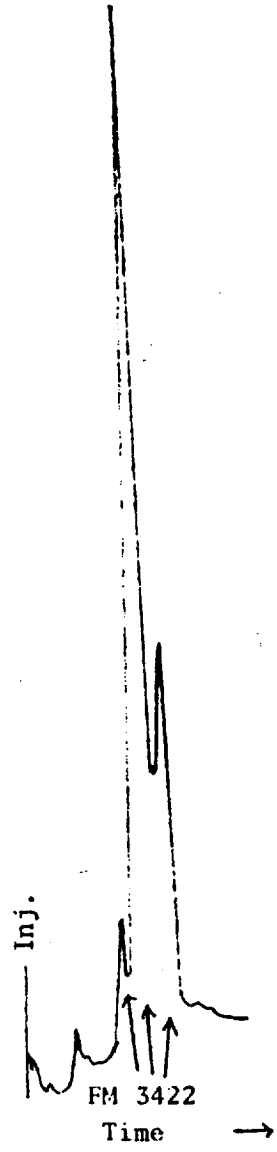

Figure 2

GAS CHROMATOGRAPHIC
PATTERN OF FM 3422

EXPERIMENTS ON THE RECOVERY OF FM 3422

A. Recovery of FM 3422 from Ethyl Acetate: (41947-42)

Ethyl acetate (ca. 1 ℓ) was stored over anhydrous sodium sulfate and used as needed. A 500 ppm standard of FM 3422 in ethyl acetate was prepared by weighing 0.050 g. of FM 3422 and diluting it to the mark (100 ml) in a volumetric flask. Similarly, a 25 ppm solution was prepared by pipetting 5 ml of the above solution into a 100 ml volumetric flask and diluting it to the mark.

To make sure that the FM 3422 in dry ethyl acetate was not lost by evaporation, 10 ml of the 25 ppm standard was pipetted into a 10 ml volumetric flask. A slow stream of nitrogen was used to evaporate the ethyl acetate and an aliquot was gas chromatographed. Comparison of GC results with the original 25 ppm solution showed a recovery of 99.99 percent.

B. Recovery of FM 3422 from Ethyl Acetate-Water and from Ethyl Acetate-Salt Water (41947-45)

It was anticipated that in future experiments involving the preferential extraction of FM 3422 from aqueous media and from media containing biological components, e.g., fish, sludge, soil, and the like, it might become necessary to use saturated sodium chloride ("salt-out" technique) for two reasons: to increase transfer of FM 3422 from aqueous media into ethyl acetate; to help prevent the potential emulsions which ethyl acetate appears to form with many biological ingredients.

Accordingly, 25 ml of 25 ppm FM 3422 in ethyl acetate was pipetted into 25 ml of water, and into 25 ml of water containing 5 ml of saturated sodium chloride, respectively. Each mixture was shaken in a separatory funnel (fifty inversions respectively) and the respective ethyl acetate layer was analyzed by gas chromatography. The results are shown in TABLE II.

TABLE II

RECOVERY OF FM 3422

Experiment	Description	Vol. EtOAc Recovered (ml)	GC INTEGRATOR RESPONSE (AREA)	FM 3422 (ppm)
1	25 ppm FM 3422 (in EtOAc)	Standard Solution (25 ml)	4,337,111	25
2	25 ml FM 3422 + 25 ml Water	23.5	4,363,283	25.15
3	25 ml FM 3422 + 25 ml water + 5 ml Sat'd NaCl	24.5	4,325,514	24.93

Note that the addition of salt water allowed approximately 1 ml more of ethyl acetate to be separated compared to water, i.e., the FM 3422 is now in 24.5 ml of ethyl acetate whereas before (not using salt-out techniques) the FM 3422 was in 23.5 ml of ethyl acetate. This explains why the result in experiment 3 is slightly lower than that in experiment 2. Nevertheless, no loss is noted using the salt-out technique. A volume correction factor may be needed, however.

C. Recovery of FM 3422 from Water (41947-38, 39, 40)

During experiments to determine the distribution coefficient of FM 3422 between 1-octanol and water, the water phase was separated and quantitatively transferred to a flask. It was rotary evaporated (50°/water aspirator pressure, 20 mm Hg) to remove water. The residue was taken up in a known volume of 1-octanol and an aliquot was gas chromatographed. Results were low indicating that FM 3422 was lost by sublimation and/or by steam distillation.

Accordingly, the all glass-to-teflon lining in the rotary evaporator was leached with a small amount of methanol. A small portion of this leaching was gas chromatographed and the results showed the presence of FM 3422.

Finally, the water condensate, collected during the rotary stripping, was extracted with a small amount of 1-octanol. Gas chromatography of the separated 1-octanol extract again showed the presence of FM 3422. It appears therefore that unless all the water is removed from FM 3422-water mixtures by azetropic distillation or by a drying agent, results will be low in FM 3422. Consultation with other workers (3) indicated that similar problems were observed with other fluorine-containing compounds. Removal of water by azetropic distillation or by evaporation with an excess of solvent, such as ethyl acetate, solved the recovery problem.

DETERMINATION OF SOLUBILITY OF FM 3422 IN WATER

The Veith-Comstock technique (2) was used for this experiment.

Glass beads (ca. 300 g, 3 mm. in diameter) were added to a solution of 100 mg of FM 3422 in about 500 ml of acetone. The solvent was allowed to evaporate, thus depositing the fluorochemical on the beads. The beads were packed into a column (ca. 25 mm. dia. x 450 mm.) whose end was prepacked with a 20 mm. layer of silanized glass wool, followed by a 20 mm. layer of sand.

The top of the column, packed with a 20 mm. layer of silanized glass wool, was attached by Mayon(R) tubing to the top inlet of a 2-liter bottle filled with water. The bottom of the column was attached by tubing through a peristaltic pump, to the bottom outlet of the 2-liter flask. The water was circulated upwards by the pump through the column for about two weeks. By volumetric pipet, one hundred milliliters of saturated liquid was withdrawn, diluted with 10 ml of aqueous saturated salt, and extracted 3 times with a total of 21 ml of ethyl acetate. The combined extract was diluted to 25 ml (volumetric flask). An aliquot was gas-chromatographed. This experiment was performed eight times. The results are reported in TABLE III.

TABLE III

SOLUBILITY OF FM 3422 IN WATER*

Experiment No.	ppm FM 3422
1	0.050
2	0.045
3	0.061
4	0.042
5	0.040
6	0.062
7	0.050
8	0.048
Mean	0.04975

*Temp. = 20° C.
Mean = 0.05 ppm; Range = 0.04-0.062 ppm; Std. Dev. = 0.0084

RECOVERY STUDIES OF AQUEOUS FM 3422 SOLUTIONS IN VARIOUS CONTAINERS (44191-42)

At the low solubility level of FM 3422 in water (0.05 ppm), the possibility was considered of incomplete recoveries due to sorption of FM 3422 by plastics and/or glass. Accordingly, the following study was made:

One hundred milliliters on 0.05 ppm FM 3422 in water (by the Veith-Comstock technique (2) as described earlier) was added to an amber glass - and to a polyethylene - container, respectively. The containers were capped and allowed to stand in the laboratory for one week. The respective contents of the containers were transferred quantitatively to a separatory funnel. The container was rinsed with two milliliters of water only. To the funnel was added 10 ml of saturated aqueous sodium chloride and 19 ml of ethyl acetate. The contents were extracted and the organic extract was transferred quantitatively to a 25 ml volumetric flask. The aqueous phase was re-extracted twice with 5 ml of ethyl acetate. The combined organic extract was diluted to the mark (ethyl acetate) and then gas chromatographed.

To each of the now empty containers used above was added (pipet) 1 ml of methanol. The respective container was sealed, rinsed with this 1 ml of methanol, and an aliquot was gas chromatographed. Experiments were performed in duplicate and the results are indicated in TABLE IV.

TABLE IV

CONTAINER STUDIES WITH FM 3422

Experiment No.	Container	FM 3422 in 100 ml water (µg)	Total FM 3422 in Container: Methanol Rinse (µg)	Total FM 3422 Recovered* (µg)
1	Glass	5.8	0.04	5.8
2	Glass	4.6	0.19	4.8
3	Polyethylene	<3	1.88	<4.9
4	Polyethylene	<3	1.15	<4.2

*Solubility of FM 3422 in water determined as 0.05 ppm or 5 µg/100 ml.

It appears therefore that glass containers may be used but polyethylene must not be used to store solutions at these concentrations; otherwise, severe losses of material are possible.

ALKALINE HYDROLYSIS OF FM 3422

The stability or instability of FM 3422 toward base was apparently studied several years ago under aqueous conditions. Because this material steam distills and because of its lack of water solubility, the stability of FM 3422 toward base in alcohol was studied in the present work as follows:

Six samples each of a 25 ml solution of 362 ppm of FM 3422 in 20% alcoholic potassium hydroxide was kept in a 50° oil bath for varying lengths of time. A sample was taken after 0.5-, 1-, 7- and 24- hrs., and neutralized with concentrated nitric acid to the phenolphthalein indicator end point; this allows precipitation of potassium nitrate and minimizes water which tends to interfere with the EC/GC analyses. GC analysis of the alcohol solution gave the results in TABLE V.

TABLE V

HYDROLYSIS STUDIES OF FM 3422

Time (in hrs.)	0	0.5	1	7	24
3422 (in ppm)	362	380	362	256	28

A sixth sample was allowed to remain in the oil bath for 50 hrs/50° C. It was neutralized as above and filtered to remove solids. The filtrate was concentrated to dryness and the residue was analyzed by TLC, and IR and NMR (Req. C46749). A comparison of the R_f value of the residue with that of authentic FC-95 showed they were the same. IR and NMR studies confirmed that the FM 3422 was broken down to FC-95 under these conditions.

GAS CHROMATOGRAPHY OF PERFLUOROOCTANE SULFONAMIDE AND FC-128 (41947-48)

The retention time of FM 3422 was 2.8 minutes isothermal at 160° using the conditions described earlier. To determine whether the above sulfonamide and FC-128 posed as an interference to FM 3422, dilute solutions (in methanol) were made for these two materials. The sulfonamide could be chromatographed isothermally at 200° (about 3.3 minutes retention) while FC-128 could not be chromatographed. Therefore, there is no interference problem.

THIN-LAYER CHROMATOGRAPHY STUDIES OF FM 3422

Radiolabeled FM 3422 (5) was examined by TLC for purity. About ten micrograms of sample was spotted on a plate which was then developed in ethyl acetate. The plate was exposed to an X-ray film for about one week and the film was developed. It revealed that the FM 3422-^{14}C had three impurities, two components of greater R_f and one component remaining at the origin. Accordingly, the entire radioactive material, nearly 1.7 g, was column chromatographed on silica gel by chloroform elution. About forty 15 ml fractions were collected and monitored by TLC-autoradiography. Pure material was combined for future studies. Impure FM 3422-^{14}C. was combined and rechromatographed as above until essentially all of the material was rendered pure (6).

The visualization technique for nonradioactive fluorochemicals was described in notebook 44191-16-17, 20-22, and in TAG (7). Briefly, the developed, dry TLC plate is sprayed with chloroplatinic acid according to Wong (8). The dry plate is then carefully sprayed with 1% aqueous starch solution until the plate is wet but not runny or soaked. The wet plate is then placed in an iodine chamber for about two minutes and examined. Fluorochemicals (and as it turns out, most chemical in general) are visualized as a white or white-to-pink spot against a dark purple background. This contrasting dark purple color will fade with time so that after about 1 hour, a faint pink-to-white spot will be noted against a light violet background. This color, however, remains stable for months and supersedes any visualization reagents to date. Between 0.1 and 1 microgram absolute of FM 3422 has been detected routinely.

TLC STUDIES ON DIE-AWAY EXPERIMENTS (44191-27-32)

Die-away studies on mixtures of FM 3422 with activated sludge-Alcanox$^{(R)}$ (commercial surfactant) - YM broth-buffer-mixtures are detailed in another report (E. A. Reiner). The final experiments were quantitatively extracted with ethyl acetate for further examination by GC for FM 3422 and by TLC evaluation for any materials not capable of being detected by GC (i.e., non-volatile materials).

Ethyl acetate extracts of seven samples from die-away experiments (labeled 18AT; 3422 #2; 61AT, 3422 Day 0; 61ATC, #1; 61AT, 3422 #2; 25 SIAT, 3422 final; 34 SAT, 3422 final; 25 SIAT, 3422 Day 0 and a reference composite containing known FM 3422 and known FC-95) were spotted on one TLC plate. It was confirmed by earlier GC studies that those samples labeled day 0 had about 500-600 ppm of FM 3422, while those samples that had been carried through biodegradation studies had considerably less (one-fifth or less) FM 3422 remaining. The TLC plate was developed (ethyl acetate) and visualized in the usual manner. Extracts from samples 61ATC #1, 61AT, 3422 #2, and 25 SIAT, 3422 final, had small amounts of FM 3422, plus a new component whose R_f value (0.45) was just below that of FM 3422 (0.52). Accordingly, these last three extracts were combined and twice preparatively thin-layer chromatographed using five developments in chloroform each to effect a complete separation between FM 3422 and the desired new material. Work up of the desired preparative layer by acetone extraction afforded about 5 mg of a semisolid which was found to be less readily soluble in methanol than FM 3422. This semisolid was examined by IR (CRL Req. C47334, C47442) which suggested a complex between FM 3422 and an unknown. Mass spectroscopy (Req. C 47585) indicated FM 3422, plus ammonia, plus carbon dioxide. GC of this complex indicated FM 3422 only. Two nonrelated materials isolated in the course of this preparative TLC study were glycerin and fatty acid, both of which probably arose from biodegradation of the YM broth, an added nutrient for the sludge.

Based on IR studies, a possible candidate as the complexing agent with FM 3422 was urea (9). Recall that the complex mass spectrum indicated FM 3422, ammonia, and carbon dioxide. Accordingly, a mixture of urea and FM 3422 in methanol and in acetonitrile was reflexed for several hours and examined by IR which suggested a physical mixture of the two components, respectively (44191-41). This complex was not further characterized.

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(3) C. D. Green (Commercial Chemicals) communication with A. Mendel.

(4) Much of the experimental work was performed by G. Vraspir and C. Schrandt.

(5) Received from D. McCown (Commercial Chemicals).

(6) Autoradiography and X-ray film development was performed in the Agrichemicals Laboratories (Commercial Chemical). The help of Agrichem personnel is acknowledged.

(7) 3M Technical Awareness Gazette (TAG), 6, No. 5, 3231 (1977).

(8) F. F. Wong, J. Chromatography, 59, 448 (1971).

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