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Journal of Fluorine Chemistry 100 (1999) 207–216

JOURNAL OF FLUORINE CHEMISTRY

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Adventures of a fluorine chemist at DuPont

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Abstract

Fluorine chemist William J. Middleton (Bill) describes his career at DuPont, including some of his discoveries, a few anecdotes and a little of his poetry.

Keywords: Tetracyanoethylene (TCNE); Fluoroacetylene; Thiocarbonyl fluoride; Hexafluorothioacetone; Hexafluoroacetone; Midaflur; Hexafluoroisopropanol (HFIP); Diethylaminosulfur trifluoride (DAST); Tris(dimethylamino)sulfonium difluorotrimethylsilicate (TASF); Periodic table; Perfluoropinacol; Perfluoroalkyl effect

1. Introduction

1.1. My first introduction to fluorine chemistry

I have been fascinated by chemistry ever since I was in grade school and discovered that vinegar reacts with soda, but my fascination with fluorine chemistry didn't develop until I was assigned a project to prepare the then unknown difluoroacetylene while working at DuPont in their Central Research Department in Wilmington, Delaware. Actually, my first brief contact with fluorine chemistry (if you can call it that) was a total disaster. In fact, I didn't even know it was a contact with fluorine chemistry at the time. It occurred when I was taking my preliminary exams for my Ph.D. degree at the University of Illinois. These 'prelims' were given to prospective Ph.D. students before their final exam and thesis defence to determine if they had the necessary broad knowledge of chemistry for recipients of this degree. The question was, 'Explain why Teflon® is chemically inert'. I had to leave the answer blank since I didn't have any idea what Teflon® was. I couldn't even guess that it was a fluoropolymer. Not a very auspicious start for someone who one day would aspire to be a fluorine chemist!

1.2. Before DuPont

To start at the beginning, I was born in Amarillo, TX, on 9 April, 1927. I spent the first 20 years or so of my life in Texas as a Texan, and the rest of my life trying to live up to (or may be live down) the typical reputation that most Texans seem to have. I received my public school education in various towns in north and west Texas, ending up in Dallas. After a brief stint in the US Navy during World War II, I continued my education at North Texas State University[1] in Denton, receiving my BS degree in 1948 and MS degree a year later. More importantly, I met my wife Millie there, and we married in 1948. After more than 50 years of marriage, I still think Millie is the best thing that ever came out of the state of Oklahoma.

With the help of Millie's earning power, I continued my education at the University of Illinois in Urbana, IL, where I studied for my doctoral degree under Nelson Leonard (my thesis was on Reductive Cyclization). I was still a few years away from my first real contact with fluorine chemistry.

1.3. On to DuPont

I was overjoyed to receive an invitation to work in DuPont's Central Research Department[2] at the Experimental Station in Wilmington, Delaware. At that time (1952), this department was regarded by many as the home of the best group of industrial chemists in the US doing fundamental research in organic chemistry, so I accepted this offer with great pleasure. Ironically, DuPont was the manufacturer of Teflon®, the material that had caused me grief during my 'prelims'.

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[1] When I enrolled, it was called North Texas State Teachers College; before I received my MS degree, the 'Teachers' part of the name was dropped; and now 'College' has been changed to 'University'.

[2] It was called the Chemical Department when I joined DuPont. Later the name was changed to the Central Research Department, which eventually merged with the Development Department.

0022-1139/99/$ – see front matter
PII: S0022-1139(99)00128-1

My first project at DuPont had nothing to do with fluorine: shortly before I arrived at DuPont, a chemist named Dick Heckert had prepared tetracyanoethylene (TCNE), and when I turned up, both he and I were assigned the task of exploring the chemistry of this new, unique compound. Dick and I entered a friendly competition to see who could do the most interesting chemistry with TCNE, and I thought that I was doing very well on that score. Unfortunately, I can't feel too smug about that now, for Dick later became president of DuPont, and I remained at the bench for my entire career at the company.

Although the TCNE project was a scientific success (our work was even featured twice in *C & E News* stories, including once as the cover story [1,31]), it was a commercial flop, so the stage was set for my induction into the world of Fluorine Chemistry. In fact, I was thrust into the area almost against my will.

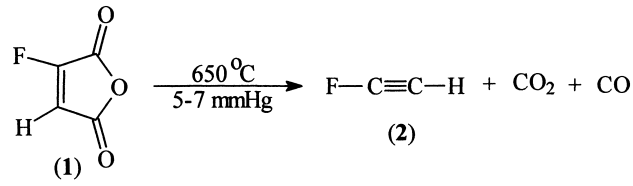
2. Fluoroacetylene

In 1955, a considerable amount of fluorine chemistry was being done at DuPont because of the commercial success associated with the company's Freons® and Teflon®; but in many ways we were very naive about some of the properties of fluorine and its compounds. There was a theory that the introduction of fluorine would always stabilize organic compounds owing to the extreme strengths of C–F bonds. So even though chloro- and dichloro-acetylene were known to be dangerously explosive, it was reasoned that fluoro- and difluoro-acetylene would be very stable and safe to handle. All this was theory, of course, because these compounds were unknown. In fact, there were no known compounds that contained fluorine bonded to an sp-hybridized carbon atom.

Although things were still going well for me in my work with TCNE, I was taken off that project and assigned a new task — to prepare fluoro- and difluoro-acetylene. This was quite a shock for me. In my previous project, I had been working with solids that in general were high-melting, crystalline compounds. Now I would be working with gases, a subject that was totally unfamiliar to me. But I received a much bigger shock a few weeks later when I was finally able to prepare the first sample of fluoroacetylene.

My first attempts to prepare the fluoroacetylenes by conventional dehalogenation and dehydrohalogenation reactions were unsuccessful, but a less conventional method yielded good results: quantitative yields of fluoroacetylene (**2**) were obtained by vacuum pyrolysis of fluoromaleic anhydride (**1**, Scheme 1) [2]. We believe that similar vacuum pyrolysis of difluoromaleic anhydride yielded difluoroacetylene, but this proved to be too unstable or reactive for us to isolate and conclusively identify.

Just a few months earlier, we had acquired an exciting new analytical tool — our first nuclear magnetic resonance spectrometer and the only such instrument in the state of



(1) (2)

Scheme 1

Delaware. It was sited in our building, so I thought this was a good opportunity to obtain my first fluorine ^{19}F NMR spectrum. I sealed a sample of fluoroacetylene in a tube and gave it to Harlen Foster, our spectroscopist. He inserted it into the probe and obtained a beautiful doublet on the oscilloscope, and then recorded it on pressure-sensitive tape, which was our recording device in those days. Before the sample could be removed from the probe, a deafening explosion occurred, and a black mushroom of smoke issued forth. The probe was completely gutted, but worse yet, the face of the heavy steel magnet was scored. To get the spectrometer back into operation, the probe had to be replaced and the face of the magnet reground. This required several weeks. You can imagine that I wasn't very popular with my co-workers for a while, having destroyed the only NMR spectrometer available to them.

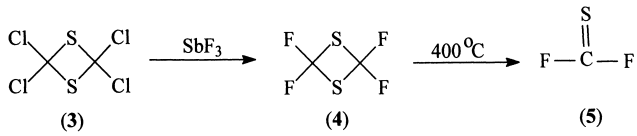
The very next day, I had an explosion in my vacuum train while I was trying to purify another sample of fluoroacetylene. I wasn't seriously injured, but I did have over a 100 small puncture wounds in my left arm, which left me picking glass out of my arm for several weeks. These explosions so scared my supervisor, Bill Sharkey, that he immediately cancelled the project, and our safety engineer, who shall remain nameless, destroyed our remaining samples by shooting at them with a rifle in an open field. Such was my introduction to fluorine chemistry.

3. Perfluorothiocarbonyl compounds

I had no input into choosing my first two projects at DuPont — they were simply assigned to me; but in spite of the explosions, I found that I really liked organofluorine chemistry. I had no say in the choice of my next project either, which turned out to be one that kept me on the road to becoming a fluorine chemist. Subsequently, DuPont was very generous in letting *me* decide what to work on, and, in most cases, I continued to work in the field that I had learned to love — organofluorine chemistry — as one project seemed to flow naturally into another.

3.1. Thiocarbonyl fluoride

My next project was to investigate perfluoro polymers that contained heteroatoms in the chain or backbone. The hope was that we could prepare polymers with the chemical resistance and other good properties that Teflon® possessed,



Scheme 2

but would also be thermoplastic, so they could be moulded, or maybe even be elastomeric or rubber-like.

We were indeed able to prepare polymers of this type. The most interesting one was poly(thiocarbonyl fluoride) [3]. The monomer, thiocarbonyl fluoride (**5**), was prepared in high yield and high state of purity by the pyrolysis of 2,2,4,4-tetrafluoro-1,2-dithietane (**4**), which was in turn prepared by the fluorination of thiophosgene dimer (**3**; Scheme 2) [4]. Polymerization of thiocarbonyl fluoride by anionic initiation at low temperatures gave an elastomeric polymer which had alternating CF_2 groups and S atoms. Even before this polymer was cured, it was bouncier than the best natural rubbers after cure. My supervisor, Bill Sharkey, was so intrigued by its properties that he had a sample made into a golf ball. This ball had remarkable properties — it was sort of a super 'super ball'. If it was dropped onto a firm surface, it would rebound to more than 95% of the release height. If it was dropped from five feet, it would continue to bounce for a long time; and after 30 bounces, it would still be bouncing higher than a foot. Bill tried it out on a golf course, thinking that he might get a super-long-distance drive. He did, but not in the direction that he suspected. The problem was that the ball was very heavy — very dense — so it didn't travel far in the air; but, oh boy!, once it hit the ground it really travelled, bounding first in one crazy direction, then another.

Poly(thiocarbonyl fluoride) might have been commercial except for two things. It lacked insufficient stability toward non-aqueous bases to be a high value-in-use, inert, stable elastomer, and it was too expensive to produce to be a superior general-purpose elastomer. It did have one property that was useful, however: in its crystalline form, it had a low coefficient of friction and it was non-stick, like Teflon®. DuPont licensed the patent to a company interested in coating razor blades.

3.2. Hexafluorothioacetone

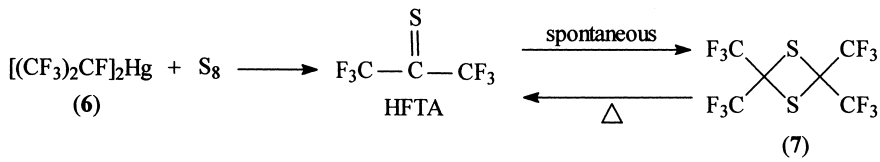
The work on thiocarbonyl fluoride led to our work on hexafluorothioacetone (HFTA) and other perfluorothiocarbonyl compounds. We first prepared HFTA by reacting bis(perfluoroisopropyl)mercury (**6**) (which could be prepared from HgF_2 and hexafluoropropylene) with molten sulfur [4]. HFTA is a deep blue liquid, bp 6°C, that can be stored for extended periods of time at −78°C, but slowly dimerizes to a dithietane (**7**) when stored at room temperature (Scheme 3).

Our original purpose was to form a polymer from HFTA, but this polymer turned out to be thermally unstable, probably because of steric strain. However, HFTA did have some remarkable properties. For example, it may be the most reactive dienophile and enophile now known that can be put in a bottle and stored. For example, it will react rapidly with the diene system in styrene, even at −78°C, and with propylene, also at –78°C, to give adducts [5]. The ene reaction with propylene is typical of many of HFTA's other reactions, in that it appears as though the sulfur atom is at the positive end of the C–S dipole, hence the sulfide **8** is produced instead of a thiol, as would be expected if it were to behave like hexafluoroacetone (Scheme 4).

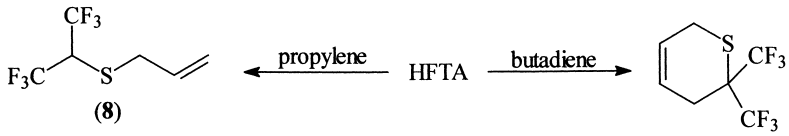
3.3. Hexafluoroacetone and its derivatives [6]

The work on HFTA led to our work with hexafluoroacetone (HFA) itself, including its many derivatives, which included (see Scheme 5): hexafluoroacetone imine (**9**) and 2,2-diaminohexafluoropropane (**10**) [7]; bis(trifluoromethyl)diazomethane (**11**) and the isomeric diazirine (**12**), and the carbene **13** derived from these compounds [8]; and 1,1-bis(trifluoromethyl)dicyanoethylene (**14**) [9]. We made many interesting discoveries while working with HFA, some by design, and some by accident. One example of an accidental discovery concerns midaflur.

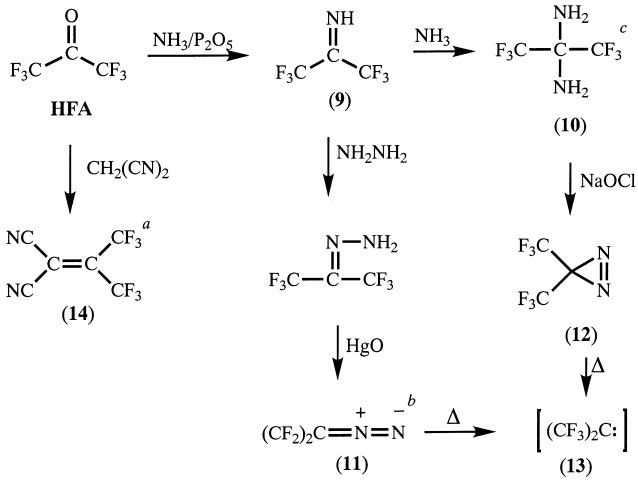
Midaflur is 4-amino-2,2,5,5-tetrakis(trifluoromethyl)imidazoline (**15**), an extremely potent muscle relaxant [10]. This compound was first formed as an unexpected by-product when we were trying to make amino acids from HFA by the reaction of sodium cyanide with hexafluoro-



Scheme 3

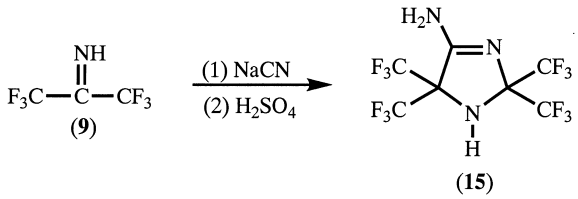


Scheme 4



[a]An analogue of TCNE, undergoing many of the same reactions.
[b]A stable diazo compound.
[c]A stable *gem*-diamine, distillable at atmospheric pressure

Scheme 5



Scheme 6

acetone imine (**9**; Scheme 6). My technician, Armand Bardales, noted a few crystals embedded in the pot residue after distillation. We fished these crystals out, identified them as the aminoimidazoline **15**, and then sent a new sample, made on purpose, to our routine biological screen. Much to our surprise, the compound was extremely potent as a muscle relaxant. It was given the generic name midaflur; and some have claimed that it was named after me, but I assure you that this was not the case.

Midaflur has some good properties. For example, it has very low toxicity. This was demonstrated when a massive dose was given to a beagle. The beagle went to sleep for a week, woke up, took a drink of water, and then went back to sleep for two days. When he finally awoke for good, he had suffered no ill effects except weight loss from not eating for several days, hence the facetious suggestion that midaflur might be the perfect diet drug. In addition to lack of toxicity, midaflur has many other good properties — for example, it does not depress heartbeat or breathing, as other muscle relaxants do; however, it failed in the clinic, partly because it was too potent, i.e. it relaxed all skeletal muscles, not just the spastic ones, and no way was found to terminate its effect prematurely once it was no longer needed, as in surgery.

3.4. Fluoroalcohols

Another accidental discovery did lead to a commercial product; however, this discovery might be considered more serendipitous than accidental. We were trying to prepare some fluorothioketones through the corresponding fluoroalcohols, but the required alcohols were unknown, so first we had to prepare them. We reduced bis(perfluoroisopropyl) ketone with $LiAlH_4$ in diethyl ether to give the corresponding alcohol (**16**), but found that we couldn't separate it from the ether solvent by distillation. Our new secondary alcohol had formed a very strong hydrogen bond with ether, and the resulting one-to-one complex couldn't be broken, either by distillation or recrystallization. This turned out to be a very general phenomenon: most highly-fluorinated secondary and tertiary alcohols form very strong hydrogen bonds with ether or other solvents or substrates that contain oxygen or nitrogen atoms [11].

$(CF_3)_2CFCH(OH)CF(CF_3)_2$ **(16)** $CF_3CH(OH)CF_3$ **HFIP**

It occurred to me that since these fluoroalcohols attached themselves so tenaciously to ethers, esters, amides, etc., perhaps they would also attach themselves to the surface of high-molecular-weight polymers; in other words, may be they would form a fluorocarbon sheath around fibres of nylon or polyesters and render them soil and water repellant. It was an interesting notion, but it didn't work out that way: when I immersed pieces of nylon fabric or polyester fabric (Dacron®) in one of our new secondary fluoroalcohols, they dissolved like magic — just like sugar in water. Even polymers for which no good solvent was previously known dissolved. This was our serendipitous discovery — an excellent class of polymer solvents. DuPont marketed one of these new alcohols, hexafluoroisopropanol (HFIP)[3], for this use, for solvent welding of polyamides, polyesters and polyethers[4], and for analytical control in the manufacture of such polymers. Deuterated derivatives of these alcohols have also become useful NMR solvents.

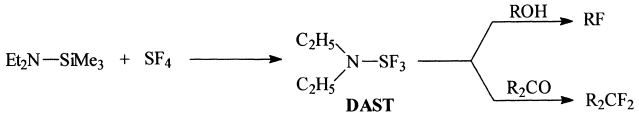
4. Fluorinating reagents

4.1. Diethylaminosulfur trifluoride

I feel that we were lucky to have made several accidental or serendipitous discoveries. However, most of our results have been the outcome of more directed research. An example is the development of DAST, or diethylaminosulfur trifluoride [12].

During the 1950s, William C. Smith and others at DuPont discovered that SF_4 could be used to replace the oxygen of carbonyl groups, and sometimes hydroxyl groups, with fluor-

[3]US Patent 3,418,337 (1968)
[4]US Patent 3,245,944 (1966)



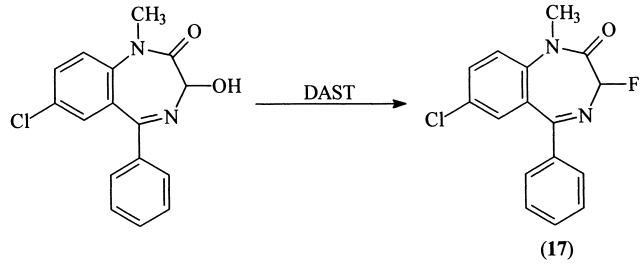
Scheme 7

ine [13]. Unfortunately, SF_4, being a toxic gas, was difficult to handle and the harsh conditions often necessary for the fluorination reactions were unsuitable for sensitive organic compounds. We prepared several derivatives of SF_4 in the hope of finding a reagent that was easy to handle and could be used to replace hydroxyl groups with fluorine in sensitive molecules of biological interest. One of these derivatives, DAST (Scheme 7), seems to have fitted the bill fairly well judging from the number of investigators that used it in the decade after we first published our work [14]. We were able to obtain patents on DAST, but because the process of publication moves so slowly in an industrial company, another group of investigators beat us to the first journal publication, although they made no mention of the fluorination of alcohols, DAST's most useful fluorination reaction.

There are several reasons why it is of interest to insert fluorine into biological molecules. The reason I find most fascinating is the theory that fluorine can block sites of metabolism. After determining with model compounds that DAST did indeed replace OH groups with fluorine in sensitive molecules, we decided to test this theory. Our idea was to prepare a fluorine-containing derivative of the tranquilizer diazepam [Valium® (Roche)] by replacing a hydrogen with a fluorine in the metabolically active 3-position. We hoped that this replacement would result in a compound with greater potency, since this derivative couldn't be metabolized by the normal pathway, and therefore would not be destroyed as rapidly. Using DAST, we were able to prepare 3-fluorodiazepam (**17**) in high yield from the corresponding hydroxy derivative (a metabolite of Valium®) [15] (Scheme 8), and found that it was indeed several times more potent in the model animals studied. I predict a bright future for pharmaceuticals and other biologically-active materials such as insecticides and herbicides that contain fluorine.

4.2. Tris(dimethylamio)sulfonium difluorotrimethylsilicate

In trying to optimize the conditions for preparing DAST, we discovered that a sulfonium salt was formed instead if



(17)

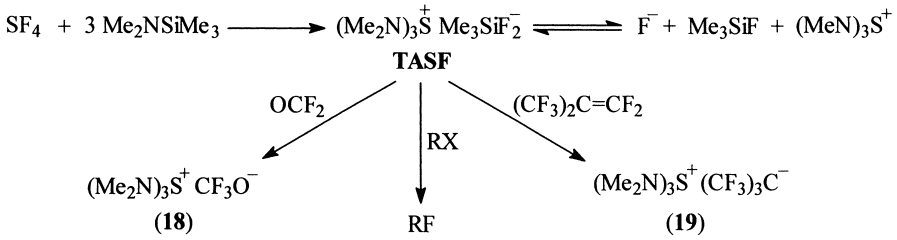
Scheme 8

the SF_4 was added to the aminosilane (Scheme 9) instead of the other way around. One of the most interesting salts prepared this way, because it was highly crystalline and easy to isolate, was tris(dimethylamio)sulfonium difluorotrimethylsilicate (TASF) [16]. This salt is very soluble in organic solvents, and serves as a source of highly reactive fluoride ion due to the dissociation of the silicate anion and the large, charge-diffuse sulfonium cation that prevents significant ion-pairing. It can be used to replace various leaving groups (Cl, Br, I, TsO, CF_3SO_2O) with fluorine, even in nonpolar solvents, to add fluoride ion to fluoroolefins or fluorocarbonyl compounds to give stable isolable perfluorcarbanions (such as **19**) or perfluoroalkoxides (such as **18**), and to fulfil a variety of uses in general organic synthesis [17,28–30]. The alkoxide (**18**) is particularly noteworthy because the X-ray crystal structure shows that the C–F bonds are exceptionally long (1.390 and 1.397 Å) and the C–O bond is exceptionally short (1.227 Å), almost approaching the length of a double bond [18]. This appears to be one of the strongest bits of evidence now known for negative fluorine hyperconjugation (no-bond resonance).

5. Fascinated by fluorine

5.1. Periodic table

A few years ago, I prepared a periodic chart of the elements (Fig. 1) to express how I feel about fluorine, and passed out copies to the audience when I gave my acceptance speech for the ACS Fluorine Award. One of the reasons why I am fascinated by fluorine is the extreme properties that fluorine and its compounds can exhibit. As a natural consequence of being the most electronegative element, some fluorine compounds have the distinction of



Scheme 9

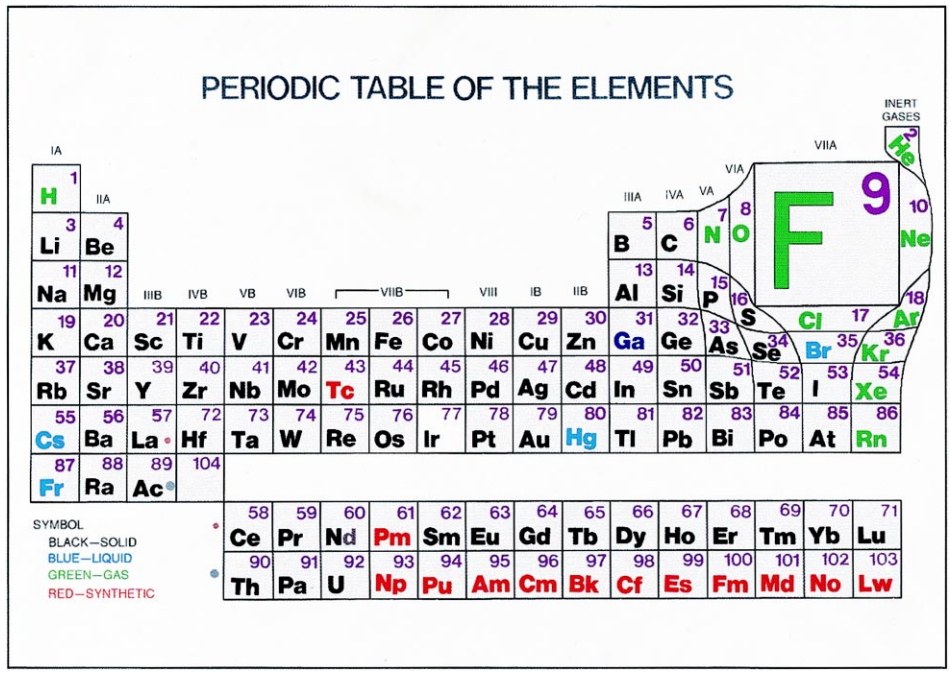


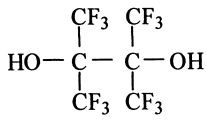
Fig. 1. A fluorine chemist's view of the Periodic Table.

being among the most reactive of all compounds, while others are found among the most inert of all compounds. Fluorine compounds also feature in lists of the least toxic of all compounds, and in those of the most toxic. Some of my own work illustrates this latter point.

5.2. Toxicity surprises

Freon® refrigerants and various fluorocarbon 'blood substitutes' are examples of some very non-toxic compounds. In our lab, however, we have prepared some very innocent-looking fluorine compounds that possess extreme toxicity.

One example is perfluoropinacol (**20**), which we prepared by a photolytic bimolecular reduction of HFA [11]. A single drop of **20** on the skin of a guinea pig is sufficient to kill it, whereas pinacol itself is practically non-toxic. Because it was an excellent solvent for polymers, we prepared over a pound of perfluoropinacol before we discovered its extreme toxicity. It is only by great good luck and good hygiene practices by almost all DuPont employees that no one was poisoned by this material before we destroyed it.



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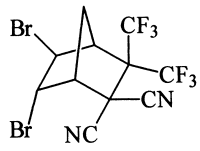


(21)

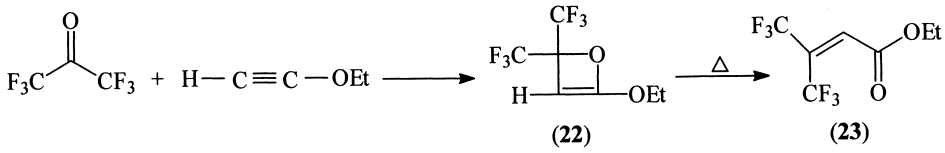
Another example is the norbornane **21**, derived from cyclopentadiene, bromine and 1,1-bis(trifluoromethyl)dicyanoethylene (**14**; Scheme 5) [19]. This is one of the most potent oral poisons known (oral LD_{50} 0.2 mg/kg), being more than 4000 times more toxic than lead arsenate. It was an extremely potent nematocide, but we abandoned all thoughts of field-testing it as soon as we discovered how toxic it was, and all existing samples were destroyed.

5.3. The perfluoroalkyl effect

Another fascinating aspect of fluorine chemistry is the remarkable tendency of perfluoroalkyl substituents to stabilize small-ring compounds. This perfluoroalkyl effect, which is thought to be a kinetic phenomenon, has enabled a number of compound types either unknown in hydrocarbon chemistry, or rarely isolable, to be prepared. In the course of our work we have found many examples of this effect, two of which I'll mention.

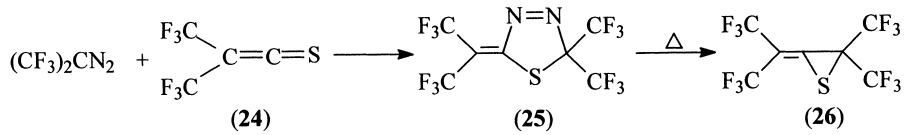
Ketones react with alkoxyacetylenes in the presence of BF_3 to give α,β-unsaturated esters in high yield (sometimes known as the Arens rearrangement.) The formation of an oxete as a cyclic intermediate has been postulated, but in general, oxetes are unstable and have not been isolated. However, we found that hexafluoroacetone reacts vigorously and exothermically with ethoxyacetylene without added catalyst to give the first example of an isolable oxete (**22**) that can be distilled and characterized [20]. It requires a mild pyrolysis or storage at room temperature for several days to be converted to the expected ester, **23** (Scheme 10).

We observed other examples of the perfluoroalkyl effect when we combined our work with perfluorodiazo compounds and perfluorothiocarbonyl compounds. Usually, 1,3,4-thiadiazolines are too unstable to isolate, but a stable,



(22) (23)

Scheme 10



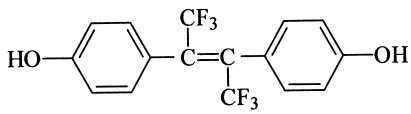
(24) (25) (26)

Scheme 11

isolable thiadiazoline (**25**) was formed when bis(trifluoromethyl)diazomethane was mixed with bis(trifluoromethyl)thioketene (**24**) [21]. Mild pyrolysis of **25** caused extrusion of nitrogen to give the vinylepisulfide **26**, also stabilized by the trifluoromethyl groups (Scheme 11).

6. A professional embarrassment

My several professional triumphs at DuPont were accompanied by a few professional embarrassments. One embarrassment in particular sticks in my mind. Our research had led us to prepare a number of CF_3-substituted phenylethylenes that possessed potent estrogenic activity [22], the most potent of which was an analogue (**27**) of diethylstilbesterol (DES), in which the ethyl groups had been replaced with trifluoromethyl groups. This compound had many times the potency of the very potent synthetic estrogen DES [23].



(27)

Using animal models, mainly rats, our biologist at DuPont, Jack Snyder, discovered that our compounds could be used as extremely effective post-coital antifertility agents, i.e. morning-after pills. But it was the interesting chemistry based on hexafluoroacetone or hexafluorothioacetone that was uppermost in our minds when we decided to give a paper on our research at the Washington DC ACS meeting in 1972. One of our PR men at DuPont, who was always looking for stories that would catch the public's eye (and who shall remain nameless), duly prepared a press release dealing with our work, but unfortunately the editors of the Wilmington papers wrote headlines for the story that really made me squirm. The headline in the *Wilmington Morning News* was 'DuPont Discovers Birth Control Pill for Rats', and The *Evening Journal*s was even worse — 'Post Mating Pill for Rats is Developed'. Regrettably, my name was mentioned, and it was said that the compounds I had prepared were related to Teflon®, DuPont's fluorocarbon resin used in non-stick frying pans; the reports then went on to explain that the compounds could also be considered non-stick because they worked by preventing a fertilized ovum from sticking to the wall of the uterus. I received some very angry phone calls the next day, particularly from the people at DuPont who were involved with non-stick pans. They were concerned that people who read the article might believe that using non-stick cookware would make them impotent or infertile!

7. My DuPont colleagues

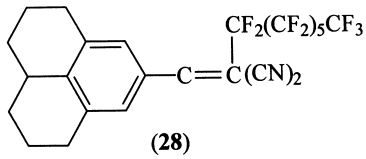
While at DuPont, I had the privilege of working and consulting with some of the best fluorine chemists anywhere in the world. There was always a free exchange of ideas, and we were always proud of each other's accomplishments. Many have considered the group of fluorine chemists assembled by the Central Research Department of DuPont during the last half of the 20th Century to be the greatest collection under one roof of industrial organic fluorine chemists anywhere in the world (the group included David C. England, Carl G. Krespan, William A. Sheppard, Bruce E. Smart, Maynard S. Raash, Charles W. Tullock, Frank S. Fawcett, William E. Burnette and William B. Farnham and myself, and for a brief time, Shlomo Rozen and Kirby Scherer). To add credence to this belief, three members of this group have been given the American Chemical Society Award for Creative Work in Fluorine Chemistry, the only such group to collect this many awards to date. Short biographies of the three award winners, of which I am one, are appended to this article.

8. After DuPont

I left DuPont in 1984 to teach chemistry at Ursinus College in Collegeville, Pennsylvania. I always wanted to try my hand at teaching in a small liberal arts college, and at Ursinus I finally got my chance. It was a delightful experi-

ence, but I found doing research there was a far different ball game than doing research at DuPont. For one thing, there was no fluorine NMR spectrometer available, and doing without ^{19}F NMR for an organofluorine chemist is almost like working blindfolded and handcuffed. I was totally dependent on friends in industry or research universities to run spectra for me. Research at a liberal arts undergraduate institution is also different from research at a university that has a graduate department, in that almost all of the research is done by junior or senior undergraduate students who can normally spend only a few hours each week in the lab, and by the time they finally become experienced, they graduate. Nonetheless, I believe that we were able to accomplish some useful research, and many of my students won awards at regional undergraduate research meetings.

One of our more significant discoveries was a new polarity scale for very non-polar substances [24]. This was a serendipitous discovery: one of my students, Beth Freed, noted that the fluorocarbon-soluble dye **28** she had prepared as a leak-detecting agent for CFCs had a distinctly different colour in every solvent that it was dissolved in, so we used its solvatochromic properties to devise a relative polarity scale.



(**28**)

Another discovery [25] which may have utility concerns the selective monofluorination of benzylic compounds (e.g. $C_6H_5CH_2CN \rightarrow C_6H_5CHFCN$) via electrolysis (with alternating current) in pyridine/HF (Olah's Reagent) instead of the usual Simons electrolysis in straight HF with direct current, which results in polyfluorination.

9. Fluorine chemistry's future?

In the past few years, the concern has arisen that the number of investigators doing fluorine chemistry may drop because much government-supported research in the area has been terminated. This is particularly true in the US. However, I believe that this will be more than offset by the increased interest that chemists of all disciplines have in fluorine.

In the past, fluorine chemistry has been regarded by many as a specialized field — not in the main stream of chemical science. I think this was especially true for organic fluorine chemistry. However, that seems to be changing now since more and more chemists who do not regard themselves as fluorine chemists are utilizing fluorine in their research. This is certainly true in the biological and medicinal area, but it is also true in other areas as well. Consequently, there is a much broader interest in what the fluorine chemist is doing today and what he has done in the past. We seem to be entering the mainstream of chemistry now. I don't know what effect this will have on those of us who regard ourselves as fluorine chemists. I hope that we are up to the challenge.

10. Addendum

Chemistry, and particularly fluorine chemistry, has been my life's blood, but I also greatly enjoy another of my hobbies — writing poetry. On rare occasions the two mix, and I have actually had two of my poems published in scientific journals. The first one appeared in *C & E News* [26], and is a form of poetry called a double dactyl:

BURNER, BURNER,
BURNING BLUE

Flamity-blamity
Robert E. Bunsen, the
Chemist we all know of
Gas burner fame,

Worked to develop the
Gas and air mixer that
Characteristic'ly
Burns a blue flame.

The second poem was published in *Fluorine Technology Bulletin* [27]. The professor in this poem is fictional, but does bear some resemblance to me. It runs as follows:

PROFESSOR McGEE'S SOLUTION

Have you ever heard of a queer old bird named Thaddeus P. McGee?
He was of late a professor of State University.

Now Thaddeus was a teacher because he loved to teach chemistry,
But the real love he had was to work in the lab whenever his time was free.

He was renowned for once he had found a new solvent for stainless steel,
But, never shirking, he kept on working, for his solvent was far from ideal.

He said, to succeed, what he'd really need was a broth to dissolve everything,
And he dreamed of the day when the world would say, 'Thad, you're the chemistry king.'

Now it was no chore to dissolve the wood floor... a little strong acid would do,
And it was no task to dissolve a glass flask and a beaker or test tube or two.

And it's easy as pie to use a little lye to dissolve both flesh and hair,
And who couldn't use whatever acid they choose to dissolve rusty nails and such fair?

But the real challenge was to try to manage to find one solvent for all.
His students all say that he worked night and day to succeed in this task before fall.

When school started that fall, his students recall, they entered his lab through the door,
But they didn't see Professor McGee. All they saw was a hole in the floor.

They looked all around. He was not to be found. All they saw was the hole in the floor.
They looked in the hole. Had McGee reached his goal? This hole was hard to ignore.

The hole was much more than a hole through the floor, for it was a bottomless pit.
His students surmized that McGee had devized a solvent that just wouldn't quit,

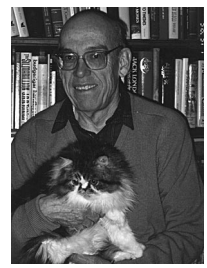
And his students all stated he miscalculated, for no flask could contain his new brew...
It dissolved the flask wall and that is not all, it dissolved the lab bench and ate through

The lab floor, and what's even more it dissolved a deep hole in the ground.
Some thought that McGee, who was nowhere to see, and was never again to be found,

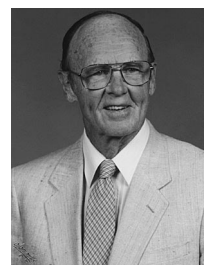
Was now dissolved, too, into his new brew, and his solution flowed into the hole.
But don't shed a tear for Thaddeus, my dear, for in death he attained his life's goal.

References

[1] Chem. and Eng. News, 28 April 1958, p. 50.
[2] W.J. Middleton, J. Am. Chem. Soc. 81 (1959) 803.
[3] W.J. Middleton, H.W. Jacobson, R.E. Putnam, H.C. Walter, D.G. Pye, W.H. Sharkey, J. Polymer Sci. A 3 (1965) 4115.
[4] W.J. Middleton, E.G. Howard, W.H. Sharkey, J. Am. Chem. Soc. 83 (1961) 2589.
[5] W.J. Middleton, J. Org. Chem. 301390 (1965) 1395.
[6] C.G. Krespan, W.J. Middleton, Fluor. Chem. Rev. 1 (1967) 145–196.
[7] W.J. Middleton, C.G. Krespan, J. Org. Chem. 30 (1965) 1398.
[8] W.J. Middleton, D.M. Gale, C.G. Krespan, J. Am. Chem. Soc. 88 (1966) 3617.
[9] W.J. Middleton, J. Org. Chem. 30 (1965) 1402.
[10] W.J. Middleton, C.G. Krespan, J. Org. Chem. 35 (1970) 1480.
[11] W.J. Middleton, R.V. Lindsey, J. Am. Chem. Soc. 86 (1964) 4948.
[12] W.J. Middleton, J. Org. Chem. 40 (1975) 574.
[13] W.C. Smith, C.W. Tollock, E.L. Muetterties, W.R. Hasek, F.S. Fawcett, V.A. Englhardt, D.D. Coffman, J. Am. Chem. Soc. 81 (1959) 3165–3166.
[14] M. Hudlicky, Fluorinations with diethylaminosulfur trifluoride and related aminosulfurans, in: Organic Reactions, vol. 35, Wiley, New York, 1988, pp. 513–637.
[15] W.J. Middleton, E.M. Bingham, D.H. Smith, J. Fluorine Chem. 23 (1983) 557–572.
[16] W.J. Middleton, Organic Synthesis 57 (1985) 221–225.
[17] O.W. Webster, W.R. Hertler, D.Y. Sogah, W.B. Farnham, T.V. RajanBabu, J. Am. Chem. Soc. 105 (1983) 5706.
[18] W.B. Farnham, B.E. Smart, W.J. Middleton, D.A. Dixon, J. Am. Chem. Soc. 107 (1985) 4565.
[19] W.J. Middleton, E.M. Bingham, J. Fluorine Chem. 20 (1982) 297.
[20] W.J. Middleton, J. Org. Chem. 30 (1965) 1307.
[21] W.J. Middleton, J. Org. Chem. 34 (1969) 3201.
[22] W.J. Middleton, D. Metzger, J.A. Synder, J. Med. Chem. 14 (1971) 1193.
[23] W.J. Middleton, US. Patent 3,683,009 (1972) [Ger. Equivalent, CA 73 : 14,425 m].
[24] B.K. Freed, J. Biesecker, W.J. Middleton, J. Fluorine Chem. 48 (1990) 63–75.
[25] S.M. Lee, J.M. Roseman, C.B. Blair, E.P. Morrison, S.J. Harrison, C.A. Stankiewicz, W.J. Middleton, J. Fluorine Chem. 77 (1996) 65–70.
[26] K.M. Reese, Chem. and Eng. News, 8 November 1993, p. 66.
[27] W.J. Middleton, Fluorine Technology Bulletin, No. 19, 1995, p. 25.
[28] R. Noyori, I. Nishida, J. Sakata, J. Am. Chem. Soc. 105 (1983) 1598.
[29] T.V. RajanBabu, T. Fukunaga, J. Org. Chem. 49 (1984) 4571.
[30] M. Fujita, T. Hiyama, J. Am. Chem. Soc. 107 (1985) 4085.
[31] Chem. and Eng. News, 11 April 1960, pp. 114–120.



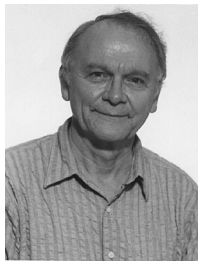
William J. Middleton (Bill) was the recipient of the 1982 ACS Award for Creative Work in Fluorine Chemistry. Born in Amarillo, TX, in 1927, he holds BS and MS Degrees in chemistry from North Texas State University, and a Ph.D. in organic chemistry from the University of Illinois. He joined DuPont's Central Research and Development Department in 1952 as a research chemist, and for the next 32 years carried out research, primarily in the field of organofluorine chemistry; his work resulted in 107 US patents on fluorine-containing pharmaceuticals, agricultural chemicals, polymers, solvents, and reagents. Bill left DuPont in 1984 and joined as the chemistry staff at Ursinus College in Collegeville, PA, where he taught organic chemistry and continued his research over the next eleven years, advising 36 junior and senior undergraduates in their research projects and thesis. Currently he is emeritus professor of research at Ursinus College. During his career, Bill has published more than 80 scientific papers and has been an invited speaker at numerous domestic and foreign universities and scientific meetings. In 1995, he received the Laughlin Professional Achievement Award for distinguished service to Ursinus College. Among his non-chemistry related honours, he was chosen to be the Poet of the Year, 1996, by the Feelings Poetry Journal.



David C. England received the American Chemical Society Award for Creative Work in Fluorine Chemistry in 1985. He was born in Portland, OR, USA, graduated from Oregon State College in 1940, and received a Ph.D. degree in organic chemistry from the University of Wisconsin three years later. He then joined DuPont's Chemical Department (now Central Research and Development Department) as a research chemist and is proud of the fact that he spent almost 40 years there 'working at the bench' on interesting projects. Dave retired in 1982, but not before he had published 30 scientific papers and received 61 US patents. Some of the more interesting compounds he has synthesized and elucidated the chemistry of include the extremely reactive perfluorocyclobutanone, the deep blue perfluorocyclobuta-1,2-dione, and the perfluoro-β-sultone derived from tetrafluoroethylene and sulfur trioxide, which is the starting material for commercial fluorinated ion-exchange polymers.

In addition to the ACS Fluorine Award, Dave's achievements have been recognized by the presentation of the ACS Delaware Section Award

(1984), DuPont's Pederson Award for Technical Excellence (1995), and DuPont's Lavoisier Medal for Technical Achievement (1997).



Carl G. Krespan received the American Chemical Society Award for Creative Work in Fluorine Chemistry in 1987. He was born in 1926, and received his BS Degree in chemistry from the University of Rochester in 1948 and his Ph.D. in organic chemistry from the University of Minnesota in 1952. Carl joined DuPont's Central Research and Development Department in 1952 and carried out much significant research in organofluorine chemistry during his 41-year career there. His broad interests in organofluorine chemistry include new synthetic methods and novel structures, anionic, cationic and free-radical reactions of fluoroolefins and fluoroketones, and the chemistries of fluorinated sulfates, aminoimidazolines, diazo compounds, diazirines, thiiranes and cyclic polysulfides. Among his many achievements is a technology he developed which gave rise to the high-performance Viton® GLT class of fluoroelastomers.

Carl's involvement with the ACS Division of Fluorine Chemistry has included two terms as chairman and the organization (with Professor Alan Clifford) of the First Winter Fluorine Conference. He is an author of more than 60 scientific papers, and has received 71 US patents. In addition to winning the 1987 ACS Fluorine Award, he was presented with DuPont's Pederson Award for Technical Excellence in 1995.