2,2,2-Trifluoroethanol (TFEA)

Its Production Process and Various Applications

TOSOH
TOSOH F-TECH, INC.

1. INTRODUCTION

Trifluoroethanol (TFEA), is a liquid with an odor similar to ethanol. It was first synthesized by Swarts in 1933[1], and produced industrially by Halocarbon Products Corporation in 1960[2]. Although the specific properties of TFEA were well known since its discovery, few commercial applications existed for the product until improved methods of manufacture made its use in medical anesthetics economically feasible[3].

More recently, the chemical and physical properties of TFEA suggest that the product may have commercial potential, not only as an intermediate building block, but as a key material in environmentally friendly applications. This report will describe TOSOH F-TECH's TFEA production flow, as well as several established and developing applications for the product.

2. PHYSICAL PROPERTIES OF TFEA

TFEA, the simplest alcohol with a CF_3 group, is a colorless, transparent liquid and has a higher molecular weight and higher density compared with ethanol. The strong electron drawing property of the fluorine atoms contributes to weak acidity, and makes TFEA unique, and different from ethanol (Table 1).

Table 1 Comparison of Physical Properties between TFEA and Ethanol

Chemical Structure	CF_3CH_2OH	CH_3CH_2OH
Molecular Weight	100.04	46.1
Boiling Point (˚C)	73.6	78.3
Melting Point (˚C)	-43.5	-130
Specific Density	1.3842	0.7905
Refractive Index (n^{20})	1.2907	1.3614
Dipole Morment (Debye)	2.04	1.68
Heat of Vaporazation (KJ/mol)	35.15	38.6
Viscosity (cp at 20˚C)	0.9	1.19

TOSOH F-TECH INC's TFEA Plant built in1993

3. TFEA PRODUCTION PROCESS

TOSOH F-TECH has developed an unique manufacturing technology for the manufacture of TFEA in large tonnage quantities. Our process is based on the reaction of trifluoroethylchloride (133a), with γ-hydroxybutyric acid potassium salt in γ-butyrolactone as a solvent[3]. The starting 133a is synthesized from trichloroethylene and HF via vapor phase fluorination (Figure 1). Our first commercial scale TFEA plant located in Nanyo, Japan was commissioned in 1985. In order to meet market demand, a second, and much larger unit was completed in 1993 (Photograph).

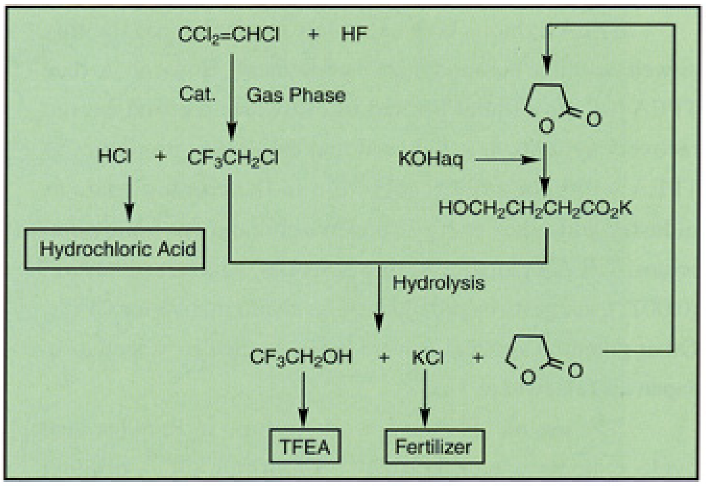

Figure 1 TFEA Process of TOSOH F-TECH

The characteristics of our TFEA process technology are extremely high purity, mild hydrolysis reaction conditions, minimal reactor corrosivity, and virtually zero waste (by product KCl is utilized as a fertilizer).

We believe the TOSOH F-TECH TFEA technology compares well with other reported technologies, including the catalytic hydrogenation of trifluoroacetic acid or its ester[4] and the stepwise process via trifluoroethylacetate[5], and a newer technolgy involving direct steam hydrolysis of 133a in the presence of a catalyst [6].

4. APPLICATIONS

1) Anesthetics

The synthesis of medical anesthetics is, by far, the most important known application for TFEA. Certain ether deriviatives of TFEA have been used as medical anesthetics for many years. Fluroxene was an early product to be successfully introduced, but Isoflurane soon garnered much of the market as a result of its lower flammability and lower toxicity. The new generation TFEA based Desflurane continues to make inroads in the marketplace and is reportedly superior to Isoflurane, in some instances[7]. Halothane, an older anesthetic derived from 133a, is still widely used in some countries (Figure 2).

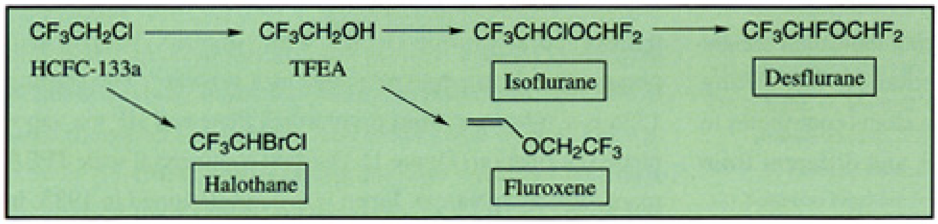

Figure 2 Anesthetics derived from TFEA

2) Energy Fields

TFEA exhibits both extremely tough thermal stability as well desirable thermodynamic properties[8]. However, to date TFEA has only found limited use in waste thermal energy recovery systems. It is believed that the unique properties of TFEA will gain more recognition in the coming years as industry addresses energy conservation and environmental issues. TFEA's global warming potential, which is almost nil (0.0072), suggests its possible use as an alternative for CFC's. Other potential applications are being studied by scientists in Japan and elsewhere.

The use of TFEA as a working fluid in Rankine heat cycle systems is well known[8]. "Fluorinol 85", a product registered in United States by Thermo Electron Corp, is a TFEA/water mixture that has been successfully utilized at the Kimitsu Plant of Nippon Steel Corporation in Chiba, Japan since 1981. It seems likely that similar environmentally friendly heat recovery systems might eventually be adopted by other steel companies, and by major energy consumers such as cement manufactures (Figure 3).

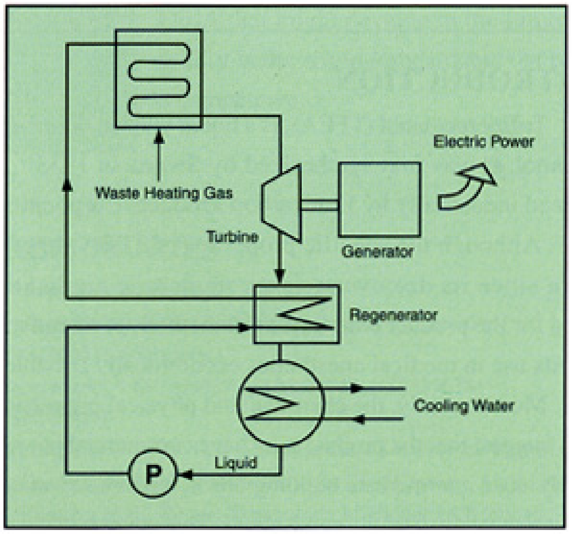

Figure 3 Rankine Cycle System for Recovering Waste Thermal Energy

Another interesting property of TFEA is its moderate evaporative heat and fairly large heat dissolution when combined with amides such as N-methylpyrolidone (NMP) and N,N-dimethylimidazolidinone (DMI). Both TFEA/NMP and TFEA/DMI based systems are presently under evaluation by absorption/compression type heat pump designers[9]. Resistant to freezing below 0°C, these TFEA based systems lend themselves to compact unit design and are expected to work well with a variety of alternative electric power energy sources such as city gas, propane and kerosene. If successfully commercialized, such heat pumps could significantly cut peak electric power consumption by business and residential air conditioner users during the hot summer months in Japan and elsewhere.

3) Intermediate For Organic Synthesis

TFEA can be a CF_3CH_2 and CF_3CH_2O donor in the synthesis of pharmaceuticals and agrochemicals. For example, "Flurotyl", a TFEA based ether is a central nerve system stimulant developed by Ohio Medical[10]. Takeda Chemical Industries introduced "Lansoprazole", a proton pump inhibitor for gastric and dodecadactylon disorders[11]. Other examples of TFEA based drugs include 3M Sante Corporation's "Flecainide", a heart antriarrhythmic12), "Quazepam", a sedative[13], and "KMD-3213", an antiacraturesis introduced by Kissei Pharmaceuticals[14].

In the agrochemicals arena, TFEA can be used in the production of the herbicide "Triflusulfuron-methyl[15] (Figure 4).

4) Building Block

TFEA based ethers and thioethers can react with alkyl-lithiums in amines or other solvents to give non-fluorinated alkyl-thioenamines and alkyl-acetylenic derivatives respectively[16]. These compounds are useful reagents.

TFEA based ether derivatives easily liberate F anions from CF_3 groups and can generate difluoroenolates when treated with certain bases or reductive agents. It has been observed by some researchers that difluoroenolates are potential building blocks for the synthesis of a variety of fluorinated organic compounds. J. Percy is one such researcher who has shown that difluoroenolates can be used for the introduction of difluoromethylene groups[17]. It has also been demonstrated that certain organic compounds that contain difluoromethylene groups might be used as antienzymatic agents (Figure 5).

5) TFEA As A Solvent

TFEA is miscible with many oxygen containing compounds such as water, alcohols, ethers and ketones. It also dissolves certain aromatic compounds such as benzene and toluene. Chloroform is highly miscible in TFEA, carbon tetrachloride is only slightly miscible in TFEA. Some polymers such as nylon, polmethacrylate, ethyl cellulose, and polyvinyl-acetate will dissolve in TFEA, while others like polyetylene and polypropylene are insoluble[18]. The Solubility of nylon in TFEA can be important to some fiber and resin makers.

TFEA has also been useful in certain polymerizations, and as a cleaning solvent. More recently, TFEA has been employed in HPLC separations as an eluent, owing to its high solubility properties, consistent high purity, and reasonable cost.

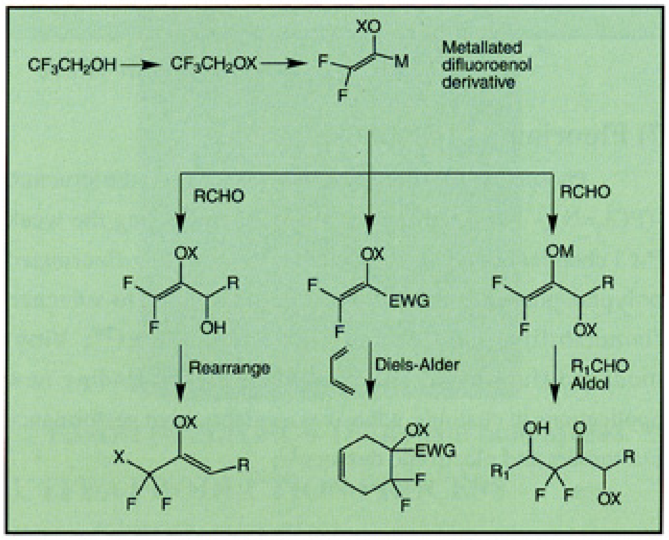

Figure 5 TFEA as Building Blocks

6) Acylating Agents

Certain enzyme reaction in organic solvents is remarkable because of reversible reaction and easy treatment after the reaction, which is different in water. TFEA displays extremely lower electrophilicity, and enzyme acylation using the ester of TFEA may occur predominantly at the counter hydroxyl group.

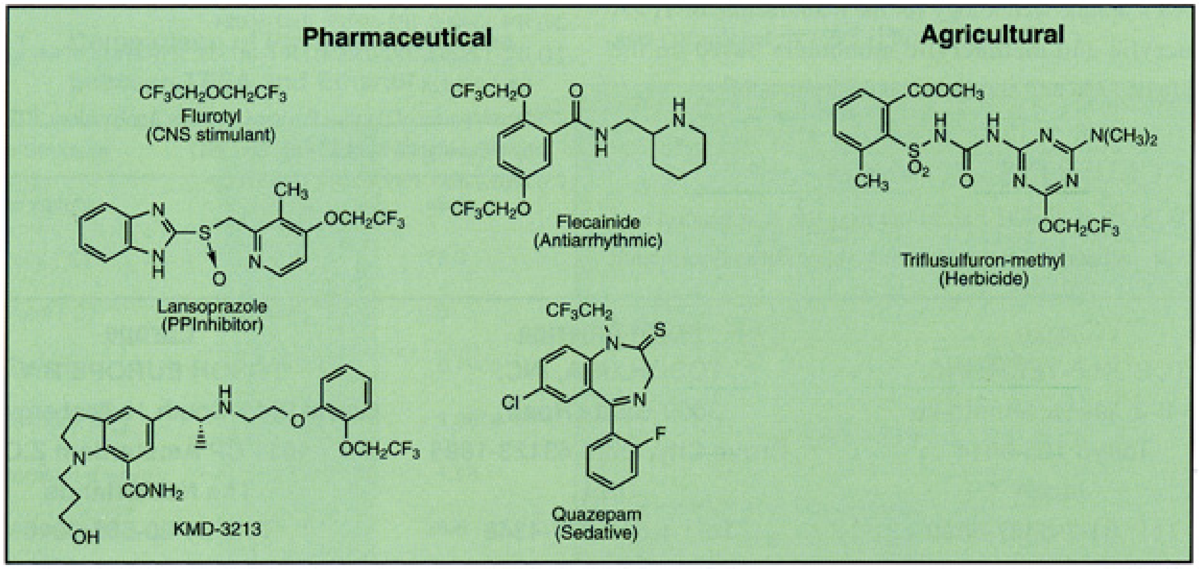

Figure 4 TFEA in Pharmaceutical and Agricultural Field

Since Klibanov found this unique properties of TFEA, enzyme acylation reaction is often carried out for esterification of optical active alcohols, regioselective acylation of steroids, optical resolution of amine compounds and synthesis of optical active compounds for medicine[19] (Figure 6).

$$ROH + R'COOCH_2CF_3 \underset{}{\overset{enzyme}{\rightleftharpoons}} ROCOR' + CF_3CH_2OH$$

ROH : Chiral Compound
$R'COOCH_2CF_3$: Acylating Agent

Figure 6 Acylation with TFEA

7) Fluorinated Polyphosphazenes

Phosphazene are inorganic polymers having the structure $-(PCl_2{=}N)_n-$. TFEA provides a way of stabilizing the weak P-Cl chemical bond by substitution, the resulting fluorinated polyphosphazenes exhibit excellent resistance to solvents, flammability, and low and high temperatures[20]. Vinyl modified fluorinated polyphosphazenes are finding new applications in coatings, adhesives, sealants, high performance elastomers and electronic devices[21].

8) TFEA Esters

The acrylic and methacrylic esters of TFEA can be easily copolymerized with a variety of other monomers to give polymers special properties such as water repellency, oxygen permeability and improved refractive properties. The use of such monomers in contact lens fabrication is well known. Newer potential applications include coatings and new generation photo resist materials[22]. TOSOH F-TECH has developed a unique technology for the manufacture of TFEA based acrylic and methacrylic monomers based on the utilization of 133a and acrylic or methacrylic acid[23].

5. CONCLUSIONS

TOSOH F-TECH has pioneered the manufacture of TFEA with its patented and proprietary vapor phase fluorination technology. The purpose of this article is to stimulate wider R&D interest in this unique product. We believe that industry will come to appreciate the commercial potentials for this unique fluoroalcohol as researchers uncover its true potential. As the world's largest TFEA supplier, TOSOH F-TECH is prepared satisfy virtually any demand for TFEA that might develop in the future. Our quality is the world standard and our pricing is competitive.

6. REFERENCES

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