

Fluoroalkanesulfonanilides, a New Class of Herbicides

Substituted fluoroalkanesulfonanilides are a new class of potent herbicides. The highest pre- and post-emergence herbicidal activity was present in a series of several mono- and disubstituted trifluoromethanesulfonanilides. Substitution in the benzene ring had large effects on activity. Disubstitution in the 2,4-positions of the benzene ring by fluoride and chloride gave the most promising com-

pounds. Chemical and physical properties were greatly affected by fluorine introduction. The change from methanesulfonamido to trifluoromethanesulfonamido gave a 10,000-fold increase in acidity and a 50-fold increase in lipophilicity. Structure-activity studies did not afford a simple correlation of herbicidal activity with a number of the parameters examined.

In the past few years numerous fluoroalkanesulfonanilides were prepared and tested in this laboratory for biological activity. A preliminary report describing two anti-inflammatory agents resulting from these studies has already appeared (Harrington *et al.*, 1970). We now wish to report that a number of these fluoroalkanesulfonanilides are potent herbicides. In addition, these compounds possess unique chemical and physical properties not previously noted.

The preparation of trifluoromethanesulfonanilide and other perfluoroalkanesulfonanilides was described in the literature more than a decade ago (Brice and Trott, 1956; Burdon *et al.*, 1957). More recently, difluoromethanesulfonanilides and fluoromethanesulfonanilides were reported (Farrar, 1960), but no herbicidal uses for such compounds have been described. In general, syntheses were accomplished by sulfonylation of the appropriate aniline with either fluoroalkylsulfonyl halide or anhydride in the presence of a base such as triethylamine or pyridine. Details of the sulfonylation procedures and subsequent chemical modifications of the products are the subject of forthcoming publications.

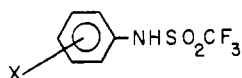
Fluoroalkanesulfonanilides are unusually acidic due to the strong electron-withdrawing effect of the fluoroalkanesulfonyl moiety. For example, trifluoromethanesulfonanilide has a pKa value of 4.5 at 25° C, while the pKa of methanesulfon-

anilide is 8.7. Half-neutralization potentials (HNP) were determined in 67% dimethylformamide/water. The pKa's were estimated from a plot of HNP's of other water soluble organic acids in 67% dimethylformamide/water *vs.* their aqueous pKa's. A pKa value of 9.9 in 50% ethanol/water was obtained by potentiometric titration (Uloth *et al.*, 1966). Similarly, lipophilicity, as measured by the partition coefficient (Fujita *et al.*, 1964) increases dramatically with fluorine introduction. Un-ionized trifluoromethanesulfonanilide partitions 582 to 1 in *n*-octanol-water in contrast to methanesulfonanilide, which partitions 9 to 1 in the same solvent system.

Many of the sulfonanilides synthesized to date have exhibited selective herbicidal activity (Table I). They were active in pre- and post-emergence assays on a variety of grasses and broadleaf weeds. In general, herbicidal activity was greatest with the more highly fluorinated compounds. The trifluoromethanesulfonamido group was the best of a variety of partially and completely fluorinated alkylsulfonamido groups investigated.

Substitution on the aromatic ring greatly altered the mode and degree of activity of these compounds. The most potent activity was exhibited by 4- and 2,4-substituted trifluoromethanesulfonanilides in which the substituents were halogen, alkyl, or sulfur-containing groups.

Table I. Pre-emergence Herbicidal Activity of Substituted Trifluoromethanesulfonanilides



X	Average Pre-emergence Herbicidal Activity ^a					
	Four Grass Species			Four Broadleaf Species		
	10 ^b	5	2.5	10	5	2.5
2-Cl	100	92	72	100	100	92
3-Cl	0	0	0	100	100	70
4-Cl	30	0	0	93	72	40
4-F	100	90	90	97	97	97
3-NO ₂	50	0	0	100	100	0
2-SCH ₃	100	100	100	87	60	52
4-SO ₂ CH ₃	93	93	85	0	0	0
2-CH ₃ , 4-Cl	40	0	0	100	100	100
2-Cl, 4-CF ₃	100	57	30	100	97	53
2,4-dichloro	100	100	100	100	100	100
2,4-difluoro	100	100	100	100	100	100

^a Weed species planted in four rows in replicated 6 in. plastic pots were: giant foxtail, *Setaria faberii*; barnyardgrass, *Echinochloa crusgalli*; crabgrass, *Digitaria ischaemum*; quackgrass, *Agropyron repens*; pigweed, *Amaranthus retroflexus*; purslane, *Portulaca oleracea*; wild mustard, *Brassica kaber*; and annual morning glory, *Ipomoea purpurea*. Aliquots of test chemical in aqueous acetone were added to give the proper treatment levels. Data were taken 2 weeks after treatment and rated on a 0-100 scale where 0 = no effect and 100 = complete kill. The soil used was a sandy loam (68% sand, 20% silt, 9% clay, 2-2.8% organic matter). The tests were run in an artificially illuminated greenhouse. ^b Dosage rate in lb/acre.

Crop selectivity was also noted. The 2,4-dichloro- and 2,4-difluorosubstituted sulfonanilides were markedly superior in this respect to other equally potent members of the series. These two compounds were field-tested and selectivity with corn and soybean crops was observed, although minor stunting occurred in some locations. The crop injury was positively correlated with high rainfall conditions, and may be correlated with low organic-content soils. Although extensive structure-activity studies have been carried out on this series, no single property of these sulfonanilides could be used to rationalize the observed herbicidal activity which is the result of a complex interplay of acidic, lipophilic, electronic, and steric properties.

ACKNOWLEDGMENT

We thank C. D. Green and J. W. Belisle for the pKa determinations.

LITERATURE CITED

- Brice, T. J., Trott, P. W., U.S. Patent 2,732,398, January 24, 1956.
 Burdon, J., Farazmand, I., Stacy, M., Tatlow, J. C., *J. Chem. Soc.* 2574, 1957.
 Farrar, W. V., *J. Chem. Soc.* 3058 (1960).
 Fujita, T., Iwasa, J., Hansch, C., *J. Amer. Chem. Soc.* **86**, 5175 (1964).
 Harrington, J. K., Robertson, J. E., Kvam, D. C., Hamilton, R. R., McGurran, K. T., Trancik, R. J., Swingle, K. F., Moore, G. G. I., Gerster, J. F., *J. Med. Chem.* **13**, 137 (1970).
 Uloth, R. H., Kirk, J. R., Gould, W. A., Larsen, A. A., *J. Med. Chem.* **9**, 88 (1966).

R. D. Trepka
 J. K. Harrington
 J. E. Robertson
 J. T. Waddington

Biochemical Research Laboratory
 3M Co.
 3M Center
 St. Paul, Minn. 55101

Received for review July 13, 1970. Accepted August 31, 1970.