SYNTHESIS OF MONOFLUORO-HETEROCYCLES USING FLUOROOLEFINS AS STARTING MATERIALS

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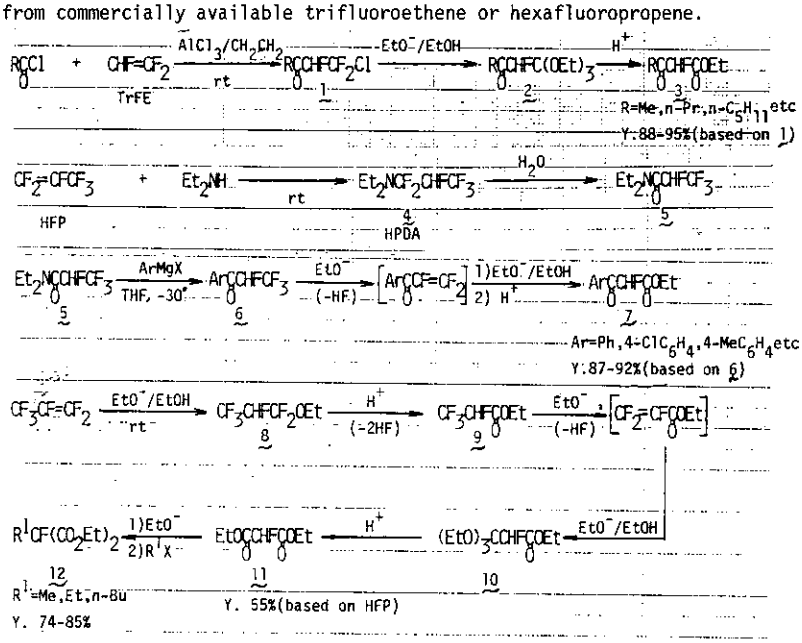
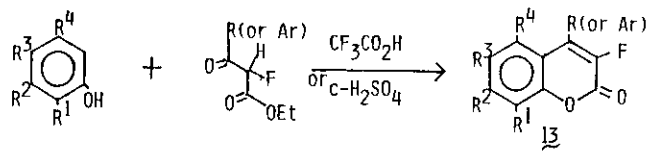
The Compounds of having an active fluoromethylene group such as α-fluoro-β-ketoesters and -diesters are recognized as useful intermediates for the synthesis of monofluoro-compounds which are of great interest from the biological point of view. These building blocks were readily prepared from commercially available trifluoroethene or hexafluoropropene.



The monofluoro-heterocycles synthesized from these building blocks include coumarins, chromones, benzodiazepines, pyrazoles, barbituric acids and cytosine derivatives etc.

α-Fluoro-β-ketoesters, 3 and 7, derived from trifluoroethene or hexafluoropropene as described above, were a potent intermediates for monofluoroheterocycles. As an example of those, 3-fluoro-4-alkyl(or aryl) coumarins were prepared by the reaction with phenols. The reactions proceeded in refluxing trifluoroacetic acid smoothly, and 3-fluoro-4-alkyl(or aryl) coumarins (13) were expectedly obtained in good yields.



The detailed synthetic methods will be presented.