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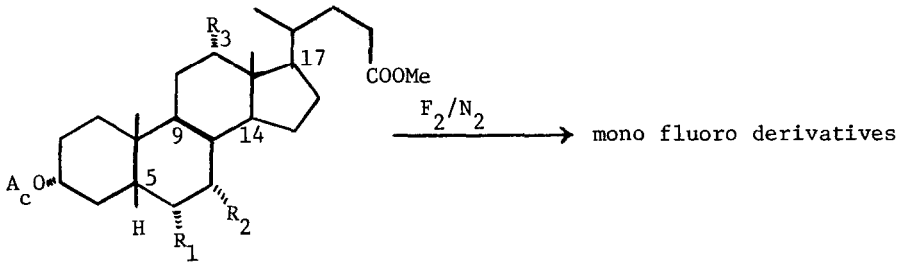
DIRECT FLUORINATION OF UNCONVENTIONAL SITES OF STEROIDS BY ELEMENTAL FLUORINE

G. Ben-Shushan* and S. Rozen

Department of Chemistry, Tel Aviv University, Tel Aviv 69978 (Israel)

Activation of remote unactivated sites in steroids is of course highly important. There are two approaches to this problem; one is of radical nature and produces a chlorinated or oxygenated derivatives, and the second which we have developed, uses elemental fluorine as a strong electrophile able to react with tertiary unactivated hydrogens.

We have shown that in the bile acid series, for example, one can direct the site of fluorination by appropriate substitution of the steroidal skeleton:



Depending on the various R's, the fluorination could be directed to the tertiary sites replacing the hydrogens attached to C-5,9,14 or 17, with full retention of configuration. Some other steroids with A/B cis configuration, with 3α oxygenated function or with only one electronegative end were also examined. A good correlation of the number of the electronegative groups with the easiness and the regioselectivity of the fluorination was found.

Although usually the fluorination is carried at -75°C, the temperature can be raised up to the more convenient, 0°C without losing the selectivity but with considerable reduction of the chemical yields. Some characteristic spectral features of the fluoro derivatives will also be outlined.