The Conversion of Diaryl-1,3-Dithiolanes into *gem*-Difluoromethylene Compounds by a Combination of Elemental Fluorine and Iodine

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Diaryl-1,3-dithiolanes are converted to *gem*-difluorides in good yield by reaction with a mixture of elemental fluorine and iodine in acetonitrile at room temperature.

The selective fluorination of organic molecules has received considerable attention because of the profound effect that fluorine can have on the physical, chemical and biological properties of a wide range of substrates.[1] In particular, the introduction of a difluoromethylene unit into a molecule is an important target because of the possible relationship between a CF_2 group and an ether oxygen. Consequently, effective methods of constructing CF_2 moieties from readily available, inexpensive fluorinating agents are highly desirable.

The conversion of a carbonyl group into a *gem*-difluoride can be accomplished by a variety of methods using reagents such as SF_4, SeF_4, MoF_6 and DAST,[2] all of which have some limitations. Consequently, recent milder methods have focused on the fluorination of carbonyl derivatives such as hydrazones[3] (with halogen monofluorides or fluorine) and diazo compounds[4] (with fluorine) but both of these types of intermediate can be unstable. Dithiolanes offer an attractive alternative and are generally difluorinated by using either a combination of a source of electrophilic halogen (*e.g. N*-bromosuccinimide) with a fluoride ion donor[5] (*e.g.* HF/pyridine) or, more recently, by difluoroiodobenzene[6] derivatives (which must be prepared by the reaction of $ArICl_2$ with HF and a mercuric oxide catalyst).

Elemental fluorine has long been considered as not viable as a laboratory reagent, but is now emerging as a realistic, selective fluorinating reagent[7] and, here, we describe the conversion of dithiolanes into *gem*-difluoro compounds using elemental fluorine and iodine in a notably simple procedure at room temperature.

A series of diaryl 1,3-dithiolanes, prepared by literature methods,[8] were converted to the corresponding *gem*-difluorides by passing a stream of fluorine gas (diluted to 10% in dry nitrogen) through a solution comprising of the dithiolane, iodine and acetonitrile. Isolation of the desired products was achieved simply by pouring the reaction mixture into a solution of sodium metabisulfite and extracting with dichloromethane followed by column chromatography on silica gel. All yields are quoted as isolated yields of pure products with spectral data consistent with literature data.[9] See Table 1 for structures and reactions.

Recently, Rozen demonstrated[10] that IF, preformed at −78 °C by adding fluorine to iodine in $CFCl_3$, converted a range of hydrazones to *gem*-difluorides at low temperature. In our process, however, no cooling is necessary and the reaction may be simply controlled by adjusting the flow rate of fluorine–nitrogen mixture into the reaction vessel. It is possible that the reaction intermediate is iodine monofluoride and the mechanism of reactions of halogen fluorides with thiolanes is well established.[5] The precise nature of the fluorinating species has not been established but this simple procedure now provides a convenient method for the synthesis of *gem*-difluoro compounds from dithiolanes.

The scope of the present reaction and development of further fluorodesulfurization methodology using this procedure is being actively pursued.

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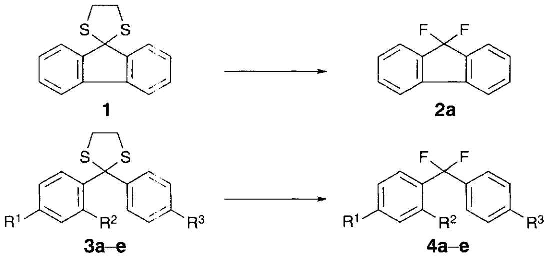
Table 1



Reagent and conditions: F_2, I_2, MeCN, room temp.

Thiolane	R^1	R^2	R^3	*gem*-Difluoride	Yield (%)
1a	—	—	—	**2a**	52
3a	H	H	H	**4a**	68
3b	Me	Me	H	**4b**	65
3c	Cl	H	H	**4c**	64
3d	Br	H	H	**4d**	61
3e	F	H	F	**4e**	66

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