N-Fluoro Perfluoroalkylsulphonimides: Efficient Reagents for the Fluorination of 1,3-Dicarbonyl Derivatives

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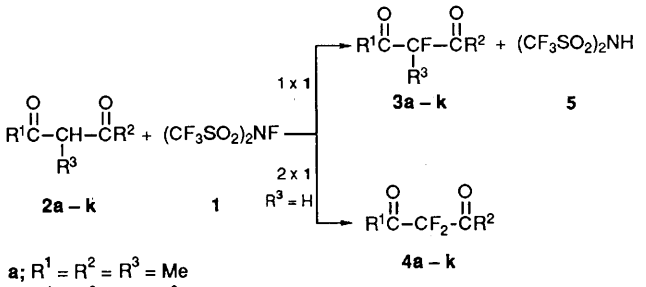
Fluorination of 1,3-dicarbonyl derivatives with *N*-fluoro sulphonimides afforded either 2-fluoro or 2,2-difluoro products in high yields.

Owing to the interesting biological, chemical and physical properties of organofluorine compounds, considerable effort has been made in the past two decades in the search for new fluorinating reagents and methodology for selective fluorination.[1] Recently, some interesting *N*-fluoro compounds have been introduced as electrophilic fluorinating reagents, which are easy to handle and effective to fluorinate a metal enolate and to transform it into an α-fluoro carbonyl compound. Among these *N*-fluoro compounds are *N*-fluoro-2-pyridone,[2] *N*-fluoro pyridinium trifluoromethanesulphonate,[3] *N*-fluoro

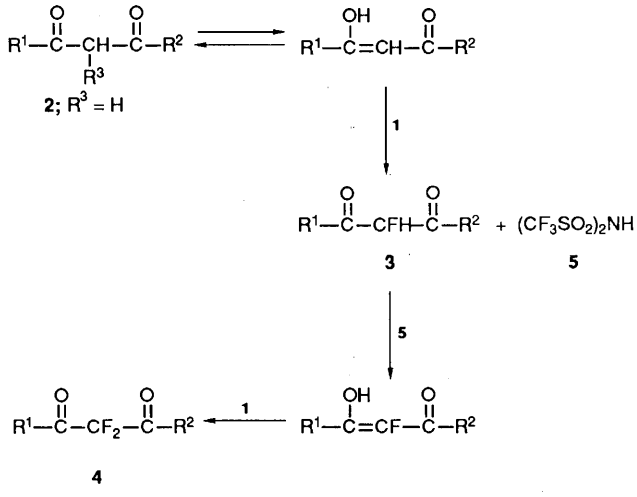
Table 1 Reaction of 1,3-dicarbonyl derivatives **2** with $(CF_3SO_2)_2NF$ **1** at 22 °C

Entry	Substrate	mol (%)	Solvent	*t*/h	Product	Yield (%)[a]
1	**2a**	100	CH_2Cl_2	7	**3a**	91
2	**2b**	100	CH_2Cl_2	7	**3b**	83
3	**2c**	100	CH_2Cl_2	4	**3c**	100
4	**2d**	200	CH_2Cl_2	3	**4d**	54
5	**2e**	200	CH_2Cl_2	20	**4e**	80
6	**2f**	200	CH_2Cl_2	24	**4f**	90
7	**2g**	200	CH_2Cl_2	24	**4g**	96
8	**2e**	150	CH_2Cl_2–H_2O	8	**3e**	86
9	**2f**	130	CH_2Cl_2–H_2O	11	**3f**	93
10	**2g**	150	CH_2Cl_2–H_2O	11	**3g**	86
11	**2h**	150	CH_2Cl_2–H_2O	10	**3h**	94
12	**2i**	130	CH_2Cl_2–H_2O	14	**3i**	91
13	**2j**[b]	100	THF[c]	5	**3j**	78
14	**2k**[b]	100	THF	3	**3k**	92

[a] Isolated yield after purification by silica gel chromatography. [b] Sodium enolate was used. [c] THF = tetrahydrofuran.



a; $R^1 = R^2 = R^3 = Me$
b; $R^1 = R^3 = Me$, $R^2 = OEt$
c; $R^1, R^3 = (CH_2)_3$, $R^2 = OEt$
d; $R^1 = R^2 = Me$, $R^3 = H$
e; $R^1 = Me$, $R^2 = OEt$, $R^3 = H$
f; $R^1 = C_6H_5$, $R^2 = Me$, $R^3 = H$
g; $R^1 = C_6H_5$, $R^2 = OEt$, $R^3 = H$
h; $R^1 = p\text{-}NO_2C_6H_4$, $R^2 = OEt$, $R^3 = H$
i; $R^1 = (Me)_2CH$, $R^2 = OEt$, $R^3 = H$
j; $R^1 = R^2 = OMe$, $R^3 = H$
k; $R^1 = R^2 = OEt$, $R^3 = Ph$



sulphonamide,[4] optically active *N*-fluoro sulphonamide,[5] *N*-fluoro quinuclidinium fluoride[6] and *N*-fluoro perfluoroalkyl sulphonimide,[7] the last of which was first synthesized in our laboratory and has been shown to be one of the best of the available reagents for electrophilic aromatic fluorination. As part of a continuing study of this new class of fluorinating agents, herein we report the fluorination of 1,3-dicarbonyl derivatives. Although some 2-fluoro- and 2,2-difluoro-1,3-dicarbonyl derivatives have been prepared by several different routes,[2–12] no general synthetic methodology has been developed.

Reactions of β-diketones and β-ketoesters with *N*-fluorobis[(trifluoromethane)sulphonyl]imide, $(CF_3SO_2)_2NF$ **1**, in dichloromethane at 22 °C proceed smoothly to give α-fluoro products. Thus, α-monofluoro compounds **3** could be obtained in good yields *via* the reaction of α-monosubstituted β-diketones and β-ketoesters **2a–c** (entry 1–3 in Table 1), and α,α-difluoro compounds **4** were formed when unsubstituted substrates **2** (R^3 = H) reacted with 2 equiv. of **1** (entry 4–7 in Table 1).

The formation of **4** and the fact that a mixture of monofluoro and difluoro products was formed in the reaction of unsubstituted substrates **2** (R^3 = H) with an equimolar amount of **1** might be atrributed to the fact that the monofluoro compounds **3** (R^3 = H) can be enolized by the very strong product acid $(CF_3SO_2)_2NH$ **5**[13] and then react further with the *N*-fluoro compound to form the difluoro derivatives.

Based on the foregoing hypothesis, the reaction could be stopped at the monofluoro stage if the acid **5** could be removed from the reaction system. In fact, when CH_2Cl_2–H_2O was used as the solvent, a high selectivity for monofluoro products **3** (R^3 = H) was observed in very good yields (entry 8–12 in Table 1). Considering that the strong acid $(CF_3SO_2)_2NH$ **5** is highly water-soluble, it is obvious that **5** could be rapidly partitioned into H_2O as formed and thereby removed from the reaction system (CH_2Cl_2 solution). Therefore, the enolization of the monofluoro compound and the subsequent fluorination are greatly reduced.

For β-diesters, in which the contribution of the enol form is small, no reaction takes place between the substrate and the *N*-fluoro compound. Fortunately, the reaction of the sodium enolate of the malonate esters with **1** is efficient and proceeds in good yield forming the monofluoro derivatives (entry 13 and 14 in Table 1).

In conclusion, *N*-fluoroperfluoroalkylsulphonimides, *i.e.* $(CF_3SO_2)_2NF$ **1**, have been demonstrated to be perhaps the best reagents for the fluorination of 1,3-dicarbonyl derivatives to form either 2-fluoro- or 2,2-difluoro-1,3-dicarbonyl analogues, depending on the reaction conditions. High yields are obtained for a variety of structural types. In the case of 1,3-dicarbonyl derivatives with low enol content, **1** only reacts with the sodium enolates. All of the products were identified by ^{19}F and ^1H NMR, IR and mass spectroscopy, and checked with reported data for known or related compounds. The monofluoro derivatives **3** (R^3 = H) are shown to exist predominantly in the keto forms.

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