

Received: November 29, 1983; accepted: January 11, 1984

SELECTIVE FLUORINATIONS WITH 1-FLUORO-2-PYRIDONE

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SUMMARY

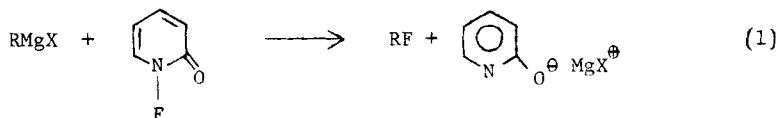
1-Fluoro-2-pyridone has been used to fluorinate selectively enamines and Grignard reagents under mild conditions.

INTRODUCTION

Recently, we reported the preparation of a new selective fluorinating reagent [1] that fluorinates malonates in the same way as perchloryl fluoride but without any of the hazards commonly associated with the perchloryl fluoride. This solid, 1-fluoro-2-pyridone, can be used as a regular organic synthetic reagent with no special safety devices and herein we describe its use in the preparation of 2-fluoroketones from enamines and of aryl and alkyl fluorides from Grignard reagents.

RESULTS AND DISCUSSION

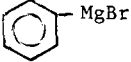

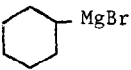
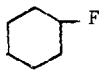
1-Fluoro-2-pyridone was prepared and purified as previously reported [1] and dissolved in methylene chloride. Equimolar solutions of aryl and alkyl Grignard reagents, prepared by standard procedures in diethyl ether, were added to the pyridone as shown in equation 1. After aqueous work-up,



the respective alkyl and aryl fluorides were analyzed by NMR (F and H) and GC. The percent yields and ^{19}F NMR signals are tabulated in Table I.

TABLE I

Fluorination of Grignard reagents

Grignard	Product	% yield ^a	¹⁹ F NMR, ppm ^b
		15	113(s)
		11	169(m)
$\text{CH}_3\underset{\text{MgBr}}{\text{CH}}(\text{CH}_2)_5\text{CH}_3$	$\text{CH}_3\text{CHF}(\text{CH}_2)_5\text{CH}_3$	5	174(m)

^a Determined by NMR. ^b Downfield from FCCl_3

Since current procedures for the preparation of α -fluoroketones include treatment of enol acetates with gaseous, toxic fluoroxytrifluoromethane [2] or enamines with gaseous, explosive perchloryl fluoride [3], we decided to attempt the fluorination with 1-fluoro-2-pyridone. N-Morpholino enamines were added to the pyridone in methylene chloride and the solutions were then refluxed. The α -fluoroketone was analyzed by NMR (F and H) and GC after aqueous work up and the sequence is summarized in equation 2. These reactions were investigated with varying ratios of pyridone to enamine as set out in Table II.

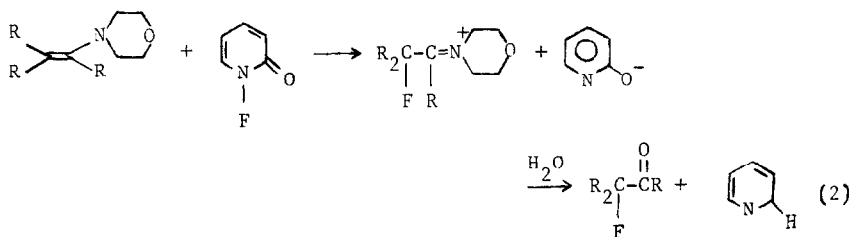

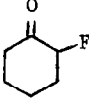




TABLE II

Fluorination of Enamines

Enamine of	$\left\{ \begin{array}{l} \text{moles pyridone} \\ \text{moles enamine} \end{array} \right\}$	Time (hr)	Product	% yield ^a	¹⁹ F NMR, ppm ^b
	1.0	24		44	187(d)
	2.0	22		36	
	2.0	49		33	177(d)
	4.0	91		11	
	5.0	38		24	
2,6-dimethyl-4-heptanone	2.0	61	3-fluoro-2,6-dimethyl-4-heptanone	23	200(dd)

^a Determined by NMR. ^b Downfield from FCCl_3

Selective fluorinations of enamines and Grignard reagents with 1-fluoro-2-pyridone both involve transfer of the fluorine from nitrogen to carbon. Although the products were produced in moderate to low yield, the ease of handling the solid reagent demonstrates its usefulness as a fluorinating reagent.

EXPERIMENTAL

¹H NMR and ¹⁹F NMR were recorded on a Varian EM-390 and are reported in parts per million (ppm). Gas-liquid partition chromatography was accomplished using a 30-m OV-17 column with a Hewlett-Packard 5880A instrument.

The 1-fluoro-2-pyridone used in this study was prepared as previously reported [1]. It was noted that 10% F_2 in N_2 gave product that was more difficult to purify than 5% F_2 in N_2 . N-Morpholino-1-cyclohexene was purchased from Aldrich Chemical Co. The N-morpholino enamines of desoxybenzoin and 2,6-dimethyl-4-heptanone and the Grignard reagents were prepared by standard procedures.

Enamines. To a solution of enamine in methylene chloride was added a solution of 1-fluoro-2-pyridone (ca. 1 to 4 molar equiv.) in methylene chloride and the reaction mixture were allowed to reflux. After an appropriate time, the reaction mixture was stirred with aqueous HCl solution and the crude fluoro-ketone mixture was analyzed by ^{19}F NMR, ^1H NMR and gas chromatography.

Aryl and Aliphatic Grignard Reagents. To a solution of Grignard reagent in diethyl ether was added a solution 1-fluoro-2-pyridone (ca. 1 molar equiv.) in methylene chloride at room temperature (phenyl magnesium bromide at 0°C). The mixture was then allowed to stir overnight at room temperature. After aqueous workup, removal of solvent, the fluorinated mixture was then analyzed by ^1H NMR, ^{19}F NMR and gas chromatography.

ACKNOWLEDGEMENT

This research was supported by a grant from Research Corporation.

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