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A FACILE METHOD FOR THE BECKMANN REARRANGEMENT USING 2-FLUOROPYRIDINIUM SALT OR 2-CHLOROPYRIMIDINIUM SALT

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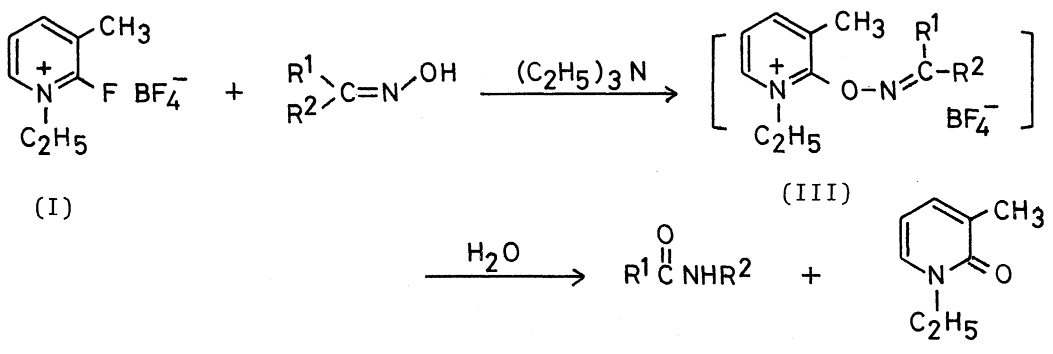
The Beckmann rearrangement of ketoximes easily proceeds under mild conditions to afford various amides in high yields by treating the oximes with 2-fluoropyridinium salt or 2-chloropyrimidinium salt.

In the course of our synthetic investigation[1)] utilizing the onium salts of azaaromatics, it was found that the Beckmann rearrangement of ketoximes easily proceeds under mild conditions to give various amides in high yields by treating oximes with 2-fluoropyridinium salt or 2-chloropyrimidinium salt.

Concerning the Beckmann rearrangement, there have numerous publications appeared which deal with the reagents for rearrangement. For example, concentrated sulfuric acid, phosphorus pentachloride, hydrogen chloride in a mixture of acetic acid and acetic anhydride, polyphosphoric acid[2)], benzenesulfonyl chloride[3)], p-toluenesulfonyl chloride , and 1,1'-carbonyldiimidazole[4)] are well known. But, the Beckmann rearrangement using most of these reagents proceeds under strongly acidic conditions or basic conditions. In the last example, the rearrangement proceeds under neutral conditions, but the yields are not always satisfactory after heating the intermediates, O-(1-imidazolylcarbonyl)oximes, in refluxing octane.

According to the present procedure to treat oximes with 2-fluoropyridinium salt or 2-chloropyrimidinium salt, the rearrangement smoothly proceeds at low temperature to afford the corresponding amides in high yields under mild conditions. The facility of the rearrangement may be explained by assuming the initial formation of O-(2-pyridinio)oximes (III) or O-(2-pyrimidinio)oximes (IV), which are in turn rearranged to afford the corresponding amides by treating with water as shown in the scheme. Especially, in the case of using pyrimidinium salt (II), the Beckmann rearrangement smoothly proceeds only by mixing oximes with II even in the absence of



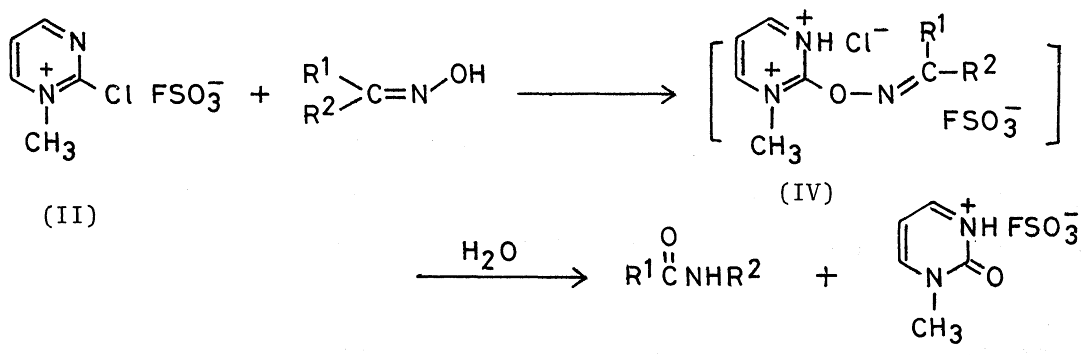


Table. The Beckmann rearrangement of oximes

Quaternary salt	R^1	R^2	Yield (%) of amide
I	C_2H_5	C_6H_5	94
II	C_2H_5	C_6H_5	92
I	$C_6H_5CH_2$	C_6H_5	93
II	$C_2H_5CH_2$	C_6H_5	95
II	CH_3	C_6H_5	94
II	CH_3	$2\text{-}C_{10}H_7$	92
II	C_6H_5	$t\text{-}C_4H_9$	91
II	C_6H_5	C_6H_5	quant
II	$-(CH_2)_5-$		94

tertiary amines. Furthermore, according to the present method, N-tert-butylbenzamide is obtained in high yield under very weakly acidic conditions from pivalophenone oxime, which is known to be rearranged to pivalanilide under the generally employed acidic conditions and to N-tert-butylbenzamide by heating with p-toluenesulfonyl chloride in alkaline solution[5].

The typical procedure for the Beckmann rearrangement using pyridinium salt (I) or pyrimidinium salt (II) is as follows.

(a) The rearrangement using 1-ethyl-2-fluoro-3-methylpyridinium tetrafluoroborate (I).

To a suspension of I (1.1 mmol, 249 mg) and deoxybenzoin oxime (1.0 mmol, 211 mg) in dry dimethoxyethane (2 ml) was added triethylamine (1.1 mmol, 111 mg) in dry dimethoxyethane (2 ml) under an argon atmosphere and the mixture was stirred for half an hour at 0°C to give a clear colorless solution. After being stirred for half an hour at room temperature, the reaction mixture was treated with water (20 ml), and then extracted with dichloromethane. The extracts, after being washed with 5% aq. HCl solution and water, were condensed under reduced pressure. Phenylacetanilide was isolated after separation by thin layer chromatography on silica gel (196 mg; 93% yield).

(b) The rearrangement using 2-chloro-1-methylpyrimidinium fluorosulfate (II).

To a mixture of II (1.1 mmol, 250 mg) and pivalophenone oxime (1.0 mmol, 177 mg) was added dry dimethoxyethane (3 ml) under an argon atmosphere and the mixture was stirred for half an hour at 0°C to give a white suspension. Then, it was stirred at room temperature for additional 6 hr. The resulting mixture, after being quenched by water (30 ml) at 0°C, was extracted with dichloromethane. The extracts were washed with water and condensed under reduced pressure to give almost pure (nmr spectrum) N-tert-butylbenzamide, which was purified by thin layer chromatography on silica gel (161 mg; 91% yield).

In a similar manner, various oximes were rearranged to the corresponding amides in high yields as shown in above table.

It should be noted that present method is of quite general utility; ketoximes are rearranged to amides in high yields under mild conditions by a simple procedure using readily available pyridinium or pyrimidinium salts.

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