## Recent Applications of Percutaneous USguided Radiofrequency Ablation in Treatment of Breast Cancer

Essay

# Submitted for partial fulfillment of the master degree in radio-diagnosis

 $\mathcal{B}y$ 

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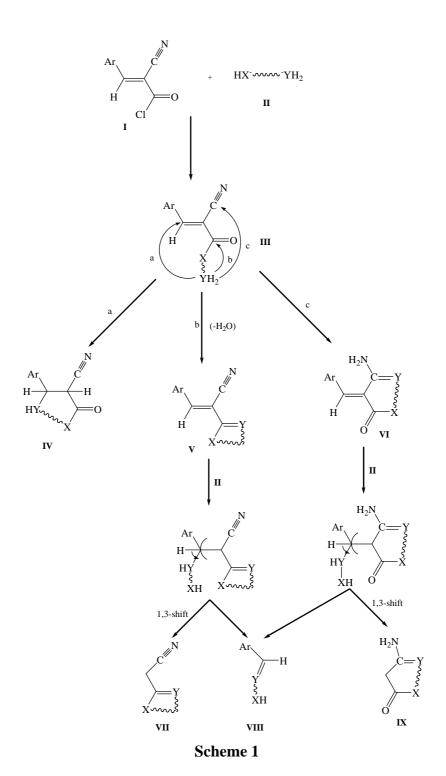
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#### I. Aims of the work

- 1) The recent widely uses of 2-propenoyl chloride derivatives in synthesis of highly important products as precursor of herbicides<sup>153</sup>, drugs, agrochemicals, pesticides and pharmaceutical intermediate<sup>63</sup>, ...etc make them worthy to be synthesized and encourage us to use new derivatives of these categories in synthesis analogous of new 2-propenoyl amides,<sup>92</sup> esters, 70,136,150,164 besides many of interesting biologically and pharmacologically active heterocyclic systems, like, oxadiazoles, 93,125 pyrazoles, 71,84 pyrazolopyrimidines, 45,109 pyridopyrimidines, benzoxbenzimidazoles, 96,161 azoles, 86,106,148 benzoxazine<sup>61</sup> quinazolines, benzothiazepines, 35,170 pyrimidinethiones and other heterocyclic systems.
- 2) The present investigation was planned, also, to study the effect of the 2-cyano group on the reactivity and stability of C<sub>2</sub>-C<sub>3</sub> double bond towards different strong to weak nucleophiles, besides its enhancement of nucleophilic addition at C<sub>2</sub>-C<sub>3</sub> double bond to give new heterocyclic derivatives.

As mentioned in (**Scheme 1**), strong nucleophiles (hydrazine hydrate and its derivatives) facilitate the breaking of  $C_2$ - $C_3$  bond.

In general (**Scheme 1**) is suggested, considering the mechanistic details of the studied reactions. The central aspect of this scheme is that there are three different routes for a ring-closure reaction of the primary product  $\mathbf{III}$  resulting from an attack of the bifunctional nucleophile  $\mathbf{II}$  with its hard nucleophilic center  $\mathbf{X}$  at the carbonyl chloride moiety of the adduct  $\mathbf{I}$  giving rise to the alternative formation of the products of type  $\mathbf{IV}$ ,  $\mathbf{V}$ , or  $\mathbf{VI}$ . These products can be incorporated into consecutive reactions, e.g., with a second equivalent of the nucleophilic reagent  $\mathbf{II}$  which reacts subsequently with its soft nucleophilic group  $\mathbf{Y}$  at  $\mathbf{C}_3$  of the arylonitrile moiety giving rise to the products of the type  $\mathbf{VII}$ ,  $\mathbf{VIII}$ , or  $\mathbf{IX}$ .



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# Chemistry of Heterocyclic Acryloyl Derivatives (amides & esters)

#### 1- Introduction

Acryloyl amides and acryloyl esters are useful reagents for Diel's-Alder reactions <sup>126,127</sup> Michael addition and conjugated substitution reactions <sup>115,143</sup>.

#### 2- Synthesis of 2-propenoyl chlorides, amides and esters:

2-propenoylamides and esters are commonly prepared from the corresponding acid via the acid chloride 80,115,116,126,127,143,151

The acid chlorides were prepared by heating the acid with chlorinating agent under conditions inhibiting side reaction and polymerization. A preferred chlorinating agent is a volatile reagent, for example, COCl<sub>2</sub>, SOCl<sub>2</sub>, F<sub>3</sub>C-COCl or COCl<sub>2</sub> which form only volatile byproduct. The polymerization is inhibited by using a catalyst which forms an intermediate complex with the chlorinating agent, there by preventing the formation of mixed anhydride<sup>37</sup>.

The chlorinating agent may afford a halogen exchange, for example, heating 3-bromo acrylic acid with thionyl chloride gave 3-chloro acryloyl chloride<sup>80,151</sup>. Reaction of 3-(5-aryl-2-furyl)propenoic acid **1** with thionyl

chloride gave thieno[3,2-b]furan-5-carboxyl acid chloride **2** as side product <sup>82</sup>.

 $R_1R_2C$ =CR-COCl were prepared in 60-83% yield by chlorination of  $R_1R_2C$ =CR-CO<sub>2</sub>H with SOCl<sub>2</sub>/DMF or reflux of  $R_1R_2C$ =CR-CONH<sub>4</sub> with COCl<sub>2</sub>; R= H, Me;  $R_1R_2$  = H, Br, Cl <sup>150</sup>.

$$\begin{array}{c} Ph\overset{H}{-}C\overset{H}{-}C\overset{H}{-}C - Cl + ROH \longrightarrow Ph\overset{-}{-}C = C\overset{-}{-}C - CR \\ Cl Cl O & H Cl O \\ \hline R = o, m, p-tolyl \\ = o, m, p-NO_2 \end{array}$$

Acrylic acid derivatives  $RCH=CHCOR_1$  [R = Cl, Br, I;  $R_1$  = OH, alkoxy, unsubstituted phenoxy, amino, alkylamino, dialkylamino] were prepared and showed fungicidal activity esp. wood. Thus, treating of propiolic acid with NaOBr and Na<sub>2</sub>CO<sub>3</sub> gave Br-C C-COOH whose photochemical iodination by iodine in  $CCl_4$  gave Br-Cl=Cl-COOH  $^{103}$ .

The esters  $CH_2=C(CI)-COOCH_2-(CF_2)_n-CF_3$  [n = 0,1,2] were prepared by reaction of  $HO-CH_2-(CF_2)-CF_3$  with acrylic acid in the presence of  $H_2SO_4$  or fuming  $H_2SO_4$ , chlorination of the resulting acrylate and removal of HCI from the resulting , -unsaturated dichloro propionate  $^{103}$ .

# 3- Applications and biological activities of 2-propenoyl chlorides, amides and esters:

When 2-propenoyl chloride and its substituted derivatives are amidated or esterified, they provide the corresponding amides and esters which have useful applications in the organic synthesis of a variety of chemicals used in our daily life.

Amides **3** were prepared by different methods. Some **3** inhibited coniferyl alc. Dehydrogenose <sup>36</sup>.

 $R_1 = H, \ and \ R_2 = Ph, \ pyridyl, \ pyridylalkyl, \ PhCHMe, \ 2\mbox{-}(3\mbox{-}indolyl)ethyl$ 

OR

 $NR_1R_2 = 2$ -thioxo-3-thiazolidinyl  $R_3 = H$ , OMe;  $R_4 = H$ , OH, OMe;  $R_5 = H$ , OMe.

The benzopyrane derivatives **4** ( $R_1$ ,  $R_4$  = H, Alkyl;  $R_2$  = H, Alkoxy;  $R_3$  = H, Alkyl, Alkoxy; n = 0, 1, 2) useful as antiallergics, were prepared by Ejiri, Katsuji <sup>40</sup>.

Thus a solution of  $\mathbf{5}$  (R = OH) and  $SOCl_2$  in benzene in the presence of DMF was refluxed to give  $\mathbf{5}$  (R = Cl) which was treated with anthranilic acid in benzene in the presence of pyridine to afford 57% of  $\mathbf{6}$ .

Thiazinobenzimidazol 7 was prepared by reacting of benzimidazol-2-thione with 2-propenoyl chloride derivative and show high herbicidal activity  $^{20,21}$ .

Esterification of mucochloric acid with propenoyl chloride derivative in benzene gave the furanone derivatives **8** as agrochemical fungicides <sup>83</sup>.

o-Alkanoyl phenols  $\bf 9$  were treated with cinnamoyl chloride and  $K_2CO_3$  in  $Me_2CO$  to yield the chromones  $\bf 10^{125}$ 

HO OH CH<sub>2</sub>R<sub>1</sub> + Ph-CH=CH-COCl R<sub>2</sub> O (9)
$$R_1 = H, \text{ Me, Ph} \\ R_2 = H, \text{ OH}$$

$$O \subset CH = CH - Ph$$

$$O \subset CH = CH - Ph$$

$$R_2 = H, OH$$

$$O \subset CH = CH - Ph$$

$$R_2 = H, OH$$

$$O \subset CH = CH - Ph$$

$$R_1 = H, OH$$

$$R_2 = H, OH$$

$$R_2 = H, OH$$

$$R_2 = H, OH$$

$$R_3 = H, OH$$

$$R_4 = H, OH$$

$$R_5 = H, OH$$

Reaction of 3-(3-pyridyl)acryloyl chloride with N-trimethylsilyl-2-piperidinone gave the lactam derivative **11** as interleukin-1- and tumor necrosis factor releasing inhibitor  $^{73}$ .

$$\begin{array}{c}
O \\
C = C - C - C \\
N = 
\end{array}$$

$$\begin{array}{c}
O \\
H H \\
\end{array}$$

$$\begin{array}{c}
O \\
1) \text{ toluene} \\
2) H C \\
\end{array}$$

$$\begin{array}{c}
C - N \\
C = C \\
\end{array}$$

$$\begin{array}{c}
O \\
C = C \\$$

$$\begin{array}{c}
O \\
C = C \\
\end{array}$$

$$\begin{array}{c}
O \\
C = C \\
\end{array}$$

$$\begin{array}{c}
O \\
C$$

Reaction of , -unsaturated acid chloride 12 with primary enaminonitrile 13 in presence of triethyl amine affords under very mild conditions, a simple and highly efficient regiospecific synthesis of poly substituted 3,4-dihydro-2(1H)-pyridones  $14^{23}$ .

Matteucinol 15 which was isolated from *Rhododendron Simsii* and has expectorant activity was prepared by cyclocondensation of 16 with p-

methoxycinnamoyl chloride or by Friedel-Craft's acylation of **16** and cyclocondensation of the resulting **17** with p-methoxy benzaldehyde  $^{165}$ .

Pyridylquinolinone **18** has positive isotropic activity and was prepared by treatment of 2-methoxy-4-pyridyl aniline **19** with 3-ethoxy-2-propenoyl chloride in THF <sup>87</sup>.