Recent Applications of Percutaneous US-guided Radiofrequency Ablation in Treatment of Breast Cancer

Essay

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

By

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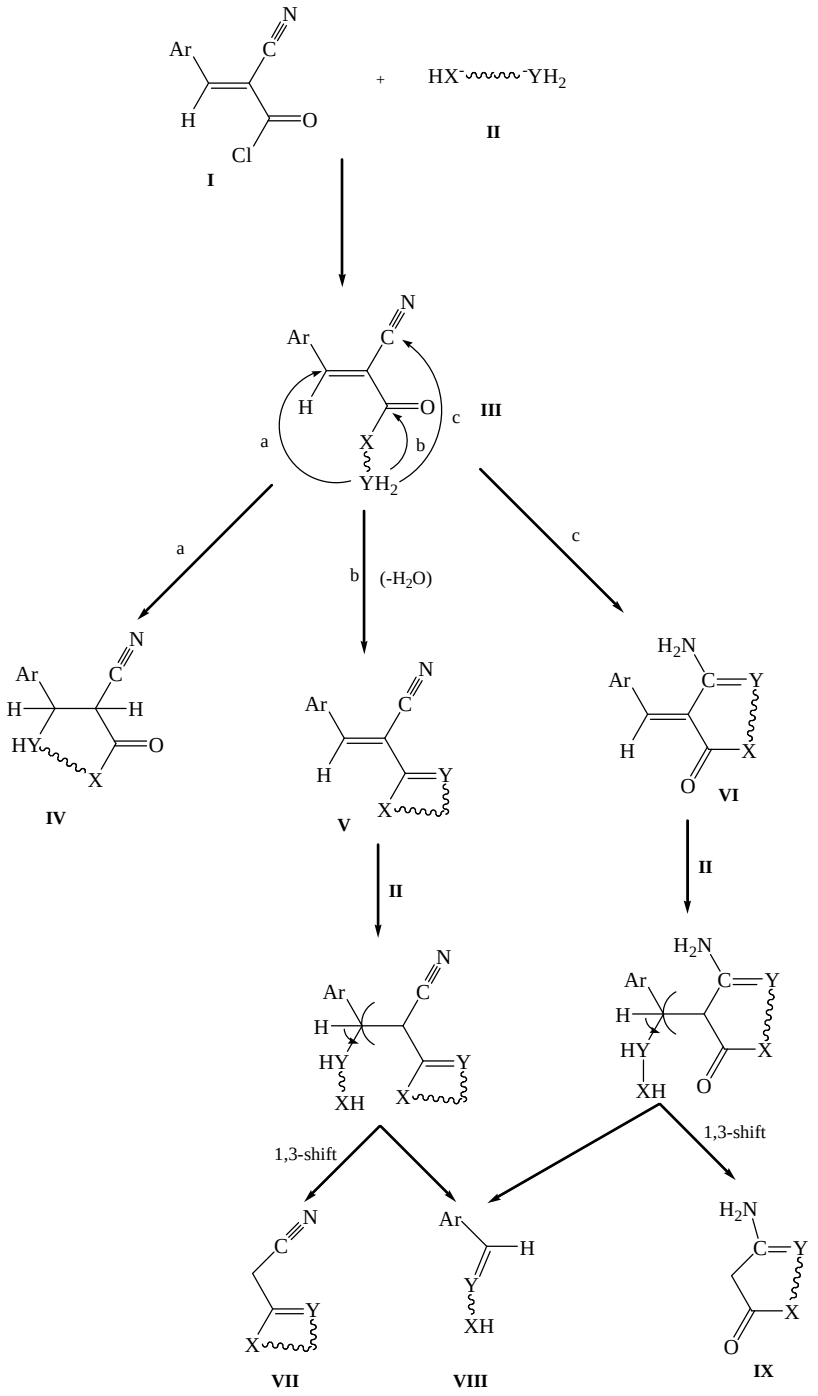
I. Aims of the work

1) The recent widely uses of 2-propenoyl chloride derivatives in synthesis of highly important products as precursor of herbicides[153], drugs, agrochemicals, pesticides and pharmaceutical intermediate[63], …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,[92] 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, benzoxazoles,[86,106,148] benzimidazoles,[96,161] benzoxazine[61] 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_2-C_3 double bond towards different strong to weak nucleophiles, besides its enhancement of nucleophilic addition at C_2-C_3 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 **III** resulting from an attack of the bifunctional nucleophile **II** with its hard nucleophilic center **X** at the carbonyl chloride moiety of the adduct **I** giving rise to the alternative formation of the products of type **IV**, **V**, or **VI**. These products can be incorporated into consecutive reactions, e.g., with a second equivalent of the nucleophilic reagent **II** which reacts subsequently with its soft nucleophilic group **Y** at C_3 of the arylonitrile moiety giving rise to the products of the type **VII**, **VIII**, or **IX**.


Ar
C
N
H
O
Cl
I
+
HX-YH2
II
III
a
b
c
X
YH2
(-H2O)
IV
V
VI
H2N
Y
HY
XH
1,3-shift
VII
VIII
IX

Scheme 1

Contents

• Part one

• Part two

• Part three

Chemistry of Heterocyclic Acryloyl Derivatives (amides & esters)

1- Introduction

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

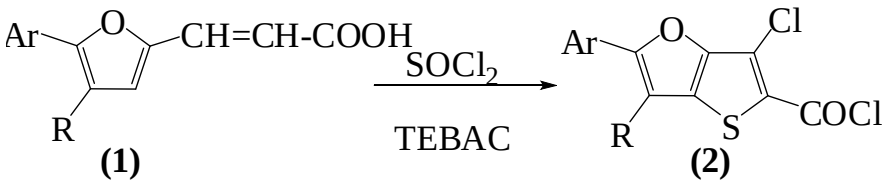
2- Synthesis of 2-propenoyl chlorides, amides and esters:

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, $COCl_2$, $SOCl_2$, F_3C-COCl or $COCl_2$ 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[37].

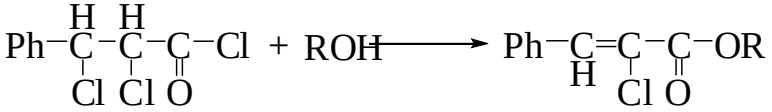
The chlorinating agent may afford a halogen exchange, for example, heating 3-bromo acrylic acid with thionyl chloride gave 3-chloro acryloyl chloride[80,151]. Reaction of 3-(5-aryl-2-furyl)propenoic acid **1** with thionyl

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

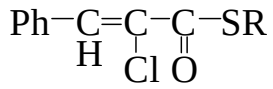


R = H Ar = $2NO_2$-C_6H_4
= Cl Ar = Ph
= Cl Ar = $4Cl$-C_6H_4

R_1R_2C=CR-COCl were prepared in 60-83% yield by chlorination of R_1R_2C=CR-CO_2H with $SOCl_2$/DMF or reflux of R_1R_2C=CR-$CONH_4$ with $COCl_2$; R= H, Me; R_1R_2 = H, Br, Cl [150] .



R = o, m, p-tolyl
= o, m, p-NO_2



Were prepared by similar manner.[81]

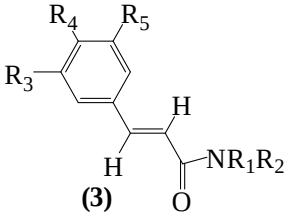
Acrylic acid derivatives RCH=CHCOR_1 [R = Cl, Br, I; R_1 = OH, alkoxy, unsubstituted phenoxy, amino, alkyl-amino, dialkylamino] were prepared and showed fungicidal activity esp. wood. Thus, treating of propiolic acid with NaOBr and Na_2CO_3 gave Br-C≡C-COOH whose photochemical iodination by iodine in CCl_4 gave Br-Cl=Cl-COOH [103] .

The esters CH_2=C(Cl)-$COOCH_2$-$(CF_2)_n$-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 HCl from the resulting α,β-unsaturated dichloro propionate[103].

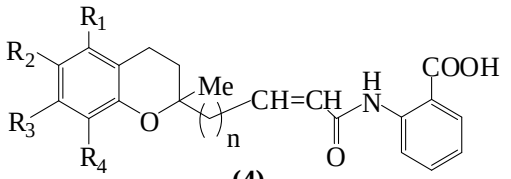
3- Applications and biological activities of 2-propenoyl chlorides, amides and esters:

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 [36].



(3)

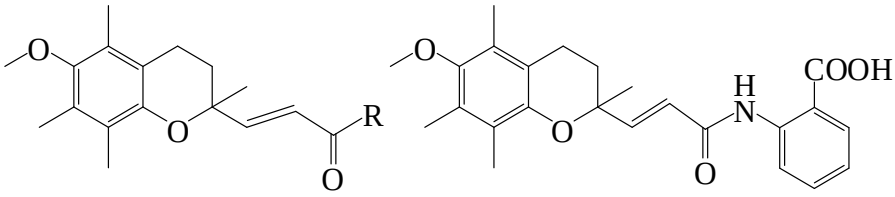


(4)

R_1 = H, and R_2 = Ph, pyridyl, pyridylalkyl, PhCHMe, 2-(3-indolyl)ethyl

OR

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

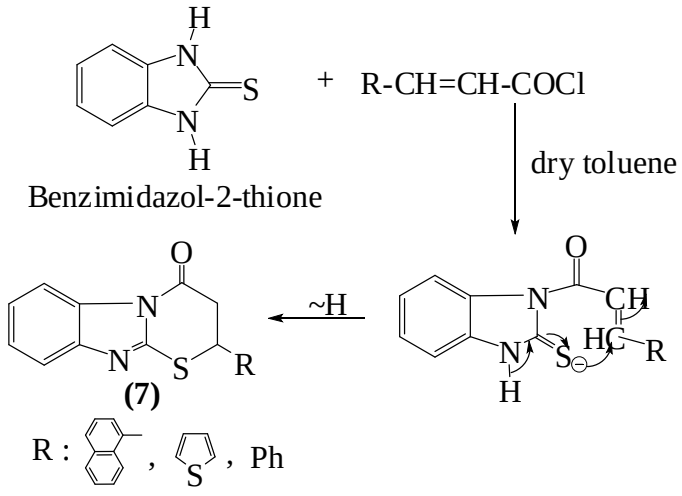


(5) **(6)**

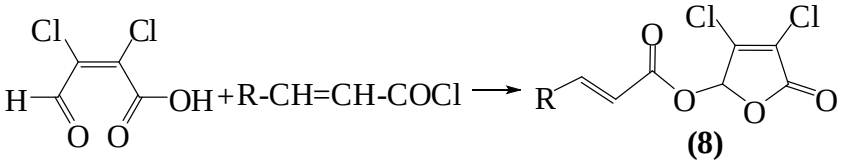
The benzopyrane derivatives **4** (R_1, R_4 = H, Alkyl; R_2 = H, Alkoxy; R_3 = H, Alkyl, Alkoxy; n = 0, 1, 2) useful as antiallergics, were prepared by Ejiri, Katsuji [40].

Thus a solution of **5** (R = OH) and $SOCl_2$ in benzene in the presence of DMF was refluxed to give **5** (R = Cl) which was treated with anthranilic acid in benzene in the presence of pyridine to afford 57% of **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 [83] .

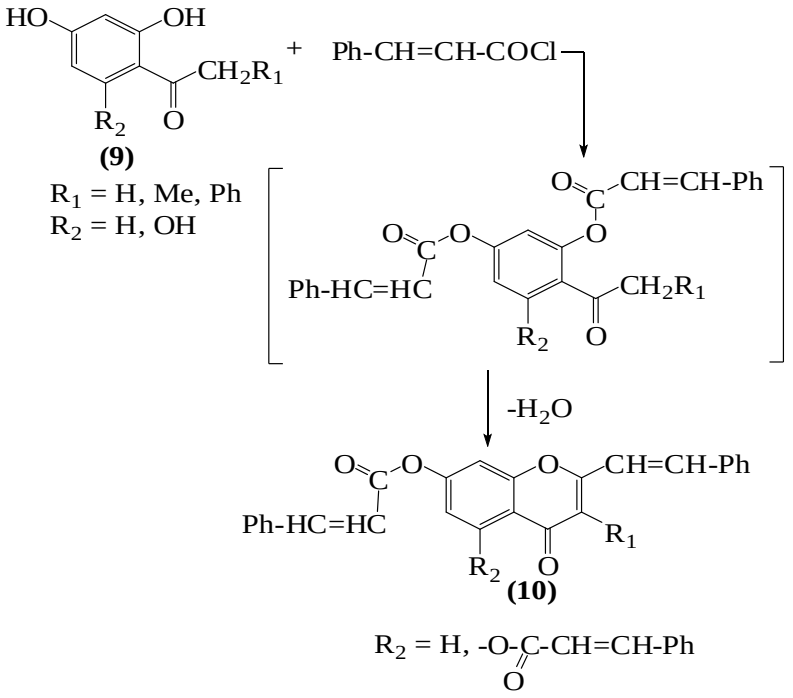


Mucochloric acid

(8)

R = Ph, 3-Cl-C_6H_4, 3,4-Cl_2-C_6H_3, 3-MeO-C_6H_4, 4-Me-C_6H_5, 2-furyl, 3-nitro-2-furyl

o-Alkanoyl phenols **9** were treated with cinnamoyl chloride and K_2CO_3 in Me_2CO to yield the chromones **10** [125]



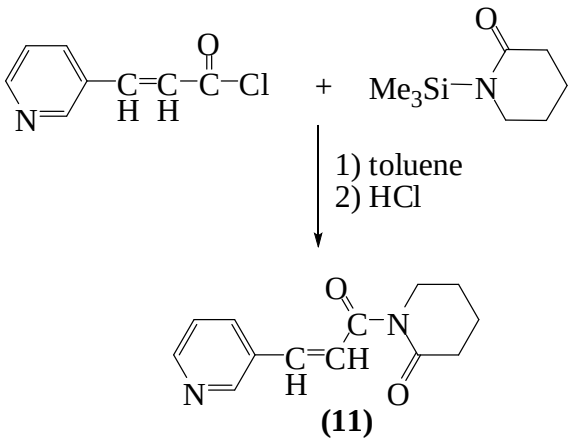
(9)

R_1 = H, Me, Ph
R_2 = H, OH

(10)

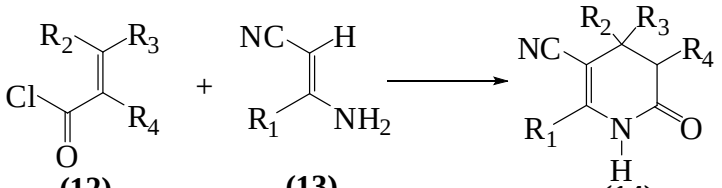
R_2 = H, -O-C(=O)-CH=CH-Ph

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



(11)

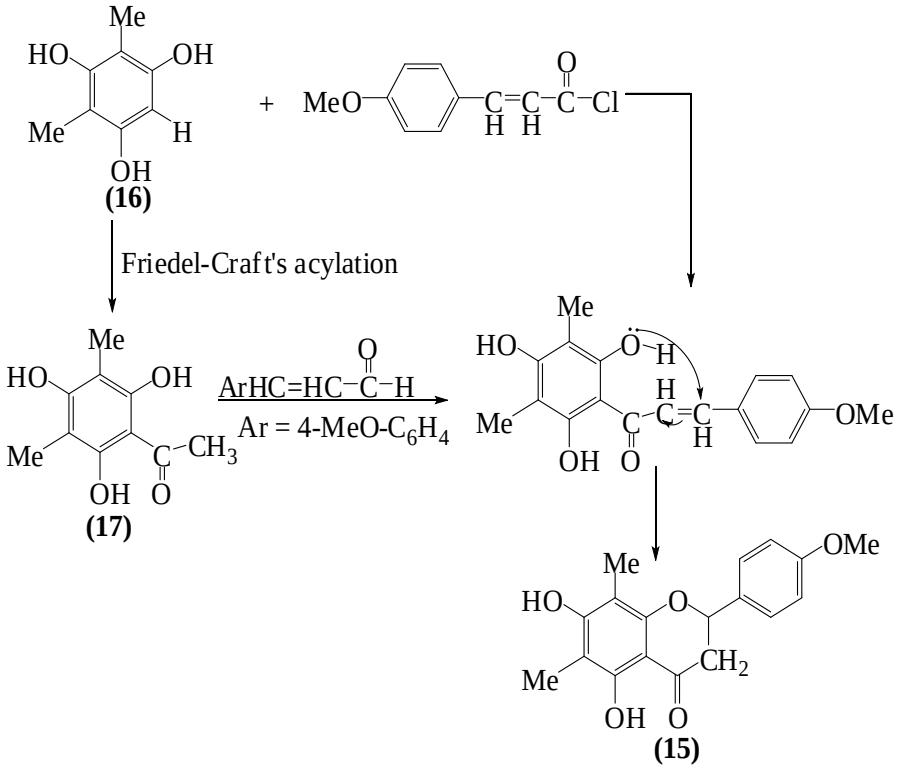
Reaction of α,β-unsaturated acid chloride **12** with primary enaminonitrile **13** in presence of triethyl amine affords under very mild conditions, a simple and highly efficient regiospecific synthesis of poly substituted 3,4-dihydro-2(1H)-pyridones **14** [23].



(12) **(13)** **(14)**

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 [87].