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FRIEDEL-CRAFTS COORDINATED PROCESSES:
SELECTIVE CYCLOOLIGOMERIZATION OF ACYL CHLORIDES

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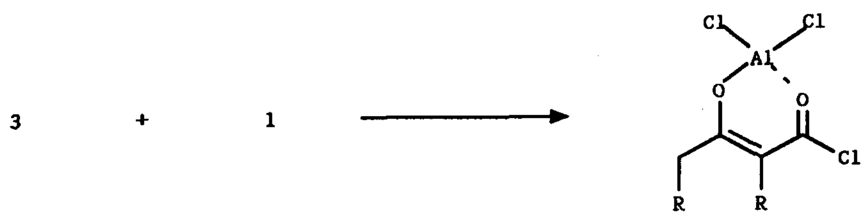
Summary - Adducts $AlCl_3.RCOCl$ undergo highly regioselective self- and cross-condensation. 4-Hydroxy-2-pyrones and 2-acetyl-indan-1,3-diones are synthesized in good yields.

Aliphatic acid chlorides and anhydrides undergo condensation with different carbonyl compounds affording polymeric materials[1] as well as oligomers, including cyclic derivatives[2] and polyhydric phenols.[3] Despite the intensive studies in this area the selective oligomerization of acyl chlorides remains a still open problem, particularly when the cross-condensation of different substrates is involved.

During our studies on the ortho-coordinated acylation of phenol salts[4] our attention turned to the evaluation of the relative stability of adducts between $AlCl_3$ and various acyl chlorides, and the reactivity of these complexes toward different carbonyl derivatives.[5] Now we found that $AlCl_3.RCH_2COCl$ adducts are able to promote strictly controlled dehydrohalogenative cross- as well as self-condensation of acyl chlorides. This study make it possible to evidence the regiochemical behaviour of the reaction solely as a function of R in RCH_2COCl.

SCHEME

$$\underset{1}{RCH_2COCl + AlCl_3} \rightleftharpoons \underset{2}{RCH_2CCl\text{-}O\bullet AlCl_3} \rightleftharpoons \underset{3}{HCl + RCH\text{=}CCl\text{-}O\text{-}AlCl_2}$$



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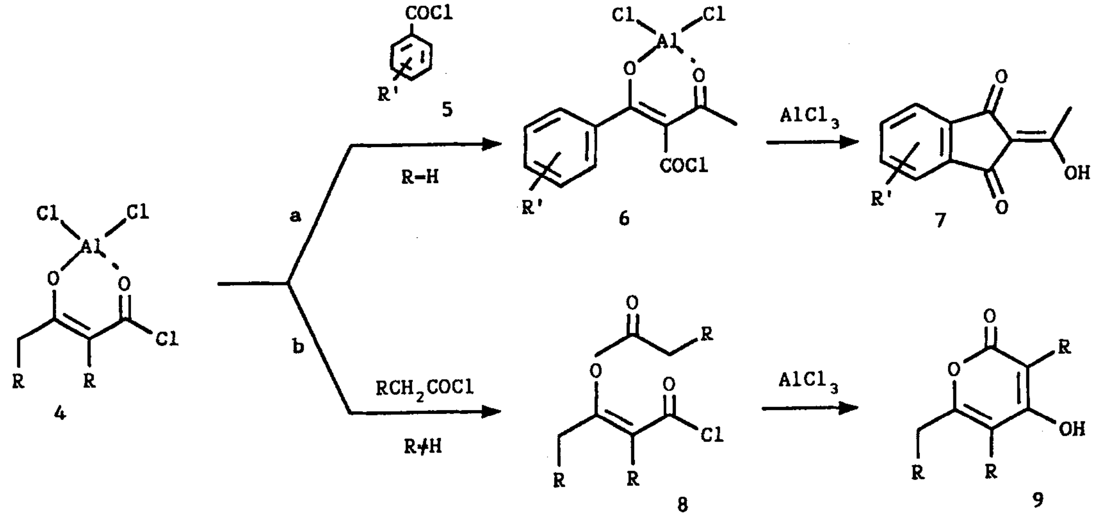

As depicted in the Scheme, 2-acetyl-indan-1,3-diones 7 (route a) or 4-hydroxy-2-pyrones 9 (route b) are obtained in high yields and complete regiochemical control.

All reactions were carried out by adding the aliphatic acid chloride 1 (0.02 mol) to a solution of $AlCl_3$ (0.03 mol) and aromatic acid chloride 5 (0.01 mol) in dry nitrobenzene and heating the mixture at 100°C for 5 h.

Table 1. Preparation of 2-acetyl-indan-1,3-diones 7 (see Scheme) by sequence cross-condensation of acetyl chloride and aroyl chlorides

Entry	R'	Yield(%)[a]	M.p.,°C (solvent)
1	H	87	109 (EtOH)
2	5-CH_3	80	79-81 (CH_2Cl_2)
3	5-OCH_3	75	90[b]
4	5-NO_2	45	110[b]

[a] Represents yields of products after extraction with 20% Na_2CO_3, treatment of the aqueous layer with 10% HCl, extraction with ether and drying with Na_2SO_4, followed by chromatography on SiO_2/eluant hexane-ethyl acetate.

[b] Decomposition point.

Table 2. Preparation of 4-hydroxy-2-pyrones 9 (see Scheme) by cyclotrimerization of acyl chlorides

Entry	R	Yield(%)[a]	M.p., °C (solvent)
1	CH_3	75	151-2 (EtOH-Tol.)
2	CH_3CH_2	70	78-80 (EtOH-Tol.)
3	$CH_3(CH_2)_2$	80	81-2 (Tol.)
4	$CH_3(CH_2)_3$	75	(foam)

[a] See note a) Table 1.

On the basis of reports from literature[6] and our previous results[7] we can hypothesize the following reaction pathway: an aldol-type condensation of the enol acyl chloride 3 with the starting matierial 1 produces the β-ketoacid chloride 4, as Aluminum chelate.[8] At this point, the intermediate 4 could react with the aromatic acyl chloride 5 (route a, cross-condensation) or the aliphatic one (route b, self-condensation). Our results demonstrate there is a fine balance between the two chemical pathways solely depending on the nature of R in RCH_2COCl. Indeed, when R = H the intermediate 4 reacts at the active methylene carbon with the aromatic acyl chloride 5 affording the highly enolized tricarbonyl derivative 6. The successive chemical evolution of 6 merits comment. Recent ^1H NMR studies suggest that the major part of the enolization of compounds like 6 may be ascribed to the β-dicarbonyl structural unit involving the benzoyl group, with the consequent loss of the electronwithdrawing effect of the aromatic C=O.[9] Moreover the chlorocarbonyl functional group lies in the proximate ortho-position with respect the aromatic C=O. As a consequence the intramolecular electrophilic acylation occurs very quickly affording 2-acetyl-indan-1,3-diones 7. It is noteworthy that the synergism of the β-dicarbonylic group enolization and the proximity effect promotes also extremely unfavored electrophilic reactions as in the case of 4-nitrobenzoyl chloride (Table 1, Entry 4).

As we anticipated in the first part of the present communication, the reactivity of the intermediate 4 strictly depends on the nature of R in RCH_2COCl. When R = CH_3, C_2H_5 or C_3H_9, a dramatic change in the chemical behaviour of 4 was observed. Indeed, in all these cases, compound 4 reacts with a third molecule of the aliphatic acyl chloride 1 affording the enol ester 8 which is extremely reactive toward cyclization[10] and 4-hydroxy-2-pyrones 9 are obtained as final reaction products.[11]

In conclusion we found that acyl chlorides-$AlCl_3$ complexes promote regiochemical control in the oligomerization of acyl chlorides including cross-condensation. The reaction opens a direct and selective route to indandiones and α-pyrones, two classes of substances playing an important role in organic synthesis[12] and occurring in several types of natural and biologically active compounds.[3,6] More detailed studies concerning this reaction are necessary to determine the mechanism which seems more complex than can be solved by the simplified hypotheses here described. However these first results indicate the large possibilities of controlling specific reaction pathways by using peculiar Lewis acids in Friedel-Crafts like processes.[13]

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13.- Preliminary results evidenced the great importance of the Lewis acid and the solvent in this specific reaction. For instance, 4-propionyloxy-3,5-dimethyl-6-ethyl-2-pyrone represents the unique product (65% yield) when propionyl chloride was cyclotrimerized in 1,2-dichloroethane instead of nitrobenzene in the presence of $AlCl_3$.

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