An Expeditious Synthesis of 4-Acyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidines (6-acyl uracils) and 4-Acyl-6-aryl-2-oxo-2,3-dihydropyrimidines

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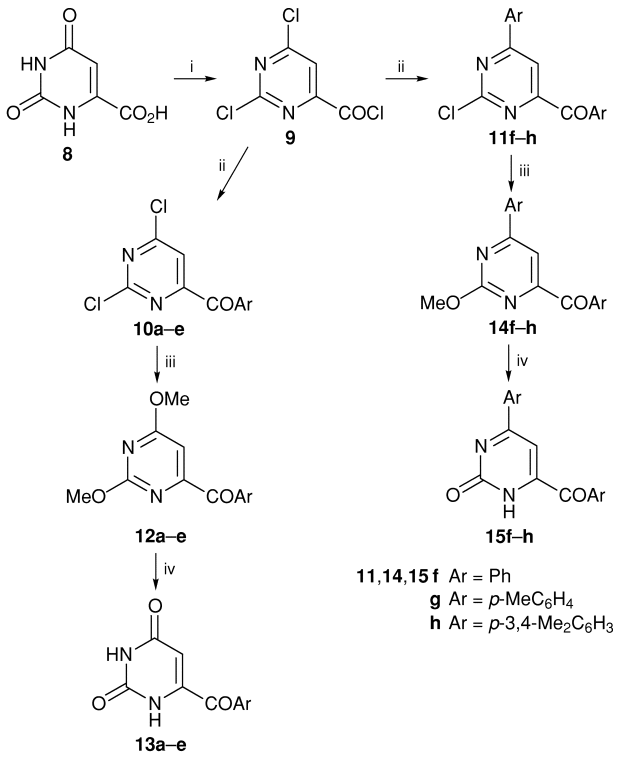
A facile synthesis of 4-acyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidines (6-acyl uracils) and 4-acyl-6-aryl-2-oxo-2,3-dihydropyrimidines is described where the Friedel–Crafts reaction on 2,6-dichloropyrimidine-4-carbonyl chloride plays a crucial role.

In view of the significant biological activities of various 6-substituted uracils and related pyrimidine derivatives,[10,13,15] we became interested in developing methods for the synthesis of novel 6-substituted uracils and pyrimidines. Recently we have described a palladium-catalysed reaction for the synthesis of novel 6-substituted uracils.[21] In this paper we report a very facile method for the synthesis of a number of 6-substituted uracils and the related pyrimidine derivatives where the classical Friedel–Crafts reaction has been utilised very effectively.

The 6-substituted uracils and the pyrimidines were synthesised according to the reaction sequence shown in Scheme 1.

2,6-Dichloropyrimidine-4-carbonyl chloride **9** was synthesised according to the procedure of Gershon.[24] Compound **9** underwent a smooth Friedel–Crafts reaction with benzene and substituted benzene derivatives in the presence of anhydrous aluminium chloride in which the acid chloride moiety was found to react predominantly (entries 1–8, Table 1).

However, it was noticed that in case of benzene and alkyl benzenes (*e.g.* toluene and *o*-xylene), further Friedel–Crafts reaction took place at the C-6 position of the pyrimidine ring leading to the disubstituted compounds **11f–h** (entries 6–8). The yields of the Friedel–Crafts products were very good (70–88%) except in case of entry 5. The dichloropyrmidines **10a–e** and the chloropyrimidines **11f–h** were converted to the corresponding dimethoxypyrimidines **12a–e** and the methoxy pyrimidines **14f–h** respectively on treatment with sodium methoxide in methanol. The latter on refluxing with 6 M hydrochloric acid were converted to 4-acyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidines (6-acyl uracils) **13a–e** and 4-acyl-6-aryl-2-oxo-2,3-dihydropyrimidines **15f–h** respectively in quantitative yields.



Scheme 1 *Reagents and conditions*: i, $POCl_3$, PCl_5, reflux, 2 days; ii, ArH, $AlCl_3$, 0 °C–rt, 2 h; iii, NaOMe, MeOH, reflux, 4 h; iv, 6 M HCl, reflux, 4 h

Table 1 Products from the Friedel–Crafts reaction of 2,6-dichloropyrimidine-4-carbonylchloride **9** with aromatic compounds (Scheme 1)

				Product	
Entry	Aromatic compounds (ArH) (Ar)	Solvent	Time/h	**10** (% yield)[a]	**11** (% yield)[a]
1	BrC_6H_4	Neat	2	88	—
2	$MeOC_6H_4$	Neat	2	84	—
3	HOC_6H_4	$Cl_2CHCHCl_2$	2	70 (*p*:*o*-isomer, 2:3)	—
4	2,3-$(HO)_2C_6H_3$	$Cl_2CHCHCl_2$	5	61	—
5	$CH_3CONHC_6H_4$	$Cl_2CHCHCl_2$	5	42	—
6	C_6H_5	Neat	2	—	80
7	$CH_3C_6H_4$	Neat	2	—	74
8	1,2-$Me_2C_6H_3$	Neat	2	—	70

[a]Yields are based on 2,6-dichloropyrimidine-4-carbonyl chloride **9**.

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The 4-acyl-2,6-dioxo-1,2,3,6-tetrahydropyrimidines (6-acyl uracils), 4-acyl-6-aryl-2-oxo-2,3-dihydropyrimidines and the other compounds synthesised were characterised by CHN analyses, ^{1}H NMR, ^{13}C NMR and IR spectroscopic data.

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Techniques used: IR, ^{1}H and ^{13}C NMR

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