

## REACTION OF URACILS WITH GRIGNARD REAGENTS

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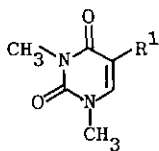
Mitahora-higashi, Gifu 502, Japan

Uracil derivatives exhibit high reactivity toward nucleophilic reagents, such as  $\text{NaHSO}_3$ ,  $\text{RSH}$ ,  $\text{RNH}_2$ ,  $\text{NaCN}$ ,  $\text{NH}_2\text{C(X)=NH}$ , bringing about addition, cine-substitution, or ring transformation.\* Here is described reaction of 5-substituted uracil derivatives with Grignard reagent as a nucleophile.

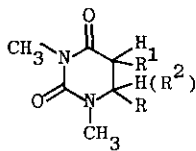
Thus, treatment of the 5-cyanouracil (I:  $\text{R}^1=\text{CN}$ ) with various  $\text{RMgX}$  reagents in THF afforded the 6-substituted 5,6-dihydrouracils (II:  $\text{R}^1=\text{CN}$ ,  $\text{R}=\text{Me}$ ,  $\text{Et}$ ,  $\text{Ph}$ ,  $\text{CH}_2\text{Ph}$ ) in good yields. The structure of II ( $\text{R}^1=\text{CN}$ ,  $\text{R}=\text{Me}$ ) was confirmed by comparison of authentic sample prepared by reduction of 5-cyano-1,3,6-trimethyluracil with  $\text{NaBH}_4$ .

The 5-nitrouracil (I:  $\text{R}^1=\text{NO}_2$ ) reacted with 1.2 eq. of  $\text{MeMgBr}$  to give the expected product (II:  $\text{R}^1=\text{NO}_2$ ,  $\text{R}=\text{Me}$ ) and the nitrone compound (III:  $\text{R}=\text{Me}$ ), and further treatment of II ( $\text{R}^1=\text{NO}_2$ ,  $\text{R}=\text{Me}$ ) with  $\text{MeMgBr}$  gave III ( $\text{R}=\text{Me}$ ). Use of excess  $\text{RMgX}$  resulted in formation of III ( $\text{R}=\text{Me}$ ,  $\text{Ph}$ ,  $\text{CH}_2\text{Ph}$ ) as the sole product. These results suggest that compound II ( $\text{R}^1=\text{NO}_2$ ) is an intermediate in the formation of III.

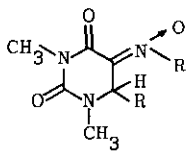
Treatment of 5-halogenouracils (I:  $\text{R}^1=\text{Br}$ ,  $\text{Cl}$ ,  $\text{F}$ ) with  $\text{MeMgBr}$  yielded abnormal products (IV:  $\text{R}^1=\text{Br}$ ,  $\text{Cl}$ ,  $\text{F}$ ,  $\text{R}^2=\text{H}$ ). Similar treatment of 5-halogeno-1,3,6-trimethyluracils (V) also gave the 4-methylene compounds (IV:  $\text{R}^1=\text{Br}$ ,  $\text{R}^2=\text{Me}$ ;  $\text{R}^1=\text{Cl}$ ,  $\text{R}^2=\text{Me}$ ). Reaction of 5-bromouracils (I and V) with other Grignard reagents ( $\text{PhMgBr}$ ,  $\text{PhCH}_2\text{MgCl}$ ) gave the expected 5,6-dihydrouracils (II:  $\text{R}=\text{Ph}$ ,  $\text{CH}_2\text{Ph}$ ,  $\text{R}^1=\text{Br}$ ,  $\text{R}^2=\text{H}$ ,  $\text{Me}$ ).



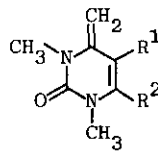
(I)



(II)



(III)



(IV)

\* K. Hirota, K. A. Watanabe, J. J. Fox, J. Org. Chem., **43**, 1193(1978) and references cited therein.