INVESTMENTS IN EDUCATION DEVELOPMENT

Inovation of education in chemistry and biology with respect to current trends in biomedicinal research
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Application of Mitsunobu Reaction in the Synthesis of *N*-Substituted 3,5-dioxo-2-phenyl-2,3,4,5-tetrahydro-1,2,4-triazine-6-carbonitrile

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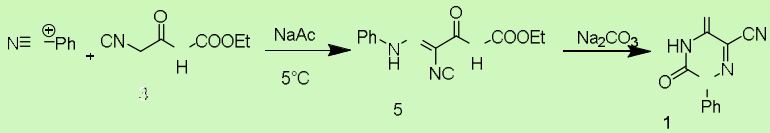
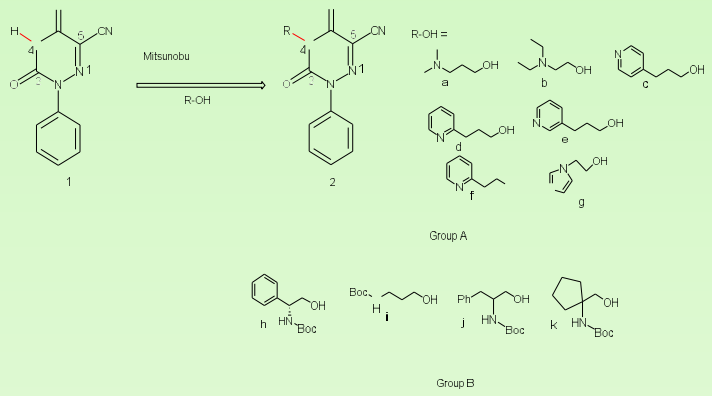
Triazine derivates belong to group of compounds that are very similar to the structure of pyrimidine bases. Biological properties of *N*-substituted triazines have been poorly explored. Therefore, we focused our attention on this type of compounds. Starting compound, 3,5-dioxo-2-phenyl-2,3,4,5-tetrahydro-1,2,4-triazine-6-carbonitrile **1**, contains imidic group, which is suitable for alkylation via Mitsunobu reaction[1,2,4].

A starting compound, triazine **1**, was prepared in two steps synthesis[3]. In the first step, 6-cyanoacetylurethane **4** was treated with phenyldiazonium salt **3** resulting in the hydrazone **5**. Subsequent cyclization in an alkaline medium afforded triazine **1**.



After the triazine **1** was prepared, our attention was focused on the substituion of the imide functionality. We decided to modify this functionality under Mitsunobu conditions. At first, reactions of primary aminoalcoholes (**group A**) containing tertiary amine were tested. After the methodology was verified, the reactions were extended to primary Boc-protected aminoalcoholes (**group B**).



Alcohol	*Conditions*	*React. time*	*Yield/purity(%)*
N,N-dimethylaminopropan-1-ol (**a**)	B,D	2h	46/96 , 60/90
N,N-diethylaminoethanol (**b**)	B,D	2,5h	33/95 , 40/98
3-pyridine-4-yl-propan-1-ol (**e**)	C,D	24h , 2h	75/99 , 95/95
3-pyridine-2-yl-propan-1-ol (**d**)	A,B,C,D	24h-30days	-/-
3-pyridine-3-yl-propan-1-ol(**e**)	C,D	24h , 2h	55/95 , 92/95
2-pyridine-2-yl-ethanol (**f**)	C,D	24h	50/90 , 80/92
2-imidazole-1-yl-ethanol (**g**)	D	24h	66,7/99
(2-hydroxy-1-phenyl-ethyl)-terc-butylcarbamate (**h**)	C,D	2h	0/0 , 60,3/93
(3-Hydroxy-propyl)-terc-butylcarbamate (**i**)	D	2h	70/99,8
(1-Hydroxymethyl-2-phenyl-ethyl)-terc-butylcarbamate (**j**)	D	1,5h	78/98
(1-Hydroxymethyl-cyclopentyl)-terc-butylcarbamate (**k**)	D	1,5h	70/95

Conditions: *A*= 1 equiv. triazine ,1 equiv. alcohol, 1,5 equiv. TPP and 1,5 equiv. DIAD, RT, THF
B= 1 equiv. triazine, 1 equiv. alcohol, 1,5 equiv. TPP and 1,5 equiv. DIAD, RT, DCM
C= 1 equiv. triazine, 1 equiv. alcohol, 1,5 equiv. TPP and 1,5 equiv. DIAD, after 1h, agents were added (1,5 equiv. TPP and 1,5 equiv. DIAD), RT, DCM
D= 1 equiv. triazine 1 equiv. alcohol, 1,5 equiv. TPP a 1,5 equiv. DIAD, RT, 1,4-dioxane

Cyclization of Boc-deprotected derivatives **2h-k**, potentially leading to triazine bicyclic systems, is under study. The attention will be focused on regioselectivity of intended cyclization.

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