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HETEROCYCLES IN ORGANIC SYNTHESIS. PART VI[1] - A FACILE SYNTHESIS OF 1-(4-ARYL-2-THIAZOLYL)-2-PROPANONES

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Abstract - Reactions of ω-(6-methyl-4-pyrimidinylthio)acetophenones (1) with aq. $HCl/HClO_4$ or $POCl_3$ followed by hydrolysis provide 1-(4-aryl-2-thiazolyl)-2-propanones (3).

Heterocyclic cations form pseudobases with water or hydroxide ion. In case the carbon attached to hydroxyl group is bonded to two heteroatoms, it undergoes easy extrusion[2] and the isolation of the residual skeleton of the precursor provides an entry into various categories of organic compounds. Thus thiazolo[3,2-c]quinazolin-4-ium cations formed as transient species by acid catalysed cyclodehydration of ω-(4-quinazolinylthio)acetophenones provide 2-(o-aminophenyl)thiazoles.[3] Here we report that ω-(6-methyl-4-pyrimidinylthio)acetophenones 1 or 2 can be converted to otherwise so far unknown 1-(4-aryl-2-thiazolyl)-2-propanones 3.

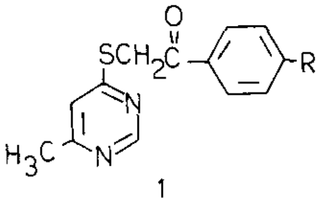
ω-(6-Methyl-4-pyrimidinylthio)acetophenones 1(R=H,Cl,Br,CH_3,OCH_3), obtained by the reactions of pyrimidine-4(3H)-thione with phenacyl halides, on refluxing in hot methanol and $HCl/HClO_4$ (1 : 1) for 35-40 h gave the corresponding 2,5-diaryl-1,4-dithiins[1] and 1-(4-aryl-2-thiazolyl)-2-propanones 3(R=H,Cl,Br,CH_3,OCH_3) (Table). Likewise, ω-(6-methyl-4-pyrimidinylthio)cyclohexanone 2 gave only 6 in 40-50 % yield. The formation of 1-(4-aryl-2-thiazolyl)-2-propanones 3 can be visualised through the cyclodehydration of ω-(6-methyl-4-pyrimidinylthio)acetophenone 1 to the transient structure, thiazolo[3,2-c]pyrimidinium cation 4 followed by hydrolytic C-2 extrusion to enamine 5, which could hydrolyse to give 3.

We argued that the use of aqueous medium in these reactions might be responsible for the relatively low yields of 3 as the nucleophilic substitution at C-4 generating mercaptoacetophenones and thereby forming 2,5-diaryl-1,4-dithiins competes with the initial cyclodehydration. Hence cyclodehydration under non-hydrolytic conditions and subsequent hydrolysis of the cation might provide the product in better yields. Thus ω-(6-methyl-4-pyrimidinylthio)acetophenones 1(R=Cl,H,Br,CH_3,OCH_3) and 2 were refluxed in $POCl_3$ for 10-12 h. After the removal of the solvent and treatment with saturated aq. solution of $NaHCO_3$ followed by workup the corresponding 3 and 6 were isolated in 45-50 % yields and dithins were formed in negligible amounts.

Table

Compound[a]	Yield (%) b		c		mp (°C)	$M^{+\cdot}$ (m/e)
3 (R = Cl)	40	(15)[d]	50	(10)[d]	103-106	251
3 (R = Br)	40	(20)	50	(10)	112-115	295
3 (R = CH_3)	35	(15)	45	(5)	oil	231
3 (R = OCH_3)	35	(20)	45	(5)	oil	247
3 (R = H)	40	(15)	50	(5)	oil	217
6	40	-	50	-	123-127	195

a) All compounds gave satisfactory i.r. and n.m.r. data. The 2H signal in the ^1H n.m.r. spectrum got completely exchanged with D_2O (ovemight) indicating the highly acidic active methylene character. b) Using $HCl/HClO_4$. c) Using $POCl_3$. d) Yields of the corresponding 2,5-diaryl-1,4-dithiins formed.



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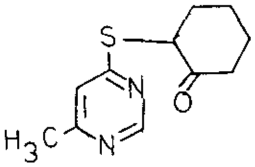

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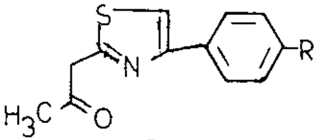

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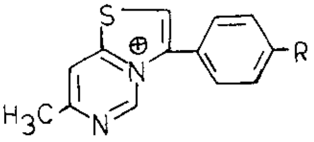

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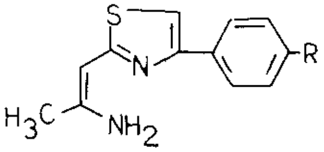

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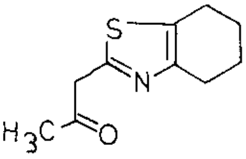

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