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Tetraorganogallate Complexes in Organic Chemistry: A Novel, Efficient and Versatile Preparation of Ketones from Acyl Chlorides

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Abstract: Tetraorganogallium ate complexes, prepared *in situ* by addition of an organolithium reagent to a triorganogallium, reacted smoothly with acyl chlorides to yield ketones in high yields and mixed ate complexes display high chemoselectivity in the transfer of one of their ligands.

The transformation of an acyl chloride into the corresponding ketone is a very useful functional group transformation in organic synthesis[1-2]. Some organometallic[3] reagents have been employed to produce ketones from acyl chlorides, such as organocopper[4], organocadmium[5] and recently reported organothallium compounds[6]. For the synthesis of ketones from organo-copper and -cadmium compounds they suffered from some limitations such as overaddition of organometallic reagent leading to tertiary alcohols. Also , it has been reported that ate complexes of In[7], Tl[8] coupled with alkyl halides. However, according to our knowledge, it has not appeared that these ate complexes reacted with acyl chlorides to form ketones in literature except for borate[9]. A simple, versatile procedure is still required.

Triethylgallium, the first organogallium compound, was prepared by Dennis in 1932[10]. Since then, a lot of new organogallium compounds have been synthesized[11]. Structural characters of these compounds have been systematically studied in many aspects. However, their chemical behavior, in particular their application to organic synthesis, has scarcely appeared[12]. The reason may be due to the very low reactivity of triorganogalliums towards most organic electrophiles and their sensitivity to moisture. Recently, the catalytic processes using gallium[13] and thallium[14] compounds have been reported. Also, we have reported that gallium-mediated highly regioselective reactions of trimethylsilylpropargyl bromide and trimethylsilylallyl bromide with carbonyl compounds[15], and $PbCl_2$/Ga bimetal redox system-mediated reactions of carbonyl compounds with ethyl trichloroacetate or iodoacetonitrile[16]. In this paper, we would like to report that a series of tetraorganogallates[17] react smoothly with acyl chlorides at 0°C-rt, giving ketones in high yields (**Scheme 1**, **Table**).

Scheme 1

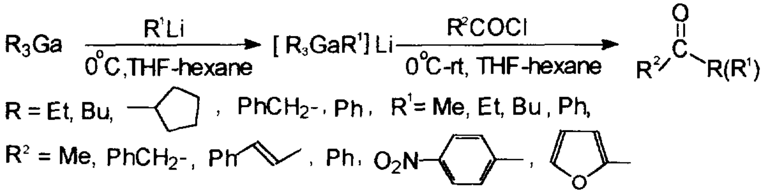
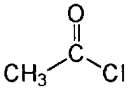
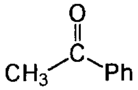
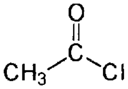
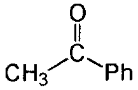
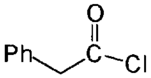
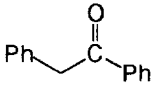
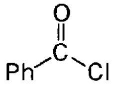
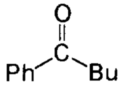
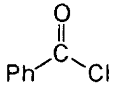
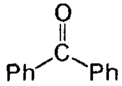
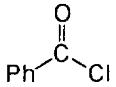
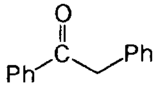
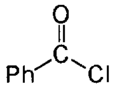
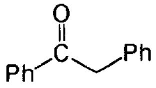
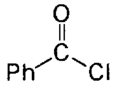
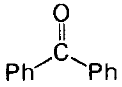
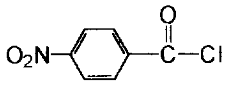
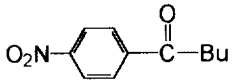
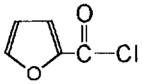
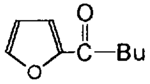
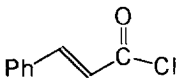
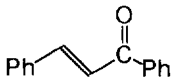
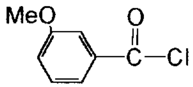
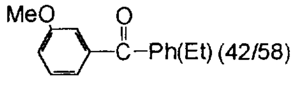
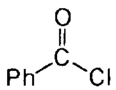
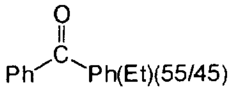


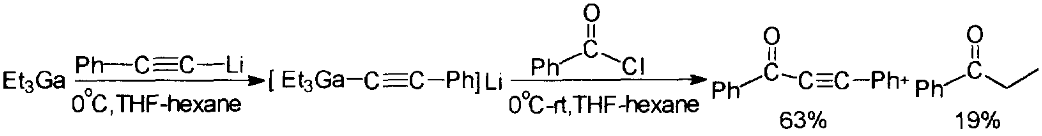
Table. Synthesis of Ketones from Acyl Chlorides Using Tetraoganogallium Ate Complexes[a]

Entry	Substrate[b]	Reagent[c]	Product	Yield(%)[d]
1		$[Ph_3GaBu]$ Li		88
2		$[Ph_3GaMe]$ Li		84
3		$[Ph_3GaBu]$ Li		82
4		Bu_4Ga Li		83
5		$[Ph_3GaBu]$ Li		90
6		$[(PhCH_2)_3GaBu]$Li		58
7		$[(PhCH_2)_3GaPh]$ Li		69
8		$[Et_3GaPh]$ Li		79
9		Bu_4Ga Li		75
10		Bu_4Ga Li		78
11		$[Ph_3GaBu]$ Li		90
12		$[Et_3GaPh]$ MgBr		34(46)
13		$[Et_3GaPh]$ MgBr		46(37)

a) All reactions were carried out with gallate(1.2 equiv.) and acyl chloride(1 equiv.) at 0°C-rt for 1h. b). All acyl chlorides except CH_3COCl and PhCOCl were prepared from the corresponding carboxylic acid and $SOCl_2$ in refluxing CCl_4. c) All the triorganogallium were obtained by means of the reaction of gallium trichloride and Grignard reagents respectively in Et_2O[17c]. d) Isolated yields based on acyl chlorides. All products gave satisfactory ^1H NMR and IR spectral datd.

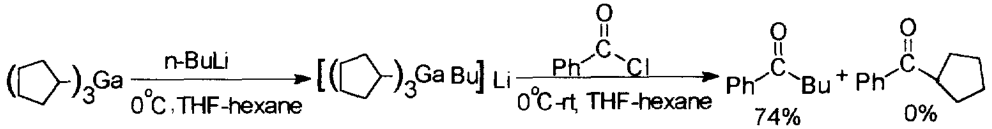
The gallates are readily prepared *in situ* by addition of an organolithium reagent to a corresponding triorganogallium in THF. When an acyl chloride in THF is added into this solution, after usual work-up, a ketone was obtained in high yield. This reaction is suitable for both aliphatic and aromatic substrates, and is chemoselective. The gallates react selectively with acyl chlorides in the presence of other functional groups such as olefin, ether and nitro group. When a mixed lithium butyl triphenylgallate or lithium phenyl tribenzylgallate react with benzoyl chloride, no valerophenone or diphenyl ketone , which would result from a competitive butyl or phenyl group transfer was obtained. Another mixed lithium phenylethynyl triethylgallate reacted with benzoyl chloride to afford mainly phenylethynyl transfer product[18] (**Scheme 2**). Organothallium compounds[6] is more selective for phenylethynyl transfer as compared with organogallium compounds.

Scheme 2



It is particularly noteworthy that, using the mixed lithium butyl tricyclopentylgallate containing primary alkyl group and secondary alkyl groups, the primary alkyl group is transferred exclusively into acyl chloride getting valerophenone without cyclopentylated product[19] (**Scheme 3**). This feature is in agreement with borate[19]. So, the group-transfer order of lithium tetraorganogallate is $PhCH_2$- > Ph- > PhC≡C- > butyl (ethyl) > c-cyclopentyl. In comparision with lithium tetraorganogallates, magnesium tetraorganogallate reacted with acyl chlorides(**Entry 12** and **13**) to produce about 1/1 phenyl and ethyl transfer products. This may be due to the low reactivity of magnesium tetraorganogallates leading to mixed products.

Scheme 3



In conclusion, we have described a novel, efficient, and versatile preparation of ketones from acyl chlorides using lithium tetraorganogallates. Its advantages lie on: (1) the mildness of the reaction condition, (2) chemoselectivity and selective transfer of one group from a mixed gallate (except for phenylethynyl gallate, **Scheme 2**), (3) without overaddition products. The formation of tetraorganogallate complexes not only overcomes the low reactivity of triorganogallium reagents but also weakens the high reactivity and basicity of the organolithium reagents. This method would broaden the scope of utility of organogallium reagents in organic synthesis.

The following experimental procedure is typical: Butyllithium (1.2 mmol, 76.8 mg, 1.6 M, 0.75 ml in hexane, Aldrich) was slowly added into triphenylgallium (361mg, 1.2 mmol) in 4 ml THF at 0°C and stirred for 30 min. under argon. The gallate was dropped by a syringe into cinnamoyl chloride (166.6 mg, 1 mmol) in 2 ml THF at 0°C for 30 min., then allowed to rise to room temperature. After aqueous work-up and chromatography on a silica gel plate, the pure trans-chalcone was obtained in 90% yield.

Acknowledgment

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18. Lithium phenylethynyl trialkylborate reacted with acyl chloride to give heterocyclic compounds containing borane without corresponding ketone. Naruse, M.; Tomita, T.; Utimoto, K. and Nozaki, H., *Tetrahedron Lett.*, **1974**, 835
19. The similar result was found that lithium butyl tricyclopentylgallate reacted with diethyl (p-nitrobenzylidene) malonate in 1,4-addition to yield only butyl transfer product.

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