

A Novel Synthesis of 1,3-Diketones by Reaction of an α -Bromoketone with Acyl Chlorides Promoted by Gallium Triiodide†

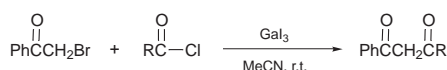
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Promoted by gallium triiodide, an α -bromoketone, bromomethyl phenyl ketone, is treated with acyl chlorides to synthesize 1,3-diketones in good yields under mild and neutral conditions.

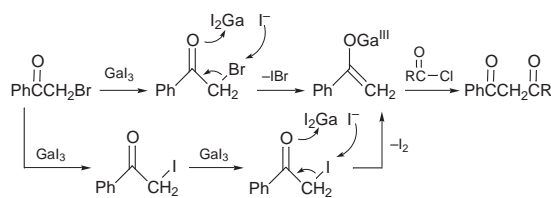
Recently gallium and its compounds are gradually attracting attention as useful reagents in organic synthesis.^{1–7} Gallium enolate-mediated intermolecular aldol reaction and addition of α -bromoketone with imine, a straightforward and versatile preparation of prop-2-ynyl alcohols from alkynes and aldehydes *via* GaI₃ and amine have been documented.³ Kobayashi reported that gallium reagents could efficiently promote the glycosidation of glycopyranosyl fluoride.⁴ The reaction of alkynes with aldehydes produce conjugated enones in the presence of GaI₃-NBu₃ in CH₂Cl₂,⁵ Ga/PbCl₂ bimetal redox system-mediated carbon-carbon bond formation reactions between carbonyl compounds and ethyl trichloroacetate and iodoacetone nitrile,⁶ gallium-mediated highly regioselective reactions of trimethylsilylprop-2-ynyl bromide and trimethylsilylallyl bromide with carbonyl compounds⁷ are known. We have also reported gallium mediated allylation and prop-2-ynylation of 1-(α -aminoalkyl)benzotriazole.⁸ All those reactions above indicated that the scope of utility of gallium reagents in organic chemistry can be broadened.

Our previous work of 1,3-diketone synthesis by reaction of α -haloketones with acyl chlorides or anhydrides promoted by samarium diiodide has been reported.⁹ Here we report that an α -bromoketone, bromomethyl phenyl ketone can reductively couple with acyl chlorides mediated by GaI₃ to give 1,3-diketones (Scheme 1).



Scheme 1

As far as we know, this was the first example of 1,3-diketone synthesis using GaI₃. The mechanism of the reaction may be through the gallium enolate intermediate (Scheme 2). In the classical procedures, 1,3-diketones may be synthesized by condensation of ketones, having an α -hydrogen atom, with acyl chlorides, but the reaction is usually effected by means of a strong basic reagent such as sodium amide,¹⁰ with anhydrides a Lewis acid such as boron trifluoride is generally used.¹¹ O-Acyl derivatives are also formed in these reaction.¹² In our methodology synthesizing 1,3-diketones with acyl chlorides, the ratio of O-acyl derivatives is negligibly small.



Scheme 2

From the result of the experiment, we found that this reaction proceeded quickly and smoothly at room temperature in neutral, mild condition and gives good yields (Table 1). The solvent (MeCN) and acyl chlorides must be dried thoroughly and freshly redistilled, otherwise the amounts of byproducts due to reduction of the α -bromoketone will be increased. This also suggests that the reaction intermediates may be gallium(III) enolates formed *in situ* from the α -bromoketone. THF can not be used as solvent as in the presence of GaI₃ acyl chlorides lead to THF ring opening.¹³

Table 1 Reaction of bromomethyl phenyl ketone with acyl chlorides

Entry	Acyl chloride	Product	Reaction time/h	Yield(%) ^a
1	MeCOCl	PhCOCH ₂ COMe	0.5	77
2	EtCOCl	PhCOCH ₂ COEt	0.5	82
3	PrCOCl	PhCOCH ₂ COPr	0.5	75
4	Me[CH ₂] ₃ COCl	PhCOCH ₂ CO[CH ₂] ₃ Me	1	83
5	Me ₂ CHCH ₂ COCl	PhCOCH ₂ COCH ₂ CHMe ₂	1	79
6	Me[CH ₂] ₄ COCl	PhCOCH ₂ CO[CH ₂] ₄ Me	1	75
7	Me[CH ₂] ₇ COCl	PhCOCH ₂ CO[CH ₂] ₇ Me	1	78
8	Me[CH ₂] ₁₀ COCl	PhCOCH ₂ CO[CH ₂] ₁₀ Me	1	72
9	PhCOCl	PhCOCH ₂ COPh	0.5	75
10	<i>p</i> -O ₂ NC ₆ H ₄ COCl	<i>p</i> -O ₂ NC ₆ H ₄ COCH ₂ COPh	0.5	68
11	Me ₃ CCOCl	PhCOCH ₂ COCMe ₃	1	69
12	PhCH ₂ COCl	PhCOCH ₂ COCH ₂ Ph	1	78

^aIsolated yields.

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Experimental

¹H NMR spectra were recorded on a JEOL PMX 60 SI instrument in CCl₄ using TMS as internal standard. IR spectra were determined on a Perkin-Elmer 683 spectrometer. Metallic gallium and other chemicals were purchased from commercial sources and used without purification. MeCN was freshly distilled prior to use.

General Procedure.—Under a nitrogen atmosphere, a metallic gallium bar (1 mmol) and iodine (1.5 mmol) were placed in a three-necked reaction flask, then MeCN (10 ml) was added in one portion. The mixture was stirred at room temperature until the colour of iodine disappeared completely. Then the α -bromoketone (1 mmol) and acyl chloride (1 mmol) were added sequentially to the mixture. After stirring at room temperature for the time indicated in Table 1, a dilute solution of HCl was added and the resulting mixture was stirred for a few minutes. The mixture was extracted with diethyl ether (20 ml \times 2) and the organic layer was washed with water (20 ml \times 2) and dried over anhydrous Na₂SO₄. The solvent was removed *in vacuo*. The residue was then purified by preparative TLC on silica gel with cyclohexane and ethyl acetate as eluent to give pure product.

PhCOCH₂COMe¹⁴: mp 60 °C; δ_{H} 1.98 (s, 3H), 5.93 (s, 1H), 7.20–7.28 (m, 3H), 7.60–7.76 (m, 2H), OH unfound; ν/cm^{-1} 1700, 1670.

PhCOCH₂COEt¹²: Oil; δ_{H} 1.01–1.25 (t, 3H), 2.16–2.51 (q, 2H), 6.10 (s, 1H), 7.33–7.42 (m, 3H), 7.73–7.90 (m, 2H), 15.97 (s, 1H); ν/cm^{-1} 1610.

PhCOCH₂COPr¹²: mp 30–31 °C; δ_{H} 0.90–1.12 (t, 3H), 1.43–2.00 (m, 2H), 2.26–2.50 (t, 2H), 6.10 (s, 1H), 7.38–7.46 (m, 3H), 7.80–7.95 (m, 2H); 16.27 (s, 1H); ν/cm^{-1} 1610.

PhCOCH₂COCH₂[CH₂]₂Me¹²: Oil; δ_{H} 0.88–0.98 (t, 3H), 1.42–1.95 (m, 4H), 2.25–2.49 (t, 2H), 6.10 (s, 1H), 7.36–7.45 (m, 3H), 7.78–7.95 (m, 2H); 16.22 (s, 1H); ν/cm^{-1} 1610.

PhCOCH₂COCH₂CH₂Me¹²: Oil; δ_{H} 0.90–0.98 (d, 6H), 1.96–2.25 (m, 3H), 6.03 (s, 1H), 7.40–7.47 (m, 3H), 7.80–7.95 (m, 2H), 126.26 (s, 1H); ν/cm^{-1} 1610.

PhCOCH₂COCH₂[CH₂]₃Me⁹: Oil; δ_{H} 0.85–1.76 (m, 9H), 2.25–2.47 (t, 2H), 6.03 (s, 1H), 7.36–7.45 (m, 3H), 7.77–7.93 (m, 2H), 16.20 (s, 1H); ν/cm^{-1} 1610.

PhCOCH₂COCH₂[CH₂]₆Me⁹: Oil; δ_{H} 0.85–1.80 (m, 15H), 2.22–2.45 (t, 2H), 6.03 (s, 1H), 7.32–7.43 (m, 3H), 7.74–7.90 (m, 2H), 16.15 (s, 1H); ν/cm^{-1} 1605.

PhCOCH₂COCH₂[CH₂]₉Me¹⁴: Oil; δ_{H} 0.85–1.80 (m, 21H), 2.22–2.45 (t, 2H), 6.03 (s, 1H), 7.32–7.43 (m, 3H), 7.74–7.90 (m, 2H), 16.15 (s, 1H); ν/cm^{-1} 1605.

PhCOCH₂COPh¹⁵: mp 74–75 °C; δ_{H} 6.73 (s, 1H), 7.42–7.50 (m, 6H), 7.90–8.05 (m, 4H), 17.00 (s, 1H), ν/cm^{-1} 1605.

p-O₂NC₆H₄COCH₂COPh¹⁶: mp 160–161 °C; δ_{H} 6.68 (s, 1H), 7.35–8.00 (m, 9H), 16.85 (s, 1H), ν/cm^{-1} 1610, 1350.

PhCOCH₂COCMe₃¹⁵: Oil; δ_{H} 1.15 (s, 9H), 6.20 (s, 1H), 7.34–7.38 (m, 3H), 7.79–7.83 (m, 2H), 16.50 (s, 1H); ν/cm^{-1} 1619.

PhCOCH₂COCH₂Ph¹⁵: mp 50–51 °C; δ_{H} 3.70 (s, 2H), 6.08 (s, 1H), 7.29–7.48 (m, 8H), 7.75–7.79 (m, 2H), OH unfound; ν/cm^{-1} 1605.

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