SHORT PAPER

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Gallium mediated barbier reactions of 1,2-diones: a facile synthesis of α-hydroxy ketones[†]

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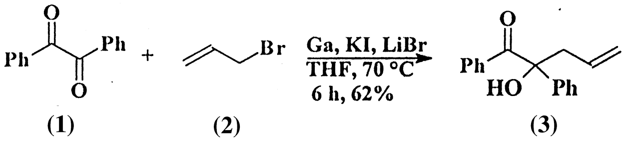
Gallium mediated allylation and cinnamylation reactions of 1,2-diones in presence of LiBr and KI afforded α-hydroxycarbonyl compounds in moderate to good yields.

Keywords: gallium, allylation, cinnamylation, 1,2-diones

The resurgence of the Barbier reaction as an important method for carbon–carbon bond formation has prompted the use of a variety of metals in this reaction. Of particular interest has been the Araki protocol using indium, which has now found extensive use in organic synthesis.[1a,1b] We have recently shown that indium mediated allylation of 1,2-diones is an efficient method for the synthesis of α-hydroxyketones.[2] In this context, it was of interest to explore the reactivity of gallium reagents also towards various electrophiles, especially 1,2-dicarbonyl compounds. There have been only limited investigations using gallium reagents,[3a–f] compared to indium reagents and there is no report on their reaction with 1,2-dicarbonyl compounds.

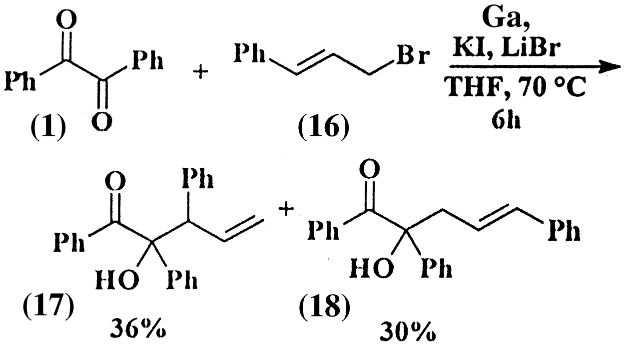
Our studies, commenced by treating benzil with allylbromide and gallium in presence of LiBr and KI in dry THF, furnished 62% of the corresponding α-hydroxy carbonyl compound (Scheme 1).



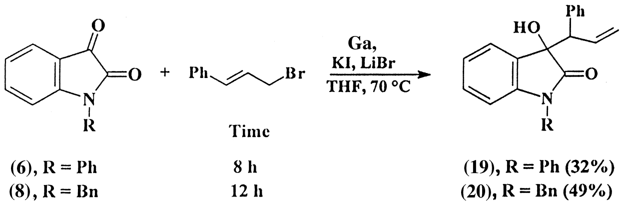
Scheme 1

In order to study the scope and limitations of the reaction,we examined the allylation of several 1,2-diones and the results are summarised in Table 1.

Further studies showed that this methodology works for cinnamylation also. Thus benzil underwent cinnamylation under similar conditions to yield a regioisomeric mixture of α- and γ-cinnamylated products (Scheme 2) which is in agreement with the characteristic behaviour of other substituted allyl organometallics.[5] With benzil, γ-product itself is an inseparable mixture of *syn* and *anti* isomers.



Scheme 2



Scheme 3

The gallium mediated cinnamylation of isatins was also found to occur (scheme 3).

In conclusion, we report a novel gallium mediated synthesis of α-hydroxy carbonyl compounds in moderate to good yields.

Experimental

α-Hydroxy carbonyl compounds. general procedure: A mixture of gallium metal (1.2 mmol), 1,2-dione (1mmol), potassium iodide (2 mmol), lithium bromide (1.2 mmol) and allylbromide/ cinnamyl bromide (2 mmol) is refluxed in 4 ml of anhydrous THF under argon atmosphere until there is no more consumption of the starting material. The reaction mixture is then concentrated, diluted with water and quenched with a few drops of 2M hydrochloric acid. It is then extracted with diethylether and the ether layer is then washed with water, brine and dried over sodium sulfate. Evaporation of the solvent followed by purification of the product by column chromatography on silica gel afforded the pure product.

Data for (**3**): Colourless solid. m.p.: 88–90°C (recrystallised from CH_2Cl_2-hexane). IR (KBr) ν_{max}: 3467, 1681 cm^{-1}. ^1H NMR: δ 2.90–2.97 (m, 1H), 3.09–3.16 (m, 1H), 4.09 (s, 1H), 4.98–5.13 (m, 2H), 5.66–5.80 (m, 1H), 7.25–7.73 (m, 10H). ^{13}C NMR: δ 44.06, 81.30, 120.28, 125.50, 127.96, 128.76, 130.10, 132.34, 141.77, 200.44. Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 81.22; H, 6.60.

Data for (**7**): Colourless solid. m.p.: 93-95 °C (recrystallised from CH_2Cl_2-hexane). IR (KBr) ν_{max}: 3317, 1706 cm^{-1}. ^1H NMR: δ 2.70–2.86 (m, 2H), 3.61 (s,1H, exchangeable by D_2O), 5.08–5.16 (m, 2H), 5.55–5.66 (m, 1H), 6.78 (d, J = 7.7 Hz, 1H) 7.11 (t, J = 7.4 Hz, 1H), 7.21 (d, J = 7.7 Hz, 1H), 7.35–7.52 (m, 6H). ^{13}C NMR δ 43.52, 76.10, 109.61, 120.55, 123.46, 124.41, 126.48, 128.17, 129.45, 129.48, 129.60, 130.46, 143.32, 177.25.

Data for (**9**): Colourless solid. m.p.: 124–126°C (recrystallised from CH_2Cl_2-hexane). IR (KBr) ν_{max}: 3290, 1692 cm^{-1}. ^1H NMR: δ 2.66–2.84 (m, 2H), 3.71 (s,1H, exchangeable by D_2O), 4.69 (d, J = 15.6 Hz, 1H), 4.97–5.14 (m, 3H), 5.55-5.60 (m, 1H), 6.66 (d, J = 7.2Hz, 1H) 7.04–7.06 (m, 1H), 7.04–7.26 (m, 6H), 7.32–7.39 (m, 1H). ^{13}C NMR: δ 43.08, 43.85, 76.00, 109.42, 120.48, 123.06, 124.20, 127.28, 127.67, 128.77, 129.52, 129.81, 130.60, 135.44, 142.48, 178.03.

Data for (**11**): Colourless solid. m.p.: 51–53°C (recrystallised from ether-light petroleum ether). IR (KBr) ν_{max}: 3425, 1738 cm^{-1}. ^1H NMR: δ 0.93 (s, 3H), 0.99 (s, 3H), 1.06 (s, 3H), 1.43–1.50 (m, 1H),

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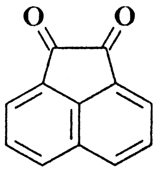
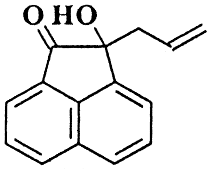
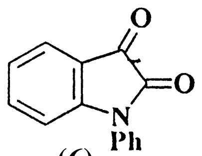
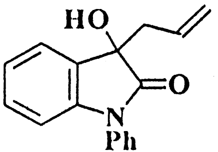
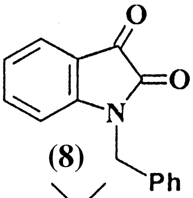
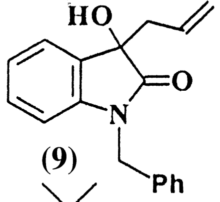
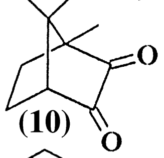
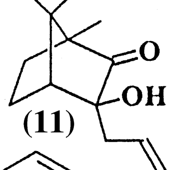
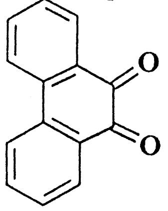
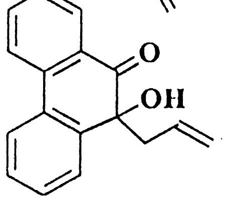
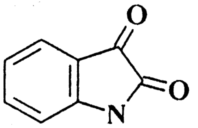
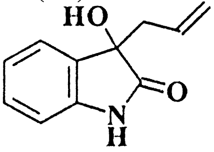
[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 Allylation of 1,2-diones

Sample no.	1,2-Diones	Time/h	Product	Yield[a]
1	 **(4)**	7	 **(5)**	96%[b]
2	 **(6)**	4	 **(7)**	80%
3	 **(8)**	5	 **(9)**	75%
4	 **(10)**	5	 **(11)**	58%
5	 **(12)**	5	 **(13)**	55%[b]
6	 **(14)**	7	 **(15)**	49%

[a]Isolated yield. [b]The products (**5**) and (**13**) were identified by comparison of their physical and spectral data with those of authentic samples.[4] Reaction condition: LiBr, KI, THF, 70°C

1.56–1.71 (m, 2H), 1.83–1.94 (m, 1H), 1.98 (d, J = 3.8 Hz, 1H), 2.29 (t, J = 6.2 Hz, 2H), 2.36 (s, 1H, exchangeable by D_2O), 5.16–5.23 (m, 2H), 5.87–6.00 (m, 1H). ^{13}C NMR: δ 9.52, 20.44, 22.42, 29.85, 41.01, 46.28, 51.69, 58.32, 76.49, 119.65, 132.34, 220.02.

Data for (**15**): Colourless solid. m.p.: 150–152°C (recrystallised from ethylacetate-hexane). IR (KBr) ν_{max}: 3334, 1720, 1626 cm^{-1}. ^{1}H NMR (DMSO-d$_6$): δ 2.55–2.62 (m, 1H), 2.69–2.76 (m, 1H), 3.43 (s, 1H), 5.07–5.12 (m, 2H), 5.57–5.71 (m, 1H), 6.84–7.35 (m, 4H), 8.43 (s, 1H). ^{13}C NMR (DMSO-d$_6$): δ 42.80, 77.20, 104.70, 110.14, 120.39, 122.90, 124.42, 129.50, 130.24, 140.21, 179.89. Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.82; H, 5.85; N, 7.40. Found: C, 70.18; H, 5.83; N, 7.79.

Data for (**17**): Colourless solid. m.p.: 112–114°C (recrystallised from CH_2Cl_2-hexane). IR (KBr) ν_{max}: 3499, 1670 cm^{-1}. ^{1}H NMR: δ 3.83 (s, 1H), 4.10 (s, 1H), 4.58 (d, J = 7.5 Hz, 1H), 4.65 (d, J = 7.8 Hz, 1H), 4.96–5.17 (m, 4H), 6.11–6.23 (m, 2H), 7.09–7.97 (m, 30H). ^{13}C NMR: δ 54.69, 55.92, 83.61, 84.51, 117.36, 117.92, 125.17, 125.48, 125.72, 125.91, 126.41, 126.80, 126.89, 126.91, 127.09, 127.16, 127.49, 127.89, 128.57, 128.74, 128.82, 128.88, 131.11, 131.14, 133.64, 135.92, 136.10, 199.97, 200.44. Anal. Calcd for $C_{23}H_{20}O_2$: C, 84.11; H, 6.13. Found: C, 84.22; H, 6.37. From the ^{1}H NMR spectrum, *syn* and *anti* isomers were found to be in the ratio 1:1.

Data for (**18**): colourless solid. m.p.: 108–111°C (recrystallised from CH_2Cl_2-hexane). IR (KBr) ν_{max}: 3494, 1676 cm^{-1}. ^{1}H NMR: δ 3.02–3.09 (m, 1H), 3.24–3.31 (m, 1H), 4.17 (s, 1H), 6.08–6.15 (m, 1H), 6.26 (d, J = 15.9 Hz, 1H), 7.18–7.73 (m, 15H). ^{13}C NMR: δ 43.50, 81.93, 123.68, 125.71, 126.42, 127.67, 128.21, 128.62, 129.04, 130.34, 132.81, 134.84, 135.45, 136.95, 142.04, 200.77. Anal. Calcd for $C_{23}H_{20}O_2$: C, 84.11; H, 6.13. Found: C, 84.39; H, 6.25.

Data for (**19**): colourless solid. m.p.: 145–147°C (recrystallised from CH_2Cl_2-hexane). IR (KBr) ν_{max}: 3317, 1692 cm^{-1}. ^{1}H NMR: δ 3.64 (s, 1H, exchangeable by D_2O), 4.05 (d, J = 7.9 Hz, 1H), 4.25 (d, J = 15.9 Hz, 1H), 4.92(d, J = 15.9 Hz, 1H), 5.26–5.41 (m, 2H), 6.38 (d, J = 7.6 Hz, 1H) 6.46 (d, J = 6.8 Hz, 2H), 6.50–6.61 (m, 1H), 6.80 (d, J = 7.2 Hz, 2H), 7.05–7.21 (m, 8H), 7.55 (d, J = 6.8 Hz, 1H). ^{13}C NMR: δ 43.38, 57.78, 76.57, 109.57, 119.85, 122.71, 125.13, 126.51, 127.21, 127.32, 128.24, 128.62, 129.40, 129.85, 134.94, 136.68, 143.36, 177.35.

Data for (**20**): colourless solid. m.p.: 130–132°C (recrystallised from CH_2Cl_2-hexane). IR (KBr) ν_{max}: 3316, 1719 cm^{-1}. ^{1}H NMR: δ 3.61 (s, 1H, exchangeable by D_2O), 3.89 (d, J = 10.09 Hz, 1H), 5.39–5.49 (m, 2H), 6.46–6.53 (m, 2H), 7.05–7.14 (m, 8H), 7.24–7.43 (m, 5H). ^{13}C NMR: δ 59.39, 76.58, 104.79, 109.21, 121.09, 123.03, 124.52, 126.39, 127.17, 127.91, 128.11, 128.31, 128.99, 129.48, 129.52, 133.86, 136.88, 143.65, 176.24.

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