

'GaI': A new reagent for chemo- and diastereoselective C–C bond forming reactions†

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The potential of 'GaI' as a reductant in organic transformations, in particular C–C bond forming reactions involving α -functionalised ketones, has been investigated. Of most interest are the diastereoselective aldol coupling reactions of the α -alkoxy ketones, PhC(O)C(H)(OR)Ph , $\text{R} = \text{Me, Et or } ^i\text{Pr}$, which give the novel γ -alkoxy, β -hydroxy ketones, $\text{PhC(O)C(H)(Ph)C(OH)(Ph)C(H)(OR)Ph}$, containing three contiguous stereogenic centres. The diastereoselectivity of these reactions was established from NMR spectroscopic and X-ray crystallographic studies of the products. When $\text{R} = \text{Me}$, the $2R,3S,4R/2S,3R,4S$ -enantiomeric pair is formed, whereas when $\text{R} = \text{Et or } ^i\text{Pr}$, $2R, 3R, 4S/2S, 3S, 4R$ -diastereoisomers result. These differences are rationalised in terms of the likely transition states of the reactions. The same products are not formed when higher oxidation salts of gallium, or InI , are employed as the inorganic reagent. The reactivity of "GaI" towards α -halo ketones, a 1,2-diketone and α,β -unsaturated ketones has also been explored. Again, the outcomes of these reactions have been compared to those involving Ga(II) and Ga(III) reagents.

Introduction

C–C bond forming reactions are fundamental to organic synthesis and have been carried out using inorganic and organometallic reagents incorporating metals from across the periodic table. From group 13, boron(III) and aluminium(III) compounds have been amongst the widely used reagents for this purpose. More recently, indium compounds have found increasing usage in organic synthetic methodology. This can involve reagents with indium in the +3 oxidation state, but there is an escalating interest in the exploitation of indium metal and indium(I) halides as reductants in processes such as Barbier allylations, Reformatsky reactions, aldol additions and propargylation reactions.^{1,2} Although not as widely studied, gallium metal is beginning to be accepted as a reagent in a similar array of reactions.^{2,3}

Low oxidation state gallium halides have been almost completely neglected as reducing agents in C–C bond forming reactions. The reasons for this most likely include the fact that the former are not commercially available, and are more oxygen and moisture sensitive than their indium counterparts. Indeed, prior to our involvement in this area, it appears that only two reports⁴ have detailed the employment of a gallium sub-halide in organic synthesis. In these, Saigo *et al.* described the use of gallium(II) chloride (which actually exists as a mixed oxidation salt, $\text{Ga}^{\text{I}}[\text{Ga}^{\text{III}}\text{Cl}_4]$) in the one-pot "reductive Friedel–Crafts" coupling reactions of carbonyl compounds or dimethylacetals with aromatics.

Our interest in low oxidation state gallium chemistry largely involves the stabilisation and coordination chemistry of gallium(I) *N*-heterocyclic carbene analogues.⁵ The most important starting material in the synthesis of such heterocycles is Green's "GaI" which acts as a source of gallium(I) iodide.⁶ This insoluble green powder is straightforwardly prepared by the reaction of gallium metal with one half of an equivalent of diiodine in toluene under ultrasonic conditions (ultrasonic bath). Although it is very oxygen sensitive, it is thermally stable and can be stored indefinitely under an inert atmosphere without loss of activity. Although its formulation is not definitely known, the results of a Raman spectroscopic study suggest it predominately consists of the mixed oxidation salt, $\text{Ga}_2^{\text{I}}[\text{Ga}_2^{\text{III}}\text{I}_6]$, with an average gallium oxidation state of +1.5.⁷

In preliminary studies, we have shown that this material is, not surprisingly, a more potent reducing reagent than InI . For example, it can readily reductively couple diynes (to give enediynes)⁸ or bulky 2-(imino)pyridines⁹ that are unreactive towards the indium reagent. Given the apparent chemoselectivity of "GaI" over InI , we were keen to extend our studies into its use in C–C bond forming reactions. In this paper we detail its unusual reactivity towards α -alkoxy ketones, α -halo ketones and α -diketones, which in the case of α -alkoxy ketones, leads to the diastereoselective formation of γ -alkoxy β -hydroxy ketones with three contiguous stereogenic centres.

Results and discussion

(i) Aldol-type coupling reactions of α -alkoxy ketones

Strong reducing agents such as SmI_2 have been shown to reduce α -alkoxy ketones, *e.g.* benzoin methyl ether, to the corresponding ketone, *e.g.* deoxybenzoin, under mild, neutral

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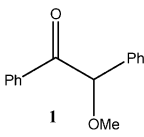
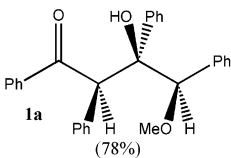
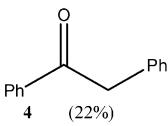
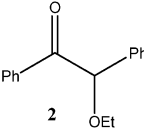
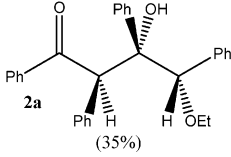
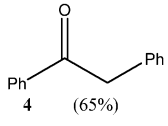
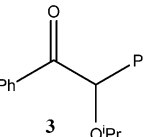
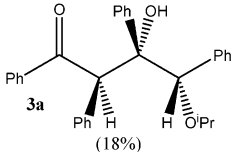
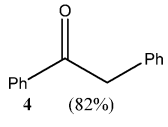
conditions.¹⁰ In attempts to carry out similar reductions of α -alkoxy ketones with “GaI”, deoxybenzoin, **4**, was formed but unexpected C–C coupled products also resulted. The reactions of benzoin methyl ether **1**, benzoin ethyl ether **2** and benzoin isopropyl ether **3**, with four equivalents of “GaI” were carried out in toluene, at $-78\text{ }^{\circ}\text{C}$, with subsequent slow warming to room temperature. These afforded the novel tri-functional aldol coupled products **1a** ($2R,3S,4R/2S,3R,4S$ -product), **2a** and **3a** ($2R,3R,4S/2S,3S,4R$ -products), respectively, with complete diastereocontrol within detection limits (see Table 1).

The reactions are thought to proceed *via* an initial reduction of the substrate to generate short-lived gallium-enolates (assumed to exist as their *E*-isomers), “[$(\text{RO})\text{IGa}\{\text{OC}(\text{Ph})=\text{C}(\text{Ph})(\text{H})\}$]” **5**, which upon formation, undergo aldol-type reactions with unreacted substrate to give the observed products. NMR spectroscopic studies of the reaction mixtures prior to aqueous work-up did not show any evidence of **5** or the expected gallium alkoxide conjugate bases of **1a–3a**. Instead, only **4** and the quenched products were present. This suggests that product quenching *via* proton abstraction from the toluene reaction solvent or another reaction component readily occurs. The increasing yield of **4** with increasing size of R could, therefore, be explained by a competition between solvent quenching of **5** (to give **4**) and its nucleophilic attack on the α -alkoxy ketone substrate. The latter process would, presumably, be slowed with increasing size of the alkoxy substituent, thus favouring the formation of **4**. When the reactions were repeated utilising benzene as the solvent, the resultant yields and diastereoselectivities were nearly identical to the toluene reactions. Intriguingly, when hexane was used as a solvent no reactions occurred. One explanation for this is

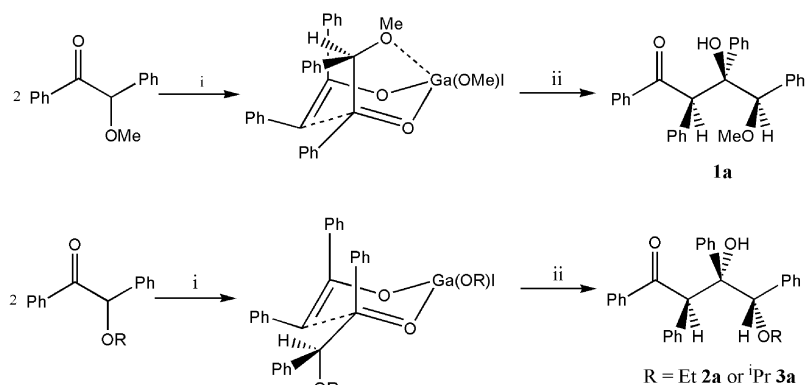
that arene solvents are required to partly solubilise the “GaI” reagent. Indeed, it is well known that Ga(I) salts engage in π -arene interactions in solution.¹¹

The diastereoselectivity of these reactions is interesting, but even more so is the change in the diastereoisomer formed upon changing the size of the substrate alkoxy group. It cannot be sure why these differences occur but analogies can be drawn with the previously reported additions of α -stannyl esters¹² or indium enolates¹³ towards α -alkoxy ketones which give *syn*-products (*cf.* formation of **1a**) with a very high degree of diastereoselectivity. It was proposed that this selectivity arose from a steric control of the enolate attack imposed by chelation of the substrate to the tin or indium centre prior to addition. In contrast, additions of indium enolates to simple ketones were found to proceed diastereoselectively to give *anti*-products (*cf.* formation of **2a** and **3a**). Here, six-membered cyclic transition states were used to explain the selectivity of the reactions. In our systems, it is feasible that the reaction of benzoin methyl ether with “GaI” could proceed *via* a chelated cyclic transition state (Scheme 1) which when quenched would lead to the observed diastereoisomer, **1a**. It is possible that the bulkier alkoxy substituents of **2** and **3** preclude chelated transition states in their reactions with “GaI” and instead six-membered transition states, akin to those of indium enolate additions to simple ketones, lead to **2a** and **3a** upon quenching. If this is the case, the stereo-control of these reactions is dominated by the electrophilic substrate rather than the enolate. It is possible that the cyclic transition state that gave **2a** and **3a** is stabilised by chelation of its alkoxy and ketone O-centres to gallium salts (*e.g.* GaI_3 from the disproportionation of “GaI”^{6a}) which are likely to be present in the reaction mixture.

Table 1 Products from the reactions of α -alkoxy ketones, $\text{PhC}(\text{O})\text{C}(\text{OR})\text{Ph}$ (R = Me, Et or $i\text{Pr}$), with “GaI”

Substrate	Products (yield) ^a	
 1	 1a (78%)	 4 (22%)
 2	 2a (35%)	 4 (65%)
 3	 3a (18%)	 4 (82%)

^a Only one enantiomer of each product is shown. Diastereoselectivities of the products are $>99\%$ in all cases.



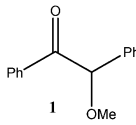
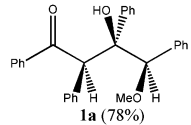
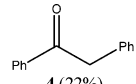
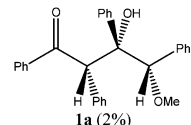
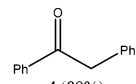
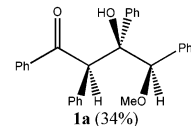
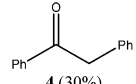
Scheme 1 Proposed mechanisms for the formation of **1a–3a**. (i) “GaI”, toluene; (ii) quench.

As the formulation of “GaI” is not definitely known, but is believed to include the mixed oxidation salt, $\text{Ga}^{\text{I}}_2[\text{Ga}^{\text{II}}_2\text{I}_6]$, it cannot be sure if the active component of the reagent is the $\text{Ga}(\text{I})$ cation, the $\text{Ga}(\text{II})$ anion, or both. In addition, “GaI” is well known to disproportionate to Ga metal and GaI_3 in the presence of Lewis base donor sites,^{6a} as are present in **1–3**. Therefore, **1** was reacted with several $\text{Ga}(\text{II})$ and $\text{Ga}(\text{III})$ halides, and gallium metal under identical conditions to its reaction with “GaI” for purposes of comparison. The outcomes of these reactions are highlighted in Table 2 and show that no reaction occurs with gallium metal or gallium(III) halides, suggesting the formation of **1a** involves a reduction process. This is perhaps confirmed by the reaction with the gallium(II) halide, a milder reducing agent than “GaI”, which only affords a very low yield of **1a**. Similarly, no reaction occurred between **1** and InI , even under reflux conditions,

which is consistent with our previous studies that point towards this being a milder reductant than “GaI”.^{8,9} Furthermore, when **1** was reacted with only two equivalents of “GaI”, a reduced yield of **1a** was obtained and much of **1** remained unreacted. If the proposed mixed oxidation state formulation of “GaI” is correct, these results suggest that its $\text{Ga}(\text{I})$ cations are the active components of the salt. Finally, all attempts at *in situ* cross condensation reactions, for example between **1** and **2** or between **1** and ketones, were not successful and yielded only **1** and **4**, or intractable mixtures of products.

Compounds **1a–3a** were characterised by X-ray crystallography and the molecular structures of one enantiomer of each are depicted in Fig. 1. These were used to assign the stereochemistry of the products. To confirm that the crystals chosen for the X-ray experiments represented the bulk materials, their ^1H NMR spectra were obtained and these were found to be

Table 2 Comparisons between the reactions of **1** with “GaI” and those with other gallium and indium reagents

Substrate	Reagent	Products (yield) ^a	
 1	4 'GaI'	 1a (78%)	 4 (22%)
	4 Ga ₂ Cl ₄ (dioxane) ₂	 1a (2%)	 4 (89%)
	2 'GaI'	 1a (34%)	 4 (30%) + 1 (36%)
	GaCl ₃ GaI ₃ 4 Ga metal 4 InI	No reaction No reaction No reaction No reaction	

^a All reactions were carried out under the conditions to prepare **1a**.

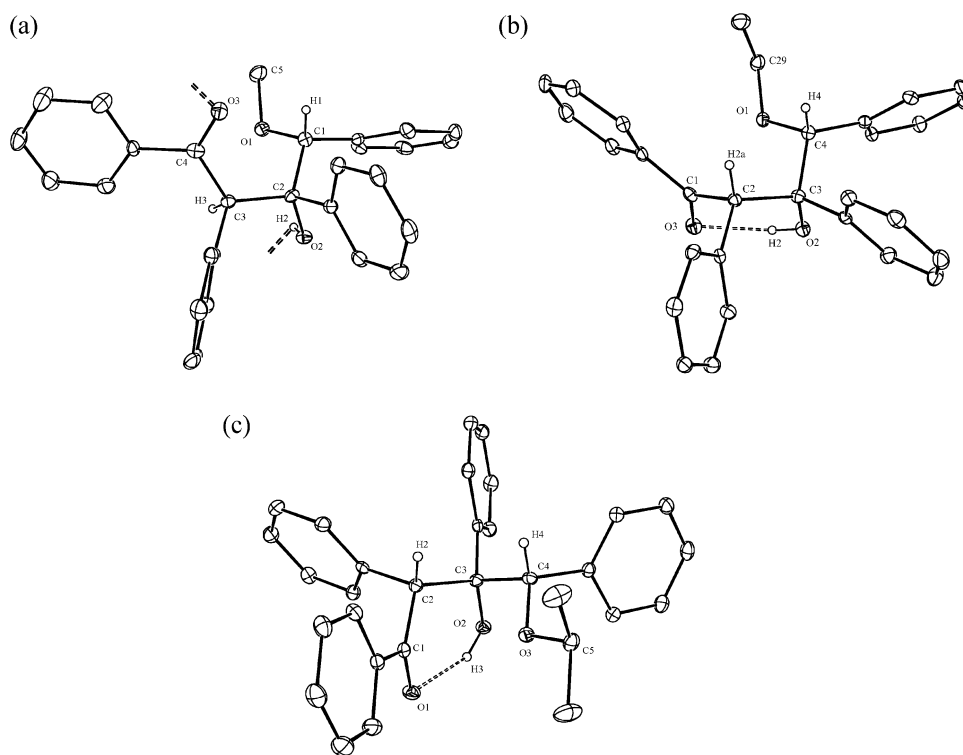


Fig. 1 Molecular structures of (a) **1a**, (b) **2a** and (c) **3a** (25% thermal ellipsoids are shown).

identical to the total crystallised product. Each compound exhibits hydrogen bonding interactions between its ketone and alcohol functionalities, though the differences in the stereochemistries of the products mean that in **1a** these interactions are intermolecular, leading to 1-dimensional hydrogen bonded polymers, whereas in **2a** and **3a** they are intramolecular.

(ii) Reactivity of “GaI” towards α -halo ketones

Considering that halides are better leaving groups than alkoxy substituents, it was thought that the reaction of α -halo ketones with “GaI” might lead to γ -halo β -hydroxy ketones (*cf.* the reactions that gave **1a–3a**). Saying this, reactions of α -halo ketones with reducing agents such as SmI_2 are known to facilitate effect halide elimination and ketone formation.¹⁰ In the case of the reaction of the α -bromo ketone, **6**, with “GaI”, this did occur to give the ketone, **8**, as the major product, though a significant amount of the known diketone, **7**, was also formed as a mixture of diastereoisomers (Table 3). We believe the mechanism of formation of **7** is similar to that reported for its synthesis from the reaction of **6** with MeMgBr .¹⁴ That is, the reaction proceeds through a dehalogenation step, to yield a gallium enolate which then attacks a second molecule of **6**, leading to bromide elimination and a concomitant 1,2-phenyl migration yielding **7** (Scheme 2). This phenyl migration helps to explain the lack of diastereoselectivity in the reaction.

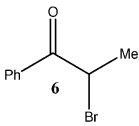
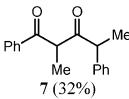



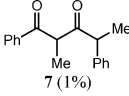

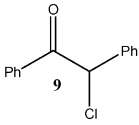
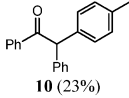

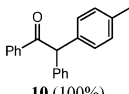
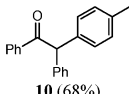

An ^1H NMR spectroscopic analysis of the reaction mixture prior to aqueous work-up revealed the presence of both **7** and **8**, suggesting that the intermediate gallium enolate readily abstracts a proton from the toluene solvent. This process

would therefore be in competition with the aldol condensation that ultimately gives **7**, thus leading to the observed mixture of **7** and **8**. The apparent facile solvent quenching of the intermediate gallium enolate contrasts with work involving the reaction of $\text{GaMe}_n\text{I}_{3-n}$ with **6** which led to room temperature stable gallium enolates that underwent successful aldol reactions with carbonyl compounds and imines.¹⁵

In order to ascertain if the Ga(I) component of “GaI” plays the active role in the formation of **7**, compound **6** was reacted with Ga(II) and Ga(III) halides under identical conditions. In these cases GaCl_3 was largely unreactive, whilst treatment of **6** with $\text{Ga}_2\text{Cl}_4(\text{dioxane})_2$ almost exclusively gave the ketone, **8** (Table 3).

As the chloride group is a poorer leaving group than bromide, but a better leaving group than alkoxides, the reaction of an α -chloro ketone, **9**, with four equivalents of “GaI” in toluene was carried out for purposes of comparison. This led to a completely different outcome to the reactions with **1–3** and **7**, namely *para*-alkylation of the toluene solvent to give a low to moderate yield of the known ketone, **10**.¹⁶ The previously observed quenched enolate, **4**, was formed as the major product. The formation of **4** is not surprising in light of the fact that **9** is known to form enolates with other reducing agents, *e.g.* barium metal,¹⁷ but the absence of any coupled products (*cf.* **7**) is unusual. More surprising is the apparent role of “GaI”, or one of its disproportionation products, as a Friedel–Crafts alkylation reagent in the formation of **10**, which was not observed in any previous reaction. Evidence for this proposal comes from the results of the reactions of **9** with the classical Friedel–Crafts alkylation reagents, AlCl_3 or GaCl_3 , which gave high or quantitative yields, respectively, of

Table 3 A comparison of the reactivity of ‘GaI’ and other group 13 halides towards α -halo ketones

Substrate	Reagents	Products (yield)
 6	4 ‘GaI’	 7 (32%)  8 (68%)
	GaCl ₃	 6 (96%)  8 (4%)
	4 Ga ₂ Cl ₄ (dioxane) ₂	 7 (1%)  8 (99%)
 9	4 ‘GaI’	 10 (23%)  4 (73%)
	GaCl ₃	 10 (100%) —
	AlCl ₃	 10 (68%)  9 (32%)

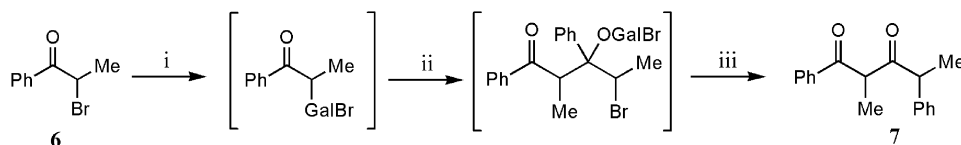
10. Of course, no evidence for **4** was seen in these reactions due to the non-reducing nature of the salts involved. The X-ray crystal structure of **10** was determined and its ORTEP diagram is included in the supplementary material.

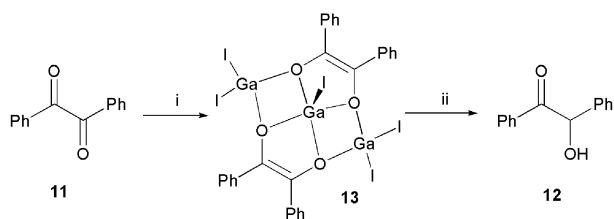
(iii) Reactivity of ‘GaI’ towards other α -functionalised ketones

Low oxidation state metal complexes are well known to reduce 1,2-diketones to give chelated enediolate complexes.¹⁸ To examine the applicability of ‘GaI’ to such reactions, it was treated with benzil, **11**, in toluene. After aqueous work-up, benzoin, **12**, was recovered in near quantitative yield (Scheme 3). Despite the reactivity of α -alkoxy ketones towards ‘GaI’, **12** was found to be completely unreactive to this reagent in

toluene. This seems unusual, given the strongly reducing nature of ‘GaI’ which one might think would lend it to the formation of **4**, or dihydrobenzoin, PhC(OH)C(OH)Ph, in this reaction.

In order to shed light on the nature of the inorganic intermediate in the reaction that gave **12**, the reaction was worked up prior to aqueous quench, affording a high yield of the novel trimetallic, bis(enediolato) complex, **13**. Presumably, this forms by a combination of diketone reduction and ‘GaI’ disproportionation processes. The molecular structure of **13** is depicted in Fig. 2. Surprisingly, this represents the first structural characterisation of a gallium enediolate complex. It possess three Ga(III) centres, two of which, Ga(2) and Ga(3), have distorted tetrahedral geometries and bridge an O-centre from each diolate ligand. The other gallium, Ga(1), has a

**Scheme 2** Proposed mechanism for the formation of **7**. (i) ‘GaI’, toluene; (ii) **6**; (iii) –GaIBr₂, 1,2-phenyl migration.



Scheme 3 (i) “GaI”, toluene; (ii) quench.

distorted square based pyramidal geometry and is coordinated to all four O-centres. Although there are differences in the Ga–O and Ga–I bond lengths within the structure, all lie within the normal ranges¹⁹ and are unremarkable.

In keeping with the theme of this study, the reduction of a series of α,β -unsaturated ketones and related compounds with “GaI” was attempted. In all cases, no reduction products were returned, but in reactions with esters, deposition of gallium metal was observed. It is thought that this arises from a disproportionation of the gallium reagent to the metal and GaI₃ upon coordination by the O-centres of the ester. Such disproportionation reactions have been previously reported for “GaI”.^{6a} Indeed, in its reaction with *trans*-ethyl cinnamate in this study, a high yield of its GaI₃ adduct, [GaI₃{OC(OEt)C(H)C(H)Ph}] **14**, was isolated and structurally characterised. Details of this structure can be found in the supplementary material.

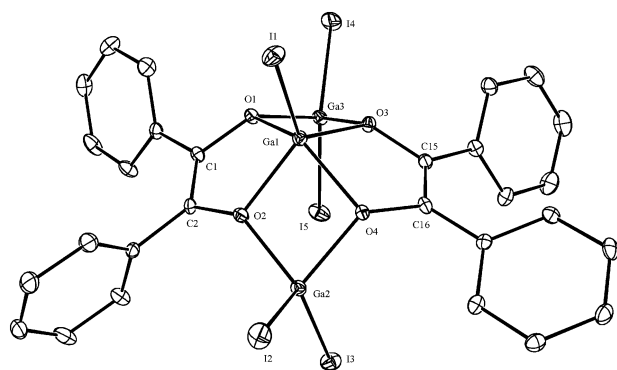


Fig. 2 Molecular structure of **13** (25% thermal ellipsoids are shown). Selected bond lengths (Å) and angles (°): I(1)–Ga(1) 2.4465(9), Ga(1)–O(3) 1.930(4), Ga(1)–O(2) 1.936(4), Ga(1)–O(1) 1.984(3), Ga(1)–O(4) 1.998(3), O(1)–C(1) 1.406(6), O(1)–Ga(3) 1.930(4), I(2)–Ga(2) 2.4618(10), Ga(2)–O(2) 1.913(4), Ga(2)–O(4) 1.943(3), Ga(2)–I(3) 2.4710(9), Ga(3)–O(3) 1.940(3), Ga(3)–I(4) 2.4617(8), Ga(3)–I(5) 2.4686(8), O(3)–Ga(1)–O(2) 123.00(16), O(3)–Ga(1)–O(1) 78.07(15), O(2)–Ga(1)–O(1) 81.27(15), O(3)–Ga(1)–O(4) 82.40(14), O(2)–Ga(1)–O(4) 78.84(14), O(1)–Ga(1)–O(4) 137.98(15), O(3)–Ga(1)–I(1) 123.29(11), O(2)–Ga(1)–I(1) 113.71(12), O(1)–Ga(1)–I(1) 112.27(11), O(4)–Ga(1)–I(1) 109.59(11), O(2)–Ga(2)–O(4) 80.78(15), O(2)–Ga(2)–I(2) 108.59(12), O(4)–Ga(2)–I(2) 110.09(11), O(2)–Ga(2)–I(3) 116.27(12), O(4)–Ga(2)–I(3) 112.41(11), I(2)–Ga(2)–I(3) 121.45(4), O(1)–Ga(3)–O(3) 79.15(15), O(1)–Ga(3)–I(4) 112.23(11), O(3)–Ga(3)–I(4) 113.93(11), O(1)–Ga(3)–I(5) 110.05(11), O(3)–Ga(3)–I(5) 111.18(11), I(4)–Ga(3)–I(5) 122.21(4).

Conclusions

In summary, the reactivity of “GaI” towards a range of α -functionalised ketones has been examined for the first time. Of most interest are the reactions of this reagent with α -alkoxy ketones which led to diastereoselective aldol coupling reactions and the formation of novel trifunctional products containing three contiguous stereocentres. The differences in the stereoselectivities of these reactions has been explained by invoking the involvement of two different transition states that depend upon the steric bulk of the alkoxy substituent. An aldol-type coupling reaction was also observed in the reaction of an α -bromo ketone with “GaI”, whilst in the reaction with an α -chloro ketone, the gallium reagent appeared to act as a Friedel–Crafts alkylation reagent. A selective, high yielding reduction of a 1,2-diketone to an α -hydroxy ketone has been achieved and the inorganic reaction intermediate structurally characterised. Throughout this work “GaI” has proved to be a stronger reducing agent than InI and has showed different chemistry to either Ga(II) or Ga(III) salts. The results of this study establish easy to prepare “GaI” as a potential specialist C–C bond forming reagent for the organic synthetic chemist. Work is ongoing in our laboratory to optimise the reported reactions and to explore new synthetic avenues for “GaI”, especially with regard to cross coupling reactions.

Experimental section

General considerations

All manipulations were carried out using standard Schlenk and glove-box techniques under an atmosphere of high purity argon. The solvents toluene and hexane were distilled over potassium whilst diethyl ether was distilled over Na–K alloy. ¹H and ¹³C NMR spectra were recorded on either a Bruker DXP400 spectrometer operating at 400.13 and 100 MHz, respectively or a JEOL Eclipse 300 spectrometer operating at 300.52 and 75.57 MHz, respectively. Spectra were referenced to either the ¹³C or residual ¹H resonances of the solvent used. High resolution mass spectra were obtained from the EPSRC National Mass Spectrometric Service at Swansea University. IR spectra were recorded as Nujol mulls between NaCl plates. Melting points were determined in sealed glass capillaries under argon and are uncorrected. “GaI”,⁶ InI²⁰ and Ga₂Cl₄ (dioxane)₂²¹ were synthesised by literature methods. All other reagents were obtained commercially and used as received.

General procedure for reactions involving “GaI”. To a suspension of “GaI” (8 mmol) in toluene (20 cm³) at –78 °C was added a solution of the organic substrate (2 mmol) in toluene (10 cm³) over 5 minutes. The resulting suspension was slowly warmed to 20 °C and stirred for 24 h. Degassed HCl (1 M, 50 cm³) was then added to the resulting suspension with vigorous shaking under an argon atmosphere. NaOH (1 M) was added to the mixture until pH 10 was reached. The organic layer was separated, dried over anhydrous magnesium sulfate, and the solvent removed by rotary evaporation to afford a crude product mixture. The composition of the product mixtures were determined by ¹H NMR and GC/MS analyses.

Table 4 Crystal data for compounds **1a–3a**, **10**, **13** and **14**^a

Compound	1a	2a	3a	10	13	14
Empirical formula	C ₂₉ H ₂₆ O ₃	C ₃₀ H ₂₈ O ₃	C ₃₁ H ₃₀ O ₃	C ₂₁ H ₁₈ O	C ₂₈ H ₂₀ Ga ₃ I ₅ O ₄	C ₁₁ H ₁₂ GaI ₃ O ₂
FW	422.50	436.52	450.55	286.35	1264.10	626.63
Temp./K	150(2)	150(2)	150(2)	150(2)	150(2)	150(2)
Crystal system	Monoclinic	Orthorhombic	Monoclinic	Triclinic	Monoclinic	Monoclinic
Space group	C2	P2 ₁ 2 ₁ 2 ₁	P2 ₁ /n	P1	P2 ₁ /n	P2 ₁ /n
<i>a</i> /Å	32.142(6)	6.0010(12)	20.793(4)	5.7983(12)	9.0898(18)	7.4458(15)
<i>b</i> /Å	6.2276(12)	18.790(4)	6.1220(12)	9.0444(18)	19.066(4)	18.197(4)
<i>c</i> /Å	11.413(2)	20.595(4)	20.961(4)	15.820(3)	20.516(4)	12.271(3)
α /°	90	90	90	94.69(3)	90	90
β /°	101.70(3)	90	114.24(3)	100.00(3)	95.84(3)	94.13(3)
γ /°	90	90	90	106.81(3)	90	90
Vol./Å ³	2237.1(8)	2322.3(8)	2433.0(8)	774.4(3)	3537.1(12)	1658.3(6)
<i>Z</i>	4	4	4	2	4	4
Density (calc.)/Mg m ⁻³	1.254	1.249	1.230	1.228	2.374	2.510
μ (Mo-K α)/mm ⁻¹	0.080	0.079	0.078	0.074	6.663	7.233
<i>F</i> (000)	896	928	960	304	2312	1136
No. of reflections collected	5064	13489	7991	4993	15044	4253
No. of independent reffs	3292	4205	4444	2689	7690	2849
<i>R</i> _{int}	0.1064	0.0683	0.0710	0.0381	0.0420	0.0499
Final <i>R</i> indices [<i>I</i> > 2 σ (<i>I</i>)]	<i>R</i> 1 = 0.0876 <i>wR</i> 2 = 0.1387	<i>R</i> 1 = 0.0500 <i>wR</i> 2 = 0.0901	<i>R</i> 1 = 0.0554 <i>wR</i> 2 = 0.1081	<i>R</i> 1 = 0.0594 <i>wR</i> 2 = 0.1280	<i>R</i> 1 = 0.0399 <i>wR</i> 2 = 0.0878	<i>R</i> 1 = 0.0533 <i>wR</i> 2 = 0.1217

^a CCDC 626737–626742. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b613669a

NB: an identical procedure was used for the reactions in Tables 2 and 3 that employed other inorganic reagents.

***R,R,S,S,R,S*-PhC(O)C(H)(Ph)C(OH)(Ph)C(H)(OMe)Ph **1a**.** Following the general procedure, the resulting crude yellow solid was recrystallised from methanol yielding colourless crystals of **1a** (78%): Mp 117–118 °C; ¹H NMR (400 MHz, CDCl₃, 298 K): δ /ppm 2.92 (s, 3H, CH₃), 3.37 (s, 1H, OH), 4.84 (s, 1H, CH), 5.50 (s, 1H, CH), 6.89–7.97 (m, 20H, ArH); ¹³C NMR (75 MHz, CDCl₃, 298 K): δ 31.0 (CH₃), 57.0 (COMe), 82.0 (COH), 87.2 (CCO) 126.9, 127.2, 127.3, 127.6, 127.7, 128.1, 128.5, 128.7, 128.9, 129.1, 130.7, 132.8, 134.9, 136.5, 137.5, 142.2 (Ar-C), 200.17 (CO); IR ν /cm⁻¹ (Nujol): 3520 (br., OH), 1681 (s, C=O); HRMS: (ES) calcd. for [M⁺ + Na]: 445.1774; found 445.1775.

***R,R,S,S,S,R*-PhC(O)C(H)(Ph)C(OH)(Ph)C(H)(OEt)Ph **2a**.** Following the general procedure, the resulting crude yellow solid was recrystallised from methanol yielding colourless crystals of **2a** (35%): mp 132–134 °C; ¹H NMR (400 MHz, CDCl₃, 298 K): δ /ppm 0.51 (t, ³*J*_{HH} = 7.0 Hz, 3H, CH₃), 2.97 (dq, ²*J*_{HH} = 9.3 Hz, ³*J*_{HH} = 7.0 Hz, 1H, diastereotopic CH₂), 3.16 (dq, ²*J*_{HH} = 9.3 Hz, ³*J*_{HH} = 7.0 Hz, 1H, diastereotopic CH₂), 3.42 (s, 1H, OH), 4.63 (s, 1H, CH), 5.23 (s, 1H, CH), 6.85–8.11 (m, 20H, ArH); ¹³C NMR (100 MHz, CDCl₃, 298 K): δ 14.2 (CH₃), 56.0 (CHOEt), 64.9 (CH₂), 83.7 (COH), 89.8 (CCO), 126.3, 126.7, 126.9, 127.1, 127.8, 128.5, 128.6, 128.7, 129.4, 129.8, 130.3, 133.1, 134.8, 137.0, 137.4, 141.5 (Ar-C), 201.3 (CO); IR ν /cm⁻¹ (Nujol): 3480 (br., OH), 1689 (m, C=O); HRMS: (ES) calcd for [MH⁺]: 437.2111; found 437.2110.

***R,R,S,S,S,R*-PhC(O)C(H)(Ph)C(OH)(Ph)C(H)(OⁱPr)Ph **3a**.** Following the general procedure, the resulting crude yellow solid was recrystallised from methanol yielding colourless crystals of **3a** (18%): mp 162–163 °C; ¹H NMR (400 MHz, CDCl₃, 298 K): δ /ppm 0.59 (d, ³*J*_{HH} = 6.12 Hz, 3H, CH₃), 0.72

(d, ³*J*_{HH} = 6.12 Hz, 3H, CH₃), 3.24 (sept, ³*J*_{HH} = 6.12 Hz, 1H, CH(CH₃)₂), 4.83 (s, 1H, CH), 5.15 (s, 1H, CH), 7.23–8.12 (m, 20H, ArH); ¹³C NMR (100 MHz, CDCl₃, 298 K): δ 19.1 (CH₃), 22.8 (CH₃), 56.3 (CH), 68.3 (CH(CH₃)₂), 83.7 (COH), 86.7 (CCO), 126.2, 126.7, 126.9, 127.1, 127.8, 128.2, 128.5, 128.8, 128.9, 130.3, 130.9, 133.1, 134.8, 136.2, 137.3, 141.3 (Ar-C), 201.1 (CO); IR ν /cm⁻¹ (Nujol): 3345 (br., OH), 1651 (m, C=O); HRMS: (ES) calcd for [MH⁺]: 451.2268; found 451.2276.

PhC(O)C(H)(Me)C(O)C(Me)Ph **7.** Following the general procedure, the resulting crude yellow solid was chromatographed using hexane–diethyl ether (10 : 1) as an eluent. Fractions containing **7** were dried *in vacuo* and the residue recrystallised from methanol to yield colourless crystals of **7** (31%). Spectroscopic data for this compound were identical to those previously reported.¹⁴

PhC(O)C(H)(*p*-MeC₆H₄)Ph **10.** Following the general procedure, the resulting crude yellow solid was chromatographed using hexane–diethyl ether (10 : 1) as an eluent. Fractions containing **10** were dried *in vacuo* and the residue recrystallised from methanol to yield colourless crystals of **10** (24%). Spectroscopic data for this compound were identical to those previously reported.¹⁶

[Ga₃I₅{PhC(O)C(O)Ph}₂]13**.** Following the general procedure, the reaction mixture was filtered rather than undergoing aqueous work-up, yielding an orange brown solution. Concentration of the filtrate and placement at –30 °C overnight yielded colourless crystals of **13** (81%) Mp 163–165 °C (dec.). ¹H NMR (400 MHz, CDCl₃, 298 K): δ 6.56–7.30 (m, 20H, ArH); ¹³C NMR (75 MHz, CDCl₃, 298 K): δ 128.8, 129.8, 131.1, 131.8, 135.9, 136.6 (Ar-C), 139.2 (COGa); IR ν /cm⁻¹ (Nujol) 1616 (m, C=O); HRMS: (EI) calcd for [C₂₈H₂₀O₄Ga₃¹²⁷I₅⁺]: 1261.4347; found 1261.4338; Anal. calcd for C₂₈H₂₀O₄Ga₃I₅: C 26.60, H 1.59; Found: C 27.34, H 1.72.

[GaI₃{*trans*-(EtO)C(O)C(H)C(H)Ph} **14**. Following the general procedure, the reaction mixture was filtered rather than undergoing aqueous work-up, yielding an orange brown solution. Concentration of the filtrate and placement at -30 °C overnight yielded colourless crystals of **14** (86%) Mp 113–115 °C; ¹H NMR (400 MHz, CDCl₃, 298 K): δ 0.50 (t, ³J_{HH} = 7.12 Hz, 3H, CH₃), 3.49 (q, ³J_{HH} = 7.12 Hz, 2H, CH₂), 6.89 (d, ³J_{HH} = 15.8 Hz, 1H, CH), 7.43 (d, ³J_{HH} = 15.8 Hz, 1H, CH), 6.66–7.05 (m, 5H, ArH); ¹³C NMR (75 MHz, CDCl₃, 298 K): δ 13.1 (CH₃), 66.7 (CH₂), 113.4 (CH), 152.9 (CH), 129.2, 129.3, 132.5, 132.7 (Ar-C), 174.4 (CO); IR ν/cm⁻¹ (Nujol): 1623 (m, CO); HRMS (EI) calcd for [M⁺-I]: 498.8177, found 498.8177; Anal. calcd for C₁₁H₁₂O₂GaI₃: C 21.08, H 1.93; Found: C 21.19, H, 1.95.

X-Ray crystallography

Crystals of **1a–3a**, **10**, **13** and **14** suitable for X-ray structural determination were mounted in silicone oil. Crystallographic measurements were made using a Nonius Kappa CCD diffractometer. The structures were solved by direct methods and refined on F² by full matrix least squares (SHELX-97)²² using all unique data. All non-hydrogen atoms are anisotropic with H-atoms included in calculated positions (riding model). Compounds **1a** and **2a** crystallised in chiral space groups but their X-ray analyses only established the relative stereochemistry of these “all light atom” structures. Compounds **3a** and **10** crystallised in centrosymmetric space groups and are racemic. Crystal data, details of data collections and refinement are given in Table 4.

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