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1,4-Addition of Bis(iodozincio)methane to α,β-Unsaturated Ketones: Chemical and Theoretical/Computational Studies

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Abstract: 1,4-Addition of bis(iodozincio)methane to simple α,β-unsaturated ketones does not proceed well; the reaction is slightly endothermic according to DFT calculations. In the presence of chlorotrimethylsilane, the reaction proceeded efficiently to afford a silyl enol ether of β-zinciomethyl ketone. The C–Zn bond of the silyl enol ether could be used in a cross-coupling reaction to form another C–C bond in a one-pot reaction. In contrast, 1,4-addition of the dizinc reagent to enones carrying an acyloxy group proceeded very efficiently without any additive. In this case, the product was a 1,3-diketone, which was generated in a novel tandem reaction. A theoretical/computational study indicates that the whole reaction pathway is exothermic, and that two zinc atoms of bis(iodozincio)methane accelerate each step cooperatively as effective Lewis acids.

Keywords: addition reactions · density functional calculations domino reactions · ketones · tandem reactions · zinc

Introduction

Bis(iodozincio)methane (**1**), which can be prepared from diiodomethane and zinc in the presence of a lead catalyst, is a useful synthetic tool. Because it has two C–Zn bonds involving the same carbon atom, it can be regarded as a dianion equivalent.[1] Taking advantage of this characteristic functionality, a number of molecular transformations have been developed. Methylenation of carbonyl compounds[2] and cyclopropanation of 1,2-diketones are representative examples.[3] In these reactions, nucleophilic attack by **1** occurs twice to form two C–C bonds in one step. When these two nucleophilic attacks occur in a stepwise manner, the first reaction can be regarded as a zinciomethylation reaction.[4] In fact, we previously reported sequential coupling of **1** with organic halides:[5] The first coupling reaction of **1** with an organic halide affords the organozinc compound, which then undergoes a further cross-coupling reaction. Similarly, 1,4-addition of **1** to α,β-unsaturated ketones would be another possible approach to the introduction of the iodozinciomethyl group into organic compounds.[6] The 1,4-addition of an organometallic reagent has been used as a highly regio- and stereoselective method for the formation of enolates without the use of a strong base.[7] It would be more attractive if the 1,4-addition of *gem*-dizinc **1** could be achieved because the enolate thus formed would also have a zinciomethyl group in the same molecule, which would allow further molecular transformations. Therefore we studied the 1,4-addition of **1** to α,β-unsaturated ketones and found new reactions that exhibit the characteristic features of the dizinc **1**.

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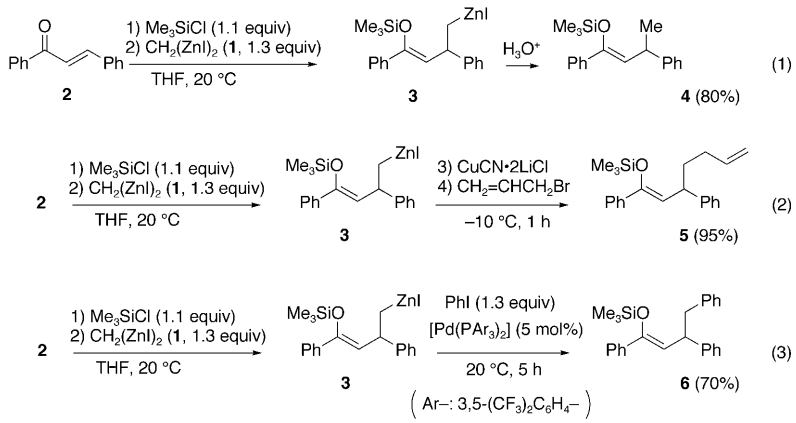
Results and Discussion

1,4-Addition of bis(iodozincio)methane (1) to α,β-unsaturated ketones: The 1,4-addition of bis(iodozincio)methane (**1**) to enones did not proceed efficiently, however, we found that the reaction went to completion in the presence of a stoichiometric amount of chlorotrimethylsilane.[6] The corresponding (*Z*)-silyl enol ethers of β-zinciomethyl ketones were formed, for example, the reaction of chalcone (**2**) with **1** in the presence of chlorotrimethylsilane. Quenching the

intermediary organozinc **3** with a saturated aqueous solution of NH_4Cl gave (*Z*)-silyl enol ether **4** in a yield of 80% [Eq. (1), Scheme 1]. The C–Zn bond in **3** was also used in a cross-coupling reaction to form a C–C bond. The copper-mediated reaction of **3** with allyl bromide gave the coupling product **5** in a yield of 95% [Eq. (2)].[8] The organozinc **3** was also treated with iodobenzene in the presence of a palladium catalyst and was converted into **6** in a yield of 70% [Eq. (3)].[9] The reactions in Scheme 1 can be classified as typical one-pot reactions. It is notable that chlorotrimethylsilane was essential for the completion of the 1,4-addition reaction. Stabilization of the intermediary zinc enolate by transformation into the silyl enol ether would be the driving force of the reactions.



Scheme 1. One-pot reactions initiated by the 1,4-addition of bis(iodozincio)methane (**1**) to chalcone (**2**).

Theoretical/computational study of the 1,4-addition of 1: Density functional theory (DFT) calculations were performed to gain an understanding of the 1,4-addition reactions of **1**. The success of this 1,4-addition in the presence of chlorotrimethylsilane is considered to be a result of 1) the different reactivity of the enone moiety at the 1,2- and 1,4-addition sites, that is, the 1,4-addition site is much more reactive than the 1,2-site, and 2) the crucial role of chlorotrimethylsilane in the 1,4-addition reaction.[10] To determine the reaction mechanism, selectivity, and the effect of chlorotrimethylsilane on the 1,4-addition reaction, we examined the reaction of **1** with acrolein as the simplest model reaction by the DFT method.

All the calculations reported herein were carried out with the Gaussian 03 program package.[11] The molecular structures and harmonic vibrational frequencies were obtained by using the hybrid density functional method based on Becke's three-parameter exchange function and the Lee–Yang–Parr nonlocal correlation functional (B3LYP).[12] We used Ahlrich and co-workers' SVP[13] all-electron basis set for the zinc and iodine atoms and the 6-31G* basis set for the other atoms (denoted as 631SVPs in the text). Geometry optimizations and vibrational analyses were performed at the same level of theory. All stationary points were optimized without any symmetry constraints and characterized by normal coordinate analysis at the same level of theory (number of imaginary frequencies (NIMAG): 0 for minima and 1 for the TSs). We employed $CH_2(ZnX)_2$ (X = Cl or I) as chemical models for the dizinc compounds.

The results of several calculations indicated that the reaction pathway for the 1,4-addition of **1** to acrolein shown in Figure 1 is the most probable. In this pathway the addition of $CH_2(ZnCl)_2$ to acrolein occurs first to form an association complex **CP1** without much energy gain (0.7 kcal mol^{-1}). In the complex **CP1**, both zinc atoms of **1** are coordinated to the same carbonyl group of the acrolein causing the Zn–C–Zn angle (107°) to be bent by 8° and the C=O bond length (1.24 Å) to be elongated by 2% as compared with those in **RT1**. C–C bond formation occurs as the methylene group bound to the two zinc atoms approaches the terminal carbon atom of the acrolein with an activation energy of 23.6 kcal mol^{-1}. The whole reaction is slightly endothermic (4.0 kcal mol^{-1}), in good agreement with the failure of the 1,4-addition of **1** to **2** to go to completion in the absence of chlorotrimethylsilane. The results of this DFT calculation clearly suggest that the 1,4-addition of **1** to α,β-unsaturated carbonyl compounds either does not proceed or it proceeds only slightly because of

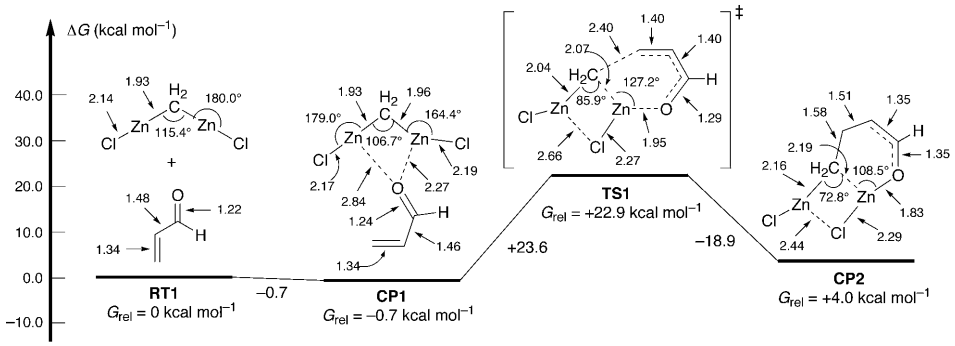


Figure 1. 1,4-Addition of bis(iodozincio)methane (**1**) to acrolein.

thermodynamic preferences rather than for kinetic reasons. Hence, we can conclude that the addition of chlorotrimethylsilane improves the conversion of the 1,4-addition by transforming the initially formed zinc enolate into the corresponding stable silyl enol ether.

We also identified a four-centered TS, **TS2**, for the 1,2-addition reaction (Figure 2). However, **TS1** is energetically much more favorable than **TS2** by $\Delta\Delta G^{\ddagger} = 12.4\ \mathrm{kcal\,mol^{-1}}$. The 1,2-addition reaction is therefore kinetically much less likely to take place than the 1,4-addition.

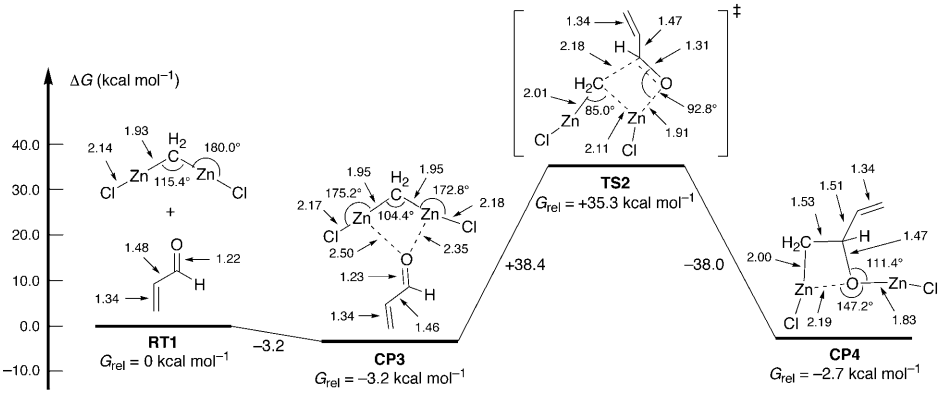
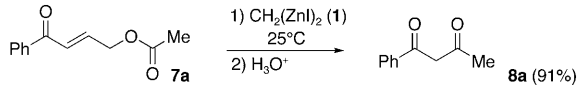


Figure 2. 1,2 -Addition of bis(iodozincio)methane (**1**) to acrolein.

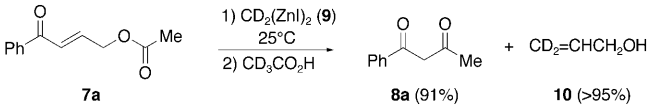
Replacement of $CH_2(ZnCl)_2$ with $CH_2(ZnI)_2$ does not much affect the geometry of the intermediates/TSs or their energy profiles and so does not change the conclusions of the above analysis (see the Supporting Information).

Tandem reactions of 1 with γ-acyloxy-α,β-unsaturated ketones: Based on the above computational analysis, we introduced an acyloxy group at the γ-position of the enone as an intramolecular electrophile in the reaction with the dizinc **1** instead of stabilizing the initially formed zinc enolate by silylation. The acyloxy group would trap the zinc enolate intramolecularly and was expected to facilitate the 1,4-addition of **1**. We treated (*E*)-4-acetoxy-1-phenylbut-2-en-1-one (**7a**; 0.5 mmol) with bis(iodozincio)methane (**1**; 0.6 mmol, 0.5 M in THF) in THF at 25 °C for 2 h and obtained an unexpected product, 1,3-diketone **8a**, in a yield of 91% after aqueous workup (Scheme 2).[14]



Scheme 2. Formation of 1,3-diketone **8a** from **7a**.

Mechanistic investigation of the reaction pathway of the tandem reaction: The reaction of **7a** was also performed with deuterium-labeled bis(iodozincio)methane ($CD_2(ZnI)_2$, **9**)[15] in [D_8]THF and quenched with [D_4]acetic acid. NMR analysis of the mixture obtained showed the quantitative formation of 1,3-diketone **8a** and 3,3-dideuterioprop-2-en-1-ol (**10**; Scheme 3).



Scheme 3. Reaction of **7a** with $CD_2(ZnI)_2$ (**9**).

To obtain additional information about the reaction pathways and mechanisms, we then examined the reaction of **1** and (*E*)-4-oxobut-2-enyl formate with two molecules of Me_2O by means of DFT (B3LYP/631SVPs) calculations (Figure 3 and Scheme 4). The reactants first form an association complex **T-CP1** with little energy gain. The cyclic intermediate **T-CP1** bears two Zn···O bridges between **1** and the substrate. The 1,4-addition reaction of the methylene group of the dizinc reagent proceeds via the TS **T-TS1**, which retains both the Zn···O coordinations, with a reasonable activation energy ($24.2\ \mathrm{kcal\,mol^{-1}}$) to give the Zn–enolate intermediate **T-CP2** with an exothermicity of approximately $10\ \mathrm{kcal\,mol^{-1}}$, probably due to the stabilization of the two Zn···O bonds. After the 1,4-addition, the geometry/orientation of the formate group changes drastically so that the enolate anion can ap-

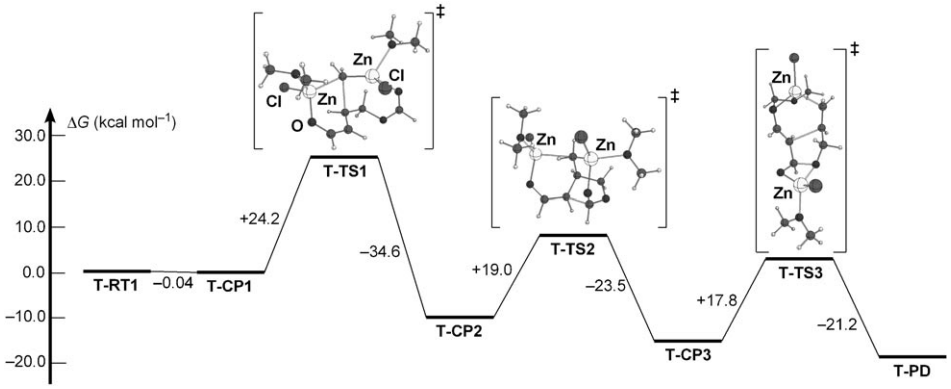
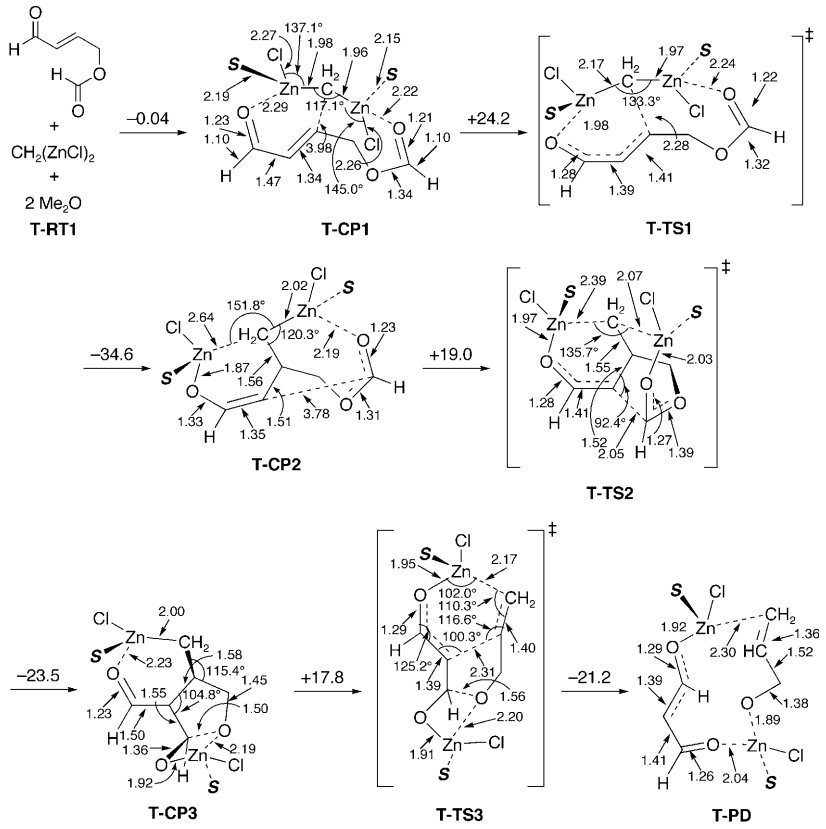


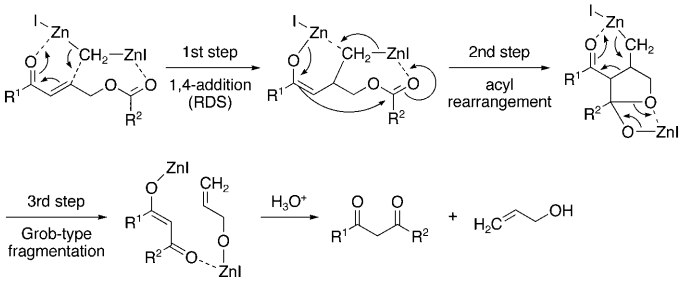
Figure 3. Tandem reaction of bis(iodozincio)methane (**1**) and (*E*)-4-oxobut-2-enyl formate.



Scheme 4. Detailed structures of the intermediates and transition states presented in Figure 3.

proach it. Intramolecular acyl rearrangement occurs with a slightly lower activation energy (19.0 kcal mol^{-1}) than that of the 1,4-addition. The intramolecular acylation reaction proceeds with the rupture of one of the two Zn–C bonds in **1** and the resultant hemiacetal moiety becomes attached to the detached Zn–Cl moiety to produce intermediate **T-CP3** with a stabilization of 23.5 kcal mol^{-1}. The hemiacetal complex **T-CP3** is further stabilized by the recombination of several bonds, including the C–Zn cleaved bond, with an overall loss of energy of only 17.8 kcal mol^{-1}. A Grob-type fragmentation product **T-PD**, which possesses the enolate of the 1,3-diketone and zinc chloride prop-2-en-1-olate, is finally formed with a reasonably large stabilization energy.

This mechanistic investigation by theoretical methods has revealed that 1) this unique reaction using the *gem*-dizinc reagent takes place as a three-step sequential reaction, that is, 1,4-addition (RDS), acyl rearrangement, and Grob-type fragmentation[16] (Scheme 5), 2) each reaction step is facilitated by the synergy of the two zinc atoms of the *gem*-dizinc reagent, and 3) the activation energies from the first to third step decrease gradually and the products become more stabilized as reaction proceeds. This is in good agreement with the fact that no intermediate was observed in this reaction and with the occurrence of the so-called "tandem reaction".[17]

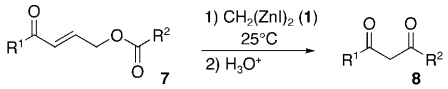


Scheme 5. Plausible pathway for the tandem reaction.

Application of the tandem reaction to triketone synthesis: The formation of enolates by 1,4-addition can be achieved selectively and various functional groups can be tolerated. Therefore we can obtain enolates with extra reactive functional groups such as a ketone group as well as an ester group. In the second step of the tandem reaction, the intramolecular addition of the enolate to the ester group should also proceed selectively, even in the presence of another ketone group, because it proceeds preferentially in a 5-*exo*-trigonal manner.[18] Thus, the preparation of 1,3-diketones based on the acylation of enolates can be realized even in the presence of an extra ketone group. As shown in Scheme 6, substrates containing another ketone group were examined in our tandem reaction. Compounds **11** and **13**

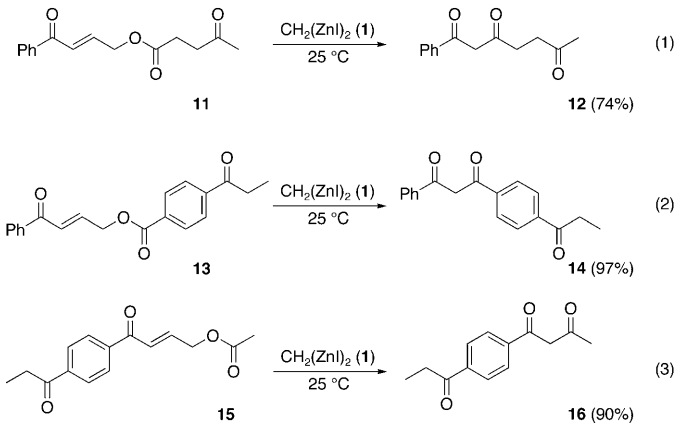
Preparation of various 1,3-diketones by the tandem reaction: Various examples of the synthesis of 1,3-diketones by using our strategy are shown in Table 1. Aryl enones produced the corresponding 1,3-diketones **8** in excellent yields (R^1 = Ar, entries 1–13) whereas alkyl enones gave the products in moderate yields (R^1 = alkyl, entries 14–17). Notably, intramolecular nucleophilic attack of the zinc enolate on the ester group proceeded smoothly, even with sterically hindered substrates, for example, entries 3 and 15. As shown in entries 4–6, the yields of **8** were not affected by the electrophilicity of the aryloyl group in the ester moiety. On the other hand, an electron-donating group on the benzene ring in the Michael acceptor slightly decreased the yield, although it was still good (entry 9).

Table 1. Preparation of the 1,3-diketones **8** by the tandem reaction of **7**.[a]



Entry	R^1	R^2	7	8	Yield [%][b]
1	Ph	Me	**7a**	**8a**	91
2	Ph	*i*Pr	**7b**	**8b**	91
3	Ph	*t*Bu	**7c**	**8c**	81
4	Ph	Ph	**7d**	**8d**	97
5	Ph	*p*-$MeOC_6H_4$	**7e**	**8e**	>99
6	Ph	*p*-$CF_3C_6H_4$	**7f**	**8f**	95
7	*o*-Tol	Me	**7g**	**8g**	88
8	*p*-Tol	Me	**7h**	**8h**	92
9	*p*-$MeOC_6H_4$	Me	**7i**	**8i**	84
10	*p*-$CF_3C_6H_4$	Me	**7j**	**8j**	91
11	*p*-BrC_6H_4	Me	**7k**	**8k**	>99
12	1-naphthyl	Me	**7l**	**8l**	73
13	2-naphthyl	Me	**7m**	**8m**	91
14	$PhCH_2CH_2$	Me	**7n**	**8n**	55
15	$PhCH_2CH_2$	*t*Bu	**7o**	**8o**	61
16	$PhCH_2CH_2$	*p*-$MeOC_6H_4$	**7p**	**8p**	69
17	Me	*p*-$CF_3C_6H_4$	**7q**	**8j**	51

[a] The substrate **7** (0.5 mmol) and bis(iodozincio)methane (**1**; 0.6 mmol) were used for the reaction. [b] Determined by ^{1}H NMR spectroscopy. All products were isolated by silica gel column chromatography for identification.

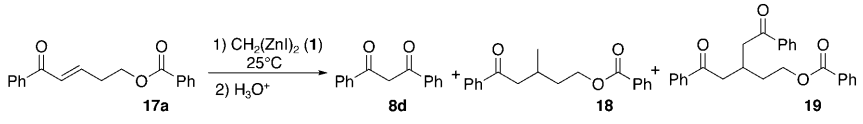


Scheme 6. Preparation of triketones by the tandem reaction.

were easily prepared by esterification of (*E*)-4-hydroxy-1-phenylbut-2-en-1-one[19] with the corresponding keto carboxylic acids. Compound **15** was also prepared by acylation of a γ-hydroxy-α,β-unsaturated ketone carrying an extra ketone group, which was easily obtained from 4-propionylbenzaldehyde according to our reported procedure.[19] The substrates **11**, **13**, and **15** were efficiently converted into the corresponding triketones **12**, **14**, and **16** in high yields. In these transformations it is notable that bis(iodozincio)methane (**1**) did not function as a base at all, which would have deprotonated the α-proton of the carbonyl group, but reacted selectively by 1,4-addition to form the enolate regioselectively.

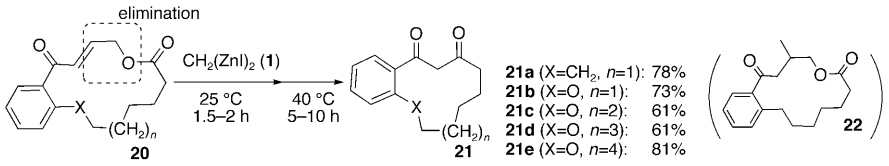
Tandem reactions of δ-acyloxy-α,β-unsaturated ketones with 1: If we consider the mechanism of this tandem reaction starting from γ-acyloxy-α,β-unsaturated ketone **7** in Scheme 5, δ-acyloxy-α,β-unsaturated ketone **17** may also be a suitable substrate to give 1,3-diketone **8**. In the latter case, the initially formed enolate from **17** will react intramolecularly with the ester group in a 6-*exo*-trigonal manner and will release homoallyl alcohol in a Grob-type fragmentation. As shown in Scheme 7, 5-benzoyloxy-1-phenylpent-2-en-1-one (**17a**) was treated with **1**. Whereas the corresponding γ-acyloxy-α,β-unsaturated ketone, 4-benzoyloxy-1-phenylbut-2-en-1-one (**7d**), was transformed into **8d** exclusively (entry 4, Table 1), **17a** gave a mixture of **8d**, **18**, and **19**. The product **18** was obtained by protonation of the enolate, which was formed by the 1,4-addition of **1** to **17a**. The product **19** was obtained by intermolecular 1,4-addition of the enolate to **17a** followed by a Grob-type fragmentation. By prolonging the reaction time, the yield of **8d** increased to 50%, but the formation of **18** and **19** could not be avoided (Scheme 7). A theoretical/computational study of the tandem reaction in Figure 3 revealed that the reaction of **T-CP2** to **T-CP3** proceeds smoothly via **T-TS2**. In particular, in **T-TS2**, the two zinc atoms on the methylene group operate cooperatively in the fused six- and five-membered-ring structure. In the case of **17a**, the transition state of the intramolecular acylation step would be unfavorable for the formation of a fused ring structure like **T-TS2**. Therefore the second step of this tandem reaction did not proceed efficiently with **17a**. Thus, in this novel tandem reaction, γ-acyloxy-α,β-unsaturated ketone **7** is more suitable as a substrate than **17**.

Preparation of cyclic 1,3-diketones by a ring-contraction reaction: Another characteristic feature of the tandem reactions of γ-acyloxy-α,β-unsaturated ketones with **1** is the elimination of three atoms. When the reaction was applied to lactones, they were transformed into the corresponding cyclic 1,3-diketones by a ring contraction with the elimination of three atoms. Thus, as shown in Scheme 8, 14-membered lactone **20a** (X = CH_2, n = 1) was treated with **1** at 25 °C for 2 h and at 40 °C for 5 h, and was converted into the cyclic 1,3-diketone **21a** in a yield of 78%. Without heating, β-methylated product **22**, which results from the 1,4-addition of **1**, was formed as the sole product after aqueous workup.



	8d	18	19
4 h	39%	26%	5%
12 h	50%	10%	14%

Scheme 7. Reaction of δ-benzoyloxy-α,β-unsaturated ketone **17a** with bis(iodozincio)methane (**1**).



Scheme 8. Preparation of cyclic 1,3-diketones **21** from lactones **20** by the tandem reaction proceeding with ring contraction.

In this transformation, the 1,4-addition of **1** to **20a** proceeded at 25 °C but the subsequent intramolecular nucleophilic attack required heating at 40 °C to enable intramolecular addition of the enolate in a 5-*exo*-trigonal manner across the ring structure along with the formation of a more strained ring. In the reactions of other lactones **20b–e**, the corresponding 1,3-diketones **21b–e** were obtained by ring contraction even at 25 °C, with heating to 40 °C improving the yield slightly. The ethereal oxygen atom in the ring (X in **20b–e**) may facilitate the reaction by reducing the ring strain of the intermediate corresponding to **T-TS2** in Figure 3.

Conclusion

The 1,4-addition of bis(iodozincio)methane (**1**) to an enone gave the zinc enolate of β-zinciomethyl ketone, but the reaction did not go to completion. The reaction was shown to be endothermic by a theoretical/computational study. Addition of chlorotrimethylsilane allowed the 1,4-addition reaction to proceed efficiently and gave the silyl enol ether of β-zinciomethyl ketone in high yield. Thus, the products formed were still reactive towards C–C bond forming reactions because the C–Zn bond in the silyl enol ether could be converted into a C–C bond in a cross-coupling reaction.

The introduction of an acyloxy group at the γ position of the α,β-unsaturated ketone also facilitated the 1,4-addition of **1** to form the zinc enolate, which underwent intramolecular nucleophilic addition and then Grob-type fragmentation to afford the 1,3-diketone effectively. By achieving the 1,4-addtion of **1** to γ-acyloxy-α,β-unsaturated ketone **7**, we introduced two nucleophilic sites, zinc enolate and a zinciomethyl group, which induced the intramolecular addition and Grob-type fragmentation, respectively. A theoretical/computational study showed that the two addition reaction steps in our tandem reaction were promoted in a cooperative manner by the two zinc atoms acting as Lewis acids.

Experimental Section

Full experimental procedures and characterization data are given in the Supporting Information.

Preparation of bis(iodozincio)methane (1): A mixture of pure zinc dust (150 mmol), diiodomethane (1.0 mmol), and $PbCl_2$ (0.005 mmol) in THF (5.0 mL) was sonicated for 1 h in an ultrasonic cleaner bath under argon. When pyrometallurgy zinc dust was used instead of pure zinc, it was not necessary to add $PbCl_2$. Both pure zinc and pyrometallurgy zinc are commercially available. Diiodomethane (50 mmol) in THF (45 mL) was added dropwise to the mixture over 30 min at 0 °C with vigorous stirring. The mixture was stirred for 4 h at 25 °C. Then the reaction vessel was allowed to stand undisturbed for several hours. Excess zinc was separated by sedimentation. The ^{1}H NMR spectrum of the supernatant obtained showed a broad singlet at −1.2 ppm at 0 °C, which corresponded to the methylene proton of **1**. The supernatant was used in subsequent reactions as a solution of **1** in THF (0.4–0.5 M). Bis(iodozincio)methane in THF can be kept without decomposing for at least a month in a sealed reaction vessel.

Preparation of 5 by 1,4-addition and Cu-mediated coupling: Bis(iodozincio)methane in THF (1, 0.4 M, 1.0 mmol) was added dropwise to a solution of chalcone (**2**; 1.0 mmol) and chlorotrimethylsilane (1.1 mmol) in THF (3 mL) at 20 °C. The mixture was stirred for 1 h and cooled to −10 °C. A solution of CuCN (1.0 mmol) and LiCl (2.0 mmol) in THF (2 mL) was added to the mixture at −10 °C and the whole was stirred for 5 min at the same temperature. Allyl bromide (1.2 mmol) in THF (1 mL) was added to the mixture and the resulting mixture was stirred for 1 h at −10 °C. Et_3N (5 mL) was then added to the mixture. The resulting mixture was stirred for 5 min and poured into an ice-cooled saturated aqueous solution of NH_4Cl, and extracted with diethyl ether. The organic layers were washed with a saturated aqueous solution of $Na_2S_2O_3$ and brine. The ethereal solution was dried over $MgSO_4$. Concentration in vacuo gave a yellow oil. Short column chromatography on neutral silica gel gave **5** in a yield of 95%. Aqueous workup before the addition of allyl bromide gave **4**[20] in a yield of 80%.

Preparation of (*E*)-4-oxo-4-phenylbut-2-enyl acetate (7a): The substrate **7a** was easily obtained by acetylation of the corresponding γ-hydroxy-α,β-unsaturated ketone, (*E*)-4-hydroxy-1-phenylbut-2-en-1-one, which was obtained in four steps from benzaldehyde in an overall yield of 49% following our reported procedure.[19]

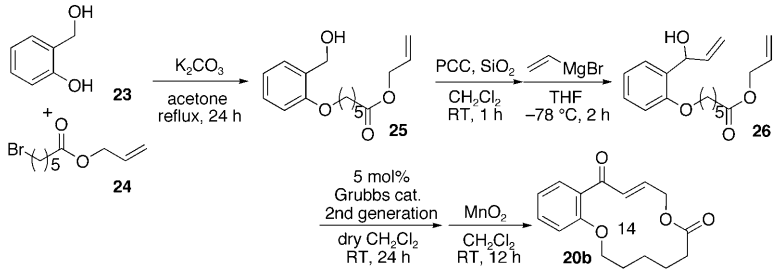
Pyridine (24 mmol), acetic anhydride (12 mmol), and *N,N*-dimethyl-4-aminopyridine (0.5 mmol) were added to a solution of (*E*)-4-hydroxy-1-phenylbut-2-en-1-one (10 mmol) in dichloromethane (10 mL) and the mixture was stirred for 12 h at 25 °C. A saturated aqueous solution of ammonium chloride was added and then the mixture was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated in vacuo. After a purification by a flash silica gel column chromatography (hexane/ethyl acetate, 5:1), the pure acetate **7a** was isolated in a yield of 96%.

The substrates **7b–q** and **15** were also synthesized by esterification of hydroxyenones with the corresponding carboxylic anhydrides or acyl chlorides in the presence of amines. The substrates **11** and **13** were prepared by esterification with the corresponding carboxylic acids and *N,N*-dicyclohexylcarbodiimide (DCC).

The precursor of lactone **20a** was prepared following the reported procedure,[19,21] and its macrolactonization was achieved by using lipase.[22] The lactones **20b–e** were prepared by the following procedure.

Preparation of macrolactones 20b–e: The substrate **20b** was obtained from commercially available 2-hydroxybenzyl alcohol (**23**) in five steps. Selective etherification of **23** with allyl 6-bromohexanoate (**24**) was performed following the reported procedure.[23] Hexanoate **24** (20 mmol) and potassium carbonate (60 mmol) were added to a solution of **23** (25 mmol) in acetone (120 mL) and the resulting mixture was vigorously stirred at reflux for 24 h and then cooled. The acetone was then removed under reduced pressure, the resulting residue was partitioned between ethyl acetate and 1.0 M aq. HCl, and the aqueous layer was washed twice with ethyl acetate. The combined organic layers were dried over sodium sulfate and concentrated in vacuo. After purification by flash silica gel column chromatography (hexane/ethyl acetate, 3:1), the corresponding pure ether **25** was obtained in 34% yield. Ether **25** was oxidized with pyr-

idinium chlorochromate (PCC) and SiO_2 in dichloromethane at room temperature for 1 h to give the corresponding aldehyde. The aldehyde was then converted into allylic alcohol **26** by using vinyl magnesium bromide in THF at −78 °C for 2 h. Purification by flash silica gel column chromatography (hexane/ethyl acetate, 10:1) gave pure **26** in a yield of 44 % in two steps.



After bubbling argon through a solution of **26** in dry dichloromethane (0.01 M) for 20 min, 5 mol % of Grubbs second generation catalyst was added and the mixture was stirred at room temperature for 24 h.[24] The catalyst was removed by filtration and a 14-membered-ring lactone was obtained. Oxidation with MnO_2 in dichloromethane at room temperature for 12 h and purification by flash silica gel column chromatography (hexane/ethyl acetate, 3:1) gave the substrate **20b** in a yield of 67 % in two steps.

The substrates **20c–e** were also obtained in the same way using the corresponding allyl esters instead of **24**.

General procedure for the preparation of 1,3-diketones: The reactions were performed in a 20 mL round-bottomed flask filled with argon. Bis(iodozincio)methane (**1**; 0.6 mmol, 0.5 M in THF) was added to a solution of a γ-acyloxy-α,β-unsaturated ketone (**7**, **11**, **13**, **15**; 0.5 mmol) in THF (2.0 mL). Then the mixture was stirred at 25 °C for 2–5 h (aryl enones: **7a–m**, **11**, **13**, **15**) or 6–12 h (alkyl enones: **7n–q**). Then a saturated aqueous ammonium chloride solution was added and the mixture was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated in vacuo. Purification by flash silica gel column chromatography gave the corresponding pure 1,3-diketones **8**, **12**, **14**, and **16**.

When the lactones **20** were used as substrates, the reaction mixtures were stirred at 25 °C and then at 40 °C. The reaction times were as follows: **20a**: 2 h at 25 °C and 5 h at 40 °C; **20b–e**: 1.5 h at 25 °C and 10 h at 40 °C. By employing higher temperatures, the desired reaction proceeded efficiently; after purification as described above, the pure cyclic 1,3-diketones **21** were obtained.

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