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Lewis Acid Catalyzed Conjugate Addition and the Formation of Heterocycles using Michael Acceptors under Solvent-Free Conditions

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Keywords: β-Dicarbonyl compounds / Dihydrofurans / Conjugate addition / Lewis acid catalysis / Dionato complexes

Conjugate addition and conjugate-addition-initiated ring closure (CAIRC) reactions of β-dicarbonyl compounds with Michael acceptors have been studied using several Lewis acid catalysts under solvent-free conditions. Excellent chemoselectivity was obtained when various Michael acceptors were treated with several β-dicarbonyl compounds. On the other hand, 2-bromo-2-cyclopentenone and 3-bromo-3-vinyl methyl ketone furnished 2,3-dihydrofurans instead of the 1,4-adducts when treated with the same reagents.

Introduction

The conjugate addition of β-dicarbonyl compounds to activated π-systems is one of the most useful C–C bond-forming methods in organic synthesis.[1] Traditionally, these reactions have been catalyzed by bases such as alkali metal alkoxides or hydroxides that may generate byproducts due to competing side reactions.[2] Therefore, the catalysis by transition metals or lanthanides, which work under neutral and mild conditions, has attracted the attention of the chemical community.[3,4] Conjugate addition of β-dicarbonyl compounds, especially β-keto esters, to several acceptors catalyzed by LiI,[2] zeolite,[5] non-ionic bases such as phosphazenes and guanidines,[6] indium metal/TMSCl,[7] some copper and nickel compounds,[8–10] $Yb(OTf)_3$ in H_2O[11] or silica gel support,[12] clay-supported $NiCl_2$/$FeCl_3$[13] and Lewis acid/surfactant systems[14] have been reported. As a consequence of the ever-increasing demand for optically active compounds, asymmetric versions have also been investigated using either chiral complexes of metal cations or organo-catalysts.[15,16]

However, most conjugate-addition and conjugate-addition-initiated ring-closure (CAIRC) reactions reported so far are performed in solution, either in aqueous or non-aqueous media. Recently, for environmental and economic reasons, attention has focused on catalytic reactions under solvent-free conditions. The reactions carried out either in water or under solvent-free methods are much sought for, as they can also be employed with noticeable increase in reactivity and selectivity.[17] Solventless techniques represent clean, economical, efficient and safe procedure that can be efficiently coupled to nonclassical methods of activation including ultrasound and microwaves.[17] However, to the best of our knowledge, there are very few studies on the Lewis acid catalyzed addition of β-dicarbonyl compounds to Michael acceptors under solvent-free conditions. Besides, most of these Lewis acids rarely show a wide range of efficiency over various β-dicarbonyl compounds. In most cases, surveys were carried out on β-keto esters, and application to other functionalities such as β-diesters and β-diketones have not been extensively investigated. For instance, Kotsuki et al.[18] reported the TfOH-catalyzed 1,4-addition reactions of β-keto esters with Michael acceptors under neat conditions. Microwave-irradiation-assisted 1,4-additions of β-dicarbonyl compounds to enones mediated by $BiCl_3$, $EuCl_3$ or CdI_2 have also been investigated.[19,20] More recently, Yadav et al.[17] reported the conjugate addition of β-keto esters to Michael acceptors mediated by $InCl_3$. Christoffers[21] also developed an $FeCl_3{\cdot}6H_2O$-catalyzed Michael addition of β-keto esters to enones without solvent. In a paper by Bartoli et al.[22] β-dicarbonyl compounds were treated with Michael acceptors in the presence of $CeCl_3{\cdot}7H_2O$/NaI to afford effectively 1,4-addition under solvent-free conditions.

However, catalysts that display broad functional group tolerance, enhanced reaction rates and high turnover numbers for an intermolecular addition are rare.[23] Thus, the metal-catalyzed conjugate addition of nucleophiles to activated olefins is still a largely unsolved, but synthetically important problem. In this paper we report our findings on Lewis acid catalyzed conjugate-addition and CAIRC reactions with the use of Michael acceptors (Figure 1). The first part will describe a mild and efficient strategy for conjugate addition of β-dicarbonyl compounds (Figure 2) to 2-cyclopentenone (**1a**). A plausible reaction mechanism which is consistent with our experimental data will be suggested. Finally, the second part will discuss the application of this catalytic process in the formation of heterocycles from β-

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dicarbonyl compounds to 2-bromoalkenones under the same reaction conditions.

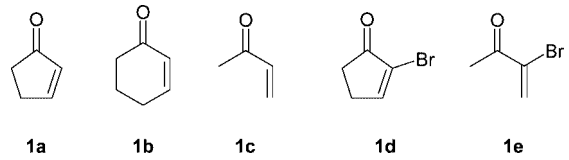


Figure 1. α,β-Unsaturated ketones **1a**–**1e** used as Michael acceptors.

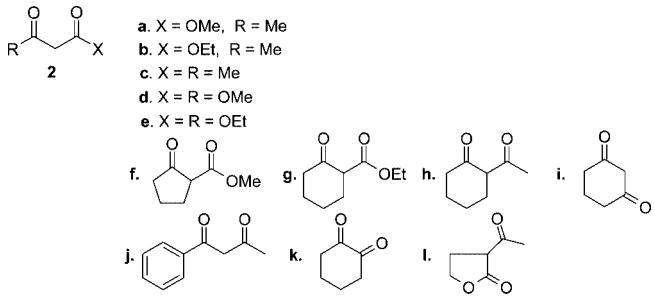
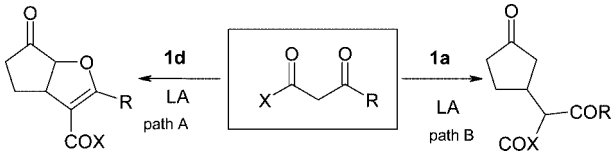


Figure 2. Michael donors **2** used in conjugate-addition and CAIRC reactions.

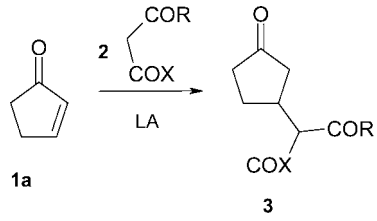
Result and Discussion

As part of a project on the synthetic use of α-donor-α,β-unsaturated ketones, 2-bromo-2-cyclopentenone (**1d**) has been of particular interest as a potentially useful synthetic intermediate. Therefore, this study was primarily designed to investigate the effect of Lewis acid catalysts on the reaction of β-dicarbonyl compounds with the α-bromoalkenones **1d** and **1e** under solvent-free reaction conditions, so that an environmentally benign procedure could be obtained. As an initial attempt, we treated **1d** with **2a** in the presence of $Zn(OTf)_2$ (Scheme 1, path A), and we obtained significant amounts of the corresponding dihydrofuran adducts through the CAIRC reaction.



Scheme 1.

However, when we searched for further information on this type of reaction, we found reports stating that the conjugate addition of β-keto esters to enones catalyzed by $FeCl_3·6H_2O$ is only possible if the enone could adopt the *cisoid* conformation.[21] According to these papers, compounds such as 2-cyclopentenone (**1a**), which can not adopt a favorable conformation, should therefore be reluctant to undergo Lewis acid catalyzed reactions (Scheme 1, path B). Thus, these reports forced us to change our strategy and also to include **1a** in our study. Nevertheless, as indicated in Scheme 2 and Table 1, the reaction between several β-dicarbonyl compounds and **1a** in the presence of $FeCl_3·6H_2O$ gave good results under solvent-free conditions. For instance, when **1a** was treated with **2a** in the presence of $FeCl_3·6H_2O$, **3a** was isolated in 69% yield.



Scheme 2.

With these inspiring results in hand, we decided to survey other types of Lewis acids under the same reaction conditions. In these experiments, **1a**, **1d** and **2a** were selected as model reactants. A series of commercially available Lewis acids with different complexation ability, such as $Sc(OTf)_3$, $Cu(OTf)_2$, $In(OTf)_3$, $Zn(OTf)_2$, $FeCl_3·6H_2O$, $Bi(NO_3)_3·5H_2O$, AgOTf, $CoCl_2·6H_2O$, $Ni(NO_3)_2·6H_2O$ and $MnCl_2$, were surveyed for their ability to induce conjugate addition of β-dicarbonyl compounds to **1a**. In the screening experiments, the triflates of Cu^{II}, Sc^{III}, In^{III}, Zn^{II} and $Bi(NO_3)_3·5H_2O$ were found to be extraordinarily effective catalysts (Table 1). On the other hand, none or only trace amounts of the expected products were detected when AgOTf, $MnCl_2$, $Ni(NO_3)_2·6H_2O$ and $CoCl_2·6H_2O$ were used. So far, there is no report on the conjugate addition reactions of β-dicarbonyl compounds with Michael acceptors mediated by triflates of Cu^{II}, Sc^{III}, In^{III}, Zn^{II} and $Bi(NO_3)_3·5H_2O$ under solvent-free conditions.

Following a screening experiment, further investigations were done to identify the appropriate reaction conditions with the model reactants **1a** and **2a**. The results indicated that the donor/acceptor ratio as well as the catalysts used, strongly influenced the yields of the desired products. For each of the reactions studied, the yields of the Lewis acid catalyzed reaction fluctuates in a surprisingly consistent fashion as the reactant ratios and metal catalysts were varied. Although, from a mechanistic point of view, little is known about the real catalytic function of the Lewis acids, during our investigation we have found that the highest catalytic activity was achieved when 10 mol-% of metal ion was employed. Consequently, the effect of the stoichiometric amount of reactants on the yield of **3a** was also investigated in the presence of 10 mol-% of Lewis acid. When an acceptor/donor ratio of 1:3 was used, the conversion rate was retarded and the yield was decreased. On the other hand, when equimolar amounts of **1a** and **2a** were used, excess **1a** was recovered (Scheme 2). Both conversion rate and yield improved significantly when an acceptor/donor ratio of 1:2 was employed.

On the basis of the above results, we also examined the generality of our Lewis acid catalyzed version in the context of the 1,4-addition of several β-dicarbonyl compounds such as β-keto esters, β-diketones and β-diesters to **1a** using the above-mentioned conditions. Several examples that demon-

Table 1. Solvent-free Lewis acid catalyzed conjugate-addition reaction of the β-dicarbonyl compounds **2a**–**l** with the Michael acceptor **1a** at room temperature.

Entry	Donor	Time (h)	Product	Yields(%)					
				Catalysts					
				$Zn(OTf)_2$	$Cu(OTf)_2$	$Sc(OTf)_3$	$In(OTf)_3$	$FeCl_3 \cdot 6H_20$	$Bi(NO_3)_3 \cdot 5H_2O$
1.	**2a**	6	**3a**[15a]	97	97	97	73	69	83
2.	**2b**	6	**3b**[15a]	95	94	95	83	72	77
3.	**2c**	6	**3c**[8]	85	97	81	88	73	47
4.	**2d**	48	**3d**[7]	75	76	69	80	43	n.d.[a]
5.	**2e**	48	**3e**[7]	61	68	63	75	31	n.d.[a]
6.	**2f**	18	**3f**	88	90	89	82	67	67
7.	**2g**	18	**3g**	70	84	82	71	13	32
8.	**2h**	72	**3h**	58	51	38	25	trace	34
9.	**2i**	72	**3i**	29	26	43	38	12	72

Table 1. (*continued*).

Entry	Donor	Time (h)	Product	Yields(%)					
				Catalysts					
				$Zn(OTf)_2$	$Cu(OTf)_2$	$Sc(OTf)_3$	$In(OTf)_3$	$FeCl_3 \cdot 6H_20$	$Bi(NO_3)_3 \cdot 5H_2O$
10.	**2j**	48	**3j**	76	89	77	91	49	76
11.	**2k**	48	**3k**	68	72	57	71	31	50
12.	**2l**	48	**3l**	81	87	68	78	54	49

[a] n.d.: not determined.

strate the general feasibility of the present method are shown in Table 1. For instance, **1a** reacted with various acyclic β-dicarbonyl compounds in high yields (Table 1, Entries 1–5), and even with cyclic β-dicarbonyl compounds, reasonable yields of the desired products were obtained (Table 1, Entries 6–10). Some interesting compounds such as **3k** and **3l** were also isolated from the 1,2-diketone **2k** and the lactone **2l**, respectively. These results clearly reflect the general and remarkable activity of these catalysts, especially the triflates of Cu^{II}, Zn^{II}, Sc^{III} and In^{III}. Although $FeCl_3 \cdot 6H_2O$ is generally regarded as good catalyst, it is not as effective as other Lewis acids in terms of reactivity and selectivity.

The β-diketones showed slightly lesser reactivity than the β-keto esters. Particularly when **2h**, **2i** and **2j** were used (Table 1, Entries 8, 9 and 10), a large amount of starting material remained unreacted, even after prolonged reaction times. The generality of the catalytic process was also further demonstrated by carrying out the Michael addition of β-diesters such as **2d** and **2e** to **1a** (Table 1, Entries 4 and 5). Though the catalysts display a wide range of structural variations of β-dicarbonyl compounds, the reaction becomes slower and needs a longer time for completion when β-diesters were used. Moreover, no or trace amounts of products were observed when the reaction was catalyzed by $Bi(NO_3)_3 \cdot 5H_2O$ (Table 1, Entries 4 and 5). When β-keto esters or β-diesters were treated with **1a** in the presence of $FeCl_3 \cdot 6H_2O$ and $Bi(NO_3)_3 \cdot 5H_2O$, the desired products were isolated along with decarboxylated side products as detected by GC-MS.

Generally, the metal triflates showed strong and almost unvarying reactivity to a wide range of β-dicarbonyl compounds. In^{III} also showed a similar catalytic behavior to that of the transition metal triflates, whereas Fe^{III} and Bi^{III} were variable. For instance, as it is indicated in Table 1 (Entries 9 and 10), Bi^{III} showed a strong catalytic activity towards the reactions of **2i** and **2j** with **1a**, whereas it was a relatively poor catalyst for the reaction of other β-dicarbonyl compounds. This clearly suggested that the mode of interaction of the Bi^{III}-mediated process is different from that of other catalysts. Furthermore, the failure of other salts to promote an effective Michael reaction also indicates their inability to produce a precise coordinating complex or other intermediates that are critical for the success of the reaction. This can be connected with the charge/size ratio and hydrolysis constants of the metal ions.[24] For instance, the oxophilicity of Ag^{I} is significantly lower than that of other ions, as a result of a lower charge/size ratio of the ion. $Ni(NO_3)_2 \cdot 6H_2O$ and $CoCl_2 \cdot 6H_2O$ were found to loose their activity possibly because of the hydrolytic decomposition in the presence of trace amounts of moisture, which indicates the sensitivity of these ions to non-anhydrous conditions.

We have also found that the catalytic activity is highly dependent upon the purity of the Lewis acids used. Another observation was that there was no reaction at all or only trace amounts of products could be isolated when the reaction was performed in the presence of a solvent such as CH_3CN. The loss of catalytic activity in the presence of a solvent is possibly due to the competitive coordination of the solvent to the catalyst which hinders the formation of

the complex. This competition could also mask the weak interactions that lead to further consequences on the reactivity and selectivity. In other words, the interaction between the reactants could be increased when solvent-free or aggregated charged species are involved, which results in a decrease in molecular dynamics and subsequent induction of special selectivities. In this catalytic process stirring has no significant effect on the rate of conversion.

The mechanism for the addition of metal enolates to Michael acceptors has been investigated by several authors.[6,8,21b] It has been suggested that metal enolates of β-dicarbonyl compounds of the general structure **I** (Figure 3), formed in situ, are the actual nucleophilic species.[6] Although the formation of the dionato complex **I** is a gen-

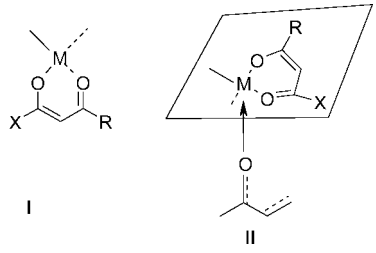
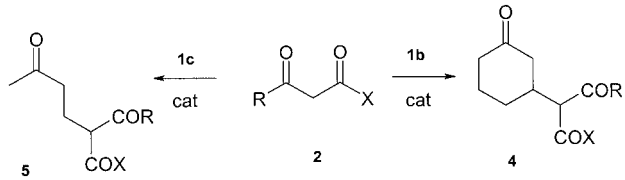


Figure 3. Possible structures of metal enolate intermediates.



Scheme 3.

Table 2. Solvent-free Lewis acid catalyzed conjugate addition reaction of β-dicarbonyl compounds with Michael acceptors **1b** and **1c** to give **4** and **5**, respectively, at room temperature.

Entry	Donor	Time (h)	Product	Yield(%)					
				Catalyst					
				$Zn(OTf)_2$	$Cu(OTf)_2$	$Sc(OTf)_3$	$In(OTf)_3$	$FeCl_3 \cdot 6H_2O$	$Bi(NO_3)_3 \cdot 5H_2O$
1.	**2a**	6	**4a**[7]	98	96	90	94	90	86
2.	**2b**	6	**4c**[22]	98	89	91	89	94	94
3.	**2c**	48	**4d**[7]	95	88	92	95	37	n.d.[a]
4.	**2a**	6	**5a**[15a]	91	87	79	86	79	75
5.	**2c**	6	**5c**[22]	83	71	69	70	74	91
6.	**2d**	48	**5d**[7]	48	37	34	39	23	n.d.[a]

[a] n.d.: not determined.

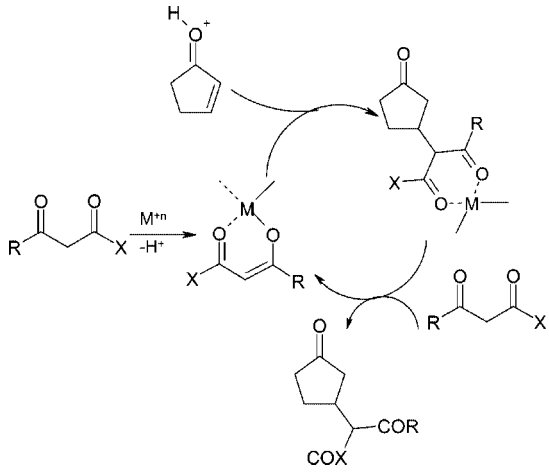
erally accepted principle for transition- and main-group-metal cations,[6,8] the attack on the Michael acceptor by the complex is yet an unresolved issue and requires further research.

However, the simultaneous coordination of both reactants to the metal center has been suggested.[21b,21c] This proposal gives great emphasis to the conformation of the Michael acceptor. If both reagents are simultaneously coordinated in the intermolecular reaction, the Michael acceptor should adopt an *s-cis* conformation as in **II** (Figure 3). This automatically excludes some enones that can not form this favorable conformation.

In order to shed some light on the role of the substrate structure upon the Lewis acid catalysis, other acceptors such as **1b** and **1c** were also included in our study as shown in Scheme 3 and Table 2. Comparison of the results of Table 1 with those of Table 2 help us to propose some structure–reactivity relationships among different Michael acceptors. The fact that there was a small difference among the acceptors in terms of isolated yields, we do not consider this to be chemically significant. Particularly, **1a**, which was considered to be inactive, showed a similar reactivity toward 2-cyclohexenone (**1b**) and the acyclic enone **1c**. In this respect, our findings do not support the criterion of the *cisoid* conformation required from the Michael acceptor.

From our experimental results, therefore, it is possible to predict that the efficiency of the catalytic process is strongly dependent on the nature of the β-dicarbonyl compounds and the metal ion to form a complex, which can be a dionato complex **I** or some other undefined complex. According to our observation, an important part of the mechanism of this reaction could be that the proton released during the formation of the dionato complex protonates the carbonyl oxygen atom of the acceptor (in situ protonation) and prevents the coordination of the oxygen atom to the metal center. On the other hand, the extent of the protonation depends on the nature of the counteranion in the Lewis acid and the Michael donor used. In this respect, the metal salts of strong protic acids having high negative standard enthalpy values, such as TfOH should have a more pronounced in situ protonation effect and make them highly efficient catalysts for the formation of stable complexes.[18] Therefore, the "dual activation" of the reacting species possibly determines the rate of addition (Scheme 4). In addition, a dionato complex **I** has a planar structure and is stabilized by π-delocalization. Therefore, the power of π-delocalization could affect the energy of the O–M^{+n} bond which is then responsible for the transfer of the enolate to the acceptor. Thus, these factors may also well explain the lesser reactivity of β-diesters in this catalytic process.

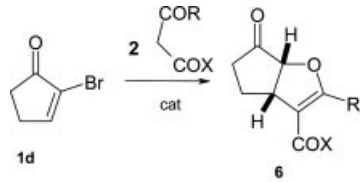
Finally, this work directed our next efforts to develop a strategy for the synthesis of heterocycles through CAIRC reaction using the same reaction conditions. During the last decades, several methods have been developed for the synthesis of dihydrofurans. However, the synthesis of polysubstituted dihydrofuran derivatives is much more difficult than the synthesis of less substituted systems.[25] Therefore, a mild and efficient method for the preparation of polysubstituted dihydrofurans is of practical importance. Indeed, it is only recently that CAIRC has been proved as a synthetic path to dihydrofurans using α-haloalkenones.[26] Though the above-mentioned and some other reports of the successful synthesis of dihydrofurans[27] have been available for quite some time, the CAIRC reaction of β-dicarbonyl compounds with α-halo-substituted Michael acceptors mediated by Lewis acids has not hitherto been exploited.



Scheme 4.

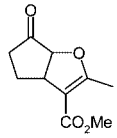
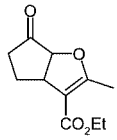
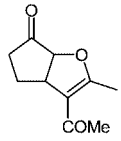
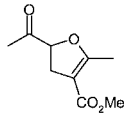
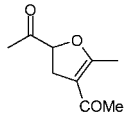
Therefore, the above-mentioned metal salts together with $FeCl_3·6H_2O$ were surveyed for the reactions of β-dicarbonyl compounds with 2-bromo enones for the synthesis of heterocycles through CAIRC reaction. $Cu(OTf)_2$, $Sc(OTf)_3$, $In(OTf)_3$, $Zn(OTf)_2$ and $FeCl_3·6H_2O$ gave moderate yields of 2,3-dihydrofuran derivatives and some selected examples, which demonstrate the general feasibility of the present method for the reaction of β-dicarbonyl compounds with **1d** and **1e**, are summarized in Scheme 5 and Table 3. Although the strong tendency of Fe^{III} to form dionato complexes to perform the conjugate addition is well known,[21b,23] catalysis of CAIRC reactions by $FeCl_3·6H_2O$ has not yet been explored. This catalytic transformation appeared to be specific as β-keto esters and acyclic β-diketones are the only reactive nucleophiles giving moderate yields. Besides, the CAIRC transformation is not as efficient as the corresponding conjugate-addition reaction, both in reactivity and yields. This is because the bromide ion traps the proton before it coordinates to the carbonyl oxygen atom and then the metal enolate is protonated by HBr.

However, the present procedure is highly selective compared with a base-mediated phase-transfer-catalyzed reaction, which gives a single product. For example, when β-



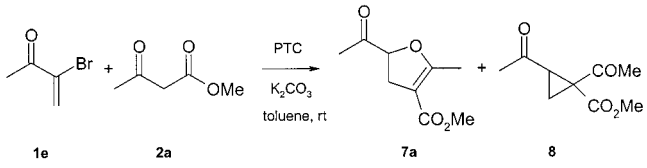
Scheme 5.

Table 3. Solvent-free Lewis acid catalyzed CAIRC reaction of the β-dicarbonyl compounds **2a**–**c** with Michael acceptors **1d** and **1e**.

Entry	Donor	Time (h)	Product	Yield(%)				
				Catalysts				
				$Zn(OTf)_2$	$Cu(OTf)_2$	$Sc(OTf)_3$	$In(OTf)_3$	$FeCl_3·6H_2O$
1.	**2a**	12	**6a** 	72	69	77	63	29
2.	**2b**	12	**6b** 	63	58	68	42	15
3.	**2c**	12	**6c** 	89	57	61	49	18
4.	**2a**	12	**7a**[28] 	62	n.d.[a]	n.d.[a]	n.d.[a]	n.d.[a]
5.	**2c**	12	**7c**[28] 	67	n.d.[a]	n.d.[a]	n.d.[a]	n.d.[a]

[a] n.d.: not determined.

keto esters were treated with acyclic 2-haloalkenones such as **1e** in a base-mediated phase-transfer-catalyzed reaction, the cyclopropanes **8** are unavoidable byproducts along with the dihydrofurans **7**.[26a] However, only dihydrofurans were isolated in Lewis acid catalyzed reactions (Scheme 6).



Scheme 6.

Conclusion

We have presented a novel Lewis acid mediated procedure for the conjugate addition of β-dicarbonyl compounds to enones as well as the CAIRC reaction of α-bromo enones under mild conditions. The method expands the applicability of conjugate-addition reactions in the presence of Lewis acids and offers a practical alternative to the existing procedures. Furthermore, this protocol is also a complement and an alternative to the base-mediated phase-transfer-catalyzed CAIRC reaction route, in which the outcome of the reaction for the synthesis of rings is crucially dependent on the choice of the appropriate bases, phase-transfer catalyst and solvent. We also believe that the present method offers considerable advantages in view of its high efficiency, experimental simplicity, wide range of applicability, catalysts stability and convenient workup procedure. The observed selectivity of the conjugate addition and CAIRC reactions may also be of value in the synthesis of polyfunctional molecules.

Experimental Section

General Methods: All ^1H and ^{13}C NMR spectra were recorded with a JEOI JNM-EX 400 FT-NMR system using $CDCl_3$ as a solvent at room temperature. Chemical shifts are given in ppm and *J* values in Hz. Analytical TLC was carried out on precoated (0.25 mm) Merck silica gel F-254 plates. Flash chromatography was carried out using granular silica (Si-60A° 35–70 μm). GLC analysis was performed with a Varian 3300 chromatograph equipped with a split injector, FID detector and a Varian 4400 integrator. IR spectra were recorded with an FT-IR spectrometer and are reported as wave numbers. GC-MS spectra were registered with a Hewlett Packard 5890 series II CP Sil 5 CB column (25 m) followed by VG Quattro mass spectrometer. Fison Prosoec-Q was used to obtain HREIMS data and the spectra were obtained at 250 °C and 70 eV.

Melting points are uncorrected and are determined in open capillaries with a Büchi 535 apparatus. All reagents and solvents, except 2-bromocyclopentenone (**1d**) and 3-bromo-3-vinyl methyl ketone (**1e**), were obtained from commercial sources and used as received without further purification. The compounds **1d** and **1e** were prepared according to a literature procedure.[29] All compounds were identified by their DEPT, ^{1}H, and ^{13}C NMR and HRMS data. Relevant references are given for known compounds.

General Experimental Procedure for the Synthesis of Compounds 3, 4 and 5: A mixture of the enone **1a**, **1b** or **1c** (1.0 mmol), a Lewis acid (0.1 mmol) and a β-dicarbonyl compound **2** (2.0 mmol) was allowed to stand at room temperature until the reaction was completed. Then the reaction mixture was diluted with a suitable solvent (usually Et_2O/CH_2Cl_2), and the desired products were obtained in high chemical purity after a simple filtration through a short pad of silica gel. In some cases, the crude mixtures were directly chromatographed on silica gel using appropriate solvents (solvents used to determine R_f values).

Methyl 2,3′-Dioxo-1,1′-bi(cyclopentyl)-1-carboxylate (3f): Yield 0.15–0.20 g, 67–90%, white crystals, R_f = 0.42 (EtOAc/pentane, 3:7); m.p. 60–61 °C. IR (neat, NaCl plates): $\tilde{\nu}_{max}$ = 3053, 2858, 1740, 1695, 1421, 1264 cm^{-1}. ^{1}H NMR: δ = 1.60–1.78 (m, 2 H), 1.90–2.05 (m, 2 H), 2.10–2.23 (m, 2 H), 2.32–2.39 (m, 2 H), 2.44–2.55 (m, 4 H), 2.82–2.9 (m, 1 H), 3.72 (d, J = 6.8 Hz, 2 H), 3.74 (s, 3 H) ppm. ^{13}C NMR: δ = 216.5 (–CO), 214.2 (–CO), 172.3 (–COO–), 61.8 (C), 52.7 (–OCH_3), 41.9 (CH_2), 41.0 (CH), 39.5 (CH_2), 31.0 (CH_2), 30.6 (CH_2), 24.6 (CH_2), 19.8 (CH_2) ppm. HRMS: calcd. for $C_{12}H_{16}O_4$ 224.1049; found 224.1049.

Ethyl 2-Oxo-1-(3-oxocyclopentyl)cyclohexane-1-carboxylate (3g): Yield 0.01–0.21 g, 13–84%, colorless oil, R_f = 0.37 (EtOAc/pentane, 3:7). IR (neat, NaCl plates): $\tilde{\nu}_{max}$ = 2940, 2866, 1740, 1710, 1447, 1240, 1206 cm^{-1}. ^{1}H NMR: δ = 1.26 and 1.30 (t, J = 7 Hz, 3 H), 1.51–1.72 (m, 2 H), 1.80–2.08 (m, 4 H), 2.05–2.25 (m, 2 H), 2.30–2.42 (m, 4 H), 2.43–2.58 (m, 2 H), 2.65–2.80 (m, 1 H), 4.20–4.34 (m, 2 H) ppm. ^{13}C NMR: δ = 217.7, 207.5, 171.5, 66.0 (–OCH_2), 62.5 (C), 61.8 (CH_2), 42.3 (CH_2), 41.2 (CH), 38.5 (CH_2), 34.6 (CH_2), 27.4 (CH_2), 24.3 (CH_2), 22.5 (CH_2), 14.3 (CH_3) ppm. HRMS: calcd. for $C_{14}H_{20}O_4$ 252.1362; found 252.1358.

2-Acetyl-2-(3-oxocyclopentyl)cyclohexanone (3h): Yiels trace–0.13 g, trace–58%, colorless oil, R_f = 0.40 (EtOAc/pentane, 3:7). IR (neat, NaCl plates): $\tilde{\nu}_{max}$ = 2956, 1742, 1404, 1265, 1230 cm^{-1}. ^{1}H NMR: δ = 1.52–1.74 (m, 2 H), 1.78–1.92 (m, 4 H), 1.98–2.14 (m, 2 H), 2.16 and 2.17 (s, 3 H), 2.20–2.44 (m, 4 H), 2.46–2.54 (dt, 1 H), 2.86–2.98 (m, 2 H) ppm. ^{13}C NMR: δ = 217.6, 214.5, 203.6, 67.6 (C), 42.3 (CH_2), 40.9 (CH), 40.0 (CH_2), 39.7 (CH_2), 38.6 (CH_2), 30.4 (CH_3), 26.2 (CH_2), 24.5 (CH_2), 22.2 (CH_2) ppm. HRMS: calcd. for $C_{13}H_{18}O_3$222.1256; found 222.1254.

2-(3-Oxocyclopentyl)cyclohexane-1,3-dione (3i): Yield 0.02–0.14 g, 12–72%, yellow crystals, R_f = 0.51 (EtOAc/pentane, 3:7). IR (neat, NaCl plates): $\tilde{\nu}_{max}$ = 2960, 1732, 1601, 1386,1328 cm^{-1}. M.p. 136–136.9 °C. ^{1}H NMR: δ = 1.70–1.95 (m, 2 H), 2.05–2.30 (m, 2 H), 2.32–2.42 (m, 2 H), 2.46 (t, J = 6.4 Hz, 2 H), 2.55–2.80 (m, 4 H), 2.90–2.98 (m, 1 H), 3.63 (d, J = 7.6 Hz, 2 H) ppm. ^{13}C NMR: δ = 204.0 (CO), 71.8 (CH), 42.8 (CH_2), 40.6 (CH), 39.0 (CH_2), 38.4 (CH_2), 33.7 (CH_2), 27.3 (CH_2), 21.0 (CH_2) ppm. HRMS: calcd. for $C_{11}H_{14}O_3$ 194.0943; found 194.0944.

2-(3-Oxocyclopentyl)-1-phenylbutane-1,3-dione (3j): Yield 0.12–0.22 g, 49–91%, brown oil, R_f = 0.29 (EtOAc/pentane, 3:7). IR (neat, NaCl plates): $\tilde{\nu}_{max}$ = 2964, 1740, 1675, 1359, 1183 cm^{-1}. ^{1}H NMR: δ = 2.15 and 2.18 (s, 3 H), 2.20–2.50 (m, 2 H), 2.72 (t, J = 4.8 Hz, 2 H), 3.15–3.24 (m, 1 H), 4.44 (dd, J = 6.0 and 4.0 Hz, 2 H), 6.16–6.25 (m, 1 H), 7.45–7.58 (m, 1 H), 7.60–7.70 (m, 2 H), 7.95–8.10 (m, 2 H) ppm. ^{13}C NMR: δ = 217.3, 203.0, 195.2 (–COPh), 165.5 (C), 134.3 (CH), 129.5 (CH), 129.0 (CH), 69.6 (CH), 43.0 (CH_2), 38.6 (CH_2), 37.3 (CH), 38.1 (CH_2), 27.4 (CH_3) ppm. HRMS: calcd. for $C_{15}H_{16}O_3$ 244.10994; found 244.10988.

2-Hydroxy-6-(3-oxocyclopentyl)cyclohex-2-enone (3k): Yield 0.06–0.14 g, 31–72%, brown oil, R_f = 0.53 (EtOAc/pentane, 3:7). IR (neat, NaCl plates): $\tilde{\nu}_{max}$ = 3084, 2940, 2248, 1738, 1706, 1402, 1381, 1181 cm^{-1}. ^{1}H NMR: δ = 1.52–2.20 (m, 4 H), 2.30–2.65 (m, 6 H), 2.75–3.05 (m, 2 H), 6.20 (s, 1 H), 7.72–7.75 (m, CH=C–) ppm. ^{13}C NMR: δ = 210.4, 204.3, 165.5 (*C*H=C–), 134.6 (C), 47.5 (CH), 39.6 (CH), 39.0 (CH_2), 34.2 (CH_2), 34.0 (CH_2), 29.3 (CH_2), 28.7 (CH_2) ppm. HRMS: calcd. for $C_{11}H_{14}O_3$ 194.0943; found 194.0939.

3-Acetyl-3-(3-oxocyclopentyl)dihydrofuran-2-one (3l): Yield 0.11–0.18 g, 54–87%, yellow oil, R_f = 0.56 (EtOAc/pentane, 3:7). IR (neat, NaCl plates): $\tilde{\nu}_{max}$ = 2966, 2919, 1743, 1712, 1405, 1376, 1173, 1027 cm^{-1}. ^{1}H NMR: δ = 1.85–2.10 (m, 2 H), 2.10–2.25 (m, 2 H), 2.30–2.45 (m, 1 H), 2.34 (s, 3 H), 2.82 (t, J = 10.0 Hz, 2 H), 3.07 (d, J = 6.4 Hz, 2 H), 4.15 (t, J = 8.0 Hz, 2 H) ppm. ^{13}C NMR: δ = 216.5, 202.0, 174.8, 66.2 (CH_2O–), 64.0 (C), 40.1 (CH), 39.9 (CH_2), 38.2 (CH_2), 25.6 (CH_2), 25.3 (CH_3), 24.4 (CH_2) ppm. HRMS: calcd. for $C_{11}H_{14}O_4$ 210.0892; found 210.0895.

Typical Experimental Procedure for the Synthesis of Compounds 6 and 7: A mixture of the 2-bromo enone **1d** or **1e** (1.0 mmol), a Lewis acid (0.1 mmol) and a β-dicarbonyl compound **2** (2.0 mmol) was kept at room temperature without stirring for several hours to ensure complete conversion. The reaction mixture was diluted with Et_2O, concentrated and purified using silica gel column chromatography (Et_2O/pentane, 30:70) to obtain the desired adducts.

Methyl 2-Methyl-6-oxo-4,5,6,6a-tetrahydro-3a*H*-cyclopenta[*b*]furan-3-carboxylate (6a): Yield 0.06–0.15 g, 29–77%, yellow oil; R_f = 0.34 (Et_2O/pentane, 3:7). IR (neat, NaCl plates): $\tilde{\nu}_{max}$ = 3010, 2992, 1732, 1585, 1321, 1193 cm^{-1}. ^{1}H NMR: δ = 2.17 (s, 3 H), 2.18–2.35 (m, 2 H), 2.28–2.41 (m, 2 H), 3.96 (s, 3 H), 4.23 (t, J = 8.0 Hz, 1 H), 4.84 (d, J = 9.6 Hz, 1 H) ppm. ^{13}C NMR: δ = 15.4 (CH_3), 25.6 (CH_2), 34.5 (CH_2), 44.3 (CH), 52.4 (CH_3), 84.0 (CH), 105.5 (C), 125.6 (C), 165, 202 ppm. HRMS: calcd. for $C_{10}H_{12}O_4$ 196.0733; found 196.0735. The signal (δ = 4.23 ppm) of the proton, which coupled to one proton along the ring junction and to two geminal protons on the ring, appeared as a triplet instead of a multiplet (ddd). The same was true for compounds **6b** and **6c**. This is because of the effect of dihedral angles and similar values of the coupling constants among the coupled protons. The same phenomenon was also observed for the cyclopropanated adducts.[30]

Ethyl 2-Methyl-6-oxo-4,5,6,6a-tetrahydro-3a*H*-cyclopenta[*b*]furan-3-carboxylate (6b): Yield 0.03–0.14 g, 15–68%, yellow oil; R_f =0.34 (Et_2O/pentane, 3:7). ^{1}H NMR: δ = 1.24 (t, J = 7.0 Hz, 3 H), 2.15 (s, 3 H), 2.10–2.36 (m, 2 H), 2.34–2.51 (m, 2 H), 4.17 (q, J = 7.0 Hz, 2 H), 4.30 (t, J = 7.6 Hz, 1 H), 4.80 (d, J = 9.6 Hz, 1 H) ppm. ^{13}C NMR: δ = 15.0 (CH_3), 20.12 (CH_3), 25.4 (CH_2), 34.0 (CH_2), 44.8 (CH), 53.0 (CH_2), 84.6 (CH), 104.7 (C), 125.0 (C), 166.5, 201.5 ppm. HRMS: calcd. for $C_{11}H_{14}O_4$ 210.0888; found 210.0892.

3-Acetyl-2-methyl-3a,4,5,6a-tetrahydro-cyclopenta[*b*]furan-6-one (6c): Yield 0.03–0.16 g, 18–89%, light yellow oil; R_f = 0.37 (Et_2O/pentane, 3:7). IR (neat, NaCl plates): $\tilde{\nu}_{max}$ = 2998, 1736, 1645, 1335, 1261, 1167 cm^{-1}. ^{1}H NMR: δ = 2.15–2.40 (m, 2 H), 2.30 (s, 3 H), 2.38 (s, 3 H) 2.48–2.57 (m, 2 H), 4.16 (t, J = 8.0 Hz, 1 H), 4.68 (d, J = 9.6 Hz, 1 H) ppm. ^{13}C NMR: δ = 16.7 (CH_3), 26.2 (CH_2), 30.0 (CH_3), 36.3 (CH_2), 44.4 (CH), 83.5 (CH), 116.2 (C), 128.0 (C), 194.8 (C=O), 214.3 (C=O) ppm. HRMS: calcd. for $C_{10}H_{12}O_3$ 180.0783; found 180.0786.

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