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Studies on Elimination Pathways of β-Halovinyl Ketones Leading to Allenyl and Propargyl Ketones and Furans under the Action of Mild Bases

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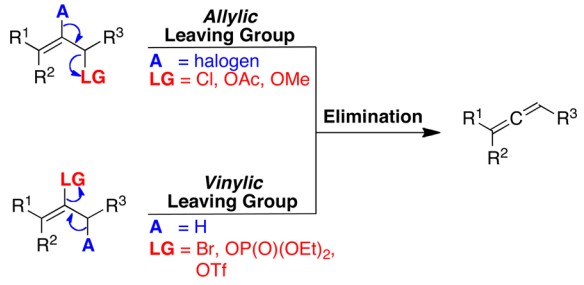
Supporting Information

ABSTRACT: The elimination pathway of stereochemically defined β-halovinyl ketones has been investigated using a mild base, NEt_3, leading to the formation of allenyl ketones and propargyl ketones. A preferential α-vinyl enolization of (*E*)-β-chlorovinyl ketones has been observed where a nonplanar *s-cis* conformation is proposed as a dominant conformation as opposed to a planar *s-cis* conformation of (*Z*)-β-chlorovinyl ketones. Other eliminative pathways, such as concerted *syn*- and *anti*-E2 as well as γ-deprotonation, are excluded on the basis of the deuterium isotope studies. The synthetic utility of the elimination reaction of β-chlorovinyl ketones was further demonstrated for a one-pot synthesis of 2,5-disubstituted furans in the presence of 1 mol % CuCl.

INTRODUCTION

The cumulated double bonds of allenes are a rich source of innovation in synthetic and medicinal chemistry.[1] As with other unsaturated hydrocarbons, a variety of reaction types have been utilized for the synthesis of allenes from alkenes, alkynes, and cyclopropane derivatives.[2] Base-mediated 1,2-eliminations to afford allenes, a key pathway to unsaturated hydrocarbons, have been investigated by using two distinctive elimination pathways (Scheme 1). Thus, allenes have been previously obtained from

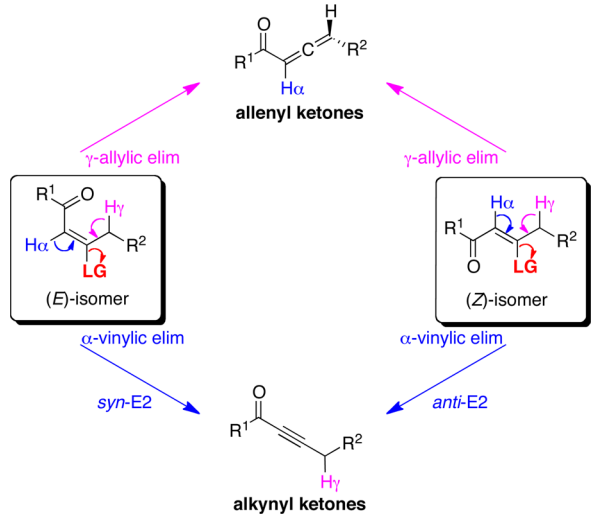
Scheme 1. Elimination Pathways to Allenes



elimination reactions of vinyl halides,[3] enol triflate,[4] and phosphate[5] in the presence of strong bases such as LDA and LiHMDS. These strong bases could pose a problem in terms of functional group tolerance in the synthesis of functionalized allenes.

An interesting selectivity issue arises in the vinylic elimination strategy when one of the alkenyl substituents (R^1 and R^2) possesses an electron-withdrawing group such as a carbonyl group. The presence of an α-hydrogen can lead to

Scheme 2. Concerted Vinylic and Allylic Elimination Pathways



elimination reaction pathways involving *syn*-E2 and *anti*-E2 to alkynyl ketones (Scheme 2). In fact, the syntheses of alkynyl ketones through *syn*- and *anti*-elimination of HBr (using K_2CO_3 or NaOPh),[6] HI (using *i*-Pr_2NEt),[7] and TfOH (using Et_3N)[4] have been reported without involvement of allene intermediacy. In contrast, the vinylic elimination of HBr (using Et_3N) has

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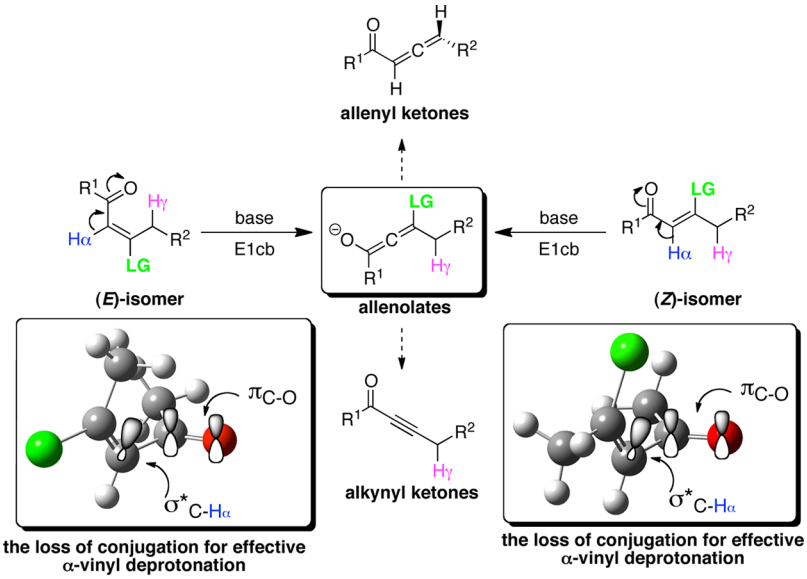
Scheme 3. Stepwise Elimination Pathways via α-Vinyl Deprotonation/Enolization



been utilized in the synthesis of allenyl ketones, in particular acetylallene derivatives.[8]

While the involvement of α-vinyl anion intermediates (i.e., allenolates) has been postulated under strong basic conditions in either a concerted process (i.e., *syn*-E2 and *anti*-E2) or a stepwise manner (i.e., *anti*-E1cB),[6] little experimental evidence for such intermediate species has been documented to date (Scheme 3). Thus, the knowledge gap continues to exist in the generation of allenol(ates) from α,β-unsaturated carbonyl compounds with an α-hydrogen. The inherent difficulty of direct α-vinyl deprotonation of α,β-unsaturated carbonyl compounds lies in the unfavorable orbital overlap between the π_{C-O} bonding orbital and the σ* antibonding orbital in a conjugate system that must precede the loss of conjugation.[9] How to exert influence on the effective orbital overlap between the π_{C-O} bonding orbital and the σ* antibonding orbital in the α,β-unsaturated carbonyl system remains unexplored. As a consequence, α,β-unsaturated carbonyl compounds with an α-hydrogen have been primarily utilized in either 1,2- or 1,4-addition reaction with basic reagents that primarily act as nucleophiles. In addition, the presence of multiple C−H bonds in the α,β-unsaturated carbonyl system under strong basic conditions adds more complexity into the degree of regiocontrol.[10]

While there are a few exceptional cases of direct α-vinyl deprotonations of α,β-unsaturated carbonyl compounds under strong basic conditions,[11] the majority of synthetic methods to allenolates have been developed to circumvent the inherent regio- and chemoselectivity issues associated with direct α-vinyl deprotonation. These synthetic strategies include conjugate additions to alkynylcarbonyl compounds,[12] nucleophilic additions of lithium alkylides to carbonyl compounds followed by a Brook rearrangement,[13] 1,3-transposition of propargylic alcohols by a vanadium oxo complex,[14] and base-promoted isomerization of alkynyl esters.[15]

Given the high synthetic potential of donor/acceptor-substituted allenes in organic synthesis[16] combined with the lack of mechanistic understanding of vinyl eliminations, we investigated the elimination pathway of β-halovinyl ketones, readily accessible through the Friedel−Crafts acylation of alkynes.[17] Herein, we describe the mechanistic studies of dehydrohalogenation of β-halovinyl ketones under mild basic conditions and the application of this technique to a one-pot approach to furan derivatives.

RESULTS AND DISCUSSION

Dehydrochlorination of (*E*)-β-Chlorovinyl Ketones. To examine the nature of the vinylic elimination pathway, (*E*)-β-chlorovinyl ketones were chosen as model elimination substrates since they are selectively accessible by the Friedel−Crafts acylation of alkynes.[18] In a recent attempt to synthesize allenyl ketones, Tsuji and co-workers found that the base-promoted elimination of (*Z*)-β-chlorovinyl ketones did not proceed using KO-*t*-Bu.[19] Thus, we first focused on the identification of suitable bases for dehydrochlorination of (*E*)-**1a** (Table 1). The use of a strong base, KO-*t*-Bu, predominantly led to the decomposition of (*E*)-**1a** without any identifiable structural information (entry 1). To our surprise, the employment of milder organic bases did not provide conjugated alkynyl ketone, the resulting product of vinyl elimination (Scheme 2), but provided a mixture of allenyl ketone **2a** and deconjugated alkynyl ketone **3a**. Further screening of bases generated the same products with different reaction rates. A class of amidine compounds, DBU, did induce the dehydrochlorination of (*E*)-**1a** albeit with a slow rate (entry 2). While the use of a proton sponge, DMAP, and pyridine was not successful, other stronger bases such as DABCO and Hünig's base exhibited similar patterns of low reactivity leading to a 2:1 mixture of **2a** and **3a** (entries 3 and 4). Pleasingly, NEt_3 was found to be the base of choice with a faster elimination rate to give products in an isolated yield of 89% within 18 h at ambient temperature (entry 5). No beneficial effect was observed upon increasing or deceasing the amount of NEt_3 (entries 6 and 7). Reactions in other solvents were slower (entries 8−13), and reactions at higher reaction temperature resulted in diminished isolated yields (entry 14). Interestingly, the ratio of **2a** and **3a** did not vary under the experimental conditions employed, including the reaction temperature (entries 14 and 15).

With the identification of mild elimination conditions, our efforts were directed to shed light on the reaction mechanism.

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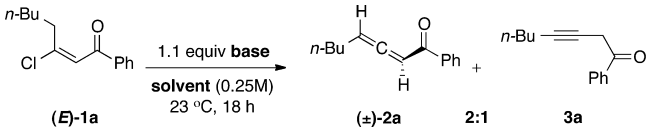
Table 1. Optimization of Dehydrochlorination of (*E*)-Chlorovinyl Ketones



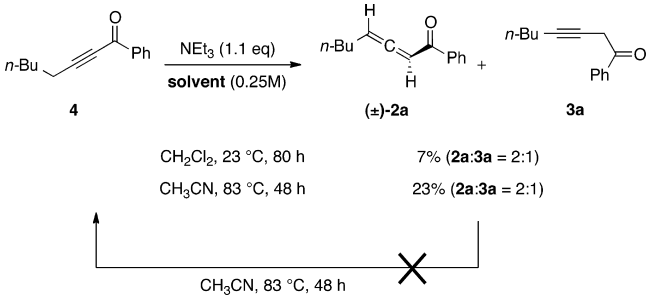
(*E*)-1a (±)-2a 2:1 3a

entry	base (pK_a)[a]	solvent	conversion[b] (%)	comment
1	*t*-BuOK (29)	CH_2Cl_2		DM[c]
2	DBU (12)	CH_2Cl_2	20	
3	DABCO (8.8)	CH_2Cl_2	15	
4	*i*-Pr_2NEt (11)	CH_2Cl_2	30	
5	NEt_3 (9.0)	CH_2Cl_2	>95 (89)	
6	NEt_3 (9.0)	CH_2Cl_2	18	0.2 equiv of NEt_3
7	NEt_3 (9.0)	CH_2Cl_2	>95 (85)	2 equiv of NEt_3
8	NEt_3 (9.0)	CH_3CN	80	
9	NEt_3 (9.0)	$CHCl_3$	57	
10	NEt_3 (9.0)	THF	71	
11	NEt_3 (9.0)	Et_2O	30	
12	NEt_3 (9.0)	$PhCH_3$	63	
13	NEt_3 (9.0)	DMF	72	
14	NEt_3 (9.0)	CH_3CN	>95 (65)	82 °C (4 h)
15	NEt_3 (9.0)	CH_2Cl_2	6	−15 °C

[a]pK_a values in DMSO. [b]Combined isolated yields are given in parentheses. [c]DM = decomposition of material.

The fact that no conjugated alkynyl ketone was observed during and after the reaction suggested a less likely case for the *syn*-E2 reaction mechanism. To explore the possibility of isomerization between a mixture of **2a** and **3a** and conjugated alkynyl ketone **4**, we treated conjugated alkynyl ketone **4** in the same elimination reaction conditions. Although the preferential isomerization of conjugated alkynyl ketone **4** to a 2:1 mixture of **2a** and **3a** was observed, the reaction proceeded very slowly (Scheme 4). While a related transformation of conjugated

Scheme 4. Isomerization Study of Conjugated Alkynyl Ketones



alkynyl esters to allenyl esters has been reported under strong basic conditions,[20] given the fact that similar propargylic isomerizations under basic conditions are much slower with an alkyl substitution on the acetylenic carbon on the order of 300-fold compared to unsubstituted propargylic compounds,[21] it was our interpretation of the result that such isomerization was too slow to account for the rapid generation of products under our elimination reaction conditions. Also, it was found that a mixture of **2a** and **3a** did not isomerize to conjugated alkynyl ketone **4** in CH_3CN with an excess of NEt_3 at 83 °C. Therefore, it was clear that (*E*)-*β*-chlrovinyl ketones underwent a different elimination pathway leading to allenyl and propargyl ketones under our mild basic conditions.

Proposed Mechanism. As for the mechanistic insight, the critical involvement of both vinylic H*α* and allylic H*γ* in the elimination was demonstrated by substrates (*E*)-**5** and (*E*)-**6**. As illustrated in Scheme 5, no elimination reactions were observed for substrates lacking either vinylic H*α* or allylic H*γ* under our elimination conditions, and even using stronger bases such as KO-*t*-Bu. Also, a possible pathway via the formation of 1,3-butadienyl species, generated by an allylic H*γ* deprotonation, was ruled out. Upon the treatment of (*E*)-**1a** with an excess of NEt_3 and (TMS)OTf, it was possible to observe a highly unstable silyl enolate, **7**, as a single stereoisomer with unidentified stereochemistry. Upon treating such intermediates with NEt_3, the elimination products **2a** and **3a** were not observed, but instead slow formation of a mixture of (*E*)-**1a** and (*Z*)-**8** (1:6.6) was observed, which clearly demonstrated that the allylic H*γ* deprotonation did not proceed as a first step in our elimination reaction. In addition, the dehydrobromination of (*E*)-**1a**-Br showed a kinetic behavior similar to that of the dehydrochlorination, leading to an identical mixture of products. Taken together, our experiments suggested a critical role of the *α*-hydrogen of *β*-halovinyl ketones in the elimination reaction pathway, but not the nature of halogen leaving groups and their acid−base chemistry.

To gain further insight into the role of *α*-hydrogen in the formation of elimination products, we examined the deuterium exchange between the *α*-hydrogen of *β*-halovinyl ketones and CD_3OD. Under the elimination conditions, the exclusive formation of (*E*)-*α*-deuterated *β*-methoxyvinyl ketone **9** was observed,[22] while recovered (*E*)-**1a** did not incorporate deuteriums from the solvent (Scheme 6). This result clearly showed the possibility of *α*-deprotonation of *β*-halovinyl ketones in our reaction conditions. A control experiment also showed that the formation of **9** was less likely to originate from the reaction of **2a** and **3a** with CD_3OD since no significant *α*-deuterium incorporation was observed in the product **10**.[23] We also performed kinetic isotope effect studies using (*E*)-**1b** with either vinylic D*α* or allylic D*γ*. Our observation of an appreciable kinetic isotope effect (KIE) of 5.9 for (*E*)-**1b**-D*γ*, but not with (*E*)-**1b**-D*α*, suggested compelling evidence for the involvement of C−H*γ* bond cleavage in the rate-determining step. Also, the fact that no deuterium incorporation was found in the elimination products **2a** and **3a** from these studies reconfirmed that the mechanistic possibility of elimination through a direct *γ*-allylic deprotonation could be excluded.

On the basis of these results, a plausible reaction mechanism that is consistent with our experimental data is depicted in Figure 1. The preferential *α*-vinyl enolization (step 1) of (*E*)-**1** using a mild base, NEt_3, provides an allenol, **11**, that subsequently undergoes elimination through an allylic C-(sp^3)−H deprotonation (step 2) to cumulenol **12**. The fact that no deuterium incorporation was found in the recovered starting material (*E*)-**1a** from the deuterium exchange studies demonstrated that the allenol intermediate **11**, generated via a direct *α*-vinyl enolization, collapsed with expulsion of halide ion faster than reprotonation, the key driving force that enabled mild base to promote elimination reactions. While the high reaction temperature and use of stronger bases in our elimination reaction were not efficient, possibly due to the competing conjugate addition/elimination pathway,[24] the distinction between *α*-vinyl enolization and *α*-vinyl deprotonation of (*E*)-**1** might account for the failure of stronger bases in our elimination process, which will produce the allenolate, not the allenol. The cumulenol **12** can in principle undergo direct

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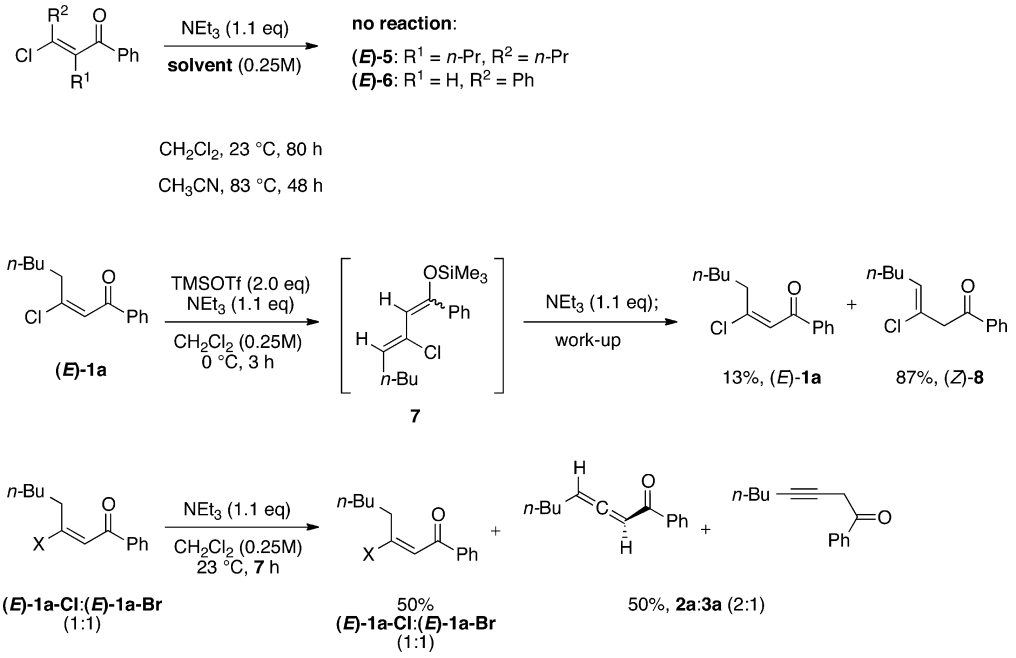
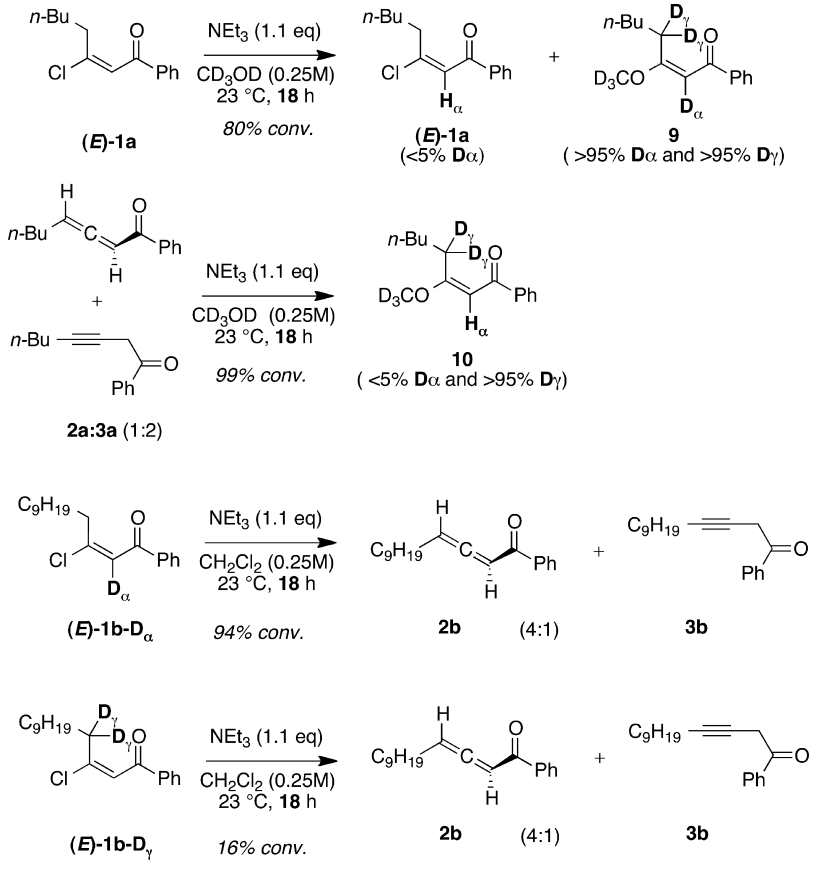
Scheme 5. Mechanistic Consideration for Dehydrohalogenation



Scheme 6. Deuterium Incorporation and Kinetic Isotope Effect Studies



protonation to allenyl ketone; however, the fact that no deuterium incorporation was found in the allenyl ketone **2b** from the elimination reaction of (*E*)-**1b**-Dγ suggests the initial formation of alkynyl enol(ate) **13** through the NEt_3-promoted isomerization of **12** to **13**, which can divergently protonate to either allenyl ketone **2** or deconjugated alkynyl ketone **3**. In a previous work of Miesch, a similar divergent protonation pathway of alkynyl ester enolate was observed to give a 3:1 mixture of allenyl ester and unconjugated alkynyl ester.[25] The involvement of the cumulenol **12** as an intermediate species during the elimination reaction pathway signifies the absence of conjugated alkynyl ketone **4** as a product. At the present time, it

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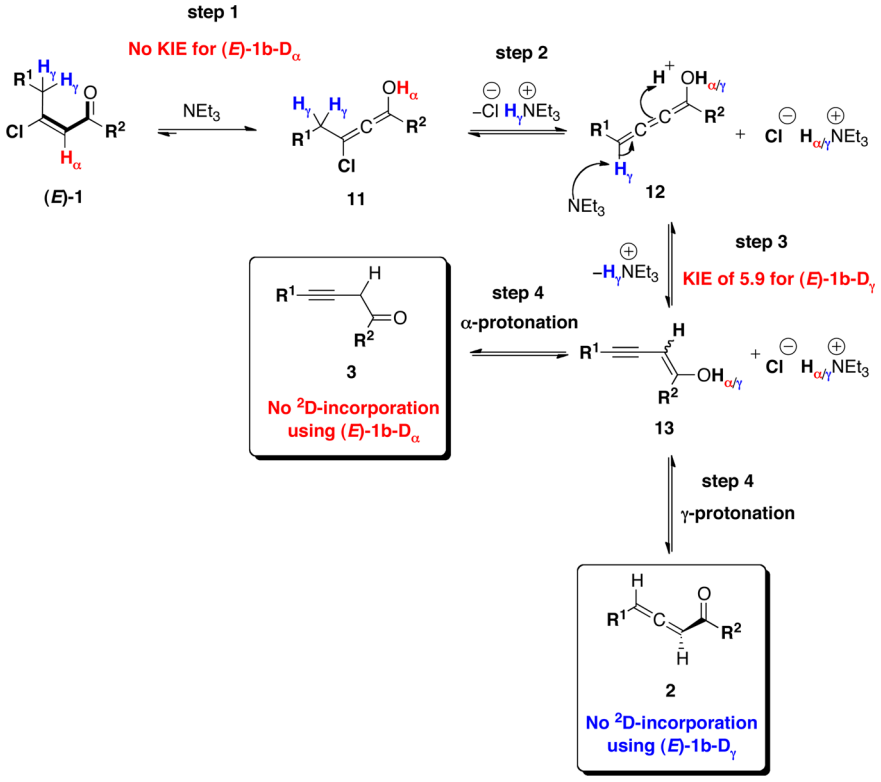
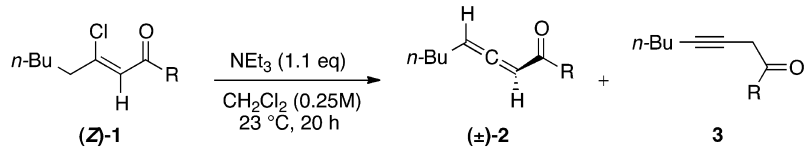


Figure 1. A proposed mechanism for dehydrochlorination of β-halovinyl ketones.

Scheme 7. Dehydrochlorination of (*Z*)-Chlorovinyl Ketones



(*Z*)-**1a**: R = Ph	25% (**2a**:**3a** = 2:1)
(*Z*)-**14**: R = 4-MePh	10% (**2l**:**3l** = 1:1)
(*Z*)-**15**: R = 4-NO_2Ph	51% (**2j**:**3j** = 5:1)

is our understanding that the rate-determining step of the elimination sequence leading to **2** and **3** from (*E*)-**1** is step 3, the generation of alkynyl enol(ate) **13**, based on the significant kinetic isotope effect of 5.9 for (*E*)-**1b**-Dγ and the absence of deuterium incorporation for the recovered (*E*)-**1a** upon the deuterium exchange experiment in CD_3OD.

Interestingly, the deuterium labeling study of (*E*)-**1b**-Dγ showed no deuterium incorporation in each of the products **2b** and **3b**. This outcome suggested a possible side reaction resulting in HCl formation under our deuterium labeling studies other than the HCl formation through α-hydrogen enolization. While our elimination reaction of (*E*)-**1a** proceeded with an excellent conversion (>95%), the isolated yield of products **2a** and **3a** was maximized at around 89% yield at ambient temperature (Table 1, entry 5) and reduced to around 65% at elevated temperature (Table 1, entry 14). Thus, it is possible to speculate that about 10% of **1a** was consumed by a side reaction under ambient temperature that could produce HCl as a byproduct. It has been previously demonstrated that tertiary amines readily displace the β-chlorine atom of β-chlorovinyl ketones to form the corresponding quaternary salts through conjugate addition/elimination reaction.[26] Thus, it is highly likely that the inadvertent appearance of HCl during our deuterium labeling studies might originate from a Hofmann-type elimination of quaternary salts.[27]

Dehydrochlorination of (*Z*)-β-Chlorovinyl Ketones. Subjection of (*Z*)-**1a** as an elimination substrate also led to the formation of a 2:1 mixture of **2a** and **3a**, but at a significantly low reaction rate (Scheme 7). Reactions at higher reaction temperature or longer reaction time failed to improve the reaction efficiency and resulted in a significant loss of isolated yields of products. Other (*Z*)-β-chlorovinyl ketones, **14** and **15**, displayed different reaction rates, favoring the presence of phenyl groups with an electron-withdrawing group.[28] Nevertheless, our results ruled out the possibility of an *anti*-E2 reaction mechanism and suggested a critical role of the stereochemistry of β-chlorovinyl ketones for the effective elimination reaction. To seek the origin of slower elimination reaction rates of (*Z*)-**1a** compared to (*E*)-**1a**, we tested the

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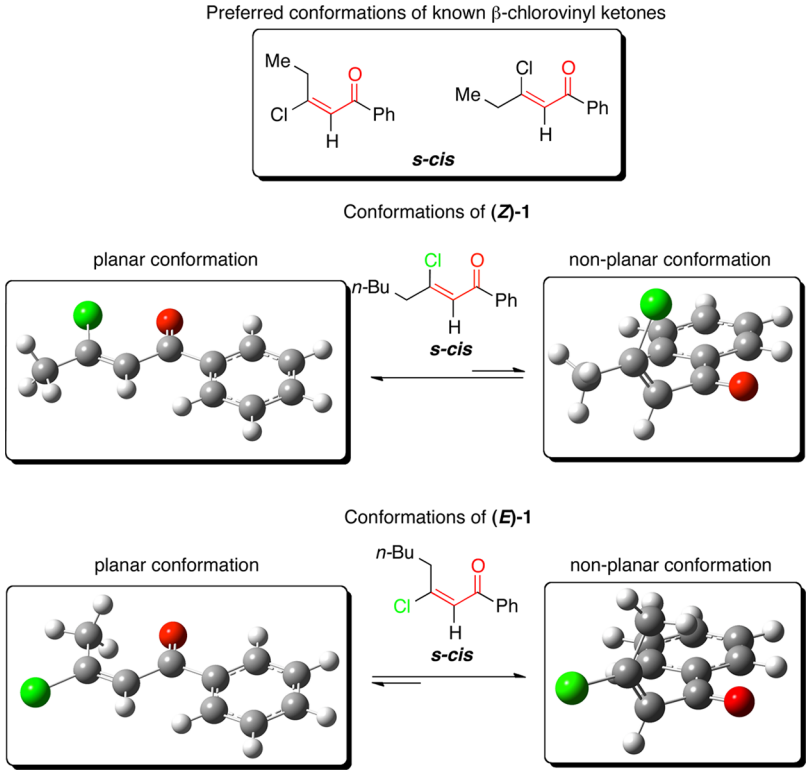

Figure 2. Preferred conformations of β-chlorovinyl ketones.

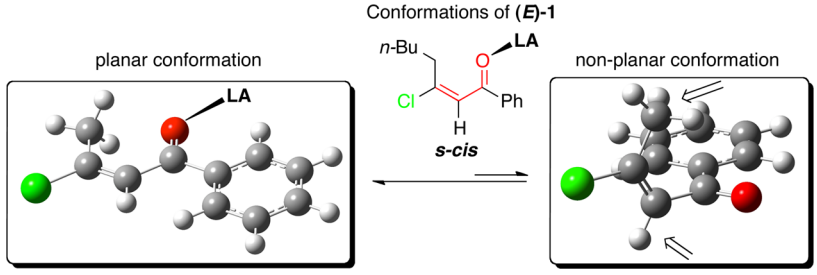

Figure 3. Shift in equilibrium between planar and nonplanar conformations under hard Lewis acids.

possibility of E/Z isomerization by monitoring the elimination of (Z)-**14**. The ^{1}H NMR analysis of the reaction mixtures at frequent intervals indicated no evidence of E/Z isomerization. While we also observed a similar mechanistic scenario for (Z)-β-chlorovinyl ketones (no KIE for (Z)-**1b**-Dα and a KIE of 5.6 for (Z)-**1b**-Dγ), the elimination reactions of (Z)-**1** were still considerably slower than those of (E)-**1**.[29]

The reason for a significantly slow elimination rate observed for (Z)-**1** might be traced to a different conformational preference of (Z)-**1** as opposed to that of (E)-**1**. In a previous spectral correlation study of β-chlorovinyl ketones by Martens, it was proposed that both (E)- and (Z)-β-chlorovinyl ketones with an α-hydrogen and an β-alkyl group preferentially adopt *s-cis* conformations (Figure 2).[30] While the degrees of nonplanarity of *s-cis*-(E)-**1a** and *s-cis*-(Z)-**1a** are difficult to estimate, given the possible steric repulsion between the C═O and the β-alkyl group in *s-cis*-(E)-**1a** as opposed to the steric interaction between the C═O and chlorine atom in *s-cis*-(Z)-**1a**, a slight deviation from the planar conformation of *s-cis*-(E)-**1a** can be envisioned to occur to relieve the steric repulsion between the C═O and the β-alkyl group (Figure 2; for clarity, the *n*-Bu group was omitted). Thus, the least sterically hindered conformation of *s-cis*-(E)-**1a** should have the C═O and the C═C angle between 0° and 90° with respect to the planar *s-cis*-(Z)-**1a**. The nonplanar conformation of *s-cis*-(E)-**1a** will allow more effective orbital overlaps between the π_{C-O} bonding orbital and σ^* antibonding orbital. With a similar steric argument, it is expected that the planar conformation of *s-cis*-(Z)-**1a** is more populated. This nonplanar conformational preference of (E)-**1a** should account for why (E)-**1a** undergoes a faster elimination reaction than (Z)-**1a**.

The equilibrium between the nonplanar and planar *s-cis*-(E)-**1a** conformations is expected to change in the presence of a Lewis acid. Indeed, from our trapping experiment involving (TMS)OTf in Scheme 5, we did not observe a preferential α-deprotonation pathway, leading to the formation of silyl enolate **7**. This is probably due to the fact that hard Lewis acids bind the oxygen atom of ketones, a hard Lewis base, through a nonlinear π-like bonding. Such nonlinear π-like bonding descriptions have been rationalized for Si(IV)-based Lewis acids[31] and might push the equilibrium to the planar *s-cis*-(E)-**1a** conformation in which an orbital overlap between the π_{C-O} bonding orbital and the σ^* antibonding orbital is no longer favored (Figure 3; for clarity, the *n*-Bu group was omitted).

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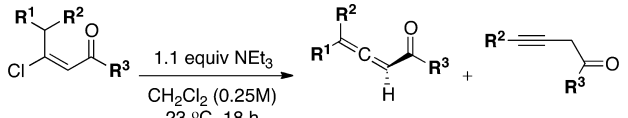
Under such a planar *s-cis*-(*E*)-**1a** conformation, the γ-deprotonation pathway is expected to prevail to provide silyl enolate **7** since the nonlinear π-like bondings between α-H (or the γ-alkyl group) and hard Lewis acids will exert a significant steric congestion in the nonplanar *s-cis*-(*E*)-**1a** conformation.

Substrate Scope. With our improved understanding of elimination pathways of β-halovinyl ketones, we investigated the reaction scope using various β-chlorovinyl ketones (Table 2). Since the stereoselective formation of (*E*)-**1** under thermodynamic control was possible through the $AlCl_3$-catalyzed Friedel–Crafts acylation of alkynes,[32] a number of alkyl- and aryl-(*E*)-**1** compounds bearing various functional groups were synthesized with varying selectivities (*E*:*Z* = 3:1 to 25:1). Subjection of various (*E*)-**1** compounds to our elimination reaction conditions demonstrated the tolerance of functional groups such as halide (entry 3), ester (entry 4), and phthalimide (entry 5), providing excellent isolated yields of products. Reactions of γ,γ-disubstituted (*E*)-**1f,g** led to slightly lower isolated yields, possibly due to the decomposition of products under prolonged exposure to high temperature (entries 6 and 7). In addition to aryl ketones, alkyl ketones underwent elimination reactions albeit with modest yields (entries 7–9). It is worth noting that while allenyl ketones were exclusively formed from the reaction of (*E*)-**1f,g**, the ratios of allenyl/unconjugated alkynyl ketones **2** and **3** varied depending on the substrates, but were not reaction-condition-dependent. Thus, the product ratios were consistent throughout the reaction under varying reaction temperature, base, and solvent. In addition, the ratio of products was independent of postreaction handlings, including aqueous workup procedures; thus, the reaction mixture was directly applied to column chromatography after removal of solvents. No change in the ratio of **2a** and **3a** (2:1) was observed from our variable-temperature ^1H NMR experiments in the presence of 1 equiv of NEt_3 in toluene-d_8 or CD_2Cl_2 at temperatures ranging from 5 to 100 °C. These results suggested the substrate-dependent protonation preference of alkynyl enolate intermediates **13** as illustrated in Figure 1. Such substrate-dependent protonation has been recently observed in the reaction leading to a mixture of allenyl esters and unconjugated alkynyl esters.[33] Our result represented herein describes a general method for the synthesis of aryl- and alkyl-substituted allenyl ketones from β-chlorovinyl ketones under mild basic conditions.[34]

Table 2. Scope of Dehydrochlorination Using (*E*)-β-Chlorovinyl Ketones



1a-m **2a-m** **3a-m**

entry	R^1	R^2	R^3	1	ratio (**2**:**3**)	yield (%)[a]
1	H		Ph	(*E*)-1a	2:1	89
2	H		Ph	(*E*)-1b	4:1	84
3	H		Ph	(*E*)-1c	2.5:1	83
4	H		Ph	(*E*)-1d	5:1	88
5	H		Ph	(*E*)-1e	5:1	81
6[b]			Ph	(*E*)-1f	2 only	77
7[b]			Et	(*E*)-1g	2 only	63
8[b]	H		Et	(*E*)-1h	5:1	68
9	H		Bn	(*E*)-1i	10:1	78
10	H		4-NO_2Ph	(*E*)-1j	5:1	70
11	H		4-BrPh	(*E*)-1k	4:1	87
12	H		4-MePh	(*E*)-1l	1:1	74
13	H		4-OMePh	(*E*)-1m	2:1	81

[a]Combined isolated yields of **2** and **3**. [b]Reaction at 83 °C in CH_3CN for 18 h.

Synthetic Utility. After establishing the preferential α-vinyl enolization of β-halovinyl ketones under mild basic conditions, we became interested in the interconversion between allenyl ketones **2** and unconjugated alkynyl ketones **3**. As previously noted, the ratios of **2** and **3** were not dependent on our reaction conditions, and our isomerization attempt using strong bases such as KO-*t*-Bu only led to the decomposition of the starting materials. A recent chiral guanidine-catalyzed isomerization of unconjugated alkynyl esters to an inseparable 2:1 mixture of allenyl esters and unconjugated alkynyl esters by Tan[35] was evaluated for our isomerization study of **3**. However, the fact that unconjugated alkynyl ketones **3** must be separated from the mixture by using either distillation or selective reactions of allenyl ketones **2** through the Diels–Alder reaction led us to consider other synthetic utility of **2** and **3**. Previously, the laboratories of Hashimi[36] and Gevorgyan[37] postulated the isomerization between allenyl ketones **2** and unconjugated alkynyl ketones **3** under the catalysis of Au(III). Our effort to effect the Lewis acid-promoted reaction of **2** and **3** to a single product led to the cycloisomerization of **2** and **3** to furan derivatives. The furan syntheses from allenyl ketones **2** under Rh(I),[38] Ag(I),[39] Pd(II),[40] and Au(I/III)[41] catalysis as well as from unconjugated alkynyl ketones **3** under Zn(II)[42] and Au(I)[43] catalysis have been well documented. While the cycloisomerization of allenyl ketones **2** to furans was previously examined under copper(I) catalysis, reactions were reported to be either inefficient or in need of a higher catalyst loading of 50 mol % at an elevated temperature of 120 °C.[40a,b] In fact, upon our investigation into the cycloisomerization of a 2:1 mixture of **2a** and **3a**, we found that, among various copper salts we screened, the employment of 30 mol % CuCl was required for an efficient furan formation in 18 h at ambient temperature (Scheme 8). Importantly, the presence of NEt_3 (1.1 equiv) did not have a deteriorating effect on the cycloisomerization, resulting in a slightly higher reaction conversion to 73% after 18 h.

While the furan synthesis from β-chlorovinyl ketones has been recently accomplished in the presence of 5 mol % IrCl(cod)(IPr) at 120 °C,[44] we felt that alkynyl enolate intermediate **13** from elimination reaction of β-chlorovinyl ketones could undergo cycloisomerization under mild reaction conditions in the presence of a catalytic amount of copper salts.

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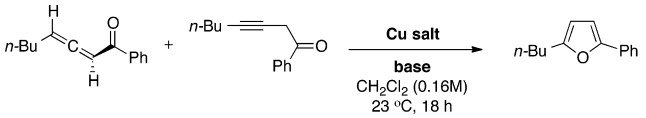
Scheme 8. Furan Formation from Allenyl and Unconjugated Alkynyl Ketones

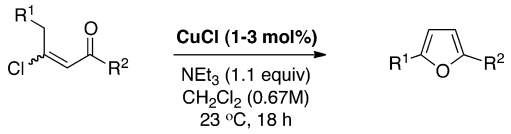


2a:3a (2:1) **16a**

CuCl (0.1 eq)	61% conv.
CuCl (0.3 eq)	99% conv.
CuCl (0.1 eq), NEt_3 (1.1 eq)	73% conv.
NEt_3 (1.1 eq)	0%

Gratifyingly,(*E*)-**1a** in the presence of 1 mol % CuCl and 1.1 equiv of NEt_3 at ambient temperature led to a facile cycloisomerization reaction in a one-pot fashion (Table 3, entry 1). To evaluate the furan formation from (*Z*)-*β*-chlorovinyl ketones, we also subjected (*Z*)-**1a** to our optimized reaction. While a slightly higher loading of CuCl (3 mol %) was necessary, a full reaction conversion of (*Z*)-**1a** to furan **16a** was also observed in 18 h at ambient temperature (entry 2). Under our optimized reaction conditions, a wide range of *β*-chlorovinyl ketones underwent furan formation in excellent yields (entries 3−12). In particular, *β*-chlorovinyl ketones with an alkyl substitution at the *α′* position underwent furan formation at ambient temperature (entries 7 and 8), while the elimination reactions of such substrates were slow and even required a higher reaction temperature in CH_3CN (Table 2, entry 8). Our results indicated that the copper salts did not interfere with the preferential *α*-hydrogen enolization of *β*-chlorovinyl ketones, suggesting a soft Lewis acid, CuCl, might interact with soft Lewis bases such as the C═C bond of (*E*)-**1** and the *β*-chlorine atom of (*Z*)-**1**. Through such interactions, nonplanar conformations are more populated for (*E*)- and (*Z*)-*β*-chlorovinyl ketones, allowing an effective orbital overlap between the π_{C-O} bonding orbital and the σ^* antibonding orbital for *α*-hydrogen enolizations. Likewise, the hard−soft acid−base principle can be applied to the postulated interaction among a hard Lewis base, the C═O bond of (*E*)-*β*-chlorovinyl ketones, and a hard Lewis acid, (TMS)OTf, in our mechanistic studies (Figure 2).

Table 3. One-Pot Approach to Furan Formation from *β*-Chlorovinyl Ketones



1a-k **16a-k**

entry	R^1	R^2	Cu salts (mol%)	yield (%)[a]
1		Ph	CuCl (1)	95
2[b]		Ph	CuCl (3)	88
3		Ph	CuCl (1)	85
4	Cl	Ph	CuCl (1)	90
5	CO_2Me	Ph	CuCl (1)	91
6	NPhth	Ph	CuCl (1)	90
7		Et	CuCl (3)	80
8		Bn	CuCl (3)	84
9		4-NO_2Ph	CuCl (1)	87
10		4-BrPh	CuCl (1)	92
11		4-MePh	CuCl (1)	88
12		4-OMePh	CuCl (3)	85

[a]Isolated yields. [b]Reaction of (*Z*)-**1a**.

■ CONCLUSION

In summary, our elimination reaction studies of *β*-halovinyl ketones revealed a preferential *α*-hydrogen enolization under mild basic conditions, leading to a facile synthesis of allenyl and unconjugated alkynyl ketones. The conformational analysis of (*E*/*Z*)-*β*-chlorovinyl ketones suggested that the different elimination reaction rates originate from the conformational preference of *s-cis*-(*E*)-**1** as a nonplanar form as opposed to a planar conformation of *s-cis*-(*Z*)-**1**. The nonplanar conformation of *s-cis*-(*E*)-**1** allows better orbital overlap between the π_{C-O} bonding orbital and the σ^* antibonding orbital, leading to an efficient *α*-hydrogen enolization. The conformational preference of *β*-chlorovinyl ketones has also been shown to switch under the hard−soft acid−base interactions. Our mechanistic finding was further utilized in the development of one-pot synthesis of 2,5-disubstituted furans from *β*-chlorovinyl ketones in the presence of 1 mol % CuCl. Further synthetic studies of *β*-halovinyl ketones are currently under way in our laboratories, and our result will be reported in due course.

■ EXPERIMENTAL SECTION

General Methods. All reactions were carried out under an argon atmosphere with oven-dried glassware. The progress of the reactions was monitored by thin-layer chromatography on precoated silica gel plates (250 mm) and visualized by ultraviolet light or by staining with $KMnO_4$ stain. The ^1H and ^{13}C NMR spectra were obtained on a 500 MHz Fourier transform spectrometer. Chemical shifts are reported in units of parts per million downfield from tetramethylsilane, and all coupling constants are reported in hertz. The infrared spectra were obtained using an infrared spectrometer. High-resolution mass spectral (HRMS) analyses were carried out using electrospray ionization time-of-flight (ESI-TOF) mass spectrometry. Silica gel (32−64 u) was used for air-flashed chromatography. HPLC-grade solvents were further dried through alumina columns. Unless otherwise specified, all chemicals were obtained from commercial sources and used without further purification.

General Procedure A: Friedel−Crafts Acylation of Alkynes for the Synthesis of *β*-Chlorovinyl Ketones. All *β*-chlorovinyl ketones were prepared on the basis of the method in a previous report.[18] To a stirred suspension of aluminum chloride (733 mg, 5.5 mmol) in dry dichloromethane (5 mL) at −40 °C (*Z*-selective) or 0 °C (*E*-selective) were added alkyne (5 mmol) and acyl chloride (5 mmol) dropwise at the same time. Stirring of the resulting solution was continued at the same temperature until the reaction was complete by TLC (20−40 min). The reaction was then quenched with H_2O, extracted with dichloromethane, and washed with brine. After drying over $MgSO_4$, the solution was concentrated under reduced pressure, and the resulting *E*/*Z* mixtures of products (*E*:*Z* = 1:1 to

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25:1) were chromatographed to isolate the desired (*E*)-isomers in 35−65% yields.

*Data for (E)-3-chloro-1-phenyloct-2-en-1-one (**1a**):* 485 mg (41%); yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.91−7.93 (m, 2H), 7.54−7.58 (m, 1H), 7.45−7.48 (m, 2H), 7.12 (s, 1H), 2.95−2.98 (m, 2H), 1.67−1.70 (m, 2H), 1.34−1.37 (m, 4H), 0.89 (t, 3H, J = 7.20 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 188.9, 157.8, 138.1, 133.0,131.4, 128.6, 128.3, 123.2, 36.4, 31.0, 27.5, 22.4, 13.9; IR (neat) 2957, 2930, 2860, 1669, 1600, 1447, 1227, 1039, 1020, 692, 639 cm^{-1}; HRMS-CI m/z 237.1040 [(MH)$^+$, calcd for $C_{14}H_{18}ClO$ 237.1041]. *Data for (Z)-**1a***: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.91−7.93 (m, 2H), 7.54−7.56 (m, 1H), 7.44−7.47 (m, 2H), 6.82 (s, 1H), 2.51−2.54 (m, 2H), 1.68−1.71 (m, 2H), 1.36−1.37 (m, 4H), 0.92 (t, 3H, J = 6.80 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 189.8, 147.7, 137.6, 133.1, 128.6(4), 128.6(1), 128.4, 121.1, 41.1, 30.6, 27.0, 22.3, 13.9; IR (neat) 2957, 2931, 2860, 1666, 1600, 1447, 1227, 1040, 692, 639 cm^{-1}; HRMS-CI m/z 237.1046 [(MH)$^+$, calcd for $C_{14}H_{18}ClO$ 237.1041].

*Data for (E)-3-chloro-1-phenyltridec-2-en-1-one (**1b**):* 613 mg (40%); yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.90−7.94 (m, 2H), 7.54−7.59 (m, 1H), 7.44−7.49 (m, 2H), 7.12 (s, 1H), 2.92−3.01 (m, 2H), 1.64−1.72 (m, 2H), 1.21−1.36 (m, 14H), 0.87 (t, 3H, J = 7.03 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 188.7, 157.9, 138.3, 133.1, 128.8, 128.4, 123.4, 36.6, 32.0, 29.7, 29.6, 29.4(9), 29.4(5), 29.0, 27.9, 22.9, 14.2; IR (neat) 2925, 2854, 1666, 1600, 1465, 1226, 1038, 692, 639 cm^{-1}; HRMS-CI m/z 307.1822 [(MH)$^+$, calcd for $C_{19}H_{28}ClO$ 307.1823].

*Data for (E)-3,7-dichloro-1-phenylhept-2-en-1-one (**1c**):* 668 mg (52%); yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.88−7.92 (m, 2H), 7.54−7.58 (m, 1H), 7.44−7.48 (m, 2H), 7.17 (s, 1H), 3.52−3.60 (m, 2H), 2.97−3.04 (m, 2H), 1.79−1.93 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 188.4, 156.5,137.9, 133.2, 128.7, 128.3, 123.8, 44.6, 35.4, 31.5, 25.0; IR (neat) 2929, 2853, 1717, 1663, 1395, 1373, 719 cm^{-1}; HRMS-CI m/z 257.0493 [(MH)$^+$, calcd for $C_{13}H_{15}Cl_2O$ 257.0494].

*Data for (E)-methyl 5-chloro-7-oxo-7-phenylhept-5-enoate (**1d**):* 866 mg (65%); yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.89−7.90 (m, 2H), 7.52−7.56 (m, 1H), 7.42−7.47 (m, 2H), 7.14 (s, 1H), 3.64 (s, 3H), 2.97−3.04 (m, 2H), 2.37−2.43 (m, 2H), 1.98−2.05 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 188.3, 173.3, 155.8, 137.9, 133.1, 128.7, 128.3, 124.1, 51.5, 35.4, 32.7, 22.8; IR (neat) 2956, 2929, 1771, 1669, 1608,1261, 1178, 1015 cm^{-1}; HRMS-CI m/z 267.0777 [(MH)$^+$, calcd for $C_{14}H_{16}ClO_3$ 267.0782].

*Data for (E)-2-(4-chloro-6-oxo-6-phenylhex-4-en-1-yl)-isoindoline-1,3-dione (**1e**):* 955 mg (54%); yellow crystalline solid; mp 159−162 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.83−7.86 (m, 2H), 7.79−7.82 (m, 2H), 7.67−7.70 (m, 2H), 7.52−7.56 (m, 1H), 7.41−7.46 (m, 2H), 7.13 (s, 1H), 3.75−3.80 (m, 2H), 3.02−3.07 (m, 2H), 2.06−2.14 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 188.2, 168.3, 155.6, 137.9, 133.8, 133.1, 132.1, 128.6, 128.3, 123.9, 123.2, 37.1, 33.8, 26.6; IR (neat) 2955, 2910, 2866, 1695, 1664, 1635, 1600, 1447, 1226, 1039, 777, 692, 638 cm^{-1}; HRMS-CI m/z 354.0882 [(MH)$^+$, calcd for $C_{20}H_{17}ClNO_3$ 354.0891].

*Data for (E)-3-chloro-3-cyclohexyl-1-phenylprop-2-en-1-one (**1f**):* 559 mg (45%); pale yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.90−7.95 (m, 2H), 7.54−7.58 (m, 1H), 7.45−7.49 (m, 2H), 7.02 (s, 1H), 3.67−3.79 (m, 1H), 1.66−1.87 (m, 5H), 1.52−1.63 (m, 2H), 1.32−1.43 (m, 2H), 1.13−1.26 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 188.4, 162.4, 138.1, 132.9, 128.6, 128.3, 122.3, 42.5, 30.6, 25.6(6), 25.6(1); IR (neat) 3062, 2920, 2854, 1667, 1603, 1368, 1224, 1034, 1016, 964, 858, 776, 717, 692, 641, 591 cm^{-1}; HRMS-CI m/z 249.1040 [(MH)$^+$, calcd for $C_{15}H_{18}ClO$ 249.1041].

*Data for (E)-1-chloro-1-cyclohexylpent-1-en-3-one (**1g**):* 351 mg (35%); pale yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.34 (s, 1H), 3.79−3.87 (m, 1H), 2.46 (q, 2H, J = 7.29 Hz), 1.73−1.78 (m, 2H), 1.62−1.69 (m, 3H), 1.44−1.54 (m, 2H), 1.31−1.34 (m, 2H), 1.14−1.21 (m, 1H), 1.07 (t, 3H, J = 7.29 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 197.6, 161.1, 124.1, 41.7, 37.5, 30.3, 25.4(8), 25.4(5), 7.54; IR (neat) 2930, 2855, 1693, 1595, 1449, 1367, 1118, 1039, 853, 799 cm^{-1}; HRMS-CI m/z 201.1035 [(MH)$^+$, calcd for $C_{11}H_{18}ClO$ 201.1041].

*Data for (E)-5-chlorodec-4-en-3-one (**1h**):* 330 mg (35%); colorless liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.42 (s, 1H), 2.89−2.95 (m, 2H), 2.46 (q, 2H, J = 7.32 Hz), 1.56−1.62 (m, 2H), 1.30−1.23 (m, 4H), 1.07 (t, 3H, J = 7.32 Hz), 0.88 (t, 3H, J = 7.28 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 198.2, 156.3, 125.2, 37.6, 35.9, 30.9, 27.3, 22.3, 13.8, 7.7; IR (neat) 2925, 2854, 1716, 1458, 1377, 775 cm^{-1}; HRMS-CI m/z 189.1032 [(MH)$^+$, calcd for $C_{10}H_{18}ClO$ 189.1041].

*Data for (E)-4-chloro-1-phenylnon-3-en-2-one (**1i**):* 727 mg (58%); yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.32−7.36 (m, 2H), 7.25−7.30(m, 1H), 7.19−7.22 (m, 2H), 6.45 (s, 1H), 3.72 (s, 2H), 2.87−2.95 (m, 2H), 1.55−1.62 (m, 2H), 1.26−1.33 (m, 4H), 0.88 (t, 3H, J = 7.20 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 195.1, 158.1, 133.9, 129.5, 128.8, 127.2, 124.9, 51.5, 36.2, 31.0, 27.4, 22.4, 14.0; IR (neat) 3024, 2956, 2929, 2859, 1692, 1598, 1455, 1069, 698 cm^{-1}; HRMS-CI m/z 251.1198 [(MH)$^+$, calcd for $C_{15}H_{20}ClO$ 251.1197].

*Data for (E)-3-chloro-1-(4-nitrophenyl)oct-2-en-1-one (**1j**):* 845 mg (60%); yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.32 (d, 2H, J = 8.86 Hz), 8.06 (d, 2H, J = 8.86 Hz), 7.11 (s, 1H), 2.97−3.05 (m, 2H), 1.68−1.74 (m, 2H), 1.34−1.39 (m, 4H), 0.90 (t, 3H, J = 7.01 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 186.6, 161.0, 150.2, 142.8, 129.2, 123.9, 122.3, 36.7, 31.0, 27.5, 22.3, 13.9; IR (neat) 2930, 2860, 1683, 1646, 1539, 1522, 1345, 1219 cm^{-1}; HRMS-CI m/z 282.0888 [(MH)$^+$, calcd for $C_{14}H_{17}ClNO_3$ 282.0891]. *Data for (Z)-3-chloro-1-(4-nitrophenyl)oct-2-en-1-one (**15**)*: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.32 (d, 2H, J = 8.70 Hz), 8.04 (d, 2H, J = 8.70 Hz), 6.82 (s, 1H), 2.51−2.60 (m, 2H), 1.66−1.77 (m, 2H), 1.29−1.40 (m, 4H), 0.91 (t, 3H, J = 7.18 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 187.9, 150.8, 150.2, 142.4, 129.4, 123.8, 120.2, 41.4, 30.8, 27.0, 22.3, 13.9; IR (neat) 2896, 2850, 1701, 1640, 1539, 1522, 1219, 965, 780 cm-1; HRMS-CI m/z 282.0889 [(MH)$^+$, calcd for $C_{14}H_{17}ClNO_3$ 282.0891].

*Data for (E)-1-(4-bromophenyl)-3-chlorooct-2-en-1-one (**1k**):* 742 mg (47%); yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.77 (d, 2H, J = 8.75 Hz), 7.60 (d, 2H, J = 8.75 Hz), 7.05 (s, 1H), 2.92−3.00 (m, 2H), 1.65−1.75 (m, 2H), 1.32−1.39 (m, 4H), 0.89 (t, 3H, J = 7.02 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 187.3, 158.8, 136.9, 131.9, 129.8, 128.2, 122.6, 36.5, 31.0, 27.5, 22.4, 13.9; IR (neat) 2956, 2930, 2860, 1666, 1594, 1396, 1225, 1042, 1008, 818 cm^{-1}; HRMS-CI m/z 315.0139 [(MH)$^+$, calcd for $C_{14}H_{17}BrClO$ 315.0146].

*Data for (E)-3-chloro-1-(p-tolyl)oct-2-en-1-one (**1l**):* 551 mg (44%); yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.82 (d, 2H, J = 8.14 Hz), 7.26 (d, 2H, J = 8.14 Hz), 7.10 (s, 1H), 2.91−2.99 (m, 2H), 2.41 (s, 3H), 1.65−1.71 (m, 2H), 1.32−1.38 (m, 4H), 0.89 (t, 3H, J = 7.12 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 188.2, 157.1,143.9, 135.6, 129.3, 128.4, 123.3, 36.3, 31.0, 27.5, 22.4, 21.6, 13.9; IR (neat) 2956, 2929, 2860, 1669, 1608, 1261, 1230, 1178, 1015 cm^{-1}; HRMS-CI m/z 251.1190 [(MH)$^+$, calcd for $C_{15}H_{20}ClO$ 251.1197]. *Data for (Z)-3-chloro-1-(p-tolyl)oct-2-en-1-one (**14**)*: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.84 (d, 2H, J = 8.14 Hz), 7.26 (d, 2H, J = 8.14 Hz), 6.78 (s, 1H), 2.50−2.54 (m, 2H), 2.41 (s, 3H), 1.65−1.73 (m, 2H), 1.33−1.41 (m, 4H), 0.91 (t, 3H, J = 7.25 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 189.5, 146.9,144.0, 135.1, 129.3, 128.7, 121.3, 41.0, 30.8, 27.0, 22.3, 21.7, 13.9; IR (neat) 2954, 2896, 2820, 1710, 1540, 1258, 1178, 985 cm-1; HRMS-CI m/z 251.1197 [(MH)$^+$, calcd for $C_{15}H_{20}ClO$ 251.1197].

*Data for (E)-3-chloro-1-(4-methoxyphenyl)oct-2-en-1-one (**1m**):* 733 mg (55%); yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.89 (d, 2H, J = 8.90 Hz), 7.06 (s, 1H), 6.91 (d, 2H, J = 8.90 Hz), 3.84 (s, 3H), 2.90−2.97 (m, 2H), 1.63−1.70 (m, 2H), 1.30−1.37 (m, 4H), 0.88 (t, 3H, J = 7.29 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 186.8, 163.5, 156.4, 131.0, 130.5, 123.2, 113.7, 55.3, 36.2, 31.0, 27.4, 22.4, 13.9; IR (neat) 2956, 2929, 2860, 1668, 1580, 1266, 1179, 1040, 815 cm^{-1}; HRMS-CI m/z 267.1153 [(MH)$^+$, calcd for $C_{15}H_{20}ClO_2$ 267.1149].

*1-Phenyloct-2-yn-1-one (**4**).* The product was prepared by the literature method, and ^{1}H and ^{13}C NMR spectra for this compound are consistent with previously reported literature data:[45] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.11−8.15 (m, 2H), 7.56−7.62 (m, 1H), 7.45−7.49 (m, 2H), 2.49 (t, 2H, J = 7.28 Hz), 1.63−1.73 (m, 2H), 1.34−1.50 (m, 4H), 0.93 (t, 3H, J = 7.29 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 178.2, 136.9, 133.8, 129.5, 128.4, 96.9, 79.6, 31.1, 27.5, 22.2, 19.2,

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13.9; IR (neat) 2957, 2932, 2861, 1686, 1644, 1581, 1264, 1175, 916, 701 cm^{-1}; HRMS-CI *m/z* 201.1271 [$(MH)^+$, calcd for $C_{14}H_{17}O$ 201.1274].

*Data for (E)-3-chloro-1-phenyl-2-propylhex-2-en-1-one (**5**):* 777 mg (62%); yellow liquid; ^1H and ^{13}C NMR spectra for this compound are consistent with previously reported literature data;[46] ^1H NMR ($CDCl_3$, 500 MHz) δ 7.87−7.91 (m, 2H), 7.57−7.61 (m, 1H), 7.45−7.51 (m, 2H), 2.43−2.52 (m, 2H), 2.13−2.19 (m, 2H), 1.54−1−61 (m, 2H), 1.38−1.49 (m, 2H), 0.91 (t, 3H, *J* = 7.44 Hz), 0.77 (t, 3H, *J* = 7.21 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 197.4, 137.2, 136.8, 136.3, 133.6, 129.4, 128.7, 39.0, 34.5, 20.9, 13.8, 13.1; IR (neat) 2962, 2932, 2872, 1669, 1638, 1449, 1273, 1118, 1024, 722, 690 cm^{-1}; HRMS-CI *m/z* 251.1198 [$(MH)^+$, calcd for $C_{15}H_{20}ClO$ 251.1197].

*Data for (E)-1-chloro-1-phenylpent-1-en-3-one (**6**):* 622 mg (64%); yellow oil; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.65−7.68 (m, 2H), 7.37−7.43 (m, 3H), 6.79 (s, 1H), 2.68−2.72 (m, 2H), 1.15 (t, 3H, *J* = 7.23 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 199.3, 142.3, 137.4, 130.5, 128.6, 127.2, 123.7, 37.6, 7.9; IR (neat) 2960, 2925, 2860, 1710, 1580, 1377 1264, 998, 775 cm^{-1}; HRMS-CI *m/z* 195.0575 [$(MH)^+$, calcd for $C_{11}H_{12}ClO$ 195.0571].

*(Z)-3-Chloro-1-phenyloct-3-en-1-one (**8**).* The flask was charged with (*E*)-**1a** (0.5 mmol, 118 mg) and dry dichloromethane (5 mL) under argon. Triethylamine (0.55 mmol, 77 mL) and trimethylsilyl trifluoromethanesulfonate (1.0 mmol, 0.18 mL) were then added at 0 °C, and the resulting solution was stirred for 3 h at this temperature. The unstable intermediate species **7** was observed by crude ^1H NMR in $CDCl_3$ (δ 7.46−7.50 (m, 2H), 7.26−7.35 (m, 3H), 6.18 (t, 1H, *J* = 7.27 Hz), 5.66 (s, 1H), 2.25−2.37 (m, 2H), 1.40−1.49 (m, 4H), 0.93 (t, 3H, *J* = 7.20 Hz), 0.11 (s, 9H)) with triethylamine salt and the remaining trimethylsilyl trifluoromethanesulfonate. The product **8** was obtained in 66% yield (781 mg) after column chromatography on silica gel with (*E*)-**1a** as a minor product: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.95−8.00 (m, 2H), 7.54−7.62 (m, 1H), 7.44−7.50 (m, 2H), 5.65 (t, 1H, *J* = 7.20 Hz), 3.96 (s, 2H), 2.19−2.27 (m, 2H), 1.28−1.42 (m, 4H), 0.89 (t, 3H, *J* = 7.20); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 195.5, 136.4, 133.4, 130.9, 128.6, 128.4, 126.7, 48.6, 30.5, 28.5, 22.2, 13.8; IR (neat) 2957, 2929, 2859, 1693, 1448, 1211, 668 cm^{-1}; HRMS-CI *m/z* 237.1034 [$(MH)^+$, calcd for $C_{14}H_{18}ClO$ 237.1041]. The stereochemistry was assigned by a 2D NOESY study.

*(E)-3-Bromo-1-phenyloct-2-en-1-one (**1a**-Br).* The product was prepared with aluminum bromide ($AlBr_3$) instead of aluminum chloride. A mixture of bromo/chloro products (5:1 ratio) was isolated: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.90−7.94 (m, 2H), 7.55−7.58 (m, 1H), 7.45−7.48 (m, 2H), 7.36 (s, 1H), 3.00−3.09 (m, 2H), 1.67−1.70 (m, 2H), 1.34−1.37 (m, 4H), 0.90 (t, 3H, *J* = 7.40 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 188.5, 150.7, 137.8, 133.1, 128.6, 128.3, 127.6, 123.2, 38.5, 31.0, 28.2, 22.4, 13.9; IR (neat) 2956, 2930, 2859, 1666, 1599, 1448, 1358, 1226 1037, 729 cm^{-1}; HRMS-CI *m/z* 281.0530 [$(MH)^+$, calcd for $C_{14}H_{18}BrO$ 281.0536].

*Data for **9**:* ^1H NMR ($CDCl_3$, 500 MHz) δ 7.87−7.91 (m, 2H), 7.47−7.52 (m, 1H), 7.40−7.46 (m, 2H), 1.57−1.63 (m, 2H), 1.31−1.39 (m, 4H), 0.89 (t, 3H, *J* = 7.04 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 190.1, 178.8, 140.7, 131.8, 128.5, 127.8, 31.8, 27.1, 22.6, 14.1; IR (neat) 3085, 3066, 3028, 2956, 2929, 2861, 1684, 1648, 1598, 1558, 1507, 1457, 1447, 1384, 1319, 1302, 1153, 1100, 990, 961, 907, 841, 719, 691, 668 cm^{-1}; HRMS-CI *m/z* 239.1911 [$(MH)^+$, calcd for $C_{15}H_{15}D_6O_2$ 239.1913].

*Data for **10**:* ^1H NMR ($CDCl_3$, 500 MHz) δ 7.86−7.90 (m, 2H), 7.48−7.54 (m, 1H), 7.41−7.48 (m, 2H), 6.17 (s, 1H), 1.64−1.69 (m, 2H), 1.31−1.39 (m, 4H), 0.89 (t, 3H, *J* = 7.02 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 197.0, 183.8, 135.2, 132.3, 128.7, 127.1, 96.2, 31.5, 25.6, 22.6, 14.1; IR (neat) 3062, 2956, 2928, 2858, 1717, 1647, 1599, 1558, 1457, 1401, 1282, 765, 694 cm^{-1}; HRMS-CI *m/z* 238.1851 [$(MH)^+$, calcd for $C_{15}H_{16}D_5O_2$ 238.1850].

*Data for (E)-**1b**-Dα:* ^1H NMR ($CDCl_3$, 500 MHz) δ 7.88−7.94 (m, 2H), 7.54−7.59 (m, 1H), 7.44−7.50 (m, 2H), 2.92−3.01 (m, 2H), 1.62−1.74 (m, 2H), 1.19−1.44 (m, 14H), 0.87 (t, 3H, *J* = 7.12 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 188.4, 157.8, 138.1, 133.0, 128.6, 128.2, 53.4, 36.4, 31.9, 29.6, 29.5, 29.3, 28.9, 27.8, 22.7, 14.1; IR (neat) 2948, 2925, 2854, 1663, 1586, 1465, 1259, 725 cm^{-1}; HRMS-CI *m/z* 308.1874 [$(MH)^+$, calcd for $C_{19}H_{27}DClO$ 308.1886]. *Data for (Z)-**1b**-Dα*: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.90−7.95 (m, 2H), 7.54−7.58 (m, 1H), 7.44−7.49 (m, 2H), 2.50−2.57 (m, 2H), 1.66−1.74 (m, 2H), 1.19−1.44 (m, 14H), 0.88 (t, 3H, *J* = 7.22 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 189.6, 147.9, 137.7, 133.1, 128.6, 128.5, 41.2, 31.9, 29.5(7), 29.5(1), 29.3, 28.6,27.3, 22.6, 14.1; IR (neat) 2961, 2925, 2854, 1668, 1599, 1456, 1259, 722 cm^{-1}; HRMS-CI *m/z* 308.1879 [$(MH)^+$, calcd for $C_{19}H_{27}DClO$ 308.1886].

*Data for (E)-**1b**-Dγ:* ^1H NMR ($CDCl_3$, 500 MHz) δ 7.88−7.95 (m, 2H), 7.54−7.59 (m, 1H), 7.43−7.50 (m, 2H), 7.12 (s, 1H), 1.63−1.70 (m, 2H), 1.18−1.39 (m, 14H), 0.87 (t, 3H, *J* = 6.98 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 188.5, 157.7, 138.1, 133.0, 128.6, 128.3, 123.3, 31.9, 29.5(7), 29.5(2), 29.3(7), 29.3(2), 28.8, 27.6, 22.6, 14.1; IR (neat) 2951, 2925, 2854, 1666, 1599, 1225, 1017, 694 cm^{-1}; HRMS-CI *m/z* 309.1945 [$(MH)^+$, calcd for $C_{19}H_{26}D_2ClO$ 309.1949]. *(Z)-**1b**-Dγ*: ^1H NMR ($CDCl_3$, 500 MHz) δ 7.88−7.95 (m, 2H), 7.50−7.57 (m, 1H), 7.42−7.47 (m, 2H), 6.82 (s, 1H), 1.62−1.71 (m, 2H), 1.23−1.35 (m, 14H), 0.88 (t, 3H, *J* = 6.87 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 189.7, 147.8, 137.8, 133.1, 128.6(7), 128.6(2), 121.1, 31.9, 29.5(9), 29.5(3), 29.4, 29.3, 28.6, 27.1, 22.7, 14.1; IR (neat) 2958, 2925, 2854, 1716, 1671, 1601, 1465, 1223, 1020, 701, 689 cm^{-1}; HRMS-CI *m/z* 309.1950 [$(MH)^+$, calcd for $C_{19}H_{26}D_2ClO$ 309.1949].

General Procedure B: Elimination of (*E*)-β-Chlorovinyl Ketones. To a flask charged with (*E*)-β-chlorovinyl ketone **1a**−**m** (0.5 mmol) under argon were added dry dichloromethane (2 mL) and triethylamine (0.55 mmol, 77 mL) at ambient temperature. The solution was stirred for 18 h and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (1−3% ethyl acetate in hexanes) to afford mixtures of allenyl ketones **2a**−**m** and deconjugated alkynyl ketones **3a**−**m** in 63−89% yields.

Preparation and Characterization of Compounds in Table 2. *Data for 1-phenylocta-2,3-dien-1-one (**2a**)/1-phenyloct-3-yn-1-one (**3a**):* 89 mg (89%); yellow liquid; **2a**:**3a** = 2:1. *Data for **2a**:* ^1H NMR ($CDCl_3$, 500 MHz) δ 7.84−7.89 (m, 2H), 7.51−7.58 (m, 1H), 7.40−7.45 (m, 2H), 6.32−6.36 (m, 1H), 5.57−5.62 (m, 1H), 2.12−2.22 (m, 2H), 1.37−1.48 (m, 2H), 1.27−1.37 (m, 2H), 0.87 (t, 3H, *J* = 7.40 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 212.9, 191.0, 136.8, 132.8, 131.4, 127.6, 127.2, 94.0, 92.9, 29.9, 26.4, 21.0, 12.7; IR (neat) 2955, 2925, 2854, 1946, 1733, 1691, 1652, 1448, 1273, 690 cm^{-1}; HRMS-CI *m/z* 201.1275 [$(MH)^+$, calcd for $C_{14}H_{17}O$ 201.1274]. *Data for **3a**:* ^1H NMR ($CDCl_3$, 500 MHz) δ 7.97−8.02 (m, 2H), 7.55−7.60 (m, 1H), 7.44−7.48 (m, 2H), 3.82 (t, 2H, *J* = 2.44 Hz), 2.12−2.22 (m, 2H), 1.37−1.48 (m, 2H), 1.27−1.37 (m, 2H), 0.87 (t, 3H, *J* = 7.40 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 193.0, 134.6, 132.3, 127.6, 127.5, 84.8, 71.1, 29.9, 29.7, 20.8, 17.5, 12.5.

*Data for 1-phenyltrideca-2,3-dien-1-one (**2b**)/1-phenyltridec-3-yn-1-one (**3b**):* 113 mg (84%); yellow liquid; **2b**:**3b** = 4:1. *Data for **2b**:* ^1H NMR ($CDCl_3$, 500 MHz) δ 7.84−7.89 (m, 2H), 7.49−7.54 (m, 1H), 7.38−7.44 (m, 2H), 6.30−6.36 (m, 1H), 5.54−5.63 (m, 1H), 2.10−2.22 (m, 2H), 1.37−1.50 (m, 2H), 1.21−1.37 (m, 12H), 0.87 (t, 3H, *J* = 7.40 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 212.8, 191.0, 136.9, 131.4, 127.6, 127.2, 94.0, 93.0, 30.8, 28.4, 28.3, 28.2, 27.9, 27.8, 26.7, 21.6, 13.1; IR (neat) 2925, 2865, 1947, 1693, 1653, 1598, 1274, 1211, 1178, 803 cm^{-1}; HRMS-CI *m/z* 271.2052 [$(MH)^+$, calcd for $C_{19}H_{27}O$ 271.2056]. *Data for **3b**:* ^1H NMR ($CDCl_3$, 500 MHz) δ 7.98−8.02 (m, 2H), 7.54−7.60 (m, 1H), 7.44−7.49 (m, 2H), 3.81 (t, 2H, *J* = 2.40 Hz), 2.12−2.22 (m, 2H), 1.37−1.50 (m, 2H), 1.23−1.37 (m, 12H), 0.87 (t, 3H, *J* = 7.26 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 193.0, 134.5, 132.3, 127.6, 127.5, 84.9, 71.2, 29.9, 28.4, 28.2, 28.1, 27.6, 21.7, 17.8, 13.3.

*Data for 7-chloro-1-phenylhepta-2,3-dien-1-one (**2c**)/phenylhept-3-yn-1-one (**3c**):* 91 mg (83%); yellow liquid; **2c**:**3c** = 2.5:1. *Data for **2c**:* ^1H NMR ($CDCl_3$, 500 MHz) δ 7.84−7.90 (m, 2H), 7.51−7.56 (m, 1H), 7.42−7.50 (m, 2H), 6.39−6.45 (m, 1H), 5.58−5.65 (m, 1H), 3.53 (t, 2H, *J* = 6.50 Hz), 2.30−2.39 (m, 2H), 1.87−1.96 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 212.7, 190.4, 136.6, 131.7, 127.5, 127.3, 93.2, 92.6, 42.8, 30.3, 23.8; IR (neat) 2959, 2939, 1948, 1689, 1652, 1448, 1275, 1064, 736 cm^{-1}; HRMS-CI *m/z* 221.0722 [$(MH)^+$, calcd for $C_{13}H_{14}ClO$ 221.0728]. *Data for **3c**:* ^1H

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NMR ($CDCl_3$, 500 MHz) δ 7.96−8.00 (m, 2H), 7.55−7.60 (m, 1H), 7.42−7.50 (m, 2H), 3.83 (t, 2H, J = 2.52 Hz), 3.61 (t, 2H, J = 6.50 Hz), 2.37−2.42 (m, 2H), 1.87−1.96 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 192.7, 134.4, 132.5, 127.6, 127.5, 82.7, 72.4, 42.6, 30.3, 29.8, 15.3.

*Data for methyl 7-oxo-7-phenylhepta-4,5-dienoate (**2d**)/methyl 7-oxo-7-phenylhept-4-ynoate (**3d**):* 101 mg (88%); yellow oil; **2d**:**3d** = 5:1. *Data for **2d***: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.84−7.88 (m, 2H), 7.51−7.55 (m, 1H), 7.40−7.45 (m, 2H), 6.37−6.45 (m, 1H), 5.65−5.73 (m, 1H), 3.63 (s, 3H), 2.43−2.49 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 213.4, 191.2, 172.7, 137.5, 132.7, 128.6, 128.3, 94.6, 93.8, 51.7, 32.8, 22.8; IR (neat) 2957, 2939, 1945, 1694, 1653, 1448, 1211, 687 cm^{-1}; HRMS-CI m/z 231.1011 [(MH)$^+$, calcd for $C_{14}H_{15}O_3$ 231.1016]. *Data for **3d***: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.95−7.98 (m, 2H), 7.54−7.58 (m, 1H), 7.44−7.48 (m, 2H), 3.79−3.82 (m, 2H), 3.65 (s, 3H), 2.50−2.53 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 193.4, 172.4, 135.4, 133.5, 128.6, 128.4, 83.7, 63.9, 51.7, 33.3, 30.8, 14.8.

*Data for 2-(6-oxo-6-phenylhexa-3,4-dien-1-yl)isoindoline-1,3-dione (**2e**)/2-(6-oxo-6-phenylhex-3-yn-1-yl)isoindoline-1,3-dione (**3e**):* 128 mg (81%); yellow glue; **2e**:**3e** = 5:1. *Data for **2e***: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.73−7.83 (m, 4H), 7.68−7.72 (m, 2H), 7.43−7.49 (m, 1H), 7.36−7.41 (m, 2H), 6.26−6.32 (m, 1H), 5.56−5.64 (m, 1H), 3.79 (t, 2H, J = 7.20 Hz), 2.50−2.63 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 213.8, 191.3, 168.1, 137.4, 134.0, 133.9, 133.4, 132.6, 131.9, 128.6, 128.3, 123.3, 94.2, 91.4, 36.9, 27.2; IR (neat) 2957, 2923, 2859, 1947, 1701, 1694, 1668, 1653, 1448, 1332, 753, 688 cm^{-1}; HRMS-CI m/z 318.1126 [(MH)$^+$, calcd for $C_{20}H_{16}NO_3$ 318.1125]. *Data for **3e***: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.90−7.93 (m, 2H), 7.80−7.83 (m, 2H), 7.69−7.72 (m, 2H), 7.51−7.55 (m, 1H), 7.38−7.43 (m, 2H), 3.83 (t, 2H, J = 7.20 Hz), 3.76 (t, 2H, J = 2.42 Hz), 2.50−2.63 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 193.3, 168.0, 136.9, 133.9, 133.4, 132.0, 128.5, 123.3, 81.6, 74.5, 36.7, 30.8, 18.9.

*Data for 3-cyclohexylidene-1-phenylprop-2-en-1-one (**2f**):* 82 mg (77%); yellow liquid; ^{1}H and ^{13}C NMR spectra for this compound are consistent with previously reported literature data;[21c] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.79−7.84 (m, 2H), 7.49−7.54 (m, 1H), 7.38−7.45 (m, 2H), 6.11−6.14 (m, 1H), 2.17−2.25 (m, 4H), 1.58−1.65 (m, 2H), 1.46−1.58 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 209.5, 193.4, 138.0, 133.1, 128.8, 128.0, 105.5, 92.7, 30.1, 26.3, 25.6; IR (neat) 2956, 2869, 1946, 1651, 1598, 1447, 1272, 1022, 695 cm^{-1}; HRMS-CI m/z 213.1282 [(MH)$^+$, calcd for $C_{15}H_{17}O$ 213.1274].

*Data for 1-cyclohexylidenepent-1-en-3-one (**2g**):* 52 mg (63%); pale yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.57−5.61 (m, 1H), 2.53−2.62 (m, 2H), 2.15−2.31 (m, 4H), 1.57−1.75 (m 6H), 1.08 (t, 3H, J = 7.50 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 202.9, 193.4, 128.3, 106.4, 94.9, 32.0, 30.2, 26.9, 25.7, 8.8; IR (neat) 2930, 2854, 1949, 1446, 1274, 1212, 686 cm^{-1}; HRMS-CI m/z 165.1284 [(MH)$^+$, calcd for $C_{11}H_{17}O$ 165.1275].

*Data for deca-4,5-dien-3-one (**2h**)/dec-5-yn-3-one (**3h**):* 51 mg (68%); pale yellow liquid. *Data for **2h***: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.69−5.73 (m, 1H), 5.56−5.62 (m, 1H), 2.55−2.62 (m, 2H), 2.12−2.19 (m, 2H), 1.42−1.49 (m, 2H), 1.34−1.42 (m, 2H), 1.07 (t, 3H J = 7.46 Hz), 0.91 (t, 3H, J = 7.20 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 211.5, 201.1, 95.9, 94.3, 31.2, 30.0, 26.4, 21.3, 12.7, 7.58; IR (neat) 2957, 2923, 2869, 1946, 1443, 1271, 1022, 993 cm^{-1}; HRMS-CI m/z 153.1286 [(MH)$^+$, calcd for $C_{10}H_{17}O$ 153.1274]. *Data for **3h***: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 3.20 (t, 2H, J = 2.60 Hz), 2.60−2.65 (m, 2H), 2.18−2.24 (m, 2H), 1.42−1.49 (m, 2H), 1.32−1.42 (m, 2H), 1.05 (t, 3H, J = 7.12 Hz), 0.88 (t, 3H, J = 7.20 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 205.5, 82.6, 71.4, 33.5, 32.9, 29.8, 21.6, 17.4, 12.5, 6.7.

*Data for 1-phenylnona-3,4-dien-2-one (**2i**)/1-phenylnon-4-yn-2-one (**3i**):* 83 mg (78%); yellow liquid; **2i**:**3i** = 10:1. *Data for **2i***: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.28−7.33 (m, 2H), 7.18−7.24 (m, 3H), 5.74−5.79 (m, 1H), 5.63−5.68 (m, 1H), 3.87 (s, 2H), 2.06−2.19 (m, 2H), 1.31−1.47 (m, 4H), 0.91 (t, 3H, J = 7.30 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 212.4, 197.5, 133.9, 128.3, 127.4, 125.7, 96.2, 94.8, 44.7, 29.6, 26.4, 21.2, 12.7; IR (neat) 2955, 2927, 2860, 1946, 1733, 1652, 1598, 1273, 1099, 710 cm^{-1}; HRMS-CI m/z 215.1431 [(MH)$^+$, calcd for $C_{15}H_{19}O$ 215.1430]. *Data for **3i***: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.31−7.35 (m, 2H), 7.22−7.26 (m, 3H), 3.87 (s, 2H), 3.26 (t, 2H, J = 2.43 Hz), 2.20−2.24 (m, 2H), 1.31−1.47 (m, 4H), 0.92 (t, 3H, J = 7.30 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 197.6, 133.8, 128.4, 127.6, 126.1, 83.0, 72.3, 47.2, 32.6, 29.7, 20.9, 17.4, 12.5.

*Data for 1-(4-nitrophenyl)octa-2,3-dien-1-one (**2j**)/1-(4-nitrophenyl)oct-3-yn-1-one (**3j**):* 86 mg (70%); yellow oil; **2j**:**3j** = 5:1). *Data for **2j***: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.28 (d, 2H, J = 8.78 Hz), 7.96 (d, 2H, J = 8.78 Hz), 6.28−6.32 (m, 1H), 5.62−5.68 (m, 1H), 2.12−2.20 (m, 2H), 1.34−1.45 (m, 2H), 1.23−1.33 (m, 2H), 0.87 (t, 3H, J = 7.35 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 214.8, 191.0, 142.7, 137.1, 129.5, 123.4, 95.8, 94.6, 30.8, 27.3, 22.0, 13.7; IR (neat) 2957, 2930, 2860, 1945, 1732, 1661, 1601, 1318, 1272, 1106, 854 cm^{-1}; HRMS-CI m/z 246.1127 [(MH)$^+$, calcd for $C_{14}H_{16}NO_3$ 246.1126]. *Data for **3j***: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.32 (d, 2H, J = 8.78 Hz), 8.18 (d, 2H, J = 8.78 Hz), 3.83 (t, 2H, J = 2.45 Hz), 2.12−2.20 (m, 2H), 1.34−1.45 (m, 2H), 1.23−1.33 (m, 2H), 0.87 (t, 3H, J = 7.35 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 192.7, 134.4, 132.5, 127.6, 127.5, 82.7, 72.4, 42.6, 30.3, 29.8, 15.3.

*Data for 1-(4-bromophenyl)octa-2,3-dien-1-one (**2k**)/1-(4-bromophenyl)oct-3-yn-1-one (**3k**):* 121 mg (87%); yellow liquid; **2k**:**3k** = 4:1. *Data for **2k***: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.72 (d, 2H, J = 8.50 Hz), 7.56 (d, 2H, J = 8.50 Hz), 6.26−6.30 (m, 1H), 5.57−5.64 (m, 1H), 2.12−2.22 (m, 2H), 1.36−1.47 (m, 2H), 1.27−1.36 (m, 2H), 0.88 (t, 3H, J = 7.30 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 213.0, 190.0, 135.4, 130.4, 129.1, 126.4, 94.2, 92.9, 29.8, 26.3, 21.0, 12.7; IR (neat) 2957, 2930, 2871, 1947, 1733, 1652, 1568, 1428, 1261, 1071, 807 cm^{-1}; HRMS-CI m/z 279.0378 [(MH)$^+$, calcd for $C_{14}H_{16}BrO$ 279.0379]. *Data for **3k***: ^{1}H NMR (CDCl3, 500 MHz) δ 7.86 (d, 2H, J = 8.50 Hz), 7.60 (d, 2H, J = 8.50 Hz), 3.76 (t, 2H, J = 2.40 Hz), 2.10−2.22 (m, 2H), 1.36−1.47 (m, 2H), 1.27−1.36 (m, 2H), 0.87 (t, 3H, J = 7.30 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 192.0, 133.2, 130.8, 129.1, 127.5, 85.2, 70.8, 30.0, 29.6, 20.8, 17.5, 12.5.

*Data for 1-(p-tolyl)octa-2,3-dien-1-one (**2l**)/1-(p-tolyl)oct-3-yn-1-one (**3l**):* 79 mg (74%); yellow liquid; **2l**:**3l** = 1:1. *Data for **2l***: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.78 (d, 2H, J = 8.47 Hz), 7.23 (d, 2H, J = 8.47 Hz), 6.32−6.36 (m, 1H), 5.57−5.62 (m, 1H), 2.40 (s, 3H), 2.11−2.23 (m, 2H), 1.40−1.51 (m, 2H), 1.29−1.40 (m, 2H), 0.87 (t, 3H, J = 7.20 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 212.5, 190.3, 142.2, 134.2, 127.9, 127.7, 93.8, 92.8, 29.9, 26.4, 21.0, 20.6, 12.5; IR (neat) 2954, 2872, 1947, 1668, 1601, 1458, 1258, 1206, 1028, 855 cm^{-1}; HRMS-CI m/z 215.1427 [(MH)$^+$, calcd for $C_{15}H_{19}O$ 215.1430]. *Data for **3l***: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.89 (d, 2H, J = 8.65 Hz), 7.26 (d, 2H, J = 8.65 Hz), 3.79 (t, 2H, J = 2.49 Hz), 2.41 (s, 3H), 2.11−2.23 (m, 2H), 1.40−1.51 (m, 2H), 1.29−1.40 (m, 2H), 0.88 (t, 3H, J = 7.20 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 192.6, 143.2, 132.1, 128.2, 127.7, 84.6, 71.3, 29.8, 29.7, 20.8, 20.6, 17.5, 12.5.

*Data for 1-(4-methoxyphenyl)octa-2,3-dien-1-one (**2m**)/1-(4-methoxyphenyl)oct-3-yn-1-one (**3m**):* 93 mg (81%); yellow liquid; **2m**:**3m** = 2:1. *Data for **2m***: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.88 (d, 2H, J = 8.70 Hz), 6.90 (d, 2H, J = 8.70 Hz), 6.31−6.36 (m, 1H), 5.55−5.61 (m, 1H), 3.85 (s, 3H), 2.12−2.22 (m, 2H), 1.40−1.48 (m, 2H), 1.30−1.39 (m, 2H), 0.88 (t, 3H, J = 7.34 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 213.1, 190.0, 163.2, 130.9, 130.6, 113.5, 94.8, 93.5, 55.4, 30.9, 27.4, 22.0, 13.9; IR (neat) 2957, 2933, 2871, 1948, 1717, 1601,1258, 1169, 1028, 865, 633 cm^{-1}; HRMS-CI m/z 231.1385 [(MH)$^+$, calcd for $C_{15}H_{19}O_2$ 231.1380]. *Data for **3m***: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.97 (d, 2H, J = 8.60 Hz), 6.94 (d, 2H, J = 8.05 Hz), 3.73−3.76 (m, 2H), 3.85 (s, 3H), 2.12−2.22 (m, 2H), 1.40−1.48 (m, 2H), 1.30−1.39 (m, 2H), 0.87 (t, 3H, J = 7.34 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 192.7, 163.7, 130.9, 128.6, 113.7, 85.5, 72.6, 55.4, 30.8, 30.7, 21.9, 18.5, 13.6.

General Procedure C: Synthesis of Furan Derivatives with CuCl. To a suspension of CuCl (0.02 mmol, 1 mol %, 2 mg) with dry dichloromethane (3 mL) was added β-chlorovinyl ketones (2 mmol) followed by triethylamine (2.2 mmol, 0.3 mL) under argon at ambient temperature. The resulting solution was stirred for 18 h at this temperature, after which it was concentrated under reduced pressure and purified by column chromatography on silica gel (1−2% ethyl acetate in hexanes) to give furans in 80−95% yields.

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Preparation and Characterization of the Compounds in Table 3. *Data for 2-butyl-5-phenylfuran (**16a**):* 380 mg (95%); yellow liquid; ^{1}H and ^{13}C NMR spectra for this compound are consistent with previously reported literature data;[47] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.63−7.67 (m, 2H), 7.35−7.41 (m, 2H), 7.20−7.26 (m, 1H), 6.56 (d, 1H, J = 3.23 Hz), 6.05−6.10 (m, 1H), 2.71 (t, 2H, J = 7.51 Hz), 1.66−1.75 (m, 2H), 1.37−1.48 (m, 2H), 0.97 (t, 3H, J = 7.25 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.4, 152.1, 131.3, 128.6, 126.7, 123.3, 106.8, 105.6, 30.2, 27.9, 22.3, 13.8; IR (neat) 2957, 2929, 2870, 1603, 1540, 1337, 1100. 852, 692 cm^{-1}; HRMS-CI m/z 201.1277 [(MH)$^+$, calcd for $C_{14}H_{17}O$ 201.1274].

*Data for 2-nonyl-5-phenylfuran (**16b**):* 459 mg (85%); yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.61−7.68 (m, 2H), 7.34−7.40 (m, 2H), 7.18−7.27 (m, 1H), 6.55 (d, 1H, J = 3.34 Hz), 6.04−6.09 (m, 1H), 2.69 (t, 2H, J = 7.50 Hz), 1.65−1.80 (m, 2H), 1.19−1.47 (m, 12H), 0.90 (t, 3H, J = 7.20 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.5, 152.1, 131.3, 128.5, 126.9, 123.3, 106.8, 105.6, 31.9, 29.5, 29.4. 29.3, 29.2, 28.2, 28.1, 22.7, 14.1; IR (neat) 2958, 2875, 1605, 1568, 1540, 1332, 1260, 768 cm^{-1}; HRMS-CI m/z 271.2058 [(MH)$^+$, calcd for $C_{19}H_{27}O$ 271.2056].

*Data for 2-(3-chloropropyl)-5-phenylfuran (**16c**):* 397 mg (90%); yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.52−7.56 (m, 2H), 7.24−7.30 (m, 2H), 7.12−7.16 (m, 1H), 6.46 (d, 1H, J = 3.30 Hz), 6.03−6.05 (m, 1H), 3.52 (t, 2H, J = 6.62 Hz), 2.78 (t, 2H, J = 7.20 Hz), 2.04−2.11 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 154.1, 152.7, 131.0, 126.9, 123.4, 107.9, 105.6, 44.1, 31.0, 25.3; IR (neat) 2965, 2880, 1669, 1652, 1275, 1064, 736 cm^{-1}; HRMS-CI m/z 221.0723 [(MH)$^+$, calcd for $C_{13}H_{14}ClO$ 221.0728].

*Data for methyl 3-(5-phenylfuran-2-yl)propanoate (**16d**):* 419 mg (91%); yellow liquid; ^{1}H and ^{13}C NMR spectra for this compound are consistent with previously reported literature data;[48] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.51−7.56 (m, 2H), 7.22−7.30 (m, 2H), 7.09−7.18 (m, 1H), 6.44 (d, 1H, J = 3.27 Hz), 5.99−6.04 (m, 1H), 3.61 (s, 3H), 2.95 (t, 2H, J = 7.65 Hz), 2.63 (t, 2H, J = 7.60 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 172.9, 153.8, 152.7, 130.9, 128.6, 126.9, 123.4, 107.5, 105.7, 51.7, 32.5, 23.6; IR (neat) 2959, 2941, 1694, 1651, 1513, 1331, 1206, 692 cm^{-1}; HRMS-CI m/z 231.1011 [(MH)$^+$, calcd for $C_{14}H_{15}O_3$ 231.1016].

*Data for 2-(2-(5-phenylfuran-2-yl)ethyl)isoindoline-1,3-dione (**16e**):* 571 mg (90%); yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.79−7.84 (m, 2H), 7.67−7.71 (m, 2H), 7.48−7.53 (m, 2H), 7.25−7.31 (m, 2H), 7.15−7.21 (m, 1H), 6.50 (d, 1H, J = 3.42 Hz), 6.15−6.18 (m, 1H), 4.03 (t, 2H, J = 7.27 Hz), 3.11 (t, 2H, J = 7.27 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 168.1, 153.1, 151.7, 133.9, 132.1, 130.8, 128.5, 126.9, 123.4, 123.3, 108.7, 105.6, 36.8, 27.1; IR (neat) 2958, 2930, 2872, 1694, 1542, 1513, 1332, 1108, 688 cm^{-1}; HRMS-CI m/z 318.1125 [(MH)$^+$, calcd for $C_{20}H_{16}NO_3$ 318.1125].

*Data for 2-benzyl-5-butylfuran (**16f**):* 360 mg (84%); yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.27−7.31 (m, 2H), 7.18−7.25 (m, 3H), 5.83−5.88 (m, 2H), 3.92 (s, 2H), 2.56 (t, 2H, J = 7.50 Hz), 1.56−1.66 (m, 2H), 1.30−1.43 (m, 2H), 0.91 (t, 3H, J = 7.54 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 155.5, 152.5, 138.5, 128.6, 128.4, 126.3, 106.6, 105.0, 34.5, 30.2, 27.7, 22.2, 13.8; IR (neat) 2958, 2931, 2872, 1652, 1586, 1513, 1322, 788 cm^{-1}; HRMS-CI m/z 215.1432 [(MH)$^+$, calcd for $C_{15}H_{19}O$ 215.1430].

*Data for 2-butyl-5-ethylfuran (**16g**):* 243 mg (80%); pale yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.82−5.88 (m, 2H), 2.48−2.66 (m, 4H), 1.53−1.66 (m, 2H), 1.33−1.40 (m, 2H), 1.20 (t, 3H, J = 7.52 Hz), 0.92 (t, 3H, J = 7.37 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 155.8, 154.6, 104.8, 104.0, 30.2, 27.7, 22.3, 21.3, 13.8, 12.2; IR (neat) 2957, 2925, 2869, 1664, 1608, 1449, 1017, 862 cm^{-1}; HRMS-CI m/z 153.1280 [(MH)$^+$, calcd for $C_{10}H_{17}O$ 153.1274].

*Data for 2-butyl-5-(4-nitrophenyl)furan (**16h**):* 427 mg (87%); yellow liquid; ^{1}H and ^{13}C NMR spectra for this compound are consistent with previously reported literature data;[49] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.21 (d, 2H, J = 8.87 Hz), 7.71 (d, 2H, J = 8.87 Hz), 6.78 (d, 1H, J = 3.26 Hz), 6.13−6.15 (m, 1H), 2.71 (t, 2H, J = 7.41 Hz), 1.65−1.73 (m, 2H), 1.38−1.46 (m, 2H), 0.96 (t, 3H, J = 7.42 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 158.1, 148.9, 144.8, 135.7, 123.3, 122.2, 109.0, 106.0, 29.0, 26.9, 21.2, 12.7; IR (neat) 2957, 2929, 2872, 1661, 1606, 1449, 1287, 1017, 817 cm^{-1}; HRMS-CI m/z 246.1128 [(MH)$^+$, calcd for $C_{14}H_{16}NO_3$ 246.1126].

*Data for 2-(4-bromophenyl)-5-butylfuran (**16i**):* 513 mg (92%); yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.48−7.53 (m, 4H), 6.57 (d, 1H, J = 3.28 Hz), 6.05−6.11 (m, 1H), 2.70 (t, 2H, J = 7.70 Hz), 1.65−1.74 (m, 2H), 1.40−1.48 (m, 2H), 0.98 (t, 3H, J = 7.45 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.9, 151.0, 131.6, 130.1, 124.8, 120.2, 107.0, 106.2, 30.1, 27.8, 22.3, 13.8; IR (neat) 2961, 2931, 1664, 1506, 1499, 1180, 817, 776 cm^{-1}; HRMS-CI m/z 279.0376 [(MH)$^+$, calcd for $C_{14}H_{16}BrO$ 279.0379].

*Data for 2-butyl-5-(p-tolyl)furan (**16j**):* 377 mg (88%); yellow liquid; ^{1}H and ^{13}C NMR spectra for this compound are consistent with previously reported literature data;[49] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.54 (d, 2H, J = 8.14 Hz), 7.17 (d, 2H, J = 8.14 Hz), 6.49 (d, 1H, J = 3.24 Hz), 6.04−6.06 (m, 1H), 2.69 (t, 2H, J = 7.30 Hz), 2.36 (s, 3H), 1.64−1.75 (m, 2H), 1.38−1.46 (m, 2H), 0.97 (t, 3H, J = 7.42 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.0, 152.3, 136.4, 129.2, 128.6, 123.3, 106.7, 104.8, 30.2, 27.9, 22.3, 12.2, 13.8; IR (neat) 2957, 2929, 2871, 1699, 1696, 1499, 1287, 1180, 1017, 817, 778 cm^{-1}; HRMS-CI m/z 215.1431 [(MH)$^+$, calcd for $C_{15}H_{19}O$ 215.1430].

*Data for 2-butyl-5-(4-methoxyphenyl)furan (**16k**):* 391 mg (85%); yellow liquid; ^{1}H and ^{13}C NMR spectra for this compound are consistent with previously reported literature data;[49] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.56 (d, 2H, J = 8.80 Hz), 6.90 (d, 2H, J = 8.80 Hz), 6.41 (d, 1H, J = 3.18 Hz), 6.00−6.04 (m, 1H), 3.83 (s, 3H), 2.67 (t, 2H, J = 7.20 Hz), 1.63−1.71 (m, 2H), 1.36−1.46 (m, 2H), 0.95 (t, 3H, J = 7.27 Hz); ^{13}C NMR (CDCl3, 125 MHz) δ 158.5, 155.7, 152.1, 124.7, 124.4, 114.0, 106.6, 103.9, 55.3, 30.2, 27.8, 22.2, 13.8; IR (neat) 2958, 2931, 2872, 1605, 1586, 1513, 1108, 1021, 852, 788, 752 cm^{-1}; HRMS-CI m/z 231.1374 [(MH)$^+$, calcd for $C_{15}H_{19}O_2$ 231.1380].

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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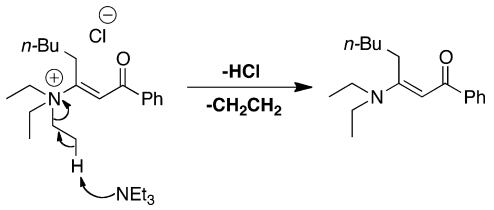

(28) No reaction was observed for (*Z*)-β-chlorovinyl ketone with a benzyl substitution at the α' position.
(29) The elimination of (*Z*)-**1** seems to be largely substrate-dependent as shown in Scheme 7 and appears to have a significantly slower reaction rate after an initial reaction period (18–40 h). For some unknown reason, the longer reaction time did not improve the isolated yields of product, possibly due to the decomposition of materials. Thus, the presence of competing decomposition/inhibitory reaction mechanisms after an initial period of reaction time (up to about 40 h at ambient temperature) cannot be ruled out.
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