Pergamon

Tetrahedron 58 (2002) 10429–10435

TETRAHEDRON

Copper(I)-catalyzed reaction of acylzirconocene chloride: cross-coupling and conjugate addition

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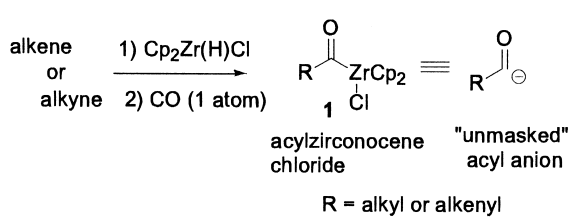
Received 4 October 2002; accepted 29 October 2002

Abstract—For the purpose of exploring a new reaction of acylzirconocene chloride as an acyl anion donor, Cu(I)-catalyzed cross-coupling and conjugate addition reactions of acylzirconocene chloride were studied. The coupling reaction with allylic or propargylic halides efficiently proceeded to yield β,γ-unsaturated ketone or allenyl ketone derivatives, respectively. The conjugated addition reaction to α,β-enones was carried out in the presence of 2 equiv. of $BF_3{\cdot}OEt_2$ giving 1,4-diketone compounds.

1. Introduction

The importance of an acyl anion in organic synthesis has been well recognized and a number of 'masked' acyl anion equivalents have been devised and applied to the nucleophilic acylation of organic molecules.[1] The use of the masked acyl anion, however, implies that an extra step is required to regenerate an acyl functional group in the product. As an 'unmasked' acyl anion donor, an acyl-metal species has long been studied by many research groups for the introduction of acyl anion.[2] However, the toxicity of metal carbonyls as a starting material for the preparation of the acyl-metal species and/or the instability of the prepared acyl-metal species could reduce the practicability of the acyl-metal species as a synthetic reagent.

Our recent studies[3] on the reactivity of stable acylzirconocene chloride complex ($RCOZrCp_2Cl$, Cp=cylopentadienyl) **1**,[4] which is easily available through the hydrozirconation of alkene or alkyne with Schwartz reagent ($Cp_2Zr(H)Cl$)[5] and subsequent insertion of carbon monoxide, have indicated a promising use of **1** as an unmasked acyl anion donor (Scheme 1). We describe herein a full account on



Scheme 1.

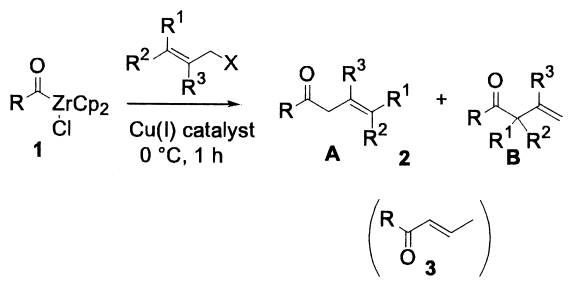
Cu(I)-catalyzed reactions of **1**: cross-coupling with organic halides and conjugate addition to α,β-enones.[6]

2. Results and discussion

2.1. Cross-coupling reaction

The cross-coupling reaction of an acyl-metal species with organic halides has attracted attention for the synthesis of unsymmetrical ketone derivatives, and several acyl-metal complexes have been employed for the purpose.[7] In 1998, we reported the preparation of unsymmetrical ketones through Pd-catalyzed cross-coupling reactions of **1** with organic halides.[3d]

However, in the Pd-catalyzed coupling reaction of **1** with allylic halides and/or acetate, the purification of coupling product **2**, β,γ-unsaturated ketone, was hampered by the formation of a side product (e.g. **3**, Scheme 2), α,β-unsaturated ketone, which was derived from the isomerization of **2** during the reaction. A further examination of the catalyst in the cross-coupling reaction showed



Scheme 2. Cu(I) catalyzed cross-coupling reaction of **1** with allylic compounds.

Keywords: acylzirconocene chloride; allenyl ketone; propargylic halides.

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0040–4020/02/$ - see front matter
PII: S0040-4020(02)01422-9

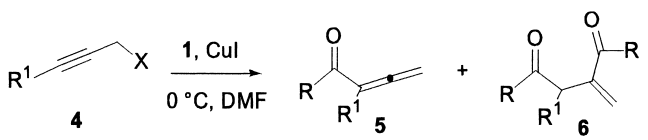
Table 1. Cu-catalyzed cross-coupling reactions of **1** with allylic compounds

Entry	R	R1	R2	R3	X	Cu(I)	Solv	**2** Yield (%)[a]
1	$Ph(CH_2)_4$ **1a**	H	H	H	Br	CuI	DMF	**2a** 91
2	**1a**	H	H	H	Cl	CuI	DMF	44
3	**1a**	H	H	H	I	CuI	DMF	76
4	**1a**	H	H	H	OTs	CuI	DMF	77
5	**1a**	H	H	H	OAc	CuI	DMF	–
6	**1a**	H	H	H	Br	CuI·2LiCl	THF	88
7	**1a**	H	H	H	Br	CuCN·2LiCl	THF	87
8	**1a**	H	H	H	Br	$CuBr{\cdot}SMe_2$	THF	<10
9	**1a**	H	H	H	Br	CuBr	DMF	78
10	**1a**	H	H	H	Br	CuCl	DMF	84
11	(*E*)-$Ph(CH_2)_2CH{=}CH$ **1b**	H	H	H	Br	CuI	DMF	**2b** 78
12	**1a**	CH_3	CH_3	H	Br	CuI	DMF	**2c** 91[b]
13	**1a**	H	CH_3	H	Br	CuI	DMF	**2d** 72[c]
14	**1a**	H	H	CH_3	Br	CuI	DMF	**2e** 84
15	**1b**	CH_3	CH_3	H	Br	CuI	DMF	**2f** 47[d]

(*E*)-crotyl bromide/(*Z*) crotyl bromide/3-bromo-1-butene=73:14:13.
[a] Yields are isolated and calculated from allylic compounds.
[b] Reaction period; 10 h. **2cA/2cB**=1:2.
[c] **2dA/2dB**=1:2.6.
[d] Reaction period; 10 h. **2fA/2fB**=1:1.6.

a promising result of Cu(I) catalyst to attain the exclusive formation of the β,γ-unsaturated ketone **2** (Scheme 2). Thus, the reaction of **1** with allyl halides in the presence of a catalytic amount (10 mol%) of Cu(I) in DMF or THF efficiently proceeded at 0°C and completed within 1 h at 0°C to give acyl–allyl coupled products **2** in good yields. No isomerized side product **3** was detected in the reaction mixture (Table 1). At the time when we published our Cu(I)-catalyzed coupling reaction,[3f] Huang et al. also reported that Cu(I)-catalyzed cross-coupling reactions of acylzirconocene chloride derivatives with alkynyl halides gave vinyl alkynyl ketone derivatives.[8]

Although the examined Cu(I) salts other than $CuBr{\cdot}SMe_2$ (entry 8) can be used as an efficient catalyst, the solubility of a Cu(I) catalyst is important for the formation of **2**. Thus, the use of a suspension of CuX in THF decreased the product yield (<20%). Allyl tosylate is also an excellent reactant in the present reaction (entry 4, Table 1) while allyl acetate is not (entry 5). α,β-Unsaturated acylzirconocene chloride **1b**, which is a poor substrate for the reported Pd-catalyzed



Scheme 3.

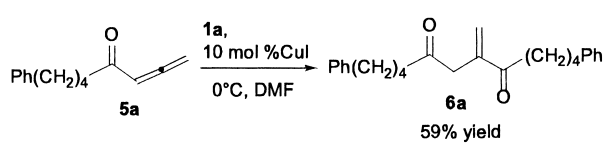
Table 2. Cu(I)-catalyzed coupling reaction with propargylic compounds

Entry	**1**	Ratio of **1/4**	**4**		Yield (%)	
			R^1	X	**5**	**6**
1	**1a**	1.5	H	Br	**5a** 65[a]	**6a** <5[a]
2	**1a**	3.0	H	Br	24[a]	48[a]
3	**1a**	0.5	H	Br	55[b]	0
4	**1a**	0.5	H	OTs	21[b]	0
5	**1a**	0.5	CH_3	Br	**5b** 61[b]	0
6	**1b**	0.5	H	Br	**5c** 52[b]	0
7	**1b**	0.5	CH_3	Br	**5d** 47[b]	0

[a] Yields are isolated and calculated from **6**.
[b] Yields are isolated and calculated from **1**.

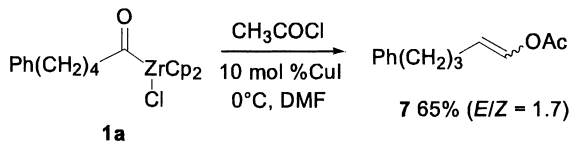
reaction, gave **2** in a good yield (entry 11). The mild reaction conditions of Cu(I)-catalyzed coupling reactions of **1** compared to the previously reported Pd-catalyzed reactions[3d] might exert a desirable influence on the exclusive formation of **2**. The reaction of the substituted allylic halides gave cross-coupled products in good yields albeit their low regioselectivity (entries 12, 13, and 15). Furthermore, a longer reaction time (10 h) was required for completion of the reaction than the case of allyl bromide (1 h). The Cu(I) catalyst was also efficient for the coupling of **1** with propargyl halides or tosylate **4** (Scheme 3).[9] The result is listed in Table 2. The reaction of **4** with **1a** afforded allenyl ketone derivative **5a** together with a trace amount of **6a** (entry 1, Table 2). The use of an increased amount (3 equiv.) of **1a** to **4** gave 1,4-dicarbonyl compound **6a** as a major product (48%) together with **5a** (24%) (entry 2).

The formation of **5** as the sole product was attained by utilizing **4** in excess amount (**4/1**=2:1) (entries 3–7, Table 2). The reaction of the isolated **5a** with **1a** under identical conditions afforded **6a** in 59% yield (Scheme 4), and the result suggests a possibility for the Cu(I)-catalyzed conjugate addition of **1** to enone compounds (vide infra).

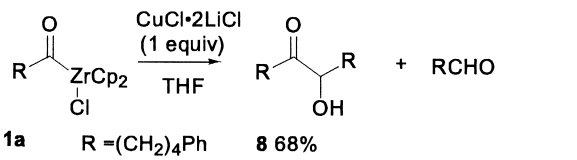


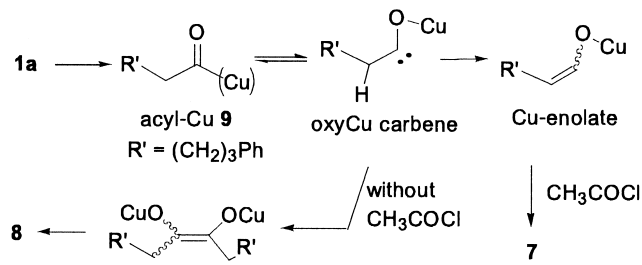
Scheme 4.

The present Cu(I)-catalyzed cross-coupling reactions of **1** did not work for alkyl-, vinyl-, homoallyl- or aryl halides. The CuI-catalyzed reaction of **1a** with acetyl chloride in DMF at 0°C for 1 h gave a mixture (*E*/*Z*=1:1) of enol acetate **7** in 65% yield, and no reaction took place in the absence of CuI catalyst (Scheme 5). It is very interesting to note that treatment of **1a** with a stoichiometric amount of CuI/DMF or CuCl·2LiCl/THF afforded α-ketol **8** in 60 or 68% yield, respectively (Scheme 6). Based on these observations and the fact that the transmetalation of alkenyl group in alkenylzirconocene complex from Zr to Cu



Scheme 5.



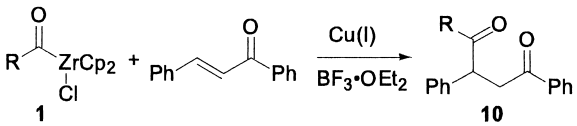


Scheme 6. Generation of RCOCu, α-ketol **8** and the supposed mechanism.

occurs,[9] we consider that the present Cu(I)-catalyzed reactions proceed through an acylcopper intermediate (RCOCu **9**) as an active species by the acyl group transfer from Zr to Cu (transmetalation). Thus, the formation of **7** could be explained by the generation of a Cu-enolate via oxy-Cu carbene, the subsequent 1,2-migration of hydrogen atom to Cu-enolate, and the reaction with acetyl chloride as shown in Scheme 6. The similar observation and the mechanistic consideration have been made by Norman et al. in the formation and reaction of acyl zinc species in ethyl acetate.[10,11]

2.2. Conjugate addition

The conjugate addition of organometallic reagents to α,β-unsaturated carbonyl compounds is an important tactic for the introduction of various carbon nucleophiles to the β-carbon of the α,β-unsaturated carbonyl compounds.[12] As the Cu(I)-catalyzed conjugate addition of hard organometallic reagents to α,β-enones is a highly useful reaction in modern organic synthesis, the observation described above prompted us to examine the Cu(I)-catalyzed conjugate addition of **1** to α,β-enones. The conjugate addition of an unmasked acyl anion to α,β-enones is an efficient procedure for the preparation of 1,4-dicarbonyl compounds, and we reported the palladium-catalyzed regiochemically tunable reactions of acylzirconocene chlorides **1** to α,β-enones by selecting the Pd-catalyst.[3c] Besides the acylzirconocene chloride complex, acyl-metal reagents, such as: nickel,[13] iron,[14] cobolt,[15] tin,[16] or acyl-lithium cuprate reagents[17] have also been reported to be efficient donors of an acyl anion in the conjugate addition to α,β-enones. The Cu(I)-catalyzed addition of alkylzirconocene chloride complexes ($RZrCp_2Cl$) to α,β-enones efficiently proceeds to give conjugate addition products.[18] At the outset, the reactivity of *n*-nonanoylzirconocene chloride (**1c**) to 1,3-diphenylpropenone was examined (Scheme 7), and the result is shown in Table 3.



Scheme 7.

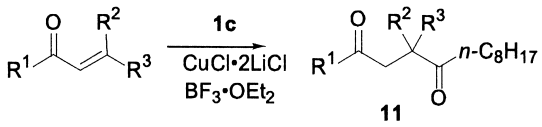
Table 3. Cu(I)-catalyzed conjugate addition of **1** to 1,3-diphenylpropenone

Entry	**1** R	Cu(I)[a]	BF_3·OEt_2 (equiv.)	Yield **10** (%)[b]
1	*n*-C_8H_{17} **1c**	CuCl·2LiCl	–	**10a** 18
2	**1c**	CuCl·2LiCl	1.0	53
3	**1c**	CuCl·2LiCl	2.0	76
4	**1c**	CuCl·2LiCl	3.0	44
5	**1c**	CuCN·2LiCl	2.0	65
6	**1c**	$CuBr·S(CH_3)_2$	2.0	42
7	*t*-$Bu(CH_2)_2$ **1d**	CuCl·2LiCl	2.0	**10b** 61
8	*cy*$C_6H_{11}CH_2$ **1e**	CuCl·2LiCl	2.0	**10c** 71
9	(*E*) *n*-$C_6H_{13}CH{=}CH$ **1f**	CuCl·2LiCl	2.0	**10d** 27

Solvent: THF/ether=1:2.
[a] 10 mol% Cu(I).
[b] Isolated yield.

The 1,4-conjugate addition proceeded efficiently to give **10a** (76% yield) by the addition of CuCl·2LiCl (10 mol%) and BF_3·OEt_2 (2 equiv.) to the reaction mixture in THF/ether (1:2), and no 1,2-addition product was isolated from the reaction mixture (entry 3, Table 3). The reaction was sluggish without adding BF_3·OEt_2 (entry 1), and no reaction took place without using the Cu(I) catalyst even in the presence of BF_3·OEt_2. The use of BF_3·OEt_2 in less than 2 equiv. to α,β-enone decreased the yield of **10a** from 76 to 53% (entry 2). In addition, in the case of more than 2 equiv. of BF_3·OEt_2, the yield of **10a** decreased to 44% (entry 4). Besides the CuCl·2LiCl catalyst, other Cu(I) catalysts, such as CuCN·2LiCl (65%), $CuBr·SMe_2$ (42%), showed catalytic activity for the 1,4-addition (entries 5 and 6). It should be mentioned that the use of CuI (10 mol%) in DMF as a catalyst at 0°C gave a low yield of **10a** (<10%). Thus, the presence of a CuX·2LiCl catalyst (10 mol%) and BF_3·OEt_2 (2 equiv.) in THF/ether (1:2) is requisite to perform the 1,4-addition of **1** to α,β-enones. Although the exact role of 2 equiv. BF_3·OEt_2 in addition to the activation of α,β-enone is unclear, BF_3·OEt_2 may have an influence on transiently formed **9** to generate RCOCu·BF_3 as suggested for RCu·BF_3 by Yamamoto et al.[19] or might generate a reactive cationic acylzirconocene species ($RCOZrCp_2^+$) by the abstraction of chloride ligand.[20] The importance of BF_3·OEt_2 for achieving optimal chemical yield has also been reported in the reactions of Cu(I)-catalyzed 1,4-addition of alkylzirconocene chloride ($RZrCp_2Cl$) to *N*-acyl oxazolidinones.[14d] Various acylzirconocene chloride derivatives (**1b–d**) also afforded 1,4-adducts **10b–d** (entries 7–9, Table 3), although the product yield was low with the use of α,β-unsaturated acylzirconocene chloride **1d** (entry 9). The present procedure (10 mol% CuX·2LiCl catalyst, 2 equiv. BF_3·OEt_2 in THF/Et_2O) can be applied to a variety of α,β-enone derivatives (Scheme 8), and the result of the reaction of **1c** is shown in Table 4.

Cyclic and acyclic α,β-enones reacted with **1c** to give conjugate addition products **11** in fair to good yields.



Scheme 8.

Table 4. Conjugate addition of **1c** to α,β-enones

Entry	R^1	R^2	R^3	**11** Yield %[a]
1		Cyclohexenone		65
2		Cyclopentenone[b]		43
3	Ph	H	CH_3	57
4	CH_3	H	Ph	65
5	CH_3	H	H	55
6	n-C_8H_{17}	H	CH_3	72
7	$Ph(CH_2)_2$	H	H	52
8	Ph	CH_3	CH_3	–

Reaction temperature: ambient temperature.
[a] Isolated yield.
[b] Reaction temperature: 0°C.

However, bis substitution at the β-carbon of α,β-enones retarded the reaction (entry 8, Table 4). This reactivity is very similar to that of the Pd-catalyzed 1,4-conjugate addition reactions of **1** to α,β-enones.[3c] In all cases examined, the isolated product was the 1,4-addition product, and the 1,2-addition product was not detected in the reaction mixture. The present Cu(I)-catalyzed 1,4-addition was restricted to α,β-enones, and no conjugate addition reaction occurred for α,β-unsaturated ester, -amide and -nitril compounds.

3. Conclusion

We indicated that the Cu(I)-catalyzed coupling and conjugate addition reactions of acylzirconocene chlorides as a donor of acyl anion proceeded efficiently under the mild conditions. In these reactions, acylcopper species (RCOCu) generated by the transfer of acyl group from Zr to Cu was speculated as a reactive species. The present Cu(I)-catalyzed reactions of acylzirconocene chloride are complementary to the palladium-catalyzed reactions and made possible to produce the β,γ-unsaturated ketones which are readily isomerized under the palladium-catalyzed reaction. Thus, the results described herein indicate the versatility of acylzirconocene chloride as an organometallic reagent in organic synthesis.

4. Experimental

4.1. General

All anhydrous solvents and reagents except $Cp_2Zr(H)Cl$ were obtained from commercial suppliers and used without further purification. The Schwartz reagent ($Cp_2Zr(H)Cl$) was prepared according to the procedure reported by Buchwald et al.[5] ^1H and ^{13}C NMR are recorded in $CDCl_3$ at 400 and 100 MHz, respectively. Melting points were determined by a micro melting point apparatus and are uncorrected. The structures of the products **11** described in Table 4 were confirmed by comparing with the authentic samples.[3h]

4.2. Preparation of a solution of acylzirconocene chloride 1

Under an argon atmosphere, to a suspension of $Cp_2Zr(H)Cl$ (1.0 equiv.) in CH_2Cl_2 (3 mL/mmol) was added alkene or alkyne (2.0 equiv.) at ambient temperature. After the mixture was stirred at the same temperature for 0.5 h, the mixture was further stirred for 2 h under CO (1 atm). The solution was concentrated in vacuo to dryness to give an acylzirconocene chloride complex **1** as a pale yellow solid. An appropriate solvent (see text) in a described amount was added to the acylzirconocene chloride, and the solution was used directly in the next reaction.

4.3. General procedure for cross-coupling reaction

All reactions were carried out by the use of 1.0 mmol amount of allylic compounds. Under an argon atmosphere, to a solution of acylzirconocene chloride complex **1** (1.5 equiv.) in DMF or THF (10 mL) was added allyllic halide or tosylate and a 0.1 equiv. amount of CuX or CuX·2LiCl (a 0.5 M solution in THF) at 0°C, and the mixture was stirred for 1 or 10 h at the same temperature. After the reaction mixture was filtered through a short silica gel column, the filtrate was concentrated in vacuo to dryness. The residue was purified by silica gel column chromatography (hexanes/ethyl acetate=60:1) to give cross-coupling products in yields described in the tables.

4.4. General procedure for 1,4-addition

All reactions were carried out by the use of 0.5 mmol amount of α,β-enones. Under an argon atmosphere, a solution of acylzirconocene chloride **1** (2.0 equiv.) in THF/ether (1:2) (9 mL/mmol) was slowly added (1 h) to a solution of α,β-enone (1.0 equiv.), CuCl·2LiCl (0.5 M solution in THF, 0.1 equiv.) and $BF_3{\cdot}OEt_2$ (2.0 equiv.) in THF/ether (1:2) (9 mL/mmol) at 0°C and the mixture was stirred at ambient temperature overnight. After being added aq. $NaHCO_3$, the mixture was extracted with ethyl acetate. The combined organic layer was washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated to dryness to give a crude product, which was purified by silica gel column chromatography (hexane/ethyl acetate=40:1) to give 1,4-diketone compound.

4.4.1. 8-Phenyl-1-octen-4-one (2a). ^1H NMR (400 MHz, $CDCl_3$) δ 1.58–1.67 (m, 4H), 2.43–2.48 (m, 2H), 2.60–2.64 (m, 2H), 3.14–3.16 (m, 2H), 5.13 (qd, 1H, J=1.6, 17.1 Hz), 5.17 (qd, 1H, J=1.4, 10.2 Hz), 5.91 (tdd, 1H, J=7.0, 10.2, 17.1 Hz), 7.16–7.29 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 23.3, 30.9, 35.7, 42.1, 47.7, 118.7, 125.7, 128.3, 128.4, 130.7, 142.2, 208.6; IR (neat) ν 1715 cm^{-1}; EIMS m/z 202 (M^+). Anal. calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 82.96; H, 8.89.

4.4.2. (5*E*)-8-Phenyl-1,5-octadien-4-one (2b). ^1H NMR (400 MHz, $CDCl_3$) δ 2.52–2.58 (m, 2H), 2.79 (t, 2H, J=7.4 Hz), 3.28–3.31 (m, 2H), 5.14 (qd, 1H, J=1.4, 17.1 Hz),

5.18 (qd, 1H, J=1.4, 10.3 Hz), 5.93 (tdd, 1H, J=6.9, 10.3, 17.1 Hz), 6.13 (td, 1H, J=1.5, 15.9 Hz), 6.89 (td, 1H, J=6.8, 15.9 Hz), 7.17–7.32 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 34.1, 34.4, 45.2, 118.6, 126.2, 128.3, 128.5, 130.1, 130.9, 140.6, 146.8, 197.9; IR (neat) ν 1697, 1671, 1628 cm^{-1}. Anal. calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.66; H, 7.97.

4.4.3. 2-Methyl-9-phenyl-2-nonen-5-one (2cA). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.56–1.68 (m, 4H), 1.62 (s, 3H), 1.75 (s, 3H), 2.40–2.46 (m, 2H), 2.57–2.63 (m, 2H), 3.08 (d, 2H, J=7.2 Hz), 5.26–5.31 (m, 1H), 7.16–7.29 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 18.0, 23.5, 25.7, 31.0, 35.7, 42.0, 42.7, 116.0, 125.7, 128.3, 128.4, 135.7, 142.2, 209.4; IR (neat) ν 1714 cm^{-1}; EIMS m/z 230 (M^+). HRMS calcd for $C_{16}H_{22}O$: 230.16706. Found: 230.16612.

4.4.4. 3,3-Dimethyl-8-phenyl-1-octen-4-one (2cB). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (s, 6H), 1.54–1.62 (m, 4H), 2.44–2.49 (m, 2H), 2.58–2.62 (m, 2H), 5.11–5.15 (m, 2H), 5.90 (dd, 1H, J=10.6, 17.6 Hz), 7.15–7.28 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 23.5, 23.7, 31.0, 35.8, 37.2, 50.8, 114.2, 125.7, 128.3, 128.4, 142.4, 142.6, 212.9; IR (neat) ν 1710 cm^{-1}. Anal. calcd for $C_{16}H_{22}O$: C, 83.43; H, 9.63. Found: C, 83.16; H, 9.45.

4.4.5. 9-Phenyl-2-nonen-5-one (*E*,*Z*-mixture) (2dA). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.57–1.70 (m, 9H), 2.42–2.48 (m, 2H), 2.58–2.62 (m, 2H), 5.49–5.70 (m, 2H), 7.13–7.32 (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 18.0, 23.4, 31.0, 35.7, 42.0, 46.8, 123.1, 125.7, 128.3, 128.4, 129.6, 142.2, 209.4; IR (neat) ν 1712 cm^{-1}; EIMS m/z 216 (M^+). HRMS calcd for $C_{15}H_{20}O$: 216.15141. Found: 216.15091.

4.4.6. 3-Methyl-8-phenyl-1-octen-4-one (2dB). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (t, 3H, J=6.8 Hz), 1.56–1.66 (m, 4H), 2.40–2.55 (m, 2H), 2.59–2.63 (m, 2H), 3.15–3.22 (m, 1H), 5.13 (td, 1H, J=1.0, 10.3 Hz), 5.15 (td, 1H, J=1.2, 17.3 Hz), 5.79 (ddd, 1H, J=8.2, 10.3, 17.3 Hz), 7.15–7.29 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 15.8, 23.3, 31.0, 35.8, 40.5, 51.3, 116.8, 125.7, 128.3, 128.4, 137.6, 142.3, 211.3; IR (neat) ν 1714 cm^{-1}; EIMS m/z 216 (M^+). HRMS calcd for $C_{15}H_{20}O$: 216.15141. Found: 216.15119.

4.4.7. 2-Methyl-8-phenyl-1-octen-4-one (2e). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.57–1.67 (m, 4H), 1.74 (s, 3H), 2.44–2.50 (m, 2H), 2.60–2.64 (m, 2H), 3.08 (s, 2H), 4.80 (s, 1H), 4.93 (s, 1H), 7.16–7.29 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 22.6, 23.4, 30.9, 35.7, 41.7, 52.2, 114.9, 125.7, 128.3, 128.4, 139.3, 142.2, 208.7; IR (neat) ν 1714 cm^{-1}; EIMS m/z 216 (M^+). Anal. calcd for $C_{15}H_{20}O$: C, 83.28; H, 9.32. Found: C, 93.01; H, 9.24.

4.4.8. (6*E*)-2-Methyl-9-phenyl-2,6-nonadien-5-one (2fA). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.63 (s, 3H), 1.75 (d, 3H, J=1.0 Hz), 2.51–2.57 (m, 2H), 2.79 (t, 2H, J=7.4 Hz), 3.21 (d, 2H, J=7.1 Hz), 5.27–5.31 (m, 1H), 6.12 (td, 1H, J=1.5, 15.8 Hz), 6.87 (td, 1H, J=6.9, 15.8 Hz), 7.17–7.31 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 18.1, 25.8, 34.1, 34.4, 40.3, 116.2, 126.2, 128.4, 128.5, 130.2, 135.6, 140.7, 146.2, 198.6; IR (neat) ν 1718 cm^{-1}; EIMS m/z 228 (M^+). HRMS calcd for $C_{16}H_{20}O$: 228.15141. Found: 228.15101.

4.4.9. (5*E*)-3,3-Dimethyl-8-phenyl-1,5-octadien-4-one (2fB). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20 (s, 6H), 2.48–2.54 (m, 2H), 2.77 (t, 2H, J=7.4 Hz), 5.10–5.15 (m, 2H), 5.88 (dd, 1H, J=10.8, 17.2 Hz), 6.39 (td, 1H, J=1.4, 15.3 Hz), 6.94 (td, 1H, J=6.9, 15.3 Hz), 7.15–7.30 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 23.4, 34.1, 34.4, 49.6, 114.5, 125.7, 126.1, 128.38, 128.42, 140.9, 142.5, 146.0, 201.3; IR (neat) ν 1692, 1625 cm^{-1}; EIMS m/z 228 (M^+). HRMS calcd for $C_{16}H_{20}O$: 228.15141. Found: 228.15196.

4.4.10. 8-Phenyl-1,2-octadien-4-one (5a). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.62–1.67 (m, 4H), 2.60–2.65 (m, 4H), 5.20 (d, 2H, J=6.5 Hz), 5.76 (t, 1H, J=6.5 Hz), 7.16–7.29 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 24.2, 30.9, 35.7, 39.0, 79.3, 96.7, 125.7, 128.3, 128.4, 142.2, 200.7, 216.6; IR (neat) ν 1932, 1681 cm^{-1}; EIMS m/z 200 (M^+). Anal. calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.71; H, 7.97.

4.4.11. 6-Methylidene-1,12-diphenyl-5,8-dodecanedione (6a). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.59–1.69 (m, 8H), 2.49–2.53 (m, 2H), 2.60–2.65 (m, 4H), 2.71–2.74 (m, 2H), 3.32 (s, 2H), 5.81 (s, 1H), 6.12 (s, 1H), 7.15–7.18 (m, 10H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 23.3, 24.0, 30.9, 31.0, 35.7, 35.8, 37.0, 42.6, 45.1, 125.7, 127.1, 128.3, 128.4, 142.2, 142.9, 200.9, 207.5; IR (neat) ν 1716, 1677 cm^{-1}; EIMS m/z 362 (M^+). Anal. calcd for $C_{25}H_{30}O_2$: C, 82.83; H, 8.34. Found: C, 82.66; H, 8.36.

4.4.12. 3-Methyl-8-phenyl-1,2-octadien-4-one (5b). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.58–1.69 (m, 4H), 1.78 (t, 3H, J=3.0 Hz), 2.59–2.64 (m, 2H), 2.65–2.70 (m, 2H), 5.10 (q, 2H, J=3.0 Hz), 7.15–7.29 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 13.1, 24.7, 31.0, 35.7, 38.7, 78.4, 103.6, 125.7, 128.3, 128.4, 142.3, 201.4, 216.3; IR (neat) ν 1678 cm^{-1}; EIMS m/z 214 (M^+). HRMS calcd for $C_{15}H_{18}O$: 214.13576. Found: 214.13549.

4.4.13. (5*E*)-8-Phenyl-1,2,5-octatrien-4-one (5c). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.52–2.58 (m, 2H), 2.79 (t, 2H, J=7.4 Hz), 5.24 (d, 2H, J=6.5 Hz), 5.90 (t, 1H, J=6.5 Hz), 6.57 (td, 1H, J=1.4, 15.5 Hz), 6.96 (td, 1H, J=6.8, 15.5 Hz), 7.17–7.31 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 34.1, 34.4, 79.5, 96.8, 126.1, 128.3, 128.5, 140.8, 146.3, 188.7, 216.5; IR (neat) ν 1669, 1622 cm^{-1}; EIMS m/z 198 (M^+). HRMS calcd for $C_{14}H_{14}O$: 198.104465. Found: 198.104331.

4.4.14. (5*E*)-3-Methyl-8-phenyl-1,2,5-octatrien-4-one (5d). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.85 (t, 3H, J=2.9 Hz), 2.50–2.56 (m, 2H), 2.78 (t, 2H, J=7.4 Hz), 5.14 (q, 2H, J=2.9 Hz), 6.76 (td, 1H, J=1.3, 15.4 Hz), 6.93 (td, 1H, J=6.8, 15.4 Hz), 7.17–7.31 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 13.4, 34.0, 34.5, 78.7, 104.4, 125.7, 126.1, 128.37, 128.44, 141.0, 145.2, 189.6, 216.3; IR (neat) ν 1667, 1624 cm^{-1}; EIMS m/z 212 (M^+). HRMS calcd for $C_{15}H_{16}O$: 212.120115. Found: 212.119156.

4.4.15. (*E*)-5-Phenyl-1-pentenyl acetate (*E*-7). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.66–1.76 (m, 2H), 2.04 (q, 2H, J=6.8 Hz), 2.12 (s, 3H), 2.63 (t, 2H, J=7.6 Hz), 5.43 (td, 1H, J=7.6, 12.4 Hz), 7.08 (d, 1H, J=12.4 Hz), 7.16–7.30 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 20.7, 26.8, 31.2, 35.2, 114.5, 125.8, 128.3, 128.4, 135.8, 142.1, 168.3; IR

(neat) ν 2933, 1756, 1222 cm^{-1}; EIMS *m/z* 204 (M^+). HRMS calcd for $C_{13}H_{16}O_2$: 204.11503. Found: 204.11566.

4.4.16. (*Z*)-5-Phenyl-1-pentenyl acetate (*Z*-7). ^1H NMR (400 MHz, $CDCl_3$) δ 1.68–1.76 (m, 2H), 2.13 (s, 3H), 2.19 (dq, 2H, *J*=1.5, 7.4 Hz), 2.64 (t, 2H, *J*=7.6 Hz), 4.89 (dt, 1H, *J*=6.5, 7.4 Hz), 7.03 (td, 1H, *J*=1.5, 6.5 Hz), 7.16–7.30 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 20.7, 23.9, 30.8, 35.3, 113.7, 125.7, 128.3, 128.5, 134.4, 142.2, 168.1; IR (neat) ν 2933, 1756, 1222 cm^{-1}; EIMS *m/z* 204 (M^+). HRMS calcd for $C_{13}H_{16}O_2$: 204.11503. Found: 204.11566.

4.4.17. 6-Hydroxy-1,10-diphenyl-5-decanone (8). ^1H NMR (400 MHz, $CDCl_3$) δ 1.50–1.82 (m, 10H), 2.37–2.51 (m, 2H), 2.58–2.64 (m, 4H), 3.44 (d, 1H, *J*=4.9 Hz), 4.11–4.15 (m, 1H), 7.16–7.30 (m, 10H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 23.2, 24.6, 30.9, 31.2, 33.6, 35.7, 35.8, 37.7, 76.2, 125.8, 125.9, 128.3, 128.4, 141.9, 142.3, 212.1; IR (neat) ν 3474 (broad), 3026, 1708 cm^{-1}; EIMS *m/z* 324 (M^+). HRMS calcd for $C_{22}H_{28}O_2$: 324.208930. Found: 324.210398.

4.4.18. 1,3-Diphenyl-1,4-dodecanedione (10a). Clear oil, ^1H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, 3H, *J*=7.1 Hz), 1.19–1.28 (m, 10H), 1.50–1.55 (m, 2H), 2.42–2.64 (m, 2H), 3.11 (dd, 1H, *J*=18.0, 3.7 Hz), 4.03 (dd, 1H, *J*=18.0, 10.1 Hz), 4.42 (dd, 1H, *J*=10.1, 3.7 Hz), 7.26–7.55 (m, 8H), 7.94–7.96 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.1, 22.6, 23.6, 29.0, 29.1, 29.3, 31.8, 41.8, 42.4, 53.3, 127.5, 128.1, 128.4, 128.6, 129.1, 133.2, 136.6, 138.3, 198.3, 209.5; IR (neat) ν 1685, 1627 cm^{-1}; EIMS *m/z* 350 (M^+). Anal. calcd for $C_{24}H_{30}O_2$: C, 82.24; H, 8.63. Found: C, 82.10; H, 8.78.

4.4.19. 7,7-Dimethyl-1,3-diphenyl-1,4-octanedione (10b). Colorless crystals, mp 51.0–52.0°C. ^1H NMR (400 MHz, $CDCl_3$) δ 0.75 (s, 9H), 1.31 (ddd, 1H, *J*=13.7, 11.3, 5.2 Hz), 1.55 (ddd, 1H, *J*=13.7, 11.3, 5.2 Hz), 2.40 (ddd, 1H, *J*=16.5, 11.2, 5.1 Hz), 2.54 (ddd, 1H, *J*=16.5, 11.2, 5.1 Hz), 3.07 (dd, 1H, *J*=18.0, 3.7 Hz), 4.00 (dd, 1H, *J*=18.0, 10.1 Hz), 4.42 (dd, 1H, *J*=10.1, 3.7 Hz), 7.20–7.95 (m, 10H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 29.0, 29.9, 37.3, 37.5, 42.3, 53.4, 126.6, 127.5, 128.0, 128.3, 128.5, 129.0, 129.5, 133.1, 136.6, 138.3, 198.1, 209.8; IR (neat) ν 1713, 1682 cm^{-1}; EIMS *m/z* 323 (M^++1). Anal. calcd for $C_{22}H_{26}O_2$: C, 81.95; H, 8.13. Found: C, 81.72; H, 8.14.

4.4.20. 5-Cyclohexyl-1,3-diphenyl-1,4-pentanedione (10c). Colorless crystals, mp 73.0–75.0°C. ^1H NMR (400 MHz, $CDCl_3$) δ 0.60 (ddd, 1H, *J*=24.4, 12.7, 3.4 Hz), 0.85 (ddd, 1H, *J*=24.4, 12.7, 3.4 Hz), 0.93–1.28 (m, 3H), 1.40–1.67 (m, 5H), 1.70–1.85 (m, 1H), 2.25 (dd, 1H, *J*=16.7, 7.4 Hz), 2.43 (dd, 1H, *J*=16.7, 7.4 Hz), 3.03 (dd, 1H, *J*=18.0, 3.7 Hz), 3.97 (dd, 1H, *J*=18.0, 10.0 Hz), 4.33 (dd, 1H, *J*=10.0, 3.7 Hz), 7.18–7.89 (m, 10H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 26.0, 26.1, 26.2, 32.7, 33.1, 33.2, 42.2, 49.4, 53.8, 127.4, 128.0, 128.4, 128.5, 129.0, 133.1, 136.6, 138.1, 198.2, 208.6; IR (neat) ν 1714, 1684 cm^{-1}; EIMS *m/z* 334 (M^+). Anal. calcd for $C_{23}H_{26}O_2$: C, 82.60; H, 7.84. Found: C, 82.30; H, 7.90.

4.4.21. (*E*)-1,3-Diphenyl-5-dodecene-1,4-dione (10d). ^1H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, 3H, *J*=7.1 Hz), 1.18–1.43 (m, 8H), 2.14 (ddd, 2H, *J*=14.8, 7.2, 1.4 Hz), 3.15 (dd, 1H, *J*=17.9, 4.1 Hz), 4.05 (dd, 1H, *J*=17.9, 9.6 Hz), 4.63 (dd, 1H, *J*=9.6, 4.1 Hz), 6.16 (dt, 1H, *J*=15.7, 1.4 Hz), 6.94 (dt, 1H, *J*=15.7, 7.2 Hz), 7.23–7.97 (m, 10H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.0, 22.5, 27.9, 28.8, 31.5, 32.4, 42.4, 51.5, 127.3, 128.1, 128.4, 128.5, 128.8, 129.1, 133.1, 136.7, 138.6, 148.5, 198.0, 198.1; IR (neat) ν 1685 cm^{-1}; EIMS *m/z* 348 (M^+). HRMS calcd for $C_{24}H_{28}O_2$: 348.208930. Found: 348.207123.

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