JOC Article

Studies on K_2CO_3-Catalyzed 1,4-Addition of 1,2-Allenic Ketones with Diethyl Malonate: Controlled Selective Synthesis of β,γ-Unsaturated Enones and α-Pyrones

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The K_2CO_3 (10 mol %)-catalyzed 1,4-addition reaction of diethyl malonate with various substituted 1,2-allenic ketones leading to polyfunctionalized β,γ-unsaturated enones **3** or **4** was studied. With 3-unsubstituted 1-substituted-1,2-allenyl ketones, the highly selective formation of β,γ-unsaturated enones **4** was observed; with 1,2-allenyl ketones bearing one or two 3-substituents in the allenyl group, only β,γ-unsaturated enones **3** with an unmigrated carbon−carbon double bond were produced; with 3-monosubstituted-1,2-allenyl ketones *Z*-β,γ-unsaturated enones **3** were formed with excellent stereoselectivity (*E:Z* > 96:4); with propadienyl ketones, mixtures of β,γ-unsaturated enones **3** and **4** were formed. α-Pyrone derivatives were synthesized via the K_2CO_3-catalyzed or -promoted reaction of 1,2-allenic ketones with diethyl malonate via a sequential Michael addition−carbon-carbon double bond migration−lactonization process.

Introduction

β,γ-Unsaturated enones can be found in some natural products[1] and are important intermediate in organic synthesis. However, due to the possible migration of the carbon−carbon double bond from the β,γ-position to the α,β-position, it is challenging to synthesize β,γ-unsaturated enones selectively. β,γ-Unsaturated enones are usually obtained indirectly by rather sophisticated long and tedious procedures. Some typical methodologies for the preparation of β,γ-unsaturated ketones are summarized as follows: (1) acylation of olefins;[2] (2) oxidation of pent-4-en-2-ol with Corey's oxidant;[3] (3) Zn−Ag couple-promoted reaction of allylic bromide with nitriles;[4] and (4) oxidative cleavage of phenylselenolates.[5] Thus, it is still highly desirable to develop new and efficient methodologies for the synthesis of β,γ-unsaturated enones.

1,2-Allenic ketones constitute an important class of compounds with numerous applications in organic synthesis,[6] showing high reactivities.[7] Among them, the nucleophilic 1,4-addition reactions have been most extensively investigated, in which the carbon−carbon double bond of the initially formed β,γ-unsaturated enones would like to migrate to form α,β-unsaturated enones or a mixture of α,β- and β,γ-unsaturated enones.[8]

Recently, during the course of our study of the chemistry of allenes,[9] we have demonstrated that electron-deficient allenes can easily accept the nucleophilic attack of a halide anion to afford β-halo-β,γ-unsaturated func-

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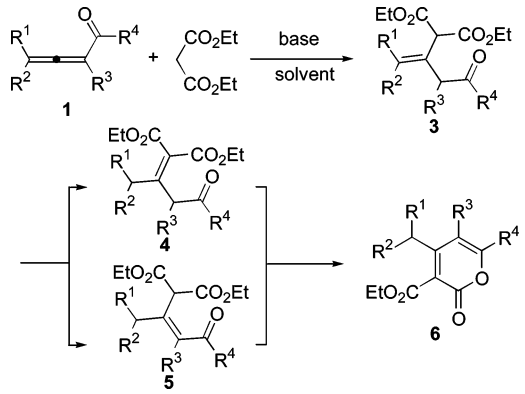
SCHEME 1

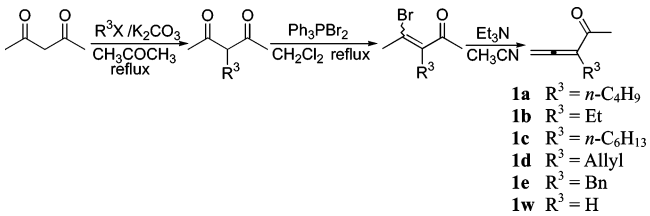


tionalized alkenes.[10] Of particular interest, we observed that β-halo-β,γ-unsaturated enones can be formed highly selectively from 1,2-allenic ketones.[11] On the basis of these results, we reasoned that in principle 1,2-allenic ketones may accept any nucleophilic attack. However, for the reaction with malonates, due to the existence of three carbonyl groups, there is a great tendency that the carbon−carbon double bond may migrate to form compounds with a conjugated carbon−carbon double bond (Scheme 1). Thus, the challenge is how to control the extent of migration of the β,γ carbon−carbon double bond and the stereoselectivity of the reaction. In a previous communication, we have demonstrate that 1,2-allenic ketones can react with malonates to afford α-pyrones.[12] In this paper, we wish to disclose the details of this nucleophilic conjugate addition.

Results and Discussion

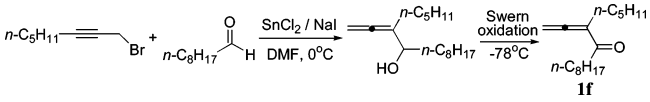
Synthesis of the Starting Materials. A number of methods[13] were reported for the preparation of 1,2-allenic ketones and all of the starting 1,2-allenic ketones used in this study were prepared through the application of known procedures (in some cases, with slight modification). 1-Substituted 1,2-allenyl ketones **1a**−**e** and 1,2-propadiennyl ketone **1w** were synthesized via the elimination of the corresponding 4-bromo-3-penten-2-ones (Scheme 2).[14] **1f** was obtained by the oxidation of the corresponding allenic alcohol[15] with the Swern oxidation procedure (Scheme 3).[16] 3,3-Disubstituted-1,2-allenyl ketones **1g**−**h** (Scheme 4),[17] 3-monosubstituted-1,2-allenyl ketone **1i**−**k** (Scheme 5),[17] and 1,3-disubstituted-1,2-allenyl ketones **1*l***−**r** (Scheme 6) were prepared via the reaction of the corresponding 1,2-allenyllithiums with *N*,*N*-dimethyl amides. 1,3-Nonsubstituted-1,2-allenyl ketones **1s**−**v** were prepared by the addition of allenic magnesium bromide to an aldehyde,[18] followed by the oxidation with DMP[19] (Scheme 7). 1,2-Propadienyl ketones **1x**[20] and **1y**[21] were prepared by the addition of allenic magnesium bromide with the corresponding esters at −78 °C (Scheme 8).

SCHEME 2



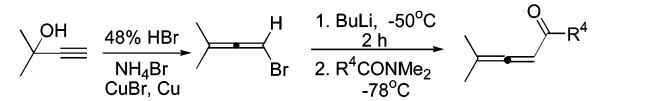
1a $R^3 = n\text{-}C_4H_9$
1b R^3 = Et
1c $R^3 = n\text{-}C_6H_{13}$
1d R^3 = Allyl
1e R^3 = Bn
1w R^3 = H

SCHEME 3



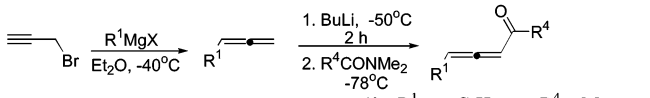
1f

SCHEME 4



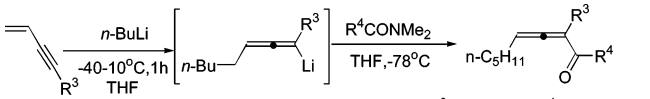
1g R^4 = Me
1h $R^4 = n\text{-}C_6H_{13}$

SCHEME 5



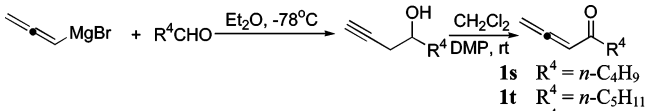
1i $R^1 = n\text{-}C_7H_{15}$, R^4 = Me
1j $R^1 = n\text{-}C_4H_9$, R^4 = Me
1k $R^1 = n\text{-}C_7H_{15}$, $R^4 = n\text{-}C_7H_{15}$

SCHEME 6



1l $R^3 = n\text{-}C_4H_9$, R^4 = Me
1m $R^3 = n\text{-}C_4H_9$, $R^4 = n\text{-}C_7H_{15}$
1n $R^3 = n\text{-}C_4H_9$, R^4 = Ph
1o $R^3 = n\text{-}C_4H_9$, R^4 = Toyl
1p $R^3 = n\text{-}C_5H_{11}$, R^4 = Me
1q $R^3 = n\text{-}C_5H_{11}$, $R^4 = n\text{-}C_7H_{15}$
1r $R^3 = n\text{-}C_5H_{11}$, R^4 = Ph

SCHEME 7



1s $R^4 = n\text{-}C_4H_9$
1t $R^4 = n\text{-}C_5H_{11}$
1u $R^4 = n\text{-}C_6H_{13}$
1v $R^4 = n\text{-}C_8H_{17}$

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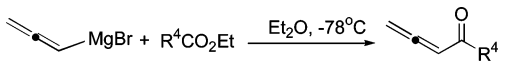
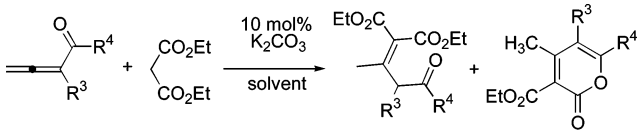
SCHEME 8



1x R^4 = Ph
1y R^4 = Bn

TABLE 1. K_2CO_3-Catalyzed 1, 4-Addition of α-Substituted γ-Nonsubstituted Allenic Ketones with Diethyl Malonate



1 **2** **4** **6**

	1			temp		yield (%)	
entry	R^3	R^4	solvent	(°C)	time	**4**	**6**
1	*n*-C_4H_9	CH_3 (**1a**)	CH_3CN	rt	16 h	48 (**4a**)	25 (**6a**)
2	*n*-C_4H_9	CH_3 (**1a**)	CH_2Cl_2	60	2.5 d	57 (**4a**)	28 (**6a**)
3	*n*-C_4H_9	CH_3 (**1a**)	DMF	rt	10 h	36 (**4a**)	34 (**6a**)
4	*n*-C_4H_9	CH_3 (**1a**)	EtOH	rt	24 h	65 (**4a**)	27 (**6a**)
5	*n*-C_4H_9	CH_3 (**1a**)	*a*	rt	4 d	47 (**4a**)	
6	*n*-C_4H_9	CH_3 (**1a**)	acetone	60	8 h	57 (**4a**)	3 (**6a**)
7	*n*-C_6H_{13}	CH_3 (**1c**)	acetone	reflux	12 h	67 (**4c**)	27 (**6c**)
8	Bn	CH_3 (**1e**)	acetone	reflux	8 h	56 (**4e**)	
9	*n*-C_5H_{11}	*n*-C_8H_{17} (**1f**)	acetone	reflux	24 h	85 (**4f**)	

[a] A mixture of DMF and CH_2Cl_2 (1:1) was used as the solvent.

K_2CO_3-Catalyzed 1,4-Addition of 1,2-Allenic Ketones with Diethyl Malonate. We examined the reaction of 1-(*n*-butyl)-1,2-propadienyl methyl ketone (**1a**) with diethyl malonate using K_2CO_3 as a catalyst in different solvents (entries 1−6, Table 1). The reactions in DMF, EtOH, and CH_3CN at room temperature afforded a mixture of β,γ-unsaturated enone **4a** with the carbon−carbon double bond conjugated with the two ethoxycarbonyl groups and α-pyrone **6a** in good combined yields and low selectivities. The reaction in DMF was faster than those in EtOH and CH_3CN (entries 1, 3, and 4, Table 1). In dichloromethane, it took 2.5 days for the reaction to produce 57% of **4a** and 28% of **6a** at 60 °C (entry 2, Table 1). However, it is interesting to observe that the corresponding reaction in acetone at 60 °C afforded **4a** with modest yields highly selectively together with only 3% of **6a** (entry 6, Table 1). In acetone, the concentration of active nucleophile may be kept level to ensure the 1,4-addition reaction while at the same time inhibit the isomerization−lactonization reaction. Thus, the key point in carrying out this experiment is to choose a modest polar solvent and control the reaction time. In the following cases we carried out the reaction in acetone with heating using 10% K_2CO_3 as the catalyst (conditions A).

The results of other 1-substituted-3-unsubstituted-1,2-allenyl ketones with diethyl malonate catalyzed by K_2CO_3 in acetone affording β,γ-unsaturated enones **4** are given in Table 1 (entries 7−9). The highly selective migration of the carbon−carbon double bond leading to **4** (entries 6, 8, and 9, Table 1) indicates that the malonate moiety in the products can stabilize the carbon−carbon double bond under conditions A.

Encouraged by the above results, we envisioned that any substitutes at the 3-position of the allenyl group might also contribute to the control of the isomerization of the β,γ-unsaturated carbon−carbon double bond. In fact, to our surprise, 3,3-disubstituted-1,2-allenyl ketones, i.e., 5-methylhexa-3,4-dien-2-one **1g** and 2-methylundeca-2,3-dien-5-one **1h**, reacted with diethyl malonate forming β,γ-unsaturated enones **3g** and **3h,** respectively. In these two compounds the carbon−carbon double bond was kept at the original position (entries 1−3, Table 2). It is interesting to observe that 3-monoalkyl-substituted-1,2-allenyl ketones (**1i** to **1r**) reacted smoothly with diethyl malonate to afford the corresponding β,γ-unsaturated enones **3** in good yields highly stereoselectively (*E*:*Z* > 96:4) (entries 4−13, Table 2). The configurations of the carbon−carbon double bond of the products **3i**−**r** (entries 4−13, Table 2) were determined by the $^1H-^1H$ NOESY spectra of *E*/*Z*-**3j** and *E*-**3o** (Figure 1).

The most reactive unsubstituted propadienyl ketones **1s**−**v** also underwent conjugate addition with diethyl malonate. The results are shown in Table 3. In contrast to the reaction discussed above, the formation of a mixture of carbon−carbon double bond isomers was observed. The general ratio of β,γ-unsaturated enones **3** to α,β-unsaturated enones **4** was ∼3/1 (determined by ^1H NMR spectra) whereas in dichloromethane the ratios drop to ∼1/1. Efforts such as other combinations of weaker bases ($KHCO_3$, KF, KOAc, $NaHCO_3$, NaOAc) with solvents (CH_3CN, CH_2Cl_2, acetone) were made to improve the stereoselectivity of the reaction, but failed.

A rationale for the observed regio- and stereochemistry is shown in Scheme 9. In this mechanism, a dienolate intermediate is produced by the attack of the anionic nucleophile from the less hindered side at the β-carbon of the allenic ketones. Thus, the configuration of the carbon−carbon double bond in the pertinent final product **3i**−**r** is *E*. The two π systems in the resulting dienolate are orthogonal to each other.[22] Selective protonation at the α-carbon afforded β,γ-unsaturated enones **3**.[22] When groups R^1 and R^2 in the substrate are hydrogens, due to the lack of stabilization effect of substituents to the unreacted carbon−carbon double bond, it has a tendency to migrate to form thermodynamically more stable products **4**, especially in the basic environment. What is surprising is that with propadienyl ketones **1s-v** the carbon−carbon double bond in the initially formed 1,4-adduct did not completely transform to product **4** as 1-substituted-3-unsubstituted-1,2-allenyl ketones did.

The new synthetic method has several noteworthy features: (1) for 3-mono- or disubstituted-1,2-allenyl ketones, only β,γ-unsaturated enones with an unmigrated carbon−carbon double bond were produced; (2) for 3-monosubstituted-1,2-allenyl ketones the corresponding **3** were formed with an excellent stereoselectivity (*E*:*Z* > 96:4); (3) polyfunctionalities in the products made them ready for further transformation; (4) the present catalytic

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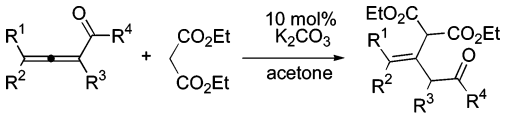
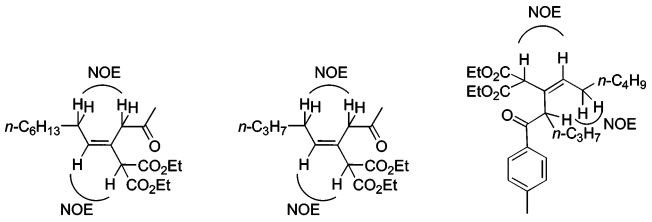
TABLE 2. K_2CO_3-Catalyzed 1,4-Addition of γ-Substituted Allenic Ketones with Diethyl Malonate



1 **3**

	1				temp		3	
entry	R^1	R^2	R^3	R^4	(°C)	time	yield (%)	$E:Z^b$
1	CH_3	CH_3	H	CH_3 (**1g**)	reflux	9 h	75 (**3g**)	
2[a]	CH_3	CH_3	H	CH_3 (**1g**)	55	11 h	83 (**3g**)	
3	CH_3	CH_3	H	n-C_6H_{13} (**1h**)	reflux	21 h	58 (**3h**)	
4	n-C_7H_{15}	H	H	CH_3 (**1i**)	reflux	12 h	75 (**3i**)	>99:1
5	n-C_4H_9	H	H	CH_3 (**1j**)	reflux	12 h	81 (**3j**)	98:2
6	n-C_7H_{15}	H	H	n-C_7H_{15} (**1k**)	reflux	24 h	58 (**3k**)	96:4
7	n-C_5H_{11}	H	n-C_4H_9	CH_3 (**1l**)	55	4 d	84 (**3l**)	>99:1
8	n-C_5H_{11}	H	n-C_4H_9	n-C_7H_{15} (**1m**)	55	2 d	71 (**3m**)	95:5
9	n-C_5H_{11}	H	n-C_4H_9	Ph (**1n**)	55	3 d	76 (**3n**)	>99:1
10	n-C_5H_{11}	H	n-C_4H_9	Toyl (**1o**)	60	2 d	47 (**3o**)	98:2
11	n-C_5H_{11}	H	n-C_5H_{11}	CH_3 (**1p**)	55	2.5 d	83 (**3p**)	>99:1
12	n-C_5H_{11}	H	n-C_5H_{11}	n-C_7H_{15} (**1q**)	55	3 d	78 (**3q**)	>99:1
13	n-C_5H_{11}	H	n-C_5H_{11}	Ph (**1r**)	55	3 d	75 (**3r**)	>99:1

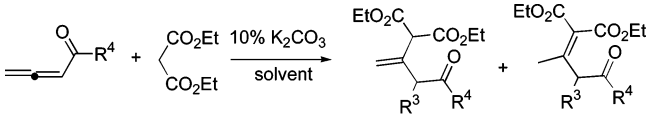
[a] DMF was used as the solvent. [b] Determined by ^{1}H NMR spectra.



***E*-3j** ***E*-3k** ***E*-3o**

FIGURE 1. NOE study of **3j** and **3o**.

TABLE 3. K_2CO_3-Catalyzed 1,4-Addition of α,γ-Nonsubstituted Allenic Ketones with Diethyl Malonate



1 **3** **4**

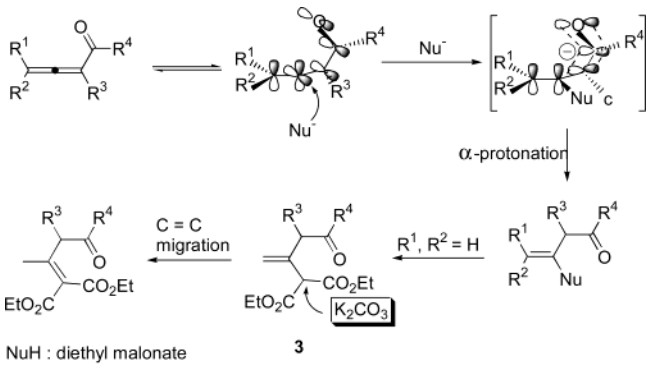
	1		temp		
entry	R^4	solvent	(°C)	time	yield (%) (**3**:**4**)[a]
1	n-C_4H_9 (**1s**)	acetone	55	55 min	88 (**3s:4s** = 2.9:1)
2	n-C_5H_{11} (**1t**)	acetone	55	50 min	89 (**3t:4t** = 3.5:1)
3	n-C_6H_{13} (**1u**)	acetone	55	50 min	86 (**3u:4u** = 3.7:1)
4	n-C_8H_{17} (**1v**)	acetone	55	50 min	74 (**3v:4v** = 3.6:1)
5	n-C_4H_9 (**1s**)	CH_2Cl_2	50	11 h	66 (**3s:4s** = 2.7:1)
6	n-C_5H_{11} (**1t**)	CH_2Cl_2	50	11 h	66 (**3t:4t** = 1.1:1)
7	n-C_6H_{13} (**1u**)	CH_2Cl_2	50	10 h	69 (**3u:4u** = 0.9:1)
8[b]	n-C_5H_{11}(**1t**)	acetone	55	8 h	71 (**3t:4t** = 3.5:1)

[a] Determined by the 300-MHz ^{1}H NMR spectra; [b] 10% Na_2CO_3 was used as the catalyst.

reaction is operationally simple; and (5) commercial solvents are good enough for this reaction.

Sequential Michael Addition−Carbon-Carbon Double Bond Migration−Lactonization Synthesis of α-Pyrones. α-Pyrones are a class of important intermediates utilized in organic synthesis[23,24] and a commonly observed structural unit in many naturally occurring products, which show a broad range of biological activities.[25,26] During the course of our study of transformation of the above products, we found that in a basic

SCHEME 9



4

environment, unsaturated enones can cyclize to form α-pyrone. Thus, combining the three sequential processes we can develop an efficient method for the synthesis of α-pyrone with diversity and regioselectivity since the allenic ketones can accommodate four different substituents at the different locations ready for assembly into the different locations of α-pyrones.

As revealed in Table 4, 1-substituted-3-unsubstituted-1,2-allenyl ketones can undergo this K_2CO_3-catalyzed sequential Michael addition−carbon-carbon double bond migration−lactonization readily with diethyl malonate in acetone, ethanol, and DMF. Structural variation in the

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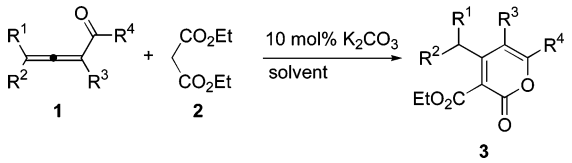
(24) For a discussion of the chemistry of α-pyrone, see also: Stauton, J. *Comprehensive Organic Chemistry*; Samnes, P. G., Ed.; Pergamon Press: Oxford, UK, 1979; Vol. 4, pp 629−646.

(25) (a) Hayashi, Y.; Yuki, Y.-i.; Matsumoto, T.; Sakan, T. *Tetrahedron Lett*. **1977**, 3637. (b) Chen, K. K.; Kovarikova, A. *J. Pharm. Sci*.**1967**, *56*, 1535. (c) Kupchan, S. M.; Moniot, J. L.; Sigel, C. W.; Hemingway, R. J. *J. Org. Chem*. **1971**, *36*, 2611.

(26) For a synthesized α-pyrone with *anti*-HIV activity, see: Prasad, J. V. N. V.; Para, K. S.; Lunney, E. A.; Ortwine, D. F.; Dunbar, J. B.; Ferguson, D., Jr.; Tummino, P. J.; Hupe, D.; Tait, B. D.; Domagala, J. M.; Humblet, C.; Bhat, T. N.; Liu, B.; Guenin, D. M. A.; Baldwin, E. T.; Erickson, J. W.; Sawyer, T. K. *J. Am. Chem. Soc.* **1994**, *116*, 6989.

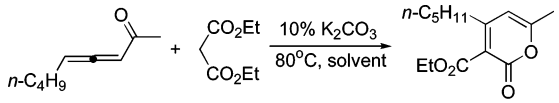
TABLE 4. K_2CO_3-Catalyzed or -Promoted Sequential Michael Addition−Carbon-Carbon Double Bond Migration−Lactonization of Allenic Ketones with Diethyl Malonate



	1							
entry	R^1	R^2	R^3	R^4	solvent	temp (°C)	time	yield (%) (**6**)
1	H	H	*n*-C_4H_9	Me (**1a**)	acetone	reflux	48 h	64[a] (**6a**)
2	H	H	*n*-C_4H_9	Me (**1a**)	DMF	80	7 h	55 (**6a**)
3	H	H	*n*-Et	Me (**1b**)	EtOH	reflux	12 h	53 (**6b**)
4	H	H	*n*-Et	Me (**1b**)	DMF	80	12 h	50 (**6b**)
5	H	H	*n*-Et	Me (**1b**)	acetone	reflux	20 h	33 (**6b**)
6	H	H	*n*-C_6H_{13}	Me (**1c**)	acetone	55	3 d	81 (**6c**)
7	H	H	allyl	Me (**1d**)	EtOH	reflux	15 h	54 (**6d**)
8	H	H	allyl	Me (**1d**)	acetone	reflux	20 h	90 (**6d**)
9	H	H	Bn	Me (**1e**)	acetone	reflux	21 h	92 (**6e**)
10	H	H	Bn	Me (**1e**)	DMF	60	2.5 h	90 (**6e**)
11	H	H	*n*-C_5H_{11}	*n*-C_8H_{17} (**1f**)	acetone	reflux	2 d	56 (**6f**)
12	H	H	H	*n*-C_4H_9 (**1s**)	acetone	55	9 h	65 (**6s**)
13	H	H	H	*n*-C_6H_{13} (**1u**)	acetone	55	9 h	63 (**6u**)
14	H	H	H	*n*-C_8H_{17} (**1v**)	acetone	55	9 h	69 (**6v**)
15	H	H	H	Me (**1w**)	EtOH	60	1.5 h	74 (**6w**)
16	H	H	H	Ph (**1x**)	acetone	reflux	4 h	71 (**6x**)
17	H	H	H	Ph (**1x**)	EtOH	reflux	1.5 h	56 (**6x**)
18	H	H	H	Bn (**1y**)	CH_2Cl_2	reflux	40 h	69 (**6y**)

[a] 1 equiv of K_2CO_3 was used.

SCHEME 10



solvent: EtOH, yield: 38%
solvent: DMF, yield: 54%

1,2-allenic ketone component has also been examined. As showed in Table 4, R^3 can be alkyl, allyl, and benzyl groups and R^4 can be alkyl, phenyl, and benzyl groups.

Propadienyl butyl ketone (**1s**) reacted smoothly with diethyl malonate in the presence of 10% K_2CO_3 as the catalyst giving the corresponding α-pyrone (**6s**) in 65% yield (entry 12, Table 4). Changing R^4 from methyl to octyl and benzyl, the yields are almost the same (entries 14 and 16, Table 4). The sequential reaction of **1y** even proceeds in dichloromethane to yield α-pyrone **6y** with prolonged time (entry 18, Table 4).

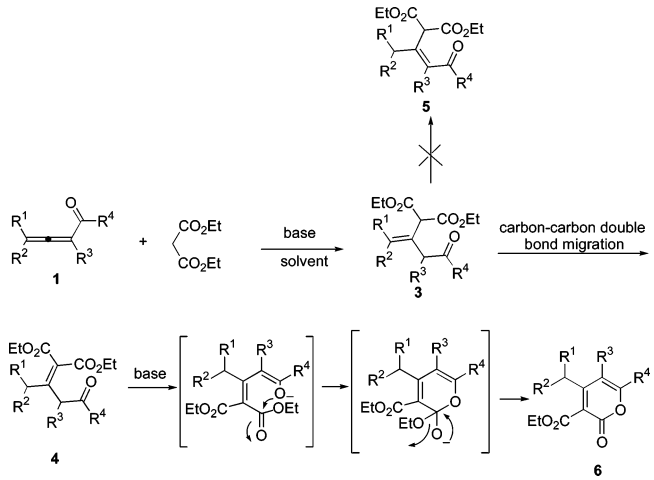
Next we examined the cyclization reaction of other 1,2-allenyl ketones with diethyl malonate. Generally speaking, the yields of the reactions of 3-substituted-1,2-allenyl ketones with diethyl malonate were notably low. The reaction of nona-3,4-dien-2-one **1j** with diethyl malonate in EtOH yielded **6j** in 38% yield, whereas in DMF the yield of **6j** is 54% (Scheme 10). When it comes to 1,3-disubstituted-1,2-allenyl ketone, α-pyrone was not formed.

According to the results of 1,4-addition, instead of the intermediacy of **5**, it is believed that α-pyrone was formed via keto−ester cyclization of *β*,*γ*-unsaturated enones **4** (Scheme 11).

Conclusion

In conclusion, we have developed an efficient methodology for the synthesis of *β*,*γ*-unsaturated ketones and a

SCHEME 11



sequential carbon−carbon double bond migration−cyclization protocol for the synthesis of various substituted α-pyrones starting from the easily available 1,2-allenic ketones with diethyl malonate. We found that the substituent of substrates has a great effect on the reaction. The 3-substituent of the allenyl group can stabilize the carbon−carbon double bond of the 1,4-addition product. The reaction shows good 1,4-regio- and *E*-stereoselecivity. Further investigation in this area is being intensively carried out in our laboratory.

Experimental Section

Starting Materials. Compounds 3-butylpenta-3,4-dien-2-one (**1a**),[11a] 3-ethylpenta-3,4-dien-2-one (**1b**),[11a] 3-allylpenta-3,4-dien-2-one (**1d**),[11b] 3-benzylpenta-3,4-dien-2-one (**1e**),[11b] 5-methylhexa-3,4-dien-2-one (**1g**),[14b] 2-methylundeca-2,3-dien-5-one (**1h**),[14] dodeca-3,4-dien-2-one (**1i**),[14a,c] nona-3,4-dien-2-one (**1j**),[14a,b] octa-1,2-dien-4-one (**1s**),[15] nona-1,2-dien-4-one

(**1t**),[15] penta-3,4-dien-2-one (**1w**),[11a] 1-phenylbuta-2,3-dien-1-one (**1x**),[17] and 1-phenylpenta-3,4-dien-2-one (**1y**)[18] are prepared as reported.

Synthesis of 3-hexylpenta-3,4-dien-2-one (1c):[11] A mixture of acetoacetone (10.0 g, 0.1 mol), 1-bromohexane (15.5 mL, 18.2 g, 0.11 mol), potassium carbonate (15.2 g, 0.11 mol), and potassium iodide (8.3 g, 0.05 mol) in acetone (50 mL) was refluxed for 43 h. After filtration and evaporation, the resulting crude 3-hexylpenta-2,4-dione was directly added dropwise into an ice-cold solution of PPh_3Br_2 (prepared from PPh_3 (21.6 g, 83 mmol) and Br_2 (17.8 g, 80 mmol)) in dichloromethane (100 mL). The mixture was stirred until the evolution of hydrogen bromide ceased. After removal of triphenylphosphine oxide by addition of ether, the residue was dissolved in 100 mL of acetonitrile followed by the addition of triethylamine (7.5 g, 75 mmol). After being stirred for 23 h at 80 °C, the precipitate was removed by filtration and the resulting mixture was washed with diluted hydrochloric acid (2 × 30 mL) and saturated NaCl solution (2 × 50 mL). The combined organic phase was dried over magnesium sulfate. After evaporation, the residue was purified by chromatography on silica gel (eluent, hexane/ether 100/1) to afford 4.5 g (36%) of **1c**: liquid; IR (neat) 1933, 1682, 1466, 1358, 1242, 1020, 843, 725 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.18 (t, J = 3.2 Hz, 2 H), 2.29 (s, 3 H), 2.12−2.20 (m, 2 H), 1.22−1.40 (m, 8 H), 0.86 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.1, 199.1, 109.4, 79.7, 31.9, 29.1, 28.0, 27.2, 26.3, 22.8, 14.3; MS m/z (%) 166 (M^+, 0.18), 43 (100); HRMS m/z (EI) calcd for $C_{11}H_{18}O$ 166.13576, found 166.13514.

Synthesis of 3-pentyldodeca-1,2-dien-4-one (1f):[12,13] A suspension of stannous chloride (2.39 g, 12.6 mmol), 1-bromooct-2-yne (1.8 g, 10.1 mmol), and sodium iodide (1.85 g, 12.4 mmol) in DMF (20 mL) was stirred at room temperature for 1 h. After the reaction mixture was cooled to 0 °C, a solution of 1.4 g (9.9 mmol) of nonanal in 10 mL of DMF was added and the mixture was stirred at 0 °C for another 24 h followed by quenching with water. Extraction, drying, evaporation, and flash chromatography on silica gel (hexane/ether 15:1) afforded 1.04 g of the crude alcohol. To a solution of 0.7 mL (6.2 mmol) of oxalyl chloride in 10 mL of dichloromethane was added 1.1 mL (12.4 mmol) of DMSO in 10 mL of CH_2Cl_2 at −78 °C. After 5 min, a solution of 1.04 g of the alcohol in 10 mL of dichloromethane was added. The mixture was stirred at −78 °C for another 30 min followed by the addition of 6.0 mL (40 mmol) of triethylamine. Then the mixture was warmed to 0 °C and stirred at 0 °C for another 10 min. The mixture was diluted with ether, washed with 10% HCl solution, extracted with ether, and dried over anhydrous magnesium sulfate. Evaporation and flash chromatography on silica gel (petroleum ether/ethyl acetate 100/1) afforded 0.84 g (82%) of **1f**: liquid; IR (neat) 1934, 1681, 1466, 1378, 1171, 1091, 841 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.13 (t, J = 2.9 Hz, 2 H), 2.60 (t, J = 7.5 Hz, 2 H), 2.08−2.18 (m, 2 H), 1.42−1.60 (m, 2 H), 1.18−1.41 (m, 16 H), 0.84 (t, J = 6.5 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 216.4, 201.8, 108.8, 79.6, 39.4, 32.0, 31.6, 29.6, 29.5, 29.4, 27.7, 26.4, 25.3, 22.9, 22.6, 14.3, 14.2; MS m/z (%) 250 (M^+, 3.28), 57 (100); HRMS m/z (EI) calcd for $C_{17}H_{30}O$ 250.22966, found 250.22745.

Synthesis of octadeca-9,10-dien-8-one (1k):[14] To a solution of deca-1,2-diene (4.4 g, 32 mmol) in THF (100 mL) was added *n*-BuLi (2.5 M in cyclohexane, 12 mL, 30 mmol) at −70 °C. Then the mixture was stirred for 1 h at −50 to −40 °C followed by the dropwise addition of *N*,*N*-dimethyl octamide (5.1 g, 30 mmol) at −78 °C. After 2 h at this temperature, the resulting solution was slowly transferred into an ice-cold aqueous HCl solution (0.2 N, 200 mL). Extraction with ether, drying over anhydrous magnesium sulfate, rotary evaporation, and flash chromatography on silica gel (eluent: hexane/ether 40/1) afforded 3.1 g (39%) of **1k**: liquid; IR (neat) 1947, 1737, 1682, 1466, 1377, 1092, 879, 723 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.68−5.73 (m, 1 H), 5.59 (q, J = 6.8 Hz, 1H), 2.55 (t, J = 7.5 Hz, 2 H), 2.12−2.20 (m, 2 H), 1.52−1.60 (m, 2 H), 1.41−1.52 (m, 2 H), 1.18−1.41 (m, 16 H), 0.78−0.91 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.0, 202.3, 97.6, 95.6, 39.2, 32.0, 31.9, 29.5, 29.3, 29.3, 29.3, 29.2, 28.1, 25.1, 22.8, 14.3; MS m/z (%) 264 (M^+, 1.80), 57 (100); HRMS m/z (EI) calcd for $C_{18}H_{32}O$ 264.24532, found 264.25030.

Preparation of 1,2-Allenic Ketones 1l−r. Typical Procedure. Synthesis of 3-butyldeca-3,4-dien-2-one (1l): To a solution of oct-1-en-3-yne (1.1 g, 10 mmol) in tetrahydrofuran (60 mL) was added 4 mL of 2.5 M *n*-BuLi at −40 °C under argon. After being stirred at −25 °C for 0.5 h, the solution was recooled to −78 °C and treated with a solution of *N*,*N*-dimethyl acetamide (5.1 g, 30 mmol) in tetrahydrofuran (10 mL) for another 2 h. Then the reaction mixture was transferred to 400 mL of 0.2 N HCl solution. After the usual workup, the residue was purified by flash chromatography on silica gel (eluent: hexane/ether 100/1) to afford 3.2 g (55%) of **1l**: liquid; IR (neat) 1944, 1680 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.59−5.39 (m, 1 H), 2.17 (s, 3 H), 2.20−2.07 (m, 4 H), 1.50−1.11 (m, 10 H), 0.95−0.82 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.4, 199.6, 109.6, 95.5, 31.3, 30.1, 28.7, 28.2, 26.9, 26.2, 22.4, 22.3, 14.0, 13.9; MS m/z (%) 208 (2.77), 43 (100); HRMS m/z (EI) calcd for $C_{14}H_{24}O$ 208.1827, found 208.1795.

Preparation of 1,2-Allenic Ketones 1u−v. Typical Procedure. Synthesis of deca-1,2-dien-4-one (1u):[16] To a suspension of magnesium turnings (3.6 g, 0.15 mol) in dry Et_2O (60 mL) was added $HgCl_2$ (0.1 g). After being stirred for 2.5 h at room temperature, the mixture was cooled to 0 °C followed by the addition of propargyl bromide (10.7 mL, 0.12 mol). After an additional 1 h, the mixture was cooled to −40 °C and treated with heptanal (16.0 mL, 0.11 mol). After 1 h, the mixture was warmed to room temperature naturally and poured into a solution of NH_4Cl. After the usual workup, the residue was distilled under reduced pressure to give dec-1-yn-4-ol (bp 99−100 °C/20 mmHg) (15.9 g, 93%).

A solution of the above prepared alcohol (8.8 g, 57 mmol) in dichloromethane (100 mL) was added to a solution of DMP (29.5 g, 69 mmol) in dichloromethane (400 mL) with stirring. After 2 h, the homogeneous reaction mixture was diluted with 500 mL of ether and the resulting suspension was added to 200 mL of 1 N sodium hydroxide. After the usual workup, the residue was purified by flash chromatography on silica gel (eluent: hexane/ethyl acetate 100/1) to afford 4.7 g (54%) of **1u**: liquid; IR (neat) 3066, 1961, 1934, 1684, 849 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.63 (t, J = 6.6 Hz, 1 H), 5.15 (d, J = 6.6 Hz, 2 H), 2.52 (t, J = 8.4 Hz, 2 H), 1.51 (t, J = 7.2 Hz, 2 H), 1.12−1.29 (m, 6 H), 0.79 (t, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 216.8, 201.2, 96.8, 79.5, 39.4, 31.8, 29.0, 24.7, 22.7, 14.2; MS m/z (%) 153 ($M^+ + 1$, 2.20), 43 (100); HRMS m/z (EI) calcd for $C_{10}H_{16}O$ 152.12012, found 152.11928.

General Procedure for K_2CO_3-Catalyzed 1,4-Addition of 1,2-Allenic Ketones with Diethyl Malonate. A solution of **1** (1.2 mmol), diethyl malonate (1.0 mmol), and 15.8 mg (10 mol %) of K_2CO_3 in 2 mL of acetone was heated to 60 °C with stirring. After the reaction was over as monitored by TLC, the solvent was evaporated and the crude product was purified by chromatography on silical gel (petroleum ether/ethyl acetate 10/1) to afford **3** or **4** or **6** or their mixture.

Synthesis of ethyl 2-(ethoxycarbonyl)-3-methyl-4-butyl-5-oxo-2-hexenoate (4a) and 3-(ethoxycarbonyl)-4,6-dimethyl-5-butyl-2-pyranone (6a): A solution of **1a** (169.7 mg, 1.2 mmol), diethyl malonate (164.5 mg, 1.0 mmol), and 16.7 mg (10 mol %) of K_2CO_3 in 2 mL of acetone was heated to 60 °C with stirring. After the reaction was over as monitored by TLC, the solvent was evaporated and the crude product was purified by chromatography on silical gel (petroleum ether/ethyl acetate 10/1) to afford 172.4 mg (57%) of **4a** and 9.1 mg (3%) of **6a**. **4a**: liquid; IR (neat) 1732, 1628, 1227, 1058, 869, 783 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.21−4.31 (m, 4 H), 4.14−4.20 (m, 1 H), 2.18 (s, 3 H), 1.87 (s, 3 H), 1.81−1.86 (m, 1 H), 1.47−1.54 (m, 1 H), 1.22−1.33 (m, 8 H), 1.10−1.19 (m, 2 H), 0.86 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ

206.8, 165.3, 165.3, 153.8, 128.0, 61.5, 61.4, 57.5, 29.7, 29.5, 28.1, 22.8, 16.5, 14.2, 14.0; MS *m*/*z* (%) 298 (M^+, 0.47), 181 (100); HRMS *m*/*z* (EI) calcd for $C_{16}H_{26}O_5$ 298.17802, found 298.18169. **6a**: yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.42 (q, J = 7.1 Hz, 2 H), 2.25−2.50 (m, 2 H), 2.26 (s, 3 H), 2.17 (s, 3 H), 1.38−1.25 (m, 7 H), 0.94 (t, J = 7.1 Hz, 3 H); MS *m*/*z* (%) 253 ($M^+ + 1$, 9), 252 (M^+, 52), 181 (100); IR 1718, 1635, 1552, 1236 cm^{-1}. Elemental Anal. Calcd for $C_{14}H_{20}O_4$: C 66.65, H 7.99. Found: C 66.67, H 7.70.

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Supporting Information Available: Analytical data for compounds **1**, **3**, **4**, and **6** and ^{1}H NMR and ^{13}C NMR spectra of these compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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