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Facile and clean synthesis of α-alkenoyl ketene-(*S*,*S*)-acetals via the aldol condensation reactions in water

Yan Ouyang, Dewen Dong,* Wei Pan, Jie Zhang and Qun Liu*

Department of Chemistry, Northeast Normal University, Changchun 130024, Jilin, PR China

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Abstract—The aldol condensation reactions of α,α-diacetyl ketene-(*S*,*S*)-acetals, **1a** and **1b**, with aromatic aldehydes **2** in the presence of NaOH in water have been investigated. At room temperature, the base-mediated condensations proceed smoothly to afford the corresponding mono-condensed products, α-alkenoyl ketene-(*S*,*S*)-acetals **3**, in high yields. At reflux temperature, the reactions produce high yields of symmetric double condensed α,α-dialkenoyl ketene-(*S*,*S*)-acetals **4** when 2 equiv of aldehyde are employed. Moreover, compounds **3** can condense with a different aldehyde to give unsymmetric double condensed α,α-dialkenoyl ketene-(*S*,*S*)-acetals **5**.

1. Introduction

The use of water as a solvent in organic chemistry was rediscovered in the 1980s in Breslow's work, which showed that hydrophobic effect could strongly enhance the rates of some organic reactions.[1] Organic reactions carried out in water, without the use of any organic solvent, can also be beneficial because water is an easily available, cheap, safe and environmentally benign solvent.[2] So far, extensive work has revealed that a variety of organic reactions including aldol reaction, allylation reaction, Diels–Alder reaction, Michael reaction, Mannich-type reaction and even dehydration reactions can be realized in water, especially in the presence of various catalysts such as inverse phase-transfer catalysts and surfactant-type Lewis or Bronsted acids.[3–5]

Very recently, we achieved a clean, facile and practical synthesis of α-oxo ketene-(*S*,*S*)-acetals based on the reaction of β-dicarbonyl compounds with carbon disulfide and alkyl bromide catalyzed by tetrabutylammonium bromide (TBAB) in the presence of potassium carbonate in water.[6] Indeed, our laboratory has also been engaging in the synthesis and application of α-oxo ketene-(*S*,*S*)-acetals.[7] During the course of our studies, we noted that α-alkenoyl ketene-(*S*,*S*)-acetals containing a dienone moiety showed promising structural features as novel organic intermediates for: (1) double Michael acceptors serving as five carbon 1,5-bielectrophilic species, (2) dense and flexible substitution patterns and (3) good leaving alkylthio groups that can be subjected to a nucleophilic vinyl substitution (S_NV) reaction. Consequently, we developed a novel synthetic strategy for the construction of highly substituted six-membered carbocycles and heterocycles, relying upon the utilization of α-alkenoyl ketene-(*S*,*S*)-acetals as a five carbon 1,5-bielectrophilic species in formal [5+1] annulations with various carbon, nitrogen and sulfur nucleophiles, respectively.[8] The important synthetic utility of such intermediates and our continuing interest in organic reactions in water prompted us to exploit the synthesis of novel α-alkenoyl ketene-(*S*,*S*)-acetals in aqueous media. In the present work, we wish to report our investigations on the aldol condensation reactions of α,α-diacetyl ketene-(*S*,*S*)-acetals with various selected aryl aldehydes affording a variety of novel α-alkenoyl ketene-(*S*,*S*)-acetals in water.

2. Results and discussion

The synthesis and application of α-oxo ketene-(*S*,*S*)-acetals have been reported elsewhere.[9] Following the procedure described in our previous work,[6] α,α-diacetyl ketene-(*S*,*S*)-acetals **1a** and **1b** were easily prepared from acetylacetone, carbon disulfide, 1,2-dibromoethane/1,3-dibromo propane catalyzed by TBAB in the presence of K_2CO_3 and water in nearly quantitative yields, respectively. Junjappa et al. and Pak et al. investigated the direct aldol condensation reactions of some α-acetyl ketene-(*S*,*S*)-acetals with aromatic aldehydes and described the synthetic utility of the condensed products.[10,11] Recently, Asokan and co-workers reported the preparation of bis(alkenoyl)ketene-(*S*,*S*)-acetals from **1a** and aldehydes in the presence of NaOEt in EtOH, and the stereoselective intramolecular [2+2] photocycloadditions of the title compounds.[12] In all these cases, the aldol condensation reactions were carried out in organic media in which strong bases, such as NaH and NaOEt, have been employed.

Keywords: Aldol condensation reactions; Aromatic aldehydes; α-Oxo ketene-(*S*,*S*)-acetals; Water.
* Corresponding authors. Tel.: +86 431 5099759; fax: +86 431 5098635; e-mail: dongdw663@nenu.edu.cn

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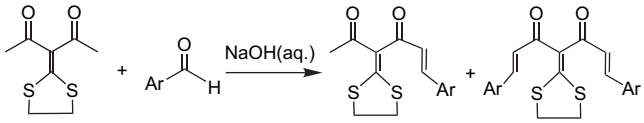
In the present work, the reaction of **1a** with 4-methoxybenzaldehyde **2a** (2 equiv) mediated by NaOH (3 equiv) at 20 °C in water was initially investigated. As indicated by TLC, a product was formed but the reaction proceeded sluggishly since some of the substrates could not be consumed even after prolonged reaction time. The reaction was stopped and a pure yellowish solid was obtained in 65% yield along with 30% recovery of the starting material **1a** after workup and column chromatography of the resulting reaction mixture (Table 1, entry 1). The only product was characterized as (*E*)-3-(1,3-dithiolan-2-ylidene)-6-(4-methoxyphenyl)hex-5-ene-2,4-dione **3aa**, a mono-condensed product, on the basis of its spectral and analytical data. Surprisingly, none of the desired double condensed product, (1*E*,6*E*)-4-(1,3-dithiolan-2-ylidene)-1,7-bis(4-methoxyphenyl)hepta-1,6-diene-3,5-dione **4aa**, could be detected in the reaction system. In a separate experiment, when **1a** and **2a** (2 equiv) were subjected to the similar conditions, namely in the presence of NaOH in ethanol at 20 °C, both **3aa** and **4aa** appeared simultaneously in the reaction system within 10 min. After 12 h, the reaction was complete, as indicated by TLC, affording **4aa** in 78% isolated yield, similar to that previously described in the literature.[12] The results reveal that the reaction media have great effect on the aldol condensations, and the clean conversion of **1a** into **3aa** in organic media is difficult.

The reactions of **1a** with **2a** were then carried out in water under various conditions to examine the reaction orientation and to optimize the yields (see Table 1). Table 1 clearly shows that the reaction temperature has a great effect on the test reactions based on the reaction time and yields. A complete conversion of **1a** could be realized at 30 °C within 20 h, which exclusively afforded compound **3aa** in 90% yield even when 2 equiv of **2a** were employed (entry 2, Table 1). With the increase of the reaction temperature, the reaction was significantly accelerated and led to the formation of **4aa** (entries 3–5, Table 1). At reflux temperature, the conversion of **1a** into **4aa** could be achieved within 4 h. It should be mentioned that much excess of base could result in a slightly lower yield of **4aa** for the formation of byproducts (entry 6, Table 1). Actually, 2.5 equiv of base were sufficient with the condensation reaction to give **4aa** (entry 7, Table 1). However, the excess of base or aldehyde **1a** did not have an obvious influence on the formation of **3aa** at low temperature (entries 8 and 9, Table 1). All the experiments have revealed that the condensation reaction can be controlled to exclusively produce **3aa** or **4aa** by simply varying the reaction temperature.

Table 1. The aldol condensation reactions of α,α-diacetyl ketene-(*S*,*S*)-acetal **1a** and 4-methoxybenzaldehyde **2a** in the presence of NaOH in water



Entry	Molar ratio[a]	Molar ratio[b]	*T* (°C)	Time (h)	Yield of **3aa** (%)[c]	Yield of **4aa** (%)[c]
1	2:1	3:1	20	20	65 (30)	0
2	2:1	3:1	30	20	90	0
3	2:1	3:1	50	15	78	9
4	2:1	3:1	70	10	62	24
5	2:1	3:1	100	4	0	80
6	2:1	5:1	100	4	0	75
7	2:1	5:2	100	4	0	82
8	1:1	3:1	30	20	90	0
9	1:1	3:2	30	20	91	0

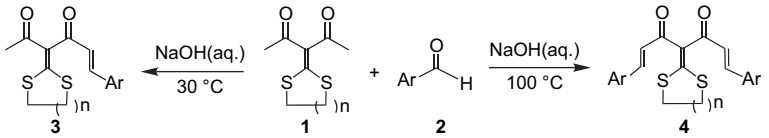
[a] Molar ratio for **2a**:**1a**.
[b] Molar ratio for NaOH:**1a**.
[c] Isolated yields, the value in bracket is recovery of **1a**.

Under the identical conditions as described in Table 1, entry 9, a range of reactions were performed on α,α-diacetyl ketene-(*S*,*S*)-acetals **1** with a variety of aromatic aldehydes **2**. Some of the results are summarized in Table 2 (entries 1–16). It is observed that all the reactions of aldehydes bearing electron-donating groups proceed smoothly under the mild basic conditions to afford the corresponding mono-condensed products **3aa**–**3bh** in high yields. It is noteworthy that these reactions are associated with very simple separation processes. In all cases, the product is a solid and deposits from the reaction system once formed. After the solid is collected, filtered and washed with water, the almost pure product is obtained. If necessary, the product can be easily purified further by flash chromatography (silica gel, diethyl ether–petroleum ether=1:4). However, the reaction of aldehyde **2i** bearing electron-withdrawing nitro group proceeded with difficulty since most of the substrates were not consumed even after a prolonged reaction time (entry 17, Table 2). In this case purification of the product had to be carried out by chromatography over silica gel.

Alternatively, a range of selected aldehydes **2** were subjected to the aldol condensation with compounds **1** under the identical conditions as described in Table 1, entry 7. Some of the results are also presented in Table 2 (entries 18–23). Within a short time, 4–5 h, all the reactions were complete affording the corresponding double condensed products **4aa**–**4af** in high yields. The results indicate that the mono-condensed products **3** can further react with aldehydes at high temperature, which suggests that compounds **3** might react with a second (different) aldehyde to generate unsymmetric double condensed α,α-dialkenoyl ketene-(*S*,*S*)-acetals **5** with different α-alkenoyl groups. This will enrich the versatility of the substituent patterns and make such intermediates even more useful, especially in library synthesis.

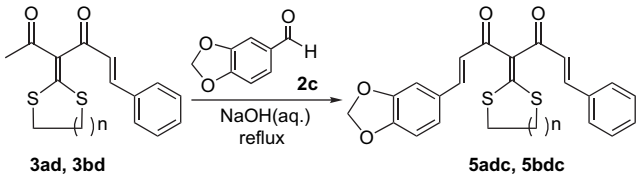
With many mono-condensed products **3** in hand, we next explored the possible transformations of these functionalities to prepare the unsymmetric double condensed α-alkenoyl ketene-(*S*,*S*)-acetals. Thus, two more experiments were carried out (Scheme 1). In one case, when **3ad** and benzo[*d*][1,3]-dioxole-5-carbaldehyde **2c** were subjected to the same aldol condensation under reflux temperature for 2 h, workup of the reaction mixture furnished a yellow product in 87% yield, which was characterized as (1*E*,6*E*)-1-(benzo[*d*][1,3]dioxol-5-yl)-4-(1,3-dithiolan-2-ylidene)-7-phenylhepta-1,6-diene-3,5-dione **5adc** on the basis of its spectral and analytical data. In another case, the reaction was performed on **3bd** and **2c** at reflux temperature for 2.5 h to give a yellow product, characterized as (1*E*,6*E*)-1-(benzo[*d*][1,3]dioxol-5-yl)-4-(1,3-dithian-2-ylidene)-7-phenylhepta-1,6-diene-3,5-dione **5bdc**, in 86% yield.

Table 2. The aldol condensation of α,α-diacetyl ketene-(*S*,*S*)-acetals **1a** and **1b** with aromatic aldehydes **2** in aqueous NaOH



Entry	Substrate **1**	*n*	Substrate **2**	Ar	*T* (°C)	Time (h)	Product **3** or **4**	Yield (%)[a]	Mp (°C)
1	**1a**	1	**2a**	4-MeOPh	30	20	**3aa**	91	156–158
2	**1b**	2	**2a**	4-MeOPh	30	20	**3ba**	90	138–140
3	**1a**	1	**2b**	4-MePh	30	18	**3ab**	92	114–116
4	**1b**	2	**2b**	4-MePh	30	19	**3bb**	93	119–121
5	**1a**	1	**2c**	3,4-OCH_2OPh	30	16	**3ac**	94	130–132
6	**1b**	2	**2c**	3,4-OCH_2OPh	30	17	**3bc**	92	141–142
7	**1a**	1	**2d**	Ph	30	21	**3ad**	92	108–109
8	**1b**	2	**2d**	Ph	30	22	**3bd**	90	116–118
9	**1a**	1	**2e**	PhCH=CH	30	24	**3ae**	86	118–120
10	**1b**	2	**2e**	PhCH=CH	30	24	**3be**	87	109–110
11	**1a**	1	**2f**	4-ClPh	30	23	**3af**	89	152–153
12	**1b**	2	**2f**	4-ClPh	30	24	**3bf**	90	135–137
13	**1a**	1	**2g**	4-NMe_2Ph	30	20	**3ag**	95	172–174
14	**1b**	2	**2g**	4-NMe_2Ph	30	21	**3bg**	93	129–131
15	**1a**	1	**2h**	2-Thioenyl	30	22	**3ah**	88	90–92
16	**1b**	2	**2h**	2-Thioenyl	30	23	**3bh**	91	101–103
17	**1a**	1	**2i**	4-NO_2Ph	30	48	**3ai**	24 (63)[b]	163–165
18	**1a**	1	**2a**	4-MeOPh	100	4	**4aa**	82	104–106
19	**1b**	2	**2a**	4-MeOPh	100	5	**4ba**	83	112–114
20	**1a**	1	**2b**	4-MePh	100	4	**4ab**	85	140–141
21	**1b**	2	**2b**	4-MePh	100	4	**4bb**	86	118–120
22	**1a**	1	**2d**	Ph	100	4	**4ad**	88	130–132
23	**1a**	1	**2f**	4-ClPh	100	4	**4af**	89	120–122

[a] Isolated yields for **3** and **4**.
[b] The value in bracket is recovery of **2i**.



Scheme 1. The reactions of benzo[*d*][1,3]dioxole-5-carbaldehyde **2c** with **3ad/3bd**.

3. Conclusion

In summary, we present here a facile, clean and practical protocol for the synthesis of α-alkenoyl ketene-(*S*,*S*)-acetals of types **3–5** via the aldol condensation of α,α-diacetyl ketene-(*S*,*S*)-acetals **1a** and **1b** with aromatic aldehydes **2** in the presence of NaOH in water. The simplicity of execution, mild conditions, high yields, ready availability of substrates and broad range of potential synthetic utility of the products, especially in relation to recent environmental concerns, make the protocol more attractive for academic research and practical applications. The scope of the aldol condensation and synthetic application of these intermediates of types **3–5** are under investigation in our laboratory.

4. Experimental

4.1. General

All reagents were purchased from commercial sources and used without treatment, unless otherwise indicated. The products were purified by column chromatography over silica gel. ^{1}H NMR and ^{13}C NMR spectra were recorded at 500 MHz and 125 MHz, respectively, with TMS as internal standard. IR spectra (KBr) were recorded on an FTIR spectrophotometer in the range of 400–4000 cm^{-1}.

4.2. Typical procedure

Preparation of α-alkenoyl ketene-(*S*,*S*)-acetal **3aa**, via the aldol condensation reactions of α,α-diacyl ketene-(*S*,*S*)-acetal **1a** with aldehyde **2a**, is described as an example: to a 25 mL flask containing NaOH (3.0 mmol) in 10 mL water were added **1a** (2.0 mmol) and **2a** (2.0 mmol) under stirring. The mixture was stirred at 30 °C for about 20 h when the reaction was complete as indicated by TLC. The crude product was collected by filtration and washed with water. Further purification was carried out by flash chromatography over silica gel (eluent: diethyl ether–petroleum ether=1:4) to give pure product **3aa** as a yellowish solid (yield: 91%).

4.3. Selected data for compounds 3aa–3bh, 4aa–4af, 5adc and 5bdc

4.3.1. (*E*)-3-(1,3-Dithiolan-2-ylidene)-6-(4-methoxyphenyl)hex-5-ene-2,4-dione (3aa). Yellowish solid, mp 114–116 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.32 (s, 3H), 3.32–3.40 (m, 4H), 3.85 (s, 3H), 6.82 (d, 1H, *J*=16 Hz), 6.92 (d, 2H, *J*=8 Hz), 7.52 (d, 2H, *J*=8 Hz), 7.54 (d, 1H, *J*=16 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=29.6, 37.0, 38.1, 55.7, 114.8, 124.3, 127.3, 127.9, 130.6, 145.4, 162.2, 172.2, 192.4, 193.6. IR (KBr, cm^{-1}): 2927, 2920, 1603, 1420, 1264, 1174, 1152, 1021, 870. Anal. Calcd for $C_{16}H_{16}O_3S_2$: C, 59.97; H, 5.03. Found: C, 60.06; H, 5.05.

4.3.2. (*E*)-3-(1,3-Dithian-2-ylidene)-6-(4-methoxyphenyl)hex-5-ene-2,4-dione (3ab). Yellowish solid, mp 119–121 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.21 (s, 3H), 2.19–2.27 (m, 2H), 2.92 (m, 4H), 3.84 (s, 3H), 6.75 (d, 1H, *J*=16 Hz), 6.91 (d, 2H, *J*=8 Hz), 7.48 (d, 1H, *J*=16 Hz), 7.50 (d, 2H, *J*=8 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=24.4, 29.1, 29.7, 29.8, 55.7, 114.8, 125.2, 127.2, 130.7, 135.8, 145.7, 162.2, 164.7, 193.3, 193.5. IR (KBr, cm^{-1}): 3420, 2936, 1630, 1602, 1570, 1511, 1472, 1420, 1250, 1174, 1021. Anal. Calcd for $C_{17}H_{18}O_3S_2$: C, 61.05; H, 5.42. Found: C, 60.95; H, 5.45.

4.3.3. (*E*)-3-(1,3-Dithiolan-2-ylidene)-6-*p*-tolylhex-5-ene-2,4-dione (3ba). Yellowish solid, mp 156–158 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.33 (s, 3H), 2.39 (s, 3H), 3.33–3.39 (m, 4H), 6.90 (d, 1H, *J*=16 Hz), 7.22 (d, 2H, *J*=8 Hz), 7.46 (d, 2H, *J*=8 Hz), 7.56 (d, 1H, *J*=16 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=21.8, 29.8, 37.0, 38.0, 125.6, 127.9, 128.8, 130.0, 131.9, 141.8, 145.4, 172.9, 192.1, 193.7. IR (KBr, cm^{-1}): 1626, 1582, 1565, 1418, 1323, 1245, 1178, 811. Anal. Calcd for $C_{16}H_{16}O_2S_2$: C, 63.13; H, 5.30. Found: C, 63.29; H, 5.34.

4.3.4. (*E*)-3-(1,3-Dithian-2-ylidene)-6-*p*-tolylhex-5-ene-2,4-dione (3bb). Yellowish solid, mp 138–140 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.21 (s, 3H), 2.22–2.26 (m, 2H), 2.38 (s, 3H), 2.92–2.96 (m, 4H), 6.84 (d, 1H, *J*=16 Hz), 7.21 (d, 2H, *J*=8 Hz), 7.46 (d, 2H, *J*=8 Hz), 7.50 (d, 1H, *J*=16 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=21.4, 24.1, 28.8, 29.3, 29.5, 126.2, 128.5, 129.7, 131.6, 135.5, 141.5, 145.4, 192.9. IR (KBr, cm^{-1}): 3420, 2925, 1638, 1587, 1564, 1455, 1421, 1322, 1244, 1158, 980. Anal. Calcd for $C_{17}H_{18}O_2S_2$: C, 64.12; H, 5.70. Found: C, 64.32; H, 5.74.

4.3.5. (*E*)-6-(Benzo[*d*][1,3]dioxol-5-yl)-3-(1,3-dithiolan-2-ylidene)hex-5-ene-2,4-dione (3ac). Yellowish solid, mp 130–132 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.32 (s, 3H), 3.34–3.38 (m, 4H), 6.03 (s, 2H), 6.77 (d, 1H, *J*=16 Hz), 6.83 (d, 1H, *J*=8 Hz), 7.05 (d, 1H, *J*=8 Hz), 7.07 (s, 1H), 7.50 (d, 1H, *J*=16 Hz) .^{13}C NMR ($CDCl_3$, 125 MHz): δ= 29.3, 36.7, 37.7, 101.6, 106.6, 108.6, 124.3, 125.3, 127.7, 128.8, 144.8, 148.4, 150.1, 172.4, 191.6, 193.3. IR (KBr, cm^{-1}): 3853, 3734, 1576, 1558, 1500, 1489, 1257, 1226, 1034. Anal. Calcd for $C_{16}H_{14}O_4S_2$: C, 57.47; H, 4.22. Found: C, 57.59; H, 4.26.

4.3.6. (*E*)-6-(Benzo[*d*][1,3]dioxol-5-yl)-3-(1,3-dithian-2-ylidene)hex-5-ene-2,4-dione (3bc). Yellowish solid, mp 141–143 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.20 (s, 3H), 2.21–2.25 (m, 2H), 2.91–2.95 (m, 4H), 6.02 (s, 2H), 6.69 (d, 1H, *J*=16 Hz), 6.82 (d, 1H, *J*=8 Hz), 7.02 (d, 1H, *J*=8 Hz), 7.06 (s, 1H), 7.43 (d, 1H, *J*=16 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=24.1, 28.8, 29.4, 29.5, 101.6, 106.6, 108.6, 125.2, 125.4, 128.7, 135.6, 145.1, 148.4, 150.1, 164.6, 192.7, 193.0. IR (KBr, cm^{-1}): 3446, 1623, 1502, 1480, 1449, 1358, 1253, 1214, 1034, 976. Anal. Calcd for $C_{17}H_{16}O_4S_2$: C, 58.60; H, 4.63. Found: C, 58.63; H, 4.61.

4.3.7. (*E*)-3-(1,3-Dithiolan-2-ylidene)-6-phenylhex-5-ene-2,4-dione (3ad). Yellowish solid, mp 108–110 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.33 (s, 3H), 3.33–3.39 (m, 4H), 6.95 (d, 1H, *J*=16 Hz), 7.39–7.41 (m, 3H), 7.50 (d, 2H, *J*=8 Hz), 7.58 (d, 1H, *J*=16 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=29.8, 37.1, 38.0, 126.5, 128.6, 129.2, 131.1, 134.7, 144.1, 145.1, 173.8, 191.8, 193.7. IR (KBr, cm^{-1}): 3425, 3058, 2922, 1629, 1583, 1572, 1448, 1407, 1331, 1283, 1245, 1178, 982. Anal. Calcd for $C_{15}H_{14}O_2S_2$: C, 62.04; H, 4.86. Found: C, 61.93; H, 4.85.

4.3.8. (*E*)-3-(1,3-Dithian-2-ylidene)-6-phenylhex-5-ene-2,4-dione (3bd). Yellowish solid, mp 116–118 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.23 (s, 3H), 2.25–2.29 (m, 2H), 2.94 (m, 4H), 6.89 (d, 1H, *J*=16 Hz), 7.40–7.42 (m, 3H), 7.53 (d, 1H, *J*=16 Hz), 7.56 (m, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=24.5, 29.2, 29.7, 29.9, 127.4, 128.8, 129.3, 131.2, 134.6, 135.8, 145.5, 165.5, 193.2, 193.3. IR (KBr, cm^{-1}): 1640, 1625, 1571, 1452, 1422, 1325, 1242, 1159, 977, 740. Anal. Calcd for $C_{16}H_{16}O_2S_2$: C, 63.13; H, 5.30. Found: C, 63.33; H, 5.31.

4.3.9. (5*E*,7*E*)-3-(1,3-Dithiolan-2-ylidene)-8-phenylocta-5,7-diene-2,4-dione (3ae). Yellowish solid, mp 118–120 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.32 (s, 3H), 3.34–3.38 (m, 4H), 6.49 (d, 1H, *J*=16 Hz), 6.96 (d, 1H, *J*= 8 Hz), 6.98 (s, 1H), 7.37–7.39 (m, 4H), 7.49 (d, 2H, *J*= 8 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=29.8, 37.1, 38.0, 126.8, 127.7, 127.9, 129.1, 129.7, 129.8, 136.1, 142.6, 145.4, 173.1, 191.9, 193.8. IR (KBr, cm^{-1}): 3446, 1716, 1683, 1615, 1509, 1393, 1282, 1251, 1217, 1002. Anal. Calcd for $C_{17}H_{16}O_2S_2$: C, 64.53; H, 5.10. Found: C, 64.54; H, 5.13.

4.3.10. (5*E*,7*E*)-3-(1,3-Dithian-2-ylidene)-8-phenylocta-5,7-diene-2,4-dione (3be). Yellowish solid, mp 109–110 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.21 (s, 3H), 2.22–2.26 (m, 2H), 2.93 (m, 4H), 6.41 (d, 1H, *J*=16 Hz), 6.95 (d, 2H, *J*=8 Hz), 7.33–7.35 (m, 4H), 7.48 (d, 2H, *J*=8 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=24.4, 29.1, 29.7, 29.9, 126.8, 127.7, 129.1, 129.7, 130.6, 135.8, 136.1, 142.6, 145.7, 165.0, 193.1, 193.4. IR (KBr, cm^{-1}): 1632, 1617, 1476. Anal. Calcd for $C_{18}H_{18}O_2S_2$: C, 65.42; H, 5.49. Found: C, 65.53; H, 5.51.

4.3.11. (*E*)-6-(4-Chlorophenyl)-3-(1,3-dithiolan-2-ylidene)-hex-5-ene-2,4-dione (3af). Yellowish solid, mp 152–154 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.33 (s, 3H), 3.37–3.39 (m, 4H), 6.92 (d, 1H, *J*=16 Hz), 7.38 (d, 2H, *J*=8 Hz), 7.49 (d, 2H, *J*=8 Hz), 7.54 (d, 1H, *J*=16 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=29.9, 37.1, 38.0, 126.9, 128.0, 129.6, 129.9, 133.2, 137.0, 143.4, 174.1, 191.2, 193.8. IR (KBr, cm^{-1}): 1623, 1572, 1490, 1405, 1379, 1182, 1087. Anal. Calcd for $C_{15}H_{13}ClO_2S_2$: C, 55.46; H, 4.03. Found: C, 55.62; H, 4.14.

4.3.12. (*E*)-6-(4-Chlorophenyl)-3-(1,3-dithian-2-ylidene)-hex-5-ene-2,4-dione (3bf). Yellowish solid, mp 135–137 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.22 (s, 3H), 2.26–2.30 (m, 2H), 2.93–2.95 (m, 4H), 6.84 (d, 1H, *J*=16 Hz), 7.37 (d, 2H, *J*=8 Hz), 7.47 (d, 2H, *J*=8 Hz), 7.49 (d, 1H, *J*=16 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=24.1, 28.9, 29.3, 29.6, 127.3, 129.2, 129.5, 132.8, 135.5, 136.7, 143.3, 165.2, 191.9, 193.2. IR (KBr, cm^{-1}): 1652, 1643, 1587, 1458, 1402, 1243, 1160, 1090. Anal. Calcd for $C_{16}H_{15}ClO_2S_2$: C, 56.71; H, 4.46. Found: C, 56.54; H, 4.50.

4.3.13. (*E*)-6-(4-(Dimethylamino)phenyl)-3-(1,3-dithiolan-2-ylidene)hex-5-ene-2,4-dione (3ag). Yellowish solid, mp 172–174 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.30

(s, 3H), 3.04 (s, 6H), 3.36–3.40 (m, 4H), 6.67 (d, 2H, J=8 Hz), 7.73 (d, 1H, J=16 Hz), 7.46 (d, 2H, J=8 Hz), 7.50 (d, 1H, J=16 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=28.9, 36.5, 37.8, 39.9, 111.8, 121.3, 122.0, 127.9, 130.5, 146.6, 152.2, 169.7, 192.7, 193.0. IR (KBr, cm^{-1}): 1624, 1560, 1525, 1435, 1244, 1165, 1053. Anal. Calcd for $C_{17}H_{19}NO_2S_2$: C, 61.23; H, 5.74; N, 4.20. Found: C, 61.41; H, 5.79; N, 4.23.

4.3.14. (*E*)-6-(4-(Dimethylamino)phenyl)-3-(1,3-dithian-2-ylidene)hex-5-ene-2,4-dione (3bg). Yellowish solid, mp 129–131 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.20 (s, 3H), 2.21–2.25 (m, 2H), 2.88–2.92 (m, 4H), 3.04 (s, 6H), 6.66 (d, 2H, J=8 Hz), 6.69 (d, 1H, J=16 Hz), 7.45 (d, 1H, J=16 Hz), 7.46 (d, 2H, J=8 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=24.3, 29.0, 29.6, 40.4, 112.0, 122.0, 122.5, 130.9, 136.1, 147.4, 152.5, 163.5, 193.2, 194.1. IR (KBr, cm^{-1}): 3446, 1645, 1589, 1525, 1463, 1182, 1104, 978. Anal. Calcd for $C_{18}H_{21}NO_2S_2$: C, 62.21; H, 6.09; N, 4.03. Found: C, 62.34; H, 6.12; N, 4.11.

4.3.15. (*E*)-3-(1,3-Dithiolan-2-ylidene)-6-(thiophen-2-yl)-hex-5-ene-2,4-dione (3ah). Yellowish solid, mp 90–92 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.33 (s, 3H), 3.34–3.38 (m, 4H), 6.73 (d, 1H, J=16 Hz), 7.08 (dd, 1H, J_1=5 Hz, J_2=4 Hz), 7.32 (d, 1H, J=4 Hz), 7.44 (d, 1H, J=5 Hz), 7.72 (d, 1H, J=16 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=29.7, 37.1, 38.1, 125.4, 127.9, 128.7, 129.8, 132.5, 137.6, 140.1, 173.3, 191.3, 193.6. IR (KBr, cm^{-1}): 3430, 1626, 1575, 1452, 1419, 1278, 1243, 1202, 1044, 718. Anal. Calcd for $C_{13}H_{12}O_2S_3$: C, 52.67; H, 4.08. Found: C, 52.75; H, 4.13.

4.3.16. (*E*)-3-(1,3-Dithian-2-ylidene)-6-(thiophen-2-yl)-hex-5-ene-2,4-dione (3bh). Yellowish solid, mp 101–103 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.22 (s, 3H), 2.23–2.27 (m, 2H), 2.93–2.95 (m, 4H), 6.66 (d, 1H, J=16 Hz), 7.08 (dd, 1H, J_1=5 Hz, J_2=4 Hz), 7.31 (d, 1H, J=4 Hz), 7.45 (d, 1H, J=5 Hz), 7.65 (d, 1H, J=16 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=24.4, 29.2, 29.7, 29.8, 126.2, 128.7, 129.9, 132.5, 135.7, 137.9, 139.9, 165.4, 192.6, 193.3. IR (KBr, cm^{-1}): 3072, 2921, 1645, 1634, 1578, 1473, 1418, 1277, 1219, 1049, 986, 855. Anal. Calcd for $C_{14}H_{14}O_2S_3$: C, 54.16; H, 4.55. Found: C, 54.29; H, 4.51.

4.3.17. (*E*)-3-(1,3-Dithiolan-2-ylidene)-6-(4-nitrophenyl)-hex-5-ene-2,4-dione (3ai). Yellowish solid, mp 163–165 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.38 (s, 3H), 3.38–3.41 (m, 4H), 7.08 (d, 1H, J=16 Hz), 7.63 (d, 1H, J=16 Hz), 7.70 (d, 2H, J=8.5 Hz), 8.26 (d, 2H, J=8.5 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=30.1, 37.2, 37.9, 124.8, 127.9, 129.1, 129.9, 140.9, 141.0, 148.8, 171.9, 189.7, 194.0. IR (KBr, cm^{-1}): 1632, 1577, 1562, 1407, 1348, 1265, 1187, 837. Anal. Calcd for $C_{15}H_{13}NO_4S_2$: C, 53.72; H, 3.91; N, 4.18. Found: C, 53.41; H, 4.03; N, 4.02.

4.3.18. (1*E*,6*E*)-4-(1,3-Dithiolan-2-ylidene)-1,7-bis(4-methoxyphenyl)hepta-1,6-diene-3,5-dione (4aa). Yellow solid, mp 140–142 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=3.38 (s, 4H), 3.81 (s, 6H), 6.85 (d, 4H, J=8 Hz), 6.88 (d, 2H, J=16 Hz), 7.45 (d, 4H, J=8 Hz), 7.68 (d, 2H, J=16 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=37.5, 55.6, 113.6, 114.6, 123.9, 127.7, 129.3, 130.5, 143.9, 161.9, 188.3. IR (KBr, cm^{-1}): 1627, 1586, 1569, 1511, 1457, 1422, 1255, 1172, 1027, 828. Anal. Calcd for $C_{24}H_{22}O_4S_2$: C, 65.73; H, 5.06. Found: C, 65.87; H, 5.10.

4.3.19. (1*E*,6*E*)-4-(1,3-Dithian-2-ylidene)-1,7-bis(4-methoxyphenyl)hepta-1,6-diene-3,5-dione (4ba). Yellow solid, mp 118–120 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.25–2.29 (m, 2H), 2.94–2.96 (m, 4H), 3.80 (s, 6H), 6.75 (d, 2H, J=16 Hz), 6.85 (d, 4H, J=8 Hz), 7.45 (d, 4H, J=8 Hz), 7.60 (d, 2H, J=16 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=24.8, 29.8, 55.7, 114.6, 124.2, 127.6, 130.6, 136.4, 144.7, 161.9, 167.8, 188.7. IR (KBr, cm^{-1}): 3626, 2928, 2837, 1772, 1563, 1509, 1383, 1250, 1150, 1028, 829. Anal. Calcd for $C_{25}H_{24}O_4S_2$: C, 66.34; H, 5.34. Found: C, 66.49; H, 5.31.

4.3.20. (1*E*,6*E*)-4-(1,3-Dithiolan-2-ylidene)-1,7-di-*p*-tolylhepta-1,6-diene-3,5-dione (4ab). Yellow solid, mp 101–103 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.38 (s, 3H), 3.29 (d, 2H), 3.70 (s, 2H), 6.78–6.79 (d, 2H, J=16 Hz), 7.19 (d, 4H), 7.43 (s, 4H), 7.75 (d, 2H, J=16 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=21.8, 43.7, 43.9, 118.9, 119.9, 128.8, 129.9, 132.4, 141.3, 143.0, 179.8, 196.3. IR (KBr, cm^{-1}): 1624, 1586, 1457, 1422, 1255, 1176, 1027, 829. Anal. Calcd for $C_{24}H_{22}O_2S_2$: C, 70.90; H, 5.45. Found: C, 70.92; H, 5.49.

4.3.21. (1*E*,6*E*)-4-(1,3-Dithian-2-ylidene)-1,7-di-*p*-tolylhepta-1,6-diene-3,5-dione (4bb). Yellow solid, mp 112–114 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.27–2.29 (m, 2H), 2.34 (s, 3H), 2.94–2.96 (m, 4H), 6.83 (d, 2H, J=16 Hz), 7.14 (d, 2H, J=8 Hz), 7.39 (d, 4H, J=8 Hz), 7.62 (d, 2H, J=16 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=21.8, 24.8, 29.8, 125.4, 128.8, 129.9, 132.1, 136.2, 141.4, 144.9, 168.7, 188.6. IR (KBr, cm^{-1}): 2917, 1632, 1586, 1420, 1298, 1151, 928, 815. Anal. Calcd for $C_{25}H_{24}O_2S_2$: C, 71.39; H, 5.75. Found: C, 71.56; H, 5.79.

4.3.22. (1*E*,6*E*)-4-(1,3-Dithiolan-2-ylidene)-1,7-diphenylhepta-1,6-diene-3,5-dione (4ad). Yellow solid, mp 130–132 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=3.37 (s, 4H), 6.93 (d, 2H, J=16 Hz), 7.27–7.30 (m, 2H), 7.29 (d, 4H, J=8 Hz), 7.38 (d, 4H, J=8 Hz), 7.62 (d, 2H, J=16 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=38.0, 122.9, 123.4, 126.4, 128.0, 128.7, 135.2, 152.7, 183.8, 200.1. IR (KBr, cm^{-1}): 2920, 1637, 1539, 1390, 1211, 1171, 987, 929, 811. Anal. Calcd for $C_{22}H_{18}O_2S_2$: C, 69.81; H, 4.79. Found: C, 69.70; H, 4.68.

4.3.23. (1*E*,6*E*)-1,7-Bis(4-chlorophenyl)-4-(1,3-dithiolan-2-ylidene)hepta-1,6-diene-3,5-dione (4af). Yellow solid, mp 120–122 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=3.41 (s, 4H), 6.95 (d, 2H, J=16 Hz), 7.30 (d, 4H, J=8 Hz), 7.42 (d, 4H, J=8 Hz), 7.65 (d, 2H, J=16 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=37.6, 126.5, 128.5, 129.5, 129.7, 133.4, 136.7, 142.5, 187.6, 201.3. IR (KBr, cm^{-1}): 2917, 1641, 1577, 1396, 1290, 1173, 930, 809. Anal. Calcd for $C_{22}H_{16}Cl_2O_2S_2$: C, 59.06; H, 3.60. Found: C, 58.98; H, 3.51.

4.3.24. (1*E*,6*E*)-1-(Benzo[*d*][1,3]dioxol-5-yl)-4-(1,3-dithiolan-2-ylidene)-7-phenylhepta-1,6-diene-3,5-dione (5adc). Yellow solid, mp 166–168 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=3.40 (s, 4H), 5.97 (s, 2H), 6.77 (d, 1H, J=8 Hz), 6.83 (d, 1H, J=16 Hz), 7.00 (d, 1H, J=16 Hz),

7.01 (d, 1H, J=8 Hz), 7.34 (d, 1H, J=8 Hz), 7.50 (d, 2H, J=8 Hz), 7.63 (d, 1H, J=16 Hz), 7.70 (d, 1H, J=16 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=37.5, 37.6, 101.8, 106.9, 108.9, 124.3, 125.4, 126.0, 128.2, 128.7, 129.2, 129.4, 130.7, 134.9, 143.9, 144.0, 148.6, 150.2, 187.9, 188.3. IR (KBr, cm^{-1}): 3734, 1635, 1590, 1559, 1447, 1251, 1034, 725. Anal. Calcd for $C_{23}H_{18}O_4S_2$: C, 65.38; H, 4.29. Found: C, 65.49; H, 4.25.

4.3.25. (1*E*,6*E*)-1-(Benzo[*d*][1,3]dioxol-5-yl)-4-(1,3-dithian-2-ylidene)-7-phenylhepta-1,6-diene-3,5-dione (5bdc). Yellow solid, mp 148–150 °C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ=2.25–2.29 (m, 2H), 2.94–2.96 (m, 4H), 5.98 (s, 2H), 6.77 (d, 1H, J=8 Hz), 6.84 (d, 1H, J=16 Hz), 7.01 (d, 1H, J=16 Hz), 7.02 (d, 1H, J=8 Hz), 7.51 (d, 2H, J=8 Hz), 7.64 (d, 1H, J=16 Hz), 7.71 (d, 1H, J=16 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ=24.8, 29.7, 29.8, 101.8, 106.9, 108.9, 124.3, 125.4, 126.0, 128.2, 128.7, 129.2, 129.5, 130.7, 143.9, 144.0, 148.6, 150.2, 187.9, 188.3. IR (KBr, cm^{-1}): 3731, 3643, 2928, 1753, 1601, 1559, 1250, 1029, 721. Anal. Calcd for $C_{24}H_{20}O_4S_2$: C, 66.03; H, 4.62. Found: C, 65.99; H, 4.58.

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References and notes

1. (a) Rideout, D. C.; Breslow, R. *J. Am. Chem. Soc.* **1980**, *102*, 7816–7817; (b) Breslow, R. *Acc. Chem. Res.* **1991**, *24*, 159–164; (c) Breslow, R. *Acc. Chem. Res.* **2004**, *37*, 471–478.
2. (a) *Aqueous-Phase Organometallic Catalysis. Concepts and Applications*; Cornils, B., Herrmann, W. A., Eds.; Wiley-VCH: Weinheim, 1998; (b) *Organic Synthesis in Water*; Grieco, P. A., Ed.; Thomson Science: Glawsgow, Scotland, 1998; (c) Li, C.-J.; Chan, T.-H. *Organic Reactions in Aqueous Media*; Wiley: New York, NY, 1997; (d) Kobayashi, S.; Manabe, K. *Stimulating Concepts in Chemistry*; Shibasaki, M., Stoddart, J. F., Vogtle, F., Eds.; Wiley-VCH: Weinheim, 2000; (e) *Clean Solvents: Alternative Media for Chemical Reactions and Processing*; Moens, L., Abraham, M., Eds.; ACS Symposium Series 819; American Chemical Society: Washington, DC, 2002.
3. (a) Li, C.-J. *Chem. Rev.* **1993**, *93*, 2023–2035; (b) Genet, J. P.; Savignac, M. *J. Organomet. Chem.* **1999**, *576*, 305–317; (c) Fringuelli, F.; Piermatti, O.; Pizzo, F.; Vaccaro, L. *Eur. J. Org. Chem.* **2001**, 439–452; (d) Kobayashi, S.; Manabe, K. *Acc. Chem. Res.* **2002**, *35*, 209–217; (e) Akiya, N.; Savage, P. E. *Chem. Rev.* **2002**, *102*, 2725–2750; (f) Li, C.-J. *Chem. Rev.* **2005**, *105*, 3095–3165; (g) Lindstrom, U. M. *Chem. Rev.* **2002**, *102*, 2751–2772.
4. (a) Manabe, K.; Mori, Y.; Kobayashi, S. *Synlett* **1999**, 1401–1402; (b) Manabe, K.; Kobayashi, S. *Org. Lett.* **1999**, *1*, 1965–1967; (c) Manabe, K.; Sun, X.-M.; Kobayashi, S. *J. Am. Chem. Soc.* **2001**, *123*, 10101–10102; (d) Kobayashi, S.; Wakabayashi, T. *Tetrahedron Lett.* **1998**, *39*, 5389–5392.
5. (a) Siskin, M.; Katritzky, A. R. *Chem. Rev.* **2001**, *101*, 825–836; (b) Otto, S.; Engberts, J. B. F. N.; Kwak, J. C. T. *J. Am. Chem. Soc.* **1998**, *120*, 9517–9525; (c) Rispens, T.; Engberts, J. B. F. N. *Org. Lett.* **2001**, *3*, 941–943; (d) Fringuelli, F.; Piermatti, O.; Pizzo, F.; Vaccaro, L. *Eur. J. Org. Chem.* **2001**, 439–455.
6. Ouyang, Y.; Dong, D.; Yu, H.; Liang, Y.; Liu, Q. *Adv. Synth. Catal.* **2006**, *348*, 206–210.
7. (a) Liu, Q.; Che, G.; Yu, H.; Liu, Y.; Zhang, J.; Zhang, Q.; Dong, D. *J. Org. Chem.* **2003**, *68*, 9148–9150; (b) Sun, S.; Liu, Y.; Liu, Q.; Zhao, Y.; Dong, D. *Synlett* **2004**, 1731–1734; (c) Dong, D.; Liu, Y.; Zhao, Y.; Qi, Y.; Wang, Z.; Liu, Q. *Synthesis* **2005**, *1*, 85–91; (d) Dong, D.; Ouyang, Y.; Yu, H.; Liu, Q.; Liu, J.; Wang, M.; Zhu, J. *J. Org. Chem.* **2005**, *70*, 4535–4537; (e) Pan, W.; Dong, D.; Sun, S.; Liu, Q. *Synlett* **2006**, 1090–1094.
8. (a) Bi, X.; Dong, D.; Liu, Q.; Pan, W.; Zhao, L.; Li, B. *J. Am. Chem. Soc.* **2005**, *127*, 4578–4579; (b) Dong, D.; Bi, X.; Liu, Q.; Cong, F. *Chem. Commun.* **2005**, 3580–3582; (c) Bi, X.; Dong, D.; Li, Y.; Liu, Q.; Zhang, Q. *J. Org. Chem.* **2005**, *70*, 10886–10889; (d) Zhao, L.; Liang, F.; Bi, X.; Sun, S.; Liu, Q. *J. Org. Chem.* **2006**, *71*, 1094–1098.
9. For reviews on the synthesis and applications of α-oxo ketene-(*S*,*S*)-acetals, see: (a) Dieter, R. K. *Tetrahedron* **1986**, *42*, 3029–3096; (b) Tominaga, Y. *J. Heterocycl. Chem.* **1989**, *26*, 1167–1204; (c) Junjappa, H.; Ila, H.; Asokan, C. V. *Tetrahedron* **1990**, *46*, 5423–5506; (d) Kolb, M. *Synthesis* **1990**, 171–190; (e) Ila, H.; Junjappa, H.; Mohanta, P. K. *Progress in Heterocyclic Chemistry*; Gribble, G. H., Gilchrist, L. T., Eds.; Pergamon: Oxford, 2001; Vol. 13, Chapter 1, pp 1–24.
10. (a) Myrboh, B.; Asokan, C. V.; Ila, H.; Junjappa, H. *Synthesis* **1984**, 50–51; (b) Asokan, C. V.; Ila, H.; Junjappa, H. *Synthesis* **1985**, 163–165; (c) Asokan, C. V.; Balu, M. P.; Ila, H.; Junjappa, H. *Synthesis* **1988**, 727–729.
11. Choi, E. B.; Youn, I. K.; Pak, C. S. *Synthesis* **1991**, 15–18.
12. Joseph, B. K.; Verghese, B.; Sudarsanakumar, C.; Deepa, S.; Viswam, D.; Chandran, P.; Asokan, C. V. *Chem. Commun.* **2002**, 736–737.