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The reaction of selenoaldehydes with 2-methoxyfuran using their generation by retro Diels–Alder reaction

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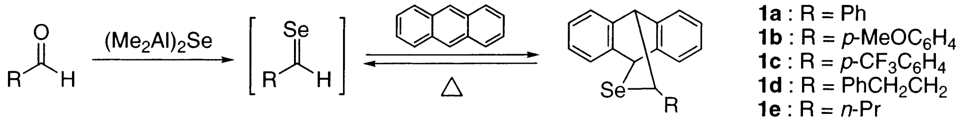
Abstract—Selenoaldehydes, regenerated by thermal retro Diels–Alder reaction of anthracene cycloadducts under neutral conditions, reacted with 2-methoxyfuran to give methyl penta-2,4-dienoates along with the deposition of elemental selenium. In a similar reaction with 2-methoxyfuran using thioaldehyde, thiirane compound was isolated. This suggests the formation of selenirane intermediates in the above reaction. © 2003 Published by Elsevier Science Ltd.

Selenoaldehydes have been generally considered to be highly reactive species as a dienophile for cycloaddition reactions because of long bond length and poor overlap in the carbon–selenium π bond, so they are one of the important intermediates in the synthesis of selenium-containing heterocycles.[1] The interest in their preparation and reactivities has significantly grown in recent years, and several synthetic methods of reactive selenoaldehydes have already been reported.[2] We have also reported an efficient and simple method for the direct conversion of a carbonyl group into a selenocarbonyl group using selenating reagents, $(Me_3Si)_2Se$-BuLi[3] or $(Me_2Al)_2Se$.[4] Selenoaldehydes generated by this method were in situ effectively trapped with conjugated dienes to afford the corresponding cycloadducts via Diels–Alder reaction. Especially, the cycloadducts **1** of selenoaldehydes with anthracene were obtained in good yields as a stable solid in the most substituents R (Scheme 1), and very stable at room temperature in all cases.[5] However, the cycloaddition by this method was inapplicable to 1,3-dienes having oxygen and/or nitrogen atoms because of the coordination of the aluminum atom in the selenating reagent. On the other hand, **1** decomposed quantitatively via thermal retro Diels–Alder reaction to regenerate the corresponding selenoaldehydes under neutral conditions, as shown in Scheme 1.[5,6] Thus **1** can serve as convenient and 'clean' precursors of selenoaldehydes. 1,3-Dienes bearing oxygen atom substituents can be tolerated by this retro Diels–Alder protocol. In this paper we describe the reaction behavior of selenoaldehydes, generated by thermal retro Diels–Alder reaction of **1**, with 2-methoxyfuran[7] which is one of reactive electron-rich dienes and the formation of methyl penta-2,4-dienoates.[8]

The toluene solution of **1a** (R = Ph) and 2-methoxyfuran was heated at 90°C for 3 h to give methyl 5-phenylpenta-2,4-dienoate (**2a**) as a mixture of four geometrical isomers in 88% yield along with the deposition of elemental selenium (Eq. (1)). Our expectation was the formation of Diels–Alder adducts **3a** and/or **4a**. However, the resulting product contained characteristic signals of four olefinic protons and methyl ester in the NMR spectrum. This reaction showed a great dependence on the reaction temperature in the isomer ratio. The results are summarized in Table 1. The reaction at



Scheme 1.

Keywords: selenium and compounds; Diels–Alder reactions; dienoates; seleniranes.

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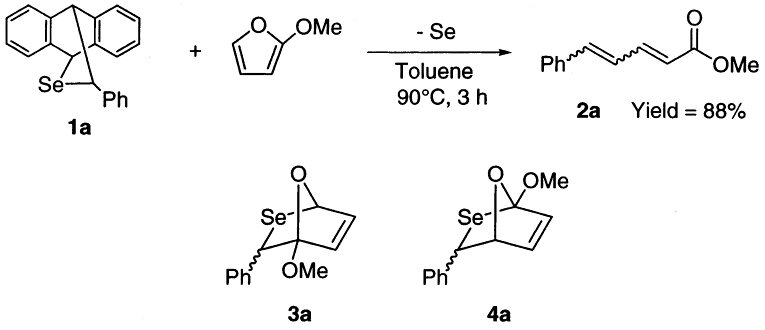
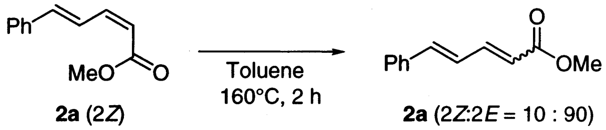


(1)

lower temperatures (70 and 90°C) gave 2*Z* isomers as a major product, whereas those at higher temperatures (140 and 160°C) resulted in the formation of 2*E* isomers as a main product. This dependence on the reaction temperature can be explained by a thermal isomerization of 2*Z* to 2*E*. Actually when the 2*Z*,4*E* isomer of **2a** was heated at 160°C for 2 h in toluene using a sealed stainless steel vessel, the ratio of 2*Z*:2*E* in **2a** after heating was 10:90 (Eq. (2)). Accordingly, the observed isomer ratio of 2*Z*:2*E* at lower temperature is the kinetically controlled one, while the ratio at higher temperature is the thermodynamically controlled one. On the other hand, the geometry of C4–C5 double bond was *E* with a high selectivity at all temperatures.



(2)

Several anthracene cycloadducts (**1**) with aromatic and aliphatic substituents were treated with 2-methoxyfuran in toluene at both 90 and 160°C to afford the corresponding penta-2,4-dienoate derivatives (**2**) in excellent yields in all cases, with similar dependency on the reaction temperature in the isomer ratio. The results are shown in Table 2. Substituent effects on the aromatic ring for the isomer ratio were effectively not observed (entries 1–6). Compound **1** having an aliphatic group

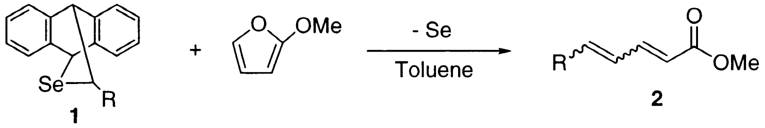
Table 1. Effect of reaction temperature in the treatment of **1a** with 2-methoxyfuran in toluene

Entry	Temp. (°C)	Time (h)	Yield (%)[a]	(2*E*,4*E*):(2*E*,4*Z*):(2*Z*,4*E*):(2*Z*,4*Z*)[b]
1	70	11	84	9:1:80:10
2	90	3	88	11:1:78:10
3	105	3	98	56:2:39:3
4	140	2	77	67:3:28:2
5	160	2	87	88:3:8:1

[a] Isolated yield.

[b] Determined by ^{1}H NMR analysis.

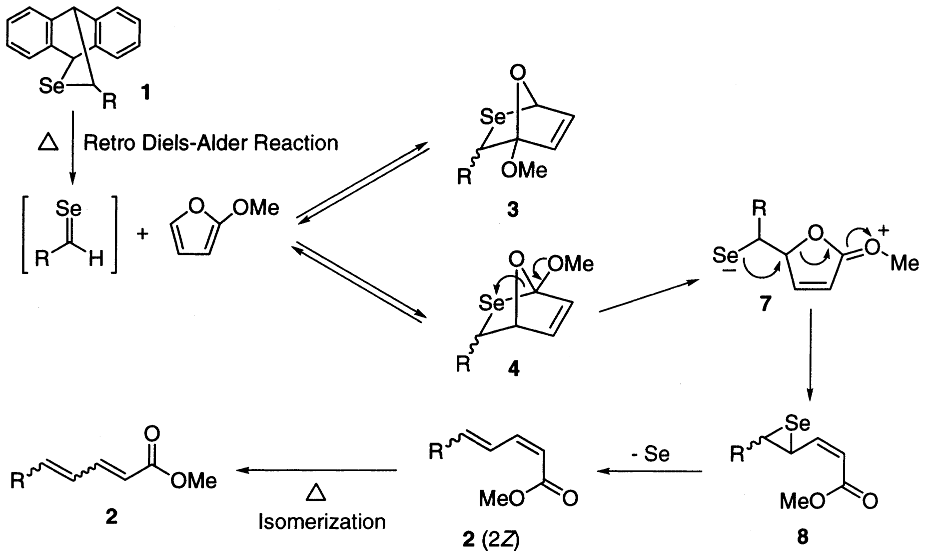
Table 2. Treatment of **1** with 2-methoxyfuran in toluene



Entry	Substrate	R	Temp. (°C)	Time (h)	Product	Yield (%)[a]	(2*E*,4*E*):(2*E*,4*Z*):(2*Z*,4*E*):(2*Z*,4*Z*)[b]
1	**1a**	Ph	90	3	**2a**	88	11:1:78:10
2	**1a**	Ph	160	2	**2a**	87	88:3:8:1
3	**1b**	*p*-$MeOC_6H_4$	90	3	**2b**	91	18:3:67:12
4	**1b**	*p*-$MeOC_6H_4$	160	2	**2b**	98	89:4:6:1
5	**1c**	*p*-$CF_3C_6H_4$	90	3	**2c**	91	18:2:72:8
6	**1c**	*p*-$CF_3C_6H_4$	160	2	**2c**	91	88:2:9:1
7	**1d**	$PhCH_2CH_2$	160	3	**2d**	95	51:10:36:3
8	**1e**	*n*-Pr	160	3	**2e**	65	50:9:39:2

[a] Isolated yield.

[b] Determined by ^{1}H NMR analysis.

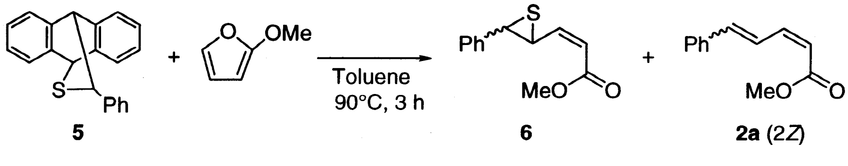


Scheme 2. Possible reaction pathway.

did not undergo retro Diels–Alder reaction at 90°C, but the generation of aliphatic selenoaldehydes from **1** at 160°C was efficient. Thus, the corresponding 2,4-dienoates in the reaction with 2-methoxyfuran were obtained with a slight preference for the 2*E* isomer (entries 7 and 8). In fact, 2*Z*-penta-2,4-dienoates substituted with an aliphatic group at the C5 position isomerized to 2*E* isomers slower than those with an aromatic group in an independent experiment.[9]

We tried to isolate some intermediates in the above reaction or to confirm their formation by the NMR measurements, but failed in our all trials because of the instability of intermediates containing a selenium atom.

Hence we next carried out a similar reaction using sulfur analog. Thus when the thioaldehyde-anthracene cycloadduct **5** was heated with 2-methoxyfuran in toluene at 90°C for 3 h, thiirane (episulfide) compound **6** was isolated as a mixture of *cis* and *trans* isomers together with 2*Z*-penta-2,4-dienoate (Eq. (3)). The geometry of the double bond in **6** was *Z* in both isomers.[10]



(3)

The mechanism for the formation of penta-2,4-dienoates in the reaction of selenoaldehydes with 2-methoxyfuran has not been established yet, but taking into account the above evidence for the formation of thiirane compound in the analogous reaction using thioaldehyde, the corresponding selenirane (episelenide) intermediate[11] is likely involved in the reaction pathway (Scheme 2). At the present stage the most likely pathway may be as follows. The [4+2] cycloaddition reaction of selenoaldehyde, generated via thermal retro Diels–Alder reaction of **1**, with 2-methoxyfuran affords cycloadducts **3** and **4** which would be at equilibrium each other under thermal conditions. Compound **4** having an orthoester structure would be expected to readily undergo C–Se bond cleavage to give the betaine intermediate **7**, followed by the formation of selenirane compound **8** via intramolecular nucleophilic substitution of the selenium anion in **7**. Subsequently, the extrusion of the selenium atom from **8** and thermal isomerization of the resulting 2*Z*-penta-2,4-dienoate yields an isomeric mixture of methyl penta-2,4-dienoate **2**. To confirm the formation of cycloadducts **3** and **4**, we carried out heating of **1** at 80°C in 2-methoxyfuran as a solvent. However, **3** and **4** were not detected in a reaction mixture. Hence there are several other mechanistic possibilities which we cannot rule out. These involve stepwise mechanisms via ionic or diradical intermediates.

In conclusion, we have demonstrated that the reaction of selenoaldehydes, generated from **1** via thermal retro Diels–Alder reaction, with 2-methoxyfuran gives methyl penta-2,4-dienoates in high yields with deposition of elemental selenium. We are currently extending the scope of cycloadditions of selenoaldehydes with heterodienes involving oxygen and/or nitrogen atoms via this thermal retro Diels–Alder protocol using **1**. The results of our findings will be reported in due course.

Acknowledgements

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9. When a 60:40 (2*Z*:2*E*) mixture of **2d** was heated at 160°C for 3 h in toluene, the ratio of 2*Z*:2*E* in **2d** after heating was 36:64. An additional 5 h heating at 160°C led to the ratio of 14:86.
10. Thiirane **6**-*trans* (major): ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.77 (s, 3H, OCH_3), 3.79 (d, 1H, PhC*H*S, $J=4.9$ Hz), 5.05 (dd, 1H, C*H*S, $J=4.9$, 10.1 Hz), 5.74 (d, 1H, $=CHCO_2$, $J=11.3$ Hz), 5.77 (dd, 1H, C*H*=, $J=10.1$, 11.3 Hz), 7.26–7.41 (m, 5H, Ph). Thiirane **6**-*cis* (minor): ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.76 (s, 3H, OCH_3), 4.41 (d, 1H, PhC*H*S, $J=6.7$ Hz), 5.13 (dd, 1H, C*H*S, $J=6.7$, 10.4 Hz), 5.49 (dd, 1H, C*H*=, $J=10.4$, 11.3 Hz), 5.80 (d, 1H, $=CHCO_2$, $J=11.3$ Hz), 7.26–7.41 (m, 5H, Ph).
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