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Journal of Organometallic Chemistry 485 (1995) 55–62

Journal of Organometallic Chemistry

Syntheses of cyclohexenone derivatives by the ruthenium complex-catalysed reactions of allylic compounds with β-keto esters

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Received 2 March 1994; in revised form 11 May 1994

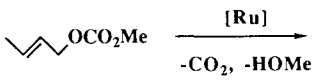
Abstract

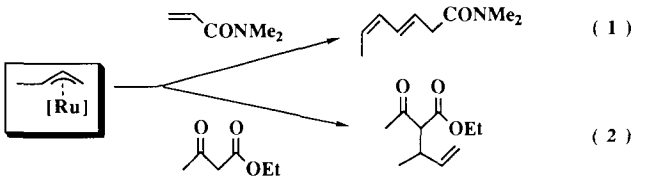
Allylic compounds such as allyl alcohols and allylamines react with two equivalent moles of acetoacetates in the presence of a catalytic amount of Ru(cod)(cot) (cod = cycloocta-1,5-diene; cot = cycloocta-1,3,5-triene) at 100°C for 5 h to give cyclohexenone derivatives in high yields.

Keywords: Ruthenium; Allyl; Cyclohexane; Catalyst; Alcohol; Amine

1. Introduction

Recently, ruthenium complex-catalysed reactions of allylic compounds have received much attention [1]. We have reported the first example of the ruthenium-catalysed coupling of allylic carbonates with acrylic compounds [2] (Eq. (1)), and allylic alkylation of carbonucleophiles with allylic carbonates, to give mono- or diallylated carbonucleophiles selectively in high yields (Eq. (2)) [3]. Ruthenium-catalysed reactions of

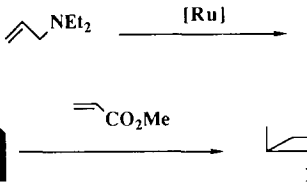




(1)

(2)

allylic carbonates, which proceed via π-allylruthenium intermediates, were mainly discussed. Furthermore, we have also studied ruthenium complex-catalysed reactions using other allylic compounds besides allylic carbonates. We also found that allylamine reacts with acrylic compounds in the presence of a catalytic amount of Ru(cod)(cot) (cod = cycloocta-1,5-diene; cot = cycloocta-1,3,5-triene) to give cyclobutane-β-amino acid derivatives in high yields [4] (Eq. (3)). In this case, the reaction proceeds *via* catalytic isomerization of



(3)

allylamines to the corresponding enamines followed by thermal cycloaddition of the enamines with acrylic compounds, not *via* a π-allylruthenium intermediate as in the reactions of Eqs. (1) and (2). In these reactions, ruthenium complexes showed different catalytic activity and chemoselectivity from those of palladium complexes [5]. These facts showed the characterization of ruthenium complexes in catalytic reactions of allylic compounds and led us to make further efforts to investigate the ruthenium-catalysed reactions of allylic compounds.

This paper deals with the ruthenium-catalysed synthesis of cyclohexenone derivatives from allylic compounds such as allyl alcohols or *N,N*-dialkylallylamines with β-keto esters (Eq. (4)). The cyclization reaction

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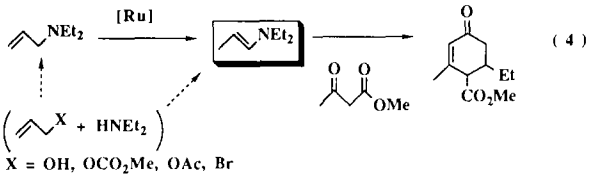
SSDI 0022-328X(94)24751-4



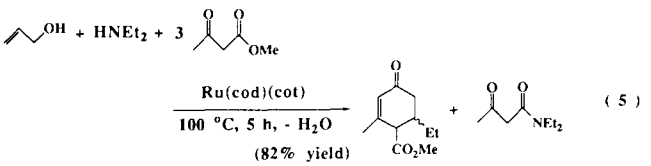
(4)

of allyl alcohols with β-keto esters in the presence of an amine provides a versatile method for the selective and effective preparation of 4-alkoxycarbonyl-2-cyclohexenone derivatives.

2. Results and Discussion

2.1. Selective synthesis of cyclohexenone derivatives from allyl alcohol and β-keto esters in the presence of a secondary amine

In the presence of a catalytic amount of Ru(cod)(cot), allyl alcohol reacted with two equivalent moles of methyl acetoacetate to give 5-ethyl-4-methoxycarbonyl-3-methyl-2-cyclohexenone in 82% yield (Eq. (5)). The product was a mixture of *trans* and

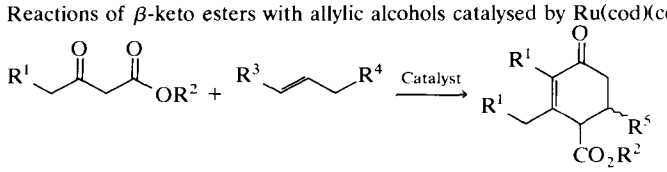


(5)

cis isomers (*trans*: *cis* = 3:2). In this reaction, it was necessary to add a secondary amine such as *N*,*N*-diethylamine with the same equivalent moles of allyl alcohol. Representative results are shown in Table 1. In the absence of *N*,*N*-diethylamine, allyl alcohol did not react with methyl acetoacetate (run 1). Addition of *N*,*N*-diethylamine led in a smooth reaction of allyl alcohol with the acetate. β-Keto esters such as methyl acetoacetate, ethyl acetoacetate, butyl acetoacetate and methyl methoxyacetoacetate gave the corresponding cyclic products in more than 80% yields (runs 2, 3, 4 and 6). In the reaction using hexyl acetoacetate, 5-ethyl-4-hexoxycarbonyl-3-methyl-2-cyclohexenone was selectively obtained in 93% yield (run 5). The reactions of crotyl alcohol and cinnamyl alcohol with methyl acetoacetate smoothly gave the corresponding products in 81% and 66% yields (runs 7 and 8).

Allyl acetate, allyl carbonate and allyl bromide also reacted with β-keto esters in the presence of secondary amine to give the cyclic products. For example, the reactions of methyl acetoacetate gave 5-ethyl-4-methoxycarbonyl-3-methyl-2-cyclohexenone as shown in Table 2 (runs 9, 10 and 11). Based on the results of runs 2, 9, 10 and 11, these reactions are considered to proceed as follows. The allylic compound first gives the corresponding allylamine in the presence of secondary amine, and then corresponding enamine is formed by the ruthenium-catalysed isomerization of allylamine. The enamine reacted with the β-keto ester thermally to give the resulting product, the cyclohexenone deriva-

Table 1
Reactions of β-keto esters with allylic alcohols catalysed by Ru(cod)(cot) [a]



Run	β-Keto ester		Allylic alcohol/amine		Product			Yield (%) [b]
	R^1	R^2	R^3	R^4	R^1	R^2	R^5	
1	H	CH_3	H	OH/–		–		–
2	H	CH_3	H	OH/$HNEt_2$	H	CH_3	C_2H_5	(1) 82 (*trans* : *cis* = 3 : 2)
3	H	C_2H_5	H	OH/$HNEt_2$	H	C_2H_5	C_2H_5	(2) 86 (*trans* : *cis* = 3 : 2)
4	H	^nBu	H	OH/$HNEt_2$	H	^nBu	C_2H_5	(3) 87 (*trans* : *cis* = 3 : 2)
5	H	^nHex	H	OH/$HNEt_2$	H	^nHex	C_2H_5	(4) 93 (*trans* : *cis* = 3 : 2)
6	OCH_3	CH_3	H	OH/$HNEt_2$	OCH_3	CH_3	C_2H_5	(5) 80 (*trans* : *cis* = 3 : 2)
7	H	CH_3	CH_3	OH/$HNEt_2$	H	CH_3	^nPr	(6) 81 (*trans* : *cis* = 3 : 2)
8	H	CH_3	C_6H_5	OH/$HNEt_2$	H	CH_3	$CH_2CH_2C_6H_5$	(7) 66 (*trans* : *cis* = 3 : 2)

[a] A mixture of allylic alcohol (2.5 mmol), methyl acetoacetate (7.5 mmol), diethylamine (2.5 mmol), *N*-methylpiperidine (2.5 mmol) and Ru(cod)(cot) (0.10 mmol) was stirred at 100°C for 5 h.

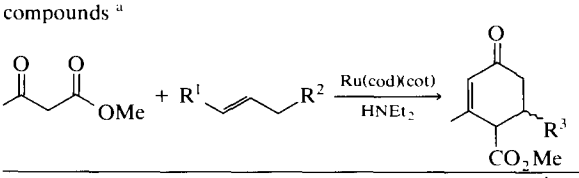
[b] Yield of the mixture of the isomers obtained by Kugelrohr distillation and yields of the products were calculated based on the amount of allylic compounds.

tive. Under the same reaction conditions, the reaction of allyl alcohol with *N,N*-diethylamine was carried out in the presence of Ru(cod)(cot) to give a complicated mixture; *N,N*-diethylamine was not delected. In the absence of the catalyst, starting materials was recovered. Since the palladium-catalysed reaction of allyl alcohol with amine gives allylamine [6], it is possible that a novel ruthenium complex was formed by adding the β-keto ester, which catalysed the reaction of allyl alcohol with secondary amine to give allylamine. Based on these facts, we investigated the reaction of allylamine with β-keto ester in detail.

2.2. Reaction of allylamine with a β-keto ester via isomerization of allylamine to the corresponding enamine

In the presence of a catalytic amount of Ru(cod)(cot), *N,N*-diethylallylamine reacted with two equivalent moles of methyl acetoacetate to give 5-ethyl-4-methoxycarbonyl-3-methyl-2-cyclohexenone in high yield (Table 3, run 15). The product was a mixture of *trans* and *cis* isomers as found in the reaction of allyl alcohol. In this case, the best yield of the product was obtained when the molar ratio of *N,N*-diethylallylamine and methyl acetoacetate was 1:2 [7]. The generated diethylamine was quenched by another molecule of acetoacetate to give acetoacetamide (see Eq. (6)). Further addition of the acetoacetate resulted in a poor selectivity of the product. Ru(cod)(cot) was

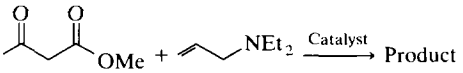
Table 2
Ru(cod)(cot)-catalysed reactions of methyl acetoacetate with allylic compounds [a]

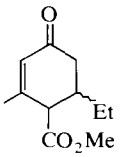
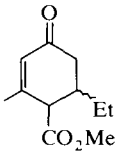
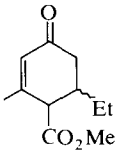
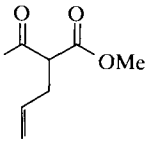
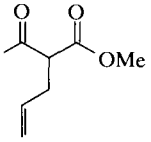


Run	Allylic compound		Product	Yield (%) [b]
	R^1	R^2	R^3	
9	H	OAc	CH_2CH_3	56 (*trans*:*cis* = 3:2)
10	H	Br	CH_2CH_3	54 (*trans*:*cis* = 3:2)
11	H	OCO_2CH_3	CH_2CH_3	68 (*trans*:*cis* = 3:2)
12	CH_3	OCO_2CH_3	^nPr	23 (*trans*:*cis* = 3:2)
13	H	OPh	–	–

[a] A mixture of allylic compound (2.5 mmol), methyl acetoacetate (7.5 mmol), diethylamine (2.5 mmol) *N*-methylpiperidine (2.5 mmol) and Ru(cod)(cot) (0.10 mmol) was stirred at 100°C for 5 h.
[b] Yield of the mixture of the isomers obtained by Kugelrohr distillation, and yields of products were calculated based on the amount of allylic compounds.

Table 3
Reactions of Methyl acetoacetate with *N,N*-Diethylallylamine Using Metal Complexes [a]

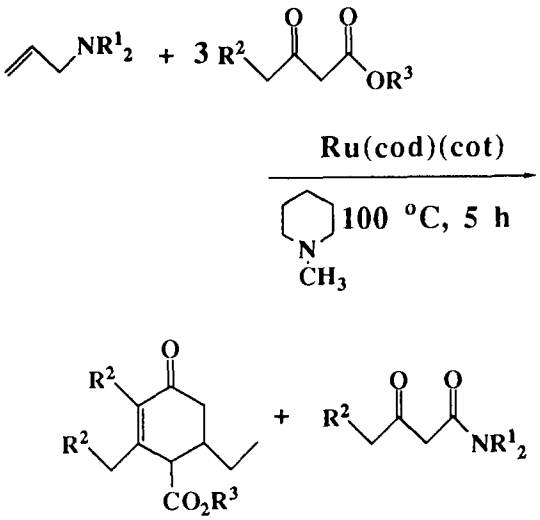


Run	Catalyst	Product	Yield (%) [b]
14	None	–	–
15	Ru(cod)(cot)		81 (*trans*:*cis* = 3:2)
16	$Ru_3(CO)_{12}$		36 (*trans*:*cis* = 3:2)
17	$RhCl(PPh_3)_3$		53 (*trans*:*cis* = 3:2)
18	$Pd(PPh_3)_4$		43
19	$Pt(PPh_3)_4$		30

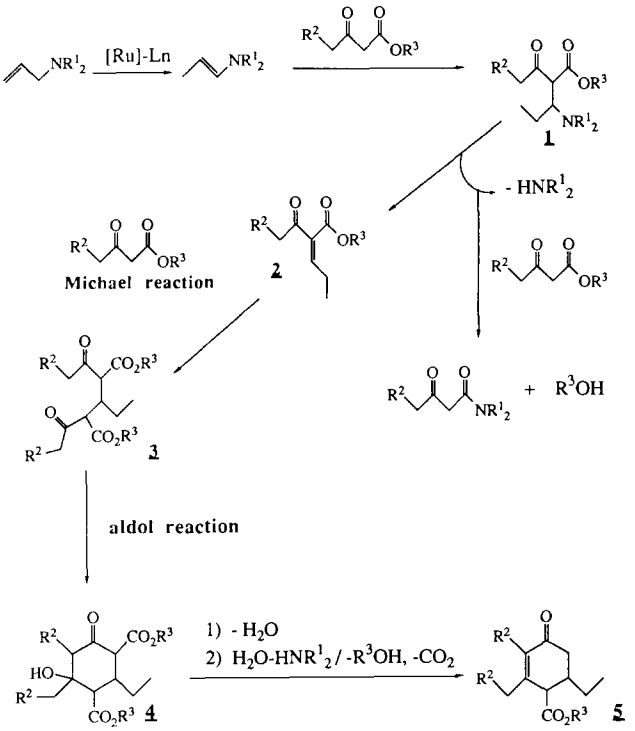
[a] A mixture of *N,N*-diethylallylamine (2.5 mmol), β-keto ester (5.0 mmol), *N*-methylpiperidine (2.5 mmol) and Ru(cod)(cot) (0.10 mmol) was stirred at 100°C for 5 h. [b] Yield of the mixture of the isomers obtained by Kugelrohr distillation.

the best catalyst. $Ru_3(CO)_{12}$ and $RhCl(PPh_3)_3$ showed definite catalytic activities (runs 16 and 17), while $Pd(PPh_3)_4$ and $Pt(PPh_3)_4$ catalysts only gave products derived by allylic alkylation of acetoacetates (runs 18 [6] and 19). $Ni(PPh_3)_4$ showed no catalytic activity for the present reaction. Addition of *N*-methylpiperidine was crucial for the selectivity, while without *N*-methylpiperidine a number of by-products were formed. The optimum reaction temperature was 100°C. β-Keto esters having a substituent such as 2-methylacetoacetate and other nucleophiles such as acetylacetone and dimethyl malonate in the present reaction conditions did not give the corresponding products.

A variety of β-keto esters are applicable for the cyclization. Representative results are shown in Table 4. *N,N*-Diethylallylamine reacted with ethyl acetoacetate to give 5-ethyl-4-ethoxycarbonyl-3-methyl-2-



R^1 = Me, Et; R^2 = H, Me, OMe;
R^3 = Me, Et, ^{n}Bu, CH_2Ph.

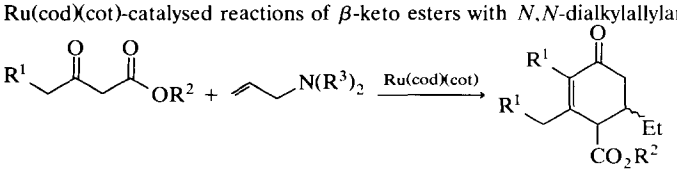


Scheme 1.

cyclohexenone in 85% yield in the stereoisomeric ratio of 1:1 (run 20). *N,N*-Diethylallylamine reacted with butyl acetoacetate or benzyl acetoacetate to give the corresponding products in 57% and 47% yields, respectively (runs 21 and 22). In the reaction of *N,N*-diethylallylamine with ethyl propionylacetate, the mixture of the corresponding products was obtained in 58% yield (*trans*:*cis* = 6:1, run 23). *N,N*-Diethylallylamine reacted with methyl 4-methoxyacetoacetate to give the corresponding product in high yield (87%, *trans* : *cis* = 3:2, run 24). tert-Butyl acetoacetate had a poor reactivity (run 25).

One of possible mechanisms of the present reaction is shown in Scheme 1. First, *N,N*-dialkylamine is isomerized by Ru(cod)(cot) to an enamine [4], *trans*-1-

Table 4
Ru(cod)(cot)-catalysed reactions of β-keto esters with *N,N*-dialkylallylamines [a]



Run	β-Keto ester		Allylamine	Product		Yield (%) [b]
	R^1	R^2	R^3	R^1	R^2	
15	H	CH_3	C_2H_5	H	CH_3	**(1)** 81 (*trans* : *cis* = 3:2)
20	H	C_2H_5	C_2H_5	H	C_2H_5	**(2)** 85 (*trans* : *cis* = 3:2)
21	H	^{n}Bu	C_2H_5	H	^{n}Bu	**(3)** 57 (*trans* : *cis* = 3:2)
22	H	$CH_2C_6H_5$	C_2H_5	H	$CH_2C_6H_5$	**(8)** 47 (*trans* : *cis* = 3:2)
23	CH_3	C_2H_5	C_2H_5	CH_3	C_2H_5	**(9)** 58 (*trans* : *cis* = 3:2)
24	OCH_3	CH_3	C_2H_5	OCH_3	CH_3	**(5)** 87 (*trans* : *cis* = 3:2)
25	H	^{t}Bu	C_2H_5	H	^{t}Bu	**(10)** Trace
26	H	CH_3	CH_3	H	CH_3	**(1)** 40 (*trans* : *cis* = 3:2)

[a] A mixture of allylamine (2.5 mmol), methyl acetoacetate (5.0 mmol), *N*-methylpiperidine (2.5 mmol) and Ru(cod)(cot)(0.10 mmol) was stirred at 100°C for 5 h.
[b] Yield of the mixture of the isomers obtained by Kugelrohr distillation.

N,*N*-dialkylamino-1-propene. In fact, *N*,*N*-diethylallylamine was isomerized to *trans*-1-*N*,*N*-diethylamino-1-propene in the presence of a catalytic amount of Ru(cod)(cot). *N*,*N*-Diethylallylamine is attacked by a nucleophile, β-keto ester, to give an adduct, **1** [8]. The elimination of HNR^1_2 would generate **2**. Intramolecular aldol condensation of **3**, derived from Michael addition of the β-keto ester to **2**, gives "propylidenebis (acetoacetate)" **4** [9]. The product **5** is obtained from **4** via dehydration followed by decarboxylation. It has been reported that propionaldehyde slowly reacts with ethyl acetoacetate in the presence of diethylamine to give **4**, and with treatment of **4** with alkali, a cylcohexenone derivative was obtained [9].

Taking into account these facts, we examined the reaction of *trans*-1-diethylamino-1-propene with ethyl acetoacetate in the absence of ruthenium catalyst. The product **5** was also obtained in 80% yield when the unstable enamine was carefully treated with acetoacetate under an argon atmosphere. The reaction of allyl alcohol, allyl acetate and carbonates with β-keto esters in the presence of diethylamine would proceed via the formation of allylamines.

Consequently, this reaction provides a versatile method for the selective preparation of cylcohexenone derivatives using β-keto esters and allyl alcohol or other allylic compounds such as allylamine.

3. Experimental details

β-Keto esters, allylic alcohols and allyamines were commercial products. Solvents were distilled before use. Allylic carbonates were prepared by published methods [10]. Ru(cod)(cot) [11], $Pd(PPh_3)_4$ [12], $Pt(PPh_3)_4$ [13], $Ni(PPh_3)_4$ [14] and $RhCl(PPh_3)_3$ [15] were prepared according to methods in the literature. $Ru_3(CO)_{12}$ was purchased from Strem Chemicals and used without further purification.

trans-1-Diethylamino-1-propene was prepared as follows. To a heavy-walled glass tube were added Ru(cod)(cot) (0.1 mmol, 0.031 g), *N*,*N*-diethylallylamine (10 mmol, 1.5 ml) and a stirring magnetic bar under an argon atmosphere. The glass tube was sealed and the mixture was stirred magnetically at 80°C for 10 h. Kugelrohr distillation afforded a colourless liquid (7.0 mmol, 70% yield). All operations must be carefully carried out under an argon atmosphere.

All products were identified by means of ^{1}H NMR, ^{13}C NMR, FT-IR, GC–MS and elemental analysis. ^{1}H NMR (270 MHz) and ^{13}C NMR (67.8 MHz) spectra were recorded on a JEOL GSX-270 spectrometer using $CDCl_3$ as a solvent and tetramethylsilane as an internal standard. Methyl, methylene and methine groups were confirmed by DEPT mode measurement. IR spectra were measured on Shimadzu FTIR-8100 spectrometer. GC analyses were performed with a Shimadzu GC-8A chromatograph with a flame ionization detector (column, SE-30, 3 m × 3 mm i.d.). Mass spectra were obtained with a Shimadzu GCMS-QP2000 spectrometer. Microanalyses were performed by the Laboratory for Organic Elemental Microanalysis of Kyoto University.

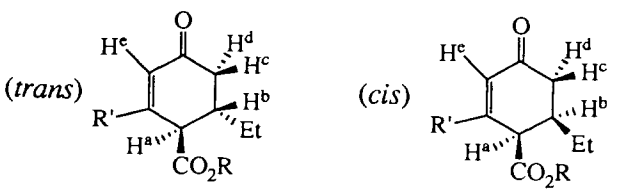
3.1. General reaction procedure

A representative procedure is as follows. (1) Reaction of allyl alcohol: to a heavy-walled glass tube were added Ru(cod)(cot) (0.1 mmol, 0.031 g), *N*-methylpiperidine (2.5 mmol, 0.30 ml), *N*,*N*-diethylamine (2.5 mmol, 0.26 ml), allyl alcohol (2.5 mmol, 0.17 ml), methyl acetoacetate (7.5 mmol, 0.81 ml) and a magnetic stirring bar under an argon atmosphere. The glass tube was sealed and the mixture was stirred magnetically at 100°C for 5 h. A mixture of stereoisomers (*trans*:*cis* = 3:2) of 5-ethyl-4-methoxycarbonyl-3-methyl-2-cyclohexenone was separated from the reaction mixture by Kugelrohr distillation (100°C/0.8 mmHg, 0.40 g, 82% yield); (2) Reaction of allylamine: to a heavy-walled glass tube were added Ru(cod)(cot) (0.1 mmol, 0.031 g), *N*-methylpiperidine (2.5 mmol, 0.30 ml), *N*,*N*-diethylallylamine (2.5 mmol, 0.38 ml), ethyl acetoacetate (5 mmol, 0.62 ml) and a magnetic stirring bar under an argon atmosphere. The glass tube was sealed and the mixture was stirred magnetically at 100°C for 5 h. A 1:1 mixture of the stereoisomers of 5-ethyl-4-ethoxycarbonyl-3-methyl-2-cylcohexenone was separated from the reaction mixture by Kugelrohr distillation (120°C/0.8 mmHg, 0.22 g, 85% yield). The stereochemistry of the product was determined by means of ^{1}H NMR, ^{13}C NMR and the DNOE technique (difference of nuclear Overhauser effect).

The spectral and analytical data for the representative products are described below (*trans* and *cis* diastereomers are shown in Scheme 2).

3.1.1. 5-Ethyl-4-methoxycarbonyl-3-methyl-2-cyclohexenone (a mixture of trans and cis isomers) (1)

Kugelrohr distillation (100°C/0.8 mmHg). IR (neat): 1736, 1670 cm^{-1}. MS (*m*/*z*) 196 (M^+). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.33; H, 8.22. Found: C, 67.13; H, 8.37%. *trans*-Isomer: ^{1}H NMR ($CDCl_3$, ppm) δ 0.88 (t, 3H, *J* = 7.3 Hz, CH_2CH_3), 1.35 (m, 2H, CH_2CH_3),



Scheme 2.

1.91 (s, 3H, CH_3), 2.12 (dd, 1H, J = 16.5 and 8.8 Hz, H^d), 2.33 (m, 1H, H^b), 2.58 (dd, 1H, J = 16.5 and 4.4 Hz, H^c), 3.10 (d, 1H, J = 6.6 Hz, H^a), 3.72 (s, 3H, OCH_3), 5.91 (s, 1H, H^e); ^{13}C NMR ($CDCl_3$, ppm) δ 10.9 (CH_2CH_3), 22.8 (CH_3), 26.4 (CH_2CH_3), 39.0 (CH^b), 39.8 (CH_2^{cd}), 52.0 (CH^a), 52.2 (OCH_3), 128.0 (CH^e), 155.5 (C), 172.4 (CO_2CH_3), 197.9 (C=O). *cis*-Isomer: ^1H NMR ($CDCl_3$, ppm) δ 0.94 (t, 3H, J = 7.3 Hz, CH_2CH_3), 1.43 (m, 2H, CH_2CH_3), 1.93 (s, 3H, CH_3), 2.09 (dd, 1H, J = 13.9 and 4.3 Hz, H^d), 2.27 (m, 1H, H^b), 2.52 (dd, 1H, J = 13.9 and 8.6 Hz, H^c), 3.24 (d, 1H, J = 5.1 Hz, H^a), 3.68 (s, 3H, OCH_3), 5.93 (s, 1H, H^e); ^{13}C NMR ($CDCl_3$, ppm) δ 11.3 (CH_2CH_3), 23.2 (CH_3), 26.2 (CH_2CH_3), 38.6 (CH_2^{cd}), 39.0 (CH^b), 50.5 (CH^a), 52.2 (OCH_3), 128.4 (CH^e), 156.4 (C), 170.6 (CO_2CH_3), 199.1 (C=O).

3.1.2. 5-Ethyl-4-ethoxycarbonyl-3-methyl-2-cyclohexenone (a mixture of trans and cis isomers) (2)

Kugelrohr distillation (100°C/0.7 mmHg). IR (neat): 1732, 1672 cm^{-1}. MS (m/z) 210 (M^+). Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.25; H, 8.65%. *trans*-Isomer: ^1H NMR ($CDCl_3$, ppm), δ 0.93 (t, 3H, J = 7.3 Hz, CH_2CH_3), 1.28 (t, 3H, J = 7.0 Hz, OCH_2CH_3), 1.40 (m, 2H, CH_2CH_3), 1.96 (s, 3H, CH_3), 2.17 (dd, 1H, J = 16.5 and 8.8 Hz, H^d), 2.37 (m, 1H, H^b), 2.59 (dd, 1H, J = 16.5 and 4.5 Hz, H^c), 3.12 (d, 1H, J = 6.6 Hz, H^a), 4.22 (q, 2H, J = 7.0 Hz, OCH_2CH_3), 5.95 (s, 1H, H^e); ^{13}C NMR ($CDCl_3$, ppm), δ 12.4 (CH_2CH_3), 15.6 (OCH_2CH_3), 24.3 (CH_3), 27.9 (CH_2CH_3), 40.5 (CH^b), 41.3 (CH_2^{cd}), 53.9 (CH^a), 62.7 (OCH_2CH_3), 129.5 (CH^e), 158.5 (C), 173.0 ($CO_2C_2H_5$), 200.5 (C=O). *cis*-Isomer: ^1H NMR ($CDCl_3$, ppm) δ 0.99 (t, 3H, J = 7.3 Hz, CH_2CH_3), 1.30 (t, 3H, J = 7.0 Hz, OCH_2CH_3), 1.46 (m, 2H, CH_2CH_3), 1.97 (s, 3H, CH_3), 2.13 (dd, 1H, J = 13.9 and 4.4 Hz, H^d), 2.29 (m, 1H, H^b), 2.58 (dd, 1H, J = 13.9 and 8.8 Hz, H^c), 3.26 (d, 1H, J = 5.1 Hz, H^a), 4.19 (q, 2H, J = 7.0 Hz, OCH_2CH_3), 5.97 (s, 1H, H^e); ^{13}C NMR ($CDCl_3$, ppm) δ 12.8 (CH_2CH_3), 15.7 (OCH_2CH_3), 24.7 (CH_3), 27.6 (CH_2CH_3), 40.2 (CH_2^{cd}), 40.5 (CH^b), 52.1 (CH^a), 62.6 (OCH_2CH_3), 129.9 (CH^e), 159.0 (C), 171.5 ($CO_2C_2H_5$), 199.5 (C=O).

3.1.3. 5-Ethyl-4-butoxycarbonyl-3-methyl-2-cyclohexenone (a mixture of trans and cis isomers) (3)

Kugelrohr distillation (130°C/0.4 mmHg). MS (m/z) 238 (M^+). Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.26; H, 9.38%. *trans*-Isomer: ^1H NMR ($CDCl_3$, ppm) δ 0.90 (t, 3H, CH_2CH_3), 0.98 (t, 3H, $OCH_2CH_2H_2CH_3$), 1.37 (m, 2H, CH_2CH_3), 1.43 (m, 2H, $OCH_2CH_2CH_2CH_3$), 1.65 (m, 2H, $OCH_2CH_2CH_2CH_3$), 1.97 (s, 3H, CH_3), 2.14 (dd, 1H, J = 16.5 and 8.8 Hz, H^d), 2.36 (m, 1H, H^b), 2.61 (dd, 1H, J = 16.5 and 4.5 Hz, H^c), 3.13 (d, 1H, J = 6.6 Hz, H^a), 4.17 (q, 2H, OCH_2CH_2), 5.95 (s, 1H, H^e); ^{13}C NMR ($CDCl_3$, ppm) δ 10.9 (CH_2CH_3), 13.5 ($OCH_2CH_2CH_2CH_3$), 18.9 ($OCH_2CH_2CH_2CH_3$), 22.9 (CH_3), 26.4 (CH_2CH_3), 30.5 (OCH_2CH_2–), 39.0 (CH^b), 39.8 (CH_2^{cd}), 52.5 (CH^a), 65.0 (OCH_2–), 128.0 (CH^e), 155.8 (C), 171.9 (CO_2CH_2), 198.1 (C=O). *cis*-Isomer: ^1H NMR ($CDCl_3$, ppm) δ 0.94 (t, 3H, CH_2CH_3), 0.98 (t, 3H, $OCH_2CH_2H_2CH_3$), 1.40 (m, 2H, CH_2CH_3), 1.45 (m, 2H, $OCH_2CH_2CH_2CH_3$), 1.69 (m, 2H, $OCH_2CH_2CH_2CH_3$), 1.98 (s, 3H, CH_3), 2.14 (dd, 1H, J = 16.5 and 8.8 Hz, H^d), 2.36 (m, 1H, H^b), 2.61 (dd, 1H, J = 16.5 and 4.5 Hz, H^c), 3.28 (d, 1H, J = 5.1 Hz, H^a), 4.19 (q, 2H, OCH_2CH_2), 5.96 (s, 1H, H^e); ^{13}C NMR ($CDCl_3$, ppm) δ 11.3 (CH_2CH_3), 13.4 ($OCH_2CH_2CH_2CH_3$), 19.0 ($OCH_2CH_2CH_2CH_3$), 23.2 (CH_3), 26.2 (CH_2CH_3), 30.4 (OCH_2CH_2–), 38.8 (CH_2^{cd}), 39.0 (CH^b), 52.7 (CH^a), 64.9 (OCH_2–), 128.3 (CH^e), 156.0 (C), 172.2 (CO_2CH_2), 199.0 (C=O).

3.1.4. 5-Ethyl-4-hexoxycarbonyl-3-methyl-2-cyclohexenone (a mixture of trans and cis isomers) (4)

Kugelrohr distillation (130°C/0.4 mmHg). MS (m/z) 266 (M^+). Anal. Calcd for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84. Found: C, 71.85; H, 9.99%. *trans*-Isomer: ^1H NMR ($CDCl_3$, ppm) δ 0.90 (t, 3H, CH_2CH_3), 0.98 (t, 3H, $O(CH_2)_5CH_3$), 1.37 (m, 2H, CH_2CH_3), 1.43 (m, 2H, $OCH_2(CH_2)_3CH_2CH_3$), 1.65 (m, 6H, $OCH_2(CH_2)_3CH_2CH_3$), 1.97 (s, 3H, CH_3), 2.14 (dd, 1H, J = 16.5 and 8.8 Hz, H^d), 2.36 (m, 1H, H^b), 2.61 (dd, 1H, J = 16.5 and 4.5 Hz, H^c), 3.13 (d, 1H, J = 6.6 Hz, H^a), 4.17 (q, 2H, OCH_2CH_2), 5.95 (s, 1H, H^e); *cis*-Isomer: ^1H NMR ($CDCl_3$, ppm) δ 0.94 (t, 3H, CH_2CH_3), 0.98 (t, 3H, $O(CH_2)_5CH_3$), 1.40 (m, 2H, CH_2CH_3), 1.45 (m, 2H, $OCH_2(CH_2)_3CH_2CH_3$), 1.69 (m, 6H, $OCH_2(CH_2)_3CH_2CH_3$), 1.98 (s, 3H, CH_3), 2.14 (dd, 1H, J = 16.5 and 8.8 Hz, H^d), 2.36 (m, 1H, H^b), 2.61 (dd, 1H, J = 16.5 and 4.5 Hz, H^c), 3.28 (d, 1H, J = 5.1 Hz, H^a), 4.19 (q, 2H, OCH_2CH_2), 5.96 (s, 1H, H^e);

3.1.5. 5-Ethyl-4-methoxycarbonyl-3-methomethyl-2-methoxyl-2-cyclohexenone (a mixture of trans and cis isomers) (5)

Kugelrohr distillation (110°C/0.75 mmHg). MS (m/z) 256 (M^+). Anal. Calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 60.55; H, 8.04%. *trans*-Isomer: ^1H NMR ($CDCl_3$, ppm) δ 0.95 (t, 3H, J = 7.3 Hz, CH_2CH_3), 1.48 (m, 2H, CH_2CH_3), 2.25 (dd, 1H, J = 16.5 and 8.8 Hz, H^d), 2.45 (m, 1H, H^b), 2.70 (dd, 1H, J = 16.5 and 4.5 Hz, H^c), 3.31 (s, 3H, CH_2OCH_3), 3.52 (d, 1H, J = 6.1 Hz, H^a), 3.72 (s, 3H, CO_2CH_3), 3.74 (s, 3H, OCH_3), 4.25 (2H, CH_2OCH_3); ^{13}C NMR ($CDCl_3$, ppm) δ 11.2 (CH_2CH_3), 26.0 (CH_2CH_3), 38.5 (CH^b), 41.0 (CH_2^{cd}), 46.8 (CH^a), 52.2 (CO_2CH_3), 58.7 (CH_2OCH_3), 60.1 (OCH_3), 68.1 (CH_2OCH_3), 138.1 (CH_3O–C–), 149.5 (CH_3OCH_2–C–), 172.6 (CO_2CH_3),

193.4 (*C*=O). *cis*-Isomer: ^{1}H NMR ($CDCl_3$, ppm) δ 0.99 (t, 3H, $J = 7.3$ Hz, CH_2CH_3), 1.40 (m, 2H, CH_2CH_3), 2.20 (dd, 1H, $J = 16.5$ and 8.8 Hz, H^d), 2.45 (m, 1H, H^b), 2.68 (dd, 1H, $J = 16.5$ and 4.5 Hz, H^c), 3.33 (s, 3H, CH_2OCH_3), 3.64 (d, 1H, $J = 4.9$ Hz, H^a), 3.70 (s, 3H, CO_2CH_3), 3.75 (s, 3H, OCH_3), 4.25 (2H, CH_2OCH_3); ^{13}C NMR ($CDCl_3$, ppm) δ 11.4 (CH_2CH_3), 26.2 (CH_2CH_3), 38.6 (CH^b), 40.3 (CH_2^{cd}), 45.9 (CH^a), 51.9 (CO_2CH_3), 58.6 (CH_2OCH_3), 60.3 (OCH_3), 68.3 (CH_2OCH_3), 139.0 (CH_3O–*C*–), 150.5 (CH_3OCH_2–*C*–), 170.5 (CO_2CH_3), 194.5 (*C*=O).

3.1.6. 5-Propyl-4-methoxycarbonyl-3-methyl-2-cyclohexenone (a mixture of trans and cis isomers) (6)

Kugelrohr distillation (90°C/0.50 mmHg). MS (*m/z*) 210 (M^+). *trans*-Isomer: ^{1}H NMR ($CDCl_3$, ppm) δ 0.85 (t, 3H, $CH_2CH_2CH_3$), 1.29 (m, 2H, $CH_2CH_2CH_3$), 1.31 (m, 2H, $CH_2CH_2CH_3$), 1.89 (s, 3H, CH_3), 2.08 (dd, 1H, $J = 16.5$ and 8.8 Hz, H^d), 2.30 (m, 1H, H^b), 2.50 (dd, 1H, $J = 16.5$ and 4.4 Hz, H^c), 3.06 (d, 1H, $J = 6.6$ Hz, H^a), 3.70 (s, 3H, OCH_3), 5.89 (s, 1H, H^e); ^{13}C NMR ($CDCl_3$, ppm) δ 13.8 ($CH_2CH_2CH_3$), 19.6 ($CH_2CH_2CH_3$), 22.9 (CH_3), 35.8 ($CH_2CH_2CH_3$), 37.2 (CH^b), 40.1 (CH_2^{cd}), 50.7 (CH^a), 52.5 (OCH_3), 128.0 (CH^e), 155.5 (*C*), 172.4 (CO_2CH_3), 198.0 (*C*=O). *cis*-Isomer: ^{1}H NMR ($CDCl_3$, ppm) δ 0.86 (t, 3H, $CH_2CH_2CH_3$), 1.30 (m, 2H, $CH_2CH_2CH_3$), 1.32 (m, 2H, $CH_2CH_2CH_3$), 1.90 (s, 3H, CH_3), 2.08 (dd, 1H, $J = 16.5$ and 8.8 Hz, H^d), 2.30 (m, 1H, H^b), 2.50 (dd, 1H, $J = 16.5$ and 4.4 Hz, H^c), 3.19 (d, 1H, $J = 5.1$ Hz, H^a), 3.67 (s, 3H, OCH_3), 5.90 (s, 1H, H^e); ^{13}C NMR ($CDCl_3$, ppm) δ 13.9 ($CH_2CH_2CH_3$), 19.7 ($CH_2CH_2CH_3$), 23.3 (CH_3), 35.3 ($CH_2CH_2CH_3$), 36.9 (CH^b), 38.8 (CH_2^{cd}), 52.0 (CH^a), 52.3 (OCH_3), 128.4 (CH^e), 156.4 (*C*), 170.7 (CO_2CH_3), 199.2 (*C*=O).

3.1.7. 5-Ethyl(3-phenyl)-4-methoxycarbonyl-3-methyl-2-cyclohexenone (a mixture of trans and cis isomers) (7)

Kugelrohr distillation (140°C/0.15 mmHg). MS (*m/z*) 272 (M^+). Anal. Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 74.75; H, 7.57%. *trans*-Isomer: ^{1}H NMR ($CDCl_3$, ppm) δ 1.71 (m, 2H, $CH_2CH_2C_6H_5$), 1.94 (s, 3H, CH_3), 2.19 (dd, 1H, $J = 16.5$ and 8.8 Hz, H^d), 2.42 (m, 1H, H^b), 2.55 (dd, 1H, $J = 16.5$ and 4.4 Hz, H^c), 2.69 (t, 2H, $CH_2CH_2C_6H_5$), 3.17 (d, 1H, $J = 6.2$ Hz, H^a), 3.74 (s, 3H, OCH_3), 5.96 (s, 1H, H^e), 7.17 (m, 5H, phenyl); ^{13}C NMR ($CDCl_3$, ppm) δ 23.0 (CH_3), 32.8 ($CH_2CH_2C_6H_5$), 35.4 ($CH_2CH_2C_6H_5$), 37.1 (CH^b), 40.0 (CH_2^{cd}), 50.6 (CH^a), 52.4 (OCH_3), 128.1 (CH^e), 128.4 (phenyl), 155.4 (*C*), 172.1 (CO_2CH_3), 197.7 (*C*=O). *cis*-Isomer: ^{1}H NMR ($CDCl_3$, ppm) δ 1.73 (m, 2H, $CH_2CH_2C_6H_5$), 1.97 (s, 3H, CH_3), 2.19 (dd, 1H, $J = 16.5$ and 8.8 Hz, H^d), 2.42 (m, 1H, H^b), 2.55 (dd, 1H, $J = 16.5$ and 4.4 Hz, H^c), 2.72 (t, 2H, $CH_2CH_2C_6H_5$), 3.29 (d, 1H, $J = 5.1$ Hz, H^a), 3.74 (s, 3H, OCH_3), 5.96 (s, 1H, H^e), 7.28 (m, 5H, phenyl); ^{13}C NMR ($CDCl_3$, ppm) δ 23.4 (CH_3), 32.7 ($CH_2CH_2C_6H_5$), 35.0 ($CH_2CH_2C_6H_5$), 36.4 (CH^b), 38.8 (CH_2^{cd}), 52.2 (CH^a), 52.3 (OCH_3), 128.2 (CH^e), 128.3 (phenyl), 156.0 (*C*), 170.0 (CO_2CH_3), 198.5 (*C*=O).

3.1.8. 5-Ethyl-4-benzoxycarbonyl-3-methyl-2-cyclohexenone (a mixture of trans and cis isomers) (8)

Kugelrohr distillation (130°C/0.3 mmHg). MS (*m/z*) 272 (M^+)., Anal. Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 75.00; H, 7.41%. *trans*-Isomer: ^{1}H NMR ($CDCl_3$, ppm) δ 0.89 (t, 3H, $J = 7.3$ Hz, CH_2CH_3), 1.37 (m, 2H, CH_2CH_3), 1.91 (s, 3H, CH_3), 2.16 (dd, 1H, $J = 16.1$ and 8.4 Hz, H^d), 2.36 (m, 1H, H^b), 2.60 (dd, 1H, $J = 16.1$ and 4.4 Hz, H^c), 3.17 (d, 1H, $J = 6.9$ Hz, H^a), 5.20 (s, 2H, OCH_2Ph), 5.95 (s, 1H, H^e), 7.36 (s 5H, phenyl); ^{13}C NMR ($CDCl_3$, ppm) δ 10.9 (CH_2CH_3), 22.9 (CH_3), 26.4 (CH_2CH_3), 39.1 (CH^b), 39.8 (CH_2^{cd}), 52.4 (CH^a), 66.9 (OCH_2Ph), 128.0 (CH^e), 128.7 (phenyl), 155.6 (*C*), 169.0 (CO_2CH_2Ph), 198.0 (*C*=O). *cis*-Isomer: ^{1}H NMR ($CDCl_3$, ppm) δ 0.95 (t, 3H, $J = 7.3$ Hz, CH_2CH_3), 1.42 (m, 2H, CH_2CH_3), 1.93 (s, 3H, CH_3), 2.22 (dd, 1H, $J = 13.2$ and 3.8 Hz, H^d), 2.30 (m, 1H, H^b), 2.40 (dd, 1H, $J = 13.2$ and 8.0 Hz, H^c), 3.31 (d, 1H, $J = 5.1$ Hz, H^a), 5.16 (s, 2H, OCH_2Ph), 5.97 (s, 1H, H^e), 7.35 (s 5H, phenyl); ^{13}C NMR ($CDCl_3$, ppm) δ 11.3 (CH_2CH_3), 23.3 (CH_3), 26.1 (CH_2CH_3), 38.8 (CH_2^{cd}), 39.2 (CH^b), 50.5 (CH^a), 67.0 (OCH_2Ph), 128.5 (CH^e), 128.7 (phenyl), 156.4 (*C*), 171.8 (CO_2CH_2Ph), 199.2 (*C*=O).

3.1.9. trans-5-Ethyl-4-ethoxycarbonyl-3-ethyl-2-methyl-2-cyclohexenone (9)

Kugelrohr distillation (100°C/0.7 mmHg). IR (neat): 1732, 1670 cm^{-1}. MS (*m/z*) 238 (M^+). ^{1}H NMR ($CDCl_3$, ppm) δ 0.93 (t, 3H, $J = 7.3$ Hz, $CH^bCH_2CH_3$), 1.05 (t, 3H, $J = 7.3$ Hz, CCH_2CH_3), 1.29 (t, 3H, $J = 6.9$ Hz, OCH_2CH_3), 1.40 (m, 2H, $CH^bCH_2CH_3$), 1.81 (s, 3H, CH_3), 2.18 (dd, 1H, $J = 16.1$ and 8.8 Hz, H^d), 2.27 (m, 1H, H^b), 2.47 (m, 2H, CCH_2CH_3), 2.71 (dd, 1H, $J = 16.1$ and 4.4 Hz, H^c), 3.26 (d, 1H, $J = 6.6$ Hz, H^a), 4.20 (q, 2H, $J = 6.9$ Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, ppm) δ 10.5 ($CH^bCH_2CH_3$), 11.3 (CCH_2CH_3), 11.6 (OCH_2CH_3), 14.1 (CH_3), 26.4 ($CH^bCH_2CH_3$), 26.9 (CCH_2CH_3), 38.4 (CH^b), 39.6 (CH_2^{cd}), 51.1 (CH^a), 61.2 (OCH_2CH_3), 132.1 (*C*–CH_3), 158.5 (*C*–CH_2CH_3), 172.6 ($CO_2C_2H_5$), 198.1 (*C*=O).

Acknowledgments

This work was partly supported by a Grant-in-Aid for Scientific Research from the Japanese Ministry of Education, Science and Culture. S.-W. Zhang thanks JSPS for postdoctoral fellowship.

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