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# Sodium Benzoate as a Mild Base Catalyst for the Tandem *Michael*-Aldol Self-Condensation of γ,δ-Unsaturated β-Ketoesters

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**Summary.** An efficient procedure has been developed for the tandem *Michael*-aldol self-condensation of δ,γ-unsaturated β-ketoesters (**1**), using sodium benzoate as a mild base catalyst to furnish conjugated vinylcyclohexenonedicarboxylates (**2**) some of which show biological activity against ectoparasites in cattle.

**Keywords.** Unsaturated β-ketoester; 2-Cyclohexenone; *Michael*-aldol condensation; Sodium benzoate.

**Natriumbenzoat als milder basischer Katalysator für die Tandem-*Michael*-Aldol-Selbstkondensation von γ,δ-ungesättigten β-Ketoestern**

**Zusammenfassung.** Natriumbenzoat ist als milder basischer Katalysator ausgezeichnet zur Anwendung bei der Tandem-*Michael*-Aldol-Selbstkondensation von γ,δ-ungesättigten β-Ketoestern (**1**) geeignet. Es entstehen Vinylcyclohexenondicarboxylate (**2**), von denen einige biologische Aktivität gegen Ektoparasiten bei Rindern zeigen.

## Introduction

Methods for the preparation of substituted 2-cyclohexenones are important in organic synthesis [1]. Whereas the *Robinson* annelation is especially useful for the synthesis of 3-oxobicyclo[4.4.0]dec-1-enes [2], new methodologies for the synthesis of simple substituted 2-cyclohexenones are of great interest. Some of the well-known methods available are the *Birch* reduction of substituted anisoles followed by hydrolysis [3, 4], *Michael*-aldol condensations of α,β-unsaturated carbonyl compounds with ketones followed by dehydration (*i.e. Robinson* type annelations) [5, 6], and alkylations of enolizable 1,3-cyclohexadiones [7]. Recently, N-*tert*-butyl-1-aza-1,3-butadienes have been reacted with β-diketones to furnish 2-cyclohexenones [8]. One of us has described the synthesis of 2-

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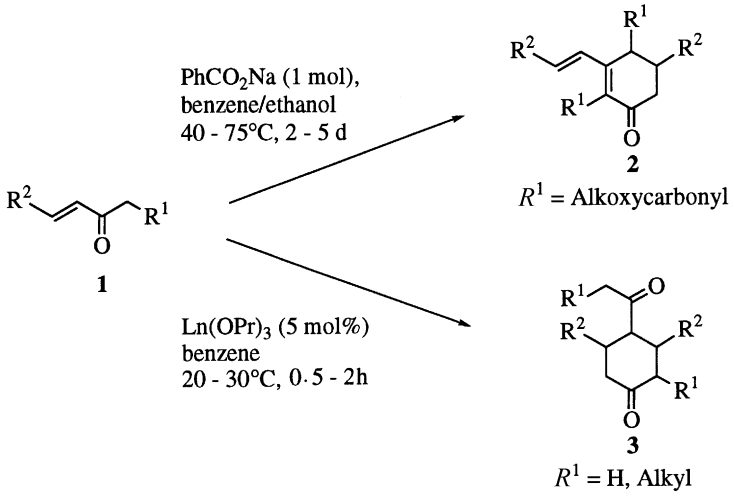
cyclohexenones *via* a *Michael-Wittig* condensation of substituted 2*H*-pyran-5-carboxylates and the $\gamma$-arsonium ylide of acetoacetate [9] which is based on a similar observation obtained from condensations of conjugated unsaturated carbonyl compounds and the $\gamma$-phosphonium ylide of acetoacetate [10].

For base catalyzed annelations, the focus is presently on the use of lanthanide triisopropoxides to induce tandem *Michael-Michael* annelations [11] and *Michael*-aldol condensations of $\alpha,\beta$-unsaturated ketones [12]. On the other hand, we had recently success using lithium carbonate and sodium or potassium benzoate as base catalysts for the synthesis of 2*H*-pyran-5-carboxylates from $\alpha,\beta$-unsaturated aldehydes and esters of acetoacetate [13]. Since we were interested in the synthesis of a new type of insect growth regulator [14], we now describe an efficient synthesis of substituted dialkyl 6-oxo-2-vinylcyclohex-1-ene-1,3-dicarboxylates (**2**). These compounds were prepared by *Michael-aldol* self-condensation of $\gamma,\delta$-unsaturated $\beta$-ketoesters (**1**) [15, 16] using sodium benzoate as a superior base catalyst for this type of reaction (Schemes 1–3).

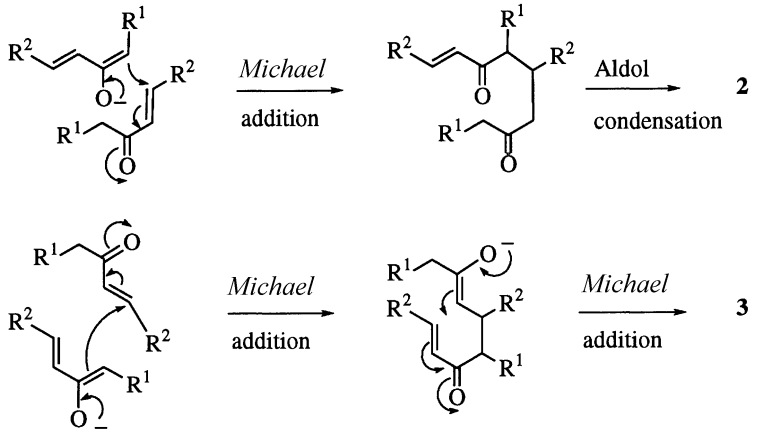
## Results and Discussion

Coincidental with our own work on self-dimerizations, *Okano* and co-workers reported on the cyclodimerization of $\alpha,\beta$-unsaturated ketones (**1**; $R = $ H, alkyl) in the presence of lanthanoid triisopropoxides to produce cyclohexanones (**3**; $R = $ H, alkyl) (Scheme 1). This reaction proceeded *via* a tandem *Michael-Michael* addition mechanism (Scheme 2) [11]. The authors reported that the rate of this reaction could be increased by performing the reactions in 2-propanol instead of non-polar solvents like benzene [12]. The self-dimerization of $\alpha,\beta$-unsaturated ketones to cyclohexenones is less well known [12].

In sharp contrast, we have found that base catalyzed dimerization of $\gamma,\delta$-unsaturated $\beta$-ketoesters (**1**; $R = $ alkoxycarbonyl) can easily be accomplished in the presence of sodium benzoate and triethylbenzylammonium chloride (*TEBAC*) as a



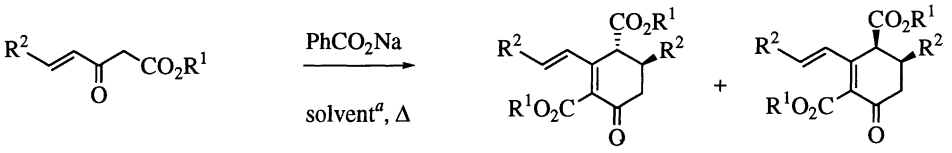

**Scheme 1.** The *Michael*-aldol and *Michael-Michael* addition of conjugated unsaturated ketones and $\delta,\gamma$-unsaturated $\beta$-ketoesters




**Scheme 2.** Mechanism of the *Michael*-aldol condensation and *Michael-Michael* addition of conjugated unsaturated carbonyl compounds

phase transfer catalyst. With this procedure, cyclohexenones (**2**; $R =$ alkoxycarbonyl) (Scheme 1) were obtained *via* a tandem *Michael*-aldol mechanism (Scheme 2). Note that the formation of **2** actually proceeds *via* the same type of intermediate as for the production of compounds **3** [11]. However, the intermediate *Michael*-adduct could not be isolated by us or by *Okano* and co-workers [11]. Likewise, we have found that alcohols as solvents enhance the tandem *Michael*-aldol self-condensation of $\gamma,\delta$-unsaturated $\beta$-ketoesters (**1**). In our case, bases like NaOEt, NaOH, or $Na_2CO_3$ were too harsh and actually led to a substantial amount of decarboxylation of **1** to the corresponding conjugated 2-enones. Sodium benzoate is an even milder catalyst for these condensations than sodium acetate. Additives like hydroquinone to curb polymerization and magnesium sulfate to remove water further increased the yield of **2**. This *Michael*-aldol [17] reaction has some similarities with the *Michael-Dieckmann* addition [18] and *Michael-Claisen* condensations [19, 20], but is closely related to the *Robinson* annelation [2, 5].

The ease by which our dimerization-annelations of **1** to **2** took place and the reason why this reaction was so regioselective is most likely due to the activating and directing effect of the alkoxycarbonyl group and the ionic sodium enolate of the intermediate *Michael* addition complex as compared to the lanthanoid enolates which eventually led to quite a different product **3** [11]. For all our investigated substrates, the $\gamma,\delta$-unsaturated-$\beta$-ketoesters **1** gave smoothly the annelated products **2** in a modest yield of the expected approx. 1:1 mixture of two diastereomers. We were able to separate most of the diastereomers of **2** by careful chromatography (Scheme 3). All products were *trans* geometric isomers (Table 2). $^1$H NMR spectroscopy revealed that the diastereomer with the *cis* configuration (designated *ii*) had only small vicinal coupling constants for both geminal protons 12, for example in the case of **2a**-*ii*: $J = 4.8$ and 4.9 Hz at $\delta = 2.80$ and 2.28 ppm, respectively. Furthermore, a small vicinal coupling constant of $J = 3.8$ Hz of the methoxycarbonyl methine ring-proton 8 at $\delta = 3.64$ ppm showed that the conformation of **2a**-*ii* is such that the methoxycarbonyl group occupies the




**1a**: $R^1 = Et$, $R^2 = (CH_3)_2C{=}CH$ — **2a**, 46%[b]
**1b**: $R^1 = Me$, $R^2 = CH_3CH{=}CH$ — **2b**, 39%
**1c**: $R^1 = Me$, $R^2 = (CH_3)_2CH(CH_2)_3(CH_3)CHCH_2$ — **2c**, 33%
**1d**: $R^1 = Et$, $R^2 = (CH_3)_2(MeO)CH(CH_2)_3(CH_3)CHCH_2$ — **2d**, 38%
**1e**: $R^1 = Et$, $R^2 = (CH_3)_2CH(CH_2)_3(CH_3)CHCH_2$ — **2e**, 35%

[a] See experimental; [b] isolated yields of both diastereomers

**Scheme 3**

equatorial position and the 2-methylprop-1-enyl group the axial position. In the *trans* configuration **2a**-*i*, one of die vicinal coupling constants of one of the geminal protons is quite large, ($J = 12.8$ Hz, *trans*-diaxial, $\delta = 2.91$ ppm), and both methoxycarbonyl- and 2-methylprop-1-enyl groups are in the equatorial position and probably slightly distorted (moved out of the plane) due to steric interaction. This has an effect on the olefinic protons 5 and 6 of the side chain. Proton 5 is more deshielded, whereas proton 6 is more shielded than that of the *cis* molecule. This feature was used as another diagnostic tool for the other molecules **2**. Biological screening tests revealed that cyclohexenonedicarboxylates **2d** and **2e** show some activity against ectoparasites (flea larvea and mites) in pets and cattle.

In summary, sodium benzoate is a soft base catalyst to induce a regioselective tandem *Michael*-aldol self-condensation of $\gamma,\delta$-unsaturated $\beta$-ketoesters (**1**) to furnish 4-vinyl-6-oxocyclohex-1-ene-1,3-dicarboxylates (**2**) in the expected two diastereomers without decarboxylation of the $\beta$-ketoester moiety of the substrate **1** or the product **2**.

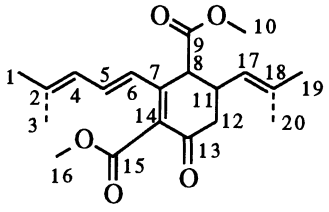
## Experimental

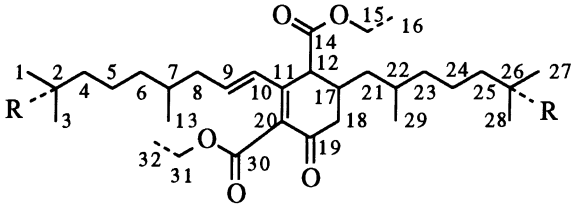
All reactions were carried out in a nitrogen atmosphere. $^1$H NMR and $^{13}$C NMR were recorded on a Varian FT-80 at 80 or 20 MHz, respectively, or on a Varian 200 spectrometer at 200 MHz and 50.3 MHz, respectively, in $CDCl_3$ with *TMS* as internal standard. High resolution electron ionization (El) mass spectra were obtained from a Varian MAT 311A instrument, and high resolution chemical ionization (Cl) mass spectra using ammonia were obtained from a Kratos Concept ISQ instrument. Ultraviolet absorbance was measured as solutions in 96% EtOH on a Varian SuperScan 3 spectrophotometer. Microanalyses were performed by Microanalytisches Labor Pascher (Bonn, Germany). Column chromatography was performed using Merck Si-60 (40–63 mm) silica gel. Diethyl ether (ether) was dried and distilled from sodium or $LiAlH_4$. Light petroleum is the hexane fraction boiling between 40 and 60°C.

*Methyl 7-methyl-3-oxoocta-4,6-dienoate* (**1a**)

Methyl 7-methyl-3-oxoocta-4,6-dienoate (**1a**; 1.00 g, 5.49 mmol) in benzene (10 ml) was condensed in the presence of sodium benzoate (0.80 g, 5.55 mmol), magnesium sulfate (0.70 g, 5.82 mmol), hydroquinone (0.60 g, 5.45 mmol), and *TEBAC* (1.25 g, 5.49 mmol) and heated at 60°C for 5 days.

**Table 1.** $^{13}C$ Chemical shifts ($\delta_C$ in ppm) of compounds **2a**, **2b**, **2c**, **2d**, and **2e**[a]





| Carbon | **2a**–*i*[b] | **2a**–*ii* | **2b**–*i*[b] | **2b**–*ii* |
|---|---|---|---|---|
| 1, 19 | 25.64, 26.50 | 25.85, 26.52 | 17.89 | 17.85 |
| 2 | 144.82 | 145.34 | 139.89 | 139.17 |
| 18 | 135.09 | 135.67 | 138.17 | 137.78 |
| 4 | 126.22 | 125.84 | 127.80 | 127.91 |
| 5 | 135.46 | 136.21 | 131.79 | 131.79 |
| 6 | 124.16 | 123.11 | 125.71 | 126.63 |
| 7 | 147.94 | 149.98 | 148.80 | 146.99 |
| 8 | 47.49 | 45.71 | 46.26 | 46.89 |
| 3, 20 | 17.88, 18.91 | 18.07, 18.95 | | |
| 9, 15 | 166.89, 171.56 | 167.17, 170.39 | 169.98, 166.92 | 166.73, 171.28 |
| 10, 16 | 52.22, 52.58 | 52.28 (2x) | 52.25 (2x) | 52.30, 52.70 |
| 11 | 35.91 | 35.45 | 39.18 | 39.57 |
| 12 | 40.22 | 39.16 | 38.26 | 39.57 |
| 13 | 193.90 | 194.98 | 194.87 | 193.77 |
| 14 | 132.04 | 131.69 | 132.32 | 130.56 |
| 17 | 125.82 | 125.34 | 129.76 | 130.56 |

| Carbon | **2c**[b,d] | **2d**-*i*[c,d] | **2d**-*ii*[e,d] | **2e**-*i*[c,d] | **2e**-*ii*[e,d] |
|---|---|---|---|---|---|
| 1, 3, 27, 28 | 22.60 (2x), 22.69 (2x) | 24.75 (4x) | 24.74 (4x) | 22.46 (2x), 22.57 (2x) | 22.49 (2x), 22.60 (2x) |
| 2, 26 | 27.97, 29.28 | 74.28 | 74.27 (2x) | 27.81 (2x) | 27.86 (2x) |
| 4, 25 | 39.25 (2x) | 39.83 (2x) | 39.81 (2x) | 39.01 (2x) | 39.03 (2x) |
| 5, 24 | 24.58, 24.76 | 28.96 (2x) | 28.95, 29.68 | 24.39, 24.66 | 24.38, 24.64 |
| 6, 23 | 37.29, 37.37 | 21.03, 20.77 | 21.01, 20.74 | 36.77, 37.24 | 36.68, 36.83 |
| 7, 22 | 33.19, 33.82 | 32.82 (2x) | 33.40, 33.97 | 32.98, 33.52 | 32.95, 33.00 |
| 8 | 41.17 | 41.03 | 40.94 | 41.16 | 41.02 |
| 9 | 142.29 | 142.04 | 141.07 | 142.17 | 141.31 |
| 10 | 128.00 | 127.70 | 128.45 | 127.75 | 128.64 |
| 11 | 149.00 | 148.64 | 146.63 | 148.77 | 146.37 |
| 12 | 46.10 | 45.88 | 47.24 | 45.94 | 45.62 |
| 13, 29 | 19.55 (2x) | 19.11, 19.30 | 18.90, 19.27 | 19.27, 19.44 | 19.43, 19.48 |
| 14, 30 | 171.65 (2x) | 166.42, 169.67 | 171.08 (2x) | 166.53, 169.78 | 166.24, 171.27 |
| 15, 31 | 52.15 (2x) | 61.15, 61.30 | 61.22 (2x) | 61.22 (2x) | 61.35, 61.50 |
| 16, 32 | | 14.02 (2x) | 14.01 (2x) | 14.11 (2x) | 14.08, 14.12 |
| 17 | 36.93 | 36.99 | 36.98 | 36.77 | 36.83 |
| 18 | 40.91 | 39.99 | 40.53 | 40.72 | 41.05 |
| 19 | 195.44 | 195.60 | 194.37 | 195.74 | 194.89 |
| 20 | 132.28 | 132.08 | 131.72 | 132.13 | 131.81 |
| 21 | 37.47 | 37.30 | 37.41 | 37.14 | 37.11 |
| $R$ = OMe | | 48.89 | 48.87 | | |

[a] At room temperature in $CDCl_3$; consult Scheme 3 for compounds; [b] at 20 MHz; [c] at 50 MHz; [d] signal assignments are not accurate; a bundle of peaks are in the aliphatic region, correlated with HETCOR $^1H$-$^{13}C$ NMR techniques and APT experiments; some signals can be interchanged; [e] an almost identical set of peaks for the diastereomer due to the racemic aldehyde mixture used was obtained in equimolar amounts, only one set is given

**Table 2.** $^1$H Chemical shifts ($\delta_H$ in ppm) of compounds **2a**, **2b**, **2c**, **2d**, and **2e**[a]

| Proton | **2a**-*i* | *J* (Hz) | **2a**-*ii* | *J* (Hz) | **2b**-*i* | *J* (Hz) | **2b**-*ii* | *J* (Hz) |
|---|---|---|---|---|---|---|---|---|
| 1, 19 | 1.69, 1.73 | 2×s | 1.66, 1.68 | 2×s | 1.70, 1.84 | 2×d, 5.3 and 5.2 | 163, 1.83 | 2×d, 4.7 and 5.2 |
| 2, 18 | | | | | 5.43–6.37 | m | 5.45–6.38 | m |
| 3, 20 | 1.86 | s | 1.84, 1.85 | 2×s | | | | |
| 4 | 6.00 | d, 11.2 | 5.97 | d, 11.0 | 5.43–6.37 | m | 5.45–6.38 | m |
| 5 | 7.20 | dd, 15.5, 11.2 | 7.01 | dd, 15.1, 11.0 | 6.75 | dm, 16.0 | 6.67 | dm, 16.0 |
| 6 | 6.19 | d, 15.5 | 6.23 | d, 15.1 | 5.43–6.37 | m | 5.45–6.38 | m |
| 8 | 3.71 | d, 5.0 | 3.64 | d, 3.8 | 3.66–3.85 | m | 3.65–3.77 | m |
| 10, 16 | 3.70, 3.82 | 2×s | 3.71, 3.83 | 2×s | 3.68, 3.84 | 2×s | 3.72, 3.85 | 2×s |
| 11 | 3.22 | m | 3.37 | m | 2.97 | sm | 3.17 | sm |
| 12 | 2.29, | ddd, 16.4, 4.6, 0.6 | 2.28, | dd, 16.6, 4.9 | 2.40 | dm, 11.6 | 2.45, | dm, 16.8 |
| | 2.91 | ddd, 16.4, 12.8, 0.6 | 2.80 | dd, 16.6, 4.8 | 2.89 | dm, 11.6 | 2.86 | dm, 16.8 |
| 17 | 4.98 | d, 8.8 | 5.14 | d, 9.3 | 5.43–6.37 | m | 5.45–6.38 | m |

| Proton | **2c** | *J* (Hz) | **2d**-*i*[b] | *J* (Hz) | **2d**-*ii*[b] | *J* (Hz) | **2e**-*i*[b] | *J* (Hz) | **2e**-*ii*[b] | *J* (Hz) |
|---|---|---|---|---|---|---|---|---|---|---|
| 1, 3, 27, 28 | 0.86 | d, 6.1 | 1.069 | s | 1.071 | s | 0.873 | d, 6.5 | 0.867 | d, 6.5 |
| 2, 7, 22, 26 | 1.5–2.3 | m | 1.4–1.7 | m | 1.4–1.7 | m | 1.4–1.7 | m | 1.4–1.7 | m |
| 4, 5, 6, 21, 23, 24, 25 | 1.0–1.5 | m | 1.1–1.5 | m | 1.1–1.5 | m | 1.1–1.5 | m | 1.1–1.5 | m |
| 13, 29 | 0.86 | d, 6.1 | 0.808 | d, 6.0 | 0.807 | d, 7.0 | 0.873 | d, 6.5 | 0.851 | d, 6.6 |
| 8 | 1.5–2.3 | m | 1.9–2.2 | m | 1.9–2.2 | m | 2.041 | dm, 14.0, 7.2 | 1.92–2.10 | m |
| | | | | | | | 2.235 | dm, 14.0, 7.0 | | |
| 9 | 6.54 | dt, 15.8, 6.1 | 6.413 | dt, 15.6, 7.4 | 6.18–6.25 | m | 6.494 | dt, 15.8, 7.2 | 6.289 | sm |
| 10 | 6.07 | d, 15.8 | 6.145 | dm, 15.6 | 6.18–6.25 | m | 6.226 | dm, 15.8 | 6.289 | sm |
| 12 | 3.6–3.8 | m | 3.648, 3.623 | 2×d, 5.2, 4.8[c] | 3.525, 3.473 | 2×d, 3.0, 3.0[c] | 3.701 | d, 4.5 | 3.600, 3.548 | 2×d, 2.4, 3.1[c] |
| 15, 31 | 3.70, 3.85 | 2×s | 4.277, 4.117 | 2×q, 7.2 | 4.283, 4.128 | 2×q, 7.2 | 4.358, 4.195 | 2×q, 7.1 | 4.343, 4.194 | 2×q, 7.1 |
| 16, 32 | | | 1.276, 1.192 | 2×t, 7.2 | 1.277, 1.196 | 2×t, 7.2 | 1.269, 1.355 | 2×t, 7.1 | 1.260, 1.344 | 2×t, 7.1 |
| 17 | 2.35–2.73 | m | 1.9–2.2 | m | 1.9–2.2 | m | 2.332–2.72 | m | 2.54–2.68 | m |
| 18 | 2.35–2.73 | m | 2.2–2.6 | m | 2.2–2.6 | m | 2.1–2.9 | m | 2.829, | dd, 16.7, 5.2 |
| | | | | | | | | | 2.294 | dd, 16.7, 3.1 |
| $R$ = OMe | | | 3.098 | s | 3.104 | s | | | | |

[a] At 80 MHz $CDCl_3$; [b] at 200 MHz in $CDCl_3$; [c] due to racemic aldehyde used for the preparation of **1c**, **1d**, and **1e**, the second set of **2d**-*i*, **2d**-*ii*, and **2e**-*ii* has almost identical chemical shifts or coupling constants except for proton 12

The reaction mixture was diluted with ether: light petroleum (1:1, 20 ml), washed with aqueous saturated sodium hydrogen carbonate solution, and the dried extract was filtered over a bed of silica gel. The filtrate was concentrated and the residue chromatographed on silica gel to give after elution with ether: light petroleum (1:4) dimethyl 4-(4-methylpenta-1,3-dienyl)-2-(2-methylprop-1-enyl)-6-oxocyclohex-1-ene-1,3-dicarboxylate (**2a**) in a mixture of two diastereomers **2a**-*i* (0.24 g, 25%) and **2a**-*ii* (0.20 g, 21%).

$C_{20}H_{26}O_5$; calcd.: C 70.56, H 8.07. found: C 70.16, H 8.07; $\lambda_{max} = 343$, 230 nm ($\varepsilon = 25800$, 4900); HRMS (El): calcd. for $C_{20}H_{26}O_5$ ($MH^+$): $m/z = 346.1780$, found: $m/z = 346.1793$.

*Methyl 3-oxoocta-4,6-dienoate* (**1b**)

Methyl 3-oxoocta-4,6-dienoate (**1b**; 2.00 g, 11.9 mmol) in benzene (12 ml) was condensed in the presence of sodium benzoate (1.80 g, 12.5 mmol), magnesium sulfate (1.50 g, 12.5 mmol), hydroquinone (1.50 g, 13.6 mmol), and *TEBAC* (2.00 g, 8.78 mmol) and heated at 75°C for 45 h. The reaction mixture was diluted with ether: light petroleum (1:1, 20 ml), washed with aqueous saturated sodium hydrogen carbonate solution, and the dried extract was filtered over a bed of silica gel. The filtrate was concentrated and the residue chromatographed on silica gel to give after elution with ether: light petroleum (1:4) dimethyl 4-(penta-1,3-dienyl)-2-(prop-1-enyl)-6-oxocyclohex-1-ene-1,3-dicarboxylate **2b** in a mixture of two diastereomers **2b**-*i* (0.41 g, 22%) and **2b**-*ii* (0.32 g, 17%).

*Methyl 7,11-dimethyl-3-oxododec-4-enoate* (**1c**)

Methyl 7,11-dimethyl-3-oxododec-4-enoate (**1c** [14]; 0.80 g, 3.14 mmol) in benzene (10 ml) was condensed in the presence of sodium benzoate (0.45 g, 3.12 mmol), magnesium sulfate (0.7 g, 5.82 mmol), hydroquinone (0.40 g, 3.63 mmol), and *TEBAC* (0.70 g, 3.1 mmol) and heated at 75°C for 36 h. The reaction mixture was diluted with ether: light petroleum (1:1, 20 ml) and filtered over a bed of silica gel. The filtrate was concentrated and the residue chromatographed on silica gel to give some recovered keto ester **1c** (10%) and after elution with ether: light petroleum (1:4) dimethyl 4-(2,6-dimethylheptyl)-2-(4,8-dimethylnon-1-enyl)-6-oxocyclohex-1-ene-1,3-dicarboxylate **2c** in a mixture of two times two diastereomers (0.25 g, 32%).

$C_{30}H_{50}O_5$; calcd.: C 73.43, H 10.27; found: C 73.79, H 10.27; $\lambda_{max} = 282.5$ nm ($\varepsilon = 20200$); HRMS (El) calcd. for $C_{30}H_{50}O_5$ ($MH^+$): $m/z = 490.3658$, found: $m/z = 490.3659$.

*Ethyl 11-methoxy-7,11-dimethyl-3-oxododec-4-enoate* (**1d**)

Ethyl 11-methoxy-7,11-dimethyl-3-oxododec-4-enoate (**1d** [14, 21]; 1.64 g, 5.50 mmol) in absolute ethanol (15 ml) was condensed in the presence of sodium benzoate (1.1 g, 7.6 mmol), magnesium sulfate (1.1 g, mmol), a catalytic amount of hydroquinone, and *TEBAC* (0.45 g, mmol) and heated at 50°C for 5 days to give after workup as described for **1a** diethyl 4-(6-methoxy-2,6-dimethylheptyl)-2-(8-methoxy-4,8-dimethylnon-1-enyl)-6-oxocyclohex-1-ene-1,3-dicarboxylate **2d** in 2 separated mixtures of 2 diastereomers (4 diastereomers) (0.60 g, 38%).

IR: $\nu_{max}$ (film) = 2970 (s), 2938 (s), 1732 (s), 1672 (s), 1632 (m), 1592 (m), 1464 (m), 1367 (m), 1237 (m), 1152 (s), 1084 (m), 1032 (m), 733 (m) $cm^{-1}$; HRMS (CI): calcd. for $C_{34}H_{59}O_7$ ($MH^+$): $m/z = 579.4261$, found: $m/z = 579.4272$; MS (CI, ammonia): $m/z = 596$ ($M+NH_4$), 100), 579 (40), 564 (20), 547 (25%), 517 (30).

*Ethyl 7,11-dimethyl-3-oxododec-4-enoate* (**1e**)

Ethyl 7,11-dimethyl-3-oxododec-4-enoate (**1e**, [14]) was condensed in the presence of sodium benzoate, magnesium sulfate, and *TEBAC* in ethanol as described for **1d** to give diethyl 4-(2,6-

dimethylheptyl)-2-(4,8-dimethylnon-1-enyl)-6-oxocyclohex-1-ene-1,3-dicarboxylate **2e** in 2 separated mixtures of 2 diastereomers (4 diastereomers) (35%).

HRMS (CI): calcd. for $C_{32}H_{55}O_5$ ($MH^+$): $m/z = 519.4061$, found: $m/z = 519.4036$; MS (CI, ammonia): $m/z = 596$ ($M+NH_4$), 100), 579 (40), 564 (20), 547 (25%), 517 (30).

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