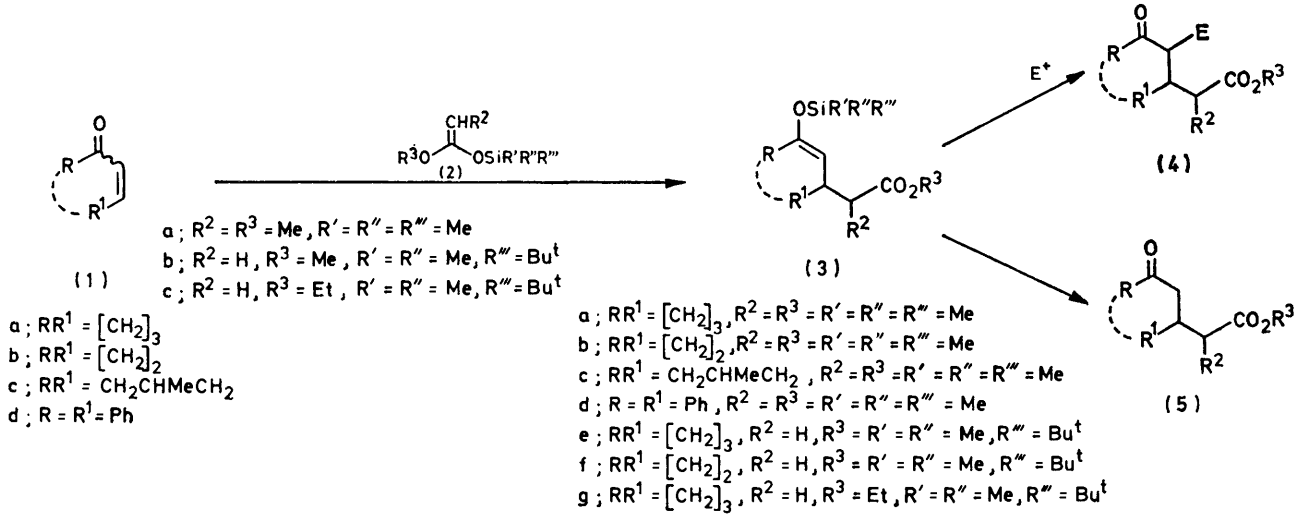
Keten Silyl Acetal Chemistry; [1] Simple Synthesis of Methyl Jasmonate † and Related Compounds by Utilising Keten Methyl Dimethyl-t-butylsilyl Acetal

By **Yasuyuki Kita, Jun Segawa, Jun-ichi Haruta, Hitoshi Yasuda,** and **Yasumitsu Tamura,*** Faculty of Pharmaceutical Sciences, Osaka University, 1–6 Yamada-oka, Suita, Osaka, Japan

Conjugate addition of keten silyl acetals to α,β-unsaturated carbonyl compounds in acetonitrile gave a quantitative yield of the corresponding methyl (3-trialkylsiloxyalk-2-enyl)acetates; subsequent site-specific electrophilic substitution yielded the corresponding 2-substituted 3-(alkoxycarbonylmethyl)alkanones. These novel addition and sequential alkylation reactions could be applied to a simple synthesis of methyl jasmonate, methyl didehydrojasmonate, and methyl dihydrojasmonate.

In a recent communication,[2] we briefly reported the conjugate addition of keten silyl acetals (2) to α,β-unsaturated carbonyl compounds (1) in acetonitrile to give a quantitative yield of the corresponding methyl (3-trialkylsiloxyalk-2-enyl)acetates (3); subsequent site specific electrophilic substitution of (3) yielded the corresponding 2-substituted 3-(alkoxycarbonylmethyl)-alkanones (4). We now give a full account of this work and of its application to a simple synthesis of methyl dihydrojasmonate (11a), methyl didehydrojasmonate (12a),‡ and methyl jasmonate (13) from cyclopent-2-enone (1b).



Scheme 1

Preparation and Reactions of Methyl (3-Trialkylsiloxyalk-2-enyl)acetates (3a—g).—The Michael addition of keten silyl acetals (2) to α,β-unsaturated carbonyl compounds (1) is reported not to proceed.§ However, Mukaiyama and his co-workers have succeeded recently in bringing about the reaction of the acetals (2) with enones (1) by an activation method with titanium tetrachloride,[4] which gives methyl (3-oxoalkyl)acetates (5). We have found that the use of acetonitrile as a solvent can greatly enhance the reactivity of the acetals (2) § towards the enones (1) without catalyst to give almost quantitative yields of the corresponding *O*-silylated Michael adducts (3) ‖ instead of their hydrolysis products, the ketones (5). The silyl enolates (3a—g) were obtained pure by this method in almost quantitative yield. The attractive feature of this reaction is that the enolate (3) is obtained from the enone (1) directly; ¶ the α-substituent can then be readily introduced *via* the *O*-silyl enolate moiety as described below.

There have been many reports [8] of site-specific

† Jasmonic acid is (*Z*)-*trans*-3-oxo-2-pent-2-enylcyclopentylacetic acid.

‡ The name methyl dehydrojasmonate has also been used for this compound (G. Büchi and B. Egger, *J. Org. Chem.*, 1971, **36**, 2021).

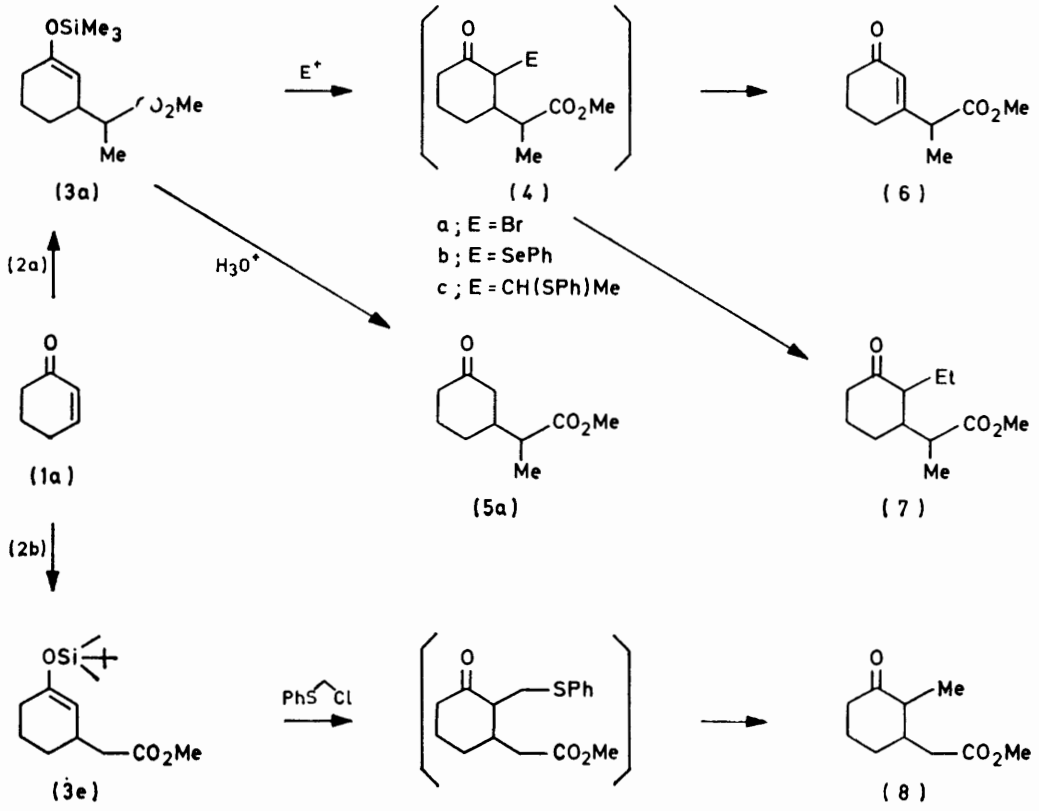
§ The aldol condensation of keten silyl acetals with carbonyl compounds is also known not to proceed except for aromatic aldehydes, which react with the acetals (2) under severe conditions (at 150 °C for 18 h), giving moderate yields of condensation products.[3]

§ A similar enhancing effect of acetonitrile has been observed in the reaction of alkyl acetylenecarboxylates with primary or secondary amines.[5]

‖ The Michael adducts could be trapped by intermolecular transfer of the mobile trialkylsilyl substituent since the reaction was performed in the absence of Lewis acid.

¶ Two approaches (i) and (ii) were examined for the preparation of (3a) but failed: (i) conjugate addition of methyl lithiopropionate to cyclohexenone (1a) at −78 °C followed by quenching with trimethylsilyl chloride (*cf.* conjugate addition of an alkyl group and subsequent silylation [6]); (ii) direct silylation of the oxo-ester (5a) to give its *O*-silyl enolate (3a) by House's methods using LDA and trimethylsilyl chloride or triethylamine, DMF, and trimethylsilyl chloride.[7]

reactions of *O*-trimethylsilyl enolates with various electrophiles, giving α-substituted carbonyl compounds. We have found that the *O*-trimethylsilyl enolate (3a) reacts with electrophiles such as *N*-bromosuccinimide (NBS),[9] phenylselenium chloride,[10] and α-chloroalkylphenylsulphide [11] to give the corresponding α-substituted cyclohexanones (4). These results and conversions of the cyclohexanones (4) into methyl 2-(3-oxocyclohex-1-enyl)propionate (6) and methyl 2-(2-ethyl-3-oxocyclohexyl)propionate (7) were mentioned in our preliminary communication.[2]



SCHEME 2

We have now found that the *O*-dimethyl-t-butylsilyl enolate (3e) obtained from (1a) and (2b) reacts with α-chloromethylphenyl sulphide in the presence of titanium tetrachloride; * desulphurization of the product with Raney nickel gives methyl (2-methyl-3-oxocyclohexyl)-acetate (8). This vicinal dialkylation of cyclohex-2-enone (1a) *via* (3e) was applied in the following simple route to jasmonoid compounds from cyclopent-2-enone (1b).

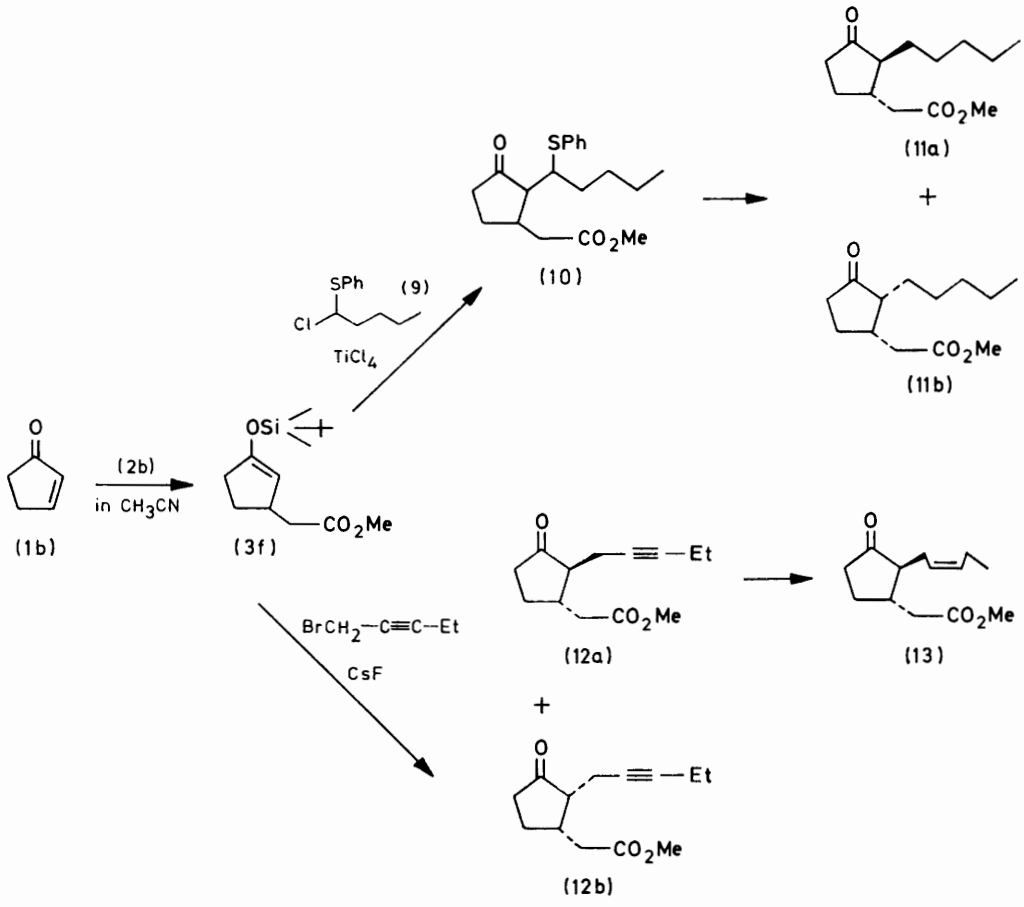
Synthesis of Methyl Jasmonate (13) *and Related Compounds* (11) *and* (12).—Much attention has been paid [13-17] to the preparation of methyl jasmonate (13) and related compounds in view of their connection with the perfume industry. Keten methyl trimethylsilyl acetal is apparently an ideal synthon for completion of the methyl jasmonate synthesis,† but its attempted production by quenching of methoxycarbonylmethanide ion with trimethylsilyl chloride gave an inseparable mixture of *C*- and *O*-silylated products.[18] Therefore, keten *S*-t-butyl *O*-trimethylsilyl thioacetal [16] and trimethylsilyl-keten methyl trimethylsilyl acetal [17] were developed as synthetic equivalents of keten methyl trimethylsilyl acetal. However, the route to methyl jasmonate (13) using the former reagent is long and the overall yield is low. The latter reagent was shown to be useful in the case of 2-alkylcyclopent-2-enones. We have now established a short and easy synthesis of jasmonoid compounds (11)—(13) based on conjugate addition of keten methyl dimethyl-t-butylsilyl acetal (2b) ‡ to cyclopent-2-enone (1b) and subsequent alkylation of the adduct (3f), in which (2b) is used as a methyl acetate equivalent. The reaction sequence is outlined in Scheme 3.

The ester (3f) obtained from (1b) and (2b) was alkylated with 1-chloro-1-phenylthiopentane (9) by using titanium tetrachloride as catalyst in methylene chloride at −60 °C to give the sulphide (10), which was desul-

* In contrast to our results, Clark [12] has reported that the *O*-dimethyl-t-butylsilyl group of cyclopentanone *O*-dimethyl-t-butylsilyl enolate is stable under the conditions of the titanium tetrachloride catalysed [2 + 2] cycloaddition with ethyl acetate.

† It is well established that keten silyl acetal derivatives react with α,β-unsaturated carbonyl compounds to give 1,4-addition products in high yields.[2,4]

‡ Although Matsuda [17] stated that the reagent (2b) could not be purified by distillation, we had already reported a high yield preparation of the reagent.[1]



SCHEME 3

phurized with Raney nickel.* A mixture of methyl dihydrojasmonate (11a) and methyl dihydro-2-*epi*-jasmonate (11b) was obtained. Epimerisation of (11b) to (11a) was carried out smoothly by the method[15] reported for methyl 2-*epi*-jasmonate. An attempt to introduce the pent-2-ynyl group into (3f) by a similar route using 1-chloro-1-phenylthiopent-2-yne failed.† However, alkylation of (3f) was performed with 1-bromopent-2-yne by using caesium fluoride in acetonitrile, to give a mixture of methyl didehydrojasmonate (12a) and its 2-epimer (12b). Epimerisation of (12b) with triethylamine in a sealed tube proceeded smoothly to give (12a). Catalytic hydrogenation of (12a) over a Lindlar catalyst to methyl (±)-jasmonate (13) is a known reaction.[14] Although none of these reactions with the acetal (2b) has been optimised, it is clear that (2b) is a useful intermediate for the preparation of methyl jasmonate and related compounds.

* A general method for the introduction of a primary alkyl group into the α-position of a silyl enolate has been reported by Fleming,[19] using Lewis acid catalysed phenylthioalkylation followed by Raney-nickel desulphurization.

† 1-Chlorophenylthiopent-2-yne could be prepared from 1-bromopent-2-yne by reaction with sodium benzenethiolate in ethanol followed by chlorination with *N*-chlorosuccinimide in CCl_4, but it decomposed under the conditions employed in the reaction of (3f) and the chloro-sulphide (9).

EXPERIMENTAL

I.r. absorption spectra were recorded with a Shimazu-IR-27G spectrometer, and n.m.r. spectra with a Hitachi R-20A (60 MHz) or R-22 (90 MHz) spectrometer. Chemical shifts are reported relative to $SiMe_4$. Low- and high-resolution mass spectra were obtained with Hitachi RMU-6E and JEOL-JMS D-300 instruments, with a direct inlet system operating at 70 eV. Column chromatography was carried out on Merck silica gel 60.

α,β-*Unsaturated Ketones* (1a—d).—The starting α,β-unsaturated ketones (1a, b, and d) were commercially available. 5-Methylcyclohex-2-enone (1c) was prepared by Heathcock's method.[20]

Keten Silyl Acetals (2a—c).[1]—These were obtained by a modification of reported methods.[18,21]

1-*Methoxy*-1-*trimethylsiloxypropene* (2a). A 1.5M-solution of n-butyl-lithium in hexane (150 ml, 225 mmol) was added dropwise to a stirred solution of di-isopropylamine (22.5 g, 225 ml) in tetrahydrofuran (THF) (150 ml) at 0 °C under argon. The mixture was stirred for 15 min under the same conditions, then cooled to −78 °C. This solution was ready for use as lithium di-isopropylamide (LDA). Methyl propionate (19.8 g, 225 mmol) was added dropwise to the freshly prepared LDA solution at −78 °C under argon, and the mixture was stirred for an additional 30 min to complete the formation of methyl lithiopropionate. Trimethylsilyl chloride (29.2 g, 270 mmol) was added dropwise with stirring at −78 °C over 10 min, and the mixture was stirred for 3 h

under the same conditions. Methyl iodide (32 g, 225 mmol) and then pentane (100 ml) were added at the same temperature. The flask was left in a refrigerator overnight and the resulting LiCl and quaternary salt precipitates were removed by filtration under reduced pressure. The filtrate was concentrated under reduced pressure. The residual oil was distilled to give the *keten acetal* (2a) as a colourless liquid (20.5 g, 57%), b.p. 46.3—46.5 °C at 23 mmHg (Found: M^+, 160.0919. $C_7H_{16}O_2Si$ requires M, 160.0919); $\nu_{max.}$ (CCl_4) 1 680 cm^{-1}; δ (CCl_4) 0.20 [9 H, s, $Si(CH_3)_3$], 1.42 (3 H, d, J 6.5 Hz, 2-$CHCH_3$), 3.45 (3 H, s, OCH_3), and 3.56 (1 H, q, J 6.5 Hz, CH=).

Dimethyl-t-butylsiloxy-1-methoxyethene (2b). Methyl acetate (2.47 g, 33 mmol) was added dropwise to a freshly prepared solution of LDA (35 mmol) in THF (35 ml) at −78 °C during 25 min. The mixture was stirred for 50 min under the same conditions, then hexamethylphosphoric triamide (HMPA) (3.5 ml) was added. The mixture was stirred for 5 min and a solution of dimethyl-t-butylsilyl chloride (5.3 g, 35 mmol) in n-pentane (10 ml) was added dropwise over 10 min. After being stirred for an additional 1 h under the same conditions, the mixture was allowed to warm to room temperature, quenched with cold water (20 ml), and extracted with n-pentane (3 × 50 ml). The extract was washed with saturated aqueous NaCl, dried($MgSO_4$), and concentrated under reduced pressure. The residual oil was distilled to give the *keten acetal* (2b) as a colourless liquid (4.54 g, 72%), b.p. 76.2—76.4 °C at 24 mmHg (Found: C, 57.0; H, 10.7. $C_9H_{20}O_2Si$ requires C, 57.4; H, 10.7%); $\nu_{max.}$ (CCl_4) 1 645 cm^{-1}; δ (CCl_4) 0.14 [6 H, s, $Si(CH_3)_2$], 0.93 (9 H, s, t-Bu), 2.95 (1 H, d, J 3 Hz, CH=), 3.10 (1 H, d, J 3 Hz, CH=), and 3.49 (3 H, s, OCH_3).

1-Dimethyl-t-butylsiloxy-1-ethoxyethene (2c). This was prepared from ethyl acetate (5.68 g, 66 mmol), LDA (70 mmol), and dimethyl-t-butylsilyl chloride (10.1 g, 70 mmol) in THF–HMPA (10 : 1; 77 ml) in 71% yield (9.3 g) by a method similar to that described for the preparation of (2b); b.p. 67—68 °C at 10 mmHg (Found: C, 59.15; H, 11.05. $C_{10}H_{22}O_2Si$ requires C, 59.35; H, 11.0%); $\nu_{max.}$ (CCl_4) 1 645 cm^{-1}; δ (CCl_4) 0.16 [6 H, s, $Si(CH_3)_2$], 0.93 (9 H, s, t-Bu), 1.30 (3 H, t, J 7 Hz, CH_2CH_3), 2.92 (1 H, d, J 3 Hz, CH=), 3.08 (1 H, d, J 3 Hz, CH=), and 3.68 (2 H, q, J 7 Hz, OCH_2).

General Procedure for the Preparation of Methyl (3-Trialkylsiloxyalk-2-enyl)acetates (3a—g).—The following procedure is typical. To a stirred solution of the α,β-unsaturated ketone (12.5 mmol) in dry acetonitrile (11 ml) was added the keten acetal (2) (12.5 mmol) under argon. The mixture was stirred at 55 °C for 2 h, and a small amount of the acetal (0.2 mmol) was added every 30 min for the requisite period (*ca.* 1—2 h) to complete the reaction. The mixture was concentrated under reduced pressure. The residual oil was distilled to give the methyl (3-trialkylsiloxyalk-2-enyl)-acetate (3).

Methyl 2-(3-trimethylsiloxycyclohex-2-enyl)propionate (3a). This *enolate* was prepared from cyclohex-2-enone (1a) (1.20 g, 12.5 mmol) and the keten acetal (2a) (2.10 g, 13.1 mmol) in dry CH_3CN (11 ml) in 88% yield (2.82 g); b.p. 140—145 °C at 2.7 mmHg (Found: C, 61.0; H, 9.6. $C_{13}H_{24}O_3Si$ requires C, 60.9; H, 9.45%); $\nu_{max.}$ (CCl_4) 1 735 and 1 660 cm^{-1}; δ (CCl_4) 0.17 [9 H, s, $Si(CH_3)_3$], 0.8—2.7 (8 H, m, 3 × CH_2 and 2 × CH), 1.08 (3 H, d, J 7 Hz, $CHCH_3$), 3.59 (3 H, s, OCH_3), and 4.58 (1 H, d, J 8.5 Hz, CH=).

Methyl 2-(3-trimethylsiloxycyclopent-2-enyl)propionate (3b). This *enolate* was prepared from cyclopent-2-enone (1b) (93.7 mg, 1.14 mmol) and the keten acetal (2b) (234 mg, 1.46 mmol) in dry CH_3CN (1 ml) in 98% yield (272 mg); b.p. 135—145 °C at 2.2 mmHg (bath temp.) (Found: C, 59.2; H, 9.2. $C_{12}H_{22}O_3Si$ requires C, 59.45; H, 9.15%); $\nu_{max.}$ (CCl_4) 1 735 and 1 640 cm^{-1}; δ (CCl_4) 0.20 [9 H, s, $Si(CH_3)_3$], 0.9—3.1 (6 H, m, 2 × CH_2 and 2 × CH), 1.08 (3 H, d, J 7 Hz, $CHCH_3$), 3.57 (3 H, s, OCH_3), and 4.3—4.6 (1 H, m, CH=).

Methyl 2-(5-methyl-3-trimethylsiloxycyclohex-2-enyl)propionate (3c). This *enolate* was prepared from 5-methylcyclohex-2-enone (1c) (98.2 mg, 0.89 mmol) and the keten acetal (2a) (265 mg, 1.65 mmol) in dry CH_3CN (1 ml) in 96% yield (230 mg); b.p. 155—165 °C at 2.5 mmHg (bath temp.) (Found: C, 62.3; H, 9.55. $C_{14}H_{26}O_3Si$ requires C, 62.15; H, 9.7%); $\nu_{max.}$ (CCl_4) 1 740 and 1 665 cm^{-1}; δ (CCl_4) 0.15 [3/8 × 9 H, s, $Si(CH_3)_3$], 0.16 [5/8 × 9 H, s, $Si(CH_3)_3$], 0.6—2.7 (13 H, m, 2 × CH_3, 2 × CH_2, and 3 × CH), 3.59 (3 H, s, OCH_3), and 4.4—4.9 (1 H, m, CH=).

Methyl 2-(1,3-diphenyl-3-trimethylsiloxyprop-2-enyl)propionate (3d). This *enolate* was prepared from benzylideneacetophenone (1d) (81.3 mg, 0.39 mmol) and the keten acetal (2a) (238 mg, 1.49 mmol) in dry CH_3CN (1 ml) in 99% yield (144 mg); b.p. 195—205 °C at 0.05 mmHg (bath temp.) (Found: M^+, 368.1855. $C_{22}H_{28}O_3Si$ requires M, 368.1806); $\nu_{max.}$ (CCl_4) 1 740 and 1 645 cm^{-1}; δ (CCl_4) 0.07 [9 H, s, $Si(CH_3)_3$], 1.01 (1/2 × 3 H, d, J 7 Hz, $CHCH_3$), 1.20 (1/2 × 3 H, d, J 7 Hz, $CHCH_3$), 3.36 (1/2 × 3 H, s, OCH_3), 3.56 (1/2 × 3 H, s, OCH_3), 5.22 (1/2 × 1 H, d, J 7.5 Hz, CH=), 5.39 (1/2 × 1 H, d, J 7 Hz, CH=), and 6.8—7.1 (10 H, m, aromatic).

Methyl (3-dimethyl-t-butylsiloxycyclohex-2-enyl)acetate (3e). This *enolate* was prepared from cyclohex-3-enone (1a) (497 mg, 5.17 mmol) and the keten acetal (2b) (1.07, 5.66 mmol) in dry CH_3CN (5 ml) in 90% yield (1.33 g); b.p. 134 °C at 0.4 mmHg (Found: C, 63.2; H, 10.2. $C_{15}H_{28}O_3Si$ requires C, 63.35; H, 9.9%); $\nu_{max.}$ (CCl_4) 1 730 and 1 665 cm^{-1}; δ (CCl_4) 0.12 [6 H, s, $Si(CH_3)_2$], 0.6—2.9 (9 H, m, 4 × CH_2 and CH), 0.92 (9 H, s, t-Bu), 3.60 (3 H, s, CH_2), and 4.5—4.7 (1 H, m, CH=).

Methyl (3-dimethyl-t-butylsiloxycyclopent-2-enyl)acetate (3f). This *enolate* was prepared from cyclopent-2-enone (1b) (105 mg, 1.28 mmol) and the keten acetal (2b) (443 mg, 2.35 mmol) in dry CH_3CN (1 ml) in 95% yield (329 mg); b.p. 142—143 °C at 1.0 mmHg (Found: M^+, 270.1659. $C_{14}H_{26}O_3Si$ requires M, 270.1652); $\nu_{max.}$ (CCl_4) 1 735 and 1 635 cm^{-1}; δ (CCl_4) 0.13 [6 H, s, $Si(CH_3)_2$], 0.91 (9 H, s, t-Bu), 1.8—2.5 (5 H, m, 2 × CH_2 and CH), 2.21 (2 H, d, J 7 Hz, $CH_2CO_2CH_3$), 3.57 (3 H, s, OCH_3), and 4.3—4.6 (1 H, m, CH=).

Ethyl (3-dimethyl-t-butylsiloxycyclohex-2-enyl)acetate (3g). This *enolate* was prepared from cyclohex-2-enone (1a) (114 mg, 1.19 mmol) and the keten acetal (2c) (475 mg, 2.26 mmol) in dry CH_3CN (1 ml) in 90% yield (317 mg); b.p. 140—150 °C at 1.2 mmHg (bath temp.) (Found: C, 64.0; H, 10.1. $C_{16}H_{30}O_3Si$ requires C, 64.35; H, 10.55%); $\nu_{max.}$ (CCl_4) 1 730 and 1 660 cm^{-1}; δ (CCl_4) 0.12 (6 H, s, $SiMe_2$), 0.6—2.3 (7 H, m, 3 × CH_2 and CH), 0.91 (9 H, s, t-Bu), 1.23 (3 H, t, J 7 Hz, OCH_2CH_3), 2.15 (2 H, d, J 8 Hz, CH_2CO_2Et), 4.06 (2 H, q, OCH_2), and 4.5—4.8 (1 H, m, CH=).

Methyl 2-(2-Bromo-3-oxocyclohexyl)propionate (4a).—To a solution of the silyl enolate (3a) (456 mg, 11 mmol) in dry THF (110 ml) was added NBS (2.02 g, 11 mmol) in portions at 15 °C under argon. The mixture was stirred for 15 min under the same conditions, washed with saturated aqueous NaCl and aqueous sodium hydrogencarbonate, and extracted with light petroleum (3 × 200 ml). The extract was

dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel [benzene–EtOAc (10 : 1 v/v) as eluant] to give *trans*-(4a) (976 mg, 34%), *cis*-(4a) (781 mg, 28%), and a mixture of both isomers (109 mg, 4%). The *trans*-ester (4a) showed $\nu_{max.}$ (CCl_4) 1 730 cm^{-1}; δ (CCl_4) 1.13 (5/7 × 3 H, d, *J* 7 Hz, $CHCH_3$), 1.23 (2.7 × 3 H, d, *J* 7 Hz, $CHCH_3$), 1.4—3.4 (8 H, m, 3 × CH_3 and 2 × CH), 3.64 (3 H, s, OCH_3), 4.32 (5/7 × 1 H, d, *J* 9.5 Hz, CHBr), and 4.64 (2/7 × 1 H, d, *J* 8 Hz, CHBr); *m/z* 263 (M^+). The *cis*-ester (4a) showed $\nu_{max.}$ (CCl_4) 1 730 cm^{-1}; δ (CCl_4) 1.16 (3/8 × 3 H, d, *J* 7 Hz, $CHCH_3$), 1.24 (5/8 × 3 H, d, *J* 7 Hz, $CHCH_3$), 1.4—3.3 (8 H, m, 3 × CH_2 and 2 × CH), 3.63 (3/8 × 3 H, s, OCH_3), 3.65 (5/8 × 3 H, s, OCH_3), and 4.15—4.3 (1 H, br, s, CHBr); *m/z* 263 (M^+). Spectroscopic data of these compounds were fully consistent with the proposed structures, but a sample for analysis could not be obtained because of decomposition upon distillation. These bromo compounds were used for the next reaction without further purification.

Methyl 2-[3-*Oxo*-2-(1-*phenylthioethyl*)*cyclohexyl*]*propionate* (4c).—To a solution of the silyl enolate (3a) (260 mg, 1.01 mmol) in dry CH_2Cl_2 (2 ml) was added 1-chloroethyl phenyl sulphide (173 mg, 1.22 mmol) in portions at 15 °C under argon. A catalytic amount of $ZnBr_2$ (10 mg, 0.04 mmol) was added, and the mixture was stirred at room temperature for 15 min and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel [benzene–EtOAc (15 : 1 v/v) as eluant] to give the sulphide (4c) (188 mg, 58%); $\nu_{max.}$ (CCl_4), 1 740 and 1 710 cm^{-1}; *m/z* 321 (M^+). This was used for the next reaction without further purification because of decomposition upon distillation.

Hydrolysis of the Enolate (3a) *to Methyl* 2-(3-*Oxocyclohexyl*)-*propionate* (5a).—A solution of (3a) (75 mg, 0.29 mmol) in aqueous N-HCl–ether (2 : 1; 6 ml) was stirred at room temperature for 24 h. The aqueous solution was neutralised with saturated aqueous $NaHCO_3$. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel [chloroform as eluant] to give the ester (5a) as a syrup (46 mg, 87%); $\nu_{max.}$ (CCl_4), 1 740 and 1 715 cm^{-1}; δ (CCl_4) 0.9—2.7 (10 H, m, 4 × CH_2 and 2 × CH), 1.13 (3 H, d, *J* 7 Hz, $CHCH_3$), and 3.60 (3 H, s, OCH_3); *m/z* 184 (M^+). All spectral data were identical with those of an authentic sample.[22]

Methyl 2-(3-*Oxocyclohex*-1-*enyl*)*propionate* (6).—(a) *From the* trans-*ester* (4a). A stirred solution of *trans*-(4a) (128 mg, 0.49 mmol), LiBr (524 mg, 6.02 mmol), and Li_2CO_3 (326 mg, 4.4 mmol) in dimethylformamide (DMF) (10 ml) was heated at 100 °C for 8 h. The mixture was partitioned between water (20 ml) and ether (20 ml). The aqueous layer was extracted with ether (2 × 20 ml). The combined organic layer was washed with saturated aqueous $NaHCO_3$ (20 ml), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel [benzene–EtOAc (7 : 1 v/v) as eluant] to give the *ester* (6) (60 mg, 68%) as an oil (Found: C, 65.55; H, 7.9. $C_{10}H_{14}O_3$ requires C, 65.9; H, 7.75%); $\nu_{max.}$ (CCl_4) 1 740, 1 675, and 1 630 cm^{-1}; δ (CCl_4) 1.31 (3 H, d, *J* 7 Hz, $CHCH_3$), 1.5—2.5 (6 H, m, 3 × CH_2), 3.23 (1 H, q, *J* 7 Hz, $CHCH_3$), 3.62 (3 H, s, OCH_3), and 5.74 (1 H, br, s, CH=); *m/z* 182 (M^+).

(b) *From the* cis-*ester* (4a). The *cis*-isomer (269 mg, 1.02 mmol) was treated with LiBr (1.09 g, 12.6 mmol) and Li_2CO_3 (682 mg, 9.23 mmol) in DMF (20 ml) at 100 °C for 5 h to give the ester (6) (125 mg, 67%), identical with the sample prepared from *trans*-(4a).

Methyl 2-(3-*Oxocyclohex*-1-*enyl*)*propionate* (6) via *Methyl* 2-(3-*Oxo*-2-*phenylselenocyclohexyl*)*propionate* (4b).—To a stirred solution of the silyl enolate (3a) (348 mg, 1.36 mmol) in dry CH_2Cl_2 (2 ml), a solution of PhSeCl (261 mg, 1.36 mmol) in dry CH_2Cl_2 (5 ml) was added dropwise at −78 °C under argon during 5 min. The mixture was allowed to warm to room temperature and diluted with dry CH_2Cl_2 (15 ml). After addition of *m*-chloroperbenzoic acid (472 mg, 2.74 mmol) in portions, the mixture was stirred at room temperature for 15 min and poured into saturated aqueous Na_2SO_3. The aqueous layer was extracted with CH_2Cl_2 (20 ml). The combined organic layer was washed with aqueous $NaHCO_3$, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to give the ester (6) (125 mg, 51%), identical with the sample prepared from (4a).

Methyl 2-(2-*Ethyl*-3-*oxocyclohexyl*)*propionate* (7).—The sulphide (4c) prepared from (3a) (260 mg, 1.01 mmol) was dissolved in EtOH (6 ml) and Raney nickel (W2; 1 g) was added. The suspension was stirred at room temperature for 15 min and the nickel was filtered off. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel [benzene–EtOAc (9 : 1 v/v) as eluant] to give a mixture of *cis*- and *trans*-esters (7) [35.7 mg, 41% overall yield from (3a)] as an oil (Found: C, 67.8; H, 9.7. Calc. for $C_{12}H_{20}O_3$: C, 67.9; H, 9.5%); $\nu_{max.}$ (CCl_4) 1 735 and 1 705 cm^{-1}; δ (CCl_4) 0.86 (1/3 × 3 H, t, *J* 7 Hz, CH_2CH_3), 0.87 (2/3 × 3 H, t, *J* 7 Hz, CH_2CH_3), 1.06 (2/3 × 3 H, d, *J* 7 Hz, $CHCH_3$), 1.16 (1/3 × 3 H, d, *J* 7 Hz, $CHCH_3$), 1.2—2.8 (10 H, m, 4 × CH_2 and 2 × CH), and 3.60 (3 H, s, OCH_3).

Methyl (2-*Methyl*-3-*oxocyclohexyl*)*acetate* (8) via *Methyl* (3-*Oxo*-2-*phenylthiomethylcyclohexyl*)*acetate*.—To a stirred solution of the silyl enolate (3e) (129 mg, 0.45 mmol) and chloromethyl phenyl sulphide (170 mg, 0.77 mmol) in dry CH_2Cl_2 (0.5 ml), a solution of $TiCl_4$ (0.55 mmol) in dry CH_2Cl_2 (0.6 ml) was added dropwise at −40 °C during 10 min under argon. The mixture was quenched with saturated aqueous Na_2CO_3 (10 ml) and extracted with ether (3 × 20 ml). The extract was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel [benzene–EtOAc (9 : 1 v/v) as eluant] to give methyl (3-oxo-2-phenylthiomethylcyclohexyl)acetate (68 mg, 51%); $\nu_{max.}$ (CCl_4) 1 730, 1 710, and 1 580 cm^{-1}.

The product was not purified because of its decomposition upon distillation. The sulphide (87 mg, 0.30 mmol) was converted into the ketone (9) by reductive desulphurisation with Raney nickel (2 g) in dry EtOH (3 ml) at room temperature for 3 h. After removal of the nickel by filtration, the solution was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel [benzene–EtOAc (9 : 1 v/v) as eluant] to give a mixture of *cis*- and *trans*-esters (8) [36 mg, 34% overall yield from (3e)] as an oil (Found: M^+, 184.1096. Calc. for $C_{10}H_{16}O_3$: *M*, 184.1097); $\nu_{max.}$ (CCl_4) 1 735 and 1 705 cm^{-1}, δ (CCl_4), 0.96 (3/10 × 3 H, d, *J* 6 Hz, $CHCH_3$), 1.01 (7/10 × 3 H, d, *J* 6 Hz, $CHCH_3$), 1.2—2.8 (10 H, m, 4 × CH_2 and 2 × CH), and 3.60 (3 H, s, OCH_3). All spectral data of the major component were identical with those of an authentic sample of *trans*-methyl (2-methyl-3-oxocyclohexyl)acetate.[23]

1-*Chloro*-1-*phenylthiopentane* (9).—To a solution of benzenethiol (2.34 g, 21.3 mmol) and NaOH (0.90 g, 22.5 mmol)

in EtOH (15 ml) was added 1-iodopentane (4.23 g, 21.4 mmol) dropwise. The mixture was stirred at room temperature for 1 h and partitioned between n-pentane (50 ml) and water (50 ml). The aqueous layer was extracted with n-pentane (3 × 50 ml). The combined organic layer was washed with saturated aqueous Na_2CO_3, dried ($MgSO_4$), and concentrated under reduced pressure to give an oil, which was distilled to give 1-*phenylthiopentane* (2.67 g, 70%), b.p. 136—137 °C at 19 mmHg (Found: C, 73.2; H, 9.05. $C_{11}H_{16}S$ requires C, 73.25; H, 8.95%); δ (CCl_4) 0.5—2.1 (9 H, m, 3 × CH_2 and CH_3), 2.81 (2 H, t, *J* 7 Hz, CH_2SPh), and 6.6—7.5 (5 H, m, aromatic). The sulphide (563 mg, 3.13 mmol) was chlorinated with *N*-chlorosuccinimide (433 mg, 3.24 mmol) in dry CCl_4 (7 ml) at 0—10 °C for 2.5 h. After removal of succinimide by filtration, the solution was concentrated under reduced pressure to give the chlorosulphide (9) (584 mg, 87%), which was used for the next reaction without further purification because of its thermal instability.

Synthesis of Methyl Dihydrojasmonate (11a) via 3-*Methoxycarbonylmethyl*-2-(1-*phenylthiopentyl*)*cyclopentanone* (10).—To a stirred solution of the silyl enolate (3f) (577 mg, 2.13 mmol) and the chloro-sulphide (9) (642 mg, 2.99 mmol) in dry CH_2Cl_2 (2.5 ml), a solution of $TiCl_4$ (2.3 mmol) in dry CH_2Cl_2 (2.7 ml) was added dropwise at −60 °C during 30 min under argon. After additional stirring for 30 min under the same conditions, the mixture was allowed to warm to −30 °C, quenched with saturated aqueous Na_2CO_3 (10 ml), and extracted with ether (3 × 20 ml). The extract was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel [benzene–EtOAc (15 : 1 v/v) as eluant] to give the sulphide (10) (508 mg, 71%); $\nu_{max.}$ (CCl_4) 1 740 cm^{-1}; *m/z* 334 (M^+), used for the next reaction without further purification. The sulphide (508 mg, 1.52 mmol) was converted into a mixture of methyl dihydrojasmonate (11a) and methyl dihydro-2-*epi*-jasmonate (11b) by reductive desulphurization with Raney nickel (W2; 5 g) in dry EtOH (25 ml) at room temperature for 3 h. After removal of nickel by filtration, the solution was concentrated under reduced pressure and the residue was purified by column chromatography on silica gel [benzene–EtOAc (20 : 1 v/v) as eluant] to give a mixture of (11a) and (11b) [250 mg, 52% overall yield from (3f)]. A solution of the mixture (46 mg, 0.20 mmol) in Et_3N (2 ml) was heated in a sealed tube at 130—140 °C for 7 h.[15] Concentration followed by distillation gave (11a) (45 mg, 99%; g.l.c. purity >95%), b.p. 57—59 °C at 0.025 mmHg; $\nu_{max.}$ (CCl_4) 1 735 cm^{-1}; δ (CCl_4) 0.89 (3 H, t, *J* 4.5 Hz, CH_2CH_3), 1.0—2.8 (16 H, m, 7 × CH_2 and 2 × CH), and 3.6 (3 H, s, OCH_3). All spectral data were identical with those of an authentic sample.[13]

Synthesis of Methyl Didehydrojasmonate (12a) *from the Silyl Enolate* (3f) *and* 1-*Bromopent*-2-*yne*.—To a stirred solution of (3f) (122 mg, 0.67 mmol) and 1-bromopent-2-yne [24] (124 mg, 0.84 mmol) in CH_3CN (1.5 ml) was added anhydrous CsF (*ca.* 200 mg, 1.3 mmol) under argon. The mixture was stirred at room temperature for 3 h, poured into water (10 ml), and extracted with ether (3 × 20 ml). The combined organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (benzene as eluant) to give a mixture of (12a) and (12b); $\nu_{max.}$ (CCl_4), 1 740 cm^{-1}; δ (CCl_4) 1.09 (3 H, t, *J* 7.2 Hz, CH_2CH_3), 1.4—3.4 (12 H, m, 5 × CH_2 and 2 × CH), and 3.71 (3 H, s, OCH_3); *m/z* 222 (M^+). A solution of the mixture in Et_3N (2 ml) was heated in a sealed tube at 130—140 °C for 7 h. Concentration followed by distillation gave racemic methyl didehydrojasmonate (12a) [28 mg, 19% overall yield from (3f)], b.p. 95—120 °C at 0.01 mmHg (bath temp.). All spectroscopic and physical data were identical with those of an authentic sample.[14]

[1/1636 *Received*, 22*nd October*, 1981]

REFERENCES

[1] Previous papers in this series: Y. Kita, J. Haruta, T. Fujii, J. Segawa, and Y. Tamura, *Synthesis*, 1981, 451; Y. Kita, J. Haruta, J. Segawa, and Y. Tamura, *Tetrahedron Lett.*, 1979,4311.

[2] Y. Kita J. Segawa J. Haruta, T. Fujii, and Y. Tamura, *Tetrahedron Lett.*, 1980, **21**, 3779.

[3] P. L. Creger, *Tetrahedron Lett.*, 1972, 79.

[4] K. Saigo, M. Osaki, and T. Mukaiyama, *Chem. Lett.*, 1975, 989; 1976, 163.

[5] B. Giese and R. Huisgen, *Tetrahedron Lett.*, 1967, 1889.

[6] J. W. Patterson, jun., and J. H. Fried, *J. Org. Chem.*, 1974, **39**, 2506.

[7] H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *ibid.*, 1969, **34**, 2324.

[8] For a review, see E. W. Colvin, *Chem. Soc. Rev.*, 1978, **7**, 15.

[9] *Cf.* reaction with NBS: L. Blanco, P. Amice, and M. Conia, *Synthesis*, 1976, 194, 196.

[10] *Cf.* reaction with PhSeBr: I. Ryu, S. Murai, I. Niwa, and N. Sonoda, *Synthesis*, 1977, 874.

[11] *Cf.* reaction with chloroalkyl phenyl sulphides: I. Paterson and I. Fleming, *Tetrahedron Lett.*, 1979, 995; I. Paterson, *ibid.*, 1979, 2179.

[12] R. D. Clark and K. G. Untch, *J. Org. Chem.*, 1979, **44**, 248.

[13] E. Demole and M. Stoll, *Helv. Chim. Acta*, 1962, **45**, 692; K. Sisido, S. Kurozumi, and K. Utimoto, *J. Org. Chem.*, 1969, **34**, 2661; P. Oberhaensli, Ger. Offen., 2 008 876/1970 (*Chem. Abstr.*, 1970, **73**, 109363d); A. I. Meyers and N. Nazarenko, *J. Org. Chem.*, 1973, **38**, 175; P. Ducos and F. Rouessac, *Tetrahedron*, 1973, **29**, 3233; T. L. Ho, *Synth. Commun.*, 1974, **4**, 265; F. Johnson, K. G. Paul, and D. Favara, Ger. Offen., 2 508 295/1974 (*Chem. Abstr.*, 1976, **84**, 59783v); S. Torii, H. Tanaka, and T. Mandai, *J. Org. Chem.*, 1975, **40**, 2221; A. E. Greene and P. Crabbé, *Tetrahedron Lett.*, 1976, 4867; H. J. Monteiro, *J. Org. Chem.*, 1977, **42**, 2324; S. Torii, H. Tanaka, and Y. Kobayashi, *ibid.*, 1977, p. 3473; P. Dubs and R. Stüssi, *Helv. Chim. Acta*, 1978, **61**, 990, 998; F. Näf and R. Decorzant, *ibid.*, p. 2524; K. Kondo, Y. Takahatake, K. Sugimoto, and D. Tunemoto, *Tetrahedron Lett.*, 1978, 907; J. Tsuji, K. Kasuga, and T. Takahashi, *Bull. Chem. Soc. Jpn.*, 1979, **52**, 216; J. Tsuji, Y. Kobayashi, H. Kataoka, and T. Takahashi, *Tetrahedron Lett.*, 1980, **21**, 1475; N. Fukamiya, M. Okano, and T. Aratani, *Chem. Ind.*, 1980, 86.

[14] G. Büchi and B. Egger, *J. Org. Chem.*, 1971, **36**, 2021.

[15] H. Tanaka and S. Torii, *J. Org. Chem.*, 1975, **40**, 462.

[16] H. Gerlach and P. Künzler, *Helv. Chim. Acta*, 1978, **61**, 2503.

[17] I. Matsuda, S. Murata, and Y. Izumi, *J. Org. Chem.*, 1980, **45**, 237.

[18] C. Ainsworth, F. Chen, and Y.-N. Kuo, *J. Organomet. Chem.*, 1972, **46**, 59.

[19] I. Paterson and I. Fleming, *Tetrahedron Lett.*, 1979, 995, and references cited therein.

[20] A. J. Birch, *J. Chem. Soc.*, 1947, 1270; R. D. Clark and C. H. Heathcock, *J. Org. Chem.*, 1976, 41, 636; 1973, **38**, 3658; R. M. Blankenship, K. A. Burdett, and J. S. Swenton, *ibid.*, 1974, **39**, 2300.

[21] C. R. Kruger and E. G. Rochow, *J. Organomet. Chem.*, 1964, **1**, 476; M. W. Rathke and D. F. Sullivan, *Synth. Commun.*, 1973, **3**, 67; Y.-N. Kuo, F. Chen, C. Ainsworth, and J. J. Bloomfield, *Chem. Commun.*, 1971, 136; A. D. Petrov, S. I. SadykhZade, and E. I. Filatova, *Zh. Obsch. Khim.*, 1959, **29**, 2936; E. Yoshii, Y. Kobayashi, T. Koizumi, and T. Oribe, *Chem. Pharm. Bull.*, 1974, **22**, 2767; I. Ojima, M. Kumagai, and Y. Nagai, *J. Organomet. Chem.*, 1976, **111**, 43; I. R. Lutsenko, J. I. Baukov, and G. S. Burlachenko, *ibid.*, 1965, **3**, 478; I. Ojima and S. Inaba, *Yuki Gosei Kagaku Kyokai Shi*, 1978, **36**, 610.

[22] D. K. Banerjee and P. S. Halwe, *J. Ind. Chem. Soc.*, 1960, **37**, 669.

[23] U. Ravid, R. Ikan, and R. M. Sachs, *J. Agric. Food Chem.*, 1975, **23**, 835; compound (8) is known as a potent inhibitor of lettuce root growth and germination.

[24] E. Michel and C. Troyanowsky, *C.R. Acad. Sci., Ser. C*, 1966, **264**, 1705 (*Chem. Abstr.*, 1966, **65**, 12098f).