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New Synthesis of Megastigma-4,6,8-trien-3-ones, 3-Hydroxy-β-ionol, 3-Hydroxy-β-ionone, 5,6-Epoxy-3-hydroxy-β-ionol, and 3-Oxo-α-ionol

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The Lewis acid-catalysed reaction of 1-trimethylsiloxy-1,3-cyclohexadienes with aldehydes and trialkyl orthoformates afforded the corresponding 4-substituted 2-cyclohexenones. A new reaction of 2,4,6-trienones with *m*-chloroperbenzoic acid followed by the reduction with zinc in acetic acid gave 7-hydroxy-3,5-dienones. Utilizing these efficient reactions, megastigma-4,6,8-trien-3-ones, 3-hydroxy-β-ionol, 3-hydroxy-β-ionone, 5,6-epoxy-3-hydroxy-β-ionol, and 3-oxo-α-ionol were successfully synthesized.

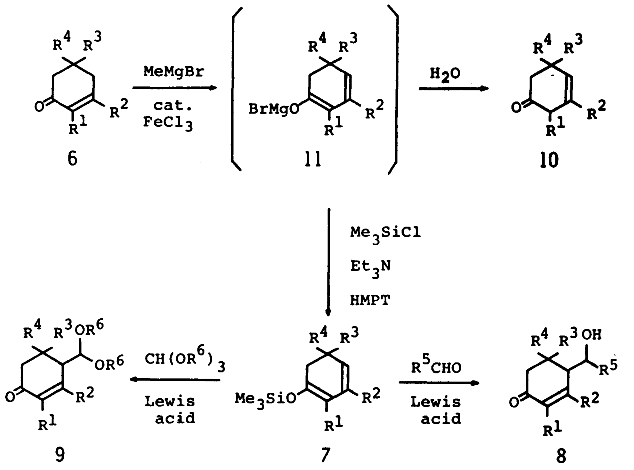
A large number of megastigmane derivatives, which are considered to be carotenoid metabolites having 13 carbon atoms, have been isolated successively from various tobacco leaves as neutral aroma constituents. Most of them have an oxygen function at the C-3 position in their cyclohexane rings, such as megastigma-4,6,8-trien-3-ones (**1**),[1] 3-hydroxy-β-ionol (**2**),[2] 3-hydroxy-β-ionone (**3**),[3] 5,6-epoxy-3-hydroxy-β-ionol (**4**),[4] and 3-oxo-α-ionol (**5**).[5] Recently, **1** and **3** were also found in Kudzu oil (Pueravia lobata Ohwi).[6] A number of synthetic methods for these megastigmane derivatives have been reported,[7] because they are considered to be potent flavoring components of tobacco and are frequently utilized as intermediates leading to carotenoids such as zeaxanthin. However, there still remain many problems, such as starting material, overall yield, and synthetic route.

In this paper, we will report a simple and efficient synthesis of **1** *via* the intermediate (**8a**) starting from readily available isophorone (**6a**), and an efficient conversion of **1** into **2**—**5** by way of an other intermediate (**13**).

Results and Discussion

The Lewis acid-catalysed aldol-type reactions of silyl enol ethers with various electrophiles such as carbonyl compounds, acetals, and trialkyl orthoformates were studied by Mukaiyama *et al.*[8] Recently, attention is focused on the reaction of dienoxysilanes with various electrophiles, which is a most useful means of organic synthesis because of its high selectivity of γ-attacking products. Mukaiyama and Ishida reported the $TiCl_4$-promoted reaction of 1-trimethylsiloxy-1,3-butadiene with acetals giving 5-alkoxy-2-enals.[9] In the course of our studies, some reports on the Lewis acid-catalysed reaction of dienoxysilanes with various electrophiles have appeared.[10]

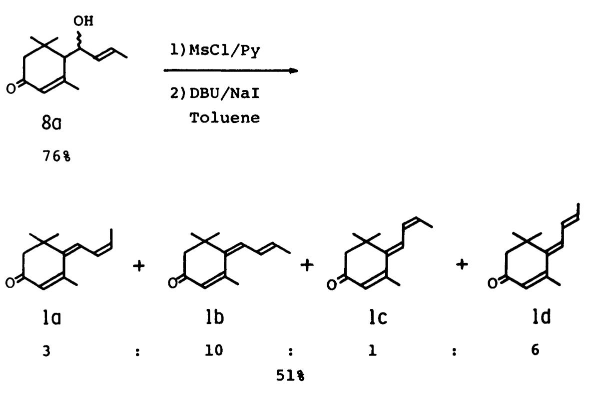
In order to apply to the syntheses of the desired megastigmane derivatives, we attempted to react 1-trimethylsiloxy-1,3-cyclohexadienes (**7**) with aldehydes or trialkyl orthoformates in the presence of Lewis acid. As a method to synthesize **7**, the reaction of 3-cyclohexenones (**10**) with lithium diisopropylamide and subsequent trapping with trimethylchlorosilane has been known, we discovered a simple synthetic method of **7** from 2-cyclohexenones (**6**) by application of the method of Kharasch *et al.*[11] Consequently, 1-hydroxyalkylated cyclohexenones (**8**) or dialkoxymethylated cyclohexenones (**9**) could be regioselectively synthesized from **6** *via* **7** as in the following (Scheme 1):



Scheme 1.

These results are listed in Tables 1 and 2.

3,5,5-Trimethyl-1-trimethylsiloxy-1,3-cyclohexadiene (**7a**) was employed to introduce an oxygen function into the C-3 position of the megastigmane skeleton. From **7a**, **1** was synthesized as in the following (Schemes 1 and 2):



Scheme 2.

Table 1. Preparation of 1-trimethylsiloxy-1,3-cyclohexadienes (**7**) from 2-cyclohexenones (**6**)

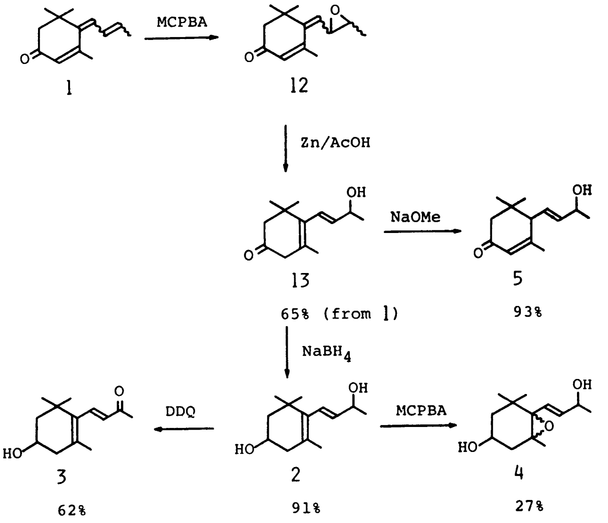
2-Cyclohexenone (**6**)	Product (**7**)					Yield[a)]
		R^1	R^2	R^3	R^4	%
Isophorone (**6a**)	**7a**	H	CH_3	CH_3	CH_3	80
l-Carvone (**6b**)	**7b**	CH_3	H	$\mathrm{C}\begin{smallmatrix}\nearrow CH_3\\ \searrow CH_2\end{smallmatrix}$	H	72

a) Isolated yields.

Treatment of 3-oxo-α-damascol (**8a**) with methanesulfonyl chloride and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)[12)] gave a mixture of **1a**—**d** in 51% total yield. The four isomers (**1a**—**d**), all of which occur in nature, were found in the ratio 3 : 10 : 1 : 6, determined by gas chromatography. All spectral data of the four isomers, isolated by means of preparative gas chromatography (20% PEG 20M), were consistent with those in the literature.[1)]

In the process of transforming **1** to ionone-type compounds (**2**—**5**), there are two problems: the introduction of an oxygen function into the C-9 position and the isomerization of double bonds from the C-4 and C-6 positions to the C-5 and C-7 positions. We resolved the problems by the synthesis of a key intermediate (**13**), which was obtained by the regioselective epoxidation of **1** with *m*-chloroperbenzoic acid in dichloromethane, followed by the selective reduction with zinc in acetic acid in 65% yield (Scheme 3). The isomers of the epoxy compound (**12**) were not isolated, but the position of epoxy function was confirmed by measurement with NMR. (This was based upon the result that two olefin protons of the C-8 and C-9 positions of **1** disappeared). The epoxy ring cleavage accompanying isomerization of double bonds was caused by treatment of **12** with zinc in acetic acid. The isomerization of double bonds of **13** to conjugated system did not take place under these conditions. Concerning the similar reduction of 4,5-epoxy-2-enones under acidic conditions, two methods have been reported.[13)] But their products were not unconjugated 5-hydroxy-3-enones but conjugated 5-hydroxy-2-enones, and the corresponding 2,4-dienones were also produced as by-products. In our synthesis of 7-hydroxy-3,5-dienone (**13**) from 6,7-epoxy-2,4-dienone (**12**), **13** could be selectively obtained as the sole product in good yield without any contamination of conjugated products. It is thought that this selectivity is due to either the conjugated effect of diene or the characteristic property of megastigmane skeleton.

The syntheses of **2**—**5** from **1** are shown in Scheme 3. Treatment of 3-oxo-β-ionol (**13**) with sodium borohydride in ethanol or sodium methoxide in methanol gave 3-hydroxy-β-ionol (**2**) or 3-oxo-α-ionol (**5**) in 91% or 93% yield, respectively. All spectral data of **2** and **5** were consistent with those in the literature.[2,5)] 3-Hydroxy-β-ionone (**3**) and 4,5-epoxy-3-hydroxy-β-ionol (**4**) had been synthesized from **2** by Mori[14)] and Takagi *et al.*,[4)] respectively.



Scheme 3.

In conclusion, megastigmane derivatives oxidized at the C-3 position (**1**—**5**) were efficiently synthesized starting from readily available isophorone (**6a**) by using a regioselective aldol-type reaction of dienoxysilanes (**7**) and selective transformation of 2,4,6-trienone (**1**) into 7-hydroxy-3,5-dienone (**13**) in each key step.

Experimental

All the boiling points are uncorrected. The IR spectra were recorded with a JASCO IRA-2 spectrometer. The NMR spectra were measured with a Hitachi R-24A spectrometer, using tetramethylsilane as the internal standered. The mass spectra were determined with a Hitachi RMU-6E mass spectrometer.

Table 2. Preparation of 4-substituted 2-cyclohexenones, **8** and **9**, from dienoxysilanes (**7**)

Dienoxysilane (**7**)	Electrophile	Lewis acid	Product (**8** or **9**)			Yield[a)]	Isomer ratio A/B
				R^5	R^6	%	
7a	$CH_3CH{=}CHCHO$	$TiCl_4$	**8a**	$CH{=}CHCH_3$	—	67	41/59[b)]
7a	$CH_3CH{=}CHCHO$	$BF_3\cdot OEt_2$	**8a**	$CH{=}CHCH_3$	—	76	43/57[b)]
7b	$(CH_3)_2CHCHO$	$BF_3\cdot OEt_2$	**8b**	$CH(CH_3)_2$	—	63	86/14[c)]
7b	PhCHO	$BF_3\cdot OEt_2$	**8c**	Ph	—	60	93/7[c)]
7a	$CH(OCH_3)_3$	$TiCl_4$	**9a**	—	CH_3	64	—
7a	$CH(OCH_3)_3$	$BF_3\cdot OEt_2$	**9a**	—	CH_3	61	—
7a	$CH(OCH_2CH_3)_3$	$TiCl_4$	**9b**	—	CH_2CH_3	62	—
7b	$CH(OCH_2CH_3)_3$	$BF_3\cdot OEt_2$	**9c**	—	CH_2CH_3	67	87/13[c)]

a) Isolated yields. b) *Threo-erythro* isomers. *c*) *Cis-trans* isomers. A/B=*trans*/*cis*.

Preparation of 3,5,5-Trimethyl-1-trimethylsiloxy-1,3-cyclohexadiene (7a). To a mixture of 2 M(1 M = 1 mol dm^{-3}) ether solution of methylmagnesium bromide (400 ml, 0.8 mol) and iron(III) chloride (2.0 g), a solution of isophorone (**6a**) (83 g, 0.60 mol) in dry ether (100 ml) was added dropwise at −20 °C, and the mixture was stirred for 0.5 h at −20 °C. Trimethylchlorosilane (87 g, 0.80 mol), triethylamine (60 ml), and hexamethylphosphoric triamide (HMPT) (60 ml) were successively added at 0 °C and the mixture was stirred for 24 h at room temperature. The mixture was poured into cold water and extracted with hexane. The extract was washed with a saturated solution of $KHSO_4$, a saturated solution of $NaHCO_3$, and brine, and then dried over $MgSO_4$. After removal of the solvent, the residue was distilled to give **7a** (101 g, 80%). Bp 88—89 °C/16 Torr (1 Torr = 133.322 Pa); IR (neat) 1655, 1595, and 850 cm^{-1}; NMR ($CDCl_3$) δ=0.22 (9H, s), 0.99 (6H, s), 1.68 (3H, d, J=2.0 Hz), 2.03 (2H, d, J=1.0 Hz), 4.87 (1H, m), and 4.96 (1H, m); MS (70 eV), m/e (%), 210 (M$^+$, 24), 195 (100), 179 (45), 105 (26), 75 (31), 73 (69), and 45 (26). Found: C, 68.63; H, 10.38%. Calcd for $C_{12}H_{22}SiO$: C, 68.51; H, 10.54%.

Preparation of 5-Isopropenyl-2-methyl-1-trimethylsiloxy-1,3-cyclohexadiene (7b). In the same manner, *l*-carvone (**6b**) (57 g, 0.38 mol) was treated with methylmagnesium bromide (2 M ether solution, 225 ml, 0.45 mol), iron(III) chloride (1.0 g), trimethylchlorosilane (49 g, 0.45 mol), triethylamine (35 ml), and HMPT (35 ml). The work-up described above gave **7b** (61 g, 72%). Bp 111—112 °C/17 Torr; IR (neat) 1670, 1640, 1585, 920, 890, and 843 cm^{-1}; NMR ($CDCl_3$) δ=0.20 (9H, s), 1.65 (3H, m), 1.76 (3H, m), 2.18 (1H, m), 2.36 (1H, m), 3.13 (1H, m), 4.80 (2H, m), 5.37 (1H, dd, J=9.5, 3.0 Hz), and 5.80 (1H, dd, J=9.5, 2.4 Hz); MS (70 eV), m/e (%), 222 (M$^+$, 21), 207 (17), 181 (15), 165 (18), 91 (21), 75 (24), 73 (100), and 45 (35). Found: C, 70.24; H, 9.79%. Calcd for $C_{13}H_{22}SiO$: C, 70.21; H, 9.97%.

Reaction of Dienoxysilanes (7) with Aldehydes Using $TiCl_4$ or $BF_3 \cdot OEt_2$. General Procedure: A solution of $TiCl_4$ (3.80 g, 20 mmol) or $BF_3 \cdot OEt_2$ (2.84 g, 20 mmol) in dry dichloromethane (5 ml) was added dropwise to a cold solution (−60 °C) of **7** (20 mmol) and aldehyde (24 mmol) in dry dichloromethane (20 ml). After being stirred for 2 h at −60 °C, the mixture was quenched with water. The dichloromethane layer was further stirred with a 10% solution of $(CO_2H)_2$ for 24 h at room temperature and washed with a saturated solution of $NaHCO_3$ and brine, and then dried over $MgSO_4$. After evaporation of the solvent, the residue was subjected to silica-gel column chromatography (hexane–ether) to afford **8**.

3-Oxo-α-damascol (8a): Two stereoisomers (*threo-erythro*), **8aA** and **8aB**, were prepared. **8aA**: IR (neat) 3450, 1650, and 970 cm^{-1}; NMR ($CDCl_3$) δ=1.02 (3H, s,) 1.13 (3H, s), 1.64 (3H, d, J=5.0 Hz), 1.90 (1H, d, J=18.0 Hz), 2.11 (3H, d, J=1.5 Hz), 2.32 (1H, d, J=3.5 Hz), 2.45 (1H, d, J=18.0 Hz), 3.30 (1H, broad s), 4.57 (1H, dd, J=7.0, 3.5 Hz), 5.60 (2H, m), and 5.98 (1H, broad s); MS (70 eV), m/e (%), 208 (M$^+$, 3), 193 (3), 190 (3), 149 (9), 138 (47), 123 (45), 96 (69), 95 (51), 82 (35), 81 (61), 70 (45), 69 (42), 41 (100), and 39 (77). Found: C, 74.77; H, 9.87%. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68%. **8aB**: IR (neat) 3370, 1645, and 985 cm^{-1}; NMR ($CDCl_3$) δ=1.00 (3H, s), 1.16 (3H, s), 1.70 (3H, dd, J=5.0, 1.5 Hz), 1.8—2.0 (1H, m), 1.98 (3H, d, J=1.5 Hz), 2.05 (1H, d, J=1.5 Hz), 2.78 (1H, d, J=18.0 Hz), 3.42 (1H, broad s), 4.67 (1H, m), 5.60 (2H, m), and 5.98 (1H, broad s); MS (70 eV), m/e (%), 208 (M$^+$, 3), 193 (3), 190 (2), 149 (8), 138 (47), 123 (43), 96 (70), 95 (53), 82 (47), 81 (61), 70 (47), 69 (38), 41 (100), and 39 (81). Found: C, 74.68; H, 9.51%. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68%.

4-(1-Hydroxy-2-methylpropyl)-5-isopropenyl-2-methyl-2-cyclohexenone (8b): *Trans*-isomer (**8bA**) and *cis*-isomer (**8bB**) were separated. **8bA**: IR (neat) 3460, 1660, and 895 cm^{-1}; NMR ($CDCl_3$) δ=0.95 (3H, d, J=6.5 Hz), 0.99 (3H, d, J=6.5 Hz), 1.76 (6H, m), 2.0—3.1 (6H, m), 3.55 (1H, m), 4.85 (2H, m), and 6.73 (1H, m); MS (70 eV), m/e (%), 150 (M$^+$−72, 100), 135 (93), 109 (74), 108 (63), 107 (51), 73 (79), 55 (79), 43 (72), and 41 (60). Found: C, 75.48; H, 9.78%. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97%. **8bB**: IR (neat) 3500, 1660, and 890 cm^{-1}; NMR ($CDCl_3$) δ=0.96 (6H, d, J=6.5 Hz), 1.76 (3H, m), 1.86 (3H, m), 2.2—3.1 (6H, m), 3.56 (1H, m), 4.48 (2H, m), and 6.65 (1H, m); MS (70 eV), m/e (%), 204 (M$^+$−18, 4), 150 (M$^+$−72, 100), 135 (59), 109 (49), 108 (93), 107 (68), 73 (56), 55 (59), 43 (73), and 41 (51). Found: C, 75.83; H, 9.72%. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97%.

4-(α-Hydroxybenzyl)-5-isopropenyl-2-methyl-2-cyclohexenone (8c): *Trans*-isomer (**8cA**) and *cis*-isomer (**8cB**) were separated. **8cA**: IR (neat) 3450, 1665, and 895 cm^{-1}; NMR ($CDCl_3$) δ=1.70 (3H, m), 1.77 (3H, m), 2.3—3.2 (5H, m), 4.85 (1H, m), 4.94 (2H, m), 6.53 (1H, m), and 7.30 (5H, s); MS (70 eV), m/e (%), 257 (M$^+$+1, 3), 256 (M$^+$, 1), 187 (5), 150 (100), 135 (43), 109 (40), 108 (31), 107 (100), 91 (21), 79 (79), and 77 (60). Found: C, 79.43; H, 7.66%. Calcd for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86%. **8cB**: IR (neat) 3400, 1660, and 900 cm^{-1}; NMR ($CDCl_3$) δ=1.73 (6H, m), 2.2—3.1 (5H, m), 4.75—4.95 (3H, m), 6.82 (1H, m), and 7.25 (5H, s); MS (70 eV), m/e (%), 256 (M$^+$, 0.3), 255 (M$^+$−1, 1), 187 (2), 150 (96), 135 (41), 109 (35), 108 (27), 107 (100), 91 (22), 79 (75), and 77 (59), Found: C, 79.49; H, 7.70%. Calcd for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86%.

Reaction of Dienoxysilanes (7) with Trialkyl orthoformates Using $TiCl_4$ or $BF_3 \cdot OEt_2$. General Procedure: To a cold solution (−60 °C) of **7** (20 mmol) and trialkyl orthoformate (26 mmol) in dry dichloromethane (20 ml), a solution of $TiCl_4$ (3.80 g, 20 mmol) or $BF_3 \cdot OEt_2$ (2.84 g, 20 mmol) in dry dichloromethane (5 ml) was added. After being stirred for 1 h at −60 °C, the mixture was quenched with methanol (5 ml). The mixture was poured into water and extracted with dichloromethane after separation of the organic layer. The extract was washed with a saturated solution of $NaHCO_3$ and dried over $MgSO_4$. After evaporation of the solvent, the residue was subjected to silica-gel column chromatography (hexane–ether) to afford **9**.

4-Dimethoxymethyl-3,5,5-trimethyl-2-cyclohexenone (9a): IR (neat) 1665, 1120, and 1075 cm^{-1}; NMR ($CDCl_3$) δ=1.02 (3H, s), 1.11 (3H, s), 1.95 (1H, d, J=17.0 Hz), 2.06 (3H, d, J=1.5 Hz), 2.24 (1H, d, J=3.0 Hz), 2.57 (1H, d, J=17.0 Hz), 3.39 (3H, s), 3.42 (3H, s), 4.53 (1H, d, J=3.0 Hz), and 5.95 (1H, broad s); MS (70 eV), m/e (%), 181 (M$^+$−31, 2), 180 (M$^+$−32, 4), 165 (5), 137 (7), 125 (7), 75 (100), 47 (15), 41 (12), and 39 (10). Found: C, 67.62; H, 9.70%. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50%.

4-Diethoxymethyl-3,5,5-trimethyl-2-cyclohexenone (9b): IR (neat) 1660, 1630, 1120, and 1065 cm^{-1}; NMR ($CDCl_3$) δ=1.04 (3H, s), 1.13 (3H, s), 1.16 (3H, t, J=7.0 Hz), 1.23 (3H, t, J=7.0 Hz), 1.95 (1H, d, J=17.0 Hz), 2.10 (3H, d, J=1.5 Hz), 2.23 (1H, d, J=3.0 Hz), 2.65 (1H, d, J=17.0 Hz), 3.3—4.0 (4H, m), 4.75 (1H, d, J=3.0 Hz), and 5.95 (1H, broad s); MS (70 eV), m/e (%), 195 (M$^+$−45, 6), 139 (8), 123 (10), 111 (15), 103 (88), 75 (81), and 47 (100). Found: C, 70.20; H, 9.88%. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07%.

4-Diethoxymethyl-5-isopropenyl-2-methyl-2-cyclohexenone (9c): GLC (10% PEG 20M) indicated two stereoisomers, **9cA** (*trans*-isomer) and **9cB** (*cis*-isomer). The analytically pure samples of both isomers were prepared by preparative GLC (20% PEG 20M). **9cA**: IR (neat) 1670, 1110, 1060, and 895 cm^{-1}; NMR ($CDCl_3$) δ=1.18 (3H, t, J=7.0 Hz), 1.25 (3H, t,

J=7.0 Hz), 1.76 (6H, m), 2.2—3.1 (4H, m), 3.3—4.0 (4H, m), 4.45 (1H, d, J=3.0 Hz), 4.85 (2H, m), and 6.88 (1H, m); MS (70 eV), *m/e* (%), 207 (M$^+$−45, 2), 135 (13), 103 (86), 75 (73), and 47 (100). Found: C, 71.11; H, 9.31%. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59%. **9cB**: IR (neat) 1670, 1110, 1060, and 895 cm^{-1}; NMR ($CDCl_3$) δ=1.17 (3H, t, J=7.0 Hz), 1.22 (3H, t, J=7.0 Hz), 1.80 (6H, m), 2.0—3.1 (4H, m), 3.2—4.0 (4H, m), 4.42 (1H, d, J=5.0 Hz), 4.84 (2H, m), and 6.80 (1H, m); MS (70 eV), *m/e* (%), 207 (M$^+$−45, 4), 135 (14), 103 (75), 75 (67), and 47 (100). Found: C, 71.15; H, 9.42%. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59%.

Preparation of Megastigma-4,6,8-trien-3-ones (1a—d). The reaction of **8a** (6.24 g, 30 mmol) with methanesulfonyl chloride (6.87 g, 60 mmol) was carried out in pyridine (25 ml) at 0 °C for 2 h. The mixture was quenched with cold 2 M HCl and extracted with ether. The extract was washed with a saturated solution of $NaHCO_3$ and brine, dried over $MgSO_4$, and then concentrated. The residue was added to a cold solution (0 °C) of DBU (9.12 g, 60 mmol), NaI (4.50 g, 30 mmol), and toluene (30 ml) and the mixture was refluxed for 1 h. The mixture was poured into cold 2 M HCl and extracted with ether. The extract was washed with a saturated solution of $NaHCO_3$ and brine, and then dried over $MgSO_4$. After removal of the solvent, the residue was distilled to give a mixture (2.90 g, bp 120—130 °C/4 Torr, 51%) of **1a**, **1b**, **1c**, and **1d** in *ca.* 3 : 10 : 1 : 6 ratio. The analytically pure samples of four isomers were prepared by preparative GLC (20% PEG 20M).

(6Z, 8Z)-Megastigma-4,6,8-trien-3-one (1a): IR (neat) 1665, 1630, 1590, and 730 cm^{-1}; NMR ($CDCl_3$) δ=1.25 (6H, s), 1.82 (3H, dd, J=7.0, 1.5 Hz), 2.23 (3H, d, J=1.5 Hz), 2.30 (2H, s), 5.70 (1H, m), 5.90 (1H, broad s), and 6.2—6.8 (2H, m); MS (70 eV), *m/e* (%), 190 (M$^+$, 100), 175 (82), 148 (82), 147 (79), 133 (79), 122 (59), 119 (68), 105 (68), 91 (91), 79 (55), 77 (61), 69 (76), 55 (61), 41 (98), and 39 (82).

(6Z, 8E)-Megastigma-4,6,8-trien-3-one (1b): IR (neat) 1665, 1635, 1595, and 970 cm^{-1}; NMR ($CDCl_3$) δ=1.19 (6H, s), 1.86 (3H, dd, J=7.0, 1.5 Hz), 2.28 (3H, d, J=1.5 Hz), 2.29 (2H, s), 5.89 (1H, dd, J=14.0, 7.0 Hz), 5.92 (1H, broad s), 6.25 (1H, d, J=11.0 Hz), and 6.55 (1H, dd, J=14.0, 11.0 Hz); MS (70 eV), *m/e* (%), 190 (M$^+$, 74), 175 (61), 148 (75), 147 (70), 133 (82), 122 (41), 119 (63), 105 (60), 91 (78), 79 (48), 77 (52), 69 (68), 55 (49), 41 (100), and 39 (59).

(6E, 8Z)-Megastigma-4,6,8-trien-3-one (1c): IR (neat) 1665, 1582, and 725 cm^{-1}; NMR ($CDCl_3$) δ=1.36 (6H, s), 1.83 (3H, dd, J=7.0, 1.5 Hz), 2.13 (3H, d, J=1.5 Hz), 2.35 (2H, s), 5.92 (1H, broad s), and 5.5—7.0 (3H, m); MS (70 eV), *m/e* (%), 190 (M$^+$, 97), 175 (67), 148 (76), 147 (76), 133 (82), 122 (55), 119 (55), 105 (64), 91 (79), 79 (48), 77 (55), 69 (73), 55 (52), 41 (100), and 39 (73).

(6E, 8E)-Megastigma-4,6,8-trien-3-one (1d): IR (neat) 1670, 1630, 1585, and 968 cm^{-1}; NMR ($CDCl_3$) δ=1.35 (6H, s), 1.89 (3H, dd, J=7.0, 1.5 Hz), 2.08 (3H, d, J=1.0 Hz), 2.35 (2H, s), 5.91 (1H, broad s), 5.94 (1H, dd, J=14.5, 7.0 Hz), 6.50 (1H, d, J=11.5 Hz), and 6.75 (1H, dd, J=14.5, 11.5 Hz). MS (70 eV), *m/e* (%), 190 (M$^+$, 100), 175 (81), 148 (98), 147 (92), 133 (98), 122 (54), 119 (77), 105 (65), 91 (94), 79 (52), 77 (63), 69 (81), 55 (60), 41 (100), and 39 (81).

Preparation of 3-Oxo-β-ionol (13). To a cold solution (0 °C) of **1** (2.25 g, 12 mmol) in dry dichloromethane (50 ml) was added *m*-chloroperbenzoic acid (2.59 g, 15 mmol) and the mixture was stirred at 0 °C for 2 h. The mixture was washed with a 1% solution of NaOH and brine, dried over $MgSO_4$, and concentrated. The residue was added to a mixture of zinc powder (3.92 g, 60 mg atom) and acetic acid (20 ml) at room temperature. After the mixture was stirred for 2 h at room temperature, the precipitate was filtered off and washed with ether (100 ml). The filtrate was washed with a saturated solution of $NaHCO_3$ and brine, dried over $MgSO_4$, and then concentrated. Purification by silica-gel column chromatography (hexane–ether) afforded **13** (1.61 g, 65%). IR (neat) 3400, 1720, 1660, and 975 cm^{-1}; NMR ($CDCl_3$) δ=1.06 (6H, s), 1.33 (3H, d, J=6.0 Hz), 1.76 (3H, s), 2.39 (2H, s), 2.86 (2H, s), 3.57 (1H, s), 4.43 (1H, quintet, J=6.0 Hz), 5.61 (1H, dd, J=16.0, 6.0 Hz), and 6.07 (1H, d, J=16.0 Hz); MS (70 eV), *m/e* (%), 208 (M$^+$, 5), 190 (15), 175 (12), 135 (30), 133 (24), 121 (26), 109 (29), 108 (46), 107 (34), 91 (36), and 43 (100).

Reduction of 13 to 3-Hydroxy-β-ionol (2). To a suspension of $NaBH_4$ (0.076 g, 2 mmol) in ethanol (10 ml) was added **13** (0.801 g, 3.9 mmol) at room temperature. After the mixture had been stirred for 1 h at room temperature, the mixture was quenched with cold 5% $(CO_2H)_2$ and extracted with ether. The extract was washed with a saturated solution of $NaHCO_3$ and brine, dried over $MgSO_4$, and then concentrated. Purification by silica-gel column chromatography (hexane–ether) afforded **2** (0.734 g, 91%).

Isomerization of 13 to 3-Oxo-α-ionol (5). To a solution of NaOMe (0.010 g) in methanol (5 ml) was added **13** (0.243 g, 1.2 mmol) at room temperature, then the mixture was stirred for 10 min at room temperature, poured into cold water, and extracted with ether. The extract was washed with brine, dried over $MgSO_4$, and then concentrated. Purification by silica-gel column chromatography (hexane–ether) afforded **5** (0.225 g, 93%).

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