Approaches to the Synthesis of the Insect Juvenile Hormone Analog Ethyl 3,7,11-Trimethyl-2,4-dodecadienoate and Its Photochemistry[1]

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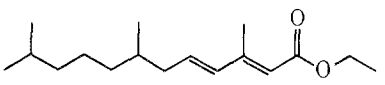
Three alternate synthetic schemes for the preparation of ethyl 3,7,11-trimethyl-2,4-dodecadienoate are described. Methods are discussed for the conversion of the 4*Z* to the 4*E* isomers and the thermodynamic equilibrium was established for the isomers. A study was made of both the direct and the sensitized photochemical *Z*–*E* isomerization of the 2*E*,4*E* and the 2*Z*,4*E* isomers. The Rose Bengal sensitized photooxygenation of the 2*E*,4*E* isomer **1** gave the 3-hydroxy-2-pyrone **19**.

In related papers[3,4] we have discussed synthetic methods for the preparation of each of the four stereoisomers of the alkyl 3,7,11-trimethyl-2,4-dodecadienoates,[5] a class of insect growth regulators in which the 2*E*,4*E* isomers (*e.g.*, **1**) have potent juvenile hormone activity.[4,5] In the preceding paper[3] we described a general stereoselective route to these compounds. The present paper describes three of the other synthetic routes which we have investigated for the preparation of **1**.



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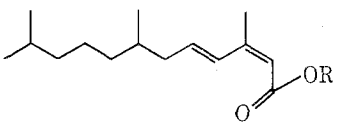


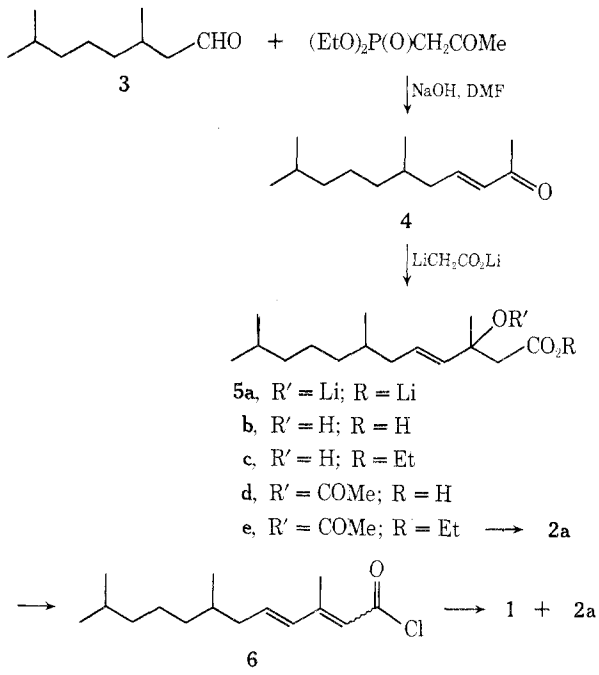
2a, R = Et
b, R = H

Method I. The condensation of a conjugated ketone such as **4** with an acetic acid derived reagent was one potential route to **1**. Reaction of the aldehyde **3** with the anion of diethyl 2-oxopropylphosphonate gave **4** in high yield with nearly exclusive *E* stereochemistry. Treatment of **4** with the dilithium salt of acetic acid[6] gave, after protonation, the hydroxy acid **5b** which could be esterified to **5c** (*cf.* Reformatsky reaction[7]) (Scheme I). Dehydration of **5c** with either phosphoryl chloride in pyridine[7a] or phosphorus pentoxide[7c] in benzene gave a mixture of **1** and **2a**, as well as variable amounts (*ca.* 40%) of isomers (presumably 3,5-dienes **16**; and perhaps some 4,6-dienes) in which the ester was no longer conjugated with the diene system (*cf.* ref 7). Reaction of **5b** with thionyl chloride or with phosphorus trichloride[7b] gave impure **6** containing up to 50% 3,5-diene isomers. However, if formation of the acid chloride was carried out in the presence of the hindered tertiary amine *N*-ethyldiisopropylamine,[8] subsequent treatment with ethanol gave a mixture of **1** and **2a** containing <10% of the 3,5-dienoate isomers. If the impure acid chloride above, prepared with thionyl chloride, was allowed to stand in the presence of *N*-ethyldiisopropylamine for 3 days before treatment with ethanol, a similar mixture of **1** and **2a** was obtained (*cf.* ref 7b).

Acetylation of the intermediate dilithium salt **5a** gave **5d** which was esterified with diazoethane to give **5e.** Treatment of the acetoxy ester **5e** with potassium *tert*-butoxide[9] in tetrahydrofuran gave a mixture of **1** and **2a** in approximately equal amounts. Both **1** and **2a** can be equilibrated readily with benzenethiol to a mixture containing 65% of **1**.[3]

Reaction of **4** with the anion of triethyl phosphonoacetate under a variety of conditions gave negligible yields of **1**

Scheme I

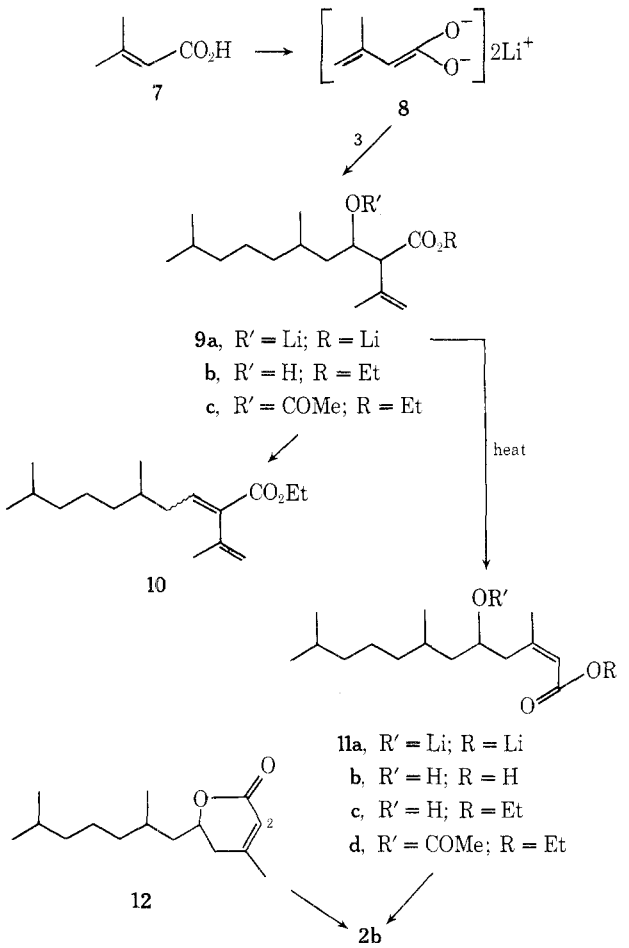


and **2a**, in contrast to the result obtained with the corresponding 3-yn-2-one analog of **4**.[4]

Method II. The direct condensation of esters of 3-methyl-2-butenoic acid (**7**) with aldehydes in the presence of alkali amides in either liquid ammonia or in ether has been reported to give (after hydrolysis) 3-methyl-2,4-dienoic acids.[10] However, the yields in our hands from such direct condensations with *saturated* aldehydes such as **3** were very poor (*cf.* ref 10b, c, and e). Alkylation reactions of the reactive metalated esters of **7** have been reported, with attack occurring predominately at the α position.[11] A recent report has also appeared on the condensation reaction of the relatively stable disalts of **7** with benzaldehyde.[12]

Dimetalation of **7** to give **8** occurred readily with lithium diisopropylamide in tetrahydrofuran (Scheme II). Reaction of **8** with the aldehyde **3** at room temperature (or at −70°) afforded predominantly the intermediate salt **9a**. Protonation of the reaction mixture and esterification with 1-ethyl-3-*p*-tolyltriazene gave **9b** (plus some **11c** and **12**). Acetylation of **9b** gave **9c** (a mixture of diastereoisomers) which could be converted to the dienoic ester **10** with potassium *tert*-butoxide in tetrahydrofuran. Heating a solution of the intermediate dilithium salt **9a** in tetrahydrofuran under reflux gave a *mixture containing ca. 95% of the isomer* **11a** *and only ca. 5% of* **9a**. Acetylation of the dilithium salt **11a** and then esterification of the recovered acetoxy acid

Scheme II

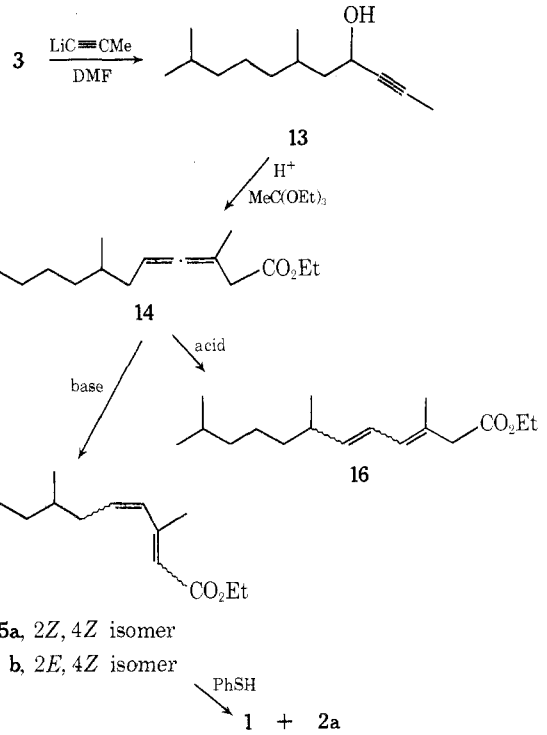


with diazoethane gave the acetoxy ester **11d** as a mixture of the *Z* and *E* isomers in the ratio 9:1, respectively. Treatment of **11d** with potassium *tert*-butoxide in tetrahydrofuran, however, gave only a slow conversion to **2a** (plus **1**) (*cf.* ref 9 and 13a).

Direct acidification of the disalt **11a** gave a mixture of the acid **11b** and the lactone **12**[3] with the latter usually predominating. The hydroxy acid **11b** lactonized readily to **12** under mild acidic conditions. Opening the lactone **12** with sodium ethoxide in ethanol[3,13] gave a high yield of the 2*Z*,4*E* acid **2b** which can be converted to **1**.[3]

It was reported by Watanabe, *et al.*,[14] that the reaction of the dilithium salt of crotonic acid with ketones gave only the 5-hydroxy-2-enoic acids. Repetition of this work by a different group[15] showed that in fact, under the conditions used by Watanabe, *et al.*, a mixture of ~40% α isomer and 60% γ isomer is obtained. Similarly it has been recently reported[12] that the disalts of 3-methyl-2-butenoic acid (**7**) react with benzaldehyde to give mixtures of the α and γ products and that the product distribution could be correlated with the nature of the two metals used to form the disalt, and with the solvent. However, none of these authors noticed that *there is an equilibrium between the disalts of the products*, and that the α product (*e.g.*, **9a**) can be converted to a mixture containing mainly the γ product (*e.g.*, **11a**) by further heating of the reaction mixture. Recently the Reformatsky reaction of alkyl γ-bromocrotonates has been reinvestigated. It was noticed that at 0° the β-hydroxy ester was obtained and that when the alkoxide corresponding to this hydroxy ester was heated, an equilibrium was established which upon hydrolysis gave the δ-hydroxy ester, corresponding to the thermodynamically more stable zinc salt.[16]

Scheme III



Method III. It has been shown by Crandall and Tindell[17] and by us[18] that reaction of aliphatic propynyl alcohols such as 2-methyl-3-butyn-2-ol with trialkyl orthoacetates gives β-allenic ester derivatives which can be rearranged under mild alkaline conditions[18] to give alkyl 5-methyl-2,4-hexadienoates. We have also investigated this reaction as a possible route to alkyl 3,7,11-trimethyl-2,4-dodecadienoates such as **1**.[19]

Reaction of aldehyde **3** with propynyllithium in dimethylformamide gave **13** in 29% yield after spinning band distillation (Scheme III). Treatment of **13** with triethyl orthoacetate (*cf.* ref 20) and a catalytic amount of propionic acid at 125° under conditions of continuous ethanol removal gave the allenic ester **14** in 83% isolated yield. The rearrangement of **14** to the 3-methyl-2,4-dienoate isomers was studied under a variety of conditions. Treatment of **14** with various acidic catalysts gave mixtures of **1**, **2a**, and the 3,5-dienoate isomers **16** with the latter predominating.[21,22] Rearrangement of **14** with basic catalysts (Table I) generally gave mixtures of **1**, **2a**, and the 4*Z* isomers, **15a** and **15b**,[4] with the 4*Z* isomers often predominating. Small variations in the basic conditions gave different ratios of **1**, **2a**, **15a**, and **15b**. The use of tetrahydrofuran or ethanol as the reaction solvent gave fewer by-products than did the use of dimethylformamide, dimethyl sulfoxide, or of dioxane. The allenic ester isomerized rapidly under basic conditions and the composition of the initially formed mixture of isomers did not generally change appreciably with time under the various conditions used. Thus addition of a catalytic amount of sodium ethoxide in ethanol to a solution of **14** in dimethylformamide gave complete reaction of the starting material in less than 10 min at 0° (or 2 hr at −20°) and produced a mixture of **1**, **2a**, and **15a** + **15b** in the ratio *ca.* 45:20:35, respectively. Little further change in the isomer ratio occurred after another 15 hr of reaction time at room temperature.

Rearrangement of **14** with Triton B in ethanol at room temperature for 2 days gave a mixture of **1** (23%), **2a** (7%), and the 4*Z* isomers (21% of **15a** and 49% of **15b**), in high yield. Further treatment of this mixture with a catalytic

Table I
Catalytic Rearrangement[a] of Ethyl 3,7,11-Trimethyl-3,4-dodecadienoate (14)

Catalyst	Solvent	Temp, °C (time, hr)	Product ratio[b] (15a + 15b)	2a	1	16
NaOEt	EtOH	24 (1)	35	50	15	
NaOEt	EtOH	24 (68)	65	15	20	
NaOEt	EtOH	50 (70)	65	15	20	
NaOEt[c]	DMF	−70 (2)				
NaOEt	DMF	−20 (2)	40	15	45	
NaOEt	DMF	−15 (48)	55	10	35	
NaOEt	DMF	0 (0.25)	35	20	45	
NaOEt	THF	24 (3)	50	30	15	5
KO-*t*-Bu	THF	24 (2)	55	40	5	
KO-*t*-Bu	*p*-Dioxane	24 (22)[e]	35	40	5	5
Triton B[d]	EtOH	24 (5)	65	10	25	
Triton B	*p*-Dioxane	24 (24)[e]	40	10	20	15
Triton B	DMSO	24 (24)[e]	30	10	20	30
Triton B	DMF	153 (18)[e]	15	10	15	40
KF	EtOH	60 (11)	40	35	15	10
DBN[f]	THF	60 (190)	30	50	10	10
Me_4N^+ $OCOMe^-$[c]	THF	60 (120)				
p-TsOH·H_2O	CH_2Cl_2	40 (5)		15	30	55
H_2SO_4	EtOH	60 (190)[e]		15	25	40
BF_3·Et_2O[g]	Et_2O	24 (48)				

[a] All rearrangements were monitored by glc analysis using *n*-docosane as an internal standard. [b] Duplicate runs varied by up to ± 10% in isomer ratio. [c] No rearrangement occurred. [d] $C_6H_5CH_2N(Me)_3OH$. [e] About 10–20% of 14 remained unreacted under these conditions. [f] 1,5-Diazabicyclo[4.3.0]non-5-ene. [g] Starting material was partially destroyed.

amount of benzenethiol[3] in the presence of a trace of 2,2′-azobis(isobutyronitrile) [AIBN] at 85° for 2 hr in the absence of solvent gave equilibration[3] to a mixture of **1** and **2a** in the ratio 67:33, respectively, with only traces (≤1%) of the 2*Z*,4*Z* isomer (**15a**) and the 2*E*,4*Z* isomer (**15b**). The latter two isomers have been prepared by an alternative route.[4] We have also shown that the same equilibrium mixture of **1** and **2a** was obtained on treatment of either pure **1** or **2a** with benzenethiol (2% by weight) and a trace of AIBN at 80° for 2 hr (*cf.* ref 3). Thus at thermodynamic equilibrium the 4*Z* stereochemistry is not favorable. Indeed examination of Dreiding stereomodels of **15a** and **15b** indicates considerable steric crowding might be expected in these isomers (*cf.* ref 4).

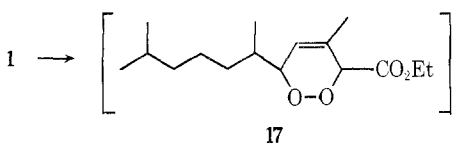
The allenic ester **14** was recovered completely unchanged after attempted isomerization with benzenethiol under the above conditions. Even more vigorous treatment such as heating **14** with 2% by weight of benzenethiol at 100° for 16 hr, gave recovered allene with no decomposition or isomerization detectable by ir, nmr, or glc.

The synthetic routes described above appear to be less useful than the 3-methylglutaconate route described in the preceding paper,[3] for the commercial production of 3,7,11-trimethyl-2,4-dodecadienoates and related analogs. The above schemes involve more steps, are more linear in outline and are less versatile.

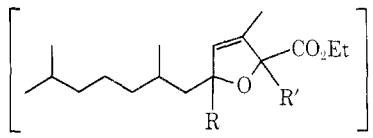
Photochemistry. Photochemical *Z*–*E* isomerization of the α,β-double bond was essentially the only process observed in solution under the conditions used, when the (2*E*,4*E*)-dienoate **1** or its 2*Z*,4*E* isomer **2a** was directly irradiated, or irradiated in the presence of a suitable photosensitizer. The direct irradiation of **1** [λ_{max} (hexane) 259 nm (ε 26,400)] or of **2a** [λ_{max} (hexane) 262 nm (ε 20,900)] or of a mixture of both using a medium-pressure mercury lamp whose light was filtered through *ca.* 2–3 mm of Pyrex glass, gave a photostationary state in which the ratio of **1** to **2a** was *ca.* 44:56, respectively. Only traces (<2%) of the 4*Z* isomers **15a** and **15b** could be detected and no other photoprocesses such as photodeconjugation, including allene formation (*i.e.*, **14**), were observed under these conditions.[23] It is interesting that when 4-methyl-3,5-heptadienone was irradiated in a dilute solution in ether, only photoisomerization about the α,β-double bond was reported to occur, in contrast to the results obtained with analogous compounds lacking the 4-methyl group.[24]

Irradiation of mixtures of **1** and **2a** (*ca.* 7:3, respectively) with a medium-pressure mercury lamp (whose light was filtered through 5–12 mm of Pyrex) in the presence of triplet-state sensitizers with triplet-excitation energies ≥53 kcal/mol gave rapid *Z*–*E* isomerization at C-2 to give mixtures of **1** and **2a** in the ratio *ca.* 1:1. For sensitizers with triplet-state energies below 53 kcal/mol the energy transfer efficiency rapidly decreased with decreasing E_t (see Experimental Section). Thus a triplet excited state of the dienoic ester with a triplet-state energy of *ca.* 46–48 kcal/mol is probably involved in this photoisomerization (*cf.* ref 25). Our inability to find an appropriate quencher with a triplet-state energy <49 kcal/mol and not absorbing uv light in the region, where the dienoic esters **1** and **2a** absorb, prevented our doing quenching experiments. Thus it was not possible to ascertain if in the case of direct irradiation, the photoisomerization could, at least in part, have occurred *via* a singlet excited state.

The Rose Bengal sensitized photooxygenation[26] of a mixture of **1** and **2a** (in the ratio 4:1, respectively) was studied using ethanol as the solvent. The reaction of singlet oxygen with the 2*E*,4*E* isomer was quite slow while the 2*Z*,4*E* isomer appeared to be completely unreactive. In a typical experiment, after 163 hr of irradiation only 57% of **1** had reacted. Analysis by tlc showed the formation of only one main product which after work-up and then chromatography gave the hydroxypyrone **19**. The formation of **19** can be rationalized *via* the initial formation of the cyclic peroxide **17** which rearranged to **18a** or to **18b** and then to **19**. Products analogous to **17** and **18a** have been obtained on photosensitized oxygenation of some carotenoid analogs.[27] Photosensitized oxygenation of **1** in d_4-deuteriomethanol in an nmr tube showed that **19** was *not* primarily formed during the irradiation. The initial product showed nmr signals (in

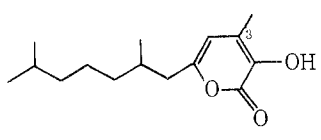


17



18a, R = H; R′ = OH
b, R = OH; R′ = H

base



19

CD_3OD) at 1.73 (triplet, J = 2 Hz) and at 5.83 ppm (broad peak) and the addition of a few drops of sodium deuteriomethoxide solution caused the rapid appearance of nmr signals due to **19** and to the liberated ethanol (see Experimental Section). The initial product appeared to be **18a** or **18b** and the conversion to **19** occurred not only with base but also upon heating or prolonged treatment with alumina or even silica gel. The formation of **19** also occurred in the injection port of the gas chromatograph. The nmr, ir, mass spectra, and uv spectra of **19** agree with that expected for the assigned 3-hydroxy-2-pyrone structure (*cf.* ref 28). Recently the analogous 3-hydroxy-2-pyrone has been obtained from the photosensitized oxygenation of isopropyl (2*E*,4*E*)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate.[29]

Experimental Section

All substances described herein are racemic compounds; the prefix *dl* is omitted. Preparative thin-layer chromatography was carried out with Merck (Darmstadt) silica gel PF-254. Nmr spectra were determined on a Varian T-60 spectrometer. Infrared spectra were measured on a Unicam SP 200G spectrophotometer. Mass spectra were measured on a Varian Mat CH-7 spectrometer, at either 20 or 70 eV ionization potential. Gas–liquid chromatographic analyses were performed on Model 402 Hewlett-Packard instruments equipped with hydrogen flame ionization detectors. Solvents were dried over activated molecular sieves.

(*E*)-6,10-Dimethyl-3-undecen-2-one (4). To a mixture of 118.0 g (0.76 mol) of 3,7-dimethyl-1-octanal and 160.5 g (0.83 mol) of diethyl 2-oxopropylphosphonate[30] in 350 ml of dimethylformamide cooled in an ice bath under N_2 was added 31.8 g (0.80 mol) of finely ground sodium hydroxide. After 30 min the cooling bath was removed and after a further 1 hr at room temperature the mixture was diluted with 1400 ml of ice–water and 1000 ml of hexane. The organic layer was separated, washed twice with 600-ml portions of brine, then dried ($CaSO_4$). Solvent removal *in vacuo* yielded 153.1 g of crude product which was purified by distillation through a 15-cm Vigreux column to give 130.0 g (87% yield) of ketone **4** [analysis by glc showed a purity of >90% with a negligible (<2%) amount of the *Z* isomer present]: bp 67–73° (0.07 mm); ir (film) 1700, 1680 (C=O), and 1630 cm^{-1} (C=C); nmr (CCl_4) δ 2.17 (s, 3, $COCH_3$), 5.97 (d, 1, J = 16 Hz, H-3), and 6.71 ppm (2t, 1, J = 16 Hz and 7 Hz, H-4); mass spectrum (20 eV) *m/e* (rel intensity) 197 (~0), 196 (~0), 181 (2), 153 (3), 111 (12), 95 (10), 84 (100), 71 (40), 69 (32), 57 (46), 43 (30).

Anal. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.75; H, 12.23.

(*E*)-3-Hydroxy-3,7,11-trimethyl-4-dodecenoic Acid (5b). To a solution of 7.9 g (0.078 mol) of diisopropylamine in 400 ml tetrahydrofuran, at 0° under N_2 was slowly added 51 ml (0.079 mol) of 1.55 *M* *n*-butyllithium in hexane solution. The mixture was stirred at 0° for 1 hr, and at room temperature for 3 hr. Then 2.26 g (0.038 mol) of acetic acid in 25 ml of tetrahydrofuran was added at 0°; the mixture was stirred 0.5 hr, heated, and stirred an additional 1.5 hr at 45°. After cooling to 0°, 7.34 g (0.037 mol) of the ketone **4** in 25 ml of tetrahydrofuran was added. The ice bath was then removed and the mixture was stirred at room temperature overnight. After removal of most of the solvent *in vacuo* aqueous 1 *N* hydrochloric acid was added and the mixture extracted with ether. The ether extract was washed with 0.1 *N* aqueous NaOH (4X) and the combined alkaline washings were acidified with 3 *N* hydrochloric acid and extracted thoroughly with ether. The combined organic extracts were washed with brine and dried ($CaSO_4$) and the solvent removed to give 7.21 g of **5b:** low melting solid; ir (film) 3600–2400 (CO_2H and OH) and 1710 cm^{-1} (C=O); nmr ($CDCl_3$) δ 0.88 (d, 9, J = 6 Hz, C-7 CH_3 + C-11 CH_3 + H-12), 1.37 (s, 3, C-3 CH_3), 2.63 (s, 2, H-2), and 5.65 ppm (m, 2, H-4 and H-5).

To 1.9 of **5b** in 25 ml of ether was added 2.38 g of 1-ethyl-3-*p*-tolyltriazene[31] and a boiling chip and the mixture heated under reflux for 3.5 hr. To the solution was added slowly aqueous 10% hydrochloric acid and then the organic layer was washed with further aqueous acid, 10% Na_2CO_3, and brine, and dried ($CaSO_4$) and the solvent was removed. Short path distillation of the residue gave 1.1 g of hydroxy ester **5c:** bp (bath) 110° (0.1 mm); ir (film) 3540 (OH) and 1725 cm^{-1} (C=O); nmr ($CDCl_3$) δ 0.87 (d, 9, J = 6 Hz, C-7 CH_3 + C-11 CH_3 + H-12), 1.25 (t, 3, J = 7 Hz, OCH_2CH_3), 1.32 (s, 3, C-3 CH_3), 1.95 (m, 2, H-6), 2.55 (s, 2, H-2), 4.16 (q, 2, J = 7 Hz, OCH_2CH_3), and 5.58 ppm (m, 2, H-4 and H-5); mass spectrum (20 eV) *m/e* (rel intensity) 269 (10), 223 (3), 84 (92), 71 (100), 69 (45), 57 (80), 43 (60).

Anal. Calcd for $C_{17}H_{32}O_3$: C, 71.79; H, 11.34. Found: C, 71.76; H, 11.20.

Ethyl (*E*)-3-Acetoxy-3,7,11-trimethyl-4-dodecenoate (5e). To about 0.025 mol of the dilithium salt **5a** in 275 ml of THF (prepared as described above for **5b**) at room temperature, under N_2 was added 5.2 g (0.051 mol) of acetic anhydride. The mixture was stirred 6 hr and then boiled overnight. After concentration *in vacuo* aqueous 1 *N* hydrochloric acid was added and the mixture was extracted twice with ether. The organic layer was then extracted with 10% aqueous Na_2CO_3 solution and the basic washes were acidified with cold 3 *N* aqueous HCl and extracted with ether. The organic layer was washed with brine and dried ($CaSO_4$) and the solvent removed *in vacuo* to give 9.56 g of acetoxy acid **5d:** ir (film) 3500–2500 (COOH), 1745, 1720, and 1615 cm^{-1}; nmr ($CDCl_3$) δ 0.88 (d, 9, J = 6 Hz, C-7 CH_3 + C-11 CH_3 + H-12), 1.65 (s, 3, C-3 CH_3) 2.02 (s, 3, CH_3CO), 3.02 (br s, 2, H-2), and 5.75 ppm (m, 2, H-4 and H-5).

A sample of the acetoxy acid **5d** was esterified with excess diazoethane in ether and the product purified by preparative tlc to yield the ester **5e:** ir (film) 1745 cm^{-1} (C=O); nmr ($CDCl_3$) δ 0.88 (d, 9, J = 6.0 Hz), 1.27 (t, 3, J = 7.0 Hz), 1.63 (s, 3, C-3 CH_3), 2.02 (s, 3, CH_3CO), 2.97 (s, 2, H-2), 4.14 (q, 2, J = 7.0 Hz, OCH_2CH_3), and 5.73 ppm (m, 2, H-4 and H-5).

Anal. Calcd for $C_{19}H_{34}O_4$: C, 69.90; H, 10.50. Found: C, 70.06; H, 10.45.

Ethyl 3,7,11-trimethyl-2,4-dodecadienoate (1 and 2a). A. From 5b with Phosphorus Trichloride. To a solution of 1.0 g (3.9 mmol) of hydroxy acid **5b** in 10 ml of benzene was added a solution of 0.91 g (6.6 mmol) of phosphorus trichloride in 5 ml of benzene, and the mixture was stirred at room temperature for 3 days. Ethanol (5 ml) and pyridine (10 ml) were then added and the mixture was stirred at room temperature for 2 hr. The reaction mixture was then diluted with ether and water and acidified with 3 *N* aqueous H_2SO_4. The organic layer was washed with 10% aqueous Na_2CO_3, water, saturated aqueous $CuSO_4$, water, and brine, and dried ($CaSO_4$) and the solvent was removed *in vacuo* to give 0.30 g of a mixture. Analysis by glc[21] showed it to contain **1, 2a,** and **16**[22] in the ratio of *ca.* 1:1:2, respectively.

Repetition of the above procedure using ether as the solvent under reflux overnight gave, apart from 10% **5c,** a mixture of **1, 2a,** and **16** in the ratio 1.5:1.2, respectively.

B. From 5b with Thionyl Chloride. To a mixture of 7.2 g (28 mmol) of **5b,** 100 ml of benzene, and 7.64 g (59 mmol) of *N*-ethyldiisopropylamine at 0° was added 5.1 ml (70 mmol) of thionyl chloride. The ice bath was then removed and the mixture was stirred at room temperature overnight. Glc analysis at this point revealed very little starting material to be present. The mixture was cooled to 0°, 6.5 g (141 mmol) of ethanol was added, and the mixture was allowed to warm to room temperature and then stirred for 4 hr. The product was then isolated as in A to yield 5.1 g of product. Distillation gave 3.54 g, bp 137–142° (0.3 mm), containing (glc analysis[21]) 5% of **5c,** 27% of **2a,** 50% of ester **1,** and 10% of the deconjugated esters **16.**

This procedure was repeated with 0.1 g (0.4 mmol) of **5b** without initial addition of the tertiary amine. After stirring overnight at room temperature an aliquot was worked up (with ethanol treatment) and analyzed by glc.[21] In addition to some **5b,** there was present a mixture of **1** + **2a** and **16** in the ratio 4:3. To the reaction mixture was now added 0.26 g (2 mmol) of *N*-ethyldiisopropylamine and the reaction followed by glc. The proportion of **16** decreased during the first few hours. After 3 days the mixture was worked up as in A and shown to contain mostly **1** and **2a** with less than 5% of **16.**

C. From 5c with Phosphoryl Chloride. To a solution of 0.10 g (0.35 mmol) of hydroxy ester **5c** in 2 ml of pyridine at 0° was added 0.05 g (0.33 mmol) of phosphoryl chloride. The mixture was allowed to warm to room temperature and stand 4 days. At this point glc analysis[21] revealed the presence of about equal amounts each of the esters **5c, 1, 2a,** and **16.**

D. From 5c with Phosphorus Pentoxide. To a mixture of 1.0 g (3.52 mmol) of **5c** in 25 ml benzene, was added 0.50 g (3.52 mmol) of phosphorus pentoxide and the mixture was stirred at 65° for 12 hr, then cooled to room temperature and an additional 0.50 g of phosphorus pentoxide was added. After the mixture had remained at room temperature for 4 days it contained, according to glc analysis,[21] a mixture of **5c, 1, 2a,** and **16**[22] in the ratio of 1:1:1:2, respectively.

E. From 5e. To a solution of 0.10 g (0.31 mmol) of the acetoxy ester **5e** in 5 ml of tetrahydrofuran was added 0.04 g (0.36 mmol) of potassium *tert*-butoxide. The solution was stirred at room temperature for 60 hr after which time the mixture contained[21] about 20% starting material **5e** and approximately equal amounts of the 2,4-dienoates **1** and **2a**.

Ethyl 3-Hydroxy-2-isopropenyl-5,9-dimethyldecanoate (9b). To 3.32 g (32.8 mmol) of diisopropylamine and 150 ml of tetrahydrofuran at 0° under N_2 was added 21 ml (33.4 mmol) of 1.59 *M n*-butyllithium in hexane solution. The mixture was stirred 1 hr at 0° and then 3 hr at room temperature. After cooling to 0°, 1.56 g (15.6 mmol) of 3-methyl-2-butenoic acid in 25 ml of THF was added; the solution was stirred 0.5 hr at 0° and then 1.5 hr at 45°. The solution was then recooled to 0° and 2.43 g (15.6 mmol) of 3,7-dimethyl-1-octanal (**3**) in 20 ml of THF was added. After the mixture was stirred 0.5 hr at 0°, it was slowly allowed to warm to room temperature overnight. Aqueous 1 *N* hydrochloric acid was then added with cooling in an ice–water bath and the mixture was extracted thoroughly with ether. The combined organic layers were extracted three times with aqueous 0.1 *N* sodium hydroxide and the combined alkaline washes were acidified at 0° with aqueous 3 *N* hydrochloric acid. The mixture was then extracted with ether and the organic layer washed with brine and dried ($CaSO_4$) and the solvent removed *in vacuo* to give 4.26 g of crude 3-hydroxy-2-isopropenyl-5,9-dimethyldecanoic acid as a low melting solid: ir (film) 1710 (C=O), 1650 (C=C), and 900 cm^{-1}; nmr (CCl_4) δ 0.88 [d, J = 6 Hz, $(CH_3)_2CH$-], 2.99 (br d, $J \sim 7$ Hz, H-2), 4.1 (m, H-3), and 4.97 ppm (m, C=CH_2). A sample of the crude hydroxy acid was esterified with 1-ethyl-3-*p*-tolyltriazene[31] in ether (at reflux temperature) to give crude **9b** contaminated with about 25% of a mixture of **11c** and **12**. Purification by preparative tlc gave pure **9b**: bp (bath, short-path) 120° (0.1 mm); ir (film) 3550 (OH), 1725 (C=O), 1650 (C=C), and 915 cm^{-1} (C=CH_2); nmr ($CDCl_3$) δ 0.88 (d, 6, J = 6 Hz, C-9 CH_3 + H-10), 0.93 (d, 3, J = 6 Hz, C-5 CH_3), 1.27 (t, 3, J = 7 Hz, OCH_2CH_3), 1.87 (m, 3, CH_3C=), 3.03 (br d, 1, $J \sim 7$ Hz, H-2), 4.1 (m, 1, H-3), 4.21 (q, 2, J = 7 Hz, OCH_2CH_3), and 5.02 ppm (m, 2, C=CH_2); mass spectrum (70 eV) *m/e* (rel intensity) 128 (100), 113 (15), 100 (55), 83 (60), 82 (65), 69 (18), 57 (30), 55 (40).

Anal. Calcd for $C_{17}H_{32}O_3$: C, 71.79; H, 11.34. Found: C, 71.78; H, 11.30.

A similar result was obtained when the aldehyde **3** was allowed to react with **8** at −70° for 2 hr followed by quenching at −70° with aqueous hydrochloric acid. Esterification of the product gave a mixture **9b** and **12** in the ratio 88:12, and a negligible amount of **11c**.

Ethyl 3-Acetoxy-2-isopropenyl-5,9-dimethyldecanoate (9c). To a mixture of 2.58 g (9.1 mmol) of hydroxy ester **9b** and 5.9 ml (73 mmol) of pyridine at 0° was added 1.7 ml (18 mmol) of acetic anhydride. The ice bath was then removed and the mixture was stirred at room temperature overnight. The mixture was then cooled to 0° and stirred for 1 hr with 3.5 ml of water. The ester was then isolated with ether in the usual manner to give 2.0 g of crude acetoxy ester which was purified by preparative tlc. Two samples (0.48 g and 0.56 g) were separated, both exhibiting identical ir, nmr, and mass spectra but each containing equal amounts of two components, all differing in glc retention times. These proved to be the four diastereoisomers of **9c** which had been partially separated into two groups: bp (bath, short-path) 80° (0.06 mm); ir (film) 1745 cm^{-1}; nmr ($CDCl_3$) δ 0.88 (d, J = 6.0 Hz), 1.27 (t, J = 7 Hz, OCH_2CH_3), 1.82 (br s, 3, CH_3C=C), 2.02 (s, 3, CH_3CO), 3.24 (d, 1, J = 9 Hz, H-2), 4.19 (q, 2, J = 7 Hz, OCH_2CH_3), 4.98 (br s, 2, C=CH_2), 5.52 ppm (m, 1, H-3); mass spectrum (20 eV) *m/e* (rel intensity) 221 (4), 170 (10), 128 (100), 127 (22), 100 (10), 43 (32).

Anal. Calcd for $C_{19}H_{34}O_4$: C, 69.90; H, 10.50; Found: C, 69.72; H, 10.35.

Ethyl 2-Isopropenyl-5,9-dimethyl-2-decenoate (10). A mixture of 0.30 g (0.92 mmol) of acetoxy ester **9c**, 10 ml of tetrahydrofuran and 0.11 g (0.98 mmol) of potassium *tert*-butoxide was stirred at room temperature overnight under N_2. Volatile material was then removed *in vacuo* and the residue diluted with 50 ml of ether and 50 ml of water. The aqueous layer was then removed and extracted with 50 ml of ether. The combined ether layers were washed with aqueous 5% sodium bicarbonate solution and water and then dried ($CaSO_4$) and the solvent was removed *in vacuo* to give 0.14 g of product **10** which was short-path distilled: bp (bath) 80° (0.06 mm); ir (film) 3080, 1725 (C=O), 1635 (C=C), and 905 cm^{-1}; nmr ($CDCl_3$) δ 0.88 (d, 9, J = 6.0 Hz, C-5 CH_3 + C-9 CH_3 + H-10), 1.28 (t, J = 7 Hz, OCH_2CH_3), 1.90 (br s, 3, CH_3C=C), 2.2 (m, 2, H-4), 4.24 (q, 2, J = 7 Hz, OCH_2CH_3), 4.78 and 5.18 (br s, C=CH_2), and 6.87 ppm (t, 1, "J" = 7.5 Hz, H-3); mass spectrum (20 eV) *m/e* (rel intensity) 266 (8), 221 (7), 195 (5), 153 (100), 140 (30), 126 (43), 125 (50), 107 (33), 95 (33), 81 (35), 69 (22), 57 (34), 43 (21).

Anal. Calcd for $C_{17}H_{30}O_2$: C, 76.64; H, 11.35. Found: C, 76.52; H, 11.20.

The stereochemistry of the 2-ene bond in **10** is unknown.

(*Z*)-5-Hydroxy-3,7,11-trimethyl-2-dodecenoic Acid (11b). A solution of 9.72 g (62.2 mmol) of **3** was added to 700 ml of a solution of about 62 mmol of the dilithium salt of 3-methyl-2-butenoic acid (prepared as described above, under N_2). The mixture was stirred 0.5 hr at 0° and 4 hr at room temperature, and then heated overnight (16 hr) under reflux. The hydroxy acid was then isolated as described above to give 8.5 g of a mixture of the hydroxy acid **11b** and the lactone **12** in the ratio 60:40 plus about 5% of the 2-isopropenyl-3-hydroxy acid, as estimated from the nmr spectrum (the ratio of **11b**:**12** obtained varied in different experiments).

Ethyl (*Z*)-5-Hydroxy-3,7,11-trimethyl-2-dodecenoate (11c) and 3-Methyl-(2,6-dimethylheptyl)-2-penten-5-olide (12). A 2.0-g sample of crude hydroxy acid above was esterified with 1-ethyl-3-*p*-tolyltriazene[31] and the product was purified by short-path distillation followed by preparative tlc, to give hydroxy ester **11c** [about 90% *Z* and 10% *E* isomers by glc]: {bp (bath, short-path) 120° (0.1 mm); ir (film) 3450 and 1720 cm^{-1}; nmr ($CDCl_3$) δ 0.88 (d, 6, J = 6 Hz, C-11 CH_3 + H-12), 0.93 (d, 3, J = 6 Hz, C-7 CH_3), 1.28 (t, 3, J = 7 Hz, OCH_2CH_3), 1.97 (d, 3, J = 1.3 Hz, C-3 CH_3), 3.95 (br m, 1, H-5), 4.18 (q, 2, J = 7 Hz, OCH_2CH_3) and 5.87 ppm (m, 1, H-2)} and the **lactone 12** {bp (bath, short-path) 110° (0.05 mm); ir (CS_2) 1730, 1655 cm^{-1}; nmr ($CDCl_3$) δ 0.88 [d, 6, J = 6 Hz, $(CH_3)_2CH$], 0.93 (d, 3, J = 6 Hz, CH_3CH), 2.00 (br s, 3, C-3 CH_3), 2.28 (d, 2, J = 7 Hz, H-4), 4.47 (br m, 1, H-5), and 5.80 ppm (m, 1, H-2); mass spectrum (20 eV) *m/e* (rel intensity) M^+ 238 ($\sim$ 0), 125 (7), 112 (8), 111 (100), 109 (5), 100 (5), 97 (5), 95 (5), 83 (17), 82 (22), 81 (8), 71 (9), 69 (9), 57 (14), 55 (8)}.

Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.66; H, 10.83.

Ethyl (*Z*)-5-Acetoxy-3,7,11-trimethyl-2-dodecenoate (11d). To a solution of about 20 mmol of the dilithium salt **11a** in tetrahydrofuran was added 3.7 ml (39 mmol) of acetic anhydride and the mixture stirred at room temperature for 6 hr and then boiled overnight. The acetoxy acid was isolated in the usual manner to give 6.5 g of crude acetoxy acid. A 1.4-g sample of the latter was treated with excess diazoethane to give the acetoxy ester **11d** [about 90% *Z* and 10% *E* stereoisomers by glc]: bp (bath, short path) 100° (0.03 mm); ir (film) 1740 (C=O), 1715 (C=O), 1650 (C=C), and 1245 cm^{-1}; nmr ($CDCl_3$) δ 0.88 (d, J = 6 Hz), 1.28 (t, 3, J = 7 Hz, OCH_2CH_3), 1.94 (d, 3, J = 1.3 Hz, C-3 Me), 2.00 (s, 3, $COCH_3$), 2.92 (m, 2, H-4), 4.25 (q, 2, J = 7 Hz, OCH_2CH_3), 5.17 (br m, 1, H-5), and 5.77 ppm (br s, 1, H-2); mass spectrum (20 eV) *m/e* (rel intensity) 266 ($\sim$0), 170 (9), 139 (38), 128 (100), 111 (12), 100 (18), 83 (14), 82 (14), 69 (9), 57 (14).

Anal. Calcd for $C_{19}H_{34}O_4$: C, 69.90; H, 10.50. Found: C, 69.99; H, 10.33.

Ethyl 3,7,11-Trimethyl-2,4-dodecadienoate (1 plus 2a). A mixture of 0.10 g (0.31 mmol) of acetoxy ester **11d** [*ca.* 90% *Z* and 10% *E* isomers by glc], 5 ml tetrahydrofuran, and 0.04 g (0.36 mmol) of potassium *tert*-butoxide was stirred at room temperature for 60 hr, at which time it contained (glc) about 80% of starting material **11d** and a mixture of the dienoates **1** plus **2a** in the ratio about 1:9, respectively.

6,10-Dimethyl-2-undecyn-4-ol (13). To a mixture of 46 g (1 mol) of 1-propynyllithium (from Foote Mineral Co) and 700 ml of dimethylformamide at 0° under N_2 was added 60 g (0.38 mol) of 3,7-dimethyl-1-octanal in 300 ml of dimethylformamide over a period of 3 hr; the ice bath was then removed and the mixture was stirred at room temperature overnight. Saturated aqueous NH_4Cl was then added with ice–water cooling and the mixture was extracted with ether–pentane (1:1). The combined organic layers were washed with water and brine and dried ($CaSO_4$), and the solvent was removed *in vacuo* to give 72.4 g of crude product which was purified by distillation through a 15-cm Vigreux column, followed by distillation on a spinning-band column to give 21.5 g (29% yield) of pure alcohol **13**: bp 68.0° (0.025 mm); ir (film) 3360 (OH) and 2220 cm^{-1} (C≡C); nmr (benzene-d_6) δ 0.88 (d, 9, J = 6 Hz, C-6 Me + C-10 Me + H-11), 1.55 (d, 3, J = 2 Hz, C≡CCH_3), and 4.40 ppm (br m, 1, H-4); nmr ($CDCl_3$) δ 0.87 (d), 1.83 (d, J = 2 Hz, H-1), and 4.4 ppm (br m, H-4); mass spectrum (20 eV) *m/e* 195 ($M^+ - 1$), 69.

Anal. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.46; H, 12.24.

Ethyl 3,7,11-Trimethyl-3,4-dodecadienoate (14). A mixture of 4.0 g (20 mmol) of the alcohol **13**, 23 g (142 mmol) of triethyl orthoacetate, and 0.05 g (0.7 mmol) of propionic acid was heated at 135° with stirring for 5 hr with a slow stream of argon being allowed to pass over the surface of the liquid such that ethanol plus some triethyl orthoacetate slowly distilled off (reaction was followed by glc). The product was then distilled *in vacuo* directly from the reaction flask after excess triethyl orthoacetate had been removed at 20 mm. There was obtained 4.4 g (83%) of the ester **14** (analysis by glc showed a purity of >96%): bp 100–101° (0.10 mm); ir (film) 1955 (C=C=C), 1740 (C=O), and 1190 cm^{-1}; nmr ($CDCl_3$) δ 0.88 (d, 9, J = 6 Hz, C-7 Me + C-11 Me + H-12), 1.27 (t, 3, J = 7 Hz, OCH_2CH_3), 1.76 (d, 3, J = 3 Hz, C-3 Me), 2.96 (br d, 2, H-2), 4.17 (q, 2, J = 7 Hz, OCH_2CH_3), and 5.03 ppm (br m, 1, H-5); mass spectrum (20 eV) *m/e* (rel intensity) 266 (1), 81 (100).

Anal. Calcd for $C_{17}H_{30}O_2$: C, 76.64; H, 11.35. Found: C, 76.53; H, 11.21.

Isomerization of 14. Small samples (25–30 mg) of **14** in 1 ml of solvent were treated with 10–30 mol % of various catalysts (Table I) and the progress of the reaction was followed by glc analysis[21] using *n*-docosane (20–30 mg) as an internal standard and using previously prepared, authentic samples of esters **1, 2a, 16, 15a,** and **15b** for comparison purposes. Some of the products were analyzed carefully by glc–mass spectrometry for confirmation of the results.

Isomerization of 14 and Equilibration of Ethyl 3,7,11-Trimethyl-2,4-dodecadienoate Stereoisomers. To a solution of 0.20 g (0.75 mmol) of ester **14** in 2 ml of ethanol at room temperature under N_2 was added 2 drops of *N*-benzyltrimethylammonium hydroxide ("Triton B"; 40% solution in methanol). After 2 days the mixture was acidified with aqueous 2 *N* sulfuric acid and the solvent removed *in vacuo*. The residue was treated with 20 ml of ether and 20 ml of water, the ether layer was separated, washed with water and brine and dried ($CaSO_4$), and the solvent was removed to give 0.16 g of product containing (in their glc elution order)[21] 21% of ester **15a,** 49% of ester **15b,** 7% of ester **2a,** and 23% of ester **1.**

To 50 mg the above ester mixture was added with stirring, 4.6 mg of benzenethiol and 2.9 mg of 2,2′-azobis(isobutyronitrile) and the mixture was heated at 85° for 2 hr under N_2. Volatile materials were then removed *in vacuo* and the mixture was examined by glc.[21] In addition to several trace impurities already present in the starting ester mixture, the final material was found by careful glc analysis to contain 31% of ester **2a** and 64% of ester **1** and very little (<1%) of the 4*Z* esters (**15a** and **15b**).

Photochemical *Z–E* Isomerization of 1 and 2a. A. Direct Irradiation. A 44-mg sample of the pure 2*E*,4*E* isomer **1** was dissolved in 3 ml of hexane in a Pyrex tube. The solution was degassed and maintained under an atmosphere of argon, and then irradiated with a 200-W Hanovia medium-pressure mercury arc lamp (S654A-36) with the light filtered through a total of *ca.* 2–3 mm of Pyrex glass. The reaction was followed by glc and after 73 hr of irradiation of photostationary state was reached with **1** and **2a** present in the ratio 44:56, respectively. No trace of the allene **14** could be detected and ≤2% each of the 2*Z*,4*Z* isomer **15a** and of the 2*E*,4*Z* isomer **15b** were present.

An identical result was obtained on repeating the above irradiation starting with the pure 2*Z*,4*E* isomer **2a** in hexane (80 hr). Very little loss of material was observed due to polymerization.

Irradiation of a mixture of **1** and **2a** (in the ratio 70:30, respectively) in either hexane or in methanol as above but in presence of air, gave essentially the same result. After 21-hr irradiation in methanol a mixture of **1** and **2a** was obtained in the ratio 48:52, respectively. Irradiation of a 30-mg sample of dienoates **1** + **2a** (70:30) in a mixture of 2 ml of hexane and 1 ml of (*E*)-1,3-pentadiene (E_t = 59 kcal/mol) in an air atmosphere gave after 21 hr, a mixture of **1** and **2a** in the ratio 44:56, respectively, as above. Thus no quenching was observed.

B. Photosensitized Isomerization. A 30-mg sample of **1** + **2a** (70:30, respectively) was dissolved in a mixture of 1 ml of hexane and 1 ml of acetophenone. The solution was irradiated as above but through a total of 12 mm of Pyrex glass. Isomerization was rapid and after 5.5 hr a photostationary state was reached containing a mixture of **1** and **2a** in the ratio 53:47, respectively. After a further 25 hr of irradiation the ratio had not altered. No allene **14** could be detected and only trace amounts of the 4*Z* isomers **15a** and **15b** were present.

Similarly 50-mg samples of a mixture of **1** + **2a** (78:22, respectively) in degassed tetrahydrofuran (5 ml) under an argon atmosphere were irradiated as above in the presence of 10–20 equiv of a variety of sensitizers, for 2–3 hr with the light filtered through 5–7 mm of Pyrex glass. Under these conditions no change at all occurred in the absence of a sensitizer. The concentrations of the sensitizers were chosen so that they would absorb >99% of the light above 300 nm. The sensitizers used with their triplet energies[32] in kcal/mol in parentheses were acetophenone (73.6), carbazole (70.1), benzophenone (68.5), fluorene (67.6), biphenyl (65), phenanthrene (62.2), 1′-acetonaphthone (56.4), biacetyl (54.9), benzil (53.7), pyrene (48.7), 1,2-benzanthracene (47), and phenazine (44). Most of the sensitizers with triplet energies ≥53 kcal/mol gave rapid isomerization under these conditions to mixtures of **1** and **2a** in *ca.* 50:50 ratio. Some decomposition of the sensitizer was noted in the experiments using phenazine, 1′-acetonaphthone, and phenanthrene, and in the experiment using benzophenone the dienoates were consumed. After 3 hr the run with pyrene contained a mixture of **1:2a** in the ratio 61:39, and after 2 hr that with 1,2-benzanthracene contained a ratio of 73:27 (**1:2a**). Phenazine under these conditions (2 hr) gave a ratio of 78:22, unchanged from that in the starting sample (some decomposition of the sensitizer did, however, occur).

Photosensitized Oxygenation of 1. A sample of 9 g of dienoate (containing **1** and **2a** in the ratio 4:1, respectively) and 500 mg of Rose Bengal were dissolved in 300 ml of dry ethanol. The photooxidation was conducted in a water-jacketed reaction flask into which the oxygen was dispersed by an extracoarse gas dispersion tube. The solution was irradiated externally with a Smith-Victor Corp (Ind.) Model Q-1 movie light containing a Type DYH 600-*W* GE quartz tungsten–iodine lamp, installed 20 cm from the flask. Efficient water cooling of the jacket kept the reaction temperature below 15° during the reaction period. The reaction was followed by glc analysis of a known aliquot diluted with a solution of *n*-docosane as an internal standard. After 163 hr of irradiation glc analysis demonstrated that whereas the amount of **2a** had remained practically constant, the 2*E*,4*E* isomer **1** had reacted to the extent of *ca.* 57%. Only one main reaction product could be detected by tlc. The solvent was then removed *in vacuo* at a bath temperature below 40°. The residue was chromatographed on 1200 g of silica gel (activity II). Elution with hexane–ether (10:3) gave 1.5 g of **19:** bp (bath, short-path) 100° (0.1 mm); uv max (hexane) 296 nm (ϵ 6500); ir (film) 3370, 1695, 1660, and 1585 cm^{-1}; nmr ($CDCl_3$) δ 0.88 (d, 9, J = 6 Hz, C-7 CH_3 + C-11 CH_3 + H-12), 2.12 (s, 3, C-3 CH_3), and 5.87 ppm (s, 1, H-4); mass spectrum (20 eV) *m/e* (rel intensity) M^+ 252 (10), 140 (100).

Anal. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.29; H, 9.67.

The nmr spectra of some of the fractions of **19** obtained from the above chromatography, contained a triplet signal at 1.73 ppm due to the presence of an impurity (see below).

In another experiment a 2-g sample of the dienoate (**1:2a** in ratio 4:1) was photooxidized at 10° with Rose Bengal (100 mg) for 115 hr as above and the ethanol removed *in vacuo*. Ether was added to the residue and the Rose Bengal was removed by filtration through a column of cellite. The solvent was then evaporated and the residue examined by nmr. The spectrum ($CDCl_3$) showed the presence of **1** and **2a** in about equal amounts (C-3 CH_3 as doublets at 2.28 and 2.00 ppm, respectively) and two new signals, a triplet (J = 2 Hz) at 1.73 ppm and a broad peak at 5.88 ppm. The singlet at 2.12 due to **19** could not be seen. Half of this crude product was distilled *in vacuo* (0.1 mm) at a bath temp of 110° to give 0.87 g of an oil. The nmr spectrum ($CDCl_3$) of this distilled product now contained (apart from signals due to **1** and **2a**) singlets due to **19** at 2.12 and 5.87 ppm. The triplet at 1.73 ppm was considerably diminished in intensity. Analysis by glc showed that the amount of **19** present was *ca.* 15%.

Chromatography of the crude photooxygenation product on alumina (Activity IV) also gave some **19.** Addition of triphenylphosphine or of hexamethylphosphorous triamide to the ethanol solution after irradiation gave after work-up, lower yields of **19** along with complex by-product mixtures.

Photosensitized Oxygenation of 1 in an Nmr Tube. To a 100-mg sample of the dienoate (containing **1** and **2a** in the ratio 4:1) in 0.5 ml of CD_3OD in an nmr tube was added 10 mg of Rose Bengal and the solution irradiated as above in a cooling bath. The oxygen was bubbled through *via* a fine glass tube. The temperature was maintained at 8°, and the reaction was followed by taking occasional nmr spectra. After irradiation for 10 hr the nmr spectrum showed that the majority of **1** had reacted to give a new product which absorbed at 1.73 ppm (triplet, J = 2 Hz) and at 5.83 ppm (broad multiplet peak). Addition of a few drops of NaOD in CD_3OD produced a complete change in the spectrum with loss of the 1.73 and 5.83 ppm signals and the appearance of singlets at

2.03 and 5.87 ppm characteristic of **19**. A quartet at 3.63 ppm (J = 7 Hz) was now observed which was probably due to liberated free ethanol.

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Registry No.—**1,** 41205-09-8; **2a,** 53042-55-0; **3,** 5988-91-0; **4,** 53042-56-1; **5a,** 53042-57-2; **5b,** 53042-58-3; **5c,** 53042-59-4; **5d,** 53042-60-7; **5e,** 53042-61-8; **8,** 53042-62-9; **9b,** 53042-63-0; **9b** free acid, 53042-64-1; **9c** isomer A, 53042-65-2; **9c** isomer B, 53109-13-0; **9c** isomer C, 53109-14-1; **9c** isomer D, 53109-15-2; **10,** 53042-66-3; **11a,** 53042-67-4; **11b,** 53042-68-5; **11c,** 53042-69-6; **11d,** 53042-70-9; **12,** 53042-71-0; **13,** 40770-70-5; **14,** 40770-71-6; **15a,** 53042-72-1; **15b,** 53042-73-2; **19,** 53042-74-3; diethyl 2-oxopropylphosphonate, 1067-71-6; 1-ethyl-3-*p*-tolyltriazene, 50707-40-9; 3-methyl-2-butenoic acid, 541-47-9; triethyl orthoacetate, 78-39-7.

References and Notes

(1) Contribution No. 25 from the Research Laboratory of Zoecon Corporation.
(2) Zoecon Postdoctoral Fellow, 1971–1972.
(3) C. A. Henrick, W. E. Willy, J. W. Baum, T. A. Baer, B. A. Garcia, T. A. Mastre, and S. M. Chang, *J. Org. Chem.*, **40,** 1 (1975).
(4) C. A. Henrick, W. E. Willy, B. A. Garcia, and G. B. Staal, *J. Agr. Food Chem.*, submitted for publication.
(5) C. A. Henrick, G. B. Staal, and J. B. Siddall, *J. Agr. Food Chem.*, **21,** 354 (1973).
(6) *Cf.* P. L. Creger, *J. Amer. Chem. Soc.*, **89,** 2500 (1967); S. Watanabe, K. Suga, T. Fujita, and K. Fujiyoshi, *Isr. J. Chem.*, **8,** 731 (1970); *Chem. Ind. (London)*, 1811 (1969); G. W. Moersch and A. R. Burkett, *J. Org. Chem.*, **36,** 1149 (1971).
(7) (a) H. O. Huisman, A. Smit, S. Vromen, and L. G. M. Fisscher, *Recl. Trav. Chim. Pays-Bas,* **71,** 899 (1952); (b) H. O. Huisman, A. Smit, P. H. Van Leeuwen, and J. H. Van Rij, *Recl. Trav. Chim. Pays-Bas,* **75,** 977 (1956); (c) F. Korte and D. Scharf, *Chem. Ber.*, **95,** 443 (1962); (d) lithio alkyl acetates have been used recently as an alternative to the Reformatsky reaction, M. W. Rathke, *J. Amer. Chem. Soc.*, **92,** 3222 (1970); M. W. Rathke and D. F. Sullivan, *ibid.*, **95,** 3050 (1973).
(8) Obtained from Aldrich Chemical Co; *cf.* S. Hünig and M. Kiessel, *Chem. Ber.*, **91,** 380 (1958); use of pyridine or of triethylamine was not satisfactory as these amines gave complex mixtures.
(9) *Cf.* K. Eiter, E. Truscheit, and H. Oediger, *Angew. Chem.*, **72,** 948 (1960); see also ref 13a.
(10) (a) M. Matsui, S. Okano, K. Yamashita, M. Miyano, S. Kitamura, A. Kobayashi, T. Sato, and R. Mikami, *J. Vitaminol. (Kyoto),* **4,** 178 (1958); (b) M. Matsui, K. Yamashita, M. Miyano, S. Kitamura, S. Okano, A. Kobayashi, T. Sato, and R. Mikami, *ibid.*, **4,** 190 (1958); (c) M. Matsui, U. S. Patent 2,951,853 (Sept 6, 1960); (d) U. Schwieter, C. v. Planta, R. Rüegg, and O. Isler, *Helv. Chim. Acta.*, **45,** 528 (1962); (e) P. E. Blatz, P. Balasubramaniyan, and V. Balasubramaniyan, *J. Amer. Chem. Soc.*, **90,** 3282 (1968).
(11) (a) M. Matsui, A. Kobayashi, and H. Kuzuhara, *Bull, Agr. Chem. Soc. Jap.*, **24,** 685 (1960); M. Matsui and A. Kobayashi, *Agr. Biol. Chem.*, **26,** 705 (1962); (b) see also M. W. Rathke and D. Sullivan, *Tetrahedron Lett.*, 4249 (1972); J. L. Herrmann, G. R. Kieczykowski, and R. H. Schlessinger, *ibid.*, 2433 (1973).
(12) G. Cainelli, G. Cardillo, M. Contento, G. Trapani, and A. Umani Ronchi, *J. Chem. Soc., Perkin Trans. 1,* 400 (1973).
(13) (a) U. Eisner, J. A. Elvidge, and R. P. Linstead, *J. Chem. Soc.*, 1372 (1953); (b) K. Eiter and E. Truscheit, German Patents 1,070,175 (Dec 3, 1959), 1,075,598 (Feb 18, 1960).
(14) S. Watanabe, K. Suga, T. Fujita, and K. Fujiyoshi, *Chem. Ind. (London),* 80 (1972); K. Suga, S. Watanabe, and T. Fujita, *Aust. J. Chem.*, **25,** 2393 (1972); see also B. Angelo, *Bull. Soc. Chim. Fr.*, 1848 (1970).
(15) P. E. Pfeffer, L. S. Silbert, and E. Kinsel, *Tetrahedron Lett.*, 1163 (1973); see also P. E. Pfeffer and L. S. Silbert, *J. Org. Chem.*, **36,** 3290 (1971).
(16) R. Couffignal and M. Gaudemar, *J. Organomental Chem.*, **60,** 209 (1973); *cf.* A. S. Dreiding and R. J. Pratt, *J. Amer. Chem. Soc.*, **75,** 3717 (1953); R. H. Wiley, E. Imoto, R. P. Houghton, and P. Veeravagu, *J. Amer. Chem. Soc.*, **82,** 1413 (1960).
(17) J. K. Crandall and G. L. Tindell, *J. Chem. Soc., Chem. Commun.*, 1411 (1970).
(18) H. J. Monteiro and J. B. Siddall, U.S. Patent 3,737,452 (June 5, 1973).
(19) C. A. Henrick and J. B. Siddall, U.S. Patent 3,716,565 (Feb 13, 1973); U.S. Patent 3,801,611 (April 2, 1974).
(20) W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, T. Li, D. J. Faulkner, and M. R. Peterson, *J. Amer. Chem. Soc.*, **92,** 741 (1970).
(21) Analytical glc analyses of ester mixtures were carried out on 2 m × 2 mm (i.d.) glass columns packed with 100–120 mesh ZPT-S, coated with 3% PDEAS or OV-101. The presence of suspected compounds was confirmed by coinjection with authentic samples.
(22) Spectral data (ir, nmr, and mass spectra) showed the presence of two major isomers in which the carbonyl function was not in conjugation with the diene system. Since proof of actual structure in this case is not trivial, we have tentatively assigned their structures as 3,5-dienoates (*cf.* ref 7). In the mass spectra of **1, 2a, 15a,** and of **15b,** the base peak is at *m/e* 139. In the mass spectra of the isomers **16,** the base peak is at *m/e* 107. Partial deconjugation of **1** can readily be carried out by treatment with triphenylmethyllithium in tetrahydrofuran at −30° followed by protonation with water to give some **16;** addition of excess deuterium oxide to the anion solution at −70° gives **16** containing one deuterium atom at C-2 (in the mass spectrum the base peak is now at *m/e* 109 with a peak at 108 of 93% of the base peak intensity).
(23) *Cf.* M. J. Jorgenson, *Chem. Commun.*, 137 (1965); J. A. Barltrop and J. Wills, *Tetrahedron Lett.*, 4987 (1968); M. J. Jorgenson and L. Gundel, *ibid.*, 4991 (1968); ethyl 6,6-dimethyl-2,4-heptadienoate has been transformed into its 3,4-allenic isomer on irradiation through a Vycor filter, M. J. Jorgenson, *J. Amer. Chem. Soc.*, **91,** 6432 (1969).
(24) A. F. Kluge and C. P. Lillya, *J. Org. Chem.*, **36,** 1988 (1971).
(25) G. S. Hammond, J. Saltiel., A. A. Lamola, N. J. Turro, J. S. Bradshaw, D. O. Cowan, R. C. Counsell, V. Vogt, and C. Dalton, *J. Amer. Chem. Soc.*, **86,** 3197 (1964); W. G. Herkstroeter and G. S. Hammond, *ibid.*, **88,** 4769 (1966).
(26) C. S. Foote, *Accounts Chem. Res.*, **1,** 104 (1968); K. Gollnick, *Advan. Photochem.*, **6,** 1 (1968); D. R. Kearns, *Chem. Rev.*, **71,** 395 (1971).
(27) J.-P. Dalle, M. Mousseron-Canet, and J.-C. Mani, *Bull. Soc. Chim. Fr.*, 232 (1969), and references therein; C. S. Foote and M. Brenner, *Tetrahedron Lett.*, 6041 (1968); cyclic peroxides have also been obtained as the major products from photosensitized oxygenation of simple acyclic 1,3-dienes, K. Kondo and M. Matsumoto, *J. Chem. Soc., Chem. Commun.*, 1332 (1972).
(28) R. H. Wiley and C. H. Jarboe, *J. Amer. Chem. Soc.*, **78,** 2398 (1956); R. Mayer, *Chem. Ber.*, **90,** 2369 (1957).
(29) G. B. Quistad, L. E. Staiger, and D. A. Schooley, *J. Agr. Food Chem.*, submitted for publication.
(30) P. A. Chopard, V. M. Clark, R. F. Hudson, and A. J. Kirby, *Tetrahedron,* **21,** 1961 (1965); G. Sturtz, *Bull. Soc. Chim. Fr.*, 2477 (1967); 2340 (1964).
(31) E. H. White and H. Scherrer, *Tetrahedron Lett.*, 758 (1961); E. H. White, A. A. Baum, and D. E. Eitel. *Org. Syn.*, **48,** 102 (1968); available from Aldrich Chemical Co. and from Willow Brook Laboratories.
(32) W. G. Herkstroeter, A. A. Lamola, and G. S. Hammond, *J. Amer. Chem. Soc.*, **86,** 4537 (1964); N. J. Turro, "Molecular Photochemistry," W. A. Benjamin, New York, N.Y., 1967, p 132.

Photochemical Reactivity of Imino Lactones. Photoreduction and Photoelimination

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The photochemical reactivity of three imino lactones, 5,6-dihydro-3,5,5-trimethyl-1,4-oxazin-2-one (**3a**), 5,6-dihydro-5,5-dimethyl-3-phenyl-1,4-oxazin-2-one (**3b**), and 3-butyl-5,6-dihydro-5,5-dimethyl-1,4-oxazin-2-one (**3c**), is described. Oxazinones **3a** and **3b** are photostable with respect to the [2 + 2] photocycloaddition reaction to the carbon–nitrogen double bond. Oxazinone **3a** undergoes photoreductive dimerization in 2-propanol solvent, oxazinone **3c** photoeliminates propene to give **3a,** and **3b** is photostable. Possible mechanisms for the reductive dimerization and elimination reactions are discussed.

In our exploration of the photochemical reactivity of conjugated imines and imino ethers, we have synthesized and studied three imino lactones. These chromophores were prepared as systems which might illustrate the elusive