(290 g; Alcoa F-20; activity grade ~2) packed in benzene–petroleum ether (3:2); elution with the same solvent mixture (1400 ml) followed by pure benzene (2000 ml) yielded 19.36 g of nearly pure keto methyl ester II, mp 92.5–96.5° after crystallization from petroleum ether. One recrystallization gave 18.52 g (41.4%; based on amount of **6** unrecovered as **14**) of II as slender bars: mp 95.6–97.3°; $[\alpha]^{30}\text{D}$ −38.4° (*c* 3.4, $CHCl_3$); ir ($CHCl_3$) 1725, 1705, 1230, 1170 and 1158 cm^{-1}; nmr τ 9.05 (d, 3, *J* = 6.5 Hz, H-15), 8.87 (s, 3, H-14) and 6.38 (s, 3, $-OCH_3$).

Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.56; H, 9.14.

An analytical sample of the corresponding acid, **3-oxo-5,7αH,-4βH-12,13-bisnoreudesman-11-oic acid (12)**, obtained after several recrystallizations from methylene chloride–diethyl ether, exhibited mp 138–140°; ir ($CHCl_3$) 3490–2500 (broad band) and 1718 cm^{-1} (three peaks); nmr ($CDCl_3$) τ 8.99 (d, 3, *J* = 6.5 Hz, H-15), 8.87 (s, 3, H-14) and 0.39 (s, 1, –COOH).

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.40; H, 8.76.

B. *Via* Potassium Hypoiodite Oxidation of 3-Ethylenedioxy-5,7αH,4βH-12-noreudesman-11-one (7).—A mixture (1.93 g) of **7**, **14** and **6**, obtained from 0.0071 mol of **6** plus **14** and ethylene glycol in a manner similar to that described for the preparation of pure **7**, was dissolved in dioxane (48 ml) and water (23 ml) containing 5.8 g of 85% KOH pellets. A solution of 18 g (0.07 mol) of iodine and 36 g of potassium iodide in 72 ml of water was then added dropwise at room temperature. After stirring for 11 hr, 10 g of 85% KOH pellets were added to destroy the purple color. Suspended solids (unreacted **14** and iodoform) were removed by filtration. The filtrate was extracted with methylene chloride to remove additional neutral materials, cooled, acidified (HCl), treated with saturated sodium bisulfite solution to destroy the remaining iodine, stirred at room temperature for 20 hr and extracted with methylene chloride. The extracts were washed with brine and dried (Na_2SO_4). Removal of the solvent gave 1.35 g of brown liquid which was treated with excess diazomethane in ether–ethyl acetate at 0° and chromatographed on 20 g of alumina (Woelm, grade I; 28 × 1.4 mm column) using benzene as eluent to give 0.43 g (26%) of keto ester II as needles, mp 89–93°. A second ester (ir, nmr) which was not investigated further was obtained in comparable yield as a yellow oil upon further elution with benzene. Studies using a wide range of similar conditions indicate that the 26% yield cited is optimum. Large-scale preparations using *ca.* 10 g of **6** and 1.2 mol equiv of ethylene glycol gave somewhat poorer yields of II.

C. *Via* Treatment of 6 with Trimethyl Orthoformate–Perchloric Acid.—Aqueous 70% perchloric acid (10 ml, 0.113 mol) was added slowly to 30 ml of trimethyl orthoformate initially at 2°; the temperature during the addition was maintained below 20° and safety precautions against possible detonation were taken. The reaction mixture was cooled to 1° and a solution of diketone **6** (2.50 g, 0.0113 mol) in 8 ml of cold trimethyl orthoformate was added dropwise with stirring over a 5.5-min period; the temperature of the reaction mixture was maintained below 2° during the addition. After stirring for 1.6 hr at 0.5–1° the crude reaction mixture was poured into 300 ml of ice–water containing 4.5 g (0.112 mol) of NaOH and 13.6 g (0.10 mol) of sodium acetate trihydrate. The cold aqueous suspension was extracted rapidly with methylene chloride and worked up as usual, taking care not to heat or expose the oily unstable product to air for prolonged periods. Nmr analysis of the product indicated the presence of ≤25% of **6** and ≤30% of a product exhibiting signals of equal area at τ 4.77 (d, 1, *J* = 7.2 Hz) and 0.29 (d, 1, *J* = 7.2 Hz) and a peak at 6.27 (s, ~3.2). The crude product was dissolved in methylene chloride and treated with an excess of ozone over a period of 18 min; the resulting solution was reduced to an *ca.* 10-ml volume *in vacuo* and treated with 6.1 g of potassium iodide in acetic acid (6 ml) and methanol (8 ml) at 0°. The cooling bath was removed and stirring continued at ambient temperature for 2.5 hr. The final reaction mixture was treated with aqueous sodium bisulfite and extracted with methylene chloride. Washing the extracts with 5% sodium bicarbonate followed by acidification of the wash solutions and extraction of the organic acids gave 0.118 g of an acidic white solid which was not **12** (nmr analysis) and was not investigated further. The neutral product (2.43 g of orange oil) which was obtained in the usual manner from the methylene chloride extracts was found to contain about 20% of the starting diketone **6** and *ca.* 15–25% of keto ester II. The total crude product was hydrolyzed using potassium hydroxide in 80% methanol. The acidic portion (1.38 g) of the product was isolated in the usual manner after removal of any neutral material in the diluted reaction mixture by extraction with methylene chloride. Esterification of the acidic product with ethereal diazomethane, followed by chromatography on 20 g of alumina as described in B, yielded 0.412 g (15.4%) of **18**, mp 93.8–95.8°. Using nmr as a monitoring technique, studies under a range of conditions similar to those described above indicate that the yield of II cited is probably optimum.

3,11-Bisethylenedioxy-5,7αH,4βH-noreudesmane (14).—A mixture of diketone **6** (2.28 g, 0.0102 mol), ethylene glycol (3.80 g, 0.061 mol) and 0.034 g of *p*-toluenesulfonic acid in 17 ml of benzene was heated at reflux temperature for 10 hr using a Dean–Stark water separator. The usual work-up procedure afforded 3.10 g (97%) of diketal **14** as prisms, mp 86.5–88.5°. Four additional recrystallizations from petroleum ether–methylene chloride gave an analytical sample, mp 89.5–90.0°; the ir spectrum indicates the absence of a characteristic absorption band for a ketonic carbonyl group; nmr τ 9.25 (d, 3, *J* = 7 Hz, H-15), 9.16 (s, 3, H-14), 8.83 (s, 3, H-13) and 6.16 (m, 8, $-OCH_2CH_2O-$).

Anal. Calcd for $C_{18}H_{30}O_4$: C, 69.64; H, 9.74. Found: C, 69.70; H, 9.77.

Registry No.—II, 18508-76-4; **2**, 18540-91-5; **3**, 18508-83-3; **4**, 18508-84-4; **5**, 18508-85-5; **6**, 18540-92-6; **7**, 18508-86-6; **12**, 18508-87-7; **13**, 18508-88-8; **14**, 18508-89-9.

Acknowledgment.—It is a pleasure to acknowledge the assistance of Mr. Edward A. Weiss in the large-scale preparation of several intermediates.

The Structure of (+)-Occidentalol. A Revision[1]

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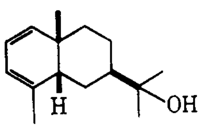
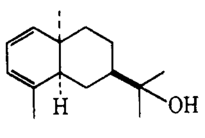
Received August 2, 1968

(+)-Occidentalol, a eudalene-type sesquiterpene alcohol obtained from *Thuja occidentalis* L., possesses a *cis* fusion and a 1,3-diene system,[2] two structural features rarely encountered in this series of natural products.[3] The recent isolation of the related *cis*-fused 1,3-dienes, dehydrochamaecynenol and -al, and several *cis*-fused Δ¹-3 ketones, from *Chamaecyparis formosensis* Matsum.,[4] has led to the suggestion[5] that these compounds arise by a unique biosynthetic pathway involving valence tautomerism of 1,3,5-*trans*,-



1



2

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[1] We thank the National Institutes of Health for partial support of this research (Grant No. 5-RO1-GM-13441-03), the National Science Foundation for funds used to purchase a Varian HA-100 spectrometer, and Professor E. von Rudloff for kindly supplying us with a sample of occidentalol.

[2] E. von Rudloff and H. Erdtman, *Tetrahedron*, **18**, 1315 (1962), and references cited.

[3] G. Ourisson, S. Munavelli, and C. Ehret, "International Tables of Selected Constants," Vol. 15 (Data Relative to Sesquiterpenoids), Pergamon Press, Oxford, 1966, pp 13, 14, 22, 25, 26. [Note that the *cis*-fused structure for juniper camphor has recently been revised to *trans:* G. L. Chetty, V. B. Zalkow, and L. H. Zalkow, *Tetrahedron Lett.*, 3223 (1968).]

[4] T. Asao, S. Ibe, K. Takase, Y. S. Cheng, and T. Nozoe, *ibid.*, 3639 (1968), and references cited.

[5] A. G. Hortmann, *ibid.*, 5785 (1968).

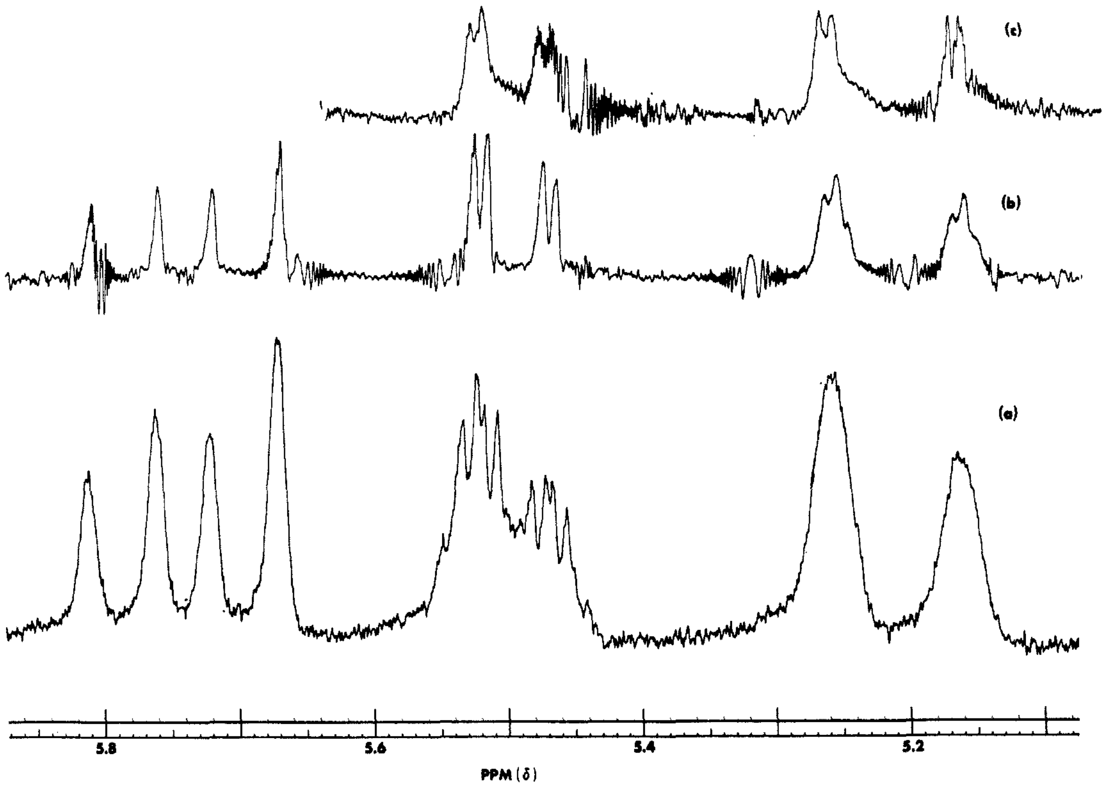
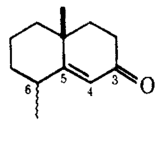


Figure 1.—Nmr spectrum (100 MHz) of the olefinic protons of (+)-occidentalol: (a) undecoupled spectrum; (b) spectrum obtained by applying a moderate irradiating field at δ 1.79 (protons on C-15 decoupled); (c) spectrum obtained by applying a strong irradiating field at δ 1.65 (protons on C-15 *and* C-5 decoupled).

cis,trans-cyclodecatriene intermediates derived from farnesol.

Of the four structures possible for (+)-occidentalol, Mislow and Moscowitz[6] considered **1** and **2** to be most likely on the basis of conformational analysis and the assumption (based on a comparison of $[\alpha]_D$ values for occidentalol and its products of hydrogenation) that occidentalol exhibits a strong positive Cotton effect which is due to skewing of the cisoid butadiene moiety in the sense of a right-handed helix. A report[7] by Ziffer, *et al.*, of the direct observation of an intense positive Cotton effect in the ORD curve of occidentalol and of a mirror-image relationship between the ORD curves of a ketone believed to be **3** (obtained as a minor product from the oxidation of tetrahydrooccidentalol) and keto acid **4** (a reduction product of α-santonin) has led to the present acceptance[3] of **1** as the structure of this terpene.



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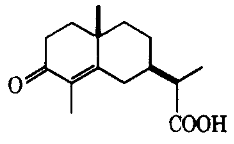

4

We wish to report that the structure **1** for (+)-occidentalol is in error and should be revised to **2**.

The nmr spectrum (100 MHz) (see Table I) of occidentalol shows signals due to the olefinic protons as three characteristic resonance patterns (see Figure 1) at δ 5.21, 5.74, and 5.49 which can be assigned to H-1, H-2, and H-3, respectively, on the basis of the magnitudes of their mutual spin-coupling interactions.[8] Upon irradiation of the signal due to the H-15 protons at δ 1.79, the broad doublet (J = 9.6 Hz) due to H-1 at 5.21 was transformed into a doublet of triplets $J_{1,2}$ = 9.6, $J_{1,3}$ = 1.0, $J_{1,5}$ = 1.0 Hz); in addition, the pattern due to H-3 at δ 5.49 (d, q, d; $J_{2,3}$ = 5.0, $J_{3,15}$ = 1.5, $J_{1,3}$ = 1.0 Hz) collapsed to a doublet of doublets ($J_{2,3}$ = 5.0, $J_{1,3}$ = 1.0 Hz). Simultaneous irradiation of the signals due to H-15 and H-5 resulted in further collapse of the signal due to H-1 to a doublet of doublets ($J_{1,2}$ = 9.6, $J_{1,3}$ = 1.0 Hz), but effected no further change in the signal due to H-3, thus confirming that $J_{1,5}$ = 1.0 and $J_{3,5}$ = 0 Hz. Taken with the observation that $J_{5,6\beta} \sim 12.5$ Hz,[9] these data indicate that occidentalol exists in a preferred conformation in which (a) the H-1-C-1-C-10-C-5-H-5 portion of the molecule exists in a coplanar zigzag (W) configuration,[4,10] (b) the H-3-C-3-C-4-C-5-H-5, portion of the molecule exists in a coplanar zigzag (W) configuration,[4] and (c) H-5 and H-6β are situated in a *trans*-diaxial relationship[4,10] to one another. Consideration of these conclusions and application of the helicity rule to the ORD data for occidentalol[7] allow only two pos-

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[6] K. Mislow and A. Moscowitz, *Tetrahedron Lett.*, 699 (1963).

[7] H. Ziffer, T. J. Batterham, U. Weiss, and E. von Rudloff, *Tetrahedron*, **20**, 67 (1964).

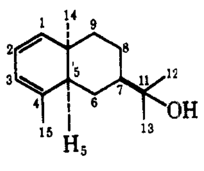
[8] E. Vogel, W. Maier, and J. Eimer, *Tetrahedron Lett.*, 655 (1966). See also ref 4.

[9] The signal for H-5 was directly observed (see Table I). The signal for H-6β in **2a** would be expected to be very broad and was not directly observed. However, its location at *ca.* δ 0.97 could be indirectly determined (see data and footnotes for H-5 and H-6β in Table I). This high-field resonance position of the 6β proton might be partly explained as being due to its axial orientation and possibly as a result of additional shielding due to its proximity to the π electrons of the diene system in **2a**. Similar effects have been recorded for α- and β-pinene: J. R. Dyer, "Applications of Absorption Spectroscopy of Organic Compounds," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1965, pp 80, 81.

[10] A. G. Hortmann, D. S. Daniel, and J. Schaefer, *J. Org. Chem.*, **33**, 3988 (1968).

TABLE I

NMR SPECTRAL DATA FOR OCCIDENTALOL[a]



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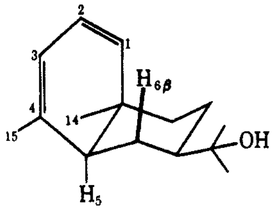
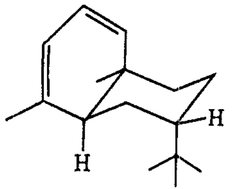


2a

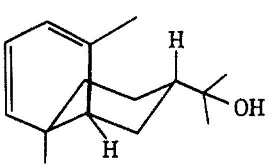
Proton(s)	Chemical shift,[b] δ	Multiplicity[c]	Observed coupling constants,[d] Hz
H-1	5.21	d (br)	$J_{1,2} = 9.6, J_{1,3} = 1.0, J_{1,5} = 1.0, J_{1,15} = 0.8$
H-2	5.74	d, d	$J_{1,2} = 9.0, J_{2,3} = 5.1$
H-3	5.49	d, q, d (sl br)	$J_{2,3} = 5.0, J_{3,15}$ 1.5, $J_{1,3} = 1.0$
H-5	1.51[e,f]	d, d, d (br)	$J_{5,6\alpha} = 12.5,^{g,h} J_{5,6\beta} \sim 3.3,^{i}$ $J_{1,5} = 1.0$
H-6β	~0.97[j]	m (v br)	
H-12,13	1.07	s	
H-14	0.85	s	
H-15	1.79	d, d	$J_{3,15} = 1.5, J_{1,15} = 0.8$
H-x	1.66[e,f]	d (?)(br)	$J_{x,y} \sim 9^{k,l}$
H-y	~1.18	m (v br)	

[a] The nmr spectrum was measured in CCl_4 solution (10%) with a Varian HA-100 spectrometer; internal benzene and tetramethylsilane (TMS) were used to provide lock signals; methanol was added to shift the –OH signal out of the upfield region. [b] Chemical shifts are relative to internal TMS at δ 0.00. [c] As observed in the undecoupled spectrum. [d] Assignments indicated by = symbol were confirmed by spin-decoupling experiments; estimated accuracies are 0.1 Hz except were stated otherwise. [e] The downfield half of the pattern due to H-5 partially overlaps the upfield half of the pattern due to H-x. [f] In the cases of H-5 and H-x (which appeared superimposed on broad absorption signals due to other protons) careful comparisons of estimated δ_5, δ_x, $J_{5,6\beta}$, and $J_{x,y}$ values were made at 60 and 100 MHz; the deviation in $\Delta(\delta_5 - \delta_x)$ was less than 10%. [g] Decoupled by applying a strong irradiating field at δ 0.97 (H-6β); the doublet at δ 1.66 (H-x) was unperturbed in this experiment. [h] Estimated accuracy, 1.5 Hz. [i] Not confirmed by spin-decoupling experiments. [j] Significantly perturbed by irradiation at δ 1.51 (H-5). [k] Estimated accuracy, 0.3 Hz. [l] Collapses to a broad peak at δ ~1.68 by irradiation at 1.18 (H-y).

sible structures for (+)-occidentalol, **2** and **5**, on the condition that each must exist preferentially in a nonsteroidal conformation, *i.e.*, **2a** and **5a**. However, since there is no reason *a priori* to favor conformer **5a** over **5b**, only structure **2**, in conformation **2a**, is possible for (+)-occidentalol.[11,14]



5a



5b

The apparent discrepancy between these results, which indicate an α orientation of the C-10 methyl group in occidentalol, and those reported earlier, which indicate β orientation,[7] can probably be attributed to the inhomogeneity of **3**.[17]

It is notable that, although the 7β orientation is considered usual for the hydroxypropyl group in naturally occurring eudesmanes, the α orientation of the C-10 methyl group relative to the 7β group, as observed in occidentalol, is very unusual.[3] This fact adds support to the hypothetical biogenetic pathway for **2** mentioned earlier and consequently suggests[19] that further examination of the essential oil of *Thuja occidentalis* L. may also lead to the isolation of **1**.

Registry No.—2, 18509-05-2.

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(11) It should be noted, in contrast to our conclusions and those of others[2,6] concerning the preferred conformation of **5**, that the structures I, II, and III in ref 4 exist predominantly in conformers having their C-7 substituents *axially* oriented. This is probably due, in part, to relief of an interaction between H-7 and the C-15 substituents in the alternate conformer and to the smaller effective steric bulk of 7-ethynyl[12] and 7-vinyl groups when compared with that of the 2-hydroxypropyl group in **5**. Further support for these conclusions can be derived from examination of data from base-catalyzed equilibration studies on chamaecynone and its derivatives from hydrogenation (T. Nozoe, *et al.*, cited in ref 4) and on 7α- and 7β-*cis*-tetrahydro-*epi*-α-cyperones.[13]

(12) R. J. Ouellette, *J. Amer. Chem. Soc.*, **86**, 3089 (1964).

(13) C. Djerassi and W. Klyne, *J. Chem. Soc.*, 4936 (1962).

(14) Implicit in our interpretation of the nmr spectrum of occidentalol is the assumption that long-range coupling between H-1 and H-5 occurs exclusively through σ bonds in the coplanar W configuration. However, a comparable coupling, $J_{1,15} = 0.8$ Hz, which could not occur *via* a W configuration, is observed between H-1 and the methyl hydrogens on C-15. This observation has lead a referee to suggest that the coupling interactions responsible for *both* $J_{1,5}$ and $J_{1,15}$ might possibly arise *via* transmission through the π system of the diene since each of the protons on C-5 and C-15 is similarly separated from H-1 by six bonds *via* the diene system. If $J_{1,5}$ did, in fact, arise exclusively as a result of such an allylic σ–π interaction, the structure **1** in its favored conformation (enantiomeric with **5b**) would have to be seriously considered as a possibility for (+)-occidentalol.[15] However, the observations that $J_{5,6\beta} = 12.5$ and $J_{5,6\alpha} \sim 3.3$ Hz, as well as the absence of coupling interactions of the allylic σ–π type[16] between H-3 and H-5 ($J_{3,5}$ = 0; carefully ascertained at both δ 1.51 and 5.49) are sufficient to exclude this possibility.[4,10]

(15) This assumes, by analogy with observations recorded for simple allylic systems,[16] that coupling between H-1 and H-5 transmitted *via* the diene system will be at a maximum where H-5 is perpendicular to the coplanar C-5–C-4–C-3–C-2–C-1–H-1 portion of the molecule. Although such an analogy with allylic systems seems reasonable, it should be noted that, to our knowledge, no examples have been recorded which define the limits of significant coupling over six bonds *via* allylic σ–π interactions in diene systems such as those present in **1** and **2**.

(16) N. S. Bhacca and D. H. Williams, "Applications of N.M.R. Spectroscopy in Organic Chemistry," Holden-Day, San Francisco, Calif., 1964.

(17) The compound believed to be **3** was obtained[7] by oxidation of tetrahydrooccidentalol (~90% pure) in *ca.* 15% yield; however, this ketone (purified by glpc) yielded no crystalline derivatives and exhibited an ε value (6300) at λ_{max} 242 mμ which was less than half that normally associated[18] with conjugated ketones of this type. The comparable, and often higher, intensities of Cotton effects observed for unconjugated ketones suggests that impurities of this type may have given rise to the relatively low-intensity curve reported[7] for **3**. In addition, the fact that anomalous rotatory dispersion curves are often exhibited[18] by 4-en-3-ones having 6- and 7-alkyl substituents indicates that any ORD data obtained using pure **3** with undetermined configuration at C-6 would result in uncertain conclusions regarding the configuration of C-10 in **3**.

(18) C. Djerassi, O. Halpern, V. Halpern, and B. Riniker, *J. Amer. Chem. Soc.*, **80**, 4001 (1958), and references cited.

(19) *Cf.* footnote 9 in ref 5.

Oxidative Introduction of Alkyloxycarbonyl Groups into Olefins

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Received July 2, 1968

It has previously been shown in this laboratory that α,β-unsaturated esters may be prepared directly from

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