

METALATION REACTIONS—IX

AN APPARENT SUPRAFACIAL 1,6-HYDROGEN SHIFT IN A PENTADIENYL-LITHIUM DERIVATIVE

J. KLEIN and S. GLILY

Department of Organic Chemistry, The Hebrew University, Jerusalem, Israel

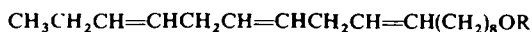
(Received in the UK 11 March 1971; Accepted for publication 29 March 1971)

Abstract—Linolenyl alcohol and its mixed methyl ether gave on metalation with butyllithium in ether after short reaction times heptatrienyllithium compounds which cyclized on standing to seven-membered pentadienyl-lithium derivative. Protonation and carbonation of this cyclized lithium compound yielded products corresponding to pentadienyl-lithium derivatives derived from the expected lithium compounds after a 1,6-hydrogen migration.

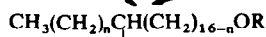
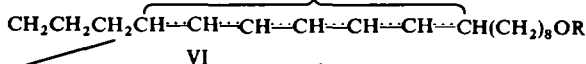
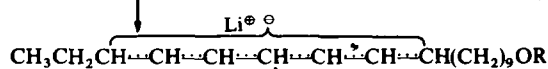
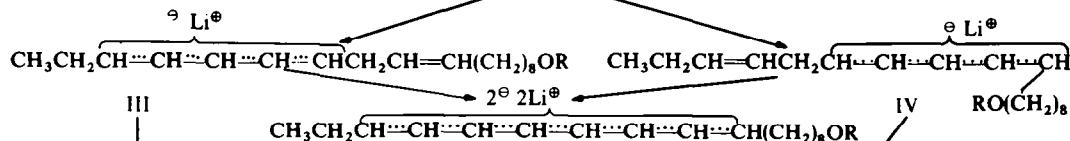
RECENTLY, we have reported a 1,6-hydrogen shift which we proved to be intramolecular in pentadienyl-lithium compounds derived from linoleyl alcohol and its Me ether. This migration proceeded along the chain in both directions yielding a number of isomeric pentadienylic compounds and stopped practically, in the conditions of our work, at the third carbon from one and at the sixth from the other end of the molecule. This last observation in conjunction with the minimum number of six carbon atoms required for an isomerization of a pentadienylic ion led us to a statement¹ that at least 14 carbon atoms were required in this system for the isomerization to be observable in ordinary metalation conditions. This generalization was based also on the fact that no isomerization even on heating solutions of short-chain pentadienylic lithium derivatives² was reported before. The statement was not intended to be a rule (as understood)³ but a simple statement of a fact valid under the conditions of our work. Later work by Bates³ has shown that on heating short chain pentadienyl-lithium compounds isomerization also occurred. Bates has supplied experimental support for the antarafacial mechanism of this 1,6 sigmatropic shift assumed by us¹ on the strength of Woodward–Hoffmann rules.⁴

We have studied the metalation of linolenyl alcohol (I) and Me ether (II) in which two methylene groups are present, each of them activated by two double bonds. Monometalation of these compounds would give the pentadienyl-lithium derivatives III and IV (Scheme 1) having neighbouring methylene groups flanked by an additional double bond. The mobility of the hydrogens of these methylene groups in a 1,6 sigmatropic rearrangement was of interest. Such rearrangement would give the heptatrienyl-lithium compounds V or VI respectively, which could in their turn undergo isomerization by 1,8-hydrogen shifts, this time in a suprafacial manner, causing migration of the heptatrienyl system along the chain. An additional process was expected, namely, the abstraction of a proton from the allylic methylene group in the monolithium derivatives III and IV which would then yield a dilithium compound VII. This last hypothetical compound was of interest since it is composed of two staggered pentadienyl systems in such a manner that no alteration of charge should

SCHEME 1



I: R = H

II: R = CH₃

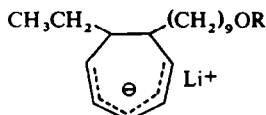
COOR

VIII

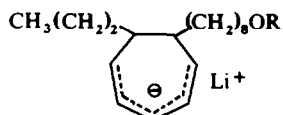
a: n = 8; b: n = 7; c: n = 6

d: n = 5; e: n = 4; f: n = 3

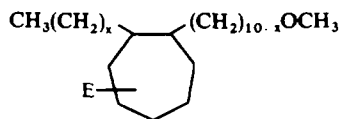
g: n = 2; h: n = 1



IX



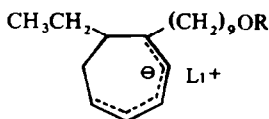
X



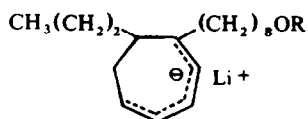
XI

k: E = H

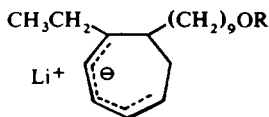
l: E = D

m: E = COOCH₃

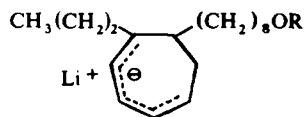
XXXVIII



XXX



XXIX



XXXI

be present and the charge would be distributed almost evenly on all the eight carbons of the dianion.

Metalation of linolenyl alcohol (I) with Bu-Li in ether for 3–4 hr and subsequent carbonation with Dry-Ice gave a mixture of carboxylic acids (45% yield). Hydrogenation of these acids, esterification and etherification of the carboxyl and hydroxyl groups with CH_2N_2 gave a mixture of the esters VIII a–h, accompanied by products of further reaction (see below), the composition of the esters was determined by mass spectrometry by comparison of the relative intensities of the $[\text{CH}_3(\text{CH}_2)_x\text{CH}=\text{C}(\text{OH})\text{OCH}_3]^+$ fragments. This method was found previously^{1,5} to be a reliable tool for the determination of the composition of mixtures of such isomeric esters. The ratio of the various isomers is recorded in Table 1. No additional isomers and

TABLE I. RATIO OF ISOMERIC ESTERS FORMED AFTER SHORT TIME METALATION OF I

Esters	VIIIa	VIIIb	VIIIc	VIIId	VIIIe	VIIIf	VIIIg	VIIIh
Ratio	1	1	1:1	1	1:4	1:3	2:2	2:4

no diesters were formed. This result showed that A: Abstraction of a proton from each of the two activated methylene group proceeded with a similar rate and the different distance from the functional group did not favour one or the other. B: The isomerization of the ions III and IV to V and VI respectively did take place during the short metalation time. C: Carboxylation of each heptatrienyl lithium derivative V and VI occurred in a similar manner, and D: No dimetalation with formation of VII occurred, apparently because isomerization of III and IV to the heptatrienyl lithium derivatives V and VI was faster than eventual abstraction of an additional proton. Isomerization of III and IV occurred since these compounds should not have given VIIIb and VIIIg. The presence of these esters in amounts similar to the esters with a carboxyl on an adjoining carbon proved that the isomerization to V and VI was complete. The two heptatrienyl lithium derivatives were obtained in similar amounts, since the sum of the esters VIIIa, VIIIc, VIIIe, VIIIg obtained from VI and of the esters VIIIb, VIIId, VIIIf, VIIIh obtained from V is similar. The ratio of the esters in each group varies also in a similar manner with the distance from the hydroxyl. The esters having the carboxyl the furthest from this function being formed in the largest amount: VIIIh > VIIIf > VIIId ~ VIIIb and VIIIg > VIIIe > VIIIc ~ VIIIa. A similar effect of the functional group was observed during the carbonation of the metalation product of linoleyl alcohol.¹ Metalation of linolenyl alcohol for longer periods (above 20 h) and then protonation or deuteration of the metalation product gave after hydrogenation and etherification of the hydroxyl group with CH_2N_2 compounds with molecular weights (mass spectrometry) of 282 or 283 respectively. Similarly, the product of carbonation (65% yield) and subsequent hydrogenation, esterification and etherification with CH_2N_2 , showed a molecular ion of mass number 340 as compared to 342 for VIII ($\text{R}=\text{CH}_3$). These results showed that the anions V and VI have undergone cyclization to IX and X respectively. Additional proof for cyclization was obtained by

ozonolysis (see below). Similar cyclization of heptatrienyl lithium to cyclic seven-membered pentadienyl compounds were recorded previously by others.^{6,7} The cyclic pentadienyl-lithium compounds IX and X gave on protonation, deuteration or carbonation (with subsequent hydrogenation and treatment with CH_2N_2) the products, XIk, XII or XIIm respectively. Analogous results were obtained on prolonged metalation of linolenyl methyl ether (II). Such cyclizations would be different from previously observed thermal cyclization of linolenic acid to cyclohexadiene⁸ and indane derivatives.⁹ The study of the structure of the cyclization products was therefore of importance.

Mass spectral analysis of the protonation and deuteration products XIk and XII obtained after prolonged metalations of I and II showed the presence of fragments (Table 2 and Scheme 2) corresponding to scission of alkyl groups from a seven but

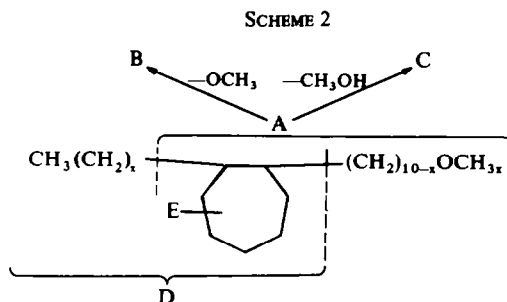


TABLE 2. CHARACTERISTIC FRAGMENTATION OF THE PRODUCTS OF PROTONATION (P)^a AND DEUTERATION (D)^a AFTER PROLONGED METALATION OF I AND II

Metalated compound (hrs) of metalation	Reaction	Fragments (%) ^b							correspondence x ^c
		M ⁺	[M--OCH ₃] ⁺	[M--CH ₃ OH] ⁺	A	B	C	D	
I(24)	P	282(7)	251(6)	256(25)	239(6)	208(6)	207(13)	139(27)	2
					253(6)	222(5)	221(12)	125(36)	1 or 2 1
II(24)	D	283(4)	252(6)	251(26)	240(6)	209(7)	208(14)	140(36)	2
					254(6)	223(7)	222(15)	126(54)	1 or 2 1
II(75)	P	282(3)	251(5)	250(21)	239(5)	208(6)	207(11)	139(26)	2
					253(5)	222(5)	221(12)	125(38)	1 or 2 1

^a and subsequent hydrogenation

^b Mass number of the fragment (% of the base peak)

^c x in the fragment is equal to the number indicated

not six-membered cyclization product. Moreover, no fragments with x in XIk or XII different from 1 or 2 were obtained, proving that no isomerization of the open heptatrienyl lithium compounds V and VI by sigmatropic hydrogen shifts occurred before cyclization to the pentadienyl lithium. The cyclization to IX and X was therefore faster than the eventual rearrangement of V and VI by hydrogen migration. In the pentadienyl-lithium compound obtained from linoleyl alcohol¹ only isomerization and no cyclization was observed. The different behaviour of the heptatrienyl and pentadienyl system in cyclization might be due partly to angle strain in a cyclopentyl compound having three trigonal atoms in the ring. This, however, cannot be the entire explanation in view of the facile cyclization of pentadienyl to cyclopentenyl carbonium ions.^{10, 11} The resistance to cyclization in the pentadienyl anion may be due to the disrotatory manner of this process which encounters probably larger steric interaction between the rotating groups than in the conrotatory process for the cyclization of pentadienyl cations or heptatrienyl anions. Mass spectral fragmentation of the ester (XI_m) did not give information on the size of the ring, since bond scission near the carboxylate group was the predominant process.

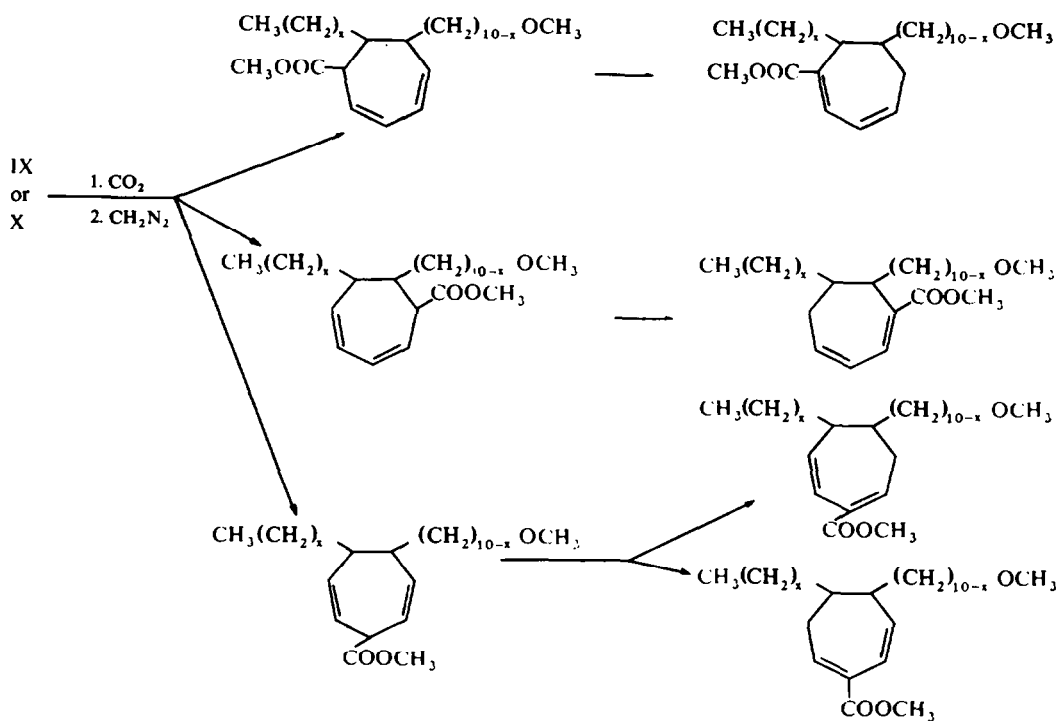
The position of protonation, deuteration and carbonation of the cyclized lithium compound and the connected problem of the position of the double bonds in the products of these reactions was then considered. Reaction at the centre of the pentadienyl system would give a 1,4-diene, but a reaction at each of the extremities of this system should yield a conjugated endocyclic diene. The UV spectra of the unsaturated protonation and deuteration products showed absorption maxima between 240 and 270 nm, characteristic for endocyclic 1,3-dienes.

The separation by TLC of the unsaturated esters, products of carbonation of the cyclic lithium compounds, led to the isolation of three fractions A, B and C (each of A and C approximately 40% of the product). Fraction A showed in the IR a band at 1740 cm^{-1} (unconjugated ester carbonyl), and in the UV maxima at the 248 nm (ϵ 8,700) and 256 nm (ϵ 9,000) for an endocyclic conjugated diene. Its NMR spectrum exhibited an ester OMe at δ 3.59 (3H, s), $-\text{CH}_2\text{OCH}_3$ protons at δ 3.25 (5H, s + m) and vinylic protons at δ 5.38–5.58 (3H, m). Fraction C exhibited a conjugated ester carbonyl at 1720 cm^{-1} , an absorption at 279 nm (ϵ 9,600), methoxycarbonyl protons at δ 3.72 (3H, s), $-\text{CH}_2-\text{O}-\text{CH}_3$ protons at δ 3.25 (5H, s + m) and vinylic protons at δ 7.01 (1H, m) (β to a conjugated carbonyl) and at δ 5.93 (1.6 H, m). The insufficient amount of vinylic protons was puzzling, but the presence in A of three instead of the four expected vinylic protons was not consistent with the expected products of carbonation of IX and X (Scheme 3). A further study aimed at the location of the double bonds in the unsaturated compounds was therefore desired.

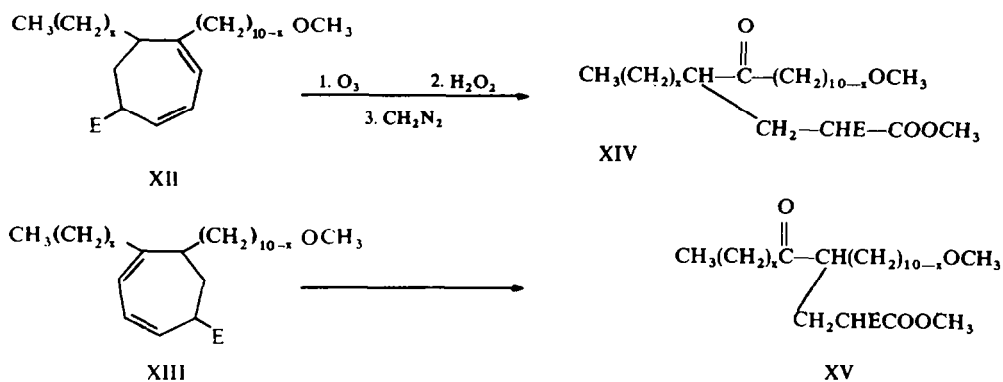
Oxidative ozonolysis of the unsaturated cyclic products of protonation or deuteration and subsequent treatment with CH_2N_2 gave a mixture of esters that was separated by GLC and TLC into two fractions, 1 (the main one) and 2 (about 10–20% of the product). Fraction 1 has a molecular weight (mass spectroscopy) of 314 for the protonation product and 315 for the deuterated one. Its IR spectrum showed an ester carbonyl at 1740 cm^{-1} and a band at 1720 cm^{-1} attributed to a ketone carbonyl (no CHO was detected by NMR.) One ester and one ether OMe were present (by NMR). These results could be accommodated with structures XII and XIII for the unsaturated cyclic hydrocarbons (Scheme 4).

Fraction 2 had a molecular weight of 330 when derived either from the protonated

SCHEME 3



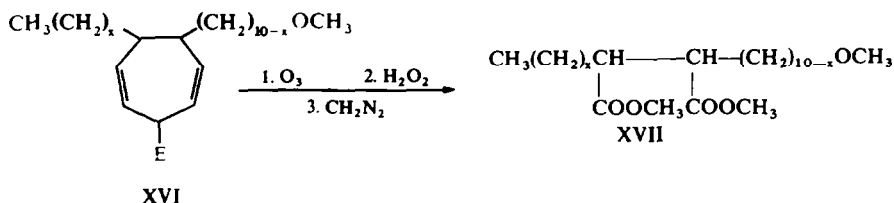
SCHEME 4



k: E = H
l: E = D
m: E = COOCH₃

or the deuterated cyclic compound. It showed an ester band at 1740 cm^{-1} two esters and one ether OMe by NMR and no other carbonyl groups. These data are consistent with structure XVII for the cyclic compound (Scheme 5).

SCHEME 5



XVI

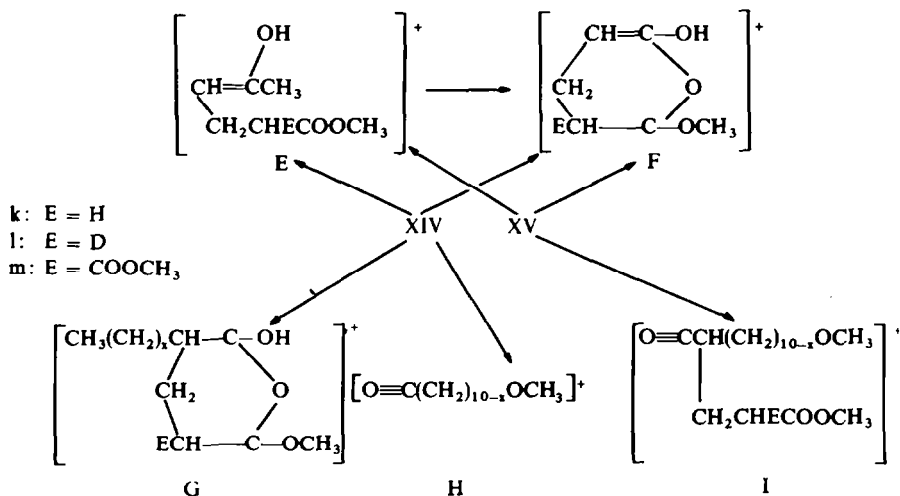
XVII

k: E = H

l: E = D

Mass spectral fragmentation of fraction 1 confirms the structures XIV and/or XV assigned (Table 3 and Scheme 6) to it. A number of fragments containing the ketone and ester carbonyls were obtained. The intensities of these fragments were relatively high and to some of them cyclic structure permitting larger delocalization of charge were assigned, although no direct proof for these structures was available. Fragment E was formed by a double rearrangement (two β -scissions). A subsequent α -scission in E could lead to F. All the fragments indicated could have been formed from XIVk or XVI (for the protonated or deuterated product respectively), but

SCHEME 6



k: E = H

l: E = D

m: E = COOCH₃

G

H

I

some of them could also have had XVk or XVI as source. The question of the presence of one or both isomers in fraction 1 was not solved.

Structure XVII for fraction 2 was also confirmed by mass spectroscopy (Table 4; Scheme 7).

TABLE 3. SOME FRAGMENTS OBTAINED IN THE MASS SPECTRUM OF FRACTION I

Metalated compound (hr) of metalation	Reaction ^a	Fragments (%) ^b								
		M ⁺	E	F	G	H	I	x ^c		
I(70)	P	314	144(46)	129(17)				1 or 2		
							172(17)	171(17)	271(5)	2
							158(31)	185(10)	285(9)	1
II(4)	D	315	145(24)	130(14)				1 or 2		
							173(27)	171(8)	272(2)	2
							159(20)	185(10)	286(5)	1
I(24)	D	315	145(88)	130(24)				1 or 2		
							173(92)	171(16)	272(8)	2
							159(35)	185(11)	286(11)	1

^a P: protonation of the lithium compound; D—deuteration

^b Mass of the fragment (% of the base peak)

^c x in the fragment is equal to the number indicated

SCHEME 7

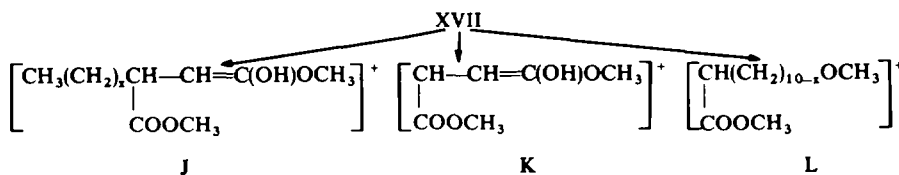


TABLE 4. SOME FRAGMENTS IN THE MASS SPECTRUM OF XVII

Metalated Compound (hr of met.)	Reaction ^a	Fragments (%)							
		M ⁺	K	K + 1	J	L	x ^b		
I(70)	P	330	145(20)	146(15)			1 or 2		
							174(17)	229(16)	1
							188(13)	215(20)	2
I(4)	D	330	145(20)	146(15)			1 or 2		
							174(16)	229(11)	1
							188(9)	215(13)	2

^a P: protonation of the lithium compound; D—deuteration

^b x in the fragment is equal to the number indicated

The unsaturated cyclic esters obtained from the product of prolonged metalation of I and II gave on ozonolysis acids that were esterified (and etherified in case of I) with CH_2N_2 and separated by TLC or GLC into three main fractions named 3, 4 and 5. Fraction 3 had a molecular weight of 372 and showed bands at 1740 (ester) and 1720 cm^{-1} (ketone). Its NMR exhibited signals at $\delta\ 3.30$ (6H, m) corresponding to $-\text{CH}_2\text{OCH}_3$ and to one additional proton α to two carboxylate groups and two singlets (6H; separation: 5Hz) near $\delta\ 3.70$ corresponding to two methoxycarbonyl groups. The structure XIVm (and eventually XVm) was attributed to this fraction. Mass spectral analysis (Table 5) showed the presence of fragments similar to those of Scheme 6 with E equal to $-\text{COOCH}_3$. An additional fragment $\text{N} = [\text{CH}_2\text{CH}_2\text{CH}(\text{COOCH}_3)_2]^+$ was also found.

Fraction 4 (ca. 70% of fraction 3) had a molecular weight of 428 (mass spectroscopy) and exhibited an ester band at 1735 cm^{-1} , a conjugated double bond at 1625 cm^{-1} and also a maximum at 220 nm ($\epsilon\ 9,400$) proving conjugation. Its NMR showed a signal at $\delta\ 3.37$ (5H) for $-\text{CH}_2\text{OCH}_3$, at $\delta\ 3.60$ (3H, s) for $-\text{COOCH}_3$, two additional three-proton singlets at $\delta\ 3.78$ (separated by 5Hz) for two conjugated $-\text{COOCH}_3$ groups, and one vinylic proton β to the methoxycarbonyl groups at $\delta\ 6.77$. Structures XXII, XXIII, XXIV and XXV were assigned to the components of this fraction and these could be formed (Scheme 8) from the unsaturated conjugated esters XVIII,

SCHEME 8

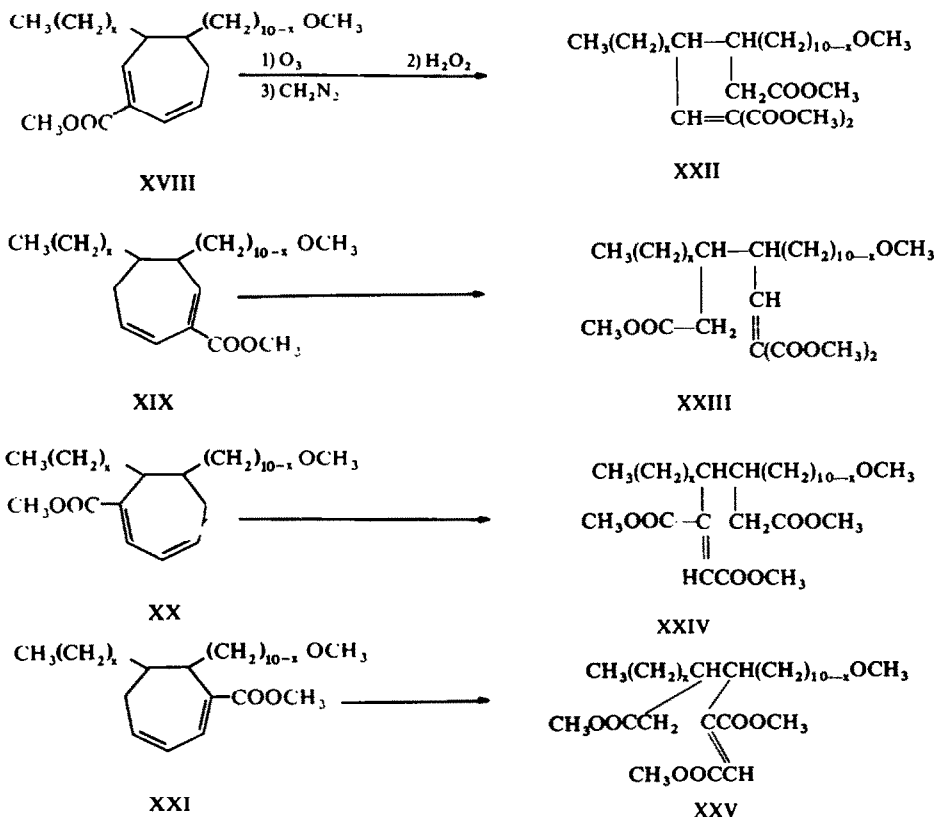


TABLE 5. SOME FRAGMENTS* OBTAINED IN THE MASS SPECTRUM OF FRACTION 3

Metalated compound (hr of met.)	Fragments (%)									
	M ⁺	I = [M-CH ₃ (CH ₂) _n] ⁺	E	[E-CH ₃ OH] ⁺	G	[G-CH ₃ OH] ⁺	H	N	x	
I(24)	372		202(9)	170(9)				159(10)	1 or 2	
	329(2)	329(2)			230(7)	198(11)	171(5)		2	
I(66)	372	343(2)	202(16)	170(13)	216(4)	184(8)	185(4)	159(17)	1	
		329(2)			230(17)	198(17)	171(8)		1 or 2	
II(75)	372	343(4)	202(10)	170(8)	216(7)	184(13)	185(6)	159(8)	1	
		329(2)			230(8)	198(9)	171(5)		2	
		343(2)			216(6)	184(5)	185(3)		1	

* R in all fragments is COOCH₃

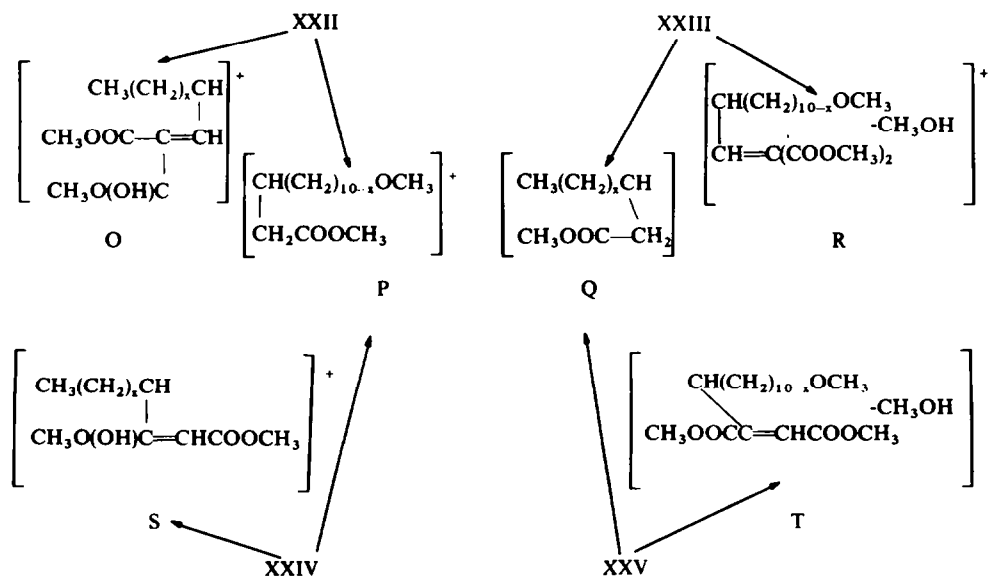
XIX, XX and XXI, where the conjugated double bond was slow to undergo ozonolysis. The fragmentation observed (Table 6 and Scheme 9) could be reconciled with the structures proposed but not with other possible ozonolysis products formed from cyclic compounds containing three vinylic protons as e.g. in Scheme 10.

Fraction 5 was obtained in lower yield than the two other (*ca.* 30% of fraction 3). It was composed of XIVk and XVk as shown by mol. wt. and fragments obtained on

TABLE 6. SOME FRAGMENTS OBTAINED IN THE MASS SPECTRUM OF FRACTION 4

Metalated compound (hr)	Fragments (%)						
	M ⁺	O or S	[(O or S)—CH ₃ OH] ⁺	P	Q	R or T	x
I (24)	428	200(11)	168(20)	299(8)	129(11)	267(7)	2
		186(10)	154(16)	243(6)	115(10)	281(6)	1
II (75)	428	200(7)	168(16)	229(5)	129(10)	267(3)	2
		186(9)	154(15)	243(4)	115(9)	281(3)	1
II (24)	428	200(8)	168(12)	229(6)	129(13)	267(4)	2
		186(8)	154(14)	243(5)	115(10)	281(2)	1

SCHEME 9



SCHEME 10

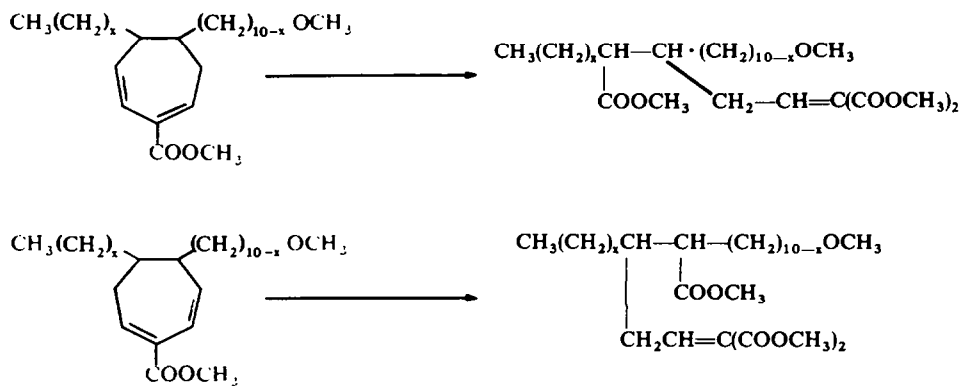
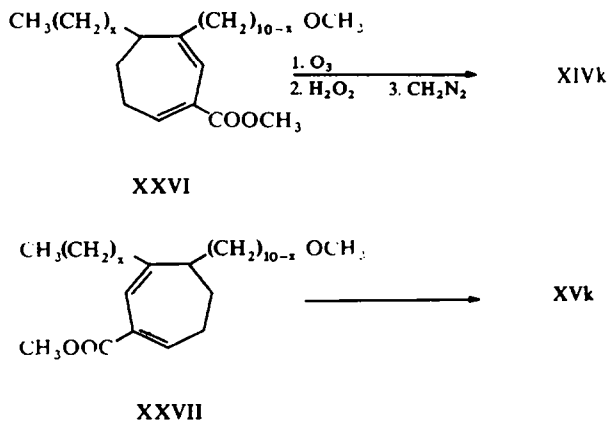


TABLE 7. FRAGMENTS IN THE OZONOLYSIS PRODUCT OF FRACTION 5

Metalated (hr of met.)	M^+	E	F	Fragments (%)			
				G	H	I	x
I (24)	314	144(10)	129(5)	172(10)	171(4)	271(1)	1 or 2
				158(6)	185(2)	285(1)	2
II (75)	314	144(17)	129(8)	172(18)	171(7)	271(2)	1 or 2
				158(13)	185(4)	285(10)	2

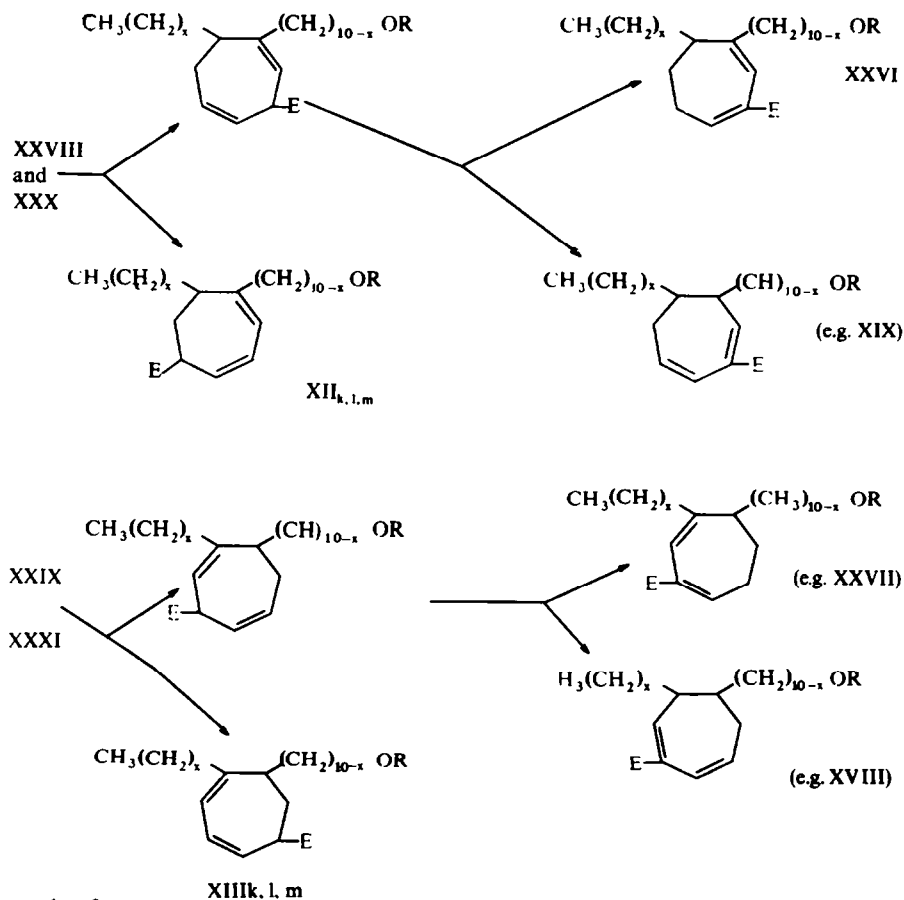
SCHEME 11



mass spectral analysis (Table 7). The structure of the compounds from which this fraction was formed was therefore XXVI and XXVII (Scheme 11).

Summarizing the results: A small part only of the products of protonation, deuteration or carbonation of the cyclic seven-membered pentadienyl-lithium compound that was formed on prolonged metalation of I or II could be accommodated with structures IX and X for these compounds. Most of the products of these reactions could not have been formed from IX or X since this would imply electrophilic attack on the uncharged instead of the charged positions. This is of particular significance in the carbonation products where the position of the carboxyl in the ring cannot change by prototropic shifts subsequent to the initial reaction. We have therefore to admit that the initially formed compounds IX and X undergo isomerization to new pentadienylic lithium derivatives, i.e. XXVIII (eventually XXIX) and XXX (eventually XXXI) respectively (Scheme 1). These compounds undergo reactions at the extremities and the central position of the pentadienyl system to give products. (Scheme 12). No carbonation was found at the tertiary position.

SCHEME 12



$x = 1$ or 2

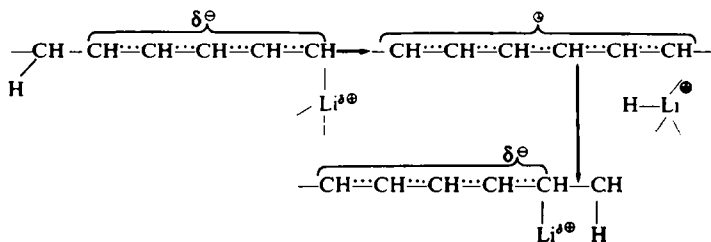
$\text{E} = \text{H}, \text{D}$ or COOCH_3

The mechanism of the rearrangement of IX to XXVIII and XXIX and of X to XXX and XXXI is of interest. Orbital correlation requirements⁴ demand 1,6-hydrogen shifts in a pentadienylic anion to be antarafacial. Such a course is prohibited in our case due to ring constraint. We considered the possibility of a two step isomerization involving protonation to a conjugated diene and an additional proton abstraction on a carbon α to a double bond to give the isomerized lithium derivatives e.g. XXVIII.

To test this possibility we submitted to prolonged metalation a mixture of the hydrocarbon products of deuteration, containing mostly XIII and XIII with 15% of XVII. The product of metalation was carbonated and the acids formed (15%) separated. The neutral fraction obtained after this metalation was again submitted to metalation but only traces of acid were obtained. It seems therefore that the 1,4-but not the 1,3-diene undergo metalation. Ozonolysis of the esterified acid fraction gave mainly XIVm, XVm, XXII–XXV corresponding to the ester XIIIm, XIIIIm, XVIII–XXI. These results prove that the mechanism of formation of XXVIII–XXXI involving protonation of the lithium derivatives IX and X to conjugated dienes and subsequent proton abstraction from the dienes has to be rejected. The compound that has undergone metalation in the mixture of cyclic hydrocarbons was XVI and this has given necessarily IX and X, which undergo an intramolecular hydrogen shift to yield the observed products, derived from XXVIII–XXXI.

Sigmatropic hydrogen shifts in organolithium compounds that were incompatible with simple orbital correlations of the anions were found by us previously.^{12, 13} It is possible that the difficulties in the orbital correlations are due to the disregard of the lithium atom. A suprafacial hydrogen shift could be obtained if the lithium atom is considered, as a sum of two antarafacial processes, each proceeding with inversion on lithium and keeping the migrating hydrogen on the same side of the ring (Scheme 13). The lithium is partly covalently linked to the carbon and probably tetrahedral

SCHEME 13



in solution, being complexed by the solvent. Migration of hydrogen to this atom inverts its configuration and as a result a tight ion pair is formed that rearranges again when the carbon atom next to the one that was initially bound to lithium displaces the hydrogen atom with inversion on lithium, the hydrogen being simultaneously transferred to the carbon originally bound to lithium. The first step is a 1,7-hydrogen shift in an eight electron system (or a 1,3-shift in a 4-electron system if the lithium is situated on the carbon vicinal to that originally linked to the migrating hydrogen). The second step is a four centre cycloaddition involving the one-electron Li—H bond and a double bond, i.e. a $\sigma_1^1 + \pi_2^2$ process. The two processes can be considered as an example of a two step concerted reaction.¹⁴ These transformations should be

of low energy. The electronic energies of a two-electron Li—H bond is 165 kcal/mol.¹⁵ We can assume that the electrostatic interactions between the positive and negative centres in the pentadienyl lithium and the intermediate obtained on hydrogen migration to lithium are similar. If we take the energy of the one electron Li—H bond as approximately 85 kcal/mole, which is close to that of an allylic C—H bond, then the energies of the two systems are similar.

An isomerization that could have been caused by a suprafacial sigmatropic rearrangement in a similar system has been observed before.^{6, 20} However, a two step isomerization cannot be eliminated as the reaction path in those cases, since a proton donating species was present during the isomerization.

EXPERIMENTAL

UV spectra were taken in EtOH and IR spectra neat. TLC analysis was run on Silica Gel PF₂₅₄.

Linolenyl alcohol I: A solution of ethyl linolenate¹⁶ (12 g) in anhyd ether (15 ml) was added to LAH (1.5 g) in ether (25 ml). The solution was refluxed for 2 hr, cooled, ethyl acetate (2 ml), then dil. HCl were added dropwise. Separation and distillation gave I (9.4 g; 87%) b.p. 158/0.8 mm; $\bar{\nu}_{\max}$ 3300–3400. 3010 cm^{-1} ; λ_{\max} 233 nm (ϵ 580).

Linolenyl methyl ether II: I was methylated¹⁷ with CH_2N_2 in CH_2Cl_2 .¹⁸ b.p. 146°/0.6 mm; $\bar{\nu}_{\max}$ 3010. 1125 cm^{-1} .

Metalation: The solvent of a soln of BuLi in hexane was distilled off in vac and ether was added under N_2 to make a 1.5 ml soln. This soln was used for metalation of I with a 4–5 mole ratio, and of III with 3–4 mole ratio of BuLi/substrate. The metalation product was left for the indicated period at room temperature and reacted (1) with water by dropwise addn of the organolithium solution to an excess of water. (2) With D_2O as above but with external cooling. (3) With CO_2 by addition of the organolithium soln to pulverized CO_2 under ether. The acids were separated, esterified and etherified with CH_2N_2 .¹⁷ (Table 8).

*Ozonolysis*¹⁹ ozone was passed through a solution of 1 g of the compound in 20 ml of acetic and formic acids 4:1 for 20 min at 0°. N_2 was then bubbled and the solution refluxed for 30 min with 4 ml of 30% H_2O_2 . Most of the solvent was evaporated at reduced pressure and the product extracted with ether. The acids were separated by extraction with NaOH 10%, then esterified and etherified with CH_2N_2 .¹⁷

Results of metalation (Table 8)

Run 1. The unsaturated esters—ethers were distilled, b.p. 173–178°/0.9 mm. (Found: C, 75.0; H, 10.6; $\text{C}_{21}\text{H}_{36}\text{O}_3$ requires: C, 75.0; H, 10.7%). These esters were separated by TLC (elution 7 times with hexane— anhyd ether, 15:1 into fraction A, B and C in the order of increasing R_f . Fraction A (41%): $\bar{\nu}_{\max}$ 1740 cm^{-1} . λ_{\max} 248 nm (ϵ , 8700), 256 nm (ϵ 9000), 260 nm (sh, ϵ 5800), 287 nm (ϵ 1050). Fraction B (20%): $\bar{\nu}_{\max}$ 1740 (m). 1720 (s), 1620 cm^{-1} . λ_{\max} 287 nm (ϵ 9200). Fraction C (39%): $\bar{\nu}_{\max}$ 1720 (s), 1605 cm^{-1} ; λ_{\max} 278 nm (ϵ 9600). (Found: C, 75.6; H, 11.0; $\text{C}_{21}\text{H}_{36}\text{O}_3$ requires: C, 75.0; H, 10.7%).

Run 2. B.p. of the unsaturated esters: 168–170°/0.9 mm. The unsaturated esters—ethers were analyzed by mass spectroscopy (Table 1).

Run 4. Oxidative ozonolysis of the unsaturated alcohols (b.p. 162°/1 mm) gave acids that were esterified and etherified with CH_2N_2 . Separation by GLC (SE30 on Chromosorb) gave fractions 1 and 2 in a ratio 5:1. (Tables 3 and 4 respectively).

Run 5. Half of the metalated product was carbonated. The composition of the carbonation product was similar to that of run 2. The second half was treated with D_2O . The product was submitted to oxidative ozonolysis. The esters—ethers that were obtained after treatment with CH_2N_2 were separated by GLC (SE30 on Chromosorb P) into three fractions. A preliminary fraction was composed of methyl 9-methoxy-nonanoate and methyl 10-methoxydecanoate, products of uncyclized lithium compounds. Then came fractions 2 and 1 (order of elution), that were submitted to mass spectral analysis (Tables 4 and 3 respectively).

Run 6. A part of the metalated compound was carbonated. CH_2N_2 gave esters b.p. 175°/0.7 mm. (Found:

TABLE 8. METALATION OF I AND II

Run	Mmoles BuLi	Substrate	Solvent ^e ml	Hr. metal.	Yield ^b %	Reaction ^f M.W. ^d	EtOH λ_{\max} nm(e) ^e	$\bar{\nu}_{\max}$ cm ⁻¹ e
1	45	I; 10	E; 30	165	40	C; 340	258 (6000), 267 (6000) 283 (5700)	3010, 1740, 1720, 1610 ^f 1125
2	45	I; 10	E; 28	3	47	C; 340, 342	242 (sh. 9600), 250 (10600) 265 (12,800), 273 (15100) 278 (12300)	3010, 1740, 1720 ^f 1610 (w), 1125
3	90	I; 20	E; 70	66	60	C; 340	248 (6200), 257 (7100) 267 (7100), 282 (6500)	3010, 1740, 1720 ^f 1610 (m), 1125
4	90	I; 20	E; 70	70		P	233 (sh. 4600), 243 (5800) 248 (6100), 257 (5200)	3300-3400, 3010
5	68	I; 16	E; 43	4	45	C; 340, 342	262 (sh. 2800) 238 (sh. 9000), 250 (sh. 10800) 263 (14100), 272 (16700) 282 (13900)	3300-3500 1740, 1720, 1600 (w) 3800-3500, 3010
						D	238 (10200) 247 (sh. 8800) 257 (7200)	
							257 (7200) 268 (6900) 268(6900)	
6	90	I; 20	E; 70	24	50	C	281 (4600) 247 (sh. 6400), 256 (7100) 272 (6500), 280 (5100)	3010, 1740, 1720 ^f 1610 (m), 1125
						P	233 (sh. 4600), 243 (6000) 249 (6200), 258 (5100) 267 (sh. 2700), 278 (sh. 840)	3010, 1125 ^f

7	45	I; 10	H; 28 ^a	20	P; 284, 282	234 (12800), 258 (7100) 268 (7400), 278 (5600)	3010, 1125 ^f
8	76	II; 18	E; 48	75	C; 340	248 (sh. 6100), 257 (7000) 267 (7050), 282 (sh. 6400)	3010, 1740, 1720 1600, 1125
9	48	II; 12	E; 30	25	D; 283	234 (sh. 4400), 242 (5800) 249 (6200), 257 (4700) 262 (sh. 2200)	3010, 1125
10	75	II; 25	E; 48	24	D	249 (6500), 257 (5300) 262 (sh. 2600)	3010, 1125
11	107	II; 36	E; 77	24	D	233 (sh. 7900), 240 (8300) 248 (8000), 258 (7100) 268 (5900), 280 (3500)	3010, 1125
12	40	II; 13	E; 30	24	C	233 (sh. 4000), 240 (sh. 5600) 248 (6400), 257 (sh. 5600)	3010, 1125
13	228	II; 54	E; 145	24	D; 283	267 (3000), 278 (sh. 500) 248 (sh. 6100), 257 (7000) 267 (7200), 280 (6700)	3010, 1740, 1720 1605, 1125
						246 (sh. 3600), 257 (6500) 267 (6900), 279 (6500) 233 (sh. 3800), 243 (5400) 249 (6000), 257 (5200)	3010, 1740, 1720 1600, 1125 3010, 1125

^a E—ether; H; hexane

^b Yield according to carbonation

^c P—protonation; D—deuteration, C—carbonation

^d By mass spectrometry after hydrogenation, esterification (in the case of carbonation) and etherification

^e Of the unsaturated product after esterification (in the case of carbonation)

^f Of the unsaturated product after esterification (in the case of carbonation) and etherification

^g 25 mmoles of TMEDA were added.

C, 74.8; H, 10.3; $C_{21}H_{36}O_3$ requires: C, 75.0; H, 10.7%). Another part of the metalated product was protonated, b.p. 130–140°/0.5 mm (Found: C, 81.5; H, 12.2; $C_{19}H_{34}O$ requires: C, 82.0; H, 11.9%). The composition of the esters, that were obtained after oxidative ozonolysis of the protonation products, was similar to that of run 4. Oxidative ozonolysis of the esters (1 g) gave after the usual work up esters (0.9 g) that were separated into three fractions 5, 3 and 4 (according to the elution order) (Tables 5, 6, 7 respectively) in addition to methyl-9-methoxynonanoate and 10-methoxydecanoate (approx. 10%).

Run 8. The unsaturated esters b.p. 164°/0.5 mm (Found: C, 74.9; H, 10.3; $C_{21}H_{36}O_3$ requires: C, 75.0; H, 10.7%), ozonolysis of 0.8 g esters gave 0.7 g of esters, that were separated by GLC into 3 fractions 5, 3 and 4. Fraction 5 had mol. wt. of 314 (Table 7). Fraction 3: mol. wt. 372 (Table 5). (Found: C, 64.5; H, 9.3; $C_{20}H_{36}O_6$ requires: C, 64.5; H, 9.7%). $\bar{\nu}_{max}$ 1740, 1715 cm^{-1} . Fraction 4: mol. wt. 428 (Table 6).

Acknowledgement—We are grateful to the United States Department of Agriculture, Agricultural Research Service, for the support of this work.

REFERENCES

- 1 J. Klein, S. Gilly and D. Kost, *J. Org. Chem.* **35**, 128 (1970)
- 2 R. B. Bates, S. Brenner, W. H. Deines, D. A. McCombs and D. E. Potter, *J. Amer. Chem. Soc.* **92**, 6345 (1970)
- 3 R. B. Bates, D. W. Gosselink and J. A. Kaczynski, *Tetrahedron Letters* 199, 205 (1967)
- 4 R. B. Woodward and R. Hoffmann, *J. Amer. Chem. Soc.* **87**, 2511 (1965)
- 5 J. Klein and E. Gurfinkel, *J. Org. Chem.* **34**, 3952 (1969)
- 6 E. A. Zuech, D. L. Crain and R. F. Kleinschmidt, *Ibid.* **33**, 771 (1968); H. Kloosterziel and Mrs. J. A. A. Van Drunen, *Rec. Trav. Chim.* **88**, 1083 (1969)
- 7 R. B. Bates, W. H. Deines, D. A. McCombs and D. E. Potter, *J. Amer. Chem. Soc.* **91**, 4608 (1969)
- 8 J. P. Friedrich, *J. Amer. Oil Chem. Soc.* **44**, 244 (1967)
- 9 W. R. Eckert, H. Scharmann and A. Zeman, *Fette Seifen Anstrichmittel* **71**, 468 (1969)
- 10 N. C. Deno, C. U. Pittman Jr and J. O. Turner, *J. Amer. Chem. Soc.* **87**, 2153 (1965)
- 11 T. S. Sorensen, *Can. J. Chem.* **42**, 2768 (1964); *J. Amer. Chem. Soc.* **87**, 5075 (1965)
- 12 J. Klein and S. Brenner, *Tetrahedron* **26**, 2345 (1970)
- 13 *Idem*, *J. Org. Chem.* **36**, 1319 (1971).
- 14 E. Baldwin, *Fortsch, Chem. Fortsch.* **15**, 281 (1970)
- 15 G. Herzberg: *Molecular Spectra and Molecular Structure, Diatomic Molecules* Van Nostrand, 2nd ed. (1950)
- 16 J. W. McCutcheon, *Org. Synth. Coll. Vol III*, p 526, 531, 532 (J. Wiley and Sons, 1955)
- 17 M. Neeman, M. C. Caserio, J. D. Roberts and W. S. Johnson, *Tetrahedron Letters* 36 (1959)
- 18 R. E. Lutz *et al.*, *J. Amer. Chem. Soc.* **68**, 1818 (1946)
- 19 T. H. Applewhite, L. A. Goldblatt and R. E. Lundin, *J. Org. Chem.* **31**, 3407 (1966)
- 20 H. Kloosterziel and Mrs. J. A. A. Van Drunen, *Rec. Trav. Chim.* **88**, 1471 (1969)