Metallation Reactions. Part X.[1] Allylic Metallation in the Presence of Amide Groups: Long Range Interactions

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The *N*-methylamide of linoleic acid is metallated by butyl-lithium in ether or in hexane α to the amide groups and/or at the doubly allylic position, without addition to the carbonyl group. The ratio of the products depends on the solvent. Metallations of *NN*-dimethyl-linoleamine were also obtained. The positions of carbonation of these lithium derivatives revealed a long-range effect of the functional groups. A series of octadecanoic acids with one additional carboxy-group in various positions in the chain was prepared for comparison. Products of metallation in the presence of tetramethylethylenediamine of the amide with the conjugated two double bonds gave addition of butyl-lithium to the diene.

LINOLEYL ALCOHOL and its methyl ether were metallated smoothly with butyl-lithium at the double allylic position.[1] It was of interest to investigate the possibility of metallation of a linoleic acid derivative containing a carbonyl group but without addition of the organometallic reagent to this group. Although monomethylamides of unsaturated acids were found to be resistant to 1,2-addition, they did undergo 1,4-addition [2] with Grignard reagents. The monomethylamide of linoleic acid (I) was, therefore, submitted to the action with butyl-lithium. The metallation of *NN*-dimethyl-linoleamine (II) and of the *NN*-dimethylamide of linoleic acid were also studied. The metallation of (I) with butyl-lithium in ether with subsequent carbonation gave acids in yields of up to 86%. This reaction was slower in hexane: after 28 h of metallation a yield of 24% of acids was obtained and this yield increased to 37% after 96 h. The main component of the product formed in hexane was, after hydrogenation, the methyl-monoamide (III) of the malonic acid, obtained from the product of

$CH_3\cdot[CH_2]_4\cdot CH{=}CH\cdot CH_2\cdot CH{=}CH\cdot[CH_2]_7R$

(I) $R = CO\cdot NH\cdot CH_3$
(II) $R = CH_2N(CH_3)_2$

$CH_3\cdot[CH_2]_{15}\cdot CHR\cdot CO\cdot NH\cdot CH_3$

(III) $R = CO_2H$
(IV) $R = Cl$
(V) $R = CO_2CH_3$

$CH_3\cdot[CH_2]_x\cdot CH(CO_2CH_3)\cdot[CH_2]_{14-x}CHR\cdot CO\cdot NH\cdot CH_3$

(VI) $R = CO_2CH_3$
(VII) $R = H$

$CH_3\cdot[CH_2]_x\cdot CH(CO_2CH_3)(CH_2)_{15-x}CO_2CH_3$

(VIII)

a; $x = 10$
b; $x = 9$
c; $x = 8$
d; $x = 7$
e; $x = 6$
f; $x = 5$
g; $x = 4$
h; $x = 3$
i; $x = 2$
j; $x = 1$

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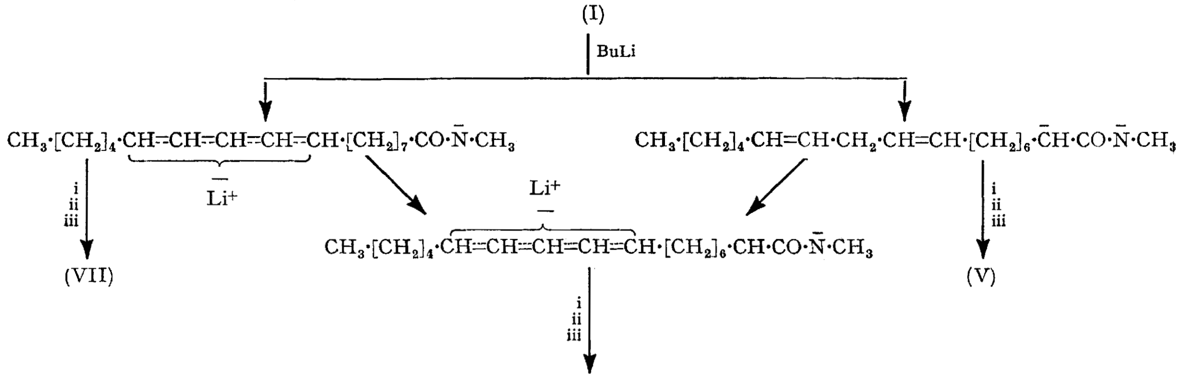
[1] J. Klein, S. Glily, and D. Kost, *J. Org. Chem.*, 1970, **35**, 1281.

[2] J. Klein, *Tetrahedron*, 1964, **20**, 465.

metallation α to the amide group. Metallation of a methylamide on nitrogen and α to the carbonyl was also found before.[3] The constitution of the compound (III) was inferred from (*a*) the n.m.r. spectrum of the product of chlorodecarboxylation[4] (IV) which exhibited a one-proton triplet at δ 4·25 p.p.m. (*b*) the mass spectrum of its methyl ester (V) which showed a molecular ion of 355 and fragments of mass number 131 and 144, corresponding to the ions $[CH_3O\cdot(OH)C{=}CH\cdot CO\cdot NH\cdot CH_3]^+$ and $[CH_2CH\cdot(CO_2CH_3)\cdot CO\cdot NH\cdot CH_3]^+$ respectively, and (*c*) the product of saponification of the amide group of (III) gave stearic acid on decarboxylation.

Metallation of (I) in ether with subsequent carbonation, esterification, and hydrogenation gave a mixture of esters that was separated by t.l.c. into three fractions (by order of elution) (1) (*ca.* 20% of the total esters), (2), and (3) (main product). Fraction (1) was proved to be identical with compound (V). This structure was confirmed by n.m.r. spectroscopy that showed a doublet at δ 2·85 p.p.m. (NCH_3), a triplet at δ 3·25 p.p.m. (proton α to the amide and ester groups), a singlet at δ 3·78 p.p.m. (OCH_3) and a broad signal at δ 6·6 p.p.m. (–CONH– proton). Fraction (2) contained two methoxycarbonyl groups (elemental analysis) and resulted from the metallation α to the amide group and at the doubly allylic position. The presence of an amide and two ester groups was confirmed by n.m.r. spectroscopy that showed a doublet at δ 2·85 p.p.m. (3H) (NCH_3 protons), a broad triplet at δ 3·38 p.p.m. (one proton α to the amide and ester groups), two singlets at δ 3·66 and 3·76 p.p.m. (each corresponding to three protons of an ester OCH_3) and a broad signal at δ 6·65 p.p.m. (CONH). Structure (VI) was therefore assigned to it. Fraction (3) contained one methoxycarbonyl group and was different from (V). It was, therefore, a product of metallation at the allylic position and structure (VII) was attributed to it (Scheme 1). Its n.m.r. spectrum showed the NCH_3 doublet at δ 2·85 p.p.m., the OCH_3 singlet at δ 3·71 p.p.m., and CONH at δ 5·8 p.p.m. (broad signal). In each of the products (VI) and (VII) three isomers with $x = 4, 6,$ or 8 were possible, resulting from the attack of carbon dioxide on one of the terminal or central positions of the pentadienylic system.[1] The ratio of these isomers could indicate a long-range effect of the amide group on the course of carbonation. Additional isomers, resulting from the isomerization of the pentadienyllithium compounds by sigmatropic hydrogen migration could also have been formed from the original products.



i, CO_2; ii, CH_2N_2; iii, H_2/PtO_2.

SCHEME 1

The unsaturated esters were also separated into three similar fractions. Various methods of degradation of the unsaturated products such as ozonolysis,[5] or of the saturated acids such as chlorodecarboxylation,[4] bromodecarboxylation,[6] or Barbier–Wieland degradation did not give isolable products in good yield and were, therefore, unsuitable as a method of determination of the ratio of isomeric acids formed. Mass spectral analysis was, therefore, used as a method of evaluation of this ratio. The amides were not suitable substrates for this analysis due to their low volatility. However, saponification of the amides to the acids and their conversion into the diesters (VIII) with diazomethane gave, in excellent yield, compounds, that could be analysed. A number of these esters were synthesized by independent methods to compare their fragmentation[7] with that of our reaction products. The amide-diesters (VI) were saponified to tricarboxylic acids (IX), that could be converted into the triesters (X) or by decarboxylation and subsequent esterification to (VIII).

$$[CH_2]_7\cdot(CO_2CH_3)_2 + CO(OC_2H_5)_2 \xrightarrow{C_2H_5ONa} NaC(CO_2C_2H_5)_2\cdot[CH_2]_6\cdot CO_2CH_3 \xrightarrow{C_{10}H_{21}Br}$$
$$CH_3\cdot[CH_2]_9\cdot C(CO_2C_2H_5)_2\cdot[CH_2]_6\cdot CO_2CH_3 \longrightarrow \text{(VIIIb)}$$

SCHEME 2

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[3] E. M. Kaiser, D. M. Von Schriltz, and C. R. Hauser, *J. Org. Chem.*, 1968, **33**, 4275.

[4] J. K. Kochi, *J. Amer. Chem. Soc.*, 1965, **87**, 2500.

[5] P. Fitton, E. H. Pryde, and J. C. Cowan, *J. Amer. Oil Chemists' Soc.*, 1965, **42**, 14.

[6] S. J. Cristol and W. C. Firth, jun., *J. Org. Chem.*, 1961, **26**, 280.

[7] These esters were used also, as reference compounds, for a similar analysis: E. N. Frankel, S. Netlin, W. K. Rohwedder, and J. Wender, *J. Amer. Oil Chemists' Soc.*, 1969, **46**, 133.

Methyl 8-methoxycarbonyloctadecanoate (VIIIb) was prepared (Scheme 2) by reaction of decyl bromide with the condensation product of diethyl carbonate with dimethyl azelate and subsequent hydrolysis, decarboxylation, and esterification with diazomethane.

Alkylation of diethyl nonylmalonate with methyl 8-bromo-octanoate and subsequent hydrolysis, decarboxylation, and esterification gave methyl 9-methoxycarbonyloctadecanoate (VIIIc) (Scheme 3).

$$HO_2C{\cdot}[CH_2]_7{\cdot}CO_2CH_3 \longrightarrow Br[CH_2]_7{\cdot}CO_2CH_3 \longrightarrow$$
$$CH_3{\cdot}[CH_2]_8C{\cdot}(CO_2C_2H_5)_2{\cdot}[CH_2]_7{\cdot}CO_2CH_3 \longrightarrow \text{(VIIIc)}$$

SCHEME 3

Alkylation of diethyl malonate first with methyl 9-bromononanoate, then with octyl bromide and subsequent hydrolysis, decarboxylation and esterification gave methyl 10-methoxycarbonyloctadecanoate (VIIId) (Scheme 4).

$$HO_2C{\cdot}[CH_2]_8{\cdot}CO_2CH_3 \xrightarrow[HgO]{Br_2} Br[CH_2]_8{\cdot}CO_2CH_3 \longrightarrow$$
$$(C_2H_5O_2C)_2CH{\cdot}[CH_2]_8{\cdot}CO_2CH_3 \longrightarrow$$
$$CH_3{\cdot}[CH_2]_7{\cdot}C(CO_2C_2H_5)_2{\cdot}[CH_2]_8{\cdot}CO_2CH_3 \longrightarrow \text{(VIIIa)}$$

SCHEME 4

Selective reduction of methyl hydrogen sebacate with diborane to methyl 10-hydroxydecanoate, reaction of the tosylate of this alcohol with diethyl malonate and additional alkylation of the malonate with heptyl tosylate gave after hydrolysis, decarboxylation, and esterification methyl 11-methoxycarbonyloctadecanoate (VIIIe) (Scheme 5).

$$HO_2C{\cdot}[CH_2]_8{\cdot}CO_2CH_3 \xrightarrow{B_2H_6} HO{\cdot}[CH_2]_9{\cdot}CO_2CH_3 \longrightarrow$$
$$TsO{\cdot}[CH_2]_9{\cdot}CO_2CH_3 \longrightarrow (C_2H_5O_2C)_2{\cdot}CH{\cdot}[CH_2]_9{\cdot}CO_2CH_3 \longrightarrow$$
$$CH_3{\cdot}[CH_2]_6{\cdot}C(CO_2C_2H_5)_2{\cdot}[CH_2]_9{\cdot}CO_2CH_3 \longrightarrow \text{(VIIIe)}$$

SCHEME 5

10-Undecenoic acid was converted by an Arndt–Eistert synthesis to methyl 11-dodecenoate.[8] Diethyl malonate was added, by a t-butyl peroxide-catalysed reaction,[9,10] to the double bond of the last-named compound and the malonate thus formed was alkylated with pentyl bromide. The usual treatment gave (VIIIg) (Scheme 6).

$$CH_2{=}CH{\cdot}[CH_2]_8{\cdot}CO_2H \longrightarrow CH_2{=}CH{\cdot}[CH_2]_9{\cdot}CO_2CH_3 \longrightarrow$$
$$(C_2H_5O_2C)_2{\cdot}CH{\cdot}[CH_2]_{11}{\cdot}CO_2CH_3 \longrightarrow$$
$$CH_3{\cdot}[CH_2]_4{\cdot}C(CO_2C_2H_5)_2{\cdot}[CH_2]_{11}{\cdot}CO_2CH_3 \longrightarrow \text{(VIIIg)}$$

SCHEME 6

11-Bromodecanoic acid[11] was converted into its monomethylamide. Alkylation of ethyl malonate with this compound, then with hexyl bromide gave, after further standard reactions, methyl 12-methoxycarbonyloctadecanoate (VIIIf) and the monomethylamide (XI) (Scheme 7).

$$Br[CH_2]_{10}{\cdot}CO_2H \longrightarrow Br[CH_2]_{10}{\cdot}CO{\cdot}NH{\cdot}CH_3 \longrightarrow$$
$$(C_2H_5O_2C)_2{\cdot}CH{\cdot}[CH_2]_{10}{\cdot}CO{\cdot}NH{\cdot}CH_3 \longrightarrow$$
$$CH_3{\cdot}[CH_2]_5{\cdot}C{\cdot}(CO_2C_2H_5)_2{\cdot}[CH_2]_{10}{\cdot}CO{\cdot}NH{\cdot}CH_3 \begin{array}{l} \nearrow \text{(XI)} \\ \searrow \text{(VIIIf)} \end{array}$$

SCHEME 7

Similarly, 8-bromo-octanoic acid was transformed into its monomethylamide and this product reacted with diethyl nonylmalonate. Partial hydrolysis, decarboxylation and esterification gave (XII) (Scheme 8).

$$Br[CH_2]_7{\cdot}CO_2H \longrightarrow Br[CH_2]_7{\cdot}CO{\cdot}NH{\cdot}CH_3 \longrightarrow$$
$$CH_3{\cdot}[CH_2]_8{\cdot}C(CO_2C_2H_5)_2{\cdot}[CH_2]_7{\cdot}CO{\cdot}NH{\cdot}CH_3 \longrightarrow \text{(XII)}$$

SCHEME 8

The fragmentation of the synthetic diesters in the mass spectrometer was similar to that of simple esters.[12,13] Th echaracteristic fragments are recorded in Table 1 and Scheme 9. The fragments A of high intensity were used for the determination of the ratio of isomeric esters in the product of metallation of (I). Two different mixtures of known compositions of three isomeric synthetic esters were submitted to mass spectral analysis in order to verify whether the relative intensities of ions A could be used to evaluate the ratio of the esters in the mixture (Table 2). The results showed that these intensities are proportional to the relative amount of each ester in the mixture and could, therefore, be used directly for analysis.

TABLE 1

Characteristic fragments of the esters (VIII)

Analysed ester	Fragments (%)					
	A	B	C	D	E	F
(VIIIg)	144(91)	112(76)	213(46)	181(20)	286(40)	254(40)
(VIIIf)	158(100)	126(24)	199(10)	167(5)	272(30)	240(13)
(VIIIe)	172(100)	140(19)	185(19)	153(11)	258(24)	226(19)
(VIIId)	186(100)	154(17)	171(11)	139(10)	244(30)	212(25)
(VIIIc)	200(100)	168(22)	157(27)	125(13)	230(30)	198(31)
(VIIIb)	214(100)	182(20)	143(45)	111(25)	216(70)	184(63)

TABLE 2

Intensities of fragments A in mass spectrum of mixtures of (VIII)

			Mixture 1 ratio		Mixture 2 ratio	
Ion	*m/e*	Ester	Esters	Intensities of A	Esters	Intensities of A
A	144	(VIIIg)	20	18	9·4	10
	172	(VIIIe)	1	1	1	1
	200	(VIIIc)	7·6	7·5	2·2	2·2

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[8] J. H. Wotiz and S. N. Bruce, *J. Org. Chem.*, 1955, **20**, 210.

[9] J. Moulines and R. Lalande, *Bull. Soc. chim. France*, 1966, 3387.

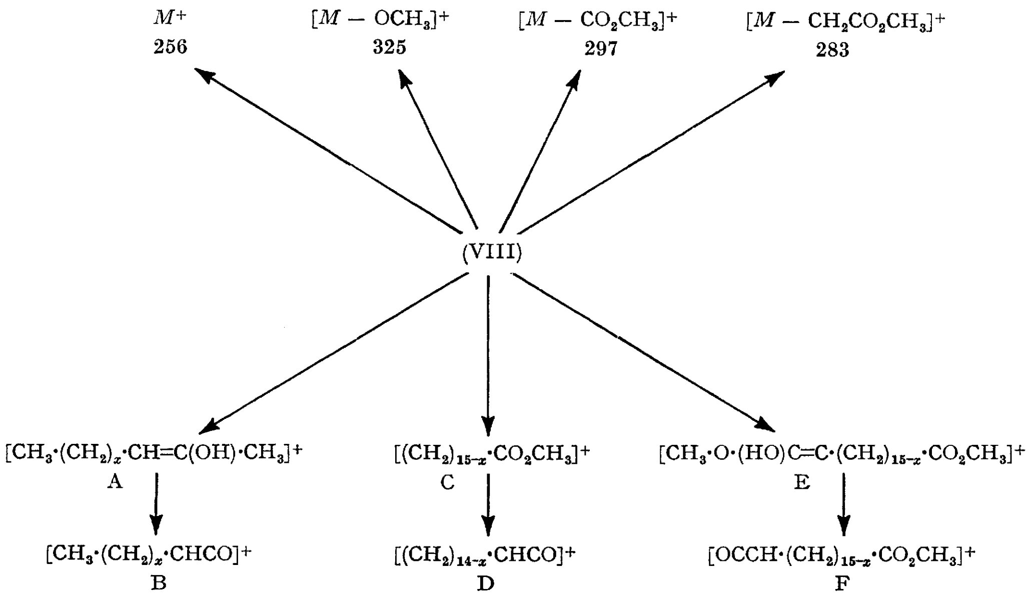
[10] J. I. G. Cadogan, D. H. Hey, and J. T. Sharp, *J. Chem. Soc.* (*C*), 1966, 1743.

[11] W. R. Sorenson and T. W. Campbell, ' Preparative Methods of Polymer Chemistry,' Interscience, New York, London, 1961, p.68.

[12] R. Ryhage and E. Stenhagen in ' Mass Spectrometry of Organic Ions,' ed. F. W. McLafferty, Academic Press, New York, 1963, p. 399.

[13] H. Budzikiewicz, C. Djerassi, and D. H. Williams, ' Mass Spectrometry of Organic Compounds,' Holden-Day, New York, 1967, p. 174.

In Table 3 are recorded the results of the metallation reactions and the ratio (by mass spectroscopy) of the diesters (VIII) obtained from the amides. The metallation of (I) in ether is much faster than in hexane, but addition of tetramethylethylenediamine (TMEDA) to hexane speeds up the reaction. The expected three isomers with the carboxyls at the positions 9, 11, and 13 were formed after short metallation periods. These isomers were not formed in equal amounts, although a similar extent of carbonation was expected at the extremities of the pentadienylic system, since it is situated in the central part of the molecule. The preferential attack of carbon dioxide at position 13 has to be attributed to the influence of the functional group. It is difficult to assume that this effect is of inductive nature in view of the large number of bonds separating the reactive site from the functional groups. Long-range effects were attributed to inductive effects[14] but were considered later, both on theoretical grounds and from experimental results,[15] to be due rather to field effect. Some effect other than inductive has to be in-



SCHEME 9

TABLE 3

Ratio[a] of isomeric diesters from metallation of (I) and (II)

Run	Substrate (mmol)	BuLi (mmol)	Solvent[b] (ml)	Duration of reaction (h)	Yield (%)	Ratio of esters[c] (VIIIj)	(VIIIi)	(VIIIh)	(VIIIg)	(VIIIf)	(VIIIe)	(VIIId)	(VIIIc)	(VIIIb	(VIIIa)
1	(I)85)	420	E(300)	20	83[d]				5·0+		1·0+		1·0+		
2	(I)(10)	51	E(28)	168	70[e]	0·2	0·2	0·6	4·3+	0·7+	1·1+	0·5+	1·0+	0·3+	
3	(I)(10)	51	E(28)	2·7	20				3·0+		0·7+		1·0+		
4	(I)(7)	35	E(23)	3·3	25[f]				3·4+		0·8+		1·0+		
5	(I)(8)	32	A(30)	28	24[g]										
6	(I)(8)	32	H(30)	96	37[g]										
7	(I)(20)	60	C(46)[h]	66	74[i]	0·5	1·0	1·4	2·0+	1·7+	1·7+	1·2+	1·0+	0·5+	0·3+
8	(II)(17)	48	E + H (30 + 30)	48	30				1·9+		0·7+		1·0+		
9	(II)(10)	48	E(25)	172	60			1·1	2·0+	1·1+	0·8+	0·8+	1·0+	0·4+	0·2+

[a] By relative intensities of fragments A in mass spectral analysis. [b] E = Ether, H = hexane, C = cyclohexane. [c] + Signifies detection by t.l.c. [d] The product contained 23% of (V). [e] The ratio of (V) : (VI) : (VII) was 1 : 3 : 3. [f] The ratio of (V) : (VI) : (VII) was 1 : 2·5 : 3. [g] Mostly (V). [h] 50 Mmoles of TMEDA were added. [i] (V) : (VI) = 1·6 and only traces of (VII).

$CH_3\cdot[CH_2]_x\cdot CH(CO_2R)\cdot[CH_2]_{14-x}\cdot CH(CO_2R)_2$

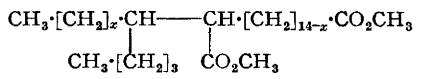
(IX) $R = H$

(X) $R = CH_3$

$CH_3\cdot[CH_2]_y\cdot CH(CO_2CH_3)\cdot[CH_2]_{15-y}\cdot CO\cdot NH\cdot CH_3$

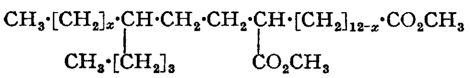
(XI) $y = 5$

(XII) $y = 8$



$CH_3\cdot[CH_2]_x\cdot\underset{CH_3\cdot[CH_2]_3}{CH}\!-\!\!-\!\!\underset{CO_2CH_3}{CH}\cdot[CH_2]_{14-x}\cdot CO_2CH_3$

(XIII)



$CH_3\cdot[CH_2]_x\cdot\underset{CH_3\cdot[CH_2]_3}{CH}\cdot CH_2\cdot CH_2\cdot\underset{CO_2CH_3}{CH}\cdot[CH_2]_{12-x}\cdot CO_2CH_3$

(XIV)

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[14] P. E. Peterson, C. Casey, E. V. Tao, A. Agtarap, and G. Thompson, *J. Amer. Chem. Soc.*, 1965, **87**, 5163.

[15] (*a*) M. J. S. Dewar and A. P. Marchand, *J. Amer. Chem. Soc.*, 1966, **88**, 354; (*b*) M. J. S. Dewar and T. G. Squires, *J. Amer. Chem. Soc.*, 1968, **90**, 210.

voked to explain the selective carbonation, *e.g.* a direct field effect as a result of coiling of the molecule or formation of a ring by co-ordination of lithium to the functional group and the reaction site.

Prolonged metallation of (I) in ether resulted in the migration of the pentadienyl-lithium system along the chain, resulting from sigmatropic 1,6-hydrogen shifts, as observed before in the case of linoleyl alcohol.[1] This isomerization is evidenced by the formation of additional isomeric diesters, having the second carboxylate group also at other positions of the chain. This isomerization is particularly easy in the presence of TMEDA. This catalyst further induces metallation at both positions, α to the amide and at the allylic position; the product formed in its presence was mostly (VI).

Metallation of (II) with butyl-lithium also proceeded satisfactorily although slower than that of (I). The selectivity of CO_2 attack was here less than in the case of metallated (I). Apparently, the charge introduced on the nitrogen of (I) by proton abstraction does also have a directive effect. However, even during the carbonation of metallated (II), there was a 2 : 1 discrimination of the position 13 relative to position 11 and 9. Prolonged metallation of the tertiary amine (II) produced isomerization of the lithium derivative and a mixture of isomeric acids was formed on carbonation. The analysis of the product of carbonation was carried out on the diesters formed from the amino-esters by hydrogenation and oxidative deamination[16] to acids and esterification.

Metallation of *NN*-dimethyl-linoleamide with butyl-lithium showed that the amide group is attacked during this reaction. A keto-acid was obtained.

Treatment of (I) with methylsulphinyl carbanion in dimethyl sulphoxide[17] gave a mixture of the conjugated 9,11- and 10,12-*N*-methyloctadecadienamides, which had the *cis–trans* configuration after short isomerization times, but were converted into the *trans–trans* isomers with larger amounts of base and longer reaction periods. These dienes were metallated with butyl-lithium in ether only at the position α to the amide group.

However, in hexane and in presence of TMEDA, addition of butyl-lithium to the diene and metallation at the position α to the amide group occurred. Carbonation of the metallated compound with subsequent hydrogenation and esterification with diazomethane gave a mixture of esters that showed in its n.m.r. spectrum six protons at δ 0·9 p.p.m. (two $C{-}CH_3$; the second coming from the butyl group), a doublet at δ 2·85 p.p.m. (NCH_3), a broad triplet at δ 3·3 p.p.m. (one proton α to the amide and ester groups), two singlets at δ 3·66 and 3·76 p.p.m. (each due to three protons of OCH_3 of two ester groups) and a broad signal at δ 6·65 p.p.m. (CONH). Hydrolysis of the amide and ester groups, decarboxylation of the malonic acid, and esterification gave a series of dicarboxylic acid diesters, that contained a butyl group in the chain, *e.g.* (XIII) and (XIV). Since the course of reaction and the products were similar to those obtained from the conjugated octadecadienols[1] we shall not describe these reactions in detail.

EXPERIMENTAL

N-*Methyl-linoleamide* (I).—This compound was prepared following a procedure described for oleamide.[18] A solution of methyl linoleate (100 g) and of methylamine (100 ml) in tetrahydrofuran (100 ml) was heated at 150° for 18 h in an autoclave. Distillation gave (I) (96 g, 94%), b.p. 197°/2 mm; $\nu_{max.}$ 3270 (NH), 3070, 1650 (CO), and 1560 cm^{-1} (Found: C, 78·1; H, 12·1; N, 4·7. Calc. for $C_{19}H_{35}NO$: C, 77·8; H, 11·9; N, 4·8%).

NN-*Dimethyl-linoleamide*.—This compound was prepared as above but substituting dimethylamine for methylamine; yield 99%, b.p. 180°/0·2 mm, $\nu_{max.}$ 1650 cm^{-1}.

NN-*Dimethyl-linoleamine* (II).—This compound was prepared following a procedure described for stearamide;[19] yield 93%, b.p. 140°/0·2 mm (Found: C, 82·2; H, 13·2; N, 4·6. Calc. for $C_{20}H_{39}N$: C, 81·9; H, 13·3; N, 4·7%), $\nu_{max.}$ 2800, 2770, and 2750 cm^{-1}; $\lambda_{max.}$ (EtOH) 230 nm (ε 710).

Metallation.—Commercial butyl-lithium in hexane (Foote) was used. The solvent was evaporated *in vacuo* and the necessary amount of dried ether was added under N_2. The amide was added to this solution and the mixture was left for the period indicated. It was then poured on pulverized solid carbon dioxide covered with ether. After several hours ice and HCl were added; the layers were separated and the ether layer was washed with 10% NaOH. The carboxylic acids, obtained after acidification, were esterified with diazomethane.

The alkaline solution obtained from the carbonation of the product of metallation of (II) was brought to pH 5—6 with HCl and the hydrochloride of the amine was extracted with CH_2Cl_2.

Hydrogenation was performed in acetic acid on PtO_2. Hydrolysis of the amides (2 g) was carried out by refluxing them for 40 h in EtOH (35 ml) with KOH (5 g) in H_2O (5 ml).

Run 1. The unsaturated acids were esterified[20] by addition of thionyl chloride at $-15°$ to a solution of the acids in methanol; b.p. 218°/0·4 mm; $\nu_{max.}$ 3280, 3070, 1740, 1650, and 1560 cm^{-1}. T.l.c. of the unsaturated esters on silical gel G (ether–hexane 2 : 1) separated three fractions. The first fraction: $\nu_{max.}$ 3274, 3075, 1740, 1650, and 1550 cm^{-1}; $\lambda_{max.}$ (EtOH) 233 nm (ε 5000), the second: $\nu_{max.}$ 3275, 3075, 1740, 1650, 1550, and 990 cm^{-1}; $\lambda_{max.}$ (EtOH) 233 nm (ε 17000), and the third: $\nu_{max.}$ 3275, 3075, 1740, 1650, 1550, and 990 cm^{-1}; $\nu_{max.}$ (EtOH) 233 nm (ε 20000) (Found: C, 71·6; H, 10·5. Calc. for $C_{21}H_{37}NO_3$: C, 71·8; H, 10·5%).

In the solution of the saturated acids in ether a precipitate separated on cooling that consisted of (III) [confirmed by the n.m.r. spectroscopy of the product of chlorodecarboxylation (IV), see below], m.p. 136° (methanol) (Found: C, 70·4; H, 11·5. Calc. for $C_{20}H_{39}NO_3$: C, 70·4; H, 11·4%).

Esterification of the saturated acids with diazomethane and separation by t.l.c. yielded fractions (1), (2), and (3)

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[16] S. S. Rawalay and H. Shechter, *J. Org. Chem.*, 1967, **32**, 3129.

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[18] E. J. Roe, *J. Amer. Chem. Soc.*, 1949, **71**, 2215.

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corresponding to (V), (VI), and (VII) respectively. Saponification of the mixture of saturated ester-amides and esterification of the acids with diazomethane gave a mixture of (VIII) and (X). Compound (VIII) was separated by g.l.c. (Found: C, 70·8; H, 11·0. Calc. for $C_{21}H_{40}O_4$: C, 70·8; H, 11·2%) and submitted to mass spectral analysis.

Chlorodecarboxylation[4] *of Compound* (III).—Lead tetraacetate (11·13 g) was added to compound (III) (1 g) in benzene (9 ml) under N_2 and the mixture was stirred for 15 min at room temperature. Lithium chloride (123 mg) was then added to the mixture which was stirred in a bath at 80° until the yellow colour of the solid disappeared; it was then cooled. The solvent was decanted and the precipitate was washed twice with benzene. The combined benzene solutions were washed with dil. $HClO_4$ and then 10% Na_2CO_3. Evaporation of the solvent gave 0·5 g of product, m.p. 79° (hexane); $\nu_{max.}$ 3270, 3085, 1660, 1570, 815, and 692 cm^{-1} (Found: C, 68·6; H, 11·3; Cl, 10·5. Calc. for $C_{19}H_{38}ClNO$: C, 68·9; H, 11·5; Cl, 10·7%).

Run 2. The ratio of (V) : (VI) : (VII) was 1 : 3 : 3. The esters (VIII) and (X) (obtained after saponification of the amides and esterification with diazomethane) were separated by g.l.c. (20% SE-30 on Chromosorb). Ester (X) showed a molecular weight of 414 (mass spectrometry).

Run 8. The amine hydrochloride obtained after evaporation of dichloromethane was dissolved in methanol and the carboxylic groups were esterified by refluxing the solution in the presence of H_2SO_4 for 5 h under N_2. Most of the methanol was then removed *in vacuo*; dichloromethane was added and the solution was washed with aqueous $NaHCO_3$. The esters were distilled; b.p. 190°/0·4 mm; $\nu_{max.}$ 2800, 2770, 2750, 1740, and 987 cm^{-1}; $\lambda_{max.}$ (EtOH) 235 nm (ε 21000) (Found: C, 74·9; H, 11·7. N, 3·7. Calc. for $C_{22}H_{41}NO_2$: C, 75·2; H, 11·7; N, 4·0%). These esters were hydrogenated in acetic acid in presence of PtO_2.

Oxidative Deamination.[14]—Potassium permanganate (2 g) and $ZnSO_4,7H_2O$ (1·5 g) were dissolved in Bu^{t}OH–water 1 : 1 (40 ml) at 80°. The amino-esters (0·5 g) in Bu^{t}OH (3 ml) were added and the mixture was stirred first for 30 min at 80° and then for 12 h at room temperature. A solution of sodium metabisulphite was added. The mixture was then acidified and the acids were extracted with ether and esterified with diazomethane.

Metallation of NN-*Dimethyl-linoleamide.*—This reaction was carried out in the usual manner. A mixture of acids (6·8 g) was obtained (i.r. indicated absence of amide and presence of acid by absorption at 1710 cm^{-1}). Esterification with diazomethane gave methyl esters containing an additional ketone band, $\nu_{max.}$ 1735 and 1715 cm^{-1} (Found: C, 75·95; H, 10·6. Calc. for $C_{24}H_{42}O_3$: C, 76·2; H, 11·1%).

Methyl 8-*Methoxycarbonyloctadecanoate* (VIIIb).—A mixture of dry sodium ethoxide (prepared from 2·3 g Na), diethyl carbonate (100 ml), and dimethyl azelate (21·6 g) was heated under reflux; the ethanol formed was distilled off slowly through a small distillation column. Decyl bromide (5·2 g) was then added, and the reaction mixture was refluxed for 40 h; it was then cooled and acidified with acetic acid (15 ml). The product was isolated by addition of water and extraction with ether. Saponification with KOH in ethanol gave the malonic acid which was decarboxylated at 200°. The carboxylic acid obtained was esterified with diazomethane; b.p. 167°/0·4 mm, yield 34 g (43%); $\nu_{max.}$ 1740 cm^{-1} (Found: C, 71·0; H, 11·3. Calc. for $C_{21}H_{40}O_4$: C, 70·8; H, 11·2%).

Methyl 8-*Bromo-octanoate.*—This compound was prepared by the procedure of Cristol;[6] it had b.p. 79°/0·2 mm; yield 59%.

Methyl 9-*Methoxycarbonyloctadecanoate* (VIIIc).—Diethyl nonylmalonate (9·4 g) was added to a suspension of sodium hydride (1·54 g of a 50% emulsion, washed with hexane) in xylene (30 ml). After dissolution had taken place, methyl 8-bromo-octanoate (7 g) was added, and the reaction mixture was refluxed for 24 h. Water was added to the cooled mixture. The residues, after distillation of the solvent and the lower boiling products from the organic layer, was saponified, decarboxylated, and esterified as above; b.p. 163°/0·2 mm; yield 3·4 g (32%); $\nu_{max.}$ 1740 cm^{-1} (Found: C, 70·9; H, 11·1. Calc. for $C_{21}H_{40}O_4$: C, 70·8; H, 11·2%).

Diethyl 8-*Methoxycarbonyloctylamalonate.*—Methyl 9-bromononanoate (6·5 g) prepared from methyl hydrogen sebacate analogously to methyl 8-bromo-octanoate) was added to diethyl sodiomalonate prepared from sodium hydride (1·9 g, 50%) and diethyl malonate (6·4 g) in xylene (40 ml). The reaction mixture was refluxed for 18 h, cooled, washed with water, and distilled; b.p. 152°/0·3 mm, yield 4·1 g (50%); $\nu_{max.}$ 1735 cm^{-1} (Found: C, 61·7; H, 8·9. Calc. for $C_{17}H_{30}O_6$: C, 61·8; H, 9·1%).

Methyl 10-*Methoxycarbonyloctadecanoate* (VIIId).—Octyl bromide (1·2 g) was refluxed for 18 h with a solution of malonate formed from the product above (4 g) and sodium (0·15 g) in absolute ethanol (10 ml). Hydrolysis, decarboxylation, and esterification gave (VIIId) (1 g, 23%), b.p. 168°/0·2 mmHg (Found: C, 70·8; H, 11·1. Calc. for $C_{21}H_{40}O_4$: C, 70·8; H, 11·2%).

Methyl 10-*Hydroxydecanoate.*—A solution of borane (25 ml; 3M) in tetrahydrofuran was added dropwise to methyl hydrogen sebacate (8 g) in tetrahydrofuran (65 ml). Excess of diborane was decomposed with water after 20 min, and the solution was concentrated and the product extracted with ether; yield 6·6 g (94%), b.p. 110°/0·2 mm (lit.,[21] 145—146°/3 mmHg), $\nu_{max.}$ 3300—3500 and 1740 cm^{-1} (Found: C, 65·5; H, 10·9. Calc. for $C_{11}H_{22}O_3$: C, 65·3; H, 10·9%). Addition in portions of toluene-*p*-sulphonyl chloride (6·5 g) to a solution of this alcohol (6·6 g) in pyridine (16 ml) cooled to −15 °C with subsequent stirring overnight at room temperature gave the tosylate. It was isolated by pouring the reaction mixture on ice and HCl and extraction with ether; $\nu_{max.}$ 1740, 1650, 668, 568, and 560 cm^{-1}.

Diethyl 9-*Methoxycarbonylnonylmalonate.*—The tosylate obtained above (6·2 g) was refluxed for 16 h with the sodiomalonate, formed from diethyl malonate (6·4 g) and sodium hydride (1·9 g, 50%) in toluene (40 ml). Work-up gave the product (1·2 g, 18%), b.p. 160°/0·3 mm, $\nu_{max.}$ 1735 cm^{-1} (Found: C, 63·3; H, 9·1. Calc. for $C_{18}H_{32}O_6$: C, 63·0; H, 9·3%).

Methyl 11-*Methoxycarbonyloctadecanoate* (VIIIe).—This compound was prepared by refluxing heptyl tosylate (6·8 g) with a solution of sodium hydride (1·3 g, 50%) and the malonate obtained above (6·2 g) in toluene (25 ml) for 16 h; yield 1 g, b.p. 168°/0·2 mm; $\nu_{max.}$ 1740 cm^{-1} (Found: C, 70·9; H, 11·3. Calc. for $C_{21}H_{40}O_4$: C, 70·8; H, 11·2%).

Diethyl 11-*Methoxycarbonylundecylmalonate.*—This compound was prepared by the method used by Lalande[9] from ethyl malonate and methyl dodec-11-enoate[8] in the presence of di-t-butyl peroxide, b.p. 195°/0·3 mm; yield 36%; $\nu_{max.}$

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[21] N. H. Lycan and R. Adams, *J. Amer. Chem. Soc.*, 1929, **51**, 627.

1735 cm^{-1} (Found: C, 64·4; H, 9·8. Calc. for $C_{20}H_{36}O_6$: H, 64·5; H, 9·7%).

Methyl 13-*Methoxycarbonyloctadecanoate* (VIIIg).—This compound was obtained by refluxing for 24 h pentyl bromide (1·5 g), the sodium derivative of the malonate described above (3·7 g), and sodium (0·23 g) in absolute ethanol (15 ml), followed by saponification, decarboxylation, and esterification; yield 0·8 g (23%), b.p. 160°/0·2 mmHg, $\nu_{max.}$ 1740 cm^{-1} (Found: C, 70·5; H, 11·3. Calc. for $C_{21}H_{40}O_4$: C, 70·8; H, 11·2%).

N-*Methyl*-11-*bromoundecanamide*.— 11-Bromoundecanoic acid[11] (15 g) was refluxed for 2 h with thionyl chloride (50 g). Excess of thionyl chloride was distilled off *in vacuo*. The solution of the residue in toluene (20 ml) was added dropwise, during 1 h, to a solution of methylamine (65 g) in toluene (150 ml) at 0°. The reaction mixture was poured on ice and HCl. The organic layer gave the product (6·5 g, 41%), m.p. 63° (hexane), $\nu_{max.}$ 3280, 3075, 1650, 1560, and 650 cm^{-1}; n.m.r. (CCl_4) NCH_3 at δ 2·69 p.p.m. (3H, d); –CONH– at δ 6·36 p.p.m. (1H) and $BrCH_2$– at δ 3·3 p.p.m. (2H, t) (Found: Br, 29·2. Calc. for $C_{12}H_{24}BrNO$: Br, 28·8%).

Diethyl 10-N-*Methylcarbamidodecylmalonate*.—This compound was prepared by refluxing for 20 h *N*-methyl-11-bromoundecanamide (8·3 g) with a solution of diethyl malonate (6·4 g) and Na (0·95 g) in absolute ethanol (60 ml); yield 7·3 g (69%), m.p. 46° (hexane), $\nu_{max.}$ 3300, 3065, 1740, 1735, 1650, and 1550 cm^{-1} (Found: N, 3·9. Calc. for $C_{19}H_{35}NO_5$: N, 3·9%).

Methyl 12-*Methoxycarbonyloctadecanoate* (VIIIf).—The malonate above (6·8 g) was added to a solution of sodium (0·46 g) in absolute ethanol (30 ml). Hexyl bromide (3·3 g) was added to the solution which was then refluxed for 17 h. Water was then added to the mixture and the product was extracted with ether and divided into two portions. One portion in ethanol (15 ml) was refluxed with KOH (3 g) in water (3 ml) for 14 h. The malonic acid obtained was decarboxylated at 200° and the carboxylic acid was esterified with diazomethane; yield 1 g; b.p. 168°/0·2 mmHg, $\nu_{max.}$ 1740 cm^{-1} (Found: C, 71·1; H, 11·1. Calc. for $C_{21}H_{40}O_4$: C, 70·8; H, 11·2%).

N-*Methyl*-12-*methoxycarbonyloctadecanamide* (XI).—The second portion in the preceding experiment was dissolved in ethanol (20 ml) and was refluxed for 2 h with a solution of sodium hydroxide (2 g) in water (10 ml). The acid obtained was decarboxylated at 200°, and then the second ester group was saponified as above and the carboxyl group esterified with diazomethane; yield 1 g, m.p. 41° (hexane); $\nu_{max.}$ 3280, 3080, 1740, 1650, and 1565 cm^{-1} (Found: C, 70·8; H, 11·5. Calc. for $C_{21}H_{41}NO_3$: C, 71·0: H, 11·6%).

N-*Methyl*-9-*methoxycarbonyloctadecanamide* (XII).—*N*-Methyl-8-bromo-octadecanamide was prepared analogously to *N*-methyl-11-bromoundecanamide and was refluxed for 48 h with a solution formed from diethyl nonylmalonate (5·7 g) and sodium (0·146 g) in absolute ethanol (20 ml). A work-up similar to that above gave (XII), m.p. 42° (hexane), $\nu_{max.}$ 3280, 3080, 1740, 1650, and 1565 cm^{-1} (Found: C, 71·2; H, 11·7. Calc. for $C_{21}H_{41}NO_3$: C, 71·0; H, 11·6%).

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