LEWIS ACID CATALYSIS OF THE ENE ADDITION OF DIMETHYL OXOMALONATE AND BUTYL GLYOXYLATE TO OLEFINS: FORMATION OF CYCLIC ETHERS AND LACTONES

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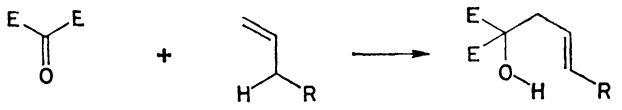
Dedicated to the memory of Professor František Šorm.

The Lewis acid ($SnCl_4$, $TiCl_4$) catalyzed ene addition of dimethyl oxomalonate and butyl glyoxylate to pent-1-ene and 3-methylbut-1-ene has been investigated. Side reactions have been noted leading variously to the formation of δ-lactones and/or cyclic ethers (tetrahydrofurans). The effect on the reaction course of the structure of the substrates has been discussed.

In recent years significant attention has been directed towards the ene reaction[1-3] of enophiles with active carbonyl group (Scheme 1).



SCHEME 1

Synthetic utility of the resulting adducts has been recognized[4-7] and in this connection the mechanism[8-12], asymmetric induction[13,14] and chemo- as well as regioselectivity[5-7,10,15] of these enophiles has been examined. Since activation energies of thermal ene reactions are higher than those of related Diels–Alder reactions[1] to obtain an ene adduct of carbonyl compound, with the exception of carbonyl cyanide[16] elevated temperatures (150–250°C) are generally required[1-3]. Hence there has been much interest in the catalysis by Lewis acids which allows to carry out ene reactions at low temperature (room temperature down to −70°C) with high yields and with remarkable improvement of the stereoselectivity[3,5-7,17,18]. In particular esters of oxomalonic and glyoxylic acid have been in this respect extensively studied[5,7,9-14]. Less attention has been paid to the formation of other products

which can arise in the Lewis acid catalyzed addition of carbonyl compounds to olefins.

Some time ago we have found that in the ene addition of dimethyl oxomalonate to pent-1-ene catalyzed by $SnCl_4$ together with ene adduct δ-lactone: methyl 3--hydroxy-2-oxo-5-propyltetrahydrofuran-3-carboxylate[19] has been formed. Since then it has been noted by others that catalyzed ene addition of carbonyl compounds can lead to the formation of cyclic ethers, derivatives of tetrahydrofuran[8,9,11,18] as well as δ-lactones (in the case of dialkyl oxomalonate)[7,20]. In the present communication we report on the Lewis acid catalyzed reaction of dimethyl oxomalonate (*I*) and butyl glyoxylate (*II*) as enophiles with pent-1-ene (*IIIa*) and 3-methylbut-1-ene (*IIIb*), respectively.

Dimethyl oxomalonate (*I*) and butyl glyoxylate (*II*) have been reacted in dichloromethane solution with 2 equiv. of alkene *IIIa* or *IIIb* in the presence of 0·5 equiv. of $SnCl_4$ or $TiCl_4$ at room temperature for 18 h. In each case the reaction gave a mixture consisting of two or three products (TLC) which have been separated by column chromatography. Yields and the ratio of resulting compounds *IV*, *V*, *VI*, *VII* and *VIII* are given in Table I.

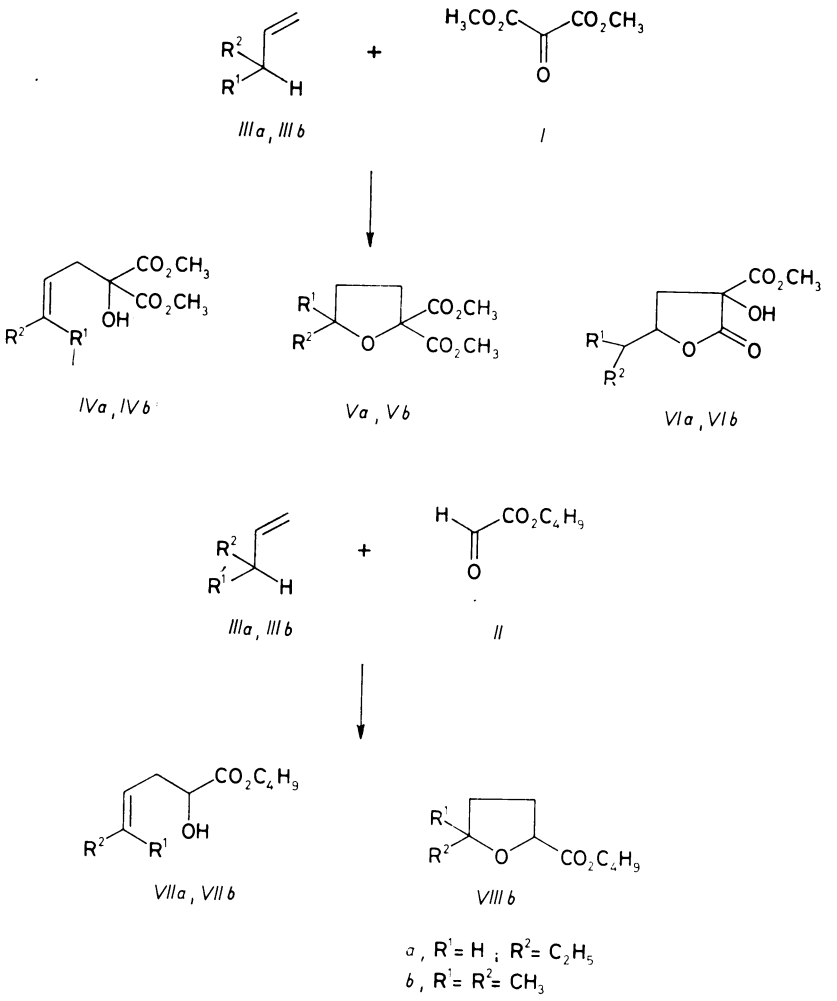
Structures of ene adducts *IVa*, *b* and *VIIa*, *b* were confirmed by direct comparison (TLC, IR, ^{1}H NMR) with reference samples obtained in the thermal reaction (1 equiv. of enophile, 2 equiv. of alkene, neat, 150°C, 24 h). Structures of cyclic ethers *Va*, *b* and *VIIIb* as well as δ-lactones *VIa*, *b* were deduced from their analytical and spectrometric data. In particular IR and ^{1}H NMR spectra of ethers *Va*, *b* and *VIIIb* indicated, as compared to the ene adducts *IVa*, *b* and *VIIa*, *b* the disappearance of a hydroxy group and vinylic protons, respectively, IR spectra of compounds

TABLE I

Yields and product distribution in the ene reactions

Entry	Substrate	Catalyst	Yield %	Product distribution		
				IV(*VII*)	*V*(*VIII*)	*VI*
1	*I* + *IIIa*	$SnCl_4$	66	76	9	15
2	*I* + *IIIa*	$TiCl_4$	60	77	13	10
3	*I* + *IIIb*	$SnCl_4$	40	—	82	18
4	*I* + *IIIb*	$TiCl_4$	42	—	90	10
5	*II* + *IIIa*	$SnCl_4$	85	100	—	—
6	*II* + *IIIa*	$TiCl_4$	72	100	—	—
7	*II* + *IIIb*	$SnCl_4$	62	24	76	—
8	*II* + *IIIb*	$TiCl_4$	60	17	83	—

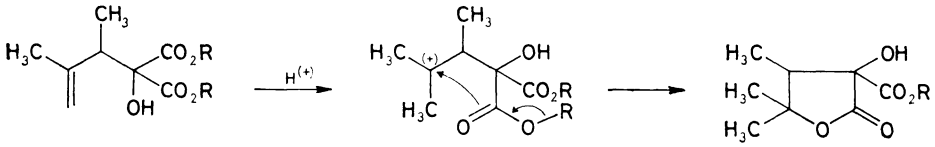
VIa, b demonstrated the presence of a hydroxy group (3 480 cm^{-1}) as well as a carbonyl group of a δ-lactone (1 780 cm^{-1}), whereas their ^1H NMR spectra clearly showed the presence of only one methoxycarbonyl group (δ 3·92 or 3·99, s, 3 H) and the absence of vinylic protons. Other resonances in the ^1H NMR spectra of compounds *Va, b*, *VIa, b* and *VIII* were also consistent with the assigned structures (see Experimental).



SCHEME 2

From our results (cf. Table I) it is apparent that of the two esters dimethyl oxomalonate (*I*) is more prone to the cyclic products formation. In the catalytic reaction

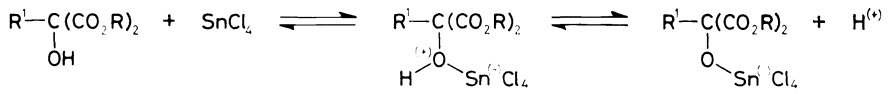
of the latter with 3-methylbut-1-ene (*IIIb*) only cyclic products have been isolated (Table I, entry 3 and 4). More remarkable difference in reactivity between esters *I* and *II* consists in the ability of only dimethyl oxomalonate (*I*) to yield, regardless of the olefin structure, δ-lactones *VIa* and *VIb*. Apart from our earlier observation[19] formation of this type of the side product has been described in the literature for the addition of dimethyl (diethyl) oxomalonate only to trisubstituted olefins (eg. 3--methylbut-2-ene) catalyzed by $SnCl_4$ (ref.[7]) or kaolin (and montmorillonite)[20]. In both cases it has been assumed that the primary product is an ene adduct *IX* which in the consecutive reaction, initiated by protonation yields δ-lactone *X*.



IX *IXa* *X*

SCHEME 3

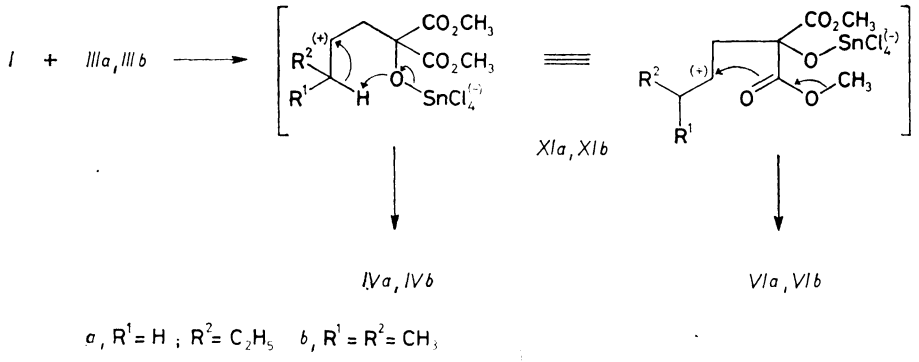
Required protonic acid can be generated from the ene adduct and Lewis acid in the equilibrium process shown in Scheme 4. On the other hand the stability of tertiary carbocation *IXa* (Scheme 3) facilitates protonation of ene adduct *IX* what makes the foregoing mechanistic rationale plausible. It has been supported experimentally by realising higher yields of δ-lactone *X* after longer reaction time[7] and by conversion of an ene adduct *IX* into the δ-lactone *X* on treatment with kaolin under the reaction conditions[20]. In the examples reported now the course of the cyclization reaction appears to be different for the following reasons.



SCHEME 4

Firstly, adduct *IVa* on protonation can not give a stable (tertiary) carbocation. Secondly, tertiary carbocation derived from adduct *IVb* obviously can not cyclize to δ-lactone *VIb*. In fact adduct *IVa* when left for 24 h with 0·5 equiv. of $SnCl_4$ in dichloromethane solution at room temperature has been recovered unchanged. On the other hand adduct *IVb* under the same conditions after 30 min reacted to completion yielding tetrahydrofuran *Vb* as a sole product. We assume therefore that the formation of δ-lactones *VIa* and *VIb* in the catalyzed reaction of dimethyl

oxomalonate (*I*) with alkenes *IIIa* and *IIIb* is not a consecutive but a parallel reaction to the ene addition. Both reactions proceed via a common dipolar intermediate *XIa* (or *XIb*) (Scheme 5). Such dipolar intermediates have been established by kinetic



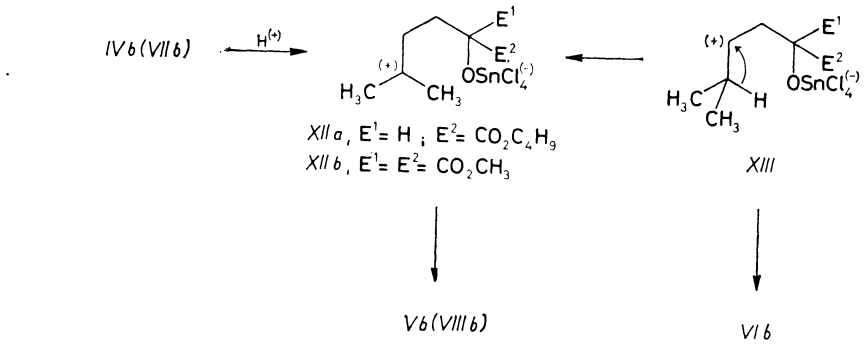
SCHEME 5

isotope effect measurements for the ene-like reactions of the acetic anhydride–zinc chloride complex[21]. They are also implicated by a large accelerating effect of an electron donating substituents observed for the $SnCl_4$ catalyzed ene reaction of diethyl oxomalonate with a series of arylcyclopentenes[7]. However it should be added that the generality of such stepwise mechanism for Lewis acid catalyzed ene reactions of dimethyl oxomalonate has been questioned on the basis of kinetic isotope effect studies[10].

3-Methylbut-1-ene (*IIIb*) adds in the presence of $SnCl_4$ or $TiCl_4$ to dimethyl oxomalonate (*I*) and butyl glyoxylate (*II*) to give relatively high yields of cyclic ether *Vb* and *VIIIb*, respectively (Table I, entries 3, 4, 7, and 8). The ease of the five-membered cyclic ether formation obviously depends on the structure of alkene *IIIb* which enables the generation of the stable carbocation *XIIa* (or *XIIb*) (Scheme 6). This becomes apparent when these results are compared with the analogous additions to pent-1-ene (*IIIa*). The latter with butyl glyoxylate (*II*) gives no cyclic product (Table I, entries 5 and 6) and with dimethyl oxomalonate (*I*) only low yield of tetrahydrofuran *Va* (Table I, entries 1 and 2). These data reflect the already mentioned higher tendency of ester *I* then *II* towards yielding cyclic products.

Postulated carbocations *XIIa* and *XIIb* can be produced by protonation of the respective ene adducts *IVb* and *VIIb*, hence cyclization leading to the five-membered ether may be regarded as the reaction consecutive to the ene addition. However on the basis of the foregoing results a parallel course of the two reactions can not be ruled out, because carbocations *XIIa* and *XIIb* can also result from the dipolar intermediate *XIII* (Scheme 6) by the hydride shift. Formation of cyclic ethers in the

$AlCl_3$ catalyzed addition of chloral or bromal to various alkenes has been rationalized in terms of the dipolar intermediate analogous to *XIII* (Scheme 6) undergoing the hydride or alkyl 1,2-shift[8,17]. Similarly in the $SnCl_4$ catalyzed addition of ester *I* to allylbenzene and 3,4,4-trimethylbut-1-ene formation of tetrahydrofuran derivatives has been observed. In the case of the latter alkene cyclization proceeded with concomitant shift of the methyl group[10].



SCHEME 6

It is interesting to note that so far in the products of the catalyzed ene reaction of dialkyl oxomalonate either a δ-lactone[7,20] or a five-membered ether[8,10] have been detected. Our results show that these products can arise side by side in the same reaction.

Conclusions. Lewis acid ($SnCl_4$, $TiCl_4$) catalyzed addition of dimethyl oxomalonate to alkenes gives besides ene adduct two types of cyclic products: δ-lactone and tetrahydrofuran derivative. The same reaction of butyl glyoxylate yields only one type of cyclic product: five-membered ether. The studied catalyzed ene reaction appears to be stepwise (not concerted) process with dipolar intermediate which can yield either the ene adduct or the δ-lactone (Scheme 5). On the other hand the tetrahydrofuran derivative can arise either from the same dipolar intermediate via a hydride shift or in the reaction subsequent to the ene addition, initiated by the protonation of the ene adduct (Scheme 6).

EXPERIMENTAL

IR spectra were recorded using films with a Specord 75 IR spectrophotometer. ^1H NMR spectra were recorded at 100 MHz in $CDCl_3$ or CCl_4 solutions with tetramethylsilane (TMS) as the internal standard using Jeol JNM-4H-100 spectrometer. TLC was performed on silica gel 60 F_{254} (aluminium pre-coated 0·2 mm layer) and column chromatography on silica gel 230 to 400 mesh (Merck). Addition of esters *I* and *II* to alkenes *IIIa* and *IIIb* has been carried out according to the general procedure given below.

General Procedure

To the stirred solution of freshly distilled ester (*I* or *II*, 5 mmol) in dry dichloromethane (10 ml) at 0°C under nitrogen, a solution of Lewis acid ($SnCl_4$ or $TiCl_4$, 2·5 mmol) in dry dichloromethane (5 ml) is added, followed by an alkene (*IIIa* or *IIIb*, 10 mmol). The solution is allowed to warm to room temperature and left for 18 h. The mixture is then dilluted with dichloromethane (10 ml) washed with water, $NaHCO_3$ solution, water and dried ($MgSO_4$). The solvent is removed on a rotatory evaporator and the residue consisting of two or three products separated by column chromatography. Homogenous (TLC) fractions are evaporated and the residue kugelrohred under reduced pressure. The yields and products ratio are collected in Table I. All new compounds gave correct elemental analyses; their b.p., IR and ^{1}H NMR spectra are given below.

IR and ^{1}H NMR spectroscopic data of compounds *IV*—*VIII*

Dimethyl (*E*)-*pent-2-enyltartronate* (IVa), b.p. 94—96°C/0·5 Torr. IR (film) ν_{max}: 3 490 (OH); 1 740 (C=O); 1 290, 1 230, 1 150 (C—O); 980 cm^{-1} (*trans* CH=CH). ^{1}H NMR ($CDCl_3$): δ 0·94 (t, J = 7·5 Hz, 3 H, —CH_3); 1·85—2·14 (m, 2 H, —C^4H_2—); 2·67—2·82 (m, 2 H, —C^1H_2); 3·89 (s, 6 H, 2× —OCH_3); 5·32 (dt, J_d = 15·1 Hz, J_t = 6·3 Hz, 1 H, =CH); 5·62 (dt, J_d = = 15·1 Hz, J_t = 5·8 Hz, 1 H, =CH).

Dimethyl (3-*methylbut-2-enyl*)*tartronate* (IVb), b.p. 90°C/0·2 Torr. IR (film) ν_{max}: 3 480 (OH); 1 730 (C=O); 1 220, 1 110 (C—O); 970 cm^{-1} (*trans* CH=CH). ^{1}H NMR (CCl_4): δ 1·60 (s, 3 H, —CH_3); 1·68 (s, 3 H, —CH_3); 2·72 (d, J = 7·2 Hz, 2 H, —CH_2—); 3·75 (s, 6 H, 2× —OCH_3); 3·85 (s, 1 H, —OH); 5·04 (bt, J = 7·4 Hz, 1 H, =CH—).

Dimethyl 5-*ethyltetrahydrofuran*-2,2-*dicarboxylate* (Va), b.p. 80°C/0·3 Torr. ^{1}H NMR (CCl_4) δ 0·98 (t, J = 6·9 Hz, 3 H, —CH_3); 1·30—1·91 (m, 4 H, 2 × —CH_2—); 2·48—2·55 (m, 2 H: —CH_2—); 3·81 (s, 3 H, —OCH_3); 3·87 (s, 3 H, —OCH_3); 4·05—4·31 (m, 1 H, H-5).

Dimethyl 5,5-*dimethyltetrahydrofuran*-2,2-*dicarboxylate* (Vb), b.p. 80°C/0·3 Torr. IR (film) ν_{max}: 1 740 (C=O), 1 290, 1 250, 1 150, 1 080 cm^{-1} (C—O). ^{1}H NMR ($CDCl_3$): δ 1·32 (s, 6 H, 2 × —CH_3); 1·85 (t, J = 7·4 Hz, 2 H, —CH_2—); 2·55 (t, J = 7·4 Hz, 2 H, —CH_2—); 3·80 (s, 6 H, 2 × —OCH_3).

Methyl 3-*hydroxy*-2-*oxo*-5-*propyltetrahydrofuran*-3-*carboxylate* (VIa), b.p. 110—112°C/ /0·3 Torr. IR (film) ν_{max}: 3 450 (OH); 1 780 (C=O, δ-lactone); 1 740 (C=O); 1 260, 1 200, 1 160 cm^{-1} (C—O). ^{1}H NMR (CCl_4): δ 1·04 (t, J = 7·4 Hz, 3 H, —CH_3); 1·40—2·00 (m, 4 H, —CH_2—CH_2—); 2·20 (dd, J_1 = 13·8 Hz, J_2 = 7·6 Hz, 1 H, H-4); 2·91 (dd, J_1 = 13·8 Hz, J_2 = 7·3 Hz, 1 H, H-4′); 3·99 (s, 3 H, —OCH_3); 4·32 (s, 1 H, —OH); 4·79 (m, 1 H, H-5).

Methyl 3-*hydroxy*-2-*oxo*-5-*prop*-2-*yltetrahydrofuran*-3-*carboxylate* (VIb), b.p. 100°C/0·2 Torr. IR (film) ν_{max}: 3 450 (OH); 1 750 (C=O, δ-lactone); 1 735 (C=O); 1 260, 1 180, 1 120 cm^{-1} (C—O). ^{1}H NMR ($CDCl_3$): δ 0·99 (d, J = 7·1 Hz, 3 H, —CH_3); 1·10 (d, J = 7·1 Hz, 3 H, —CH_3); 1·93 (dd, J_1 = 13·8 Hz, J_2 = 7·0 Hz, 1 H, H-4); 2·20 (m, 1 H, >CH—); 2·71 (dd, J_1 = = 13·8 Hz, J_2 = 7·0 Hz, 1 H, H-4′); 3·92 (s, 3 H, —OCH_3); 4·31 (m, 1 H, H-5).

Butyl (*E*)-2-*hydroxyhept*-4-*enoate* (VIIa), b.p. 95°C/0·5 Torr. IR (film) ν_{max}: 3 480 (OH): 1 725 (C=O); 1 200, 1 090 cm^{-1} (C—O). ^{1}H NMR ($CDCl_3$): δ 0·93 (t, J = 6·6 Hz, 3 H, —CH_3); 0·95 (t, J = 7·1 Hz, 3 H, —CH_3); 1·20—1·81 (m, 4 H, —CH_2—CH_2—); 1·86—2·16 (m, 2 H, —C^6H_2—); 2·35—2·50 (m, 2 H, —C^3H_2—); 3·15 (bs, 1 H, —OH); 4·16 (t, J = 6·4 Hz, 2 H, —OCH_2—); 4·19 (s, 1 H, —C^1H<); 5·35 (dt, J_d = 15·2 Hz, J_t = 5·8 Hz, 1 H, =CH—); 5·60 (dt, J_d = 15·2 Hz, J_t = 5·1 Hz, 1 H, =CH—).

Butyl 2-hydroxy-5-methylhex-4-enoate (VIIb), b.p. 99°C/0·4 Torr. IR (film) ν_{max}: 3 480 (OH); 1 730 (C=O); 1 210, 1 100 cm^{-1} (C—O). ^1H NMR (CCl_4): δ 0·95 (t, J = 6·6 Hz, 3 H, —CH_3); 1·20—1·74 (m, 4 H, —CH_2—CH_2—); 1·60 (s, 3 H, =C—CH_3); 1·68 (s, 3 H, =C—CH_3); 2·12—2·50 (m, 2 H, —CH_2—); 2·90 (bs, 1 H, —OH); 4·08—4·27 (m, 3 H, —OCH_2— and —C^2H<)*; 5·19—5·45 (m, 1 H, =CH—).

Butyl 5,5-dimethyltetrahydrofuran-2-carboxylate (VIIIb), b.p. 80°C/0·4 Torr. IR (film) ν_{max}: 1 750, 1 725 cm^{-1} (C=O). ^1H NMR ($CDCl_3$): δ 0·95 (t, J = 7·0 Hz, 3 H, —CH_3); 1·20 (s, 3 H, —CH_3); 1·30 (s, 3 H, —CH_3); 1·16—2·49 (m, 8 H, 2 × —CH_2—CH_2—); 4·05 (t, J = = 6·2 Hz, 2 H, —OCH_2—); 4·32 (dd, J_1 = 7·6 Hz, J_2 = 5·3 Hz, 1 H, H-2).

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* In the $CDCl_3$ solution the multiplet was resolved into two signals: δ 4·18 (t, J = 6·2 Hz, 2 H, —OCH_2—) and 4·38 (t, J = 5·1 Hz, 1 H, —C^2H<).