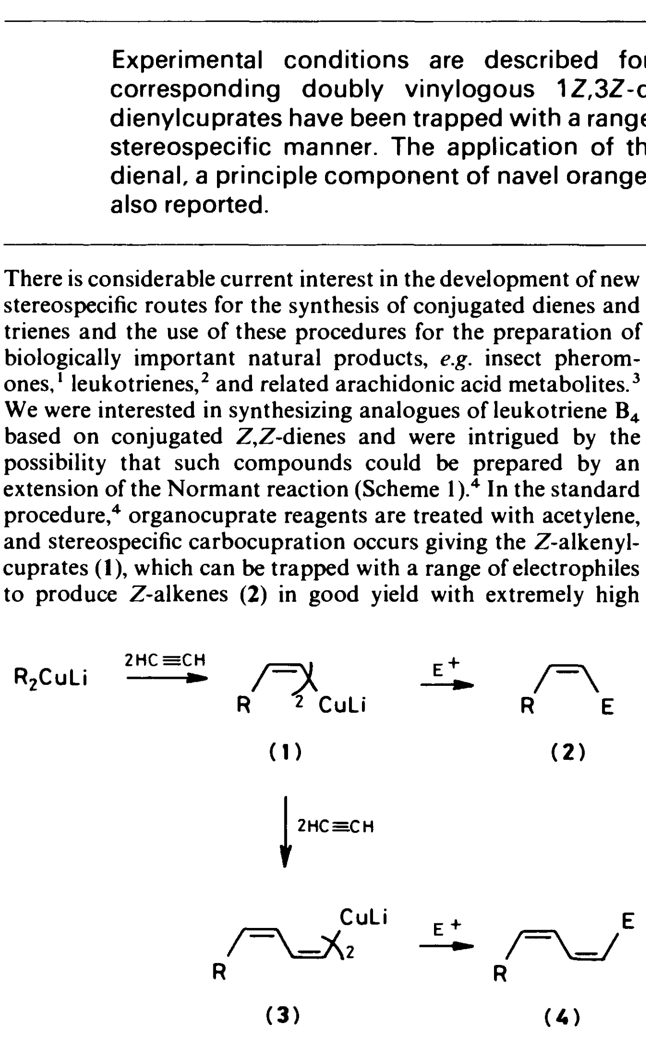
Stereospecific Diene Synthesis using Acetylene Carbocupration; Preparation of Navel Orangeworm Pheromone and Leukotriene Analogues

Mark Furber and Richard J. K. Taylor*
School of Chemical Sciences, University of East Anglia, Norwich NR4 7TJ
S. Cliff Burford
Fisons Pharmaceutical Division, Loughborough LE11 0RH

Experimental conditions are described for the conversion of lithium dialkylcuprates into the corresponding doubly vinylogous 1*Z*,3*Z*-dienylcuprates using acetylene carbocupration. These dienylcuprates have been trapped with a range of electrophiles to form conjugated *Z*,*Z*-dienes in a highly stereospecific manner. The application of this methodology to the synthesis of hexadeca-11*Z*,13*Z*-dienal, a principle component of navel orangeworm pheromone, and simple leukotriene B_4 analogues is also reported.

There is considerable current interest in the development of new stereospecific routes for the synthesis of conjugated dienes and trienes and the use of these procedures for the preparation of biologically important natural products, *e.g.* insect pheromones,[1] leukotrienes,[2] and related arachidonic acid metabolites.[3] We were interested in synthesizing analogues of leukotriene B_4 based on conjugated *Z*,*Z*-dienes and were intrigued by the possibility that such compounds could be prepared by an extension of the Normant reaction (Scheme 1).[4] In the standard procedure,[4] organocuprate reagents are treated with acetylene, and stereospecific carbocupration occurs giving the *Z*-alkenylcuprates (**1**), which can be trapped with a range of electrophiles to produce *Z*-alkenes (**2**) in good yield with extremely high stereospecificity. In principle, vinylcuprates (**1**) could react with an excess of acetylene to give *Z*,*Z*-dienylcuprates (**3**) which should provide access to a wide range of dienes (**4**). In comparison with existing procedures for *Z*,*Z*-diene synthesis,[1,5] this 'double carbocupration' reaction seemed attractive in view of its potential ease and versatility.



Scheme 1.

At the commencement of the studies described in this paper there had been no reported examples of this 'double carbocupration' process or of *Z*-alkenyl cuprates, generated by other means, undergoing addition to acetylene.† Investigations were therefore carried out to establish the viability of the carbocupration procedure for the synthesis of *Z*,*Z*-dienes.[7]

Organocuprates readily absorb 2 equiv. of acetylene to form alkenylcuprates (**1**) at -50 °C.[4] We found that further acetylene absorption is negligible at this temperature, but partial absorption occurs at a reasonable rate on warming the reaction mixture to 0 °C. Good conversion into the dienylcuprate (**3**) is observed if twice the calculated amount of acetylene is bubbled into the reaction mixture at this higher temperature. Under these conditions the green solution of the alkenylcuprate reagent (**1**) turns deep brown as the dienylcuprate (**3**) forms. It should be emphasized that the temperature must be carefully maintained at 0 °C or lower, as at higher temperatures the alkenyl and dienylcuprate reagents decompose. The utility of this process was demonstrated by trapping the dienyl cuprate reagents (**3**) with a range of electrophiles, giving the expected dienes in fair to good yields.

As can be seen from Table 1 and from reactions discussed later, the double-carbocupration procedure is successful with a range of simple lithium dialkylcuprates. The intermediate dienylcuprates (**3**) can be alkylated in the presence of hexamethylphosphoric triamide (HMPA) (entries i—iii), and trapped with Michael acceptors (entries iv and v) carbon dioxide (in the presence of HMPA–triethyl phosphite[4]), aldehydes, or iodine (entries vi—ix respectively).

A range of related reagents are known to react with organocuprates[4] and there seems no reason why they should not be successfully employed in the double-carbocupration reaction. With reactive electrophiles (entries v—vii and ix) it seems that both dienyl ligands on copper are transferred, whereas only a single ligand transfer occurs with alkylating agents and cyclopentenone. The dienyl products (**4**) were usually accompanied by a small amount ($< 10\%$) of the corresponding alkene (**2**) resulting from incomplete insertion of acetylene. In most cases the two products were chromatographically identical but readily separable by Kugelrohr distillation. With two exceptions (entries v and ix) this procedure gave the expected dienes as single stereoisomers according to g.l.c. and ^{1}H and ^{13}C n.m.r. spectroscopy. High-field ^{1}H n.m.r. spectroscopy confirmed the *Z*,*Z*-stereospecificity of the reaction, *e.g.* (**8**), $J_{1,2} = J_{3,4} = 11$ Hz.

When methyl propiolate was employed as electrophilic trapping agent (entry v), purification had to be carried out using chromatography on silver nitrate-impregnated silica gel rather than by distillation. This procedure gave the *E*,*Z*,*Z*-triene (**9**) as a single stereoisomer according to ^{13}C n.m.r. spectroscopy. The geometry of the C-2 olefinic linkage was confirmed as *E* by ^{1}H n.m.r. spectroscopy ($J_{2,3}$ 14.5 Hz). Confirmation that the

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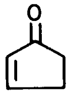
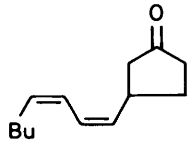
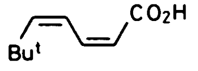
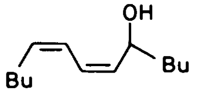
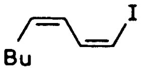
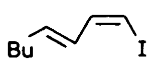
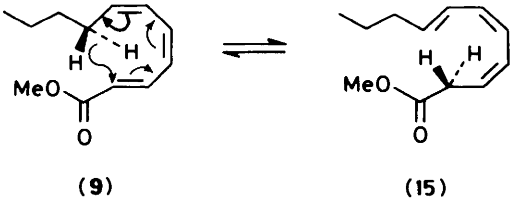
[†] It should be noted that 1-substituted vinylcuprates add smoothly to acetylene to produce substituted dienylcuprates[6] and that the double carbocupration of trimethylsilylacetylene has recently been reported (H. Westmijze, H. Kleijn, and P. Vermeer, *J. Organomet. Chem.*, 1984, **276**, 317).

Table 1. $R_2CuLi \xrightarrow[\text{iii, } E^+, \ -50 \text{ to } -80\ ^\circ C]{\text{i, 2 HC≡CH, } -50\ ^\circ C \quad \text{ii, 4 HC≡CH, } 0\ ^\circ C}$

R in R_2CuLi		Trapping agent (E^+)	Product		Isolated yield (%)
(i)	Bu	MeI		(5)	71[a]
(ii)	Bu	CH_2=$CHCH_2Br$		(6)	62[a]
(iii)	Bu	$PhCH_2Br$		(7)	59[a]
(iv)	Bu			(8)	52[a]
(v)	Bu	HC≡CCO_2Me		(9)	51[b]
(vi)	Bu^t	CO_2		(10)	46[b]
(vii)	C_8H_{17}	CO_2		(11)	48[b]
(viii)	Bu	C_4H_9CHO		(12)	53[a,c]
(ix)	Bu	I_2	 	(13) (14)	30[b,d]

[a] 1 Equiv. of electrophilic trapping agent added; yield based on trapping agent. [b] 2 Equiv. or excess of electrophilic trapping agent added; yield based on organocuprate. [c] Product contaminated with corresponding alkenol. [d] Ratio (*Z,Z*):(*Z,E*) *ca.* 2:3.

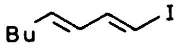
remaining double bonds were both *Z* came from the observation that triene (**9**) undergoes a [1,7]-sigmatropic rearrangement on being heated [equation (1)].



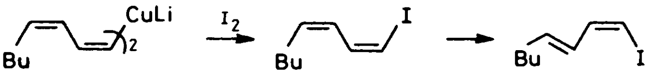
(**9**) (**15**) (1)

A 1:1 mixture of triene (**9**) and methyl undeca-3*Z*,5*Z*,7*E*-trienoate (**15**) was obtained which could be separated on silver nitrate-impregnated silica gel, and the trienes re-equilibrated on being heated to 100 °C.

The only non-stereospecific reaction observed involved the use of iodine as the electrophilic trapping agent (Table 1, entry ix). In this reaction a mixture of two co-distilling stereoisomeric dienyl iodides was obtained according to ^{13}C n.m.r. analysis. The corresponding *E,E*-dienyl iodide (**16**) was prepared and shown not to be present in the reaction mixture. Given the thermal stability of (*Z*)-1-iodohex-1-ene[8] it seems likely that the expected *Z,Z*-diene (**13**) was formed and then underwent partial iodine-catalysed isomerization at the 3,4-olefinic linkage (possibly during distillation) to give the *Z,E*-isomer (**14**) as an impurity (Scheme 2).



(**16**)

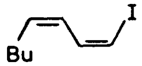
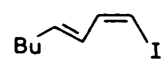
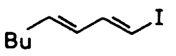
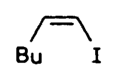
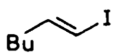


(**13**) (**14**)

Scheme 2.

Support for this hypothesis comes from an inspection of ^{13}C n.m.r. chemical-shift data for C-1 of a series of dienyl and vinyl iodides (Table 2). The C-1 resonances in *E*-alkenyl iodides (**16**) and (**18**) occur at higher field than those of the *Z*-alkenyl iodide (**17**). The C-1 resonances for dienyl iodides (**13**) and (**14**) are 3—7 p.p.m. downfield from C-1 for the *E,E*-isomer (**16**), *i.e.* consistent with the assignment of *Z*-geometry.

Table 2. ^{13}C Chemical-shift data (p.p.m.) for C-1 of a range of vinyl iodides

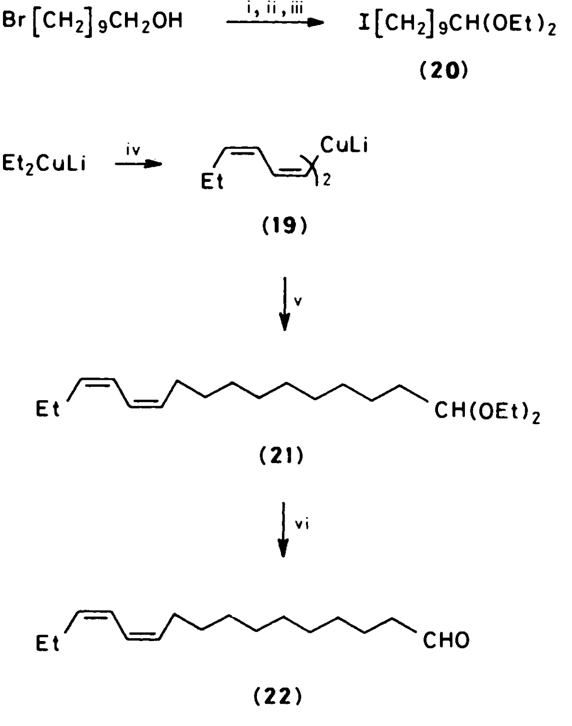
		δ_C
	(**13**)	83.2
	(**14**)	79.3
	(**16**)[a]	76.2
	(**17**)[b]	82.1
	(**18**)[b]	75.3

[a] See Experimental for preparation. [b] Prepared by literature procedures: (**17**),[8] (**18**) (G. Zweifel and R. B. Steele, *J. Am. Chem. Soc.*, 1976, **89**, 2754).

The results in Table 1 demonstrate that the double acetylene-carbocupration procedure provides an extremely useful method of preparing a range of conjugated *Z,Z*-dienes. It was surprising, therefore, that after the completion of this work Alexakis and Normant reported[6] that double acetylene carbocupration was not synthetically viable. The main difference between the two experimental procedures concerns the amount of acetylene employed. Alexakis and Normant[6] used only 2.19 mol equiv. for the conversion of alkenylcuprates into dienylcuprates [Scheme 1; (**1**) ⟶ (**3**)] whereas we found that 4 mol equiv. were essential; when only 2.19 equiv. of acetylene were used under our conditions a considerable amount of monoene (**2**) was isolated along with the expected diene (**4**). Alexakis and Normant also reported[6] that their yields were lowered by acetylene metallation which produced insoluble copper acetylides. Such side-reactions were not observed using our experimental procedure.

Having established a useful procedure for the stereospecific synthesis of *Z,Z*-conjugated dienes, applications of the methodology were investigated.

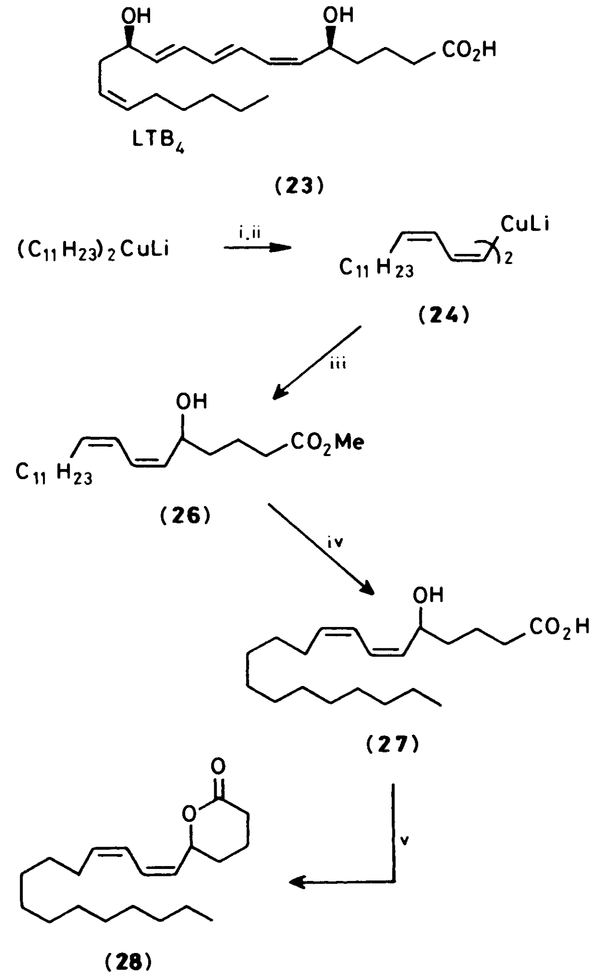
Synthesis of Navel Orangeworm Pheromone.—The recently discovered[9] pheromone of *Amyelois transitella* (Wlk), the navel orangeworm, is structurally unique amongst pheromones in that it contains a *Z,Z*-conjugated diene system as shown in structure (**22**). Four syntheses of pheromone (**22**) have now been published,[1a,5,9] two using organocopper chemistry,[1a] but all of these syntheses are considerably longer than the double-carbocupration approach outlined in Scheme 3.[7] Lithium diethylcuprate was treated with 2 mol equiv. of acetylene at −50 °C and then with 4 mol equiv. of acetylene at −10 °C to generate the hexadienylcuprate (**19**). Alkylation of cuprate (**19**) with 10-iodododecanal diethyl acetal (**20**), readily obtained from 10-bromodecanol[10] by the sequence outlined in Scheme 3, gave acetal (**21**). It should be noted that when the preparation of dienylcuprate (**19**) was carried out at 0 °C as before, the subsequent alkylation reaction was unsuccessful. Presumably, dienyl cuprate (**19**) [or its precursor, lithium di(but-1*Z*-enyl)cuprate] is thermally unstable at 0 °C.



Scheme 3. *Reagents:* i, PCC; ii, EtOH–H$^+$; iii, NaI; iv, 2 HC≡CH, −50 °C, then 4 HC≡CH, −10 °C; v, (**20**); vi, H$^+$

The unpurified acetal (**21**) was treated directly with oxalic acid in aqueous tetrahydrofuran (THF) to remove the acetal protecting group and the product was subjected to *rapid* Kugelrohr distillation. This procedure gave navel orangeworm pheromone (**22**) in 33% overall yields [based on iodoalkane (**20**)] as a single isomer according to ^{13}C n.m.r. spectroscopy. Prolonged heating during distillation caused some isomerization as shown by ^{13}C n.m.r. spectroscopy, and so rapid Kugelrohr distillation is essential.

Synthesis of Leukotriene B_4 *Analogues.*—There has been considerable recent interest in the biology and chemistry of hydroxylated icosatetraenoic acids derived from arachidonic acid by lipoxygenase metabolic pathways. Leukotriene B_4 (LTB_4), (**23**) has attracted particular attention because of its potent chemotactic properties and potential role in inflammation and allergy.[2] In view of our interest in the synthesis of LTB_4 analogues[7] the double acetylene-carbocupration reaction was applied to the synthesis of the 12-deoxytetrahydro LTB_4 analogue (**27**) (Scheme 4).



Scheme 4. *Reagents and conditions:* i, 2 HC≡CH, −25 °C; ii, 4 HC≡CH, 0 °C; iii, $OHC[CH_2]_3CO_2Me$ (**25**) + $BF_3 \cdot Et_2O$; iv, K_2CO_3; iv, K_2CO_3, aq. MeOH; v, heat ($-H_2O$)

Lithium diundecylcuprate was prepared and converted into the dienylcuprate (**24**) by treatment with 2 mol equiv. of acetylene at −25 °C (in this case, acetylene absorption was very slow at −50 °C) and 4 mol equiv. of acetylene at 0 °C. We have previously shown[7] that methyl 5-oxopentanoate (**25**) can be successfully employed as an aldehyde-trapping agent for alkenylcuprates, provided that boron trifluoride–diethyl ether is added to the reaction mixture. These conditions were employed with the dienylcuprate (**24**) to produce hydroxy ester (**26**) which, on saponification, gave the target LTB_4 analogue (**27**). Purification of compound (**27**) was best achieved by Kugelrohr distillation, the diene lactone (**28**) being formed during this procedure. Lactone (**28**) was obtained in 41% overall yield from aldehyde (**25**), as a single diene isomer according to ^{13}C n.m.r. analysis. The biological properties of LTB_4 analogues (**27**) and (**28**) are currently being evaluated. The procedure outlined in Scheme 4 is obviously well suited to the synthesis of a range of 6*Z*,8*Z*-LTB_4 analogues by varying the initial cuprate reagent.

Experimental

All organometallic and low-temperature reactions were conducted in flame-dried glassware under an atmosphere of dry, oxygen-free nitrogen. Alkyl-lithium preparations were carried out under a blanket of argon. BuLi and Bu^tLi were purchased from Aldrich as solutions in hexane. All alkyl-lithium reagents were standardized at regular intervals and transferred using gas-tight syringes. Copper(I) bromide–dimethyl sulphide complex ($CuBr \cdot SMe_2$) was purchased from Fluka. Acetylene was purified and dispensed in accurately measured volumes using the gas burette apparatus illustrated in the Figure. Two traps cooled in solid CO_2–acetone baths served to remove acetone impurities. Water vapour was removed by passage through two $CaCl_2$ drying tubes. Acetylene was introduced beneath the solvent surface by means of a wide-bore syringe needle.

Light petroleum is that fraction with b.p. 40—60 °C, ether is diethyl ether. Column chromatography was carried out using silica gel (Merck 7734) or silver nitrate-impregnated silica gel. The latter was prepared by addition of a solution of silver nitrate (5 g) in acetonitrile to silica gel (Merck 7734; 100 g), mixing thoroughly, and removal of the solvent under reduced pressure: all operations were conducted in the dark.

^1H N.m.r. spectra were recorded on Jeol PMX 60 or Bruker AM 360 spectrometers. ^{13}C Spectra were recorded on a Jeol FX 100. All n.m.r. spectra were recorded using $CDCl_3$ as solvent. I.r. spectra were obtained on a Perkin-Elmer 297 spectrophotometer, u.v. spectra on a Pye-Unicam SP800A spectrophotometer, and mass spectra on Kratos MS25 (low resolution) and Kratos MS30 or VGZAB-IF (high resolution) instruments.

General Procedure for Preparing Lithium Di-(1*Z*,3*Z-dienyl*)*-cuprate Reagents* (**3**).—The alkyl-lithium reagent (2 mol equiv.) was added dropwise to a stirred suspension of $CuBr \cdot SMe_2$ (1 mol equiv.) in ether (*ca.* 5 ml $mmol^{-1}$) at −40 °C. After being stirred at −30 °C for 30 min, the solution was cooled to −50 °C and acetylene (2.2 mol equiv.) was slowly passed into the reaction *via* a syringe needle (Figure), and total absorption occurred. The resulting green solution was stirred at −25 °C for 30 min, and then warmed to 0 °C. The temperature was carefully maintained at 0 °C while more acetylene (4.0 mol equiv.) was added during 10 min, when only partial absorption occurred. The resulting brown solution of dienylcuprate (**3**) was cooled to the appropriate temperature and used immediately.

Standard Work-up Procedure for Organocopper Reactions.—The reaction mixture was quenched with a mixture of saturated aqueous NH_4Cl and 2M-HCl (2:1) at *ca.* −30 °C, the organic layer was decanted, and the product was extracted with ether or light petroleum. The combined organic extracts were washed successively with 5% aqueous NH_4OH and then saturated aqueous NH_4Cl, then dried over $MgSO_4$ and concentrated under reduced pressure.

*Nona-*2*Z*,4*Z-diene* (**5**).—To a stirred solution of lithium di(octa-1*Z*,3*Z*-dienyl)cuprate (7.9 mmol) (from Bu_2CuLi and HC≡CH according to the general procedure) in ether (40 ml) at −50 °C were added iodomethane (0.50 ml, 7.9 mmol) and HMPA (1.4 ml, 7.9 mmol). A thick yellow precipitate developed immediately. After 1 h at −50 to 0 °C, the reaction mixture was subjected to a standard light petroleum work-up. Kugelrohr distillation yielded diene (**5**) (0.70 g, 71%) as an oil, b.p. 110 °C/32 mmHg; $\nu_{max.}$ (thin film) 3 040, 3 010, 1 650, and 1 600 cm^{-1}; δ_H (60 MHz) 0.90 (3 H, br t), 1.40 (4 H, m), 1.76 (3 H, d, *J* 7 Hz), 2.20 (2 H, dt, *J* 7 and 7 Hz), 5.45 (2 H, m), and 6.20 (2 H, m); δ_C 13.86, 22.31, 27.18 (2C), 31.82, 123.35, 124.64, 125.52, and 131.69. This compound proved to be too volatile for microanalytical characterization.

*Undeca-*1,4*Z*,6*Z-triene* (**6**).—To a stirred solution of lithium di(octa-1*Z*,3*Z*-dienyl)cuprate (9.7 mmol) in ether (45 ml) at −50 °C were added 3-bromoprop-1-ene (0.8 ml, 9.7 mmol) and

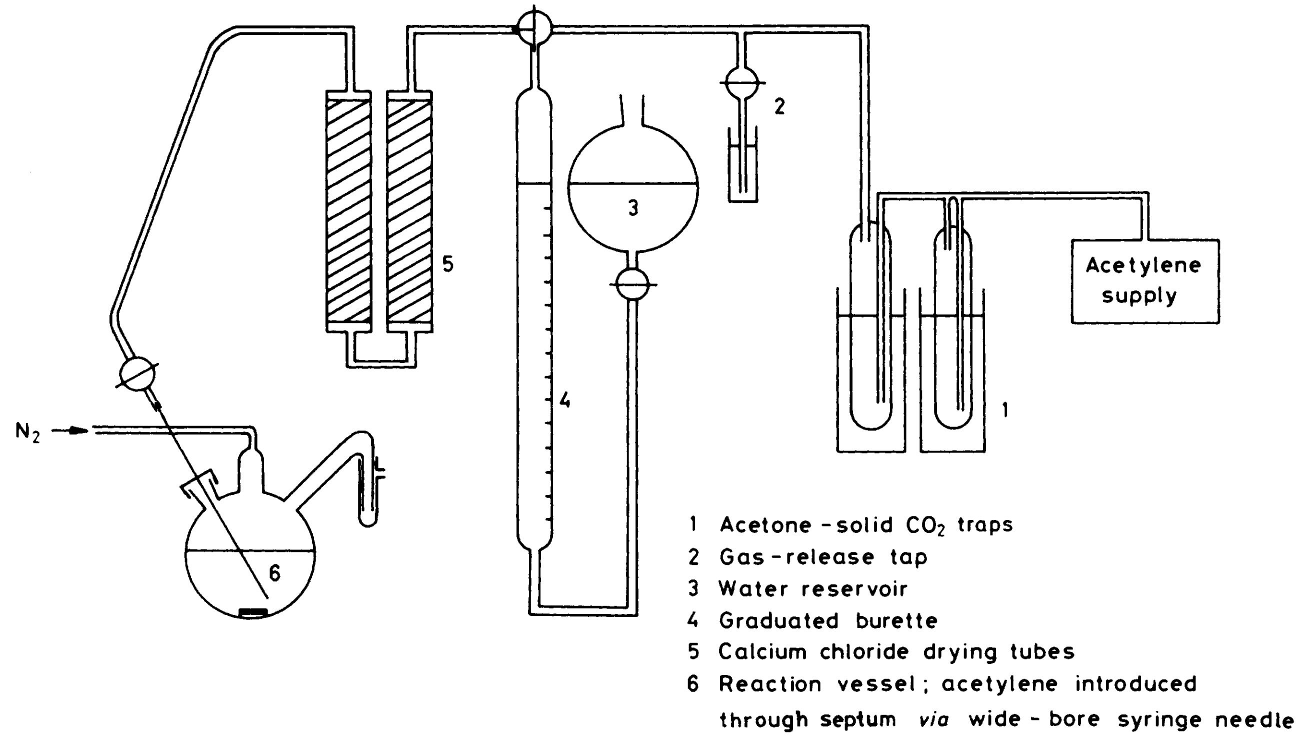


Figure. Apparatus used for double acetylene carbocupration

HMPA (1.7 ml, 9.7 mmol). A thick yellow precipitate developed. After being stirred at −50 to 0 °C for 1 h, the reaction mixture was subjected to a standard light petroleum work-up. Kugelrohr distillation yielded the *triene* (**6**) (0.905 g, 62%), b.p. 100 °C/6 mmHg; $\nu_{max.}$ (liquid film) 3 080, 3 040, 3 010, 1 640, and 1 600 cm^{-1}; $\lambda_{max.}$(EtOH) 234 nm (ε 18 280); δ_H (60 MHz) 0.90 (3 H, br t), 1.36 (4 H, m), 2.30 (2 H, br dt), 2.92 (2 H, dd, *J* 7 and 7 Hz), and 4.80—6.60 (7 H, m); δ_C 13.91, 22.43, 27.30, 31.82 (2C), 114.89, 123.41, 124.67, 128.22, 132.69, and 136.44; *m/z* 150 (M^+) (Found: C, 87.9; H, 12.3. $C_{11}H_{18}$ requires C, 87.9; H, 12.1%).

1-*Phenylnona*-2Z,4Z-*diene* (**7**).—To a stirred solution of lithium di(octa-1*Z*,3*Z*-dienyl)cuprate (4.87 mmol) in ether (25 ml) at −70 °C were added α-bromotoluene (0.58 ml, 4.8 mmol) and HMPA (0.85 ml, 4.8 mmol). After being stirred at −40 to 0 °C for 2 h, the reaction was subjected to a standard light petroleum work-up. Kugelrohr distillation yielded the *diene* (**7**) (0.574 g, 59%); $\nu_{max.}$ (liquid film) 3 080, 3 060, 3 030, 3 000, 1 600, and 1 495 cm^{-1}; δ_H (60 MHz) 0.90 (3 H, br t), 1.40 (4 H, m), 2.20 (2 H, m), 3.50 (2 H, d, *J* 7.5 Hz), 5.50 (2 H, m), 6.35 (2 H, m), and 7.15 (5 H, m); δ_C 13.97, 22.37, 27.30, 31.82, 33.70, 123.29, 124.41, 125.88, 128.34 (4C), 129.57, 133.09, and 140.61; *m/z* 200 (M^+) (Found: C, 89.6; H, 10.0. $C_{15}H_{20}$ requires C, 89.9; H, 10.1%).

3-(*Octa*-1Z,3Z-*dien*-1-*yl*)*cyclopentanone* (**8**).—To a stirred solution of lithium di(octa-1*Z*,3*Z*-dienyl)cuprate (4.87 mmol) in ether (25 ml) at −70 °C was added cyclopent-2-enone (0.43 ml, 4.87 mmol) in one portion. After being stirred at −70 to 0 °C for 4 h, the mixture was subjected to a standard ether work-up. Chromatography on silica [CH_2Cl_2–light petroleum (1:1)] followed by Kugelrohr distillation yielded *dienone* (**8**) (0.486 g, 52%), b.p. 125 °C/0.5 mmHg; $\nu_{max.}$ (liquid film) 3 035, 3 000, 1 740, and 1 600 cm^{-1}; $\lambda_{max.}$(EtOH) 233 nm (ε 18 230); δ_H (60 MHz) 0.90 (3 H, br t), 1.00—2.50 (12 H, m), 3.25 (1 H, m), 5.00—5.70 (2 H, m), and 5.80—6.40 (2 H, m); δ_H (360 MHz) 5.37 (1 H, dd, *J* 11 and 9.6 Hz), 5.53 (1 H, dt, *J* 11 and 8 Hz), 6.27 (1 H, dd, *J* 11 and 11 Hz), and 6.31 (1 H, dd, *J* 11 and 11 Hz); δ_C 13.91, 22.31, 27.24, 30.35, 31.76, 35.29, 38.16, 45.27, 123.23, 124.35, 133.45, 133.56, and 217.58; *m/z* 192 (M^+); g.l.c. purity >97% (OV 101; 0.9 m; start 80 °C, prog. rate 8 °C/min^{-1}, R_t 7.77 min) (Found: C, 81.05; H, 10.6. $C_{13}H_{20}O$ requires C, 81.2; H, 10.5%).

Methyl Undeca-2E,4Z,6Z-*trienoate* (**9**) *and Methyl Undeca*-3Z,5Z,7E-*trienoate* (**15**).—(*a*) To a stirred solution of lithium di(octa-1*Z*,3*Z*-dienyl)cuprate (2.9 mmol) in ether (20 ml) at −80 °C was added a solution of methyl propiolate (0.48 ml, 5.35 mmol) in THF (3 ml). After being stirred at −80 °C for 30 min, the reaction mixture was subjected to a standard ether work-up. The solvent was removed under reduced pressure and the product was filtered through a plug of silica (light petroleum, then CH_2Cl_2) to remove non-polar impurities. Chromatography on silica impregnated with 5% $AgNO_3$ (20 g) [light petroleum–ether (7:1)] yielded the E,Z,Z-*triene ester* (**9**) (0.53 g, 51% based on the transfer of both dienyl ligands) uncontaminated by isomer (**15**); $\nu_{max.}$ (liquid film) 3 025, 1 720, and 1 600 cm^{-1}; $\lambda_{max.}$(EtOH) 304 nm (ε 18 190); δ_H (60 MHz) 0.90 (3 H, br t), 1.32 (4 H, m), 2.20 (2 H, m), 3.70 (3 H, s), 5.40—6.80 (5 H, m), and 7.70 (1 H, dd, *J* 14.5 and 11.5 Hz); δ_C 13.91, 22.37, 27.48, 31.64, 51.37, 121.18, 123.23, 125.99, 131.98, 137.38, 139.14, and 167.26; *m/z* 194 (M^+) (Found: C, 74.5; H, 9.5. $C_{12}H_{18}O_2$ requires C, 74.2; H, 9.3%).

(*b*) The above reaction was repeated using lithium di(octa-1*Z*,3*Z*-dienyl)cuprate (9.7 mmol) and the resulting product was fractionally distilled. The main fraction (2.26 g), b.p. 96 °C/0.15 mmHg, consisted of two isomers according to ^{13}C n.m.r. spectroscopy. These were separated by chromatography of a portion of the mixture (1.1 g) on silica gel impregnated with 5% $AgNO_3$ (30 g) [light petroleum–ether (7:1)] to give triene ester (**9**) (0.47 g) followed by *methyl undeca*-3Z,5Z,7E-*trienoate* (**15**) (0.48 g); $\nu_{max.}$ (liquid film) 3 040, 3 020, 1 742, and 1 640 cm^{-1}; $\lambda_{max.}$(EtOH) 261 nm (ε 26 560); δ_H (60 MHz) 0.90 (3 H, br t), 1.40 (2 H, m), 2.10 (2 H, dt, *J* 7 and 7 Hz), 3.20 (2 H, d, *J* 7.5 Hz), 3.64 (3 H, s), and 5.30—6.80 (6 H, m); δ_C 13.74, 22.43, 32.88, 35.11, 51.72, 121.24, 122.17, 125.64, 126.40, 131.33, 137.20, and 171.67; *m/z* 194 (M^+) (Found: C, 74.2; H, 9.5%).

(*c*) Pure samples of trienes (**9**) and (**15**) (20 mg) were heated *in vacuo* (100 °C; 5 mmHg) for varying lengths of time, as neat liquids. ^{1}H N.m.r. spectroscopy showed that both samples were rapidly equilibrated to a 1:1 mixture of isomers, as judged by integration of the methyl ester peaks at δ_H 3.70 and 3.64.

*6,6-Dimethylhepta-*2Z,4Z-*dienoic acid* (**10**).—Following the general procedure, a solution of lithium di-(5,5-dimethylhexa-1*Z*,3*Z*-dienyl)cuprate (4.87 mmol) was prepared in ether (25 ml) from Bu^{t}Li and HC≡CH. To this solution at −50 °C were added HMPA (0.85 ml, 4.87 mmol), triethyl phosphite (2 drops), and dry gaseous carbon dioxide (excess). Following the initial exothermic reaction, a continuous stream of carbon dioxide was passed through the reaction mixture for 1 h, the temperature being allowed to rise slowly to 0 °C. The reaction mixture was hydrolysed with saturated aqueous NH_4Cl (30 ml) and 3M-HCl (10 ml), and the product was extracted with ether (3 × 50 ml). The combined organic extracts were re-extracted with aqueous Na_2CO_3 (5 × 50 ml), and the combined aqueous fractions were washed with ether (2 × 50 ml). The aqueous layer was acidified to pH 4 with dil. HCl, then extracted with CH_2Cl_2 (3 × 100 ml). After being dried over $MgSO_4$, the product was concentrated *in vacuo* and distilled (Kugelrohr) to yield *diene acid* (**10**) (0.689 g, 46% based on the transfer of both dienyl ligands); b.p. 100 °C/0.5 mmHg; $\nu_{max.}$ (liquid film) 3 600—2 300, 1 690, 1 630, and 1 590 cm^{-1}; $\lambda_{max.}$(EtOH) 262 nm (ε 16 550); δ_H (60 MHz) 1.20 (9 H, s), 5.74 (2 H, m), 7.15 (2 H, m), and 12.00 (1 H, br s); *m/z* 154 (M^+) (Found: C, 70.0; H, 9.4. $C_9H_{14}O_2$ requires C, 70.1; H, 9.15%).

*Trideca-*2Z,4Z-*dienoic acid* (**11**).—A stirred suspension of finely cut lithium wire (0.5 g, 71 mmol) in hexane (20 ml) at 0 °C was subjected to ultrasonification, and 1-bromo-octane (2 g, 10.3 mmol) was added dropwise. Once reaction was complete (*ca.* 30 min), titration gave the organolithium reagent molarity as 0.3M (57%). According to the general procedure, a solution of lithium di(dodeca-1*Z*,3*Z*-dienyl)cuprate (2.63 mmol) was prepared in ether (30 ml). To this solution at −30 °C were added HMPA (0.46 ml, 2.6 mmol), triethyl phosphite (1 drop), and dry gaseous carbon dioxide (excess). After being stirred at −30 to 0 °C for 2 h with a continuous stream of carbon dioxide passing through the solution, the reaction was subjected to an acid–base–acid work-up, as for compound (**10**). Kugelrohr distillation yielded *diene acid* (**11**) (0.53 g, 48% based on the transfer of both dienyl ligands) as a low melting solid, m.p. *ca.* 17 °C; b.p. 110 °C/0.02 mmHg; $\nu_{max.}$ (liquid film) 3 600—2 250, 1 695, and 1 630 cm^{-1}; $\lambda_{max.}$(EtOH) 256 nm (ε 13 970); δ_H (60 MHz) 0.90 (3 H, br t), 1.36 (12 H, m), 2.25 (2 H, m), 5.50—6.30 (2 H, m), 6.80—7.50 (2 H, m), and 12.30 (1 H, br s), δ_C 14.03, 22.72, 27.65, 29.30 (2C), 29.47 (2C), 31.94, 116.77, 124.76, 140.96, 142.37, and 172.14; *m/z* 210 (M^+) (Found: C, 74.3; H, 10.6. $C_{13}H_{22}O_2$ requires C, 74.2; H, 10.55%).

*Trideca-*6Z,8Z-*dien-5-ol* (**12**).—To a stirred solution of lithium di(octa-1*Z*,3*Z*-dienyl)cuprate (4.87 mmol) in ether (30 ml) at −70 °C were added simultaneously boron trifluoride–ether complex (0.6 ml, 3.66 mmol) and pentanal (0.5 ml, 4.70 mmol). After 30 min at −70 °C, standard ether work-up followed by chromatography on silica [CH_2Cl_2–ether (5:1)] gave the dienol (**12**) (0.49 g, 53%); $\nu_{max.}$ (liquid film) 3 420 cm^{-1}; δ_H (60 MHz) 0.90 (6 H, m), 1.35 (10 H, m), 2.20 (2 H, m), 2.55 (1 H, br s, OH), 4.50 (1 H, m), 5.40 (2 H, m), and 6.30 (2 H, m); δ_C 13.91, 14.09, 22.43, 22.78, 27.18, 27.59, 31.88, 37.34, 67.52, 123.53, 124.17, 133.56, and 134.27. The ^{13}C n.m.r. spectrum indicated the presence of undec-6*Z*-en-5-ol[7] (δ_C 131.50, 133.21, *etc.*) as a minor impurity. Fractional distillation could almost certainly be used to separate these compounds.

1-*Iodo-octa-*1Z,3Z-*diene* (**13**) *and* 1-*Iodo-octa-*1Z,3E-*diene* (**14**).—To a stirred solution of lithium di(octa-1*Z*,3*Z*-dienyl)cuprate (7.3 mmol) in ether (40 ml) at −70 °C was added a solution of iodine (3.7 g, 14.3 mmol) in THF (20 ml). The resulting solution was stirred in the dark at −50 to −30 °C for 3 h, then hydrolysed with 2M-HCl (50 ml). The product was extracted with ether (3 × 200 ml), and the combined extracts were washed with saturated aqueous sodium thiosulphate (3 × 200 ml). After being dried over $MgSO_4$, the mixture was evaporated under reduced pressure and the product was distilled (Kugelrohr) in the dark to yield a mixture of dienes (**13**) and (**14**) (1.03 g, 30% based on the transfer of both dienyl ligands) [(**13**):(**14**) *ca.* 2:3], b.p. 90—100 °C/3 mmHg; $\nu_{max.}$ (liquid film) 3 070, 3 020, 1 645, 970, and 690 cm^{-1}; δ_H (60 MHz) 0.90 (3 H, br t), 1.36 (4 H, m), 2.16 (2 H, m), 5.40—6.30 (3 H, m), 6.55 (0.4 H, m), and 6.93 (0.6 H, dd, *J* 9.6 and 7.2 Hz). The individual ^{13}C data could be extracted from the composite spectrum: (**13**) δ_C 13.91, 22.19, 28.53, 31.41, 83.25, 128.46, 133.33, and 137.15; (**14**) δ_C 13.91, 22.19, 31.00, 32.58, 79.26, 130.34, 138.32, and 140.08.

Owing to the thermal instability of these compounds, full characterization was not possible.

1-*Iodo-octa-*1E,3E-*diene* (**16**).—For ^{13}C n.m.r. comparison, a sample of 1-iodo-octa-1*E*,3*E*-diene was prepared by dehydration of 1-iodo-oct-1*E*-en-3-ol.[11] This was achieved by heating a solution of the alcohol (1 g, 4.2 mmol) in HMPA (4 ml) to 220 °C for 30 min. After having cooled, the brown solution was diluted with ether (50 ml) and washed with aqueous NH_4Cl solution (4 × 50 ml). After the solution had been dried over $MgSO_4$, the solvent was removed under reduced pressure and the product was chromatographed on silica (light petroleum) to give dienyl iodide (**16**) (0.23 g, 25%); $\nu_{max.}$ (liquid film) 3 060, 3 030, 1 640, and 980 cm^{-1}; δ_C 13.86 (q), 22.13 (t), 31.00 (t), 32.06 (t), 76.15 (d), 130.16 (d), 135.74 (d), and 145.19 (d). Owing to the thermal instability of this compound, full characterization was not possible.

1,1-*Diethoxy-*10-*iododecane* (**20**).—10-Bromodecanol[10] (25 g, 0.105 mol) was oxidized using pyridinium chlorochromate (34.5 g, 0.16 mol) in CH_2Cl_2 (400 ml) at room temperature for 3 h. The organic layer was decanted and the residual tar was extracted with light petroleum. Removal of solvent from the combined organic layers under reduced pressure gave a dark oil. Re-extraction with light petroleum (200 ml) and removal of the solvent under reduced pressure gave crude 10-bromodecanal (24.87 g, 100%).

All of this product was converted into the corresponding diethyl acetal by treatment with anhydrous ethanol (150 ml) and toluene-*p*-sulphonic acid (0.1 g). After being refluxed for 14 h, the solution was cooled and the solvent was removed under reduced pressure. The product was stirred with K_2CO_3 (1 g) for 10 min, diluted with ether (100 ml), then washed with saturated aqueous K_2CO_3 and dried over $MgSO_4$. The solvent was removed under reduced pressure and the product was chromatographed on silica [CH_2Cl_2–light petroleum (5:1)]. Although this process removed minor non-polar impurities, partial acetal hydrolysis also occurred. The resulting mixture of acetal and aldehyde was therefore subjected to the above acetalization procedure again but without the chromatography. This procedure gave crude 1,1-diethoxy-10-bromodecanal (24.10 g, 74%).

This product was converted into the title iodide (**20**) by being stirred for 14 h in the dark with sodium iodide (60 g, 0.4 mol) in dry acetone (350 ml) at room temperature. Two-thirds of the solvent was removed under reduced pressure, the mixture was diluted with water (200 ml), and the product was extracted with light petroleum (2 × 200 ml). After the extracts had been dried over $MgSO_4$, the solvent was removed under reduced pressure to yield 1,1-*diethoxy*-10-*iododecane* (**20**) as an oil (27.3 g, 98%); $\nu_{max.}$ (liquid film) 1 120 and 1 060 cm^{-1}; δ_H (60 MHz) 1.00—2.00 (22 H, m), 3.17 (2 H, t, *J* 7 Hz), 3.55 (4 H, m), and 4.45 (1 H, t, *J* 5 Hz); *m/z* 327 (M^+ − Et) and 311 (M^+ − OEt) (Found: C, 47.35; H, 8.1; I, 35.6. $C_{14}H_{29}IO_2$ requires C, 47.2; H, 8.2; I, 35.6%).

Hexadeca-11*Z*,13*Z*-*dienal* (**22**), *Navel Orangeworm Pheromone*.—A stock solution of ethyl-lithium was prepared by addition of bromoethane (2.61 ml, 25 mmol) to a suspension of finely cut lithium wire (1 g, 143 mmol) in hexane (30 ml) at −20 °C. After being stirred at this temperature for 1 h, the mixture was allowed to warm to room temperature during an additional 2 h. Titration gave the molarity as 0.85M (73%). A portion of this ethyl-lithium solution (8 ml, 6.8 mmol) was added dropwise to a stirred suspension of $CuBr{\cdot}SMe_2$ (0.689 g, 3.36 mmol) in ether (25 ml) at −40 °C. A homogeneous blue-black solution of lithium diethylcuprate formed. After being stirred at −35 °C for 30 min, the solution was cooled to −50 °C and treated with acetylene (165 ml, 7.4 mmol). The mixture was allowed to warm to −25 °C for 30 min and then to −10 °C. More acetylene (300 ml, 13.4 mmol) was added during *ca.* 10 min, while the temperature was maintained at −10 °C. Once addition was complete, the solution was cooled to −40 °C and treated with iodo acetal (**20**) (1.0 g, 2.79 mmol) and HMPA (0.5 ml, 2.8 mmol). After being stirred at −40 to 0 °C for 3 h, the reaction was quenched with water (30 ml), diluted with brine (50 ml), and the product was extracted with ether (2 × 30 ml). The combined extracts were washed with brine (50 ml) and dried over $MgSO_4$. After chromatography on silica (CH_2Cl_2), the product acetal (**21**) was treated with oxalic acid (2 g) in water (20 ml). THF was added until the mixture became homogeneous and the solution was stirred for 2 h at 60 °C. The product was extracted with light petroleum (3 × 100 ml), and the extract was dried over $MgSO_4$ and concentrated under reduced pressure. *Rapid* distillation from a Kugelrohr oven (125 °C/0.3 mmHg) gave hexadeca-11*Z*,13*Z*-dienal (**22**) (0.22 g, 33%); $\nu_{max.}$ 3 040, 3 000, 2 720, 1 730, 1 600, and 725 cm^{-1}; δ_H (60 MHz) 1.00 (3 H, t, *J* 7.2 Hz), 1.32 (14 H, m), 1.90—2.60 (6 H, m), 5.45 (2 H, m), 6.20 (2 H, m), and 9.68 (1 H, br t); δ_C 14.21, 20.78, 22.08, 27.48, 29.36 (5 × C), 29.65, 43.86, 123.06, 123.53, 131.92, 133.45, and 202.43; *m/z* 236 (M^+). The ^1H n.m.r. data were consistent with published[5,9] values.

6-(*Pentadeca*-1*Z*,3*Z*-*dien*-1-*yl*)*tetrahydropyran*-2-*one* (**28**).—A stirred suspension of finely cut lithium wire (1.0 g, 143 mmol) in hexane (25 ml) at 0 °C was subjected to ultrasonification, and 1-bromoundecane (5.0 g, 21.28 mmol) was added dropwise. Once reaction was complete (*ca.* 30 min), titration gave the molarity of undecyl-lithium as 0.74M (80%). A portion of this alkyl-lithium solution was employed in the general procedure (**N.B.**: The initial acetylene addition was carried out at −25 °C, not at −50 °C as in the general procedure) to prepare lithium di(pentadeca-1*Z*,3*Z*-dienyl)-cuprate (**24**) (6.94 mmol) in ether (80 ml). To this solution at −80 °C were added methyl 5-oxopentanoate[12] (**25**) (0.72 g, 5.5 mmol) and $BF_3{\cdot}OEt_2$ (0.68 ml, 5.5 mmol). After 1 h at −70 °C the mixture was subjected to a standard ether work-up and the product was chromatographed on silica (CH_2Cl_2) to give the crude hydroxy ester (**26**) (0.917 g, 52%). All of this crude material was treated with 1.5M-K_2CO_3 in CH_3OH–water (4:1; 20 ml). After being stirred overnight at room temperature the reaction mixture was diluted with water (30 ml) and washed with ether (3 × 20 ml). The aqueous layer was then acidified to pH 3 with dil. hydrochloric acid and extracted with ether (3 × 50 ml). The latter combined extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give hydroxy acid (**27**). Kugelrohr distillation gave the title *lactone* (**28**) (0.695 g, 41%), b.p. 200 °C/0.02 mmHg; $\nu_{max.}$ (liquid film) 3 020, 1 740, 1 650, 1 240, and 1 040 cm^{-1}; δ_H (60 MHz) 0.90 (3 H, br t), 1.30 (18 H, m), 1.60—2.70 (8 H, m), and 4.80—6.60 (5 H, m); δ_C 14.09, 18.49, 22.72, 27.53, 28.53, 29.47 (3C), 29.65 (4C), 31.94 (2C), 76.38, 122.29, 126.52, 127.75, 136.03, and 171.37; *m/z* 306 (M^+) (Found: M^+ 306.2560. $C_{20}H_{34}O_2$ requires *M*, 306.2559).

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