Nickel(0)-promoted Synthesis of Tetralin Lactones from the Co-cyclisation of Monoynes and Octa-1,7-diynes Terminally Substituted with Ester or Amide Groups

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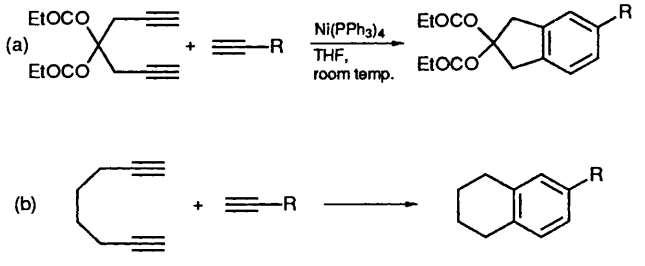
The co-cyclisation of octa-1,7-diynes with a variety of monoynes mediated by nickel(0) requires ester or amide groups at the terminal positions of the diyne and is subject to steric hindrance about the diyne rather than the monoyne; fused tetralin lactones are the most common products obtained in moderate to good yields. Intramolecular cyclisation of two triynes to the same type of product gives superior yields.

We have recently shown that the co-cyclisation of hepta-1,6-diynes and monoalkynols, or monoalkynyl ethers, mediated by a nickel(0) reagent generated *in situ* [stoichiometric $Ni(PPh_3)_4$; THF (tetrahydrofuran), room temp.] proceeds smoothly to give a range of indane derivatives in moderate to good yields (Scheme 1a).[1] This conversion complements similar chemistry



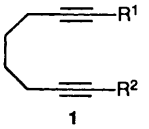
Scheme 1

developed by Grigg[2] [catalytic $RhCl(PPh_3)_3$; benzene, reflux] and Vollhardt[3] [catalytic $CpCo(CO)_2$; xylene, heat + irradiation] and their respective co-workers. The extension of this type of synthesis to the preparation of tetralins (Scheme 1b) is dependent upon the metal complex used as catalyst or mediator. The rhodium complex is unreactive, apart from exceptional substrates,[4] whereas the cobalt one[5] appears uniformly successful. Only one case of the preparation of a tetralin by a nickel complex $[Ni(CO)_2(PPh_3)_2]$ has been recorded[6] but the co-cyclisation of octa-1,7-diynes with aldehydes,[7] carbon dioxide,[8] silanes[9] and isocyanides[10] under the influence of nickel(0) [Ni(COD)–R_3P or $Ni(acac)_2$–DIBAL] showed that these diynes are not unresponsive to this metal.

In this paper we record that the use of octa-1,7-diynes terminally substituted with esters (and, in one case, an amide) leads to successful co-cyclisation with monoynes in the presence of our nickel(0) reagent to give tetralins, many isolated as their fused lactones.[11] The method provides a quick and convenient access to this type of compound.

Results and Discussion

Intermolecular Synthesis of Tetralin Lactones.—Octa-1,7-diynes **1** terminally disubstituted with groups which had



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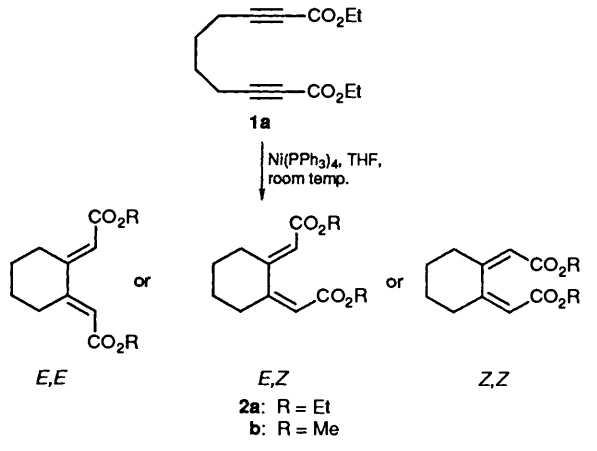


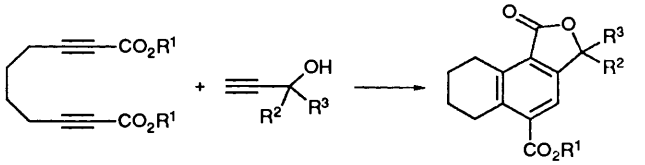
Scheme 2

electronically neutral ($R^1 = R^2$ = H, Me, Et), electronically withdrawing (COMe, COPh), electronically donating (SMe) or potentially coordinative [$CH(OH)Ph$, CH_2CH_2OH] properties all failed to give more than traces of cyclised products in the presence or absence of a monoalkyne. Apart from the parent and the thiomethyl compounds all the starting diynes were recovered in good yields (generally > 75%).

Fortunately one of the first groups which we had tried had proved very successful. In the absence of a monoalkyne trap diethyl deca-2,8-diynedioate **1a**, on addition to a solution of the nickel(0) reagent in THF,[12] disappeared completely and gave one geometrical isomer of 1,2-bis(ethoxycarbonylmethylene)-cyclohexane **2a** in low yield (8%) (Scheme 2). One fine triplet for the olefinic protons at δ 5.8 ruled out the *E,Z*-geometry for this product on symmetry grounds (for the product of *E,Z*-geometry the spectrum should show two olefinic peaks). Our data did not allow us to distinguish between the other two but we favour the *E,E*-structure on the basis of reduced steric hindrance.

In the presence of four equivalents of prop-2-ynyl alcohol co-cyclisation occurred to give a tetralin† lactone **3a** (46%) wherein the hydroxy group of the monoalkyne had condensed with one of the ester groups (Scheme 3). With the corresponding methyl ester **1b**, the yield of the co-cyclisation–lactonisation was even higher (78%) and consequently methyl esters were used for the remaining studies. Using diester **1b** as the test diyne, the effect of steric encumbrance in the monoalkyne on the reaction was probed with but-1-yn-3-ol, 3-methylbut-1-yn-3-ol and 1-ethyn-

† 1,2,3,4-Tetrahydronaphthalene.

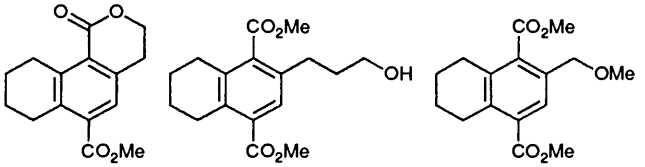


1a R^1 = Et
b R^1 = Me

3a R^1 = Et, R^2 = R^3 = H (46%)
b R^1 = Me, R^2 = R^3 = H (78%)
c R^1 = Me, R^2 = Me, R^3 = H (51%)
d R^1 = Me, R^2 = R^3 = Me(58%)
e R^1 = Me, R^2 + R^3 = $(CH_2)_5$ (58%)

Scheme 3

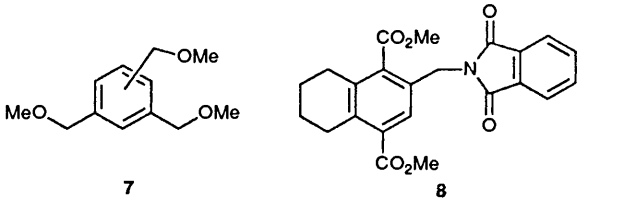
ylcyclohexanol. In contrast to the indane synthesis [1] where alkyl substitution next to the OH group in the monoalkyne had resulted in a 4–6 fold reduction in yield compared to the unfettered prop-2-ynyl alcohol, in the present case yields of product lactones **3c–e** were not drastically lowered (51, 58 and 58% respectively). Thus, there appeared to be no substantial problem of steric hindrance from substituents on the monoalkyne. A homoprop-2-ynylic alcohol, but-3-yn-1-ol, also co-cyclised to a lactone but less well; δ-lactone **4** was isolated in only 24% yield. Pent-4-yn-1-ol gives a respectable yield (42%) of the cyclisation product **5** without, however, the concomitant lactonisation. Unexpectedly, hex-5-yn-1-ol, which had worked well in the indane synthesis,[1] was largely (80%) recovered in the present case. Likewise, methyl prop-2-ynyl ether, the champion indane precursor, was disappointing in the tetralin synthesis; the tetralin **6** was obtained as an inseparable 1:1 mixture with the trimers **7** (both 1,2,4 and 1,3,5) of the monoyne (the estimated yield of **6** from the ^{1}H NMR spectrum of this mixture was 35%).



4

5

6

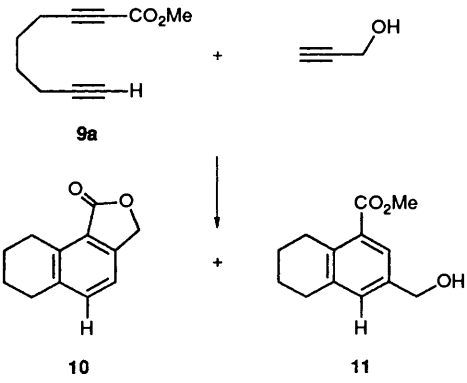


7

8

In an attempt to synthesise lactams instead of lactones by this route we substituted prop-2-ynylamine for prop-2-ynyl alcohol in the reaction with ester **1b**. Unexpectedly, only traces of a product which might be the lactam were formed but rather the diene **2b** was isolated in respectable yield (47%). In contrast *N*-prop-2-ynyl phthalimide presented no problem and provided the tetralin, **8**, in the highest yield yet for this type of reaction (87%).

In order to test whether both terminal ester groups on the diyne were necessary for the success of the reaction, methyl nona-2,8-diynoate **9a** was subjected to co-cyclisation with prop-2-ynyl alcohol (4 equiv.) (Scheme 4). The total yield of tetralin products was 91%, distributed between lactone **10** (19%) and alcohol ester **11** (72%). Since the lactone products were more valuable synthetically, we hoped that perturbation of **9a** by replacing hydrogen on the terminal acetylene by bulky silyl groups might force the CH_2OH group into proximity with



9a

10 **11**

Scheme 4

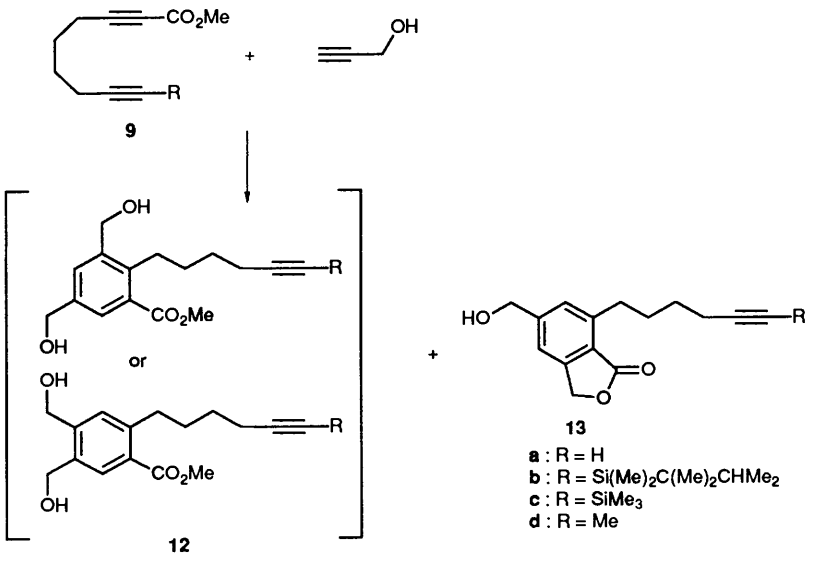
the ester during co-cyclisation. This was not to be. Reaction of the thexylsilyl analogue **9b** resulted in none of the desired lactone but rather in two aromatic compounds **12b** (38%) and **13b** (31%) in which the ester bearing alkyne had cocyclised with 2 equiv. of prop-2-ynyl alcohol (Scheme 5). The same types of product **12c,d** (34, 36%) and **13c,d** (21, 20%) were obtained when the smaller trimethylsilyl and methyl congeners **9c** and **9d** were employed. The regiochemistry of the diols **12** was not completely certain whereas the structures of lactones **13** were more secure. For one of these latter, **13d**, an X-ray crystal structure proved definitive (Fig. 1).[13] Thus, the problem of steric hindrance in the monoalkyne which had led to low yields in the earlier indane synthesis,[1] has resurfaced here but rather in the diyne component with yields following the substituent order CO_2Me, H > CO_2Me, CO_2Me > CO_2Et, CO_2Et ≫ CO_2Me, Me or CO_2Me, SiR_3.

Nona-2,8-diynoic acid amide **14** reacted totally regiospecifically to give lactone **10** (Scheme 6). This result indicates that the regiochemical problem may be overcome, although in modest yield (36%), and that a $CONH_2$ group on the diyne is not as damaging to the reaction as an NH_2 group on the monoyne.

Intramolecular Synthesis of Tetralin Lactones.—We were keen to test triynes as suitable precursors to tetralin lactones since the problem of regiochemical control will be absent for these cyclisation substrates. To this end nona-2,8-diynoic acid **15** was separately esterified with prop-2-ynyl alcohol and but-3-yn-1-ol to give the requisite cyclisation substrates **16** (84%) and **17** (79%) respectively. Both were cyclised very cleanly by nickel(0) to their respective lactones **10** (70%) and **18** (46%) (Scheme 7). Clearly, the intramolecular reaction represents the best approach to this type of tetralin lactone especially in view of the short route to the cyclisation precursors.

Conclusions.—It could be argued that the success of the intermolecular reactions with diynes bearing ester substituents is a consequence of transesterification with the monoyne alcohols followed by intramolecular cyclisation. The following observations suggest otherwise: (a) the major product of the co-cyclisation of monoester **9a** was the non-lactonic product **11**; (b) co-cyclisation of diester **1b** with pent-4-yn-1-ol proceeded to **5** in moderate yield without lactonisation; (c) no lactones corresponding to **3** were isolated in which the remaining ester group on the aromatic ring had been transesterified with the monoyne alcohol; and (d) methyl prop-2-ynyl ether and *N*-prop-2-ynyl phthalimide, for which transesterification is impossible, do produce tetralins (35 and 87% respectively).

The synthesis of tetralins is clearly different in its requirements from that of indanes. The necessity for ester or amide groups on the diyne, the fact that the reaction is subject to steric hindrance on the diyne but not on the monoyne component and



Scheme 5

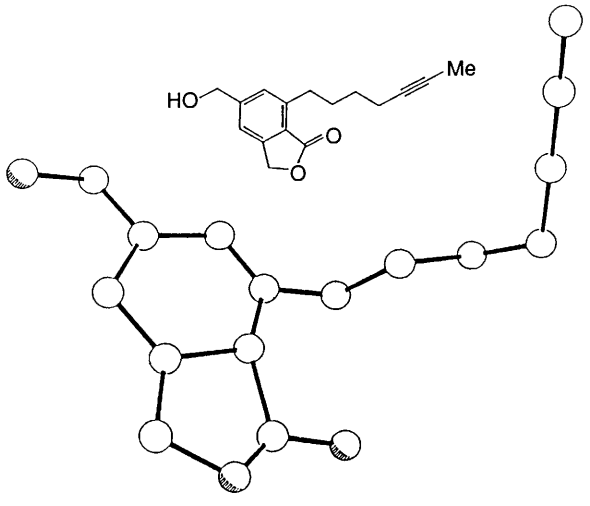
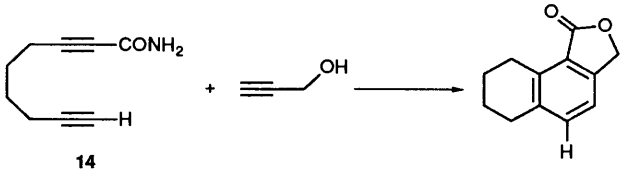
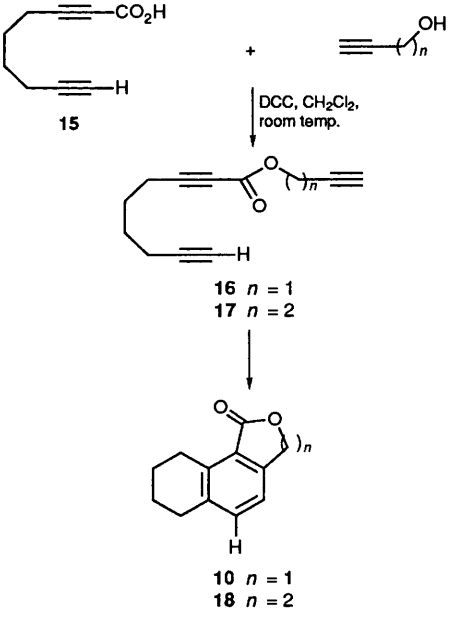


Fig. 1



Scheme 6



Scheme 7

that no coordination effects of alcohol or ether groups on the monoyne are shown towards nickel all point to a different emphasis in the mechanism for the tetralin synthesis (or a different mechanism entirely) despite its structural similarity to the indane one. The nature of this mechanistic divergence is currently under investigation.

Experimental

M.p.s were determined on a Kofler hot-stage or Gallenkamp apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 881 spectrophotometer as thin films (neat) or as mulls (Nujol). ^1H and ^{13}C NMR spectra were recorded on JEOL FX90Q, JEOL GSX 270, or Bruker WM 500 instruments, using tetramethylsilane or chloroform as internal standards in $CDCl_3$ unless otherwise stated, J values are given in Hz. Signals are quoted as singlet (s), doublet (d), triplet (t), quartet (q), quintet (quin), hexaplet (hex), heptaplet (hep), multiplet (m) and broad (br). Mass spectra were recorded on a VG Micromass 7070B machine by the EI method.

Preparative gravity column chromatography was performed on Crosfield Sorbsil C60 silica gel. Light petroleum refers to that fraction of b.p. 40–60 °C. Ether refers to diethyl ether. Ether and THF (tetrahydrofuran) were distilled from sodium and potassium metal respectively under argon immediately prior to use. Dichloromethane was distilled from phosphorus pentoxide under argon just prior to use. Butyllithium was purchased from Aldrich Chemicals as a solution in hexanes. All other solvents and chemicals were purified by standard methods.

Diethyl deca-2,8-diynedioate **1a**, m.p. 54–56 °C (23%), dimethyl deca-2,8-diynedioate **1b**, m.p. 36–39 °C (98%), and methyl nona-2,8-diynoate **9a** (oil, 78%) were made by a minor modification of the literature method [14] whereby BuLi was used instead of MeLi for the deprotonation of octa-1,7-diyne prior to reaction with the chloroformates.

Methyl 9-(*Dimethylthexylsilyl*)*nona*-2,8-*diynoate* **9b**.—To a solution of 1-(dimethylthexylsilyl)octa-1,7-diyne (500 mg, 2.02 mmol) in dry THF under argon at −78 °C was added BuLi (1.6 mol dm^{-3}; 3.2 cm^3, 2 mmol) dropwise. The reaction mixture was stirred at this temperature for 1 h, then allowed to warm briefly to 0 °C followed by cooling to −78 °C again. To the lithio species thus formed was added neat methyl chloroformate (0.2 cm^3, 282 mg, 3 mmol) dropwise. After stirring at −78 °C for 30 min, the reaction was allowed to warm to room temperature over a period of 30 min. Water (15 cm^3) was added to the mixture carefully and the THF was removed on the rotary evaporator. The aqueous residue was extracted with ether (3 × 15 cm^3), the extracts were dried ($MgSO_4$), filtered and concentrated to an oil which was distilled in a Kugelrohr apparatus to give the product as a colourless oil (550 mg, 89%), b.p. 110 °C at 0.2 mmHg; ν_{max}(neat)/cm^{-1} 2237, 2174 and 1724; δ_H(270 MHz) 0 (6 H, s, Me_2Si), 0.8 (12 H, s + d, thexyl 4 × Me), 1.45–1.65 (5 H, m, 2 × CH_2 + thexyl CH), 2.15 (2 H, t, *J* 7.5, $CH_2C{\equiv}$),2.25 (2 H, t, *J* 7.5, $CH_2C{\equiv}$) and 3.65 (3 H, s, CO_2Me); the ^1H NMR spectrum showed that this material was contaminated with a little starting alkyne which was difficult to remove. Consequently, this product was used without further purification.

Methyl 9-(*Trimethylsilyl*)*nona*-2,8-*diynoate* **9c**.—This was made in identical fashion from 1-trimethylsilylocta-1,7-diyne (525 mg, 2.94 mmol) to give the crude product as a yellow oil. This was distilled in a Kugelrohr apparatus, b.p. 150 °C at 0.3 mmHg, and then chromatographed on silica gel using light petroleum–ether (9:1) as eluent to give the product as a pale yellow oil (550 mg, 79%) (Found: M^+ − Me, 221.1004. $C_{12}H_{17}O_2Si$ requires *M*, 221.0998); ν_{max}/cm^{-1} 2236, 2175 and 1717; δ_H(270 MHz) 0.1 (9 H, s, Me_3Si), 1.5–1.7 (4 H, m, 2 × CH_2), 2.2 (2 H, t, *J* 7.5, $CH_2C{\equiv}$), 2.3 (2 H, t, *J* 7.5, $CH_2C{\equiv}$) and 3.7 (3 H, s, CO_2Me); δ_C(67.5 MHz) 0 (Me_3Si), 18 (CH_2), 20 (CH_2), 27 (CH_2), 28 (CH_2), 52 (OMe), 73 (alkynic C), 85 (alkynic C), 89 (alkynic C), 106 (alkynic C) and 154 (CO); *m*/*z* 235 (M^+ − 1), 221 (M^+ − Me), 162 (M^+ − 1 − Me_3Si), 73 (Me_3Si), 59, 45 and 43.

Methyl Deca-2,8-*diynoate* **9d**.—This was made in identical fashion from mona-1,7-diyne (130 mg, 1.08 mmol) to give the crude product. This was distilled in a Kugelrohr apparatus, b.p. 120 °C at 0.4 mmHg, and then chromatographed on silica gel using light petroleum–ether (1:1) as eluent to give the product as a pale yellow oil (139 mg, 78%); ν_{max}(neat)/cm^{-1} 2240 and 1717; δ_H(90 MHz) 1.4–1.7 (7 H, m, MeC≡ + 2 × CH_2), 1.9–2.1 (2 H, m, $CH_2C{\equiv}$), 2.1–2.4 (2 H, m, $CH_2C{\equiv}$) and 3.6 (3 H, s, CO_2Me). This material was contaminated with traces of the starting alkyne and was used without further purification.

Nona-2,8-*diynamide* **14**.—To a solution of methyl nona-2,8-diynoate **9a** (380 mg, 2.26 mmol) in methanol (18 cm^3) was added aqueous ammonia (35% solution, 0.125 cm^3, 38.5 mg, NH_3, 2.26 mmol) and the reaction was stirred vigorously at room temperature for 1 h. Water (10 cm^3) was then added and the aqueous solution was extracted with ether (3 × 10 cm^3). The ethereal extracts were combined, dried ($MgSO_4$), filtered and concentrated to a beige solid. This was chromatographed on silica gel to give the product as a white solid, m.p. 103 °C (300 mg, 87%) (Found: C, 72.3; H, 7.05; N, 9.05. $C_9H_{11}NO$ requires C, 72.46; H, 7.43; N, 9.39%); ν_{max}(Nujol) 3297, 3188, 2244, 1656 and 1613; δ_H(90 MHz) 1.6–1.9 (4 H, m, 2 × CH_2), 2.05 (1 H, t, *J* 2, HC≡), 2.2–2.6 (4 H, m, 2 × $CH_2C{\equiv}$),6.1 (1 H, br s, NH) and 6.7 (1 H, br s, NH); δ_C(22.5 MHz) 18 (2 × CH_2), 26.5 (CH_2), 27.5 (CH_2), 69 (CH), 76 (alkynic C), 84 (alkynic C), 88 (alkynic C) and 156 (CO); *m*/*z* 149 (M^+), 148 (M^+ − H), 134 (M^+ − NH), 131 (M^+ − H_2O), 121, 120, 105 (M^+ − $CONH_2$), 91, 79, 77, 65, 44, 41 and 39.

Nona-2,8-*diynoic Acid* **15**.—Methyl nona-2,8-diynoate **9a** (1 g, 5.95 mmol) was dissolved in ethanol (10 cm^3) and a solution of KOH (390 mg, 6.96 mmol) in water (3 cm^3) was added dropwise. The resultant mixture was warmed to 70 °C and stirred at this temperature for 1 h. The mixture was cooled in an ice-bath and chloroform (15 cm^3) was added. To this mixture ice-cold sulfuric acid (2 mol dm^{-3}; 10 cm^3) was added dropwise. The organic layer was separated and the aqueous layer was further extracted with chloroform (3 × 10 cm^3). The extracts and organic layer were combined, dried (Na_2SO_4), filtered and concentrated to give the acid as a colourless oil (713 mg, 80%) (Found: M^+ − H, 149.0603. $C_9H_9O_2$ requires *M*, 149.060 25); ν_{max}(neat)/cm^{-1} 3297, 3400–2700, 2236 and 1700; δ_H(90 MHz) 1.7–2.0 (4 H, m, 2 × CH_2), 2.1 (1 H, m, HC≡), 2.4–2.7 (4 H, m, 2 × $CH_2C{\equiv}$) and 8.9 (1 H, br s, CO_2H); *m*/*z* 150 (M^+), 149 (M^+ − H), 135, 133 (M^+ − OH), 132, 131, 122, 121, 105 (M^+ − CO_2H), 91, 79, 77, 65, 44, 41 and 39.

4-*Oxatrideca*-1,6,12-*triyn*-5-*one* **16**.—To a solution of prop-2-ynyl alcohol (126 mg, 2.25 mmol) and acid **15** (340 mg, 2.26 mmol) in dry dichloromethane (20 cm^3) under calcium chloride was added dicyclohexylcarbodiimide (466 mg, 2.26 mmol). The reaction mixture was stirred for 2 h and then filtered to remove dicyclohexylurea. The filtrate was concentrated to a yellow oil which was chromatographed on silica gel using light petroleum–ether (5:1) as eluent to give the product as a pale yellow oil (376 mg, 89%) (Found: M^+, 188.0841. $C_{12}H_{12}O_2$ requires *M*, 188.0837); ν_{max}(neat)/cm^{-1} 3297, 2239, 1712 and 1239; δ_H(90 MHz) 1.6–1.8 (4 H, m, 2 × CH_2), 2.0 (1 H, m, HC≡), 2.2–2.4 (4 H, m, 2 × CH_2), 2.5 (1 H, m, HC≡) and 4.75 (2 H, m, CH_2OCO); *m*/*z* 188 (M^+), 141, 103, 79, 77, 39 and 28.

5-*Oxatetradeca*-1,7,13-*triyn*-6-*one* **17**.—Prepared in exactly the same manner as ester **16** using but-3-yn-1-ol (200 mg, 2.86 mmol), acid **15** (430 mg, 2.86 mmol), dicyclohexylcarbodiimide (590 mg, 2.86 mmol) and dry dichloromethane (20 cm^3). The crude product was subjected to column chromatography on silica gel using light petroleum–ether (5:1) as eluent to give the *ester* as a colourless oil (457 mg, 79%) (Found: M^+ − H, 201.0917. $C_{13}H_{13}O_2$ requires *M*, 201.091 55); ν_{max}(neat)/cm^{-1} 3297, 2237, 1707 and 1247; δ_H(270 MHz) 1.7 (4 H, m, 2 × CH_2), 1.98 (1 H, t, *J* 2, HC≡), 2.03 (1 H, t, *J* 2, HC≡), 2.3 (4 H, m, 2 × $CH_2C{\equiv}$), 2.55 (2 H, dt, *J* 2, *J'* 7, CH_2CH_2OCO) and 4.2 (2 H, t, *J* 7, CH_2OCO); *m*/*z* 201 (M^+ − H), 150, 149 (M^+ − C_4H_5), 105, 79, 77 and 53 ($C_4H_5^+$).

Co-cyclisations. General Procedure.—A red–brown solution of the nickel(0) reagent (0.76 mmol) in dry, degassed THF (40 cm^3) under argon was prepared according to the literature procedure.[12] To this solution was added at room temperature a solution of the diyne (0.76 mmol) in dry, degassed THF (5 cm^3) when the red tinge of the brown mixture was replaced by a green one. After 10 min a solution of the monoyne (3.04 mmol) in dry, degassed THF (5 cm^3) was added and the reaction mixture was allowed to stir under argon at room temperature for 17 h. The reaction was quenched by the addition of hydrochloric acid (5 mol dm^{-3}; 5 cm^3), the flask was opened to the air and the solvent was removed on the rotary evaporator. Water (50 cm^3) was added to the resultant brown sludge and the mixture was extracted with ether (3 × 20 cm^3). The extracts were combined, dried ($MgSO_4$), filtered and concentrated to give the crude product. In all cases this material was chromatographed on silica gel with the indicated solvent as eluent.

1,2-*Bis*(*ethoxycarbonylmethylene*)*cyclohexane* **2a**.—Obtained

from diester **1a**, after chromatography using light petroleum–ether (1:1), as a colourless oil (8%) (Found: M^+, 252.1355. $C_{14}H_{20}O_4$ requires *M*, 252.136 15); ν_{max}(neat)/cm^{-1} 1717 and 1657; δ_H(270 MHz) 1.25 (6 H, t, *J* 7, 2 × Me), 1.75 (4 H, m, 2 × CH_2), 2.97 (4 H, m, 2 × CH_2), 4.15 (4 H, q, *J* 7, 2 × CH_2OCO) and 5.8 (2 H, t, *J* < 1, CH=); *m/z* 252 (M^+), 206 (M^+ − EtOH), 179, 151, 133, 105 and 57.

1,2-*Bis*(*methoxycarbonylmethylene*)*cyclohexane* **2b**.—Obtained from diester **1b** and prop-2-ynylamine, after chromatography using light petroleum–ether (1:1), as a pale yellow oil (47%) (Found: M^+, 224.1053. $C_{12}H_{16}O_4$ requires *M*, 224.1049); ν_{max}(neat)/cm^{-1} 1731 and 1653; δ_H(270 MHz) 1.7 (4 H, m, 2 × CH_2), 2.95 (4 H, m, 2 × CH_2), 3.6 (6 H, s, 2 × Me) and 5.8 (2 H, t, *J* < 1, CH=); *m/z* 224 (M^+), 192 (M^+ − MeOH) and 165.

Ethyl 1,3,6,7,8,9-*Hexahydro*-1-*oxonaphtho*[1,2-c]*furan*-5-*carboxylate* **3a**.—Obtained from diester **1a** and prop-2-ynyl alcohol, after chromatography using light petroleum–ether (1:1), as a white solid (46%), m.p. 62 °C (Found: C, 69.1; H, 5.85. $C_{15}H_{16}O_4$ requires C, 69.22; H, 6.20%); ν_{max}(Nujol)/cm^{-1} 1761, 1727 and 1620; δ_H(90 MHz) 1.4 (3 H, t, *J* 8, Me), 1.8 (4 H, m, 2 × CH_2), 3.0 (2 H, m, benzylic CH_2), 3.25 (2 H, m, benzylic CH_2), 4.35 (2 H, q, *J* 8, MeCH_2OCO), 5.2 (2 H, s, benzylic CH_2OCO) and 7.6 (1 H, s, ArH); δ_C(67.5 MHz) 14, 21, 22, 25.5, 27, 31, 61 (CH_2O), 68.5 (CH_2O), 120, 124, 136, 136.5, 140, 141, 144, 163, 167.5 and 170.5; *m/z* 260 (M^+, 100%), 231 (M^+ − Et), 215 (M^+ − EtO), 187 and 128.

Methyl 1,3,6,7,8,9-*Hexahydro*-1-*oxonaphtho*[1,2-c]*furan*-5-*carboxylate* **3b**.—Obtained from diester **1b** and prop-2-ynyl alcohol, after chromatography using light petroleum–ether (1:1), as a white solid (78%), m.p. 120–122 °C (Found: C, 68.25; H, 5.65. $C_{14}H_{14}O_4$ requires C, 68.28; H, 5.73%); ν_{max}(Nujol)/cm^{-1} 1765, 1727 and 1683; δ_H(90 MHz) 1.8 (4 H, m, 2 × CH_2), 3.0 (2 H, m, benzylic CH_2), 3.3 (2 H, m, benzylic CH_2), 3.9 (3 H, s, OMe), 5.2 (2 H, s, CH_2OCO) and 7.6 (1 H, s, ArH); δ_C(22.5 MHz) 22 (CH_2), 23 (CH_2), 26 (CH_2), 28 (CH_2), 53 (OMe), 69 (CH_2OCO), 120, 143, 163 (CO) and 186 (CO); *m/z* 246 (M^+, 100%), 231 (M^+ − Me), 214, 186 (M^+ − H − CO_2Me) and 128.

Methyl 1,3,6,7,8,9-*Hexahydro*-3-*methyl*-1-*oxonaphtho*[1,2-c]-*furan*-5-*carboxylate* **3c**.—Obtained from diester **1b** and but-1-yn-3-ol, after chromatography using light petroleum–ether (1:1), as a beige solid (51%), m.p. 192–194 °C (Found: C, 69.0; H, 6.4. $C_{15}H_{16}O_4$ requires C, 69.21; H, 6.19%); ν_{max}(Nujol)/cm^{-1} 1765, 1727 and 1612; δ_H(90 MHz) 1.55 (3 H, d, *J* 7, Me), 1.8 (4 H, m, 2 × CH_2), 3.0 (2 H, m, benzylic CH_2), 3.25 (2 H, m, benzylic CH_2), 3.9 (3 H, s, OMe), 5.45 (1 H, q, *J* 7, CHOCO) and 7.6 (1 H, s, ArH); δ_C(22.5 MHz) 21 (Me), 22 (CH_2), 23 (CH_2), 26 (CH_2), 28 (CH_2), 53 (OMe), 79 (CHO), 119, 168 (CO) and 188 (CO); *m/z* 262 (M^+ + 2, 100%), 183 and 108.

Methyl 1,3,6,7,8,9-*Hexahydro*-3,3-*dimethyl*-1-*oxonaphtho*-[1,2-c]*furan*-5-*carboxylate* **3d**.—Obtained from diester **1b** and 3-methylbut-1-yn-3-ol, after chromatography using light petroleum–ether (1:1), as a cream-coloured solid (58%), m.p. 134–136 °C (Found: C, 70.05; H, 6.65. $C_{16}H_{18}O_4$ requires C, 70.06; H, 6.61%); ν_{max}(Nujol)/cm^{-1} 1751, 1726 and 1607; δ_H(90 MHz) 1.4 (6 H, s, 2 × Me), 1.8 (4 H, m, 2 × CH_2), 3.0 (2 H, benzylic CH_2), 3.25 (2 H, m, benzylic CH_2), 3.9 (2 H, s, OMe) and 7.55 (1 H, s, ArH); δ_C(22.5 MHz) 22, 22.5, 26, 27.5, 28, 52.5 (OMe), 84 (*C*OCO), 119 and 168 (CO); *m/z* 274 (M^+, 100%), 259 (M^+ − Me).

Methyl-1,3,6,7,8,9-*Hexahydro*-1-*oxo*(*naphtho*[1,2-c]*furan*-3-*spirocyclohexane*)-5-*carboxylate* **3e**.—Obtained from diester **1b** and 1-ethynylcyclohexanol, after chromatography using light petroleum–ether (1:1), as a thick, colourless oil (58%) (Found: C, 73.0; H, 8.25%; M^+, 314.1513. $C_{19}H_{22}O_4$ requires C, 72.59; H, 7.05%; *M*, 314.1518); ν_{max}(neat)/cm^{-1} 1759, 1728 and 1612; δ_H(90 MHz) 1.8 (14 H, m, 7 × CH_2), 3.0 (2 H, m, CH_2), 3.25 (2 H, m, CH_2), 3.9 (3 H, s, OMe) and 7.55 (1 H, s, ArH); δ_C(22.5 MHz), 21, 22, 22.5, 23, 24.5, 25, 25.5, 28, 36, 40, 52 (OMe), 85 (*C*OCO), 119 and 168 (CO); *m/z* 314 (M^+, 100%), 237.

Methyl 3,4,7,8,9,10-*Hexahydro*-1-*oxo*-1H-*naphtho*[1,2-c]-*pyran*-6-*carboxylate* **4**.—Obtained from diester **1b** and but-3-yn-1-ol, after chromatography using light petroleum–ether (1:1), as a pale yellow oil (24%) (Found: M^+,260.1045. $C_{15}H_{16}O_4$ requires *M*, 260.1049); ν_{max}(neat)/cm^{-1} 1721; δ_H(90 MHz), 1.75 (4 H, m, 2 × CH_2), 3.0 (4 H, m, 2 × benzylic CH_2), 3.2 (2 H, m, benzylic CH_2), 3.9 (3 H, s, OMe), 4.4 (2 H, t, *J* 5, CH_2OCO) and 7.4 (1 H, s, ArH); δ_C(62.9 MHz) 22.2 (CH_2), 22.4 (CH_2), 28 (CH_2), 29 (CH_2), 29.3 (CH_2), 52 (OMe), 67 (CH_2O), 125, 127, 135, 138, 143, 164 (CO) and 168 (CO); *m/z* 260 (M^+, 100%), 245 (M^+ − Me), 227 and 200 (M^+ − H − CO_2Me).

Dimethyl 5,6,7,8-*Tetrahydro*-2-(3-*hydroxypropyl*)*naphthalene*-1,4-*dicarboxylate* **5**.—Obtained from diester **1b** and pent-4-yn-1-ol, after chromatography using light petroleum–ether (1:4), as a colourless oil (42%) (Found: C, 66.4; H, 7.85. $C_{17}H_{22}O_5$ requires C, 66.64; H, 7.64%); ν_{max}(neat)/cm^{-1} 3401 and 1727; δ_H(270 MHz) 1.75 (4 H, m, 2 × CH_2), 1.85 (2 H, quin, *J* 7, chain CH_2), 2.6 (2 H, t, *J* 7, chain benzylic CH_2), 2.7 (2 H, m, ring benzylic CH_2), 3.0 (2 H, m, ring benzylic CH_2), 3.6 (2 H, t, *J* 7, CH_2O), 3.85 (3 H, s, OMe), 3.9 (3 H, s, OMe) and 7.55 (1 H, s, ArH); δ_C(22.5 MHz) 22, 22.5, 27, 27.5, 29, 31.5, 52 (OMe), 61 (OMe), 77 (CH_2OH), 128, 128.5, 131.5, 132, 168 (CO) and 170 (CO); *m/z* 306 (M^+), 288 (M^+ − H_2O), 274 (M^+ − MeOH) and 111.

Dimethyl 5,6,7,8-*Tetrahydro*-2-(*phthalimidomethyl*)*naphthalene*-1,4-*dicarboxylate* **8**.—Obtained from diester **1b** and *N*-prop-2-ynyl phthalimide, after chromatography using light petroleum–ether (1:1), as a white solid (87%), m.p. 162–164 °C (Found: C, 67.8; H, 5.2; N, 3.35. $C_{23}H_{21}NO_6$ requires C, 67.81; H, 5.20; N, 3.44%); ν_{max}(Nujol)/cm^{-1} 1774 and 1725; δ_H(270 MHz) 1.7 (4 H, m, 2 × CH_2), 2.7 (2 H, m, benzylic CH_2), 3.0 (2 H, m, benzylic CH_2), 3.85 (3 H, s, OMe), 3.95 (3 H, s, OMe), 4.85 (2 H, s, CH_2N), 7.3 (1 H, s, ArH), 7.7 (2 H, m, ArH) and 7.85 (2 H, m, ArH); δ_C(67.5 MHz) 22, 22, 27.5, 28, 39 (CH_2N), 52 (OMe), 52.5 (OMe), 123, 129, 129.5, 131.5, 132, 134, 135.5, 136.5, 138.5, 160 (CO), 167.6 (CO), 167.7 (CO) and 169 (CO); *m/z* 407 (M^+ − H), 375 (M^+ − H − MeOH, 100%), 347 and 130.

6,7,8,9-*Tetrahydro*-3H-*naphtho*[1,2-c]*furan*-1-*one* **10**.—Obtained from monoester **9a** and prop-2-ynyl alcohol, after chromatography using light petroleum–ether (1:1), as a white solid (19%), m.p. 79 °C (Found: M^+, 188.0836. $C_{12}H_{12}O_2$ requires *M*, 188.0837); ν_{max}(Nujol)/cm^{-1} 1763; δ_H(270 MHz) 1.86 (4 H, m, 2 × CH_2), 2.85 (2 H, m, benzylic CH_2), 3.25 (2 H, m, benzylic CH_2), 5.2 (2 H, s, CH_2OCO), 7.15 (1 H, 1/2 ABq, *J* 8, ArH) and 7.35 (1 H, 1/2 ABq, *J* 8, ArH); δ_C(125.8 MHz) 22 (CH_2), 22.5 (CH_2), 25 (CH_2), 29 (CH_2), 69 (CH_2O), 118, 135, 138, 138.5, 145 and 171 (CO); *m/z* 188 (M^+, 100%) and 143.

Methyl 5,6,7,8-*Tetrahydro*-3-*hydroxymethylnaphthalene*-1-*carboxylate* **11**.—Obtained from monoester **9a** and prop-2-ynyl alcohol, after chromatography using light petroleum–ether (1:1), as a colourless oil (72%) (Found: M^+, 220.1095. $C_{13}H_{16}O_3$ requires *M*, 220.1099); ν_{max}(neat)/cm^{-1} 3388 and 1722; δ_H(270 MHz) 1.75 (4 H, m, 2 × CH_2), 2.0 (1 H, br s, OH), 1.8 (2 H, m, benzylic CH_2), 3.05 (2 H, m, benzylic CH_2), 3.85 (3 H, s, OMe), 4.6 (2 H, s, CH_2O), 7.2 (1 H, s, ArH) and 7.65

(1 H, s, ArH); δ_C(22.5 MHz) 22.5 (CH_2), 23 (CH_2), 28 (CH_2), 30 (CH_2), 52 (OMe), 65 (CH_2O), 127, 131, 137, 138, 139 and 168 (CO); *m/z* 220 (M^+), 188 (M^+ − MeOH), 131 and 91.

Methyl 3(4),5-*Bis*(*hydroxymethyl*)-2-(6-*dimethylthexylsilyl*-*hex*-5-*ynyl*)*benzoate* **12b**.—Obtained from monoester **9b** and prop-2-ynyl alcohol, after chromatography using light petroleum–ether (1:1), as a colourless oil (38%); ν_{max}(neat)/cm^{-1} 3335, 2175 and 1725; δ_H(270 MHz) 0.1 (6 H, s, $SiMe_2$), 0.9 (12 H, s + d, thexyl Me groups), 1.55–1.8 (5 H, m, 2 × CH_2 + thexyl CH), 2.3 (3 H, br s + t, *J* 7, $CH_2C\equiv$ + OH), 3.0 (2 H, t, *J* 7, benzylic CH_2), 3.5 (1 H, br s, OH), 3.9 (3 H, s, OMe), 4.7 (4 H, 2 × s, 2 × CH_2O), 7.25 (1 H, s, ArH) and 7.85 (1 H, s, ArH, *ortho*-ester group); δ_C(125.8 MHz) 18.5, 19.5, 20.5, 23, 28.5, 31, 33.5, 34.5, 52 (OMe), 63.3 (CH_2O), 63.4 (CH_2O), 84, 108, 129, 131.8, 132, 136.5, 143, 144.5 and 168 (CO); *m/z* 389 (M^+ − CHO), 387 (M^+ − MeO), 333, 89 and 75.

7-(6-*Dimethylthexylsilylhex*-5-*ynyl*)-5-*hydroxymethyl*-3H-*benzo*[c]*furan*-1-*one* **13b**.—Obtained from monoester **9b** and prop-2-ynyl alcohol, after chromatography using light petroleum–ether (1:1), as a yellow oil (31%) [Found: M^+ − $C(Me)_2CHMe_2$, 301.1256. $C_{17}H_{21}O_3Si$ requires *M*, 301.1260]; ν_{max}(neat)/cm^{-1} 3449, 2174 and 1750; δ_H(270 MHz) 0.1 (6 H, s, $SiMe_2$), 0.8 (12 H, s + d, thexyl Me groups), 1.5–1.8 (5 H, m, 2 × CH_2 + thexyl CH), 1.9 (1 H, br s, OH), 2.3 (2 H, t, *J* 7, $CH_2C\equiv$), 3.1 (2 H, t, *J* 7, benzylic CH_2), 4.8 (2 H, s, CH_2O), 5.3 (2 H, s, CH_2OCO), 7.25 (1 H, s, ArH) and 7.35 (1 H, s, ArH); *m/z* 387 (M^+ + H), 301 [M^+ − $C(Me)_2CHMe_2$], 89 and 75.

Methyl 3(4),5-*Bis*(*hydroxymethyl*)-2-(6-*trimethylsilylhex*-5-*ynyl*)*benzoate* **12c**.—Obtained from monoester **9c** and prop-2-ynyl alcohol, after chromatography using light petroleum–ether (1:1), as a pale yellow oil (34%); ν_{max}(neat)/cm^{-1} 3302, 2171 and 1724; δ_H(270 MHz) 0.1 (9 H, s, $SiMe_3$), 1.55–1.75 (4 H, m, 2 × CH_2), 2.25 (2 H, t, *J* 7, $CH_2C\equiv$), 2.95 (2 H, t, *J* 8, benzylic CH_2), 3.9 (3 H, s, OMe), 4.7 (4 H, 2 × s, 2 × CH_2O), 7.25 (1 H, s, ArH) and 7.85 (1 H, s, ArH); δ_C(67.5 MHz) 20, 29, 30, 31, 33, 52 (OMe), 63 (2 peaks, 2 × CH_2O), 85, 108, 132, 132.5, 137, 143, 145 and 168 (CO); *m/z* 333 (M^+ − Me), 317, 269, 226, 197, 91 and 73 (Me_3Si^+).

5-*Hydroxymethyl*-7-(6-*trimethylsilylhex*-5-*ynyl*)-3H-*benzo*-[c]*furan*-1-*one* **13c**.—Obtained from monoester **9c** and prop-2-ynyl alcohol, after chromatography using light petroleum–ether (1:1), as an oil (21%) (Found: M^+, 316.1484. $C_{18}H_{24}O_3Si$ requires *M*, 316.1495); ν_{max}(neat)/cm^{-1} 3398, 2173 and 1751; δ_H(270 MHz) 0.1 (9 H, s, $SiMe_3$), 1.5–1.8 (4 H, m, 2 × CH_2), 2.25 (2 H, t, *J* 7, $CH_2C\equiv$), 3.1 (2 H, t, *J* 8, benzylic CH_2), 4.8 (2 H, s, CH_2O), 5.2 (2 H, s, CH_2OCO), 7.25 (1 H, s, ArH) and 7.3 (1 H, s, ArH); *m/z* 316 (M^+), 301 (M^+ − Me, 100%), 75 and 74.

Methyl 3(4),5-*Bis*(*hydroxymethyl*)-2-(*hept*-5-*ynyl*)*benzoate* **12d**.—Obtained from monoester **9d** and prop-2-ynyl alcohol, after chromatography using light petroleum–ether (1:1), as a pale yellow oil (36%); ν_{max}(neat)/cm^{-1} 3407 and 1717; δ_H(270 MHz) 1.5–1.7 (4 H, m, 2 × CH_2), 1.75 (3 H, t, *J* 2, $MeC\equiv$), 2.15 (2 H, m, $CH_2C\equiv$), 2.9 (2 H, t, *J* 9, benzylic CH_2), 3.6 (2 H, br s, 2 × OH), 3.9 (3 H, s, OMe), 4.7 (4 H, 2 × s, 2 × CH_2O), 7.25 (1 H, s, ArH) and 7.8 (1 H, s, ArH); *m/z* 290 (M^+), 258 (M^+ − MeOH), 229 and 211.

7-(*Hept*-5-*ynyl*)-5-*hydroxymethyl*-3H-*benzo*[c]*furan*-1-*one* **13d**.—Obtained from monoester **9d** and prop-2-ynyl alcohol, after chromatography using light petroleum–ether (1:1), as a white solid (20%), m.p. 84–85 °C; ν_{max}(CH_2Cl_2)/cm^{-1} 3434 and 1749; δ_H(270 MHz) 1.5–1.8 (4 H, m, 2 × CH_2), 1.75 (3 H, t, *J* 1, $MeC\equiv$), 2.2 (2 H, m, $CH_2C\equiv$), 3.1 (2 H, t, *J* 7.5, benzylic CH_2), 4.8 (2 H, s, CH_2O), 5.2 (2 H, s, CH_2OCO), 7.25 (1 H, s, ArH) and 7.3 (1 H, s, ArH); *m/z* 258 (M^+), 241 (M^+ − OH), 229, 191, 178, 81 and 44.

3,4,7,8,9,10-*Hexahydronaphtho*[1,2-c]*pyran*-1-*one* **18**.—Obtained from the triyne **17**, after chromatography using light petroleum–ether (1:5), as a colourless oil (46%) (Found: M^+, 202.0990. $C_{13}H_{14}O_2$ requires *M*, 202.0994); ν_{max}(neat)/cm^{-1} 1724; δ_H(270 MHz) 1.7 (4 H, m, 2 × CH_2), 2.7 (2 H, m, benzylic CH_2), 2.9 (2 H, t, *J* 5, CH_2CH_2OCO), 3.1 (2 H, m, benzylic CH_2), 4.35 (2 H, t, *J* 5, CH_2OCO), 6.9 (1 H, 1/2 ABq, *J* 7, ArH) and 7.15 (1 H, 1/2 ABq, *J* 7, ArH); δ_C(125.8 MHz) 22 (CH_2), 23 (CH_2), 28.5 (CH_2), 29 (CH_2), 30 (CH_2), 66.5 (CH_2O), 123.5, 124, 134, 137.5, 138, 142 and 164.5 (CO); *m/z* 202 (M^+, 100%), 187, 159, 129 and 115.

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