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Ring Expansion of Benzocyclic Ketones *via* Transient Alkoxyl Radicals: The Side Chain Incorporation Approach†

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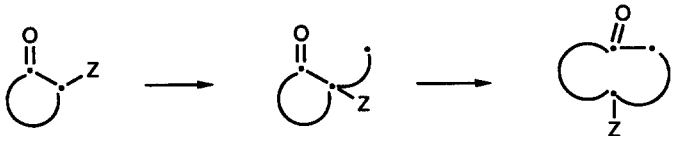
Key Words: radical cyclisation; radical ring opening; alkoxy radicals; tributyltin hydride; ring expansion

Abstract: *Radical cyclisation onto carbonyl groups followed by β-sission of the resulting alkoxy radicals provides a method for the one-carbon ring expansion of benzocyclic ketones. The radicals are generated by Bu_3SnH reduction of bromomethyl moieties α to the carbonyl group of benzocyclic ketones.*

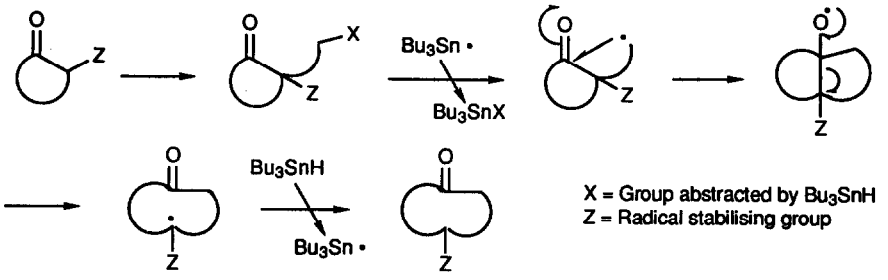
Many benzocyclic compounds have important pharmacological activity.[1] However, systematic screening of benzocyclic compounds, especially with eight-membered or larger rings, has been hindered due to difficulties in synthesising suitable examples by conventional means. Ring expansion of easily obtained 5-, 6-, or 7-membered rings can overcome the problem of cyclising to large rings.[2a] We considered that radical ring expansion of benzocyclic ketones offered a novel and potentially useful synthetic route to this group of compounds. In this paper we give an account of out initial studies of the ring expansion of available benzocyclic ketones, with 5-, 6-, 7-membered benzo-fused ring, as a means of circumventing this synthetic problem. We have employed the 'Ring Enlargement by Side Chain Incorporation' approach (Scheme 1),[2b] which has hitherto been applied mainly to monocyclic compounds, and offer a rationalisation of its limitations.



Scheme 1. Ring Enlargement by Side Chain Incorporation

The use of free radicals in synthesis has increased dramatically in recent years.[3] The discovery that radicals readily add to suitable carbonyl groups has initiated a new direction to the synthetic use of radical cyclisations.[4] One particularly novel synthetic method using a radical 'Ring Enlargement by Side Chain Incorporation' has been reported by Dowd and Choi[5] (see Scheme 2). The side chain, containing a group abstractable by tributyltin hydride (Bu_3SnH),[3] is added by conventional alkylation. Bu_3SnH is used to generate a nucleophilic alkyl radical on the side chain which cyclises onto the carbonyl group to give an alkoxyl radical.

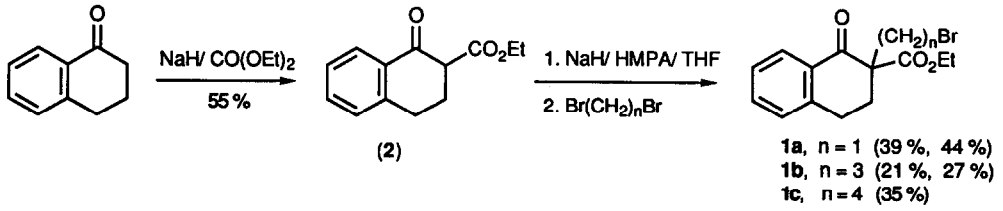
† ***Dedicated to the memory of our friend and colleague Barrie C.Uff; 13 Feb 1937 - 19 Oct 1991***



Scheme 2. Ring enlargement using radical cyclisation onto a ketone and β-sission of the alkoxyl radical

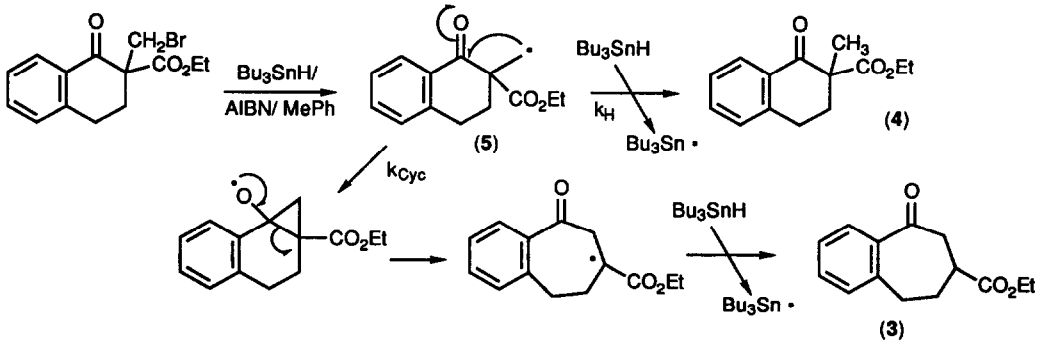
The alkoxyl radical undergoes a regiospecific β-scission to give a stable radical, centred at a tertiary carbon atom with an optional radical stabilising group (Z), which is reduced by Bu_3SnH to perpetuate the chain. A similar mechanism is believed to operate where the carbonyl group is replaced by an exocyclic methylene double bond.[6] The general method has been reviewed[2c] and analogous reactions have been reported by several groups.[7] The aim of our studies was to observe whether this general procedure (Scheme 2), used for monocyclic ketones, could be applied to benzocyclic ketones.

1-Tetralone, the most readily available benzocyclic ketone, was chosen as the initial model, *i.e.* the ring expansion of ethyl 2-(ω-bromoalkyl)-1-tetralone-2-carboxylates (**1**) were studied first. The tetralone substrates (**1**) were synthesised from ethyl 1-tetralone-2-carboxylate[8] (**2**) (Scheme 3).



Scheme 3. Synthesis of ethyl 2-(ω-bromoalkyl)-1-tetralone-2-carboxylates

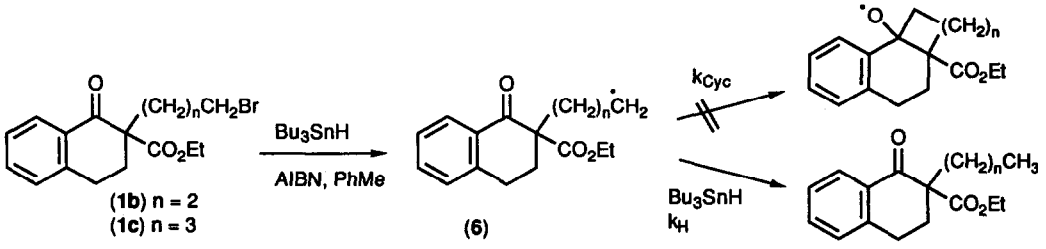
Treatment of tetralone (**1a**) with tributyltin hydride and a catalytic amount of azoisobutyronitrile (AIBN) in refluxing toluene gave two products, ethyl 1-benzosuberone-2-carboxylate[9] (**3**) and ethyl 2-methyl-1-tetralone-2-carboxylate[8] (**4**). Tetralone (**4**) was also prepared by independent synthesis.[10] Under conditions, *i.e.* immediate complete addition of the tributyltin hydride [3 mM], the ring-expanded product (**3**)



Scheme 4. Radical ring enlargement of ethyl 2-bromomethyl-1-tetralone-2-carboxylate by one carbon

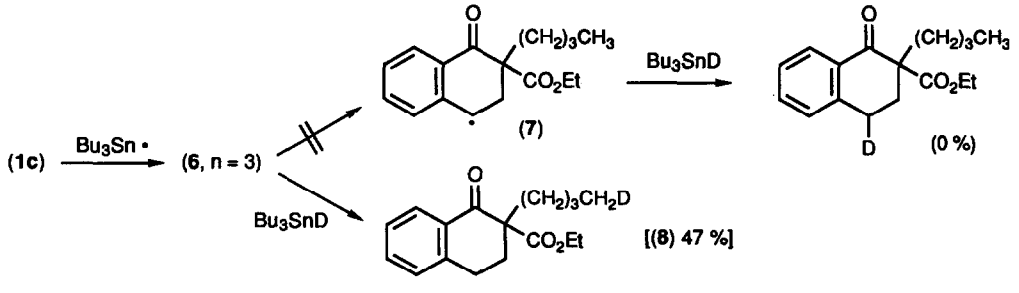
and the non-expanded reduction product (4) were obtained in approximately equal yields (10% and 9% respectively after extensive purification). Use of a syringe pump to add the tributyltin hydride over a number of hours, lowering the concentration to *ca.* 0.8 mM gave a higher yield of the ring-expanded product (3, 39%) than the non-expanded product [(4), 20%]. The likely mechanism, shown in Scheme 4, is analogous to that of the monocyclic reaction.[5] More of the ring-expanded product was obtained in the monocyclic example[5] in which a syringe pump was not used. In our benzocyclic reaction the rate of reduction (k_H) of the intermediate radical (5), even though a bimolecular reaction, is faster than the rate of cyclisation (k_{cyc}). Even use of the syringe pump was not sufficient to prevent some reduction of (5).

Cyclisation to a cyclobutyl-alkoxyl radical would be much less favoured and was not attempted. Attempts to carry out 3- and 4-carbon ring-enlargement by Bu_3SnH reduction of (1b) and (1c) failed even though a syringe pump and varied reaction conditions were used; no traces of ring-expanded material could be detected (Scheme 5). The rate of reduction (k_H) of the intermediate radical (6) by Bu_3SnH is obviously much faster than the rate of cyclisation (k_{cyc}) onto the ketone group, unlike the results for the monocyclic analogues.[5]



Scheme 5. Reduction of ethyl 2-bromo(propyl and butyl)-1-tetralone-2-carboxylate

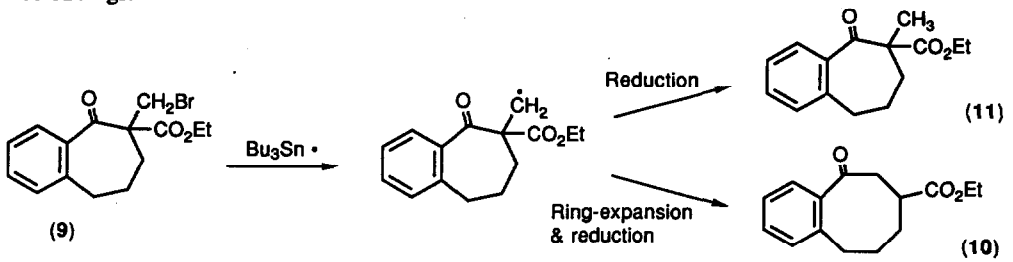
We considered that intramolecular abstraction of a benzylic (or other) hydrogen [e.g. (7)] may explain the absence of cyclisation, even though the S_H2 reaction would have to take place *via* 7- and 8-membered transition states (*e.g.* Scheme 6). However, reaction between Bu_3SnD and (1c) gave a product (8) with the deuterium only on the end of the side-chain which indicates that the lack of cyclisation is probably due to $k_H > k_{Cyc}$ and not due to intramolecular hydrogen abstraction. Dowd and Choi[5a] have also reported that in certain systems the 3- and 4-carbon expansion failed whereas the 1-carbon expansion was successful.



Scheme 6. Absence of intramolecular hydrogen abstraction

The methodology was extended to a benzo-7-membered cyclic ketone, benzosuberone (Scheme 7). Ethyl 5,6,8,9-tetrahydrobenzocycloheptene-5-one-6-carboxylate was synthesised[11] and bromomethylated to yield the required substrate (9). Reaction between (9) and Bu_3SnH yielded the ring-expanded benzo-8-membered ring cyclic ketone (10) in 25% yield and the non-expanded benzosuberone (11) in 21% yield (Scheme 7). This one-

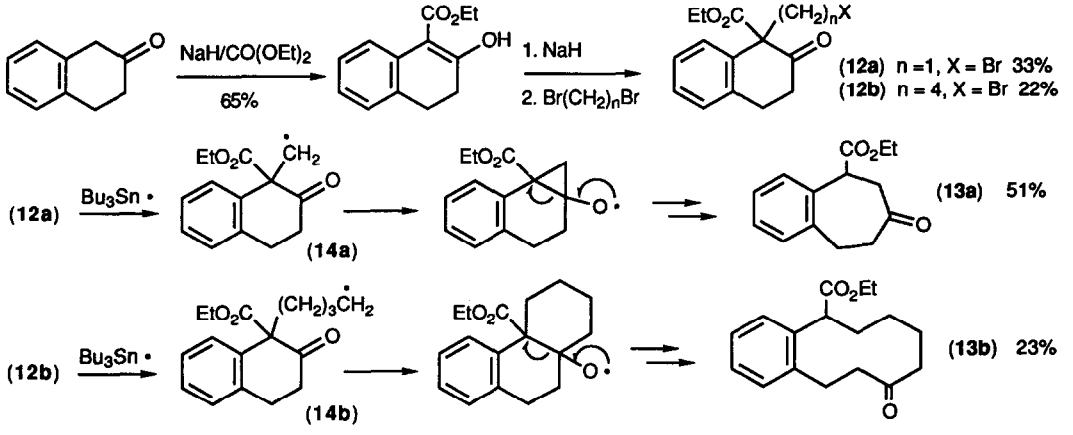
carbon expansion gave similar results to the 1-tetralone analogue indicating little difference between 6- and 7-membered rings.



Scheme 7. One-carbon ring-enlargement of a benzosuberone

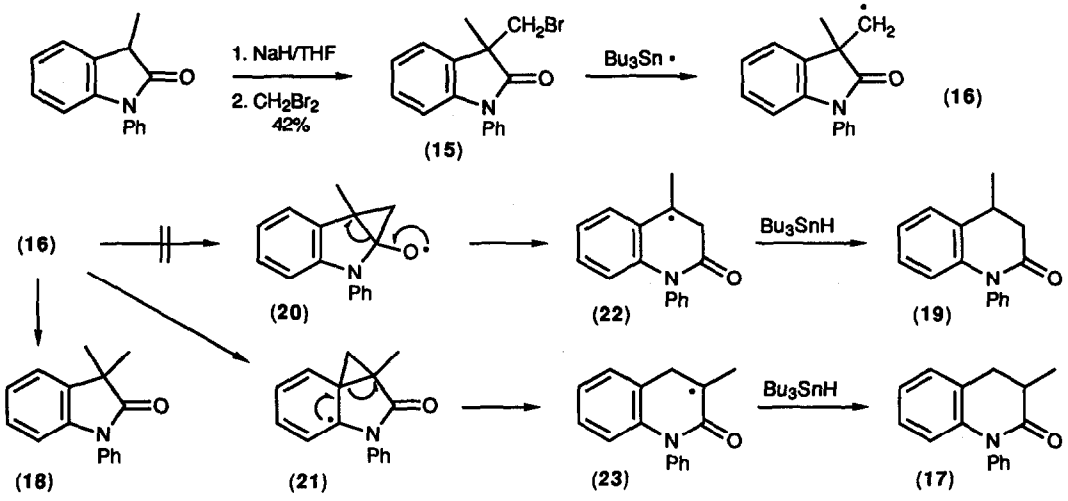
The benzocyclic ketones do not cyclise/ring-open as readily as the monocyclic analogues. Conformational restraint on the initial cyclisation reaction may be an explanation. The radical stability of the final radical should be close to that of the final monocyclic radical and is not a likely reason. We consider that the higher stability of the conjugated aryl-ketone moiety makes the initial cyclisation less favourable, but favours the ring-opening, in which the conjugated aryl-ketone is reformed. The less favourable cyclisation to form the intermediate alkoxy radical is the most likely explanation for the results.

In order to overcome this problem, we investigated the 2-tetralone analogues in which the ketone is not conjugated and the final radical intermediate should also have benzylic stabilisation. Both of these facets should encourage the ring-enlargement sequence and would be expected to give similar results to the monocyclic analogues unless conformational factors are important. The analogous 1-(ω-bromoalkyl)-2-tetralone substrates (**12**) for 1- and 4-carbon ring expansion were synthesised[12] from 2-tetralone *via* the β-ketoester (Scheme 8). Reaction between the 1-bromomethyl-2-tetralone (**12a**) and Bu_3SnH, using a syringe pump, gave the ring-enlarged benzocycloheptenone [(**13a**), 51% yield] as the only product (Scheme 8). As expected from the above premise, the intermediate radical (**14a**) undergoes cyclisation/ ring-opening faster than reduction by Bu_3SnH indicating that the aryl-ketone is the problem for the 1-tetralones. The reduction of the 1-(4-bromobutyl)-2-tetralone (**12b**) using a syringe pump gave a mixture of the ring enlarged benzocyclodecenone (**13b**) (23%) and the non-ring expanded ethyl 1-butyl-2-tetralone-1-carboxylate (16%). As observed for monocyclic ketones,[5a] the four-carbon expansion *via* a 6-membered ring cyclisation of the intermediate radical (**14b**) is less favoured than the related one-carbon expansion *via* a three-membered ring cyclisation. These reactions indicate the potential for this ring-enlargement methodology to be applied to non-conjugated benzocyclic ketones.



Scheme 8. Synthesis of 1-(ω-bromoalkyl)-2-tetralones and reaction between (**12a**) and (**12b**) and Bu_3SnH

The general method would not be predicted to be successful for lactams because of the energy barrier to cyclisation onto the stable lactam carbonyl group. However, we considered that when the nitrogen free-electrons were delocalised in two arene rings the carbonyl may react. To this end, 3-methyl-1-phenyloxindole was synthesised by a literature procedure[13] and bromomethylated to yield the substrate (**15**) (Scheme 9). Treatment of (**15**) in refluxing toluene with Bu_3SnH, using a syringe pump gave a ring-expanded product, 3,4-dihydro-3-methyl-1-phenyl-quinolin-2(1H)-one (**17**), and a product of direct reduction, 3,3-dimethyl-1-phenyl-oxindole (**18**) (Scheme 9). The quinolinone (**17**) has the assigned structure rather than that of its isomer (**19**), due to the absence of any nOe interaction between the methyl group and the aromatic protons in the ^1H NMR spectrum. The initial radical (**16**) can be intercepted by Bu_3SnH to yield (**17**) or undergo cyclisation onto the carbonyl to yield the cyclopropyl-alkoxyl radical (**20**) or cyclisation onto the arene to yield (**21**). Ring-opening of the two possible cyclopropyl intermediates would yield (**22**) or (**23**) and, on reduction with Bu_3SnH, yield the quinolinones (**19**) and (**17**) respectively. Cyclisation onto the arene (see reference 14 for a precedent) is more favoured than the cyclisation onto the amide carbonyl indicating that even very ketonic amides are not sufficiently electrophilic.



Scheme 9. Synthesis of 3-bromomethyl-3-methyl-1-phenyloxindole and reaction with Bu_3SnH

Our results indicate that the radical ring-enlargement methodology has potential in the synthesis of a wide range of compounds including benzoheterocyclic ketones but that the parameters of the reaction need to be carefully considered to ensure success. The stability of the carbonyl group and the intermediate radicals appear to be the key factors. One-carbon enlargements are in general more successful than 3- and 4-C enlargements.

Acknowledgements

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EXPERIMENTAL

General Procedures

IR spectra were obtained using a Pye Unicam PU9516 spectrometer. Elemental analyses, 360 MHz NMR spectra, and mass spectra were provided by The Boots Company PLC. 400 MHz and nOe difference spectra were provided by the SERC High Field NMR Service at the University of Warwick. 250 MHz NMR spectra

were obtained using a Bruker AC250 spectrometer. $CDCl_3$ was used as the NMR solvent with TMS as internal standard. Temperatures quoted for Kugelrohr distillations are those of the heating bath. TLC was performed on aluminium plates coated with Merck silica gel 60F254 and compounds visualised by UV light. Flash chromatography and TLC were carried with silica gel as absorbent and with mixtures of light petroleum (b.p. 40-60°C) and ethyl acetate as eluent. Solvents were purified by standard procedures.

Ethyl 1-tetralone-2-carboxylate (2). General procedure for carboxyethylation of ketones

1-Tetralone (9.4 g, 64 mmol) was added to a stirred suspension of sodium hydride (80% dispersion; 2.2 g, 75 mmol) in diethyl carbonate (50 ml) under an atmosphere of nitrogen. After effervescence had ceased, the solution was refluxed for 2 h. The resultant solid was dissolved in hydrochloric acid (2 M) and the phases were separated. The aqueous phase was extracted with ethyl acetate. The organic extracts were dried and evaporated to dryness to give a brown liquid. Kugelrohr distillation gave ethyl 1-tetralone-2-carboxylate[8](2) (7.7 g, 35 mmol, 55%) as a yellow liquid, b.p. 140°C [0.4 mm Hg] (lit.[8] 183°C [15 mm Hg]), TLC gave one spot; υ_{max} (neat) 3068, 2976, 1738, 1686, 1634, 1568, and 1482 cm^{-1}; δ_H (250 MHz) 12.49 (1 H, s, D_2O ex., enol 1-OH), 7.80 (1 H, d, J = 9.0 Hz, 8-H, ketone), 7.49 (1 H, d, J = 1.4 Hz, 8-H, enol), 7.35 - 7.15 (3H, m, 7-H, 6-H, and 5-H, ketone and enol), 4.28 (2 H, q, J = 7.1 Hz, OCH_2, ketone), 4.25 (2 H, q, J = 5.5 Hz, OCH_2, enol), 3.70 - 3.50 (1 H, 2-H, ketone), 3.04 -2.53 (4 H, m, 4-H and 3-H, ketone and enol), 1.34 (3 H, t, J = 5.5 Hz, Me, enol), and 1.29 (3 H, t, J = 5.5 Hz, Me, ketone). The ratio ketone:enol is 1:2; δ_C (62.5 MHz) 193.2 (1-C, ketone), 172.7 and 170.2 (ester CO, ketone and enol), 165.0 (2-C, enol), 143.7 and 139.4 (8a-C, ketone and enol), 133.8 and 130.5 (8-C, ketone and enol), 131.8 and 130.0 (4a-C, ketone and enol), 128.8 and 127.6 (7-C, ketone and enol), 127.4 and 126.8 (6-C, ketone and enol), 126.5 and 124.3 (5-C, ketone and enol), 97.0 (2-C, enol), 61.2 and 60.5 (OCH_2, ketone and enol), 54.6 (2-C, ketone), 27.7 and 27.6 (4-C, ketone and enol), 26.4 and 20.5 (3-C, ketone and enol), and 14.3 and 14.2 (Me, ketone and enol); *m/z* (E.I.) 218.0945 (M^+, 91%, $C_{13}H_{14}O_3$ requires 218.0943), 173 (30, M - EtO), 172 (89, M - EtOH), 145 (42, M - CO_2Et), 144 (100), 118 (67), and 90 (38).

General procedure for the alkylation of ketones using α, ω-dibromoalkanes. Alkylation of ethyl 1-tetralone-2-carboxylate (2)

(a) Ethyl 2-bromomethyl-1-tetralone-2-carboxylate (**1a**). Ethyl 1-tetralone-2-carboxylate (**2**) (3.4 g, 16 mmol) was added to a stirred suspension of sodium hydride (80% dispersion; 0.6 g, 19 mmol) and HMPA (3.5 ml, 3.6 g, 20 mmol) in THF (40 ml) under an atmosphere of nitrogen. After stirring for 1 h, dibromomethane (5.5 ml, 14 g, 78 mmol) was added and the solution was refluxed for 22 h. The mixture was taken up in diethyl ether (150 ml) and washed with water (5 x 10 ml), dried, and evaporated to dryness to give an orange oil. Flash chromatography gave ethyl 2-bromomethyl-1-tetralone-2-carboxylate[9](**1a**) (2.1 g, 6.9 mmol, 44%) as a yellow oil; TLC showed one spot; (Found: C, 56.1; H, 5.1. $C_{14}H_{15}O_3Br$ requires C, 54.0; H, 4.9%); υ_{max} (neat) 2980,1726, 1686, 1600, and 1450 cm^{-1}; δ_H (250 MHz) 8.04 (1 H, d, J = 7.8 Hz, 8-H), 7.49 (1 H, t, J = 7.4 Hz, 7-H), 7.44-7.20 (2 H, m, 6-H and 5-H), 4.19 (2 H, q, J = 7.3 Hz, OCH_2), 3.93 and 3.88 (2 H, 2 d, J_{AB} = 10.4 Hz, CH_2Br), 3.18-2.92 (2 H, m, 4-H), 2.70-2.42 (2 H, m, 3-H), and 1.22 (3 H, t, J = 8.6 Hz, Me); δ_C (62.5 MHz) 192.4 (1-C), 169.0 (ester CO), 143.2 (8a-C), 134.0 (8-C), 131.3 (4a-C), 128.9 (7-C), 128.0 (6-C), 126.9 (5-C), 62.0 (OCH_2), 58.3 (2-C), 34.5 (CH_2Br), 30.2 (4-C), 25.4 (3-C), and 14.0 (Me); *m/z* (E.I.) 312.0315 and 310.0186 (M^+, 31 and 29%, $C_{14}H_{15}O_3Br$ requires 312.0185 and 310.0205), 231 (76, M - Br), 217 (100, M - CH_2Br), 158 (99), 157 (78), 130 (29), and 118 (61).

(b) Ethyl 2-(3-bromopropyl)-1-tetralone-2-carboxylate (**1b**). The general procedure was used with ethyl 1-tetralone-2-carboxylate (**2**) and 1,3-dibromopropane. Flash chromatography on silica gel with light petroleum (b.p. 40-60°C): ethyl acetate (15:1) as eluent gave *ethyl 2-(3-bromopropyl)-1-tetralone-2-carboxylate* (**1b**) (21, 27%) as an orange oil; one spot on TLC; (Found: C, 56.6; H, 5.7; Br, 29.8. $C_{16}H_{19}O_3Br$ requires C, 56.65; H, 5.65; Br, 23.55%); υ_{max} (neat) 3064, 2960, 1730, 1682, and 1450 cm^{-1}; δ_H (250 MHz) 8.04 (1 H, d, J = 7.8 Hz, 8-H), 7.49 (1 H, t, J = 7.4 Hz, 7-H), 7.44-7.20 (2 H, m, 6-H and 5-H), 4.15 (2 H, q, J = 7.1 Hz, OCH_2), 3.44 and 3.42 (2 H, 2 d, J_{AB} = 4.6 Hz, CH_2Br), 3.07-2.90 (2 H, m, 4-H), 2.62-2.53 (1 H, m, 3-H),

2.19-1.89 (5 H, m, 3-H and 2-CH_2CH_2CH_2Br), and 1.17 (3 H, t, J = 8.6 Hz, Me); δ_C (62.5 MHz) 195.2 (1-C), 171.6 (ester CO), 142.8 (8a-C), 133.5 (8-C), 131.9 (4a-C), 128.7 (7-C), 127.9 (6-C), 126.8 (5-C), 61.4 (OCH_2), 57.0 (2-C), 33.7 (CH_2Br), 32.7 (CH_2CH_2Br), 30.8 (4-C), 28.2 (CH_2CH_2CH_2Br), 25.8 (3-C), and 14.0 (Me); *m/e* (E.I.) 340.0555 and 338.0503 (M^+, 12% and 13%, $C_{16}H_{19}O_3Br$ require 340.0498 and 338.0518), 259 (70, M - Br), 218 (14), 217 (48), 186 (14), 185 (79), and 118 (100).

(c) Ethyl 2-(4-bromobutyl)-1-tetralone-2-carboxylate (**1c**). The general procedure was used with ethyl 1-tetralone-2-carboxylate (**2**) and 1,4-dibromobutane. Flash chromatography gave *ethyl 2-(4-bromobutyl)-1-tetralone-2-carboxylate* (**1c**) (35%) as an orange oil; one spot on TLC; (Found: C, 57.5; H, 5.7; Br, 21.9. $C_{17}H_{21}O_3Br$ requires C, 57.8; H, 6.0; Br, 22.6%); υ_{max} (neat) 3060, 1728, 1686, 1600, and 1452 cm^{-1}; δ_H (250 MHz) 8.04 (1 H, d, J = 7.8 Hz, 8-H), 7.47 (1 H, t, J = 1.3 Hz, 7-H), 7.31-7.20 (2 H, m, 6-H and 5-H), 4.15 (2 H, q, J = 7.1 Hz, OCH_2), 3.42 (2 H, t, J = 6.7 Hz, CH_2Br), 3.09-2.94 (2 H, m, 4-H), 2.62 - 2.53 (1 H, m, 3-H), 2.21-2.11 (1 H, m, 3-H), 2.01-1.85 (4 H, m, CH_2CH_2CH_2CH_2Br), 1.65 - 1.48 (2 H, m, CH_2CH_2CH_2Br) and 1.17 (3 H, t, J = 7.1 Hz, Me); δ_C (62.5 MHz) 195.4 (1-C), 171.7 (ester CO), 143.0 (8a-C), 133.4 (8-C), 132.0 (4a-C), 128.7 (7-C), 128.0 (6-C), 126.8 (5-C), 61.3 (OCH_2), 57.4 (2-C), 33.3, 33.0, 32.9, 30.5 (4-C), 25.9 (3-C), 23.4, and 14.1 (Me); *m/z* (E.I.) 354.0759 and 352.0658 (M^+, 4% and 6%, $C_{17}H_{21}O_3Br$ require 354.0654 and 352.0674), 273 (10), 218 (100), 217 (24), 172 (40), and 118 (67).

Ethyl 2-methyl-1-tetralone-2-carboxylate (4)

Sodium ethoxide (0.03 mol) was prepared *in situ* and taken up in diethyl carbonate (20 ml). 1-Tetralone (0.9 g, 6 mmol) was added and the solution was refluxed for 2 h. Iodomethane (1.8 ml, 4.1 g, 29 mmol) was added and the solution was stirred for 66 h. The solution was refluxed for 0.5 h, cooled and neutralised with acetic acid (2 M). The solvent was evaporated to dryness, taken up in toluene (50 ml), filtered, and the solvent removed *in vacuo*. Flash chromatography yielded ethyl 2-methyl-1-tetralone-2-carboxylate[8] (**4**) (0.4 g, 2 mmol, 24%) as a yellow oil; one spot on TLC; (Found: C, 72.0, H, 6.9. $C_{14}H_{16}O_3$ requires C, 72.4; H, 6.9%); υ_{max} (neat) 3064, 2984, 1732, 1600, and 1456 cm^{-1}; δ_H (250 MHz) 8.04 (1 H, d, J = 7.8 Hz, 8-H), 7.25-7.20 (3 H, m, 5-H, 6-H, and 7-H), 4.14 (2 H, q, J = 7.1 Hz, OCH_2), 3.05-2.89 (2 H, m, 4-H), 2.66-2.56 (1 H, m, 3-H), 2.11-1.99 (1 H, m, 3-H), 1.50 (3 H, s, 2-Me), and 1.16 (3 H, t, J = 7.1 Hz, ester Me); δ_C (62.5 MHz) 196.1 (1-C), 172.8 (ester CO), 143.1 (8a-C), 133.4 (8-C), 131.8 (4a-C), 128.7 (7-C), 127.9 (6-C), 126.7 (5-C), 61.2 (OCH_2), 53.8 (2-C), 33.9 (4-C), 26.0 (3-C), 20.5 (2-Me), and 14.0 (ester Me); *m/z* (E.I.) 232.1143 (M^+, 41%, $C_{14}H_{16}O_3$ requires 232.1099), 217 (7, M - Me), 187 (4, M - EtO), 159 (40, M - CO_2Et), 158 (100), 131 (24), 118 (58), and 90 (41).

General procedure for Bu_3SnH reductions

Bu_3SnH reductions of 2-bromoalkyl-1-tetralone-2-carboxylates

(a) *Ethyl 2-bromomethyl-1-tetralone-2-carboxylate* (**1a**). Bu_3SnH (0.2 g, 0.7 mmol) in toluene (10 ml) was added by syringe pump over a set time (50 h and [Bu_3SnH] *ca.* 0.8 mM in this case) under an atmosphere of nitrogen, to a refluxing solution of ethyl 2-bromomethyl-1-tetralone-2-carboxylate (**1a**) (0.1 g, 0.3 mmol) in toluene (15 ml). AIBN was normally included with the halide; in this case *ca.* 2 mg in toluene (1 ml) was added at 0, 18, 30, and 40 h. The solution was allowed to reflux for a further 12 h, and then the solvent was removed in vacuo to give a yellow liquid. Flash chromatography and preparative TLC gave ethyl 6,7,8,9-tetrahydrobenzocyclohepten-5-one-7-carboxylate[9] (**3**) (0.031 g, 0.13 mmol, 39%) as an orange oil; one spot on TLC; (Found: C, 72.7; H, 7.1. $C_{14}H_{16}O_3$ requires C, 72.4; H, 6.9%); υ_{max} (neat) 3056, 1726, 1676, 1598, and 1478 cm^{-1}; δ_H (250 MHz) 7.71 (1 H, d, J = 6.3 Hz, 4-H), 7.42 (1 H, t, J = 3.7 Hz, 3-H), 7.30 (1 H, t, J = 7.6 Hz, 2-H), 7.21 (1 H, d, J = 7.5 Hz, 1-H), 4.08 (2 H, q, J = 7.1 Hz, OCH_2), 3.11-2.82 (5 H, m, 6-H, 7-H, and 9-H), 2.28-2.10 (2 H, m, 8-H), and 1.21 (3 H, t, J = 7.1 Hz, Me); δ_C (62.5 MHz) 202.7 (5-C), 174.2 (ester CO), 140.7 (4a-C), 138.1 (9a-C), 132.5 (4-C), 129.7 (3-C), 128.7 (2-C), 126.9 (1-C), 60.9 (OCH_2), 42.8 (6-C), 38.2 (7-C), 31.1 (9-C), 28.5 (8-C), and 14.1 (Me); *m/z* (E.I.) 232.1075 (M^+, 76%, $C_{14}H_{16}O_3$ requires 232.1099). 187 (24, M - EtO), 159 (100, M - CO_2Et), 158 (29), and 131 (16). The spectra correspond to those reported.[9]

As a by-product, ethyl 2-methyl-1-tetralone-2-carboxylate[8] (4) (0.016 g, 0.069 mmol, 20%) was obtained as an orange liquid, identical with authentic material.

(b) *Ethyl 2-(3-bromopropyl)-1-tetralone-2-carboxylate* (**1b**). Using the general procedure, Bu_3SnH was added to ethyl 2-(3-bromopropyl)-1-tetralone-2-carboxylate (**1b**) over 50 h ([Bu_3SnH] *ca.* 0.2 mM). Flash chromatography and preparative TLC gave *ethyl 2-propyl-1-tetralone-2-carboxylate* (22%) as a yellow oil; one spot on TLC; (Found: C, 72.2; H, 7.35. $C_{16}H_{20}O_3$ requires C, 73.8; H, 7.7%); υ_{max} (neat) 3060, 2956, 2872, 1730, 1682, 1600, and 1452 cm^{-1}; δ_H (250 MHz) 8.04 (1 H, d, J = 7.8 Hz, 8-H), 7.45-7.42 (1 H, m, 7-H), 7.32-7.19 (2 H, m, 6-H and 5-H), 4.14 (2 H, q, J = 7.1 Hz, OCH_2), 3.05-2.92 (2 H, m, 4-H), 2.59-2.54 (1 H, m, 3-H), 2.19-2.09 (1 H, m, 3-H), 1.97-1.84 (2 H, m), 1.42-1.26 (2 H, m), 1.16 (3 H, t, J = 7.1 Hz, ester Me), and 0.95 (3 H, t, J = 7.1 Hz, Me); δ_C (62.5 MHz) 195.6 (1-C), 171.9 (ester CO), 143.1 (8a-C), 133.3 (8-C), 132.1 (4a-C), 128.7 (7-C), 128.0 (6-C), 126.7 (5-C), 61.1 (OCH_2), 57.6 (2-C), 36.0, 30.4 (4-C), 25.9 (3-C), 18.1, 14.6 (ester Me), and 14.1 (Me); *m/z* (E.I.) 260.1442 (M^+, 29%, $C_{16}H_{20}O_3$ requires 260.1412), 218 (100), 217 (48, M - Pr), 215 (27, M - EtO), 187 (20, M - CO_2Et), and 118 (64). Ethyl 2-(3-bromopropyl)-1-tetralone-2-carboxylate (**1b**) (15%) was obtained as a by-product.

(c) *Ethyl 2-(4-bromobutyl)-1-tetralone-2-carboxylate* (**1c**). Using the general procedure Bu_3SnH was added to ethyl 2-(4-bromobutyl)-1-tetralone-2-carboxylate (**1c**) over 50 h ([Bu_3SnH] *ca.* 0.2 mM). Dry flash chromatography and preparative TLC gave *ethyl 2-butyl-1-tetralone-2-carboxylate* (20%) as a yellow oil; one spot on TLC; (Found: C, 74.1; H, 8.0%. $C_{17}H_{22}O_3$ requires C, 74.4; H, 8.1%); υ_{max} (neat) 2956, 1726, 1686, 1600, and 1452 cm^{-1}; δ_H (250 MHz) 8.04 (1 H, d, J = 7.9 Hz, 8-H), 7.48-7.42 (1 H, m, 7-H), 7.33-7.06 (2 H, m, 6-H and 5-H), 4.14 (2 H, q, J = 7.1 Hz, OCH_2), 3.51-2.81 (2 H, m, 4-H), 2.61-2.54 (1 H, m, 3-H), 2.20-2.12 (1 H, m, 3-H), 1.99-1.88 (2 H, m), 1.41-1.26 (4 H, m), 1.16 (3 H, t, J = 7.1 Hz, ester Me) and 0.91 (3 H, t, J = 6.9 Hz, Me); δ_C (62.5 MHz) 195.7 (1-C), 171.9 (ester CO), 143.0 (8a-C), 133.3 (8-C), 132.1 (4a-C), 128.6 (7-C), 128.0 (6-C), 126.6 (5-C), 61.1 (OCH_2), 57.5 (2-C), 33.5, 30.3 (4-C), 26.8, 25.9 (3-C), 23.1, 14.0 (ester Me), and 13.9 (Me); *m/z* (E.I.) 274.1489 (M^+, 9%, $C_{17}H_{22}O_3$ requires 274.1569), 218 (100), 217 (14, M - Bu), 229 (4, M - EtO), 201 (22, M - CO_2Et), 118 (57), and 90 (24). Ethyl 2-(4-bromobutyl)-1-tetralone-2-carboxylate (**1c**) (71%) was also isolated. Repetition at [Bu_3SnH] *ca.* 0.6 mM gave ethyl 2-butyl-1-tetralone-2-carboxylate (67%).

A repeat reaction using ([Bu_3SnH] *ca.* 14 mM, not using a syringe pump) gave ethyl 2-butyl-1-tetralone-2-carboxylate (55%) and recovered ethyl 2-(4-bromobutyl)-1-tetralone-2-carboxylate (**1c**) (9%).

(d) Ethyl 2-(4-bromobutyl)-1-tetralone-2-carboxylate (**1c**) *with Bu_3SnD.* Bu_3SnD in cyclohexane was added using the general procedure to ethyl 2-(4-bromobutyl)-1-tetralone-2-carboxylate (**1c**) in cyclohexane over 24 h ([Bu_3SnD] *ca.* 3 mM). Dry flash chromatography (twice) gave ethyl 2-(4-d-butyl)-1-tetralone-2-carboxylate (**8**) (47%) as a yellow liquid; one spot on TLC; (Found: C, 73.6; H, 7.9%. $C_{17}H_{21}DO_3$ requires C, 74.2; H, 8.4%); υ_{max} (neat) 2920, 2860, 2160 (C-D), 1730, 1690, 1600, and 1450 cm^{-1}; δ_H (360 MHz) 8.04 (1H, dd, J = 7.9, J = 1.1 Hz, 8-H), 7.46 (1 H, dt, J = 3.0 Hz, J = 7.4 Hz, 7-H), 7.30 (1 H, t, J = 9.2 Hz, 6-H), 7.21 (1 H, d, J = 7.6 Hz, 5-H), 4.14 (2 H, q, J = 7.1 Hz, OCH_2), 3.06-3.03 and 2.94-2.89 (2 H, 2 m, 4-H), 2.59-2.53 and 2.18-2.12 (2 H, 2 m, 3-H), 1.99-1.87 (2 H, m), 1.39-1.29 (4 H, m), 1.17 (3 H, t, J = 7.1 Hz, ester Me), and 0.93-0.89 (2 H, m, CH_2D); δ_C (90 MHz) 195.6 (1-C), 171.9 (ester CO), 143.0 (8a-C), 133.3 (8-C), 132.1 (4a-C), 128.6 (7-C), 128.0 (6-C), 126.6 (5-C), 61.1 (OCH_2), 57.5 (2-C), 33.5, 30.3 (4-C), 26.8, 25.9 (3-C), 23.1, 14.0 (ester Me), and 13.9 (t, CH_2D); *m/z* (E.I.) 275.1589 (M^+, 15%, $C_{17}H_{21}DO_3$ requires 275.1632), 230 (3, M - EtO), 218 (100), 217 (19, M - d-Bu), 202 (12, M - CO_2Et), and 118 (40).

Ethyl 6,7,8,9-tetrahydrobenzocyclohepten-5-one-6-carboxylate

Using the general procedure for carboxyethylations of ketones, 1-benzosuberone (9.4 g, 59 mmol) was reacted with diethyl carbonate (50 ml) to yield ethyl 6,7,8,9-tetrahydrobenzocyclohepten-5-one-6-carboxylate[11] after distillation (7.9 g, 34 mmol, 58%, repeat 67%); b.p. 125-130°C [0.8 mm Hg] (lit.[11] 125-134°C [1 mm Hg]); one spot on TLC; (Found: C, 72.7, H, 7.5. $C_{14}H_{16}O_3$ requires C, 72.4; H, 6.9%); υ_{max} (neat) 2940, 2860, 1740, 1680, 1590, and 1450 cm^{-1}; δ_H (250 MHz) 12.70 (1 H, s, D_2O ex., enol 5-OH), 7.75 (1 H, d, J = 7.6 Hz, 4-H, ketone), 7.63-7.60 (1 H, m, 4-H, enol), 7.42-7.14 (3 H, m, 3-H, 2-H, and 1-H, ketone and

enol), 4.28 (2 H, q, J = 7.1 Hz, OCH_2, ketone and enol), 2.96-2.92 (1 H, m, 6-H, ketone), 2.66-2.60 (2 H, m, 9-H, ketone and enol), 2.17-2.00 (4 H, m, 8-H and 7-H, ketone and enol), 1.34 (3 H, t, J = 7.2 Hz, Me, enol), and 1.26 (3 H, t, J = 7.2 Hz, Me ketone) (The ratio of ketone:enol is 1:2); δ_C (62.5 MHz) 200.6 (5-C, ketone), 173.0 and 170.3 (ester CO, ketone and enol), 165.0 (5-C, enol), 141.2 and 138.1 (9a-C and 4a-C, enol), 141.1 and 132.4 (9a-C and 4a-C, ketone), 130.0, 128.9, 127.1, and 126.3 (1-C, 2-C, 3-C, and 4-C, enol), 129.9, 129.1, 127.8, and 126.7 (1-C, 2-C, 3-C, and 4-C, ketone), 100.4 (6-C, enol), 61.2 and 60.6 (OCH_2, ketone and enol), 56.7 (6-C, ketone), 33.5 and 32.9 (9-C, enol and ketone), 31.8 and 25.4 (8-C, ketone and enol), 24.4 and 21.8 (7-C, ketone and enol), and 14.3 and 14.1 (Me, ketone and enol); *m/z* (E.I.) 232.101 (M^+, 81%, $C_{14}H_{16}O_3$ requires 232.110), 187 (22, M - EtO), 186 (100, M - EtOH), 158 (45, M - CO_2Et), 157 (20), and 129 (54).

Ethyl 6-bromomethyl-6,7,8,9-tetrahydrobenzocyclohepten-5-one-6-carboxylate (9)

Using the general procedure for alkylation, ethyl 1-benzosuberone-2-carboxylate (5.7 g, 25 mmol) was reacted with dibromomethane (20 g, 114 mmol). Dry flash chromatography gave *ethyl 6-bromomethyl-6,7,8,9-tetrahydrobenzocyclohepten-5-one-6-carboxylate* (9) (2.9 g, 9.0 mmol, 37%); one spot on TLC; (Found: C, 58.3; H, 5.3; Br, 21.8%. $C_{15}H_{17}O_3Br$ requires C, 55.4; H, 5.3; Br, 24.6%); υ_{max} (neat) 2940, 1740, 1680, 1600, and 1450 cm^{-1}; δ_H (250 MHz) 7.35 (1 H, d, J = 7.4 Hz, 4-H), 7.31 (1 H, t, J = 13.4 Hz, 3-H), 7.22 (1 H, t, J = 10.3 Hz, 2-H), 7.14 (1 H, d, J = 7.4 Hz, 1-H), 4.07 (2 H, q, J = 7.1 Hz, OCH_2), 3.89 and 3.81 (2 H, 2 d, J_{AB} = 10.2 Hz, 6-CH_2Br), 3.09-3.01 and 2.88-2.80 (2 H, 2 m, 9-H), 2.62-2.53 (1 H, m, 7-H), 2.04-1.85 (3 H, m, 7-H and 8-H) and 1.07 (3 H, t, J = 7.1 Hz, Me); δ_C (62.5 MHz) 202.6 (5-C), 169.5 (ester CO), 139.3 (4a-C), 139.1 (9a-C), 131.5 (4-C), 129.3 (3-C), 129.0 (2-C), 128.4 (1-C), 63.0 (6-C), 61.8 (OCH_2), 37.2 (6-CH_2Br), 33.2 (9-C), 32.3 (7-C), 23.8 (8-C), and 13.8 (Me); *m/z* (E.I.) 326.0342 and 324.0321 (M^+, 8 and 10%, $C_{15}H_{17}O_3Br$ requires 326.0341 and 324.0361), 245 (100, M - Br), 200 (17), 199 (65), 172 (31), 171 (58), and 144 (70).

Bu_3SnH reduction of ethyl 6-bromomethyl-6,7,8,9-tetrahydrobenzocyclohepten-5-one-6-carboxylate (9)

Using the general procedure, Bu_3SnH (0.8 g, 2.6 mmol) was added over 5 h ([Bu_3SnH] *ca.* 4.2 mM) to ethyl 6-bromomethyl-6,7,8,9-tetrahydrobenzocyclohepten-5-one-6-carboxylate (0.5 g, 1.6 mmol). Dry flash chromatography (twice) gave *ethyl 6,7,8,9-tetrahydro-6-methylbenzocyclohepten-5-one-6-carboxylate*(**11**) (0.1 g, 0.5 mmol, 32%) as an orange oil; one spot on TLC; (Found: C, 74.3; H, 7.6%. $C_{15}H_{18}O_3$ requires C, 73.15; H, 7.4%); υ_{max} (neat) 3064, 2976, 2932, 2864, 1736, 1684, 1598, and 1448 cm^{-1}; δ_H (250 MHz) 7.44 (1 H, dd, J = 7.4 Hz, J = 1.5 Hz, 4-H), 7.33 (1 H, dd, J = 7.4 Hz, J = 1.6 Hz, 3-H), 7.25 (1 H, dt, J = 1.3 Hz, J = 7.4 Hz, 2-H), 7.12 (1 H, dd, J = 7.4 Hz, J = 0.8 Hz, 1-H), 4.05 (2 H, q, J = 7.1 Hz, OCH_2), 2.94-2.89 and 2.84-2.78 (2 H, 2 m, 9-H), 2.37-2.30 (1 H, m, 7-H), 2.03-1.70 (3 H, m, 7-H and 8-H), 1.48 (3 H, s, 6-Me), and 1.07 (3 H, t, J = 7.1 Hz, ester Me); δ_C (62.5 MHz) 206.1 (5-C), 173.3 (ester CO), 140.2 (4a-C), 138.4 (9a-C), 131.1 (4-C), 129.0 (3-C), 128.8 (2-C), 126.4 (1-C), 61.1 (OCH_2), 57.9 (6-C), 34.3 (9-C), 32.8 (8-C), 23.6 (7-C), 22.1 (6-Me), and 13.8 (ester Me); *m/z* (E.I.) 246.1218 (M^+, 83%, $C_{15}H_{18}O_3$ requires 246.1256), 218 (21, M - CO), 201 (22, M - EtO), 200 (66, M - EtOH), 173 (25, M - CO_2Et), 172 (36), and 145 (100); and *ethyl 7,8,9,10-tetrahydro-5(6H)-benzocyclo-octenone-7-carboxylate* (**10**) (0.1 g, 0.4 mmol, 21%) as an orange oil; one spot on TLC; (Found: C, 73.1; H, 7.2%. $C_{15}H_{18}O_3$ requires C, 73.15; H, 7.4%); υ_{max} (neat) 3056, 2932, 1722, 1664, 1596, 1476, and 1462 cm^{-1}; δ_H (250 MHz) 7.79 (1 H, dd, J = 7.7 Hz, J = 1.5 Hz, 4-H), 7.41 (1 H, dd, J = 7.4 Hz, J = 6.1 Hz, 3-H), 7.30 (1 H, dd, J = 6.1 Hz, J = 7.4 Hz, 2-H), 7.18 (1 H, dd, J = 7.6 Hz, J = 0.8 Hz, 1-H), 4.17 (2 H, q, J = 7.2 Hz, OCH_2), 3.48-3.37 (2 H, m, 10-H), 3.07-2.91 (2 H, m, 6-H), 1.83-1.76 (3 H, m, 7-H and 8-H), 1.24 (3 H, t, J = 7.2 Hz, ester Me) and 0.87 (2 H, qu, J = 6.7 Hz, 9-H); δ_C (62.5 MHz) 203.6 (5-C), 174.1 (ester CO), 139.9 (4a-C), 139.1 (10a-C), 132.3 (4-C), 131.3 (3-C), 128.6 (2-C), 126.6 (1-C), 60.9 (OCH_2), 44.8 (6-C), 40.8 (7-C), 34.3 (10-C), 27.0 (8-C), 25.1 (9-C), and 14.2 (Me); *m/z* (E.I.) 246.1247 (M^+, 46%, $C_{15}H_{18}O_3$ requires 246.1256), 201 (15, M - EtO), 200 (22, M - EtOH), 173 (100), 172 (13), and 145 (18).

Ethyl 2-tetralone-1-carboxylate

2-Tetralone was reacted with diethyl carbonate using the general procedure for carboxethylations. Kugelrohr distillation of the crude product gave *ethyl 2-tetralone-1-carboxylate* (65, 58%) as a yellow liquid; b.p. 140°C (2 mm Hg); one spot on TLC; (Found: C, 71.4; H, 6.55. $C_{13}H_{14}O_3$ requires C, 71.5; H, 6.5%); υ_{max} (neat) 1740, 1712 1638, 1566, 1486, and 1452 cm^{-1}; δ_H (250 MHz) 13.43 (1 H, s, D_2O ex., 2-OH), 7.72 (1 H, d, J = 7.8 Hz, 8-H), 7.23 - 7.00 (3 H, m, 5-H, 6-H, and 7-H), 4.37 (2 H, q, J = 7.1 Hz, 1-OCH_2), 2.79 (2 H, t, J = 7.0 Hz, 4-H), 2.50 (2 H, t, J = 7.1 Hz, 3-H), and 1.34 (3 H, t, J = 7.1 Hz, Me); δ_C (62.5 MHz) 178.4 (1-C), 172.1 (ester CO), 133.2 (8a-C), 131.5 (4a-C), 127.2 (8-C), 126.4 (7-C), 125.9 (6-C), 124.9 (5-C), 99.9 (2-C), 61.0 (OCH_2), 29.6 (4-C), 27.8 (3-C), and 14.3 (Me); *m/z* (E.I.) 218.0927 (M^+, 29%, $C_{13}H_{14}O_3$ requires 218.0943), 173 (16, M - EtO), and 172 (100, M - EtOH).

Alkylation of Ethyl 2-tetralone-1-carboxylate

(a) Ethyl 1-bromomethyl-2-tetralone-1-carboxylate (**12a**). Ethyl 2-tetralone-1-carboxylate was alkylated with dibromomethane using the general procedure. Flash chromatography gave *ethyl 1-bromomethyl-2-tetralone-1-carboxylate* (**12a**) (33%) as a yellow oil; one spot on TLC; (Found: C, 55.35; H, 5.05. $C_{14}H_{15}O_3Br$ requires C, 54.0; H, 4.9%); υ_{max} (neat) 3060, 2976,1740, 1718, and 1492 cm^{-1}; δ_H (250 MHz) 7.45-7.23 (4 H, m, 8-H, 7-H, 6-H and 5-H), 4.33 (1 H, d, J_{AB} = 10.2 Hz, CH_2Br), 4.09 (2 H, q, J = 7.2 Hz, OCH_2), 3.95 (1 H, d, J_{AB} = 10.2 Hz, CH_2Br), 3.22-3.16 (2 H, m, 4-H), 3.03-2.91 (1 H, m, 3-H), 2.79-2.68 (1 H, m, 3-H), and 1.13 (3 H, t, J = 7.2 Hz, Me); δ_C (62.5 MHz) 205.8 (2-C), 168.9 (ester CO, 137.2 (8a-C), 134.5 (4a-C), 128.7 (8-C), 128.1 (7-C), 127.4 (6-C), 126.3 (5-C), 62.9 (1-C), 62.4 (OCH_2), 39.0 (1-CH_2Br), 35.8 (4-C), 27.7 (3-C), and 13.7 (Me); *m/z* (E.I.) 312.0193 (M^+, 2%, $C_{14}H_{15}O_3Br$ requires 312.0185 and 310.0205), 231 (83, M - Br), 217 (35, M - CH_2Br), 158 (12), and 157 (33).

(b) Ethyl 1-(4-bromobutyl)-2-tetralone-1-carboxylate (**12b**). Ethyl 2-tetralone-1-carboxylate was alkylated with 1,4-dibromobutane using the general procedure. Dry flash chromatography gave ethyl 1-(4-bromobutyl)-2-tetralone-1-carboxylate (**12b**) (22, 24, 20%) as an orange oil; one spot on TLC; (Found: C, 56.6; H, 5.7. $C_{17}H_{21}O_3Br$ requires C, 57.8; H, 6.0 %); υ_{max} (neat) 3060, 2956, 1728, 1600, and 1492 cm^{-1}; δ_H (250 MHz) 7.26-7.23 (1 H, m, 8-H), 7.15-7.05 (3 H, m, 7-H, 6-H and 5-H), 4.35 (2 H, q, J = 7.1 Hz, OCH_2), 3.96 and 3.46 (2 H, 2 d, J = 6.0 Hz, CH_2Br), 2.92 (2 H, t, J = 8.0 Hz, 4-H), 2.52 (2 H, t, J = 8.0 Hz, 3-H), 2.05-1.96 (2 H, m), 1.89-1.81 (2 H, m), 1.37 (3 H, t, J = 7.1 Hz, Me), and 1.12 (2 H, t, J = 7.1 Hz); δ_C (62.5 MHz) 208.0 (2-C), 167.8 (ester CO), 135.9 (8a-C), 131.6 (4a-C), 127.1 (8-C), 126.7 (7-C), 125.6 (6-C), 123.3 (5-C), 62.7 (1-C), 60.7 (OCH_2), 35.4 (4-C), 33.4, 33.0, 32.8, and 23.7 [$(CH_2)_4Br$], 29.1 (3-C), and 14.4 (Me); *m/z* (C.I.) 355 and 353 (22 and 25 %, M+ H), 273 (10, M - Br), 219 (100, M + H - CH_2=C=O), 218 (22, M - CH_2=C=O); *m/z* (E.I.) 218.0953 (45, M - CH_2=$CHCH_2CH_2Br$, $C_{13}H_{14}O_3$ requires 218.0943), 217 (5, M - $CH_2CH_2CH_2CH_2Br$), and 172 (100).

(c) Ethyl 1-butyl-2-tetralone-1-carboxylate. Ethyl 2-tetralone-1-carboxylate was alkylated with 1-iodobutane using the general procedure. (9 %); υ_{max} (neat) 2959, 2929, 2873, 1728, and 1464 cm^{-1}; δ_H (250 MHz) 7.26-7.19 (4 H, m, 8-H, 7-H, 6-H and 5-H), 4.08 (2 H, q, J = 7.1 Hz, OCH_2), 3.13-2.87 (4 H, m, 4-H), 2.65-2.25 (2 H, m, 3-H), 2.20-2.10 (1 H, m), 1.39-0.76 (3 H, m), 1.11 (3 H, t , CO_2CH_2*Me*) and 0.79 (3 H, t, 1-$CH_2CH_2CH_2$*CH*$_3$); δ_C (62.5 MHz) 208.0 (2-C), 171.2 (ester CO), 136.5 (8a-C), 136.4 (4a-C), 128.4 (8-C), 127.3 (7-C), 126.7 (6-C), 125.5 (5-C), 62.9 (1-C), 61.6 (OCH_2), 39.4 (*C*H_2Pr), 36.4 (4-C), 28.0 (3-C), 26.3 (CH_2*C*H_2Et), 23.0 (1-CH_2*C*H_2*C*H_2CH_3), 13.8 (2 Me's); the NMR spectroscopic assisgnments were identified using COSY and HETCOR techniques.

Bu_3SnH reduction of ethyl 1-bromomethyl-2-tetralone-1-carboxylate (9)

Ethyl 1-bromomethyl-2-tetralone-1-carboxylate (**12c**) was reacted with Bu_3SnH using the general procedure ([Bu_3SnH] *ca.* 0.4 mM). Dry flash chromatography and preparative TLC gave *ethyl 5,6,8,9-tetrahydrobenzocyclohepten-7-one-5-carboxylate* (**13**) (51%) as a yellow oil; one spot on TLC; (Found: C, 71.6; H, 7.3. $C_{14}H_{16}O_3$ requires C, 72.4; H, 6.9%); υ_{max} (neat) 2956, 1726, 1696, and 1492 cm^{-1}; δ_H (250 MHz) 7.29-7-12 (4 H, m, 4-H, 3-H, 2-H and 1-H), 4.17 (2 H, q, J = 7.1 Hz, OCH_2), 4.04 and 4.01 (1 H, 2 d, J_{AB}

= 4.1 Hz, 5-H), 3.16-3.02 (2 H, m, 6-H), 2.90-2.55 (4 H, m, 9-H and 8-H), and 1.22 (3 H, t, J = 7.1 Hz, Me); δ_C (62.5 MHz) 208.9 (7-C), 172.3 (ester CO), 140.2 (4a-C), 137.2 (9a-C), 130.1 (4-C), 129.8 (3-C), 128.2 (2-C), 127.4 (1-C), 61.5 (OCH_2), 47.3 (5-C), 45.3 (9-C), 44.3 (8-C), 29.8 (6-C), and 14.1 (Me). The assigned structure was confirmed by nOe difference spectroscopy. *m/z* (E.I.) 232.1137 (M^+, 39%, $C_{14}H_{16}O_3$ requires 232.1099), 187 (24, M - EtO), 159 (100, M - CO_2Et), 158 (29), and 131 (35).

Bu_3SnH reduction of ethyl 1-(4-bromobutyl)-2-tetralone-1-carboxylate (12b)

Ethyl 1-(4-bromobutyl)-2-tetralone-1-carboxylate (**12b**) was reacted with Bu_3SnH using the general procedure with a syringe pump. Dry flash chromatography and preparative TLC gave a clean mixture of two products with identical R_T in several different TLC systems. GLC using a Pye Unicam Series 104 Chromatograph at 258°C on a 3% Apiezon L column and ^1H NMR spectroscopy indicated two components: ethyl 1-butyl-2-tetralone-1-carboxylate (16%) and the ethyl 5,6,7,8,9,10,11,12-octahydro-7-oxo-benzocyclodecene-12-carboxylate (**13b**) (23 %). The TLC, GLC, and ^1H and ^{13}C NMR spectra indicated that the minor component was ethyl 1-butyl-2-tetralone-1-carboxylate. The major component is assigned to (**13b**) and further characterisation is underway; υ_{max} (mixture, neat) 2957, 2935, 2873, 1731, and 1451 cm^{-1}; δ_H (250 MHz) 3.65 (1 H, m, C*H*-CO_2Et); δ_C (62.5 MHz) 208.0 (7-C, ketone), 172.4 (ester CO), 61.2 (OCH_2), 54.2 (12-C, Ar*C*H-CO_2Et), 39.4, 36.4, and 31.8 (C-5, 6, 8), 14.3 (ester Me).

3-Bromomethyl-3-methyl-1-phenyloxindole (15)

(a) *3-Methyl-1-phenyloxindole.*[13] Anhydrous aluminium chloride (38.3 g, 287 mmol) was added portionwise to a stirred solution of *N,N*-diphenyl-2-chloropropionamide (30) (35.0 g, 135 mmol) in methylcyclohexane (100 ml) and refluxed for 2 h. The cooled solution was poured into crushed ice (500 ml) and hydrochloric acid (5 M, 50 ml). The precipitate was filtered and recrystallised from ethanol to give 3-methyl-1-phenyloxindole (18.2 g, 82 mmol, 61%), m.p. 76-78°C (lit.[13] 80-81°C), one spot on TLC; (Found C, 80.3; H, 5.9; N, 6.15%. $C_{15}H_{13}NO$ requires C, 80.7 ; H, 5.9; N, 6.3%); υ_{max} (KBr disc) 3340, 3060, 3000, 2940, 2920, 2840, 1710, 1620, 1600, 1500, and 1460 cm^{-1}; δ_H (360 MHz, d_6-DMSO) 7.52 (2 H, t, J = 5.4 Hz, *N*-Ph), 7.41 (3 H, d, J = 7.7 Hz, *N*-Ph), 7.28 (1 H, t, J = 8.5 Hz, 7-H), 7.19 (1 H, t, J = 7.6 Hz, 6-H), 7.08 (1 H, t, J = 7.0 Hz, 5-H), 6.81 (1 H, d, J = 7.6 Hz, 4-H), 3.62 (1 H, q, J = 7.6 Hz, 3-H), and 1.59 (3 H, d, J = 7.6 Hz, 3-Me); δ_C (90 MHz, d_6-DMSO) 178.0 (2-C), 143.9 (3a-C), 134.6 (7a-C), 130.5, 129.6, 128.0 and 127.8 (*N*-Ph), 126.6 (4-C), 123.8 (5-C), 122.9 (6-C), 109.3 (7-C), 40.8 (3-C), and 15.7 (3-Me); *m/z* (E.I.) 223.1016 (100%, M^+, $C_{15}H_{13}NO$ requires 223.0997) and 195 (27).

(b) *3-Bromomethyl-3-methyl-1-phenyloxindole* (**15**). 3-Methyl-1-phenyloxindole (8.1 g) was alkylated with dibromomethane using the general procedure. Recrystallisation of the residue from ethanol gave *3-bromomethyl-3-methyl-1-phenyloxindole* (**15**) (4.9 g, 15 mmol, 42%), m.p. 112-113°C; one spot on TLC; (Found C, 60.9; H, 4.55; N, 4.4; Br, 25.2%. $C_{16}H_{14}NOBr$ requires C, 60.8 ; H, 4.5; N, 4.4; Br, 25.3%); υ_{max} (KBr disc) 3080, 3040, 2960, 2920, 2860, 1720, 1610, 1600, 1490, 1480, 1460, and 1440 cm^{-1}; δ_H (250 MHz) 7.49 (2 H, t, J = 14.2 Hz, *N*-Ph), 7.38 (3 H, t, J = 11.8 Hz, *N*-Ph), 7.34 (1 H, d, J = 7.3 Hz, 7-H), 7.22 (1 H, t, J = 7.6 Hz, 6-H), 7.13 (1 H, t, J = 7.4 Hz, 5-H), 6.84 (1 H, d, J = 7.9 Hz, 4-H), 3.83 and 3.68 (2 H, 2 d, J = 9.9 Hz, 3-CH_2Br), and 1.60 (3 H, s, 3-Me); δ_C (62.5 MHz) 177.0 (2-C), 144.0 (3a-C), 135.0 (7a-C), 132.0, 129.6, 128.5 and 128.2 (*N*-Ph), 126.7 (4-C), 123.2 (5-C), 123.0 (6-C), 109.5 (7-C), 49.2 (3-C), 37.4 (3-CH_2Br) and 22.4 (3-Me); *m/z* (E.I.) 317.0170 and 315.0212 (40 and 38%, M^+, $C_{16}H_{14}NOBr$ require 317.0239 and 315.0259), 236 (8, M - Br), and 222 (100, M - CH_2Br).

Bu_3SnH reduction of 3-bromomethyl-3-methyl-1-phenyloxindole (15)

3-Bromomethyl-3-methyl-1-phenyloxindole (**15**) (0.5 g, 1.6 mmol) was reduced with Bu_3SnH (0.5 g, 1.8 mmol) using the general procedure (5 h, [Bu_3SnH] *ca.* 1.7 mM). The solution was refluxed for a further 1 h, and then stood overnight. A further portion of Bu_3SnH (0.5 g, 1.8 mmol) and AIBN was added by syringe pump over 5 h. Dry flash chromatography gave two oils. Trituration of one of the oils with chloroform gave *3,3-dimethyl-1-phenyloxindole* (**18**) (0.08 g, 0.33 mmol, 21%) as a colourless solid, m.p. 70-75°C, one spot

on TLC; (Found C, 79.6; H, 6.6; N, 5.7%. $C_{16}H_{15}NO$ requires C, 81.0; H, 6.4; N, 5.9%); υ_{max} ($CDCl_3$) 3056, 2968, 2928, 1722, 1610, and 1494 cm^{-1}; δ_H (250 MHz) 7.51-7.48 (2 H, m, ArH), 7.44-7.38 (3 H, m, ArH), 7.26-7.09 (3 H, m, ArH), 6.86 (1 H, d, J = 0.9 Hz, ArH), and 1.49 (6 H, s, 3-Me); δ_C (62.5 MHz) 181.0 (2-C), 142.5 (3a-C), 135.6 (7a-C), 135.0, 129.6, 127.9 and 127.6 (1-Ph), 126.6 (4-C), 123.0 (5-C), 122.6 (6-C), 109.4 (7-C), 44.3 (3-C), and 24.8 (3-Me); *m/z* (E.I.) 237.1163 (100%, M^+, $C_{16}H_{15}NO$ requires 237.1154), 222 (51, M - Me), and 194 (37). Trituration of the other oil with light petroleum (b.p. 40-60°C) gave *3,4-dihydro-3-methyl-1-phenyl-quinolin-2(1H)-one* (**17**) (0.12 g, 0.50 mmol, 31%) as a colourless solid, m.p. 89-93°C, one spot on TLC; (Found C, 81.0; H, 6.9; N, 5.9%. $C_{16}H_{15}NO$ requires C, 81.0; H, 6.4; N, 5.9%); υ_{max} ($CDCl_3$) 3060, 1676, 1602, 1492, and 1458 cm^{-1}; δ_H (250 MHz) 7.52-7.39 (3 H, 5-H, 6-H and 7-H), 7.24-7.17 (3 H, 8-H and 1-Ph), 7.03-6.96 (2 H, 1-Ph), 6.35-6.32 (1 H, 1-Ph), 3.13-2.99 (1 H, m, 3-H), 2.93-2.75 (2 H, m, 4-H), and 1.33 (3 H, d, J = 6.4 Hz, no nOe with ArH, 3-Me); δ_C (62.5 MHz) 173.0 (2-C), 142.0 (8a-C), 138.8 (4a-C), 129.9 (5-C), 129.8 (8-C), 129.0 (7-C), 128.0 (6-C), 127.0, 125.2, 122.8, 116.8 (1-Ph), 35.9 (3-C), 33.5 (4-C), and 15.5 (3-Me); the structure was confirmed by nOe difference spectroscopy; *m/z* (E.I.) 237.1164 (100%, M^+, $C_{16}H_{15}NO$ requires 237.1154), 222 (6), and 209 (8, M - CO).

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