SHORT PAPER

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The synthesis of highly substituted decahydrocarbazoles as potential chain-breaking antioxidants†

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Two methyl groups have been introduced into the positions α to the N-atom in 1,2,3,4,4a,5,6,7-octahydrobenzo[*d*]carbazoles in a 'one-pot' procedure; additionally bromination of 1*H*-2,3,4,4a-tetrahydro-6-isopropylcarbazoles has been shown to occur at C-8 and the derived bromides converted into 8-alkenylated derivatives as precursors of chain-breaking antioxidants of tuneable lipophilicity.

We have shown that certain highly substituted reduced carbazoles are effective chain-breaking antioxidants,[1] some of which have been tested as inhibitors of mammalian arterial plaque development.[2] Critical to this application is the selective affinity of the antioxidant for low-density lipoprotein (LDL), rather than for other forms of lipoproteins.[3] This selectivity is shown well by cyclohexano-fused carbazoles **1**, where R^2 is an alkyl chain, the lipophilicity of which can be varied.[4]

The cyclohexanocarbazoles can be synthesised from 1-decalone by Fischer reactions with aryl hydrazines,[5] followed by the addition of a suitable side chain by the addition of an alkyllithium (R^2Li) to the imine bond of the product 1,2,3,4,4a,5,6,7-octahydrobenzo[*d*]carbazoles **2**.[5] Although this approach works reasonably well for certain compounds **1** (where R^1 = H), when R^1 = Me the yield in the Fischer reaction drops sharply.[5]

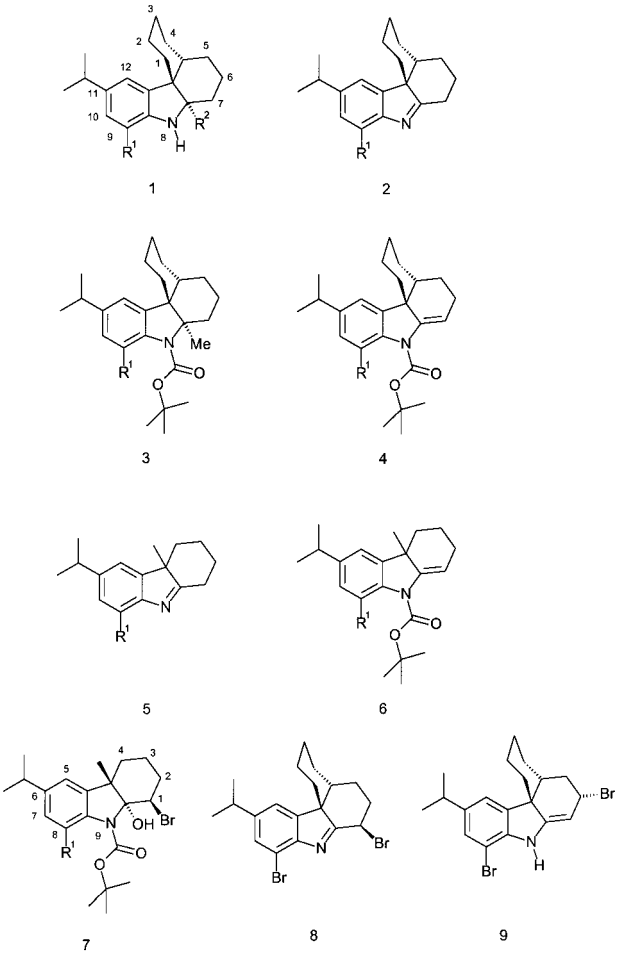
We have now devised a 'one-pot' synthesis of **1** ($R^1 = R^2$ = Me) from the 1,2,3,4,4a,5,6,7-octahydrobenzo[*d*]carbazole **2** (R^1 = H). Thus, when this compound in THF is reacted with methyllithium and the reaction mixture is quenched with di(tert-butyl) dicarbonate the carbamate **3** (R^1 = H) is obtained. This, without isolation, may now be treated with tert-butyllithium and then with methyl iodide to afford the carbamate **3** (R^1 = Me) in 44 % yield. *N*-Deacylation of **3** (R^1 = Me) is effected simply by treatment of the product with trifluoroacetic acid giving **1** ($R^1 = R^2$ = Me) in 88 % yield. Despite this success, when higher alkyllithiums replace methyllithium in the first step of the reaction sequence the procedure either fails or is very low yielding.

In an attempt to overcome this problem we next sought to introduce a side chain α to the N atom *late* in the synthesis. The 1,2,3,4,4a,5,6,7-octahydrobenzo[*d*]carbazole **2** (R^1 = H) was reacted with di(tert-butyl) dicarbonate in the presence of sodium acetate. After 4-5 weeks at reflux in THF the 8-acyl-1,2,3,4,4a,5,6,7-octahydrobenzo[*d*]carbazole **4** (R^1 = H) was formed in 48 % yield, but when this compound was treated with tert-butyllithium, and the bright yellow solution was quenched with methyl iodide, only the starting material **4** (R^1 = H) was returned.

Rather than pursue this work with the relatively expensive 1,2,3,4,4a,5,6,7-octahydrobenzo[*d*]carbazole **2** (R^1 = H) at this point we switched to the simpler model compound **5** (R^1 = H). In this case *N*-acylation with di(tert-butyl) dicarbonate under the same conditions was somewhat faster and the carbamate **6** (R^1 = H) was obtained in 36 % yield within 3 days. However, an attempted *ortho*-metallation/methylation reaction on the product failed and **6** (R^1 = H) was recovered unchanged. A similar failure was noted using Katritzky's conditions,[6] where the acylating agent was carbon dioxide rather than di(tert-butyl) dicarbonate.

Next we considered forming the carbamate **6** (R^1 = Br), which could be subjected to bromine/lithium exchange, prior to 8-alkylation, but direct bromination experiments upon **6** (R^1 = H) under very mild conditions always led to multi-component mixtures. On the other hand, a reaction with NBS in the presence of hydrogen peroxide gave mainly a mono-brominated product, but this was not the required compound **6** (R^1 = Br), rather the bromohydrin **7**.

The ^{1}H NMR spectrum of this compound, in $CDCl_3$ at ambient temperature, showed the H-7 resonance as a double



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doublet at 7.1 ppm ($^{1,3}J$ = 9 Hz and $^{1,4}J$ = 3 Hz), but that of H-8 at 7.4 ppm was broad. Moreover, the OH proton resonance could not easily be detected. Once the NMR was re-recorded at 50 °C the signal of H-8 was resolved into a doublet ($^{1,3}J$ = 9 Hz) and that of the OH proton appeared as a singlet at 6.9 ppm.

When the 1*H*-2,3,4,4a-tetrahydrocarbazole **5** (R^1 = H) was brominated with NBS the most abundant product was the required aryl bromide **5** (R^1 = Br) (29 % yield). A metal-halogen exchange experiment on this aryl bromide caused only hydrodebrom-ination, so it was coupled directly with methyl acrylate in the presence of triphenylphosphine and palladium acetate. This gave the 8-alkenyl derivative **5** [R^1 = CH=CHCO$_2$Me (*trans*)] in 41 % yield, a compound that contains the right type of side chain, *i.e.* capable of modification by, for example, hydrolysis and amide coupling to give units of variable lipophilicity. Now a similar series of reaction steps were then carried out upon the cyclohexano analogue **2** (R^1 = H). These were also successful and led to the desired alkenylated product **2** [R^1 = CH=CHCO$_2$Me (*trans*)]. This compound could be hydrolysed by treatment with aqueous sodium hydroxide to the corresponding acid **2** [R^1 = CH=CHCO$_2$H] in 40 % yield.

Unfortunately the overall yield of the ester **2** [R^1 = CH=CHCO$_2$Me] was half that obtained in the model series. In particular, the intermediate aryl bromide **2** (R^1 = Br) had to be separated from an intractable mixture of what appears to be the two dibromides **8** and **9** (relative stereochemistry assumed). In the ^{1}H NMR spectrum both components show closely similar aromatic ^4J related AB spin–spin patterns (J = 1.8 Hz) and in the mass spectrum molecular ion peaks at *m/z* 423, 425 and 427 [M^+], [$M+2^+$], [$M+4]^+$ (ratio 1:2:1).

Experimental

Unless stated otherwise, all solvents used were distilled and dried prior to use. Petrol refers to petroleum ether, b.p. 60–80°C. Solvents were removed by rotary evaporation at, or below 45ºC. Where necessary, the glass apparatus was dried in an oven and cooled under nitrogen. Most reactions were monitored by TLC, on Whatman aluminium backed UV$_{254}$ silica gel plates visualised under UV light, or developed with iodine, or a PMA dip. Flash-column chromatography was carried out under medium pressure on Amicon 60 Å silica gel. ^{1}H NMR spectra were run in deuteriochloroform using tetramethylsilane as an internal standard. These spectra were recorded at 270 MHz on a JEOL JNM GX FT 270 spectrometer. Mass spectra were determined on a Fisons VG Autospec instrument and were obtained by the method of electron impact at 70eV, unless stated otherwise.

8-Tert-butoxycarbonyl-1,2,3,4,4a,5,6,7,7a,8-decahydro-7a,9-dimethyl-11-iso-propylbenzo[d]carbazole **3** *(R^1 = Me)*: The carbazolenine **2** (R^1 = H)[4] (5.4 g, 20 mmol) in THF (30 cm^3) at 0 ºC under a nitrogen atmosphere was treated with 1.2M methyllithium (19 cm^3, 22.8 mmol) during 15 min. The temperature of the reaction mixture was then raised to 45 ºC and maintained at this level for 45 min. It was then cooled to 0 ºC and di-tert-butyl dicarbonate (5.2 g, 24 mmol) in THF (10 cm^3) was added *via* a syringe, then the mixture was heated at 40 ºC for 30 min. After this time, the reaction mixture was cooled to –78 ºC and tert-butyllithium (43 cm^3, 56 mmol) was added over 40 min, then the temperature was allowed to rise to –20 ºC over 45 min, and it was maintained at this temperature for 1 h. The reaction mixture was again cooled to –78 ºC and methyl iodide (5 cm^3) was added over 3 min. Excess reagent was then destroyed by the addition of a saturated aqueous solution of ammonium chloride (5 cm^3) and the residue was then partitioned between AcOEt (50 cm^3) and brine 25 cm^3). The aqueous phase was extracted with AcOEt (2 × 10 cm^3) and the combined organic layer and extracts were dried and evaporated to give an oil (10 g). Some of this material (2 g) was chromatographed on silica (40 g) eluting with 0.5–0.75 % AcOEt in petrol.

The first fraction 90 mg (0.5 % AcOEt/petrol), consisted of the dimethylated- octahydrocarbazole carbamate **3** (R^1 = Me), plus the corresponding unprotected decahydrocarbazole **1** (R^1 = R^2 = Me).

The second fraction 990 mg (0.5 % AcOEt/petrol), contained the dimethylated decahydrocarbazole **3** (R^1 = Me), 90 % by ^{1}H NMR), plus small amounts of the corresponding decahydrocarbazole **1** (R^1 = R^2 = Me) and the mono-methylated decahydrocarbazole carbamate **3** (R^1 = H).

The final fraction 510 mg (0.75 % AcOEt/petrol) contained 85 % (by ^{1}H NMR) of the title decahydrocarbazole carbamate **3** (R^1 = Me) and 10 % the corresponding decahydrocarbazole **1** (R^1 = R^2 = Me). Fractions 2 and 3 crystallised on standing to give **3** (R^1 = Me) as colourless cubes, 60 mg (after recrystallisation from petrol), m.p. 110–112 ºC; ν_{max} 1700 cm^{-1}; δ_H 1.22 (3 H, d , J = 7 Hz, (C$\underline{H}_3$)$_2$CH), 1.23 [3H, d, J = 7 Hz (C$\underline{H}_3$)$_2$CH)], 1.23 – 1.50 (5H, m), 1.54 [9H, s, (C$\underline{H}_3$)$_3$CO)], 1.55–1.87 (7H, m), 1.64 (3H, s, 7a-C$\underline{H}_3$), 2.04 (1H, m), 2.14 (3H, s, 9-C$\underline{H}_3$), 2.70 (2H, brd, J = 12 Hz), 2.84 [1H, sept, J = 7 Hz, (CH$_3$)$_2$C$\underline{H}$)], 6.81 (1H, d, J = 1.0 Hz, H-10), 7.22 (1H, d, J = 1.0 Hz, H-12) [Found: C, 78.4; H, 10.0; N, 3.4 $C_{26}H_{39}NO_2$ requires: C, 78.5; H, 9.8; N, 3.5 %].

1,2,3,4,4a,5,6,7,7a,8-Decahydro-7a,9-dimethyl-11-isopropyl-benzo[d]carbazole 1 (R^1 = R^2 = Me): A solution of **3** (R^1 = Me), (0.7 g, 1.8 mmol) in trifluoroacetic acid (4 cm^3) at room temperature was stored overnight, before the reagent was removed by evaporation. The residue was partitioned between AcOEt (30 cm^3) and water (30 cm^3) and the organic layer was collected. The aqueous phase was extracted with AcOEt (15 cm^3) and the combined organic phase and the extract were evaporated to afford an oil. This was redissolved in diethyl ether (5 cm^3) and a saturated solution of hydrogen chloride in diethyl ether (1 cm^3) was added. A colourless micro-crystalline solid separated out and this was collected and washed with a little diethyl ether to give the hydrochloride of the title compound (0.52 g, 88 %), m.p. 209–211 ºC; ν_{max} 2700, 2600, 1630 cm^{-1}; δ_H 1.23 [6H, d, J = 7 Hz, (C$\underline{H}_3$)$_2$ CH)], 1.40–1.75 (8H, m), 1.61 (3H, s, 7a-C$\underline{H}_3$), 1.75-2.00 (5H, m), 2.15-2.40 (2H, m), 2.71 (3H, s, 9-C$\underline{H}_3$), 2.88 [1H, sept, J = 7 Hz (CH$_3$)$_2$C$\underline{H}$)], 6.94 (1H, brs), 7.17 (1H, brs), 11.0 (2H, brs) [Found: C, 75.2; H, 9.7; N, 4.1 $C_{21}H_{31}N$.HCl requires: C, 75.6; H, 9.6; N, 4.2%].

*8-Tert-butoxycarbonyl-1,2,3,4,4a,5,6,12b-octahydro-11-isopropyl-benzo[*d*]-carbazole* **4** *(R^1 = H)*: The carbazolenine **2** (R^1 = H) (0.5g, 1.0 mmol) di-tert-butyl dicarbonate (0.41g, 1.9 mmol) and sodium acetate (0.13g, 1.9 mmol) in tetrahydrofuran (5 cm^3), protected under a nitrogen atmosphere, were heated at *ca* 70ºC for 4–5 weeks, during which time a further 6 mmol of di-tert-butyl dicarbonate were added. After this time, the solvent was evaporated and the dark coloured oil that remained was redissolved in AcOEt (40 cm^3) and washed with water (3 × 20 cm^3) and brine (3 × 20 cm^3). Removal of the solvent gave an oil, which was chromatographed on silica (40g), eluting with 5 % AcOEt in petrol, to afford the title compound as a colourless gum (327 mg, 48 %); 1.25 [6H, d, J = 7 Hz, (C$\underline{H}_3$)$_2$CH)], 1.4-1.58 (5H, s), 1.60 (9H, s), 1.75–2.0 (4H, m), 2.11–2.40 (4H, m), 2.91 [1H, sept, J = 7 Hz (CH$_3$)$_2$C$\underline{H}$)], 5.90 (1H, m, 7-$\underline{H}$), 7.04 (1H, dd, J = 6.5, 2 Hz, H-9), 7.0 (1H, d, J = 2 .0 Hz, H-12), 7.61 (1H, J = 6.5 Hz, H-8); δ_C 20.2(t), 20.8 (t), 23.6 (t), 24.4 (t), 27.3 (q), 27.8 (q), 28.9 (t), 33.0 (t), 33.8 (s), 34.7 (d), 45.3 (d), 81.5 (s), 103.3 (d), 115.1 (d), 123.0 (d), 124.5 (d), 138.5 (s), 142.5 (s), 145.8 (s), 146.7 (s), 151.1 (s), 152.1 (s) [Found: *m/z* 367.2516, $C_{24}H_{33}NO_2$ requires *m/z* 367.2511].

1H-2,3,4,4a-Tetrahydro-4a-methyl-6-isopropylcarbazole **5** *(R^1 = H):* 4-Isopropylphenylhydrazine hydrochloride (5.0 g, 33 mmol), 2-methylcyclohexanone (3.7 g, 4 cm^3, 33 mmol), freshly fused sodium acetate (4.6 g, 66 mmol) and glacial acetic acid (40 cm^3) were heated in an oil bath firstly at 60 ºC for 30 min and then at 110 ºC for 2 h. The solvent was removed and residue partitioned between AcOEt (60 cm^3) and brine (30 cm^3). The organic layer was collected, washed with brine (2 × 10 cm^3) and then with saturated sodium hydrogen carbonate (2 × 10 cm^3), then dried. The solvent was removed to afford a brown oil, which was chromatographed eluting with 30 % AcOEt in petrol to give the title compound as a pale yellow oil (5.1g, 68 %), ν_{max} 1583 cm^{-1} (C=N), δ_H 1.3 [6H, d, J = 7.0, (C$\underline{H}_3$)$_2$CH)], 1.3 (3H, s, Me), 2.6 (1H, m), 2.9 (1H, m), 3.0 [1H, sept, J = 7.0, (CH$_3$)$_2$C$\underline{H}$)], 7.2 (1H, d, J = 1.8 Hz, H-5), 7.2 (1H, dd, J = 7.9, 1.8 Hz, H-7), 7.5 (1H, d, J = 7.9 Hz, H-8); δ_C 19.7 (q), 21.2 (t), 24.2 (q), 28.9 (t), 29.4 (t), 34.0 (d), 38.5 (t), 53.5 (d), 119.2 (d), 119.5 (d), 125.3 (d), 145.7 (s), 146.6 (s), 151.9 (s), 189.4 (s) [Found: *m/z*: 227.1673 $C_{16}H_{21}N$ requires 227.1674].

Synthesis of 9-tert-butoxycarbonyl-2H-3,4,4a,9-tetrahydro-4a-methyl-6-isopropylcarbazole **6** *(R^1 = H)*: A solution of the carbazolenine **5** (0.5 g, 2.2 mmol), di-tert-butyl dicarbonate (0.48 g, 2.2 mmol) and freshly fused sodium acetate (0.15 g, 2.2 mmol) were dissolved in THF and stirred under nitrogen for a few minutes. The reaction was then left at 60–70 ºC for 3 days, during which a further equivalent of di-tert-butyl dicarbonate was added. Then the tetrahydrofuran was removed and the resultant brown oil was taken up in AcOEt (40 cm^3) and washed with water (2 × 15 cm^3) and then brine (2 × 15 cm^3). The organic phase was dried and evaporated to afford a

brown oil. This was chromatographed eluting with 4 % AcOEt in petrol to afford the title compound as a viscous colourless oil (0.37 g, 51 %); ν_{max} 1713 cm^{-1} (C=O); δ_H 1.2 [6H, d, *J* = 7.0 Hz, $(C\underline{H}_3)_2CH$], 1.3 (3H, s, Me), 1.6 [9H, s, $(C\underline{H}_3)_2C$], 1.6-2.3 (6H, m), 2.9 [1H, sept, *J* = 7.0 Hz, $(CH_3)_2C\underline{H}$], 5.9 (1H, bs, 1-H), 7.0 (1H, d, *J* = 2.0 Hz, H-5), 7.03 (1H, dd, *J* = 8.2, 2.0 Hz, H-7), 7.6 (1H, d, *J* = 8.2, H-8); δ_C 17.5 (t), 23.0 t, 24.2 q 24.2 q, 27.7 q, 23.4 q, 31.4 t, 33.8, 41.6, 81.5, 107.5, 115, 119.4, 124.9, 138.7, 139.6, 143.8, 145.2, 151.8 [Found: *m/z* 327.2203 $C_{21}H_{29}NO_2$ requires 327.2198].

*Preparation of 1-bromo-9-tert-butoxycarbonyl-1*H*-2,3,4,4a,9,9a-hexahydro-9a-hydroxy-4a-methyl-6-isopropylcarbazole* (**7**): The carbamate **6** (R^1 = H) (0.17 g, 0.5 mmol) in DCM (10 cm^3) was treated with *N*-bromosuccinimide (0.1 g, 0.5 mmol) in one portion and a catalytic amount of hydrogen peroxide was added dropwise (0.1 cm^3, 27 % solution in water). The reaction mixture was then left at room temperature for 16 h., before being poured into water (20 cm^3) and extracted with AcOEt. The extract was evaporated to give an oil that was chromatographed eluting with 10 % AcOEt in petrol. This yielded the title compound as a colourless gum (0.1 g, 4.7 %); δ_H 0.9 (1H, m), 1.2 [6H, d, *J* = 7.1 Hz $(C\underline{H}_3)_2CH$], 1.3 (3H, s, Me), 1.6–1.7 (1H, m), 1.7–2.2 (4H, m), 2.9 [1H, sept, *J* = 7.1 Hz, $(CH_3)_2C\mathit{H}$], 4.1 (1H, m, 1-H), 7.1 (1H, dd, *J* = 7.9, 1.8 Hz, 7-H), 7.2 (1H, d, *J* = 1.8 Hz, 5-H), 7.4 (1H, brs, H-8); δ_C 23.6 (t), 24.6 (q), 27.6 (q), 28.9 (q), 28.9 (t), 30.2 (t), 34.3 (d), 50.8 (q), 82.6 (s), 117.4 (d), 119.5 (d), 125.6 (s), 126.5 (s), 136.6 (s), 144.8 (s) [Found: *m/z* (+ FAB) 424.1495/426.1473 $(M^+{+}1)$ $C_{21}H_{31}BrNO_3$ requires 424.1487/426.1470]

*8-Bromo-1*H*-2,3,4,4a-tetrahydro-4a-methyl-6-isopropylcarbazole* **5** *(R^1 = Br)*: To a solution of the carbazolenine **5** (R^1 = H) (0.2 g, 0.9 mmol) in DCM (10 cm^3) was added *N*-bromosuccinimide (0.16 g, 0.9 mmol) and a catalytic amount of hydrogen peroxide (0.1 cm^3, 27.5 % solution in water). The reaction mixture was then left for 16 h, before being poured into water. The organic layer was separated and the residue extracted with DCM (2 × 5 cm^3). The combined organic layer and extracts were then dried and evaporated to afford a brown oil, which was chromatographed eluting with 30 % AcOEt in petrol. This gave the title compound as a pale yellow oil (0.08 g, 29 %); δ_H 1.3 [6H, d, *J* = 7.0 Hz, $(C\underline{H}_3)_2CH$], 1.3 (3H, s, Me), 1.4–1.5 (2H, m), 1.7–1.8 (2H, m), 2.2–2.3 (2H, m), 2.6 (1H, m), 2.9 (1H, m), 2.9 [1H, sept, *J* = 7.0 Hz $(CH_3)_2C\underline{H}$], 7.1 (1H, d, *J* = 1.5 Hz, H-5), 7.3 (1H, d, *J* = 1.5 Hz, H-7); δ_C 19.8 (q), 21.2 (t), 24.1 (q), 28.8 (t), 29.7 (t), 33.9 (s), 38.6 (t), 55.4 (d), 113.4 (d), 118.5 (d), 128.6 (s), 147.7 (s), 148.4 (s), 150.4 (s), 190.8 (s) [Found: *m/z* 305.0780/307.0759 $C_{16}H_{20}BrN$ requires 305.0779/307.0760].

Trans-*8-(2-methoxycarbonylvinyl)-1*H*-2,3,4,4a-tetrahydro-4a-methyl-6-isopropylcarbazole* **5** *(R^1 = CH=CHCO$_2$Me)*: Triphenylphosphine (0.1 g, 1.2 mmol) and 10 % palladium(II) acetate (0.013 g, 0.005 mmol) in freshly distilled toluene (10 cm^3) were stirred for a few minutes under nitrogen and triethylamine (0.1 g, 0.1 cm^3, 0.09 mmol) was then added dropwise. The bromo compound **5** (R^1 = Br) (0.12g, 0.4 mmol) in toluene (5 cm^3) was added next and then methyl acrylate (0.04 g, 0.04 cm^3, 0.4 mmol). The reaction mixture was left at 80 °C for 2 days, then quenched with water the organic phase separated and the aqueous layer extracted with DCM (2 × 5 cm^3). The combined organic layer and extracts were evaporated to afford a brown oil that was chromatographed, eluting with 30 % AcOEt in petrol, to afford the title compound as a pale yellow oil (0.05 g, 41 %); δ_H 1.27 (6H, d, *J* = 7.0 Hz, $(C\underline{H}_3)_2CH$)], 1.2-1.75 (11H, m), 2.9 [1H, septet, *J* = 7.0 Hz, $(CH_3)_2C\underline{H}$)], 3.81 (3H,s, $OC\underline{H}_3$), 6.9 (1H, d, *J* = 16.1 Hz, C<u>H</u>=), 7.2 (1H, d, *J* 1.7 Hz, H-5), 7.4 (1H, d, *J* = 1.7 Hz, H-7), 8.3 (1H, d, *J* = 16.1 Hz, C<u>H</u>=); δ_C 19.9 (q), 21.3 (t), 24.2 (q), 29.0 (t), 29.8 (t), 34.1 (d), 38.2 (t), 51.5 (q), 53.6 (d), 119.5 (d), 121.1 (d), 124.2 (d), 125.8 (s), 141.4 (s), 146.0 (s), 148.5 (s), 151.7 (s), 167.7 (d), 190.5 (s) [Found: *m/z* (+ FAB) 312.1964 $C_{20}H_{26}NO_2$ $(M+1)^+$ requires 312.1964].

*9-Bromo-1,2,3,4,4a,5,6,7-octahydro-11-isopropylbenzo[*d*]carbazole (2, R^1 = Br)*: To a solution of the carbazolenine **2** (R^1 = Br) (1.27g, 4.8 mmol) in DCM (20 cm^3) was added *N*-bromosuccinimide (0.85 g, 4.8 mmol) and a catalytic amount of hydrogen peroxide (0.5 cm^3, 27.5 % solution in water). The reaction mixture was then left over the weekend. It was then poured into water and the organic layer was collected extracted and the aqueous phase was washed with DCM (2 x 5 cm^3). The organic phases were combined, dried and evaporated to afford a brown oil, which was chromatographed, eluting with 30 % AcOEt in petrol. This gave the title compound as a pale yellow oil (0.25 g, 15 %); δ_H 1.0 (1H, brd, *J* = 12.6 Hz), 1.28 [6H, d, *J* = 7.0 Hz, $(C\underline{H}_3)_2CH$], 1.4–1.8 (7H, m), 2.0-2.2 (5H, m), 2.6 (1H, m), 2.9 (2H, m), 7.4 (1H, d, *J* = 1.5 Hz, H-12), 7.5 (1H, d, *J* = 1.5Hz, H-10); δ_C 20.1 (t), 21.8 (t), 24.7 (q), 26.7 (t), 27.5 (t), 27.7 (t), 28.5 (t), 34.5 (d), 39.9 (t), 41.6 (s), 59.6 (d), 114.1 (d), 122.3 (d), 128.8 (s), 146.8 (s), 147.5 (s), 150.9 (s), 191.0 (s) [Found: 345.1092/347.1080 $C_{19}H_{24}BrN$ requires 345.1092/347.1074].

Trans-*9-(2-methoxycarbonylvinyl)-1,2,3,4,4a,5,6,7-octahydro-11-isopropylbenzo[*d*]carbazole (2; R^1 = CH=CHCO$_2$Me):* Triphenylphosphine (0.9 g, 3.3 mmol) and 10 % palladium(II) acetate (0.013 g, 0.005 mmol) in freshly distilled toluene (10 cm^3) were stirred for a few min. under nitrogen. Triethylamine (0.24 g, 0.3 cm^3, 2.4 mmol) was then added dropwise and then the bromo compound **2,** (R^1 = Br) (0.39 g, 1.1mmol) in toluene. Finally methyl acrylate (0.09 g, 0.1 cm^3, 1.1 mmol) was introduced and the reaction mixture was left at 80 °C for 2 days. It was then quenched with water, the organic phase separated and the aqueous layer extracted with DCM (15 cm^3). The combined organic layer and extract were evaporated to afford a brown oil that was chromatographed, eluting with 30 % AcOEt in petrol, to afford the title compound as a pale yellow oil (0.05 g, 41 %); δ_H 1.0 (brd, 1H, *J* = 11.9 Hz), 1.3 [6H, d, *J* = 7.0 Hz $(C\underline{H}_3)_2CH$)], 1.4–2.2 (12H, m), 2.6 (1H, m), 2.9 (2H, m), 6.9 (1H, d, *J* = 16.1 Hz, C<u>H</u>=), 7.4 (1H, d, *J* 1.7 Hz, H-12), 7.6 (1H, d, *J* = 1.7 Hz, H-10), 8.3 (1H, d, *J* = 16.1 Hz, C<u>H</u>=): δ_C 19.7 (t), 21.5 (t), 24.2 (q), 26.4 (t), 27.1 (t), 27.4 (t), 28.3 (t), 29.5 (t), 34.2 (d), 41.4 (s), 51.5 (q), 57.5 (d), 119.1 (d), 123.5 (d), 124.5 (d), 126.2 (s), 141.4 (s), 144.9 (s), 146.7 (s), 152.1 (s), 167.7 (d), 190.5 (s) [Found: 351.2190 $C_{23}H_{29}NO_2$ requires 351.2198].

Trans-*9-(2-carboxyvinyl)-1,2,3,4,4a,5,6,7-octahydro-11-isopropylbenzo[*d*]carbazole (2; R^1 = CH=CHCO$_2$H)*: The ester **2** (R^1 = CH=CHCO$_2$Me) (0.2 g, 0.6 mmol) was mixed with 2M sodium hydroxide (15 cm^3) and stirred at 60 °C for 2 h. The reaction mixture was cooled and filtered through a pad of celite. The mixture was then mixed with ice, before the addition of conc. HCl (5 cm^3) and AcOEt (25 cm^3). The organic layer was separated and the aqueous phase extracted with DCM (2 x 10 cm^3). The combined organic phases were combined, dried and evaporated to afford the title compound as a pale yellow oil (0.08 g, 40 %); δ_H ($CDCl_3$ + D_2O) 1.2 (1H, brd, *J* = 11.5 Hz), 1.3 (6H, d, *J* = 6.8 Hz $(C\underline{H}_3)_2CH$)], 1.5-2.1 (12H, m), 2.6 (1H, m), 2.9 (1H, m), 3.6 (1H, m), 6.5 (1H, d, *J* = 15.9 Hz), 7.5 (1H, d, *J* = 1.7 Hz, H-12), 7.6 (1H, d, *J* = 1.7 Hz, H-10), 8.7 (1H, d, *J* = 15.9 Hz, C<u>H</u>=); δ_C 19.7 (t), 21.4 (t), 24.3 (q), 26.4 (t), 27.1 (t), 27.3 (t), 28.3 (t), 28.5 (t), 34.3 (d), 41.5 (s), 57.4 (d), 120.0 (d), 122.4 (d), 124.6 (d), 126.0 (s), 141.0 (s), 145.5 (s), 146.2 (s), 169.6 (d), 192.5 (s) [Found: *m/z* (+ FAB) 338.2116 $C_{22}H_{27}NO_2$ requires 338.2120 $(M+1)^+$].

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