Reductive alkylation of pyridinium salts. Part 2.[1] Utilisation of di-, tetra- and hexa-hydropyridine esters

Kevin J. McCullough,†[b] John MacTavish,[a] George R. Proctor *[,a] and James Redpath[c]

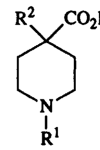
[a] *Department of Pure and Applied Chemistry, University of Strathclyde, Glasgow G1 1XL, UK*

[b] *Department of Chemistry, Heriot-Watt University, Riccarton, Edinburgh EH14 4AB, UK*

[c] *Organon Laboratories Ltd., Newhouse, Lanarkshire ML1 5SH, UK*

4-Benzyl-4-ethoxycarbonyl-1-substituted piperidines 1 (R^1 = $PhCH_2$, PhCO; R^2 = $PhCH_2$) cyclise with polyphosphoric acid (PPA) to give spiro[indane-2,4′-piperidin]-1-ones 3 (R = $PhCH_2$, PhCO), while 2-benzyl-2-ethoxycarbonyl-1-methylpiperidine 4 gives the *N*-methylspiro[indane-2,2′-piperidin]-1-one 5. 3,4,4a,5-Tetrahydrobenz[*g*]isoquinolin-10(2*H*)-one 8 arises from PPA treatment of 1-benzoyl-4-benzyl-5-ethoxycarbonyl-1,2,3,4-tetrahydropyridine 7 (R = PhCO) while *o*-chloranil converts 1-benzoyl-4-benzyl-4-ethoxycarbonyl-1,4-dihydropyridine 6 (R = PhCO) into 4-benzyl-3-ethoxycarbonylpyridine 9. Phenyl(tribromomethyl)mercury reacts with 1-benzoyl-4-benzyl-4-ethoxycarbonyl-1,4-dihydropyridine 2 (R^1 = PhCO, R^2 = $PhCH_2$) yielding 2-benzoyl-5-benzyl-7,7-dibromo-5-ethoxycarbonyl-2-azabicyclo[4.1.0]hept-3-ene 11, and with 1-benzoyl-4-benzyl-3-ethoxycarbonyl-1,4-dihydropyridine 6 (R = PhCO) to give 2-benzoyl-5-benzyl-7,7-dibromo-4-ethoxycarbonyl-2-azabicyclo[4.1.0]hept-3-ene 12. The structure of the latter is confirmed by X-ray crystallographic analysis. Catalytic hydrogenation of 2-benzoyl-5-benzyl-7,7-dichloro-5-ethoxycarbonyl-2-azabicyclo[4.1.0]hept-3-ene 16 yields 2-benzoyl-5-benzyl-7,7-dichloro-5-ethoxycarbonyl-2-azabicyclo[4.1.0]heptane 21 which cyclises with PPA to give the tetracyclic product 22 in good yield. When 2-benzoyl-5-benzyl-7,7-dichloro-4-ethoxycarbonyl-2-azabicyclo[4.1.0]hept-3-ene 17 is hydrogenated it yields mainly 2-benzoyl-5-benzyl-7,7-dichloro-4-ethoxycarbonyl-2-azabicyclo[4.1.0]heptane 25 but the dibromo analogue 12 under the same conditions gives two components thought to be 2-benzoyl-5-benzyl-7-*endo*-bromo-4-ethoxycarbonyl-2-azabicyclo[4.1.0]hept-3-ene 24 and 2-benzoyl-5-benzyl-7-*exo*-bromo-4-ethoxycarbonyl-2-azabicyclo[4.1.0]hept-3-ene 23.

As described in the preceding paper, some di-, tetra- and hexa-hydropyridines may be prepared by reductive alkylation of pyridinium ester salts using activated zinc in acetonitrile. In this paper we describe some useful synthetic applications for the reduced and partially reduced pyridines so obtained.



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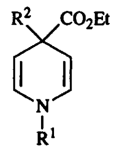

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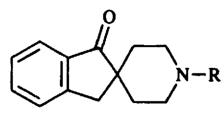

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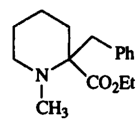

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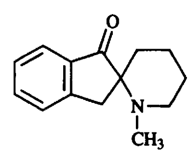

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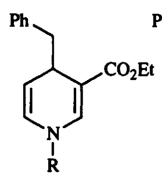
Discussion

4,4-Disubstituted piperidines 1 (R^2 = CH_2Ph) are readily available by catalytic hydrogenation of 1,4-dihydropyridines 2 [1-3] and may then be cyclised to spiro[indane-2,4′-piperidin]-1-ones 3 (R = CH_3, CH_2Ph) in polyphosphoric acid (PPA). In the present work the dihydropyridines 2 (R^1 = COPh, R^2 = $PhCH_2$ and PhCO) were prepared and reduced to the piperidines 1 (R^1 = COPh, R^2 = $PhCH_2$ and PhCO). The first of these cyclised to the spiro compound 3 (R = PhCO) with PPA: this further demonstrates the usefulness of such an approach to this ring system. The 2,2-disubstituted piperidine 4 [1] could also be cyclised in PPA (37%) yielding the *N*-methylspiro[indane-2,2′-piperidin]-1-one 5. The latter is the first example of this ring-system which is, in effect, a rigid β-phenylethylamine and worthy of further study.

As noted before,[1] catalytic hydrogenation of dihydropyridines 6 obtained from reductive alkylation of nicotinate salts leads to tetrahydropyridines, *e.g.* 7 (R = CH_3 and PhCO). Somewhat surprisingly, sodium hydroxide hydrolysis of ester 7 (R = PhCO) gave the ester 7 (R = H). However, hydrolysis/cyclisation in PPA at 95 °C gave a 75% yield of the



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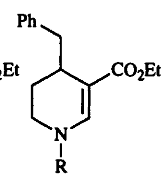

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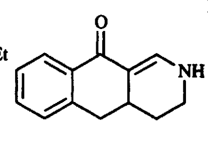

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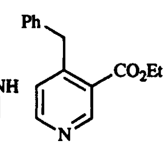

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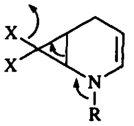
benz[*g*]isoquinolinone 8: some examples of this ring system were previously claimed by cyclising 3-benzylpiperidine-4-carboxylates.[4,5] This new synthesis of benz[*g*]isoquinolinone 8 is facile and productive. The dihydropyridine ester 6 (R = PhCO) was shown to be useful in another way: oxidation of it with *o*-chloranil[6] yielded ethyl 4-benzylnicotinate 9. The latter also appears to be novel, suggesting that the two-step protocol

† To whom enquiries regarding X-ray crystallographic studies should be addressed.

of reductive alkylation followed by oxidation may be a useful method to bring about substitiution of pyridines.

Carbene reactions

Availability of 1,4-dihydropyridines **2** and **6**[1] suggested that *they might undergo* dihalocarbene addition to yield 2-azabicyclo[4.1.0]heptenes **10** from which azepine derivatives might arise (as shown) under the influence of suitable reagents. Precedents exist for the analogous ring-expansion of quinoline and isoquinoline derivatives into benzazepines.[7–9] In the event, unstable dihydropyridines **2** (R^1 = CH_3 and $PhCH_2$) and **6** (R = CH_3 and $PhCH_2$) failed to give recognisable products when treated with phenyl(tribromomethyl)mercury,[7,10,11] but the *N*-benzoyl esters **2** (R^1 = PhCO) and **6** (R = PhCO) gave the adducts **11** and **12** respectively.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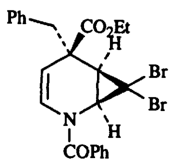
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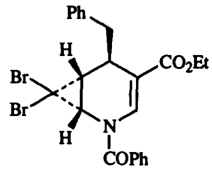
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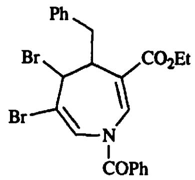
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Although elemental analysis and mass spectra indicated that both adducts ($C_{23}H_{21}Br_2NO_3$) were as illustrated, line broadening in the ^1H NMR spectra and a failure to identify cyclopropyl protons conclusively, cast some doubts on these structures. Moreover, ^{13}C NMR and 2-D spectroscopy did not clarify the situation and it became necessary to consider alternative structures, (*e.g.* **13**) which might have arisen due to spontaneous ring-expansion. The latter hypothesis seemed quite plausible when it was discovered that compounds **11** and **12** failed to react with silver nitrate[7] or silver trifluoroacetate in several different solvents, or with collidine (2,4,6-trimethylpyridine) in the case of **11**; collidine caused compound **12** to decompose.

From suitable single crystals, the structure of adduct **12** was determined by X-ray crystallographic analysis. The results of this study, depicted in Fig. 1, were entirely consistent with structural formula **12** and supported our assumption that the cyclopropyl ring would be *anti* to the pendant benzyl group. Although compound **11** is not crystalline, it seemed inconceivable that the same relative stereochemistry would not apply to it.

There is no obvious explanation for the failure of **11** and **12** to undergo ring-expansion. It has to be conceded that assistance from the unpaired electrons on nitrogen as shown in **10** would be minimal in *N*-benzoyl structures, although there is an example[9] of *N*-acetyl group participation under vigorous conditions giving a fairly low yield of a 2-benzazepine product. There are cases where lithium aluminium hydride has been shown to induce ring-expansion of dihalocarbene adducts containing *N*-acyl substituents;[12,13] presumably the reagent restores the basicity of the nitrogen atom by reducing the amidic carbonyl groups, thus allowing the electrons on the nitrogen atom to participate in the process induced by bromide ion expulsion. When compound **11** was treated with lithium aluminium hydride, both carbonyl group reduction and debromination took place; the unstable product, not fully characterised, was thought to be the hemiaminal ether **14**.

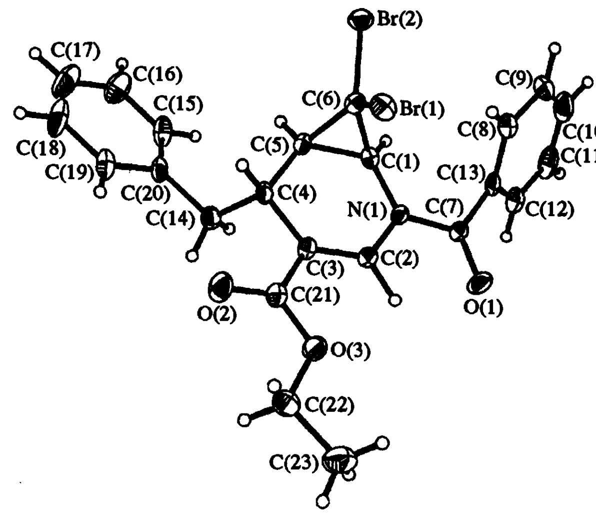
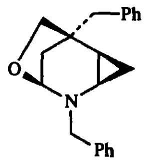


Fig. 1 Molecular structure of adduct **12** as determined by X-ray crystallographic analysis (ORTEP, the non-hydrogen atoms are represented by 30% probability ellipsoids).[19] Hydrogen atom labels have been omitted for clarity.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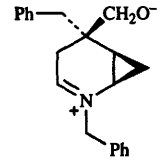
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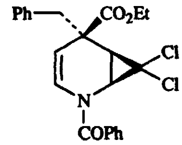
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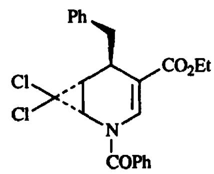
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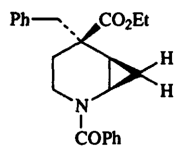
A plausible mechanism can be written which involves the iminium zwitterion **15**. Similar treatment of **12** caused decomposition.

The dichloroadducts **16** and **17** were made from dihydropyridines **2** (R^1 = PhCO, R^2 = $PhCH_2$) and **6** (R = PhCO) respectively using a phase transfer technique.[14,15] Yields were consistently satisfactory (91%) for compound **16** but very poor for compound **17** (11%). The method, however, was more convenient than that employing organomercurials.[7,10,11]

The aforementioned problem in allocating structures to dihalocarbene adducts **11** and **12** prompted a study of their behaviour on hydrogenolysis, along with comparison with similar treatment of **16** and **17**. Prolonged catalytic hydrogenation of compound **11** over palladium gave the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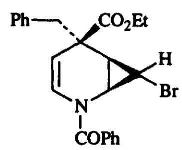
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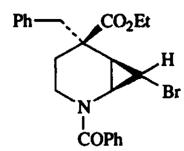
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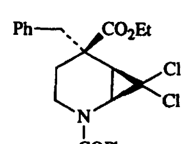
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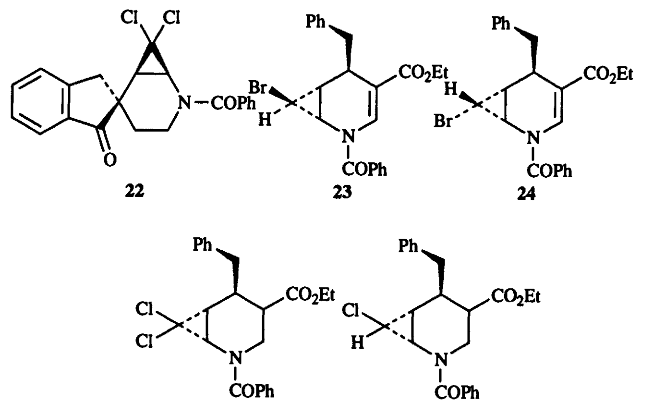
debrominated and reduced product **18**. Interrupted hydrogenation gave a mixture, not fully characterised, of **19** and **20**. For the latter, all data (including elemental analysis) were consistent, but the precise stereochemistry could not be defined.

Contrastingly adduct **16** was converted by similar catalytic hydrogenation into the dichloroazabicycloheptane **21** which, like related examples (**1**→**3**) cyclised (PPA, 120 °C) to the tetracyclic product **22**. On the other hand, the dibromoadduct



22 **23** **24** **25** **26**

12 gave two monobromo azabicycloheptenes, **23** and **24**, of which only **24** was solid. Although only small amounts of **23** and **24** were available, mass spectrometry and ^{1}H NMR spectroscopy served to establish with fair certainty the relevant structures. In particular these isomers ($C_{23}H_{22}BrNO_3$) could be distinguished by the differing coupling constants between 1-H, 6-H and 7-H. Thus in the *endo* bromo isomer **24** 6-H is a double doublet with coupling constants *J* 9.1 and *J* 9.1 Hz characteristic of the expected *cis* vicinal couplings. The ^{1}H NMR spectrum of the *exo* bromo isomer **23** was even more convincing: not only did 6-H exhibit a *cis* (*J* 9.7 Hz) coupling with 1-H and a *trans* (*J* 4.6 Hz) coupling with 7-H, but 7-H was a clearly resolved double doublet showing the two *trans* couplings (*J* 2.7 Hz and *J* 4.6 Hz) with 1-H and 6-H respectively.

Surprisingly and in contrast, the dichloro analogue **17** underwent double-bond reduction on catalytic hydrogenation: the principal product ($C_{23}H_{23}Cl_2NO_3$) (50%) was solid and had structure **25** although the relative stereochemistry of the ester group could not be estimated from the ^{1}H NMR spectrum since both 4-H and 5-H were multiplets (250 MHz). A trace of a second compound ($C_{23}H_{24}ClNO_3$) **26** was isolated by chromatography but the data did not allow a decision as to which chlorine atom (in **25**) had been lost, although the *exo* chlorine might be expected to be more labile.

To conclude, this study demonstrates that the alkylated and reduced pyridines obtained from reductive alkylation of pyridinium salts have several useful synthetic outlets involving bi-, tri- and tetra-cyclic fused and spiro ring systems.

Experimental

For general procedures, see previous paper.

1-Benzoyl-4-benzyl-4-ethoxycarbonylpiperidine 1 (R^1 = PhCO, R^2 = $PhCH_2$)

1-Benzoyl-4-benzyl-4-ethoxycarbonyl-1,4-dihydropyridine[1] **2** (R^1 = PhCO, R^2 = $PhCH_2$) (5.89 g, 16.95 mmol), ethanol (200 cm^3) and platinum oxide (200 mg) were hydrogenated at 45 psi in a Cook hydrogenator. The catalyst was then removed by filtration through kieselguhr and the filtrate was concentrated *in vacuo*, to yield a viscous oil (5.34 g, 90%). Purification by column chromatography (2.165 g) (eluent: 25% ethyl acetate–hexane) produced the product as a viscous, colourless oil (1.37 g, 58%), bp 180 °C/0.04 mmHg (Found: C, 75.05; H, 7.3; N, 3.9%; M$^+$, 351.1839. $C_{22}H_{25}NO_3$ requires C, 75.2; H, 7.2; N, 4.0%; *M*, 351.1835); ν_{max}(film)/cm^{-1} 1720 and 1660 (C=O str); δ_H(250 MHz, $CDCl_3$) 1.19 (3 H, t, *J* 7.1, CH_2CH_3), 1.3–1.7 (2 H, br m, 3-H and 5-H), 2.0–2.4 (2 H, br m, 3-H and 5-H), 2.80–3.0 (3 H, d and br m, *J* 5.0, $PhCH_2$ and ring C–H), 3.09 (1 H, br m, ring C–H), 3.65 (1 H, br d, ring C–H), 4.12 (2 H, q, *J* 7.1, CH_2CH_3), 4.56 (1 H, br d, ring C–H), 7.03 (2 H, m, aryl), 7.25 (3 H, m, aryl), 7.35 (5 H, m, aryl).

N-Benzoylspiro[indane-2,4′-piperidin]-1-one 3 (R = PhCO)

1-Benzoyl-4-benzyl-4-ethoxycarbonylpiperidine **1** (R^1 = PhCO, R^2 = $PhCH_2$) (5.0 g, 14.23 mmol) was added to polyphosphoric acid (40 g) and stirred at 110 °C, for 6 days. The reaction was then cooled to 60 °C, poured onto ice–water, basified with aqueous sodium hydroxide and extracted with dichloromethane. The combined extracts were dried (Na_2SO_4), filtered and concentrated *in vacuo*, to produce a dark viscous oil (3.65 g, 84%). Purification by column chromatography (eluent: 2% ethanol in $CHCl_3$), gave the product (2.9 g, 67%). Recrystallisation (ethanol–activated charcoal) afforded colourless crystals, mp 152–154 °C (Found: C, 78.5; H, 6.3; N, 4.5%; M$^+$, 305.1410. $C_{20}H_{19}NO_2$ requires C, 78.7; H, 6.3; N, 4.6%; *M*, 305.1416); ν_{max}(KBr)/cm^{-1} 1727 and 1651 (C=O str); δ_H(250 MHz, $CDCl_3$) 1.5 (2 H, br d, ring C–H), 2.0 (2 H, br s, ring C–H), 3.15 (4 H, m, ring C–H and $PhCH_2$), 3.9 (1 H, br s, ring C–H), 4.65 (1 H, br s, ring C–H), 7.35–7.5 (7 H, m, aryl), 7.63 (1 H, ddd, *J* 1.2, 7.2 and 7.7, aryl), 7.75 (1 H, d, *J* 7.7, aryl).

N-Methylspiro[indane-2,2′-piperidin]-1-one 5

2-Benzyl-2-ethoxycarbonyl-1-methylpiperidine[1] **4** (4.0 g, 15.3 mmol) was stirred in polyphosphoric acid (40 g) for 4 days, at 130–150 °C. The mixture was cooled to 60 °C, poured onto ice–water, basified with aqueous sodium hydroxide and extracted with dichloromethane. The extracts were dried (Na_2SO_4), filtered and concentrated *in vacuo*, to produce a dark residual oil. Purification by column chromatography (eluent: 300:8:1, $CHCl_3$–C_2H_5OH–NH_3) and Kugelrohr distillation, produced the title compound as a mobile, orange oil (1.21 g, 37%), bp 135 °C/0.01 mmHg (Found: C, 77.9; H, 8.3; N, 6.2%; M$^+$, 215.1319. $C_{14}H_{17}NO$ requires C, 78.1; H, 8.0; N, 6.5%; *M*, 215.1310) [the methiodide salt had mp 215 °C (decomp.) (Found: C, 50.8; H, 5.7; I, 34.2; N, 3.4%. $C_{15}H_{20}INO$ requires C, 50.4; H, 5.6; I, 35.5; N, 3.9%)]; ν_{max}(film)/cm^{-1} 1725 (C=O str); δ_H(400 MHz, $CDCl_3$) 1.45 (2 H, m, ring C–H), 1.8 (4 H, m, ring C–H), 2.08 (3 H, s, N–CH_3), 2.39 (1 H, dt, *J* 2.9 and 11.4, ring C–H), 2.80–2.95 (2 H, m and d, *J* 17.3, $PhCH_2$ and ring C–H), 3.31 (1 H, d, *J* 17.3, $PhCH_2$), 7.38 (1 H, td, *J* 0.8 and 7.4, aryl), 7.48 (1 H, dt, *J* 1 and 7.7, aryl), 7.61 (1 H, dt, *J* 1 and 7.4, aryl), 7.8 (1 H, dd, *J* 1 and 7.7, aryl); δ_C(100.625 MHz, $CDCl_3$) 21.09 (CH_2), 25.66 (CH_2), 29.08 (CH_2), 35.28 ($PhCH_2$), 39.76 (N–CH_3), 52.20 (C-6), 70.25 (C-2), 124.69, 127.07, 127.71, 135.43 (aryl *C*–H), 135.89, 152.27 (*ipso*-aryl), 208.7 (C=O).

1-Benzoyl-4-benzyl-3-ethoxycarbonyl-1,4,5,6-tetrahydropyridine 7 (R = PhCO)

1-Benzoyl-4-benzyl-3-ethoxycarbonyl-1,4-dihydropyridine[1] **6** (R = PhCO) (2.8 g, 8.06 mmol) was hydrogenated in ethanol (200 cm^3) over platinum oxide (200 mg) in a Cook hydrogenator (45 psi/25 °C). The catalyst was then removed by filtration through kieselguhr and the filtrate was concentrated *in vacuo* to give a viscous oil (2.75 g, 98%) (TLC indicated one major component). Purification by column chromatography (eluent: 20% ethyl acetate–hexane) gave the product as a colourless solid (2.59 g, 92%), mp 66–68 °C. HPLC indicated a single fraction was present (retention time, 10 min; eluent: 70% acetonitrile–water) (Found: C, 75.5; H, 6.4; N, 3.8%; M$^+$, 349.1687. $C_{22}H_{23}NO_3$ requires C, 75.6; H, 6.6; N, 4.0%; *M*, 349.1678); ν_{max}(film)/cm^{-1} 1705 and 1680 (C=O str); δ_H(400 MHz, $CDCl_3$) 1.27 (3 H, t, *J* 7.1, CH_2CH_3), 1.64 (1 H, m, 5-H), 1.86 (1 H, m, 5-H), 2.4 (1 H, dd, *J* 10.7 and 13.4, PhCH_2), 2.99 (1 H, m, 4-H), 3.15 (1 H, dd, *J* 3.3 and 13.4, PhCH_2), 3.4 (1 H, dt, *J* 3.3 and 13.4, 6-H), 4.18 (3 H, q, *J* 7.1, 6-H and CH_2CH_3), 7.21–7.34 (5 H, m, aryl), 7.45–7.6 (5 H, m, aryl), 7.97 (1 H, br s, 2-H).

4-Benzyl-3-ethoxycarbonyl-1,4,5,6-tetrahydropyridine 7 (R = H)

1-Benzoyl-4-benzyl-3-ethoxycarbonyl-1,4,5,6-tetrahydropyridine 7 (R = PhCO) (1.0 g, 2.86 mmol), sodium hydroxyde (0.126 g, 3.15 mmol), water (5 cm^3) and ethanol (10 cm^3) were boiled under reflux for 6 days. The system was then cooled, diluted with water (100 cm^3) and extracted with dichloromethane. The combined extracts were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Recrystallisation (light petroleum, bp 80–100 °C) yielded the product as colourless crystals (0.625 g, 92%), mp 65–67 °C (Found: C, 73.6; H, 7.9; N, 5.5%; M^+, 245.1417. $C_{15}H_{19}NO_2$ requires C, 73.45; H, 7.8; N, 5.7%; *M*, 245.1416); ν_{max}(KBr)/cm^{-1} 1675 (C=O str); δ_H(250 MHz, $CDCl_3$) 1.30 (3 H, t, *J* 7.1, CH_2CH_3), 1.51 (1 H, m, 5-H), 1.69 (1 H, m, 5-H), 2.32 (1 H, dd, *J* 10.7 and 13.4, PhCH_2), 2.93 (1 H, m, 4-H), 3.11 (1 H, dd, *J* 3.4 and 13.4, PhCH_2), 3.15–3.28 (2 H, m, 6-H), 4.18 (2 H, dq, *J* 2.0 and 7.1, CH_2CH_3), 4.66 (1 H, br s, exch., N–H), 7.15–7.33 (5 H, m, aryl), 7.54 (1 H, d, *J* 6.25, 2-H).

3,4,4a,5-Tetrahydrobenz[*g*]isoquinolin-10(2*H*)-one 8

1-Benzoyl-4-benzyl-3-ethoxycarbonyl-1,4,5,6-tetrahydropyridine 7 (R = PhCO) (2.0 g, 5.72 mmol) was stirred in polyphosphoric acid (20 g) for 3 days at 95 °C. The reaction mixture was then cooled to 60 °C, added to ice–water, basified with aqueous sodium hydroxide and extracted with dichloromethane. The combined extracts were dried (Na_2SO_4), filtered and concentrated *in vacuo*, to produce a brown solid residue. Purification by column chromatography (eluent: 150:8:1 $CHCl_3$–C_2H_5OH–NH_3) yielded a colourless solid (0.804 g, 71%). Recrystallisation (ethanol–decolourising charcoal) gave colourless crystals, mp 182–183 °C (Found: C, 78.1; H, 6.6; N, 7.0%; M^+, 199.0990. $C_{13}H_{13}NO$ requires C, 78.4; H, 6.6; N, 7.0%; *M*, 199.0997); ν_{max}(KBr)/cm^{-1} 3190 (N–H str), 1675 (C=O str); δ_H(250 MHz, $CDCl_3$) 1.79 (1 H, m, 4-H), 2.07 (1 H, m, 4-H), 2.6–2.94 (3 H, m, 4a-H and PhCH_2), 3.37–3.52 (2 H, m, 3-H), 7.1–7.4 (5 H, m, aryl and exch., N–H), 7.62 (1 H, d, *J* 2.3, 1-H).

4-Benzyl-3-ethoxycarbonylpyridine 9

A solution of 1-benzoyl-4-benzyl-3-ethoxycarbonyl-1,4-dihydropyridine 6 (R = PhCO)[1] (1.04 g, 3.0 mmol), *o*-chloranil (3,4,5,6-tetrachloro-*o*-benzoquinone) (0.811 g, 3.3 mmol) and Na-dried toluene (20 cm^3) were refluxed under nitrogen for 6 h. Ether (50 cm^3) and 1 M aqueous sodium hydroxide were added to the cooled reaction mixture which was then stirred for 5 min and filtered through kieselguhr. The organic layer was washed with water, brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*, to yield a dark residual oil. Purification by Kugelrohr distillation produced a colourless, mobile oil (0.29 g, 40%), bp 120 °C/0.03 mmHg (Found: C, 74.35; H, 6.2; N, 5.7%; M^+, 241.1098. $C_{15}H_{15}NO_2$ requires C, 74.7; H, 6.3; N, 5.8%; *M*, 241.1103); ν_{max}(film)/cm^{-1} 1727 (C=O str); δ_H(250 MHz, $CDCl_3$) 1.35 (3 H, t, *J* 7.1, CH_2CH_3), 4.35 (2 H, q, *J* 7.1, CH_2CH_3), 4.4 (2 H, s, PhCH_2), 7.08 (1 H, d, *J* 5.2, H-5), 7.1–7.4 (5 H, m, aryl), 8.57 (1 H, d, *J* 5.2, H-6), 9.09 (1 H, s, H-2).

2-Benzoyl-5-benzyl-7,7-dibromo-5-ethoxycarbonyl-2-azabicyclo-[4.1.0]hept-3-ene 11

1-Benzoyl-4-benzyl-4-ethoxycarbonyl-1,4-dihydropyridine 2 (R^1 = PhCO, R^2 = $PhCH_2$) (0.5 g, 1.43 mmol) in benzene (10 cm^3) was refluxed under nitrogen, while a solution of phenyl-(tribromomethyl)mercury (0.825 g, 1.57 mmol) in benzene (10 cm^3) was added, over 3 min. After refluxing for 18 h (TLC indicated the mercurial had been consumed), the cooled solution was filtered and concentrated *in vacuo*, to give a colourless oil. Purification by column chromatography (eluent: 15% ethyl acetate–hexane) produced a colourless, viscous oil, which crystallised slowly (0.53 g, 72%), mp 104 °C (Found: C, 53.4; H, 4.0; Br, 30.95; N, 2.6%; M^+, 520.9859, 518.9869, 516.9855. $C_{23}H_{21}Br_2NO_3$ requires C, 53.2; H, 4.1; Br, 30.8; N, 2.7%; *M*, 520.9848, 518.9868, 516.9888); ν_{max}(KBr)/cm^{-1} 1728 and 1675 (C=O str); δ_H(250 MHz, $CDCl_3$) 1.35 (3 H, br t, *J* 7.1, CH_2CH_3), 2.53 (1 H, br s, 6-H), 3.0–3.4 and 4.0 (3 H, br m and br s, PhCH_2 and 1-H), 4.12–4.44 (2 H, m, CH_2CH_3), 4.9–5.5 (1 H, br d, 4-H), 6.36 and 7.1–7.7 (11 H, br s and br m, 3-H and aryl).

2-Benzoyl-5-benzyl-7,7-dibromo-4-ethoxycarbonyl-2-azabicyclo-[4.1.0]hept-3-ene 12

A solution of 1-benzoyl-4-benzyl-3-ethoxycarbonyl-1,4-dihydropyridine 6 (R = PhCO) (3.47 g, 10 mmol) in benzene (10 cm^3) was refluxed under nitrogen, while a solution of phenyl(tribromomethyl)mercury (5.3 g, 11 mmol) in benzene (10 cm^3) was added over 3 min. After refluxing for 18 h (TLC indicated the mercurial had been consumed), the cooled solution was filtered and concentrated *in vacuo*, to produce a brown solid. Purification by column chromatography (eluent: 30% ethyl acetate–hexane) and recrystallisation (ethanol–activated charcoal) produced colourless needles (3.52 g, 68%), mp 163–165 °C. HPLC indicated a single fraction (retention time 10 min, eluent: 60% acetonitrile–water) (Found: C, 53.4; H, 4.0; Br, 30.7; N, 2.7%; M^+, 520.9866, 518.9877, 516.9900. $C_{23}H_{21}Br_2NO_3$ requires C, 53.2; H, 4.1; Br, 30.8; N, 2.7%; *M*, 520.9848, 518.9868, 516.9888); ν_{max}(Nujol)/cm^{-1} 1695 and 1685 (C=O str); δ_H(400 MHz, $CDCl_3$) 1.31 (3 H, t, *J* 7.1, CH_2CH_3), 2.23 (1 H, d, *J* 10.4, 6-H), 2.64 (1 H, dd, *J* 9.1 and 13.5, PhCH_2), 3.16 (1 H, dd, *J* 3.3 and 9.1, 5-H), 3.31 (1 H, dd, *J* 3.3 and 13.5, PhCH_2), 3.63 (1 H, br s, 1-H), 4.25 (2 H, q, *J* 7.1, CH_2CH_3), 7.22–7.36 (5 H, m, aryl), 7.49–7.61 (5 H, m, aryl), 8.06 (1 H, br s, 3-H).

2-Benzoyl-5-benzyl-7,7-dichloro-5-ethoxycarbonyl-2-azabicyclo-[4.1.0]hept-3-ene 16

Aqueous sodium hydroxide (6 cm^3, 50% w/w) was added, dropwise, to a solution of 1-benzoyl-4-benzyl-4-ethoxycarbonyl-1,4-dihydropyridine 2 (R^1 = PhCO, R^2 = $PhCH_2$) (1.34 g, 3.85 mmol) and benzyltriethylammonium chloride (0.1 g, 0.35 mmol) in $CHCl_3$ (8 cm^3). The two-phase system was stirred for 20 h, then poured into water (100 cm^3) and extracted with dichloromethane. The combined extracts were washed with water, dried (Na_2SO_4), filtered and concentrated *in vacuo*, to produce a brown residue. Purification by column chromatography (eluent: 20% ethyl acetate–hexane) produced a colourless, viscous oil, which crystallised slowly (1.55 g, 94%), mp 67–73 °C (decomp.) (Found: C, 64.4; H, 4.7; Cl, 16.3; N, 3.0%; M^+, 431.0876, 429.0911. $C_{23}H_{21}Cl_2NO_3$ requires C, 64.2; H, 4.9; Cl, 16.5; N, 3.25%; *M*, 431.0869, 429.0899); ν_{max}(film)/cm^{-1} 1734 and 1663 (C=O str); δ_H(250 MHz, $CDCl_3$) 1.32 (3 H, t, *J* 7.1, CH_2CH_3), 2.43 (1 H, br d, 6-H), 3.10 (2 H, s, PhCH_2), 3.2–4.05 (1 H, 2 × br s, 1-H), 4.10–4.40 (2 H, m, CH_2CH_3), 4.9 and 5.35 (1 H, 2 × br s, 4-H), 6.3–7.5 (11 H, br s and br m, 3-H and aryl).

2-Benzoyl-5-benzyl-7,7-dichloro-4-ethoxycarbonyl-2-azabicyclo-[4.1.0]hept-3-ene 17

Aqueous sodium hydroxide (6 cm^3, 50% w/w) was added, dropwise, to a solution of 1-benzoyl-4-benzyl-3-ethoxycarbonyl-1,4-dihydropyridine[1] 6 (R = PhCO) (1.34 g, 3.85 mmol) and benzyltriethylammonium chloride (0.1 g, 0.35 mmol) in $CHCl_3$ (8 cm^3). The two-phase system was stirred for 26 h, then poured into water (100 cm^3) and extracted with dichloromethane. The combined extracts were washed with water, dried (Na_2SO_4), filtered and concentrated *in vacuo*, to produce a dark residue. Purification by column chromatography (eluent: 20% ethyl acetate–hexane) produced a yellow, crystalline solid.

Recrystallisation (ethanol) afforded colourless plates (0.18 g, 11%), mp 134–135 °C (Found: C, 64.15; H, 4.8; Cl, 16.45; N, 3.0%; M^+, 433.0818, 431.0882, 429.0897. $C_{23}H_{21}Cl_2NO_3$ requires C, 64.2; H, 4.9; Cl, 16.5; N, 3.25%; *M*, 433.0840, 431.0869, 429.0899); ν_{max}(KBr)/cm^{-1} 3130, 3080 and 3055 (aromatic C–H str), 2980 and 2925 (aliphatic C–H str), 1700 and 1650 (C=O str); δ_H(250 MHz, $CDCl_3$) 1.32 (3 H, t, *J* 7.1, CH_2CH_3), 2.14 (1 H, d, *J* 10.5, 6-H), 2.62 (1 H, dd, *J* 8.9 and 13.2, PhCH_2), 3.24 (1 H, dd, *J* 3.3 and 8.9, 5-H), 3.32 (1 H, dd, *J* 3.3 and 13.2, PhCH_2), 3.60 (1 H, br s, 1-H), 4.24 (2 H, q, *J* 7.1, CH_2CH_3), 7.2–7.4 (5 H, m, aryl), 7.45–7.6 (5 H, m, aryl), 8.02 (1 H, br s, 3-H).

2-Benzoyl-5-benzyl-7,7-dichloro-5-ethoxycarbonyl-2-azabicyclo-[4.1.0]heptane 21

2-Benzoyl-5-benzyl-7,7-dichloro-5-ethoxycarbonyl-2-azabicyclo[4.1.0]hept-3-ene **16** (1.5 g, 3.49 mmol), lithium carbonate (0.75 g, 10.5 mmol), ethanol (150 cm^3) and 10% palladium on charcoal (150 mg) were hydrogenated in a Cook hydrogenator (50 psi/25 °C), for 7 days. The catalyst was then removed by filtration through kieselguhr and the filtrate was concentrated *in vacuo*, to produce a viscous oil. Purification by column chromatography (eluent: 30% ethyl acetate–hexane), produced a colourless solid (1.01 g, 61%), mp 114–115 °C (Found: C, 64.2; H, 5.4; Cl, 16.4; N, 3.15%; M^+, 435.0971, 433.1017, 431.1051. $C_{23}H_{23}Cl_2NO_3$ requires C, 63.9; H, 5.4; Cl, 16.4; N, 3.2%; *M*, 435.0996, 433.1026, 431.1055); ν_{max}(KBr)/cm^{-1} 1750 and 1651 (C=O str); δ_H(400 MHz, $CDCl_3$) 1.25 (3 H, t, *J* 7.2, CH_2CH_3), 1.6–2.4 (3 H, m, ring C–H), 2.8–3.2 (3 H, m, ring C–H and PhCH_2), 3.3–3.7 (1 H, 2 × br d, ring C–H), 3.8–4.5 (3 H, m, ring C–H and CH_2CH_3), 7.05 (2 H, m, aryl), 7.30 (3 H, m, aryl), 7.45 (3 H, m, aryl), 7.65 (2 H, m, aryl).

Cyclodehydration of 2-benzoyl-5-benzyl-7,7-dichloro-5-ethoxy-carbonyl-2-azabicyclo[4.1.0]heptane 21

The azabicycloheptane (0.45 g, 1.04 mmol) and polyphosphoric acid (40 g) were stirred for 5 days at 120 °C. The system was cooled to 60 °C and poured into ice–water, then basified with aqueous sodium hydroxide and extracted with dichloromethane. The dried (Na_2SO_4) extracts were filtered and concentrated *in vacuo*, to produce a dark solid. Purification by column chromatography (eluent: 50% ethyl acetate–hexane) and recrystallisation (ethyl acetate) yielded 2-benzoyl-7,7-dichlorospiro[(2-azabicyclo[4.1.0]heptane)-5,2′-indan]-1′-one **22** as a colourless micro-crystalline solid (0.33 g, 82%), mp 184–185 °C (Found: C, 65.2; H, 4.5; Cl, 18.3; N, 3.6%; M^+, 389.0576, 387.0616, 385.0626. $C_{21}H_{17}Cl_2NO_2$ requires C, 65.3; H, 4.45; Cl, 18.4; N, 3.6%; *M*, 389.0578, 387.0607, 385.0636); ν_{max}(KBr)/cm^{-1} 3080, 3055 and 3005 (aromatic C–H str), 2955 and 2900 (aliphatic C–H str), 1727 and 1650 (C=O str); δ_H(250 MHz, $CDCl_3$) 1.25–2.05 (2 H, m, ring C–H), 2.5–3.05 (2 H, br dt and br t, ring C–H), 3.05–3.4 (3 H, m, ring C–H and PhCH_2), 3.8–4.7 (1 H, 2 × br d, ring C–H), 7.45 (6 H, m, aryl), 7.6 (2 H, m, aryl), 7.85 (1 H, d, aryl).

Hydrogenolysisof2-benzoyl-5-benzyl-7,7-dichloro-4-ethoxycarb-onyl-2-azabicyclo[4.1.0]hept-3-ene 17

The 2-azabicyclo[4.1.0]heptene (0.18 g, 0.42 mmol), triethylamine (0.5 cm^3), ethanol (150 cm^3) and 10% palladium on charcoal (100 mg) were shaken in a Cook hydrogenator (50 psi/25 °C), for 7 days. The catalyst was then removed by filtration through kieselguhr and the filtrate was concentrated *in vacuo*, to produce a two component system (TLC). Purification by column chromatography (eluent: 25% ethyl acetate–hexane) afforded starting material (0.05 g, 28%), 2-azabicycloheptane **25** (0.09 g, 49%), mp 112–114 °C and 2-azabicycloheptane **26** (trace amount), mp 118 °C.

2-Benzoyl-5-benzyl-7,7-dichloro-4-ethoxycarbonyl-2-azabicyclo[4.1.0]heptane 25 (Found: C, 63.7; H, 5.4; N, 3.2%; M^+, 435.1004, 433.1021, 431.1045. $C_{23}H_{23}Cl_2NO_3$ requires C, 63.9; H, 5.4; N, 3.2%; *M*, 435.0996, 433.1026, 431.1055); ν_{max}(KBr)/cm^{-1} 1730 (C=O str); δ_H(250 MHz, $CDCl_3$) 1.32 (3 H, t, *J* 7.1, CH_2CH_3), 1.72 (1 H, dd, *J* 4.4 and 10.4, 6-H), 2.4 (2 H, m, 4-H and 5-H), 2.62 (1 H, dd, *J* 9.8 and 13.8, PhCH_2), 3.15 (3 H, m, 1-H, 3-H and PhCH_2), 4.21 (2 H, q, *J* 7.1, CH_2CH_3), 4.42 (1 H, dd, *J* 3.8 and 12.8, 3-H), 7.1–7.6 (10 H, m, aryl).

2-Benzoyl-5-benzyl-7-chloro-4-ethoxycarbonyl-2-azabicyclo-[4.1.0]heptane 26. (Found: M^+, 399.1409, 397.1454. $C_{23}H_{24}ClNO_3$ requires *M*, 399.1415, 397.1445); ν_{max}(KBr)/cm^{-1} 1730 (C=O str); δ_H(250 MHz, $CDCl_3$) 1.32 (4 H, t, *J* 7.1, CH_2CH_3 and ring C–H), 2.3–2.7 (2 H, m, ring C–H and PhCH_2), 2.81 (1 H, m, ring C–H), 3.05–3.25 (2 H, m, ring C–H and PhCH_2), 3.55 (1 H, br s, ring C–H), 4.07 (1 H, br s, ring C–H), 4.20 (2 H, q, *J* 7.1, CH_2CH_3), 4.38 (1 H, dd, *J* 4.1 and 13.2, ring C–H), 7.15–7.50 (10 H, m, aryl).

Hydrogenolysis of 2-benzoyl-5-benzyl-7,7-dibromo-5-ethoxy-carbonyl-2-azabicyclo[4.1.0]hept-3-ene 11

The 2-azabicyclo[4.1.0]heptene (0.2 g, 0.39 mmol), lithium carbonate (0.06 g, 0.85 mmol), ethanol (150 cm^3) and 10% palladium on charcoal (100 mg) were hydrogenated in a Cook hydrogenator (50 psi/25 °C), for 3 days. The catalyst was then removed by filtration through kieselguhr and the filtrate was concentrated *in vacuo*, to produce a two component system (TLC). Purification by column chromatography (eluent: 20% ethyl acetate–hexane) afforded some starting material (mp, TLC and ^{1}H NMR were consistent with authentic starting material), 7-bromo-2-azabicycloheptene **19** (0.08 g, 45%), a viscous oil and 7-bromo-2-azabicycloheptane **20** (trace amount), a colourless solid, mp 94–97 °C.

2-Benzoyl-5-benzyl-7-bromo-5-ethoxycarbonyl-2-azabicyclo-[4.1.0]hept-3-ene 19. (Found: M^+, 439.0777. $C_{23}H_{22}BrNO_3$ requires *M*, 439.0783); ν_{max}(film)/cm^{-1} 1727 and 1651 (C=O str); δ_H(250 MHz, $CDCl_3$) 1.26 (3 H, m, CH_2CH_3), 1.9–2.4 (1 H, m, ring C–H), 2.9–3.3 (3 H, m, ring C–H and PhCH_2), 3.4–3.8 (1 H, m, ring C–H), 4.2 (2 H, m, CH_2CH_3), 4.4–6.6 (2 H, 4 × br d, *J* 8.5, 3-H and 4-H), 7.0–7.6 (10 H, m, aryl).

2-Benzoyl-5-benzyl-7-bromo-5-ethoxycarbonyl-2-azabicyclo-[4.1.0]heptane 20. (Found: C, 62.8; H, 5.6; N, 3.1%; M^+, 443.0908, 441.0932. $C_{23}H_{24}BrNO_3$ requires C, 62.45; H, 5.5; N, 3.2%; *M*, 443.0919, 441.0940); ν_{max}(KBr)/cm^{-1} 1735 and 1660 (C=O str); δ_H(250 MHz, $CDCl_3$) 1.30 (3 H, t, *J* 7.1, CH_2CH_3), 1.65 (1 H, dt, *J* 3.4 and 14.4, 4-H), 1.85–1.90 (2 H, m, 4-H and cyclopropyl C–H), 2.83 (1 H, dd, *J* 2.7 and 4.5, cyclopropyl C–H), 3.05–3.15 (3 H, m, cyclopropyl C–H, PhCH_2 and 3-H), 3.28 (1 H, d, *J* 13.8, PhCH_2), 4.14 (1 H, m, 3-H), 4.14–4.35 (2 H, m, CH_2CH_3), 7.07 (2 H, d, *J* 6.5, aryl), 7.28 (3 H, m, aryl), 7.45–7.5 (3 H, m, aryl), 7.6 (2 H, m, aryl).

2-Benzoyl-5-benzyl-5-ethoxycarbonyl-2-azabicyclo[4.1.0]heptane 18

The dibromo-2-azabicyclo[4.1.0]heptene **11** (0.2 g, 0.39 mmol), lithium carbonate (0.06 g, 0.85 mmol), ethanol (150 cm^3) and 10% palladium on charcoal (100 mg) were hydrogenated in a Cook hydrogenator (50 psi/25 °C), for 10 days. The catalyst was then removed by filtration and the filtrate was concentrated *in vacuo*. Purification by column chromatography (eluent: 40% ethyl acetate–hexane) afforded the product (0.06 g, 43%), mp 131–133 °C (Found: C, 75.7; H, 6.7; N, 3.75%; M^+, 363.1831. $C_{23}H_{25}NO_3$ requires C, 76.0; H, 6.9; N, 3.85%; *M*, 363.1834); ν_{max}(KBr)/cm^{-1} 1729, 1640 (C=O str); δ_H(400 MHz, $CDCl_3$) 0.50–0.65 (1 H, m, cyclopropyl C–H), 0.75–1.25 (1 H, m, cyclopropyl C–H), 1.28 (3 H, t, *J* 7.1, CH_2CH_3), 1.40–1.65 (2 H, m, cyclopropyl C–H and 4-H), 1.75 (1 H, m, 4-H), 2.8–4.1 (5 H, m, cyclopropyl C–H, 3-H and PhCH_2), 4.19 (2 H, m, CH_2CH_3), 7.0–7.15 (2 H, m, aryl), 7.2–7.3 (3 H, m, aryl), 7.4–7.45 (3 H, m, aryl), 7.6–7.65 (2 H, m, aryl).

Hydrogenolysis of 2-benzoyl-5-benzyl-7,7-dibromo-4-ethoxycarbonyl-2-azabicyclo[4.1.0]hept-3-ene 12

The dibromo-2-azabicyclo[4.1.0]heptene (0.2 g, 0.39 mmol), triethylamine (0.5 cm^3), ethyl acetate (150 cm^3) and 10% palladium on charcoal (100 mg) were hydrogenated in a Cook hydrogenator (50 psi/25 °C), for 9 days. The catalyst was then removed by filtration and the filtrate was concentrated *in vacuo*, to produce a two component system (TLC). Purification by column chromatography (eluent: 20% ethyl acetate–hexane) afforded 7-*exo*-bromo-2-azabicycloheptene **23** (0.05 g, 29%), a colourless, viscous oil and 7-*endo*-bromo-2-azabicycloheptene **24** (0.04 g, 23%), a colourless solid, mp 128–130 °C.

2-Benzoyl-5-benzyl-7-*exo*-bromo-4-ethoxycarbonyl-2-azabicyclo[4.1.0]hept-3-ene 23. (Found: M^+, 439.0779. $C_{23}H_{22}BrNO_3$ requires *M*, 439.0783); ν_{max}(film)/cm^{-1} 1730, 1700 and 1650 (C=O str); δ_H(250 MHz, $CDCl_3$) 1.29 (3 H, t, *J* 7.1, CH_2CH_3), 1.91 (1 H, dd, *J* 4.6 and 9.7, 6-H), 2.69 (1 H, dd, *J* 8.2 and 13.3, $PhCH_2$), 3.10 (1 H, dd, *J* 2.7 and 4.6, 7-H), 3.18 (1 H, dd, *J* 3.5 and 13.3, $PhCH_2$), 3.52 (1 H, dd, *J* 3.5 and 8.2, 5-H), 3.58 (1 H, br s, 1-H), 4.21 (2 H, q, *J* 7.1, CH_2CH_3), 7.2–7.4 (5 H, m, aryl), 7.45–7.6 (5 H, m, aryl), 7.75 (1 H, br s, 3-H).

2-Benzoyl-5-benzyl-7-*endo*-bromo-4-ethoxycarbonyl-2-azabicyclo[4.1.0]hept-3-ene 24. (Found: M^+, 441.0752, 439.0774. $C_{23}H_{22}BrNO_3$ requires *M*, 441.0763, 439.0783); ν_{max}(KBr)/cm^{-1} 1700, 1650 (C=O str); δ_H(250 MHz, $CDCl_3$) 1.30 (3 H, t, *J* 7, CH_2CH_3), 1.72 (1 H, dd, *J* 9.1 and 9.1, 6-H), 2.60 (1 H, dd, *J* 10 and 13, $PhCH_2$), 3.02 (1 H, dd, *J* 3 and 10, 5-H), 3.26 (1 H, br s, 7-H), 3.35 (1 H, dd, *J* 3 and 13, $PhCH_2$), 3.5 (1 H, br s, 1-H), 4.23 (2 H, q, *J* 7, CH_2CH_3), 7.2–7.35 (5 H, m, aryl), 7.4–7.6 (5 H, m, aryl), 7.9 (1 H, br s, 3-H).

Lithium aluminium hydride reduction of 2-benzoyl-5-benzyl-7,7-dibromo-5-ethoxycarbonyl-2-azabicyclo[4.1.0]hept-3-ene 11

The dibromo-2-azaheptene (0.01 g, 193 mmol) in dried THF (5 cm^3) was added to a stirred suspension of lithium aluminium hydride (190 mg, 5.1 mmol) in dry THF (15 cm^3). The reaction was stirred at room temperature for 1.5 h, before excess hydride was destroyed by dropwise addition of a minimum amount of water. The organic phase was filtered and the remaining solid was washed with dichloromethane (3 × 15 cm^3). The organic extracts were dried (Na_2SO_4), filtered and concentrated *in vacuo*, to give a mobile, orange oil. Purification by column chromatography (eluent: 20% ethyl acetate–hexane) afforded the unstable hemiaminal ether **14** as a colourless oil (40 mg, 68%) (Found: M^+, 305.1780. $C_{21}H_{23}NO$ requires *M*, 305.1780); ν_{max}(film)/cm^{-1} 3080, 3030 and 3005 (aromatic C–H str), 2940 and 2875 (aliphatic C–H str), 1651 and 1625 (C=C str); δ_H(250 MHz, $CDCl_3$) 0.23 (1 H, dt, *J* 6 and 9, 7-H), 0.72 (1 H, dt, *J* 4 and 6, 7-H), 1.42 (1 H, dt, *J* 6 and 9, 6-H), 1.71 (1 H, dd, exch., *J* 5.3 and 10.5, 4-H), 1.82 (1 H, d, exch., *J* 10.5, 4-H), 2.01 (1 H, ddd, *J* 4, 6.6 and 8.1, 1-H), 2.89 (1 H, d, *J* 13.6, $PhCH_2$), 3.01 (1 H, d, *J* 13.6, $PhCH_2$), 3.38 (1 H, d, *J* 7.8, CH_2-O), 3.58 (1 H, d, *J* 7.8, CH_2–O), 3.78 (1 H, d, *J* 13.2, $PhCH_2$), 3.89 (1 H, d, *J* 13.2, $PhCH_2$), 4.78 (1 H, d, collapses to singlet with D_2O, *J* 5.3, 3-H), 7.2–7.4 (10 H, m, aryl).

1,4-Dibenzoyl-4-ethoxycarbonylpiperidine 1 (R^1 = R^2 = PhCO)

1,4-Dibenzoyl-4-ethoxycarbonyl-1,4-dihydropyridine **2** (R^1 = R^2 = PhCO) (0.6 g, 1.66 mmol), ethanol (200 cm^3) and platinum oxide (200 mg) were hydrogenated at atmospheric temperature and pressure. The catalyst was then removed by filtration through kieselguhr and the filtrate concentrated *in vacuo*. Purification by Kugelrohr distillation and column chromatography (eluent: 40% ethyl acetate–hexane), afforded the product **1** (R^1 = R^2 = PhCO) as a colourless, viscous oil (0.12 g, 19%), bp 170 °C/0.01 mmHg, 1-benzoyl-4-ethoxycarbonylpiperidine **1** (R^1 = PhCO, R^2 = H), a colourless crystalline solid (0.09 g, 21%), mp 73–75 °C and benzoic acid (trace amount).

1,4-Dibenzoyl-4-ethoxycarbonylpiperidine 1 (R^1 = R^2 = PhCO). (Found: C, 72.0; H, 6.45; N, 3.7%; M^+, 365.1634. $C_{22}H_{23}NO_4$ requires C, 72.3; H, 6.3; N, 3.8%; *M*, 365.1627); ν_{max}(film)/cm^{-1} 1730 and 1680 (C=O str); δ_H(250 MHz, $CDCl_3$) 1.10 (3 H, t, *J* 7.1, CH_2CH_3), 2.1–2.45 (4 H, br d, 3-H and 5-H), 3.52 (2 H, br s, ring C–H), 3.77 (1 H, br s, ring C–H), 3.91 (1 H, br s, ring C–H), 4.17 (2 H, q, *J* 7.1, CH_2CH_3), 7.35–7.6 (8 H, m, aryl), 7.82 (2 H, dd, *J* 1.5 and 7.2, aryl).

1-Benzoyl-4-ethoxycarbonylpiperidine[16] 1 (R^1 = PhCO, R^2 = H). (Found: C, 68.9; H, 7.5; N, 5.2%. Calc. for $C_{15}H_{19}NO_3$: C, 68.9; H, 7.3; N, 5.4%); ν_{max}(KBr)/cm^{-1} 1727 (C=O str); δ_H(250 MHz, $CDCl_3$) 1.27 (3 H, t, *J* 7.1, CH_2CH_3), 1.9 (4 H, br d, 3-H and 5-H), 2.57 (1 H, m, 4-H), 3.05 (2 H, br t, ring C–H), 3.75 (1 H, br s, ring C–H), 4.16 (2 H, q, *J* 7.1, CH_2CH_3), 4.55 (1 H, br s, ring C–H), 7.4 (5 H, m, aryl).

Crystal structure determination of dibromocarbene adduct 12

The single crystal of **12** used for X-ray data collection (approx. dimensions 0.5 × 0.4 × 0.35 mm) was grown by slow evaporation from ethanol and mounted in a sealed Lindemann capillary tube.

Crystal data. $C_{23}H_{21}Br_2NO_3$, $M = 519.23$, colourless prisms, triclinic, space group $P\bar{1}$ (No. 2), $a = 6.1634(12)$, $b = 8.851(2)$, $c = 20.354(4)$ Å, $\alpha = 87.34(3)$, $\beta = 89.33(3)$, $\gamma = 74.07(3)°$, $V = 1066.5(4)$ Å^3, $Z = 2$, $D_c = 1.617$ g cm^{-3}, $F(000) = 520$, μ(Mo-Kα) = 3.825 mm^{-1}.

Data collection. The intensity data were collected on an Enraf-Nonius 4-circle diffractometer [temperature 293(2) K; θ range: 1.00 to 24.97°; $0 \leqslant h \leqslant 7$, $-10 \leqslant k \leqslant 10$, $-24 \leqslant l \leqslant 24$] using graphite monochromated Mo-Kα X-radiation (λ 0.710 69 Å) and ω–2θ scanning. Of the 3752 unique data [R(int) = 0.040] data measured, 2714 had $F > 4\sigma(F)$. The data were corrected for Lorentz and polarisation effects, and for absorption (DIFABS[17]).

Structure solution. The approximate positions of the non-hydrogen atoms were determined by direct methods (SHELXS-86[18]). The structure was refined by full-matrix least-squares methods on F^2 (SHELXTL[19]) using all F^2 data and anisotropic temperature factors for all the non-hydrogen atoms. All the hydrogen atoms were located on Fourier difference maps and included in the refinement process at idealised positions with isotropic temperature factors 1.5 times U_{iso} of the bonded heavy atom. At convergence, the discrepancy factors R and R_w [$F > 4\sigma(F)$] were 0.042 and 0.104 respectively. The weighting scheme, $w^{-1} = [\sigma^2(F_o^2) + (0.0617\ P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$, was found to give satisfactory analyses of variance. The final difference Fourier map was essentially featureless (general noise level less that ±0.3 e Å^{-3}) with largest difference peak and hole of 0.436 and −0.848 e Å^{-3} respectively.‡

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‡ Atomic coordinates, thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1996, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/42.

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