Bridged-ring Nitrogen Compounds. Part 2.[1] Synthesis and Reduction of 6,7,8,9-Tetrahydro-6,9-iminobenzocyclohepten-5-ones

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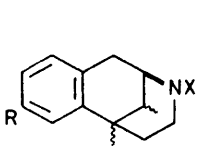
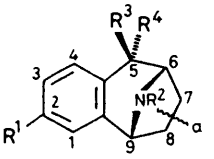
A novel synthesis of the title compounds is described: their reduction and reaction with Grignard reagents have been studied.

ANALOGUES of benzomorphans (hexahydro-2,6-methano-3-benzazocines) (1) are of current interest [2] as potential analgesics.

We have endeavoured to obtain bridged-ring systems which contain parts of the benzomorphan (or morphine) molecule in which the bond angles have been distorted by changing the ring sizes (in principle). The title compounds (2) comprise the first of these systems.



(1)

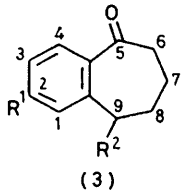


(2)

The one previous synthesis [3] of simple examples of this type of compound employed the strategy of utilising a 1,3-difunctionalised isoquinoline derivative [bond fission 'a' in (2)] which gave a 2,3-dimethoxy-7-oxo-derivative which was reduced by the Wolff–Kishner method. Our previous work on 6,7,8,9-tetrahydrobenzocyclohepten-5-ones [4] (benzosuberones) led us to hope that these might serve as more accessible precursors for the present task and this proved to be so.

RESULTS AND DISCUSSION

It has been known for some time [5] that benzosuberone (3; $R^1 = R^2 = H$) reacts with *N*-bromosuccinimide (NBS) to give the 9-bromo-compound (3; $R^1 = H$, $R^2 = Br$). We found that reaction of the latter with several primary amines led to elimination rather than nucleophilic displacement. However, reaction of the bromide (3; $R^1 = H$, $R^2 = Br$) with ethylamine in



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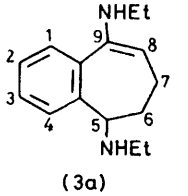
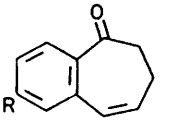


(3a)

ethanol gave the enamine (3a) of the desired amino-compound (3; $R^1 = H$, $R^2 = NHEt$) isolated *via* the hydrobromide salt. When the enamine was brominated in acetic acid a new substance was isolated in good yield (75—85%); this was the hydrobromide of compound (2; $R^1 = H$, $R^2 = Et$, $R^3,R^4 = O$), which was liberated as the free base in the usual way. It was a relatively stable pale yellow oil; the structure assigned is based on satisfactory elemental analysis, and mass spectral, i.r., and n.m.r. data (see Experimental section): of particular significance was the double quartet for the methylene hydrogens of the ethyl group in the n.m.r. spectrum, which confirm prochirality in this group of molecules. A minor by-product was the de-ethylated compound (2; $R^1 = R^2 = H$, R^3, $R^4 = O$) which we presume was due to the action of hydrogen bromide (generated in the reaction) upon the product or its precursor.

Synthesis of the methoxy-analogue (2; $R^1 = OMe$, $R^2 = Et$, $R^3,R^4 = O$) was more troublesome. In the first place, NBS treatment of methoxybenzosuberone [4] (3; $R^1 = OMe$, $R^2 = H$) gave a less clean conversion to one major monobromo-compound, and it was necessary to confirm that this was the desired product (3; $R^1 =$ OMe, $R^2 = Br$) and not an isomer (*cf.* ref. 6). This was done by dehydrobromination to (4; R = OMe) and



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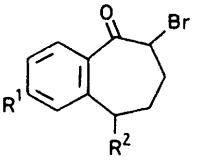

(5)

relation of this product to materials prepared previously.[7] Thus the acetate (4; R = OAc) was hydrolysed to the phenol (4; R = OH) which was methylated giving the same enone (4; R = OMe) as that described above. After repeated attempts to react the bromo-compound (3; $R^1 = OMe$, $R^2 = Br$) with ethylamine had given very complex mixtures, an alternative procedure was desirable. Bromination of the monobromide (3; $R^1 = OMe$, $R^2 = Br$) with copper bromide in ethyl acetate [8] gave the dibromide as an inseparable mixture of isomers (5; $R^1 = OMe$, $R^2 = Br$); its structure was confirmed by ^1H n.m.r. spectroscopy which showed, *inter alia*, two triplets for protons at C-6 and C-9 in about the same positions as the relevant signals in the monobromo-ketones (3; $R^1 = OMe$, $R^2 = Br$) and (5; $R^1 = OMe$, $R^2 = H$). Reaction of the dibromide (5; $R^1 = OMe$, $R^2 = Br$) mixture with ethylamine yielded a mixture of bases from which the desired compound (2;

R^1 = OMe, R^2 = Et, R^3,R^4 = O) was obtained in 20% yield by chromatography. Its structure was confirmed by spectroscopy as in the case of the amino-ketone (2; R^1 = H, R^2 = Et, R^3,R^4 = O) above. The latter was also obtained by the modified method using the dibromide (5; R^1 = H, R^2 = Br) but the overall yield was poorer than that obtained originally. It is probably not surprising that a double nucleophilic displacement by ethylamine on a dibromide (*e.g.* 5; R^1 = OMe, R^2 = Br) was not particularly fruitful since such a reaction requires *cis*-geometry of the two bromine atoms. Attempts to partially invert the dibromide mixture (5; R^1 = OMe, R^2 = Br) with iodide ion, before reaction with ethylamine, led to no improvement in yield. Working with the *O*-benzoates or *O*-acetates (3; R^1 = OCOPh or OAc) led to no improvements; for example, reaction of the bromobenzoate (3; R^1 = OCOPh, R^2 = Br) with ethylamine gave a complex reaction mixture from which *N*-ethylbenzamide was crystallised.

It is known that reduction or Grignard addition to bridged α-amino-ketones is mostly governed by steric rather than electronic effects.[9-11] N.m.r.[10] or i.r. spectroscopy [9,11] has been used to determine the stereochemistry of the products. In the present case, models indicate that the relevant dihedral angles of the C–H bonds at C-5 and C-6 are either around 45 or 80°, depending on whether the hydroxy group is α or β, and indeed the n.m.r. spectra of the two isomers obtained by borohydride reduction of ketone (2; R^1 = OMe, R^2 = Et, R^3, R^4 = O) showed $J_{5,6}$ = 5 and 2 Hz respectively; the minor (β) isomer showed a weak but distinct intramolecular hydrogen bond not seen in the major isomer. Accordingly we deduce that the minor isomer is (2; R^1 = OMe, R^2 = Et, R^3 = OH, R^4 = H) and that the major isomer has structure (2; R^1 = OMe, R^2 = Et, R^3 = H, R^4 = OH). The latter was the only product obtained by catalytic hydrogenation (Pd–C); no further reduction could be brought about by hydrogenation in the presence of acid at 4.5 atm. The fully reduced material (2; R^1 = OMe, R^2 = Et, R^3 = R^4 = H) could not be obtained by $LiAlH_4$ treatment of the tosyl derivative of (2; R^1 = OMe, R^2 = Et, R^3 = H, R^4 = OH) nor by a modified Wolff–Kishner reduction.[12] Traditional Wolff–Kishner [13] treatment gave the amino-alcohol (2; R^1 = OMe, R^2 = Et, R^3 = H, R^4 = OH) along with unreacted amino-ketone (2; R^1 = OMe, R^2 = Et, R^3, R^4 = O).

Reaction of both bridged amino-ketones with phenyl magnesium bromide gave the expected tertiary alcohols, neither of which showed intramolecular hydrogen-bonding in their i.r. spectra; accordingly they are regarded as having structures (2; R^1 = H and OMe, R^2 = Et, R^3 = Ph, R^4 = OH).

None of the 6,9-iminobenzocycloheptenes (2) prepared in this work showed any biological activity; presumably this ring system differs structurally from benzomorphans too drastically. Future work will be directed towards molecules with less disparate bond angles to those of benzomorphans.[2]

EXPERIMENTAL

5,9-Bis(ethylamino)-6,7-dihydro-5H-benzocycloheptene (3a).—9-Bromo-6,7,8,9-tetrahydrobenzocyclohepten-5-one [5,7] (3; R^1 = H, R^2 = Br) (2.3 g) in ethanol (5 ml) was added dropwise during 1 h with stirring to ethanolic ethylamine (10 ml; 10% w/v). After rapid extraction of the mixture with dilute hydrochloric acid the *product* (1.35 g) was obtained by basification (cooling), extraction, and distillation at 98—102 °C and 0.1 mmHg (Found: C, 78.25; H, 9.55; N, 12.5%; M^+, 230.177 8. $C_{15}H_{22}N_2$ requires C, 78.35; H, 9.65; N, 12.2%; *M*, 230.178 3); $\nu_{max.}$ (film) 3 340 (NH) and 1 685w (C=C) cm^{-1}; τ 2.7—3.15 (4 H, m, aryl-H), 5.8 (1 H, s, 8-H), 7.1—7.85 (4 H, m, 2 CH_2CH_3), 8.0—9.2 [13 H, m, overlapping 5-H, 6-H_2, 9-H_2, 2 CH_3CH_2 and 2 NH (exchangeable)]. The hydrobromide had m.p. >250 °C (Found: C, 46.0; H, 5.85; N, 7.35. $C_{15}H_{24}Br_2N_2$ requires C, 45.95; H, 6.15; N, 7.15%).

9-Ethylamino-6,7,8,9-tetrahydro-5-hydroxybenzocycloheptene Hydrobromide.—5,9-Bis(ethylamino)-6,7-dihydro-5*H*-benzocycloheptene (3a) (1 g) was hydrogenated in acetic acid with platinum oxide (0.1 g). The usual work-up yielded an oily base which was converted into the *hydrobromide* (0.5 g) with hydrogen bromide in acetic acid. It had m.p. >250 °C (Found: C, 54.8; H, 7.2; N, 4.7. $C_{13}H_{20}BrNO$ requires C, 54.45; H, 7.3; N, 4.9%). The free base was a mixture of *cis* and *trans* isomers; τ 2.66—2.98 (4 H, m, aryl-H), 6.2—6.4 (2 H, m, CH_2CH_3), 7.0—8.65 [10 H, m, ring CH and CH_2, and NH and OH (exchangeable)], and 8.65—9.1 (3 H, m, CH_3CH_2).

6,9-Ethylimino-6,7,8,9-tetrahydrobenzocyclohepten-5-one (2; R^1 = H, R^2 = Et, R^3,R^4 = O).—5,9-Bis(ethylamino)-6,7-dihydro-5*H*-benzocycloheptene hydrobromide (3a·HBr) (20 g), anhydrous sodium carbonate (10 g), and chloroform (800 ml) were stirred while bromine (16 g) in chloroform (200 ml) was added dropwise during 1 h. After being stirred overnight the reaction mixture was filtered, evaporated to dryness, and the residue crystallised from methanol to give the hydrobromide of the *product* (7.1 g), m.p. >250 °C (Found: C, 54.5; H, 6.8; N, 5.2. $C_{13}H_{16}BrNO$ requires C, 54.75; H, 6.65; N, 4.9%). A second crop (2.5 g) was set aside (see below). The *free base* (4.9 g) had b.p. 130 °C at 0.1 mmHg (Found: C, 77.0; H, 7.45; N, 6.7%; M^+, 201.114 5. $C_{13}H_{15}NO$ requires C, 77.5; H, 7.5; N, 6.95%; *M*, 201.115 4); $\nu_{max.}$ (film) 1 685 (br) cm^{-1} (C=O); τ 2.05 (1 H, dd, *J* 9 and 1 Hz, 4-H), 2.45—2.9 (3 H, m, 1-, 2-, and 3-H), 5.75—5.8 (1 H, m, 6-H), 6.15—6.25 (1 H, m, 9-H), 7.5 (2 H, dq, CH_2CH_3), 7.5—7.75 (2 H, m, ring CH_2), 8.25—8.43 (2 H, m, ring CH_2), and 8.93 (3 H, t, CH_3CH_2). The second crop of hydrobromide from above was basified to yield a further quantity of free base (80%) contaminated with a second base (20%) which was separated by p.l.c. It was *6,7,8,9-tetrahydro-6,9-iminobenzocyclohepten-5-one* (2; R^1 = R^2 = H, R^3,R^4 = O), b.p. 100 °C at 0.05 mmHg (Found: M^+, 173.081 7. $C_{11}H_{11}NO$ requires *M*, 173.084 1); τ 2.2 (1 H, dd, *J* 9 and 1 Hz, 4-H), 2.6—3.03 (3 H, m, 1-, 2-, and 3-H), 5.6—5.7 (1 H, m, 6-H), 5.95—6.1 (1 H, m, 9-H), 7.3—7.6 (1 H, br, exchangeable, NH), 7.6—7.8 (2 H, m, ring CH_2), and 8.2—8.4 (2 H, m, ring CH_2). The deuteriated sample was redistilled (Found: C, 75.55; H, 6.3; N, 8.0. $C_{11}H_{10}DNO$ requires C, 75.9; H, 6.75; N, 8.05%).

6,9-Ethylimino-(6,7,8,9-tetrahydro-5α-hydroxybenzocycloheptene (2; R^1 = R^3 = H, R^2 = Et, R^4 = OH).—6,9-Ethylimino-6,7,8,9-tetrahydrobenzocyclohepten-5-one (2; R^1 = H, R^2 = Et, R^3,R^4 = O) (2 g) in ethanol (100 ml)

was stirred overnight with sodium borohydride (1.14 g). The usual work-up yielded a mixture of two epimers (1.45 g), b.p. 140 °C at 0.05 mmHg, from which the desired material was obtained (775 mg) by repeated crystallisation from benzene–light petroleum (b.p. 60—80 °C). It had m.p. 95—96 °C (Found: C, 76.3; H, 8.55; N, 6.65%; M^+, 203.130 1. $C_{13}H_{17}NO$ requires C, 76.8; H, 8.35; N, 6.9%; M, 203.131 0); $\nu_{max.}(CCl_4)$ 3 600 and 3 050—3 400 (br, OH, disappears on dilution) cm^{-1}; τ 2.7—3.3 (4 H, m, aryl-H), 5.15 (1 H, d, J 7 Hz, 5-H), 5.9—6.2 (1 H, m, 6-H), 6.45—6.8 (1 H, m, 9-H), 6.8—7.2 (1 H, br s, exchangeable, OH), 7.6 (2 H, dq, CH_2CH_3), 7.75—8.6 (4 H, m, ring CH_2CH_2), and 8.9 (3 H, t, CH_3CH_2).

6,9-*Ethylimino*-6,7,8,9-*tetrahydro*-5α-*hydroxy*-5β-*phenylbenzocycloheptene* (2; R^1 = H, R^2 = Et, R^3 = Ph, R^4 = OH).—6,9-Ethylimino-6,7,8,9-tetrahydrobenzocyclohepten-5-one (2; R^1 = H, R^2 = Et, R^3,R^4 = O) (2.01 g) in dry ether (50 ml) was treated with the Grignard reagent from bromobenzene (3.14 g), magnesium (0.5 g), and dry ether (120 ml). The usual work-up yielded, after chromatography, the product, m.p. 125 °C (decomp.) (2.28 g) (Found: C, 82.05; H, 7.85; N, 5.35%; M^+, 279.162 7. $C_{19}H_{21}NO$ requires C, 81.8; H, 7.6; N, 5.0%; M, 279.162 3); $\nu_{max.}(CCl_4)$ 3 600 and 3 050—3 500 (br, OH, disappears on dilution) cm^{-1}; τ 2.7—3.2 (9 H, m, aryl-H), 6.0—6.1 (1 H, m, 6-H), 6.6—6.73 (1 H, m, 9-H), 7.45—7.65 (1 H, br, exchangeable, OH), 7.6—8.55 (6 H, m, ring CH_2CH_2 and CH_2CH_3), and 9.37 (3 H, t, CH_3CH_2).

9-*Bromo*-6,7,8,9-*tetrahydro*-2-*methoxybenzocyclohepten*-5-*one* (3; R^1 = OMe, R^2 = Br).—6,7,8,9-Tetrahydro-2-methoxybenzocyclohepten-5-one [7] (12 g), *N*-bromosuccinimide (11.2 g), carbon tetrachloride (150 ml), and benzoyl peroxide (200 mg) were refluxed over a 150 W bulb until all the *N*-bromosuccinimide was consumed. The usual work-up gave the product (15 g), b.p. 140 °C at 0.05 mmHg (Found: C, 53.2; H, 4.8; Br, 29.45. $C_{12}H_{13}BrO_2$ requires C, 53.6; H, 4.85; Br, 29.7%); $\nu_{max.}$ (film) 1 670 (C=O) cm^{-1}; τ 2.35—2.65 (1 H, m, aryl-H), 3.2—3.48 (2 H, m, aryl-H), 5.2—5.33 (1 H, dd, 9-H), 6.25 (3 H, s, OMe), and 7.0—8.35 (6 H, m, 6-, 7-, and 8-H_2).

cis- *and* trans-6,9-*Dibromo*-6,7,8,9-*tetrahydro*-2-*methoxybenzocyclohepten*-5-*one* (5; R^1 = OMe, R^2 = Br).—9-Bromo-6,7,8,9-tetrahydro-2-methoxybenzocyclohepten-5-one (8.7 g), copper(II) bromide (11.27 g), chloroform (50 ml), and ethyl acetate were stirred and refluxed for 6 h. Work-up [8] gave the *product* (9 g), b.p. 150 °C at 0.05 mmHg (Found: Br, 45.7%; M^+, 349.915 6, 347.919 2, and 345.918 3. $C_{12}H_{12}Br_2O_2$ requires Br, 45.9%; M, 349.916 6, 349.918 5, and 345.920 5. Carbon analyses were *ca.* 2% high); $\nu_{max.}$ (film) 1 680 and 1 690 cm^{-1} (C=O); τ 2.4—2.54 (1 H, m, aryl-H), 3.2—3.4 (2 H, m, aryl-H), 4.6—4.72 (1 H, m, 6-H), 5.0—5.12 (1 H, m, 9-H), 6.23 (3 H, s, OMe), and 7.0—8.1 (4 H, m, 7- and 8-H_2). T.l.c. showed that this material consisted of two closely spaced spots. Bromination with bromine in chloroform on a small scale yielded the same products but, on a larger scale, an exothermic reaction ensued and material, m.p. 169—171 °C, was obtained (Found: C, 28.6; H, 2.05%; M^+, 509.740 6, 507.734 6, 505.736 6, 503,738 1, and 501.740 4. $C_{12}H_{10}Br_4O_2$ requires C, 28.5; H, 2.0%; M, 509.740 6, 507.735 7, 505.737 7, 503.739 7, and 501.741 6); $\nu_{max.}$ (Nujol) 1 695 cm^{-1} (C=O); τ 2.25 (1 H, s, 4-H), 3.2 (1 H, s, 1-H), 4.6—4.8 (1 H, m, 9-H), 6.0 (3 H, s, OMe), and 6.3—7.8 (4 H, m, 7- and 8-H_2). This material was therefore 3,6,6,9-*tetrabromo*-6,7,8,9-*tetrahydro*-2-*methoxybenzocyclohepten*-5-*one*.

6-*Bromo*-6,7,8,9-*tetrahydro*-2-*methoxybenzocyclohepten*-5-*one* (5; R^1 = OMe, R^2 = H).—6,7,8,9-Tetrahydro-3-methoxybenzocyclohepten-5-one [7] (5 g), copper(II) bromide (11.15 g), chloroform (50 ml), and ethyl acetate (50 ml) were refluxed for 6 h. Work-up [8] gave an oil, b.p. 120 °C at 0.05 mmHg (Found: C, 52.65; H, 4.8; Br, 29.65. $C_{12}H_{13}BrO_2$ requires C, 53.6; H, 4.85; Br, 29.7%); τ 2.46 (1 H, d, J 9 Hz, 4-H), 3.22—3.48 (2 H, m, 1- and 3-H), 5.16—5.3 (1 H, dd, 6-H), 6.23 (3 H, s, OMe), and 7.0—8.2 (6 H, 3 m, 7-, 8-, and 9-H_2).

6,7-*Dihydro*-2-*methoxybenzocyclohepten*-5-*one* (4; R = OMe).—(*a*) 9-Bromo-6,7,8,9-tetrahydro-2-methoxybenzocyclohepten-5-one (3; R^1 = OMe, R^2 = Br) (2.9 g) and collidine (7 ml) were refluxed for 2.5 h, filtered, and worked up in the usual fashion to yield the *product* (0.5 g), b.p. 115 °C at 0.2 mmHg [Found: C, 76.05; H, 6.65%; M^+, 188.084 2 (100%). $C_{12}H_{12}O_2$ requires C, 76.5; H, 6.4%; M, 188.083 7]; τ 2.2 (1 H, d, 4-H), 3.3—4.06 (4 H, m, aryl + olefinic), 6.25 (3 H, s, OMe), 7.2—7.35 (2 H, m, 6-H_2), and 7.5—7.75 (2 H, m, 7-H_2). (*b*) 6,7-Dihydro-2-hydroxybenzocyclohepten-5-one [7] (4; R = OH) (1.74 g) was refluxed with iodomethane (6 g), potassium carbonate (1.4 g), and acetone (30 ml) for 18 h. The usual work-up gave the *product*, b.p. 120 °C at 0.1 mmHg (1.1 g), identical to that obtained in (*a*).

6,9-*Ethylimino*-6,7,8,9-*tetrahydro*-2-*methoxybenzocyclohepten*-5-*one* (2; R^1 = OMe, R^2 = Et, R^3,R^4 = O).—6,9-Dibromo-6,7,8,9-tetrahydro-2-methoxybenzocyclohepten-5-one (5; R^1 = OMe, R^2 = Br) (27.8 g), ethylamine (27 ml, 40% solution in ethanol), and benzene (50 ml) were refluxed for 1.5 h and the basic fraction (6.2 g) was purified by short-path chromatography on silica (Whatman SO.TLC); ether eluted the *product* (1.55 g), b.p. 160 °C at 0.05 mmHg (Found: C, 72.35; H, 7.6; N, 6.45%; M^+, 231.123 4. $C_{14}H_{17}NO_2$ requires C, 72.8; H, 7.4; N, 6.05%; M, 231.125 9); $\nu_{max.}$ (film) 1 672 (C=O) cm^{-1}; τ 2.25 (1 H, d, 4-H), 3.2—3.5 (2 H, m, 1- and 3-H), 5.8—5.9 (1 H, m, 6-H), 6.1—6.35 (1 H, m, 9-H), 6.2 (3 H, s, OMe), 7.4—7.8 (2 H, m, ring CH_2), 7.5 (2 H, dq, CH_2CH_3), 8.15—8.45 (2 H, m, ring CH_2), and 8.94 (3 H, t, CH_3CH_2).

Reduction of 6,9-*Ethylimino*-6,7,8,9-*tetrahydro*-2-*methoxybenzocyclohepten*-5-*one with Sodium Borohydride*.—The ketone (2; R^1 = OMe, R^2 = Et, R^3,R^4 = O) (3.4 g), sodium borohydride (1.75 g), and ethanol (110 ml) were stirred for 8 h. Work-up gave a gum (2.7 g), partly purified by column chromatography (SiO_2) giving material (2.0 g) comprising two closely spaced spots on t.l.c. A sample (765 mg) of the latter was purified by p.l.c. (15% EtOH–$CHCl_3$) giving first 6,9-*ethylimino*-6,7,8,9-*tetrahydro*-5β-*hydroxy*-2-*methoxybenzocycloheptene* (2; R^1 = OMe, R^2 = Et, R^3 = OH, R^4 = H) (113 mg), R_F 0.85, b.p. 130 °C at 0.05 mmHg [Found: C, 72.0; H, 8.35; N, 5.9%; M^+, 233.140 4 (100%). $C_{14}H_{19}NO_2$ requires C, 72.15; H, 8.2; N, 6.0%; M, 233.141 6]; $\nu_{max.}$ (CCl_4) 3 600, 3 540 (persisting on dilution), and 3 400 cm^{-1} (OH); τ 2.82 (1 H, d, J 9 Hz, 4-H), 3.25—3.65 (2 H, m, 1- and 3-H), 5.94 (1 H, d, J *ca.* 2 Hz, 5-H), 6.08—6.18 (1 H, m, 6-H), 6.3 (3 H, s, OMe), 6.4—6.64 (1 H, m, 9-H), 6.76 (1 H, s, exchangeable, OH), 7.65 (2 H, dq, CH_2CH_3), 7.8—8.8 (4 H, m, 7- and 8-H_2), and 8.88 (3 H, t, CH_3CH_2).

Eluted second was 6,9-*ethylimino*-6,7,8,9-*tetrahydro*-5α-*hydroxy*-2-*methoxybenzocycloheptene* (2; R^1 = OMe, R^2 = Et, R^3 = H, R^4 = OH) (450 mg), R_F 0.5, b.p. 130 °C at 0.05 mmHg [Found: C, 72.0; H, 8.3; N, 6.0%; M^+, 233.140 9 (100%). $C_{14}H_{19}NO_2$ requires C, 72.15; H, 8.2;

N, 6.0%; *M*, 233.141 6]; $\nu_{max.}$ (CCl_4) 3 600 and 3 100—3 400 (br) cm^{-1} (OH, variable with dilution); τ 2.82 (1 H, d, *J* 9 Hz, 1-H), 3.42 (1 H, dd, *J* 9 and 2 Hz, 2-H), 3.61 (1 H, d, *J* 2 Hz, 1-H), 5.13 (1 H, d, *J* 5 Hz, 5-H), 6.18 (1 H, d, *J* 5 Hz, 6-H), 6.33 (3 H, s, OMe), 6.5 (1 H, s, exchangeable, OH), 6.6—6.75 (1 H, m, 9-H), 7.4—7.6 (2 H, q, CH_2CH_3), 7.8—8.6 (4 H, m, 7- and 8-H_2), and 8.86 (3 H, t, CH_3CH_2).

6,9-*Ethylimino*-6,7,8,9-*tetrahydro*-5α-*hydroxy*-2-*methoxy*-5β-*phenylbenzocycloheptene* (2; R^1 = OMe, R^2 = Et, R^3 = Ph, R^4 = OH).—6,9-Ethylimino-6,7,8,9-tetrahydro-2-methoxybenzocyclohepten-5-one (586 mg) in dry ether (30 ml) was added to the Grignard reagent [from magnesium (182 mg) and bromobenzene (1 g)] in dry ether (80 ml). Work-up gave a gum which was purified by p.l.c., yielding the *product* (503 mg), b.p. 150 °C at 0.05 mmHg (Found: C, 78.4; H, 7.4; N, 4.4. $C_{20}H_{23}NO_2$ requires C, 77.75; H, 7.5; N, 4.55%); τ 2.75—3.58 (8 H, m, aryl-H), 6.05—6.15 (1 H, m, 6-H), 6.57—6.73 (1 H, m, 9-H), 6.3 (3 H, s, OMe), 7.35 (1 H, br s, exchangeable, OH), 7.65—7.85 (2 H, dq, CH_2CH_3), 7.8—8.45 (4 H, m, 7- and 8-H_2), and 9.38 (3 H, t, CH_3CH_2).

2-*Benzoyloxy*-6,7,8,9-*tetrahydrobenzocyclohepten*-5-*one* (3; R^1 = OCOPh, R^2 = H).—Treatment of the correspondng phenol [7] (11.7 g) with benzoyl chloride (15 g) in pyridine (70 ml) gave the *product* (16.9 g), b.p. 180—185 °C at 0.1 mmHg (Found: C, 77.55; H, 5.55. $C_{18}H_{16}O_3$ requires C, 77.2; H, 5.75%); $\nu_{max.}$ (film) 1 790, 1 720—1 740 (br) (ester), and 1 680 (C=O) cm^{-1}; τ 1.9—3.1 (8 H, m, aryl-H), 7.05—7.45 (4 H, m, 6- and 9-H_2), and 8.0—8.4 (4 H, m, 7- and 8-H_2). This material (2.8 g) was reacted with *N*-bromosuccinimide as usual giving one major product (t.l.c.) which was reacted with ethylamine in ethanol–benzene as before. The only product isolated was *N*-ethylbenzamide (1.5 g), m.p. 70 °C (lit.,[14] 70—71 °C) (Found: C, 72.5; H, 7.35; N, 9.45. Calc. for $C_9H_{11}NO$; C, 72.5; H, 7.4; N, 9.4%).

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