

Photocyclisation of Enamides. Part 23.¹ Reductive Photocyclisation of Enamides²

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Irradiation of the enamides (1), (9), and (13) in the presence of sodium borohydride led to reductive photocyclisation to afford two types of hydrogenated lactams, the lactams with a conjugated diene moiety (4a–c), (5), (10a and b), and (11) and the lactams with an unconjugated diene moiety (6a–c), (12a and b), and (14) respectively, whose ratios were dependent on the solvent used. Deuterium-incorporation experiments provided important information on the mechanism of this reductive photocyclisation.

In connection with our interest in the reactivity of enamides as unique synthons and also in the evaluation of enamide photocyclisation as an inherently useful synthetic tool, we have undertaken a basic study of the photocyclisation of enamides under newly discovered reductive conditions in the presence of a hydride reagent.

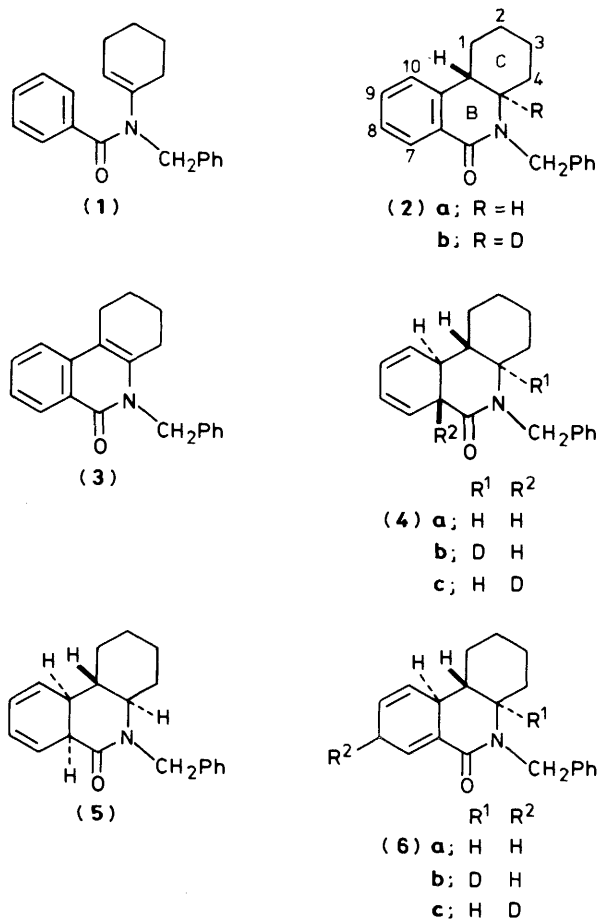
In addition to oxidative and non-oxidative photocyclisations of enamides,^{3,4} this newly discovered reductive photocyclisation disclosed a broader aspect of the cyclisability of enamides, thus establishing the enamide photocyclisation as a simple and most useful methodology for the construction of various types of six-membered lactams (2)–(6) with various oxidation levels.

To a 0.005M solution of the enamide (1) in ether was added an eight-molar amount of sodium borohydride and an amount of methanol sufficient to dissolve the hydride reagent. Irradiation of the above reaction mixture at 5–10 °C with a high-pressure mercury lamp (with Pyrex filter) afforded three hydrogenated lactams (4a), (5), and (6a) and the aromatised lactam (2a) in 11, 16, 43, and 5% yields respectively, of which the latter stable lactam (2a) was found to be identical with an authentic sample of the known octahydrophenanthridone (2a).⁵ Isolation of these products was accomplished by repeated preparative t.l.c. (p.l.c.). On the other hand, similar irradiation of the enamide (1) using acetonitrile as solvent in place of ether gave exclusively the hydrogenated lactam (6a), with an unconjugated diene moiety, in 78% yield. Since these three hydrogenated lactams (4a), (5), and (6a) were readily dehydrogenated into the known B/C-*trans*-lactam (2a)⁵ simply by refluxing in benzene, the B/C-*trans* stereochemistry of these lactams (4a), (5), and (6a) was firmly established.

The diene structures and the remaining stereochemical problems of the lactams (4a), (5), and (6a) were solved from their spectral data along with their behaviour toward the Diels–Alder reaction with maleic acid derivatives as follows.

The first hydrogenated lactam (4a) showed a molecular ion peak at m/z 293 in the mass spectrum, a u.v. absorption at 254 nm (conjugated diene), and n.m.r. peaks at δ_H 6.57 (br d, J 9 Hz, 7-H), 6.20–5.98 (m, 8-, 9-, and 10-H), 2.93 (br d, J 21 Hz, 6a-H), 2.92 (td, J 11 and 3 Hz, 4a-H), 2.18 (ddd, J 21, 11, and 2 Hz, 10a-H), and 1.56 (qd, J 11 and 3 Hz, 10b-H). Among these spectral data, the peaks and the signal patterns of the 6a-, 10a-, and 10b-proton in the n.m.r. spectrum, upon comparison with those of the deuteriated congeners (4b and c) described later, firmly established a *trans-anti-trans*† stereochemistry‡ of the lactam (4a).

Although the Diels–Alder reaction of the *trans-anti-trans*-

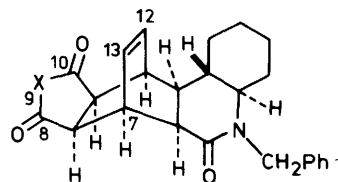


lactam (4a) with *N*-phenylmaleimide at a refluxing temperature in toluene was unsuccessful, similar reaction with maleic anhydride gave a mixture of the *exo-endo*-adduct (7) and the unchanged isomerised lactam (6a) which were readily separated by p.l.c. The adduct (7) exhibited a molecular ion peak at m/z 391 in the mass spectrum, i.r. absorptions at 1 850, 1 780 (anhydride), and 1 625 (NCO) cm^{-1} , and n.m.r. peaks at δ_H 6.50 (br dd, J 8 and 6 Hz, 13-H), 6.30 (br dd, J 8 and 6 Hz, 12-H), 4.21

† Although the stereochemistry of the lactams (4a and b) was deduced incorrectly to be *cis-anti-trans* (IUPAC: *cis-transoid-trans*) in the preliminary communication (ref. 2), their isolation, together with comparison of the spectral data of both isomers (4a and b) and (5), established their stereochemistry as shown.

† Stereochemical terms refer to the relative configurations at the 6a-, 10a-, 10b-, and 4a-position respectively. IUPAC conventions: *trans-transoid-trans* for '*trans-anti-trans*'.

(br ddd, J 6, 3, and 2 Hz, 7-H), 3.45 (br ddd, J 6, 3, and 2 Hz, 11-H), 3.26 (dd, J 9 and 3 Hz, 7a-H), 3.20 (dd, J 9 and 3 Hz, 10a-H), 3.08 (m, 4a-H), 2.75 (dd, J 11 and 2 Hz, 6a-H), and 1.96 (td, J 11 and 2 Hz, 11a-H). The assignment of the *exo-endo* structure to this Diels–Alder adduct (7) is also supported by the work of Jacobson *et al.*⁶ who found that the *exo-endo* adducts were the sole products formed from the Diels–Alder reaction of hexahydronaphthalenes with some dienophiles.



(7) X = O
(8) X = NPh

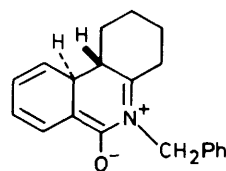
The second hydrogenated lactam (5) was isolated only after repeated p.l.c. and had a very similar R_F value to that of the lactam (6a) and showed a molecular ion peak at m/z 293 in the mass spectrum, u.v. absorptions at 252 and 258 (sh) nm (conjugated diene), and n.m.r. peaks at δ_H 5.98 (m, 7- and 10-H), 5.80 (m, 8- and 9-H), 3.63 (dm, J 9 Hz, 6a-H), 2.86 (td, J 10 and 3 Hz, 4a-H), and 2.26 (m, 10a-H). The Diels–Alder reaction of the lactam (5) with *N*-phenylmaleimide and maleic anhydride proceeded smoothly to give the adducts (8) and (7) in 58 and 60% yield respectively, the latter adduct being identical with the adduct (7) obtained from the *trans-anti-trans*-lactam (4a). All the spectral data of the adduct (8) were similar to those of the adduct (7) formed from the reaction with maleic anhydride, thus suggesting the stereochemistry of the adduct (8) as being *exo-endo* as shown. Consequently, the spectroscopic data of the lactam (5) and the ready formation of the Diels–Alder adducts (7) and (8) established the lactam (5) as having a *cis-anti-trans* stereochemistry.

The above results of the Diels–Alder reaction of the lactams (4a) and (5), namely, (4a) giving the adduct (7) with maleic anhydride accompanied by the formation of the isomerised lactam (6a), but no adduct with *N*-phenylmaleimide, while (5) affords the adducts (7) and (8) with both dienophiles, are well explained as follows. During the course of the Diels–Alder reaction, the *A/B-trans-anti-trans*-lactam (4a) with a conjugated diene structure was first isomerised to the *A/B-cis*-lactam (5) and the lactam (6a) with an unconjugated diene moiety upon heating with assistance of the catalytic action of maleic acid present in the reaction mixture. The n.m.r. spectrum of the product, obtained by refluxing (4a) in toluene in the presence of a trace amount of maleic acid, clearly showed the occurrence of two lactams (5) and (6a).

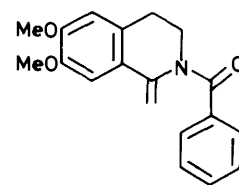
In order to clarify the reaction mechanism of reductive photocyclisation, we next carried out irradiation of the enamide (1) in the presence of sodium borodeuteride in ether–methanol and obtained three lactams (4b),[†] (2b), and (6b) in 10, 7, and 40% yield respectively, all of which were found to be deuteriated at the same 4a-position by analysis of their spectral data as follows. The lactam (4b) showed a molecular ion peak at m/z 294 in the mass spectrum and had similar u.v. and n.m.r. spectra to those of the *trans-anti-trans*-lactam (4a) except that an n.m.r. peak appeared at δ_H 1.55 (td, J 11 and 3 Hz, 10b-H) and a peak for 4a-H disappeared. The lactam (6b) also exhibited a molecular-ion peak at m/z 294 in the mass spectrum and had similar u.v. and n.m.r. spectra to those of the lactam (6a) except that an n.m.r. peak appeared at δ_H 1.53 (td, J 11 and 3 Hz, 10b-H) and a peak for 4a-H disappeared.

On the other hand, irradiation of the enamide (1) in the

presence of sodium borohydride in ether–methan[²H]ol (CH₃OD) afforded a mixture of three lactams (4c), (2a), and (6c). They were isolated and characterised by their spectral analyses, which established selective incorporation of deuterium into the 6a-position in the lactam (4c) and into the 8-position in the lactam (6c).



(A)



(9)

Thus, with the establishment of the *trans* configuration between 10a-H and 10b-H in the photocyclised lactams (4a–c), (5), and (6a–c), the proposed structure of an intermediate (A) was firmly ascertained. Therefore, the mechanism of reductive photocyclisation of the enamide (1) can be explained as follows. Upon irradiation, the photochemical electrocyclic ring closure⁷ of the 6 π -electron system would occur to give a 10a/10b-*trans* cyclic intermediate (A), which would then be subjected to reduction in the presence of a hydride reagent to yield the hydrogenated lactams (4a–c), (5), and (6a–c) as a result of concomitant incorporations of a proton into either the 6a- or 8-position and of a hydride ion into the 4a-position respectively.

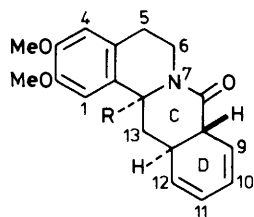
Next, we picked the enamide (9) for its reductive photocyclisation, aiming at the development of an effective synthetic route to protoberberine alkaloids. The enamide (9) was prepared⁸ from the 1-methyl-3,4-dihydroisoquinoline and benzoyl chloride in a usual way. Irradiation of the enamide (9) in ether–methanol afforded a mixture of three hydrogenated lactams (10a),* (11), and (12a) in 12, 12, and 23% yield respectively, though the lactam (11) was obtained only as a mixture with the lactam (12a) and was characterised from its n.m.r. spectrum. On the other hand, irradiation of the enamide (9) in acetonitrile–methanol afforded the lactam (12a), with an unconjugated diene moiety, as the sole product in 80% yield. When sodium borodeuteride was employed as the reducing agent in the irradiation of the enamide (9), two hydrogenated lactams (10b)* and (12b) were obtained and they were both found to be deuteriated at the 13a-position. Their mass and n.m.r. spectra [(10b); m/z 312 (M^+); δ_H 1.67 (dd, J 12 and 11 Hz, 13-H_{ax}); and (12b); m/z 312 (M^+); δ_H 1.59 (t, J 13 Hz, 13-H_{ax})] established their structures. Though n.m.r. signals for 8a- and 12a-H in the lactams (10a and b), which have a conjugated diene moiety, overlapped with other proton signals, their *C/D-trans* ring juncture was deduced by comparison of the peaks for the 9-, 10-, 11-, 12-, and 13_{ax}-proton [(10a); δ_H 6.40 (br d, J 9 Hz, 9-H), 6.05 (m, 10- and 11-H), 5.77 (br d, J 9 Hz, 12-H), and 1.67 (ddd, J 12, 11.5, and 11 Hz, 13-H_{ax})] with those of the analogous *trans*-lactam⁹ whose stereochemistry had been already established.}}

The other lactam (11), isomeric with (10a), was shown to have a *C/D-cis* ring juncture from the comparison of n.m.r. peak at δ_H 3.56 (br d, J 8.5 Hz, 8a-H) with that of the analogous, known *cis*-lactam.¹⁰ In addition, the chromatographic behaviour (R_F values on t.l.c.) of the compounds involved, which showed the largest R_F value for the *trans*-lactam (10a), followed by the enamide (9), the *cis*-lactam (11), and the hydrogenated lactam

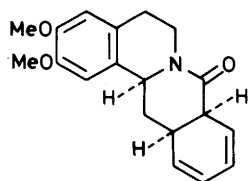
* Although the stereochemistry of the lactams (10a and b) was deduced incorrectly to be *C/D-cis* in the preliminary communication (ref. 2), their isolations, together with comparison of the spectral data of the two *trans*-lactams (10a and b) and *cis*-lactam (11), established their stereochemistry as shown.

with an unconjugated diene moiety, (12a), in that order, are in good agreement not only with the above spectral assignment, but with the R_F values described in the case of reductive photocyclisation of the enamide (1).

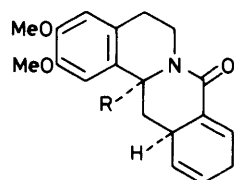
Further, reductive photocyclisation was also shown to occur with the enamide (13) which yielded the hydrogenated lactam (14) as the sole product in 42% yield upon irradiation in acetonitrile-methanol.



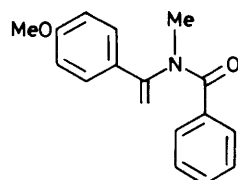
(10) a; R = H
b; R = D



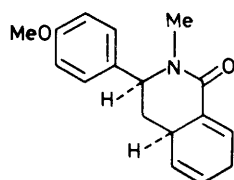
(11)



(12) a; R = H
b; R = D



(13)



(14)

In addition to the results reported previously, the above-mentioned reductive photocyclisation of enamides thus established that enamides are capable of undergoing smooth photocyclisation under non-oxidative, oxidative, and reductive conditions, to yield the corresponding *trans*-lactam, the didehydrolactam, and the hydrogenated lactams respectively, thus assuring a firm position for enamide photocyclisation as a useful synthetic methodology for the construction of various heterocyclic compounds.

Experimental

^1H N.m.r. spectra were measured with JEOL PMX-60 and Varian XL-200 instruments for solutions in deuteriochloroform unless otherwise stated (tetramethylsilane as internal reference), mass spectra with JEOL JMS01SG and Hitachi M-80 machines, i.r. spectra for solutions in chloroform on a Hitachi 215 spectrophotometer, and u.v. spectra for solutions in ethanol on a Hitachi 124 spectrophotometer. M.p.s were determined with a Kofler-type hot-stage apparatus. The extracts from the reaction mixtures were dried over anhydrous sodium sulphate. The photochemical reactions were carried out by irradiation with an internal, quartz, pencil-shaped high-pressure (100 or 300 W) mercury lamp through a Pyrex filter (Eikosha, Osaka, Japan, PIH-100 or PIH-300); during irradiation, the solutions were kept at 5–10 °C while being stirred and treated with bubbling nitrogen.

Reductive Photocyclisation of the Enamide (1).—(a) *In ether-methanol.* To a stirred solution of the enamide (1) (300 mg) in ether (200 ml) in the photochemical reaction vessel were successively added sodium borohydride (300 mg) and methanol (15 ml) at room temperature. After the added sodium borohydride had dissolved, the resulting solution was cooled to 5–10 °C and irradiated for 5 h. Water was then added carefully to the cooled reaction mixture to decompose an excess of sodium borohydride and the organic layer was separated. The aqueous layer was extracted with benzene. The combined extracts were washed with brine, dried, and evaporated to give a yellow viscous oil. Purification by Chromatotron (Model 7924, Harrison Research) on silica gel separated three fractions. The first fraction eluted with n-hexane was (4a α ,6a β ,10a α ,10b β)-5-benzyl-1,2,3,4,4a,6a,10a,10b-octahydrophenanthridin-6(5H)-one (4a) (33 mg, 11%) obtained as unstable crystals, m.p. 148–149 °C (from ether); λ_{max} 254 nm (ϵ 3 100 dm³ mol⁻¹ cm⁻¹); ν_{max} 1 635 cm⁻¹ (NCO); δ_{H} 7.39–7.02 (5 H, m, CH₂Ph), 6.57 (1 H, br d, *J* 9 Hz, 7-H), 6.20–5.98 (3 H, m, 8-, 9-, and 10-H), 4.99 and 4.56 (together 2 H, ABq, *J* 16 Hz, CH₂Ph), 2.93 (1 H, br d, *J* 21 Hz, 6a-H), 2.92 (1 H, td, *J* 11 and 3 Hz, 4a-H), 2.18 (1 H, ddd, *J* 21, 11, and 2 Hz, 10a-H), 2.30–2.08 (2 H, m, 4- and 1-H_{eq}), 1.56 (1 H, qd, *J* 11 and 3 Hz, 10b-H), and 1.90–1.68 (2 H, m) and 1.42–0.86 (4 H, m) (together 4-H_{ax}, 3- and 2-H₂, and 1-H_{ax}) (Found: M^+ , 293.1779. C₂₀H₂₃NO requires M , 293.1778). The second fraction eluted by n-hexane was a mixture of the enamide (1) (30 mg, 10%) and the known ⁵B/C-*trans*-lactam (2a) (15 mg, 5%), each of which was identical with the respective authentic samples upon comparison of their i.r. and n.m.r. spectra and R_F values in t.l.c. The last fraction eluted by a mixture of n-hexane and ether (2:1) was further purified by p.l.c. on silica gel to afford two hydrogenated lactams (5) and (6a). The former, (5), with the higher R_F value, was (4a α ,6a α ,10a α ,10b β)-5-benzyl-1,2,3,4,4a,6a,10a,10b-octahydrophenanthridin-6(5H)-one (50 mg, 16%), obtained as an unstable glass; λ_{max} 258sh (ϵ 4 900) and 252 nm (5 600); ν_{max} 1 635 cm⁻¹ (NCO); δ_{H} 7.40–7.16 (5 H, m, CH₂Ph), 5.98 (2 H, m, 7- and 10-H), 5.80 (2 H, m, 8- and 9-H), 4.99 and 4.60 (together 2 H, ABq, *J* 16 Hz, CH₂Ph), 3.63 (1 H, dm, *J* 9 Hz, 6a-H), 2.86 (1 H, td, *J* 10 and 3 Hz, 4a-H), 2.26 (1 H, m, 10a-H), and 2.20–0.80 (9 H, m, 10b-H, and 4-, 3-, 2-, and 1-H₂) (Found: M^+ , 293.1769. C₂₀H₂₃NO requires M , 293.1778). The second product (with the lower R_F value) was (4a α ,10a α ,10b β)-5-benzyl-1,2,3,4,4a,8,10a,10b-octahydrophenanthridin-6(5H)-one (6a) (130 mg, 43%), obtained as crystals, m.p. 104–106 °C (from ether-n-hexane); λ_{max} 234 nm (ϵ 6 300); ν_{max} 1 680, 1 635, and 1 600 cm⁻¹ (C=C and NCO); δ_{H} 7.40–7.16 (5 H, m, CH₂Ph), 7.00 (1 H, br s, 7-H), 5.84 (2 H, s-like, 9- and 10-H), 5.08 and 4.57 (together 2 H, ABq, *J* 16 Hz, CH₂Ph), 3.05 (1 H, td, *J* 11 and 3 Hz, 4a-H), 2.89 (2 H, m, 8-H₂), 2.74 (1 H, m, 10a-H), 2.20–2.04 (2 H, m, 4- and 1-H_{eq}), 1.54 (1 H, qd, *J* 11 and 3 Hz, 10b-H), and 1.80–1.62 (2 H, m) and 1.30–0.90 (4 H, m) (together 4-H_{ax}, 3- and 2-H₂, and 1-H_{ax}) (Found: C, 82.15; H, 7.45; N, 4.8. C₂₀H₂₃NO requires C, 81.85; H, 7.90; N, 4.75%).

(b) *In acetonitrile-methanol.* According to the photochemical procedure given for the enamide (1) in ether-methanol, a solution of a mixture of the enamide (1) (582 mg) and sodium borohydride (608 mg) in acetonitrile (600 ml)-methanol (30 ml) was irradiated for 7 h. The reaction mixture was then evaporated at low temperature under reduced pressure. Benzene and water were then added to the residue to separate the organic layer. The aqueous layer was extracted with benzene. The combined organic extracts were washed with water, dried, and evaporated to give a residue which was purified by p.l.c. on silica gel and recrystallised from ether-n-hexane to afford the lactam (6a) with an unconjugated diene moiety (457 mg, 78%). This product was identical with the lactam (6a) obtained by irradiation in ether-methanol.

Reductive Photocyclisation of the Enamide (1) using Sodium Borodeuteride.—According to the photochemical procedure given for the enamide (1) in ether–methanol, irradiation of the enamide (1) (580 mg) in ether (500 ml)–methanol (40 ml) using sodium borodeuteride (500 mg) as a reducing agent was performed. Separation of the crude product by p.l.c. afforded three lactams (4b), (2b), and (6b), all of which were found to be deuteriated at the same 4a-position; (4b) (59 mg, 10%), m.p. 148–149 °C (from ether); λ_{\max} 254 nm (ϵ 3 100); ν_{\max} 1 635 cm^{-1} (NCO); δ_{H} 7.39–7.16 (5 H, m, CH_2Ph), 6.57 (1 H, br d, J 9 Hz, 7-H), 6.19–5.97 (3 H, m, 8-, 9-, and 10-H), 4.98 and 4.54 (together 2 H, ABq, J 16 Hz, CH_2Ph), 2.93 (1 H, d, J 21 Hz, 6a-H), 2.16 (1 H, ddd, J 21, 11, and 2 Hz, 10a-H), 2.30–2.07 (2 H, m, 4- and 1- H_{eq}), 1.55 (1 H, td, J 11 and 3 Hz, 10b-H), and 1.90–1.68 (2 H, m) and 1.40–0.86 (4 H, m) (together 4- H_{ax} , 3- and 2- H_2 , and 1- H_{ax}) (Found: M^+ , 294.1839. $\text{C}_{20}\text{H}_{22}\text{DNO}$ requires M , 294.1841); (2b) (41 mg, 7%), m.p. 154–155 °C (from n-hexane); ν_{\max} 1 635 cm^{-1} (NCO); δ_{H} 8.25 (1 H, dd, J 8 and 2 Hz, 7-H), 7.58–7.20 (8 H, m, CH_2Ph , and 8-, 9-, and 10-H), 5.41 and 4.60 (together 2 H, ABq, J 16 Hz, CH_2Ph), and 2.83 (1 H, m), 2.52 (1 H, m), 2.20 (1 H, br d, J 13 Hz), 1.96–1.75 (2 H, m), and 1.58–1.10 (4 H, m) (together 10b-H and 4-, 3-, 2-, and 1- H_2), and no peaks around δ_{H} 3.35 assignable to 4a-H (Found: C, 81.95; H, 7.2; N, 4.85%; M^+ , 292.1693. $\text{C}_{20}\text{H}_{20}\text{DNO}$ requires C, 82.15; H, 6.9; N, 4.8%; M , 292.1684); (6b) (235 mg, 40%), m.p. 104–106 °C (from ether–n-hexane); λ_{\max} 234 nm (ϵ 6 300); ν_{\max} 1 685, 1 640, and 1 605 cm^{-1} (C=C and NCO); δ_{H} 7.38–7.18 (5 H, m, CH_2Ph), 7.00 (1 H, br s, 7-H), 5.82 (2 H, s-like, 9- and 10-H), 5.08 and 4.56 (together 2 H, ABq, J 16 Hz, CH_2Ph), 2.88 (2 H, m, 8- H_2), 2.73 (1 H, m, 10a-H), 2.25–2.04 (2 H, m, 4- and 1- H_{eq}), 1.53 (1 H, td, J 11 and 3 Hz, 10b-H), and 1.80–1.65 (2 H, m) and 1.26–0.98 (4 H, m) (together 4- H_{ax} , 3- and 2- H_2 , and 1- H_{ax}) (Found: C, 81.6; H, 7.8; N, 4.75%; M^+ , 294.1824. $\text{C}_{20}\text{H}_{22}\text{DNO}$ requires C, 81.60; H, 7.55; N, 4.75%; M , 294.1841).

Reductive Photocyclisation of the Enamide (1) in Ether–Methan[^2H]ol.—According to the photochemical procedure given for the enamide (1) in ether–methanol, irradiation of the enamide (1) (300 mg) in ether (200 ml)–methan[^2H]ol (10 ml) in the presence of sodium borohydride (300 mg) was performed and the separation of the crude product by p.l.c. afforded three lactams (4c), (2a), and (6c); (4c) (30 mg, 10%) as an unstable glass; λ_{\max} 256 nm (ϵ 3 100); ν_{\max} 1 625 cm^{-1} (NCO); δ_{H} 7.44–7.14 (5 H, m, CH_2Ph), 6.57 (1 H, br d, J 9 Hz, 7-H), 6.20–5.96 (3 H, m, 8-, 9-, and 10-H), 4.99 and 4.57 (together 2 H, ABq, J 16 Hz, CH_2Ph), 2.92 (1 H, td, J 11 and 3 Hz, 4a-H), 2.31–2.08 (3 H, m, 10a- and 4-, and 1- H_{eq}), 1.57 (1 H, qd, J 11 and 3 Hz, 10b-H), and 1.96–0.85 (6 H, m, 4- H_{ax} , 3- and 2- H_2 , and 1- H_{ax}) (Found: M^+ , 294.1849. $\text{C}_{20}\text{H}_{22}\text{DNO}$ requires M , 294.184); (2a) (27 mg, 9%), identical with an authentic sample⁵ upon comparison of their i.r. and n.m.r. spectra and R_{F} values; (6c) (115 mg, 38%) as an unstable glass; λ_{\max} 234 nm (ϵ 6 300); ν_{\max} 1 675, 1 630, and 1 600 cm^{-1} (C=C and NCO); δ_{H} 7.40–7.10 (5 H, m, CH_2Ph), 7.00 (1 H, br s, 7-H), 5.85 (2 H, s-like, 9- and 10-H), 5.06 and 4.58 (together 2 H, ABq, J 16 Hz, CH_2Ph), 3.06 (1 H, td, J 11 and 3 Hz, 4a-H), 2.90 (1 H, m, 8-H), 2.74 (1 H, t-like, J 8 Hz, 10a-H), 2.30–2.40 (2 H, m, 4- and 1- H_{eq}), and 2.00–0.90 (7 H, m, 10b-H, 4- H_{ax} , 3- and 2- H_2 , and 1- H_{ax}) (Found: M^+ , 294.1838. $\text{C}_{20}\text{H}_{22}\text{DNO}$ requires M , 294.1841).

Dehydrogenation of the Hydrogenated Lactams (4a), (5), and (6a).—Solutions of 15 mg of each of the three hydrogenated lactams (4a), (5), and (6a) in benzene (10 ml) was heated on a steam-bath, with a reflux condenser open to air, for 13 h. After evaporation of the solvent, the resulting residue was purified by p.l.c. on silica gel to give the lactam (2a) (about 10 mg, 67%) in each case.

Diels–Alder Reaction of the trans-anti-trans-Lactam (4a).—(a) *With maleic anhydride.* A solution of a mixture of the lactam (4a) (65 mg) and maleic anhydride (43 mg) in benzene (10 ml) was refluxed under a nitrogen stream for 24 h. After evaporation of the solvent, the resulting residue was purified by p.l.c. on silica gel to give two products. The first product, with the higher R_{F} value, was found to be the lactam with an unconjugated diene moiety, (6a), (7 mg, 11%) which was identical with the photocyclised lactam (6a) obtained by reductive photocyclisation of the enamide (1). The second product, with the lower R_{F} value, was found to be the Diels–Alder adduct (7) (47 mg, 54%) obtained as crystals, m.p. 242–244 °C (from ethanol); m/z 391 (M^+), 241, and 91; ν_{\max} 1 850 and 1 780 (anhydride) and 1 625 cm^{-1} (NCO); δ_{H} 7.38–7.08 (5 H, m, CH_2Ph), 6.50 (1 H, br dd, J 8 and 6 Hz, 13-H), 6.30 (1 H, br dd, J 8 and 6 Hz, 12-H), 5.18 and 4.37 (together 2 H, ABq, J 16 Hz, CH_2Ph), 4.21 (1 H, br ddd, J 6, 3, and 2 Hz, 7-H), 3.45 (1 H, br ddd, J 6, 3, and 2 Hz, 11-H), 3.26 (1 H, dd, J 9 and 3 Hz, 7a-H), 3.20 (1 H, dd, J 9 and 3 Hz, 10a-H), 3.08 (1 H, m, 4a-H), 2.75 (1 H, dd, J 11 and 2 Hz, 6a-H), 1.96 (1 H, td, J 11 and 2 Hz, 11a-H), and 2.28–2.05 (2 H, m), 1.96–1.60 (2 H, m), and 1.28–0.98 (5 H, m) (together 11b-H and 4-, 3-, 2-, and 1- H_2) (Found: C, 73.65; H, 6.45; N, 3.65. $\text{C}_{24}\text{H}_{25}\text{NO}_4$ requires C, 73.65; H, 6.45; N, 3.6%).

(b) *With N-phenylmaleimide.* According to the procedure given for maleic anhydride, the Diels–Alder reaction of the lactam (4a) with N-phenylmaleimide in toluene for 8.5 h was unsuccessful and the starting lactam (4a) was recovered.

Diels–Alder Reaction of the cis-anti-trans-Lactam (5).—(a) *With maleic anhydride.* According to the procedure given for the reaction of the lactam (4a) with maleic anhydride, the Diels–Alder reaction of the cis-anti-trans-lactam (5) (100 mg) containing a small amount of the lactam (6a) with maleic anhydride (150 mg) in toluene (15 ml) for 8 h gave the adduct (7) (68 mg, 60%) and the recovered lactam (6a) (15 mg). The adduct was identical with the adduct (7) obtained from the lactam (4a).

(b) *With N-phenylmaleimide.* According to the procedure given for the reaction of the lactam (4a) with N-phenylmaleimide, the Diels–Alder reaction of the lactam (5) (100 mg), which contained a small amount of the lactam with an unconjugated diene moiety, (6a), with N-phenylmaleimide (200 mg) in toluene (15 ml) for 8 h gave the adduct (8) (78 mg, 58%) as a glass; m/z 466 (M^+), 293, and 91; ν_{\max} 1 775, 1 710, and 1 630 cm^{-1} (NCO); δ_{H} 7.55–7.10 (10 H, m, 2Ph), 6.48 (1 H, br dd, J 8 and 6 Hz, 13-H), 6.27 (1 H, br dd, J 8 and 6 Hz, 12-H), 5.23 and 4.38 (together 2 H, ABq, J 16 Hz, CH_2Ph), 4.26 (1 H, br ddd, J 6, 3, and 2.5 Hz, 7-H), 3.48 (1 H, m, 11-H), 3.15 (1 H, dd, J 8 and 3 Hz, 7a-H), 3.10 (1 H, m, 4a-H), 3.07 (1 H, dd, J 8 and 3 Hz, 10a-H), 2.81 (1 H, dd, J 10.5 and 2.5 Hz, 6a-H), 2.04 (1 H, br t, J 10.5 Hz, 11a-H), and 2.25–2.08 (2 H, m), 1.80–1.65 (2 H, m), and 1.20–1.00 (5 H, m) (together 11b-H and 4-, 3-, 2-, and 1- H_2) (Found: M^+ , 466.2256. $\text{C}_{30}\text{H}_{30}\text{N}_2\text{O}_3$ requires M , 466.2255), and the lactam with an unconjugated diene moiety, (6a), was recovered (15 mg).

Isomerisation of the trans-anti-trans-Lactam (4a).—A solution of the trans-anti-trans-lactam (4a) (20 mg) in toluene (4 ml) was refluxed under a nitrogen stream for 14 h and evaporated. The n.m.r. spectrum and t.l.c. of the resulting residue showed the presence of the cis-anti-trans-lactam (5) and the lactam with an unconjugated diene moiety, (6a).

Reductive Photocyclisation of the Enamide (9).—(a) *In ether–methanol.* According to the photochemical procedure given for the enamide (1), a solution of a mixture of the enamide (9) (100 mg) and sodium borohydride (100 mg) in ether (100 ml)–methanol (5 ml) was irradiated for 20 min. Separation of the crude product by p.l.c. afforded three hydrogenated lactams

(10a), (11), and (12a), though we failed to isolate the lactam (11) which was, however, characterised by the n.m.r. spectrum of a mixture with the lactam (12a); (10a) (12 mg, 12%) as an unstable glass; m/z 311 (M^+); ν_{\max} 1 640 cm^{-1} (NCO); δ_{H} 6.63 (1 H, s, 1-H), 6.54 (1 H, s, 4-H), 6.40 (1 H, br d, J 9 Hz, 9-H), 6.05 (2 H, m, 10- and 11-H), 5.77 (1 H, br d, J 9 Hz, 12-H), 4.84 (1 H, m, 6-H), 4.64 (1 H, dd, J 11.5 and 5.5 Hz, 13a-H), 3.82 and 3.79 (each 3 H, s, 2OMe), 3.00—2.40 (6 H, m, 5-H₂, and 6-, 13-, 8a-, and 12a-H), and 1.67 (1 H, ddd, J 12, 11.5, and 11 Hz, 13-H_{ax}) (Found: M^+ , 311.1519. $\text{C}_{19}\text{H}_{21}\text{NO}_3$ requires M , 311.1519); (11) (about 12 mg, 12%) as an unstable glassy mixture with the lactam (12a); δ_{H} 6.10—5.90 (4 H, m, 9-, 10-, and 12-H), 4.59 (1-H, br dd, J 13 and 4 Hz, 13a-H), 3.56 (1 H, br d, J 8.5 Hz, 8a-H), 2.16 (1 H, br dt, J 13 and 4 Hz, 13-H_{eq}), and 1.92 (1 H, q, J 13 Hz, 13-H_{ax}); (12a) (23 mg, 23%) as an unstable glass, ν_{\max} 1 640 and 1 615 cm^{-1} (C=C and NCO); δ_{H} 6.97 (1 H, br s, 9-H), 6.72 (1 H, s, 1-H), 6.64 (1 H, s, 4-H), 5.90—5.59 (2 H, m, 11- and 12-H), 4.89 (1 H, m, 6-H_{eq}), 4.57 (1 H, dd, J 11.5 and 4.5 Hz, 13a-H), 3.89 and 3.88 (each 3 H, s, 2OMe), 3.02—2.56 (5 H, m, 13-H_{eq}, 12a-H, 6-H_{ax}, and 5-H₂), 2.90 (2 H, m, 10-H₂), and 1.61 (1 H, ddd, J 13, 12, and 11.5 Hz, 13-H_{ax}) (Found: M^+ , 311.1514. $\text{C}_{19}\text{H}_{21}\text{NO}_3$ requires M , 311.1520).

(b) In acetonitrile-methanol. According to the photochemical procedure given for the enamide (1) in acetonitrile-methanol, a solution of a mixture of the enamide (9) (50 mg) and sodium borohydride (50 mg) in acetonitrile (25 ml)-methanol (5 ml) was irradiated for 1 h and separation of the crude product by p.l.c. afforded the lactam with an unconjugated diene moiety, (12a), (40 mg, 80%) which was identical with the lactam (12a) obtained by irradiation in ether-methanol as described above.

Reductive Photocyclisation of the Enamide (9) using Sodium Borodeuteride.—According to the photochemical procedure given for the enamide (9) in ether-methanol, irradiation of the enamide (9) (100 mg) in ether (100 ml)-methanol (5 ml) using sodium borodeuteride (100 mg) as reducing agent, and separation of the crude product by p.l.c., afforded two hydrogenated lactams (10b) and (12b) which were found to be deuteriated at the 13a-position; (10b) (10 mg, 10%) as an unstable yellow glass, ν_{\max} 1 640 cm^{-1} (NCO); δ_{H} 6.64 (1 H, s, 1-H), 6.56 (1 H, s, 4-H), 6.42 (1 H, br d, J 9 Hz, 9-H), 6.02 (2 H, m, 10- and 11-H), 5.77 (1 H, br d, J 9 Hz, 12-H), 4.85 (1 H, m, 6-H), 3.82 and 3.80 (each 3 H, s, 2OMe), 2.92—2.42 (6 H, m, 5-H₂ and 6-, 8a-, 12a-, and 13-H), and 1.67 (1 H, dd, J 12 and 11 Hz, 13-H_{ax}) (Found: M^+ , 312.1587. $\text{C}_{19}\text{H}_{20}\text{DNO}_3$ requires M , 312.1583); (12b) (22 mg, 22%) as an unstable yellow glass, ν_{\max} 1 640 and 1 615 cm^{-1} (C=C and NCO); δ_{H} 6.96 (1 H, br s, 9-H), 6.68 (1 H, s, 1-H), 6.62 (1 H, s, 4-H), 5.84—5.56 (2 H, m, 11- and 12-H), 4.86 (1 H, m, 6-H_{eq}), 3.87 and 3.86 (each 3 H, s, 2OMe), 3.04—2.50 (5 H, m, 13-H_{eq}, 12a-H, 6-H_{ax}, and 5-H₂), 2.88 (2 H, m, 10-H₂), and 1.59 (1 H, t, J 13 Hz, 13-H_{ax}) (Found: M^+ , 312.1583. $\text{C}_{19}\text{H}_{20}\text{DNO}_3$ requires M , 312.1583).

N-Benzoyl-4-methoxy-N-methyl- α -methylenebenzylamine (13).—Anhydrous methylamine gas was bubbled into an ice-cooled solution of 4-methoxyacetophenone (1.5 g) in anhydrous benzene (40 ml) for 20 min. The resulting mixture was added dropwise to an ice-cooled solution of titanium tetrachloride (0.8 ml) in anhydrous chloroform (10 ml). After the mixture had been refluxed for 1 h, the precipitate was filtered off and washed

with benzene. The combined extracts were evaporated to dryness under reduced pressure. The residue was dissolved in anhydrous benzene and the solution was filtered. The filtrate was condensed to give a yellow oil. To an ice-cooled, stirred solution of the resulting oil and triethylamine (1.5 g) in anhydrous benzene (30 ml) was added dropwise a solution of benzoyl chloride (1.5 g) in anhydrous benzene (20 ml). After being stirred at room temperature for 3 h, the solution was cooled and filtered to remove triethylamine hydrochloride. The filtrate was evaporated to give a viscous oil. Trituration with ether afforded the unstable enamide (13) (2.2 g, 83%) as pale yellow solid, δ_{H} 7.50—6.70 (9 H, m, ArH), 5.17 and 4.69 (each 1 H, s, C=CH₂), 3.76 (3 H, s, OMe), and 3.20 (3 H, s, NMe), which was used for irradiation without further purification.

3,4,4a,7-Tetrahydro-3-(4-methoxyphenyl)-2-methylisoquinolin-1(2H)-one (14).—According to the photochemical procedure given for the enamide (1) in acetonitrile-methanol, a solution of a mixture of the enamide (13) (1.67 g) and sodium borohydride (1.67 g) in acetonitrile (1 190 ml)-methanol (60 ml) was irradiated for 7 h. Recrystallisation of the crude product which was obtained as a solid from ether afforded the hydrogenated lactam (14) (709 mg, 42%), m.p. 126—127 °C; ν_{\max} 1 680, 1 640, and 1 610 cm^{-1} (C=C and NCO); δ_{H} 7.16 and 6.90 (each 2 H, d, J 8 Hz, ArH), 6.94 (1 H, br s, 8-H), 5.77 (1 H, br d, J 12 Hz, 6-H), 5.60 (1 H, dd, J 12 and 3.5 Hz, 5-H), 4.48 (1 H, dd, J 12 and 5 Hz, 3-H), 3.82 (3 H, s, OMe), 3.08 (1 H, tm, J 10 Hz, 4a-H), 3.00—2.84 (2 H, m, 7-H₂), 2.73 (3 H, s, NMe), 2.25 (1 H, ddd, J 14, 5, and 3 Hz, 4-H_{eq}), and 1.72 (1 H, ddd, J 14, 12, and 10 Hz, 4-H_{ax}) (Found: C, 76.1; H, 7.1; N, 5.25. $\text{C}_{17}\text{H}_{19}\text{NO}_2$ requires C, 75.8; H, 7.1; N, 5.20%).

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