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PHOTOCHEMICAL SYNTHESIS OF DIAZA-STEROIDS

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Abstract—N-Iminopyridinium ylides **12** and **13** readily undergo regio-specific photoinduced ring expansion to the isomeric 1,2-diazepines **14** and **15** respectively. Similarly UV irradiation of the steroidal N-iminopyridinium ylide **25**, which can be obtained from 19-nortestosterone, leads quantitatively and in a regiospecific manner to the corresponding diazepine **26**. In a second photochemical reaction **26** gives the cyclobutene derivative **27**. Variable temperature ^{1}H NMR and OCD measurements of the optically active diazepine **26** indicate that one of the two possible diastereoisomeric conformations is preferred.

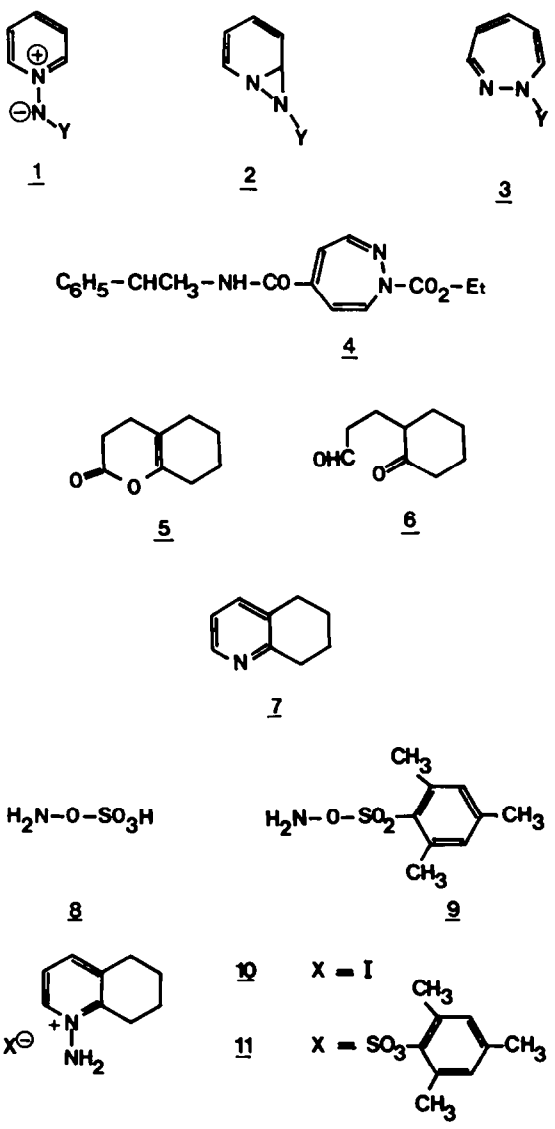
The photoinduced ring-enlargement of 1-iminopyridinium ylides **1** to the isomeric 1,2-diazepines **3** is by now a well established reaction[1-4] which may be widely applied[1,2,5,6] provided that the exocyclic N atom bears a stabilising chromophore, e.g. –COR, $-CO_2R$, $-SO_2R$ where R is an alkyl or an aryl group.[1,2,5,6] 1,7-Diazanorcaradienes **2** have been postulated as intermediates[1,5] in these reactions although their existence has not yet been proved.

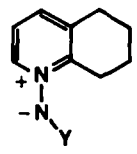
The synthesis of azasteroids[7,8] and diazasteroids[8-10] constitutes an extension of the physiological spectrum of steroidal compounds. In addition, steroids have been widely used for studying the scope and limitations of new reactions. Along these lines it seemed desirable to synthesize a diaza-A-homosteroid starting from a steroidal pyridine, namely 17-acetoxy-4-azaestra-1(10), 2,4-triene **24**, utilising the aforementioned photoinduced ring-expansion reaction. In order to realise the synthesis of the diaza-A-homosteroid the following scheme was considered: (i) synthesis of the steroidal pyridine **24**, (ii) introduction of a suitable stabilizing chromophore in order to obtain ultimately the pyridinium ylide **25** and (iii) photoinduced ring expansion of **25** to the diazasteroid **26**.

We have already described the synthesis of the optically active 1,2-diazepine **4**,[11] the 7-membered ring being boat-shaped and therefore asymmetric. Its conformational inversion leads to an equilibrium between diastereoisomeric conformations which should be temperature dependent. Indeed optical circular dichroism of **4**, as measured at −192° and +20°, showed this to be so[11] and was simultaneously definite and qualitative proof for the conformational mobility of the diazepine ring. Variable temperature NMR did not permit us to determine the thermodynamic parameters of the ring inversion. The optically active and annulated 1,2-diazepine **26** was expected to ring-invert at a slightly slower rate compared to **4**, all other conditions being equal.

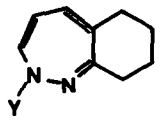
Model synthesis of a monoannulated 1,2-*diazepine*

Before entering the field of optically active diazasteroids we wanted to carry out a model synthesis of a monoannulated diazepine from readily available starting materials. To begin with we prepared 5,6,7,8-

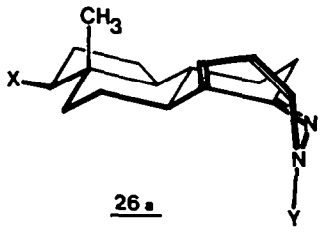




12 Y = $COCH_3$
13 Y = CO_2Et

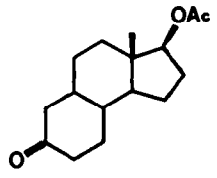


14 Y = $COCH_3$
15 Y = CO_2Et



26a

X = OAc



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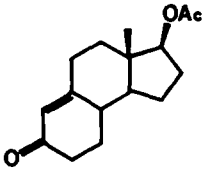

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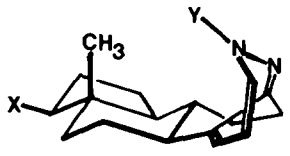
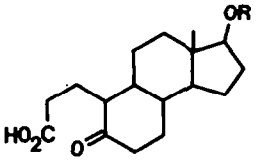
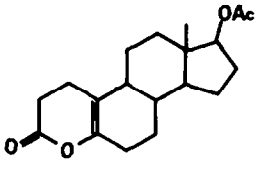


26b

Y = CO_2Et



18 R = H
19 R = $COCH_3$



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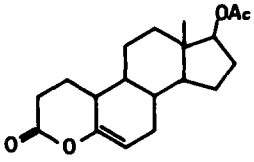

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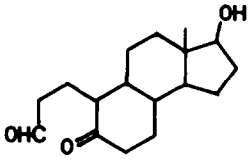

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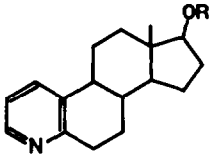
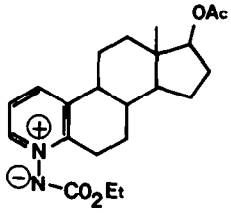


23 R = H
24 R = $COCH_3$



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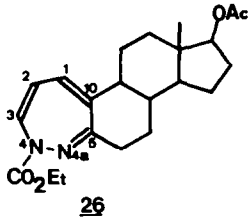

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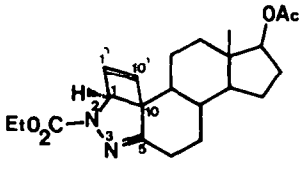
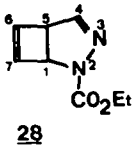


27



28

tetrahydroquinoline **7** from cyclohexanone. This synthesis could be achieved in several ways. Firstly condensation of acrylonitrile with cyclohexenanone pyrrolidinoenamine gave 2(β-cyanoéthyl)cyclohexanone[12] which, when treated with sulphuric acid led to 5,6,7,8-tetrahydrocarbostyril.[13] Treatment of the latter compound with phosphorus oxychloride followed by zinc reduction in the presence of hydrochloric acid gave 5,6,7,8-tetrahydroquinoline **7**.[14] The overall yield for this straightforward synthesis is 28%. Alternatively condensation of ethyl acrylate with cyclohexanone in the presence of base, followed by saponification of the ester function[15] and enol-lactonization, led to **5**. Low temperature reduction of **5** with diisobutylaluminium hydride gave the keto-aldehyde **6** in 82% yield. Compound **6** could also be prepared in a more straightforward manner by reaction of the morpholino-enamine of cyclohexanone with acrolein according to Allan's procedure.[10] The reaction of the ketoaldehyde **6** with hydroxylamine hydrochloride in acetic acid led to the desired tetrahydroquinoline **7** in 50% yield. N-Amination of **7** was performed using either of the two O-substituted hydroxylamines **8** and **9**, the N atom of both of the latter two compounds exhibiting an electrophilic character.[17,18] Reaction of **7** with the potassium salt of hydroxylamine-O-sulphonic acid **8** (H.A.S.) in aqueous solution, followed by treatment of the resulting salt with hydroiodic acid led to the N-aminopyridinium iodide (**10**). Acetylation, followed by Amberlite IRA 400 ion exchange,[19] resulted in the formation of the 1-iminopyridinium ylide **12** in 16% overall yield with respect to **7**. UV irradiation of **12** in benzene solution, followed by chromatographic separation of the photoproducts gave a mixture of 1-acetyl-3,4-tetramethylene-1,2-diazepine **14**, (27%), tetrahydroquinoline **7**, (25%) and a compound $C_9H_{11}NO$, m.p. 66–67° (3%) of unknown structure.

For reasons, which will become apparent in the next section, we used Tamura's method for the synthesis of 1-iminopyridinium ylides.[20] Thus, reaction of **7** with mesitylsulphonylhydroxylamine **9** (M.S.H.) in methylene chloride solution, followed by treatment of the resulting pyridinium salt **11** with éthyl-chloroformate in the presence of potassium carbonate,[5] led directly to the

N-iminopyridiniym ylide **13** in 39% overall yield. UV irradiation of **13** in benzene solution gave 1 - ethoxy - carbonyl - 3,4 - tetramethylene - 1,2 - diazepine **15** in 90% yield.

Only the diazepine having been obtained in this second approach, and furthermore in quantitative yield, the photoinduced ring enlargement obviously proceeds regiospecifically. According to the mechanism which we have postulated in the introduction for the ring expansion process, quantitative isolation of compound **15** as the sole diazepine can be explained by assuming, firstly photoinduced electrocyclic ring-closure between the exocyclic nitrogen atom and carbon atom C-2, and, secondly thermal valence tautomerism of the resulting diazanorcaradiene.

The structure of the ylide **13** and of the diazepines **14** and **15** were firmly established spectroscopically (Table 1) by comparison with known 1-iminopyridinium ylides and 1,2-diazepines.[1,2,5,6] Tamura's method[18,20] using M.S.H. **9** in organic solvents instead of H.A.S. **8** in aqueous media, is obviously more useful for hydrophobic pyridine derivatives. As will be seen in the next section M.S.H. proved to be best-suited for the synthesis of steroidal N-iminopyridinium ylides.

Table 1. NMR spectral data of hydrogen atoms attached to the heterocyclic rings in ylides **13** and **25** and in diazepines **14**, **15** and **26**[a,b]

Compound	H_α	H_β	H_γ
ylide 13	8.36 J = 6.0	7.26 J=6.0; 7.0	7.53 J = 7.0
ylide 25	8.65 J = 7.0	7.75 J=7.0; 7.5	8.18 J = 7.5
diazepine 14	6.43 J = 7.0	5.74 J=7.0; 5.0	6.24 J=5.0 ; 1.8
diazepine 15	6.22 J = 7.0	5.60 J=7.0; 5.0	6.15 J=5.0 ; 2.0
diazepine 26	6.27 J = 7.0	5.60 J=7.0; 5.3	6.13 J=5.3 , 2.3

a) Chemical shifts and coupling constants expressed respectively in δ(ppm) and Hz values

b) Solvent : $CDCl_3$

Synthesis of steroidal diazepines

At this stage we had at our disposal three methods for the synthesis of annulated pyridines of the 5,6,7,8-tetrahydroquinoline type and two routes for the preparation of 1-iminopyridinium ylides. Our next goal was the synthesis of the steroidal pyridine **24** using the preceding model reactions. The pyrrolidino-enamine of the known ketone **16** did not lead to the expected cyano-ketone on reaction with acrylonitrile according to the method described previously. Instead a complex reaction mixture was obtained from which only starting material **16** could be isolated. Reaction of the enone **17**[22] with methyl acrylate, according to the procedure of Chinn and Dryden, followed by saponification and hydrogenation,[23] gave the keto-acid **18**. It should be noted that the overall yield for the synthesis of **18** from **17** is low (30%) when compared to the one step ozone degradation of 19-nortestosterone to the keto-acid **19** (83%).[24]

Cyclisation of **19** gave a mixture of the enol-lactones **20** m.p. 137–141° and **21** m.p. 120–123° in 78% yield. Low temperature reduction of the lactone mixture **20** + **21** with diisobutylaluminium hydride gave the keto-aldehyde **22**, m.p. 61–63°, in 58% yield. Reaction of **22** with hydroxylamine afforded the desired steroidal pyridine **24** m.p. 130–132°. One actually obtains a mixture of the acetoxy derivative **24** and the 17-hydroxy compound **23** m.p. 218–22°, the latter being readily acetylated back to **24**.

H.A.S. potassium salt did not react with **24**, probably because the latter compound is not very hydrophilic. On the contrary reaction of **24** with M.S.H. facilitated the formation of the pyridinium ylide **25** after functionalisation with ethylchloroformate *in situ*.

UV irradiation of **25** gave in high yield the expected 4 - ethoxycarbonyl - 17 - acetoxy - A - homo - 4,4a - diaza - 19 - norandrosta - 1(10), 2,4a - triene **26**, as the only isolated 1,2-diazepine derivative. As in the case of the tetrahydroquinolinium ylide **13** we observed a regiospecific ring-expansion, the photoinduced electrocyclic step being entirely directed towards 3-membered ring formation between the exocyclic N atom and the unsubstituted C atom (in this case C-3). Similar observations have been made with unsubstituted 1-iminopyridinium ylides:[1,2,4] α-alkyl groups direct the electrocyclic ring closure entirely towards the α′ position.

It has already been shown that 1-ethoxycarbonyl-1,2-diazepines undergo photoinduced disrotatory ring closure of their butadiene moiety leading to the corresponding cyclobutene derivatives.[2] This photochemical reaction usually proceeds at a much slower rate than that of ring-expansion of the parent 1-imino pyridinium ylides. We have found that the steroidal diazepine **16** behaves in a similar manner, C atoms C-3 and C-10 being the termini of the photoinduced disrotatory electrocyclisation.[26] 1,10 - Ethylidino - 2 - ethoxycarbonyl - 1,7 - acetoxy - A - nor - 2,3 - diazaandrost - 3(5) - ene **27** could be obtained directly when the ylide **25** was excited with UV light for a longer period than normal.

Of the two possible isomers only **27**, having probably the cyclobutene moiety in the β-configuration is isolated. Indeed Dreiding models show that **27** as depicted would have the more stable configuration, ring B being in a quasi-chair conformation. If the cyclobutene ring were α, there would be more steric crowding and ring B would be in a quasi-boat shaped conformation. Although we cannot give any compelling spectroscopic arguments in favour of a β-configuration for the cyclobutene moiety, NMR data does agree with the proposed structure **27**. In a preceding paper concerning NMR data of 2,3-diazabicyclo [3.2.0] heptadienes **28** we discussed the relative magnitude of coupling constants in the strained 4-membered ring.[27] The conclusions we reached entirely agree with those reported by Paquette for similar bicyclo[3.2.0] systems:[28] *vis* allylic coupling constants $J_{1,6}$ and $J_{5,7}$ are of higher magnitude than vinylic coupling constants $J_{1,7}$ and $J_{5,6}$ for geometric and ring strain reasons. The three cyclobutene protons of **27** have the following ^1H NMR characteristics which agree well with those found in similar series:[28] δ 4.63 (H-1, $J_{1,10}$ = 1.5 Hz); 6.12 (H-1′, $J_{1',1} = OH_2$, $J_{1'10}$ = 3.5 Hz) 6.46 (H-10′, $J_{10',1}$ = 1.5 Hz, $J_{10',1'}$ = 3.5 Hz).

Unlike the bicyclic compounds of type **28** which isomerise back to the monocyclic 1,2-diazepines when heated to 130–170°, **27** did not isomerise to **26** when heated to 170°. Higher temperatures were not employed in this

reaction. Since the ^{1}H NMR spectrum of **26** did not show any additional splitting when measured at low temperature we were unable to compute or estimate the inversion barrier between the two probable diastereoisomeric boat-shaped conformations of the 7-membered ring. Similarly variable temperature optical circular dichroism measured between −190° and +22° did not show any appreciable change in shape or amplitude.[22]

These findings are in marked contrast to OCD measurements obtained with the optically active but non-annulated diazepine **4**. We conclude therefore that one of the two possible diastereoisomeric conformations is thermadynamically preferred. This preference was confirmed by the use of molecular models: in conformation **26a** ring B has a stable chair conformation whereas in the diastereoisomeric conformation **26b** ring B has been forced into a boat form. Conformation **26a** is thus the more stable geometry for **26**. It is from this preferred conformation that the photoinduced disrotatory electrocyclisation leading to the pentacyclic diazasteroid **27** occurs since the cyclobutene ring would be β-orientated.

EXPERIMENTAL

Element analyses of new compounds were determined either in the Institute of Organic Chemistry of the Technical University in Lodz, Poland, or by the Service Central de Microanalyse of CNRS, divisions of Lyon and Strasbourg, France. Melting points were measured on a Buchi SMP-20 apparatus and are uncorrected. IR spectra were determined with a Beckman IR-20-A or with Spectromom 2000 (MOM, Budapest) spectrophotometer for KBr discs. UV spectra were measured on a Beckman DB or with a Varian Techtron UV-VIS 635 spectrophotometer. NMR spectra were obtained with Bruker 90 MHz, Model HFX-72, Varian A-60-A, JEOL CD. LTS, JNM-C-60HL and Tesla 80 MHz, BS 487C spectrophotometers in $CDCl_3$, unless otherwise stated, using TMS as an internal standard (chemical shifts are given in δ values). Mass spectra were measured with a mass spectrometer GCMS-LKB-type 9000 S. Rotation measurements were carried out on Perkin-Elmer No. 141 or 241 MC polarimeters. OCD measurements were performed with a Roussel Jouan type II dichrographe. Column, thin- and thick-layer chromatography was carried out with silicic acid (Merck). Solvents were reagent grade and distilled before use. Photochemical reactions were carried out in Pyrex glass, the reactor being of the Hanovia cooling finger type.

Diisobutylaluminium hydride reduction of enol-lactone **5** *to the keto-aldehyde* **6**. A soln of **5** (3.0 g; 0.2 mole), which has been prepared according to Susherina's method,[29] in dry toluene (500 ml), was cooled to −70°, and kept under N_2. To this stirred mixture was added dropwise over 15 min a 20% soln of diisobutylaluminium hydride in toluene (30 ml; 0.035 mole). After 30 min the resulting soln was poured into a mixture of AcOH (150 ml), water and ice (total amount of water: 300 ml) Extraction of the products with chloroform (450 ml) and treatment of the organic soln with water and $NaHCO_3$aq, after evaporation of the solvent, gave an oil which was distilled under reduced pressure yielding **6**, 2.52 g (82%); b.p. 82–84°/05 mm; n_D^{20} 1.4761; IR 3450, 2940, 1705, 1650 cm^{-1}; ^{1}H NMR 9.7 (1 H, t, J = 1 Hz).[16]

Synthesis of 5,6,7,8-*tetrahydroquinoline* **7**. A soln of **6** (10.8 g; 0.07 mole) and hydroxylamine hydrochloride (6.0 g; 0.086 mole) in AcOH (150 ml) was heated for 1.5 hr at reflux temp. under N_2. AcOH was separated by steam distillation; non basic compounds were extracted with ether and discarded; the remaining soln was made basic with NaOH and extracted several times with ether. The combined ether extracts were dried over Na_2SO_4 and evaporated to dryness. The remaining oil was distilled under reduced pressure and **7** obtained as a colourless oil 3.8 g; (41%); [14] b.p. 130–132°/70 mm; n_D^{24} 1.5407.

Synthesis of 1-*imino*-5,6,7,8-*tetrahydroquinolinium iodide* **10**. A soln of **8** (11.3 g; 0.1 mole) in water (50 ml) was neutralized at 0° with 2N NaOH (about 50 ml). The resulting soln was poured into a suspension of **7** (13.3 g; 0.1 mole) in water (75 ml) and the stirred mixture heated at 70° for 3 hr. After addition of K_2CO_3 (6.9 g; 0.05 mole) in water (40 ml) the resulting soln was heated for another hr at 20°. Unreacted tetrahydroquinoline (8.5 g) was extracted with ether and the aqueous soln concentrated *in vacuo* to about 150 ml. Addition of EtOH (300 ml) caused K_2SO_4 to precipitate. After separation of the crystals the soln was treated at −30° with 57% HI (22.3 g; 0.1 mole) and then evaporated *in vacuo* to dryness at 40–50°. The residue was dissolved in 1 l EtOH and the resulting brown soln treated with charcoal. After filtration ether (500 ml) was added which led to crystallization of **10**, 8.4 g (34%); m.p. 121–122°, recrystallized from EtOH. (Found: C, 39.0; H, 4.7; N, 10.2; Calc. for $C_9H_{13}N_2I$: C, 39.15; H, 4.74; N, 10.15%).

Synthesis of 1-*acetylimino*-5,6,7,8-*tetrahydroquinolinium ylide* **12**. A soln of **10** (5.52 g; 0.02 mole) in Ac_2O (40 ml) was heated at 90–100° for about 2 hr under N_2. Excess Ac_2O was removed *in vacuo* and the residue treated with ether whence a solid precipitated which on crystallization from EtOH gave N-acetylamino-5,6,7,8-tetrahydroquinolinium iodide 3.45 g (54%) m.p. 167–168°, UV λ_{max} (MeOH) 275 nm (=7500).

A soln of this latter compound (5.72 g; 0.018 mole) in EtOH (150 ml) was percolated over an Amberlite IRA 410 column (90 g) which had been prepared as follows: treatment of the resin with 10% NaOH aq and removal of the excess base with distilled water was followed by displacement of water with EtOH. After ion exchange the EtOH solns were evaporated *in vacuo* to dryness, the residue was chromatographed over sililic acid thick layer plates with EtOH. About 3 g (87%) of **12** were thus isolated as colourless hygroscopic crystals; m.p. 116–118°; λ_{max} (MeOH) 275 nm, ϵ = 5700. (Found: C, 69.3; H, 7.4; N, 14.7; Calc. for $C_{11}H_{14}N_2O$: C, 69.44; H, 7.42; N, 14.73%).

Photoinduced synthesis of 1-*acetyl*-3,4-*tetramethylene*-1,2-*diazepine* **14**. A soln of **12** (3 g; 0.016 mole) in benzene (1.8 l) was irradiated through Pyrex filter by means of a 125 W Philips HPK high pressure mercury lamp under N_2 for 7 hr, whence all starting material was consumed. After evaporation of the solvent *in vacuo* the crude mixture was chromatographed over a silicic acid column (300 g) with a cyclohexane-ethyl acetate 80/20 v/v mixture. Three compounds were successively eluted; -5,6,7,8-Tetrahydroquinoline **7**, 535 mg (25%); -1-Acetyl-3,4-tetramethylene-1,2-diazepine **14**, 790 mg (27%) as a viscous yellow oil which slowly crystallized after distillation under reduced pressure; b.p. 68–74°/0.02 mm; m.p. 47°; λ_{max} (MeOH) and 333 nm (ϵ = 6100 and 475 Resp). See Table 1 for ^{1}H NMR data. (Found: C, 69.5; H, 7.5; N, 14.6. Calc. for $C_{11}H_{14}N_2O$: C, 69.44; H, 7.42; N, 14.73%).

Iron tricarbonyl complex of **14**, prepared in standard way[1]; m.p. 131–132°; ^{1}H NMR: 6.34 (1 H, J = 2.0 and 6.5 Hz), 5.02 (1 H, J = 2.0 and 4.5 Hz), 4.47 (1 H, J = 6.5 and 4.5 Hz), 2.34 (3 H, s) (Found: C, 50.9; H, 4.3; N, 8.5. Calc. for $C_{14}H_{14}N_2O_4Fe$: C, 50.94; H, 4.27; N, 8.49%). Colourless crystals, 70 mg (3%) of unknown structure; m.p. 66–67°; mass spectrum: *m/e* 148.

Synthesis of 1-*amino*-5,6,7,8-*tetrahydroquinolinium mesityl sulphonate* **11**. To a stirred soln of **7** (3.59 g; 0.027 mole) in CH_2Cl_2 (20 ml) was added dropwise a soln of MSH **9**[18,30] (5.8 g; 0.027 mole) in CH_2Cl_6 (60 ml), the resulting mixture being kept at room temp. for 1 hr. Addition of diethyl ether (300 ml) led to crystallization of **11**, 7.5 g (80%), m.p. 125–126°, recrystallized from CH_2Cl_2–ether. (Found: C, 61.9; H, 6.8; N, 7.9. Calc. for $C_{18}H_{24}N_2O_3S$: C, 62.05; H, 6.94; N, 8.04%).

Synthesis of 1-*ethoxycarbonylimino*-5,6,7,8-*tetrahydroquinolinium ylide* **13**. To a stirred soln of **11** (5.25 g; 0.015 mole) in abs EtOH (100 ml) was added dropwise ethyl chloroformate (1.63 g; 0.015 mole) in abs EtOH (10 ml) followed by anhyd K_2CO_3 (4.14 g). After about 10 hr at room temp., the inorganic salts were filtered off and the remaining soln was evaporated to dryness *in vacuo*. After chromatography of the mixture over silicic acid (50 g) with a $CHCl_3$–EtOH 80/20 v/v mixture **13**, 1.6 g (48%) was obtained, m.p. 126–128°; UV λ_{max} (MeOH) 277 and 245 nm (ϵ = 6900 and 12500 resp.), UV λ_{max} (C_6H_6) 342 and 245 nm (ϵ = 5900 and 700 resp.); IR 1640 cm^{-1}; for ^{1}H NMR spectral data see Table 1. (Found: C, 65.4; H, 7.3; N, 12.8. Calc. for $C_{12}H_{16}N_2O_2$: C, 65.43; H, 7.32; N, 12.72%).

Photoinduced synthesis of 1-*ethoxycarbonyl*-3,4-*tetramethylen-*

1,2-diazepine **15**. A soln of **13** (440 mg; 0.002 mole) in benzene (450 ml) was irradiated as previously described for photochemical synthesis of **14** for 2 hr. After evaporation of the solvent *in vacuo* and chromatography of the residue over silicic acid with EtOAc–cyclohexane–chloroform 1/1/1 v/v mixture one isolated **15**, 430 mg (98%), as a homogenous orange oil; UV λ_{max} (MeOH) 330 and 255 nm (ϵ = 480 and 3700 resp.), UV λ_{max} (C_6H_6) 342 and 280 nm (ϵ = 600 and 2000 resp.); for ^{1}H NMR spectral data see Table 1; mass spectrum: *m/e* 220 (M+). (Found: C, 65.3; H, 7.3; N, 12.7. Calc. for $C_{12}H_{16}N_2O_2$: C, 65.43; H, 7.32; N, 12.72%).

Formation of enol-lactones **20** *and* **21** *from keto-acid* **19**. A soln of **19** (17 g; 0.05 mole) which had been synthesized according to Chinn's[23] or Dreiding's[24] procedure, and anhyd NaOAc (34 g) in Ac_2O (850 ml), was heated at reflux temp. under N_2 over a 10 hr period. Excess Ac_2O was removed *in vacuo*, the residue taken up in EtOAc and washed with water. After treatment with Na_2SO_4, the solvent was evaporated *in vacuo* and the mixture chromatographed over silicic acid (300 g) with the chloroform–EtOAc–cyclohexane 1/1/1 v/v system. Lactones **20** and **21**, 12.65 g (78% overall yield), were partially separated for individual identification.

Enol-lactone **20**, m.p. 137–141° (crystallized from isopropyl ether); $[\alpha]_D^{20}$ ($CHCl_3$) + 62.7°; ^{1}H NMR: 4.7 (1 H), 2.0 (3 H, s) 0.8 (3 H, s). (Found: C, 71.5; H, 8.1. Calc. for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23%).

Enol-lactone **21**, m.p. 120–123° (crystallized from isopropyl ether); $[\alpha]_D^{20}$ ($CHCl_3$)–68.5°; ^{1}H NMR: 5.35 (1 H), 4.68 (1 H), 2.0 (3 H, s), 0.8 (3 H, s). (Found: C, 71.7; H, 8.2. Calc. for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23%).

Preparation of keto-aldehyde **22**. A mixture of **20** and **21** (5.4 g: 0.017 mole) was dissolved in 600 ml toluene and the resulting soln cooled to −70°. To this a soln of 20% diisobutylaminium hydride in toluene (45 ml) was added dropwise under a dry N_2, the resulting mixture being kept at −70° for another 30 min. The mixture was then poured into an ice cold mixture of AcOH (150 ml) and water (total amount of water: 300 ml) Extraction by $CHCl_3$ and treatment of the organic soln with water and $NaHCO_3$ led, after evaporation of $CHCl_3$ *in vacuo* to a crude mixture which was chromatographed over silicic acid (280 g) with EtOAc–cyclohexane–$CHCl_3$ 1/1/1 v/v. Ketoaldehyde **22**, 2.4 g, (58%) is thus isolated as colourless crystals, m.p. 61–63°; IR 1705 and 1715 cm^{-1} (C=O); ^{1}N NMR: 9.8 (1 H, t, J = 0.5 Hz), 3.7 (1 H), 0.85 (3 H, s). (Found: C, 73.1; H, 9.5. Calc. for $C_{17}H_{26}O_3$: C, 73.34; H, 9.41%).

Synthesis of 17-acetoxy-4-azaestra-1(10),2,4-triene **24**. A soln of **22** (2.1 g–0.075 mole) and hydroxylamine hydrochloride (0.58 g; 0.083 mole) in AcOH (20 ml) was heated under N_2 for 2 hr. AcOH was then removed by steam distillation; the non basic compounds were extracted with diethyl ether and the remaining aqueous soln was basified with NaOH at 0–5°. Extraction with $CHCl_3$, drying of the resulting organic soln over Na_2SO_4 and evaporation of the solvent *in vacuo* led to a residue which was chromatographed over silicic acid (300 g) with an EtOAc—cyclohexane—$CHCl_3$ 2/1/1 v/v mixture. Compound **24**, 890 mg, was thus isolated along with **23**, 350 mg, in 58% combined yield.

17-Hydroxy-4-aza-estra-1(10),2,4-triene **23**. M.p. 217–220° (crystallized from dioxane); $[\alpha]_D^{20}$ ($CHCl_3$) + 88.6°; UV λ_{max} (EtOH) 268 nm (ϵ = 4800); ^{1}H NMR: 8.2 (1 H, d, J = 4.5 Hz), 7.5 (1 H, d, J = 8.0 Hz) 6.95 (1 H, q, J = 8.0 and 4.5 Hz), 2.2 (1 H, t, J = 7.8 Hz) 0.8 (3 H, s); mass spectrum: *m/e* 257 (M+). (Found: C, 79.3; H, 8.9; N, 5.2. Calc. for $C_{17}H_{23}NO$: C, 79.51; H, 9.01; N, 5.44%).

17-Acetoxy-4-aza-estra-1(10),2,4-triene **24**. M.p. 130–132° (crystallized from hexane); $[\alpha]_D^{20}$ ($CHCl_3$) + 57.4°; IR 1730, 1560, 1240, 1100, 710 cm^{-1}; UV λ_{max} (EtOH) 270 nm (ϵ = 6650); ^{1}H NMR: 8.27 (1 H, d, J = 4.7 Hz), 7.48 (1 H, d, J = 7.6 Hz), 6.98 (1 H, q, J = 7.6 and 4.7 Hz), 4.63 (1 H, t, J = 7.6 Hz), 1.99 (3 H, s), 0.77 (3 H, s); mass spectrum: *m/e* 299 (M+) (Found: C, 76.1; H, 8.3; N, 4.8. Calc. for $C_{19}H_{25}NO_2$: C, 76.20; H, 8.42; N, 4.68%).

Synthesis of N-ethyoxycarbonyliminopyridinium ylide **25**. To a stirred soln of **24** (300 mg: 1 mmole) in CH_2Cl_2 (20 ml) were added 215 mg MSH **9** (1 mmole) at room temp. After 1 hr addition of 300 ml diethyl ether led to crystallization of the corresponding pyridinium mesitylsulphonate salt, 407 mg, (79%), m.p. 227–230°. To a stirred soln of the latter compound (400 mg); 0.8 mmole) in abs EtOH (8 ml) were added successively ethyl chloroformate (84 mg; 0.8 mmole) in abs EtOH (2 ml) and anhyd K_2CO_3 (200 mg). After 2 hr the reaction reached completion as checked by TCL. After removal of the inorganic salts, the soln was evaporated to dryness and the products were separated by thick layer chromatography eluting with $CHCl_3$–EtOH 4/1 v/v. Ylide **25** 204 mg (69%) was obtained as colourless crystals, m.p. 55–68°, $[\alpha]_D^{20}$ ($CHCl_3$) −19.3°; UV λ_{max} (MeOH) 228, 278 and 310 nm (ϵ = 9800, 7800 and 2600 resp.); UV λ_{max} (C_6H_6) 279 and 342 nm (ϵ = 3200 and 3360 resp.); ^{1}H NMR (acetone-d_6): see Table 1. (Found: C, 68.1; H, 7.6; N, 7.0. Calc. for $C_{22}H_{30}N_2O_4$: C, 68.34; H, 7.82; N, 7.25%).

Photoinduced synthesis of 4-ethoxycarbonyl-17-acetoxy-A-homo-4,4a-diaza-19-norandrosta-1/10/,2,4a-triene **26**. A soln of **25** (116 mg; 0.3 mmole) in benzene (200 ml) was irradiated by UV light as described above, consumption of starting material being monitored by UV spectroscopy (gradual disappearance of the λ_{max} 342 nm absorption band) and by TLC. After 0.5 hr no starting material remained and the soln was evaporated *in vacuo* to dryness. The products were separated by means of thick layer chromatography with an EtOAc–cyclohexane–$CHCl_3$ 1/1/1 v/v mixture. Diazepine **26** was thus isolated as yellow crystals (104 mg; yield 90%), m.p. 70–71°; $[\alpha]_D^{20}$ ($CHCl_3$) + 94.5°; UV λ_{max} (MeOH) 239 nm (ϵ = 5400); UV λ_{max} (C_6H_6) 280 nm (ϵ = 2300); OCD(EPA) at +20°C: $\Delta\epsilon_{400}$ − 2.4; $\Delta\epsilon_{343}$ − 15.0; $\Delta\epsilon_{292}$ 0.0; $\Delta\epsilon_{254}$ + 22.2; $\Delta\epsilon_{230}$ + 14.3; OCD(EPA) at −190°: $\Delta\epsilon_{400}$ − 0.7; $\Delta\epsilon_{343}$ − 12.2; $\Delta\epsilon_{287}$ 0.0; $\Delta\epsilon_{254}$ + 26.8; $\Delta\epsilon_{230}$ + 19.4; ^{1}H NMR (CCl_4 + acetone-d_6) see Table 1; mass spectrum: *m/e* 386(M+). (Found: C, 68.3; H, 7.7; N, 7.2. Calcd. for $C_{22}H_{30}N_2O_4$: C, 68.34; H, 7.82; N, 7.25%).

Photoinduced synthesis of 1,10-ethylidino-2-ethoxycarbonyl-17-acetoxy-A-nor-2,3-diaza-androst-3(5)-ene **27**. A soln of **25** (160 mg; 0.42 mmole) in benzene (200 ml) was irradiated in the usual manner (see above) for 10 hr. After evaporation of the solvent *in vacuo* the products were separated by means of thick layer chromatography eluting with a mixture of EtOAc–cyclohexane 1/1 v/v mixture, elution being performed three times. Pentacyclic photoisomer **27** was obtained as a semi-crystalline compound (27 mg); UV λ_{max} ($CHCl_3$) 253 nm (ϵ = 4200); ^{1}H NMR (CCl_4 and acetone-d_6 mixture) data are indicated in the discussion; mass spectrum *m/e* 386 (M+). (Found: C, 68.4; H, 7.9; N, 7.1. Calc. for $C_{22}H_{30}N_2O_4$: C, 68.34; H, 7.82; N, 7.25%).

A soln of **27** (40 mg; 0.1 mmole) in CCl_4 (10 ml) was heated in a sealed tube under N_2 atm at 170° during 4 hr. After evaporation of the solvent *in vacuo* and thick layer chromatography of the residue only starting material **27** 15 mg was isolated; diazepine **26** could not be detected.

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