Potentially carcinogenic cyclopenta[*a*]phenanthrenes. Part 13. Synthesis of the 11-trifluoro, 11-cyano, and 11-amino analogues of the carcinogen 15,16-dihydro-11-methylcyclopenta[*a*]-phenanthren-17-one[1]

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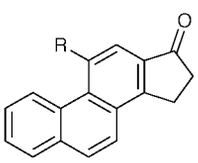
Received (in Cambridge, UK) 23rd March 1999, Accepted 26th August 1999

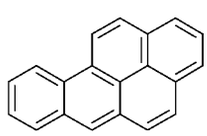
The preparation of 11,12,13,14,16,17-hexahydro-15*H*-cyclopenta[*a*]phenanthren-11,17-dione has been optimised, and the derived 17,17-ethylene diketal has been employed in the synthesis of the bay-region 11-trifluoromethyl-, 11-cyano-, and 11-amino-15,16-dihydrocyclopenta[*a*]phenanthren-17-ones.

Introduction

It is well established that methyl substitution in the bay-region of polycyclic aromatic compounds often leads to carcinogenicity.[2] Thus in the cyclopenta[*a*]phenanthrene series addition of a methyl group in the bay-region at C-11† in the inactive 17-ketone, 15,16-dihydrocyclopenta[*a*]phenanthren-17-one (**1a**), gives the methyl homologue **1b** with carcinogenic potency[3] approximately equal to that of the classical polycyclic aromatic hydrocarbon carcinogen benzo[*a*]pyrene (**2**). This is surprising in that **1b** contains only three fused aromatic rings whereas usually four or more are required for marked biological activity.[4] This makes cyclopenta[*a*]phenanthrenes the simplest system in which the relationship between structure and carcinogenic activity can be examined, and has warranted the thorough study of these compounds.[5]



1a, R = H
1b, R = CH_3
1c, R = C_2H_5
1d, R = C_4H_9
1e, R = CH_2OH
1f, R = NH_2
1g, R = CN
1h, R = CF_3
1i, R = OAc



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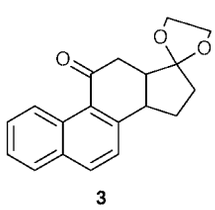

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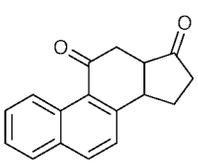

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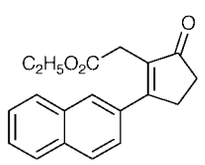

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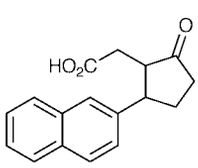


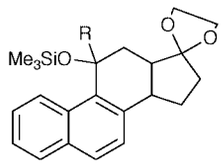
6

Although several different syntheses of this carcinogen (**1b**) are now known,[5,6] originally it was made in a straightforward manner in high yield from the oxo-ketal **3** through a Grignard reaction followed by acid dehydration and oxidation.[7] This oxo-ketal has the merit of allowing the introduction of a variety of substituents at the bay-region; the 11-ethyl (**1c**) and 11-*n*-butyl (**1d**),[8] and 11-hydroxymethyl (**1e**)[9] derivatives have all been obtained in this way. The synthesis of the 11,17-diketone **4**, the precursor of this oxo-ketal, was first described by Koebner and Robinson[10] in 1938, but little further work has been reported. A multi-step synthesis involving an anionic Cope rearrangement of a 1-naphthylbicyclo[2.2.1]heptene has been reported[11] and optical resolution of **4** by a microbiological method has been achieved.[12] This paper reports attempts to optimise the yield of the racemic diketone by Robinson's method, and describes its use in the synthesis of the bay-region 11-amino (**1f**), 11-cyano (**1g**) and 11-trifluoromethyl (**1h**) analogues. A preliminary account of the latter has been published;[13] this electronegatively substituted analogue **1h** of the carcinogen **1b** has been found to lack carcinogenic response.[14] Since X-ray structures of these two compounds show similar bay-region distortions[15] it is reasonable to conclude that it is the electronic nature of the bay-region substituent and not its steric influence that is important in conferring activity. The other two compounds have been prepared to investigate this relationship further.

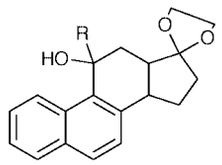
Results and discussion

In Robinson's synthesis[10] the unsaturated ester **5** is readily obtained from 2-acetylnaphthalene in three steps, and the analogous acid is cyclised in high yield simply by boiling it with acetic anhydride to give 11-acetoxy-15,16-dihydrocyclopenta[*a*]phenanthren-17-one (**1i**). To avoid aromatisation of the third ring and preserve the ketone function at C-11 required for further elaboration, it is necessary first to reduce the cyclopentene C=C double bond. It is now found that this is best achieved by reduction over 5% palladium-on-carbon catalyst obtainable from Engelhard, giving the saturated keto-acid **6** isolated after hydrolysis in 60–70% yield. Other commercial catalysts led to lower yields. Cyclisation of this acid to the diketone **4** by exposure to polyphosphoric acid under strictly

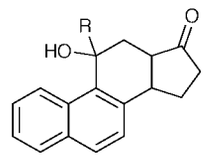
† Throughout this paper steroidal numbering has been used for the cyclopenta[*a*]phenanthrene compounds.



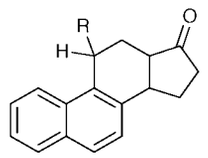
7a, R = CN
7b, R = CF_3



8a,**b**



9a,**b**



10a,**b**

controlled conditions consistently gave yields of ~60%, but inferior results were obtained with other methods. Conversion of the diketone to the 11-keto-17-ketal (**3**) was carried out in 86% yield as described.[7]

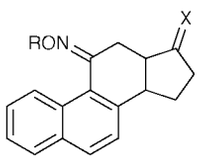
Reactions of the oxo-ketal **3** with trimethylsilyl cyanide and trifluoromethyltrimethylsilane gave the 11-cyano (**1g**) and 11-trifluoromethyl (**1h**) derivatives respectively. Both reactions occurred smoothly to give the corresponding protected tertiary alcohols **7a** and **b** in high yield, but in each case elimination of the hydroxy group proved difficult, although for different reasons. The trifluoro compound **7b** resisted removal of the siloxy oxygen with boron trifluoride–diethyl ether in dichloromethane, a method recommended for this purpose with siloxy tertiary alcohols;[16] the product was the hydroxy-ketal **8b** which was obtained more conventionally by treatment of **7b** with tetrabutylammonium fluoride in damp THF. This compound (**7b**) was unchanged on treating with phosphoryl chloride in pyridine at room temperature, but on being heated, it slowly gave rise to small amounts of several products, including the expected 11,12-ene. Boiling **7b** with concentrated hydrochloric acid converted it into the keto-alcohol **9b**. Dehydration was finally achieved, although in disappointing yield, by treatment of the latter with thionyl chloride in pyridine at 0 °C, a reaction reported for the dehydration of hindered tertiary alcohols.[17] As expected[7] with a keto-group at C-17, the product was not the 11,12-ene, but a mixture of similar amounts of the required 11-trifluoromethyl-17-ketone **1h** and its 11,12,13,14-tetrahydro derivative **10b**, obtained together in about 25% yield. However dehydrogenation of **10b** to **1h** could be accomplished by heating the former with palladium on charcoal at 220 °C.

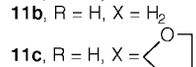
Acid hydrolysis of the fully protected cyanohydrin **7a** readily yielded the 17-keto cyanohydrin **9a** which was however rather unstable, losing HCN under mildly alkaline conditions or even on storage at ambient temperature. An attempt to dehydrate **9a** by heating it with phosphorus oxychloride in pyridine led mainly to the diketone **4**, but with thionyl chloride in pyridine at 0 °C the desired 11-cyano-17-ketone **1g** was obtained in low yield, together with the diketone and several other unidentified products.

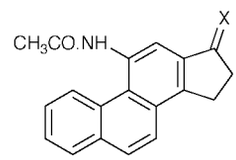
For the synthesis of the 11-amino derivative **1f**, the oxime **11c** was heated with acetic anhydride and crystalline phosphoric acid (Semmler reaction). The product was a sparingly soluble brown solid, indicated on IR spectroscopic evidence to be an amide. However, prolonged acid hydrolysis provided the 11-amino-17-one **1f** in only 13% yield. In order to examine this reaction without the complication of the 17-ketal function, the 11-oxime **11b** was submitted to Semmler conditions. The product was not the expected phenanthrene **12b**, but the ring C expanded internal amide **13b** resulting from a Beckmann rearrangement in 88% yield. The structure of this compound

Table 1

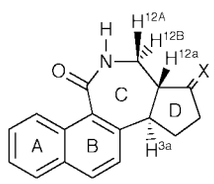
Bay region substituent (R in **1**)	$\delta_{H\text{-}12}$ ($CDCl_3$) (ppm)	
CF_3	8.43	inactive
CN	8.38	?
CH_3	7.97	carcinogen
NH_2	7.86	?
OCH_3	7.39	carcinogen



11a, R = H, X = O
11b, R = H, X = H_2
11c, R = H, X = 
11d, R = CH_3CO, X = O



12a, X = O
12b, X = H_2



13a, X = O
13b, X = H

follows from its elemental analysis ($C_{17}H_{17}NO$), from its UV spectrum which is similar to that of the oxime **11b** (carbonyl group at C-11), its strong infrared absorption at 1660 cm^{-1} (secondary amide), and its NMR spectrum which is consistent with this structure.

Mild acid treatment of the original oxime **11c** gave the corresponding 17-ketone **11a**, which was also submitted to the Semmler conditions in anticipation that the trigonal carbon at C-17 would promote aromatisation. The product was in fact a mixture of the required 11-amino-17-ketone **1f** along with a smaller quantity of its acetate **12a**, isolated together in 38% yield. In addition to some unchanged starting oxime as its acetate **11d** there was also the expected Beckmann ketone **13a** (12%) with spectroscopic properties almost identical with those of **13b**. The effect of the fused five-membered ring on the ratio of Semmler : Beckmann products is unexpected, for in the simpler case of the oxime of 7-methyltetralone the Semmler product 1-acetamido-7-methylnaphthalene was obtained in 91% yield.[19]

Since the nature of the bay region substituent is all-important in conferring carcinogenicity in this series, it is interesting to estimate the electron release or withdrawal by these groups. A measure of this is provided by the ^1H NMR chemical shift of the adjacent H-12 (Table 1).

On this basis it seems likely that the 11-nitrile will be inactive, whereas the 11-amine will be carcinogenic. In support of this it is now found that the 11-amine is a potent bacterial mutagen; details of this will be published elsewhere.

Experimental

Materials and methods were generally as described in Part 12.[1] Ultraviolet spectra were recorded for ethanolic solutions and infrared spectra as Nujol mulls; 300 MHz NMR spectra were obtained in deuteriochloroform with tetramethylsilane as reference.

13,14,15,16-Hexahydrocyclopenta[*a*]phenanthrene-11,17(12*H*)-dione (4)

15 g (5.56 mmol) of the unsaturated ethyl ester[10] (**5**) and 1 g of 5% palladium on charcoal catalyst (Engelhard, 5157, lot 04734) in ethanol (150 mL) was stirred in hydrogen at atmospheric pressure. After 5 days slightly more than one equivalent had been absorbed and TLC showed virtual absence of starting material. After removal of the catalyst the solution was evaporated to about 65 mL, water (50 mL) containing sodium hydroxide (5 g) was added, and the mixture was kept overnight at ambient temperature. After dilution with water (400 mL), acidification with dilute hydrochloric acid, and extraction with ether, the extract was washed with water, dried, and evaporated to give a syrup. This crystallised slowly from warm toluene (10 mL) on keeping in the refrigerator as almost colourless prisms of the saturated acid **6**, mp 108–110 °C (Found: C, 75.9; H, 6.2. Calculated for $C_{17}H_{16}O_3$: C, 76.1; H, 6.0%); λ_{max} 267 and 274 nm; ν_{max} 1742 and 1702 cm^{-1}. Koebner and Robinson[10] quote a mp of 132 °C for this acid obtained from hydrogenation at 40 °C over palladium on strontium carbonate. Yields ranging between 60–70% of the crystalline dihydro keto-acid were obtained in eight separate runs.

The dihydro acid (11.6 g) was ground into a fine powder and added quickly to polyphosphoric acid (100 g) held at 120 °C in an open beaker in an oil bath. The solid was rapidly stirred giving a dark green solution which after a total of 2 minutes was added to ice–water (~700 g) with good mixing. The suspension was extracted several times with dichloromethane which was washed with saturated aqueous sodium hydrogen carbonate, then with water, and dried; evaporation gave an oil that crystallised. This material was extracted repeatedly with boiling hexane, leaving a brown insoluble powder and giving on evaporation pale yellow crystals of the 11,17-diketone **4**, mp 118–120 °C (lit.,[10] 115 °C) λ_{max} 249 and 314 nm; ν_{max} 1744 and 1679 cm^{-1}. Yields of 55–65% were realised in eight separate runs under these conditions, but attempts to alter the time or temperature all led to inferior results. Stirring the dihydro acid (0.5 g) with trifluoromethanesulfonic acid (2.5 mL) at room temperature for 1 h, followed by addition of the deep orange solution to water, and workup as described above afforded the diketone in 40% yield.

Conversion to the 11-keto-17-ketal **3** was carried out as previously described[7] with the exception that it was advantageous to extract the ketal from the crude brown reaction product with boiling hexane before crystallisation from ethanol; the yield was 86%. Its *oxime* **11c**, separated from ethanol as small colourless needles, mp 174–175 °C (Found: C, 73.3; H, 6.1; N, 4.3. $C_{19}H_{19}NO_3$ requires C, 73.7; H, 6.2; N, 4.5%); λ_{max} (ε/dm^3 mol^{-1} cm^{-1}) 232 (4.59), 300.5 (3.82) nm; ν_{max} 3320 (N–OH), 1720 (17-C=O) cm^{-1}.

15,16-Dihydro-11-trifluoromethylcyclopenta[*a*]phenanthren-17-one (1h)

A solution of the 11-keto-17-ketal **3** (3.20 g) in dry tetrahydrofuran (20 mL) was cooled in ice and treated with tetrabutylammonium fluoride (40 mg), then dropwise with trifluoromethyltrimethylsilane (2.50 mL); stirring was continued at room temperature overnight. Because TLC showed that some starting material remained, treatment with the two reagents was repeated and the reaction was again left overnight. Water was added and the product was extracted with dichloromethane, washed with water, and dried; evaporation gave a syrup which soon crystallised as rosettes (4.75 g). These crystals were dissolved in a mixture of tetrahydrofuran (50 mL) and 3 M hydrochloric acid (5 mL) and kept at room temperature for 48 h; most of the THF was then removed at 40 °C *in vacuo*, more water was added, and the product was extracted with ethyl acetate. The extract was washed with aqueous sodium hydrogen carbonate, with water, dried, and evaporated to afford *11,12,13,14,15,16-hexahydro-11-hydroxy-11-trifluoromethylcyclopenta[a]phenanthren-17-one* (**9b**) as a light brown solid (3.44 g, 99%); ν_{max} 3394 (OH) and 1722 (C=O) cm^{-1}.

A solution of this tertiary alcohol **9b** (1.30 g) in dry pyridine (5 mL) was cooled in ice during the dropwise addition of thionyl chloride (0.80 mL); the solution became orange. After being stirred at room temperature for 1 h, ice and 3 M hydrochloric acid were added and the mixture was extracted with dichloromethane. The solution was washed with water, dried, and evaporated to leave a red oil which was added to a column (16 × 3.5 cm diameter in dichloromethane) of flash silica and eluted with the same solvent. The first material to be eluted formed an oil (69 mg) that partly crystallised; it appeared to be mainly the tetrahydro derivative **10b**. Later fractions gave the required *11-trifluoromethyl-17-ketone* **1h** as small beige prisms (70 mg), mp 171–172 °C; this compound was identical with that which has already been fully characterised by UV, IR, and ^1H and ^{13}C NMR spectra,[13] its mass spectrum,[18] and X-ray diffraction.[15]

The supposed tetrahydro compound (69 mg), λ_{max} 227, 280.5 nm, was heated at 220 °C in triglyme (5 mL) with 5% Pd/C for several hours. Water was then added, the reaction mixture was extracted with dichloromethane, and the latter was chromatographed as before. A further quantity of **1h** (11 mg) identical with that described above was obtained.

11-Cyano-15,16-dihydrocyclopenta[*a*]phenanthren-17-one (1g)

To a cooled solution of the 11-keto-17-ketal **3** (3.0 g) in tetrahydrofuran (60 mL) was added tetrabutylammonium fluoride (60 mg) followed by trimethylsilyl cyanide (1 mL), dropwise with stirring. At the end of 1 h, when TLC showed absence of **3**, water was added and the product was extracted with dichloromethane. After being dried, evaporation of the extract left a honey-coloured syrup which was dissolved in a mixture of tetrahydrofuran (45 mL) and 3 M hydrochloric acid (15 mL) and kept at room temperature overnight. Addition of water (300 mL) caused the separation of a gum that solidified. *11-Cyano-11-hydroxy-11,12,13,14,15,16-hexahydrocyclopenta[a]-phenanthren-17-one* (**9a**) formed off-white crystals from methanol (2.35 g, 83%), λ_{max} 217, 232.5, 282.5 nm; ν_{max} 1735 cm^{-1} (5-membered ring C=O); the CN peak at 2235 cm^{-1} was barely discernible in the infrared spectrum, but readily seen in its Raman spectrum at the same wavenumber.

This keto-cyanohydrin **9a** (500 mg) in dry pyridine (3 mL) was cooled in ice during the dropwise addition of thionyl chloride (0.20 mL). After a further 2 h at room temperature water was added and the products were extracted with dichloromethane. The latter was washed free of pyridine with dilute hydrochloric acid, then with water, and dried; the off-white solid (0.37 g) obtained on evaporation was triturated with dichloromethane (5 mL) leaving the starting keto-cyanohydrin **9a** (0.164 g). The residual solution was chromatographed on a column of flash silica, eluted with the same solvent and monitored by TLC. Fractions identified by their ultraviolet spectra as the *11-cyano-17-ketone* **1g** were pooled and evaporated to give white crystals (20 mg), mp 260–261 °C (Found: C, 83.7; H, 3.8; N, 5.4. $C_{17}H_{11}NO$ requires C, 84.0; H, 4.3, N, 5.5%) λ_{max} (ε/dm^3 mol^{-1} cm^{-1}) 233.5 (4.61), 261 (4.54), 271 (4.62), 280 sh (4.58), 339.5 (3.11), 357 (3.16), 375 (3.15) nm; ν_{max} 2250 (CN), 1717 (C=O) cm^{-1}; δ_H 9.90 (1H, d, H-9), 8.38 (1H, s, H-11), 8.05–7.96 (3H, m, ArH), 7.86 (2H, m, ArH), 3.60 (2H, m, H-3), 2.94 (2H, m, H-2).

11-Amino-15,16-dihydrocyclopenta[*a*]phenanthren-17-one (1f)

From the 11-hydroxyimino-17-ketal 11c. This compound (0.61 g), acetic anhydride (4 mL), and anhydrous crystalline phosphoric acid (4 g) were heated together with stirring at 70–80 °C. After 35 minutes the clear solution was poured into water and the brown solid was collected, washed with water

and dried (0.52 g). This material was boiled under reflux with constant-boiling HCl for 20 h, filtered hot, and the insoluble fraction was washed with water and dried (0.35 g); a second acid treatment left this brown solid unchanged. Neutralisation of the pink acid solution with sodium hydroxide gave a yellow turbid solution which was extracted with dichloromethane; on removal of the solvent and recrystallisation of the residue from ethanol *11-amino-15,16-dihydrocyclopenta[a]phenanthren-17-one* (**1f**) was obtained as small yellow needles (65 mg, 13%), mp 220 °C, with brilliant yellow fluorescence in UV light, λ_{max} (ε/dm^3 mol^{-1} cm^{-1}) 264.5 (4.63), 303.5 (4.16), and 401 (3.65) nm [after *in situ* reduction with $NaBH_4$, λ_{max} (ε/dm^3 mol^{-1} cm^{-1}) 230.5 (4.70), 241 (4.47), 249 (4.50), 285 (4.25), 369.5 (3.55) nm, almost identical with the values for 11-amino-16,17-dihydro-15*H*-cyclopenta[*a*]phenanthrene synthesised by an entirely different route,[20] λ_{max} 230.5, 242, 249.5, 283.5, 369.5 nm]; ν_{max} 3400, 3333 (N–H stretch), 1683 (C=O) cm^{-1}; δ_H 9.43 (1H, m, H-9), 7.99–7.96 (2H, m, ArH), 7.86 (1H, s, H-12), 7.70–7.64 (3H, m, ArH), 4.94 (2H, br s, NH_2), 3.40 (2H, m, H-15), 2.84 (2H, m, H-16). The yellow crystals darkened in the presence of air and several attempts at combustion analysis gave somewhat low C, H, and N figures; the amine was therefore characterised as the *N*-acetate **12a**, prepared from **1f** with acetic anhydride in pyridine overnight at ambient temperature. *11-Acetylamino-15,16-dihydrocyclopenta[a]phenanthren-17-one* (**12a**) formed pale cream crystals from ethanol, mp ~245 °C (decomp.) (Found: C, 78.5, H, 5.05, N, 4.4. $C_{19}H_{15}NO_2$ requires C, 78.9; H, 5.2; N, 4.85%), purple fluorescence in UV light, λ_{max} (ε/dm^3 mol^{-1} cm^{-1}) 265 (4.50), 285 (4.08), 300 sh (3.96), 355.5 (3.06), 373 (3.11) nm; ν_{max} 3220, 1660 (sec. amide), 1710 (17-C=O) cm^{-1}; δ_H 8.66 (1H, t, H-1), 8.03–7.96 (3H, m, ArH), 7.74–7.66 (3H, m, ArH), 3.81 (2H, t, H-15), 2.94 (2H, t, H-16), 1.56 (3H, s, CH_3).

From 11-hydroxyimino-17-ketone (11a). The 11-hydroxyimino-17-ketal **11c** (1 g) was dissolved in tetrahydrofuran (15 mL) containing 3 M HCl (1.5 mL), and kept overnight at ambient temperature. The acid was neutralised by addition of sodium hydrogen carbonate solution, more water was added, and the oil that separated was extracted with dichloromethane. After being dried, evaporation left a solid which was recrystallised from ethanol. The *11-hydroxyimino-17-ketone* **11a** formed pale fawn prisms (0.46 g), mp ~190 °C (decomp.) (Found: C, 76.65; H, 5.55; N, 5.0. $C_{17}H_{15}NO_2$ requires C, 76.95; H, 5.7; N, 5.3%) λ_{max} (ε/dm^3 mol^{-1} cm^{-1}) 231 (4.49), 301 (3.87) nm; ν_{max} 3317 (N–OH), 1721 (C=O) cm^{-1}; δ_H 8.89 (1H, d, *J* 8.5, H-1), 7.84 (1H, d, *J* 8.8, ArH), 7.57–7.45 (3H, m, ArH), 7.41 (1H, d, *J* 8.5, ArH), 3.8 (1H, q, $J_{13,14}$ 15, $J_{14,15}$ 6.8, H-13), 3.15 (2H, d, $J_{12,13}$ 7.45, H-12), 2.86 (1H, q, $J_{13,14}$ 15, $J_{12,13}$ 7.5, H-13), 2.55–2.16 (4H, m, H-15,16). Its *acetate* **11d** formed needles from methanol, mp 178–179 °C (Found: C, 74.1; H, 5.4; N, 4.4. $C_{19}H_{17}NO_3$ requires C, 74.3; H, 5.5; N, 4.55%); λ_{max} (ε/dm^3 mol^{-1} cm^{-1}) 221.5 (4.57), 239 sh (4.36), 305 (3.84) nm; ν_{max} 1764 (acetate C=O), 1739 (17-C=O) cm^{-1}.

This hydroxyimino ketone (**11a**) (2.3 g) was heated at 80 °C with acetic anhydride (15 mL) and anhydrous phosphoric acid (15 g) for 1 h. The clear deep yellow solution was diluted with water giving a solid which was collected, washed with water and dried. The yellow mother liquor was neutralised with sodium hydroxide and extracted with dichloromethane; evaporation gave a small amount of material which was pooled with the main solid. This was dissolved in dichloromethane and added to a column of silica (17 × 3.5 cm) which was eluted with this solvent containing 10% *v*/*v* of ethyl acetate. The oxime acetate **11d** (0.394 g) was eluted first followed by the 11-amino-17-ketone **1f** (0.565 g), then the Beckmann keto-amide **13a** (0.288 g), λ_{max} 231, 297, 325 nm; ν_{max} 1735 (17-C=O) (amide), 1665 cm^{-1} (see **13b** below). Further elution with ethyl acetate gave the 11-acetamido-17-ketone (**12a**) (0.12 g).

Semmler reaction with the 11-hydroxyimino-12,13,14,15,16,17-hexahydro-11*H*-cyclopenta[*a*]phenanthrene (11b)

11-Oxo-12,13,14,15,16,17-hexahydro-11*H*-cyclopenta[*a*]phenanthrene (0.3 g, mp 115–117 °C, lit.,[10] 119 °C), hydroxylamine hydrochloride (0.5 g), pyridine (0.5 mL), and ethanol (5 mL) were stirred together overnight. Water was added and the solid was collected and dried (0.3 g); the *oxime* **11b** crystallised from ethanol as cream prisms, mp 188–190 °C, λ_{max} (ε/dm^3 mol^{-1} cm^{-1}) 231 (4.44), 305 (3.92) nm; ν_{max} 3260 (NO–H) cm^{-1}.

This oxime (**11b**) (0.187 g) was heated at 70–80 °C with acetic anhydride (1.5 mL) and anhydrous phosphoric acid (1 g); after 45 minutes the deep yellow solution was diluted with water and the precipitate was collected and dried (0.166 g). Recrystallisation from ethanol gave clusters of golden leaflets (0.135 g), of the *Beckmann rearrangement product* (**13b**), mp 218–220 °C (Found: C, 80.9; H, 6.75; N, 5.5. $C_{17}H_{17}NO$ requires C, 81.2; H, 6.8; N, 5.6%); λ_{max} (ε/dm^3 mol^{-1} cm^{-1}) 229 (4.36), 297.5 (3.63), 325 (3.05) nm; ν_{max} 3407, 1660 (amide) cm^{-1}; δ 7.93 (1H, d, *J* 8.4, ArH), 7.87 (1H, d, *J* 7.8, ArH), 7.74 (1H, d, $J_{6,7}$ 8.5, H-6), 7.59–7.52 (2H, m, ArH), 7.45 (1H, d, $J_{6,7}$ 8.5, H-7), 7.39 (1H, br s, N-H), 3.09 (1H, sextet, H-14), 2.51 (1H, q, $J_{12A,13}$ 9.7, $J_{12A,12B}$ 13.8, H-12A), 2.50 (1H, d, $J_{12A,12B}$ 13.8, H-12B), 2.17 (1H, quintet, H-13), 2.06–1.88 (6H, m, ring D methylene H).

Acknowledgements

The author wishes to thank Professor J. J. Sepiol for kindly providing a specimen of 11-amino-16,17-dihydro-15*H*-cyclopenta[*a*]phenanthrene, Dr H. Herman for the Raman spectrum of **9a**, and Professor J. R. Jones for his continued support.

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Paper 9/02329A