

Studies in Metal-Ammonia Reduction. Part 4. Reduction and Reductive Methylation of 7-Methoxy-3,4-dihydrophenanthren-1(2H)-one and 7-Methoxy-1,2-dihydrophenanthren-4(3H)-one

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Birch reduction and reductive methylations of the title compounds have been investigated. 7-Methoxy-3,4-dihydrophenanthren-1(2H)-one (2) yields the *cis*-3,4,9,10,11,12-hexahydro-derivative (15) while the 7-methoxy-1,2-dihydrophenanthren-4(3H)-one (5) is reduced to the corresponding 1,2,9,10-tetrahydro-derivative (7). The factors influencing the mechanism of the reduction process have been discussed. The reductive methylation products of the ketone (2) are useful substrates in the synthesis of 9-methyl steroids.

MEJER observed² that Birch reduction of the ketone (1) gives the alcohol (3) while the isomeric ketone (4) gave the compound (6). However, the results of Mejer indicate that the influence of the carbonyl group is felt only in the reduction of the ketone (4) and not in the ketone (1). Watanabe and Narisada have shown³ that reductive alkylation of acetophenones yields the corresponding 1-alkylated-1,4-dihydroacetophenones (8) and Brown *et al.* described⁴ the reductive alkylation of 5-methoxy-tetralone to the ketone (9). These observations conclusively establish the predominant role of the carbonyl group in deciding the course of metal-ammonia reductions of aromatic carbonyl compounds.

We have recently shown¹ that the metal-ammonia

reduction of 1-acetylnaphthalene (10) affords the dihydro-derivative (11) while 2-acetylnaphthalene (12) yields the tetrahydro-derivative (13). We have also reported that the metal-ammonia reduction of 2-acetylnaphthalene (12) can be controlled in order to afford the dihydro-derivative (14) either by using potassium instead of lithium or sodium or in the presence of anhydrous ferric chloride with lithium or sodium. Our results further demonstrated the predominant influence of the carbonyl group in the reduction, without carbonyl hydrolysis of aromatic carbonyl compounds. In continuation of our interest in the metal-ammonia reduction of carbonyl compounds, we describe the results of reduction and reductive methylation of the title compounds in this paper.

Reductions and Reductive Methylations of 7-Methoxy-3,4-dihydrophenanthren-1(2H)-one.—The results of reduction and reductive methylation of the ketone (2) are presented in Table 1. It is seen from the data that reduction of the ketone (2) affords mainly the *cis*-3,4,9,10,11,12-hexahydrophenanthren-1(2H)-one (15) and in the presence of added proton sources, like ethanol, the alcohol (17) is obtained, while the reductive methylation affords a mixture of *cis*- and *trans*-ketones (18) and (19) respectively in the ratio of 4 : 1. No significant change in the reduction pattern was observed even in the presence of anhydrous ferric chloride, unlike the reduction of 2-acetylnaphthalenes,¹ and reduction with 2 g-atom equivalents of metal afforded only the hexahydro-derivative (15) and the starting material.

It is interesting to note that reduction of the ketone (2) exclusively gave the *cis*-isomer (15), which could be readily isomerised to the *trans*-isomer (16) with base indicating that the protonation of the enolate anion (25) is regioselective. Similarly the methylation of enolate anion (15) afforded a mixture of *cis*- and *trans*-isomers (18) and (19), the former being the predominant isomer. The structures of compounds (18) and (19) were deduced from ¹H n.m.r. spectral results, the methyl resonances for the two isomers having different chemical shifts (δ 1.20 for the *cis*- and δ 0.95 for the *trans*-isomer). These assignments were based on a comparison with authentic *trans*-isomer (19) prepared⁵ by the catalytic hydrogenation of compound (21). Reductive methylation of the ketone

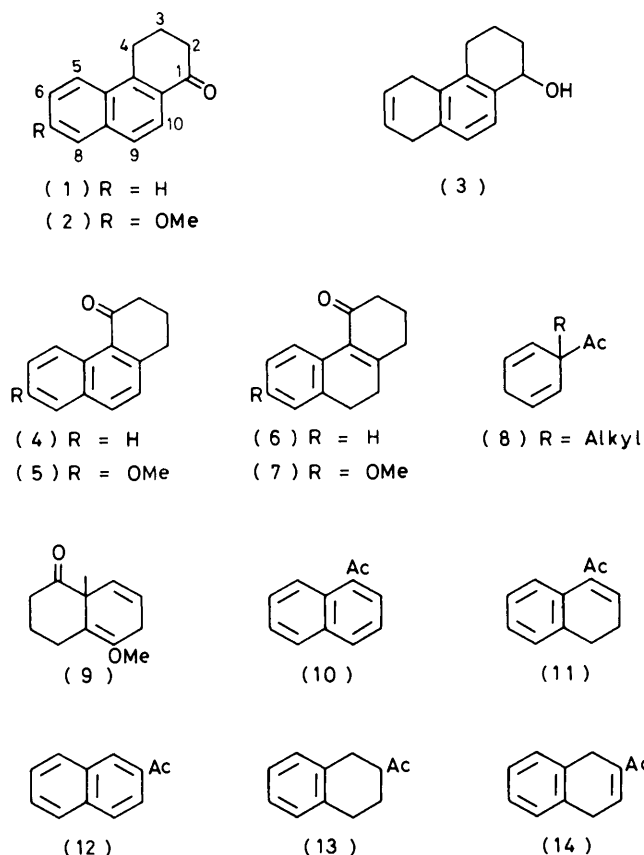


TABLE 1

Reduction and reductive methylation of the ketone (2)				
Substrate ^a (2)	Metal (g-atom/mol of substrate) Li (2)	Other conditions —	Quenching agent Ammonium chloride or sodium benzoate ^b	Product and yield (%) (2) and (15) [50 : 50]
	Li (4,6)	—	Ammonium chloride or sodium benzoate ^b	(15) [70,60]
	Li (4)	FeCl ₃	Ammonium chloride or sodium benzoate ^b	(15) [80]
(2)	Na (2)	—	Ammonium chloride or sodium benzoate ^b	(2) and (15) [50 : 50]
	Na (4)	—	Ammonium chloride or sodium benzoate ^b	(15) [65]
	Na (4)	FeCl ₃	Ammonium chloride or sodium benzoate ^b	(15) [85]
(2)	Na	—	EtOH	(17) and (15) [65 : 35]
	K (2)	—	EtOH	(2) and (15) [50 : 50]
	K (4,6)	—	EtOH	(15) [70,60]
	K (4)	FeCl ₃	—	(15) [90]
	Li (4,6)	—	MeI	Mixture of (18) and (19) [75,80]
	Li (4)	FeCl ₃	MeI	Mixture of (18) and (19) [80]
	Na (4)	—	MeI	(20) and (15) [70,30]
	Na (4)	FeCl ₃	MeI	(20) and (15) [60,40]
	K (4,6)	—	MeI	20 (80,85)

^a 10 mmol in THF (20 ml) and liquid ammonia (100 ml). ^b No significant change in yield.

(2) with sodium afforded the dimethyl derivative (20). The ¹H n.m.r. spectra of compound (20) showed a doublet at δ 0.80 (2-methyl), two singlets at δ 1.15 and 3.85 (*cis*-11-methyl and methoxy respectively) and a multiplet around δ 6.90 (ArH).

The mechanism of reduction of the ketone (2) is similar to that of 2-acetylnaphthalene.¹ Addition of two electrons to the ketone (2) affords the dianion (23). Protonation of the dianion (23) at the benzylic position

reductive methylation of the ketone (22). However, reductive methylation of the ketone (21) gave an equimolar mixture of compounds (18) and (19); these results, which contribute towards the mechanism of reduction of styrenes, will be discussed elsewhere.⁷

Reductions and Reductive Methylations of 7-Methoxy-1,2-dihydrophenanthren-4(3H)-one (5).—Reduction of the ketone (5) with metals in ammonia afforded the expected product (7), the structure of which was deduced from the

TABLE 2

Reduction and reductive methylation of the ketone (5)				
Substrate ^a (5)	Metal (g-atom/ mole of substrate)	Other conditions	Quenching agent	Product and yield (%)
	Li (2,4,6)	—	Ammonium chloride or sodium benzoate or EtOH ^b	(7) [70]
	Na (2,4,6)	—	Ammonium chloride or sodium benzoate or EtOH ^b	(7) [70—80]
	K (2,4,6)	—	Ammonium chloride or sodium benzoate or EtOH ^b	(7) [75—80]
(5)	Li (4,6)	—	MeI	(26) [75,60]
	Na (4,6)	—	MeI	(26) [75,60]
	K (4,6)	—	MeI	(26) [70,65]

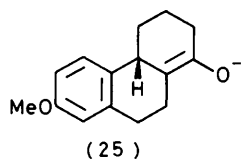
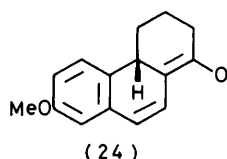
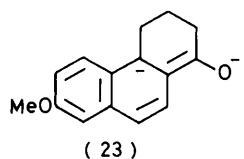
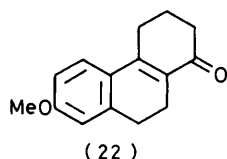
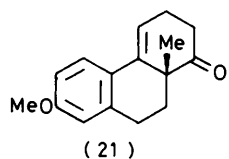
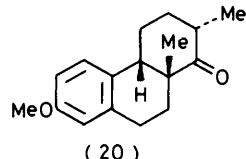
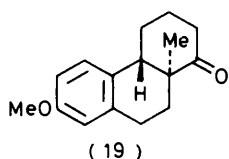
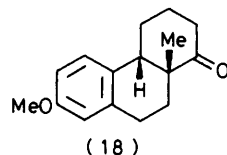
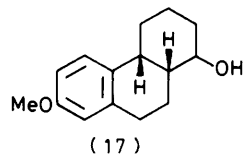
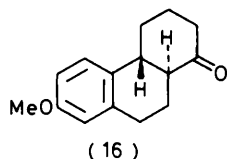
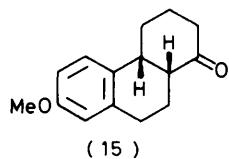
^a 10 mmol in THF (20 ml) and liquid ammonia (100 ml). ^b No significant change in yield.

results in the dienolate anion (24) which is susceptible to further reduction to give the enolate anion (25). Protonation of the latter during work up yields the ketone (15). The production of the *cis*-isomer (15) in the reduction is due to the kinetic ketonisation of the enolate anion as explained by Birch⁶ during the reduction of the ketone (22) to the *cis*-ketone (15). Protonation of the ketone takes place from the sterically less hindered equatorial side by the proton donor to yield the thermodynamically less stable *cis*-isomer. Similarly, methylation takes place from the less hindered equatorial side producing mostly the *cis*-isomer. Similar results were obtained in the

spectral and analytical data, while reductive methylation gave exclusively the ketone (26). The results of these reactions are presented in Table 2.

The reduction of 3,4-dihydrophenanthrene-4(3H)-one (4) was first reported by Mejer who isolated the unsaturated ketone (6) and pointed out the influence of the carbonyl on the reduction. Hence, the formation of compound (7) from the reduction of the ketone (5) is not unexpected and the results are consistent with our previous observation¹ on the reduction of 1-acetylnaphthalene. The mechanism of reduction of the ketone (5) involves the addition of two electrons to yield the

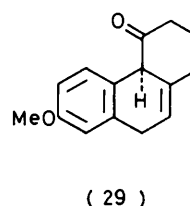
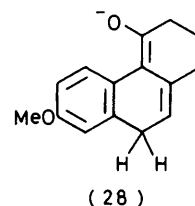
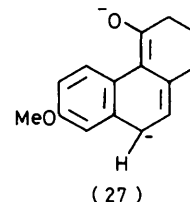
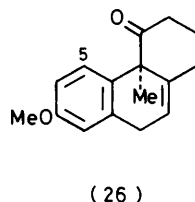
dianion (27) in which the more basic benzylic anion is initially protonated by ammonia to give the enolate anion (28). Protonation of the latter yields the β,γ -unsaturated ketone (29) which undergoes isomerisation during work-up to yield the more stable α,β -unsaturated ketone (7). Methylation of the enolate anion yields the ketone (26).



From the above results on reduction of the ketones (2) and (5), it follows that the carbonyl group influences the course of metal-ammonia reduction which is consistent with our previous observations.

EXPERIMENTAL

M.p.s are uncorrected. U.v. spectra were determined in 95% ethanol on a Unicam SP 700A spectrophotometer. I.r. spectra of liquids were measured as liquid films and those of solids were taken in Nujol on a Perkin-Elmer Infracord or model 237 spectrometer. ^1H N.m.r. spectra (chemical shifts in p.p.m. from SiMe_4) were recorded in CCl_4 solutions



on a Varian T-60 (60 MHz) spectrometer. T.l.c. and p.l.c. were carried out using silica gel (N.C.L. India). Tetrahydrofuran was distilled over lithium aluminium hydride and liquid ammonia was distilled from sodium before use; reductions were carried out at -33°C . Whenever a mixture of compounds was obtained, separation of pure components was effected by p.l.c. 2,4-Dinitrophenylhydrazones were prepared in the usual way and, unless otherwise stated, were crystallised from ethanol.

Reductions of Aryl Ketones using Metal-Ammonia.—To a well stirred solution of the substrate (10 mmol) in ammonia (100 ml) and tetrahydrofuran or diethyl ether (20 ml) an appropriate quantity of the alkali metal was added in portions. After 30 min the reaction was quenched by adding solid ammonium chloride, sodium benzoate, or absolute ethanol. The ammonia was evaporated off, water added, and the organic matter was thoroughly extracted with diethyl ether. The ethereal solution was washed until neutral and dried (Na_2SO_4). The solvent was removed and the residue was purified further, either by p.l.c. or by distillation under reduced pressure.

For reactions in the presence of a proton source ethanol was used as co-solvent, and when studies were made on the effect of anhydrous ferric chloride, catalytic amounts (10 mg/1 g of the substrate) were added to the substrate solution prior to the addition of the reducing agent.

Reductive Methylations of Aryl Ketones.—An appropriate quantity of the alkali-metal was added in portions to a well stirred solution of the substrate (10 mmol) in tetrahydrofuran or diethyl ether (20 ml) and ammonia (100 ml), and the resultant deep-blue solution was agitated for 30 min. A solution of methyl iodide in diethyl ether was added dropwise until the blue colour of the solution was discharged; the pale-yellow reaction mixture was stirred for a further 15 min. After evaporation of the ammonia the residue was worked-up in the usual manner.

cis-7-Methoxy-3,4,9,10,11,12-hexahydrophenanthren-1(2H)-one (15).—This compound had m.p. $67-68^\circ\text{C}$, ν_{max} , 1705, 1605, 1585, and 1470 cm^{-1} ; δ 1.6–3.1 (12 H, m, methylene and methines), 3.8 (3 H, s, OMe), and 6.6–7.10 (3 H, m, Ar) (Found: C, 78.0; H, 8.2. Calc. for $\text{C}_{15}\text{H}_{18}\text{O}_2$: C, 78.2; H, 7.9%); 2,4-dinitrophenylhydrazone, m.p. $143-145^\circ\text{C}$ (Found: N, 13.65. Calc. for $\text{C}_{21}\text{H}_{22}\text{N}_4\text{O}_5$: N, 13.6%).

trans-7-Methoxy-3,4,9,10,11,12-hexahydrophenanthren-1(2H)-one (16).—This compound was prepared by the method of Birch,⁶ m.p. $107-108^\circ\text{C}$; 2,4-dinitrophenylhydrazone, m.p. $188-190^\circ\text{C}$.

cis-7-Methoxy-1,2,3,4,9,10,11,12-octahydrophenanthren-1-ol (17).—This compound was obtained as a gum, ν_{\max} 3 400, 1 605, and 1 585 cm^{-1} ; δ 1.4—3.8 (14 H, m, methylene and methines), 4.1 (1 H, s, OH), 3.8 (3 H, s, OMe), and 6.6—7.0 (3 H, m, ArH) (Found: C, 77.15; H, 9.1. $\text{C}_{15}\text{H}_{20}\text{O}_2$ requires C, 77.55; H, 8.68%).

cis- and *trans*-1-7-Methoxy-11-methyl-3,4,9,10,11,12-hexahydrophenanthren-1(2H)-ones (18) and (19).—These compounds were obtained as a gum, ν_{\max} 1 700, 1 605, 1 590, 1 480, and 1 410 cm^{-1} ; δ 0.95 (3 H, s, *cis*-11-Me), 1.20 (3 H, s, *trans*-11-Me), 1.4—3.0 (11 H, m, methylenes and methines), 3.75 (3 H, s, OMe), and 6.60—7.15 (3 H, m, ArH) (Found: C, 78.4; H, 8.4. $\text{C}_{16}\text{H}_{20}\text{O}_2$ requires C, 78.65; H, 8.25%); 2,4-dinitrophenylhydrazone, m.p. 207—208 °C (Found: N, 13.3. $\text{C}_{22}\text{H}_{24}\text{N}_4\text{O}_5$ requires N, 13.20%).

trans-7-Methoxy-11-methyl-3,4,9,10,11,12-hexahydrophenanthren-1(2H)-one (19).—This compound was prepared following the method of Banerjee,⁵ m.p. 88—89 °C, ν_{\max} 1 710, 1 600, and 1 490 cm^{-1} ; δ 0.9 (3 H, s, *trans*-11-Me), 1.6—2.9 (11 H, m, methylenes and methines), 3.70 (3 H, s, OMe), and 6.5—7.0 (3 H, m, ArH).

cis-7-Methoxy-2,11-dimethyl-3,4,9,10,11,12-hexahydrophenanthren-1(2H)-one (20).—This compound was obtained as a gum, ν_{\max} 1 705, 1 610, and 1 580 cm^{-1} ; δ 0.8 (3 H, d, 2-Me), 1.15 (3 H, s, 11-Me), 1.3—3.0 (10 H, m, methylenes and methines), 3.85 (3 H, s, OMe), and 6.60—7.05 (3 H, m, Ar H) (Found: C, 78.9; H, 9.05. $\text{C}_{17}\text{H}_{22}\text{O}_2$ requires C, 79.03; H, 8.58%); 2,4-dinitrophenylhydrazone, m.p. 180—185 °C (Found: N, 12.55. $\text{C}_{23}\text{H}_{26}\text{N}_4\text{O}_5$ requires N, 12.78%).

7-Methoxy-1,2,9,10-tetrahydrophenanthren-4(3H)-one (7).—This had m.p. 109—110 °C; λ_{\max} 247 nm (ϵ 13 200); ν_{\max}

1 660, 1 600, 1 570, 1 500, 1 480, and 1 400 cm^{-1} ; δ 2.1—2.7 (10 H, m, methylene), 3.80 (3 H, s, OMe), 6.7—6.9 (2 H, m, ArH) and 8.2 (1 H, d, *peri*-proton) (Found: C, 78.74; H, 7.30. $\text{C}_{15}\text{H}_{16}\text{O}_2$ requires C, 78.92; H, 7.06%); 2,4-dinitrophenylhydrazone, m.p. 210—212 °C (ethyl acetate) (Found: N, 13.45. $\text{C}_{21}\text{H}_{20}\text{N}_4\text{O}_5$ requires N, 13.59%).

7-Methoxy-12-methyl-1,2,9,12-tetrahydrophenanthren-4(3H)-one (26).—This compound was obtained as a gum, λ_{\max} 227 nm (ϵ , 12 300); ν_{\max} 1 710, 1 600, 1 580, 1 490, 1 470, and 1 040 cm^{-1} ; δ 1.60 (3 H, s, 12-Me), 1.8—2.6 (6 H, m, methylenes), 3.35 (2 H, br s, benzylic allylic), 3.85 (3 H, s, OMe), 5.8 (1 H, t, vinylic), and 6.8—7.2 (3 H, m, ArH) (Found: C, 79.1; H, 7.25. $\text{C}_{16}\text{H}_{18}\text{O}_2$ requires C, 79.31; H, 7.41%); 2,4-dinitrophenylhydrazone, m.p. 148—150 °C (Found: N, 13.45. $\text{C}_{22}\text{H}_{22}\text{N}_4\text{O}_5$ requires N, 13.2%).

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