Metal Hydride Reduction of 9-Anthryl Ketones. Steric Influence on Reaction Path

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Reduction of 9-anthryl styryl ketone and of anthracene-9,10-diyl bis(styryl ketone) by metal hydrides yields the corresponding saturated ketones, 9-anthryl phenethyl ketone and anthracene-9,10-diyl bis(phenethyl ketone), as sole products regardless of the metal hydride or the conditions used. The absence of the corresponding allylic and saturated alcohols normally associated with the reduction of αβ-unsaturated ketones by metal hydrides is attributed to the steric influence of the adjacent *peri*-hydrogen atoms of the anthracene ring. In the first case, steric hindrance to nucleophilic attack on the carbonyl carbon atom suppresses 1,2- in favour of 1,4-reduction and, in the second, a similar effect prevents further reduction of the enolate or enol precursors of the saturated ketones. Saturated 9-anthryl ketones may be reduced to the corresponding alcohols with lithium aluminium hydride and aluminium hydride, but not with the more selective reagents sodium borohydride and lithium tri-t-butoxyaluminium hydride.

REDUCTION of αβ-unsaturated ketones by metal hydrides has been investigated extensively in recent years (refs. 1—5, and references cited therein). The products are normally the corresponding allylic alcohol, saturated ketone, and saturated alcohol, whose relative yields vary according to the conditions of the reaction, the nature of the metal hydride, and the structure of the substrate. The allylic alcohol is derived from 1,2-reduction and appears to be stable once formed.[1] The saturated ketone and the saturated alcohol, on the other hand, are believed to arise from 1,4-reduction, which gives first an enolate complex which may or may not be reduced further under the conditions of the reaction.[1,5] Acidic hydrolysis of a stable enolate gives first the enol and then, usually, the saturated ketone but at the same time destroys the excess of metal hydride so that reduction of the liberated ketone does not take place. This mechanism is supported by the isolation of the enol in certain cases, *e.g.* 1,2-dimesitylprop-1-en-1-ol from the lithium aluminium hydride reduction of 1,2-dimesitylprop-2-en-1-one.[6] In non-protic solvents the saturated alcohol is derived from reduction of the enolate, a relatively slow process as shown by the time factor which favours the saturated alcohol at the expense of the saturated ketone.[1] However, in protic solvents (*e.g.* reduction with sodium borohydride–ethanol) interconversion amongst the enolate, the enol, and the saturated ketone takes place within the reducing medium,[3,5] with the result that in the presence of an excess of the metal hydride 1,4-reduction leads exclusively to the saturated alcohol.[1-5]

The literature shows that preference for 1,2- or 1,4-reduction of αβ-unsaturated ketones is delicately balanced and not easily predictable. As a rule 1,2-reduction is preferred for aliphatic open-chain compounds [2] and derivatives of cyclohex-2-en-1-one [1,2,4] although 1,4-reduction is more important for derivatives of cyclopent-2-en-1-one.[1,3] The mode of reduction is also a function of the metal hydride used and a distinct order of the common metal hydrides in preference for 1,2- or 1,4-attack can be discerned (1,2 : aluminium hydride > lithium aluminium hydride > lithium tri-t-butoxyaluminium hydride > sodium borohydride : 1,4). An attempt to explain parts of this sequence in terms of the HSAB theory has recently been published.[7]

The effect of the solvent is also important. Thus, reduction with lithium aluminium hydride in ether consistently gives a higher ratio of the 1,2-adduct than reduction with lithium aluminium hydride in tetrahydrofuran,[1] and reduction of simple chalcones with sodium borohydride, predominantly 1,2 when methanol or ethanol is used as solvent,[8] gives chiefly the 1,4-adducts in less polar solvents such as propan-2-ol, tetrahydrofuran, and bis-(2-methoxyethyl) ether.[5]

We have investigated the reduction of a number of saturated and αβ-unsaturated 9-anthryl ketones with various metal hydrides. The results (Table) differ from established trends in several important respects.

(*a*) Sodium borohydride reduces the two αβ-unsaturated ketones (1) and (2) to the corresponding saturated ketones rather than the expected saturated alcohols and does not react at all with the saturated 9-anthryl ketones (3)—(5).

(*b*) Reduction of the unsaturated ketones (1) and (2) with aluminium hydride and lithium aluminium hydride–ether also yields the saturated ketones as sole products and therefore proceeds by a 1,4-mechanism. Although small percentages of 1,4-adducts have previously been reported from reduction of other αβ-unsaturated ketones with these reagents [1] the yields have in no case been more than 20% (aluminium hydride) or 35% (lithium aluminium hydride–ether) of the total product, and 1,2-reduction to the allylic alcohol is usual.[1,3,9]

(*c*) The successful reduction of the unsaturated ketones (1) and (2) with lithium tri-t-butoxyaluminium hydride

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[1] H. C. Brown and H. M. Hess, *J. Org. Chem.*, 1969, **34**, 2206.

[2] M. R. Johnson and B. Rickborn, *J. Org. Chem.*, 1970, **35**, 1041.

[3] W. L. Dilling and R. A. Plepys, *J. Org. Chem.*, 1970, **35**, 2971.

[4] (*a*) H. Haubenstock, *J. Org. Chem.*, 1972, **37**, 656; (*b*) H. Haubenstock and P. Quezada, *ibid.*, p. 4067.

[5] K. Iqbal and W. R. Jackson, *J. Chem. Soc.* (*C*), 1968, 616.

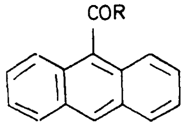
[6] R. E. Lutz and D. F. Hinkley, *J. Amer. Chem. Soc.*, 1950, **72**, 4091.

[7] J. Bottin, O. Eisenstein, C. Minot, and N. Trong Anh, *Tetrahedron Letters*, 1972, 3015.

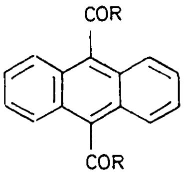
[8] (*a*) R. E. Lutz and J. O. Weiss, *J. Amer. Chem. Soc.*, 1955, **77**, 1814; (*b*) P. L. Southwick, N. Latif, B. M. Fitzgerald, and N. M. Zaczek, *J. Org. Chem.*, 1966, **31**, 1.

[9] M. J. Jorgenson, *Tetrahedron Letters*, 1962, 559.

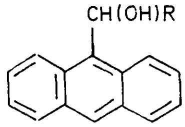
and sodium borohydride and the failure of these reagents to reduce the saturated 9-anthryl ketones (3)—(5) is contrary to Haubenstock's general conclusion from competitive experiments that sterically hindered, as well as sterically unhindered, αβ-unsaturated ketones are consistently less reactive than the corresponding saturated ketones.[4]



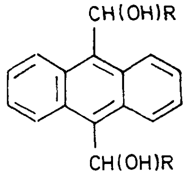
(1) R = PhCH:CH
(3) R = Ph
(4) R = $PhCH_2·CH_2$



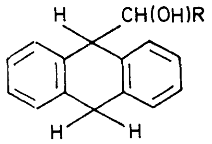
(2) R = PhCH:CH
(5) R = $PhCH_2·CH_2$



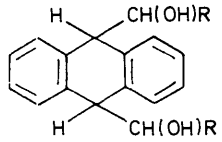
(6) R = Ph
(7) R = $PhCH_2·CH_2$



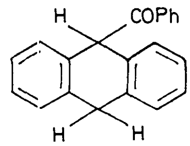
(8) R = $PhCH_2·CH_2$



(9) R = Ph
(10) R = $PhCH_2·CH_2$



(11) R = $PhCH_2·CH_2$



(12)

The only parallel in the literature to the behaviour of 9-anthryl ketones towards metal hydride reduction is an early report [8a] that reduction of mesityl styryl ketone with lithium aluminium hydride gives a 97% yield of the 1,4-adduct, mesityl phenethyl ketone, whereas reduction of chalcone under similar conditions gives an 88% yield of the allylic alcohol, 1,3-diphenylprop-2-en-1-ol. In both mesityl styryl ketone and the 9-anthryl ketones the carbonyl group is flanked by two 'bulky' groups—the two *ortho* methyl groups in the former and the two *peri* hydrogen atoms of the anthracene ring in the latter. It appears that the presence of these groups is responsible for the unusual direction of reduction by preventing free rotation of the carbonyl group *vis-à-vis* the ring and hindering normal nucleophilic attack by the metal hydride, which is believed to proceed along the π axis of the carbonyl carbon.[10,11] Initial nucleophilic attack on the conjugate carbon atom (C-4) to give first the enolate and thence, on hydrolysis, the saturated ketone is therefore preferred.

Reduction products of 9-anthryl ketones

Substrate (0·01 mol)	Method †	Product	(g, % yield)
(1)	(a)	(4)	(2·92, 94)
	(b)	(4)	(2·80, 90)
	(c)	(4)	(2·97, 96)
	(d)	(4)	(2·65, 85)
	(e)	(4)	(2·51, 81)
(2)	(a)	(5)	(4·14, 94)
	(b)	(5)	(4·05, 92)
	(c)	(5)	(4·10, 93)
	(d)	(5)	(3·85, 87)
	(e)	(5)	(3·82, 86)
(3)	(a)	(6)	(2·20, 78)
	(c)	(6)	(2·36, 83)
	(d), (e)	No reaction	(—)
(4)	(a)	(7)	(2·90, 93 ‡)
	(c)	(7)	(3·01, 96 ‡)
	(d), (e)	No reaction	(—)
(5)	(a)	(8)	(4·10, 92 ‡)
	(c)	(8)	(4·06, 91 ‡)
	(d), (e)	No reaction	(—)

† (a) $LiAlH_4$–ether; (b) $LiAlH_4$–ether (reverse addition); (c) AlH_3–ether; (d) $LaAlH(OBu^t)_3$–ether; (e) $NaBH_4$–ethanol. ‡ Crude product.

With regard to reduction with aluminium hydride, Dilling and Plepys [3] have proposed initial electrophilic attack by the aluminium centre on the carbonyl oxygen atom followed by hydride transfer to the carbonyl carbon atom to account for the usually exclusive 1,2-reduction of αβ-unsaturated ketones with this reagent.[3,9] There are also strong indications, notably Wiberg and Jahn's isolation of aluminium ethylate from the aluminium hydride reduction of acetaldehyde,[12] that such a mechanism operates in the reduction of simple carbonyl compounds. However, although steric hindrance to electrophilic attack on the carbonyl oxygen atom of compounds (1) and (2) would be much less than that towards nucleophilic attack on the carbonyl carbon atoms, reaction with aluminium hydride yields only 1,4-reduction products. It appears therefore that, for these compounds at least, the mechanism of reduction with aluminium hydride proceeds *via* initial nucleophilic attack as for other metal hydrides.

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[10] M. Cherest, H. Felkin, and N. Prudent, *Tetrahedron Letters*, 1968, 2199.

[11] H. O. House, 'Modern Synthetic Techniques,' 1st edn., Benjamin, New York, 1965, ch. 2.

[12] E. Wiberg and A. Jahn, *Z. Naturforsch.*, 1952, **7b**, 581.

Since no trace of the corresponding saturated alcohols was found on reduction of the unsaturated ketones (1) and (2), even with sodium borohydride–ethanol, the enolates and, in protic solvents, the enols are apparently immune to further attack by the metal hydride. This would be reasonable only if reduction of enolates and enols proceeded *via* initial nucleophilic attack on the carbon atom bonded to oxygen. As with attack on the carbonyl carbon of 9-anthryl ketones this would be hindered by the *peri* hydrogen atoms of the anthracene ring and, with a deuterium-labelling technique, Dauben and Eastham[13] have in fact shown such a mechanism to operate in the lithium aluminium hydride reduction of enol acetates derived from cholestan-3-one and coprostan-3-one. The failure of lithium tri-t-butoxylaluminium hydride and sodium borohydride to reduce the saturated 9-anthryl ketones (3)—(5) is consistent with these facts, although the successful reduction of these ketones with aluminium hydride and with lithium aluminium hydride–ether shows that 1,2-reduction of the sterically hindered carbonyl group is possible under forcing conditions.

Of the alcoholic end-products (6)—(8), (6) is a known compound[14] and was readily obtained in a solid form and purified by recrystallisation. Compounds (7) and (8), however, could only be obtained as gums, which deteriorated and, in the presence of oxygen, slowly deposited crystals of anthraquinone both in the presence and in the absence of light. Compounds (7) and (8), as well as (6), also deposited anthraquinone from solution, and this reaction was accelerated on attempts to purify the gums by chromatography on alumina. The possibility that the alcohols were in fact the dihydro-derivatives (9)—(11) was discounted first by their n.m.r. spectra, which showed aromatic absorption patterns similar to those of their ketonic precursors, and by the synthesis of the dihydro-alcohol (9) from 9-benzoylanthracene [by reduction with zinc–acetic acid to the known 9-benzoyl-9,10-dihydroanthracene[15] (12), followed by treatment of this product with lithium aluminium hydride]. The gums (7) and (8) gave satisfactory analytical figures, i.r. spectra and n.m.r. spectra, although their n.m.r. spectra revealed the presence of small quantities of unidentified impurities in each.

Models of the alcohols (6)—(8) showed that accommodation of the tetrahedral carbon atom attached to the anthracene ring involves considerable strain, and further research into the nature of these compounds and the mode of their decomposition is in progress.

EXPERIMENTAL

I.r. spectra were determined for Nujol mulls or transparent films prepared by allowing solutions in toluene to evaporate, and were recorded on a Unicam SP 200 G spectrometer. N.m.r. spectra were determined for solutions in deuteriochloroform with tetramethylsilane as internal reference and were recorded at 60 MHz on a Varian A60 D or a Perkin-Elmer R11 instrument.

All reductions were carried out under an atmosphere of dry nitrogen.

Starting Materials.—9-Benzoylanthracene, 9-anthryl styryl ketone, and anthracene-9,10-diyl bis(styryl ketone) were prepared by direct acylation of anthracene following the methods of ref. 16.

9-Anthryl phenethyl ketone and anthracene-9,10-diyl bis(phenethyl ketone) were prepared by reduction of 9-anthryl styryl ketone and anthracene-9,10-diyl bis(styryl ketone), respectively, as described later.

9-Benzoyl-9,10-dihydroanthracene, prepared by heating 9-benzoylanthracene with zinc powder in acetic acid,[15] had m.p. 100—101° (lit.,[15] 101°), and gave a deep yellow colour with sulphuric acid; $\nu_{max.}$ 1672 cm^{-1} (C=O), τ 1·87—2·14 (2H, m, ArH), 2·50—2·84 (11H, m, ArH), 4·01 (1H, s), and 5·86 (2H, q, *J* 38 Hz).

General Procedures for Reduction.—(a) *Lithium aluminium hydride–ether.* The finely powdered ketone (0·01 mol) was added in portions to a stirred solution of lithium aluminium hydride (0·38 g, 0·01 mol) in anhydrous ether (100 ml). The mixture was allowed to reflux gently for 15 min [(1)—(4)] or 2 h (5) and the excess of metal hydride was then destroyed by slow addition of water-saturated ether. The ethereal solution was washed once with dilute sulphuric acid, dried (Na_2SO_4), and distilled. Final traces of ether were removed under vacuum.

(b) *Lithium aluminium hydride–ether (reverse addition).* This was similar to (a) except that a solution of lithium aluminium hydride (0·38 g, 0·01 mol) in ether (75 ml) was added slowly to a stirred suspension of the powdered ketone (0·01 mol) in ether (50 ml).

(c) *Aluminium hydride.*[9] Lithium aluminium hydride (0·38 g, 0·01 mol) was dissolved in ether (100 ml) and anhydrous aluminium chloride (0·466 g, 0·035 mol) was then added slowly with stirring. To this mixture the finely powdered ketone (0·1 mol) was added in portions and the procedure described in (a) was then followed.

(d) *Lithium tri-t-butoxyaluminium hydride.* To a stirred solution of lithium aluminium hydride (1·52 g, 0·04 mol) in ether (100 ml) was added dropwise a solution of t-butyl alcohol (9·26 g, 0·125 mol) in ether (50 ml). To this mixture the finely powdered ketone (0·01 mol) was added in portions and the mixture was then stirred at 20° for $\frac{1}{2}$ h [(1) and (2)] or 5 h [(3)—(5)] and worked up as described in (a).

(e) *Sodium borohydride.* A mixture of the finely powdered ketone (0·01 mol), sodium borohydride (0·38 g, 0·01 mol), and ethanol (50 ml) was refluxed for $\frac{1}{2}$ h [(1) and (2)] or 5 h [(3)]—(5)]. The mixture was then treated with dilute sulphuric acid and extracted with ether or chloroform. The organic extracts were worked up as described in (a).

Products.—Unless stated the yields of the products are given in the Table.

9-Anthryl styryl ketone (all procedures) gave a yellow gum which on trituration with ether gave pale yellow crystals of *9-anthryl phenethyl ketone*, m.p. 79—80° (ethanol), giving a red colour rapidly changing to olive green with sulphuric acid, $\nu_{max.}$ (neat) 1703s (C=O) and 890s cm^{-1} (isolated Ar-H) (Found: C, 88·7; H, 6·2. $C_{23}H_{18}O$ re-

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[13] W. G. Dauben and J. F. Eastham, *J. Amer. Chem. Soc.*, 1953, **75**, 1718.

[14] O. Cervinka, V. Suchan, and B. Masar, *Coll. Czech. Chem. Comm.*, 1965, **30**, 1693.

[15] E. Lippmann and P. Keppich, *Ber.*, 1900, **33**, 3086.

[16] A. T. Dlamini, H. J. Williams, and R. G. Shotter, *Tetrahedron*, 1973, **29**, 1327.

quires C, 89·0; H, 5·8%); τ 1·64 (1H, s, ArH), 1·98—2·16 (2H, m, ArH), 2·47—2·77 (11H, m, ArH), and 6·75 (4H, triplet approximation to singlet, A_2X_2 approximating to A_2B_2). The i.r. spectrum of the initial gum revealed no trace of peaks attributable to OH.

Anthracene-9,10-diyl bis(styryl ketone) (all procedures) gave pale yellow crystals of *anthracene*-9,10-*diyl bis*(*phenethyl ketone*), m.p. 155° (ethanol), giving a red colour with sulphuric acid; $\nu_{max.}$ (Nujol) 1695 cm^{-1} (C=O) (Found: C, 86·8; H, 6·0. $C_{32}H_{26}O_2$ requires C, 86·55; H, 5·9%); τ 2·30—2·86 (18H, m, ArH) and 6·75 (8H, triplet approximating to singlet, two equivalent A_2X_2 systems approximating to A_2B_2).

9-Benzoylanthracene [procedures (a) and (c)] gave a yellow gum which on trituration with ether gave pale yellow crystals of α-(9-anthryl)benzyl alcohol, m.p. 107—109° (ethanol) (lit.,[14] 110—114°), giving a persistent deep green colour with sulphuric acid; $\nu_{max.}$ (neat) 3520m (free OH), 3450br (H-bonded OH), 1051s (OH), and 890s cm^{-1} (isolated Ar-H) (Found: C, 88·65; H, 5·7. Calc. for $C_{21}H_{16}O$: C, 88·75; H, 5·65%). With procedures (d) and (e) unchanged 9-benzoylanthracene was recovered in *ca.* 90% yield.

9-Anthryl phenethyl ketone [procedures (a) and (c)] gave a pale yellow gum which could not be crystallised and which was identified as 1-(9-*anthryl*)-3-*phenylpropan*-1-*ol*, giving a persistant blood red colour with sulphuric acid, and showing mauve fluorescence; $\nu_{max.}$ 3530m (free OH), 3390br (H-bonded OH), 1051s (OH), and 889s cm^{-1} (isolated Ar-H) (Found: C, 89·05; H, 6·55. $C_{23}H_{20}O$ requires C, 88·45; H, 6·4%), τ 1·89 (1H, s, ArH), 2·14—2·31 (2H, m, ArH), 2·60—3·00 (11H, m, ArH), and 7·08—8·00 (6H, m). One of the major peaks of the high-field multiplet (τ 7·48; 1H) disappeared after shaking with D_2O and was assigned to OH. Small absorptions assigned to impurities were centred at τ 1·61, 4·08, and 8·69. With procedures (d) and (e) unchanged starting material was recovered in *ca.* 90% yield.

Anthracene-9,10-diyl bis(phenethyl ketone) [procedures (a) and (c)] gave a yellow gum which could not be crystallised and which was identified as 1,1′-*anthracene*-9,10-*diylbis*-(3-*phenylpropan*-1-*ol*), very soluble in ether, giving an indigo colour rapidly turning to red-brown with sulphuric acid, and showing strong mauve fluorescence; $\nu_{max.}$ 3530m (free OH), 3380br (H-bonded OH), and 1049s cm^{-1} (OH) (Found: C, 87·15; H, 6·95. $C_{32}H_{30}O_2$ requires C, 86·1; H, 6·75%), τ 2·58—2·97 (18H, m, ArH) and 6·83—7·92 (multiplet approximating to strong singlet at τ 7·28, 12H). After shaking the sample with D_2O the high-field multiplet integrated for 10H instead of 12H, and it appears that OH absorption corresponds with the main peak at τ 7·28. Small absorptions assigned to impurities were centred at τ 1·48, 3·92, and 8·65. With procedures (d) and (e) unchanged starting material was recovered in *ca.* 90% yield.

9-Benzoyl-9,10-dihydroanthracene [procedure (a)] gave α-(9,10-*dihydro*-9-*anthryl*)*benzyl alcohol* (2·46 g, 86%), small white needles (ethanol), m.p. 150—151°, $\nu_{max.}$ (Nujol) 3420br (OH) and 1045s cm^{-1} (OH) (Found: C, 88·05; H, 6·15. $C_{21}H_{18}O$ requires C, 88·1; H, 6·3%), τ 2·66—3·28 (13H, ArH), 5·18 (1H, d, *J* 7 Hz, showing splitting by OH, *J* 2·5 Hz), 5·73 (1H, d, *J* 7 Hz), 6·40 (2H, q, *J* 22 Hz), and 7·85 (1H, d, *J* 2·5 Hz). After shaking the sample with D_2O the doublet at τ 5·18 was no longer split and that at τ 7·85 had disappeared.

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