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CONFORMATIONAL EFFECTS IN COMPOUNDS WITH SIX-MEMBERED RINGS—V

REDUCTION OF UNSATURATED KETONES BY DISSOLVING METALS $\Delta^{1(9)}$-2-OCTALONES

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Abstract—*Cis*-2-decalones have been detected for the first time in the reduction of $\Delta^{1(9)}$-2-octalones by metals and alcohols in liquid ammonia. The effects of alkyl substituents on the ratio of *cis*- to *trans*-ring fused products and the high stereoselectivity are *not* consistent with product determining transition states in which the β-carbon atom (i.e. C9), is nearly tetrahedral, as has been previously supposed. The product ratios may be accounted for qualitatively if in accordance with Hammond's postulate the transition states are similar to the conformations of the highly basic intermediate anion (IV), in which the C9-carbon atom is trigonal, rather than to the products in which the C9-carbon atom is tetrahedral. A considerable improvement in the yield and purity of the products from metal in liquid ammonia reductions of unsaturated ketones results when the reaction time is minimized by rapid mixing of the reagents.

Solutions of alkali and alkaline earth metals in liquid ammonia are widely used for reductions because, among other reasons, the stereochemistry of the products may generally be successfully predicted from Barton's empirical generalization that when a new asymmetric carbon atom results the more stable of the two possible diastereoisomers predominates.[1,2] Since the relative stabilities of stereoisomers are often predictable in six-membered ring compounds metal-ammonia reductions are particularly valuable in rational synthesis of the most important groups of alicyclic compounds.

The steric course of the reduction of unconjugated double bonds in olefines and ketones may generally be explained by postulating an intermediate tetrahedral carbanion in its most stable conformation, either formed directly or resulting from rapid inversion of the alternative less stable conformation.[2] Since the more stable conformation of the carbanion is similar in shape to the more stable diastereoisomeric product and the highly exothermic protonation appears to be comparatively insensitive to steric hindrance, the relative stabilities of the transition states for the product determining protonation usually reflect qualitatively the relative stabilities of the products. In a few instances relatively large differences have been observed for different metals, and ion-pairs rather simple carbanions must then be explicitly considered.[3,4]

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[1] H. Smith, *Organic Reactions in Liquid Ammonia* (Edited by G. Jander, H. Spandau and C. C. Addison) Vol. 1; Part 2, Chap 11. Interscience, New York and London (1963); [a] pp. 213–230; [b] pp. 237–261.

[2] D. H. R. Barton and C. H. Robinson, *J. Chem. Soc.* 3045 (1954).

[3] G. Ourisson and A. Rassat, *Tetrahedron Letters No.* 21, 16 (1960).

[4] G. E. Arth, G. I. Poos, R. M. Lukes, F. M. Robinson, W. F. Jones, M. Feurer and L. H. Sarett, *J. Amer. Chem. Soc.* **76**, 1715 (1954).

The factors controlling the steric course of reduction are commonly less simple for conjugated systems than for isolated double bonds. Firstly, if we assume that there is stepwise addition of electrons and protons (see below), it is uncertain whether the first protonation precedes or follows the second electron addition, and whether any of the trigonal carbon atoms in the original conjugated system become tertahedral in the intermediate mesomeric anions. Secondly, a single conformation of a mesomeric anion already containing an asymmetric carbon atom can often give more than one pair of diastereoisomeric products. Finally, a mesomeric anion may differ considerably in shape from the products resulting from its protonation. α,β-Unsaturated ketones, however, are relatively simple to study because the first proton usually adds very selectively to the β-carbon atom and the succeding reactions of the enol anion are quite well understood.[5–7] The problem is thereby reduced to determining the factors which influence the steric course of a protonation giving one pair of stereoisomers.

Two sequences of reactions, differing only in the timing of the addition of the first proton and the second electron, appear plausible for the reduction of α,β-unsaturated ketones. The stepwise addition of electrons and protons, rather than concerted addition, in the early steps seems likely by analogy with the addition of electrons to other unsaturated[1a,8,9] or aromatic[1b] compounds and is confirmed in two instances by direct evidence for an intermediate with a nucleophilic β-carbon atom.[10,11] The enolate anion B has been shown to be the final product in the absence of alcohols by reaction with alkyl halides,[12,13] while in the presence of an alcohol the anion B is protonated and the resulting ketone is reduced further.[14] $\Delta^{1(9)}$-2-Octalones are suitable for detailed study because they are readily available, are reducible to compounds of known or determinable configuration and convenient for gas chromatographic analysis, are good models for important classes of compounds such as the steriods and have been the subject of some important qualitative studies.

All the early examples of the reduction of $\Delta^{1(9)}$-2-octalones and analogous ketones gave the presumably more stable *trans* ring fused products exclusively, with one exception,[15] in agreement with Barton's generalization. Birch has supposed that these results are explained by the very high basicity of the β-carbon atom in the di-anion A so that the relative amounts of the products are related to the stabilities of the conformations of the reactant di-anion A, in which, apparently, the β-carbon atom was considered to be tetrahedral as in the products. More recently, however, the $\Delta^{1(9)}$-2-octalones If-h[16,17] have been found to be reduced to *trans*-2-decalones, without the *cis*-isomers being detected. These are clear exceptions to Barton's rule that the

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[5] H. E. Zimmerman, *J. Amer. Chem. Soc.* **78**, 1163 (1956).

[6] A. J. Birch, H. Smith and R. E. Thornton, *J. Chem. Soc.* 1339 (1957).

[7] E. J. Corey and R. A. Sneen *J. Amer. Chem. Soc.* **78**, 6269 (1956).

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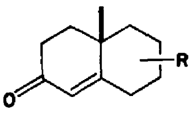
[14] F. Sondheimer, R. Yashin, G. Rosenkranz and C. Djerassi, *J. Amer. Chem. Soc.* **74**, 2696 (1952).

[15] M. J. T. Robinson, *Tetrahedron* **1**, 49 (1957).

[16] R. Howe and F. J. McQuillin, *J. Chem. Soc.* 2670 (1956).

[17] G. Stork and S. D. Darling, *J. Amer. Chem. Soc.* **82**, 1512 (1960); **86**, 1761 (1964).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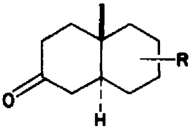
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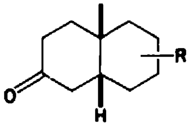
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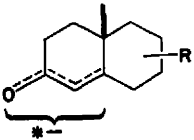
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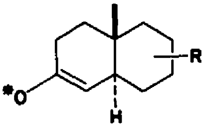
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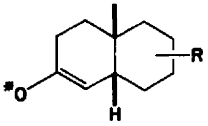
VI

R =

a; H
b; 10β-Me
c; 5β,7β-Me_2
d; 6,6-Me_2
e; 7,7-Me_2
f; 1,10β-Me_2; 7α-i-Pr

R =

g; 6β-OMe; 10β-Me
h; 6β-OMe; 7α,10β-Me_2
i; 6β-OMe; 7β,10β-Me_2
j; 6α-OMe; 10β-Me
k; 6α-OMe; 7β,10β-Me_2

more stable stereoisomers results because in each instance one of the conformations of the *cis*-enol radical or anion should be more stable than the *trans*-enol radical or anion. Stork and Darling explained these observations by postulating an over-riding stereoelectronic requirement for axial* protonation at the β-carbon atom, with the relative stabilities of the products being subsiduary factors. The conclusion that the observed axial protonation is the result of stereoelectronic control, however, is a valid deduction only if unstated and, in the present author's view, improbable assumptions about the shapes of the transition states are correct (see Results and Discussion). The probable magnitude of the stereoselectivity for some ketones, furthermore, seemed likely to be greater than plausible estimates of the differences in stabilities of the products resulting from axial protonation, so that it was doubtful whether either of the two factors supposed to control the stereoselectivity is really important. I chose to study the reduction of $\Delta^{1(9)}$-2-octalones in which the effects of the substituents on the relative stabilities of the conformations of the reactants and products are at least qualitatively predictable if small, using only these compounds which gave analysable mixtures of *cis*- and *trans*-2-decalones. The preparation and proof of configuration of the ketones will be published separately.[18]

EXPERIMENTAL

Reductions with metal ammonia

The following procedure was found to be most convenient for minimizing by-products in small scale reductions when product ratios were being measured. A solution of a $\Delta^{1(9)}$-2-octalone (2 mmoles), except for the 10-methyl derivative Ib (see below), in dry ether was added rapidly to a freshly prepared solution of Na (12–16 mg atoms) in liquid ammonia (*c*, 40 ml). Liquid ammonia from some commercial cylinders could be used under these conditions without purification, even though it was not suitable for slower reductions,[19] but usually the liquid ammonia was distilled immediately before use. The addition of the ketone–alcohol–ether mixture was most conveniently made from a hypodermic syringe with a wide bore needle, the jet of liquid causing rapid mixing and diminishing the risk of excessive foaming resulting from the strongly exothermic reaction and the evolution of H_2. When

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* Axial (or equatorial) protonation means that the added proton is axial (or equatorial) in the *unsaturated* ring in the product.

[18] W. D. Cotterill, D. R. Elliott and M. J. T. Robinson, unpublished work.

[19] H. L. Dryden, G. M. Webber, R. R. Burtner and J. A. Cella, *J. Org. Chem.* **26**, 3237 (1961).

necessary mixing was completed by hand swirling and after a few sec excess NH$_4$Cl was added. After the ammonia had evaporated the mixture of 2-decalols was isolated with ether in the usual way and oxidized in acetone ("AnalaR") at 5–10° with CrO$_3$[20] the small excess of the latter being destroyed after *c* 1 min by isopropyl alcohol. The mixtures of *cis*- and *trans*-2-decalones were isolated with ether and analysed by gas chromatography[21] using 1,2,3-tri-(2-cyanoethoxy)propane or sucrose acetate isobutyrate (1 % on celite) at 110° as the stationary phase.

Reductions of 10-methyl-$\Delta^{1(9)}$-2-octalone were carried out on a larger scale (5–10 mmoles) and the resulting mixtures of *cis*- and *trans*-10-methyl-2-decalone, which could not be separated by gas chromatography, were analysed with a Varian A60 spectrometer using the peak heights of the 10-methyl group absorptions at 8·75 τ (unchanged 10-methyl-$\Delta^{1(9)}$-2-octalone, always <1 %), 8·81 τ (*cis*) and 8·96 τ (*trans*). The heights of the 10-methyl group peak for the *cis* isomer were multiplied by a factor 0·65 (when the half width of the tetramethylsilane line was 0·6 vc/s) determined from standard mixtures run under the same conditions; suitable concentrations and spectrometer settings were 50 % (w/v) solutions (not de-gassed, 0·35 ml) in ethanol-free chloroform, sweep width 250 c/s, sweep time 250 sec and rf field 0·04 mgauss.

Table 1. Analysis of mixtures of 2-decalones from the reduction of $\Delta^{1(9)}$-2-octalones I with sodium in liquid ammonia

$\Delta^{1(9)}$-2-Octalone I, Substituents	% *cis*-2-Decalone III	Ratio of products (*trans*/*cis*)
a; Nil	1·0 ± 0.1	100 ± 10
b; 10β-Me	1·3 ± 0·2	80 ± 20
c; 5β,7β-Me$_2$	0·4 ± 0·1	250 ± 50
d; 6,6-Me$_2$	0·15 ± 0·05	700 ± 200
e; 7,7-Me$_2$	0·9 ± 0·1	110 + 10

RESULTS AND DISCUSSION

Preliminary experiments with (Ia) showed that complete reduction could not be obtained using an alkali metal in liquid ammonia without an alcohol as a proton source.[22,23] The unreduced unsaturated ketone interfered with the analysis of the resulting mixture of 2-decalones because the β,γ-isomer,[24] Δ^9-2-octalone, and *cis*-2-decalone, have similar gas chromatographic properties. The reductions were accordingly carried out in the presence of an alcohol, usually methanol and the resulting mixtures of 2-decalols were oxidized to 2-decalones with chromic acid in acetone.[20] Even samples of $\Delta^{1(9)}$-2-octalones containing equilibrium amounts of the unconjugated Δ^9-isomers were completely reduced. Although this shows that the β,γ-isomers rearrange to the conjugated ketones much more readily than they are reduced to unsaturated alcohols, so that their presence does not lead to incomplete reduction, most reductions were carried out on ketones purified by low temperature crystallization and therefore free from the Δ^9-isomers because this was sometimes the only way to remove impurities which interfered with the analyses. The preparation and proof of the stereochemistry of the ketones will be described later.

Although complete reduction was obtained when alcohols were used as proton sources, it was apparent that the previously published conditions often give relatively

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[20] R. G. Curtis, I. Heilbron, E. R. H. Jones and G. F. Woods, *J. Chem. Soc.* 457 (1953).

[21] W. D. Cotterill and M. J. T. Robinson, *Tetrahedron* **20**, 765 (1964).

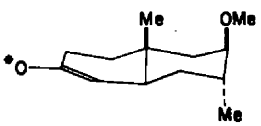
[22] cf. E. E. van Tamelen and W. C. Proost, *J. Amer. Chem. Soc.* **76**, 3632 (1954).

[23] cf. H. Bruderlein, N. Dufort, H. Favre and A. J. Liston, *Canad. J. Chem.* **41**, 2908 (1963).

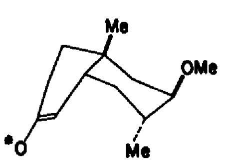
[24] D. J. Baisted and J. S. Whitehurst, *J. Chem. Soc.* 4089 (1961).

low yields of difficulty purifiable material. After many trial reactions it was found that practically instantaneous and quantitative reduction occurred when a solution of an unsaturated ketone and an alcohol, usually methanol, in ether was added during a few seconds to a freshly prepared solution of an alkali metal in liquid ammonia, with immediate addition of ammonium chloride. Such conditions make possible the use of sodium or potassium in undistilled liquid ammonia from some cylinders in open flasks and the products are more readily purified in preparative reactions. When the reaction time was increased by slow addition of one of the reagents, or by prolonged stirring, coloured and basic by-products were often obtained. The results for all the ketones are striking because the stereoselectivity is very high (Table 1), in contrast to the reduction of alkylcyclohexenones,[18] and explain the earlier failures to detect *cis*-2-decalones.[22,25] Variation on the metal or alcohol used caused some change in the isomer ratios but these changes were not large enough to alter the effects of alkyl substituents qualitatively, and only results obtained using sodium and methanol, the most convenient combination of reagents, will be discussed here. The effect of changing the metal or alcohol is being studied in more detail for the reduction of alkylcyclohexenones.[18]

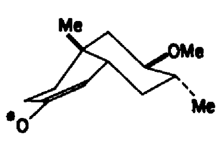
Before the observed isomer ratios for the reduction of alkyl-$\Delta^{1(9)}$-2-octalones, I can be used to elucidate the factors influencing the stereochemistry of the protonation of the β-carbon atom it is necessary to estimate the effects of the alkyl substituents on the relative stabilities of the conformations of the Δ^1-octalin enol radicals or anions (V and VI) and of the radical anions or di-anions (IV). There are three conformations of the anions (IV) differing in the unsaturated ring and a total of six related conformations of the Δ^1-octalin derivatives (V and VI). The various transition states for protonation are assumed to be part way, both electronically and geometrically, between those pairs of conformations of IV and V or VI which have the most closely related shapes. Stork and Darling[17] appear to have considered only one conformation of the anion IV and concentrated their attention principally on the products. Until experimental values become available for the conformations of Δ^1-octalin derivatives,



VII



VIII



IX

only rather crude estimates for the enol derivatives (V and VI) can be made by conventional conformational analysis.* If differences in angle strain between the *cis* and *trans* isomers, and skew interactions between trigonal and tetrahedral carbon atoms are neglected, then the energies of the chair conformations (VIB and VIC) of the *cis* enols relative to the *trans* isomers in the conformation VA are those given in columns 8 and 10 of Table 2; the higher energy boat conformations (VB, VC and VIA) are discussed below. The errors in these approximations tend to cancel because the

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* It does not appear to be useful to consider the relative stabilities of the *cis*- and *trans*-2-decalones II and III, as has been done by Stork and Darling[17] since these ketones are *not* the immediate products of the step which determines the configuration of the bridgehead carbon atom.

[25] F. Sondheimer and D. Rosenthal, *J. Amer. Chem. Soc.* **80**, 3995 (1958).

trans-Δ^1-octalins appear to have greater angle strain than their *cis* isomers,* while in the latter the neglected interactions are probably small but not negligible. Alternatively, the skew interactions between tetrahedral and trigonal carbon atoms may be taken to be 0·4 kcal mole^{-1}, which appears to be consistent with the '3-alkylketone effect'[28] in 3-methylcyclohexanone[29,30] and in *cis*-2-decalones,[30] (Table 2, columns 9 and 11). In passing it may be noted that Rickborn[31] has suggested that this modified skew interaction is as large as 0·9 kcal mole^{-1}, i.e. the '3-alkylketone effect' is non-existent. This conflicts both with Allinger and Blatter's analysis, which Rickborn accepts, of the conformational equilibrium in 2-ethylcyclohexanone[31,32] and with experimentally more direct estimates.[29,30] Comparison of the estimated differences of stability for Δ^1-octalins with the observed stereoselectivity expressed as $\Delta\Delta F = -RT \ln$ (ratio of *cis*- to *trans*-2-decalone) (Table 2, column 12) shows that in general there is no correlation. The qualitative evidence provided by the reduction of the ketone (If–h) shows that the ratios of products are not determined by the relative stabilities of the most stable conformations of the *trans*-enols VA and *cis*-enols VIC (for the substituents concerned), the latter resulting from equatorial protonation. For example, in the reduction of the ketone (Ih) the more stable conformation (IX) of the *cis*-enol radical or anion (VIh) which should be more stable than the *trans*-isomer, results from equatorial protonation while the less stable conformation (VIII), although formed by axial protonation, should be much less stable than the *trans*-isomer (VII), which also results from axial protonation. It was this evidence which led Stork and Darling to propose that a stereoelectronic requirement for axial protonation was more important than the relative stabilities of the products, which were, however, supposed to determine the ratio of products formed in chair conformations by axial protonation, i.e. VA and VIB. This latter assumption is not compatible with the stereoselectivity of the reduction of 10-methyl-$\Delta^{1(9)}$-2-octalone because little or no difference in stability is predicted for the enols (VAb and VIBb). Even making generous allowances for the approximations, many of which cancel, in the estimates of the relative stabilities of VA and VIB in Table 2, the observed stereoselectivities *exceed* the probable differences in stability in all but three instances, including four of Stork and Darling's examples! Furthermore *differences* in stereoselectivity do not correlate with the expected effects of alkyl substituents on the relative stabilities of those products formed by axial protonation. *cis*-5,7- and 6,6-dimethyl substituents, which increase the stereoselectivity, should have no significant effect on the difference of stability between the enols (VA and VIB). The axial 7-methyl group in Ve and VIe will greatly decrease the stability of the *cis* enol derivative (VIBe) relative to the *trans* but will also hinder the approach of a proton to give the enol (VAe). The importance of steric hinderance in

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* This is not apparent from Corey and Sneen's[26] calculations in which bond angles at tetrahedral carbon atoms were assumed to be 109½° and the calculated strains were numerically nearly equal but opposite in sign. The presently accepted bond angles in cyclohexane (111–112°)[27] tend to lower the strain calculated for *cis*-Δ^1-octalin but to increase it for the *trans* isomer.

[26] E. J. Corey and R. A. Sneen, *J. Amer. Chem. Soc.* **77**, 2505 (1955).

[27] M. Davis and O. Hassel, *Acta Chem. Scand.* **17**, 1181 (1963).

[28] W. Klyne, *Experientia* **15**, 119 (1956).

[29] N. L. Allinger and L. A. Freiberg, *J. Amer. Chem. Soc.* **84**, 2201 (1962).

[30] W. D. Cotterill and M. J. T. Robinson, *Tetrahedron* **20**, 777 (1964).

[31] B. Rickborn, *J. Amer. Chem. Soc.* **84**, 2414 (1962).

[32] N. L. Allinger and H. M. Blatter, *J. Amer. Chem. Soc.* **83**, 994 (1961).

TABLE 2. STABILITIES OF THE CHAIR CONFORMATIONS OF THE *cis*-Δ^1-OCTALINS VI RELATIVE TO THE *trans*-OCTALINS VA COMPARED WITH THE STEREOSELECTIVITY OF SODIUM-METHANOL-AMMONIA REDUCTIONS OF $\Delta^{1(9)}$-2-OCTALONES (I)

Substituents	Interactions in conformations of Δ^1-octalins						Relative stabilities of *cis*-Δ^1-octalins (kcal.mole^{-1})				Observed stereo-selectivity $-RT\ln$ *cis*-/*trans*-2-decalone
	VA (*trans*)		VIB (*cis*)		VIC (*cis*)		VIB		VIC		
(1)	(2)[a]	(3)[b]	(4)[a]	(5)[b]	(6)[a]	(7)[b]	(8)[c]	(9)[d]	(10)[c]	(11)[d]	(12)
a; Nil	—		1(2)	-	2(1)	-	0·9	1·7	1·8	2·2	+2·18 ± 0·04
b; 10β-Me	3(1)	-	3(2)	-	3(2)	-	0·0	0·4	0·0	0·4	+2·07 ± 0·1[e]
c; 5β,7β-Me$_2$	1	-	2(2)	-	4(1)	1	0·9	1·7	4·6	5·0	+2·61 ± 0·1
d; 6,6-Me$_2$	2	-	3(2)	-	2(1)	1	0·9	1·7	2·8	3·2	+3·11 ± 0·2
e; 7,7-Me$_2$	2	-	2(1)	(1)	4(1)	-	2·0	2·4	1·8	2·2	+2·22 ± 0·04
f; 1,10β-Me$_2$; 7α-i-Pr	7(1)	-			5(2)	-	High[f]		−1·8	−1·4	>0
g; 6β-OMe; 10β-Me	2(1)	(1)	2(2)	(1)	3(2)	-	0·0	0·4	−1·1	−0·7	>0[g]
h; 6β-OMe; 7α,10β-Me$_2$	4(1)	(1)	3(1)	(2)	3(2)	-	1·1	1·1	−2·9	−2·5	>0[g]
i; 6β-OMe; 7β,10β-Me$_2$	2(1)	(1)	2(2)	(1)	5(2)	-	0·0	0·4	0·7	1·2	>0[g]
j; 6α-OMe; 10β-Me	3(1)	-	3(2)	-	2(2)	(1)	0·0	0·4	1·1	1·5	>0[g]
k; 6α-OMe; 7β,10β-Me$_2$	3(1)	-	3(2)	-	4(2)	(1)	0·0	0·4	2·9	3·3	>0[g]

[a] Skew butane interactions, 0·9 kcal mole^{-1}; the numbers of modified skew butane interactions ('3-alkylketone effects') are given in parentheses, see text and footnotes *c* and *d*.

[b] 1,3-Di-axial interactions between methyl groups,[23] 3·7 kcal mole^{-1}. The numbers of 1,3-di-axial interactions between a methyl group and a trigonal carbon atom or a methyl group are given in parentheses; each may reasonably be supposed to be *c*, 2·0 kcal mole^{-1} by analogy with interactions between two acetoxyl groups (2·0 kcal mole^{-1})[24] and between methyl and hydroxyl groups (2·2–2·4 kcal mole^{-1}).[25]

[c] Modified skew interactions neglected, see text.

[d] Modified skew interactions taken as +0·4 kcal mole^{-1}.

[e] Sondheimer and Rosenthal's results imply a value $\not<$ +1·4.[25]

[f] There is a very small separation between the 7α-isopropyl and 1-methyl groups in this conformation which may therefore be assumed to have a high energy.

[g] Stork and Darling[17] found that there was at least 50% of the *trans*-2-decalone formed but set no upper limit to the amount of *cis* isomer present; it seems unlikely that as much as 10% of the latter could have been present without detection so that the stereoselectivity is probably > +1·0 kcal mole^{-1}.

protonation seems to vary with the hybridization of the carbanion (see below) but the relatively large amount of *cis*-enol (VIe) formed would not be expected if the relative stabilities of products formed by axial protonation controlled the course of these reductions. The absence of correlation between the stereoselectivity of the reduction of $\Delta^{1(9)}$-2-octalones and the relative stabilities of the products is not suprising because the protonation of the anion V by an alcohol should be highly exothermic reactions in which the transition states should resemble the reactant more closely than the products.[36] The relative stabilities of the latter should only be important if the differences between the stabilities of the conformations of the reactant were small.

Previous discussions have considered neither the conformations of the anions IV with the C9 carbon atom trigonal nor the possibility of protonation leading to products in boat conformations and an examination of both these points is now necessary. The first problem is to determine the hybridization of the β-carbon atom in the transition state. A tetrahedral β-carbon atom has often been assumed and Zimmerman,[37] in a very clear exposition of the evidence on this basis, has called this "the important conclusion" deriving from Barton's paper. In fact the formation of *trans*-fused ring systems in Barton's examples was merely consistent with and did not require the conclusion that the transition state resembled the products. Zimmerman has rationalized the idea of a tetrahedral β-carbon atom in the intermediate di-anion A by saying "intuitively one would guess that there would be only weak interaction of the β-carbon electron pair and accompanying negative charge with the already electron rich enolate system." He went on, perhaps a little inconsistently, to consider the π-electron localization energy (ΔE_π) for localizing two electrons on the terminal carbon atom in the di-anion A ($\Delta E_\pi = 0{\cdot}56\beta$; $\delta = 1$, or $\Delta E_\pi = 0{\cdot}66\beta$; $\delta = 2$, depending on the value assumed for the electronegativity parameter δ). Although this is less than half the localization energy for the α-carbon atom in the enolate anion B($\Delta E_\pi = 1{\cdot}28\beta$; $\delta = 1$, or $\Delta E_\pi = 1{\cdot}52\beta$; $\delta = 2$) this is not a convincing reason for supposing that the β-carbon atom in the di-anion A is tetrahedral because a more appropriate ion for comparison would be the allyl anion ($\Delta E_\pi = 0{\cdot}82\beta$), in which the the carbon atoms are presumably trigonal. Such calculations, for what they are worth, are inconclusive for the di-anion A but there is no reason to suppose that in the radical anion C the β-carbon atom will be tetrahedral. In the absence of evidence about the sequence of electron and proton additions the distinction between the two mechanisms will be ignored for the remainder of this paper.

The experimental results discussed above clearly show that the β-carbon atom, i.e. C9 in the decalin system, in the di-anion A is far from tetrahedral in the transition state for protonation because there is no correlation between product stability and stereoselectivity. In contrast, the protonation of the more stable product increases with the difference between the stabilities of the products in reductions of isolated double bonds and cycloalkyl halides for which tetrahedral carbanion intermediates

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[33] N. L. Allinger and M. A. Miller, *J. Amer. Chem. Soc.* **83**, 2145 (1961).

[34] R. U. Lemieux and P. Chu, *Abstracts, Meeting of American Chemical Society* p. 31N. San Francisco (1958).

[35] E. L. Eliel and C. A. Lukach, *J. Amer. Chem. Soc.* **79**, 5986 (1957); E. L. Eliel and H. Haubenstock, *J. Org. Chem.* **26**, 3504 (1961).

[36] G. S. Hammond, *J. Amer. Chem. Soc.* **77**, 334 (1955).

[37] H. E. Zimmerman, *Molecular Rearrangements* (Edited by P. de Mayo) pp. 355–358. Interscience, New York (1963).

are not in doubt. Steric hindrance to the protonation of tetrahedral carbanions does not seem to be important even in the reduction of the extremely hindered carbonyl groups in 11-oxosteroids, which give exclusively the 11α-alcohols.[14,38,39] The relatively high proportion of the *cis*-2-decalone (VIe) from the reduction of the $\Delta^{1(9)}$-2-octalone (Ie) is therefore particularly strong evidence against a tetrahedral β-carbon atom in the transition state. For the remainder of this discussion a planar trigonal β-carbon atom in the anion A or B will be assumed although it is recognised that this planarity will not be perfectly retained in the transition states, which should nevertheless resemble the anion A or B closely in shape.

As a good first approximation the conformations of the anions IV may be supposed to be very similar in shape to the conformations of the parent ketones (I). The principal differences will be in the bond lengths in the conjugated system and, probably most important, a much greater need for planarity in the latter. Each of the three conformations of the anion IV (Fig. 1) can be protonated to give the *trans*- and *cis*-octalins (V and VI) sometimes with the cyclohexylidene ring in a half-boat. The most stable conformation of the anion IV is IVa, in which there appears to be very little angle or torsion strain and the conjugated system is planar; protonation leads directly to the most stable conformation of the *trans*-octalin (VA) or to the *cis* isomer with a half-boat cyclohexene ring (VIA). Judging from Dreiding models the conformation IVB has somewhat greater angle and torsion strain, the latter due mainly to partial eclipsing along the C1–C2 bond, than IVA, and the conjugated system is twisted. Protonation of the conformation IVB leads either to the *cis*-octalin in the conformation VIB or to the *trans*-octalin with a half-boat ring in the conformation VB. The third and least stable conformation is extremely strained and cannot be satisfactorily represented by Dreiding models because the strain results mainly from eclipsing and from non-planarity of the conjugated system. It is uncertain whether the cyclohexylidene ring must be forced into a boat, as has been suggested for similar structures by Balasubramanian[40] and by Ireland,[41] or will adopt a more or less highly distorted chair form. The latter shape is shown in IVC because similar distorted chair rings are now known to be present in very strained molecules such as 4,4-dimethyl-3-oxosteroids and bicyclo(3,3,1) nonane,[42–44] which were previously thought to have boat rings. Whatever the shape of this conformation protonation would lead either to the *trans* octalin (VC) with the cyclohexane ring in a boat or to *cis* octalin in the conformation VIC. The great strain present in the conformation IVC and the somewhat smaller but still large strain to be expected in the transition state for protonation appears to account adequately for the formation of the *trans*-octalins (Vf–h) to the exclusion of the *cis*-octalins (VIf–h) in the reduction of the ketones (If–h) irrespective of any stereoelectronic preference for axial protonation. Thus Stork and Darling's main conclusion is not warranted by their evidence. The preparation and reduction of a $\Delta^{1(9)}$*l*-2-octalone which will be constrained to adopt a

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[38] S. Bernstein, R. Littel and J. H. Williams, *J. Amer. Chem. Soc.* **75**, 1481 (1953).

[39] F. Sondheimer, O. Mancera, G. Rosenkranz and C. Djerassi, *J. Amer. Chem. Soc.* **75**, 1282 (1953).

[40] S. K. Balasubramanian, *Tetrahedron* **12**, 196 (1961).

[41] R. F. Church and R. E. Ireland, *J. Org. Chem.* **28**, 17 (1963).

[42] N. L. Allinger and M. A. DaRooge, *J. Amer. Chem. Soc.* **84**, 4561 (1962).

[43] W. A. C. Brown, G. Eglinton, J. Martin, W. Parker and G. A. Sim, *Proc. Chem. Soc.* 57 (1964).

[44] N. W. J. Pumphrey and M. J. T. Robinson, Part VI, in preparation; cf. I.U.P.A.C. Congress Abstracts A3–19, p. 135. London (1963).

conformation such as IVC is being undertaken and the course of the reduction should clearly show the relative importance of stereoelectronic and product stability factors.

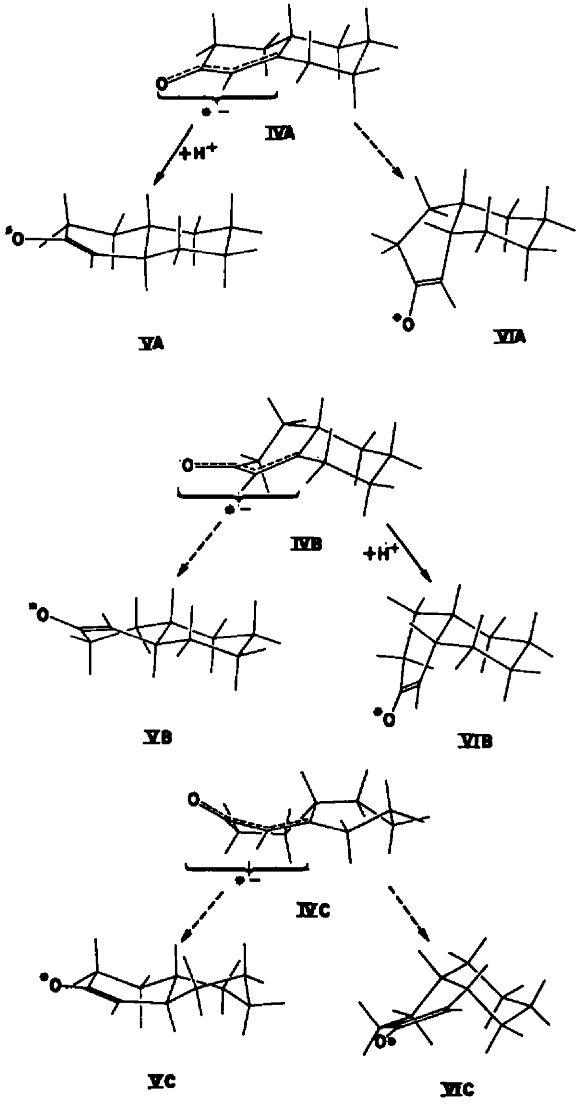

Fig. 1. Conformations of the anions IV and the related conformations of the Δ^1-octalin enol anions or radicals V and VI (• implies either an odd electron or a negative charge depending on whether the protonation takes place on the radical anion C or on the di-anion A; the substituents R are the same as those listed under formulae I–VI).

If the conformation IVC and the related transition states for protonation are so strained that they might be neglected then there remain the problems of whether the observed mixtures of *cis*- and *trans*-decalins are formed from one or both of the remaining chair conformations IVA and IVB and whether the half-boat conformations VB and VIA are formed to any significant extent. The conformations IVA and IVB differ in angle and torsion strain as well as in the nearness to coplanarity of the conjugated system, the conformation IVA being subject to less strain of each type, but these strains should be essentially independent of the methyl substituents in the anions IVa–e. The effects of the methyl groups in changing the relative stabilities of IVA and IVB were predicted qualitatively from the 1,3-methyl-hydrogen distances

TABLE 3. DIFFERENCES IN 1,3-METHYL-HYDROGEN DISTANCES[a] FOR THE CONFORMATIONS OF THE $\Delta^{1(9)}$-2-OCTALONES (I) USED AS MODELS FOR THE CONFORMATIONS OF THE ANIONS (IV)

Substituents	1,3-Methyl-hydrogen interactions	Distance in IVA	Difference in distance IVB–IVA	Predicted effect on stereoselective
b; 10β-Me	10β-Me—3βH	$2{\cdot}61 \pm 0{\cdot}05$A	*c*	Small
	10β-Me—6βH	$2{\cdot}73 \pm 0{\cdot}07$	$-0{\cdot}31 \pm 0{\cdot}04$	
	10β-Me—8βH	$3{\cdot}40 \pm 0{\cdot}07$	$-0{\cdot}67 \pm 0{\cdot}08$	
c; $5\beta,7\beta$-Me$_2$	5β-Me—4βH[d]	$2{\cdot}66 \pm 0{\cdot}03$	$-0{\cdot}37 \pm 0{\cdot}06$[e]	+
d; 6,6-Me$_2$	6β-Me—8βH	$2{\cdot}54 \pm 0{\cdot}09$	$+0{\cdot}08 \pm 0{\cdot}04$	+
	6β-Me—10βH	$2{\cdot}64 \pm 0{\cdot}06$	$-0{\cdot}25 \pm 0{\cdot}03$[f]	
e; 7,7-Me$_2$	7α-Me—5αH	$2{\cdot}36 \pm 0{\cdot}04$	$+0{\cdot}14 \pm 0{\cdot}05$	− (?)
	(7α-Me—π-electrons—negative[g])			

[a] Determined from Dreiding models.

[b] Based on the changes of methyl-hydrogen distances when individual Dreiding models were changed from conformation IVA to IVB; this procedure gives more reproducible values than does taking the difference between average values for the two conformations.

[c] The 3β-hydrogen atom is no longer axial in conformation IVB so that the skew interaction present in IVA is completely removed.

[d] This becomes a 1,3-interaction between the 5β-methyl group and the 4α-hydrogen atom in conformation IVBc.

[e] Decreased in *magnitude* (by *c*, 0·1 A) if the conjugated system is forced to be planar.

[f] Increased in *magnitude* (by *c*, 0·1 A) if the conjugated system is forced to be planar.

[g] Although the distance from the 7α-methyl group to the nearest carbon atom, C9, of the conjugated system is almost unchanged, the distance to the middle of the nearer lobe of the C1–C9 π-orbital decreases by *c*, 0·2 A.

found in Dreiding models* (Table 3). The effect of the 10-methyl group in IVb is relatively complex. The distance between the 10-methyl group and the axial 6- and 8-hydrogen atoms are less in IVBb than in IVAb but the resulting increases in skew interactions will be offset by the loss of the skew interaction between the 10-methyl group and the 3β-hydrogen atom which is axial in IVAb but not in IVBb. In addition the 10-methyl group may change the relative stabilities of IVA and IVB by raising the barrier to rotation about the C4–C10 bond, which is partly eclipsed in IVB, and by altering the bond angles at C10, but these should be minor effects. On balance the 10-methyl substituent would not be expected to have a large effect on the relative stabilities of IVA and IVB, unlike the clear-cut effect on the products (V and VI). The equatorial 5-methyl group in IVc is significantly closer to the equatorial 1α-hydrogen atom in IVBc than to the equatorial 1β-hydrogen atom (IVAc); no significant differences were detected in the octalins (VAc and VIBc). The increased buckling of the cyclohexylidene ring in IVB compared with IVA moves the axial 6-methyl

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* The models used were new and carefully matched and the rods and tubes fitted closely. Distorted or loose fitting models can easily obscure the changes in intramolecular distances in the methyl derivatives.

group in IVd closer to the 10-hydrogen atom but slightly further from the 8-hydrogen atom; the former should be more important effect energetically. Thus the methyl groups in the octalones (IVc and IVd) should lead to increased stereoselectivity. The axial 7-methyl group in the $\Delta^{1(9)}$-2-octalone (IVe) is somewhat closer to the axial 5-hydrogen atom but further from the π-electrons in the conformation IVAe than in IVBe. At most a small decrease in stereoselectivity might be anticipated if the transition states resemble the anion IVe in contrast to a large increase predicted from the relative stabilities of the products (VAe and VIBe). The qualitative correlation between the predicted effects of methyl substituents on the relative stabilities of the conformations IVA and IVB and the observed changes in the stereoselectivity of the reductions is most satisfactorily accounted for if IVA yields VA, with at most *c* 0·2% of the *cis*-enol VB (corresponding to the maximum observed stereoselectivity, for the reduction of the octalone (Id), for the total reaction), and IVB yields mainly VIB, in both instances protonation leading to half-chair cyclohexene rings. The correlation is improved in a quantitative sense if planarity is forced on the conjugated system because the change of methyl-hydrogen is thereby decreased in the anion IVc but increased in the anion IVd so as to accord with the greater selectivity in the latter. Measurements on distorted models have not been recorded in general, however, because they are less reproducible and do not otherwise differ much for other distances in the anions IV.

TABLE 4. STRAIN[a] IN THE HALF-CHAIR AND HALF-BOAT CONFORMATIONS OF THE *cis*- AND *trans*-Δ^1-OCTALINS DERIVATIVES (V AND VI)

Conformation	Dihedral angles[b] (±5°) C2–C3	C3–C4	C4–C10	C10–C9	Strain[c] (kcal mole^{-1})
VA	15	50	70	25	1·4
VB	40	40	15	50	6·4
VC	20	50	50	20	6·4[d]
VIA	40	30	20	50	6·8
VIB	5	40	65	25	1·5
VIC	5	40	65	25	1·5

[a] Based only on torsion strain since none of these conformations seem to have large or widely differing angle strains

[b] The torsion atoms for each of the sequences of four consecutive carbon atoms in the cyclohexene rings; each sequence is designated by the central pair of carbon atoms.

[c] Calculated from the dihedral angles assuming cosine barriers to rotation and using values for ethane (2·9 kcal mole^{-1})[45] and for propene (2·0 kcal mole^{-1})[46] as appropriate.

[d] Includes 5 kcal mole^{-1} for the boat cyclohexane ring.

Since product stability has been shown not to be an important factor in these reductions and even the whole of the difference in stabilty between the *trans*-octalin in the half-chair form VA and the *cis*-octalin in the half-boat form VIA (Table 4) is not greatly in excess of the stereoselectivity apparent in the protonation of IVA there may be another factor favouring the formation of *trans*-fused products. This is unlikely

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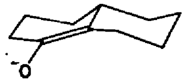
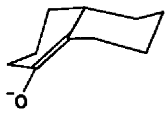
[45] D. R. Lide and D. E. Mann, *J. Chem. Phys.* **27**, 868 (1957).

[46] D. R. Lide, *J. Chem. Phys.* **29**, 1426 (1958).

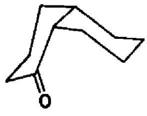


Xa



Xb

XI



XII

to be steric hindrance which is probably greater for *trans*-fused products than for *cis*. In the octalins (V and VI) the angles between the C9–H bond projected along C1–C2 and the nodal plane of the π-bond are very close to 90° when the cyclohexene ring is in a half-chair but are only about 60–70° for the half-boat rings; this suggests that there is indeed a stereoelectronic requirement favouring "axial" protonation in the sense of maximum overlap between the developing sp^3 orbitial at C9 and the p orbitals at C1 and C2. It must be emphasized, however, that this conclusion may be drawn tentatively from the selectivity shown in the protonation of a single conformation of the anion IV but that it does *not* follow from Stork and Darling's qualitative evidence. The quantitative importance of 'axial' protonation may not be very great since there is a substantial difference in stability between the *trans*-octalin in the conformation VA and the *cis*-octalin in the conformation VIB, and the need to invoke a stereoelectronic factor only arises because the transition states appear to resemble the common reactant IVA more closely than the products (VA and VIA).

One apparent discrepancy between the present conclusions about the protonation of the anions IV and the results of Zimmerman's many studies of ketonization remains to be noted. Ketonization of the $\Delta^{1(9)}$-enol of 1-decalone (X)[47] gives *trans*-1-decalone (XI), presumably from the conformation Xa, and *cis*-1-decalone (XII), presumably by axial protonation of the conformation Xb. The *cis*-decalone is formed greatly in excess of the equilibrium amount[47,48] and the protonation varies with the proton source. The transition states for this reaction and the one now proposed for metal-ammonia reductions are superficially similar yet the observed product ratios are very different. The two conformations of the $\Delta^{1(9)}$-enol anion (X) differ very little in stability and even the one skew interaction, between C3 and C5 in the conformation Xb which by axial protonation leads to *cis*-1-decalone (XII) is essentially completely eliminated (the shortest distance between hydrogen atoms being *c* 2·6A) by the partial rotation about the C4–C10 bond imposed by the double bond. If the transition states for ketonization are not too far along the reaction coordinate the large difference in stability of the product should be unimportant in controlling the course of the reaction. The conformation IVB, however, is far more strained than IVA and the transition state for protonation should be even nearer the reactant anion than in the case in the ketonization. The important difference between the two reactants is that the two trigonal carbon atoms fit into both the conformations Xa and Xb of the enol anion X with little strain while the three trigonal carbon atoms in the anion IV are accommodated with little or no strain only in the conformation IVA.

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[47] H. E. Zimmerman and A. Mais, *J. Amer. Chem. Soc.* **81**, 3644 (1959).

[48] W. D. Cotterill and M. J. T. Robinson, to be published.